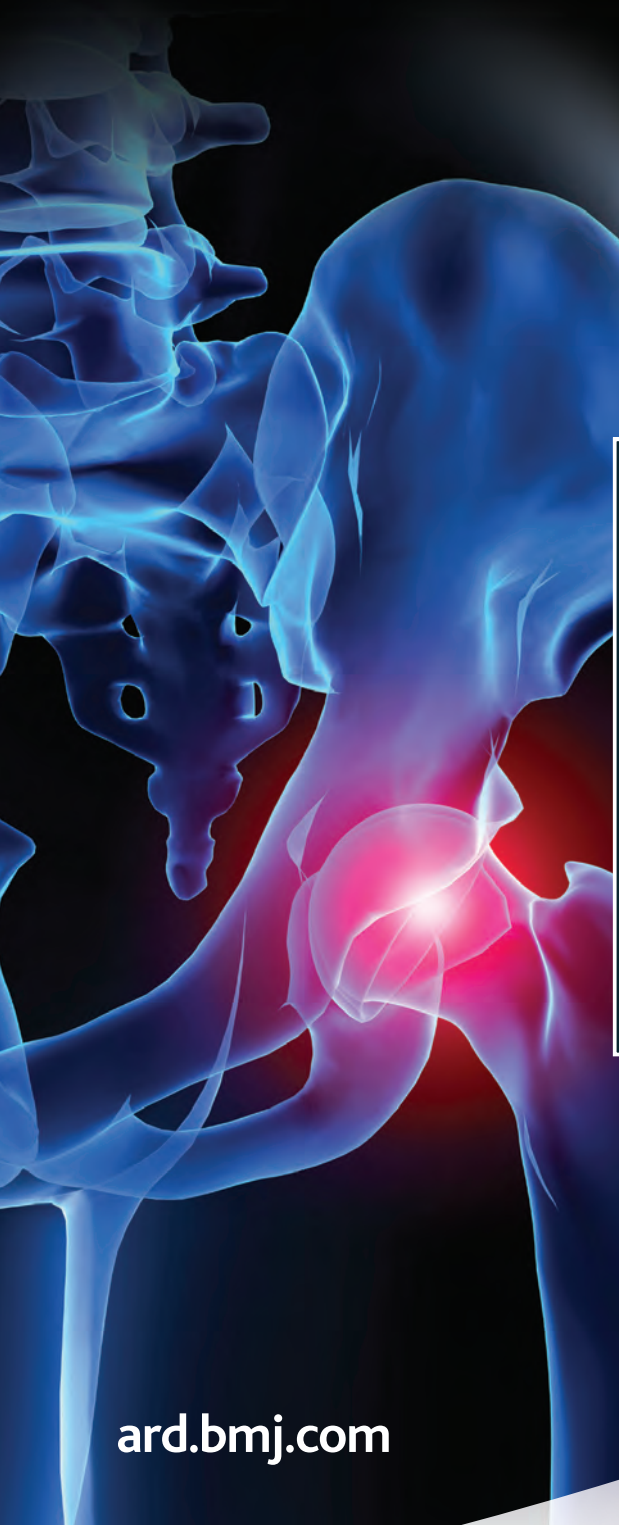
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tsDMARD therapy of rheumatoid arthritis

OP0001

BARICITINIB, TOFACITINIB, UPADACITINIB, FILGOTINIB, AND CYTOKINE SIGNALING IN HUMAN LEUKOCYTE SUBPOPULATIONS: AN UPDATED EX-VIVO COMPARISON

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Background: everal JAKi are now used for the treatment of RA; approved doses include baricitinib (bari) 2- and/or 4-mg QD, tofacitinib (tofa) 5-mg BID, upadacitinib (upa) 15-mg QD. The JAK selectivity these agents is proposed to vary across the class.

Objectives: In vitro cellular pharmacology of bari to tofa, upa, and filgotinib (filgo) were compared.

Methods: PBMCs from 6 healthy donors were incubated with the JAKis over a 7- to 8-point concentration range. Following cytokine stimulation, levels of pSTAT were measured and IC50 calculated in gated leukocyte subpopulations. Therapeutic dose relevance was assessed using calculated mean concentration-time (CT) profiles over 24 hours for bari 2- and 4-mg QD; tofa 5- and 10-mg BID; upa 15- and 30-mg QD; filgo 100- and 200-mg QD. Average daily % inhibition of pSTAT (%SI) was calculated for each JAKi, cytokine, and cell type; filgo %SI integrated parent drug + metabolite.

Results: The cytokines did not signal in all cell types (Figure 1). When signaling was detected, IC50 and %SI for a particular JAKi were generally similar across cell types, with dose-dependent inhibition (Figures 1 & 2). Based on IC50s, upa was most and filgo/metabolite least potent across JAK2/2 or JAK2/TYK2-dependent (IL-3, GM-CSF, G-CSF), JAK1/3-dependent (IL-2, 4, 15, 21), and JAK1/2/TYK2 dependent (IL-6 & 10, IFN-α & γ) signaling pathways.

Incorporating CT profiles, no agent potently or continuously inhibited an individual cytokine signaling pathway throughout the dosing interval. Comparing bari 4-mg to tofa 5-mg BID, upa 15-mg QD, and filgo 100-mg QD, %SI of JAK2/2 or JAK2/TYK2-dependent cytokines was highest with bari 4-mg and upa. Inhibition of JAK1/2/TYK2 cytokines was highest with bari 4-mg. Inhibition of JAK2/2 or



Figure 1. IC50 values (nM) for baricitinib, tofacitinib, upadacitinib, filgotinib (parent and metabolite) in cytokine-stimulated human PBMC preparations.*p<0.01, **p<0.001, ***p<0.0001 vs. bari.

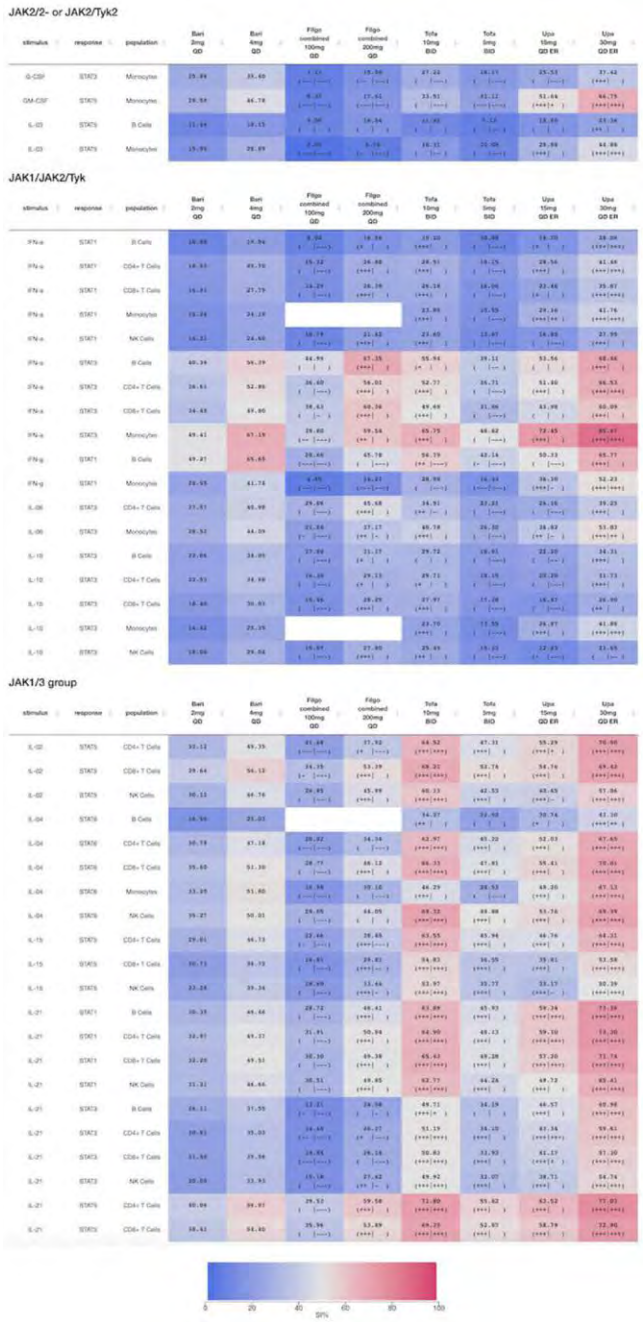


Figure 2. Baricitinib, tofacitinib, upadacitinib, filgotinib: calculated average percent daily STAT inhibition for selected cytokines.-p<0.01, --p<0.001, ---p<0.0001 significantly lower compared to bari (vs. 2-mg if left of vertical line "|", vs. 4-mg if right of vertical line "|"). +p<0.01, ++p<0.001, +++p<0.0001 significantly higher compared to bari (vs. 2-mg if left of vertical line "|", vs. 4-mg if right of vertical line "|").

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JAK2/TYK2, and of JAK1/3-dependent cytokines was lowest for filgo 100-mg QD. For bari 2-mg QD vs. these other JAKi doses, %SI of JAK2/2 or JAK2/TYK2 was highest with upa followed by bari 2-mg. The highest inhibitors of the JAK1/2/TYK2-dependent cytokines varied by cytokine / cell type though consistently included upa. Inhibition of JAK1/3 was highest for upa and tofa. Across comparisons, filgo 100-mg QD showed the least %SI of JAK2/2 or JAK2/TYK2-dependent, and of JAK1/3-dependent cytokines. Filgo reached the highest levels of %SI among agents only for 200-mg QD vs. lower doses of the other JAKi (for selected JAK1/2/TYK2-dependent cytokines).

Conclusion: JAKis display different in vitro pharmacologic profiles which, coupled to their in vivo pharmacokinetics, suggest they modulate distinct cytokine pathways to differing degrees and durations over 24 hours. Ex vivo whole cell assays seem distinct from cell free kinase inhibition assays in determining the overall cytokine modulatory potential of members of the JAKi class.

References:

[1] McInnes IB, et al. Arthritis Res Ther. 2019 Aug 2;21(1):183

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Cardiovascular risk and management in IMIDS

OP0002 INCIDENCE OF FIRST CARDIOVASCULAR EVENT IN SPANISH PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATIC DISEASES: PROSPECTIVE DATA FROM THE CARMA PROJECT AFTER 5 YEARS OF FOLLOW-UP

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Objectives: To determine the incidence and risk factors implicated in the development of first cardiovascular (CV) event (CVE) in patients with chronic inflammatory rheumatic diseases (CIRD) attending Spanish rheumatology clinics after 5 years of follow-up

Methods: Analysis of data of patients included in an observational prospective study [CARdiovascular in rheuMAtology (CARMA) project] after 5 years of follow-up. The study includes a cohort of 2234 patients with rheumatoid arthritis (RA), ankylosing spondylitis (AS) and psoriatic arthritis (PsA), and another cohort of matched individuals (n=677) without CIRD from 67 hospitals in Spain. Cumulative incidence per 1000 patients of CVE was estimated in both cohorts at 5 years from the start. Weibull proportional hazard model was used to calculate the Hazard Ratio (HR) and 95% confidence intervals (CI) of the risk factors involved in the development of CV events. Losses to follow-up and their causes were also analyzed.

Results: The total number patient who completed the follow-up visit at 5 years was 2.382 (81.9%). Fifteen patients died due to CVE and sixty due to non-CVE. The patients with CIRD showed higher cardiovascular cumulative incidence (40.5; 95% CI: 36.2-44.8) than controls (28.3; 95% CI: 21.8-34.8). The higher risk of developing a first CVE during the 5 years of follow-up was seen in patients with AS (HR: 4.60; 95% CI: 1.32-15.99; p=0.02), those with older age (HR:1.09; 95% CI: 1.05-1.13; p<0.001), higher systolic blood pressure (HR: 2.64; 95% CI: 1.32-5.25; p=0.006), and those with longer duration of the rheumatic disease (HR: 1.07; 95% CI: 1.03-1.12; p=0.002). In contrast, woman gender was a protective factor (HR: 0.45; 95% CI: 0.21-0.99; p=0.047).

Conclusion: Patients with AS prospectively followed-up at rheumatology outpatient clinics showed higher risk of developing a first CVE than those without CIRD. Besides traditional CV disease risk factors, a longer time course of the disease is a risk factor for the development of CV disease in patients with CIRD.

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Detection of type I interferon – Bridges into clinical applications

OP0003 EARLY AND SUSTAINED RESPONSES WITH ANIFROLUMAB TREATMENT IN PATIENTS WITH ACTIVE SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) IN 2 PHASE 3 TRIALS

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Background: In the phase 3 TULIP-2 and TULIP-1 trials in SLE, treatment with the type I interferon receptor antibody anifrolumab resulted in higher percentages of patients with BICLA responses vs placebo at Week 52, with differences of 16.3% (primary endpoint; P=0.001, 95% CI 6.3–26.3) and 16.4% (secondary endpoint; 95% CI 6.7–26.2), respectively.1,2

Objectives: To better understand the time course of BICLA responses to anifrolumab, we examined responses over time compared with placebo in TULIP-2 and TULIP-1, including those that were sustained from attainment through Week 52.

Methods: The TULIP-2 and TULIP-1 randomized, double-blind, placebo-controlled trials evaluated the efficacy and safety of anifrolumab (300 mg Q4W) over 52 weeks in patients with moderately to severely active SLE who were receiving standard-of-care treatment. Time to onset of BICLA response that was sustained

from attainment through Week 52 was evaluated using a Cox proportional hazards model. For TULIP-1, BICLA response rate and time to onset of BICLA response were analyzed using the amended restricted medication rules.[2]

Results: Overall, 180 patients each in TULIP-2 and TULIP-1 received anifrolumab compared with 182 and 184 patients in the placebo arms, respectively. At the first 3 assessments in TULIP-2 (Weeks 4, 8, and 12), numerically greater percentages of patients treated with anifrolumab (26.8%, 35.3%, and 42.9%, respectively) were classified as having a BICLA response compared with placebo (21.3%, 21.6%, and 31.8%). A similar trend was observed in TULIP-1 with anifrolumab (23.3%, 34.2%, and 36.5%) vs placebo (18.3%, 23.2%, and 27.5%). The time to onset of BICLA response sustained from onset through Week 52 favored anifrolumab in both TULIP-2 (HR 1.55, 95% CI 1.11–2.18) and TULIP-1 (HR 1.93, 95% CI 1.38–2.73) (**Figure**). In TULIP-2, 86 (47.8%) patients treated with anifrolumab had BICLA responses that were sustained from time of onset through Week 52 compared with 57 (31.3%) patients in the placebo group. In TULIP-1, 85 (47.2%) patients in the anifrolumab treatment arm had BICLA responses that were sustained from time of onset through Week 52 compared with 55 (29.9%) patients in the placebo group.

Conclusion: In 2 Phase 3 studies, a greater proportion of patients achieved BICLA responses sustained from onset through Week 52 with anifrolumab treatment compared with placebo. Anifrolumab resulted in numerically favorable differences in time to onset of BICLA responses maintained through Week 52 across the TULIP studies. These data support the sustainability of clinical benefit derived from anifrolumab treatment of patients with active SLE.

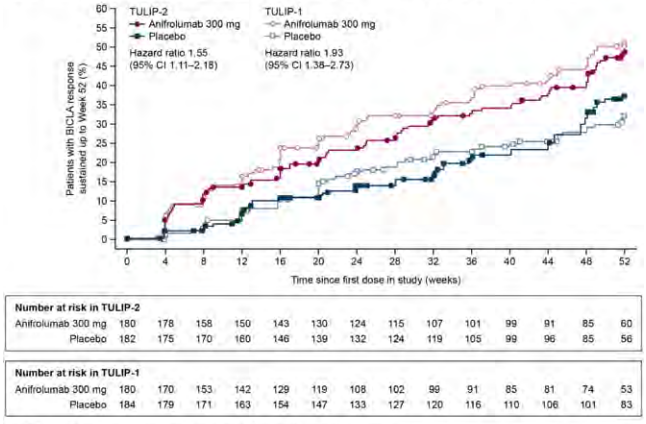
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Figure. Time to Onset of BICLA Response That Was Sustained From Attainment Through Week 52 in TULIP-2 and TULIP-1



BICLA, British Isles Lupus Assessment Group–based Composite Lupus Assessment.
Note: Evaluated using a Cox proportional hazards model; time course of sustained BICLA response is not multiplicity adjusted.
Patients without a BICLA response sustained up to Week 52 are censored at the date of study treatment discontinuation or Week 52, whichever occurred earlier. Points on graph show censored patients. Data were analyzed for TULIP-1 data using the amended restricted medication rules.[2]

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OP0004

THE EXPRESSION OF INTERFERON-STIMULATED GENES IN PERIPHERAL BLOOD OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) ASSOCIATES WITH AFRICAN ANCESTRY

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Background: Type I Interferons (IFNs), and especially INF-alpha, play a crucial role in the pathogenesis of SLE. Interferon-stimulated genes (ISGs) are generally up-regulated in SLE patients. Their pattern of up-regulation is often termed as an IFN signature. Even though composite IFN-scores are already used to express the up-regulation of the IFN-system, e.g. in studies testing therapeutic anti-IFN-antibodies, we are still lacking an in-depth understanding of the IFN signature.

Objectives: To summarize the available data on the expression of ISGs in peripheral blood of patients with SLE compared to healthy controls; to assess which ISGs are most up-regulated in SLE patients; and to analyse if up-regulations of 6 ISGs typically used in IFN-scores [1,2] are associated with SLE disease activity and ethnicity.

Methods: The electronic databases PubMed and EMBASE were searched using the terms "interferon signature", "SLE", "interferon-stimulated genes", "microarray" and "gene expression" with inception date until Jan. 28, 2020. Original case-control studies containing quantitative data of ISG expression were included. Exclusion criteria were studies with animal models, clinical trials of drug treatment and studies with *ex* vivo stimulation of cells prior to gene-expression analysis. Fold changes (FCs) (ISG expression in SLE/ISG expression in healthy controls) for the ISGs analysed in each study were extracted. FCs were plotted gene-wise on a heatmap for studies analysing ≥ 7 genes and for genes that were analysed in ≥ 5 studies. Cluster analysis using principle component analysis (PCA) and association analyses using generalized linear modelling (GLM) were performed for 6 ISGs (IFI27, IFI44, IFI44L, RSAD2, PRKR and IFIT1) as well as disease activity and ethnicity (SPSS).

Results: 16 case-control studies comprising a total of 851 SLE patients were included in the analyses, see Tab. 1. 24 ISGs had an average FC of ≥ 4. IFI27, RSAD2, IFI44L, IFI44, HERC5 and IFIT5 had an average FC > 6. The heatmap showed great variation in the expression of ISGs within the individual studies but also gene-wise between the studies, see Fig. 1. The inter-study variation was statistically explored for the selected 6 ISGs. PCA showed that PRKR, RSAD2, IFIT1, IFI44 and IFI44L clustered with African ancestry, see Fig. 2. Subsequent GLM confirmed that RSAD2 and PRKR were positively associated with African ancestry. However, none of the 6 ISGs were positively correlated with disease activity.

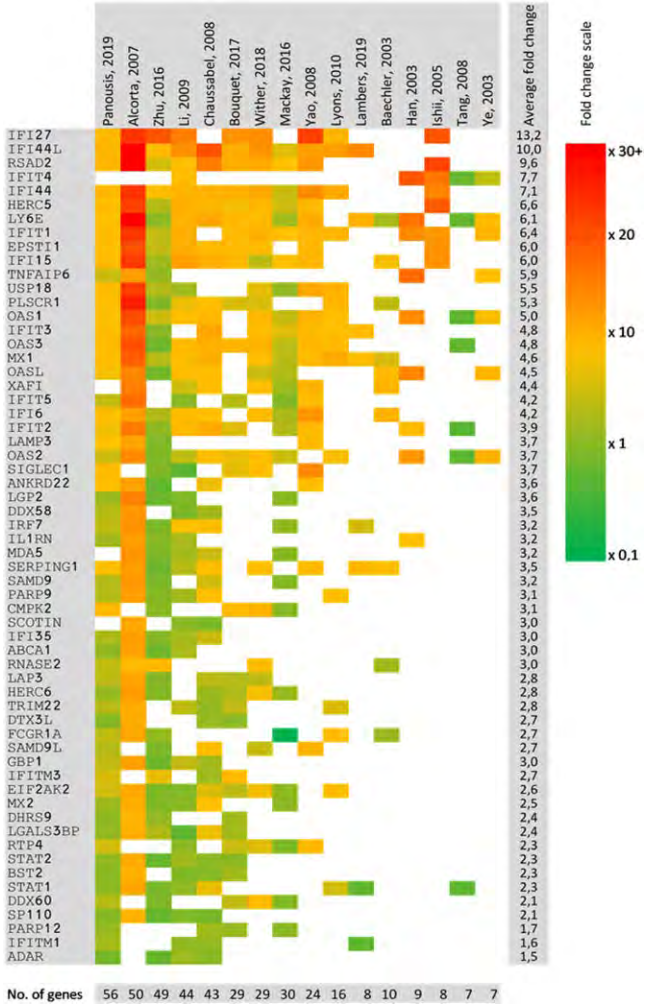


Figure 1. Heatmap of ISG up-regulation.

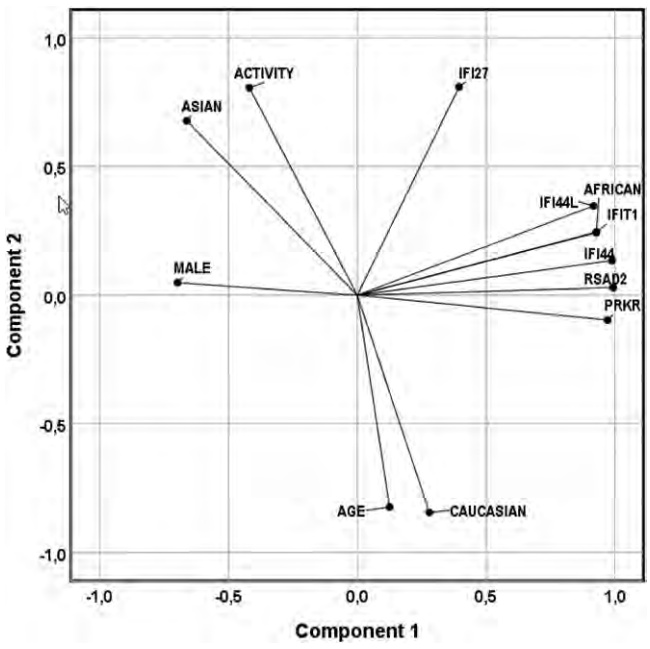


Figure 2. Principal component analysis.

Conclusion: The degree of up-regulation of ISGs in SLE patients shows considerable variation within and between the individual studies. However, a pattern of up-regulation clearly emerges. We find a clustering of 5 prominent genes of the IFN signature (PRKR, RSAD2, IFIT1, IFI44 and IFI44L) and a positive correlation of RSAD2 and PRKR with African ancestry, pointing to the need to take ethnicity into account when using the IFN signature. Our results do not support the use of the IFN signature as traditionally defined as a surrogate marker for disease activity.

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Table 1. Demographics on the studies in the heatmap. Characteristics refer to SLE patients. HC = healthy controls, SLEDAI = SLE Disease Activity Index, BILAG = British Isles Lupus Assessment Group.

Paper	SLE (N)	HC (N)	Female (N)	Age (Mean)	SLEDAI (Mean)	African (N)	Caucasian (N)	Asian (N)
Panousis, N.I. 2019	142	58	120	40	5.2		138	
Alcorta, D.A., 2007	40	28	40	35	BILAG: 6.7	20	18	
Assassi, S., 2010	17	21	16	39		2	6	
Zhu, H., 2016	30	25	4	29	12			
Li, Q.Z.,2009	27	11	25	39		12		
Chaussabel, D., 2008	22	12	20	14	12.1	6	3	
Bouquet, J., 2017	11	25	11	51		3	5	3
Wither, J.E. 2018	170	22	149	34	8.5	40	80	50
Mackay, M., 2016	11	20	11	34	13		1	4
Yao, Y., 2008	41	24	39	40			41	
Lyons, P.A., 2010	13	25	13	47			12	1
Lambers, W.M., 2019	39	22	32	43	<4		35	1
Baechler, E.C., 2003	48	42		45				
Han, G.M., 2003	10	18	9	29	6.1			10
Ishii, T., 2005	31	30	30	34	3.8			31
Tang, J., 2008	144	60	132	33	6.4			144
Ye, S., 2003	50	39	45	29				50

Disclosure of Interests: None declared
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OP0005

ELEVATED STAT1 EXPRESSION BUT NOT PHOSPHORYLATION IN LUPUS B CELLS CORRELATES WITH DISEASE ACTIVITY AND INCREASED PLASMABLAST SUSCEPTIBILITY

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Background: Systemic lupus erythematosus (SLE) is characterized by two pathogenic key signatures, type I interferon (IFN) (1.) and B-cell abnormalities (2.). How these signatures are interrelated is not known. Type I-II IFN trigger activation of Janus kinase (JAK) – signal transducer and activator of transcription (STAT).

Objectives: JAK-STAT inhibition is an attractive therapeutic possibility for SLE (3.). We assess STAT1 and STAT3 expression and phosphorylation at baseline and after IFN type I and II stimulation in B-cell subpopulations of SLE patients compared to other autoimmune diseases and healthy controls (HD) and related it to disease activity.

Methods: Expression of STAT1, pSTAT1, STAT3 and pSTAT3 in B and T-cells of 21 HD, 10 rheumatoid arthritis (RA), 7 primary Sjögren's (pSS) and 22 SLE patients was analyzed by flow cytometry. STAT1 and STAT3 expression and phosphorylation in PBMCs of SLE patients and HD after IFNα and IFNγ incubation were further investigated.

Results: SLE patients showed substantially higher STAT1 but not pSTAT1 in B and T-cell subsets. Increased STAT1 expression in B cell subsets correlated significantly with SLEDAI and Siglec-1 on monocytes, a type I IFN marker (4.). STAT1 activation in plasmablasts was IFNα dependent while monocytes exhibited dependence on IFNγ.

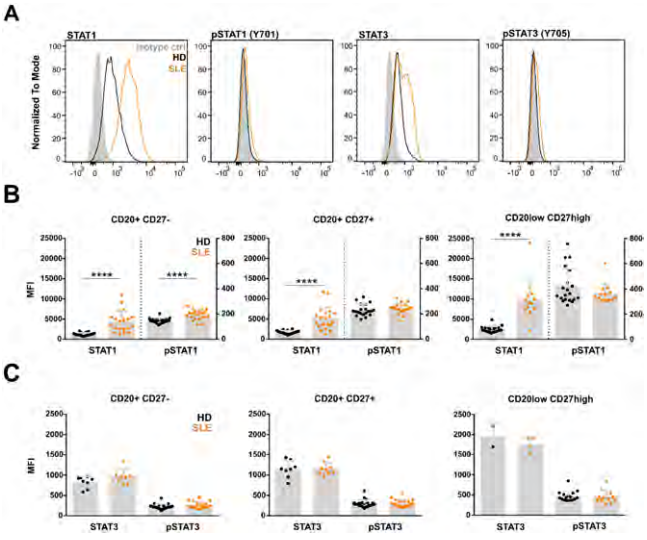


Figure 1. Significantly increased expression of STAT1 by SLE B cells(A) Representative histograms of baseline expression of STAT1, pSTAT1, STAT3 and pSTAT3 in CD19+ B cells of SLE patients (orange), HD (black) and isotype controls (grey). (B) Baseline expression of STAT1 and pSTAT1 or (C) STAT3 and pSTAT3 in CD20+CD27-, CD20+CD27+ and CD20lowCD27high B-lineage cells from SLE (orange) patients compared to those from HD (black). Mann Whitney test; ****p≤0.0001.

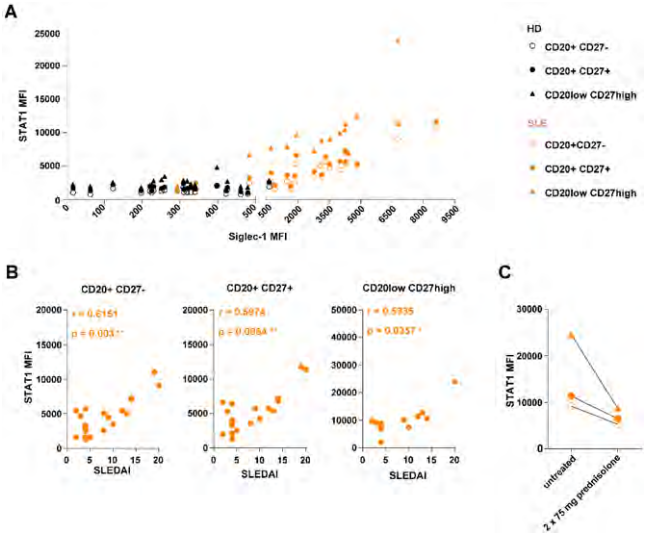


Figure 2. Correlation of STAT1 expression by SLE B cells correlates with type I IFN signature (Siglec-1, CD169) and clinical activity (SLEDAI). Correlation of STAT1 expression in CD20+CD27- näive (p<0.0001, r=0.8766), CD20+CD27+ memory (p<0.0001, r=0.8556) and CD20lowCD27high (p<0.0001, r=0.9396) B cells from SLE patients with (A) Siglec-1 (CD169) expression on CD14+ cells as parameter of type I IFN signature and (B) lupus disease activity (SLEDAI score). Spearman rank coefficient (r) was calculated to identify correlations between these parameters. *p≤0.05, **p≤0.01. (C) STAT1 expression in B cell subsets of a previously undiagnosed, active SLE patient who was subsequently treated with two dosages of prednisolone and reanalyzed.

Conclusion: Enhanced expression of STAT1 by B-cells candidates as key node of two immunopathogenic signatures (type I IFN and B-cells) related to important immunopathogenic pathways and lupus activity. We show that STAT1 is activated upon IFNα exposure in SLE plasmablasts. Thus, Jak inhibitors, targeting JAK-STAT pathways, hold promise to block STAT1 expression and control plasmablast induction in SLE.

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Metabolic pathways during the regulation of inflammation and immunity

OP0006

ABNORMAL IRON METABOLISM AND MITOCHONDRIAL DYSFUNCTION: INVESTIGATING A NOVEL PATHOLOGICAL MECHANISM IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Iron is vital for numerous essential physiological processes including erythropoiesis and energy metabolism (as iron is found in the mitochondrial electron transport chain, the central site of ATP production). Iron homeostasis is tightly controlled by a number of regulators including; 1. Hepcidin, which prevents iron release from stores (under the influence of IL6 and IL1β); 2. Ferritin, an iron storage protein; 3. Lipocalin-2 (LCN2), which is released upon innate immune activation that induces iron sequestration; 4. Transferrin, which binds circulating iron and enables its transport to effector cell targets; 5. Haptoglobin, which binds free haemoglobin and assisting iron recycling; 6. Erythropoietin (EPO), which stimulates erythropoiesis as a result of hypoxia.

Chronic inflammation may result in dysregulation of iron metabolism and in turn impair mitochondrial function yet little is known regarding how these processes change in systemic lupus erythematosus (SLE).

Objectives: In this study, we investigated how dysregulation of iron metabolism may occur in SLE and subsequently sought to identify how a lack of iron may ultimately induce abnormal mitochondrial function.

Methods: *1. Investigating abnormal iron metabolism in SLE.* Serum samples from patients with SLE (n=39) and healthy controls (HC, n=17) were assessed hepcidin, IL-1ß, IL-6, ferritin, LCN2, EPO, haptoglobin and transferrin levels by ELISA. Hierarchical cluster analysis of normalised data (converted to Z-scores) was performed using MeV software in order to characterise patient groups based upon iron metabolism profile. Anti-dsDNA antibody titres, complement C3 levels and SLEDAI-2K were excluded to limit the influence of these variables on cluster analysis. Results were presented as a heatmap.

2. Studying mitochondrial function in iron deficiency and SLE. Peripheral blood mononuclear cells (PBMCs) from HCs and patients with SLE were analysed using Seahorse Respirometry, which measures mitochondrial oxygen consumption rate (a measure of energy metabolism dependent upon oxidative phosphorylation). To assess differences between health, iron deficiency and SLE 3 groups were assessed; 1. PBMCs derived from HCs; 2. PBMCs from patients with SLE; 3. Healthy PBMCs cultured in iron deficient condition, in which cells were treated with the potent iron chelator, Deferiprone.

Results: Figure 1a demonstrates that four groups were identified following cluster analysis. In spite of excluding markers of disease activity, these groups showed significant differences in SLEDAI-2K (shown in Figure 1b). In summary, patients with more active disease (Groups C and D) showed higher levels of hepcidin (which prevents the release of iron from stores, under the influence of IL-1ß and IL-6) and reduced transferrin thus suggesting that iron is inefficiently transported when compared with those with less active disease (in Groups A and B).

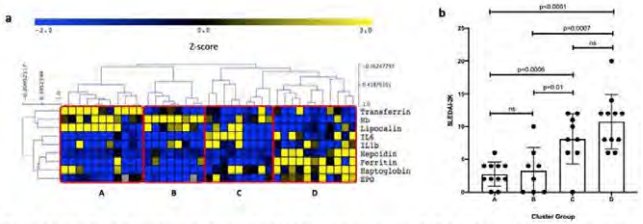
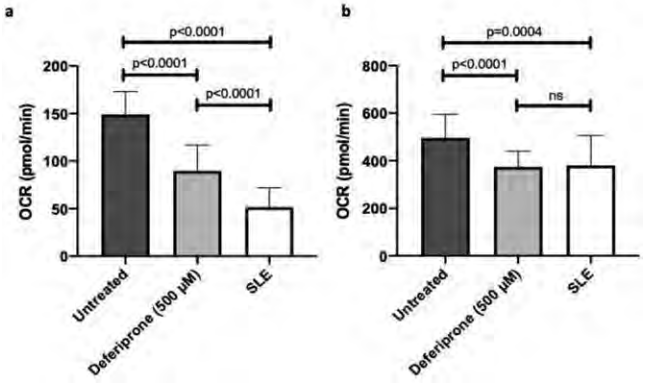


Figure 1a: Results of hierarchical clustering identified four patient groups (A-D) based upon key regulators of iron metabolism

Figure 1b: Differences in disease activity (SLEDAI-2K) between each group produced from hierarchical cluster analysis (A-D)

Figure 2a demonstrates that basal mitochondrial respiration is significantly reduced in PBMCs derived from healthy controls when grown in iron deficiency conditions (following treatment with Deferiprone and is lower still in those with SLE. Figure 2b shows that PBMCs from patients with SLE have reduced maximal mitochondrial respiration capacity that is comparable to the levels seen in iron deficient healthy PBMCs.

Figure 2



Conclusion: Patients with SLE demonstrate abnormalities in iron metabolism that results in cellular iron deficiency as iron is not released from stores, nor adequately transported at the rate required to meet physiological demands. Furthermore, PBMCs derived from patients with SLE who impaired basal and maximal respiration that is comparable with healthy PBMCs treated potent iron chelation. This suggests that abnormal iron metabolism may in turn limit mitochondrial energy metabolism in SLE and represents a potential future therapeutic target.

References: Nil

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Disclosure of Interests: None declared

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OP0007-PARE

CAMPAIGN TO PROMOTE PHYSICAL ACTIVITY & EXERCISE TO RMD PATIENTS THROUGH EDUCATION AND PRACTICE

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Background: Eular give' s a lot of attention to outline the need of a change in RMD patients life style that is very well outlined into the 2018 Eular recommendations for Physical Activity (PA).

Objectives: Driven by those recommendations that says that "PA should be an integral part of standard care throughout the course of disease", CypLAR decided to create a campaign to promote PA through educating RMD patients on the PA benefits, make them to change their life style and enroll them to PA programs. More over we want to inform Rheumatologist and HPR's on that effort and enroll them to that campaign.The CypLAR' s goal through that campaign is to manage and enroll as much as possible patients to PA Programs for a continual period of about 10 months.

Methods: To achieve all the above we decided to move to the following steps:

- Offer PA Programs organized by CypLAR or HPR associates
- Increase awareness regarding the benefits of the PA (Land based & Aquatic) programs to Rheumatologists, HPR's and RMD patients
- Integrate PA into National Health System and procedures
- Offer incentives

Results:

- We managed to increase the PA programs that we used to offer from 1 to 3 in every major cities with also some more opportunities ahead. That also increases the number of participants attracting around 100 participants instead of 20 that we uses to before.
- Towards awareness, we presented Exercise rehabilitation in conferences around Europe (Agora 2017,2018,2019, Eular 2018, Cyprus – Crete Conference 2017, 2019, Enfa 2019, Pain Conference, Athens 2019) and also published related articles on CypLAR's magazine that is published twice a year that is distributed to more than 5000 members.
- We managed to include the Aquatic Exercise Rehabilitation to the new National Strategic plan for Rheumatic Diseases.
- As incentives, we created a fund that is addressed to partially support low income patients. Furthermore we acquire special discount membership fees to our members on PA programs that are offered by associates.
- We organize our own sport related fund events and also participate in others sport funding events. Especially the Charity Swimming Event "Swim for my fellow" which is co-organized by the Iacovou Swimming Centre and Cyplar for the last 5 years is also under the Limassol Municipality Annual Sport Events called "Lemesia" which this year will have an International promotion due Limassol's Award as the "European City of Sports" for 2020.
- We are in the process and in contact with big companies in order to become our campaign Sponsors

We attracted a fund of €2000 from Cyprus Sport Organization that offered a partial financial support to 30 patients for their participation in PA programs for 3 months.

Conclusion: We all believe that the success on that campaign is based on Education (articles, presentations), the available options (programs/positions to participate) and Incentives (financial) that all of them needs further development.

Disclosure of Interests: None declared

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How to build and choose an appropriate outcome measure

OP0008

DEVELOPMENT AND VALIDATION OF AN ALTERNATIVE ANKYLOSING SPONDYLITIS DISEASE ACTIVITY SCORE WHEN PATIENT GLOBAL ASSESSMENT IS UNAVAILABLE

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Background: Ankylosing Spondylitis Disease Activity Score (ASDAS) is a composite index measuring disease activity in axial spondyloarthritis (axSpA). It includes questions from the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Patient Global Assessment (PGA), and inflammation biomarkers. However, ASDAS calculation is not always possible because PGA is sometimes not collected.

Objectives: To develop an alternative ASDAS to be used in research settings when PGA is unavailable.

Methods: Longitudinal data from 4 axSpA cohorts and 2 RCTs were combined. Observations were randomly split in a development (N=1026) and a validation cohort (N=1059). Substitutes of PGA by BASDAI total score, single or combined individual BASDAI questions, and a constant value, were considered. In the development cohort, conversion factors for each substitute were defined by Generalized Estimating Equations. Validation was performed in the validation cohort according to the OMERACT filter, taking into consideration: 1) Truth (agreement with original-ASDAS in the continuous score, by intraclass correlation coefficient -ICC- and in disease activity states, by weighted kappa) 2) Discrimination (standardized mean difference –SMD- of ASDAS scores between high/low disease activity states defined by external anchors e.g Patient Acceptable Symptom State –PASS-; agreement -kappa- in the % of patients reaching ASDAS improvement criteria according to alternative vs. original formulae) 3) Feasibility.

Results: Taking all psychometric properties into account and comparing the different formulae (Table), alternative-ASDAS using BASDAI total as PGA replacement proved to be: 1) truthful (agreement with original-ASDAS: ICC=0.98, kappa=0.90); 2) discriminative: it could discriminate between high/low disease activity states (e.g. scores between PASS no/yes: SMD=1.37 versus original-ASDAS SMD=1.43) and was sensitive to change (agreement with original-ASDAS in major improvement/clinically important improvement criteria: kappa=0.93/0.88; 3) feasible (BASDAI total often available; conversion coefficient≈1).

Conclusion: Alternative-ASDAS using BASDAI total score as PGA replacement is the most truthful, discriminative and feasible instrument. This index enables ASDAS calculation in existing cohorts without PGA.

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Table. Psychometric properties of alternative ASDAS formulae

	Truth N= 823		**Discrimination (disease activity states)** N=381			**Discrimination (sensitivity to change)** N=375	
	Agreement with original-ASDAS		**Patient Acceptable Symptom State (PASS)**			**Agreement with:**	
			PASS =no	**PASS=yes**		**major improvement**	**clinically important improvement**
	ICC	**Weighted Kappa**	**Mean ASDAS, SD**		**SMD**	**Kappa**	
Original-ASDAS	-	-	3.19, 0.97	1.86, 0.88	1.43	-	-
ASDAS-Q1	0.97	0.86	3.02,0.90	1.80,0.87	1.37	0.90	0.78
ASDAS-Q14	0.98	0.88	3.08,0.94	1.80,0.89	1.39	0.92	0.83
ASDAS-Q145	0.98	0.89	3.13,0.96	1.82,0.91	1.40	0.92	0.86
ASDAS-BT	0.98	0.90	3.15,0.99	1.83,0.93	1.37	0.93	0.88
ASDAS–C3	0.97	0.84	3.02,0.98	1.71,0.94	1.36	0.87	0.80

Legend. The alternative Ankylosing Spondylitis Disease Activity Scores (ASDAS) formulae were calculated using as PGA replacement: question 1 (Q1), average of questions 1 and 4 (Q14), average of questions 1,4,5 (Q145) and total score (BT) of the Bath Ankylosing spondylitis Disease Activity Score (BASDAI) or a constant value (ASDAS-C3); original-ASDAS= ASDAS according to the usual formula; ICC =Intraclass Correlation Coefficient; SD= Standard Deviation; SMD=Standardized mean difference

OP0009

DERIVATION AND VALIDATION OF THE SCLERODERMA LUNG 3-STAGE INDEX (SL3SI), A NEW FUNCTIONAL INDEX FOR INTERSTITIAL LUNG DISEASE WITH PROGNOSTIC IMPLICATIONS

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Background: The staging of interstitial lung disease (ILD) is important to monitor disease progression and for prognostication. A disease severity scale of Systemic Sclerosis (SSc)-related lung disease has long been proposed (i.e. Medsger's severity scale). This scale was mostly developed by discussion and consensus and stage thresholds were not computed by a data-driven approach. Hidden Markov models (HMM) are methods to estimate population quantities for chronic diseases with a staged interpretation which are diagnosed by markers measured at irregular intervals.

Objectives: To build a SSc-ILD specific disease severity scale with prognostic relevance via HMM modeling.

Methods: A total of 358 SSc patients at risk for or with ILD were enrolled in a discovery (207 cases, Milan1) and in a validation (151 cases, Milan2, Pavia and Rome) cohort. Patients were included if satisfied the following criteria: 1) Diagnosis of SSc according to the EULAR/ACR 2013 criteria, 2) absence of anticentromere antibodies, 3) dcSSc subset or 4) other subsets with either 4a) ILD-related antibodies (Scl70, PmScl, Ku) or 4b) evidence of ILD on HRCT, 5) disease duration < 5 years at the time of the first pulmonary function test (PFT). Serial PFTs were retrieved and the time up to the last available visit -if the patient alive-, or to death due to pulmonary complications, was recorded. HMM were used to estimate the threshold of a 3-stage model (SL3SI, Scleroderma Lung 3-Stage Index) based on PFT functional values (normal/mild, moderate, severe involvement) in the discovery cohort. Survival estimates of the SL3SI model were compared to Medsger's severity classes estimates and their predictive capability evaluated via the explained residual variation (R^2) of prediction errors (the higher the better). One-hundred random replicates were generated to simulate the prediction effort in patients with different disease duration and lung severity.

Results: Patients characteristics are summarized in the Table. Fifteen-years survival estimates for Mesdger's classes in the discovery set were: normal=0.88, mild=0.86, moderate=0.84 and severe=0.71. The SL3SI was defined by the following thresholds: normal/mild, FVC and DLco >=75%; moderate FVC or DLco 74-55%; severe, FVC or DLco <55%. SL3SI 15-yrs survival estimates were: normal/mild=0.89, moderate=0.82 and severe=0.63. Prediction analysis showed a higher R^2 values at 15 yrs for the SL3SI compared to Medsger's classes, providing evidence for a better predictive capability of the former (discovery: 0.31 vs 0.25; validation: 0.28 vs 0.19).

Conclusion: The SL3SI, a simplified 3-stage functional model of SSc-ILD, yields better survival estimates and long-term prognostic information than Medsger's classes. Its reproducibility and ease of use make it a useful tool for the functional and prognostic evaluation of SSc patients at risk for or with ILD.

Table:

Variables	Discovery (n=207)	Replication (n=151)
DcSSc	62 (30%)	98 (64%)
Age at first PFR	48.6±12	49.1±14.4
Disease duration at first PFR	1.7±1.6	1.3±2.4
FVC	90.5±18.1	91.1±20.2
DLco	70.7±19.8	61.3±20.1
ILD on HRCT	179 (86%)	125 (80%)
Scl70	157 (76%)	153 (78%)
SSA	63 (30%)	32 (21%)
n of visits	3857	1473
Follow-up time, yrs	11±5.6	10.6±5.7
Deaths	27 (13%)	23 (15%)

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Opening Plenary abstract session

OP0010

EFFECTIVENESS OF THE MAKING IT WORK™ PROGRAM AT IMPROVING PRESENTEEISM AND WORK CESSATION IN WORKERS WITH INFLAMMATORY ARTHRITIS – RESULTS OF A RANDOMIZED CONTROLLED TRIAL

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Background: Arthritis often leads to presenteeism (decreased at-work productivity), missed days from work and permanent work disability, leading to reduced quality of life and high costs to individuals and society. Yet, health services addressing the employment needs of people with arthritis are lacking.

Objectives: We evaluated the effectiveness of the Making-it-Work™ (MiW) program, an online self-management program developed to help people with inflammatory arthritis (IA) deal with employment issues.

Methods: A multi-center RCT evaluated the effectiveness of MiW at improving presenteeism and preventing work cessation (WC) over two years. Participants were recruited from rheumatologist practices, consumer organizations and arthritis programs, in three Canadian provinces. Eligibility criteria: diagnosis of IA, employed, age 18-59, and concerned about ability to work. Participants were randomized 1:1 to MiW or usual care plus printed material on workplace tips. MiW consists of five online self-learning modules and group meetings, and individual vocational counselling and ergonomic consultations. Questionnaires were administered every 6 months. Outcomes were presenteeism [Rheumatoid Arthritis Work Instability Scale (RA-WIS)], time to WC ≥ 6 months, and time to WC ≥ 2 months (secondary outcome). Baseline characteristics (age, gender, ethnicity, occupation, education, disease duration and self-employment) were collected. Intention-to-treat (ITT) longitudinal analysis of RA-WIS using linear mixed effect regression models with 2-year comparison as primary endpoint and survival analysis for time to WC using Kaplan-Meier and Cox Proportional Hazard models were performed. Robustness analyses were conducted by using various missing values imputation methods like last observation carried forward, imputation using worse possible outcomes and model-based multiple imputations; using square root transformation of RA-WIS outcome; and adjusting for baseline covariates. SAS version 9.4 was used.

Results: A total of 564 participants were recruited, with 478 (84.75%) completing 2-year follow-up. Baseline characteristics were similar between groups. Mean RA-WIS scores were significantly lower in the intervention group from 6 months onwards, with the greatest difference observed at 2 years (-1.78, 95%CI: -2.7, -0.9, p < .0001), yielding a standardized effect size of 32%. Satisfactory robustness was observed. Work cessation occurred less often in intervention than control groups, but only reached statistical significance for WC ≥ 2 months (WC ≥ 6 months: 31 versus 44 events, aHR 0.70, 95%CI: 0.44, 1.11, p = 0.13; WC ≥ 2 months: 39 versus 61 events, aHR: 0.65, 95%CI: 0.43, 0.98, p = 0.04).

Conclusion: Results of the RCT reveal the program was effective at improving presenteeism and preventing short-term WC. Effectiveness at preventing long-term work disability will be assessed at 5 years. This program fills one of the most important and costly unmet needs for people with inflammatory arthritis.

References:

[1] Carruthers EC, Rogers P, Backman CL, et al. "Employment and arthritis: making it work" a randomized controlled trial evaluating an online program to help people with inflammatory arthritis maintain employment (study protocol). *BMC Med Inform Decis Mak*. 2014;14:59. Published 2014 Jul 21. doi:10.1186/1472-6947-14-59

Figure 1. Mean RA-WIS by allocation group over 2 years of follow-up. Mean ± Standard Error are plotted.

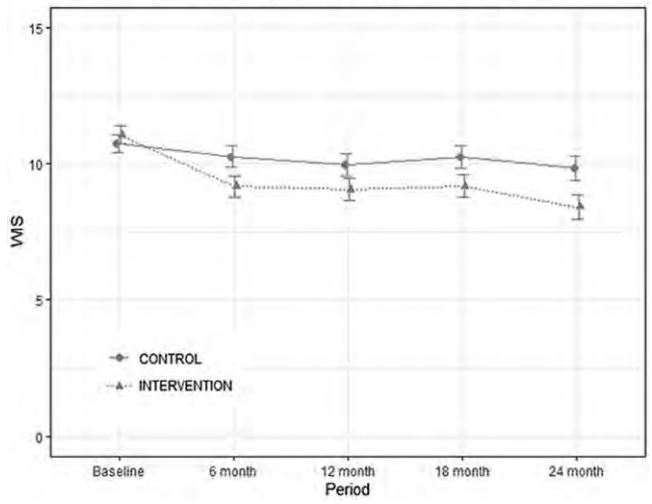
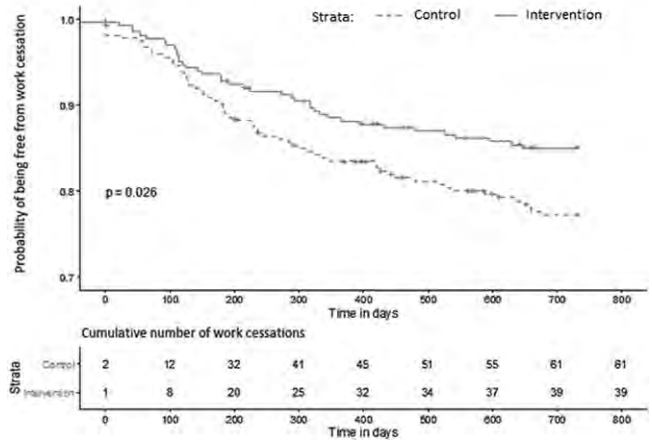


Figure 2. Kaplan Meier analysis of time to work cessation ≥2 months



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OP0011

A RANDOMIZED, DOUBLE-BLIND, ACTIVE-CONTROLLED STUDY OF AVACOPAN IN ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY (ANCA)-ASSOCIATED VASCULITIS

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Background: Complement fragment C5a is strongly linked to the pathogenesis of Anti-Neutrophil Cytoplasmic Antibody (ANCA)-associated vasculitis (AAV). C5a receptor (C5aR), present on neutrophils, is a G protein-coupled receptor for C5a. Avacopan (previously CCX168) is an orally-administered selective antagonist of C5aR which blocks C5a-induced cell activation. Two previous Phase 2 clinical trials provided evidence of effectiveness of avacopan in AAV and its potential to eliminate extensive use of glucocorticoids (GC) and GC-related toxicities.

Objectives: This Phase 3 study evaluated the efficacy and safety of avacopan for the treatment of AAV.

Methods: Eligible subjects were randomized 1:1 to receive either prednisone or avacopan in combination with either a) cyclophosphamide (oral or IV) followed by azathioprine or b) rituximab (four IV infusions). Randomization was stratified by the treatment regimen (rituximab, IV cyclophosphamide, or oral cyclophosphamide), ANCA serotype, and newly-diagnosed or relapsing disease. Treatment period was 52 weeks; primary efficacy endpoints were the proportion of subjects achieving disease remission at Week 26, and sustained disease remission at Week 52. Remission was defined as a Birmingham Vasculitis Activity Score (BVAS) of zero and not taking glucocorticoids for AAV within 4 weeks prior to Week 26. Sustained remission was defined as being in remission at Week 26 and also subsequently in remission as defined above at Week 52. Any relapse of AAV between Weeks 26 and 52 was considered not achieving sustained remission.

Results: 330 subjects were randomized and dosed: 166 in avacopan and 164 in prednisone arms. At Week 26, 72.3% subjects achieved remission in the avacopan arm compared to 70.1% in the prednisone arm ($p<0.0001$ for non-inferiority). At Week 52, 65.7% subjects achieved sustained remission in the avacopan arm compared to 54.9% in the prednisone arm achieving both non-inferiority and superiority to prednisone arm ($p=0.0066$ for superiority of avacopan).

The avacopan arm had a significant reduction in glucocorticoid-related toxicity compared to the prednisone arm as measured by the Glucocorticoid Toxicity Index (GTI) of Cumulative Worsening Score ($p=0.0002$) and Aggregate Improvement Score ($p=0.0082$).

In subjects with renal disease at baseline, the avacopan arm showed a mean increase in estimated glomerular filtration rate (eGFR) of 7.3 mL/min/1.73 m2 from baseline to week 52 as compared to 4.0 mL/min/1.73 m2 increase in the prednisone arm ($p=0.0259$).

Overall subject incidence of serious adverse events (SAEs) was generally consistent with previous AAV trials at 45.1% and 42.2% for prednisone and avacopan groups, respectively. Serious infections were 15.2% and 13.3%, serious hepatic adverse events 3.7% vs 5.4%, and SAEs of white blood cell count decreases were 4.9% vs 2.4% for prednisone and avacopan, respectively. No meningococcal infections were reported.

Conclusion: Avacopan treatment resulted in remission in AAV patients receiving rituximab or cyclophosphamide/azathioprine at a rate that was non-inferior to the active comparator prednisone at week 26 and superior to prednisone in sustained remission at Week 52. A significant reduction in glucocorticoid-related toxicity was observed in the avacopan vs. prednisone arms. Significant increase in eGFR in subjects with renal disease was also observed in avacopan vs. prednisone. The safety profile of avacopan appears acceptable for development in AAV. Avacopan treatment for AAV is efficacious and exhibits benefits not seen with chronic prednisone therapy.

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OP0012

TNF INHIBITORS ARE ASSOCIATED WITH A REDUCED RISK OF VENOUS THROMBOEMBOLISM COMPARED TO CSDMARDS IN RA PATIENTS

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Background: While the short-term use of bDMARDs up to 180 days has been associated with an increased risk of venous thromboembolism (VTE) compared to csDMARDs in patients with rheumatoid arthritis (RA), the long term use of more than 730 days has been associated with a decreased risk based on claims data [1]. Among patients with inflammatory bowel disease, observational data indicated that TNF inhibitors may have a protective effect regarding the VTE risk [2].

Objectives: To assess the effects of TNF inhibitors and newer bDMARDs (including abatacept, rituximab, sarilumab, and tocilizumab) on the VTE risk based on observational data from RA patients.
Methods: The German register RABBIT is a prospective longitudinally followed cohort of RA patients enrolled with a new start of a DMARD after at least one csDMARD failure. This analysis comprises patients who were enrolled with start of a bDMARD between 01/2009 and 04/2019 and had at least one follow-up.
Cox regression models were used to calculate hazard ratios (HRs) for VTEs, for csDMARDs, TNF inhibitors and other bDMARDs. Propensity score weighting was used to adjust for confounding by indication.
Results: Patients receiving TNF inhibitors or other bDMARDs on average had higher CRP levels and a higher prevalence of cardiovascular diseases at baseline than patients receiving csDMARDs. They also received more often glucocorticoids (Table 1).

Table 1. Patient characteristics at baseline for DMARD groups

Parameter	csDMARDs	TNFi	Other bDMARDs
N	3500	5060	2534
VTE event	38 (1.1)	55 (1.1)	23 (0.9)
Age [years]	58.8 (12.6)	56.5 (12.9)	58.1 (12.4)
Female sex	2575 (73.6)	3734 (73.8)	1933 (76.3)
Disease duration [years]	6.2 (7.2)	9.4 (8.6)	11.9 (9.2)
Seropositivity	2189 (62.6)	3739 (73.9)	2048 (80.8)
Joint erosions	1024 (31.0)	2566 (52.4)	1523 (63.3)
Prior bDMARD therapies	0 (0.2)	0.3 (0.6)	1.2 (1.2)
CRP	8.8 (8.1)	11.6 (10.6)	12.4 (11.8)
DAS28-ESR	4.4 (1.3)	4.9 (1.2)	5.1 (1.3)
% of full physical capacity	71.3 (21.8)	66.2 (22.6)	62.1 (23.5)
Current glucocorticoid therapy	2564 (73.3)	3951 (78.1)	2036 (80.4)
Heart failure	36 (1)	113 (2.2)	93 (3.7)
Coronary artery disease	196 (5.6)	326 (6.4)	183 (7.2)
Cerebrovascular disease	60 (1.7)	86 (1.7)	44 (1.7)
Osteoporosis	400 (11.4)	771 (15.2)	530 (20.9)
Ever smoker	1875 (53.6)	2738 (54.1)	1402 (55.3)

Results are presented as mean ± SD or number (percentage).

The HR of patients receiving TNF inhibitors for a serious VTE event was 0.53 (95% CI: 0.33 – 0.86) compared to csDMARDs, while the HR for patients receiving other bDMARDs was 0.66 (95% CI: 0.40 – 1.09). A CRP level of more than 5 mg/L (HR 2.09, 95% CI: 1.39 – 3.14) and an age above 65 years (HR 2.96, 95% CI: 1.94 – 4.52) increased the risk for a serious VTE event. Better physical function was associated with a decreased risk for VTEs (Table 2).

Table 2. Hazard ratios for VTE events

Parameter (at time of event/end of observation unless specified otherwise)	Hazard ratio	95% confidence interval	
TNF inhibitors (reference: csDMARDs)	**0.53**	**0.33**	**0.86**
Other bDMARDs (reference: csDMARDs)	0.66	0.40	1.09
Age ≥ 65 years (baseline)	**2.96**	**1.94**	**4.52**
CRP ≥ 5 ml	**2.09**	**1.39**	**3.14**
> 5 mg and ≤ 10 mg glucocorticoids/day	1.04	0.55	1.98
> 10 mg and ≤ 15 mg glucocorticoids/day	2.35	0.81	6.79
> 15 mg glucocorticoids/day	2.03	0.76	5.41
% of full physical capacity (per 10 percentage points increase, time of event)	**0.85**	**0.78**	**0.92**
Current smoking (baseline)	0.98	0.61	1.55
Former smoking (baseline)	0.80	0.45	1.43

Conclusion: Treatment with TNF inhibitors (compared to csDMARDs) and better physical function significantly reduced the risk of serious VTE events, while age above 65 years and high CRP levels increased this risk.
References:
[1] Kim S. C. et al. Am. J. Med. 2015; 128(5): 539.e7–539.e17.
[2] Desaj R.J. et al. CMAJ 2017; 189:E1438-47.
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OP0013

SINGLE CELL PROFILE OF SKIN STROMAL AND IMMUNE CELLS AND PERIPHERAL BLOOD IMMUNE CELLS OF SCLERODERMA PATIENTS TOWARDS IDENTIFICATION OF DISEASE MECHANISM, PROGNOSTIC BIOMARKERS AND POTENTIAL THERAPEUTIC TARGETS

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Background: Despite many years of research, our understanding of Systemic Sclerosis (SSc) pathogenic processes, patient-to-patient variability, and diversity of stromal and immune cells within the involved tissues microenvironment, their interaction, as well as the genes and pathways leading to the pathogenesis remains largely unclear. Current technologies for characterizing SSc have limited depth and resolution, which needed for molecular define the small skin stromal and immune cells sub-populations supposed to drive SSc pathogenesis. Single-cell sequencing technologies hold a great potential in genomic medicine since they offer high resolution and sensitivity for unbiased profiling of disease versus normal niches.
Objectives: Comprehensive characterization of stromal and immune cells in the skin and blood of SSc patients, and healthy controls, their specific intra-skin cell states, pathways, cell-cell interactions, and unbiased characterization of cell types profile, biomarkers, drivers, and regulatory pathways associated with specific SSc patient subgroups.
Methods: We applied the massively parallel single cell RNA-seq (MARS-seq) developed in our laboratory to conduct a comprehensive single-cell genomics analysis of skin stromal and immune cells obtained through punch biopsy and blood immune cells from 73 SSc patients (39 DcSSc, 34 LcSSc) and 30 healthy controls. We used the MetaCell analytical method to identify homogeneous and robust groups of cells from single cell RNA-seq data. The perturbed signaling pathways, pathogenic stromal or immune cell subsets are characterized using CyTOF, immunohistochemistry, **P**hysical **I**nteracting **C**ell sequencing (**PIC**-seq), and *in vitro* functional assays.
Results: We collected data from a total of 46,742 high-quality skin stromal cells, and 57,475 high-quality blood and skin immune cells. Analysis of stromal cell compartment led to a detailed map of 261 meta cells organized into 16 broad lineages including: Fibroblasts, Pericytes, Vascular cells, and other cells. In the immune cell compartment, we found 361 meta cells organized into 14 broad lineages (e.g unique skin T, B, NK and dendritic cells). We observed a unique population of stromal and immune cells in the skin and blood of SSc patients as compared to controls. The major and dramatic changes were observed in the stromal cell compartment of the patient's skin compared to controls. In the fibroblast lineage we found a small cluster of cells that were significantly diminished in the SSc patients compared with control, expressed genes associated with fibrosis and vascular remodeling. Significantly higher number of specific subsets of pericytes and vascular cells was found in SSc patients compared to controls. Analysis of the immune cell compartment revealed only minor changes in the immune cell composition in patients compared with controls. Finally, we found known and novel pathways (e.g Wnt/Notch signaling, IFN type I/II, AP-1 pathway, complement cascade activation) and cell-cell interactions that play crucial roles in SSc pathogenicity.
Conclusion: Our study provides a detailed and unprecedented high-resolution atlas of the immune and stromal cells that make up the skin and peripheral blood in a large cohort of SSc patients with diverse disease duration and clinical settings. Our findings of candidate stromal and immune cell subpopulation, genes and pathways constitute the basis for understanding of SSc pathogenesis and heterogeneity and holds great potential to provide clinicians with new and powerful molecular tools for understanding of the immune-stromal cell crosstalk, for finding new biomarkers for SSc activity and complications and for tailoring and identification of new therapeutic targets.
Disclosure of Interests: Chamutal Gur: None declared, Alexandra Balbir-Gurman Consultant of: Novartis, Hagit Peleg: None declared, Suhail Aamar: None declared, Fadi Kharouf: None declared, Yolanda Braun-Moscovici: None declared, Shuang-Yin Wang: None declared, Ido Amit: None declared
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OP0014

COMPARISON OF ANTERIOR UVEITIS OCCURRENCE DURING TREATMENT WITH SECUKINUMAB, ADALIMUMAB, INFLIXIMAB AND ETANERCEPT IN SPONDYLOARTHRITIS

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Background: Randomized controlled trials indicate that compared to tumor necrosis factor inhibitors (TNFi), secukinumab (SEC) has similar efficacy

regarding axial inflammation in spondyloarthritis (SpA), better efficacy regarding cutaneous psoriasis, but is inferior in inflammatory bowel disease (IBD). However, the efficacy of SEC compared to TNFi in anterior uveitis (AU) has not been extensively studied.

Objectives: To compare the occurrence of AU in patients with SpA treated with SEC, adalimumab (ADA), infliximab (IFX) or etanercept (ETN), in clinical practice.

Methods: Patients with ankylosing spondylitis or undifferentiated SpA starting either SEC, ADA, IFX or ETN, in 2015 through 2017, were identified in the Swedish Rheumatology Quality register, and were linked to the national patient register for identification of AU. AU-flares were defined as the number of visits with an AU diagnosis, separated by a ≥60 days penalty interval, within ophthalmology outpatient care, during the respective bDMARD treatment.

Follow-up started at the bDMARD initiation, and ended at the first of Dec 31st 2017, death, emigration or discontinuation date of the bDMARD.

To assess and accommodate treatment channeling, crude incidence rates for AU-flares were determined (A) for all bDMARD treatment starts, (B) excluding patients with an AU diagnosis during the year prior to the bDMARD start, and (C) in addition, excluding all first line bDMARD treatment starts.

Hazard ratios (HR) for time until a first on-treatment AU diagnosis were estimated using Cox regression (ADA=reference), adjusted for sex, age, and any history of AU, and estimating robust confidence intervals to account for the individuals contributing multiple lines of treatment.

Results: In total, 2,684 patients (52% women) contributed 3,255 treatment initiations. SEC was less frequently used as first line bDMARD and there was channeling of patients with previous AU, towards treatment with ADA, and away from ETN (Table 1). Further, AU occurred almost exclusively in patients with a pre-treatment history of AU (data not shown).

Table 1.

Analysis	Treat-ment starts, N	Previous AU [1]	Age at treat-ment start, mean (sd)	N Previous bDMARD, median	HR (95% CI) for first AU-diagnosis	AU flares, N	Follow-up[2], years
A. All treatment starts, N=3255							
SEC	333	21%	48 (13)	2	2.0 (1.2-3.3)	52	241
ADA	872	34%	44 (12)	1	Ref	175	973
IFX	714	21%	43 (14)	0	0.9 (0.6-1.4)	68	677
ETN	1336	17%	44 (14)	0	0.9 (0.7-1.3)	102	1290
B. Excluding patients with prior AU within 1 year before treatment start, N=2907							
SEC	304	13%	47 (13)	2	3.1 (1.4-7.3)	10	212
ADA	711	19%	44 (13)	1	Ref	18	792
IFX	633	11%	43 (14)	0	1.0 (0.4-2.3)	8	599
ETN	1259	12%	44 (14)	0	1.8 (1.0-3.4)	43	1204
C. Excluding patients with prior AU within 1 year before treatment start and first line bDMARD, N=1288							
SEC	284	14%	48 (13)	2	2.5 (1.0-6.2)	10	198
ADA	374	18%	45 (13)	1	Ref	11	384
IFX	185	12%	45 (14)	2	1.3 (0.4-4.0)	4	166
ETN	445	17%	47 (14)	1	1.9 (0.9-4.0)	23	439

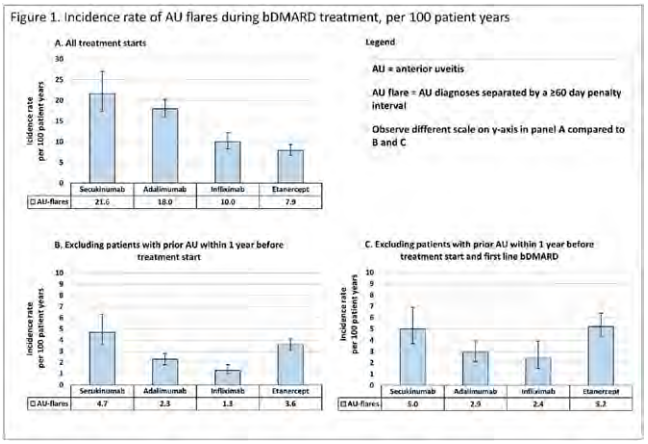
1) Anterior uveitis between 2001 and treatment start; 2) Total follow-up time for analyses of incidence rate.

The incidence rates of AU-flares were higher for SEC and ETN compared to ADA and IFX, in the analyses (B, C) accommodating for channeling, figure 1.

Compared to ADA, the adjusted HRs of a first on-treatment AU-diagnosis were also higher for SEC and ETA, Table 1.

Conclusion: In clinical practice, SEC and ETN are associated with a higher incidence of AU than ADA and INF, suggesting a poorer protective effect of SEC and ETN against AU. These preliminary results should be interpreted in light of pronounced treatment channeling, which was only partly accommodated for.

Figure 1. Incidence rate of AU flares during bDMARD treatment, per 100 patient years



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OP0015

SEX-SPECIFIC U-SHAPED RELATIONSHIP BETWEEN SERUM URATE AND MORTALITY IN THE UNITED STATES GENERAL POPULATION

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Background: A U-shaped relationship may exist between serum urate (SU) and cardiovascular events, although the relationship between SU and mortality is unclear. The most recent EULAR recommendations for gout advise against maintaining SU <3 mg/dl for prolonged periods.

Objectives: To examine the relationship between SU and all-cause and cause-specific mortality in large cohorts in the United States (US).

Methods: We examined National Health and Nutrition Examination Survey (NHANES) data from 1988-1994 (NHANES III) and 1999-2007 including subjects

Table. Multivariable hazard ratios for all-cause and cause-specific mortality in NHANES III and 1999-2007.

			Men			
Serum urate range (mg/dL)	**<4**	**4-5**	**5-6**	**6-7**	**7-8**	**>8**
Deaths (N)	325	934	1513	1412	872	658
All-cause	**1.33 (1.17, 1.51)**	**1.17 (1.07, 1.28)**	1.00**	1.04 (0.96, 1.13)	**1.13 (1.04, 1.24)**	**1.52 (1.37, 1.69)**
Cardiovascular	0.97 (0.75, 1.27)	1.10 (0.93, 1.30)	1.00	0.93 (0.80, 1.08)	1.13 (0.96, 1.34)	**1.22 (1.00, 1.49)**
Chronic lower respiratory disease	0.92 (0.51, 1.68)	0.96 (0.64, 1.43)	1.00	1.01 (0.69, 1.47)	0.86 (0.53, 1.38)	**1.91 (1.18, 3.10)**
Alzheimer's disease	1.13 (0.50, 2.55)	0.88 (0.48, 1.61)	1.00	1.14 (0.69, 1.91)	0.87 (0.45, 1.69)	**0.23 (0.05, 0.99)**
Diabetes mellitus	**3.39 (1.89, 6.09)**	**1.81 (1.10, 3.00)**	1.00	0.86 (0.51, 1.44)	0.93 (0.51, 1.69)	1.60 (0.87, 2.95)
			Women			
Serum urate range (mg/dL)	**<3**	**3-4**	**4-5**	**5-6**	**6-7**	**>7**
Deaths (N)	181	750	1321	1170	776	703
All-cause	1.11 (0.93, 1.31)	1.03 (0.93, 1.14)	1.00 (0.92, 1.09)	1.00	**1.11 (1.00, 1.22)**	**1.45 (1.31, 1.61)**
Cardiovascular	1.23 (0.88, 1.71)	1.11 (0.92, 1.34)	0.94 (0.80, 1.11)	1.00	1.06 (0.89, 1.28)	1.16 (0.95, 1.41)
Chronic lower respiratory disease	1.26 (0.62, 2.57)	1.11 (0.72, 1.72)	0.87 (0.58, 1.30)	1.00	0.66 (0.39, 1.12)	0.85 (0.49, 1.45)
Alzheimer's disease	1.38 (0.57, 3.36)	0.97 (0.54, 1.73)	1.15 (0.73, 1.81)	1.00	0.79 (0.44, 1.41)	**0.54 (0.25, 1.15)**
Diabetes mellitus	1.69 (0.71, 4.02)	1.50 (0.89, 2.53)	0.91 (0.56, 1.46)	1.00	1.11 (0.68, 1.82)	**1.66 (1.02, 2.71)**

aged ≥18 with an enrollment SU measurement. We used Cox proportional hazards regression models to estimate sex-specific mortality risk relative to a referent SU 5-6 mg/dL, adjusting for NHANES cycle, age, race, body mass index (BMI), education, alcohol use, smoking, hypertension, total cholesterol, estimated glomerular filtration rate (GFR), and competing risks, using age as a time scale for survival analysis.
Results: Among 19,954 men and 21,853 women, there were 5,714 male deaths and 4,901 female deaths (median follow-up 14.2 ± 6.9 years). Among men, there was a 33% increased all-cause mortality risk at SU <4 mg/dL (HR 1.33, 95% CI 1.17-1.51) and 52% increased all-cause mortality risk at SU >8 mg/dL (HR 1.52, 95% CI 1.37-1.69) compared to subjects with SU 5-6 mg/dL, driven by cause-specific mortality from diabetes at low SU and chronic lower respiratory diseases and cardiovascular disease at high SU (**Table**). In women, there was no increased mortality risk at low SU and a 45% increased all-cause mortality risk at SU >7 mg/dL (HR 1.45, CI 1.31-1.61) compared to subjects with SU 5-6 mg/dL, driven by cause-specific mortality from diabetes. Mortality from Alzheimer's disease was lower at high SU among men (HR 0.23, 95% CI 0.05-0.99) and women (HR 0.54, 95% CI 0.25-1.15).
Conclusion: In large cohorts representative of the US population, there was a U-shaped relationship between SU and all-cause mortality in men but not women. In men with low SU, mortality was driven primarily by diabetes, which may be explained by the uricosuric effect of uncontrolled hyperglycemia in diabetes patients. The lower mortality from Alzheimer's disease at high SU agrees with previously shown inverse associations between gout and Alzheimer's disease. Further studies are needed to determine the presence of causality underlying these associations.
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OP0016

GUT MICROBIOTA DYSBIOSIS IN THE HIGH-RISK INDIVIDUAL FOR RA TRIGGERS THE MUCOSAL IMMUNITY PERTURBATION AND PROMOTES RHEUMATOID ARTHRITIS DEVELOPMENT

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Background: The early treatment of rheumatoid arthritis (RA) is associated with better outcomes. In recent years, studies in our understanding of the preclinical events in RA help to define the "at-risk" populations who might go on to develop RA. Emerging evidence indicate that initiating events may occur at mucosal surfaces including oral cavity, lung and gut influenced by the local microbiome. Therefore, identifying the microbiome characteristics in prospective cohorts of at-risk individuals enables risk prediction or prevention of RA.
Objectives: Here, we undertook this study to clarify the intestinal microbiota changes in individuals at high risk for RA. Meanwhile, we performed fecal transplantation study to investigate whereby the intestinal dysbiosis in the pre-RA population contributes to RA initiation and development, and provide a new prevention strategy for the treatment of this disease.
Methods: 42 high-risk for RA individuals (Pre-RA), who were defined as having a positive serum antibody for anti-cyclic citrullinated peptide (CCP), 31 RA patients and 38 healthy individuals (HC) were recruited in this study. The V3-V4 region of 16S ribosomal RNA of fecal samples from these individuals were sequenced. We evaluated the gut permeability and the gut barrier dysfuction using HE staining and RT-PCR in mice receiving fecal transplantation (FMT). Flow cytometry was applied to measure the proportions of T cell subsets in immune organs. The disease severity of collagen-induced arthritis (CIA) was also evaluated after the mice receiving FMT.
Results: Alpha diversity analysis showed a comparable community richness and a lower community diversity of the intestinal microbiota in Pre-RA compared to HC (Fig 1A). At the family level, the abundance of *Bacteroidaceae* gradually decreased from HC to Pre-RA individuals and to RA patients (Fig 1B). On the contrary, the enriched abundances of *Streptococcaceae, Lactobacillus, Lactococcus, Weissella* and *unclassified_o_Lactobacillales* were observed in RA patients (Fig 1B). There was different intestinal microbiota construction between groups based on principal coordinate analysis (PCoA). The intestinal microbiota communities dynamically shifted from HC to Pre-RA and to RA patients (Fig.1C). Fecal transplantation study showed that gut microbiota from Pre-RA group (P) significantly increased the fluorescence intensity (Fig 2A), accompanied with a significantly decreased ZO-1 gene expression (Fig 2B), and injured epithelial microvilli of the small intestine (Fig 2C). Moreover, the percentages of Th17 cells in the mesenteric lymph nodes (mLN) and peyer patches (PP) were also significantly increased in P and R groups (Fig 2D, E). Importantly, in CIA models, the joints redness and swelling in the mice receiving Pre-RA faeces occurred earlier and were more severe compared to HC-transplanted mice (Fig 2F, G and H).

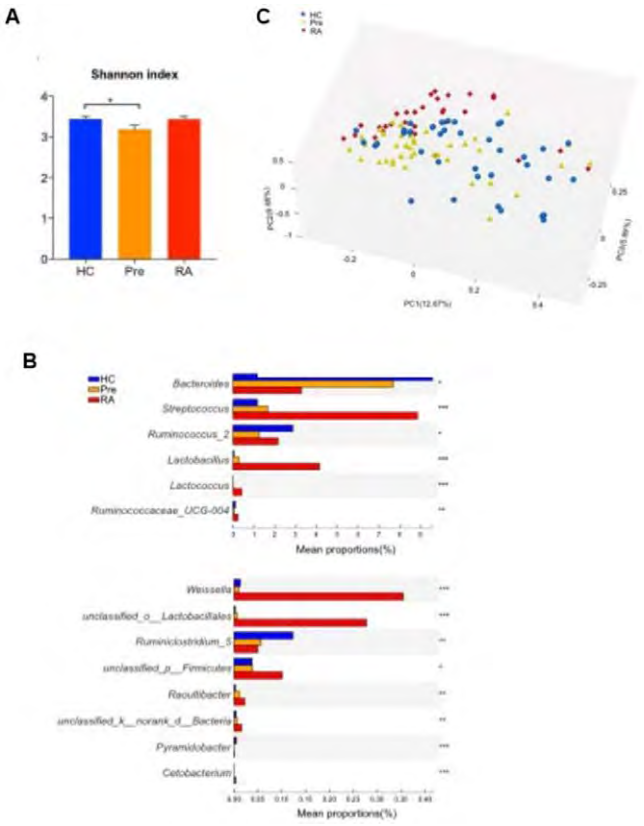


Figure 1.

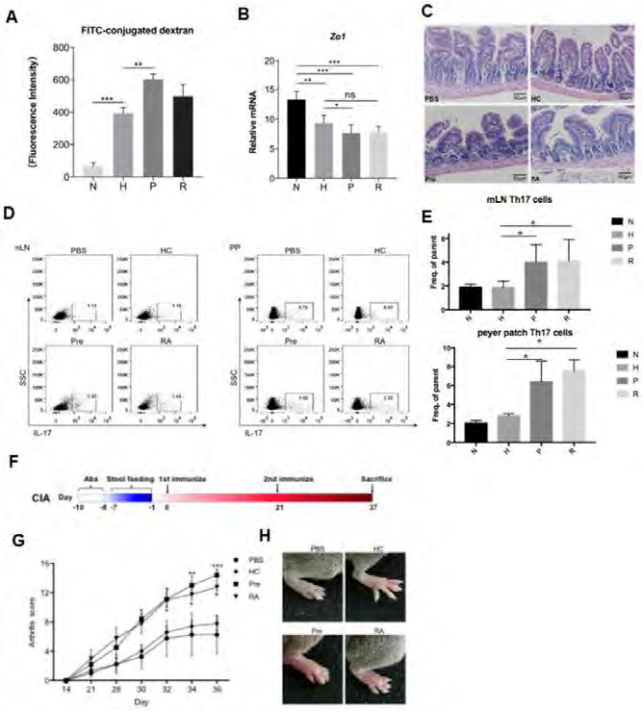


Figure 2.

Conclusion: The intestinal microbiota changed gradually during disease progression of human rheumatoid arthritis. The gut microbiota from Pre-RA individuals can trigger the gut barrier dysfunction and intestinal mucosal immunity imbalance, which may further contribute to the arthritis initiation and development.
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OP0017 THERAPEUTIC DRUG MONITORING COMPARED TO STANDARD TREATMENT OF PATIENTS STARTING INFLIXIMAB THERAPY: RESULTS FROM A MULTICENTRE RANDOMISED TRIAL OF 400 PATIENTS

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Background: A lack or loss of response to TNFα inhibitors (TNFi) has been associated with low serum drug levels and formation of anti-drug antibodies (ADAb). Therapeutic drug monitoring (TDM), an individualised treatment strategy based on regular assessments of serum drug levels, has been suggested to optimise efficacy of TNFi. It is still unclear if TDM improves clinical outcomes, and the value of TDM has recently been included in the research agenda across different specialities. This first randomised controlled trial on the effectiveness of TDM in a range of immune mediated inflammatory diseases including rheumatic diseases, the NORwegian DRUg Monitoring trial part A (NOR-DRUM (A)) focus on the induction period of infliximab (INX) treatment.
Objectives: To assess if TDM is superior to standard treatment in order to achieve remission in patients starting INX.
Methods: In the investigator-initiated, randomised, open-label, multicentre NOR-DRUM (A) study, adult patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), spondyloarthritis (SpA), ulcerative colitis (UC), Crohn's disease (CD) and psoriasis (Ps) starting INX therapy were randomly assigned to administration of INX according to a treatment strategy based on TDM (TDM arm) or to standard administration of INX without TDM (control arm). Study visits were conducted at each infusion. The primary endpoint was remission at week 30. In the TDM arm, the dose and interval were adjusted according to INX trough levels to reach the therapeutic range (Figure 1). If the patient developed significant levels of ADAb, INX was terminated. To guide the investigators, the TDM strategy was integrated in an interactive eCRF. The primary endpoint was analysed by mixed effect logistic regression in the full analyses set (FAS), adjusting for diagnoses. Infections and infusion reactions were specified as adverse events (AEs) of special interest. Clinical trial.gov: NCT03074656
Results: We enrolled 411 patients at 21 study centres between January 2017 and December 2018. 398 patients (RA 80, PsA 42, SpA 117, UC 80, CD 57, Ps 22) received the allocated strategy and were included in the FAS population. Demographic and baseline characteristics were comparable in both arms. TDM was not found to be superior to standard treatment with regard to the primary outcome. Remission at week 30 was reached in 100 (53%) and 106 (54%) of the patients in the TDM and control arm, respectively (adjusted difference, 1.5%; 95% confidence interval (CI), -8.2 to 11.1, p=0.78) (Figure 2). Consistent results were shown for all the secondary endpoints (Figure 3) and in the sensitivity analyses. Twenty patients (10%) in the TDM arm and 30 patients (15%) in the control arm developed significant levels of ADAb. The number of adverse events (AE) was similar in both groups, however infusion reactions were less frequent (5 patients (2.5%) vs 16 patients (8.0%)) in the TDM arm (difference 5.5% (95% CI 1.1, 9.8%))
Conclusion: NOR-DRUM (A) is the first randomised trial to address effectiveness of TDM in the induction period of TNFi treatment, and the first trial to address TDM in rheumatic diseases. In this study, TDM was not superior to standard treatment in order to achieve remission. Although improved safety is indicated by a reduction in infusion reactions, implementation of TDM as a general strategy in the induction period of INX is not supported by the NOR-DRUM (A) study.

Figure 1 Treatment strategy in the TDM arm

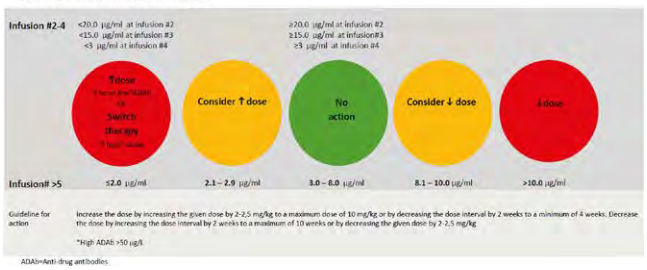


Figure 2. Difference in remission rate, overall and by disease

	TDM (n=198)	Control (n=200)	Difference in remission rate
Rheumatoid Arthritis	21/36 (58.3%)	21/42 (50.0%)	-8.3% (-30.4,13.8)
Psoriatic Arthritis	5/18 (27.8%)	12/21 (57.1%)	29.4% (-0.2,59.0)
Spondyloarthritis	23/57 (40.4%)	21/57 (36.8%)	-3.5% (-21.4,14.4)
Ulcerative Colitis	25/38 (65.8%)	29/41 (70.7%)	4.9% (-15.6,25.5)
Crohn's Disease	17/28 (60.7%)	17/26 (65.4%)	4.7% (-21.1,30.4)
Psoriasis	9/12 (75.0%)	6/9 (66.7%)	-8.3% (-47.7,31.0)
Overall	**100/189 (52.9%)**	**106/196 (54.1%)**	**1.5% (-8.2,11.1)**

TDM=Therapeutic drug monitoring arm, Control=Standard therapy arm

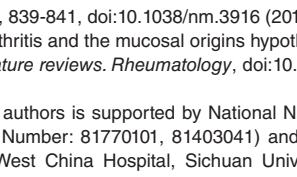
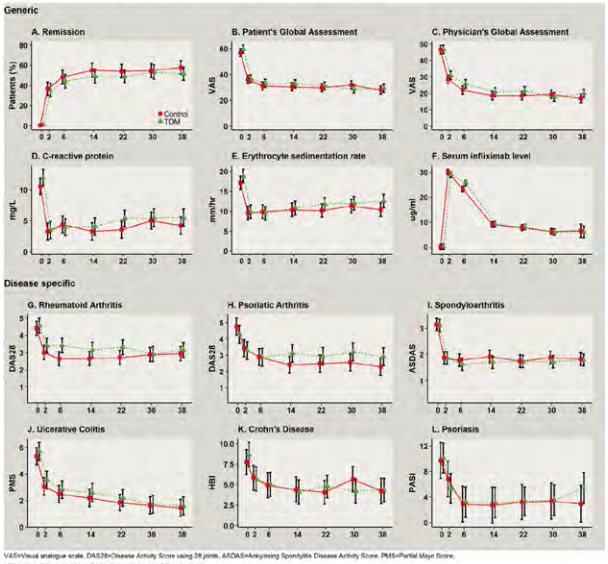


Figure 3. Generic (A-F) and disease specific (G-L) composite measures over study period.



VAS=Visual analogue scale, DAS28=Disease Activity Score using 28 joints, ASDAS=Ankylosing Spondylitis Disease Activity Score, PMS=Partial Mayo Score, HBI=Harvey-Bradshaw Index, PASI=Psoriasis Area and Severity Index

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LB0001 EFFICACY AND SAFETY OF UPADACITINIB VERSUS PLACEBO AND ADALIMUMAB IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS AND INADEQUATE RESPONSE TO NON-BIOLOGIC DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS (SELECT-PSA-1): A DOUBLE-BLIND, RANDOMIZED CONTROLLED PHASE 3 TRIAL

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Background: Upadacitinib (UPA) is an oral, reversible, JAK inhibitor approved for treatment of rheumatoid arthritis (RA) and currently under evaluation for treatment of psoriatic arthritis (PsA).
Objectives: To assess the efficacy and safety of UPA vs placebo (PBO) and adalimumab (ADA) in patients (pts) with PsA and prior IR or intolerance to ≥1 non-biologic DMARD (non-bDMARD).
Methods: Pts with active PsA (≥3 swollen and ≥3 tender joints), active or historical psoriasis, and on ≤2 non-bDMARDs were randomized 1:1:1:1 to once daily UPA 15mg (UPA15), UPA 30mg (UPA30), ADA 40mg every other week, or PBO. The primary endpoint was the proportion of pts achieving ACR20 for UPA vs PBO at Wk 12. Multiplicity controlled secondary endpoints for each dose of UPA vs PBO included change in HAQ-DI, FACIT-F, and SF-36 PCS (Wk 12); static Investigator Global Assessment of Psoriasis of 0 or 1, PASI75, and change in Self-Assessment of Psoriasis Symptoms (Wk 16); change in modified Sharp/van der Heijde Score (mTSS), proportion of pts achieving MDA, and resolution of enthesitis (LEI=0) and dactylitis (LDI=0) (Wk 24). For each dose of UPA, the multiplicity-controlled analysis also included non-inferiority and superiority vs ADA for ACR20 and superiority for HAQ-DI and pt's assessment of pain NRS (Wk 12). ACR50/70 at Wk 12 and ACR20 at Wk 2 were additional secondary endpoints. Treatment-emergent adverse events (TEAEs) through 24 wks are reported for pts who received ≥1 dose of study drug.
Results: 1705 pts were randomized; 1704 received study drug (53.2% female, mean age 50.8 yrs, mean duration of PsA diagnosis 6.1 yrs). 82% were on ≥1 concomitant non-bDMARD, of whom 84% received MTX +/- another non-bDMARD. At Wk 12, ACR20 rates were 70.6% with UPA15 and 78.5% with UPA30 vs 36.2% with PBO ($p < .001$ for UPA15/30 vs PBO) and 65.0% with ADA (non-inferiority, $p < .001$ for UPA15/30 vs ADA; superiority, $p < .001$ for UPA30 vs ADA). A greater proportion of pts achieved ACR50/70 with UPA15/30 vs PBO and UPA30 vs ADA. Improvements were observed with UPA15/30 vs PBO for all multiplicity controlled secondary endpoints and for UPA 15/30 vs ADA for HAQ-DI and UPA 30 vs ADA for improvement in pain (**Figure 1A-1B**). At Wk 24, change in mTSS was 0.25 for PBO, -0.04 for UPA15, 0.03 for UPA30, and 0.01 for ADA ($p < 0.001$ for UPA15/30 vs PBO). The rates of TEAEs and serious AEs, including serious infections, were similar in the PBO, UPA15, and ADA arms and higher with UPA30 (**Figure 2**). The rate of herpes zoster was similar for PBO and UPA15/30. No MACE was reported with UPA. One malignancy occurred in each of the PBO and UPA15 arms, and 3 malignancies were reported in each of the UPA30 and ADA arms. VTE were reported in 1 pt on PBO, 1 pt on UPA30, and 2 pts on ADA. One death occurred in the PBO arm.
Conclusion: In this non-bDMARD-IR PsA population, treatment with UPA15/30 demonstrated improvement in musculoskeletal symptoms, psoriasis, physical function, pain, and fatigue and inhibited radiographic progression; improvements were observed by Wk 2. At Wk 12, UPA15/30 were non-inferior to ADA for ACR20, with superiority demonstrated for UPA30. Greater percentages of UPA vs PBO pts achieved stringent measures of disease control (MDA, ACR50/70, sIGA 0/1). No new safety signals were identified compared with the safety profile observed in RA.

Figure 1. Efficacy Outcomes

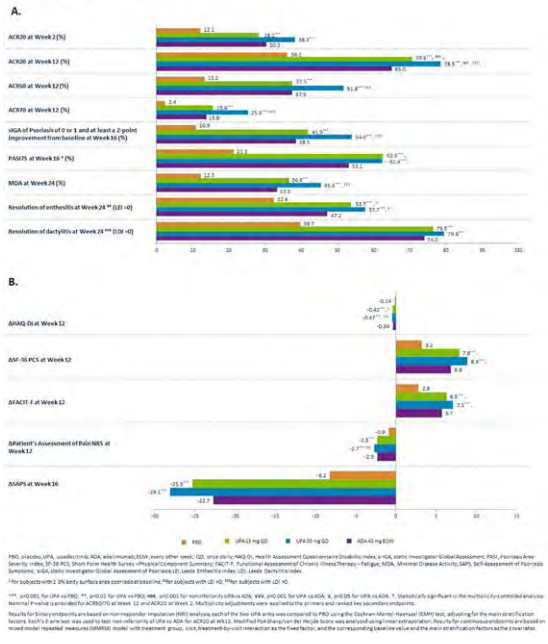
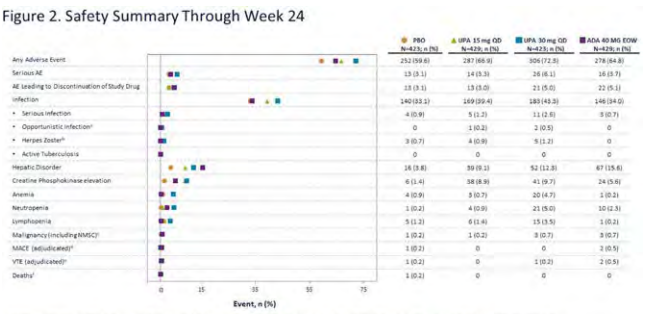


Figure 2. Safety Summary Through Week 24



PBO: placebo; UPA, upadacitinib; ADA, adalimumab; QD, once daily; EOW, every other week; NMSC, non-melanoma skin cancer; MACE, major adverse cardiovascular event; VTE, venous thromboembolic events

†Opportunistic infections: UPA15, candida urethritis; UPA30, 1 pneumocystis jirovecii pneumonia, 1 cytomegalovirus infection. ‡Herpes zoster. All events of herpes zoster were mild or moderate in severity involving 1-2 dermatomes. §Malignancies: PBO, basal cell carcinoma; UPA15, 1 neuroendocrine carcinoma; UPA30, 2 basal cell carcinoma, 1 lung neoplasm malignant; ADA, 1 colon cancer, 1 ovarian cancer, 1 uterine cancer. ¶MACE (includes CV death, non-fatal myocardial infarction, non-fatal stroke): PBO, 1 non-fatal myocardial infarction; ADA, 1 non-fatal myocardial infarction, 1 cerebrovascular accident. #VTE: PBO, 1 deep vein thrombosis; UPA30, 1 pulmonary embolism; ADA: 2 deep vein thrombosis. ‖Deaths: PBO, 1 cardiac arrest (death adjudicated to unknown cause).

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Biological DMARDs in RA I

OP0018

A MULTICENTER RANDOMIZED STUDY IN EARLY RHEUMATOID ARTHRITIS TO COMPARE ACTIVE CONVENTIONAL THERAPY VERSUS THREE BIOLOGICAL TREATMENTS: 24 WEEK EFFICACY RESULTS OF THE NORD-STAR TRIAL

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Background: The optimal first-line treatment of patients (pts) with early rheumatoid arthritis (RA) is yet to be established.
Objectives: The primary aim was to assess and compare the proportion of pts who achieved remission with active conventional therapy (ACT) and with three different biologic therapies after 24 wks. Secondary aims were to assess and compare other efficacy measures.
Methods: The investigator-initiated NORD-STAR trial (NCT01491815) was conducted in the Nordic countries and Netherlands. In this multicenter, randomized, open-label, blinded-assessor study pts with treatment-naïve, early RA with DAS28>3.2, and positive RF or ACPA, or CRP >10mg/L were randomized 1:1:1:1. Methotrexate (25 mg/week after one month) was combined with: 1) (ACT): oral prednisolone (tapered quickly); *or*: sulphasalazine, hydroxychloroquine and mandatory intra-articular (IA) glucocorticoid (GC) injections in swollen joints <wk 20; 2) certolizumab 200 mg EOW SC (CZP); 3) abatacept 125 mg/wk SC (ABA); tocilizumab 162 mg/wk SC (TCZ). IA GC was allowed in all arms <wk 20. Primary outcome was clinical disease activity index remission (CDAI≤2.8) at wk 24. Secondary outcomes included CDAI remission over time and other remission criteria. Dichotomous outcomes were analyzed by adjusted logistic regression with non-responder imputation (NRI). Non-inferiority analyses had a pre-specified margin of 15%.
Results: 812 pts were randomized. Age was 54.3±14.7 yrs (mean±SD), 31.2% were male, DAS28 5.0±1.1, 74.9% were RF and 81.9% ACPA positive. Fig 1 shows the adjusted CDAI remission rates over time with 95% CI. Table shows crude remission and response rates and absolute differences in adjusted

Table. Primary and key secondary outcomes at 24 weeks (ITT)

	Active conventional therapy (ACT)	Certolizumab +MTX	Abatacept +MTX	Tocilizumab +MTX
No of pts (ITT)	200	203	204	188[§]
		Crude remission and response rates		
CDAI remission	**42.0%**	**47.8%**	**52.5%**	**41.0%**
ACR/EULAR Boolean remission	34.0%	38.4%	37.3%	31.4%
DAS28 remission	63.5%	68.5%	69.6%	63.3%
SDAI remission	41.5%	49.8%	51.5%	42.6%
EULAR good response	71.5%	76.9%	79.9%	71.3%
		Difference (95% CI) in rates with Arm 1 as reference (adjusted)		
CDAI remission	**Ref**	**4% (-5 to 13%)**	**9% (0.1 to 19%)**	**-1% (-10 to 9%)**
ACR/EULAR Boolean remission	Ref	4% (-6 to 13%)	5% (-5 to 14%)	-4% (-13 to 6%)
DAS28 remission	Ref	3% (-6 to 11%)	5% (-4 to 13%)	-1% (-10 to 8%)
SDAI remission	Ref	6% (-3 to 18%)	9% (-0.3 to 18%)	1% (-8 to 11%)
EULAR good response	Ref	4% (-4 to 14%)	8% (-2 to 18%)	0.4% (-10 to 11%)

[§]17 patients allocated to Tocilizumab did not receive it due to its unavailability and were excluded from ITT.

remission and response rates (superiority analysis). Differences in remission and response rates with CZP and TCZ, but not with ABA, remained within the pre-defined non-inferiority margin versus ACT, Fig 2.

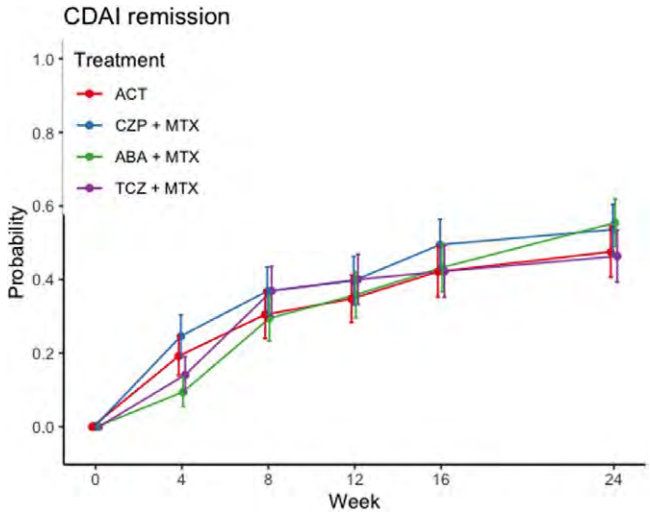


Figure 1. CDAI remission over time (adj. estimates with 95% CI)

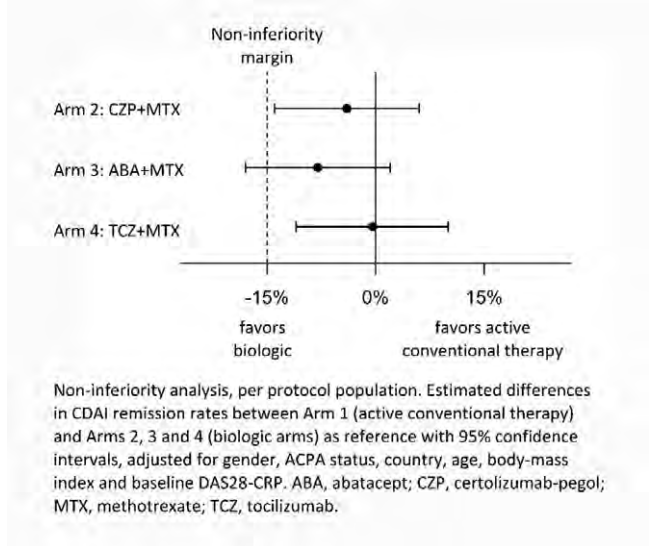


Figure 2. Non-inferiority analysis of protocol population. Estimated differences in CDAI remission rates between Arm 1 (active conventional therapy) and Arms 2, 3, and 4 (biologic arms) as reference with 95% confidence intervals, adjusted for gender, ACPA status, country, age, body-mass index and baseline DAS28-CRP. ABA, abatacept; CZP, certolizumab-pegol; MTX, methotrexate; TCZ, tocilizumab.

Conclusion: High remission rates were found across all four treatment arms at 24 wks. Higher CDAI remission rate was observed for ABA versus ACT (+9%) and for CZP (+4%), but not for TCZ (-1%). With the predefined 15% margin, ACT was non-inferior to CZP and TCZ, but not to ABA. This underscores the efficacy of active conventional therapy based on MTX combined with glucocorticoids and may guide future treatment strategies for early RA.

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OP0019

STABLE VERSUS TAPERED AND WITHDRAWN TREATMENT WITH TUMOR NECROSIS FACTOR INHIBITOR IN RHEUMATOID ARTHRITIS REMISSION (ARCTIC REWIND): A RANDOMISED, OPEN-LABEL, PHASE 4, NON-INFERIORITY TRIAL

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Background: Remission is the preferred treatment target in rheumatoid arthritis (RA), and many patients require biologic DMARDs to reach this state. It is debated whether tapering of tumor necrosis factor inhibitor (TNFi) treatment to discontinuation should be considered in RA patients who sustain remission on treatment (1).

Objectives: The primary study objective was to assess the effect of tapering and withdrawal of TNFi on the risk of flares in RA patients in clinical remission.

Methods: In the non-inferiority ARCTIC REWIND trial, RA patients in remission for at least 12 months on stable TNFi therapy were randomly assigned to continued stable TNFi or tapering (half-dose TNFi for 4 months, thereafter withdrawal of TNFi), with visits every four months. csDMARD co-medication was kept stable in both arms. Patients had to be in DAS remission at inclusion with 0/44 swollen joints. The primary endpoint was the proportion of patients with disease flare during the 12-month study period (defined as DAS>1.6, change in DAS>0.6 and 2 or more swollen joints, or the physician and patient agreed that a clinically significant flare had occurred). Full-dose TNFi was reinstated in case of flares in the tapering arm. The non-inferiority margin was 20%, with a predefined superiority test if non-inferiority was not shown. The inferiority null-hypothesis was tested in the per-protocol population by mixed effect logistic regression. Radiographs were scored by van der Heijde modified Sharp score (0 and 12 months, average of two readers, progression: ≥1 unit change). Clinicaltrials NCT01881308.

Results: We randomised 99 patients, 92 received the allocated treatment strategy, 84 were included in the per-protocol population. Baseline characteristics, clinical and ultrasound disease activity were balanced (Table). csDMARD co-medication was used by 93% in the stable and 88% in the tapering arm. In the primary analysis, 5% of patients in the stable TNFi arm experienced a flare during 12 months, compared to 63% in the tapering TNFi arm. The risk difference (95% CI) was 58% (42% to 74%, Fig 1), with stable treatment being deemed superior to tapering. 90% in the stable and 81% in the tapering arm did not show progression of radiographic joint damage, difference (95% CI) -9% (-24%, 6%). At 12 months, DAS scores, DAS remission and function were similar between groups (Fig 2). The numbers of adverse events (AE)/serious AE in the stable and tapering arm were 57/2 and 50/3, respectively, with 26 and 15 infections.

Conclusion: In a randomised clinical trial assessing patients in prolonged and deep RA remission, we observed a large increase in the flare rate in patients who tapered and discontinued TNFi. Patients responded well to reinstated treatment and remission rates in the two study arms were comparable at 12 months.

References:

[1] Smolen et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2019 update. ARD 2020

Table. Baseline values – n (%), mean (SD), or median (IQR)

	Stable, n=45	Tapering, n=47
Age, yrs	57 (11)	58 (13)
Female	30 (67%)	25 (53%)
ACPA+	35 (78%)	36 (77%)
Symptom duration, yrs	10 (7)	12 (7)
DAS	0.9 (0.4)	0.8 (0.3)
CRP mg/L	1 (1 – 2)	1 (1 – 3)
No ulttrasound power Doppler signal in any of 32 joints	42 (96%)	44 (94%)

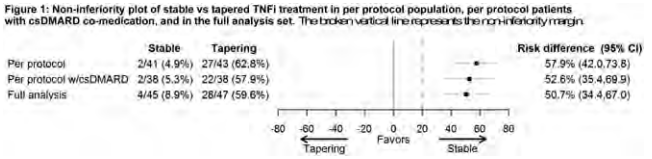
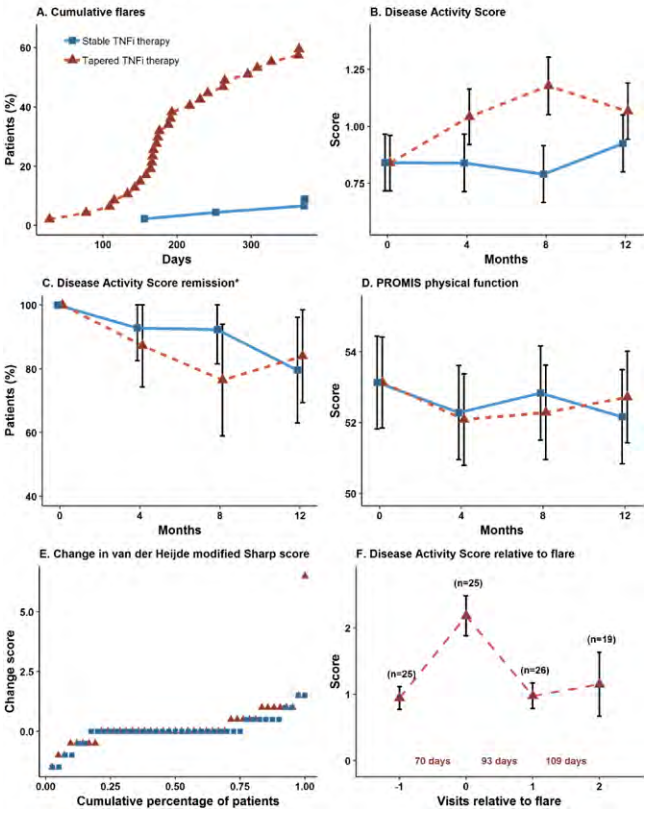


Figure 2: Secondary endpoints



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OP0020 IMPACT OF BDMARDS WITH DIFFERENT MODES OF ACTION ON FATIGUE IN RA PATIENTS

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Table 1. Patient characteristics for different DMARD modes of action

Parameter	csDMARDs	TNFi	RTX	ABA	IL-6	JAKi
N	2376	2772	115	166	357	110
Fatigue at baseline	5.9 (2)	6.1 (2)	5.9 (2)	5.9 (1.9)	6.1 (2)	6.3 (1.9)
Age [years]	58.5 (12.7)	56.3 (12.4)	62.7 (10.9)	59.7 (12.6)	57.9 (12.5)	61.5 (11.5)
Female sex	1809 (76.1)	2060 (74.3)	82 (71.2)	118 (71)	272 (76.3)	79 (70.1)
Disease duration [years]	6.2 (7.2)	8.7 (8.1)	10.8 (9.7)	9.8 (9.2)	7.9 (7.6)	8.5 (10)
Joint erosions	634 (28.4)	1358 (50.5)	62 (56.8)	91 (55.4)	158 (46.4)	45 (41.3)
Prior csDMARD therapies	1.3 (0.6)	2.3 (1)	2.5 (1.1)	2.2 (1)	2.2 (0.9)	1.8 (0.8)
DAS28-ESR	4.6 (1.2)	5 (1.2)	5.3 (1.3)	5.3 (1.2)	5.2 (1.3)	4.9 (1.3)
% of full physical capacity	67.4 (21.6)	64.6 (22)	57 (23.5)	59.5 (21.3)	63.8 (20.9)	61.6 (23)
Glucocorticoid therapy (last 6 months)	1161 (48.9)	1747 (63)	76 (66.4)	93 (56)	198 (55.5)	42 (38.1)
Fibromyalgia	73 (3.1)	111 (4)	6 (5.2)	7 (4.2)	11 (3.1)	1 (0.9)
Depression	180 (7.6)	218 (7.9)	10 (8.7)	14 (8.4)	26 (7.3)	16 (14.6)
Ever smoker	1252 (52.7)	1497 (54)	68 (59)	84 (50.7)	200 (56)	59 (53.5)

Results are presented as mean ± SD or number (percentage). Absolute numbers may be rounded due to multiple imputation.

Background: Fatigue is an important patient-reported outcome. It has been reported to be potentially targetable by DMARDs with specific modes of action, particularly IL-6 inhibition [1].

Objectives: To assess to which extent patients on DMARDs with different modes of action reach fatigue levels of 2 or less on a 0 (no fatigue) to 10 (high fatigue) scale after 6 months of treatment.

Methods: The German register RABBIT is a prospective longitudinally followed cohort of RA patients enrolled with a new start of a DMARD after at least one csDMARD failure. This analysis comprises bionaive patients who were enrolled with start of a b/tsDMARD between 01/2009 and 04/2019, who had at least 1 follow-up, did not switch during the first 3 months and afterwards only within the same substance, and presented fatigue levels of > 2 at baseline.

Poisson regression models with a robust error variance were used to calculate risk ratios (RRs) for reaching fatigue values ≤ 2, for all DMARD modes of action. Propensity score weighting was used to adjust for confounding by indication. Multiple imputation of missing values was performed.

Results: Baseline fatigue levels were 5.1 overall and 6.1 among patients with a fatigue level of > 2 points on average. They were comparable among different DMARD modes of action. csDMARD patients had lower values than others regarding disease duration, disease activity, or joint erosions (Table 1).

The RR of IL-6 inhibitors for achieving a fatigue level of ≤ 2 was 1.34 (95% CI: 1.09 – 1.64) compared to csDMARDs. Among other factors, current smoking, prevalent fibromyalgia and depression had a negative impact on achieving a low fatigue level (Table 2).

Table 2. Risk ratios for achieving fatigue levels ≤2

Parameter (at baseline)	RR	95% confidence interval	
Fatigue (1 point higher)	**0.83**	**(0.80;**	**0.86)**
TNF inhibitor (vs. csDMARDs)	1.11	(0.99;	1.24)
Rituximab (vs. csDMARDs)	1.10	(0.71;	1.68)
Abatacept (vs. csDMARDs)	1.13	(0.82;	1.54)
IL-6 inhibitor (vs. csDMARDs)	**1.34**	**(1.09;**	**1.64)**
JAK inhibitor (vs. csDMARDs)	1.19	(0.81;	1.75)
Age (5 years more)	**0.97**	**(0.95;**	**0.99)**
Female sex	**0.83**	**(0.74;**	**0.92)**
Patient global health (1 point higher)	**0.97**	**(0.94;**	**0.997)**
Joint erosions	**1.19**	**(1.07;**	**1.32)**
Current smoking	**0.86**	**(0.76;**	**0.98)**
Former smoking	0.92	(0.82;	1.04)
Fibromyalgia	**0.56**	**(0.35;**	**0.90)**
Depression	**0.75**	**(0.59;**	**0.95)**

Conclusion: Treatment with IL-6 inhibitors significantly increases the chance of reaching low fatigue levels within half a year in RA patients, while current smoking reduces it.

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OP0021

OLOKIZUMAB, MONOCLONAL ANTIBODY AGAINST IL6, IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE RHEUMATOID ARTHRITIS INADEQUATELY CONTROLLED BY METHOTREXATE: EFFICACY AND SAFETY RESULTS OF PHASE III CREDO-1 STUDY

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Background: Olokizumab (OKZ) is a new humanized monoclonal antibody targeting IL-6 [1, 2]. Here we present the results of the first phase III study of OKZ in patients with Rheumatoid Arthritis (RA).

Objectives: The primary objective was to evaluate the safety and efficacy of OKZ administered subcutaneously (SC) every 2 weeks (q2w) and 64mg SC every 4 weeks (q4w) vs placebo in the treatment moderate-to-severe RA.

Methods: In this randomized, double-blind, placebo-controlled, multicenter study in patients with moderately to severely active RA despite methotrexate (MTX) (ClinicalTrials.gov Identifier NCT02760368, CREDO-1) patients received SC injections of OKZ 64 mg q2w, OKZ 64 mg q4w and PBO q2w for 24 weeks. Starting at Week (Wk) 14, non-responders were rescued. After Wk 24, subjects were eligible for an open-label study extension.

The primary endpoint was American College of Rheumatology 20% (ACR20) response at Wk 12.

Secondary endpoints included: percentage of subjects with low disease activity, improvement of physical ability. Safety outcomes, including treatment-emergent adverse events (TEAEs), treatment-emergent serious adverse events (TESAEs) and laboratory abnormalities (via central lab) were assessed.

Results: 428 patients were randomized to OKZ 64mg q2w (n=143), OKZ 64mg q4w (n=142), and PBO (n=143). Baseline characteristics were comparable between treatment arms: mean (SD) age was 51.3 (12.0) years, 82.7% of patients were female, disease duration 8.14 (7.6) and all patients were on MTX. Mean (SD) baseline DAS28-CRP was 6.0 (0.76) and HAQ-DI was 1.72 (0.49). 130 (90.9%) patients in q2w, 134 (94.4%) in q4w and 132 (92.3%) in PBO arms completed the study. Both regimens of OKZ were significantly better than PBO in all primary and secondary endpoints (Table 1).

Table 1. Key efficacy results (intent-to-treat population) NRI [1]

	OKZ q2w	OKZ q4w	PBO
Number of Subjects	143	142	143
ACR20 Response, n (%) Wk 12 (primary endpoint)	91(63.6)***	100(70.4)***	37(25.9)
DAS28<3.2 Response, n (%) Wk 12	48(33.6)***	55(38.7)***	5(3.5)
HAQ-DI Wk 12 LSM (SE)	-0.54(0.041)	-0.56(0.042)	-0.20(0.042)
Treatment Comparison vs PBO LSM Difference (SE)	-0.34***(0.059)	-0.36***(0.059)	
97.5% CI for LSM Difference	-0.47, -0.21	-0.49, -0.23	
ACR50 Response, n (%) Wk 24	61(42.7)***	69(48.6)***	11(7.7)
CDAI ≤2.8 Response, n (%) Wk 24	12(8.4)**	11(7.7)**	0

[1] – NRI, Non-Responder Imputation; LSM, Least Squares Mean; **p-value difference from PBO <0.001; ***p-value difference from PBO <0.0001; SE, Standard Error

The key efficacy outcomes were maintained throughout the 24-week.

Overall incidence of TEAEs was 58.0% in OKZ q2w arm; 57.0% in OKZ q4w arm and 43.7% in PBO, TEAEs leading to study treatment discontinuation were reported in 4.9%, 3.5% and 0.7% patients, respectively.

At least one TESAE (subcutaneous abscess, pulmonary tuberculosis, staphylococcal sepsis, toxic shock syndrome, cervix carcinoma, obstructive pancreatitis, diabetic vascular disorder) was reported in 8 (5.6%) of OKZ groups, numerically higher than 4(2.8%) in PBO. There was one death due to septic shock in the OKZ q2w arm.
Conclusion: Treatment with OKZ over a 24-week period was associated with significant improvements in the signs, symptoms and physical function of RA, with a safety profile consistent with Phase II data for OKZ and with the data for the agents with similar mechanism of action.
There were no discernible differences between the two regimens of OKZ in efficacy or safety outcomes.
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OP0022 RISK OF DIVERTICULITIS AND GASTRO-INTESTINAL PERFORATION IN RHEUMATOID ARTHRITIS TREATED WITH TOCILIZUMAB COMPARED TO RITUXIMAB AND ABATACEPT: A PROSPECTIVE PROPENSITY-MATCHED COHORT STUDY

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Background: There are discordant results regarding a potential increased risk of gastro-intestinal perforation (GIP) in rheumatoid arthritis (RA) patients treated with tocilizumab (TCZ) compared to conventional synthetic disease modifying anti rheumatic drugs (csDMARDs) or TNF inhibitors (TNFis) (1–3).
Objectives: The aim of our study was to compare the risk of diverticulitis and GIP in RA patients treated with TCZ compared to rituximab (RTX) and abatacept (ABA).
Methods: We conducted a multicentric study of patients with RA, prospectively followed in 3 observational French registries evaluating the effectiveness and safety of RTX (Autoimmunity and Rituximab (AIR)), ABA (Orencia and Rheumatoid Arthritis (ORA)), and TCZ (REGistry–RoAcTEmra (REGATE)). Using a propensity score approach, we compared the risk of diverticulitis or GIP during treatment with TCZ vs RTX and ABA. The following covariates were included in the propensity score: age, sex, history of diabetes and neoplasia, Charlson Comorbidity Index, number of previous csDMARDs and TNFi, history of TNFi, daily dose of glucocorticoids (GCs) at baseline, co-treatment with a csDMARDs, average DAS28 during follow-up, duration of RA, and exposure time to the considered bDMARDs.
Results: 4501 patients (1496 treated by TCZ, 1986 by RTX and 1019 by ABA) were included. 21 and 9 GIP occurred in the TCZ treated patients, compared to 10 and 8 in the RTX treated patients and 10 and 2 in the ABA treated patients (corresponding incidence rate (IR) are shown in table 1). Two deaths occurred in patients experiencing GIP: 1 (12.5%) due to undetermined rectal perforation among a RTX treated patient, and 1 (11.1%) due to a perforated ulcer among a TCZ treated patient. Based on inverse probability weighting (IPW), there was an increased risk of diverticulitis and GIP in the TCZ treated patients compared with RTX or ABA (table 1). In a subgroup analysis, we confirmed an increased risk of GIP due to diverticulitis but not to any other etiology. Older age (p=0.05), GCs at baseline (p=0.10) and average daily dose of GCs during follow-up (p=0.08) seemed associated with GIP only in univariate analysis. Compared to RTX and ABA, diverticulitis and GIP among TCZ patients occurred earlier after the last perfusion (p=0.01), with atypical clinical presentation (slow transit in 30%, p=0.04) and lower acute phase reactants when the event occurred (C-reactive protein: 31.2±58.4 vs 88.2±89.6 mg/L, p=0.005). Perforated diverticulitis seemed to have higher dose of GCs at the time of the event compared to diverticulitis without perforation in univariate analysis (p=0.06).
Conclusion: TCZ was associated with an increased risk of diverticulitis, and GIP due to diverticulitis, compared to RTX and ABA. Our study confirms an increased risk of GIP in RA patients treated with TCZ, which might be explained by an increased risk of diverticulitis with misleading clinical presentation.
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OP0023 PREDICTION OF REMISSION FOR EACH BIOLOGICS BASED ON PATIENT'S CLINICAL INFORMATION BEFORE STARTING BIOLOGICS USING EXPLAINABLE ARTIFICIAL INTELLIGENCE: DATA FROM THE KOREAN COLLEGE OF RHEUMATOLOGY BIOLOGICS REGISTRY

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Background: Many studies have identified predictive factors of response to biologics in patients wirh rheumatoid arthritis (RA). However, there is still a lack in using them in daily clinical practice. Therefore, it is necessary to develop a method that can assist the physician in selecting effective biologics.
Objectives: The purpose of this study is to establish machine learning model that predicts remission in patients treated with biologics using data of RA patients from the Korean College of Rheumatology Biologics (KOBIO) registry, and to identify the important features that have the most influence on the response to biologics using explainable artificial intelligence (AI).
Methods: A total of 1,527 patients who started with biologics such as etanercept, adalimumab, golimumab, infliximab, abatacept, and tocilizumab from December 2012 to June 2019 were enrolled. Remission was predicted using 46 variables corresponding to baseline profiles at the starting of each biologics. We used five machine learning methods such as lasso, ridge, SVM, random forest, and XGBoost. For explainability of those models, we used Shapley plot to interpret the feature importance for each biologics.

Table 1. Incidence (/1000 PY) and risk of diverticulitis or GIP

							IPW analysis			
	AE (n)	IR	AE (n)	IR	AE (n)	IR	OR [95 CI]	p	OR [95 CI]	p
Exposition (PY)	TCZ (ref) 3 990		RTX 6 322		ABA 2 389		TCZ vs RTX		TCZ vs ABA	
Diverticulitis	21	5.3	10	1.6	10	4.2	4.5 [2.6-7.6]	<0.0001	3.4 [1.7-6.5]	<0.0001
GIP	9	2.3	8	1.3	2	0.8	2.8 [1.5-5.1]	0.001	5.4 [1.4-19.9]	0.01
* *Diverticular GIP*	6	1.5	3	0.5	2	0.8	3.8 [1.7-8.5]	0,001	6.9 [1.9-25.4]	0.004
* *Due to another etiology*	3	0.7	5	0.8	0	0	1.4 [0.5-3.9]	0.5	-	-

AE=adverse events; PY=person-years

Results: In all machine learning methods, the accuracy and the area under the receiver operating characteristic (AUROC) were 57.2%~74.5%, 0.547~0.747, respectively (Table 1). The accuracy and AUROC of each biologics were similar between machine learning methods. Figure 2 showed interpretation of feature importance with the Shapley plot for remission. The most important feature was age in adalimumab (younger were closer to remission), daily corticosteroid dose in etanercept, golimumab, and all TNF inhibitors (using fewer doses daily were closer to remission), baseline erythrocyte sedimentation rate in infliximab (lower ESR were closer to remission), disease duration in abatacept (longer disease durations showed difficulty determining remission), baseline c-reactive protein in tocilizumab (higher CRP were closer to remission).

Table 1. Predicting remission for all biologics in various machine learning method.

	Measure	Lasso	Ridge	SVM	Random Forest	XGBoost	No info rate	Sample
Abatacept	Accuracy	74.1%	74.1%	70.6%	71.8%	68.8%	70.6%	216
	AUROC	0.725	0.742	0.707	0.677	0.647	0.500	
Adalimumab	Accuracy	73.6%	72.0%	70.4%	72.0%	70.4%	68.8%	315
	AUROC	0.710	0.729	0.700	0.675	0.663	0.500	
Etanercept	Accuracy	72.0%	72.0%	70.0%	71.5%	70.0%	68.0%	250
	AUROC	0.741	0.747	0.726	0.719	0.704	0.500	
Golimumab	Accuracy	71.3%	68.5%	66.7%	68.5%	68.5%	68.5%	138
	AUROC	0.746	0.727	0.701	0.690	0.655	0.500	
Infliximab	Accuracy	72.8%	73.5%	67.6%	73.5%	69.1%	72.5%	172
	AUROC	0.663	0.683	0.616	0.597	0.527	0.500	
TNF inhibitors	Accuracy	73.9%	74.5%	73.9%	74.2%	73.6%	70.3%	875
	AUROC	0.739	0.741	0.726	0.747	0.724	0.500	
Tocilizumab	Accuracy	62.4%	63.6%	62.4%	59.5%	57.2%	59.5%	436
	AUROC	0.633	0.640	0.633	0.615	0.547	0.500	

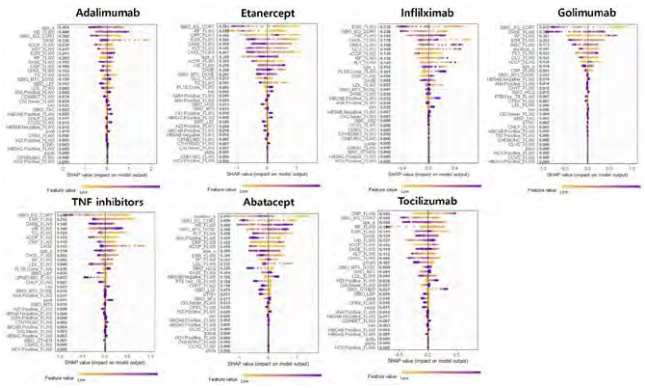


Figure 2. Shapley plots and SHAP values for the feature importance from clinical information in patients with RA.

Conclusion: We developed machine learning models for predicting remission as a response to each biologics in active RA patients based on their clinical profiles, and found important clinical features using explainable AI. This approach may support clinical decisions to improve treatment outcomes in patients with RA.
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OP0024 USE OF HYDROXYCHLOROQUINE AND RISK OF HEART FAILURE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Hydroxychloroquine (HCQ) is a disease-modifying anti-rheumatic drug (DMARD) used as a long-term treatment for rheumatoid arthritis (RA) patients. Cardiotoxicity is a rare but potentially life-threatening side effect of HCQ and may present as conduction disorders, cardiomyopathy, and resulting heart failure (HF). The evidence of cardiotoxicity associated with the use of HCQ largely relies on case reports and case series while large cohort studies on the subject are lacking.
Objectives: To examine the relationship between the use of HCQ and risk of developing HF in RA.
Methods: In this nested case-control study, cases were Olmsted county, Minnesota residents with incident RA (based on 1987 ACR criteria) in 1980-2013 who developed HF after RA incidence. Each case was matched on year of birth, sex and year of RA incidence with an RA control who did not develop HF. Each non-HF control was assigned an index date corresponding to the HF diagnosis date of the case. Controls were allowed to later become cases to avoid bias. HF was defined using the Framingham criteria. Data on HCQ use including start and stop dates and dose changes was manually abstracted via medical record review, and used to calculate HCQ duration and cumulative dose. Age-adjusted logistic regression models were used to examine the association between HCQ and HF.
Results: From a cohort of 1078 subjects, the study identified 143 RA cases diagnosed with HF (mean age 65.8, 62% females) and 143 non-HF RA controls (mean age 64.5, 62% female). Cases and controls had similar RA duration, proportion of patients positive for rheumatoid factor (RF) and/ or cyclic citrullinated antibody (CCP), body mass index, and smoking status (Table). The duration of HCQ use prior to the diagnosis of HF was 2.8 years in cases and 2.6 years in controls. A total of 71 cases and 69 controls used HCQ at some time before index date. Among these, the median (interquartile range) duration of HCQ use was 2.8 (0.6, 10.0) years for cases and 2.5 (0.7, 8.2) for controls. The median cumulative dose of HCQ was 371 g and 302 g in cases and controls, respectively, with 55% of cases receiving a cumulative dose of ≥ 300 g compared to 54% in controls. HCQ cumulative dose was not associated with HF (Odds Ratio [OR]: 0.96 per 100g increase in cumulative dose, 95% confidence interval [95% CI]: 0.90-1.03). Likewise, no association was found for patients with a cumulative dose ≥300g (OR 0.92, 95% CI 0.41-2.08). The duration of use of HCQ prior to index was not associated with HF (OR 0.98, 95% CI 0.91-1.05). Retinal toxicity rates were similar in cases and controls.

Table. Characteristics of patients with rheumatoid arthritis with and without heart failure.

Variable	HF	non-HF
Age at RA diagnosis (years)	65.8 ± 12.3	64.5 ± 12.5
Female	62%	62%
RA duration at baseline (years)	11.3 ± 8.5	10.3 ± 8.2
RF positive	66%	65%
CCP positive	46%	53%
RF/ CCP positive	68%	66%
BMI (at RA diagnosis)	28.6 ± 6.5	27.7 ± 5.4
Smoking status at RA incidence		
Former	45%	41%
Current	22%	22%

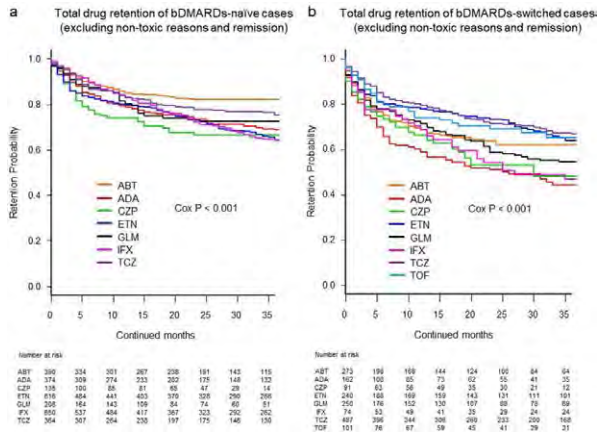
Conclusion: Use of HCQ was not associated with development of HF in patients with RA in this study. While there was no statistically significant association between the cumulative dose of HCQ and HF, the confidence interval for HCQ dose ≥300 g was wide suggesting that more studies are needed to understand the impact of higher doses of HCQ on development of HF in RA.
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OP0025 DRUG RETENTION OF 7 BIOLOGICS AND TOFACITINIB IN BIOLOGICS-NAÏVE AND BIOLOGICS-SWITCHED PATIENTS WITH RHEUMATOID ARTHRITIS -THE ANSWER COHORT STUDY

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Background: EULAR recommendation announced that biological disease-modifying antirheumatic drugs (bDMARDs) and janus kinase inhibitors (JAKi) are considered as equivalent in the treatment of rheumatoid arthritis (RA). However, we still lack reliable evidence of direct comparison between these agents' retention, which may reflect both effectiveness and safety.

Objectives: The aim of this multi-center (7 university-related hospitals), retrospective study is to clarify retention rates and reasons for discontinuation of 7 bDMARDs and tofacitinib (TOF), one of the JAKi, in both bDMARDs-naïve and bDMARDs-switched cases.
Methods: This study assessed 3,897 patients and 4,415 treatment courses of with bDMARDs and TOF from 2001 to 2019 (2,737 bDMARDs-naïve patients and 1,678 bDMARDs-switched patients [59.5% switched to their second agent], female 82.3%, baseline age 57.4 years, disease duration 8.5 years; rheumatoid factor positivity 78.4%; DAS28-ESR 4.3; concomitant prednisolone [PSL] 6.1 mg/day [42.4%] and methotrexate [MTX] 8.5 mg/week [60.9%]). Treatment courses included abatacept (ABT; n=663), adalimumab (ADA; n=536), certolizumab pegol (CZP; n=226), etanercept (ETN; n=856), golimumab (GLM; n=458), infliximab (IFX; n=724), tocilizumab (TCZ; n=851), and TOF (n=101/only bDMARDs-switched cases). Reasons for discontinuation were classified into four categories by each attending physician: 1) lack of effectiveness, 2) toxic adverse events, 3) non-toxic reasons, and 4) remission. Retention rates of each discontinuation reason were estimated at 36 months using the Kaplan-Meier method and adjusted for potential clinical confounders (age, sex, disease duration, concomitant PSL and MTX, starting date and number of switched bDMARDs) using Cox proportional hazards modeling.
Results: Adjusted drug retention rates for each discontinuation reason were as follows: lack of effectiveness in the bDMARDs-naïve group (from 70.8% [CZP] to 85.1% [ABT]; P=0.001 between agents) and the bDMARDs-switched group (from 52.8% [CZP] to 78.7% [TCZ]; P<0.001 between agents). Toxic adverse events in the bDMARDs-naïve group (from 86.9% [IFX] to 96.3% [ABT]; P<0.001 between agents) and the bDMARDs-switched group (from 81.1% [ADA] to 95.4% [ETN]; P=0.01 between agents). Finally, overall retention rates excluding discontinuation for non-toxic reasons or remission ranged from 64.2% (IFX) to 82.0% (ABT) (P<0.001 between agents) in the bDMARDs-naïve group (figure a) and from 44.2% (ADA) to 66.8% (TCZ) (P<0.001 between agents) in the bDMARDs-switched group (figure b).
Conclusion: Remarkable differences were observed in drug retention of 7 bDMARDs and TOF between bDMARDs-naïve and bDMARDs-switched cases.



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Vasculitis

OP0026

A RANDOMIZED, CONTROLLED TRIAL OF RITUXIMAB VERSUS AZATHIOPRINE AFTER INDUCTION OF REMISSION WITH RITUXIMAB FOR PATIENTS WITH ANCA-ASSOCIATED VASCULITIS AND RELAPSING DISEASE

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Background: Rituximab (RTX) is an effective therapy for induction of remission in ANCA-associated vasculitis (AAV). However, the effect of RTX is not sustained, and subsequent relapse rates are high, especially in patients with a history of relapse.
Objectives: The RITAZAREM trial is an international, multi-center, open-labelled, randomized, controlled trial of patients with AAV with relapsing disease comparing the efficacy, after induction of remission with RTX, of two relapse-prevention strategies: repeat dosing of RTX or daily oral azathioprine (AZA).
Methods: Patients with AAV were recruited at the time of relapse and received induction therapy with RTX and glucocorticoids. If remission was achieved by month 4, patients were randomized in a 1:1 ratio to receive either RTX (1000 mg every 4 months for 5 doses) or AZA (2 mg/kg/day) as maintenance therapy. Patients were followed for a minimum of 36 months, with the primary outcome being time to disease relapse.
Results: 190 patients were enrolled and 170 randomized at 4 months (85 to RTX; 85 to AZA). The data are complete on all patients up to at least month 24. Median age was 59 years (range 19-89), with a prior disease duration of 5.3 years (0.4-38.5). 123/170 (72%) patients had a history of testing positive for anti-proteinase 3 ANCA; 47/170 (28%) for myeloperoxidase ANCA; 104/170 (61%) were enrolled having suffered a major relapse, and 48/170 (28%) received a pre-specified higher dose glucocorticoid induction regimen (Table 1).

Table 1. Baseline characteristics of patients enrolled in RITAZAREM trial

	Rituximab (N=85)	Azathioprine (N=85)	Total (N=170)
Age, years: median (range)	57 (18-89)	61 (27-83)	59 (18-89)
Female, number (%)	42 (49.4%)	44 (51.8%)	86 (50.6%)
Disease duration, years: median (range)	5.8 (0.4-38.5)	4.9 (0.4-25.8)	5.3 (0.4-38.5)
Prior cyclophosphamide therapy			
Number of patients (%)	67/85 (78.8%)	66/85 (77.6%)	133/170 (78.2%)
Cumulative dose, grams (g): median (range)	7.1 g (0.2-301)	12 g (1.0-146)	10 g (0.2-301)
Prior rituximab therapy			
Number (%) patient	33/85 (38.8%)	27/85 (31.8%)	60/170 (35.3%)
Cumulative dose, grams (g): median (range)	3.2 g (2.0-16.0)	5.4 g (1.5-14.0)	3.9 g (1.5-16.0)
Glucocorticoid induction regimen			
1mg/kg/day starting dose	24/85 (28.2%)	24/85 (28.2%)	48/170 (28.2%)
0.5mg/kg/day starting dose	61/85 (71.8%)	61/85 (71.8%)	122/170 (71.8%)
ANCA type			
Anti-proteinase 3	61/85 (71.8%)	62/85 (72.9%)	123/170 (72.4%)
Anti-myeloperoxidase	24/85 (28.2%)	23/85 (27.1%)	47/170 (27.6%)
Relapse type upon entry into trial			
Severe	52/85 (61.2%)	52/85 (61.2%)	104/170 (61.2%)
Non-severe	33/85 (38.8%)	33/85 (38.8%)	66/170 (38.8%)

RTX was superior to AZA in preventing disease relapse with a preliminary overall hazard ratio (HR) estimate of 0.36 (95% CI 0.23-0.57, p <0.001) and a during-treatment HR estimate of 0.30 (95% CI 0.15-0.60, p<0.001) (Figure 1). After adjustment, none of the randomization stratification covariates (ANCA type,

glucocorticoid induction regimen, or relapse severity) had a significant differential effect on the primary outcome. By 24 months after entry, 20 months after randomization, 11/85 (13%) patients in the RTX group had experienced a relapse compared to 32/85 (38%) patients in the AZA group. 19/85 (22%) patients in the RTX group and 31/85 (36%) patients in the AZA group experienced at least one severe adverse event (SAE). 25/85 (29%) and 42/85 (49%) patients in the RTX group developed hypogammaglobulinaemia (IgG <5g/l) and non-severe infections respectively, compared to 21/85 (25%) and 41/85 (48%) in the AZA group.

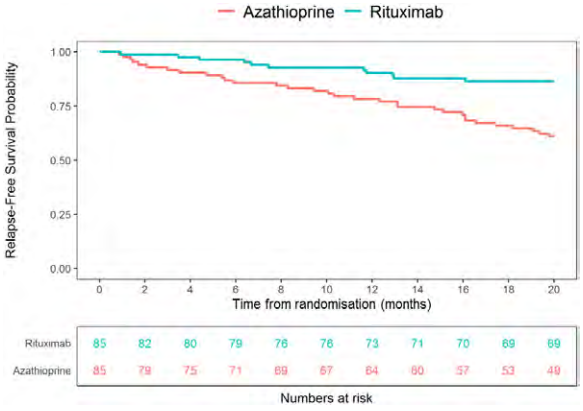


Figure 1. Relapse-free survival in RITAZAREM trial: rituximab versus azathioprine

Conclusion: In the RITAZAREM trial, following induction of remission with RTX, RTX was superior to AZA for preventing disease relapse in patients with AAV with a prior history of relapse. There were no new major safety signals for use of these medications in this population.

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OP0027 TIME TO FLARE AND GLUCOCORTICOID EXPOSURE IN PATIENTS WITH NEW-ONSET VERSUS RELAPSING GIANT CELL ARTERITIS TREATED WITH TOCILIZUMAB OR PLACEBO PLUS PREDNISONE TAPERING: 3-YEAR RESULTS FROM A RANDOMIZED CONTROLLED PHASE 3 TRIAL

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Background: In part 1 of the 52-week, double-blind GiACTA trial, tocilizumab (TCZ) every week (QW) or every other week (Q2W) + prednisone tapering reduced the risk for flare versus placebo (PBO) + 26-week prednisone tapering among patients with new-onset giant cell arteritis (GCA) at baseline. Among patients with relapsing GCA, TCZ QW but not Q2W + prednisone reduced the risk for flare versus both PBO groups, and there was separation in the time to flare between the TCZ QW and Q2W groups.[1]

Objectives: To report time to first flare and potential cumulative glucocorticoid (GC) sparing over 3 years of the GiACTA trial (part 1+2-year open-label part 2) among patients with new-onset or relapsing GCA.

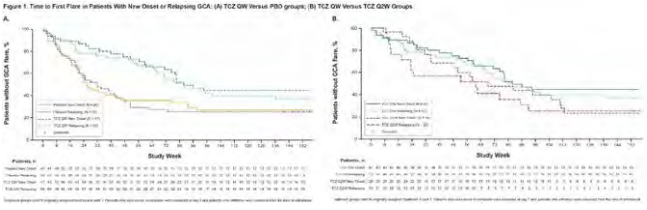
Methods: At the end of part 1, patients entered open-label part 2, in which GCA therapy (including initiation/termination of open-label TCZ and/or GCs) was given at the investigator's discretion according to disease status. Time to first GCA flare during the 3-year study period was assessed using Kaplan-Meier analysis for patients in the intention-to-treat population according to disease onset status at baseline (new-onset/relapsing) based on their originally assigned treatment groups: TCZ QW, TCZ Q2W, or pooled PBO (PBO+26-week and PBO+52-week prednisone taper).

Results: Among patients randomly assigned in part 1, 47 of 100 (47%) in the TCZ QW group, 26 of 49 (53%) in the TCZ Q2W group, and 46 of 101 (46%) in the pooled PBO group had new-onset GCA at baseline; the rest had relapsing GCA. Median time to first flare over 3 years was longer for patients assigned to TCZ treatment in part 1 than for patients assigned to PBO; Kaplan-Meier analysis showed a clear separation between the TCZ QW and the pooled PBO groups over 3 years for patients with new-onset and relapsing GCA (Figure 1A). Separation between the TCZ QW and TCZ Q2W groups was also observed over 3 years in patients with new-onset and relapsing GCA, although this was more evident in patients with relapsing GCA (Figure 1B). Higher proportions of patients in the TCZ QW group (new-onset, 49%; relapsing, 47%) than the pooled PBO group (new-onset, 28%; relapsing, 31%) and the TCZ Q2W group (new-onset, 27%; relapsing, 35%) remained flare-free during their entire treatment period. Cumulative prednisone dose over 3 years was lower for patients originally assigned to TCZ QW versus those originally assigned to PBO for patients with new-onset GCA and those with relapsing GCA at baseline (Figure 2).

Conclusion: In this 3-year analysis of GiACTA parts 1 and 2, time to first flare favored TCZ QW over TCZ Q2W in patients with new-onset and relapsing GCA. TCZ QW delayed time to first flare and resulted in lower cumulative GC exposure compared with PBO in patients with new-onset and relapsing GCA, supporting TCZ QW dosing in patients with GCA regardless of disease onset.

References:

[1] Stone JH et al. N Engl J Med 2017;377:317-28.



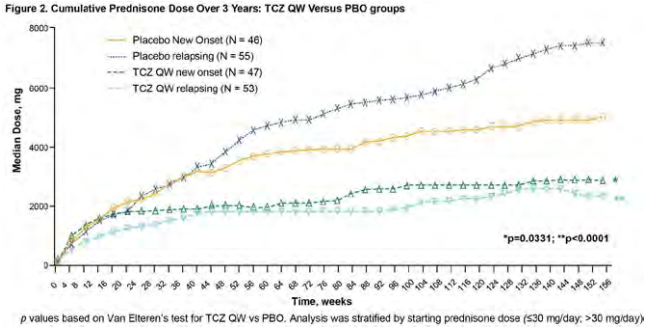


Figure 2. Cumulative Prednisone Dose Over 3 Years: TCZ QW Versus PBO groups

p values based on Van Elteren's test for TCZ QW vs PBO. Analysis was stratified by starting prednisone dose (≤30 mg/day; >30 mg/day)

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OP0028 EFFICACY OF APREMILAST FOR THE PAIN OF ORAL ULCERS ASSOCIATED WITH ACTIVE BEHÇET'S SYNDROME: 12-WEEK RESULTS FROM THE RANDOMIZED, PHASE III RELIEF STUDY

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Background: Oral ulcers (OU) associated with Behçet's syndrome are often painful, may interfere with the ability to eat and can negatively affect quality of life.[1,2] Apremilast (APR), an oral phosphodiesterase 4 inhibitor, demonstrated efficacy in the treatment of OU associated with Behçet's syndrome in a phase III, multicenter, randomized, double-blind, placebo (PBO)-controlled study (RELIEF; BCT-002).[3]

Objectives: To describe the efficacy of APR treatment in improving OU pain associated with Behçet's syndrome in RELIEF.

Methods: Patients were randomized (1:1) to APR 30 mg twice daily (APR 30 BID) or PBO twice daily for a 12-week PBO-controlled phase, followed by a 52-week active treatment extension. Eligible patients were ≥18 years of age and had active Behçet's syndrome with ≥3 OU at randomization or ≥2 OU at screening and randomization and without active major organ involvement. Clinical improvement in OU was evaluated by the area under the curve for the number of OU through Week 12 ($AUC_{Wk0\text{-}12}$; primary efficacy endpoint) and by assessments of OU number. Patient-reported OU pain was evaluated by the 100-mm visual analogue scale (VAS). The statistical tests were 2-sided (α=0.05). The proportions of patients achieving the minimal clinically important difference (MCID) and higher rates of improvement, defined as ≥10-mm,[4] ≥30-mm (3-fold MCID), ≥50-mm (5-fold MCID) improvements in OU pain VAS scores, respectively, were analyzed through Week 12. An ANCOVA model was used to analyze the primary endpoint and assessments of OU number and OU pain (VAS). The proportion of patients achieving improvement in OU pain VAS scores at Week 12 were summarized descriptively.

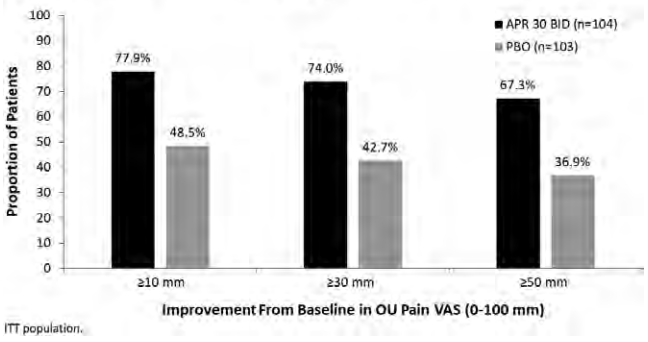
Results: A total of 207 patients were randomized and received ≥1 dose of study medication (APR: n=104; PBO: n=103). At baseline, the mean (SD) number of OU was 4.2 (3.7) in the APR 30 BID group and 3.9 (2.7) in the PBO group, and the mean (SD) OU pain VAS scores were 61.2 (27.6) and 60.8 (26.9), respectively. At Week 12, significantly greater improvements were observed with APR 30 BID vs. PBO in $AUC_{Wk0\text{-}12}$ (least-squares [LS] mean [SE]: 129.5 [15.9] vs. 222.1 [15.9]; P<0.0001), number of OU (LS mean [SE]: 1.1 [0.2] vs. 2.0 [0.3]; P=0.0003) and OU pain VAS scores (LS mean [SE] change from baseline: –40.7 [3.3] vs. –15.9 [3.3]; P<0.0001). The proportion of patients who achieved the MCID of ≥10-mm improvement in OU pain VAS scores at Week 12 was greater with APR 30 BID vs. PBO; this pattern was also observed for the higher 3- and 5-fold improvements in MCID (Figure 1). Greater proportions of APR 30 BID vs. PBO patients achieved ≥10-mm and ≥30-mm improvements in OU pain VAS scores over 12 weeks. Notably, greater achievement of ≥50-mm improvement in OU pain VAS scores was observed with APR 30 BID vs. PBO as early as Week 1 and maintained up to Week 12 (Figure 2).

Conclusion: For patients with active Behçet's syndrome, APR 30 BID provided significantly greater improvements vs. PBO in OU number and OU pain at Week 12, including the greater proportion of patients achieving MCID and 3- and 5-fold MCID of OU pain in the APR 30 BID group vs. the PBO group. These results indicate a clinically meaningful treatment effect of APR 30 BID on the OU associated with Behçet's syndrome.

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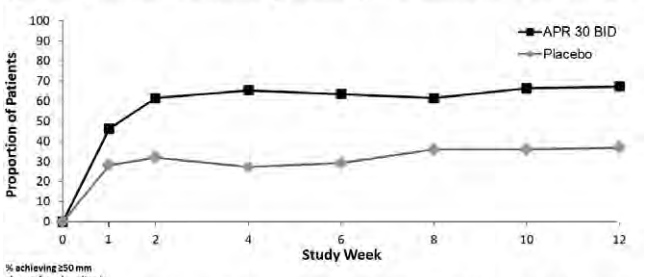
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Figure 1. Proportion of Patients Achieving Improvements in OU Pain VAS at Week 12



ITT population.

Figure 2. Proportion of Patients Achieving ≥50-mm Improvements in OU Pain VAS Over 12 Weeks



% achieving ≥50 mm change from baseline in VAS (0-100 mm), n (%)	Week 1	Week 2	Week 4	Week 6	Week 8	Week 10	Week 12
APR 30 (n=104)	48 (46.2)	64 (61.5)	68 (65.4)	68 (65.5)	64 (61.5)	69 (66.3)	70 (67.3)
PBO (n=103)	29 (28.2)	33 (32.0)	28 (27.2)	30 (29.1)	37 (35.9)	37 (36.9)	38 (36.9)

ITT population.

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OP0029

MAINTENANCE TREATMENT FOR ANCA-ASSOCIATED VASCULITIS IN REAL WORLD PRACTICE IN EUROPE – REALITY OF VASCULITIS REMISSION AND RELAPSE AND SIGNIFICANT BURDEN OF DISEASE

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Background: After successful remission induction, ANCA associated vasculitis (AAV) is a relapsing remitting long term condition and patients are at risk of organ damage from both active AAV and therapy in particular glucocorticoids (GC). The remission maintenance phase of AAV is critical for preventing relapse and ensuring organ protection.

Objectives: This retrospective study aimed to examine the definition of maintenance start, therapy used and clinical outcomes in patients managed in routine clinical practice.

Methods: 1478 AAV patients (France, Germany, Italy, Spain and UK) managed by 493 physicians (37% Rheumatologists) who completed induction therapy for organ or life threatening AAV and initiated maintenance therapy between 2014-16 were studied. Data were collected at the time maintenance was determined to begin by the physician and then at 6, 12, 18 and 36 months.

Results: 49% had granulomatosis with polyangiitis,; mean age 54.2 years with 56% male. 49% had incident AAV and 51% were studied from a relapse. 70% received cyclophosphamide and GC and 30% received rituximab and GC. Physicians defined time of the start of maintenance from induction treatment start with mean of 5.7 months on basis of fixed time point 40%, starting new drug for maintenance 26%, reaching full remission 26% and no specific criteria 8%. At this time 43% were in full remission vs 50% in partial and 7% refractory. Various maintenance regimes were used, 21% received rituximab (88% 6 monthly and 8% 12 monthly, 4% other) at varying planned doses 34% 1g, 40% 500mg and 23% 375mg/m2, 4% other regime. Remission rates varied, relapse of different severity still occurs and many patients experienced adverse events (AE) and infections with prolonged GC use being common.

At the most recent clinic review patients had been followed for a mean of 50.7 months – 6% had died, 38% had relapsed at least once, and 11% required renal replacement therapy. 54% had no vasculitis activity, 26% were ANCA positive

	Maintenance start	6 months	12 months	18 months	36 months
Remission full/partial %	43 / 50	59 / 38	67 / 30	72 / 25	74 / 22
Total relapse / major %		12/49	9 / 45	6/ 44	7 / 32
Receiving GC%	65	61	53	46	39
At least one AE %	66	52	48	43	42
At least one infection %	54	42	32	27	26

without active disease and 19% still experiencing active disease. 32% were still receiving GCs - 22% of them receiving > 5mg/ day. There was negative impact on functional status with 14% reducing working hours, 13% restricted social life, 6% leaving employment, 6% registered as disabled and 2% leaving full time education.
Conclusion: The start of maintenance treatment in AAV is variably defined but typically at 6 months after start of remission induction therapy. Achieving full remission and preventing relapse are still clinical problems and many patients require ongoing GC therapy to maintain remission. Infectious complications and adverse events are common and there is significant negative impact on patient functional status over time.
Disclosure of Interests: Peter Rutherford Shareholder of: Vifor Pharma, Employee of: Vifor Pharma, Baxter Healthcare, Dieter Götte Shareholder of: Vifor Pharma, Employee of: Vifor Pharma
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OP0030 GRANULOMATOSIS WITH POLYANGIITIS SUSTAINED REMISSION OFF-THERAPY: DATA FROM THE FRENCH VASCULITIS STUDY GROUP REGISTRY

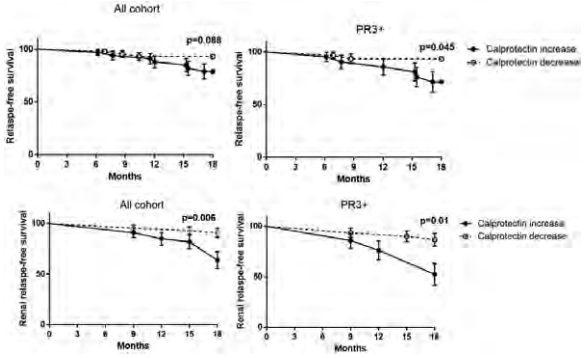
X. Puéchal[1], M. Iudici[2], C. Pagnoux[3], A. Karras[4], P. Cohen[1], F. Maurier[5], T. Quéméneur[6], F. Lifermann[7], M. Hamidou[8], L. Mouthon[1], B. Terrier[1], L. Guillevin[1]. *[1]Cochin Hospital, Paris, France; [2]University Hospitals, Geneva, Switzerland; [3]Mount Sinai Hospital,Toronto, Canada; [4]HEGP, Paris, France; [5]HP, Metz, France; [6]CH, Valenciennes, France; [7]CH, Dax, France; [8]CHU, Nantes, France*

Background: Data on granulomatosis with polyangiitis (GPA) sustained remission off-therapy (SROT) are limited and it is unknown whether disease characteristics or treatment regimen may affect it.
Objectives: This study aimed to assess SROT of GPA patients from the French Vasculitis Study Group registry, and identify factors associated with its occurrence and durability during follow-up.
Methods: GPA had to satisfy the 1990 ACR classification criteria and/or revised Chapel Hill Nomenclature for study inclusion. SROT was defined as remission (BVAS=0) without glucocorticoids (GC) or immunosuppressants (IS), the latter for ≥6 months (ie 2 consecutive visits). SROT and its duration were extracted from the database. Data from patients with 3-, 5- and 10-year SROT were analyzed. Baseline characteristics of patients with 3-year GPA SROT were compared to those of registry GPA patients with available data at 3 years but not in SROT (controls), and 3-year SROT achieving 5-year SROT vs those who relapsed between 3 & 5 years. Patients with 3-year GPA SROT follow-up +7 years were analyzed according to maintained SROT or not.
Results: Among 795 database patients with new-onset GPA, 259 achieved at least 1 SROT at some time during their disease, after a median [IQR] of 36 [28–63] months post-diagnosis. The first SROT lasted a median of 14 [I8-32] months. Among 202 of those patients who had follow-up, 73 (36%) remained in SROT for a median follow-up of 34 [14-45] months post-SROT. Among 434 (54%) patients followed for ≥3 years post-diagnosis, 82% had received GC and cyclophosphamide induction therapy. At 3 years post-diagnosis, 92 (21%) patients in SROT were compared to 342 (79%) controls who had relapsed or were still taking GC or IS. Patients achieving 3-year SROT vs controls, respectively, had more frequently received intravenous cyclophosphamide as induction therapy (89% vs 77%, P=0.01), with a higher median number of infusions (7.5 vs 6; P=0.05); no other clinical or biological baseline difference was found. Among those 92 3-year SROT patients, 74 had ≥2 years of additional follow-up: 46 (62%) attained 5-year SROT and 28 (38%) had relapsed after a mean follow-up of 13 months. Baseline clinical and biological characteristics of patients achieving 5-year SROT did not differ from those of 3-year SROT patients who relapsed. Among those 92 3-year SROT patients, 16 had ≥7 additional years of follow-up: 6 (38%) achieved 10-year SROT, ie 8% of 75 GPA with available data at 10 years, and 10 (63%) had relapsed a mean 35 ± 28 months after achieving 3-year SROT.
Conclusion: Only 8% of GPA patients achieved 10-year SROT after conventional induction and maintenance therapies. No baseline clinical or biological characteristics helped distinguish patients achieving or maintaining SROT and those who relapsed. However, patients achieving 3-year SROT had received more intensive induction therapy than those who relapsed or were still on GC or IS at 3 years.
Disclosure of Interests: None declared
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OP0031 AN INCREASE IN SERUM CALPROTECTIN LEVEL IN ANCA-ASSOCIATED VASCULITIDES PATIENTS DURING MAINTENANCE THERAPY IS ASSOCIATED WITH MORE RELAPSE AND ACCELERATED RENAL FUNCTION DECLINE

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Background: Calprotectin (S100A8/A9), a protein secreted by activated neutrophils and monocytes in inflammatory conditions, is upregulated in active ANCA-associated vasculitides. Serum calprotectin level variation during induction therapy is associated with disease relapse in PR3-ANCA-associated vasculitides (1). However, the place of this biomarker during maintenance therapy is unknown.
Objectives: To demonstrate whether variation in serum calprotectin level during maintenance therapy could be used as a biomarker predicting subsequent relapse in ANCA-associated vasculitides.
Methods: Patients with ANCA-associated vasculitides in complete remission (BVAS=0) after induction therapy with cyclophosphamide and included in the MAINRITSAN trial (2) were analyzed. Patients were randomized to receive rituximab or azathioprine as maintenance therapy. Relapse was defined as the re-occurrence or new onset of disease attributable to active vasculitis. Accelerated decline renal function (estimated Glomerular Filtration Rate (eGFR) assessed using the MDRD equation) was defined in concordance with NICE 2015 guideline (3) as "a decrease in eGFR of 25% or more and a change in GFR category or a sustained decrease in eGFR of 15 ml/min/1.73m^2 over 12 months". Calprotectin was assessed in the serum at inclusion and 6 months by ELISA (IDK® Calprotectin ELISA kit, Immunodiagnostik). We defined an increase in serum levels of calprotectin as a positive variation of calprotectin level at M6 compared to baseline.
Results: Of all, 96 patients (female 45.8%, mean age 55.3±13.5, 69.8% PR3+, 62.5% ANCA positive at inclusion) had at least a calprotectin dosage (86 at baseline, 86 at M6 and 76 patients at this 2 time-point). Calprotectin level at baseline or 6 months was not significantly different between relapsing patients and those without relapse after 18 months of follow-up, whereas the calprotectin variation at M6 compared to baseline was higher in relapsing patients (n=10) (mean (SD) 17991 (±28972) ng/ml) than in patients not experiencing any relapse (n=66) (9419 (±50002) ng/mL; p=0.03). An increase in serum calprotectin level at 6 months was significantly associated with an increased risk of relapse in PR3-ANCA patients (OR=5.6 (95%CI, 1.0-31.3; p=0,049) but not in the whole study group (OR=3.3 (95%CI, 0.8-14.1; p=0.1), and identified patients with accelerated renal function decline (all cohort: OR=10.6 (95%CI, 2.9-39.6; p=0.002; PR3+ patients: OR=5.909 (95%CI, 2.9-39.6; p=0.01)), whereas calprotectin level did not correlate with glomerular filtration rate (r = -0.07, p=0.35).
Conclusion: An increase in serum calprotectin during the first 6 months of maintenance therapy in ANCA-associated vasculitides is a useful biomarker predicting vasculitis relapse and accelerated renal function deterioration in the following 12 months.



Increase calprotectin serum at 6 months identify relapser and accelerated decline renal function at 1 year. Kaplan-Meier survival curves of ANCA-associated vasculitis patients with an increase in serum calprotectin at 6 months (solid line) or not (dotted line) remaining total relapse-free or accelerated decline renal function-free. Gehan-Beslow-Wilcoxon test.

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Disclosure of Interests: Xavier Romand Consultant of: Xavier ROMAND has received honorarium fees from Abbvie, Anais Courtier: None declared, Minh Vu Chuong Nguyen: None declared, Marie-Hélène Paclet: None declared, Philippe Gaudin Speakers bureau: Lilly, Loïc Guillevin: None declared, Benjamin Terrier: None declared, Athan Baillet Consultant of: Athan BAILLET has received honorarium fees from Abbvie for his participation as the coordinator of the systematic literature review
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OP0032 ERAP1-MEDIATED IMMUNOGENICITY AND IMMUNE-PHENOTYPES IN HLA-B51+ BEHÇET'S DISEASE POINT TO PATHOGENIC CD8 T CELL EFFECTOR RESPONSES

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Background: HLA-B51 is a definite risk factor for Behçet's disease (BD). A coding variant of ERAP1, Hap10 – with low peptide-trimming activity – vastly potentiates this risk, but is mechanistically unclear[1,2)].

Objectives: To test the hypothesis that low or absent ERAP1 activity alters CD8 T cell immunogenicity through changes in the HLA-B51 peptidome and shapes the CD8 T cell immune response in affected subjects.
Methods: We generated HLA-B51$^+$ ERAP1 KO LCL clones using CRISPR-Cas9, performed mass spectrometry of the immunoprecipitated MHC-class I peptidome with subsequent computational deconvolution for HLA-B51-binding peptides. We then assessed single cell (ICS), bulk (ELISA) and proliferative (CFSE) CD8 effector (IFNg, granzyme B, perforin) T cell responses through stimulation of allogeneic donor cells with WT vs KO LCL and determined ERAP1 haplotypes in 49 untreated Turkish BD subjects with ocular and/ or major vascular involvement as well as healthy donors (HD) whose PBMC were profiled using 6 multicolour flow cytometry panels.
Results: WT and KO peptidomes differed significantly ($p<0.0005$ Fisher's exact test) with a distinctive shift of peptide length frequencies exceeding 9-mer (binding optimum) in the KO vs WT. This held true for computationally deconvoluted HLA-B51 binders. IFNg secretion from CD8 T cells stimulated with KO LCL was significantly different from WT (ICS, $p=0.0006$; ELISA, $p=0.0059$) as were CD8 T cell proliferation and ICS of perforin/granzyme B$^+$ CD8 T cells. Analysis of 133 T, B, NK and monocyte cell populations revealed predominance of CD8 T and NKT cell subset in HLA-B51+/Hap10+ BD vs HLA-B51+/Hap10- BD and HD, accounting for 80% of all populations reaching significance ($p<0.05$, Mann-Whitney). Naive and effector memory CD8 T cell subsets were inversely correlated. Cohen's effect sizes were large (>0.8) or very large (>1.2).
Conclusion: We show that absence of functional ERAP1 alters human CD8 T cell immunogenicity. This is mediated by an HLA-class I peptidome with propensity for longer peptides above 9mer and suggests loss or de-novo presentation of peptide-HLA-B51 complexes to cognate CD8 TCR. The reciprocal changes in antigen- experienced vs naive CD8 T cell subsets in affected subjects point to biologic significance of HLA-B51/Hap10 in BD. Collectively, our findings suggest that an altered HLA-B51 peptidome modulates immunogenicity of CD8 effector T cells in ERAP1-Hap10 carriers with BD and identify targets for future drug development.
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OP0033 OPTIMIZATION OF TOCILIZUMAB THERAPY IN GIANT CELL ARTERITIS. A MULTICENTER REAL-LIFE STUDY OF 134 PATIENTS

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Background: Tocilizumab (TCZ) is the only biological agent approved in Giant Cell Arteritis (GCA). There is general agreement on the initial and the standard maintenance dose of TCZ. However, information on duration and optimization of TCZ in GCA is scarce.
Objectives: Our aim was to assess efficacy and safety of TCZ therapy optimization in an unselected wide series of GCA in clinical practice.
Methods: Multicenter study, 134 patients with GCA who received TCZ due to inefficacy/adverse events of previous therapy. Once complete remission was reached and based on a shared decision between patient and physician TCZ was optimized in some cases. Optimization was done by decreasing the dose and/or prolonging the TCZ dosing interval progressively.
Results: 134 GCA patients treated with TCZ (101w/33m); mean age 73.0±8.8 years. TCZ was administered IV to 106 (79.1%) patients and SC to 28 (20.9%). TCZ was optimized in 43 (32.1%) patients. No demographic, clinical manifestations or laboratory data differences had been found at TCZ onset (TABLE). After a follow up of 12 [6-15.5] months, and a complete remission for 6 [3-12] months; the first TCZ optimization was performed. Median prednisone dose at first TCZ optimization was 2.5 [0-5] mg/day. TCZ IV was optimized from 8 to 4 mg/kg/4weeks in 12 of 106 (11.3%) and from 162 mg/SC/week to 162 mg/SC/2weeks in 9 of 28 (32.1%) cases. Five (11.6%) of the 43 optimized cases relapsed. In 4 cases, the relapses were treated increasing TCZ up to the pre-optimization dose, in 1 case the route of administration was change (4 mg/kg/4week to 162 mg/SC/week). In 8 of 43 optimized patients (18.6%), it was possible to withdraw TCZ after complete remission for 30 [16.25-45.75] months. Regarding adverse events and severe infections were similar in both groups. The mean TCZ treatment costs were lower in the optimized group.
Conclusion: Once remission is reached in GCA patients under TCZ treatment, optimization of TCZ may be performed. Based on our experience it could be performed by reducing the dose with IV TCZ or by prolonging dosing interval with SC TCZ.
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TABLE

	OPTIMIZED-TCZ GROUP (n=43)	NON-OPTIMIZED TCZ GROUP (n=91)	p
BASAL FEATURES AT TCZ ONSET			
GENERAL FEATURES			
Age, years, mean± SD	68.9±8.7	71.4±8.5	0.125
Sex, female/male n(%)	32/10	68/24	0.779
Time from GCA diagnosis to TCZ onset (months), median [IQR]	19.5[7.75-45]	10.5[4 – 25]	0.047
SYSTEMIC MANIFESTATIONS			
Fever, n(%)	1(2.4)	8(8.7)	0.176
Constitutional syndrome, n(%)	11(26.2)	19(20.7)	0.476
PMR, n(%)	18(42.9)	56(60.9)	0.052
ISCHEMIC MANIFESTATIONS			
Visual involvement, n(%)	5(11.9)	23(25)	0.084
Headache, n(%)	26(61.9)	42(45.7)	0.081
Jaw claudication, n(%)	1(2.4)	11(12)	0.072
CORTICOSTEROIDS AT TCZ ONSET			
Prednisone dose, mg/d mean (SD)	15.1±11.1	25±17.4	0.001
FOLLOW-UP ON TCZ THERAPY (MONTHS), MEDIAN [IQR]	24[18-27]	6 [3-18]	0.000
Relapses, n(%)	5(11.6)	5(5.5)	0.207
End follow-up remission, n(%)	40(93)	84(92)	0.99
Severe side efects, n(%)	14(32.6)	22(24.2)	0.307
Seriuos infections, n(%)	6(14)	10(11)	0.878
Cost, (mean) euros per year			
IV	7 538.4	11 726.4	-
SC	7 329.0	11 726.4	-

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Lung diseases and other comorbidities in RA

OP0034 DOES THE RISK OF VENOUS THROMBOEMBOLISM VARY WITH DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS?

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Background: Patients with rheumatoid arthritis (RA) are at increased risk for venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE) (1). Several established risk factors of VTE, such as age, immobilization and comorbid conditions, occur more often patients with RA (2). In addition, inflammation may in itself also increase VTE risk by upregulating procoagolatory factors and causing endothelial damage (3). Recent reports indicate an increased risk of VTE in RA patients treated with JAK-inhibitors (4), pointing to the need to better understand how inflammation measured as clinical RA disease activity influences VTE risk.
Objectives: To investigate the relationship between clinical RA disease activity and incidence of VTE.
Methods: Patients with RA were identified from the Swedish Rheumatology Quality Register (SRQ) between July 1st 2006 and December 31st 2017. Clinical rheumatology data for these patients were obtained from the visits recorded in SRQ, and linked to national registers capturing data on VTE events and comorbid conditions. For each such rheumatologist visit, we defined a one-year period after the visit and determined whether a VTE event had occurred within this period or not. A visit followed by a VTE event was categorized as a case, all other visits were used as controls. Each patient could contribute to several visits. The DAS28 score registered at the visit was stratified into remission (0-2.5) vs. low (2.6-3.1), moderate (3.2-5.1) and high (>5.1) disease activity. Logistic regression with robust cluster standard errors was used to estimate the association between the DAS28 score and VTE.
Results: We identified 46,311 patients with RA who contributed data from 320,094 visits. Among these, 2,257 visits (0.7% of all visits) in 1345 unique individuals were followed by a VTE within the one-year window. Of these, 1391 were DVT events and 866 were PE events. Figure 1 displays the absolute probabilities of a VTE in this one-year window, and odds ratios for VTE by each DAS28 category, using DAS28 remission as reference. The one-year risk of a VTE increased from 0.5% in patients in DAS28 remission, to 1.1% in patients with DAS28 high disease activity (DAS28 above 5.1). The age- and sex-adjusted odds ratio for a VTE event in highly active RA compared to RA in remission was 2.12 (95% CI 1.80-2.47). A different analysis, in which each patient could only contribute to one visit, yielded similar results.

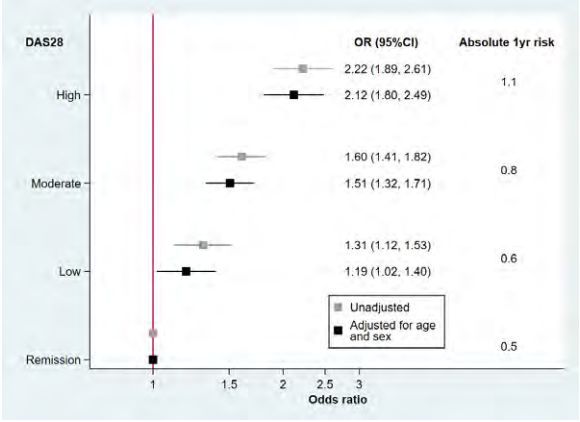


Figure 1. Odds ratios (OR) comparing the odds of VTE for DAS28 activity categories versus remission. Grey estimates are from unadjusted logistic regression models, black estimates are from logistic regression models adjusted for age and sex. Absolute one-year risk of VTE are estimated from unadjusted models.

Conclusion: This study demonstrates a strong association between clinical RA inflammatory activity as measured through DAS28 and risk of VTE. Among patients with high disease activity one in a hundred will develop a VTE within the coming year. These findings highlight the need for proper VTE risk assessment in patients with active RA, and confirm that patients with highly active RA, such as those recruited to trials for treatment with new drugs, are already at particularly elevated risk of VTE.
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OP0035 EXAMINATION OF INTERSTITIAL LUNG DISEASE IN PATIENTS WITH RHEUMATOID ARTHRITIS – PREVALENCE, TIME TO ONSET, AND CLINICAL CHARACTERISTICS

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Background: Interstitial lung disease (ILD) is a known extraarticular manifestation of rheumatoid arthritis (RA). Previous studies have shown variability in the prevalence of RA-ILD, as well as clinical characteristics and risk factors of RA-ILD.
Objectives: To evaluate the prevalence and time to onset of ILD and compare the clinical characteristics between RA patients (pts) with or without ILD using a large US electronic medical record (EMR)-based dataset.
Methods: Pts with an initial RA diagnosis (ICD-9-CM code: 714.0; ICD-10-CM codes: M05 & M06) during the study period (01JAN2009-20SEP2019) were included from the Discus Analytics JointMan database. The initial RA diagnosis date was defined as the index date. Pts with ILD were identified by ICD diagnosis codes or by provider indication in the JointMan record. Pts who developed ILD before RA were excluded from this analysis. The prevalence and time to onset of ILD were reported. Pt demographics, comorbidities, RA characteristics and disease activity scores were compared for 6 months prior to or on the index date (baseline period) for selected adult RA pts with available information.
Results: Among 8,963 identified RA pts, 337 (3.8%) were diagnosed with ILD on or after RA diagnosis. The median time to ILD onset post-RA was 2.3 years, and 47% had ILD within 2 years after RA diagnosis. RA-ILD pts were significantly older than those without ILD (65.8 years vs. 59.1 years; p<0.001; Table 1). At baseline, a higher percentage of RA-ILD pts had history of chronic obstructive pulmonary disease, positive rheumatoid factor, rheumatoid nodules, erosive joint disease, positive anti-cyclic citrullinated peptide antibody, and joint swelling compared to RA-only pts (Table 2). The mean ESR and RA disease activity scores were also significantly higher for RA-ILD pts.

Table 1. Patient Demographics

Patient demographics	RA-ONLY COhort (N = 5,612)	RA-ild coHORT (N = 205)	P-value
Age, Mean ± SD, years	59.1 ± 14.2	65.8 ± 11.8	**<.001**
Male, N (%)	1,375 (24.5%)	72 (35.1%)	**0.001**
Race, N (%)			
White	4,014 (71.5%)	165 (80.5%)	**0.005**
African American	365 (6.5%)	9 (4.4%)	0.226
Other/Missing	1,233 (22.0%)	31 (15.1%)	**0.020**

Table 2. Baseline Clinical Characteristics

Clinical Characteristics	RA-ONLY COhort (N = 3,846)	RA-ild coHORT (N = 115)	P-value
History of Chronic Obstructive Pulmonary Disease, N (%)	102 (2.7%)	8 (7.0%)	**0.006**
Hypertension, N (%)	900 (23.4%)	23 (20.0%)	0.395
Serious Infection, N (%)	38 (1.0%)	3 (2.6%)	0.091
Rheumatoid Factor Positive, N (%)	1,388 (36.1%)	69 (60.0%)	**<.001**
Joint Stiffness, N (%)	1,092 (28.4%)	39 (33.9%)	0.197
Rheumatoid Nodules, N (%)	153 (4.0%)	17 (14.8%)	**<.001**
Erosive Joint Disease, N (%)	459 (11.9%)	23 (20.0%)	**0.009**
Anti-CCP Antibody Positive, N (%)	858 (22.3%)	45 (39.1%)	**<.001**
Joint Swelling*, N (%)	2,861 (58.0%)	123 (68.0%)	**0.008**
Joint Tenderness*, N (%)	3,728 (75.6%)	138 (76.2%)	0.851
ESR**, Mean ± SD, mm/hr	22.0 ± 22.6	30.1 ± 25.5	**<.001**
CRP**, Mean ± SD, mg/L	22.5 ± 13.0	60.6 ± 25.0	0.086
CDAI, Mean ± SD	16.4 ± 12.3	18.9 ± 15.7	**0.044**
DAS28-CRP, Mean ± SD	2.6 ± 1.2	3.1 ± 1.4	**<.001**
DAS28-ESR, Mean ± SD	3.3 ± 1.4	3.9 ± 1.5	**<.001**
SDAI, Mean ± SD	20.2 ± 29.3	28.6 ± 40.2	**0.048**

* A total of 4,929 non-ILD and 181 ILD patients had joint swelling and tenderness data.
** Variables were calculated among patients who had available information.

Conclusion: This large real-world RA population provides insight into the burden of ILD in RA pts. Pts with ILD had a higher proportion of comorbidities and RA-related conditions and higher RA activity. Further analysis is warranted to assess the risk factors of ILD and its prognosis.
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Employee of: I am a paid employee of Discus Analytics., Yuexi Wang Consultant of: I am a paid employee of STATinMED Research which is a paid consultant to Bristol-Myers Squibb Company., Cynthia Gutierrez Consultant of: I am a paid employee of STATinMED Research which is a paid consultant to Bristol-Myers Squibb Company., Ding He Consultant of: I am a paid employee of STATinMED Research which is a paid consultant to Bristol-Myers Squibb Company., Lin Xie Consultant of: I am a paid employee of STATinMED Research which is a paid consultant to Bristol-Myers Squibb Company., Sonie Lama Shareholder of: I own shares of Bristol-Myers Squibb Company., Employee of: I am a paid employee of Bristol-Myers Squibb Company., Gary Craig Consultant of: I have served as a consultant to Bristol-Myers Squibb Company., Employee of: I am a paid employee of Arthritis Northwest and VP of Discus Analytics., Speakers bureau: I am a member of the speakers bureau for Bristol-Myers Squibb Company.

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OP0036 METHOTREXATE AND RHEUMATOID ARTHRITIS ASSOCIATED INTERSTITIAL LUNG DISEASE

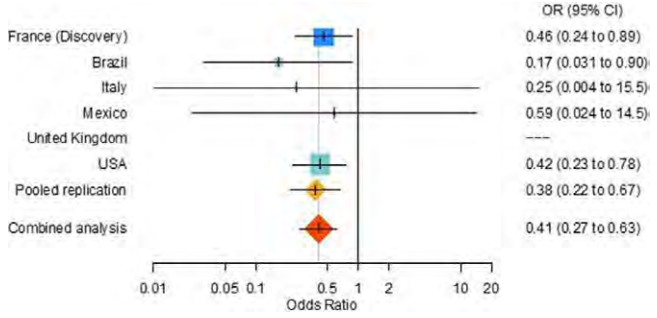
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Background: Methotrexate (MTX) is a key anchor drug for rheumatoid arthritis (RA) management. Its use has been associated with hypersensitivity pneumonitis and diffuse lung disease. Whether MTX exposure increases the risk of interstitial lung disease (ILD) in patients with RA is disputed.

Objectives: We aimed to evaluate the association of antecedent MTX use with development of RA-ILD.

Methods: Through a case-control study design with derivation and international validation samples, we examined the association of MTX exposure with ILD in 482 patients with RA-ILD and 741 patients with RA without ILD. Estimates were pooled over the different samples using meta-analysis techniques.

Results: Analysis of the derivation sample revealed an inverse relationship between MTX exposure and RA-ILD (adjusted odds ratio [OR], 0.48; 95% confidence interval [CI], 0.25 to 0.92; P=0.028), which was confirmed in the validation samples (pooled adjusted OR, 0.39; 95% CI, 0.23 to 0.68; P<0.001). The combined estimate using both the derivation and validation samples revealed an adjusted OR of 0.43 (95% CI, 0.28 to 0.65; P<0.0001). MTX ever users were less frequent among patients with RA-ILD compared to those without ILD, irrespective of chest high resolution computed tomography pattern. In patients with RA-ILD, ILD onset was significantly delayed in MTX ever users compared to never users (11.5 ± 10.6 years and 3.7 ± 7.1 years, respectively; P<0.001).



Conclusion: Our results suggest that MTX is not a risk factor for RA-ILD and support a possible disease modifying effect of MTX on development of RA-ILD.

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OP0037 NON–ANTI-TNF BIOLOGIC AGENTS ARE ASSOCIATED WITH LESS MARKED PROGRESSION OF INTERSTITIAL LUNG DISEASE SECONDARY TO RHEUMATOID ARTHRITIS

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Background:

Objectives: To analyze the effect of disease-modifying antirheumatic drugs (DMARDs) on the outcome of interstitial lung disease secondary to rheumatoid arthritis (ILD-RA).

Methods: We performed a multicenter, prospective, observational study of patients with ILD-RA receiving DMARDs between 2015 and 2017. The patients were assessed using high-resolution computed tomography and lung function tests at baseline and at 24 months. The radiological assessment was centralized. The main outcome measure at 24 months was change in lung function (improvement, non-progression, progression, or death). We recorded the 28-joint Disease Activity Score 28 (DAS28) and adverse events. A logistic regression analysis was performed to identify factors associated with progression of ILD.

Results: We included 70 patients with ILD-RA treated with DMARDs. The main baseline characteristics are shown in Table 1. After 24 months, lung disease did not progress in 40 patients (57.1%), improved in 8 (11.4%), and progressed in 21 (30.0%). One patient (1.4%) died. The factors associated with progression of ILD in the multivariate analysis were treatment with abatacept, tocilizumab, or rituximab (OR, 0.102 [95%CI, 0.015-0.686]), DAS28 (OR, 1.969 [95%CI, 1.005-3.857]), and smoking (OR, 6.937 [95%CI, 1.378-4.900]). During follow-up, 30 patients (42.9%) experienced an adverse event, which was severe in 12 cases (17.1%).

Conclusion: Lung function is stable and inflammatory activity well controlled in most patients with ILD-RA receiving treatment with DMARDs. Non–anti-TNF DMARDs reduce the risk of progression of lung disease in 90% of patients, whereas the inflammatory activity of RA and smoking are associated with progression.

Table:

Variable	Patients=70
Epidemiological characteristics	
Female sex, n (%)	39 (55.7)
Age, y, mean (SD)	68.8 (7.8)
Clinical-laboratory characteristics	
Smoking history	
Never smoked, n (%)	23 (32.9)
Smoked, n (%)	47 (67.1)
Time since diagnosis of RA, (months), **mean (SD)**	161.0 (125.9)
Diagnostic delay, (months), **median (IQR)**	12.0 (5.9-24.0)
Time since diagnosis of ILD, (months), **mean (SD)**	42.3 (48.3)
Positive rheumatoid factor (>10), n (%)	65 (92.0)
Anticitrullinated protein antibody (>20), n (%)	58 (82.9)
Synthetic DMARDs	64 (91.4)
Methotrexate, n (%)	30 (42.9)
Leflunomide, n (%)	16 (22.9)
Sulfasalazine, n (%)	8 (11.4)
Hydroxychloroquine, n (%)	10 (14.3)
Biologic DMARDs	27 (38.1)
Infliximab, n (%)	1 (1.4)
Etanercept, n (%)	4 (5.7)
Adalimumab, n (%)	1 (1.4)
Golimumab, n (%)	1 (1.4)
Certolizumab, n (%)	0 (0.0)
Tocilizumab, n (%)	5 (6.2)
Abatacept, n (%)	5 (6.2)
Rituximab, n (%)	10 (14.3)
Other immunosuppressants	
Mycophenolate, n (%)	4 (5.7)
Azathioprine, n (%)	1 (1.4)

Disclosure of Interests: None declared
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OP0038

IMPROVING RISK-STRATIFICATION OF RHEUMATOID ARTHRITIS PATIENTS FOR INTERSTITIAL LUNG DISEASE

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Background: Interstitial lung disease (ILD) is the most common pulmonary manifestation of rheumatoid arthritis (RA). It has emerged in recent series as a key prognostic factor including survival. The big challenge for rheumatologists is now the risk-stratification of RA patients for ILD. Chest high-resolution computed tomography (HRCT) is the gold standard for RA-ILD diagnosis, but costs and ionizing radiation may limit its use in clinical practice. Thus, circulating biomarkers could aid in this risk-stratification.
Objectives: to evaluate the merit of 3 circulating markers for the diagnosis and the progression of RA-ILD.
Methods: We included consecutive patients with RA, >18 years of age, from 3 tertiary rheumatology centers (Paris, France, Tokyo, Japan and Zurich, Switzerland) over a 36-month period. All patients had at least one chest HRCT during the inclusion period. In the subset of French patients with ILD, HRCT lung images were obtained both at baseline (time of blood sample collection) and at a follow-up visit. The ILD status of patients with RA was established by chest HRCT. The chest HRCT pattern was classified as usual interstitial pneumonia, UIP or non-specific interstitial pneumonia, NSIP, by the local radiologist. Serum levels of *lung epithelial-derived surfactant protein D*, SDP, CCL-18 et *Krebs von den Lungen-6 glycoprotein*, KL-6 were measured by ELISA.
Results: 147 patients were included (age: 66+/-12 ans, 69% of women, disease duration 11+/-10 years). Among these patients, 40 (27%) had fibrosing ILD on HRCT: 21 had a UIP pattern, 17 a NSIP pattern, and 2 had NSIP associated with chronic obstructive pulmonary disease.
SPD (21.91+/-2.17 *vs.* 15.76+/-1.34 ng/mL, p=0.017) CCL18 (102+/-13 *vs.* 78+/-5 ng/mL, p=0.026) and KL6 (961+/-128 *vs.* 376+/-26 U/mL, p<0.001) concentrations (Figure 1**A-C**) were significantly higher in patients with RA-ILD *vs.* unaffected RA patients. KL6 values were also higher in patients with UIP compared to the other HRCT patterns and in patients with lesion extension> 15% as compared to patients with milder disease. ROC curve analysis to assess the diagnostic abilities of the three markers for the diagnosis of RA-ILD showed a superiority of KL-6 (Area under the curve, AUC: 0.79 95% CI 0.72-0.86) compared to SPD (AUC: 0.66 95% CI 0.58-0.74) and CCL18 (AUC: 0.62, 95% CI 0.53-0.70) (Figure 1**D**). The sensitivity of KL-6 for the diagnosis of RA-ILD was 68% with a specificity of 83%. In the French subset with longitudinal data (n=15), extension of ILD was detected on 7 patients. Baseline KL6 serum levels were significantly increased in patients who experienced ILD progression (1987+/-1294 vs. 799+/-375 U/mL, p=0.027) (Figure 1**E**). The degree of ILD progression on HRCT was also proportional to baseline KL-6 concentrations (Figure 1**F**).
Conclusion: KL-6 is relevant for the diagnosis and the prognosis of RA-ILD. It may be used as a circulating non-invasive first-line marker to stratify for indication of HRCT. Indeed, given the emerging lung issues in RA patients, this simple and highly reproducible marker, which is already available in routine care in some countries, could be a good prerequisite to chest HRCT in rheumatology clinics.

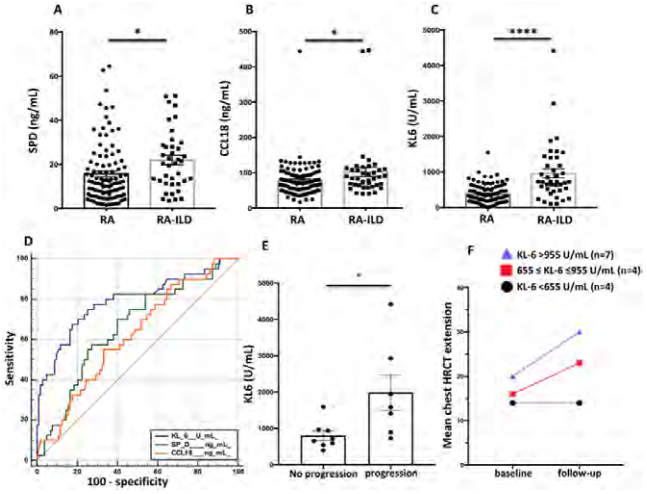


Figure 1A-F. Concentrations of serum markers, diagnostic value and performance of KL-6 for the progression of rheumatoid arthritis-associated interstitial lung disease A-C, Concentrations of SPD (ng/mL) (A), CCL18 (ng/mL) (B) and KL-6 (U/mL) (C) in patients with with or without RA-associated ILD. **D,** ROC curve illustrating the diagnostic value of SPD, CCL18 and KL-6 for diagnosis of RA-ILD. **E,** Concentrations of KL-6 (U/mL) according to the progression on chest HRCT of RA-ILD. **F,** Degree of mean ILD progression on chest HRCT according to baseline KL-6 concentrations. *p<0.05 and **** p <0.0001 by Student's t test

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OP0039

HOSPITALIZATION AND MORTALITY OUTCOMES IN RHEUMATOID ARTHRITIS PATIENTS WITH LUNG DISEASE

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Background: Pulmonary manifestations such as interstitial lung disease (ILD) and chronic obstructive pulmonary disease (COPD) are frequent extra-articular features that carry a poor prognosis in rheumatoid arthritis (RA). Prior studies have demonstrated that respiratory-related mortality is the most overrepresented cause of death in RA.

Objectives: To assess the risk of all-cause and respiratory-related hospitalization and mortality in RA patients with comorbid lung disease (LD) in comparison to those without and the differential risks associated with DMARD treatments.
Methods: Eligible RA patients included those enrolled in the Forward Databank with ≥1 year observation after 2000 and had initiated a DMARD. Forward is a large longitudinal rheumatic disease registry in the US. RA patients' diagnoses were rheumatologist-confirmed, and every 6 months participants completed comprehensive questionnaires regarding symptoms, disease outcomes, medications, and clinical events. LD was defined as one of the following: emphysema, asthma, bronchitis, COPD, pleural effusion, fibrosis of the lung, "RA lung", or ILD (England 2019). DMARDs were categorized hierarchically into four groups: csDMARDs, TNFi and NTNFi (bDMARDs), and tsDMARDs. Patients were followed from DMARD initiation until event (death and/or hospitalization) or end of follow-up, whatever came first. Events were validated using medical records and the US National Death Index. Respiratory hospitalizations and deaths were identified with ICD9 (460-519). Events were analyzed using incidence rates (IR) and Cox regression models. Models were adjusted for LD, DMARDs, age, sex, education, HAQ disability, Rheumatic Disease comorbidity index, smoking, pain, glucocorticoids, year of entry, prior bDMARDs and csDMARDs counts and MRC breath scale.
Results: Of the 21,525 eligible RA patients, 13.8% had LD at the time of DMARD initiation. Patients had 59 years old in both groups and 15% were male for LD+ vs 21% for LD-. Patients with LD+ showed worse disease outcomes (HAQ: 1.3 (0.7) vs 1.0 (0.7)) and comorbidities (2.9 (1.9) vs 1.5 (1.4)) overall and for all treatment groups, especially for NTNFi and tsDMARDi. The overall IR of any all-cause or respiratory-related events were higher in LD+ than LD- RA patients and across any DMARD treatments, with NTNFi having higher IR (Figure). In survival analyses, LD+ was associated with an increased risk for all-cause hospitalizations/deaths (HR 1.3; 95% CI 1.1-1.4) and a 3.95-fold increased risk of respiratory-related events (HR 4.0; 3.2-4.9) (Table). These risks did not differ significantly across DMARD treatment groups. Increased age, HAQ disability, comorbidities, glucocorticoids, prior bDMARDs and worse MRC breath scales were associated with an increased risk in both outcomes and smoking in respiratory-specific events.
Conclusion: An increased risk of hospitalizations and/or deaths was demonstrated for RA patients with lung disease, most notably a 4-fold increased risk for respiratory-related events. No differences were found between incident DMARD groups. Additional studies accounting for channeling of treatments by baseline health status are needed.
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[1] England BR, et al *Arth Care Res*. doi:10.1002/acr.24043.

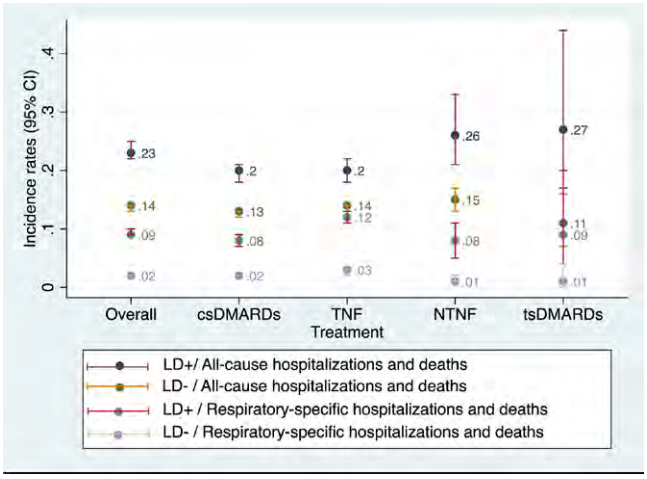


Figure. IR (95% CI): all-cause and respiratory-related events by LD+/LD- and DMARDs

Table. HR (95% CI) for Cox models.

Variables	All cause	All respiratory specific
LD+ vs LD-	1.3 (1.1 - 1.4)	4.0 (3.2 - 4.9)
Tnf vs csDMARD	1.0 (0.8 - 1.1)	1.1 (0.8 - 1.5)
NTNF vs csDMARD	1.0 (0.8 - 1.2)	0.9 (0.6 - 1.5)
tsDMARD vs csDMARD	0.8 (0.4 - 1.4)	1.8 (0.7 - 4.7)

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OP0040

ANTI-CITRULLINATED PROTEIN AUTOANTIBODIES ARE ASSOCIATED WITH ONGOING SYSTEMIC BONE LOSS IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS TREATED ACCORDING TO THE PRINCIPLES OF TREAT-TO-TARGET AND TIGHT-CONTROL

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Background: Anti-citrullinated protein antibodies (ACPA) are a major risk factor for local and systemic bone loss in patients with rheumatoid arthritis (RA). We previously demonstrated that early RA patients at disease presentation already show reduced systemic bone mineral density (BMD) in association with ACPA-positivity (1). Whether the negative impact of ACPA on bone continues over time despite treatment institution is however unknown.
Objectives: To investigate longitudinally the course of systemic bone loss in patients with early RA after institution of treatment with disease modifying anti-rheumatic drugs (DMARDs) according to the principles of treat-to-target and tight-control.
Methods: The study population included 100 consecutive early RA patients (<12 months of symptoms) recruited at our Early Arthritis inception cohort and already evaluated for systemic BMD at disease presentation before treatment start (1). After diagnosis, patients were prospectively followed-up at three-months intervals upon initiation of therapy with conventional synthetic DMARDs (methotrexate in 85% of the cases) aimed at the achievement of low disease activity (LDA, 28-joints disease activity score [DAS28] <3.2). BMD was re-assessed after 24 months at the lumbar spine (L1-L4) and hip by the same dual X-ray absorptiometry (DXA) equipment used at baseline. Differences in BMD from baseline were evaluated in relation to demographic and clinical variables (listed in Table 1).

Table 1. Predictors of bone mineral density changes over 24 months

	% change in BMD					
	lumbar spine		total hip		femoral neck	
	r	p	r	p	r	p
Age	0.269	0.008	0.069	0.50	0.258	0.01
female gender	0.085	0.42	-0.023	0.54	-0.121	0.23
menopause	0.137	0.20	0.067	0.53	0.087	0.41
disease duration	0.074	0.47	0.044	0.67	0.016	0.87
cumulative DAS28	0.018	0.86	0.002	0.87	0.011	0.91
time to LDA	0.142	0.16	-0.023	0.76	-0.044	0.66
time to remission	0.035	0.74	-0.002	0.97	-0.011	0.91
ACPA	-0.251	0.01	0.126	0.22	-0.130	0.04
RF	-0.113	0.27	0.111	0.28	0.001	0.99
months of bisphosphonates	0.368	0.003	0.171	0.09	0.291	0.04
cumulative steroids	-0.143	0.16	-0.007	0.78	-0.009	0.93
months of bDMARDs	-0.163	0.11	-0.054	0.48	-0.063	0.54

Results: The study population was mainly composed of females (84%), of whom 64.3% were in post-menopause; the mean (SD) age was 57.4 (13.5) years. Median (IQR) symptoms duration before treatment start was 14 (9-24) weeks. Fourty-three percent of the patients was ACPA positive. After 24 months of treatment, LDA was achieved in 79% of the cases, and remission in 46%; 17.7% of the patients had initiated a biological DMARD. At DXA re-scanning, the BMD at the lumbar spine and total hip remained largely unchanged, whilst at the femoral neck decreased from 0.726 g/cm2 to 0.713 g/cm2 (mean difference [SD] -0.013 [0.056], p=0.02). Predictors of BMD changes at different sites are shown in Table 1. The cumulative dose of prednisone was borderline significant for more BMD loss at the lumbar spine. Cumulative disease activity did not significantly affect BMD changes. Rather, ACPA-positive patients had higher percent changes at both the lumbar spine and the femoral neck. In multivariable analyses, ACPA remained associated with more BMD loss even when adjusting for confounders (age, gender, cumulative steroids, bisphosphonate treatment) (r -0.126, p=0.04 at the lumbar spine; r -0.126, p=0.04 at the femoral neck).
Conclusion: Treatment of patients with early RA according to treat-to-target strategies prevents systemic bone loss. However, despite optimal disease control, ACPA positivity continues to be associated with progressive decline in systemic BMD.

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[1] Bugatti S et al. Arthritis Res Ther 2016;18:226.
Disclosure of Interests: Laura Bogliolo: None declared, Francesca Motta: None declared, Paolo Del Vino: None declared, Carlomaurizio Montecucco: None declared, Serena Bugatti Speakers bureau: Bristol-Myers Squibb, Sanofi, Lilly, Novartis, Pfizer, Abbvie
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Pathogenic insights transforming the treatment of Sjögren's and SLE 2020 and beyond

OP0042 THE TRANSCRIPTOME OF PAIRED MINOR AND MAJOR SALIVARY GLAND TISSUE IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME: TWO OF A KIND?

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Background: In patients with primary Sjögren's syndrome (pSS), both minor and major salivary glands are targets of the disease. Infiltration of salivary glands by immune cells is characteristic for pSS. However, significant inter- and intra-individual variation exists in the size and composition of the infiltrates. Potential differences between minor and major salivary glands in immune cell presence and inflammatory pathway activation are unclear. This knowledge is essential for clinical trial design and precision therapy.
Objectives: To compare the transcriptome of paired labial and parotid salivary gland tissue of patients with pSS and non-SS sicca controls.
Methods: Thirty-nine pSS patients and 20 age- and sex-matched non-SS sicca controls, who participated in a prospective diagnostic cohort[1], were included. All pSS patients fulfilled 2016 ACR-EULAR criteria. RNA was isolated from formalin-fixed, paraffin-embedded labial and parotid gland tissue sections from the same individuals. Complementary DNA libraries were prepared and sequenced. Biopsies with evidence of sclerosing chronic sialoadenitis or mucosa-associated lymphoid tissue lymphoma were excluded in the current analysis. For differential gene expression analysis, patients were subdivided in four categories: I) non-SS sicca without lymphocytic infiltration, II) non-SS sicca with aspecific infiltration, III) pSS with negative biopsy (focus score<1), IV) pSS with positive biopsy (focus score≥1). For each differentially expressed gene (DEG), a false detection rate (FDR) was calculated. FDR<0.05 was considered significant.
Results: Principal component analysis (PCA) showed that only pSS patients with a positive biopsy (group IV) could be separated from the non-SS sicca patients based on gene expression. When comparing the labial and parotid gland transcriptome, resp. 798 and 1461 DEGs (FDR-adjusted p-value<0.05, log2 fold change >1) were identified between groups I and IV. The top differentially regulated genes were mostly related to T and B cells. *CXCL13, CCR6, MS4A1* (CD20)*, FCRL4* and *DAZL* were among the genes with the highest positive fold change in both glands of biopsy-positive pSS patients. Overall, there was a moderate to strong correlation between fold changes in labial and parotid glands (R^2=0.58, p-value<0.0001). Between biopsy-negative and biopsy-positive pSS (groups III and IV), 226 and 962 DEGs were identified for labial and parotid gland tissue, respectively. Interestingly, we could not identify DEGs between biopsy-negative pSS (group III) and non-SS sicca patients (group I).
Conclusion: The transcriptome of labial and parotid gland tissue from pSS patients with a positive biopsy is overall comparable, while salivary gland tissue from biopsy-negative pSS patients shows a comparable gene expression profile to non-SS sicca controls. These results indicate that different treatment strategies may be necessary for biopsy-negative and biopsy-positive pSS patients.
References:
[1] van Nimwegen JF, *et al.* Validation of the ACR-EULAR criteria for primary Sjögren's syndrome in a Dutch prospective diagnostic cohort. *Rheumatology (Oxford)* 2018;**57**:818–25.
Disclosure of Interests: Gwenny M. Verstappen: None declared, Lu Gao Employee of: BMS, Sarah A. Pringle: None declared, Silvia C. Liefers: None declared, Bert van der Vegt Consultant of: Advisory board member for Philips and Visiopharm., Vishal Patel Employee of: BMS, Sarah Hu Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Sumanta Mukherjee Employee of: BMS, Arjan Vissink: None declared, Hendrika Bootsma Grant/research support from: Unrestricted grants from Bristol-Myers Squibb and Roche, Consultant of: Consultant for Bristol-Myers Squibb, Roche, Novartis, Medimmune, Union Chimique Belge, Speakers bureau: Speaker for Bristol-Myers Squibb and Novartis., Frans G.M. Kroese Grant/research support from: Unrestricted grant from Bristol-Myers Squibb, Consultant of: Consultant for Bristol-Myers Squibb, Speakers bureau: Speaker for Bristol-Myers Squibb, Roche and Janssen-Cilag
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OP0043 RENAL TUBULAR COMPLEMENT C9 DEPOSITION IS ASSOCIATED WITH RENAL TUBULAR DAMAGE AND FIBROSIS IN LUPUS NEPHRITIS

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Background: Tubulointerstitial damage in lupus nephritis (LN) is a strong predictor of progression to chronic kidney disease and end stage renal disease (ESRD). While prior studies showed complement activation mediates glomerular injury (1), the role of complement in renal tubular damage has not been evaluated.
Objectives: To investigate the association between complement activation and tubulointerstitial fibrosis. Specifically, to study the role of tubular complement C9 deposition as a marker of tubular damage and fibrosis in LN.
Methods: LN biopsies stored in the pathology department between July 2014 to July 2016 were evaluated. Chromogenic immunohistochemistry was performed on formalin-fixed, paraffin-embedded, 4-µm human renal biopsy sections using unconjugated, murine anti-human Complement C9 (Hycult Biotech, clone X197) as a marker of the terminal complement activation. C3 glomerulopathy was used as a positive control, and normal kidney from resected tumor served as a negative control. Tubular basement membrane C9 staining intensity were analyzed on a semi-quantitative scale from 0 to 3 by a renal pathologist. The degree of Interstitial fibrosis/tubular atrophy was categorized as low (0–10%), medium (11–20%), or high (≥21%). Clinical parameters were assessed at the time of biopsy and 6 months post biopsy.
Results: Renal biopsies from 30 LN were studied, 23 (77%) of which had proliferative LN (Table). There were 24 (80%) women, mean (SD) age 33 (12) years. Positive tubular C9 staining (C9+) was observed in 7 (23%) biopsies. There was no significant difference in eGFR at renal biopsy between the two groups. At the time of renal biopsy, C9+ patients had significantly higher proteinuria, compared to C9- patients: median (IQR) 6.2g (3.3-13.1) vs. 2.4g (1.3-4.6), p<0.01. The differences persisted at 6 months after induction therapy with cyclophosphamide, cellcept or clinical trial drug: 1.08g (1.0-8.3) in C9+ vs. 0.68g (0.2-2.1) in C9- patients, p=0.06 Tubular C9 deposition was associated with interstitial fibrosis: 3 out of 7 (42.9%) had severe interstitial fibrosis vs. none in the C9- group, p=<0.01. Higher proportion of C9+ patients had moderate NIH Chronicity index: 3 out of 7 (42.9%) vs 2 out of 23 (8.7%) in the C9- group, p=0.07.
Conclusion: Tubular C9 deposition is significantly associated with proteinuria, interstitial fibrosis and increased chronicity which predict progression to ESRD and mortality. Complement activation in the tubules may be linked to proteinuria and more studies are needed to elucidate its mechanism in tubulointerstitial damage in LN.

Table. Comparisons of C9+ and C9- biopsies

	Positive for Tubular C9 (n = 7)	Negative for Tubular C9 (n = 23)	P- Value
eGFR, median (IQR)	57.9 (16.1-139.6)	118.2 (95.2-13.0)	0.17
Creatinine, median (IQR)	1.6 (0.5-3)	0.7 (0.6-0.8)	0.23
Urine protein, median (IQR), g/24hr at biopsy	6.2 (3.3- 13.1)	2.4 (1.3-4.6)	**<0.01**
Urine protein, median (IQR), g/24hr at 6 months	1.08 (1.03-8.25)	0.68 (0.21-2.12)	0.06
Proliferative (class 3, 4, 3/5, 4/5) ISN/RPS classification, n (%)	6 (85.7%)	17 (73.9%)	1.0
Moderate NIH Chronicity Index, n (%), score 4-7	3 (42.9%)	2 (8.7%)	0.07
Moderate NIH Activity Index, n (%), score 6-14	2 (28.6%)	10 (43.5%)	0.67
≥ 20% Interstitial fibrosis, n (%),	3 (42.9%)	0 (0%)	**0.01**
>10% Global glomerulosclerosis, n (%)	5 (71.3%)	5 (21.7%)	**0.03**
Number of crescents,	1 (0-2)	0 (0-2)	0.82

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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.2394

OP0044 WHOLE KIDNEY TRANSCRIPTOMIC ANALYSIS OF FORMALIN-FIXED PARAFFIN-EMBEDDED LUPUS NEPHRITIS KIDNEY BIOPSY TISSUE USING THE NANOSTRING NCOUNTER PLATFORM

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Background: There is an ongoing effort to elucidate the molecular pathways that are key to kidney injury in lupus nephritis (LN). One approach is to study the transcriptome utilising kidney tissue obtained during diagnostic renal biopsy [1]. In clinical practice the most common tissue that is surplus to diagnostic requirements is formalin-fixed paraffin-embedded (FFPE) tissue. However, due to RNA degradation, transcriptomic analysis has been sub-optimal and challenging using standard procedures. The NanoString technology platform has the advantage that reliable detection of transcripts can be achieved even with degraded RNA. In this study we explored the utility of NanoString technology in identifying transcripts in RNA isolated from archival FFPE kidney biopsy sections in a cohort of patients with LN.
Objectives: To explore the utility of the NanoString platform in elucidating a renal transcriptomic signature in formalin-fixed paraffin-embedded Lupus Nephritis kidney biopsy tissue.
Methods: We utilised well defined Class III (n=11); Class IV (n=22) and Class V (n=24) LN FFPE kidney biopsies from female patients attending the Imperial College Healthcare NHS Trust. We excluded biopsies with mixed lesions or chronic lesions (i.e. significant glomerular scarring). Kidney biopsies from patients with Thin Basement Membrane (TBM; n=14) disease were used as controls. Six 10 micron thick sections were obtained from each biopsy and RNA isolated using the Qiagen RNeasy FFPE Kit. 100 micrograms of RNA was used for the detection of transcripts. We used the NanoString PanCancer immune profiling panel (770 transcript probes) and an additional 30 custom designed probes, enabling us to detect 800 transcripts, including 40 reference genes. Transcript analysis was performed according to manufacturer's instructions using the NanoString nSolver software. When analysing differential gene expression (DGE) we used Benjamini-Hochberg adjustment to account for multiple testing. The threshold for statistical significance was an adjusted P value of 0.05 (5% false discovery rate).
Results: Transcriptomic data passing NanoString nSolver quality control metrics was obtained from all sections. Notably sections included biopsies up to 16 years old (range: 1-16 years). Our transcript panel contained several Type I interferon (IFN) responsive genes, including sialic acid-binding Ig-like lectin 1 (Siglec-1). We detected a type I IFN signature using 8 IFN-responsive transcripts in 39 (68.4%) of the LN biopsies but in none of the TBM biopsies. This signature was present in Class III (n=9, 81.8%), Class IV (n=16, 72.7%) and Class V (n=14, 58.3%) LN samples. When we performed DGE analysis using TBM as the baseline we detected significantly increased expression across the classes (Class III = 202; Class IV = 357 and Class V = 237 differentially expressed transcripts, Figure 1).
Conclusion: We have successfully identified transcriptomic signatures in RNA samples derived from a relatively large cohort of FFPE LN samples. Consistent with published reports we could detect a type I IFN signature in the LN kidney tissue [1]. Consistent with a recent study [1], we detected increased expression of OPN (osteopontin) and FN1 (fibronectin-1) in proliferative (Class III and IV) but not Class V LN. We are now performing clinical correlations to determine if the differentially expressed transcripts are clinically informative.

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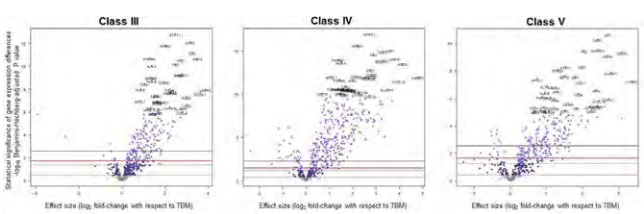


Figure 1: Volcano plots showing log2 fold-change and statistical significance of gene expression differences between each histologically defined LN classification and the TBM control group. Horizontal red line represents a Benjamini-Hochberg adjusted P value of 0.05 (5% false discovery rate)

Disclosure of Interests: Alyssa C. Gilmore: None declared, Hannah Wilson: None declared, Tom Cairns: None declared, Marina Botto: None declared, Liz Lightstone Grant/research support from: Roche - ended 2018, Consultant of: GSK, Aurinia, Pfizer, Achillion, Speakers bureau: Alexion, Ian N. Bruce Grant/research support from: Genzyme Sanofi, GSK, and UCB, Consultant of: Eli Lilly, AstraZeneca, UCB, Iltoo, and Merck Serono, Speakers bureau: UCB, Terry Cook Grant/research support from: Achillion funding for natural history study on C3 glomerulopathy, Consultant of: Scientific consultant to Apellis, Alexion, Achillion, GSK, Speakers bureau: Alexion, Matthew Pickering Grant/research support from: Funding for investigation of therapeutic compounds in pre-clinical models of complement-mediated kidney disease; Achillion funding for natural history study on C3 glomerulopathy, Consultant of: Scientific Advisor for Alexion, Achillion, Apellis
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OP0045 DELINEATION OF A PROINFLAMMATORY CYTOKINE PROFILE TARGETED BY JAK1/2 INHIBITION USING BARICITINIB IN A PHASE 2 SLE TRIAL

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Background: Given the unmet clinical needs in systemic lupus erythematosus (SLE), including poor disease control and drug toxicities, new therapies are needed. In a phase 2, randomized, placebo-controlled, double-blind study (JAHH), once-daily baricitinib (bari) resulted in significant clinical improvement in patients (pts) with active SLE versus PBO. Bari inhibits JAK1 and JAK2 signalling, and in turn may affect STAT1, STAT2, STAT4 pathways. Therefore, bari has the potential to simultaneously impact several pro-inflammatory immune cytokines implicated in the pathogenesis of SLE, including IFN-α, IFN-γ, IL-6, IL-12, and IL-23.
Objectives: The objectives of the current study were: 1) to examine baseline serum cytokines in the JAHH phase 2 clinical trial for correlations with clinical or immunologic assessments; 2) to determine if changes in serum cytokine levels were associated with bari treatment.
Methods: Pts enrolled in the JAHH phase 2 trial received daily treatment with PBO, bari 2 mg, or bari 4 mg through week 24. Serum samples were collected at baseline (week [wk] 0), wk 12, and wk 24) from SLE pts (n=270) and 50 sex- and age-matched controls. Samples were analyzed for: IL-2, IL-3, IL-5, IL-6, IL-10, IL-17A, IL-21, IL-12/23p40, IL-12p70, GM-CSF, IFN-α and IFN-γ using ultrasensitive quantitative assays. IFN gene signature, autoantibodies, C3 and C4 were measured as previously described [1].
Results: At wk 0, serum IL-17A, IL-12/23p40, IL-6, IFN-γ and IFN-α were readily detectable. IL-12/23p40 was detectable in 100% of pts vs. 100% of

Figure 1

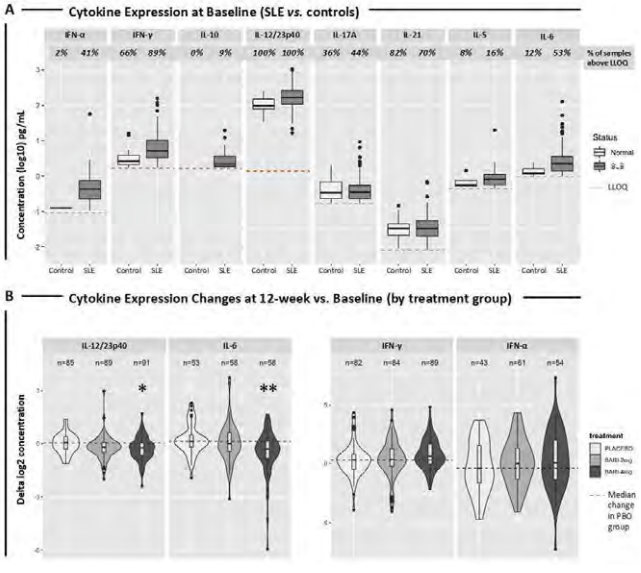


Figure 1. * p = 0.015; ** p = 0.001; Abbreviations: LLOQ, Lower limit of quantification.

controls, IFN-γ in 89% of pts vs. 66% of controls, IL-6 in 53% of pts vs. 12% of controls and in IFN-α 41% of pts vs. 2% of controls; detection of serum IL-2, GM-CSF, IL-5, IL-10 and IL-17A was variable (Fig 1). At baseline (wk 0), IL-12/23p40 was positively correlated with SLEDAI and IFN gene signature and negatively correlated with serum C4. IL-6 was positively correlated with joint swelling, joint tenderness, IFN-γ and C3. Serum IFN-α was positively correlated with serum IFN-γ, anti-Sm and anti-RNP, and the IFN gene signature (Fig 2). Treatment with bari 4 mg (Fig 1B) significantly decreased serum IL12/23p40 and IL-6 cytokine levels at wk 12 ($p<0.05$) but not serum IFN-α or IFN-γ levels (Fig 1B).

Figure 2

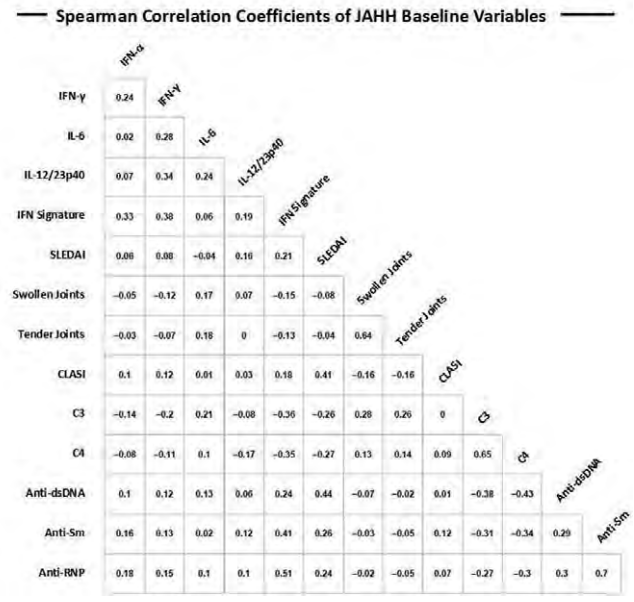


Figure 2. Abbreviations: Anti-dsDNA, Anti-double stranded DNA; Anti-RNP, Anti-ribonucleoprotein; CLASI, Cutaneous lupus erythematosus disease area and severity index; SLEDAI, SLE disease activity index.

Conclusion: Bari 4 mg treatment was associated with statistically significant decreases of serum IL-12/23p40 and IL-6 at week 12 which continued through week 24. Serum IFN-α or IFN-γ were not reduced with bari treatment. Thus, bari 4 mg simultaneously impacted multiple pro-inflammatory cytokines implicated in the pathogenesis of SLE.

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[1] Hoffman RW, et al. *Arthritis Rheumatol.* 2017;69(3):643-654.

Disclosure of Interests: Thomas Dörner Grant/research support from: Janssen, Novartis, Roche, UCB, Consultant of: Abbvie, Celgene, Eli Lilly, Roche, Janssen, EMD, Speakers bureau: Eli Lilly, Roche, Samsung, Janssen, Yoshiya Tanaka Grant/research support from: Asahi-kasei, Astellas, Mitsubishi-Tanabe, Chugai, Takeda, Sanofi, Bristol-Myers, UCB, Daiichi-Sankyo, Eisai, Pfizer, and Ono, Consultant of: Abbvie, Astellas, Bristol-Myers Squibb, Eli Lilly, Pfizer, Speakers bureau: Daiichi-Sankyo, Astellas, Chugai, Eli Lilly, Pfizer, AbbVie, YL Biologics, Bristol-Myers, Takeda, Mitsubishi-Tanabe, Novartis, Eisai, Janssen, Sanofi, UCB, and Teijin, Michelle A Petri Grant/research support from: GSK, Eli Lilly and Company, Consultant of: Eli Lilly and Company, Josef S. Smolen Grant/research support from: AbbVie, AstraZeneca, Celgene, Celltrion, Chugai, Eli Lilly, Gilead, ILTOO, Janssen, Novartis-Sandoz, Pfizer Inc, Samsung, Sanofi, Consultant of: AbbVie, AstraZeneca, Celgene, Celltrion, Chugai, Eli Lilly, Gilead, ILTOO, Janssen, Novartis-Sandoz, Pfizer Inc, Samsung, Sanofi, Daniel Wallace Consultant of: Amgen, Eli Lilly and Company, EMD Merck Serono, and Pfizer, Brenda Crowe Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Ernst Dow Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Richard E Higgs Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Guilherme Rocha Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Robert Benschop Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Maria Silk Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Stephanie de Bono Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Robert Hoffman Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Damiano Fantini Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company

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OP0046 TARGETING IRAK1 AND 4 SIGNALING WITH R835, A NOVEL ORAL SMALL MOLECULE INHIBITOR: A POTENTIAL NEW TREATMENT FOR SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is a complex autoimmune disease characterized by loss of immunological tolerance, hyperactivation of immune cells, proinflammatory cytokine production and, ultimately, end organ damage due to immune complex deposition. Toll-like receptors (TLRs), which are essential to the innate immune response to microbes and other danger signals, play a key role in the pathogenesis of SLE by recognition of self-molecules (1). Interleukin receptor associated kinases (IRAK)1 and 4 are responsible for initiating MyD88-dependent signaling from most TLRs and Interleukin-1 Receptors (IL-1R) and represent attractive targets for the therapeutic treatment of SLE (2). We have identified a potent and selective IRAK1/4 inhibitor, R835, that substantially suppressed the elevation of LPS (TLR4 agonist)-induced serum cytokines in healthy human volunteers in a recently completed phase 1 study.

Objectives: The aim of our study was to investigate the effect of IRAK1/4 selective inhibition as potential therapeutic approach for SLE. We evaluated the effect of our clinical candidate R835 on TLR7 signaling and in a mouse model of lupus-like disease.

Methods: Human primary dendritic cells and whole blood were stimulated with gardiquimod (TLR7 agonist) to evaluate the effect of R835 on Interferon-alpha (IFN-α) production. R835 was further evaluated for its efficacy on survival and disease progression in lupus-prone NZB/W F1 mice with early or active signs of disease.

Results: R835 inhibited TLR7-induced cytokine production in human dendritic cells and whole blood. Given orally to mice, R835 dose-dependently decreased serum IFN-α in response to administration of a TLR7 agonist. Furthermore, treatment of NZB/W F1 lupus-prone mice with R835 reversed the progression of lupus-like disease and the establishment of a pro-inflammatory environment, as demonstrated by decreased levels of proteinuria, blood urea nitrogen and autoantibodies, and reversal of renal pathology.

Conclusion: To our knowledge, R835 is the first dual IRAK1/4 inhibitor to enter clinical development and provides an attractive approach to treat a range of autoimmune and rheumatic diseases, including lupus.

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Disclosure of Interests: Chrystelle Lamagna Shareholder of: Rigel Pharmaceuticals, Employee of: Rigel Pharmaceuticals, Meagan Chan Shareholder of: Rigel Pharmaceuticals, Employee of: Rigel Pharmaceuticals, Art Bagos Shareholder of: Rigel Pharmaceuticals, Employee of: Rigel Pharmaceuticals, Ernest Tai Shareholder of: Rigel Pharmaceuticals, Employee of: Rigel Pharmaceuticals, Chi Young Shareholder of: Rigel Pharmaceuticals, Employee of: Rigel Pharmaceuticals, Yan Chen Shareholder of: Rigel Pharmaceuticals, Employee of: Rigel Pharmaceuticals, Lu Chou Shareholder of: Rigel Pharmaceuticals, Employee of: Rigel Pharmaceuticals, Gary Park Shareholder of: Rigel Pharmaceuticals, Employee of: Rigel Pharmaceuticals, Esteban Masuda Shareholder of: Rigel Pharmaceuticals, Employee of: Rigel Pharmaceuticals, Vanessa Taylor Shareholder of: Rigel Pharmaceuticals, Employee of: Rigel Pharmaceuticals

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OP0047 GENOME-WIDE ASSOCIATION STUDY OF SJÖGREN'S SYNDROME IDENTIFIES TEN NEW RISK LOCI

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Background: Sjögren's syndrome (SS) is a complex autoimmune disease with exocrine gland dysfunction leading to substantial morbidity. There are 10 published genetic susceptibility loci.
Objectives: Our genome-wide association study (GWAS) aimed to identify additional risk loci of genome-wide significance (GWS; p<5E-08) in European-derived primary SS.
Methods: A total of 3232 cases and 17481 controls genotyped on GWAS arrays and 619 cases and 6171 controls genotyped on ImmunoChip (IC) arrays were imputed after quality control. Logistic regression was calculated adjusting for ancestry using the first 4 principal components to identify SS-associated SNPs. GWAS and IC results were meta-analyzed using weighted Z-scores. Bayesian statistics were used to assign posterior probabilities and define credible SNP sets for each locus. Bioinformatic analyses were used to predict functionality.
Results: Seven novel loci exceeded GWS in the GWAS analysis: *NAB1*, *MIR146A-PTTG1*, *XKR6*, *MAPT-CRHR1*, *RPTOR-CHMP6-BAIAP2*, *TYK2* and *SYNGR1*. Meta-analysis with IC data identified three more novel loci exceeding GWS: *CD247*, *PRDM1-ATG5* and *TNFAIP3*. Several additional loci with suggestive association (p<1E-05) were also identified: *ADAMTSL2*, *CGNL1* and *PHRF1*. Several identified loci have reported functional implications in immune regulation and autoimmune disease. In lupus, rs2431697 correlated with rs2431098, which was shown to alter *MIR146A* expression, resulting in type I interferon pathway imbalance. Similarly, *TYK2* risk association reportedly drives interferon, IL10 and RET signaling pathways. *PRDM1* encodes Blimp-1, a master regulator of immune cell differentiation. *CD247* encodes the zeta subunit of the T cell receptor complex. *XKR6* is implicated in apoptotic cell ingestion. *ATG5* is also involved in apoptosis, as well as autophagy and antigen presentation.
Additional bioinformatics analyses (Haploreg, Regulome DB, ENCODE, etc.) revealed immune-relevant functional implications for each risk locus. The SS-associated credible set included variants downstream of *TNFAIP3* in a region reported to abolish looping between an enhancer and the*TNFAIP3* promoter in lupus and a coding variant that has been shown to alter NF-kB activity and neutrophil extra-cellular traps. The rs2293765 in the 5' UTR of *NAB1* showed evidence of enhancer/promoter activities. The rs2069235 in the *SYNGR1* locus showed enhancer and transcription start site activities in B and T cells. The rs7210219 in the *MAPT-CRHR1* locus showed enhancer/promotor activities in various tissues.
Conclusion: We have identified ten novel genetic susceptibility loci associated with SS pathology. Our finding increases the current number of GWS regions in SS patients of European origin, from 10 to 20. Future work is needed to identify and characterize the functional variants in each region.
Disclosure of Interests: Bhuwan Khatri: None declared, Tove Ragna Reksten: None declared, Kandice L Tessneer: None declared, Astrid Rasmussen Speakers bureau: Novartis, ThermoFischer, R Hal Scofield Grant/research support from: Pfizer, Simon J. Bowman Consultant of: Astrazeneca, Biogen, BMS, Celgene, Medimmune, MTPharma, Novartis, Ono, UCB, xtlbio, Glapagos, Speakers bureau: Novartis, Joel Guthridge Grant/research support from: Xencor, Bristol Myers Squibb, DXterity, Judith A. James Grant/research support from: Progentec Diagnostics, Inc, Consultant of: Abbvie, Novartis, Jannsen, Lars Ronnblom Grant/research support from: AZ, Speakers bureau: AZ, Blake M Warner: None declared, Xavier Mariette: None declared, Roald Omdal: None declared, Javier Martin Ibanez: None declared, Maria Teruel: None declared, Janicke Liaaen Jensen: None declared, Lara A Aqrawi: None declared, Øyvind Palm: None declared, Marie Wahren-Herlenius: None declared, Torsten Witte: None declared, Roland Jonsson: None declared, Maureen Rischmueller: None declared, A Darise Farris Speakers bureau: Biogen, Marta Alarcon-Riquelme: None declared, Wan-fai Ng: None declared, Kathy L Sivils: None declared, Gunnel Nordmark: None declared, Christopher Lessard: None declared
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OP0048 **TYPE I INTERFERON EXPRESSION IDENTIFIES DIFFERENT SUBSETS OF ANTIPHOSPHOLIPID SYNDROME**

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Background: Type I Interferons (IFN) play a key role in the pathogenesis and development of various autoimmune conditions. Among them, a solid amount of data demonstrates that the expression of various IFN regulated genes (IRGs), the so-called "IFN signature", has been linked to disease activity and disease progression in systemic lupus erythematosus (SLE) patients. Nevertheless, to date, a limited number of studies have analysed the IFN signature in antiphospholipid syndrome (APS) setting.
Objectives: This study aims to describe the activation and structure of the type I IFN signature among different subsets of APS, including primary APS (PAPS) and when associated with other autoimmune conditions (secondary APS - SAPS), and antiphospholipid antibodies positive individuals ("aPL carriers").
Methods: A total of 116 patients were enrolled, including 19 PAPS patients, 13 SAPS, 75 SLE patients, and 9 aPL carriers [1,2]. Thirty-two subjects were also recruited as healthy controls (HCs). IFI44, IFI44L, IFI6, MX1 and IRF4 gene expression was determined in whole blood in the entire cohort. Expression levels were normalized to Z-scores and averaged into a global IFN signature. Differences were measured by Kruskal-Wallis tests and associations among genes were studied by cluster and correspondence analyses. Correlations were plotted by network analyses.
Results: A global activation of the type I IFN signature was observed (HCs: -0.44±0.08, aPL carriers: -0.38±0.12, PAPS: -0.31±0.80, SAPS: -0.17±0.39, SLE: 0.09±0.80; p(Kruskal-Wallis)< 0.001). A certain degree of heterogeneity was observed among IRGs: MX1 being increased in all patient groups (all p< 0.001), whereas IFI44 was only increased in SLE (p< 0.001) and PAPS (p< 0.001), and both IFI44L and IFI6 were increased in SLE (both, p< 0.001) and a trend was observed in SAPS (p=0.060 and p=0.080) (Figure 1). By means of an unsupervised analysis, 3 clusters (I to III) were identified, which correlated with clinical status of the patients by correspondence analysis (p< 0.0001, Figure 2a). Network analyses revealed different structures of the IRGs networks among groups, from weaker networks in HCs and aPL carriers to stronger degree of correlations among IRGs in SAPS and SLE, thus pointing to diverse expression programs (Figure 2b). Among APS patients (both SAPS and PAPS), the IFN signature was positively associated with anti-phosphatidylserine/prothrombin antibodies IgG levels (r=0.478, p=0.003), but no associations were observed for the IgM isotype nor with other autoantibodies specificities (all p >0.050). No associations were observed with traditional cardiovascular risk factors or current treatments (all p >0.050).
Conclusion: In line with other autoimmune conditions, APS is associated with a broad type I IFN activation, with distinct profiles of the IFN signature structure among different clinical subsets, suggesting that different pathogenic pathways are involved in the pathogenesis of these conditions.
References:
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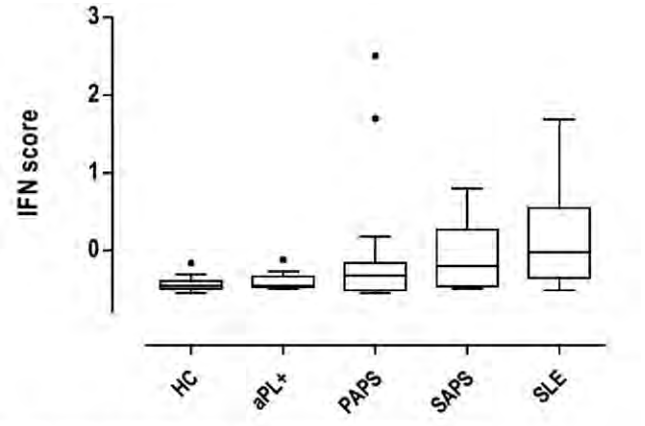


Figure 1. Global activation of the type I IFN signature among all groups of patients.

IFN means Interferon; HC, healthy controls; aPL+, antiphospholipid antibodies positive; PAPS, primary antiphospholipid syndrome; SAPS, secondary antiphospholipid syndrome; SLE, systemic lupus erythematosus.

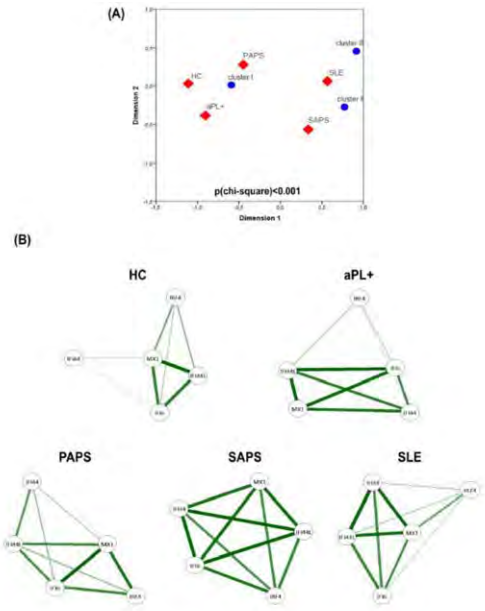


Figure 2. Panel A) Clusters analysis, correlated with clinical status of the patients by correspondence analysis (p<0.0001). Panel B) Network analyses of the interferon regulated genes networks among groups.

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Disclosure of Interests: None declared
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OP0049

EFFICACY OF ANIFROLUMAB IN ACTIVE SYSTEMIC LUPUS ERYTHEMATOSUS: PATIENT SUBGROUP ANALYSIS OF BICLA RESPONSE IN 2 PHASE 3 TRIALS

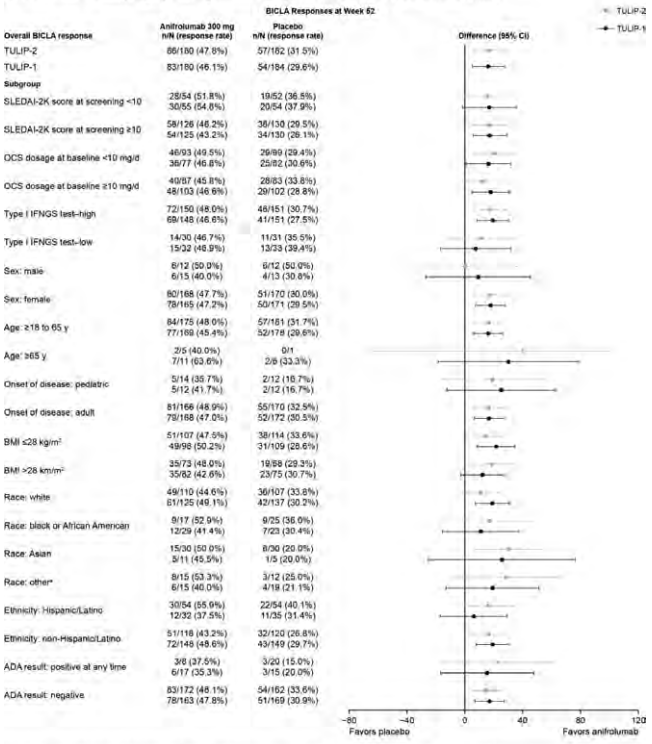
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Background: Treatment of patients with systemic lupus erythematosus (SLE) with the type I interferon (IFN) receptor inhibitor anifrolumab resulted in higher British Isles Lupus Assessment Group (BILAG)–based Composite Lupus Assessment (BICLA) response rates vs placebo at Week 52 in the phase 3 randomized trials, TULIP-2 (primary endpoint; 16.3% difference)[1] and TULIP-1 (secondary endpoint; 16.4% difference).[2] BICLA is a validated composite global disease measure that registers both partial and complete improvement within organ systems.
Objectives: TULIP-2 and TULIP-1 data were analyzed to evaluate BICLA responses to anifrolumab vs placebo at Week 52 in protocol-defined subgroups of patients with active SLE.
Methods: TULIP-2 and TULIP-1 were randomized, double-blind, placebo-controlled trials that evaluated efficacy and safety of intravenous anifrolumab vs placebo administered every 4 weeks, with the primary endpoints assessed at Week 52, in patients with moderate to severe SLE despite standard-of-care treatment.[1,2] BICLA responses are defined by all of the following: reduction of baseline BILAG-2004 A and B domain scores to B/C/D and C/D, respectively, and no worsening in any organ system; no worsening of the SLE Disease Activity Index 2000 (SLEDAI-2K) score; no worsening of ≥0.3 points in the Physician's Global Assessment (range 0–3); no trial treatment discontinuation; and no use of medications restricted by the protocol.[3] BICLA responses were compared between anifrolumab 300 mg and placebo groups, and robustness of BICLA responses was assessed across protocol-defined subgroups. TULIP-1 data were analyzed incorporating the amended restricted medication rules, as described.[2]
Results: In TULIP-2 and TULIP-1, 180 patients in each trial received anifrolumab 300 mg (182 and 184 patients received placebo, respectively). Baseline demographics, disease characteristics, and standard-of-care medications were balanced between anifrolumab and placebo groups within both TULIP trials. Patients in TULIP-2 and TULIP-1 had comparable BICLA responses (**Figure**). Across multiple subgroups, higher percentages of patients achieved BICLA responses at Week 52 in the anifrolumab vs placebo arms (**Figure**). There was concordance of BICLA responses favoring anifrolumab across the protocol-defined subgroups of baseline disease severity (SLEDAI-2K <10 points [difference 15.3%, TULIP-2; 16.9%, TULIP-1] vs ≥10 points [difference 16.7%, TULIP-2; 17.1%, TULIP-1]) and baseline oral corticosteroid use (prednisone or equivalent <10 mg/d [difference 20.1%, TULIP-2; 16.2%, TULIP-1] vs ≥10 mg/d [difference 12.0%, TULIP-2; 17.7%, TULIP-1]). Numerically different BICLA effect sizes between the anifrolumab vs placebo arms were observed in both studies in relation to baseline IFN gene signature status (high [difference 17.3%, TULIP-2; 19.1%, TULIP-1] vs low [difference 11.2%, TULIP-2; 7.5%, TULIP-1]). Other subgroups including age, sex, age at onset, race, and anti-drug antibody status showed similar uniformity of response.
Conclusion: The uniformity of robust BICLA response rates across prespecified subgroups in both phase 3 trials shows consistent clinical benefit of anifrolumab irrespective of patient baseline characteristics. However, given the small patient numbers in some subgroups, these results should be interpreted with caution.

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[1] Morand EF, et al. *N Engl J Med.* 2020;382:211–221.
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[3] Wallace DJ, et al. *Ann Rheum Dis.* 2014;73:183–190.

Figure. BICLA Response Rates by Subgroup Comparing Anifrolumab 300 mg With Placebo in the TULIP-2 and TULIP-1 Trials at Week 52



ADA, anti-drug antibody; BICLA, BILAG-based Composite Lupus Assessment; BILAG, British Isles Lupus Assessment Group; BMI, body mass index; CI, confidence interval; IFNGS, interferon gene signature; N, number of patients in treatment group; n, number of patients with response; OCS, oral corticosteroid; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000.
Note: TULIP-1 data were analyzed using the amended restricted medication rules.[2]
*Includes native Hawaiian or other Pacific Islander and American Indian or Alaska natives.

Disclosure of Interests: Eric F. Morand Grant/research support from: AstraZeneca, Consultant of: AstraZeneca, Speakers bureau: AstraZeneca, Richard Furie Grant/research support from: AstraZeneca, Biogen, Consultant of: AstraZeneca, Biogen, Yoshiya Tanaka Grant/research support from: Asahi-kasei, Astellas, Mitsubishi-Tanabe, Chugai, Takeda, Sanofi, Bristol-Myers, UCB, Daiichi-Sankyo, Eisai, Pfizer, and Ono, Consultant of: Abbvie, Astellas, Bristol-Myers Squibb, Eli Lilly, Pfizer, Speakers bureau: Daiichi-Sankyo, Astellas, Chugai, Eli Lilly, Pfizer, AbbVie, YL Biologics, Bristol-Myers, Takeda, Mitsubishi-Tanabe, Novartis, Eisai, Janssen, Sanofi, UCB, and Teijin, Rubana Kalyani Employee of: AstraZeneca, Gabriel Abreu Employee of: AstraZeneca, Lilia Pineda Employee of: AstraZeneca, Raj Tummala Employee of: AstraZeneca
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Psoriatic arthritis and its management: it's more than just synovitis…

OP0050

ADALIMUMAB INTRODUCTION VERSUS METHOTREXATE DOSE ESCALATION IN PATIENTS WITH INADEQUATELY CONTROLLED PSORIATIC ARTHRITIS: RESULTS FROM RANDOMIZED PHASE 4 CONTROL STUDY

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Background: Methotrexate (MTX) is often used as first-line therapy for patients (pts) with psoriatic arthritis (PsA) despite limited efficacy and data on appropriate dosage. Minimal Disease Activity (MDA) is suggested as an optimal treat-to-target outcome. Biologic disease-modifying antirheumatic drugs (bDMARDs) have demonstrated improved outcomes (including MDA rates) over MTX. However, more data are needed to define the optimal timing of bDMARD initiation and characterize efficacy of MTX dose escalation, to achieve optimal outcomes.

Objectives: To compare achievement of MDA between adding adalimumab (ADA) vs escalating MTX dose in PsA pts with inadequate disease control after initial MTX therapy.

Methods: The open-label, 2-part CONTROL study enrolled bDMARD-naive adult pts with active PsA (not in MDA at screening and ≥3 tender and ≥3 swollen joints) despite MTX 15 mg every wk (ew) for ≥4 wks. Pts were randomized to ADA 40 mg every other wk + MTX 15 mg (ADA+MTX) or escalated MTX to 20–25 mg ew or highest tolerable dose during 16-wk part 1 (Fig 1). The primary endpoint was achievement of MDA, defined as fulfilling ≥5 of the 7 criteria: tender joint count 68 (TJC68) ≤1, swollen joint count 66 (SJC66) ≤1, Psoriasis Area Severity Index (PASI) ≤1 or body surface area (BSA) ≤3%, pt's pain (visual analogue scale [VAS] 0–100) ≤15, Pt's Global Assessment of disease activity (PtGA) VAS ≤20, Health Assessment Questionnaire Disability Index (HAQ-DI) ≤0.5 and tender entheseal points (0–8) ≤1. Key secondary efficacy endpoints were achievement of ACR20 and PASI75 and change from baseline in HAQ-DI and Leeds Enthesitis Index (LEI) at wk 16.

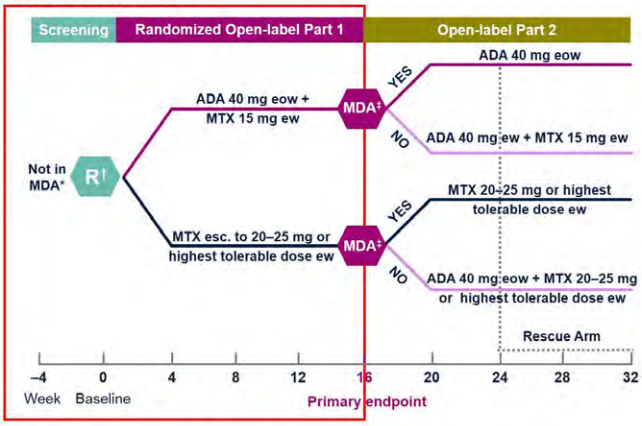
Results: Overall, 246 pts were randomized; 245 received treatment (ADA+MTX, n=123; escalated MTX, n=122); 117 (95%) pts and 110 (90%) pts, respectively, completed part 1. Baseline characteristics were similar between groups (**Table**). During part 1, the average dose of MTX was 21.8 mg/wk (55% on oral MTX) in the escalated MTX group. Significantly higher proportion of pts in ADA+MTX (42%) vs escalated MTX (13%) group achieved MDA at wk 16 (non-responder imputation [NRI]; difference [95% CI] 28% [18%–39%]; $P<0.001$; **Fig 2**). Observed case analysis confirmed the NRI analysis. Lower MDA rates at wk 16 were observed in the escalated MTX arm regardless of prior MTX duration (**Fig 2**). Significant improvements in key secondary endpoints were also observed with ADA+MTX vs escalated MTX (all $P<0.05$; **Fig 2**). In part 1, the proportion of patients with adverse events was similar between groups (ADA+MTX, 62% vs escalated MTX, 57%); no opportunistic infections, tuberculosis, malignancies, or deaths were reported during part 1.

Conclusion: A significantly higher proportion of pts achieved MDA at wk 16 after introducing ADA compared with escalating MTX dose; higher rates were observed regardless of prior MTX duration. Significantly higher responses in musculoskeletal, skin, and quality of life measures were observed with ADA+MTX vs escalated MTX. No new safety signals with ADA were identified in this pt population.

Table 1. Baseline Demographics

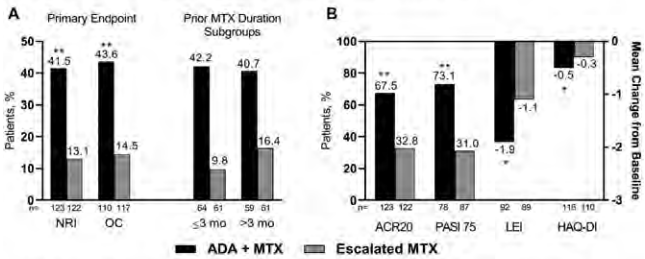
Characteristics, mean (SD)	ADA+MTX n=123	Escalated MTX n=122
Female, n (%)	64 (52.0)	59 (48.4)
Age, y	51.4 (12.2)	48.8 (12.7)
BSA >3%, n (%)	74 (60.2)	78 (63.9)
Pt pain	63.7 (19.5)	62.3 (20.9)
PtGA	65.0 (19.9)	62.9 (20.9)
HAQ-DI	1.2 (0.6)	1.2 (0.7)
LEI + plantar count	3.5 (2.1)	3.5 (2.1)

Figure 1. Study Design



*Active PsA patients (not in MDA) after MTX treatment for at least 4 weeks.
†Patients stratified by duration of prior MTX (MTX 15 mg/week for ≤3 months or >3 months).
‡Patients were assigned to treatment arms based on their MDA status.

Figure 2. MDA (A) and Secondary (B) Endpoints at Week 16



ACR, American College of Rheumatology; ADA, adalimumab; HAQ-DI, Health Assessment Questionnaire Disability; LEI, Leeds Enthesitis Index; MTX, methotrexate; NRI, nonresponder imputation; OC, Observed case; PASI, Psoriasis Area Severity Index.
Subgroup analysis stratified by prior MTX duration ≤3 months vs >3 months.
*$P<0.01$; **$P<0.001$.

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OP0051

STRUCTURAL ENTHESEAL LESIONS IN PSORIASIS PATIENTS ARE ASSOCIATED WITH AN INCREASED RISK OF PROGRESSION TO PSORIATIC ARTHRITIS - A PROSPECTIVE COHORT STUDY

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Background: We have previously reported that the presence of musculoskeletal pain in psoriasis patients is associated with a higher risk of developing psoriatic arthritis (PsA) (1). Furthermore, a subset of psoriasis patients shows evidence for structural entheseal lesions (SEL) in their hand joints (2), sometimes also referred as "Deep Koebner Phenomenon", which are highly specific for psoriatic disease and virtually absent in healthy controls, rheumatoid arthritis and hand osteoarthritis patients (2-4). However, it remains unclear whether SEL alone or in combination with musculoskeletal pain are associated with the development of PsA.

Objectives: To test whether the presence of SEL in psoriasis patients increases the risk for progression to PsA and how this is related to the presence of musculoskeletal pain.

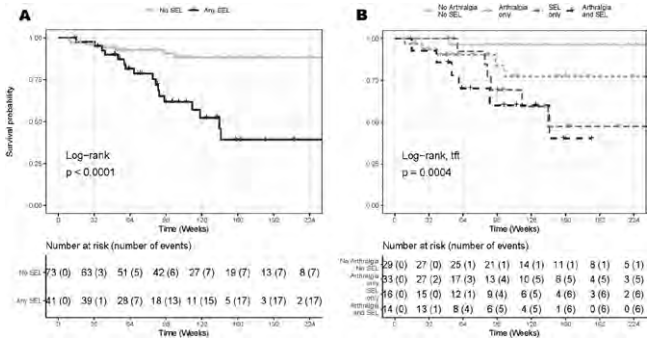
Methods: Psoriasis patients without evidence of PsA were enrolled in a prospective cohort study between 2011 and 2018. All patients underwent baseline assessment of SEL in their 2nd and 3rd MCP joints by high-resolution peripheral quantitative computed tomography (HR-pQCT). The risk of PsA development associated with SEL and arthralgia was explored using survival analyses and multivariable Cox regression models.

Results: 114 psoriasis patients (72 men/42 women) with a mean (SD) follow-up duration of 28.2 (17.7) months were included, 24 of whom developed PsA (9.7 /100 patient-years, 95%CI 6.2 to 14.5) during the observation period. Patients with SEL (N=41) were at higher risk of developing PsA compared to patients without such lesions (21.4/100 patient-years, 95%CI 12.5 to 34.3, HR 5.10, 95%CI 1.53 to 16.99, p=0.008) (Kaplan Meier plot A). Furthermore, while patients without arthralgia and without SEL had a very low progression rate to PsA (1/29; 3.4%), patients with arthralgia but no SEL showed higher progression (5/33; 15.2%), which was in line with previous observations (1) (Kaplan Meier plot B). Presence of SEL further enhanced the risk for progression to PsA both in the absence (6/16; 37.5%) and presence (6/14; 42.8%) of arthralgia with the highest progression rate in those subjects with both arthralgia and SEL (p<0.001 by log rank test for trend) (Kaplan Meier plot B).

Conclusion: Presence of SEL is associated with an increased risk of developing PsA in patients with psoriasis. If used together with pain, SEL allow defining subsets of psoriasis patients with very low and very high risk to develop PsA.

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OP0052

COMPARISON OF PATIENTS WITH PSORIATIC ARTHRITIS (PSA) AND INVESTIGATOR-DEFINED AXIAL PSA TO PATIENTS WITH PSA AND ELEVATED PATIENT-REPORTED SPINE PAIN: FINDINGS FROM THE CORRONA PSORIATIC ARTHRITIS/ SPONDYLOARTHRITIS (PSA/SPA) REGISTRY

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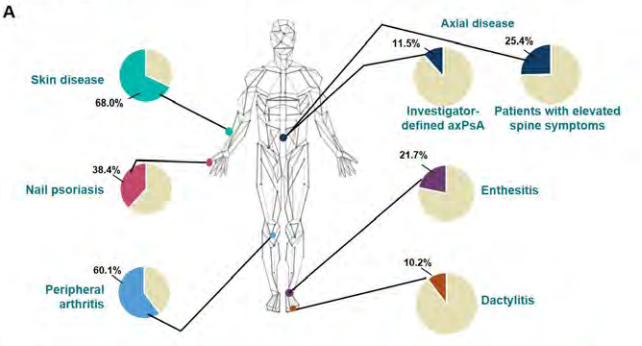
Background: Efforts are underway by GRAPPA and ASAS to define axial disease in psoriatic arthritis (axPsA).[1] AxPsA is typically diagnosed based on clinical evaluation and judgement, imaging, and patient-defined axial symptoms. In the MAXIMISE trial, part of the inclusion criteria for axPsA required patients to have a BASDAI ≥ 4 and patient-reported spine pain ≥ 40 in addition to clinician judgement.[2]

Objectives: To compare characteristics of patients with PsA and investigator-identified axPsA to patients with PsA with BASDAI ≥ 4 and patient-reported spine pain ≥ 40.

Methods: Adult patients with PsA enrolled in the registry from March 2013–December 2019 were included. Investigators identified the subset of patients with axPsA based on clinical assessments, imaging, and laboratory workup. All patients completed a BASDAI questionnaire and spine pain VAS. Patients with investigator-identified axPsA were compared with those who had BASDAI ≥ 4 and spine pain VAS ≥ 40 (elevated spine symptoms; non-mutually exclusive groups). Presence of other manifestations at enrollment was also evaluated: enthesitis (SPARCC enthesitis count > 0), dactylitis (dactylitis count > 0), peripheral arthritis (PA; tender and/or swollen joint count > 0), nail psoriasis (VAS > 0), skin psoriasis (affected body surface area > 0%). The prevalence of investigator-defined axPsA and elevated spine symptoms, alone and with other manifestations, was summarized for all patients and those who initiated biologics at enrollment using frequency counts and percentages.

Results: Of 3393 patients with PsA, 391 (11.5%) had investigator-defined axPsA and 863 (25.4%) had elevated spine symptoms (Figure 1**A**); 127 (3.7%) patients met both criteria. In the total population with PsA, 2982 patients had ≥ 1 PsA manifestation when axPsA was investigator defined, of whom 2235 (74.9%) had multiple manifestations. Among those with ≥ 1 manifestation, the most common presentations were PA + skin (14.6%), skin (13.1%), and PA + nail + skin (11.3%). When using the criteria for elevated spine symptoms, 2996 patients had ≥ 1 PsA manifestation, of whom 2299 (76.7%) had multiple manifestations. Among those with ≥ 1 manifestation, the most common presentations were skin (12.3%), PA + skin (11.2%), and PA + nail + skin (8.8%). Of 769 patients who initiated a biologic at enrollment, 109 (14.2%) had investigator-defined axPsA and 270 (35.1%) had elevated spine symptoms (Figure 2**A**). Among all biologic initiators with PsA, 733

Figure 1. Prevalence of (**A**) PsA Disease Manifestations and (**B**) Other Manifestations With Axial Disease in the Overall Population



B

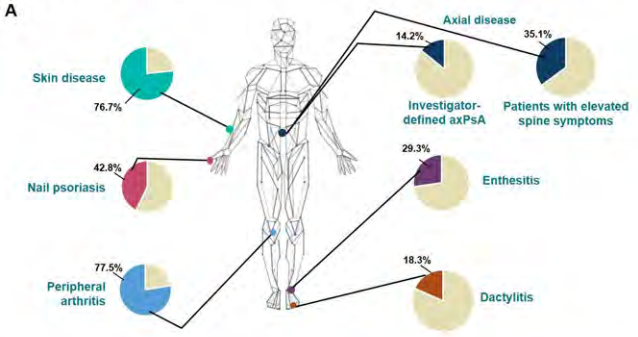
Manifestation, n (%)	Axial Disease Definition	
	Investigator-Defined AxPsA (n = 391)	Patients With Elevated Spine Symptoms (n = 863)
Enthesitis	154 (39.4)	311 (36.0)
Dactylitis	39 (10.0)	112 (13.0)
Peripheral arthritis	268 (68.5)	673 (78.0)
Nail	195 (49.9)	392 (45.4)
Skin	273 (69.8)	651 (75.4)

The heat map represents the frequency of any 2 domain combinations by the range of blue shades, with the darkest blue color specifying the highest frequency and the lightest blue specifying the lowest frequency of combinations.

had ≥ 1 PsA manifestation when axPsA was investigator defined, of whom 630 (85.9%) had multiple manifestations; the most common presentations were PA + skin (16.2%), PA + skin + nail (12.8%), and enthesitis + PA + nail + skin (7.8%). When using the criteria for elevated spine symptoms, 732 biologic initiators had ≥ 1 disease manifestation, of whom 650 (88.8%) had multiple manifestations; the most common presentations were PA + skin (11.7%), PA + skin + nail (8.5%), and PA + axPsA + skin (6.3%). The prevalence of skin, PA, and dactylitis was higher in those with elevated spine symptoms vs investigator-defined axPsA, whereas the prevalence of enthesitis was higher in those with investigator-defined axPsA (Figure 1**B and 2B**).

Figure 2. Prevalence of (**A**) PsA Disease Manifestations and (**B**) Other Manifestations With Axial Disease in the Biologic Initiator Population

A



B

Manifestation, n (%)	Axial Disease Definition	
	Investigator-Defined AxPsA (n = 109)	Patients With Elevated Spine Symptoms (n = 270)
Enthesitis	52 (47.7)	102 (37.8)
Dactylitis	17 (15.6)	53 (19.6)
Peripheral arthritis	84 (77.1)	234 (86.7)
Nail	53 (48.6)	131 (48.5)
Skin	81 (74.3)	218 (80.7)

The heat map represents the frequency of any 2 domain combinations by the range of blue shades, with the darkest blue color specifying the highest frequency and the lightest blue specifying the lowest frequency of combinations.

Conclusion: In the Corrona PsA/SpA Registry, there was a higher number of patients with elevated spine symptoms than with investigator-defined axPsA; these patients also had more coexisting manifestations. Although they may have had other reasons for back pain (ie, degenerative spine disease or central sensitization), it is possible that axPsA could be present in some and this warrants further evaluation.

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OP0053 SECUKINUMAB IMPROVES CLINICAL AND IMAGING OUTCOMES IN PATIENTS WITH PSORIATIC ARTHRITIS AND AXIAL MANIFESTATIONS WITH INADEQUATE RESPONSE TO NSAIDS: WEEK 52 RESULTS FROM THE MAXIMISE TRIAL

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Background: Although axial disease may affect up to 70% of patients (pts) with Psoriatic Arthritis (PsA), evidence on the efficacy of biologics in the treatment of axial manifestations in such pts is limited,[1] particularly as validated classification criteria for this subtype of PsA are not yet available. MAXIMISE (NCT02721966) is the first randomised controlled trial evaluating the efficacy of a biologic in the management of the axial manifestations of PsA and showed that secukinumab (SEC) 300 and 150 mg provided rapid and significant improvement in ASAS20 responses in these pts through week (Wk) 12.[2]
Objectives: To present 52 wks efficacy results and imaging data from the MAXIMISE trial.
Methods: This phase 3b, double-blind, placebo (PBO)-controlled, multicentre 52-wk trial included 498 pts (aged ≥18 years) with a diagnosis of PsA and classified by CASPAR criteria, spinal pain VAS score ≥ 40/100 and BASDAI score ≥ 4 despite use of at least two NSAIDs. Pts were randomised to SEC 300 mg (N=167) or SEC 150 mg (N=165) or PBO (N=166) wkly for 4 wks and every 4 wks thereafter. At Wk 12, PBO pts were re-randomised to SEC 300/150 mg. The primary endpoint was ASAS20 response with SEC 300 mg at Wk 12. The key secondary endpoint was ASAS20 response with SEC 150 mg at Wk 12. Wk 52 data are presented as observed. Bone marrow oedema of the entire spine and sacroiliac joints were assessed centrally with Berlin MRI scores at Baseline, Wk 12 and Wk 52.
Results: Primary and key secondary endpoints were met; ASAS20 responses were sustained and increased further through Wk 52. 75%/79.7% of the PBO pts re-randomised at Wk 12 to SEC 300/150 mg achieved ASAS20 response at Wk 52 (Figure 1). ASAS40 responses at Wk 52 were 69.1% [SEC 300 mg], 64.5% [SEC 150 mg], 62.5% [PBO-SEC 300 mg], and 54.1% [PBO-SEC 150 mg]. At baseline, 59.5% [SEC 300 mg], 53.5% [SEC 150 mg] and 64.2% [PBO] of the pts had positive MRIs for the sacroiliac joints and/or the spine with Berlin MRI score ≥1. The reductions of Berlin MRI score for entire spine and sacroiliac joints were statistically significant for pts treated with SEC 300/150 mg vs. placebo (Figure 2 **a and b**). There were no new or unexpected safety findings.

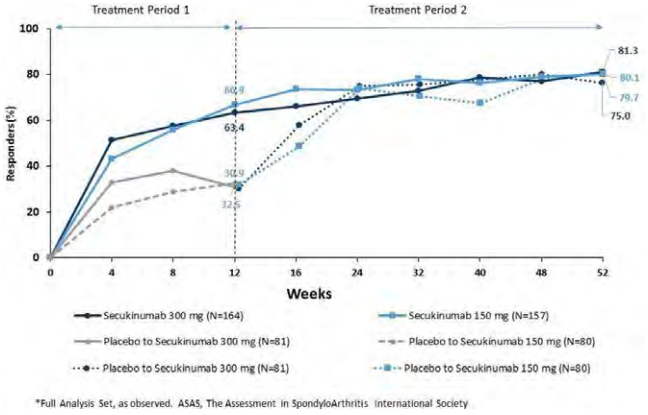


Figure 1. ASAS20 Response over 52 Wks*

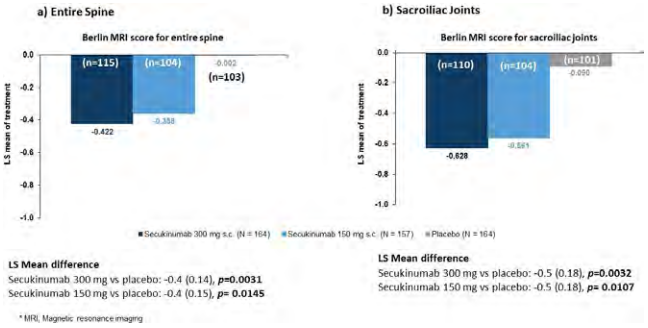


Figure 2. Total Berlin MRI score for the Entire Spine and Sacroiliac Joints at Wk 12

Conclusion: Secukinumab improved all evaluated ASAS responses through Wk 52 in PsA pts with axial manifestations and inadequate responses to NSAIDs

and led to significant reduction of inflammatory MRI lesions in the spine and the Sacroiliac Joints. The safety profile of secukinumab through Wk 52 was consistent with previous reports.[3-4]

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OP0054

EFFICACY OF GUSELKUMAB, A MONOCLONAL ANTIBODY THAT SPECIFICALLY BINDS TO THE P19-SUBUNIT OF IL-23, ON ENDPOINTS RELATED TO AXIAL INVOLVEMENT IN PATIENTS WITH ACTIVE PSA WITH IMAGING-CONFIRMED SACROILIITIS: WEEK-24 RESULTS FROM TWO PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDIES

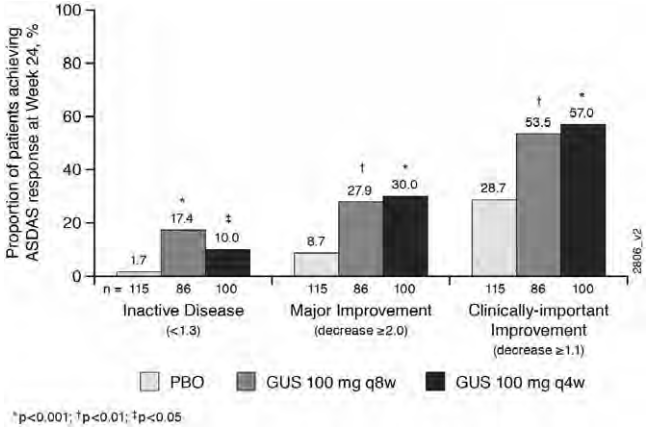
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Background: Guselkumab (GUS), an interleukin-23 inhibitor, was efficacious in reducing signs and symptoms of active psoriatic arthritis (PsA) in patients (pts) in two phase 3 trials (DISCOVER-1 and DISCOVER-2).
Objectives: To evaluate the efficacy of GUS in PsA pts with imaging-confirmed axial involvement consistent with sacroiliitis in DISCOVER-1&2.
Methods: In DISCOVER-1, 381 pts with active PsA (≥ 3 swollen joints, ≥ 3 tender joints; C-reactive protein ≥ 0.3mg/dL despite standard therapies) and in DISCOVER-2, 739 pts with active PsA (≥ 5 swollen joints, ≥ 5 tender joints, CRP ≥ 0.6mg/dL despite standard therapies) were randomized 1:1:1 to GUS 100mg Q4W, GUS 100mg Q8W (Wk0, Wk4, then Q8W), or PBO. This analysis included pts with sacroiliitis at baseline who had either documented imaging confirmation of sacroiliitis in the past or pelvic X-ray confirmation of sacroiliitis at screening (pooled data from DISCOVER-1&2) based on investigators' judgment of presence/absence of sacroiliitis. Efficacy was assessed by BASDAI score, BASDAI50, modified BASDAI (mBASDAI; excludes Q#3), spinal pain (BASDAI Q#2), ASDAS-CRP score, and ASDAS responses of inactive disease (<1.3), major improvement (decrease ≥2.0), and clinically important improvement (decrease ≥1.1). Pts with missing data at wk24 were classified as nonresponders.
Results: 312 pts presented with axial involvement (PBO, n= 118; GUS q8w, n = 91; GUS q4w, n = 103). The LS mean changes from baseline to wk24 in BASDAI, spinal pain, mBASDAI, and ASDAS-CRP were greater in the two GUS groups vs PBO (Table). Greater proportions of GUS-treated pts achieved BASDAI50 (Table) and ASDAS responses of inactive disease, major improvement, and clinically important improvement (Figure) at wk24 vs PBO.
Conclusion: GUS improved axial symptoms over 24 weeks in active PsA patients with imaging-confirmed sacroiliitis.

Table. Efficacy of GUS in PsA patients with axial involvement at week 24.[a]

	PBO (n=118)	GUS 100 mg every 8 weeks (n=91)	GUS100 mg every 4 weeks (n=103)
LS Mean change in BASDAI	-1.35	-2.67*	-2.68*
LS Mean change in spinal pain[b]	-1.30	-2.73*	-2.48*
BASDAI50[c], %	21/110 (19.1%)	34/84 (40.5%)**	36/95 (37.9%)**
LS Mean change in modified BASDAI[d]	-1.13	-2.16*	-2.18*
LS Mean change in ASDAS-CRP	-0.71	-1.43*	-1.46*

[a]Pts with axial involvement consistent with sacroiliitis at baseline and either a history of imaging confirmation or pelvic X-ray at screening (pooled data from DISCOVER-1 & 2)
[b]Question 2 of the BASDAI.
[c]Pts with BASDAI > 0 at baseline.
[d]Excludes question 3 of the BASDAI.
Unadjusted p-values as noted: *p < 0.001, ** p < 0.01



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OP0055 MINIMAL RADIOGRAPHIC DAMAGE OF SACROILIAC JOINTS DETECTED IN PSORIATIC ARTHRITIS PATIENTS

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Background: Psoriatic arthritis (PsA) is an inflammatory joint disease that is traditionally included in the Spondyloarthritis (SpA) spectrum. Prevalence and impact of axial involvement in PsA remains understudied but increasingly affects treatment decisions.

Objectives: The first step, in this multi-purpose radiographic study, is to report on baseline radiographic damage of the sacroiliac joints (SIJ) in PsA patients from a prospective multicentre cohort study in private and academic rheumatology practices.

Methods: Data from the Belgian Epidemiological Psoriatic Arthritis Study (BEPAS), a prospective multicentre cohort involving 17 Belgian rheumatology practices. Recruitment was from December 2012 until July 2014. Patients were included in the study when the local rheumatologist could diagnose an existing or new PsA and when patients fulfilled the Classification criteria for Psoriatic Arthritis (CASPAR). Radiographs of the SIJ were obtained at baseline and after 2 years. Two calibrated readers assessed radiographic damage by grading the SIJ according to the modified New York (mNY) criteria. When assessing the images, readers were blinded for clinical data and information from other obtained images (radiographs of the hands, feet and spine). Individual scores as well as consensus scores are described.

Results: In total 461 patients where included in BEPAS. Mean age was 52.79±12.29 years and 43.0% (n=198) were female; average disease duration was 8.5 ± 9.3 yrs and approximately 34% of the patients report inflammatory axial pain. From 338 patients SIJ radiographs were obtained. At baseline, the vast majority of patients did not fulfil the mNY criteria (n=325, 96.2%), according to both readers. In 8 cases (2.4%) there was concordance on fulfilment of the mNY criteria. Discordant cases (n=5, 1.4%) were equally distributed. Agreement between the 2 readers was good with 98.5% overall agreement and kappa=0.75. Therefore, with a more sensitive approach (any of the 2 readers scores mNY positive) we see slight differences; 13 patients (3.8%) fulfil the mNY criteria. Table 1 shows radiographic damage by individual readers

Table. Baseline data on radiographic damage of the sacroiliac joints in Belgian patients with newly diagnosed or existing PsA included in the BEPAS.

N=338		Right sacroiliac joint		Left sacroiliac joint	
Grades	Type of lesion	Reader 1	Reader 2	Reader 1	Reader 2
0	No abnormalities	298 (88.2%)	301 (89.1%)	298 (88.2%)	296 (87.6%)
1	Indefinite abnormalities	32 (9.5%)	23 (6.8%)	27 (8.0%)	23 (6.8%)
2-3	Abnormalities	5 (1.5%)	12 (3.6%)	9 (2.7%)	19 (5.6%)
	Erosion	3 (0.9%)	11 (3.3%)	4 (1.2%)	18 (5.3%)
	Sclerosis	4 (1.2%)	12 (3.6%)	5 (1.5%)	13 (3.9%)
	Joint space alteration (narrowing or widening)	1 (0.3%)	1 (0.3%)	4 (1.2%)	2 (0.6%)
	Partial ankylosis	2 (0.6%)	3 (0.9%)	5 (1.5%)	8 (2.4%)
4	Total ankylosis	3 (0.9%)	2 (0.6%)	4 (1.2%)	-

In 128 patients (37.9%) a follow-up x-ray after 2 years was available. In 124 patients (96.9%) there was reader agreement on mNY negative status. There was disagreement between readers on a positive mNY in 2 patients (equally distributed) and agreement on 2 patients (1.6%). There were no patients with consensus between readers on the change in mNY over 2 years, but 1 reader reported 1 patient becoming mNY positive after 2 years.

Conclusion: Despite the patient self-identified presence of axial disease in up to 34% in this cohort of PsA patients, there was minimal radiographic damage on SIJ, suggesting that SIJ disease is not a major manifestation of PsA.

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OP0056 PERSISTENCE OF BIOLOGIC TREATMENT IN PSORIATIC ARTHRITIS: A POPULATION-BASED STUDY IN SWEDEN

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Background: Psoriatic arthritis (PsA) is a chronic, heterogeneous, immune-mediated seronegative arthritis characterized by joint inflammation in people with skin psoriasis (PsO). In recent years several effective biologic treatments such as tumour necrosis factor inhibitors (TNFi), interleukin (IL) 12 and 23 inhibitors (IL-12/23i), and IL 17 inhibitors (IL-17i) have been introduced for PsA. Discontinuation (non-persistence) of therapy is usually a consequence of lack of effect and intolerability.

Objectives: Compare time to discontinuation of TNFi (adalimumab, ADA), IL-17i (secukinumab, SEC), and IL-12/23i (ustekinumab, UST) treatment exposures and the association with previous biologic treatment experience.

Methods: Population-based national health data from the Swedish Patient Registry, Prescribed Drug Registry and Cause of Death Registry were linked at the patient level and used to identify treatment exposures in PsA patients initiating ADA, SEC, or UST between January 2008 and September 2018. Discontinuation was defined as a treatment switch to any other PsA-indicated biologic, or failure to re-dispense treatment within a grace period following end of drug supplied. The grace period, defined as the number of days between end of drug supply and re-dispensation during which a patient is considered to be on active treatment, was set dynamically to the number of days of drug supplied in the primary analysis. As a sensitivity analysis, a fixed 90-day grace period was used. Supply was calculated as total milligrams dispensed divided by maintenance dose posology, where the following assumptions were made due to the limitations of the administrative data used: UST patients' weight corresponded to the amount of drug dispensed (both 45mg and 90mg dispensations last 84 days), SEC patients with prior TNFi experience consumed 300mg/28 days and all others consumed 150mg/28 days, and ADA patients consumed 40mg/14 days. Adjusted hazard ratios (HR) for time to discontinuation were calculated using a Cox proportional hazards model. Covariates for age, marital status, and previous biologic treatment experience were assessed at the initiation of treatment exposure, while comorbidity including skin PsO was assessed during the two years prior. Exposures without discontinuation events were censored at death or end of follow-up. The study was approved by the Stockholm Regional Ethical Review Board.

Results: 3,620 discontinuation events were observed in the main analysis across 4,649 treatment exposures (ADA: 3,255; SEC: 887; UST: 507) (Figure 1, unadjusted). 3,162 events were observed in the sensitivity analysis. Average age at treatment initiation was 50, 54% were female, 47% were biologic treatment naïve, and 39% had skin PsO. In the multivariate main analysis, UST exhibited lower discontinuation rates vs ADA (HR=0.56, 95% CI: 0.49-0.64) while there

was no significant difference between SEC and ADA (HR=1.01, 95% CI: 0.88-1.15). In the multivariate sensitivity analysis, both UST (HR=0.81, 95% CI: 0.70-0.94) and SEC (HR=0.82, 95% CI: 0.70-0.95) were associated with significantly lower discontinuation rates ratio relative to ADA. Overall, patients with more biologic treatment experience were statistically significantly (p<0.05) associated with higher risk of treatment discontinuation.

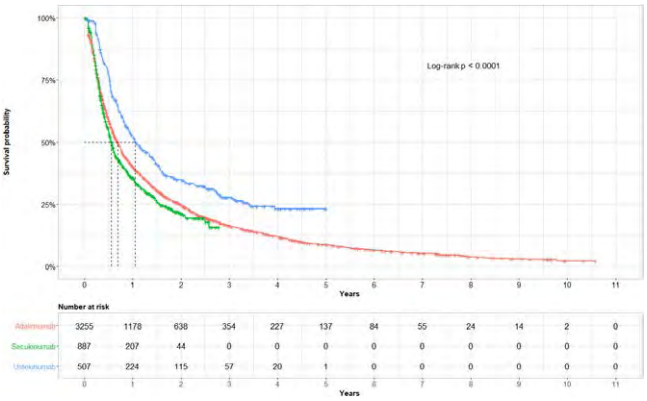


Figure 1. Unadjusted Kaplan-Meier curves of time to treatment discontinuation (main analysis, dynamic grace period)

Conclusion: UST exhibits a favourable treatment persistency profile relative to ADA, regardless of the grace period definition. The relative risk of discontinuing SEC vs ADA is sensitive to the grace period. Treatment discontinuation was higher in treatment exposures with more biologic experience.

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OP0057 SEX SPECIFIC DIFFERENCES IN EARLY PSORIATIC ARTHRITIS

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Background: Although the prevalence of Psoriatic Arthritis (PsA) is the same in men and women, women experience a higher burden of disease (pain, disability, fatigue) (1).The persistent belief that women tend to over-report their symptoms compared to men may also contribute to under or delayed diagnosis in women. The clinical pattern of PsA also differs, with men presenting more commonly with peripheral and axial joint damage and women being affected more frequently by polyarthritis (2). Furthermore, most disease activity measures contain pain and quality of life measurement metrics that may perform differently by sex. As a result, this may affect the clinician's perception of disease severity, influence management decisions and subsequently introduce sex bias in prescribing.

Objectives: To assess sex-related differences in baseline demographics, disease characteristics and evolution over 1 year in patients with newly diagnosed PsA.

Methods: Our study is embedded in the Dutch south-west Early Psoriatic Arthritis prospective cohort study. We described patient characteristics using simple descriptive analysis techniques. For the comparison across sexes and baseline and 1 year follow up, appropriate tests depending on the distribution were used.

Results: 273 men and 294 women with no significant differences in age and ethnicity were included. Women reported significantly longer duration of symptoms before diagnosis and significantly fewer of them were in paid employment at baseline. Oligoarthritis was the most common pattern of arthritis in both sexes. Polyarthritis and enthesitis were more prevalent in women who also presented at baseline a significantly higher tender joint count (Fig.1) than men but no difference in swollen joint count.

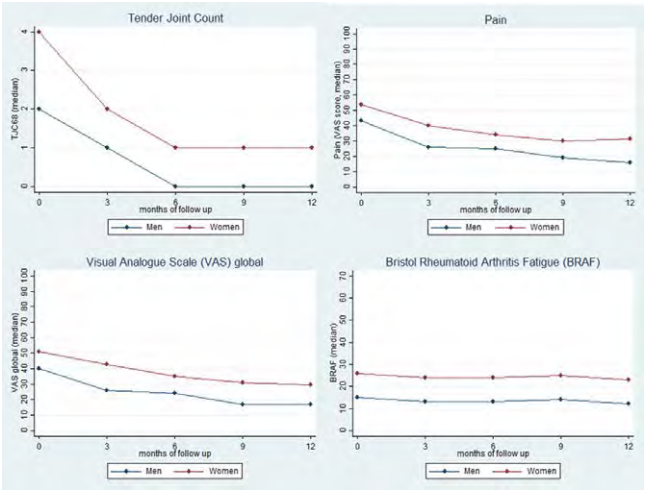


Figure 1. Longitudinal evolution of TJC68, Pain, VAS global, BRAF for men and women in the first year of PsA.

All composite indices (CPDAI, DAPSA, GRACE, MDA, Psoriatic ArthritiS Disease Activity Score) showed significantly worse results in women at baseline. Women also suffered more frequently from comorbid medical conditions, fatigue and anxiety, and reported more severe limitations in function and worse quality of life.

At 12 months women, despite the improvement they made, reported significantly higher levels of pain compared to men. Although MDA rates increase over time for both sexes,(Fig.2), it remained significantly more prevalent among men (19.0% vs 11.1% at inclusion, *p<0.05*, and 58.1% vs 35.7%, *p<0.00*, at T12). DAPSA was significantly higher in women at both timepoints and a significantly higher percentage of men presented remission according to DAPSA score at 12 months.

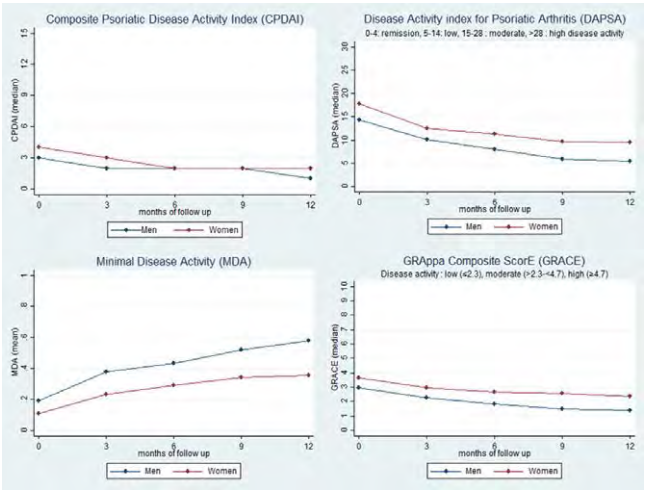


Figure 2. Longitudinal evolution of composite measures for men and women in the first year of PsA.

Conclusion: After 1 year of follow-up women didn't surpass their baseline disadvantages and despite the improvement, they still present higher disease activity, more pain and lower functional capacity than men. The nature of these findings may advocate a need for sex specific adjustment of treatment strategies and evaluation in psoriatic arthritis as sex-related difference in outcome persisted over time.

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OP0058-PARE **MY SJÖGREN'S DIARY: AN ONLINE PATIENT PORTAL FOR PATIENT LED SJÖGREN'S SYNDROME RESEARCH**

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Background: Sjögren's Syndrome is a chronic autoimmune disease affecting the exocrine glands accompanied by variable extra-glandular manifestations. Symptom flares, including dry eyes, dry mouth, dry skin, fatigue, myalgia and arthralgia, are frequent. Many of these symptoms have a considerable impact on quality of life, but are variable, sensitive to external factors, and difficult to measure objectively.
Clinical research on Sjögren's Syndrome is advancing with the help of patient registries: an array of clinical data is collected and available for approved studies. However, many of these registries focus on collecting clinical information and often fail to capture the diverse patient experience adequately. Thus, there is an unmet need for an online 'patient portal', secure and encrypted with the capability of interacting with existing registries, while also patient-facing to encourage active involvement in research and personal healthcare. Patient demand for this resource was highlighted in 2017 when the Cambridgeshire regional support group of the British Sjögren's Syndrome Association (BSSA) contacted the Patient Led Research Hub (PLRH). The PLRH provides research expertise to co-produce research ideas with patient organisations[1]; the PLRH and Cambridgeshire group have since secured funding and initiated work on this project with the Cambridge Clinical Trials Unit.
Objectives: Develop 'My Sjögren's Diary' a cross-platform patient portal to:
1.Act as an interactive tool to help patients manage their healthcare needs and aid communication with healthcare providers.
2.Function as a research platform, enabling patients to consent to contact, as well as support home-based data entry, allowing real-time capture of symptom scores and ensuring ease of participation for patients. Link with the UK Primary Sjögren's Syndrome Registry and NHS Digital to provide complementary clinical datasets.
Methods: The PLRH has coordinated a team of rheumatologists, database programmers, patients and family members to develop My Sjögren's Diary. Regular meetings, national surveys and correspondence with patients ensures the project remains relevant to patient needs, while collaborating with rheumatologists ensures the database is reliable, valid and of benefit to clinical care. Workshops hosted at key stages of database development have allowed both patients and rheumatologists to direct and refine My Sjögren's Diary. A prototype was presented at the 2019 BSSA Annual Conference before further improvements and beta release.
Results: A beta version of My Sjögren's Diary enabling BSSA members to track their medication and symptoms is now active. Feedback will be incorporated into the final version before it is publicly available to Sjögren's Syndrome patients. Further funding is required to develop the research platform.
Conclusion: My Sjögren's Diary encourages equal partnership between patients, clinicians and researchers. It presents a unique opportunity for comprehensive analysis of Sjögren's Syndrome and associated health utilities. Research participation is not mandatory, encouraging all patients to have an active role in personal healthcare management.
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[1] Mader LB, Harris T, Kläger S, Wilkinson IB, Hiemstra TF. Inverting the patient involvement paradigm: defining patient led research. *Research Involvement and Engagement* 4, 21 (2018).
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Artificial intelligence and machine learning in imaging of rheumatology: Are we ready?

OP0059 **AUTOSCORA: DEEP LEARNING TO AUTOMATE SCORING OF RADIOGRAPHIC PROGRESSION IN RHEUMATOID ARTHRITIS**

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Background: The prevention of joint destruction is an important goal in the management of rheumatoid arthritis (RA) and a key endpoint in drug trials. To quantify structural damage in radiographs, standardized scoring systems[1], such as the Sharp/van der Heijde (SvdH) score[2], which separately assesses joint space narrowing (JSN) and erosions, have been developed. However, application of these scores is time-consuming, requires specially trained staff, and results are subject to considerable intra- and inter-reader variability[1]. This makes their application poorly feasible in clinical practice and limits their reliability in clinical trials.
Objectives: We aim to develop a fully automated deep learning-based scoring system of radiographic progression in RA to facilitate the introduction of quantitative joint damage assessment into daily clinical practice and circumvent inter-reader variability in clinical trials.
Methods: 5191 hand radiographs and their corresponding SvdH JSN scores from 640 adult patients with RA without visible joint surgery were extracted from the picture archive of a large tertiary hospital. The dataset was split, on a patient level, into training (2207 images/270 patients), validation (1150/133), and test (1834/237) sets. Joints were automatically localized using a particular deep learning model[3] which utilizes the local appearance of joints combined with information on the spatial relationship between joints. Small regions of interest (ROI) were automatically extracted around each joint. Finally, different deep learning architectures were trained on the extracted ROIs using the manually assigned SvdH JSN scores as ground truth (Fig. 1). The best models were chosen based on their performance on the validation set. Their ability to assign the correct SvdH JSN scores to ROIs was assessed using the unseen data of the test set.

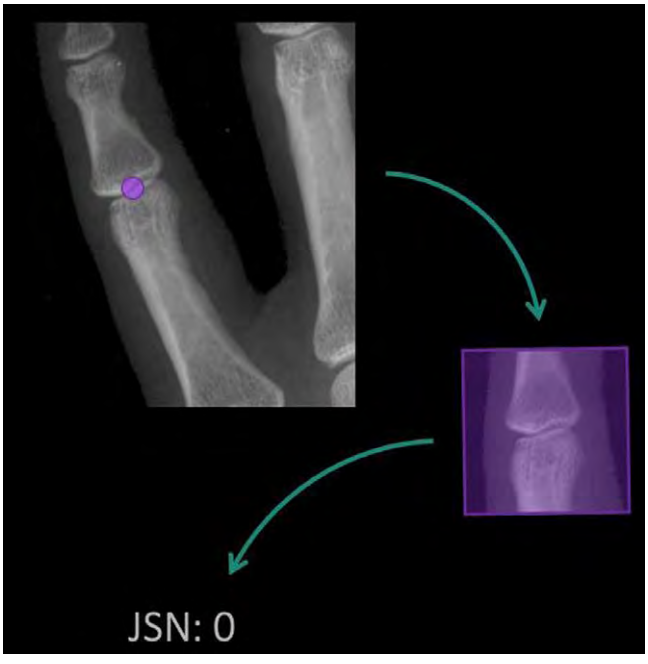


Fig. 1. 3-step approach to automated scoring: joint localization, ROI extraction, JSN scoring.

Results: ROI extraction was successful in 96% of joints, meaning that all structures were visible and joints were not malrotated by more than 30 degrees. For JSN scoring, modifications of the VGG16[4] architecture seemed to outperform adaptations of DenseNet[5]. The mean obtained accuracy (i.e., the percentage of

joints to which the human reader and our system assigned the same score) for MCP joints was 80.5 %, that for PIP joints was 72.3 %. In only 1.8 % (MCPs) and 1.7 % (PIPs) of cases did the predicted score differ by more than one point from the ground truth (Fig. 2).

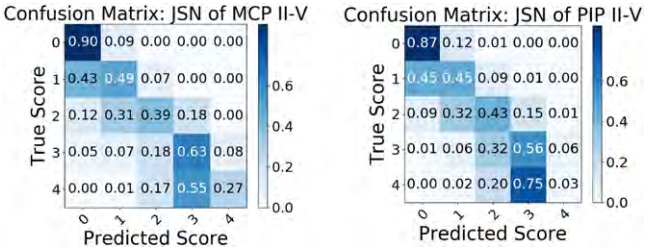


Fig. 2. Confusion matrices of automatically assigned scores ('predicted score') vs. the human reader ground truth ('true score').

Conclusion: Although a number of previous efforts have been published, none have succeeded in replacing manual scoring systems at scale. To our knowledge, this is the first work that utilizes a dataset of adequate size to apply deep learning to automate JSN scoring. Our results are, even in this early version, in good agreement with human reader ground truth scores. In future versions, this system can be expanded to the detection of erosions and to all joints contained in the SvdH score.

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OP0060

MACHINE LEARNING BASED BERLIN SCORING OF MAGNETIC RESONANCE IMAGES OF THE SPINE IN PATIENTS WITH ANKYLOSING SPONDYLITIS FROM THE MEASURE 1 STUDY

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Background: Magnetic resonance imaging (MRI) offers a non-invasive and objective method of early diagnosis and classification, monitoring disease burden and treatment response for patients (pts) with axial spondyloarthritis (axSpA) including ankylosing spondylitis (AS).[1] Numerous scoring schemes such as the AS Spine MRI Activity (ASspiMRIa) score are available for the quantitative assessment of MRI, but are subject to intra- and inter-rater variability, labor intensive and costly. Nevertheless, quantification of MRI changes has become an important tool to demonstrate treatment success of biologic drugs in axSpA.

Objectives: To evaluate the performance of machine learning (ML) based software for automated Berlin grading of spinal MRI bone marrow oedema in pts with AS and compare with expert scoring.

Methods: Fully automated ML software (Figure) was developed to detect and label 23 vertebrae, define vertebral units (VU) as per the Berlin modification of the ASspiMRIa score, and score each VU as either 0 (score of 0) or 1 (score of 1, 2 or 3). The ML algorithm was based on the previously developed SpineNet software.[2] Analysis included 108 pts from the secukinumab MEASURE 1 study[3], in which imaging was done using T1 and STIR sagittal MRI at baseline and Weeks 16, 52, 104, 156 and 208. Two expert readers, blinded to treatment and visit, evaluated all images by ASspiMRIa score. The scores from Reader 2 (R2) were binned into two groups: 0 vs 1, 2, or 3. As a result of multiple pt time points and expert reading sessions, the complete dataset comprised of 10,988 VU. Ten-way cross-validation at per-VU was used to train and validate the ML software. The dataset was split into 10 randomly selected subsets, ensuring that each pt appears in only one subset, after which 8 subsets were used for training the ML software, 1 was used to check for correct training and 1 was used for validation. The process was repeated ten times such that all 10 subsets were used for validation. Accuracy weighted for the frequency of each category, sensitivity and specificity were calculated using scores from R2 as reference. Intra-reader accuracy was also calculated.

Results: Accuracy of the software in relation to expert reader scores was 67% with a sensitivity of 0.63 and specificity of 0.70. The intra-reader accuracy was 71% and 77% for R1 and R2, respectively. Individual VU scoring of the Software vs. R2 are presented in the Table as a confusion matrix.

Conclusion: Automated scoring of MR images in AS pts provided moderate agreement to that of expert reader-based assessments. ML software has potential to provide an automated guided-reading approach to scoring MR images, which may enable further clinical insights.

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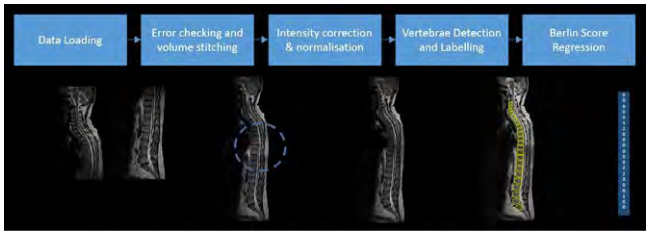


Figure. Processing pipeline of automated Berlin scoring software

Table. Confusion matrix between the software and R2

	Software Score = 0	Software Score = 1, 2 or 3	Total VU scored
R2 Score = 0	7199 (70%)	3068 (30%)	10,267
R2 Score = 1, 2 or 3	251 (35%)	475 (65%)	726
	7,450	3,543	10,993

Percentages calculated as a fraction over the total in each row. Overall accuracy is the average of the highlighted percentages.

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OP0061 FEASIBILITY STUDY ON AN AUTOMATED QUANTITATIVE SYSTEM FOR ULTRASOUND JOINT INFLAMMATION ASSESSMENT IN RHEUMATOID ARTHRITIS USING DEEP LEARNING

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Background: The most widely accepted ultrasound (US) joint inflammation scoring system in rheumatoid arthritis (RA) is semi-quantitative in nature. This process involves manual image acquisition followed by image interpretation. The subjectivity inherent in manual scoring may be overcome by the development of an automated quantitative system to measure joint inflammation.
Objectives: To develop an automated quantitative system to measure US detected power Doppler (PD) joint inflammation in patients with RA.
Methods: The synovial region of interest (sROI) on US images at the metacarpophalangeal joints (MCPJs) and the metatarsophalangeal joint (MTPJs) within the Doppler box is manually segmented by a clinician experienced in musculoskeletal US (figure 1). PD joint inflammation was scored manually semi-quantitatively (0-3). Deep learning based image segmentation was applied to the US images to automatically identify sROI and quantify the amount of PD signals within the sROI (figure 1) to obtain a computer derived PD reading reflecting the extent of PD vascularity within the sROI. The performance of computer derived PD reading was evaluated in comparison with the clinician's manual scoring.
Results: 820 joints from bilateral 1st to 5th MCPJs and MTPJs in 41 adult RA patients (baseline characteristics: 75.6% Chinese; 73.2% female; mean (SD) DAS28, 4.23 (1.25); mean (SD) disease duration, 73.3 (57.8) months) were evaluated in this cross-sectional study. The respective mean (SD)/ median (IQR) computer derived PD readings were 0.13 (0.75)/0.04 (0.08), 1.62 (1.77)/1.21 (1.19) and 10.12 (6.86)/7.51 (5.24) for manual score 0, 1 and 2 (no joints had manual score 3), with statistically significant differences found among the different manual score classes (for non-normally distributed data, Kruskal-Wallis H-test, $p=1.69 \times 10^{-92}$, Mann-Whitney Test: manual score 0 versus 1, $p=1.04 \times 10^{-62}$; manual score 0 versus 2, $p=3.28 \times 10^{-43}$; manual score 1 versus 2, $p=1.53 \times 10^{-28}$). Area under the ROC curve (AUC) based on computer derived PD reading cut-off of 0.26 to identify manual score 0 versus 1 was 0.98, while AUC based on computer derived PD reading cut-off of 3.37 to identify manual score 1 versus 2 was 0.98. The overall agreement of the score classes (0, 1 and 2) based on computer prediction using the above cut-offs versus manual scores of 0, 1 and 2 is 791/820=96.46%. Table 1 summarizes the performance of computer prediction using the above cut-offs when compared to clinician evaluation (i.e. score 0 versus 1, comparing computer prediction with clinician evaluation, sensitivity=99.14% and specificity=97.00%; score 1 versus 2, comparing computer prediction with clinician evaluation, sensitivity=97.14% and specificity=93.97%).

Figure 1. Manual and automated segmentation of synovial region of interest

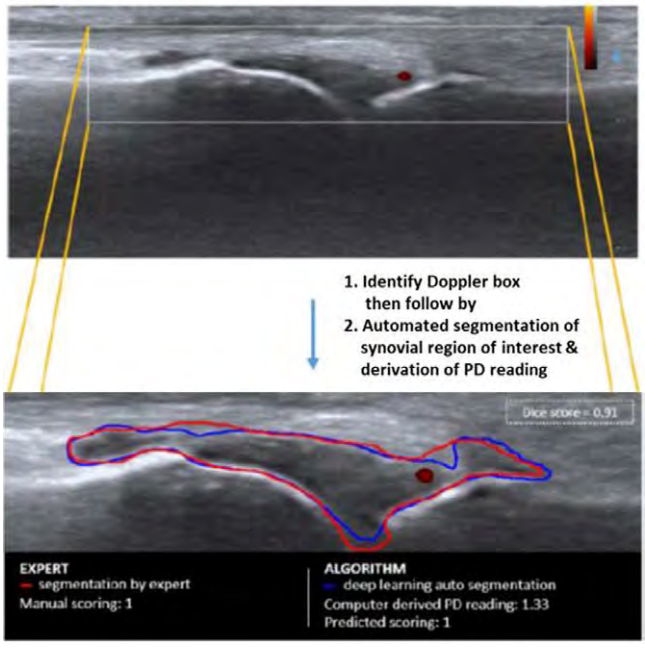


Table 1. Performance of computer prediction versus clinician evaluation

Score 0 vs. 1		
Assessor	*Clinician Evaluation: Score 0*	*Clinician Evaluation: Score 1*
Computer Prediction: Score 0	615	1
Computer Prediction: Score 1	19	115
Sensitivity=99.14%, Specificity=97.00%		
Score 1 vs. 2		
Assessor	*Clinician Evaluation: Score 1*	*Clinician Evaluation: Score 2*
Computer Prediction: Score 1	109	2
Computer Prediction: Score 2	7	68
Sensitivity=97.14%, Specificity=93.97%		

Conclusion: An automated quantitative system for US PD joint inflammation assessment using deep learning showed high sensitivity and specificity when results from computer prediction were compared to clinician evaluation. Further validation in a larger RA cohort with a longitudinal study design would be required.
References: Nil
Disclosure of Interests: None declared
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OP0062 PREDICTIVE VALUE OF BONE TEXTURE FEATURES EXTRACTED BY DEEP LEARNING MODELS FOR THE DETECTION OF OSTEOARTHRITIS: DATA FROM THE OSTEOARTHRITIS INITIATIVE

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Background: Osteoarthritis is a degenerative disorder characterized by radiographic features of asymmetric loss of joint space, subchondral sclerosis, and osteophyte formation. Conventional plain films are essential to detect structural changes in osteoarthritis. Recent evidence suggests that fractal- and entropy-based bone texture parameters may improve the prediction of radiographic osteoarthritis.[1] In contrast to the fixed texture features, deep learning models allow the comprehensive texture feature extraction and recognition relevant to osteoarthritis.
Objectives: To assess the predictive value of deep learning-extracted bone texture features in the detection of radiographic osteoarthritis.
Methods: We used data from the Osteoarthritis Initiative, which is a longitudinal study with 4,796 patients followed up and assessed for osteoarthritis. We used a training set of 25,978 images from 3,086 patients to develop the textual model. We use the BoneFinder software[2] to do the segmentation of distal femur and proximal tibia. We used the Deep Texture Encoding Network (Deep-TEN)[3] to encode the bone texture features into a vector, which is fed to a 5-way linear classifier for Kellgren and Lawrence grading for osteoarthritis classification. We also developed a Residual Network with 18 layers (ResNet18) for comparison since it deals with contours as well. Spearman's correlation coefficient was used to assess the correlation between predicted and reference KL grades. We also test the performance of the model to identify osteoarthritis (KL grade≥2).
Results: We obtained 6,490 knee radiographs from 446 female and 326 male patients who were not in the training sets to validate the performance of the models. The distribution of the KL grades in the training and testing sets were shown in Table 1. The Spearman's correlation coefficient was 0.60 for the Deep-TEN and 0.67 for the ResNet18 model. Table 2 shows the performance of the models to detect osteoarthritis. The positive predictive value for Deep-TEN and ResNet18 model classification for OA was 81.37% and 87.46%, respectively.

Table 1. Distribution of KL grades in the training and testing sets.

KL grades	0	1	2	3	4	Total
Training set	10893	4582	6114	3320	799	25,978
	41.9%	18.7%	23.5%	12.8%	3.1%	
Testing set	2472	1353	1696	775	194	6,490
	38.1%	20.8%	26.1%	11.9%	3.0%	

Table 2. Performance matrices of the Deep-Ten and ResNet18 models to detect osteoarthritis

	Deep-TEN	ResNet18
Sensitivity	62.29% (95% CI, 60.42%–64.13%)	59.14% (95% CI, 57.24%–61.01%)
Specificity	90.07% (95% CI, 89.07%–91.00%)	94.09% (95% CI, 93.30%–94.82%)
Positive predictive value	81.37% (95% CI, 79.81%–82.84%)	87.46% (95% CI, 85.96%–88.82%)
Negative predictive value	77.42% (95% CI, 77.64%–79.65%)	76.77% (95% CI, 75.93%–77.59%)

Conclusion: This study demonstrates that the bone texture model performs reasonably well to detect radiographic osteoarthritis with a similar performance to the bone contour model.

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OP0063 QUANTITATIVE COMPUTED TOMOGRAPHY PREDICTS 10-YEAR MORTALITY IN INTERSTITIAL LUNG DISEASE RELATED TO SYSTEMIC SCLEROSIS

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Background: Interstitial lung disease (ILD) is the main cause of death in Systemic Sclerosis (SSc). Chest CT is the gold standard in detecting ILD although it is not easy to understand its prognostic value. ILD qualitative assessment is almost worthless. Goh et al. semi quantitative score of ILD extent is related to mortality risk but it is burdened by relevant inter/intra-readers variability. An operator independent algorithm based on voxel-wise analysis proved to identify SSc patients with an increased risk of mortality according to prediction models.

Objectives: To verify if quantitative analysis of chest CT (QCT) predict 10 years-mortality in SSc patients.

Methods: SSc patients with availability of a chest CT were enrolled in 13 different centers. The CT voxel-wise analysis with a free software (www.horosproject.com) provided QCT indexes: kurtosis, skewness, mean lung attenuation and standard deviation. Patients characteristics, autoimmune profile and pulmonary function test were collected. The follow-up interval lasted from the date of chest CT to the one of the last visit or death. Each QCT index cutoff, established in a previous study (1), clustered patients in two groups. Kaplan-Meier analysis estimated and compared survival in the above mentioned groups. $p < 0.05$ was considered statistically significant.

Results: Five hundred sixty three SSc patients were enrolled (35938 patient-months); 52.4% had ILD detectable at CT scan. For each QCT index cutoff the cohort was split in two subgroups without differences in terms of sex, age, disease duration, autoimmune profile. All QCT indexes' cutoff selected subgroups with statistically different survival rate (e.g in Figure 1).

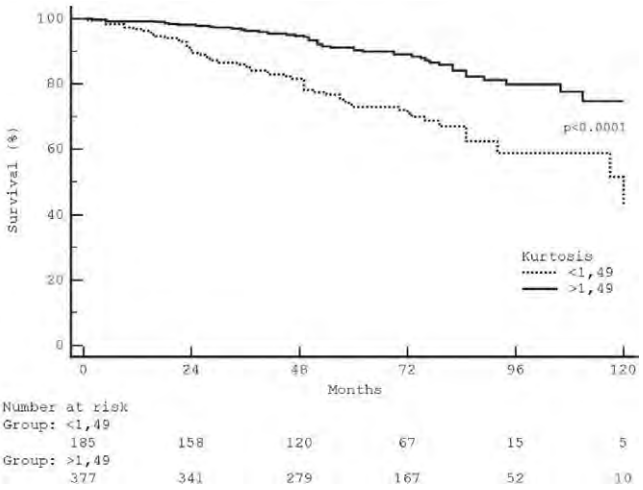


Figure 1

Conclusion: QCT can arise as the new gold standard in identifying SSc patients with poor prognosis. The real possibility to stratify SSc subjects according mortality risk will have a pivotal role in ILD treatment decisional process with the incoming anti-fibrotic drugs.

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OP0064 AUTOMATIC SCORING OF ARTHRITIS DISEASE ACTIVITY ON ULTRASOUND IMAGES FROM RHEUMATOID ARTHRITIS PATIENTS WITH CASCADED CONVOLUTIONAL NEURAL NETWORKS

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Background: Systematic Power or Color Doppler (CD) ultrasound (US) of joints can be used for early detection of Rheumatoid Arthritis (RA), predicting radiographic progression and early detection of disease flare in established

RA [1, 2]. The international standard for performing RA US scanning and evaluation of disease activity is the OMERACT-ELUAR Synovitis Scoring (OESS) system [1, 3].

To further mitigate the operator-dependency in scoring disease activity on CD US images in future trials and clinical practice, we proposed the use of convolutional neural networks (CNN) to automatically grade CD US images according to the OESS definitions. This study is a continuation of the findings in our previous work, where we developed a CNN for four-class CD US OESS scoring with a test accuracy of 75.0% [4].

Objectives: Since our last contribution, we have further developed the architecture of this neural network and can here present a new idea applying a Cascaded Convolutional Neural Network design. We evaluate the generalizability of this method on unseen data, comparing the CNN with an expert rheumatologist.

Methods: The images used for developing the algorithms were graded by a single expert rheumatologist according to the OESS system. The CNNs in the cascade were trained individually, after which they were combined to form the cascade model as shown in figure 1. The algorithms were evaluated on a separate test dataset, which came from the same distribution as the training dataset. The algorithms were compared to the gradings of an expert rheumatologist on a per-joint basis using a Kappa test, and on a per-patient basis using a Wilcoxon Signed Rank test.

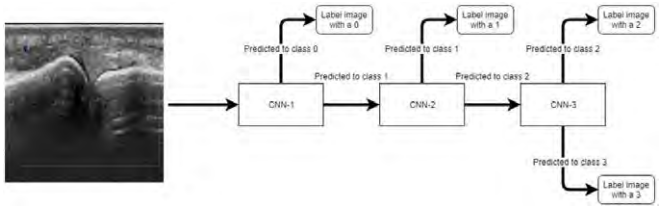


Figure 1. CNN-1 is the first CNN in the model and distinguishes between RA disease grade (DG) 0 and DG's 1, 2 and 3. CNN-2 is the second CNN and distinguishes between DG 1 and DG's 2 and 3. CNN-3 is the final CNN which distinguishes between DG's 2 and 3.

Results: With 1678 images available for training and 322 images for testing the model, the model achieved an overall 4-class accuracy of 83.9%. On a per-patient level, there was no significant difference between the classifications of the model and of a human expert (p=0.85).

Conclusion: We have shown that dividing a four-degree classification task into three successive binary classification tasks has resulted in a model capable of making correct classifications in 83.9% of the cases for a test set of ultrasound images with a naturally occurring distribution of RA joint disease activity scores. Furthermore, we have shown that the cascade model can produce classification decisions comparable with a human rheumatologist when applied on a per-patient basis. This emphasizes the potential of using CNNs with this architecture as a strong assistive tool for the objective assessment of disease activity of RA patients.

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Disclosure of Interests: None declared

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OP0065

INTER-RATER RELIABILITY AND VALIDITY OF MEDIAL AND LATERAL FEMORAL BONE MARROW LESIONS IN PATIENTS WITH OSTEOARTHRITIS UNDERGOING TIBIAL OSTEOTOMY USING THE KNEE INFLAMMATION MRI SCORING SYSTEM (KIMRISS)

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Background: The Knee Inflammation MRI Scoring System (KIMRISS) is a semi-quantitative grading tool (range 0-500) used to measure features of inflammation in knee osteoarthritis (OA), including compartment-specific BML scores.

Objectives: To investigate; 1) Inter-rater reliability of KIMRISS BML change scores including expert readers and a trainee reader, 2) Validity of KIMRISS BML scores by comparing medial and lateral femoral compartments in surgical and contralateral limbs before and 1 year after medial opening wedge high tibial osteotomy (HTO).

Methods: We included 27 patients with varus alignment and medial compartment knee OA [preoperative Kellgren-Lawrence grades ≤3, age = 53.1 ± 5.9, 22 males (81%), body mass index = 29.9 ± 4.3] undergoing unilateral HTO. Sagittal 2D turbo spin-echo sequences were acquired at 3-Tesla in both knees pre and 1-year post HTO after surgical removal of hardware. Femoral BML scores in the medial and lateral compartments were assessed on images blinded to limb and time by masking surgical evidence. Three reviewers independently graded the same 108 images (27 patients, 2 limbs, 2 time points). We evaluated reliability pre-to-post HTO BML change scores in the medial and lateral femur by calculating intraclass correlation coefficients (ICC) and Bland-Altman plots with 80% Limits of Agreement (LoA) for each rater pair.

Results: Means and standard deviations are shown in Figure 1. Cumulative percent distribution plots of changes after surgery show both increases and decreases in the medial and lateral femur (Figure 2). When combining all raters, the ICC (95% confidence interval (CI)) for the change in BML score for the surgical knee was 0.81(0.64, 0.91) in the medial femur and 0.73 (0.49, 0.87) in the lateral femur. 80% LOA for change in BML score in the surgical knee was -3.56 to 5.44. ICCs and LoAs for rater pairs are in Table 1. The surgical limb medial femur BML score was significantly greater than all other scores pre and post HTO (Figure 1). There were no significant changes after HTO. The mean change (95% CI) in medial femur BML score of the surgical knee was 1.08 (-1.21, 3.38). Using the mean scores of all raters, we compared BML scores in surgical and contralateral limbs before and after HTO using a 2-way repeated measures (limb by time) ANOVA, seperately for the medial and lateral compartments.

Table 1. Intraclass Correlation Coefficients (95% Confidence Intervals) and 80% Limits of Agreement for change in BMLs scores in the surgical knee.

a)	Medial compartment		
	1	2	3
1	0.63 (0.34, 0.81)		
2			
3	0.69 (0.43, 0.85)	0.42 (0.06, 0.69)	
b)	Lateral compartment		
	1	2	3
1			
2	0.67 (0.41, 0.83)		
3	0.79 (0.60, 0.90)	0.47 (0.11, 0.72)	
c)	Medial compartment		
	1	2	3
1			
3	-6.09, 8.61		
4	-8.10, 9.65	-6.03, 7.58	
d)	Lateral compartment		
	1	2	3
1			
2	-3.49, 5.41		
3	-4.73, 6.99	-3.43, 4.95	

ICCs in the medial (a) and lateral (b) compartments, and 80% LoA in the medial (c) and lateral (d) compartments. Rater 1 = trainee reader, raters 2-3 = expert readers (one MSK radiologist and one rheumatologist).

Conclusion: The KIMRISS can reliably detect differences between femoral BML scores in symptomatic and contralateral limbs, supporting the inter-rater reliability, feasibility and validity of compartment-specific BML scores.

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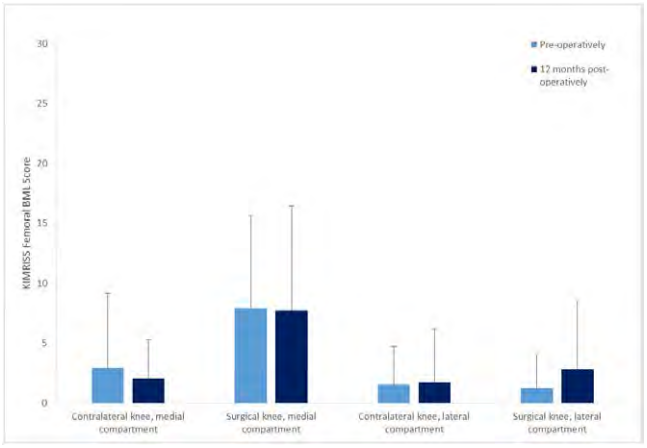


Fig 1. Means and standard deviations for KIMRISS femoral BML scores in the medial and lateral compartment for the surgical and contralateral knee.

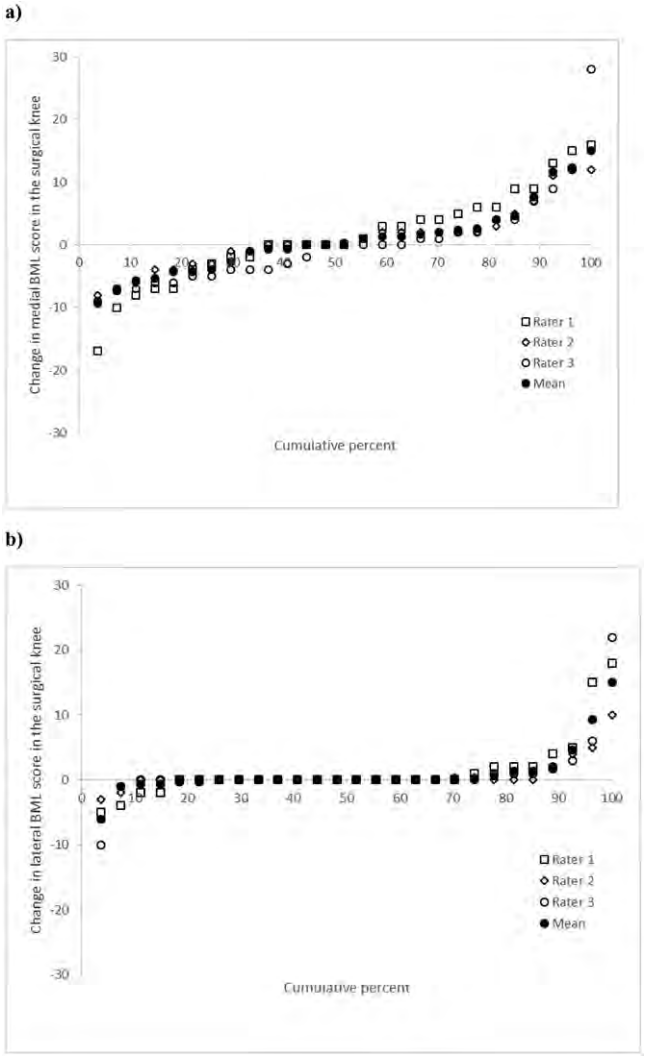


Fig 2. Probability plots for the 12-month change after surgery in femoral BML score in the medial (a) and lateral (b) compartments of the surgical knee. Change scores from each of the three raters is shown, as well as the average of all four raters.

UCB, Consultant of: WPM is Chief Medical Officer of CARE Arthritis Limited, has received consultant/participated in advisory boards for Abbvie, Boehringer, Celgene, Eli-Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, UCB, Speakers bureau: Received speaker fees from Abbvie, Janssen, Novartis, Pfizer, UCB., Robert G Lambert: None declared, Stephany Pritchett: None declared, Frank Beier: None declared, J. Robert Giffin: None declared, Thomas Appleton Grant/ research support from: AbbVie and Pfizer
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OP0066

IMAGING-DETECTED FEATURES OF HAND OSTEOARTHRITIS ASSOCIATE WITH SYMPTOMS AND RADIOGRAPHIC CHANGE OVER TIME: A SYSTEMATIC REVIEW AND META-ANALYSIS OF OBSERVATIONAL STUDIES

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Background: Osteoarthritis (OA) commonly affects joints in the hand. The natural history of hand OA is not well understood, and the local determinants of symptoms and structural changes over time remain unclear.
Objectives: To investigate, in both cross-sectional and prospective studies, the association between imaging (ultrasound [US] and magnetic resonance imaging [MRI]) features and symptoms of hand OA, and to examine in prospective studies whether imaging-detected features at baseline predict subsequent clinical and radiographic outcomes.
Methods: A systematic literature search was conducted in five databases including Medline, Web of Science, EMBASE, CINAHL and AMED in April 2018. The search was designed to capture published observational studies on the use of US and MRI in hand OA with no language restrictions. Odds ratios (OR), risk ratios (RR), and 95% confidence interval (CI) between [1] imaging features and hand OA symptoms at baseline, and [2] baseline-imaging features and follow-up outcomes were extracted and pooled using random effects model. Outcomes were defined as either incidence or progression of pre-existing features. Risk of bias assessment was performed using the Newcastle-Ottawa Scales. Heterogeneity and publication bias were assessed.
Results: The search identified 2818 citations, which reduced to 2216 after duplicate removal. Screening of titles and abstracts found 140 articles which met the inclusion criteria. After full text screening, 25 were included for analysis, including 452 participants (87% women) for US and 298 participants (86% women) for MRI with mean ages 60.3 and 62.5, respectively. Imaging-detected structural OA features were preferentially found in distal interphalangeal joints (DIPJs) followed by carpometacarpal (CMCJ) and proximal interphalangeal (PIPJ) joints. Metacarpophalangeal joints were least affected. However, the distribution pattern was different for inflammatory features for which the CMCJ was the most affected, and with no clear difference between DIPJs and PIPJs (Figure 1).

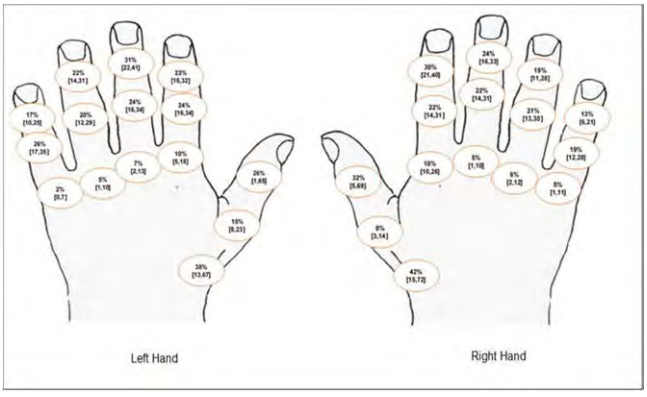


Figure 1. Hand map of grey-scale synovitis derived from pooled estimates of prevalence across studies (%[95% CI])

Of 10 US and 5 MRI studies examining association at baseline, joint tenderness was associated with US osteophytes (pooled ORs 2.30, 95% CI 1.90-2.79), grey-scale synovitis (3.00, 2.33-3.84), synovial effusion (2.92, 2.29-3.72), and power Doppler (PD) (2.30, 1.68-3.15). Similar relationships were observed with MRI features (Figure 2). Six studies did not find any association between imaging features and self-reported outcomes. However, association was observed with US- and MRI-detected synovitis in one study each, and MRI-detected structural features in two. Statistical pooling was not possible for these outcomes due to heterogeneous data.
Of the 9 US and 5 MRI studies for prediction, a dose-dependent relationship was observed between baseline PD and radiographic change at follow-up (Figure 3). Similar results were observed for MRI features and Kellgren-Lawrence change. The pooled ORs (95% CI) was 2.66 (1.88, 3.78) for bone marrow lesions, and 2.18 (1.53, 3.10) and 4.7 (3.08, 7.18) for grades 1 and 2 synovitis, respectively. Data to predict change in clinical outcomes however, were lacking.

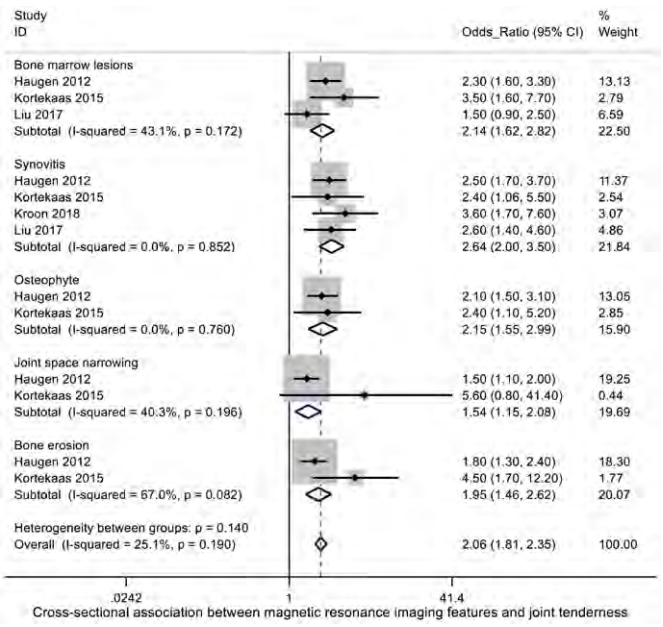


Figure 2. Forest plot showing pooled odds ratio between baseline magnetic resonance imaging features of hand osteoarthritis and joint tenderness.

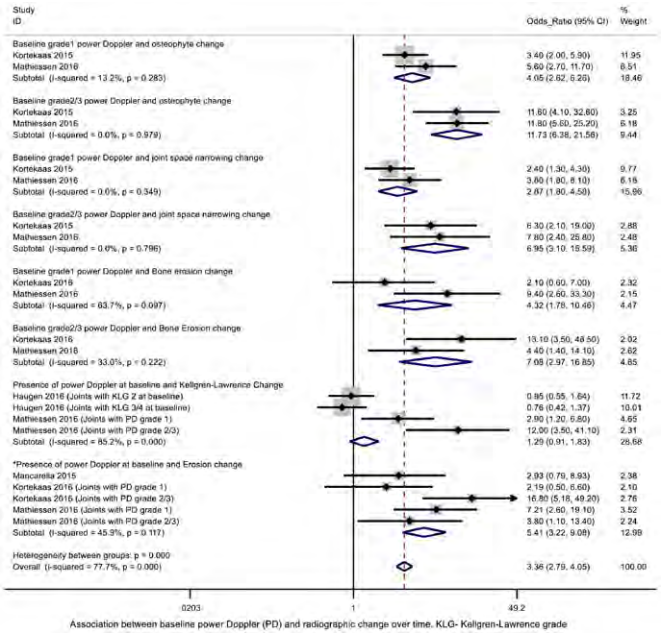


Figure 3. Forest plot showing pooled odds ratio between baseline power Doppler and radiographic change over time

Conclusion: Imaging-detected inflammatory features and osteophytes associate with joint tenderness. In addition, imaging-detected inflammatory changes at baseline predict future development and progression of structural OA changes, indicating that inflammation may precede radiographically-detectable structural changes.

Disclosure of Interests: Abasiama Obotiba: None declared, Subhashisa Swain: None declared, Jaspreet Kaur: None declared, Khalid Yaseen: None declared, Michael Doherty Grant/research support from: AstraZeneca funded the Nottingham Sons of Gout study, Consultant of: Advisory borads on gout for Grunenthal and Mallinckrodt, Weiya Zhang Consultant of: Grunenthal for advice on gout management, Speakers bureau: Bioiberica as an invited speaker for EULAR 2016 satellite symposium, Abhishek Abhishek Grant/research support from: AstraZeneca and OxfordImmunotech, Speakers bureau: Menarini pharmaceuticals

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Epidemiology

OP0067

CUMULATIVE ANTIBIOTIC USE AND THE RISK OF DEVELOPING ANKYLOSING SPONDYLITIS: A POPULATION-BASED CASE CONTROL STUDY

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Background: Recent studies show possible mechanisms of microbiota alterations that lead to the development of Ankylosing spondylitis (AS). These disturbances in the microbiota can be caused by long-term and high dose intake of antibiotics

Objectives: To analyze the association between antibiotic/s use and the risk of developing AS.

Methods: Population based case-control study using electronic medical records data from SIDIAP, covering >80% of the population in Catalonia, Spain. AS diagnoses with 2+ years data available were matched to up to 5:1 controls of same age, sex, and GP practice, and similar follow-up. Tracking of antibiotic use in the previous two years was done through pharmacy dispensation data standardized with ATC codes, and categorized in terms of recency of use and quartiles of cumulative dose. Adjusted odds ratios were estimated using conditional logistic regression analyzing antibiotic use (yes/no), recency of intake (current, recent, past, no use) and cumulative dose (quartiles of daily defined doses in the previous two years). All analyses were adjusted for age, body mass index, smoking, co-morbidity, socio-economic deprivation and number of GP visits as a proxy for healthcare resource use.

Results: The study included 4,493 cases diagnosed with AS and 22,016 controls. 46.3% of cases and 28.2% of controls had taken antibiotics. An association between taking beta-lactams (OR 1.18 [95% CI: 1.09-1.28]) and taking macrolides (OR 1.34 [95% CI: 1.18-1.52]) and getting diagnosed with AS was found. This association was stronger with current/recent use (Figure 1), but no dose-response pattern was seen (Figure 2).

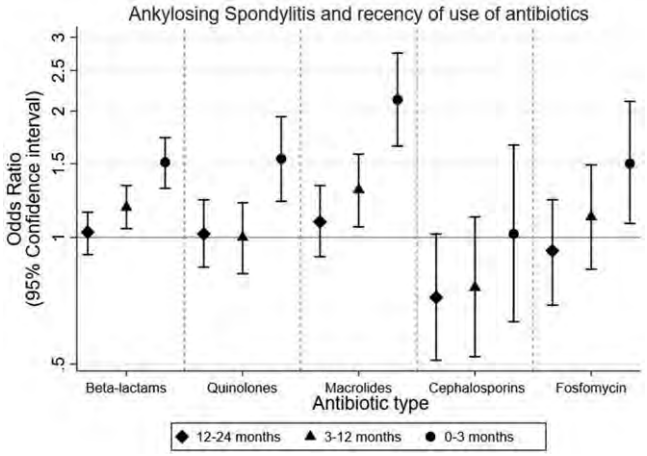


Figure 1. Recency of use and AS diagnosis.

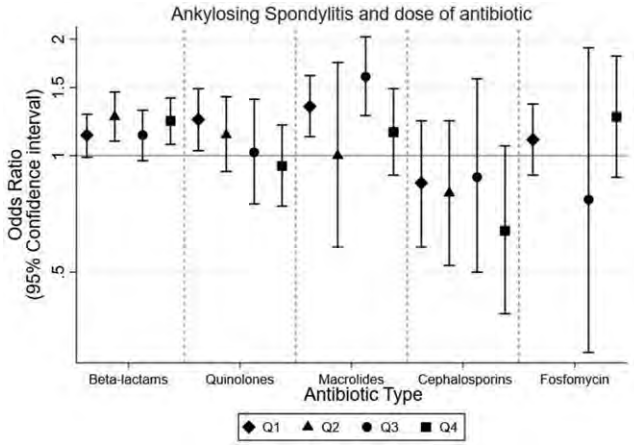


Figure 2. Cumulative use and AS diagnosis

Conclusion: There is an association between use of certain types of antibiotics and the diagnosis of AS, but no dose-response gradient. These data do not support a causal effect of cumulative antibiotic use on the development of AS. More research is needed on the impact of microbiome disturbance on the risk of developing AS.

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Disclosure of Interests: Ana Pascual-Dapena: None declared, Albert Prats-Uribe: None declared, Daniel Prieto-Alhambra Grant/research support from: Professor Prieto-Alhambra has received research Grants from AMGEN, UCB Biopharma and Les Laboratoires Servier, Consultant of: DPA's department has received fees for consultancy services from UCB Biopharma, Speakers bureau: DPA's department has received fees for speaker and advisory board membership services from Amgen

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OP0068 INCIDENCE AND PREVALENCE OF RHEUMATOID ARTHRITIS IN DENMARK: A NATIONWIDE POPULATION-BASED STUDY INVESTIGATING THE EFFECT OF FOUR DIFFERENT CASE DEFINITIONS

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Background: The incidence rate (IR) and point prevalence (PP) of rheumatoid arthritis (RA) in Denmark is largely unknown. Two challenges in estimating the "true" IR and PP using nationwide registry data are the choice of the RA case definition, and the denominator used, i.e. the exact amount of person years (PY) or census count data.

Objectives: To investigate the incidence and prevalence of RA in the adult Danish population using four different case definitions and two different denominator strategies.

Methods: Nationwide register-based cohort study. Patients with RA between 1996 and the end of 2016 were identified using the Danish National Patient Registry (DNPR) and information on DMARD prescriptions were obtained through linkage with the Danish National Prescription Registry. Age and sex standardised incidence and prevalence of RA were calculated in different ways: we estimated the IR (denominator = actual recorded number of PY in each year using migration and vital data) and the incidence proportion (IP) (denominator = census count data); and the PP (%) of RA was calculated for years 2000, 2009, 2011 and 2016. The four case definitions were: Model A, a first time RA diagnosis (ICD-10: M05-06) in DNPR and a redeemed prescription of a conventional DMARD in the following year[1]; Model B, an RA diagnosis recorded twice in DNPR within 90 days with both records originating from a department of rheumatology or general internal medicine[2]; Model C, any RA diagnosis recorded in DNPR with a DMARD prescription redeemed in the year before or after the diagnosis; Model D, similar to Model A but with the additional requirement that cases had no registered ICD code for inflammatory diseases prior to the RA diagnosis[1].

Results: The overall IR of RA from 1996 to 2016 based on model A was 35.2 (95%CI 34.8 to 35.6) per 100,000 PY while the IP was 34.7 (95%CI 34.3 to 35.1) per 100,000 individuals. The age standardised IR was higher for women than for men (Figure 1), and this was observed across all age groups. The IR peaked at age 70 to 74 in both men and women. Regardless of which case definition was used, the temporal trend showed a peak in IR in 2010 followed by a plateau (Figure 2). The overall PP estimate for all four models increased from 2000 to 2016, data shown for Model A in Table 1.

Table 1. Point prevalence (PP) of rheumatoid arthritis in years 2000, 2009, 2011 and 2016 based on Model A

	2000 N = 5906 70.3 % women	2009 N = 15037 70.9 % women	2011 N = 17363 71.0 % women	2016 N = 22991 70.3 % women
	PP (%) (95% CI)	PP (%) (95% CI)	PP (%) (95% CI)	PP (%) (95% CI)
All	0.16 (0.15 to 0.16)	0.37 (0.36 to 0.37)	0.41 (0.41 to 0.42)	0.52 (0.51 to 0.52)
Women	0.21 (0.20 to 0.22)	0.50 (0.49 to 0.51)	0.57 (0.56 to 0.58)	0.71 (0.70 to 0.72)
Men	0.10 (0.10 to 0.11)	0.23 (0.22 to 0.23)	0.25 (0.25 to 0.26)	0.32 (0.31 to 0.33)

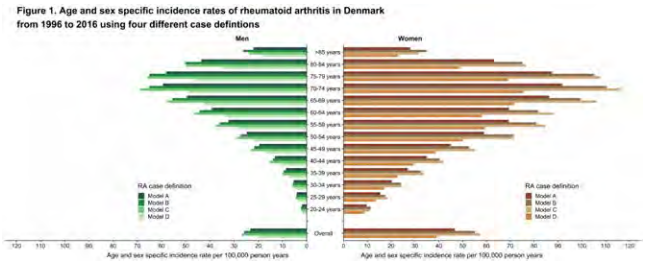


Figure 1. Age and sex specific incidence rates of rheumatoid arthritis in Denmark from 1996 to 2016 using four different case defintions

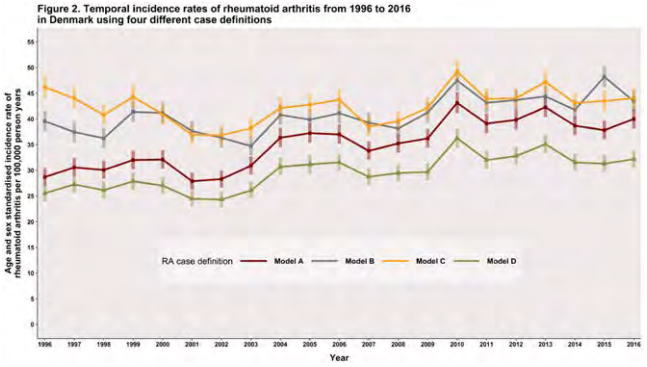


Figure 2. Temporal incidence rates of rheumatoid arthritis from 1996 to 2016 in Denmark using four different case definitions

Conclusion: A peak in the IR of RA was observed in 2010, regardless of which case definition was used. We believe this was due to introduction of the new EULAR/ACR diagnostic criteria at that time. IP estimates were systematically lower than IRs calculated using exact migration and vital data as denominator. The PP increased over time regardless of which case definition we used. We conclude that the choice of RA case definition had a larger influence than the choice of denominator.

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OP0069 FACTORS ASSOCIATED WITH THE RISK OF SEPSIS IN PATIENTS WITH IMMUNE-MEDIATED INFLAMMATORY DISEASES TREATED WITH ANTI-TUMOR NECROSIS FACTOR-ALPHA: A NATIONWIDE, POPULATION-BASED COHORT STUDY

B. C. Hsu[1], H. H. Chen[2,3], C. H. Lin[2], Y. M. Chen[2,3], K. L. Lai[3], D. Y. Chen[4], W. N. Huang[3], Y. H. Chen[3]. *[1]Taichung Veterans General Hospital Puli Branch, Internal Medicine, Nantou, Taiwan, Republic of China; [2]Taichung Veterans General Hospital, Medical Research, Taichung, Taiwan, Republic of China; [3]Taichung Veterans General Hospital, Internal Medicine, Taichung, Taiwan, Republic of China; [4]China Medical University, College of Medicine, Taichung, Taiwan, Republic of China*

Background: Anti-TNF-α agents have been proven to be effective for patients with immune-medicated inflammatory diseases (IMIDs) including rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriasis (PsO), psoriatic arthritis (PsA), Crohn's disease (CD) and ulcerative colitis (UC). Prior studies have shown an increased risk of infection in IMID patients treated with anti-TNF-α but limited studies investigated factors associated with the development of sepsis in patients with IMIDs.

Objectives: To investigate factors associated with the development of sepsis in patients with IMIDs using the Taiwanese National Health Insurance Research Database (NHIRD).
Methods: We identified all biologic-naïve patients with RA, AS, PsO, PsA, or CD/UC from the claim data via the NHIRD who started their first anti-TNF-α agent (etanercept (ETN), adalimumab (ADA) or golimumab (GOL)) between 2003 and 2017 as study subjects. The index date was the first date of anti-TNF-α prescription. Sepsis was defined based on the sepsis-3 definition. We identified sepsis patients using a validated ICD-9-CM coding system proposed by Angus et al, in which a diagnosis of bacterial/fungal infection with one or more acute organ dysfunction is required to define an episode of sepsis. All study subjects were followed up till the date of first hospitalization due to sepsis, 90 days after the last date of anti-TNF-α prescription, withdrawal from NHIRD or death, whichever came first. We used a Cox regression analysis to assess the associations of covariates with the risk of sepsis shown as hazard ratios (HRs) with 95% confidence interval (CIs). Covariates included anti-TNF-α agent, IMID, age, sex, insured amount, level of urbanization, disease duration, Charlson comorbidity index (CCI), a history of prior hospitalization due to sepsis within 3 months before the index date and medication use within 12 months before the index date and during the follow-up period.
Results: We identified 18105 biologic-naïve patients with IMIDs, including 8123 ETN users, 7623 ADA users and 2359 GOL users. The incidence rates (IRs) of sepsis in patients treated with ETN, ADA and GOL were 1080, 1181, and 617 per 10^5 years respectively. Multivariable regression analyses showed that factors associated with an increased risk of sepsis were use of ADA (ETN as reference: HR, 1.21; 95% CI, 1.02–1.42), male (HR, 1.24; 95% CI, 1.04–1.48), age (HR, 1.06; 95% CI, 1.05–1.07), CD/UC (HR, 2.35; 95% CI, 1.57–3.53), CCI (HR, 1.30; 95% CI, 1.23–1.38), prior sepsis (HR, 2.42; 95% CI, 1.78–3.29), prior use of sulfasalazine (HR, 1.25, 95% CI, 1.00-1.55), lower levels of urbanization (level III: HR, 1.37; 95% CI, 1.06–1.77; level IV: HR, 1.68, 95% CI, 1.35–2.10). Factors associated with a decreased risk of sepsis were use of GOL (ETN as reference: HR, 0.59; 95% CI, 0.39–0.84), use of methotrexate (HR, 0.78; 95% CI, 0.65–1.00), and higher insured amount (reference: ≤ 15480 NTD; 15480–28800 NTD: HR, 0.83; 95% CI, 0.68–0.99; 28800–45800 NTD: HR, 0.58; 95% CI, 0.45–0.74; >45800 NTD: HR, 0.33; 95% CI, 0.21–0.54).
Conclusion: Our study revealed that among biologic-naïve IMID patients initiating anti-TNF-α treatment, use of ADA, age, sex, CD/UC, CCI, prior sepsis, prior use of sulfasalazine and lower levels of urbanization were associated with an increased risk of sepsis, while use of GOL, use of methotrexate, and higher insured amount were associated with a decreased risk of sepsis.
Disclosure of Interests: BO-CHUEN HSU: None declared, Hsin-Hua Chen: None declared, Ching-Heng Lin: None declared, Yi-Ming Chen: None declared, Kuo-Lung Lai: None declared, Der-Yuan Chen: None declared, Wen-Nan Huang: None declared, Yi-Hsing Chen Grant/research support from: Taiwan Ministry of Science and Technology, Taiwan Department of Health, Taichung Veterans General Hospital, National Yang-Ming University, GSK, Pfizer, BMS., Consultant of: Pfizer, Novartis, Abbvie, Johnson & Johnson, BMS, Roche, Lilly, GSK, Astra& Zeneca, Sanofi, MSD, Guigai, Astellas, Inova Diagnostics, UCB, Agnitio Science Technology, United Biopharma, Thermo Fisher, Gilead., Paid instructor for: Pfizer, Novartis, Johnson & Johnson, Roche, Lilly, Astra& Zeneca, Sanofi, Astellas, Agnitio Science Technology, United Biopharma., Speakers bureau: Pfizer, Novartis, Abbvie, Johnson & Johnson, BMS, Roche, Lilly, GSK, Astra& Zeneca, Sanofi, MSD, Guigai, Astellas, Inova Diagnostics, UCB, Agnitio Science Technology, United Biopharma, Thermo Fisher, Gilead.
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OP0070 THE RISK OF PRECANCEROUS LESIONS OF THE BREAST AND CERVIX UTERI IN PATIENTS WITH AUTOIMMUNE RHEUMATIC DISEASES: A NATIONWIDE POPULATION STUDY IN TAIWAN

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Background: Precancerous lesions are pathologically atypical tissues which share part of abnormal features of cancerous tissue under microscopic examination but lack the ability of uninhibited growth and distant metastasis. Some of the measures to screen for precancerous tissues have gained popularity because supporting evidence indicates the beneficial effects on cancer incidence and mortality [1, 2]. However, the roles of these screenings and the risk of precancerous lesions in patients with autoimmune diseases have not been clarified. We aim to exam the risk of precancerous lesions among different autoimmune diseases.
Objectives: To determine whether the Taiwanese autoimmune rheumatic diseases (ARDs) patients have a higher risk of precancerous lesions of the breast and cervix uteri.
Methods: The Taiwan national breast cancer screening program provides biennially mammography for women above 45 years old or with a positive family history of breast cancer above 40 years old. The national cervical cancer screening program provides Pap smear test once every three years for women age above 30 years old. Using the National Health Insurance (NHI) database, we identified a cohort of 6 different groups of ARDs patients in Taiwan between 2004 and 2014. We linked the data from the national screening program of breast and cervical cancer and the NHI database to estimate the standardized incidence ratios (SIRs) of precancerous lesions (atypical lobular and ductal hyperplasia of the breast, carcinoma in situ of the breast, cervical intraepithelial neoplasia 1 to 3 of cervix uteri and carcinoma in situ of cervix uteri) in patients with ARDs compared with the general population.
Results: From 2004-2014, we identified 64,904 patients with autoimmune diseases. Table 1 shows the number of patients receiving the screening programs. The standardized incidence ratio (SIR) of precancerous lesion of the breast was elevated in patients with rheumatoid arthritis (SIR, 2.21; 95% CI, 1.21-3.46) and Sjögren syndrome (SIR, 5.77; 95% CI, 2.63-9.85). The incidence of precancerous lesion of cervix uteri was elevated in patients with surveyed ARDs compared with the normal population, particularly for patients with systemic lupus erythematosus (SIR 28.94; 95% CI, 24.52-33.70) and inflammatory bowel disease (SIR, 27.50; 95% CI, 7.40-56.32) (Table 2).

Table 2 Standardized incidence ratio (SIR) of precancerous lesion of the breast and cervix uteri in patients with autoimmune rheumatic diseases

	Precancerous lesion of Breast	Precancerous lesion of Cervix
	SIR (95% CI)	SIR (95% CI)
Rheumatoid arthritis	2.21 (1.21-3.46)	5.32 (4.25-6.50)
Systemic lupus erythematosus	1.34 (0.27-2.93)	28.94 (24.52-33.70)
Sjögren syndrome	5.77 (2.63-9.85)	8.32(5.72-11.34)
Systemic sclerosis	6.45 (0.72-15.54)	7.93 (2.90-14.80)
Vasculitis	0.00	7.68 (1.54-16.83)
Inflammatory bowel diseases	0.00	27.50 (7.40-56.32)

Conclusion: Precancerous lesions in the breast and cervix uteri were higher in female patients with ARDs and they should receive stringent screening program.
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OP0071 PREDICTING PERSISTENT HIGH-DOSE OPIOID USE AFTER TOTAL KNEE REPLACEMENT

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Table 1 Breast screen and Pap smear test in patients with autoimmune rheumatic diseases

	Rheumatoid arthritis (n=28289)	Systemic lupus erythematosus (n=11609)	Sjögren syndrome (n=17647)	Systemic sclerosis (n=1489)	Vasculitis (n=3050)	Inflammatory bowel disease (n=2820)
Female patients	21199	9808	15785	1043	1225	1034
Breast screening (n, %)	6296 (29.70%)	1382 (14.09%)	4737 (30.01%)	276 (26.46%)	67 (5.47%)	215 (20.79%)
Pap smear (n, %)	12827 (60.51%)	6495 (66.22%)	9961 (63.10%)	670 (64.24%)	1114 (90.94%)	665 (64.31%)

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Background: Patients undergoing total knee replacement (TKR) are at increased risk of persistent opioid use and dependence
Objectives: To identify patients with persistent high-dose opioid use after TKR using group-based trajectory models (GBTM) and determine predictors of persistent high-dose opioid users using pre-TKR patient characteristics
Methods: Using US Medicare claims (2010-2014), we identified patients aged ≥65 years who underwent a TKR and had no history of cancer or high-dose opioid use (>25 mean morphine equivalents (MME)/day) in the year prior. All patients were continuously enrolled in Medicare for ≥360 days prior to and ≥30 days after the TKR. To determine opioid filling patterns after the surgery, patients were followed up to 360 days from the day of TKR. We modeled 12 monthly indicators of opioid prescription fills as a continuous (MME/day) variable using a censored normal GBTM and categorized patients into 4 groups. The primary outcome was persistent high-dose opioid use defined as patients in trajectory Group 3 (38.8 MME/day) or Group 4 (22.4 MME/day). We split the data into training (2010-2013 data) and test (2014 data) sets and used logistic regression to predict high-dose opioid use vs low-dose opioid use (Groups 1 and 2) as a binary outcome utilizing pre-TKR patient characteristics as candidate predictors using the least absolute shrinkage and selection operator (LASSO) regression for variable selection. A reduced model with only 10 pre-specified variables readily available for clinical use was also considered
Results: The final study cohort included 142,089 patients. The GBTM identified 4 distinct trajectories (Group 1- Short-term, low-dose, Group 2- long-term, low-dose, Group 3- medium-term, high-dose, Group 4-long-term, high-dose) of opioid use in the year after TKR **(Figure)**. Using logistic regression and LASSO, we predicted the probability of persistent high-dose opioid use (N=17,171) (vs. low-dose opioid use) in the training set (N=101,810) for an AUC=0.80. The AUC in the test set (N=40,279) predicting high opioid use (N=5,893) was 0.77. The final model selected 33 variables and identified baseline history of opioid use as the strongest positive predictor of high-dose persistent opioid use. The reduced model with only ten predictors also performed equally well (AUC=0.77) **(Table)**.
Conclusion: In this cohort of older patients with no history of cancer or high-dose opioid use at baseline, 16.2% became high dose (28.1 MME/day) opioid users during the year after TKR. Our prediction model with 10 readily available clinical factors may help identify patients at high risk of future adverse outcomes from persistent opioid use and dependence after TKR

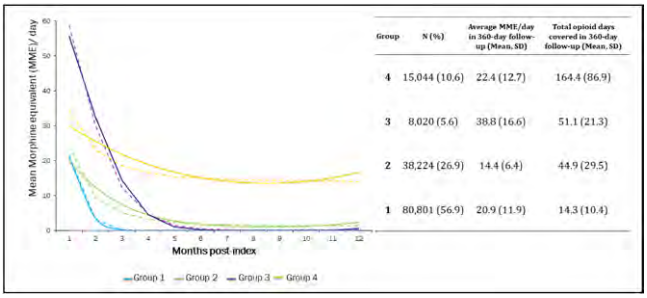


Figure. Trajectories of opioid use patterns after TKR

Table. Predictors of persistent high-dose opioid use in the reduced model

Variable	Multivariable Odds Ratio (95% CI) Predicting High dose vs. Low dose opioid use	P-value
Age (in years)	0.94 (0.93-0.94)	<0.001
Females (Ref=Males)	0.99 (0.93-1.06)	0.78
White race (Ref=Other)	1.25 (1.04-1.50)	0.02
Baseline opioid use (MME/day)	1.22 (1.22-1.23)	<0.001
Substance use (Yes/No)	1.10 (1.02-1.20)	0.02
Benzodiazepine use (Yes/No)	1.22 (1.12-1.32)	<0.001
Anxiolytic use (Yes/No)	1.30 (1.19-1.43)	<0.001
Anticonvulsant use (Yes/No)	0.94 (0.87-1.03)	0.19
Antidepressant use (Yes/No)	1.03 (0.96-1.11)	0.36
NSAID use (Yes/No)	1.07 (1.00-1.14)	0.04

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OP0072

IDENTIFYING POLYMYALGIA RHEUMATICA RELAPSE AND ITS ASSOCIATIONS IN A RETROSPECTIVE COHORT

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Background: Polymyalgia rheumatica (PMR) relapse occurs frequently when tapering glucocorticoids (GC)[1]. Some risk factors for varying definitions of relapse have been identified, although with conflicting results[2]. Identification of relapse and its associations can help identify patients in need of tighter follow up or additional medication.
Objectives: To identify PMR GC-taper related relapse (proportion 1 and 2 years after starting treatment and per year of treatment) and candidate predictors, for a future prediction model.
Methods: In a retrospective cohort of new PMR patients, visiting our hospital from April 2008 – January 2018, all visits > 30 days after starting GC treatment and with > 2.5mg oral prednisolone were used to identify substantial relapses. Relapse was defined in two ways: rheumatologist judgement (RJ) and treatment intensivation (TI). Agreement between RJ and TI at visits was assessed. TI relapse was used going forward for treatment based prediction. The proportion of relapsers after 1 and 2 years (cumulative incidence) and the amount of relapses per year of treatment (incidence rate (IR)), were assessed. Unadjusted associations with candidate predictors, present when starting GC treatment, were assessed using logistic and Poisson regression respectively.
Results: Data from 417 patients was used (figure 1). Relapse occurred at 405 and 325 (of 2455) visits based on RJ and TI respectively. TI relapse (cumulative incidence) after 1 and 2 years was 134 (32%) and 184 (44%) and IR was 0.35 per patient year. Unadjusted significant associations for the cumulative incidence were CRP and ESR at baseline, and symptom duration before treatment (table 1), but only CRP and ESR were significantly associated with yearly IR.

Table 1: Associations between predictors and relapse after 1 and 2 years of treatment and the amount of relapses per year of treatment.

	Within first year			Within first 2 years			Incidence rate		
Predictors	OR	CI		OR	CI		IRR	CI	
Age – years	1.00	0.98	1.03	1.00	0.98	1.02	1.00	0.99	1.01
Sex – ref. Male	1.44	0.95	2.20	1.38	0.94	2.05	1.38	0.79	1.27
Medical history – ref. No									
- inflammatory	1.18	0.75	1.86	1.00	0.65	1.53	1.00	0.95	1.60
- malignancy	0.69	0.36	1.35	0.96	0.53	1.73	0.96	0.64	1.35
- cardiovascular	1.68	0.07	2.95	1.74	1.00	3.03	1.74	0.89	1.66
Smoking – ref. no, n=336									
Stopped	0.85	0.49	1.46	1.16	0.70	1.92	1.16	0.96	1.74
Yes	0.81	0.412	1.57	0.98	0.53	1.82	0.98	0.67	1.40
Symptom duration before baseline – per week, n=411	0.98	0.96	0.998	0.98	0.964	0.997	0.98	0.98	1.00
Clinical disease severity – score 0-8	0.93	0.82	1.07	0.93	0.82	1.05	0.93	0.87	1.02
(Suspected) presence of peripheral arthritis – ref. No	0.73	0.40	1.33	0.67	0.38	1.16	0.67	0.55	1.16
Presence of systemic symptoms – ref. No	0.78	0.51	1.19	0.84	0.57	1.25	0.84	0.79	1.28
CRP – per mg/L, n=363	1.01	1.00	1.01	1.01	1.00	1.01	1.01	1.00	1.01
ESR – per mm/h, n=396	1.02	1.01	1.03	1.02	1.01	1.03	1.02	1.00	1.01
Hb – per mmol/L, n=316	1.03	0.75	1.39	0.99	0.74	1.32	0.99	0.86	1.25
APR – ref. normal, n=376	0.99	0.41	2.40	0.79	0.34	1.83	0.79	0.63	1.68

Ref., reference category; Hb, haemoglobin; APR, acute phase reactants; CI, 95% confidence interval

Conclusion: PMR relapse while tapering GC occurs frequently, and some – although weak – associations were found. Longer symptom duration before treatment decreased chance of relapse, but did not increase the amount of relapses per year of treatment, potentially indicating a more self-limiting disease course. A uniform definition of relapse and identifying further predictors for a potential prediction model is needed to focus GC sparing agents for patients.

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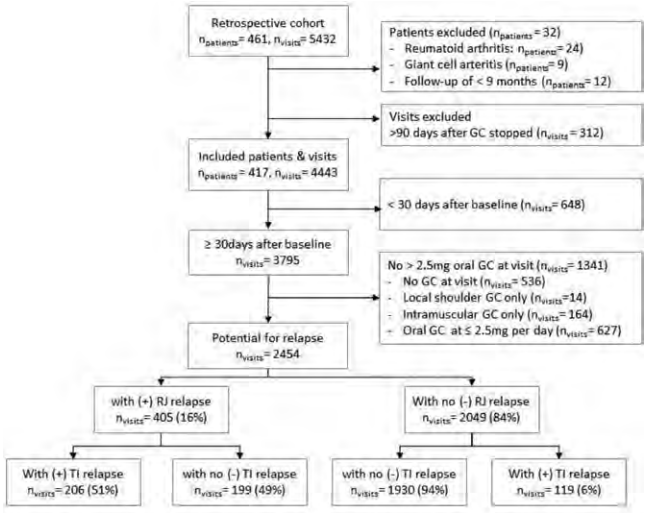


Figure 1: Flow chart detailing eligibility of patients, visits with a potential relapse, and relapse based on different definitions (Reumatologist Judgement (RJ) and Treatment Intensivation (TI)).

Disclosure of Interests: None declared
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OP0073 RISK OF DEVELOPING RHEUMATIC DISEASES IN PATIENTS WITH PALINDROMIC RHEUMATISM IN SOUTH KOREA: A NATION-WIDE POPULATION-BASED STUDY

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Background: Palindromic rheumatism (PR) has known to be three patterns of disease course: clinical remission of attacks, persistent attacks, and evolution to chronic arthritis or systemic disease. The spectrum in progression to chronic diseases of PR, however, is quite variable; rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), systemic sclerosis (SSc), Sjögren's syndrome (SjS), ankylosing spondylitis (AS), relapsing polychondritis (RP), Behçet's disease (BD), sarcoidosis, and psoriatic spondylitis and arthropathy. Because of the small numbers in case-control studies and too aged investigations, now we needs to shed new light on the fate of PR.
Objectives: The aim was to investigate the epidemiology of PR and the risk of developing various rheumatic diseases compared with non-PR individuals, employing the National Health Insurance Service (NHIS) medical claims data, which covers all medical institutions of South Korea.
Methods: The study used 2007-2018 claims data from the Korean Health Insurance Review and Assessment Service (HIRA). The identified 19,724 PR patients from 2010 to 2016 were assessed for the incidence rate (IR) compared with the population in the given year by 100,000 person-year (py). The date of diagnosis was the index date. After matching with non-PR individuals (1:10) for age, sex and the year of index date, we calculated the hazard ratios (HRs) with 95% confidence intervals (CIs). The risk of developing the various rheumatic diseases and adult immunodeficiency syndrome (AIDS) as the outcome diseases in PR cohort was estimated. This risk was compared with that of matched non-PR cohort.
Results: Of 19,724 PR patients (8,665 males and 11,059 females), the mean age was 50.2 ± 14.9 years (47.7 ± 14.4 years in males and 52.6 ± 14.9 years in females, p < 0.001). The ratio of male to female patients with PR was approximately 1:1.28. The annual IR of PR was 7.02 (6.92-7.12) per 100,000 py (6.22 (6.09-6.35) and 7.80 (7.66-7.95) per 100,000 py in males and females, respectively). The mean duration to develop the outcome diseases was significantly shorter in PR cohort compared that of non-PR cohort (19.4 vs. 35.8 months, p < 0.001). The most common outcome disease was RA (7.34% of PR patients; 80.0% of total outcome diseases), followed by AS, SLE, BD, SjS, MCTD, DM/PM, SSc, RP, psoriatic arthropathy, and AIDS in PR cohort. The patients with PR had an increased risk of RA (HR 46.6, 95% CI [41.1-52.7]), psoriatic arthropathy (44.79 [15.2-132.4]), SLE (24.5 [16.2-37.2]), MCTD (22.0 [7.7-63.3]), BD (21.0 [13.8-32.1]), SjS (12.4 [8.5-17.9]), AS (9.0 [6.7-12.2]), DM/PM (6.1 [2.6-14.8]), and SSc (3.8 [1.5-9.6]) but not of AIDS. The risk of developing RA was greater in male patients (HR 58.9, 95% CI [45.6-76.2] vs. 43.2 [37.4-49.8], p for interaction = 0.037) while female patients encountered a higher risk of developing AS (15.8 [8.9-28.1] vs. 7.2 [5.0-10.3], p for interaction = 0.023). The risk of developing RA, SLE, SjS, and BD were significantly more highly affected in younger age (p for interaction < 0.001, = 0.003, 0.002, and 0.017, at each).
Conclusion: This nationwide, population-based cohort study demonstrated that patients with PR had an increased risk of developing various rheumatic diseases, not only RA but also psoriatic arthropathy. Therefore, patients with PR needs to be cautiously followed up for their potential of diverse outcome other than RA: RA, SLE, SjS, and BD in younger patients, RA in males, and AS in females, in particular.
Disclosure of Interests: None declared
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OP0074 MULTIMORBIDITY CLUSTERS, DETERMINANTS AND TRAJECTORIES IN OSTEOARTHRITIS IN THE UK: FINDINGS FROM THE CLINICAL PRACTICE RESEARCH DATALINK

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Background: Multimorbidity (≥2 chronic conditions) escalates the risk of adverse health outcomes. However, its burden in people with osteoarthritis (OA) remains largely unknown.
Objectives: To identify the clusters of patients with multimorbidity and associated factors in OA and non-OA populations and to estimate the risk of developing multimorbidity clusters after the index date (after diagnosis).
Methods: The study used the Clinical Practice Research Datalink – a primary care database from the UK. Firstly, age, sex and practice matched OA and non-OA people aged 20+ were identified to explore patterns and associations of clusters of multimorbidity within each group. Non-OA controls were assigned with same index date as that of matched OA cases. Secondly, multimorbidity trajectories for 20 years after the index date were examined in people without any comorbidities at baseline in both OA and non-OA groups. Latent class analysis was used to identify clusters and latent class growth modelling was used for cluster trajectories. The associations between clusters and age, sex, body mass index (BMI), alcohol use, smoking habits at baseline were quantified through multinomial logistic regression.
Results: In total, 47 long-term conditions were studied in 443,822 people (OA-221922; non-OA- 221900), with a mean age of 62 years (standard deviation ± 13 years), and 58% being women. The prevalence of multimorbidity was 76.6% and 68.9% in the OA and non-OA groups, respectively. In the OA group five clusters were identified including relatively healthy (18%), 'cardiovascular (CVD) and musculoskeletal (MSK)' (12.3%), metabolic syndrome (28.2%), 'pain and psychological (9.1%), and 'musculoskeletal' (32.4%). The non-OA group had similar patterns except that the 'pain+ psychological' cluster was replaced by 'thyroid and psychological'. (Figure 1) Among people with OA, 'CVD+MSK' and metabolic syndrome clusters were strongly associated with obesity with a relative risk ratio (RRR) of 2.04 (95% CI 1.95-2.13) and 2.10 (95% CI 2.03-2.17), respectively. Women had four times higher risk of being in the 'pain+ psychological' cluster than men when compared to the gender ratio in the healthy cluster, (RRR 4.28; 95% CI 4.09-4.48). In the non-OA group, obesity was significantly associated with all the clusters.

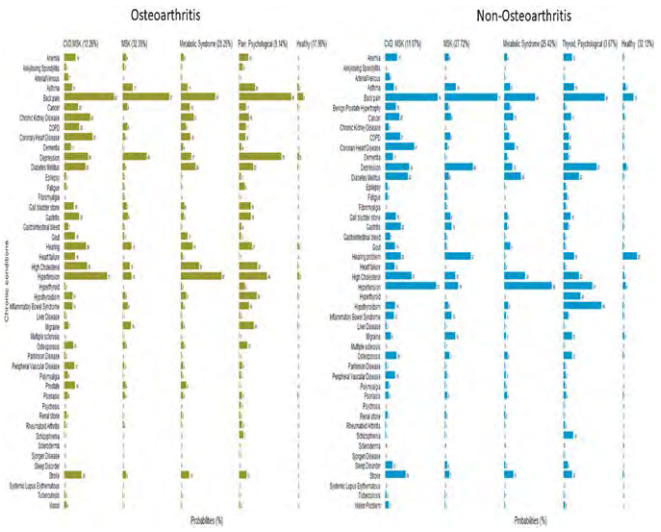


Figure 1 : Posterior probability distribution of chronic conditions across the clusters in Osteoarthritis (OA, n=221922) and Non-Osteoarthritis (Non-OA, n=221900) group COPD- Chronic Obstructive Pulmonary Disease; CVD- Cardiovascular; MSK- Musculoskeletal

OA (n=24139) and non-OA (n=24144) groups had five and four multimorbidity trajectory clusters, respectively. Among the OA population, 2.7% had rapid onset of multimorbidity, 9.5% had gradual onset and 11.6% had slow onset, whereas among the non-OA population, there was no rapid onset cluster, 4.6% had gradual onset and 14.3% had slow onset of multimorbidity. (Figure 2)

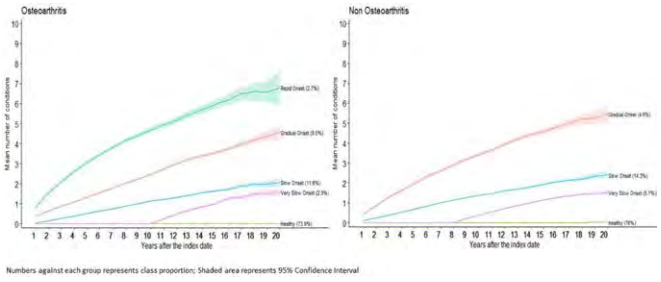


Figure 2 : Clusters of multimorbidity trajectories after index date in OA (n=24139) and Non-OA (n=24144)

Conclusion: Distinct identified groups in OA and non-OA suggests further research for possible biological linkage within each cluster. The rapid onset of multimorbidity in OA should be considered for chronic disease management.
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What is new in axial spondyloarthritis: clinical and imaging outcomes?

OP0075

SPINAL RADIOGRAPHIC PROGRESSION IN AXIAL SPONDYLOARTHRITIS AND THE IMPACT OF CLASSIFICATION AS NONRADIOGRAPHIC VERSUS RADIOGRAPHIC DISEASE

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Background: Data on spinal radiographic progression is more limited in nonradiographic axial spondyloarthritis (nr-axSpA) than in the radiographic disease state (r-axSpA). It remains unclear, whether radiographic sacroiliitis is by itself associated with progression of spinal structural damage.
Objectives: To investigate whether spinal radiographic progression relates to structural damage at the sacroiliac level in axSpA by means of statistical mediation analyses in a large prospective real-life cohort of patients with axSpA.
Methods: Patients from the Swiss Clinical Quality Management cohort were included if they fulfilled the ASAS classification criteria and could be classified as nr-axSpA or r-axSpA after central scoring of pelvis radiographs. Spinal radiographs performed every 2 years were scored according to the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS). The relationship between classification status and spinal progression over 2 years was investigated using binomial generalized estimating equations models with adjustment for sex, ankylosing spondylitis disease activity score (ASDAS) and tumor necrosis factor inhibitor treatment. Baseline spinal damage was considered an intermediate variable and included in sensitivity analyses, as were additional variables potentially influencing radiographic progression.
Results: In total, 88 nr-axSpA and 418 r-axSpA patients contributed to data for 725 radiographic intervals (Table 1). Mean (SD) mSASSS change over 2 years was 0.16 (0.62) units in nr-axSpA and 0.92 (2.78) units in r-axSpA, p=0.01. Nr-axSpA was associated with a significantly lower progression over 2 years (defined as an increase in ≥2 mSASSS units) in adjusted analyses (OR 0.33, 95%CI 0.13; 0.83), confirmed with progression defined as the formation of ≥1 syndesmophyte. Mediation analyses revealed that sacroiliitis exerted its effect on spinal progression indirectly by being associated with the appearance of a first syndesmophyte (OR 0.09, 95%CI 0.02; 0.36 for nr-axSpA vs r-axSpA) (Fig. 1 and 2). Baseline syndesmophytes were predictors of further progression.

Table 1. Baseline characteristics at first radiograph.

Parameter	N 506	nr-axSpA N = 88	r-axSpA N = 418	P
Female sex, %	506	54.5	33.7	<0.001
Age, y	506	39.5±11.1	40.4±11.0	0.52
Symptom duration, y	498	10.0±9.9	14.0±9.8	<0.001
HLA-B27 positive, %	452	71.6	80.7	0.09
BASDAI	427	4.6±2.0	4.2±2.3	0.26
ASDAS	408	2.8±0.9	2.8±1.1	0.74
Elevated CRP, %	422	30.6	40.6	0.14
BASFI	433	2.8±2.2	3.1±2.5	0.71
BASMI	435	1.1±1.4	2.2±2.0	<0.001
mSASSS	506	0.9±1.5	6.8±12.7	<0.001
Syndesmophytes, %	506	9.1	35.2	<0.001
On TNFi, %	506	19.3	36.4	0.002

Conclusion: Spinal structural damage is mainly restricted to patients with r-axSpA, leading to relevant prognostic and therapeutic implications.
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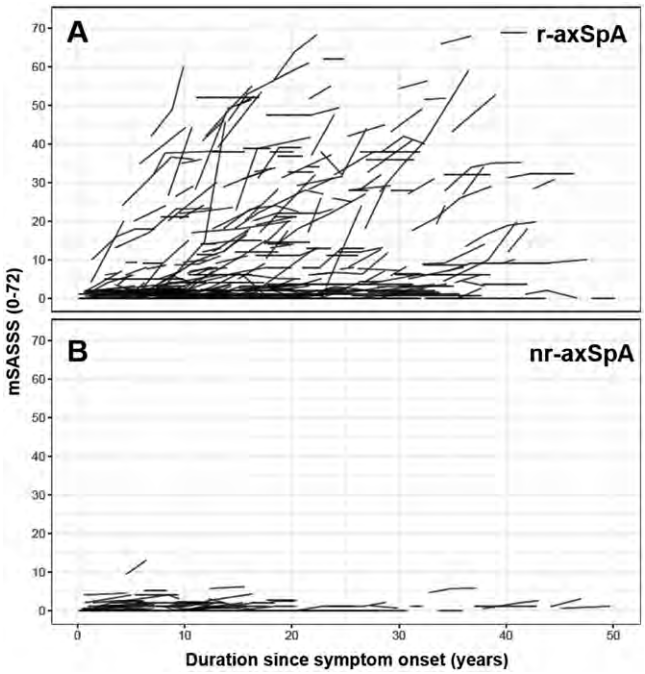


Fig. 1. Modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) for individual patients plotted as a function of duration since symptom onset.

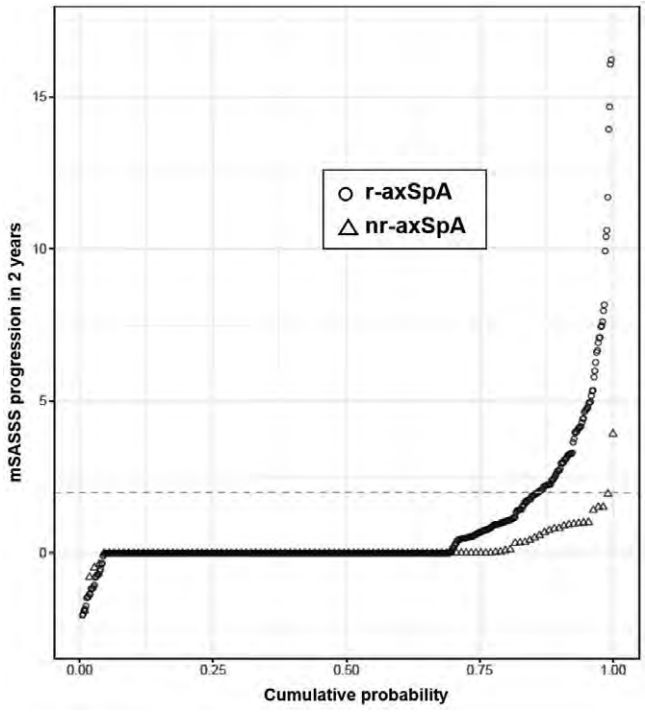


Fig. 2. Two-year mSASSS progression depicted in a cumulative probability plot. Progression was defined as an increase in mSASSS of at least 2 units (dotted line) in 2 years.

Pharma; Director of Imaging Rheumatology BV, Robert B.M. Landewé Consultant of: AbbVie; AstraZeneca; Bristol-Myers Squibb; Eli Lilly & Co.; Galapagos NV; Novartis; Pfizer; UCB Pharma, Kristina Buerki: None declared, Michael Nissen Grant/research support from: Abbvie, Consultant of: Novartis, Lilly, Abbvie, Celgene and Pfizer, Speakers bureau: Novartis, Lilly, Abbvie, Celgene and Pfizer, Burkhard Moeller: None declared, Pascal Zufferey: None declared, Pascale Exer: None declared, Adrian Ciurea Consultant of: Consulting and/or speaking fees from AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Merck Sharp & Dohme, Novartis and Pfizer.

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OP0076

CLINICAL DISEASE ACTIVITY, MRI SPINAL INFLAMMATION AND ENTHESITIS ARE KEY DETERMINANTS OF IMPAIRMENT OF SPINAL MOBILITY IN EARLY AXIAL SPONDYLOARTHRITIS – DATA FROM THE DESIR COHORT

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Background: It has been shown that spinal mobility impairment in axial spondyloarthritis (axSpA) is independently determined both by irreversible spinal damage and by reversible spinal inflammation. However, these relationships have only been investigated in patients with longstanding disease (ankylosing spondylitis). Moreover, only the composite score Bath Ankylosing Spondylitis Metrology Index (BASMI) has been evaluated rather than individual mobility assessments.
Objectives: Our aim was to investigate the determinants of spinal mobility in patients with early axSpA.
Methods: We analysed longitudinal data from the DEvenir des Spondyloarthrites Indifférenciées Récentes (DESIR) cohort, collected during the first five years of follow-up. We selected patients with a definite diagnosis of axSpA according to the treating rheumatologist, at the end of follow-up (month 60). Associations were tested using generalised estimating equations (GEE), a multilevel approach that adjusts for within-patient correlation. The Bath Ankylosing Spondylitis Metrology Index (BASMI) or the individual components of BASMI (lateral spinal flexion, tragus-to-wall distance, cervical rotation, anterior lumbar flexion, maximal intermalleolar distance) were used as dependent variables, and clinical and demographic variables were used as independent variables in univariable models. Spinal MRI inflammation was assessed using the Berlin scoring system and radiographic structural damage was assessed using the modified Stoke ankylosing spondylitis spinal score (mSASSS)]. As physical function and quality of life are considered to be hierarchically superior to spinal mobility, they were not included in the analysis. Multivariable models were built, adjusting for potential confounding. Variables with a p-value <0.10 were re-tested in the multivariable models. Six models were built, one regarding the BASMI total score and five regarding the individual components of BASMI.
Results: Data from 644 patients and 5152 visits were analysed. In the multivariable analyses (table), we found an independent association between higher BASMI values and age [adjusted B (aB)=1.02, confidence interval (CI)=1.01-1.03], Ankylosing Spondylitis Disease Activity Score-C Reactive Protein (ASDAS-CRP) (aB=1.23, CI=1.15-1.32), enthesitis score (aB=1.02, CI=1.01-1.04) and MRI inflammation score (aB=1.13, CI=1.05-1.23). All individual BASMI components were independently associated with ASDAS-CRP. Apart from maximal intermalleolar distance, all other mobility measures were associated with MRI spinal inflammation. Lateral spinal flexion, cervical rotation and maximal intermalleolar distance were associated with the enthesitis score. mSASSS was associated with lateral

Table: Multivariable GEE results (aB; 95% CI) presenting independent associations between BASMI (or its components) and clinical and demographic variables

	Mobility measures where higher values represent worse mobility		Mobility measures where higher values represent better mobility			
	BASMI	Tragus-to-wall distance	Lateral spinal flexion	Cervical rotation	Anterior lumbar flexion (modified Schober)	Maximal intermalleolar distance
Age	1.02 (1.01-1.03)		0.91 (0.87-0.96)	0.79 (0.69-0.90)		0.71 (0.61-0.82)
Male gender	#	2.35 (1.73-3.18)	5.01 (2.15 11.67)	#		171.35 (16.85-1742.22)
Education*	#	2.10 (1.06-4.16)	#	#		388.23 (32.09-4696.38)
BMI	0.97 (0.95-0.99)	1.04 (1.00-1.09)			1.08 (1.05-1.11)	
HLA-B27 positive	0.82 (0.70-0.97)		#	13.99 (1.09-180.20)		19.07 (1.56-233.62)
Symptoms' duration			0.76 (0.65-0.88)		1.07 (1.03-1.12)	1.72 (1.30-2.27)
Currently employed					#	
Current arthritis		#		0.01 (0.00-0.86)	#	
ASDAS-CRP	1.23 (1.15-1.32)	1.28 (1.07-1.52)	0.56 (0.39-0.79)	0.12 (0.04-0.38)	0.87 (0.79-0.97)	0.14 (0.08-0.25)
Enthesitis score	1.02 (1.01-1.04)		0.92 (0.86-1.00)	0.73 (0.59-0.89)		0.78 (0.67-0.89)
mSASSS	#	1.17 (0.90-1.51)**	0.77 (0.610-0.98)	0.42 (0.16-1.11)**	#	
MRI inflammation score	1.13 (1.05-1.23)	1.33 (1.08-1.64)	0.59 (0.44-0.80)	0.41 (0.17-0.95)	0.92 (0.86-0.98)	

#Statistically significant in the univariable models but excluded from the best-fit multivariable model; *Education at baseline (university or equivalent); **mSASSS not significant in the multivariable model but included as it was found to be a contributory variable improving model-fit

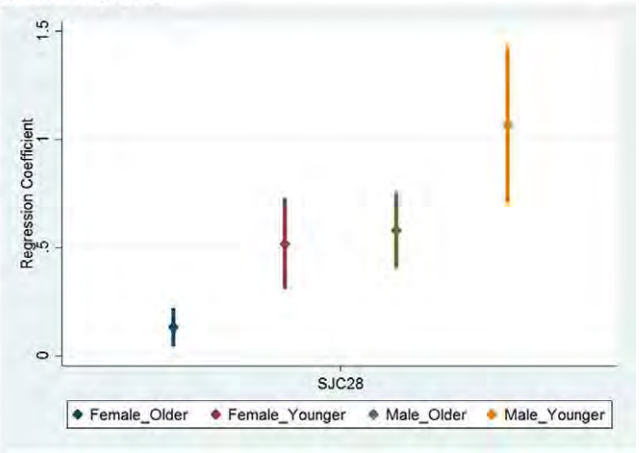
spinal flexion and a contributory factor to tragus-to-wall distance and cervical rotation.
Conclusion: In early axSpA, spinal mobility impairment is independently determined by clinical disease activity, MRI spinal inflammation and the severity of enthesitis. Maximal intermalleolar distance (which is not a true measure of spinal mobility) was the only measure not associated with MRI spinal inflammation. The influence of spinal inflammation prevails in the early phase of axSpA while spinal damage becomes more relevant in later disease stages.
References: None.
Disclosure of Interests: Pedro Carvalho: None declared, Ana Marreiros: None declared, Joao Eurico Fonseca: None declared, Adeline Ruyssen-Witrand Grant/research support from: Abbvie, Pfizer, Consultant of: Abbvie, BMS, Lilly, Mylan, Novartis, Pfizer, Sandoz, Sanofi-Genzyme, Pedro M Machado Consultant of: PMM: Abbvie, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Roche and UCB, Speakers bureau: PMM: Abbvie, BMS, Lilly, MSD, Novartis, Pfizer, Roche and UCB
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OP0077 DETERMINANTS OF THE PHYSICIAN'S GLOBAL ASSESSMENT AND INFLUENCE OF CONTEXTUAL FACTORS IN EARLY AXIAL SPONDYLOARTHRITIS

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Background: In RMDs, the physician's global assessment (PhGA) is a major factor of treatment decision. It is not well-known which disease manifestations contribute to PhGA in early axSpA and if contextual factors have an impact.
Objectives: To investigate determinants of PhGA and the influence of contextual factors on this relationship in patients with early axSpA.
Methods: Five-year data from DESIR, a cohort of early axSpA, were analysed. Clinical data were collected every 6 months up to 2 years and annually thereafter. The primary analysis included all patients, and the subgroup analysis patients with follow-up MRI at 2 and/or 5 years. PhGA over 5 years was the outcome of interest. Univariable generalized estimating equation (GEE) models were used to investigate relationships between potential determinants and PhGA. Longitudinal relationships were investigated in autoregressive models. Effect modification by contextual factors (educational level, gender and age) was tested and, if significant, models were stratified. Univariable analyses were chosen to better assess the contributory explanatory effects of each of the determinants in each of the strata.
Results: A total of 708 patients were included, mean age 33.7 (SD 8.6) years, 46% male, 41% lower educated. The subgroup consisted of 220 patients with similar characteristics. Higher BASDAI questions 1-6, SJC28, TJC53, Maastricht Ankylosing Spondylitis Enthesitis Score (MASES), CRP and BASMI were associated with a higher PhGA (Table 1). Gender and age were effect modifiers of SJC28; the effect was largest in the younger male stratum (β [95% CI]; 1.07 [0.71, 1.43]), and smallest in the older female stratum (0.13 [0.04, 0.22]) (Figure 1). Autoregressive GEE models revealed the same determinants of PhGA and the same pattern of effect modification by gender and age.
Conclusion: Patient's subjective symptoms, peripheral arthritis, enthesitis, higher CRP and impaired spinal mobility contribute to explain PhGA in patients with early axSpA irrespective of gender and age. But physicians consider the presence of swollen joints as more important in males than in females.

Figure. Impact of swollen joint count on the physician's global assessment across gender and age groups



Regression coefficients (95% CI) of the effect of SJC28 on PhGA in the univariable GEE analyses across gender/age-stratified groups (in an ascending order).

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OP0078 MAPPING FROM THE ANKYLOSING SPONDYLITIS DISEASE ACTIVITY SCORE (ASDAS) TO EQ5D IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: Clinical studies often omit outcomes that allow the direct estimation of Quality Adjusted Life Years (QALYs) for use in cost effectiveness analyses crucial for informing policy decisions. This means analysts often have to estimate the relationship, "map", between included outcomes and preference based ones like the EuroQoL EQ5D. In ankylosing spondylitis (AS), the relationship between BASDAI/BASFI and EQ5D has been established but the emergence and growing use of the Ankylosing Spondylitis Disease Activity Score (ASDAS), a new composite index used to assess clinical disease activity, means new mapping tools are required. Furthermore mapping has never been done for the entire axial

Table 1. Factors associated with PhGA over time in gender/age-stratified groups in univariable analysis

	Female/Older (n=200)	Female/Younger (n=181)	Male/Older (n=154)	Male/Younger (n=173)
		Coefficient (95% CI)		
BASDAI Q1 (fatigue, 0-10)	0.39 (0.34, 0.44)	0.39 (0.34, 0.44)	0.41 (0.35, 0.46)	0.46 (0.41, 0.51)
BASDAI Q2 (back pain, 0-10)	0.49 (0.45, 0.54)	0.53 (0.49, 0.57)	0.48 (0.43, 0.53)	0.58 (0.54, 0.63)
BASDAI Q3 (peripheral joint pain, 0-10)	0.31 (0.27, 0.36)	0.36 (0.31, 0.41)	0.32 (0.27, 0.37)	0.43 (0.37, 0.48)
BASDAI Q4 (enthesitis, 0-10)	0.37 (0.33, 0.41)	0.42 (0.37, 0.46)	0.36 (0.31, 0.41)	0.52 (0.47, 0.56)
BASDAI Q5 (severity of morning stiffness, 0-10)	0.42 (0.37, 0.46)	0.45 (0.40, 0.49)	0.44 (0.40, 0.49)	0.58 (0.54, 0.63)
BASDAI Q6 (duration of morning stiffness, 0-10)	0.30 (0.25, 0.35)	0.35 (0.30, 0.39)	0.36 (0.31, 0.41)	0.50 (0.45, 0.56)
BASMI linear (0-10)	0.61 (0.45, 0.78)	0.67 (0.48, 0.86)	0.49 (0.30, 0.68)	0.95 (0.75, 1.15)
SJC28 (0-28)	**0.13 (0.04, 0.22)**	**0.52 (0.31, 0.73)**	**0.58 (0.40, 0.76)**	**1.07 (0.71, 1.43)**
TJC53 (0-159) ¶	0.05 (0.04, 0.06)	0.13 (0.11, 0.16)	0.13 (0.11, 0.16)	0.15 (0.13, 0.18)
MASES (0-39)	0.10 (0.08, 0.12)	0.15 (0.12, 0.17)	0.18 (0.14, 0.23)	0.30 (0.25, 0.35)
CRP (mg/L)	0.02 (0.01, 0.04)	0.03 (0.01, 0.05)	0.06 (0.04, 0.07)	0.04 (0.03, 0.05)
Any EAM (presence vs absence)	-0.13 (-0.49, 0.23)	-0.20 (-0.58, 0.19)	-0.26 (-0.68, 0.17)	-0.28 (-0.69, 0.14)
SPARCC-spine (0-414) §	0.06 (-0.11, 0.22)	0.05 (-0.11, 0.20)	0.02 (-0.03, 0.06)	0.05 (-0.04, 0.14)
SPARCC-SIJ (0-72) §	-0.02 (-0.13, 0.09)	0.01 (-0.08, 0.10)	0.05 (-0.01, 0.11)	0.01 (-0.04, 0.06)

¶ Each joint graded 0-3
§ Coefficients were estimated in the subgroup

spondyloarthritis (axSpA) spectrum of patients i.e. including not only patients with AS but also those with non-radiographic axSpA.

Objectives: To estimate a robust mapping between ASDAS and EQ5D (3 level version) and to test its performance out of sample (external validation) in patients with axSpA.

Methods: Data from an electronic, prospective, nationwide Rheumatic Disease Portuguese Register (Reuma.pt) provided data pertaining to 1140 patients (5483 observations) with a confirmed diagnosis of axSpA was used to develop a model to predict EQ5D from the ASDAS score. We compared a range of different statistical models developed to deal with the complex distributional features of health utility data. A range of criteria examining model fit across the spectrum of disease severity were used to select preferred models. A smaller dataset for out of sample validation from the SPondyloArthritis Caught Early (SPACE) cohort was used, providing data from 317 patients (1225 observations) at five European centres.

Results: Characteristics of patients from the Reuma.pt and SPACE are presented in the table. There is a non-linear relationship between ASDAS and EQ5D. We found that a four component mixture model based on a bespoke distribution, with one component constrained to reflect the mass of observations at full health, was the best fitting of the ASDAS models estimated (figure). ASDAS squared and age squared featured as within component variables. The model demonstrated close fit to the observed data where ASDAS was less than 4 but diverged from the mean of the data where ASDAS was higher. There is a very limited data at this more severe level of disease activity. In the out of sample testing, the model continued to perform well overall and exhibited the same divergence from the observed data only where data was sparse.

Conclusion: There is a clear relationship between ASDAS and EQ5D that we were able to model reliably using bespoke mixture model based methods. There is more uncertainty regarding model fit at very high levels of disease activity owing to the relative paucity of data from patients in such disease activity state. Future analyses may wish to focus on these severely affected patients in order to improve the robustness of model estimates.

Table. Characteristics of patients from the Reuma.pt and SPACE datasets

	REUMA (n = 1140)					SPACE (n = 317)				
	N	Mean	sd	min	max	N	mean	sd	min	max
Age at visit (yrs)	5483	46.58	11.99	17.70	82.70	1225	31.44	7.78	16.14	50.46
Number of visits	5483	4.81	5.26	1.00	39.00	1225	4.05	1.60	1.00	8.00
ASDAS total score	4886	2.02	0.97	0.60	6.30	1181	2.10	0.96	0.64	5.44
BASDAI total score	5383	2.97	2.26	0.00	10.00	1211	3.27	2.20	0.00	9.80
BASFI total score	5258	2.84	2.41	0.00	9.88	1205	1.92	2.09	0.00	9.30
EQ-5D-3L	5483	0.70	0.26	-0.59	1.00	1225	0.69	0.25	-0.59	1.00
Proportion Male	5483	0.56				1225	0.50			

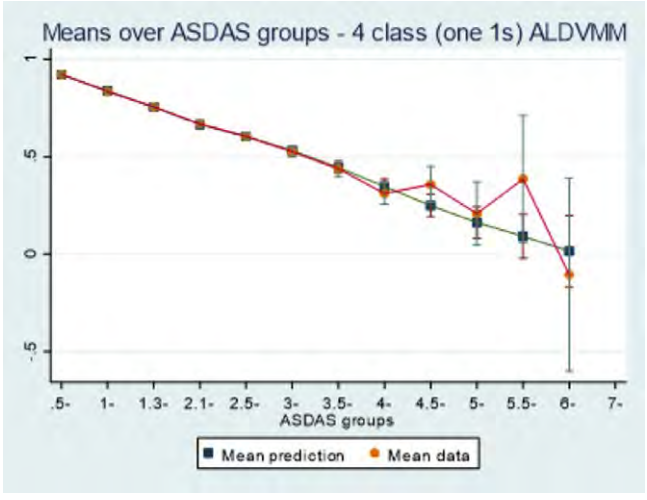


Figure. Mean observed versus fitted values for the preferred model mapping EQ5D-3L from ASDAS (Reuma.Pt dataset)

Acknowledgments: We would like to that all the contributors to the Reuma.Pt and SPACE datasets.

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OP0079 PRELIMINARY DEFINITION OF A POSITIVE MRI FOR STRUCTURAL LESIONS IN THE SACROILIAC JOINTS IN AXIAL SPONDYLOARTHRITIS

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Background: There is lack of international consensus as to what defines a structural lesion on MRI of the sacroiliac joints (SIJ) typical of axial spondyloarthritis (axSpA). The ASAS MRI group has generated updated consensus lesion definitions that describe each of the MRI lesions in the SIJ[1]. These definitions have been evaluated by 7 readers from the ASAS-MRI group on MRI images from the ASAS Classification Cohort.

Objectives: We aimed to identify quantitative cut-offs based on numbers of slices and SIJ quadrants that define a positive MRI for structural lesions typical of axSpA, the gold standard being majority central reader decision as to the presence of a structural lesion typical of axSpA with high confidence.

Methods: MRI structural lesions meeting ASAS definitions were recorded in an eCRF that comprises global assessment (structural lesion typical of axSpA present/absent and degree of confidence (-4 (absent) to +4 (present)), and detailed scoring of lesions per SIJ quadrant. Detailed scoring was based only on assessment of DICOM images (n =148). We calculated sensitivity and specificity for numbers of SIJ quadrants and consecutive slices with erosion, sclerosis, and fat lesions where a majority of readers (≥4/7) agreed as to the presence of a structural lesion typical of axSpA with high confidence (≥ +3). We tested candidate lesion definitions for predictive diagnostic utility in cases assessed after 4.4 years of follow up by the local rheumatologist.

Results: Structural lesions typical of axSpA were observed by majority read in 33 (32.4%) of 102 cases diagnosed with axSpA, and 3 (6.8%) of 44 cases without axSpA and 29 cases were assigned a high degree of confidence (≥ +3) by a majority of readers. Cut-offs achieving specificity of 95% were erosion in ≥2 consecutive slices (sensitivity 83%), erosion ≥3 SIJ quadrants (sensitivity 90%), and fat lesion (≥1cm horizontal depth) in ≥1 SIJ quadrant (sensitivity 59%) (Table). These had very high positive predictive values (>95%) for diagnosis of axSpA in cases diagnosed by the rheumatologist after 4.4 years follow up.

Conclusion: ASAS-defined erosion in ≥2 consecutive slices or in ≥3 SIJ quadrants and ASAS-defined fat lesion with depth >1cm in ≥1 SIJ quadrant are high priority candidates for defining an MRI structural lesion typical of axSpA. This will require similar assessment in additional axSpA cohorts.

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Table 1. Majority readers agree structural lesion indicative of axSpA is present with confidence ≥3/4 is the gold-standard external reference

	Sensitivity	Specificity
Erosion Score ≥1 SIJ qdr	93.1 (77.2-99.2)	80.6 (72.4-87.3)
Erosion Score ≥2 SIJ qdr	93.1 (77.2-99.2)	90.8 (84.1-95.3)
Erosion Score ≥3 SIJ qdr	89.7 (72.6-97.8)	95.8 (90.5-98.6)
Erosion in 2 consecutive slices	82.8 (64.2-94.2)	95.0 (89.3-98.1)
Fat lesion ≥1 SIJ qdr	82.8 (64.2-94.2)	81.5 (73.4-88.0)
Fat lesion ≥2 SIJ qdr	69.0 (49.2-84.7)	86.6 (79.1-92.1)
Fat lesion ≥3 SIJ qdr	62.1 (42.3-79.3)	91.6 (85.1-95.9)
Fat lesion in 2 consecutive slices	55.2 (35.7-73.6)	93.3 (87.2-97.1)
Fat lesion (>1cm depth) ≥1	58.6 (38.9-76.5)	**95.0 (89.3-98.1)**
Fat lesion (>1cm depth) ≥2	55.2 (35.7-73.6)	95.8 (90.5-98.6)
Fat lesion (>1cm depth) ≥3	51.7 (32.5-70.6)	97.5 (92.8-99.5)
Fat lesion (>1cm depth) in 2 consecutive slices	48.3 (29.4-67.5)	97.5 (92.8-99.5)

Table. SIJ qdr: sacroiliac joint quadrant

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OP0080 CENTRAL SENSITIZATION AND ILLNESS PERCEPTIONS SHOULD BE TAKEN INTO ACCOUNT WHEN INTERPRETING DISEASE ACTIVITY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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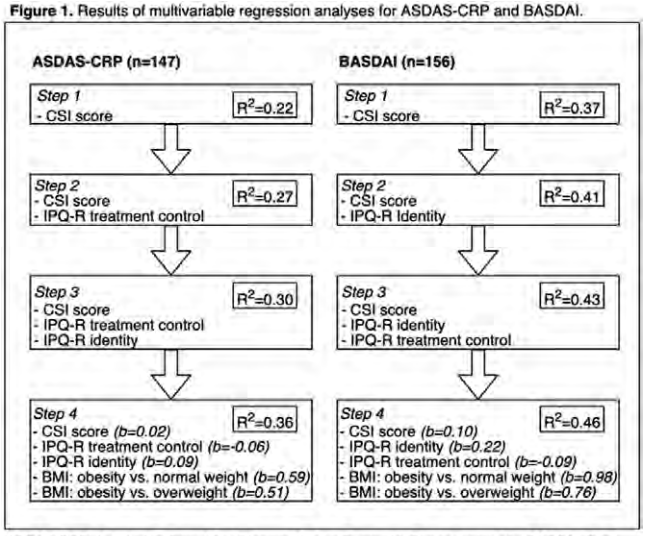
Background: Up to 40% of ankylosing spondylitis patients report persistently high pain scores of >4 (scale of 0-10) even after responding to long-term TNF-alpha blocking therapy.[1] In other rheumatic diseases, nociplastic pain (due to altered functioning of the nervous system leading to peripheral and central sensitization) is common.[2] In axial spondyloarthritis (axSpA), patient illness and pain perceptions were shown to influence disease outcome.[3] Therefore, we hypothesized that central sensitization and patients' illness perceptions are associated with persistently high disease activity in axSpA.

Objectives: To investigate to what extent central sensitization, pain catastrophizing and patients' perceptions play a role in axSpA and to explore associations with disease activity.

Methods: Between April and September 2019, consecutive outpatients from the Groningen Leeuwarden axSpA (GLAS) cohort,[4] an ongoing large prospective cohort, were included in this study. Besides the standardized assessments, patients filled out three additional questionnaires: Central Sensitization Inventory (CSI), Pain Catastrophizing Scale (PCS) and Revised Illness Perception Questionnaire (IPQ-R). Univariable and multivariable linear regression analyses were used to investigate the association of CSI, PCS and each of the eight subscales of the IPQ-R, and disease activity assessments ASDAS-CRP, BASDAI, and CRP. We corrected for the following potential confounders: gender, symptom duration, BMI, educational level, smoking status and HLA-B27 status.

Results: Of 171 included patients, 58% were male, 79% were HLA-B27 positive, median symptom duration was 21 (IQR 10-32), mean ASDAS-CRP 2.1 ± 1.0, mean BASDAI 3.9 ± 2.2 and median CRP 2.9 (IQR 1.2-6.3). Mean CSI score was 37.8 ± 14.1 (scale of 0-100), and 44% of patients scored ≥40 on the CSI.[5] Median PCS score was 15 (IQR 7-22) (scale of 0-52), median IPQ-R illness identity subscore 3 (IQR 2-4) (scale of 0-14) and mean IPQ-R treatment control subscore 18.1 ± 3.4 (scale of 5-25). In univariable regression analysis, CSI and PCS scores and IPQ-R subscores all showed significant associations with ASDAS-CRP, and all except the IPQ-R subscale personal control showed significant associations with BASDAI. Only IPQ-R treatment control was significantly associated with CRP. Central sensitization, two IPQ-R subscales (perceived treatment control and the number of symptoms patients attributed to their axSpA: illness identity) and BMI were independently associated with disease activity assessments BASDAI (R^2=0.46) and ASDAS-CRP (R^2=0.36) (Figure 1).

Figure 1. Results of multivariable regression analyses for ASDAS-CRP and BASDAI.



ASDAS-CRP: Ankylosing Spondylitis Disease Activity Score with C-reactive protein; BASDAI: Bath Ankylosing Spondylitis Disease Activity Score; CSI: Central Sensitization Inventory; IPQ-R: Revised Illness Perception Questionnaire; BMI: Body Mass Index.

Conclusion: In this axSpA population with long-term disease, 44% scored above the CSI cutoff point of 40, indicating a high probability of central sensitization. CSI score, illness identity and treatment control were independently associated with disease activity assessments.

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OP0081 THE IMPACT OF AXIAL SPONDYLOARTHRITIS ON PATIENTS' SEXUAL LIFE: RESULTS FROM THE EUROPEAN MAP OF AXIAL SPONDYLOARTHRITIS (EMAS)

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Background: Axial Spondyloarthritis (axSpA) involves a great degree of functional limitation in daily activities and psychological health, which can impact patients' sexual life.

Objectives: To study the determinants of reduced frequency of sexual activity and intimacy since disease onset in axSpA patients.

Methods: Data from 2,846 unselected patients of the European Map of Axial Spondyloarthritis (EMAS) through an online survey (2017-2018) across 13 countries were analysed. The impact of axSpA on patients' sexual life was evaluated by a question assessing changes in the frequency of intimate relations since the onset of axSpA on a 5 point Likert scale. Impact of axSpA on the spousal relationship since disease onset was also assessed using 5 point Likert scale. Other lifestyle variables included smoking and physical activity and burden of disease [BASDAI (0-10), spinal stiffness (3-12), functional limitation in intimate relations (0-2), and psychological distress (GHQ-12)]. Regression analysis were carried out to determine the relative weight of the assessed variables.

Results: EMAS total sample mean age was 43.9 years, 61.3% were female, 48.1% had a university degree, and 67.9% were married. Out of the 2,515 participants that reported on the frequency of intimate relations since disease onset, 56.4% declared that it was less or much less than before; 74.1% declared high or medium limitation in intimate relations; and 30.4% reported worsening relations with their spouse. A lower frequency of intimate relations was related to: older age, female gender, higher BASDAI, spinal stiffness, higher functional limitation in intimate relations, higher psychological distress, self-reported diagnosis of depression, worsening relationship with spouse since disease onset, higher BMI, smoking, lack of physical activity, and lack of biologics use. In the multivariate regression analysis, the most strongly associated variables with lower frequency of intimate relations were: functional limitation in intimate relations (β = 0.218; 95% CI 0.185 – 0.251), worse relationship with spouse (β = 0.207; 95% CI = 0.165 - 0.250), female gender (β = 0.150; 95% CI 0.071 – 0.229), and no engaging in physical activity (β = -0.135; 95% CI -0.234 – -0.036) (Table 2).

Conclusion: EMAS results reveal a great impact of axSpA on patients' sexual life, with multiple sociodemographic, lifestyle and PROs being associated with a lower frequency of intimate relations.

Table 1. Regression analysis to predict frequency of intimate relations

	Simple linear regression			Multivariable stepwise linear regression		
	B	95% CI	p	B	95% CI	p
Age (Years)	0.007	0.004,0.010	**<0.001**	0.010	0.007,0.013	**<0.001**
Gender (Female)	0.215	0.146,0.284	**<0.001**	0.150	0.071,0.229	**<0.001**
BASDAI	0.124	0.107,0.141	**<0.001**	0.029	0.007,0.050	**0.010**
Spinal Stiffness	0.089	0.075,0.102	**<0.001**	NA	NA	0.214
Functional Limitation – Intimate relations	0.297	0.271,0.323	**<0.001**	0.218	0.185,0.251	**<0.001**
GHQ-12	0.067	0.059,0.075	**<0.001**	0.035	0.024,0.045	**<0.001**
Depression (Yes)	0.375	0.298,0.452	**<0.001**	NA	NA	0.064
Relationship with spouse	0.343	0.306,0.380	**<0.001**	0.207	0.165,0.250	**<0.001**
BMI	0.017	0.011,0.024	**<0.001**	0.008	0.001,0.015	**0.031**
Smoking (Yes)	0.075	0.002,0.148	**0.044**	NA	NA	0.907
Physical activity (Yes)	-0.212	-0.306,-0.119	**<0.001**	-0.135	-0.234,-0.036	**0.007**
Biologics (Yes)	0.188	0.110, 0.267	**<0.001**	NA	NA	0.185

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OP0082

GROWTH AND DEVELOPMENT OF CHILDREN FROM MOTHERS WITH ANKYLOSING SPONDYLITIS

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Background: Ankylosing spondylitis (AS) is a chronic inflammatory disease featured with involvement of sacroiliac joint and starts in the second or third decade of life. Female patients with AS are mostly in childbearing ages. There are several studies of pregnancy outcomes but no studies about their offsprings.

Objectives: The objective of our study was to invetigate the growth and developement of offsprings from AS mothers.

Methods: This is a nationwide population-based case-control study using two South Korean databases that are managed by the National Health Insurance Service (NHIS): (1) the National Health Screening Program for Infants and Children (NHSIC) database, which records screening data of the growth and development of all children; (2) the NHIS database, which covers the entire population and includes comprehensive health claims data. In Korea, the NIH supports patients with 133 rare severe, intractable diseases including AS via a registration system of rare intractable disease (RID). We enrolled subjects born from 2008–2013 who had participated in the NHSIC program at three consecutive times; during 4-6 months (1st), 9-12 months (2nd), either 54-65months or 66-71 months (6th, 7th). The Korean Developmental screening test (K-DST) was used to assess development. By linking maternal and offspring healthcare data through their unique personal identification numbers, we constructed a mother-child database to track the growth of the child. We classified childrens from AS mothers using RID system (ICD code M45.X) and those from non-AS mothers. The primary outcome was to compare the growth and developement of offsprings from AS mothers and those from general popuulation. The secondary outcome was to copare the growth and developement of offsprings from mothers who diagnosed AS before delivery (ante-partum, AS-AP) and those from mothers who diagnosed AS after delivery (postpartum, AS-PP). Low birth weight (LBW) was defined as a birth weight below 2500 g. Growth retardation (GR) was defined as a body wight below 10th percentile according to birth weight reference curves for the south Korean population.

Results: A total of 794,544 subjects were identified. Among those cohort subject, there were 369 subjects with AS mother (124 subjects from AS-AP, 245 subjects from AS-PP) while 794,175 subjects with non-AS mother. Offsprings with LBW were comparable between those from AS mother and non-AS mother (OR 1.3, 95% CI 0.74-2.02). At 4-6 months, an OR of GR was comparable between two groups (OR 1.18, 95% CI 0.72-1.92) but increased at 9-12 months (OR 1.62, 95%CI 1.14-2.31) in infants from AS mothers.This difference disappered at 54-71months (OR 0.24,95% CI 0.87-1.74). An OR of development abnormality (i.e. children needed the further evaluation or the follow-up test by K-DST) was also comparable between two groups (OR 0.94, 95% CI 0.71-1.25). Mothers with AS-AP had as about three times as a higher OR for having babies with LBW than mothers with AS-PP (OR 2.8, 95% CI 1.15-6.86). At 4-6 months, an OR of GR was comparable between two groups (OR 0.59, 95% CI 0.19-1.86) but decreased at 9-12 months (OR 0.39, 95%CI 0.16-0.98) in infants from AS-PP. This difference disappered at 54-71months (OR 0.63,95% CI 0.29-1.39). An OR of development abnormality (i.e. children needed the further evaluation or the follow-up test by K-DST) was also comparable between two groups (OR 1.37, 95% CI 0.77-2.43).

Conclusion: Growth and development of children from AS mothers were comparable with those from non-AS mothers. Although mothers with AS-AP had significantly higher ORs for having LBW babies than those with AS-PP, their growth and development were comparable between two groups in young childhood.

Disclosure of Interests: None declared

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Pain pathology, progression and pharmacotherapy_

OP0083

DORSAL ROOT GANGLIA INFILTRATING MACROPHAGES MAINTAIN OSTEOARTHRITIS PAIN

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Background: Pain is a major debilitating symptom of knee osteoarthritis (OA). However, the extent of joint damage in OA does not correlate well with the severity of pain. The mechanisms that govern OA pain are poorly understood. Immune cells infiltrating nervous tissue may contribute to pain maintenance.

Objectives: Here we investigated the role of macrophages in the initiation and maintenance of OA pain.

Methods: Knee joint damage was induced by an unilateral injection of mono-iodoacetate (MIA) or after application of a groove at the femoral condyles of rats fed on high fat diet. Pain-like behaviors were followed over time using von Frey test and dynamic weight bearing. Joint damage was assessed by histology. Dorsal root ganglia (DRG) infiltrating immune cells were assessed over time using flow cytometry. To deplete monocytes and

macrophages, Lysm^{cre} x Csfr1-Stop-DTR were injected intrathecal or systemically with diptheria toxin (DT).
Results: Intraarticular monoiodoacetate injection induced OA and signs of persistent pain, such as mechanical hyperalgesia and deficits in weight bearing. The persisting pain-like behaviors were associated with accumulation of F4/80^{+} macrophages with an M1-like phenotype in the lumbar DRG appearing from 1 week after MIA injection, and that persisted till at least 4 weeks after MIA injection. Macrophages infiltrated DRG were also observed in the rat groove model of OA, 12 weeks after application of a groove at the femoral condyles. Systemic or local depletion of DRG macrophages during established MIA-induced OA completely ablated signs of pain, without affecting MIA-induced knee pathology. Intriguingly when monocytes/macrophages were depleted prior to induction of osteoarthritis, pain-like behaviors still developed, however these pain-like behaviors did not persist over time. *In vitro,* sensory neurons innervating the affected OA joint programmed macrophages into a M1 phenotype. Local repolarization of M1-like DRG macrophages towards M2 by intrathecal injection of M2 macrophages or anti-inflammatory cytokines resolved persistent OA-induced pain.
Conclusion: Overall we show that macrophages infiltrate the DRG after knee damage and acquire a M1-like phenotype and maintain pain independent of the lesions in the knee joint. DRG-infiltrating macrophages are not required for induction of OA pain. Reprogramming M1-like DRG-infiltrating macrophages may represent a potential strategy to treat OA pain.
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OP0084 PRESSURE PAIN THRESHOLDS AND THE ASSOCIATIONS WITH CHRONIC WIDESPREAD PAIN, KNEE OSTEOARTHRITIS AND OBESITY IN INDIVIDUALS WITH KNEE PAIN

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Background: Approximate 30% of individuals with symptomatic knee osteoarthritis (OA) had developed chronic widespread pain (CWP) over a period of 20 years [1]. In order to prevent CWP in those with knee pain, it is important to study associated factors.

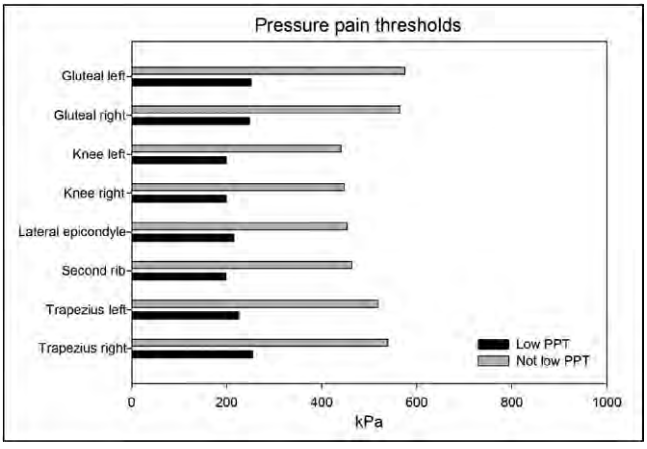


Figure 1 Differences in mean PPT in the eight tender points

Objectives: The aim was to study pressure pain thresholds among individuals with knee pain with or without radiographic changes, and associations with CWP, radiographic knee OA, and obesity.
Methods: Out of 300 individuals with knee pain (with or without radiographic changes) from an ongoing longitudinal study, 279 conducted pressure pain thresholds (PPT) measurement at baseline in this cross-sectional study (71% women; mean age 51 years). The PPT were measured using a computerized pressure algometry on eight predefined tender points (Figure 1) out of the 18 points as part of the definition of fibromyalgia [2]. PPTs were dichotomised based on the lowest tertial vs the two higher tertials for each of the eight points. A group that had ≥4 points with low PPT (low PPT group) was compared to a group that had <4 low PPT (not low PPT group). A pain mannequin categorised the participants in three different pain groups: CWP, chronic regional pain (CRP), and no chronic pain (NCP) according to the definition of the ACR [2]. Radiographic knee OA was defined according to the Ahlbäck five grading scale as having score ≥1 vs score 0 [3]. Obesity was measured by bioimpedance measuring BMI and visceral fat area (VFA, cm^2). To study associations, a crude logistic regression model controlled for age and sex was used including main and significant variables
Results: The prevalence of CWP was 37% and higher in the low PPT group compared to those in the not low PPT group (Table 1). No differences were found between the groups in BMI, VFA or radiographic knee OA (Table 1). The low PPT group had significantly lower mean PPT on all eight tender points, was younger, had more pain sites, and more cases of fibromyalgia compared to the group with not low PPT (Table 1, Figure 1). Age (OR 0.95; 95% CI 0.92–0.97), having CWP (OR 3.00; CI 1.66–5.06), fibromyalgia (OR 21.91; CI 2.45–194.69) and increased number of pain sites (OR 1.13; CI 1.05–1.22) were associated with low PPT.

Table 1. Descriptive statistics for the whole sample and for the groups: low PPT and not low PPT

	All n = 279	Low PPT n = 99	Not low PPT n = 180	p-value
Age, mean years (sd)	51 (9)	49 (9)	53 (8)	<0.001
Women, n (%)	197 (71%)	69 (70%)	128 (71%)	0.804
Pain group, n (%)				<0.001
NCP/CRP	160 (63%)	41 (47%)	119 (71%)	
CWP	95 (37%)	46 (53%)	49 (29%)	
Numbers of pain sites, mean (sd)	5 (4)	6 (5)	4 (3)	0.003
Fibromyalgia, n (%)	8 (3%)	7 (9%)	1 (1%)	0.001
Knee OA Ahlbäck, n (%)	59 (23%)	16 (18%)	43 (26%)	0.132
BMI, n (%)	127 (48%)	42 (47%)	85 (48%)	0.801
Normal Overweight/Obese	139 (52%)	48 (53%)	91 (52%)	
VFA, mean cm^2 (sd)	114 (54)	115 (51)	113 (55)	0.788

Conclusion: Baseline characteristics of individuals with knee pain showed a higher prevalence of CWP than in the general population [4]. In the group with low PPT, the prevalence was even higher. The study found associations between CWP and low PPT, however, almost half of the individuals with low PPT reported NCP/CRP. Moreover, a third in the group that not had low PPT reported CWP. The development of widespread pain in individuals with knee pain needs to be further studied over time to increase the knowledge of CWP's origin in order to prevent the condition.
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OP0085 THE CHANGING STATES OF FIBROMYALGIA IN A LONGITUDINAL COHORT OF PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: The identification of predictors for longitudinal fibromyalgia (FM) development has been identified as a research priority in a recent systematic review and meta-analyses (1). This paper examines the

Table 1.

Variable	Models of FM development		Models of FM recovery	
	Adjusted univariate OR (95% CI)	Multivariate model OR (95% CI)	Adjusted univariate OR (95% CI)	Multivariate model OR (95% CI)
Age years	1.01 (0.98-1.03)	1.00 (0.98-1.03)	1.00 (0.97-1.02)	1.02 (0.99-1.06)
Female gender	1.89 (1.01-3.53)*	2.04 (0.99-4.21)[$]	0.90 (0.40-2.04)	1.20 (0.48-3.03)
BASDAI per unit	1.39 (1.21-1.60)**	1.27 (1.08-1.49) *	0.79 (0.63-1.00)*	
BASFI per unit	1.22 (1.08-1.38)*		0.70 (0.56-0.88)*	0.68 (0.53-0.86)*
ASDAS-CRP per unit	1.47 (1.11-1.95)*		0.63 (0.39-1.01)[$]	
Started on TNF	1.95 (0.92-4.15)[$]		2.78 (1.21-6.38)*	4.23 (1.63-11.00)*
Symptomscale per unit	1.28 (1.13-1.45)**		0.76 (0.61-0.96)*	
WPI index per unit	1.24 (1.13-1.36)**	1.14 (1.02-1.28) *	0.84 (0.73-0.96)*	0.84 (0.72-0.97)*
HADS Anxiety per unit	1.12 (1.05-1.20)*		0.96 (0.88-1.04)	
Chalder per unit	1.14 (1.05-1.24)*		0.91(0.81-1.02)	
Jenkins baseline	1.07 (1.01-1.13)*		0.90 (0.83-0.98)*	
ROC/sensitivity/specificity		0.75/55.6/75.6		0.78/62.3/73.7

Logistic regression models. OR; Odds ratio, BASDAI; Bath Ankylosing Spondyilits Disease Activity IndexBASFI; Bath Ankylosing Spondylitis Functional Index, TNF; Tumour Necrosis Factor inhibitor, HADS; Hospital Anxiety Scale, WPI; widespread pain index, Chalder; Chalder fatigue index, Jenkins; Jenkins sleep evaluation, ROC; receiver operator curve.

longitudinal development of, or recovery from, FM in patients with axial Spondyloarthritis(axSpA).

Objectives: To identify predictors for FM development and recovery in patients with axSpA.

Methods: The British Society of Rheumatology Biologics Register (BSRBR-AS) recruited patients with axSpA from 83 centres in a prospective study. Fibromyalgia was diagnosed using the self-reported Fibromyalgia Survey Diagnostic Criteria (FSDC). Measures of axSpA disease activity and clinical findings were recorded at regular intervals. We identified predictors for developing FM, and for recovering from FM, between yearly visits using uni- and multivariate logistical regression models.

Results: Eight hundred and one patients had two or more visits and were eligible for inclusion. 686 patients did not have FM at baseline, of whom 45 had developed FM by follow-up. 115 patients had FM at baseline, of whom 77 had recovered by follow-up. The uni- and multivariate models are presented in table 1.

Conclusion: The development of FM in patients with axSpA can be predicted by high levels of axSpA activity and presence of widespread pain, while low levels of the same variables, and starting a TNF-inhibitor predict recovery from FM. The presence of co-morbid FM should be considered in patients with a history of high axSpA disease activity and wide spread pain.

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OP0086 THE DEGREE OF BONE MARROW EDEMA AS DETECTED BY MAGNETIC RESONANCE IMAGING IN THE SACROILIAC JOINTS AND THE SPINE SUSPICIOUS OF AXIAL SPONDYLOARTHRITIS IN THE GENERAL POPULATION IS ASSOCIATED WITH DIFFERENT FACTORS

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Background: Taking advantage of a large population-based study we have recently reported that the frequency of bone marrow edema (BME) and fatty lesions (FL) in the sacroiliac joints (SIJ) and the spine of individuals <45 years detected by magnetic resonance imaging (MRI) suggestive of axial spondyloarthritis (axSpA) is higher than expected.

Objectives: To identify and compare factors associated with the extension of MRI lesions in the spine and the SIJ in the general population.

Methods: All available spinal- (sagittal T1/T2 sequences) and SIJ- (semicoronal STIR sequences) MRIs were evaluated by two trained readers blinded to clinical data. BME (SIJ and spine) suggestive of axSpA were recorded. The extension of BME was quantified using the Berlin MRI score. Discrepancies were resolved by consensus. Degenerative lesions of the Modic type were excluded. The association of age (increase per decade), sex, HLA-B27 and hsCRP positivity, smoking (ever smoker vs. no smoker), spinal pain (yes vs. no in last 3 months), body mass index (BMI) categories (WHO definition), physically demanding job, and giving birth within the last 12 month with the severity of BME were examined. Associations between clinical factors and the Berlin MRI score were analyzed by negative binomial regression models resulting in incidence rate ratios (IRRs).

Results: MRIs of 793 volunteers from the general population, mean age 37.3±6.3 years, 49.4% male, 8.9% HLA B27+, 7% CRP-positive, 56.9% with back pain in the last 3 months (28.8% with back pain NRS ≥4/10), 35.7% reported physically heavy work, 55% with BMI > 25 kg/m^2, 16.2% current smokers, and 5% of females with pregnancy in the last year before MRI examination, were evaluated.

For BME on SIJ-MRIs, significant associations (IRR, 95% confidence level) were found for pregnancy in the last year (3.82, 1.17-14.24), HLA-B27+ (2.42, 1.33-4.55), BMI (25-30 vs. <25; 2.09 (1.33-3.31)) and presence of back pain in the last 3 months (1.54, 1.02-2.33).

For BME on spinal MRIs, significant associations were found for age per decade increase (1.45, 1.10-1.91) and physically demanding work (1.45, 1.04-2.00), while HLA-B27+ (1.32, 0.79-2.24), BMI (>30: 0.84, 0.53-1.32 (<25 reference)) and back pain in the last 3 months (1.29, 0.95-1.77) showed no association. Overall, spinal BME was more frequent than SIJ BME in the participants working at a desktop (61.5% vs. 54.4%), while smokers (66.9% vs. 63.8%) and participants with back pain in the last 3 months (62.5% vs. 56.9%) had more often SIJ BME than spinal BME, respectively.

Conclusion: In this population-based study, individuals aged <45 years, HLA-B27+, women with pregnancy in the last year and presence of back pain were associated with the extent of BME in the SIJ, while age and physically demanding work were associated with the extent of BME in the spine. These data support the hypothesis of a mechanic origin of BME in the general population aged <45 years, while HLA B27 is a severity but not a susceptibility factor for BME in the SIJ.

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OP0087

NATIONAL VARIATION AND FACTORS ASSOCIATED WITH THE TRANSITION FROM FIRST USE TO LONG-TERM OPIOID USE FOR NON-CANCER PAIN

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Background: Prescribing behaviour of physicians has been described as a key driver of rising opioid prescriptions and long-term opioid use. However, the effect of prescribers requires interpretation within context. No studies have investigated the extent to which regions, practices and prescribers, vary in opioid prescribing accounting for case-mix by considering this hierarchy together.
Objectives: (i) Quantify and identify risk factors for the transition from new-user to long-term opioid user (ii) Quantify variation of long-term use attributed to region, practice and prescriber, accounting for patient mix and chance variation.
Methods: We conducted a retrospective observational UK study between 2006-2017 using Clinical Practice Research Datalink. Opioids new users, ≥18 years, without cancer were identified. Long-term opioid use was defined as ≥3 opioid prescriptions issued within a 90-day period from index date, or ≥1 opioid prescription lasting at least 90 days in the first year. A multi-level random-effects logistic regression model was used to examine the association of patient characteristics with the odds of becoming a long-term opioid user. To examine variation in opioid use amongst prescribers, GP practices and region after adjusting for patient case-mix, we used a nested random-effect structure. A 'high-risk' region, prescriber or practice was defined as those where the entire adjusted 95% CI lay above the population average.
Results: 1,968,742 new opioid users were included; 14.6% patients transitioned to long-term use. In the fully adjusted model, factors associated with higher odds of long-term opioid use included high morphine milligram equivalents (MME)/day at first prescription, older age, deprivation, fibromyalgia, rheumatological conditions, major surgery (Table). After adjustment for case-mix, the North-West, Yorkshire and South-West were found to be high-risk regions for long-term use. 103 practices (25.6%) and 540 prescribers (3.5%) were associated with a significantly higher risk of long-term use. The odds of becoming a long-term user for a patient belonging to these prescribers reached up to >3.5 times than the population average.
Conclusion: Prescribing factors, age, deprivation and conditions including fibromyalgia and rheumatological conditions were associated with higher odds of long-term opioid use. In the first UK study evaluating long-term opioid prescribing with adjustment for patient-level characteristics, variation in regions and especially practices and prescribers were observed. Our findings support greater calls for action to reduce practice and prescriber variation by promoting safe practice in opioid prescribing.

Table. Factors associated with long-term opioid use using a multi-level model accounting for clustering of individuals within prescriber, practice and region

Individual factors	Adjusted Odds Ratio (95% CI) *
Prescribing factors	
Index daily MME >200	7.59 (6.29, 9.16)
Index daily MME 100-200	1.12 (1.03, 1.21)
Index daily MME 50-100	1.58 (1.49, 1.68)
Index daily MME <50	Ref
Gabapentinoid use	2.51 (2.43, 2.60)
Psychotropic use	1.28 (1.17, 1.40)
Age	
>75	4.35 (4.26, 4.45)
65-75	3.57 (3.50, 3.65)
55-65	3.03 (2.96, 3.09)
35-55	1.91 (1.88, 1.95)
Age <35	Ref
Deprivation (Townsend score)	
Quintile 5 (Most deprived)	1.54 (1.51, 1.57)
Quintile 4	1.34 (1.31, 1.36)
Quintile 3	1.20 (1.18, 1.22)
Quintile 2	1.09 (1.07, 1.11)
Quintile 1 (Least deprived)	Ref
Pre-existing conditions/ prior procedures	
Fibromyalgia	1.81 (1.49, 2.20)
Substance use disorder	1.76 (1.70, 1.83)
Suicide and self-harm	1.56 (1.51, 1.61)
Rheumatological conditions Ψ	1.54 (1.49, 1.59)
Alcohol abuse	1.50 (1.45, 1.55)
Depression	1.28 (1.26, 1.30)
Major Surgery	1.09 (1.06, 1.13)

Abbreviations: MME, Morphine Milligram Equivalent; *p<0.05. Index daily MME/day is the MME/day at first prescription (MME= daily dose in milligrams X opioid conversion ratio). Ψ Defined by Charlson score including rheumatoid arthritis, SLE, myositis.

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OP0088

INITIATING TNF INHIBITORS IN INFLAMMATORY ARTHRITIS DOES NOT DECREASE THE AVERAGE OPIOID ANALGESIC CONSUMPTION

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Background: TNFα-inhibitor (TNFi) therapy is effective in controlling several rheumatic diseases and has been shown to reduce pain in patients with arthritis. Opioids are often prescribed for chronic pain, a common issue in inflammatory joint disease.
Objectives: To explore the impact of the initiation of TNFi therapy as a first-line biologic disease-modifying anti-rheumatic drug (DMARD) on the prescription rates of opioids in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis (AS) and undifferentiated arthritis (UA) in Iceland.
Methods: All patients receiving biologic DMARD therapy for rheumatic diseases in Iceland are registered in a nationwide database (ICEBIO). The Icelandic Directorate of Health operates a Prescription Medicines Register that includes over 90% of all drug prescriptions in Iceland. The study group included patients with RA, PsA, AS, and UA registered in ICEBIO and for each of them five randomly selected comparators from the general population matched on age, sex, and calendar time. On February 1st 2016 we extracted data on all filled opioid analgesic prescriptions two years before and two years after the date of TNFi initiation.
Results: Data from 359 RA, 217 AS, 251 PsA and 113 UA patients and 4700 comparators were collected. In total, 75% of patients compared to 43% of comparators received ≥1 opiate prescription during the study period. The proportion of patients using opioids (regardless of dose) two years prior to TNFi initiation was 41%, increasing to 49% the following year. After TNFi initiation the proportion returned to 40% (Figure 1). Despite this, the mean yearly opiate dose used by the patients followed a rising trajectory throughout the study period (Figure 2). In total, patients were prescribed nearly 6 times more opioids than the comparators, corresponding to a bootstrapped mean (95% CI) dose of 818 (601-1073) mg MED per patient and year compared to 139 (111-171) mg for comparators.
Conclusion: Three out of four patients with inflammatory arthritis in Iceland use opioid analgesics in the two years prior to and/or after the initiation of TNFi therapy and the mean doses were significantly higher than in matched comparators. The proportion of patients receiving opioids increased before TNFi therapy and then decreased again to the previous level. The initiation of the first-line TNFi did not reduce opioid consumption by dose at the group level. On the contrary, there was a trend towards increasing doses over time in both patients and comparators, possibly reflecting the development of opiate tolerance.

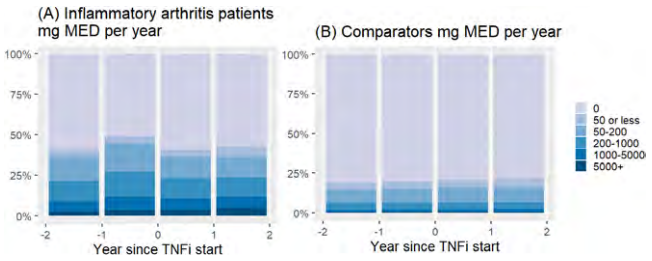


Figure 1. Percental distributions of opioid analgesic use by dose (according to dispensed prescriptions) among patients with inflammatory arthritis (A) and matched comparators (B). All doses are oral morphine equivalent dose (MED) in milligrams.

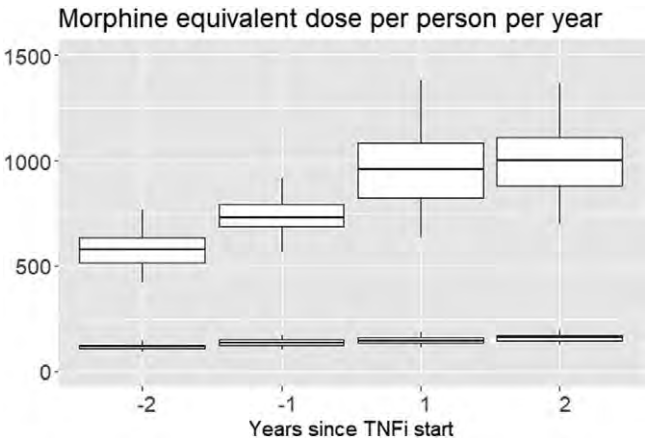


Figure 2. Bootstrapped mean oral morphine equivalent dose per person per year for patients with inflammatory arthritis (above) and age and sex matched comparators (below). Box edges represent 25-75th percentiles and whiskers 95% confidence intervals.

Table 1. Baseline demographic data. Mean ± SD unless specified. * defined from diagnosis to baseline.

	All patients	Rheumatoid arthritis	Psoriatic arthritis	Ankylosing spondylitis	Undifferentiated arthritis
Total n (%)	940 (100)	359 (38)	251 (27)	217 (23)	113 (12)
Age (years)	49 ± 14	53 ± 14	49 ± 13	43 ± 13	44 ± 15
Disease duration (years)*	7.8 ± 8.5	8.2 ± 8.2	7.4 ± 7.8	8.3 ± 10.2	6.3 ± 6.6
Female	58%	73%	59%	34%	52%

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OP0089

EFFICACY OF CLOMIPRAMINE FOR CHRONIC LUMBAR RADICULAR PAIN A RANDOMIZED CLINICAL TRIAL

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Background: Lumbar radicular pain is the most common chronic neuropathic pain syndrome. Antidepressants are highly recommended for neuropathic pain, but there is no evidence for their efficacy.
Objectives: The aim of this double-blind, randomised, placebo-controlled trial is to determine whether Clomipramine (an antidepressant) is more effective than placebo in reducing pain in individuals with resistant chronic lumbar radicular pain.
Methods: A double-blind, randomized, clinical trial. Sixty-two patients with resistant chronic lumbar radicular pain were included. (The sample size was calculated on the assumption that clomipramine would reduce the incidence of lumbar radicular pain of 35%, compared with placebo, with a two-sided test, an alpha level of 0.05, and a power of 85%). Patients were randomly allocated to receive either Clomipramine by slow intravenous infusion for 10 days in a hospital setting with progressively increasing doses, 25 mg on the first day, 50 mg on the second day and 75 mg on the third day until the tenth day, or placebo (500 ml of physiological serum a day). For both groups, paracetamol is added intravenously at a dose of 3g per day for ten days, Parecoxib for 3 days and ten sessions of lumbar spine rehabilitation including analgesic massage, muscle strengthening and joint maintenance. At the exit, clomipramine was relayed with 25 mg per day orally until the 90th day for clomipramine group, and paracetamol was authorized in both groups, in case of severe pain. The primary outcome was pain intensity, measured at baseline, 5th day, 10th day and 90th day using VAS pain (10 mm). Secondary outcome included DN4-questionnaire, lumbar radicular discomfort (VAS 10 mm), pain-free perimeter of walking (min), disability assessed using the Roland Morris Disability questionnaire and severity of mood symptoms assessed using the Hospital Anxiety and Depression scale (HAD), measured on days 0, 5, 10 and 90.
Results: 31 patients were assigned to the clomipramine group and 31 to the placebo group. There were no differences between the groups in demographic characteristics. Treatment by Clomipramine had a significantly greater reduction in pain, discomfort and DN4 from the 5th day ($p = 0.000$, $p = 0.001$ and $p = 0.004$ respectively) than the placebo, with an improvement maintained until 90th day. There was a statistically significant improvement in pain-free walking distance and disability for the clomipramine group from the 10th day ($p = 0.02$ and 0.001 respectively) and that maintained until 90th day. However, there was no significant improvement in HAD between the 2 groups. ($p \geq 0.1$).
Conclusion: This double-blind, randomized, clinical trial shows that clomipramine is quickly effective and maintained over time in the management of resistant chronic lumbar radicular pain. It can therefore be part of the therapeutic arsenal in this sense.
Disclosure of Interests: None declared
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OP0090

EFFICACY OF SUBCUTANEOUS TANEZUMAB FOR THE TREATMENT OF CHRONIC LOW BACK PAIN: AN ANALYSIS OF BRIEF PAIN INVENTORY-SHORT FORM SCORES FROM A 56-WEEK, RANDOMIZED, PLACEBO- AND TRAMADOL-CONTROLLED, PHASE 3 TRIAL

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Background: Tanezumab, a monoclonal antibody against nerve growth factor, was recently evaluated in an 80 week placebo and tramadol-controlled trial in patients with chronic low back pain (CLBP) and a history of inadequate response to standard-of-care analgesics (NSAIDs, opioids, etc). Primary endpoint was change in Low Back Pain Intensity (LBPI) at week 16 vs placebo. Key secondary endpoints were the proportion of patients with ≥50% improvement in LBPI at week 16, change in Roland Morris Disability Questionnaire score at week 16, and change in LBPI at week 2 (all vs placebo). Tanezumab 10mg met the primary and all key secondary endpoints. Tanezumab 5mg did not meet the primary endpoint, but improved 2 of 3 key secondary endpoints. Due to the primary endpoint result and the statistical gate-keeping approach to control for multiple comparisons, a conclusion of superiority over placebo could not be made for the 5mg dose.
Objectives: To further characterize tanezumab's effects on pain and function in this trial through analysis of Brief Pain Inventory-short form (BPI-sf) scores.
Methods: Patients received placebo (n=406), subcutaneous (SC) tanezumab 5mg (every 8 weeks; n=407), SC tanezumab 10mg (every 8 weeks; n=407) or oral tramadol prolonged-release (100-300mg/day; n=605). Pre-specified secondary endpoints included BPI-sf worst pain, average pain, the overall pain interference index, and selected individual domains of the index (general activity, walking ability, sleep, and normal work). Least squares (LS) mean (standard error [SE]) changes from baseline in BPI-sf scores were compared between groups (unadjusted for multiplicity) at week 16 using an analysis of covariance model. Scores range from 0-10 with higher scores indicating greater pain severity or functional impairment.
Results: LS mean (SE) differences from placebo for worst pain were -0.52 (0.19) for tanezumab 5mg (p≤0.01), -0.54 (0.19) for tanezumab 10mg (≤0.01), and -0.24 (0.17) for tramadol (p=0.17). LS mean (SE) differences from placebo for average pain were -0.37 (0.18) for tanezumab 5mg (p=0.04), -0.46 (0.18) for tanezumab 10mg (≤0.01), and -0.17 (0.16) for tramadol (p=0.29). LS mean (SE) differences from placebo for the pain interference index were -0.41 (0.18) for tanezumab 5mg (p=0.03), -0.58 (0.18) for tanezumab 10mg (≤0.01), and -0.15 (0.17) for tramadol (p=0.39). Effects of tanezumab were not statistically different (p>0.05)

from tramadol for worst pain, average pain, and the pain interference index, with exception of the pain interference index for tanezumab 10mg (p=0.01). Mean dose of tramadol was 203mg/day at week 16.
Tanezumab 10mg significantly (p<0.05) improved individual domains of the pain interference index (general activity, walking ability, sleep, and normal work) vs placebo and vs tramadol. Tanezumab 5mg significantly (p<0.05) improved pain interference with general activity and normal work vs placebo, and sleep vs placebo and vs tramadol. No statistical differences in any domain was observed for tramadol vs placebo.
Conclusion: Tanezumab 5mg and 10mg significantly improved worst pain, average pain, and overall pain interference index scores vs placebo in patients with CLBP. Tanezumab 10mg also significantly improved the overall pain interference index vs tramadol. Tanezumab 5mg significantly improved most individual domains of the pain interference index vs placebo, while tanezumab 10mg significantly improved all domains assessed vs placebo and vs tramadol.
Disclosure of Interests: John Markman Consultant of: Consultant: Trigemina, Editas Medicine, and Plasma Surgical; Advisory board: Clexio Biosciences, Flexion Therapeutics, Quark Pharmaceuticals, Quartet Medicine, Collegium Pharmaceutical, Purdue Pharma, Biogen, Novartis, Aptinyx, Nektar, Allergan, Grünenthal, Eli Lilly and Company, Depomed, Janssen Pharmaceuticals, Teva Pharmaceutical Industries, KemPharm, Abbott Laboratories, Plasma Surgical, Chromocell, Convergence Pharmaceuticals, Inspirion, Pfizer, Sanofi, Daiichi Sankyo, and Trevena; Data safety monitoring boards for Novartis and Allergan, Serge Perrot Consultant of: Grunenthal, Pfizer, Lilly, MSD, Sanofi, Menarini, Seiji Ohtori: None declared, Thomas Schnitzer Consultant of: Pfizer, Lilly, AstraZeneca, GSK, Said Beydoun Grant/research support from: Argenx, Catalyst Pharma, Mallinckrodt, Pfizer, UCB, Consultant of: Alexion, Akcea, Alnylam, CSL, Takeda, Mitsubishi Tanabe, Speakers bureau: Alexion, Akcea, Alnylam, CSL, Takeda, Mitsubishi Tanabe, Lars Viktrup Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Ruoyong Yang Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Candace Bramson Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Christine West Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Ken Verburg Shareholder of: Pfizer Inc, Employee of: Pfizer Inc
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SLE, Sjögren's and APS clinical aspects

OP0091 A TWO-SCORE INTERFERON SIGNATURE AND MUSCULOSKELETAL IMAGING EXPLAIN THE ASSOCIATION BETWEEN INTERFERON AND ARTHRITIS IN SLE

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Background: Interferon (IFN) signature is associated with disease activity and flare in SLE. We previously described two independent IFN gene expression scores; IFN Score A (the most commonly measured ISGs) and IFN Score B (less commonly measured ISGs which may also respond to IFN-II or other immune mediators)[1]. Many more clinical outcomes are associated with IFN Score B than with a "classic" interferon signature. These include progression of At-Risk individuals to SLE, response to rituximab, and differentiation of IFN signature in RA and SLE.
In previous work, the relationship of IFN Signatures with arthritis was less clear than for other SLE features. This may be related to the local regulatory effects of IFN-beta in the synovium, contrasting with the pro-inflammatory effects of other interferons. Another reason may be the proven imprecision of clinical examination as a measure of MSK inflammation in SLE.
USEFUL was a multicentre longitudinal study including serial ultrasound assessment of SLE patients with inflammatory MSK pain receiving treatment with glucocorticoids (GC).
Objectives: To determine whether IFN scores A and B are associated with imaging-proven synovitis in SLE and measure the responsiveness of IFN scores to GC treatment.
Methods: 133 SLE patients were recruited into the USEFUL study if the referring physician deemed they had inflammatory pain warranting treatment. Participants received depomedrone 120mg IM then were assessed at 0, 2 and 6 weeks using clinical instruments and ultrasound (US). OMERACT US criteria were used to categorise patients as active (GS2 or PD1 in at least one joint or tendon), active in both joints and tendons, or non-active (no GS1 and PD0 or better in all joints).
Expression of 26 interferon stimulated genes, normalised to PP1A was measured in whole blood collected in TEMPUS tubes using a custom Taqman array. IFN scores A and B were calculated as previously described[1]. Missing data was imputed using expectation-maximisation method. Parametric tests were applied with post hoc Tukey to compare scores between groups.
Results: At baseline, there was no significant difference in IFN Score A between ultrasound groups (F = 1.045, p = 0.355). In contrast, IFN Score B differed significantly between ultrasound groups (F = 4.168, p = 0.018). The greatest difference was between active ultrasound for both joints and tendons (n=22) and non-active ultrasound (n=53) (difference = 0.75, 95% CI 0.13, 1.37, p=0.013).
There was no significant change from baseline in IFN Score A at week 2 (mean difference 0.08, 95% -0.14, 0.31, p = 0.45) or week 6 (mean difference -0.03, 95% -0.25, 0.19, p = 0.79). Similarly, there was no significant change in IFN Score B at week 2 (mean difference -0.01, 95% -0.18, 0.17, p = 0.93) or week 6 (mean difference -0.07, 95% -0.21, 0.08, p = 0.36).
Conclusion: Previous studies were unable to demonstrate an association between a typical interferon signature and arthritis in SLE. Our study includes a homogenous patient population and therapy, objective measure of synovitis, and a more detailed assessment of IFN Status. We found that imaging-proven synovitis is associated with increased expression of a specific subset of ISGs (IFN score B), but not a the more typical interferon signature genes (IFN Score A).
This increases the body of evidence for the value of IFN score B in predicting clinical outcomes. GC treatment did not affect systemic IFN signature scores at follow up. Future analysis will explore the role of IFN Scores in predicting clinical responses to therapy in this study.
References:
[1] El-Sherbiny, Y.M., et al. Scientific Reports, 2018. **8**(1): p. 5793.
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OP0092 OPTIMIZING A DEFINITION OF LUPUS LOW DISEASE ACTIVITY STATE (LDA) FOR DAILY CLINICAL PRACTICE: SLE-DAS LDA VS LLDAS

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Background: The Lupus Low Disease Activity State (LLDAS)[1] is a proposed target for the management of Systemic Lupus Erythematosus (SLE). However, the LLDAS definition is cumbersome to apply, as it requires comparison with manifestations in the previous visit, scoring of Systemic Lupus Erythematosus disease activity index (SLEDAI), Physician Global Assessment (PGA), treatment conditions and exclusion of additional features. The SLE disease activity score (SLE-DAS)[2] is a validated continuous measure with higher sensitivity to change and validity in predicting damage accrual as compared to SLEDAI-2K. SLE-DAS is quickly quantified with its online calculator. The SLE-DAS low disease activity (SLE-DAS LDA) was recently defined [3] and it is easier to apply than the LLDAS.
Objectives: To compare the performance of SLE-DAS and LLDAS for defining LDA state in a real-life clinical setting.
Methods: Cross-sectional study of SLE patients fulfilling ACR'97 and/or SLICC'12 classification criteria followed at an academic lupus clinic, from January to December 2019. Fulfillment of LLDAS and SLE-DAS LDA state was verified for each patient. The SLE-DAS LDA state was defined as (1) SLE-DAS ≤3.77[3] with (2) prednisolone dose ≤7.5 mg/day. The proportion of cases in LDA state using LLDAS and SLE-DAS LDA was compared with McNemar's test. Agreement between LLDAS and SLE-DAS LDA was tested with Cohen's Kappa coefficient.
Results: We included 292 patients (86.6% female, mean age: 48.7±14.4 years, mean disease duration: 14.4±9.3 years). From these, 245 (83.9%)

and 248 (85%) were in LDA according to LLDAS and SLE-DAS LDA, respectively. There was no statistically significant difference between LLDAS and SLE-DAS LDA (p=0.581 regarding the identification of patients in LDA. Agreement between these two sets of criteria was almost perfect (k=0.831, p<0.01).

There were 13 discordant cases, fulfilling only the SLE-DAS LDA (n=8) or the LLDAS (n=5), and their manifestations of disease activity (excluding serologic features) are summarized in table 1.

Patients fulfilling only SLE-DAS LDA

Number of cases	PGA (range)	Active clinical manifestations (range)	SLEDAI-2K (range)	SLE-DAS (range)	Prednisolone (range, mg/day)
6	0.1-0.2	Leukopenia 2.2-2.7x10^9/L	1-3	1.46-3.03	0-2.5
2	0.2-0.3	Thrombocytopenia 71-96x10^9/L	1-3	1.97-2.86	0-5

Patients fulfilling only LLDAS

Number of cases	**PGA** (range)	**Active clinical manifestations** (range)	**SLEDAI-2K** (range)	**SLE-DAS** (range)	**Prednisolone** (range, mg/day)
2	0.2-0.4	Arthritis (2-4/28 swollen joints)	4	4,41-5.31	0-5
1	0.5	Panniculitis (face and torso)	3	5,53	0
1	0.1	Generalized rash	4	5,01	5
1	0.4	Leukopenia 2.1x10^9/L Thrombocytopenia 62x10^9/L	2	4,99	0

Conclusion: A LDA state, by either definition, was achieved by most patients in this real-life setting. LLDAS and SLE-DAS LDA identify almost exactly the same population. The SLE-DAS LDA definition is easier to apply and hence might be the optimal definition for use in daily clinical practice.

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[2] Jesus D, Matos A, Henriques C, *et al.* Derivation and validation of the SLE Disease Activity Score (SLE-DAS): a new SLE continuous measure with high sensitivity for changes in disease activity. Ann Rheum Dis 2019; 78: 365-71.

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OP0093 FREQUENCIES AND PREDICTORS OF THE LUPUS LOW DISEASE ACTIVITY STATE AND REMISSION IN TREATMENT-NAÏVE PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS -- A REAL-WORLD COHORT STUDY

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Background: After the introduction of treat-to-target strategy in systemic lupus erythematosus (SLE), Lupus Low Disease Activity State (LLDAS) and definitions of remission in SLE (DORIS) were developed and validated. Several studies had demonstrated that the achievement and maintenance of LLDAS or DORIS was associated with good prognosis.

Objectives: To evaluate the attainability of LLDAS and DORIS in a treatment-naïve cohort of SLE.

Methods: LDAS5 was defined as LLDAS with a prednisone dose ≤5 mg/d. There were 4 definitions in DORIS: clinical remission on treatment (RONT), complete RONT, clinical remission off treatment (ROFT) and complete ROFT. The treatment-naïve patients from Peking University First Hospital SLE cohort were enrolled. The time to each state and their annual cumulative probabilities were estimated by Kaplan-Meier approach. The frequencies of patients who achieved each component of LLDAS or DORIS during follow-up were determined.

Results: A total of 218 treatment-naïve patients were included, with a median follow-up of 4.48 years. Respectively, 190 (87.2%), 160 (73.4%), 148 (67.9%), 94 (43.1%), 23 (10.6%) and 18 (8.3%) patients achieved LLDAS, LLDAS5, clinical RONT, complete RONT, clinical ROFT and complete ROFT at least once during the follow-up time. The median time to LLDAS, LLDAS5, clinical RONT and complete RONT were 1.4, 2.3, 2.6 and 4.7 years, respectively.

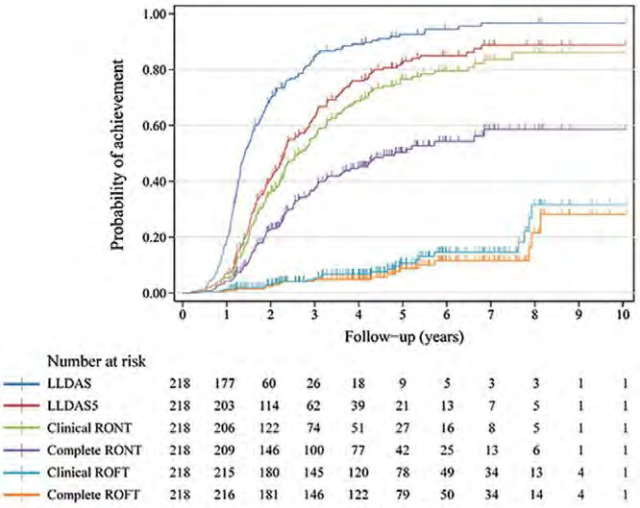


Figure 1 Kaplan-Meier curves of time to LLDAS, LLDAS5 and each state of DORIS.

Table 1. Frequencies, time to achieve and annual cumulative probabilities of each state by Kaplan-Meier approach

States	Achieved patients Number (%)	Time to achieve (years)	Cumulative probabilities of achievement (%)				
			Year 1	Year 2	Year 3	Year 4	Year 5
LLDAS	190 (87.2)	1.4	18.8	69.7	86.7	89.1	92.6
LLDAS5	160 (73.4)	2.3	6.9	40.7	63.3	76.0	82.3
Clinical RONT	148 (67.9)	2.6	5.5	36.1	56.1	68.8	76.6
Complete RONT	94 (43.1)	4.7	4.1	22.6	37.5	45.3	50.4
Clinical ROFT	23 (10.6)	NA	1.4	2.9	5.4	6.7	10.6
Complete ROFT	18 (8.3)	NA	0.9	2.5	4.8	4.8	8.8

Table 2. Patients who achieved each component of LLDAS or DORIS during follow-up

Components	Number (%)
SLEDAI-2K ≤4, with no activity in major organ systems (renal, central nervous system, cardiopulmonary, vasculitis, fever), and no haemolytic anaemia or gastrointestinal active	213 (97.7)
Clinical SLEDAI-2K =0	210 (96.3)
PGA ≤1	217 (99.5)
PGA <0.5	199 (91.3)
Serology (anti-dsDNA and complement) negative	148 (67.9)
Prednisone dose ≤7.5 mg/day	201 (92.2)
Prednisone dose ≤5 mg/day	171 (78.4)
No prednisone dose	40 (18.3)
No prednisone dose and Immunosuppressants	32 (14.7)

Conclusion: Our data confirmed that LLDAS is an attainable early treatment target for SLE. Though with more difficulty, RONT can be achieved in two-thirds of our patients. ROFT may not be an ideal treatment target at present as it is only attained in few patients.

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[1] Franklyn, K. et al. Ann Rheum Dis. 2016 Sep;75(9):1615-21.

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Disclosure of Interests: None declared

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OP0094 EULAR-ACR 2019 CLASSIFICATION CRITERIA FOR SLE: CAN WE CLASSIFY USING LABORATORY TESTS ALONE?

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Background: The EULAR-ACR 2019 (EULAR19) classification criteria for systemic lupus erythematosus (SLE) were developed to improve the sensitivity and specificity of previous criteria. Notably, both the EULAR19 and existing SLICC-SLE 2012 (SLICC12) criteria can classify patients as having SLE by the presence of immunology and haematological abnormalities in the absence of any signs or symptoms.

Objectives: To validate the EULAR19 criteria, with comparison to existing criteria, in a large cohort of patients with an established systemic autoimmune rheumatic disease (SARD).

Methods: We recruited 227 adult patients who were ANA positive with ≥1 clinical feature suggestive of a SARD, from three hospitals in the North West of England. Clinician diagnosis was used as gold standard; we then applied the EULAR19, SLICC12 and the ACR-SLE 1997 (ACR97) criteria.

Results: Of the 227 patients recruited, by clinician diagnosis, 89 patients (36%) had SLE, 43 (17%) primary Sjögren's (pSS), 62 (25%) undifferentiated CTD (UCTD), 25 (10%) systemic sclerosis (SSc) and 8 (3%) an inflammatory myositis. The characteristics of these patients and the breakdown of the EULAR19 criteria are outlined in figure 1.

	SLE n=89	pSS n=43	UCTD n=62	SSc n=25	Myositis n=8
Female N (%)	82 (92)	42 (98)	53 (85)	24 (96)	8 (100)
Age, mean (SD) /years	44 (13)	52 (12)	47 (13)	60 (9)	53 (7)
Disease duration, mean (SD) /years	12 (10)	6 (5)	5 (7)	9 (11)	3 (3)
SLE classification criteria					
EULAR SLE 2019, N (%)	75 (84)	10 (23)	20 (32)	1 (4)	0
ACR SLE 1997, N (%)	77 (87)	9 (21)	21 (34)	2 (8)	1 (13)
SLICC SLE 2012, N (%)	84 (94)	15 (35)	33 (53)	4 (16)	2 (25)
EULAR-ACR 2019 criteria					
Constitutional, N (%)	10 (11)	2 (5)	1 (2)	0	1 (13)
Neuropsychiatric, N (%)	3 (3)	0	1 (2)	1 (4)	0
Mucocutaneous, N (%)	71 (80)	13 (30)	27 (44)	2 (8)	2 (25)
Serosal, N (%)	13 (15)	1 (2)	2 (3)	0	0
Musculoskeletal, N (%)	52 (58)	14 (33)	22 (35)	3 (12)	3 (38)
Renal, N (%)	30 (34)	0	0	1 (4)	0
Haematological, N (%)	44 (49)	12 (28)	10 (16)	3 (12)	0
Antiphospholipid antibodies, N (%)	43 (48)	7 (16)	17 (27)	4 (16)	0
Low complement, N (%)	48 (54)	10 (23)	10 (16)	3 (12)	1 (13)
Anti-Sm, N (%)	19 (21)	2 (5)	4 (6)	1 (4)	0
Anti-dsDNA, N (%)	50 (56)	8 (19)	12 (19)	0	1 (13)

Figure 1. Baseline characteristics and classification criteria compared across five SARD diagnoses.

The sensitivity and specificity of the EULAR19 is similar to ACR97 (sensitivity 84% (95% CI 75-91%) vs. 87% (95% CI 78-93%) and specificity 78% (95% CI 70-84%) vs. 76% (95% CI 68-83%) respectively). The SLICC12 criteria by contrast are more sensitive (94% (95% CI 87-98%)) and less specific (61% (95% CI 52-69%)) in this cohort.

Figure 2 illustrates patients with a clinician diagnosis of SLE or UCTD who meet each of the classification criteria. Of the 89 patients with a clinician diagnosis of SLE, 39 (44%) patients would have sufficient points to meet EULAR19 criteria on blood test results alone in the absence of clinical symptoms. Four pSS patients and 4 UCTD patients would also meet EULAR19 criteria from positive blood results alone.

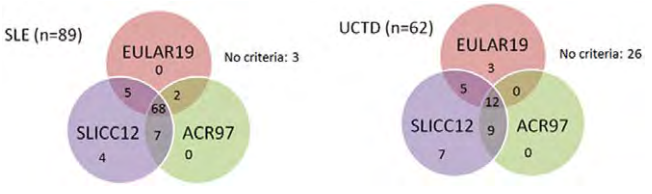


Figure 2. Venn diagrams illustrating patients with SLE and UCTD who meet the EULAR19, ACR97 and SLICC12 classification criteria. No criteria refers to the patients not meeting any of the three SLE classification criteria.

Conclusion: These results suggest that the EULAR19 criteria perform comparably to the ACR97 criteria when applied to an established cohort of SARDs. Similar to SLICC12, it is possible to classify patients as having SLE using the EULAR19 criteria by haematological and other laboratory tests. To what extent haematological abnormalities can be potentially used as the sole 'clinical criteria' needs consideration.

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OP0095 A DECISION MODEL OF LABIAL GLAND BIOPSY BASED ON B-MODE ULTRASONOGRAPHY WITH SHEAR-WAVE ELASTOGRAPHY IN PATIENTS WITH SUSPECTED SJÖGREN'S SYNDROME

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Background: Focal lymphocytic sialadenitis defined as focus score (FS) ≥1 on labial gland (LG) biopsy plays an integral role in various classification criteria of Sjögren's syndrome (SS). However, suspected patients often hesitate to receive a biopsy; and rheumatologists hope a decision for biopsy based on a high predicted incidence of FS≥1, or against biopsy based on an absolutely low predicted incidence.

Objectives: To build a decision model of LG biopsy based on B-mode ultrasonography (US) with shear-wave elastography (SWE) in patients with suspected SS.

Methods: Patients who had at least one symptom of oral dryness (based on AECG questions) or had anti-SSA positive were recruited and signed a written informed consent. Bilateral parotid (PG) and submandibular glands (SMG) were examined with B-mode US which graded the echostructure of each gland on a scoring system scaled 0 to 4 (US score), and SWE which described the elasticity of glands. Then LG biopsy was performed.

Results:

(1) Ninety-one patients whose mean age was 43±15 years were enrolled and 93% of them were female. Anti-SSA was detected in 77 patients (85%) and 28 patients (31%) showed unstimulated whole saliva flow rate (USFR)≤0.1mL/mim. There were 57 patients (63%) showing FS≥1 on LG biopsy. Sixty-three patients (69%) were classified as primary SS, 10 patients (10%) were secondary SS, 18 patients (20%) were uCTD and one patient was RA without SS.

(2) US scores were equal between PG and SMG in 59 patients (65%), while the rest patients showed different US scores between two glands: 7 patients (8%) showed higher US scores in PG and 25 patients (27%) showed higher scores in SMG. In each pair of glands US scores were equal. SWE values in PG or SMG of US score 1, 2 or 3 were significantly

higher than those of US score 0, while SWE values in glands of US score 4 became declined and showed no significant difference from those with US score 0 (Figure 1A).

(3) Heatmap showed US scores in either major salivary gland of patients with FS≥1 on LG biopsy were significantly higher than those with FS<1 (all p<0.001, Figure 1B). ROC curve showed a total US score (including bilateral PG and SMG) ≥9 and a total SWE value (including bilateral PG and SMG)≥30 could significantly recognize patients with FS≥1, respectively with specificity of 100% and 93% (Figure 1C). In this cohort, among 51 patients with a total US score ≥9 and/or a total SWE value≥30, 49 patients (96%) showed FS≥1 on LG biopsy; while two outliers showed total US scores were both 8 although combined SWE values≥30. Other 29 patients showed total US scores≤6 with total SWE values <30 and only one patient (3%) showed FS≥1 on LG biopsy. The remaining 11 patients showed total US scores were 8 with total SWE values <30 and 64% of them (n=7) showed FS≥1.

Conclusion: A preliminary decision model of LG biopsy based on B-mode US with SWE in patients with suspected SS were built in Table 1. For example, rheumatologists should reassess the need for biopsy if the incidence of FS≥1 would be <5%. Another cohort of patients with suspected SS is needed for further validation.

Table 1. A preliminary decision model of LG biopsy based on B-mode US with SWE in patients with suspected SS

Algorithm*	Comments on the decision of LG biopsy
A total US score≥9 and/or a total SWE≥30	The specificity of FS≥1 on biopsy is >93%. Biopsy is recommended. In some special cases (e.g. contraindicated to biopsy), this item is a potential alternative to LG biopsy.
A total US score 7~8 with a total SWE <30	It is hard to predict the result of FS, so biopsy is strongly recommended.
A total US score≤6 with a total SWE <30	The incidence of FS≥1 would be <5%. Rheumatologists should reassess the need for biopsy.

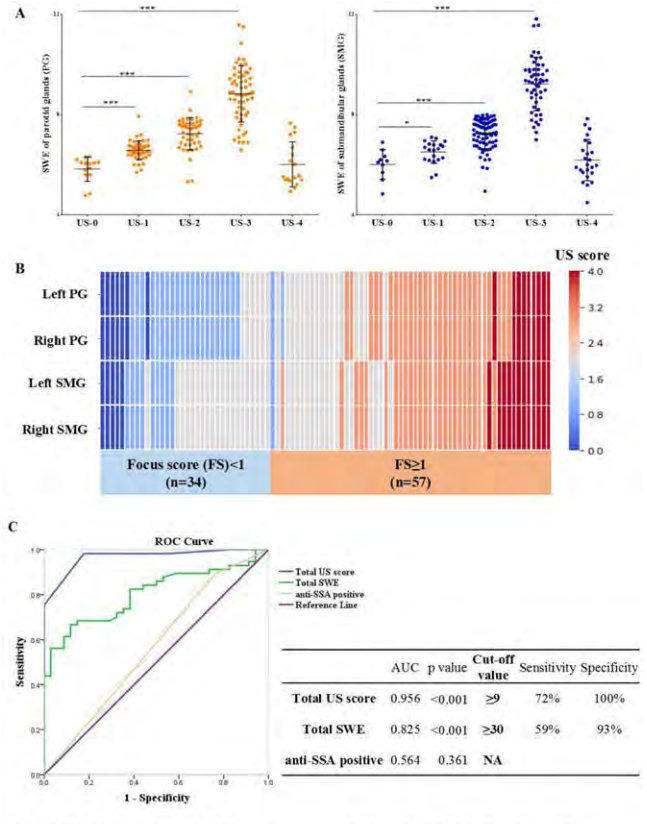


Figure 1 B-mode ultrasonography (US) with shear-wave elastography (SWE) in 91 patients with suspected SS. **A**: SWE values in 182 parotid glands (PG, left) or 182 submandibular glands (SMG, right) of US score 0 to 4. **B**: Heatmap showed US scores in either major salivary gland of 57 patients with FS≥1 on labial gland biopsy and 34 patients with FS<1. **C**: ROC curve was used to evaluate the predicting role of a total US score (including bilateral PG and SMG), a total SWE (including bilateral PG and SMG) and anti-SSA positive on the incidence of FS≥1 on labial gland biopsy.

References: None

Disclosure of Interests: None declared
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OP0096

THE DIFFERENCES BETWEEN SJÖGREN'S SYNDROME PATIENTS WITH COMBINED SERONEGATIVITY AND ANTI-RO/SSA SEROPOSITIVITY

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Background: Sjögren's syndrome (SS) is characterized by B cell hyperactivity reflected by hypergammaglobulinemia as well as a plethora of autoantibodies including antinuclear antibodies (ANA), anti-Ro/SSA, anti-La/SSB and rheumatoid factors (RF). Previous studies have focused on the phenotype of single positive (ANA or anti-Ro/SSA or anti-La/SSB) or double positive (anti-Ro/SSA and anti-La/SSB positive) SS patients, showing differences regarding the age of diagnosis, sicca manifestations and specific extraglandular manifestations. To our knowledge, no study has ever explored the clinical spectrum of triple seronegative (anti-Ro/SSA + anti-La/SSB + RF negative) and quadruple seronegative (ANA +anti-Ro/SSA + anti-La/SSB + RF negative) SS patients.

Objectives: To study the differences in the clinical phenotype of triple and quadruple seronegative (SS) patients in a large cohort of well characterized patients, after comparison with anti-Ro/SSA positive patients.

Methods: From a total cohort of 1723 consecutive SS patients who fulfill the 2016 EULAR/ACR criteria and are followed up in 4 clinical centers ([Universities of Pisa and Athens, Harokopio and Ioannina, (PAHI)], those who have been found triple or quadruple seronegative were identified and compared with matched anti-Ro/SSA positive SS patients according to age of SS onset, disease duration and gender, in 1:1 and 1:2 ratio respectively. Glandular (dry mouth, dry eyes, parotid gland enlargement) and extra-glandular manifestations (Raynaud's phenomenon, chronic fatigue arthralgias/myalgias, arthritis, palpable purpura, liver involvement, kidney involvement, lung involvement, neurologic involvement, long standing lymphadenopathy and lymphoma) were compared between the 2 seronegative groups and the anti-Ro/SSA positive control group. Statistical analysis for categorical variables was performed by Fisher exact or chi-square tests and for continuous variables with t test or Mann-Whitney accordingly.

Results: Two hundred and four SS patients (11,8%) were identified as triple negatives and 53 (3,0%) as quadruple, with a median disease duration of 6 years (range: 0-41) and 5 years (range: 0-32) respectively. The matched anti-Ro/SSA controls were 204 for the triple and 103 for the quadruple negatives. Triple negatives had lower frequency of monoclonal gammopathy (5,5% vs 12,1% p=0,04), low C4 serum levels (23% vs 36%, p=0,009) and lymphoma (3,4% vs 9,8%, OR= 3,06, 95% CI =1,27-7,85) while quadruple negatives exhibited higher prevalence of dry eyes (100% vs 90%) and lower prevalence of long standing lymphadenopathy (2,7% vs 19,5%, p=0,001) and lymphoma (0% vs 15%, p=0,001) compared to anti-Ro/SSA matched controls.

Conclusion: Combined seronegativity account for more than 10% of SS population and is associated with lower prevalence of lymphoma compared to anti-Ro/SSA positive patients.

Disclosure of Interests: Loukas Chatzis: None declared, Vasileios Pezoulas: None declared, Francesco Ferro: None declared, Valentina Donati: None declared, Aliki Venetsanopoulou: None declared, Evangelia Zampeli: None declared, Maria Mavromati: None declared, Paraskevi Voulgari: None declared, Clio Mavragani: None declared, Dimitris Fotiadis: None declared, Fotini Skopouli: None declared, Salvatore De Vita Consultant of: Roche, Human Genome Science, Glaxo Smith Kline and Novartis, Chiara Baldini: None declared, Haralampos M. Moutsopoulos: None declared, Athanasios Tzioufas: None declared, Andreas Goules: None declared
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OP0097 DEVELOPMENT OF NEW INTERNATIONAL CLASSIFICATION CRITERIA FOR ANTIPHOSPHOLIPID SYNDROME: PHASE III CASE COLLECTION RESULTS

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Background: An international multi-disciplinary effort is underway to develop rigorous, new, consensus- and evidence-based classification criteria for Antiphospholipid Syndrome (APS). The methodological approach includes four phases; we have previously presented phases I and II (item generation and reduction), which resulted in 27 candidate criteria[1] organized in laboratory and clinical domains.

Objectives: Phase III (item weighting/threshold identification) is currently underway; here we report initial Phase III case collection results.

Methods: We used REDCap, a secure data system, for Phase III international case collection. The candidate criteria of 27 items at the end of Phase II was represented in a standardized case collection form. We asked international physicians interested in APS to provide and rate cases using a Likert scale (+3 to -3: highly likely to highly unlikely to be APS). Cases with higher scores (+2 or +3) were categorized as "highly likely" APS, whereas lower scores (+1 to -3) were categorized as "equivocal or unlikely" APS.

Results: We collected 314 potential APS cases (mean age 43.8±14.4 years; 79% female; and 77% white) between 6/2019-8/2019 from 17 sites in Europe (47%), North America (41%), and South America (11%). Majority of cases were potential primary APS (64%); 137 were rated as "highly likely" and 177 as "equivocal or unlikely" APS. Lupus anticoagulant, anti$\beta_2$glycoprotein-I antibody IgG/M, anticardiolipin antibody IgG, arterial thrombosis, venous thromboembolism, microvascular disease, fetal loss between 16-34 weeks, severe preeclampsia, severe placental insufficiency, cardiac valve disease, and low platelet count occurred with higher frequency in the APS cases categorized as "highly likely" (Table).

Conclusion: International collection of cases spanning the spectrum of "highly likely" to "equivocal or unlikely" APS provide "real world" assessment of patients being referred for APS evaluation. In next steps, proposed candidate criteria will be further refined, organized, and weighted, and a preliminary threshold for APS classification will be determined.

Table. Characteristics of Potential APS Cases Categorized by Physician Assessment

Candidate Relative Criteria, n (%)	Total (n=314)	Highly Likely APS (n=137)	Equivocal or Unlikely APS (n=177)
LABORATORY			
Lupus Anticoagulant Test	208 (66)	117 (85)	91 (51)
Anticardiolipin Antibody			
• IgG	170 (54)	90 (66)	80 (45)
• IgM	138 (44)	61 (45)	77 (44)
Anti$\beta_2$glycoprotein-I Antibody			
• IgG	99 (32)	66 (48)	33 (19)
• IgM	79 (25)	47 (34)	32 (18)
CLINICAL			
Macrovascular			
• Superficial Vein Thrombosis	15 (5)	4 (3)	11 (6)
• Venous Thromboembolism	95 (30)	63 (46)	32 (18)
• Transient Ischemic Attack	27 (9)	13 (10)	14 (8)
• Arterial Thrombosis	82 (26)	58 (42)	24 (14)
Microvascular*	86 (27)	62 (45)	24 (14)
Obstetric**			
• Embryonic Loss (<10 weeks [w])	85 (45)	34 (42)	51 (48)
• Fetal Loss (10w–<16w)	20 (11)	9 (11)	11 (10)
• Fetal Loss (16w–34w)	42 (22)	32 (40)	19 (18)
• Severe Preeclampsia (<34w)	27 (14)	18 (22)	9 (8)
• Severe Placental Insufficiency (<34w)	22 (12)	13 (16)	9 (8)
Cardiac Valve Disease***	32 (10)	21 (15)	11 (6)
Thrombocytopenia <150 G/L	72 (23)	43 (31)	29 (16)

*Livedo racemosa, livedoid vasculopathy, adrenal hemorrhage, acute ischemic enceophalopathy, cardiac microvascular disease, pulmonary hemorrhage, acute and/or chronic antiphospholipid-related nephropathy; **Total number of patients ever pregnant: 188 (highly likely APS: 81; unlikely APS: 107) ***Valve thickening and/or vegetation.

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OP0098 TRAJECTORIES OF GROWTH IN OFFSPRING FROM MOTHERS WITH PREVALENT OR PRE-SYSTEMIC LUPUS ERYTHEMATOSUS: A NATIONWIDE POPULATION-BASED STUDY IN KOREA

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease that primarily affects women of childbearing age and is known to have poor maternal and fetal outcomes associated with pregnancy.

Objectives: We planned on the long-term follow-up studies to find out whether SLE offspring with low birth weight would properly catch up in future childhood life.

Methods: Korean National Health Insurance (NHI) service is a mandatory, single public health insurance system that covers more than 50,000,000 Korean population. It consists of inpatient and outpatient diagnosis and treatment data for the purpose of reimbursement. Rare and Intractable Diseases (RID) registration system is a copayment reduction scheme which provides financial support to patients with certain rare disease, include SLE. National Health Screening Program for Infants and Children (NSHPIC) is a population screening system for children aged 4 to 71 months, requiring 7 visits to participating clinic at pre-specified times.

Among the children who were born between 2008 and 2013, we identified those who completed the first (between 4-6th month), second (between 9-12th month) and either sixth or seventh examination (between 54-65th month and 66-71th month, respectively) of NSHPIC. By linking maternal and offspring healthcare data through their unique personal identification numbers, we constructed a mother-child database to track the growth of the child. Among their mothers, we could identify SLE patients who had given live singleton births using RID database (V136) and the international classification of disease code (M32.x) for SLE. Therefore, we were able to follow birth weight and subsequent growth of offspring according to their mother's disease status.

Results: We could identify 1,007 offspring from SLE mothers and 793,537 control from non-SLE mothers. Offspring from SLE mothers showed the higher risk of low birth weight defined as less than 2500g [hazard ratio (HR) 4.79, 95% confidence interval (CI) 4.08–5.63]. In terms of subgroups analysis according to the time of diagnosis, the risk of low birth weight was the highest in offspring from those who diagnosed SLE during pregnancy (HR 8.22, 95% CI 3.18–21.26). In addition, the risk of low birthweight increased not only in offspring from already diagnosed SLE before pregnancy (HR 5.63, 95% CI 4.41–7.19), but also in offspring from those who diagnosed with SLE after delivery (pre-SLE) compared to general population (HR 2.03, 95% CI 1.33–3.09).

Subsequent growth failure defined as less than 3 percentile was more prevalent in SLE offspring compared to general population at 4-6 month (HR 3.28, 95% CI 2.22–4.77). However, at 6-9 months and 54-71 months, the gap was reduced, showing no statistical difference with the general population (HR 1.22, 95% CI 0.73–2.03 and HR 1.26, 95% CI 0.88–1.80, respectively).

Among SLE offspring with low birth weight (< 2500g), 89.34% showed the body weight of 3 percentile or more and 75.84% showed the body weight 10 percentile or more at 4-6 month. The proportion of children who catch up afterwards has not increased since then, as the proportion of children who

were more than 10 percentile was 81.46% at 6-9 months and 80.34% at 54-71 months.
Conclusion: The offspring of SLE patients were more likely to have low birthweight compared to general population, but majority of them showed the catch up growth at 4-6 month of age. The risk of low birthweight was especially high in the offspring from mothers who diagnosed SLE during pregnancy.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.4002

New technologies in basic research

OP0099 FUNCTIONAL MAPPING OF SYNOVIAL FIBROBLAST POPULATIONS IN HEALTH AND ARTHRITIC DISEASE: INSIGHTS INTO THE PATHOGENIC REMODELING OF SYNOVIAL MICROENVIRONMENT

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Background: Our previous studies highlighted the fundamental in vivo role of synovial fibroblasts (SFs) in TNF-mediated murine chronic arthritis[1,2] and recent findings identified different SF identities based on their transcriptomic profiles with distinct contributions in acute, autoimmunity-based, murine arthritis[3].
Objectives: In this study, we focus on delineating the map of SF subpopulations in healthy joint and in the course of arthritic disease and the underlying regulatory networks functioning towards pathogenicity.
Methods: Sorted single cell suspensions (CD45-, Pdpl+) and their fragmented nuclei from synovial joints of WT, early and late arthritic hTNFtg mice were processed for scRNAseq and scATAC employing a droplet-based technology (10x Genomics). To define the transcriptional and epigenetic signatures originating from the two different assays, we developed an integrative analysis pipeline based on the Seurat software package (v3.1). Meta-analysis of previously reported data of K/BxN serum transfer of arthritis was employed to define commonalities and differences in SF subsets among murine modelled disease.
Results: The transition from healthy to chronically affected synovial microenvironment (SME) due to overexpression of hTNF is characterized by a dynamic transformation of SF clusters. The Lining arthritic Thy1^{low} synovial layer (L-SFs) is hyper-populated while Sub-Lining Thy1^{high} SF clusters (SL-SFs) are remodeled towards catabolic and inflammatory phenotypes compared to naïve SF organization pattern. Interestingly, trajectory analysis revealed that the SL clusters, which normally exhibit a gradual developmental-like process towards different profiles, differentially change during disease. We identified that the previously reported proliferating SL cluster is absent in healthy synovium, dominates mainly in early stages of chronic arthritis and it is closely related to the L-SFs. Mapping of the gene regulatory networks by RNAseq was supported by scATAC analysis. Similarly, meta-analysis of SF profiles derived from naïve and the K/BxN-serum–treated mice showed significant differences, possibly reflecting the phenotypes of the two established models of arthritis.
Conclusion: Our approach unravels for the first time the regulatory heterogeneity and gene expression profiling of SF subpopulations in normal synovium, and reveals deep biological insights of the functional re-organization of SME during development of disease. It further identifies the common and divergent features of the different subtypes of murine arthritis that may well reflect the diversity of RA subtypes and the response to therapies.
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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.1839

OP0100 MOLECULAR PROFILING OF PERIPHERAL IMMUNE CELL SUBSETS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease that affects 1% of the world's population. Several key biological functions are dysregulated in RA, manifesting clinically as pain, fatigue, and synovitis, with articular destruction, organ-based comorbidities, and functional decline. Defining immune dysregulation in the peripheral blood of patients (pts) with RA will help inform future work to assess the extent to which immune homeostasis can be therapeutically achieved for these pts.
Objectives: To identify baseline molecular characteristics of the peripheral immune system, at the level of individual immune cell subsets, in pts with RA recruited to clinical trials of the oral, selective Janus kinase 1 (JAK1) inhibitor, filgotinib.
Methods: Peripheral blood mononuclear cells (PBMC) were collected from 324 pts with moderate to severely active RA, who had an inadequate response to methotrexate ([MTX], FINCH-1; NCT02889796; n=109) or who were MTX naïve (FINCH-3; NCT02886728; n=215). PBMC were also collected from 50 demographically matched healthy volunteers (HV). The Immune Profiler platform was used to sort PBMC into 24 immune cell subsets, then quantify their gene expression and chromatin accessibility using RNA-seq and the assay for transposase-accessible chromatin with high-throughput sequencing (ATAC-seq), respectively. Differentially expressed genes (DEGs) and differentially accessible regions (DARs) were identified among immune cell subsets from pts with RA versus HV. Gene set signature scores of Molecular Signatures Database hallmark pathways were calculated using single sample gene set enrichment analysis (ssGSEA) to examine differences in pathway activity between groups.
Results: A total of 14,500 sequencing datasets were generated from the pt and HV immune cell subsets. Among these, over 26,000 DEGs and 220,000 DARs were identified in RA versus HV (false discovery rate <0.05) across the 24 immune cell subsets. DEGs were identified in all immune cell subsets tested and were most pronounced in natural killer (NK) subsets; most DARs were detected in myeloid and NK subsets. ssGSEA revealed differential pathway signaling in RA versus HV across multiple functions at the immune cell subset level. Myeloid subsets from pts with RA often showed elevated pathway activities versus HV whereas B, T and NK subsets showed a general decrease. In particular, monocyte populations from pts with RA versus HV had elevated pathway activities involved in inflammatory response and interleukin-6/Janus kinase/signal transducer and activator of transcription 3 signaling. The B, T and NK subsets showed a general decrease in tumor necrosis factor-α signaling; conversely, monocyte subsets showed an increase. Prior MTX exposure did not have a notable impact on the detected molecular profile.
Conclusion: Differences in gene expression, hallmark pathway activity, and chromatin accessibility were identified in RA versus HV at the immune cell subset level. Significant contributions to differences in chromatin accessibility identified in the myeloid and NK cell populations suggest that there are more active regulatory sequences in these cell types that are associated with RA. Further investigations based on these findings may increase understanding of the immune regulatory paradigm in the context of RA.
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Disclosure of Interests: Peter C. Taylor Grant/research support from: Celgene, Eli Lilly and Company, Galapagos, and Gilead, Consultant of: AbbVie, Biogen, Eli Lilly and Company, Fresenius, Galapagos, Gilead, GlaxoSmithKline, Janssen, Nordic Pharma, Pfizer Roche, and UCB, Jinfeng Liu Shareholder of: Gilead Sciences Inc., Roche, Employee of: Gilead Sciences Inc., Luting Zhuo Employee of: Gilead Sciences Inc., Yuan Tian Employee of: Gilead Sciences Inc., Thomas Snyder Employee of: Verily Life Sciences, Charlie Kim Employee of: Verily Life Sciences, Pouya Kheradpour Employee of: Verily Life Sciences, Kat Drake Employee of: Verily Life Sciences, Sam Kim Shareholder of: Gilead Sciences Inc., Employee of: Gilead Sciences Inc., Rachael E. Hawtin Shareholder of: Gilead Sciences Inc., Employee of: Gilead Sciences Inc.
DOI: 10.1136/annrheumdis-2020-eular.3967

OP0101-HPR **QUALITY OF LIFE IN PEOPLE WITH SYSTEMIC SCLEROSIS WITH DIFFERENT DEGREES OF LUNG DISEASE - A CROSS-SECTIONAL STUDY**

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Background: There are few studies evaluating different aspects of quality of life including depressive symptoms and physical capacity and physical activity in patients with systemic sclerosis (SSc) with different degrees of lung disease.
Objectives: The aim of this study was to evaluate differences in self-reported disability, physical capacity and activity, depressive symptoms and quality of life, between patients with SSc with no-mild lung disease and those with moderate-endstage lung disease.
Methods: In this cross-sectional study, 279 patients with SSc fulfilling the 2013 ACR/EULAR criteria for SSc (84% limited and 16% diffuse SSc) were included. Medsger disease severity scale was used to subgroup the patients into no-mild (n=156) or moderate- endstage lung disease (n=115). Disability was measured with Health Assessment Questionnaire-Disability Index (HAQ-DI); physical capacity (ability to walk, jog/run); and physical activity (different intensities) was measured with three single questions; depressive symptoms with Hospital Anxiety and Depression-scale (HADs); and quality of life was measured with The *Short Form* (36) Health Survey (SF-36).
Results: Patients with moderate-endstage lung disease reported higher scores on HAQ-DI ($p<0.001$) and lower scores on SF-36 physical component ($p<0.0001$) than patients with no-mild lung disease. Patients with moderate-endstage lung disease reported lower physical capacity ($p<0.0001$), less physical activity on low to moderate intensity the past 6 months ($p<0.016$) and less exercise on moderate to high intensity the past year ($p=0.022$) compared to those with no-mild lung disease. There was no difference between the two subgroups when it comes to the mental component in SF-36 ($p=0.2$), however patients with moderate-endstage lung disease had lower scores on the subscales vitality (($p=0.003$), social function ($p=0.002$) and emotional role function ($p=0.005$) as well as higher scores on the HADs depressive symptoms scale ($p=0.024$), than the patients with no-mild lung disease.
Conclusion: Patients with SSc with moderate-endstage lung disease report more disability, lower physical capacity and activity, are more depressed and the physical aspects of quality of life is lower, as well as vitality, social function and emotional role function, compared to patients with no-mild lung disease. Studies evaluating whether increased physical activity and exercise may improve depressive symptoms and aspects of quality of life in patients with moderate-endstage lung disease are needed.
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Immunodeficiency and autoimmune disease

OP0102 **GENE SCREENING OF PRIMARY IMMUNODEFICIENCY DISEASES IN PATIENTS WITH JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS**

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Background: Systemic lupus erythematosus (SLE) is one of the most common auto-immune diseases in childhood. Primary immunodeficiency disease (PID) patients may present or combine with autoimmune diseases.
Objectives: This study aimed to perform gene sequencing via high-throughput sequencing technology in a series of Chinese pediatric SLE patients, and investigate the concomitant situation of PIDs and SLE. Gene sequencing results may help clarify the pathogenesis of SLE.
Methods: This was a retrospective case series of SLE children who referred to the Peking Union Medical College Hospital between 01/2016 and 09/2019. Genetic tests were performed in patients who met the inclusion criteria. We then collected demographic, clinical, and treatment information of all involved patients. Descriptive statistics were used.
Results: Seventy-one patients were finally included (eighteen boys and fifty-three girls). The median age at the time of disease onset was 9.5 (range, 3-15) years. It is notable that five patients experienced their first attack before the age of five. Twenty-seven patients showed a persistent increase in ESR during treatment, while thirteen cases presented with repeated CMV infection, thirty-four cases with persistent low complement levels, seven with basal ganglia calcification showed in skull CT or MRI, four with special type of rash (i.e., frostbite-like rash, discoid erythema, reticular erythema), two with obvious hepatosplenomegaly, and one case with type I diabetes. Gene sequencing results showed that about ten patients combine with primary immunodeficiency disease, including Aicardi-Goutières Syndrome (AGS) (n=4), Spondyloenchondro-dysplasia with immune dysregulation (SPENCDI) (n=1), STING-associated vasculopathy with onset in infancy (SAVI) (n=1), lysinuric protein intolerance (LPI) (n=1), Ras-associated autoimmune leukoproliferative disorder (RALD) (n=2).
Conclusion: SLE patients who present atypical or refractory manifestations should attach importance to the existence of primary immunodeficiency disease. Genetic tests are recommended for patients with early-onset SLE, especially those with recurrent frostbite-like rash or persistent CMV infection since childhood.
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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.4199

Spondyloarthritis - treatment

OP0103 **DOES GENDER, AGE OR SUBPOPULATION INFLUENCE THE MAINTENANCE OF CLINICAL REMISSION IN AXIAL SPONDYLOARTHRITIS FOLLOWING CERTOLIZUMAB PEGOL DOSE REDUCTION?**

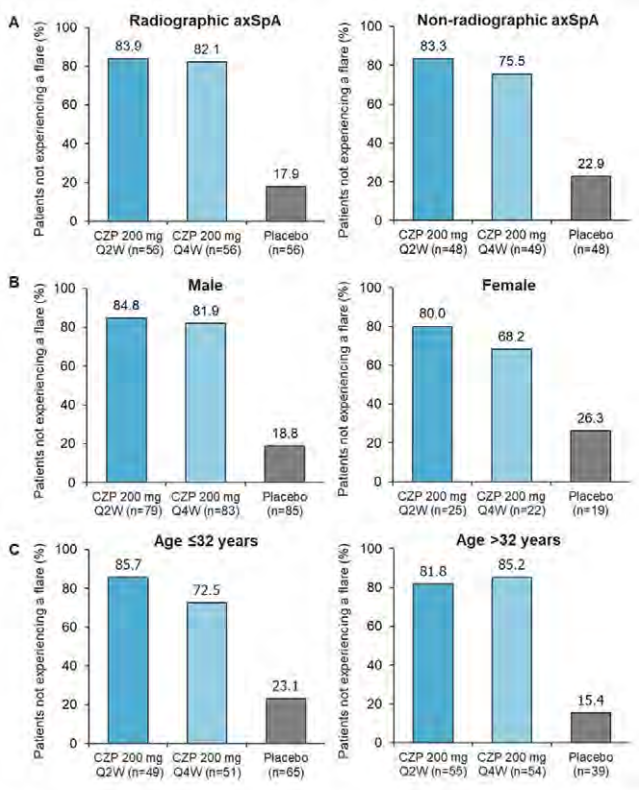
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Background: Previous studies have shown that withdrawing tumour necrosis factor inhibitors (TNFi) in patients (pts) with axial spondyloarthritis (axSpA) who have achieved sustained remission often leads to relapse.[1] However, none have formally tested TNFi dose reduction strategies in a broad axSpA population or evaluated whether relapse following TNFi dose reduction and withdrawal is associated with a specific demographic subgroup.
Objectives: C-OPTIMISE evaluated the percentage of pts without flare after TNFi dose continuation, reduction or withdrawal in adults with early axSpA treated with the Fc-free, PEGylated TNFi certolizumab pegol (CZP). Here, we analyse whether responses to reduced maintenance dose were comparable in pts stratified by axSpA subpopulation, gender and age.
Methods: C-OPTIMISE (NCT02505542) was a multicentre, two-part phase 3b study in adults with early (<5 years' symptom duration) active axSpA (stratified for radiographic [r]- and non-radiographic [nr]- axSpA). Pts received CZP 200 mg every 2 weeks (wks) (Q2W; 400 mg loading dose at Wks 0, 2 and 4) during the open-label induction period. At Wk 48, pts in sustained remission (Ankylosing Spondylitis Disease Activity Score [ASDAS] <1.3 at Wk 32 or 36 [if ASDAS <1.3 at Wk 32, it must be <2.1 at Wk 36, or vice versa] and at Wk 48) were randomised to double-blind full maintenance dose (CZP 200 mg Q2W); reduced maintenance dose (CZP 200 mg every 4 wks [Q4W]) or placebo (PBO) for a further 48 wks (maintenance period). The primary endpoint was the percentage of pts not experiencing a flare (ASDAS ≥2.1 at two consecutive visits or ASDAS >3.5 at any timepoint) during Wks 48–96. Analyses were conducted on subgroups according

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to axSpA subpopulation, gender and age ≤/> the median age of the randomised set (32 years).
Results: During the 48-wk induction period, 43.9% of patients (323/736) achieved sustained remission and 313 pts entered the 48-wk maintenance period (r/nr-axSpA: 168/145 pts; males/females: 247/66 pts; age ≤32/>32: 165/148 pts). During the maintenance period, responses in r- and nr-axSpA pts were comparable across all three randomised arms. 83.9% r-axSpA and 83.3% nr-axSpA pts receiving the full CZP maintenance dose did not experience a flare, and in the reduced maintenance dose arm 82.1% r-axSpA and 75.5% nr-axSpA pts did not experience a flare. In the PBO group this was reduced to 17.9% and 22.9%, respectively. Similar responses were seen in pts stratified by gender or age, with substantially higher percentages of pts randomised to CZP full or reduced maintenance dose remaining free of flares compared to PBO in all subgroups (Figure).
Conclusion: The results of C-OPTIMISE indicate that a reduced maintenance dose is suitable for pts with axSpA who achieve sustained remission following 1 year of CZP treatment, regardless of axSpA subpopulation, gender or age. Complete treatment withdrawal is not recommended due to the high risk of flare.
References: **[1]**Landewe R. Lancet 2018;392:134–44.

Figure. Patients not experiencing flares during the maintenance period of C-OPTIMISE, stratified by: A) disease subpopulation (radiographic vs non-radiographic axSpA); B) gender (male vs female); C) age (≤32 years vs >32 years)



axSpA: axial spondyloarthritis; CZP: certolizumab pegol; Q2W: every 2 weeks; Q4W: every 4 weeks.

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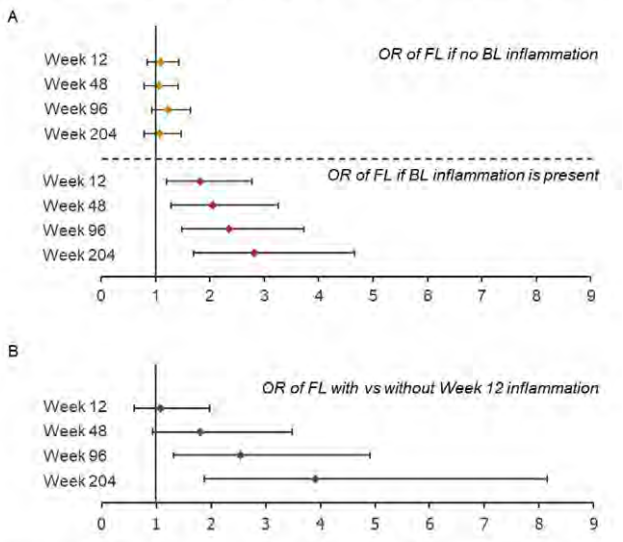
OP0104

THE IMPACT OF PERSISTENT INFLAMMATORY CHANGES ON PREVALENCE OF FATTY LESIONS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS TREATED WITH CERTOLIZUMAB PEGOL: 4-YEAR MRI RESULTS FROM RAPID-AXSPA

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Background: Axial spondyloarthritis (axSpA) is a chronic disease characterised by inflammation in the sacroiliac joints and spine, causing severe back pain and stiffness. Emerging evidence suggests chronic spinal inflammation may be associated with osteoproliferation leading to syndesmophyte formation and spinal ankylosis, with subsequent worsening of patient mobility and function.[1] Fatty lesions (FLs) on magnetic resonance imaging (MRI) T1 sequences are considered to be post-inflammatory precursors to these changes. Certolizumab pegol (CZP), an Fc-free, PEGylated tumour necrosis factor inhibitor (TNFi), has proven efficacy in treating the signs and symptoms of axSpA.[2,3] CZP has also been shown to decrease spinal and sacroiliac joint MRI inflammation, and limit radiographic progression of the spine over 4 years of treatment.[4]
Objectives: To report the effect of early post-baseline (BL) inflammatory changes on fatty lesion prevalence over 4 years in a broad axSpA patient population treated with CZP.
Methods: RAPID-axSpA (NCT01087762) was a phase 3 trial which was double-blind and placebo (PBO)-controlled to Week (Wk) 24, dose-blind to Wk 48 and open-label to Wk 204. CZP-randomised axSpA patients (Wk 0 CZP: 200 mg every 2 wks [Q2W] or 400 mg Q4W) continued their assigned dose throughout; PBO-randomised axSpA patients (Wk 0 PBO) received CZP from Wk 24, or if non-responders, from Wk 16 onwards. Blinded spinal MRI scans at Wks 0, 12, 48, 96 and 204 were assessed by 2 central readers to evaluate FL and inflammatory lesions in vertebral edges (VEs). Changes in FL prevalence are reported as odds ratios (OR; FL+/FL-) between time points or inflammation states, with nominal 95% confidence intervals (CI), for Wk 0 CZP. ORs were estimated from a logistic regression model for VE level data with random effects for patient and VE (within patient). The fixed model effects included time point, inflammatory status of VEs at BL and Wk 12, FL status at BL, and interactions if appropriate.
Results: Of 325 axSpA patients, 89 and 47 initially randomised to CZP or PBO, respectively, had a BL and ≥1 post-BL MRI and therefore were eligible for these analyses. In these patients, a total of 3,127 of VEs were assessed at BL; inflammation was observed in 21.6% and FL in 29.3% of VEs, equating to mean counts of 5.0 and 6.7 per patient; 10.5% of VEs had both inflammation and FL at BL. At BL, FLs were relatively more often observed in inflamed VEs vs non-inflamed VEs: OR (95% CI) of 3.30 (1.94, 5.61). This difference increased over time, as the OR of FL at Wk 204 vs BL was 2.82 (1.70, 4.66) in VEs that were inflamed at BL compared with 1.08 (0.79, 1.48) in VEs that were not inflamed at BL (Figure 1A). Resolution of inflammation by Wk 12 appeared to lower the risk of FL prevalence over 4 years. When adjusted for BL VE status with respect to inflammation and FL, if inflammation prevailed at Wk 12, the OR of FL vs no FL was 1.80 (0.93, 3.49) at Wk 48, 2.54 (1.32, 4.91) at Wk 96 and 3.91 (1.87, 8.15) at Wk 204 (Figure 1B).
Conclusion: This is the first report from a clinical interventional PBO-controlled study in a broad axSpA population showing that inflammation that prevailed after the start of TNFi treatment was associated with increased FL prevalence over 4 years. Reduction of inflammation by Wk 12 mitigated the risk of FL over the long-term, indicating the importance of early, effective and long-term treatment targeting inflammation. Similarly, a complete and persistent reduction of inflammation appears to be critical in these patients.
References:
[1] Maksymowych WP. Ann Rheum Dis 2013;72:23–8; **2.** Van der Heijde D. Rheumatology (Oxford) 2017;56:1498–509; **3.** Deodhar A. Arthritis Rheumatol 2019;71:1101–11; **4.** Van der Heijde D. Ann Rheum Dis 2018;77:699–705.

Figure 1. (A) OR for changes in FL prevalence vs presence or absence of inflammation at BL; (B) OR of FL for VEs with vs without inflammation at Week 12



A: An OR >1 represents an increase in FL from BL. A logistic regression with fixed effects for BL inflammation status by visit (including BL) and random effects for patient and VE (within patient). B: An OR >1 represents increased FL in VEs with vs without inflammation at Week 12, adjusted for BL VE status with respect to inflammation and FL. A logistic regression with fixed effects for Week 12 inflammation by visit (excluding BL) and BL inflammation by BL FL, and random effects for patient and VE (within patient). BL: baseline; FL: fatty lesion; OR: odds ratio; VE: vertebral edge.

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OP0105

EFFICACY AND SAFETY OF BIMEKIZUMAB IN ANKYLOSING SPONDYLITIS: 48-WEEK PATIENT-REPORTED OUTCOMES FROM A PHASE 2B, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, DOSE-RANGING STUDY

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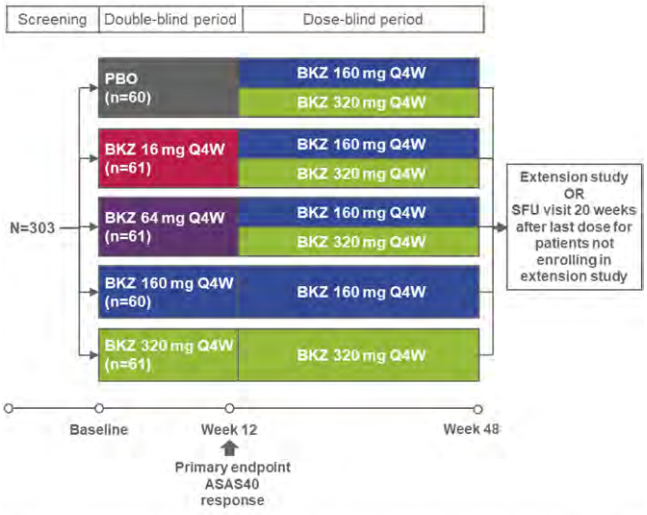
Background: Bimekizumab (BKZ), a monoclonal antibody that selectively neutralises interleukin (IL)-17A and IL-17F, is a potential therapeutic option in ankylosing spondylitis (AS).

Objectives: To report 48-week (wk) patient-reported outcomes (PROs) in patients (pts) with AS treated with BKZ in a phase 2b dose-ranging study (BE-AGILE; NCT02963506).

Methods: Pts with active AS (Bath AS Disease Activity Index [BASDAI] ≥4; spinal pain ≥4 [0–10]), fulfilling modified New York criteria (central reading), and inadequate response/intolerance to NSAIDs were randomised according to the study design (Figure 1). PROs included spinal pain, fatigue (BASDAI Q1), morning stiffness (mean of BASDAI Q5+6), Bath AS Functional Index (BASFI), Medical Outcomes Study (MOS) Sleep Problems Index II and AS Quality of Life questionnaire (ASQoL). Efficacy is reported for pts initially randomised to placebo (PBO) or BKZ 160/320 mg every 4 weeks (Q4W); treatment-emergent adverse events (TEAEs) are reported for pts who received ≥1 dose of study drug (Safety Set).

Results: Of 303 pts, 181 were randomised to PBO or BKZ 160/320 Q4W mg at Wk 0; 179/181 completed Wk 12 and 161/181 completed Wk 48. At Wk 12, improvements in pain, fatigue, morning stiffness, BASFI, sleep and ASQoL were greater in BKZ pts vs PBO pts. Responses were further improved or maintained to Wk 48, with no meaningful differences between BKZ 160 mg and 320 mg (Table 1). Serious TEAEs occurred in 13/303 (4.3%) pts (Table 2), which included 2 major adverse cardiac events considered not related to study drug. Oral candidiasis occurred in 16 (5.3%) pts.

Figure 1. Study design



ASAS40: Assessment of SpondyloArthritis international Society improvement of ≥40%; Q4W: every 4 weeks; SFU: safety follow-up.

Table 1. PRO efficacy endpoints to Week 48 (multiple imputation)

Mean (SD)	Wk	PBO – BKZ 160 mg (n=24)	PBO – BKZ 320 mg (n=36)	BKZ 160 mg (n=58)	BKZ 320 mg (n=61)
Spinal pain	0	6.9 (1.4)	7.0 (1.9)	6.6 (2.0)	7.3 (1.5)
CfB	12	-1.5 (1.6)	-0.7 (1.7)	-2.6 (2.2)	-3.6 (2.4)
	48	-3.7 (2.0)	-3.7 (2.6)	-3.8 (2.4)	-4.7 (2.1)
Fatigue	0	6.4 (1.7)	6.8 (1.6)	6.4 (1.7)	6.4 (1.9)
CfB	12	-0.7 (2.5)	-1.0 (1.7)	-2.1 (2.2)	-2.1 (2.5)
	48	-2.7 (2.2)	-2.8 (2.4)	-3.1 (2.1)	-3.3 (2.4)
Morning stiffness	0	6.9 (1.7)	6.7 (2.0)	6.5 (1.8)	6.6 (2.1)
CfB	12	-1.5 (1.7)	-1.1 (1.5)	-2.8 (2.0)	-3.4 (2.7)
	48	-3.9 (2.2)	-3.6 (2.4)	-3.9 (2.2)	-4.4 (2.4)
BASFI	0	5.8 (1.8)	5.5 (2.2)	5.5 (2.2)	5.9 (2.0)
CfB	12	-1.0 (2.1)	-0.3 (1.7)	-1.7 (1.8)	-2.2 (2.0)
	48	-2.9 (2.2)	-2.4 (2.2)	-2.5 (2.0)	-2.9 (2.2)
MOS Sleep Problems Index II	0	45.5 (8.1)	45.3 (7.9)	46.9 (7.5)	47.2 (9.4)
CfB	12	2.1 (8.3)	1.8 (6.8)	5.6 (6.7)	6.8 (7.5)
	48	7.6 (8.7)	8.0 (9.1)	6.5 (6.1)	8.0 (7.9)
ASQoL	0	8.4 (4.7)	9.2 (4.7)	8.4 (4.3)	8.7 (4.3)
CfB	12	-1.3 (5.5)	-1.3 (3.7)	-3.5 (4.3)	-4.6 (4.8)
	48	-4.2 (5.6)	-5.3 (5.6)	-4.9 (4.1)	-5.4 (4.8)

CfB: change from baseline

Conclusion: Pts with active AS demonstrated rapid and sustained improvements in PROs, sleep and quality of life over 48 wks of BKZ treatment. BKZ was generally well tolerated with no unexpected safety findings versus previous studies.

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Table 2. Overview of TEAEs to Week 48 (Safety Set; N=303)

n (%)	BKZ 160 mg (n=149)	BKZ 320 mg (n=150)	All BKZ [a] (N=303)
Any TEAE	103 (69.1)	122 (81.3)	235 (77.6)
Drug-related TEAEs	48 (32.2)	54 (36.0)	110 (36.3)
Serious TEAEs	5 (3.4)	6 (4.0)	13 (4.3)
Discontinuations due to TEAEs	7 (4.7)	10 (6.7)	20 (6.6)

[a] Includes TEAEs for 16 and 64 mg BKZ

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OP0106

SECUKINUMAB 150 MG SIGNIFICANTLY IMPROVED SIGNS AND SYMPTOMS OF NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: 52-WEEK RESULTS FROM THE PHASE III PREVENT STUDY

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Background: Axial spondyloarthritis (axSpA) spectrum covers radiographic axSpA and non-radiographic axSpA (nr-axSpA). PREVENT (NCT02696031) is the first phase III, placebo (PBO) controlled study evaluating secukinumab (SEC) 150 mg with (LD) or without loading (NL) dose, in patients (pts) with nr-axSpA.[1] The study had 2 independent analysis plans as per EU (Wk 16) and US (Wk 52) regulatory requirements.

Objectives: To report efficacy through Wk 52 and safety up to two years for the PREVENT study.

Methods: 555 pts fulfilling ASAS criteria for axSpA plus abnormal CRP and/or MRI, without evidence of radiographic changes in sacroiliac (SI) joints according to modified New York Criteria for AS were enrolled. All images were assessed centrally before inclusion. Pts were randomised (1:1:1) to SEC 150 mg with LD, NL, or PBO at baseline (BL). LD pts received SEC 150 mg at Wks 1, 2, 3, and 4, and then every 4 wks (q4wk) starting at Wk 4. NL pts received SEC 150 mg at BL and PBO at Wks 1, 2, and 3, and then 150 mg q4wk. Switch to open-label (OL) SEC 150 mg or standard of care (SoC) was permitted after Wk 20. Primary endpoint was ASAS40 at Wk 16 (LD) and at Wk 52 (NL) in anti-TNF-naïve pts. Secondary endpoints (overall population) included ASAS40, BASDAI50, SI joint bone marrow edema (BME) score by MRI at Wks 16 and 52 and ASDAS-CRP inactive disease (ID) at Wk 52. Endpoints were analysed according to statistical hierarchy. Analysis used non responder imputation through Wk 52. Safety analyses included all pts who received ≥1 dose of study treatment.

Results: Overall, 481 pts completed 52 wks with no major differences in retention across groups: 84.3% (156/185; LD), 89.7% (165/184; NL) and 86.0% (160/186; PBO). BL characteristics were similar across groups; 90% pts were anti-TNF-naïve, 56-58% pts had elevated CRP, 71-75% pts had evidence of SI joint inflammation by MRI. Proportion of pts who switched to OL or SoC between Wks 20 and 48 was 52.1% (LD), 49.2% (NL), and 67.4% (PBO). Primary endpoints at Wk 16 and Wk 52 were met (Table). SEC 150 mg LD or NL significantly improved secondary endpoints at Wk 16 and 52 vs PBO (Table). SEC significantly reduced SI joint MRI BME score vs PBO at Wk 16 (-1.68 and -1.03 vs -0.39; $P = 0.0197$ and 0.026, LD and NL respectively). No unexpected safety signals were reported.

Conclusion: SEC 150 mg provided significant and sustained improvement in signs and symptoms of pts with nr-axSpA through Wk 52. MRI BME scores were reduced accordingly. There was no major difference between LD and NL. Safety of SEC was consistent with previous reports.[2]

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[1] Deodhar A, et al. *Arthritis Rheumatol*. 2019;71(suppl 10).

[2] Deodhar A, et al. *Arth Res Ther*. 2019;21:111.

Table

Endpoints, % responders	Wk	SEC 150 mg LD (N = 185)	SEC 150 mg NL (N = 184)	PBO (N = 186)
Primary				
ASAS40 in anti-TNF-naïve pts	16	41.5‡	42.2‡	29.2
	52	35.4‡	39.8‡	19.9
Secondary				
ASAS40	16	40.0‡	40.8‡	28.0
	52	33.5‡	38.0‡	19.4
BASDAI50	16	37.3‡	37.5‡	21.0
	52	30.8‡	35.3‡	19.9
ASDAS-CRP ID	16	20.5†	21.7†	8.1
	52	15.7	23.9‡	10.2

†$P < 0.001$; ‡$P < 0.05$ vs PBO (P values are adjusted for multiplicity of testing at Wks 16 and 52. Unadjusted P value for ASDAS-CRP ID at Wk 16). Missing values were imputed as non-response.

N, number of randomised pts

Disclosure of Interests: Juergen Braun Grant/research support from: Abbvie (Abbott), Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, Eli Lilly and Company, Medac, MSD (Schering Plough), Mundipharma, Novartis, Pfizer (Wyeth), Roche, Sanofi- Aventis, and UCB Pharma, Consultant of: Abbvie (Abbott), Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, EBEWE Pharma, Eli Lilly and Company, Medac, MSD (Schering-Plough), Mundipharma, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis, and UCB Pharma, Speakers bureau: Abbvie (Abbott), Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, EBEWE Pharma, Eli Lilly and Company, Medac, MSD (Schering-Plough), Mundipharma, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis, and UCB Pharma, Ricardo Blanco Grant/research support from: AbbVie, MSD, Roche, Consultant of: Abbvie, Eli Lilly, Pfizer, Roche, Bristol-Myers, Janssen, UCB Pharma and MSD, Speakers bureau: Abbvie, Eli Lilly, Pfizer, Roche, Bristol-Myers, Janssen, UCB Pharma. MSD, Eva Dokoupilova Grant/research support from: Eli Lilly, AbbVie, Novartis, Lianne S. Gensler Grant/research support from: Pfizer, Novartis, UCB, Consultant of: AbbVie, Eli Lilly, GSK, Novartis, UCB, Alan Kivitz Shareholder of: AbbVie, Amgen, Gilead, GSK, Pfizer Inc, Sanofi, Consultant of: AbbVie, Boehringer Ingelheim, Flexion, Genzyme, Gilead, Janssen, Novartis, Pfizer Inc, Regeneron, Sanofi, SUN Pharma Advanced Research, UCB, Paid instructor for: Celgene, Genzyme, Horizon, Merck, Novartis, Pfizer, Regeneron, Sanofi, Speakers bureau: AbbVie, Celgene, Flexion, Genzyme, Horizon, Merck, Novartis, Pfizer Inc, Regeneron, Sanofi, Stephen Hall Grant/research support from: Abbvie, UCB, Janssen, Merck, Hideto Kameda Grant/research support from: Abbvie, Asahi-Kasei, Chugai, Eisai, Mitsubishi-Tanabe and Novartis, Consultant of: Abbvie, Boehringer, Celgene, Eli Lilly, Janssen, Novartis, Sanofi, UCB, Speakers bureau: Abbvie, Asahi-Kasei, BMS, Chugai, Eisai, Eli Lilly, Janssen, Mitsubishi-Tanabe, Novartis and Pfizer, Denis Poddubnyy Grant/research support from: AbbVie, MSD, Novartis, and Pfizer, Consultant of: AbbVie, Bristol-Myers Squibb, Eli Lilly, MSD, Novartis, Pfizer, Roche, UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, MSD, Novartis, Pfizer, Roche, UCB, Marleen van de Sande Grant/research support from: Novartis, Eli Lilly, Boehringer Ingelheim, Janssen, Consultant of: Abbvie, Novartis, Eli Lilly, Speakers bureau: Novartis, MSD, Désirée van der Heijde

Consultant of: AbbVie, Amgen, Astellas, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Cyxone, Daiichi, Eisai, Eli-Lilly, Galapagos, Gilead Sciences, Inc., Glaxo-Smith-Kline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB Pharma; Director of Imaging Rheumatology BV, Anna Wiksten Shareholder of: Novartis, Employee of: Novartis, Brian Porter Shareholder of: Novartis, Employee of: Novartis, Hanno Richards Shareholder of: Novartis, Employee of: Novartis, Sibylle Haemmerle Shareholder of: Novartis, Employee of: Novartis, Atul Deodhar Grant/research support from: AbbVie, Eli Lilly, GSK, Novartis, Pfizer, UCB, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myer Squibb (BMS), Eli Lilly, GSK, Janssen, Novartis, Pfizer, UCB, Speakers bureau: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myer Squibb (BMS), Eli Lilly, GSK, Janssen, Novartis, Pfizer, UCB

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OP0107 ETANERCEPT WITHDRAWAL AND RE-TREATMENT IN PATIENTS WITH INACTIVE NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS AT 24 WEEKS: RESULTS OF RE-EMBARK, AN OPEN-LABEL, PHASE IV TRIAL

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Background: In the RE-EMBARK trial (NCT02509026), etanercept (ETN)-treated patients with non-radiographic axial spondyloarthritis (nr-axSpA) who achieved inactive disease (defined as Ankylosing Spondylitis Disease Activity Score with C-reactive protein [ASDAS CRP] <1.3) in Period 1 (P1)[1] discontinued ETN for ≤40 weeks.

Objectives: To assess the proportion of patients with inactive disease after P1 who experienced disease flare (ASDAS with erythrocyte sedimentation rate [ASDAS ESR] ≥2.1) within 40 weeks of ETN withdrawal and to estimate time to flare following ETN withdrawal.

Methods: RE-EMBARK was a multicenter, open-label, Phase IV trial of ETN in patients with active nr-axSpA (meeting Assessment in SpondyloArthritis international Society criteria and with ASDAS CRP ≥2.1) and an inadequate response to ≥2 nonsteroidal anti-inflammatory drugs (NSAIDs) while taking a stable dose of 1 NSAID for ≥2 weeks before the first ETN dose. All patients received ETN (50 mg/week) plus NSAID for the first 24 weeks (P1). At week 24, patients with inactive disease discontinued ETN for ≤40 weeks (Period 2 [P2]). Those who experienced flare during P2 were re-treated with ETN for 12 weeks in Period 3 (P3). Kaplan-Meier (KM) analysis and Cox proportional hazard models were used to 1) estimate the probability of experiencing flare within a given time period, and 2) compare data between RE-EMBARK and the EMBARK trial (NCT01258738) of patients with nr-axSpA who met RE-EMBARK P2 entry criteria (achieved inactive disease after 24 weeks of ETN treatment) and continued treatment for a further ≤40 weeks.

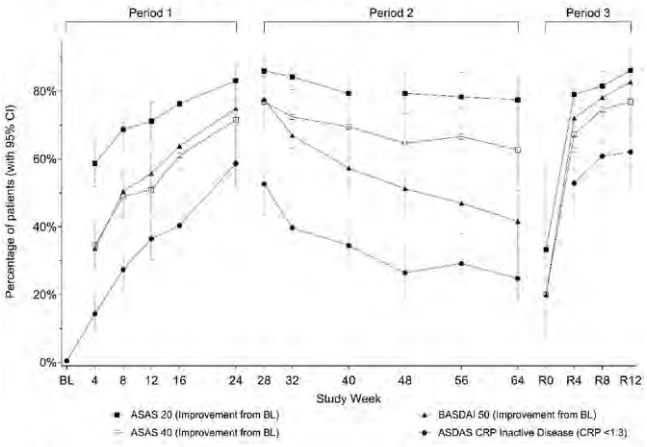
Results: Of the 209 patients in P1 (mean age, 33 years; women, 46%; white, 89%), 119 (57%) entered P2. The proportion of patients experiencing ≥1 flare increased from 22% (25/112) at P2 week 4 to 67% (77/115) at P2 week 40. Overall, 75% (86/115) of patients in P2 experienced flare and 50% experienced flare within 16 weeks (95% CI: 13-24 weeks, KM analysis). Conversely, data from the comparator EMBARK trial suggested that <25% of patients receiving continuous ETN treatment over 40 weeks experienced flare. Cox proportional hazard model analysis showed an 85% relative risk reduction of experiencing flare during P2 in patients with inactive disease who continued ETN treatment vs those who discontinued. By P3 end 62% (54/87) of patients re-treated with ETN re-achieved inactive disease; 50% of patients who re-achieved inactive disease in P3 did so within 5 weeks (95% CI: 4-8 weeks, KM analysis). The observed trend of clinical improvement (P1), worsening (P2), and improvement (P3) was reflected in other clinical measures (Figure) plus measures of joint damage (Spondyloarthritis Research Consortium of Canada Sacroiliac Joint magnetic resonance imaging score) and quality of life (EQ-5D visual analog scale score); mean (standard deviation) score changes from each study period baseline–end were –6.1 (11.7) [P1], +1.5 (4.4) [P2], –2.0 (8.8) [P3] and +27.7 (26.7) [P1], –26.4 (30.5) [P2], +32.1 (26.3) [P3], respectively. There were no unexpected safety signals.

Conclusion: For patients with nr-axSpA who achieved inactive disease with ETN and then discontinued treatment, a quarter maintained treatment-free inactive disease for 40 weeks and 50% maintained an ASDAS ESR score of <2.1 for ≥16 weeks. Re-starting ETN allowed 62% of patients who flared to re-achieve inactive disease within 12 weeks.

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Figure: Clinical Assessments by RE-EMBARK Study Period



ASAS, Assessment of SpondyloArthritis International Society; ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BL, baseline; CI, confidence interval; CRP, C-reactive protein; R, re-treatment

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Disclosure of Interests: Filip van den Bosch Consultant of: AbbVie, Celgene Corporation, Eli Lilly, Galapagos, Janssen, Novartis, Pfizer, and UCB, Speakers bureau: AbbVie, Celgene Corporation, Eli Lilly, Galapagos, Janssen, Novartis, Pfizer, and UCB, James Cheng-Chung Wei Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer Inc, UCB, Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Chugai, Eisai, Janssen, Novartis, Pfizer Inc, Sanofi-Aventis, UCB Pharma, Peter Nash Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Gilead, Janssen, MSD, Novartis, Pfizer Inc, Roche, Sanofi, UCB, Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, MSD, Novartis, Pfizer Inc, Roche, Sanofi, UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, MSD, Novartis, Pfizer Inc, Roche, Sanofi, UCB, Francisco J. Blanco Grant/research support from: Sanofi-Aventis, Lilly, Bristol MS, Amgen, Pfizer, Abbvie, TRB Chemedica International, Glaxo SmithKline, Archigen Biotech Limited, Novartis, Nichi-iko pharmaceutical Co, Genentech, Jannsen Research & Development, UCB Biopharma, Centrexion Theurapeutics, Celgene, Roche, Regeneron Pharmaceuticals Inc, Biohope, Corbus Pharmaceutical, Tedec Meiji Pharma, Kiniksa Pharmaceuticals, Ltd, Gilead Sciences Inc, Consultant of: Lilly, Bristol MS, Pfizer, Daniela Graham Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Chuanbo Zang Shareholder of: Pfizer, Employee of: Pfizer, Edmund Arthur Shareholder of: Pfizer, Employee of: Pfizer, Cecilia Borlenghi Shareholder of: Pfizer, Employee of: Pfizer, Bonnie Vlahos Shareholder of: Pfizer, Employee of: Pfizer, Atul Deodhar Grant/research support from: AbbVie, Eli Lilly, GSK, Novartis, Pfizer, UCB, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myer Squibb (BMS), Eli Lilly, GSK, Janssen, Novartis, Pfizer, UCB, Speakers bureau: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myer Squibb (BMS), Eli Lilly, GSK, Janssen, Novartis, Pfizer, UCB

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OP0108 RANDOMIZED CONTROLLED TRIAL OF ORAL CORTICOSTEROIDS IN AXIAL SPONDYLOARTHROPATHY: MODIFIED COBRA REGIME

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Background: There is an unmet need of anti-inflammatory agents in AxSpA after NSAID failure. This is especially true for patients with persisting high disease activity and not having access to anti-TNFα. In this regard, corticosteroids may be helpful as a short-term measure. However, current guidelines recommend against oral corticosteroids citing insufficient evidence of efficacy. [1]. Also, there is an assumption that the dose required for benefit is much higher than RA, and thus untenable. It is unclear whether starting with a high dose followed by rapid taper would be effective (like the COBRA regime in RA)[2].

Objectives: To study the efficacy of the COBRA regime of oral corticosteroids in axial SpA over 24 weeks.

Methods: This was a double blind placebo controlled randomized trial. Patients with active axial SpA (BASDAI ≥ 4) despite NSAIDs were randomized to either

receive oral prednisolone or placebo as per COBRA regime, started on oral prednisolone at a dose of 60 mg, rapidly tapered weekly to reach a dose of 10 mg by 6 weeks and subsequently maintained on a low dose of 5 mg till 24 weeks. Primary end point was 50% improvement in BASDAI at week 24. Secondary end points were improvement in ASDAS and BASFI. Analysis was by intention-to-treat. Trial Registration# CTRI/2018/01/011342

Results: This study enrolled 65 patients (62 males) who were randomized to corticosteroid (n=32) or placebo (n=33) with mean ± SD age 28.5 ± 8.4 years and BASDAI 5.4 ± 1.0. Primary end point was reached in 12 (37.5%) and 3 (9%) patients treated with steroids and placebo respectively (p=0.007). On repeated measures analysis by general linear model, there was a significant difference between the two-groups in BASDAI (p= 0.03) (Figure-1). Patients in the corticosteroid group had significant improvement in BASDAI, ESR, CRP, ASDAS ESR and ASDAS CRP at 24 weeks (Table-1). Clinically important improvement in ASDAS CRP was achieved by significantly higher number of patients in steroid group (17 (55%) vs 6 (18%), p= 0.002). Major improvement in ASDAS ESR and ASDAS CRP was also higher in the steroid group (Figure-2). At 24 weeks, patients in the steroid group had significant reduction in IL-6 levels compared to that in placebo group (p= 0.007, data for 41 patients). Patients in the steroid group had more weight gain and facial puffiness, however no serious adverse events were noted in both the groups.

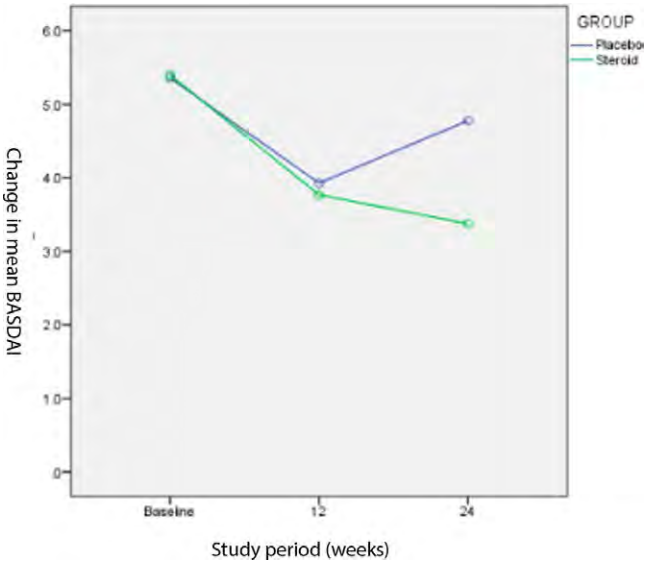


Figure 1. Change in mean BASDAI

Table 1. Changes in disease indices and inflammatory markers at 24 weeks

Changes in Parameters (24 weeks-baseline)	Placebo	Corticosteroid	P value
ESR, Median (IQR)	0 (-11 to 21)	-13 (-37 to 4)	0.01
CRP mg/L Median (IQR)	0 (-8.8 to 13)	-9 (-22.7 to 0)	0.03
BASDAI (mean ± SD)	- 0.51 ± 1.6	- 1.88 ± 2.5	0.03
BASMI (mean ± SD)	-0.25 ± 0.8	-0.56 ± 0.9	0.23
BASFI (mean ± SD)	-0.35 ± 2.3	-1.48 ± 3.1	0.28
BAS-G (mean ± SD)	-1.02 ± 2.7	-1.86 ± 2.5	0.32
ASDAS-ESR (mean ± SD)	-0.13 ± 1.0	-1.11 ± 1.1	0.001
ASDAS-CRP (mean ± SD)	-0.24 ± 1.1	-1.17 ± 1.3	0.006

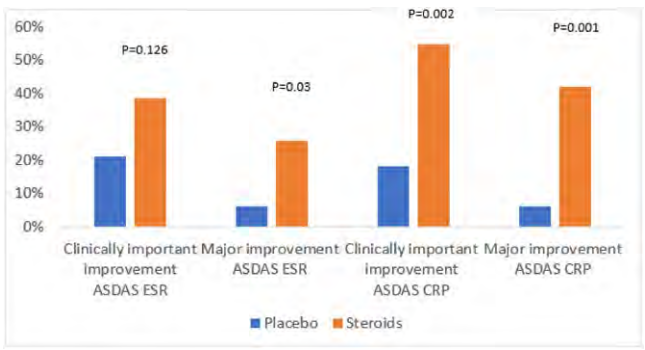


Figure 2. Clinically important and Major improvement at 24 weeks

Conclusion: Oral prednisolone given by COBRA regime was associated with significant improvement in disease activity scores in axial SpA at 24 weeks. This extends and supports results from a previous short term study.[3] Thus, corticosteroids may be an option for patients not having access to biologics, atleast for the short-term.

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OP0109

CO-MEDICATION WITH A CONVENTIONAL SYNTHETIC DMARD IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS IS ASSOCIATED WITH IMPROVED RETENTION OF TNF INHIBITORS: RESULTS FROM THE EUROSPA COLLABORATION

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[1]EuroSpA Research Collaboration, on behalf of the DANBIO (Denmark), ARTIS (Sweden), SCQM (Switzerland), NOR-DMARD (Norway), ATTRA (Czech Republic), Reuma.pt (Portugal), BIOBADASER (Spain), ROB-FIN (Finland), biorx.si (Slovenia), ICEBIO (Iceland), TURKBIO (Turkey), RRBR (Romania), ARC (Netherlands), BSRBR-AS (United Kingdom), GISEA (Italy), Copenhagen, Denmark

Background: Axial spondylarthritis (axSpA) patients treated with a tumour necrosis factor inhibitor (TNFi) may receive a concomitant conventional synthetic disease-modifying anti-rheumatic drug (csDMARD), although the value of combination therapy remains unclear.

Objectives: Describe the proportion and phenotype of patients with axSpA initiating their first TNFi as monotherapy compared to TNFi+csDMARD combination therapy, and to compare the 1-year TNFi retention between the two groups.

Methods: Data from 13 European registries was collected. Two exposure treatment groups were defined: TNFi monotherapy at baseline (=TNFi start date) and TNFi+csDMARD combination therapy. TNFi retention rates were assessed with Kaplan-Meier curves for each country and combined. Hazard ratios (HR, 95% CI) for discontinuing the TNFi were obtained with Cox models: (i) crude; adjusted for (ii) country, and (iii) country, sex, age, calendar year, disease duration and BASDAI. Participating countries were dichotomized into two strata, depending on their 1-year retention rate being above (stratum A) or below (stratum B) the average retention rate across all countries.

Results: 22,196 axSpA patients were included with 34% on TNFi+csDMARD combination therapy. Baseline characteristics are presented in table 1. Overall, the crude TNFi retention rate was marginally longer in the combination therapy group (80% (79-81%)) compared to the monotherapy group (78% (77-79%)) and was primarily driven by differences in stratum B (fig. 1). TNFi retention rates varied significantly across countries (range:-11.0% to +11.3%), with a clear distinction between the 2 strata. The HRs for discontinuation over 1-year (reference=TNFi monotherapy) in the 3 models were: (i) 0.88 (0.82-0.93), (ii) 0.87 (0.82-0.92), (iii) 0.88 (0.82-0.93).

Conclusion: Considerable differences were observed across countries in the use of combination therapy and TNFi retention in axSpA patients. The overall 1-year TNFi retention was higher with csDMARD co-therapy compared to TNFi monotherapy. TNFi monotherapy had a 12-13% higher risk of treatment discontinuation.

Acknowledgments: Novartis Pharma AG and IQVIA

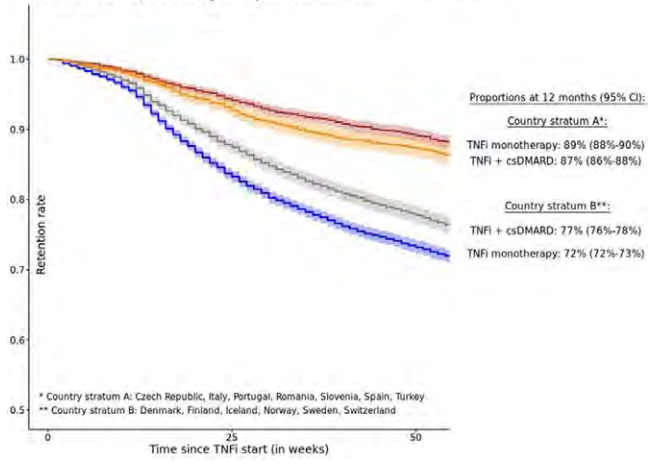
MN and BD participated equally

Disclosure of Interests: Michael Nissen Grant/research support from: Abbvie, Consultant of: Novartis, Lilly, Abbvie, Celgene and Pfizer, Speakers bureau: Novartis, Lilly, Abbvie, Celgene and Pfizer, Bénédicte Delcoigne: None declared, Daniela Di Giuseppe: None declared, Lennart T.H. Jacobsson Consultant of: AbbVie, Eli Lilly, Janssen, Novartis and Pfizer, Karen Fagerli: None declared,

Table 1

Baseline characteristics	All patients (n=22196)	Country stratum A		Country stratum B	
		TNFi mono (n=4940)	csDMARD + TNFi (n=2547)	TNFi mono (n=9693)	csDMARD + TNFi (n=5016)
Age (years), mean (SD)	42.6 (12.5)	43.4 (12.0)	42.8 (12.2)	41.6 (12.7)	43.7 (12.7)
Females, %	41.1	37.7	38.2	42.0	44.2
Disease duration (yrs), mean (SD)	5.7 (8.0)	6.2 (7.7)	6.7 (7.4)	4.9 (8.2)	6.1 (8.2)
Enthesitis, %	50.3	16.7	33.9	57.8	59.7
SJC-28, median (IQR)	0 (0-1)	0 (0-0)	0 (0-2)	0 (0-0)	0 (0-2)
VAS pain (0-100), mean (SD)	60.9 (24.5)	63.3 (26.5)	67.8 (23.3)	60.2 (23.4)	57.2 (24.3)
CRP (mg/L), median (IQR)	8 (3-20)	7.8 (2-20)	18 (6.7-32.6)	6.0 (2.7-15)	8.0 (3-22)
BASDAI (0-10), mean (SD)	5.7 (2.1)	5.7 (2.2)	6.2 (2.1)	5.6 (2.0)	5.4 (2.2)
BASFI (0-10), mean (SD)	4.4 (2.5)	4.4 (2.6)	4.9 (2.5)	4.3 (2.4)	4.2 (2.9)
ASDAS, mean (SD)	3.5 (1.1)	3.7 (1.0)	4.0 (1.0)	3.3 (1.0)	3.3 (1.1)
On Infliximab, %	25.7	21	22	24	36
Baseline csDMARD use, %					
-Methotrexate		0	45	0	63
-Sulfasalazine		0	68	0	33
-Leflunomide		0	8	0	1

Figure 1. Retention rate of TNFi monotherapy vs TNFi and csDMARD comedication, stratified by each country's one-year retention rate being above (stratum A) or below (stratum B) the average one-year retention rate



Anne Gitte Loft Grant/research support from: Novartis, Consultant of: AbbVie, MSD, Novartis, Pfizer and UCB, Speakers bureau: AbbVie, MSD, Novartis, Pfizer and UCB, Adrian Ciurea Consultant of: Consulting and/or speaking fees from AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Merck Sharp & Dohme, Novartis and Pfizer., Dan Nordström Consultant of: Abbvie, Celgene, Lilly, Novartis, Pfizer, Roche and UCB., Speakers bureau: Abbvie, Celgene, Lilly, Novartis, Pfizer, Roche and UCB., Ziga Rotar Consultant of: Speaker and consulting fees from Abbvie, Amgen, Biogen, Eli Lilly, Medis, MSD, Novartis, Pfizer, Roche, Sanofi., Speakers bureau: Speaker and consulting fees from Abbvie, Amgen, Biogen, Eli Lilly, Medis, MSD, Novartis, Pfizer, Roche, Sanofi., Florenzo Iannone Consultant of: Speaker and consulting fees from AbbVie, Eli Lilly, Novartis, Pfizer, Roche, Sanofi, UCB, MSD, Speakers bureau: Speaker and consulting fees from AbbVie, Eli Lilly, Novartis, Pfizer, Roche, Sanofi, UCB, MSD, Maria Jose Santos Speakers bureau: Novartis and Pfizer, Manuel Pombo-Suarez Consultant of: Janssen, Lilly, MSD and Sanofi., Speakers bureau: Janssen, Lilly, MSD and Sanofi., Björn Gudbjornsson Speakers bureau: Novartis and Amgen, Heřman Mann: None declared, Nurullah Akkoc: None declared, Catalin Codreanu Consultant of: Speaker and consulting fees from AbbVie, Accord Healthcare, Alfasigma, Egis, Eli Lilly, Ewopharma, Genesis, Mylan, Novartis, Pfizer, Roche, Sandoz, UCB, Speakers bureau: Speaker and consulting fees from AbbVie, Accord Healthcare, Alfasigma, Egis, Eli Lilly, Ewopharma, Genesis, Mylan, Novartis, Pfizer, Roche, Sandoz, UCB, Irene van der Horst-Bruinsma Grant/research support from: AbbVie, Novartis, Eli Lilly, Bristol-Myers Squibb, MSD, Pfizer, UCB Pharma, Consultant of: AbbVie, Novartis, Eli Lilly, Bristol-Myers Squibb, MSD, Pfizer, UCB Pharma, Brigitte Michelsen: None declared, Gary Macfarlane: None declared, Merete L. Hetland Grant/research support from: BMS, MSD, AbbVie, Roche, Novartis, Biogen and Pfizer, Consultant of: Eli Lilly, Speakers bureau: Orion Pharma, Biogen, Pfizer, CellTrion, Merck and Samsung Bioepis, Matija Tomsic: None declared, Burkhard Moeller: None declared, Pedro Ávila-Ribeiro Grant/research support from: Novartis, Carlos Sánchez-Piedra: None declared, Heikki Relas Grant/research support from: Abbvie., Consultant of: Abbvie, Celgene, and Pfizer., Speakers bureau: Abbvie, Celgene, and Pfizer., Arni Jon Geirsson: None declared, Lucie Nekvindova: None declared, Gozde Yildirim Cetin Speakers bureau: AbbVie, Novartis, Pfizer, Roche, UCB, MSD, Ruxandra Ionescu Consultant of: Consulting fees from Abbvie, Eli-Lilly, Novartis, Pfizer, Roche, Sandoz, Speakers bureau: Consulting and speaker fees from Abbvie, Eli-Lilly, Novartis, Pfizer, Roche, Sandoz, Niels Steen Krogh: None declared, Johan Askling Grant/research support from: JA acts or has acted as PI for agreements between Karolinska Institutet and the following entities, mainly in the context of the ARTIS national safety monitoring programme of immunomodulators in rheumatology: Abbvie, BMS, Eli Lilly, Merck, MSD, Pfizer, Roche, Samsung Bioepis, Sanofi, and UCB Pharma, Bente Glintborg Grant/research support from: Grants from Pfizer, Biogen and Abbvie, Ulf Lindström: None declared
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OP0110

IS VERY EARLY TREATMENT EFFECTIVE? SIX MONTHS RESULTS OF THE PREVAS STUDY, A PLACEBO-CONTROLLED TRIAL WITH ETANERCEPT IN PATIENTS SUSPECTED OF NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS

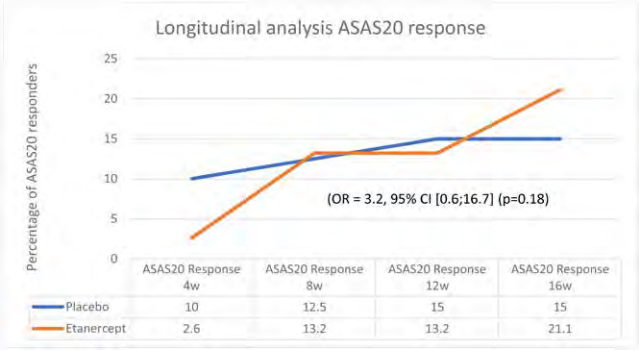
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Background: Despite the new classification criteria for non-radiographic axial spondyloarthritis (nr-axSpA) patients according to the Assessment of Spondyloarthritis International Society (ASAS), there are limited data on disease progression in nr-axSpA patients.
Objectives: First to assess the improvement in disease activity in patients suspected of nr-axSpA after 16 weeks treatment with Etanercept (ETN) or Placebo (PBO). Second, to assess the changes of active inflammation on MRI of the SI-joints (SIJ) between the ETN and PBO group after 16 and 24 weeks without study medication.
Methods: The PrevAS study is a randomized, double blind, placebo-controlled trial with ETN performed in the VU University medical center (VUmc) (EudraCT number 2009-015515-40), with a screening period from 2009 until 2014. Patients suspected of nr-axSpA were included if they had chronic back pain for ≥ 3 months, were ≥ 18 years, fulfilled the Calin criteria of inflammatory back pain and had to be either HLA-B27 positive with at least ≥ 1 Spondyloarthritis (SpA)-feature (as defined by the European Spondyloarthropathy Study Group (ESSG), or HLA-B27 negative with at least ≥ 2 SpA-features and had a high disease activity score (Bath Ankylosing Spondylitis Disease Activity Index ≥ 4) plus insufficient response to at least two NSAIDs. Excluded were patients who fulfilled the modified New York criteria for ankylosing spondylitis, or in case of previous biological use. Included patients were randomly assigned (1:1) for 16 weeks treatment with ETN (N=40) or PBO (N=40) and followed after the treatment period for 24 weeks. The primary endpoint was the number of patients achieving the ASAS20 response at week 16. MRI was performed at baseline, 16 and 24 weeks and scored using the Spondyloarthritis Research Consortium of Canada (SPARCC) index for number of active inflammatory lesions.
Results: The majority of included patients was female (63.8%). Patient characteristics, like the presence of the HLA-B27 antigen and number of SpA-features

at baseline, were comparable between the ETN and PBO group. Mean compliance to the study medication at sixteen weeks was 72.1%. Longitudinal regression analysis over the first 16 weeks showed a trend towards a three times higher chance to achieve the ASAS20 response in the ETN compared to the PBO group (OR = 3.2, 95% CI [0.6;16.7] *p*=0.18) (Figure 1). No differences were observed in ASAS20 response at 24 weeks. A positive SPARCC score (SPARCC ≥ 2.5) of the SIJ was observed in the ETN and PBO group in 33.3% (13/39 patients) vs. 30.8% (12/39 patients) at baseline, 16.7% (6/36 patients) vs. 17.5% (7/40 patients) at 16 weeks and 21.9% (7/32 patients) vs. 20.0% (7/35 patients) at 24 weeks, respectively. Increased CRP-levels (CRP_UL ≥ 10.0mg/L) nor a positive SPARCC score at baseline, had significant influence on the ASAS20 response at 16 weeks follow-up. The safety profile was consistent with what is known for ETN in AS.

Conclusion: Patients suspected of nr-axSpA with high disease activity showed a trend towards a three times higher chance to achieve the ASAS20 response in the ETN group, compared to the PBO group at 16 weeks, regardless of a raised CRP level or positive MRI-SIJ at baseline.

Figure:



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Rheumatoid arthritis - prognosis, predictors and outcome I

OP0111

RHEUMATOID ARTHRITIS SEROLOGIC PHENOTYPE AT DIAGNOSIS AND SUBSEQUENT RISK FOR PNEUMONIA IDENTIFIED USING MACHINE LEARNING APPROACHES

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Background: Patients with rheumatoid arthritis (RA) are at increased risk of serious infections, with considerable excess morbidity and mortality after pneumonia. RA-related autoantibodies such as anti-cyclic citrullinated peptide (CCP) and rheumatoid factor (RF) may be generated at inflamed pulmonary mucosa prior to clinical RA onset. Therefore, patients with seropositive RA may be at increased risk for pneumonia after RA diagnosis due to subclinical pulmonary injury.

Objectives: We investigated whether seropositive RA was associated with increased pneumonia risk compared to seronegative RA.

Methods: We performed a retrospective cohort study among RA patients seen at a health care system in Boston, MA. RA patients were identified using a previously validated electronic health record (EHR) algorithm incorporating billing codes, natural language processing (NLP) of notes, medications, and laboratory results at 97% specificity[1]. We constructed an incident RA cohort using NLP for the index date of initial mention of RA. All patients were required to have both CCP and RF data from clinical care to determine serologic RA phenotype. We used semi-supervised machine learning approaches to identify pneumonia using billing codes and terms extracted using NLP, with the Centers for Disease Control definition of pneumonia from medical record review as a gold standard. The area under the receiver operating curve (AUROC) for this billing code+NLP pneumonia algorithm was 0.94 compared to the standard rule-based pneumonia algorithm (billing code on inpatient discharge) AUROC of 0.86 (p<0.001). Smoking status was extracted using NLP methods. Other covariates, including a previous validated weighted RA multimorbidity score[2], were determined using structured EHR data. We used Cox regression to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for pneumonia adjusting for potential confounders.

Results: We analyzed a total of 4,110 patients with incident RA and both CCP/RF data available. Mean age at index date was 53.0 years (SD 14.8), 77.2% were female, and 79.8% were CCP+ or RF+. During 32,248 patient-years of follow-up (mean 7.8 years/patient), we identified 240 pneumonia cases. Patients with seropositive RA had a HR of 1.99 (95%CI 1.30-3.01, Table) for pneumonia compared to patients with seronegative RA, adjusted for age, sex, smoking, index year, ESR level, glucocorticoid use, DMARD use, and weighted RA multimorbidity score. While CCP+ RA (HR 1.91, 95%CI 1.23-2.97) and RF+ RA (HR 2.07, 95%CI 1.35-3.16) had increased pneumonia risk compared to seronegative RA, the CCP+RF- RA subgroup had no association with pneumonia (HR 0.67, 95%CI 0.23-1.93).

Conclusion: Patients with incident seropositive RA, particularly RF+ RA, had increased risk for pneumonia throughout the RA disease course that was not explained by measured confounders including smoking status, multimorbidity, medications, and ESR level. Further studies should investigate how RF+ may predispose RA patients to later develop pneumonia after clinical RA diagnosis.

Table. Hazard ratios for pneumonia by CCP and RF status among patients with incident RA (n=4,110).

	Pneumonia cases	Patient-years	Unadjusted HR (95%CI)	Multivariable HR (95%CI)	n in model
Seronegative (CCP- and RF-)	24	6,154.98	1.00 (Ref)	1.00 (Ref)	4,110
Seropositive (CCP+ or RF+)	216	26,092.60	**2.15 (1.41-3.28)**	**1.99 (1.30-3.01)**	
Seronegative (CCP- and RF-)	24	6,154.98	1.00 (Ref)	1.00 (Ref)	2,973
CCP+	136	17,225.63	**2.05 (1.33-3.16)**	**1.91 (1.23-2.97)**	
CCP-	104	15,021.95	1.00 (Ref)	1.00 (Ref)	4,110
CCP+	136	17,225.63	1.14 (0.88-1.48)	1.10 (0.84-1.43)	
Seronegative (CCP- and RF-)	24	6154.98	1.00 (Ref)	1.00 (Ref)	3,909
RF+	212	24,560.64	**2.25 (1.47-3.43)**	**2.07 (1.35-3.16)**	
RF-	28	7,686.94	1.00 (Ref)	1.00 (Ref)	4,110
RF+	212	24,560.64	**2.40 (1.62-3.57)**	**2.22 (1.50-3.30)**	
CCP- and RF-	24	6,154.98	1.00 (Ref)	1.00 (Ref)	4,110
CCP+ and RF-	4	1,531.96	0.67 (0.23-1.94)	0.67 (0.23-1.93)	
CCP- and RF+	80	8,866.98	**2.36 (1.50-3.73)**	**2.22 (1.40-3.52)**	
CCP+ and RF+	132	15,693.67	**2.18 (1.41-3.38)**	**2.00 (1.29-3.01)**	

*Adjusted for age (continuous, years), sex (male, female), race (white, non-white), smoking status (never, past, current), index calendar year, ESR level (continuous, mm/hr), glucocorticoids (use, non-use), disease-modifying antirheumatic drug (use, non-use), weighted rheumatoid arthritis multimorbidity score (continuous).

CCP, cyclic citrullinated peptide; CI, confidence interval; ESR, erythrocyte sedimentation rate; HR, hazard ration; RF, rheumatoid factor.

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[2] Radner H, Yoshida K, Mjaavatten MD, et al. Development of a multimorbidity index: Impact on quality of life using a rheumatoid arthritis cohort. Semin Arthritis Rheum. 2015;45(2):167–173.

Disclosure of Interests: Jeffrey Sparks Consultant of: Bristol-Myers Squibb, Optum, Janssen, Gilead, Weixing Huang: None declared, Bing Lu: None declared, Sicong Huang: None declared, Andrew Cagan: None declared, Vivian Gainer: None declared, Sean Finan: None declared, Guergana Savova: None declared, Daniel Solomon Grant/research support from: Funding from Abbvie and Amgen unrelated to this work, Elizabeth Karlson: None declared, Katherine Liao: None declared

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OP0112

IN INDIVIDUALS AT RISK OF INFLAMMATORY ARTHRITIS, PATIENT REPORTED OUTCOMES DETERIORATE IN THE 12 WEEKS BEFORE PROGRESSION TO CLINICAL DISEASE

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Background: Subjects with clinically significant arthralgia who will eventually develop inflammatory arthritis (IA) had a higher HAQ at baseline (1). Here we investigated the change in patients reported outcomes (PRO) over time in ACPA+ at risk of IA subjects.

Objectives: In ACPA+ subjects at risk of developing IA, to analyse the change in PRO results in order to identify an imminent phase of progression.

Methods: In a single centre prospective observational cohort, PRO from 109 ACPA+ subjects without clinical arthritis were collected prospectively at 0, 12, 26, 39 weeks; the last time-point was 52 weeks for the individuals who did not progress to IA (non-progressors) or the last visit preceding progression (within 12 weeks) for those who developed IA (progressors). Data on the following PRO were collected: HAQ, "general health" (GH-VAS), "fatigue" (fatigue-VAS), and "global pain" (GP-VAS) using visual analogic scale measures graded 0 to 100. We firstly used mixed models repeated measures ANOVA analysis then included covariates such as gender, shared epitope (SE) (HLA DRB1*01, *04 and/or *10), anti-CCP2 antibody (CCP2) and/or rheumatoid factor (RF) high titre (≥3ULN), and smoking exposure (Ever/Never).

Results: All analysis met sphericity assumption. In this selection, 20% of subjects (24/109) developed IA within a median of 77 weeks (Range 37-369.43), non-progressors were followed for a median of 216 weeks (Range 50-590), 74 subjects were SE positive (68%), 81 had a CCP2 and/or RF high titre (74%), and 66 were previous or current smokers (61%).

Analysis revealed significant differences between both groups for the last visit, and within the progressor group for the last visit compared to all previous visits regarding the GH-VAS, GP-VAS and HAQ (Table 1, figure 1). Between subject analysis showed a significant influence of GH-VAS and GP-VAS change on progression. Covariate analysis showed a significant influence of previous smoking history on HAQ results (p=0.033, F=2.645 (4,408), Eta = 0.025).

Conclusion: These results show for the first time a significant deterioration in the PRO of general health, global pain, and HAQ weeks just preceding clinical arthritis development. This phase prior progression needs to be thoroughly studied to improve the accuracy of predicting imminent progression.

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[1] Ten Brinck RM et al. Functional limitations in the phase of clinically suspect arthralgia are as serious as in early clinical arthritis; a longitudinal study. RMD open. 2017;3(1):e000419.

Disclosure of Interests: Laurence Duquenne: None declared, Kulveer Mankia: None declared, Leticia Garcia-Montoya: None declared, Jacqueline Nam: None declared, Andrea Di Matteo Grant/research support from: the publication was conducted while Dr. Di Matteo was an ARTICULUM fellow, Paul Emery Grant/research support from: AbbVie, Bristol-Myers Squibb, Merck Sharp & Dohme, Pfizer, Roche (all paid to employer), Consultant of: AbbVie (consultant, clinical trials, advisor), Bristol-Myers Squibb (consultant, clinical trials, advisor), Lilly (clinical trials, advisor), Merck Sharp & Dohme (consultant, clinical trials, advisor), Novartis (consultant, clinical trials, advisor), Pfizer (consultant, clinical trials, advisor), Roche (consultant, clinical trials, advisor), Samsung (clinical trials, advisor), Sandoz (clinical trials, advisor), UCB (consultant, clinical trials, advisor)

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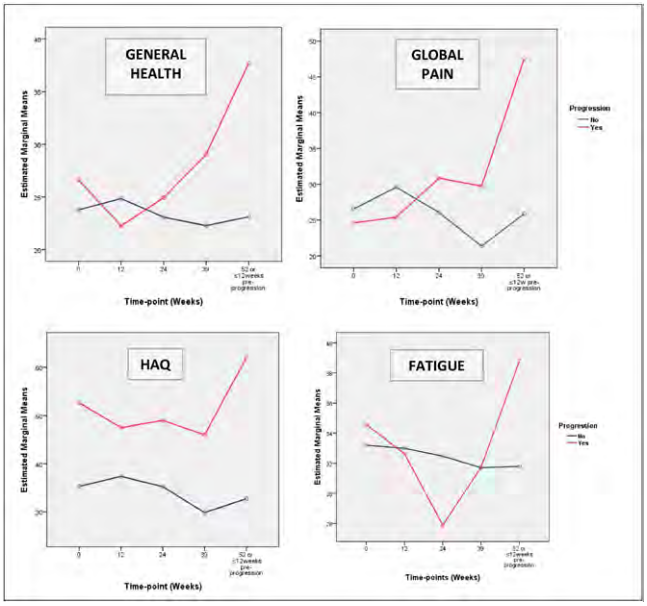


Figure 1. Repeated measure ANOVA between groups

OP0113

WHOLE BLOOD RNA EXPRESSION IN CLINICALLY SUSPECTED ARTHRALGIA PATIENTS SHOWS A POTENTIAL ADDED VALUE IN PREDICTION OF INFLAMMATORY ARTHRITIS

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Table 1. Mixed Models repeated measures

	General Health	Global Pain	HAQ	Fatigue
Within subject effects; VAS change over time depending on group.	**P= 0.004** F(4, 428) = 3.883 Partial Eta Square= 0.35	**P < 0.001** F(4, 400) = 5.754 Partial Eta Squared = 0.054	P = 0.115	P = 0.459
Pairwise comparison within group	**Non-progressors:** all p > 0.05 **Progressors:** Time-point 1 to 5: **p = 0.010** SE = 4.199 Time-point 2 to 5: **p = 0.001** SE = 4.709 Time-point 3 to 5: **P = 0.001** SE = 3.842 Time-point 4 to 5: **P = 0.043** SE = 4.239	**Non-progressors:** all p > 0.05 **Progressors:** Time-point 1 to 5: **p < 0.001** SE = 6.172 Time-point 2 to 5: **p < 0.001** SE = 5.518 Time-point 3 to 5: P = 0.002 SE = 5.246 Time-point 4 to 5: **P = 0.001** SE = 5.333	**Non-progressors:** all p > 0.05 **Progressors:** Time-point 1 to 5: p = 0.215 Time-point 2 to 5: **P = 0.036** SE = 0.068 Time-point 3 to 5: **P = 0.040** SE = 0.062 Time-point 4 to 5: **P = 0.017** SE = 0.066	**Non-progressors:** all p > 0.05 **Progressors:** Time-point 1 to 5: p = 0.448 Time-point 2 to 5: P =0.292 Time-point 3 to 5: **P = 0.047** SE = 5.421 Time-point 4 to 5: P = 0.202
Pairwise comparison between group	**Last visit:** **P = 0.009** SE = 5.454 **All other visits:** P > 0.05	**Last visit:** **P = 0.003** SE = 7.082 **All other visits:** P > 0.05	**Last visit:** **P = 0.016** SE = 0.119 **All other visits:** P > 0.05	P-value > 0.05
Mauchly's test of sphericity	P = 0.099	P = 0.050	P = 0.057	P = 0.722
N (Progressors/total)	24/109	15/102	24/107	19/102

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Background: Clinically suspect arthralgia (CSA) can precede development of clinically evident inflammatory arthritis (IA). Autoantibody, C-reactive protein (CRP), and subclinical inflammation are known predictors, but risk estimation remains insufficiently accurate. Especially CRP has a small effect size and is inadequately reflective of inflammation that can be measured systemically. RNA expression in whole blood of patients with rheumatoid arthritis (RA) have shown differences compared to healthy individuals. Therefore, we hypothesized that differences in RNA expression can be found between CSA patients that do and do not progress to IA.
Objectives: This study assessed whole blood RNA expression levels of inflammatory and immune genes as potential biomarkers for prediction of IA-development in patients with arthralgia.
Methods: Between April 2012-March 2015, 234 patients were consecutively included in the Leiden CSA-cohort. Follow-up ended when patients developed clinically apparent IA (determined at physical examination), or else after 2-years. RNA expression in whole blood, at the moment of inclusion, was determined for 135 genes of the innate and adaptive immune system by dual color Reverse-Transcription Multiplex Ligation-dependent Probe Amplification (dcRT-MLPA) profiling. Cox proportional hazard models were used to associate time-to-event with gene expression level at inclusion, while adjusting for age, gender, and assay plate (model 1). The false discovery rate was used to correct for multiple testing. Genes with significantly different expression were subsequently studied for reproducibility by qPCR, and mutual independence in their association with IA-development. For the latter, we employed a forward selection strategy, starting with the most significantly associated gene and iteratively adding more genes. Resulting mutually independent genes were further investigated for their added predictive value over known risk factors, CRP, ACPA, and subclinical joint inflammation.
Results: 21% of CSA-patients developed IA after mean 3.6 months (IQR:1.6-10.7) follow-up. After correction for multiple testing, six genes were significantly associated with IA-development (model 1), namely IFN-γ, PHEX, IGF-1, IL7R, CD19, or CCR7 (ordered by significance). For all six genes, a lower expression at inclusion was associated with an increased risk of IA-development. IFN-γ was only weakly expressed in peripheral blood, hampering the technical reproducibility between MLPA and qPCR results, and was excluded for further analyses. PHEX and IGF-1 were highly correlated (R^2 0.97) and only IGF-1, but not PHEX, was included in further analyses. Of the remaining significant genes (IGF-1, IL7R, CD19, CCR7), an independent association with IA-development was observed for IGF-1 and IL7R, but not for CD19 or CCR7. qPCR data of IL7R correlated with MLPA results (p<0.001), confirming the robustness of the transcriptomic outcome. Lastly, when analysing IGF-1 and IL7R with known clinical predictors, both IGF-1 and IL7R remained independently associated with progression to IA.
Conclusion: Six genes were differentially expressed between CSA-patients that did or did not progress to IA. Expression of IGF-1 and IL7R showed added value to regularly used predictors. Validation is warranted.
References: None.

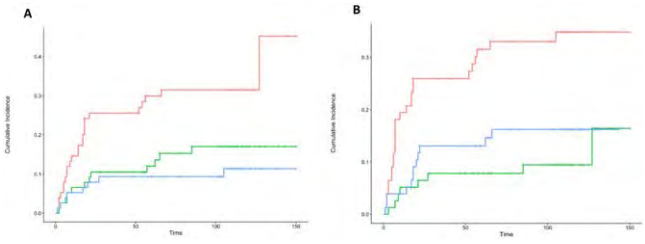


Figure 1. Association between RNA expression divided in tertiles of IGF-1 (A) and IL7R (B), and development of inflammatory arthritis

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OP0114

PREDICTING RHEUMATOID ARTHRITIS USING THE SYMPTOMS IN PERSONS AT RISK OF RHEUMATOID ARTHRITIS (SPARRA) QUESTIONNAIRE

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Background: Accurate prediction of rheumatoid arthritis (RA) development in persons at risk of RA can help to select individuals for early intervention trials. Currently, RA prediction mostly relies on biomarkers such as genetic factors, autoantibodies and imaging abnormalities, with symptoms being only a minor component [1-3]. However, at-risk individuals exhibit a high prevalence of diverse and often severe symptoms [4,5] and information on the predictive ability of individual symptoms or symptom complexes is still largely lacking.
Objectives: We investigated the prevalence and predictive ability of symptoms in persons at-risk of RA, using the validated 'Symptoms in Persons At Risk of Rheumatoid Arthritis' (SPARRA) questionnaire.
Methods: Individuals at-risk of RA from four different cohorts from the Netherlands (n=122), United Kingdom (N=90), Sweden (N=13) and Switzerland (N=20), were asked to fill out the SPARRA questionnaire, consisting of 69 questions (previously described [6]). Individuals were either defined as persons with anticitrullinated protein antibodies (ACPA) and/or rheumatoid factor (RF; n=193), having relevant symptoms (i.e. clinically suspect arthralgia with or without RA-specific antibodies, n=70) or being first degree relatives (FDR, n=20) of RA patients. All were followed for a minimum of 24 months or until clinical arthritis development. Univariable analyses were performed for possible predictor selection (p<0.2), followed by stepwise forward selection (by Cox regression, p<0.1) to create a multivariable prediction model.
Results: The mean age of all participants was 49 years and 69% was female. In total, 56 persons (23%) developed clinical arthritis (n=22, 25, 7, 2 respectively in the 4 groups) after a median of 11.9 months (IQR 5.3 - 17.8). In total, 23 SPARRA questions were selected from the univariable analyses and entered in the stepwise forward selection procedure. Time to development of RA was predicted by the following questions: pain moving from joint to joint, having moderate or severe swelling in joints, feeling ≥1 days fatigue per month and feeling stiffness in joints of one and both feet (table 1).

Table 1. Multivariable prediction model of SPARRA questions to predict clinical arthritis

	HR (95% CI), p
Does your joint pain move from joint to joint?	
No; from arms to legs; from legs to arms (ref)	1
From ons side to the other	2.96 (1.57; 5.57), p = 0.001
Over the past month how much joint swelling have you had?	
None or mild (ref)	1
Moderate or severe	3.04 (1.48; 6.25), p = 0.003
Over the past month how many days of the month have you had fatigue?	
0 (ref)	1
≥ 1	0.32 (0.15; 0.67), p = 0.003
Where did you feel joint stiffness?	
Neither feet (ref)	
One foot	0.93 (0.42; 2.08), p = 0.865
Both feet	0.40 (0.17; 0.93), p = 0.032

Conclusion: Asking persons at-risk of RA about joint pain, swelling and stiffness is common clinical practice. However, specific details such as pain moving from one side to the other or degree of joint swelling may provide useful additional information to estimate a person's RA risk. The protective effect noted for fatigue and stiff feet may reflect an underlying pain syndrome rather than RA risk. We are currently performing analyses of the potential added value of SPARRA questions over the clinical prediction model by van der Stadt et al [3] which will help determine the final format of the SPARRA questionnaire.
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Disclosure of Interests: Laurette van Boheemen: None declared, Marieke ter Wee: None declared, M. Falahee: None declared, M.H. van Beers - Tas: None declared, Axel Finckh Grant/research support from: Pfizer: Unrestricted research grant, Eli-Lilly: Unrestricted research grant, Consultant of: Sanofi, AB2BIO, Abbvie, Pfizer, MSD, Speakers bureau: Sanofi, Pfizer, Roche, Thermo Fisher Scientific, Aase Hensvold: None declared, Karim Raza Grant/research support from: KR has received research funding from AbbVie and Pfizer, Consultant of: KR has received honoraria and/or consultancy fees from AbbVie, Sanofi, Lilly, Bristol-Myers Squibb, UCB, Pfizer, Janssen and Roche Chugai, Speakers bureau: KR has received honoraria and/or consultancy fees from AbbVie, Sanofi, Lilly, Bristol-Myers Squibb, UCB, Pfizer, Janssen and Roche Chugai, Dirkjan van Schaardenburg: None declared
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OP0115

EFFECT OF NINTEDANIB ON PROGRESSION OF INTERSTITIAL LUNG DISEASE (ILD) IN PATIENTS WITH AUTOIMMUNE DISEASE-RELATED ILDS: FURTHER DATA FROM THE INBUILD TRIAL

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Background: In the INBUILD trial in patients with progressive fibrosing ILDs, nintedanib reduced the rate of decline in forced vital capacity (FVC) versus placebo over 52 weeks both in the overall population and in the subgroup with autoimmune disease-related ILDs. Patients continued blinded randomised treatment until the end of the trial.

Objectives: Assess the effects of nintedanib on the risks of death, acute exacerbation of ILD or death, and disease progression or death over the whole INBUILD trial in patients with autoimmune disease-related ILDs and a progressive phenotype.

Methods: Patients with progressive fibrosing ILDs other than idiopathic pulmonary fibrosis (IPF) were randomised to receive nintedanib 150 mg bid or placebo. Time to i) death, ii) first acute exacerbation of ILD or death, and iii) disease progression (absolute decline in FVC ≥10% predicted) or death, over the whole trial were analysed in patients with autoimmune disease-related ILDs. Incidence rates of adverse events per 100 patient–years were calculated based on events with onset between the first trial drug intake and the last intake plus 28 days. Analyses were descriptive.

Results: Of 663 patients, 170 (82 nintedanib, 88 placebo) had autoimmune disease-related ILDs (89 RA-ILD, 39 SSc-ILD, 19 MCTD-ILD, 23 other autoimmune ILDs including Sjogren's disease-related ILD [n=7], interstitial pneumonia with autoimmune features [n=5] and undifferentiated CTD-ILD [n=3]). Over the whole trial, in the nintedanib and placebo groups, respectively, mean (SD) exposure to drug was 15.4 (7.4) and 16.9 (6.1) months and maximum exposure was 26.0 and 25.2 months; 62 (75.6%) and 68 (77.3%) patients in these groups, respectively, completed the planned observation time. Over the whole trial, in the nintedanib and placebo groups, respectively, 9.8% and 12.5% of patients died, 12.2% and 20.5% of patients had ≥1 acute exacerbation of ILD or died, and 40.2% and 53.4% of patients had disease progression or died (Table). Diarrhoea was the most common adverse event, with incidence rates of 139.2 and 26.3 events per 100 patient–years in the nintedanib and placebo groups, respectively. Adverse events led to treatment discontinuation in 20.7% of patients in the nintedanib group and 13.6% of patients in the placebo group.

Conclusion: Data from the INBUILD trial suggest that nintedanib has a clinically meaningful effect on slowing the progression of ILD in patients with progressive fibrosing autoimmune disease-related ILDs, with adverse events that can be tolerated by most patients.

Table.

	Nintedanib (n=82)	Placebo (n=88)	HR (95% CI)*
Death	8 (9.8)	11 (12.5)	0.80 (0.32, 1.98)
≥1 acute exacerbation of ILD or death	10 (12.2)	18 (20.5)	0.58 (0.27, 1.27)
Disease progression (absolute decline in FVC ≥10% predicted) or death	33 (40.2)	47 (53.4)	0.72 (0.46, 1.13)

n (%) with event over the whole trial (mean [SD] exposure: 15.4 [7.4] and 16.9 [6.1] months in nintedanib and placebo groups, respectively). *Based on time to first event.

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OP0116

TEN-YEAR ANALYSIS OF VERY LOW-DOSE GLUCOCORTICOIDS IN EARLY RA (ESPOIR COHORT) SUPPORTS A TIME-DEPENDENT RISK OF SEVERE OUTCOMES

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Background: We previously failed to find any significant difference with regard to severe outcomes (death, severe infections, fractures, cardiovascular diseases [CVD]) between recent-onset RA patients taking or not low-dose GC treatment in a 7-year analysis of the ESPOIR cohort (1).

Objectives: To explore the 10-year tolerability profile of GC use in patients with early RA.

Methods: We analysed data from the early arthritis (less than 6 months disease duration) ESPOIR cohort. Patients were stratified in two groups, with or without GC treatment at least once during their follow-up (median 10 years IQR [9-10]). The primary outcome was a composite of death, CVD (including myocardial ischemia, cerebrovascular accident and heart failure), severe infection and fracture. In order to reduce the impact of treatment selection bias and potential confounding factors, the weighted Cox time-dependent analysis model was used with inverse probability of treatment weighting (IPTW) propensity score method.

Results: Among the 608 RA patients (480 women, mean age of 47.5 ± 12.1 years), 397 patients (65%) received low-dose prednisone (median 1.9 mg/day [IQR 0.6-4.2], mainly during the first 6 months (70%). The mean duration of GC treatment was 44.6 months ± 40.1. Overall, 95 events were identified during follow-up: 10 deaths, 18 CVD, 32 fractures and 35 severe infections. Based on univariate analysis at 10 years, patients taking GC experienced significantly more events (n=71) than those without GC (n=24) (p=0.035), especially severe infections (n=30 with GC versus 5 without GC, p=0.009) (table 1), with a cumulative dose effect (p=0.007). *On weighted Cox time-dependent analysis, using the IPTW propensity score method, the risk of events over time was significantly associated with GC treatment (p <0.001), age, history of hypertension and erythrocyte sedimentation rate. The risk associated with GC treatment, estimated by the hazard ratio (HR), increased between the first follow-up visit (HR at 6 months = 0.39, 95% CI 0.19-0.82) and 10 years (HR=6.83, 95% CI 2.29-20.35)* (figure 1 and table 2).

Table 1. Primary outcome and events at 10 years: univariate analysis

	Total study population (n=608)	Without GC	With CG	P Value
Primary outcome	95 (15.6%)	24 (11.4%)	71 (17.9%)	0.035
Death	10 (1.6%)	1 (0.5%)	9 (2.3%)	0.103
Cardiovascular diseases	18 (3%)	3 (1.4%)	15 (3.8%)	0.177
Severe infections	35 (5.8%)	5 (2.4%)	30 (7.6%)	0.009
Fractures	32 (5.3%)	15 (7.1%)	17 (4.3%)	0.137

Table 2. Time-dependent relationship between glucocorticoids treatment and risk of events *estimated by hazard ratio*

Time (Months)	Hazard Ratio (95% CI)
12	0.46 (0.23 - 0.90)
24	0.62 (0.36 - 1.08)
36	0.83 (0.52 - 1.33)
48	1.12 (0.73 - 1.72)
60	1.52 (0.96 - 2.40)
72	2.05 (1.19 - 3.52)
84	2.77 (1.44 - 5.34)
96	3.74 (1.69 - 8.26)
108	5.05 (1.98 - 12.91)
120	6.83 (2.29 - 20.35)

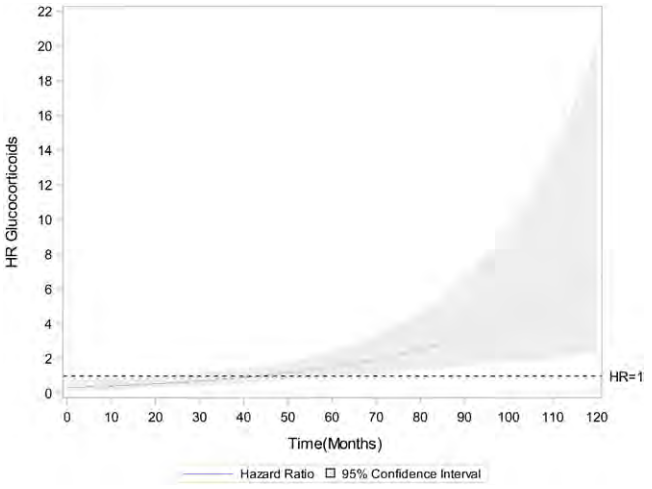


Figure 1. Time-dependent relationship between glucocorticoids treatment and risk of events *estimated by hazard ratio (HR)*

Conclusion: This 10-year analysis of the ESPOIR cohort supports a dose and time-dependent impact of very low-dose GC treatment in early RA, with a long-term high risk of severe outcomes.

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OP0117

LONGITUDINAL CHANGE IN THE CENTRAL NERVOUS SYSTEM PAIN RESPONSE AFTER TREATMENT WITH CERTOLIZUMAB OR PLACEBO. A POST-HOC ANALYSIS FROM THE PRECEPRA TRIAL

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Background: Tumor necrosis factor inhibitors have revolutionized the treatment of rheumatoid arthritis (RA). However, only about 50% of the patients respond well to TNF inhibitors. Therefore, markers that predict response to TNF inhibitors are valuable. Previously we demonstrated that central nervous system (CNS) response to nociceptive stimuli, measured by fMRI of the brain as blood oxygen level dependent (BOLD) signals, decreases already after 24 hours of anti-TNF administration a higher pre-treatment BOLD signal volume seems to predict clinical response to treatment with certolizumabpegol (CZP) [1,2]. We therefore hypothesized that the baseline volume of BOLD signal in the CNS could predict anti-TNF treatment response.

Objectives: To perform a randomized placebo controlled trial in active RA patients to test the effect of TNF inhibition on arthritis induced pain activity in the brain and to test whether patients with high-level RA-related brain activation react differently to TNF-inhibitors than patients with low-level brain activation.

Methods: Adult RA patients fulfilling the 2010 ACR/EULAR classification criteria with a DAS28>3.2 receiving stable DMARD treatment for at least 3 months were eligible. Patients underwent the first fMRI at screening measuring BOLD signal upon MCP joint compression and were stratified into low (< 700 units) and high (>700 units) voxel counts. Then patients were randomized to CZP or placebo with a 2:1 ratio. The second and third fMRI were performed after 12 and 24 weeks, respectively. Control stimulation was done by measuring brain activation after non-painful finger tapping.

Results: 156 RA patients with moderate-to-high disease activity participated in the study. In the finger tapping control, fMRI showed no significant changes in BOLD signal in the CZP-L and CZP-H arms, but a slight but significant decrease (p=0.043) was observed. After joint compression, the CZP-L group showed significant increase in the BOLD signal volume (p=0.043) in fMRI-2 as compared to fMRI-1 with no further significant changes. In contrast, in the CZP-H group, the BOLD signal volume significantly decreased (p=0.037) in fMRI-2 and continued

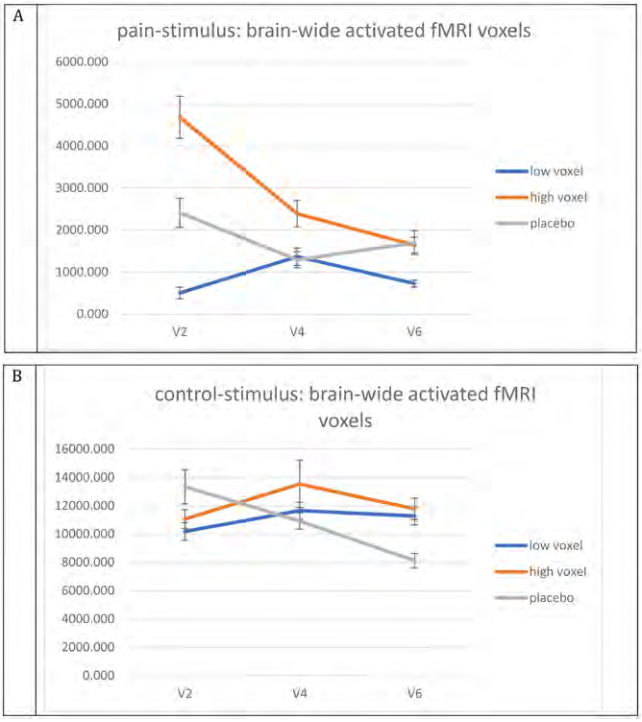


Fig 1. BOLD fMRI responses to painful stimulation

to decrease further, p=0.007. No significant changes were observed in the placebo arm over time.

Conclusion: TNF inhibition improves arthritis-related brain activity in the subgroup of RA patients with high baseline BOLD activity in the fMRI.

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OP0118

DECIPHERING THE ANTI-PROTEIN-ARGININE DEIMINASE (PAD) RESPONSE IDENTIFIES PAD1 AND PAD6 AS NOVEL AUTOANTIGENS IN RHEUMATOID ARTHRITIS

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Background: Protein-arginine deiminase (PAD) 4 enzymes play a central role in the pathogenesis of rheumatoid arthritis (RA) and represents an antigenic target. Among the five known family members (PAD1, PAD2, PAD3, PAD4 and PAD6), only PAD2, PAD3 and PAD4 have been described to have autoantigenic properties. Furtheremore, very little is known on the the isotype usage of these autoantibodies. Understanding the molecular basis of the anti-PAD antibody reponse has the potential to open novel approaches for precision medicine in RA.

Objectives: The objectives of this study were to screen for the presence of antibodies to the five PAD family members and to evaluate the isotype usage of the anti-PAD4 response in RA.

Methods: First, we developed a panel for the detection of anti-PAD IgG based on a particle-based multi-analyte technology (PMAT), that utilized paramagnetic particles coupled with the different human recombinant PAD proteins (PAD1, PAD2, PAD3, PAD4 and PAD6) and anti-human IgG conjugate. This panel was used to test sera from RA patients (n=33) and non-RA controls (n=36). The controls were comprised of apparently healthy individuals (n=10), and patients with infectious diseases (n=10), systemic lupus erythematosus (n=7), systemic sclerosis (n=9) and Sjogren's syndrome (n=1). Next, the PAD4-coupled beads were tested with anti-human IgM, IgA and IgG conjugates on an extended cohort of RA patients (n=62) and the same non-RA controls.

Results: All five anti-PAD IgG (Figure 1) demonstrated the ability to discriminate between RA patients and controls. At greater than 90% specificity, anti-PAD4 IgG, followed by anti-PAD3 IgG, showed the best diagnostic performance. Significantly higher levels of the five antibodies were observed in RA *vs.* controls (*p*-values of 0.0041, <0.0001, 0.0014, 0.0039, and 0.0140 for anti-PAD1, 2, 3, 4 and 6, respectively). Significant correlation was observed between all the antibodies, with the highest between anti-PAD1 and anti-PAD4 (Spearman´s *rho*=0.87, *p*<0.0001) and the lowest between anti-PAD4 and anti-PAD2 (Spearman's *rho*=0.38, *p*=0.0015) and anti-PAD4 and anti-PAD6 (Spearman's *rho*=0.38, *p*=0.0011). While principal component analysis (PCA) (Figure 2) showed an association between all anti-PAD antibodies, there was further discrimination that displayed closer association between anti-PAD1, 3 and 4 on one hand, and between anti-PAD2 and 6. For the extended testing of anti-PAD4 with IgG, IgA and IgM, all three isotypes were identified in the sera of RA patients. Higher levels of the three isotypes were observed in RA patients with erosive disease when compared with the patients without erosion, but this association was only significant for anti-PAD4 IgA (*p*=0.0086).

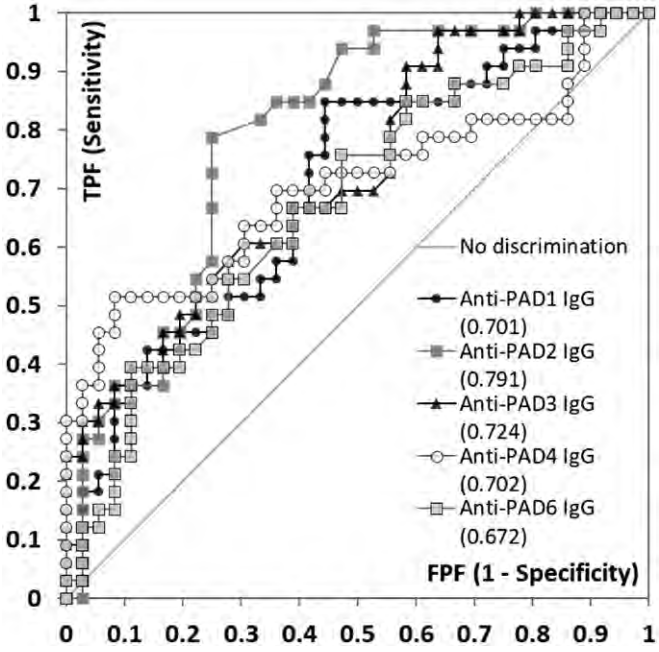


Figure 1. Receiver operating characteristics (ROC) analysis of the discrimination between rheumatoid arthritis (RA) and controls of IgG to protein-arginine deiminase (PAD) 1, PAD2, PAD3, PAD4 and PAD6. The area under the curve (AUC) values are shown in brackets for each biomarker.**Abbreviations:** TPF: true positive fraction; FPF: false positive fraction

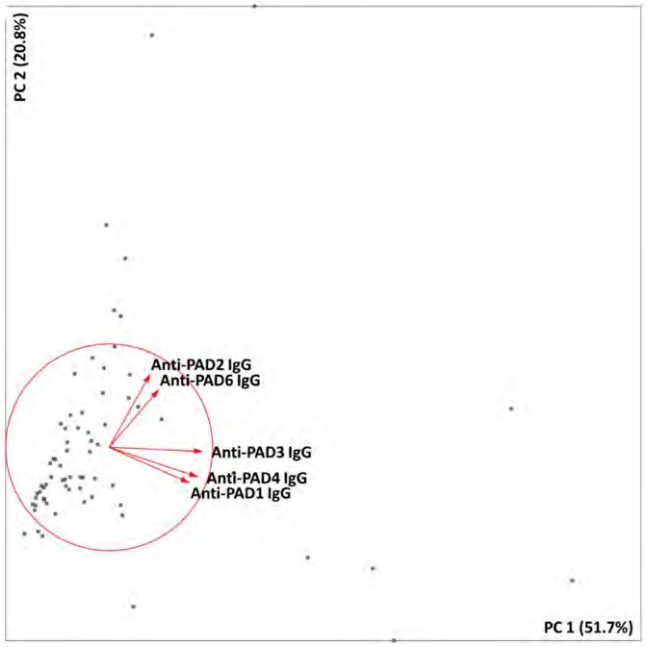


Figure 2. Two dimensional principal component analysis (PCA) plot of the anti-PAD levels in RA patients (n=33) and controls (n=36). Anti-PAD1, 3 and 4 have the main contribution to PC1, which explains 51.7% of the variance, and anti-PAD2 and 6 to PC2, that represents 20.8% of it.**Abbreviations:** PC: principal component

Conclusion: Our study is the first to describe PAD1 and PAD6 as novel antigenic targets in RA and to demostrate that the anti-PAD4 B-cell immune response uses all three isotypes (IgG, IgA and IgM). The strong and significant association between anti-PAD4 IgA and joint erosion is of particular clinical relevance.

Disclosure of Interests: Laura Martinez-Prat Employee of: I am an employee of Inova Diagnostics, an in vitro diagnostics company., Mary Ann Aure Employee of: I am an employee of Inova Diagnostics, an in vitro diagnostics company., Chelsea Bentow Employee of: I am an employee of Inova Diagnostics, an in vitro diagnostics company., David Lucia Employee of: I am an employee of Inova Diagnostics, an in vitro diagnostics company., Marcos Lopez-Hoyos Consultant of: Inova Diagnostics, an in vitro diagnostics company., Michael Mahler Employee of: I am an employee of Inova Diagnostics, an in vitro diagnostics company.

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Cardiovascular disease and malignancies in RA

OP0119

NOT ALL THE SAME? REACHING REMISSION REDUCES THE RISK OF CVD IN PATIENTS WITH RA, BUT PATIENTS ON BIOLOGICS MAY BE BETTER PROTECTED

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Background: Disease activity is a risk factor for the development of cardiovascular disease (CVD) in patients with rheumatoid arthritis (RA). Remission is the preferred treatment target in RA, and may be achieved by treatment with both conventional synthetic DMARDS (csDMARDs) and biologic DMARDS (bDMARDs).

Objectives: To compare the risk of CVD in patients reaching RA disease remission vs. non-remission by 6 months. Additionally; to compare the risk of CVD in RA patients reaching remission on bDMARDs vs. csDMARDs

Methods: The NOR-DMARD is a multi-centre prospective observational study that was established in 2000. Until 2012, patients who started on any DMARD were included, while only patients starting bDMARDSs were included after 2012. Disease activity and markers of inflammation (Erythrocyte Sedimentation Rate (ESR) and C-reactive protein (CRP mg/L) were measured at regular intervals. In these analyses we used data from baseline, 3-month and 6-month visits in patients with clinical RA included in the study from 2009. Patients with prior CVD were excluded from the study. Remission was assessed according to several criteria, and should be attained by the 6-month visit.

NOR-DMARD data were linked to the National Death Registry and National Patient Register. The latter records all diagnoses given at any hospital admission, inpatient and outpatient, from 2009. CVD was defined as a diagnosis of myocardial infarction, chronic heart failure, cerebrovascular disease or sudden CV death in ICD10. Using cox-regression models, we compared the time until the first recorded CVD diagnosis RA disease remission vs non-remission for the first 4 years after start of therapy. The models were adjusted for age and gender. Additionally, we explored interactions between bDMARD vs. csDMARD, remission and non-remission in age and gender adjusted models.

Results: Data were available for 3251 patients, mean (SD) age, 53.6 (13.5) years, number (%) females 2483 (76.4). The total patient years at risk were 5784, during which there were 65 CVD events. The HR across remission criteria are presented in table 1. Patients in disease remission had a significantly lower HR for CVD compared to those not in remission. There was no statistically significant difference in HR for CVD between patients in remission who were treated with bDMARDs vs csDMARDs.

Table 1.

	NOR-DMARD N=3251	p	bDMARDs N=2622	p	csDMARDs N=629	p
	HR (95% CI)		HR(95% CI)		HR(95% CI)	
DAS28-ESR remission vs non-remission	0.40 (0.21,0.74)	0.01	0.30 (0.14,0.65)	0.002	0.75 (0.26,2.22)	0.61
DAS28-CRP remission vs non-remission	0.48 (0.28,0.83)	0.01	0.42 (0.23,0.81)	0.01	0.68 (0.2,1.90)	0.46
CRP <=10	0.55 (0.30,1.03)	0.06	0.67 (0.31,1.47)	0.32	0.46 (0.16,1.36)	0.16
Boolean remission	0.63 (0.34,1.84)	0.33	0.49 (0.15,1.59)	0.23	0.93 (0.21,4.10)	0.92
SDAI remission	0.70 (0.37,1.34)	0.28	0.61 (0.28,1.34)	0.22	1.04 (0.33,3.30)	0.95
CDAI remission	0.69 (0.37,1.29)	0.25	0.61 (0.28,1.34)	0.25	1.04 (0.33,3.30)	0.98

DAS28-ESR and DAS28-CRP remission: <2.6, Boolean remission: tender and swollen joint count <=1, CRP mg/L<=10, patient global <1 (0-10), CDAI remission: <=2.8, SDAI remission <=3.3

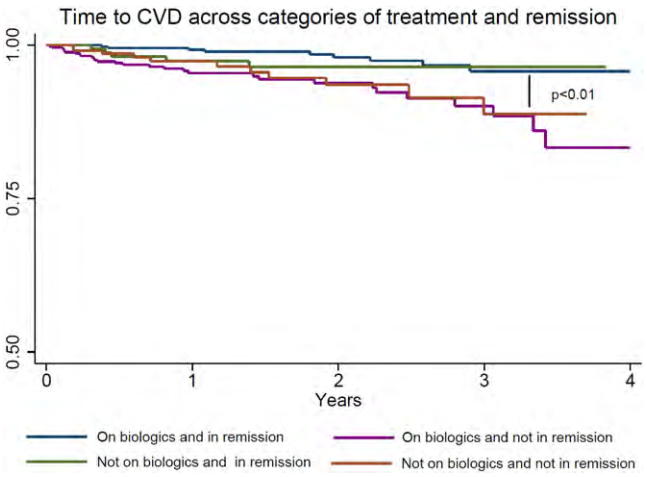


Figure 1

Conclusion: Patients on bDMARDs who achieved DAS28, DAS28-CRP remission, or CRP less than 10 mg/L by the 6-month follow-up were less likely to experience a CVD, compared to patients not achieving remission. The HRs for CVD were higher for patients in remission on csDMARDS, compared to patients on bDMARDss, but the difference was not statistically significant and should be further explored.

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OP0120

BIOLOGICS MAY PREVENT CARDIOVASCULAR EVENTS IN RHEUMATOID ARTHRITIS BY INHIBITING CORONARY PLAQUE FORMATION AND STABILIZING HIGH-RISK LESIONS

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Background: Biologic disease-modifying antirheumatic drugs (bDMARDs) effectively control inflammation and may improve cardiovascular outcomes in Rheumatoid arthritis.

Objectives: To evaluate if bDMARDs decrease long-term cardiovascular disease (CVD) risk in rheumatoid arthritis and whether potential benefits might be rendered by impacting coronary plaque formation or progression.

Methods: In this single-center observational cohort study, 150 patients underwent computed tomography angiography for evaluation of coronary atherosclerosis (total, non-calcified, mixed/calcified and low-attenuation or high-risk plaque); 101 had repeat assessments within 6.9±0.3 years to evaluate plaque progression. All CVD events were prospectively recorded, including cardiac death, myocardial infarction, unstable angina, revascularization, stroke, claudication, and heart failure hospitalization. The Framingham-D'Agostino score assessed clinical risk. Segment stenosis score (cumulative stenosis) measured plaque burden. The effect of bDMARD treatment on CVD events was assessed using marginal structural models. The inverse probability of treatment and censoring weights were used in a weighted pooled logistic regression with current bDMARD use and time since study entry included in the model to approximate a Cox proportional hazards model allowing for time-varying weights. Robust logistic regression evaluated the effect of bDMARD exposure (>50 percent of follow-up period) on likelihood of new plaque formation or change in plaque composition in per-segment models adjusted for Framingham-D'Agostino score, time between scans, statin duration, cumulative prednisone dose and time-averaged CRP.

Results: Sixteen patients incurred 19 CVD events. Current bDMARD use associated with lower CVD risk (OR=0.20 [95%CI=0.05-0.75], p=0.018, Figure 1). However, the effect of bDMARDs was no longer significant when a 6-month exposure extension was applied (OR=0.42 [95% CI 0.13-1.38], p=0.15). The effect of bDMARD use on CVD risk was moderated by non-calcified plaque and low-attenuation plaque presence (Figure 1); specifically, bDMARDs were associated with lower CVD risk only in patients with non-calcified plaque (p=.048) or low-attenuation plaque (p=0.036) at baseline. Per-segment plaque progression analyses showed no main effect of bDMARD exposure on likelihood of new plaque formation (Figure 2). However, bDMARD exposure predicted lower likelihood of new plaque forming in segments without plaque among patients without mixed/calcified plaque in other coronary segments (OR=0.40 [95%CI=0.17-0.93]), but not among those with mixed/calcified plaque elsewhere in their arteries (OR=1.60 [95%CI=0.71-3.62]). Moreover, transition of non-calcified to mixed/calcified plaque associated with bDMARD exposure (OR=4.00 [95%CI=1.05-15.32]). bDMARD use also predicted low-attenuation plaque loss (p=0.042).

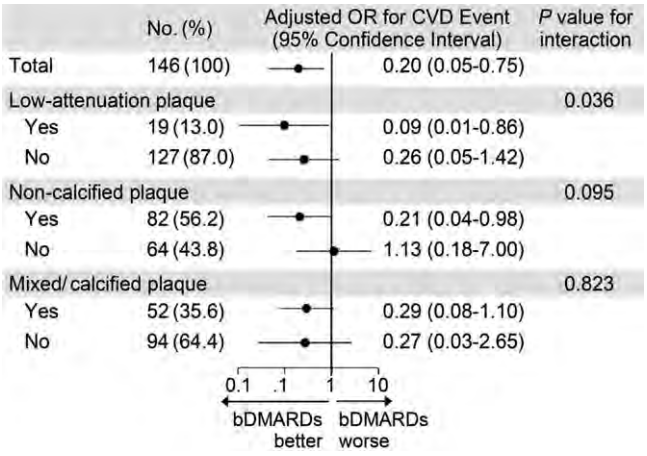


Figure 1. Effect of bDMARD use on cardiovascular disease risk stratified by coronary plaque presence

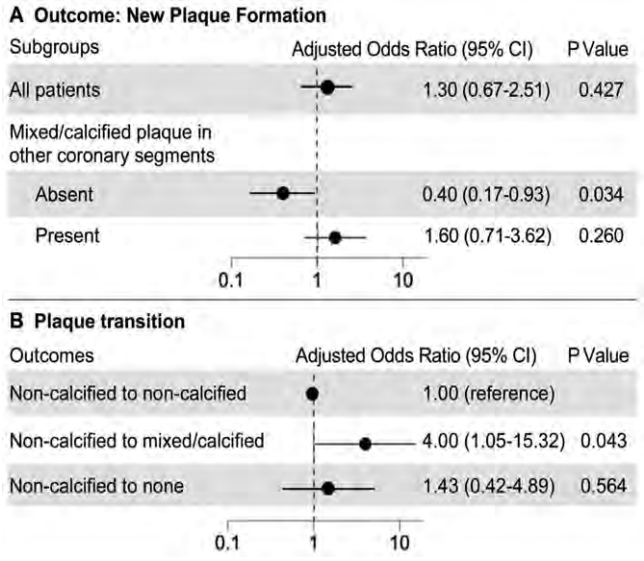


Figure 2. Effect of bDMARD exposure on plaque formation and transition from baseline to follow-up

Conclusion: In rheumatoid arthritis, bDMARD use associated with reduced long-term CVD risk, lower likelihood of new plaque formation in patients with early atherosclerosis, stabilization of high-risk plaque and protective calcification of non-calcified lesions.

Disclosure of Interests: George Karpouzas Grant/research support from: Pfizer, Consultant of: Sanofi-Genzyme-Regeneron, Janssen, Speakers bureau: Sanofi-Genzyme-Regeneron, BMS, Sarah Ormseth: None declared, Elizabeth Hernandez: None declared, Matthew Budoff: None declared

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OP0121 MANAGEMENT OF DYSLIPIDAEMIA AND HYPERTENSION IN PATIENTS WITH RHEUMATOID ARTHRITIS – DATA FROM 19 COUNTRIES

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Background: The realisation that subjects with rheumatoid arthritis (RA) are at increased risk of cardiovascular disease (CVD) has led to a growing interest in risk factor control in such people, but whether this has influenced the management of dyslipidaemia and hypertension (HT) is uncertain. In subjects with coronary heart disease (CHD), audits of CVD risk factor control are regularly performed, which makes it possible to evaluate guideline implementation over time.[1] Updated surveys on CVD risk management in patients with RA are needed.

Objectives: To describe differences in lipid and blood pressure (BP) levels among patients with RA from five world regions. Furthermore, to evaluate attainment of guideline recommended targets for lipid lowering and antihypertensive treatment.

Methods: The SUrvey of CVD Risk Factors in patients with RA (SURF-RA) was conducted at 53 centres in 19 countries from 2014 to 2019. Data including demographics, RA disease characteristics, CVD comorbidity, risk factors and use of preventive treatment was collected. HT was defined as self-reported HT, and/or measured BP ≥140/90 mmHg, and/or use of anti HT medication (a-HT). The treatment goal of a-HT was BP <140/90 mmHg. The 10-year risk of a fatal CVD event was calculated by the European CVD risk calculator, the Systematic COronary Risk Evaluation (SCORE), and was thereafter multiplied with 1.5 as recommended by the European League Against Rheumatism. Patients were classified in a high or very high CVD risk group according to the 2012 European Society of Cardiology guidelines, with low density lipoprotein cholesterol (LDL-c) goal at <2.6 and <1.8 mmol/L, respectively.[2]

Results: In total, 14503 RA patients were included. The mean age was 59.8±13.6 years, and it was a strong female preponderance (74%). Nearly 2/3 of the patients were hypertensive. Use of a-HT in the total population differed substantially between the cohorts with limited use in West Europe and Latin America (17.4% and 24.8%), in contrast to North America and East Europe (46.8% and 57.0%). On average, half of those with HT were at the recommended BP goal. The lowest BP goal attainment was seen in Asia, West and East Europe (40.8-43.1%), and the highest in North America (63.5%). Overall 51.5% had an indication for lipid lowering therapy (LLT), and of these 43.5% were taking LLT. Only 34.0% of patients with an indication for LLT were at recommended LDL-c goals. The proportion of RA patients on target for LDL-c varied greatly between regions, from 23.1% in East Europe to 51.0% in North America. The LDL-c goal attainment was higher in RA patients at high risk (45.1%) compared to those at very high risk of CVD (18.0%).

Conclusion: This large international survey on RA patients revealed considerable geographical differences in CVD preventive treatment. Lower goal attainment for LLT than reported for subjects with CHD was observed. We conclude that there is a substantial need for improvement in CVD preventive measures in RA patients.

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Disclosure of Interests: Silvia Rollefstad: None declared, Eirik Ikdahl: None declared, Joe Sexton: None declared, Georeg Kitas: None declared, Piet van Riel: None declared, Cynthia S. Crowson Grant/research support from: Pfizer research grant, Ian Graham: None declared, Anne Grete Semb: None declared

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OP0122 SUBCLINICAL ATHEROSCLEROSIS OF FEMORAL ARTERIES IN RHEUMATOID ARTHRITIS. AN ULTRASOUND STUDY

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Background: Cardiovascular morbidity and mortality is increased in patients with rheumatoid arthritis (RA). This cannot be entirely explained by traditional risk factors. Inflammation and autoimmunity may play a role in the cardiovascular risk excess. Subclinical atherosclerosis is associated with a risk comparable to

established coronary heart disease. In RA it has been investigated by carotid artery ultrasound and carotid atherosclerotic plaques are more prevalent in RA patients than controls. EULAR recommendations for cardiovascular disease risk management consider that carotid ultrasound may be part of the risk evaluation in patients with RA. Recent studies in general population have shown that plaques in femoral arteries are more common and are associated with higher cardiovascular risk.

Objectives: To study the usefulness of femoral artery ultrasound for the detection of subclinical atherosclerosis and its ability to improve cardiovascular risk assessment in RA patients.

Methods: Cross-sectional observational study of prevalence in 140 RA patients aged 40 to 65 years. Subclinical atherosclerosis was evaluated by carotid and femoral artery ultrasound.

Results: Atherosclerotic plaques were found in 86.4% of RA patients (60.7% in carotid arteries and 78.6% in femoral arteries). Patients with plaques were older and more frequently past or present tobacco users. Femoral plaques were larger and more numerous than the carotid plaques and people with plaques in both locations had more extensive subclinical atherosclerotic disease (table). Only 7.9% of RA patients were considered as having very high cardiovascular risk by clinical factors, after carotid ultrasound this increased to 57.1% and after femoral ultrasound to 86.4%.

Conclusion: Ultrasound examinations of the femoral artery in addition to the carotid artery increased the detection of subclinical atherosclerosis and determine a group of patients with higher intensity of atherosclerotic disease. Examinations of both arteries allowed a greater number of RA patients previously considered to have low to moderate cardiovascular risk to be classified as very high cardiovascular risk.

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Table

	Only carotid plaques n= 11	Only femoral plaques n= 36	Femoral and carotid plaques n= 74
Number of carotid plaques per patient	1,3 ± 0,5	-	2,5 ±2,0*
Carotid plaques size (mm)	1,63 ±0,20	-	2,08 ±0,69*
Number of femoral plaques per patient	-	2,3 ±1,7	3,7 ± 2,9**
Femoral plaque size (mm)	-	2,20 ± 0,59	3,10 ± 1,10**
Total number of plaques per patient	1,3 ± 0,5	2,3 ± 1,7*	6,2 ± 4,3***

†Results in mean ± sd. *p<0,05 vs only carotid plaques. **p<0,05 vs only femoral plaques. ***p<0,05 vs only carotid plaques and only femoral plaques.

Disclosure of Interests: Julio Medina: None declared, Francisco Aramburu: None declared, Carmen González Montagut: None declared, Dolores Sánchez: None declared, Estíbaliz Loza Grant/research support from: Roche, Pfizer, Abbvie, MSD, Novartis, Gebro, Adacap, Astellas, BMS, Lylly, Sanofi, Eisai, Leo, Sobi
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OP0123 RISK OF BREAST CANCER BEFORE AND AFTER RHEUMATOID ARTHRITIS, AND THE IMPACT OF HORMONAL FACTORS

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Background: Large cohort studies have consistently reported decreased occurrence of breast cancer among women with RA. However, both the reasons behind this decreased risk and if it is present already before RA diagnosis, is unclear. The occurrence of RA following breast cancer is clinically and etiologically important also for other reasons. Long-term adjuvant anti-hormonal treatment with tamoxifen or aromatase inhibitors has become mainstay for estrogen receptor positive breast cancer, but are often associated with arthralgia as a side effect. Some studies have suggested that these therapies not only induce arthralgia, but also inflammatory arthritis.

Objectives: To examine the risk of incident breast cancer in women with RA, and the risk of RA in women with a history of breast cancer, taking anti-hormonal treatment for breast cancer into account.

Methods: Using nationwide Swedish registers, women with new-onset RA diagnosed 2006-2016 were identified. Each RA patient was matched on age, sex, and place of residence to 5 randomly selected control subjects from the general population. Through register linkages, we collected information on breast cancer, breast cancer risk factors (age at childbirth, number of children, hormone replacement therapy), and socio-economy. The relative risk of breast cancer after RA was assessed using Cox regression, and the relative risk of RA in women with a history of breast was assessed using conditional logistic regression.

Results: The risk of incident breast cancer in women with RA was reduced and the association was not attenuated by adjustment for breast cancer risk factors (HR=0.80, 95%CI 0.68-0.93)(Table 1). The risk was similar among seronegative RA, (HR=0.77, 95%CI 0.58-1.02), and seropositive RA, (HR=0.81, 95%CI, 0.67-0.98), and for all age groups. We noted reduced risks for all TNM stages, and for both pre- and postmenopausal breast cancer (assessed with age cutoff 50 years). The risk of RA in women with a history of breast cancer was similarly reduced (OR=0.87, 95%CI, 0.79-0.95). Odds ratios (OR) stratified by serostatus and age at RA diagnosis yielded similar results. There was no clear trend in the level of risk reduction when examining the risk by menopausal status, or cancer stage at breast cancer diagnosis. Women with breast cancer treated with tamoxifen (OR=0.86, 95%CI 0.62-1.20), or aromatase inhibitors (OR=0.97, 95%CI 0.69-1.37), did not have an increased risk of RA compared to women with breast cancer treated differently.

Table 1. Risk of breast cancer in women with RA, overall and by serostatus (events and hazard ratios), and risk of RA in women with a history of breast cancer, overall and by serostatus (events and odds ratios)

	No. of breast cancers, patients with RA	No. of breast cancers, comparators/ controls	RR (95% CI)
Risk of breast cancer in women with RA	190	1191	0.80 (0.68-0.93)
Seronegative RA	55	346	0.77 (0.58-1.02)
Seropositive RA	124	772	0.81 (0.67-0.98)
Risk of RA in women with breast cancer	555	3193	0.87 (0.79-0.95)
Seronegative RA	157	921	0.85 (0.71-1.01)
Seropositive RA	367	2088	0.88 (0.78-0.98)

Conclusion: There is a decreased risk of breast cancer in patients with RA, and a similar decrease in risk of breast cancer before RA diagnosis. We did not find evidence to support that the decreased risk of breast cancer was due to known risk determinants. Furthermore, adjuvant anti-hormonal therapy as used in secondary breast cancer pharmacoprevention did not seem to increase the risk of RA.

Disclosure of Interests: Hjalmar WADSTRÖM: None declared, Andreas Pettersson: None declared, Karin Ekström Smedby: None declared, Johan Askling Grant/research support from: JA acts or has acted as PI for agreements between Karolinska Institutet and the following entities, mainly in the context of the ARTIS national safety monitoring programme of immunomodulators in rheumatology: Abbvie, BMS, Eli Lilly, Merck, MSD, Pfizer, Roche, Samsung Bioepis, Sanofi, and UCB Pharma
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OP0124 RISK OF MALIGNANCIES ACROSS BIOLOGIC CLASSES IN RHEUMATOID ARTHRITIS: ANALYSIS OF A NATIONAL CLAIM DATABASE

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Background:

Objectives: To estimate the incidence rate of malignancies in biologic-treated RA patients, and to compared it to the general population and across different classes of biologics

Methods: We conducted an historical cohort study within the French the national claim database, named SNDS. This database prospectively records individual health resource of 86% of the entire French population (65 million inhabitants) since 2007. RA adult patients were identified based on ICD-10 code (M05 or M06). Patients with cancer history were excluded. Treatment exposures focused on incident first use of biologics including all anti-TNF, rituximab, abatacept, tocilizumab, ustekinumab, anakinra. To identify incident treatment periods, only patients who did not receive any biologics in the 1-year period before the index date were

selected. In the base case analysis, exposure was defined with a 90-day latency after treatment initiation and a 180-day carry-over period after drug discontinuation. To compare the risk of malignancies between biologic treated patients and general population, Standardized incidence ratio (SIR [95%CI]) were calculated using FRANCIM ("France Cancer Incidence et Mortalité") estimations as reference.

To compare the risk of malignancies between biologics, a propensity score (including age, sex, year of first occurrence of RA code, date of treatment initiation, number of previous DMARDs, Charlson comorbidity index, diagnosis of tobacco and/or alcohol-associated disorders, number of hospitalizations for RA, cumulative corticosteroid dose) was calculated for each comparison. Hazard Ratios (HRs) for risk of cancer were estimated using Cox proportional hazard model using inverse probability of treatment weighting (IPTW) with propensity score. Exposure was considered as a time-dependent variable and propensity scores were estimated dynamically using pooled logistic regression reassessed for each new exposure.

Results: Between 2007 and 2016, 31,792 patients (112,802 patient-years)- were exposed to biologics. The annual incidence rate of overall malignancies was 0.865 per 100 patients-years. Malignancies occurred in 730 patients exposed to anti-TNF, 235 patients exposed to another biologic and 11 exposed to both.

As compared to the general population, biologic treated patients had an increased risk of lung cancer (SIR=1.35 [1.14;1.60]), a decreased risk of pancreatic cancer (SIR=0.52[0.31-0.85]) and no significant increased risk of invasive melanoma (SIR=1.15 [0.82;1.61]). Results were similar for anti-TNF-treated patients. Other biologics were not analyzed separately due to small sample sizes.

The overall risk of malignancies and risk of lymphoma did not differ between anti-TNF and other biologics (analysed all together), or abatacept. Within the anti-TNF class, the overall risk of malignancies and risk of lymphoma did not differ between etanercept and monoclonal anti-TNF (table).

Type of malignancies	HR [95% CI]	p-value	HR [95% CI]	p-value	HR [95% CI]	p-value
	Anti-TNF (ref) vs. other biologics		**Anti-TNF (ref) vs. Abatacept**		**Monoclonal anti-TNF (ref) vs. Etanercept**	
P-Y exposure	*83256 vs. 25649*		*91770 vs. 4681*		*49620 vs. 36790*	
All malignancies (excl. non-melanoma skin cancer)	**0.97 [0.81;1.17]**	p=0.7	**1.27 [0.89;1.81]**	p=0.2	**1.11 [0.94;1.32]**	p=0.2
Solid cancer (excl. non-melanoma skin cancer)	**0.98 [0.80;1.20]**	p=0.8	**1.23 [0.84;1.82]**	p=0.4	**1.10 [0.92;1.32]**	p=0.3
Lymphoma	**0.69 [0.32;1.46]**	p=0.3	**1.73 [0.55;5.48]**	p=0.5	**0.87 [0.49;1.57]**	p=0.7

Conclusion: Using a large nationwide healthcare database, representative of the French population, the overall risk of malignancies did not seem to differ across the different classes of biologic. Among anti-TNF, the risk of malignancies of lymphoma did not differ between etanercept and monoclonal antibodies. The risk of organ specific cancers, except lung cancer, did not differ from that of general population.

Disclosure of Interests: Raphaèle Seror Consultant of: BMS, Medimmune, Novartis, Pfizer, GSK, Lilly, Bruno Fautrel Grant/research support from: AbbVie, Lilly, MSD, Pfizer, Consultant of: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celgene, Lilly, Janssen, Medac MSD France, Nordic Pharma, Novartis, Pfizer, Roche, Sanofi Aventis, SOBI and UCB, Alexandre Lafourcade: None declared, yann de-rycke: None declared, Xavier Mariette Consultant of: BMS, Gilead, Medimmune, Novartis, Pfizer, Servier, UCB, Florence Tubach Grant/research support from: Florence TUBACH is head of the Centre de Pharmacoépidémiologie (Cephepi) of the Assistance Publique – Hôpitaux de Paris and of the Clinical Research Unit of Pitié-Salpêtrière hospital, both these structures have received research funding, grants and fees for consultant activities from a large number of pharmaceutical companies, that have contributed indiscriminately to the salaries of its employees. Florence Tubach didn't receive any personal remuneration from these companies.

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OP0125

LYMPHOMAS COMPLICATING RHEUMATOID ARTHRITIS: RESULTS OF A FRENCH MULTI-CENTRE CASE-CONTROL STUDY

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Background: Rheumatoid arthritis (RA) is associated with an increased risk of non-Hodgkin B-cell lymphoma (B-cell NHL).

Objectives: 1)To study the characteristics of B-cell NHL complicating RA 2)To identify the factors associated with their occurrence.

Methods: A multi-centre case-control study was performed in France. Cases were patients with RA fulfilling the ACR-EULAR 2010 criteria, who developed a B-cell NHL after the diagnosis of RA. Cases were reported following a call for observations by the "Club Rhumatismes et Inflammation" network, registries from the French society of Rheumatology (AIR, ORA and REGATE) and the ESPOIR cohort. For each case, 2 control patients were drawn at random from patients in the ESPOIR cohort with RA fulfilling the ACR-EULAR 2010 criteria; cases and controls were matched on age (age at lymphoma diagnosis for cases and age at the 10-year ESPOIR visit for controls). Patients with associated Sjögren's syndrome were excluded. Cases and controls characteristics were compared for parameters associated with the occurrence of lymphoma.

Results: A total of 54 cases were included and matched to 108 controls. Lymphomas were mostly diffuse large B-cell lymphomas (n=26, 48.2%) *(Figure 1)*. EBV positivity was found in 4 cases among 27 tested (14.8%). Cases had a mean age of 63.5 years (SD=10.9), and had a mean RA duration of 12.4 years (SD=10.5) at the time of diagnosis of lymphoma; there was no significant difference with controls (p=0.47 and p=0.40 respectively). The mean duration of follow-up after the diagnosis of lymphoma was 5.2 years (SD=5.8). In univariate analysis, factors associated with occurrence of B-cell NHL were: male gender (OR=3.3, 95%CI: 1.7-6.7), positive ACPA (OR=5.1, 95%CI: 2.0-15.7), positive Rheumatoid Factor (RF) (OR=3.9, 95%CI=1.6-12.2), erosions on X-rays (OR=15.4, 95%CI: 6.9-37.7) and DAS28 (OR=2.0, 95%CI: 1.5-2.7). Methotrexate, TNF-blockers and the number of previous biologics were not associated with the occurrence of B-cell NHL. Hydroxychloroquine and sulfasalazine were more frequent in cases versus control, which could be linked to a date bias. Erosions and DAS28 remained significant in multivariate analysis *(Table 1)*.

Conclusion: This study revealed an association between markers of activity (DAS28), severity (erosions) and autoimmune B-cell activation (RF and ACPA) and the risk of B-cell NHL in patients with RA, supporting the continuum between autoimmunity and lymphomagenesis in RA.

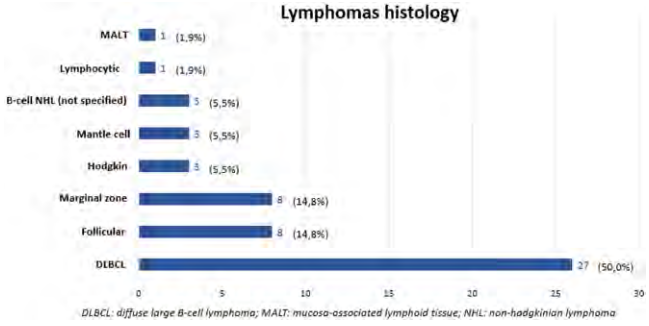


Figure 1. lymphomas histology

Table 1. association between RA characteristics and B-cell NHL in univariate and multivariate analysis

Variables	Cases (N=54)	Controls (N=108)	Univariate analysis		Multivariate analysis	
			OR (95%CI)	p-value	OR (95%CI)	p-value
Male gender, N (%)	27 (50.0)	25 (23.2)	3.3 (1.7-6.7)	*0.0006*	2.2 (0.8-6.1)	*0.13*
Positive ACPA, N (%)	49 (90.7)	71 (65.7)	5.1 (2.0-15.7)	*0.0006*	-	-
Positive RF, N (%)	49 (90.7)	77 (71.3)	3.9 (1.6-12.2)	*0.005*	-	-
Positive RF or ACPA, N (%)	49 (90.7)	80 (74.1)	3.4 (1.3-10.6)	*0.01*	2.9 (0.7-15.0)	*0.16*
Erosions on X-rays, N (%)	44 (81.5)	26 (24.1)	15.4 (6.9-37.7)	*< 0.0001*	*9.8 (3.8-28.2)*	*< 0.0001*
DAS28 at B-cell NHL diagnosis/at the 10th year visit*, mean(SD)	4.1 (1.6)	2.6 (1.4)	2.0 (1.5-2.7)	*< 0.0001*	*1.9 (1.3-2.8)*	*0.0007*

*B-cell NHL diagnosis for cases, 10th year visit for controls

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OP0126

IS IMMUNE CHECKPOINT INHIBITORS THERAPIES SAFE AND EFFECTIVE FOR PATIENTS WITH CANCER AND PREEXISTING AUTOIMMUNE DISEASE?

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Background: Immune checkpoints inhibitors (ICIs) are associated with frequent immune-related adverse events (irAEs). Most patients with preexisting autoimmune disease (PAD) have been universally excluded from clinical trials and ICIs are not recommended for patients with cancer and PAD due to the unknown safety. In this study, we aim to evaluate the safety and efficacy of ICIs in patients with PAD and cancer.

Objectives: Systematic searches were performed of PubMed, EMBASE, and the Cochrane library from inception through September 2019 for observational studies reporting safety and efficacy data among ICIs-treated patients with cancer and PAD. A random effects meta-analysis was performed to calculate pooled incidence rates of PAD flare, irAEs and response.

Methods: Systematical search of PubMed, EMBASE and Cochrane Library plus a hand search of conference proceedings were performed for observational studies that reported cancer incidence in patients with RA treated with biologics or tofacitinib with active comparator of conventional DMARDs (csDMARDs) or TNFi. The pooled relative risk (RR) and 95% confidence interval (CI) were calculated with fix-effects or random-effects model.

Results: A total of 619 ICI-treated patients with PAD in 14 publications were finally identified. In the random effects meta-analysis, pooled incidence of PAD flares, *de novo* irAEs or both of any grade was 60% (95% CI 52%-68%). Viewed separately, there were 219 and 206 patients experiencing PAD exacerbation and *de novo* irAEs of any grade, yielding a pooled incidence of 35% (95% CI 29%-41%) and 33% (95% CI 24%-42%) respectively. Of these, most of flare and *de novo* irAEs were graded as mild (grade 1-2) (pooled proportion: 82%, 95%CI 72%-91%; 65%, 95%CI 54%-76%, respectively). Rheumatoid arthritis was associated with a trend toward higher flare occurrence compared with another individual PADs (RR=1.25-1.88). With respect to efficacy, 136 patients showed complete or partial response, corresponding to a pooled response rates of 30% (95% CI 22%-39%). There were no statistical differences between patients with and without immunosuppressive therapy at ICI start regarding flare (RR: 1.08, 95% CI 0.72-1.62), but a trend towards lower response rates was observed in patients with baseline immunosuppressants (RR: 0.58, 95% CI 0.26-1.33).

Conclusion: Immune toxicities are frequent in ICI-treated patients with PAD but often mild and manageable without discontinuing therapy. Rheumatoid arthritis is associated with a trend toward more flares. ICI treatment are effective and not absolute contraindication in PAD patients, but close monitoring and multidisciplinary collaboration should be contemplated, especially for those concomitantly receiving immunosuppressant or having rheumatoid arthritis.

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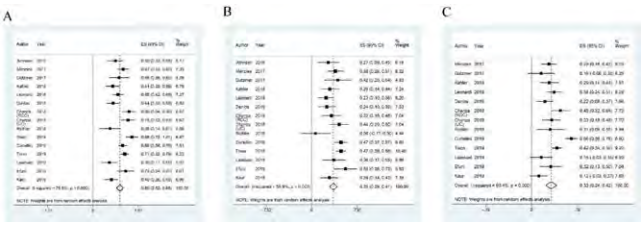


Figure 1. Pooled effect estimates in ICI-treated patient with PAD (A) PAD flare, *de novo* irAEs or both; (B) PAD flare; (C) *de novo* irAEs. ICI: Immune checkpoint inhibitors; PAD: Preexisting autoimmune disease; irAEs: Immune-related adverse events.

Disclosure of Interests: None declared

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Immunity in rheumatic disease

OP0127

TRANSCRIPTIONAL ACTIVITY OF SURVIVIN CONTRIBUTES TO MATURATION AND FUNCTION OF THE INTERFERON-GAMMA PRODUCING T CELLS IN RHEUMATOID ARTHRITIS

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Background: Interferon gamma (IFNg) signalling and downstream effects make important contribution in pathogenesis of rheumatoid arthritis (RA). Here, we propose a mechanism by which oncoprotein survivin participates in development of IFN-dependent repertoire of T cells in RA patients.

Objectives: We study the role of survivin in the phenotype of CD4 T cells of RA patients.

Methods: CD4 cells of RA patients and healthy controls were purified from blood, activated and subjected to RNAseq, ChIPseq with antibodies to survivin (BIRC5) was performed on CD4+ cells. Histone H3 ChIPseq was performed using antibodies to H3K27ac, H3K27me3 and H3K4me3. Statistical analysis was performed In R-studio using the Bioconductor package DESeq2, clustering using Spearman and Ward.D2.

Results: Unsupervised clustering of CD4 samples by expression of 48 core Th cell markers identified subsets of $CD28^{hi}CD27^{hi}IFN^{neg}$ central memory cells (Tcm), $CD28^{lo}CD27^{lo}IFN^{lo}$ effector memory cells (Tem) and $CD28^{null}CD27^{null}IFN^{hi}$ terminal effector cells (Tte). Tte cells showed classical features of Th1 cells including high levels of TBX21, TNFa and IL32 and signs of activation in IFN signalling machinery. Interestingly, they combined the features of peripheral Tregs $CD25^{hi}Foxp3^{hi}IKZF2^{neg}$ and IL10 producing cells together with type 1 regulatory cells, which rely on transcription factors BATF and IRF1 for the differentiation and produced high amounts of perforin and granzyme B. Importantly, Tte CD4 cells had also high transcription of BIRC5 (p=1.15e-18).

To study if BIRC5 is a part of IFN signalling, CD4 cells were cultured with survivin inhibitor YM155 and activated with IFNg. RNAseq analysis revealed 2033 (FC<2.0, n=336) differentially expressed genes in the IFN stimulated cultures. Interestingly, a substantial number of these IFN-dependent genes was significantly reduced in the survivin-deficient cultures and included among others CD28, FoxP3, IKZF2, ICOS, BATF, PRDM1, CXCR3, IRF4 and IRF8. Analysis of the peak sequences identified enrichment for composite motifs for IRFs (ETS:IRF, p1.0e-124; bZIP:IRF, p=1.0e-640), indicating that survivin is important for IFNg signalling. Numerically, the peaks containing ETS:IRF motifs were most prevalent and identified in total within 49.7% of all survivin-ChIP peaks. Frequent was co-localisation of the IRF:bZIP and IRF:ETS motifs within the survivin peaks. Among the IRF motifs dominated those suitable for IRF1 (p=1,0e-127) and IRF8 (p=1,0e-84). However, the DNA binding motifs of these two are alike.

Encouraged by the survivin ChIPseq results, we wanted to know its relation to histone marks. We observed that 50% of survivin peaks containing both IRF:bZIP and IRF:ETS motifs are co-localized with the H3K27ac marks. In total, 16 of 48 core Th cell markers used for patients clustering were identified by survivin ChIPseq, co-localized with IRF composite motifs and histone marks. They were also dependent of survivin for expression.

Conclusion: his study showed that survivin binds to DNA and regulates the core gene expression contributing to maturation and function of the IFNg producing Th1 cells.
References: -
Disclosure of Interests: Malin Erlandsson: None declared, Karin ME Andersson: None declared, Nisha Nair: None declared, Anastasius Damdimopoulos: None declared, Sofia Töyrä Silfverswärd: None declared, Rille Pullerits: None declared, Anne Barton Consultant of: AbbVie, Maria I Bokarewa: None declared
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OP0128 DISTINCT FEATURES OF HLA-DR+ AND HLA-DR- PD-1HI CXCR5- T PERIPHERAL HELPER CELLS IN SEROPOSITIVE RHEUMATOID ARTHRITIS

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Background: PD-1hi CXCR5- T peripheral helper (Tph) cells are newly identified pathogenic CD4+ helper T cells in rheumatoid arthritis (RA). Since Tph cells have been emerged quite recently, the characteristics of Tph cells as a biomarker of RA are not fully understood.
Objectives: The aim of the study is to evaluate how useful Tph cells in peripheral bloods are when compared to other immune cell subsets, and to clarify which Tph subset most accurately reflects the disease activity of RA.
Methods: The RA patients who visited our rheumatology department between January 2000 and February 2017, and met the 2010 ACR/European League Against Rheumatism (EULAR) classification criteria were included. We first assessed correlation with 40 immune cell subsets and the disease activity of RA. Next, the proportions of these immune cells were compared between RA and healthy controls (HCs). We also investigated the immune cell subsets which reflected the time course change of the disease activity after the methotrexate (MTX) treatment. The study protocol was approved by the ethics committee at Keio University School of Medicine.
Results: Thirty-four seropositive RA, 12 seronegative RA and 34 HCs were included. The Immune cell subsets which showed correlation with DAS28-ESR (r> 0.2 or r> -0.2) were activated CD4 T cells (r= 0.31), HLA-DR+Th1 cells (r= 0.20), HLA-DR+Th1-17 cells (r= 0.25), Tfh1-17 cells (r= -0.25), HLA-DR+Tph cells (r= 0.22), CD3+CD8+naïve T cells (r= -0.25), CD3+CD8+effector memory T cells (r= -0.26), plasma cells (r= 0.40) and CD14++CD16+intermediate monocyte (r= 0.23). The proportions of HLA-DR+Th1 cells (2.3% vs. 5.7%), HLA-DR+Th1-17 cells (0.7% vs. 2.2%), Tfh1-17 cells (1.7% vs. 2.0%), HLA-DR+Tph cells (0.02% vs. 0.1%), CD3+CD8+effector memory T cells (16.6% vs 25.7%), plasma cells (0.04% vs. 0.17%) were statistically higher in the patients with RA compared to HCs. While the proportion of Tph cells showed weak correlation with DAS28-ESR (r= 0.18), that was extremely higher in RA (0.08% vs. 0.25%). Interestingly, when assessing the correlations with the disease activity in seropositive and seronegative RA separately, the proportions of Tph cells (r= 0.52) and HLA-DR+Tph cells (r= 0.50) were highly reflected in seropositive RA, but not in seronegative RA. Regarding the disease activity after the MTX treatment, the change of proportion of Tph cells between week 0 and 52 significantly reflected the change of DAS28-ESR (r= 0.75, p= 0.025), but not HLA-DR+Tph cells because of the non-specific reduction by the MTX treatment. Rather, HLA-DR-Tph cells significantly reflected the change of DAS28-ESR while receiving the MTX treatment (r= 0.76, p= 0.021).
Conclusion: Tph cells and HLA-DR+Tph cells highly reflected the disease activity of seropositive RA. However, after the treatment, the proportion of HLA-DR+Tph cells decreased independent from the disease activity, and that of HLA-DR-Tph cells more accurately reflected the change of the disease activity during the treatment.
References:
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Disclosure of Interests: Hiroki Yamada: None declared, Takanori Sasaki: None declared, Katsuya Suzuki: None declared, Masaru Takeshita: None declared, Shuhei Tanemura Employee of: I am employed by Mitsubishi Tanabe Pharma Corporation, Noriyasu Seki Employee of: I am employed by Mitsubishi Tanabe Pharma Corporation, Hideto Tsujimoto Employee of: I am employed by Mitsubishi Tanabe Pharma Corporation, Tsutomu Takeuchi Grant/research support from: Eisai Co., Ltd, Astellas Pharma Inc., AbbVie GK, Asahi Kasei Pharma Corporation, Nippon Kayaku Co., Ltd, Takeda Pharmaceutical Company Ltd, UCB Pharma, Shionogi & Co., Ltd., Mitsubishi-Tanabe Pharma Corp., Daiichi Sankyo Co., Ltd., Chugai Pharmaceutical Co. Ltd., Consultant of: Chugai Pharmaceutical Co Ltd, Astellas Pharma Inc., Eli Lilly Japan KK, Speakers bureau: AbbVie GK, Eisai Co., Ltd, Mitsubishi-Tanabe Pharma Corporation, Chugai Pharmaceutical Co Ltd, Bristol-Myers Squibb Company, AYUMI Pharmaceutical Corp., Eisai Co., Ltd, Daiichi Sankyo Co., Ltd., Gilead Sciences, Inc., Novartis Pharma K.K., Pfizer Japan Inc., Sanofi K.K., Dainippon Sumitomo Co., Ltd.
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OP0129 AUTOREACTIVE, CITRULLINATED PEPTIDE-SPECIFIC T CELLS IN RHEUMATOID ARTHRITIS

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Background: Self-reactive CD4+ T cells are thought to play a key role in the pathogenesis of rheumatoid arthritis (RA) and represent a target for antigen-specific, tolerogenic therapies[1]. Phenotyping such cells could provide the means with which to monitor these treatments. Here, we aimed to demonstrate antigen-induced T cell responses to RA relevant epitopes using peptide stimulation of peripheral blood mononuclear cells (PBMC). Several autoantigens have been described in RA, including various citrullinated peptide (cit-peptide) epitopes[2]; here we have used a combination of cit-peptides that will be used to load tolerogenic dendritic cells in a forthcoming experimental medicine study (AuToDeCRA II).
Objectives: To detect peripheral blood T cell proliferation in response to candidate autoantigens in RA patients and healthy controls (HCs) using flow cytometry.
Methods: PBMC from RA patients and HCs were obtained following informed consent and were cryopreserved. Prior to use, cells were thawed in medium supplemented with human serum and were labelled with a proliferation tracking dye (PTD). $2x10^5$ labelled cells were plated into 96 well plates with a minimum of 7 replicates per condition and were either cultured alone or stimulated with individual peptides at varying concentrations or a peptide pool. On day 9, cells from replicate wells were harvested, pooled and stained for surface markers and viability. Samples were acquired on a BD Fortessa X20 and analysis was performed in FlowJo version 10. A manual gating strategy was used to identify CD45RO+ (memory) CD4+ T cells and amongst this population, activated/proliferated cells were defined as CD25+ PTD low. Stimulation indices (SI) were calculated as the percentage of activated/proliferated cells from stimulated wells divided by the percentage from unstimulated wells.
Results: Ten RA patients (including early and established disease) were recruited alongside seven HCs. Cit-peptides were initially titrated on an individual basis to determine the optimum concentration for use (n = 2). We then compared stimulation with either single peptides or a pool (n = 2), and found that PBMC stimulated with the pooled cit-peptides had a higher proliferative response. Both single and pooled cit-peptide induced T cell proliferation was observed in both RA and HC samples (Figure 1); the largest responses were seen amongst RA

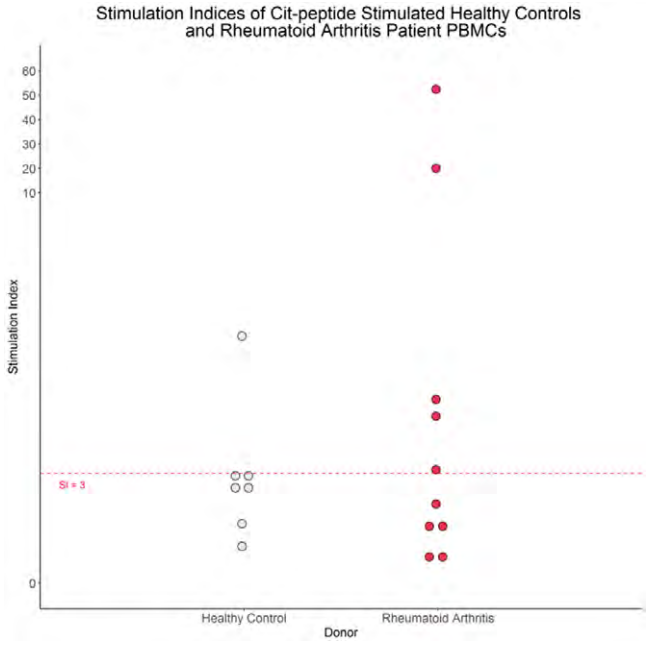


Figure 1 Antigen-specific CD4+ CD45RO+ responses of citrullinated peptide stimulated PBMC from HCs and RA patients.

patients, with a maximum stimulation index of 52.4 compared to a maximum of 6.75 in the HC group. Only 1 HC sample responded with an SI greater than 3.0, whereas 50 % of RA patients elicited responses above this. Two of the RA patients failed to respond to the peptide pool (SI < 1.0). Of note, RA patients were not selected on the basis of tissue type whereas selected peptides bind preferentially to class II HLA containing the shared epitope (SE).

Conclusion: In non-HLA typed individuals, cit-peptide induced proliferative T cell responses were detectable in both RA patients and HCs, and although SIs overall were higher amongst RA patients this did not reach statistical significance in this small sample. Not all RA patients responded to the peptide pool which may be due to the limited number of citrullinated epitopes used, or to RA patients with a non-SE HLA type. Additional work should establish the need for HLA typing in this assay; around half of seropositive RA patients would be expected to be SE positive[3]. Furthermore, a wider array of cit-peptides may be needed to demonstrate autoreactivity in a broader cross-section of RA patients. Our future plans are to further phenotype the cellular subsets responding to the peptide pool and to study assay data in the context of clinical outcomes, to assess its utility for immune monitoring.

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Disclosure of Interests: Jessica Swift: None declared, James Stanway: None declared, Catharien Hilkens: None declared, Amy Anderson: None declared, Arthur Pratt Grant/research support from: Pfizer, GlaxoSmithKlein, John Isaacs Consultant of: AbbVie, Bristol-Myers Squibb, Eli Lilly, Gilead, Janssen, Merck, Pfizer, Roche

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OP0130 IN VITRO CHARACTERIZATION OF INFLAMMATORY ARTHRITIS ASSOCIATED WITH IMMUNE CHECK POINT INHIBITION

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Background: During cancer treatment with immune checkpoint inhibitors (ICI) such as the anti-PD-1 antibody pembrolizumab, 2-4% of patients develop inflammatory arthritis as an immune related adverse event and half of patients with pre-existing inflammatory arthritis have disease flares. This type of adverse events shows striking similarities with traditional immune mediated inflammatory arthritis. However, the underlying immunological mechanisms of inflammatory arthritis associated with ICI are not fully understood.

Objectives: We aimed to develop an in vitro model of inflammatory arthritis associated with ICI, and to use this model to investigate monocyte differentiation and activation following treatment with pembrolizumab.

Methods: First, synovial fluid mononuclear cells (SFMCs) and peripheral blood mononuclear cells (PBMCs) from patients with immune mediated inflammatory arthritis (rheumatoid arthritis and peripheral spondyloarthritis, n=22) and PBMCs from healthy controls were incubated with pembrolizumab and assessed for monocyte chemoattractant protein 1 (MCP-1) secretion by ELISA. Then, cytokine production in SFMCs was studied in more detail by the multiplex V-PLEX proinflammatory panel and by intracellular flow cytometry. Finally, pembrolizumab treated SFMCs were incubated with the different disease modifying anti-rheumatic drugs adalimumab, tocilizumab, tofacitinib, and baricitinib.

Results: Pembrolizumab significantly increased MCP-1 production in the SFMCcultures (P=0.0031). In contrast, pembrolizumab did not change MCP-1 production by PBMCs from neither patients nor healthy controls (P=0.77 and P=0.43). Pembrolizumab also increased the production of TNFα (P=0.049), IFNγ (P=0.047), and IL-12p70 (P=0.031), but did not change the production of IL-6 (P=0.98). Among SFMCs treated with pembrolizumab there was an increased frequency of intermediate monocytes (P=0.044). Interestingly, pembrolizumab also increased the MCP-1 production within the intermediate monocytes only (P=0.028). In contrast, among SFMCs treated with LPS, only the classical monocyte subset was increased (P=0.0045) and MCP-1 production increased in both intermediate and classical monocyte subsets. Lastly, the TNFα inhibitor adalimumab and the Janus kinase inhibitors baricitinib and tofacitinib attenuated the pembrolizumab-induced MCP-1 production (P=0.0004, P=0.033, and P=0.025, respectively) while this was not seen with the IL-6 inhibitor tocilizumab (P=0.75).

Conclusion: We have developed a very simple in vitro model of inflammatory arthritis associated with ICI. Using this model, we found that pembrolizumab specifically activated intermediate monocytes and induced TNFα, IFNγ, and IL-12p70 production, whereas IL-6 was unchanged. These findings were supported by effectful reduction of MCP-1 secretion with TNFα inhibition but not with IL-6 inhibition. This model could potentially be used to further study the effects of ICIs and the underlying immunological mechanisms of inflammatory arthritis associated with ICI.

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OP0131 GUT DERIVED ACETATE PROMOTES REGULATORY B CELLS WITH ANTI-INFLAMMATORY EFFECTS

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Background: Regulatory B cells (Bregs) are defective in many auto-immune diseases, i.e. rheumatoid arthritis (RA). The short-chain fatty acid (SCFA) acetate, derived mostly from gut microbial fermentation of dietary fiber, promotes anti-inflammatory regulatory T cells and protects mice from type 1 diabetes and colitis. We hypothesized that acetate could be a good candidate to promote Bregs in auto-immune diseases.

Objectives: To assess the effect of acetate on Breg number and function, *in vitro* and *in vivo* in mice and humans.

Methods: Bregs were defined as IL-10 producing regulatory B cells (B10 cells). Their number was assessed after overnight exposure to acetate (Ac 10 mM) and 4 hours of CpG, ionomycin and PMA in mice and after 24 hours of acetate +/- CpG and 4 hours of ionomycin and PMA in humans. Acetate was given to mice either intraperitoneally (twice at a 12-hour interval) or in drinking water for 3 weeks. Acetate-treated B cells were transferred to mice with collagen-antibody -induced arthritis to assess their function. To decipher the mechanisms behind the effect of acetate, we used inhibitors of GPR43 (CATPB), ATP synthase (oligomycin), glycolysis (2-DG), ACSS2 and ACLY and assessed protein lysine acetylation by flow cytometry on human B cells. Acetate and B10 cells were also assessed before and after a 7-day high-fibre diet in 12 healthy volunteers.

Results: In mice, acetate promoted B10 cell differentiation both *in vitro (*medians [IQR] 3.1 [0.4-3.7] and 9.9 [5.9-17.6]% of B for CpG and CpG+Ac respectively, p=0.002) and *in vivo* when intraperitoneal injected *(22 [14-29] and 31 [25-37]% of B for PBS and acetate respectively,* p=0.03) or added to drinking water (17 [6-25] and 39 [26-40]% of B for water or acetate respectively, p=0.02). Adoptive transfer of acetate-treated B cells protected mice from arthritis compared to non-exposed B cells (ANOVA p=0.008). Acetate also promoted B10 cells from human blood cells (2.5 [1.6-2.7] and 3.4 [2.6-4.5] for unstimulated [Un] and Ac respectively, p=0.0001). Conversely to CpG, acetate specifically promoted IL-10, with no impact or a decrease of proinflammatory cytokines (IL-6: 17 [5-29]; 12 [3-21] and 40 [20-47]% B cells for Un, Ac and CpG respectively, p<0.01 for all comparisons and TNF-a: 48 [29-61]; 41 [28-67] and 69 [64-78]% B cells for Un, Ac and CpG respectively, p<0.01 for CpG vs Un or Ac, NS for acetate vs Un). Inhibition of GPR43 and ACLY did not impact acetate response, while inhibition of glycolysis significantly decreased its effect. Blockade of ACSS2, converting acetate into acetyl-CoA, decreased acetate-induced B10 cells. Acetate was associated with an increase of protein lysine acetylation which was not observed in presence of CpG alone, suggesting a different mechanism of action (2.0 [1.3-3.4]; 3.3 [2.4-5.4] and 1.4 [0.5-1.7]% B cells for Un, Ac and CpG respectively, p=0.002 for Un vs Ac, NS with CpG). Conversion of acetate into acetyl-CoA could thus be used for the acetylation of cytoplasmic protein, a post-translational modification that regulates key cellular processes, including energy metabolism. In addition, B10 cells had significantly more lysine-acetylated proteins than IL-10^{neg} B cells or TNF^{+} B cells (5.3[3.9-7.3]; 3.2 [2.4-5.4] and 3.9 [2.7-6.2] % of B for B10, IL-10^{neg} B cells or TNF^{+} B cells respectively, p<0.01 for all comparisons). Finally, dietary fiber supplementation in healthy individuals was associated with increased acetate and B10 cells in the blood, which were significantly correlated (R^2=0.20, p=0.02).

Conclusion: Our results suggest that acetate induces functional Bregs, through its conversion into acetyl-CoA, used for cell metabolism and protein acetylation. Delivery of acetate or acetate producing diets or bacteria might be a promising approach to restore Bregs in non-communicable diseases such as RA in which they are defective.

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OP0132

ALLERGIC ASTHMA INDUCES THE ACCUMULATION OF SYNOVIAL RESIDENT EOSINOPHILS, TRIGGERING THE RESOLUTION OF INFLAMMATORY ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disorder, involving synovial joints, which affects approximately 1 percent of the world population[1]. Our former work demonstrated that the Th2-eosinophil pathway is a strong anti-inflammatory mediator of inflammatory arthritis[2]. Allergic asthma is an inflammatory disease of the airway, triggered by type 2 immune response. Hitherto, clinical observations on the impact of asthma on RA showed controversial results. Herein, we investigated the action of allergic asthma on inflammatory arthritis.

Objectives: We aimed to delineate the molecular and cellular responses induced by allergic asthma on inflammatory arthritis, particularly depicting the role of eosinophil subsets in arthritic synovium.

Methods: Allergic asthma was induced in wild type and genetically modified mice by ovalbumin (OVA) treatment. After the initiation of allergic asthma, K/BxN serum was transferred into the asthmatic mice or control mice to trigger serum induced arthritis (SIA). Then, arthritis severity, circulating cytokines and the cytology of lung and synovium were analyzed. Eosinophil subsets were studied by flow cytometry, single cell RNA sequencing analysis, and were isolated and transferred into the synovial cavity of eosinophil deficient arthritic mice. Clinical data of patients with both RA and asthma were collected and checked for the relapse of RA after asthma treatment with anti-interleukin (IL)-5 antibody.

Results: Mice induced with allergic asthma exhibited a rapid resolution of SIA. The OVA-triggered resolution disappeared in eosinophil deficient mice (ΔdblGATA), and was partially blocked by IL-5 neutralization. We could detect that IL-5 was mainly produced by type 2 innate lymphoid cell (ILC2) in the lung. Allergic asthma exclusively induced the proliferation ($Ki67^+$) and accumulation of synovial resident eosinophils (rEos, Siglec-F^{int}), which switched classical macrophages into alternatively activated macrophages. Synovial induced eosinophils (iEos, Siglec-F^{high}) appeared only in the acute phase of SIA. Single cell RNA sequencing analysis showed that rEos played an anti-inflammatory role, while iEos had pro-inflammatory properties in arthritis. The roles of rEos and iEos in arthritis were confirmed by transferring rEos/iEos into the synovial cavity of arthritic mice. Patiens with both RA and asthma showed a remission relapse of RA after using humanized monoclonal IL-5 antibody for treating sever eosinophilic asthma.

Conclusion: Allergic asthma induced an IL-5 mediated proliferation and accumulation of synovial rEos. The latter triggered the resolution of inflammatory arthritis. In human, eosinophils induced by asthma were essential for the sustaining of RA remission.

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OP0133

PRECLINICAL EFFICACY OF R835, A NOVEL IRAK1/4 DUAL INHIBITOR, IN RODENT MODELS OF JOINT INFLAMMATION

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Background: Interleukin receptor associated kinases (IRAK) 1 and 4 are kinases involved in Toll-Like Receptor (TLR) and Interleukin-1 Receptor (IL-1R) signaling pathways, which regulate innate immunity and inflammation. Dysregulation of IRAK1/4 signaling can lead to a variety of inflammatory conditions including rheumatoid and gouty arthritis. As a result, IRAK1/4 are promising therapeutic targets for rheumatic diseases (1). We have identified a potent and selective IRAK1/4 inhibitor, R835, that substantially suppressed the elevation of LPS (TLR4 agonist)-induced serum cytokines in healthy human volunteers in a recently completed phase 1 study.

Objectives: The aim of our study was to investigate the effect of IRAK1/4 selective inhibition as a potential therapeutic approach for rheumatological diseases. We evaluated the inhibition by our clinical candidate, R835, on TLR-, IL-1R- and NLRP3 inflammasome-induced cytokine production, as well as in preclinical models of arthritis.

Methods: The effect of R835 on TLR- or IL-1R-induced cytokine production was evaluated in vitro using THP-1, human primary endothelial cells and human primary dendritic cells. The activity of R835 on the NLRP3 inflammasome was also tested in vitro using THP-1 cells. The pharmacokinetic-pharmacodynamic relationship of R835 was evaluated in a mouse model of IL-1b-induced cytokine release. Mice were pre-treated orally with vehicle or R835 prior to challenge; serum cytokine and plasma compound levels were determined. The efficacy of IRAK1/4 inhibition by R835 in rodent models of joint inflammation was evaluated in a mouse model monosodium (MSU)-induced peritonitis, in rat model of MSU-induced gouty arthritis and in a rat model of collagen-induced arthritis (CIA).

Results: In human cells, R835 blocked proinflammatory cytokine production in response to TLR, IL-1R and NLRP3 inflammasome activation. In mice, R835 dose-dependently decreased serum cytokines in response to administration of IL-1b. Mice pre-treated with R835 demonstrated dose-dependent reductions in MSU crystal-induced serum and peritoneal cytokine levels, as well as neutrophil influx in the peritoneal cavity. Prophylactic and therapeutic treatment with R835 also resulted in significant inhibition of MSU crystal-induced knee edema and pain in a rat model of human gouty arthritis. In the rat model of CIA, R835 blocked both onset and progression of disease, by reducing inflammation, cartilage degeneration and synovial inflammation.

Conclusion: R835 is a promising clinical candidate for the treatment of a range of cytokine-driven rheumatological diseases. R835 has proven to have desirable pharmacokinetic properties, was well tolerated and suppressed LPS-induced serum cytokines in healthy volunteers in a recent phase 1 study.

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OP0134

MACROPHAGES SKEWED BY GM-CSF PRODUCE YKL-40, INSTIGATING ANGIOGENESIS IN GIANT CELL ARTERITIS

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Background: Giant cell arteritis (GCA) is an inflammatory disease affecting the medium- and large-sized arteries. The pathology of GCA is characterized by an infiltrate of mainly CD4+ T-cells and macrophages. These macrophages release a wide range of inflammatory, tissue destructive and proangiogenic proteins, including YKL-40. Previously, we demonstrated that macrophage populations in the vessel wall of GCA patients are heterogeneous; one such macrophage subset highly expressed CD206 and MMP-9, and was located in or near the media layer. Cancer studies have implicated YKL-40 production by tumor-associated macrophages in various inflammatory and tissue remodeling processes,

including angiogenesis. Less is known about the role of YKL-40 in inflammatory diseases such as GCA.

Objectives: Our objective was to investigate the cellular source and the pro-angiogenic function of YKL-40 in GCA patients.

Methods: For this study we performed immunohistochemistry (IHC) and cell culture experiments. IHC for YKL-40 and CD206 was performed on GCA positive temporal artery biopsies (TABs; n=12) and GCA positive aortas (n=10) of treatment-naive patients. Expression of YKL-40 by macrophages was confirmed by double staining with macrophage transcription factor PU.1. Additionally, the TABs were stained for IL-13Rα2, recently described as the receptor for YKL-40. The effect of skewing signals on YKL-40 production was assessed by cell culture of monocyte-derived macrophages of GCA patients with either M-CSF or GM-CSF (n=8). Subsequently, the supernatant was assayed by ELISA. Finally, the angiogenic potential of YKL-40 was investigated by tube formation experiments using human microvascular endothelial cells (HMVECs).

Results: YKL-40 is produced by a distinct subset of macrophages in GCA TABs and aortas, usually located in or near the media (Figure 1 shows representative stainings in consecutive slides of a GCA TAB). We here show YKL-40 to be expressed by CD206+/MMP-9+ macrophages in all GCA TABs and aortas. In vitro, macrophages were found to produce YKL-40 (Figure 2 shows an increasing YKL-40 production during the maturation of monocytes towards macrophages over 8 days of culture). GM-CSF stimulation, which is known to upregulate CD206 expression in macrophages, gave rise to higher YKL-40 production by GCA macrophages, when compared to M-CSF stimulated macrophages from GCA patients (p=0.038). In addition, YKL-40 stimulation of HMVECs induced more tube formation compared to unstimulated HMVECs. Finally, we showed, by IHC, abundant expression of the YKL-40 receptor IL-13Rα2 in TABs of GCA patients.

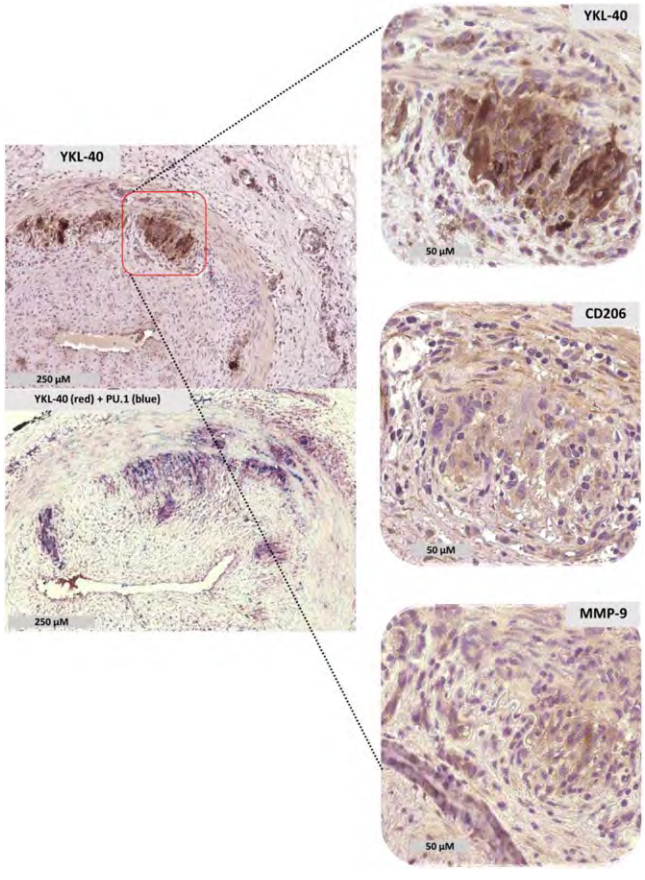


Figure 1

Conclusion: Taken together, we show here that a distinct subset of macrophages, skewed by GM-CSF and highly positive for CD206, is responsible for the production of YKL-40 in GCA. The results are in line with previous reports demonstrating that CD206 expression distinguishes YKL-40 positive macrophages from YKL-40 negative macrophages (1). Thus, YKL-40 production by CD206+ macrophages may be involved in angiogenesis in GCA tissues, a process important for the continuation of the inflammatory process.

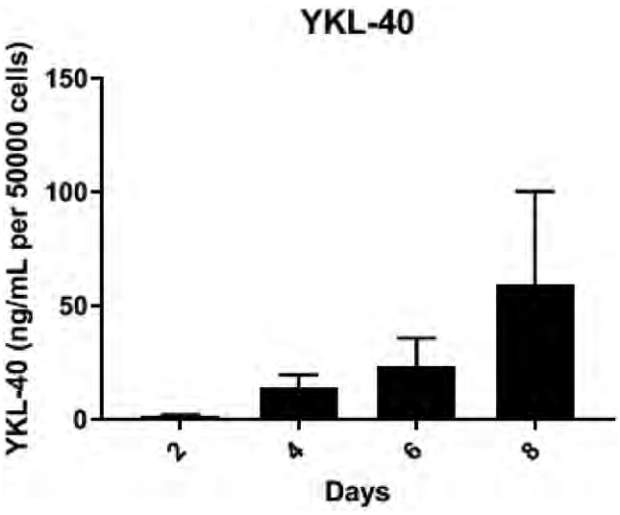


Figure 2

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Connective tissue diseases - genomics, proteomics and pathogenesis

OP0135

INHIBITION OF HSP90 REDUCES PROGRESSION OF DERMAL FIBROSIS AND INDUCES REGRESSION OF ESTABLISHED EXPERIMENTAL DERMAL FIBROSIS INDUCED BY BLEOMYCIN

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Background: Our previous study demonstrated that Heat shock protein 90 (Hsp90) is overexpressed in the skin of patients with systemic sclerosis (SSc), in cultured SSc fibroblasts and preclinical models of SSc. HSP90 is a new regulator of canonical TGF-β signalling and its inhibition prevents the stimulatory effects of TGF-β on collagen synthesis and dermal fibrosis in three preclinical models of SSc.

Objectives: Herein, we aimed to evaluate the efficacy of Hsp90 inhibitor (17-DMAG) in the treatment of established experimental dermal fibrosis induced by bleomycin.

Methods: Design consisted of three control groups, I (NaCl-s.c./6 weeks), II (bleomycin-s.c./3w and NaCl-s.c./3w), III (bleomycin-s.c./6w), and 2 treatment groups (bleomycin-s.c./6w). During the last 3 weeks, one group was treated with 17-DMAG 0.5mg/kg-i.p. every third day, whereas one group (with nintedanib 50mg/kg-p.o. twice daily) served as a comparator with already published efficacy in this setting. Total of 40 BL6 mice were examined weekly for weight, activity and fur texture. The effects of 17-DMAG were determined by assessment of dermal thickness (HE-staining), collagen content (hydroxyproline assay), myofibroblast

counts (α-SMA staining) and of 23 serum inflammatory cytokines/chemokines (Mouse-Cytokine-23-plex, Bio-Rad-Laboratories).
Results: 17-DMAG decreased dermal thickening by 53±3% (p<0.001) (nintedanib by 46±2%,p<0.001), collagen content by 48±5% (p=0.004) (nintedanib by 50±4%,p=0.003), myofibroblast counts by 42±9% (p<0.001) (nintedanib by 44±7%,p<0.001), and levels of IL-1α, IL-6, IL-12(p40), CXCL1, MCP-1, MIP-1α/β, RANTES (in all: p<0.05) compared to vehicle-treated mice injected with bleomycin for 6w. Moreover, 17-DMAG also induced regression of pre-established fibrosis to below the levels of vehicle-treated mice injected with bleomycin for 3w and NaCl for 3w (dermal thickness by 14±3%, collagen content by 20±5%, myofibroblast counts by 13±9%; whereas in nintedanib by 10±3%, 21±4%, 17±7%, respectively; in all: p<0.05), and levels of IL-12(p40), CXCL1, MCP-1, MIP-1β, RANTES (in all: p<0.05). No significant weight loss, decrease in activity or changes in fur texture were observed upon 17-DMAG treatment.
Conclusion: This is the first study on effects of Hsp90 inhibitor 17-DMAG in the treatment of established dermal fibrosis. We demonstrate that 17-DMAG effectively prevents the progression and induces regression of established bleomycin-induced dermal fibrosis, in an extent that was comparable to nintedanib in this study (which was recently FDA approved for slowing the rate of decline in lung function in adults with SSc-ILD). 17-DMAG was well tolerated without obvious clinical signs of toxicity. These data suggest that Hsp90 could be a novel potential target in the treatment of SSc dermal fibrosis.
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OP0136 THE INFLUENCE OF LONG-TERM EXERCISE AND IN VITRO EXERCISE-MIMICKING STIMULATION ON THE PRODUCTION OF MYOKINES AND CYTOKINES IN MYOTUBES OF PATIENTS WITH CHRONIC IDIOPATHIC INFLAMMATORY MYOPATHIES

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Background: It has been demonstrated several times that endurance exercise has beneficial effects on the condition of patients with idiopathic inflammatory myopathies (IIM). Muscle contraction during exercise is a major stimulus for the release of myokines that are supposed to take part in the beneficial adaption to exercise.
Objectives: The aim of this study was to find out how a six-month physiotherapy and *in vitro* exercise-mimicking treatment affect myokine and cytokine production in myotubes of IIM patients.
Methods: Seven patients with chronic IIM took part in a six-month physiotherapy (stretching and strengthening), which significantly improved their muscle strength and endurance. IIM patients (n=7) before and after the six months exercise and their respective healthy counterparts (HC, n=9) underwent a *musculus vastus lateralis* biopsy. Isolated skeletal muscle cells were grown, differentiated into myotubes, which were treated with a pharmacological cocktail: palmitate, forskolin and ionomycin (PFI) to mimic exercise-stimulated contractions in vitro. Myokine and cytokine concentrations produced by myotubes to the culture medium were analyzed with ELISA and the multiplex immunoassay, respectively. RT-PCR was used for the evaluation of myokine gene expression in the cultured myotubes.
Results: Compared to myotubes of healthy controls, myotubes of IIM patient released more myostatin and activin A into the medium. The myostatin gene was expressed significantly more in muscle cells of patients than in healthy controls' cells (p<0.05). After a six-month rehabilitation program, activin A secretion was four-fold reduced in myotubes of patients with IIM, while myostatin release and gene expression remained unchanged. In myotubes of IIM patients, less follistatin and more follistatin like 3 were detected in the culture medium compared to HC myotubes. Myotubes derived from IIM patients after six months of rehabilitation secreted twice as much follistatin and half the amount of follistatin like 3 into the medium than myotubes derived from IIM patients prior to rehabilitation (p<0.05). There was no difference in secretion of interleukin (IL) 6, IL-17, tumor necrosis factor (TNF) and vascular endothelial growth factor (VEGF) between myotubes of IIM patients and myotubes of HC. However, six-month exercise significantly (p<0.05) reduced release of IL-6, TNF and VEGF in myotubes of IIM patients. Contrary to our expectation, stimulation of PFI had no effect on the release of myostatin, activin A, follistatin and follistatin like 3, or the expression of their genes. PFI treatment significantly (p<0.05) increased IL-6 secretion in myotubes from HC and IIM patients prior to six months of rehabilitation. On the other hand, it was observed that myotubes of HC and IIM patients exposed to the PFI cocktail secreted significantly less inflammatory cytokines IL-17, TNF and VEGF into the medium compared to unstimulated myotubes (p<0.05).
Conclusion: In conclusion, long-term exercise influenced the production of myokines and decreased release of inflammatory cytokines in myotubes of IIM patients. *In vitro* exercise-mimicking treatment increased the secretion of IL-6 and decreased the release of inflammatory cytokines as IL-17, TNF-α and VEGF in myotubes of patients with IIM and healthy individuals.
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OP0137 GENOME-WIDE WHOLE-BLOOD TRANSCRIPTOME PROFILING IN A LARGE EUROPEAN COHORT OF SYSTEMIC SCLEROSIS PATIENTS

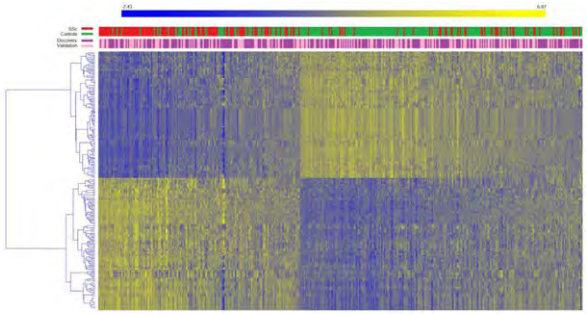
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Background: The analysis of annotated transcripts from genome-wide expression studies data is of paramount importance to understand the molecular phenomena underlying the occurrence of complex diseases, such as systemic sclerosis (SSc).
Objectives: To perform whole-blood transcriptome and pathway analysis on whole-blood (WB) RNA collected in two cohorts of European SSc patients. Via a discovery and validation strategy we aimed at characterizing the molecular pathways that differentiate SSc from controls and that are reproducible in geographically diverse populations.
Methods: WB samples from 252 controls and 162 SSc patients were collected in RNA stabilizers. Patients were divided into a discovery (n=79; Southern Europe) and validation cohort (n=83; Central-Western Europe). RNA sequencing was performed by an Illumina assay. Functional annotations of Reactome pathways were performed with the FAIME algorithm. In parallel, a immunophenotyping analysis on 28 circulating cell populations was assessed. We then tested: the presence of differentially expressed genes or pathways and the correlation between absolute cell counts and RNA transcripts/FAIME scores in regression models. Results significant in both populations were considered as replicated.
Results: A total of 15224 genes and 1277 related functional pathways were available for analysis. Among these, 99 genes and 225 pathways were significant in both sets. The heatmap in figure shows the relative expression of replicated pathways and the distribution of cases and controls (red and green bars). Among the significant pathways we found a deregulation in: type-I IFN, TLR-cascade and signalling, function of the tumor suppressor p53 protein, platelet degranulation and activation. Correlation analysis showed that the count of several cell

subtypes is jointly associated with RNA transcripts or FAIME scores with strong differences in relation to the geographical origin of samples; neutrophils emerged as the major determinant of gene expression in SSc-whole-blood samples.

Conclusion: We discovered a set of differentially expressed genes and pathways that could be validated in two independent sets of SSc patients highlighting a number of deregulated molecular processes that have relevance for the pathogenesis of autoimmunity and SSc.

Figure:



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OP0138 CLUSTERIN ASSOCIATES WITH DISEASE MECHANISMS AND INFLAMMATION IN MYOSITIS PATIENTS

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Background: Idiopathic inflammatory myopathies (IIM, myositis) are a heterogeneous group of autoimmune muscle disorders characterized by skeletal muscle weakness and damage, inflammation and extramuscular manifestations. Recent findings suggest that immunological as well as nonimmunological processes, such as endoplasmic reticulum stress, hypoxia, mitochondrial and metabolic dysfunction are involved in the pathogenesis of IIMs [1]. Clusterin (CLU) has been reported to play a protective function in the development of tissue injury, inflammation and autoimmunity, and is involved in the maintenance of immune homeostasis [2].

Objectives: This study aimed to explore a potential involvement of the circulating levels and skeletal muscle expression of CLU in pathogenic mechanisms of IIM.

Methods: A total of 85 IIM patients and 86 healthy controls (HC) were recruited. In addition, 20 IIM patients and 21 HC underwent a muscle biopsy. Circulating concentrations of CLU were measured by ELISA. Serum cytokine profile of patients and HC was assessed by Cytokine 27-plex Assay. Immunohistochemical localisation of CLU was assessed in 10 IIM and 4 control muscle tissue specimens. The expression of CLU and myositis related cytokines in muscle tissue was determined by real-time PCR.

Results: We observed a significant increase of circulating CLU in all IIM patients compared to HC (86.2 (71.6-99.0) vs. 59.6 (52.6-68.4) µg/mL, $p < 0.0001$). Moreover, CLU serum levels were positively correlated with myositis disease activity assessment (MYOACT) ($r = 0.337$, $p = 0.008$), myositis intention-to-treat activity index (MITAX) ($r = 0.357$, $p = 0.004$) and global disease assessment evaluated by physician ($r = 0.309$, $p = 0.015$). In addition to that, a multivariate redundancy analysis revealed a combined effect of serum CLU and cytokine profile (represented by cytokines and chemokines known to be involved in IIM) on disease activity measures. In muscle tissue, CLU mRNA was significantly increased in IIM patients compared to controls ($p = 0.032$) and correlated with IL-1β ($r = 0.489$, $p = 0.034$), IL-6 ($r = 0.581$, $p = 0.009$), TNF ($r = 0.485$, $p = 0.035$) and PGC-1α ($r = 0.709$, $p = 0.001$) mRNA. Immunohistochemistry revealed CLU accumulation in the cytoplasm of regenerating myofibers.

Conclusion: Our results show an up-regulation of clusterin in circulation and skeletal muscle of IIM patients that associates with disease activity and inflammation, and its specific expression in regenerating myofibres. Based on our data and the known cytoprotective function of CLU we suggest an attempt of the organism to limit further muscle damage induced by myositis disease mechanisms.

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OP0139 FUNCTIONAL EVALUATION OF THE SJÖGREN'S SYNDROME AND SYSTEMIC LUPUS ERYTHEMATOSUS DDX6-CXCR5 RISK INTERVAL

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Background: Sjögren's Syndrome (SS) and Systemic Lupus Erythematosus (SLE) are distinct chronic, complex autoimmune diseases with shared characteristics such as autoantibodies, heightened interferons, and polyarthritis. SS and SLE genome-wide association studies (GWAS) report strong associations with the *DDX6-CXCR5* risk interval. DDX6 suppresses interferon stimulated gene expression and CXCR5 regulates T cell functions implicated in autoimmunity.

Objectives: To identify functional variants that impact regulation in the *DDX6-CXCR5* interval.

Methods: Fine-mapping was done using ImmunoChip data from 3785 SLE, 1916 SS cases and 6893 population controls of European ancestry that were imputed and tested for SNP-trait association. Bayesian statistics assigned posterior probabilities to SNPs and defined a credible set of risk variants. Bioinformatic analyses further prioritized variants with predicted functionality. Electrophoretic mobility shift assays (EMSAs) and luciferase expression were used to validate predicted SNPs in EBV transformed B (EBV B) cells.

Results: While some differences were observed, the overall SS and SLE association signals were similar. SNP-SS rs9736016 near *CXCR5* and SNP-SLE rs76409436 near *DDX6* were the most significant but did not show evidence of functionality. Bayesian statistics defined credible sets of variants in strong D' in common between both SS and SLE. Bioinformatics analyses (Haploreg, RegulomeDB, ENCODE data, etc) further refined the credible set and identified 5 common SNPs with strong evidence of functionality in immune cell types: rs4938572, rs4936443, rs57494551, rs7117261 and rs4938573. EMSAs showed a significant increase in protein binding to the risk allele of rs57494551 ($p=0.0001$), rs7117261 ($p=0.0001$) and rs4938573 ($p=0.0003$), but not the others, using nuclear lysates from EBV B cells. Luciferase vectors with a minimal promoter or no promoter were used to test for enhancer or promoter activity, respectively. To this end, the rs57494551 risk allele exhibited a significant increase in enhancer activity ($p=0.0001$). In contrast, the rs7117261 risk allele decreased enhancer activity

(p=0.018). The rs4938573 risk allele decreased enhancer (p=0.043) and promoter (p=0.024) activity. While rs7117261 or rs4938573 were not reported in eQTL databases, GTex data reported rs57494551 as an eQTL that alters *DDX6* expression in whole blood (p=1.8E-7). Additionally, these functional SNPs have been associated with looping events to several proximal promoters in nearby genes in immune cells.

Conclusion: SS and SLE have similar genomic architecture across the *DDX6-CXCR5* risk interval. Multiple variants in the credible set exhibited allele specific changes in protein binding, as well as modified enhancer activity, promoter activity or both. Ongoing studies will use Cas9 in EBV B cells to determine which other loci are within the local regulatory network.

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OP0140 DYSREGULATED EXPRESSION OF THE LONG NON-CODING RNA, LINC01871, IMPLICATED IN SJÖGREN'S SYNDROME PATHOGENESIS

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Background: Sjögren's syndrome (SS) is a chronic, heterogenous autoimmune disease characterized by inflammatory destruction of the exocrine glands. Long non-coding RNAs (lncRNAs) have emerged as a functionally diverse class of non-protein coding RNA (ncRNA) with increasing implications in interferon signaling, immune cell regulation, and autoimmune disease pathology. The potential role of lncRNAs in SS pathogenesis is unknown.

Objectives: To identify and characterize candidate lncRNAs with potential relevance to SS pathology.

Methods: RNA-seq was used on whole blood from SS patients (n=30 antibody negative (Ro^-); n=27 antibody positive (Ro^+)) and healthy controls (HC, n=27) to identify differentially expressed (DE) lncRNAs (log2 fold change (FC) ≥ 2 or ≤ 0.5; p_{adj} <0.05). Bioinformatic and pathway analyses were used to predict lncRNA function. *In vitro* time course experiments in HSB2 T cell lymphoblasts stimulated with PMA/Ionomycin (PMA/I) or type I interferon (IFN) were used to assess biological relevance. *LINC01871* function was further investigated by RNA-seq on a single cell clone of HSB2 with confirmed CRISPR-targeted *LINC01871* deletion (*LINC01871*$^{-/-}$).

Results: We identified a total of 1054 unique DE ncRNAs between Ro^+, Ro^- and/or a combined analysis relative to HC; of these, 45 (1 long intergenic ncRNA (lincRNA), 1 antisense, 43 pseudogenes) were overexpressed in all 3 SS subsets. To begin investigating the function of the previously undescribed lincRNA, *LINC01871* (SS^{Ro-}: FC=2.85; $p_{adj}=1.1x10^{-4}$), we performed a correlation analysis of the SS^{Ro-} transcriptome, which found several co-expressed protein coding RNAs involved in immune regulation (*THEMIS*, *TBX21*, *IL10RA*, *IL2RB,* among many others). Similarly, Ingenuity Pathway Analysis of the SS transcriptome compared to HC, as well as several gene ontology enrichment analyses of publicly available RNA expression correlation databases, identified shared immune-related pathways including cytotoxic T cell, natural killer cell, and T cell regulation. To further study the role of *LINC01871* in cytotoxic T cells, we used qRT-PCR to resolve the effects of PMA/I or type I IFN stimulation on *LINC01871* expression in the T lymphoblastoid HSB2 cells. *LINC01871* expression was downregulated after PMA/I stimulation, but unchanged with type I IFN stimulation. To explore the regulatory function of *LINC01871* in T cells, we targeted *LINC01871* in HSB2 cells using CRISPR. To this end, we generated a single cell *LINC01871*$^{-/-}$ clone with no RNA expression by qPCR and confirmed homozygous deletion using DNA sequencing. RNA-seq analysis of *LINC01871*$^{-/-}$ compared to unmodified HSB2 cells identified 1166 DE transcripts. Pathway analyses clustered the DE transcripts into similar immune regulatory, cytotoxic and T cell pathways identified in SS^{Ro-} whole blood RNA-seq and publicly available RNA-seq databases. Further, several prominent T cell regulatory transcripts that exhibited correlated upregulation with *LINC01871* in SS^{Ro-} whole blood RNA-seq also demonstrated downregulation after *LINC01871* deletion: *CD109* (FC=-9.7; $p_{adj}=5.3x10^{-16}$), *IL22* (FC=-8.1; $p_{adj}=7.6x10^{-11}$), *PDCD1* (FC=-6.2; $p_{adj}=1.1x10^{-6}$), *THEMIS* (FC=-3.8; $p_{adj}=2.7x10^{-165}$) and *TBX21* (FC=-2.1; $p_{adj}=3.3x10^{-25}$).

Conclusion: LncRNAs are emerging as important regulators of immune function with increasing evidence of autoimmune disease relevance. Here, we leveraged RNA-seq, extensive bioinformatic data, and CRISPR technology to identify and functionally characterize *LINC01871* as a potential mediator of the dysregulated T cell inflammatory response pathways implicated in SS pathogenesis.

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OP0141 HIGH DIMENSIONAL ANALYSIS REVEAL A NETWORK OF CERTAIN TRANSCRIPTION FACTORS THAT LINK VASCULOPATHY AND ORGAN FIBROSIS IN SYSTEMIC SCLEROSIS

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Background: Since vascular manifestations such as Raynaud's phenomenon often precede the onset of other clinical manifestations of systemic sclerosis (SSc), the identification of pathways linking vasculopathy to organ fibrosis might thus provide important insights into early disease mechanisms and allow early targeted intervention for both fibrotic and vascular events.

Objectives: In this study we performed high dimensional (HD) analyses to identify mediators that link vasculopathy to organ fibrosis.

Methods: HD techniques including RNA-seq, ChIP-seq, ATAC-seq and FISH-seq have been performed to identify mediators in vessels and fibrotic lesions of human skin samples of SSc patients and healthy volunteers. In addition, murine skin and lung tissue samples were analyzed by multi-channel immunofluorescence (IF) and confocal laser scanning microscopy. Microvascular endothelial cells, smooth muscle cells and fibroblasts have been further processed to address their functional attributes with regard to their proliferative, migratory and chemotactic capacity. In vivo models and e*x vivo* mouse fetal metatarsal assays were performed to study fibrotic and angiogenic processes.

Results: Bioinformatic HD analyses revealed the ETS transcription factor PU.1 as molecular checkpoint of a network of factors that drive matrix production and fibrotic imprinting in SSc. Within this network ATF3 was significantly upregulated in fibroblasts of skin biopsies of SSc patients and of various organs of fibrosis models. ATF3 deficiency ameliorated fibrosis in various mouse models. Notably, ATF3 was significantly upregulated in vascular cells of fibrotic tissues of SSc patients. Multi-channel IF and confocal laser scanning microscopy of skin and lung biopsies of SSc patients revealed an increased expression of ATF3 especially in microvascular endothelial cells and smooth muscle cells. ATF3 overexpression in smooth muscle cells led to an extensively enhanced proliferation and increased migratory capacity whereas endothelial cells showed a SSc-like phenotype with reduced proliferation and migration. After ATF3 overexpression, tube formation capacity was completely altered as assessed by cumulative tube length, tube numbers and capillary sprouting. To investigate vessel outgrowth from a different perspective, we used the *ex vivo* fetal mouse metatarsal assay. ATF3 knockout mice showed a completely altered angiogenic response as assessed by tube length, number of branches and number junctions compared to wildtype controls.

Conclusion: We identified PU.1 and ATF3 as key factors in disturbed vasculature and endogenous activated fibroblasts suggesting this axis as a potential therapeutic target intervening both fibrotic and vascular manifestations.

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OP0142

FIBROBLAST GROWTH FACTOR RECEPTOR 3 REGULATES THE ACTIVITY OF PROFIBROTIC CYTOKINE AND GROWTH FACTOR PATHWAYS TO DRIVE FIBROBLAST ACTIVATION AND TISSUE FIBROSIS IN SYSTEMIC SCLEROSIS

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Background: Fibroblast growth factor receptor 3 (FGFR3) is a member of the family of different fibroblast growth factor receptors with several ligands called fibroblast growth factors (FGFs) in humans. Each FGFR has different isoforms resulting from natural alternative splice variants. Upon binding FGF ligands, fibroblast growth factor receptors (FGFRs) trigger various intracellular signaling pathways to regulate important biological processes. Systematic evaluation of FGF/FGFR signaling in the context of SSc has not been performed so far.
Objectives: The aim of this study was to characterize FGFR3/FGF9 signaling in the context of fibroblast activation and to evaluate FGFR3 as a potential molecular target for antifibrotic treatment in SSc.
Methods: Differential expression profiling of dermal cells from SSc patients and healthy volunteers were performed employing GEArray cDNA microarray. Real-time PCR, Western Blot, immunohistochemistry and immunofluorescence were done in skin tissues and fibroblasts from SSc patients. Selective inhibitors in conjunction with genetic knockdown and knockout strategies were used to target FGFR3 signaling *in vitro* and in mouse models of SSc: skin fibrosis induced by bleomycin and by overexpression of a constitutively active transforming growth factor receptor 1 (TBR) and tight skin-1 (TSK) mice. Affymetrix gene arrays in dermal fibroblasts from mice with constitutive FGFR3 signaling and mice lacking FGFR3.
Results: Expression of FGFR3, specifically the isoform FGFR3IIIb and its ligand FGF9, was significantly upregulated in the dermis and dermal fibroblasts of SSc patients as compared to healthy volunteers. Furthermore, an increase of FGFR3 IIIb/FGF9 expression comparable to that in SSc fibroblasts could also be obtained by stimulating normal healthy dermal fibroblasts with transforming growth factor (TGFβ) *in vitro* and in mice constitutively overexpressing active TGFβ receptor type I.
Transcriptome profiling, *in silico* analysis and functional experiments revealed that FGFR3 synergistigically induces multiple profibrotic pathways including Endothelin-, Interleukin-4- and CTGF-signaling in a CREB-dependent manner. FGFR3 exerts profibrotic effects by modulating phosphorylation of CREB by ERK-, AKT-, CAMK2- and p38-kinases. Activation of FGFR3 in healthy or SSc dermal fibroblasts by stimulation with recombinant FGF9 was sufficient to induce resting fibroblast-to-myofibroblast differentiation along with increased collagen secretion and alpha-SMA production.
Genetic knockout of Fgfr3 abrogates myofibroblast differentiation *in vitro* and ameliorates skin fibrosis in TSK and TBR mice and in bleomycin-induced fibrosis. Further confirming the translational potential of these findings in the preclinical models of SSc, we demonstrate that pharmacological inactivation of FGFR3 by PD173074 could induce the regression of experimental fibrosis in *vitro* and in bleomycin-challenged, TSK and TBR mice.
Conclusion: Our findings characterize FGFR3 as an upstream regulator of a network of profibrotic mediators in SSc and thus, we could demonstrate successfully that the targeted inhibition of FGFR3 could inhibit multiple signaling pathways *in vitro* and ameliorated fibrosis in different preclinical models of SSc. These findings may have direct translational implications as FGFR3 inhibitors are currently in development.
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Vasculitis

OP0143

CANCER IN GIANT-CELL ARTERITIS PATIENTS: A LARGE NATIONWIDE STUDY

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Background: The association between giant-cell arteritis (GCA) and malignancy is controversial.
Objectives: To asses malignancy rates and risk in GCA patients in a large-scale population-based study.
Methods: We utilized the medical database of Clalit-Health-Services for this retrospective cohort study. Follow-up was from January 1,2002 and continued until death or end of follow-up on September 1,2018. Incident GCA patients were compared with age-and-sex-matched controls. Hazard-ratios for subtypes of malignancies were obtained by the Cox proportional-hazard model, adjusted for socio-demographic variables and cancer risk factors.
Results: The study population included 7,213 GCA patients and 32,987 age- and sex-matched controls who were not diagnosed with the disease. The mean age of GCA diagnosis was 72.3±9.9 years (median 73.1 years) and 69.1% were women. At Kaplan–Meier survival analysis, assessing cumulative cancer-free survival in GCA patients and controls, GCA patients had worse curve than controls (chi-squared = 49.84; degrees of freedom = 1; $p < 0.0001$; Figure 1). At the cox-survival analysis adjusted for age, sex, SES and cancer risk factors GCA patients showed increased risk for overall cancer (HR 1.29 [95%CI 1.20-1.39]),

Table 1. Cox survival analysis assessing crude and adjusted hazard for cancer in GCA patients compare to controls

Type of malignancy	Adjusted HR	
	HR	95% CI
Any malignancy	1.29	1.20, 1.39
Oropharyngeal cancer	0.96	0.69, 1.35
Thyroid cancer	1.20	0.66, 2.16
Breast cancer	0.93	0.75, 1.14
Lung cancer	1.26	0.99, 1.59
Esophagus cancer	1.86	0.93, 3.75
Stomach Cancer	0.61	0.37, 0.98
Colorectal Cancer	1.12	0.93, 1.36
Liver and bile ducts cancer	1.06	0.69, 1.62
Kidney cancer	1.60	1.15, 2.23
Bladder cancer	1.15	0.88, 1.50
Uterus cancer	0.85	0.55, 1.30
Cervical cancer of the uterus	0.45	0.37, 1.46
Ovary Cancer	0.96	0.58, 1.59
Prostate Cancer	1.07	0.80, 1.43
Sarcoma	2.14	1.41, 3.24
Melanoma	1.11	0.80, 1.55
Acute Leukemia	1.81	1.06, 3.07
Chronic Leukemia	1.82	1.19, 2.77
Myelodysplastic syndrome	1.84	0.94, 3.60
Hodgkin's Lymphoma	2.42	1.12, 5.20
Non-Hodgkin's Lymphoma	1.66	1.21, 2.29
Multiple Myeloma	2.40	1.63, 3.53

kidney cancer (HR 1.60 [95%CI 1.15-2.23]), sarcoma (HR 2.14 [95%CI 1.41-3.24]), acute-leukemia (HR 1.81 [95%CI 1.06-3.07]), chronic-leukemia (HR 1.82 [95%CI 1.19-2.77]), Hodgkin's lymphoma (HR 2.42 [95%CI 1.12-5.20]), non-Hodgkin's lymphoma (HR 1.66 [95%CI 1.21-2.29]) and multiple myeloma (HR 2.40 [95%CI 1.63-3.53) (Table 1). The time (mean [months] ± SD) to the diagnosis of any malignancy was significantly shorter in GCA patients (48.6 ± 41.3) compared to controls (58.1 ± 43.6; p<0.001).

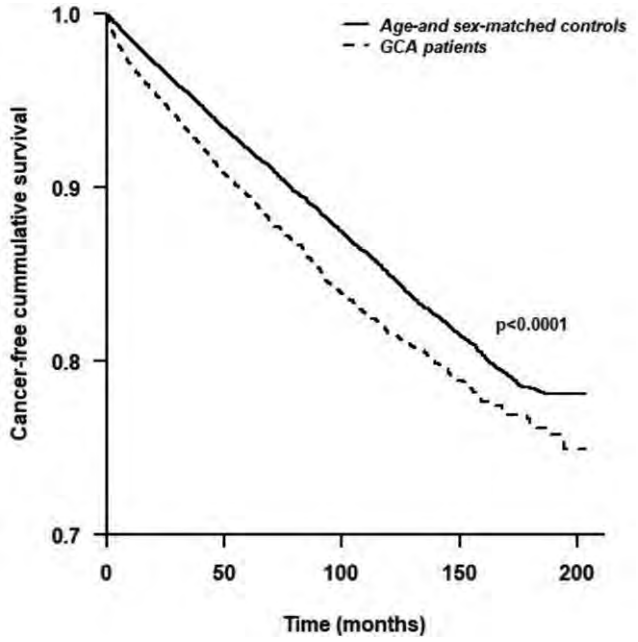


Figure 1. Kaplan-Meier cancer-free survival curve

Conclusion: GCA patients are at increased risk for sarcoma, kidney cancer, hematological malignancies and overall malignancies compared to age-and-sex matched controls from the general population.

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OP0144

EFFECT OF TOCILIZUMAB ON VASCULAR INFLAMMATION BY 18F-FLUORODEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY: A PROSPECTIVE, LONGITUDINAL STUDY

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Background: Two randomized controlled trials have demonstrated clinical efficacy of tocilizumab for the treatment of giant cell arteritis (GCA)(1, 2). In these trials, clinical and laboratory measures were used to define the outcome measures. The direct effect of tocilizumab on vascular inflammation remains poorly characterized.

Objectives: To prospectively evaluate vascular inflammation as measured by ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography (PET) in a longitudinal cohort of patients with GCA treated with tocilizumab over a several year follow-up period.

Methods: Patients with GCA were recruited into a prospective, observational cohort. All patients fulfilled modified 1990 American College of Rheumatology (ACR) Classification Criteria for GCA. All patients underwent FDG-PET computed tomography (CT) prior to initiation of tocilizumab. A single reader reviewed all PET scans, blinded to clinical data. Qualitative assessment of FDG uptake relative to liver uptake by visual assessment (scale 0-3) was assessed in 9 arterial territories. A summary score, PET Vascular Activity Score (PETVAS), was calculated (scale 0-27).

Patients underwent imaging at 6-12 month intervals per a standardized imaging protocol. In a subset of patients in whom tocilizumab was discontinued due to established remission, a repeat FDG-PET scan was obtained within 6 months of drug discontinuation.

Change in PET activity over time was measured by linear regression. PET activity during established remission was compared to PET activity after discontinuation of tocilizumab. For some patients, tocilizumab was added to the existing treatment regimen without a substantive change in concomitant glucocorticoid dose. In a secondary analysis, patients were stratified by prednisone dosing (high dose prednisone >10mg/day prednisone, low dose prednisone ≤10mg/day prednisone during the imaging interval) to determine if tocilizumab had an effect on vascular inflammation independent of glucocorticoids.

Results: 22 patients were included in the study. All patients had clinically active disease at baseline with median baseline PETVAS 24.5 (23-27). There was a significant reduction in PETVAS over 2 years follow up (p<0.01 for linear trend) (Figure). Of note, there was continued progressive improvement in PETVAS in both year 1 and year 2 of treatment. Eight patients received concomitant high dose glucocorticoids and 14 patients remained on low dose glucocorticoids with the addition of tocilizumab. In patients who only received low dose prednisone, significant reduction in PETVAS was still observed with addition of tocilizumab (PETVAS 25.5 to 19.5, p=0.04). In a subset of 5 patients who discontinued tocilizumab due to established remission [median PETVAS 19 (17.5-22) at time of remission], a repeat FDG-PET scan within 6 months after treatment discontinuation showed worsening PET activity in 4 out of 5 patients [median PETVAS 23 (20-23)]. Two of these patients subsequently experienced a clinical disease relapse.

Conclusion: Tocilizumab was associated with improved vascular inflammation as assessed by FDG-PET. There was continued improvement of vascular inflammation at both year 1 and year 2 of treatment, and early evidence suggests a rebound of vascular inflammation when tocilizumab was discontinued. These data provide rationale for long-term tocilizumab therapy in patients with GCA and for consideration of FDG-PET as an outcome measure in future clinical trials.

References:

[1] Stone JH, et al. N Engl J Med 2017;377:317-28.

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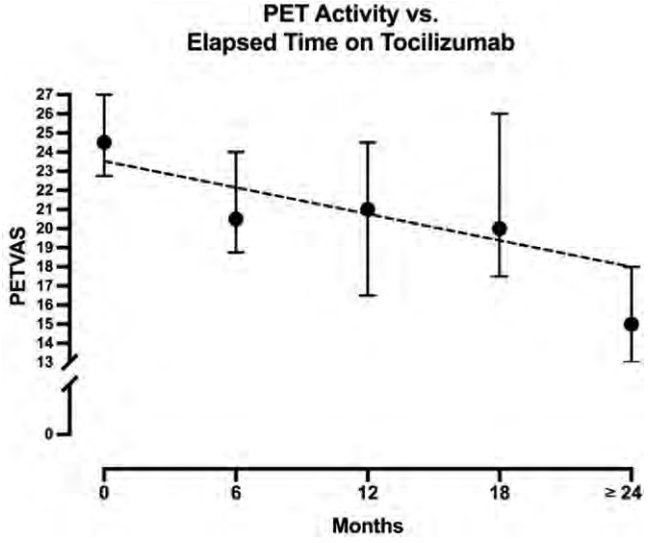


Figure. XXX

Disclosure of Interests: None declared

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OP0145

MALIGNANCY IN ANCA-ASSOCIATED VASCULITIS AND POLYARTERITIS NODOSA: AN AUSTRALIAN POPULATION-BASED STUDY

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Background: The increased risk of malignancy in patients with ANCA-associated vasculitis (AAV) and polyarteritis nodosa (PAN) has been attributed to late

treatment related effects, with non-melanoma skin and genitourinary cancers most frequently reported in European studies[1,2,3]. Malignancy has not been examined in patients with AAV/PAN in Australia, where environmental factors may influence risk.

Objectives: To determine the risk and timing of incident cancer in Western Australian (WA) AAV/PAN patients compared to controls.

Methods: Patients and controls were ascertained through the WA Hospital Morbidity Data collection System (HMDS). Administrative hospitalisation data were linked with the WA cancer and death registries. Data was available between 1980-2015. Patients were classified into two sub-groups using International Classification of Disease (ICD) -9 and/or -10 codes: (1) GPA/MPA- granulomatosis with polyangiitis (GPA)/microscopic polyangiitis (MPA), and (2) other-AAV/PAN-eosinophilic granulomatosis with polyangiitis (EGPA), PAN, and other patients with any AAV or PAN where more specific ICD-10 coding was not available. Controls were age, sex and temporally matched (at patient diagnosis date) and had no rheumatological diagnosis. Patients and controls with prior cancer were excluded from the analysis.

Spline-based estimation of time-varying hazard ratios (HR) for incident cancer in patients *vs* controls was performed using the Stata library stpm2cr[4]. Results for cause-specific models, which treated deaths in patients without cancer as censored, were confirmed using models treating death as a competing risk. The risk of specific cancers was analysed by Cox regression.

Results: The analysis included 391 patients (165 GPA/MPA, 217 other-AAV/PAN) and 4913 controls, with 86 incident cancers (over 3556.7 person-years) observed in patients and 1119 (over 64997.0 person-years) in controls. Patients and controls were well matched for age (mean ± standard deviation GPA/MPA: 55 ± 18 years, other AAV/PAN: 59 ± 17 years, controls 57 ± 16 years), and sex (female: GPA/MPA 48%, other AAV/PAN 46%, controls 46%).

Incident cancer risk and timing differed between the two patient subgroups (Figure 1). The risk of incident cancer in GPA/MPA patients, compared to controls, increased with disease duration, whilst other-AAV/PAN patients had a greater risk within the first two years of diagnosis, but a similar risk to controls in the longer term.

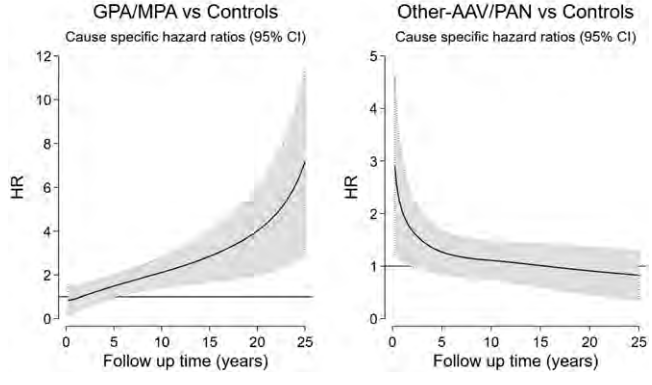
By specific cancers, GPA/MPA patients had an increased risk of skin cancers (excluding squamous and basal cell carcinomas): hazard radio (HR) 2.71 95% confidence interval (CI) 1.55 – 4.74, and genitourinary cancers: HR 3.64, 95% CI 1.58, 8.39, which was not observed in other-AAV/PAN patients. While there was trend for an overall increase in haematological cancers, this was inconclusive.

Conclusion: Incident cancer risk, driven by skin and genitourinary cancers, increased with disease duration in GPA/MPA patients, consistent with previous studies, suggestive of a treatment related effect. In contrast, cancer was more frequently observed early after diagnosis in other-AAV/PAN patients. Our findings suggest that vigilance for incident cancers is required for all patients with AAV and PAN after diagnosis and in long term management, considering distinct periods of greater risk by disease subgroup.

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Figure 1: Incident Cancer Risk



Disclosure of Interests: Joanna Tieu: None declared, Susan Lester: None declared, Warren Raymond: None declared, Helen Keen Speakers bureau: Pfizer Austrlaia, Abbvie Australia, Catherine Hill: None declared, Johannes ("Hans") Nossent Speakers bureau: Janssen

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OP0146 LONG TERM OUTCOME AND PROGNOSIS FACTORS OF ISOLATED AORTITIS

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Background: Aortitis is a group of disorders characterized by the inflammation of the aorta. The most common causes of aortitis are the large-vessel vasculitis i.e. giant cell arteritis (GCA) and Takayasu arteritis (TA). However, aortitis may be isolated. Because of the wide variation in the course of aortitis, predicting outcome is challenging. The optimal management strategy of isolated aortitis (IA) is still unclear as IA is poorly defined, with data consisting of small retrospective and case control studies.

Objectives: To assess the long-term outcome and prognosis factors for vascular complications in patients with isolated aortitis.

Methods: Retrospective multicenter study of 353 patients with non-infectious aortitis including 136 giant cell arteritis (GCA), 96 Takayasu arteritis (TA) and 73 isolated aortitis (IA). Factors associated with event-free survival, vascular event-free survival and revascularization-free survival were assessed. Risk factors for vascular complications were identified in multivariate analysis.

Results: After a median follow up of 52 months, vascular complications were observed in 32.3 %, revascularization in 30 % and death in 7.6%. The 5-year cumulative incidence of vascular complications was 58% (41; 71), 20% (13; 29), and 19 % (11; 28) in IA, GCA and TA, respectively. In multivariate analysis, IA [HR, 1.85 (1.19 to 2.88), p=0.017] and male gender [1.77 (1.26 to 2.49), p<0.0001] were independently associated with vascular events. The 5-year surgery-free survival was 45% (31; 65), 71% (62; 81) and 76% (68; 86) in IA, TA and GCA, respectively.

Conclusion: IA has a worse vascular prognosis than GCA and TA. Sixty percent of IA patients will experience a vascular complication within 5 years from diagnosis.

Disclosure of Interests: None declared

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OP0147 MEASUREMENT OF FLOW VELOCITIES OF THE CENTRAL RETINAL ARTERY IN PATIENTS WITH GIANT CELL ARTERITIS WITH VISUAL SYMPTOMS AND CONTROLS

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Background: Giant cell arteritis (GCA) is the most common form of systemic vasculitis in patients aged 50 years and older.[1] Visual symptoms such as amaurosis, diplopia, temporary or permanent visual field loss secondary to optic nerve ischemia are common manifestations.[2] The value of vascular ultrasound of extra-ocular vessels in diagnosing GCA is well established.[3] However, the role of transocular ultrasound of the central retinal artery in GCA patients has not yet been established.

Objectives: To identify changes in flow velocities of the central retinal artery in GCA patients with visual symptoms and controls with transocular high resolution ultrasound.

Methods: Prospective analysis of GCA patients with visual symptoms and controls. Ultrasound of the central retinal artery was performed in 18 newly diagnosed consecutive GCA patients with visual symptoms (GCA-group) and 25 controls without ocular pathology. Visual symptoms included amaurosis, diplopia and temporary or permanent visual field loss. For each eye, peak systolic values (PS) and end diastolic values (ED) were recorded. Furthermore, the resistance index of each central retinal artery was measured.

Results: Twenty-one of 36 eyes of 18 GCA patients were affected. Therefore 21 central retinal were measured. The control group consisted of 50 central retinal arteries of 25 eye-healthy individuals. The mean age and gender distribution of the GCA-group were 75.6 years (SD± 8.1) with eight females (44 %) and 67 years (SD± 8.9) with twelve females (48%) in the control group. The mean flow velocity of the central retinal artery was PS 12.2 cm/s (SD± 3.5) and ED 3.7 cm/s (SD± 1.2) in the GCA group and PS 14.4 cm/s (SD± 3.2) and ED 5.1 cm/s (SD± 1.6) in the control group. The mean RI was 0.9 (SD± 0.3) in the GCA group and 0.8 (SD± 0.3) in the control group. Mean reduction

in flow velocity in the GCA-group was PS 2.1 cm/s (p= 0.039) and ED 1.4 (p= 0.0004) cm/s, while the RI was increased by 0.14 (p= 0.077). The results for PS and ED measurements were statistically significant, while the results for RI were not significant.

Conclusion: In GCA patients with ocular symptoms, a reduction of flow velocities of the central retinal artery compared to the eye-healthy control group was found. Results for PS and ED were significant. There seems to be a trend for decreased flow velocities in coexistence with visual symptoms in patients with GCA.

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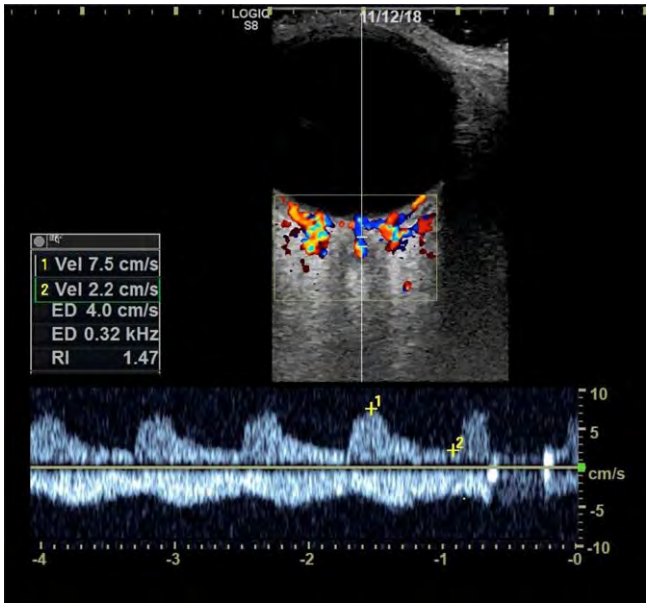


Figure 1. Transocular ultrasound of an affected eye in giant cell arteritis with reduced flow velocities and increased resistance index.

Disclosure of Interests: None declared
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OP0148

MEPOLIZUMAB FOR EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS (EGPA): A RETROSPECTIVE REAL-WORLD EUROPEAN STUDY ON 142 PATIENTS

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Background: Evidence on the efficacy of Mepolizumab (MEPO) in Eosinophilic Granulomatosis with Polyangiitis (EGPA) is scarce [1].

Objectives: To assess the efficacy and safety of MEPO in real-life clinical practice.

Methods: We retrospectively included patients diagnosed with EGPA and treated with MEPO (100 or 300 mg/month). MEPO efficacy was evaluated in the first 12 months in terms of systemic disease and asthma control. The occurrence of any adverse event (AE) was recorded.

Results: 142 patients were included (38% males; median age 46.4 (IQR 36.7-54.4); 110 and 32 on MEPO 100 and 300 mg/month, respectively). General, ear-nose-throat, pulmonary, and neurological symptoms significantly decreased during treatment (table 1). MEPO accounted for a significant reduction in the BVAS (figure 1) and for a steroid sparing effect (figure 2). The proportion of patients with asthma attacks decreased by 90% at 12 months compared to t0, and asthma-related emergency accesses dropped from 17.4% to 2.3%. Overall, 21.1% of patients had a non-serious AE.

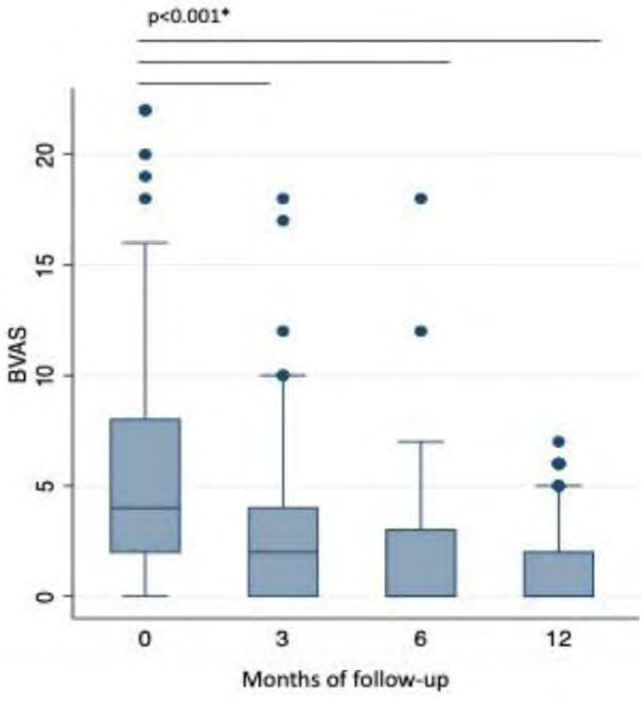


Figure 1. Changes in BVAS

Table 1. Control of clinical symptoms

	MEPO beginning (t0)	3 months	p-value (t3 vs t0)	6 months	p-value (t6 vs t0)	12 months	p-value (t12 vs t0)
N obs	N=142	N=135		N=123		N=89	
General symptoms	40 (28.2%)	17 (12.6%)	<0.001	19 (15.5%)	<0.001	13 (14.6%)	0.002
Cutaneous manifestations	13 (9.2%)	6 (4.4%)	0.008	5 (4.1%)	0.025	4 (4.5%)	0.180
ENT manifestations	106 (74.7%)	52 (38.5%)	<0.001	44 (35.8%)	<0.001	29 (32.6%)	<0.001
Pulmonary manifestations	130 (91.6%)	59 (43.7%)	<0.001	39 (31.7%)	<0.001	28 (31.5%)	<0.001
Cardiac manifestations	6 (4.2%)	2 (1.5%)	0.083	2 (1.6%)	0.083	0	0.157
Intestinal manifestations	10 (7.0%)	1 (0.7%)	0.005	4 (3.3%)	0.059	3 (3.4%)	0.059
Renal manifestations	5 (3.5%)	3 (2.2%)	0.414	0	0.046	1 (1.1%)	0.317
Neurological manifestations	36 (25.4%)	22 (16.3%)	0.012	18 (14.6%)	0.003	10 (11.2%)	0.035

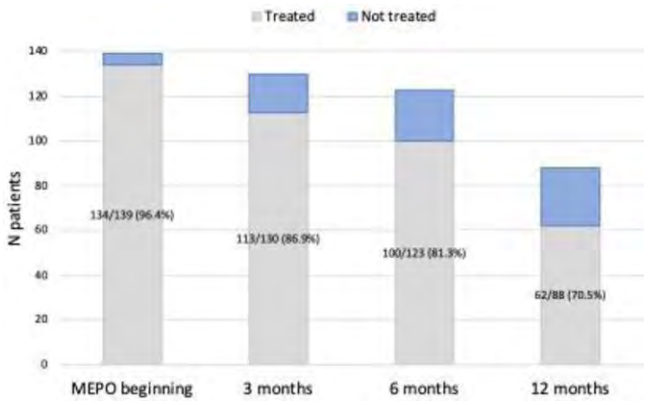


Figure 2. Steroid treatment

Conclusion: MEPO effectively controlled systemic and respiratory EGPA symptoms in a large European cohort, with no major safety concerns.

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Disclosure of Interests: Alessandra Bettiol: None declared, Maria Letizia Urban: None declared, Federico Alberici: None declared, Carlo Agostini: None declared, Chiara Baldini: None declared, Enrica Bozzolo: None declared, Paolo Cameli: None declared, Nunzio Crimi: None declared, Stefano Del Giacco: None declared, Allyson Egan: None declared, Georgina Espigol-Frigole Consultant of: Roche and Janssen, Mara Felicetti: None declared, Marco Folci: None declared, Paolo Fraticelli: None declared, Marcello Govoni: None declared, Anna Kernder Grant/research support from: Grant/research support from: GlaxoSmithKline and UCB Pharma for performing the LuLa-study., Carlo Lombardi: None declared, Giuseppe Lopalco: None declared, Claudio Lunardi: None declared, Aladdin J Mohammad Speakers bureau: lecture fees from Roche and Elli Lilly Sweden, PI (GiACTA study), Frank Moosig: None declared, Simone Negrini: None declared, Thomas Neumann: None declared, Pavel Novikov Grant/research support from: This work was supported by the 5-100 Project, Sechenov University, Moscow, Giuseppe Paolazzi: None declared, paola parronchi: None declared, Luca Quartuccio Consultant of: Abbvie, Bristol, Speakers bureau: Abbvie, Pfizer, Vito Racanelli: None declared, Carlo Salvarani: None declared, Maxime Samson: None declared, Jan Schroeder: None declared, Savino Sciascia: None declared, Renato A. Sinico: None declared, Benjamin Terrier: None declared, Paola Toniati: None declared, Domenico Prisco: None declared, Augusto Vaglio: None declared, Giacomo Emmi: None declared

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OP0149 VISUAL LOSS IN PATIENTS WITH GIANT CELL ARTERITIS TREATED WITH TOCILIZUMAB

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Background: Whether Tocilizumab (TCZ) may prevent vision loss in Giant Cell Arteritis (GCA) to the same extent as glucocorticoids remains a key and unanswered question. A patient cohort observed over up to 8 years addresses this issue.

Objectives: To investigate the frequency of vision loss/visual impariment in a GCA cohort treated with TCZ.

Methods: In this observational monocentric study, the courses of 192 patients with GCA treated with TCZ between 01.01.2011 and 31.12.2018 were analyzed. Data were extracted from medical records and collected in a Clinical Trial Unit (CTU) - based registry. Demographic, clinical and laboratory data were analyzed.

Results: 192 patients with GCA were treated with TCZ; 121 (63%) were female, 112 (58%) fulfilled 1990 American College of Rheumatology (ACR) criteria, all others had large vessel vasculitis based on magnetic resonance-angiography (MRA). The cumulative duration of TCZ treatment was 3467 months; the median treatment duration was 13.8 (8.5; 22.8) months. At baseline, visual impairment was present in 71 (37%) and vision loss in 21 (7.8%) patients. Visual loss was associated with higher age (74 (70; 82) vs. 70 (63; 76) years; p=0.029), lower C-reactive protein at baseline (14.0 (3.5; 42.0) vs. 54.5 (21.0; 101.0) mg/l; p<0.001), cranial symptoms (p<0.0001), jaw claudication (p=0.030) and negative MRA of the aorta (p=0.020). Over the observed time span only one patient taking part in a clinical trial developed vision loss. In total 4 (2%) patients with vision impairment showed deterioration and 61 (32%) improvement.

Conclusion: Collectively, our data suggest that TCZ is able to prevent visual loss and may have a favorable effect on visual impairment.

Disclosure of Interests: Jennifer Amsler: None declared, Iveta Kysela: None declared, Lisa Christ Consultant of: BMS, Christoph Tappeiner: None declared, Luca Seitz: None declared, Godehard Scholz: None declared, Florian Kollert Employee of: Novartis, Stephan Reichenbach: None declared, Peter Villiger Consultant of: MSD, Abbvie, Roche, Pfizer, Sanofi, Speakers bureau: Roche, MSD, Pfizer

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OP0150 WHAT IS THE ROLE OF TEMPORAL ARTERY BIOPSY IN GIANT CELL ARTERITIS FAST-TRACK PATHWAYS WHEN TEMPORAL ARTERY ULTRASOUND IS NEGATIVE?

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Background: A number of centres are now running fast track pathways for diagnosis and management of Giant cell arteritis with ultrasound as the first port of call for diagnosis[1]. Temporal artery biopsies (TABs) have become the second line of investigation, and it is unclear how useful TAB is in this setting.

Objectives: This study looked at accuracy of Temporal artery biopsy (TAB) in patients with suspected Giant Cell arteritis (GCA) with negative/inconclusive ultrasound (U/S) and how duration of treatment on steroids prior to these investigations and arterial specimen size affected it.

Methods: Prospective study of all patients with suspected GCA referred for TAB when U/S was negative or inconclusive, as part of the local fast-track pathway (Coventry). Database included clinical findings, serological work up, U/S and TAB results and treatment. Sensitivity and specificity of U/S and TAB was calculated and compared based on duration of treatment with steroids.

Results: One hundred and nine patients were referred for TAB via Coventry fast-track-pathway. The sensitivity of U/S in this cohort of patients was 9.08% and specificity was 93.33%. After 3 days of steroid this was 0% and 100% respectively. For TAB when done within 10 days of starting steroids, this was 65% and 87.5% respectively. After 20 days of steroids this was 0 % and 100%. The sensitivity and specificity was 20% and 85% when arterial specimen size was 11-15mm and 47% and 100% when specimen size was 16 mm or more. Sensitivity and specificity of U/S of 644 suspected GCA patients was 48% and 98%.

Conclusion: Our study demonstrates that TAB plays a relevant role in GCA fast-track-pathways, when U/S is negative/inconclusive. TAB was more sensitive than U/S in this cohort of patients, but overall sensitivity of U/S was higher when calculated for all patients suspected with GCA. Both remain useful tests if performed early. TAB specimen size should ideally be 16mm or more and done within 10 days of starting steroids.

References:

[1] Jonathan Pinnell, Carl Tiivas, Kaushik Chaudhuri, Purnima Mehta, Shirish Dubey, O38 The diagnostic performance of ultrasound Doppler in a fast-track pathway for giant cell arteritis, *Rheumatology*, Volume 58, Issue Supplement_3, April 2019, kez105.036, https://doi.org/10.1093/rheumatology/kez105.036

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.6534

OP0151-PARE WORK IMPACTS EXPERIENCED BY YOUNGER PEOPLE WITH ARTHRITIS: A SYSTEMATIC REVIEW

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Background: On a global scale, it is estimated that adults in their peak income-earning years are disproportionately impacted by arthritis (1). Younger adults with arthritis are less likely to be employed and are more likely to face productivity challenges at work when compared to healthy similar-aged peers (2). The work-related impacts of arthritis on younger adults remain largely unexplored and are rarely considered in routine clinical care for arthritis.

Objectives: To systematically identify, appraise and synthesise the available evidence on work impacts experienced by individuals aged 16-50 years with arthritis.

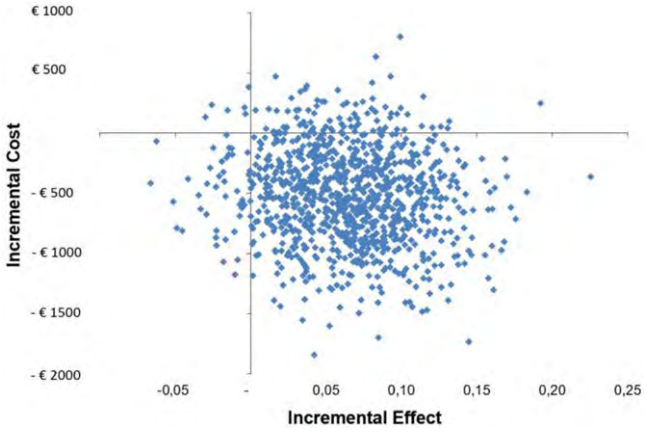
Methods: Eligible studies from 2000 - 2020 were identified in OVID Medline, PsycINFO, Embase, and CINAHL databases using a comprehensive search strategy. Quantitative and qualitative studies containing self-reported data on the work impacts of arthritis on younger people were included. Quality assessment was undertaken using validated quality appraisal tools (3).
Results: From a yield of 300 studies, 35 were included in the review. After quality assessment and exclusion of the lowest-ranked studies, 28 studies (17 quantitative, 11 qualitative) were analysed. Work outcomes data were organised into five themes (1-3 for quantitative outcomes, 4-5 for qualitative outcomes): (1) the impacts of arthritis on work productivity; (2) the impacts of arthritis on work participation; (3) other arthritis attributable workplace challenges; (4) barriers to work participation associated with arthritis, and (5) enablers to work participation associated with arthritis. For quantitative themes, arthritis was strongly associated with other workplace challenges: scores on the Workplace Activity Limitations Scale ranged from 5.9 (moderate workplace difficulty) to 9.8 (considerable workplace difficulty); and work disability relative to the healthy population (prevalence ranging from 6% - 80%). For qualitative themes, barriers to work participation included lack of workplace support; enablers included workplace support and intrinsic motivation to work.
Conclusion: Arthritis is associated with poorer work outcomes for younger people relative to healthy peers. The available evidence was heterogeneous across studies. Additional research focusing solely on the unique workplace needs of younger population groups is required. This would inform the development of tailored intervention or workplace support strategies to maximise productive working years.
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[1] European League Against Rheumatism. Horizon 2020 Framework Programme: EULAR's positions and recommendations. EULAR 2011.
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[3] Joanna Briggs Institute. Critical Appraisal Tools. The University of Adelaide 2019.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.1461

Innovative care

OP0152-HPR A COST-UTILITY ANALYSIS OF MULTIMODAL OCCUPATIONAL THERAPY IN PATIENTS WITH THUMB BASE OSTEOARTHRITIS

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Background: Patient education, hand exercises, and use of assistive devices and orthoses are regarded as first-line treatment for patients with hand osteoarthritis (OA) (1), however there is limited evidence for the cost-effectiveness of such treatment.
Objectives: The objective of this study is to assess the cost-utility of a multimodal occupational therapy treatment delivered in the waiting period before surgical consultation in patients with thumb base OA compared to usual care.
Methods: This study presents an economic evaluation assessing the difference in health care use and quality-of-life during a 24-month period in a Norwegian multicenter randomized controlled trial. All patients referred to surgical consultation due to thumb base OA at three departments of rheumatology between 2013 and 2015 were eligible for inclusion. In total, 180 patients were included and randomized to a control group or a multimodal occupational therapy group (90 patients in each group). During the waiting period between referral and actual surgical consultation, the control group continued with usual care which was staying on the waiting list and receiving information on hand OA. The intervention group got information on hand OA, ergonomic principles and use of assistive devices, and they were instructed in home-based hand exercises and received a day and a night orthosis. The intervention group was instructed to use the orthoses and assistive devices as much as possible and perform home exercises three times per week for 12 weeks. The patients were assessed at baseline and after 4, 18 and 24 months. The within-trial economic analysis reports the incremental cost-effectiveness ratio (ICER) reflecting the between-group difference in incremental cost per adjusted life years (QALY) over 24 months. A generic health-related quality of life questionnaire, the EuroQol 5 Dimension, was used to calculate the QALYs at baseline, 4, 18 and 24 months. Costs were collected from different sources, taking a health care perspective; The occupation therapist reported the number of consultations related to the intervention; surgical procedure and post-operative follow-up were collected from patients' journals; and additional consumption of primary and specialist health care was self-reported by the patient. Sensitivity analyses were performed. The results are presented in a cost-effectiveness plane using bootstrapping. Willingness-to-pay threshold is set to be € 27 500 linked to the severity of this condition.
Results: The mean age of the included patients was 63 years (SD 7.6) and 79% were women. There was a total between-group difference in QALYs of 0.07 utilities after 24 months, in favour of the intervention group. Operations constituted the main costs with 22 operations in the intervention group compared to 33 in the control group. The between-group difference in costs due to health care consumption was estimated to € 500 in favour of the intervention group (Figure 1).



Conclusion: The results in this within-trial analysis indicate that multimodal occupational therapy in the waiting period before surgical consultation compared to usual care is a cost-effective alternative taking a health care perspective.
References:
[1] Kloppenburg, M., et al. (2018). "2018 update of the EULAR recommendations for the management of hand osteoarthritis." Ann Rheum Dis.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.3345

OP0153-HPR HOW CAN WE HELP PEOPLE WITH FIBROMYALGIA? NO EFFECTS OF AN EVIDENCE-BASED MULTICOMPONENT REHABILITATION PROGRAMME

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Background: Patients with fibromyalgia (FM) suffer from high symptom burden, lack of understanding and few available treatments. EULAR evidence-based recommendations for the management of FM state that optimal management should focus on prompt diagnosis, patient education and initially non-pharmacological treatments[1]. Physical exercise is recommended for all patients and may be combined with tailored psychological therapies for those with unhelpful coping strategies. The evidence for these combined therapies is still weak and further studies are warranted. A Norwegian mindfulness- and acceptance-based intervention, the Vitality Training Programme (VTP), has shown beneficial effects in groups of patients with rheumatic and musculoskeletal diseases[2,3], but has previously not been tested in combination with physical exercise.
Objectives: To test the effects of a multicomponent rehabilitation programme comprising the VTP followed by supervised physical exercise for patients with recently diagnosed FM.
Methods: Patients with widespread pain ≥3 months; aged 20 to 50, who were working or had not been out of work >2 years, were referred to rheumatologists for diagnosis clarification according to ACR 2010 FM diagnosis criteria. All eligible patients participated in a 3-hour group-based patient education programme before inclusion and randomization. The intervention group received the VTP, a 10-session group programme followed by 12 weeks supervised physical exercise. The control group followed treatment as usual. Self-reported data were collected electronically. Primary outcome was Patient Global Impression of Change

(PGIC), scored as 1= much worse, through 4=no change, to 7=much better, measured at 12 months follow-up. Values 6 - 7 were considered clinically relevant improvement. Secondary outcomes were pain, fatigue, sleep quality, psychological distress, mindfulness, physical activity, motivation and barriers for physical activity and work impairment. Effects were analysed by Analysis of Covariance (ANCOVA).

Results: 170 patients were randomised, 85 to intervention and 85 to control. There were no statistically significant differences between groups in PGIC at 12 months; 13% in the intervention group and 8% in the control group reported clinically relevant improvement (Figure 1). No statistically significant between-group differences were found in pain (p=0.05), fatigue (p=0.72), sleep quality (p=0.52), psychological distress (p=0.34), physical activity (p=0.78) or work impairment (0.27). There were significant between-group differences in patients' tendency to be mindful (p=0.02) and 'perceived benefits of exercise' (p=0.03), in favour of the intervention group.

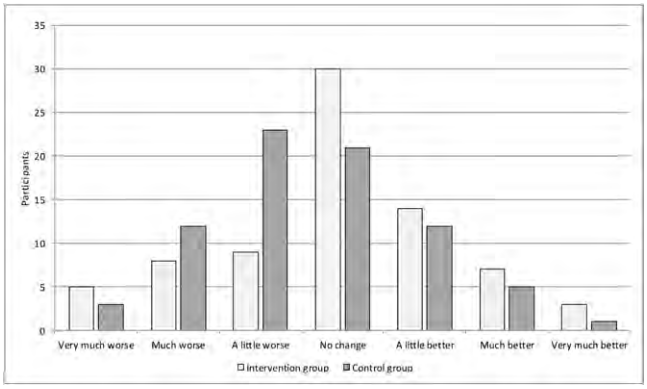
Conclusion: At 12 months follow-up, a multicomponent rehabilitation programme had no significant health effects compared to treatment as usual. The results differ from previous studies on the VTP in patients with inflammatory joint diseases. The question, how can we help people with FM, remains unresolved.

References:

[1] Macfarlane GJ et al. EULAR revised recommendations for the management of fibromyalgia. Ann Rheum Dis 2017;76:318-28

[2] Zangi HA et al. A mindfulness-based group intervention to reduce psychological distress and fatigue in patients with inflammatory rheumatic joint diseases: a randomised controlled trial. Ann Rheum Dis 2012;71:911-17

[3] Haugli L et al. Learning to have less pain - is it possible? A one-year follow-up study of the effects of a personal construct group learning programme on patients with chronic musculoskeletal pain. Patient Educ Couns 2001;45:111-18



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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.1408

OP0154-HPR

EFFECT OF NURSE-LED-CARE ON PATIENT OUTCOMES IN RHEUMATOID ARTHRITIS IN GERMANY: A MULTICENTRE RANDOMISED CONTROLLED TRIAL

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Background: Inflammatory rheumatic disorders are very complex and require high medical resources. However, there is a shortage of care for these patients, which results in suboptimal reach of therapy objectives. Nevertheless, these very objectives need to be pursued quickly to prevent permanent joint damage. In order to ensure adequate care, multidisciplinary teams which include clinical nurse specialists are required. These clinical nurse specialists play an important role in improving standard-of-care in addition to the rheumatologist. The current standard of care ensures that essential medical provision remains intact, however, psychological, social, rehabilitative and educational needs are often skipped due to time constraints. While studies from e.g. the UK and Denmark have already supported the non-inferiority of nurse-led care (NLC)[1], no such studies have yet been published in Germany.

Objectives: To demonstrate the non-inferiority of NLC to the current standard-of-care, rheumatologist-led care (RLC), for patients with seropositive rheumatoid arthritis (RA) with induction, escalation or change of therapy regarding disease activity as well as different patient reported outcomes (PROs).

Methods: This trial was conducted as a prospective multi-centered RCT with a non-inferiority design over the course of 12 months. Based on power calculations, 236 adults with RA were included in the study and randomized to either NLC or RLC. The primary outcome measure is disease activity (DAS28), assessed at baseline (T0), 6 weeks (T1), 3,6, 9, and 12 months (T3, T6, T9, T12). Secondary measures are health related quality of life (RAID), functionality (FFbH) and depression (PHQ9).

Results: There are no significant differences between intervention group (IG) (n=117) and control group (CG) (n=119) at baseline. The mean age of the IG is 58.80 years (SD=12.09) and of the CG 58.34 years (SD=11.72). 72.4% of the IG and 78.1% of the CG are female. The mean duration of symptoms was 147 months (SD=144.63) for the IG and 116 months (108.89) for the CG. The mean DAS28 for the IG is 4.36 (SD=1.24) and 4.51 (SD=1.24) for the CG.

A mixed one-way repeated measures ANOVA showed that the DAS28 improves significantly over time, Huyn-Feldt $F(4.42, 751.72) = 105.701$, $p < .001$, partial $\eta^2 = 0.383$, but the interaction of the DAS28 and the randomization is not significant, Huyn-Feldt $F(4.42, 751.72) = 1.464$, $p = 0.260$, partial $\eta^2 = 0.009$. No main effect for randomization was found, meaning that the IG and CG did not differ significantly, $F(1, 170) = 1.005$, $p = 0.317$, partial $\eta^2 = 0.006$.

The Mann-Whitney-Test showed that the change of the secondary outcomes does not depend on the randomization FFbH $U = 4978.50$, $Z = -.755$, $p = .450$. RAID $U = 5121.00$, $Z = -.539$, $p = .590$. PHQ9 $U = 4800.50$, $Z = -1.281$, $p = .200$. The secondary outcomes improve significantly over time, as shown by a Wilcoxon Signed Rank test for the FFbH $Z = -5.589$, $p < .001$, the RAId $Z = -9.884$, $p < .001$ and the PHQ9 $Z = -7.960$, $p < .001$.

Conclusion: The results support the non-inferiority of NLC in the management of RA regarding the primary and secondary outcome measures and provide first evidence that NLC could improve care and help carry the doctors' workflow.

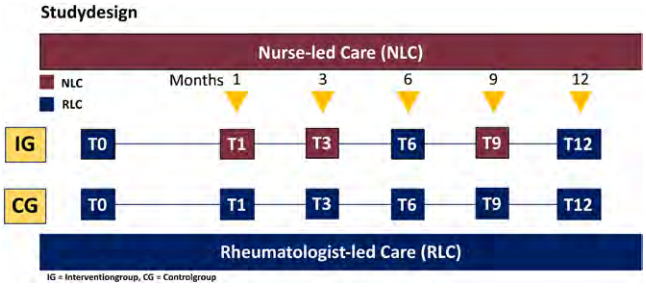


Figure 1.

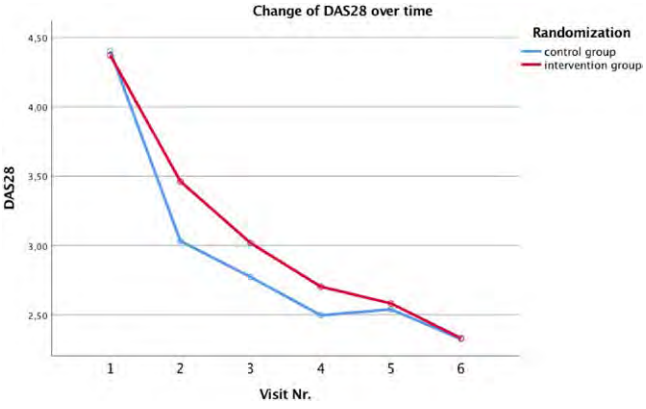


Figure 2.

References:

[1] de Thurah A, Esbensen BA, Roelsgaard IK, et al. Efficacy of embedded nurse-led versus conventional physician-led follow-up in rheumatoid arthritis: a systematic review and meta-analysis. RMD Open 2017;3:e000481.

Disclosure of Interests: Juliana R Hoeper: None declared, Georg Gauler Consultant of: Abbvie, Lilly, MSD, Speakers bureau: Abbvie, Celgene, Novartis, Sanofi,, Dirk Meyer-Olson Grant/research support from: Novartis, Sandoz Hexal, Consultant of: Abbvie, Amgen, Bristol Myers Squibb, Chugai, Lilly, Mylan, Novartis, Sandoz Hexal, Sanofi, Speakers bureau: Abbvie, Bristol Myers Squibb, Chugai, Lilly, Novartis, Pfizer, Sandoz Hexal, Sanofi, Karin Rockwitz Consultant of: Janssen Cilag, Speakers bureau: Janssen Cilag, Patricia Steffens-Korbanka Consultant of: Abbvie, Chugai, Novartis, Sanofi, Mylan, Lilly, Speakers bureau: Abbvie, Chugai, Novartis, Sanofi, Lilly, Carsten Stille: None declared, Jochen Walter Consultant of: Pfizer, Speakers bureau: AbbVie, Frauenhofer Institut, Gilead, Janssen-Cilag, Medac, Novartis, Pfizer, Martin Welcker Grant/research support from: Abbvie, Novartis, UCB, Hexal, BMS, Lilly, Roche, Celgene, Sanofi, Consultant of: Abbvie, Actelion, Aescu, Amgen, Celgene, Hexal, Janssen, Medac, Novartis, Pfizer, Sanofi, UCB, Speakers bureau: Abbvie, Aescu, Amgen, Biogen, Berlin Chemie, Celgene, GSK, Hexal, Mylan, Novartis, Pfizer, UCB, Joerg Wendler Consultant of: Janssen, AbbVie, Sanofi, Speakers bureau: Roche, Chugai, Janssen, AbbVie, Novartis, Jan Zeidler: None declared, Kirsten Hoeper Consultant of: AbbVie, Celgene,, Speakers bureau: Abbvie, Chugai, Novartis, Lilly, Celgene, Sandoz Hexal
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OP0155-HPR EFFECT OF THE DR. BART APPLICATION ON HEALTHCARE USE AND CLINICAL OUTCOMES IN PEOPLE WITH OSTEOARTHRITIS OF THE KNEE AND / OR HIP IN THE NETHERLANDS; A RANDOMIZED CONTROLLED TRIAL

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Background: Self-management is of paramount importance in non-surgical treatment of knee and/or hip osteoarthritis(OA). Modern technologies offer the possibility to support self-management 24/7. We developed an e-self-management application (dr. Bart app) for people with knee and/or hip OA. A central element of the dr. Bart app is that the app proposes a selection of 72 preformulated goals to induce health behaviors based on the 'tiny habits method'[1]
Objectives: To evaluate the short-term effects of the use of the dr. Bart app, compared to usual care, on the number of secondary health care consultations and clinical outcomes in people with knee/hip OA in the Netherlands.
Methods: A randomized controlled design involving participants ≥50 years with self-reported knee and/or hip OA, randomly allocated to the dr. Bart app or usual care. Participants were recruited from the community through advertisements in local newspapers and social media campaigns. In Figure 1 the theoretical framework of the dr. Bart app is presented. Participants received online questionnaires at baseline and after 3 and 6 months of follow-up. The primary outcome was the number of consultations in secondary health care due to OA in the knee/hip in the past six months. Secondary outcome measures were self-management behavior, pain, symptoms, functional limitations, physical activity, quality of life, and illness perceptions. Data were analyzed using negative binomial regression or linear mixed models, as appropriate, corrected for baseline, main OA-location (knee or hip), and interaction between treatment group and time.

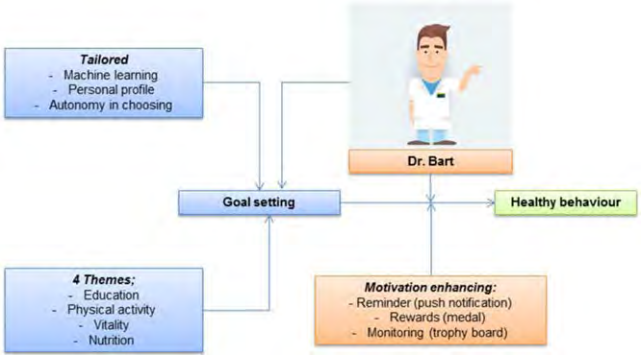


Figure 1. Theoretical framework of the dr. Bart app.

Results: In total 427 eligible participants were allocated to either the dr. Bart group (n=214) or usual care (n=213). Mean age of the participants was 62.1 (SD 7.3) years, with the majority being female (72%) and having symptoms predominantly in their knee(s) (73%). Response rates for the follow-up questionnaires were 75.4% and 69.3% at 3 and 6 months, respectively. With respect to the number of consultations in secondary health care we found a non-significant incidence rate ratio (1.20 (95% CI: 0.67; 2.19)) between the dr. Bart app group and the usual care group. We found a positive overall treatment effect of the dr. Bart app on symptoms (2.6 (95% CI: 0.4; 4.9)), pain (3.5 (95% CI: 0.9; 6.0)) and, activities of daily living (2.9 (95% CI: 0.2; 5.6)), see Table 1. We found non-significant differences between groups for self-management behavior, physical activity, health-related quality of life and illness perceptions.

Table 1. Overall treatment effect and treatment effects at 3 and 6 months of the dr. Bart app.

Measures	Treatment effects of dr. Bart app		
	Δ3 months§ ∞ (95 % CI)	Δ6 months§ ∞ (95 % CI)	Δ overall§ (95 % CI)
Number of consultations in secondary health care †	1.05 (0.55; 2.02)	1.32 (0.89; 2.87)	1.20 (0.67; 2.16)
KOOS/HOOS			
- Symptoms	*1.5 (-1.2;4.1)*	*2.6 (-0.4; 5.6)*	***2.6 (0.4; 4.9)****
- Pain	***3.1 (0.2; 5.9)****	*0.9 (-2.0; 3.8)*	***3.5 (0.9; 6.0)****
- Activities of daily living	*2.5 (-0.7; 5.7)*	*0.9(-2.6; 4.4)*	***2.9 (0.2; 5.6)****
- Functioning in sport and recreation	*-1.7 (-6.4; 2.9)*	***7.7 (2.7; 12.7)****	*1.9 (-2.0; 5.9)*

* Indicates p-value < 0.05
† Reported as incidence rate ratio
§Adjusted for baseline value, treatment group and main OA-location (knee/hip)
∞ Adjusted for time, and interaction between treatment group and time
Abbreviations: KOOS; Knee Injury and Osteoarthritis Outcome Score; HOOS; Hip Disability and Osteoarthritis Outcome Score.

Conclusion: The dr. Bart app did not reduce the number of secondary health care consultations compared to usual care. However, we found positive effects attributable to the dr. Bart app on pain, symptoms, activities of daily living and functioning in sport and recreation in people with knee/hip OA, suggesting that the dr. Bart app has potential to positively influence health in people with knee/hip OA.
References:
[1] Fogg GJ. 2009: ACM; 2009: 40.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.1720

OP0156-HPR COST EFFECTIVENESS OF TELE-HEALTH FOLLOW-UP IN RHEUMATOID ARTHRITIS BASED ON A NON-INFERIORITY RANDOMIZED CONTROLLED TRIAL

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Background: The clinical effectiveness of a patient-reported outcome (PRO) based telehealth intervention offered to rheumatoid arthritis (RA) patients with low disease activity or remission has previously been reported[1]. The TeRA study showed that PRO-based telehealth follow-up in RA achieved similar disease control as conventional outpatient follow-up among patients with low disease activity or remission. The degree of disease control did not differ between telehealth follow-up offered by rheumatologists or rheumatology nurses.
Objectives: To compare the cost-effectiveness of PRO–based telehealth follow-up to patients with RA performed by rheumatologists or rheumatology nurses with conventional outpatient follow-up.
Methods: A total of 294 patients were randomized (1:1:1) to either PRO-based telehealth follow-up carried out by a nurse (PRO-TN) or a rheumatologist (PRO-TR), or conventional outpatient follow-up by physicians. Quality of life (EQ-5D) was measured at baseline and at follow-up after one year. The primary outcome was a change in the Disease Activity Score, C-reactive Protetin in 28 joints (DAS-28, CRP).
The focus in the health economic evaluation was on the relation between costs and EQ-5D in the period between one year prior to and one year after the intervention. All costs were measured at the individual level and consisted of: intervention costs, health and social care costs, and productivity costs. All cost

data were retrieved from Danish population-based registers. Incremental cost-effectiveness rates (ICERs) were calculated on the basis of a comparison of the development in costs and effects in the two intervention groups (separately and combined) with the control group. Bootstrap with 10,000 replications were used to access significance.

Results: The difference in health and social care costs during the intervention period compared to the year before were €1,072, - €50 and €519 for the control group, the PRO-TR group and the PRO-TN respectively. Hence, the change in health and social care costs was lower for both intervention groups. The PRO-TR group had a small decrease and it was significantly lower than for the control group (p=0.0027). The difference between health and social care costs in the PRO-TN group compared to the control group was only borderline significant (p=0.067). No statistically significant differences were found in QALY's between the three groups, all three groups experienced minor, non-significant, declines in QALY over the intervention period. ICER's were not statistically significant but below known threshold values for the PRO-RN group (ICER=€17,121).

Conclusion: It is difficult to obtain statistically significant results for cost-effectiveness in small samples. However, the results point towards a possible cost-saving impact of PRO interventions in patients with low disease activity or remission. The study was unable to conclude if PRO-TR or PRO-TN were most cost-effective. Other relevant considerations, like patient satisfaction or organisational issues, should determine the way of organizing RA disease management in these patients.

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Disclosure of Interests: Annette de Thurah Grant/research support from: Novartis (not relevant for the present study)., Speakers bureau: Lily (not relevant for the present study)., Christian Skovsgaard: None declared, Thomas Maribo: None declared, Niels Henrik Hjøllund: None declared, Marie Kruse: None declared

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OP0157-HPR

DISSEMINATION AND ASSESSING IMPLEMENTATION OF THE EULAR RECOMMENDATIONS FOR PATIENT EDUCATION FOR PEOPLE WITH INFLAMMATORY ARTHRITIS ACROSS EUROPE

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Background: EULAR recommendations for patient education for people with inflammatory arthritis (IA) were published in 2015.[1] This is the first systematic dissemination and implementation study, reporting qualitative data identifying barriers to implementation of the recommendations.

Objectives: To (i) disseminate and assess the level of acceptability and applicability of the EULAR recommendations for patient education among healthcare professionals and rheumatologists and (ii) assess potential barriers and facilitators to their application in clinical practice.

Methods: This was a cross-sectional study using survey methods. Survey items were developed in English and translated into 20 different languages before being distributed to health professionals by snowball sampling using an online platform. The items covered demographic information and 10-point rating scales assessing the level of acceptability and applicability of each of the eight recommendations. In addition, textual data fields were provided to assess reasons for disagreeing and barriers to implementation of the recommendations in practice. Quantitative data were analysed descriptively with agreement and applicability levels summarised as median (IQR) scores. Textual data were analysed by content analysis and presented in themes. Finally, collaborators in each country reviewed the top barriers to implementation and proposed facilitators to implementation in their respective countries.

Results: A total of 2442 responses were recorded from 23 countries, but only 1495 contained complete data. Of complete responses, 74% were women. Most of the professionals were nurses (n=640), rheumatologists (n=369) and physiotherapists (n=232).

Table 1 presents the levels of agreement and applicability of the recommendations. For all recommendations, the level of agreement was high (median=10). However, the level of applicability was generally lower compared to each corresponding agreement level, especially for recommendation 6, which states that the effectiveness of patient education should be evaluated. Lack of an effective evaluation tool was the biggest barrier to implementation.

Table 1. Levels of agreement and applicability of each recommendation.

	Agreement		Applicability	
	Median	IQR	Median	IQR
Recommendation 1	10	10 to 10	8	7 to 10
Recommendation 2	10	10 to 10	8	6 to 10
Recommendation 3	10	9 to 10	8	7 to 10
Recommendation 4	10	8 to 10	7	5 to 10
Recommendation 5	10	8 to 10	7	5 to 9
Recommendation 6	10	8 to 10	6	4 to 8
Recommendation 7	10	9 to 10	8	5 to 8
Recommendation 8	10	10 to 10	8	5 to 8

There were notable similarities between barriers and facilitators for implementation of the recommendations across countries. The 3 most common barriers to application were; (i) lack of time (ii) lack of training in how to provide patient education and (iii) not having enough staff to provide patient education. The most common facilitators were: tailoring the content and delivery of patient education to individual patients; training providers, and evaluating the effectiveness of patient education with individual patients.

Conclusion: This project has disseminated the EULAR recommendations for patient education across 23 countries. There was high agreement with the recommendations among health professionals but their application to clinical practice was lower. Some barriers to application are amenable to change such as addressing training needs of health professionals and developing evaluation tools for patient education.

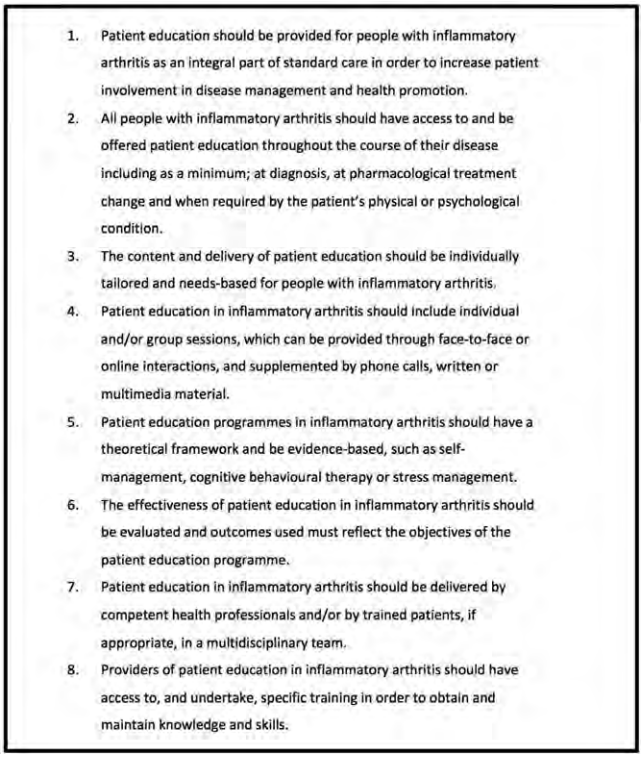

1. Patient education should be provided for people with inflammatory arthritis as an integral part of standard care in order to increase patient involvement in disease management and health promotion.
2. All people with inflammatory arthritis should have access to and be offered patient education throughout the course of their disease including as a minimum; at diagnosis, at pharmacological treatment change and when required by the patient's physical or psychological condition.
3. The content and delivery of patient education should be individually tailored and needs-based for people with inflammatory arthritis.
4. Patient education in inflammatory arthritis should include individual and/or group sessions, which can be provided through face-to-face or online interactions, and supplemented by phone calls, written or multimedia material.
5. Patient education programmes in inflammatory arthritis should have a theoretical framework and be evidence-based, such as self-management, cognitive behavioural therapy or stress management.
6. The effectiveness of patient education in inflammatory arthritis should be evaluated and outcomes used must reflect the objectives of the patient education programme.
7. Patient education in inflammatory arthritis should be delivered by competent health professionals and/or by trained patients, if appropriate, in a multidisciplinary team.
8. Providers of patient education in inflammatory arthritis should have access to, and undertake, specific training in order to obtain and maintain knowledge and skills.

Figure 1. Recommendations for patient education in inflammatory arthritis.[1]

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[1] Zangi HA, et al. EULAR recommendations for patient education for people with inflammatory arthritis *Ann Rheum Dis*. 2015;**74**:954-962.

Disclosure of Interests: Sarah Bennett: None declared, Heidi A. Zangi: None declared, Astrid van Tubergen Consultant of: Novartis, Mwidimi Ndosi Grant/research support from: Bristol Myers Squibb, Consultant of: Janssen, Pfizer

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OP0158-HPR **TELEMEDICINE CONSULTATIONS IN POLYMYALGIA RHEUMATICA PATIENTS. A TWO YEARS' EXPERIENCE REPORT**

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Background: Polymyalgia rheumatica (PMR) is the most common inflammatory rheumatic disease of people over 50 years in Scandinavian countries and people of northern European descent, characterized by proximal pain, stiffness, raised inflammatory markers and prompt response to steroids(1). Relapse free during tapering off prednisone, are common in approximately 50% of patients. Studies reported that up to 70% of PMR patients are successfully tapered of prednisone due to remission, within 1-2 years from treatment initiation (1). Telemedicine has found a wider application in a number of chronic diseases resulting in a decreased number of hospital visits; however, no telemedicine studies on PMR patients have been performed before (2).
Objectives: To evaluate the use of telemedicine consultation in newly diagnosed PMR patients.
Methods: Telemedicine consultations managed by rheumatic nurses for newly diagnosed PMR patients was established in 2017 at our department. Patients diagnosed with PMR by a rheumatologist received written information concerning the nature of the disease, a "follow-up" schedule and a prednisone treatment/tapering plan. Telephone consultations (TC) including relevant blood analysis was planned after 4, 16, 52 and 78 weeks from the time of diagnosis. TC was managed by 4 nurses specialized in rheumatic diseases, who received appropriate education of PMR prior to the establishment. A predefined questionnaire was used for every telephone consultation.
All PMR patients were initially treated with 15 mg of prednisone daily, with slowly tapering to 5 mg daily at week 16 and reduced to zero at week 48. In the case of relapse symptoms, patients were instructed to contact the treating nurses. In that case, relevant biomarkers were taken and a rheumatologist evaluated the need for a physical consultation and potential treatment adjustment.
Only patients with minimum disease duration of 3 months were included in the study.
Results: In a period of two years, 76 patients were evaluated. The mean age was 73 years and the mean follow up period was 10, 67 ± standard deviation (SD) 5,2 months. At the time of diagnosis, all patients fulfilled the 2012 Classifications criteria for PMR (3). The Mean number of TC was 4.27(± SD 2, 3).
In 45 cases (60%) no additional physical consultation was necessary. In patients examined physically due to relapse suspicion, the most common findings were PMR relapses (66%), followed by non-inflammatory muscle and joint pain (18,5%), arthritis (14%), while one patient was diagnosed with giant cell arteritis.
Successfully prednisone tapering was achieved in 23 cases (30%) while 27 patients (35,5%) at the time of data evaluation were treated with only 2,5 mg of prednisone daily. The mean current daily prednisolone dosage was 3.95 mg (± SD 3.25) while disease-modifying-anti-rheumatic-drugs had been initiated in 6 patients.
Conclusion: Telemedicine consultations in PMR diminish the need for physical consultations in this patient cohort. More than half of all patients were either out of- or received only a very low dose of prednisone at the time of evaluation of data.
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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.3261

OP0159 **EFFICACY OF COMPREHENSIVE TECHNOLOGY-ASSISTED HOME-BASED EXERCISE IN ANKYLOSING SPONDYLITIS: A RANDOMIZED, CONTROLLED TRIAL**

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Background: Clinical practice guidelines recommend that exercise is an essential component in the self-management of Ankylosing Spondylitis (AS). Attending supervised interventions requiring periodic medical center visits can be burdensome and patients may decline participation, whereas, effective home-based exercise interventions that do not need regular medical center visits are likely to be more accessible and acceptable for patients with AS. Recently, increasing evidences have been accumulated that the wearable devices could facilitate patients with inflammatory arthritis by giving exercise instructions and improving self-efficacy. Therefore, patients with AS may benefit from an effective technology-assisted home-based exercise intervention.
Objectives: To investigate the efficacy of a comprehensive technology-assisted home-based exercise intervention on disease activity in patients with AS.
Methods: This study was a 16-week assessor-blinded, randomized, waiting-list controlled trial (ChiCTR1900024244). Patients with AS were randomly allocated to the home-based exercise intervention group and the waiting-list control group. A 16-week comprehensive exercise program consisting of a moderate intensity (64%-76% HR_{max}) aerobic training for 30min on 5 days/week and a functional training for 60min on 3 days/week was given to patients in the intervention group immediately after randomization, with 1.5h training sessions for two consecutive days by a study physical therapist at baseline and Week 8. The aerobic exercise intensity was controlled by a Mio FUSE Wristband with a smartphone application. The functional training consisted of the posture training, range of motion exercises, strength training, stability training and stretching exercises. Patients in control group received standard care during the 16-week follow-up and started to receive the exercise program at Week 16. The primary outcome was ASDAS at Week 16. The secondary outcomes were BASDAI, BASFI, BASMI, ASAS HI, peak oxygen uptake, body composition and muscle endurance tests. The mean difference between groups in change from baseline was analyzed with the analysis of covariance.
Results: A total of 54 patients with AS were enrolled (26 in intervention group and 28 in control group) and 46 (85.2%) patients completed the 16-week follow-up. The mean difference of ASDAS between groups in change from baseline to 16-week follow-up was −0.2 (95% CI, −0.4 to 0.003, P = 0.032), and the mean change from baseline was -0.4 (95% CI, -0.5 to -0.2) in the intervention group vs -0.1 (95% CI, -0.3 to 0.01) in the control group, respectively. Significant between-group differences were found between groups for BASDAI (−0.5 [95% CI, −0.9 to −0.2], P = 0.004), BASMI (−0.7 [95% CI, −1.1 to −0.4], P <0.001), BASFI (−0.3 [95% CI, −0.6 to 0.01], P=0.035), peak oxygen uptake (2.7 [95% CI, 0.02 to 5.3] ml/kg/min, P=0.048) and extensor endurance test (17.8 [95% CI, 0.5 to 35.2]s, P=0.044) at Week 16. Between-group differences were detected in ASAS HI (−0.9 [95% CI, −1.7 to −0.1], P=0.030), body fat percentage (−1.0 [95% CI, −2.0 to −0.01] %, P=0.048) and visceral adipose tissue (−4.9 [95% CI, −8.5 to −1.4] cm^2, P=0.008) at Week 8, but not at Week 16. No significant between-group differences were detected in the total lean mass, time up and go test and the flexor endurance test during the follow-up.
Conclusion: Comprehensive technology-assisted home-based exercise has been shown to have beneficial effects on disease activity, physical function, spinal mobility, aerobic capacity, and body composition as well as in improving fatigue and morning stiffness of patients with AS.
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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.5100

Advances in treating SLE and lupus nephritis

OP0160 **HYDROXYCHLOROQUINE BLOOD LEVELS AND RISK OF THROMBOTIC EVENTS IN SYSTEMIC LUPUS ERYTHEMATOSUS**

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Background: Hydroxychloroquine (HCQ) has a primary role in the treatment of systemic lupus erythematous (SLE). Beyond its pleiotropic immunomodulatory effects on Toll-like receptor and type I interferon signaling, HCQ use has been found to be protective for thrombosis in SLE (1). Optimal dosing of HCQ in SLE is unknown. The longitudinal measurement of HCQ blood levels may provide an opportunity to individualize weight-based dosing strategies and reduce risk of toxicity.
Objectives: Examine the association of HCQ blood levels with thrombotic events in a longitudinal SLE cohort.
Methods: 812 SLE patients with HCQ blood level measured prior to the thrombosis were included: 93% female, 43% African-American, 46% Caucasian. HCQ blood levels were quantified by liquid chromatography-tandem mass

spectrometry. Mean HCQ blood levels (± standard deviation) over all cohort visits prior to occurrence of thrombosis were calculated for each patient. Thromboses were defined as venous (DVT/PE or other venous) or arterial thrombosis (stroke, myocardial infarction, digital gangrene or other arterial).

Results: Thrombosis had occurred during prospective follow up in 43 patients (5.5%), venous in 3.0% and arterial in 2.9%. Lupus anticoagulant was strongly associated with a history of any thrombosis (OR 3.25, p<0.0001), venous thrombosis (OR 3.53, p<0.0001), and arterial thrombosis (OR 3.08, p<0.0001). A prospective analysis shows that for any thrombosis and for venous thrombosis, the HCQ blood level was significantly lower (Table 1). Higher prescribed doses of HCQ (as opposed to HCQ blood levels) were also associated with decreased odds of any thrombosis and venous thrombosis in a separate cross-sectional analysis (OR 0.88, p=0.04 and OR 0.83, p=0.009, respectively for each 1 mg/kg increase in prescribed HCQ).

Table 1. Thrombotic Events are Associated with Lower Mean HCQ Blood Level

	Mean HCQ Blood Level (± Std. Dev.)		
	Thrombotic Event	No Event	P-value
Any thrombosis	695 ±464	887 ± 562	0.029
Any venous thrombosis	682 ± 374	881 ± 560	0.10
DVT/PE only	615 ± 384	881 ± 559	0.055
Any arterial thrombosis	708 ± 539	882 ± 558	0.13
Stroke	720 ± 643	880 ± 557	0.27

Conclusion: HCQ blood levels are inversely associated with risk of any thrombosis and of venous thrombosis in patients with SLE in a prospective analysis. Reduction of HCQ dosing, as suggested by the American Academy of Ophthalmologists (2), could reduce or eliminate the benefit of hydroxychloroquine to prevent thrombosis.

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OP0161

ASSOCIATION OF BASELINE CYTOTOXIC GENE EXPRESSION WITH USTEKINUMAB RESPONSE IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic Lupus Erythematous (SLE) is a clinically and biologically diverse disease, for which only one new therapy has been approved in the past 60 years. In a phase 2 trial on patients with mild-to-moderate SLE, ustekinumab (UST) improved clinical and laboratory measures of disease activity compared with placebo (PBO).[1]

Objectives: We previously reported an association of IFN-γ reduction with response to UST,[2] suggesting an impact on the IL12/Th1 axis. To extend these findings, we performed unbiased transcriptomic analysis from baseline whole blood samples to identify genes that discriminate UST responders (UST-R) from non-responders (UST-NR) using the primary endpoint of Systemic Lupus Erythematosus Responder Index (SRI)-4 at week 24 to define response.

Methods: UST was studied in a Ph2 PBO-controlled study of 102 patients with seropositive SLE and active disease despite standard therapy. Patients were randomized 3:2 to receive IV UST 6 mg/kg or placebo followed by subcutaneous injections of UST 90 mg or PBO every 8 weeks. Whole blood gene expression at baseline was measured via microarray using RNA samples from 100 patients, as samples from 2 patients failed quality control. An unbiased approach was used to identify gene signatures present at baseline that associate with UST response. Recombinant IL-12 or IL-23 was incubated *in vitro* with whole blood from 6 healthy donors for 24h and RNA-Seq was performed to determine the effect of these treatments on representative genes comprising the UST response signature.

Results: A non-biased machine learning algorithm identified a 9-gene whole blood signature composed primarily of cytotoxic cell-associated transcripts (PRF1, KLRD1, GZMH, NKG7, GNLY, FGFBP2, TRGC2, TARP, TRGV2) that was enriched at baseline in UST-R vs UST-NR. By Gene Set Variation Analysis, the cytotoxic signature enrichment in UST-NR was less at baseline than both UST-R and a healthy control cohort (P=0.0087, P=0.056, respectively), whereas UST-R cytotoxic gene enrichment was similar to healthy controls (P=0.31). No significant difference in cytotoxic signature enrichment was observed at baseline between PBO responders and PBO non-responders or healthy controls (Figure). Enrichment levels of the cytotoxic gene signature remained stable over time in PBO and UST-NR groups while a trend of decreased cytotoxic signature was observed in UST-R, although never reaching levels seen in UST-NR. To begin to understand the relationship between IL-12 and IL-23, the targets of UST, and the cytotoxic signature, whole blood was stimulated with these cytokines *in vitro*. Recombinant IL-12, but not IL-23, resulted in increased expression of representative members of this cytotoxic gene signature.

Conclusion: We identified a novel cytotoxic signature in baseline blood samples that associated with UST response in SLE. The observation that IL-12 can increase this signature *in vitro* and that IL-12 is a robust inducer of cytotoxic cell activity[3] as well as IFN-γ[3] suggests an important role of IL-12 blockade in the mechanism of action of UST in SLE.

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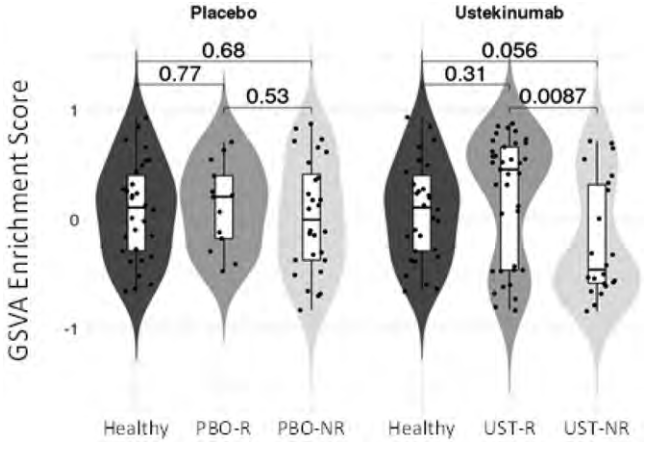


Figure.

Disclosure of Interests: Loqmane Seridi Employee of: Janssen Research & Development, LLC, Matteo Cesaroni Employee of: Janssen Research & Development, LLC, Matthew J Loza Employee of: Janssen Research & Development, LLC, Jessica Schreiter Employee of: Janssen Research & Development, LLC, Kristen Sweet Employee of: Janssen Research & Development, LLC, Yevgeniya Orlovsky Employee of: Janssen Research & Development, LLC, Spring House, PA, United States of America, Isabelle Baribaud Employee of: Janssen Research & Development, LLC, Ashley Orillion Employee of: Janssen Research & Development, LLC, Peter Lipsky Consultant of: Horizon Therapeutics, Ronald van Vollenhoven Grant/research support from: AbbVie, Amgen, Arthrogen, Bristol-Myers Squibb, GlaxoSmithKline (GSK), Janssen Research & Development, LLC, Lilly, Pfizer, Roche, and UCB, Consultant of: AbbVie, AstraZeneca, Biotest, Bristol-Myers Squibb, Celgene, Crescendo Bioscience, GSK, Janssen, Lilly, Medac, Merck, Novartis, Pfizer, Roche, UCB and Vertex, Speakers bureau: AbbVie, AstraZeneca, Biotest, Bristol-Myers Squibb, Celgene, Crescendo Bioscience, GlaxoSmithKline, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, UCB, Vertex, Bevra H. Hahn Grant/research support from: Janssen Research & Development, LLC, George Tsokos Grant/research support from: Janssen Research & Development, LLC, Marc Chevrier Employee of: Janssen Research & Development,

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OP0162

ABATACEPT TREATMENT FOR PATIENTS WITH EARLY ACTIVE PRIMARY SJÖGREN'S SYNDROME: OPEN-LABEL EXTENSION PHASE OF A RANDOMIZED CONTROLLED PHASE III TRIAL

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Background: Abatacept (CTLA-4-Ig) targets the CD80/CD86:CD28 co-stimulatory pathway required for full T-cell activation and T-cell dependent activation of B-cells. The Abatacept Sjögren Active Patients phase III (ASAPIII) trial is a mono-center, investigator-initiated, placebo controlled study with an open-label extension phase (NCT02067910), which assessed the efficacy and safety of weekly subcutaneous abatacept (125mg) in patients with early active primary Sjögren's syndrome (pSS). Previous analyses of the double blind phase showed no significant effect of abatacept treatment compared to placebo on the primary endpoint, difference in EULAR Sjögren's syndrome disease activity index (ESSDAI) at week 24.[1]

Objectives: To evaluate the efficacy and safety of extended (48 weeks) open label abatacept treatment in pSS patients.

Methods: Included patients had biopsy-proven pSS, fulfilled the AECG and ACR-EULAR criteria, had disease duration ≤7 years (median 2 years), ESSDAI ≥5, and 89% were anti–SSA positive. All 40 patients who received abatacept (ABA) in week 0-24 were subsequently treated with abatacept from week 24-48. Of the 40 patients who received placebo (PLB) in week 0-24, 2 were lost to follow up, and 38 were treated with abatacept from week 24-48. Systemic disease activity (ESSDAI), patient reported symptoms (ESSPRI), serological outcomes (RF and IgG), ocular staining score (OSS) and unstimulated whole salivary flow (UWS) were assessed. We evaluated whether outcomes improved within treatment groups, from week 0 to subsequent visits and from week 24 to subsequent visits:

1. Within ABA→ABA treated patients:
a. Week 0-48 to assess overall efficacy.
b. Week 24-48 to assess additional efficacy of long term treatment.
2. Within PLB→ABA treated patients:
a. Week 0-24 to assess whether a placebo effect occurred.
b. Week 24-48 to assess short-term efficacy of open label ABA.

GEE modeling was used to test significance of changes over time. Missing data were not imputed.

Results: ESSDAI and ESSPRI were improved within ABA/ABA patients between week 0-48 with additional efficacy after week 24, and within PLB/ABA patients after switching to ABA. Significant decreases in ESSDAI and ESSPRI were also seen within PLB treated patients between week 0-24 (Figure 1). IgG and RF were improved within ABA/ABA patients between week 0-48 with additional efficacy after week 24, and within PLB/ABA patients after switching to ABA. OSS was improved within ABA/ABA treated patients between week 0-48. UWS only showed significant improvement in week 36 within ABA/ABA treated patients. No changes in IgG, RF, OSS or UWS were seen within PLB treated patients. No deaths occurred. One serious adverse event possibly related to intervention occurred during ABA treatment.

Conclusion: ESSDAI and ESSPRI improved significantly during 48-week treatment with abatacept. Placebo treated patients also showed significant improvement in both indices and further improvement occurred after switching to abatacept. Biological activity was decreased by abatacept treatment. 48-week abatacept treatment improved OSS, and might improve UWS. Abatacept was well tolerated by pSS patients.

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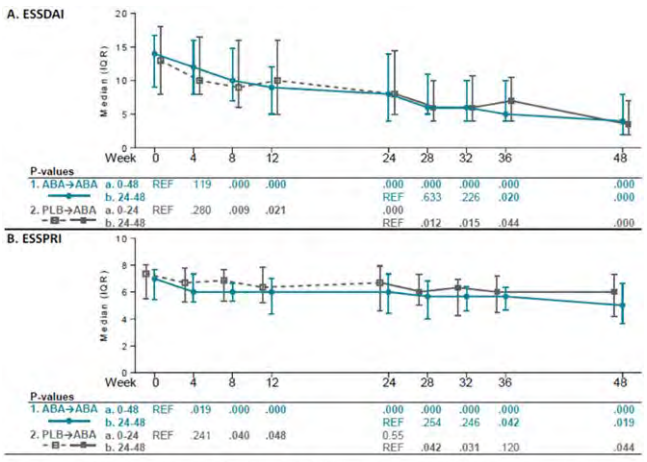


Figure 1. ESSDAI (A) and ESSPRI (B) during ABA/ABA treatment and PLB/ABA treatment in pSS

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OP0163

2019 UPDATE OF THE JOINT EUROPEAN LEAGUE AGAINST RHEUMATISM AND EUROPEAN RENAL ASSOCIATION–EUROPEAN DIALYSIS AND TRANSPLANT ASSOCIATION (EULAR/ERA-EDTA) RECOMMENDATIONS FOR THE MANAGEMENT OF LUPUS NEPHRITIS

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Background: Up to 40% of systemic lupus erythematosus (SLE) patients develop kidney disease, which represents a major cause of morbidity.

Objectives: To update the 2012 EULAR/ERA-EDTA recommendations for the management of lupus nephritis (LN).

Methods: We followed the EULAR standardised operating procedures for the publication of treatment recommendations. Delphi-based methodology led to 15 questions for systematic literature review (SLR), which was undertaken by three fellows.

Results: The changes include recommendations for treatment targets, use of glucocorticoids and calcineurin inhibitors (CNI), and management of

end-stage-kidney-disease (ESKD). The target of therapy is complete response (proteinuria <0.5-0.7gr/24h with [near-]normal glomerular filtration rate) by 12 months, but this can be extended in patients with baseline nephrotic-range proteinuria. Hydroxychloroquine is recommended with regular ophthalmological monitoring. In active proliferative LN, initial (induction) treatment with mycophenolate mofetil (MMF 2-3g/day, or mycophenolic acid at equivalent dose) or low-dose intravenous cyclophosphamide (CY; 500mg x6 biweekly doses), both combined with glucocorticoids (pulses of intravenous methylprednisolone, then oral prednisone 0.3-0.5mg/kg/day) is recommended. MMF/CNI (especially tacrolimus) combination and high-dose CY are alternatives, for patients with nephrotic-range proteinuria and adverse prognostic factors. Subsequent long-term maintenance treatment with MMF or azathioprine should follow, with no or low-dose (<7.5 mg/day) glucocorticoids. The choice of agent depends on the initial regimen and plans for pregnancy. In non-responding disease, switch of induction regimens or rituximab are recommended. In pure membranous LN with nephrotic-range proteinuria or proteinuria >1g/24h despite renin-angiotensin-aldosterone blockade, MMF in combination with glucocorticoids is preferred. Assessment for kidney and extra-renal disease activity, and management of comorbidities is lifelong with repeat kidney biopsy in cases of incomplete response or nephritic flares. In ESKD, transplantation is the preferred kidney replacement option with immunosuppression guided by transplant protocols and/or extra-renal manifestations.

Conclusion: The updated recommendations intend to inform rheumatologists, nephrologists, patients, national professional societies, hospital officials, social security agencies and regulators about the treatment of LN based on most recent evidence.

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OP0164

BLISS-LN: A RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE 3 TRIAL OF INTRAVENOUS BELIMUMAB IN PATIENTS WITH ACTIVE LUPUS NEPHRITIS

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Background: Lupus nephritis (LN), a serious manifestation of systemic lupus erythematosus (SLE), affects nearly 70% of patients (pts) in high-risk groups. To preserve renal function, LN requires fast and effective treatment. Despite medical advances, progression rates at 15 years to end-stage renal disease (ESRD) remain >40% for pts with diffuse proliferative LN. Belimumab (BEL), approved in pts aged ≥5 years with active SLE, improved renal parameters in pts with baseline renal involvement in a *post hoc* analysis of Phase 3 trials data.

Objectives: To assess efficacy and safety of intravenous (IV) BEL vs placebo (PBO), plus standard therapy (ST), in pts with active LN.

Methods: BLISS-LN is a Phase 3, randomised, double-blind, PBO-controlled, 104-week study (GSK Study BEL114054, NCT01639339). Adults with SLE and biopsy-proven LN (class III, IV, and/or V) were randomised (1:1) to monthly BEL 10 mg/kg IV or PBO, plus ST. Primary endpoint: Primary Efficacy Renal Response (PERR); defined as urine protein creatinine ratio [uPCR] ≤0.7; estimated glomerular filtration rate [eGFR] within 20% of the pre-flare value or ≥60 ml/min/1.73m^2; no rescue therapy) at Week (Wk) 104. Key secondary endpoints: Complete Renal Response (CRR; defined as uPCR <0.5; eGFR within 10% of the pre-flare value or ≥90 ml/min/1.73m^2; no rescue therapy) at Wk 104; PERR at Wk 52; time to renal-related event (defined as ESRD/doubling of serum creatinine/renal worsening/renal disease-related treatment failure) or death. Other endpoints: time to PERR/CRR sustained through Wk 104; SLEDAI-S2K score <4 points at Wk 104; safety.

Results: Overall, 448 pts were randomised (efficacy: 223/group; safety: 224/group). Significantly more BEL (43%) than PBO (32.3%) pts achieved PERR at Wk 104 (OR 1.55, 95% CI 1.04, 2.32; p=0.0311). More BEL than PBO pts achieved key secondary and other efficacy endpoints (Table).

Overall, 214 (95.5%) BEL and 211 (94.2%) PBO pts had ≥1 adverse event (AE); 58 (25.9%) BEL and 67 (29.9%) PBO pts had ≥1 serious AE; 29 (12.9%) pts in each group had ≥1 AE resulting in study treatment discontinuation; 4 (1.8%) BEL and 3 (1.3%) PBO pts developed on-treatment fatal AEs.

Conclusion: In the largest LN study to date, data from BLISS-LN demonstrate that BEL plus ST significantly improves LN renal responses compared with ST alone with a favourable safety profile.

Study funding: GSK.

Table.

Endpoint, n (%)	PBO (n=223)	BEL (n=223)	OR/HR (95% CI) vs PBO	p-value
CRR at Wk 104*	44 (19.7)	67 (30.0)	OR 1.74 (1.11, 2.74)	0.0167
PERR at Wk 52*	79 (35.4)	104 (46.6)	OR 1.59 (1.06, 2.38)	0.0245
Time to PERR through Wk 104†	72 (32.3)	96 (43.0)	HR 1.46 (1.07, 1.98)	0.0157
Time to CRR through Wk 104†	44 (19.7)	67 (30.0)	HR 1.58 (1.08, 2.31)	0.0189
Time to renal-related event or death†	63 (28.3)	35 (15.7)	HR 0.51 (0.34, 0.77)	0.0014
SLEDAI-S2K score <4 points at Wk 104*	41 (18.4)	62 (27.8)	OR 1.76 (1.11, 2.78)	0.0164

*PBO and BEL columns represent the n (%) responders

†Data presented as n (cumulative incidence)

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OP0165

LONG-TERM OUTCOME OF A RANDOMIZED CONTROLLED TRIAL COMPARING TACROLIMUS WITH MYCOPHENOLATE MOFETIL AS INDUCTION THERAPY OF SEVERE LUPUS NEPHRITIS

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Background:
Objectives: To report the 10-year outcome of a cohort of patients with lupus nephritis (LN) treated with combined glucocorticoids with either mycophenolate mofetil (MMF) or tacrolimus (TAC) as induction in a randomized controlled trial (RCT).
Methods: 150 patients with active lupus nephritis were randomized to receive either MMF (2-3g/day) (N=76) or TAC (0.1-0.06mg/kg/day) (N=74) in combination with high-dose prednisolone (0.6mg/kg/day for 6-8 weeks and tapered) as induction therapy between 2005 and 2012. Complete renal (CR) or good partial renal responders were switched to azathioprine (AZA) (2mg/kg/day) for maintenance. We hereby report the 10-year outcomes of the patients in terms of renal flares (proteinuric/nephritic), renal function decline (drop in eGFR by ≥30% from baseline), development of chronic kidney disease (CKD) stage 4/5 (eGFR<30ml/min) and mortality. Factors affecting renal prognosis were studied by Cox regression analysis. Renal parameters (urine P/Cr ratio [uPCr], eGFR) at different time points from 6 to 24 months were studied for their predictive value of a poor renal prognosis by ROC analysis.
Results: 150 patients (92% women) with active LN were studied (ISN/RPS class III±V 36%; IVG/S±V 46%; pure V 19%). The mean age was 35.5±12.8 years and SLE duration was 50.2±62 months. The mean histological activity and chronicity score was 8.2±3.4 and 2.6±1.6, respectively. At baseline, 59(39%) patients were hypertensive, 62(41%) had active urinary casts, 112(75%) had microscopic hematuria and 67% patients had eGFR<90ml/min. As reported previously, the rate of complete renal response (CR) was 59% in the MMF and 62% in the TAC group (p=0.71). Maintenance therapy with AZA was given to 79% patients. After a follow-up of 118.2±42 months, proteinuric and nephritic renal flares occurred in 34% and 37% of patients treated initially with MMF and 53% and 30% in those treated with TAC, respectively. There was a total of 77 renal flares in 43 (57%) patients treated with MMF (0.11/patient-year) and 92 renal flares in 46 (62%) of patients treated with TAC (0.12/patient-year; p=0.44). The cumulative risk of having a renal flare of patients treated with MMF/AZA was 28% at 3 years, 42% at 5 years and 58% at 10 years, whereas the corresponding figures for patients treated with TAC/AZA was 32% at 3 years, 53% in 5 years and 66% in 10 years (p=0.43). For those who achieved CR after induction therapy, the mean time to first renal flare was 70.4±47.1 months in the MMF group and 65.2 ±50 months in the TAC group (p=0.61). The cumulative incidence of a composite outcome of decline of eGFR by ≥30%, development of CKD stage 4/5 or death at 5 and 10 years was 24% and 33%, respectively, in patients treated with MMF, and 17% and 33%, respectively, in those treated with TAC (p=0.90). Factors significantly associated with this outcome were first time lupus nephritis (HR 0.26[0.11-0.59]; p=0.001), uPCR at 6 months (HR 1.33[1.02-1.76]; p=0.04) and eGFR at 6 months (HR 0.98[0.97-0.997]; p=0.02). Exploratory ROC analysis demonstrated that an eGFR cut-off of 80ml/min (AUC 0.70; sensitivity 0.64, specificity 0.66) and uPCR cut-off of 0.75 (AUC 0.73; sensitivity 0.69, specificity 0.74) at month 18 best predicted CKD stage 4/5 or decline of eGFR by ≥30%.
Conclusion: Long-term data of our RCT showed that TAC remained non-inferior to MMF as induction therapy of LN in terms of renal flares, renal function decline and mortality. Relapsed renal disease, lower eGFR and more proteinuria post-induction therapy were associated with a poorer outcome. An uPCR ≤0.75 and eGFR of >80ml/min at 18 months best predicted a better outcome at 10 years, and should be considered as a target for induction/consolidation therapy.
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Disclosure of Interests: None declared
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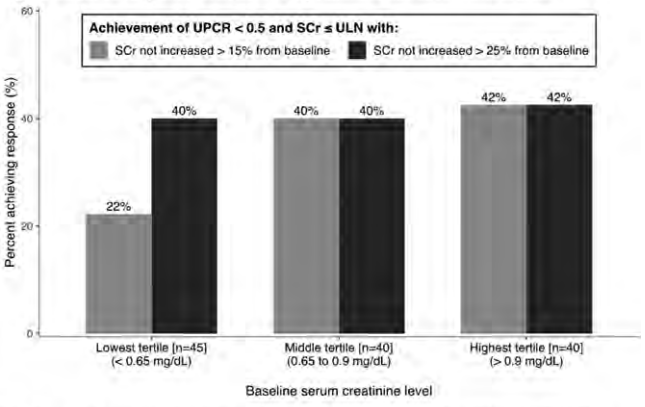
OP0166

ALTERNATIVE RENAL RESPONSE DEFINITIONS IN A RANDOMIZED, CONTROLLED TRIAL OF OBINUTUZUMAB FOR PROLIFERATIVE LUPUS NEPHRITIS

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Background: Obinutuzumab, a type II anti-CD20 mAb, resulted in rapid and complete B-cell depletion and improved renal responses in proliferative lupus nephritis (LN) in the Phase 2 NOBILITY trial and will be further evaluated in the Phase 3 REGENCY trial. Recent analyses suggest alternative urinary sediment, serum creatinine (SCr), and urine protein/creatinine ratio (UPCR) requirements may be better measures of response in LN than those used in NOBILITY [1,2].
Objectives: To evaluate the NOBILITY response definitions and to report the results of NOBILITY using alternative definitions of renal response.
Methods: 126 patients with active Class III/IV LN were randomized to obinutuzumab or placebo in combination with mycophenolate and glucocorticoids. NOBILITY complete renal response (CRR) required UPCR < 0.5, SCr ≤ the upper limit of normal (ULN) of the reference laboratory and not increased > 15% from baseline SCr, and inactive urinary sediment. Exploratory analyses were conducted, and alternative response definitions were evaluated post hoc.
Results: NOBILITY CRR was increased with obinutuzumab over placebo at Week 52 (35% vs. 23%, P = 0.11) and Week 76 (40% vs. 18%, P = 0.007). Response rates were low among patients with baseline SCr < 0.65 mg/dL (n = 45) due to the requirement that SCr not increase > 15% from baseline; increasing this threshold to 25% increased the response rate to a level similar to other groups (Figure). Alternative response definitions demonstrated increased rates of response in both treatment groups and similar benefits of obinutuzumab over placebo at Weeks 52 and 76 (Table).
Conclusion: Obinutuzumab resulted in consistent treatment benefits across a range of renal response definitions in NOBILITY and will be further evaluated in REGENCY. A requirement that SCr not increase > 15% from baseline may be overly restrictive in patients with low baseline SCr (< 0.65 mg/dL), where a change of 15% represents < 0.1 mg/dL and is of questionable clinical relevance. These findings may inform LN clinical trial design and more accurately reflect clinical practice.
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Figure. Week 76 response in NOBILITY by baseline serum creatinine level



UPCR, urine protein/creatinine ratio; SCr, serum creatinine; ULN, upper limit of normal.

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Table. Data from NOBILITY at weeks 52 and 76 using several response definitions

Definition of response	Week 52			Week 76		
	OBI (n = 63)	PBO (n = 62)	Diff.	OBI (n = 63)	PBO (n = 62)	Diff.
NOBILITY complete response UPCR < 0.5, SCr ≤ ULN and not increased > 15% from baseline SCr, and < 10 RBC/hpf without casts	35%	23%	12%*	40%	18%	22%**
REGENCY complete response UPCR < 0.5, SCr ≤ ULN and not increased > 25% from baseline SCr	43%	29%	14%*	54%	31%	23%**
UPCR < 0.8 only	64%	48%	15%*	64%	47%	17%*
UPCR < 0.8 with SCr requirement UPCR < 0.8 and SCr ≤ ULN or not increased > 15% from baseline SCr	60%	48%	12%*	64%	45%	18%**
NOBILITY overall response CRR or ≥ 50% reduction in UPCR[a] with SCr not increased > 15% from baseline and urinary RBCs not increased > 50% from baseline	56%	36%	20%**	51%	29%	22%**
REGENCY overall response CRR or ≥ 50% reduction in UPCR[a] with SCr not increased > 25% from baseline	68%	45%	23%**	67%	50%	17%**

OBI, obinutuzumab; PBO, placebo.

* P < 0.2 vs. placebo group. ** P < 0.05 vs. placebo group.

[a] ≥ 50% reduction in UPCR to a value < 1 (< 3 if the baseline UPCR was ≥ 3). All response definitions required no use of rescue medications or early withdrawal.

OP0167

SUCCESSFUL WITHDRAWAL OF MYCOPHENOLATE MOFETIL IN QUIESCENT SLE: RESULTS FROM A RANDOMIZED TRIAL

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Background: Trials and clinical observations have demonstrated the efficacy of mycophenolate mofetil (MMF) for SLE treatment. Long-term use of MMF is associated with adverse events, pregnancy risks, drug monitoring, and increased cost. Current management continues therapy indefinitely. Whether immunosuppression may be safely withdrawn or whether risks of withdrawal outweigh the benefits of continuation is unknown.

Objectives: To compare rates of clinically significant disease reactivation (CSDR), major flares, and all flares in patients with quiescent SLE on stable MMF randomized to maintain or withdraw MMF. The goal is to provide guidance for clinicians and patients on the risks of MMF withdrawal.

Methods: Adults with quiescent SLE (SELENA-SLEDAI without serologies <4) receiving MMF for ≥2 years for nephritis or ≥ 1 year for non-nephritis were randomized 1:1 to unblinded MMF (maintenance arm, MA) or to a 12-week taper off MMF (withdrawal arm, WA) and followed through 60 weeks. Subjects were on stable hydroxychloroquine; steroids limited to ≤ 10 mg. CSDR, defined as a SLEDAI flare requiring immunosuppression, BILAG flares and adverse events were assessed. Event rates and time to flare were compared using Kaplan-Meier.

Results: 102 subjects were randomized (50 MA, 52 WA); 1 subject in each arm was ineligible and 10 terminated early (7 MA, 3 WA). Mean disease duration was 13 years; 76% had a history of nephritis; mean baseline SLEDAI was 2.2. 5 MA subjects (10%) had CSDR, compared to 9 WA (17%). Median time to CSDR was 38 weeks in both arms. BILAG A flares occurred in 1MA subject (pancreatitis) vs. 4 WA (cranial neuropathy, panniculitis, 2 nephritis). Kaplan-Meier curves overlapped for CDSR, BILAG A flares, and all SLEDAI flares (Figure). Based on these data, we are 86% confident that the increased risk of CDSR with MMF withdrawal is less than 15% over 60 weeks. AEs were similar between groups; infections occurred more commonly in MA (63 vs. 49).

Conclusion: In this cohort of subjects with quiescent SLE on long term MMF serious flares occurred infrequently in subjects continuing or withdrawing MMF without differences in time to flare. MMF withdrawal may be considered in subjects with prolonged quiescent disease.

Table 1. Baseline and Demographic Characteristics

	Maintenance arm	Withdrawal arm	Total
Randomized	50	52	102
Female, n (%)	39 (78)	47 (90)	86 (84)
White, n (%)	25 (50)	19 (37)	44 (43)
Black, n (%)	19 (38)	22 (42)	41 (40)
Hispanic/Latino, n (%)	10 (20)	12 (23)	22 (22)
Age, Years, mean (SD)	42.4 (12.9)	41.6 (12.5)	42.0 (12.6)
Disease Duration, Years, mean (SD)	13.6 (8.2)	12.2 (7.9)	12.9 (8.0)
H/O Lupus Nephritis, n (%)	40 (80)	38 (73)	78 (76.5)
On Baseline Steroids, n (%)	18 (36)	23 (44)	41 (40)
Prednisone Dose, mg, mean (SD)	4.8 (2.7)	3.3 (1.7)	4.0 (2.3)
MMF Duration, Years, mean (SD)	6.8 (4.3)	6.4 (4.3)	6.6 (4.3)
Baseline MMF Dose, mg, mean	1,612	1,668	1,640
SELENA-SLEDAI*, mean (SD)	2.4 (1.76)	1.9 (1.76)	2.2 (1.77)
Positive DsDNA, n (%)	35 (70)	27 (52)	62 (61)
Low C3[1], n (%)	14 (28)	9 (17)	23 (23)
Low C4[1], n (%)	6 (12)	5 (10)	11 (11)

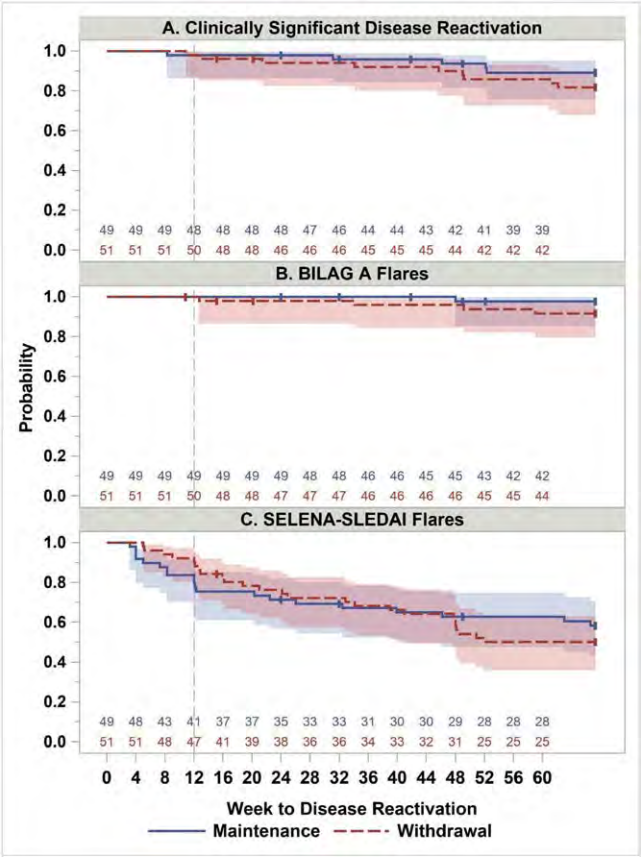


Figure. Kaplan-Meier Estimates of Flare Endpoints

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C Kalunian: None declared, Cynthia Aranow: None declared, Megan Clowse Grant/research support from: GSK, Pfizer, Consultant of: UCB, Astra-Zeneca, Speakers bureau: UCB, Ellen Goldmuntz: None declared, Jessica Springer: None declared, Lynette Keyes-Elstein: None declared, Bill Barry: None declared, Ashley Pinckney: None declared, Judith James: None declared
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Crystals and bones: A selection of best abstracts

OP0168 CARDIOVASCULAR EVENT ASSOCIATED WITH INITIATING ALLOPURINOL AND FEBUXOSTAT - ACUTE GOUT ATTACK AND CARDIOVASCULAR GOUT ATTACK

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Background: When serum uric acid rapidly increases or decreases due to such as alcohol consumption or fasting, free urate crystals are formed, which induce an acute joint inflammation referred to as an acute gout attack. In 86.4% of patients with gout, dual energy computed tomography demonstrated the deposition of urate crystals in vasculature, and urate crystals have been observed in coronary arteries and various tissues in 10.9% of patients with a heart transplant. However, whether hyperuricemia and urate crystal directly cause cardiovascular disease is not well known. We previously reanalyzed the CARES trial to calculate the mortality rates based on the median duration of exposure to study drugs and the median follow-up duration. A sharp increase in mortality was observed after allopurinol and febuxostat were discontinued. Even in view of the Sick-Stopper Effect, for about 40-fold increase in mortality following drug discontinuation, we postulated that the sharp increase in mortality may be associated with rapid changes in uric acid level (rebound hyperuricemia), and that withdrawal of hypouricemic agent leads to an acute inflammatory response due to an abrupt increase in serum uric acid level with subsequent free urate crystal formation in the cardiovascular system (cardiovascular gout attack)(1).
Objectives: Based on this hypothesis that some cardiovascular events may be cardiovascular gout attacks, we investigated the association between the cardiovascular event and initiation of hypouricemic agent, when is accompanied by acute gout attack and/or fluctuation of uric acid, in gout patients.
Methods: Using the Korean National Health Insurance Service (KNHIS) database, which covers the entire Korean population, we conducted a population-based cohort study among gout patients who initiated allopurinol or febuxostat between 2012 and 2018. The initiators were defined as those who had no prior dispensing of any urate-lowering therapy for at least 60 months before the first dispensing date (i.e. index date) of either allopurinol or febuxostat. We excluded patients with a diagnosis of cancer and patients treated with benzbromarone. We investgated a composite cardiovascular event of hospitalized myocardial infarction, ischemic stroke, and cerebral hemorrhage.
Results: We identified hospitalizations for cardiovascular event (acute myocardial infarction (n = 3538), cerebral infarction (n = 5127), and cerebral hemorrhage (n = 1593)) that occurred within 2 year before and 2 year after initiation of allopurinol or febuxostat. Of these, 4333 cardiovascular event (0.014 per person-time, 95% confidence interval [CI], 0.014 to 0.015) occurred in 2 years before initiation of allopurinol or febuxostat, 1032 cardiovascular event (0.081 per person-time, 95% confidence interval [CI], 0.076 to 0.086) occurred in 30 days before initiation of allopurinol or febuxostat. And, 83 cardiovascular event (0.030 per person-time, 95% CI, 0.024 to 0.037) occurred in 7 days after initiation of allopurinol or febuxostat. (Figure)

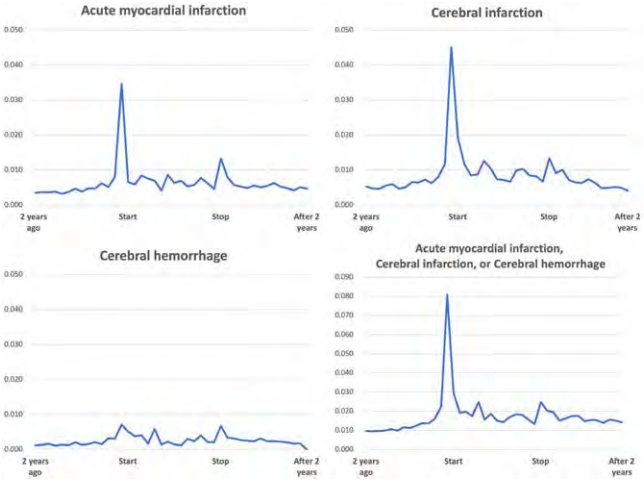


Figure. The cardiovascular event in gout patients who initiated and discontinued allopurinol and febuxostat.

Conclusion: Initiation of febuxostat and allopurinol was significantly associated with acute myocardial infarction, cerebral infarction, and cerebral hemorrhage. Considering that allopurinol and febuxostat usually are initiated a few weeks after a acute gout attack. Acute gout attack and/or fluctuation of uric acid level might be significantly associated with cardiovascular event. Some of cardiovascular events might be cardiovascular gout attack.
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Disclosure of Interests: None declared
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OP0169 AMPUTATION PROCEDURES IN PATIENTS WITH GOUT COMPARED TO PATIENTS WITH DIABETES

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Background: Gout is the most common inflammatory arthritis in the United States (U.S.) and is associated with specific comorbidities, including hypertension, renal disease, cardiovascular disease, hyperlipidemia, and metabolic syndrome (1). This set of comorbidities is known for carrying an increased risk of macrovascular complications (e.g., myocardial infarction, stroke) and peripheral limb problems (e.g., skin ulcers, amputations). Diabetics are known to have an elevated risk of undergoing ulcer and amputation procedures, which have been shown to increase morbidity and mortality in this population (2,3). It is currently not known if patients with gout have an elevated independent risk for limb amputations or whether gout potentiates amputation rates in patients with diabetes.
Objectives: To assess and compare the rate of amputation procedures conducted in patients with gout, diabetes, both gout and diabetes, and neither gout nor diabetes.
Methods: In September 2019, a large U.S. claims database (includes data from 190 million patients over 7 years, TriNetX "Diamond" network) was used to determine amputation rates in patients with gout and diabetes. TriNetX only provides aggregate data and statistical summaries of de-identified patient information. Initial cohorts were developed to understand the amputation rate in patients with gout, regardless of diabetes comorbidity (n=4,467,721), and the amputation rate in patients with diabetes, regardless of gout comorbidity (n=25,972,726). Subsequently, the following four cohorts were constructed to isolate these two diseases: 1) presence of gout without diabetes (n=2,471,430), 2) presence of diabetes without gout (n=23,976,435), 3) presence of both gout and diabetes (n=1,996,291), and 4) absence of both gout and diabetes (control cohort, n=144,705,645). Demographic features of these groups were tabulated and amputation (foot, toes, hand, fingers) rates were calculated using procedural codes reported in each group.
Results: The overall rate of amputations in patients with gout (0.434%) was similar to the amputation rate in patients with diabetes (0.484%). However, when separating these patients into distinct, non-overlapping cohorts, the amputation rate in patients with gout but not diabetes (0.162%) differed from the rate in patients with diabetes but not gout (0.461%). The control population (no gout or diabetes) had an amputation rate of 0.035%. Unexpectedly, patients with both gout and diabetes had an amputation rate of 0.770%, the highest of all groups examined.
Conclusion: Gout is increasingly being linked to unfavorable cardiovascular, renal, and metabolic complications. Our analysis showed that having gout also increased the likelihood of undergoing an amputation procedure. Patients with gout but not diabetes suffered an approximately 3-fold increase in amputations compared to patients without either disease. Additionally, patients with both gout and diabetes had a notably increased risk of amputation compared to patients with only diabetes (no gout). Because amputations are an unfavorable outcome associated with procedural complication risk and long-term sequelae, this apparent increased risk of amputation in patients with gout warrants further exploration.
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Disclosure of Interests: Brian LaMoreaux Shareholder of: Horizon Therapeutics, Employee of: Horizon Therapeutics, Megan Francis-Sedlak Shareholder of: Horizon Therapeutics, Employee of: Horizon Therapeutics, Robert Holt Shareholder of: Horizon Therapeutics, Employee of: Horizon Therapeutics
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OP0171 MENDELIAN RANDOMIZATION SHOWS NO CAUSAL ASSOCIATION BETWEEN SERUM URATE OR GOUT AND TYPE-2 DIABETES

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Background: Positive associations between gout[1,2] or serum urate (SU)[3] and risk of type-2 diabetes (T2D) have been reported in population-based observational studies, but may be due to residual confounding. As such, causal roles of SU and gout on development of T2D are unclear.
Objectives: Use two-sample mendelian randomization to estimate the causal effects of SU and gout on T2D and glycemic traits.
Methods: Aggregate data from three large genome-wide association studies were used to identify genetic variants (SNPs) associated with the exposures and outcomes. Exposure SNPs were sourced from Global Urate Genetics Consortium (> 140,000 individuals); outcome SNPs sourced from DIAbetes Genetics Replication And Meta-analysis consortium (DIAGRAM; > 34,000 T2D cases and > 114,000 controls) and Meta-Analyses of Glucose and Insulin-related traits Consortium (MAGIC; > 46,000 non-diabetics).
We analysed SNPs associated with SU levels (n=28) and gout (n=6) for associations with T2D and three glycemic traits (insulin resistance, fasting insulin levels, and HbA1c) using inverse variance weighted meta-analysis methods. We also specifically examined two SNPs mapping to the *SLC2A9* gene, which encodes the GLUT9 transporter (for glucose and urate), estimating Wald ratios for these individual SNPs. Analyses were performed with TwoSampleMR package in R and mRnd power calculator.
Results: Estimated effects of genetically-determined gout on each of the four outcomes (T2D, insulin resistance, fasting insulin levels, and HbA1c) were small and non-significant ($p \geq 0.18$), as were the effects of changes in genetically-determined SU levels (Table).
Although the two SNPs in the *SLC2A9* gene were strongly associated with SU (rs12498742: R^2=2.7%, beta=0.37 per mg/dL, $p < 10^{-700}$) and gout (rs4475146: odds ratio=0.63, $p=4.1x10^{-26}$), neither was associated with T2D nor any of the glycemic traits (**Table**).
Applying R^2 values ≥ 1.9%, we had ≥ 90% power to detect the increased odds of T2D (OR ≥1.15[1,3]) from observational studies.

All Risk SNPs (meta-analysis)

OUTCOME	n SNPs	Gout (vs. non-gout)		Serum urate (per 1 mg/dL increase)	
		Effect size (95% CI)	p	Effect size (95% CI)	p
HbA1c (%)	45	0.0046 (-0.0087 to 0.0179)	0.50	-0.0046 (-0.0275 to 0.0183)	0.70
Insulin resistance (HOMA-IR: log units)	45	0.0108 (-0.0049 to 0.0265)	0.18	0.0016 (-0.0240 to 0.0272)	0.90
Fasting insulin levels (log pmol/L)	18	0.0046 (-0.0037 to 0.0129)	0.28	-0.0221 (-0.1035 to 0.0593)	0.59
Type 2 Diabetes: odds ratio	43	0.98 (0.90 to 1.07)	0.72	1.01 (0.88 to 1.16)	0.84

SNPs in *SLC29A* Gene (single-SNP analysis)

OUTCOME	**rs4475146 Gout (vs. non-gout)**		**rs12498742 Serum urate (per 1 mg/dL increase)**	
	Effect size (95% CI)	**p**	**Effect size (95% CI)**	**p**
HbA1c (%)	0.0032 (-0.0139 to 0.0203)	0.71	0.0005 (-0.0205 to 0.0216)	0.96
Insulin resistance (HOMA-IR: log units)	0.0128 (-0.0073 to 0.0328)	0.21	0.0126 (-0.0121 to 0.0373)	0.32
Fasting insulin levels (log pmol/L)	0.0038 (-0.0070 to 0.0147)	0.49	0.0048 (-0.0088 to 0.0185)	0.49
Type 2 Diabetes: odds ratio	0.98 (0.87 to 1.10)	0.70	0.98 (0.85 to 1.13)	0.75

HOMA-IR=homeostasis model assessment of insulin resistance

Conclusion: Evidence from this instrumental variable analysis suggests gout and SU are signals for future T2D, but neither SU or gout itself are causally associated with the development of this condition. As such, interventions targeting SU levels alone are unlikely to lower the risk of T2D.
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Disclosure of Interests: Natalie McCormick: None declared, Jeewoong Choi: None declared, Shelby Marozoff: None declared, Hyon Choi Grant/research support from: HC reports research support from Ironwood and Horizon, Consultant of: HC reports consulting fees from Ironwood, Selecta, Horizon, Takeda, Kowa, and Vaxart.
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OP0172 EFFECT OF WEIGHT LOSS AND LIRAGLUTIDE ON SERUM URATE LEVELS AMONG OBESE KNEE OSTEOARTHRITIS PATIENTS: SECONDARY ANALYSIS OF A RANDOMISED CONTROLLED TRIAL

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Background: There is a strong association between gout and obesity. Lowering urate is the cornerstone of gout management [1] and urate levels correlate strongly with central obesity. Previous studies suggest that weight loss has a positive effect on serum urate, however, the studies are sparse and small [2].
Objectives: To assess the impact of an initial low-calorie diet-induced weight loss and subsequent randomisation to the body weight-lowering drug liraglutide (a glucagon-like peptide 1 receptor agonist) or placebo on serum urate levels.
Methods: In the LOSE-IT trial (NCT02905864), a randomised, double-blinded, placebo-controlled, parallel group, single-centre trial [3], 156 obese individuals with knee osteoarthritis, but without gout, were offered an initial 8-week intensive diet intervention (week -8 to 0) on Cambridge Weight Plan (800-1000 kcal/day) followed by a weight loss maintenance period in which participants were randomised to either liraglutide 3 mg/day or placebo for 52 weeks. We conducted a secondary analysis of blood samples collected at week -8, 0 and 52. The primary outcome measure was change in serum urate. We used paired t-test for the change from week -8 to 0, and for change from week 0 to 52 we used an ANCOVA model adjusted for stratification factors (sex, age category and obesity class), and the level of the outcome at baseline. Data were analysed as observed (i.e. no imputation of missing data).
Results: 156 individuals were randomised and 155 had blood samples taken at baseline. In the initial intensive diet intervention period (week -8 to 0) they lost a mean of 12.5 kg (95% CI -13.1 to -11.9, n 156). In the following 52 weeks, the liraglutide group lost an additional 4.1 kg (SE 1.2, n 71) whereas the control group was almost unchanged with a weight loss of 0.2 kg (SE 1.2, n 66). Looking at the main outcome of serum urate levels change, the initial intensive diet resulted in a mean decrease of 0.21 mg/dL (95% CI 0.35 to 0.07, n 155) for the entire cohort. In the following year (week 0 to 52) the liraglutide group exhibited a further mean decrease in serum urate of 0.48 mg/dL (SE 0.11, n 69), whereas the placebo group exhibited a slight decrease in mean serum urate of 0.07 mg/dL (SE 0.12, n 65) resulting in a significant between-group difference of -0.40 mg/dL (95% CI -0.69 to -0.12, n 134) – see Figure 1. Four participants in each group experienced serious adverse events; no deaths were observed.
Conclusion: This secondary analysis of the LOSE-IT trial suggests that liraglutide provides a potential novel serum urate lowering drug mechanism in obese patient populations, with potential implication for gout treatment.

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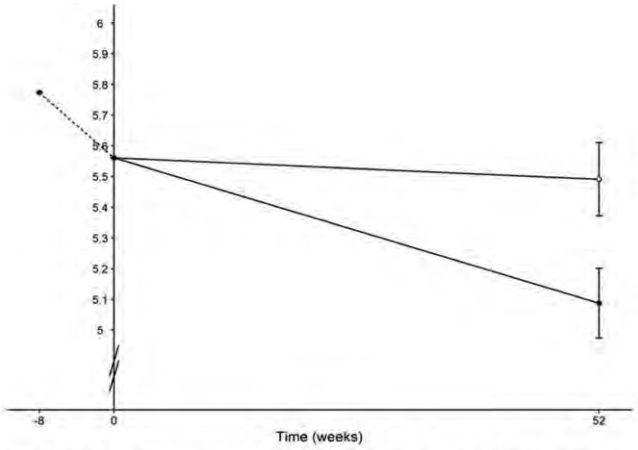


Figure 1: Serum urate at different timepoints: Estimates are unadjusted means at week -8 and 0 (dotted line; n=155) and least square means estimates from an ANCOVA model (adjusted for stratification factors, i.e. sex, age category, obesity class as well as the level of the outcome at baseline) for data at 52 weeks (solid lines; n=134). Solid points at week 52 indicate the liraglutide group (n=69) and open points indicate the placebo group (n=65). The error bars indicate SE.

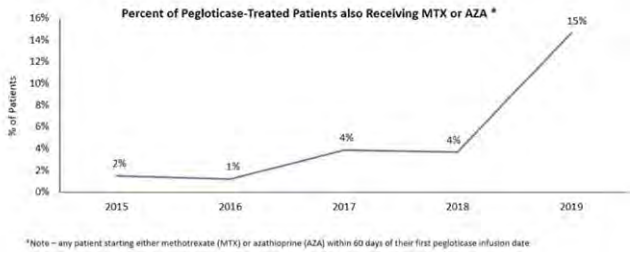
Disclosure of Interests: Kristian Zobbe: None declared, Sabrina Mai Nielsen: None declared, Robin Christensen: None declared, Anders Overgaard: None declared, henrik gudbergsen Speakers bureau: Pfizer 2016, Marius Henriksen: None declared, Henning Bliddal Grant/research support from: received research grant fra NOVO Nordic, Consultant of: consultant fee fra NOVO Nordic, Lene Dreyer: None declared, Lisa Stamp: None declared, Filip Krag Knop Shareholder of: Minority shareholder in Antag Therapeutics Aps, Grant/research support from: AstraZeneca, Gubra, Novo Nordisk, Sanofi and Zealand Pharma, Consultant of: Amgen, AstraZeneca, Boehringer Ingelheim, Carmot Therapeutics, Eli Lilly, MSD/Merck, Mundipharma, Novo Nordisk, Sanofi and Zealand Pharma., Speakers bureau: AstraZeneca, Bayer, Boehringer Ingelheim, Eli Lilly, MedImmune, MSD/Merck, Mundipharma, Norgine, Novo Nordisk, Sanofi and Zealand Pharma., Lars Erik Kristensen Consultant of: UCB Pharma (Advisory Board), Sannofi (Advisory Board), Abbvie (Advisory Board), Biogen (Advisory Board), Speakers bureau: AbbVie, Amgen, Biogen, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Forward Pharma, Janssen Pharmaceuticals, MSD, Novartis, Pfizer, and UCB Pharma
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OP0173 IMMUNOMODULATION CO-THERAPY WITH PEGLOTICASE: DATABASE TRENDS 2014-2019

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Background: Pegloticase is a PEGylated biologic therapy for patients with uncontrolled gout who have not improved on or could not tolerate conventional urate-lowering therapies.[1] All biologics have the ability to engender anti-drug antibodies (ADAs) and it is known that some patients given pegloticase develop ADAs that cause them to stop treatment prior to recieving a complete course of therapy.[2-3] In other rheumatic autoimmune diseases, DMARDs such as methotrexate or azathioprine are used as standard of care to prevent the development of ADAs to biologics. These DMARDs often allow patients to remain on biologic therapies longer and recieve the full therapeutic benefits while minimizing adverse events.[4] While pegloticase has been used traditionally as monotherapy, recent case series have demonstrated the therapeutic benefit of immunomodulator co-administration, allowing more patients to receive a full course of pegloticase therapy.[5-6] Little has been published on how widespread this practice is and whether it has changed over time.
Objectives: To examine medical claims database from 2014-2019 for trends in immunomodulating therapies being co-prescribed with pegloticase.
Methods: An IQVIA claims database (November 2014 to October 2019) representing 1.3 billion claims, covering 30 million patients diagnosed with gout or CKD, was utilized to search for patients who had received pegloticase. Patients who had recieved pegloticase were classified as having been on an immunomodulating co-therapy if they were prescribed methotrexate or azathioprine within 60 days before or after initiation of their first pegloticase infusion.
Results: We found relatively steady low rates of immunomodulation co-therapy with pegloticase from 2014 through 2018 ranging from 1% in 2016 to 4% in 2018 (Figure 1). In 2019 however, the proportion of pegloticase patients that were co-treated with methotrexate or azathioprine therapy increased to 15%. Most patients were started on immunomodulating therapy 20 days before to 10 days after initiation of pegloticase. Methotrexate was the more frequently used immunomodulaton co-therapy as compared to azathioprine.

Figure 1: Proportion of pegloticase patients receiving immunomodulation therapy by year



*Note – any patient starting either methotrexate (MTX) or azathioprine (AZA) within 60 days of their first pegloticase infusion date

Conclusion: We found evidence of a relatively dramatic increasing initiation of immunomodulation therapy with pegloticase beginning soon after a November 2018 presentation of a case series which demonstrated improved response rates of pegloticase when co-administered with methotrexate. These data indicate that clinicians began to more frequently employ a strategy of DMARD co-treatment with pegloticase in 2019 to improve response rates to this important gout medicine.
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Disclosure of Interests: Brian LaMoreaux Shareholder of: Horizon Therapeutics, Employee of: Horizon Therapeutics, Megan Francis-Sedlak Shareholder of: Horizon Therapeutics, Employee of: Horizon Therapeutics, Karl Svensson Shareholder of: Horizon Therapeutics, Employee of: Horizon Therapeutics, Robert Holt Shareholder of: Horizon Therapeutics, Employee of: Horizon Therapeutics
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OP0174 POLYDATIN PREVENTS CALCIUM PYROPHOSPHATE CRYSTAL-INDUCED ARTHRITIS IN MICE

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Background: Acute calcium pyrophosphate (CPP) crystal-induced inflammation is characterized by the massive release of cytokines and pro-inflammatory mediators and, from a clinical point of view, pain and limited joint function. Contrary to the precipitation of urate crystals that can be prevented through the use of hypouricemic drugs, there is no pharmacological therapy that can prevent the formation of pyrophosphate crystals.
Polydatin (PD),a natural precursor of resveratrol, is a stilbenoid mainly contained in grape juice and bark of Polygonum Cuspidate. Its antioxidant, anti-inflammatory and immunomodulating properties have been demonstrated in several experimental models. We have recently shown that this compound is able to prevent the inflammatory response to pathogenic crystals in vitro (1).
Objectives: The aim of this study was to assess the anti-inflammatory preventing effect of polydatin in the mouse model of acute crystal-induced arthritis.
Methods: A suspension of sterile CPP crystals (0.3 mg/20 µL PBS) have been injected intra-articularly (i.a.) into one ankle joint of Balb/c mice under isoflurane anesthesia. Animals were randomized in 5 groups: 1- CPP injection, 2- CPP + PD, 3- CPP + colchicine (control drug), 4- CPP + vehicle (control. N 1), 5- PBS injection (control N. 2). Polydatin and colchicine were administered by gavage (respectively 40 mg/kg and 1 mg/kg in 200 µL PBS/EtOH/glucose) at 24, 15 and 1 h before and 1, 6 and 24 h after (prophylactic model) or 1, 6 and 24 h after (therapeutic model) i.a. injection of CPP crystals.
Ankle swelling was measured at different time points using a precision caliper. After 48h (peak of the acute phase) mice were euthanized and blood and ankle

joints were collected for inflammatory cytokine (IL-1ß and KC) determination and histological analysis, respectively.
Results: The mean change in ankle swelling after i.a injection was 0.595±0.434 mm. Prophylactic treatment with PD and colchicine significantly diminished ankle swelling to 0.175±0.115 mm and 0.137±0.100 mm, respectively (Kruskal Wallis p 0.0025; Dunn's post test p < 0.01 CPP vs PD+CPP). The therapeutic administration of PD did not have significant effects on delta swelling (0.468±0.372 mm - PD vs 0.243±0.152 mm - colchicine). In mice treated with CPP crystals, histological analysis revealed areas of edema and increased cell infiltrate in articular and periarticular tissues and the presence of reactive lymphnodes. Tissue necrosis around inflamed tissue has been observed. Treatment with PD importantly reduced cell infiltrate in the prophylactic but not in the therapeutic protocol.
Serum IL-1ß and KC levels, which increased significantly (p<0.05) after 48h from i.a injection, diminished in non significant manner after prophylactic and therapeutic treatment. The gene expression study revealed a reduction of IL-1ß and KC mRNA after PD and colchicine treatment in both groups.
Conclusion: PD can effectively prevent acute inflammatory response to crystals in the mouse model of CPP arthritis. Oral PD prophylactic treatment showed a similar effect of colchicine in reducing ankle swelling and cell infiltrate. However, only colchicine showed to be effective in the therapeutic protocol.
These results raise the possibility that PD might have utility in the prevention of crystal-induced acute attacks in humans.
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Disclosure of Interests: Francesca Oliviero: None declared, Francesca Galuppini: None declared, Anna Scanu: None declared, Paola Galozzi: None declared, Vanni Lazzarin: None declared, Paolo Sfriso: None declared, Gianpietro Ravagnan: None declared, Roberta Ramonda Speakers bureau: Novartis, Celgene, Janssen, Pfizer, Abbvie, Lilly, Paolo Spinella: None declared, LEONARDO PUNZI: None declared, Gianmaria Pennelli: None declared, Roberto Luisetto: None declared
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OP0175 **IDENTIFYING PERIPHERAL VASCULAR MONOSODIUM URATE CRYSTAL DEPOSITION WITH DUAL-ENERGY CT: FACT OR FICTION? THE VASCURATE STUDY**

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Background: The close relationship between gout and cardiovascular diseases is well established. A growing hypothesis explaining this association would be that monosodium urate (MSU) crystals are deposited within vessel walls. Dual-energy computed tomography (DECT) can identify and quantify MSU crystal deposition in soft tissues. It remains unclear whether vascular spots exhibiting DECT attenuation characteristics of MSU are artefacts or true MSU crystal deposits.
Objectives: The objectives of this study were to determine whether the presence of peripheral vascular MSU crystal deposition identified with DECT is associated with the extent of MSU deposits in joint soft tissues, and if this association persists over time under urate-lowering therapy.
Methods: Patients with a clinical suspicion or established gout diagnosis prospectively underwent DECT for identification and quantification of the MSU crystal burden in their knees and feet. Some of these patients were also enrolled in the GOUT-DECTUS longitudinal study, and thus underwent follow-up DECT scans of their knees and feet at 6, 12 and 24 months. DECT scans were examined for the presence of vascular spots ≥0.01 cm3 classified as MSU crystal deposits according to the default post-processing settings. Multiple linear regressions adjusting on serum urate levels and gout diagnosis were implemented to determine the association between DECT MSU crystal volume in joint soft tissues, and the presence of vascular MSU deposits. Mixed linear models were used to compare DECT volumes of MSU crystal deposition in soft tissues between vascular MSU positive and negative patients during follow-up.
Results: A total of 169 patients were included, of which 140 had a final diagnosis of gout, including 15 also included in the longitudinal study. Patients were mostly male (78.8%) and were 65.5 ± 14.6 years old. Among gout patients, disease duration was 9.3 ± 9.9 years and 56.5% were urate lowering therapy-naive. A total of 11/29 (37.9%) controls and 40/140 (28.6%) gout patients presented with a least one vascular spot of DECT MSU deposition, with an average volume of 0.02 ± 0.02 cm3, and all subjects also presented at least one vascular calcification. In the feet, patients positive for vascular DECT MSU crystal deposition had an MSU volume of 3.81 ± 10.06 cm3 in joint soft tissues, compared with 1.85 ± 7.72 cm3 for those without vascular MSU deposition (p=0.018). In the knees, patients with vascular MSU deposition had an MSU crystal volume of 6.03 ± 24.13 cm3 in joint soft tissues, compared with 0.83 ± 2.88 cm3 for those without vascular evidence of MSU deposition. In the longitudinal subgroup analysis, coefficients of the fixed effects for the presence of vascular MSU deposits on the MSU crystal volume in joint soft tissues was 0.4 (p=0.35) in the feet and 1.21 (p=0.03) in the knees. The presence of vascular DECT MSU deposits was associated with a 3.4-fold increase in MSU crystal volume in knee joint soft tissues throughout follow-up.
Conclusion: This study suggests that some vascular spots identified with DECT as MSU crystal deposition may be real and not artefacts. This correlation remains throughout follow-up in the knees. However, the comparable prevalence of vascular DECT MSU deposits between gout patients and controls, the systematic co-existence of vascular calcifications and the uneven regression under urate-lowering therapy requires further analysis to determine which DECT spots are artefacts and which are not.
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Disclosure of Interests: Tristan Pascart Grant/research support from: Research Grant Horizon Pharma, Consultant of: Novartis, BMS, Sanofi, Pfizer,, Speakers bureau: Novartis, BMS, Paul Carpentier: None declared, Laurène Norberciak: None declared, Julie Legrand: None declared, Eric Houvenagel Speakers bureau: Janssen, Novartis, Fabio Becce: None declared, Jean-François Budzik: None declared
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Diagnostics and imaging procedures

OP0176 **CHRONOLOGICAL ORDER OF DECREASE OF SYNOVITIS, OSTEITIS AND TENOSYNOVITIS IN ARTHRITIS PATIENTS RECEIVING FIRST DMARD-TREATMENT**

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Background: During the last decennium advanced imaging modalities have refined our understanding of the tissues involved in RA and have shown that not only joints but also bones and tendons can be inflamed at diagnosis. However, the time-order of decrease of these inflammatory features after initiation of DMARDs is unknown. Whether this differs for ACPA-positive and ACPA-negative patients is also unknown.
Objectives: To achieve better understanding of the time order in which the different inflamed tissues (joint, tendon, bone) respond to DMARD-treatment and whether this differs between ACPA-subgroups.
Methods: 216 consecutive patients with early undifferentiated or rheumatoid arthritis, who received DMARD-treatment, were studied. Unilateral 1.5 Tesla contrast-enhanced MRIs of MCPs, wrists and MTPs were performed at baseline (before treatment) and after 4, 12 and 24 months. MRIs were scored for synovitis, osteitis and tenosynovitis in line with the RAMRIS, in known time-order but blinded for clinical data. Data of 4 serial time-points (three time intervals) were studied with autoregressive cross-lagged models. These models evaluated the influence of two time patterns in one model: 1) a simultaneous pattern ("extra change in one inflammatory feature was associated with extra change in another feature") and 2) a subsequent pattern ("change in one inflammatory feature preceded change in another feature"). All analyses were repeated stratified for ACPA-status (anti-CCP2).
Results: In all patients, all combinations of inflammatory features showed significant simultaneous decrease in all time intervals (0 – 4 /4 – 12/12 – 24 months; all p<0.05). In addition to simultaneous changes there were also time orders identified: synovitis change between 0 – 4 months preceded tenosynovitis change between 4 – 12 months (p=0.03) and synovitis change between 4 - 12 months preceded tenosynovitis change between months 12 - 24 months (p=0.02).
When considering ACPA-negative and ACPA-positive patients separately, similar results were obtained. In addition, in ACPA-positive patients, synovitis change between 4 - 12 months preceded osteitis change at 12 – 24 months (p = 0.002); this was significantly different from ACPA-negative patients (p<0.001).
Conclusion: This study increased the understanding of the response to treatment on tissue level. In addition to simultaneous decrease of synovitis, osteitis and tenosynovitis, also time orders of inflammation decrease were identified.

These differed between ACPA-subgroups, implying a different interaction of synovium and bone in these patients.

Disclosure of Interests: None declared

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OP0177 PROPERTIES AND LOCATIONS OF COLOR-CODED DUAL ENERGY CT LESIONS IN GOUT PATIENTS – A SYSTEMATIC EVALUATION

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Background: Dual energy CT (DECT) has diagnostic potential in gout patients. DECT can automatically colour-code presumed urate deposits based on radiodensity (Hounsfield Units, HU) and DECT ratio (difference in attenuation between high and low kV series) of lesions. However, other materials may imitate properties of urate deposits, most importantly calcium-containing material, dense tendons and artefacts, which may lead to misinterpretations. The characteristics of DECT lesions in gout patients have not yet been systematically investigated.

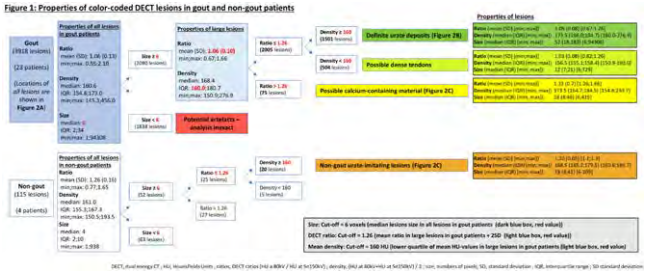
Objectives: To evaluate the properties and locations of colour-coded DECT lesions in gout patients.

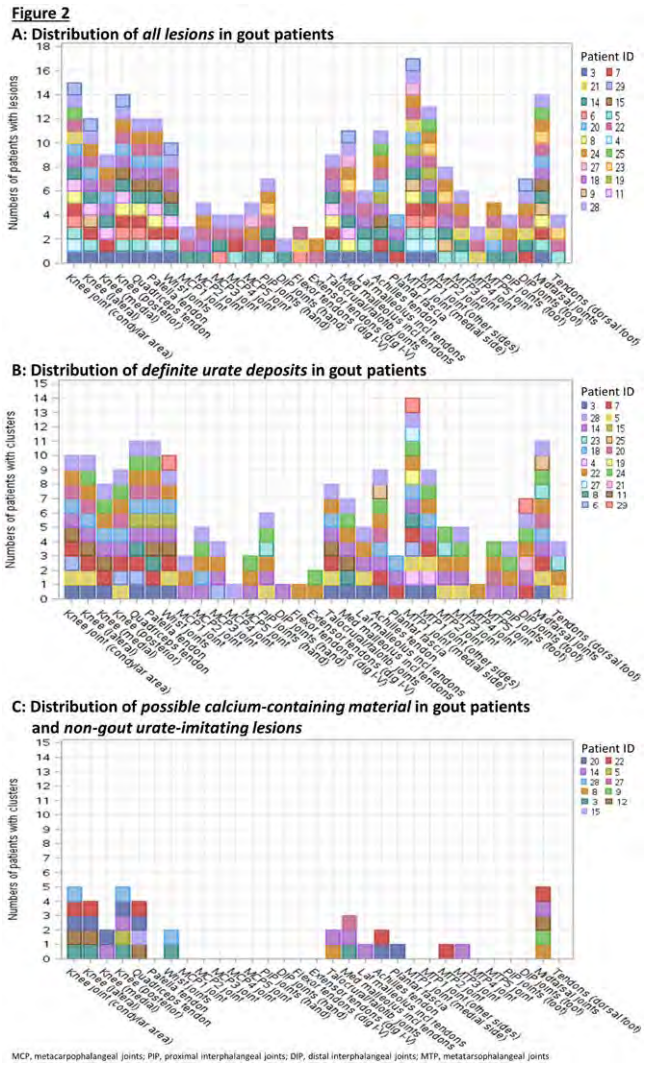
Methods: DECT were performed in patients with suspected gout. Patients were separated into gout and non-gout patients based on joint fluid microscopy findings. DECT of the hands, knees and feet were performed using default gout settings and colour-coded lesions were registered. Only location-relevant lesions were analysed (e.g. nail bed artefacts excluded). Mean density (mean of HU at 80 kV and Sn150 kV), mean DECT ratio, size and location of each lesion was determined. Subgroup analysis was performed post-hoc evaluating potential differences in properties and locations of lesions. Lesions were separated into groups according to properties (Figure 1, grey box): 1) *Size*—to separate artefacts characterised by small volume (*possible artefacts*). 2) *DECT ratios*—to separate calcium-containing material characterised by high DECT ratio (*possible calcium-containing material*). 3) *Density*—to separate dense tendons characterised by low DECT ratio and low HU values (*possible dense tendons*). Lesion fulfilling all urate characteristics (large volume, low DECT ratio, high density) were labelled *definite urate deposits*. Finally, for non-gout patients, properties of *non-gout urate-imitation lesions* (properties as *definite urate deposits*) were analysed.

Results: In total, 3918 lesions (*all lesions*) were registered in gout patients (n=23), with mean DECT ratio 1.06 (SD 0.13), median density 160.6 HU and median size 6 voxels (Figure 1, blue box). Lesions were seen in all analysed joints, most frequently MTP1 joints (medial side), knee joints and midtarsal joints (Figure 2a). Tendon affections were also common, especially in the knee tendons (patella and quadriceps), malleolus-related tendons (e.g. peroneus and tibialis posterior) and the Achilles tendons (Figure 2a).

Subgroup analyses showed that *definite urate deposits* (figure 2b) were found at the same locations as *all lesion* in gout patients (figure 2a), with the four most common sites being MTP1 joints, midtarsal joints, and quadriceps and patella tendons (Figure 2b). *Possible dense tendon* lesions had a mean HU value of 156.5 HU—markedly higher than expected for dense tendons (<100HU)—and lesion-locations were similar to *definite urate deposits* (data not shown), indicating that they primarily consisted of true urate deposits. In contrast, *possible calcium-containing material* and *non-gout urate-imitating lesions* had distinctly different properties (ratios 1.33 and 1.20, respectively) (Figure 1, yellow and orange box). Furthermore, the locations of these lesions were different from *definite urate deposits* since they were primarily found in a few weight-bearing joints (knee, midtarsal and talocrural including malleolus regions) and tendons (Achilles and quadriceps), whereas no lesions were found in either MTP1 joints or patella tendons (figure 2c).

Conclusion: DECT color-coded lesions in gout patients are heterogeneous in properties and locations. Subgroup analyses found that locations such as MTP1 joints and patella tendons were characterised by almost only showing *definite urate deposits*. A sole focus on these regions in the evaluation of gout patients may therefore improve specificity of DECT scans.





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OP0178 IMAGING NEOANGIOGENESIS IN RHEUMATOID ARTHRITIS (INIRA): WHOLE-BODY SYNOVIAL UPTAKE OF A 99MTC-LABELLED RGD PEPTIDE IS HIGHLY CORRELATED WITH POWER DOPPLER ULTRASOUND

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Background: Power Doppler ultrasound (PDUS) is superior to clinical examination in detecting synovitis in patients with rheumatoid arthritis (RA). Although dynamic and cheap it is impractical to scan large numbers of joints in routine clinical settings. MRI, whilst sensitive for synovitis, is expensive and routine use is limited to targeted joints. Bone scintigraphy produces whole body images but due to limited specificity is not routinely used.

^{99m}Tc-maraciclatide (Serac Healthcare) is a radiolabelled tracer which binds with high affinity to integrin $\alpha_v\beta_3$, a cell-adhesion molecule up-regulated on neoangiogenic blood vessels. It therefore has the potential to image synovial inflammation at the whole-body level. We previously showed in a pilot study that uptake was seen in the inflamed joints of five RA patients and that this correlated with PDUS. This study explores correlation with PDUS in a larger groups of patients with varied disease activity.

Objectives: To determine the correlation between ultrasound and ^{99m}Tc-maraciclatide imaging in patients with rheumatoid arthritis.

Methods: 50 patients with RA fulfilling ACR 2010 classification criteria were recruited. Patients underwent an ultrasound scan of 40 joints with grey scale (GS) and PD quantification. Each joint was scored on a scale of 0-3 for GS and PD with a total score calculated for each patient. Within 3 hours of the ultrasound patients were injected with 740 MBq of ^{99m}Tc-maraciclatide. Using a gamma camera, whole body planar views and dedicated hand and foot views were taken 2 hours after injection (Figure 1). Acquisition time was 20 minutes for whole body and 20 minutes for hand and foot views.

^{99m}Tc-maraciclatide images were scored as positive or negative uptake for each joint (binary score). A quantitative score was also calculated for each joint where there was uptake with this corrected for background uptake. Total binary and quantitative scores per patient were calculated.

Ultrasound and ^{99m}Tc-maraciclatide scores were tested for correlation with Pearson's correlation coefficient (r). Interrater agreement for 2 scorers was calculated using kappa (κ) and concordance correlation coefficient (*Pc)*.

Results: Strong correlation was seen when total PDUS was compared to binary scores (r=0.92, r^2=0.85) (Figure 2) and quantitative scores (r=0.85, r^2=0.72). κ was 0.82 and 0.79 for binary and ultrasound scores respectively. *Pc* was 0.82 for quantitative scores. p was <0.0005 for all results. ^{99m}Tc-maraciclatide uptake was also seen in inflamed tendons/tendon sheaths. The imaging procedure was well-tolerated. There were no tracer-related adverse events.

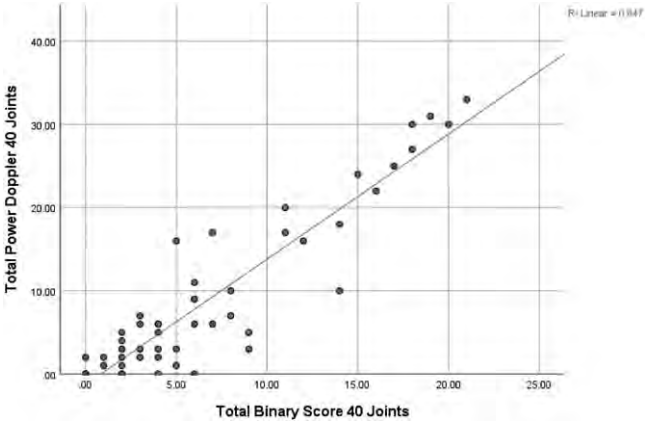


Figure 1. ^{99m}Tc-maraciclatide imaging with dedicated hand and foot views

Conclusion: ^{99m}Tc-maraciclatide uptake was highly correlated with PDUS highlighting its potential as an alternative imaging modality. ^{99m}Tc-based planar imaging has the unique capacity to image the whole body and hence the total synovial inflammatory load in a quick acquisition. The imaging equipment to perform these scans is already widely available in radiology departments. Interpretation of scans is also much simpler compared to US/MRI. It could therefore have a role in key decision-making points in pathways for diagnosis, treatment failure, and remission prior to dose tapering.



Figure 2. Correlation between total power doppler and ^{99m}Tc-maraciclatide binary scores

Disclosure of Interests: None declared

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OP0179

USEFUL STUDY I: A MULTICENTRE LONGITUDINAL STUDY TO TEST WHETHER ULTRASOUND CAN IDENTIFY PATIENTS WITH MUSCULOSKELETAL SYMPTOMS OF LUPUS WITH BETTER RESPONSE TO THERAPY

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Background: In SLE, musculoskeletal manifestations impact on quality of life and trial outcomes. We previously showed that assessments based on joint swelling lack sensitivity, specificity and responsiveness compared to ultrasound (US).

Objectives: To determine clinical features predicting US synovitis and whether patients with US synovitis respond better to therapy

Methods: SLE patients were recruited if the referring physician deemed they had inflammatory pain warranting treatment. Swollen joints were not required. At baseline, physicians recorded features of inflammation, concurrent fibromyalgia and osteoarthritis. Stable doses of prednisolone (≤5mg/day), antimalarials or immunosuppressants were allowed. Participants received depomedrone 120mg IM then were assessed at 0, 2 and 6 weeks for 66/68 swollen and tender joint counts, BILAG-2004, SLEDAI-2K, physician global and MSK-VAS, inflammatory markers, patient pain and disease activity-VAS, HAQ-DI, LupusQoL, US of hands and wrists (blinded to patient and clinical assessor). An internal pilot determined the primary endpoint:(Early Morning stiffness-VAS (EMS-VAS) at 2 weeks (adjusted for baseline) between patients with US-synovitis (GS≥2 or PD≥1 in ≥1 joint) vs. normal US at baseline. 20% difference was considered clinically meaningful. Sensitivity analyses adjusted for prednisolone and immunosuppressants.

Results: 122/133 patients completed all visits. There was significant disagreement between clinical examination and US. 78/133 had US synovitis; 68% of these had ≥1 swollen joint. Of 66/133 patients with ≥ 1 swollen joint, 20% had normal US. US-synovitis was more likely with joint swelling, a symmetrical small joint distribution and active serology. Physician-determined EMS, other lupus features or prior response to therapy were not associated. Fibromyalgia or osteoarthritis did not reduce the probability of US synovitis.

In the full analysis set (n=133) there was no difference in EMS VAS at 2 weeks according to US synovial status at baseline (difference -8mm, 95% CI -19, 4mm, p=0.178). 32 patients had fibromyalgia. After excluding them, we found a statistically and clinically significantly better clinical response to depomedrone in patients with US-synovitis at baseline (baseline-adjusted EMS VAS at 2 weeks -12mm, 95% CI -24, 0mm, p=0.049). This difference was greater in the treatment-adjusted sensitivity analysis (-12.8 (95% CI -22, -3mm), p=0.007) and the per-protocol-adjusted sensitivity analysis (-14.8mm (95% CI -20.8, -8.8mm), p<0.001). Patient with US synovitis had higher rates of improvement in the MSK BILAG-2004 (56% vs. 26%, p=0.09) and SLEDAI-2K (37% vs. 15%, p=0.03).

Conclusion: In lupus arthritis, distribution and serology, but not other features, help identify US-synovitis. US-synovitis was independent of features of fibromyalgia, but fibromyalgia confounded assessment of clinical response. US should be used to select SLE arthritis patients for therapy and clinical trials, especially when there are inflammatory symptoms without swollen joints.

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OP0180 DIAGNOSTIC VALIDITY OF ULTRASOUND INCLUDING EXTRA-CRANIAL ARTERIES IN GIANT CELL ARTERITIS

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Background: Giant cell arteritis (GCA) is a chronic vasculitis of the medium and large arteries. The involvement of large vessel (LV) either isolated or associated with cranial artery is frequent, so it is necessary to use imaging techniques for diagnosis, because the biopsy in these cases is not useful. European League Against Rheumatism (EULAR) recommends an early imaging test in patients with suspected GCA, and ultrasound of temporal±axillary arteries is recommended as the first imaging modality in patients with suspected predominantly cranial GCA (1).
Objectives: To assess the validity of Colour Doppler ultrasound (CDUS) of temporal superficial arteries (TA) and LV (axillary, subclavian and carotid) in the diagnosis of GCA, using as gold standard the patient's definitive clinical diagnosis. Analyse if routine ultrasound examination of LV improves the diagnostic accuracy.
Methods: This was an observational, descriptive and analytical study of 198 consecutive patients with GCA suspicion. A baseline CDUS of the TA and LV was performed. Ultrasound diagnosis was made according to the OMERACT (Outcome Measures in Rheumatology) definitions of halo sign and was established as a limit of average intimal thickness ≥ 0.34 mm for superficial temporal arteries and ≥ 1 mm for axillary, subclavian and carotid arteries. Statistical analysis was performed using SPSS version 25.
Results: Eighty-seven patients (43.9%) were CDUS compatible with GCA, and 111 patients (56.1%) had a negative CDUS. Among the patients with positive CDUS three different patterns were detected: 45 patients (51.7%) had an exclusive cranial involvement, 31 (35.6%) had a mixed pattern with involvement of both TA and LV and 11 (12.6%) had an exclusive LV involvement. The validity (sensitivity and specificity) and security (positive predictive value and negative predictive value) of diagnostic are shown in table.
When we analyse patients with LV involvement, 87.8% have axillary artery involvement, 77.4% subclavian involvement and 34.4% carotids involvement. If we only explored the axillary arteries, 12.2% of patients with LV involvement would not be diagnosed. However, if we explored axillary and subclavian arteries, 100% of patients with LV involvement would be diagnosed.
Conclusion: Half of the patients with GCA have LV involvement and up to 12.8% exclusively LV affectation in our series. Adding CDUS exploration of LV arteries to TA increases both sensitivity and diagnostic specificity. The minimum ultrasound examination of LV should include both axillary and subclavian arteries.
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	Sensitivity	Specificity	Positive predictive value	Negative predictive value
CDUS TA and LV	97,7%	97,3%	96,6%	98,2%
CDUS TA	83,9%	97,3%	96,1%	88,5%

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OP0181 FUNCTIONAL CUT-OFFS TO DISTINGUISH PULMONARY VASCULAR AND PARENCHYMAL INVOLVEMENT IN SYSTEMIC SCLEROSIS (SSC): A QUANTITATIVE ANALYSIS OF IMAGING FEATURES AT CHEST COMPUTED TOMOGRAPHY (CT)

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Background: Interstitial lung disease (ILD) and pulmonary arterial hypertension represent the most frequent causes of morbidity and mortality in SSc, with chest CT representing the gold standard in ILD assessment, while FVC and DLco allow functional assessment.
Objectives: As qualitative analysis of given chest CT scans is hampered by low reproducibility, we aimed to perform a quantitative analysis (QA) of CT scans able to investigate the parenchymal and vascular features in SSc-ILD and thus testing the relationship with clinical-functional data.
Methods: We prospectively enrolled 80 patients who underwent PFTs and spirometry-gated chest CT scan at TLC on the same day. Clinical, lung functional and diffusion data, as well as disability indexes were collected. CT images were analyzed by a computational platform for texture analysis of ILD patterns (CALIPER) through Imbio LTA. It quantified the extent of normal lung (%N), ground-glass opacities (%GG), reticulation (%RET), honeycombing (%HC), hyperlucent (%HL), absolute (PVV, cm^3) and normalized (PVV/LV, %) pulmonary vascular volumes. Cut-offs of normality for %FVC and %DLco of 80% and 70% were tested to differentiate parenchymal and vascular features.
Results: 73 patients/CT scans were eligible for both software analyses. CALIPER showed GG% as the most frequent radiological pattern (mean 5.5±10.4%). %FVC and % TLC negatively correlated with all ILD patterns, while %DLco with RET% only; PVV and PVV/LV negatively correlated with %FVC and %TLC, while %DLco with PVV/LV only. Positive correlations were found between all ILD patterns and vascular volumes (Table 1).

		LV (cm^3)	%N	%GG	%RET	%HC	%HL	PVV (cm^3)	% PVV/LV
FVC%	r	.60	-.19	-.40	-.34	-.30	.35	-.26	-.44
	p	<.001	-	<.001	.004	.01	.003	.04	<.001
FEV_1%	r	.58	-.02	-.38	-.25	-.24	.23	-.35	-.49
	p	<.001	-	.002	.04	.05	-	.004	<.001
FEV_1/FVC	r	-.16	.33	.22	.16	.21	-.35	-.15	-.08
	p	-	.02	-	-	-	-	-	-
TLC%	r	.71	-.14	-.42	-.37	-.48	.40	-.43	-.64
	p	<.001	-	.001	.01	<.001	.002	<.001	<.02
DLco%	r	.38	-.05	-.21	-.31	-.22	.30	-.21	-.33
	p	.01	-	-	.01	-	-	-	.006
FVC/DLco	r	.03	-.08	-.06	-.003	-.09	.08	-.06	-.08
	p	-	-	-	-	-	-	-	-

Cut-offs equal to 80 for %FVC and 70 for %DLco distinguished both parenchymal and vascular features, while 80 for %DLco characterized vascular features only. These results were confirmed also when patients were stratified according to absent/single/combined %FVC and %DLCO impairments with 80% cut-offs (Table 2).

Conclusion: In SSc a cut-off at 80 for %DLco may help identifying vascular changes as automatically assessed on chest CT scan, without any underlying

	FVC<80%	FVC ≥80%	p	DLco<80%	DLco ≥80%	p	DLco <70%	DLco ≥70%	p
%N	82.7 (9.6)	86.2 (14.7)	-	86.6 (12.7)	80.8 (15.8)	-	84.1 (13.9)	86.4 (13.5)	-
%GG	10.3 (8.9)	2.4 (3.9)	<.001	5.0 (6.7)	3.9 (6.9)	-	6.2 (7.5)	2.4 (4.8)	.002
%RET	2.9 (2.9)	0.8 (1.3)	<.001	1.6 (2.1)	0.7 (0.9)	-	1.9 (2.4)	0.6 (0.8)	.007
%HC	0.4 (0.6)	0.1 (0.1)	<.001	0.2 (0.3)	0.1 (0.1)	-	0.2 (0.4)	0.05 (0.2)	.010
%HL	3.6 (6.8)	8.9 (12.1)	-	5.4 (8.8)	14.1 (15.4)	.050	6.3 (10.1)	9.2 (12.7)	-
PVV	125.6 (39.1)	90.9 (26.9)	<.001	101.9 (34.8)	84.7 (19.4)	.016	106.9 (38.3)	87.5 (20.5)	.012
PVV/LV	3.8 (1.6)	2.0 (0.7)	<.001	2.51 (1.3)	1.7 (0.6)	.002	2.76 (1.4)	1.83 (0.6)	.001

ILD. The 80% cut-off for %DLco may be proposed to identify isolated vascular involvement, while %FVC at 80% or %DLco at 70% to identify significant parenchymal involvement. These results need to be confirmed in larger multi-centric cohorts.

Disclosure of Interests: Cosimo Bruni Speakers bureau: Actelion, Eli Lilly, Mariaelena Occhipinti Consultant of: Imbio, Gianna Camiciottoli: None declared, Maurizio Bartolucci: None declared, Gemma Lepri: None declared, Alessio Fabbrizzi: None declared, Alessandra Tottoli: None declared, Anna Bassetto: None declared, Giuglia Ciardi: None declared, Dilia Giuggioli: None declared, Giovanna CUOMO: None declared, Francesco Masini: None declared, Federico Lavorini: None declared, Linda Calistri: None declared, Marco Matucci-Cerinic Grant/research support from: Actelion, MSD, Bristol-Myers Squibb, Speakers bureau: Acetelion, Lilly, Boehringer Ingelheim

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OP0182 PROTEOGLYCAN LOSS IN ARTICULAR CARTILAGE IS ASSOCIATED WITH JOINT INFLAMMATION SEVERITY IN PSORIATIC ARTHRITIS – A COMPOSITIONAL MAGNETIC RESONANCE IMAGING STUDY

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Background: Even though cartilage loss is a known feature of psoriatic arthritis (PsA), little is known about its role in the pathogenesis of PsA. Using delayed gadolinium-enhanced magnetic resonance imaging of cartilage (dGEMRIC) as a non-invasive marker of the tissue's proteoglycan content, such early (i.e. pre-morphological) changes have been associated with inflammation in rheumatoid arthritis (RA). Yet, this association has not been studied before in PsA.

Objectives: Is the severity of local joint inflammation associated to local proteoglycan loss in PsA patients?

Methods: Metacarpophalangeal (MCP), proximal interphalangeal (PIP), and distal interphalangeal (DIP) joints of 17 patients with active PsA were evaluated by high-resolution clinical standard morphological and dGEMRIC sequences using a 3T MRI scanner (Magnetom Skyra, Siemens) and a dedicated 16-channel hand coil. Images were analyzed by two independent raters for dGEMRIC indices, PsA MRI scores (PsAMRIS) and total cartilage thickness (TCT). Kendall-Tau correlation coefficients (τ) were calculated.

Results: We found significant negative correlations between dGEMRIC indices and total PsAMRIS (τ = -0.5, p= 0.012), synovitis (τ = -0.56, p= 0.006), flexor tenosynovitis (τ = -0.4, p= 0.049), and periarticular inflammation (τ = -0.72, p< 0.001). Significant positive correlations were found between TCT and dGEMRIC indices in all joint levels (τ = 0.43, p<0.001). No significant correlations were determined between dGEMRIC indices and bone erosion, bone edema or bone proliferation.

Conclusion: In PsA, proteoglycan loss as assessed by dGEMRIC is associated with periarticular inflammation, synovitis, and flexor tenosynovitis, but not with bone erosion or proliferation, thereby highlighting the need for effective anti-inflammatory treatment regimes. Beyond morphology, advanced MRI techniques may be used to assess cartilage composition in PsA and to identify early changes in cartilage as an imaging biomarker with potential application in detection and monitoring of PsA.

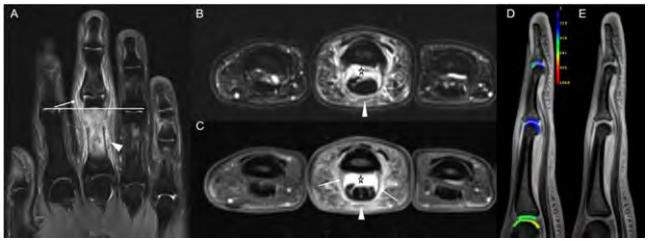


Figure 1 *Right hand of a 26-year-old male with psoriatic arthritis Coronal STIR image (*A*) of digits 1-5, transversal fat-saturated (fs) T2-weighted image of digits 2-4 (*B*) and the corresponding transversal fs contrast-enhanced T1-weighted image (*C*) at the distal portion of the proximal phalanges. Horizontal white bar in (*A*) indicates level of transversal slices (*B*) & (C). Sagittal fs Proton Density-weighted image of the third digit (*D*). A: Increased signal at the collateral ligaments and synovitis of the proximal interphalangeal (PIP) joint of the third digit (white arrow). Periarticular inflammation around the PIP joint and the body of the proximal phalanx of the third digit (arrowhead).* B & C: *Extensive flexor tenosynovitis (asterix) and periarticular inflammation in the subcutaneous tissues (arrowhead) alongside thickened flexor tendon pulleys (arrow).* D & E*: Representative sagittal T1-weighted images of the MCP, PIP and DIP joint of the 3rd digit. Following iv contrast administration and appropriate delay of 40 min,* A *gives the morphological T1 map, while* B *gives the corresponding parameter map with dGEMRIC values [ms] overlaid. Note the significant decrease in dGEMRIC indices of the PIP joint as compared to the MCP joint.*

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OP0183 DO CARTILAGE LAMINAR COMPOSITIONAL CHANGES AS ASSESSED BY T2 RELAXOMETRY PREDICT INCIDENT AND WORSENING OF STRUCTURAL MORPHOLOGIC DAMAGE IN THE SAME PLATE 3 YEARS LATER?

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Background: To address the question whether laminar changes in knee cartilage T2 are relevant for prediction of lesion onset or progression in the same articular plate we included two different samples from the Osteoarthritis Initiative (OAI) study without radiographic osteoarthritis (ROA), i.e. so-called "healthy controls" with no ROA in either knee and being free of risk factors, and those with K-L 0 in one knee and ROA in the contralateral knee. Given the concept of the osteochondral unit, we hypothesize that superficial T2 is elevated in cartilage plates with subsequent surface damage development or worsening and deep layer T2 is elevated for those with subsequent bone marrow lesion (BML) development or worsening.

Objectives: To analyze whether knees with subsequent morphologic cartilage and BML development or worsening exhibit elevated cartilage T2 compared to those that do not develop such structural damage in the same plate 3 years later.

Methods: We included 63 knees from the OAI without ROA (K-L 0), but with definite ROA (K-L ≥2) in the contralateral knee, and 78 participants from the OAI healthy reference cohort.

Cartilage integrity or damage and subchondral bone marrow lesions (BMLs) were assessed for year 1 (i.e. baseline (BL) in this analysis) and year 4 (Y4) in chronological order using the semi-quantitative MOAKS scoring system.

BL deep and superficial layer cartilage T2 was computed from sagittal multi-echo spin echo MR images. Because cartilage T2 is known to display spatial variation with tissue depth, the segmented cartilages were computationally divided into superficial and deep 50%, based on the distance between the segmented cartilage surface and bone interface. Statistical analyses were performed for the femoro-tibial (FT) joint on a plate level, i.e. medial femur (MF), medial tibia (MT), lateral femur (LF) and lateral tibia (LT), using UNIANOVA with adjustment for age, body mass index, sex, and sample.

Results: 141 participants were included. Of these 79 (56%) were women, had a mean age of 59.4 ± 9.1 years and a mean body mass index of 25.8 ± 4.1 m/kg^2.

52 (37%) had prevalent cartilage lesions in the medial FT joint and 67 (48%) in the lateral FT joint. For BMLs these numbers were 15 (11%) medially and 14 (10%) laterally. Worsening of FT cartilage lesions from BL to Y4 were seen in 10 (7%) medially and 21 (15%) in the lateral FT compartment. Incident FT cartilage lesions were seen in 11 (11.5%) medially and 8 knees laterally. No worsening BMLs were seen

medially and 2 knees showed worsening BMLs laterally. 10 (7%) knees showed incident BMLs medially and 8 (6%) knees in the lateral FT compartment.
Deep layer T2 showed prolongation in the LT in knees with incident LT cartilage lesions (n=8, 34.5 vs. 32.7 ms, p=0.02) and for MF in knees with MF cartilage lesion worsening (n=9, 47.6 vs. 41.4 ms, p=0.01) and MF BML incidence (n=6, 45.4 vs.41.6 ms, p=0.000). Superficial T2 showed prolongation in the MT only in those knees with MT cartilage lesion worsening (n=2, 47.3 vs. 43.4 ms, p=0.03). No additional associations were seen for the superficial layer.
Conclusion: For knees without ROA, BL deep layer T2 prolongation was seen for those who developed incident cartilage damage in the LT, and those with worsening cartilage damage and incident BMLs in the MF, respectively. Superficial T2 showed prolongation only in the MT for those with MT cartilage lesion worsening. In summary and contrary to our hypothesis the deep cartilage layer seems to be more relevant for cartilage damage development or worsening in the same FT plate than the superficial layer.
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Osteoarthritis: clinical

OP0184

RISK OF COMORBIDITIES FOLLOWING INCIDENT CLINICIAN-DIAGNOSED KNEE OR HIP OSTEOARTHRITIS: A REGISTRY-BASED COHORT STUDY

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Background: Osteoarthritis (OA) is associated with increased comorbidity, but knowledge of the temporal relationships between OA and comorbidities is limited.
Objectives: To estimate the risk of consulting for comorbidities in people with incident clinician-diagnosed knee or hip OA.
Methods: Using the Swedish Population Register, we identified all residents aged 35 years or above in the Skåne region, Sweden (total pop. 1.23 million) in the year 2009. We used the Skåne Health Care Register (SHR), a comprehensive register based on physicians' International Classification of Disease (ICD) 10, to identify persons who had at least one diagnosis of knee or hip OA – the exposures of interest – and 18 other diagnoses (Figure 1) – the outcomes of interest – between 1 January 2010 and 31 December 2017. To minimize potential confounding due to propensity to seek care, persons had to have at least one health-care visit with any diagnosis registered between 1 January 1998 and 31 December 2009 to be included. We excluded persons with a knee or hip OA diagnosis before 1 January 2010, and for each analysis, persons with a previous diagnosis of the outcome diagnosis of interest. People were followed from 1 January 2010 until relocation outside of the region, death, outcome diagnosis, or 31 December 2017, whichever came first. We calculated hazard ratios (HR) of each outcome diagnosis using Cox proportional hazard models with incident knee and hip OA as time-varying exposure. Time from start of follow-up to the date of an OA diagnosis was treated as unexposed, while time from an OA diagnosis to the outcome diagnosis was treated as exposed. Models were adjusted for residential area, if born in Sweden, annual income, years of education, marital status, sex, and age (all retrieved from Statistics Sweden), and baseline conditions (i.e. the other outcome diseases of interest, and alcohol-related disorders) as registered in SHR before 1 January 2010.
Results: We included 548,681 persons in the Skåne population having at least one health-care visit during 1998 to 2009 and no doctor-diagnosed knee or hip OA. Of these, 36,465 persons consulted for knee OA and 14,477 for hip OA during the follow-up period (Table 1). Persons with clinician-diagnosed incident knee or hip OA have 8-61% higher hazard of depression, cardiovascular diseases, back pain, and osteoporosis than persons without an OA diagnosis (Fig. 1). Both knee and hip OA persons have increased risk of diabetes, however the 95% confidence interval excluded 1 only for knee OA (Fig. 1). Also, only knee OA patients have an increased risk of fracture to the forearm. For the rest of the diagnoses, we found either no increased risk for knee or hip OA persons, or estimates with wide confidence intervals, excluding any clear interpretations of the direction or size of the effects.

Table 1. Demographics of the study cohort at start of follow-up (Jan. 1, 2010).

	No OA (n=497,739)	Incident knee OA (n=36,465)	Incident hip OA (n=14,477)
Age, yrs (SD)	57.3 (14.6)	62.2 (12.2)	65.3 (11.7)
Women, n (%)	254,593 (51)	21,553 (59)	8,306 (57)
Married[a], n (%)	350,172 (70)	27,955 (77)	10,937 (76)
Born in Sweden[b], n (%)	422,713 (85)	31,292 (86)	12,949 (89)
Education[c], n (%)			
<10 yrs	128,738 (26)	11,364 (31)	4,745 (33)
10-12 yrs	222,147 (45)	16,390 (45)	6,050 (42)
13-14 yrs	59,950 (12)	3,908 (11)	1,556 (11)
≥15 yrs	83,620 (17)	4,590 (13)	2,065 (14)
Income in 100,000 SEK[d], mean (SD)	2.3 (3.0)	2.1 (2.4)	2.1 (2.6)

Missings: [a]29 [b]44, [c]3,558, [d]2

Conclusion: Incident clinician-diagnosed knee and hip OA are associated with increased risk of consultation for depression, cardiovascular disease, back pain, osteoporosis, and diabetes. Results support previous findings for cardiovascular diseases and diabetes, however suggesting that the risk of diabetes is mainly associated with knee OA.

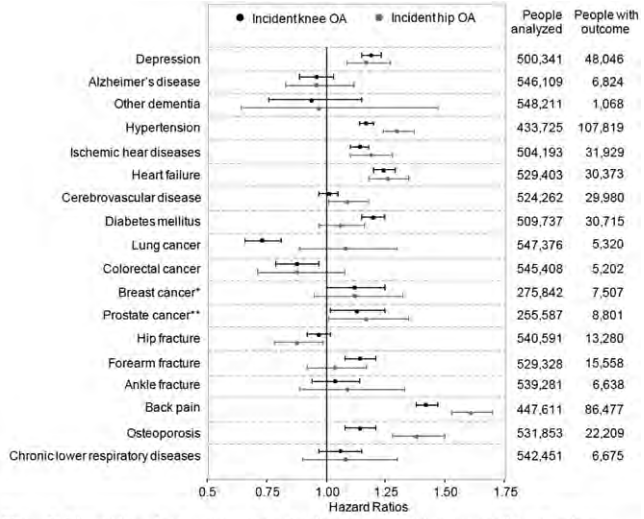


Figure 1. Adjusted hazard ratios of consultation for diseases occurring in persons with incident doctor-diagnosed knee or hip OA compared to non-OA persons. *Only women included in analysis. **Only men included in analysis.

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OP0185

KNEE JOINT DISTRACTION IS MORE EFFICIENT IN RESTORING CARTILAGE THICKNESS THAN HIGH TIBIAL OSTEOTOMY IN PATIENTS WITH SEVERE KNEE OSTEOARTHRITIS

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Background: Both high tibial osteotomy (HTO) and knee joint distraction (KJD) are joint preserving surgical techniques unloading the affected femorotibial

compartment in patients with knee osteoarthritis (OA). While HTO permanently unloads the more affected compartment (MAC) by overcorrecting the leg axis, KJD temporarily unloads the whole joint by separating the tibia and femur for 5 mm for 6 weeks. In a previous randomized controlled trial (RCT), comparable clinical benefit and radiographic joint space width (JSW) increase over 2 years follow-up were demonstrated for both treatments[1]. Yet, comparison of JSW before and after HTO may be unreliable, as pseudo-widening of the unloaded compartment may occur due to the induced leg axis change. Therefore, direct cartilage thickness measurements need to be compared between KJD and HTO, to accurately evaluate the efficacy of both treatment options on cartilage structure.

Objectives: To compare two-year cartilage thickness changes after treatment with KJD *vs* HTO and identify factors predicting cartilage thickness restoration.

Methods: Patients indicated for HTO were randomized to KJD (KJD_{HTO}) or HTO treatment. Patients indicated for total knee arthroplasty received KJD (KJD_{TKA}). Standardized semi-flexed weight-bearing radiographs and 3T MRIs with 3D spoiled gradient recalled imaging sequence with fat suppression (SPGR-fs) were acquired before and two years after surgical treatment. Cartilage thickness in the knee was measured using Chondrometrics Works 3.0 software. On the radiographs the mean JSW in the MAC were measured with KIDA software. Readers were blinded to the type of intervention and acquisition order. The primary and secondary outcomes were the mean MAC cartilage thickness (ThCtAB) and percentage of denuded bone area (dABp) change before and two years after treatment (MRI), with radiographic joint space width (JSW) used as a reference.

Results: No statistically significant differences in the baseline characteristics were seen between KJD_{HTO} (n=18) and HTO (n=33). The KJD_{TKA} group (n=18) had a higher age and Kellgren-Lawrence grade (KLG) than the HTO and KJD_{HTO} groups.

KJD_{HTO} patients did not show significant changes in MAC cartilage thickness, dABp, or JSW over time (all p>0.10; figure 1). HTO patients displayed a decrease in MAC cartilage thickness and an increase in dABp (both p<0.03), but an increase in JSW (p=0.006). KJD_{TKA} showed a significant increase in MAC cartilage thickness and JSW and decrease in dABp (all p<0.01). Baseline OA severity was the strongest predictor of cartilage restoration. KJD patients with severe OA (KJD_{severe}; KLG ≥3) showed significant restoration (all p<0.01; figure 2); mild OA patients (KJD_{mild}; KLG ≤2) showed a slight deterioration. KJD_{severe} showed a significantly greater cartilage restoration response in the MAC than HTO_{severe} for cartilage thickness (p=0.005) and dABp (p=0.003), but not JSW change (p=0.521). The changes in all three parameters did not differ significantly between KJD_{mild} and HTO_{mild} (all p>0.08).

Conclusion: In patients with severe knee OA, KJD is more efficient in restoring cartilage thickness than HTO is. In these patients, KJD causes significant cartilage restoration while HTO, despite shifting the leg axis and demonstrating radiographic joint space widening, shows loss of cartilage as measured on MRI. In patients with mild knee OA, neither HTO nor KJD treatment results in significant cartilage restoration and both treatments show a slight deterioration that is likely the result of natural OA progression. As such, this research promotes the choice KJD as joint-preserving surgery in case of knee OA patients with more severe structural damage.

References:

[1] MP Jansen *et al*, Cartilage 2019.

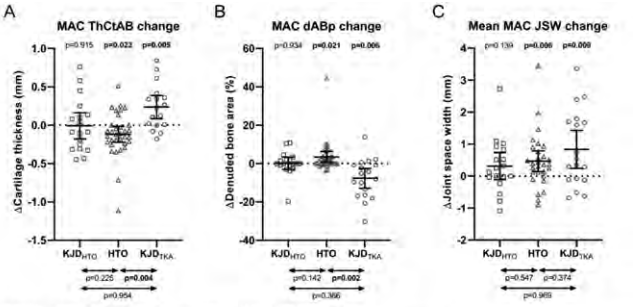


Figure 1: Two-year change in radiographic and MRI cartilage parameters.
(A) Change in MRI mean cartilage thickness over the total subchondral bone area (ThCtAB) of the most affected compartment (MAC), for the three groups: KJD_{HTO} = KJD patients with indication high tibial osteotomy (HTO); KJD_{TKA} = knee joint distraction (KJD) patients with indication total knee arthroplasty. (B) Change in MRI percentage of denuded subchondral bone area (dABp) of the MAC for the three groups. (C) Change in mean radiographic joint space width (JSW) of the MAC for the three groups. Markers represent individual patients, dashes represent the group mean and 95% confidence interval. P-values above groups indicate statistical significance of two-year changes while p-values between groups indicate the differences between each two groups, corrected for baseline patient characteristics statistically significantly different between each two groups.

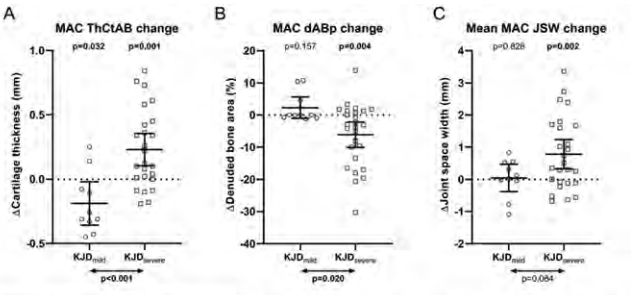


Figure 2: Two-year change in radiographic and MRI cartilage thickness parameters for knee joint distraction (KJD) patients with mild (KJD_{mild}) and severe (KJD_{severe}) osteoarthritis.
(A) Change in MRI mean cartilage thickness over the total subchondral bone area (ThCtAB) of the most affected compartment (MAC). (B) Change in MRI percentage of denuded subchondral bone area (dABp) of the MAC for both groups. (C) Change in mean radiographic joint space width (JSW) of the MAC for both groups.
Markers represent individual patients, dashes represent the group mean and 95% confidence interval. P-values above groups indicate statistical significance of two-year changes while p-values between groups indicate the differences between each two groups, corrected for statistically significantly different baseline characteristics.

Disclosure of Interests: Mylène Jansen: None declared, Susanne Maschek Shareholder of: Stock/stock options at Condrometrics GmbH, Employee of: Employment at Condrometrics GmbH, Ronald Van Heerwaarden: None declared, Simon Mastbergen: None declared, Wolfgang Wirth Shareholder of: Stock/stock options at Condrometrics GmbH, Consultant of: Consultancy to Galapagos NV, Employee of: Employment at Condrometrics GmbH, Floris Lafeber Shareholder of: Co-founder and shareholder of ArthroSave BV, Felix Eckstein Shareholder of: Stock/stock options at Condrometrics GmbH, Consultant of: Consultancy at Merck KGaA, Samumed, Bioclinica, Galapagos, Servier, Novartis, Employee of: Employment at Condrometrics GmbH, Speakers bureau: Development of educational presentations for Medtronic

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OP0186

HYDROXYCHLOROQUINE IN PATIENTS WITH INFLAMMATORY AND EROSIVE OSTEOARTHRITIS OF THE HANDS: RESULTS OF A RANDOMIZED, DOUBLE-BLIND, PLACEBO CONTROLLED, MULTI-CENTRE, INVESTIGATOR-INITIATED TRIAL (OA TREAT)

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Background: Hand osteoarthritis (OA) is a very common condition with cartilage degradation and frequently erosive bone changes. It may be very painful and can greatly affect everyday activities. Common analgesics and NSAIDs are used for symptomatic relief but are often poorly tolerated or contraindicated especially in elderly patients. There is no effective and proven disease modifying therapy available. Previous publications and anecdotal reports suggest hydroxychloroquine (HCQ) as a possible treatment, and some physicians use HCQ off-label for the treatment of OA

Objectives: To investigate the efficacy and safety of HCQ in patients with inflammatory and erosive hand OA in a randomized, double-blind, placebo controlled, multi-centre, investigator-initiated trial

Methods: Patients with inflammatory and erosive hand OA, according to the ACR criteria, with radiographically proven erosive disease were randomized 1:1 to HCQ 200-400mg per day or matching placebo (PBO) for 52 weeks. Both groups received standard therapy (stable NSAIDs). The primary endpoint was AUSCAN for pain and hand disability at week 52 (W52). A secondary endpoint was radiographic progression from baseline (BL) to W52. A multiple endpoint test and analysis of covariance was used to compare changes between groups. All analyses were conducted on an intention-to-treat base

Results: Of 156 patients 3 were excluded and 75 were randomized to HCQ and 78 to PBO. Mean age was 52.4 (SD 8.1) in the HCQ and 50.2 (SD 6.6) years in the PBO group. 68 (90.7%) of the patients were female in the HCQ and 60 (76.9%) in the PBO group. Disease duration was 9.5 (SD 7.5) in HCQ and 10.8 (SD 8.8) years in PBO group. CRP and ESR were normal in both groups. BL pain (AUSCAN) was 31.1 (SD 8.2) and 30.7 (SD 8.9), BL function (AUSCAN) was 58.5 (SD 15.5) in HCQ and 57.8 (SD 17.1) in PBO patients. Table 1 shows clinical and functional parameters at W52. Only morning stiffness was significantly reduced in the HCQ group (p=0.001). Changes in radiographic scores did not

differ significantly (p>0.05) between treatment groups. There were 7 SAE in the HCQ and 15 in the PBO group. No new safety issues were detected

Table 1. Results of the covariance analysis (ANCOVA)-adjusted mean values and 95%-confidence intervals for primary and secondary outcomes at W52, as well as a p-value for group comparison

Outcome	Adj. Mean HCQ	95%-CI HCQ		Adj. Mean PBO	95%-CI PBO		P-value HCQ x PBO
AUSCAN Function	48.1	43	53.3	51.3	46.6	56	0.36
AUSCAN Pain	26.7	23.9	29.4	26.5	23.9	29.1	0.92
tender joint	6.4	4.8	7.9	7.1	5.4	8.7	0.49
swollen joint	2	1.3	2.7	2.1	1.4	2.7	0.93
ESR (mm/h)	8.2	6.9	9.6	11.7	10.1	13.5	<0.01
HAQ	0.9	0.8	1	0.8	0.7	0.9	0.46
Phys. Global	3.2	2.8	3.6	3.5	3	3.9	0.39
Pat. Global	4.5	3.9	5.1	5.2	4.6	5.8	0.14
SF36 mental	48.8	46.6	51	50.8	48.7	52.8	0.22
SF36 physical	39.8	38	41.6	39.9	38.2	41.6	0.95
Morning Stiffness (min)	30.2	24	36.3	16.3	10.3	22.3	0.001
Modif. Kallmann Score	53.6	52.1	55.1	52.8	51.4	54.2	0.24

The associated BL value or, if available, a mean value from BL and screening was included in the ANCOVA model as a covariate.

Conclusion: The OATREAT trial examined the clinical and radiological efficacy and safety of HCQ as a treatment option for inflammatory and erosive OA over 52 weeks. OATREAT is the first large randomized PBO controlled trial focusing on erosive hand OA. HCQ was no more effective than PBO for changes in pain, function and radiographic scores in the 52-week period. Overall safety findings were consistent with the known profile of HCQ. Thus, our data failed to show that HCQ is effective in patients with inflammatory, erosive hand OA

Disclosure of Interests: Claudia Kedor Consultant of: Advisory Board for Novartis Pharma GmbH, Jacqueline Detert: None declared, Rolf Rau: None declared, Siegfried Wassenberg: None declared, Joachim Listing: None declared, Pascal Klaus Employee of: Pfizer Pharma GmbH, Tanja Braun: None declared, Walter Hermann: None declared, Stefan Weiner: None declared, Martin Bohl-Bühler: None declared, Frank Buttgereit Grant/research support from: Amgen, BMS, Celgene, Generic Assays, GSK, Hexal, Horizon, Lilly, medac, Mundipharma, Novartis, Pfizer, Roche, and Sanofi., Gerd Rüdiger Burmester Consultant of: AbbVie Inc, Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB Pharma, Speakers bureau: AbbVie Inc, Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB Pharma

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OP0187

DETERMINING OPTIMAL COOLING AND ADMINISTRATION METHODS FOR CNTX-4975 INTRA-ARTICULAR INJECTION IN SUBJECTS WITH MODERATE TO SEVERE OSTEOARTHRITIS KNEE PAIN

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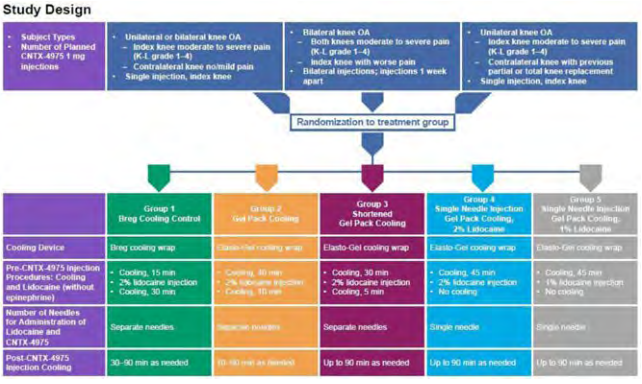
Background: CNTX-4975 is a highly purified, synthetic capsaicin being developed to provide long-term analgesia after a single intra-articular (IA) injection for patients with moderate to severe osteoarthritis (OA) knee pain. CNTX-4975 IA administration is associated with short-term post-procedural pain that can be attenuated with preemptive joint cooling.

Objectives: To evaluate cooling and administration procedures for CNTX-4975 IA injection, with goals of balancing patient comfort and ease of use and assessing clinical response 8 weeks after injection.

Methods: This phase 3, open-label, 8-week study (NCT03661996) enrolled subjects aged 40–95 y with Kellgren-Lawrence grade 1–4, BMI ≤45 kg/m2, and stable, moderate to severe OA knee pain and who failed ≥2 therapies. Subjects were assigned to unilateral/bilateral CNTX-4975 1 mg IA injections as determined by OA pain/joint replacement status, then randomized by study site to 1 of 5 treatment regimens (Figure). The primary outcome measure assessed Breg cooling control vs other cooling regimens on day 1 using a combined sum of 1) pain (0, none; 4, severe) 30 minutes after CNTX-4975 injection; 2) subject satisfaction (SS) with cooling/injection procedures; and 3) investigator satisfaction (IS) with procedures. SS and IS were measured on a 1–7 scale (1, completely dissatisfied; 7, completely satisfied); pain was reverse scored and normalized (1, severe; 7, none) for equal weighting. Geometric mean ratios (GMR) with 95% CIs were constructed for each regimen vs Breg control (ANCOVA); lower 95% CI >0.7 was considered clinically acceptable. Secondary endpoints included percentage of subjects by subject type meeting criteria for Outcome Measures in Rheumatology-Osteoarthritis Research Society International (OMERACT-OARSI) responders 8 weeks after injection. Safety assessments included TEAEs.

Results: The intent-to-treat population included 848 subjects. The primary combined outcome showed that all cooling and administration regimens were clinically acceptable, with the evaluated cold gel wraps being at least as effective as the Breg circulating ice-water wrap (Table). For subjects with unilateral OA, OMERACT-OARSI response rates were 67% in those with no/mild nonindex knee pain and 81% in those with nonindex knee single joint replacement. For subjects with bilateral knee OA receiving bilateral injections, response rates for index and nonindex knees were 73% and 79%. TEAEs were reported in 22% of subjects; <1% were serious. TEAEs occurring in >2% of subjects were procedural pain (2.9%), arthralgia (2.2%), and nausea (2.1%), with no meaningful differences across groups.

Conclusion: All cooling regimens for CNTX-4975 IA administration were clinically acceptable and well tolerated, offering feasible options for use in routine practice. Importantly, high levels of clinical response were observed 8 weeks after unilateral or bilateral knee injections for moderate to severe OA knee pain.



Primary Combined Endpoint Outcome in the Index Knee, Normalized Scale, by Cooling and Administration Procedure (ANCOVA Model)

	Breg Cooling Control N=162	Gel Pack Cooling N=179	Shortened Gel Pack Cooling N=175	Single Needle Injection, Gel Pack Cooling, 2% Lidocaine N=160	Single Needle Injection, Gel Pack Cooling, 1% Lidocaine N=172
Mean (SD)	17.23 (2.660)	18.23 (2.023)	16.81 (2.891)	17.57 (3.049)	16.43 (3.138)
Geometric LS Mean (SE)	17.18 (1.016)	18.26 (1.015)	16.48 (1.016)	17.40 (1.016)	16.00 (1.015)
95% CI	16.66, 17.72	17.74, 18.80	15.99, 16.99	16.87, 17.95	15.53, 16.49
Comparison vs Breg Cooling					
GMR (SE)		1.06 (1.022)	0.96 (1.022)	1.01 (1.022)	0.93 (1.022)
95% CI		1.02, 1.11	0.92, 1.00	0.97, 1.06	0.89, 0.97
Clinically Acceptable?		Yes	Yes	Yes	Yes

LS, least squares; SD, standard deviation; SE, standard error.
GMR lower 95% CI >0.7 considered clinically equivalent.

Disclosure of Interests: Randall Stevens Shareholder of: Centrexion Therapeutics Corp, Employee of: Centrexion Therapeutics Corp, Peter Hanson Shareholder of: Centrexion Therapeutics Corp, Employee of: Centrexion Therapeutics Corp, Paul Tiseo Employee of: Centrexion Therapeutics Corp, Kimberly Guedes Shareholder of: Centrexion Therapeutics Corp, Employee of: Centrexion Therapeutics Corp, James Campbell Shareholder of: Centrexion Therapeutics Corp, Employee of: Centrexion Therapeutics Corp, James Connolly Employee of: Centrexion Therapeutics Corp, Stephanie Ruggiero Employee of: Centrexion Therapeutics Corp, Meg Corliss Employee of: Centrexion Therapeutics Corp, Valerie Smith Consultant of: Centrexion Therapeutics Corp, Philip G Conaghan Consultant of: AbbVie, BMS, Eli Lilly, EMD Serono, Flexion Therapeutics, Galapagos, GSK, Novartis, Pfizer, Speakers bureau: AbbVie, Eli Lilly, Novartis, Pfizer

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OP0188

INTEGRATED SAFETY SUMMARY OF THE NOVEL, INTRA-ARTICULAR AGENT LORECIVIVINT (SM04690), A CLK/DYRK1A INHIBITOR THAT MODULATES THE WNT PATHWAY, IN SUBJECTS WITH KNEE OSTEOARTHRITIS

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Background: Concerns over the safety of available osteoarthritis (OA) treatments have led to revision of treatment guidelines and highlight the need for new therapies. Lorecivivint (LOR; SM04690) is an intra-articular (IA), small-molecule CLK/DYRK1A inhibitor that modulates the Wnt pathway and is in development as a potential disease-modifying treatment for knee OA.[1,2]
Objectives: To evaluate pooled early-phase LOR clinical data for safety, including bone health-related adverse events (AEs).
Methods: Safety data were pooled from 3 randomized controlled trials (one Phase 1, two Phase 2) evaluating 4 doses (0.03 mg, 0.07 mg, 0.15 mg, 0.23 mg) of a single IA injection of LOR in subjects with moderately to severely symptomatic knee OA. Two trials (NCT02095548; NCT03122860) evaluated subjects for 24 weeks and one trial (NCT02536833) for 52 weeks. AEs, serious AEs (SAEs), and bone health AEs were categorized by Medical Dictionary for Regulatory Activities (MedDRA) classification. Incidences of AEs and SAEs were compared between the combined LOR-treated group (subjects who received any dose of LOR) and a control group (subjects not treated with LOR).
Results: This analysis includes 848 LOR-treated and 360 control subjects. The incidence of AEs was similar in LOR-treated (350/848 [41.3%]) and control subjects (138/360 [38.3%]). Incidence of SAEs was 20/848 (2.4%) in LOR-treated and 4/360 (1.1%) in control subjects. The most commonly reported AE in LOR-treated subjects was arthralgia (treated 7.6%, control 7.2%) and was the only AE reported at >5% in either group (Fig. 1). Target-knee arthralgia was the most common joint-specific AE (treated 6.5%, control 5.3%) (Fig. 2). No AEs in other joints exceeded an incidence of 2% in either group. In all categories, individual AEs were reported at similar rates between groups and no SAEs were deemed related to LOR by investigators.

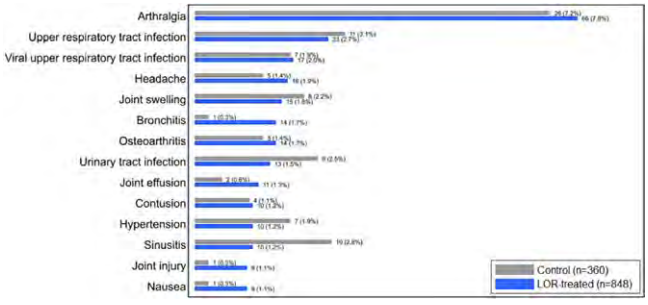


Figure 1. Adverse event summary for events occurring in at least 1% of the treated population (N=1208).

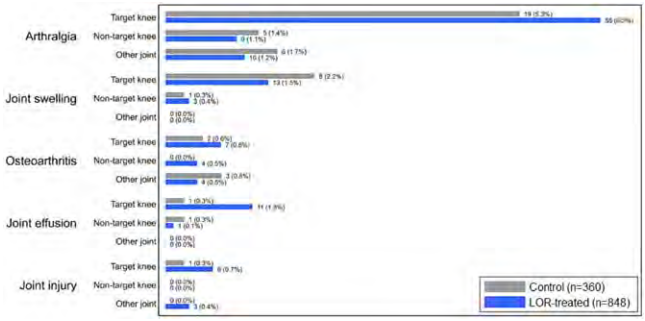


Figure 2. Joint-specific adverse event summary, subcategorized by affected joint, for events occurring in at least 1% of the treated population (N=1208).

There were 16 bone health-related AEs in 9/848 (1.1%) LOR-treated and 3/360 (0.8%) control subjects. Of the bone health AEs, 2 were osteopenia/osteoporosis in 2 LOR-treated postmenopausal women and 14 were fractures in 10 subjects (7 LOR-treated, 3 control). All fractures (3 patellar [1 target knee, 2 non-target knee], 3 vertebral, 2 foot, 2 wrist, 2 rib, 1 fibula, 1 hand) were adjudicated and determined to be caused by trauma; all healed uneventfully within the expected time frame.
Conclusion: In exposure to date of 848 subjects, IA LOR for the treatment of knee OA appeared to be safe and well tolerated. These data support the continued evaluation of LOR as a potential treatment for knee OA.
References:
[1] Deshmukh V, et al. *Osteoarthritis Cartilage*. 2017.
[2] Deshmukh V, et al. *Osteoarthritis Cartilage*. 2019.
Disclosure of Interests: Ismail Simsek Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Christopher Swearingen Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Sarah Kennedy Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Jeyanesh Tambiah Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Cristina Damatarca Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Yusuf Yazici Shareholder of: Samumed, LLC, Grant/research support from: Bristol-Myers Squibb, Celgene, and Genentech, Consultant of: Celgene and Sanofi, Employee of: Samumed, LLC, Nancy Lane Consultant of: Samumed, LLC, Marc Hochberg: None declared
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OP0189

ASSESSMENT OF CARTILAGE DEGRADATION AND PROTECTIVE MARKERS IN SYNOVIAL FLUID FROM OSTEOARTHRITIS PATIENTS BEFORE AND AFTER CYCLES OF INTRA-ARTICULAR INJECTIONS WITH SPRIFERMIN

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Background: It is challenging to monitor treatment effects after intra-articular (IA) injection with tissue modifying drugs. Assessment of biomarker levels in synovial fluid may be one solution to the challenge. Sprifermin is a truncated form of fibroblast growth factor (FGF) 18 known to induce chondrocyte proliferation and type II collagen formation [1,2]. Data from preclinical investigations show that cartilage formation happens in different phases after therapy with sprifermin, starting with a phase of cartilage degradation during the induction of proliferation of chondrocytes followed by a phase of cartilage formation/production of extracellular matrix.
Objectives: The aim was to investigate the effect of IA administrated sprifermin on cartilage turnover activity as compared to placebo in the injected joint by measurement of markers using longitudinal synovial fluid samples of patients participating in the FORWARD study.
Methods: Each included patient had baseline and at least one FU sample available. Synovial fluid (SF) from participants receiving injections at three consecutive weeks in six month intervals through to week (wk) 80 (fig.A) available from the phase II clinical trial evaluating the efficacy and safety of intraarticularly delivered sprifermin [3] were selected for the investigations. Biochemical markers were measured in available SF samples of the placebo (containing saline IA, n=38) and the highest sprifermin dose group (100 mcg/IAx4, n=59). Samples were pretreated with ultrasound and centrifugation to decrease viscosity. Markers measured were PRO-C2 (type II collagen formation), huARGS (aggrecan degradation), and FBN-C (fibronectin). Markers are technically validated for synovial fluid measurement. Data were individually normalized to baseline to investigate the median proportional change over time.
Results: Baseline mean (SD) levels of the markers in SF at BL were: PRO-C2, 21.4 (13.6) ng/mL, huARGS, 1117 (516) pM and FBN-C, 2556 (1959) ng/mL. PRO-C2 was initially decreased (from BL to wk 2) after injection with sprifermin; however, the level was increased at the beginning of each new injection cycle followed by a decrease after injection of sprifermin (Fig.B). Overall synovial PRO-C2 levels increased over time in therapy with sprifermin, while no change was observed for the placebo arm. huARGS showed a similar pattern as PRO-C2 – there was an overall increase in ARGS over time in the sprifermin group (fig.C). Interestingly ARGS continuously decreased over time in the placebo group. FBN-C is continuously increased after injection's cycles, whereas no effect was seen in the placebo group (fig.D).
Conclusion: Confirmatory of the preclinical investigations a biphasic response on cartilage turnover after injection with sprifermin was observed. Biochemical indications of cartilage formation and chondrocyte proliferation was only modulated in the sprifermin group, and cartilage degradation (ARGS) was temporal induced and reduced by sprifermin and placebo injections, respectively.
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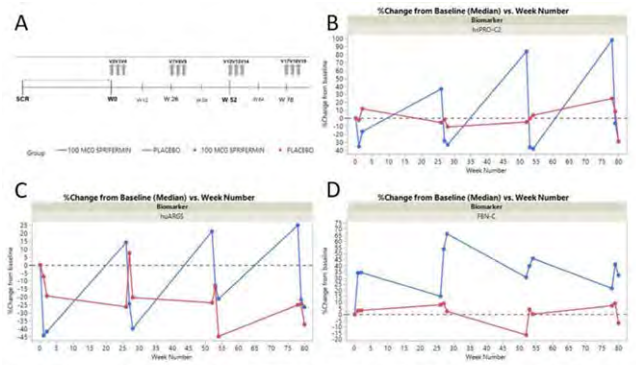


Fig. Assessment of cartilage markers in synovial fluid at the 4 cycles. A) Study overview. B) type II collagen formation, PRO-C2. C) Aggrecan degradation, huARGS. D) Fibronectin degradation, FBN-C. Data are shown as median of available samples at each timepoint.

Disclosure of Interests: Anne-Christine Bay-Jensen Shareholder of: Nordic Bioscience A/S, Employee of: Full time employee at Nordic Bioscience A/S., Angela Manginelli Employee of: Merck KGaA, Flavie Moreau Employee of: Merck KGaA, Yi He Employee of: YH is a full time employee of Nordic Bioscience A/S, Yunyun Luo Employee of: Nordic Bioscience A/S, Jeppe Ragnar Andersen Shareholder of: Nordic Bioscience A/S., Employee of: Full time employee of Nordic Bioscience., Asger Reinstrup Bihlet Shareholder of: Nordic Bioscience A/S., Morten Karsdal Shareholder of: Nordic Bioscience A/S., Employee of: Full time employee at Nordic Bioscience A/S., Hans Gühring Employee of: Merck KGaA, Christoph Ladel Employee of: Merck KGaA
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OP0190 UNDERSTANDING CURRENT PRESCRIPTION DRUG TREATMENT PARADIGMS FOR PATIENTS WITH OSTEOARTHRITIS IN EUROPE

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Background: Joint pain is the most prevalent symptom for sufferers of osteoarthritis (OA). Pharmacological management of OA is restricted by limited efficacy and considerable toxicity, with growing fears about opioid use.
Objectives: To understand the current real-world prescribed drug treatment paradigm related to OA disease severity for patients in 5 EU countries; France, Germany, Italy, Spain and the UK.
Methods: Data were drawn from the Adelphi OA Disease Specific Programme (2017-18), a point-in-time study of physicians and their patients. Physicians classified their patients as currently having mild, moderate or severe disease severity, and provided details on currently prescribed OA therapy and physician satisfaction with therapy, rated from very satisfied to very dissatisfied. Patients were excluded from these analyses if they suffered from back and neck OA only, and shoulder OA that had not been diagnosed by X-ray. Comparisons among disease severity groups were made using analysis of variance and chi-squared tests.
Results: The study included 489 physicians (primary care physicians, rheumatologists, orthopaedists) reporting on 3596 of their OA patients: 24% mild (n=874), 53% moderate (n=1904), and 23% severe (n=818). Overall, 73% patients were prescribed at least one drug for their OA (65% of mild; 76% of moderate; 77% of severe patients [<0.001]). Paracetamol (34%) was the most commonly prescribed OA treatment. NSAIDs (31%) and opioids (27%) were also frequently prescribed treatments, and worsening severity was associated with an increase in opioid use (11% of mild; 26% of moderate, 47% of severe patients [<0.001]), but not NSAID (Table 1). The mean number of prescription medications increased (0.9 for mild; 1.4 for moderate; 1.6 for severe patients [<0.001]) and physician satisfaction with treatment decreased (86% for mild; 70% for moderate; 41% for severe [<0.001]) with worsening OA disease severity.

Table 1. Prescribed treatment by physician-reported OA severity

	Mild (n=874)	Moderate (n=1904)	Severe (n=818)
Current class of medication prescribed for OA, n (%)			
Paracetamol	186 (21.3)	663 (34.8)	313 (38.3)
NSAIDs	267 (30.5)	605 (31.8)	237 (29.0)
Any opioid	93 (10.6)	501 (26.3)	386 (47.2)
Weak opioid	82 (9.4)	407 (21.4)	255 (31.2)
Strong opioid	11 (1.3)	99 (5.2)	146 (17.8)
Opioid + analgesic (combined)	6 (0.7)	15 (0.8)	7 (0.9)
Corticosteroid	31 (3.5)	150 (7.9)	92 (11.2)
Glycosaminoglycan	50 (5.7)	149 (7.8)	62 (7.6)
Viscosupplement	12 (1.4)	93 (4.9)	42 (5.1)
Number of currently prescribed drug classes, mean (SD)	0.9 (0.8)	1.4 (1.1)	1.6 (1.2)

Conclusion: Physicians reported decreasing satisfaction with treatment for their OA patients as disease severity increased, despite increasing use of opioids and numbers of classes of prescribed drugs.
Disclosure of Interests: Philip G Conaghan Consultant of: AbbVie, BMS, Eli Lilly, EMD Serono, Flexion Therapeutics, Galapagos, GSK, Novartis, Pfizer, Speakers bureau: AbbVie, Eli Lilly, Novartis, Pfizer, Lucy Abraham Shareholder of: Pfizer, Employee of: Pfizer, Peita Graham-Clarke Shareholder of: Eli Lilly and Co, Employee of: Eli Lilly and Co, Lars Viktrup Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Joseph C Cappelleri Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Craig Beck Shareholder of: Pfizer, Employee of: Pfizer, Andrew G Bushmakin Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Niall Hatchell: None declared, Emily Clayton: None declared, James Jackson: None declared
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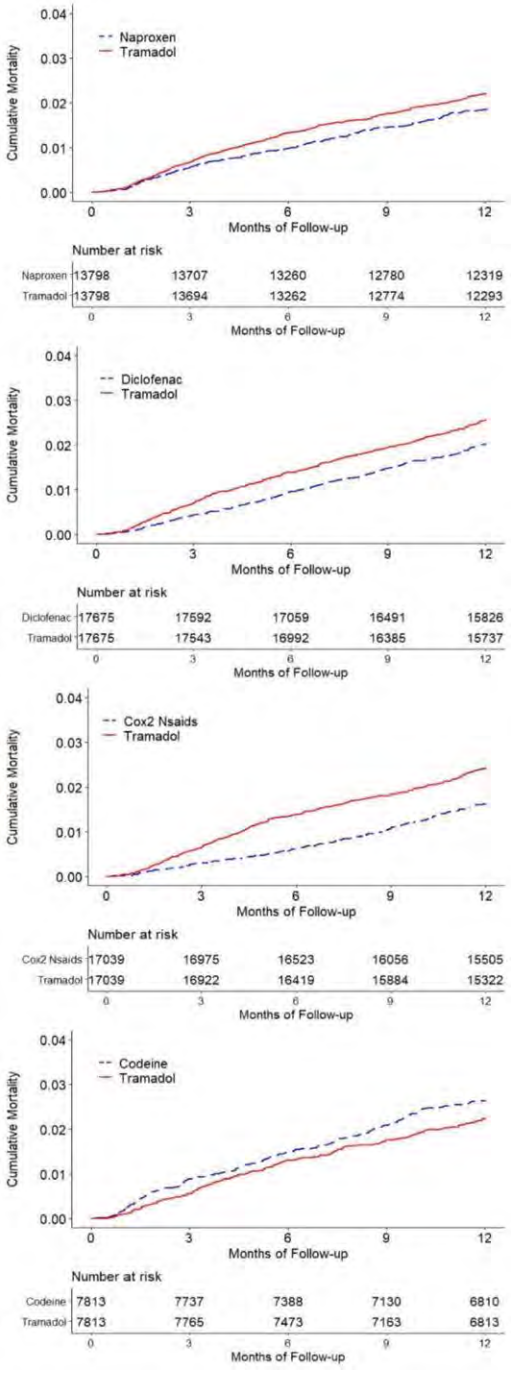
OP0191 ASSOCIATION OF TRAMADOL WITH ALL-CAUSE MORTALITY, CARDIOVASCULAR DISEASE, VENOUS THROMBOEMBOLISM AND HIP FRACTURES AMONG PATIENTS WITH OSTEOARTHRITIS. A POPULATION-BASED STUDY

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Background: Both tramadol (narcotic-like drug) and nonsteroidal anti-inflammatory drugs (NSAIDs) are prescribed for pain relief among osteoarthritis (OA) patients. Evidence comparing risks of adverse events between tramadol and NSAIDs users is inconclusive.
Objectives: To examine the association of tramadol with all-cause mortality, cardiovascular disease (CVD), venous thromboembolism (VTE) and hip fractures (HFx) compared with NSAIDs and codeine in OA.
Methods: Design: Sequential propensity score-matched cohort study. Sample: All patients with OA who received medical care from 2005 to 2014 in the entire province of British Columbia, Canada. Tramadol cohort: Initial prescription of tramadol (n=56325). Four comparator cohorts: the initiation of one of the following: naproxen (n=13798), diclofenac (n=17675), cyclooxygenase-2 [Cox-2] inhibitor (n= 17039), or codeine (a weak opioid) (n=7813). Patients required to be prescribed neither tramadol nor its comparators during the year before the initial prescription date (i.e., index date). Outcomes: 1) all-cause mortality; first ever 2) CVD, 3) VTE, 4) HFx within the 1st year after the initiation of tramadol or its comparators. Follow-up: from index date until the event occurred, disenrollment, or the end of a 1-year follow-up period. Statistical analysis: We created baseline covariates (demographics, comorbidities, medications and health resource utilization) from the year prior to the index date. Calendar years from 2005 to 2014 were divided into 10 blocks; propensity scores were calculated using logistic regression within each block. We used 1:1 greedy matching method. We estimated hazard ratios (HRs) using Cox proportional hazard models.
Results: After propensity score matching, 112650 patients with OA were included (mean age of 68 years, 62.8% were females). During the 1-year follow-up, 296 deaths (21.5/1000 person-years) occurred in the tramadol cohort and 246 (17.8/1000 person-years) in the naproxen cohort (Table 1). All-cause mortality was higher for tramadol compared with all NSAIDs cohorts, but not with the codeine cohort (Table 1, Figure 1). Tramadol initiators have also a higher risk of CVD and VTE compared with the diclofenac and Cox-2 inhibitor initiators with HRs ranging from 1.2 to 1.7. Furthermore, tramadol was also associated with a higher risk of HFx compared with all NSAIDs cohorts (HRs ranging from 1.4 to 1.5). No significant difference was found between tramadol and codeine (Table 1).
Conclusion: OA patients initiating tramadol have an increased risk of mortality, CVD, VTE, and HFx within 1 year compared with NSAIDs, but no statistically significant difference in the risk was observed between tramadol and codeine.

Table 1

		Group1		Group2		Group3		Group4	
		Tramadol	Naproxen	Tramadol	Diclofenac	Tramadol	Cox-2 inhibitor	Tramadol	Codeine
All-cause Mortality	OA (n)	13798	13798	17675	17675	17039	17039	7813	7813
	Death (n)	296	246	439	345	402	267	168	199
	Rate (/1000 PY)	21.5	17.8	24.8	19.5	23.6	15.7	21.5	25.5
	HR (95% CI)	1.2 (1.0-1.4)	1.0	1.3 (1.1-1.5)	1.0	1.5 (1.3-1.8)	1.0	0.8 (0.7-1.0)	1.0
CVD	OA (n)	11708	11708	14924	14924	14779	14779	6809	6809
	CVD (n)	309	319	410	349	404	353	156	164
	Rate (/1000 PY)	26.4	27.3	27.5	23.4	27.3	23.9	22.9	24.1
	HR (95% CI)	1.0 (0.9-1.1)	1.0	1.2 (1.1-1.3)	1.0	1.2 (1.0-1.3)	1.0	0.9 (0.8-1.1)	1.0
VTE	OA (n)	13472	13472	17230	17230	16699	16699	7660	7660
	VTE (n)	41	37	60	40	70	40	28	30
	Rate (/1000 PY)	3.0	2.8	3.5	2.3	4.2	2.4	3.7	3.9
	HR (95% CI)	1.2 (0.9-1.6)	1.0	1.5 (1.1-1.9)	1.0	1.7 (1.3-2.3)	1.0	1.0 (0.7-1.4)	1.0
HFx	OA (n)	13378	13378	17216	17216	16670	16670	7593	7593
	HFx (n)	66	49	88	59	91	60	35	40
	Rate (/1000 PY)	5.0	3.7	5.1	3.4	5.5	3.6	4.6	5.3
	HR (95% CI)	1.4 (1.0-1.8)	1.0	1.5 (1.2-1.9)	1.0	1.5 (1.2-1.9)	1.0	0.9 (0.7-1.2)	1.0



Disclosure of Interests: None declared
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OP0192

PSORIATIC ARTHRITIS IS ASSOCIATED WITH A METABOLICALLY ADVERSE BODY COMPOSITION PROFILE PREDICTIVE OF GREATER CHD AND TYPE 2 DIABETES RISK – MRI FINDINGS FROM THE IMAPA AND UK BIOBANK STUDIES

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Background: Increased Body Mass Index (BMI) is associated with Psoriatic Arthritis (PsA) but with uncertain pathophysiological significance. BMI does not reflect body fat distribution, but fat storage site is important as increased ectopic fat including visceral adipose tissue (VAT), liver fat, and muscle fat infiltration (MFI), are associated with increased type 2 diabetes and coronary heart disease (CHD) risk[1]. To date no study has compared detailed body composition in PsA with the general population and other metabolic diseases.
Objectives: 1. To characterize the body composition profile of PsA compared to age, sex, and BMI-matched metabolic disease free (MDF) individuals, and type 2 diabetes. 2. To relate body composition to risk of type 2 diabetes and CHD in PsA versus MDF controls.
Methods: MRI body composition profiles were available for 29 PsA participants in the IMAPA study[2]. After excluding 3 participants with concomitant type 2 diabetes, body composition was compared in 26 PsA participants with 130 age, sex, and BMI-matched healthy MDF controls (matched 1:5) and 454 individuals with type 2 diabetes from UK Biobank, using Wilcoxon signed-rank test. Analyses were repeated adjusted for age, sex, and BMI. The propensity of PsA patients to develop CHD or type 2 diabetes based on their body composition profile was compared to that of matched MDF controls.
Results: PsA participants had significantly more ectopic fat including greater visceral adipose tissue (VAT) volume and liver fat percentage compared to MDF controls (table 1, figure 1A). This difference persisted after adjustment for age, sex, and BMI. Individuals with PsA shared a similar body composition to type 2 diabetes (table 1, figure 1B). Body composition-predicted propensity for CHD or type 2 diabetes was 1.3 and 1.8 times higher, respectively, for PsA compared to matched MDF controls.

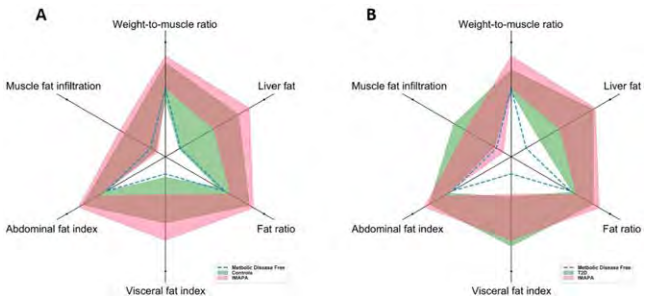


Figure 1. Body Composition Profiles of IMAPA PsA participants (pink) versus A. UK Biobank matched MDF controls (green), and B. type 2 diabetes (T2D) (green).

Table 1. Comparison of body composition parameters in PsA, MDF controls, and type 2 diabetes

Variable	PsA	MDF controls	p-value*	Adj. p value**	Type 2 diabetes	p-value†	Adj. p value‡
Age (years)	56.0 (9.0)	57.4 (6.5)	0.766	-	65.4 (6.9)	< 0.001	-
BMI (kg/m^2)	31.2 (6.4)	30.5 (5.3)	0.799	-	29.9 (5.2)	0.397	-
VAT (L)	5.89 (2.10)	4.34 (1.83)	<0.001	<0.001	5.93 (2.56)	0.662	0.301
Visceral fat index (L/m^2)	2.06 (0.73)	1.52 (0.64)	<0.001	<0.001	2.03 (0.84)	0.337	0.175
Abdominal subcutaneous adipose tissue (L)	10.48 (4.90)	9.42 (4.86)	0.288	0.071	8.58 (3.93)	0.109	0.339
Abdominal fat index (L/m^2)	5.87 (2.39)	4.93 (2.29)	0.084	<0.001	5.04 (1.92)	0.052	0.024
Liver fat (%)	8.88 (4.42-13.18)	3.29 (1.98-7.25)	0.002	0.002	6.13 (2.77-11.63)	0.392	0.656
MFI (%)	7.74 (2.57)	7.43 (1.95)	0.748	0.292	8.61 (2.29)	0.736	0.191

Values are mean (SD) (liver fat, median (IQR)). *PsA vs. MDF controls. **PsA vs. MDF controls adjusted for age, sex, and BMI. †PsA vs. Type 2 diabetes. ‡ PsA vs. Type 2 diabetes adjusted for age, sex, and BMI.

Conclusion: This is the first study to report that individuals with PsA have a body composition profile associated with an adverse metabolic phenotype, with greater VAT and ectopic liver fat than the general population and more similar to that of type 2 diabetes, in line with their greater cardiometabolic risk. These data mandate a revision of the management approach to PsA that includes attention to weight loss interventions.

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Dendritic cells as therapeutics

OP0193

BIIB059, A HUMANIZED MONOCLONAL ANTIBODY TARGETING BDCA2 ON PLASMACYTOID DENDRITIC CELLS (PDC), SHOWS DOSE-RELATED EFFICACY IN THE PHASE 2 LILAC STUDY IN PATIENTS (PTS) WITH ACTIVE CUTANEOUS LUPUS ERYTHEMATOSUS (CLE)

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Background: CLE represents an unmet medical need with no approved therapy. BIIB059, a humanized monoclonal antibody, binds to BDCA2 and inhibits pro-inflammatory mediators production, including type I interferons. BIIB059 was evaluated in Phase 1 studies NCT02106897 and NCT03224793. LILAC is a 2-part Phase 2 study: Part A enrolled SLE pts; Part B enrolled pts with active CLE (NCT02847598).

Objectives: Evaluate efficacy and safety of BIIB059 in pts enrolled in Part B at Week 16, end of treatment (EOT) period.

Methods: Pts with active CLE, SCLE and/or CCLE and adjudicated Cutaneous Lupus Disease Area and Severity Index – Activity (CLASI-A) ≥8 were enrolled and randomized to receive either BIIB059 (50, 150 or 450 mg) or placebo (PBO) s.c. Q4W. Primary endpoint was dose response defined by % change in CLASI-A score from baseline (BL) to Week 16. Secondary endpoints included CLASI-50 response rate and ≥ 7-point reduction in CLASI-A score from baseline to EOT. Adverse events and serious adverse events were recorded throughout the study.

Results: 132 pts with active CLE were randomized. The study met its primary endpoint, demonstrating a dose response (p= 0.0005) and a statistically significant difference in % change from BL in CLASI-A score in BIIB059-treated pts vs PBO. Table 1 and Table 2 summarize efficacy and safety results, respectively.

Conclusion: BIIB059 administration to pts with active CLE resulted in statistically significant dose-related improvement in disease activity vs PBO with no untoward safety signals. Further development of BIIB059 in CLE is warranted.

Disclosure of Interests: Victoria Werth Grant/research support from: Biogen, Celgene, Gilead, Janssen, Viela, Consultant of: Biogen, Gilead, Janssen, Abbvie, GSK, Resolve, AstraZeneca, Amgen, Eli Lilly, EMD Serono, BMS, Viela, Kyowa Kirin, Richard Furie Grant/research support from: AstraZeneca, Biogen, Consultant of: AstraZeneca, Biogen, Juanita Romero-Diaz Consultant of: Biogen, Sandra Navarra Speakers bureau: Astellas, Novartis, Pfizer, Johnson & Johnson, Abbvie, Kenneth Kalunian Grant/research support from: Pfizer, Lupus Research

Table 1. Efficacy Endpoints

		BIIB059								
	PBO	50 mg			150 mg			450 mg		
	LS Mean (SE)	LS Mean (SE)	LSMD* from PBO (95% CI)	P val.	LS Mean(SE)	LSMD* from PBO (95% CI)	P val.	LS Mean (SE)	LSMD* from PBO (95% CI)	P val.
Primary Endpoint CLASI-A % change from BL	-14.5 (6.4)	-40.8 (7.5)	-26.3 (-45.7; -7.0)	0.008	-47.9 (7.4)	-33.5 (-52.7; -14.3)	0.001	-43.5 (5.5)	-28.0 (-44.5; -11.5)	0.001
Secondary Endpoints	n(%)	n(%)	LSMD* from PBO (95% CI)	P val.	n(%)	LSMD* from PBO (95% CI)	P val.	n(%)	LSMD* from PBO (95% CI)	P val.
Prop. of participants achieving CLASI 50	7/32 (21.9%)	10/26 (38.5%)	15.8% (-7; 39)	0.133	11/25 (44.0%)	21 (-2.8; 45)	0.059	20/43 (46.5%)	23 (3; 44)	0.024
Prop. of participants achieving a ≥7-point CLASI-A reduction from BL	7/32 (21.9%)	9/26 (34.6%)	12.3 (-11.3; 35.8)	0.228	12/25 (48.0%)	22.2 (-2.0; 46.3)	0.055	18/43 (41.8%)	16.8 (-6.7; 40.4)	0.048

*LSMD=LS Mean Difference

Table 2. Safety Profile: Number of participants (%) experiencing any event

	PBO	BIIB059				OVERALL
	N=33	50 mg N=26	150 mg N=25	450 mg N=48	Pooled N=99	N=132
Any Event, n(%)	18 (54.5)	17 (65.4)	12 (48)	33 (68.8)	62 (62.6)	80 (60.6)
Severity						
Mild	11 (33.3)	11 (42.3)	8 (32.0)	19 (39.6)	38 (38.4)	49 (37.1)
Moderate	4 (12.1)	6 (23.1)	3 (12.0)	12 (25.0)	21 (21.2)	25 (18.9)
Severe	3 (9.1)	0	1 (4.0)	2 (4.2)	3 (3.0)	6 (4.5)
Related events	6 (18.2)	9 (34.6)	4 (16.0)	16 (33.3)	29 (29.3)	35 (26.5)
Serious events	2 (6.1)	0	3 (12.0)	2 (4.2)	5 (5.1)	7 (5.3)
Related serious events	1 (3.0)	0	1 (4.0)	1 (2.1)	2 (2.0)	3 (2.3)
Events leading to drug withdrawal	0	1 (3.8)	1 (4.0)	1 (2.1)	3 (3.0)	3 (2.3)
Events leading to study withdrawal	0	0	0	1 (2.1)	1 (1.0)	1 (0.8)
Fatal events	0	0	0	0	0	0

Alliance, Sanford Consortium, Consultant of: Genentech, Nektar, BMS, Janssen, AstraZeneca, Biogen, Vielabio, Equillium, Eli Lilly, ILTOO, Abbvie, Amgen, Roche, Gilead, Ronald van Vollenhoven Grant/research support from: AbbVie, Arthrogen, Bristol-Myers Squibb, GlaxoSmithKline, Lilly, Pfizer, and UCB, Consultant of: AbbVie, AstraZeneca, Biotest, Bristol-Myers Squibb, Celgene, GSK, Janssen, Lilly, Medac, Merck, Novartis, Pfizer, Roche, and UCB, Filippa Nyberg Consultant of: Biogen, Benjamin Kaffenberger Grant/research support from: Amgen, Biogen, InflaRx, Veloce Biopharmaceuticals, Dermatology Foundation, Saira Sheikh: None declared, Goran Radunovic: None declared, XIAOBI HUANG Shareholder of: Biogen, Employee of: Biogen, HUA CARROLL Shareholder of: Biogen, Employee of: Biogen, Francois Gaudreault Shareholder of: Biogen, Employee of: Biogen, Adam Meyers Shareholder of: Biogen, Employee of: Biogen, Catherine Barbey Shareholder of: Biogen, Employee of: Biogen, Cristina Musselli Shareholder of: Biogen, Employee of: Biogen, NATHALIE FRANCHIMONT Shareholder of: Biogen, Employee of: Biogen

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OP0194 **IMMUNOSUPPRESSIVE EFFECT OF TOLEROGENIC DENDRITIC CELLS ON AUTOLOGOUS T-CELLS IN PATIENTS WITH RHEUMATOID ARTHRITIS**

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Background: Dendritic cells (DCs) are known to contribute to the pathogenesis of rheumatoid arthritis (RA) through presentation of cartilage glycoprotein, production of proinflammatory cytokines and activation of Th1/Th17 responses. Along with stimulating activity, DCs may exhibit suppressive functions via capacity to induce T cell apoptosis/anergy and to generate regulatory T cells. Since these DCs have potential to control autoreactive T-lymphocytes, the enhancing of tolerogenic properties of DCs seems to be a new important strategy in treatment of RA. However, it remains unclear whether autoreactive T lymphocytes are sensitive to the immunosuppressive effects of DC.
Objectives: The aim of our study is to investigate the mechanisms of the inhibitory effect of dexamethasone-modified DCs (dexDCs) in patients with RA on autologous T cells.
Methods: Twenty patients with RA with high and moderate activity of disease were recruited in this study. All patients fullfield ACR/EULAR criteria (2010). All studies were performed after receiving informed consent. DCs were generated from blood monocytes culturing for 5 days with GM-CSF and IFN-α in the presence dexamethasone, applied on third day. LPS as maturation stimuli was added on fourth day. The study evaluated the ability of dexDCs to induce T cell apoptosis, inhibit the production of Th1 and Th17 cytokines in auto-mixed leukocytes culture (MLC), induce the activation of T-regulatory cells, and inhibit the purified protein derivative (PPD)-specific immune response.
Results: We revealed that dexDCs markedly suppressed the production of IFN-γ and IL-17, while the decreasing of IL-4 and IL-13 was less pronounced. Thus, in comparison with Th2 cells, Th1 and Th17 T lymphocytes were more sensitive to suppressor effects of dexDCs. We also revealed a significant increasing of cells in the stage of late apoptosis (An+Pi+) during the cultivation of autologous T cells with dexDCs. We have also proved the suppressive effect of dexDCs on culture T cells that are co-cultivated with mature DCs (reduction of proliferation from 2700 cpm to 1500 cpm, p=0.0015). In addition, we have shown the ability of dexDCs to induce T-regulatory cells with a phenotype CD4+IL10+Tr1. In conclusion, we have shown the ability of PPD-loaded dexDCs to inhibit the proliferative response of both mature DCS and mature dexDCs-loaded PPD, that indicates the ability of dexDCs to possess antigen-specific suppression.
Conclusion: The data obtained indicate that, dexDCs from RA patients have an immunosuppressive effect on autologous T cells through the induction of apoptosis, anergia and activation of T regulatory cells that authorise their application as a DCs-vaccine.
Disclosure of Interests: None declared
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Creating in vitro patients - how to best model disease

OP0195 **VASCULARIZED THREE-DIMENSIONAL MODELS OF HUMAN SKIN FIBROSIS**

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Background: The complex pathophysiological processes that result in fibrotic tissue remodeling in systemic sclerosis involve interplay between multiple cell types (1). Experimental models of fibrosis are essential to provide a conceptual understanding of the pathogenesis of these diseases and to test antifibrotic drugs. Current models of fibrosis have important limitations: the *in vivo* models rely on species that are phylogenetically distant, whereas the *in vitro* models are oversimplified cultures of a single cell type in an artificial two-dimensional environment of excessive stiffness, which imposes an unphysiological cell polarization (2).
Objectives: Here we evaluated the potential use of vascularized, three-dimensional *in vitro* human skin equivalents as a novel model of skin fibrosis and a platform for the evaluation of antifibrotic drugs.
Methods: Skin equivalents were generated by seeding human endothelial cells, fibroblasts and keratinocytes on a decellularized porcine extracellular matrix with perfusable vascular structure. The skin models were cultured for one month in a system that ensured perfusion of the vascular network at physiological pressure. Fibrotic transformation induced by TGFβ and response to nintedanib as an established antifibrotic drug was evaluated by capillary Western immunoassays, qPCR, histology and immunostaining.
Results: The vascularized human skin equivalents formed the major skin structures relevant for the pathogenesis of fibrosis: a polarized, fully matured epidermis, a stratified dermis and a perfused vessel system with small capillaries. Exposure to TGFβ led to the fibrotic transformation of the skin equivalents, with activated TGFβ downstream pathways, increased fibroblast-to-myofibroblast transition and excessive deposition of extracellular matrix. Treatment of models exposed to TGFβ with nintedanib (a drug with proven antifibrotic effects) ameliorated the fibrotic transformation of skin equivalents with reduced TGFβ signaling, fibroblast-to-myofibroblast transition and decreased extracellular matrix deposition.

Conclusion: Here we describe a novel *in vitro* model of skin fibrosis. Our data show that vascularized skin equivalents can reproduce all skin layers affected by fibrosis, that, upon exposure to TGFβ, these models recapitulate key features of fibrotic skin and that these skin models can be used as a platform for evaluation of antifibrotic drugs in a setting with high relevance for human disease.

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Time2Work - why and how to act

OP0196-PARE **#ARTHRITISATWORK: USING TWITTER TO ENGAGE THE INTERNATIONAL ARTHRITIS COMMUNITY**

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Background: In 2019, EULAR launched the #Time2Work campaign [1] to raise awareness of the impact of rheumatic and musculoskeletal diseases on individuals, society, and the economy. Building on this theme, the Canadian Arthritis Patient Alliance (CAPA) developed a social media campaign and Twitter chat in collaboration with international patient advocates and organizations. The Twitter chat built upon CAPA's successful development of workplace resources for people living with arthritis [2].

Objectives: To deliver an international #ArthritisAtWork social media campaign on Twitter, in support of the #Time2Work campaign.

Methods: A one-hour Twitter Chat was held on World Arthritis Day (October 12, 2019) on arthritis in the workplace (#ArthritisAtWork) from 18:00 to 19:00 UTC. The chat was hosted by CAPA and co-hosted by Simon Stones, a patient advocate from the United Kingdom (UK) and CreakyJoints, patient-driven arthritis organization in the United States (US). The Twitter Chat questions were co-developed in advance by the hosts, and blog posts were shared from CAPA's website. Each host also promoted the Twitter Chat through their websites, newsletters and online communities. A social media analytical tool, Symplur, was used to measure audience engagement using the hashtag #ArthritisAtWork. In addition, pertinent Tweets before, during, and after the chat were obtained. The analysis of themes was undertaken to identify common issues and questions.

Results: One hundred and ten users participated in the Twitter chat between 17:20 and 19:20 UTC. Participants included people living with arthritis, researchers, patient organizations, health information outlets and academic institutions. During this period, 565 tweets were shared between participants in Australia, Canada, Ireland, Spain, UK and US. There were 3.352 million Twitter impressions. This represents the number of times a tweet appears to users in either their timeline or search results. Emergent themes of the analysis include:

- common workplace challenges such as employer attitudes and stigma;
- effective workplace supports such as prioritizing tasks and requesting workplace accommodations; and
- areas of improvement such as instituting workplace policies, flexible workplace approaches and education for employees and managers.

Conclusion: The social media campaign was successful in reaching a diverse audience and supporting the #Time2Work campaign. Social media tools can provide an important social support for people living with arthritis as they navigate workplace challenges. It also offers a more contemporary platform to engage the international community on issues of common interest. Working together, internationally helps expand reach and reduce barriers in communication. Research can be conducted to measure potential behavior change that leverages digital social support for people living with arthritis.

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Making rational the therapeutic approach to Still's disease in children and adults

OP0197

THE INITIAL TREATMENT OF SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS: AN INTERNATIONAL COLLABORATION AMONG 10 REGISTRIES

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1: Medication Usage within First Year (pre/post 2012 where available)

	Glucocorticoids (IV+PO) %	Methotrexate %	Biologic %	Anti-IL-1 %	Anakinra %	Tocilizumab %
USA 2010-2011 n=9	22	56	33	33	33	0
USA 2012-2018 n=91	50	17	71	70	57	17
Canada 2005-2010 n=88	76	60	17	10	10	0
UK 2001-2011 n=69	78	71	10	3	3	0
UK 2012-2018 n=31	48	58	29	19	19	19
Portugal 2008-2011 n=73	42	36	4	3	3	0
Portugal 2012-2018 n=19	74	47	32	16	16	21
Sweden 2009-2015 n=50	96	46	62	30	28	30
Denmark 1997-2011 n=83	86	40	13	6	6	2
Denmark 2012-2018 n=32	50	12.5	75	63	63	19
Turkey 2000-2011 n=71	93	77	58	42	37	20
Turkey 2012-2018 n=114	98	52	40	32	28	9
Germany 2000-2011 n=271	73	62	13	7	6	<1
Germany 2012-2018 n=249	57	47	27	19	10	20
Norway 1997-2011 n=26	81	62	12	4	4	8
Norway 2012-2018 n=5	100	60	100	20	20	80
Finland 2006-2011 n=12	42	42	17	0	0	8
Finland 2012-2018 n=12	25	8	8	0	0	8

Background: The introduction of biologics has transformed care for children with systemic juvenile idiopathic arthritis (SJIA). Differences in treatment approaches between countries and how they have changed over time are not well studied.
Objectives: We contrast the initial features, treatment and 12-month outcome in SJIA across 10 JIA registers in Europe and North America.
Methods: Data were extracted locally from 10 Registers including manifestations at diagnosis, medication use over first year and outcomes (Physician Global Assessment (PGA), active joint count (AJC)) at 12 months. Data was compared before/after 2012 to assess change over time. Weighted (w) means were used to adjust for varying number of patients/Register.
Results: 1,149 patients; 553 had medication data for 2012-2018; primarily female and Caucasian; median age at diagnosis 5.3-8 years. Median duration of symptoms prior to first visit varied (0-3.3 months). Glucocorticoid (GC) use was common in the first year (w_average 72% (range 33-96%)). Biologic use included IL-1, IL-6 and TNF inhibitors. The proportion of patients treated with biologics, primarily anakinra, increased after 2012 (Table 1). W_mean PGA and AJC at the 12±3 month visit were 1.55 and 1.57, respectively (Table 2). At one year, the proportion of patients prescribed GC varied (w_mean 40%, range 26-60%).
Conclusion: Analysis of SJIA patients across 10 countries show that time to first rheumatology visit was highly variable. Although local factors influence treatment decisions, biologic use increased after 2011; anakinra most common. Nearly 75% of patients were prescribed steroids within the first year but seemed to decrease after 1 year. More study is needed on long-term outcomes in SJIA patients within this modern era.

2: Clinical Outcomes at 12 Months -all years

	AJC Median [IQR]	PGA Median [IQR]	GC Use, %
USA	0 [0, 0]	0 [0,0]	47
Canada	0 [0, 2]	0.1 [0, 2.7]	41
UK	0 [0, 0]	0.5 [0, 1.7]	53
Portugal	0 [0, 0]	0.3 [0, 1]	53
Sweden	0 [0, 0.5]	0 [0, 0.5]	31
Denmark	0 [0, 0]	-	26
Turkey	4 [2, 7]	4 [3, 7]	60
Germany	0 [0, 1]	0 [0,2]	36
Norway	0 [0, 0]	0.5 [0, 2]	45
Finland	0 [0, 0]	0 [0, 0]	33

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OP0198

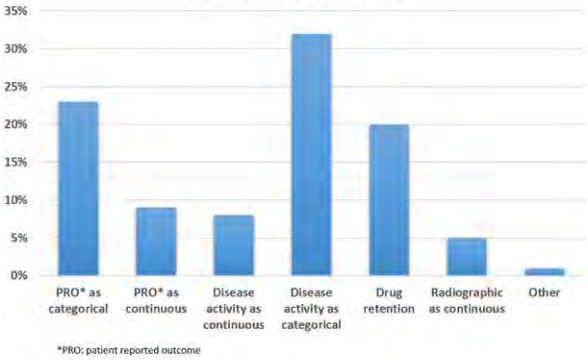
A SYSTEMATIC REVIEW TO INFORM THE EULAR POINTS TO CONSIDER WHEN ANALYSING AND REPORTING COMPARATIVE EFFECTIVENESS RESEARCH WITH OBSERVATIONAL DATA IN RHEUMATOLOGY

K. Lauper[1], J. Kedra[2], M. De Wit[3], B. Fautrel[4], T. Frisell[5], K. Hyrich[6], F. Iannone[7], P. M. Machado[8], L. Midtbøll Ørnbjerg[9], Z. Rotar[10], M. J. Santos[11], T. Stamm[12], S. Stones[13], A. Strangfeld[14], R. B. M. Landewé[15,16], A. Finckh[17], S. A. Bergstra[18], D. Courvoisier[1].
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Background: Comparative effectiveness studies using observational data are increasingly used. Despite their high potential for bias, there are no detailed recommendations on how these studies should best be analysed and reported in rheumatology.
Objectives: To conduct a systematic literature review of comparative effectiveness research in rheumatology to inform the EULAR task force developing points to consider when analysing and reporting comparative effectiveness research with observational data.
Methods: All original articles comparing drug effectiveness in longitudinal observational studies of ≥100 patients published in key rheumatology journals (Scientific Citation Index > 2) between 1.01.2008 and 25.03.2019 available in Ovid MEDLINE® were included. Titles and abstracts were screened by two reviewers for the first 1000 abstracts and independently checked to ensure sufficient agreement has been reached. The main information extracted included the types of outcomes used to assess effectiveness, and the types of analyses performed, focusing particularly on confounding and attrition.
Results: 9969 abstracts were screened, with 218 articles proceeding to full-text extraction (Figure 1), representing a number of rheumatic and musculoskeletal diseases. Agreement between the two reviewers for the first 1000 abstracts was 92.7% with a kappa of 0.6. The majority of the studies used several outcomes to evaluate effectiveness (Figure 2A). Most of the studies did not explain how they addressed missing data on the covariates (70%) (Figure 2B). When addressed (30%), 44% used complete case analysis and 10% last observation carried forward (LOCF). 25% of studies did not adjust for confounding factors and there was no clear correlation between the number of factors used to adjust and the number of participants in the studies. An important number of studies selected covariates using bivariate screening and/or stepwise selection. 86% of the studies did not acknowledge attrition (Figure 2C). When trying to correct for attrition (14%), 38% used non-responder (NR) imputation, 24% used LUNDEX[1], a form of NR imputation, and 21% LOCF.

Figure 2: Results of the Systematic Literature Review

Figure 2A: Main outcomes



*PRO: patient reported outcome

Figure 2B: Missing Data

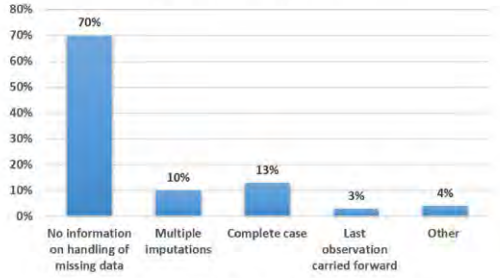
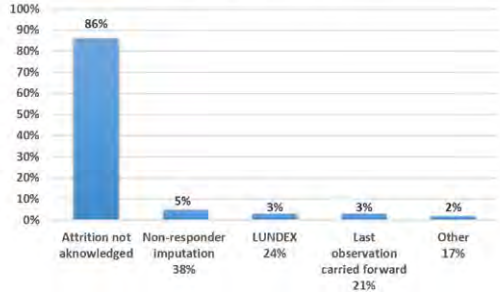


Figure 2C: Attrition



Conclusion: Most of studies used multiple outcomes. However, the vast majority did not acknowledge missing data and attrition, and a quarter did not adjust for any confounding factors. Moreover, when attempting to account for attrition, several studies used methods which potentially increase bias (LOCF, complete case analysis, bivariate screening…). This systematic review confirms the need for the development of recommendations for the assessment and reporting of comparative drug effectiveness in observational data in rheumatology.
References:
[1] Kristensen et al. A&R. 2006 Feb;54(2):600-6.
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OP0199

POINTS TO CONSIDER WHEN ANALYSING AND REPORTING COMPARATIVE EFFECTIVENESS RESEARCH WITH OBSERVATIONAL DATA IN RHEUMATOLOGY

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Background: Comparing drug effectiveness in observational settings is hampered by several major threats, among them confounding and attrition bias bias

(patients who stop treatment no longer contribute information, which may overestimate true drug effectiveness).

Objectives: To present points to consider (PtC) when analysing and reporting comparative effectiveness with observational data in rheumatology (EULAR-funded taskforce).

Methods: The task force comprises 18 experts: epidemiologists, statisticians, rheumatologists, patients, and health professionals.

Results: A systematic literature review of methods currently used for comparative effectiveness research in rheumatology and a statistical simulation study were used to inform the PtC (table). Overarching principles focused on defining treatment effectiveness and promoting robust and transparent epidemiological and statistical methods increase the trustworthiness of the results.

Points to consider

Reporting of comparative effectiveness observational studies must follow the STROBE guidelines
Authors should prepare a statistical analysis plan in advance
To provide a more complete picture of effectiveness, several outcomes across multiple health domains should be compared
Lost to follow-up from the study sample must be reported by the exposure of interest
The proportion of patients who stop and/or change therapy over time, as well as the reasons for treatment discontinuation must be reported
Covariates should be chosen based on subject matter knowledge and model selection should be justified
The study baseline should be at treatment initiation and a description of how covariate measurements relate to baseline should be included
The analysis should be based on all patients starting a treatment and not limited to patients remaining on treatment at a certain time point
When treatment discontinuation occurs before the time of outcome assessment, this attrition should be taken into account in the analysis.
Sensitivity analyses should be undertaken to explore the influence of assumptions related to missingness, particularly in case of attrition

Conclusion: The increased use of real-world comparative effectiveness studies makes it imperative to reduce divergent or contradictory results due to biases. Having clear recommendations for the analysis and reporting of these studies should promote agreement of observational studies, and improve studies' trustworthiness, which may also facilitate meta-analysis of observational data.

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Multiple issues in inherited connective tissues - more than 'just' hypermobility

OP0200 PATIENTS WITH HYPERMOBILITY RELATED DISORDERS HAVE A SIGNIFICANT NUMBER OF ORTHOPAEDIC INTERVENTIONS ON MULTIPLE SITES AND AT A YOUNG AGE: DATA FROM A TERTIARY REFERRAL CENTRE

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Background: Mechanisms of pain associated with joint hypermobility are poorly understood and include nociceptive pain from structural joint changes along with soft tissue injuries linked to impaired proprioception; central sensitisation associated with chronic pain and muscle weakness alongside deconditioning. Anxiety and depression are also thought to play a role in patients presenting with pain and hypermobility. We have observed an increase in the rate of orthopaedic surgical procedures undertaken in patients attending the hypermobility clinics compared to those attending the general rheumatology and chronic pain clinics. There is limited published data regarding orthopaedic interventions in patients with hypermobility related disorders especially those with confirmed genetic mutations.

Objectives: We aimed to evaluate the characteristics of patients in our hypermobility cohort focusing on those who had received prior surgical intervention in order to understand the underlying mechanism behind their presentations.

Methods: A retrospective review of medical records was conducted of patients attending a hypermobility clinic at our tertiary referral centre, University College London Hospital, between January 2018 and December 2018.

Results: There were 350 patients (300 females, 50 males) with a mean age of 36 years (range 18-71 years). 63% had a diagnosis of Hypermobility Spectrum Disorder or Hypermobility Syndrome and 37% had a type of Ehlers-Danlos Syndromes (EDS) (hypermobile, classical, vascular or other rare type). 46 patients (13%) had documented genetic mutations. 83 patients (24%) had undergone orthopaedic interventions including 9 who had EDS with confirmed genetic mutations. 54% of patients who had surgical intervention were under the age of 40. The total number of surgical procedures in the cohort was 227 (equating to 0.6485 interventions per patient). Of those requiring operative intervention, the average number of interventions per patient was 2.73. One third of patients had surgery on two or more joint groups, including 8 patients (2%) who had surgery in four or more joint groups. Knees (24%) and hips (23%) were the most common sites for operative intervention with 9% having surgery on their shoulders. 29% of pts had significant hypermobility with a Beighton score of 7 and above but there was no correlation between Beighton score and number of surgical procedures. Only 2% of cases were referred from an orthopaedic team thereby excluding a referral bias.

Conclusion: Patients with hypermobility related disorders have a significant number of orthopaedic surgical procedures on multiple sites and at a young age, with indication of mechanical pathology playing an important role in their symptoms. The Beighton score does not appear to be a reliable predictor of surgical intervention. This is not surprising given that the score only covers 5 joint areas and excludes common surgical sites such as the hips and shoulders. Early diagnosis and a holistic non-operative approach combining physiotherapy and chronic pain management is essential to reduce the need for multiple surgical procedures.

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OP0201 INCREASED RISK OF DEMENTIA IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is a chronic inflammatory disease that can affect any organ of the body. Nervous system involvement of SLE lead to a variety of neurologic and psychiatric manifestations, which are called neuropsychiatric lupus. Cognitive dysfunction may appear as part of neuropsychiatric lupus. There are several papers on the increase in dementia risk in SLE patients, but data are not sufficient and there is little data on whether SLE affects dementia differently depending on the dementia subtype.
Objectives: We evaluate dementia incidence and risk in SLE patients in a nationwide population-based cohort and determine whether the risk is different for each dementia subtype.
Methods: We identified patients aged 40 years or more, with systemic lupus erythematosus between 2008 and 2014 using the database of the National Health Insurance Service (NHIS) of south Korea. Patients who had previously been diagnosed with dementia were excluded from the study. A total of 11,288 SLE patients and 56,440 control subjects with a 1:5 age- and sex-matching were included in the study. The primary outcome of the study was incident dementia, which was defined by an ICD-10 code and the use of dementia medications. Kaplan-Meier curves and Cox proportional hazards regression analysis were used for the analysis.
Results: The incidence rate of dementia was higher in SLE cohort (3.90 per 1,000 person-years) than control cohort (2.73 per 1,000 person-years). Incidence rates of Alzheimer disease and vascular dementia were also higher in SLE cohort than control. SLE patients had a higher risk of dementia compared to control cohorts without SLE (crude hazard ratio 1.43, 95% CI 1.25-1.63). In patients with SLE, the risk of Alzheimer's disease was 1.4 times higher and the risk of vascular dementia 1.6 times higher than non-SLE control.
Conclusion: In this nationwide population-based cohort study, SLE patients had a 1.4-fold higher risk of incident dementia compared to patients without SLE. Further studies are warranted to identify mechanisms of increased risk of dementia in SLE patients. Monitoring of dementia incidence in SLE patients is needed in clinical practice.
Disclosure of Interests: None declared
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OP0202 STRESS-ACTIVATED MIR-204 GOVERNS SENESCENT PHENOTYPES OF CHONDROCYTES TO PROMOTE OSTEOARTHRITIS DEVELOPMENT

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Background: A progressive loss of cartilage matrix leads to the development of osteoarthritis (OA). Matrix homeostasis is disturbed in OA cartilage as the result of reduced production of cartilage-specific matrix and increased secretion of catabolic mediators by chondrocytes. Chondrocyte senescence is a crucial cellular event contributing to such imbalance in matrix metabolism during OA development.
Objectives: We sought to identify a previously unknown, senescence-associated signaling pathway in chondrocytes linked to major OA cartilage manifestations such as PG loss and cartilage degeneration.
Methods: We particularly aimed to screen miRNAs whose inhibition could effectively modulate senescent phenotypes of chondrocytes to treat OA. We investigated the regulatory mechanisms of miR-204 under various stress-eliciting stimuli in primary cultured human and mouse chondrocytes. We examined the in vivo effects of miR-204 overexpression and its antagonism in surgically induced OA mouse models. DMM surgery was used to induce posttraumatic OA in 12-week-old mice. Small RNAs were delivered to mouse knee joints by intra-articular injection. Various OA manifestations including cartilage destruction, subchondral bone sclerosis, osteophyte maturity, and synovial inflammation in mice were histologically inspected.
Results: We identify miR-204 as a senescence-associated microRNA (miRNA) which is markedly upregulated in OA cartilage. The upregulated miR-204 simultaneously targets multiple components of the sulfated proteoglycan (PG) biosynthesis pathway, effectively shutting down PG anabolism. Ectopic expression of the miR-204 in joints triggers spontaneous cartilage loss and OA development, whereas inhibition of miR-204 ameliorates experimental OA, with concomitant recovery of PG synthesis and suppression of inflammatory senescence-associated secretory phenotype (SASP) factors in cartilage
Conclusion: we unravel a stress-activated senescence pathway that underlies disrupted matrix homeostasis in OA cartilage.
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Disclosure of Interests: None declared
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OP0203-HPR EVALUATION OF A 10-WEEK PROGRESSIVE RESISTANCE TRAINING PROGRAMME FOR PEOPLE WITH INFLAMMATORY ARTHRITIS

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Background: Inflammatory Arthritis [IA] adversely affects well-being, function, fatigue and strength[1]. Guidelines recommend people with IA should exercise to improve strength and cardiovascular fitness[2]. In 2015, our team introduced an evidence-based Progressive Resistance Training Programme [PRTP] for IA[3].
Objectives: To evaluate the effectiveness of a PRTP within a United Kingdom National Health Service setting.
Methods: A pre- to post-treatment evaluation was conducted. People with IA attending Rheumatology Physiotherapy were offered a supervised PRTP (1 hour x 10 weeks): 7 exercises at 70-80% 1-repetition maximum (3 x 8-12 repetitions). Treatment outcomes included Health Assessment Questionnaire [HAQ], EQ5D-5L, 30s sit-to-stand [STS], Self-Efficacy (SARAH Trial) [SE], Grip Strength and FACIT-Fatigue [FACIT-F]. Changes in outcomes were analysed using Paired Samples t-tests and standardised mean difference (SMD).
Results: 201 patients commenced the programme between May 2015 and April 2019, with 121 participants providing complete pre-post HAQ data. Diagnoses included Rheumatoid Arthritis (n=149), Psoriatic Arthritis (n=42), Juvenile Idiopathic Arthritis (n=5), Enteropathic IA (n=2), Oligoarthritis (n=1), Reactive Arthritis (n=1) and Undifferentiated IA (n=1). Age (mean ± SD) = 56.8 ± 14.8 years; number of sessions attended = 7.7 ± 3.4.
There were no differences between those recorded as not completing the PTRP (n=54; 72% women; age 55.0 ± 14.6 years; HAQ 0.99 ± 0.70) versus the others (n=147; 78% women; age 57.5 ± 14.8; HAQ 0.86 ± 0.65). A pragmatic decision was made to analyse all available data for each outcome.

Table 1. Analysis of PRTP outcomes * Indicates clinical improvement.

Outcome measure	Pre-treatment	Post-treatment	Mean difference (95% CI)	p-value	Standardised mean difference (95% CI)
HAQ max score 3 (n=121)	0.83 ± 0.65	0.70 ± 0.67	-0.13 (-0.07, -0.19)	p<0.001	-0.20* (-0.46, 0.07)
EQ5D VAS max score 100 (n=119)	70.0 ± 16.3	76.7 ± 15.2	6.7 (9.4, 3.9)	p<0.001	0.42* (0.17, 0.68)
STS number in 30s (n=118)	13.2 ± 4.9	16.2 ± 5.3	3.0 (3.6, 2.5)	p<0.001	0.59* (0.33, 0.85)
SE max score 70 (n=117)	52.3 ± 10.4	58.6 ± 8.0	6.3 (8.3, 4.4)	p<0.001	0.68* (0.41, 0.94)
Grip Strength kg force (n=62)	20.3 ± 9.4	23.6 ± 10.6	3.3 (4.8, 1.7)	p<0.001	0.33* (-0.03, 0.68)
FACIT-F max score 52 (n=58)	30.9 ± 11.5	35.5 ± 12.0	4.6 (7.2, 2.1)	p=0.001	0.39* (0.02, 0.76)

Conclusion: All outcome measures demonstrated statistically significant improvements. Notably, minimal clinically important differences were achieved in STS and FACIT-F. STS correlates to lower limb power, balance and endurance, and is a predictor of falls[4]. Fatigue significantly impacts function in people with IA[5], often limiting confidence and willingness to participate in exercise activities[6].
Effective evidence-based PRTPs for people with IAs can be delivered by Physiotherapists. Improvements in function, wellbeing, self-efficacy, strength and fatigue are achievable, however, exploration of the clinical relevance of these observed changes is recommended. Further research exploring patients' perspectives of the PRTP and adherence to long-term exercise is needed.

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Disclosure of Interests: None declared
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OP0204 LUPUS COMPREHENSIVE DISEASE CONTROL IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: APPLICATION OF A NEW INDEX

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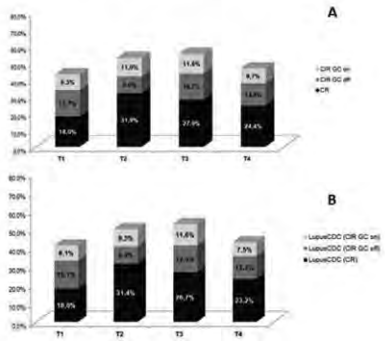
Background: The main outcomes in SLE patients management are represented by the remission achievement and chronic damage prevention. Even though activity and damage are intimately connected, to date indices including both these outcomes are not available.
Objectives: In the present study, we aimed at assessing the application of a new index, the Lupus comprehensive disease control (*LupusCDC*), including disease activity and chronic damage progression.
Methods: We performed a longitudinal analysis, including SLE patients according to ACR 1997 criteria, followed-up in the period between January 2014 and December 2018, and with at least one visit per year. Disease activity was assessed by SLE Disease Activity Index 2000 (SLEDAI-2K) and three different remission levels were evaluated, as reported in Table 1 (1).

Table 1. Remission levels considered in the study (1).

Remission level	Definition
Complete Remission (*CR*)	No clinical and serological activity (SLEDAI-2K=0) in corticosteroid-free and immunosuppressant-free patients (antimalarials allowed)
Clinical remission off-corticosteroids (*CIR-GCoff*)	Serological activity with clinical quiescent disease according to SLEDAI-2K in corticosteroid-free patients (stable immunosuppressive therapy and antimalarials allowed)
clinical remission on-corticosteroids (*CIR-GCon*)	Clinical quiescent disease according to SLEDAI-2K in patients on prednisone 1–5 mg/day (stable immunosuppressants and antimalarials allowed)

Chronic damage was registered according to SLICC damage index (SDI). All the patients were evaluated at baseline (T0) and every 12 months (T1, T2, T3, T4). At each time-point, we calculated the prevalence of LupusCDC, defined as remission achievement plus absence of chronic damage progression in the previous one year. We calculated this outcome including separately the different remission levels.
Results: According with inclusion criteria, 172 SLE patients were evaluated in the present analysis [M/F 16/156, median age 49 years (IQR 16.7), median disease duration 180 months (IQR 156)]. At first assessment, we observed a mean±SD SDI value of 0.7±1.1. In details, 56 patients (32.5%) showed damage in at least one organ/system and the presence of damage was significantly associated with age (p<0.0001, r=0.3) and disease duration (p=0.0003, r=0.3). During the follow-up, we observed a significant increase in SDI values compared with T0 (T1: mean±DS 0.8±1.3, p<0.0001; T2: 0.8±1.4, p<0.0001; T3: 0.9±1.4 p=0.0001; T4: 1.0±1.5 p<0.0001).
In figure 1A and 1B we reported the proportion of patients achieving the different levels of remission and LupusCDC, respectively. In particular, the LupusCDC definition including CR was the most frequently detected in all time-points evaluated (T1: 18.0%; T2: 31.9%; T3: 27.9%; T4: 24.4%), with a significant difference at T2 [LupusCDC(CR) *versus* LupusCDC(CIR-GCoff), p=0.0002; LupusCDC(CR) *versus* LupusCDC(CIR-GCon) p=0.0002)], T3 [LupusCDC(CR) *versus* LupusCDC(CIR-GCoff), p=0.03; LupusCDC(CR) *versus* LupusCDC(CIR-GCon) p=0.006], T4 [LupusCDC(CR) *versus* LupusCDC(CIR-GCon), p=0.002]. No significant differences were found when comparing the prevalence of different remission levels and the prevalence of LupusCDC including the corresponding remission.
Conclusion: In the present analysis we proposed for the first time a new index including disease activity and chronic damage, in order to evaluate the proportion of SLE patients reaching a comprehensive disease control. We found that CR is most frequently associated with the absence of damage progression.
References:
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Figure 1. Proportion of patients achieving one of the three levels of remission (A), and of patients reaching LupusCDC according with different remission levels (B).



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OP0205 PHASE I STUDY OF D-0120, A NOVEL URAT1 INHIBITOR IN CLINICAL DEVELOPMENT FOR HYPERURICEMIA AND GOUT

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Background: D-0120 is a novel oral selective uric acid transporter (URAT1) inhibitor being developed for the treatment of hyperuricemia and gout by blocking the reabsorption of uric acid (UA) within the renal proximal tubule, thereby reducing serum uric acid concentrations. As a novel URAT1 inhibitor, D-0120 is anticipated to have more potent serum UA reducing effect than the approved URAT1 inhibitor lesinurad, but with less toxicity and wider therapeutic window. The pharmacological potential of D-0120 for the treatment of hyperuricemia and gout was demonstrated in preclinical studies. The results of the in vitro hURAT1 expressed CHO cell model showed that the inhibitory activity of D-0120 is 150-fold more potent than lesinurad and slightly more potent than verinurad.
Objectives: The purpose of this dose escalation study is to evaluate the safety and tolerability of D-0120 in multiple ascending doses in healthy volunteer, to characterize the pharmacokinetics (PK) of D-0120 and to assess pharmacodynamic (PD) effects and determine the drug-drug interaction (DDI) effect of febuxostat and D-0120 in healthy volunteers.
Methods: This is a randomized, double blind, multiple ascending doses Phase I study of D-0120 in healthy volunteers conducted at one site. Thirty-two healthy eligible volunteers with serum uric acid level ≥ 4.5 mg/dL but within normal range at screening were enrolled and dosed with D-0120 within 4 different single agent cohorts for a period of 7 days. Each cohort had 8 subjects randomized at 3:1 ratio for D-0120:placebo. A fifth cohort of 8 healthy eligible volunteers were enrolled and dosed with 5 mg of D-0120 in combination with 40 mg of febuxostat over a period of 9 days. Evaluation of safety, PK and PD was conducted at various timepoints while the patients were in

confinement. Further safety evaluation took place on Day 14. A Safety Review Committee reviewed safety, PK and PD data for each cohort of D-0120 dose level (2.5 mg, 5 mg, 10 mg, 20 mg) as well as when D-0120 5 mg was combined with 40 mg febuxostat. PK evaluation for multiple dose parameters included AUC0-τ, Cmax, Cmin, Tmax and FI.

Results: Dose escalation of D-0120 from 2.5 mg/day to 20 mg/day was completed without any dose limiting toxicities. Most AEs occurred during the study were mild to moderate in severity and did not require any treatment before resolution. There was no SAE and no dose reduction during the treatment period. The pharmacokinetic (PK) evaluation of ascending dose levels of D-0120 suggested a dose proportional increase in drug exposure and there was no significant change of PK profile between Day 1 and Day 7 of dosing. For pharmacodynamic (PD) evaluation, the serum uric acid (UA) levels before and after D-0120 dosing was evaluated on multiple days. The UA reduction effect achieved maximum at about 4-8 hours after dosing and the effect lasted for at least 24 hours. After the 7-day dosing period, the mean percentage of UA reduction from baseline showed an increasing trend as the dose level increased.

More detailed safety, PK and PD data from multiple D-0120 dose cohorts and D-0120/febuxostat combination cohort will be presented at the meeting.

Conclusion: The oral daily administration of a novel URAT1 inhibitor, D-0120, in healthy volunteers for 7 days was well tolerated at dose levels from 2.5 mg/day to 20 mg/day. The PK profile demonstrated a dose proportional increase. D-0120 administration for 7 days resulted in significant reduction of serum UA levels. Further evaluation of this novel agent in longer treatment period and in patients with hyperuricemia and/or gout is warranted.

References: Not Applicable.

Disclosure of Interests: Ling Zhang Employee of: INVENTISBIO, David Wyatt: None declared, Kathryn Stazzone Employee of: INVENTISBIO, Zhe Shi Employee of: INVENTISBIO, Yaolin Wang Employee of: INVENTISBIO

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OP0206 ALLANTOIN - A BIOMARKER OF OXIDATIVE STRESS - IS HIGHER IN PATIENTS WITH GOUT THAN IN HEALTHY VOLUNTEERS, AND CORRESPONDS WITH SEVERITY OF DISEASE

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Background: Uric acid can be non-enzymatically oxidized into allantoin and other products by reactive oxygen species. Allantoin has emerged as a reliable biomarker for monitoring oxidative status both *in vitro* and *in vivo*[1]. In gout patients, significantly increased plasma levels of allantoin have been found compared to healthy controls[2].

Objectives: The aim of this pilot study was to measure allantoin as a biomarker of oxidative stress in patients with gout using newly developed UHPLC-HILIC-MS/MS method[3] and to investigate whether the allantoin levels are higher in patients with more severe disease (tophaceous gout).

Methods: We used clinical data and frozen serum (-80°C) from 10 patients with chronic tophaceous gout, 10 patients with chronic gout without tophi and 10 healthy controls. Allantoin was determined in serum with sensitive UHPLC-MS/MS method using an isotopically labeled internal standard as we described before[3]. In addition, the concentrations of serum CRP, creatinine and uric acid were measured. Data are summarized as medians with interquartile range [IQR]. Differences between two patient groups were evaluated using the Wilcoxon signed-rank test.

Results: The median concentrations of allantoin in the serum from patients with tophaceous gout were significantly higher than in patients with gout without tophi (4.2 [2.6] vs. 3.2 μM [1.5], p = 0.0273). There was no significant difference in other biochemical or demographic parameters (CRP, uric acid, creatinine, BMI, weight) between these two groups. Allantoin levels in healthy controls were significantly lower (0.5 vs. 4.2 [2.6], p = 0.0020, 0.5 vs. 3.2 [1.5], p < 0.0001) (Fig. 1).

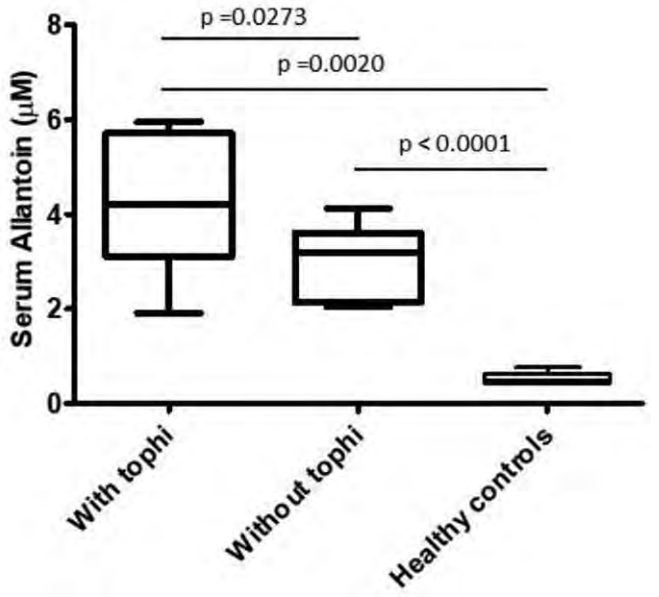


Fig. 1. Box plots of allantoin concentration in patients with tophaceous gout with tophi, without tophi and in healthy controls.

Conclusion: We have observed significantly higher levels of serum allantoin in the patients with more advanced gout with tophi compared with the patients with chronic gout without tophi. We have found elevated values of allantoin in both groups in comparison with healthy controls. In our small cohort the level of allantoin correspond with the severity of disease presented by tophi. However, further studies in large cohorts are needed. We can speculate, whether higher level of oxidative stress may contribute to increased cardiovascular risk and mortality in patients with gout (and more so in severe gout)[4].

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Cartilage - heal thyself!

OP0207 MECHANISM OF CHONDROPROTECTIVE EFFECTS OF 2-DEOXYGLUCOSE

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Background: We recently reported that the inhibitor of hyaluronan (HA) biosynthesis, 4-methylumbelliferone (4-MU) blocked IL-1β activation of MMP13 mRNA and protein expression in human osteoarthritic (OA), bovine as well as bovine or OA cartilage explants [1]. This was a somewhat counterintuitive observation

because we have also demonstrated that the overexpression of HAS2 (HAS2-OE) exerted the same chondroprotective effects on human and bovine chondrocytes. Others [2] have reported that HAS2-OE in tumor cells generates a flux in intracellular UDP-sugar pools that resulted in changes in cell metabolism; switching from a dependence on glycolysis to aerobic respiration. HAS2-OE and 4-MU likely also cause dramatic fluxes in intracellular UDP-GlcUA pools. From these results, we hypothesized that the effect of HAS2-OE and 4-MU relate to changing metabolism and the possibility of inhibition of glycolysis induce chondroprotective effect. To determine that, we used the glycolysis inhibitor, 2-Deoxyglucose (2DG) as an alternative agent to change metabolism in chondrocytes.

Objectives: The objective of this study was to investigate the mechanism of chondroprotective effects of 2DG

Methods: Bovine and human chondrocyte were stimulated with IL-1β (2ng/ml) in the presence or absence of 4MU (1.0 mM), 2DG (0.2-20 mM). Bovine chondrocytes were tested using Seahorse Flux Analyzer (Agilent Tech) to determine rate changes in medium accumulation of +H protons (indicative of lactic acid accumulation: ECAR) and for O2 consumption (indicative of mitochondrial respiration: OCR). Accumulation of MMP13 and phosphor AMPK (pAMPK) protein was quantified with Western blotting. Human and Bovine cartilage explants were cultured with L-1β in the presence or absence of 2DG (20 mM) and d 5-Aminoimidazole-4-carboxamide 1-β-D-ribofuranoside (AICAR) to pharmacologically induce AMPK for 7 days and stained with Safranin O.

Results: Reduced mitochondrial potential and enhanced dependence on glycolysis was observed in IL-1β stimulated chondrocytes. Co-treatment with 4-MU and 2DG returned the cell metabolism to levels at or below baseline (Fig 1A, B). The Seahorse ATP Rate Assay means the contributions of glycolysis and mitochondrial respiration to chondrocyte ATP production (Fig 1C). In control chondrocytes, the use of glycolysis contributes to the majority of ATP produced (grey bars) approximately 1/5th from the TCA cycle (red bars). IL1β-activated chondrocytes display increase in glycolysis and decrease in mitochondrial contributions. These changes are reversed by co-treatment with 4MU and 2DG. As shown in Figs 2A, 2DG reversed the IL1β-induced increases accumulation of MMP13 protein in human OA chondrocytes by Western blotting analysis. Although IL-1β lost safranin O staining in human and bovine samples, co-incubation with 2DG blocked in the loss of proteoglycan (Fig 2B). pAMPK is associate with energy homeostasis in chondrocytes. IL-1β treatment decreased accumulation of phosphor AMPK. Co-treatment with 4-MU and 2DG resulted in a rescue of the pAMPK status (Figure 3A). Co treatment with AICAR, which is inducer of AMPK, also blocked in the loss of proteoglycan (Fig 3B).

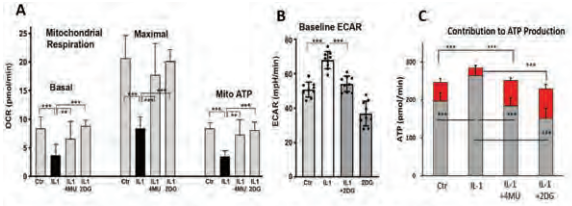


FIGURE 1 Bovine chondrocytes were incubated 24h ± IL1β (2 ng/ml) and without or with 4MU (1.0mM) or 2DG (2.0 mM).
Panel A depicts a representative *Mito Stress Test* wherein bars represent basal and maximal mitochondrial respiration as a corrected OCR value
Panel B show summaries of ECAR data representative of changes in basal glycolysis rates as labeled.
Panel C show a representative *ATP rate assay* wherein the contribution of glycolysis (grey bars) and mitochondrial respiration (red bars) to ATP production. (**: p<0.01 ***: p<0.001)

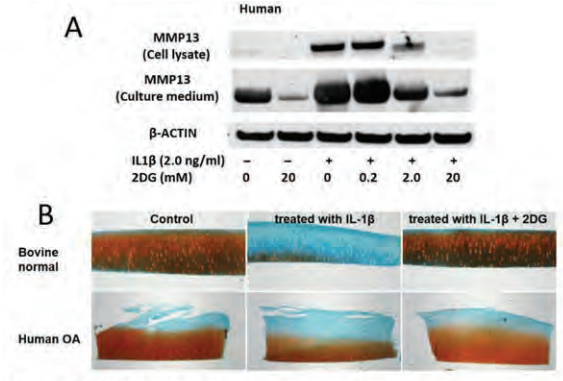


FIGURE 2. Effect of 2DG on chondrocytes activated with IL-β.
Panel A represent the experiment with human OA chondrocytes treated ± 2 ng/ml IL1β in the absence or presence of 0.2, 2.0 or 20 mM 2DG for 24h.
Panel B depict representative examples of bovine and human OA cartilage explants stained by Safranin O.

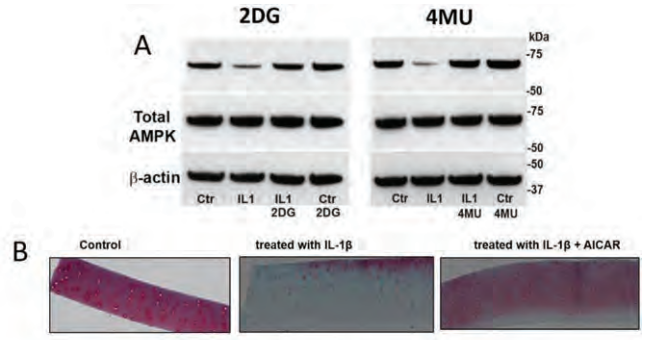


FIGURE 3. The effect of 4MU and 2DG on p-AMPK changes in IL1β activated chondrocytes.
Panel A: Bovine chondrocytes were treated for 24 h without (Ctr) or with IL1β (2 ng/ml) and ±2DG (2.0 mM), ±4MU (0.5 mM).
Panel B depict representative examples of bovine cartilage explants stained by Safranin O treatment with AICAR or not.

Conclusion: 4-MU and 2DG have chondroprotective effect by changing metabolism and upregulate AMPK. We propose that 4MU and 2DG become useful when these endogenous responses are not enough to rescue cells from a pro-catabolic phenotype.

References:

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Disclosure of Interests: KENYA TERABE: None declared, Nobunori Takahashi Speakers bureau: AbbVie, Asahi Kasei, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eisai, Eli Lilly, Janssen, Mitsubishi Tanabe, Ono, Pfizer, Takeda, and UCB Japan, Ohashi Yoshifumi: None declared, Maeda Masataka: None declared, Warren Knudson: None declared, Cheryl Knudson: None declared, Toshihisa Kojima Grant/research support from: Chugai, Eli Lilly, Astellas, Abbvie, and Novartis, Consultant of: AbbVie, Speakers bureau: AbbVie, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eli Lilly, Janssen, Mitsubishi Tanabe, Pfizer, and Takeda, Naoki Ishiguro Grant/research support from: AbbVie, Asahi Kasei, Astellas, Chugai, Daiichi-Sankyo, Eisai, Kaken, Mitsubishi Tanabe, Otsuka, Pfizer, Takeda, and Zimmer Biomet, Consultant of: Ono, Speakers bureau: Astellas, Bristol-Myers Squibb, Daiichi-Sankyo, Eli Lilly, Pfizer, and Taisho Toyama

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Biological DMARDs in RA II

OP0208

PATIENTS REPORT FATIGUE AS AN ADVERSE DRUG REACTION OF BIOLOGICS

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Background: Chronic fatigue is a well-known symptom in patients with rheumatic diseases and other immune-mediated inflammatory diseases (IMIDs). Therefore, fatigue as an adverse drug reaction (ADR) to biologics may remain unrecognised or may erroneously be attributed to the disease.

Objectives: To assess patient-reported fatigue attributed to biologics for IMIDs and investigate predisposing factors of patient-reported fatigue.

Methods: The Dutch Biologic Monitor is a multicenter patient-reported ADR monitoring system that surveys patients using a biologic for an IMID. Patients completed web-based questionnaires regarding ADRs attributed to biologics and the course and experienced burden (5 point Likert scale) of these ADRs. All patient-reported ADRs with MedDRA Preferred Term 'fatigue' were defined as biologic-associated fatigue (BA-fatigue). Basic demographics and treatment characteristics were compared between patients reporting BA-fatigue and patients not reporting BA-fatigue (reported other ADRs or no ADRs).

Results: Out of 1369 participating IMID patients, 696 patients reported 1844 unique ADRs. BA-fatigue was reported by 100 patients and 48 patients described a consistent pattern of recurring fatigue after each administration. Most of these patients (88%) described recovery from BA-fatigue within one week after biologic administration and 73 patients reported health care

professional (HCP) contact following BA-fatigue, with dose adjustment in 8 and discontinuation in 5 patients.
Basic demographics and characteristics that differ significantly between patients reporting BA-fatigue and patients not reporting BA-fatigue are summarized in table 1. No significant difference was found for other biologics, IMIDs, combination therapy and comorbidities. BA-fatigue was reported by 27% of rituximab users (n=33), 27% of vedolizumab users (n=26), 16% of tocilizumab users (n=50), 14% of infliximab users (n=159) and 3% of etanercept users (n=418). Although 29 patients in the BA-fatigue population had RA and 29 patients had Crohn's disease (CD), 571 patients in our overall study population had RA and 194 patients had CD, suggesting BA-fatigue was reported by CD patients more often. The mean burden of BA-fatigue was higher than the mean burden of other ADRs (p<0.001).

Table 1. Characteristics of patients with BA-fatigue compared to patients with other ADRs and without ADRs

		Patients with BA-fatigue n (%)	Patients with other ADRs n (%)	Patients without ADRs n (%)
	n	100 (100%)	596 (100%)	673 (100%)
Basic demographics	Age (years) (mean ± SD)	50.0 ± 14.6	53.4 ± 13.6 *	55.7 ± 14.2 ***
	Gender (Female)	59 (59%)	398 (67%) ns	342 (51%) ns
	Smoking n (%)	25 (25%)	97 (16%) *	100 (15%) *
	BMI (kg/m^2) (mean ± SD)	25.7 ± 4.4	25.9 ± 4.7 ns	26.6 ± 5.5 ns
Biologic	Infliximab	22 (22%)	53 (9%) ***	84 (12%) *
	Etanercept	13 (13%)	177 (30%) ***	228 (34%) ***
	Rituximab	9 (9%)	18 (3%) **	6 (1%) ***
	Tocilizumab	8 (8%)	29 (5%) ns	13 (2%) **
	Vedolizumab	7 (7%)	12 (2%) *	7 (1%) ***
IMID	Rheumatoid arthritis	29 (29%)	270 (45%) **	272 (40%) *
	Crohn's disease	29 (29%)	77 (13%) ***	88 (13%) ***
	Other indication	16 (16%)	53 (9%) *	39 (6%) ***
Combination therapy	Methotrexate	23 (23%)	167 (28%) ns	227 (34%) *
Comorbidity	Psychiatric disorder	11 (11%)	49 (8%) ns	31 (5%) *
	Other comorbidity	30 (30%)	124 (21%) *	102 (15%) ***
	Mean burden of ADR ± SD	2.9 ± 0.9	2.4 ± 1.1 ***	

Mann Whitney U, independent t-test and Fisher's exact as appropriate

ns: not significant *p ≤ 0.05 **p ≤ 0.01 ***p ≤ 0.001

Conclusion: HCPs should be aware that fatigue may be associated with biologic therapy and has a significant burden on patients. Evaluating the course of the symptoms might be helpful in recognizing BA-fatigue.
Disclosure of Interests: Jette van Lint: None declared, Tom Bakker: None declared, Jouke Ubbink: None declared, Martijn van Doorn Grant/research support from: Unrestricted grants, advisory board, speaker fees and/or other (investigator) from Novartis, Abbvie, Janssen Cilag, Leopharma and Pfizer, Speakers bureau: Unrestricted grants, advisory board, speaker fees and/or other (investigator) from Novartis, Abbvie, Janssen Cilag, Leopharma and Pfizer, Phyllis Spuls Grant/research support from: Departmental independent research grant for TREAT NL registry LeoPharma December 2019; Contract support: I am involved in performing clinical trials with many pharmaceutical industries that manufacture drugs used for the treatment of e.g. psoriasis and atopic dermatitis for which we get financial compensation paid to the department/hospital, Consultant of: Consultancies in the past for Sanofi 111017 and AbbVie 041217 (unpaid), Sander Tas: None declared, Harald Vonkeman: None declared, Frank Hoentjen Grant/research support from: Received grants from Dr Falk, Janssen-Cilag, and AbbVie., Consultant of: Served on advisory boards, or as speaker or consultant for AbbVie, Celgene, Janssen-Cilag, MSD, Takeda, Celltrion, Teva, Sandoz, and Dr Falk, Speakers bureau: Served on advisory boards, or as speaker or consultant for AbbVie, Celgene, Janssen-Cilag, MSD, Takeda, Celltrion, Teva, Sandoz, and Dr Falk, Bart van den Bemt Grant/research support from: UCB, Pfizer and Abbvie, Consultant of: Delivered consultancy work for UCB, Novartis and Pfizer, Speakers bureau: Pfizer, AbbVie, UCB, Biogen and Sandoz., Michael Nurmohamed Grant/research support from: Not related to this research, Consultant of: Not related to this research, Speakers bureau: Not related to this research, Eugène van Puijenbroek: None declared, Naomi Jessurun: None declared
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OP0209

INTERVAL PROLONGATION IN ETANERCEPT-TREATED PATIENTS WITH RHEUMATOID ARTHRITIS, ANKYLOSING SPONDYLITIS OR PSORIATIC ARTHRITIS: AN OPEN-LABEL, RANDOMISED CONTROLLED TRIAL

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Background: The majority of patients with a rheumatic disease treated with etanercept may be overexposed. Data regarding etanercept tapering is scarce, particularly in psoriatic arthritis (PsA) and ankylosing spondylitis (AS). Dose reductions can potentially reduce blood drug levels too much, resulting in loss of effect.
Objectives: We compared extending the dose interval to continuation of the standard dose and studied the success rate of etanercept discontinuation. Etanercept concentrations were measured throughout the study.
Methods: 160 consecutive patients with rheumatoid arthritis (RA), PsA or AS with sustained minimal disease activity (MDA) were enrolled in this 18-month, open-label, randomised controlled trial. The intervention group doubled the dosing-interval at baseline and discontinued etanercept 6 months later. The control group continued the standard dose up to 6 months, after which the dosing-interval was doubled. Primary outcome was the proportion of patients maintaining MDA after 6 months follow-up.
Results: At 6 months, MDA status was maintained in 47 (63%) patients in the intervention group and 56 (74%) in the control group (p=0.15), with comparable results in all rheumatic diseases. Median etanercept concentrations decreased from 1.50 µg/mL (25-75th percentile 1.06-2.65) to 0.46 µg/mL (0.28-0.92) after 6 months of interval prolongation (figure 1). In total, 40% discontinued etanercept successfully with maintained MDA for at least 6 months.

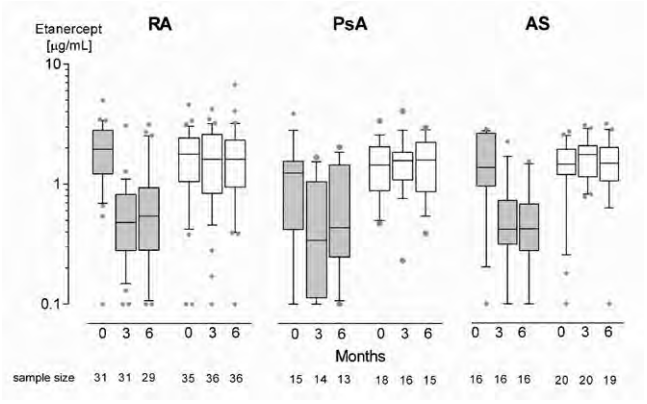


Figure 1. Median (with Q1 to Q3 boxplots) etanercept concentrations (per protocol) during the first 6 months of follow-up in the intervention group (prolongation; gray boxplots) and the control group (continuation; white boxplots), separated by disease (RA, PsA, AS). Bars represent 10-90 percentile and outliers are shown separately (dots).

Conclusion: As observed in RA, etanercept tapering can be safely attempted in PsA and AS patients in sustained MDA. A substantial proportion of patients could stop etanercept for at least 6 months. In many patients low drug concentrations proved sufficient to control disease activity. However, the risk of minor and major flares is substantial, even in patients continuing standard dosing.
References: none
Disclosure of Interests: Merel J. l'Ami Speakers bureau: Novartis, Jill Ruwaard: None declared, Eva L. Kneepkens: None declared, Charlotte L.M. Krieckaert: None declared, Michael Nurmohamed Grant/research support from: Not related to this research, Consultant of: Not related to this research, Speakers bureau: Not related to this research, Femke Hooijberg: None declared, J.C. van Denderen: None declared, Arno Van Kuijk: None declared, Lot Burgemeister: None declared, Maarten Boers: None declared, Gert-Jan Wolbink: None declared
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OP0210

EFFICACY AND SAFETY OF SM03, A RECOMBINANT ANTI-HUMAN CD22 MONOCLONAL ANTIBODY IN CHINESE PATIENTS WITH RHEUMATOID ARTHRITIS: A PHASE II RANDOMIZED, DOUBLE-BLIND, MULTI-DOSE, PLACEBO-CONTROLLED STUDY

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Background: Rheumatoid arthritis (RA) is a common chronic inflammatory rheumatic disease in China. SM03 is a novel chimeric monoclonal antibody (mAb) specific to the B cell restricted antigen CD22 developed for the treatment of rheumatoid arthritis (RA) and other B cell related immunological diseases.
Objectives: We aim to evaluate the efficacy and safety of SM03 in patients with moderately-to-severely active RA in China.
Methods: In this 24-week Phase II randomized, double-blind, multi-dose, placebo-controlled study, 156 patients were randomized with ratio of 1:1:1 to receive 3600mg cumulative dose of SM03 (group A, 600mg * 6 infusions at 0, 2, 4, 12, 14, and 16 week), 2400mg cumulative dose of SM03 (group B, 600mg*4 infusions at 0, 2, 12, and 14 week) and placebo (group C). All patients remained on background treatment of MTX. Efficacy and safety were assessed at weeks 4, 8, 12,16 and 24.The primary efficacy end point was the American College of Rheumatology 20% improvement criteria (ACR20) response rate at week 24.Safety profile was also assessed.
Results: ACR20 response rates at 24-week were significant for group A (65.3%, p=0.002) and B (56.9 %, p=0.024) versus group C (34.0%). There is no significant difference in ACR20 between group A and B(Table 1 & Fig 1). We did not observe significant difference in any adverse event (AE) among group A (35.3%), B (51.9%) and C (34.6%)(Table 2). In groups A and B, 13 (12.6%) patients reported treatment-related infection, and 5 (6.8%) patients were positive in anti-drug antibodies analysis. In group A (higher dose), 3.9% patient had AE of treatment-related infections. No patients reported treatment-related severe infection or any malignancies caused by treatment in groups A and B.

Table 1. Summary of ACR/DAS EULAR Responses of Patients with RA to SM03 at Week 24

Response	Group C Placebo+MTX (n=47)	Group A SM03 600mg*6+MTX (n=49)	Group B SM03 600mg*4 +MTX (n=51)
ACR 20	34.0%	65.3% *	56.9% *
ACR 50	17.0%	44.9%**	29.4%
ACR 70	4.3%	18.4%***	9.8%
EULAR response good & moderate	40.4%	75.5%^	70.6%^
EULAR response good	12.8%	30.6%^^	15.7%
Change of DAS28 from baseline	-0.70	-1.65^^^	-1.38^^^
DAS28≤3.2	14.9%	30.6%	19.6%
DAS28<2.6	8.5%	18.4%	5.9%

Compared with group C(Placebo), results of group A and B were shown respectively
*P=0.002, P=0.024; **P= 0.003; ***P= 0.03;
^ P<0.001, P=0.003; ^^ P=0.034; ^^^P=0.008, P=0.047

Table 2. Profile of Adverse Events

Adverse event, N (%)	Group C(N=52)	Group A(N=51)	Group B(N=52)
Any AE	18(34.6)	18(35.3)	27(51.9)
AE-drug related	7(13.5)	5(9.8)	8(15.4)
AE-mild	16 (30.8)	15(29.4)	24(46.2)
AE-moderate	2(3.8)	2(3.9)	3(5.8)
AE-severe	-	1(2.0)	-
AE-leading to discontinuation	-	2(3.9)	-
Serious adverse event, SAE	1(1.9)	1(2.0)	-
AE-1st cycle(week 0-12)	15	13	22
AE-2nd cycle(week 12-24)	9	9	14

Conclusion: In Chinese patients with active RA, both 2400mg and 3600mg cumulative doseof SM03,in combination with MTX were efficacious and well tolerated. throughout the 24 weeks of treatment.Moreover, SM03 has demonstrated a good safety profile, especially in terms of treatment-related infection, malignancy and immunogenicity.
References: None
Disclosure of Interests: None declared
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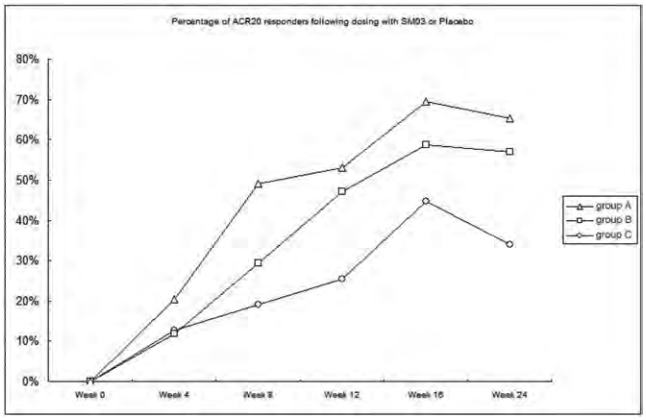


Fig 1. Percent of Patients Achieving ACR 20 Response by Visit

OP0211

TIME TO DISCONTINUATION OF TOFACITINIB AND TNF INHIBITORS IN RHEUMATOID ARTHRITIS PATIENTS WITH AND WITHOUT METHOTREXATE: DATA FROM A RHEUMATOID ARTHRITIS COHORT

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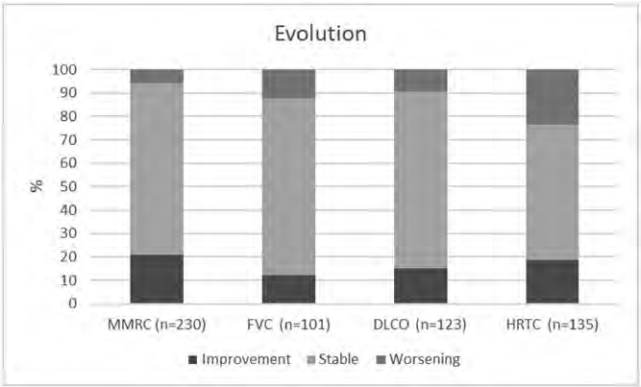
Background: Tofacitinib (TOFA) is an oral, small molecule drug used for rheumatoid arthritis (RA) treatment and is prescribed alone or with methotrexate (MTX). Tofa can be used as an alternative to biologic disease modifying antirheumatic drugs (bDMARDs) including tumor necrosis factor inhibitors (TNFi).
Objectives: We aimed to evaluate the discontinuation rate of this drug, with and without concurrent MTX in comparison with TNFi, in patients with RA in the Ontario Best Practices Research Initiative (OBRI).
Methods: RA patients enrolled in the OBRI initiating their TOFA or TNFi (adalimumab, certolizumab, etancercept, golimumab, and infliximab) within 30 days prior to or any time after enrolment between 1st June 2014 (TOFA approval date in Canada) and 31st Dec 2018 were included. Time to discontinuation (due to any reason) were assessed using Kaplan-Meier survival (adjusted for propensity score using inverse probability of treatment weight) to compare patients with and without MTX use at initiation of TOFA or TNFi.
Results: A total of 565 patients initiated TOFA (n=208) or TNFi (n=357). Of those, 106 (51%) and 222 (62%) were treated with MTX in the TOFA and TNFi group, respectively and mean (SD) disease duration were 13.1 (9.4) and 9.5 (9.4) years. In the TOFA group, 86% were female and mean (SD) age at treatment initation was 60.4 (10.6) years. In the TNFi group 82% were female and mean age (SD) at treatment initation was 57.0 (12.6) years. The TOFA group was more likely to have prior biologic use (61.5%) compared with the TNFi group (31%). At treatment initiation, the mean (SD) clinical disease activcity index was 24.8 (12.1) in the TOFA group and 21.8 (12.0) in the TNFi group.
Over a mean of 17.3 month follow-up, discontinuation was reported in 75 (36%) and 103 (29%) of all TOFA and TNFi patients, respectively. After adjusting for propensity score, patients treated with TNFi and MTX remained on treatment longer than those treated without MTX (Logrank p=0.002) while there was no significant difference in TOFA discontinuation in patients with and without MTX (Logrank p=0.31).
Conclusion: In this real world data study, we found that TOFA retention is similar in patients with and without MTX, while patients treated with TNFi and MTX remained on treatment longer than those treated without MTX. Merging data with other RA registries in Canada is proposed to increase study power and to provide more robust results.
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OP0212 ABATACEPT IN INTERSTITIAL LUNG DISEASE ASSOCIATED WITH RHEUMATOID ARTHRITIS. NATIONAL MULTICENTER STUDY OF 263 PATIENTS

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Background: Interstitial Lung Disease (ILD) is a severe complication of Rheumatoid Arthritis (RA). Several conventional disease-modifying anti-rheumatic drugs (cDMARDs) and biologic (b) DMARDs may induce or impaired ILD-RA. Abatacept (ABA) may be useful in ILD-RA (1).
Objectives: To assess the efficacy and safety of ABA in a large series of ILD-RA for a long-term follow-up.
Methods: Multicenter open-level study of ILD-RA treated with at least 1 dose of ABA. ILD was diagnosed by high-resolution computed tomography (HRTC). We study these outcomes: a) 1-point change Modied Medical Research Council (MMRC); b) forced vital capacity (FVC) and/or DLCO improvement or decline ≥10%; c) change in HRCT, d) change in DAS28. e) Prednisone dose. Values were collected at 0, 3, 6, 12 and then every 12 months.
Results: We studied 263 patients (150 women/113 men) (mean age;64.6±10 years), with ILD-RA. At ABA-onset they were smokers or exsmoker (53.8%), positive APCC (88.6%), median [IQR] duration of ILD of 12 [3-41.25] months, mean DLCO (65.7±18.3) and FVC (85.9±21.8).
The ILD-pattern were usual interstitial pneumonia (UIP) (40.3%), non-specific interstitial pneumonia (NSIP) (31.9%) and others (27.8%).
ABA was prescribed at standard subcutaneous (125 mg/w) in 196 (74.5%) or intravenously (10 mg/kg/4 w) in 67 (25.5%); in monotherapy (n=111) or combined with cDMARDs (n=152); especially leflunomide (n=55), MTX (n=46), or antimarials (n=21).
After a mean follow-up of 22.7±19.7 months most outcomes remain stable (Figure). Moreover, DAS28 improved from 4.5±1.5 to 3.1±1.3; prednisone dose reduced from a median 7.5 [5-10] to 5 mg [5-7.5] and retention rate was 76.4%. The main adverse effects were serious infections (n=28), neoplasia (n=3), serious infusion reaction (n=1) and myocardial infarction (n=1).
Conclusion: ABA seems effective and relatively safe in ILD-RA.
References:
[1] Fernández-Díaz C et al. Semin Arthritis Rheum. 2018; 48:22-27
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CLARA AGUILERA CROS: None declared, Ignacio Villa-Blanco Consultant of: UCB, Speakers bureau: Novartis, MSD, Lilly, Sergi Ordoñez: None declared, Susana Romero-Yuste: None declared, C. Ojeda-Garcia: None declared, Manuel Moreno: None declared, Gemma Bonilla: None declared, I. Hernández-Rodriguez: None declared, Mireia Lopez Corbeto: None declared, José Luis Andréu Sánchez: None declared, Trinidad Pérez Sandoval: None declared, Alejandra López Robles: None declared, Patricia Carreira Grant/research support from: Actelion, Roche, MSD, Consultant of: GlaxoSmithKline, VivaCell Biotechnology, Emerald Health Pharmaceuticals,



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OP0213 THE IMPACT OF TNFA INHIBITORS ON GLUCOCORTICOIDS USE AMONG PATIENTS WITH ARTHRITIS

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Background: Glucocorticoid steroid (GC) use among patients with arthritis is common. The introduction of TNFα inhibitors (TNFi) has been a breakthrough in the treatment of arthritis leading to remission for many patients. However, there is scarce information on the impact of TNFi on the use of GC among patients with inflammatory joint diseases.
Objectives: To explore oral GC use in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), and axial spondyloarthritis (axSpA) before and after the initiation of TNFi therapy. Furthermore, to evaluate if patients on long term GC treatment were receiving active preventive osteoporosis treatment and how treatment with TNFi affected the use of topical steroids in patients with PsA.
Methods: Clinical data on patients with RA, PsA and axSpA who initiated TNFi therapy with etanercept, infliximab, adalimumab or golimumab for the first time between 2005-2015 was collected from the ICEBIO registry. ICEBIO is a nationwide registry on all patients treated with biologics for rheumatologic disorders in Iceland. The use of oral GC, topical steroids and bisphosphonates was collected from the Icelandic Prescription Medicines Registry (IPMR) for a period of four years, two years before and after the initiation of TNFi. Medication use was then evaluated by counting the number of individuals receiving a medication in a given year, the total number of prescriptions, and the defined daily dose (DDD). Five controls were randomly selected from IPMR and matched on age, sex and time frame.
Results: 621 patients with RA, PsA or axSpA received 2630 prescriptions (4.2 prescription per patient; 3105 controls received 1337 prescriptions or

0.4 prescription per individual) for GC during the study period. GC use varied between patient groups (Figure 1). The total GC use (DDD) doubled over the two-year period leading up to TNFi treatment but decreased sharply after the initiation of TNFi. The number of individuals on GC decreased by one third after initiating TNFi therapy and the majority of those who continued GC treatment were patients with RA (Figure 1). Of those patients on long term GC treatment (>7.5 mg/day for three months) 38% were receiving bone protective therapy against corticosteroid induced osteoporosis. The use of topical steroids decreased by half among PsA patients and one third discontinued the treatment after initiating TNFi (Figure 2).

Conclusion: TNFi therapy does impact GC use among patients with arthritides, however a large portion of RA patients are still on GC two years after initiating TNFi therapy. Better osteoporosis prophylaxis and treatment is warranted for those patients on long term GC

Figure 1: Percentage of patients that received glucocorticosteroids

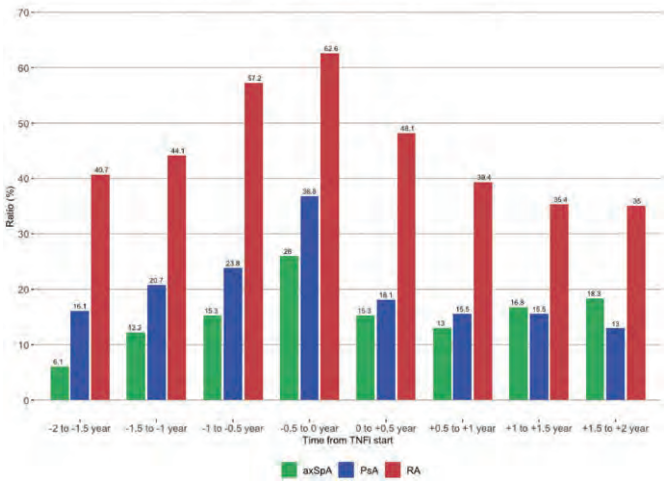
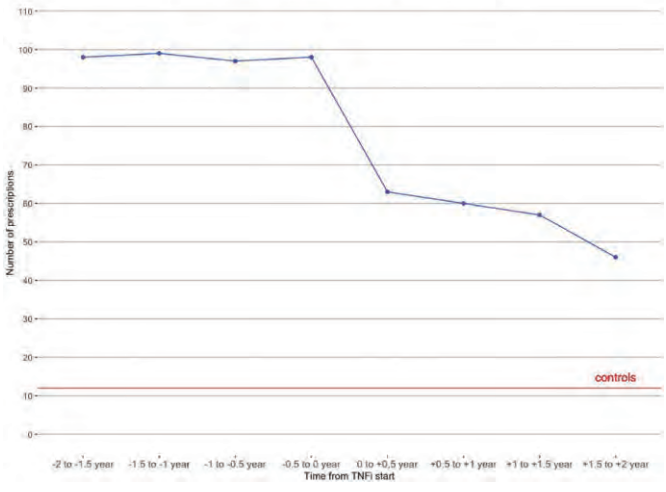


Figure 2: Total number of prescriptions on topical corticosteroids in PsA



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OP0214 INCIDENCE OF CANCER (RELAPSE OR NEW ONE) FOLLOWING BDMARDS INITIATION IN PATIENT WITH RHEUMATOID ARTHRITIS AND HISTORY OF CANCER: A SYSTEMATIC REVIEW WITH META-ANALYSIS OF OBSERVATIONAL STUDIES

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Background: The tolerance of targeted biologic therapies (bDMARDs) used in rheumatoid arthritis (RA) has been studied in patients with no history of cancer. A 5-year cancer remission is recommended to initiate treatment with bDMARDs. However, in the context of the aging of the population and the increase in screening for neoplasia, the question of targeted treatment in a patient with RA with a history of cancer is usual.

Objectives: To determine the risk of recurrence or a new malignancy when exposed to a b-DMARDs in adults with RA and a history of cancer.

Methods: A systematic literature search of EMBASE, MEDLINE, Cochrane Library, and electronic abstract databases of the annual scientific meetings of both the European League Against Rheumatism and the American College of Rheumatology was conducted through June 2019 and selected all cohort follow-up studies including adults with RA with a history of cancer and treated with b-DMARDs (TNF inhibitors, rituximab, abatacept and tocilizumab). We compared the risk of relapse or new cancer onset between the groups treated with and without b-DMARDs. The RevMan 5.3 software was used to calculate the cumulative risks from each group's Hazard Ratio (HR), with their 95% confidence intervals. The heterogeneity of the studies was evaluated by the Cochran Q test and expressed with the I^2 value.

Results: 26 observational cohort studies were selected, of which 12 were included in the meta-analysis. The overall risk of new cancer or recurrence of neoplasia in RA patients with a history of cancer, compared to control subjects, for all b-DMARDs combined was 1.09 (p=0.29, 95%CI [0.92-1.32], I^2=16%). The risk of relapse or new cancer onset in patients exposed to TNF inhibitors was 1.11 (p=0.45, 95%CI [0.85-1.46], I^2=48%) and 0.79 (p=0.49, 95%CI [0.41-1.53], I^2=10%) for rituximab. The rate of recurrence was 1.32 (p=0.04, 95%CI [1.02-1.72], I^2=0%) for skin cancer, 1.28 (p=0.07, 95%CI [0.98-1.67], I^2=0%) for skin cancers excluding melanoma and 1.21 (p=0.31, 95%CI [0.84-1.72], I^2=0%) for breast neoplasia.

Conclusion: This is the first meta-analysis evaluating the risk of recurrence or new cancers in a RA population with a history of neoplasia exposed to b-DMARD. For patients with a history of cancer, for whom the benefit / risk balance has been found to be favorable, the initiation of b-DMARD treatment for RA does not seem to significantly increase the risk of recurrence or new cancer compared to patients naïve to biological treatments, apart from skin cancers including melanoma.

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OP0215 FUNCTIONAL ABILITIES IMPROVEMENT IN RHEUMATOID ARTHRITIS PATIENTS WITH DEPRESSIVE AND ANXIETY DISORDERS TREATED WITH BIOLOGIC DMARDS AND/OR ANTIDEPRESSANTS

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Background: Anxiety and depressive disorders (ADD) significantly increase functional limitations in patients with rheumatoid arthritis (RA). Successful psychopharmacotherapy (PPT) of ADD can potentially improve the functional abilities of RA-patients.

Objectives: To compare changes in functional disability of RA patients with comorbid ADD treated with conventional disease-modifying antirheumatic drugs (cDMARDs) alone or in combination with biologic DMARDs (bDMARDs) and/or PPT.

Methods: 128 RA-patients (pts) were enrolled, 86% were women with a mean age of 47,4±11,3 (M±SD) yrs. All patients met the full ACR/EULAR 2010 criteria for RA. Functional limitations were assessed using Health Assessment Questionnaire (HAQ), mean HAQ was 1,42±0,78 at baseline. 69,4% RA-pts were already taking prednisone (9 [5; 10] mg/day (Me (25%; 75%)), 84,4% - cDMARDs, 7,8% - bDMARDs (anti-TNF-α – 6,3%, rituximab – 1,6%). ADD were diagnosed by psychiatrist in 123 (96,1%) of RA-pts in accordance with ICD-10 in semi-structured interview. Severity of depression and anxiety was evaluated with

Montgomery–Asberg Depression Rating Scale (MADRS) and Hamilton Anxiety Rating Scale (HAM-A). RA-pts with ADD were divided into the following treatment groups: 1 – cDMARDs (n=39), 2 – cDMARDs + PPT (sertraline or mianserine) (n=43), 3 – cDMARDs + bDMARDs (n=32), 4 – cDMARDs + bDMARDs + PPT (sertraline or mianserine) (n=9). Biologics treatment duration varied from 1 to 6 years, antidepressants – from 6 to 96 weeks.

Results: HAQ scores were high in all 4 groups at baseline and after five years remained high in all groups except group 2 with the lowest endpoint scores among 4 groups (table 1). To measure changes in HAQ scores between groups we compared the differences between baseline and endpoint HAQ scores (Δ HAQ = endpoint HAQ – baseline HAQ) (table 2). The table shows an improvement in HAQ scores in groups 2 and 3, no significant changes in group 4 and a worsening of HAQ scores in group 1. HAQ scores in groups 2 and 3 significantly improved compared to group 1.

Table 1 Mean HAQ scores in RA patients with ADD at baseline and after 5 years, by groups.

Groups	At baseline (n=128)	After 5 years (n=83)	P between time points
1 (cDMARDs), n=39	1,39±0,75	1,61±0,7	>0,05
2 (cDMARDs + PPT), n=43	1,42±0,9	0,85±0,66	0,011
3 (cDMARDs + bDMARDs), n=32	1,58±0,76	1,36±0,71	>0,05
4 (cDMARDs + bDMARDs + PPT), n=9	1,38±0,83	1,49±0,26	>0,05
P between groups	>0,05	P_{2-1}<0,001; P_{2-3}=0,023 P_{2-4}=0,015	

Table 2. Differences between baseline and 5-years endpoint HAQ scores, by groups

	cDMARDs, n=24	cDMARDs + PPT, n=29	cDMARDs + bDMARDs, n=21	cDMARDs + bDMARDs + PPT, n=9	
	1	2	3	4	p
Δ HAQ	0,23±0,49	-0,3±0,42	-0,28±0,94	0±0,82	P_{1-2}=0,002; P_{1-3}=0,033

Conclusion: Functional abilities measured by HAQ scores significantly improved in RA-patients with ADD receiving cDMARDs in combination with bDMARDs or PPT compared to cDMARDs only. The lowest HAQ scores were observed in patients receiving cDMARDs in combination with PPT.

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Rheumatoid arthritis - prognosis, predictors and outcome II

OP0216 DEVELOPMENT AND VALIDATION OF PATIENT-LEVEL PREDICTION MODELS FOR ADVERSE HEALTH OUTCOMES AMONGST ADULT RA PATIENTS INITIATING FIRST-LINE TREATMENT OF METHOTREXATE MONOTHERAPY: A MULTINATIONAL REAL-WORLD COHORT ANALYSIS INCLUDING 164,735 SUBJECTS

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Background: EULAR guidelines recommend the early initiation of methotrexate (MTX) monotherapy as soon as possible after the diagnosis of rheumatoid arthritis (RA). Evaluating patient-level risks for adverse outcomes after MTX initiation would allow clinicians to provide more personalised care.

Objectives: To develop and validate patient-level prediction models for adverse health outcomes including leukopenia, pancytopenia, infection (serious, opportunistic, all), cardiovascular disease (CVD) (myocardial infarction (MI), stroke), and cancer (breast, colorectal, uterus) in adult RA patients initiating first-line treatment of MTX monotherapy

Methods: Health data from claims and electronic health records were used including patients from 7 European countries (Spain, Estonia, Netherlands, Belgium, Germany, France, and the UK), the United States of America, Australia, and Japan. All RA patients initiating first-line treatment of MTX monotherapy with at least one year of prior observation were included. Prediction models for the outcomes were developed for a time at risk of 3 months (infections, leukopenia, pancytopenia), 2 years (MI and stroke), and 5 years (cancers) on the Optum© De-Identified Clinformatics® Data Mart Database. Models were developed using LASSO logistic regression and were evaluated using the area under the receiver operator characteristic curve (AUROC) for discrimination and graphically assessed for calibration. The models were externally validated on all other databases.

Results: A total of 21,307 subjects were used for training and validated against 143,427 patients from 14 sites. MI (AUROC internal 0.77, AUROC external ranging from 0.49 to 0.78), stroke (AUROC internal 0.78, AUROC external ranging from 0.68 to 0.79) and serious infection (AUROC internal 0.75, AUROC external ranging from 0.63 to 0.79) had good predictive validity [Table 1]. Discrimination for all other outcomes was lower, with all AUC<0.7 in internal validation. For detailed results see: https://data.ohdsi.org/ehdenRaPrediction/

Table 1. Internal (Optum) and external validation results: AUC ROC for discrimination

Database	Acute MI within 2y	Stroke within 2y	Serious Infection within 3m
Optum (internal)	0.77	0.78	0.75
PanTher	0.76	0.78	0.74
IQVIA_AMBEMR	0.76	0.72	
CCAE	0.73	0.73	0.66
IQVIA_GERMANY	0.64	0.70	
IQVIA_THIN	0.62	0.65	
MDCR	0.68	0.68	0.67
IQVIA_HOSPITAL	0.67	0.63	0.61
MDCD	0.72	0.79	0.63
JMDC	0.49	0.75	0.71
IQVIA_LPDFRANCE	0.69		
Estonia	0.67	0.77	0.82
IQVIA_AUS	0.58		
IPCI	0.68		
SIDIAP	0.65	0.75	

Conclusion: Clinical tools were developed that successfully identify subjects at risk of MI, stroke and serious infection at the initiation of first-line MTX therapy. The developed algorithms had good transportability and generally, the models with high AUROC had adequate internal calibration although some external validations show they could benefit from recalibration. For short-term opportunistic and all infections, as well as 5-year cancer models, we were unable to achieve a high enough AUROC to warrant validating externally.

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OP0217 INVOLVEMENT OF LARGE JOINTS AT DISEASE PRESENTATION IS ASSOCIATED WITH DIVERSE HISTOPATHOLOGICAL FEATURES AND CLINICAL OUTCOMES IN EARLY RHEUMATOID ARTHRITIS

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Background: The involvement of large joints at disease presentation in early Rheumatoid Arthritis (RA) has been associated with severe disease activity. At the same time, the clinical heterogeneity of RA is known to be mirrored by heterogeneity of synovial inflammation, with specific histological patterns (pathotypes)

associated with treatment response and disease progression. However, it is not known whether joint size is associated with specific pathotypes.

Objectives: To analyse histopathological features of synovial biopsies from joints of different sizes and establish the relationship with clinical outcomes in patients with early RA.

Methods: 167 patients with early (<1 year) treatment-naïve RA, fulfilling the 2010 RA criteria and recruited at Barts Health NHS Trust, underwent US-guided synovial biopsy of the most inflamed joint, either large (knee), medium (e.g. wrist, ankle, elbow) or small (MCPs, MTPs), before starting treatment with csDMARDS with a treat to target approach. Upon SQ scoring (0-4) of immune cell infiltration, tissues were classified into lympho-myeloid, diffuse-myeloid and pauci-immune pathotypes. Synovial samples from 111 patients underwent RNA-seq.

Results: The majority of synovial biopsies were performed on medium and small joints (60.6% and 19.4%) as compared to 21.3% in large joints (Table 1). At baseline, patients who underwent large joint biopsy showed significantly higher levels of inflammation (CRP 27.9±32.4 large, 20.7±26.9 medium, 10.4±9.8 small, p=0.007) and higher HAQ (1.8 ± 0.7 large, 1.4 ± 0.8 medium, 1.2 ±0.9 small, p=0.012), with no differences in DAS28. Significantly higher inflammatory scores and higher proportion of lympho-myeloid pathotype were observed in large joints (Table 1 and Figure 1). 6 months after treat-to-target treatment with csDMARDs, large joints patients had significantly higher HAQ and lower response (RR for low disease activity in large vs medium joints 0.5, 95%CI 0.2-0.9, p=0.03). Finally, differentially expressed genes by RNA-seq showed segregation according to joint size (Figure 2), with upregulation of genes of the Homeobox transcription factors family in large joints.

Table 1. EULAR 2010 RA (n=167)

		Large joints# 33 (19.4%)	Medium joints# 100 (60.6%)	Small Joints# 34 (20%)	P*
Clinical features					
ESR mm/h, mean (SD)		48.2 (31.5)	39.6 (30.8)	29.2 (17.3)	ns
CRP mg/L, mean (SD)		27.9 (32.4)	20.7 (26.9)	10.4 (9.8)	0.007
DAS28, mean (SD)		6 (1.2)	5.7 (1.4)	5.7 (1.5)	ns
HAQ, mean (SD)		1.8 (0.7)	1.4 (0.8)	1.2 (0.9)	0.012
ACPA-positive, %		70.9%	77.3%	83.9%	ns
RF-positive, %		71.9%	74.2%	80.6%	ns
Histology					
Inflammatory score, median IQR)		5 (3)	4 (4)	2 (2.75)	<0.001
Pathotype, %	Ungraded	6.1%	7.8%	2.9%	0.014
	Fibroid	6.1%	24.3%	32.3%	
	Myeloid	30.3%	28.1%	47.1%	
	Lympho-myeloid	57.6%	39.8%	17.6%	
Clinical outcomes at 6 months					
DAS28 6m, mean (SD)		4.2 (1.8)	3.4 (1.9)	3.7 (1.5)	ns
HAQ 6m, mean (SD)		1.2 (0.8)	0.8 (0.8)	0.8 (0.8)	0.012
DAS28 6m <3.2, %		23.3%	48.8%	37.9%	0.04

#Large joints: knees; Medium joints: wrists, ankle, elbows; Small joints: MCPs, MTPs, PIPs; * Chi-squared or Kruskal–Wallis as appropriate;

Conclusion: Synovial biopsy of large joints as the most inflamed joints at disease presentation identified patients with early RA with specific histopathological features and clinical outcomes. Together with clustering of differentially expressed genes according to joint size, this suggests that the involvement of different joint compartments in early RA contributes to disease heterogeneity with potential physiopathological and clinical implications.

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F. Rivellese NIHR Fellowship TRF-2018-11-ST2-002

Figure 1

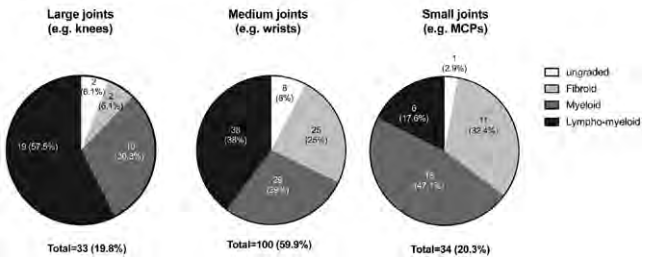
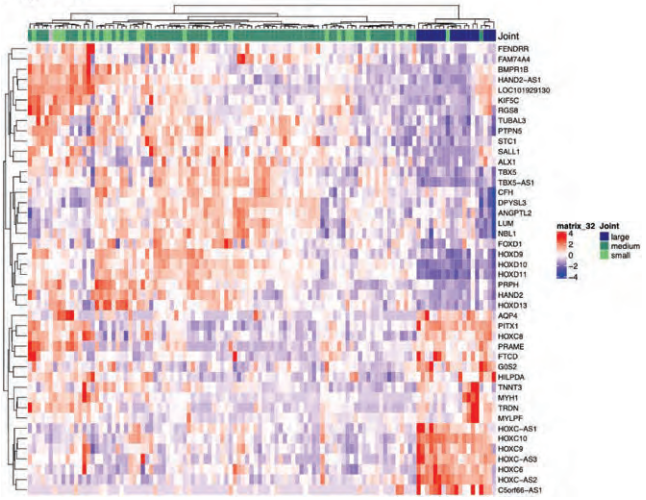


Figure 2



Disclosure of Interests: None declared

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OP0218

CENTRAL NERVOUS SYSTEM PAIN RESPONSE AND COMPONENTS OF DISEASE ACTIVITY IN RA PATIENTS AFTER TREATMENT WITH CERTOLIZUMAB OR PLACEBO: A POST-HOC ANALYSIS FROM THE PRECEPRA TRIAL

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Background: We have previously observed in RA patients that central nervous system (CNS) response to compression of a painful joint, measured using functional MRI (fMRI) of the brain as the number of blood oxygen level dependent (BOLD) signal positive voxels, is rapidly ameliorated, much earlier than any clinical response with anti-TNF treatment and a high baseline CNS pain response could predict better response to certolizumab pegol (CZP) treatment. Pre-CePRA was designed and conducted to test this effect in a randomized, placebo controlled trial of CZP and showed an incremental linear trend of DAS28 low disease activity (LDA) across study groups treated with placebo, and two CZP arms stratified as low or high pre-treatment CNS pain response.

Objectives: To explore and describe pre-treatment CNS pain response associations with post treatment course of RA disease activity components and patient-physician discrepancy in global disease assessment.
Methods: Patients fulfilling the 2010 ACR/EULAR classification criteria with moderate-severe disease activity (DAS-28>3.2) under stable DMARD treatment were recruited. Patients underwent an fMRI scan, stratified by a whole-brain BOLD positive voxel count threshold of 700 units and randomized to treatment with CZP or placebo in a 2:1 ratio. We descriptively assessed components of RA disease activity (Table 1 + 2). We summarized the mean results and 95% confidence intervals of these measurements at study timepoints and compared the 3 study groups at week 12 using one-way ANOVA and post-hoc Tukey tests.
Results: 156 eligible patients were screened and 139 (99 females, 71%) patients with moderate-high disease activity were randomized. ANOVA and pairwise comparisons showed that PGA-VAS improvement was larger in the CZP-H group whereas more similar to that in placebo in the CZP-L group. PhysGA-VAS however was similarly reduced in both CZP groups. Patients in the CZP-L group constantly rated their pain numerically higher than physicians whereas in the CZP-H group an initially higher discrepancy numerically reduced over time.
Conclusion: These results suggest that improved patient global disease activity assessment could be the main driver of improved DAS-28 LDA rates with CZP treatment in patients with a high CNS pain response. Our findings indicate a potential role of fMRI imaging of the brain to further understand disease activity perception in RA patients.
Disclosure of Interests: Hannah Schenker: None declared, Jürgen Rech Consultant of: BMS, Celgene, Novartis, Roche, Chugai, Speakers bureau: AbbVie, Biogen, BMS, Celgene, MSD, Novartis, Roche, Chugai, Pfizer, Lilly, Koray Tascilar: None declared, Melanie Hagen: None declared, Verena Schönau: None declared, Marina Sergeeva: None declared, Mageshwar Selvakumar: None declared, Laura Konerth: None declared, Jutta Prade: None declared, Sandra Strobelt: None declared, Larissa Valor: None declared, Axel Hueber Grant/research support from: Novartis, Lilly, Pfizer, EIT Health, EU-IMI, DFG, Universität Erlangen (EFI), Consultant of: Abbvie, BMS, Celgene, Gilead, GSK, Lilly, Novartis, Speakers bureau: GSK, Lilly, Novartis, David Simon Grant/research support from: Else Kröner-Memorial Scholarship, Novartis, Consultant of: Novartis, Lilly, Arnd Kleyer Consultant of: Lilly, Gilead, Novartis,Abbvie, Speakers bureau: Novartis, Lilly, Frank Behrens Grant/research support from: Abbvie, Pfizer, Roche, Chugai, Janssen, Consultant of: Abbvie, Pfizer, Roche, Chugai, UCB, BMS, Celgene, MSD, Novartis, Biotest, Janssen, Genzyme, Lilly; Boehringer; Sandoz, Speakers bureau: Abbvie, Pfizer, Roche, Chugai, UCB, BMS, Celgene, MSD, Novartis, Biotest, Janssen, Genzyme, Lilly; Boehringer; Sandoz, José Antonio P. da Silva Grant/research support from: Pfizer, Abbvie, Consultant of: Pfizer, AbbVie, Roche, Lilly, Novartis, Christoph Baerwald Consultant of: CGB received speaker or consulting fees from AbbVie, Paid instructor for: CGB received speaker or consulting fees from AbbVie, Speakers bureau: CGB received speaker or consulting fees from AbbVie, Stephanie Finzel: None declared, Reinhard Voll: None declared, Eugen Feist Consultant of: Novartis, Roche, Sobi, Lilly, Pfizer, Abbvie, BMS, MSD, Sanofi, Speakers bureau: Novartis, Roche, Sobi, Lilly, Pfizer, Abbvie, BMS, MSD, Sanofi, Arnd Doerfler: None declared, Nemanja Damjanov Grant/research support from: from AbbVie, Pfizer, and Roche, Consultant of: AbbVie, Gedeon Richter, Merck, Novartis, Pfizer, and Roche, Speakers bureau: AbbVie, Gedeon Richter, Merck, Novartis, Pfizer, and Roche, Andreas Hess: None declared, Georg Schett Speakers bureau: AbbVie, BMS, Celgene, Janssen, Eli Lilly, Novartis, Roche and UCB
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Table 1: Baseline patient characteristics.

			Study group		
			Certolizumab-High	Certolizumab-Low	Placebo
N			43	49	47
Age		Mean(SD)	54.3 (10.8)	56.5 (12.2)	52.1 (12.0)
Sex	female	n(%)	34 (79.1)	35 (71.4)	30 (63.8)
	male	n(%)	9 (20.9)	14 (28.6)	17 (36.2)
Disease duration		Mean(SD)	6.0 (8.3)	6.4 (8.6)	6.2 (7.6)
		Median(IQR)	2.0 (1.0-9.0)	3.0 (1.0-8.0)	3.0 (1.0-8.0)
ACPA	Negative	n(%)	15 (34.9)	9 (18.4)	10 (21.3)
	Positive	n(%)	28 (65.1)	40 (81.6)	37 (78.7)
RF	Negative	n(%)	12 (27.9)	13 (26.5)	14 (29.8)
	Positive	n(%)	31 (72.1)	36 (73.5)	33 (70.2)
Tender joints (28)		Mean(SD)	9.3 (6.4)	11.3 (6.7)	9.9 (6.2)
Swollen joints (28)		Mean(SD)	7.0 (4.4)	8.7 (6.3)	8.0 (4.8)
Patient global VAS, mm		Mean(SD)	57.2 (19.9)	59.1 (17.8)	57.6 (22.5)
Physician global VAS, mm		Mean(SD)	46.0 (20.2)	49.5 (19.2)	53.1 (16.2)
Pain VAS		Mean(SD)	53.5 (18.0)	57.1 (17.0)	54.9 (22.7)
ESR		Mean(SD)	23.7 (19.0)	25.2 (17.1)	28.2 (23.2)
CRP		Mean(SD)	6.8 (12.7)	7.9 (8.7)	11.2 (16.5)
DAS28		Mean(SD)	4.7 (1.0)	5.0 (1.1)	4.9 (1.0)

Table 2: Between group comparisons of disease activity components

	Comparison	Difference	95%CI	P value
Pain-VAS	CZP-L-CZP-H	6.26	-1.87 to 17.38	0.379
	Placebo-CZP-H	8.28	-2.85 to 19.41	0.186
	Placebo-CZP-L	2.02	-8.85 to 12.89	0.899
PGA-VAS	CZP-L-CZP-H	9.49	-1.23 to 20.20	0.094
	Placebo-CZP-H	14.99	4.27 to 25.70	**0.003**
	Placebo-CZP-L	5.50	-4.97 to 15.97	0.429
PhysGA-VAS	CZP-L-CZP-H	1.59	-8.91 to 12.08	0.932
	Placebo-CZP-H	11.22	0.67 to 21.77	**0.034**
	Placebo-CZP-L	9.64	-0.54 to 19.81	0.068
PGA-PhysGA Discrepancy	CZP-L-CZP-H	6.90	-0.50 to 14.30	0.073
	Placebo-CZP-H	3.30	-4.14 to 10.74	0.546
	Placebo-CZP-L	-3.60	-10.78 to 3.57	0.461
SJC-28	CZP-L-CZP-H	0.47	-1.26 to 2.19	0.796
	Placebo-CZP-H	1.21	-0.52 to 2.93	0.225
	Placebo-CZP-L	0.74	-0.95 to 2.43	0.554
TJC-28	CZP-L-CZP-H	0.16	-0.28 to 0.61	0.664
	Placebo-CZP-H	0.25	-0.20 to 0.69	0.389
	Placebo-CZP-L	0.08	-0.35 to 0.52	0.889
ESR	CZP-L-CZP-H	6.53	-2.80 to 15.85	0.225
	Placebo-CZP-H	11.77	2.44 to 21.09	**0.009**
	Placebo-CZP-L	5.24	-3.87 to 14.35	0.363
CRP	CZP-L-CZP-H	0.79	-7.01 to 8.59	0.969
	Placebo-CZP-H	8.24	0.48 to 16.00	**0.035**
	Placebo-CZP-L	7.45	-0.17 to 15.07	0.057

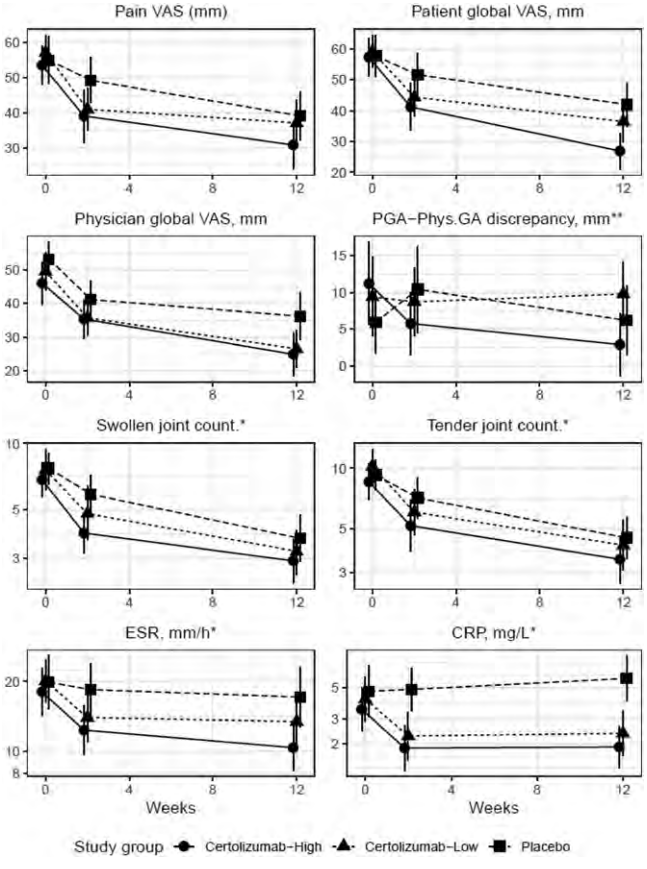


Figure 1. Course of disease activity components through trial timepoints. *indicates log-transformed y axis. ** Discrepancy equals Patient global minus physician global assessment.

OP0219

MORTALITY OF RHEUMATOID ARTHRITIS PATIENTS, TREATED TO TARGET AT LOW DISEASE ACTIVITY: 17-YEARS FOLLOW-UP OF THE BEST COHORT

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Background: Rheumatoid arthritis is known to be associated with increased mortality over the years when compared to the general population. In the BeSt study, 508 patients were treated to target (Disease Activity Score ≤2.4) for 10 years between April 2000 and August 2012. At the end of the initial study follow-up, the observed mortality in the BeSt cohort was similar to mortality in the general population. In the current study we evaluated the mortality in the BeSt cohort after 17 years follow-up and compared it to the general Dutch population.
Objectives: Evaluate long-term mortality in the BeSt study cohort.
Methods: In the BeSt study 508 patients diagnosed with early RA were randomized to four initial treatment strategies: 1. Sequential monotherapy; 2. Step-up

combination therapy; 3. Initial combination therapy with prednisone; or 4. Initial combination therapy with infliximab. During the 10-year follow-up period treatment was steered at low disease activity (DAS ≤2.4) and adjusted every three months when necessary. After 10-years patients were treated and followed-up according to regular care. We explored mortality through the Dutch state registry for mortality (Centrum voor Familiegeschiedenis) and treating rheumatologist. Mortality in the BeSt cohort was compared to the general Dutch population (Statistics Netherlands) matched by gender, age and calendar year using the standardized mortality ratio (SMR). Kaplan-Meier curves and the log-rank test were used to compare survival among the initial treatment strategies.

Results: The mean duration of follow-up in non-deceased patients was 17 years (range 16-18). In total, 143 patients died (28%) compared to a total of 105 (21%) expected deaths in the reference population. The overall SMR after 17 years was 1.37 (95% CI: 1.16-1.61). Within the study population, no statistically significant difference in survival-curves was observed between the four initial treatment strategies (log-rank p=0.76) (table 1, and figure 1).

Table 1. BeSt study cohort mortality - stratified for initial treatment strategy

	Sequential monotherapy n=126	Step-up combination therapy n=121	Initial combination therapy with prednisone n=133	Initial combination therapy with infliximab n=128
N (%) †	38 (30)	31 (26)	41 (31)	33 (26)
SMR (95% CI)	1.41 (1.03–1.94)	1.20 (0.84-1.70)	1.53 (1.13-2.09)	1.31 (0.93-1.85)

SMR: standardized mortality ratio (number observed deaths/number expected deaths); CI: confidence interval.Conclusion:

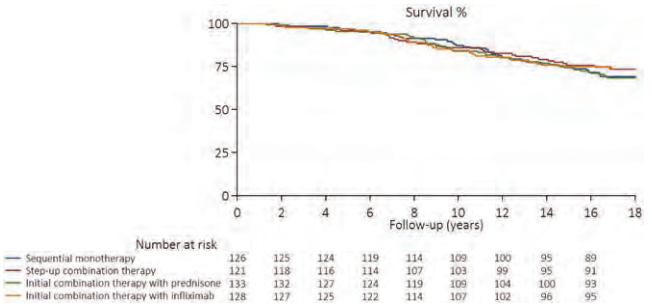


Figure 1. Survival curves – stratified for initial treatment strategy

After a mean of 17 years follow-up the mortality was increased in the BeSt study cohort when compared to the general Dutch population. We observed no difference in survival curves among the four treatment strategies.

Disclosure of Interests: Johanna M. Maassen: None declared, Yvonne Goekoop-Ruiterman: None declared, Hans van Groenendael: None declared, WIllem Lems Grant/research support from: Pfizer, Consultant of: Lilly, Pfizer, Pit Kerstens: None declared, Thomas Huizinga Grant/research support from: Ablynx, Bristol-Myers Squibb, Roche, Sanofi, Consultant of: Ablynx, Bristol-Myers Squibb, Roche, Sanofi, Cornelia Allaart: None declared

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OP0220 ASSESSING THE EFFECT OF INCREASED BODY MASS INDEX ON RESPONSE TO TNF INHIBITORS IN ESTABLISHED RHEUMATOID ARTHRITIS: RESULTS FROM THE METEOR DATABASE

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Background: Rheumatoid arthritis (RA) is associated with increased body mass index (BMI)- 60% of patients are either overweight or obese. Obesity in RA has been shown to predict reduced response to biologic therapy including tumour-necrosis-factor inhibitors (TNFi) [1]. However, it is not clear whether increased BMI influences response to all TNFi drugs in RA.

Objectives: 1.To explore whether BMI is associated with response to TNFi in patients with established rheumatoid arthritis (estRA), including those newly-starting on these drugs.

Methods: Participants with estRA (>1year since diagnosis) taking biologic medications, registered on METEOR (international database of RA patients), 2008-2013, were included. EULAR response, DAS28 remission (including components), and treatment regimens were recorded at baseline, 6, and 12 months. WHO definitions of overweight (BMI≥ 25) and obese (BMI≥30) were explored as predictors of TNFi response (good EULAR response and DAS28 remission) using normal BMI as comparator. Logistic and linear regression models (controlling for age, gender, smoking, and baseline outcomes) and sensitivity analyses were performed. Subgroup analyses were performed for grouped TNFi and individual TNFi (infliximab, IFX; adalimumab, ADA; etanercept, ETN).

Results: 247 patients with estRA were taking a biologic at 6 months, and 231 patients were taking a biologic at 12 months. Obese patients taking any biologic were significantly less likely to achieve DAS28 remission (OR 0.33 [95%CI 0.12-0.80]) or good EULAR response (OR 0.37 [95%CI 0.16-0.81]) after 6 months, compared to those of normal BMI; this was also demonstrated in those co-prescribed methotrexate (DAS28 remission: OR 0.23 [95%CI 0.07-0.62]; good EULAR response: OR 0.39 [95%CI 0.15-0.92]). These associations did not remain statistically significant at the 12 months assessment.

Regarding specific anti-TNF therapies, RA patients treated with monoclonal antibody (-mab) TNFis (IFX/ADA/ GOL) were significantly less likely to achieve good EULAR response at 6 months if they were obese RA (n=38), compared to those of normal weight (n=44) (OR 0.17 [95%CI 0.03-0.59]). A similar non-significant difference was demonstrated for DAS28 remission, and 12-month remission. Specifically, obese individuals were significantly less likely to achieve good EULAR response at 6 months with IFX (OR 0.09 [95%CI 0.00-0.61]; n=20), and significantly less likely to achieve DAS28 remission at 6 months when newly-starting ADA (OR 0.14 [95%CI 0.01-0.96]; n=17), compared to those of normal weight. There were no significant differences in remission outcomes between individuals of different BMI taking ETN. A small number of individuals stopped taking their respective biologic after 6months; reason for cessation was not recorded.

Similar outcomes were seen in patients already established on anti-TNF therapy, with overweight and obese individuals less likely overall to be in DAS28 remission at all time points.

Conclusion: In established RA, obesity is associated with reduced treatment response to -mab TNFi. No association between increased BMI and response to ETA was observed. Using BMI to direct biologic drug choice could prove to be a simple and cost-effective personalised-medicine approach to prescribing.

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OP0221 HAVE 5-YEAR SURVIVAL RATE AND MORTALITY CHANGED IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS IN THE PAST TWENTY YEARS?-RESULTS FROM THE IORRA COHORT

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Background: The mortality of patients with rheumatoid arthritis (RA) had been reported as being worse than that of the general population [1, 2], but is expected to have improved over time because the progress in treatment of RA during the past twenty years has been actively adopted to RA management [3, 4]. However, the change in the mortality still remains controversial in patients with early RA [5, 6].

Objectives: To investigate whether the vital prognosis of patients with early RA has changed in the past twenty years.

Methods: The IORRA cohort is a large observational cohort established in 2000 at the Institute of Rheumatology, Tokyo Women's Medical University. Essentially, all Japanese patients diagnosed with RA at our institute were registered and clinical parameters were assessed biannually. As there is no National Death Registry in Japan, we obtained death report from residual families who responded to our mail query to patients who failed to conduct the subsequent IORRA survey, from physicians of affiliated hospitals and from police in case they found dead

patient outside of a hospital. In this study, the patients with early RA (less than 2 years of disease duration) who participated in the survey for the first time from 2001 to 2012 were included and observed for five years from the date of the initial survey. We classified patients into group A (enrolled in 2001-2006) and B (enrolled in 2007-2012). Five-year survival rate and standardized mortality ratio (SMR) were calculated for each group. SMR was calculated using the life tables in Japanese general population reported by the Ministry of Health, Labour and Welfare, Japan. The effects of loss to follow-up cases were evaluated by multiple imputation method as a sensitivity analysis of SMR.

Results: A total of 3,217 patients with early RA were analyzed. The number of patients was 1,609 (79.4% female) in the group A and 1,608 (81.8% female) in B. The median age at baseline was 55 in both groups. Among a total of 3,217 patients, 486 (15.1%) patients were lost during 5-year follow-up; 213 (13.2%) in the group A and 273 (17.0%) in B, respectively. During the observational period, deaths were confirmed in 47 cases (2.9%) in the group A and 45 (2.8%) in B. Major causes of death included malignancies (28% in the group A, 38% in B), respiratory involvement (23% in the group A, 40% in B), cerebrovascular disorders (11% in the group A, 2% in B), and cardiovascular disorders (11% in the group A, 0% in B). The five-year survival rate was 88.8% for the group A and 87.8% for B, and the SMR was 0.81 (95%CI: 0.59-1.08) for the group A and 0.78 (0.57-1.04) for B when assuming all the lost to follow-up patients were alive for 5 years. In the sensitivity analysis assuming that the mortality rate of patients who were lost to follow-up was twice as that of the general population, the SMR was 0.90 (0.68-1.19) for the group A and 0.92 (0.68-1.23) for B.

Conclusion: The mortality of patients with early RA in the past twenty years has been comparable to that of the Japanese general population. In addition, the SMR and the five-year survival rate did not change overtime.

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OP0222

IS REFERRING EARLY ARTHRITIS PATIENTS WITHIN 6 WEEKS ASSOCIATED WITH BETTER LONG-TERM OUTCOMES THAN REFERRING WITHIN 12 WEEKS AFTER SYMPTOM ONSET? – INVESTIGATING THE EVIDENCE FOR THE FIRST EULAR RECOMMENDATION FOR EARLY ARTHRITIS IN TWO OBSERVATIONAL COHORTS

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Background: EULAR- recommendations for management of early arthritis formulated that patients should be referred to, and seen by a rheumatologist, within 6-weeks after symptom onset. The mentioned period of ≤6-weeks after symptom onset is shorter than ≤12-weeks, the period that is generally considered as the 'window-of-opportunity'. Because implementation provides challenges, and evidence supporting that referral ≤6-weeks is better than e.g. <12-weeks is missing, we investigated if ≤6-weeks relates to improved long-term outcomes.

Objectives: We used an observational study design to investigate in two cohorts if time-to-encounter (TtE) a rheumatologist ≤6-weeks, compared to 7-12-weeks, results in better disease long-term outcomes, measured with sustained DMARD-free remission (SDFR) and radiographic progression.

Methods: Consecutive 1987-RA patients of the Leiden EAC (n=1025) and ESPOIR (n=514) were studied during median 7 and 10 years follow-up. Patients were categorized on duration between symptom onset and first encounter with a rheumatologist; ≤6-, 7-12-, and >12-weeks. Multivariable Cox regression (SDFR), linear mixed models (radiographic progression), and meta-analyses were used.

Results: Leiden RA-patients encountered the rheumatologist within 6-weeks obtained SDFR more often than patients seen within 7-12-weeks (HR 1·59, 95%CI:1·02-2·49), and >12-weeks (HR 1·54, 95%CI:1·04-2·29). In ESPOIR, similar but non-significant effects were observed; meta-analysis showed that within 6-weeks was better than 7-12-weeks (HR 1·69, 95%CI:1·10-2·57, Figure 1-A) and >12-weeks (HR 1·67, 95%CI:1·08-2·58). Patients encountered the rheumatologist within 6-weeks had similar radiographic progression than those seen 7-12-weeks, in any cohort, or meta-analysis (Figure 1-B).

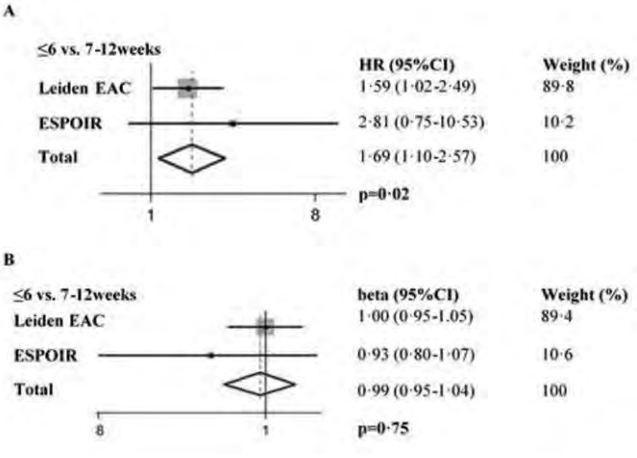


Figure 1 Meta-analyses of time-to-encounter the rheumatologist and the chance of achieving sustained DMARD-free remission (A) and radiographic progression (B)

Conclusion: Scientific evidence underlying the first EULAR recommendation depends on the outcome of interest; visiting a rheumatologist within 6-weeks of symptom-onset had clear benefits for achieving SDFR, but not for radiographic progression.

References: None.

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Update on new treatment options for psoriatic arthritis

OP0223 **EFFICACY AND SAFETY OF UPADACITINIB IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS AND INADEQUATE RESPONSE TO BIOLOGIC DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS (SELECT-PSA-2): A DOUBLE-BLIND, RANDOMIZED CONTROLLED PHASE 3 TRIAL**

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Background: Upadacitinib (UPA) is an oral, reversible, JAK inhibitor approved for treatment of moderate to severe rheumatoid arthritis (RA) and currently under evaluation for treatment of psoriatic arthritis (PsA).

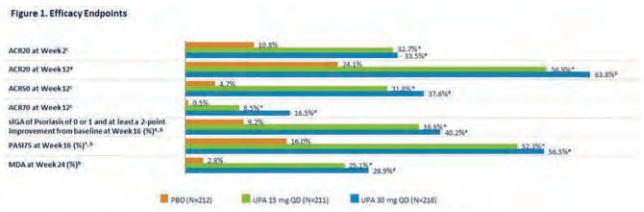
Objectives: To assess the efficacy and safety of UPA versus placebo (PBO) in patients (pts) with PsA and prior inadequate response or intolerance to ≥1 biologic disease-modifying anti-rheumatic drug (bDMARD).

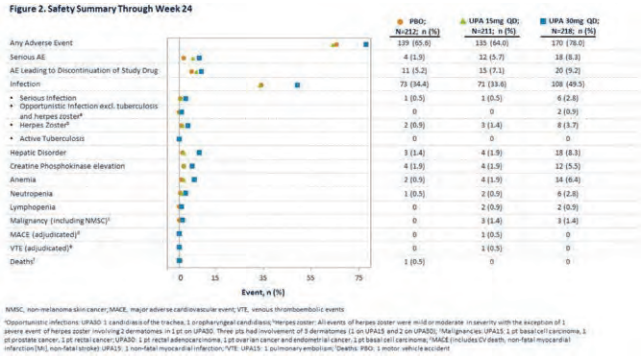
Methods: In SELECT-PsA-2, pts were randomized 1:1:1 to once daily UPA 15 mg (UPA15), UPA 30 mg (UPA30), or PBO. Pts were stratified by baseline DMARD use, number of prior failed bDMARDs, and extent of psoriasis. The primary endpoint was the proportion of pts achieving ACR20 response at Wk 12. Multiplicity controlled secondary endpoints included change in HAQ-DI, FACIT-Fatigue (FACIT-F), and SF-36 Physical Component Summary (PCS) at Wk 12; static Investigator Global Assessment (sIGA) of Psoriasis of 0 or 1 and at least a 2-point improvement from baseline, PASI75, and change in Self-Assessment of Psoriasis Symptoms (SAPS) at Wk 16; and proportion of pts achieving MDA at Wk 24. Additional key secondary endpoints were ACR50 and ACR70 at Wk 12, and ACR20 at Wk 2. Treatment-emergent adverse events (TEAEs) are reported for pts who received ≥1 dose of study drug.

Results: 641 pts were randomized and received study drug; 54.3% were female with mean age of 53.4 years, and mean duration since PsA diagnosis of 10.1 years. 61% of pts failed 1 bDMARD, 18% failed 2 bDMARDs, and 13% failed ≥3 bDMARDs. 543 (84.6%) pts completed Wk 24 study drug.

At Wk 12, a significantly greater proportion of pts receiving UPA15 and UPA30 vs PBO achieved ACR20 (56.9% and 63.8% vs 24.1%; p < .0001 for both comparisons). Statistically significant improvements were observed in the UPA15 and UPA30 arms vs PBO in all multiplicity controlled secondary endpoints, including ΔHAQ-DI (PBO, -0.10; UPA15, -0.30; UPA30, -0.41), ΔSF-36 PCS (PBO, 1.6; UPA15, 5.2; UPA30, 7.1), ΔFACIT-F (PBO, 1.3; UPA15, 5.0; UPA30, 6.1), and ΔSAPS (PBO, -1.5; UPA15, -24.4; UPA30, -29.7; p < .0001 for all endpoints; **Figure 1**). In addition, a greater proportion of pts achieved ACR50 and ACR70 at Wk 12 with UPA vs PBO. Generally, TEAEs were reported at similar frequencies in the PBO and UPA15 arms and at a higher frequency in the UPA30 arm (**Figure 2**). Numerically higher rates of serious AEs were reported in the UPA arms. Herpes zoster was more frequent with UPA30. Three malignancies occurred in each of the UPA arms. One adjudicated non-fatal myocardial infarction and one adjudicated pulmonary embolism were reported with UPA15.

Conclusion: In this bDMARD-IR PsA population, UPA15 and UPA30 demonstrated significant improvements across PsA domains including improvements in joint and skin signs and symptoms vs PBO through Wk 24 with improvement observed by Wk 2. A greater percentage of pts treated with UPA achieved MDA and ACR50/70, stringent composite measures of disease control. No new safety signals were identified compared to what has been observed with UPA in RA.





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OP0224

FILGOTINIB TREATMENT LEADS TO RAPID AND SUSTAINED REDUCTIONS IN INFLAMMATORY BIOMARKERS IN PATIENTS WITH MODERATE TO SEVERE PSORIATIC ARTHRITIS

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory musculoskeletal disease characterized by musculoskeletal and cutaneous inflammation. In the recent EQUATOR study (NCT03101670), patients (pts) with active PsA receiving the oral, selective Janus kinase 1 (JAK1) inhibitor filgotinib (FIL) had significant and sustained improvements versus placebo (PBO) in clinical signs and symptoms. We present here updated results of the EULAR 2019 presentation of EQUATOR on circulating biomarkers in PsA.

Objectives: To evaluate the impact of FIL on the levels of circulating proinflammatory cytokines and chemokines, adhesion molecules, and markers of matrix remodeling in EQUATOR pts with active PsA.

Methods: EQUATOR was a 16-week, double-blind, multicenter, Phase 2 study in pts with active PsA. Pts were randomized 1:1 to FIL 200 mg (n=65) or PBO (n=66) once daily. Serum samples (FIL n=60 and PBO n=61) were collected at baseline (BL) and at Weeks 1, 4, and 16. The association of BL biomarkers with PsA disease characteristics was analyzed by Spearman's rank-order correlation. Biomarker changes from BL were assessed in time-paired serum samples using multiplex and high sensitivity ELISA-based assays. Analytes were grouped by hierarchical clustering; treatment effect on a biomarker was defined as a difference in change from BL between pts receiving FIL versus PBO. Improvements in PsA clinical signs and symptoms were determined by assessing changes from BL in a number of clinical disease activity scores including psoriatic arthritis disease activity score (PASDAS), psoriasis area and severity index (PASI) and disease activity index for psoriatic arthritis (DAPSA) scores.

Results: BL levels of numerous biomarkers were associated ($p<0.05$) with clinical measures of PsA. Several clusters of biomarkers were identified based on the rate and magnitude of FIL treatment response. Cluster 1 included biomarkers with substantial reductions from BL with FIL by week 1, such as the acute phase proteins CRP and SAA (>50%), and the inflammatory mediators IL-6, CXCL10, and IL-23 (>25%). Cluster 2 included biomarkers of cell adhesion (ICAM-1, VCAM1) with a 5%–15% reduction from BL with FIL by week 1. Cluster 3 included biomarkers of matrix remodeling (MMP1, SC1M) with a delayed >25% reduction from BL with FIL that was significant by Week 4. Finally, Cluster 4 included biomarkers with a modest (5%–10%) increase from BL with FIL (Eotaxin, IL-15, and adiponectin). Spearman rank correlation analyses showed that at BL, many biomarkers were positively associated with disease scores, and tended to segregate between psoriasis weighted scores such as PASI and arthritis weighted scores such as DAPSA. The observed decrease in proinflammatory cytokines were associated with on-treatment improvements from BL in disease score for pts receiving FIL.

Conclusion: Compared with PBO, FIL significantly decreased BL levels of circulating biomarkers associated with PsA disease activity, including proinflammatory cytokines and chemokines, adhesion molecules, and markers of matrix remodeling. The observed decreases in circulating proinflammatory cytokines and biomarkers of both bone pathobiology and psoriatic disease suggest that FIL improves PsA clinical signs and symptoms at a molecular level. These findings are consistent with reduced disease activity in pts with PsA and suggest that FIL treatment leads to a rapid and sustained reduction of inflammation in PsA.

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Disclosure of Interests: Dafna D Gladman Grant/research support from: AbbVie, Amgen Inc., BMS, Celgene Corporation, Janssen, Novartis, Pfizer, UCB – grant/research support, Consultant of: AbbVie, Amgen Inc., BMS, Celgene Corporation, Janssen, Novartis, Pfizer, UCB – consultant, Wendy Jiang Shareholder of: Gilead Sciences Inc., Employee of: Gilead Sciences Inc., Angie Hertz Shareholder of: Gilead Sciences Inc, Employee of: Gilead Sciences Inc, Vlad Malkov Shareholder of: Gilead Sciences Inc., Employee of: Gilead Sciences Inc., Oh Kyu Yoon Shareholder of: Gilead Sciences Inc., Employee of: Gilead Sciences Inc., Mona Trivedi Shareholder of: Amgen and Gilead Sciences, Employee of: Gilead Sciences, Muhsen Alani Employee of: Gilead Sciences, Lene Vestergaard Shareholder of: Gilead Sciences Inc., Employee of: Gilead Sciences Inc., Robin Besuyen Shareholder of: Galapagos, Employee of: Galapagos, René Galien Shareholder of: Galapagos, Employee of: Galapagos, Amer M. Mirza Shareholder of: Gilead Sciences Inc., Employee of: Gilead Sciences Inc., Vinod Chandran Grant/research support from: Abbvie, Celgene, Consultant of: Abbvie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lily, Janssen, Novartis, Pfizer, UCB, Employee of: Spouse employed by Eli Lily

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OP0225

TOFACITINIB AS MONOTHERAPY FOLLOWING METHOTREXATE WITHDRAWAL IN PATIENTS WITH PSORIATIC ARTHRITIS PREVIOUSLY TREATED WITH OPEN-LABEL TOFACITINIB + METHOTREXATE: A RANDOMISED, PLACEBO-CONTROLLED SUBSTUDY OF OPAL BALANCE

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Background: Tofacitinib is an oral JAK inhibitor for the treatment of psoriatic arthritis (PsA).

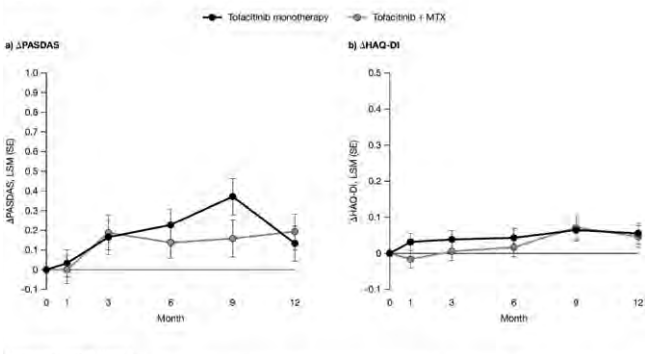
Objectives: To assess tofacitinib 5 mg BID as monotherapy after methotrexate (MTX) withdrawal vs with continued background MTX in patients (pts) with PsA.

Methods: OPAL Balance (NCT01976364) was an open-label (OL) long-term extension (LTE) study of tofacitinib in pts with PsA who participated in Phase (P)3 studies (OPAL Broaden, NCT01877668; OPAL Beyond, NCT01882439). Pts who completed ≥24 months' tofacitinib treatment in the LTE (stable 5 mg BID for ≥3 months) and were receiving oral MTX (7.5–20 mg/week; stable for ≥4 weeks) entered the multicentre, 12-month, double-blind, MTX withdrawal substudy. Pts remained on OL tofacitinib 5 mg BID and were randomised 1:1 to receive placebo (tofacitinib monotherapy, ie, blinded MTX withdrawal) or MTX (tofacitinib + MTX; same stable doses). Primary endpoints were changes from substudy baseline (Δ) in PASDAS and HAQ-DI at Month (M)6. Secondary efficacy endpoints were assessed at all time points. Safety was assessed throughout the substudy.

Results: Of 180 pts randomised, 179 were treated (tofacitinib monotherapy n=90; tofacitinib + MTX n=89). Pt characteristics were similar between treatment arms. At M6, least squares mean (LSM) (standard error [SE]) ΔPASDAS was 0.229 (0.079) for tofacitinib monotherapy and 0.138 (0.081) for tofacitinib + MTX, and LSM (SE) ΔHAQ-DI was 0.043 (0.027) and 0.017 (0.028), respectively (Figure 1); no clinically meaningful differences were observed. Efficacy and pt-reported outcomes were generally similar between treatment arms at M6 and M12 (data not shown). Rates of pts achieving minimal disease activity, and maintaining an absence of enthesitis and dactylitis, were sustained to M12 in both treatment arms (Figure 2). Adverse event rates (Table) and laboratory parameters were comparable between treatment arms, but liver enzyme elevations were more common with tofacitinib + MTX.

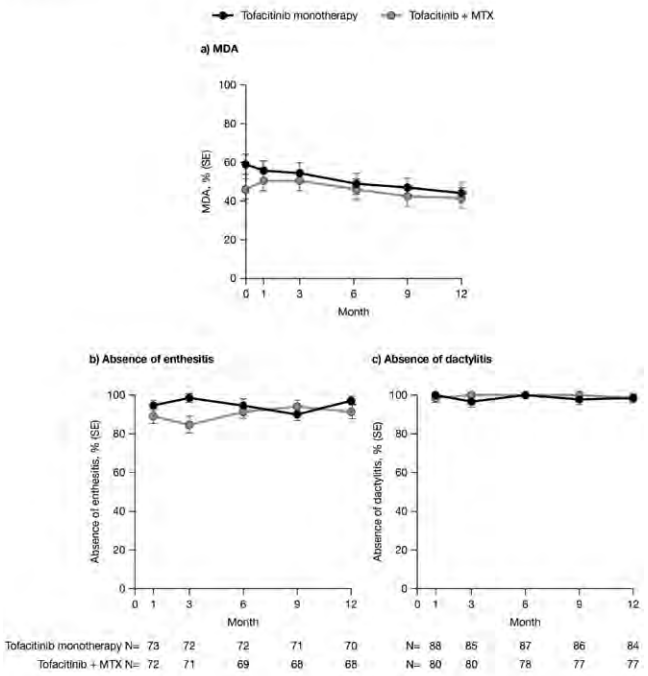
Conclusion: No clinically meaningful differences in efficacy and safety were observed in PsA pts who received OL tofacitinib 5 mg BID as monotherapy after MTX withdrawal vs with continued MTX. Safety was consistent with previous P3 studies. The substudy was an estimation study and not powered for hypothesis testing.

Figure 1. LSM (SE) a) ΔPASDAS[a] and b) ΔHAQ-DI[a] up to Month 12 of the MTX withdrawal substudy



[a]Primary endpoints at Month 6
Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction, and baseline value, without imputation for missing values; a common unstructured covariance matrix was used. The numbers of patients included in the repeated measures model from tofacitinib monotherapy and tofacitinib + MTX arms were 90 and 89, respectively, for both PASDAS and HAQ-DI. For each endpoint at each time point, the 95% CI of the LSM difference between the tofacitinib monotherapy and tofacitinib + MTX arms included 0
Δ, change from substudy baseline; CI, confidence interval; HAQ-DI, Health Assessment Questionnaire-Disability Index; LSM, least squares mean; MTX, methotrexate; PASDAS, Psoriatic Arthritis Disease Activity Score; SE, standard error

Figure 2. Proportion (SE) of patients achieving a) MDA,[a] and maintaining absence of b) enthesitis[b] and c) dactylitis,[c] up to Month 12 of the MTX withdrawal substudy



[a]Missing response=non-response. The numbers of patients included in this analysis were 90 and 89 for tofacitinib monotherapy and tofacitinib + MTX, respectively; [b]In patients with LEI=0 at baseline, no imputation; [c]In patients with DSS=0 at baseline, no imputation DSS, Dactylitis Severity Score; LEI, Leeds Enthesitis Index; MDA, minimal disease activity; MTX, methotrexate; SE, standard error

Table. Safety outcomes to Month 12

Pts with events, n (%) AEs of special interest	Tofacitinib monotherapy N=90	Tofacitinib + MTX N=89
AE	43 (47.8)	41 (46.1)
Serious AE	4 (4.4)	3 (3.4)
Discontinuations due to AE	3 (3.3)	4 (4.5)
Death	0	0
Herpes zoster (serious/non-serious)	1 (1.1)	2 (2.2)
Serious infection	0	2 (2.2)
Opportunistic infection[a]	0	1 (1.1)
Malignancy (excl. NMSC)[a]	1 (1.1)	1 (1.1)
NMSC[a]	0	0
Major adverse cardiovascular event[a]	0	0
Venous thromboembolism[c]	0	0
Arterial thromboembolism[c]	1 (1.1)	0
Gastrointestinal perforation[a]	0	0
Interstitial lung disease[b]	0	0
Laboratory parameters[d]		
ALT ≥3×ULN	0	5 (5.6)
ALT (IU/L), mean (SE)	-2.7 (1.6)	2.5 (1.3)
AST ≥3×ULN	0	3 (3.4)
AST (IU/L), mean (SE)	-1.5 (1.2)	1.7 (0.8)

Reviewed by independent [a]external/[b]internal adjudication committee
[c]Per Standardised MedDRA Query terms
[d]Without regard to baseline abnormality
ALT, alanine aminotransferase; AST, aspartate aminotransferase; ULN, upper limit of normal

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OP0226

NETAKIMAB DECREASES DISEASE ACTIVITY IN PATIENTS WITH PSORIATIC ARTHRITIS: RESULTS FROM A RANDOMIZED DOUBLE-BLIND PHASE 3 CLINICAL TRIAL (PATERA)

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Background: Netakimab (NTK) is a humanized anti-interleukin 17A antibody approved for the treatment of moderate-to-severe plaque psoriasis.
Objectives: To determine the efficacy and safety of NTK in patients (pts) with active psoriatic arthritis (PsA), based on 24-week (Wk) data from an ongoing phase 3 study (NCT03598751, PATERA).
Methods: 194 eligible adult pts with PsA (CASPAR, 2006) with inadequate response to csDMARD or one TNFi, were randomized (1:1) to receive NTK 120 mg or placebo (PBO) subcutaneously at Wk 0, 1, 2, 4, 6, 8, 10, 14, 18, 22. 84 pts from PBO arm who did not meet ACR20 (20% improvement of the American College of Rheumatology criteria) by Wk 16 were switched to NTK 120 mg. The primary endpoint was ACR20 at Wk 24. DAPSA (Disease Activity Index for Psoriatic Arthritis), the proportion of pts achieved ACR50/70, minimal disease activity (MDA) (≥5/7 MDA criteria) and Psoriatic arthritis response criteria (PsARC) were also analyzed.
Results: Baseline demographics and disease characteristics were similar across treatment arms (Table 1). 80 (82.47%) pts in NTK arm and 9 (9.28%) in the PBO arm achieved ACR20 at Wk 24 (p<0.0001). A significantly greater percentage of NTK-treated pts had ACR50/70, PsARC response, MDA at Wk 24 (Figure 1). By Wk 24 DAPSA significantly improved for NTK vs PBO. DAPSA remission was achieved by 36.08% and 13.40% in NTK and PBO arms, respectively (p=0.003). NTK was well tolerated. The most frequent AEs (≥3%) were lymphopenia, neutropenia, hypercholesterolemia, ALT increased, upper respiratory tract infection, systolic blood pressure increased, hyperglycemia, hyperbilirubinemia. Most AEs were mild to moderate. Severe treatment-related AEs were observed in 1.03% vs 2.06% for NTK and PBO, respectively. No treatment-related SAEs were reported. No anti-drug antibodies were detected.

Table 1. Baseline demographics and disease severity characteristics

Arm	NTK (N=97)	PBO (N=97)
Age (years) *	44.0 (11.66)	43.1 (11.88)
Male, n (%)	52 (53.61)	50 (51.55)
PsA duration, mo*	63.1 (73.12)	68.2 (77.49)
DAS28-CRP*	4.62 (0.97)	4.41 (1.11)
DAPSA*	32.19 (12.23)	33.54 (15.98)
TJC (66/68) *	12.9 (9.97)	12.0 (9.88)
SJC (66/68) *	7.0 (4.93)	7.2 (7.18)
MTX at baseline	83 (85.6)	83 (85.6)
Previous PsA therapy		
Sulfasalazine, n (%)	9 (9.28)	11 (11.34)
Leflunomide, n (%)	4 (4.12)	8 (8.25)
Anti-TNFα, n (%)	22 (22.68)	17 (17.53)

* mean (standard deviation); Mo=months, PsA=psoriatic arthritis, SJC=swollen joint count, TJC=tender joint count, DAS28=Disease Activity Score, MTX=methotrexate, CRP=C-reactive protein, DAPSA=Disease activity index for psoriatic arthritis, TNF=tumor necrosis factor

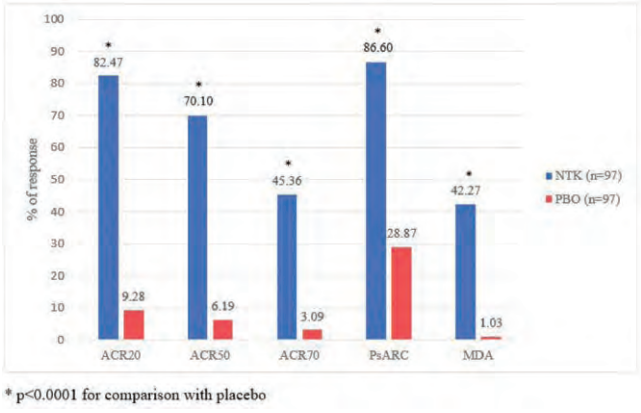


Figure 1. Treatment response at Wk 24

Conclusion: NTK is a well-tolerated monoclonal antibody, that provided sustained improvements in signs and symptoms of active PsA through 24 Wks of therapy.

Table 2. Safety data

Arm	NTK (N=97)	PBO (N=97)	p-value
Treatment-related AEs	12 (12.37)	7 (7.22)	0.227[1]
Treatment-related SAEs	0 (0)	0 (0)	1.00[2]
Treatment-related AEs (grade 3-4)	1 (1.03)	2 (2.06)	1.00[2]
Local reactions	0 (0)	0 (0)	-
Grade 3-4 treatment-related AEs			
blood pressure increased	1 (1.03)	0(0)	1.00[2]
lymphopenia	0 (0)	2 (2.06)	0.497[2]

n (%) are presented, [1] Pearson's χ^2 test, [2] Fisher's exact test; N=number of patients, AE=adverse event, SAE=serious adverse event, ALT=Alanine transaminase

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OP0227

SECUKINUMAB VERSUS ADALIMUMAB HEAD-TO-HEAD COMPARISON IN BIOLOGIC-NAÏVE PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS THROUGH 52-WEEKS (EXCEED): A RANDOMISED, DOUBLE-BLIND, PHASE-3B STUDY

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Background: Secukinumab (SEC), an interleukin-17A inhibitor, has demonstrated improvements on multiple domains of psoriatic arthritis (PsA).[1] Adalimumab (ADA), a TNF inhibitor, is widely used as a first–line biologic in PsA.
Objectives: To report efficacy and safety outcomes from the head-to-head EXCEED trial (NCT02745080) that compares SEC *vs.* ADA as first–line biologic monotherapy through 52-weeks (wks), with a musculoskeletal primary endpoint in pts with active PsA.
Methods: Head-to-head, phase-3b, randomised, double-blind trial: biologic naïve active PsA pts were randomised to receive SEC 300mg subcutaneous at baseline, Wk1-4, and then every 4wks (q4w) until Wk48 or ADA 40mg subcutaneous at baseline and then q2w until Wk50. The primary endpoint was superiority of SEC *vs.* ADA on ACR20 response at Wk52. Binary and continuous variables were analysed using logistic-regression model and MMRM, respectively. Safety analysis included patients who received ≥1 dose of study-drug.
Results: 853 pts were randomised to receive SEC (n=426) or ADA (n=427). Baseline demographics and disease characteristics were comparable between treatment-groups except higher proportion of female pts and pts without enthesitis in the SEC group. ACR20 response at Wk52 for SEC *vs.* ADA were 67·4% *vs.* 61·5%, respectively (p=0·0719) (Figure). Higher clinical responses were observed with SEC *vs.* ADA for a range of musculoskeletal, skin, and higher-hurdle outcomes (Table). A higher retention rate was observed for SEC (85.7%) *vs.* ADA (76.3%). Safety profiles of SEC and ADA were consistent with previous reports.[2,3]
Conclusion: Results suggest that SEC is at least as efficacious as ADA on musculoskeletal endpoints whilst providing higher responses on skin endpoints, and is associated with a higher retention rate. No new safety signals were reported.
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[1] van der Heijde, et al. Rheumatol. (Oxford).2019; DOI10.1093/rheumatology/kez420.
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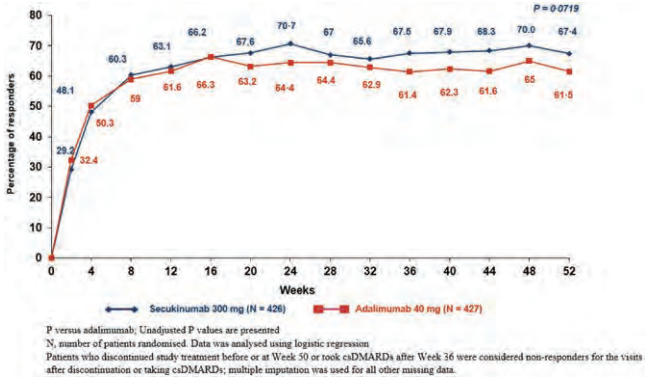


Figure. ACR20 Response through Wk 52

Table. Efficacy Outcomes at Wk 52

Endpoints, % response unless specified otherwise	SEC 300 mg (N=426)	ADA 40 mg (N=427)	P-value (unadjusted)*
ACR20	67·4	61·5	0·0719
[a]ACR20	66·9	59·5	0·0239
Key Secondary			
[b]PASI 90	65·4	43·2	<0·0001
ACR50	49·0	44·8	0·2251
HAQ-DI mean change from baseline ± SE	-0·58 ± 0.03	-0·56 ± 0.03	0·5465
[c]Resolution of enthesitis (based on LEI)	60·5	54·2	0·1498
Exploratory			
MDA	43·0	37·9	0·1498
VLDA	18·1	16·6	0·6107
DAPSA LDA+Remission	61·7	53·1	0·0178
PASDAS LDA+Remission	51·1	44·1	0·0557

*Unadjusted P-values *vs* ADA
Binary variables were analysed using logistic regression. Pts who discontinued study treatment prematurely or took csDMARDs after week-36 were considered non-responders. Multiple imputation was used for all other missing data. HAQ-DI mean change from baseline was analysed using mixed-effect model repeated measures
[a]Non-responder imputation was used for pre-specified sensitivity analysis
[b]N=215 in SEC and N=202 in ADA in psoriasis subset
[c]N=234 in SEC and N=264 in ADA in enthesitis subset

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OP0228

EFFICACY AND SAFETY OF IXEKIZUMAB VERSUS ADALIMUMAB (SPIRIT-H2H) WITH AND WITHOUT CONCOMITANT CONVENTIONAL SYNTHETIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS (DMARD) IN BIOLOGIC DMARD-NAÏVE PATIENTS WITH PSORIATIC ARTHRITIS: 52-WEEK RESULTS

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Background: Ixekizumab (IXE), a high-affinity monoclonal antibody selectively targeting IL-17A, was superior to adalimumab (ADA) at Week (Wk) 24 for simultaneous achievement of ACR50 and 100% improvement from baseline in the Psoriasis Area and Severity Index (PASI 100) (primary endpoint) in patients (pts) with active PsA from SPIRIT-H2H[1]. SPIRIT-H2H had two major secondary endpoints and achieved both: noninferiority of IXE to ADA for ACR50 at Wk 24, and superiority of IXE to ADA for PASI 100 at Wk 24.

Objectives: To determine how concomitant conventional synthetic DMARD (csDMARD) use affects safety and efficacy of IXE and ADA in prespecified subgroups defined by biologic monotherapy, concomitant MTX use, and concomitant csDMARD use through Wk 52 in SPIRIT-H2H.

Methods: SPIRIT-H2H (NCT03151551) was a 52-week, multicentre, randomised, open-label, assessor-blinded, parallel-group study evaluating the efficacy and safety of IXE versus ADA in adults with PsA and naïve to biologic DMARDs. Patients were required to have active PsA fulfilling Classification for Psoriatic Arthritis (CASPAR) criteria and ≥3/68 tender and ≥3/66 swollen joints, ≥3% plaque psoriasis BSA involvement, no prior treatment with bDMARDs, and with prior inadequate response to ≥1 csDMARD (but not necessarily current treatment with csDMARDs). Randomization (1:1) was stratified by concomitant use of csDMARD and the presence/absence of moderate to severe PsO (baseline: BSA≥10% + PASI≥12, + static Physician's Global Assessment≥3). Patients (N=566) received IXE/ADA through 52 wks according to the labelled dose dependent on presence/absence of moderate-to-severe PsO. In this prespecified subgroup analysis by presence or absence of csDMARDs, efficacy outcomes through wk 52 were compared between IXE and ADA using logistic regression models and Fisher's exact tests. Missing data were imputed using non-responder imputation.

Results: At baseline, 167 of 283 IXE-treated patients and 169 of 283 ADA-treated patients had concomitant MTX use. Of these, 9.0% (15/167) and 7.1% (12/169) treated with IXE and ADA, respectively, were taking an additional csDMARD (sulfasalazine, cyclosporine, or leflunomide). A significantly greater proportion of patients on IXE versus ADA achieved the primary endpoint or PASI 100 when used as monotherapy or in combination with csDMARD (Figure 1A and 1C). At Wk 52, the proportion of patients achieving ACR50 was not statistically different between IXE and ADA, regardless of monotherapy or concomitant csDMARD use (Figure 1B). A significantly higher proportion of patients achieved MDA on IXE compared to ADA in the monotherapy subgroup (49% vs 33%), while the response rates were similar in both combination subgroups (Figure 1D). These data support consistent ACR50, PASI 100, and MDA response for IXE across all three subgroups. Frequencies of adverse events were similar across the three subgroups for IXE and ADA (Figure 2).

Conclusion: As with prior studies,[2,3] consistent efficacy across multiple PsA disease-specific endpoints was observed with IXE in SPIRIT-H2H, regardless of whether IXE was taken as monotherapy or in combination with MTX or another csDMARD. No unexpected safety signals were found for either agent.

References:

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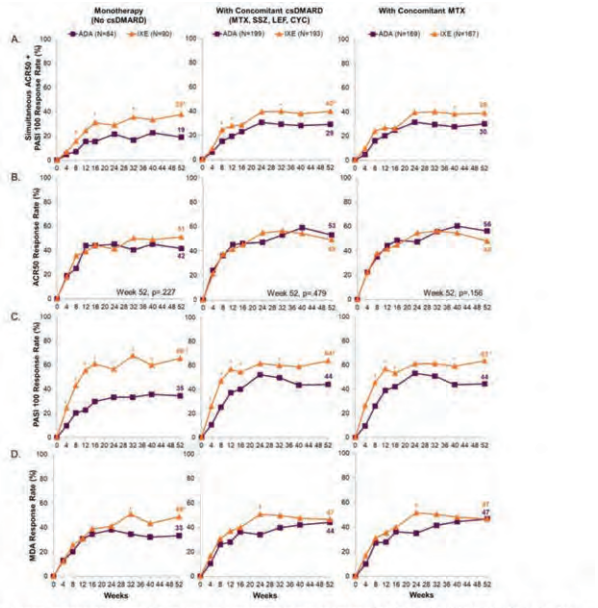
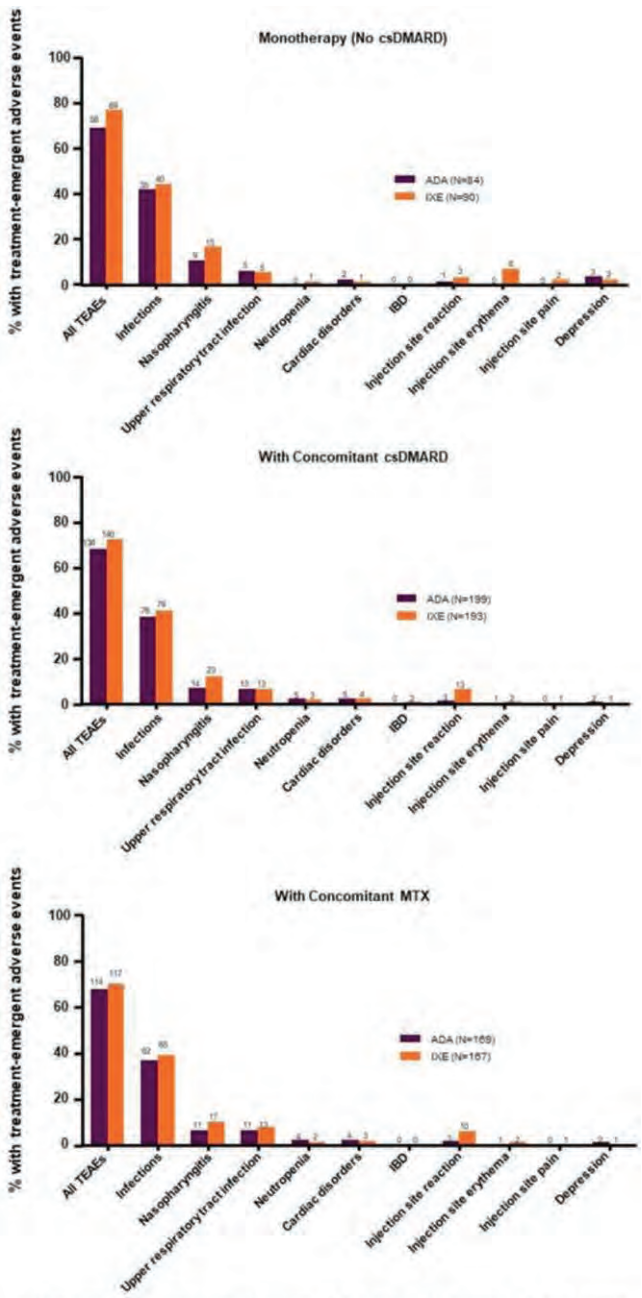


Figure 1. Proportion patients through 52 weeks with simultaneous achievement of ACR50 + PASI 100, ACR50, PASI 100, and MDA-18 Entheseal Points. Nine patients with active PsO and BSA≥3% were assessed as PASI=0 at baseline, a medical inconsistency that was resolved using medical judgement. These patients were considered PASI 100 responders if PASI=0 and BSA=0 at post baseline visit. *p≤.05 vs. ADA; †p<.01 vs. ADA; ‡p≤.001 vs. ADA.

Abbreviations: ACR, American College of Rheumatology criteria; ADA, adalimumab; csDMARD, conventional synthetic DMARD; IXE, ixekizumab; MTX, methotrexate; MDA, minimal disease activity – PsA; PASI, Psoriasis Area Severity Index score.



Safety data for patients through 52 weeks. 2 events of IBD were reported in the ixekizumab treatment arm but only 1 case met the adjudication criteriaof confirmed inflammatory bowel disease.
Abbreviations: ADA, adalimumab; csDMARD, conventional synthetic DMARD; IBD, inflammatory bowel disease; IXE, ixekizumab; MTX, methotrexate; TEAE, treatment emergent adverse event.

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OP0229

GUSELKUMAB INDUCES SUSTAINED REDUCTION IN ACUTE PHASE PROTEINS AND TH17 EFFECTOR CYTOKINES IN ACTIVE PSORIATIC ARTHRITIS IN TWO PHASE-3 CLINICAL TRIALS (DISCOVER-1 AND DISCOVER-2)

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Background: Guselkumab (GUS), an IL-23 inhibitor monoclonal antibody (Mab) that specifically binds to the IL-23p19 subunit, demonstrated efficacy compared to placebo (PBO) in reducing skin and musculoskeletal signs and symptoms in patients (pts) with active psoriatic arthritis (PsA) in two phase-3 studies, DISCOVER 1 & 2.[1,2] Previous results from a GUS PsA Phase-2 trial[3] and Ustekinumab (UST, anti-IL12/23p40 MAb) PsA Phase-3 trials (PSUMMIT 1 & 2)[4] showed associations of baseline IL-17A, IL-17F, and CRP with baseline disease characteristics, and associations of GUS-induced cytokine reductions with clinical responses.

Objectives: To investigate plausible cytokine expression in PsA and alterations after exposure to GUS therapy.

Methods: In DISCOVER 1 & 2, pts were treated with GUS 100 mg at Wk 0, 4, then every 8Wks (q8w); GUS 100mg q4w; or matching PBO. 21 serum biomarkers were measured in a random subset of 300 PsA pts from the DISCOVER program at Weeks (Wks) 0, 4, & 24 and in 34 healthy controls matched for age, sex, and ethnicity. Serum proteins measured were acute phase reactants CRP & SAA (Meso Scale Discovery (MSD) Platform) and inflammatory cytokines/chemokines: Th17 effector cytokines IL-17A, IL-17F, & IL-22 (Single Molecule Counting Erenna® Immunoassay Platform) and soluble ICAM-1, soluble VCAM-1, IL-6, CXCL-8, IL-10, IL-13, IL-12p70, CCL22, IFN-γ, CCL2, CCL4, TNFα, IL-1β, IL-2, IL-4 (MSD), & YKL-40 (Quantikine Immunoassay). Serum IL-17A, IL-17B, & CRP measured in the Phase-3 PSUMMIT trials of UST for PsA[4] were included for comparison with GUS.

Results: At baseline, serum levels of acute phase proteins CRP, SAA, & IL-6, and Th17-effector cytokines IL-17A & IL-17F were elevated in pts with PsA compared with healthy controls ($p<0.05$, geometric mean ≥ 40% higher, FIG 1). There was no significant dysregulation in the other cytokines measured in PsA pts compared to healthy controls. Baseline IL-17A, IL-17F, IL-22, & CCL22 were significantly associated with baseline psoriasis disease activity (Body Surface Area & Psoriatic Area and Severity Index, Spearman Signed Rank $p<0.05$, $r>0.25$). Baseline CRP, SAA, IL-6, & YKL40 were significantly associated with baseline joint disease (Disease Activity Score 28-CRP, Spearman $p<0.05$, $r>0.25$). Baseline SAA, IL-6, IL-17A, & IL-17F were higher in pts with prior TNF inhibitor exposure than without ($p<0.05$, geometric mean ≥ 40% higher), although pts with PsA both with and without prior TNF inhibitor had higher levels than the healthy control set.

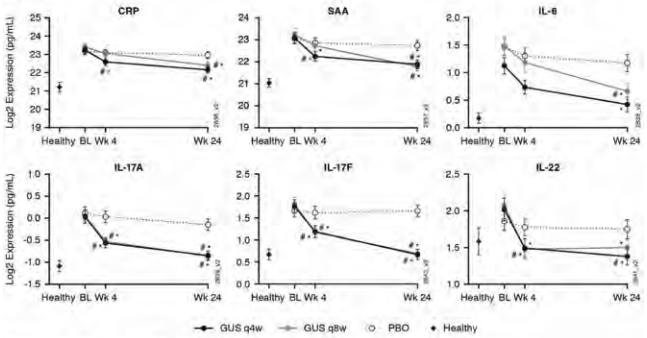
GUS treatment resulted in decreases in serum CRP, SAA, IL-6, IL-17A, IL-17F, & IL-22 that were significantly greater than PBO as early as Week 4 (FIG 1). These protein levels continued to decrease through Wk 24 in GUS-treated pts with both dosing regimens ($p<0.05$, geometric mean decrease from baseline ≥ 33%). Further, Wk 24 IL-17A & IL-17F levels for pts treated with either dose of GUS were not significantly different from healthy controls, suggesting a normalization of peripheral effector cytokines associated with the IL-23/Th17 axis following treatment with GUS. Effects on IL-17A/IL-17F were greater in GUS treated pts than UST treated pts, while CRP levels were similar in both programs (FIG 2).

Conclusion: Comprising a strong pharmacodynamic effect, GUS treatment reduced serum protein levels of acute phase and Th17-effector cytokines (whose elevations at baseline were associated with PsA disease characteristics) and achieved comparable levels to those in healthy controls. In pts with PsA, reductions of IL-17A and IL-17F by GUS were of greater magnitude than those by UST.

References:

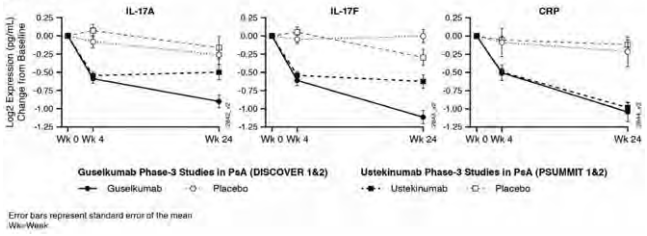
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[2] Mease et al. ACR 2019, abs #L13. Arth Rheumatol. 2019;71 S10:5247
[3] Siebert et al. EULAR 2019, abs #479. Ann Rheum Dis. 2019;78 S2:293
[4] Siebert et al. Arth Rheumatol. 2019;71:1660

FIGURE 1.



* P vs. baseline ≤0.05, |fold difference| ≥1.4
# P vs. placebo ≤0.05, |fold difference| ≥1.4
Error bars represent 2 standard errors of the mean (~95% confidence interval)
BL=Baseline, GUS=Guselkumab, PBO=Placebo, Wk=Week

FIGURE 2.



Error bars represent standard error of the mean
Wk=Week

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OP0230

EFFICACY AND SAFETY OF TILDRAKIZUMAB, A HIGH-AFFINITY ANTI–INTERLEUKIN-23P19 MONOCLONAL ANTIBODY, IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS IN A RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, MULTIPLE-DOSE, PHASE 2B STUDY

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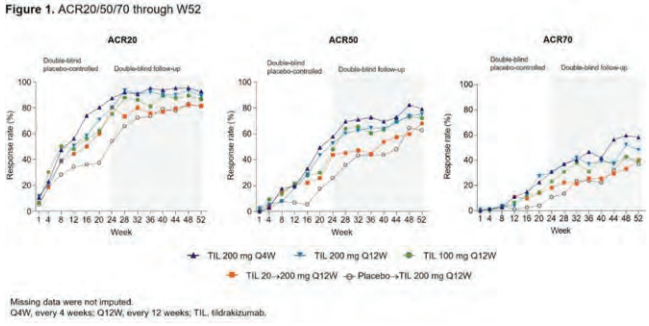
Background: Tildrakizumab (TIL), a high-affinity anti–interleukin-23p19 monoclonal antibody, is approved to treat moderate to severe plaque psoriasis and is under investigation for treatment of psoriatic arthritis (PsA).[1]

Objectives: To evaluate efficacy and safety of TIL up to week (W)52 in a randomised, double-blind, placebo-controlled, multiple-dose, phase 2b study in PsA (NCT02980692).

Methods: Patients (pts) ≥18 years with active PsA[2] were randomised 1:1:1:1:1 to TIL 200 mg every 4 weeks (Q4W) to W52, TIL 200 mg Q12W to W52, TIL 100 mg Q12W to W52, TIL 20 mg Q12W until W24 then TIL 200 mg Q12W to W52, or placebo (PBO) Q4W until W24 then TIL 200 mg Q12W to W52. Efficacy assessments included ACR20/50/70, 75%/90%/100% improvement in Psoriasis Area and Severity Index (PASI), proportion of pts with residual minimal disease activity (MDA) response; and mean change from baseline (BL) in HAQ-DI, Leeds Dactylitis Index (LDI, pts with BL LDI ≥1), and Leeds Enthesitis Index (LEI, pts with BL LEI ≥1) to W52. Treatment-emergent adverse events (TEAEs) were monitored.

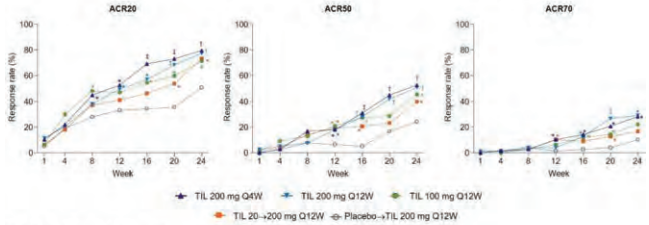
Results: Of 500 pts screened, 391 were randomised and received ≥1 dose of drug. Proportions of ACR20/50/70 responders were superior with TIL vs PBO through W24; after W24 rates of responses further increased for TIL 20→200 mg Q12W and PBO→200 mg Q12W through W52 (Figure 1, 2). Other efficacy results are shown in Table. Overall from BL→W24/W25→W52, 50.4%/39.9% and 2.3%/1.0% of pts experienced a TEAE and serious AE, respectively. From BL→W24, 1 case of pyelonephritis and urinary tract infection was reported in the TIL 100 mg Q12W arm and 1 case of chronic tonsillitis was reported in the TIL 20 mg→200 mg Q12W arm. During W25→W52, 1 malignancy (intraductal proliferative breast lesion) was reported with TIL 20 mg→200 mg Q12W. No deaths or major adverse cardiac events occurred.

Figure 1. ACR20/50/70 through W52



Missing data were not imputed.
Q4W, every 4 weeks; Q12W, every 12 weeks; TIL, tildrakizumab.

Figure 2. ACR20/50/70 through W24



*P <0.05; †P <0.001; ‡P <0.0001 vs PBO.
Missing responses were imputed as nonresponses.
Q4W, every 4 weeks; Q12W, every 12 weeks; TIL, tildrakizumab.

Table. W52 clinical efficacy

	TIL 200 mg Q4W n=78	TIL 200 mg Q12W n=79	TIL 100 mg Q12W n=77	TIL 20→ 200 mg Q12W n=78	PBO→ TIL 200 mg Q12W n=79
HAQ-DI, BL[a]	1.0 ± 0.6	1.0 ±0.6	1.0 ± 0.7	1.1 ± 0.6	1.2 ± 0.6
W52[b]	−0.5 ± 0.5	−0.5 ± 0.6	−0.5 ± 0.6	−0.5 ± 0.5	−0.5 ± 0.5
LEI, BL[a,c]	1.9 ± 2.0	1.5 ± 1.9	2.2 ± 2.1	2.2 ± 2.0	1.5 ± 1.9
W52[b]	−1.3 ± 1.9	−1.0 ± 1.6	−1.7 ± 2.1	−1.2 ± 1.8	−1.2 ± 1.8
LDI, BL[a,d]	32.8 ± 32.9	61.3 ± 73.5	93.8 ± 146.5	71.4 ± 118.5	99.6 ± 170.7
W52[b,d]	−21.4 ± 37.1	−42.1 ± 76.7	−41.6 ± 89.3	−56.5 ± 123.4	−81.5 ± 173.0
BL, W52 median[d]	21.8, 7.4	28.3, 3.2	32.1, 20.0	28.6, 0	34.0, 5.6
MDA[e]	56.9	64.4	45.0	47.1	42.0
PASI 100[e]	54.0	44.4	43.9	47.5	35.0
PASI 90[e]	72.0	80.6	58.5	55.0	50.0
PASI 75[e]	82.0	94.4	82.9	75.0	67.5

[a]BL mean ± SD. [b]Mean change from BL ± SD. [c]Pts with BL LEI ≥1 will be presented at EULAR. [d]Pts with BL LDI ≥1 (n = 27, 21, 21, 19, 25) using nonresponder imputation. [e]% at W52
Missing data not imputed.
SD, standard deviation.

Conclusion: TIL was well tolerated and improved joint and skin manifestations of PsA through W52.

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Disclosure of Interests: Philip J Mease Grant/research support from: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Eli Lilly, Novartis, Pfizer, Sun Pharmaceutical, UCB – grant/research support, Consultant of: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Eli Lilly, Novartis, Pfizer, Sun Pharmaceutical, UCB – consultant, Speakers bureau: Abbott, Amgen, Biogen Idec, BMS, Eli Lilly, Genentech, Janssen, Pfizer, UCB – speakers bureau, Saima Chohan Employee of: Partner/physician at Arizona Arthritis and Rheumatology Associates, Ferran J García Fructuoso Grant/research support from: AbbVie, Eli Lilly, Gedeon Richter, MedImmune, Nichi-Iko, Pfizer, Sanofi-Aventis, Takeda, and UCB, Consultant of: AbbVie, Eli Lilly, Gedeon Richter, MedImmune, Nichi-Iko, Pfizer, Sanofi-Aventis, Takeda, and UCB, Speakers bureau: AbbVie, Eli Lilly, Gedeon Richter, MedImmune, Nichi-Iko, Pfizer, Sanofi-Aventis, Takeda, and UCB, Alice B Gottlieb Grant/research support from:: Research grants, consultation fees, or speaker honoraria for lectures from: Pfizer, AbbVie, BMS, Lilly, MSD, Novartis, Roche, Sanofi, Sandoz, Nordic, Celltrion and UCB., Consultant of:: Research grants, consultation fees, or speaker honoraria for lectures from: Pfizer, AbbVie, BMS, Lilly, MSD, Novartis, Roche, Sanofi, Sandoz, Nordic, Celltrion and UCB., Speakers bureau:: Research grants, consultation fees, or speaker honoraria for lectures from: Pfizer, AbbVie, BMS, Lilly, MSD, Novartis, Roche, Sanofi, Sandoz, Nordic, Celltrion and UCB., Michael E Luggen Grant/research support from: AbbVie; Amgen; Eli Lilly; Genentech; Nichi-Iko; Novartis; Pfizer; R-Pharm; and Sun Pharmaceutical Industries, Inc., Consultant of: AbbVie; Amgen; Eli Lilly; Genentech; Nichi-Iko; Novartis; Pfizer; R-Pharm; and Sun Pharmaceutical Industries, Inc., Speakers bureau: AbbVie; Amgen; Eli Lilly; Genentech; Nichi-Iko; Novartis; Pfizer; R-Pharm; and Sun Pharmaceutical Industries, Inc., Proton Rahman Grant/research support from: Janssen and Novartis, Consultant of: Abbott, AbbVie, Amgen, BMS, Celgene, Lilly, Janssen, Novartis, and Pfizer., Speakers bureau: Abbott, AbbVie, Amgen, BMS, Celgene, Lilly, Janssen, Novartis, Pfizer, Siba P Raychaudhuri Grant/research support from: AbbVie; Janssen; Novartis, Pfizer; Sun Pharmaceutical Industries, Inc, Consultant of: Amgen; Eli Lilly; Janssen; Novartis and Pfizer, Richard C Chou Consultant of: Sun Pharmaceutical Industries, Inc, Alan M Mendelsohn Shareholder of: Johnson and Johnson, Employee of: Sun Pharmaceutical Industries, Inc, Stephen Rozzo Employee of: Sun Pharmaceutical Industries, Inc, Ana-Maria Orbai Grant/research support from: Abbvie, Eli Lilly and Company, Celgene, Novartis, Janssen, Horizon, Consultant of: Eli Lilly; Janssen; Novartis; Pfizer; UCB. Ana-Maria Orbai was a private consultant or advisor for Sun Pharmaceutical Industries, Inc, not in her capacity as a Johns Hopkins faculty member and was not compensated for this service.
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Rheumatoid arthritis - non biologic treatment and small molecules

OP0231

COMPARATIVE EFFECTIVENESS OF JAK-INHIBITORS, TNF-INHIBITORS, ABATACEPT AND IL-6 INHIBITORS IN AN INTERNATIONAL COLLABORATION OF REGISTERS OF RHEUMATOID ARTHRITIS PATIENTS (THE "JAK-POT" STUDY)

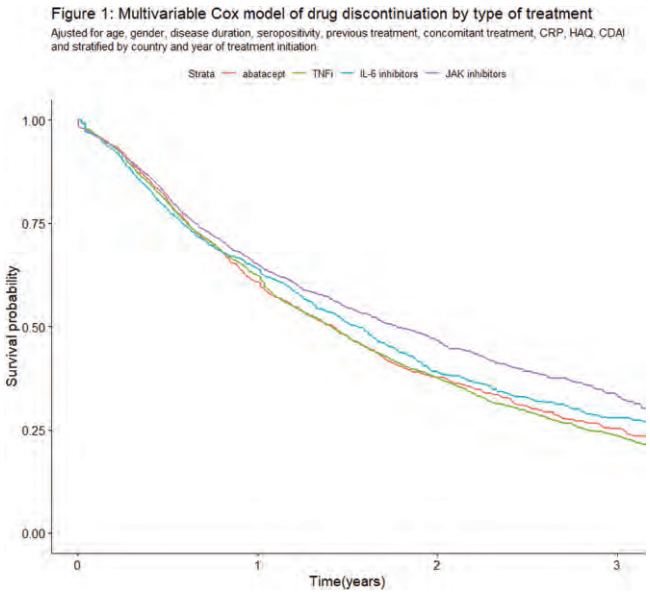
K. Lauper[1], D. Mongin[1], S. A. Bergstra[2], D. Choquette[3], C. Codreanu[4], D. De Cock[5], L. Dreyer[6], O. Elkayam[7], K. Hyrich[8], F. Iannone[9], N. Inanc[10], E. Kristianslund[11], T. K. Kvien[11], B. Leeb[12], G. Lukina[13], D. Nordström[14], K. Pavelka[15], M. Pombo-Suarez[16], Z. Rotar[17], M. J. Santos[18], A. Strangfeld[19], D. Courvoisier[1], A. Finckh[1]. *[1]HUG, Geneva, Switzerland; [2]LUMC, Rheumatology, Leiden, Netherlands; [3]Institut de Recherche en Rhumatologie, Montréal, Canada; [4]Center of Rheumatic Diseases, Bucharest, Romania; [5]KU Leuven, Skeletal Biology and Engineering Research Unit, Leuven, Belgium; [6]Aalborg University Hospital, DANBIO, Aalborg, Denmark; [7]Tel Aviv University, Rheumatology,Tel Aviv, Israel; [8]University of Manchester, Centre for Epidemiology Versus Arthritis, Manchester, United Kingdom; [9]University Hospital of Bari, GISEA, Bari, Italy; [10]Marmara University, Rheumatology, Istanbul,Turkey; [11]Diakonhjemmet Hospital, Rheumatology, Oslo, Norway; [12]State Hospital Stockerau, Rheumatology, Stockerau, Austria; [13]V.A.Nasonova Research Institute of Rheumatology, Moscow, Russian Federation; [14]Helsinki University, ROB-FIN, Helsinki, Finland; [15]Institute of Rheumatology, Prague, Czech Republic; [16]Hospital Clinico Universitario, Rheumatology, Santiago de Compostela, Spain; [17]biorx.si, Rheumatology, Ljubljana, Slovenia; [18]Faculdade de Medicina, Reuma.pt, Lisboa, Portugal; [19]DRFZ, Programme Area Epidemiology, Berlin, Germany*

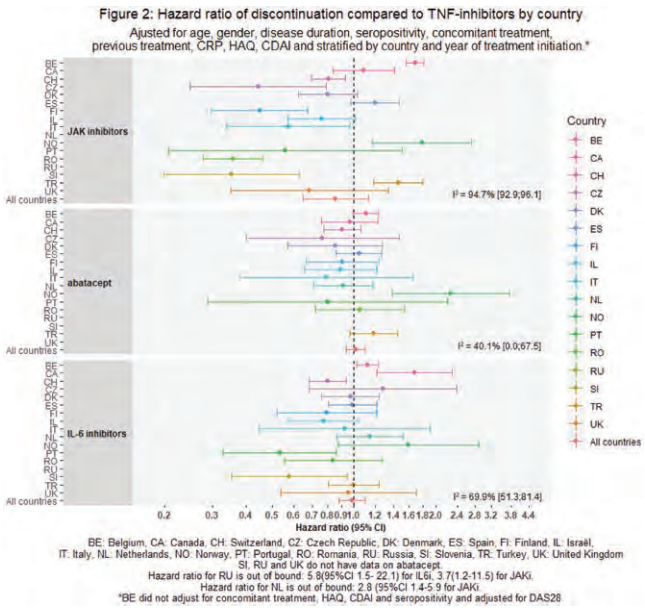
Background: In many countries, JAK-inhibitors (JAKi) have only recently been approved as treatment for patients with rheumatoid arthritis (RA).
Objectives: To evaluate the effectiveness of JAKi compared to bDMARDs in RA patients in the real-world population in an international collaboration of registers (the "JAK-pot" collaboration).
Methods: Patients initiating either JAKi, TNFi, IL-6i or abatacept (ABA) during a time period when JAKi were available in each country (19 registers, Table) were included. We compared the effectiveness of JAKi and bDMARDs in terms of retention using crude and adjusted survival analysis. Missing covariates were imputed using multiple imputation.
Results: Among 25521 included patients, 6063 initiated a JAKi, 13879 a TNFi, 2348 ABA, and 3231 an IL-6i. Patients were on average 55 years old, with a mean disease duration 10 years, mostly seropositive (67%), female (77%) and with moderate disease activity at treatment initiation. The main reason of stopping treatment was ineffectiveness (49%), followed by adverse events (21%). Patients on JAKi were treated more often as monotherapy, had higher CRP and disease activity at baseline and had experienced more previous ts/bDMARDs. Crude median retention was 1.4 (95% CI 1.2-1.5) years for JAKi, 1.6 (1.6-1.7) for TNFi, 1.5 (1.3-1.7) for IL6i and 1.1 (1.0-1.3) for ABA. After adjustment, the hazard ratio (HR) for discontinuation tended to be lower for JAKi (HR 0.86 (0.65-1.13)) compared to TNFi, but comparable for ABA (1.02 (0.94-1.10)) and IL6i (0.99 (0.88-1.10)) (Figure 1). HRs differed notably between countries (Figure 2).

Table 1. Registers

Country, register	N	JAKi, n (%)
Austria, BIOREG*		
Belgium, TARDIS	6288	2113 (33.6)
Canada, RHUMADATA	528	114 (21.6)
Czech Republic, ATTRA	374	253 (67.6)
Denmark, DANBIO	4721	506 (10.7)
Finland, ROB-FIN	807	234 (29.0)
Germany, RABBIT*		
Italy, GISEA	757	250 (33.0)
Israel, I-RECORD	400	94 (23.5)
Netherlands, METEOR	1642	4 (0.2)
Norway, NOR-DMARD	507	99 (19.5)
Portugal, REUMA.PT	797	44 (5.5)
Romania, RRBR	593	328 (55.3)
Russia, ARBITER	526	483 (91.8)
Slovenia, BIORX.SI	583	146 (25.0)
Spain, BIOBADASER	781	139 (17.8)
Switzerland, SCQM	2956	796 (26.9)
Turkey, TURKBIO	2150	397 (18.5)
UK, BSRBR	1111	63 (5.7)

*Registers planning to participate in future studies but not included yet





Conclusion: The adjusted overall drug retention of JAKi tended to be higher than for TNFi, with large variation between countries. Other measures of effectiveness, such as the evaluation of CDAI remission and low disease activity are planned to shape a more comprehensive picture of JAKi effectiveness in the real world.

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OP0232

TREATMENT WITH METHOTREXATE AND RISK OF LUNG DISEASE IN PATIENTS WITH RHEUMATOID ARTHRITIS: A NATIONWIDE POPULATION-BASED COHORT STUDY FROM DENMARK

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Background: Methotrexate (MTX) is the recommended first-line drug in EULAR and ACR treatment guidelines for rheumatoid arthritis (RA) and hence the most commonly prescribed DMARD in the treatment of this group of patients. However, lung disease is considered a potential adverse effect of MTX treatment.

Objectives: To investigate the risk of interstitial lung disease (ILD) and acute and chronic respiratory failure in RA patients treated with MTX and other medications.

Methods: From the Danish National Patient Register (DNPR) and the clinical DANBIO Register for rheumatic diseases, we retrieved data on RA patients registered between 1997 and 2015. Information on ILD and respiratory failure outcomes was obtained from DNPR, and information on redeemed prescriptions for MTX and other medications was obtained through linkage to the Danish Prescription Register. Associations between MTX and lung disease outcomes were analyzed in Cox regression models adjusted for age, calendar time, sex and use of other medications possessing the potential for pulmonary toxicity. Standardized Incidence Ratios (SIRs) of lung disease were calculated to compare RA patients to the general population.

Results: Of the 30,512 RA patients identified, 60% patients had redeemed at least one prescription for MTX, 35% had redeemed a prescription for sulphasalazine, 6% had redeemed a prescription of either amiodarone or

Table. Hazard ratios (HR) with 95% confidence intervals (95%CI) for the risk of interstitial lung disease (ILD) and acute or chronic respiratory failure in 30,512 patients with rheumatoid arthritis up to 5 years after diagnosis.

ILD (incl. drug-induced cases)	1 year of follow up		5 years of follow up	
	Events, N	HR (95% CI)	Events, N	HR (95% CI)
Methotrexate, ≥1 redeemed prescription(s) vs. none	62	1.03 (0.71 to 1.48)	166	1.00 (0.78 to 1.27)
Sulphasalazine, ≥1 redeemed prescription(s) vs. none	21	0.88 (0.54 to 1.43)	90	1.14 (0.89 to 1.48)
Amiodarone and/or nitrofurantoin, ≥1 redeemed prescription(s) vs. none	1	0.57 (0.08 to 4.10)	7	0.65 (0.31 to 1.38
Women	72	Ref.	155	Ref.
Men	55	1.51 (1.06 to 2.16)	130	1.74 (1.38 to 2.21)
Acute or chronic respiratory failure	**1-year of follow up**		**5-years of follow up**	
	Events, N	**HR (95% CI)**	**Events, N**	**HR (95% CI)**
Methotrexate, ≥1 redeemed prescription(s) vs. none	36	0.48 (0.32 to 0.73)	158	0.54 (0.43 to 0.67)
Sulphasalazine, ≥1 redeemed prescription(s) vs. none	14	0.70 (0.39 to 1.26)	99	1.09 (0.86 to 1.38)
Amiodarone and/or nitrofurantoin, ≥1 redeemed prescription(s) vs. none	6	3.01 (1.31 to 6.94)	22	1.33 (0.86 to 2.06)
Women	71	Ref.	239	Ref.
Men	38	1.07 (0.72 to 1.59)	120	1.04 (0.83 to 1.29)

nitrofurantoin, and 27% had not received any of the included drugs at the end of the 5-year follow-up for ILD and respiratory failure. MTX treatment was not associated with an increased risk of lung disease (≥1 redeemed prescription(s) compared to no prescriptions), HR 1.00 (95% CI 0.78 to 1.27) for ILD and 0.54 (95%CI 0.43 to 0.67) for respiratory failure at 5-year follow-up (Table). The SIR was 3-4 times increased for ILD in MTX-treated RA patients, but this was no different from the RA population in general compared to the background population.

Conclusion: RA patients had an increased risk of ILD compared to the general population, but that risk was not further increased in patients treated with MTX compared to non-MTX treated.

Disclosure of Interests: None declared

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OP0233 EFFICACY, SAFETY, AND PHARMACODYNAMIC EFFECTS OF THE BRUTON'S TYROSINE KINASE INHIBITOR, FENEBRUTINIB (GDC-0853), IN MODERATE TO SEVERE SYSTEMIC LUPUS ERYTHEMATOSUS IN A PHASE 2 CONTROLLED STUDY

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Background: Fenebrutinib (GDC-0853, FEN) is an oral, non-covalent, and selective inhibitor of Bruton's tyrosine kinase (BTK) in clinical development for autoimmune diseases.

Objectives: This was a randomized, placebo-controlled, multi-center study to evaluate the efficacy, safety, and pharmacodynamic effects of FEN in patients with moderate-to-severe systemic lupus erythematosus (SLE) activity.

Methods: Patients who met SLICC or revised ACR SLE criteria, had ≥1 serologic marker of SLE, SLEDAI ≥8, and were on ≥1 standard of care (SOC) therapy were included; patients with renal or CNS involvement, or exposure to B cell depleting or calcineurin inhibitor therapy were excluded. Patients were randomized to placebo (PBO), FEN 150 mg QD, or FEN 200 mg BID, for 48 weeks. A corticosteroid taper was recommended, with burst and taper permitted from Week 0 (W0) to W12 and W24 to W36. The primary endpoint was SRI-4 at W48. Post hoc subgroup analyses were conducted based on patient baseline disease characteristics.

Results: This study enrolled 260 patients, with the majority recruited in Latin America, USA, and Western Europe. At W48, the SRI-4 response rates for FEN 150 mg QD and FEN 200 mg BID were 51% (95% CI: -8.5, 21.2; p value 0.37) and 52% (95% CI: -7.3, 22.4; p value 0.34), respectively, compared to 44% for PBO (Table 1). Post-hoc analysis showed larger responses in subgroups of patients with higher baseline disease activity (Table 1). Safety results were similar between FEN and PBO arms, although more serious adverse events were observed in the FEN 200 mg BID arm. Study discontinuations were balanced across the 3 arms (24-26%). FEN treatment significantly reduced levels of CD19+ B cells, anti-dsDNA autoantibodies, IgG, and a BTK-dependent RNA signature highly expressed in plasmablasts by W48 compared to PBO; C4 levels modestly improved with FEN vs. PBO (Table 2).

Table 1. SRI-4 Response (%) at W48 in Primary Analysis and in Post-hoc Patient Subgroups

	PBO	FEN 150 mg QD	FEN 200 mg BID
SRI-4 Response (%) at W48	**44**	**51**	**52**
	n=84	*n*=87	*n*=88
SRI-4 Response (%) in Baseline Subgroups			
At least 1 BILAG A	**48**	**54**	**59**
	n=42	*n*=39	*n*=46
At least 1 BILAG A and SLEDAI increased DNA binding	**37**	**53**	**65**
	n=19	*n*=17	*n*=26
SLEDAI arthritis with at least 4 swollen joints	**39**	**50**	**57**
	n=57	*n*=54	*n*=54
SLEDAI arthritis with at least 4 tender joints	**39**	**53**	**59**
	n=71	*n*=70	*n*=69
CLASI >=10	**21**	**36**	**31**
	n=14	*n*=11	*n*=16

Table 2. Key Biomarker Results

	PBO	FEN 150 mg QD	FEN 200 mg BID
Median (%) Change from Baseline at W48			
Plasmablast signature	**-19.7%**	**-54.3%***	**-51.7%***
	n=52	*n*=53	*n*=57
$CD19^+$ B cells (cells/µl)	**-0.50**	**-57.0***	**-57.5***
	n=38	*n*=49	*n*=48
Anti-dsDNA# (IU/ml)	**+6.9**	**-38.3***	**-75.7***
	n=31	*n*=36	*n*=33
Total IgG (g/L)	**-0.20**	**-1.25***	**-1.56***
	n=65	*n*=64	*n*=64
C3 (g/L)	**-0.02**	**+0.01**	**-0.01**
	n=65	*n*=67	*n*=66
C4 (g/L)	**0.00**	**+0.02***	**+0.01***
	n=65	*n*=67	*n*=66

#Patients who were positive at baseline (>30 IU/mL)

*Denotes significant vs. PBO; Kruskal-Wallis false-discovery rate controlled two sided (*p*-value ≤0.05)

Conclusion: The primary endpoint of SRI-4 for FEN was not met despite evidence of strong BTK target and pathway inhibition. FEN had an acceptable safety profile. Several disease activity subgroups were suggestive of a greater treatment effect on SRI-4 compared to PBO

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OP0234 MBS2320, A NOVEL SELECTIVE MODULATOR OF IMMUNE METABOLISM, IN PATIENTS WITH SEVERE RHEUMATOID ARTHRITIS: SAFETY, TOLERABILITY AND EFFICACY RESULTS OF A PHASE 2 STUDY

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Background: Despite the availability of several treatment options for Rheumatoid Arthritis (RA), many patients are classed as 'non-responders' who show little or no improvement. Hence, there remains a need for new therapies with a differentiated mechanism of action, to be used alone or in combination. MBS2320 is a selective modulator of immune metabolism displaying distinctive dual pharmacology: strong anti-inflammatory activity as well as a broader spectrum of osteoprotection than TNFα inhibition in preclinical models[1].

Objectives: To evaluate the safety, tolerability and efficacy of MBS2320 in patients receiving a stable dose of methotrexate (MTX).

Methods: Patients with active RA on a stable dose of MTX were randomised 2:1 to receive MBS2320 (80mg) or matching placebo once daily for 4 weeks. Subject to a satisfactory safety and tolerability assessment, patients were escalated to a dose of 120 mg qd or remained on 80 mg qd for a further 8 weeks. Safety, efficacy, pharmacokinetics and pharmacodynamics were evaluated.

Results: 121 patients were randomised (Safety analysis set) to MBS2320 or matching placebo and 96 completed the study. Sixteen subjects were excluded from the efficacy analysis set due to evidence of poor compliance or absence of efficacy evaluations. Enrolled patients were mostly female (86.8%), white and with a mean (range) age at baseline (BL) of 52 (19-69) years.

The study population had hard-to-treat, severe, active and erosive disease as indicated by high BL DAS28-CRP and DAS28-ESR, low Week-12 placebo ACR50 and DAS28-CRP responder rates (2.5% and 5% respectively) and a low ratio of synovitis-to-erosion volume despite treatment with DMARD(s).

There were no serious treatment emergent adverse events (TEAEs). 15 patients (19%) randomised to MBS2320 withdrew due to TEAEs, predominantly of nausea. TEAEs were typically reported soon after dosing, were mostly mild in severity and resolved without treatment. Onset of TEAEs reduced as the study proceeded.

Gastrointestinal disorders were the most frequently reported TEAEs (all causalities) with a higher incidence in patients receiving MBS2320 (68.8%) than placebo (14.6%). Nausea was most frequently reported during Week 1 (27.3% patients). Asthenia and/or fatigue was reported more frequently in the MBS2320 treatment group (23.8% patients) than with placebo (7.3% patients), with the majority being considered related to study drug. Infections were more frequently reported by patients receiving placebo (22.0%) than those receiving MBS2320 (12.5%). There were no clinically relevant treatment-related trends in the biochemistry, haematology, urinalysis, vital signs or ECG data.

Higher ACR20 response rates were observed in patients receiving MBS2320 versus those receiving placebo at all time points and increased with time. At Week 12, ACR50 response rates with MBS2320 treatment were increased by >4-fold compared with placebo (11.6% vs 2.5%). Greater mean reductions from baseline in DAS28-CRP were also observed in patients receiving MBS2320 versus those receiving placebo at Week 12 (-18.6% vs -8.4%). DAS28-CRP responder rates were more than doubled with MBS2320 treatment compared to placebo (5% vs 14%). These changes were mirrored by improvements in tender joint counts, reduced hsCRP and improvements in Patient Reported Outcomes of pain VAS, Patients' and Clinicians' Global Assessments of Disease Activity and Patients' Global Impression of Change.

Conclusion: MBS2320 was generally well tolerated for up to 12 weeks in this RA study population. Nausea was the most common TEAE, was generally mild in severity and resolved without treatment. In this population of patients with hard-to-treat, severe, active, erosive disease MBS2320 showed evidence of a clinical benefit on both ACR20 responses and DAS28-CRP.

References:

[1] Patel et al, Ann Rheum Dis, 78, S2, 2019, A228

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Disclosure of Interests: Lisa Patel Shareholder of: Istesso Ltd, Employee of: Istesso Ltd, Laurence Skillern Consultant of: Istesso Ltd, Martyn Foster Shareholder of: Istesso Ltd, Consultant of: Istesso Ltd, Andy Gray Shareholder of: Istesso Ltd, Consultant of: Istesso Ltd, Richard Leff Consultant of: Istesso Ltd, Sam Williams Shareholder of: Istesso Ltd, Employee of: Istesso Ltd

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OP0235 ACHIEVING A LOW DAS IN THE FIRST 4-MONTHS AFTER DIAGNOSIS IS IMPORTANT FOR THE LONG-TERM CHANCE OF ACHIEVING DMARD-FREE REMISSION

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Background: Sustained DMARD-free remission (SDFR) is increasingly achievable in RA. The pathogenesis underlying SDFR-development is unknown and patient-characteristics at diagnosis poorly explain whether SDFR will be achieved. This limits substantiated decisions to discontinue DMARD-treatment in clinical practice.

Objectives: To increase the understanding of SDFR, we studied the course of disease activity scores (DAS) over time in relation to SDFR-development. Subsequently, we explored whether DAS-time course could be helpful to identify patients likely to achieve SDFR.

Methods: 761 RA-patients consecutively included in the Leiden Early Arthritis Clinic, treated with initial methotrexate and treat-to-target treatment, were studied (median follow-up 7 years). The course of DAS was compared between patients achieving SDFR within 7 years and those who did not, using linear mixed models, stratified for ACPA. Subsequently, the relation between DAS at 4 months and the probability of achieving SDFR within 7 years was studied with logistic regression. Kaplan-Meier curves were constructed to illustrate cumulative incidence of SDFR for different DAS categories at 4 months, respectively <1.6, 1.6-2.4, 2.4-3.6, >3.6.

Results: Patients achieving SDFR were characterized by a remarkedly different DAS response within 4 months after diagnosis. Compared to patients who did not achieve SDFR, the SDFR-group showed a prominently stronger decline in DAS between baseline and 4 months; 1.59 units decline (95%CI,1.24-1.95) versus 0.96 units (95%CI, 0.85-1.07) decline (p<0.001) (figure 1). Stratification for ACPA yielded a similar and statistically significant effect in ACPA-negative RA. In ACPA-positive RA this effect was absent. Subsequently, the probability of achieving SDFR during 7 years was studied in ACPA-negative RA and it was observed to be lower for patients with higher DAS at 4 months. After 7 years of disease, the cumulative incidence for SDFR in ACPA-negative patients with DAS<1.6 at 4 months was high (71.0%), whilst SDFR was rare among those with DAS>3.6 at 4 months (7.1%) (figure 2).

Conclusion: In RA-patients treated according to current guidelines, SDFR is predominantly achieved in patients with a strong decline in DAS during the first four months after diagnosis. Especially in ACPA-negative RA, the DAS at 4-months can be useful for later decisions to stop DMARDs.

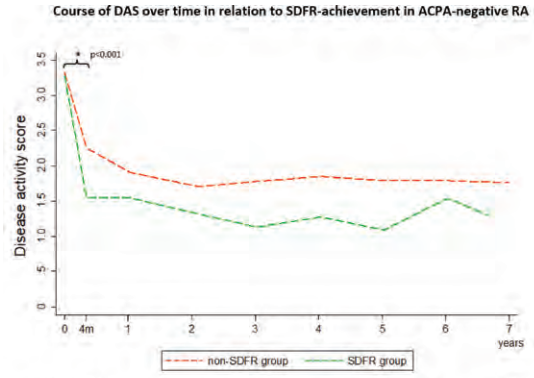


Figure 1. Course of disease activity scores over time in relation to SDFR-achievement in 7 years of follow-up in ACPA-negative RA. Course of disease activity scores (DAS) over time between ACPA-negative patients achieving SDFR (SDFR group) and those not achieving SDFR (non-SDFR group). * indicates significant stronger decline in DAS in SDFR-group. ACPA: anti-citrullinated protein antibodies, SDFR: sustained DMARD-free remission.

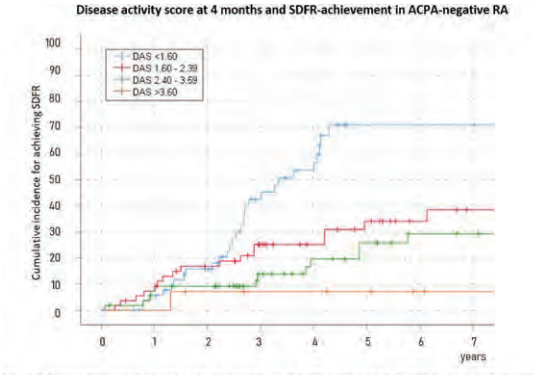


Figure 2. Kaplan-Meier analysis demonstrating incidence of SDFR-achievement for DAS levels after 4 months in ACPA-negative RA. Cumulative incidence demonstrated using Kaplan-Meier curves to visualize differences in SDFR-achievement for patients achieving lower DAS 4 months after diagnosis. SDFR: sustained DMARD-free remission.

Disclosure of Interests: None declared

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OP0236 RELEVANCE OF BIASED PAR2 INHIBITORS IN REDUCING INFLAMMATION AND CARTILAGE DEGRADATION IN IN VITRO AND IN VIVO MODELS OF RHEUMATOID ARTHRITIS

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Background: Protease-activated receptor-2 (PAR2) is a member of a family of G-protein-coupled receptors involved in multiple physiological mechanisms. Compelling evidences have unravelled the key roles of PAR2 in the pathology of both rheumatoid arthritis (RA) and osteoarthritis (OA)[1]. Indeed, in vitro, in vivo and ex vivo experiments showed that this receptor promotes inflammation, cartilage erosion (and subsequent bone degradation), and pain. However, the signalling pathways involved in these functions are not well understood[2]. This is of importance as some pathways can promote the pathogenesis[3] while others prevent it[4]. We developed a new series of small molecules as novel biased PAR2 inhibitors to treat rheumatic diseases.

Objectives: To evaluate the efficacy and mechanism of action of new biased PAR2 inhibitors on cartilage erosion and inflammation.

Methods: The potency of compounds to inhibit human PAR2 signalling was evaluated in vitro by FLIPR calcium assay in HEK293 cells. The same assay was used to determine their selectivity over human PAR1 and PAR4 as well as murine versions of PAR2. The effect of several PAR2 inhibitors on 9 signalling pathways (Gi2, GoB, Gz, Gq, G13, G14, G15, B arrestin 2, EPAC) was evaluated by the BRET-based bioSens-All™ technology. In vitro anti-hypertrophic effect was determined by measuring the mRNA level of type II collagen, aggrecan

and MMP13 in rat chondrocytes after IL1β stimulation. In vitro anti-inflammatory effect was determined by measuring the secretion of IL6, IL8, IL1β, TNFα and IFNγ by human monocytes. In vivo, the pharmacodynamic of our small molecules was assessed after intravenous and oral administration. Therapeutic efficacy of a compound was then evaluated in a collagen-induced arthritis model in DBA1/J mice. In this model, measures of the arthritis index score, body weight, plasma level of TNFα, IL6, IL8 and IL1β and histological evaluation of cartilage erosion were performed.

Results: Our new series of small molecules are potent PAR2 inhibitors (IC50<1nM in calcium assay) with some selectivity over PAR1 and PAR4. Our compounds significantly inhibited PAR2 mediated recruitment of Gz, Gq, G13, G14 and G15. However, surprisingly, these small molecules had no effect on B arrestin 2, EPAC, Gi2 and GoB demonstrating that they are biased inhibitors. The effect of our compounds on PAR2 signalling was clearly different from 3 already existing PAR2 inhibitors described in the literature (I-117, AZ3451 and P2pal-18s). We compared the in vitro anti-hypertrophic effect on chondrocyte and anti-inflammatory effect on monocytes of these compounds to determine the importance of PAR2 signalling pathways in these cellular functions. In vivo, our small molecules had good bioavailability after oral administration of 10mg/kg in mice (clearance = 0.038L/h/kg; T½ = 9.9h; AUC= 162564 ng.h/mL; Cmax = 9005 ng/mL). The in vivo therapeutic efficacy of a biased PAR2 inhibitor in a model of collagen-induced arthritis will be presented.

Conclusion: Our results show the potency of biased PAR2 inhibitors to reduce both the inflammation and cartilage erosion in rheumatoid arthritis. They confirm the huge potential of PAR2 as a therapeutic target and unravel the relevance of biased antagonism of this receptor to treat rheumatic diseases.

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Disclosure of Interests: Thibaut Brugat Employee of: Domain Therapeutics, Baptiste Rugeri Employee of: Domain Therapeutics, Gaël Hommet Employee of: Domain Therapeutics, Alexia Dumont Employee of: Domain Therapeutics, Luc Baron Employee of: Domain Therapeutics, Célia Halter Employee of: Domain Therapeutics, Meriem Sémache Employee of: Domain Therapeutics, Arturo Mancini Employee of: Domain Therapeutics, Camille Amalric Employee of: Domain Therapeutics, Marie Giambelluco Employee of: Domain Therapeutics, Nathalie Lenne Employee of: Domain Therapeutics, Marjorie Sidhoum Employee of: Domain Therapeutics, Christel Franchet Employee of: Domain Therapeutics, Stanislas Mayer Employee of: Domain Therapeutics, Xavier Leroy Employee of: Domain Therapeutics, Stephan Schann Employee of: Domain Therapeutics

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OP0237 THROMBOEMBOLIC SAFETY PROFILE OF TOFACITINIB AND BARICITINIB: AN ANALYSIS OF WHO VIGIBASE

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Background: The Janus Kinase (JAK) inhibitors tofacitinib and baricitinib are new targeted treatments for rheumatoid arthritis. Recent concerns regarding the risk of thrombosis have led to warnings by the European Medicines Agency (EMA) and the Food and Drug Administration (FDA)[1,2].

Objectives: To examine the safety reporting of tofacitinib and baricitinib, with focus on thromboembolic events.

Methods: Individual case safety reports (ICSRs) for tofacitinib and baricitinib were retrieved from the World Health Organization (WHO) global database (VigiBase) in April 2019. The primary outcomes were deep vein thrombosis (DVT) and pulmonary thrombosis (PT) or pulmonary embolism (PE). A disproportionality analysis was conducted by estimating the reporting odds ratio (ROR) and 95% confidence intervals (CIs) to compare the observed versus expected reporting ratio of DVT or PT|PE for tofacitinib or baricitinib. The ROR were calculated worldwide and stratifying by reporting from Europe or the US. In a secondary analysis, further thrombotic-related outcomes were investigated.

Results: In both tofacitinib (n=40,017) and baricitinib (n=2,138) ICSRs, patients with reported DVT or PT|PE were older and had higher reporting of pro-thrombotic medications (e.g., contraceptives) or indicators of thromboembolic risk (i.e., antithrombotic treatment). The use of tofacitinib was associated with a significant increased reporting for DVT (ROR: 2.37 95% CI 1.23-4.56) and PT|PE (ROR 2.38 95% CI 1.45-3.89) in Europe. In the US, tofacitinib was only associated with an elevated reporting of PT (ROR: 2.05 % CI 1.45-2.90). Baricitinib was associated with a 3-fold increased risk of reporting for DVT (ROR: 3.47 95% CI 2.18-5.52) or PT|PE (ROR: 3.44 95% CI 2.43-4.88) in Europe, which accounted for 97% of all baricitinib ICSRs. Secondary thrombotic-related outcomes were poorly reported overall in VigiBase.

Conclusion: This study supports the cautious use of JAK inhibitors in patients with rheumatoid arthritis who have a high thrombotic risk profile. Moreover, a potential class effect of JAK inhibitors cannot be ruled out.

References:

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Acknowledgments: We are thankful to every pharmacovigilance centre and contributor to the WHO Programme for International Drug Monitoring and VigiBase.

While the authors used data from the VigiBase, the WHO global database of ICSRs as a source of information, the conclusions do not represent the opinion of the Uppsala Monitoring Centre (UMC) or the WHO.

Disclosure of Interests: Enriqueta Vallejo-Yagüe Employee of: Synovo GmbH 2012-2018 (not related to this abstract), Stefan Weiler Consultant of: Gedeon-Richter for drug safety 2017 (not related to this abstract), Andrea Michelle Burden: None declared

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OP0238 RISK OF HERPES ZOSTER IN PATIENTS WITH RHEUMATOID ARTHRITIS UNDER BIOLOGICAL, TARGETED SYNTHETIC, AND CONVENTIONAL SYNTHETIC DMARD TREATMENT

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Background: The risk of herpes zoster (HZ) is higher in patients with rheumatoid arthritis (RA) than in the general population. This risk is further increased with biologic disease-modifying anti-rheumatic drugs (bDMARDs) such as tumour necrosis factor inhibitors (TNFi) and targeted synthetic (ts)DMARDs such as Janus kinase inhibitors (JAKi) compared to patients taking conventional synthetic (cs)DMARDs such as methotrexate (MTX).

Objectives: To compare incidence rates of HZ in RA patients under treatment with bDMARDs, tsDMARDs and csDMARDs with different modes of action and to find potential risk factors.

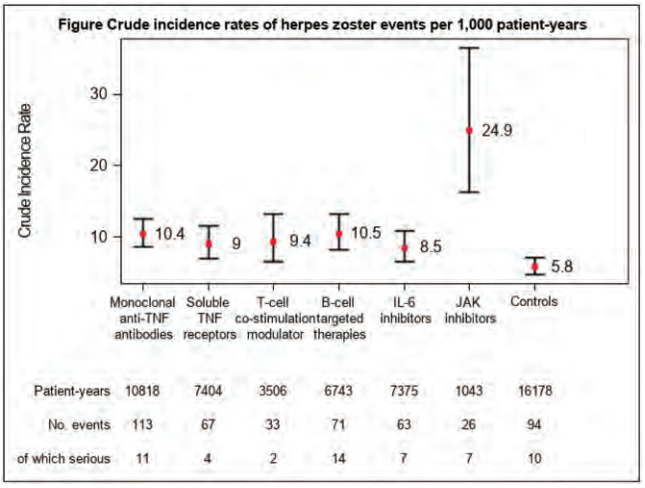
Methods: Data of patients enrolled in the German biologics register RABBIT from 2007 onwards with the start of a bDMARD, tsDMARD or a change in csDMARD treatment were analysed. Patients were included when at least one follow-up documentation was available. All HZ events reported until 30 April 2019 were identified and assigned to treatments administered within the 3 month period prior to the HZ event. Crude incidence rates (IR) of HZ were calculated per 1,000 patient years (py). Cox regression was applied to investigate risk factors for the occurrence of HZ with and without inverse probability weights (IPW) to adjust for confounding by indication.

Results: Data of 12,470 patients (53,218 py of observation) were included in the analysis. A total of 452 HZ cases in 433 patients were reported, of which 52 events were serious. The crude IRs per 1,000 py are illustrated by Figure. Adjusted for age, sex, and glucocorticoid use, a significantly increased risk was observed for treatment with monoclonal TNF antibodies (hazard ratio [HR], 1.55 [95% CI, 1.21-2.00]), B-cell targeted therapies (HR, 1.45 [95% CI, 1.07-1.97]), and tsDMARDs (HR, 3.55 [95% CI, 2.33-5.41]). Treatment with soluble TNF receptors, T-cell co-stimulation modulator, and IL-6 inhibitors were not significantly associated (Table). Adjustment with IPW amplified the effect and treatment with T-cell co-stimulation modulator and IL-6 inhibitors were also significantly associated with a higher risk compared to csDMARD treatment (Table).

Conclusion: This is the first analysis in a European prospective cohort study comparing the incidence rates and risk of HZ in RA patients under treatment with six different modes of action within one cohort to csDMARD treatment. We found a significant association between HZ and treatment with JAKi. Our results also confirm a higher risk for monoclonal TNF antibodies and show a similar result for the T-cell co-stimulation modulator and B-cell targeted therapies. This study clearly supports systematic HZ vaccination of RA patients.

Table. Risk of herpes zoster: Results of adjusted regression analyses with and without inverse probability weights

	Multivariate Analysis without IPW		Multivariate Analysis with IPW	
	Adjusted HR (95% CI)	P Value	Adjusted HR (95% CI)	P Value
Female sex	1.42 (1.12-1.82)	**0.0042**	1.21 (0.96-1.53)	0.1095
Age per 10 years	1.23 (1.13-1.33)	**<.0001**	1.31 (1.2-1.43)	**<.0001**
Glucocorticoids, 5-10 vs 0 mg/d	1.16 (0.95-1.41)	0.1577	1.23 (1-1.52)	0.0501
Glucocorticoids, >10 vs 0 mg/d	1.58 (1.02-2.46)	**0.0417**	1.92 (1.27-2.92)	**0.0022**
csDMARD treatment	*Reference*		*Reference*	
Monoclonal TNFi antibodies	1.55 (1.20-2.00)	**0.0009**	1.63 (1.25-2.12)	**0.0003**
Soluble TNF receptors	1.32 (0.98-1.77)	0.0683	1.34 (0.98-1.83)	0.0631
T-cell co-stimulation modulator	1.41 (0.97-2.05)	0.0746	1.69 (1.17-2.45)	**0.0048**
B-cell targeted therapies	1.45 (1.07-1.97)	**0.0156**	1.66 (1.19-2.3)	**0.0026**
IL-6 inhibitors	1.31 (0.97-1.77)	0.0737	1.55 (1.15-2.09)	**0.0045**
JAK inhibitors	3.55 (2.33-5.41)	**<.0001**	5.01 (3.45-7.28)	**<.0001**



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Disclosure of Interests: Anja Strangfeld Speakers bureau: AbbVie, BMS, Pfizer, Roche, Sanofi-Aventis, Imke Redeker: None declared, Jörn Kekow Speakers bureau: BMS, MSD, Pfizer, Roche, Gerd Rüdiger Burmester Consultant of: AbbVie Inc, Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB Pharma, Speakers bureau: AbbVie Inc, Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB Pharma, Juergen Braun Grant/research support from: Abbvie (Abbott), Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, Eli Lilly and Company, Medac, MSD (Schering Plough), Mundipharma, Novartis, Pfizer (Wyeth), Roche, Sanofi- Aventis, and UCB Pharma, Consultant of: Abbvie (Abbott), Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, EBEWE Pharma, Eli Lilly and Company, Medac, MSD (Schering-Plough), Mundipharma, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis, and UCB Pharma, Speakers bureau: Abbvie (Abbott), Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, EBEWE Pharma, Eli Lilly and Company, Medac, MSD (Schering-Plough), Mundipharma, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis, and UCB Pharma, Angela Zink Speakers bureau: AbbVie, Amgen, BMS, Gilead, Hexal, Janssen, Lilly, MSD, Pfizer, Roche, Sanofi Aventis, UCB

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Preclinical models of arthritis and bone disease

OP0239 WHY DOES ALCOHOL INHIBIT ARTHRITIS? - AN EXPLANATION OF THE MECHANISM OF ARTHRITIS INHIBITION BY ETHANOL

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Background: Alcohol consumption has emerged as consistent protective factor for the development of autoimmune diseases such as rheumatoid arthritis (RA). The underlying mechanism for this tolerance-inducing effect of alcohol, however, is unknown.

Objectives: To understand the anti-arthritogenic effect of alcohol

Methods: The immune-regulatory properties of alcohol consumption in vivo were tested in the collagen-induced arthritis (CIA) and serum-induced arthritis (SIA) model as well as after immunization with T cell- dependent (NP-CGG) and independent (TNP-FICOLL) antigens. Additional experiments in vivo experiments in these models were done with acetate- the metabolite of ethanol. The models were analysed for T- cell lineage and plasma cell differentiation, germinal centre formation and IgG levels and sialylation. Molecular expression of T follicular helper cell (TFH) activation such as IL-21, Bcl-6 and PD-1, as well as TFH: B cell conjugates were also assessed. Furthermore, TFH cells were generated in vitro, exposed to ethanol or acetate and tested for IL-21 production, PD1 expression and conjugate formation with B cells.

Results: Ethanol exposure significantly inhibited arthritis in the active adaptive immunity-driven model of arthritis (CIA) but not in the passive innate immunity-driven model (STA) suggesting that the immune suppressive effect of alcohol is based on interference of T- and B- cell activation. In line ethanol and even more its metabolite acetate, suppressed T cell dependent antibody formation after NP-CGG immunization, while T cell independent antibody formation after TNP-FICOLL immunization was not suppressed. Ethanol, as well as its metabolite acetate, specifically altered the functional state of T follicular helper (T_{FH}) cells in vitro and in vivo, thereby exerting immune regulatory and tolerance-inducing properties. Alcohol-exposed mice showed reduced Bcl6 and PD-1 expression as well as interleukin (IL)-21 production by TFH cells, preventing proper spatial organization of TFH cells to form TFH: B cell conjugates in the germinal centre. This effect of alcohol on T_{FH} cells was associated with impaired autoantibody formation, higher sialylation of autoantibodies and less arthritis. In accordance, overexpression of IL-21 in vivo completely reversed the immune regulatory effects of alcohol.

Conclusion: In summary, these data provide a new mechanistic explanation for the immune regulatory and tolerance-inducing effect of alcohol consumption in arthritis.

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OP0240 A MULTIMODAL MASS SPECTROMETRY APPROACH REVEALS SPECIFIC CARTILAGE MOLECULAR PROFILES ASSOCIATED TO TYPE 2 DIABETIC PATIENTS

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Background: Osteoarthritis (OA) is mainly characterized by the progressive deterioration of articular cartilage. Recent studies support that type 2 diabetes (TD2) is a risk factor to develop OA [1, 2]. However, the molecular cartilage profile of patients combining these two diseases remains unclear, and a better understanding of the different OA phenotypes should be considered for the development of personalized medicine.

Matrix-assisted laser desorption/ionization (MALDI) mass spectrometry imaging (MSI) is used to investigate the bimolecular distribution of proteins, lipids or metabolites through the *in-situ* analysis of tissue sections. Bottom-up proteomics focuses on the relative quantification of proteins. The combination of both technologies could be considered to reveal specific molecular profiles and help for patient classification.

Objectives: The main goal of this study is to apply a multimodal mass spectrometry approach on cartilage to reveal specific lipidomic and proteomic profiles associated to TD2 patients.

Methods: Human cartilages from OA (n_a=10) and OA/TD2 human patients (n_b=10) were obtained from donors undergoing total knee joint replacement. Cartilage punches of 8*8mm were sectioned at 12 µm thickness for MALDI-MSI and bottom-up proteomics.

For MALDI-MSI experiments (n_a=6; n_b=6), norharmane matrix was sprayed over the samples for the detection of lipids. Experiments were then performed in positive ion polarity at 50 µm of lateral resolution using a RapifleX MALDI

Tissue-typer instrument. LipostarMSI and in-house ChemomeTricks toolbox for MATLAB software were used for data processing and analysis.
For bottom-up proteomics experiment (n_a=10; n_b=10), proteins were extracted, separated using SDS-PAGE and digested prior to liquid chromatography separation coupled to an orbitrap MS Q-Exactive HF mass spectrometer. Proteome Discoverer, enrichR and Reactome software were used for data processing and analysis.
Results: MALDI-MSI showed overall differences between OA and OA/TD2 patients based on their specific lipidomic profiles. In particular, sphingomyelin and phosphatidylcholine species were significantly more abundant in OA patients whereas lysolipids such as lysophosphatidylcholine species were mainly present in OA/TD2 patients, providing therefore phenotype-specific OA molecular panels. Additionally, we observed that phosphatidylcholine and sphingomyelin species were more present in the superficial layer of the cartilage whereas lysophosphatidylcholine species were more abundant in the deep layer (Fig. 1A, B). Proteomics experiments applied on cartilage enables the quantification of 114 proteins. Among those, 73 were overexpressed in OA samples whereas 41 were overexpressed in OA/TD2 patients. Among the differentially regulated proteins (Fig. 1C), phospholipase A2 was increased in the diabetic cohort, in line with the elevated level of lysolipids found in the imaging data. Our results also involved the fatty acid omega oxidation and the fatty acid biosynthesis pathways as relevant to explain this deregulation of the lipid metabolism.
Conclusion: MALDI–MSI combined with proteomics experiments showed different profiles between OA and OA/TD2 patients and could be employed for patient classification.
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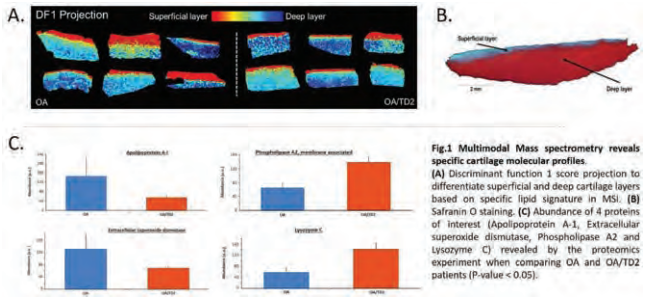


Fig.1 Multimodal Mass spectrometry reveals specific cartilage molecular profiles. **(A)** Discriminant function 1 score projection to differentiate superficial and deep cartilage layers based on specific lipid signature in MSI. **(B)** Safranin O staining. **(C)** Abundance of 4 proteins of interest (Apolipoprotein A-1, Extracellular superoxide dismutase, Phospholipase A2 and Lysozyme C) revealed by the proteomics experiment when comparing OA and OA/TD2 patients (P-value < 0.05).

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OP0241 IL9 MODULATION OF OSTEOCLASTS DIFFERENTIATION AND IMPACTS ON BONE METABOLISM

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Background: Osteoclasts are multinucleated cells originating from the monocytes/macrophage lineage and require receptor activator of NF-κB ligand (RANK-L) and macrophage-colony-stimulating factor (M-CSF) for their development. They play a major role in bone remodeling by degrading the calcified bone matrix. They are considered as one of the culprits in bone destruction in many inflammatory diseases e.g. rheumatoid arthritis and osteoporosis. In previous work by our group, it was observed that IL-9 mediated the resolution of inflammation in rheumatoid arthritis and hence protected against bone degradation in animal models. Despite this protection was particularly associated to the resolution of inflammation, our data also supported the hypothesis of a direct signalling of IL-9 to osteoclasts.
Objectives: The aim of this study was to investigate the modulating effect of IL-9 on osteoclasts and on the bone metabolism.
Methods: Osteoclasts differentiation was studied in the mouse models of antigen induced arthritis (AIA) and KBxN serum induced arthritis (SIA) in the presence and absence of IL-9 by histomorphometric analysis and microcomputed tomography scans (μCT). Osteoclasts were generated from bone marrow derived monocytes of BALB/c mice with M-CSF, RANKL and IL-9, which were added in varying concentrations to induce osteoclast differentiation. Tartrate-resistant acid phosphatase (TRAP) staining was performed to follow the differentiation steps from monocytes into multinucleated osteoclasts and to determine the effects of IL-9 on osteoclastogenesis. Additionally, we performed RNA-seq and seahorse analysis to detect IL-9 dependent, differentially expressed genes and metabolites. Intracellular signaling as induced by IL9R activation was followed by western blot analysis.
Results: IL-9 KO mice showed higher numbers of osteoclasts as compared to wild-type mice in the mouse models of AIA and SIA. Microcomputed tomography showed pronounced loss of the trabecular network and bone volume as signs of inflammation-induced osteopenia in Il9–/– mice. We found that osteoclasts express high levels of IL-9R. Next, monocytes were differentiated into osteoclasts in the presence of different concentrations of recombinant IL-9. Cells cultured in the presence of IL-9 showed significantly impaired differentiation into osteoclasts. We observed phosphorylation of STAT3 and STAT5 in cultured osteoclasts in dependency of IL-9. Furthermore, the presence of IL-9 during osteoclast differentiation impacted the gene expression levels of characteristic osteoclast related genes such as NFATc1, Cathepsin K and TRAP. Furthermore, IL-9 showed a major impact on mitochondrial respiration rate and glycolysis as assessed by Seahorse assays.
Conclusion: IL-9 exerted direct effects on osteoclast differentiation and modulated the expression of several genes that are related to osteoclast differentiation and function.
Disclosure of Interests: mina saad: None declared, Simon Rauber: None declared, Georg Schett Speakers bureau: AbbVie, BMS, Celgene, Janssen, Eli Lilly, Novartis, Roche and UCB, Andreas Ramming Grant/research support from: Pfizer, Novartis, Consultant of: Boehringer Ingelheim, Novartis, Gilead, Pfizer, Speakers bureau: Boehringer Ingelheim, Roche, Janssen
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OP0242 META-ANALYSIS OF SINGLE-CELL RNA SEQUENCING DATA OF THE SYNOVIUM TO DEFINE SYNOVIAL FIBROBLAST PHENOTYPES ACROSS JOINT LOCATION AND DISEASE

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Background: Up to now, three groups used single cell RNA sequencing (scRNA-seq) to analyse the synovium in arthritis using different methods and material to measure RNA expression on a single cell level: Ref. 1 used unsorted dissociated synovial cells and a droplet based method; Refs 2 and 3 performed scRNA-seq on sorted cell populations.
Objectives: The aim of this study was to perform a meta-analysis of scRNA-seq data of the synovium in arthritis: 1) to define synovial fibroblast (SF) phenotypes, 2) to confirm differences across SF clusters between rheumatoid arthritis (RA) and osteoarthritis (OA) and 3) to analyse joint specific differences between SF phenotypes.
Methods: In addition to the available count matrices [1-3], we used unsorted dissociated synovial cells from three patients with undifferentiated arthritis (UA) with a droplet-based method (10x Genomics). We followed a standard protocol [4] to integrate the datasets into a shared space, even in the presence of extensive technical and/or biological differences ("batch-corrected"). SF were selected as previously described (*PDPN*+, *ISLR*+, *COL1A2*+, *PTPRC*-) [1-3]. We used a minimum log2 FC of 0.25 for average expression of genes in a cluster relative to the average expression in all other clusters combined to define marker genes. R with Seurat, Monocle and clusterProfiler packages were used for scRNA-seq analysis, pseudotime trajectory analysis and pathway enrichement analysis, respectively. Quantitative PCR (qPCR) (n=6-14 per location and disease), immunohistochemistry (IHC) and Krenn synovitis score (n=5-15 per location and disease) were performed according to standard protocols.
Results: Data from 29 RA, 3 UA and 6 OA patients were analysed. From a total of 29'448 cells, we identified 14'787 (50%) with a fibroblast phenotype. Of those, we determined 5 subpopulations (Fig. 1): 1) *THY1*$^{-}$ *CD55*^{hi} fibroblasts with high

expression of *MMP1* and *MMP3* (SF1), 2) *THY1*^{lo} *CD34*$^{+}$ fibroblasts expressing high levels of *PI16* (SF2) 3) *THY1*^{hi} fibroblasts expressing high levels of periostin (*POSTN)* and collagens (e.g. *COL1A1, COL3A1*) (SF3), 4) *THY1*^{hi} fibroblasts expressing *CXCL12* (SF4) and 5) *THY1*^{lo} fibroblasts expressing *CXCL12*, *NR4A1* and *CCL2* (SF5). Fig. 2 shows pathway enrichment map of all marker genes; it organizes enriched terms into a network with edges connecting overlapping gene sets. Pseudotime trajectory axis derived from Monocle indicated that SF4 represent a state between SF3 and SF5. Pseudotemporal expression dynamics of *THY1* marked the progression of these three subtypes (Graph 1). SF1 and SF2 were proportionally underrepresented and SF3-5 overrepresented in RA (chi-squared = 37.18, p = 1.65e-07). The expression of POSTN, a signature gene of SF3, was not different between RA and OA tissues, but significantly correlated with the synovitis score (Spearman ρ = 0.55, p=0.02), in particular with pathological changes in the sublining. POSTN expression was higher in hand than in knee synovial tissues (mean ± SD IHC score: hand 8 ±2, knee 5 ±2) and in cultured SF (qPCR: 10-fold difference). Accordingly, SF3 was enriched in hand versus knee synovial tissues in the scRNA-seq dataset (chi-squared = 944.87, p < 2.2e-16).

Fig. 1

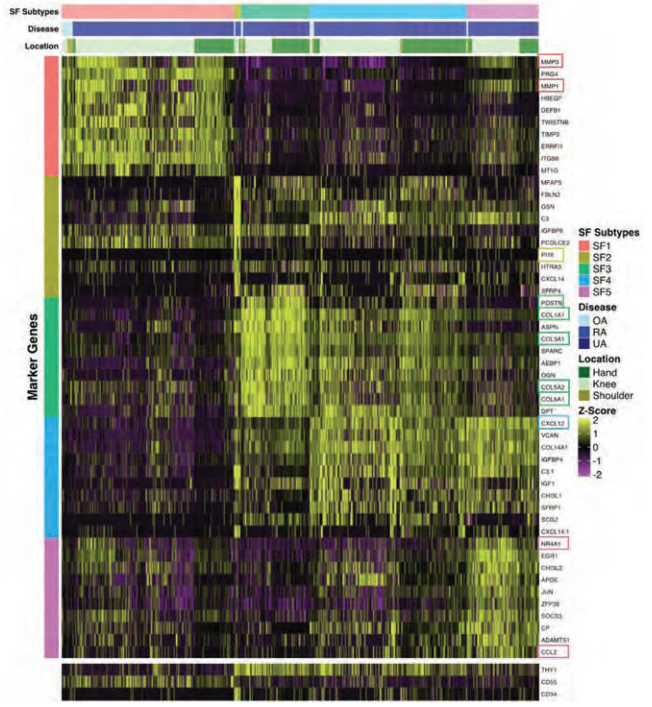


Fig. 1

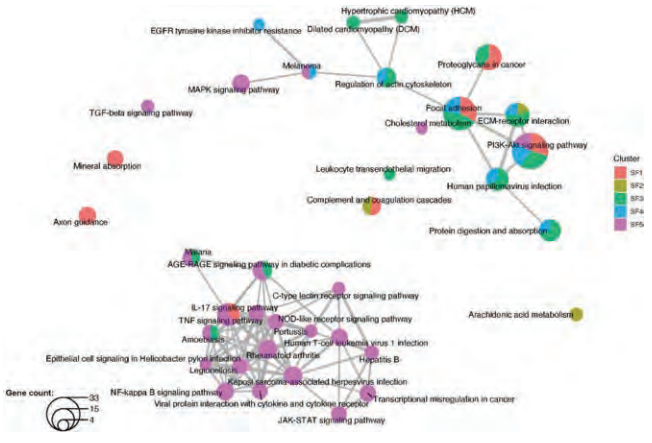
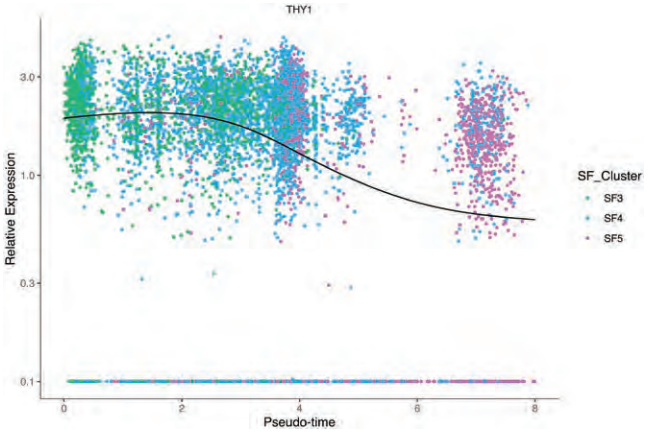


Fig. 2

Graph 1



Conclusion: In our meta-analysis, we found comparable subtypes of fibroblasts as in the individual analyses [1-3], showing the robustness of cell phenotype identification using scRNA-seq. The different SF phenotypes appear to be plastic cell states rather than fixed cell subtypes, whose development is controlled by an interrelation between pathological changes in the synovium and joint location.

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Disclosure of Interests: Raphael Micheroli: None declared, Mojca Frank-Bertoncelj: None declared, Sam G. Edalat: None declared, Kerstin Klein: None declared, Tadeja Kuret: None declared, Kristina Buerki: None declared, Adrian Ciurea Consultant of: Consulting and/or speaking fees from AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Merck Sharp & Dohme, Novartis and Pfizer., Oliver Distler Grant/research support from: Grants/Research support from Actelion, Bayer, Boehringer Ingelheim, Competitive Drug Development International Ltd. and Mitsubishi Tanabe; he also holds the issued Patent on mir-29 for the treatment of systemic sclerosis (US8247389, EP2331143)., Consultant of: Consultancy fees from Actelion, Acceleron Pharma, AnaMar, Bayer, Baecon Discovery, Blade Therapeutics, Boehringer, CSL Behring, Catenion, ChemomAb, Curzion Pharmaceuticals, Ergonex, Galapagos NV, GSK, Glenmark Pharmaceuticals, Inventiva, Italfarmaco, iQvia, medac, Medscape, Mitsubishi Tanabe Pharma, MSD, Roche, Sanofi and UCB, Speakers bureau: Speaker fees from Actelion, Bayer, Boehringer Ingelheim, Medscape, Pfizer and Roche, Caroline Ospelt Consultant of: Consultancy fees from Gilead Sciences.
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OP0243

SERPINA3N LIMITS CARTILAGE DESTRUCTION IN OSTEOARTHRITIS BY INHIBITING MACROPHAGE-DERIVED LEUKOCYTE ELASTASE

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Background: Interleukin-6 (IL-6) plays an important role in osteoarthritis (OA). Transcriptomic analyses (RNAseq) revealed that SerpinA3N, a serine protease inhibitor, is a key target of IL-6 in chondrocyte.

Objectives: This study aimed to examine the role of SerpinA3N and Leukocyte Elastase (Elane), a serine protease targeted by SerpinA3N, in cartilage destruction during OA.

Methods: The role of SerpinA3N was investigated in the destabilization of medial meniscus (DMM) model of murine OA with 1) mice with conditional inducible knockdown of *Serpina3n* in cartilage (*Col2*Cre^{ER};*Serpina3n*$^{fl/fl}$ mice [ΔSerpina3n^{Col2}]) and 2) C57BL/6 wild type (WT) mice treated with intra-articular injection of SerpinA3N (1,5 or 15 nM/week). OA joint lesions were assessed by histology (OARSI and synovitis scores) and micro-CT analysis (osteophyte volume, subchondral bone remodeling).

Because serine proteases targeted by SerpinA3N are not produced by murine chondrocytes, *Elane* expression (qRT-PCR) was determined in murine macrophages (Raw) stimulated or not by IL-6 (100 ng/ml). Recombinant

SerpinA3N (30 nM) and a specific Elane inhibitor, Sivelestat (100 µg/ml) were used on cartilage explants treated by conditioned medium of macrophages pre-treated or not by IL-6 (CM–IL-6). Cartilage catabolism was determined by histology and matrix metalloproteinase MMP-3 production was evaluated by Western Blot and immunohistochemistry (IHC). Weekly intra-articular injections of Sivelestat (1mM) were performed in the DMM to determine the role of Elane in OA.

Results: ΔSerpina3n^{Col2} mice had more severe OA lesions than control littermates 6 weeks after DMM, with greater cartilage damage (mean±SD OARSI score: 5.6±0.4 vs 3.4±0.5, p=0.01), increased synovitis scores (3.0±0.3 vs 1.9±0.3, p=0.03) and bigger osteophytes (7.2±0.8x107 vs 3.8±0.8x107 µ3, p=0.048). Conversely, WT mice treated with intra-articular injections of SerpinA3N 15nM exhibited less severe cartilage loss than mice treated with PBS after DMM (OARSI score: 2.1±0.4 vs 3.9±0.5, p=0.02). Elane mRNA expression was increased in macrophages upon IL-6 stimulation. In cartilage explants, CM–IL-6 activated cartilage catabolism and MMP-3 production, and effect that was blunted by SerpinA3N and Sivelestat. Finally, mice treated with intra-articular injections of Sivelestat had less severe cartilage damage than those treated with PBS after DMM (OARSI score: 3.3±0.47 vs 5.8±0.53, p=0.0046).

Conclusion: SerpinA3N protects against experimental OA via the inhibition of Elane, a pro-catabolic serine protease produced by macrophages. This results highlight the crosstalk between cartilage and surrounding macrophages and open up new therapeutic perspectives.

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Disclosure of Interests: None declared

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OP0244 A PRECLINICAL TESTING TOOL: THE IN VITRO 3D FRACTURE GAP MODEL

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Background: Approximately 10% of fractures lead to significant fracture healing disorders, with a tendency to further increase due to the aging population. Of note, especially immunosuppressed patients with ongoing inflammation show difficulties in the correct course of fracture healing leading to fracture healing disorders. Most notably, invading immune cells and secreted cytokines are considered to provide an inflammatory microenvironment within the fracture gap, primarily during the initial phase of fracture healing. Current research has the focus on small animal models, facing the problem of translation towards the human system. In order to improve the therapy of fracture healing disorders, we have developed a human cell-based *in vitro* model to mimic the initial phase of fracture healing adequately. This model will be used for the development of new therapeutic strategies.

Objectives: Our aim is to develop an *in vitro* 3D fracture gap model (FG model) which mimics the *in vivo* situation in order to provide a reliable preclinical test system for fracture healing disorders.

Methods: To assemble our FG model, we co-cultivated coagulated peripheral blood and primary human mesenchymal stromal cells (MSCs) mimicking the fracture hematoma (FH model) together with a scaffold-free bone-like construct mimicking the bony part of the fracture gap for 48 h under hypoxic conditions (n=3), in order to reflect the *in vivo* situation after fracture most adequately. To analyze the impact of the bone-like construct on the *in vitro* FH model with regard to its osteogenic induction capacity, we cultivated the fracture gap models in either medium with or without osteogenic supplements. To analyze the impact of Deferoxamine (DFO, known to foster fracture healing) on the FG model, we further treated our FG models with either 250 µmol DFO or left them untreated. After incubation and subsequent preparation of the fracture hematomas, we evaluated gene expression of osteogenic (*RUNX2*, *SPP1*), angiogenic (*VEGF*, *IL8*), inflammatory markers (*IL6*, *IL8*) and markers for the adaptation towards hypoxia (*LDHA*, *PGK1*) as well as secretion of cytokines/chemokines using quantitative PCR and multiplex suspension assay, respectively.

Results: We found via histology that both the fracture hematoma model and the bone-like construct had close contact during the incubation, allowing the cells to interact with each other through direct cell-cell contact, signal molecules or metabolites. Additionally, we could show that the bone-like constructs induced the upregulation of osteogenic markers (*RUNX2, SPP1*) within the FH models irrespective of the supplementation of osteogenic supplements. Furthermore, we observed an upregulation of hypoxia-related, angiogenic and osteogenic markers (*RUNX2*, *SPP1*) under the influence of DFO, and the downregulation of inflammatory markers (*IL6*, *IL8*) as compared to the untreated control. The latter was also confirmed on protein level (e.g. IL-6 and IL-8). Within the bone-like constructs, we observed an upregulation of angiogenic markers (RNA-expression of *VEGF*, *IL8*), even more pronounced under the treatment of DFO.

Conclusion: In summary, our findings demonstrate that our established *in vitro* FG model provides all osteogenic cues to induce the initial bone healing process, which could be enhanced by the fracture-healing promoting substance DFO. Therefore, we conclude that our model is indeed able to mimic correctly the human fracture gap situation and is therefore suitable to study the influence and efficacy of potential therapeutics for the treatment of bone healing disorders in immunosuppressed patients with ongoing inflammation.

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OP0245 MICROBIOTA-INDUCED INTESTINAL BARRIER DYSFUNCTION PRECEDES THE ONSET OF ARTHRITIS AND ALLOWS THE SHUTTLING OF IMMUNE CELLS FROM THE GUT THE JOINTS

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Background: While it is known that microbial dysbiosis is associated with the onset of rheumatoid arthritis, mechanistic insights how it facilitates the development of arthritis remained largely elusive to date. It is especially interesting how microbial dysbiosis affects the transition from asymptomatic autoimmunity to arthritis. We speculated that a breakdown of intestinal barrier function caused by microbial dysbiosis allows immune cells to shuttle from the gut to the joints.

Objectives: To test whether intestinal barrier function is impaired before the onset of human RA and experimental arthritis and to seek for evidence that immune cells from the gut migrate to the joints.

Methods: In a longitudinal cohort of RA-at risk individuals markers of disturbed intestinal barrier function, such as zonulin, were analysed and linked to RA onset. Furthermore, new-onset RA patients were assessed for gut leakiness and their intestinal biopsies for the expression of tight junction proteins and immune cell infiltration. In the murine model of collagen-induced arthritis, sequential analysis of intestinal dysbiosis, intestinal barrier function and arthritis onset was carried out. Additionally, barrier function was assessed on intestinal organoids exposed to faecal supernatants from eu- and dysbiotic mice with and without inhibition of zonulin. Furthermore, three types of interventions restoring intestinal barrier function were carried out for testing their effects on the inhibition of arthritis onset. Finally, photo- converted cells from the gut were traced in the joints to test for cellular trafficking from one to the other compartment.

Results: Zonulin, a potent regulator for intestinal tight junctions, was elevated in autoimmune mice and men before the onset of arthritis and predicted the onset of human RA. Intestinal barrier functions as well as epithelial tight junctions were decreased before the onset of experimental arthritis and at onset of human RA. In mice, induction of autoimmunity was followed by rapid intestinal dysbiosis followed by gut leakiness before arthritis started. Faecal supernatants of arthritic mice induce epithelial barrier dysfunction in intestinal organoids in zonulin dependent manner. Restoration of the intestinal barrier in the pre-phase of arthritis using butyrate, CB1R agonist or zonulin antagonist larazotide inhibited the development of arthritis. Finally, using photoconvertible mice, gut-borne immune cells were identified that homed to the joints when barrier function was impaired.

Conclusion: In summary, these data show the intestinal barrier dysfunction precedes the onset of RA and allows the trafficking of immune cells from the gut to the joints. Targeting of intestinal tight junction function may therefore allow preventing the onset of RA.

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Disclosure of Interests: Mario Zaiss: None declared, Narges Taijc: None declared, Kerstin Sarter: None declared, Vugar Azizov: None declared, laura Bucci: None declared, Yubin Luo: None declared, Juan de Dios Cañete: None declared, francesco ciccia Grant/research support from: pfizer, novartis, roche, Consultant of: pfizer, novartis, lilly, abbvie, Speakers bureau: pfizer, novartis, lilly, abbvie, Georg Schett Speakers bureau: AbbVie, BMS, Celgene, Janssen, Eli Lilly, Novartis, Roche and UCB

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OP0246 **MIR-214-3P PROTECTS AGAINST OSTEOARTHRITIS BY DIRECTLY TARGETING NF-κB PATHWAY**

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Background: Osteoarthritis (OA) is a degenerative disease associated with changes in the articular cartilage and bone, severely affecting patients' mobility and quality of life. Multiple factors including mechanical stress, metabolic alteration and inflammatory mediators are involved in the complex pathogenesis of OA[1]. Interventions targeting these pathogenic factors may contribute to the treatment of OA. MiRNAs are single strand non-coding small RNAs, which are regulated in chondrogenesis and OA[2,3]. Recent studies demonstrated that miRNAs are involved in the regulation of NF-κB signaling pathway by different mechanisms[4]. These interactions suggest that NF-κB related miRNAs may be used as potential biomarkers and drug therapeutic targets in clinical treatment of OA. However, the relationship between miR-214-3p and NF-κB pathway remains poorly understood in OA.
Objectives: This study aimed to test the expression and biological function of miR-214-3p in OA, and explore its mechanism in osteoarthritic chondrocytes.
Methods: Articular primary chondrocytes were isolated from human cartilage samples, which were acquired from patients with end-stage knee OA at the time of total knee replacement surgery (n = 27), according to protocols approved by the Ethic Committee of Zhujiang Hospital. Real time PCR (RT-PCR) and in situ hybridization (ISH) were used to detect the expression of miR-214-3p in OA and non-OA cartilage tissues. Interference of miR-214-3p was conducted using inhibitor, while overexpression of miR-214-3p was performed with mimics. Metabolism of extracellular matrix was detected by RT-PCR, western blotting and immunofluorescence in vitro. Flow cytometry were conducted to determine cell apoptosis. A luciferase reporter assay, was used to evaluate the interaction between miR-214-3p and its downstream target. Human chondrocytes were cotransfected with miR-214-3p and the IKBKB-overexpressing plasmid to confirm the interaction between miR-214-3p and NF-κB pathway. For in vivo studies, experimental OA was induced in 12-week-old male C57BL/6J mice by destabilization of the medial meniscus (DMM) surgery with miR-214-3p agomir intra-articular (IA) injection (once weekly for 12 days) or by IA injection (once weekly for 12 days) of miR-214-3p antiagomir. Mice were sacrificed 10 weeks after the first IA injection, and subjected to histological analyses.
Results: MiR-214-3p was significantly reduced in human OA cartilage. The decreased expression of miR-214-3p in the OA cartilage tissues was directly associated with excessive apoptosis and imbalance between anabolic and catabolic factors of ECM. Mechanistically, we determined that miR-214-3p directly targeted IKBKB/IKK-b and thereby suppressed the activation of NF-κB pathway. IKBKB overexpression attenuated the inhibitory effect of miR-214-3p on NF-κB pathway. Furthermore, inhibition of miR-214-3p in mice joints triggered spontaneous cartilage loss and OA development, while IA injection of miRNA-214-3p agomir alleviated OA in the DMM mouse model.
Conclusion: Our results reveal an important role of miR-214-3p in OA progression. MiR-214-3p was down-regulated while IKBKB was upregulated in OA. MiR-214-3p inhibits the NF-kB signaling pathway and suppresses the progression of OA through targeting IKBKB. Thus, miR-214-3p maybe a therapeutic target for OA.
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Disclosure of Interests: None declared
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Progress in scleroderma and myositis

OP0247 **PERSISTENT PREMATURE MORTALITY GAP IN IDIOPATHIC INFLAMMATORY MYOPATHY: A GENERAL POPULATION-BASED COHORT STUDY**

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Background: Idiopathic inflammatory myopathy (IIM) is associated with significant premature mortality; however, whether the mortality gap has improved over recent years is unknown.
Objectives: To determine trends in premature mortality in patients with IIM in a large cohort, representative of the United Kingdom (UK) general population.
Methods: Using The Health Improvement Network (THIN), an electronic medical record database representative of the UK general population, we identified patients with incident IIM between 18 and 89 years of age (defined by at least one Read diagnosis code for dermatomyositis, polymyositis, or interstitial myositis with at least one year of continuous enrollment in THIN prior to the cohort entry date) and up to 10 controls without IIM matched on age, sex, birth year, and database entry year. The cohort was divided in two based on the year of IIM diagnosis: the early cohort (1999-2006) and the late cohort (2007-2014). We calculated adjusted hazard ratios for death using a multivariable Cox-proportional hazards model and adjusted rate differences using an additive hazard model.
Results: The early cohort consisted of 355 patients with IIM and 3182 matched controls, while the late cohort consisted of 396 IIM patients and 3551 matched controls. In both cohorts, IIM patients had excess mortality compared to matched controls [57.4 vs. 15.2 deaths/1000 person-years (PY) in the early cohort and 43.2 vs. 14.1 deaths/1000 PY in the late cohort] (Table). The corresponding multivariate mortality hazard ratios were 2.73 (95% CI, 1.85 to 4.03) vs. 2.61 (95% CI, 1.75 to 3.89) in the early and late cohorts, respectively (p-value for interaction = 0.63) (Figure). The absolute multivariate mortality differences were 36.6 (95% CI, 20.4 to 52.8) and 25.8 (95% CI, 13.7 to 37.9) deaths/1000 PY, in the early and late cohorts, respectively (p-value for interaction = 0.24).
Conclusion: In this general population-based cohort study, patients with IIM had over 2.5 times the risk of death compared to matched controls, even after adjusting for comorbidities and medications. Unlike trends seen in rheumatoid arthritis and granulomatosis with polyangiitis, there appears to be no improvement in mortality in IIM in recent years. This highlights the need for improved strategies for the management of patients with IIM and its comorbidities.

Table. Association between idiopathic inflammatory myopathy (IIM) and all-cause mortality according to time period.

	1999-2006		2007-2014		
	IIM cohort (n=355)	Non-IIM cohort (n=3182)	IIM cohort (n=396)	Non-IIM cohort (n=3551)	p-value for interaction
Follow-up time, years (mean ± SD)	2.6 ± 2.1	2.9 ± 2.1	3.2 ± 2.4	3.5 ± 2.4	
Number of deaths	53	140	55	177	
Death rate/1000 PY (95% CI)	57.4 (43.0, 75.1)	15.2 (12.7, 17.9)	43.2 (32.5, 56.2)	14.1 (12.1, 16.3)	
Age-, sex-, and entry year-matched hazard ratio (95% CI)	4.02 (2.89, 5.59)	1.00 (ref)	3.43 (2.49, 4.73)	1.00 (ref)	0.50
Multivariable-adjusted hazard ratio (95% CI)*	2.73 (1.85, 4.03)	1.00 (ref)	2.61 (1.75, 3.89)	1.00 (ref)	0.63
Age-, sex-, and entry year-matched rate difference/1000 PY (95% CI)	42.2 (26.6, 57.9)	0.0 (ref)	29.1 (17.5, 40.7)	0.0 (ref)	0.24
Multivariable-adjusted rate difference/1000 PY (95% CI)	36.6 (20.4, 52.8)	0.0 (ref)	25.8 (13.7, 37.9)	0.0 (ref)	0.24

* Multivariable models were adjusted for age, sex, entry year, number of GP visits, BMI, smoking status (i.e., non-smokers, ex-smokers, current smokers), alcohol consumption (i.e., non-drinkers, ex-drinkers, current drinkers), comorbidities, and medication use.
PY, person-year; BMI, body mass index; GP, general practitioner

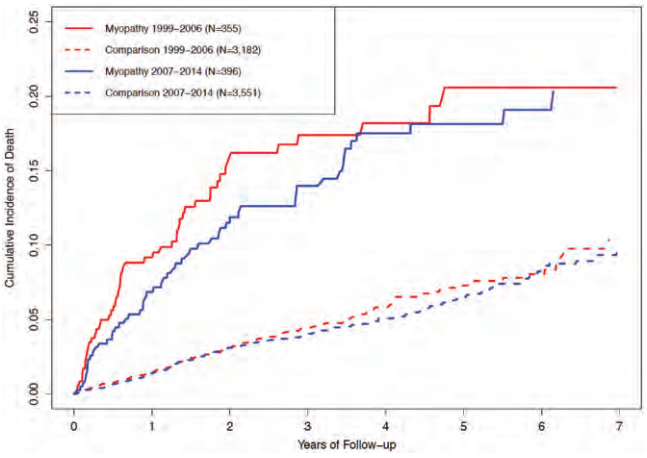


Figure. Cumulative mortality of patients with idiopathic inflammatory myopathy and matched controls without IIM in early versus late cohorts (1999-2006 versus 2007-2014).

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OP0248 PREMATURE MORTALITY BURDEN FOR SYSTEMIC SCLEROSIS: NATIONWIDE POPULATION-BASED STUDY

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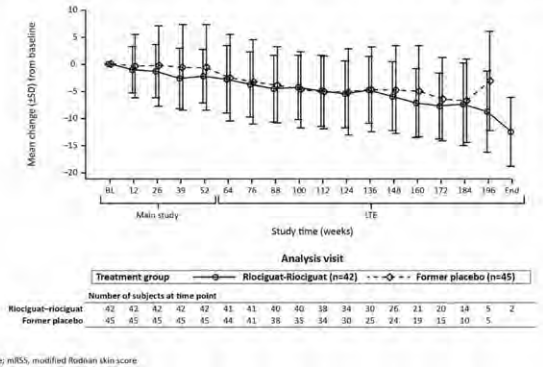
Background: Premature mortality is an important way to quantify disease burden. Patients with systemic sclerosis (SSc) can die prematurely of disease, however, the premature mortality burden of SSc is unknown. The years of potential life lost (YPLL), in addition to age-standardized mortality rate (ASMR) in younger ages, can be used as measures of premature death.
Objectives: To evaluate the premature mortality burden of SSc by calculating: 1) the proportions of SSc deaths as compared to deaths from all other causes (non-SSc) by age groups over time, 2) ASMR for SSc relative to non-SSc-ASMR by age groups over time, and 3) the YPLL for SSc relative to other autoimmune diseases.
Methods: This is a population-based study using a national mortality database of all United States residents from 1968 through 2015, with SSc recorded as the underlying cause of death in 46,798 deaths. First, we calculated the proportions of deaths for SSc and non-SSc by age groups for each of 48 years and performed joinpoint regression trend analysis[1] to estimate annual percent change (APC) and average APC (AAPC) in the proportion of deaths by age. Second, we calculated ASMR for SSc and non-SSc causes and ratio of SSc-ASMR to non-SSc-ASMR by age groups for each of 48 years, and performed joinpoint analysis to estimate APC and AAPC for these measures (SSc-ASMR, non-SSc-ASMR, and SSc-ASMR/non-SSc-ASMR ratio) by age. Third, to calculate YPLL, each decedent's age at death from a specific disease was subtracted from an arbitrary age limit of 75 years for years 2000 to 2015. The years of life lost were then added together to yield the total YPLL for each of 13 preselected autoimmune diseases.
Results: 23.4% of all SSc deaths as compared to 13.5% of non-SSc deaths occurred at <45 years age in 1968 (p<0.001, Chi-square test). In this age group, the proportion of annual deaths decreased more for SSc than for non-SSc causes: from 23.4% in 1968 to 5.7% in 2015 at an AAPC of -2.2% (95% CI, -2.4% to -2.0%) for SSc, and from 13.5% to 6.9% at an AAPC of -1.5% (95% CI, -1.9% to -1.1%) for non-SSc. Thus, in 2015, the proportion of SSc and non-SSc deaths at <45 year age was no longer significantly different. Consistently, SSc-ASMR decreased from 1.0 (95% CI, 0.8 to 1.2) in 1968 to 0.4 (95% CI, 0.3 to 0.5) per million persons in 2015, a cumulative decrease of 60% at an AAPC of -1.9% (95% CI, -2.5% to -1.2%) in <45 years old. The ratio of SSc-ASMR to non-SSc-ASMR also decreased in this age group (cumulative -20%, AAPC -0.3%). In <45 years old, the YPLL for SSc was 65.2 thousand years as compared to 43.2 thousand years for rheumatoid arthritis, 18.1 thousand years for dermatomyositis,146.8 thousand years for myocarditis, and 241 thousand years for type 1 diabetes.
Conclusion: Mortality at younger ages (<45 years) has decreased at a higher pace for SSc than from all other causes in the United States over a 48-year period. However, SSc accounted for more years of potential life lost than rheumatoid arthritis and dermatomyositis combined. These data warrant further studies on SSc disease burden, which can be used to develop and prioritize public health programs, assess performance of changes in treatment, identify high-risk populations, and set research priorities and funding.
References:
[1] Yen EY….Singh RR. Ann Int Med 2017;167:777-785.
Disclosure of Interests: None declared
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OP0249 LONG-TERM EXTENSION RESULTS OF RISE-SSC, A RANDOMIZED TRIAL OF RIOCIGUAT IN PATIENTS WITH EARLY DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS (DCSSC)

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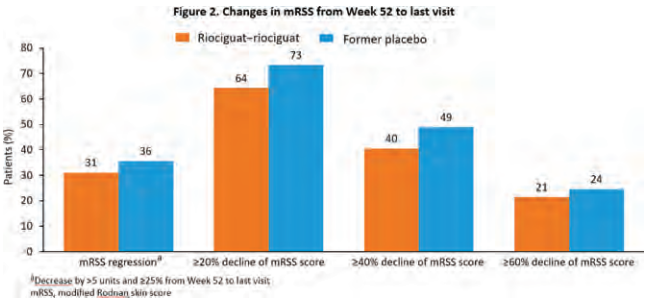
Background: RISE-SSc (NCT02283762) was a multicenter Phase IIb trial of riociguat in pts with early (duration ≤18 months) dcSSc and modified Rodnan skin score (mRSS) 10–22 units. Pts were randomized double-blind to placebo or riociguat 0.5–2.5 mg t.i.d. for 52 weeks. The primary endpoint, mRSS change from baseline to Week (Wk) 52, did not reach statistical significance (p=0.08, riociguat vs placebo), but there were favorable trends in some other outcomes.
Objectives: To present open-label long-term extension (LTE) results of RISE-SSc.
Methods: Pts who completed Wk 52 of double-blind therapy could enter LTE on riociguat. Endpoints included mRSS, adverse events (AEs), and serious AEs (SAEs).
Results: Of 60 pts randomized to riociguat and 61 to placebo, 42 (riociguat–riociguat group) and 45 (former placebo group), respectively, entered LTE. At LTE start, mean±SD mRSS was 16.4±3.2 and 16.3±4.2 units, and mean disease duration was 8.9±7.8 and 8.9±5.8 months, in the riociguat–riociguat and former placebo groups, respectively. Other demographics/disease characteristics were also comparable. Median duration of riociguat treatment was 1092 d in riociguat–riociguat pts and 649 d in former placebo pts. Throughout the study, mRSS decreased in both groups (Figure 1). From Wk 52 to last visit, mRSS fell by –3.02±5.51 in riociguat–riociguat patients and –3.96±5.43 in former placebo pts. Rates of mRSS regression (decrease by >5 units and ≥25% from Wk 52 to last visit) and of % declines in mRSS were similar in the two groups (Figure 2). mRSS progression (increase by >5 units and ≥25% from Wk 52 to last visit) occurred in 1 pt (2%) in each group. During the entire study, rescue therapy agents were used in 15 (36%) riociguat–riociguat pts and 17 (38%) former placebo pts. AEs were reported from Wk 52 to last visit in 82 pts (94%): 40 (95%) riociguat–riociguat and 42 (93%) former placebo. Most common AEs overall: nasopharyngitis (24%), gastroesophageal reflux disease (17%), diarrhea (15%), and hypotension (14%). AEs of special interest (dizziness, postural dizziness, or hypotension) occurred in 5 riociguat–riociguat pts (12%) and 4 former placebo pts (9%). SAEs were reported in 21 (24%) pts: 10 (24%) riociguat–riociguat pts and 11 (24%) former placebo pts, with no SAE reported in >1 patient, no SAEs of special interest, and no deaths.
Conclusion: During LTE riociguat treatment, mRSS decreased in both groups from Wk 52 onwards and mRSS progression was uncommon. Riociguat had acceptable safety, similar to the main study, with no new safety signal.

Figure 1. Mean change from baseline in mRSS by time point from baseline to the last visit (long-term safety analysis set)



BL, baseline; mRSS, modified Rodnan skin score

Figure 2. Changes in mRSS from Week 52 to last visit



[a]Decrease by >5 units and ≥25% from Week 52 to last visit
mRSS, modified Rodnan skin score

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OP0250 EFFICACY AND SAFETY OF ROMILKIMAB IN DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS (DCSSC): RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, 24-WEEK, PROOF OF CONCEPT STUDY

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Background: Systemic sclerosis (SSc) is a progressive, multi-organ disease with limited treatment options. Interleukin-4 (IL-4) and IL-13 have been implicated in the fibrotic pathway and pathogenesis of SSc and are promising targets. Romilkimab (RKB) is an engineered humanized bispecific Ig-G4 antibody that binds and neutralizes both IL-4/IL-13. We report a Phase IIa randomized, double-blind, placebo-controlled trial (NCT02921971, Sanofi funded) employing RKB in SSc.
Objectives: To evaluate the efficacy and safety of RKB in dcSSc.
Methods: Patients with dcSSc duration ≤36 months, mRSS 10-35, with or without immunosuppressive background therapy were randomized (1:1) to subcutaneous RKB 200mg or placebo (PBO) for 24 weeks and stratified on history of SSc-ILD. Primary endpoint was mean change in mRSS at Week 24 and FVC/DLco and HAQ-DI were secondary endpoints. All analyses used a 1-sided p-value <0.05 as reaching statistical significance.
Results: Ninety-seven patients with similar baseline characteristics between arms, including use of background therapy (RKB 59.2% vs. PBO 52.1%) were randomized. Six (12.2%) and 4 (8.3%) patients discontinued study treatment early in the PBO and RKB arms, respectively. Primary endpoint showed an absolute change in mRSS of -2.45 (0.85) and -4.76 (0.86) for PBO and RKB groups, respectively with a difference of -2.31 (1.21) favoring RKB (p=0.029). Subgroup analysis based on background therapy showed a similar treatment effect with a PBO subtracted difference in mRSS of -2.69 (1.83) and -2.38 (1.59), suggesting an additive effect between background therapy and RKB. Secondary endpoints did not show a statistically significant difference between RKB vs. PBO arms, although there was numerically less decline in FVC with RKB with a PBO subtracted difference of 70ml (p=0.06). Exploratory endpoints suggested possible effect of RKB on overall pain, Raynaud's, digital ulcers, and EQ-5D-5L. Post-hoc analysis was undertaken to determine time to progression (first event defined as death, ≥10% relative decline in % predicted FVC, ≥15% relative decline in % predicted DLCO, ≥20% increase or +5 in mRSS, or other events: cardiac, SRC, PAH development) and showed a benefit for RKB (HR: 0.47 p=0.04). Adverse events were balanced between the two groups (RKB 83.3% vs. PBO 83.7%). There were 5 and 4 SAEs in the PBO and RKB arms, respectively. One death occurred in each arm (SRC – RKB, cardiomyopathy – PBO).
Conclusion: Patients with dcSSc who were treated with RKB showed a statistically significant reduction in mRSS compared to those receiving PBO. Secondary outcomes were not met, although RKB was associated with a smaller decline in FVC than PBO. Post-hoc analysis showed a possible reduction on time to progression with RKB. RKB was well tolerated with no major safety concerns.
References: None.
Disclosure of Interests: Yannick Allanore Grant/research support from: Yannick Allanore has received grants from Inventiva, Roche and Sanofi, Consultant of: Yannick Allanore has received fees from Actelion, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Curzion, Inventiva, Roche, Sanofi, Peter Wung Shareholder of: I own Sanofi stock, Employee of: I work for Sanofi, Christina Soubrane Employee of: I work for Sanofi., Corinne Esperet Employee of: I work for Sanofi., MARRACHE Frederic Employee of: I work for Sanofi,

Raphael Bejuit Employee of: I work for Sanofi., Amel Lahmar Employee of: I work for Sanofi., Dinesh Khanna Shareholder of: Eicos Sciences, Inc./Civi Biopharma, Inc., Grant/research support from: Dr Khanna was supported by NIH/NIAMS K24AR063120, Consultant of: Acceleron, Actelion, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Corbus Pharmaceuticals, Horizon Therapeutic, Galapagos, Roche/Genentech, GlaxoSmithKline, Mitsubishi Tanabe, Sanofi-Aventis/Genzyme, UCB, Christopher Denton Grant/research support from: GlaxoSmithKline, CSL Behring, and Inventiva, Consultant of: Medscape, Roche-Genentech, Actelion, GlaxoSmithKline, Sanofi Aventis, Inventiva, CSL Behring, Boehringer Ingelheim, Corbus Pharmaceuticals, Acceleron, Curzion and Bayer

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OP0251

THE EULAR SYSTEMIC SCLEROSIS IMPACT OF DISEASE (SCLEROID) SCORE – A NEW PATIENT-REPORTED OUTCOME MEASURE FOR PATIENTS WITH SYSTEMIC SCLEROSIS

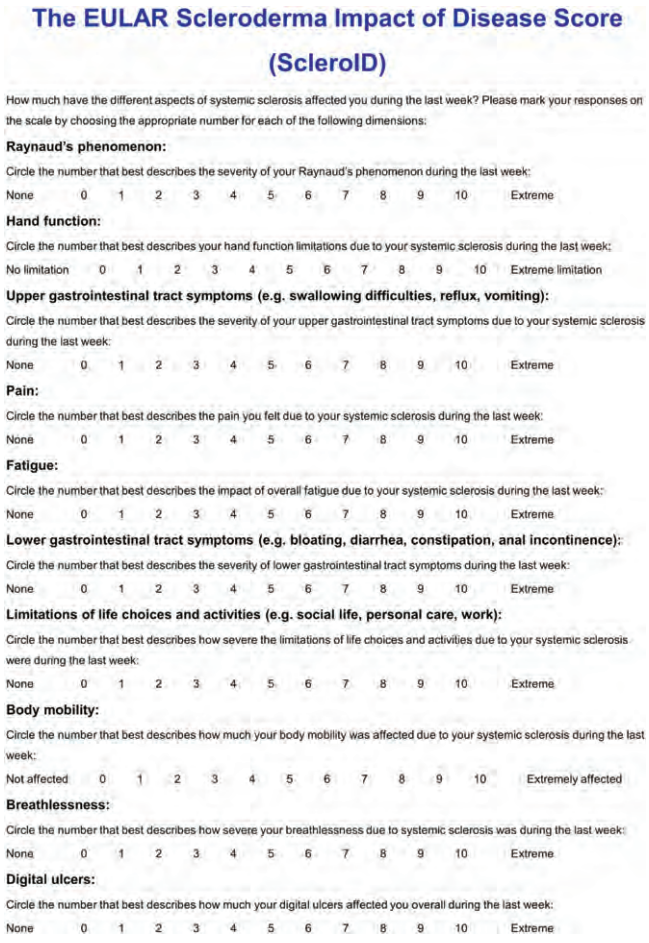
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Background: Patient reported outcome measures (PROM) are important for clinical practice and research. Given the unmet need for a comprehensive PROM for systemic sclerosis (SSc), the ScleroID questionnaire was developed by a joint team of patients with SSc and medical experts. This is intended as a brief, specific, patient-derived, disease impact score for research and clinical use in SSc.

Objectives: Here, we present the validation and final version of the ScleroID.

Methods: This EULAR-endorsed project involves 9 European expert SSc centers. Patients fulfilling the ACR/EULAR 2013 criteria were prospectively included since 05/16 in a large observational cohort study. Patients completed the ScleroID and comparators SHAQ, EQ5D, SF36. They also weighted the 10 dimensions of the ScleroID by distributing 100 points according to the perceived impact on their health. The final score calculation is based on the ranking of the weights. The validation study included a reliability arm and a longitudinal arm, looking at sensitivity to change at follow-up.

Results: Of the 472 patients included at baseline, 109 patients also had a reliability visit and 113 patients a follow-up visit. 84.5% of patients were female, 29.8% had diffuse SSc, mean age was 54.6 years, and mean disease duration 9.5 years. The highest weights were assigned by the patients to Raynaud`s phenomenon, fatigue, hand function and pain, confirming our previous results. The total ScleroID score showed good Spearman correlation coefficients with the comparators (SHAQ, 0.73; EQ5D -0.48; Patient's global assessment, VAS 0.77; HAQ-DI 0.62; SF36 physical score -0.62; each p<0.001). The internal consistency was good: Crohnbach's alpha 0.866, similar to SS-HAQ (0.88) and higher than EQ5D (0.77). The ScleroID had a very good reliability: intra-class correlation coefficient 0.839 (ranging 0.608 to 0.788 for the individual items), superior to all comparators. Twenty of 113 patients reported a change in their disease status at follow up. Sensitivity to change: the standardized response mean was 0.34 for the total ScleroID score and highest for lower GI (0.633) and life choices domains (0.521), superior to all other PROM. Figure 1 shows the final ScleroID.



The EULAR Scleroderma Impact of Disease Score (ScleroID)

How much have the different aspects of systemic sclerosis affected you during the last week? Please mark your responses on the scale by choosing the appropriate number for each of the following dimensions:

Raynaud's phenomenon:

Circle the number that best describes the severity of your Raynaud's phenomenon during the last week:

None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Hand function:

Circle the number that best describes your hand function limitations due to your systemic sclerosis during the last week:

No limitation 0 1 2 3 4 5 6 7 8 9 10 Extreme limitation

Upper gastrointestinal tract symptoms (e.g. swallowing difficulties, reflux, vomiting):

Circle the number that best describes the severity of your upper gastrointestinal tract symptoms due to your systemic sclerosis during the last week:

None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Pain:

Circle the number that best describes the pain you felt due to your systemic sclerosis during the last week:

None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Fatigue:

Circle the number that best describes the impact of overall fatigue due to your systemic sclerosis during the last week:

None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Lower gastrointestinal tract symptoms (e.g. bloating, diarrhea, constipation, anal incontinence):

Circle the number that best describes the severity of lower gastrointestinal tract symptoms during the last week:

None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Limitations of life choices and activities (e.g. social life, personal care, work):

Circle the number that best describes how severe the limitations of life choices and activities due to your systemic sclerosis were during the last week:

None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Body mobility:

Circle the number that best describes how much your body mobility was affected due to your systemic sclerosis during the last week:

Not affected 0 1 2 3 4 5 6 7 8 9 10 Extremely affected

Breathlessness:

Circle the number that best describes how severe your breathlessness due to systemic sclerosis was during the last week:

None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Digital ulcers:

Circle the number that best describes how much your digital ulcers affected you overall during the last week:

None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Figure 1.

Conclusion: The EULAR ScleroID is a novel PROM designed for use in clinical practice and clinical trials to reflect the disease impact of SSc, showing good performance in the validation study. Importantly, Raynaud syndrome, impaired hand function, pain and fatigue were the main patient reported drivers of disease impact.

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OP0252 CIRCULATING COLLAGEN TURNOVER MARKERS ARE SPECIFICALLY CHANGED IN VERY EARLY SYSTEMIC SCLEROSIS

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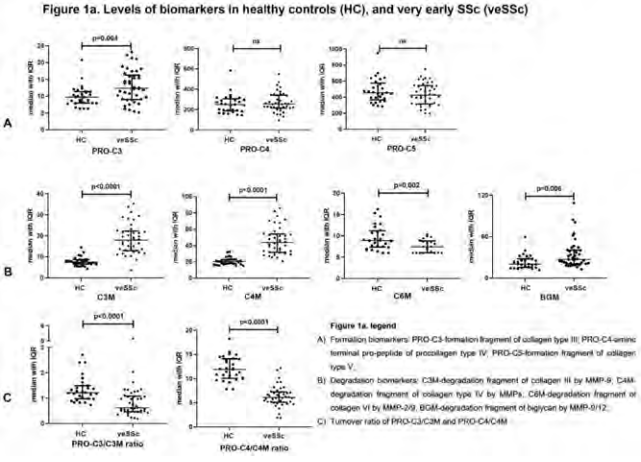
Background: Timely diagnosis of patients with very early systemic sclerosis (veSSc) is essential for their personalized and optimal management. We hypothesise that changes in serum-based extracellular matrix (ECM) turnover biomarkers are already detectable in patients with veSSc, even before occurrence of specific clinical signs.

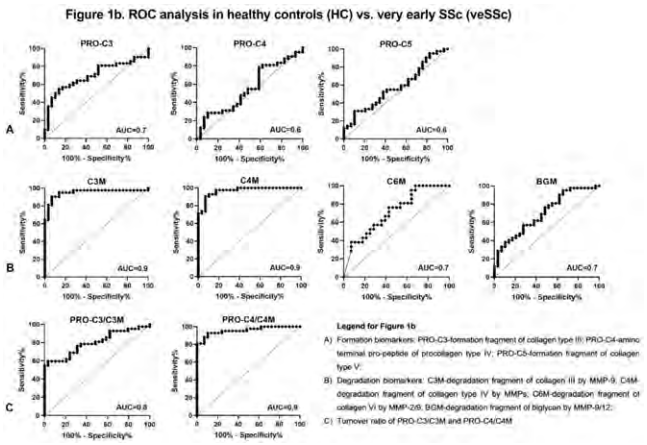
Objectives: To investigate circulating ECM turnover markers as potential biomarkers for veSSc.

Methods: Patients with veSSc, n=42, defined as presence of Raynaud's syndrome and at least one of puffy fingers, positive antinuclear antibodies or pathological nailfold capillaroscopy, who did not meet any classification criteria for SSc, were compared to healthy controls (HC, n=29). Longitudinal assessment, data and sera collection were conducted by EUSTAR standards. ECM-degradation (BGM, C3M, C4M, C6M) and ECM-formation biomarkers (PRO-C3, PRO-C4, PRO-C5) were measured in serum using ELISA assays. The statistical analyses included Mann-Whitney U, Spearman correlation and ROC analysis. Using Kaplan-Meier plots and univariable Cox regression, we explored if biomarkers can predict progression towards definite SSc (fulfillment of ACR/EULAR criteria or minimum two points increase in the criteria score) during the longitudinal follow-up.

Results: Compared to HC, veSSc patients showed a deregulated turnover of type III and IV collagen, with higher degradation (higher C3M, C4M, both p<0.0001 and PRO-C3, p=0.004, Figure 1a, resulting in lower turnover ratios PRO-C3/C3M and PRO-C4/C4M, both p<0.0001). The biglycan degradation biomarker BGM was also higher in veSSc (p=0.006), whereas the degradation biomarker for type VI collagen, C6M, was lower than in HC (p=0.002). In the ROC analysis, biomarkers of type III and IV collagen distinguished between veSSc and HC: C3M, AUC=0.95, p<0.0001; C4M, AUC=0.97, p<0.0001; turnover ratios PRO-C3/C3M, AUC=0.80, p<0.0001; PRO-C4/C4M, AUC=0.97; p<0.0001 (Figure 1b).

Median follow up was 4.5 years (range 0.5-7.9 years), mean age was 50±2.2 years, 88% female gender, 24% with puffy fingers, 92% were ANA positive, 64% had an abnormal capillaroscopy, none had organ involvement or skin fibrosis. 14/42 veSSc patients fulfilled the ACR/EULAR classification criteria at follow-up (time to fulfilment of criteria ranged between 0.5 and 6.8 years from inclusion) and in addition, 18/42 veSSc patients gained at least two classification criteria-points. This resulted in 14, respectively 18 progressors for the longitudinal analysis. However, in univariable Cox regression, the baseline levels of the markers did not predict progression over time.





Conclusion: ECM turnover is already altered in veSSc patients compared to HC. Biomarkes of type III and IV collagen distinguished between veSSc patients and HC, which may indicate them as potential biomarkers for the detection of veSSc in addition to the established immunological and capillaroscopic criteria.

Disclosure of Interests: Rucsandra Dobrota: None declared, Suzana Jordan: None declared, Pernille Juhl Employee of: Nordic Bioscience, Britta Maurer Grant/research support from: AbbVie, Protagen, Novartis, congress support from Pfizer, Roche, Actelion, and MSD, Speakers bureau: Novartis, Mike O. Becker: None declared, Carina Mihai: None declared, Anne-Christine Bay-Jensen Shareholder of: Nordic Bioscience A/S, Employee of: Full time employee at Nordic Bioscience A/S., Morten Karsdal Shareholder of: Nordic Bioscience A/S., Employee of: Full time employee at Nordic Bioscience A/S., Anne Sofie Siebuhr Employee of: Nordic Bioscience, Oliver Distler Grant/research support from: Grants/Research support from Actelion, Bayer, Boehringer Ingelheim, Competitive Drug Development International Ltd. and Mitsubishi Tanabe; he also holds the issued Patent on mir-29 for the treatment of systemic sclerosis (US8247389, EP2331143)., Consultant of: Consultancy fees from Actelion, Acceleron Pharma, AnaMar, Bayer, Baecon Discovery, Blade Therapeutics, Boehringer, CSL Behring, Catenion, ChemomAb, Curzion Pharmaceuticals, Ergonex, Galapagos NV, GSK, Glenmark Pharmaceuticals, Inventiva, Italfarmaco, iQvia, medac, Medscape, Mitsubishi Tanabe Pharma, MSD, Roche, Sanofi and UCB, Speakers bureau: Speaker fees from Actelion, Bayer, Boehringer Ingelheim, Medscape, Pfizer and Roche

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OP0253 AUTOANTIBODY STATUS IN DERMATOMYOSITIS AND POLYMYOSITIS PATIENTS DEFINES BOTH CANCER RISK AND SURVIVAL WITH ANA NEGATIVITY IN CASES WITH CONCOMITANT CANCER HAVING A WORSE SURVIVAL

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Background: We previously reported that ANA-negative cases with systemic sclerosis (SSc) and concomitant cancer had a worse survival than ANA-positive cases with associated cancer possibly suggesting that humoral mediated autoimmunity conferred a survival advantage (1). Dermatomyositis (DM) and polymyositis (PM) are two immune-mediated myopathies associated with numerous autoantibodies.

Objectives: The present large-scale, population-based study tested the hypothesis that humoral autoimmunity associated with cancer in solid/haematological malignancies impacted on DM/PM patient survival.

Methods: Over 2000 cases with either DM or PM were recruited from the Clalit Health Service (CHS) chronic diseases registry, one of the largest healthcare maintenance Israeli organization, serving approximately half of the entire country's population. Over 10000 matched controls were recruited. The data collected range from 2000 to 2018.

Results: Altogether 12,278 subjects were recruited (2,085 cases, and 10,193 controls, 5,042 males, 41.1%, and 7,236 females, 58.9%). Among cases, 1,475 individuals (70.7%) were diagnosed with DM, whereas 610 (29.3%) with PM. Mean age was 47.81±22.51 years. 1,379 cases of cancers (11.2%) were diagnosed. At the univariate analysis and as expected, the rate of malignancies was

significantly (p<0.0001) higher in DM/PM (n=361, 17.3%) with respect to controls (n=1,018, 10.0%).
Concerning prognosis, ANA positivity in PM/DM was associated with a better prognosis for all cancers (OR 0.39 [95% 0.24-0.63], p=0.0001). For individual cancer types; thyroid cancer (OR 0.39 [95% 0.24-0.63], p=0.0001), gastric cancer (OR 0.40 [95% 0.25-0.64], p=0.0001), kidney cancer (OR 0.39 [95% 0.24-0. 62], p=0.0001), acute leukaemia (OR 0.40 [95% 0.25-0.65], p=0.0002), non-Hodgkin's lymphoma (OR 0.39 [95% 0.25-0.63], p=0.0001), but not for myelodysplastic syndrome.
The main cancers linked to PM/DM were thyroid cancer (OR 3.17 [95%CI 2.27-4.43]), gastric cancer (OR 5.96 [95%CI 4.24-8.38]), kidney cancer (OR 3.83 [95%CI 1.02-14.31], p=0.0462), and myelodysplastic syndrome (OR 2.01 [95%CI 1.17-3.46], p=0.0111). Regarding gastric cancer, positivity for anti-RNP (OR 5.68 [95%CI 3.02 to 10.71], p<0.0001), anti-SSA (OR 21.99 [95%CI 11.21 to 43.14], p<0.0001), and anti-Jo1 (OR 12.23 [95%CI 7.12 to 21.01], p<0.0001) was associated with a higher risk of cancer development.
Conclusion: ANA positivity is an independent predictor of favorable prognosis in PM/DM patients with cancer, possibly suggesting that cancer directed humoral autoimmunity may have some benefit. Therefore, humoral autoimmunity in SSc and PM/DM is a broad mechanism that confers a survival advantage and is relevant for disease understanding and elucidating optimal anti tumoural immunity in the current age of cancer immunotherapy.
References:
[1] Watad A, McGonagle D, Bragazzi NL, Tiosano S, Comaneshter D, Shoenfeld Y, Cohen AD, Amital H. Autoantibody status in systemic sclerosis patients defines both cancer risk and survival with ANA negativity in cases with concomitant cancer having a worse survival. Oncoimmunology. 2019 Mar 24;8(6):e1588084.
Disclosure of Interests: Abdulla Watad: None declared, Dennis McGonagle Grant/research support from: Janssen Research & Development, LLC, Merav Lidar: None declared, Nicola Luigi Bragazzi: None declared, Doron Comaneshter: None declared, Arnon Cohen: None declared, Howard Amital: None declared
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OP0254 CHROMATIN CONFORMATION SIGNATURE ANALYSIS IN EARLY VS LATE SCLERODERMA PHENOTYPES

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Background: Systemic sclerosis (scleroderma, SSc) is a heterogeneous disease in which clinical outcomes vary widely. Predicting outcomes on an individual basis remains challenging despite progress made through autoantibody analysis and gene expression profiling. Effective targeted therapies are evolving and accurately predicting outcomes is important to enable patient stratification for therapy.
Chromatin Conformation Signature (CCS) profiling of peripheral blood for systemic epigenetic deregulations could be used for such a purpose. The EpiSwitch platform offering high throughput and resolution chromosome conformation (3C) capture detects significant regulatory changes in 3D genome architecture and maps long range interaction between distant genomic locations. This then reveals the spatial disposition and physical properties of the chromosome, such as chromatin loops and inter-chromosomal connections, which have a role in network organization and genetic epistasis controlling gene expression. EpiSwitch automated platform has been successfully utilised in patient stratification in RA, MS and other indications.
This methodology could be applied to patients with SSc to identify CCS associated with different phenotypes and may ultimately be used to stratify and identify patients into pathogenic subtypes.
Objectives: We aimed to determine significant CCSs associated with early and late phenotypes of SSc.
Methods: The EpiSwitch-based chromosome conformation capture (3C) method was applied to blood samples from early phenotype, and late phenotype SSc patients. Intact nuclei were isolated from peripheral blood mononuclear cells and subjected to formaldehyde fixation resulting in crosslinking between physically touching segments of the genome via contacts between their DNA bound proteins. For quantification of cross-linking frequencies, the cross linked DNA was digested and then subjected to ligation. Cross-linking was then reversed and individual ligation products detected and quantified by EpiSwitch custom oligo array annotated across the whole genome to the anchoring sites of 3D genome architecture.
Results: 7 significant CCSs were found over the HLA-C, HLA-B and TNF regions on Chromosome 6 in the early phenotype. The top 8 pathways for genetic locations associated to the CCSs are shown in Table 1.

Table 1. Top 8 pathways for genetic locations associated to significant CCS for the early phenotype.

	GeneSet
1	Natural Killer cell mediated cytotoxicity
2	Immunoregulatory interations between a lymphoid cell and a non-lymphoid cell
3	Antigen Processing & presentation
4	Phagosome
5	Graft versus host disease
6	Type 1 diabetes mellitus
7	Osteoclast differentiation
8	Class 1 MHC mediated antigen processing & presentation

2 significant CCSs were found centred around the IFNG region of chromosome 12 in the late phenotype. The top 8 pathways for genetic locations associated to significant CCSs are shown in Table 2.

Table 2. Top 8 pathways for genetic locations associated to significant CCS for the late phenotype.

	GeneSet
1	Surfactant metabolism
2	IL12 signalling mediated by STAT4
3	Protein digestion & absorption
4	Calcineruin regulated NFAT dependent transcription in lymphocytes
5	Transcriptional misregulation in cancer
6	Kaposi's sarcoma associated herpes virus infection
7	IL2 mediated signalling events
8	Inflammatory bowel disease

Conclusion: Significant CCSs, as part of 3D genomic regulatory control, and their associated pathways for the genetic locations, were identified in both late and early phenotypes. There were distinct CCSs in the early phenotype compared to the late suggesting the CCSs change as the disease progresses and varies between phenotypes. If CCSs could be linked to each clinically defined subgroup across a SSc cohort they could be used as a biomarker tool to predict outcome and progression in patients.
Disclosure of Interests: Megan Galloway: None declared, Ewan Hunter: None declared, Alexandre Akoulitchev: None declared, Shivanee Vigneswaran: None declared, Bahja Abdi: None declared, Christopher Denton Grant/research support from: GlaxoSmithKline, Inventiva, CSF Behring, Consultant of: Roche-Genentech, Actelion, GlaxoSmithKline, Sanofi Aventis, Inventiva, CSL Behring, Boehringer Ingelheim, Bayer, David Abraham: None declared, Richard Stratton: None declared
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PARE abstract session

OP0255-PARE USING AN EDUCATIONAL APPLICATION TO FACILITATE UNDERSTANDING OF THE ANATOMY AND FUNCTION OF THE BRAIN AND TO EXPLORE THE EFFECTS OF CLINICAL FATIGUE FROM A PATIENT PERSPECTIVE

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Background: Rheumatic and musculoskeletal diseases are a group of devastating autoimmune disorders that all commonly share the debilitating symptom of fatigue. Despite the fact that fatigue can often cause some of the greatest impairments to quality of life, it is frequently reported by patients as the least successfully managed symptom of these conditions.
Fatigue is routinely misunderstood within the general population, with many people using the word fatigue as a synonym for tired. Fatigue is not the same as tiredness, which is a normal state that is experienced by most of the population, therefore it is important to help the general public understand what fatigue actually is and how it imposes consequences and limitations on those who suffer from it. To aid this understanding an educational application has been created to reinforce the patient perspective of living with fatigue. Furthermore, this application will also aid the understanding of brain anatomy and function, using Augmented Reality (AR), as research has now shown that brain function may be altered in the state of fatigue.
Currently, educational AR applications show great potential for increasing comprehension and understanding of complex concepts. AR expands user engagement by enhancing the learner's enjoyment and enriching their learning environment. We hope to utilise this technology in the education of fatigue.

Objectives: We aimed to create an AR application that has informative content designed to educate users on the topics of basic brain anatomy and function. Furthermore, we aimed to increase the users understanding of the complete impairment of fatigue by creating a short video that describes living with fatigue from the patient's perspective.
Methods: The application was created using medical scan dataset, a variety of 3D modelling software, and a game engine to create a functional and interactive augmented application. The short video regarding a patient's perspective on living with fatigue was developed in collaboration with the Glasgow Arthritis Involvement Network patient partners. In order to determine if the application met its primary objectives a pilot test was conducted on 14 participants. After consenting to taking part in the study, individuals were guided through a pre-application test, the use of the application itself and finally a post-application test.
Results: Initial results from the pilot test showed promise in the educational potential of the application. With regards to the questions pertaining to the brain anatomy, the percentage of questions answered correctly increased from 36% in the pre-test to 60% in the post-test. Furthermore, after using the application the participants reported a significant increase in their confidence for their answers. An additional six questions ascertained a participants perceptions of fatigue. From these questions, the answer that was most significantly changed after use of the application, was in relation to the impact that fatigue has on a patient's quality of life (t-Test p=0.02). After use of the application participants' opinions changed to reflect the fact that fatigue can completely impair a person's quality of life, showing an increase in their understanding of the debilitating nature of fatigue.
Conclusion: This research explored the development and effectiveness of an AR application that was centered around fatigue and basic neuroanatomy education within the general population. From the pilot test conducted we are able to report that the application was successful in delivering educational material about brain anatomy and was successful in increasing awareness about the impact that fatigue can have on an individual's quality of life.

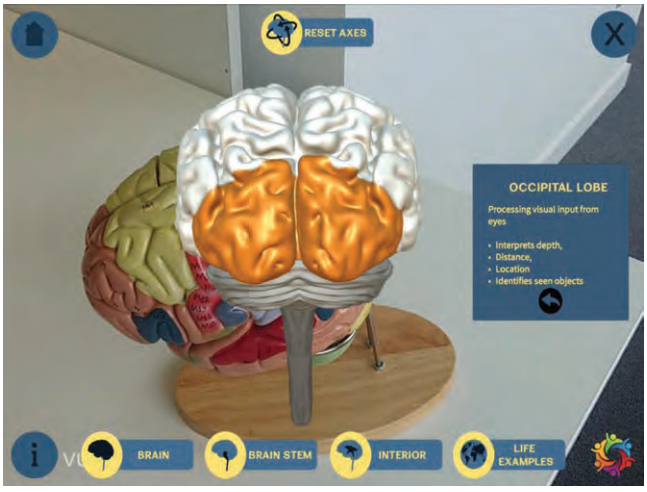


Figure 1. Augmented brain model scene using brain model as trigger

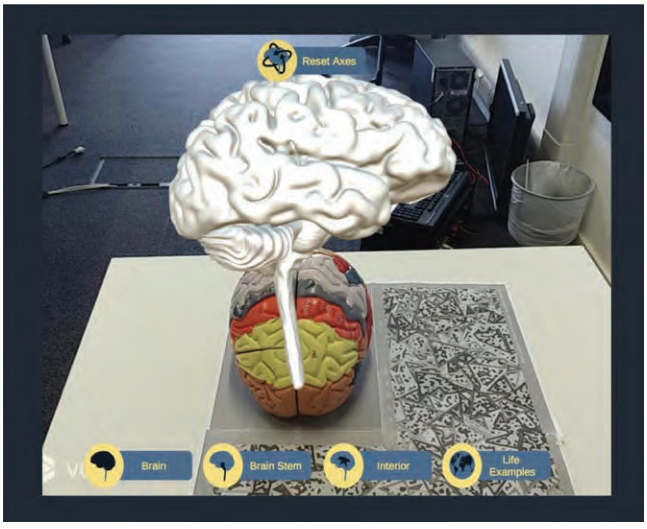


Figure 2. Example of material change upon selection of Occipital Lobe option

Acknowledgments: The Glasgow Arthritis Involvement Network (GAIN)
Disclosure of Interests: None declared
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OP0256-PARE

A PAW? YES, THANK YOU AN ANIMAL ASSISTED INTERVENTION (AAI) PILOT PROJECT FOR CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA)

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Background: Animal-Assisted Interventions (AAI) is the new way to indicate what was previously known as "Pet Therapy", as activities can be done either with the conventional "pets" (dogs, cats and rabbits) or with horses and donkeys. Children with JIA have several problems in terms of adherence both due to the atavistic fear of the needle and due to nausea and vomiting - the most important side effects of Methotrexate – often since the 2-3 days before the assumption to immediately after it.
Sure that animals can help children to forget this fear and to avoid the psycological conditions which enhance nausea, for the first time in Italy (and probably in Europe) it was designed a specific AAI program for these children.
Objectives: To promote a general state of psycho-physical well-being in children and families about:
manage of therapy; reduce discomfort and anxiety caused by entering hospital; improve self-esteem and the response to the stress generated by the execution of therapy and disease management; strengthen communication and socialization; stimulate the affective area through the activities of animal care.
Methods: Dogs and cats are part of the recreational activities once a week in an equipped area in the OIRM Hospital (no alternative gateway was needed).
Paediatric Rheumatologists selected two different groups of children: the first one (5 children in the pilot study) every 15 days; the second one (5 children) every month; the selection was made looking at the therapeutic scheme.
Every session, one hour, has 3 clearly distinct stages:
Welcome and organization: children say hello to dogs and cats, open the toolkits specifically designed for the intervention, express their state of mind and are encouraged to tell their own stories.
Therapy: parents prepare and inject the drug to their children under medical or Health Professional control without discontinuation of the activities with animals.
Play and socializing: children are involved in petting and other activities with animals; they are also involved in manipulative activities (design, puppets shows, modelling clay, animal care, ball retriving, etc). This step has the aim to relieve stress and discomfort due to medical procedures.
Visual Analogic Scales (VAS) were part of the toolkit, to let the researchers evaluate the effects of the activity directly from the children experience.
For the first time, we will control also the animal health status and wellness condition monitoring behavioural parameters and salivary cortisol level during each session.
Results: The pilot project started in October 2019 and nowaday we closed 12 meetings, 4 on October, 4 on November, 3 on December and 2 on January, with the participation of 2 dogs (Golden and Labrador Retriever) and 1 cat (Devon Rex) in each one.
All children love to play with animals, seek their closeness at the time of therapy and enjoy playing all together with the dogs; no one cry or refuse therapy and, since the third session, no one has nausea before, during or after the injection. Parents have reached a certain level of confidence: they stay quietly in the waiting room or go away to have a drink or to run an errand (it becomes a moment of relaxing for them too).
Animals remain in healthy and wellness conditions during the activity.
Conclusion: These preliminary data seem that AAI to be useful in helping patients in JIA to overcome some problems related to their pathology.
Disclosure of Interests: UGO VIORA: None declared, Patrizia Ponzio: None declared, Maria Teresa Mascarino: None declared, Barbara Picco: None declared, Paolo Guiso: None declared, Eleonora Battista: None declared, Silvana Martino: None declared, Davide Montin Speakers bureau: Not relevant for the topic, Marta Dellepiane: None declared, Germana Rosso: None declared
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OP0257-PARE USING PATIENT HEALTH LITERACY PROFILES TO IDENTIFY SOLUTIONS TO CHALLENGES FACED IN RHEUMATOLOGY CARE

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Background: The prevalence of limited health literacy (i.e. cognitive and social resources of individuals to access, understand and apply health information to promote and maintain good health) in the Netherlands is estimated to be over 36% [1]. Access to and outcomes of rheumatological care may be compromised by limited patient health literacy, yet little is known about how to address this, thus action is required. As influencing individual patients' health literacy in the rheumatology context is often unrealistic, it is paramount for the health system to be tailored to the health literacy needs of its patients. The OPtimising HEalth LIteracy and Access (Ophelia) process offers a method to inform system change [2].

Objectives: Following the Ophelia approach:

a. Identify health literacy profiles reflecting strengths and weaknesses of outpatients with RA, SpA and gout.
b. Use the health literacy profiles to facilitate discussions on challenges for patients and professionals in rheumatological care and identify possible solutions the health system could offer to address these challenges.

Methods: Patients with RA, SpA and gout attending outpatient clinics in three centres in the Netherlands completed the Health Literacy Questionnaire (HLQ) and questions on socio-demographic and health-related characteristics. Hierarchical cluster analysis using Ward's method identified clusters based on the nine HLQ domains. Three researchers jointly examined 24 cluster solutions for meaningfulness by interpreting HLQ domain scores and patient characteristics. Meaningful clusters were translated into health literacy profiles using HLQ patterns and demographic data. A patient research partner confirmed the identified profiles. Patient vignettes were designed by combining cluster analyses results with qualitative patient interviews. The vignettes were used in two two-hour co-design workshops with rheumatologists and nurses to discuss their perspective on health literacy-related challenges for patients and professionals, and generate ideas on how to address these challenges.

Results: In total, 895 patients participated: 49% female, mean age 61 years (±13.0), 25% lived alone, 18% had a migrant background, 6.6% did not speak Dutch at home and 51% had low levels of education. Figure 1 shows a heat map of identified health literacy profiles, displaying the score distribution per profile across nine health literacy domains. Figure 2 shows an excerpt of a patient vignette, describing challenges for a patient with profile number 9. The workshops were attended by 7 and 14 nurses and rheumatologists. Proposed solutions included health literacy communication training for professionals, developing and improving (visual) patient information materials, peer support for patients through patient associations or group consultations, a clear referral system for patients who need additional guidance by a nurse, social worker, lifestyle coach, pharmacist or family doctor, and more time with rheumatology nurses for target populations. Moreover, several system adaptations to the clinic, such as a central desk for all patient appointments, were proposed.

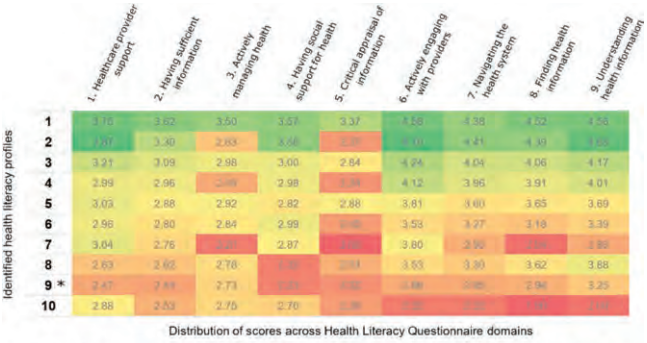


Figure 1. Heat map of identified health literacy profiles, with patterns of scores across nine health literacy domains. Range for domains 1-5 is [1-4]; Range for domains 6-9 is [1-5]. Orange and red scores represent low to very low levels, yellow and green scores represent moderate to good levels. * indicates the profile displayed in figure 2.

1	2	3	4	5	6	7	8	9
Healthcare provider support	Having sufficient information	Actively managing health	Having social support for health	Critically appraising information	Actively engaging with providers	Navigating the health system	Finding health information	Understanding health information
2.47	2.44	2.73	2.23	2.32	2.86	2.85	2.94	3.25

Ms. Spanjer is a 61-year-old unmarried woman who lives in a small Dutch city, together with her cat and two parakeets (scale 4). She is working reduced hours as a result of her continuously active Psoriatic Arthritis, besides several other health complaints, including moderate COPD and polyneuropathy.

Ms. Spanjer tries her best to take care of her health, and makes an effort to figure things out by herself (domain 3). That is not easy. She finds it hard to get enough health information (domains 2 and 8), let alone to make sense out of different sources of information that apply to her personal combination of health issues (domains 5 and 9). *„Sometimes you hear someone talk about cold therapy, or fasting. Then I try it for a while, but I'm not really sure if it really works for me"* (domain 5). Ideally, she'd like to leave it all up to her healthcare providers, but sometimes she feels like her doctor doesn't understand what is important to her (domain 1). *(…)*

Figure 2. Excerpt of a health literacy vignette corresponding to a hypothetical patient with profile number 9. Range for domains 1-5 is [1-4], range for domains 6-9 is [1-5]. Orange and red scores represent low to very low levels, yellow to green scores represent moderate to good levels.

Conclusion: This study identified several distinct health literacy profiles of patients with rheumatic conditions. Engaging with health professionals in co-design workshops led to numerous bottom-up ideas to improve care. Next steps include co-design workshops with patients, followed by prioritising and testing proposed interventions.

References:

[1] Heijmans M. et al. Health Literacy in the Netherlands. Utrecht: Nivel 2018
[2] Batterham R. et al. BMC Public Health 2014, 14:694

Disclosure of Interests: Mark Bakker: None declared, Polina Putrik: None declared, Jany Rademakers Speakers bureau: In March 2017, Prof. Dr. Rademakers was invited to speak about health literacy at the "Heuvellanddagen" Conference, hosted by Janssen-Cilag., Mart van de Laar Consultant of: Sanofi Genzyme, Speakers bureau: Sanofi Genzyme, Harald Vonkeman: None declared, Marc R Kok Grant/research support from: BMS and Novartis, Consultant of: Novartis and Galapagos, Hanneke Voorneveld: None declared, Sofia Ramiro Grant/research support from: MSD, Consultant of: Abbvie, Lilly, Novartis, Sanofi Genzyme, Speakers bureau: Lilly, MSD, Novartis, Maarten de Wit Grant/research support from: Dr. de Wit reports personal fees from Ely Lilly, 2019, personal fees from Celgene, 2019, personal fees from Pfizer, 2019, personal fees from Janssen-Cilag, 2017, outside the submitted work., Consultant of: Dr. de Wit reports personal fees from Ely Lilly, 2019, personal fees from Celgene, 2019, personal fees from Pfizer, 2019, personal fees from Janssen-Cilag, 2017, outside the submitted work., Speakers bureau: Dr. de Wit reports personal fees from Ely Lilly, 2019, personal fees from Celgene, 2019, personal fees from Pfizer, 2019, personal fees from Janssen-Cilag, 2017, outside the submitted work., Richard Osborne Consultant of: Prof. Osborne is a paid consultant for pharma in the field of influenza and related infectious diseases., Roy Batterham: None declared, Rachelle Buchbinder: None declared, Annelies Boonen Grant/research support from: AbbVie, Consultant of: Galapagos, Lilly (all paid to the department)
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OP0258-PARE ESTABLISHMENT AND DEPLOYMENT OF PATIENT EXPERT PROGRAM

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Background: Patient Expert on RMD's is a Patient Instructor who can train on the clinical examination technique of hand, hip, or knee for Rheumatoid Arthritis or Osteoarthritis. This Patient can explain the differences between RA and OS, can give information about symptoms for RMDs, and can share personal experience. Having a Patient Expert Program in a patient organisation helps on Raising awareness with future Health Professionals, gives strength and makes a stronger voice. After a very successful development of the Patient Expert Program, with the help of Eular Pare Knowledge Transfer Program, the time for installation of the program in universities has come.

Objectives: The aim was Medical Schools and Health Professional Universities to accept the program, in order for it to be a part of their education or training program. Having the program as part of their education or training program would benefit the next generation of Physicians or Health Professionals in the following ways. Better understanding for RMD's and the patient perspective, increaseing awareness and early diagnosis, to build a rapport with the patient. The challenge was in having the program accepted by the schools and universities, as is the only program on this kind in the country.

Methods: We created a task force to achieve our goal. The task force developed a strategic plan using the Swot analysis, to be able to achieve our goal. From that analysis the following plan was made: First we needed to prepare a presentation for the program. Second, we needed to demostrate it. Third, we had to have all our evaluation forms ready. And lastly, we had to make contacts with Medical schools by writing and by calling them. The stronger weakness and threat that came up was the possible refusal of the Universities, to accept the program.

Results: We started our communications with the Medical Schools when all of the steps were ready. The Medical School that had undergraduate students accepted to have a meeting with us. During our meeting, we made the oral presentation of our program and the Professors' response was positive and they proposed it to the Academic Board. The Academic Board asked for a demostration

and so we did. In the end, the Academic Board accepted our proposal. The program runs on students in the fourth Academic Year, in small groups, and on the premises of the school. The other one with postgraduate Medical Students didn't accept the proposal of our program, with the justification that as a department of a foreign Medical school, they couldn't implement anything in the students program. So far, more than 10 trainings have been conducted. At the end of the first year that the program was implemented, the Medical School asked from the organisation for a Patient Instructor to take part at the Musculoskeletal Examination and be a model for the Examination. Seeing our success, and taking into consideration the students' evaluation of the program, especially the fact that 95% of them said, 'It was very important for them to have a Patient Expert Program during their studies' our organisation decided to expland our collaboration with more Healthcare Professions Universities. Our original goal had been to collaborate with one of the medical schools/universities, but now we have bigger plans. Now we want this program to be established in all the universities in the country with the Patient Expert RMD's program implemented in all health professional curriculums.

Conclusion: The importance of the Patient Expert in RMD's is unquestionable. Patient Expert Program is an excellent tool to raise awareness on RMD's. Also it is very helpful for the Medical or Health care Professions student as it can help them better understand the disease and the patients. The success of the program is also giving motivation to the organisation to expand and improve the program. It also shows the significance of the program for the next generation of Physicians and Healthcare Professionals. Our organisation is leading in patient centered care and is proof that making the patient the most important is the target of treatment for RMD's in our country.

Disclosure of Interests: None declared

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OP0259-PARE WORLD YOUNG RHEUMATIC DISEASES (WORD) DAY: THE FIRST INTERNATIONAL AWARENESS DAY FOR PAEDIATRIC RHEUMATIC DISEASES

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Background: There is a lack of awareness of paediatric rheumatic diseases (PRDs), among the public, and certain groups of healthcare professionals, such as general practitioners [1]. To help improve awareness and understanding of PRDs, World Young Rheumatic Diseases Day (WORD Day) was established in 2019.

Objectives: The aim of WORD Day, which took place on 18 March 2019, was to raise awareness of PRDs, while informing young people, families, healthcare professionals, teachers, and the public about the importance of timely referral plus early diagnosis and access to appropriate treatment and support.

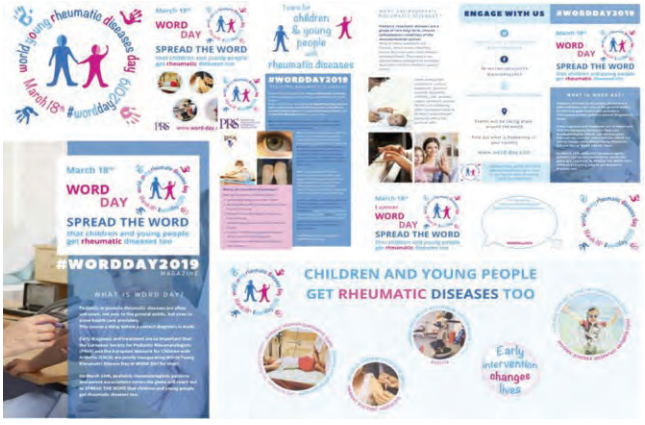
Methods: A steering committee was established for the inaugural campaign. An external agency was appointed to provide digital support, with an official social media campaign launching in December 2018. Social media analytics were used to measure the impact of official social media platforms. A range of branded materials were also made available (Fig 1), including an official campaign video. In addition, a specific engagement activity (#ButtonChallenge2019) was launched. This challenged participants to button up a piece of clothing while wearing gloves, to simulate the difficulties that young people with PRDs face undertaking daily activities. As part of the campaign launch, a list of suggested activities were provided, along with template press releases.

Results: Several face-to-face and virtual events took place globally on or around WORD Day 2019, with 34 countries reporting events (Fig 2). Examples of events included lectures, social gatherings and media appearances. An official WORD Day tweet chat was also hosted. Regarding social media impact, between December 2018 and March 2019, a total of 2,585 and 660 individuals followed the official Facebook and Twitter accounts, respectively. Facebook posts were seen 646,000 times since the start of the campaign, with over 60,000 of Facebook reach from posts published on 18 March 2019 exclusively. A total of 270,800 impressions were observed on Twitter. The official #WORDDay2019 hashtag was seen by 533,955 unique accounts on 18 March 2019 alone, with 3,334,699 impressions. Posts with the hashtag were retweeted 1,112 times on WORD Day, with a total of 1,568 tweets recorded that day. With regards to the #ButtonChallenge2019, the challenge video was viewed for 6,700 minutes and received participation from across the world. Compared to the industry benchmark, the average engagements per post for WORD Day-related content was significantly higher compared to other medical and non-for-profit social media pages.

Conclusion: WORD Day 2019 was the first international campaign focused solely on PRDs. Organic and paid social media content aided the dissemination of the WORD Day message, with Facebook proving to be the most popular social platform. Despite a wealth of different content published, authentic materials, namely video content, proved to be the most popular with users, particularly when it featured material designed by and with young people with PRDs. It was demonstrated that awareness events can often be resource-light and easily implemented across a range of diverse countries. It is anticipated that the global reach of WORD Day will increase over time as the campaign becomes more established.

References:

[1] Egert Y et al. Children and young people get rheumatic disease too. The Lancet Child & Adolescent Health. 2019;3(1):8-9.





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OP0260-PARE EXPERIENCE EXCHANGE – FUNDRAISING AND PATIENT EXPERT PROGRAM

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Background: Since the establishment of ORS, we have been organising different activities for rheumatic diseases patients and their supporters within our five branches. After celebrating our 10th anniversary in 2017 we were keen to expand and improve our activities, learning from an organisation with long tradition, in order to strengthen our position and to start reaching another level – growing from a small to a medium-sized organization in the next three years.

The main source of our income were the pharmaceutical companies (94%). We wanted to reduce their contribution to our budget by 20% in the next three years. We had established good cooperation with two medical high schools and we would like to consider cooperation with a medical faculty. We were keen to gain insight into the Patient Expert Programme (PEP) project that Swedish Rheumatism Association had developed and hoped to then begin and steadily develop

successful cooperation with target institutions in Serbia in the next years. We would like to improve the cooperation with medical faculties and become a part educational program. And the PEP was the best way to achieve this aim

Objectives: The aims of this knowledge transfer programme were for us to:

1. Fundraising
   – Learn how to gather more voluntary contributions of money and other resources. Following the knowledge transfer visits we will organise a seminar to disseminate information with the representatives of all our branches. After the seminar our activists will have been trained to collect money for different activities. Those activities will attract more members and provide better life for people with RMDs.
2. Patient Expert Program
   – Implement the Patient Expert Program. The implementation of this program would strengthen the connections with medical institutions, provide first/hand knowledge for future doctors, provide better care for RMDs patients in the future. The PEP will allow the organization to collaborate closer with the universities, the doctors, researchers, health professionals.
3. Cooperation among sister organisations

Develop strong relationships with the sisters EULAR organisations.

Methods: From 4th September – 8th September 2018 we visited Swedish Rheumatism Association in Stockholm in order to gain insight into the structure and activities of their association.

From 14th October-16th October 2019 Swedish delegation (president, two trainers and secretary) visited Serbian association for rheumatic diseases. It was organized the two-days PEP training as well as the visits to relevant institutions.

From 23th January-26th January 2020 two trainers from Sweden came to Serbia in order to hold the exams.

Results: Association of Rheumatic Diseases Patients of the Republic of Serbia now has six Patient Experts for RA. They will be involved in the education of future doctors through the lectures within the subject Intern Medicine.

ORS improved cooperation with Faculty of Medicine in Belgrade, as well as, with Ministry of Health.

Conclusion:

- We achieve to have six Patient Experts. Unofficially right now we have confirmation how they will be included in the education of future doctors through the lectures within the subject Intern Medicine in next school year at the Belgrade University
- We reduced contribution of the pharmaceutical companies of our income for 10% to our budget.
- We increased donations from personal donators In past year.

Disclosure of Interests: None declared

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OP0261-PARE BIOSIMILAR SWITCHING PROCESS - UK PATIENTS' EXPERIENCE STUDY

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Background: The introduction of 4 adalimumab biosimilars was challenging for the health service and patients alike. A group of patient organisations representing rheumatology, dermatology and gastroenterology patients worked with NHS England in producing materials for disseminating information to prescribers and patients to ensure smooth and appropriate transition to biosimilar products from the originator product as appropriate. These patient groups wanted to know how the 'switch' process was implemented and if shared decision making was practiced.

Objectives: To gather patient feedback on biosimilar switch process and report findings back to NHS England as well as provide the patient organisations information to develop any future resources to help improve patient and physician shared decision making.

Methods: A working group of the 4 organisations collaborated on designing an online survey asking questions around how the individual was communicated with regarding their treatment being switched to a biosimilar; was there any choice or perceived input into the decision making process; how queries or issues were handled and overall satisfaction on how the individual felt their personal preferences/needs were met.

Results: 899 useable responses were gathered representing 52% Rheumatology patients; 42% Gastroenterology patients and 5% Dermatology patients with remaining 1% more complex specialties. More than half of patients were not asked for their consent before their treatment was switched to a biosimilar of adalimumab with only 40% giving consent 7% couldn't remember or were unsure if consent was given. 75% were not at all satisfied or not satisfied with the ability to decline being switched with only 12% feeling that they had been given an option to decline being switched.

Conclusion: Shared Decision Making (SDM) needs to be put into action not just words. There is a clear majority that are dissatisfied with the communication they had prior to the switch and are very dissatisfied with the lack of patient engagement in the decision-making process. NRAS, NASS, Crohn's & Colitis UK and the Psoriasis Association will continue to collaborate with NHS England and other stakeholders as appropriate to make Shared Decision Making a reality not just rhetoric.

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Disease consequences

OP0262-HPR COST OF ILLNESS IN PATIENTS WITH PSORIASIS AND PSORIATIC ARTHRITIS. COEPSO STUDY

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Background: Psoriasis (Ps) and psoriatic arthritis (PsA) have a major impact on patients' health-related quality of life. Cost of illness of patients with Ps, PsA and both diseases (PsA+Ps) is an important subject as they are associated with a substantial economic impact, with implications from a health management perspective.

Objectives: To describe the economic burden of direct non-healthcare and indirect resources of patients with Ps, PsA and PsA+Ps in Spain.

Methods: COEPSO ("Evaluation of Costs in patients with Psoriatic Disease") was an observational, retrospective, cross-sectional study performed in 22 Spanish centers (17 Dermatology and 14 Rheumatology Services), from February 2017 to February 2018, including moderate to severe Ps and PsA patients (with or without Ps), naive to biologics. Direct non-healthcare (social services, home care, physical adaptations, private health and non-health professionals, non-reimbursed and non-pharmaceutical therapies), indirect (loss of productivity) and total costs (direct non-healthcare and indirect costs) related to the disease during the previous year to the study were obtained. Unitary costs (€, 2018) were calculated: out-of-pocket costs were specified directly by patients and loss of productivity costs by means of average salaries based on occupation specified by patients. The information was collected through a case report form filled out by the investigators and a telephone survey administered to the patients.

Results: A total of 318 patients were included (196 Ps; 43 PsA and 79 PsA+Ps), mean age 48.7 years and 51.3% males. Metabolic syndrome was the most frequent comorbidity in all groups. The average annual total cost per patient was 1,042.71€ (SD 3,817.55), 1,137.84€ (SD 3,070.39) and 1,830.26€ (SD 5,835.81) for Ps, PsA and PsA+Ps, respectively. The average annual direct non-healthcare cost per patient was 749.57€ (SD 2,393.77), 750.50€ (SD 1,641.82) and 1,247.56€ (SD 4,467.19) for Ps, PsA and PsA+Ps, respectively. The average annual indirect cost per patient was 293.14€ (SD 2,855.27), 387.35€ (SD 2,409.63) and 582.71€ (SD 3,842.12) for Ps, PsA and PsA+Ps, respectively.

Patients with combined PsA+Ps had higher annual total cost (direct non-healthcare and indirect costs) than patients with only one of these manifestations separately (75.5% and 60.9% above patients with Ps and PsA, respectively). Total costs in patients with Ps and PsA were similar. Direct non-healthcare costs represent between 66.0% (patients with PsA) to 71.9% (patients with Ps) of total cost. Indirect costs represent between 28.1% (patients with Ps) to 34.0% (patients with PsA) of total cost.

Conclusion: PsA and Ps have proved to be diseases with a high economic burden, and the total costs were mainly driven by direct non-healthcare costs. Moreover, although annual total costs in patients with PsA were similar to those of Ps patients, the combination of both manifestations yielded the highest costs suggesting the importance of the increased disease load.

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OP0263-HPR MAJOR STRESSORS IN THE YEAR PRIOR TO RA DIAGNOSIS: IMPACT ON PATIENT-REPORTED OUTCOMES ONE YEAR LATER

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Background: Stress is implicated in RA onset and poorer prognoses through changes in neuro-endocrine and autoimmune function. Although many people with RA link disease onset to recent stressful life events, results from retrospective studies are unclear.

Objectives: To describe the incidence of major stressors **(+STRESS)** in year prior to diagnosis and compare characteristics and patient-reported outcomes (PROs) of newly diagnosed RA patients with and without **+STRESS** at 0 and 12 months.

Methods: Data were from early RA patients (symptoms <1 yr) enrolled in the Canadian Early Arthritis Cohort (CATCH) from 2007-17 who met 1987/2010 ACR/EULAR criteria and had ≥12 months of follow-up. Patients reported major psychological (death, divorce/separation, family, financial, other) and physical (motor vehicle accident, surgery, major illness/infection, other) stressors in previous year. We used independent t-tests and chi square to compare characteristics by stressors at baseline, and multivariable regression to examine the impact of **+STRESS** on disease activity and PROs at 1 year, adjusting for age, sex, education, fibromyalgia, and SJC.

Results: The 1933 adults were mostly female (72%), with a mean (SD) age of 55 (15) years. 52% reported 1+ stressors in previous year; family (48%), financial stress (36%), death (35%), surgery (28%), and major illness (26%) were the most common stressors. Patients with +STRESS were more likely to be women, younger, have more comorbidities including fibromyalgia, and higher mean DAS28. Patients with +STRESS also had significantly higher mean pain, fatigue, depression, sleep disturbance, patient global, and HAQ scores at baseline.

At 1 year, SJC and the proportion in DAS28 REM was similar between groups. However, PROs (pain, HAQ, Fatigue, Pt Global, Depression, Poor Sleep) remained higher in **+STRESS**, with evidence of an additive effect for number of stressors and having both physical and psychological stressors (Table). The greatest impacts were on mood, sleep disturbance, and fatigue.

Conclusion: In this pan-Canadian early RA cohort, more than half reported 1+ stressful life events in the year prior to diagnosis. Individuals reporting major stressors had significantly worse pain, patient global, disability, depression, fatigue, and sleep disturbance at diagnosis; 1 year later, though disease activity was similar between groups, the effects of +STRESS on PROs persisted. Early RA patients with recent major stressors may benefit from emotional support and stress reduction to optimize how they feel and function.

Mean (SD) or N (%)	No Stress (N=928; 48%)	Physical (N=131; 7%)	Psychological (N=658; 34%)	Both (N=216; 11%)
Age	56 (15)	56 (15)	53 (14)	52 (15)
Women	622 (67%)	82 (63%)	512 (78%)	174 (81%)
College Education	464 (50%)	76 (58%)	345 (52%)	126 (58%)
Rheum Dis Comorbid Index	1.1 (1.2)	1.4 (1.4)	1.1 (1.3)	1.4 (1.3)
OA or Spinal pain	168 (18%)	35 (27%)	117 (18%)	55 (25%)
Fibromyalgia diagnosis	15 (2%)	2 (2%)	13 (2%)	11 (5%)
Symptom duration (months)	5.6 (3.0)	5.7 (3.0)	5.9 (3.0)	5.9 (3.0)
DAS28 – mean	5.0 (1.4)	5.1 (1.5)	5.0 (1.5)	5.2 (1.4)
MTX ±csDMARDs	679 (73%)	100 (76%)	489 (74%)	166 (77%)
Oral Steroids	295 (32%)	40 (31%)	215 (33%)	55 (25%)
Pain (0-10)	5.3 (2.8)	5.5 (2.9)	5.7 (2.8)	6.2 (2.8)
HAQ-DI	1.0 (0.7)	1.2 (0.7)	1.1 (0.7)	1.3 (0.7)
Fatigue (0-10)	4.7 (3.1)	5.0 (3.0)	5.7 (2.9)	5.9 (2.9)
Patient Global (0-10)	5.6 (2.9)	6.0 (2.9)	6.0 (2.9)	6.4 (3.0)
Depression (SF12 MCS < 45.6)	329 (35%)	54 (41%)	356 (54%)	123 (57%)
Poor sleep (0-10)	4.5 (3.4)	4.8 (3.3)	5.3 (3.2)	6.0 (3.1)

Effect of stress in year prior to diagnosis on outcomes at 12 months (N=1933).*

	Pain	Fatigue	Patient Global	Depression	Poor Sleep	HAQ-DI	DAS28 REM	Swollen Joints
Any Stress	0.27 (0.02, 0.53)	0.39 (0.12, 0.66)	0.25 (-0.01, 0.51)	1.55 (1.24, 1.95)	0.49 (0.21, 0.76)	0.05 (-0.01, 0.11)	1.02 (0.82, 1.27)	0.12 (-0.19, 0.42)
Total stressors	0.24 (0.12, 0.37)	0.32 (0.18, 0.45)	0.24 (0.11, 0.37)	1.30 (1.17, 1.45)	0.37 (0.24, 0.51)	0.05 (0.02, 0.08)	1.00 (0.90, 1.12)	0.05 (-0.10, 0.20)
0 (n=928, 48%)	REF	REF	REF	REF	REF	REF	REF	REF
1 (n=575, 30%)	-0.02 (-0.31, 0.28)	0.14 (-0.17, 0.46)	-0.04 (-0.34, 0.26)	1.31 (1.00, 1.71)	0.18 (-0.14, 0.50)	0.00 (-0.07, 0.06)	1.12 (0.87, 1.43)	0.06 (-0.29, 0.42)
2 (n=295, 15%)	0.54 (0.17, 0.92)	0.59 (0.19, 0.99)	0.54 (0.16, 0.92)	1.79 (1.29, 2.48)	0.80 (0.40, 1.20)	0.10 (0.02, 0.18)	0.99 (0.72, 1.35)	0.20 (-0.25, 0.65)
3 (n=88, 5%)	1.06 (0.45, 1.66)	0.73 (0.08, 1.39)	0.81 (0.19, 1.44)	1.90 (1.15, 3.16)	0.72 (0.06, 1.38)	0.18 (0.04, 0.32)	0.90 (0.53, 1.52)	0.23 (-0.50, 0.96)
4+ (n=47, 2%)	0.75 (-0.11, 1.61)	1.78 (0.84, 2.72)	1.02 (0.12, 1.91)	3.45 (1.70, 6.99)	2.10 (1.16, 3.04)	0.19 (0.00, 0.38)	0.46 (0.21, 1.03)	0.03 (-0.99, 1.05)

*Multivariable linear regression coefficient adjusted for age, sex, education, baseline fibromyalgia diagnosis and swollen joints.

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Janssen (CATCH)
Celgene (Clinical nurse)
Eli Lilly (Registry of biologics, Clinical nurse), Consultant of: Eli Lilly, Janssen, Novartis, Pfizer, Speakers bureau: Merck, BMS, Pfizer, Janet Pope Grant/research support from: AbbVie, Bristol-Myers Squibb, Eli Lilly & Company, Merck, Roche, Seattle Genetics, UCB, Consultant of: AbbVie, Actelion, Amgen, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Eicos Sciences, Eli Lilly & Company, Emerald, Gilead Sciences, Inc., Janssen, Merck, Novartis, Pfizer, Roche, Sandoz, Sanofi, UCB, Speakers bureau: UCB, Glen Hazlewood: None declared, Louis Bessette Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer, Roche, Sanofi, UCB Pharma, Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer, Roche, Sanofi, UCB Pharma, Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer, Sanofi, Carol Hitchon Grant/research support from: UCB Canada; Pfizer Canada, Diane Tin: None declared, Carter Thorne Consultant of: Abbvie, Centocor, Janssen, Lilly, Medexus/Medac, Pfizer
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OP0264-HPR PERSPECTIVES ON APPROACHES TO PREDICT THE DEVELOPMENT OF RHEUMATOID ARTHRITIS: A QUANTITATIVE ASSESSMENT OF PATIENTS AND THEIR FIRST DEGREE RELATIVES

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Background: There is considerable interest within the medical research community in the identification of individuals at risk of developing rheumatoid arthritis

(RA), to identify those who may benefit from preventive interventions. However, it is important to understand the views of those who may be candidates for such predictive tests, to inform the development of effective approaches. First degree relatives (FDRs) of patients with RA are at an increased risk of developing RA. RA patients can provide access to FDRs. Qualitative investigations have explored the views of these groups about predictive testing for RA[1,2], but quantitative approaches are needed to develop a robust understanding.

Objectives: To identify predictors of interest in predictive testing for FDRs and patients, and to assess the likelihood of patients communicating information about RA risk to their FDRs.

Methods: Surveys were completed by 482 RA patients and 397 of their FDRs. Patients were invited to complete the survey and to provide another to their relatives. Spearman's Rank Correlations were used to assess relationships between interest in predictive testing/ likelihood of risk communication and potential predictor variables.

Results: FDRs had a median age of 41 years, 64% were female. 57% were definitely interested and 36% were probably interested in taking a predictive test for RA. Several predictors were found to be associated with interest (table 1).

Table 1. Spearman's correlations for relatives' and patients' interest in predictive testing. After applying a Bonferonni adjustment, p values were taken as statistically significant at p≤0.003.

	FDRs		Patients	
Predictors of interest in predictive testing	rs	P	rs	P
Brief Illness Perception Questionnaire	0.11	0.03	0.09	0.05
Consequences	0.16*	0.002*	0.10	0.03
Timeline	0.09	0.07	-0.05	0.28
Personal control	-0.03	0.59	-0.02	0.68
Treatment control	-0.02	0.76	0.02	0.74
Identity	0.09	0.09	0.12	0.01
Concern	0.21*	<0.001*	0.16*	<0.001*
Coherence	0.11	0.03	0.007	0.88
Emotional	0.12	0.02	0.11	0.02
Information Seeking	0.35*	<0.001*	0.22*	<0.001*
Decision making	-0.05	0.33	0.07	0.13
Health literacy	0.03	0.52	0.02	0.62
Health numeracy	-0.06	0.23	-0.02	0.72
Brief Avoidance Coping Questionnaire	0.12	0.02	-0.01	0.76
Optimism	0.06	0.26	-0.07	0.12
Health anxiety	0.16*	0.001*	-	-
Perceived risk	0.37*	<0.001*	-	-
Rheumatoid Arthritis Impact of Disease	-	-	0.05	0.31

– not applicable

Patients had a median age of 65 years, 71% were female. 47% were definitely interested and 30% were probably interested in their children taking a predictive test. Several predictors were found to be associated with interest (table 1). On a Likert scale from extremely unlikely (0) to extremely likely (4), most patients indicated that they were likely to communicate RA risk information to their children (median score=3).

Conclusion: Interest in predictive testing for RA was high amongst FDRs, and factors including information seeking preference, RA risk perception, concern about RA, perceived consequences of RA and health anxiety were significantly associated with interest. Patients were also willing to communicate information about RA risk to their children. These findings increase understanding of perceptual variation in those at risk of RA, and will inform the development of information to support decision making in individuals considering predictive tests and preventive interventions. We are currently extending this preliminary analysis by building multivariate models incorporating a range of attitudes about predictive testing, assessing predictors of patients' likelihood of communicating to their FDRs about risk, and the relationship between patients' and FDRs' responses.

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OP0265-HPR FACTORS ASSOCIATED WITH MEETING WORK DEMANDS FOR INDIVIDUALS WITH RHEUMATIC DISEASES

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Background: Almost 65% of individuals with rheumatic diseases have severe fatigue with the majority of these reporting difficulties in work leading to absenteeism and early retirement. However, there is a lack of research investigating how different types of fatigue impact on work ability.

Objectives: To identify the prevalence of different types of fatigue and explore the association between different types of fatigue and various demands involved in work

Methods: A cross-sectional study was carried out with 234 individuals with rheumatic diseases currently in employment. Study measures examined demographics, different types of fatigue (general, physical reduced activity, reduced motivation and mental), ability to meet work demands, disease activity and quality of life.

Results: The majority of participants were female (70%), had rheumatoid arthritis (42.7%), were between 41-50 years (30.3%) and worked full-time (70%). One hundred and twenty-eight participants (55%) had severe fatigue. Physical fatigue was the most prevalent category of fatigue (Table 1). Participants reported managing 50% of their work demands with physical demands being the most challenging (Table 1). All types of fatigue were significantly associated with the total WRF score (Table 2). Mental fatigue had the strongest association with the total WRF score (r=0.53, p<0.001). On examining the impact of different types of fatigue on meeting work demands, mental fatigue was the most significant predictor of difficulty meeting work demands (β =1.6, SE=0.37, p<0.001)

Table 1. MFI and WRF total and category scores

WRF n=212	Total mean (SD)	Work Scheduling Demands mean (SD)	Output demands mean (SD)	Physical Demands mean (SD)	Mental Demands mean (SD)	Social Demands mean (SD)
	50.3% (19.0)	44.6% (25.8)	52.9% (22.1)	43.3% (27.9)	53.4% (22.5)	62.4% (17.7)
MFI n=220	**Total mean (SD)**	**Physical fatigue mean (SD)**	**Reduced activity mean (SD)**	**Reduced motivation mean (SD)**	**Mental fatigue mean (SD)**	
	13.4 (2.8)	12.5 (4.3)	10.1 (4.2)	10.2 (3.5)	10.3 (4.2)	

Table 2. Correlations for WRF and MFI fatigue categories

MFI Category	Correlations with total WRF	p-values
General fatigue	.53	<0.001
Mental fatigue	.57	<0.001
Physical fatigue	.48	<0.001
Reduced motivation	.48	<0.001
Reduced activity levels	.41	<0.001

Conclusion: Fatigue interferes with many aspects of work performance. However, this study identifies that mental fatigue is the greatest predictor of difficulty in managing work. Self-management interventions focusing on mental fatigue and work ability are required for individuals with rheumatic diseases to manage the demands of their work.

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OP0266-HPR WORK PRODUCTIVITY IN PATIENTS WITH AXIAL AND PERIPHERAL SPONDYLOARTHRITIS

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Background: Work disability is an important outcome in the treatment of Spondyloarthritis (SpA) since this disease affects people in the most productive stage of life.
Objectives: The aim of this study is to investigate the working status and the factors associated with work productivity loss (WPL) in patients with axial (axSpA) and peripheral SpA (pSpA).
Methods: Patients with SpA according to ASAS criteria were included consecutively in this multicentric cross-sectional study. Evaluation of activity through a visual analogue scale (0-100), enthesitis (LEI), functional capacity (HAQ and BASFI), disease activity (DAS28 and BASDAI), health status (ASAS Health Index) and quality of life (ASQoL) were calculated. The Ankylosing Spondylitis Disease Activity Score (ASDAS) was recorded. The Work Productivity and Activity Impairment Spondyloarthritis (WPAI SpA) questionnaire was used to assess work productivity.
Spearman's correlation coefficient (ρ) was used to assess the correlation with the percentage of WPL.
Results: 274 patients with SpA were recruited, 129 (47.1%) with axSpA and 145 (52.9%) with pSpA. 56.6% were women and 33.2% stopped working due to the underlying disease.
Among axSpA patients, 70% were radiographic and 30% non radiographic, mean age 45.5 (SD14) yrs, median disease duration 72 (IQR 36-144) months and diagnosis delay 20 (IQR 11-70) months. 45.7% were employed, median hours worked in the last week was 40 (IQR 25-45), median scores for absenteeism was 0% (IQR 0-2), presenteeism 30% (IQR 5-40), WPL 30% (IQR 10-52.5) and activity impairment 30% (IQR 10-50). A positive correlation was found between WPL and the following variables: HAQ (ρ:0.40, p<0.001), BASDAI (ρ:0.48, p<0.001), ASDAS (ρ:0.46, p<0.001), BASFI (ρ:0.59, p<0.001), ASQoL (ρ:0.60, p<0.0001), LEI (ρ:0.31, p:0.02) and ASAS health index (ρ:0.54, p<0.001).
Among pSpA patients, mean age was 52.3 (SD13) yrs, median disease duration 60 (IQR 14-120) months and diagnosis delay 12 (IQR 3-24) months. 46.9% were employed, median hrs worked in the last week was 30 (IQR 14-40), absenteeism 0% (IQR 0-7), presenteeism 30% (IQR 2.5-58), WPL 30% (IQR 5-52) and activity impairment 20% (IQR 0-40). A positive correlation was found between WPL and: HAQ (ρ:0.49, p<0.001), ASDAS (ρ:0.58, p<0.001), ASQoL (ρ:0.57, p<0.0001), DAS28 (ρ:0.50, p<0.001), LEI (ρ:0.36, p:0.04) and ASAS health index (ρ:0.52, p<0.001). No statistically significant differences were found in absenteeism, presenteeism, WPL and activity impairment between axSpA and pSpA.
Conclusion: Our study showed that WPL in this national cohort was 30% in both groups of patients and is associated with disease activity, enthesitis, health status, quality of life and functional ability.
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OP0267-HPR "I NEVER THOUGHT EXERCISE COULD HELP IMPROVE MY SLEEP": EXPERIENCES OF PEOPLE WITH RHEUMATOID ARTHRITIS ON THE IMPACT OF EXERCISE ON SLEEP

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Background: OMERACT has identified sleep quality as one of the key outcomes for people with RA [1]. Poor sleep and reduced total sleep time (TST) are common complaints among people with RA. Poor sleep can in turn lead to deterioration in function, reduce activity levels and also impact mental health. Although sleep and mental health outcomes have been identified as important, they are frequently not measured in clinical trials. Involving key stakeholders, like people with RA, is important when designing exercise interventions as it allows consideration of particular issues that may influence future intervention delivery. This study involved people with RA who participated in a pilot RCT group exercise class to improve sleep quality.
Objectives: To explore participants experiences of an exercise intervention in improving sleep quality and TST, to capture their reality.
Methods: A descriptive qualitative study design of face-to-face semi-structured interviews was employed. The interview schedule explored a number of areas: experience of the intervention; outcome measures used; views regarding the intervention; perceptions regarding exercise and sleep and the impact on sleep. Interviews were transcribed verbatim by a professional transcriber. Inductive thematic analysis was used as an analytical approach. Interview transcripts were read, notes made, and ideas formulated to facilitate coding. The research team searched for patterns, analysed and coded the data, and generated themes and sub-themes. Themes were reviewed by the research team to check if they worked in relation to the coded extracts and the entire data set. The COREQ checklist provided guidance.
Results: Twelve females participated with a mean age of 58 (SD 7.4); mean RA diagnosis of 9.9 (SD 7.4) years; moderate to severe disability (HAQ-DI: 1.5 (SD 0.60). Four main themes were generated: 1) Positive impact of exercise on sleep - *"I really didn't think any type of exercise would help me sleep better if I'm honest.";* 2) Positive experiences of exercise intervention to improve sleep -*"I learnt so much regarding walking that I didn't even think about.";* 3) Clear mental health benefits – *"If you don't sleep well then it will have a knock-on effect to your mental health"*; 4) Achieving empowerment and ownership when exercising - *"I feel empowered now and confident that I'm not doing harm to myself".* The findings demonstrated that participants were clearly surprised that exercise could improve sleep.
Conclusion: In a variety of inflammatory conditions exercise is recommended as an effective intervention for the treatment of sleeping disorders. Although there is a growing consensus that exercise will benefit sleep, research is severely lacking in those with RA. This study demonstrates that participants were clearly surprised that exercise could improve their sleep. Due to the multifactorial nature of RA, engaging in exercise may not only improve sleep quality but also mitigate some of its symptoms.
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OP0268-HPR RHEUMATIC DISEASE PATIENTS' PREFERENCES IN ADVERSE DRUG REACTION INFORMATION REGARDING BIOLOGICS

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Background: Patient-reported outcomes (PROs) are increasingly used in studies and medical practice to obtain information on patients' perspectives towards their treatment or disease. However, study outcomes are primarily directed at and shared with healthcare professionals, even though the results may also be relevant for patients.
Objectives: The objective of this study was to obtain insight in which results patients with immune-mediated inflammatory diseases (IMIDs), including inflammatory rheumatic disease patients, prefer to receive after participating in the Dutch Biologic Monitor.
Methods: The Dutch Biologic Monitor is a PRO-based prospective cohort event monitoring study focused on adverse drug reactions (ADRs) [1]. A survey was conducted among the participants of the Dutch Biologic Monitor who wanted to be informed about the results. Patients' preferences were identified using twelve statements and rated with five-point Likert-type scales. Averages described the preference per statement. Preference for the results per IMID or altogether was assessed using Mann-Whitney U Test.
Results: Respondents (N=591, response rate 67.6%) preferred results per IMID over aggregated results (p=<0.001). Information on whether patients with the same IMID experience ADRs (average 4.5), which biologics are most likely to cause ADRs (4.4) and whether the ADRs subside or disappear (4.4) were regarded as most interesting. Outcomes of patients with other IMIDs (3.5), patient characteristics (3.7) and injection site reactions (3.8) were least interesting.

Table 1. Respondent characteristics.

	Characteristics	All		Inflammatory rheumatic disease patients	
		(*n*=591)	(%)	(*n*=453)	(%)
	Female gender, *n* (%)	353	(59.7)	286	(63.1)
	Age, median (IQR), years	59.0	(51.0-67.0)	60.0	(51.0-67.5)
Biologics	Adalimumab	220	(37.2)	164	(36.2)
	Etanercept	196	(33.2)	189	(41.7)
	Infliximab	43	(7.3)	8	(1.8)
	Tocilizumab	21	(3.6)	17	(3.8)
	Ustekinumab	21	(3.6)	7	(1.5)
	Other	90	(15.2)	68	(15.0)
Combination therapy	Methotrexate	195	(33.0)	183	(40.4)
	Corticosteroids	65	(11.0)	51	(11.3)
	Thiopurines	41	(6.9)	10	(2.2)
	No combination therapy	231	(39.1)	157	(34.7)
	Other	123	(20.8)	106	(23.4)
Indications for biologic therapy	Rheumatoid arthritis	277	(46.9)	277	(61.1)
	Psoriatic arthritis	111	(18.8)	111	(24.5)
	Ankylosing spondylitis/ axSpA	83	(14.0)	83	(18.3)
	Other	159	(26.9)	17	(3.8)

IQR: interquartile range; axSpA: axial spondyloarthritis.

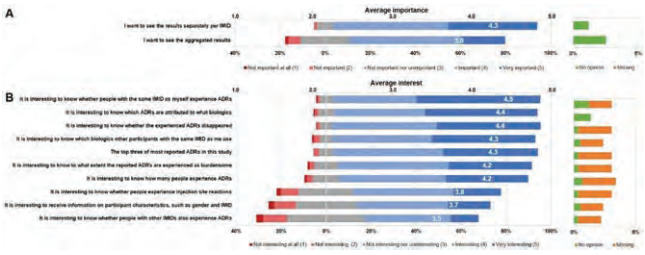


Figure 1. The preferences of patients on the communication of the reported adverse drug reaction information resulting from the Dutch Biologic Monitor.

Conclusion: Participants of the Dutch Biologic Monitor that use a biologic for their IMID prefer to receive ADR information tailored to their own biologic and IMID. Furthermore, they want to obtain insight in the course of ADRs. Therefore, we advocate to generate disease-specific information on ADRs for IMID patients.

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OP0269-HPR

ASSOCIATION OF SARC-F PERFORMANCE WITH COMORBIDITIES, PHYSICAL DISABILITY AND LOWER ALBUMIN LEVELS IN SYSTEMIC SCLEROSIS PATIENTS

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Background: Systemic sclerosis (SSc) is a multisystem autoimmune disease of complex etiopathogeny, heterogeneous in its phenotypic expression and with a limited prognosis (1). The loss of muscle mass is a serious consequence of many chronic diseases and also is observed in SSc (2). This body composition alterations results in weakness, limitations and physical disability (3). SARC-F simple questionnaire, validated, is a key diagnostic feature for the fast assessment of geriatric syndromes associated with skeletal muscle wasting. However, there is no data about the SARC-F in SSc.

Objectives: To assess the association between the SARC-F questionnaire with clinical features in patients with systemic sclerosis (SSc).

Methods: Ninety-four patients diagnosed with systemic sclerosis were recruited and evaluated. Sarcopenia was assessed by the SARC-F questionnaire. Clinical features as disease duration time, comorbidities, body mass index (BMI), functional capacity by the Health Assessment Questionnaire (HAQ), inflammatory markers (C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), creatine phosphokinase (CPK), hemoglobin, creatinin and albumin) were medical record. Frequency analysis, descriptive analysis and Pearson's correlation were performed. Statistical significance was considered as p<0,05.

Results: Of the 94 patients analyzed, most were women (87/94;92.6%) with mean age of 60.5±10.3 years, median disease duration time of 11.2 (7.5-18.9) and median number of comorbidities was 1.00 (1.00-2.00). The mean of BMI was 25.9±4.7 Kg/m^2. Twenty-one of the patients were classified as active or passive smokers, thirty-five said they were former smokers and thirty-eight never smoked. Sixty-nine (80, 2%) out of the ninety-four patients in the study had at least one type of comorbidity (mean 1, 44±1, 04). Eighty-three patients (88.3%) showed a SARC-F score without signs suggestive of sarcopenia (0-5) and eleven patients (11.7%) showed suggestive to sarcopenia (6-10). In HAQ, fifty-seven (60.6%) patients had mild incapacity, thirty-five (37.2%) had moderate incapacity, and two patients (2.2%) had severe incapacity. Higher SARC-F scores were associated with greater number of comorbidities (r=0.2; p=0.027), higher physical disability by HAQ (r= 0.5;p=0.000) and lower albumin levels (r= -0.3; p= 0.048). On other hand, SARC-F was not associated with time of diagnosis, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), creatine Phosphokinase (CPK), hemoglobin, hematocrit and creatinine.

Conclusion: SARC-F scores were associated with comorbidities, physical disability and lower albumin levels in systemic sclerosis patients. Considering that comorbidities, physical disability and the albumin deficit enhances the patient's muscle loss, SARC-F appears to be a good tool to screen sarcopenia risk factors in systemic sclerosis patients. Longitudinal studies are necessary to validate the SARC-F questionnaire in this population.

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Other orphan diseases

OP0270

TRHEUMA REGISTRY EXPLORES CHARACTERISTICS AND SUITABLE DIAGNOSTIC AND THERAPEUTIC MANAGEMENT OF RHEUMATIC IMMUNE-RELATED ADVERSE EVENTS (IRAES)

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Background: Reports of rheumatic immune-related adverse events (irAEs) in patients receiving immune checkpoint inhibitors (ICPi) have recently attracted new attention to the complex interrelations of malignancies and *rheumatic and musculoskeletal diseases (RMDs)*. Since those two entities represent two sides of a dysregulated immune response, further research on rheumatic irAEs and mechanisms underlying the better tumor response rates in irAE-affected patients may contribute to a better understanding of the different pathophysiology characterizing tumor and rheumatic disease.
Objectives: Given the heterogeneity of the patient population with rheumatic irAEs, a registry-based study has been conducted to provide first evidence regarding characteristics of rheumatic irAEs and further insights into the optimal diagnostic and therapeutic management of rheumatic irAEs.
Methods: The TRheuMa registry is a long-term, open-end observational study of a patient cohort suffering from rheumatic symptoms as a result of ICPi or other cancer therapies. The TRheuMa registry is one of the three subregistries of the MalheuR project, a registry-based study initiated in July 2018 at the at the university hospital Heidelberg to explore interrelations of malignancies and RMDs.
Results: Over 18 months, 52 of 63 patients in the TRheuMa registry were recruited with a rheumatic irAE under ICPi treatment (pembrolizumab n=21, nivolumab n=28, ipilimumab n=11, durvalumab n=1, atezolizumab n=2, avelumab n=1, history of >1 ICPi n=11). Of the 52 patients, 22 (42.3%) had non-small cell lung cancer and 23 (44.2%) had a melanoma. Eight (15.3%) patients experienced a flare of a preexisting RMD under ICPi treatment. The remaining 44 patients with *de novo* irAEs were characterized by rheumatoid arthritis-like (20.5%) or polymyalgia rheumatica-like (18.1%) and psoriatic or other spondyloarthritis-like phenotypes (50.0%). However, laboratory findings differed from classical RMDs with elevated CRP-levels in 73.1% particularly in psoriatic arthritis-like, but not necessarily in polymyalgia rheumatica-like irAEs. On the contrary, autoantibody positivity was very rare. The majority of patients (78.8%) showed signs of inflammation upon ultrasound examination.
Based on the severity of signs and symptoms as well as treatment response, we developed a therapeutic algorithm for rheumatic irAEs: non-steroidal anti-inflammatory drugs and/or low dosed glucocorticoids (≤10mg prednisone equivalent) as first treatment step were sufficient for 75% patients, whereas 17.3% required higher dosed glucocorticoids and 11.5% patients required further treatment with a cs- or bDMARD. In two cases ICPi-treatment was discontinued on patients' request due to the pain and functional impairment caused by the rheumatic irAE, although a satisfactory symptom control was reached in the further course.
Complete remission of cancer was observed in 43.5% of melanoma patients, 66.7% experienced additional severe irAEs in other organ systems.
Conclusion: Overall, data from the TRheuMa-registry show that rheumatic irAEs mostly resemble classical RMDs, however show distinct characteristics. Our diagnostic and therapeutic management of rheumatic irAEs demonstrated efficacy in the majority of patients. These findings contribute to the further understanding of rheumatic irAEs and malignancies. Future research agenda includes a correlation of irAE severity with tumor response.
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OP0271 REAL-WORLD CLINICAL BURDEN AND GLUCOCORTICOID USE IN PATIENTS WITH POLYMYALGIA RHEUMATICA

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Background: Polymyalgia rheumatica (PMR) is a chronic inflammatory condition characterized by aching and morning stiffness in the neck, shoulders and pelvic girdle. It is a common inflammatory rheumatic disease in patients age >50 years, particularly women. While giant cell arteritis (GCA) is present in 9–21% of PMR cases, many PMR patients have symptoms independent of GCA. Current treatment options are limited to long-term glucocorticoid (GC), however, with risks of GC-related complications, including cardiovascular disease, osteoporosis, and diabetes mellitus.
Objectives: To compare GC use and subsequent GC-related complications in patients with PMR vs a general population (GnP) cohort.
Methods: This retrospective, observational cohort study was based on Optum's de-identified Clinformatics® Data Mart Database (study period 01Jan2006-30June2018). The PMR cohort included patients with ≥1 inpatient or ≥2 outpatient claims ≥30 days apart with PMR related diagnosis codes (ICD-9: 725.xx or ICD-10: M35.3x) between 01Jan2006–30June2017 (patient identification period) during which first occurrence of a PMR-related medical claim was set as the index date (ID). Patients with ≥1 medical claim related to rheumatoid arthritis (RA) or GCA during the study period were excluded. The GnP cohort included patients without any RA, GCA or PMR diagnosis codes during the study period, with their ID set as 12 months from the start of continuous health plan enrollment. Patients in both cohorts were required to be age ≥50 years (on ID) with continuous health plan enrollment ≥12 months pre- and post-ID. Cohorts were 1:1 propensity score matched. GC use and incidence of GC-related complications were assessed from GC initiation, starting from the baseline period (12-months pre-ID) through to the end of GC use during the post-index period (i.e. the end of data availability, end of the study period or death [whichever occurred first]). Mean, standard deviation (SD) and median values for continuous variables, and frequency (n and %) for categorical variables were compared between the matched cohorts. Wilcoxon sum rank tests and *t*-tests on continuous variables and Chi-square tests or Fisher's exact tests on categorical variables between matched cohorts were conducted. Duration of GC use was analyzed using the Kaplan-Meier method and compared between matched cohorts using log-rank tests.
Results: In each of the PMR and GnP cohorts, 16,865 patients were included. In both matched cohorts, median age was 76 years, median Elixhauser comorbidity index score was 2.0, and the majority (~65%) were women. The median follow-up duration was 45 months and 51 months in the PMR and GnP cohorts, respectively. A higher proportion of patients in the PMR cohort than the matched GnP cohort (90.4% vs 62.8%; $p<0.001$) used GC. The mean (SD) duration of GC therapy was significantly longer in the PMR cohort than in the matched GnP cohort (242.1 [±317.2] days vs 35.5 [±124.6] days; $p<0.001$). Although patients in the PMR cohort had a lower average daily dose of GC (prednisone equivalent) vs the GnP cohort (mean [SD] mg 16.3 [± 21.9] vs 27.8 [±24.5], respectively [$p<0.0001$)], the cumulative GC dose was significantly higher in the PMR cohort than the GnP cohort (2125.4 [±3689.5] mg vs 476.6 [±1450.9] mg; $p<0.001$). This indicates PMR patients used chronic low dose GC while the GnP patients utilized higher dose GC burst therapy less frequently. The number of incident complications associated with GC use were significantly greater in the PMR cohort, and included hypertension, diabetes, skin toxicity, infections, neuropsychiatric effects, endocrine abnormalities, renal dysfunction/ failure, ocular effects, and cardiovascular disease ($p<0.05$).
Conclusion: The overall GC burden in patients with PMR is high. With a higher incidence of GC-related comorbidities among PMR patients, early onset of these complications may be a significant contributor to long-term healthcare costs in these patients.
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OP0272 LONG-TERM EFFICACY AND SAFETY OF CANAKINUMAB IN PATIENTS WITH COLCHICINE-RESISTANT FAMILIAL MEDITERRANEAN FEVER: RESULTS FROM THE RANDOMISED PHASE 3 CLUSTER TRIAL

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Background: Familial Mediterranean Fever (FMF) is a hereditary autoinflammatory disease associated with mutations in the *MEFV* gene. Colchicine is the cornerstone of current therapy for FMF; however, a subset of patients are resistant or intolerant to it. Previously published results from the CLUSTER trial [NCT02059291] demonstrated that canakinumab, a fully human anti-interleukin-1β monoclonal antibody, was effective in controlling and preventing flares in patients with colchicine-resistant familial Mediterranean fever (crFMF).[1]
Objectives: To evaluate the long-term efficacy and safety of canakinumab to treat patients with crFMF during Epoch 4 of the CLUSTER study.
Methods: Patients with active crFMF (baseline flare) were enrolled in the CLUSTER study. During Epoch 4 (weeks 40 to 113), patients received open-label canakinumab 150 or 300 mg, every 4 or 8 weeks (q4w or q8w). Patients started Epoch 4 on the same regimen that they were receiving at the end of Epoch 3, and stepwise up-titration of canakinumab was allowed in patients who experienced a flare, to a maximum dose of 300 mg q4w. We evaluated disease activity every 8 weeks using the physician global assessment of disease activity (PGA), counting the number of flares (defined as PGA ≥2 and CRP >30 mg/L), and measuring serum concentrations of C reactive protein (CRP) and serum amyloid A (SAA). Safety was assessed by the determination and classification of adverse events (AEs). We analysed safety and efficacy separately in two subgroups of patients receiving a cumulative dose of canakinumab lower than 2700 mg, or equal or higher than 2700 mg.
Results: Of the 61 patients with active crFMF who started the CLUSTER study, 60 entered Epoch 4 and 57 completed it. During the 72-week period, 35/60 (58.3%) patients experienced no flares, and 23/60 (38.3%) had one single flare, as compared with a median of 17.5 flares per year reported at baseline. The incidence of flares was similar in the two cumulative dose groups. PGA scores indicated no disease activity for the majority of patients throughout the study, in both cumulative dose groups. 23/57 (40%) of patients remained in the lower dosing group (150 mg q8w) until study end, whereas 9/57 (16%) required the highest dose allowed (300 mg q4w). Patients with higher body weight had an increased probability to require up-titration of canakinumab to control disease activity. Median CRP concentrations were lower than 10 mg/L at every time point in both cumulative dose groups, while median SAA concentrations remained in the 16-70 mg/L range, and were higher in the group receiving ≥2700 mg canakinumab (Figure 1). No opportunistic infections, renal disease caused by amyloidosis, new or unexpected AEs were reported.

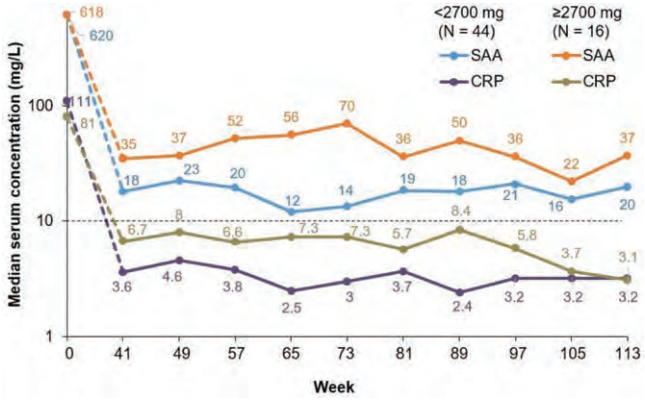


Figure 1. SAA and CRP blood levels in Epoch 4 of the CLUSTER study, in two subgroups of patients treated with a cumulative dose of canakinumab <2700 mg or ≥2700 mg

Conclusion: Patients with crFMF treated with canakinumab during 72 weeks experienced a minimal incidence of flares and good control of clinical disease activity, with no new safety signals reported.
References:
[1] De Benedetti F et al. *N Engl J Med* 2018;378:1908–19.
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OP0273 ADHERENCE TO COLCHICINE TREATMENT AND COLCHICINE RESISTANCE IN A MULTICENTRIC FMF NATIONAL COHORT

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Background: Colchicine is the standard treatment for Familiar Mediterranean Fever (FMF), however about 5% of patients experience colchicine resistance. There is no standard definition of colchicine resistance. Recently a panel of experts elaborated a new definition based on a Delphi consensus approach.
Objectives: We aim to describe main features of the disease and clinical outcome of a cohort of FMF patients with particular interest on the colchicine resistance and tolerability according to the definitions proposed by the recent consensus.
Methods: Since November 2009, 425 Italian pediatric and adult FMF patients (pts) from 13 centers were enrolled in a national longitudinal cohort study, using the international EUROFEVER registry. Demographic, genetic and clinical data, including response to treatment, were analyzed. Supplementary information on health related quality of life and treatment adherence was also collected by a specific questionnaire.
Results: Complete information were available in 341 pts (189 M and 152 F, 211 children and 120 adults). The median age at disease onset was 5.0 years (1 m-59 y); the mean diagnostic delay was 8.7 y (range 0-61 y). The median age at enrollment was 12.1 y (range 3 m - 82 y). The MEFV genotype was the following: 103 (30.2%) pts carried biallelic pathogenic variants; 59 (17.3%) one pathogenic variants and one VOUS /LB variant; 27 (7.9%) had biallelic VOUS/LB variants; 97 (28.45%) were heterozygous for pathogenic variants; 30 (8.8%) were heterozygous for VOUS/LB, 25 (7.33%) were genetically negative.
Colchicine treatment was used in 280 pts; during treatment, biologic treatment (anti-IL1) in 22 pts. 61 pts received NSAID or steroid on demand.
We analyzed the behavior of the pts treated with colchicine according to the statements on colchicine resistance/intolerance defined by Ozen et al (1) (Table 1).

Table 1.

Adherence	62% displayed a total adherence (> 90% of prescription); 10.8% a good adherence (50-89% of prescriptions); 1.9% poor adherence (< 50% of prescriptions); 0.9% no adherence
Dose adjustment criteria/ Recommended maximum colchicine dose	Mean colchicine dose: Pts <5 years: 0.57mg/de (std. dev. 0.18) 5-10 year: 0.77mg/die (std. dev. 0.23) 10-18 years: 1.1mg/die (std. dev. 0.39) Adults: 1.16 mg/die (std. dev. 0.37) Pts with a dose inferior to the minimum recommended dose 5-10 years: 2.5% 10-18 years: 15% Adults: 4%
Resistance to Colchicine	Resistance was be defined as persistence of fever attacks, despite optimal treatment. 41.6% pts had a complete disease control 32.8% Pts had < 1 episode/month for 3 months 25.5% had ≥1 episode/month for 3 months
Inclusion of secondary amyloidosis in the definition of colchicine resistance	5 adult pts (1.5%) displayed amyloidosis
Colchicine intolerance	11 pts (3.2%) withdraw colchicine because of drug intolerance
Patient quality of life and patient-reported outcomes	20.7% of pts experience fatigue or chronic pain, 16.9% limitations in daily activities, and 16.9% have lost school/ work days.

Conclusion: Almost 58% of FMF pts display disease activity despite colchicine treatment. The treatment is generally under-dosed, especially in children. The adherence and the compliance to the treatment is generally good.
References:
[1] Ozen S et all. Recommendation on colchicine dosing and definition of colchicine resistance/intolerance in the management of FMF. Pediatric Rheumatology, 2019.
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Giovanna Fabio: None declared, Laura Obici: None declared, Maria Alessio: None declared, Donato Rigante: None declared, Luca Cantarini: None declared, Antonella Insalaco: None declared, Marco Cattalini: None declared, Maria Cristina Maggio: None declared, Gabriele Simonini: None declared, Alma Nunzia Olivieri: None declared, Serena Pastore: None declared, Maddalena Lancieri: None declared, Nicolino Ruperto Grant/research support from: Bristol-Myers Squibb, Eli Lily, F Hoffmann-La Roche, GlaxoSmithKline, Janssen, Novartis, Pfizer, Sobi (paid to institution), Consultant of: Ablynx, AbbVie, AstraZeneca-Medimmune, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Eli Lily, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, Sanofi, Servier, Sinergie, Sobi, Takeda, Speakers bureau: Ablynx, AbbVie, AstraZeneca-Medimmune, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Eli Lily, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, Sanofi, Servier, Sinergie, Sobi, Takeda, Marco Gattorno Consultant of: Sobi, Novartis, Speakers bureau: Sobi, Novartis

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OP0274 CLINICAL ASPECTS, LABORATORY CHARACTERISTICS AND TREATMENT RESPONSES OF AA AMYLOIDOSIS: SINGLE CENTER EXPERIENCE WITH 163 PATIENTS

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Background: AA amyloidosis has been associated with uncontrolled chronic inflammatory diseases such as rheumatoid arthritis (RA), ankylosing spondylitis (AS), inflammatory bowel disease (IBD) and hereditary periodic fever syndromes, and the most common cause is familial Mediterranean fever (FMF) in Turkey.

Objectives: We herein aimed to evaluate clinical and laboratory characteristics and treatment responses of patients with AA amyloidosis retrospectively in a tertiary referral center.

Methods: Study group was consisting of patients with biopsy proven AA amyloidosis, and their data were recorded from their charts. Treatment responses were categorized as follows: *complete response* was defined as no increase in serum creatinine and a proteinuria below 1gr/day; *partial response* as 50% decrease in proteinuria; and *stable disease* as no significant change in serum creatinine and proteinuria. Progressive disease was defined as increase in serum creatinine and/or proteinuria under treatment.

Results: 173 patients were identified, and 10 patients with no biopsy result and/or missing data were excluded. A total of 163 patients (79 females, 84 males) were included in the study. Median age of patients was 45.4, and median age at diagnosis of amyloidosis was 33.5. Most common cause of amyloidosis was FMF (78.5%), followed by idiopathic cases (7.9%) and patients with AS (4.9%). A quarter (26%) of amyloidosis patients had a family history for AA amyloidosis, and 59% of patients with FMF had a family history of FMF. Amyloidosis was confirmed by renal biopsy in 76.1%, by gastrointestinal (GIS) biopsy in 11.7%, and by other biopsies in the remaining. Renal involvement was documented in 160 (98.2%) patients, while GIS involvement in 20.9%, heart in 13.5%, thyroid in 3.7% and bone marrow in 3.1%. In FMF patients, most common MEFV mutation was M694V (77.7%); and 66.7% of the patients had homozygous, 14.6% had compound heterozygous, and 18.7% heterozygous exon 10 variants. Mean age at diagnosis of amyloidosis was earlier in homozygotes (29.1) and compound heterozygotes (32.3) compared to heterozygotes (43.9) (p = 0.001). There was no difference in treatment responses, organ involvement, progression to end stage renal disease (ESRD) and mortality between monoallelic and biallelic exon 10 mutations (p = 0.42). While 44.3% (n = 70) of patients had chronic renal disease (CRD) at time of diagnosis, ESRD developed in 45.3% (n = 73) of patients. During follow-up, 55 patients underwent renal transplantation and recurrence of renal amyloidosis occurred in 24% of them. Mean creatinine and proteinuria levels at time of diagnosis were higher in patients with ESRD than those without ESRD (p <0.001, p = 0.03 respectively). Progression to ESRD was significantly higher in patients with GFR≤60 ml/min at time of admission (%14.5 vs %41.7, p=0.005, Figure 1). A total of 113 (70.2%) patients used biological agents, most commonly used biological agent was anakinra (n = 81). Canakinumab was used in 17 and other biological agents in 17 patients. Complete response was observed in 49.1%, partial response was observed in 6.2%, and progressive progression was observed in 21.7%. GIS and cardiac involvements were associated with progressive course (p <0.001) and increased mortality (p = 0.002, p <0.001, respectively), and overall mortality rate was 8.7%.

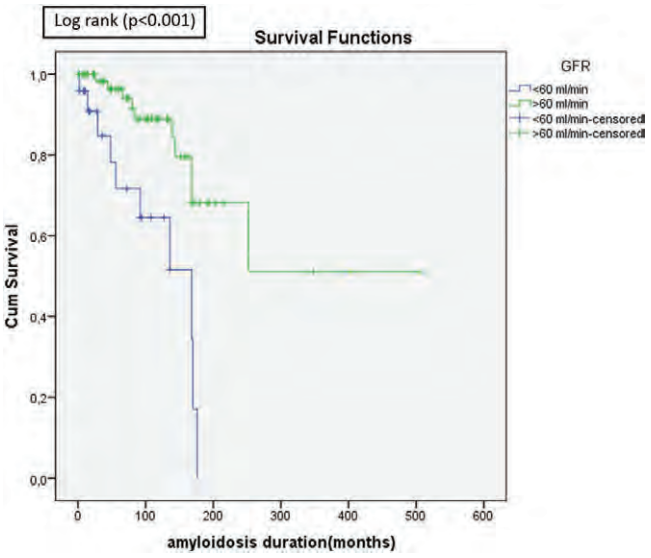


Figure 1 : Survival graphic of AA amyloidosis patients who developed ESRD according to their baseline GFR status

Conclusion: Increased rate of ESRD and progression of amyloidosis findings in patients who presented with GFR<60 ml/min emphasize the importance of early diagnosis. Although mortality rate is very high in patients with AA amyloidosis due to FMF disease, it may be possible to reduce mortality with an effective treatment.

Disclosure of Interests: None declared

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OP0275 REAL-WORLD CLINICAL BURDEN AND GLUCOCORTICOID USE IN PATIENTS WITH GIANT CELL ARTERITIS

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Background: Giant cell arteritis (GCA) is a rare form of vasculitis usually manifesting in people aged ≥50 yr and is more common in women. Symptoms include headache, jaw claudication, fatigue, polymyalgia; and blindness if untreated. While risks of complications can be reduced with promptly administered high-dose glucocorticoids (GC; 20-60 mg for 2-4 wk, then slowly tapered), further risks of high GC exposure and related complications over the course of therapy remain.

Objectives: To compare GC use and GC-related complications in GCA patients (pts) vs a general population (GnP) cohort.

Methods: This retrospective, observational cohort study was based on Optum's de-identified Clinformatics® Data Mart Database (01/01/06-30/06/18, study period). The GCA cohort included pts with ≥1 inpatient or ≥2 outpatient claims ≥30 days apart with GCA-related diagnosis codes (ICD-9: 446.5x/ICD-10: M31.6x) between 01/01/06-30/06/17 (pt identification period) during which first occurrence of a GCA-related medical claim was set as index date (ID). The GnP cohort included pts without any medical claims for rheumatoid arthritis, GCA or polymyalgia rheumatica diagnosis codes during the study period, with their ID set as 12 mo from start of continuous health plan enrollment. Pts in both cohorts were required to be age ≥50 yr (on the ID) with continuous health plan enrollment ≥12 mo pre- and post-ID. Cohorts were 1:1 propensity score matched. GC use and incidence of GC-related complications were assessed from GC initiation, starting from the baseline period (12-mo pre-ID) to the end of GC use during the post-index period (ie the end of data availability, end of the study period, or death, whichever occurred first). Descriptive analyses included mean, standard deviation (SD) and median values for continuous variables, and frequency (n and %) for categorical variables. Continuous variables were compared between matched cohorts using *t*-tests and Wilcoxon sum rank tests. Categorical variables were compared between matched cohorts using Chi-square tests or Fisher's exact tests. Duration of GC use was analyzed using the Kaplan-Meier method and compared between matched cohorts using log-rank tests.

Results: There were 6071 pts included in each of the GCA and matched GnP cohorts; median age per cohort was 76 yr, median Elixhauser comorbidity index score was 3.0, and the majority (~75%) were women. The median follow-up duration was 44 and 48 mo in the GCA and GnP cohorts, respectively. A higher proportion of pts in the GCA cohort than the GnP cohort (90.6 vs 63.8%; $p<0.001$) used GC. The mean (SD) duration of GC therapy was 230.5 (±326.8) days in

the GCA cohort vs 36.3 (±107.2) days in the GnP cohort (p<0.001). Although the mean (SD) daily dose of GC (prednisone equivalent) was similar in both cohorts (27.6 [±28.20] vs 27.7 [±25.18] mg), the mean (SD) cumulative GC dose was significantly higher in the GCA cohort than the GnP cohort (3503.0 (±4622.6) mg vs 503.7 (±1593.51) mg; p<0.001). This indicates that GCA pts had chronic GC exposure over the study period while GnP pts likely utilized higher dose GC burst therapy less frequently. The number of incident complications associated with GC use were significantly greater in the GCA cohort, and included hypertension, diabetes, skin toxicity, infections, neuropsychiatric effects, gastrointestinal complications, ocular effects, and cardiovascular disease (p<0.05).

Conclusion: The overall GC burden in pts with GCA is significantly higher than the general population and may result in downstream complications related to GC exposure. The incidence of GC-related complications was statistically significantly higher in GCA pts compared with GnP pts, even with a short duration of GC use. The early onset of these complications may be a significant contributor to long-term healthcare costs in GCA pts.

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OP0276 CLINICAL PATTERNS AND FOLLOW-UP OF INFLAMMATORY ARTHRITIS AND OTHER IMMUNE-RELATED ADVERSE EVENTS INDUCED BY CHECKPOINT INHIBITORS. A MULTICENTER STUDY

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Background: Immune checkpoint inhibitors (ICI), such as anti-CTLA-4and anti-PD1/PD-L1 monoclonal antibodies, have produced impressive clinical results in different types of cancer. However, immune-related adverse events (irAEs) may develop a wide spectrum of disabling syndromes. Knowledge of different rheumatic irAEs induced by ICI is increasing over the last years, however clinical patterns, time to onset of different irAEs according to treatment and follow-up are less well known.

Objectives: To describe different clinical patterns of rheumatic irAEs induced by ICI and their rheumatic and oncologic outcomes.

Methods: We included consecutive patients with rheumatic irAEs from 3 different referral centers in Barcelona with special emphasis in articular irAEs. Four main clinical syndromes were identified: inflammatory arthritis (IA), non-inflammatory arthralgias (NIA), psoriatic arthritis (PsA)-like and polymialgia (PMR)-like. We conducted a baseline visit and then follow-up in order to determine their clinical pattern, treatment response and outcome. Longitudinal visits were done from January 2017 to January 2020. Patients with other non–articular diagnosis were not included in the follow-up analysis.

Results: We included 55 patients. A total of 34 patients were male (61.8%) with a mean age of 65.0 ± 11.4 years. Oncologic underlying diagnosis was lung carcinoma in 24 (43.6%) patients, followed by melanoma in 17 (29%), urothelial cancer in 4 (7.3%), breast in 2 (3.6%) and 2 (3.6%) acute myeloid leukemia among others. Seven (12.7%) patients received ICI as combined therapy. Different ICI were used including: Pembrolizumab in 21 (38.2%), Nivolumab 13 (23.6 %), Atezolizumab 6 (10.9%), Nivolumab + ipilimumab 5 (9.0%), Durvalumab 3 (5.5%), Pembrolizumab + epacadostat in 2 (3.6%), 2 anti TIM3, Atezolizumab+ Ibatasertib, Avelumab and Ipilimumab in one case each. 12 out of 55 patients had an underlying rheumatic disease before ICI treatment. Eleven patients developed other irAEs before or at the same time as rheumatic syndromes (mainly colitis and thyroiditis). Main rheumatic irAE included: IA in 23 (41.8%), NIA in 16 (29.1%), PsA-like in 6 (10.9%), PMR-like in 5 (9.1%) among others. Time from ICI to irAEs was 8.3 ± 8.4 months(mo). irAE presented earlier in patients with combined ICI therapy than in patients with monotherapy (6.5 ± 4.0 vs 8.6 ± 8.9 mo, p=NS, Figure 1A). Time (in mo) from ICI initiation to irAE onset was different according to treatments. For Nivolumab 10.0 ± 10.6, Anti TIM3 10.0 ± 1.4, Durvalumab 9.0 ± 2.0, Ipilimumab 7.98 ± 9.21, Pembrolizumab 7.28 ± 7.53, Avelumab 6.0 and Atezolizumab 4.4 ± 5.38 mo (Figure 1B). Time from ICI initiation and onset also differs among rheumatic irAEs (Figure 2). Mean time follow-up was 13.4 ± 10.9 mo. At the last visit, 45% were under GC, mean dose of 3.6 mg/d (range 0-40). DMARD were needed in 15% of patients (6 patients MTX, 1 with LEF and 1 SFZ). At the last visit, 11 (22.9%) patients remain with persistent arthritis, 25% intermittent flares and 52% had a self-limited pattern. Regarding oncologic outcome, 30.2% were on remission, 30.2% in partial response and 39.6% with tumor progression. Eleven (20%) of patients died.

Conclusion: We described different clinical patterns according treatment and irAEs. Combined ICI therapy and patients treated with Atezolizumab had earlier onset of symptoms. Vasculitis and PMR-like syndromes appear in earlier phases. After a mean follow-up of around 1 year, one-quarter of the patients remain with persistent arthritis and 15% require DMARD therapy.

Figure 1

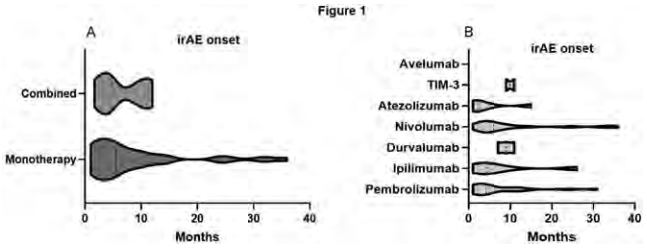
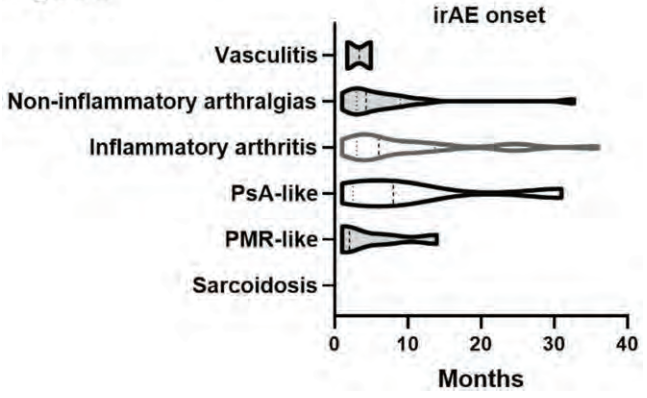


Figure 2



Disclosure of Interests: Jose A. Gómez-Puerta Speakers bureau: Abbvie, BMS, GSK, Lilly, Pfizer, Roche, Carolina Perez-Garcia: None declared, David Lobo Prat: None declared, Roberto Gumucio: None declared, Fabiola Ojeda: None declared, Ana Milena Millán Arciniegas: None declared, Sebastian Rodriguez Garcia: None declared, Virginia Ruiz Speakers bureau: Lilly, Pfizer, Héctor Corominas Speakers bureau: Abbvie, Lilly, Pfizer, Roche

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OP0277 AURORA PHASE 3 STUDY DEMONSTRATES VOCLOSPORIN STATISTICAL SUPERIORITY OVER STANDARD OF CARE IN LUPUS NEPHRITIS (LN)

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Background: Voclosporin (VCS) is a novel high potency calcineurin inhibitor (CNI) with a favorable metabolic profile and a consistent predictable dose response potentially eliminating the need for therapeutic drug monitoring. LN occurs more frequently and is more severe in Hispanic/Latino ethnicity SLE patients. The recently completed phase 3 AURORA study builds on the favorable efficacy seen in the Phase IIb AURA-LV study in patients with active LN.

Objectives: Document efficacy and safety of VCS vs placebo over one year when used with 2 grams of MMF daily and a rapid steroid taper in patients with active LN.

Methods: AURORA is a Phase III multicenter, randomized, double-blind, placebo-controlled 52-week study of active LN patients. Patients were randomized 1:1 to VCS (23.7 mg BID) or placebo in combination with mycophenolate (MMF, 1 g BID) and rapidly tapered oral steroids. The primary endpoint was renal response (RR) at 52 weeks, defined as UPCR of ≤ 0.5 mg/mg, eGFR ≥ 60 mL/min, or no confirmed decrease from baseline in eGFR of > 20%, presence of sustained, low dose steroids and no administration of rescue medication. Ethnicity subgroup analyses of RR was also undertaken given the higher severity of disease in the Hispanic/Latino LN patients.

Results: There were 357 patients enrolled, 88% female, median age of 31 and 33% of Hispanic/Latino ethnicity. Renal response by intention to

treat analysis at 52 weeks was 40.8% for the voclosporin arm and 22.5% for the control arm (OR: 2.65; 95% CI: 1.64, 4.27; p< 0.001); therefore, AURORA met its primary endpoint. These findings were consistent with those observed in the previously completed pivotal AURA-LV study. Ethnicity subgroup analysis of RR at 52 weeks noted benefit of VCS in both Hispanic/Latino (VCS 38.6% and control 18.6%, p=0.0062, OR 3.45) and non-Hispanic/Latino patients (VCS 41.8% and control 24.6%, p=0.0045, OR 2.29). The benefits of VCS were also seen for all pre-specified hierarchical secondary endpoints: RR at 24 weeks, partial renal response (PRR) at 24 and 52 weeks, time to achieve UPCR ≤ 0.5, and time to 50% reduction in UPCR. Furthermore, all pre-specified subgroup analyses (age, sex, race, biopsy class, region, and prior MMF use) favored VCS. VCS was well tolerated with no unexpected safety signals. The overall incidence of SAEs were similar in both groups (VCS 20.8% and control 21.3%); with infection most commonly reported (VCS 10.1% and control 11.2%). Overall mortality in the trial was low, with one death in the voclosporin arm and five in the control arm. Additionally, the VCS arm showed no significant decrease at week 52 in eGFR or increase in BP, lipids, or glucose.

Conclusion: The AURORA study met its primary endpoint and VCS was efficacious in Hispanic/Latino ethnicity patients, a difficult to treat group.

Disclosure of Interests: Cristina Arriens Grant/research support from: - BMS: Investigator Initiated Trial Research Funding, GSK: Investigator Initiated Trial Research Funding, Exagen: Research Grant, Consultant of: AstraZeneca (Sci Ad Board Dec 2017), GSK (Sci Ad Board Oct 2018), BMS (Sci Ad Board April 2019), Svetlana Polyakova: None declared, Igor Adzerikho: None declared, Simrat Randhawa Shareholder of: Aurinia Pharmaceuticals, Inc. stock, Employee of: Aurinia Pharmaceuticals, Inc., Neil Solomons Shareholder of: Aurinia Pharmaceuticals, Inc. stock, Employee of: Aurinia Pharmaceuticals.

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Public health, health services, and health economics in RMDs

OP0278

IDENTIFICATION OF PARAMETERS ASSOCIATED WITH A DIAGNOSTIC DELAY IN AXIAL SPONDYLOARTHRITIS: RESULTS FROM THE EUROPEAN MAP OF AXIAL SPONDYLOARTHRITIS (EMAS)

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Background: Early diagnosis of Axial Spondyloarthritis (axSpA) is crucial for timely access to specialist care and effective treatment.

Objectives: To assess the current diagnostic delay in axSpA and identify the parameters associated with increased diagnostic delay in a European sample.

Methods: Data from unselected patients participating in the European Map of Axial Spondyloarthritis (EMAS) study through an online survey (2017- 2018) across 13 countries were analysed. Mean differences in diagnostic delay were analysed using Mann-Whitney and Kruskal-Wallis tests, among sociodemographic and disease-related factors. A multivariate linear regression analysis was carried out to identify the relative weight of the associated parameters in determining diagnostic delay.

Results: 2,846 patients participated in EMAS. Mean age was 43.9 years, 61.3% were female, 48.1% had a university degree, and 53.9% were employed. Of the 2846 participants, 2652 provided information for calculating diagnostic delay. Mean age at symptom onset was 26.6 ± 11.1, mean age at diagnosis was 33.7 ± 11.5, and mean diagnostic delay was 7.4 ± 8.4 (Fig. 1). The following variables were associated with longer diagnostic delay in the bivariate analysis: older age, female gender, being diagnosed by a rheumatologist (Table 1). In the multivariate regression analysis younger age at symptom onset, number of HCPs seen before were associated with diagnostic delay (Table 2).

Table 1. Associations between sociodemographic and disease-related variables and diagnostic delay (N: 2,652)

Variable		Diagnostic Delay (years) Mean ± SD	P-value
Age categories	18-34	4.4 ± 5.5	**<0.001**
	35-51	7.9 ± 8.2	
	52-68	9.5 ± 10.2	
	>68	7.3 ± 9.7	
Gender	Male	6.1 ± 7.4	**<0.001**
	Female	8.2 ± 8.9	
Education level	No school completed	8.0 ± 10.7	0.397
	Primary school	7.6 ± 8.9	
	High school	7.6 ± 8.4	
	University	7.3 ± 8.3	
Occupation	Manual worker	6.7 ± 8.3	0.163
	Non-manual worker	7.3 ± 8.4	
Diagnosed by rheumatologist	Yes	7.9 ± 8.7	**<0.001**
	No	5.7 ± 7.3	
HLA-B27	Positive	8.3 ± 8.3	0.775
	Negative	8.7 ± 9.0	
Uveitis (ever)	Yes	8.0 ± 8.3	0.098
	No	7.6 ± 8.4	
IBD (ever)	Yes	7.7 ± 8.7	0.944
	No	7.5 ± 8.5	

Table 2. Regression analysis between sociodemographic and clinical variables in relation to diagnostic delay

Variable	Univariable linear regression		Multivariable stepwise linear regression	
	B	95% CI	B	95% CI
Age at symptoms onset	**-0.289**	**-0.316, -0.262**	**-0.321**	**-0.390, -0.253**
Female gender	**2.099**	**1.442, 2.755**	NA	NA
Employed, Manual worker	-0.604	-1.953, 0.746	NA	NA
Educational status, University	-0.343	-0.986, 0.299	NA	NA
Diagnosed by rheumatologist, Yes	**2.117**	**1.321, 2.913**	NA	NA
Number of HCPs seen before diagnosis	**1.723**	**1.486, 1.960**	**1.258**	**0.739, 1.776**
HLA-B27, Positive	-0.471	-1.347, 0.404	NA	NA
Uveitis (ever), Yes	0.463	-0.392, 1.319	NA	NA
IBD (ever), Yes	0.123	-0.971, 1.217	NA	NA

Conclusion: In this large sample of axSpA patients from 13 different European countries, the average diagnostic delay was more than seven years. The fact that one of the most strongly associated parameters to diagnostic delay was number of HCPs seen before diagnosis suggests the need for urgent action to reduce incorrect referrals to shorten the patient journey to diagnosis across Europe.

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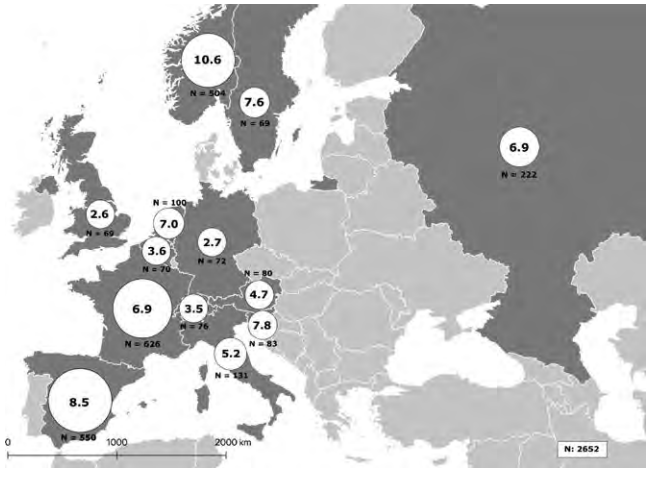


Figure 1. Average years of diagnostic delay across EMAS countries (N: 2,652)

Jesús Delgado-Domínguez: None declared, Denis Poddubnyy Grant/research support from: AbbVie, MSD, Novartis, and Pfizer, Consultant of: AbbVie, Bristol-Myers Squibb, Eli Lilly, MSD, Novartis, Pfizer, Roche, UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, MSD, Novartis, Pfizer, Roche, UCB
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OP0279 THE IMPACT OF A REFERRAL STRATEGY FOR AXIAL SPONDYLOARTHRITIS: 12 MONTHS FOLLOW-UP OF PATIENT REPORTED OUTCOMES

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Background: Early recognition of axial spondyloarthritis (axSpA) patients is difficult for general practitioners within the large amount of chronic low back pain (CLBP) patients[1]. As a result, several referral strategies have been developed to help physicians identify patients at risk for axSpA. Most referral strategies were developed in secondary care patients with no available data on their impact. The only referral strategy that was developed and validated in primary CLBP patients is the Case Finding Axial Spondyloarthritis (CaFaSpA) strategy, but required an impact analysis before implementation in daily clinical practice[2-3].
Objectives: The purpose of this study was to assess the impact of using the CaFaSpA referral strategy on patient reported outcome outcomes (PROs) in primary care patients with CLBP at risk for axSpA.
Methods: A clustered randomized controlled trial was performed in a primary care setting in the Netherlands. (ClinicalTrials.gov Identifier: NCT01944163). Each cluster contained the general practices from a single primary care practice and their included patients. Clusters were randomized to either the intervention (use of CaFaSpA referral strategy) or the control group (usual care). Primary outcome was disability after 12 months. Secondary outcome was quality of life, pain and fatigue after 12 months. A linear mixed-effects model was used to explore the effects over time according to intention to treat analysis.
Results: In total 679 patients were included within 93 GP clusters. Sixty-four percent of our study population were female and mean age was 36 (7.5) years. Overall RMDQ reduced over time both in the intervention and control group (figure 1). The difference in decrease was not statically significant between the groups (p-value 0.81).
EQ-5D increased by 0.03 after 12 months within the intervention group and 0.01 in the control group (not significant) (table 1). The decrease in pain and fatigue did not differ significantly between the intervention and control group.

Table 1. Mean change in PROs after 12 months in the intervention and control group

PROs	Intervention			Usual care		
	Baseline	12 months	p-value	Baseline	12 months	p-value
EQ-5D mean (SD)	0.69 (0.26)	0.72 (0.27)	0.14	0.72 (0.24)	0.73 (0.25)	0.53
VAS-pain mean (SD)	5.03 (2.42)	4.68 (2.69)	0.07	4.96 (2.42)	4.55 (2.69)	0.02
VAS-fatigue mean (SD)	5.19 (2.50)	5.01 (0.21)	0.35	5.23 (2.45)	4.86 (2.73)	0.04



Figure 1. Estimated mean RMDQ scores over time for the overall intervention and usual care group.

Conclusion: Although the functional disability due to pain reduces over time, there was no positive effect by referring based on the CaFaSPA model. Further data on PROMs for the axSpA patients are under investigation.
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OP0280 TEMPORAL TRENDS OF OPIOID USE AMONG INCIDENT OSTEOARTHRITIS PATIENTS IN CATALONIA, 2007-2016: A POPULATION-BASED COHORT STUDY

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Background: Opioids are not recommended as first-line treatments for chronic pain management in osteoarthritis (OA), but recent data suggest they are commonly used in routine practice in North America and northern Europe.
Objectives: To characterise the secular trends of opioid and strong opioids use in patients with incident OA from 2007 to 2016, and to explore the impact of patient characteristics on the use of opioid/s for OA.
Methods: Data was obtained from the SIDIAP (The System for the Development of Research in Primary Care) database, which contains primary care records and

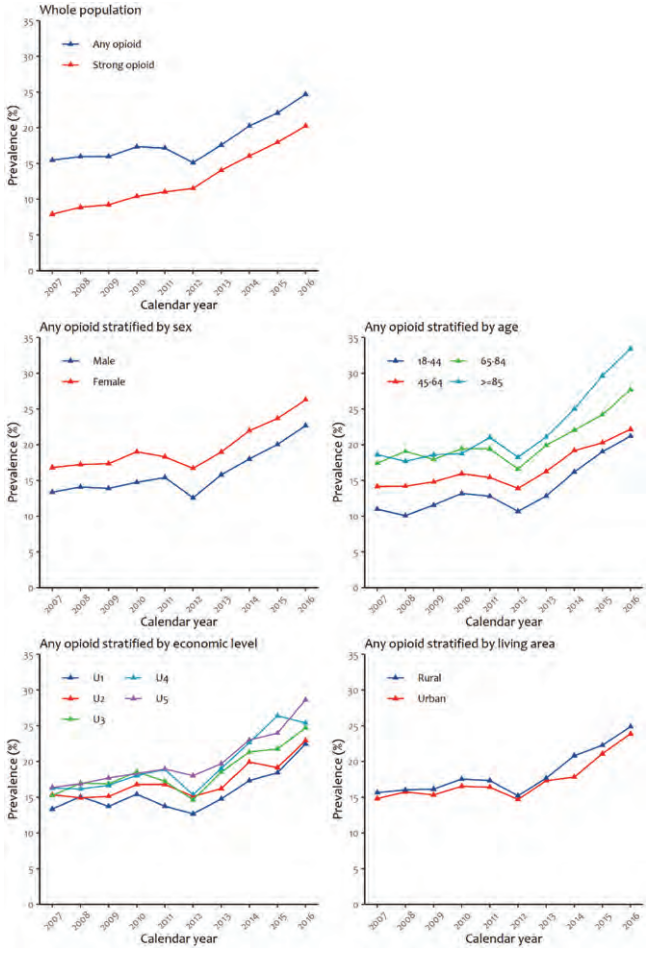


Figure 1. Trends of 1-year prevalence of opioid/s use among incident OA patients, whole and subgroup population.

pharmacy dispensing data for 80 % of the population in Catalonia (~ 6 million people). All persons aged 18 or older at the beginning of each calendar year with an incident OA diagnosis (including both peripheral and central joints) in the study period were included. Index date was the date of first OA diagnosis, and the observation period of opioid use was 1-year after index date. Opioids considered included codeine, tramadol, fentanyl, and morphine, with the latter three classified as strong opioids. The period prevalence of any opioid use was estimated in whole and sub-population stratified by sex, age, socio-economic status (U1 – U5, higher values of the indicator equivalent to deprivation) and residence area (rural/urban).

Results: The 1-year prevalence of any opioid use among incident OA patients was around 15% from 2007 to 2012. After that, this figure grew by 10% approaching 25% in 2016. However, strong opioid use increased continuously to nearly triple, from 8% in 2007 to 20% in 2016. The different subgroups followed similar trends over time, with women 4% higher than men, oldest 10% higher than youngest, most deprived 6% higher than least deprived, and rural 1% higher than urban.

Conclusion: The use of opioids (and especially strong opioids) has substantially increased in recent years among newly diagnosed OA patients in Catalonia. Our findings call for urgent action for safe opioid prescribing to avoid opioid abuse in OA patients especially amongst older women living in deprived areas.

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OP0281 TWO-YEAR COST-EFFECTIVENESS BETWEEN TWO GRADUAL TAPERING STRATEGIES IN RHEUMATOID ARTHRITIS: COST-UTILITY ANALYSIS OF THE TARA TRIAL

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Background: Current guidelines recommend to consider tapering treatment in rheumatoid arthritis (RA) patients who are in sustained remission, but the optimal approach to de-escalate conventional synthetic and biological DMARDs (respectively csDMARDs and bDMARDs) remains unknown. The benefits of tapering are a decreased risk of long-term adverse events and a reduction of health care costs, especially when bDMARDs are tapered. However, tapering treatment may lead to more transient or persistent disease flares, which have a direct impact on patients' lives and societal costs.

Objectives: To evaluate the two year cost-utility ratio between tapering the csDMARD first followed by the TNF-inhibitor, and tapering the TNF-inhibitor first followed by the csDMARD.

Methods: The TARA trial is a multicenter single-blinded randomized controlled trial. RA patients that used a csDMARD(s) plus a TNF-inhibitor and who had a well-controlled disease for at least 3 months, defined as a DAS≤2.4 and a swollen joint count (SJC)≤1, were included. Patients were randomized into gradual tapering their csDMARD followed by the TNF-inhibitor or vice versa. Medication was tapered in three steps over the course of 6 months. Gradual tapering was done by cutting the dosage into half, a quarter and thereafter it was stopped. Data on QALYs (measured with the Dutch EuroQol [EQ5D]), direct and indirect costs were used to calculate the Incremental Cost Effectiveness Ratio (ICER). The incremental cost-effectiveness ratio (ICER) and the incremental net monetary benefit (iNMB) were used to assess cost-effectiveness between both tapering strategies. Direct costs comprises costs for treatment and medical consumption, while indirect costs comprises costs due to loss of productivity (i.e. sick leave and unemployment).

Results: Of the 189 included patients, 94 started tapering their TNF-inhibitor first, while the other 95 tapered their csDMARD first. QALYs (sd) were, respectively, 1.64 (0.22) and 1.65 (0.22). Medication costs were significantly lower in the patients who tapered the TNF-inhibitor first, but indirect cost were higher due to more productivity loss. Therefore, total costs per QALY were similar for both tapering strategies (p=0.62). The ICER between tapering csDMARDs and the TNF-inhibitor was -€184534 (-€417314, €48245; 95% CI)(figure 1). The mean iNMB was €2831 at a willingness-to-pay (WTP) level of €80000. At all WTP levels the probability of being cost-effective was higher (62% vs. 28%) for tapering the TNF-inhibitor first (figure 2)

Conclusion: Medication costs are lower when the TNF-inhibitor is tapered first, but this is counterbalanced by higher indirect costs due to loss of productivity. Therefore, overall cost savings are smilar for both tapering strategies. However, tapering the TNF-inhibitor first has a higher chance of being cost-effective at all WTP thresholds. For this reason we advise to taper the TNF-inhibitor first when tapering medication is considered.

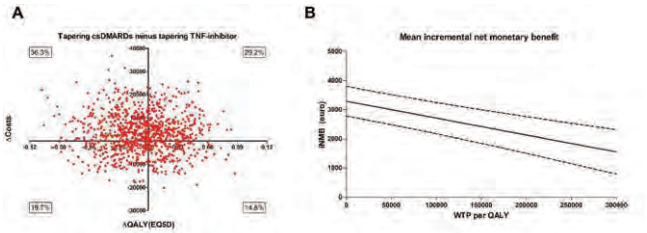


Figure 1 Summary of economic evaluation of tapering csDMARDs first minus tapering TNF-inhibitor first. (A) Results of 1000 bootstrapped replications, presented in a cost-effectiveness plane which represents uncertainty of the cost-effectiveness ratio. (B) Mean incremental net monetary benefit for tapering csDMARDs minus tapering TNF-inhibitors with 95% confidence intervals plotted against different levels of willingness to pay (WTP) per quality adjusted life year (QALY). csDMARDs: conventional synthetic DMARDs; iNMB: incremental net monetary benefit; QALY: quality adjusted life year; WTP: willingness to pay.

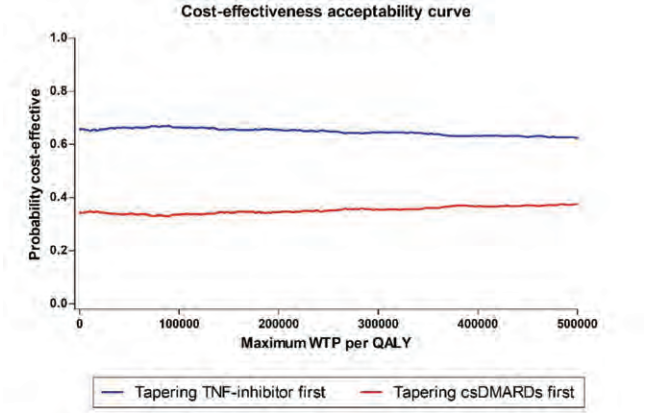


Figure 2 Cost effectiveness acceptability curve for tapering csDMARDs first versus tapering TNF-inhibitor first. Results of 1000 bootstrapped replication, presented for several levels of willingness to pay, indicated per quality adjusted life year (QALY). csDMARDs: conventional synthetic DMARDs; QALY: quality adjusted life year; WTP: willingness to pay.

Disclosure of Interests: None declared

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OP0282 COST-EFFECTIVENESS ANALYSIS OF A CAFASPA REFERRAL MODEL FOR AXIAL SPONDYLOARTHRITIS

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Background: Chronic low back pain (CLBP) poses a significant individual and socio-economic burden. A substantial amount of patients with CLBP have axial spondyloarthritis (axSpA), but early recognition of these patients is difficult for general practitioners (GPs). Guidelines form primary care and secondary care differ in criteria for referral recommendation. The Dutch primary care guideline is restrictive in referring CLBP patients to secondary care whereas ASAS recommend to refer CLBP patients having at least 1 axSPA feature[1]. Therefore several referral models have been developed to assist GPs. Although the validated CaFaSpA referral model[2] is able to identify CLBP patients at risk for axSpA, its cost-effectiveness is yet unknown and essential before implementation in daily clinical practice.

Objectives: Primary objective to assess the cost-effectiveness of the CaFaSpA referral model for axSpA in primary care. Secondary objective to evaluate the costs made for screening by following the CaFaSpA vs ASAS referral model.

Methods: A clustered randomized controlled trial was performed with GPs as clusters. Clusters were randomized into the intervention (CaFaSpA referral, CS) or usual care (UC). Cost-effectiveness analysis from a societal perspective was performed to compare the CS and UC. Clinical outcomes were disability

(Roland-Morris Disability Questionnaire (RMDQ)) and health-related quality of life (EuroQol (EQ-5D)) after 12 months. Direct (Medical Consumption Questionnaire IMCQ) and indirect healthcare (Productivity Cost Questionnaire IPCQ) costs were evaluated. Complete case analysis was performed. Incremental cost-effectiveness ratios (ICERs) were calculated for both clinical effects. Fictive costs according to the Dutch standard prices were assessed if the ASAS guideline would be followed (screening costs)[3].

Results: Of all 679 patients sixty-four percent were female and mean age was 36 (SD) years. In the CS 333 patients were included and in the UC. Non-significant differences in clinical outcomes were for RMDQ: 0.78 (95% CI: -0.38-2.07) and for EQ5D 0.03 (95% CI: -0.04-0.11). Costs were significantly higher in the UC group €19,748 (95% CI: € 15,327-25,022) vs CS € 14,169 (95% CI: € 10,723-18,066).

Productivity loss was the largest contributor to the total costs (CS group: 62%, UC group: 96%). The majority of the bootstrapped ICERs presented were located in the south-eastern quadrant of the cost-effectiveness planes (Figure 1a and 1b), indicating that the CS is cost-effective. The ICER for RMDQ was €-5,579, indicating that per point improvement on the RMDQ the intervention saved €5,579. The difference in QALY's between the CS and UC was very small resulting in a large ICER of €16,9583.

The fictive screening costs by using the ASAS referral advice, i.e. referring 85% of 679 patients, results in €876 per patient. The total screening costs per patient by using the CaFaSpA model, i.e. referring 60% of 679 patients is €618.

Conclusion: Although the clinical effects between the CaFaSpA referral strategy and usual care were comparable, the CaFaSpA referral strategy resulted in a better cost-effectiveness. Lower costs were mainly driven by the increased productivity.

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[2] van Hoeven L et al. PLoS One 2015; 22;10(7):e0131963.
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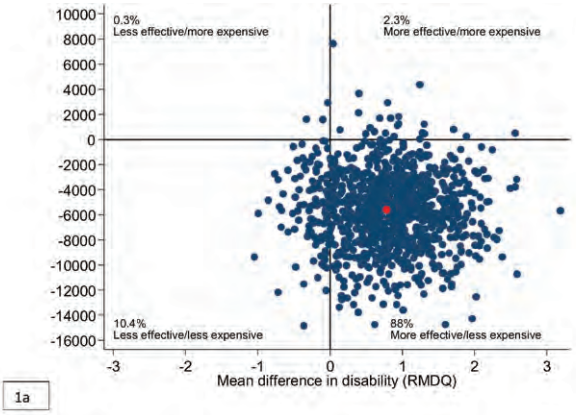


Figure 1. Cost-effectiveness plane for disability (RMDQ) (figure 1a) and health related quality of life (EQ-5D) in which the CaFaSpA referral strategy is compared to usual care.

Disclosure of Interests: None declared
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OP0283

COMPARING COST-UTILITY OF DMARDS IN SERONEGATIVE RHEUMATOID ARTHRITIS PATIENTS; A TREACH SUBANALYSIS

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Background: The diversity of the clinical phenotype of rheumatoid arthritis (RA) is increasing due to the emphasis on early diagnosis and treatment. This resulted in an increased number of RA patients without autoantibodies, also known as seronegative RA. We recently showed that newly diagnosed seronegative RA patients initially treated with hydroxychloroquine (iHCQ) had a similar clinical efficacy to initial methotrexate (iMTX). To our knowledge, however, there are no data on the cost-effectiveness of different initial treatment strategies in seronegative RA patients.

Objectives: To evaluate the 1-year cost-effectiveness between three different initial treatment strategies in seronegative rheumatoid arthritis (RA) patients, according to 2010 criteria.

Methods: For this analysis we selected all seronegative RA patients (n=131) within the intermediate probability stratum of the tREACH trial (table 1). Selected patients either received initial methotrexate 25mg/week (iMTX), hydroxychloroquine 400mg/day (iHCQ) or oral glucocorticoids, starting dose 15mg, in a 10-week tapering scheme without csDMARDs (iGCs). Quality adjusted life year (QALY) were derived from the EQ-5D. Costs were calculated with data from patient records and questionnaires. Direct costs are health care costs, whereas indirect costs are costs due to productivity loss. The incremental cost-effectiveness ratio (ICER) was used to assess the cost-effectiveness between treatment strategies.

Table 1. Baseline characteristics and response after 1 year.

	A.iMTX (n=50)	B.iHCQ (n=40)	C.iGCs (n=41)
Baseline (t=0)			
Age (years), mean (SD)	57 (14)	54 (14)	53 (15)
Sex, female, n (%)	38 (76)	24 (60)	27 (66)
Symptom duration (days), mean (SD)	143 (86-209)	146 (102-226)	126 (94-192)
Das, mean (SD)	3.43 (0.92)	2.93 (0.84)	3.50 (0.93)
HAQ, mean (SD)	1.20 (0.56)	0.90 (0.61)	1.03 (0.69)
Response after 1 year (t=12)			
Das, mean (SD)	1.71 (0.81)	1.78 (0.97)	1.72 (1.00)
HAQ, mean (SD)	0.78 (0.55)	0.77 (0.60)	0.71 (0.68)

Results: Average QALYs (sd), for iMTX, iHCQ and iGCs were respectively 0.71 (0.14), 0.73 (0.13) and 0.70 (0.15). The average total costs (sd) per QALY for iMTX, iHCQ and iGCs were respectively €11.004 (17.611), €13.231 (19.886) and €18.415 (35.660). Direct and indirect costs were higher in the iGCs group compared to iMTX and iHCQ (table 2). The ICERs did not differ between the initial treatment strategies (figure 1A-C). For WTP levels <€33.900 iMTX has the highest probability of being cost-effective, while for WTP levels >€33.900 iHCQ has the highest probability (figure 1D).

Table 2. Total costs per QALY after 1 year of follow-up.

	A.iMTX (n=50)	B.iHCQ (n=40)	C.iGCs (n=41)
QALYs (AUC)	0.71 (0.14)	0.73 (0.13)	0.70 (0.15)
Cost per QALY (EQ5D)			
Total direct costs, €	€3873 (4706)	€3262 (4434)	€5008 (6869)
•Medication, €	€2224 (4025)	€1134 (2493)	€3135 (5343)*
•Medical consumption, €	€1394 (1067)	€1915 (3274)	€1874 (2367)
•Hospitalization, €	€256 (1353)	€213 (785)	-
Total indirect costs, €	€7131 (15164)	€9969 (17340)	€13406 (31255)
Total costs, €	€11004 (17611)	€13231 (19886)	€18415 (35660)

Results shown are mean (SD) unless stated otherwise. *p<.05 for HCQ vs. GCs (student t test)

Conclusion: iMTX and iHCQ are more cost-effective than iGCs. However, depending on the WTP threshold either iMTX or iHCQ has the highest probability of being cost-effective.

Figure:

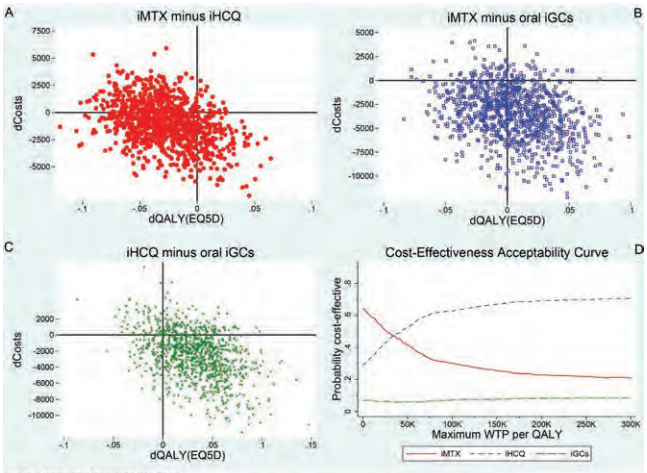


Figure 1 Summary of economic evaluation.
(A-D) Cost-effectiveness planes and cost-acceptability curves for the different initial treatment strategies compared to each other.
MTX 25mg/wk, HCQ 400mg/day, GCs oral tapering scheme starting with 15mg/day.
Abbreviations: EQ-5D, Dutch EuroQol; HAQ, iHCQ, initial hydroxychloroquine; iGCs, initial glucocorticoids; iMTX, initial methotrexate; QALYs, Quality Adjusted Life Years; WTP, willingness-to-pay.

Disclosure of Interests: None declared
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OP0284

AN AGENT-BASED SIMULATION OF THE EFFECTS OF VARYING TIME TO TREATMENT WITH BIOLOGICAL AGENTS ON PATIENT HEALTH AND COST IN AXIAL SPONDYLOARTHRITIS USING NATIONAL REGISTER DATA

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Background: Evaluating the long-term impacts of healthcare policies on patient's health and treatment costs for people with axial spondyloarthritis (axSpA) is challenging due to its chronic nature, and the variation in individual patient journeys post-diagnosis. Agent-based simulations are a novel approach to interrogating this complexity, and allow the consequences of different policy scenarios on outcomes to be explored.

Objectives:

1. Develop and validate an agent-based simulation of the UK axial spondyloarthritis healthcare system, using real-world data.
2. Interrogate the effects of earlier biologic treatment on costs and patient outcomes.

Methods: Anonymised data were obtained from the UK National Early Inflammatory Arthritis Audit, and BSR Biologics Register (BSRBR-AS). This provided data on 162 units, and 702 patients with 1,631 patient-years of follow-up. An agent-based model was designed and programmed on the Netlogo platform to simulate patients and units individually over time. New patients were created based on national disease prevalence statistics. Patients' disease journeys were modelled with a Bath AS Disease Activity Index (BASDAI) score. The model included hospital outpatient attendances, treatment histories, drug costs, and key patient demographics. The baseline simulation was run for two simulated years, repeated 10 times, and assessed against the BSRBR-AS dataset for validation. The model was subsequently used to explore five experimental scenarios in which the time between the date of diagnosis, to first introduction to biologics (d-b) was varied by increasing the number of appointments. The experiment was run 10 times for each parameter setting.

Results: In the baseline model in a typical two year run, 13,631 new patients attended 5,167 baseline, and 6,966 follow-up appointments. Of these, 6,324 and 623 were prescribed ≥1NSAID, and biologics, respectively. The validation comparison tests showed a high-level of similarity between simulated output and target datasets. In the target data, d-b was 250 days. In the experimental scenarios, as might be expected, earlier biologic access improved outcomes but at higher-costs (Figure 1; Table 1). Reducing d-b to 150 days doubled the number of patients on biologics at 2 years from 623 to 1,286. It also led to 8% more patients achieving a BASDAI of 0 to 2.5 at 2 years, with 5%, 1%, and 2% less patients achieving 2.5 - 5, 5 to 7.5 and 7.5 to 10 BASDAI, respectively. Reducing d-b to 150 days increased drug costs from £3.2 million to £8.8 million. However, the total number of appointments (a proxy for staff costs) increased proportionality less from 16,000 to 20,000.

Table 1. Influence of varying the time between diagnosis to biologic treatment (d-b) on drug-use and staffing costs

Diagnosis to Biologic (d-b)	Drug Costs Unit (£k)	Total Appointments	No. patients prescribed NSAIDs	No. patients prescribed Biologics
150	8,796	20,384	7,154	1,283
220	5,702	18,592	6,796	971
250	3,259	16,214	6,324	621
260	2,054	14,700	5,968	382
265	1,297	13,411	5,562	233

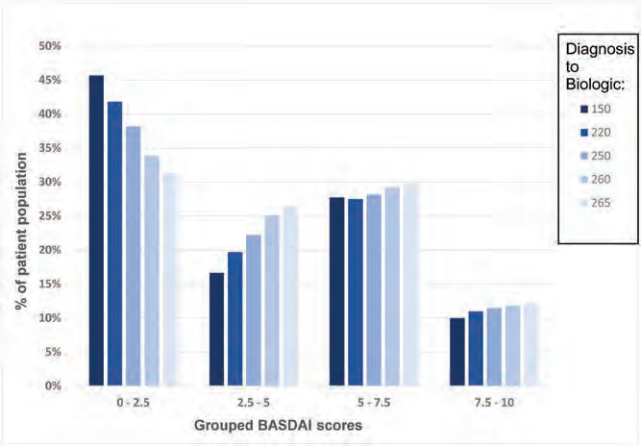


Figure 1. Influence of varying the time between diagnosis to biologic treatment (d-b) on 2 year BASDAI outcome

Conclusion: We have successfully developed, and validated an agent-based approach to model the effect of key policy changes on the whole healthcare system, providing output estimates of cost and patient outcomes, based on integrated real-world data. To our knowledge this is the first attempt to explore the patient journey in people with axSpA in this way. The model provides a useful tool for exploring the effects of changing the way healthcare is delivered to patients with this disease. Our experimental analysis lends support to the case for increasing staffing and drug expenditure to achieve current NICE standards of care in AS.

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OP0285

TOWARDS IMPLEMENTING THE OMOP CDM ACROSS FIVE EUROPEAN BIOLOGIC REGISTRIES

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Background: The Observational and Medical Outcomes Partnerships (OMOP) common data model (CDM) provides a framework for standardising health data.

Objectives: To map national biologic registry data collected from different European countries to the OMOP CDM.

Methods: Five biologic registries are currently being mapped to the OMOP CDM: 1) the Czech biologics register (ATTRA), 2) Registro Español de Acontecimientos Adversos de Terapias Biológicas en Enfermedades Reumáticas (BIOBADASER), 3) British Society for Rheumatology Biologics Register for Rheumatoid Arthritis (BSRBR-RA), 4) German biologics register 'Rheumatoid arthritis observation of biologic therapy' (RABBIT), and 5) Swiss register 'Swiss Clinical Quality Management in Rheumatic Diseases' (SCQM).
Data collected at baseline are being mapped first. Details that uniquely identify individuals are mapped to the person table, with the observation_period table defining the time a person may have had clinical events recorded. Baseline comorbidities are mapped to the condition_occurrence CDM table, while baseline medications are mapped to the drug_exposure CDM table. This mapping is summarised in Figure 1.

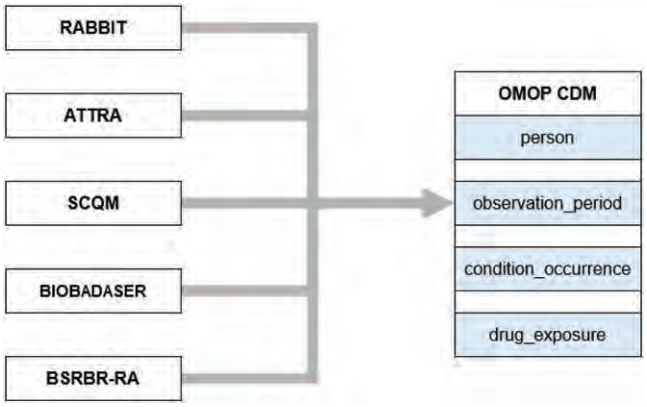


Figure 1. Overview of initial mapping

Results: A total of 64,901 individuals are included in the 5 registries being mapped to the OMOP CDM, see table 1. The number of unique baseline conditions being mapped range from 17 in BSRBR-RA to 108 in RABBIT, while the number of baseline medications range from 26 in ATTRA to 802 in BSRBR-RA. Those registries which captured more comorbidities or medications generally allowed for these to be inputted as free text.

Table 1. ***Summary of initial code mapping***

Registry	Number of individuals	Number of mapped baseline conditions	Number of mapped baseline medications
ATTRA	5,326	26	26
BIOBADASER	6,496	30	51
BSRBR-RA	21,695	17	802
RABBIT	13,062	108	78
SCQM	18,322	26	33

Conclusion: Due to differences in study design and data capture, the baseline information captured on comorbidities and drugs across registries varies greatly. However, these data have been mapped and mapping biologic registry data to the OMOP CDM is feasible. The adoption of the OMOP CDM will facilitate collaboration across registries and allow for multi-database studies which include data from both biologic registries and other sources of health data which have been mapped to the CDM.
Disclosure of Interests: Edward Burn: None declared, Lianne Kearsley-Fleet: None declared, Kimme Hyrich Grant/research support from: Pfizer, UCB, BMS, Speakers bureau: Abbvie, Martin Schaefer: None declared, Doreen Huschek: None declared, Anja Strangfeld Speakers bureau: AbbVie, BMS, Pfizer, Roche, Sanofi-Aventis, Jakub Zavada Speakers bureau: Abbvie, UCB, Sanofi, Elli-Lilly, Novartis, Zentiva, Accord, Markéta Lagová: None declared, Delphine Courvoisier: None declared, Christoph Tellenbach: None declared, Kim Lauper: None declared, Carlos Sánchez-Piedra: None declared, Nuria Montero: None declared, Jesús-Tomás Sanchez-Costa: None declared, Daniel Prieto-Alhambra Grant/research support from: Professor Prieto-Alhambra has received research Grants from AMGEN, UCB Biopharma and Les Laboratoires Servier, Consultant of: DPA's department has received fees for consultancy services from UCB Biopharma, Speakers bureau: DPA's department has received fees for speaker and advisory board membership services from Amgen
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Novel diagnostic and therapeutic approaches in paediatric rheumatic diseases

OP0286

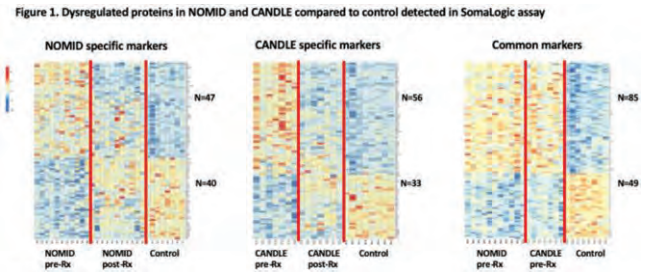
PROTEOMICS AND RNA SEQUENCING APPROACHES HIGHLIGHT THE ROLE OF ENDOTHELIAL CELL DYSREGULATION IN IL-1 AND IFN MEDIATED AUTOINFLAMMATORY DISEASES, NOMID AND CANDLE

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Background: Systemic Autoinflammatory diseases present with sterile inflammation. NOMID (Neonatal-Onset Multisystem Inflammatory Disease) is caused by gain-of-function mutations in *NLRP3* and excess IL-1 production, presents with fever, neutrophilic dermatosis, aseptic meningitis, hearing loss and eye inflammation; CANDLE (Chronic Atypical Neutrophilic Dermatosis, Lipodystrophy and Elevated Temperature) is caused by loss-of-function mutations in proteasome genes that lead to type-1 interferon signaling, characterized by fever, panniculitis, lipodystrophy, cytopenia, systemic and pulmonary hypertension and basal ganglia calcification. IL-1 blockers are approved for NOMID and JAK-inhibitors show efficacy in CANDLE treatment.
Objectives: We used proteomic analysis to compare differentially expressed proteins in active NOMID and CANDLE compared to healthy controls before and after treatment, and whole blood bulk RNA seq to identify the immune cell signatures.
Methods: Serum samples from active NOMID (n=12) and CANDLE (n=7) before and after treatment (table 1) and age matched healthy controls (HC) (n=7) were profiled using the SomaLogic platform (n=1125 proteins). Differentially expressed proteins in NOMID and CANDLE were ranked after non-parametric tests for unpaired (NOMID p <0.05, CANDLE, p<0.1) and paired (p<0.05) analysis and assessed by enriched Gene Ontology pathways and network visualization. Whole blood RNA seq was performed (NOMID=7, CANDLE=7, Controls =5) and RPKM values were used to assess immune cells signatures.
Results: Compared to control, 205 proteins (127 upregulated, 78 downregulated) were significantly different at baseline in NOMID, compared to 163 proteins (101 upregulated, and 62 downregulated) in CANDLE. 134 dysregulated proteins (85 upregulated, 49 downregulated) overlapped in NOMID and CANDLE (Figure 1). Pathway analysis identified neutrophil and monocyte chemotaxis signature in both NOMID and CANDLE. NOMID patients had neutrophilia and active neutrophils. CANDLE patients exhibited active neutrophils in whole blood RNA. Endothelial cell activation was the most prominent non-hematopoietic signature and suggest distinct endothelial cell dysregulation in NOMID and CANDLE. In NOMID, the signature included neutrophil transmigration (SELE) endothelial cell motility in response to angiogenesis (HGF, VEGF), while in CANDLE the endothelial signatures included extracellular matrix protein deposition (COL8A) suggesting increased vascular stiffness. CANDLE patients had higher expression of Renin, 4 out of 7 had hypertension, NOMID patients did not have hypertension. Treatment with anakinra and baricitinib normalized 143 and 142 of dysregulated proteins in NOMID and CANDLE respectively.
Conclusion: Differentially expressed proteins in NOMID and CANDLE are consistent with innate immune cell activation. Distinct endothelial cell signatures in NOMID and CANDLE may provide mechanistic insight into differences in vascular phenotypes. Treatment with anakinra and Baricitinib in NOMID and CANDLE leaves 30% and 13% of the dysregulated proteins unchanged.

Table 1. Patient's characteristics

	NOMID N=12, Male =6		**CANDLE** N=7, Male =6	
Age Median (range)	12 (2, 28)		16 (3, 20)	
Ethnicity %White (Hispanic)	80 (20)		100 (30)	
Genetics	*NLRP3* mutation (2 Somatic, 10 Germline)		mutations in proteasome component genes (1 digenic, 6 Homozygous/compound Heterozygous)	
	Before treatment	After treatment	Before treatment	After treatment
CRP Median (range) mg/L	52 (16-110)	5 (0-23)	5 (0-101)	1 (0-4)
IFN score median (range)	0	NA	328 (211-1135)	3 (0-548)



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Disclosure of Interests: None declared
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OP0287 A MACHINE LEARNING APPROACH FOR PRECISION STRATIFICATION OF JUVENILE-ONSET SLE

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Background: Juvenile-onset systemic lupus erythematosus (JSLE) is a complex and heterogeneous disease characterised by diagnosis and treatment delays. An unmet need exists to better characterise the immunological profile of JSLE patients and investigate its links with the disease trajectory over time.
Objectives: A machine learning (ML) approach was applied to explore new diagnostic signatures for JSLE based on immune-phenotyping data and stratify patients by specific immune characteristics to investigate longitudinal clinical outcome.
Methods: Immune-phenotyping of 28 T-cell, B-cell and myeloid-cell subsets in 67 age and sex-matched JSLE patients and 39 healthy controls (HCs) was performed by flow cytometry. A balanced random forest (BRF) ML predictive model was developed (10,000 decision trees). 10-fold cross validation, Sparse Partial Least Squares-Discriminant Analysis (sPLS-DA) and logistic regression was used to validate the model. Longitudinal clinical data were related to the immunological features identified by ML analysis.
Results: The BRF-model discriminated JSLE patients from healthy controls with 91% prediction accuracy suggesting that JSLE patients could be distinguished from HCs with high confidence using immunological parameters. The top-ranked immunological features from the BRF-model were confirmed using sPLS-DA and logistic regression and included CD19+ unswitched memory B-cells, naïve B-cells, $CD14^+$ monocytes and total $CD4^+$, $CD8^+$ and memory T-cell subsets.
K-mean clustering was applied to stratify patients using the validated signature. Four groups were identified, each with a distinct immune and clinical profile. Notably, $CD8^+$ T-cell subsets were important in driving patient stratification while B-cell markers were similarly expressed across the JSLE cohort. JSLE patients with elevated effector memory $CD8^+$ T-cell frequencies had more persistently active disease over time, and this was associated with increased treatment burden and prevalence of lupus nephritis. Finally, network analysis identified specific clinical features associated with each of the top JSLE immune-signature variables.
Conclusion: Using a combined ML approach, a distinct immune signature was identified that discriminated between JSLE patients and HCs and further stratified patients. This signature could have diagnostic and therapeutic implications. Further immunological association studies are warranted to develop data-driven personalised medicine approaches for JSLE.
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OP0288 ANTI-IL1 TREATMENT IN COLCHICINE RESISTANT PEDIATRIC FMF PATIENTS-REAL LIFE DATA FROM THE HELIOS REGISTRY

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Background: FMF is a prototype of autoinflammatory diseases associated with excess IL1 production. Anti-IL1 treatments are the first-line alternatives in colchicine resistant/intolerant FMF patients.
Objectives: We aimed to investigate the efficacy and safety of anti-IL1 treatment in pediatric FMF patients in our local (HELIOS) registry.
Methods: HELIOS (Hacettepe univErsity eLectronIc research fOrmS) is a web-based biological drug registry for pediatric rheumatology patients (helios.hacettepe.edu.tr). Data were recorded at biological treatment onset (month 0), at month 6 and yearly thereafter in patients. We have analysed the clinical features, disease activity parameters, treatment responses and safety outcomes in FMF patients treated with anti-IL1 agent.
Results: Forty pediatric FMF patients were included to the study group (67% female).
Thirty-four patients received continous anti-IL1 treatment. The mean age at the start of the colchicine was 5.55±3.87 years. Age at onset of the anti-IL1 treatment was 11.47±5.41 with a mean follow-up duration of 3.87±1.96 years. Apart from two patients, all of them had biallelic exon-10 mutations.
We have also given anti-IL1 treatment on an on-demand basis in six adolescent patients. Five of them were having very severe attacks during menstrual periods and one was having attacks during extreme stress periods along with very high CRP levels. The quality of life has markedly improved and these patients no longer reveal any CRP elevation.
Anakinra was used as the first-line anti-IL1 treatment. During the last visit, six patients were treated with anakinra and 28 patients were treated with canakinumab. Anti-IL1 treatment decreased the CRP levels, number and severity of the attacks. (Figure 1.) There were three hospitalizations reported due to mild infections. Eleven patients had local skin reactions, two patients had leukopenia with anakinra and one patient had thrombocytopenia with canakinumab. We have discontinued anti-IL1 treatment until the cytopenia subsided. We have switched to on-demand therapy in one patient, started the same treatment and gradually increased the dose in the other two patients. There were no malignancy or other severe adverse reactions.

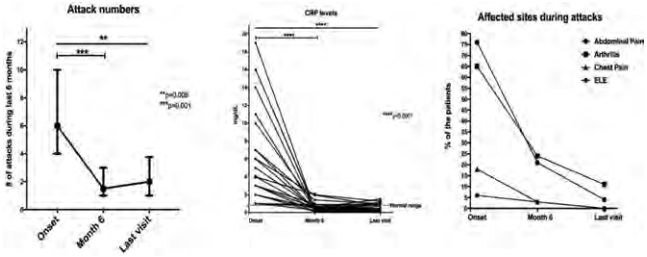


Figure 1.

Conclusion: Anakinra and canakinumab are efficient and safe alternatives in colchicine resistant and intolerant pediatric FMF patients. We also for the first time, report on-demand use of anti-IL1 in pediatric FMF patients. We suggest that on-demand treatment should be considered under certain circumstances where the trigger is known and short-lasting (such as menstruation and periods of extreme stress)
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the establishment of infrastructure, Yelda Bilginer Grant/research support from: Novartis and SOBI financially supported the HELIOS registry during the establishment of infrastructure, Seza Özen Consultant of: Novartis, Pfizer, Speakers bureau: SOBI, Novartis

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OP0290 EMAPALUMAB (ANTI-INTERFERON-GAMMA MONOCLONAL ANTIBODY) IN PATIENTS WITH MACROPHAGE ACTIVATION SYNDROME (MAS) COMPLICATING SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS (SJIA)

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Background: MAS is a severe complication of rheumatic diseases and occurs most frequently in patients with sJIA. Data from animal models and from observational studies in patients suggest that interferon gamma (IFNγ) is a driver of the hyperinflammation and hypercytokinemia observed in MAS.

Objectives: To assess the pharmacokinetics, efficacy, and safety of intravenous (IV) infusions of emapalumab, a fully human anti-IFNγ monoclonal antibody, in patients with MAS in the context of sJIA.

Methods: This ongoing, pilot, open-label, single-arm study (NCT03311854) includes patients with MAS (2016 ACR/EULAR criteria) on a background of confirmed, or high presumption of, sJIA, and with inadequate response to high-dose IV glucocorticoids. Emapalumab is initiated at 6 mg/kg (1 dose) and continued at 3 mg/kg twice weekly for a total of 4 weeks, or less upon achievement of complete response (CR). CR is defined as an absence of MAS clinical signs plus white blood cell and platelet counts above the lower limit of normal, LDH, AST and ALT <1.5 x upper limit of normal, fibrinogen >100 mg/dL, and ferritin decreased by ≥80% or to <2,000 ng/mL.

Results: We report preliminary data from the first 9 patients (median age [range] 11.6 [2.1-25.3] years) enrolled (7 in Europe and 2 in the USA). All patients had failed high-dose methylprednisolone, of which there were prior treatment failures from cyclosporin A (n=4) and from anakinra (n=4). Treatment with emapalumab resulted in rapid IFNγ neutralization, as demonstrated by the decrease in CXCL9 levels (Figure 1), and subsequent deactivation of T cells, as indicated by the decrease in sIL-2R levels. CR was achieved in all patients after a median of 23 (12-56) days. A progressive improvement in all clinical and laboratory parameters of MAS was observed (Table 1 and Figure 2). Glucocorticoids were tapered in all patients (median % tapering -92%; range -45% to -98% at Week 8). Emapalumab infusions were well tolerated by all patients, with no discontinuation. CMV reactivation was reported in 1 patient as a serious event possibly related to emapalumab and resolved with antiviral treatment.

Table 1. Time to response for key clinical and laboratory parameters.

Parameters	Median baseline value (range)	Median days of treatment (range)
D-dimers to <1000 mg/L	12,480 (550-89,552)	15 (1-49)
sIL-2R to <2000 ng/L	4596 (1664-20,954)	21 (6-37)
Ferritin <500 mg/L	29,240 (716-192,584)	21 (9-42)
Physician visual analog scale of MAS activity ≤1	9.0 (2-10)	19 (9-56)
All MAS laboratory parameters within range of CR	NA	21 (15-55)
All MAS parameters within range of CR	NA	23 (12-56)
Glucocorticoid tapering at ≤1 mg/kg prednisolone equivalent*	NA	42 (16-50)

*Data incomplete for 1 patient

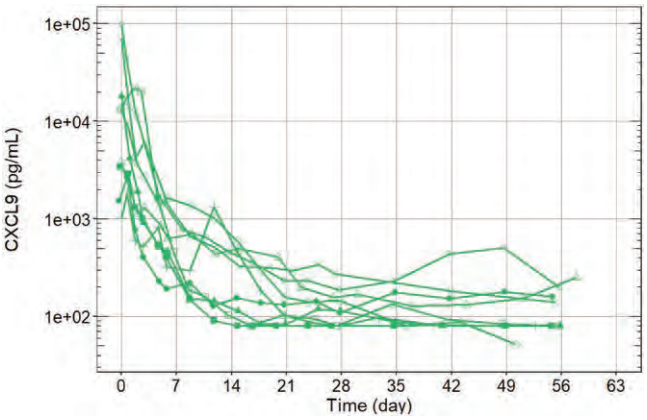


Figure 1. Rapid neutralization of IFNγ. Each line represents an individual patient (n=9).

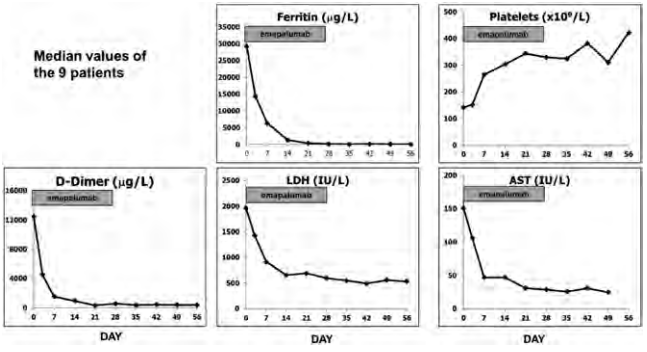


Figure 2. Ferritin levels and platelet counts over time.

Conclusion: Emapalumab administration led to rapid neutralization of IFNγ and was efficacious in controlling MAS with a favorable safety profile. These results support the pathogenic role of IFNγ in MAS/sJIA and the therapeutic value of IFNγ neutralization in MAS patients who have failed standard of care.

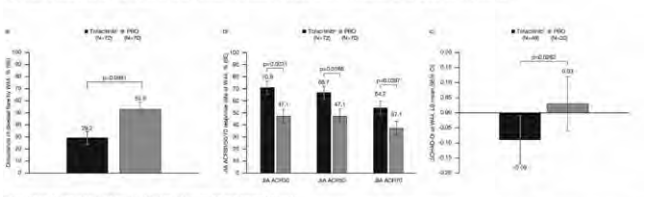
Disclosure of Interests: Fabrizio De Benedetti Grant/research support from: AbbVie, Pfizer, Novartis, Novimmune, Sobi, Sanofi, Roche, Speakers bureau: AbbVie, Novartis, Roche, Sobi, Paul Brogan Grant/research support from: Sobi, Novartis, Roche, Chemocentryx, Consultant of: Roche, Sobi, Speakers bureau: Sobi, Roche, Novartis, UCB, Claudia Bracaglia: None declared, Manuela Pardeo: None declared, Giulia Marucci: None declared, Emanuela Sacco: None declared, Despina Eleftheriou Speakers bureau: Sobi, Charalampia Papadopoulou: None declared, Alexei Grom Grant/research support from: Novartis, AB2Bio, Consultant of: Novartis, Pierre Quartier Consultant of: AbbVie, Chugai-Roche, Lilly, Novartis, Sanofi, Sobi, Speakers bureau: AbbVie, BMS, Chugai-Roche, Novartis, Pfizer, Sobi, Rayfel Schneider Grant/research support from: Roche, Novartis, Sobi, Pfizer, Consultant of: Sobi, Novartis, Novimmune, Philippe Jacqmin Consultant of: Sobi, Rikke Frederiksen Employee of: Sobi, Maria Ballabio Employee of: Sobi, Cristina De Min Employee of: Sobi

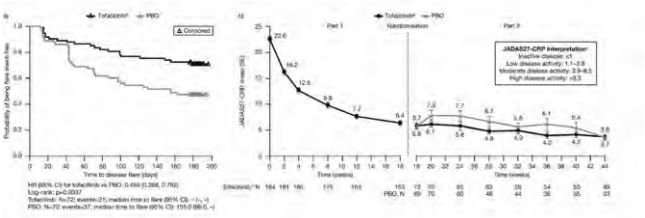
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OP0291 TOFACITINIB FOR THE TREATMENT OF POLYARTICULAR COURSE JUVENILE IDIOPATHIC ARTHRITIS: RESULTS OF A PHASE 3, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED WITHDRAWAL STUDY

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Background: Tofacitinib is an oral JAK inhibitor that is being investigated for JIA.
Objectives: To assess tofacitinib efficacy and safety in JIA patients (pts).
Methods: This was a Phase 3, randomised, double-blind (DB), placebo (PBO)-controlled withdrawal study in pts aged 2–<18 years with polyarticular course JIA (pcJIA), PsA or ERA (NCT02592434). In the 18-week open-label Part 1, pts received weight-based tofacitinib doses (5 mg BID or lower). Pts with ≥JIA ACR30 response at Week (W)18 were randomised 1:1 in the DB Part 2 (W18–44) to continue tofacitinib or switch to PBO. Primary endpoint: disease flare rate by W44. Key secondary endpoints: JIA ACR50/30/70 response rates; change from Part 2 baseline (Δ) in CHAQ-DI at W44. Other efficacy endpoints: time to disease flare in Part 2; JADAS27-CRP in Parts 1 and 2. PsA/ERA pts were excluded from these efficacy analyses. Safety was evaluated in all pts up to W44.
Results: 225 enrolled pts with pcJIA (n=184), PsA (n=20) or ERA (n=21) received tofacitinib in Part 1. At W18, 173/225 (76.9%) pts entered Part 2 (pcJIA n=142, PsA n=15, ERA n=16). In pcJIA pts, disease flare rate in Part 2 was significantly lower with tofacitinib vs PBO by W44 (p=0.0031; Fig 1a). JIA ACR50/30/70 response rates (Fig 1b) and ΔCHAQ-DI (Fig 1c) at W44, and time to disease flare in Part 2 (Fig 2a), were improved with tofacitinib vs PBO. Tofacitinib reduced JADAS27-CRP in Part 1; this effect was sustained in Part 2 (Fig 2b). Overall, safety was similar with tofacitinib or PBO (Table): 77.3% and 74.1% had adverse events (AEs); 1.1% and 2.4% had serious AEs. In Part 1, 2 pts had herpes zoster (non-serious) and 3 pts had serious infections (SIs). In Part 2, SIs occurred in 1 tofacitinib pt and 1 PBO pt. No pts died.
Conclusion: In pcJIA pts, tofacitinib vs PBO resulted in significantly fewer disease flares, and improved time to flare, disease activity and physical functioning. Tofacitinib safety was consistent with that in RA pts.





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Table. Safety in all pts

	Part 1	Part 2	
	Tofacitinib[a] N=225	Tofacitinib[a] N=88	PBO N=85
Pts with events, n (%)			
AEs	153 (68.0)	68 (77.3)	63 (74.1)
SAEs	7 (3.1)	1 (1.1)	2 (2.4)
Permanent discontinuations due to AEs	26 (11.6)	16 (18.2)	29 (34.1)
AEs of special interest			
Death	0	0	0
Gastrointestinal perforation[b]	0	0	0
Hepatic event[b]	3 (1.3)	0	0
Herpes zoster (non-serious and serious)	2 (0.9)[c]	0	0
Interstitial lung disease[b]	0	0	0
Major adverse cardiovascular events[b]	0	0	0
Malignancy (including non-melanoma skin cancer)[b]	0	0	0
Macrophage activation syndrome[b]	0	0	0
Opportunistic infection[b]	0	0	0
SI	3 (1.3)	1 (1.1)[d]	1 (1.2)
Thrombotic event (deep vein thrombosis, pulmonary embolism[b] or arterial thromboembolism)	0	0	0
Tuberculosis[b]	0	0	0

[a]5 mg BID or equivalent weight-based lower dose in pts <40 kg
[b]Adjudicated events
[c]Both non-serious
[d]One SAE of pilonidal cyst repair was coded to surgical procedures instead of infections, and was inadvertently not identified as an SI. Following adjudication, the SAE did not meet opportunistic infection criteria; it is also included in the table as an SI
AE, adverse event; BID, twice daily; PBO, placebo; pts, patients; SAE, serious AE; SI, serious infection

OP0292

HIGH EFFICACY OF CANAKINUMAB IN SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS (SJIA) ACROSS AGE GROUPS: COMPARISON OF CHILDREN, ADOLESCENTS AND YOUNG ADULTS BASED ON POOLED CLINICAL TRIAL RESULTS

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Background: Still's disease is a systemic auto-inflammatory disease with a pediatric form, sJIA, and an analogous condition in adults, adult-onset Still's disease (AOSD). The role of interleukin-1 (IL-1) in the pathophysiology of Still's disease is well established. Canakinumab, a monoclonal antibody against IL-1ß, is approved to treat patients with Still's disease in Europe (sJIA and AOSD) and the United States (sJIA).
Objectives: To study the efficacy of canakinumab in sJIA patients categorized by age, we performed an intention-to-treat analysis of pooled data from 5 clinical trials, as an addition to a previously communicated analysis including 3 of the studies[1]
Methods: The age categories were children (2-<12 years), young adolescents (12-<16 years) and older adolescents and young adults (16-<20 years). We pooled efficacy results from patients with active disease at baseline treated during a 12-week period with canakinumab (4mg/kg every 4 weeks), including the presence of intermittent fever, serum concentrations of C reactive protein (CRP), improvement of sJIA (adapted pediatric ACR 30, 70 and 100 responses) and JIA ACR inactive disease status. Safety was assessed by analysis of reported adverse events (AEs).
Results: 302 children, 82 young adolescents and 34 older adolescents and young adults were included in the analysis, with a mean disease duration of 922, 1708 and 2615 days, respectively. Prior therapy with other biologics was common, with anakinra used in 33%, 35% and 47% of patients in each group. Disease severity was comparable among groups, with the mean number of active joints ranging from 11.8 to 13.7. Adapted pediatric ACR responses revealed a rapid response to canakinumab, with all groups showing similar rates of responders at most time points (Table 1). In each age group, the proportion of patients with inactive disease progressively increased to Day 57. At all time points after Day 15, the 16-<20 years group presented the highest proportion of patients with inactive disease. Median CRP levels decreased from baseline to reach values in the normal range (<10 mg/L) from Day 29 onwards in the three groups, with improvements more marked in the 16-<20 years group. The safety profile was similar in the three age groups analyzed, with a lower proportion of 16-<20 years old patients experiencing serious AEs (28%) as compared to children (35%) and young adolescents (42%).

Table 1. Percentages of patients with Adapted pediatric ACR responses and inactive disease status over time*

	Time of treatment (Days)	2 - <12 years[a]	12 - <16 years[b]	16-<20 years[c]
ACR30	15	72.7	81.7	83.9
(%)	29	77.5	84.1	82.4
	57	76.2	82.9	88.2
	85	65.5	74.5	83.3
ACR70	15	51.5	58.3	64.5
(%)	29	61.9	62.2	70.6
	57	65.2	58.5	79.4
	85	58.6	61.8	75.0
ACR100	15	21.6	25.0	12.9
(%)	29	29.5	30.5	35.3
	57	36.1	34.1	38.2
	85	34.1	30.9	33.3
Inactive disease	15	19.0	30.0	19.4
(%)	29	34.1	34.1	47.1
	57	39.4	36.6	55.9
	85	36.7	43.4	52.2

*Some studies did not include visits at Day 15 and/or 85. For Day 15, 29, 57 and 85 the respective denominators for each age group were: [a]N = 231, 302, 302, 232; [b]N = 60, 82, 82, 55; [c]N = 31, 34, 34, 24.

Conclusion: The efficacy and safety profile of canakinumab was consistent in children, adolescents and young adults with sJIA. Since sJIA and AOSD represent pediatric- and adult- onset variants of the Still's disease continuum, these results further support the therapeutic effect of canakinumab 4 mg/kg every 4 weeks in both children and adults with Still's disease.
References:
[1] Feist et al. *Clin Exp Rheumatol.* 2018;36(4):668-75.
Disclosure of Interests: Pierre Quartier Consultant of: AbbVie, Chugai-Roche, Lilly, Novartis, Sanofi, Sobi, Speakers bureau: AbbVie, BMS, Chugai-Roche, Novartis, Pfizer, Sobi, Eugen Feist Consultant of: Novartis, Roche, Sobi, Lilly, Pfizer, Abbvie, BMS, MSD, Sanofi, Speakers bureau: Novartis, Roche, Sobi, Lilly, Pfizer, Abbvie, BMS, MSD, Sanofi, Daniel J Lovell Consultant of: Abbott (consulting and PI), AbbVie (PI), Amgen (consultant and DSMC Chairperson), AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb (PI), Celgene, Forest Research (DSMB Chairman), GlaxoSmithKline, Hoffman-La Roche, Janssen (co-PI), Novartis (consultant and PI), Pfizer (consultant and PI), Roche (PI), Takeda, UBC (consultant and PI), Wyeth, Employee of: Cincinnati Children's Hospital Medical Center, Speakers bureau: Wyeth, Hiroaki Umebayashi: None declared, Nicolino Ruperto Grant/research support from: Bristol-Myers Squibb, Eli Lily, F Hoffmann-La Roche, GlaxoSmithKline, Janssen, Novartis, Pfizer, Sobi (paid to institution), Consultant of: Ablynx, AbbVie, AstraZeneca-Medimmune, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Eli Lily, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, Sanofi, Servier, Sinergie, Sobi, Takeda, Speakers bureau: Ablynx, AbbVie, AstraZeneca-Medimmune, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Eli Lily, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, Sanofi, Servier, Sinergie, Sobi, Takeda, Hermine Brunner Consultant of: Hoffman-La Roche, Novartis, Pfizer, Sanofi Aventis, Merck Serono, AbbVie, Amgen, Alter, AstraZeneca, Baxalta Biosimilars, Biogen Idec, Boehringer, Bristol-Myers Squibb, Celgene, EMD Serono, Janssen, MedImmune, Novartis, Pfizer, and UCB Biosciences, Speakers bureau: GSK, Roche, and Novartis, Cornelia Dunger-Baldauf Employee of: Novartis, Stephanie Noviello Employee of: Novartis, sarah whelan Employee of: Novartis
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OP0293

USE OF WHOLE-BODY MAGNETIC RESONANCE TO IDENTIFY POTENTIAL DIAGNOSTIC CLUES IN CHILDREN WITH FEVER OF UNKNOWN ORIGIN (FUO)

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Background: Whole-body magnetic resonance imaging (WBMRI) is a fast and accurate method to detect diseases throughout the entire body without exposure to ionizing radiation. Possible emerging applications for this technique include rheumatologic field and evaluation of fever of unknown origin (FUO).
Objectives: To evaluate the ability of WBMRI to identify significant potential diagnostic clue (PDC) in patients presenting a non specific inflammatory clinical picture.
Methods: We retrospectively collected cases of pediatric patients followed in a single pediatric rheumatology center who underwent WBMRI between January 2010 and December 2015 for the following indications: i) FUO (temperature greater than 38.3°C for more than three weeks or failure to reach diagnosis after one week of investigations), iii) recurrent fever (febrile episodes separated by periods of normal temperature), iii) Inflammation of unknown origin, IUO (an illness of at least 3 weeks' duration, with raised inflammatory markers and fever below 38.3°C).WBMRI studies were acquired with coronal and sagittal planes (slice thickness 5mm) with acquisition of several image sets with automatic direct image realignment after acquisition creating a whole-body scan.Sequences include short τ inversion recovery (STIR) and T1-weighted. All studies have been evaluated twice, the second time according to a predefined checklist, defined by an experienced radiologist, considering systematically single /multifocal bone lesion, bone marrow, joint effusion, soft tissues, adenopathies, parenchymal and vessels looking for PDC. We considered as a Potential Diagnostic Clue each alteration of the examined district that can potentially guide the diagnosis. Each alteration found is a PDC. We retrospectively evaluated patients' clinical history and final diagnosis and we classified the PDCs identified during both first evaluation and re-evaluation as: Not useful (the identified PDC did not guide the diagnosis and is not coherent with the final diagnosis), consistent (the identified PDC is congruent with the patient's final diagnosis) or diagnostic (the identification of the considered PDC strongly orient the final diagnosis).
Results: We collected 104 patients who underwent WBMRI; 24 (23%) of them presenting FUO, 28 (27%) presenting recurrent fever and 52 (50%) presenting IUO. The mean age of onset symptoms was 6 years and nine months (range: 2 weeks old- 17 years and 6 months). The mean age of execution of WBMRI was 9 years (range: 5 months old- 19 years). After the whole diagnostic work-out a final diagnosis was achieved in 44 patients (42%).PDCs were identified at the first evaluation in 78/104 cases (75%). In 22 cases (21%) the identified PDCs were consistent with the diagnosis, whereas in 9 cases (8.5%) the identified PDCs were considered diagnostic. Globally we can consider that at first evaluation PDCs were somehow contributory to the diagnosis in 31 cases (30%; 6 JIA, 7 systemic infections, 5 monogenic inflammatory diseases, 4 ALPS, 2 Goldbloom's Syndrome,2 Vasculitis,1 eosinophilic fasciitis, 1 hystiocytosis, 3 oncologic diagnosis).Blind re-evaluation of WBMRI allowed the identification of additional PDCs in 52 patients (12 of them previously negative). In 10 cases the PDC found after re- evaluation were consistent with the final diagnosis (2 JIA, one infectious disease, one neuroblastoma, 3 ALPS, 1 monogenic inflammatory disease, 1Takayasu arteritis, 1 Goldbloom's syndrome).
Conclusion: WBMRI can be a powerful diagnostic tool in patients with FUO. A predefined checklist increases sensitivity of WBMRI in the identification of PDC.
Disclosure of Interests: Sara Signa: None declared, Roberta Caorsi: None declared, Giorgio Stagnaro: None declared, Francesca Minoia: None declared, Paolo Picco: None declared, Angelo Ravelli: None declared, Maria Beatrice

Damasio: None declared, Marco Gattorno Consultant of: Sobi, Novartis, Speakers bureau: Sobi, Novartis
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Osteoporosis

OP0294 **DIFFERENTIAL INFLUENCE OF CO-MORBIDITIES ON SITE OF FRAGILITY FRACTURES**

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Background: Fragility fractures (FF) can occur at various sites of the skeleton, and are associated with multiple risk factors [1]. The prevalence of FF markedly increases with age. As the longevity of the population increases, so will the incidence of FF, and that of associated co-morbidities and risk factors. There are few data on co-morbidities associated with fractures at each site.
Objectives: Identify associations of co-morbidities with sites of FF, by applying cluster analysis.
Methods: We reviewed 28868 patients presenting for BMD estimation at a district general hospital in North West England, 2004-2016. We identified patients who had sustained one or more FF at time of presentation. Site(s) of FF were recorded for each patient, including femur, forearm, humerus, pelvis, ribs, spine, tibia or fibula. The following co-morbidities or treatments were recorded: excess alcohol consumption (previous or current); bisphosphonates; coeliac disease; family history of FF; hormone replacement therapy; hyperparathyroidism; hyperthyroidism; inflammatory bowel disease; polymyalgia rheumatica; rheumatoid arthritis; smoking (previous or current); corticosteroids (previous or current). Cluster analysis was performed on fracture sites and co-morbidities, using Jaccard similarity coefficient, and plotted on a dendrogram. Results were divided into an optimal number of clusters, derived using the elbow and silhouette methods.
Results: 11003 of 28868 patients had sustained one or more FF at time of BMD estimation. Overall, 84.6% patients were female, mean age 67.5years, and median T-score -1.12 SD. Cluster analysis was performed for FF sites and co-morbidities, with Jaccard similarity coefficients calculated. 4 clusters were identified (Figure 1): FF of forearm (n=5054), tibia/fibula (n=2617), spine (n=2352), associated with family history of FF, smoking, corticosteroids, and bisphosphonate treatment; FF of pelvis (n=300) associated with hyperparathyroidism, PMR, coeliac disease, and HRT; FF of femur (n=1181) and humerus (n=1131) associated with IBD and RA; FF of ribs (n=1022) associated with alcohol and hyperthyroidism.
Conclusion: Cluster analysis demonstrated 4 distinct subgroups of FF sites and associated co-morbidities. To our knowledge, this is the first study applying cluster analysis to evaluate co-morbidities associated with FF sites. Risk factors may influence trabecular more than cortical bone, accounting for the difference in clusters. Knowledge of risk factors associated with FF site subgroups will aid prophylaxis and management in at-risk patients.
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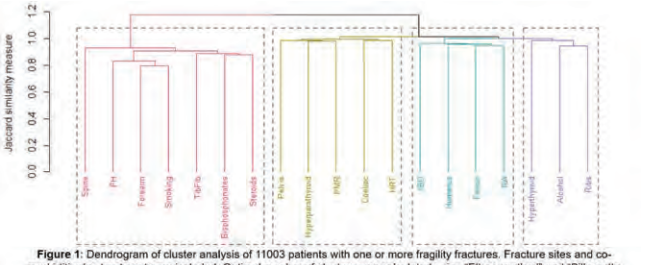


Figure 1: Dendrogram of cluster analysis of 11003 patients with one or more fragility fractures. Fracture sites and co-morbidities/co-treatments are included. Optimal number of clusters was calculated using "Elbow method" and "Silhouette method." Clusters are defined by colour and grey dashed boxes. FH= family history; TibFib= fracture of tibia or fibula; Hyperparathyroid= hyperparathyroidism; PMR= polymyalgia rheumatica; Coeliac= coeliac disease; HRT= hormone replacement therapy; IBD= inflammatory bowel disease; RA= rheumatoid arthritis; Hyperthyroid= hyperthyroidism.

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OP0295 **CORRELATION BETWEEN CORTICAL THICKNESS RELATIVE TO TRANSVERSE DIAMETER ON MID-PORTION OF THIRD METACARPAL BONE AND BONE MINERAL DENSITY IN LUMBAR SPINE AND FEMORAL NECK FOR PATIENTS WITH RHEUMATOID ARTHRITIS**

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Background: Rheumatoid arthritis (RA) is a determinant risk factor of osteoporosis. BMD is clearly defined as diagnosis criteria of osteoporosis in Japan; that is less than -2.5 with T-score measured with dual-energy X-ray absorptiometry (DXA). The marker of T-score <-2.5 is widely used worldwide; however, the testing system is very expensive, preventing its extensive adoption.
Objectives: We tried to evaluate BMD not measuring with DXA, but the other method that substituting DXA with another X-ray picture of hand that is routinely taken for Sharp/van der Heijde score (SHS) calculation.
Methods: Patient with RA, who met the American College of Rheumatology/European League Against Rheumatism classification criteria, visited our institute has been routinely calculated SHS in taking X-ray pictures of bilateral hands and feet at first consultation. Cortical thickness was calculated from mid-portion of third metacarpal bone in X-ray picture that was taken for the calculation of SHS as taking cancellous bone diameter of the third metacarpal bone from transverse diameter at the same point. We set Cortical Thickness Ratio (CTR) as cortical thickness relative to transverse thickness (Figure 1). BMD measurements at the lumbar spine (LS) and femoral neck (FN) were obtained, and BMD values are presented as g/cm^2 and T-score showing dissociation of the BMD compared with the mean BMD in healthy 30-year-old of the same sex with standard deviation was also presented. Patient with RA who underwent SHS calculation and BMD measurement at first consultation was picked up for the study. Relationship between BMD and the other parameters such as sex (male/female), age, disease duration (years), ACPA titer, RF titer, body mass index (BMI), CTR, the HAQ score, DAS28-CRP, SHS, PS-VAS, tartrate-resistant acid phosphatase-5b value (TRACP-5b), previous treatment for osteoporosis and RA before initial consultation (pTx_OP and pTx_RA) (Yes/No) at initial consultation was evaluated with linear regression analysis.
T-score<-2.5 was statistically evaluated with binary regression analysis for the parameters that demonstrated significant correlation in multivariate linear regression analysis.
Then, Cut-off index (COI) of CTR for the BMD represented with T-score <-2.5 for both of LS and FN was evaluated with Receivers Operation Characteristics technique (ROC). Sensitivity, specificity, area under curve, odds ratio with 95% confidence interval (95%CI) for T-score <-2.5 was also calculated.
Results: A total of 300 patients were picked up for the study. BMDs were 0.867 and 0.682 with 0.203 and 0.143 for standard deviations, that means T-score was -1.93 and -1.86 with 1.64 and 1.15 for standard deviations in LS and FN, respectively. Mean transverse width of third metacarpal bone was 7.3 mm and thickness of the cortex was 2.00 mm, so CTR was 0.279 in average and 0.124 for standard deviation.
In linear regression analysis, BMD in LS demonstrated significant correlation with sex, CTR, and DAS28-CRP, while BMD in FN demonstrated significant correlation with sex, age, and CTR.
In binary regression analysis, CTR and DAS28-CRP demonstrated significant positive correlation with T-score <-2.5 in LS, while age and CTR demonstrated significant correlation in FN.
In ROC, cut-off index of CTR was 0.25 in both of LS and FN, and sensitivities demonstrated 67.9% and 76.1%, and specificity demonstrated 83.0% and 81.6% in LS and FN, respectively. Area under curve was 0.78 and 0.81 with 4.17 (95%CI: 2.51 – 6.92) and 4.90 (95%CI: 2.75 – 8.73) of odds ratios for LS and FN, respectively (Figure 2).
Conclusion: Results of this cross-sectional study encourages our hypothesis that thickness of cortical bone relative to full thickness in the long bone reflects BMD. CTR correlated with BMD in both of LS and FN. CTR of third metacarpal bone was suggested that has close correlation with BMD in both LS and FN. CTR could be strong candidate marker for screening of osteoporosis in patient with RA with the index less than 0.25.

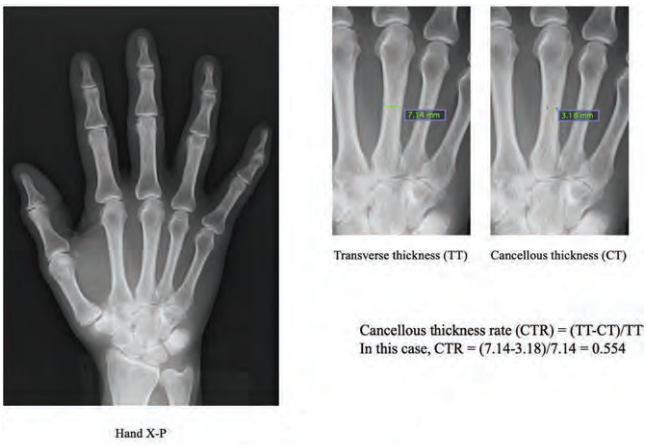


Figure 1: Calculation of CTR

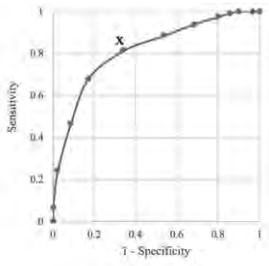


Figure 2-a: LS

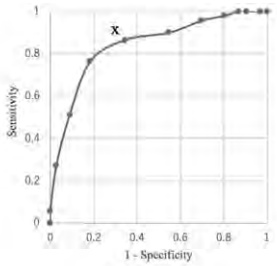


Figure 2-b: FN

X: COI; CTR < 0.25 for T-score < -2.5

	Sensitivity	Specificity	AUC	odds ratio	95%CI	p-value
LS	67.90%	83.00%	0.78	4.17	2.51 - 6.92	$3.43x10^{-8}$
FN	76.10%	81.60%	0.81	4.90	2.75 - 8.73	$6.90x10^{-8}$

Figure 2-c: Sensitivity, Specificity, odds ratio, 95%CI, and p-value

Figure 2: Area under curve graph and statistics of cut-off index for LS and FN

Disclosure of Interests: None declared
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OP0296

SUPERIOR EFFICACY OF CALCIFEDIOL SOFT GELATIN CAPSULES VS CHOLECALCIFEROL FOR THE MANAGEMENT OF VITAMIN D DEFICIENCY IN POSTMENOPAUSAL WOMEN: A TREATMENT TO BE CONSIDERED IN THERAPEUTIC GUIDELINES

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Background: Vitamin D deficiency is a highly prevalent entity worldwide, with relevance in specific diseases and stages of life[1]. Few guidelines assess the indications and optimal dosing in the general population, and although there is no international consensus, 800IU/day is associated with benefits in bone metabolism. Calcifediol, a vitamin D analog, is presented as a therapeutic alternative.

Objectives: To assess the efficacy of calcifediol in the treatment of vitamin D deficiency, compared with therapeutic guidelines recommendations for cholecalciferol in postmenopausal women.

Methods: Phase III-IV, double blind, randomised, controlled, multicentre superiority clinical trial. Postmenopausal women with baseline levels of 25(OH)D < 20 ng/mL were randomised to three arms: 266 mcg of calcifediol/month for 4 or 12 months (standard and test regime), or to cholecalciferol 25000 IU/month for 12 months (as per therapeutic guidelines).

Results from an interim analysis - performed upon completion of month 4 visit by 100% of evaluable patients - are presented and reported without unblinding the study treatments. Both calcifediol groups are summarised for analysis.

The trial has been approved by the corresponding ethics committees and national competent authorities.

Results: 298 women were included in the ITT analysis. The average age was 63.4 ± 8.2 years, mean BMI was 29.3 ± 6 Kg/m^2, 10.7% had osteoporosis and received treatment. All demographic characteristics and risk factors for osteoporosis were balanced amongst groups.

When analysing per treatment group,13.5% and 35% of women in the calcifediol group reached values of 25(OH)D > 30ng/mL at 1 and 4 months when compared to 0% and 8.2% respectively in the cholecalciferol group (p<0.01), achieving target levels in a rapid manner (Figure 1).

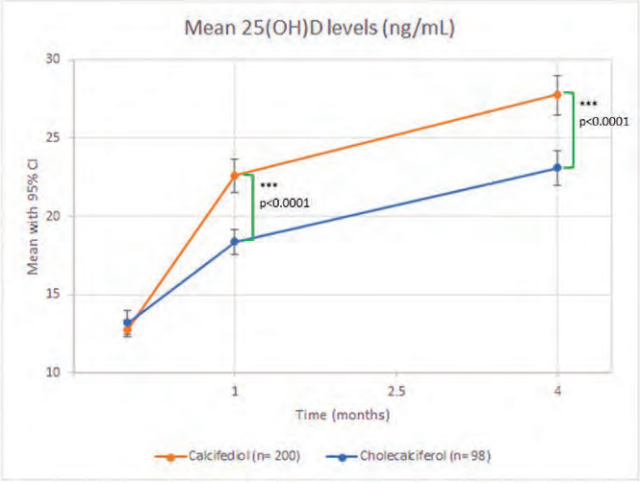


Figure 1. Regarding baseline levels, 25% of the population had levels <10ng/mL; in this group there were no statistically significant differences between both treatments, possibly due to the limited sample size. In the group with baseline levels from 10 to<20 ng/mL, a statistically significant mean difference was observed at months 1 and 4, with a greater proportion of patients achieving both therapeutic levels in the calcifediol group (Table 1). No relevant safety issues were reported for the present analysis.

Table 1.

		Basal 25(OH)D levels			
		< 10ng/mL^{NS}		10 to <20 ng/mL**	
		Calcifediol (n= 54)	Cholecalciferol (n= 20)	Calcifediol (n= 146)	Cholecalciferol (n= 78)
Month 1	>30 ng/mL	2 (3.7%)	0 (0%)	25 (17.1%)	0 (0%)
	>20 ng/mL	12 (22.2%)	2 (10%)	106 (72.6%)	31 (39.7%)
Month 4	>30 ng/mL	8 (14.8%)	1 (5%)	62 (42.5%)	7 (9%)
	>20 ng/mL	27 (50%)	8 (40%)	135 (92.5%)	63 (80.8%)

^{NS}p>0.05; **p≤0.01

Conclusion: Calcifediol shows a greater efficacy than cholecalciferol regime (as recommended in therapeutic guidelines), for the treatment of vitamin D deficiency in postmenopausal women and in a timely manner, which could impact osteoporosis treatment. Cholecalciferol fails to achieve recommended levels in a significant proportion of this population. Baseline vitamin D levels are to be considered for the supplementation of vitamin D.

References:

[1] Amrein, K., Scherkl, M., Hoffmann, M. *et al.* Vitamin D deficiency 2.0: an update on the current status worldwide. *Eur J Clin Nutr* (2020).

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OP0297

EFFICACY AND SAFETY OF ROMOSOZUMAB AMONG POSTMENOPAUSAL WOMEN WITH OSTEOPOROSIS AND MILD-TO-MODERATE CHRONIC KIDNEY DISEASE

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Background: Osteoporosis and renal insufficiency are coexisting disease states in a substantial proportion of postmenopausal women. Since bisphosphonates are generally contraindicated in patients with estimated glomerular filtration rate (eGFR) <35 mL/min, it is important to evaluate other osteoporosis treatments in this setting.

Objectives: To determine if baseline renal function affects the efficacy and safety of romosozumab.

Methods: We performed post hoc analyses of two clinical trials of romosozumab in postmenopausal women with osteoporosis. In ARCH (NCT01631214), 4,093 patients were randomised 1:1 to romosozumab 210 mg monthly or alendronate 70 mg weekly for 12 months (mean age: 74.3 years; 96.1% with prevalent vertebral fractures [VFx]). In FRAME (NCT01575834), 7,180 patients were randomised 1:1 to romosozumab 210 mg or placebo monthly for 12 months (mean age: 70.9 years; 18.3% with prevalent VFx). For these analyses, patients were categorised by baseline eGFR (mL/min/1.73m^2): normal renal function (eGFR ≥90), mild renal insufficiency (eGFR 60–89), or moderate renal insufficiency (eGFR 30–59). Least squares mean (LSM) percent change from baseline in bone mineral density (BMD) at the lumbar spine, total hip, and femoral neck; incidence of new VFx and adverse events (AEs); and changes in renal function were assessed for each eGFR category at Month 12 of the double-blind treatment period.

Results: At baseline, most patients had mild/moderate renal insufficiency: 84% in ARCH, 88% in FRAME. In both studies, change from baseline in BMD was significantly higher in the romosozumab group across baseline eGFR categories (Figure). There was an interaction between BMD increase and renal function, and although BMD increase was not as large in women with impaired renal function, differences between romosozumab and control groups remained significant (Figure). In ARCH, among patients with eGFR ≥90, 60–89, and 30–59, the incidence of new VFx (romosozumab vs alendronate) at Month 12 was 3.3% vs 7.3%, 3.2% vs 3.9%, and 3.4% vs 6.2% in ARCH. In FRAME, the incidence of new VFx (romosozumab vs placebo) at Month 12 was 0.5% vs 3.0%, 0.4% vs 1.5%, and 0.6% vs 2.1%.

In both studies, the incidences of AEs and serious AEs were similar in both treatment groups within and across eGFR categories. AEs of mild-to-moderate hypocalcaemia (investigator reported) occurred in two patients in ARCH (one romosozumab [eGFR 60–89] and one alendronate [eGFR ≥90]), and one patient in FRAME (romosozumab [eGFR 60–89]). Five patients in ARCH (all in the alendronate group) and 19 patients in FRAME (14 romosozumab, 5 placebo) had decreases in serum Ca levels (albumin adjusted); in the romosozumab group all were mild (<LLN–8.0 mg/dL) or moderate (<8.0–7.0 mg/dL). A similar percentage of patients in each group had changes in renal function over 12 months of treatment.

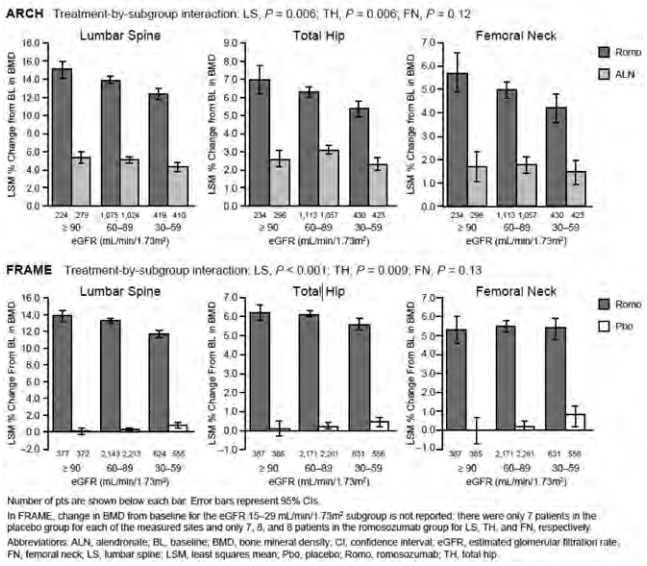
Conclusion: The efficacy and safety of romosozumab vs alendronate or placebo was similar among postmenopausal women with osteoporosis and different levels of renal function.

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Figure. LSM (95% CI) % Change in BMD From Baseline to Month 12



Number of pts are shown below each bar. Error bars represent 95% CIs.

In FRAME, change in BMD from baseline for the eGFR 15–29 mL/min/1.73m² subgroup is not reported; there were only 7 patients in the placebo group for each of the measured sites and only 7, 8, and 8 patients in the romosozumab group for LS, TH, and FN, respectively.

Abbreviations: ALN, alendronate; BL, baseline; BMD, bone mineral density; CI, confidence interval; eGFR, estimated glomerular filtration rate; FN, femoral neck; LS, lumbar spine; LSM, least squares mean; Pbo, placebo; Romo, romosozumab; TH, total hip.

OP0298

STUDY OF RISK OF VERTEBRAL FRACTURES AFTER THE WITHDRAWAL OF DENOSUMAB TREATMENT

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Background: The discontinuation of treatment with denosumab (Dmab) has been associated with a reactivation effect of bone metabolism that manifests itself with a loss of bone mass and an increased risk of vertebral fractures (VF). The incidence and risk factors that may lead to such loss are not clearly established.

Objectives: Determine the incidence of VF and bone loss in patients who have withdrawn treatment with Dmab and objectify possible associated risk factors.

Methods: Retrospective review study of patients treated with Dmab and monitored the last two years in monographic osteoporosis consultations. . We selected patients who withdrew treatment with Dmab and registered demographic characteristics, risk factors for osteoporosis and densitometries prior to treatment and during the period of suspension. We identified patients who presented fractures during treatment withdrawal period, assessing: number of fractures, time from withdrawal to fracture presence, location and if they had received osteoactive treatment in that period.

Results: Of 415 patients treated with Dmab, 83 discontinued treatment. The average age was 63.91 years, 95.2% of them women. The average duration of treatment prior to withdrawal was 2.73 years. 43.4% of the patients had previous fractures, 47.2% vertebral. The data of the previous bone mineral density and during the follow-up are shown in Table 1. 60 patients presented risk factors for osteoporosis, the most frequent being low calcium intake (36.6%) and 15.6% had disease and osteopenizing treatment. 92.7% of the patients had received prior osteoactive treatment. The most frequent reason for withdrawal of Dmab was for therapeutic vacations (56.6%). 39 patients performed post-withdrawal osteoactive treatment, mostly zoledronate (51.3%). During the two years after the rest, 9 patients had fractures (10.9%), seven of vertebral location (77.7%) and ≥ 2 VF were observed in five of them. 5 patients (71.4%) already had fractures prior to the onset of Dmab. The average time from withdrawal from treatment to fracture presentation was 15 months. None of the fractured patients had received treatment after Dmab withdrawal. Although the mean BMD analyzed by DXA at the end of treatment and that the loss of BMD during rest was higher in patients with fracture compared to those without fracture (-7.8% vs -4.3% in the spine and -8.6% vs -4.4% in total femur), the differences were not significant.

Conclusion: The incidence of VF in patients who interrupted Dmab was 8.43%. Fractured patients had lower BMD gain despite the treatment than non-fractured patients and also the loss of BMD at rest was greater, without significant differences probably due to low number of patients. Neither the presence of previous fractures nor the duration of treatment could be related to the presence of VF at rest.

Disclosure of Interests: None declared

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Table 1. BMD values and percentage of BMD change at the start of treatment with denosumab and during two years of withdrawal.

	Previous Stop Dmab (n=83)		Stop Dmab (n=54)		Break Dmab1 (n=28)		Break Dmab2 (n=20)	
DMO (mean)	(g/cm2)	T-score	(g/cm2)	T-score	(g/cm2)	T-score	(g/cm2)	T-score
Lumbar spine	0,861 ± 0,1	-2,61	0,949 ± 0,1	-1,94	0,965 ± 0,2	-1,93	0,920 ± 0,2	-2,22
Femoral neck	0,735 ± 1	-1,96	0,774 ± 0,1	-1,71	0,758 ± 0,1	-1,84	0,740 ± 0,1	-2,02
Total femur	0,784 ± 0,1	-1,81	0,823 ± 0,1	-1,48	0,805± 0,1	-1,63	0,801 ± 0,1	-1,68
% change DMO								
Lumbar spine			12,2 ± 10,3		-5 ± 7,9		-5,44 ± 7,9	
Femoral neck			6 ± 8,5		-4,2 ± 3,9		-5,35 ± 5,8	
Total femur			3,9 ± 4,2		-5,2 ± 4,9		-0,33 ± 19,6	

OP0299 CLINICAL FEATURES ASSOCIATED WITH FRAGILITY FRACTURE AFTER DISCONTINUATION OF TREATMENT WITH DENOSUMAB: A CASE-CONTROL STUDY

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Background: Discontinuation of denosumab treatment causes an increase in bone resorption that has been linked to the emergence of vertebral fractures.
Objectives: To evaluate the association of clinical features and demographic characteristics with the emergence of new fragility fractures in patients with osteoporosis who interrupt treatment with denosumab.
Methods: Retrospective case-control study. Medical records of all patients with osteoporosis, from our local densitometry database, who received treatment with denosumab (at least one dose) and discontinue the treatment, have been studied.
Information was collected on demographic variables (age, sex), risk factors for osteoporosis (alcohol and tobacco consumption, personal history of fragility fracture and history of maternal hip fracture), secondary osteoporosis (due to early menopause, disease or osteopenizing treatment), previous treatment for osteoporosis, start and end date of denosumab treatment and subsequent treatments.
All patients who suffered a fragility fracture from 6 months after the last dose of denosumab up to 20 months later were defined as a case. Prior treatment with bisphosphonate was considered to those who had received it for at least 1 year, and subsequent treatment with bisphosphonate was considered to those who received it immediately or up to 8 months after the last dose of denosumab.
Results: In total, 63 patients who discontinued treatment with denosumab were included. Ten of them presented fragility fractures (6 vertebral, 3 forearm and 1 hip). Two patients had a fracture after 24 months of the last dose of denosumab, so don't were considered cases. 61 patients were women (96.83%) and the mean age (SD) was 70.22 (8.95) years. The mean time (SD) of treatment with denosumab was 42.25 (17.32) months, with a mean (SD) doses of 7.85 (2.78). The reasons for interruption of denosumab were: improvement 39 (65%), dental procedure 9 (15%), patient decision 6 (10%), adverse event 4 (6.66%) and inefficacy 2 (3.33%). Demographic and clinical features by fragility fracture are shown in Table 1. We found that subsequent treatment with bisphosphonates after denosumab was initiated in less patients in the fracture group than in the control group (10% vs 42,9%; p=0,05), and we found no fractures in patients diagnosed with secondary osteoporosis. No statistically significant differences were found in the rest of the variables.

Table 1. Demographic and clinical features by fragility fracture.

	No fracture	Fracture	Total	p
Age, mean (SD)	70.2 (9.5)	70.5 (5.5)	70.2 (8.9)	0.956
BMI, mean (SD)	25.0 (4.8)	25.3 (3.2)	25.1 (4.6)	0.844
Secondary OP (%)	26 (49.1)	0 (0)	26 (41.3)	0.004
Tobacco (%)	17 (32.1)	2 (25.0)	19 (31.1)	0.687
Alcohol (%)	3 (5.7)	0 (0.0)	3 (4.9)	0.490
Previous fracture (%)	20 (37.7)	6 (66.7)	26 (41.9)	0.104
Mother hip (%)	6 (11.3)	0 (0.0)	6 (9.8)	0.316
Previous BP (%)	29 (67.4)	2 (50.0)	31 (66.0)	0.481
Denosumab dose, mean (SD)	7.9 (2.8)	7.5 (3.0)	7.9 (2.8)	0.676
Subsequent BP (%)	21 (42.9)	1 (10.0)	22 (37.3)	0.050

BMI: body mass index; BP: bisphosphonate; OP: osteoporosis; SD: standard deviation.

Conclusion: Sequential treatment with bisphosphonates and diagnosis of secondary osteoporosis are related to the absence of fractures after discontinuation of denosumab treatment.
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OP0300 A CROSS-SECTIONAL, MATCHED-PAIR ANALYSIS OF ACPA POSITIVE AND ACPA NEGATIVE RHEUMATOID ARTHRITIS PATIENTS COMPARING THE PREVALENCE OF OSTEOPOROSIS, FRAGILITY FRACTURES AND UNDERLYING RISK FACTORS

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Background: Rheumatoid arthritis (RA) is associated with increased systemic bone loss, leading to a high risk for fragility fractures. Especially anti-citrullinated protein antibody (ACPA) positivity is considered a risk factor for local bone erosions and systemic bone loss[1].
Objectives: The purpose of this study was to compare ACPA positive versus ACPA negative RA patients in terms of the prevalence of osteoporosis and fragility fractures and to identify differences in underlying risk factors that influence bone health.
Methods: Rh-GIOP is an ongoing prospective observational study collecting and analyzing disease- and bone-related data from patients with chronic rheumatic diseases or psoriasis treated with glucocorticoids (GC). In this cross-sectional analysis, we performed a matched-pair analysis, matching 114 ACPA positive to 114 ACPA negative RA patients according to age (5-year-steps), sex, and body mass index (BMI, 2-unit-steps). Descriptive analyses were performed, with values displayed as mean ± standard deviation for continuous variables. Non-parametric tests were used at a two-sided significance level of 5% to compare differences in underlying and potential risk factors without adjustment for multiple testing.
Results: At same mean age (63.9 ±10.2 years) and BMI (27.9 ±5.6kg/m^2), the matched groups had a female proportion of 82.5%. APCA positive patients had a significantly longer mean disease duration (13.9 vs 9.9 years, p<0.001), a higher mean cumulative GC-dose (22.3 vs 13.2g, p<0.01) and mean duration of GC therapy (10.1 vs 6.6 years, p<0.01). There was no significant difference in the prevalence of osteoporosis as defined by dual-energy X-ray absorptiometry (DXA) (18.4 vs 20.2%), nor in the prevalence of vertebral (7.0 vs 5.3%) or non-vertebral fractures (31.6 vs 29.8%). C-reactive protein levels as a marker of disease activity were significantly higher in ACPA positive patients (mean: 8.8 vs 4.3mg/l, p= 0.02), while mean disease activity score (DAS)28 levels were slightly lower in ACPA positive patients (2.4 vs 2.7, p= 0.05). No difference in health assessment questionnaire (HAQ) score was found. RA-specific treatments were similar, especially concerning current mean daily GC-dose (6.7 vs 4.9mg/day), except for Rituximab and targeted synthetic disease modifying anti-rheumatic drugs (DMARDs) which were more commonly used in ACPA positive patients (9.6 vs 2.6%, p=0.05) and (5.3 vs 0%, p=0.029), respectively. ACPA positive patients did not differ significantly from ACPA negative patients in specific anti-osteoporotic treatment, nor in the prevalence of comorbidities or concomitant medication. There were no significant differences in bone-specific laboratory parameters.
Conclusion: In a cross-sectional analysis of our cohort, the prevalence of osteoporosis and fragility fractures was similar between ACPA positive and ACPA negative RA patients, despite longer disease duration and GC-treatment in ACPA positive patients. This is remarkable since it implies that ACPA negative patients are at a similar risk for osteoporosis and associated fractures. Optimal management of disease activity with or without GCs may represent a mainstay in preventing disease-related comorbidities such as osteoporosis.
References: **[1]**Steffen, U., Schett, G., & Bozec, A. (2019). How Autoantibodies Regulate Osteoclast Induced Bone Loss in Rheumatoid Arthritis. Frontiers in immunology, 10, 1483. doi:10.3389/fimmu.2019.01483
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OP0301

PREDICTION OF LOW BONE MINERAL DENSITY AND FRAX SCORE BY ASSESSING HIP BONE TEXTURE WITH DEEP LEARNING

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Background: Osteoporosis is a widespread health concern associated with an increased risk of fractures in individuals with low bone mineral density (BMD). Dual-energy x-ray absorptiometry (DXA) is the gold standard to measure BMD, but methods based on the assessment of plain films, such as the digital radiogrammetry,[1] are also available. We describe a novel approach based on the assessment of hip texture with deep learning to estimate BMD.
Objectives: To compare the BMD estimated by assessing hip texture using a deep learning model and that measured by DXA.
Methods: In this study, we identified 1,203 patients who underwent DXA of left hip and hip plain film within six months. The dataset was split into a training set with 1,024 patients and a testing set with 179 patients. Hip images were obtained and regions of interest (ROI) around left hips were segmented using a tool based on the curve Graph Convolutional Network. The ROIs are processed using a Deep Texture Encoding Network (Deep-TEN) model,[2] which comprises the first 3 blocks of Residual Network with 18 layers (ResNet-18) model followed by a dictionary encoding operator (Figure 1). The encoded features are processed using a fully connected layer to estimate BMD. Five-fold cross-validation was conducted. Pearson's correlation coefficient was used to assess the correlation between predicted and reference BMD. We also test the performance of the model to identify osteoporosis (T-score ≤ -2.5)

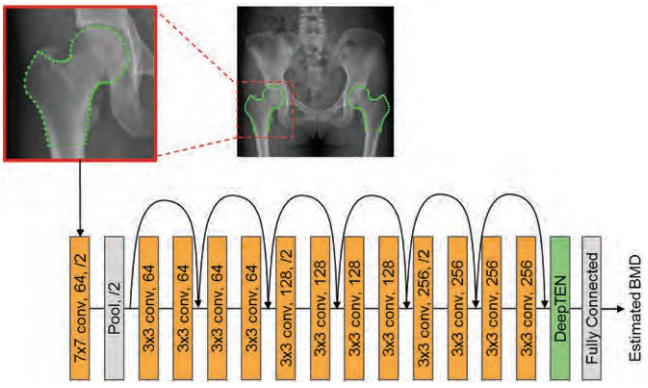


Figure 1. Schematic representation of deep learning models to extract and encode texture features for estimation of hip bone density.

Results: We included 151 women and 18 men in the testing dataset (mean age, 66.1 ± 1.7 years). The mean predicted BMD was 0.724 g/cm^2 compared with the mean BMD measured by DXA of 0.725 g/cm^2 (p = 0.51). Pearson's correlation coefficient between predicted and true BMD was 0.88. The performance of the model to detect osteoporosis/osteopenia was shown in Table 1. The positive predictive value was 87.46% for a T-score ≤ -1 and 83.3% for a T-score ≤ -2.5. Furthermore, the mean FRAX® 10-year major fracture risk did not differ significantly between scores based on predicted (6.86%) and measured BMD (7.67%, p=0.52). The 10-year probability of hip fracture was lower in the predicted score (1.79%) than the measured score (2.43%, p = 0.01).

Table 1. Performance matrices of the deep texture model to detect osteoporosis/osteopenia

	T-score ≤ -1	T-score ≤ -2.5
Sensitivity	91.11% (95% CI, 83.23% to 96.08%)	33.33% (95% CI, 17.29% to 52.81%)
Specificity	86.08% (95% CI, 76.45% to 92.84%)	98.56% (95% CI, 94.90% to 99.83%)
Positive predictive value	88.17% (95% CI, 81.10% to 92.83%)	83.33% (95% CI, 53.58% to 95.59%)
Negative predictive value	89.47% (95% CI, 81.35% to 94.31%)	87.26% (95% CI, 84.16% to 89.83%)

Conclusion: This study demonstrates the potential of the bone texture model to detect osteoporosis and to predict the FRAX score using plain hip radiographs.
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The new art of phenotyping and treating Sjögren's syndrome

OP0302

IANALUMAB (VAY736), A DUAL MODE OF ACTION BIOLOGIC COMBINING BAFF RECEPTOR INHIBITION WITH B CELL DEPLETION, REACHES PRIMARY ENDPOINT FOR TREATMENT OF PRIMARY SJOGREN'S SYNDROME

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Background: Primary Sjogren's syndrome (pSS) is a multi-organ autoimmune disease mainly affecting excretory glands and characterised by B-cell hyperactivity. No approved systemic treatment is available. Ianalumab (VAY736) is an anti-B-cell activating factor (BAFF) receptor fully human monoclonal antibody, engineered for direct ADCC-mediated B-cell depletion.
Objectives: This phase 2b study aimed at establishing a dose-response relationship over a range of VAY736 doses, using change from baseline (BL) in EULAR Sjogren's Syndrome Disease Activity index (ESSDAI) over 24 Weeks (Wks) as primary endpoint. The study is ongoing with a second blinded treatment period up to Wk52. Here we report efficacy and safety Wk24.
Methods: 190 patients (pts) were randomised 1:1:1:1 to receive monthly s.c. doses of VAY736 (5, 50, 300mg) or placebo (PBO). Prior to 1st-dose of study treatment, pts received methylprednisolone i.v. 250mg. Eligible pts fulfilled American European Consensus Group (AECG) criteria, were anti-Ro/SSA+, had ESSDAI ≥6 and EULAR Sjogren's Syndrome Patient Reported Index (ESSPRI) ≥5. Statistical methods included MCP-Mod to assess dose-response on change of ESSDAI from BL and responder rate analysis to calculate the proportion of pts with ≥3 points improvement on ESSDAI. Secondary endpoints included ESSPRI, Functional Assessment of Chronic Illness Therapy Fatigue (FACIT-F), Physician's (PhGA) and Patient's Global Assessments (PaGA), SF-36, stimulated salivary flow (sSF), Schirmer's test.
Results: Primary endpoint was met with statistically significant dose-response for ESSDAI (Figure). The largest ESSDAI reduction was 1.92 points over PBO for VAY736 300mg at Wk24. Responder rate analysis on ESSDAI revealed for 300mg vs PBO responder rates of 42/47 (89.4%) vs 30/49 (61.2%), a difference of 28.1% (p=0.0019). No differences were seen for 5mg and 50mg vs PBO. PhGA change from BL was significantly different between 300mg and PBO (p=0.022). A numerical trend for sSF improvement for VAY736 300mg compared to PBO was notable at Wk24 (p=0.092). For secondary endpoints ESSPRI and FACIT-F, VAY736 treatment showed no benefits over PBO. PBO responses were generally high. Incidence of treatment emergent AEs was comparable across all studied groups, whereby site injection reactions were most frequent, mostly mild and showed a dose-response.
Conclusion: Primary endpoint assessing ESSDAI was met, showing statistically significant dose-response for ianalumab with clinically important improvement for 300mg vs PBO. Preliminary safety profile of ianalumab was good.

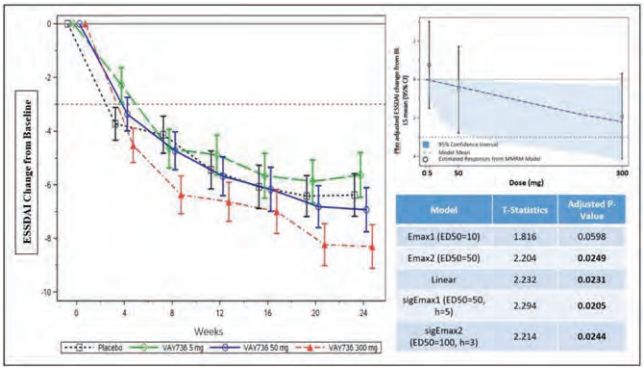


Figure. ESSDAI Change from Baseline over Time up to Week 24 Reveals a Statistically Significant Dose Response Relationship

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Meniscus : an innocent bystander in osteoarthritis?

OP0303

CORTICOSTEROID INJECTION IN KNEE OSTEOARTHRITIS IS ASSOCIATED WITH REDUCTION IN MENISCAL THICKNESS AND JOINT SPACE WIDTH WITH NO EFFECT ON CARTILAGE THICKNESS: A CASE CONTROL STUDY

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Background: Intra-articular corticosteroid injections (IACI) are commonly used for the treatment of symptomatic knee osteoarthritis (OA) and therapeutic guidelines have recommended their use. However, their safety regarding the evolution of structural changes remains unknown.
Objectives: This study explored the effects of IACI on the evolution of knee OA structural changes assessed by magnetic resonance imaging (MRI).
Methods: Participants were selected from the Osteoarthritis Initiative database. In this nested case-control design study, participants who received one treatment with IACI and had MRI exams available at the yearly follow-up visits before (pre-treatment), during (treatment), and after (post-treatment) were defined as "cases". Each case was matched with one control for age, gender, body mass index (BMI), height, joint space width (JSW), cartilage volume, bone marrow lesion (BML), meniscal extrusion, and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain at baseline. Ninety-three (93) participants fulfilling the inclusion criteria were selected and matched to controls (n=93). The study structural variables were MRI (cartilage volume, meniscal thickness, bone marrow lesion (BML), bone curvature), X-rays (JSW), and symptoms (WOMAC pain), assessed at the yearly consecutive visits and changes measured within the follow-up periods.
Results: At baseline, the control and treatment groups were balanced. In the pre-treatment period, the cartilage volume loss in the medial compartment was significantly greater in the IACI (p=0.006) compared to the control group, with a numerical trend (p=0.071) in the lateral compartment. In the treatment period, the cartilage loss was not different between groups, with the exception of a significantly greater loss in the lateral compartment in the IACI group (p=0.041). In the post-treatment period there was no difference in the cartilage loss between the groups in both compartments. For the meniscal thickness loss in the pre-treatment period, no difference was found between groups; however, there was a significantly greater loss (p=0.007) during the treatment period in the IACI. In the post-treatment period, the loss of the medial meniscus was similar in both groups. For the lateral meniscus, there was no significant difference at any time between the two groups. The loss in JSW in the pre- and post-treatment periods was not different between groups, but was significantly greater (p=0.011) in the IACI group in the treatment period. The changes in the BML sizes over time were small and similar between groups. For the bone curvature, IACI group showed a smaller change compared to the control (p=0.037) at the treatment period. The WOMAC pain changes in both groups were small and unlikely to be clinically relevant.
Conclusion: This study provides evidence that in knee OA, IACI were not associated with the occurrence of any deleterious effect on knee structures post-treatment, including cartilage volume and loss. The increase in the rate loss of medial meniscal thickness, which was associated with a loss of JSW, was a transient phenomenon and its clinical relevance unknown at that time.
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SpA: Innovative techniques in spondyloarthritis research – Is there light at the end of the tunnel for our patients?

OP0304

METABOLOMICS PROFILING OF HUMAN SERUM FOR DISCOVERING BIOMARKERS TO DIAGNOSE PSORIATIC ARTHRITIS AND ANKYLOSING SPONDYLITIS WITH HIGH SPECIFICITY

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Background: High-specificity biomarkers that can differentiate PsA and AS patients from healthy people, as well as RA patients, would be extremely helpful for early diagnosis and treatment of these two diseases. Based on the hypothesis that each disease state may cause specific changes to the metabolome, metabolomics is becoming a powerful tool for biomarker discovery. In this work, we applied a high-performance chemical isotope labeling (CIL) LC-MS platform to search for biomarker candidates of PsA and AS in human serum samples.
Objectives: We aimed to identify metabolite biomarkers with high specificity for PsA and AS.
Methods: Serum samples were collected from 331 subjects, including 100 healthy controls, 48 PsA patients, 52 AS patients and 131 RA patients. The average age of each group was: 52.6 (control), 50.7 (PsA), 51.8 (AS) and 53.1 (RA) years. After pre-treatment, each sample was incubated with ^{12}C-dansyl chloride, which can label the amine/phenol-containing metabolites. The reference sample for relative quantification was prepared by mixing all individual samples and then labeled by ^{13}C-dansyl chloride. With this normalization, the individual samples and the reference sample were mixed at an equal amount. Finally, we used an LC-QTOF-MS platform to analyze the mixtures and measure the ^{12}C/^{13}C peak pairs.
Results: We detected 1,149 peak pairs commonly existing in the serum samples. Using our dansyl-library of 700 dansyl-labeled standards and a prediction library, which contains the predicted retention times and mass values of 3,431 dansylated human metabolites, we identified 134 and 141 peak pairs, respectively. The relative concentrations are calculated from the intensity ratios of ^{12}C/^{13}C peak pairs. We first visualized the entire amine/phenol-submetabolome for all phenotypes using the partial least squares discriminant analysis (PLS-DA). We found that the most significant between-group separation was between healthy controls and all the patients. No significant sex or age effect was observed. Furthermore, among the three diseases, PsA and AS samples were closely clustering, while the RA group was well separated from them. Therefore, we chose a two-step diagnosis approach that first differentiates PsA patients from controls/RA patients and then filters out the AS patients wrongly classified as PsA in the first step. The same strategy was conducted for AS. Stipulating a fold change larger than 1.5 with the false discovery rate lower than 5%, we found 74 metabolites having significantly

higher or lower concentrations in the PsA group compared to the control or the RA group. We selected two of these significant metabolites to build a classification model based on the linear support vector machine (SVM) method, and the area-under-the-curve (AUC) value of the resulting receiver operating characteristic (ROC) curve was 0.929 (95% confidence interval: 0.899-0.956). Similarly, 37 metabolites could differentiate AS samples from RAs and controls. A proposed diagnostic panel containing four metabolites demonstrated an AUC value of 0.890 (0.843-0.934). For the last step, distinguishing between PsA and AS, there were 15 significantly increased metabolites and 9 lowered ones. The biomarker panel consisting of the top three metabolites also achieved good discriminatory power with AUC = 0.827 (0.717-0.919).

Conclusion: Isotope-labeling-LC-MS-based metabolomics has revealed biomarker candidates that can specifically differentiate PsA or AS patients from control populations.

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OP0305 RHO-GTPASE PATHWAYS MAY DIFFERENTIATE RESPONDER AND NON-RESPONDERS TO TUMOUR NECROSIS FACTOR INHIBITOR (TNFI) AND INTERLEUKIN-17A INHIBITOR (IL-17AI) THERAPY IN PSORIATIC ARTHRITIS (PSA)

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Background: In PsA there is a pressing need to develop a coherent strategy for identifying initial and subsequent biologic responders. PsA patients present substantial heterogeneity in response to biologics, and molecular subtyping will help to identify the right patient for the right treatment.

Objectives: To identify transcript profiles (biomarkers) that will select TNFi and IL-17Ai responders in PsA using baseline CD4+ cells; and elucidate novel signaling pathways relevant to biologic disease modifying antirheumatic drug (bDMARD) response using a systems biology approach.

Methods: Consenting patients initiating TNFi agents (20 patients) or IL-17Ai agents (20 patients) with moderate-to-severe PsA were assessed with a comprehensive standardized protocol at baseline and at 3 months. Responder to bDMARDs was defined by Disease Activity index for PSoriatic Arthritis (DAPSA) score of less than 14 (low disease activity). Global transcript profiling was performed on all patients prior to initiation of and 3 months post bDMARDs. We mapped RNA-seq reads to the hg19 reference genome using STAR and quantified transcripts with Cufflinks. The transcripts per million (TPM) values were log-transformed for statistical analyses

Results: The demographics of PsA patients for both treatment groups are presented (Table 1). Differentially expressed genes (DEGs) were identified using the limma tool for TNFi and IL-17Ai responders and non-responders (Figure 1) as well as DEGs that differentiated TNFi from IL-17Ai response and non-response. Integration of differential gene expression data with tissue-specific protein-protein interactions (IID version 2018-11) identified 117 and 132 DEGs between responders and non-responders to TNFi and IL-17Ai treatments, respectively. Comprehensive pathway enrichment analysis of these genes using pathDIP (v 4.1) revealed 576 (out of 5380) pathways enriched in 117 DEGs between responders and non-responders to TNFi, and 125 pathways enriched in 132 DEGs between responders and non-responders to IL-17Ai. Interestingly, while these two gene lists share only 17 genes, they have 79 enriched pathways in common suggesting potential effect of two different treatments on similar pathways but through different pathway members (Figure 2). Moreover, it suggests potential importance of the 17 shared genes in association with these pathways. Most of these pathways are related to innate and adaptive immune system, and to "osteoclast differentiation". Among 46 pathways specific to response to IL-17Ai, multiple Rho-GTPase-related pathways were identified. It has been shown that experimental inhibition of ROCK2, a target of Rho-GTPase family is effective in psoriatic disease through regulation of IL-17/23/10, but not IL-6 and TNFα.

Table 1. Demographics of psoriatic arthritis (PsA) patients.

	IL-17Ai	TNFi
Number of PsA patients	20	20
Gender (% female)	55%	75%
Mean Age (Years)	55.9 (9.5)	56.8 (7.9)
Mean Disease Duration (Years)	10.4 (6.9)	7.3 (7.9)
Mean DAPSA baseline	38.8 (17.5)	45.6 (28.9)
Responders (%) (DAPSA <14)	35%	65%
Biologic naïve (%)	40%	60%

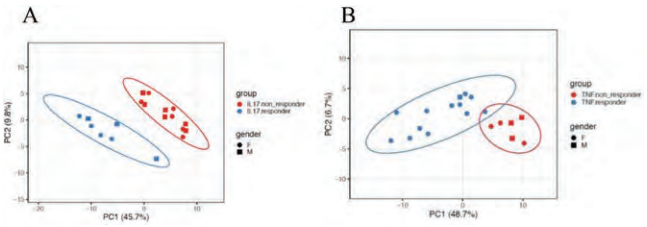


Figure 1. PCA plots illustrating that DEGs of CD4+ cells can differentiate responders from non-responders when treated with: **A.** IL-17Ai; and **B.** TNFi.



Figure 2. Over-represented terms in significantly enriched pathways considering DEGs between: **A.** IL-17i responders and non-responders (125 pathways); **B.** TNFi responders and non-responders (576 pathways).

Conclusion: Integration of cell-specific transcriptomic data with protein networks represents a very promising strategy for identifying biologic responders and pathways involved in predicting response that may have identified the Rho-GTP pathway as a potential marker to guide the choice of biologic agents for individual patients.

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Newly identified cell subsets driving disease pathogenesis

OP0306 CD11C-SPECIFIC ABLATION OF SHP1 INDUCES AUTOIMMUNE SIALADENITIS SIMILAR TO SJÖGREN'S SYNDROME

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Background: Dendritic cells (DCs) play important roles in inducing immune response as well as maintaining immune tolerance. Src homology 2 domain-containing protein tyrosine phosphatase-1 (Shp1) is a negative regulator of signaling in hematopoietic cells and is expressed in a variety of immune cells including DCs. Shp1 homozygous mutant mice (motheaten mice) develop multiple immunological abnormalities and they die around four weeks after birth because of severe pneumonitis. Motheaten mice produce large amounts of autoantibodies, and besides, B-1a cells, a distinct B cell subset, which are an important source of autoantibodies increase in these mice. The functional abnormality of DCs in motheaten mice has not been characterized, but DCs and macrophages increase in various organs of motheaten mice.
To analyze the function of Shp1 in DCs, we generated Shp1 conditional knockout mice (Shp1 CKO) in which *Shp1* gene is specifically depleted in $CD11c^+$ cells. We found that aged shp1 CKO developed autoimmune glomerulonephritis. We also found that they developed severe tubulointerstitial nephritis (TIN) at the age of 40 weeks, which is characterized by the infiltration of $CD11c^+$ and $F4/80^+$ cells. $CD4^+$ T cells from Shp1 CKO produce much more amount of IFNγ. Collectively, Shp1 in DCs acts as a key regulatory molecule to protect against autoimmunity.
Objectives: We analyzed salivary glands of CKO to confirm whether they have autoimmune sialadenitis because TIN is known to be the most common renal manifestations of Sjögren's syndrome in human.
Methods: Shp1 CKO are generated by crossing a mouse line carrying floxed *Shp1* allele to mice expressing Cre recombinase under the control of the CD11c promoter. Sex- and age-matched *Ptpn6*$^{fl/fl}$ littermates without *Cre* gene were studied as controls. We analyzed secretory function of the salivary glands in response to pilocarpine stimulation in Shp1 CKO at the age of 40 weeks or older. We then performed histological examination of salivary glands (submandibular glands and sublingual glands) with light-microscopy and immunohistochemical staining. The mononuclear cells prepared from the salivary glands were analyzed by flow cytometry (FCM). We also quantified anti-SSA/Ro60 antibodies and anti-SSB/LA antibodies by ELISA.
Results: Shp1 CKO secreted less saliva flow compared to control mice by pilocarpine stimulation. Histological study showed Shp1 CKO exhibited massive infiltration of inflammatory cells in salivary glands associated with periductal foci and periductal fibrosis. Most of infiltrated cells were stained by anti- CD4 or B220 mAbs. FCM revealed that B cells increased in the salivary glands of Shp1 CKO. In addition, B-1a cells also increased in the salivary glands of the mice. The levels of anti-SSA/Ro60 antibodies and anti-SSB/LA antibodies were increased in Shp1 CKO.
Conclusion: CD11c-specific ablation of Shp1 induces the ectopic generation of lymphoid structure in salivary glands and impairment of salivary secretion. Autoantibody profile in Shp1 CKO resembled that in human Sjögren's syndrome. Our findings suggest that aged Shp1 CKO have the potential to become a new mouse model for the analysis of Sjögren's syndrome.
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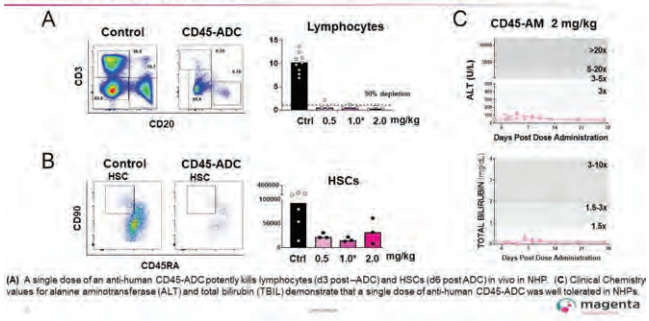
OP0307

A NOVEL TARGETED APPROACH TO ACHIEVE IMMUNE SYSTEM RESET: CD45-TARGETED ANTIBODY DRUG CONJUGATES AMELIORATE DISEASE IN PRECLINICAL AUTOIMMUNE DISEASE MODELS AND ENABLE AUTO-HSCT

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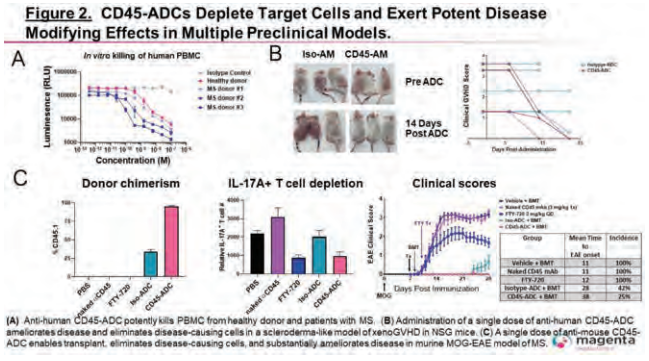
Background: Resetting the immune system through autologous hematopoietic stem cell transplant (autoHSCT) is a highly effective treatment in selected patients with autoimmune diseases. AutoHSCT can induce long-term remission with 80% progression free survival in multiple sclerosis patients (Muraro 2017, Burt 2019). Use of autoHSCT in scleroderma patients has achieved superior outcomes in two randomized studies compared to standard of care (Tyndall 2014, Sullivan 2018). These impressive results are achieved by a combination of the eradication of autoreactive immune effector cells and re-establishment of self-tolerance, i.e., immune system reset. However, only a small fraction of eligible patients undergo autoHSCT, largely due to toxicity associated with current conditioning protocols.
Objectives: As part of our goal to enable more patients to benefit from immune system reset, we have generated novel anti-human CD45 ADCs that cross react with nonhuman primates (NHP) and an anti-mouse CD45 ADC to model the approach in mouse models of AID.
Methods: The human-targeted CD45-ADC is an affinity-matured mAb that targets an epitope present on all human CD45 isoforms, is cross-reactive with NHP CD45, and is conjugated to a payload that efficiently kills both quiescent and cycling cells. This ADC is engineered to eliminate Fc-mediated effector function, enable site-specific conjugation of linker/payload, and enable rapid clearance. This ADC was evaluated in vitro and in vivo in hNSG and NHPs. The murine tool ADC specifically targets the CD45.2 isoform of mouse CD45, and is also engineered to eliminate effector function, allow for site-specific conjugation of linker payload, and be rapidly cleared. The payload for this murine tool ADC is potent and preferentially kills dividing cells. This ADC was tested for the ability to enable immune reset and ameliorate autoimmune disease in multiple disease models.
Results: The anti-human CD45-ADC showed efficient killing of human HSCs and human and cyno PBMC, including $CD3^+$ cells from healthy donors and patients with MS. In hNSG, single doses of the CD45-ADC were well-tolerated and led to substantial depletion of human cells. In NHPs, single doses of CD45-ADC were well tolerated and depleted both peripheral lymphocytes and HSCs. Administration of a single dose of anti-human CD45-ADC to hNSGs with sclerodermatous xenoGVHD resulted in depletion of human T cells and resolution of symptoms. A single-dose of the anti-mouse CD45-ADC enabled full myeloablation and complete durable donor chimerism with congenic HSCT at 16 weeks. In a murine immunization model of MS, MOG-induced EAE, a single dose of the CD45-ADC followed by congenic HSCT prior to disease onset enabled full donor chimerism, significantly delayed disease onset and reduced disease severity. We are generating additional data in an adoptive transfer model of EAE to confirm and extend these results. In a murine model of arthritis, therapeutic treatment with a single dose of the CD45-ADC followed by congenic HSCT enabled complete donor chimerism and halted disease progression, comparable to with the effects of an anti-TNFα antibody. The ADC is being further evaluated in a model of type 1 diabetes and those data will be presented. These data demonstrate that CD45-ADC conditioning followed by congenic HSCT is sufficient for full myeloablation and immune reset.
Conclusion: These results demonstrate that targeted immune depletion with a single dose of CD45-ADC can enable auto-HSCT and immune reset in multiple AID indications without toxic side effects. Targeted conditioning with CD45-ADC may represent a better tolerated approach for removing disease-causing cells as part of immune reset through auto-HSCT and enable more patients to benefit.

Figure 1. Anti-human CD45-ADC Depletes lymphocytes and HSCs at well tolerated doses *in vivo* in NHP



(A) A single dose of an anti-human CD45-ADC potently kills lymphocytes (d3 post–ADC) and HSCs (d6 post ADC) in vivo in NHP. (C) Clinical Chemistry values for alanine aminotransferase (ALT) and total bilirubin (TBIL) demonstrate that a single dose of anti-human CD45-ADC was well tolerated in NHPs.

Figure 2. CD45-ADCs Deplete Target Cells and Exert Potent Disease Modifying Effects in Multiple Preclinical Models.



(A) Anti-human CD45-ADC potently kills PBMC from healthy donor and patients with MS. (B) Administration of a single dose of anti-human CD45-ADC ameliorates disease and eliminates disease-causing cells in a scleroderma-like model of xenoGVHD in NSG mice. (C) A single dose of anti-mouse CD45-ADC enables transplant, eliminates disease-causing cells, and substantially ameliorates disease in murine MOG-EAE model of MS.

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OP0308-PARE PREGNANCY AND ARTHRITIS - A PATIENT EDUCATION PROGRAMME IN IRELAND

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Background: The relationship between pregnancy and arthritis is a complex one. Because of the variability of arthritic conditions, it is important for patients to get advice from their doctor or a specialist nurse before trying for a baby. There can be implications for medication regimes, while the pregnancy itself can also affect the inflammatory arthritis. In the postpartum period, other considerations include breastfeeding and the frequent return of flares.

Through this education programme, Arthritis Ireland developed information resources primarily targeting women of child-bearing age. The multichannel campaign provided information about the wide range of issues of concern to women with inflammatory arthritis who are planning a family or are pregnant.

Objectives:

- To provide information and increase awareness around inflammatory arthritis and pregnancy;
- To support women living with inflammatory arthritis through their illness and life journey;
- To increase awareness of the work of Arthritis Ireland as a patient organisation.

Methods: In developing and executing this education programme, Arthritis Ireland worked extensively with a team of healthcare professionals, who are regarded internationally as leaders in this field.

A multi-channel approach was taken to the development, production and dissemination of information, with public information events, literature and a suite of videos developed

Up to this point, there had not been any Irish-produced material on this subject. he topic was seen to be an important one and an issue of significant public health interest.

The series of information talks on pregnancy and inflammatory arthritis was delivered by consultant rheumatologists and were held in cities around Ireland. The information booklet covered topics such as planning for a baby, medication and pregnancy, the role of the father, fertility, genetics, during the pregnancy, after the pregnancy and breastfeeding.

Video was seen to be central to the success of the campaign. Working with the expert healthcare team, six information videos were developed around obstetrics, rheumatology, physiotherapy and occupational therapy. The videos were published and promoted across Arthritis Ireland's social media channels and website.

The capstone video featured a young mother who was diagnosed with JIA when she was two. Her story was an incredibly powerful testimony of overcoming and dealing with adversity and complex health issues.

Results: This educational campaign was developed to meet a significant need in the health information landscape. While there are no little resources produced focusing on pregnancy and parenting, there wasn't anything in Ireland which specifically addressed the needs of women and men with inflammatory arthritis who are looking to have a family. The materials produced are a valuable part of Arthritis Ireland's canon of patient education materials.

Conclusion: It is anticipated that the materials developed will have a long lifespan and will support prospective parents for several years to come. Central to the success of the project was the involvement of the expert healthcare teams. Their commitment to the project spoke volumes of its importance and the considerable need for the clearly communicated information, which the project provided.

Ultimately, Arthritis Ireland has produced a suite of resources which will be referenced and used by patients, and will hopefully make a considerable impact on their quality of life.

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OP0309-PARE REUMASUTRA: RETHINKING SEXUALITY IN RHEUMATIC AND MUSCULOSKELETAL DISEASES

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Background: Rheumatic and musculoskeletal diseases (RMDs) have a great impact on people's quality of life affecting daily tasks. Research has shown that sexual relationships are also affected by RMDs. This occurs by one or a combination of: (1) the symptoms of the disease and (2) the side effects of the medication. Although we are all here because of sex, talking about sex and sexuality remains taboo. Physicians themselves report that embarrassment, lack of time, lack of knowledge about the topic, or age are barriers that prevent them from starting a conversation about the subject. Consequently, the sexual sphere of people with RMDs is neglected; producing uncertainty in the people affected by them and their partners.

In 2016, we set ourselves the task of studying what has already been created. The only material we found was a book with drawings that showed several sexual positions. We realized that the existing material fell short and we knew that we could make an original contribution. That's why using participatory action research (PAR) approach we decided to create Reumasutra (LLC): The kamasutra for people with rheumatic diseases.

Objectives: To understand the complexities and the difficulties of sexuality in people with RMDs,

To offer a solution to the problems previously identified,

To (un)validate the proposed solution using the feedback of people with RMDs.

Methods: PAR affirms that experience can be a basis of knowing and that experiential learning can lead to a legitimate form of knowledge that influences practice.

PAR differs from conventional research in three ways. Firstly, it focuses on research whose purpose is to enable action. Secondly, PAR pays careful attention to power relationships, advocating for power to be deliberately shared between the researcher and the researched: blurring the line between them until the researched become the researchers. Thirdly, PAR contrasts with less dynamic approaches that remove data and information from their contexts, by advocating that those being researched should be involved in the process actively.

Results: Our project is divided into three phases.

In the first phase, interviews with people with RMDs were conducted. The interviewees expressed that sex remains a taboo topic, which is often ignored by physicians. Besides, we opened a suggestion box on the website www.reumaxxx.com. Last year, we received feedback from approximately >30.000 people. After evaluating the feedback, it was clear that the best way to educate in sex in RMDs was by showing real people practicing adapted sexual positions.

For that task, we asked a couple with RMDs to validate the sexual positions that appear as drawings on the only book we found on the topic. Also, the couple added new sexual positions that they have been using and adapting to be sexually active despite having RMDs.

In the second phase, we recruited sex surrogates with experience with people with functional diversity to recreate the sexual position previously validated. The sex surrogates received coaching in real-time from a person with RMDs. The positions were filmed in January 2020.

For the last phase, we expect to upload the audiovisual content to the website. Afterward, we will send out surveys so that the users themselves can determine the validity and usefulness of the solution created.

Conclusion: Mobility in rheumatic diseases is affected. Sex is dynamic and a person cannot properly learn a new dynamic reality using static resources. We need to cross the taboo line to offer real solutions anchored to the reality of people with RMDs.

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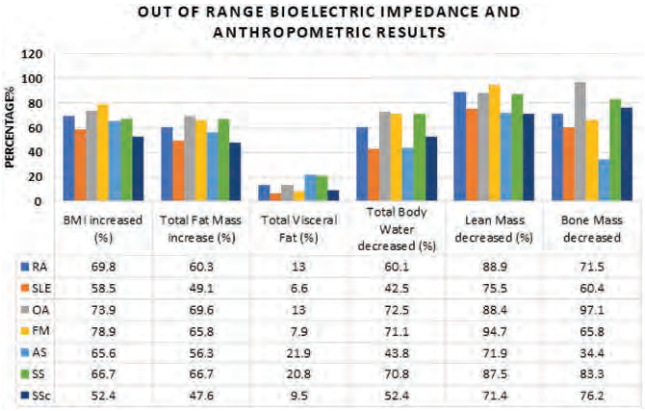
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OP0310-HPR METABOLIC ABNORMALITIES IN MEXICAN PATIENTS WITH RHEUMATIC DISEASES

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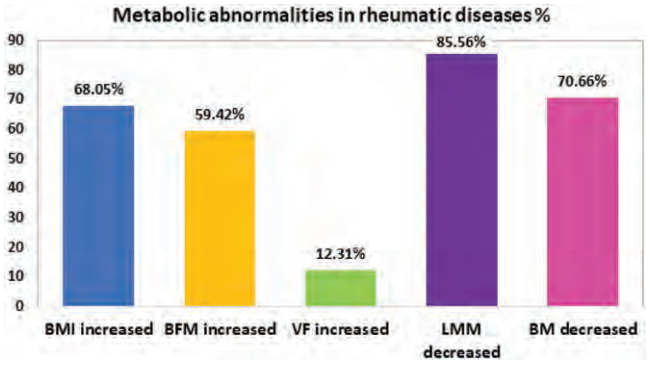
Background: Nutritional status plays an essential role in the etiopathogenesis of rheumatic diseases either as a triggering factor or as a contributor in the progression of disease activity, comorbidities and ineffective therapeutic response.[1] An increased Body Mass Index (BMI) and a low lean muscle mass (LMM) have been associated to a worse clinical prognosis in rheumatic diseases.[1]
Objectives: To describe the nutritional status and alterations in a cohort of patients with rheumatic diseases.
Methods: 658 mexican rheumatic patients from a rheumatology public center were included. Anthropometrical measurements were assessed using bio-electrical impedance analysis (BIA) Tanita. including weight, height, BMI, Body Fat Percentage and Body Fat Mass (FM), Visceral Fat (VF), MM, Total Body Water (TBW) and Bone Mass (BM) which were classified according to validated parameters as normal and abnormal.
Results: A total of 658 patients were evaluated, 368 (55.92%) had Rheumatoid Arthritis. Table 1. The different diagnosis and anthropometric measures for each pathology are listed in Graphic 1.
More than half of the patients (68.05%) presented an increased BMI and 85.56% a decreased MM. **Graphic 2.**
Conclusion: This study showed that sarcopenic obesity, defined as low MM with an increased BMI[1], is a common disorder among rheumatic patients, found in more than half of our studied population. Since nutrition is a modifiable factor, important investigation in the detection and approach of metabolic abnormalities should be done.
References:

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	BMI increased (%)	Total Fat Mass increase (%)	Total Visceral Fat (%)	Total Body Water decreased (%)	Lean Mass decreased (%)	Bone Mass decreased
RA	69.8	60.3	13	60.1	88.9	71.5
SLE	58.5	49.1	6.6	42.5	75.5	60.4
OA	73.9	69.6	13	72.5	88.4	97.1
FM	78.9	65.8	7.9	71.1	94.7	65.8
AS	65.6	56.3	21.9	43.8	71.9	34.4
SS	66.7	66.7	20.8	70.8	87.5	83.3
SSc	52.4	47.6	9.5	52.4	71.4	76.2

Graphic 1. RA: Rheumatoid Arthritis, LES: Systemic Lupus erythematosus, OA: Osteoarthritis, FM: Fibromyalgia, EA: Spondyloarthropaties, SS: Sjögren's Syndrome, SSc: Scleroderma. A BMI >25 kg/m2 was classified as overweight and > 30 kg/m2 obesity, BFM >35% in women and 24% in men was classified as high,as well as VF >12%; a low LMM was <68% in women and <75% in men, BM <2.4 was considered low.



Graphic 2. Metabolic abnormalities in rheumatic diseases. **BMI=** Body Mass Index; **BFM=** Body Fat Mass; **VF**= Visceral Fat; **LMM**= Lean Muscle Mass; **BM=** Bone Mass

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OP0311 DETECTION OF SUBCLINICAL SKIN MANIFESTATION IN PATIENTS WITH PSORIASIS AND PSORIATIC ARTHRITIS BY FLUORESCENCE OPTICAL IMAGING

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Background: Fluorescence optical imaging (FOI) as new imaging technique enables visualization of an impaired microcirculation in both hands caused by joint inflammation. A detection of psoriatic skin inflammation which may also signify an altered vessel composition via FOI has not yet been examined.
Objectives: The aim of the present study was to investigate potential subclinical skin inflammation in both hands of psoriasis (Pso) and psoriatic arthritis (PsA) patients in comparison to rheumatoid arthritis (RA) and healthy individuals by FOI, and to correlate these findings with cardiovascular risk factors or events, since a connection to Psoriasis skin involvement is assumed.
Methods: FOI scans of patients with Pso and PsA as well as RA and healthy subjects were analyzed retrospectively to detect subclinical skin enhancement in both hands that did not clinically show overt psoriasis skin changes. According to the 'fluorescence optical imaging activity score' (FOIAS) (1) used for evaluation of joint enhancement so far, a standardized definition was set in order to describe the degree of skin enhancement via a semi-quantitative (0-3) score (see **Figure**). The score was applied for the first third of the FOI exam sequence (0-120 sec.). To be scored as potential subdermal skin enhancement, it had to be localized on the back of the hands without relationship to an underlying joint or blood vessel since the ICG enhancement was then most likely localized in the area of the (sub)dermis. Using this analysis method, we further characterized the patterns and sorted the scans into the groups PsA/Pso, RA and healthy controls to compare these with the final physician's diagnosis. Furthermore, cardiovascular risk factors (e.g. obesity, smoking status, hypertension) were collected and correlated to imaging findings.

Table 1. Bioelectric impedance and anthropometric results in Rheumatic diseases

	RA	LES	OA	FM	EA	SS	SSc
N	368	106	69	38	32	24	21
Female	335 (91)	98 (92.5)	63 (91.3)	38 (100)	19 (59.4)	23 (95.8)	21 (100)
Hight	1.56 (0.07)	1.58 (0.07)	1.56 (0.09)	1.57 (0.06)	1.62 (0.1)	1.57 (0.06)	1.57 (0.06)
Age	51.71 (12.29)	37.61 (12.57)	58.67 (10.27)	48 (11.43)	44.1 (14.93)	55.79 (12.90)	48.33 (9.51)
Weight (kg)	70.02(14.94)	69.1 (16.77)	70.34 (16.63)	71.82 (12.56)	71.43 (16.55)	70.82 (15.53)	62.9 (18.18)
Total fat (%)	35.99 (8.60)	32.78 (10.43)	37.11 (7.70)	38.06 (6.48)	30.38 (12.4)	38.02 (9.09)	31.98 (8.68)
Total fat (kg)	26.06 (10.81)	24.41 (12.31)	27.13 (11.16)	28.08 (9.47)	22.97 (12.56)	28.12 (12.12)	21.28 (10.52)
Total body water (%)	44.71 (6.06)	47.41 (7.41)	43.45 (4.31)	43.21 (3.82)	49.59 (10.47)	42.99 (5.74)	46.87 (4.99)
Visceral fat	8.69 (3.68)	6.33 (4.37)	9.71 (3.90)	8.32 (3.06)	8.28 (4.85)	9.21 (4.32)	7.27 (4.19)
Lean mass (%)	60.75 (8.18)	63.71 (9.98)	59.67 (7.75)	58.82 (6.14)	65.98 (11.77)	58.47 (9.21)	66.3 (11.38)
Lean mass (kg)	41.68 (6.13)	42.86 (6.70)	41.14 (6.98)	41.54 (3.48)	45.92 (8.74)	40.11 (4.74)	40.13 (6.92)
Bone mass	2.38 (0.79)	2.69 (1.40)	2.64 (2.42)	2.32 (0.5)	2.79 (1.19)	2.14 (0.21)	2.48 (1.16)
BMI	28.69 (6.15)	27.79 (6.52)	28.72 (5.5)	29.36 (5.19)	27.41 (6.55)	28.6 (5.98)	25.58 (7.40)

RA: Rheumatoid arthritis, SLE: Systemic Lupus Erythematosus, OA: Osteoarthritis, FM: Fibromyalgia, EA: Spondyloarthropaties, SS: Sjogren Syndrome, SSc: Scleroderma

Results: We included FOI scans of patients with PsA/Pso (n=80), patients with RA (n=78) and healthy controls (n=25). Significantly more PsA/Pso patients showed subclinical skin enhancement on the back of their hands than RA and healthy individuals (PsA/Pso: 72.5%, RA: 20.5%, healthy controls: 28.0%; p<0.001). By using the pattern of skin enhancement, it was possible to categorize 58 of 80 patients correctly as PsA/Pso (72.5%), 60 out of 78 as RA (76.9%) and seventeen out of 25 as healthy controls (68.0%; p-value <0.001). We could show an influence of the body weight (kg) (p<0.001, OR 1.04, CI 1.02; 1.06) on the FOI results; no further correlation with cardiovascular risk factors was detected.
Conclusion: We were able to proof our primary hypothesis that it is possible to visualize subclinical subdermal skin inflammation in PsA/Pso patients using FOI. Furthermore, we were also able to categorize PsA/Pso and RA patients correctly by using our newly developed method. Although we could not establish a correlation between subdermal skin enhancement and cardiovascular risk factors, we demonstrated an important influence of the body weight on our FOI results. FOI may be a helpful novel tool to study microcirculation in rheumatic diseases with skin involvement.
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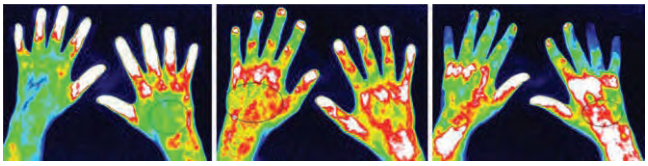


Figure. Left picture: The enhancement is mostly yellow on green ground classified as grade 1. Middle picture: The enhancement is red with minimal white signals classified as grade 2. Right picture: The enhancement in the marked area shows more white than red signals which presents grade 3.

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OP0312 THE IMPACT OF AN ULTRASOUND ATLAS FOR SCORING SALIVARY GLANDS IN PRIMARY SJÖGREN'S SYNDROME: A RELIABILITY EXERCISE

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Background: Salivary gland ultrasound (SGUS) may have the potential of facilitating diagnosis and therapy monitoring of salivary gland disease in patients with primary Sjögren's syndrome (pSS). A novel consensus based OMERACT SGUS scoring system for the parotid and submandibular glands has recently been developed.(1)
Objectives: To assess the reliability of 3 readers using the written definition of the scoring system provided by the OMERACT group and subsequent the impact of a SGUS-atlas based on the OMERACT SGUS scoring system.
Methods: 3 sonographers with 6 months to 10 years US experience performed a US exercise of 30 SGUS images of patients with SS. 16 images were of the submandibular gland (SMG) and 14 images of the parotid gland (PG) ranging from normal to varying degrees of abnormalities. The images were scored using the US scoring system provided by the OMERACT-group and subsequently using a SGUS atlas made for the study consisting of 4 images of every grade 0-3 of both the SMG and the PG. The readings were performed over 4 rounds: the first reading without using the atlas and second reading using the atlas 1 week later. The 30 images were scrambled by a physician not included in the readings and a third and fourth reading were performed without and with the atlas respectively – with 1 week in between. Inter- and intra-reader reliability were calculated by kappa-tests.
Results: Light weighted Kappa for intra- and inter-reliability was determined for each reading. The results of the intra-reader reliability was ranging from moderate to almost perfect with improvement in the 2nd round of readings and with use of the atlas. The inter-reader reliability was moderate and better in the 2nd round of readings. Readings improved with the atlas. Details are shown in table 1.

Tabel 1

Intrareader reliability Weighted Kappa:	**Weighted Kappa, reader 1-3**
Reading 1 without atlas vs. reading 1 with atlas	0.93, 0.85, 0.80
Reading 2 without atlas vs. reading 2 with atlas	0.78, 0.93, 0.78
Reading 1 without atlas vs. reading 2 without atlas	0.78, 1.00, 0.58
Reading 1 with atlas vs. reading 2 with atlas	0.93, 0.93, 0.86
Interreader reliability Weighted Kappa:	**Weighted Kappa: mean (min – max)**
Reading 1 without atlas	0.50 (0.33 – 0.72)
Reading 1 with atlas	0.55 (0.39 – 0.86)
Reading 2 without atlas	0.55 (0.33 – 0.93)
Reading 2 with atlas	0.60 (0.40 – 0.93)

Conclusion: The results of the inter- and intra-reliability showed a moderate to almost perfect agreement respectively, of scoring SGUS in patients with pSS and especially in the 2nd round of readings indicating that training and the SGUS atlas increased the reliability.
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Fractures, more than bone alone: the role of sarcopenia

OP0313 THERAPEUTIC APPROACHES TO OSTEOSARCOPENIA: DENOSUMAB EFFECT ON FALLS RISK, PHYSICAL PERFORMANCE AND WALKING SPEED

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Background: There is a strong association between osteoporosis and skeletal muscle dysfunction. Heparan-sulfate proteoglycans are abundant in skeletal muscles and may represent a target for RANKL inhibitor. It was noted that patients who completed their planned denosumab therapy course (5-years) started to sustain falls.
Objectives: To assess the effect of Denosumab on falls risk, physical performance, grip strength and gait speed and whether there is a relation with bone mineral density.
Methods: 127 osteoporotic patients treated with denosumab were assessed prior to starting denosumab therapy for: baseline BMD using DXA scan, blood test for osteoporosis bone profile, self-reported falls risk using (FRAS score [1]), fracture risk using FRAX, handgrip strength using a calibrated dynamometer (the best of three trials of the dynamometer testing was recorded), the patient's physical performance assessed by testing for: Short Physical Performance Battery (SPPB), Timed Up and Go (TUG), and the 4 Meter Walk Gait Speed. Same measures were assessed again after completing 5-years of denosumab therapy. Comparison groups included 112 patients diagnosed to have osteoporosis and treated with zoledronate (Zol), once yearly IV injection, for 3-years; and 134 patients treated with once weekly oral alendronate (Aln) 70mg for 5-years. The patients were assessed for the same parameters as in the denosumab therapy. All the measures were reassessed 1-year after stopping the osteoporosis therapy.

Results: No differences were seen on comparing the baseline parameters of the 3 groups. In comparison to the baseline, there was significant increase in the BMD in the 3 groups, Denosumab /Zol/Aln at both spine and hip (P = 0.02) at 5-, 3- and 5-years of treatment respectively. In the denosumab group, at 5-years of therapy, there was significant decrease in falls risk score (-1.4, 95% CI = –2.8 to –0.7; P = .01), significant improvements in the grip strength (+4.2Kg, P = 0.01), SPPB score (1.2 points; 95% CI = –0.07 to 2.2; P = .02), TUG (1.7 seconds; 95% CI = –2.2 to 0.1; P = .031) and gait speed (0.1 m/s; 95% CI = 0.03-0.2; P = .01). Zol and Aln improved significantly SPPB score (0.9 and 0.8 points; P = .04), TUG (1.4 and 1.3 seconds; P = .05) and gait speed (0.2 and 0.3 m/s; P = .02) respectively, however, there was no significant change in the falls risk (p = 0.06 and 0.07 respectively). 1-year after stopping Denosumab, there was significant worsening of the falls risk score, grip strength, SPPB score, TUG and gait speed (P = 0.1). There was no difference in all the measures 1-year after stopping Zol and Aln. There was no relation to the increase in BMD gained.
Conclusion: Denosumab displayed positive impact and significant improvements in physical performance, grip strength and gait speed. Also, Denosumab, enhanced multidirectional agility as depicted by TUG. Collectively, this would explain the reduction of falls risk which got worse on stopping the medication.
Osteoporosis and sarcopenia share similar risk factors, highlighting muscle-bone interactions, which may result in debilitating consequences, such as falls and fractures. RANK/RANKL/OPG pathway, a key regulator of bone homeostasis, may contribute also to the regulation of skeletal muscle integrity and function.
References:
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Clinical symposium axSpA: Treat-to-target in axSpA: myth or reality?

OP0314 FACTORS ASSOCIATED WITH 5-YEAR DRUG-FREE REMISSION IN EARLY ONSET AXIAL SPONDYLOARTHRITIS PATIENTS: DATA FROM DESIR COHORT

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Background: It is recommended to target remission when treating a patient with a chronic inflammatory rheumatism. To date, drug-free (DF) remission has been poorly investigated in axial Spondyloarthritis (axSpA).
Objectives: 1/To estimate the frequency of patients in DF remission after 5 years of follow-up in a cohort of early axSpA and 2/to assess the factors associated with 5-year DF Remission.
Methods: *Patients*: All patients included in DESIR (DEvenir des Spondyloarthrites Indifférenciées Récentes) cohort were selected for this analysis. *Definition of 5-year DF Remission*: 1/all patients in ASAS partial remission and/or ASDAS<1.3 at 5 year visit and 2/ taking no disease modifying anti-rheumatic drugs (DMARDs, including synthetic and biologics) only at 5-year visit (patients could have received DMARD before the 5-year visit) and 3/ with a NSAIDs score ≤ 25 at the 5-year visit. *Covariates analysed*: age, gender, smoking status, body mass index, disease classification criteria (ASAS, Amor, ESSG, New York), presentation at onset (peripheral or extra-articular features), disease activity at onset (BASDAI, ASDAS-CRP, CRP, MASES, TJC or SJC), functional impairment at baseline (BASFI, HAQ-AS, BASMI), comorbidities, baseline imaging data (radiographic sacroiliitis, mSASSS, MRI sacroiliitis, spine MRI Berlin score), NSAID intake within 6 months before baseline visit and 5-year treatment intake (including DMARDs, corticoids and NSAIDs). *Statistical analysis*: The associations between each of these clinical factors and the 5-year DF remission were tested by logistic regression. A multivariate model was built, stepwise procedure, to identify the independent variables associated with 5-year DF remission.
Results: Of the 708 patients included in DESIR cohort, 419 were seen at the 5-year visit and 72 (17.0%) were in DF remission (50% of males, aged of 33.08 years (SD:8.0), disease duration: 1.26 years (SD: 0.72), HLA-B27 in 71%, 26.4% had a MRI sacroiliitis). Patients in 5-year DF remission had lower symptom duration (1.3 year versus 1.6 year, p=0.01) had lower disease activity (BASDAI at baseline: 30.1 versus 46.1, p<0.0001, ASDAS-CRP: 1.96 versus 2.75, p<0.0001, CRP: 3.9 versus 8.6, p=0.01) had less peripheral involvement (at least 1 enthesitis at baseline: n=33 (45.8%) versus n=226 (65.1%), p=0.002; at least 1 painful joint at baseline: n=24 (33.3%) versus n=196 (56.5%), p=0.0006) less functional impairment (HAQ-AS: 0.32 versus 0.69, p< 0.0001, BASFI: 14.3 versus 32.1, p<0.0001, BASMI: 1.98 versus 2.51, p<0.0001), and had lower NSAIDs intake at baseline (NSAIDs score: 28.2 versus 48.1, p=0.0001). Interestingly, there was no difference in sacroiliac bone marrow oedema on MRI while Berlin scores on spine MRI were lower in patients in 5-year DF remission (Berlin score mean: 0.41 versus 1.24, p=0.03). During the 5 years of follow-up, patients in 5-year DF remission received less often analgesics (n=46 (63.9%) versus n=297 (85.3%), p<0.0001) and anti-TNF (n=1 (1.4%) versus n=182 (52.5%), p<0.0001), but there was no difference in NSAID or csDMARD intake between groups until the 4-year visit. After multivariate analysis, the variables that remained associated with 5-year DF remission were lower symptom duration (OR[95%CI]=0.58[0.36-0.88], p=0.01), lower baseline ASDAS-CRP (OR[95%CI]=0.50[0.32-0.76], p=0.002) or NSAIDs score (OR[95%CI]=0.54[0.34-0.81], p=0.004) and not initiating an anti-TNF during the 5 years of follow-up (OR[95%CI]=0.029[0.00-0.14], p=0.0005).
Conclusion: DF remission is rare, 5 years after onset of axSpA. Patients with longer symptom duration, higher baseline ASDAS-CRP and NSAIDs scores were less often in DF remission, while imaging and biological data did not predict DF remission.
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OP0315 WHICH RESPONSE OR STATUS CRITERION DISCRIMINATES BEST IN AXSPA?

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Background: Response criteria and disease activity status used to assess treatment efficacy in axial spondyloarthritis (axSpA) are: the ASAS response criteria (ASAS20; 40; 5/6 and partial remission - PR), BASDAI50 and ASDAS-based criteria (clinically important/major improvement –CII/MI; low disease activity/inactive disease –LDA/ID). These outcomes are variably used in RCTs testing biological (b) and targeted-synthetic (ts)DMARDs. However, it remains unknown which are the most discriminative.
Objectives: To compare the ability of different criteria to discriminate between the response to active treatment and placebo in axSpA.
Methods: A systematic literature review was performed in Medline and Embase to identify RCTs of b- and tsDMARDs. Placebo-controlled RCTs meeting the primary endpoint were included provided they reported ≥2 response/status criteria. Outcomes were collected at the timepoint of primary endpoint assessment (PEA). Risk of bias was evaluated by The Cochrane tool. Meta-analysis with the Mantel-Haenszel method was conducted to calculate the Chi-square ($\mathbf{X}^2$) between percentages of patients fulfilling each criterion in the treatment arm versus the placebo arm (higher $\mathbf{X}^2$, better discrimination). Comparisons among criteria were conducted evaluating their performances across RCTs reporting the exact same outcomes at the PEA. Different sets of RCTs were used for the comparisons depending on the available outcomes (Table).
Results: 29 RCTs fulfilled inclusion criteria. In total, 23/29 RCTs with PEA at 12, 14 or 16 weeks, all at a low risk of bias, could be considered for meta-analysis. Other 6 RCTs had later (e.g 24 weeks) or earlier (e.g. 6 weeks) PEA. Out of the 23 RCTs, only 16 reported at least a minimum set of ASAS20,-40, -PR and BASDAI50 (Table, Set 1): discriminative performances for ASAS40 were >ASAS20>BASDAI50>ASAS-PR. In 11/16 RCTs ASAS5/6 was also included (Table, Set 2): this criterion showed the best performances among ASAS-based response criteria. 8/16 RCTs additionally included some ASDAS-based criteria (Table, Set 3): ASDAS-CII and -MI showed a much higher discrimination compared to the ASAS-based criteria. In only 3 trials could all criteria be compared, with the ASDAS-CII and -MI appearing as the most discriminative criteria, followed by ASAS 5/6 (Table, Set 4).

Conclusion: Response criteria are more discriminative than status criteria. ASDAS-CII and ASDAS-MI showed the best discrimination between treatment/placebo arms. Using the ASDAS-CII as primary outcome in future RCTs can reduce the number of patients needed to be included while keeping the same statistical power.

Table. Discriminative performances of response and status criteria in RCTs of biological and targeted synthetic DMARDs in axial spondyloarthritis

Minimum set of outcomes	Set 1: ASAS20,-40,-PR, BASDAI50		Set 2: ASAS20,-40,-5/6, -PR BASDAI50		Set 3: ASAS20,-40, -5/6, -PR BASDAI50 ASDAS-CII, -MI, -ID		Set 4: All	
N° of RCTs Total=16*	16		11		8		3	
Descending X^2 order		X^2		X^2		X^2		X^2
1	ASAS40	339	ASAS5/6	334	ASDAS-CII	309	ASDAS-CII	124
2	ASAS20	316	ASAS40	266	ASDAS-MI	253	ASDAS-MI	65
3	BASDAI50	297	ASAS20	254	ASAS40	169	ASAS5/6	48
4	ASAS-PR	146	BASDAI50	248	BASDAI50	163	BASDAI50	39
5	-		ASAS-PR	119	ASDAS-ID	117	ASAS40	34
6	-		-		ASAS20	98	ASDAS-LDA	27
7	-		-		ASAS-PR	80	ASAS-PR	22
8	-		-		-		ASAS20	21
9	-		-		-		ASDAS-ID	7

Legend. *total of 16 RCTs analysed, with different sets of RCTs within the 16 analysed based on the availability of response criteria; X^2=Chi-square; RCTs=randomized controlled trials; BASDAI= Bath Ankylosing Spondylitis Disease Activity Index; ASAS= Assessment in SpondyloArthritis International Society; PR= partial remission; CII= clinically important improvement; MI= major improvement; LDA= low disease activity; ID= inactive disease

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New perspectives on therapeutic immune tolerance

OP0316

EMERGING BEST-IN-CLASS IL-2 VARIANT HIGHLIGHTS TREG-DIRECTED THERAPY FOR AUTOIMMUNE DISEASE

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Background: Impairment or deficiency of regulatory T cells (Treg) is associated with chronic inflammation and autoimmune diseases. Interleukin 2 (IL-2) is a cytokine indispensable for Treg expansion and immunosuppressive function. However, expansion of cytotoxic effector T (Teff) and NK cells and the associated vascular leakage side effect limit the use of IL-2 in autoimmune diseases [1].
Objectives: Cugene developed a long-acting IL-2 variant with high Treg specificity and low toxicity to restore immune homeostasis and self-tolerance, and potentially cure autoimmune and inflammatory diseases.
Methods: IL-2 variants were generated based on the quaternary structure of IL-2 and IL-2Rαβγ (alpha, beta, gamma) complex. Biological activity was determined by examining differential signaling activity in induction of STAT5 phosphorylation in defined lymphocyte populations of human PBMC using flow cytometry. Binding activity was evaluated by ELISA. Pharmacokinetics, pharmacodynamics, safety and tolerability were assessed in mice and cynomolgus monkeys. Treg suppressive function was determined *in vivo/ex vivo,* and anti-inflammatory and anti-antibody production efficacy were determined in delayed-type hypersensitivity (DTH) and T-cell-dependent antibody response (TDAR) models.
Results: Structure-based rational design and activity-guided fine-tuning generated an optimized IL-2 variant, CUG252. It demonstrated a strong and near wild-type IL-2 ability to stimulate STAT5 phosphorylation in IL-2Rαβγ dominant Treg cells but abolished activities in IL-2Rβγ dominant effector CD4, CD8 and NK cells. This was a result of biased binding activity to IL-2Rα while dramatically attenuated binding to IL-2Rβγ complex. In mice and monkeys, administration of CUG252 resulted in dose-dependent increases in Treg proliferation and expansion by more than 10- and 30-fold, respectively, with largely abolished activities in CD4+ T conventional, cytotoxic CD8+ Teff and NK cells. The ratio of Treg/Teff cells achieved was as high as 0.4 in mice and 1.2 in monkeys. Both CD4+ and CD8+ Tregs were expanded with preferential increases in memory over naïve subsets. A substantial increase in Treg-suppressive capacity over T effector cells was corroborated by enhanced expression of functional and inhibitory markers, including CD25, Foxp3, PD-1, CTLA-4, Tim3 and ICOS. In DTH and TDAR models, CUG252 strongly inhibited antigen-driven inflammation, B cell maturation, and antibody production. The sustained PK/PD profile supports monthly dosing or better in humans. CUG252 was well-tolerated and no changes in body weight, body temperature, clinical pathology or signs of vascular leakage were observed. Moreover, CUG252 demonstrated superior manufacturability.
Conclusion: CUG252 demonstrates an emerging best-in-class profile among IL-2 variants. It displayed exquisite Treg-selectivity while retaining potency comparable to wild-type IL-2. It showed strong anti-inflammatory and anti-antibody production efficacy with significantly improved therapeutic index and manufacturability. Its favorable drug-like property and robust preclinical efficacy warrant further evaluation in patients with a variety of inflammation and autoimmune diseases.

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Pathological calcification in rheumatic diseases

OP0317

ACCURACY OF THE OMERACT DEFINITIONS FOR IDENTIFICATION OF CALCIUM PYROPHOSPHATE CRYSTALS WITH ULTRASOUND: FINAL RESULTS OF THE OMERACT US IN CPPD SUB-TASK FORCE STUDY

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Background: The OMERACT Ultrasound (US) in calcium pyrophosphate deposition disease (CPPD) sub-task force has been working on the use of US in CPPD since 2014 first creating definitions for CPPD identification and then assessing the reliability[1].
Objectives: Objective of this study is to assess the diagnostic accuracy (truth) of US in CPPD.
Methods: Consecutive patients waiting to undergo knee replacement surgery due to osteoarthritis were enrolled in 12 centres from 6 countries. Each patient underwent US examination of the knee, focusing on the menisci and the hyaline cartilage, the day prior to surgery, scoring each site for presence/absence of CPP as defined previously[1]. After surgery, the menisci and the condyles were retrieved and examined microscopically. Six samples were collected, both from the surface and from the internal part of menisci and cartilage trying to cover a large part of it. All slides were observed under transmitted light microscopy and by compensated polarised microscopy. A dichotomous score was given for the presence/absence of CPP. US and microscopic analysis were performed by different operators, blind to each other's findings.

Sensitivity and specificity of US were calculated using microscopic findings as the gold standard.

Results: 101 patients have been enrolled in the study. 33 patients have been excluded due to loss of anatomical pieces at surgery. The mean age of the remaining 68 pts was 71yo (±8), 44 women, 34 were affected by CPPD according to microscopy. Overall and per site diagnostic US accuracy results are presented in table 1

	Diagnostic accuracy	Sensitivity	Specificity	Positive Predictive value	Negative Predictive value
Global	0.75	0.91	0.59	0.69	0.87
Medial meniscus	0.82	0.87	0.77	0.77	0.87
Lateral meniscus	0.75	0.83	0.68	0.68	0.83
Medial cartilage	0.86	0.79	0.92	0.88	0.85
Lateral cartilage	0.82	0.71	0.88	0.77	0.84
Medial side (combined cartilage and meniscus)	0.82	0.88	0.76	0.79	0.87
Lateral side (combined cartilage and meniscus)	0.78	0.88	0.69	0.73	0.86

Conclusion: Our results demonstrate that US is an accurate exam for identification of CPPD. The best combination of sensitivity and specificity is achieved by examining the medial aspect of the knee.

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OP0318 THE ROLE OF DUAL ENERGY COMPUTED TOMOGRAPHY (DECT) IN THE DIFFERENTIATION OF GOUT AND CALCIUM PYROPHOSPHATE DEPOSITION DISEASE

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Background: Differentiation of gout and calcium pyrophosphate deposition disease (CPPD) is sometimes difficult as patients often present with a similar clinical picture. Arthrocentesis and subsequent polarization microscopy (PM) remains the gold standard but novel diagnostic approaches such as non-invasive dual energy computed tomography (DECT) have recently been validated for gout. Currently, limited data is available on DECT in patients with CPPD.

Objectives: To analyse the diagnostic impact of DECT in gout and CPPD when compared to the gold standard of PM. We further compared the results of PM to ultrasound (US), conventional radiographs (CR), and suspected clinical diagnosis (SCD). Additionally, 15 laboratory parameters were analysed.

Methods: Twenty-six patients diagnosed with gout (n = 18) or CPPD (n = 8) who received a DECT and underwent arthrocentesis were included. Two independent readers assessed colour coded, as well as 80 and 120 kV DECT images for signs of monosodium urate (MSU) crystals or CPP deposition. US and CR from the patient's initial visit along with the SCD were also compared to PM. US examinations were performed by certified musculoskeletal ultrasound specialists. The association of up to 15 laboratory parameters such as uric acid, thyroid stimulating hormone, and C-reactive protein (CRP) with the PM results was analysed.

Results: Sensitivity of DECT for gout was 67% (95% CI 0.41-0.87) with a specificity of 88% (95% CI 0.47-1.0). Concerning CPPD, the sensitivity and specificity of DECT was 63% (95% CI 0.25-0.91) and 83% (95% CI 0.59-0.96) respectively. US had the highest sensitivity of 89% (95% CI 0.65-0.99) with a specificity of 75% (95% CI 0.35-0.97) for gout, while the sensitivity and specificity for CPPD were 88% (95% CI 0.47-1.0) and 89% (95% CI 0.65-0.99) respectively. The SCD had the second highest sensitivity for gout at 78% (95% CI 0.52-0.94) with a comparable sensitivity of 63% (95% CI 0.25-0.92) for CPPD. Uric acid levels were elevated in 33% of gout patients and 25% of CPPD patients. While elevated CRP levels were observed in 59% of gout patients and in 88% of CPPD patients, none of the 15 analysed laboratory parameters were found to be significantly linked.

Conclusion: DECT provides a non-invasive diagnostic tool for gout but might have a lower sensitivity than suggested by previous studies (67% vs 90%[1]). DECT sensitivity for CPPD was 63% (95% CI 0.25-0.91) in a sample group of eight patients. Both US and the SCD had higher sensitivities than DECT for gout and CPPD. Further studies with larger patient cohorts are needed in order to determine the diagnostic utility of DECT in CPPD.

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OP0319-PARE SEE ME HEAR ME: AN ANCA-ASSOCIATED VASCULITIS PATIENT CO-CREATION INITIATIVE

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Background: ANCA-associated Vasculitis (AAV) is a rare, severe small vessel vasculitis that affects multiple organs with a high acute mortality risk. As every patient presents differently, diagnosis is often delayed. Although treatments exist, responses vary, and remission is often not achieved or sustained. From the time of initial diagnosis onwards, patients suffer from an impaired quality of life. Coping with pain, fatigue, ongoing symptoms and combating challenges becomes a complex task and patients may be challenged in how best to communicate these emotions with health care professionals. We aimed to develop an initiative with Art and Voice, that would seek to empower people living with AAV and their carers in feeling understood, seen and heard in a meaningful way. This would invite a collective understanding of 'how people make sense of key life experiences and what it means to them' by creating a common language to address poorly addressed issues.

Objectives: This project aims to provide a voice to patients to express personal experiences and complexity of everyday living and empower people to feel in control of their own health through an online platform. It should also allow practitioners to gain new awareness about issues faced by their patients, to better understand the relationships between caring and curing, hearing and listening.

Methods: We collaborated with 10 patient association groups representatives, 17 AAV patients and 9 of their carers across 7 European countries. A series of workshops were set up to discuss issues faced and aid the subsequent production of a range of materials designed to provide clear, comprehensive content that would help individuals cope with the physical and emotional impact of AAV from diagnosis to living with it. This work was supported by a digital artist who is a rheumatologist living with vasculitis.

Results: The co-creation of patient information materials featuring real life patients was successful and led to the development of a creative initiative called SEE ME.HEAR ME with an online platform www.myancavasculitis.com. This includes: (1) an awareness programme featuring artwork created by the digital artist and advised by the patients which captures the essence of AAV from the patients view (see Figure). (2) a series of first-hand patient and carer stories capturing their authentic voice on 'what it is like to live with the disease'. (3) extensive

Table 1. Sensitivities and specificities of examinations in gout and calcium pyrophosphate deposition disease

	DECT **n=26**	US **n=26**	Conventional radiographs **n=19**	Suspected clinical Diagnosis **n=26**
Gout				
Sensitivity	66.67% (0.410-0.867)	88.9% (0.652-0.986)	61.5% (0.316-0.861)	77.8% (0.523-0.936)
Specificity	87.5% (0.473-0.997)	75% (0.349-0.968)	100% (0.541-1.000)	75% (0.349-0.968)
CPPD				
Sensitivity	62.5% (0.245-0.915)	87.5% (0.473-0.997)	0% (0.000-0.459)	62.5% (0.245-0.915)
Specificity	83.3% (0.586-0.964)	88.9% (0.653-0.986)	92.3% (0.640-0.998)	94.4% (0.727-0.999)

*95% CI in brackets

written content designed to fill information gaps around AAV diagnosis, investigations and treatment and what to expect during clinical follow up. The platform supports patients in asking questions and seeking information while signposting them to their own healthcare professional for advice and their local country patient association for support.



Conclusion: People with AAV need support throughout life, the profound psychosocial influence from illness makes the lived experience, challenging. SEE ME. HEAR ME online patient platform aims to generate awareness around AAV, improve physician and patient dialog, and enhance people's experiences of living and coping with the disease. In addition it provides support for carers and giving valuable insights to friends, family and the general public about what the lived experience with AAV looks like.

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OP0320-PARE FIBROMYALGIA NETWORK – A MULTIDIMENSIONAL PROJECT FOR PEOPLE WITH FIBROMYALGIA SYNDROME

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Background: Fibromyalgia Syndrome (FMS) is a clinical non-joint syndrome characterized by diffuse, prolonged, and unexplained muscle pains. The health effects of FMS are pervasive and wide ranging. It is frequently associated with depression, anxiety and post-traumatic stress disorder. Patients describe living with daily unrelenting chronic widespread pain, persistent chronic fatigue, sleep issues, and cognitive effects. Fibromyalgia impacts all aspects of patients' lives. Patients report severe limitations in maintaining relationships, performing at work or school, and caring for self and family. They experience stigma within society, social isolation, healthcare and financial challenges of treatment, and fears of living with an often misunderstood condition. In 2019 APMARR launched Fibromyalgia Network a project that aimed at improving the quality of life of patients with FMS.

Objectives:

- Experiment a set of good practices at territorial level to be expanded nationally to improve the FMS patients' conditions
- Create a multisectoral, patient-oriented network with different stakeholders
- Launch a communication campaign to inform and change the perception of the pathology
- Train the General Practitioners in order to increase early diagnosis
- Empower the Patients
- Promote innovative treatments and the data acquisition about hyperbaric oxygen therapy
- Provide free psychological and information support

Methods: The project was based on the assumption supported by evidence that a multi-modal treatment approach improves the quality of life of person with FMS including a combination of drug and non-drug treatments and a range of health care specialties. All the activities implemented were shaped on a holistic approach to treating Fibromyalgia, including lifestyle management, diet and exercise, and psychosocial techniques, in addition to medical treatments.

Results:

1) A territorial network coordinated by APMARR was created involving Puglia Region, Health Authorities, Professional board of Psychologists, National Association of People with FMS, Professional board of Physicians, Italian Society Of Rheumatology-Puglia
2) A communication campaign was widely spread among social network, a brochure was written in collaboration with the Italian Society of Rheumatology and distributed to the general public, a national level conference was organized in Bari
3) A training program acknowledged by the Italian Health Minister Program involved more than 120 GPs
4) A patients expert program involved more than 100 patients
5) A group of patients were tutored in their treatment with hyperbaric oxygen therapy and a report was sent to the HTA Italian Program in collaboration with the Puglia Region HTA Center. It was the first HTA report elaborated in collaboration with a patient organization in Italy
6) Self-mutual help groups were organized with free psychological support, as well as an information desk and a toll-free number
7) High satisfaction and pain relief of the participants as detected by a qualitative satisfaction questionnaire





Conclusion: The project demonstrated the good results of the holistic approach in the patients who took part in the program that reported the improvements of their quality of lives and relieve from their daily pains. The

Self-mutual help group was the most appreciated free service, in which participants shared personal stories and perspectives thoughtfully and courageously. The training initiatives organized in collaboration with physicians helped them to learn tips for a better lifestyle management, diet and exercise, and psychosocial techniques but above all helped to overcame concerns and frustration regarding the lack of understanding in the medical community. The network succeeds to increased awareness and understanding of FMS across the public opinion and GPs.

References:

[1] Author: S.Mingolla, APMARR Project Manager; Co-authors: A.Celano, APMARR President; I. Cinieri, Psychologist, A. Marsico, Rheumatologist

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OP0321-HPR

HIGHER QUALITY OF CARE AND LESS SURGERY AFTER IMPLEMENTING OSTEOARTHRITIS GUIDELINES IN PRIMARY CARE– LONG-TERM RESULTS FROM A CLUSTER RANDOMIZED CONTROLLED TRIAL

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Background: To improve quality of care for patients with hip and knee osteoarthritis (OA), a structured model for integrated OA care was developed and implemented among general practitioners (GPs) and physiotherapists (PTs) in primary care. The model was developed based on international treatment recommendations. After 6 months, patient-reported quality of care and satisfaction with care were greater, more patients were referred to physiotherapy and fewer to orthopaedic surgeon, and more patients fulfilled physical activity criteria among OA patients receiving the new model of care compared to the usual care control group[1].

Objectives: To assess the long-term effects 12 months after implementing the model in primary care.

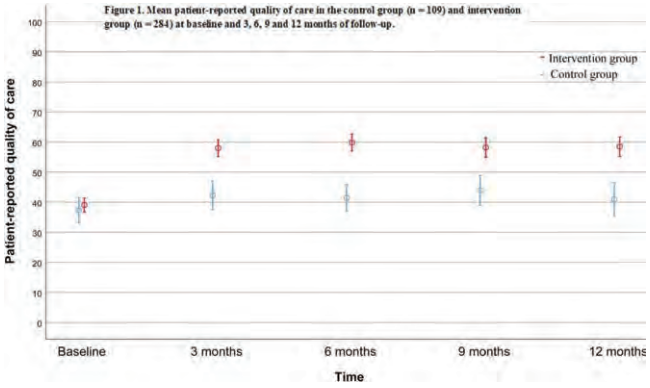
Methods: A cluster-randomised controlled trial with a stepped-wedge design was conducted in six Norwegian municipalities (clusters). The intervention included implementation of the model, facilitated by interactive workshops for GPs and PTs. The main components of the model were a PT led, 3 hour patient education programme followed by 8-12 weeks of individually tailored, supervised exercise. Patient participants were ≥45 years with symptomatic hip or knee OA. Primary outcome was patient-reported quality of care (OsteoArthritis Quality Indicator questionnaire; 0–100, 100 = optimal quality). Secondary outcomes included satisfaction with care, referrals to physiotherapy, orthopaedic surgeon and magnetic resonance imaging (MRI), joint replacement surgery, fulfilment of physical activity recommendations, and proportion with overweight (body mass index ≥25 kg/m2). Data was analysed using multilevel mixed models adjusted for age, sex and secular time.

Results: In all, 40 of 80 GPs and 37 of 64 PTs attended the workshops. A total of 393 patients with hip and knee OA were included, with 284 in the intervention and 109 in the usual care control group. In the intervention group, 92% attended the OA education programme and 64% completed ≥8 weeks of exercise. At 12 months the intervention group reported significantly higher quality of care (score 58 vs. 41, mean difference: 17.6; 95% CI 11.1, 24.0) compared to the control group. The intervention group reported significantly higher satisfaction with care (Odds ratio (OR) 7.8; 95% CI 3.55, 17.27) and a significantly larger proportion (OR: 4.0; 95% CI 1.27, 12.63) met the recommendations for physical activity compared to the control group. A smaller proportion was referred to orthopaedic surgeon (OR 0.5; 95% CI 0.29, 1.00) and a smaller proportion received joint replacement surgery in the intervention (4%) compared to the control group (11%) (OR 0.3; 95% CI 0.14, 0.74). The proportion of patients referred to physiotherapy or MRI and the proportion with overweight were similar between the groups.

Conclusion: Implementation of a structured model for OA care led to improved quality of care, higher satisfaction with care and higher physical activity levels after 12 months. These results are comparable to the 6 months results, which indicate a long-term persistence in the beneficial effects of the intervention. The lower surgical rate in the intervention compared to the control group suggests that higher uptake of OA recommendations in primary care may reduce or postpone the need for surgery in people with hip or knee OA.

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How to communicate effectively with the patients

OP0322-PARE

HOW TO COMMUNICATE DIAGNOSTIC INFORMATION AND CUTTING EDGE SCIENCE TO PATIENTS WITH RHEUMATIC DISEASES

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Background: According to the 2017 Swedish Rheumatology Association (SRA) member strategy a recurring member survey as well as a member withdrawal survey was stipulated. The strategy was developed to evaluate to what extent SRA fulfills the requirements and expectations of its members. According to the 2019 survey, the most important output from a SRA membership, the members rank information about their diagnosis (#1) and supporting the research of these diagnoses (#2) most valuable.

Objectives: To transfer the medical and scientific expertise of the rheumatic diagnoses into lay information in order to meet the member's needs; to take part of the results of the cutting edge science and research progress, funded by SRA, that are relevant and important to individuals living with rheumatic conditions.

Methods: A targeted scientific communication strategy was made consisting of lectures, interviews and scientific writing created for multi-channel distribution.

Results: Actions taken upon the survey result

- Brief summaries of every research project funded by SRA in 2019 was written and distributed via social media.
- A research day for lay people was arranged in collaboration with a regional SRA branch and invited speakers. The filmed lectures are also available online.
- A research report with in-depth interviews with researchers and brief summaries about the research funded by SRA was produced. The report was printed and distributed in 70,000 copies to the SRA members, donors and at SRA meetings and conferences.
- Diagnosis sheets aimed to newly diagnosed patients with the most essential information has been developed in collaboration with a patient research partner and an expert researcher within the field. The sheet is printable and can be distributed by any healthcare practitioner or by patients/public.
- Online patient school prototype - gout. In collaboration with the SRA funded gout network we are gathering high quality information about the diagnosis, treatment, self-care and support in the meeting with the healthcare provider for patients to easily navigate and to find robust answers to their inquiries about their disease.

Conclusion: As a member of SRA, regardless of rheumatic disease, the main interest is knowing more about their diagnosis and about the ongoing research in the field. Through collaborations and communicating rheumatic conditions and

research within the field in lay language the patients can experience self-empowerment and the need for patient education can be met.
Disclosure of Interests: None declared
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The cost-opportunity of screening: osteoporosis in the general population

OP0323 INCIDENCE OF CLINICAL FRAGILITY FRACTURES IN POSTMENOPAUSAL WOMEN WITH RHEUMATOID ARTHRITIS. A MULTICENTRIC CASE-CONTROL STUDY

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Background: Incidence of clinical fractures in rheumatoid arthritis (RA) is not as well-known as hip or vertebral fracture incidence.
Objectives: 1. To estimate the incidence of clinical fragility fractures in a population of postmenopausal women diagnosed with RA and compare it with that of the general population; 2. To analyze the risk factors for fracture.
Methods: 330 postmenopausal women with RA from 19 Spanish Rheumatology Departments, randomly selected from the registry of RA patients in each center. The control group consisted of 660 Spanish postmenopausal women from the Camargo Cohort. Clinical fractures during the previous 5 years were recorded. Assessed risk factors for fracture were: sociodemographic characteristics, BMD and variables related to RA.
Results: Median age of RA patients was 64 yrs. vs. 63 yrs. in controls (ns). Evolution of the disease was 8 yrs. 78% and 76% had RF and ACPA+, respectively. 69% of patients were in remission or low activity. 85% had received glucocorticoids and methotrexate and 40% at least one biological DMARD. We identified 105 fractures (87 fragility and 18 traumatic) in 75 patients. Fifty-four patients and 47 controls had at least one major fracture (MF) ($p < 0.001$). Incidence of MF was 3.55 per 100 patient-year in patients and 0.72 in controls. Risk factors for MF in RA patients were age, previous fracture, parental hip fracture, postmenopausal period, hip BMD and cumulative dose of glucocorticoids. In controls, risk factors were age, age at menopause and lumbar BMD.
Among RA-associated factors, MFs were associated with erosions, disease activity and disability. Previous fracture in RA patients was a strong risk for MF (HR: 10.37 [95% CI: 2.95-36.41]).
Conclusion: Between 3 and 4 of every 100 postmenopausal women with RA have a major fracture per year, four times more than the general population. Disease activity and disability associated with RA, the cumulative dose of glucocorticoids and mainly previous fracture are associated with the development of fragility fractures.
References: None
Acknowledgments: Funded in part by ISCIII (PI18/00762) that included FEDER funds from the EU.
Disclosure of Interests: Carmen Gómez Vaquero: None declared, Jose Manuel Olmos: None declared, J. Luis Hernández: None declared, Dacia Cerda: None declared, Cristina Hidalgo: None declared, JA Martínez López: None declared, Luis Marcelino Arboleya Rodríguez: None declared, Javier Aguilar del Rey: None declared, Silvia Martinez Pardo: None declared, Inmaculada Ros: None declared, Xavier Surís: None declared, Dolors Grados Canovas: None declared, Chesús Beltrán Audera: None declared, Evelyn Suero-Rosario: None declared, Inmaculada Gómez Gracia: None declared, Asunción Salmoral: None declared, Irene Martín-Esteve: None declared, Helena Florez: None declared, Antonio Naranjo Grant/research support from: amgen, Consultant of: UCB, Speakers bureau: AMGEN, Santos Castañeda: None declared, Soledad Ojeda Speakers bureau: AMGEN, LILLY, GEBRO, S García Carazo: None declared, Alberto García-Vadillo: None declared, Laura López Vives: None declared, À Martínez-Ferrer: None declared, Helena Borrell Paños: None declared, Pilar Aguado: None declared, Raul Castellanos-Moreira: None declared, Cristian Tebé: None declared, Núria Guañabens: None declared
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OP0324 CLUSTERING OF FRAGILITY FRACTURES BY SITE IN PATIENTS REFERRED FOR BONE MINERAL DENSITY ESTIMATION: AN OBSERVATIONAL STUDY

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Background: Fragility fractures (FF) are those resulting from mechanical forces equivalent to a fall from standing height or less [1]. They most commonly occur in the spine (vertebrae), forearm, and femur, but also occur at other sites. Prevalence markedly increases with age, due to age-related and menopause-related bone loss. FF cause substantial pain and disability, and are associated with decreased life expectancy. While many studies have investigated risk factors associated with FF, there are few data on the association between FF sites in at-risk patients.
Objectives:
1. Establish the most common sites of FF in patients presenting for bone mineral density (BMD) estimation.
2. Identify patterns of co-existing FF in the above cohort by applying cluster analysis.

Methods: We retrospectively reviewed the clinical records of 28868 patients presenting for BMD estimation at a district general hospital in North West England, 2004-2016, identifying those who had sustained one or more FF. Site(s) of FF were recorded for each patient, categorised as: ankle, elbow, femur, forearm, humerus, pelvis, ribs, spine, tibia or fibula (recorded as "tibfib"). Cluster analysis was performed on fracture sites, using Jaccard similarity coefficient. Results were plotted on a dendrogram and divided into clusters, as per results derived from elbow and silhouette cluster methods.
Results: Out of 28868 patients presenting for BMD estimation, 11003 were identified as having sustained one or more FF. 84.6% patients were female, with overall mean age 67.5years and median T-score -1.12 SD. The most common site of FF was the forearm (n=5045), most commonly co-existing with fractures of the tibia or fibula. Frequencies of the most common and co-existing FF sites are shown in Figure 1 (top). Cluster analysis identified 3 clusters: ankle and elbow; forearm, tibia/fibula, ribs, and spine; pelvis, femur, and humerus. The second half of Figure 1 displays the dendrogram of cluster analysis results, with Jaccard similarity measure.
Conclusion: We applied cluster analysis to a large cohort of patients presenting for BMD estimation. Our results are in keeping with previous studies demonstrating the FF to most commonly occur in the forearm, and in those with osteopenia (T-score -2.5 < -1 SD) [2]. To our knowledge, this is the first study to apply cluster analysis to sites of FF. Results may be due to differences in cortical and trabecular bone structure, and have potential to aid prevention, monitoring, and management in at-risk patients.
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Disclosure of Interests: Mrinalini Dey: None declared, Marwan Bukhari Speakers bureau: Bristol-Myers Squib, UCB celltech, Roche/Chugai, Pfizer, Abbvie, Merck, Mennarini, Sanofi-aventis, Eli-Lilly, Janssen, Amgen and Novartis.
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EFIS-EULAR - origin of autoantibodies

OP0325 EFFECT OF CITRULLINATION ON THE PROCESSING AND PRESENTATION OF RHEUMATOID ARTHRITIS AUTOANTIGENS

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Background: Citrullinated proteins are hallmark targets of the autoimmune response in rheumatoid arthritis (RA),[1] but the mechanism by which immune tolerance is broken to these self-proteins is poorly understood. $CD4^+$ T cells are implicated as important drivers of the autoimmune response due to the high-affinity, class-switched nature of anti-citrullinated protein antibodies (ACPAs) present in the majority of RA patients and the prominent genetic contribution of certain HLA-DR alleles to RA susceptibility.[2,3] However, the precise effect of citrullination on MHC class II antigen processing and presentation of autoantigens to $CD4^+$ T cells remains unknown.

Objectives: Here we aimed to examine the hypothesis that citrullination impacts the processing and presentation of RA autoantigens via destabilization of protein folding and modification of protease cleavage sites, altering the peptide repertoire presented by antigen-presenting cells (APCs).

Methods: Using fibrinogen as a model RA autoantigen, the native and citrullinated forms were digested *in vitro* by a cocktail of lysosomal cathepsins (cathepsins B, S, and H) for proteolytic mapping, or incubated with monocyte-derived dendritic cells (mo-DCs) in a natural antigen processing assay (NAPA). Peptides generated by digestion with the cathepsin cocktail or presented by HLA-DR molecules on mo-DCs were then isolated and identified by mass spectrometry.

Results: We found that the repertoire of peptides generated by each method was altered by citrullination. By proteolytic mapping, we detected both changes in the pattern of cathepsin cleavage and an increased number of peptides in the citrullinated samples. Utilizing NAPA, we observed the creation of newly presented peptides in the citrullinated samples in some cases, and loss of presented peptides in others (Fig. 1). Strikingly, all peptides whose presentation was destroyed by citrullination contained a citrullination site. Together these results suggest that both protease cleavage and selection of peptides by HLA-DR are impacted by citrullination.

Conclusion: Citrullination alters the peptide repertoire presented by APCs. Interestingly, no citrullinated peptides were identified by NAPA, suggesting that presentation of citrulline-containing peptides to T cells may not be the primary mechanism by which tolerance is broken to citrullinated antigens. Rather, citrullination-induced destabilization of protein folding and modification of protease cleavage sites, leading to the generation of a new peptide repertoire, could play a role in activating autoreactive T cells. This mechanism could thus drive the loss of immune tolerance to the citrullinated forms of RA autoantigens.

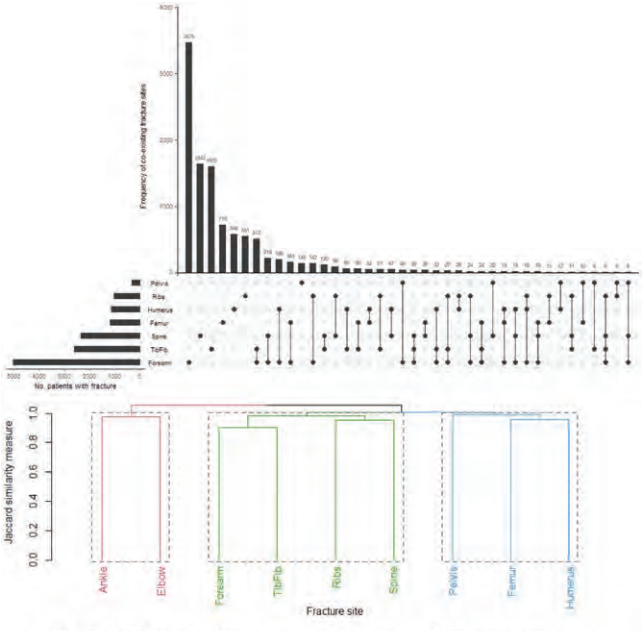


Figure 1: **Top** – Distribution of fracture sites and co-existing fractures (7 most common sites shown). **Bottom** – Dendrogram of cluster analysis of 11003 patients with one or more fragility fracture. Optimal number of clusters was calculated using "Elbow method" and "Silhouette method". Clusters are defined by colour (left-right: red, green, blue) and grey dashed boxes.

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OP0326 ACPA-INDUCED PAIN-BEHAVIOR, BONE LOSS AND TENDON INFLAMMATION IN MICE: A NOVEL MODEL FOR THE PRE-DISEASE PHASES OF ACPA-POSITIVE RHEUMATOID ARTHRITIS

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Background: In rheumatoid arthritis (RA), anti-citrullinated protein antibodies (ACPAs) are associated with bone loss and pain. Recently, tenosynovitis has been suggested as a predicting factor for arthritis progression in individuals at-risk for RA.

Objectives: We aimed to investigate if transfer of human ACPAs into mice could induce tenosynovitis and/or subclinical inflammation.

Methods: Monoclonal ACPA (1325:04C03 and 1325:01B09) and control (1362:01E02) antibodies (mAbs) were generated from synovial plasma or memory B cells of RA patients. 2mg of combination of monoclonal ACPAs or control antibody were injected in BALB/c female mice (age 12-16 weeks) (n= 9). Pain-like behavior was monitored by measuring mechanical hypersensitivity using von Frey filaments every 3 days and estimation by up-down Dixon method. Bone morphometrics was analyzed by micro-CT. Using specially designed mobilization casts, dedicated mouse MRI coils, and gadolinium enhanced contrast medium, the hind limbs of these mice were scanned in a 9.4 T scanner and resulting T1-weighted images were evaluated for signs of soft tissue joint inflammation. The MRI images were scored for the presence of joint involvement and tendon inflammatory changes by 3 readers in a blinded manner.

Results: ACPAs (1325:04C03 and 1325:01B09) induced pain-like behavior (lasting for at least 4 weeks) and reduction of the trabecular and cortical bone thickness in the hind limbs as compared to control monoclonal antibodies ($p<0.05$). While no macroscopic or MRI signs of synovial inflammation were detected, MRI subclinical inflammation of the tendon sheaths was present in mice injected with ACPAs, but not in those injected with control mAb. Semi-quantitative scoring of the inflammatory tendon changes showed significant higher values in mice injected with ACPA (median of 1, range 0 to 2) than those injected with control mAb (median of 0, range 0 to 1).

Conclusion: We show that ACPA induces pain-like behavior, bone loss and tendon sheath inflammation in mice, a model that mimics the preclinical state of ACPA positive RA.

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Disclosure of Interests: Akilan Krishnamurthy: None declared, Yogan Kisten: None declared, Alexandra Circiumaru: None declared, Koji Sakurabas: None declared, Patrik Jarvolli: None declared, Juan Jimenez Jimenez Andrade: None declared, Peter Damberg: None declared, Heidi Wähämaa: None declared, Vivianne Malmström Grant/research support from: VM has had research grants from Janssen Pharmaceutica, Lars Klareskog: None declared, Camilla Svensson: None declared, Bence Réthi: None declared, Anca Catrina: None declared

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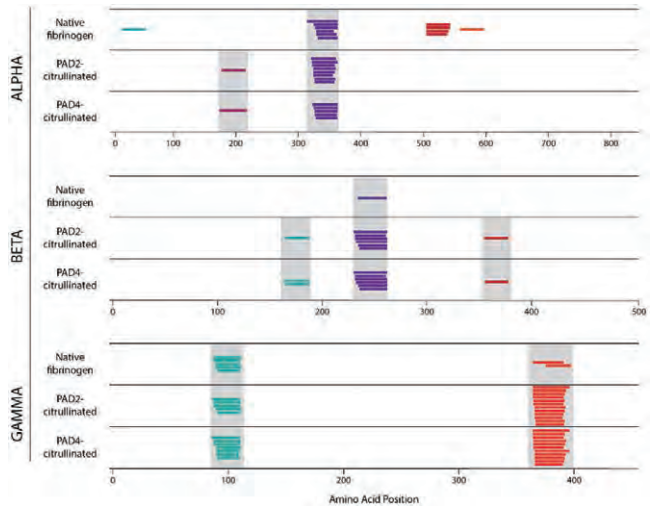


Figure 1. NAPA performed on healthy donor mo-DCs incubated with native, PAD2-citrullinated, and PAD4-citrullinated fibrinogen. Alpha, beta, and gamma chains of fibrinogen are shown separately. Each colored line represents a unique peptide. Nested peptides with a common core motif are shown in the same color. Grey bar denotes peptides with identical core motif between samples.

Artificial intelligence and osteoarthritis

OP0327 EVALUATION OF THE ARTIFICIAL INTELLIGENCE SYSTEM ACCURACY IN DETERMINING THE RADIOGRAPHIC STAGE OF KNEE OSTEOARTHRITIS

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Background: Within the last decade, rapid development of artificial neural networks and machine reading programs and their introduction into medical practice is reported [1,2,3]. Recently, an innovative program, based on the artificial intelligence (AI) technologies (a neural network and machine reading) that analyses knee X-ray images for determining the radiographic stage of OA was created. It was launched on the Osteoscan.ru website and is available for use by patients and doctors.

Objectives: to validate the system ability to accurately stage OA through machine interpretation of standard knee radiographs.

Methods: Initially, 1300 x-rays of both knee joints where used to teach the neural network. Of these, 350 were presented in the form of film scans, 950 in the DICOM format.

The accuracy of the system in recognition of OA stage by knee radiographs was evaluated on a quality control sample of 130 cases (of all 1300). Independently, the radiographs were assessed by certified radiologists (considered the "gold standard") and the System.

Results: In 124 out of 130 cases the conclusion of a specialist and the System was the same, which represents 95.4% predictive power. Coincidence or discrepancy is a qualitative attribute, so, the accuracy of the estimation was calculated. Assuming a discrepancy of 0, and coincidence - of 1, μ = 0,954, the standard error s_p = 1.8%. It can be concluded that in 95% of cases the accuracy of the system assessment will be in the range from 91.8% to 99%.

Conclusion: Osteosan is a program developed on the base of AI technologies, analyzes radiographic images of the knee joints for determining OA stage. It provides high accuracy in OA stage determining by assessing knee radiographs, in 95% of cases, the accuracy of the system varies from 91.8% to 99%.

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Disclosure of Interests: Olga Georginova Speakers bureau: GlaxoSmithKline Consumer Healthcare, Margarita Kobzar Employee of: GSK Consumer Healthcare

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Autoimmune diseases by abnormal T cell function

OP0328 A UNIQUE PD1+CD38+ CD8+ T CELL POPULATION CHARACTERIZES CHECKPOINT INHIBITOR-ASSOCIATED INFLAMMATORY ARTHRITIS

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Background: Immune checkpoint inhibitors (CI) are monoclonal antibodies that block CTLA-4, PD-1 or PD-L1, resulting in cytotoxic T cell activation in the tumor microenvironment. They have revolutionized the management of metastatic cancer but unleash "immune related adverse events" in > 80% of treated patients, including inflammatory arthritis in ~4%[1]. CI-associated arthritis (CI-A) often presents as a symmetrical polyarthritis, phenotypically indistinguishable from rheumatoid arthritis (RA), but whether it shares cellular and molecular features of RA has not been determined.

Objectives: To compare synovial fluid (SF) T cell populations from CI-A patients to those in patients with RA, phenotypically and functionally.

Methods: We immunophenotyped SF mononuclear cells from patients with CI-A caused by anti-PD-(L)1 therapy (n=9), seropositive RA (n=5), and psoriatic arthritis (PsA) (n=5) using a 39-marker mass cytometry (CyTOF) panel. FlowSOM was used to cluster CD4 and CD8 T cells into 15 'metaclusters' based on multidimensional phenotypes. We used Kruskal-Wallis or Mann-Whitney tests to identify significantly altered populations ($p<0.05$), which we confirmed by biaxial gating. Flow cytometry was used to confirm SF findings in an independent cohort, and to identify cells of interest in peripheral blood. Cytokine staining was performed on sorted T cells populations after CDCD3/CD28 stimulation for 72 hours, followed by 4 hour PMA/ION+BRA/MON restimulation.

Results: In CI-A patients, T cells represented 50% of SF mononuclear cells (53% CD4, 40% CD8), followed by monocytes (24%) and NK cells (8%), comparable to RA and PsA. However, FlowSOM analysis revealed expansion of a distinct population of PD-1$^+$ CD38^{hi} CD127$^-$ CD8 T cells (CD8 metacluster2) (Fig. 1). These cells comprised 30% of CD8+ SF T cells in CI-A, a 3.4-fold increase over RA/PsA, p=0.0002 (Fig. 2). Over 40% of these cells expressed Ki67 in CI-A, suggesting active proliferation. Flow cytometry on SF cells from an independent cohort of CI-A patients (n= 5) and RA/PsA comparators (n= 9) confirmed our findings. PD-1$^+$ CD38^{hi} CD127$^-$ CD8 T cells were also expanded in the blood of CI-A patients, where they represented 4.6% of CD8 Tcells, a 2.8-fold increase over RA, p = 0.0057. In addition to expressing high levels of PD-1, CD38^{hi} CD127$^-$, these CD8 T cells express other immune checkpoint receptors including ICOS and TIGIT. After in vitro stimulation, CD38^{hi} CD127$^-$ CD8 T cells produced granzyme B along with TNF and IFN-γ at comparable levels to other CD8 populations, suggesting that they are not functionally exhausted.

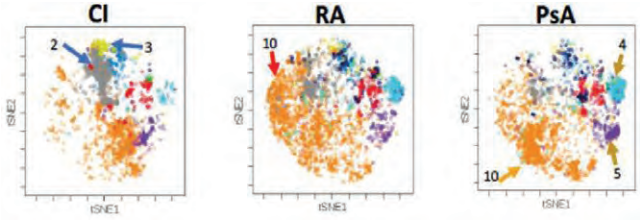


Figure 1. Mass cytometry CD8$^+$ T cells (tSNE plots) with FlowSOM metaclusters.

FlowSOM analysis of SF CD4 T cells in CI-A patients revealed the expansion of a subpopulation of CD4 cells with a similar surface phenotype of PD-1$^+$ CD38^{hi} CD127$^-$ (metacluster2, 10% of CD4s in CI-A, a 2.4-fold increase over RA/PsA, p=0.0047). In contrast, RA patients had a significantly expanded population of PD-1^{hi} ICOS+ CD4 T peripheral helper (Tph) cells (metacluster5, 30% of CD4s in RA, p=0.006), but these cells were not expanded in CI-A (**Fig 3**).

Conclusion: CyTOF analysis of SF revealed a uniquely expanded PD-1$^+$ CD38^{hi} CD127$^-$ CD8 T cell population in CI-A not present in RA or PsA, and a similar PD-1$^+$ CD38^{hi} CD127$^-$ CD4 T cell population. These cells may contribute to the amplified immune response seen in CI-A patients. Further functional and transcriptional analysis of these cells will help to elucidate their function may reveal key mechanisms driving CI-associated immune related adverse events.

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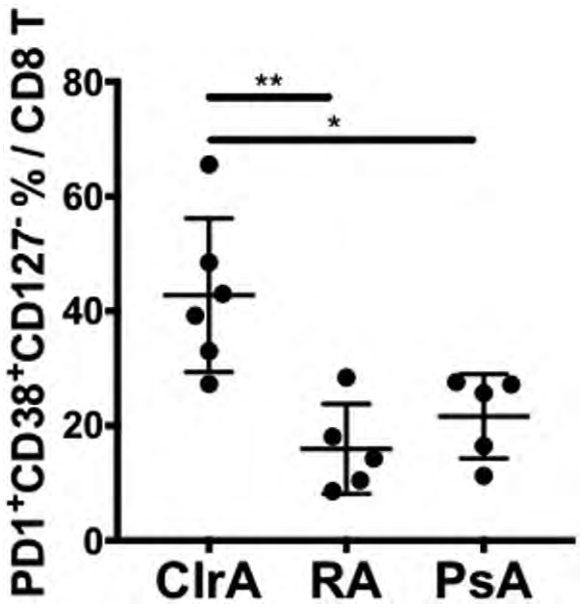


Figure 2. Synovial fluid PD-1^{+} CD38^{hi} CD127^{-} CD8^{+} T cells

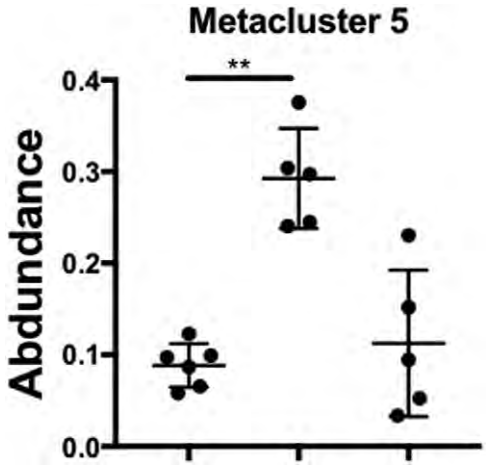


Figure 3. Synovial fluid CD4^{+} T peripheral helper cells

Disclosure of Interests: Runci Wang: None declared, Karmela Kim Chan: None declared, Amy Cunningham-Bussel: None declared, Laura Donlin Consultant of: Consultant – Genentech/Roche, Gregory Vitone: None declared, Aidan Tirpack: None declared, Caroline Benson: None declared, Gregory Keras: None declared, A. Helena Jonsson: None declared, Michael Brenner: None declared, Anne Bass: None declared, Deepak Rao Grant/research support from: Has received research grant support from Celgene and Merck., Consultant of: Has received consulting fees or honoraria from Merck, Pfizer, GlaxoSmithKine, Bristol-Myers Squibb, Janssen, and Scipher Medicine

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OP0329-PARE **IN SHORT: EASY-TO-UNDERSTAND INFORMATION FOR VULNERABLE GROUPS**

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Background: Some 800,000 people in Switzerland have trouble reading (1). For people with reading or learning difficulties, many texts are too complex or simply too long. People with a migrant background likewise often lack access to health information, in their case due to language barriers.

Objectives: One of the top priorities set out in Switzerland's "National Strategy on Musculoskeletal Diseases (2017–2022) is to develop low-threshold services for vulnerable groups. In keeping with this strategy, the Swiss League against Rheumatism (SLR) wants to reach out to people with a migrant background as well as those with reading difficulties by making available to them helpful and readily understandable information material on rheumatic diseases.

Methods: During the planning phase, the SLR collaborated with migesplus, the portal for equal health opportunities operated by the Swiss Red Cross. Their input flowed into the conception of the new publication series "kurz & knapp" (in short).

The texts for the new series are written in accordance with the rules for Easy Language, with the help of an expert committee from Pro Infirmis, the Swiss professional organisation for people with disabilities (www.buero-leichte-sprache.ch). After being evaluated, the final texts then receive a seal of approval. Easy Language is a key component of accessibility, because it makes complex content accessible to a wider audience.

For the benefit of people with a migrant background, the SLR has the texts translated not only into the three Swiss national languages German, French and Italian but also into Albanian, Bosnian/Croatian/Montenegrin/Serbian, Portuguese, Spanish and Turkish.

Brochures on "Gout" and "Arthrosis" have already been published in the "kurz & knapp" series. In 2020, a publication on the subject of "Back Pain" will follow.

In order to make the publications known to the intended target groups, the SLR wrote to various multipliers, such as immigration offices and foreign media.

The publications are available free of charge in the online shop.

Results: The new series "kurz & knapp" has been commended in particular by migration experts. Within the last ten months, the SLR has already distributed over 1,000 copies.

Conclusion: To reach people with reading difficulties or a migrant background – groups that make up a large part of the Swiss population – specially designed communication tools are needed. An interdisciplinary network is indispensable for the development and dissemination of such tools.

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OP0330-HPR

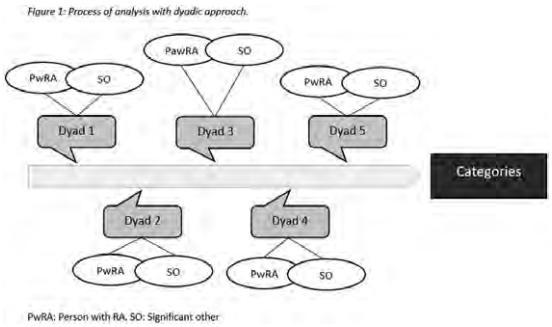
'THE BEST THING WE HAVE IS EACH OTHER' – A QUALITATIVE DYADIC APPROACH TO EXPLORE SUPPORT IN EVERYDAY LIFE BETWEEN PERSONS WITH RA AND THEIR SIGNIFICANT OTHERS

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Background: Participation in everyday life and the relationships between persons with rheumatoid arthritis (RA) and their significant others are often affected by the disease. Usually, both parts need to adapt to new roles [1]. However, the dyadic interaction between them in everyday life is yet to be understood on a deeper level.
Objectives: To explore *I)* How dyads consisting of persons with RA and their significant others comprehend support and participation in everyday life, and *II)* how the dyadic interaction can influence their experience of participation in everyday life.
Methods: In-depth individual interviews were conducted both with the persons with RA 12-13 years after diagnosis and inclusion in the Swedish multicenter project TIRA-2 [2], and with their significant others as defined by the persons with RA. Demographic data and the Valued Life Activity Scale (VLA-swe) [3] was reported by the persons with RA. To avoid bias, the persons with RA and their significant others were interviewed by different researches. Data from the interviews were transcribed verbatim and content analysis with a dyadic approach was undertaken [4]. The process of coding and categorizing was discussed between the researchers. The study was approved by the Regional Ethics Committee at Linköping University (Dnr. 2018/158-31), all participants gave their written consent.
Results: Three women and two men with RA and five significant others, all represented by spouses, participated (N=10). The age of the persons with RA ranged from 34 to 67 years and a majority experienced difficulties in ≥ 12 valued life activities.
Three categories were revealed: *1) A strong willpower affecting the dyadic relationship*, meaning that the understanding within the dyads was that the persons with RA were not so keen to share status, which was mentioned in connection to tenacity and expectations. *2) Being a support to each other*, referring to the mutual understanding within the couples that there was a constant exchange of support, forming a basis for participation in everyday life. However, disagreement was expressed concerning an unequal amount of support. *3) The dyads' potential issues with awareness*, addressing the difficulty in fully comprehending the impact of the diagnosis. The couples mentioned an unwillingness from the person with RA to share information, and the significant other viewing comments as complaining. This type of miscommunication was interpreted as a potential negative effect on participation in everyday life.
Conclusion: A constant exchange of support within the dyads was evident. However, the dyadic relationships were often affected by the willpower of the persons with RA to be independent in everyday life. In addition, the dyads faced the concern of fully understanding the diagnosis. The results indicate further needs for interventions for both the persons with RA as well as the significant others, in order to boost the dyadic interaction, and thereby facilitate optimal participation in everyday life of persons with RA.

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OP0331-HPR

BARRIERS TO SHARED DECISION-MAKING WITH WOMEN OF REPRODUCTIVE AGE AFFECTED BY CHRONIC INFLAMMATORY DISEASES

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Background: Previous research has indicated that women with a chronic inflammatory disease (CID) are likely to discontinue treatment during pregnancy. [1] Reasons for this are complex, including sub-optimal integration of shared decision-making (SDM) into practice.
Objectives: The purpose of this study was to assess: 1) physicians' competencies in risk assessment, treatment and management of women of reproductive age (WoRA) with a CID, and 2) clinical gaps, barriers and challenges to SDM with these patients.
Methods: A mixed-methods needs assessment was conducted. [2] Participants included rheumatologists and dermatologists practicing in Germany, United Kingdom, or United States, with at least three years of experience. Exposure to patients diagnosed with rheumatoid arthritis, psoriatic arthritis, axial spondyloarthritis or psoriasis was required. A first phase involved collection and thematic analysis of data from semi-structured interviews to identify main challenge areas. The second phase consisted of online surveys to validate and quantify identified challenges, gaps and barriers. Chi-square and Kruskal Wallis H statistical tests were performed to assess differences by specialty, country and gender. Qualitative and quantitative findings were triangulated with insight from experts in medical education and relevant behavioural and clinical fields. [3] The present summary reports data pertaining to rheumatologists only.
Results: A total of 24 interviews and 173 surveys were completed with rheumatologists. Depending on the country and specific item, 22% to 64% reported having sub-optimal knowledge of treatment options, patient education aids, and strategies to assess treatment adherence among WoRA with a CID (see figure 1). In addition, 36% reported having sub-optimal knowledge of methods to achieve SDM. Unplanned pregnancies were reported as a barrier to prescribing biologics to WoRA with a CID. Yet, 61% of rheumatologists reported having sub-optimal skills discussing contraceptive methods with patients. In addition, 41% reported having sub-optimal skills adjusting treatment according to changes in pregnancy status or child-bearing aspirations. Few differences in clinical gaps were observed by gender. Notably, a greater proportion of male rheumatologists reported having sub-optimal skills approaching WoRA in a way that makes them feel comfortable discussing their health concerns, compared to female rheumatologists (52% vs. 30%, p=0.046). This skill gap was identified as a contributing barrier to SDM with these patients.
Conclusion: This study identified multiple challenges, gaps and barriers relevant to rheumatologists that prevent optimal SDM, risk assessment, treatment and management of WoRA with CID. Findings may be used to develop medical education and continuous professional development interventions for target learners.

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Quantitative imaging

OP0332

MUSCLE DETERIORATION DUE TO RHEUMATOID ARTHRITIS: ASSESSMENT BY QUANTITATIVE MRI AND STRENGTH TESTING

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Background: As well as joint damage, rheumatoid arthritis (RA) is also associated with altered body composition known as rheumatoid cachexia (RC). RC is characterised by reduced skeletal muscle and increased (white) fat mass and decreased strength. RC is associated with increased disease severity and disability (1). It is unknown at what stage muscle involvement begins in RA, and if the muscle damage is modifiable when patients achieve disease control.

Quantitative MRI (qMRI) can measure the biomarkers associated with RC. MRI T2 is sensitive to fluid related to physiological changes at the molecular level, and is regarded as an indirect measure of muscle inflammation (2). MRI muscle fat fraction (FF) measurements are useful for identifying myosteatosis (3).

Objectives: To obtain preliminary estimates of the extent to which muscle imaging phenotype differs between RA and healthy controls (HC); and to describe the RA phenotype at different levels of disease activity.

Methods: 39 RA patients (comprising three groups) and 13 age and gender directly matched HC had a MRI scan of their dominant thigh. The RA groups were:

[1] 13 'New RA' - newly diagnosed, treatment naïve
[2] 13 'Active RA' - diagnosed >1 year, persistent DAS28 >3.2 for >1 year
[3] 13 'Remission RA' - diagnosed >1 year, persistent DAS28 <2.6 for >1 year

MR images of the mid-thigh were acquired using Dixon imaging to assess FF and a fat-suppressed multi-echo spin-echo to measure T2. Regions of interest were drawn around the quadriceps and hamstrings. All participants had knee extension and flexion torque measured on an isokinetic dynamometer, and isometric dynamometer to measure grip strength. One-Way ANOVA with Dunnett's post-hoc analysis provided preliminary indication of potential differences between T2, FF, muscle volume and strength measurements between the disease stages.

Results: 39 RA patients were recruited: 13 new RA (mean age [years] 63 ± 15, DAS28 5.2 ± 3), 13 active RA (mean age [years] 65 ± 10, DAS28 4.8 ± 3), 13 remission RA (mean age [years] 67 ± 19, DAS28 1.7 ± 0.7) and also 13 HC. T2 and FF were higher in RA patients compared to HC (fig. 1). Within the hamstrings for T2, the mean differences between HC versus new, active and remission patients were 4.5ms (95% CI 2.5, 6.4; p<0.001), 3ms (95% CI 1.1, 4.9; p=0.001), and 5.0ms (95% CI 3.0, 6.4; p<0.001) respectively. Quadriceps results were similar. For muscle volume, the mean differences between HC versus new, active and remission patients were -517.3cm^3 (95% CI -751, -283; p<0.001), -370.5cm^3 (95% CI -605, -136; p=0.001), and -312.3cm^3 (95% CI -546. -77; p=0.006) respectively (fig. 2). Knee flexion/extension and handgrip strength were lower in all 3 groups of RA patients compared to HC. For knee flexion, the mean differences between HC versus new, active and remission patients were 18.4Nm (95% CI -35, -1; p=0.03), 10.1Nm (95% CI -27, 7; p=0.3), and 13.3Nm (95% CI -33, 0; p=0.1) respectively.

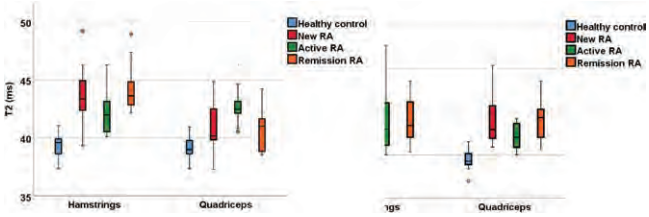


Figure 1. Quantitative T2 and FF MRI of RA patients and healthy controls

Conclusion: This pilot study suggests muscle health may be adversely affected in RA patients compared to matched HC. Our results suggest that muscle changes occur in the earliest stages of RA and persist throughout the disease duration, even in clinical remission. If confirmed, these data imply the need for adjunctive muscle intervention to current RA treatment strategies in order to improve patient outcomes.

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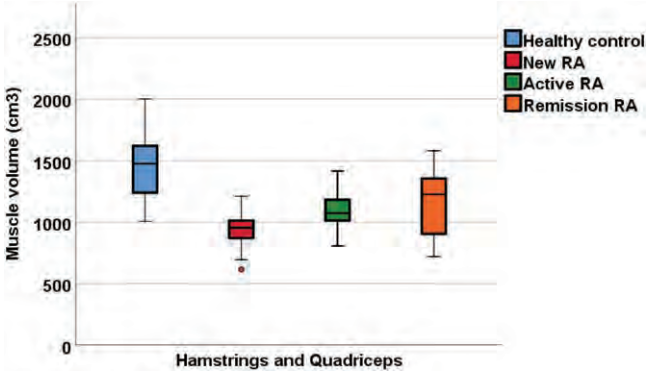
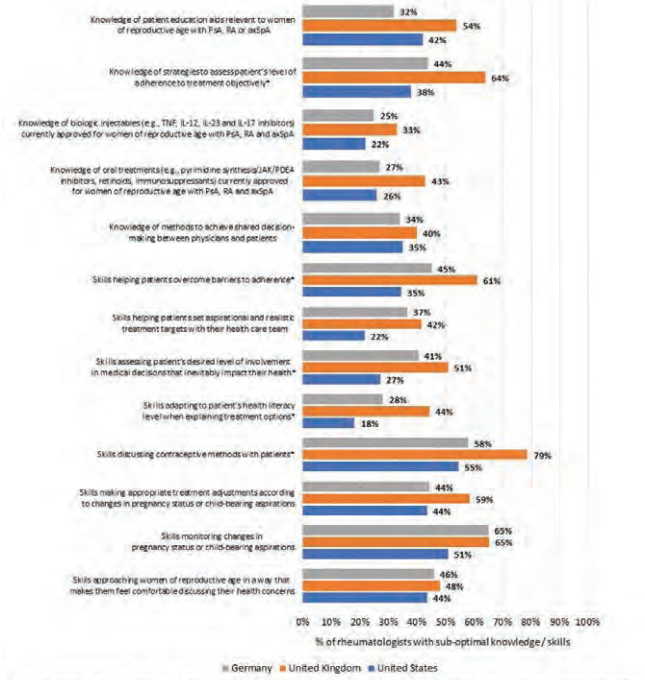


Figure 2. MRI muscle volume in RA patients and healthy controls



Description: For each item above, participants were asked to rate their level of knowledge / skills, compared to what is expected in their professional role, using a 5-point scale (1=None, 2=Basic, 3=Intermediate, 4=Advanced, 5=Expert, NR=Not relevant). Data shows percent (%) of those who selected 1, 2 or 3 in each country.
Legend: *Significant differences between countries at p=0.05. PsA=psoriatic arthritis RA=rheumatoid arthritis axSpA= axial spondyloarthritis

Figure 1- *Percent of rheumatologists in Germany (n=55), United Kingdom (n=54) and United states (n=64) who reported sub-optimal level of relevant knowledge and skills*

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OP0333

RISK FACTORS OF ANTIMALARIAL-INDUCED RETINOPATHY IN SYSTEMIC LUPUS ERYTHEMATOSUS AND OTHER AUTOIMMUNE CONDITIONS

H. Y. Liu[1], G. Cramarossa[1], J. Pope[1]. [1]*Western University, London, Canada*

Background: Hydroxychloroquine (HCQ) and chloroquine (CQ) are effective antimalarial (AM) medications for systemic lupus erythematosus (SLE) and other autoimmune conditions such as rheumatoid arthritis (RA). AM-induced retinopathy is a well-recognized irreversible complication with variable incidences [1]. Few studies have compared the AM-induced retinopathy between rheumatologic conditions.

Objectives: To describe the pattern of AM-associated retinopathy, including diagnosis of SLE as a risk factor.

Methods: A chart review was conducted at an urban Canadian center. Each patient was classified as SLE, based on ACR criteria, or non-SLE. Minimum duration of AM use was 3 months. AM-induced retinopathy was classified as possible or definite, and was determined based on characteristic visual field loss, abnormal retinal imaging, and eye specialists' opinion. Univariate and multivariate logistic regressions were performed to determine factors associated with definite AM-induced retinopathy. Sensitivity analyses included inclusion of possible AM-induced retinopathy and stratification of analysis by diagnosis and by CQ versus HCQ.

Results: Of the 680 patients, 282 patients had SLE and the remaining had RA (N=224), cutaneous lupus (N=41), or other connective tissue diseases (N=131). Patients with SLE tended to be younger, female, and had relatively more CQ and total AM exposure (Table 1). Definite AM-induced retinopathy was observed in 12 patients, 11 of whom had SLE and 7 had chloroquine exposure (Figure 1). The earliest toxicity occured after 5.4 years of AM use, and prevalence beyond 5 years was 2.7%.

Table 1. Patient characteristics. Data represented as N (%) or means (SD)

	SLE (N=282)	Non-SLE (N=398)*	Total (N=680)	P
Age	40.1 ± 15	51 ± 13.8	46.5 ± 15.3	5.72×10^{-21}
Female	258 (91%)	333 (84%)	591 (87%)	4.19×10^{-3}
AM duration (years)	11.5 ± 8.1	7.3 ± 6.2	9.1 ± 7.3	3.52×10^{-11}
CQ ever	35 (12%)	21 (5%)	56 (8%)	1.41×10^{-3}

*other connective tissue diseases and RA

In univariate logistic regression (Table 2), a diagnosis of SLE ($P=7.95\times10^{-3}$; OR= 16.1; 95% confidence interval (CI)= [2.1, 125]), and cumulative CQ dose ($P=1.13\times10^{-2}$; OR= 1.002; 95% CI=[1.000, 1.003]) were significantly associated with definite AM-induced retinopathy. When possible retinopathy was included in the analysis, both SLE ($P=7.27\times10^{-3}$; OR=3.12, 95% CI=[1.39, 7.00]) and CQ cumulative dose ($P= 6.16\times10^{-7}$; OR= 1.002; 95% CI=[1.001, 1.003]) remained significant. Total AM duration and hypertension also had significant associations. In multivariate analysis, diagnosis of SLE was significantly associated with ocular toxicity ($P=1.49\times10^{-2}$; OR=14.2; 95%CI: [1.83-127]) after adjusting for CQ/HCQ dosages, age, sex, weight, hypertension and renal impairment.

Table 2. Univariate logistic regression for risk of AM-induced retinopathy. Data represented as N (%) or mean ± SD

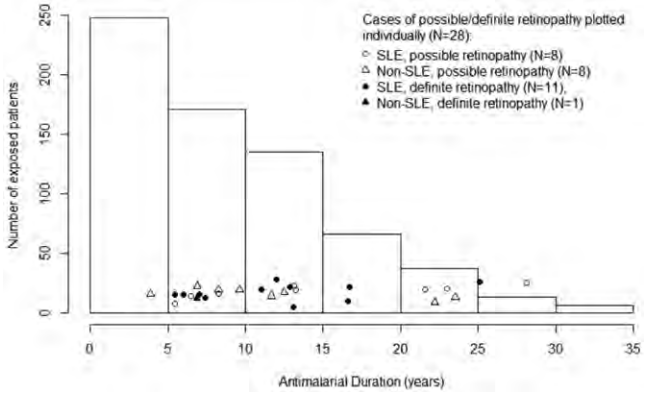
	Definite retinopathy			Possible or definite retinopathy		
	No retinopathy N=668	Retinopathy N=12	P	No retinopathy N=652	Retinopathy N=28	P
Age	46.5 ± 15.3	43.2 ± 14.3	0.452	46.4 ± 15.4	47.1 ± 12.4	0.832
Female	580 (87%)	11 (92%)	0.626	567 (87%)	24 (86%)	0.848
Weight (kg)	76.5 ± 19.5	67.3 ± 12.8	0.098	76.5 ± 19.5	73.5 ± 17.8	0.424
SLE Diagnosis	271 (41%)	11 (92%)	**0.008**	263 (40%)	19 (68%)	**0.006**
AM duration (years)	9 ± 7.4	11.7 ± 5.8	0.215	8.9 ± 7.3	12.8 ± 6.8	**0.007**
AM> 5 years	417 (63%)	0	-	250 (40%)	1 (3%)	**0.006**
HCQ dose (mg/kg/day)	5.2 ± 15.5	5.9 ± 1.5	0.891	5.2 ± 15.6	5.3 ± 1.4	0.971
HCQ total dose (g)	1042 ± 913.8	1235 ± 1032	0.471	1340 ± 914	1187 ± 955	0.404
CQ total dose (g)	46 ± 205.1	225± 291	**0.011**	37.6 ± 174)	318 ± 529	**6.16×10^{-7}**
Renal Impairment	100 (15%)	2 (17%)	0.883	99 (15%)	3 (11%)	0.506
Hypertension	298 (45%)	5 (42%)	0.832	285 (44%)	18 (64%)	0.038
Diabetes	61 (9%)	1 (8%)	0.924	59 (9%)	3 (11%)	0.765

Conclusion: The risk of AM-induced retinal toxicity increases after 5 years of use. SLE patients may be at increased risk due to longer treatment duration, AM choice, and underlying disease processes.

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Figure 1: Distribution of duration of antimalarial use and onset of AM-induced retinopathy



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Origin and role of myeloid cells during homeostasis and inflammation

OP0334

GGTASE DEFICIENT MACROPHAGES ALTER INTEGRIN EXPRESSION ON LYMPHOCYTES AND FACILITATE DEVELOPMENT OF ARTHRITIS

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Background: Geranylgeranyltransferase type I (GGTaseI) is the enzyme responsible for the prenylation/ lipidation of the RhoA family proteins, which keeps them attached to the cell membrane. We reported that GGTaseI-deficient (GLC) mice develop a spontaneous and age-dependent arthritis, reproducing the pathology of RA[1]. Targeting GGTaseI activates RhoA proteins.

Objectives: To study which of the activated Rho proteins is responsible for development of arthritis, we deleted individual RhoA, Rac1 or Cdc42 genes in GLC mice. We study consequences of GGTaseI deficiency for lymphocyte function.

Methods: Double deficient mice that lack Rac1 (GLC Rac1fl/fl), RhoA (GLC RhoAfl/fl) and Cdc42 (GLC Cdc42fl/fl) were developed by Cre-technology using the LysM-promotor, and were on a mixed genetic background (129Ola/Hsd-C57BL/6)[2]. Joints of the hind paws were assessed for signs of arthritis histologically and by micro CT at age of 16 weeks. Phenotype of spleen CD4 and CD8 T cells was analysis by flow cytometry. Proliferation and cytokine production was assessed in spleen cultures by ELISA. Gene expression profile was analyzed by RT-PCR.

Results: Deletion of Rho proteins had divergent effect on development of arthritis in GLC mice. We observed a reduction of the arthritis index in GLC Rac1fl/fl (n=19, p=0.027) and GLC RhoAfl/fl (n=4, p=0.007) mice compared to GLC (n=16), while GLC Cdc42fl/fl (n=4) had no change in arthritis development. GLC RhoAfl/fl mice increased the bone mass compared to GLC (p=0.029).

Flow cytometry analysis showed that RA-prone GLC and GLC Cdc42fl/fl mice had lower number of CD4 cells in spleen. CD4 cells of RA-prone GLC and GLC Cdc42 mice had significantly higher subsets of the regulatory FoxP3+ and FOXp3+CD25+ cells (p=0.016-0.029 and p=0.016-0.029 respectively) compared to control and GLC

RhoAfl/fl mice. Additionally, RA-prone mice had higher expression of receptors to extracellular matrix proteins collagen (α2β2) and fibronectin (α5β1) compared to control mice (p=0.016 and p=0.011 resp) and to RA-protected mice (GLC Rac1fl/fl and GLC RhoAfl/fl, p=0.0004 and p=0.011, resp). In total, both the number of FoxP3+ CD4 cells and the expression of α5β1 receptors on CD4 cells correlated strongly with the synovitis score (r=0.72, p=0.0017 and r=0.59, p=0.012, respectively).
GGTaseI gene lays under the control of HOX proteins essential for cell homing. Importantly, HOX regulate the expression of integrins. Studying the expression of HoxA genes in spleen, we found that RA prone GLC and GLC Cdc42 mice tended to have lower expression of HoxA2 and higher expression of HoxA9 compared to RA-protected GLC Rac1 and GLC RhoA and to control mice. The Hoxa9/Hoxa2 ratio was significantly higher in RA prone mice compared to RA-protected mice (p=0.0085) and control mice (p=0.019). This ratio correlated with α5β1 receptors (r=0.55, p=0.0084), FOXP3+ CD4 cells (r=0.50, p=0.017), and the arthritis index (r=0.50, p=0.033).
Conclusion: Taken together this study shows that Rho proteins play divergent role in development of arthritis. Activation of Rac1 and RhoA by GGTaseI deletion changes the pattern of HOXA proteins and increases expression of integrin receptors, which facilitates leukocyte influx in the paw joints. Deletion of Rac1 and RhoA has RA-protective effect in GLC mice.
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Disclosure of Interests: None declared
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OP0335-PARE **MODERNISATION OF PATIENT ORGANIZATION THROUGH ONLINE COURSES**

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Background: A big and very crucial part of every membership organization is the continuing education of members and elected representatives in regional and local chapters.
Given the geographical long distances in Sweden, attending courses in person can be difficult, and expensive for the Swedish Rheumatism Association, the SRA. In 2019 the SRA developed a method to modernise our educational efforts by offering online courses to our elected representatives. Thus making it possible for anyone who has access to a computer to participate when it suits him or her. The courses can be done individually or in groups.
Objectives: The goal is to offer modern and cost effective ways to educate in matters selected by the SRA, and for elected representatives and members to be able to attend courses at any times.
Methods: The courses consists of films, texts and study exercises.
The staff of the SRA record films and make as much of the content themselves as possible. The content must be relaxed, easy to do and enhance the feeling of familiarity. Those who complete the courses should feel like they are in the same room as the lecturers.
Results: In 2019, the SRA completed two courses for elected representatives. The first course was on the matter of democratic structures at the annual general meeting of the SRA, and all decision making that applies for the SRA, for example, statutes, how to elect new board members and decide on an activity plan for the coming year. The course circled around these topics:

1. How do you write a motion and how do you send it to the annual meeting?
2. How do you prepare as a representative?
3. What happens at an annual general meeting?
4. How do you ask for the word and how do you argue for your cause?
5. How do you report from a general meeting to your local organization?

During the evaluation, the SRA received positive comments from those who attended. By the end of 2019, the SRA finished developing an online course on membership recruitment.
Conclusion: In 2020, the SRA plan to do three more online courses on the topic of systemic sclerosis, rheumatoid arthritis and fibromyalgia.
Online courses will not replace physical meetings, but offer a good alternative in the field of patient education.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.1018

Improving work participation

OP0336-HPR **RISK FACTORS FOR PERSISTENCE AND DEVELOPMENT OF FREQUENT MUSCULOSKELETAL PAIN IN ADOLESCENT ATHLETES**

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Background: Physical activity has a positive impact on health, but adolescent athletes often report musculoskeletal pain (MP) which is negative in the aspect of sustaining physical activity over time. There is a lack of longitudinal assessments of MP and potential risk factors, such as timing of physical maturation, in adolescent athletes.
Objectives: To identify risk factors associated with the persistence or development of frequent MP at a 2-year follow-up in adolescent sport school students.
Methods: Fourteen-year-old sport school students (n=233) were invited to participate in this 2-year longitudinal study. Self-reports of MP was assessed as frequency, distribution, and intensity, and health status by EQ-5D. Physical maturation was calculated by the Mirwald equation (height, weight, and sitting height) (1), and categorized as early (>1 year), average (±1 year), or late (<–1 year). Students were grouped at baseline and follow-up into infrequent (never to monthly) or frequent (weekly to daily) MP groups. Logistic regression analysis was used to study associations between frequent MP at follow-up and baseline variables.
Results: 131 students (79 boys and 52 girls) were included in the study. Development or persistence of frequent MP at follow-up (n=61) was associated with being a girl, late physical maturation (only boys were categorized as late), non-contact sports participation, frequent MP at baseline, and reporting ≥2 MP sites at baseline. Students with a better health status at baseline were less likely to belong to the frequent MP group at follow-up (Table).
Conclusion: Frequent MP is common in sport school students. MP in young athletes may become a future health problem and there is a need for recognition and interventions by coaches and health services to prevent MP from becoming persistent.
References:
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Table. Associations between background variables at baseline and frequent MP at follow-up based on crude logistic regression analysis controlling each variable for sex.

Baseline variables		Model Infrequent MP vs. Frequent MP	
		OR	(95% CI; p-value)
Sex	Boys	1.00	
	Girls	2.76	(1.34–5.68; p<0.01)
Physical maturation	Average (±1 year)	1.00	
	Early (>1 year)	0.41	(0.05–3.65; p=0.42)
	Late (<–1 year)	3.83	(1.13–12.95; p=0.03)
Sport categories	Contact	1.00	
	Non-contact	5.16	(2.07–12.88; p<0.001)
MP groups	Infrequent	1.00	
	Frequent	2.74	(1.31–5.72; p<0.01)
MP intensity last week (NRS 0–10, best to worst)		1.15	(0.98–1.35; p=0.10)
Number of MP sites	0	1.00	
	1	2.32	(0.71–7.58; p=0.16)
	≥2	2.87	(1.32–6.25; p<0.01)
EQ-5D (0.00–1.00, worst to best)		0.03	(0.001–0.58; p=0.02)

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.1800

New technologies in translational rheumatology

OP0337 **DIFFERENTIAL METHYLATION OF PERIPHERAL BLOOD ADAPTIVE IMMUNE CELLS IN INDIVIDUALS AT HIGH RISK FOR RA AND WITH EARLY RA COMPARED WITH CONTROLS IDENTIFIES PATHWAYS IMPORTANT IN TRANSITION TO ARTHRITIS**

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Background: The "Targeting Immune Responses for Prevention of RA" (TIP-RA) collaboration studies individuals at high risk for developing RA because of serum anti-citrullinated protein antibody positivity in absence of arthritis, and is focused on defining how they transition from at-risk to classifiable disease. One potential mechanism is through alterations in epigenetics patterns in adaptive immune cells.
Objectives: Previous studies showed that DNA methylation patterns of early RA (ERA) synoviocytes differ from long-standing RA, suggesting that abnormal methylation occurs early in synovium and evolves over time. To extend these observations, we performed

a cross-sectional analysis in TIP-RA of DNA methylation signatures in peripheral blood cells in ERA, at-risk anti-CCP3+ individuals and demographically matched CCP- controls.
Methods: Genomic DNA was isolated from two independent cohorts of CCP- (cohorts 1 and 2, respectively: B cell: n = 17/34; memory T cell: n = 21/34; and naïve T cell: n = 21/33), CCP3+ (B cell: n = 18/37; memory T cell: n = 20/36; and naïve T cell: n = 20/35), and CCP3+ ERA (B cell: n = 4/18; memory T cell: n = 5/18; and naïve T cell: n = 5/18) after separating PBMCs using antibodies and magnetic beads. Methylation was measured by Illumina Infinium MethylationEPIC chip. Differentially methylated loci (DMLs) were identified using Welch's t-test and mapped to gene promoter regions to define DM genes (DMGs). Principal component analysis (PCA) was used to represent relationship among groups. Pathway analysis was applied by Reactome.
Results: For the initial cohort, 1494, 1097 and 1330 DMLs were identified among CCP+, CCP- and ERA in B cells, memory T cells and naïve T cells, respectively. For the confirmatory cohort, 523, 793 and 548 DMLs were found in corresponding cell populations. The DML overlap between the 2 cohorts was highly significant (p = 2.48E-77). The DMLs were combined for both groups and corresponded to 411, 412, and 351 DMGs in B cells, memory T cells and naïve T cells. Of these, we found 246, 198 and 195 DMGs between CCP3+ and ERA in each peripheral blood cell population, respectively. PCA showed separation of CCP+, CCP- and ERA in each of the three blood cell types by DMLs (Fig. 1). DMGs were mapped to biological pathways to identify DM pathways. Although most were not significant, there were several highly significant differences comparing CCP+, ERA and CCP- in memory T cells involving pathways, including "Interferon gamma signaling" (FDR 7.48E-14), "PD-1 signaling" (FDR 8.71E-10), "Translocation of ZAP-70 to Immunological synapse" (FDR 4.75E-10), and "Phosphorylation of CD3 and TCR zeta chains" (FDR 8.71E-10).

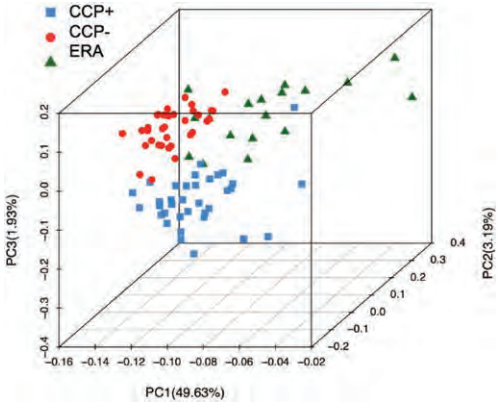


Figure 1. PCA shows the separation of CCP+, CCP- and ERA patients in memory T cells in confirmatory cohort.

Conclusion: We identified reproducible methylation signatures of CCP-, CCP+, and ERA in peripheral blood B cells, memory T cells and naïve T cells in initial and confirmatory cohorts. The methylome of ERA also demonstrated a distinctive pattern from CCP+, indicating that progression to RA is accompanied by epigenetic remodeling, especially in T cell signaling and interferon responses. These signatures identify critical pathways in CCP positivity and classifiable RA and could provide the basis of novel interventions to prevent disease.
Disclosure of Interests: Rizi Ai: None declared, David Boyle: None declared, Deepa Hammaker: None declared, Kevin Deane Grant/research support from: Janssen, Consultant of: Inova, ThermoFisher, Janseen, BMS and Microdrop, V. Michael Holers Grant/research support from: Janssen, Celgene, and BMS, Andre Matti: None declared, William Robinson: None declared, Jane Buckner Grant/research support from: Bristol-Myers Squibb, Janssen, Navin Rao Shareholder of: Janssen Pharmaceuticals, Employee of: Janssen Pharmaceuticals, Frederic Baribaud Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC, Alyssa Johnsen Employee of: Janssen, Sunil Nagpal Shareholder of: Janssen Pharmaceuticals, Employee of: Janssen Pharmaceuticals, Wei Wang: None declared, Gary Firestein Grant/research support from: Lilly, Janssen, Abbvie
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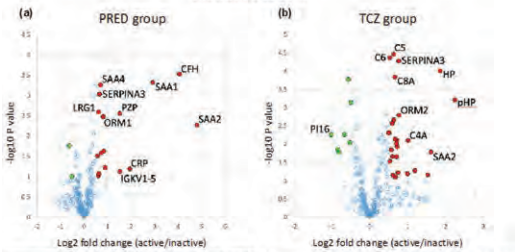
OP0338

MASS SPECTROMETRY IDENTIFIES NOVEL BIOMARKERS IN GIANT CELL ARTERITIS, USEFUL IN PATIENTS ON INTERLEUKIN-6 RECEPTOR BLOCKADE

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Background: Acute phase reactants (erythrosedimentation rate [ESR], C-reactive protein [CRP]) have limited utility in GCA, even in patients treated with prednisone alone. Furthermore, the lack of reliable biomarkers in patients receiving interleukin (IL)-6 blockade therapy is a major unmet need.
Objectives: To identify biomarkers of disease activity in GCA patients treated with prednisone monotherapy and with prednisone in combination with tocilizumab (TCZ).
Methods: We mapped the serum proteome of GCA patients with active and inactive disease in an unbiased manner using high-throughput multiplexed mass spectrometry. Proteomic analyses were performed in 5 µl serum samples with 11-plexed tandem mass tag (TMT) technology using an Orbitrap Lumos mass spectrometer. A SEQUEST-based database search engine was employed for peptide identification. Quantification was based on TMT reporter ion intensities. All patients were sampled during their participation in the GiACTA trial,[1] in which they received TCZ plus 26 weeks of prednisone (TCZ group) or placebo plus 26 or 52 weeks of prednisone (PRED group). Active disease was defined as the presence of cranial or PMR symptoms requiring treatment intensification regardless of ESR and CRP levels. Samples were selected if patients were in clear states of active or inactive disease at GiACTA systematic sample collection timepoints (baseline and weeks 4, 12, 24, 48). An exhaustive leave-2-out strategy was used to identify classification markers. All possible pairs of samples were isolated as test samples and the remaining training samples were used to identify the protein markers. Proteins with an absolute log2 fold concentration difference ≥0.5 between active and inactive samples and a P-value <0.1 were retained and sorted based on the metric -log10(P-value)*absolute(log2 fold change). Top markers within each training set were selected to generate normalized ranks {0,1} across all samples. A mean rank was calculated for every sample. The set of normalized ranks for the test samples across all sets of top markers were bootstrapped for each test sample 100 times with replacement. The bootstrapped rankings were evaluated by determining areas under the curves (AUC) of receiver operator characteristic (ROC) curves.
Results: The PRED group included 21 patients (active, n = 16; inactive, n = 5) and the TCZ group included 21 patients (active, n = 14; inactive, n = 7). Using high-throughput sample preparation methods without applying any depletion of known highly abundant serum proteins, we quantified 760 proteins across all samples and 344 proteins in at least half the samples. Compared to inactive PRED-treated patients, active PRED-treated patients showed significant overexpression of several acute phase reactants including serum amyloid A1 and 2 (SAA1, SAA2) and complement factor H (CFH) (Fig. 1a). The magnitude of concentration change and the level of statistical significance observed for SSA1, SSA2 and CFH in PRED-treated patients were higher than those of CRP (Fig. 1a). Compared to inactive TCZ-treated patients, active TCZ-treated patients demonstrated significant overexpression of multiple biomarkers including haptoglobin, haptoglobin precursor, SSA2 and complement factor 4A, and underexpression of peptidase inhibitor 16 (Fig. 1b), a protein involved in vascular and regulatory T cell biology. Sets of 10 biomarkers resulted in a classification of active versus inactive disease with ROC AUCs of 0.89 (95% CI 0.79-0.96) in the PRED group (Fig. 2a) and 0.97 (95% CI 0.95-0.97) in the TCZ group (Fig. 2b).
Conclusion: We identified several differentially expressed serum proteins in GCA patients with active and inactive disease receiving prednisone monotherapy or TCZ-based treatment regimens. In both treatment groups, a signature of biomarkers classified disease activity status with high accuracy. Haptoglobin, a readily available laboratory test, may be useful in monitoring disease activity in GCA patients receiving IL-6 blockade therapy.
References:
[1] Stone *et al*. *NEJM* 2017

Figure 1. Differentially expressed serum proteins in giant cell arteritis patients with active and inactive disease

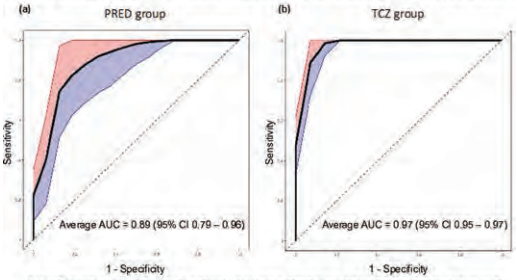


	log2 fold change	P-value
Serum amyloid A2 (SAA2)	4.8	0.0054
Complement factor H (CFH)	4.1	0.0003
Serum amyloid A1 (SAA1)	2.9	0.0025
C-reactive protein (CRP)	2	0.0650
Pregnancy zone protein (PZP)	1.5	0.0028
Immunoglobulin Kappa Variable 1-5 (IGKV1-5)	1.5	0.0740
Alpha-1-acid glycoprotein 1 (ORM1)	0.8	0.0033
Serum amyloid A4 (SAA4)	0.7	0.0005
Alpha-1-antitrypsin (SERPINA3)	0.7	0.0026
Leucine-rich alpha-2-glycoprotein 1 (LRG1)	0.6	0.0028

	log2 fold change	P-value
Haptoglobin precursor (pHP)	2.3	0.0006
Haptoglobin (HP)	1.9	0.0001
Serum amyloid A2 (SAA2)	1.6	0.0165
Complement factor 4A (C4A)	1	0.0079
Alpha-1-acid glycoprotein 2 (ORM2)	0.8	0.0016
Alpha-1-antitrypsin (SERPINA3)	0.8	0.0001
Complement factor 8A (C8A)	0.7	0.0001
Complement factor 5 (C5)	0.6	<0.0001
Complement factor 6 (C6)	0.5	<0.0001
Peptidase inhibitor 16 (PI16)	-1	0.0055

(a) Top 10 markers in patients treated with prednisone monotherapy (PRED group); (b) top 10 markers in patients treated with tocilizumab and prednisone (TCZ group)

Figure 2. Accuracy of top biomarkers for discrimination between active and inactive giant cell arteritis



(a) Top 10 markers in patients treated with prednisone monotherapy (PRED group); (b) top 10 markers in patients treated with tocilizumab and prednisone (TCZ group)

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LB0002 **A FIRST IN CLASS THERAPEUTIC NANOPARTICLE FOR SPECIFIC TARGETING OF ANTI-CITRULLINATED PROTEIN ANTIBODY AMELIORATES SERUM TRANSFER AND COLLAGEN INDUCED ARTHRITIS**

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Background: Rheumatoid arthritis (RA) is an immune mediated inflammatory disease with autoimmune features, including antibodies to citrullinated proteins and peptides (ACPAs). Several in vitro studies have suggested a pathogenic role of ACPAs in RA. However, in vivo proof of this concept has been hampered by the lack of therapeutic strategies to reduce or deplete ACPA in serum and synovial fluid. Previously, we constructed a chitosan-hyaluronic acid nanoparticle formulation with the ability to use neutrophil recruitment as a delivery mechanism to inflamed joints. Specifically, nanoparticles got phagocytosed and then released to synovial fluid upon death of the short-lived neutrophils
Objectives: We hypothesized that reducing ACPA levels would have a therapeutic effect by blocking cytokine production. In this study, we prepared and tested a series of therapeutic nanoparticles for specific targeting of ACPA in synovial fluid.
Methods: Nanoparticles were prepared by the microdroplet method and then decorated with synthetic cyclic citrullinated peptide aptamer PEP2, PEG/hexanoic acid and fluorophore (Cy5.5). Nanoparticles were characterized by dynamic light scattering (DLS), scanning electron microscopy (SEM) and high-performance liquid chromatography (HPLC). Nanoparticles were then used in a series of in vitro assays, including cell uptake with flow cytometry (FACS) detection, and in vivo studies including disease activity scores, cytokine measurements and near-infrared imaging.
Results: We screened a series of citrullinated peptide epitopes and identified a fibrinogen-derived 21-amino-acid-long citrullinated peptide showing high selectivity toward autoantibodies in RA samples. We incorporated this aptamer in the chitosan-hyaluronic acid nanoparticle formulation previously described. Average nanoparticle size was 230 nm ± 10 nm by DLS and SEM; z potential was -0.0012. Purity by HPLC was over 95%. Attachment efficiency of the aptamer was 92% by HPLC. FACS study showed selective uptake of Cy5.5 labelled aptamer-nanoparticle conjugates by neutrophils in the concentration range 0.5-4 nM. Similar to previous studies,[1] there was no apparent immunogenicity for this nanoparticle formulation measured by cytokine secretion from human peripheral blood leukocytes. In vivo, over 50% reduction of disease activity was achieved in three weeks treatment using as little as 1 nM drug candidate (dosed every 48 hours) in the collagen-induced (CIA) mouse model of RA (N=30; p<0.001 for treated vs placebo). Same was observed in the serum transfer model (N=10). The aptamer-nanoparticle conjugate significantly reduced IL-6 and TNFα levels in the mouse sera (p<0.01). The effects were not inferior to tocilizumab treated controls (N=30). To confirm mode of action, we applied Cy5.5-labelled aptamer-nanoparticles in the collagen-induced mouse model (N=10) and analyzed the resulting uptake by near-infrared imaging. We confirmed over 6-fold higher signal accumulation in inflamed vs healthy joints (p<0.01), which strongly supports the fact that the aptamer is highly specific to the inflammatory process.
Conclusion: Overall, we have designed a first-in-class therapeutic nanoparticle drug for specific targeting of anti-citrullinated protein antibodies. The marked effect of this nanoparticle observed in vivo holds promise for targeting ACPAs as a therapeutic option in RA.
References:
[1] Khatri S, Hansen J, Mendes AC, Chronakis IS, Hung S-C, Mellins ED, Astakhova K. Bioconjug Chem. 2019 Oct 16;30(10):2584–259
Disclosure of Interests: Sangita Khatri: None declared, Jonas Hansen: None declared, Mads Hartvig Clausen Shareholder of: iBio Tech ApS, Tue Wenzel Kragstrup Shareholder of: iBio Tech ApS, Consultant of: Bristol-Myers Squibb, Speakers bureau: TWK has engaged in educational activities talking about immunology in rheumatic diseases receiving speaking fees from Pfizer, Bristol-Myers Squibb, Eli Lilly, Novartis, and UCB., Shu-Chen Hung: None declared, Elisabeth Mellins: None declared, Kira Astakhova: None declared
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Science communication skills for young rheumatologists

OP0339 **ALTMETRIC - DOES SOCIAL MEDIA IMPACT CITATION RATE IN RHEUMATOLOGY JOURNALS?**

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Background: The coloured altmetrics donut has become a standard feature of online publications. The colours depict different online sources by which an article was mentioned, while the number in the donut, the Altmetric Score (AS), reflects the summarised attention an article has received. The Dimensions database joins citations from any kind of scientific or mainstream publication. Studies analysing the link between the AS and the citation rate of an article suggest that this connection is strongly dependent on the field of research, the type of article and the type of analysis used.
Objectives: To analyse the connection between AS and citation rate in articles published in rheumatology journals.
Methods: We retrieved data on article usage, AS and citations of articles published in ARD and RMD Open between January 2015 and November 2019. For time-dependent analyses on the influence of AS on citations, articles published in 2019 were excluded. Forward-stepwise regression models were used to explore factors influencing total citation rates. We performed subanalyses, dividing articles in categories of correspondence, original research and editorials/viewpoints. We dichotomised articles by reaching the top 25% in terms of citation count within the first, second, third and fourth year after publication according their category. We explored the risk of reaching these top 25% in dependency of AS using logistic regression (log transformed AS) and receiver operating curve analyses (ROC, reported cut-offs were identified coinciding with 80% specificity).
Results: We used 1597 articles published in ARD and 409 articles of RMD Open with complete data on AS and article usage within the mentioned timeframe. AS are higher in more recently published articles (p=0.04, ß: 1.3 per year), but the number of Dimensions citations is lower in more recently published articles (ß: -8.5 per year, p≤0.001). Twitter shows by far the highest activity among the AS subcategories (highly correlating with AS r=0.8, p≤0.001). The total number of twitter mentions increased by 2.8/year from 2015 to 2019, indicating that more recently published articles were more often picked up on twitter. Changes in R^2 in the regression model indicated that besides time since publication and AS, also the type of article influences citation count. For original research and editorials, AS may significantly add to the variability of the citation count, which was not the case for correspondences. The influence of AS on citation count of editorials added 16% to the 12% variability explained by publication time. Both factors showed similar ß-coefficients (months: ß: 0.76; ß: AS: 0.83). This effect was smaller in original articles (month: ß=0.74; AS: ß=0.11, Total R^2: 23.7%). AS significantly coincides with reaching the top 25% of citation counts according to time since publication. For the first year those articles with AS >15 showed a positive Likelihood Ratio (+LR; 95%CI) of 1.6 (1.4-1.9) to reach the top 25%, the second year AS>15: +LR: 1.9 (1.6-2.2), the third year AS>13: +LR 2.3 (1.9-2.7) and in the fourth year AS>12 +LR: 2.1 (1.7-2.7). This effect was again different between publication categories, with no effect of AS in correspondence articles. Figure 1 highlights that AS influences citations of editorials to a larger extent than of original articles, except within the first year of publication.

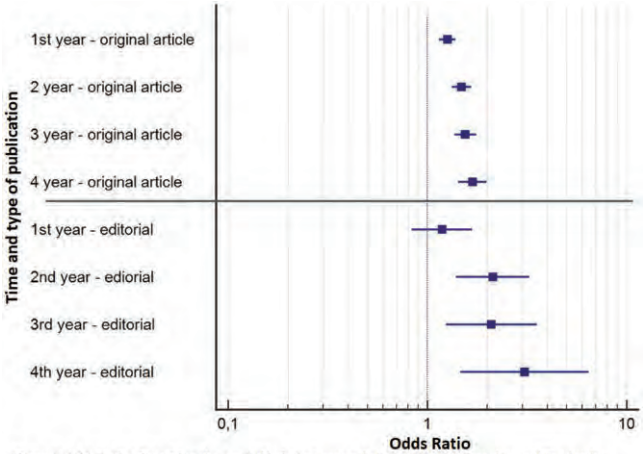


Figure 1: Odds Ratio of reaching the top 25% of cited papers in the respective year since publication by Altmetric score, separately shown for original and editorial/viewpoint articles.

Conclusion: We could show, that Altmetric scores are higher in more recent publications and seem to have an influence on the number of citations, particularly early citations in the first two years after publication. The early implementation of published articles in social media could help to increase overall citation.
Acknowledgments: We thank Lindsey Fountain from BMJ for providing citation and usage data.
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COVID-19 Pathophysiology leading to the drugs to be used

CO0001 MAVRILIMUMAB IMPROVES OUTCOMES IN SEVERE COVID-19 PNEUMONIA AND SYSTEMIC HYPER-INFLAMMATION

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Background: Patients with severe COVID-19 pneumonia and hyperinflammation face increased mortality. There is an urgent need for effective treatments to reduce the burden of the COVID-19 pandemic.
Objectives: Our protocol aimed at evaluating the potential improvement in clinical outcomes with mavrilimumab, an anti-Granulocyte/Macrophage Colony-Stimulating Factor Receptor alpha (GM-CSFRα) monoclonal antibody, in patients with COVID-19 pneumonia and systemic hyper-inflammation.
Methods: Single-center, open-label, single active arm intervention; Adult patients with severe COVID-19 pneumonia (as evaluated by CT scanning), hypoxia (PaO2:FiO2 ratio ≤ 300 mmHg), and systemic hyper-inflammation (increased C-reactive protein [CRP] ≥ 100 mg/mL and/or ferritin ≥ 900 µg/L, increased lactate dehydrogenase [LDH]) received a single intravenous dose of mavrilimumab added to standard of care; follow-up 28 days. Main outcomes measure was time to clinical improvement (reduction ≥ 2 categories on the 7-point WHO clinical status scale, 1=discharge, 7=death); others included time to discharge from hospital; % of pts achieving a clinical improvement; survival; mechanical-ventilation free survival; time to fever resolution; CRP; PaO2:FiO2 ratio.
Results: A mavrilimumab group (n=13 COVID-19 patients, non-mechanically ventilated, median age 57 [IQR, 52-58], males 12 [92%], febrile 11 [85%]; PaO_2:FiO_2 195.5[166.7–215.0]) was compared to a cohort of 26 contemporaneous patients with similar baseline characteristics. Death occurred in 0% (n=0/13) of mavrilimumab recipients and 27% (n=7/26) of comparison-group patients (log rank p=0.046) during the 28-day follow-up. 100% (n=13) of mavrilimumab recipients and 65% (n=17) of comparison-group patients achieved clinical improvement (p=0.018) at Day 28, with earlier improvement (median 8.0 [IQR, 5.0–11.0] days vs 18.5 [11.0–NE] days) (p<0.001) in mavrilimumab recipients. Fever had resolved in 91% (n=10/11 febrile patients) of mavrilimumab recipients by Day 14, compared to 61% (n=11/18 febrile) of patients in the comparison group (p=0.110); fever resolution was faster in mavrilimumab recipients versus controls (median 1.0 [IQR, 1.0–2.0] day vs 7.0 [3.0 - NE] days, respectively, p=0·009). Mavrilimumab was well tolerated in all patients.
Conclusion: Patients with severe COVID-19 pneumonia and systemic hyper-inflammation who received treatment with mavrilimumab had better clinical outcomes compared to patients receiving routine care. Mavrilimumab was well-tolerated. Randomized controlled trials are warranted to confirm our findings.
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Disclosure of Interests: Giacomo De Luca Speakers bureau: SOBI, Novartis, Celgene, Pfizer, MSD, Giulio Cavalli Speakers bureau: SOBI, Novartis, Pfizer, Corrado Campochiaro Speakers bureau: Novartis, Pfizer, Roche, GSK, SOBI, Emanuel Della Torre: None declared, Piera Angelillo: None declared, Alessandro Tomelleri: None declared, nicola boffini: None declared, Stefano Tentori: None declared, Francesca Mette: None declared, Patrizia Rovere-Querini: None declared, Annalisa Ruggeri: None declared, Teresa D'Aliberti: None declared, Paolo Scarpelllini: None declared, Giovanni Landoni: None declared, Francesco De Cobelli: None declared, John F. Paolini Shareholder of: Kiniksa, Employee of: Kiniksa, Alberto Zangrillo: None declared, Moreno Tresoldi: None declared, Bruce C. Trapnell Consultant of: Kiniksa, Fabio Ciceri: None declared, Lorenzo Dagna Grant/research support from: Abbvie, BMS, Celgene, Janssen, MSD, Mundipharma Pharmaceuticals, Novartis, Pfizer, Roche, SG, SOBI, Consultant of: Abbvie, Amgen, Biogen, BMS, Celltrion, Novartis, Pfizer, Roche, SG, and SOBI
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CO0002 LOSS OF SELF-TOLERANCE IN SARS-COV-2 INFECTION: IMMUNOLOGICAL ASSESSMENT OF A CONVALESCENT COHORT

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Background: Some infectious agents may act as inducers of autoimmune conditions[1]. Despite SARS-CoV-2 infection can induce autoimmune phenomena in infected people[2], individual risk factors or underlining mechanisms leading to loss of immunological tolerance are still unknown.
Objectives: To assess the rate of development of autoantibodies in convalescent SARS-CoV-2 patients and their relation on infection clinical course and disease parameters.
Methods: One-hundred and nine convalescent SARS-CoV-2 patients were studied and underwent multidisciplinary assessment in a Day Hospital clinical setting. For each patient, demographic, clinical and immunological data were collected and, at study entry, autoimmune profile [antinuclear antibodies (ANAs), antibodies reacting with extractable nuclear antigens (anti-ENA), antineutrophil cytoplasmic antibodies (ANCAs), Lupus anticoagulant (LA), anticardiolipin antibodies (aCL) IgM and IgG, anti-β2 glycoprotein I (anti-β2GPI) IgM and IgG] was assessed by Fluorescent immunoassay. Moreover, IL-6 plasma levels were assessed by ELISA (ELLA).
Results: After a median time from hospitalization for SARS-CoV-2 infection of 53.3 ± 0.9 days, 55(50.5%) SARS-CoV-2 convalescent patients showed the positivity (AB^{pos}) of at least one autoantibody. In particular, 31(28.4%) were positive for LA, 11(10.1%) for IgM-RF, 8(7.3%) for ANA and 6(5.5.%) for IgG-aCL whilst less than 2% showed other autoantibody positivities (IgM-aCL, IgG-anti-β2GPI, ENA, ACPA, c-ANCA, Scl70 and RNP). Analyzing the patient-related characteristics associated with the development of autoimmunity, convalescent male patients were more likely characterized by the development of antiphospholipid antibodies (aPL) (37.3%) than female (16.7%; p=0.02). Considering the disease-related characteristics, convalescent SARS-CoV-2 patients who experienced severe pneumonia (i.e., oxygen support need) during hospitalization, more likely received IL-6R-inhibitor administration (47.3%) and developed more than one autoantibody (87.5%) (aPL + another AB) than convalescent SARS-CoV-2 patients who did not need oxygen support [(12.5%; p=0.02) (OR95%IC: 9.5(1.4-109.1)] or IL-6R-inihibitor (1.9%; p<0.001). Finally, assessing cytokines plasma levels in convalescent SARS-CoV-2 patients stratified based on the development of autoantibodies we found that, despite a significant reduction of IL-6 plasma levels from hospitalization, convalescent SARS-CoV-2 patients who developed autoantibody positivity had higher IL-6 plasma levels (8.5 ± 2.5 pg/ml) than convalescent SARS-CoV-2 AB^{neg} patients (5.6 ± 1.5 pg/ml; p=0.07), mostly if considered autoantibodies other than aPL (15.4 ± 7.7 pg/ml)(p=0.01).
Conclusion: Loss of self-tolerance is a common phenomenon in the medium-term follow-up of SARS-CoV-2 convalescent patients whose occurrence is dependent by a severe disease course and by an aberrant host inflammatory response. Long-term follow-up will reveal AB persistency and their clinical impact.
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CO0005 C-C CHEMOKINE RECEPTOR TYPE 5 AND ITS LIGANDS CCL4, 8 AND 11 CAN LINK COVID-19, RHEUMATOID ARTHRITIS AND HYDROXYCHLOROQUINE

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Background: Coronavirus disease (COVID-19) caused by SARS-COV2 represents an unprecedented global public health concern with a particular burden on patients with chronic diseases and those on immune-modulating drugs. It is especially worrisome to patients with rheumatoid arthritis (RA) who are on immune suppression regimens[1]. On the other side, many reports showed and recommended the use of some Disease-Modifying Drugs commonly used to treat rheumatic diseases like hydroxychloroquine. However, the general understanding of COVID-19 characteristics in this population and the mechanism of action of these drugs in COVID-19 is still unknown[2].

Objectives: Explore publicly available transcriptomic dataset of patients infected with SARS-COV2 compared to uninfected to identify differentially expressed genes (DEGs) related to the immune system that might be pathogenic in RA synovium. Then explore the effect of Disease-Modifying Drugs on their local expression that might give hints about their possible mechanism of action.
Methods: RNAseq dataset (GSE147507) were retrieved using the Gene Expression Omnibus (GEO) and used to identify DEGs between infected and uninfected lung samples using BioJupies tools [3]. The DEGs were explored for common pathways using Metascape online tool (http://metascape.org) [10], as shown in figure (1). The chemokines genes were filtered out, and their common receptor (CR) was identified. The immune cells that express a higher level of the identified receptor were explored using DICE project tool (https://dice-database.org/). The expression of CR was searched in a microarray dataset (GSE77298) of synovial biopsies of RA and healthy controls. RNAseq dataset (GSE97165) of synovial biopsies taken from 19 early RA patients at baseline and after six months of Triple Disease-Modifying Anti-rheumatic drugs (tDMARD; methotrexate, sulfasalazine, and hydroxychloroquine) treatment.
Results: 84 DEGs were identified between uninfected and COVID-19 infected lung samples. These DEGs were enriched in pathways specific to (response to the virus, response to interferon, leukocyte activation, and chemotaxis). Interestingly, SARS-COV-2 infected lungs express more CCL4, CCL8, and CCL11; the three ligands shared the same receptor, which is CCR5. Top immune cells that express CCR5 were CD4 T memory T reg cells, Th17, Th1, and monocytes. CCR5 was significantly upregulated in RA compared to healthy controls synovium (p=0.04) and was dramatically downregulated after six months of tDMARD treatment (p=0.004), as shown in figure (2).
Conclusion: Using publicly available transcriptomic datasets properly highlighted the possible beneficiary effect of DMARDs in patients with COVID-19, which can block CCR5 rich immune cells recruitment.
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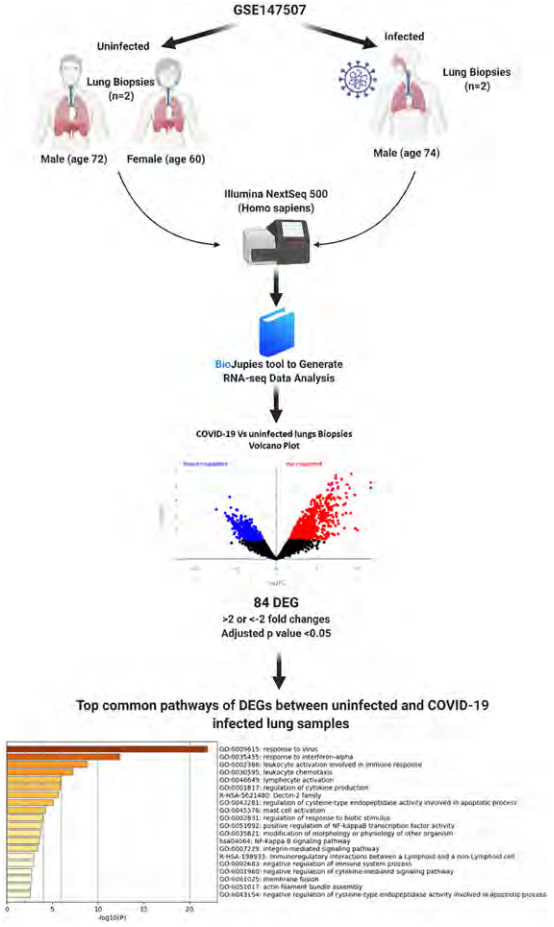


Figure 1. Flowchart of transcriptomic analysis

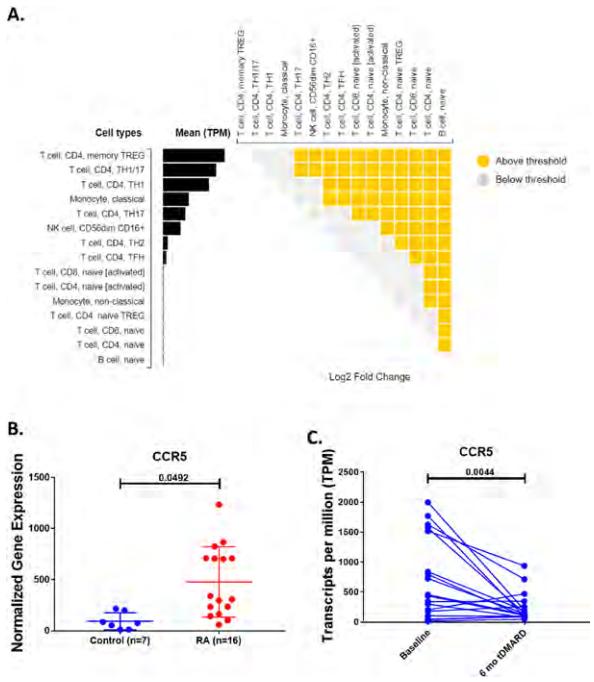


Figure 2. (A) Top immune cells that express CCR5 (B) CCR5 expression in synovial biopsies of RA and control (C) CCR5 expression at baseline and after 6 months of tDMARD treatment.

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Talk about the consequences of COVID-19 on RMDs

CO0003

TREATMENT WITH BIOLOGICAL THERAPIES AND RISK OF BEING ADMITTED TO THE HOSPITAL FOR COVID19 INFECTION

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Objectives: To analyze the risk of admission for COVID19 infection and outcome of patients treated with bDMARD or tsDMARD from our biologic therapy center, to compare with all patients admitted for COVID-19 infection in our hospital.
Methods: Records of the patients from our center admitted for COVID-19 infection between March 8 and May 8, 2020 were analyzed retrospectively. Age, gender, and outcome of all patients admitted for COVID19 infection to our hospital on the same dates were collected. Chi-square, Student's t and Man-Whitney U tests were used for comparisons when appropriate.
Results: 1,668 patients with inflammatory diseases treated with bDMARD or tsDMARD were included. Median age 53.0 years (range 17-91), 52.4% women. Diagnoses and DMARD distribution are shown in tables 1 and 2. 19/1668 (1.1%; 6.8 patient-years) were admitted for severe COVID19 infection. Mortality ratio: 4/19 (21.1%). Median age of the admitted patients was higher: 61.0y (SD 14.2) vs 53.0y (SD 15.0); p <0.009. Median age of deceased patients was also higher 69.5y (SD 20.3) vs 53.0y (SD 15.0); p: NS. Female gender had a worse prognosis trend: 52.4% of all group, 68.4% of those hospitalized, 75.0% of those who died. Females had a higher median age than men: 55.0y (SD 14.9) vs. 50.0y (SD 14.9); p <0.001.
When comparing patients treated with DMARD admitted for COVID19 infection with all patients hospitalized for the same reason (4,601patients), no differences were found neither in age (61.0y [SD 14.2] vs 58.3y [SD 18.1]; NS) nor gender (female: 68.4% vs 54.7%; NS). However, DMARD group seemed to have higher mortality: 4/19 (21.1%) vs 551/4601 (12.0%); p: NS, at a younger age: 69.5y (SD 20.3) vs 82.4 (SD 11.4); p: NS.

Rheumatoid arthritis patients were admitted more frequently: (9/392 (2.3%) vs 10/1276 (0.8%); p <0.025. And were older: median 62y (SD 13.5) vs 50.0y (SD 14.4); p <0.001.
Patients treated with anti-TNF suffered less admissions: 6/1055 (0.6%) vs 13/613 (2.1%); p<0.001 and were younger: median 51.0y (SD 15.0) vs 55.0y (SD 14.7); p <0.001. Anti-TNF were less used in patients with rheumatoid arthritis 188/392 (48.0%) vs 867/1276 (67.9%); p<0.001.

Table 1.

Disease	N (%)	Admitted	deaths
Rheumatoid arthritis	392 (23.5%)	9/392 (2.3%)	1
Spondylarthritis	277 (16.6%)	2/277 (0.7%)	1
Psoriatic arthritis	124 (7.4%)	1/124 (0.8%)	0
JIA	30 (1.8%)	0/30 (0.0%)	0
CTD	31 (1.9%)	1/31 (3.2%)	1
Vasculitis	20 (1.2%)	0/20 (0.0%)	0
IBD	582 (34.9%)	4/578 (0.7%)	1
Psoriasis	202 (12.1%)	2/202 (1.0%)	0
Others	10 (0.6%)	0/10 (0.0%)	0
TOTAL	1,668 (100%)	19/1668 (1.1%)	4/19 (21.1%)

JIA: Juvenile Idiopathic Arthritis; CTD: Connective Tissue Disease; IBD: Inflammatory Bowel Disease

Table 2.

Treatment	N (%)	Admitted	deaths
Anti-TNF	1055 (63.2%)	6/1055 (0.6%)	2
Anti-CD20	79 (4.7%)	3/79 (3.8%)	1
Anti-IL6	96 (5.8%)	3/96 (3.1%)	0
CTLA4-Ig	44 (2.6%)	3/44 (6.8%)	1
Anti-IL17	92 (5.5%)	2/92 (2,2%)	0
Anti-IL12/23	143 (8.6%)	1/143 (0.7%)	0
Anti-integrin	79 (4.7%)	0/79 (0.0%)	0
JAK inhibitor	34 (2.0%)	1/34 (2.9%)	0
PDE4 inhibitor	32 (1.9%)	0/32 (0.0%)	0
Anti-IL23	14 (0.8%)	0/14 (0.0%)	0
TOTAL	1,668 (100%)	19/1668 (1.1%)	4/19 (21.1%)

Conclusion: It seems reasonable that patients with inflammatory diseases treated with bDMARD or tsDMARD continue their treatment during the COVID19 epidemic. The different rates of hospitalization based on the diagnosis or DMARD may be due to comorbidity, confounding by indication and other bias. The study is not powerful enough to study these confounders.
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CO0004

OLDER AGE, CARDIOVASCULAR COMORBIDITY AND GLUCOCORTICOSTEROIDS ARE RISK FACTORS FOR COVID-19 HOSPITALISATION IN PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES: FIRST RESULTS OF THE GERMAN COVID-19-IRD REGISTRY

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Background: Patients with inflammatory rheumatic diseases (IRD) and infection with SARS-CoV-2 may be at risk to develop a severe course of COVID-19. To gather knowledge about SARS-CoV-2 infections in IRD patients, a national registry was established to elucidate IRD specific profiles of COVID-19.
Objectives: To identify risk factors for hospitalisation.
Methods: Patients from the German registry on SARS-CoV-2 infection in IRD were analysed. Patients are enrolled with a pre-existing IRD and a positive lab-result for a SARS-CoV-2 infection. The main outcome parameter was hospitalisation versus non-hospitalisation. Multivariable logistic regression was used to estimate odds ratios (OR) and 95% confidence intervals (CI). Covariates included in the model were age group, gender, key comorbidities (cardiovascular, lung diseases, chronic renal insufficiency), prior and/or current use of glucocorticosteroids (GC) or NSAIDs and remission.
Results: Until May 17th, 2020, data from 192 IRD patients with SARS-CoV-2 infection were reported (67 males; 124 females; 1 diverse). 64 patients were hospitalised, 21 patients were ventilated non-invasively/invasively and 15 patients died.
Baseline characteristics are shown in table 1, stratified into the patient groups non-hospitalisation, hospitalisation without ventilation, and hospitalisation with ventilation. Non-hospitalised patients were younger, had less comorbidities and were less often treated with GC. In the group of hospitalised patients compared to non-hospitalised patients more patients were male (42% vs 32% male) with an even higher proportion in the ventilated patient group (57% male).
In the multivariable logistic regression model, age>65 years (OR 5.1; 95%CI 2.3-11.4), cardiovascular comorbidity (OR 2.3; 95%CI 1.0-5.0), and prior and/or current treatment with GC (OR 2.6; 95%CI 1.2-5.4) were independently associated with hospitalisation.

Parameter, N (%)	Non-hospitalisation 128 (66.7)	Hosp. without ventilation 42 (22.4)	Hosp. with ventilation 21 (10.9)
Age [years], mean (SD)	53.8 (13.4)	65.2 (15.5)	69.7 (9.9)
Female	87 (68.5)	28 (65.1)	9 (42.9)
RA	60 (46.9)	24 (55.8)	12 (57.1)
Psoriasis	23 (18)	3 (7)	3 (14.3)
Axial spondyloarthritis	14 (10.9)	2 (4.7)	0
Lupus	7 (5.5)	1 (2.3)	0
Remission of IRD	67 (52.3)	23 (53.5)	4 (19)
Number of comorbidities, mean (SD)	1 (1.2)	1.8 (1.4)	2.4 (1.5)
Cardiovascular disease	42 (32.8)	25 (58.1)	16 (76.2)
Pulmonary disease	16 (12.5)	8 (18.6)	8 (38.1)
Chronic renal insufficiency	5 (3.9)	7 (16.3)	4 (19)
Cancer	2 (1.6)	4 (9.3)	2 (9.5)
Obesity (BMI>30)	23 (18)	5 (11.6)	3 (14.3)
Diabetes	3 (2.3)	7 (16.3)	4 (19)
Other comorbidities	20 (15.6)	9 (20.9)	6 (28.6)
csDMARD (without HCQ)	59 (46.1)	25 (58.1)	8 (38.1)
HCQ	13 (10.2)	1 (2.3)	2 (9.5)
bDMARD	48 (37.5)	15 (34.9)	8 (38.1)
tsDMARD	5 (3.9)	1 (2.3)	1 (4.8)
Glucocorticosteroids	47 (37)	29 (67.4)	13 (61.9)
NSAIDs	21 (16.4)	5 (11.6)	1 (4.8)

Conclusion: As has been described for COVID-19 in general, also in IRD male gender may be associated with a more severe course of the infection as the descriptive analysis of data shows. Risk factors for SARS-CoV-2 infection-dependent hospitalisation in IRD patients include age (>65 years), cardiovascular comorbidities, and prior and/or current treatment with GC.
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Treating RMD patients in the context of the COVID-19 pandemic - between overburdening and lockdown

C00006

PSYCHOLOGICAL IMPACT OF COVID 19 PANDEMIC ON PATIENTS WITH RHEUMATOLOGICAL DISORDERS - A WEB BASED CROSS-SECTIONAL MULTICENTRE SURVEY

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Background: The COVID-19 pandemic has resulted in uncertainty and negative psychological outcomes for patients with autoimmune rheumatic diseases for several reasons.[1] The anxiety is due to "underlying conditions" that are expected to increase the risk of infection and / or severe complications. Patients with rheumatological disorders fall into this group as they are believed to be immunosuppressed due to disease or the treatment. It is essential to understand the level of anxiety among the rheumatic disease patients at the current situation of COVID-19.

Objectives: To study difference in Anxiety score (Mean/Avg Score) among following groups-underlying rheumatic disease, age, gender, marital status, educational status, employment status, medications, those who were on steroids/not, those who are Biologicals / Not.

Methods: A web-based cross-sectional multi-centre survey was done across 5 rheumatology centres in India. The study duration was between 9th May and 16th May 2020.The questionnaire included consent, demographic details, medication history, opinion about tele rheumatology services and anxiety score measured by Beck Anxiety Inventory (BAI)[2].

Results: The survey was sent to 2987 patients, there were 933 responses and 581 were complete (Male =175). Complete responses were considered for data analysis. Most respondents were less than 50 years of age (70.6%). Rheumatoid arthritis (RA) was the most frequent (50.6%) diagnosis followed by other conditions. Most of the patients (43%) were on combination DMARD therapy, 12.7% of patients were on biological drugs and 23.9% of patients were on glucocorticoids. Statistically significant higher anxiety scores were observed in females, patients suffering from fibromyalgia, patients on glucocorticoids and biological agents. There was no difference in the anxiety scores with regard to age, educational status, and employment status.Difficulty in meeting rheumatologists and getting medications was expressed by 327 (56.2%) and 73 (29.7%) respondents respectively. Majority of respondents (86.6 %) agreed/strongly agreed regarding use of telemedicine to access health care during the crisis.

Conclusion: The findings of the study revealed that anxiety is a major concern in patients with autoimmune rheumatic diseases. Fibromyalgia patients and those who were on glucocorticoids and biological drugs were found to have more anxiety levels compared to other groups of patients. In such periods of public health crises, telemedicine is a great tool for patients to access healthcare without fear of going to hospital. There is a need to intensify the awareness and address the mental health issues of rheumatology patients during this COVID-19 pandemic.

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Poster Presentations

THURSDAY, 04 JUNE 2020

Genomics, genetic basis of disease and functional genomics

THU0001 GENOME-WIDE ASSOCIATION STUDY ON JOINT EROSIONS IN RHEUMATOID ARTHRITIS SUPPORTS DIFFERENTIAL PATHOLOGICAL MECHANISMS ACCORDING TO ANTI-CCP STATUS

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Background: Joint damage is the pathological hallmark of rheumatoid arthritis (RA). To identify the genetic variation associated with a higher level of erosions has proven elusive.

Objectives: The objective of the present study was to perform a genome-wide association study on joint damage in a cohort of RA patients of the Spanish population. Our aims were to provide independent validation of previously reported variants and to identify new candidate risk loci. A stratified analysis was performed based on positivity to ACPA status.

Methods: A total of 1,135 patients diagnosed with RA using the ACR-EULAR criteria recruited by the IMID Consortium were genotyped using a 550,000 single-nucleotide polymorphism array. Additional SNPs were imputed using the 1KG genome data. Joint damage was performed using the S-score, a simplified radiographic erosion score that has a high correlation with the Sharp-van der Hejde score (1). Association testing of SNPs with joint damage was performed via linear regression with the addition of the years of evolution as covariate. The two main components of genetic variation were also added to adjust for potential population stratification. A total of 50 SNPs representing previously reported loci associated with joint damage were selected. Genetic association was also performed at the pathway level using Pascal.

Results: 45 out of 50 SNPs representing 31 previously reported loci for joint damage could be satisfactorily imputed. Association testing of the whole patient cohort replicated the association with *IL2RA* and *TRAF1*. Of relevance, after stratifying for anti-CCP five new loci were replicated: *KIF5A* and *SOST* in ACPA-positive RA and *CD40, DKK1* and *TNF* in ACPA-negative RA. *IL2RA* was only significant in the ACPA-positive group and *TRAF1* was not significant in either strata. GWAS on the ACPA-positive cohort and on the ACPA-negative group identified n=7 and n=18 loci with P-values < 1x10-5, respectively. From these, however, only 1 SNP showed nominal significant association in the other patient group. Based on this evidence, we performed a pathway-based analysis to understand the biological mechanisms underlying this difference. Pathway analysis showed 52 biological processes associated with joint damage in ACPA-negative RA and 32 pathways in the ACPA-positive group, with only two shared biological processes between the two groups. Fc Gamma receptor mediated phagocytosis was the topmost biological process associated with erosions specifically in ACPA-negative RA and Signalling by Fibroblast Growth Factor mutants was the top process specific for ACPA-positive patients.

Conclusion: The results from our study provide suggestive evidence that the genetic basis for joint damage is different according to the presence of ACPA. Replication of the new candidate loci in an independent patient cohort is underway.

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THU0002 SOLVING THE COMPLEX MHC ASSOCIATIONS IN SLE IDENTIFIES SEX-RELATED GENE EFFECTS

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Background: Genome-wide association analyses reveal that the Major Histocompatibility Complex (MHC) is the site of the strongest association signals in SLE and Sjögren's syndrome. This associations in lupus and Sjögren's syndrome are linked to *HLA* alleles: HLA-DRB1*03:01 and HLA-DRB1*15:01 (in Europeans). The DRB1*03:01 allele resides on an extended MHC haplotype which includes loss of the complement C4A gene. Whether C4 makes a genetic contribution to SLE/Sjogren's risk has been a long standing issue of contention[1]. In comparison, it has been shown that elevated copy number of C4 is a genetic risk factor for schizophrenia[2].

Objectives: To define the causal MHC genes in SLE/Sjogren's accommodating both structural and highly polymorphic variation.

Methods: Use NG sequencing data from across the MHC to generate a panel of variants that inform class III structural variation involving the candidate genes coding complement *C4A* and *C4B* as described[2]. To further improve the resolution of the association using transancestral mapping approach in SLE: examining cohorts of European ancestry (from ImmunoChip) and data from the MHC region of an African-American GWAS in SLE.

Results: Comparing European and African data, we have shown that the association signals in SLE can be best explained by signals arising from 1) copy number variation of the complement component 4 (*C4*) genes in the MHC locus (Fig. 1) and 2) by a shared region in the class II region on the HLA-DRB1*15:01 (in Europeans) and HLA-DRB1*15:03 (in Africans) that likely operates to elevated HLA class II gene expression (Fig. 2). The *C4* locus generates a 7-fold variation in risk for lupus (95% CI: 5.88-8.61; $p<10^{-117}$ in total) and 16-fold variation in risk for Sjögren's syndrome (95% CI: 8.59-30.89; $p<10^{-23}$ in total), with *C4A*

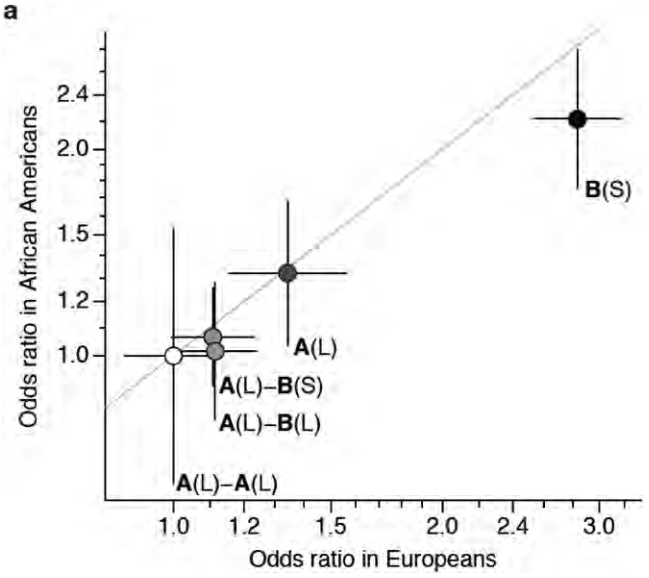


Figure 1. Loss of *C4* is risk in African and European ancestry cohorts. A = C4A, B = C4B, A-B = C4A + C4B(L) = Long form (with HERV), (S) = short form

protecting more strongly than *C4B* in both illnesses. In schizophrenia, elevated C4 copy number elevates disease risk, whereas in SLE and Sjögren's lower copy numbers of *C4* genes correlate with higher disease risk. In all three illnesses, *C4* alleles acted more strongly in men than in women: common combinations of *C4A* and *C4B* generated 14-fold variation in risk for lupus and 31-fold variation in risk for Sjögren's syndrome in men (versus 6-fold and 15-fold among women respectively) and affected schizophrenia risk about twice as strongly in men as in women. At a protein level, both C4 and its effector (C3) were present at greater levels in men than women in cerebrospinal fluid ($p<10^{-5}$ for both C4 and C3) and plasma among adults ages 20-50, corresponding to the ages of differential disease vulnerability. Sex differences in complement protein levels may help explain the larger effects of *C4* alleles in men, women's greater risk of SLE and Sjogren's, and men's greater vulnerability in schizophrenia.

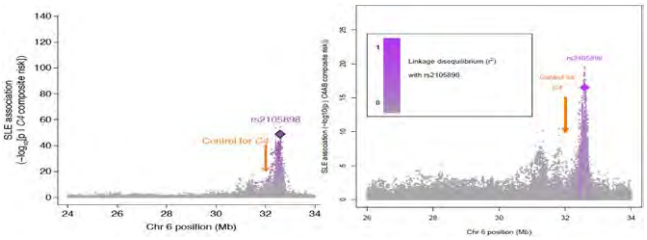


Figure 2. Common class II association after removing C4 signal

Conclusion: These results nominate the complement system as a source of sexual dimorphism in vulnerability to diverse illnesses.

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THU0003 ALTERED DNA METHYLATION AND DIFFERENTIAL EXPRESSION OF GENES INFLUENCING CARDIOVASCULAR RISK AND IMMUNITY IN CD4+ T CELLS FROM SUBJECTS WITH PSORIATIC ARTHRITIS.

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Background: Cardiovascular risk factors are increased in Psoriatic Arthritis (PsA). In fact, around 60% out of PsA patients display insulin resistance (IR), a hallmark of metabolic syndrome, which might significantly contribute to the cardiovascular disease. Latest studies suggested that inflammatory and metabolic disorders may be under epigenetic control, including DNA methylation. DNA methylation is an unexplored area in the field of PsA.

Objectives: To study the alterations in the genome-wide DNA methylation profile of $CD4^+$T cells from PsA patients and its relationship with its pathology and the risk of cardiovascular comorbidity.

Methods: Twenty healthy controls (HC) and 20 PsA patients were included in the study. PsA patients were classified into insulin resistant and non-insulin resistant according to HOMA-IR index. $CD4^+$ T lymphocytes were isolated from peripheral blood by positive immunomagnetic selection. The Illumina Infinium MethylationEPIC Beadchip was used to obtain DNA methylation profiles across approximately 850,000 CpGs (TSS1500, TSS200, 5UTR, 3UTR, first exon, gene body). Beta values (β) estimating methylation levels were obtained at each CpG site, and differentially methylated genes (DMG) between PsA and HC were identified. Functional classification of these genes was carried out through gene ontology analysis (PANTHER database). Gene expression analysis of the selected genes was also evaluated by RT-PCR. Vascular parameters including carotid intima-media thickness (cIMT) and endothelial function was analyzed by ecodoppler and periflux respectively.

Results: The genome-wide methylation analysis identified 112 DMGs including 41 hypomethylated and 71 hypermethylated. These differentially methylated genes were enriched with several signaling pathways and disease categories including immune response, metabolic processes, oxidative stress, vascular and inflammatory pathways. The altered gene expression of selected genes with altered methylation levels in PsA was also validated. Correlation and association analysis of these DMGs with clinical and analytical variables, cardiovascular risk factors and endothelial microvascular function revealed that the degree of methylation of these genes was significantly associated with cIMT (IGF1R, NDRG3, SMYD3, HLA-DRB1, WDR70), arterial pressure (METT5D1, NRDG3, ADAM17, SMYD3, WNK1, CBX1), insulin resistance (AKAP13, SEMA6D, PLCB1), altered lipid profile and atherogenic index (MYBL1, METT5D1, MAN2A1, SLC1A7, SEMA6D, PLCB1, TLK1, SDK1, CBX1), inflammation (MYBL1, NDUFA5, METT5D1, SEMA6D, PLCB1, TLK1), and endothelial dysfunction (ADAMST10, GPCPD1, CCDC88A). In addition, this analysis also identified 435 DMGs including 280 hypomethylated and 155 hypermethylated in $CD4^+$ T cells from IR-PsA vs non IR-PsA patients. Between these two groups of PsA patients, CHUK, SERINC1, RUNX1, TTYH2, TXNDC11, FAF1, BICD1, SCD5, PDE5A, FAS, NFIA and GRP75 displayed the most significantly altered methylation, suggesting the role of these genes in the metabolic complications associated with PsA.

Conclusion: These findings help our understanding of the pathogenesis of PsA and advance epigenetic studies in regards to this disease and the cardiometabolic comorbidities associated. Funded by ISCIII (PI17/01316 and RIER RD16/0012/0015) co-funded with FEDER.

Disclosure of Interests: Iván Arias de la Rosa: None declared, María Dolores López Montilla Speakers bureau: Celgene, Javier Rodríguez: None declared, Esteban Ballester: None declared, Carmen Torres-Granados: None declared, Carlos Perez-Sanchez: None declared, Maria del Carmen Abalos-Aguilera: None declared, Gómez García Ignacio: None declared, Desiree Ruiz: None declared, Alejandra M. Patiño-Trives: None declared, María Luque-Tévar: None declared, Eduardo Collantes-Estévez Grant/research support from: ROCHE and Pfizer., Speakers bureau: ROCHE, Lilly, Bristol and Celgene., Chary Lopez-Pedrera Grant/research support from: ROCHE and Pfizer., Alejandro Escudero Contreras Grant/research support from: ROCHE and Pfizer, Speakers bureau: ROCHE, Lilly, Bristol and Celgene., Nuria Barbarroja Puerto Grant/research support from: ROCHE and Pfizer., Speakers bureau: ROCHE and Celgene.

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THU0004 GENOME-WIDE DNA METHYLATION PROFILING IN MONOCYTES FROM PRIMARY ANTIPHOSPHOLIPID SYNDROME PATIENTS IDENTIFIES AN ABERRANT METHYLATION SIGNATURE ASSOCIATED WITH THEIR ATHEROTHROMBOTIC PHENOTYPE

C. Perez-Sanchez[1], A. M. Patiño-Trives[1], M. A. Aguirre[1], P. S. Laura[1], M. Luque-Tévar[1], I. Arias de la Rosa[1], C. Torres-Granados[1], M. D. C. Abalos-Aguilera[1], P. Seguí Azpilcueta[1], J. Rodríguez[2], E. Ballester[2], N. Barbarroja Puerto[1], E. Collantes Estevez[1], C. Lopez-Pedrera[1]. [1]*IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba, Spain*; [2]*Epigenetics and Immune Disease Group, Josep Carreras Research Institute (IJC), Barcelona, Spain*

Background: Recent studies underlined the crucial role of DNA methylation in several autoimmune diseases by altering gene expression profiles, thus influencing disease severity. Yet, aberrant methylation patterns in monocytes, key players in the pathogenesis of APS patients, has not been evaluated.

Objectives: To analyze the genome-wide DNA methylation profile of monocytes from APS patients and its relationship with the cardiovascular (CV) pathology. 2. To evaluate the role of antiphospholipid antibodies (aPL) in the regulation of this process.

Methods: Thirty-three APS patients and 15 healthy donors (HD) were included in the study. Monocytes were isolated from peripheral blood by positive immunomagnetic selection. The Illumina Infinium Methylation EPIC Beadchip was used to obtain DNA methylation profiles across approximately 850,000 CpGs (TSS1500, TSS200, 5UTR, 3UTR, first exon, intergenic, gene body). Beta values (β) estimating methylation levels were obtained at each CpG site, and differentially methylated genes (DMG) between APS and HD were identified. Functional classification of that genes was carried out by gene ontology analysis (PANTHER database). Gene expression of selected DMG genes was evaluated by RT-PCR. CV-risk parameters, including carotid intima-media thickness (CIMT) and microvascular endothelial function were further assessed, and correlation/association studies were developed with clinical and analytical variables. The effects of aPLs were also evaluated by *in vitro* studies.

Results: Genome-wide DNA methylation analysis identified 813 DMG, including 279 hypomethylated and 534 hypermethylated. Functional classification of these genes revealed signatures associated with biological processes and pathways related to their clinical profile, including immune response, adhesion, oxidative stress and vascular signaling. Correlation and association studies showed that the methylation levels of genes related to immune response were associated with the CV-risk score, aGAPSS (CCR2, TXLNB, GLIPR), type of thrombosis (SIGLEC11, COLEC11, LRRC16A, AHSA1, TRIL) and aPL titers (CLEC4G, RGS4, HLA-DPA1, GBP6, RAET1E, HLA-G, HLA-DPA1, HLA-H, TXLNB). Besides, methylation levels of DMG related to vascular signaling and adhesion processes were associated with the presence of thrombotic recurrences (VEGFA, MAPK14, ITGA8, EPCAM, PCDHA6, DLG1) as well as with traditional CV-risk factor such as hypertension and dyslipidemia (ITGA11, DSCAM, CLEC4F, CDH4, LTBP2, PCDHB14). In addition, methylation levels of DMG genes related to oxidative stress (GP2, PGD, ADH1) were associated with microvascular endothelial dysfunction. An altered mRNA expression of some of those genes with aberrant methylation and related to increased CV-risk and thrombotic recurrences in APS was also identified. Both, abnormal methylation and transcription levels of several genes were further associated with a pathological increase of the CIMT. Finally, in vitro studies supported the role of aPLs as key players in the altered methylation and transcriptomic profiles of APS patients.

Conclusion: APS patients showed an impaired methylation profile in monocytes of genes associated with clinical features of the disease, including aPL titers, CV risk, thrombotic recurrences, endothelial dysfunction and early atherosclerosis. These results offered a map to the monocytes methylome and shed light on the pathophysiology of APS, paving the way for the development of new, more effective biomarkers and therapeutics.

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THU0005 VARIABILITY OF DNA METHYLATION IS A DRIVER OF LYMPHOCYTE DYSREGULATION IN EARLY RHEUMATOID ARTHRITIS.

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Background: DNA methylation patterns differ between leukocyte subsets and mediate the impact of environmental exposures on the molecular and functional phenotype of immune cells. Besides differences in mean methylation of CpG positions amongst patients with immune mediated diseases, recent evidence indicates variability of site-specific DNA methylation also contributes to pathogenesis[1,2].

Objectives: To seek evidence of altered DNA methylation patterns in RA, controlling for systemic inflammation and immunotherapy use.

Methods: Patients with confirmed clinical diagnoses were enrolled from the Northeast Early Arthritis Cohort (NEAC). $CD4^+$ and $CD19^+$ lymphocytes were isolated from fresh blood by positive selection prior to therapeutic immune modulation. Methylation was quantified in cell subset-specific DNA (Infinium MethylationEPIC BeadChip, Illumina)[3]. Differentially methylated positions and regions (DMPs, DMRs) between RA and non-RA patients were identified (linear modelling, filtering on 5% pairwise difference in mean DNA methylation, and DMRcate package). Next, to identify instances where methylation variance differed between comparator groups, Bartlett's test was performed using the iEVORA package, which accounts for outlier values[4]. Findings were controlled for technical confounders and subject to multiple test correction (FDR). A validated hypergeometric test was used to annotate enriched pathways.

Results: After sample- and probe-level quality control, CD4+ and B lymphocyte specific data were respectively available for 45 and 49 RA patients, and 64 and 81 disease controls matched for systemic inflammation (CRP, ESR). No DMPs were identified in either cell type at FDR < 0.05 and $\Delta\beta \geq 0.05$. Only following relaxation of multiple test correction was it possible to identify DMRs in either cell type, most notably encapsulating 10 CpGs relatively hypomethylated at the promoter of the endosome protein-encoding *RUFY1* gene in CD4+ lymphocytes of RA patients ($\Delta\beta = 0.076$). By contrast, striking evidence for differential variation in DNA methylation was observed at 291 and 601 CpGs of CD4+ and B lymphocytes, respectively (exemplars depicted in Figure 1). Only 15 of these differentially variable positions (DVPs) were common to both cell types. Pathway analysis highlighted potential functional consequences of DVP associations; for example, RA-specific hypervariability implicates prostaglandinsignalling in CD4+ lymphocytes.

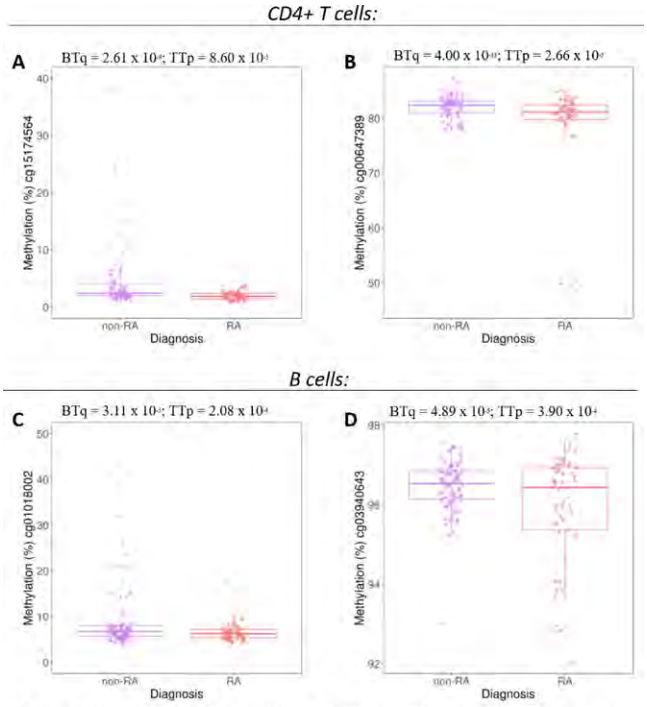


***Figure 1**. Plots are shown for CpGs in CD4+ T cells that were found to be either (**A**) hypo-variable or (**B**) hyper-variable in rheumatoid arthritis patients, with equivalent B cell plots again depicting (**C**) rheumatoid arthritis hypo-variable and (**D**) hyper-variable positions. BTq = Bartlett's q-value, a false discovery rate adjusted measure of group differences in DNA methylation variance; TTp = T-test p-value, applied to test for differences between the group means of any positions found to exhibit differential variance between cases and controls in the Bartlett's test (q < 0.001).*

Conclusion: We highlight a role for altered variability in DNA methylation during the molecular pathogenesis of RA, and emphasise the importance of its study in relevant cell subsets.

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THU0006 ASSOCIATION BETWEEN ALTERED MICRORNA EXPRESSION AND ARTERIAL WALL REMODELING IN GIANT CELL ARTERITIS

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Background: Immunopathology of giant cell arteritis (GCA) results from dysregulated interactions between arterial wall-resident non-immune cells, e.g. vascular smooth muscle cells (VSMCs), and components of the immune system [1]. In spite of several efforts at identifying microRNAs (miRNAs) implicated in the pathogenesis of GCA, the overall information on miRNA involvement in GCA and its related arterial fibro-sclerotic alterations remains scarce.
Objectives: To analyze miRNA expression and identify target genes of dysregulated miRNAs in temporal arteries from GCA patients, and to determine their association with GCA-associated arterial wall remodeling.
Methods: The study included formalin-fixed, paraffin-embedded temporal artery biopsies (TABs) from 71 clinically diagnosed treatment-naïve patients fulfilling the ACR 1990 classification criteria, and 22 non-GCA subjects (control group). Of GCA patients, 54 histologically positive and 17 histologically negative TABs were included. miRNA expression profiling was performed with quantitative real-time PCR (qPCR)-based miRNA PCR panels and qPCR. The miRDB database and STRING protein-protein network analysis were used for identification of miRNA gene targets and their pathway enrichment analysis, respectively.
Results: Of 356 detected miRNAs, we determined significant under-expression of 78 and significant over-expression of 22 miRNAs (≥ 2-fold; $p < 0.05$) in TAB-positive GCA arteries compared to non-GCA controls, pointing to a strong dysregulation of miRNA expression in inflamed GCA arteries. Several dysregulated miRNAs targeted genes involved in the ubiquitin-proteasome system and the RNA silencing complex, suggesting a novel role of these pathways in GCA. qPCR validation confirmed a 1.9–14.2-fold ($p < 0.001$) over-expression of "pro-synthetic" (miR-21-3p/-21-5p/-146a-5p/-146b-5p/-424-5p) and 3.4–9.4-fold ($p < 0.001$) under-expression of "pro-contractile" (miR-23b-3p/-125a-5p/-143-3p/-143-5p/-145-3p/-145-5p/-195-5p/-365a-3p) VSMC phenotype-associated regulatory miRNAs in TAB-positive GCA arteries. These miRNAs targeted gene pathways involved in the arterial remodeling and regulation of the immune system, and their expression significantly correlated with the extent of intimal hyperplasia in TABs from GCA patients ($p \leq 0.015$). Additionally, the expression of miR-21-3p/-21-5p/-146a-5p/-146b-5p/-365a-3p differentiated TAB-negative GCA arteries from non-GCA temporal arteries, making these miRNAs potential biomarkers of GCA.
Conclusion: Our study demonstrated an extensive dysregulation of arterial miRNA networks in GCA, favoring the pathogenic switch in the VSMC phenotype and associated intimal hyperplasia. We identified several miRNAs, which could represent potential novel GCA biomarkers. Furthermore, our results imply that the ubiquitin-proteasome system and the RNA silencing complex are targets of dysregulated arterial miRNA networks in GCA lesions, providing new insight into the complexity of GCA pathogenesis.
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THU0007 INDIVIDUALIZED PATHWAY ANALYSIS FROM WHOLE BLOOD TRANSCRIPTOMIC IN SSC PATIENTS DEMONSTRATES UNIQUE CORRELATIONS WITH DISEASE SEVERITY

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Background: Genome-wide gene expression profiles and pathways analysis may help to discover deregulated processes underlying the pathogenesis of complex diseases or their phenotypic expression. Little or nothing is currently known about pathways associated with disease severity and damage in SSc.
Objectives: To perform a whole blood transcriptome analysis and to characterize the individualized functional pathways associated with disease severity scores in SSc patients via a discovery and replication strategy.
Methods: Whole blood samples were collected in RNA stabilizers from a discovery and a replication cohort of 67 and 34 patients, respectively. RNAseq data were generated by Illumina sequencing in two independent experiments pathways analysis was conducted according to the Functional Analysis of Individual Microarray Expression (FAIME) protocol (1). FAIME scores from Reactome pathways were correlated with the Scleroderma Clinical Trial Consortium Damage Index (SCTC-DI) total scores or with each of its two components (mortality and morbidity) as calculated from regression coefficient previously published (2). A non-parametric partial correlation analysis correcting the results for the use of steroids, immunosuppressants and disease duration was performed. Results independently associated with damage in both cohorts at the 0.1 level after 1000-fold permutation-testing were considered as significant and replicated.
Results: A total of 1116 pathways were analyzed. None of them was associated in both cohorts with the total SCTC-DI; similarly, no association was found with the SCTC mortality component. On the contrary, 26 pathways showed an independent and replicated association with the SCTC morbidity component, including platelet degranulation, the transcriptional activity of SMAD2/SMAD3, Toll Like Receptor 2 (TLR2) cascade and related intracellular signaling events involving MyD88, IRAK and NF-kB, and the deregulation of selected transcription factors (TFAP2, E2F6).
Conclusion: Selected molecular events involving the innate immune system, signaling and platelet metabolism are associated with the morbidity component of the SCTC-DI in SSc patients, reflecting an irreversible loss of function in several organs and apparatus. The sensitivity of these associations to individual change in accrual damage is to be determined.
References:
[1] PMID: 22291585; (2) PMID: 30928903
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THU0008 DEVELOPMENT OF A NOVEL TRANSLATIONAL IN SILICO INDICATION DISCOVERY FRAMEWORK: EXEMPLIFIED BY THE CLINICAL COMPOUND CENERIMOD

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Background: To explore the full therapeutic spectrum of a drug it is crucial to consider its potential effectiveness in all diseases. Serendipitous clinical observations have often shown that approved drugs and those in development to be efficacious in indications different to those originally tested for. Traditional approaches to match a drug candidate with possible indications are mostly based on matching drug mechanistic knowledge with disease pathophysiology. Proof-of-concept trials or elaborate pre-clinical studies in animal models do not allow for a broad assessment due to high costs and slow progress. Gene expression changes in patients or animal models represent a good proxy to comprehensively assess both disease and drug effects. Furthermore, this data type can be integrated with a plethora of publicly available data.
Objectives: Generation of a novel in silico framework to support the selection and expansion of potential indications which associate with a compound or approved drug. The framework was exemplified by the clinical compound cenerimod, a potent, selective, and orally active sphingosine-1-phosphate receptor 1 modulator (Piali et al., 2017).
Methods: A total of ~13'000 public patient gene expression datasets from ~140 diseases were evaluated against cenerimod gene expression data generated in mouse disease models. To improve comparability of studies across platforms and species, computer algorithms (neural networks) were trained and employed to reduce noise within the data sets and improve signal. The predicted response to cenerimod for individual patients was contrasted against clinical patient characteristics.
Results: The neural network algorithm efficiently reduced experimental noise and improved sensitivity in the gene expression data. The results predicted cenerimod to be efficacious in several auto-immune diseases foremost SLE. Additionally, focused analysis on individual patients rather than disease cohorts revealed potential determinants predictive of maximal clinical response, with the highest predicted clinical response for cenerimod in patients with severe inflammatory endotype and/or high SLE Disease Activity Index (SLEDAI).
Conclusion: Combining preclinical compound data with the wealth of public disease gene expression data, provides great potential to support indication

selection. The novel in silico framework identified SLE as a prime potential indication for cenerimod and supported the cenerimod phase 2b clinical trial in patients with SLE (CARE study, NCT03742037).

References:

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Disclosure of Interests: Dominik Hartl Shareholder of: Idorsia shares, Employee of: Idorsia employee, Marcel Keller Shareholder of: Idorsia options/shares, Employee of: Idorsia employee, Axel Klenk Shareholder of: Idorsia option/shares, Employee of: Idorsia employee, Mark Murphy Shareholder of: Idorsia shares and stock options, Employee of: Idorsia employee, Marianne Martinic Shareholder of: Idorsia options/shares, Employee of: Idorsia employee, Gabin Pierlot Shareholder of: Idorsia options/shares, Employee of: Idorsia employee, Peter Groenen Shareholder of: Idorsia options/shares, Employee of: Idorsia employee, Daniel Strasser Shareholder of: Idorsia options/shares, Employee of: Idorsia employee

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THU0009 SYSTEMIC DEREGULATION OF LONG NON-CODING RNAS IN PATIENTS WITH SYSTEMIC SCLEROSIS AND THEIR ASSOCIATION WITH REGULATORS OF FIBROSIS.

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Background: Microvascular dysfunction is one of the major clinical challenges in systemic sclerosis (SSc) and mesenchymal transformation of the major event for micovascular dysfunction. Recent studies have shown epigenetic regulation of long non coding RNAs (lncRs) in different disease pathophysiology.

Objectives: To study the differential expressions of lncRs in patients with SSc and to study their associations with regulatory molecules of fibrosis

Methods: Peripheral Blood were collected from 15 diffused cutaneous SSc patients (dSSc) [ACR, 2013] and 10 age-sexes matched healthy controls. RNA was isolated from the peripheral blood & cDNAs were prepared and the Relative mRNA expressions were measured with respect to an endogenous control gene by real-time PCR. Protein expressions were measured by ELISA.

Results: Increased expression of MEG3, MALAT1and NEAT1 (3.5, 3, 4fold respectively) has been found in SSc patients with respect to healthy individuals and they are mutually correlated (MEG3 and NEAT1: *r=0.9, p<0.0001;* MALAT1and NEAT1: *r=0.7, p<0.0001;* MEG3 and MALAT1 *r=0.7, p<0.0001*). The expression of NEAT1 is significantly higher (*p= 0.0009*) in case patients with disease duration (DD) >5 years compare to the patients with DD≤5 years. No significant difference was found in the expression of MEG3 and-MALAT1 between these two subpopulations. Modified Rodnan's skin score (mRDss): the clinical parameter of measuring fibrosis, was significantly up regulated (*p=0.004*) in patients with long disease duration (>5 years) and also have a positive correlation with DD(*r=0.2,p=0.2*) and the regulatory RNAs: MEG3 (*r=0.4,p=0.003*), MALAT1 (*r=0.2, p=0.2*), and NEAT1(*r=0.3, p=0.009*).

The master regulator of fibrosis TGFβ which is significantly up regulated at both transcriptional (p<0.0001) and translational (*p=0.0009*) level has significant positive correlation with MEG3 (*r=0.3, p=0.02*), MALAT1 (*r=0.5, p=0.0005*), and NEAT1(*r=0.3p=0.006*).MEG3, MALAT1and NEAT1 also have significant high correlation (*r=0.7,* p<0.0001*; r=0.6* p<0.0001 and *r=0.7*p<0.0001 respectively) with αSMA: the marker of fibroblast activation and the collagen-I (*r=0.3,* p=0.03; *r=0.3,* p=0.03 and *r=0.3* p=0.03 respectively).

In multivariate analysisMEG3 and NEAT1 together could explain 37.5% variability of fibrotic marker and NEAT1 alone could explain 35.5% of the same.

Conclusion: mRDSS probably does not reflect the underlying fibrotic process occurring sub-clinically, as no significant correlation was observed either with the disease duration or with the pro-fibrotic molecules (TGFβ, αSMA, and collagen1). The strong inter-correlation of NEAT1, MALAT1 and MEG3 suggest that any one of them might well be studied as specific marker of sub-clinical fibrosis.The long non coding RNAs (MALAT1, MEG3, NEAT1) better reflects the sub-clinical fibrosis occurring in the patients, suggested by strong correlation with fibrotic markers (TGFβ, αSMA, collagen1). The linear regression values suggest that NEAT1 could be an important biomolecule in SSc pathogenesis.

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Disclosure of Interests: None declared

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THU0010 GENES ASSOCIATED WITH NUCLEOTIDE OLIGOMERIZATION DOMAIN-LIKE RECEPTOR SIGNALING PATHWAY ARE UPREGULATED IN CUTANEOUS LUPUS ERYTHEMATOSUS

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Background: Cutaneous Lupus Erythematosus (CLE) is a disfiguring autoimmune skin disorder with several subtypes: discoid lupus, subacute cutaneous lupus, and acute cutaneous lupus. CLE is associated with defects in the adaptive immune system, and, at times, systemic involvement. The innate immune system is likely involved as seen in the presence of interface dermatitis, which is observed in viral exanthems, and improvement of CLE using inhibitors to membrane-bound Pattern Recognition Receptors.

Objectives: Compare the expression of genes associated with the innate immune system in active CLE skin lesions of different subtypes compared to normal skin controls.

Methods: Five datasets selected from the Gene Expression Omnibus (GEO) were analyzed using GEO2R to compare the gene expressions between different subtypes of CLE. Search Tool for the Retrieval of Interacting Genes/Proteins (STRING) database, Gene Card, and Kyoto Encyclopedia of Genes and Genomes (KEGG) Pathway analysis were used to identify the interaction and function of specific genes.

Results: There were a total of 147 CLE skin samples and 52 normal controls. Genes associated with the Nucleotide-Binding Oligomerization Domain-Like Receptor (NLR) signaling pathway were upregulated in CLE skin samples (adjusted p-value < 0.001). Five genes associated with the NLR signaling pathway, STAT1, OAS1, OAS2, OAS3, and AIM2, were found to be upregulated in skin samples of CLE patients in all datasets, regardless of type, compared to normal controls in all datasets. These five genes are associated with transcription activation, regulation of viral infection, and interferon response.

Conclusion: Genes associated with the NLR signaling pathway are upregulated in the skin lesions of CLE patients compared to normal controls, supporting the role of the innate immune system in CLE. Further validation studies using experimental methods are needed.

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THU0011 ANALYSIS OF METABOLIC STATUS IN CYBRIDS REVEALED IMPAIRED METABOLIC FLEXIBILITY IN OA PROCESS.

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Background: There are several metabolic pathways involved in cell metabolism, including glycolysis, tricarboxylic acid (TCA) cycle and fatty acid (FA) oxidation. Metabolic flexibility has previously described as the ability to respond or adapt to changes in metabolic demand; assessed by the ability to switch from fat to carbohydrate oxidation. In the last years there is a growing interest to assess the influence of metabolic flexibility, as a mechanism to explain how lipids can accumulate in the tissue. During OA, it has been established a relationship between mitochondrial dysfunction and cellular damage due to impairments in mitochondrial function and metabolic flexibility. Several studies have suggested that fatty acids may play an important role in OA development and progression.

Objectives: The aim of this work was to examine the differences in glucose and fatty acid metabolism, with special focus on metabolic flexibility, in cybrids from healthy (N) or OA donors.

Methods: Cybrids were developed using 143B.TK$^-$ Rho-0 cell line (nuclear donor) and platelets (mitochondrial donors) from healthy (N) and OA donors. Glucose and FA metabolism were measured using D-[^{14}C(U)]glucose and [1-^{14}C] oleic acid respectively. Metabolic flexibility was evaluated by co-culturing with glucose and oleic acid acutely by using inhibitors against glucose and FA oxidation, 20μM UK5099 and 10μM etomoxir, respectively. Incorporation of FA into lipid droplet (LD) was evaluated by thin layer chromatography and LD were stained by LD540 and analyzed by confocal microscope and flow cytometry. Mitochondrial dynamics was measured by real-time PCR method. Percentage of mitochondrial Anion Superoxide (O_2^-) production was evaluated incubating cells with MitoSox® using Flow Cytometer. Appropriate statistical analyses were performed with GraphPad Prism v6.

Results: There were no changes in basal glucose metabolism between cybrids. N cybrids had higher acid-soluble metabolites, reflecting incomplete FA β-oxidation than OA cybrids. Comparing glucose and FA metabolism showed that both types of cybrids preferred to oxidize glucose. Co-culturing with glucose and Oleic acid, increased total cellular uptake and oxidation of glucose in N compared to basal condition (Figure-1) and in this condition the OA cybrids showed an increase in mitochondrial O_2^- production. Inhibition of FA oxidation by etomoxir increased complete glucose oxidation of N cybrids but not in OA cybrids that had a preference to oxidize oleic acid compared to basal condition. Gene expression of mitofusin-2 (*MFN2)* was higher in N than OA cybrids under inhibiting conditions. Combine these data indicate that N cybrids are more metabolically flexible and have better adaptative response than OA. Cybrids presented different lipid distribution patterns. Lipid droplet (LD) formation increased in both groups incubated in presence of FA. Furthermore, N cybrids showed less LD formation than OA.

Conclusion: The results indicated that cybrids from OA patients had reduced metabolic flexibility compared to N cybrids. These results enhance our understanding of the mitochondria metabolism in OA, suggesting a mitochondrial dysfunction and impairment of metabolic flexibility during the OA process.

Figure-1

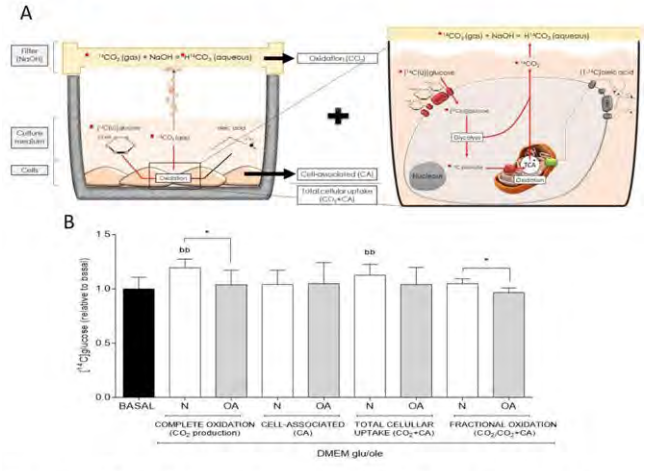


Figure -1. Effect of oleic acid in glucose metabolism. **A**. Scheme of substrate oxidation protocol: cybrids were cultured for 48 h in DMEM-glu/ole and glucose metabolism was evaluated using D-[14C(U]glucose **B**. Effect of 100 μM oleic acid compared to 5.5 mM glucose (basal) on glucose metabolism in N and OA cybrids. Values are presented as mean ± SEM relative to basal. * N versus OA cybrids (*p≤0.05, unpaired t test). b versus basal (bb p≤0.01, paired t test).

Disclosure of Interests: Andrea Dalmao-Fernandez: None declared, Jenny Lund: None declared, Tamara Hermida Gómez: None declared, Maria Eugenia Vazquez Mosquera: None declared, Ignacio Rego-Perez: None declared, Francisco J. Blanco Grant/research support from: Sanofi-Aventis, Lilly, Bristol MS, Amgen, Pfizer, Abbvie, TRB Chemedica International, Glaxo SmithKline, Archigen Biotech Limited, Novartis, Nichi-iko pharmaceutical Co, Genentech, Jannsen Research & Development, UCB Biopharma, Centrexion Theurapeutics, Celgene, Roche, Regeneron Pharmaceuticals Inc, Biohope, Corbus Pharmaceutical, Tedec Meiji Pharma, Kiniksa Pharmaceuticals, Ltd, Gilead Sciences Inc, Consultant of: Lilly, Bristol MS, Pfizer, Mercedes Fernandez-Moreno: None declared

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THU0012

IMPACT OF RS12107036 POLYMORPHISM OF TP63 ON THE RISK OF RAPID PROGRESSIVE OSTEOARTHRITIS OF THE KNEE. DATA FROM THE OSTEOARTHRITIS INITIATIVE

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Background: There is a need to identify patients with the rapid progressive phenotype of Osteoarthritis (RPOA) to include them in clinical trials and to implement prevention strategies. During the last years, nuclear single nucleotide polymorphisms (SNPs) were associated with susceptibility and progression of the disease, but not with the rapid progression phenotype.

Objectives: Analyze the influence of previously knee OA-associated nuclear SNPs on the risk of RPOA in patients of the OAI.

Methods: Caucasian patients from the OAI were selected and assigned into three different groups (N=252/group) based on the following criteria:

A.rapid progressors; baseline KL grade 0-1 in at least one knee and increase up to KL≥ 3 during a 48-month period; or baseline KL grade 2 in at least one knee and increase up to KL 4 or total knee replacement during the follow-up.

B.no-rapid progressors; baseline KL grade 0-1 in at least one knee and increase up to KL 2 during 48-month period; or baseline KL grade 2 in at least one knee and increase up to KL 3 during the follow-up.

C.no-progressors; KL grade 0-2 at baseline in at least one knee and bilaterally stable during 48-month period.

Groups were re-categorized into two groups: non-progressors and progressors (pooling A and B). Nuclear SNPs were previously assigned by mini-sequencing techniques. Preliminary chi-square analyses and binary and multinomial logistic regression models adjusted by gender, age, body mass index (BMI), contralateral OA, previous injury in target knee and WOMAC pain, were performed with IBM SPSS Statistics v24.

Results: We analyzed the effect of 7 SNPs that had been strongly associated with knee OA susceptibility in different GWAS studies: rs11177, rs4730250, rs11842874, rs12107036, rs8044769, rs10948172 and rs143383. Chi-square analyses only showed differences in the frequency distribution of rs12107036 between groups (p=0,028), being the GG genotype over-represented in the rapid progressors group and the AA genotype in the non-progressors group (Figure 1). The binary logistic regression showed that G allele was significantly over-represented in the (pooled) progressors group when compared with non-progressors (p=0,008) (Table 1). And the multinomial logistic regression showed that, in

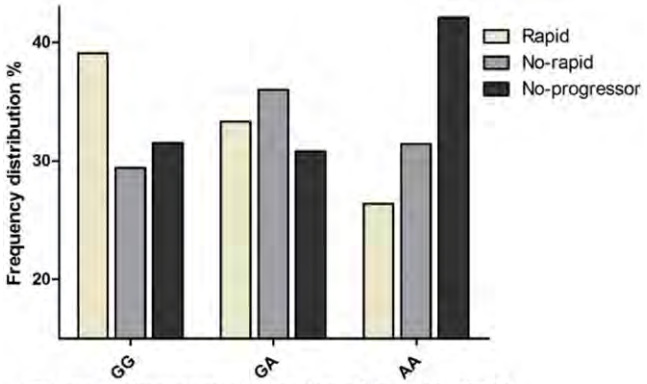


Figure 1. Frequency distribution of the rs12107036 genotypes among the different progression groups

Table 1. Binary regression model comparing progressors pool vs. no-progress

Variables	p-value	OR	C.I. 95%	
			Min.	Max.
Age	0,217	1,012	0,993	1,030
Sex (Female)	**0,000#**	2,049	1,478	2,842
BMI	**0,000#**	1,085	1,044	1,127
Contralateral OA (Yes)	**0,044#**	1,400	1,009	1,942
Previous Injury (Yes)	**0,002#**	1,723	1,223	2,429
WOMAC pain	**0,003#**	1,102	1,033	1,177
rs12107036 G (Yes)	**0,008#**	1,682	1,148	2,463

CI: confidence interval; OR: Odd Ratio; #: statistical significance declared at P ≤ 0.05

addition to age and previous injury in target knee, the GG genotype (p=0,032) emerged as a potential risk factor for the RPOA when compared with non-rapid progressors (Table 2).

Table 2. Multinomial regression model comparing rapid vs. no-rapid progressors.

Variables	p-value	OR	C.I. 95%	
			Min.	Max.
Age	**0,000#**	1,064	1,041	1,088
Sex (Female)	0,498	0,875	0,595	1,287
BMI	0,096	1,034	0,994	1,077
Contralateral OA (Yes)	0,792	1,052	0,719	1,539
Previous Injury (Yes)	**0,028#**	1,523	1,047	2,216
WOMAC pain	0,091	1,055	0,992	1,123
rs12107036 GG (Yes)	**0,032#**	1,574	1,039	2,382

CI: confidence interval; OR: Odd Ratio; #: statistical significance declared at P ≤ 0.05

Conclusion: The G allele of the nuclear SNP rs12107036 of TP63 gen increases the risk of knee OA progression. Depending on the number of risk allele copies the level of progression varies, being the GG genotype a risk factor for the RPOA of the knee. The assignment of this nuclear polymorphism could be useful as complementary genetic biomarker for the early identification of this phenotype.

Disclosure of Interests: Alejandro Durán-Sotuela: None declared, Mercedes Fernandez-Moreno: None declared, Maria Eugenia Vazquez Mosquera: None declared, Paula Ramos-Louro: None declared, Andrea Dalmao-Fernandez: None declared, Sara Relaño-Fernandez: None declared, Natividad Oreiro: None declared, Francisco J. Blanco Grant/research support from: Sanofi-Aventis, Lilly, Bristol MS, Amgen, Pfizer, Abbvie, TRB Chemedica International, Glaxo SmithKline, Archigen Biotech Limited, Novartis, Nichi-iko pharmaceutical Co, Genentech, Jannsen Research & Development, UCB Biopharma, Centrexion Theurapeutics, Celgene, Roche, Regeneron Pharmaceuticals Inc, Biohope, Corbus Pharmaceutical, Tedec Meiji Pharma, Kiniksa Pharmaceuticals, Ltd, Gilead Sciences Inc, Consultant of: Lilly, Bristol MS, Pfizer, Ignacio Rego-Perez: None declared

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THU0013 INTEGRATED ANALYSIS OF SYNOVIAL SINGLE CELL RNA SEQUENCING DATA DEEPENS THE CURRENT KNOWLEDGE OF SYNOVIAL PATHOLOGY IN ARTHRITIS

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Background: The heterogeneity of synovial tissues from patients with arthritis could contribute to the interpatient variability in disease course, prognosis and treatment response. Single-cell RNA sequencing (scRNA-seq) permits in-depth analysis of tissue heterogeneity, which could facilitate drug discovery and patient stratification for precision medicine.

Objectives: To construct a comprehensive landscape of synovial cell types and molecular pathways in arthritis by integrating our and published scRNA-seq data, generated across different scRNA-seq technologies [Smart-seq2, Drop-seq], cell preparation protocols [dissociated unsorted, sorted cells] and types of arthritis [undifferentiated (UA), rheumatoid arthritis, osteoarthritis].

Methods: Synovial tissues were obtained by ultrasound-guided biopsy from patients with UA [not fulfilling the classification criteria for a specific arthritis, n=3]. Biopsies were disintegrated [enzymatic and mechanical disruption] and cell viability assessed with trypan blue. ScRNA-seq libraries [2 per patient] were prepared with 10X Genomics Drop-Seq and sequenced on NovaSeq6000. Bioinformatics analysis of our and published [n=35] datasets[1-3] was performed using Seurat protocol[4] with correction for batch effects and filtering low-quality cells. Functional enrichment analysis of marker genes in clusters was done with STRING Protein-Protein networks. Synovitis was assessed with ultrasound and histology.

Results: Our tissue disintegration protocol resulted in good cell yield and viability (92%, 72%, 100%). The synovial cellular heterogeneity detected by scRNA-seq reflected the histological findings [Krenn score, pathotype]. These were supported with the ultrasound and clinically assessed disease activity. The integrated analysis of 41 datasets from 38 donors yielded 41845 scRNA-seq cell profiles, 50% contributed by our dataset. An independent analysis of our data and their integration with published data showed that different scRNA-seq methods and protocols can identify all the major synovial cell types and their activation states (Figure 1) with large heterogeneity between donors. We identified a previously undescribed synovial cell population, which was located near the fibroblast cluster, was negative for canonical cell markers, but highly enriched in cell division genes (80% of marker genes). These cells comprised a mixed population of CD34-, podoplanin (PDPN)^{high} or PDPN^{low} cells that were mostly negative for the sub-lining fibroblast marker THY. Furthermore, they appeared to be highly secretory (extracellular matrix components) and their gene expression profile was inclined towards cell migration, vascular development and insulin growth factor-dependent processes.

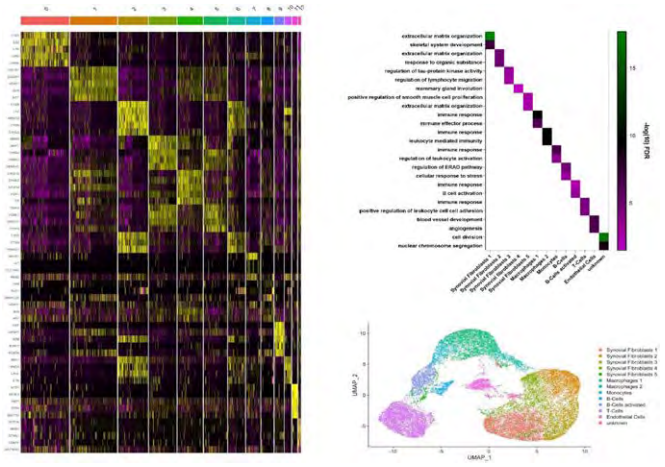


Figure 1. Heatmap with top 20 cluster gene markers, gene enrichment analysis and UMAP plot of synovial cell clusters.

Conclusion: By integrating synovial scRNA-seq data from 41845 cells, we identified a previously undescribed, highly proliferative and secretory synovial cell population in arthritis. We increased the number of known scRNA-seq synovial cell profiles in arthritis by two-fold and demonstrated the robustness of synovial scRNA-seq data outputs across different technologies and protocols. This broadens the current knowledge of synovial tissue heterogeneity and pathology in arthritis.

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THU0014

COMPARATIVE TRANSCRIPTOME ANALYSES ACROSS TISSUES AND SPECIES IDENTIFY TARGETABLE GENES FOR HUMAN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) AND LUPUS NEPHRITIS (LN)

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Background: Systemic Lupus Erythematosus (SLE) is a complex disease associated with the dysfunction of multiple tissues and cells. The causal tissue for each disease phenotype is not known a priori. Despite improvements in diagnosis and treatment, major organ involvement (such as the kidneys) contributes significantly to morbidity and mortality that still remain increased. There is an unmet need for timely targeted therapy.
Objectives: RNA-sequencing was performed to investigate the patterns of transcription variation across tissues between healthy and lupus-prone mice at different stages of lupus, and how these patterns associate with human Systemic Lupus Erythematosus (SLE).
Methods: NZB/W-F1 lupus prone mice were sacrificed at the pre-puberty, pre-autoimmunity and nephritic stage. Age-matched C57BL/6 were used as controls. An "effector" tissue (spleen) and "end-organs" (kidneys, brain) were collected. Total RNA was isolated, and mRNA-sequencing was performed. A time-series analysis was developed and differentially expressed genes (DEGs) were analyzed with DESeq. Hierarchical clustering and functional enrichment analysis were performed with gProfiler. Human orthologs of mouse tissue DEGs were identified in the whole-blood RNA-sequencing dataset comprised of 55 lupus-nephritis (LN), 65 non-LN SLE patients and 58 healthy individuals (HI). Human orthologs were compared to human DEGs. Using machine learning, human orthologs identified in the mouse dataset were used to predict kidney involvement in the human dataset, which was split in training and validation sets.
Results: Lupus susceptibility and progression signatures at different tissues and different stages of the disease were identified. Tissue-specific signatures and a common cross-tissue signature were also described. Previously described and novel biological processes and pathways were revealed. The comparative murine-human transcriptome analysis identified human orthologs from the mouse spleen-signature (including CCL5, IFIT and HLA genes) that are involved in systemic autoimmunity. It also identified human orthologs from the kidney- and brain-signature (including FCGR2A, C1Q, JAK1 and APOA2) that are involved in major "end-organ" damage and response mechanisms. Using a neural network model, 193 human orthologs accurately predicted LN patients vs HI (accuracy=0.86, sensitivity=0.82, specificity=0.91 in the validation set). Using a support vector machine model, 30 human orthologs and age and gender were the best predictors of LN vs non-LN SLE patients (accuracy=0.71, sensitivity=0.73, specificity=0.69 in the validation set).
Conclusion: Murine tissue gene signatures identified by RNA-sequencing analysis revealed biological processes and pathways that could be potentially used as biomarkers or therapeutic targets in human SLE. Comparison of the murine tissue-transcriptome with the whole-blood human-transcriptome revealed common gene signatures, demonstrating similar biological processes and pathways. Machine learning identified a murine kidney lupus signature that can accurately predict kidney involvement in human SLE. Validation in other datasets is ongoing.
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THU0015

TYPE I INTERFERON SIGNATURE PREDICTS PROGRESSION TO INFLAMMATORY ARTHRITIS IN ACPA+ AT-RISK INDIVIDUALS WITHOUT CLINICAL SYNOVITIS

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Background: Interferon (IFN) is known to play a role in the pathogenesis of many autoimmune diseases, among them, rheumatoid arthritis (RA). A study showed that two interferon-stimulated gene expression scores (IFN-Score-A and IFN-Score-B) can be used to predict progression to connective tissue disease (CTD) in at-risk individuals, positive for anti-nuclear antibodies (ANA+) [1]. This validated score could potentially be applied to individuals at-risk of RA.
Objectives: To investigate the role of type I IFN in patients at-risk of RA and assess its potential role as a biomarker to predict progression to inflammatory arthritis (IA).
Methods: PBMC samples were taken from 36 at-risk individuals positive for anti-citrullinated protein antibodies (ACPA+), with a non-specific musculoskeletal complaint but no clinical synovitis and a normal ultrasound scan at baseline (BL). 17 of them developed IA later on, and had a second sample taken at the moment of progression. The other 19 did not progress and had a second sample taken after 1 year. Expression of IFN stimulated genes was assessed using TaqMan. T-test was used to compare the expression of the genes at the two time points of each individual. Binary logistic regression was used to assess BL predictors of progression. Multivariable analysis was adjusted for confounders such as C-reactive protein (CRP) rheumatoid factor (RF) and ACPA titre.
Results: Table 1 shows the list of tested genes. There were no differences in the gene expression of progressors at BL and at the moment of IA diagnosis. Similarly, no differences were found between the non-progressors at BL and after 1 year. Comparing BL samples from progressors and non-progressors, there was a trend to higher expression of IFN-score-B in the progressors (Mann Whitney p=0.055), whereas IFN-score-A was similarly expressed in both groups. This is similar to the results found in a cohort of ANA+ individuals at risk of progressing to CTD [1]. Multivariable analysis showed that IFN-score-B and RF titre were predictive for IA progression with an odds ratio (OR) of 2.18 (p=0.048) and OR 1.01 (p=0.035).

Table 1. Interferon stimulated genes and scores A and B

GENE	IFN score	GENE	IFN score
CCL8		BST2	
CEACAM1		IFI16	
CXCL10		IFIH1	
GBP1		LAMP3	
IFI27		NT5C3B	
IFI44		PHF11	
IFI44L	A	SERPING1	B
IFIT1		SOCS1	
IRF7		SP100	
ISG15		STAT1	
RSAD2		TAP1	
XAF1		TRIM38	
		UBE2L6	
		UNC93B1	

Conclusion: These exploratory results suggest that IFN changes in IA progressors precede subclinical inflammation on ultrasound. A preliminary risk model shows that IFN-score-B could be useful to predict progression to IA in at-risk of RA individuals; however, these results require validation in a larger at-risk cohort.

Table 2. Baseline characteristics and predictors of progression

	PROGRESSORS N= 17	NON-PROGRESSORS N=19	UNIVARIABLE OR (95% CI)	MULTIVARIABLE OR (95% CI)
Mean age y.o.(SD)	50.12 (10.01)	52.53 (9.22)	0.97 (0.91-1.04) p=0.446	-
Female (%)	11 (64.7)	14 (73.7)	1.52 (0.37-6.35) p=0.560	-
RF titre, mean (SD)	77.18 (99.93)	36.58 (53.39)	1.01 (0.99-1.02) p=0.162	**1.01 (1.01-1.03) p=0.035**
ACPA titre, mean (SD)	123.44 (109.44)	103.77 (116.18)	1.00 (0.99-1.01) p=0.594	0.99 (0.98-1.00) p=0.283
ANA+ (%)	2 (11.8)	5 (26.3)	2.68 (0.45-16.11) p=0.282	-
CRP, mean (SD)	5.41 (5.31)	2.97 (1.96)	1.21 (0.96-1.52) p=0.104	1.31 (0.99-1.73) p=0.055
ESR, mean (SD)	12.24 (11.97)	12.16 (8.44)	1.00 (0.94-1.07) p=0.981	-
Shared epitope (%)	8 (47.1)	10 (52.6)	1.25 (0.34-4.63) p=0.739	-
IFN-Score-A (−ΔCt), mean (SD)	-5.81 (1.07)	-6.23 (1.08)	1.45 (0.76-2.77) p=0.253	1.97 (0.83-4.66) 0.124
IFN-Score-B (−ΔCt), mean (SD)	-4.21 (0.56)	-4.52 (0.45)	3.53 (0.83-14.97) p=0.087	**8.82 (1.02-76.38) p=0.048**

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THU0016 EPIGENOMIC ANALYSIS OF RA PATIENTS SHOWS DISTINCT BIOLOGICAL PROCESSES ASSOCIATED WITH ANTI-TNF RESPONSE

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Background: Blocking Tumor Necrosis Factor (TNF) activity is a successful therapeutic approach for approximately 60% of patients with rheumatoid arthritis (RA). To date, however, the biological basis of the lack of efficacy of anti-TNF agents is unknown.
Objectives: The objective of present study was to characterize the biological basis of anti-TNF lack of efficacy in RA using an epigenomic data approach in two steps: first, to assess the differential methylation changes between responders and non-responders and second, to use this differential methylation profile in a systems biology approach to infer differential methylated biological modules according to anti-TNF response.
Methods: A total of n=68 patients diagnosed with RA according to the ACR-EULAR criteria belonging to 16 Hospitals across Spain were recruited. All patients were >18 years old, with more than 6 months of disease evolution and a baseline disease activity of DAS28 > 3.2. Treatment response was defined according to the EULAR criteria at week 12. Good and moderate responders were aggregated into a single responder group. Genomic DNA was collected at baseline and the methylation profile was assessed using the Illumina Infinium EPIC array, which interrogates 850,000 methylation CpG sites across the genome. Differential Methylation analysis, biological pathway association and the systems Biology approach using Protein-Protein Interaction Networks, were conducted using the R statistical language and the Bioconductor libraries.
Results: From 68 anti-TNF treated patients, n=27 (39.7%) were good responders, n=26 (38.2%) moderate responders and n=15 (22.05%) non-responders at week 12 of treatment. Differential methylation analysis identified two distinctive biological profiles associated with the clinical response: responders were associated to interleukin and cytokine production, and non-responders were associated with biological pathways associated to TGF-Beta production and T cell regulation. Using these differentially methylated profiles, epigenetic modules with differentially methylated hotspots between responders and non-responders were also found. Two epigenetic modules with significant enrichment in inflammatory and interleukin production and immune regulatory processes were validated in an independent patient cohort.
Conclusion: The epigenetic analysis of whole blood from RA patients using a module-based approach shows reproducible biological mechanisms associated with the response to anti-TNF therapy.
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Disclosure of Interests: Antonio Julià: None declared, Antonio Gómez: None declared, Antonio Fernández Nebro: None declared, Francisco J. Blanco Grant/research support from: Sanofi-Aventis, Lilly, Bristol MS, Amgen, Pfizer, Abbvie, TRB Chemedica International, Glaxo SmithKline, Archigen Biotech Limited, Novartis, Nichi-iko pharmaceutical Co, Genentech, Jannsen Research & Development, UCB Biopharma, Centrexion Theurapeutics, Celgene, Roche, Regeneron Pharmaceuticals Inc, Biohope, Corbus Pharmaceutical, Tedec Meiji Pharma, Kiniksa Pharmaceuticals, Ltd, Gilead Sciences Inc, Consultant of: Lilly, Bristol MS, Pfizer, Alba Erra: None declared, Simon Sánchez Fernandez: None declared, Jordi Monfort: None declared, Mercedes Alperi-López: None declared, Isidoro González-Álvaro Grant/research support from: Roche Laboratories, Consultant of: Lilly, Sanofi, Paid instructor for: Lilly, Speakers bureau: Abbvie, MSD, Roche, Lilly, Rosario Garcia de Vicuna Grant/research support from: BMS, Lilly, MSD, Novartis, Roche, Consultant of: Abbvie, Biogen, BMS, Celltrion, Gebro, Lilly, Mylan, Pfizer, Sandoz, Sanofi, Paid instructor for: Lilly, Speakers bureau: BMS, Lilly, Pfizer, Sandoz, Sanofi, Raimón Sanmartí Speakers bureau: Abbvie, Eli Lilly, BMS, Roche and Pfizer, Cesar Diaz Torne: None declared, Carlos Marras Fernandez Cid: None declared, Jesús Tornero Molina: None declared, Núria Palau: None declared, Raquel M Lastra: None declared, Jordi Lladós: None declared, Sara Marsal: None declared
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THU0017 ATTEMPTS TO LINK EXONIC GENE POLYMORPHISMS TO SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)-ASSOCIATED PROTEIN MODIFIED FUNCTIONALITY: A STRUCTURAL BIOLOGY APPROACH

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Background: Gene association studies and genome wide association studies (GWAS) have played a primary role in depicting genetic contributions to systemic lupus erythematosus (SLE) development, while accommodating the exonic polymorphisms on the protein structure level, when available, enhances our understanding of protein function modification or depletion. Linking human genetics with therapeutic targets requires the biological function of the causal gene and variant to be known.
Objectives: To investigate recently identified SLE-associated functional gene polymorphisms, such as *PARP1*, *ITGAM, TNFAIP3, NCF1, PON1, IFIH1, SH2B3* and *TYK2* [1-4] by correlation to protein structure and function.
Methods: Three-dimensional (3D) homology modeling and molecular mechanics/dynamics studies were applied for the localization of the polymorphisms under study on the respective proteins. The mutants were constructed using molecular modeling with the program Maestro (Schrodinger, LLC), which was also used to analyze the conformational changes caused by the mutation. All figures depicting 3D models were created using the molecular graphics program PyMOL V.2.2 [5].
Results: Modeling revealed that rs1136410 SNP encodes the less common polymorphism Val762Ala on *PARP1* that reduces enzymatic activity of Poly(ADP-ribose) polymerase 1 (Figure 1), *ITGAM* polymorphism rs1143679 (Arg77His) on Integrin alpha M, component of the macrophage-1 antigen complex affects protein surface recognition, *TNFAIP3* rs2230926 polymorphism encodes Cys instead of Phe at residue 127 of the ubiquitin editing A20 protein, while rs201802880 polymorphism of the neutrophil cytosolic factor 1 (*NCF1*) gene modifies the function of the cytosolic subunit of neutrophil NADPH oxidase with the mutation Arg90His. *PON1* is involved in the oxidative stress process that cause tissue damage observed in SLE and anti-phospholipid syndrome (APS). The *PON1* Gln192Arg mutation (rs662 SNP) affects shape and recognition of the ligand recognition site as part of the evolutionary process, while *IFIH1* (rs35667974) helicase C domain1 mutant I923V is located on an essential RNA beta loop interacting directly with the nucleic acid (Figure 2). Finally, the rs3184504 SNP of *SH2B3* gene generates mutant Arg262Trp on SH2 adapter protein 3, acting as a signaling pathway involved in autoimmune disorders, while in *TYK2 gene*, one of the Janus kinases, the rs35018800 producing mutant Ala928Val modifies the ADP binding site.

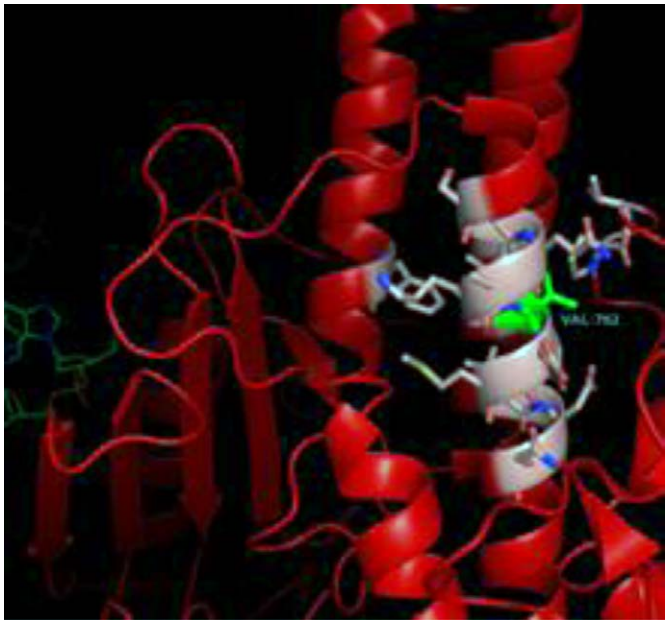


Figure 1. Details of the Val762 interaction where V762A mutation occurs in PARP1protein.

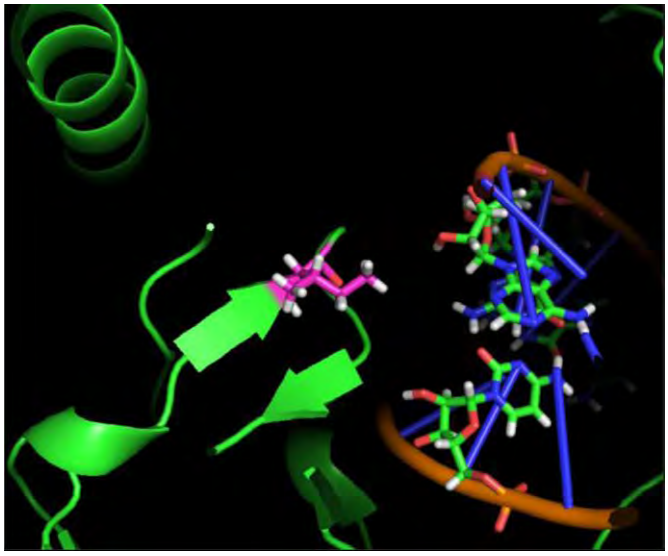


Figure 2. Nucleic acid interacting IFIH1 helicase beta-loop where I923V mutation occurs (in purple).

Conclusion: Based on several examples, we have tried to define a rational link from SLE-associated gene polymorphisms to structure and to modified function, including metagenomic analysis of SNPs, protein crystallography, protein molecular modeling, molecular mechanics and dynamics. Locating, shaping and understanding the target protein interaction interface plays a decisive role in most cases and provides clues for further pharmacological or medical actions [6].

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THU0018

GENETIC FACTORS AND RESPONSE TO RITUXIMAB THERAPY IN SLE

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Background: The biologic drug Rituximab (anti-CD20) is used therapeutically in SLE, however the clinical response to the therapy, which is expensive, is quite variable. Factors influencing the efficacy have been challenging to determine. The MRC funded MASTERPLANS consortium has investigated prognostic factors that determine the therapeutic response to biologic therapy in SLE. Genetics has not been studied on a large scale in this context. SLE is a complex clinical phenotype, it is likewise a complex genetic trait, although it has recently been shown that polygenic risk scores do have a relationship to the severity of the disease (1). In addition, genetic risk factors for SLE, coded at the IgG Fc gamma receptor locus, have the potential to influence antibody-dependent cell-mediated cytotoxicity.
Objectives: To determine whether the genetics influences the clinical outcome of therapy with Rituximab. The study used both genome-wide data in the form of genetic risk scores as well as specific genetic data at a candidate locus, namely the IgG Fc gamma receptor locus
Methods: Samples from the BILAG Biologics Register (BILAG BR) of individuals treated with Rituximab were subject to genome-wide genotyping with Illumina GSA V2 chip. Genetic risk scores (GRS) were calculated through a weighted risk sum. Genetic variation at the IgG Fc gamma receptor locus is not captured well on genotyping chips and hence common coding and copy number variation was studied using Multiplex Ligation-dependent Probe Amplification (MLPA) and sequencing.
Results: BILAG-BR samples for SLE part of receiving Rituximab therapy were genotyped on GSA chip, 573 samples passed QC and were used in principal components analysis (PCA), among them, 310 samples both have RTX treatment information and GRS calculated. Examining the population using PCA in the informative samples revealed that the largest distinction, European versus African ancestry did not correlate with Rituximab response. When GRS was determined in the Responders versus the Non-responders there was a weak correlation with those with a higher risk score showing a tendency to be in the responder group (Fig. 1). We also examined variation at the IgG Fc gamma receptor locus, polymorphisms of which are associated with SLE and have been correlated with therapeutic outcome in lymphoma (2). In a subset of the BILAG-BR cohort, we show that carriage of the SLE risk allele at *FCGR3A* (158F) was enriched in the 'responder at some point' group compared to the non-responder group (P=0.03, Chi-square).
Conclusion: We present preliminary data indicating that genetics at both the genome wide level and at the *FCGR* locus show some influence on the outcome of therapy with Rituximab in SLE; more data are required in order to draw firm conclusions.

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THU0019 INTRON REGIONS OF PIK3AP1 (BCAP) AND SPON2 (SPONDIN-2) GENES ARE DIFFERENTIALLY METHYLATED IN PATIENTS WITH PERIODIC FEVER, APHTHOUS STOMATITIS, PHARYNGITIS AND ADENITIS (PFAPA) SYNDROME

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Background: Periodic fever, aphthous stomatitis, pharyngitis and adenitis (PFAPA) syndrome is the most common autoinflammatory disease in children, often grouped together with hereditary periodic fever syndromes, although its cause and hereditary nature remain unexplained.
Objectives: We investigated whether a differential DNA methylation was present in DNA from peripheral blood mononuclear cells (PBMC) in patients with PFAPA versus a group of healthy young individuals.
Methods: A whole epigenome analysis (MeDIP and MBD) was performed using pooled DNA libraries enriched for methylated genomic regions. Of identified candidate genes, two with most significantly different methylation leves were further evaluated with methylation specific restriction enzymes coupled with qPCR (MSRE-qPCR).
Results: The analysis showed that *PIK3AP1* and *SPON2* intronic gene regions are differentially methylated in patients with PFAPA. MSRE-qPCR proved as a quick, reliable and cost-effective method to confirm results from MeDIP and MBD.
Conclusion: Our findings indicate that B cell adapter protein (BCAP) as PI3K binding inhibitor of inflammation and spondin-2 (SPON2) as a pattern recognition molecule and integrin ligand could play a role in etiology of PFAPA. Their role and impact of changed DNA methylation in PFAPA etiology and autoinflammation need further investigation.
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THU0020 NO CAUSAL ASSOCIATION OF SERUM URATE OR GOUT WITH ALZHEIMER'S DISEASE: A MENDELIAN RANDOMIZATION ANALYSIS

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Background: Several epidmiologic studies have found a lower risk of Alzheimer's disease (AD) among individuals with a history of gout[1] or high serum urate levels[2], which are the precursor to gout. Serum urate may have neuroprotective benefits for AD, however it is possible that reverse causation and residual confounding could explain the observational evidence.
Objectives: To study the causal associations of serum urate and gout with Alzheimer's disease using Mendelian Randomization (MR) methods.
Methods: Two-sample MR was performed to examine the causality of: 1) serum urate on Alzheimer's disease and 2) gout on Alzheimer's disease. Single nucleotide polymorphisms (SNP) identified from a genome-wide association study of 457,690 adults described 183 SNPs associated with serum urate and gout, which were used as instrumental variables[3]. Additional single-SNP analyses were conducted using SNPs from three genes identified as major determinants of urate levels (SLC2A9, SLC22A12, and ABCG2). SNPs for AD came from the International Genomics of Alzheimer's Project, comprised of 35,274 AD cases and 59,163 cognitively normal elderly controls[4]. Inverse-variance weighted (IVW) models were the primary method used to examine the associations between each exposure and risk of AD. Additional analyses examined the potential impact of pleiotropy via MR-Egger models. Single-SNP analyses used the Wald ratio. All analyses were performed using R.
Results: There was no evidence of a causal association between genetically-determined serum urate or gout and risk of AD from IVW analyses (both p>0.1) (Table 1). MR-Egger analyses yielded similar estimates (both p>0.1) and the intercepts of the MR-Egger regressions did not suggest the presence of directional pleiotropy (p=0.64 for serum urate exposure and p=0.98 for gout exposure) (Table 1). Additionally, none of the three individual SNPs were significantly associated with risk of AD (all p>0.05) (Table 2).

Table 1. Association of combined SNPs for serum urate and gout with Alzheimer's disease

	Number of SNPs	OR	95% CI	p value	MR-Egger intercept (p value)
Serum urate exposure (per 1 mg/dL increase)					
IVW	158	1.04	0.98-1.11	0.187	
MR-Egger	158	1.06	0.96-1.17	0.228	-0.001 (0.645)
Gout exposure (gout vs. non-gout)					
IVW	158	1.03	0.99-1.06	0.161	
MR-Egger	158	1.03	0.98-1.07	0.290	5.477 (0.976)

Table 2. Association of individual SNPs for serum urate and gout with Alzheimer's disease

Gene	SNP	OR	95% CI	p-value
Serum urate exposure (per 1 mg/dL increase)				
SLC2A9	rs3775947	1.12	1.00-1.26	0.059
SLC22A12	rs531763	0.92	0.71-1.20	0.545
ABDG2	rs74904971	1.22	0.99-1.50	0.059
Gout exposure (gout vs. non-gout)				
SLC2A9	rs3775947	1.08	1.00-1.17	0.059
SLC22A12	rs531763	0.94	0.77-1.15	0.545
ABCG2	rs74904971	1.06	1.00-1.13	0.059

Conclusion: Using both serum urate and gout as instrumental variables in MR analysis, these findings suggest that serum urate and gout are not causal determinants for the development of AD. The inverse associations described in observational studies may in part be due to confounding or reverse causality.
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THU0021 IDENTIFICATION OF MUSCLE ASSOCIATED KEY GENES TO SUPPORT AXIAL SPONDYLOARTHRITIS DIAGNOSIS BY TRANSCRIPTOMIC APPROACH, THE MYOSPA STUDY

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Background: Early diagnosis of axial Spondyloarthritis (axSpA) represents a major clinical challenge nowadays. Increasing evidence has determined that early diagnosis, prompt treatment initiation and early achievement of remission are the best predictors of long-term clinical, functional and radiographic outcomes. New tools to support the diagnosis are needed.
Objectives: This study aims to identify differentially expressed genes that may improve the current clinical diagnosis approach for early axSpA.
Methods: A cross-sectional study was conducted on 50 participants, 25 patients with axSpA (according to ASAS criteria) and 25 Healthy Controls, matched by gender, age and levels of physical activity. Peripheral blood samples were collected and RNA-Seq technology was performed. Normalization of raw data, and identification of differentially expressed genes was obtained using edgeR and limma-voom R packages. Gene Set Enrichment Analysis (GSEA) and Functional Enrichment analysis using Gene ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) annotations were also performed. A number of Differently Expressed Genes were highlighted.
Results: 311 genes were identified as being significantly differentially expressed between patients and controls. In details, 129 downregulated (7 genes have fold change more than 1) and 182 upregulated genes (3 genes have fold change more than 1) are highlighted. These genes are mostly involved in Myogenesis, Innate Immune Signalling and JAK/STAT pathways. Several genes with functions of skeletal muscle development and muscle contraction were identified.
Conclusion: The evidence disclosed that regulation of muscle development and contraction may be also engaged in physiopathology mechanisms of axSpA. These new cues open new perspectives for diagnosis and therapeutic approaches in axSpA.
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THU0022 DIFFERENTIAL DNA METHYLATION AS A PREDICTOR OF TOCILIZUMAB RESPONSE IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Tocilizumab (TCZ) is a biological disease-modifying antirheumatic drug that blocks IL-6 signalling and is effective in ameliorating disease activity in rheumatoid arthritis (RA). However, approximately 50% of patients do not respond adequately to TCZ and some patients report adverse events. Considering there is growing evidence that DNA methylation is implicated in RA susceptibility and response to some biologics (1, 2), we investigated DNA methylation as a candidate biomarker for response to TCZ in RA.
Objectives: To identify differential DNA methylation signatures in whole blood associated with TCZ response in patients with RA.
Methods: Epigenome-wide DNA methylation patterns were measured using the Infinium EPIC BeadChip (Illumina) in whole blood-derived DNA samples from patients with RA. DNA was extracted from blood samples taken pre-treatment and following 3 months on therapy, and response was determined at 6 months using the Clinical Disease Activity Index (CDAI). Patients who had good response (n=10) or poor response (n=10) to TCZ by 6 months were selected. Samples from secondary poor responders (n=10) (patients who had an improvement of CDAI and were in remission at 3 months, followed by a worsening of CDAI at 6 months) were also analysed. Differentially methylated positions and regions (DMPs/DMRs) were identified using linear regression, adjusting for gender, age, cell composition, smoking status, and glucocorticoid use. Gene Set Enrichment Analysis (GSEA) was used to identify significant pathways associated with response and Functional Epigenetic Module analysis of interactome hotspots in regions of differential methylation.
Results: 20 DMPs were significantly associated with response status at 6 months in the pre-treatment samples. Another 21 DMPs were associated with response in the 3 month samples. Within good responders, 10 DMPs showed significant change in methylation level between pre-treatment and the 3 month samples (unadjusted P-value $<10^{-6}$). One DMP, cg03121467, was significantly less methylated in good responders compared to poor responders in the pre-treatment samples. This DMP is close to *EPB41L4A* and thought to have a role in β–catenin signalling. GSEA of DMRs in non- and secondary non- responders identified histone acetyltransferase pathways and included the *KAT2A* gene, which is a repressor of NF-κB. Additional analysis of interaction hotspots of differential methylation identified significant interactions with *STAMBP* and *PTPN12* associated with response status.
Conclusion: These preliminary results provide evidence that DNA methylation patterns may predict response to TCZ. Validation of these findings in other larger data sets is required.
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THU0023 DETAILED PROFILE OF CO-OCCURRENCE OF RELAPSING POLYCHONDRITIS AND AUTOIMMUNE THYROID DISEASE

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Background: Relapsing polychondritis (RP) is a rare inflammatory disease, which is characterized by recurrent inflammation and destruction of cartilage tissues. RP also has the profile of autoimmune disease and is often complicated with other autoimmune disease. Autoimmune thyroid disease (AITD) is one of common autoimmune diseases, which consists of Graves' disease (GD) and Hashimoto's thyroiditis (HT). While RP is reported to be complicated with AITD[1)], there has been no study on detailed profile of co-occurrence of RP and AITD.
Objectives: We aimed to reveal whether there is common (statistically significant) co-occurrence of RP and AITD. We also analyzed clinical and genetic profiles characterizing the co-occurrence.
Methods: We recruited 117 patients with RP and checked their medical records in order to obtain the information about compilation of AITD and clinical features. In addition, we genotyped Human Leucocyte Antigen (HLA) A, B Cw, DRB1, DQB1 and DPB1 alleles for 88 of the 117 patients. Co-occurrence ratio was compared with prevalence of AITD in the Japanese population. Associations of co-occurrence of AITD with clinical manifestations or HLA alleles were analyzed among the patients.

Results: Among the 117 patients with RP, 5 (4.3%) and 6 (5.1%) patients had GD and HT, respectively. Patients with RP were more likely to be complicated with GD ($p=1.04\times10^{-3}$, OR: 7.15, 95%CI 2.68~ 18.14) but not with HT (p=0.50, 95%CI 0.59~1.27), compared with prevalence in general Japanese population (0.62% and 5.9%, respectively[2]). RP patients with GD showed a trend to have nasal involvement (100% vs 45.5%, p=0.023, OR: 2.58, 95%CI 1.09~∞). We did not observe any differences in clinical manifestation in patients with RP and HT. HLA- DPB1*02:02 demonstrated a trend toward GD complication (20% vs 2.3%, p=0.035, OR: 10.41, 95%CI 1.23~65.38). There were no association of HLA in the complication of HT among patients with RP.

Conclusion: Patients with RP have high co-occurrence ratio of GD. Patients with the two diseases may be characterized by nasal involvement and HLA-DPB1*02:02.

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THU0024 METHYLATION ANALYSIS OF VITAMIN D SIGNALING PATHWAY GENES IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Vitamin D is known for its immunomodulatory and epigenome interacting effects. Vitamin D deficiency is frequently observed in rheumatoid arthritis (RA) patients compared to healthy controls, is also named as a potential risk factor in RA ethiopatogenesis and may alter DNA methylation of certain genes [1,2]. Still, causality of vitamin D deficiency in RA patients needs to be elucidated.

Objectives: The aim of the study was to evaluate relationship between DNA methylation status of vitamin D related genes (*VDR*, *CYP24A1*, *CYP2R1*), miRNA-155 expression, vitamin D level and its association with RA.

Methods: CpG islands in promoter region of the *VDR*, *CYP24A1*, *CYP2R1* genes were chosen for DNA methylation analysis by means of pyrosequencing. DNA from blood mononuclear cells of 31 RA patients and 31 age and sex matched healthy controls was assessed for methylation pattern after informed consent was obtained in Vilnius university Hospital Santaros klinikos Centre of Rheumatology. For miRNA analysis quantitative reverse transcription PCR was used. Chemiluminescent microplate immunoassay was used to asses 25(OH) D serum levels.

Results: 25(OH)D concentrations varied from deficiency (<50 nmol/l), insufficiency (50-75 nmol/l) to normal range (≥75-100 nmol/l) in RA (mean 47.49 nmol/l; SD ± 27.93) and healthy controls (mean 57.38 nmol/l; SD ± 29.93)). *CYP24A1* methylation level was significantly higher in comparison to *VDR* (p<0.0001) and *CYP2R1* (p<0.0001) genes in both groups. *CYP24A1* hypermethylation was also observed in older subjects (p=0.012). The study demonstrated a significant positive correlation between vitamin D concentration and *VDR*, *CYP2R1* genes methylation intensity (r^2=0.31, p=0.014; r^2=0.25, p=0.042, respectively). However, gene methylation frequency and methylation intensity showed no significant difference between RA patients and healthy controls (*VDR* – 2.4 *vs* 2.6 %, *CYP24A1* – 16.6 *vs* 15.3 %, *CYP2R1* – 2.6 *vs* 2.6 %) (p>0.05). To note, miRNA-155 expression negatively correlated with *CYP24A1* methylation intensity (r^2=-0.43, p=0.009).

Conclusion: Our study identified significant associations between the *VDR* and *CYP2R1* promoter methylation and vitamin D concentration. However, no significant differences in DNA methylation pattern between RA patients and healthy controls were detected. MiR-155 expression was associated with *CYP24A1* methylation level, confirming its possible involvement in vitamin D metabolism. The data of our study suggests that epigenetic phenomena are significantly involved in vitamin D metabolism and may have an indirect effect on RA ethiopatogenesis.

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THU0025 MICRO-RNA DIFFERENTIALLY REGULATE THE ALTERNATIVE PRTN3-MRNA IN GRANULOMATOSIS WITH POLYANGIITIS

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Background: Micro-RNAs (miRNA) are short non-coding RNAs that regulate inflammation mostly by translational repression. Previously, we screened 847 miRNAs in nasal tissue from GPA patients and found a disease associated alteration of miRNA expression compared to healthy controls and chronic rhinosinusitis. MiR-184 was most over expressed in nasal tissue from GPA (13.4x). The dual-luciferase reporter assay confirmed a significant reduction of Proteinase-3 (PRTN3) expression by miR-184 (1).

PRTN3 transcripts with an alternative 3' untranslated region (UTR) have been described in GPA (2). The pathophysiological relevance of this alternative transcript remains unclarified.

Objectives: To identify new miRNA targets of potential pathophysiological relevance in GPA, we validated the effect of the 21 most dysregulated miRNAs on the mRNA of PRTN3. Further, we included the alternative PRTN3 mRNA in our screen to look for new regulatory differences.

Methods: The inhibitory capacity of miRNAs on Proteinase-3 mRNA was estimated by a dual-luciferase reporter system. The sequences of the alternative (132bp longer) and the regular 3'UTR-PRTN3 were cloned and inserted into the pmirGLO vector and co-transfected with 21 miRNA mimics into HeLa cells. Co-transfection with *Caenorhabditis elegans* miRNA 67 mimic (cel-miR-67) was used as negative control. Statistical significance was evaluated by students t-test adjusted for multiple comparisons (Holm-Sidak).

Results: For 18 of 21 investigated miRNAs no effects could be observed on the alternative and the regular 3'UTR-PRTN3. But there were remarkable differential effects of let-7f, miR-184 and miR-708. Let-7f (-29,2%) and miR-708 (-23,6%) both showed a suppression of the alternative 3'UTR-PRTN3 but no effect on the regular 3'UTR-PRTN3 while miR-184 only suppressed the regular 3'UTR (-17,5 %) and not the alternative variant (fig. 1-2).

Conclusion: Disease specific miRNA signatures together with an increased PRTN3 level and in alternative PRTN3 mRNA in GPA suggest a dysregulation of PRTN3 expression in GPA. To our knowledge this is the first analysis in GPA showing that miRNAs can differentially regulate the expected and the alternative 3'UTR variants of PRTN3-mRNA. As miR-184 is markedly upregulated in GPA, a repression of PRTN3 is to be anticipated, possibly as a reaction to previous neutrophil activation with PRTN3 overexpression. Our findings also strengthen the potential pathophysiological role of the alternative PRTN3 mRNA.

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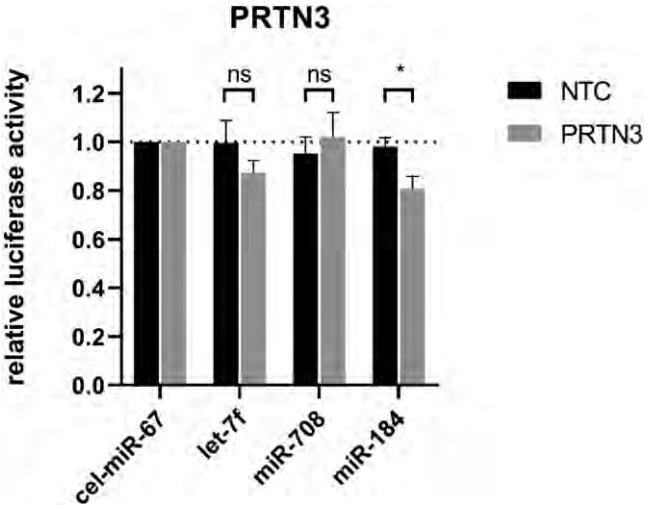


Fig. 1. Dual-luciferase reporter assay with the regular 3'UTR of PRTN3 cloned into the pmirGLO vector compared to empty vector (NTC). Significant effect for miR-184 (17,5 %), miR-708 no effect and let-7f small but not significant reduction in luciferase activity (12,3 %). Data represent 3 independent experiments with triplicate measurements. miR-184 was tested 6 times. *P<0.05; ns = not significant; error bars display standard deviation.

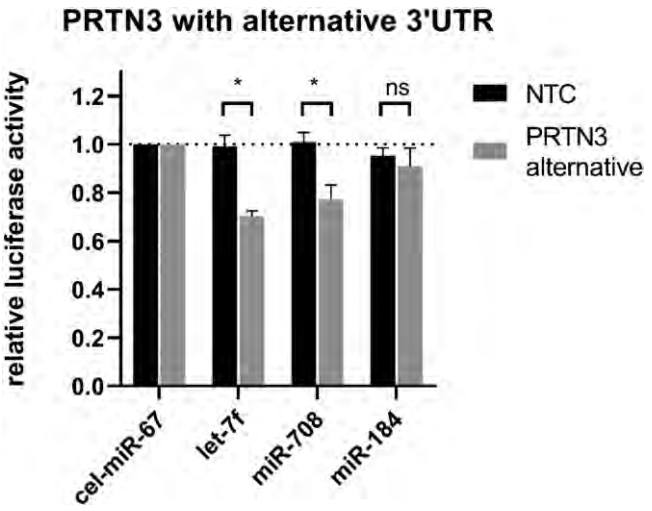


Fig. 2. Dual-luciferase reporter assay with the alternative 3'UTR of PRTN3. Significant effects of let-7f (29,2 %) and miR-708 mimic (23,6 %) but no significant effects of miR-184 of luciferase activity. 3 independent experiments with triplicate measurements. *P<0.05

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THU0026 CLONAL HAEMATOPOIESIS ASSOCIATED SOMATIC MUTATIONS IN RHEUMATOID ARTHRITIS

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Background: Clonal haematopoiesis of indeterminate potential (CHIP) occurs when somatic mutations arise in myeloid neoplasia driver genes of haematopoietic progenitor cells, in the absence of overt cytopenia or dysplasia. The prevalence of CHIP increases with age. The most common genes affected by CHIP mutations in unselected populations are DNMT3A, ASXL1, and TET2. The presence of CHIP is linked to increased basal level of inflammation and a high risk of cardiovascular disease and all-cause mortality. Rheumatoid arthritis (RA) is one of the most common and debilitating multi-system autoimmune disorders, affecting up to 1% of adults in developed countries. The role of somatic mutations in the pathogenesis of autoimmune diseases is an unexplored area; therefore, we aimed to test the hypothesis that clonal haematopoiesis (CH) is associated with the incidence and severity of RA.
Objectives: To evaluate the association of CH somatic mutation with severity of RA.
Methods: 163 RA patients were recruited from the following cohorts: (i) **E**arly RA/ treatment naive (n=31), (ii) **R**efractory RA - non-responders to Disease-Modifying Anti-Rheumatic Drugs (DMARDs) and biologics (n=48), (ii) **F**lare (n=41) vs **R**emission patients (n=43) –patients treated with DMARDs and withdrawn from treatment on achieving remission. Six months later, 50% relapse and 50% sustain remission. Single molecule molecular inversion probes (smMIPs) were used to screen for somatic mutations in 40 loci known to carry clonal haematopoiesis driver mutations (CHDMs). Whole exome sequencing was also performed on Flare/Remission patients (n = 84) to screen for CHDMs and other somatic mutations. In-house bioinformatics pipelines were used to call mutations from both the datasets.
Results: We identified CH in RA with an overall prevalence of 14%. Twenty-four unique variants with a variant allele frequency (VAF) of 2-35% were found in ten genes including ASXL1, CBL, DNMT3A, GNAS, GNB1, PTPN11, PTPN12, SF3B1, TET2, and TP53. The number of unique patients carrying mutations in these genes are follows: **refractory**: n=12/48**, flare**: n=6/41, **remission**: n=4/43 and **early RA**: n=2/31. The majority of the mutations occurred in DNMT3A (n=6) followed by TP53 (N=4) and TET2 (n=3). Two variants with VAF of 15% were identified in two patients under the age of 30, both with clinically severe disease. In patients between the ages of 50-59 yrs., 60-69 yrs., and 70-79 yrs., CH was observed at 11% (4/35), 23% (11/46) and 17%(7/41), respectively.
Conclusion: We here report the prevalence of CH in RA, affecting more patients with clinically advanced/refractory disease compared to those with early/less severe disease.
Further study will be conducted to confirm the results.
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THU0027 THE ASSOCIATION OF THE RS35677470 DNASE1L3 GENE POLYMORPHISM WITH SLE, RA AND SSC: STRUCTURAL/BIOLOGICAL INSIGHTS

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Background: Genome-wide association studies (GWAS) have identified hundreds of autoimmune diseases-associated loci so far but much of the heritability of these diseases remains unknown. In an attempt to identify potential causal variants, various studies revealed that the missense variant rs35677470 at *DNASE1L3* is associated with the development of systemic lupus erythematosus

(SLE), rheumatoid arthritis (RA) and systemic sclerosis (SSc), thus exhibiting a pleiotropic effect. Deoxyribonuclease I-like 3 (DNase1L3) is a member of human DNase I family, representing a nuclease that cleaves double-stranded DNA during apoptosis and is involved in the development of autoimmune diseases [1].
Objectives: To investigate the role of the rs35677470 polymorphism at *DNASE1L3* gene leading to the R206C mutation in SLE, RA and SSc [2-3] and the mechanism that may affect the loss of function in the protein structure.
Methods: The *DNASE1L3* evolution was investigated to define conservation elements in the protein sequence using, BLASTP extended searches [4], TCOFFEE [5] multiple sequence alignments, and MEGAX [6] for phylogenetics analysis. Three-dimensional (3D) homology modeling was used to localize the polymorphism under study. The mutant was constructed by molecular modeling using the structures of homologous DNAses (PDB entries 1atn, 4awn, 3d3w; [7-9]). Molecular mechanics/dynamics studies were applied to validate structural/functional changes caused by the R206C substitution. All figures depicting 3D models were generated using the PyMOL molecular-graphics system V.2.2 (Schrodinger, LLC).
Results: The evolutionary analysis shows heavily conserved sequence elements among species indicating structural/functional importance. Structural analysis revealed that the rs35677470 SNP codes for a nonconservative amino acid variation, R206C, disrupts the conserved electrostatic network holding protein secondary structure elements to place. Specifically, the R206 to E170 interaction, part of a salt bridge network stabilizing two a-helices, is being interrupted, thereby affecting the molecular architecture (Fig. 1). Indeed, previous studies on the effect of this SNP in Caucasian populations resulting in a lower level of DNAse1L3 activity are consistent with this observation [10].

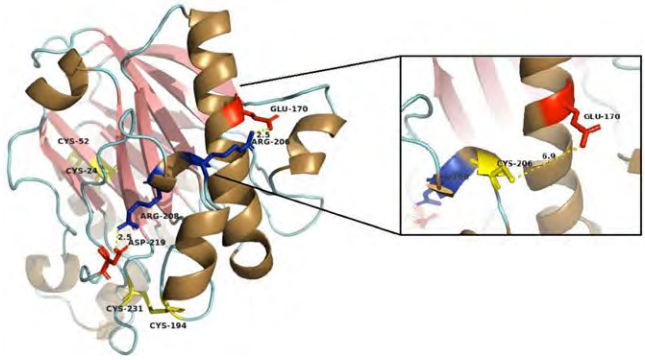


Figure 1. Ribbon representation of the DNAse1L3 homology model showing the position of the stabilizing salt bridge network (E170- R206, R208- D219). Insert figure shows the R206C mutation. Positively charged R (in blue), negatively charged D,E (in red) and C (in yellow) are shown. Distances are in Angstroms.

Conclusion: This study represents a comprehensive evaluation of the shared autoimmune loci of *DNASE1L3* (rs35677470), reported to produce an inactive form of DNaseIL3 [10]. The structural analysis, explains the potential role of the produced mutation by modifying the placement of structural elements and consequently introducing disorder in the protein folding and affecting biological function. Altogether, this study contributes to the delineation of the genetic architecture of SLE, RA and SSc.
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THU0028 AN EXPLANTION FOR HOW VIRAL INFECTION MAY TRIGGER SPONDYLOARTHROPATHY BASED ON TLR9 DRIVEN TNF RESPONSES FROM ENTHESEAL DERIVED PLASMACYTOID DENDRITIC CELLS

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Background: It is well known that viral infections may trigger psoriatic arthritis (PsA), a disease that typically has extensive pre-clinical entheseal abnormalites. Skin resident plasmacytoid dendritic cells (pDCs) produce IFNα that contribute to T cell expansion and the development of experimental psoriasis [1, 2]. IFN pathway SNPs have been reported in both PsA and psoriasis and we previously reported the presence of pDCs at the human enthesis [3].
Objectives: To investigate whether the TLR9 agonist ODN that replicates viral infection activate a wide array of of entheseal derived pDCs molecular cascades including the TNF pathway that might provide a link between viral infection and PsA.
Methods: pDCs were sorted from enthesis and blood and stimulated with ODN as previously described (n=16) [3, 4]. IFNα protein pre and post stimulation were detected by ELISA. Intracellular flow cytometry (IFC) of entheseal pDCs was used to detect TNF protein. RNA was extracted post-stimulation. The mRNA were hybridised and tagged by probes then measured on the nCounter platform. Data was analysed using nSolver 4.0. Log2 |fold change| >1 and P-value <0.05 were considered statistically significant. The gene ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) of differentially expressed genes (DEGs) were analyzed using DAVID. Protein-protein interaction (PPI) network was drawn by STRING.
Results: Stimulated entheseal pDCs showed a strong DEGs pattern pointing towards increased TNF expression. There were 11 genes significantly upregulated including TNF. RIPK3 is involved in TNF signalling pathway. TNF, RIPK3 and ZBP1 are involved in necroptosis. TNF and ITGB2 are involved in IL-4 and IL-13 signaling pathway. TNF, HLA-DOA, ITGB2/TLR7 are involved in virus infection. Together it highlights extremely activated TNF pathway genes.
IFN protein was induced in sorted entheseal pDCs following stimulation (n=8). TNF protein was detected by IFC on stimulated entheseal pDCs (CD45+HLA-DR+CD123+CD303+ CD11c-) (n=3). We also compared entheseal and matched peripheral blood pDCs (n=8) following stimulation where no major differences in the TNF pathway were present between groups.
The KEGG analysis was mapped in Figure 1. GO analysis showed the most significant change in biological processes was enriched in the positive regulation of DNA binding transcription factor activity. The change in molecular function was mainly enriched in p53 binding.

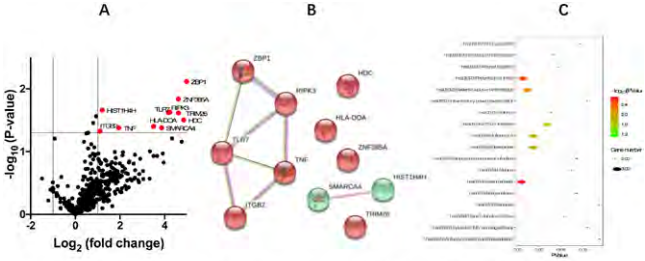


Figure 1. DEGs between stimulated and unstimulated entheseal pDCs. (A) Volcano map showing significantly upregulated genes (red). (B) PPI network. (C) KEGG pathway enrichment.

Conclusion: Entheseal pDCs, upon viral molecule stimulation, show several markers of activation. However, TNF pathway genes were highly activiated which provides a novel mechanistic link between viral infection and PsA as reported in epidemiological studies.
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THU0029 **IDENTIFICATION AND COMPARING OF HUB GENES IN SYSTEMIC LUPUS ERYTHEMATOSUS T AND B CELLS BY BIOINFORMATIC ANALYSIS**

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Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder that can virtually involve any organ system of the body. Many efforts have been made to elucidate the pathogeny, but the molecular mechanisms are still not understood. Lymphocytes are considered to play an important role in SLE pathogenesis. Aberrantly activated T cells mediate inflammatory responses and activate B cells to differentiate and produce autoantibodies, resulting in multisystem manifestations [1, 2]. With the wide use of gene technique, more genetic studies on SLE were performed and differentially expressed genes (DEGs) were identified. Integrating and re-analyzing these data can help us understand the molecular mechanisms and identify diagnostic and therapeutic targets of SLE.
Objectives: In this study, we downloaded the microarray datasets GSE4588 and GSE10325 from Gene Expression Omnibus (GEO) database to identify the candidate genes in T and B cells respectively.
Methods: Datasets GSE4588 and GSE10325 were downloaded from GEO (http://www.ncbi.nlm.nih.gov/geo). The DEGs between T or B cells and control samples were screened using GEO2R (http://www.ncbi.nlm.nih.gov/geo/geo2r). logFC |fold change| >1 and P-value <0.05 were considered statistically significant. To analyze the function of DEGs, biological analyses were performed using DAVID database (http://david.ncifcrf.gov). P<0.05 was considered statistically significant. The PPI networks of DEGs were constructed using STRING database, and an interaction with a combined score >0.4 was considered statistically significant. The PPI networks were drawn using Cytoscape and the most significant module was identified using MCODE. The criteria for selection were: MCODE scores >5, degree cut-off=2, node score cut-off=0.2, Max depth=100 and k-score=2. The hub genes were selected with degrees ≥10.
Results: After standardization of the microarray results, DEGs in T and B cells were identified respectively (Fig. 1).

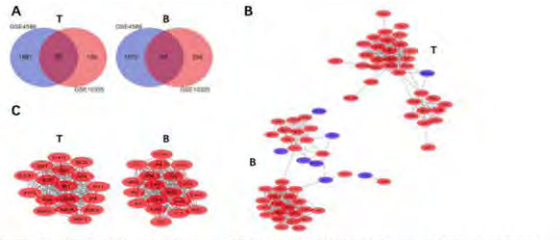


Figure 1. Venn diagram, PPI network and the most significant module of DEGs in SLE. (A) The overlap between 2 datasets contained 56 genes in T cells and 83 in B cells. (B) PPI networks were constructed using Cytoscape. (C) The most significant module in T cells had 17 nodes and 193 edges, while that in B cells had 19 nodes and 171 edges. Upregulated genes are in red; downregulated genes are in blue.

Changes in biological processes in T and B cells were both mainly enriched in type I interferon signalling pathway, defense response to virus, and negative regulation of viral genome replication. Changes in cell component in T cells was enriched in the cytosol while in B cells it was in cytoplasm. KEGG pathway analysis revealed that the DEGs of T cells were mainly enriched in influenza A, measles, herpes simplex infection and hepatitis C, while DEGs of B cells were mainly enriched in measles. Changes in molecular function were not listed because the p values were ≥0.05.
4 genes were identified as hub genes (2 in each cell population). In T cells, the hub genes are PLSCR1 and GINS2. PLSCR1 may contribute to the prothrombotic tendency in SLE. GINS2 is involved in the initiation of DNA replication and cell cycle progression. In B cells, the hub genes are ISG15 and TOP2A. Increased ISG15 is correlated with lymphocytopenia in SLE patients. TOP2A encodes a DNA topoisomerase and anti-topoisomerase II antibody could be found in SLE.
Conclusion: In our study, 2 mRNA microarray datasets were analyzed to obtain DEGs between SLE T and B cells versus healthy controls. A total of 56 DEGs were identified in T cells and 83 in B cells. Most of the DEGs were upregulated. Changes in biological processes in T and B cells were mainly related to type I interferon signalling pathway and anti-virus function. KEGG also showed the same. PLSCR1 and GINS2 were hub genes in T cells while ISG15 and TOP2A were hub genes in B cells. Overexpression of these genes might play an important role in the pathogenesis of SLE.
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Disclosure of Interests: None declared
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THURSDAY, 04 JUNE 2020

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

THU0030 **DISTINCT EFFECTS OF FIVE JAK INHIBITORS IN THE MODULATION OF HUMAN B CELL ACTIVATION**

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Background: JAK inhibitors have been successfully introduced in the treatment of rheumatoid arthritis (RA) and psoriatic arthritis and are in clinical trials for numerous other autoimmune diseases. JAK inhibition effectively reduces cytokine-mediated activation and survival of pathology-driving immune cells by targeting signaling downstream of cytokine receptors. The outcome of such immunomodulation hence will largely depend on the intrinsic expression of the four different JAKs, the cytokine environment and the targeted cell type. Comparative studies investigating the effect on B cells are lacking. In light of the use of JAK inhibitor treatment in autoantibody mediated diseases, the study of the B cell compartment represents a milestone to assess their potential.
Objectives: We thus aimed to study the B cell compartment as well as B cell function under JAK inhibition in RA patients and to compare the specific effect the JAK inhibitors tofacitinib (pan-JAK), baricitinib (JAK1/2), ruxolitinib (JAK1/2), upadacitinib and filgotinib (selective JAK1) on in vitro B cell activation, differentiation, proliferation, and class switch.
Methods: B cell subpopulations in RA patients treated with baricitinib or tofacitinib was assessed by flow cytometric analysis of peripheral blood mononuclear cells. For in vitro studies, magnetically isolated total B cells from healthy donors were stimulated T-cell -independently with CpG and treated with scalar doses of the JAK inhibitors tofacitinib, baricitinib, ruxolitinib, upadacitinib and filgotinib. Flow cytometric analysis was performed on days 0, 3 and 6. Cytokine secretion was measured by Cytokine Multiplex Assay.
Results: B cell phenotyping of RA patients treated with JAK inhibitors baricitinib or tofacitinib showed an increase in marginal zone (MZ) B cells. To investigate this further, we turned to an in vitro model of T-cell-independent B cell activation with CpG via TLR9, known to support MZ B cell expansion. Here, JAK1/2 and selective JAK1 inhibitor treatment led to a dose-dependent decrease of total B cell numbers. When assessing B cell-subpopulations, we observed an altered B cell differentiation with a significant increase in MZ-like B cells under JAK inhibition, which led to a subsequent increase in plasmablast differentiation in the first days. This effect was more pronounced upon pan-JAK inhibitor treatment than JAK1 or JAK1/2 inhibition, indicating that broader JAK inhibition is associated with a stronger effect (tofa > ruxo > bari > upa > filgo).
Notably, we further detected a significant dose-dependent reduction of switched memory formation, strongest with JAK1/2 inhibition (upa > ruxo > bari > tofa > filgo). Consistent with this finding, we observed decreased AID expression under JAK inhibition. Concomitantly, induction of STAT3 expression and STAT3 phosphorylation were reduced under JAK inhibition, suggesting that downstream signalling was abrogated.
To assess the role of autocrine signaling in this system, we measured cytokine secretion upon JAK inhibition and found that JAK2 inhibition led to reduced IL10 secretion. This in turn resulted in an increase of inflammatory cytokines such as IL6, TNF, highlighting the importance of B cell as cytokine-secreting cell type.
Conclusion: In a T-independent in vitro B cell model JAK inhibition led to a reduced total B cell number as well as reduced switched memory development, whereas MZ-like B cells were increased. Especially JAK2 inhibition strongly impaired switched memory formation. JAK inhibition does not only impact cytokine signalling but also leads to changes in cytokine secretion dynamics and amounts, potentially impacting other cell types.
In conclusion, JAK inhibition has a major effect on B cell activation and maturation, with differential outcomes between JAK inhibitors hinting towards distinct and unique effects on B cell homeostasis.

Disclosure of Interests: None declared
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THU0031 ABATACEPT ALTERS THE FREQUENCY OF IMMUNOREGULATORY AND EFFECTOR T CELL SUBPOPULATIONS IN RHEUMATOID ARTHRITIS

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Background: Under physiological conditions, T regulatory cells (Tregs) are responsible for the downregulation of the immune response. In autoimmune diseases, such as rheumatoid arthritis (RA), auto-inflammation is driven by an imbalance of activation and downregulation of immunological pathways. Thus, treatment plans for autoimmune diseases often involve the enhancement of immunoregulatory pathways by administering inhibitors of costimulation, i.e. CTLA-4-Ig (abatacept, ABA). ABA binds specifically to CD80 and CD86 on antigen presenting cells (APC). Consequently, T cell activation via the CD28 receptor is blocked. Previous studies have demonstrated surprising effects of abatacept on Tregs, specifically decreased frequency of these cells but enhancement in their function[1]. Whether these alterations can only be found in patients with ABA treatment, or whether they are also present in patients receiving other anti-inflammatory drugs is currently unknown.
Objectives: The aim of our research was to delineate the impact of ABA on the different subsets of effector and regulatory T cells in RA and compare these findings with patients receiving tocilizumab (TCZ) or rituximab (RTX).
Methods: Peripheral blood samples from 56 RA patients (median ± SE; age: 60.5 ± 1.3 years, female ratio: 0.7, disease duration: 17.9 ± 2.1 years; respectively) were drawn over a sampling period of 2 years. Freshly isolated PBMCs of RA patients were stained with fluorochrome-labelled antibodies and T cell subsets were identified by flow cytometric means. $CD3^+CD4^+$ T cells were further classified using different T cell markers (CD25, CD127, CD39, CD95). All cytometric measurements were performed using a standardized BD LSR-Fortessa platform. RA patients were compared according to their treatment with ABA, TCZ or RTX.
Results: Eighteen out of 56 RA patients (32%) received ABA, 25 patients (45%) received TCZ and 13 patients (23%) were under CD20+ cell depletion therapy with RTX. RA patients receiving ABA displayed a significant decrease in $CD3^+CD4^+CD25^+CD127^{dim}$ Tregs (3.7% ± 0.4) compared to patients with TCZ (5.4% ± 0.4, p = 0.041) and patients under RTX treatment (7.52% ± 0.93, p = 0.026). $CD39^+$ Tregs were significantly higher in RA patients treated with TCZ (49.5% + 3.2, p = 0.000) or RTX (50.5% ± 5.3, p = 0.026) compared to patients receiving ABA (24.5% ± 3.1). In addition, the frequency of $CD95^+$ Tregs was significantly reduced in ABA patients compared to RTX patients (59.6% ± 3.1 vs.76.7% ± 3.6, p = 0.014; respectively). Interestingly, T cells displaying an effector T cell phenotype ($CD3^+CD4^+CD25^{+/-}CD127^+$) were increased in ABA treated patients compared to RTX treated patients (59.6% ± 3.1 and 76.7% ± 3.6, p = 0.002). Since none of our patients were a non-responder or had high disease activity, we could not analyse whether these changes are associated with treatment outcome.
Conclusion: Our data demonstrate that blockage of T cell stimulation via ABA leads to characteristic alterations in different regulatory and effector T cells not seen in patients treated with TCZ or RTX. Further studies must clarify whether the analysis of regulatory and effector T cell subpopulations before treatment initiation can be used as biomarker for treatment response.
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Disclosure of Interests: None declared
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THU0032 MODIFIED PEPTIDES AS A NOVEL IMMUNOTHERAPY FOR RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a highly prevalent and severe systemic autoimmune disease associated with permanent disability and strong socio-economic burdens. Currently, there is no therapeutic treatment and RA patients rely on lifelong, costly treatments. Imcyse develops modified peptides eliciting antigen specific cytolytic CD4 T cells (cCD4+) that induce apoptosis of antigen presenting cells (APC) in a contact dependent manner. cCD4+ also induce apoptosis of autoantigen-specific bystander T-cells, activated by the same APC thus eliminating the risk of general immunosuppression. Peptides consist of MHC class II T cell epitopes of a target autoantigen modified in their flanking region by the addition of an amino acid sequence containing a thiol-disulphide oxidoreductase active motif[1].
Objectives: The goal of this study was to synthesize modified peptides from a target RA autoantigen and test their potency to generate *in vitro* specific and cytolytic CD4+ T cells from RA patients.
Methods: We designed modified peptides from a target RA autoantigen after in silico and in vitro assessment to identify MHC II core binding region, HLA class II binding capacities and physiochemical properties.
CD4+ T cells were purified from PBMC of a newly diagnosed seropositive RA patient and co-cultured with autologous APC in the presence of the modified peptide. The CD4+ T cells were restimulated periodically. Peptide's ability to generate specific CD4+ T cells was evaluated by flow cytometric analysis of the expression of surface activation marker CD154 (CD40L). The peptide specific CD4+ T cell lines were sorted based on their surface CD154 expression. Their pro-apoptotic activity was assessed after overnight (O/N) co-culture of CD4+ T cells with fluorescent tracer labelled autologous lymphoblastoid cells lines (LCL). Flow cytometry quantification of LCL apoptosis was measured by annexin V staining. MHC II restriction of CD4+ T cells was demonstrated by the addition of blocking antibodies against HLA-DR, DP or DQ molecules.
Results: CD4+ T cells were in vitro expanded after six consecutive stimulations with the peptide. We investigated their specificity by flow cytometry and showed that 69% of CD4+ T cells that were stimulated O/N in the presence of the peptide expressed the activation marker CD154 versus 29% of CD4+ T cells that were stimulated in its absence. These cells were sorted based on CD154 expression following specific stimulation. Cell enrichment was then assessed by flow cytometric analysis. Data showed that more than 91% (background 3%) were peptide specific based on CD154 expression.
After co-culture of CD4+ T cells with LCL, in independent experiments, Annexin V binding was detected on peptide loaded LCL, ranging from 69% to 89%, while when LCL were kept unloaded these values were between 30% and 55%, respectively, indicating that when specifically activated, these CD4+ T cells had pro-apoptotic activity. When both the peptide and blocking antibodies against HLA-DR, DP or DQ molecules added in the co-culture the pro-apoptotic activity was inhibited by 68%, 20% and 25%, respectively.
Conclusion: The preliminary but very promising data show that our modified peptide generates peptide-specific CD4+ T cells with lytic properties that lyse target APC in an HLA class II specific manner. Our plan is to show that these CD4+ T cells can also induce apoptosis in bystander T cells and to further validate our results in additional RA donors.
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THU0033

ALTERATIONS IN THE PHENOTYPIC LANDSCAPE AND SPECIFICITY OF CD4+ T CELLS IN CCP+ AT RISK SUBJECTS BEFORE THE ONSET OF RHEUMATOID ARTHRITIS

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Background: The "Targeting Immune Responses for Prevention of RA" (TIP-RA) collaboration studies individuals at high risk for developing rheumatoid arthritis (RA) because of serum anti-citrullinated protein antibody (ACPA) positivity in absence of arthritis at baseline, and is focused on defining how they transition from at-risk to classifiable disease. One potential mechanism is the expansion of antigen specific T cells that recognize self-antigens and acquisition of disease associated T cell phenotypes. ACPA emerge years prior to clinically apparent disease and subsequently increase in their titer and breadth of specificity. However, few studies have characterized T cells during this transition.
Objectives: To identify features associated with progression to RA by examining the specificity and surface phenotype of CD4+ T cells in individuals from the TIP-RA cohort by HLA class II tetramer staining and multi-parameter flow cytometry.
Methods: Tetramer staining and flow cytometry were performed on peripheral blood samples from a baseline visit from CCP3- controls (n=34), CCP3+ at-risk (n=26), CCP3+ positive individuals who transitioned in the near-term to RA (called "RA converters", n=4), and seropositive early-RA (n=21). Our staining panel allowed us to measure the frequencies of T cells specific for citrullinated alpha-enolase, aggrecan, cartilage intermediate layer protein (CILP), fibrinogen and vimentin. We then applied both supervised phenotyping and a cluster-based computational approach to compare the phenotypic landscape and specificity of antigen specific and total CD4+ T cells in each cohort.
Results: We observed higher overall frequencies of T cells that recognize citrullinated epitopes in CCP3+ at-risk subjects than CCP- controls ($p< 0.05$). Among the individual specificities, elevated frequencies prior to disease onset were most prominent for CILP specific T cells. Supervised phenotypic analysis revealed an increase in CCR4+ CD4+ T cells in CCP3+ at risk subjects ($p< 0.001$) and a corresponding decrease in CXCR3+ CD4+ T cells that was most pronounced in RA converters and seropositive early-RA ($p< 0.05$). Cluster-based phenotypic analysis defined ten distinct phenotypic states present within all subjects. Each of these ten immunotypes contained T cells that recognize citrullinated epitopes. However, the predominant immunotype varied for different antigens. During progression, the frequencies of Ag specific T cells diminished when onset was imminent, but rebounded shortly after diagnosis. Concomitantly, Ag specific T cells with memory phenotypes were diminished, but subsequently reverted to TSCM, Th1, and Th1-17 like phenotypes.
Conclusion: Our data show that disease associated changes in the antigen specificity of CD4+ T cells are present in CCP3+ at-risk subjects. Furthermore, the number of antigen specific T cells and their phenotype are perturbed before the onset of symptoms and development of classified RA. These findings support a continuum of immunologic changes that underlie risk and drive disease, motivating new approaches for early intervention.
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THU0034

AUTOREACTIVE B CELLS ESCAPE PERIPHERAL CHECKPOINT IN ANCA-ASSOCIATED VASCULITIS AND SJÖGREN'S SYNDROME

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Background: B cells play a central role in many autoimmune diseases (AIDs) including ANCA-associated vasculitis (AAV) and primary Sjögren's syndrome (pSS). Most of the research that has been conducted on AID has focused on the production, secretion, and pathogenicity of auto-antibodies, but little is known on the characteristics of autoreactive B cells in humans.
Objectives: This study aims at characterizing circulating autoantigen (PR3 ou SSA)-specific B-cells in patients with AAV and pSS compared to healthy subjects to better understand their role in the **natural and pathological autoimmunity** and define the mechanisms leading to the breakdown of self-tolerance in patients with AID.
Methods: First, we developed a new flow-cytometry method to detect circulating auto-reactive B cell based on the specificity of their B-cell receptor (BCR). To study surface phenotype of specific B cells by flow cytometry, blood samples were collected from patient with PR3-ANCA AAV, pSS and from healthy subjects. Functional analysis of antigen-specific B cells was also elicited by in vitro analysis of their capacity to secrete immunoglobulins against SSA or PR3 antigens by ELISPOT
Results: Phenotype analysis showed that antigen-specific B cells in patients have a memory phenotype compared with healthy controls (**5 to 9% are IgG-expressing memory B cells**). It suggests that in AID, theses auto-reactive cells are able to differentiate into IgG isotype-switched cells and escape peripheral tolerance checkpoint but not in healthy subjects. Interestingly, Natural auto-reactive B cells are able to secrete only IgM isotype autoantibodies upon *in vitro* stimulation but not IgG class switched antibodies. In order to better understand what differentiates auto-reactive B cells and the mechanisms leading to pathological autoimmunity, a **genomic analysis** of the antibody repertoire as well as a **transcriptional profiling** of these cells by single-cell RNA seq is ongoing to understand further the differences of these autoreactive B cells between healthy subjects and patients with AIDs.
Conclusion: We developed a technology to identify and isolate antigen-specific B cells from the peripheral blood of patients with AID. Our results suggest that autoreactive B cells escape peripheral tolerance checkpoint and are able to differentiate into IgG isotype-switched cells in patients with AIDs but not in healthy subjects.
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THU0035

OX40L EXPRESSING NEUTROPHILS INDUCE CD4 T FOLLICULAR AND PERIPHERAL HELPER CELL DIFFERENTIATION IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Neutrophils have been described as potent antigen-presenting cells able to activate T cells by MHC/TCR interaction and costimulatory molecules in tumor immunity. However, little is known about the direct interaction between neutrophils and CD4 T cells with respect to systemic lupus erythematosus (SLE). We have previously shown that OX40L expressed by monocytes from SLE patients promote the differentiation of naïve and memory cells into IL21 secreting T cells that are able to help B cells[1,2].
Objectives: In this study, we investigate OX40L expression on neutrophils from SLE patients and contribution of these $OX40L^+$ neutrophils in SLE pathogenesis to modulation of the B cell helper role of CD4 T cells.
Methods: Surface expression of co-stimulatory molecules (OX40L, ICOSL, GITRL, 4-1BBL) on neutrophils from SLE patients and healthy donors (HD) was measured by flow cytometry (FC). Neutrophils from HD were stimulated with TLR7 or TLR8 agonists and IFNα after 5 hours of culture, OX40L expression was measured by FC and Western Blotting. CD4 T cells were cultured with the stimulated neutrophils for 3 days. At the end of the co-culture, percentages of

IL21-expressing T follicular (Tfh) and peripheral helper (Tph) cells measured by FC. These generated T cells were also cultured in the presence of memory B cells. After 5 days of co-culture, plasmablast generation and Ig levels were assessed by FC and ELISA, respectively. Inhibition of OX40-OX40L interaction in vitro was achieved using ISB 830, a novel anti-OX40 mAb currently used in clinical trials.

Results: Among the co-stimulatory molecules tested, percentages of $OX40L^+$ neutrophils in SLE (n=54) were increased compared to HD (n=25)(mean + SD: HD = 1,34%±1.62 vs SLE = 4,53%±8.1; p=0.29). OX40L expression positively correlated with SLE disease activity score (SLEDAI) (p = 0,04; r = 0,31) and with anti-DNA antibodies (p= 0,04, r = 0,33). Of note, the percentage of $OX40L^+$ neutrophils was higher in anti-sm-RNP^+ patients (n=16, mean= 9%±9.8), compared to anti-sm-RNP^- patients (n=27, mean = 1,4%±2.5; p = 0,02). The percentage of $OX40L^+$ neutrophils was higher in patients with class III or IV lupus nephritis, and inflammatory infiltrate within the kidney biopsy disclosed $OX40L^+$ neutrophils, in close contact with T cells. Neutrophils from HD express OX40L with TLR8 agonist, or IFNα priming followed by TLR7 agonist. When memory CD4 T cells were cultured in the presence of TLR8-stimulated neutrophils, the proportion of IL21-expressing Tfh ($CXCR5^+PD1^+$) and Tph ($CXCR5^-PD1^{hi}$) were increased, compared to culture with unstimulated neutrophils. This process was dependent on OX40-OX40L interactions, since in vitro treatment with the anti-OX40 blocking antibody ISB 830, inhibited the differentiation of memory T cells into Tfh and Tph. Both generated Tfh and Tph were able to promote the differentiation of memory B cells into Ig-secreting plasmablasts.

Conclusion: Our results disclose an unprecedented phenomenon where cross-talk between TLR7/8-activated neutrophils and CD4 lymphocytes operates through OX40L-OX40 costimulation, and neutrophils promote the differentiation of pro-inflammatory Tfh and Tph, as well as IL21 production. Therefore, OX40L/OX40 should be considered as a potentially therapeutic axis in SLE patients.

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THU0036 FIRST-IN-HUMAN TRIAL OF BCMA-CD19 COMPOUND CAR IN THE TREATMENT OF AUTOANTIBODY MEDIATED DISORDERS

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Background: Donor-specific anti-HLA antibodies (DSAs) are antibodies in the recipient directed against donor class I/II HLA antigens. The existence of DSAs before allogenic hematopoietic stem cell transplantation (AHSCT) are known to cause primary graft failure. Currently there's no established method of DSA desensitization due to the long half-life of plasma cells.

Systemic lupus erythematosus (SLE) is a heterogeneous autoimmune disease involving in multiple organ systems mediated by numerous autoantibodies. Recent results have shown that depletion of B cells by CD19 CAR-T cells effectively reversed some manifestations in two SLE mouse models. However, plasma cells could be spared with single CD19 CAR-T cells, and peripheral circulating anti-DNA IgG and IgM autoantibodies remain elevated or increased in treated mice.

Objectives: We present the efficacy of BCMA-CD19 compound CAR (cCAR), which target on antibody- producing "root", both B cells and plasma cells in preclinical study and in our first-in-human phase 1 clinical trial.

Methods: We constructed a BCMA-CD19 cCAR composed of a complete BCMA-CAR fused to a complete CD19 CAR, separated by a self-cleaving P2A peptide. We assessed the functional activity of cCAR in co-culture assay with multiple cell lines. We also verified cCAR efficacy with two mouse models, injected with either BCMA-expressing MM.1S cells or CD19-expressing REH cells. In our phase 1 clinical trial, we enrolled patients with hematologic malignancies with antibody mediated disorders.

Results: BCMA-CD19 cCAR exhibited robust cytotoxic activity against the K562 cells engineered to express either CD19 or BCMA in co-culture assays, indicating the ability of each complete CAR domain to specifically lyse target cells. In mouse model study, cCAR-T cells were able to eliminate tumor cells in mice injected with MM.1S cells and REH cells, indicating that both BCMA and CD19 are specifically and equally lysing B cells and plasma cells in vivo, making BCMA-CD19 cCAR a candidate for clinical use.

In our first-in-human clinical trial, the first case is a 48-year-old female patient having resistant B-ALL with high DSA titers. She exhibited complete remission of B-ALL at day 14 post-CAR T treatment. MFI of DSA dropped from 7800 to 1400 at 8 weeks post cCAR treatment, the reduction percentage was approximately 80% (Figure 1). The patient had no CRS, and no neurotoxicity was observed.

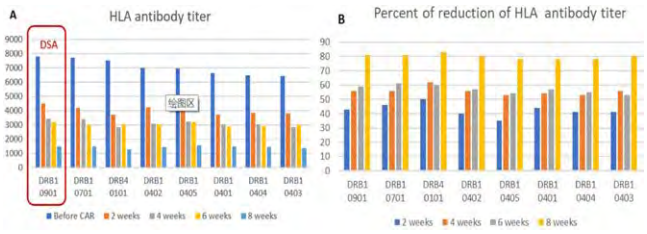


Figure 1. 1. A) MFI of DSA and other HLA antibodies before and at different time points after cCAR T infusion. B) the percent reduction post-transfusion of cCAR T cells at different time points.

The second case is a 41-year-old female patient having a refractory diffuse large B cell lymphoma with bone marrow (BM) involvement. Furthermore, she has a 20 years of SLE, with manifestation of fever dependent of corticosteroids. On day 28 after cCAR treatment, PET/CT scan showed CR, and BM turned negative. In addition, she is independent of steroids, has no fever and other manifestations, C3/C4 are within normal ranges, and all the ANA dropped significantly, especially the nuclear type ANA, which turned from> 1:1000 to be negative at day 64. She had Grade 1 CRS but with no neurotoxicity observed. The absence of B cells and plasma cells persisted more than 5 months post CAR therapy.

Conclusion: Our first in human clinical trial on BCMA-CD19 cCAR demonstrated profound efficacy in reducing DSA levels in an AHSCT candidate and ANA titer in a SLE patient. There was strong clinical evidence of depletion of antibody-producing roots, B-cells and plasma cells in both patients. Our results further suggested that BCMA-CD19 cCAR has the potential to benefit patients receiving solid organ transplants or those with other antibody-mediated diseases.

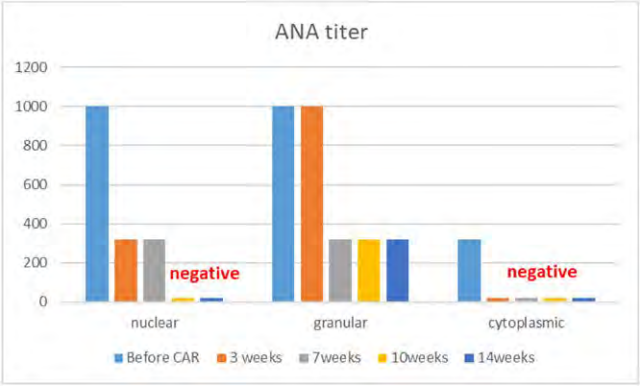


Figure 2. Reduction of different type of ANA titer at different time points.

Acknowledgments: patients and their families

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THU0037 SURVIVIN INHIBITS TRANSCRIPTION OF PBX1 AND SUPPORTS THE EFFECTOR PHENOTYPE OF THE MEMORY CD4 T CELLS IN RHEUMATOID ARTHRITIS

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Background: The oncogenic protein survivin is a marker of severe rheumatoid arthritis (RA). High serum levels of Survivin predict progressive joint damage[1] and poor treatment response[2].
Objectives: To study the role of survivin in the transcriptional regulation of phenotype in $CD4^+$ T cells.
Methods: $CD4^+$ T cells of RA female patients were isolated from the perpheral blood. Activated $CD4^+$ cells were treated with survivin inhibitor YM155. Transcriptional analysis was done by RNAseq (Illumina) and conventional qPCR. Chromatin of CD4 cells was immunoprecipitated using polyclonal antibodies to survivin and subjected to deep sequencing (survivin ChIPseq, Hiseq2000, Illumina) and aligned to GRCh38. Statistical analysis of differentially expressed genes (DEG) was done in R-studio using Benjamini-Hochberg adjustment for multiple testing (Bioconductor, DESeq2 package).
Results: Survivin ChIPseq of the activated $CD4^+$ T cells was enriched with the genes engaged in regulatory transcription factor specific DNA binding (GO:0000987, adj p=0.0005) and RNA polymerase II regulatory transcription (GO:0000978, adj p = 0.0004). Among survivin targets were the genes of HOX-B cluster and TALE family proteins MEIS, PKNOX and PBX1 controlling early leukopoesis and T cell maturation. Inhibition of survivin in PBMC resulted in significant upregulation of PBX1 (p=0.023), MEIS3 (p=0.0036), similar tendency was observed for HOXB6 and HOXC4 genes. RNAseq analysis CD4 cells of RA patients with different transcription of PBX1, identified 1636 genes (adj p<10-5). BIRC5, coding for survivin, was 8.3 folds higher in $CD4^+$ cells with low PBX1 (p=0.0005). Among the core transcription factors of T helper cell differentiation, we identifed NF-kB1 and NF-kB2, TBX21, IRF4, IRF8 and STAT3, BATF and BATF3. This followed by significantly higher TNF, IFNg and IL17A and IL17F in PBX1lo CD4 T cells. The pathway enrichment analysis of DEG identified strong over-representation of cytokine-specific genes (GO:005125, GO:0005126, GO:0048018, GO:0030545, FDR q-values 10^{-12}-10^{-9}). The genes of IL4, IL5, IL13, IL9, IL3 and CSF2 located within the chromosome 5 were common for all GO-lists, and were higher in PBX1lo, but none of those genes was identified by survivin-ChIPseq or PBX1-ChIPseq. Analysis of ChIPseq data identified the genes of STAT3, IRF4, IRF8 and BATF as common targets for PBX1 and survivin.
Conclusion: This genome-wide analysis indicates that survivin regulates transcription of the TALE family protein PBX1 in CD4+ T cells, which has essential effect for differentiation and phenotype of Th subsets. Low PBX1 in RA patients is associated with terminally differentiated effector CD4+ T cells.
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THU0038 DIFFERENTIAL ROLES OF TNFRI AND TNFRII IN THE MORPHOLOGY OF SECONDARY LYMPHOID ORGANS

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Background: Tumour necrosis factor (TNF) induced signaling events are important in lymphoid organ development and function, both in health and in immune-mediated inflammatory diseases such as arthritis. Important receptors involved in this process include TNF receptors (R) I and II that exert distinct functions. Mice overexpressing transmembrane (tm)TNF develop various features of chronic inflammation, including arthritis, that are mediated via TNFRI and/or TNFRII.
Objectives: To investigate the importance of TNFRI and TNFRII in spleen and peripheral lymph node (PLN) morphology in mice overexpressing tmTNF.
Methods: Spleen and PLN were collected from 13 week old mice with the following genotypes: WT, tmTNF transgenic heterozygotes (tmTNF tg HET), WT x $TNFRI^{-/-}$, tmTNF tg HET x $TNFRI^{-/-}$, WT x $TNFRII^{-/-}$ and tmTNF tg HET x $TNFRII^{-/-}$. Spleens were cut and stained by immunofluorescence for B and T cell markers, imaged by confocal microscopy and analyzed using FIJI software. PLN were used for whole mount tissue staining for B and T cell markers, cleared, 3D imaged by light sheet microscopy and analyzed using Imaris software.
Results: Although no macroscopic differences were observed, spleens of tmTNF tg HET animals exhibited an altered morphology characterized by smaller follicles (69,73 ± 72,25 μm^2) compared to spleens of WT mice (139,3 ± 71,36 μm^2), which was accompanied by a decrease in central T cell areas as measured by % of the total follicle (15,22 ± 9,685; WT 26,60 ± 10,46). WT mice lacking either TNFRI or TNFRII had a morphology comparable to WT (follicle size: TNFRI 234,0 ± 166,9 μm^2; TNFRII 154,2 ± 87,92 μm^2; % of T cell area: TNFRI 27,81 ± 11,03; TNFRII 28,14 ± 19,66). tmTNF tg x $TNFRI^{-/-}$ exhibited a normal spleen architecture (follicle size: 239,2 ± 250,5 μm^2; % of T cell area: 29,92 ± 11,46), whereas the spleen follicles of tmTNF tg x $TNFRII^{-/-}$ mice had T cell areas (17,31 ± 8,88) that were comparable to tmTNF tg HET mice.
The size of PLN of tmTNF tg HET mice (3,74 ± 1,31 mm^3) was increased compared to WT (2,41 ± 0,60 mm^3), also in combination with deficiency of TNFRI (3,98 ± 2,07 mm^3) or TNFRII (4,01 mm^3). tmTNF tg HET mice had an increase in absolute B cell volume (0,86 ± 0,33 mm^3) vs WT (0,51 ± 0,07 mm^3) but no change in B cell area as % of total PLN volume. The increased B cell volume was critically dependent on TNF-RII (tmTNF tg HET x $TNFRII^{-/-}$ (14,87). Interestingly, whereas B cell area morphology of tmTNF tg HET, tmTNF tg HET x $TNFRII^{-/-}$ and WT x $TNFRII^{-/-}$ PLN was similar to WT, TNFRI deficiency caused profound alterations in the morphology of the B cell areas that appeared as one peripheral layer of B cells covering a central T cell area rather than properly developed follicles.
Conclusion: The current study demonstrates that overexpression of tmTNF leads to an aberrant spleen architecture, characterized by smaller follicles and a decrease in central T cell areas, which is critically dependent on TNFRI. In addition, overexpression of tmTNF results in enlarged PLN and increased total B cell volume, which is dependent on TNFRII, whereas TNFRI is more important in the proper organization of B cell follicles. Overall, this study employing different state-of-the-art (3D) imaging techniques highlights the importance of tmTNF-TNFR-induced signaling events in secondary lymphoid organ morphology and function, and reveals distinct roles for TNFRI and II. Advancing our knowledge in this field might provide a better understanding of the pathophysiology of TNF-associated diseases such as arthritis, which may be important to develop new or improved treatment strategies.
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THU0039 DECIPHERING DISEASE-RELEVANT T CELL SUBSETS IN RHEUMATOID ARTHRITIS IDENTIFIES A NOVEL CELLULAR SUBSET OF PATHOGENETIC IMPORTANCE IN THERAPEUTIC RESISTANCE.

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Background: Aberrant T cell responses are key in driving autoimmunity and are commonly associated with rheumatoid arthritis (RA). Unravelling pathways of importance in therapeutic partial response and failure is of critical importance, as this will potentially provide new insights into key drivers of immune-mediated pathogenesis.
Objectives: To delineate disease-relevant T cell subsets in RA and assess their potential to act as cellular markers amenable to precision medicine approaches, particularly in the context of therapeutic partial or non-response.
Methods: FACS-based immunophenotyping and ex-vivo functional response profiles of $CD4^+CD161^+CCR2^+CCR5^+$ T cells were performed in peripheral blood mononuclear cells (PBMC) obtained from patients with RA and healthy controls, using previously characterised methodologies. RA patients fulfilled the 2010 ACR/EULAR criteria for RA. All samples were obtained after written consent, with the appropriate ethical approvals in place.
Results: RA patients harboured a higher frequency of $CCR2^+CCR5^+$ cells within the $CD4^+CD161^+$ T cell compartment compared with healthy controls. In RA patients this T cell subset had a higher proportion of cells that secrete pro-inflammatory cytokines such as IL-17A, GM-CSF, IFN-γ, and TNF. Importantly, the $CD4^+CD161^+CCR2^+CCR5^+$ T cell subset was significantly increased in DMARD non-responders compared to both responders and healthy controls. Moreover, in DMARD non-responders, these cells had a propensity to express increased proportions of pro-inflammatory cytokines. Notably, there was also a significant increase in the ratio of effector: regulatory T cell (Teff: Treg) compared to both responders and healthy controls. In addition, the $CD4^+CD161^+CCR2^+CCR5^+$ T cell subset was less responsive to suppression by Tregs. In further support of a role for this T cell population in disease pathogenesis, the frequency of $CD4^+CD161^+CCR2^+CCR5^+$ T cells significantly correlated with disease activity, as measured by the DAS28 (R^2 = 0.65; p = 0.003; n=11).

Conclusion: Combined, our findings suggest that the $CD4^+CD161^+C$-$CR2^+CCR5^+$ T cell subset represents a substantially abnormal T cell subset in RA, exhibiting exaggerated pro-inflammatory responses, numerical abundance relative to Tregs, and resistant to regulation by Tregs. The $CD4^+CD161^+C$-$CR2^+CCR5^+$ T cell subset appears to be a marker of therapeutic response status in RA, via its contribution to disease pathology and highlights this subset as a potential therapeutic target in RA.

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THU0040 PROTEINASE 3-REACTIVE B CELL RECONSTITUTION AFTER TREATMENT WITH RITUXIMAB FOR ANCA-ASSOCIATED VASCULITIS

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Background: Proteinase 3 (PR3)-reactive B cells are present in PR3-ANCA-associated vasculitis (AAV) at levels higher than healthy controls.

Objectives: To evaluate the dynamics of the PR3-reactive B cell repopulation in patients with PR3-AAV after treatment with rituximab, and to analyze possible associations between these immunological changes and long-lasting remissions.

Methods: We analyzed all available frozen peripheral blood mononuclear cells (n=148) from 23 randomly-selected PR3-AAV patients who participated in the RAVE trial and achieved complete remission (BVAS=0, prednisone=0) after treatment with rituximab.

We measured PR3-reactive B cells and the relative subsets by a multi-color flow cytometry panel including CD19, IgD, CD27, CD38, CD24, and a biotinylated PR3 revealed by fluorescent streptavidin. The clinical data of the trial were correlated with flow-cytometry data.

Results: 10/23 (43%) patients relapsed during the follow up, 8/10 relapses were severe. At baseline, clinical features, PR3-ANCA levels, % of total PR3-reactive B cells and PR3-reactive B cell subsets were similar between relapsers and non-relapsers. All patients were followed until the end of the trial, for a mean of 44 months (25-75%IQR 31-54), without difference in follow-up time between relapsers and non-relapsers (p=0.98).

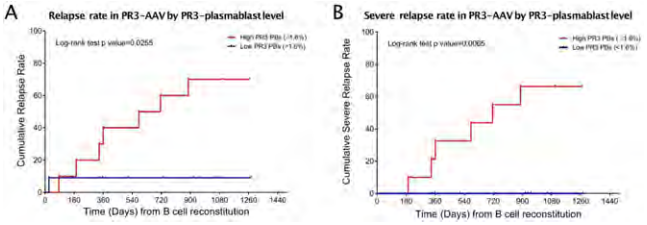
The majority of patients had B cell repopulation at 12 (range 12-24) months after rituximab. At the time of B cell repopulation, transitional (CD19+CD24+CD38+) and naïve (CD19+CD27+IgD-) B cells were higher compared to baseline, while total plasmablasts (PB) were unchanged, and mature B cells significantly decreased in both relapsers and non relapsers. PR3-reactive B cells reappeared in all the patients, and the % of PR3-reactive of B cells were higher at the B cell repopulation visit compared to baseline (5.82% vs 4.25%, p<0.05), while total B cells were lower (66/µL vs 151/µL, p<0.01), regardless of future relapse.

Within PR3-reactive B cells, only the % of PB (CD19+CD27+CD38+PR3+) were higher in relapsers vs. non-relapsers (median [25-75%IQR]; 1.95% [1.315-3.845] vs 0.84% [0.05-1.66], p=0.022) and severe relapsers vs non-severe relapsers (2.165% [1.66-4.315] vs 0.84% [0.1-1.74], p=0.015). Time-to-relapse and time-to severe-relapse were significantly shorter in patients with circulating PR3-PB higher than the median value of the cohort (1.6%) during B cell reconstitution (Figure 1A-B).

Conclusion: In PR3-AAV, during B cell reconstitution after rituximab, the total fraction of PR3-B cells increases, due to the expansion of the transitional and naïve B cell compartments. Circulating PR3-PB within PR3-B cells are enriched in the peripheral blood of relapsing and severely relapsing patients compared to non-relapsing patients. Higher levels of PR3-PB after rituximab during B cell reappearance significantly increased the risk of subsequent relapse and severe relapse.

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THU0041 IFNA AND IL21 PROMOTE DISTINCT POPULATIONS OF EFFECTOR B CELLS

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Background: B cells play a crucial role in the pathogenesis of systemic autoimmunity through various effector functions, including auto-antibody production, secretion of pro-inflammatory cytokines and antigen presentation to T cells. Interferon alpha (IFNα), mainly produced by innate cells (Menon et al., 2016), and interleukin (IL)-21 which is secreted by follicular helper T cells (Berglund et al., 2013), promote the generation of auto-reactive IgG-secreting plasma cells. However, it is suggested that IFNα participate also to the generation of regulatory B cells.

Objectives: To further understand the disturbing microenvironmental signals leading to autoimmune diseases, we aim to define a coherent framework integrating the B-cell subsets having different ability to respond to microenvironmental signals, and the signalling pathways driving the differentiation and the functional fate of B cells.

Methods: Naïve and several populations of memory B cells were isolated from peripheral blood of healthy donors and differentiated *in vitro* in the presence of IL21 or IFNα. The phenotype and the expression of transcription factors were analysed by flow cytometry and molecular identity of these cells was further determined by transcriptomic approaches. Functional analyses were performed to assess the effector functions of B cells and their potential regulatory effects on T cells.

Results: IFNα, in synergy with CpG, promote the generation of $CD27^{high}$ $CD38^{high}$ plasmablasts (PB), mainly arising from memory subsets, but not IL21. However, IFNα and IL21 induce the transcriptional program of B-cell differentiation by up-regulating IRF4 and Blimp1 expression. Unlike IFNα, IL21 drive the expansion of $CD11c^+$ T-bet^+ cells only from switched memory subsets, suggesting T-bet may be a footprint of long-lived memory B cells.

Even though subtle differences were observed in the antibody production between IFNα and IL21-stimulated memory B cells, naïve cells secreted less amount of IgM and IL10 when stimulated with IL21.

Transcriptomic studies are still in progress to further define the molecular profile of those distinct effector B cells.

Conclusion: Taken together, these findings suggest that IFNα promote a rapid differentiation of B cells into IL10 and Ig-secreting PB whereas IL21 contributes to the generation of T-bet^+ atypical pre-PB that may have a role in chronic autoimmune disorders.

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THU0042 DIFFERENTIAL EFFECT OF ABATACEPT VS TNF BLOCKERS, ON THE FREQUENCY OF CIRCULATING FOLLICULAR HELPER (TFH) AND PERIPERAL HELPER (TPH) T CELLS IN RHEUMATOID ARTHRITIS

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Background: CXCR5+PD-1^{hi} follicular helper (Tfh) and CXCR5-PD-1^{hi} peripheral helper (Tph) T cells play an important role in the pathogenesis of Rheumatoid Arthritis (RA) by providing help to autoantibody secreting B cells. Whereas Tfh cells typically dwell in the germinal centers of lymphoid organs, Tph cells accumulate at inflamed tissues. An increased frequency of Tph cells and of circulating counterparts of Tfh cells have been described in the peripheral blood of patients with seropositive RA.
Objectives: To examine the effect of treatment escalation using biological agents (TNF blockers or abatacept), on the frequency of circulating Tfh (cTfh) and Tph (cTph) cells in RA.
Methods: Peripheral blood was drawn from seropositive RA patients with an incomplete response to csDMARDS (n=29) who initiated biological therapy with TNF blockers (TNFb) (n= 17) or abatacept (n= 12), prescribed based on routine clinical practice. cTfh and cTph cell frequencies were determined by flow cytometry of freshly isolated PBMCs at the basal visit and 6 months after starting treatment escalation. For each patient, an age and gender-matched healthy control (HC) was also studied at both time points (n=29).
Results: As compared with HC, active RA patients receiving csDMARDs demonstrated a baseline increased frequency of both cTfh and cTph cells. A significant improvement of disease activity as determined by the DAS28 score (ΔDAS28>2.0) was apparent in all of the patients 6 months after initiating biologicals. At that time point, a significant reduction of the previously elevated cTph cell frequency was observed in both treatment groups. However, cTfh cells remained elevated in patients receiving TNFb notwithstanding a good therapeutic response, whereas subjects receiving abatacept experienced a significant abatement of their cTfh cell frequency. Experimental variation of the cTfh and cTph cell numbers in HC was minimal.
Conclusion: Abatacept but not TNFb, are able to bring down cTfh cell numbers in RA. This indicates that costimulation blockade can help attain an immunological remission, whereas TNF neutralization may allow a persistent pathogenic germinal center overactivity. At the same time, treatment with both abatacept and TNF blockers results in a downmodulation of the previouly elevated cTph cell numbers, in parallel with the remitting local joint inflammation.
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Disclosure of Interests: Paula Fortea-Gordo Grant/research support from: BMS, Diana Peiteado: None declared, Alejandro Villalba: None declared, Maria-Jose Santos-Bornez Grant/research support from: BMS, Laura Nuño: None declared, Irene Monjo: None declared, Alejandro Balsa Grant/research support from: BMS, Roche, Consultant of: AbbVie, Gilead, Lilly, Pfizer, UCB, Sanofi, Sandoz, Speakers bureau: AbbVie, Lilly, Sanofi, Novartis, Pfizer, UCB, Roche, Nordic, Sandoz, Maria-Eugenia Miranda-Carus Grant/research support from: BMS, Roche
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THU0043 EXPRESSION OF B CELL CHEMOKINE-CHEMOKINE RECEPTOR PATHWAYS IS ALTERED IN GIANT CELL ARTERITIS

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Background: The presence of organised B cells in both cranial-giant cell arteritis (C-GCA) (temporal artery) and large vessel (LV)-GCA (aorta) has previously been documented. The number and the extent of organisation of B cells in tertiary lymphoid organs (TLO) was more prominent in the aorta than in the temporal artery, suggesting possible differences in B cell phenotype, kinetics and tropism between C-GCA and LV-GCA.
Objectives: We sought to analyse B cell differentiation subsets in both C-GCA and LV-GCA and to investigate differences in the expression of chemokine pathways involved in B cell migration and TLO organisation.
Methods: Blood was collected from C-GCA (n=11) and LV-GCA (n=22) patients at baseline, before start of glucocorticoid treatment, and after 3 months of treatment. The LV-GCA groups consisted of 11 patients with isolated LV-GCA and 11 patients with overlap LV/C-GCA. Also, age- and sex- matched healthy controls (HC, n=24) were included. The following chemokines were measured with Luminex in the sera of patients and HC: BAFF, CCL19, CCL21, CXCL9, CXCL10, CXCL11, CXCL12, and CXCL13. Thawed PBMC of 7 C-GCA, 10 LV-GCA and 24 HC were stained with antibodies against CD19, CD27, IgD, IgM, CD38, CXCR3, CXCR4, CXCR5, and CCR7 to allow identification of B cell differentiation subsets and their chemokine receptor expression.
Results: We found a lower absolute number of CXCR3+ memory and double negative (late stage) B cells in GCA patients when compared to healthy controls. Also, the absolute number of CXCR5+ memory B cells was lower in patients than in controls. Chemokine receptor expression on circulating B cells did not significantly differ between C-GCA and LV-GCA at baseline. After 3 months of treatment, frequencies and absolute numbers of both CXCR3+ and CXCR5+ memory B cells increased. In sera of all GCA patients, CXCL9 (which is a chemokine involved in migration of B cells to sites of inflammation) and CXCL13 (which is involved in local organization of B cells) were significantly increased. BAFF and CCL21 were increased only in LV-GCA when compared to HC. Serum chemokine levels did not differ between C-GCA and LV-GCA patients. An inverse correlation was observed between B cell counts and CXCL9 as well as CXCL13 in LV-GCA, only. After 3 months of treatment, CXCL9 levels remained elevated whereas CXCL13 increased even further.
Conclusion: At diagnosis, CXCL9 and CXCL13 were significantly increased in all GCA patients as compared to HC. Elevated CXCL9 levels inversely correlated with B cells numbers in LV-GCA, only, which may suggest that B cells preferentially migrate to the inflamed aorta via a mechanism involving CXCL9. In addition, CXCL13 may be linked to local TLO organization in LV-GCA. Currently, we are studying the local expression of chemokines and chemokine receptors at the site of inflammation in both C- and LV-GCA.
Disclosure of Interests: Jacoba Graver: None declared, Annemieke Boots Consultant of: Grünenthal Gmbh until 2017, Wayel Abdulahad: None declared, Johan Bijzet: None declared, Daphne Wolbers: None declared, Elisabeth Brouwer Consultant of: Roche (consultancy fee 2017 and 2018 paid to the UMCG), Speakers bureau: Roche (2017 and 2018 paid to the UMCG), Maria Sandovici: None declared
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THU0044 SINGLE CELL ANALYSIS OF BONE MARROW AND PERIPHERAL ALTERED B CELL DIFFERENTIATION IN PATIENTS WITH ACTIVE SLE AND THE MECHANISM OF ABNORMAL EARLY B CELL DEVELOPMENT

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Background: B cell differentiation and dysfunction play a key role in the pathogenesis of Systemic lupus erythematosus (SLE). Bone marrow (BM) is the development organ of B cells, and also the home and residence place of plasma cells and memory B cells. However, there is a lack of studies on B cells in BM with lupus.
Objectives: To map the development of BM and peripheral B cells and investigate the mechanism of abnormal early B cell development in SLE.
Methods: A total of 11 SLE patients and 5 age- and sex-matched controls were recruited.BM and peripheral B cell subsets were measured by flow cytometry. sorting-purified B cell subsets were subject toSingle-cell RNA sequencing (scRNA-seq) and functional studies. Plasma cytokines and secreted immunoglobulins were detected by Luminex or ELISA. Disease activity of SLE patients was measured using the SLE Disease Activity Index (SLEDAI).
Results: In the present study, we find out that the percentage of monocytes in MNC (p=0.070) and plasma cells(p=0.001)in CD19+ were significantly decreased in BM of SLE, compared to healthy controls. While, SLE patients had increased T%MNC(p=0.008) and B%CD19+(p=0.002) in BM that controls. In detail, the B cell subsets of bone marrow in patients with active lupus (SLEDAI≥8 score) were seriously disordered, showing the increasing T%MNC(p=0.049), propre-B%CD19+ (p=0.006)and immature B cell%CD19+ (p=0.010) than healthy donors. propre-B%CD19+ exhibited good relationship with SLEDAI. By

integrating single B cell expression profiling and repertoire analysis, we map the development of B cells in BM and peripheral and pathogenic characteristics of early B cells, especially propre-B.

Conclusion: These findings demonstrated that early B cells in BM, especially propre-B are abnormally differentiated with dysregulations. BM is an important organ targeted by SLE. This studyis not only to clarify the internal mechanism of the disorder of differentiation of B cells, but also to provide new clues for the targeted diagnosis and treatment of SLE.

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Disclosure of Interests: None declared

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THU0045 IDENTIFICATION OF NOVEL CENTROMERE AUTOANTIGENS IN SJÖGREN'S SYNDROME, SYSTEMIC SCLEROSIS AND PRIMARY BILIARY CHOLANGITIS.

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Background: Anti-centromere antibodies (ACA) are detected in the serum of patients with various autoimmune diseases including Sjögren's syndrome (SjS), systemic sclerosis (SSc) and primary biliary cholangitis (PBC). ACA positivity is correlated with clinical manifestations such as Raynaud's phenomenon and sclerodactyly and these features are commonly seen across diseases. Although CENPB is thought to be the major antigen against ACA, autoimmune features of other centromere proteins have not been fully evaluated.

Objectives: The aim of this study is to elucidate centromere autoantigens comprehensively and clarify their association with pathogenesis of SjS, SSc and PBC.

Methods: A centromere protein library was created by cloning 6 single proteins and 10 complexes consisting of 35 proteins belonging to human centromere region. The centromere antigens were immobilized on beads and incubated in the serum of patients with SjS (n = 86), SSc (n = 35), PBC (n = 10), patients with two or more diseases above (n = 44), and healthy volunteers (n = 68). Autoantibodies to each centromere protein were analyzed by flow cytometry.

Results: Patients had a wide variety of antibodies against most of centromere antigens including 4 newly identified autoantigens. The hierarchical clustering of each antigen distinguished 2 antigen clusters. The reactivity of autoantibodies against a centromere protein of one cluster was mutually correlated regardless of disease types, indicating that these proteins/protein complexes might be the target of ACA. In addition, our method enabled us to detect sera reacted against multiple centromere antigens in some of the ACA-negative patients with existing methods.

Conclusion: We identified 4 novel centromere autoantigens and our data suggested that the main target of ACA was the protein complex rather than a single specific antigen in SjS, SSc and PBC patients. Using the combination of centromere proteins may be useful to detect ACA with higher sensitivity.

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THU0046 A PIPELINE TO STUDY ANTIGEN-SPECIFIC CD4+ T CELLS IN RHEUMATOID ARTHRITIS

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Background: Autoimmunity to citrullinated autoantigens forms a critical component of disease pathogenesis in rheumatoid arthritis (RA). Presence of anti-citrullinated protein antibodies (ACPAs) in patients has high diagnostic value. Recently, several citrullinated antigen specific CD4+T cells have been described. However, detailed studies of their T-cell receptor usage and in-vivo profile suffer from the disadvantage that these cells are present at very low frequencies. In this context, we here present a pipeline for TCR repertoire analysis of antigen-specific CD4+T cells from RA patients, including both citrulline and influenza (control) specificities using in-vitro peptide challenge induced-cell expansion.

Objectives: To enable studies of the T cell repertoire of citrullinated antigen-specific CD4+T cells in rheumatoid arthritis

Methods: Peripheral blood mononuclear cells (PBMCs) (n=7) and synovial fluid mononuclear cells (SFMCs) (n=5) from HLA-DR*0401-postive RA patients were cultured in the presence of citrullinated Tenascin C peptide cocktails or influenza peptides (positive control). Citrulline reactive cells were further supplemented with recombinant human IL-15 and IL-7 on day 2. All cultures were replenished with fresh medium on day 6 and rIL-2 was added every 2 days from then. Assessment of proportion of peptide-HLA-tetramer positive cells was performed using flow cytometry whereby individual antigen-specific CD4+T cells were sorted into 96-well plates containing cell lysis buffer, followed by PCR-based alpha/beta TCR sequencing. TCR sequencing data was demultiplexed and aligned for TCR gene usage using MiXCR. Some tetramer positive cells were sorted into complete medium containing human IL-2 and PHA for expansion of antigen-specific cells. Cells were supplemented with irradiated allogenic PBMCs (30 times number of antigen specific cells). Clones of antigen specific CD4+T cells were further subjected to tetramer staining to confirm expansion of cells.

Results: As evidenced by increase in frequency of tetramer positive CD4+T cells, in vitro peptide stimulation resulted in expansion of both influenza specific (Fig. 1a) and citrullinated antigen specific (Fig. 1b) CD4+T cells. Polyclonal in-vitro expansion of tenascin C tetramer positive sorted cells followed by tetramer staining further confirmed antigen specificity and enrichment for antigen specific CD4+T cells after polyclonal stimulation (Fig.1c). TCR repertoire analysis in PB and SF dataset from the first patient showed clonal expansion of influenza specific cells in both sites. Synovial fluid had more diversity of expanding clones as compared to paired PB, with few expanded clones being shared among SF and PB. We observed a more diverse TCR repertoire in citrulline specific CD4+T cells. We also observed sharing of TCR alpha chains among different citrulline specific CD4+T cell clones.

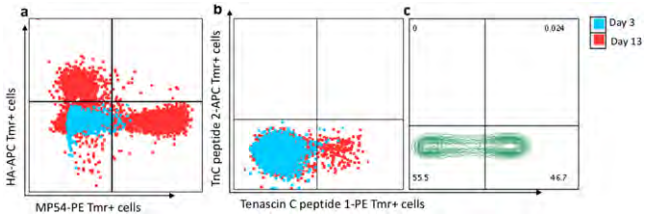


Fig. 1 ***In-vitro*** **expansion of antigen specific CD4+T cells:**

Conclusion: This method provides a highly suitable approach for investigating TCR specificities of antigen specific CD4+T cells under conditions of low cell yields. Building on this dataset will allow us to assess specific features of TCR usage of autoreactive T cells in RA.

PBMCs were cultured in presence of (a) influenza (HA, MP54) and (b) citrullinated tenascin peptides. The proportion of antigen specific CD4+T cells was assessed using HLA-class II tetramer staining. We observed an increase in frequency of (a) Infleunza specific cells (red dots in upper left and lower right quadrants) and (b) citrullinated tenascin C specific cells (red dots in lower right quadrant), at day 13 post culture as compared to day 3. (c) Sorting of citrullinated

tenascin specific CD4+T cells, followed by PHA expansion resulted in visible increase in proportion of citrullinated tenascin specific CD4+T cells.
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THU0047 THE SYNOVIUM REWIRES AN IMMUNOLOGICAL RHEOSTAT THAT DEFINES TWO FUNCTIONALLY DISPARATE PATHOGENIC CD4+HLA-DR+ SUBSETS IN HUMAN ARTHRITIS

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Background: Despite advances in understanding how the adaptive T cell landscape is affected in human arthritis, specific T cell subset knowledge has yet to be utilised in clinical settings. We have previously discovered within active arthritic patients, a circulating pathogenic-like lymphocyte (CPLs; CD4+HLA-DR+) within the T-effector compartment, that is phenotypically similar to their synovial counterparts. CPLs are inflammatory, correlate with disease activity and overlap in synovial TCR repertoire. A similar inflammation-associated T-regulatory (iaTreg; CD4+HLA-DR+) subset, that is activated, poised to migrate to inflamed site and sharing synovial TCR overlap, suggest a common disease ontogeny that may exist between CPLs and iaTregs.
Objectives: Here we seek to determine whether and how the synovial microenvironment plays a role in modulating these two functionally divergent (Teff/Treg compartments) yet pathogenically homologous subsets. This modulation, akin to an immunological rheostat, may be a feature of the disease process.
Methods: We examined CD45+ immune cells from synovial and PBMCs (active JIA, inactive JIA, paediatric healthy) through mass cytometry (CyToF). CD4 T cells were sorted into CPLs, iaTregs, Teff and Treg through FACS Aria II, from active JIA PBMCs, paired JIA SFMCs and healthy paediatric PBMCs and examined through ngRNASEQ.
Results: Mass cytometric analysis reveal a significant enrichment of synovium signatures in both circulatory CPLs and iaTregs subsets from active arthritic PBMCs, as compared with the conventional pool of Teff/Tregs. This immunological relationship between CPLs/iaTregs is reaffirmed by comparative differential gene expression (DEG) and phylogenetic tree analysis, which indicated transcriptomic convergence between circulatory pathogenic CPLs/iaTreg subsets and divergence from their respective conventional Teff/Treg pools. Circulatory CPLs/iaTregs exhibit (a) common pathway dysregulation in T cell signalling, (b) restriction in TCR oligoclonality and (c) common transcription factor drivers within the gene regulatory network, suggesting a common pathogenic mechanism acting on these two disparate compartments.
To understand how the microenvironment plays a role in modulating these two subsets, we compared the transcriptome of CPLs/iaTreg and conventional Teff/Treg subsets from (a) healthy PBMCs, (b) JIA PBMCs and (c) paired JIA SFMCs. The convergence between CPLs/iaTreg increases across the spatial/disease continuum, culminating in 7 key common dysregulated pathways within synovium CPLs/iaTregs. Importantly we detected higher clonotypic sharing of TCRs in CPLs/iaTregs across the spatial and disease continuum, suggesting a common precursor driven by antigenic selection.
Conclusion: Our data suggest that CPLs/iaTregs are dichotomic components of a systemic immune rheostat, shape through the synovium environment, modulating autoimmunity in human arthritis. As iaTreg and CPL most likely have the capacity to morph into each other, the molecular crossroads which control this plasticity represent novel therapeutic targets.
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THU0048 THE FUNCTION CHANGES OF SNPS IN THE P2X7 RECEPTOR BY ALA348TO THR, GLU496TO ALA A ND ARG307TO GLN IN THP-1 CELLS WITH HIGH URIC ACID

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Background: Previous studies[1] have shown that ATP acts on the sputum receptor P2X ligand-gated ion channel 7 (P2X7R) as a second signal to induce gouty arthritis.
Objectives: In this study, the functional changes of three SNP genotypes, Ala348 to Thr, Glu 496 to Ala and Arg307 to Gln, in P2X7R were analyzed with high uric acid.
Methods: After transfection of HEK-293T cells by lentivirus, observing the uptake ability of HEK-293T cells to ethidium bromide. The effect of three different mutants on the P2X7 receptor was thus observed on the P2X7 channel. In addition, THP-1 cells were also transfected, stable expression of a THP-1 cell line that has been transfected with a wild-type or different mutants and thus established. Then three types were set up separately, and each type was randomized into three groups: MSU(labeled M), MSU+ATP (labeled MA), and unstimulated control group (labeled C).Detection of IL-1β protein expression level in serum by ELISA and NLRP3, ASC and Caspase-1 mRNA levels in transfected THP-1 cells by qRT-PCR.
Results:

1. These three variants have different effects on the uptake function of ATP-induced ethidium^{+} bromide in transfection of HEK-293T cells by lentivirus. Ala^{348}to Thr increased $P2X_7$-dependent ethidium^{+} bromide uptake (145% of wild-type $P2X_7$ response, P<0.001). In contrast, Absent or very reduced $P2X_7$ function was found in Glu^{496}to Ala and Arg^{307}to Gln subjects, appeared to abolish $P2X_7$-dependent dye uptake (38% and 32% of wild-type $P2X_7$ responses, P<0.001,), who were compared with wild-type.
2. Compared the IL-1β levels of the three variants with the wide-type and empty virus in THP-1 cells, the Ala^{348}to Thr mutation significantly up-regulated the serum levels of IL-1β compared with the wide-type and empty virus in group MA with high uric acid (P=0.0007;P=0.013, respectively). Moreover, similar results have also been shown in IL-1β mRNA expressions (P=0.0334; P=0.0307, respectively). The Glu^{496}to Ala and Arg^{307}to Gln mutations down-regulated the serum levels of IL-1β compared with the wide-type in group MA (P=0.0189;P=0.0164, respectively).
3. NLRP3 mRNA was significantly increased in the Ala^{348}to Thr mutation compared with the wide-type and empty virus in group MA (p =0.0003;P=0.0001, respectively). However, NLRP3 mRNA was significantly reduced in the Glu^{496}to Ala and Arg^{307}to Gln mutations compared with the wide-type in group MA (p =0.0294;P=0.0279, respectively).
4. Wild-type was signifcantly higher than empty virus in the ASC gene expression in group MA(P=0.0022). Morever, the Ala^{348}to Thr mutation was higher than empty virus while Arg^{307}to Gln mutation was lower than that in group MA (P=0.0138;P=0.0283, respectively).
5. Unlike NLRP3 gene expression, the data showed that the expression of caspase-1 mRNA in group C, M and MA all with no statistical significance, respectively (P>0.05).

Conclusion: Our data revealed that Ala^{348}to Thr up-regulate the functional status of P2X7R and Glu ^{496}to Ala and Gln^{460}to Arg down-regulate the functional status of P2X7R, which resulted in a significant increase or decrease in IL-1β and NLRP3 expression levels with high uric acid.
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THU0049 DISTINCT EXPRESSION OF COINHIBITORY MOLECULES ON ALVEOLAR T CELLS IN PATIENTS WITH RHEUMATOID ARTHRITIS- AND IDIOPATHIC INFLAMMATORY MYOPATHIES-ASSOCIATED INTERSTITIAL LUNG DISEASE

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Background: Interstitial lung disease (ILD) is a common extra-articular manifestation of rheumatoid arthritis (RA) and also the most common non-musculoskeletal manifestation of idiopathic inflammatory myopathies (IIM), including polymyositis, dermatomyositis and clinically amyopathic dermatomyositis.

Previous studies have suggested that alveolar macrophages (AMs) and T cells are associated with the pathogenesis of ILD. Recently, it is reported that coinhibitory molecules are expressed at the site of inflammation such as RA synovium; however, detailed lung immunophenotyping has not been reported.

Objectives: To identify immunologic factors in the lungs of patients with RA-associated ILD (RA-ILD) and IIM-associated ILD (IIM-ILD) and to examine their pathological mechanisms.

Methods: A total of 11 patients with RA-ILD, 16 with IIM-ILD, and 6 with drug-induced ILD (DI-ILD) and 8 healthy controls were enrolled. Peripheral blood and bronchoalveolar lavage fluid (BALF) were immunophenotyped by flow cytometry. AMs were analyzed by RNA-sequence and coculture assay with peripheral naïve CD4+ T cells of healthy individuals.

Results: Several coinhibitory molecules were coexpressed on BALF T cells in the order of CTLA-4, PD-1, Tim-3, and LAG-3 from most to least, whereas only PD-1 was expressed on peripheral T cells among them. In RA-ILD, PD-1+ and Tim-3+ CD4+ T cells in the BALF were increased. PD-1+CD4+ T cells populations correlated differentiated B cells and Tim-3+CD4+ T cells populations correlated with ILD severity and RF titer. In contrast, in IIM-ILD, activated CD8+ T cells were increased and they coexpressed CTLA-4, PD-1 and Tim-3. BALF PD-1+CD4+ T cells rarely expressed CXCR5, and they positively correlated with plasmablasts and plasma cells, indicating most of them are considered Tph cells. In the coculture experiments, AMs of RA-ILD and IIM-ILD induced more PD-1 and Tim-3 on CD4+ T cells, suggesting that coinhibitory molecule expression on BALF T cells was partly due to AMs. In RNA-sequence, PD-ligand (PD-L) 1 and PD-L2 genes were significantly downregulated in AMs from RA-ILD compared with DI-ILD.

Conclusion: We identified T cell subsets that play a central role in the pathogenesis of RA-ILD and IIM-ILD; PD-1 on T cells in RA-ILD and Tim-3 on CD8+ T cells in IIM-ILD might be key factors in the disease process. The evaluation of coinhibitory molecules on BALF T cells could be clinically useful.

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THU0050 CXCL13 IS A KEY DRIVER FOR MIGRATION AND DIFFERENTIATION OF REGULATORY B CELLS

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Background: Regulatory B cells in human still need to be characterized. Given the absence of a phenotypical definition of these cells, a functional definition based on their ability to secrete IL-10 is often used (corresponding to B10+ cells). Chemokine receptors (CKR) profiles are useful to characterize some populations of T cells but have never been explored among $B10^+$ cells. Moreover, very little is known about $B10^+$ cell migration. Chemokines (CK) have also been implicated in the differentiation of naïve T cells towards regulatory T cells.

Objectives: Therefore, the aims of our study were to first characterize the profile of CKR on $B10^+$ cells, and second to investigate CK implicated in their migration and differentiation, this, both in control (CTL) and in patients with rheumatoid arthritis (RA).

Methods: B cells were isolated with Rosette Sep Human B cells enrichment followed by Ficoll separation. B cells were then activated 24 hours with CpG and CD40L to generate $B10^+$ cells. IL-10 secretion from B cells was assessed by FACs and ELISA. We compared the expression of several CKR between $B10^+$ and IL-10^{neg} B cells ($B10^{neg}$) from CTL and RA patients by flow cytometry. For migration assay, $B10^+$ and $B10^{neg}$ cells were sorted by FACSaria. Their ability to migrate, in response to ligand of CKR found differentially expressed in the first part (CCL21, CCL22, CXCL11, CXCL12 or CXCL13) or synovial fluid (SF) from RA patients, were evaluated by migration assay in 5µM Transwell chambers and expressed as fold increase compare to basal migration towards control media.

Results: $B10^+$ cells expressed a different profile of CKR compared to $B10^{neg}$ both in CTL and RA patients and these profiles differed between $B10^+$ cells of CTL and RA patients. However, no CKR profile could phenotypically define $B10^+$ cells. Of note, CXCR5 was under-expressed on $B10^+$ cell surface compared to $B10^{neg}$ in CTL (75% [IQR 72.9-81.4] positive cells among $B10^+$ vs 99.2% [98.4-99.4] positive cells among $B10^{neg}$, p=0.006, n=10) and also in RA patients (78.3% [70.8-82.3] vs 98.2% [96.9-99.54, p=0.008, n=8). Nevertheless, mRNA expression of CXCR5 was higher among $B10^+$ versus $B10^{neg}$ cells in CTL and RA patients. As CpG-stimulated cells over-expressed CXCL13, ligand of CXCR5, we hypothesized that the binding of its ligand induced the internalisation of CXCR5. Indeed, among all CK tested, only CXCL13, attracted significantly more $B10^+$ than $B10^{neg}$ from CTL (9.1[5.6-14.6] fold increase migration of $B10^+$ vs 5.2 [3.1-7.5] fold increase migration of $B10^{neg}$, p<0.0001, n=21). This was also true in RA patients (10.9 [3.6-29.9] fold increase migration of $B10^+$ vs 4.8[2.1-7.7] fold increase migration of $B10^{neg}$, p=0.009, n=12). SF from RA patients induced a significant migration of $B10^+$ cells in CTL (7.3-fold increase [4.1-21.7], p=0.004, n=9) and RA patients (5.7-fold increase [2.3-7.9], p=0.008, n=10). This migration was correlated with the levels of CXCL13 in these SF, in CTL (r=0.7, p=0.05, n=9) but not in RA patients (n=10). Lastly, CXCL13 was also found to increase IL-10 secretion in B cells stimulated with CpG in CTL (1.5-fold increase [1.3-1.5], p=0.0002, n=13) and in RA patients (1.2-fold increase [1.1-1.3], p=0.005, n=12).

Conclusion: We showed that CXCL13 is a key driver for migration and differentiation of B10+ cells in CTL and in RA patients. However, the migration of $B10^+$ cells in RA patients was not correlated with the level of CXCL13 in SF from RA patients, suggesting the implication of other CK in the migration of $B10^+$ cells in RA.

Disclosure of Interests: None declared

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THU0051 LOW-DOSE INTERLEUKIN-2 SELECTIVELY EXPAND AND ACTIVATE REGULATORY T CELLS ACROSS 13 AUTOIMMUNE DISEASES.

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Background: Regulatory T cells (Tregs) prevent autoimmunity and control inflammation. As low-dose interleukin-2 (ld-IL2) expands and activates Tregs, it has a broad therapeutic potential for any autoimmune or inflammatory disease (AIID). We performed a disease-finding "basket trial" (TRANSREG NCT01988506) in patients affected by one of 11 different AIID and reported the outcome of the first 46 patients (*Rosenzwajg et al, ARD 2019*).

Objectives: Here we analyzed and discussed results from deep immunophenotyping, of 78 patients, to comprehensively study the effect of ld-IL2 on the immune system of patients affected by various AIID

Methods: We performed a prospective, open label, phase I-IIa study in 78 patients with a mild to moderate form of one of 13 selected AIID. All patients received ld-IL2 (1 million IU/day) for 5 days, followed by fortnightly injections for 6 months. Deep immunophenotyping was performed before and after 5 days of ld-IL2.

Results: ld-IL2 significantly expands both memory Tregs as well as naïve Tregs, including recent thymic emigrant Tregs. It also activates Tregs as demonstrated by the significantly increased expression of HLA-DR, CD39, CD73, GITR, CTLA-4. Similar results were observed across the different AIID.

Conclusion: ld-IL2 "universally" improves Treg fitness across 13 autoimmune and inflammatory disease.

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THU0052 RELATIONSHIP BETWEEN INTERFERON-Γ-PRODUCING IMMUNOCOMPETENT CELLS AND DISEASE ACTIVITY IN ADULT-ONSET STILL'S DISEASE

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Background: In the acute phase of adult-onset Still's disease (AOSD), elevated levels of proinflammatory cytokines including interferon-γ (IFN-γ) are shown. Moreover, IFN-γ impacts on activating macrophages which play a crucial role in the pathogenesis of AOSD. Natural killer (NK) cells and T helper cells are in charge of secreting IFN-γ in the innate and adaptive immune systems of disease, respectively. However, the features of their IFN-γ-producing variation depending on disease activity are still uncertain in AOSD.
Objectives: We investigated characteristics of IFN-γ-producing $CD4^+$ T cells and NK cells in patients with AOSD.
Methods: Twenty-four patients in the acute phase of AOSD (active AOSD), 8 of them after treatment (remission), and 12 healthy controls (HC) were recruited in this study. Peripheral blood mononuclear cells and serum samples were provided from them for the experimental analysis. Flow cytometry was used for analyzing $CD4^+$ T cells, $CD4^+$ regulatory T cells (Tregs), NK cells, and their intracellular IFN-γ expression levels as well as suppression assay of Tregs. The serum concentration of interleukin-18 (IL-18) was measured using commercially available ELISA kit. Relationship between the analyzed data and clinical findings related to disease activity were statistically evaluated.
Results: IFN-γ expression in $CD4^+$ T cells was significantly higher in active AOSD than in HC ($p < 0.05$). Tregs also significantly indicated higher expression of IFN-γ in active AOSD than in HC ($p < 0.0001$); and moreover, Tregs were significantly impaired in their suppression ability ($p < 0.05$). In both $CD4^+$ T cells and Tregs, expression of IFN-γ was significantly correlated with serum ferritin levels in active AOSD ($p < 0.05$). IFN-γ expression in $CD4^+$ T cells was significantly higher in patients with splenomegaly than those without that ($p < 0.05$). The proportion of NK cells was significantly lower in active AOSD than in HC ($p < 0.005$), whereas IFN-γ expression in NK cells was significantly higher in active AOSD than in HC ($p < 0.0005$). The number of NK cells and IFN-γ-expressing NK cells had inverse relationship with serum ferritin levels in active AOSD ($p < 0.05$ and $p < 0.005$, respectively). Increased number of NK cells and their decreased expression of IFN-γ were significantly demonstrated in remission ($p < 0.05$). In the analyses of NK cell subsets, lower expression of IFN-γ in $CD56^{bright}$ NK cells and higher that in $CD56^{dim}$ NK cells were significantly indicated in active AOSD than HC ($p < 0.05$). In remission, IFN-γ expression was significantly decreased in $CD56^{dim}$ NK cells ($p < 0.05$) despite no significant recovery of that in $CD56^{bright}$ NK cells ($p = 0.311$). Meanwhile, increased expression of IFN-γ in $CD56^{bright}$ NK cells was demonstrated in only patients who were treated with biologics. Although serum levels of IL-18 were significantly higher in active AOSD than in remission and HC; however, they had no significant correlations with any analyzed data.
Conclusion: $CD4^+$ T cells and NK cells promote IFN-γ expression in the acute phase of AOSD. Meanwhile, increased expression of IFN-γ in $CD4^+$ T cells and decreased number of NK cells were correlated with serum ferritin levels, suggesting that they are indicators of disease activity. Furthermore, high disease activity may impact on the alteration of IFN-γ-producing balance in two distinct population of NK cells, and the plasticity of Tregs leading to defect in suppression ability.
Disclosure of Interests: None declared

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THU0053 CONTRIBUTION OF DEFECTIVE NON-APOPTOTIC FAS SIGNALING TO IMMUNE DYSREGULATION IN AUTOIMMUNE LYMPHOPROLIFERATIVE SYNDROME (ALPS)

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Background: ALPS patients show impaired generation of humoral memory for T independent antigens whereas they generate memory for self-antigens due to impaired FAS-dependent removal of autoreactive germinal center B cells. It is known that FAS signaling via caspase activation results in cell apoptosis. However, FAS ligation may also initiate or modulate non-apoptotic signaling as shown for example by its ability to activate NF-κB. Recent data implicate a regulatory role of FAS in the modulation of mTOR signaling in ALPS double-negative T cells. Moreover, a recently described C194V FAS mutation disturbs its post-translational modification leading to impaired apoptosis induction while non-apoptotic signalling is still intact. Consequently, C194V FAS protects from the autoimmune phenotype in the murine ALPS system. This supports the view that FAS may prevent autoimmunity with other mechanisms than inducing apoptosis.
Objectives: We hypothesize that FAS mutations impair this modulatory signaling, leading to hyper-activation of B cells. Therefore we aim to investigate non apoptotic FAS signaling in B cells derived from healthy individuals and ALPS patients.
Methods: We studied resting and activated B cells in ALPS patients in presence or absence of FAS ligand by flow cytometry analysing relevant molecules to the CD40 signaling pathway. We used mass cytometry to perform functional phenotyping of B cells isolated from secondary lymphoid organs. Proteomic studies were performed to identify potential signaling circuits and RNA sequencing to study the consequences of FAS signaling on B cell fate.
Results: In CD40L activated B cells, FAS signaling results in specific modulation of the mTOR signaling pathway. This modulation is absent in ALPS derived B cells. In line with these data germinal center B cells and plasmablast from secondary lymphoid organs of ALPS patients show hyperactive mTOR signaling pathway. Proteomic studies identify a circuit that links FAS to the phosphatase PTEN via DAXX and the deubiquitinase USP7.
Conclusion: We describe a new role of FAS in the regulation of B cell activation. Defects in FAS signaling in ALPS contribute to dysregulation of the mTOR signaling pathway and disturbed B cell development.
Disclosure of Interests: None declared

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THU0054 NKTR-358, A NOVEL IL-2 CONJUGATE, STIMULATES HIGH LEVELS OF REGULATORY T CELLS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Impaired IL-2 production and dysfunction of regulatory T cells (Tregs) have been identified as key immunological defects leading to the breakdown of immune self-tolerance in SLE. Low-dose IL-2 can expand Tregs, but

the effect is limited by a narrow therapeutic window for Treg selectivity. Furthermore, the short half-life of IL-2 necessitates frequent administration. NKTR-358 is a polyethylene glycol (PEG) conjugate of recombinant human IL-2 (aldesleukin sequence) and is differentiated from native IL-2 by its altered binding to the IL-2 receptor and prolonged biological activity. NKTR-358 resulted in marked and selective stimulation of Tregs when administered as a single SC injection to healthy volunteers.

Objectives: This multiple ascending dose study assessed the safety, tolerability, pharmacokinetics (PK), and immune effects of NKTR-358 in patients with SLE after repeated administration of SC doses. The time course and extent of changes in numbers and percentages of Tregs, conventional CD4+ and CD8+ T cells, NK cells, and cytokine levels in peripheral blood were investigated.

Methods: In this double-blind, multiple ascending dose study, patients with mild to moderate SLE received 3 SC doses q2w in 4 cohorts ranging from 3.0 to 24.0 µg/kg (9 active:3 placebo per cohort); patients were followed for a total of 79 days.

Results: There were no dose-limiting toxicities, deaths, or clinically significant abnormalities in either vital signs or electrocardiograms. Adverse events attributed to NKTR-358 were primarily limited to mild (grade 1) injection site reactions. At the highest dose, one subject had transient and mild (grade 1) symptoms of a flu-like syndrome after administration, without associated elevated cytokine levels, and another subject had dosing stopped due to elevated eosinophil levels. No other individual at any dose level had systemic signs or symptoms known to be associated with IL-2 therapy. No anti-drug antibodies were detected. NKTR-358 demonstrated dose-proportional PK with repeated dosing; plasma levels peaked 3-6 days post-dose and declined with a terminal half-life of ~10-13 days.

The primary and consistent effect of NKTR-358 was seen on Tregs. In the four dose cohorts, dose-dependent and sustained increases in absolute numbers and percentages of circulating CD4+FoxP3+CD25^{bright} Tregs were observed. Treg levels remained elevated throughout the dosing period, peaking at Day 10 after the first administration of NKTR-358 and returning to baseline ~ 20-30 days following last administration. At 24.0 µg/kg, the mean peak increase in numbers of CD25^{bright} Tregs was 11-fold above baseline. In addition, there was an increase in Treg activation markers at doses ≥12.0 µg/kg. In contrast to effects on Tregs, no changes in percentages or numbers of conventional CD4+ or CD8+ T cells were observed at any dose tested. At the highest dose, there were low-level increases in the percentages and numbers of NK cells. Overall, NKTR-358 selectively induced Tregs, evidenced by a 12-fold increase in the mean peak Treg:CD8 ratio over baseline in the 24.0 µg/kg group.

Conclusion: NKTR-358, an IL-2 conjugate Treg stimulator, was well tolerated when repeatedly administered (q2w) at doses up to 24 µg/kg. Its administration led to marked, selective, prolonged, and dose-dependent increases in circulating CD25^{bright} Tregs. This clinical study in SLE patients extends the previous results in healthy volunteers and provides strong support for continued testing of NKTR-358 as a new therapeutic in SLE and other inflammatory diseases.

Disclosure of Interests: Suresh Siddhanti Shareholder of: Nektar Therapeutics, Employee of: Nektar Therapeutics, Christie Fanton Shareholder of: Nektar Therapeutics, Employee of: Nektar Therapeutics, Neha Dixit Shareholder of: Nektar Therapeutics, Employee of: Nektar Therapeutics, Lin Lu Shareholder of: Nektar Therapeutics, Employee of: Nektar Therapeutics, Vishala Chindalore Grant/research support from: Nektar Therapeutics for conducted studies, Speakers bureau: > 5 years ago, Robert Levin Grant/research support from: Payments for clinical research for industry-sponsored trials, Consultant of: Gilead, Exagen, Myriad Rheumatology, Speakers bureau: Sanofi/Genzyme, Regeneron, Bristol-Myers Squibb, AbbVie, Isam Diab: None declared, Richard Furie Grant/research support from: Nektar Therapeutics to Northwell Rheumatology to conduct this study, Consultant of: Nektar Therapeutics, Jonathan Zalevsky Shareholder of: Nektar Therapeutics, Employee of: Nektar Therapeutics, Brian Kotzin Shareholder of: Nektar Therapeutics, Employee of: Nektar Therapeutics

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THURSDAY, 04 JUNE 2020

OA, aetiology, pathology and animal models

THU0055 ANTI-DEGRADATIVE AND PRO-CHONDROGENIC PROPERTIES OF LIRAGLUTIDE, A GLUCAGON-LIKE-PEPTIDE 1 RECEPTOR AGONIST: EVIDENCE FROM PRECLINICAL STUDIES AND IMPLICATION FOR OSTEOARTHRITIS

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Background: Osteoarthritis (OA) is a degenerative joint disease affecting millions of individuals worldwide. Its development has been reported to be associated with cartilage degradation and inflammatory responses leading to pain, swelling and reduced function. Although OA is a disorder of the whole joint, the progressive destruction of cartilage extracellular matrix is considered as its hallmark. To date, approved OA treatments are only symptomatic. Therefore, there is an urgent need to explore disease-modifying OA drugs (DMOADs) that can mitigate, stop, or even reverse the development of OA.

Objectives: In this context, the objective of this study was to assess the effect of liraglutide, a Glucagon-Like-Peptide 1 Receptor (GLP-1R) agonist approved for type 2 diabetes, on chondrogenesis, catabolism/inflammation and cartilage protection in *in vitro* and *in vivo* preclinical models of OA.

Methods: The capacity of liraglutide to induce chondrogenesis was evaluated using primary human mesenchymal stem cells (hMSCs). Alcian blue staining was used to assess differentiation of hMSC into chondrocyte spheroids. IL-1β-stimulated mouse articular chondrocytes were treated with different concentrations of liraglutide for 24h. Production of matrix metalloproteinase MMP-13, prostaglandin E2 (PGE2) and nitrite was measured by ELISA and Griess reaction, respectively. Exendin 9-39, a GLP-1R antagonist, was used to confirm target engagement in the *in vitro* experiments. Intra-articular (IA) injections of liraglutide or vehicle were performed in the type II collagenase rat model. Histopathological analyses (OARSI scores[1]) were conducted blindly by one investigator.

Results: Liraglutide induced the differentiation of hMSCs into chondrocytes. Indeed, 21 days after differentiation initiation, 5/6 and 4/6 alcian-blue positive spheroids were observed for 10 and 100nM liraglutide, respectively, versus 0/6 for vehicle. Liraglutide significantly reduced dose-dependently the IL-1β-induced production of PGE2 (5808±178 for vehicle vs 4560±140, 2933±171 and 2365±85 pg/ml for liraglutide 10, 100 and 500nM, respectively, p≤0.001), nitrite (24.9±0.4 for vehicle vs 20.9±1.5, 19.1±0.9 and 16.5±0.5 µM for liraglutide 10, 100 and 500nM, respectively, p≤0.001) and MMP-13 (686±9 for vehicle vs 553±3, 402±5 and 297±8 pg/ml for liraglutide 10, 100 and 500nM, respectively, p≤0.001) in murine chondrocytes. Effects of liraglutide were GLP-1R dependent since exendin 9-39 significantly counteracted both chondrogenesis and inflammation/catabolism markers expression. Histological assessment of rat collagenase-injected knee joint revealed a significant (p≤0.05) decrease of the total joint score in the IA Liraglutide treated group (8±4) compared to vehicle (11±4).

Conclusion: Liraglutide induced chondrogenesis, decreased metalloproteinase and inflammatory mediators production by chondrocytes and protected cartilage in *in vitro* and *in vivo* preclinical OA models, opening the way for repositioning this drug as a potential DMOAD.

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THU0056 SM04755, A POTENTIAL DISEASE-MODIFYING TREATMENT FOR TENDINOPATHY, MODULATES THE WNT PATHWAY VIA INHIBITION OF CLKS AND DYRK1A

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Background: Tendinopathy is an inflammatory and degenerative disorder of tendons caused by injuries and/or overuse. Left untreated, tendinopathy can lead to pain and rupture. Current therapeutic options only treat symptoms. Stem cell- and growth factor-based treatments are under investigation but have not

established safety or efficacy, leaving considerable unmet need. The Wnt pathway is upregulated in chronic tendinopathy, affecting inflammation and tenocyte differentiation. SM04755, a novel, topical, small-molecule Wnt pathway inhibitor, has previously been shown to inhibit inflammation, protect tenocytes, and increase tenocyte differentiation in nonclinical models.[1]

Objectives: To identify molecular targets of SM04755 and its associated mechanism of action.

Methods: Wnt pathway inhibition was measured using a cell-based luciferase reporter assay controlled by a β-catenin/TCF-responsive promoter in SW480 colon cancer cells. A kinome screen (318 kinases) and kinase assays were performed. Effects of SM04755 on phosphorylation of proteins, including serine/arginine-rich splicing factor (SRSF) proteins in rat tendon-derived stem cells (rTDSCs) and peripheral blood mononuclear cells (PBMCs), were measured using western blot. SiRNA-mediated knockdown of CDC-like kinases (CLKs) and dual-specificity tyrosine kinase (DYRK1A) were performed in human mesenchymal stem cells (hMSCs), rTDSCs, and rat tenocytes. Effects of SM04755 and siRNA knockdowns on Wnt pathway gene expression and catabolic enzymes (MMPs) were measured using qPCR. SM04755 and siRNA effects on tenocyte marker expression were assessed by qPCR and immunostaining. Effects of SM04755 on LPS-induced expression of inflammatory cytokines in PBMCs were measured by MSD-based ELISA. Statistical analyses used one-way ANOVA for multiple group comparisons and t-tests for comparison between two groups.

Results: SM04755 was a potent inhibitor (EC_{50}=156 nM) of Wnt signaling. Biochemical assays identified CLKs and DYRK1A as molecular targets of SM04755. SM04755 potently inhibited CLK-mediated phosphorylation of SRSF proteins compared with DMSO controls. Knockdowns of CLKs and DYRK1A led to inhibition of Wnt pathway genes (*AXIN2*, *LEF1*, *TCF4*, *TCF7*, etc.) compared with siRNA controls (siCtrl). CLK1, 2, and 4 and DYRK1A knockdowns also induced expression of tenocyte markers in rTDSCs and inhibited IL-1β-induced expression of catabolic enzymes (MMP1, 3, 9, 13) in tenocytes compared with siCtrl. SM04755 treatment of LPS-stimulated PBMCs resulted in reduced phosphorylation of NF-kB and STAT3 and inhibited production of inflammatory cytokines compared with DMSO.

Conclusion: SM04755 inhibited CLKs and DYRK1A, which led to Wnt pathway modulation. Knockdowns of CLKs and DYRK1A, compared with control siRNA, induced tenocyte differentiation and reduced tendon-destroying proteases in tenocytes. This supports the potential disease modification of tendinopathy with SM04755. Furthermore, the anti-inflammatory effects of SM04755 are mechanistically supported by the decreased phosphorylation of STAT3 and NF-kB. These data support that SM04755, as a single agent, may potentially improve symptoms and provide disease modification in tendinopathy. Human tendinopathy trials are planned.

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Acknowledgments: Brian Hofilena for chemistry, Josh Stewart for pharmacokinetics, and Luis Dellamary for formulation.

Disclosure of Interests: Vishal Deshmukh Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Alyssa O'Green Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Tim Seo Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Yusuf Yazici Shareholder of: Samumed, LLC, Grant/research support from: Bristol-Myers Squibb, Celgene, and Genentech, Consultant of: Celgene and Sanofi, Employee of: Samumed, LLC

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THU0057 A NEO-EPITOPE FRAGMENT OF CARTILAGE DEGRADATION GENERATED FROM TYPE II COLLAGEN PROCESSING: A NOVEL SERUM BIOMARKER TO ACCESS TYPE II COLLAGEN DEGRADATION IN JOINT DEGENERATIVE DISEASES

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Background: Altered extracellular matrix (ECM) remodelling is an important part of the pathology seen in joint degenerative diseases. Type II collagen is the most abundant ECM protein in the cartilage and provides the tissue with essential tensile strength in order to withstand high compressive loading. During cartilage erosion, type II collagen is cleaved by matrix metallopeptidases (MMPs) which generates new protein fragments called neo-epitopes. These fragments are released into circulation and may potentially serve as biomarkers by indicating the degree of cartilage destruction.

Objectives: The aim of this study is to develop a highly specific immunoassay targeting a neo-epitope fragment of type II collagen cleaved, named T2CM. Moreover, we investigated the assays potential to evaluate type II collagen degradation in an *ex vivo* bovine full-depth cartilage explants model (BEX) with catabolic treatment and in healthy controls and osteoarthritis (OA) patients.

Methods: A monoclonal antibody was raised in mouse against the C-terminus from protease cleavage site of type II collagen and a direct competitive ELISA was developed and technically validated. The assay specificity was evaluated for the standard peptide excluding cross-reactivity with elongated and truncated peptides, and a non-sense coating peptide. Human OA cartilage was cleaved with MMP-1, -2, -9 and -13 and measured with the T2CM-assay to investigate which MMPs generated the neo-epitope. T2CM levels were measured in supernatant from BEX explants cultured for 21 days in serum free DMEM/F12 medium with six different doses of OSM+TNF-α (O+T) treatment (20/10, 20/20, 20/40, 10/10, 10/20, 10/40 ng/mL) including a control group without (w/o) treatment. The supernatant was harvested 3 times weekly and replaced with new culture medium with O+T treatment. Biomarker results were confirmed by western blot, where T2CM was measured in supernatant from explants with O+T treatment 20/20 ng/mL and 20/40 ng/mL harvested on day 14 and day 21. To confirm the preclinical data, serum samples from 23 healthy controls (age range from 44-59 years with mean 51.4 ± SD 5.1, gender distribution was 56% female and 44% male, and 100% Caucasian) and 23 OA patients (age range from 41-77 years with mean 57.7 ± SD 13.7, gender distribution was 61% female and 39% male, and 100% Caucasian) were measured by T2CM.

Results: A technically robust and T2CM-specific assay was developed. The assay linearity and spike-recovery were accepted with percentage of 99.69% and 93.15%. The assay showed no cross-reaction with the elongated, truncated or non-sense coating peptide. In addition, it was demonstrated that the T2CM neo-epitope was derived from MMP-1 and MMP-13 cleavage of type II collagen. O+T treatment induced the T2CM release in BEX compared to the untreated (Figure 1-2). Moreover, the western blot confirmed the T2CM results by the presence of two T2CM bands on day 21 from O+T treated explant compared to day 14 where no bands appeared. T2CM showed to be significantly elevated in patients with OA compared to controls (p=0.036; mean 3.262 ng/mL ± SD 1.065 vs 2.698 ng/mL ± SD 1.118).

Conclusion: The newly developed assay was specific for the T2CM neo-epitope and was determined to be generated by MMP-1 and MMP-13. Additionally, the assay detected elevated levels of T2CM in supernatant from explants treated with O+T after 19 days of treatment compared to untreated. This was further confirmed in human OA patients, where the level of T2CM was elevated compared to healthy controls. This suggests that T2CM may have potential as biomarker for type II collagen degradation. Future preclinical and clinical studies are needed to validate these findings.

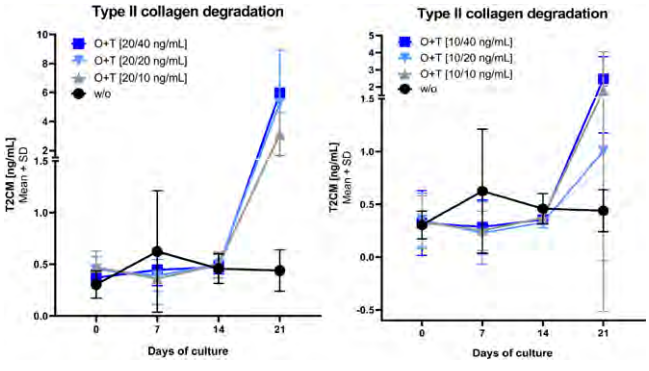


Figure 1-2. *T2CM measurements in BEX model. OSM + TNF-a (O+T) ng/mL.*

Disclosure of Interests: Solveig Skovlund Groen Employee of: Nordic Bioscience, Dovile Sinkeviciute Grant/research support from: Industrial PhD Student, Employee of: Industrial PhD Student, Christian Thudium Employee of: Employee at Nordic Bioscience A/S., Patrik Önnerfjord: None declared, Morten Karsdal Shareholder of: Nordic Bioscience A/S., Employee of: Full time employee at Nordic Bioscience A/S., Anne-Christine Bay-Jensen Shareholder of: Nordic Bioscience A/S, Employee of: Full time employee at Nordic Bioscience A/S., Signe Holm Nielsen Employee of: Full time employee at Nordic Bioscience

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THU0058 ENHANCEMENT OF CARTILAGE REGENERATION EFFICIENCY WITH HUMAN ADIPOSE STEM CELL THREE-DIMENSIONAL SPHEROID

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Background: 3D (three-dimensional) cell culture technology has been researched steadily because of its high potential of biocompatibility compared to single cells since 1990s, and is being developed to 3D spheroids recently. Spheroids are considered to reflect the natural organization of cells better than 2D cell cultures, and stem cells spheroids have been studied extensively in therapeutic transplantation. Stem cells were considered as a method of replacing autologous chondrocyte in regenerative treatment of articular cartilage. Compared to conventional single cells, 3D cell culture is artificially created an environment similar to a living body in vitro so that all cells collectively, a cell culture model that allows growth or interaction with the environment. Therefore, the findings of this study indicate that enhancement of treatment efficiency of stem cells caused by potential of survival and proliferation of hASC spheroid in Osteoarthritis. In conclusion, spheroid positive subpopulation of hASCs has high cell proliferation and survival but not apoptosis and cell death potential, which may contribute to successful cartilage regeneration and the development of stem cell therapies in the future.
Objectives: Studied for 3D spheroids to investigate the mechanism of enhancement of survival and proliferationof hASC (human adipose stem cells) spheroid, which may contribute to successful improvement of therapeutic efficacy of stem cells.
Methods: Cell isolation and culture / 3D cell culture dish preparation / hASCs culture on 3D cell culture dish / Real-time PCR analysis / Western blotting / Alcian blue staining / ACLT + MM (Anterior cruciate ligament transection with Medial meniscectomy) model / In vivo fluorescence for cell tracking / In vivo effects of spheroids in OA joint / Histological analysis / Enzyme-linked immunosorbent assay (ELISA) results for inflamma -tory cytokines in rat synovial fluid / Statistical Analysis
Results: In order to see how the spheroid showed more residual than single, and how effective it was in actual cartilage regeneration, the result of paraffin tissues were confirmed by safranin O staining for each condition. The tendency of cartilage regeneration efficiency was good for spheroid. Although the differences between the single and spheroid groups were small, they reaffirmed that they could somewhat protect cartilage and help regeneration treatment. However, immunohistochemistry of HN(Human nucleic antigen) staining showed that cells of single and spheroid were not observed in the wound but disappeared by the paracrine effect.
Conclusion: Spheroids do not exhibit differentiation characteristics, but they could be seen as a result of expression of related genes such as Bax, Bcl-XL and Alcian blue staining. Spheroids tend to have low potential of cell death rather than proliferation and reduction in the proliferation. So, we conclude the fact that instead of hASCs going directly to the surgical site to regenerate cartilage, they can help catrilage regeneration.

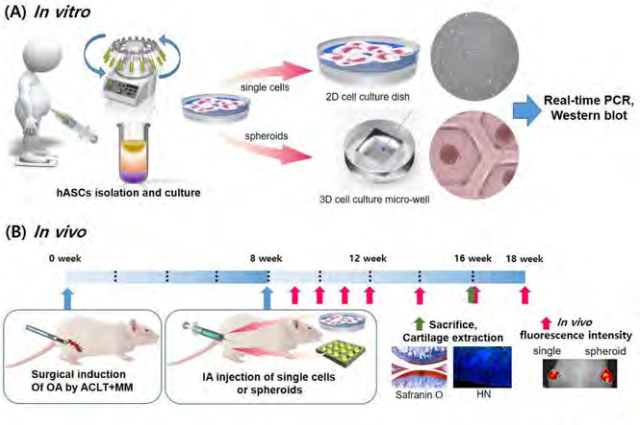


Figure 1. General scheme of *in vitro* and *in vivo* experiments using spheroid. (A) *in vitro* experimental procedures to identify single and spheroid. (B) *in vivo* experimental procedures in surgically-induced OA model to identify the cartilage regeneration efficiency of spheroid.

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THU0059 INCREASING SURFACE LUBRICATION WITH POLY(2-METHYL-2-OXAZOLINE) HALTS DEGENERATIVE CHANGES IN THE CARTILAGE IN A COLLAGENASE INDUCED OSTEOARTHRITIS (CIOA) RAT MODEL

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Background: Degenerative lesions of articular cartilage (AC) surface are related to disruption of the well-organized collagen network and allow proteoglycans to escape from the tissue. Ultimately, this leads to the development of osteoarthritis (OA). Targeted therapy for early AC lesions could provide an effective way to halt the OA development process.
Objectives: This study aims to evaluate the effectiveness of an engineered surface lubricant; poly(2-methyl-2-oxazoline) (PMOXA)[1] to prevent the destruction of the AC surface. Our recently developed contrast-enhanced μCT (CEμCT) method was used to quantify AC surface erosion[2].
Methods: OA was induced in 12-18 week-old male Wistar rats (N=17) with an injection of 250 U Collagenase within 25 μL solution into the left hind limb. Both hind legs were treated with a second injection three days after the collagenase injection (CI). Three groups were formed by using either PMOXA (N=5), hyaluronic acid (HA; N=6), or saline (N=6) during the second injection. The animals were sacrificed after 45 days, and harvested knees were fixed in phosphate-buffered formalin for a week. Knees were stored in 70% ethanol, and tibia and femur were carefully dissected free of other tissue, stained with 1% phosphotungstic acid[3], and scanned with a desktop μCT with 2.8μm pixel size. The medial and lateral AC surfaces were manually segmented from 3D projections using an in-house developed program (Matlab sofware). These surfaces were analyzed by iteratively fitting a reference surface (RS) to a median-filtered smoothed surface representing a perfectly smooth surface, capturing the realistic shape AC. An offset of 5 pixels (14 μm) was added between the RS and the original surface (OS). Two quantitative parameters were calculated from the data: Average of Maximum Void Depth (MVD) (depth of lesion) and Degeneration-% (area exceeding 20 μm MVD / whole area) *100). Estimates of mean differences from all groups against the CI+Saline -group were determined using a linear mixed model.
Results: Boxplots from tested groups are shown in Fig. 1A and MVD results are visualized in Fig. 1B. Collagenase caused structural defects only on the medial and lateral tibial AC surfaces, which was seen as increased MVD and Degeneration-%. CI changes were not seen in PMOXA or HA treated groups. Furthermore, MVD and Degeneration% were lower in CI knees that were treated with PMOXA.
Conclusion: Our CEμCT analysis method was able to detect subtle changes of the AC surface in the medial and lateral tibial cartilage, caused by the CI. In contrast, the CI did not cause detectable changes in the AC of the femur, which indicates that in the CIOA model, the tibia is more susceptible to structural degradation. Our results show that early intervention with HA or PMOXA can halt the degenerative AC changes caused by CI. However, HA did not suppress the effects of CI in the medial tibia, which indicates that PMOXA could be more effective to prevent the development of OA.

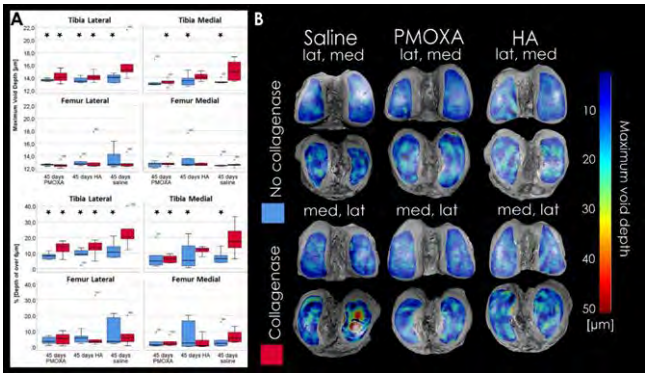


Figure 1. A) Boxplots of Maximum Void Depth (MVD) and Degeneration-%. Lateral and medial side are analyzed separately for both tibias and femurs. Stars indicate if a group was statistically different from control group (CI+Saline).CI= red, no CI= blue. B) Representative visualizations for maximum void depth overlayed on top of the 3D AC surface.

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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.1673

THU0060 KNEE JOINT DISTRACTION INDUCED SHIFT FROM CATABOLIC TO ANABOLIC STATE OCCURS AFTER DISTRACTION PERIOD

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Background: Knee joint distraction (KJD) is a validated joint-preserving treatment strategy for severe osteoarthritis (OA) that provides long-term clinical and structural improvement. Human trials and animal models indicate clear cartilage regeneration from 6 months and onwards post-KJD [1]. Recent work showed that during distraction, the balance between catabolic and anabolic indicators is directed towards catabolism, as indicated by collagen type 2 markers, proteoglycan (PG) turnover and a catabolic transcription profile.

Objectives: To investigate the cartilage changes directly and 10 weeks after joint distraction in order to elucidate the shift from a catabolic to an anabolic cartilage state.

Methods: Knee OA was induced bilaterally in 8 dogs according to the groove model. After 10 weeks of OA induction, all 8 animals were treated with knee joint distraction, employing the left knee as an OA control. After 8 weeks of distraction, 4 dogs were euthanized (KJD_{direct}) and after 10 weeks of follow-up the 4 remaining dogs (KJD_{+10}). Macroscopic and microscopic cartilage degeneration was assessed using the OARSI canine scoring system. RT-qPCR was used to determine relative expression of aggrecan (*ACAN)*, collagen type II *(COL2a1)*, cartilage oligomeric matrix protein (*COMP)* and matrix metalloproteinase-3 (*MMP3)* in the cartilage. PG content was determined by the Alcian Blue assay and the synthesis of PGs was determined using $^{35}SO_4^{2-}$ as a tracer, as published before.

Results: Macroscopic cartilage damage of the tibial plateau in the KJD_{direct} group was higher as compared to the OA control (OARSI score: 1.7±0.2 vs 0.6±0.3; $p < 0.001$). For KJD_{+10} this difference persisted (OARSI score: 1.4±0.6 vs 0.6±0.3; $p = 0.05$). Microscopically, an increase in the total OARSI score was seen after 10 weeks post-KJD. This was mainly due to an increase of chondrocyte clusters at 10 weeks of follow-up, resulting in an increased sub score chondrocyte pathology. Remarkedly the sub score intensity of proteoglycan staining decreased directly after KJD (indicating a loss of PGs) but increased after 10 weeks of follow-up suggesting a mixed response depending on the item scored.

Cartilage gene expression analysis showed downregulation of *COL2a1* (-1.3 ± 0.3), *ACAN* (-4.4 ± 1.0, $p < 0.01$) and *COMP* (-1.7 ± 0.5) in the $_t$ group compared to OA control suggesting enhanced catabolic activity during KJD. In contrast, after 10 weeks of follow-up the expression of *COL2a1* and *COMP* were increased as compared to the OA control (2.6 ± 1.1 and 2.5 ± 1.2 respectively) as well as compared to the KJD_{direc} situation (3.3 ± 1.4 and 4.2 ± 2.0*)*. Expression of *MMP3* was upregulated directly after KJD (4.4 ± 0.8) and downregulated after 10 weeks of follow up (-3.3 ± 0.8).

Biochemical analysis of the tibia cartilage of the KJD_{direct} group revealed a lower PG content compared to the OA joint (20.1±10.3 mg/g vs 23.7±11.7 mg/g). At 10 weeks post-KJD this difference in PG content was gone (24.8±6.8 mg/g vs 25.4±7.8 mg/g). The PG synthesis rate directly after KJD appeared significantly lower vs. OA (1.4±0.6 nmol/h.g vs 5.9±4.4 nmol/h.g; $p < 0.001$)). 10 weeks post-KJD this difference was not detected (3.7±1.2 nmol/h.g vs 2.9±0.8 nmol/h.g), and the synthesis rate in the distracted knee was increased compared to directly after distraction ($p < 0.01$) indicating a shift upon follow-up.

Conclusion: Further in-depth investigation of the material is ongoing and also includes the other joint tissues such as the bone and the synovial tissue. Irrespective, these first results on cartilage changes suggest that the shift from a catabolic to an anabolic state occurs within the weeks **after** joint distraction. As such, the post-distraction period seems to be essential in identifying key-players that support intrinsic cartilage repair.

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THU0061 EVALUATION OF SAFETY AND EVOLUTION OF OSTEOARTHRITIC JOINTS AFTER THE ADMINISTRATION OF HETEROLOGOUS MESENCHYMAL STROMAL CELLS IN AN ANIMAL MODEL

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Background: One of the main osteoarthritis (OA) consequences is the cartilage loss. Nowadays there is not cure for the OA, so there is an intense research focused on finding a therapy to solve this problem. In this paradigm heterologous mesenchymal stromal cells (MSCH) rise as a solution. Different studies used them as a cellular therapy in order to regenerate damaged cartilage. Furthermore, MSCH have shown anti-inflammatory effects.

Objectives:

1) Study the safety of a single intraarticular injection of MSCH derived from healthy canine fat tissue (adMSCH) in OA joints of dogs
2) Observe the evolution of functionality and range of articular mobility of these treated joints 6 months after the injection.

Methods: adMSCH obtained (n=10) were phenotypically characterized by flow cytometry, including the Major Histocompatibility Complex type II (MHC-II). Those with the best morphology and growth (n=5) were used for the injection. The infiltrated dogs (n=7) met our inclusion/exclusion criteria. The adMSCH were injected in 11 joints by 1 million of cells/kilogram of weight.

Before the infiltration we evaluated the joints (basal visit, BV), the vital signs and the animal pain by the owner (Visual Analogical Scale, VAS). The same data were collected one week after the infiltration (V1) and also studied the injected zone. Six months after treatment (V2), joint functionality and range of articular mobility were evaluated, also data of behavioural changes and pain observed by the owners.

Table 1. Functionality and range of articular mobility comparison between BV and V2. Visits column show the number of joints in that state

	Variable	Answers	Visits		t-student (p-value)	n
			BV	V2		
FUNCTIONALITY	Load changes	Normal	3	7	0.095	11
		Change load	8	4		
		Support fingers	0	0		
		No support	0	0		
	Load changes when getting up	Correctly	1	6	0.024*	11
		Position modification	10	5		
		Difficulty to get up	0	0		
		No get up	0	0		
	Lameness in cold	No lameness	1	2	0.062	11
		Mild lameness	6	9		
		Intense lameness	4	0		
		No support	0	0		
	Lameness when warmed	No lameness	1	3	0.106	11
		Mild lameness	8	8		
		Intense lameness	2	0		
		No support	0	0		
RANGE OF ARTICULAR MOBILITY	Articular passive manual mobility	Without pain	0	0	0.400	11
		Mild pain	3	5		
		Raised pain	8	6		
		Disabling pain	0	0		
	Flexion limitation	Total flexion	9	8	0.750	11
		Mild limitation	1	2		
		Severe limitation	1	1		
	Extension limitation	Total extension	0	3	0.749	11
		Mild limitation	9	4		
		Severe limitation	2	4		

*. Statistical significance stablished at P ≤ 0.05

Results: All cells obtained were negative for the MHC-II (0.45 ± 0.32).
Vital signs did not change between BV and V1. No dog suffered by severe inflammation of the injected joint. One of them during two days had difficulty to support the load in the posterior limbs, but at the third day it performed that without difficulty. Other dog suffered mild inflammation which was solved in two days. The other animals did not show any adverse effect after the infiltration. In the V1 none of them showed any inflammation in the joint. The pain evaluation by the owners showed that all dogs have less pain or it did not increase since BV. This indicate that after the infiltration the animals did not suffer a pain increase.
Data collected in V2 showed that the joint functionality tend to improve, one of the items showing significant differences between BV and V2. The range of articular mobility did not have neither differences nor tendencies to the improvement (Table 1).
Conclusion: The administration of adMSCH did not show adverse effects, rejection, infection or complications, only a probably of a mild inflammation in the treated zone. Also, joint functionality tends to improve, so these cells seem to have, at least, an anti-inflammatory effect into the OA joint.
Acknowledgments: Special thanks to the owners of the dogs who participated in this study.
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THU0062 FUNCTIONAL MR IMAGING OF HUMAN MENISCUS IS ASSOCIATED WITH HISTOLOGICAL DEGENERATION

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Background: In OA, there is a close association of meniscus and cartilage pathologies. Meniscus degeneration and lesioning are critical risk factors for development of early OA. Hence, this *ex-vivo* study assessed the responses to standardized loading of human meniscus samples as a function of degeneration and based on changes in their T1, T2 and T1ρ maps (as surrogate parameters of the tissue's functionality).
Objectives: Can meniscus functionality be visualized by serial quantitative MRI mapping technics?
Methods: During total knee replacements, 45 meniscus samples of variable degeneration were harvested from the center of the lateral meniscus body (Fig. 1a_1-a_3). After preparation to standard, samples were subject to force-controlled loading using an MRI-compatible lever device that created compressive loading by torque ((Fig. 1a_4-a_5). For each sample and loading position, MRI measurements (as detailed below) were performed in the unloaded (δ_0) and loaded configurations, i.e. loaded to 2 bar (δ_1, 37.1 N compressive force, 0.67 Nm torque) and to 4 bar (δ_2, 69.1 N, 1.24 Nm). Throughout all loading positions, morphological and quantitative imaging was performed using Proton Density-weighted and T1, T1ρ, and T2 mapping sequences (3.0 T, Achieva, Philips) based on standard turbospin-echo, inversion-recovery, spin-lock multi-gradient-echo, and multi-spin-echo sequences. For reference purposes, histological (i.e. Pauli classification) and biomechanical measures (i.e. Elastic Modulus) were obtained for each sample. Based on Pauli sum scores, samples were trichotomized as grossly intact, (n=14), mildly degenerated (n=16), and moderate-to-severely degenerated (n=15).

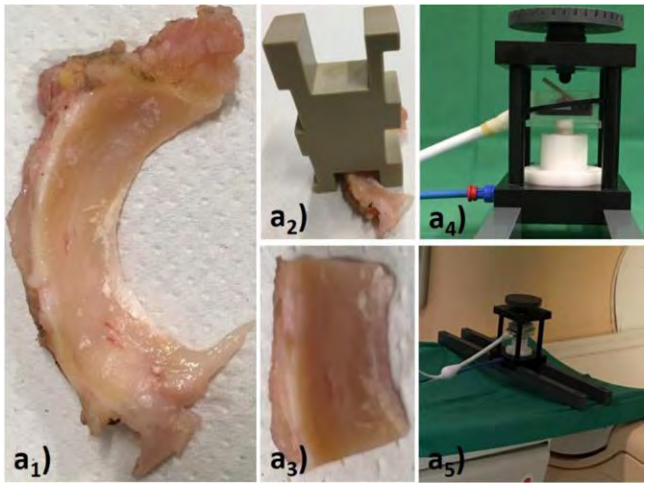


Figure 1. Preparation of meniscus samples and details of the MRI-compatible loading device. The lateral meniscus (a_1) was cut to standard size by use of a dedicated cutting block (a_2) to eventually obtain lateral meniscus samples (from the body region) of standard dimensions (a_3). These samples were then placed in a dedicated MRI-compatible loading device for pressure-controlled, quasi-static and torque-induced loading under simultaneous MR imaging (a_4). Two parallel support beams allowed standardized positioning in the MRI scanner's bore (a_5).

Results: Morphologically, loading induced deformation and flattening in all samples (Fig. 2a). For T1, homogeneous loading-induced decreases in all samples were found, irrespective of degeneration (Fig. 2b). For T1ρ, increases in the apical zones of intact samples were observed, and decreases in degenerated samples (Fig. 2c). For T2, changes were ambiguous and incoherent (Fig. 2d).

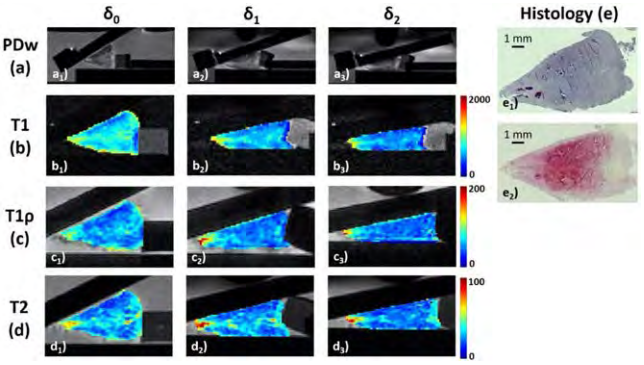


Figure 2. Serial morphological images and functional maps of histologically moderately degenerative human meniscus as a function of force-controlled loading. Serial PDw (a), T1 (b), T1ρ (c), and T2 maps (d) are displayed at increasing loading intensity (δ_0: unloaded [a_1-d_1]; δ_1: loaded to 2 bar [a_2-d_2]; δ_2: loaded to 4 bar [a_3-d_3]). Histologically, this sample demonstrated signs of severe surface desintegration and disruption. Pauli sum score 12, i.e. moderate to severe degeneration (Pauli Grade III). In b – d, color-coded parameter value maps are overlaid onto the corresponding morphological images. Histological sections are stained with Hematoxylin-Eosin (e_1) and Safranin O (e_2).

Conclusion: Meniscus functionality may be visualized using serial quantitative MRI mapping techniques. T1ρ may provide an imaging biomarker of relevant intra-tissue adaptations that seem to be associated with histological degeneration. The perspective evaluation of meniscus functionality may be indicative of incipient or manifest load transmission failure to the adjacent cartilage layer.
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THURSDAY, 04 JUNE 2020

Rheumatoid arthritis - aetiology, pathogenesis and animal models

THU0063 DIFFERENTIAL PHARMACODYNAMIC EFFECTS OF ABATACEPT AND ADALIMUMAB ON THE SERUM PROTEOME OF PATIENTS WITH RA USING THE SOMASCAN® PLATFORM

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Background: Abatacept (ABA) versus adaliMumab (ADA) comParison in bioLogic-naïvE RA subjects with background MTX (AMPLE) was a Phase IIIb clinical trial to compare the safety, efficacy and radiographic outcomes of ABA vs ADA in patients with RA who exhibited an inadequate response to MTX and who were naïve to biologic DMARDs.[1] While both therapies demonstrated similar efficacy across multiple outcomes, their mechanisms of action (MoAs) are quite different; ABA is a T-cell co-stimulation modulator and ADA is a TNFα inhibitor. Previous transcriptomic analysis of the whole blood samples showed differential pharmacodynamic (PD) effects between the treatments.[1–3]

Objectives: To expand our understanding of differential PD changes in the serum proteome over time in patients treated with ABA or ADA in AMPLE using a novel proteomic platform.

Methods: Serum was available from 440 patients in AMPLE at four time points (Days 1, 85, 365 and 729). Serum samples from the patients in AMPLE and 123 healthy individuals with matching demographics were subjected to proteomic quantification by a highly multiplexed DNA aptamer technology with wide dynamic ranges (SomaLogic SomaScan® platform).[4] A linear model analysis was used to identify protein abundance changes over time and changes specific to treatment. Other covariates included in the model were country of origin, ethnicity and sex. Additionally, patient effect was adjusted for as a random factor.

Results: Both treatments exhibited a significant PD effect on serum proteome over the course of the 2-year trial, with 73 proteins modulated by ABA and 125 by ADA. There were large overlaps between the two treatments, including proteins associated with RA, such as C-X-C motif chemokine ligand 13 (CXCL13), matrix metalloproteinase-3 (MMP3) and serum amyloid A1/A2 (SAA1/2). Changes in the levels of these proteins may be indicative of general improvement of the disease. The proteins modulated by the treatments were enriched in the G-protein coupled receptor (GPCR) signalling and innate immunity pathways. Among the proteins that exhibited significantly different PD effects between the treatments were CRP, CC chemokine ligand 17 (CCL17) and β-defensin 112 (Figure). While patients showed marked improvement in their symptoms after 2 years of treatment, the overall serum proteomic profiles of the patients were still different from those of a normal healthy population.

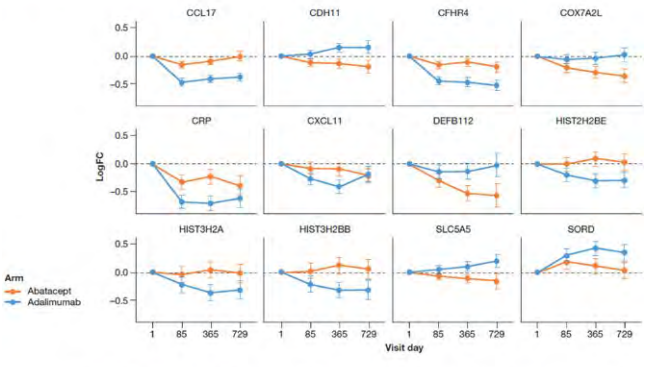
Conclusion: The SomaScan® platform provides a robust method for quantifying the PD change in a broad portion of the serum proteome in clinical trials. In AMPLE, abatacept was more selective than adalimumab in modulating protein biomarkers in patients with RA, though there was large overlap in proteins modulated by both treatments. The treatment-specific changes may reflect the different MoAs leading to similar clinical outcomes. While patients in both groups benefited from treatments, their serum proteome remained notably different from that of a healthy population. Further analysis by responder status may provide additional links between the treatment responses and proteomic changes. Proteomic approaches as described in our study could contribute to clinical trials and help shape treatment strategies for patients with RA.

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Figure. Serum Proteins With Differential PD Effects to Abatacept and Adalimumab



CCL17=CC chemokine ligand 17; CDH11=cadherin 11; CFHR4=complement factor H-related protein 4; COX7A2L=cytochrome c oxidase subunit 7A-related protein, mitochondrial; CXCL11=C-X-C motif chemokine ligand 11; DEFB112=β-defensin 112; HIST2H2BE=histone H2B type 2-E; HIST3H2A=histone H2A type 3; HIST3H2BB=histone H2B type 3-B; PD=pharmacodynamic; SLC5A5=sodium/iodide cotransporter; SORD=sorbitol dehydrogenase

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THU0064 ANTIBODY-RESPONSE MATURATION IN THE PHASE OF CLINICALLY SUSPECT ARTHRALGIA AND ITS RELATION WITH PROGRESSION TO RHEUMATOID ARTHRITIS

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Background: Auto-antibodies in rheumatoid arthritis (RA) are often present years before disease onset but their mere presence does not seem enough to induce RA. Because several nested-case control studies have shown that autoantibody-response maturation precedes disease onset, it is suggested that it plays a role in disease triggering. At present, it is undetermined whether autoantibody-response maturation occurs in the symptomatic phase preceding clinical arthritis (i.e. Clinically Suspect Arthralgia, CSA), or whether it occurs even earlier in the asymptomatic phase. Secondly, if autoantibody-response maturation is a final step towards clinical disease development, maturation is expected to be present in the patients that progress from CSA to RA, but not in CSA-patients that do not progress.

Objectives: To better understand the timeframe of autoantibody-response maturation and its relation to development of RA, we investigated autoantibody-response maturation in patients with CSA that did and did not progress to clinically apparent inflammatory arthritis (IA).

Methods: In serum from 148 CSA-patients, we determined the presence and levels of three autoantibodies (ACPA, anti-CarP and AAPA), with three isotypes each (IgM, IgG, IgA), resulting in 9 autoantibody measurements per patient per time-point. Measurements were performed on sera obtained at first presentation at the outpatient clinic and when patients developed IA or else after two years. In-house ELISA was used for all measurements. Three analyses were performed, in patients that progressed to IA (n=56) and in patients that did not progress (n=92) separately. First, in patients negative for all measurements at baseline, we determined the frequency of conversion to seropositivity. Second, in patients with at least one positive test at baseline, we studied the frequency of autoantibody positivity over time. Finally, we determined the change in autoantibody levels in patients positive for the respective autoantibodies at baseline. Frequencies and medians were reported. Statistical significance was tested with Fisher's Exact test and GEE, taking into account that measurements within one autoantibody type (ACPA, anti-CarP or AAPA) can be correlated.

Results: First we studied patients negative for all antibodies at baseline (54% of patients that progressed to IA and 76% of patients that did not progress). 17% of patients that progressed to IA became positive over time, compared to 6% of the patients that did not develop IA (p=0.12). Then we studied patients in whom at least one autoantibody was present at baseline and evaluated autoantibody-positivity over time. In patients that progressed to IA, the number

of autoantibodies detected at baseline did not change significantly during follow-up (median 1.5 (IQR 1-3, max. 6) to 1.0 (IQR 1-4, max. 6) (p=0.18)). In the patients with CSA that did not progress similar findings were made (1.0 (IQR 1-2, max. 4) at baseline and 1.0 (IQR 0-2, max. 5) after 2-years (p=0.07)). Increase in number of positive measurements over time took place in only few patients: in 15% of the patients that progressed to IA and in 18% from those that did not progress (p=1.00). Likewise, autoantibody levels did not significantly change over time, both in patients that progressed and in patients that did not progress.

Conclusion: The presence of IgM, IgG and IgA ACPA, anti-CarP and AAPA, as well as autoantibody levels, did not significantly increase over time in patients with CSA; this was similar for patients that did and did not develop clinical arthritis. These findings suggest that antibody-response maturation occurs before presenting with symptoms and also that broadening of the autoantibody response is not specific for progression from arthralgia to RA.

Disclosure of Interests: None declared
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THU0065 OXYLIPIN PROFILING DURING THE VERY EARLY PHASE OF RHEUMATOID ARTHRITIS: ASSOCIATIONS WITH DISEASE STAGE, CLINICAL FEATURES AND TREATMENT RESPONSE

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Background: traditional approaches and lipidomics support the relevance of eicosanoids in rheumatic conditions, such as rheumatoid arthritis (RA). Previous studies from our group and others have revealed altered levels of arachidonic acid in RA, pointing to a possible consumption or enhanced metabolisation. However, the potential alterations of its actual metabolites are difficult to assess with conventional approaches, and new, untargeted, high-throughput technologies are needed. More importantly, whether these alterations are related to the disease course and could be found at the very early stage of the disease is unknown.

Objectives: to characterize the eicosanoid profiles during the earliest stages of RA and their potential clinical associations.

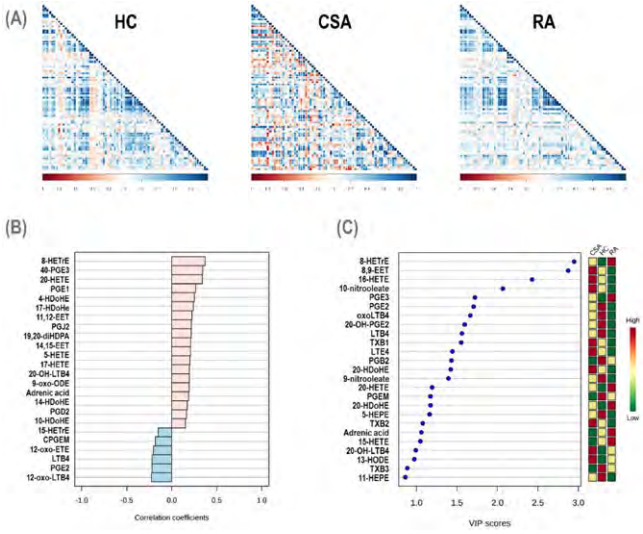
Methods: 60 very early RA patients (50 recruited at diagnosis and treatment-naïve) fulfilling 2010 ACR/EULAR criteria, 11 clinical suspect arthralgia (CSA) individuals and 28 healthy controls (HC) were recruited. Samples were collected at the moment of the diagnosis. Serum oxylipins profiles were analyzed by mass spectrometry (LC-MS/MS). Treatment-naïve patients underwent csDMARD treatment and were followed for 6 (n=49) and 12 months (n=38). Data analysis was performed in R and MetaboAnalyst.

Results: A total of 75 oxylipins, mostly derived from arachidonic (AA), eicosapentanoic (EPA) and linoleic (LA) acid, were identified. No effect was observed for age, gender or BMI. Correlation and network analyses revealed different patterns among oxylipins across RA patients, CSA and HC (Figure 1A). The 8-HETrE, PGE3 and 20-HETE showed the pattern (linear increase) HC→CSA→RA (p=1.47·10-4, 5.34·10-4 and 5.68·10-4, respectively; and adjusted FDR<0.050) (Figure 1B). A PLS-DA (explaining 12.3% of the total variance, with a 71.0% cross-validation accuracy and permutation p=5·10-4) confirmed that oxylipins profiles differ among groups, although a certain overlap existed. A total of 22 oxylipins had VIP scores>1 (Figure 1C), which allowed the identification of two clusters (I and II). Cluster usage (I/II) differed among groups (p=0.003): HC (27/1), CSA (7/4) and RA (37/23). Patients exhibiting cluster II showed higher VAS global assessment (p=0.016) and pain (p=0.003) than their cluster I-counterparts. More importantly, cluster II patients were less likely to achieve DAS28 remission at 6 (12/17 vs 10/32, p=0.008) and 12 months (6/9 vs 9/29, p=0.066) upon conventional DMARD treatment compared to those showing cluster I.

OPLS-DA analyses revealed a good discrimination between CSA and HC groups, and 7 compounds (13-HODE, PGB2, 9-oxo-ODE, 12-oxo-ETE, 19,20-di-HDPA, 5-HETrE and 15-HEPE) were associated with the course HC->CSA. Different precursors (2 LA, 3 AAA, 1 EPA and 1 DHA) and pathways were noted (3 LOX, 4 CYP450). Regarding RA subsets, differences were noted by seropositivity. Whereas 9 compounds were associated with the pattern HC→seronegative RA (8-HETrE, PGE3, 20-HETE, 19,20-di-HDPA, PGEM, PGJ2, 12-oxo-LTB4, 14,15-EET and LTB4), a distinct set was observed for the pattern HC→seropositive RA (PGE3, 20-oh-PGE2, 5-HETE, PGE2, 12-oxo-ETE, 20-HETE, PGEM, 4-HDoHE, LTB4, 9-oxo-ODE, 12-oxo-LTB4, 8,9-EET). No differences in the major pathways were noted.

Conclusion: Oxylipin networks differ across disease stages during the very early phase of RA, and can inform on specific signatures related to the disease progression. Oxylipins can delineate profiles with clinical relevance and are able to predict treatment response.

Figure:



Disclosure of Interests: None declared
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THU0066 DOES PORPHYROMONAS GINGIVALLIS MODULATE GUT MICROBIOME RESULTING IN AGGRAVATION OF DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS?

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Background: Oral Porphyromonas gingivalis (Pg) infection in rheumatoid arthritis (RA) model revealed aggravation of arthritis, dysbiosis and higher serum LPS (1). We reported that IgA/IgG antibody against Pg-LPS ratio among the patients with RA related to disease marker levels and disease activities (2). However, there are still few reports related to Gut-Oral axis.

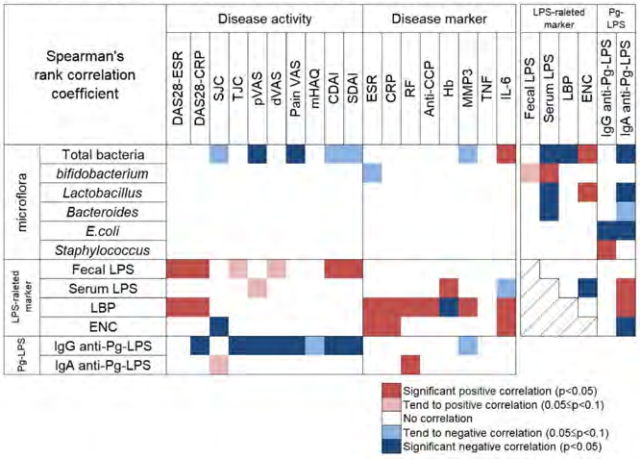
Objectives: Firstly, how total intestinal bacteria, well-known 5 species of gut bacteria behave in relation to disease activities and markers. Secondly, how infection by Pg aggravate RA in relation to microflora, disease activities and markers.

Methods: Eighty-seven RA patients with inadequate response to conventional synthetic DMARDs were evaluated. Age: 68.1±8.7 years, female (%): 79.3, disease duration: 136±91 months, DAS28-ESR: 4.68±0.98. Fecal bacteria numbers of total bacteria, Bifidobacterium, Lactobacillus, E. coli, Bacteroides and Staphylococcus were determined by PCR analysis. Fecal and serum LPS levels were measured by LAL assay. Serum endotoxin neutralizing activity (ENC) was determined along with RA disease activity and markers measurement. Infection of Pg was proofed by IgG and IgA anti-LPS antibody measurement. The statistical relationships between variables were analyzed by Spearman's non-parametric rank correlation analysis and expressed as Spearman's rank correlation coefficient "ρ".

Results: At first, we could neglect background effects as duration, methotrexate dose for measuring total or each bacterial number (data not shown). As shown in Figure 1, total bacteria only showed positive correlation with IL-6 levels (ρ= 0.230, p = 0.034), however inversely correlated with disease activities such as pVAS (ρ= -0.223, p = 0.038) and Pain VAS (ρ= -0.260, p = 0.015). While no significant relationship was observed between the numbers of each of 5 species of bacteria and the disease activities and makers except Bifidobacterium. In contrast, LPS-related markers showed positive correlation with disease activities and markers. Among LPS-related biomarker values, serum LBP levels mainly correlated with most of RA biomarker-ESR (ρ= 0.497, p <0.0001), CRP (ρ= 0.697, p <0.0001), MMP3 (ρ= 0.546, p <0.0001) and so on. Fecal LPS level was shown significant positive correlation with disease activities, however almost no correlation was observed in serum LPS level. IgA anti-LPS antibody levels to Pg, resulted in inverse correlation with total bacteria (ρ= -0.441, p<0.0001), Lactobacillus (ρ= -0.224, p=0.037), Bacteroides (ρ = -0.200, p = 0.064) and E. coli

(ρ= -0.260, p = 0.015), moreover, positive correlation with serum LPS (ρ= 0.284, p = 0.008) and LBP (ρ= 0.247, p = 0.021) and inverse correlation with ENC (ρ = -0.321, p = 0.002) were found. On the other hand, IgG anti-Pg-LPS antibody levels which reflect systemic infection, inversely correlated SDAI (ρ = -0.308, p = 0.004), PainVAS (ρ = -0.433, p < 0.0001), and so on.

Figure 1. Relationships between intestinal bacterial population and disease activity, Disease marker, LPS related marker and anti-Pg LPS antibody levels



Conclusion: Serum LBP highly associated with RA activity and markers, which suggests bacterial LPS as roles in triggering and perpetuating disease activity in RA. In contrast, IgA anti-Pg-LPS, IgG anti-Pg-LPS antibody reflecting infection of Pg, negatively associated with intestinal total bacteria (ρ=-0.4405, p<0.0001), RA disease activities, respectively. These results may show a possible oral -gut relationship resulting in aggravation of disease activity in RA.

Disclosure of interest: None declared

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Disclosure of Interests: None declared

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THU0067 JAK SELECTIVITY AND THE IMPACT ON CYTOKINE SIGNALING INHIBITION AT CLINICAL RHEUMATOID ARTHRITIS DOSES

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Background: Janus kinase 1 (JAK1) inhibitors are efficacious in rheumatoid arthritis (RA). Despite having similar efficacy, in vitro studies have shown differences in JAK selectivity profiles for the small-molecule JAK inhibitors (JAKi) baricitinib (BARI), tofacitinib (TOFA), and upadacitinib (UPA).[1] For example, BARI and UPA are JAK1/JAK2 selective, while TOFA is JAK1/JAK3 selective, but each JAKi has some activity against other JAKs. As JAKs form signaling pairs, differences in selectivity could lead to distinct pharmacologic profiles that may impact clinical efficacy and safety.

Objectives: As a first step to understand the basis of potential differences at therapeutic doses, we compared the selectivity and potency of filgotinib (FIL) and its major metabolite (MET) to those of BARI, TOFA, and UPA in cytokine-stimulated peripheral blood mononuclear cells (PBMCs) and whole blood (WB).

Methods: PBMCs and WB from healthy donors were incubated in vitro with 8 doses of each JAKi, and levels of signal transducer and activator of transcription phosphorylation (pSTAT) were measured following cytokine stimulation. Half maximal inhibitory concentration (IC_{50}) values were calculated in phenotypically sorted leukocyte populations by flow cytometry. Therapeutic dose relevance of the in vitro analyses was assessed using calculated mean concentration-time profiles from JAKi population pharmacokinetic data in RA subjects. For each JAKi, the time above IC_{50} and average daily pSTAT inhibition were calculated for each cytokine/STAT pair in B cells, CD4+ T cells, CD8+ T cells, monocytes, and/or NK cells.

Results: Cellular assays in PBMCs and WB showed dose-dependent inhibition of cytokine-induced pSTATs with all JAKi (correlation between the protein-adjusted IC_{50} values from PBMCs and IC_{50} values from WB, r^2=0.98). Among the most potently inhibited pathways were JAK1/TYK2-dependent cytokine, interferon alpha (IFNα), and the JAK1/2-dependent cytokine, interleukin (IL)-6. FIL and MET had weaker potencies against JAK2/TYK2 (G-CSF/pSTAT3), JAK1/2 (IFNγ/pSTAT1), and JAK2/2 (granulocyte-macrophage colony-stimulating factor [GM-CSF])-dependent pathways compared to JAK1/TYK2 (IFNα/pSTAT5). FIL and MET showed the greatest selectivity vs the JAK2/2 pathway (GM-CSF/pSTAT3) in monocytes.

The mean concentration-time profiles and time above IC_{50} over 24 hr for each cytokine/STAT pathway showed that JAK1/2 (IL-6/pSTAT1) and JAK1/TYK2 (IFNα/pSTAT1) pathways were strongly modulated with all tested JAKi. FIL (200 mg) showed similar activity in average target coverage and time above IC_{50} to the approved low doses of TOFA (5 mg) and UPA (15 mg); conversely, FIL had reduced mean average inhibition and time above IC_{50} levels against JAK1/2 (IFNγ/pSTAT1), JAK1/3-dependent cytokines (IL-2, -4, and -15), JAK2/TYK2 (G-CSF/pSTAT3), and JAK2/2 (GM-CSF/pSTAT5)-dependent pathways compared to TOFA and UPA, and in certain cases to BARI (2 mg).

Conclusion: Different JAKi modulate distinct cytokine pathways to varying degrees, and no agent potently and continuously inhibited an individual cytokine signaling pathway throughout the dosing interval. FIL (200 mg) showed a similar inhibition profile to TOFA, BARI, and UPA against the JAK1/TYK2- (IFNα/pSTAT1) or JAK1/2-dependent (IL-6/pSTAT1) responses, consistent with the role of these pathways in clinical efficacy.[2] However, FIL displayed a differentiated pharmacologic profile from the other JAKi, showing biologically reduced activity on the JAK1/2 (IFNγ)-, JAK1/3 (IL-2, -4 and -15)-, JAK2/TYK2 (G-CSF)-, and JAK2/2 (GM-CSF)-dependent pathways, which play important roles in hematopoiesis and immune function. These data suggest that FIL (200 mg) may have less impact on a subset of homeostatic immune functions signaling via JAK2 and JAK3 than those observed at the clinically approved doses of TOFA (5 mg and 10 mg), UPA (15 mg), and BARI (4 mg).

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Disclosure of Interests: Paqui Gonzalez-Traves Employee of: Gilead, Bernard Murray Employee of: Gilead, Federico Campigotto Employee of: Gilead, Amy Meng Shareholder of: Gilead Sciences, Employee of: Gilead, Julie A. Di Paolo Employee of: Gilead

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THU0068 COMPARISON OF INFLAMMATION DURING METABOLIC CHANGES IN RHEUMATOID AND OSTEOARTHRITIS MOUSE MODELS

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Background: Arthritis is influenced by metabolic changes. Adipokines are bioactive factors produced by adipose tissue with important effects on energy homeostasis and immune responses but are also involved in the pathogenesis of rheumatoid arthritis (RA) and osteoarthritis (OA).

Objectives: To evaluate inflammation during metabolic and adipokine induced changes in experimental models of RA and OA at different time points, an obesity model (high-fat-died, HFD) was therefore combined with an OA (DMM, destabilization of the medial meniscus) and RA (collagen induced arthritis, CIA) mouse model.

Methods: Mice were fed with HFD or ND (normal diet) for 12 (OA) or 6 (RA) weeks prior to arthritis induction. DMM was performed in C57Bl/6 mice and CIA was induced in DBA/1Rj mice. After 4, 6 and 8 (DMM) or after 4, 5 and 7 weeks (CIA) of arthritis induction animals were sacrificed to collect histological and serological data. Clinical scoring for CIA and histological scorings for both models were performed to evaluate disease development and progression. Diet-induced effects were monitored by weight, fatty liver score and crown-like structures (CLS) counts in adipose tissue. To evaluate HFD-induced adipokine levels adiponectin, leptin and visfatin serum concentrations were measured in parallel to the CRP. Local tissue adipokine expression was evaluated by immunohistochemistry.

Results: Induction of OA and RA was successful in an HFD setting, shown by histological joint destruction and the increased fatty liver score and bodyweight. Compared to healthy animals, CRP levels were significantly increased after CIA induction, confirming systemic inflammation. In DMM, the number of CLS

were significantly higher in HFD (0.2 ± 0.16, n=7) compared to ND (5.2 ± 0.98, n=8). No difference was found in CIA-severity between HFD and ND. However, CIA induction increased the number of CLS in HFD (2.77 ± 1.07, n=6) and interestingly in ND animals (8.14 ± 0.23, n=5) compared to healthy ND (0.45 ± 0.03, n=4) and healthy HFD mice (2.57 ± 0.53, n=4) without CIA. As expected, HFD led to a significant increase in systemic leptin in healthy animals in both models. Interestingly, CIA and DMM induction decreased systemic leptin levels significantly in ND and HFD, which was more prominent in CIA. The systemic effect was not reflected by local leptin distribution in the joints (CIA) which were not altered by diet. 5. and 7 weeks after CIA induction HFD led to a reduction in local adiponectin and visfatin expression, which were not reflected in systemic levels.

Conclusion: The data show that HFD deteriorates OA, which is similar to observations in humans. In contrast, HFD induction showed no significant difference in CIA severity compared to ND. Furthermore, CIA reduced local adipokine expression under HFD at later time points but not under ND. According to high numbers of CLS in ND/CIA animals and the strong reduction of leptin in CIA with HFD, CIA onset and severity seems to be obesity independent and more dependent on inflammation while OA appears to be directly influenced by obesity. However, HFD-induced obesity seems to alter local and systemic adipokine expression also in CIA. Interestingly, local adipokine distribution in affected joints was independent from systemic adipokine levels.

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THU0069 MIMICKING ARTHRITIS IN VITRO TO TEST DIFFERENT TREATMENT APPROACHES

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Background: Our ultimate goal is to study potential drug candidates in an experimental setting of arthritis. Therefore, we aim to develop a valid human *in vitro* 3D joint model mimicking features of joint inflammation by applying inflammatory conditions namely immune cells and pro-inflammatory cytokines. Our *in vitro* 3D joint model consists of different components including an osteogenic and chondrogenic part, the joint space filled with synovial fluid, and the synovial membrane. Developed as an alternative experimental setup to animal experiments, our 3D joint model will enable us to study efficiently the effects of potential drug candidates in a human-based *in vitro* model.

Objectives: Here, we aimed to demonstrate the suitability of our human-based *in vitro* 3D osteochondral model by analyzing the influence of the main cytokines involved in the pathogenesis of RA as well as the impact of a specific therapeutic intervention.

Methods: Based on human bone marrow-derived mesenchymal stromal cells (hMSCs), we developed 3D bone and cartilage tissue components that were characterized in detail (e.g. cell vitality, morphology, structural integrity) using histological, biochemical and molecular biological methods as well as µCT and scanning electron microscope (SEM). In brief, to establish the osteogenic component, we populated β-tricalcium phosphate (TCP) – mimicking the mineral bony part – with hMSCs, while the scaffold-free cartilage component was generated by cellular self-assembly and intermittent mechanical stimulation (fzmb GmbH). Subsequently, we co-cultivated both tissue components for three weeks to generate an interconnected 3D osteochondral model. To test the suitability, we applied a cocktail of TNFα, IL-6 and MIF using concentrations reported from RA synovial fluid alone or in combination with specific therapeutic drugs and analyzed their impact by qPCR.

Results: We verified the osteogenic phenotype of our 3D bone tissue component by demonstrating an increase in mineralized bone volume and the induction of bone-related gene expression (*RUNX2*, *SPP1* and *COL1A1)* as compared to the corresponding control. Secondly, we verified the chondrogenic phenotype of our cartilage tissue component by HE and Alcian Blue staining as well as by the reduced expression of *COL1A1* and an abundant expression of *COL2A1*. Interestingly, co-cultivation of both components for up to 3 weeks demonstrated colonization, connectivity and initial calcification implying a transitional bridging area. Cytokine stimulation with a cocktail of TNF, IL-6 and MIF leads to an upregulation of the metabolic marker *LDHA* and the angiogenic marker *VEGF* in both bone and cartilage. The inflammation markers *IL8* and *TNF* are also upregulated in both components, while *IL6* is downregulated in bone compared to the unstimulated control. In addition, a cytokine-induced upregulation of matrix-metalloproteases was observed especially in the cartilage component. All these cytokine-related effects could be antagonized with a cocktail of therapeutics (milatuzumab, adalimumab and tocilizumab).

Conclusion: The results of our study showed cytokine related effects of both tissue components, which can be therapeutically antagonized. By combining the components in a 96 well format, we aim to provide a mid-throughput system for preclinical drug testing.

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THU0070 DEFINING SYNOVIAL SIGNATURES IN THE RAT CIA MODEL: WHAT CAN WE LEARN ABOUT RA PROGRESSION?

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Background: Patients showing inadequate or no response to current therapies represent a key unmet need in rheumatoid arthritis (RA). To address this, novel or combination therapies are of high clinical interest. Identification of novel therapeutic targets requires a greater understanding of the pathogenic molecular drivers in the RA synovium. However, our current knowledge of human molecular patterns that emerge as a result of disease progression is complicated by patient-to-patient heterogeneity and access to synovial tissue.

Objectives: Here we use the current knowledge of human synovial heterogeneity to conduct a longitudinal study of global molecular responses in the rat collagen-induced arthritis (CIA) model to better understand synovial biology, improve the preclinical modeling of human disease, and discover novel targets for RA.

Methods: A rat CIA model was performed as previously described.[1] RNA-Seq was performed on 56 knee synovial tissues collected at multiple time points throughout the course of disease. Differential gene expression was determined at each individual time point and longitudinally with disease progression. Published human synovial datasets were used to categorize these genes into myeloid, lymphoid, fibroid, and low inflammatory signatures.[2] Differentially expressed genes (DEGs) at each time point were compared to human synovial datasets of RA patients before and after treatment. In addition, we compared disease-driven genes in CIA to genes in RA patients that are unchanged following therapy to identify possible combination therapies.

Results: Disease pathology in the rat CIA natural history study progressed as expected: significant decreases were seen in body weight, as well as increases in ankle diameter, paw weight, and histopathology scores of joints in collagen-injected vs noninjected rats. There were 1900 DEGs identified between diseased and naïve rats over the course of disease, representing disease-induced gene signatures (Fig. 1). Comparing these DEGs to reported human RA synovial signatures, both the lymphoid and myeloid signatures were found to be highly upregulated. Interestingly, there were no significant DEGs representing the human fibroid and low inflammatory synovial signatures identified in the CIA rat model. This suggests that the rat CIA model most closely models RA patients with an immune synovial phenotype. In addition, we examined the overlap between disease-driven genes in CIA and genes in RA patients that are unchanged following therapy to identify signaling pathways that may be of utility in combination therapy. Of genes that were upregulated in CIA, 94% of genes that mapped to extracellular matrix-receptor pathways remained unchanged in the synovial tissue of RA patients following tocilizumab treatment.

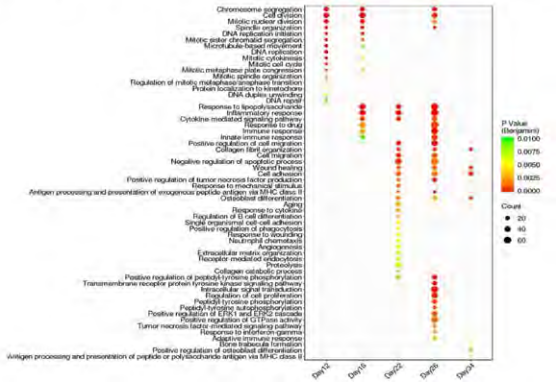
Conclusion: Previous studies have shown that nearly 30% of treatment-naïve early RA patients exhibit a strong fibroid phenotype that correlates with less severe disease and a relatively poor response to disease-modifying anti-rheumatic drugs.[3] These data indicate that the synovial biology associated with such patients (fibroid or pauci-immune) is not well captured in CIA, the most common preclinical RA model. To assess potential new therapies targeting these patients, it will be necessary to develop alternative animal models with more intact fibroid signatures. In addition to these findings, we also characterized the global molecular changes that occur with disease progression in the CIA rat and made a comparison to RA patients on treatment, providing an overall understanding of

disease-relevant pathways in the synovium that may point to possible combination therapies.

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Figure 1. Differentially expressed genes from collagen-injected versus naïve rat synovial tissue were identified over the course of disease and mapped to biological processes.



Disclosure of Interests: Debbie Ruelas Employee of: Gilead, Ruidong Li Employee of: Gilead, Christian Franci Employee of: Gilead, Victor Lira Employee of: Gilead, David Lopez Employee of: Gilead, Li Li Employee of: Gilead, Gundula Min-Oo Employee of: Gilead, Julie A. Di Paolo Employee of: Gilead

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THU0071 CD5L IN RHEUMATOID ARTHRITIS: PROTECTIVE OR PROMOTER?

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Background: Rheumatoid Arthritis (RA) is an aggressive auto-immune disease characterized by synovial hyperplasia and chronic inflammation. The main players of RA pathogenesis are T-cell and B-cell dependent pathways and some myeloid cells are also abundant in the synovial tissue. However, how inflammation is initiated, propagated and maintained remains controversial. Unbiased proteomic reports revealed an enrichment in the scavenger receptor CD5L, a component of serum and synovial tissues of arthritic patients.1 Upon secretion, this blood circulating glycoprotein represses pathogenic Th17 cells, promotes M2 polarization and binds and aggregates Gram-negative and -positive bacteria.2-4 However, its mechanisms of action has not been established either in health or disease.

Objectives: We intend to clarify whether CD5L is an immune component that helps resolving RA or a factor that aggravates the disease.

Methods: We analyzed by ELISA the presence of CD5L in samples from RA patients covering different stages of the disease, and correlated with other markers of RA. In parallel, we experimentally induced collagen induced arthritis (CIA) in CD5L knockout (KO) mice to evaluate the incidence and severity of the disease. The differences between the cellular groups in circulation vs the composition on secondary lymph organs using flow cytometry were also investigated in KO and WT mice. The histopathology of the joints was examined, while cytokine concentrations at several timepoints and total Ig levels were measured by ELISA and cytometric bead assays, respectively.

Results: The samples from RA patients showed increased CD5L levels concomitant with the severity of the disease and a direct correlation with Sharp RTG Score or IL-6 serum levels, and inversely correlated with COMP levels. However, these correlations did not clarify whether CD5L helps to resolve RA or is a component that aggravates the disease. To clarify this aspect, we provoked CIA in CD5L KO mice and observed a higher incidence of RA, higher severity and a much lower recovery rate when compared with WT mice. To corroborate these data, the H&E staining of sagittal section of fore- and hindpaws revealed histopathology consistency with RA, with notable inflammatory signs especially in KO mice. WT animals with RA also showed higher levels of CD5L when compared with the control group, which confirms the observations obtained for human samples. Total serum IgG levels did not correlate with the disease severity but KO mice presented higher quantities of IgG and IL-6 when compared with WT mice.

Conclusion: Overall, these data imply that CD5L is not a promoter of the disease but rather a fundamental protective molecule against inflammation.

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Disclosure of Interests: None declared

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THU0072 THE RELATIONSHIP BETWEEN INFLAMMATION AND COGNITIVE IMPAIRMENT IN RHEUMATOID ARTHRITIS

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Background: The pathophysiology of cognitive impairment remains unclear, however, several studies have demonstrated that pro-inflammatory cytokines such as Interleukin-6 (IL-6), Tumor necrosis factor-α (TNF-α) and lipocalin-2 (LCN2) are related with cognitive impairment by activation of microglia and astrocyte in brain. Rheumatoid arthritis (RA) is a representative inflammatory disease; however, the association of pro-inflammatory cytokines and LCN2 with cognitive impairment has seldomly been investigated in RA.

Objectives: Here, we determined the effect of pro-inflammatory cytokines and LCN2 on cognitive impairment in collagen-induced arthritis (CIA) mouse model. In addition, we studied the effect of TNF-α inhibitor (etanercept) on cognitive impairment.

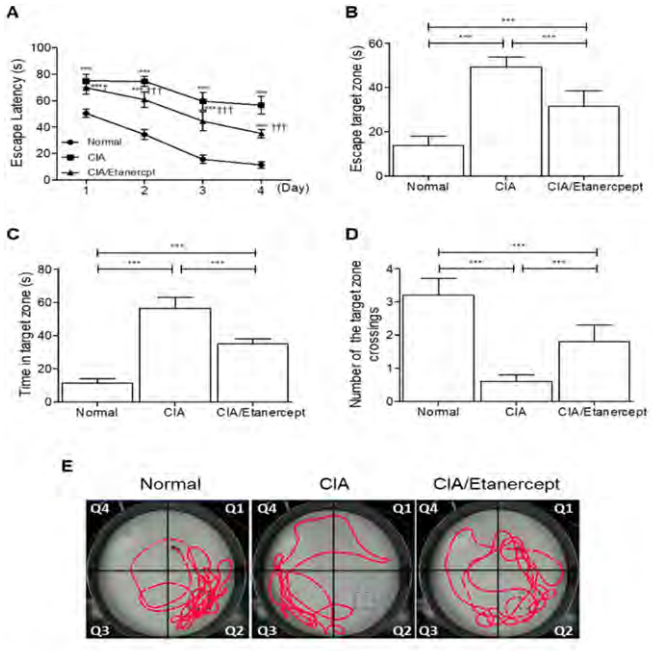


Figure 1. Comparison of learning and memory abilities in CIA mice.
For the Morris water maze, the learning phase was conducted four times per day over 5 days. (A) Escape latency to reach the platform during the training session (days 1–4), (B) escape latency to the reach the platform, (C) time spent in the target zone, (D) number of the target zone crossing and (E) tracking figures in the final trial of the last training day was also shown. Normal; Healthy group, CIA; collagen-induced arthritis group, CIA/Etanercept; collagen-induced arthritis and etanercept treatment group. Values are the means ± SEM (n = 10 mice per group). *, $p<0.05$, **; $p<0.01$, ***; $p<0.001$ and ns=not significant.

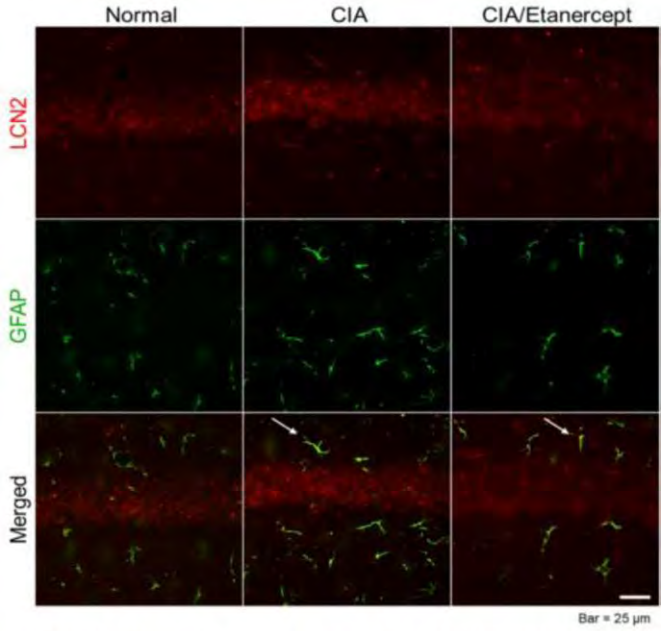


Figure 2. Effects of etanercept on expression of LCN2 and GFAP in the hippocampus of CIA mice. Double immunofluorescence of LCN2 and GFAP in the hippocamopal CA1 region of CIA mice. Dual labeling (white arrow point) showed LCN2 (red) co-localized with GFAP (Green), demonstrating the close relationship between LCN2 and GFAP. Normal; Healthy group, CIA; collagen-induced arthritis group, CIA/Etanercept; collagen-induced arthritis and etanercept treatment group. Values are the means ± SEM (n = 4 mice per group).

Methods: We induced CIA mice and randomly divided into three groups: Normal (n=10), CIA group (n=10), CIA/Etanercept group (n=10). We evaluated severity of arthritis using clinical scoring system. Joint inflammation, cartilage damage, and osteoclastic bone resorption has checked. Level of pro-inflammatory cytokines (TNF-α, and IL-6) and LCN2 checked in mice sera using enzyme-linked immunosorbent assay (ELISA). The expression of pro-inflammatory cytokines and LCN2 in ankle and hippocampus analyzed using real-time PCR. The activation of glial fibrillary acidic protein (GFAP) and ionized calcium-binding adapter molecule 1 (Iba-1) in hippocampus analyzed using immunohistochemistry (IHC). The LCN2 evaluated by western blot using hippocampal tissue. Cognitive impairment determined by morris water maze (MWM) test.

Results: Compared to normal group, CIA mice showed increased severity of arthritis, inflammation and destruction of joint. In MWM test, CIA mice significantly exhibited increased escape latencies and escape time, reduced the time in the target quadrant, and the number of target zone crossings during five study days compared with normal group. The level of pro-inflammatory cytokines (TNF-α, IL-6) and LCN2 in both sera, ankle tissue and hippocampal tissue was significantly increased. We examined whether inhibiting inflammation can mitigate the severity of arthritis and cognitive impairment. Compared to CIA mice, CIA/Etanercept group showed decreased severity of arthritis and joint inflammation. In MWM test, CIA/Etanercept group showed reduced escape latencies and escape time, increased the time in the target quadrant and the number of target zone crossings. The level of pro-inflammatory cytokines and LCN2 significantly decreased in both peripheral tissue and hippocampal tissue. In addition, the expression level of GFAP, Iba-1 and inflammatory markers decreased after treatment of etanercept. The results indicated that inhibition of inflammation may improve cognitive impairment.

Conclusion: The results suggest that peripheral arthritis induced inflammation is a possible cause for cognitive impairment by increasing pro-inflammatory cytokines and LCN2 in both peripheral tissue and hippocampal tissue in RA. In addition, we indicate that early anti-inflammatory treatment using etanercept may mitigate or inhibit the progression of cognitive impairment in RA.

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THU0073 THE ANTI-ANGIOGENIC ROLE OF TOFACITINIB DURING EXPERIMENTAL MODEL OF ARTHRITIS.

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Background: During rheumatoid arthritis (RA), a chronic autoimmune disease, the loop existing between inflammation and angiogenesis, characterised by new vessels formation associated with the increased recruitment of inflammatory cells, via the abnormal neo-angiogenesis in the synovial tissues, is considered an early important pathogenic mechanism.
Tofacitinib, a potent and selective JAK inhibitor, showed a good profile of safety and efficacy in RA patients, slowing the radiographic progression of the disease. In the last years, many works confirmed that some pro-angiogenic genes are targets of STATs family, and among them, vascular endothelial growth factors (VEGF), a potent pro-angiogenic molecule, may promote the new vessels formation via JAK/STAT pathways.

Objectives: The aim of this work was to investigate the inhibiting role of tofacitinib, on the angiogenic mechanisms occurring during experimental model of arthritis.

Methods: Healthy control (HC) ECs were stimulated with VEGF and/or tofacitinib and assessed for tube formation and migration, by matrigel and Boyden chamber assay. Furthermore, after ethical approval the experimental model of arthritis was obtained, stimulating 32 mice with collagen (CIA) and 32 mice with PBS (control). At day-19, CIA and controls mice were divided in 16 mice receiving vehicle and 16 mice receiving tofacitinib. At day-35, the mice were scarified and the thickness of paw joints, the synovial vessels and the serum levels of VEGF and Ang-2 were evaluated

Results: *In vitro*, after tofacitinib-treatment, HC-ECs lose their ability to form vessels and to migrate. *In vivo*, tofacitinib significantly prevented the increase of paw thickness induced by the collagen administration and reduced the vessel density in synovial tissues of joints, when compared to CIA that did not received tofacitinib. Furthermore, the serum levels of VEGF and Ang-2 were higher in CIA mice, than in control mice. The administration of tofacitinib was able to prevent the VEGF and Ang-2 accumulation in CIA mice.

Conclusion: During the last decade, the biological analogies between solid tumors and synovial pannus, and the encouraging results of anti-angiogenic treatments in oncology, lead to increasing interest for angiogenesis as a possible therapeutic target in RA. The present study demonstrated the anti-angiogenic efficacy of tofacitinib, opening a new perspective application for this molecule and improving our therapeutic skill to control the clinical evolution of RA.

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THU0074 ANTI-ARTHRITIC EFFECT OF RECOMBINANT CYSTATIN 3 FROM FASCIOLA HEPATICA IN COLLAGEN-INDUCED ARTHRITIS

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Background: Cystatins are cysteine proteases-inhibitors secreted by *Fasciola hepatica* in order to modulate the host immune response to promote survival of the parasite. These molecules are able to inhibit different mammal cathepsins, to regulate the immune balance via Th2 and T regulatory responses, to downregulate antigen presentation and the release of pro-inflammatory cytokines (1,2) – mechanisms that are important in the development and maintenance of several immunopathology, as rheumatoid arthritis (RA) (3).
Objectives: To evaluate the therapeutic effect of recombinants cystatin 1 and cystatin 3 from *Fasciola hepatica* in a mice model of collagen-induced arthritis (CIA).
Methods: Twenty-seven DBA/1J mice were induced with CIA by an injection of collagen type-II and Freund's adjuvant at days 0 and 18. Animals were randomly divided into three groups: vehicle (n=9, treated with phosphate-buffered saline), cystatin 1 (n=9, treated with 100 µg/dose of recombinant cystatin 1) and cystatin 3 (n=9, treated with 100 µg/dose of recombinant cystatin 3). Treatment started after day 18 by intraperitoneal injection once a day until the end of the experiment, at day 45 after CIA induction. Clinical arthritis score, nociception, paw edema, body and spleen weight were evaluated. Lymphocytes were isolated from lymph nodes and CD4+CD25+Foxp3+ T regulatory subset was assessed by flow cytometry. Data are expressed as mean ± SEM and were evaluated by one-way or two-way ANOVA followed by Bonferroni post-test.
Results: Treatment with cystatin 1 did not alter any of the analyzed parameters. On the other hand, cystatin 3 was able to reduce clinical arthritis score from day 38 with 32% of reduction at day 45 (9.22±1.22) compared to vehicle (13.56±0.73) ($p<0.05$). In addition, treatment with cystatin 3 diminished nociception (cystatin 3: 4.0±0.36g, vehicle: 2.7±0.32g) ($p<0.05$) and paw edema (cystatin 3: 0.051±0,012ml, vehicle: 0.093±0.007ml) ($p<0.05$). Moreover, the treatment did not alter body weight (cystatin 3: 21.67±0.31g, vehicle: 21.05±0.38g) and spleen weight (cystatin 3: 7.04±0.31, vehicle: 7.16±0.38), as well as the T regulatory population (cystatin 3: 63.38±3.66%; vehicle: 58.31±6.77%).
Conclusion: Treatment with cystatin 3 improved collagen-induced arthritis by attenuating the disease score, nociception and paw edema. Moreover, the treatment did not induce body weight loss or spleen weight alteration. These results suggest that recombinant cystatin 3 from *Fasciola hepatica* has the potential as a treatment for inflammatory and autoimmune diseases such as RA.
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Disclosure of Interests: Mirian Farinon: None declared, Renata Ternus Pedo: None declared, Thales Hein da Rosa: None declared, Barbara Jonson Bartikoski: None declared, Thaís Karnopp: None declared, Martin Cancela: None declared, Henrique Bunselmeyer Ferreira: None declared, Ricardo Xavier Consultant of: AbbVie, Pfizer, Novartis, Janssen, Eli Lilly, Roche
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THU0075 MIR-21 IN EXOSOMES DRIVED FROM DENTAL PULP STEM CELLS AMELIORATE THE TREGS/TH17 IMMUNE RESPONSE VIA TARGETING STAT3 IN COLLAGEN-INDUCED ARTHRITIS MICE

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Background: Rheumatoid arthritis (RA) is a common and systemic autoimmune disease[1].It is vital for deciphering pathogenesis to define the precise $CD4^+$Tcell subsets that are expanded or dysregulated in RA patients[2].An increase in the Th17 cell subset and a decrease in Tregs resulting imbalance of Tregs/Th17 may be responsible for the occurrence and development of RA[3]. Dental pulp stem cells (DPSCs) appear be a new therapeutic tool for immunological diseases[4,5].InRA, the mechanism of the effect of miR-21 drivedfromDPSCsexosomes (DPSCs-exo) on the balance of Tregs/Th17 is still unclear.
Objectives: We explored the effect of exosomes drived from DPSCson RA and investigated the correlation between DPSCs-exo and Tregs/Th17 balance.
Methods: Exosomes were isolated through differential centrifugation. Collagen-induced arthritis(CIA) mice were builded to detect histological change and Tregs/Th17 ratio.$CD4^+$Tcells were isolated from PBMCs. Exosomes and $CD4^+$T cells were co-cultured to study the regulation of Tregs/Th17 balance.The relationship between miR-21 and Tregs/Th17 balance was studied by flow cytometry, qRT-PCR and Western blotting etc.
Results: After Dpscs-exo treatment, the clinical scores and paw swelling of CIA mice decreased.At the same time, the expression of Treg cells increased and the expression of Th17 cells decreased in the spleen,changing the ratio of Tregs/Th17.Exosomes and $CD4^+$T cells were co-culture,showing that Treg cellsincreased and Th17 cellsdecreased. MiR-21 is highly expressed in RA patients. MiR-21 in exosomes were Knockout and overexpressed.The balance ofTregs/Th17 decreased when miR-21 were knockout and increased when miR-21were overexpressed. In addition, STAT3 in $CD4^+$T cells were overexpressed and co-culture with DPSCs-exo,which inhibited Tregs/Th17.
Conclusion: We elucidated the mechanism of the regulation of Tregs/Th17 balance by DPSCs-exo, that is, miR-21 in exosomes drived from dental pulp stem cells ameliorate the Tregs /Th17 immune response via targeting STAT3 in collagen-induced arthritis mice.
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THU0076 SONIC HEDGEHOG PROMOTES SYNOVIAL HYPERPLASIA AND BONE DAMAGE THROUGH P38 MAPK SIGNALING IN EXPERIMENTAL ARTHRITIS

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Background: Abnormal activation of sonic hedgehog (SHH) signaling has been found in synovium from patients with rheumatoid arthritis (RA). Inhibition of SHH signaling is reported to attenuate inflammation and cartilage damage in adjuvant-induced arthritis (AIA). Previously we have demonstrated that SHH signaling promoted the tumor-like behavior of fibroblast-like synoviocytes (FLSs) through p38 MAPK *in vitro*.
Objectives: In the current study, we aim to further explore the role of SHH-p38 MAPK signaling in regulating synovial hyperplasia and bone erosion in experimental arthritis.
Methods: Collagen-induced arthritis (CIA) mouse model was induced and the mice were injected with adenovirus associated virus (AAV) overexpressing SHH or treated with small molecule inhibitors GDC-0449. SB203580 was administrated for the inhibition of p38 MAPK. The severity of paw inflammation was graded and serum levels of TNFα, IL-6 were detected. The histological features of arthritis were evaluated by H&E staining. The bone erosion was identified by micro-CT assessment and the number and function of osteoclasts were determined.

Results: Blockade of SHH by GDC-0449 significantly alleviated the symptoms and decreased the synovial hyperplasia, inflammatory infiltration, cartilage and bone damage in ankles of CIA. The bone erosions in the area of the metatarsophalangeal and ankle joints and production of TNFα, IL-6 were decreased by SHH inhibition. In addition, the administration of GDC-0449 significantly decreased the number of TRAP positive cells and the expression of NFATc1. On the contrary, SHH overexpression led to increased severity of arthritis and pathological changes. We also observed the accelerated bone injury accompanied with increased number and activity of osteoclasts and increased production of serum IL-6 in mice with upregulation of SHH expression. Of note, the administration of p38 MAPK inhibitor reversed the effects of SHH overexpression, with a reduction of joint swelling and histological scores. Inhibition of p38 MAPK prevented the bone erosion and decreased the number of TRAP positive cells and the expression of NFATc1, which were promoted by SHH overexpression.

Conclusion: The study indicates that SHH promotes the synovial hyperplasia and bone erosion of CIA in a p38 MAPK-dependent manner. SHH-p38 MAPK signaling could be a potential target for the treatment of RA.

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Disclosure of Interests: None declared

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THU0077 CADHERINS GUIDE THE DIRECTIONAL MIGRATION OF THE SYNOVIOCYTES IN RHEUMATOID ARTHRITIS

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Background: Aggressiveness of synoviocytes and collective migration of organized synovial tissues play a key role in the pathogenesis of pannus invasion into adjacent joint structure. Interactions among synovial cells for grouped movement, however, have not been properly elucidated.

Objectives: We hypothesized that cadherins which have functions on the synovial invasion in RA, may play a critical role in collective migration of rheumatoid synoviocytes.

Methods: Cadherins expression patterns on the synoviocytes isolated from patients with RA were evaluated using RT-PCR, flow cytometry, and western blot analysis. Mesenchymal and epithelial phenotypes were examined in cadherin overexpressing cell line by flow cytometry. L-cells with overexpression of CDH2 ($CDH2^{hi}$), CDH11 ($CDH11^{hi}$), and combination of CDH2/CDH11 ($CDH2^{hi}$/$CDH11^{hi}$) were prepared. Migration of cells was observed by taking time-lapse images with laser confocal microscope. *In vitro* collective migration and directional movement in response to inflammatory mediators and different matrix rigidity were evaluated. *In vivo* homing of $CDH2^{hi}$/$CDH11^{hi}$-L-cells into joint tissues was performed in collagen induced arthritis (CIA) mouse. *In vivo* and *ex vivo* migration pattern of $CDH11^{hi}$-L-cells were investigated in nude mice using optical imaging system.

Results: In rheumatoid synovial tissues, CDH2 and CDH11 were highly expressed compared to synovial tissues from osteoarthritis. CDH2 and CDH11 were also highly expressed on synovial fibroblasts isolated from RA. Phenotype analysis of mesenchymal and epithelial cells in $CDH11^{hi}$-L-cells and $CDH2^{hi}$/$CDH11^{hi}$-L-cells showed increased expression of α5β1, CD44s, vimentin, and α-SMA compared with MOCK-L-cells. We then analyzed the pattern of migration of MOCK, $CDH2^{hi}$, $CDH11^{hi}$, and $CDH2^{hi}$/$CDH11^{hi}$-L-cells using time lapse images. During migration over a hard ECM, $CDH2^{hi}$ and $CDH11^{hi}$-L cells represented higher aspect ratio compare to a soft ECM. Aspect ratio relatively found lower in $CDH2^{hi}$/$CDH11^{hi}$-L-cell lines than MOCK cells. $CDH2^{hi}$/$CDH11^{hi}$-L-cells showed significantly higher migration velocity and Euclidean distance with narrower angle of migratory directions in a cytokine mediated migration. Compared to the MOCK cells, persistence ratio and aspect ratio of migration were also higher in $CDH2^{hi}$, $CDH11^{hi}$, and $CDH2^{hi}$/$CDH11^{hi}$-L-cells. $CDH2^{hi}$/$CDH11^{hi}$-L-cells collectively migrated with the formation of leader and follower cells. In a chemokine mediated hard stiffness of ECM, durotaxis was observed in $CDH11^{hi}$-L-cells. After 24 hours of intraarticular knee injection in CIA mouse, higher number of $CDH2^{hi}$/$CDH11^{hi}$-L-cells invaded into the cartilage than MOCK cells. *In vivo* migration of $CDH2^{hi}$/$CDH11^{hi}$-L-cells was also found towards the chemokine and cartilage mixed matrigel plug in the subcutaneous space of mice.

Conclusion: The expression of CDH2 and CDH11 promotes directional migration of synoviocytes, indicating the potential role of these cadherins on the pannus tissues in the invasion into adjacent joint structure in RA.

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THU0078 EXPRESSION PROFILE ANALYSIS OF LONG NONCODING RNAS INDUCED BY IL-1SS IN RHEUMATOID ARTHRITIS FIBROBLAST-LIKE SYNOVIOCYTES

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Background: Long noncoding RNAs (lncRNAs) have recently emerged as important biological regulators and the aberrant expression of lncRNAs has been reported in various diseases including cancer, cardiovascular disease, and diabetes mellitus. However, the role of lncRNAs in the pathogenesis of rheumatoid arthritis (RA) remains unknown.

Objectives: Thus, we studied lncRNAs influenced by IL-1, which is one of the key mediators in the pathogenesis of RA, and also investigated whether regulation of NF-κB activation, which is known to be induced by IL-1, could lead to the changes of expression of those lncRNAs.

Methods: Fibroblast-like synoviocytes (FLS) were obtained from the knee joints of the patients with RA. The next-generation sequencing (NGS) data were analyzed to identify differentially expressed lncRNAs between unstimulated RA FLS and IL-1-stimulated RA FLS. The expression levels of the top 5 candidates in NGS data were validated by RT-qPCR using extended number of unstimulated RA FLS and IL-1-stimulated RA FLS. IMD-0560, an inhibitor of IκB kinase (IKK) was used for the regulation of NF-κB activation. Activation and inhibition of NF-κB were confirmed by Western blotting. Changed expressions of the lncRNAs were identified by RT-qPCR.

Results: NGS analysis revealed up-regulated 30 lncRNAs and down-regulated 15 lncRNAs in IL-1-treated RA FLS compared with unstimulated RA FLS. Top 5 lncRNAs were selected among 30 lncRNAs up-regulated by IL-1 in RA FLS based on fold-change with P-value cutoff. The up-regulated lncRNAs including NR_046035, NR_027783, NR_033422, NR_003133, and NR_049759 were validated by RT-qPCR. IMD-0560 inhibited phosphorylation of IκBα induced by IL-1 in RA FLS. Overexpression of lncRNAs induced by IL-1 was also inhibited by IMD-0560 in RA FLS.

Conclusion: Our study revealed that IL-1 increased the expression of NR_046035, NR_027783, NR_033422, NR_003133, and NR_049759 in RA FLS. In addition, the expression of these lncRNAs was regulated by inhibition of NF-κB activation. Thus, our data suggest that the lncRNAs might be involved in the pathogenesis of RA through NF-κB signaling pathway.

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THU0079 THE MICROBIOME OF NEW-ONSET RHEUMATOID ARTHRITIS (NORA) PATIENTS DRIVES TLR4-DEPENDENT TH17 RESPONSES

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Background: Intestinal microbiota plays a prominent role in shaping the T cell immune response. Increasing evidence suggests that the gut microbiota is perturbed in patients with RA, and a variety of animal models demonstrated involvement of (mouse) microbiota in arthritis development. This underlines the necessity of understanding whether and how indigenous human NORA-associated microbiota may trigger RA.

Objectives: To comprehensively investigate the intestinal mucosa cytokine production and DC, T and B cell responses to human gut microbiota associated with new-onset RA.

Methods: We utilized *in vitro* cultures of mucosal-like DCs (differentiated from bone marrow cells) and primary splenic DCs, as well as *ex vivo* cultures of healthy human intestinal biopsies, cultured in the presence of heat-killed fecal microbiota from either NORA or control donors. Furthermore, we performed studies in humanized mice carrying intestinal NORA microbiota, to study the effect on immune response during homeostasis and upon joint inflammation during collagen-induced arthritis (CIA).

Results: In 24h DC cultures, NORA fecal microbiota more potently induced the expression of co-stimulatory molecules CD40 and CD80, and this enhanced DC maturation was partially mediated through TLR4 as demonstrated using the TLR4 antagonist TAK242. Interestingly, HC and NORA fecal microbiota differentially induced IL-12 and IL-6 production, with significantly enhanced IL-6 and reduced IL-12 secretion by the NORA microbiome. Furthermore, in *ex vivo* cultures of human ileum biopsies, the production of IL-1 and IL-33, as well as IL-23/Th17 cytokines IL-23, IL-22, and GM-CSF, were significantly increased by NORA-derived microbiome. Interestingly, in the small intestine lamina propria (SILP) of NORA-colonized mice, we observed enhanced Th17 polarization, increased innate GM-CSF expression and higher B cell CD40 and IgA levels during homeostasis. To study whether colonization with HC and NORA microbiota alters arthritis development, humanized mice and controls (mock, autologous, HC and NORA microbiota) were used in a CIA experiment. Macroscopic scoring of the arthritis severity at weekly intervals demonstrated that arthritis severity was significantly enhanced in NORA-colonized mice compared to HC-colonization and mock controls.

Conclusion: Our data reveal that NORA microbiota, in addition to the previously described Th17 differentiation, induce higher levels of GM-CSF and B cell IgA in LP and have increased potential to aggravate arthritis through the activation of TLR4.

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Disclosure of Interests: Marije Koenders: None declared, Heather Evans-Marin: None declared, Joyce Aarts: None declared, Parvathy Girija: None declared, Rebecca Rogier: None declared, Sergei Koralov: None declared, Julia Manasson: None declared, Peter van der Kraan: None declared, Shahla Abdollahi-Roodsaz: None declared, Jose Scher Consultant of: Novartis, Janssen, UCB, Sanofi.

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THU0080 PRECLINICAL CHARACTERIZATION OF TLL018, A NOVEL, HIGHLY POTENT AND SELECTIVE JAK1/TYK2 INHIBITOR FOR TREATING AUTOIMMUNE DISEASES

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Background: Janus kinases (JAKs) are important regulators of intracellular responses triggered by many key proinflammatory cytokines and are clinically validated therapeutic targets for treating various autoimmune diseases. However, current approved JAK inhibitors failed to achieve maximal clinical benefit in part due to their unfavorable selectivity for individual JAKs such as JAK2 and/or JAK3, leading to dose-limiting toxicities or severe toxicities (e.g., thrombosis, anemia, immune suppression). Selective inhibition of JAK1 and/or TYK2 may minimize or avoid some of the toxicities and potentially offer a better therapeutic window for treating autoimmune diseases. No highly selective JAK1/TYK2 inhibitor has been reported to date.

Objectives: Discovery of a highly selective JAK1/TYK2 inhibitor that maximally avoids JAK2 and JAK3 inhibition. We described preclinical characterization of a novel, highly potent and selective JAK1/TYK2 inhibitor TLL018 and its potential utility in treating autoimmune diseases such as rheumatoid arthritis (RA).

Methods: Using predicting SAR, TLL018 was designed to achieve exquisite selectivity for both JAK1 and TYK2 while sparing JAK2, JAK3 and other human kinases. Its enzyme and cell activities, kinase selectivity, and *in vivo* efficacy were assessed in a battery of relevant enzyme, cell and whole blood assays, and *in vivo* arthritis animal models. Additional preclinical DMPK and toxicology studies were conducted to support its clinical development.

Results: TLL018 is a highly potent and selective, orally bioavailable JAK1/TYK2 inhibitor against JAK1 (IC_{50} = 4 nM) and TYK2 (IC_{50} = 5 nM) as measured in *in vitro* kinase assays with ATP concentrations at individual Km. Its potency against JAK2 or JAK3 is greater than 1 μM. Profiling against a panel of over 350 human kinase showed that TLL018 is exclusively selective for JAK1 and TYK2, with ≥ 90-fold selectivity against all other kinases tested. TLL018 exhibited potent cellular activity for JAK1-mediated IL-6 signaling (IC_{50} = 0.6 μM) with greater than 100-fold selectivity against JAK2-mediated cytokine (e.g., TPO) signaling in human whole blood-based assays.

Oral administration of TLL018 demonstrated dose-dependent efficacy in commonly studied rat adjuvant-induced arthritis (rAIA) model and mouse collagen-induced arthritis (mCIA) model. Significant inhibition of inflammation, bone resorption, splenomegaly and body weight change was observed in adjuvant-induced disease in rats. In addition, significant inhibition of inflammation, cartilage destruction, bone resorption and histological signs was demonstrated in collagen-induced arthritis in mice. Noticeably, TLL018 exhibited significant anti-inflammation activity at doses that only blocked JAK1 and TYK2 and exerted little inhibition of JAK2 and JAK3.

In support of clinical development of TLL018, preclinical ADME and PK studies and IND-enabling toxicology and safety pharmacology studies were completed, confirming that TLL018 possesses excellent ADME and PK properties, and exhibits a clean on-target safety profile.

Conclusion: TLL018 is a highly potent and selective JAK1/TYK2 inhibitor that demonstrated excellent efficacy and tolerability in relevant mouse and rat arthritis models. The collective data of its preclinical pharmacology, PK and toxicology showed a favorable pharmaceutical profile, further supporting its development for treating autoimmune diseases including RA. Clinical evaluation of TLL018 is ongoing.

Disclosure of Interests: Xiangdong Liu Shareholder of: I own shares of TLL Pharmaceutical LLC, Employee of: I am employed by TLL Pharmaceutical LLC, Fenlai Tan Shareholder of: I own shares of TLL Pharmaceutical LLC, Employee of: I am employed by TLL Pharmaceutical LLC, Chris Liang Shareholder of: I own shares of TLL Pharmaceutical LLC, Employee of: I am employed by TLL Pharmaceutical LLC

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THU0081 MIR-17-5P REDUCES INFLAMMATION AND BONE EROSIONS IN COLLAGEN INDUCED ARTHRITIS MICE AND DIRECTLY TARGETS THE JAK-STAT PATHWAY IN RHEUMATOID ARTHRITIS FIBROBLAST-LIKE SYNOVIOCYTES.

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Background: micro-RNAs (miR) are strong regulators of gene expression. Their involvement in RA key cytokines pathway regulation entitles them as important players in RA pathophysiology. The miR 17-92 cluster has been widely studied in cancer as they regulate cell apoptosis.

Objectives: The aims of this study were to screen miR 17-92 cluster's expression in different RA phenotypes (erosive and non erosive), further elucidate the mechanisms and direct targets involved in miR-17-5p anti-inflammatory role and to investigate miR-17-5p therapeutic effect in arthritis.

Methods: A miR array was performed in synovial tissue from naïve erosive and non-erosive RA patients. Intra-articular delivery of miR-17 lipoplex was performed in collagen induced arthritis model in mice. Clinical, histological and structural effects were studied over the course of arthritis. In depth studies of miR-17 mechanisms of action were performed in primary RA-FLS isolated from RA synovial tissue.

Results: Among others, miR-17-5p expression was reduced in erosive RA. miR-17 transfection in arthritic paws significantly reduced clinical inflammation. Moreover, synovial B cells, T cells, macrophages and polynuclear neutrophils infiltrates were significantly reduced. Structural damage was also decreased as shown by a reduction in the number of osteoclasts and erosion score by CT analysis. Pro-inflammatory cytokines of the IL-6 family, STAT3 target genes and IL-1β expression were also significantly reduced, but not TNF-alpha. miR17 directly targeted the 3'-untranslated region of STAT3 and JAK1. STAT3 and JAK1 mRNA and protein expression were reduced in RA-FLS following miR-17 transfection. STAT3 and JAK1 mRNA and activation of STAT3 as assessed by immunohistochemistry were also reduced in injected paws.

Conclusion: We demonstrate an anti-inflammatory and anti-erosive role of miR-17 in vivo. This effect involves the suppression of the IL-6 family autocrine amplifying loop through the direct targeting of JAK1 and STAT3 as shown in RA-FLS.

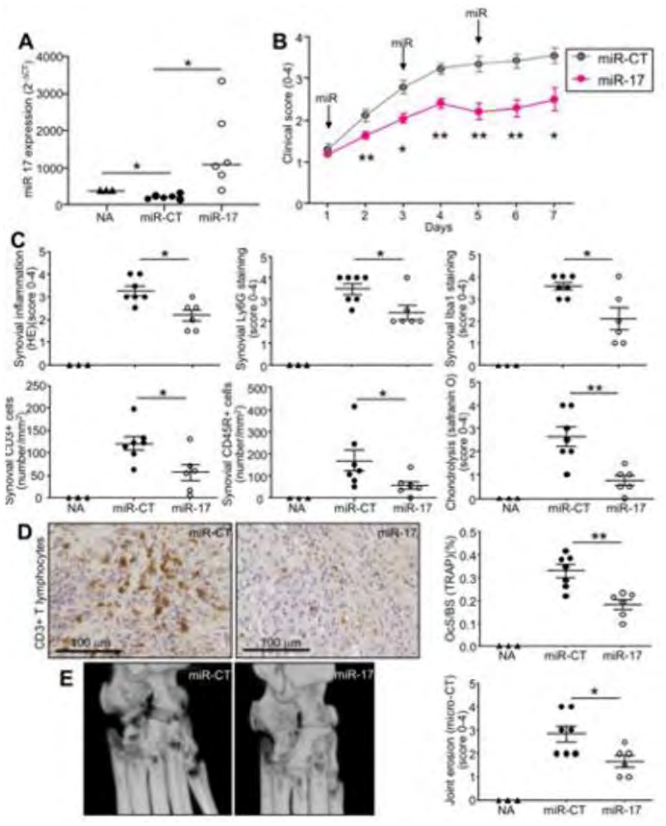


Figure Effect of miR-17 lipoplex injection in Collagen induced arthritis (CIA) mice's ankles.

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THU0082 MERTK SYNOVIAL EXPRESSION CORRELATES WITH TREATMENT RESPONSE IN RHEUMATOID ARTHRITIS

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Background: Despite substantial improvements in long-term clinical outcomes, a significant proportion of rheumatoid arthritis (RA) patients still fail to respond to treatment adequately, and early prognostic biomarkers of response are missing. Single-cell transcriptomic studies on RA synovial tissue (ST) have shown that MerTK is highly expressed in "anti-inflammatory" macrophages [1]. It has also been suggested that synovial macrophages isolated from RA patients in remission are characterised by a CD206+/MerTK+ signature [2]. Finally, monocyte-derived macrophages from RA patients treated with TNF-inhibitors (TNF-i) up-regulate MerTK.
Objectives: To assess i) the modulation of synovial tissue MerTK+ macrophages upon treatment with conventional synthetic (cs) disease-modifying anti-rheumatic drugs (DMARDs) and ii) the relationship between baseline *MerTK* gene expression and response to TNFi.
Methods: ST was obtained by US-guided synovial biopsies of an inflamed peripheral joint in patients with early (<12 months) treatment-naïve RA (as per ACR/EULAR 2010 criteria). A second biopsy of the same joint was repeated six months after starting treatment with single or multiple csDMARDs. ST (n=15) was stained for CD68, MerTK and CD206 by immunofluorescence using a tyramide amplification signal system. Quantification of the percentage of single- (MerTK+ or CD206+) and double-positive (CD206+MerTK+) CD68+ macrophages was obtained by digital image analysis (Image J). Gene expression analysis was performed on RNA sequences of 22 baseline ST samples (treatment-naïve).
Results: Before any treatment intervention, the percentage of MerTK+CD206+ macrophages was significantly higher in RA patients with low (DAS28<3.2) versus high (DAS28>5.1) disease activity (24.5±20.1 versus 4.8±4.8, p<0.05). There were no differences in the relative number of MerTK+ or CD206+ or MerTK+CD206+ macrophages at baseline in relationship with the clinical response to csDMARDs at 6-months. On the other hand, patients (n=5) achieving remission (DAS<2.6) upon receiving csDMARDs significantly increased the number of MerTK+ macrophages from pre- to six-months post-treatment (23.6±23.8 to 55.5±15.4, p<0.05) in comparison with patients (n=5) who were still active after treatment (18±15.6 to 30.4±11.17, p=ns). MerTK synovial gene expression at baseline (i.e., in newly diagnosed treatment-naïve RA patients) was significantly higher in patients subsequently treated with TNFi and achieving a good/moderate EULAR response at 12 months in comparison with those who did not respond (n=14, n=8, p adjusted 0.003).
Conclusion: Our whole-tissue protein expression data further support the hypothesis that a selective expansion of the MerTK+ macrophage subset characterise patients achieving remission. Moreover, the pre-treatment up-regulation of the MerTK gene in future responders to TNFi suggest that MerTK is implicated in modulating synovial inflammatory responses and may be exploited as a therapeutic target in RA.
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Acknowledgments: Versus Arthritis
Disclosure of Interests: None declared
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THU0083 THE DISPROPORTION OF NK CELLS AND NON-CONVENTIONAL NK-T CELLS AND ΓΔ-T CELLS IN INDIVIDUALS AT RISK OF DEVELOPING RHEUMATOID ARTHRITIS

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Background: Natural killer (NK) cells and non-conventional T cells (NK-T and γδ-T cells) are involved in the regulation of immune system and their alteration was previously described in patients with established rheumatoid arthritis (RA). The positivity of antibodies against citrullinated proteins (ACPA) significantly increases the risk of progression to RA. The clinical characteristics of individuals at risk of progression to RA (clinically suspect arthralgia, CSA) has recently been established by EULAR irrespective of the ACPA status.
Objectives: We aimed to study lymphocyte subpopulations in individuals at risk of developing RA.
Methods: Our study included 95 individuals with arthralgia at risk of developing RA based on ACPA positivity and/or meeting CSA definition and 70 age and gender matched healthy controls (HC). Whole blood samples were analysed by flow cytometry. The percentage and absolute count of CD3+ T cells, CD3-CD16/56+ NK cells, CD3+CD16/56+ NK-T cells and CD3bright γδ-T cells were evaluated in CD45+CD14- lymphocyte populations.
Results: Out of 95 individuals with arthralgia (median age 47 years [IQR=16], 92% females), 58 were ACPA+ and 62 met CSA definition (26 of them were ACPA+). Median symptom duration was 12 months [IQR=53], CRP 2.43 [IQR=3.32]. As per definition, there was no evidence of clinical arthritis on examination of 66 joints at baseline. Fourteen individuals developed RA within a median of 3 months of follow up with CRP 4.34 [IQR=17.46] and DAS28(CRP) score 4.84 [IQR=2.43].
Analysis of lymphocyte subpopulations showed higher %CD3+ T cells (p=0.001) and lower %NK (p=0.002) as well as absolute count of NK (p≤0.001), NK-T (p=0.016) and γδ-T cells (p=0.025) and trend to lower %NK-T (p=0.054) in all individuals with arthralgia compared to HC. Similarly, higher %CD3+ T cells (p=0.005) and lower %NK (p=0.004), %NK-T (p=0.027), %γδ-T cells (p=0.050) and absolute count of NK (p=0.002), NK-T (p=0.016) and γδ-T cells (p=0.019) were confirmed in a subgroup of ACPA+ individuals compared to HC. In addition, individuals who met CSA criteria irrespective of ACPA status had higher %CD3 T cells (p=0.004) and lower %NK cells (p=0.002) and absolute count of NK (p≤0.001), NK-T (p=0.019) and γδ-T cells (p=0.042) compared to HC. We observed no differences either between ACPA- or CSA- and HC or between ACPA+ and ACPA- or CSA+ and CSA- individuals with arthralgia. In addition, there were no differences in lymphocyte subsets in individuals

who have developed RA so far and patients with arthralgia or at the time of RA manifestation.

Conclusion: We identified lower number of NK cells as well as NK-T and γδ-T cells in individuals at risk of developing of RA. The decrease in non-conventional T cells was observed despite the increased percentage of the classical T cells. We hypothesize that the disproportion of these lymphocyte subpopulations, described previously in established RA, observed here in at-risk individuals may reflect their predisposition for further development of RA.

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THU0084 TOFACITINIB REVERSED ENDOTHELIAL DYSFUNCTION IN RHEUMATOID ARTHRITIS: MECHANISTIC INSIGHTS FROM THE RAT ADJUVANT-INDUCED ARTHRITIS MODEL.

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Background: Tofacitinib, an inhibitor of JAK3 and JAK1, is approved for the treatment of rheumatoid arthritis (RA)[1]. Cardiovascular (CV) risk[2] and events[3] in RA patients treated with Tofacitinib is a matter of debate, but the vascular mechanisms involved are unknown.

Objectives: The aim of this study was to investigate whether Tofacitinib improves endothelial dysfunction (ED) and if so to explore the underlying mechanisms in the model of adjuvant-induced arthritis (AIA) in rats.

Methods: AIA was induced by injection of *Mycobacterium butyricum* in the tail of male Lewis rats. A group of rats without arthritis served as controls. At the first signs of arthritis, AIA received Tofacitinib (10 mg/kg twice daily, s.c.) or 33%DMSO/PEG_{300} (Vehicle). Arthritis score was daily evaluated. After 21 days, preconstricted isolated aortic rings were relaxed with acetylcholine (Ach, 10^{-11}-10^{-4} moles/liter) in the presence or not of inhibitor of nitric oxide (NO) synthase (L-NAME), cyclooxygenase-2 (NS398), arginase (nor-NOHA), endothelium-derived hyperpolarizing factor (EDHF) (apamin/charybdotoxin) and superoxide anions production (Tempol). Endothelium-denuded rings were used to determine the vasorelaxant response to the NO-donor sodium nitroprussiate (SNP, 10^{-11}-10^{-4} moles/liter). Blood pressure and heart rate were measured by invasive method. A radiographic score was attributed to hind paws.

Results: Compared to AIA-Vehicle, Tofacitinib dramatically reduced arthritis (-76%) and radiographic (-73%) scores ($p<0.001$), and improved Ach-induced vasorelaxation ($p<0.05$). Of note, Ach-induced vasorelaxation was not different between Tofacitinib-AIA and control rats. The response to SNP was not different between groups. The effect of Tofacitinib on ED was mediated by decreased cyclooxygenase-2 and arginase activities, decreased superoxide anions production, increased NO synthase activity and EDHF synthesis. As compared to AIA-Vehicle, Tofacitinib changed neither blood pressure nor heart rate.

Conclusion: The present results demonstrated that Tofacitinib reversed arthritis-induced ED, through the correction of all the acknowledged impaired endothelial pathways in the AIA model. As ED is the *primum movens* of atherogenesis, these data provide a mechanistic explanation to the potential benefits of Tofacitinib on the cardiovascular comorbidities associated to RA.

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THU0085 RESOLVIN D5 MODULATES TH17/TREG CELL DIFFERENTIATION AND SUPPRESSES OSTEOCLASTOGENESIS

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Background: Resolution phase of acute inflammation has been recognized not passive but active process during the last 2 decades. This active process is highly regulated by novel families of potent bioactive lipid mediators, which are coined as specialized proresolving mediators (SPMs) including resolvins. Little has been known, however, about how resolvins are involved in chronic inflammation, such as rheumatoid arthritis (RA).

Objectives: To investigate whether lipid mediators (LM) are involved in the pathogenesis of RA.

Methods: We investigated lipid mediator profiling in the paws of SKG arthritis mice by using lipid chromatography (LC) /mass spectrometry (MS) /MS-based LM metabololipidomics. $CD4^+$ T cells from spleens of SKG mice were cultured on anti-CD3/ CD28Abs precoated plate with IL-6/TGF-β, anti-IFNγ/IL-4 and analyzed by flow cytometry. $CD4^+$ T cells were labeled with CFSE, and cell proliferation was analyzed by flow cytometry. Mouse bone marrow cells were cultured with M-CSF and RANKL, and TRAP-positive multinucleated cells were defined as osteoclasts. Osteoclast differentiation markers were analyzed by qRT-PCR. RvD5 or normal saline was administered daily into the peritoneal cavity of arthritic SKG mice.

Results: RvE3, RvD1, RvD3, RvD5 and Maresin2 were significantly elevated on the paws of arthritic SKG mice. Among the elevated SPMs, only RvD5 levels on arthritic paws were significantly correlated with arthritis disease activity (Figure 1). We demonstrated that RvD5 suppressed Th17 cell differentiation, and facilitated Treg cell differentiation *in vitro*. In addition, RvD5 inhibited $CD4^+$ T cell proliferation. Furthermore, RvD5 attenuated osteoclast differentiation (Figure 2) and interfered osteoclastogenesis at the molecular level. In the *in vivo* experiment, incidence of arthritis tended to be lower in RvD5-treated mice than that in control group, although there was no significant difference.

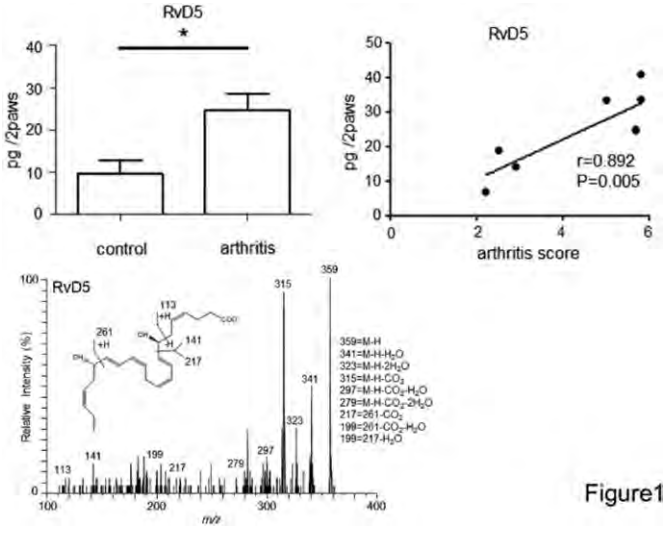


Figure1

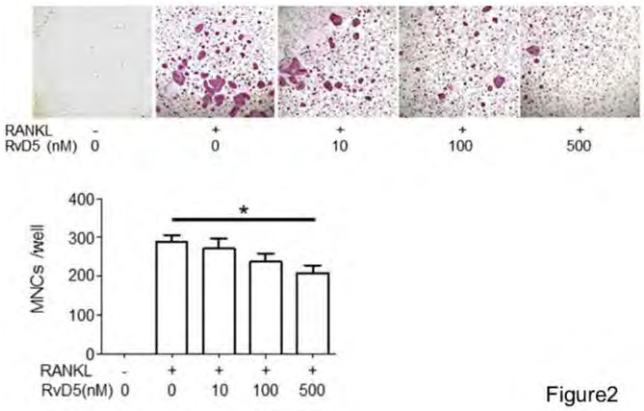


Figure2

Conclusion: RvD5 is increased in the paws of arthritic mice, and that RvD5 suppresses Th17 cell differentiation and $CD4^+$ T cell proliferation, facilitates Treg cell differentiation, and suppresses osteoclastogenesis.

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Disclosure of Interests: None declared

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THURSDAY, 04 JUNE 2020

Rheumatoid arthritis - prognosis, predictors and outcome

THU0086

FACTORS ASSOCIATED WITH TREATMENT RESPONSE IN PATIENTS WITH ELDERLY-ONSET RHEUMATOID ARTHRITIS: 3-YEAR OBSERVATION USING THE IORRA COHORT.

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Background: Patients with elderly-onset rheumatoid arthritis (EORA) are on the rise in the aging or super-aging society, especially in Japan. Patients with EORA have more comorbidities than those with younger-onset RA, a higher risk of adverse drug reactions due to reduced drug metabolism, and a higher risk of infections [1)]. Therefore, patients with EORA tend to receive suboptimal treatment, resulting in insufficient control of disease activity [2)]. Although several studies reported treatment responsiveness in patients with EORA, many of them have a limited observation period [3-8)], and long-term treatment responses and their associated factors need to be clarified.

Objectives: We retrospectively evaluated treatment responses of patients with EORA for 3 years and their associated factors in a clinical setting.

Methods: The Institute of Rheumatology Rheumatoid Arthritis (IORRA) cohort is a large, single institute-based, observational cohort of RA patients established at Institute of Rheumatology, Tokyo Women's Medical University, in 2000. The subjects were RA patients who first enrolled in the IORRA cohort from 2010 to 2014, were over 60 years old with less than 1-year disease duration, and had a DAS28-ESR over 3.2 at entry. The primary endpoint was DAS28-ESR <3.2 after 3-year observation. A multivariate logistic regression analysis was conducted to identify factors at baseline associated with the primary endpoint. The missing values of DAS28-ESR were imputed by using the last observation carried forward method.

Results: Among a total of 250 patients in this study, 152 patients (60.8%) achieved DAS28-ESR <3.2 after 3-year observation (remission/low disease activity (RL) group), and 98 patients did not (moderate/high disease activity (MH) group). Baseline characteristics of the patients were as follows (average ± SD or %): the RL group, age 69.9 ± 6.5, female 77%, DAS28-ESR 4.3 ± 0.8, J-HAQ 0.9 ± 0.7, PSL user 23.7%, MTX user 64.5%, and biologics user 4.0%; the MH group, age 69.4 ± 6.7, female 80.6%, DAS28-ESR 4.4 ± 0.8, J-HAQ 1.0 ± 0.7, PSL user 36.7%, MTX user 64.3%, and biologics user 6.1%. Proportions of the patients with cardiovascular disease and malignancy were 13.3% and 11.2% in the MH group and 5.9% and 1.3% in the RL group, respectively. DAS28-ESR and J-HAQ score after 3-year observation of the RL group were 2.3±0.5 and 0.4±0.5, respectively, and those of the MH group were 3.4±0.9 and 1.0±0.8, respectively. Corticosteroid use and having malignancy at baseline were associated with not achieving DAS28-ESR <3.2 after 3-year observation using multivariate analysis (Table 1). Similar results were obtained when MTX use and corticosteroid use were replaced by the average dose of each drug.

Conclusion: The majority of the patients with EORA achieved DAS28-ESR <3.2 after 3-year observation, and no use of corticosteroid and absence of malignancy at baseline were associated with the good outcome.

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Table 1. Factors associated with not achieving DAS28 <3.2 after 3-year observation in patients with EORA.

	Odds ratio (95%CI)	P value
Gender (female)	1.35(0.65-2.8)	0.41
Age (per year)	1.00(0.96-1.04)	0.99
Body mass index	0.98(0.90-1.07)	0.63
DAS28-ESR	1.14(0.77-1.67)	0.51
J-HAQ	0.95(0.60-1.50)	0.81
Rheumatoid factor positivity	1.00(0.99-1.00)	0.75
Corticosteroid use	1.82(0.99-3.25)	0.05
Biologics use	1.67(0.48-6.00)	0.42
Methotrexate use	0.88(0.48-1.62)	0.69
Interstitial lung disease	1.36(0.37-4.94)	0.64
Cardiovascular disease	1.98(0.73-5.34)	0.18
Diabetes mellitus	1.32(0.53-3.32)	0.55
Malignancy	10.3(2.05-51.6)	<0.001
Hypertension	0.80(0.42-1.54)	0.51

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THU0087 THE RELATIONSHIP BETWEEN THE LEVEL OF FETUIN-A, THE PRESENCE OF OSTEOPOROSIS AND OSTEOPORETIC FRACTURES IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: According to the literature, a number of markers (irisin, adiponectin, visfatin, and others) have a positive correlation with the frequency of osteoporosis, osteoporotic fractures and inflammatory response in patients with rheumatoid arthritis.

Objectives: to study the relationship between the level of fetuin-A (FA), the presence of osteoporosis (OP) and osteoporetic fractures in patients with rheumatoid arthritis (RA).

Methods: We examined 110 patients with a reliable diagnosis of RA, verified on the basis of the ACR / EULAR 2010 criteria. The age of the examined was from 18 to 69 years, all patients were female. The comparison group consisted of 30 conditionally healthy women. Patients in both groups was determined by the level of FA using a commercial kit ELISA BioVendor, bone mineral density was assessed using dual energy X-ray absorptiometry method DEXA (Lunar DPX-NT GE). The diagnosis of OP was made on the basis of WHO criteria (for women over 50 in the postmenopausal period) and the Recommendations of the International Society of Clinical Densitometry (for women in the premenopausal period).

Results: The average level of FA in patients with RA was 765.67±120.66 μg/ml, which was significantly lower than in healthy individuals - 812.95±76.21 μg/ml (p=0.0437). OP was detected in 52 (47.2%) patients with RA. The level of FA in serum in patients with OP was 733.65±135.84 μg/ml, which is also lower than that of healthy individuals (p=0.002).

We divided all patients with RA into 2 groups, depending on the presence of osteoporetic fractures. The average level of FA in the group of patients with osteoporetic fractures (n=24) was 694.79±110.47 μg/ml, which is significantly lower than the level of the group without fractures (n=86) - 785.45±116.43 μg/ml (p=0.00091).

Conclusion: The average level of FA in patients with RA is significantly lower than in healthy individuals. In addition, in patients with the presence of OP and osteoporetic fractures, the level of FA in the blood serum is also lower than in patients without OP and fractures. Thus, a decreased level of FA in the blood serum of patients with RA may indicate the presence of OP and an increased risk of osteoporetic fractures.

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THU0088 PREDICTORS OF DISEASE FLARE AFTER DISCONTINUATION OF CONCOMITANT METHOTREXATE IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH TOCILIZUMAB

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Background: All biologics should primarily be combined with a conventional synthetic DMARD, such as methotrexate (MTX), in rheumatoid arthritis (RA) patients. However, the use of MTX may lead to the development of adverse events (AEs), and de-escalation of MTX while maintaining a favorable disease activity state may be beneficial from the perspective of reducing AEs during long-term RA treatment. Several studies have evaluated the impact of MTX discontinuation in RA patients who achieved good clinical response with tocilizumab (TCZ) plus MTX combination therapy, finding that discontinuing MTX is noninferior to continuing MTX in terms of maintaining clinical response (1-3). However, information on risk factors for disease flare after MTX discontinuation is lacking.

Objectives: To investigate predictors of disease flare after MTX discontinuation in Japanese RA patients with sustained low disease activity undergoing TCZ plus MTX combination therapy.

Methods: Participants of this multicenter, open-label, uncontrolled, prospective study were RA patients maintaining low disease activity (Clinical Disease Activity Index [CDAI] ≤10) for ≥12 weeks with TCZ plus MTX. Patients had to be receiving MTX orally at a stable dose of ≥6 mg/week, and TCZ at a stable dosage regimen irrespective of the route of administration, for ≥12 weeks prior to obtaining informed consent. MTX was discontinued after 12 weeks of biweekly administration while continuing TCZ therapy (Fig. 1). Disease flare was defined as a CDAI score >10 or intervention with rescue treatments for any reason. The impact of baseline characteristics on disease flare at week 64 (52 weeks after MTX discontinuation) was assessed with logistic regression models.

Results: Efficacy analyses were performed in 49 patients, of whom 15 had a disease flare by week 64. The proportion [95% confidence interval (CI)] of patients who maintained low disease activity without a flare at week 64 was 69.4% (54.6 – 81.8%) (Fig. 2A). According to Kaplan-Meier estimates, the cumulative flare-free rate was 70.0% at week 64 (Fig. 2B). The dosing interval of TCZ was longer than that described on the drug label (i.e., intravenously every 4 weeks, or subcutaneously every 2 weeks) in 27% and 6% of patients with and without a flare, respectively (Table 1). Multivariate analysis revealed that male sex [odds ratio (OR): 18.00, 95% CI: 2.80-115.56] and extended dosing interval of TCZ (OR: 12.00, 95% CI: 1.72-83.80) were independent predictors of disease flare.

Conclusion: Male patients and those receiving TCZ at an extended dosing interval are at high risk of disease flare after discontinuation of concomitant MTX.

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Table 1. Impact of baseline variables on disease flare

	Non-flare	Flare	Odds ratio (95% confidence interval)	
	(n=34)	(n=15)	Univariate	Multivariate
Age, years	62 ± 11	63 ± 9	1.01 (0.95-1.08)[a]	
Male, %	6	40	10.67 (1.83-62.18)*	18.00 (2.80-115.56)*
Weight, kg	54 ± 8	58 ± 15	1.03 (0.98-1.09)[a]	
Disease duration, years	11 ± 8	13 ± 9	1.03 (0.95-1.11)[a]	
RF positive, %	76	86	1.85 (0.34-10.04)	
ACPA positive, %	85	100	-[b]	
Route of TCZ, intravenous, %	59	80	2.80 (0.66-11.79)	
Extended TCZ dosing interval, %	6	27	5.82 (0.93-36.28)†	12.00 (1.72-83.80)*
MTX dose, mg/week	8.2±2.2	8.0±2.6	0.95 (0.73-1.25)[a]	
Use of glucocorticoids, %	26	33	1.39 (0.37-5.18)	
Use of csDMARDs other than MTX, %	9	33	5.17 (1.04-25.57)*	-
Previous biologic use, %	56	80	3.16 (0.75-13.26)	
CDAI remission, %	65	73	1.50 (0.39-5.75)	
CRP, mg/dl	0.04 ± 0.06	0.04 ± 0.06	0.42 (0.00-15115.38)[a]	
MMP-3, ng/ml	58.5 ± 22.4	76.6 ± 37.6	1.02 (1.00-1.05)[a]†	-

Data are shown as mean ± SD or percentage. [a]Odds ratio for 1-unit increase in each item. [b]Odds ratio was not evaluated. *P <0.05. †P <0.10.

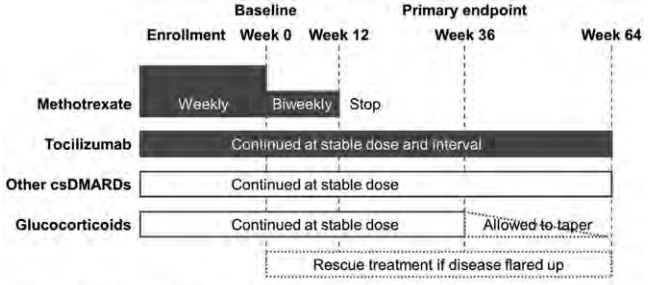


Figure 1. Schematic of treatment protocol.
At week 0, the dosing frequency of methotrexate was decreased from weekly to biweekly without changing the dose, regardless of the initial dose. At week 12, methotrexate was discontinued if low disease activity was maintained. csDMARDs: conventional synthetic disease-modifying antirheumatic drugs.

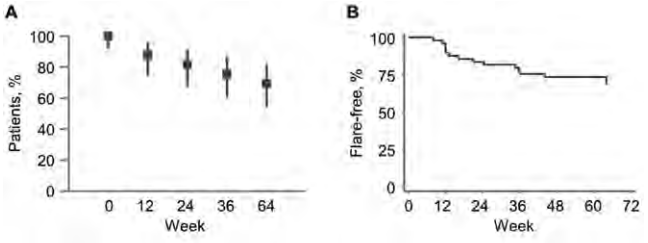


Figure 2. Maintenance of low disease activity based on CDAI score
(A) Proportion (95% confidence interval) of patients maintaining low disease activity without a flare. (B) Kaplan-Meier estimates of cumulative flare-free rate.
CDAI: Clinical Disease Activity Index.

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THU0089 TRENDS AND PREFERENCES IN RA CLINICAL SCORES WORLDWIDE

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Background: Different scores are used for patient management in rheumatoid arthritis (RA), including patient characterization such as ACR/EULAR criterion [1], disease activity monitoring by healthcare professionnals such as DAS28 [2], DAS28-CRP [2], CDAI [1], SDAI [3], or by patients such as HAQ-DI [4] or RAPID3 [5]. Most of these scores involve computations that are difficult to perform mentally (such as a square root function). Accordingly, several software tools have been designed over the years to help clinicians and patients compute these scores [6].

Objectives: This work reports for the first time usage statistics for one of these software tools, the RheumaKit online platform, from 2016 to 2020, showing that it has become a standard tool used worldwide by the rheumatology community. It also investigates the increasing use of repeated measurements, as enabled by that platform. Finally, a comparison between different disease activity scores is proposed, and usage preferences are documented.

Methods: Until January 2020, RheumaKit online portal has allowed users to compute scores without registering on the portal. In such cases, the computations and results are not stored, yet this activity is tracked by Google Analytics (as per explicit cookie policy). Users may also create an account, enabling storage and retrospective access to the computed results. Such entry recording in the RheumaKit database is only available for healthcare professionnals. The system then allows users to create individual patient files in which multiple scores and timepoints are recorded. These two data sources (Google Analytics and internal database) are used to perform this study: counts and trends are reported over the period ranging from 01 Jan 2016 to 31 Dec 2019.

Results: RheumaKit online application had been accessed by 7,300 distinct users in 2016; this number has grown to 86,000 distinct users in 2019. User distribution has also evolved: in 2016, users were reported from Russia (13% of the 7,300 users), USA (12.2%), Belgium (9.7% – this figure being explained by the fact that the tool is developed in Belgium), France (7.3%), and UK (7.2%); wereas in 2019, users are from the USA (21.1% of the 86,000 users), France (14.4%), Germany (5.4%), Brazil (5.3%), UK (5.3%). With respect to scores, the usage ranking over 2016-2019 outlines a preference for DAS28-CRP (93,900 computations) followed by HAQ-DI (72,800), DAS28 (63,600), CDAI (56,500), SDAI (42,700), RAPID3 (33,800), and ACR-EULAR2010 (19,800). The tendency in registering scores is also increasing, as the number of registered healthcare professionnals went from 117 on the 1st of Jan 2016 to almost 1,200 on 31 Dec 2019.

Conclusion: The use of computer-assisted clinical scoring for RA patients is an increasing trend observed worldwide, with dominance in Europe and America. The tendency to perform repeated, longitudinal measurements of these scores for a given patient is also increasing exponentially. DAS28-CRP and HAQ-DI are the most used scores among those available in this study.

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THU0090 AGREEMENT BETWEEN REFERRING PHYSICIANS AND RHEUMATOLOGISTS AND PREDICTORS OF INFLAMMATORY ARTHRITIS: ANALYSIS BASED ON 8 YEARS OF EXPERIENCE IN AN EARLY ARTHRITIS CLINIC

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Background: Early recognition of patients with arthritis is a crucial opportunity for optimal outcome. The Early Arthritis Clinic (EAC) of our department was created in 2012 to ensure a prompt access of these patients to efficient medical care. Patients may be referred based on a set of clinical criteria with less than 12 months duration and laboratory parameters: arthritis, inflammatory arthralgias, squeeze test, morning stiffness > 30 minutes, rheumatoid factor (RF), erythrocyte sedimentation rate (ESR)>30mm/h and C-reactive-protein>0.5mg/dL (CRP).
Objectives: To assess the level of agreement between the referring physician and the rheumatologist, regarding the presence of each of the six referral criteria and to identify predictors of inflammatory arthritis.
Methods: Cross sectional study including patients aged ≥ 18-year-old observed in the EAC between January 2012 and October 2019. Subjects who were referred to the EAC by a rheumatologist and those without available referral letter/medical records from the first visit to the EAC were excluded. Demographic data, provenience, referral criteria (presence/absence) and the final diagnosis [presence or not of an inflammatory rheumatic disease (IRD)] were collected from medical records. For the six referral criteria, the agreement between the referring physician and the rheumatologist was assessed using the Cohen's Kappa. The presence of each referral criteria was compared between patients with and without an IRD using $\chi 2$ tests. Variables with $p<0.1$ or clinically relevant were included in forward stepwise multivariable logistic regression analysis to identify possible predictors for IRD. The statistical analysis was performed using SPSS® v21 and $p<0.05$ was considered statistically significant.
Results: 376 patients (70% female; mean age (±SD) 56.3±16.2 years) were included. Most patients were referred from primary care (84%); the remaining 16% include those referred from emergency department and other hospital specialties. We diagnosed an inflammatory arthritis in 62% (n = 232) of the patients. Table 1 shows the level of agreement between the referring physician and the rheumatologist, regarding the presence of the referral criteria.

Table 1. Agreement between the referring physician and the rheumatologist, regarding the presence of the referral criteria.

Referral criteria	Kappa	p
Arthritis	0.23	0.05
Squeeze test	0.09	0.04
Inflammatory arthralgias	0.11	0.04
Morning stiffness	0.18	0.04
RF	0.27	0.04
ESR	0.26	0.04
CRP	0.25	0.04
ANA	0.02	0.47

ANA- antinuclear antibodies; CRP- C-reactive-protein; ESR-erythrocyte sedimentation rate; RF-Rheumatoid factor

In univariable analysis (IRD Vs non-IRD), inflammatory arthralgias (74% Vs 93%, p=0.01), squeeze test (24% Vs 55%, p=0.01), morning stiffness (49% Vs 63%, p=0.05), ESR (63% Vs 46%, p=0.01), CRP (62% Vs 48%, p=0.04) were associated to IRD. In multivariable analysis, only ESR (OR 5.0 [95% CI 1.9-13.0], p < 0.05) and inflammatory arthralgias (OR 0.15 [95% CI 0.04-0.52], p < 0.05) remained as predictors of IRD.
Conclusion: Agreement between the referring physicians and the rheumatologist regarding then presence/absence of the referral criteria was poor in all clinical criteria and fair in laboratory criteria. Elevated ESR was an independent predictor of IRD and the description of inflammatory arthralgias was negatively correlated with IRD. These findings suggest the need to clarify the referral criteria used and to improve education among the physicians referring patients to the EAC.
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THU0091 BODY MASS INDEX TRAJECTORY IN RHEUMATOID ARTHRITIS

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Background: Obesity is a known risk factor for development of refractory rheumatoid arthritis (RA) [1]. While past studies have examined associations between BMI and disease activity [1, 2, 3], and rheumatoid cachexia is a well-recognized phenomenon, few studies have characterized BMI trajectory over the disease course of RA.
Objectives: 1) To compare BMI trends between RA and matched non-RA subjects. 2) To determine predictors of BMI trends within RA subjects.
Methods: The study population comprised Olmsted County, Minnesota residents with incident RA (age > 18 years, 1987 ACR criteria met in 1995-2009) and non-RA subjects from the same underlying population with similar age, sex and calendar year of index. All subjects were followed until death, migration, or 01/July/2019. Follow-up was truncated for comparability. Generalized additive models with smoothing splines were used to illustrate trends in BMI measurements over time.
Results: The study included 558 patients with RA (mean age 55.6 years, 69% female) and 556 patients without RA (mean age 55.7 years, 69% female). Mean BMI of patients with incident RA (28.8) was not significantly different from that of non-RA subjects (28.9). Models demonstrating time trends in BMI showed a significant decline in BMI over time in both cohorts ($p<0.001$). A model including the interaction between RA/non-RA status and time revealed a significant interaction ($p<0.001$), indicating that patients with RA have a larger decline in BMI per year than patients without RA. There was no significant difference in BMI trends over time between seropositive (RF/CCP) and seronegative RA patients ($p=0.16$). In examining sex differences in BMI trends, female RA patients demonstrated a steeper decline in BMI compared to men ($p<0.001$).

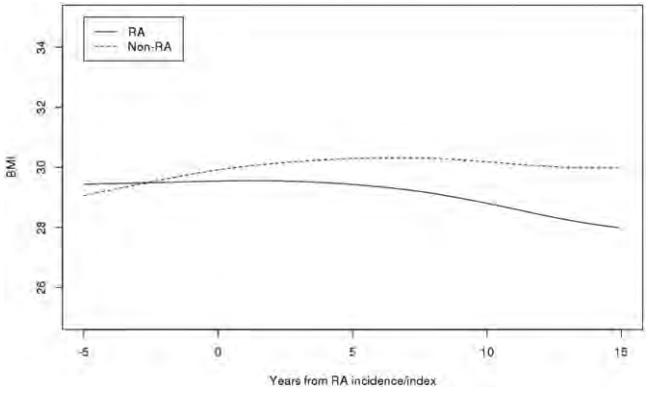


Figure 1. Time trends within BMI in the rheumatoid arthritis (RA) and non-RA cohorts, adjusted for age, sex, and calendar year of RA incidence

Conclusion: Our findings demonstrate a significant decline in BMI over time in both RA and non-RA populations, with a significantly larger decline per year in RA patients. The decline in the RA population is most pronounced beyond 5 years from RA incidence. Given that the mean age of patients in this study at baseline was 56 years, the finding of declining BMI in the healthy population fits with prior studies that demonstrate that BMI tends to decrease in the elderly population [4, 5, 6, 7]. The greater extent of BMI loss in the RA population may reflect the phenomenon of rheumatoid cachexia. More studies are needed to understand the reasons and implications of these trends.
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THU0092 USING EVIDENCE-BASED RESEARCH TO DESIGN A RANDOMISED TRIAL ON PERIODONTAL TREATMENT FOR INDIVIDUALS WITH RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW PUTTING EXISTING RESEARCH INTO CONTEXT

D. Santos Silva[1], F. Costa[2], I. Poiares Baptista[1], T. Santiago[2], H. Lund[3], S. Tarp[4], J. A. P. Da Silva*[2,5], R. Christensen[4,6]. [1]*Institute of Periodontology, University of Coimbra, Coimbra, Portugal*; [2]*Rheumatology Unit, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal*; [3]*Centre for Evidence-Based Practice, Western Norway University of Applied Sciences, Bergen, Norway*; [4]*Musculoskeletal Statistics Unit,The Parker Institute, Bispebjerg and Frederiksberg Hospital, Copenhagen, Denmark*; [5]*i.CBR - Coimbra Institute for Clinical and Biomedical Research, Faculty of Medicine, University of Coimbra, Coimbra, Portugal*; [6]*Hospital & Research Unit of Rheumatology, Department of Clinical Research, University of Southern Denmark, Odense University Hospital, Odense, Denmark*

Background: It has been suggested that RA is triggered by genetic and environmental factors that lead to a breakdown of immune tolerance at mucosal surfaces (e.g. periodontium) (1, 2). The theory that Periodontitis (PD) affects RA process/measurement has deep implications: PD treatment might improve disease activity and/or prevent overtreatment. It is urgent to confirm available evidence and design research strategies to cover knowledge gaps.(3)
Objectives: To gauge the evidence of non-surgical periodontal therapy (NSPT) impact upon measures of disease activity and inflammatory burden in individuals with RA and derive recommendations for research needed to address the knowledge gaps.
Methods: Based on a prespecified Protocol (CRD42018103359), a search for RA and Periodontitis and controlled or randomised trials was conducted on the 7th April 2019 in PubMed, Cochrane Library (CENTRAL), Embase, ClinicalTrials.gov and WHO ICTRP portal. Two independent reviewers screened titles and abstracts and selected papers were full text reviewed. Outcome domains were those OMERACT-endorsed for RA CTs: disease activity (DAS28, SDAI, CDAI), life impact (patient-reported outcome measures) and inflammation markers (CRP, ESR). We summarised continuous outcomes using standardised mean differences (SMDs) with 95% confidence intervals (95% CIs). We evaluated inconsistency using the I^2 statistic, and combined SMDs using the standard inverse variance random effects for the meta-analyses; fixed-effect meta-analysis was applied for the purpose of sensitivity.
Results: From 1909 studies identified, 9 reports (5 RCTs, 4 NRSIs) were eligible for quantitative synthesis (n=388). The evidence suggested a moderate effect on the disease activity domain in response to NSPT in RA patients (SMD -0.59 [95% CI, -1.21 to 0.03], n = 311; Figure 1). Using GRADE approach, as judged from the study's Risk of bias, imprecision around the estimate, and the results' inconsistency (I^2= 83%), the evidence was rated down to 'very low certainty evidence' indicating that any possible effect of NSPT is likely to change as more prospective evidence is provided. A RCT in PD-RA patients would need a sample size of at least 90 individuals, randomised 1:1 (80% power) to detect an effect size of 0.59. Anticipating withdrawals and attrition, a more adequate sample size would be 120 (90% power).

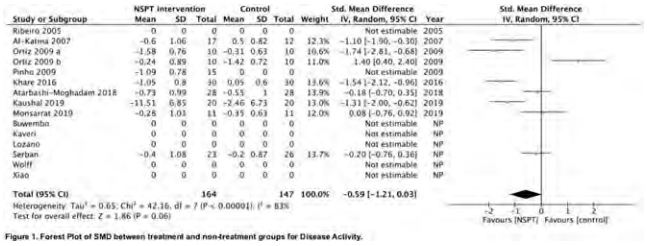


Figure 1. Forest Plot of SMD between treatment and non-treatment groups for Disease Activity.

Conclusion: Our results summarise the current evidence on the likely impact of NSPT on RA outcomes. There is an urgent need to assemble a well designed RCT, or prospective (multicenter) cohorts of RA-PD patients using rigorous protocols, standardized diagnosis criteria, data collection and duration of follow-up.

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THU0093 EARLY REMISSION IS ASSOCIATED WITH LOWER FATIGUE LEVELS ON THE LONG TERM IN PATIENTS WITH RECENT ONSET RHEUMATOID ARTHRITIS

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Background: Fatigue is mentioned as a symptom with high impact in many patients with Rheumatoid Arthritis (RA) and this symptom remains difficult to be managed by both the patient and the physician.
Objectives: To investigate if rapid suppression of disease activity in early RA could impact fatigue complaints in the long run.
Methods: For this study, we included patients from the 2-year pragmatic investigator-initiated Care in Early Rheumatoid Arthritis (CareRA) trial. Most patients were treated intensively, with different combinations of csDMARDs and glucocorticoid remission induction schemes, except one group without classic markers of poor prognosis that was treated with MTX weekly in monotherapy. Patients were followed up at least every 3 months, with more mandatory visits in the first 6 months of treatment. Clinical parameters including DAS28 components were registered at every visit. Fatigue was measured by the multi-dimensional fatigue inventory (MFI), a self-reported instrument consisting of 20 questions with a Likert scale from 1-5 as answer. These 20 questions can be subdivided in five subscales (0-20) of four questions (higher scores indicating higher fatigue levels): general fatigue, mental fatigue, physical fatigue, reduced activity and reduced motivation. General fatigue means the general feeling of being tired. Mental fatigue implicates concentration and memory problems. Physical fatigue implicates a lack of energy and strength. Reduced activity means that patients can do less activities for example on one day. Reduced motivation means that patients don't want to plan or do things due to no motivation. MFI was obtained at baseline, at week 16, week 52 and week 104. Only patients with a filled-out MFI at baseline and available DAS28CRP at week 16 were included in this study.
Patients were divided in 2 groups based on their response, defined as achieving or not achieving DAS28CRP remission (<2.6) at week 16. These patients were classified as early responders and controls respectively. The 2 groups were compared by Mann-Whitney-U test. A generalized estimating equation (GEE) compared the 2 groups over the course of the 2-year trial per each of the 5 domains of the MFI, adjusting for baseline DAS28CRP and baseline MFI domain score.
Results: Of the 379 patients recruited in the CareRA trial, 343 (90.5%) had a MFI score available at baseline and a DAS28CRP available at week 16 with 236 (68.8%) patients achieving remission, and 107 (31.2%) patients not achieving remission at week 16. After 2 years of treatment, the proportion of patients in DAS28CRP remission was still higher in the early responders versus controls (82.3% versus 63.5%, p=0.001). Every MFI domain after 2 years of treatment showed lower scores for early responders including general fatigue (p=0.017), physical fatigue (p=0.011), reduced activity (p=0.040) and mental fatigue (p=0.042) except reduced motivation (p=0.062) (see figure 1). GEE analysis demonstrated that all MFI domains differed over 2 years between patients in remission or not at week 16, including general fatigue (p<0.001), physical fatigue

(p<0.001), reduced activity (p<0.001), mental fatigue (p=0.037) and also reduced motivation (p=0.005).

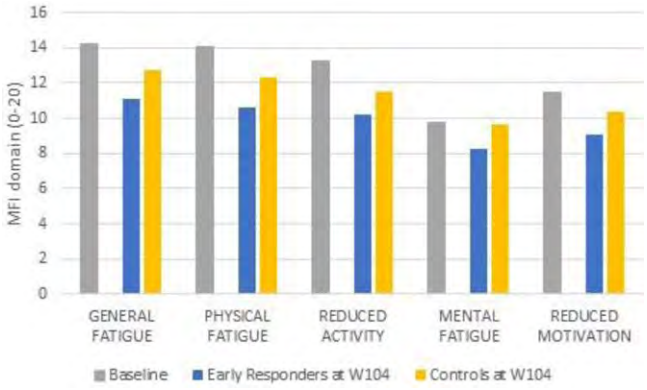


Figure 1. MFI domain scores at baseline and at week 104 per group

Conclusion: Patients reaching remission after 16 weeks of treatment achieve lower fatigue levels over 2 years compared to patients not reaching this early remission. This study underlines the importance of early disease control. Successful early intensive treatment improves in the long run not only clinical outcomes but also an important patient preferred outcome such as fatigue.

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THU0094

IN ACPA POSITIVE AT-RISK INDIVIDUALS WITHOUT CLINICAL ARTHRITIS, IS ULTRASOUND SUFFICIENTLY ACCURATE TO PREDICT PROGRESSION TO INFLAMMATORY ARTHRITIS?

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Background: In a cohort of Anti-Cyclic Citrullinated Peptide Positive (ACPA+) At-Risk of developing inflammatory arthritis (IA) individuals without clinical synovitis, we previously demonstrated the predictive value of Power Doppler for progression depending on the number of joints involved (1). Here we update these results in a larger population combining all ultrasound (US) features and incorporating them in a multivariable analysis with clinical, genetic, immunological and serological markers.

Objectives: To investigate the ability of US to predict progression to clinical arthritis using multivariable Cox analysis with and without including other variables.

Methods: In a single centre prospective cohort, 488 at risk ACPA+ individuals with new musculoskeletal symptoms underwent an US scan of 30 small joints and 18 tendons at first visit (metacarpophalangeal, interphalangeal and metatarsophalangeal joints and flexor tendons, and extensor carpi ulnaris). The predictive value of US abnormalities (Power Doppler grade ≥ 1 (PD), Grey Scale grade ≥ 2 (GS), or erosion (E) presence) for progression to IA was analysed using Cox regression analysis and adjusted for tenosynovitis (TSV) presence, age, sex, ≥3 ULN CCP2 antibody titre and/or rheumatoid factor titre (RF), early morning stiffness duration, shared epitope (HLA-DRB1*01, *04 and/or *10), number of small joints tender, elevated CRP and intermittent symptoms. A complete dataset considering all variables was available for 324 patients.

Results: Consecutive at-risk ACPA+ individuals (n=488, mean age 50.47 years old, 72.9% women) were followed up for at least 24 weeks or up to progression, for a median of 96 weeks (range 0.43-590). 130 of them (26.7%) developed IA after a median of 51.5 weeks (range 0.43 – 486).

Multivariable analysis focusing on intra-articular ultrasound features showed that individuals with 1-3 joints with a PD signal or 1-2 with E were twice as likely to develop IA (Table 1), those with ≥ 4 joints with a PD signal were more than six times more likely (Figure 1). All variables data was available in 324 participants, showing a significant predictive value of TSV presence in ≥1 joint (HR= 1.973, p= 0.024, CI= 1.095-3.553), smoking exposure (HR= 2.597, p= 0.003, CI= 1.369-4.929), shared epitope positivity (HR= 1.979, p=0.044, CI= 1.019-3.843), ≥5 small joints tender (HR= 2.111, p= 0.030, CI= 1.073-5.463), and a high titre CCP and/or RF (HR= 4.334, p= 0.003, CI=1.651-11.374).

Table 1. Multivariate Cox analysis of joint ultrasound features: non-adjusted for confounders

Joints Involved	Feature	HR	CI	P-value	PPV	NPV	N
Small joints (wrists excluded)	PD ≥1:	2.109	1.364-3.262	<0.001	44%	78.3%	488
	1-3 joints	6.524	3.465-	0.001	76.5%		
	≥4 joints		12.289	<0.001			
	GS ≥2:			0.381	20.3%	71.9%	
	1-3 joints				30.8%		
	≥4 joints						
	E presence in ≥1 joint	1.865	1.206-2.884	0.005	47.6%	76%	

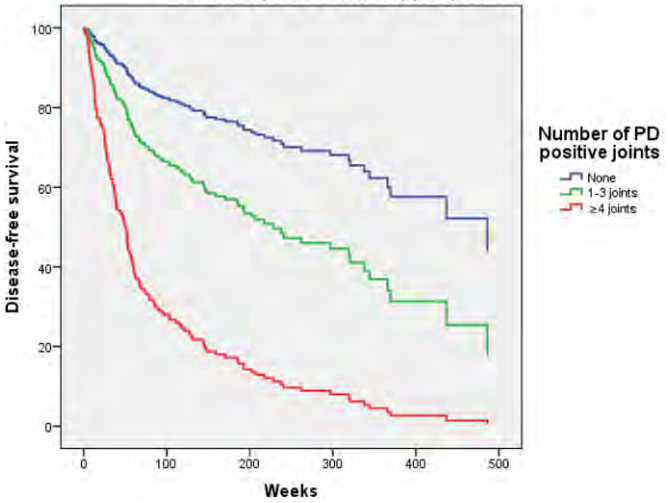
Conclusion: In at-risk ACPA+ individuals, ultrasound alone - especially Power Doppler- is a powerful predictive factor of progression to IA, therefore of high clinical value for rheumatologists. The multivariable integrated risk prediction values indicates the role of other factors to be considered in future risk model development.

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Figure 1: Cox regression analysis: Disease-free survival dependant on the number of joints Power Doppler positive



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THU0095

IMPACT OF BASELINE EROSION SCORE ON RESPONSE TO TREATMENT AND FUTURE RADIOLOGICAL DAMAGE IN AVERT-2, A RANDOMISED PHASE IIIB STUDY OF ABATACEPT IN MTX-NAÏVE, ANTI-CITRULLINATED PROTEIN ANTIBODY–POSITIVE (ACPA+) PATIENTS WITH EARLY RA

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Background: Bone erosions are associated with poor prognosis in patients (pts) with RA. They can be associated with subclinical inflammation and independently predict future radiological damage.[1] The Phase IIIb Assessing Very Early RA Treatment (AVERT)-2 (NCT02504268) trial evaluated abatacept (ABA)+MTX in MTX-naïve, ACPA+ pts with early RA.[2]

Objectives: To explore the impact of baseline (BL) X-ray erosion scores (ES) on clinical response and future radiological damage over 1 yr in different groups of pts from AVERT-2.

Methods: BL and Wk 52 X-ray data were evaluated using Sharp/van der Heijde score. SDAI remission rates (RRs; ≤3.3), unadjusted mean changes from BL (CfB) and duration of/time to sustained remission over 52 wks were evaluated. Radiographic progression was assessed at Wk 52 using CfB in ES. A range of BL ES cut-offs were evaluated to highlight key findings through comparison of pts with low and high ES.

Results: Of 994 pts in the study, 964 (97%) had BL (median 2.0, interquartile range [IQR] 0.5–5.1) and 792 (80%) had BL and Wk 52 (median 2.5, IQR 1.0–6.5) ES. Results in Table 1 are based on ES cut-offs of 2 and 5, resulting in 53% and 75%, respectively, of pts in low ES groups. In pts who received ABA+MTX, those with low ES had higher SDAI RRs over 52 wks vs pts with high ES. The relationship was more pronounced for higher cut-offs. This was not observed with ABA placebo+MTX (MTX). Greater reduction of mean CfB in SDAI was achieved in pts with high vs low ES who received ABA+MTX. This was not observed with MTX. Pts who received ABA+MTX had longer duration and shorter time to sustained SDAI remission vs MTX. With ABA+MTX, pts with low ES had longer duration and shorter time to sustained SDAI remission vs high ES. This was not observed with MTX. Mean CfB in ES at Wk 52 was lower in the ABA+MTX arm vs the MTX arm. ABA seemed to equally protect pts with low and high ES; with MTX, pts with high ES had higher mean CfB in ES at Wk 52 than pts with low ES.

Conclusion: This erosion-based stratification of the AVERT-2 early seropositive RA population emphasizes the importance of treating pts prior to the accumulation of erosive disease. Abatacept+MTX led to higher SDAI RRs in pts with low vs high ES and provided further protection vs MTX alone against future radiological damage in pts with high ES. Additional statistical modelling and adjustment for confounding factors at BL is warranted.

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THU0096

REVISITING THE REMISSION CRITERIA FOR RHEUMATOID ARTHRITIS BY EXCLUDING PATIENT GLOBAL ASSESSMENT: AN INDIVIDUAL PATIENT META-ANALYSIS INCLUDING 5792 PATIENTS

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Background: Remission nowadays is the guiding target of management of rheumatoid arthritis (RA). However, no gold standard definition of remission exists and the inclusion of patient global assessment (PGA) in remission definitions is debated (1).

Objectives: To determine the impact of excluding PGA from the ACR/EULAR Boolean remission criteria, upon prediction of radiographic outcome of RA.

Methods: Meta-analyses using individual patient data from randomized controlled trials (identified through PubMed and Clinicaltrials.gov until 2017) testing the efficacy of biological agents on radiographic outcomes at ≥2 years. Remission was defined using the ACR/EULAR remission criteria with 4 variables (Figure 1): (i) tender and swollen 28-joint counts (TJC28/SJC28), C-reactive protein (CRP, mg/dl), and PGA (0-10=worst) all ≤1 (4V-remission), (ii) the same, except PGA>1 (4V-near-remission) (iii) 3V-remission (similar to 4V, but

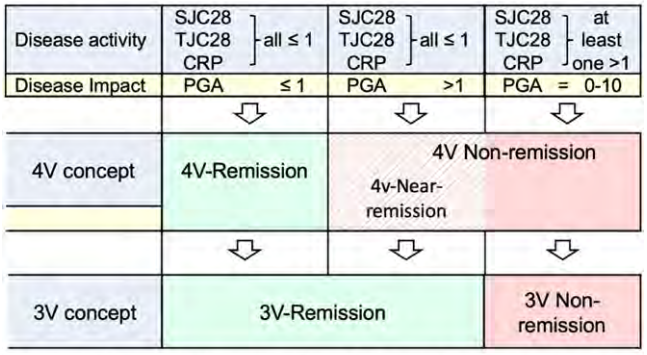
Table 1. Key Findings Based on Low and High ES Cut-offs

		ABA+MTX		ABA PBO +MTX		ABA+MTX		ABA PBO +MTX	
	ES cut-off	≤2	>2	≤2	>2	≤5	>5	≤5	>5
	n (%)	377 (56)	294 (44)	131 (45)	162 (55)	516 (77)	155 (23)	207 (71)	86 (29)
	BL SDAI	37.4 (13.4)	40.6 (13.9)	37.7 (12.6)	40.6 (14.5)	37.5 (13.4)	42.9 (13.9)	38.6 (12.7)	41 (15.9)
Wk 52	SDAI RR (≤3.3), %	35	29	20	16	34	26	17	19
	CfB in SDAI	–29.8 (14.3)	–31.5 (13.7)	–26.3 (13.6)	–25.9 (15.3)	–29.7 (14.0)	–33.5 (13.9)	–26.6 (13.4)	–24.9 (16.7)
	CfB in ES	0.3 (1.1)	0.4 (2.0)	0.9 (2.0)	1.3 (3.0)	0.3 (1.2)	0.4 (2.4)	0.9 (2.0)	1.5 (3.6)
	Time to SDAI sREM, wks	18.7 (10.7)	22.0 (10.5)	24.7 (11.5)	22.5 (9.8)	19.6 (10.7)	22.0 (10.8)	23.1 (10.7)	24.2 (10.2)
	Duration of SDAI sREM, wks	24.1 (13.0)	22.0 (11.5)	18.7 (10.1)	20.5 (11.3)	23.5 (12.8)	21.9 (10.5)	19.8 (11.0)	19.6 (10.4)

Data are mean (SD) unless otherwise stated
sREM=sustained remission

without PGA, i.e. equal to the combination of i and ii), and (iv) non-remission (TJC28 and/or SJC28 and/or CRP >1). Meta-analyses were performed using the DerSimonian-Laird random-effects method. Good radiographic outcome (GRO) was defined as an increase of ≤0.5 modified Total Sharp score (mTSS) units. The relationship between the most stringent remission class achieved at 6 or 12 months and GRO during the second year was analysed. The pooled probabilities of GRO for the different definitions of remission were estimated and compared.

Figure 1 – Definitions of remission tested in the study



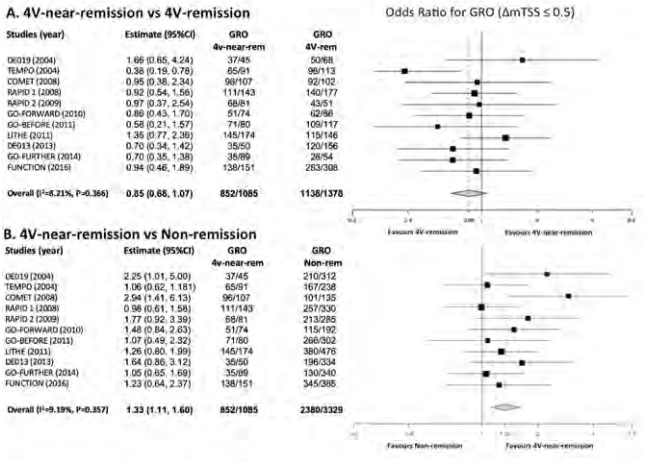
Legend: SJC28 = swollen 28-joint count, range 0-28; TJC28 = tender 28-joint count, range 0-28; CRP = C-reactive protein, mg/dl; PGA = patient global assessment, range 0-10 = worst.

Results: Individual patient data (n=5,792) from eleven trials were analysed. 4V-remission was achieved by 23% of patients (95%CI: 18-28%) and 4V-near-remission by 19% (95%CI: 15-22%) and thus, 3v-remission by 42% (95%CI: 36-48%). The probability of GRO in the 4V-near-remission group was similar to that of 4V-remission (78 vs 81%, ns) and significantly higher than that for non-remission (72%; difference 6%; 95%CI: 2-10%) (Table 1). These results were confirmed by meta-analyses of odds ratios of obtaining GRO of these groups (Graph 1). 3V-remission showed a higher predictive value for GRO (51%, 95%CI: 47-55%) than 4V-remission (41%, 95%CI: 35-46%) (Figure 2).

Table 1. Pooled outcomes and measures of association between remission categories and good radiographic outcome (GRO, defined as ΔmTSS≤0.5), during the second year of follow-up.

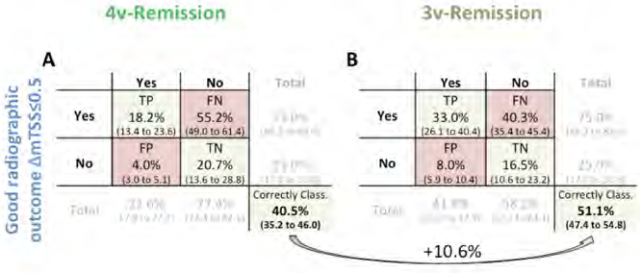
Groups	*4V-remission (n=1,378)*	*4V-near-remission (n=1,085)*	*Non-remission (n=3,329)*
Percentage GRO (95%CI)	81 (74 to 87)	78 (70 to 86)	72 (62 to 81)
Comparisons	*4V-near-remission vs 4V-remission*	*4V-near-remission vs Non-remission*	
Δ percentage GRO (95%CI)	–2.9 (–7.3 to 1.5)	6.2 (2.3 to 10.1)	

Graph 1. Meta-analyses of odds ratios of obtaining good radiographic outcome (ΔmTSS≤0.5 units); 4V-near-remission vs 4V-remission and vs Non-remission.



Legend: 4V-remission = SJC28, TJC28, CRP (in mg/dl), and PGA (0-10), all ≤1; 4V-near-remission= SJC28, TJC28, CRP (in mg/dl) ≤1 and PGA (0-10)>1; Non-remission = SJC28 >1 OR TJC28>1 OR CRP (in mg/dl)>1, irrespective of PGA value; at 6 OR 12 months of follow-up in all cases; ΔmTSS = change in the modified Total Sharp Score during the second year of follow-up

Figure 2 – Pooled meta-analytic prediction accuracy of 4V- and 3V-remission status for good radiographic outcome (n=5,792 analysed patients)



Legend: 4V-remission = SJC28, TJC28, CRP (in mg/dl), and PGA (0-10), all ≤1; 3V-remission= SJC28, TJC28, CRP (in mg/dl) ≤1; ΔmTSS = change in the modified Total Sharp Score from 12 months to 24 months. TP = True Positive; TN = True Negative; FP = False Positive; FN = False Negative; Correctly classified = TP + TN. Between brackets is the pooled 95% confidence interval.

Note: The sum of the meta-analytic percentages of TP, FN, FP, and TN is slightly less than 100%, due to error estimation when multi-category (k>2) prevalence is estimated. We used in all meta-analyses double arcsine transformation as the preferred method to correct for this effect as much as possible.

Conclusion: 4V-near-remission and the original 4V-remission are similarly predictive of GRO, therefore combining these in the 3V-remission definition potentially reduces the risk of overtreatment compared to the 4V definition. This supports the use of 3V-remission as the target for immunosuppressive therapy. The patient's perspective, which must remain central, requires a separate treatment aim: a dual-target approach.

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THU0097 PREDICTIVE VALUE OF IMMUNOLOGICAL AND IMAGING BIOMARKERS ON ACHIEVING GOOD CLINICAL RESPONSE AT 6 MONTHS IN RHEUMATOID ARTHRITIS PATIENTS TREATED BY INTRAVENOUS BDMARDS

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Background: RA is the most prevalent chronic inflammatory rheumatism, responsible of functional impairment.
Objectives: To investigate the value of biological and imaging biomarkers on predicting good clinical response at 6 months, in RA patients initiating IV bDMARD.

Methods: From 2008 to 2017, 317 RA patients fulfilling ACR 1987 and/or ACR-EULAR 2010 criteria for RA, initiated IV bDMARDs in our department of Rheumatology. Patients were excluded in cases of lack of information on disease activity assessment before and at 6 months of treatment and on immunological status and titers (ACPA, RF, ANA) at baseline. For patients receiving successive IV bDMARDs during this time period (n=30), a randomization permitted to select 1 treatment sequence for the analysis. On 173 patients eligible to the study, 4 were loss to follow-up and 14 stopped treatment due to adverse events before 6 months. Clinical, biological and imaging (US and RX) data were collected when available at baseline. US examination was performed on 12 joints (wrist, MCP2-3-5 and MTP2-3-5) with qualitative and quantitative evaluation on B mode and Power Doppler (PD) for synovitis, tenosynovitis and erosion. The modified Sharp/van der Heijde erosion score was performed by 2 independent readers blindly from clinical and US informations. Good clinical response was defined by a DAS 28 < 3.2 and/ or DAS 28 decrease > 1.2 at 6 months. Only variables with a p<0.2 in univariate analysis were included in the multivariate model.

Results: On 155 RA patients, 11 present a disease duration < 2 year, 44 (28.3%) were on first line of IV bDMARDs and 111 patients received at least one IV bDMARD (mean 2.5 (1.3)).

Table 1. Characteristics of the patients (n=155) at baseline

Variables	N (%)	Mean (SD)
Clinical characteristics Age (years)		54.8 (12.2)
Female	113 (72.9)	
Disease duration (months)		166.9 (118.8)
DAS 28		5.2 (1)
Treatment Corticosteroids / dose (mg/day)	99 (85.3)	10.9 (6)
Monotherapy	56 (36.1)	
IV bDMARD Abatacept	27 (17.4)	
Infliximab	11 (7.1)	
Rituximab	84 (54.2)	
Tocilizumab	33 (21.3)	
Immunology ACPA + /titer(IU)	132 (85.2)	618.5 (791.0)
RF + /titer (IU/ml)	114 (74.5)	184.7 (351.3)
ANA + / level	87 (56.1)	1453 (3836)
Radiography Sharp's erosion score (n=110)		49.4 (46.2)
US Nb Erosion (n=95)		3.0 (2.3)
Nb B mode Synovitis (n=128)		6.0 (4.1)
Nb PD+ Synovitis (n=130)		4.8 (3.8)
Nb B mode Tenosynovitis (n=129)		1.6 (2)
Nb PD+ Tenosynovitis (n=129)		1.3 (2.1)

At 6 months, 87 patients (56.1%) were in good clinical response. Predictive values of biomarkers are presented in table 2.

Table 2. Variables predictive of a good clinical response at 6 months

Biomarkers	Response		Multivariate Logistic regression Analysis	
	All N = 101	Response (N=60)	OR (CI95%)	P value
Immunology				
RF +	75	51 (68.0%)	**5.1 (1.8-14.4)**	**0.002**
ACPA +	87	56 (64.4%)		
ANA +	55	36 (65.5%)		
Radiography				
Erosive RA	74	48 (64.9%)		
Ultrasonography				
Erosive RA	88	55 (62.5%)		
Nb B mode synovitis	101	60 (59.4%)	**1.2 (1.1-1.4)**	**0.002**
Nb PD+ synovitis	101	60 (59.4%)		

All qualitative variables with a p value <0.2 on bivariate analysis were incorporated in the multivariate model (RF +, ACPA +, US erosive RA, Nb B mode synovitis, Nb PD+ synovitis, RX erosive RA). Only patients with all data available are incorporated in the multivariate logistic regression analysis (n=101/155)

Conclusion: We showed that positive RF was predictive of good clinical response to IV bDMARDs. For the first time, we demonstrated that number of US B-mode synovitis was also predictive to good clinical response.

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THU0098 ANTIBODIES AGAINST THREE POST-TRANSLATIONAL PROTEIN MODIFICATIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Autoantibodies to some post-translational modifications (PTMs) of proteins have a relevant role in rheumatoid arthritis (RA). Antibodies to other PMTs such as carbonylation (aCarbo) [1], nitration (aNitra) [2] and homocysteinylation (aHCis) [3] have also been described but they have been scarcely studied.

Objectives: We aimed to evaluate the presence of antibodies against three poorly studied PTMs in patients with RA and explore their value as biomarkers.

Methods: Serum samples from 196 healthy controls and RA patients meeting the 1987 ACR classification criteria that had either early RA (< 2 years from symptom onset) (n=182) or established RA (n=143) were analyzed. The antibodies were evaluated by indirect ELISA following the described protocols [1-3]. They include as antigens: HOCl- or ribose- carbonylated bovine type II collagen (HOCl-CII and GLI-CII, respectively) for aCarbo antibodies; homocysteinylated human serum albumin (Hcy-HSA) for aHCis antibodies; and *in vitro* nitrated synovial proteins and synthetic nitrated peptides (3-NT-PS and 3-NT-pep, respectively) for aNitra antibodies. The efficiency of the reactions to produce these PTMs was verified. The study was approved by the CEIC of Galicia. The results were analyzed as differences between the optical densities (OD) obtained without correction, or the specific OD after subtracting reactivity to the native protein.

Results: The aCarbo antibodies were studied in patients with early RA, as reported [1]. Despite this, uncorrected ODs against the two carbonylated forms of CII were not greater in the patients than in the controls (Table 1). Consequently, the corrected reactivity to GLI-CII that was significantly higher in patients than controls did not reflect aCarbo antibodies but differences in reactivity to native bovine CII.

Table 1. Antibodies against three post-translational protein modifications in RA patients and controls

		RA		Controls		
Antigen	Correction	Median DO	IQR	Median DO	IQR	*P*
HOCl-CII	no	0.141	0.127/0.173	0.160	0.141/0.188	0.0001
HOCl-CII	yes	-0.003	-0.011/0.008	-0.004	-0.020/0.005	0.02
GLI-CII	no	0.234	0.171/0.285	0.222	0.163/0.305	0.5
GLI-CII	yes	0.072	0.016/0.115	0.028	-0.010/0.100	0.0005
3-NT-pep	no	0.250	0.201/0.329	0.209	0.190/0.230	0.02
3-NT-pep	yes	0.137	0.097/0.185	0.113	0.100/0.133	0.1
Hcy-HSA	no	0.160	0.145/0.178	0.145	0.130/0.155	0.00011
Hcy-HSA	yes	-0.041	-0.074/-0.015	-0.038	-0.069/-0.20	0.5

The other antibodies were analyzed in patients with established RA as previously done [2,3]. However, none of them showed specific reactivity (Table 1). In effect, although an excess of uncorrected reactivity to 3-NT-pep was observed in the patients with RA, it disappeared when corrected (Table 1). Also, the vast majority of patients and controls showed no reactivity to 3-NT-SP (not shown). In turn, the aHCis antibodies were significantly elevated in patients, but only in the uncorrected analysis because the difference disappeared when corrected for reactivity against native HSA (Table 1).

Conclusion: The presence in RA patients of specific antibodies against the three PTMs has not been replicated. None of the observed reactivities were attributable to the PTMs. If confirmed, these results would indicate that only particular PTMs are relevant for RA and that carbonylation, nitration or homocysteinylation are not among them.

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Disclosure of Interests: None declared

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THU0099 THE TIME REQUIRED TO ESCALATE THE DOSAGE OF METHOTREXATE TO THERAPEAUTIC LEVELS AFFECTS THE TREATMENT SUCCESS ACHIEVED DURING PHASE I OF THE TREATMENT ALGORITHM FOR RHEUMATOID ARTHRITIS RECOMMENDED BY THE EUROPEAN LEAGUE AGAINST RHEUMATISM

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Background: In the treatment of rheumatoid arthritis (RA), methotrexate (MTX) monotherapy is undoubtedly the most cost-effective therapy available. However, no clear evidence exists for the adopted method of MTX usage, except for guidelines that have been formulated using empirical knowledge.
Objectives: We aimed to retrospectively evaluate the treatment method used to administer MTX in order to identify factors influencing the success rate of MTX treatment in phase I of the European League Against Rheumatism (EULAR) recommendation in the treatment algorithm of RA.
Methods: A total of 520 RA patients were considered for inclusion in this study, of whom 183 were eligible as they had been treated with MTX monotherapy from 2013 to 2018. The exclusion criteria included the following: unknown MTX prescription details (200 cases), deviation from the treatment algorithm i.e. use of a combination of conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) before MTX therapy (4 cases), and a long duration of MTX escalation that deviated from the treat-to-target concept (133 cases).
Patients who received csDMARD monotherapy (including switching between csDMARDs) prior to MTX monotherapy were not excluded.
The primary outcome was failed MTX monotherapy with transition to phase II.
The escalation time to the required maximum therapeutic dose of MTX and the lower limit of the required maintenance therapeutic dose that resulted in successful MTX monotherapy was determined using the receiver operating characteristic (ROC) curve. Accordingly, previous results obtained from ROC curve analyses were categorized into two groups for regression analysis: patients who tolerated MTX monotherapy and those who failed MTX monotherapy.
We performed a regression analysis on the background factors observed during their first visit to our department and two previously identified factors. The background factors included prognostically unfavourable factors related to joint destruction despite RA treatment (i.e. rheumatoid factor [RF] levels, anti-citrullinated peptide antibody [ACPA] levels, acute phase reactant levels, swollen joint counts, joint damage, and disease activity).
Results: The background factors that were statistically different were age at onset, RF levels, ACPA levels, current dose and continuity of MTX therapy, glucocorticoid (GC) use, and time until first DMARD use. After this analysis, we determined to exclude GC use from subsequent analyses as it was found to be statistically different between age groups.
Using the ROC analysis, we found that the escalation time to the maximum dose of MTX was 2.07 weeks. Further, logistic regression analysis was used to analyse each of the previously reported statistically significant factors. Statistical differences were observed in the age at onset and the escalation time of initial MTX induction therapy.
We also performed a backward stepwise logistic regression analysis on the previous two factors and conventional risk factors related to joint destruction with RA treatment. Statistical difference was observed in the escalation time of initial MTX induction therapy.
Furthermore, propensity score matching was performed by analysing the previously mentioned influencing factors and prognostically unfavourable factors of joint destruction using a backward stepwise logistic regression analysis. We identified statistical difference in the escalation time of MTX induction therapy (odds ratio: 1.957 [95% confidential interval: 1.036-3.697], p=.039).
Conclusion: These results suggest that rapid escalation to the required MTX therapeutic dose, within 2.07 weeks, during initial RA treatment can shorten the time required to achieve the treatment target. By doing this, RA patients on MTX therapy in phase I may achieve a greater treatment responsive. Thus, the short escalation time is an important factor influencing successful MTX monotherapy in the RA treatment algorithm.
Disclosure of Interests: None declared
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THU0100 FATIGUE: A PREVALENT AND PERSISTENT SYMPTOM IN EARLY RHEUMATOID ATHRITIS

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Background: Fatigue is associated with poor quality of life in people with Rheumatoid Arthritis (RA). The exact burden of fatigue in RA is uncertain. Evidence shows that fatigue may persist, even in people with well-controlled inflammatory disease. However, this is largely based on cross sectional data, and data from people with long standing or refractory disease. This study aims to examine the nature of fatigue in early RA.
Objectives: Describe the prevalence of fatigue and longitudinal course of fatigue Investigate heterogeneity in the course of fatigue and identify risk factors associated with fatigue heterogeneity
Methods: Data were from the early Rheumatoid Arthritis Network (ERAN), an inception cohort of people with a disease duration of <24mths, recruited from 2002-11 (n=1236). ERAN collected demographic, clinical, quality of life, comorbidities and laboratory data at baseline, 3-6 mths, and then annually.
Fatigue was measured using the Vitality subscale of the Short Form Health Survey questionnaire (SF36VT). Fatigue and severe fatigue were classified as SF36VT values lower than 1 and 2 standard deviations (SD) below the UK healthy population average respectively. Baseline prevalence rates standardized to Eurostat 2013 by age and sex were calculated.
The course of fatigue was examined using linear mixed effect models. Group Based Trajectory Modelling (GBTM) was used to examine heterogeneity in the course of fatigue. Baseline characteristics were then used to identify predictors of group membership using univariate and multiple regression analysis.
Results: Baseline characteristics include female sex (67%), mean age = 57(SD±14) yrs. Mean SF36VT score = 41(SD±11), median disease duration was 11 mths (IQR:7 – 18).
The age and sex standardized prevalence rates of fatigue and severe fatigue were 44%(CI:38-50) and 18% (CI:15 – 22) respectively.
729 (59%) participants were included in the longitudinal analysis. Over the course 4 years follow up, and after accounting for the effect of age, sex, patient's global assessment of disease activity, BMI, pain and mental health, there was a reduction in the population vitality levels from baseline,(β: -0.14CI: -0.26 to -0.02, $p \leq 0.001$). Inflammation measured by erythrocyte sedimentation rate (ESR) was not significantly associated with the course of fatigue.
GBTM analysis identified 2 sub-groups. These groups were named 'Fatigue' and 'No-fatigue' groups and comprised about 52% and 47% of the population respectively (Fig 1).
Females, participants with, at baseline, higher BMI, higher disability score (HAQ), disease activity score (DAS28), worse pain, mental health scores and higher comorbidity score (RDCI) were more likely to belong to the Fatigue group (each $p \leq 0.05$) in univariate analysis. However, higher BMI (OR 1.05 (CI: 1.0 – 1.1), HAQ (OR 2: CI: 1.5 - 2.7), RDCI(OR 1.3, CI: 1.2 – 1.5), worse SF36 pain and mental health scores (OR 0.93 CI: 0.92 – 0.95) and (OR 0.97, CI: 0.95 – 0.99) were collectively associated with fatigue group membership (AUROC=0.81).

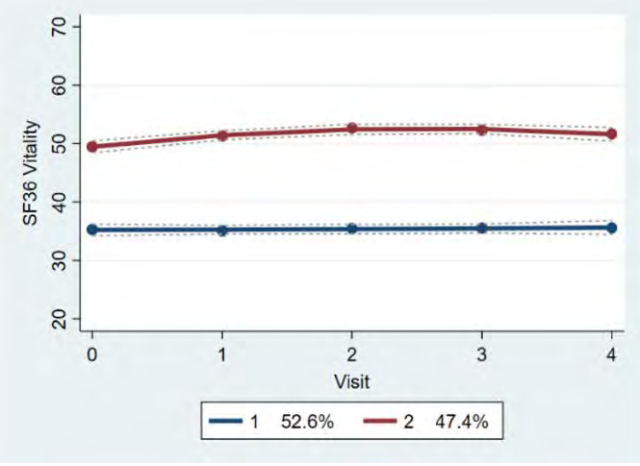


Fig 1. Fatigue Trajectories

Conclusion: Fatigue is a prevalent symptom in RA, even in early disease. Embedded within the RA population are distinct sub-populations, with or without fatigue. Those with fatigue at baseline were likely to continue to report fatigue over 4 years of follow up. Unlike our previous data on pain trajectories within this cohort, a 'resolving fatigue' was not found. Diverse baseline characteristics, including pain, were associated with persistent fatigue. Management of fatigue might require strategies additional to disease modification, and people who require such interventions might be identified at presentation with early RA.
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THU0101 **IMPACT OF TREATMENTS ON RADIOGRAPHIC PROGRESSION OVER THE FIRST 10 YEARS OF DISEASE IN EARLY RHEUMATOID ARTHRITIS: RESULTS FROM THE ESPOIR COHORT**

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Background: Long-term observational studies on the prediction of structural damage progression (SDP) in rheumatoid arthritis (RA) have mostly considered patients baseline characteristics and have rarely evaluated the specific impact of treatments in real world settings.
Objectives: To assess the impact of treatments exposure on the 10-year radiographic progression in early rheumatoid arthritis (RA).
Methods: The 310 patients of the ESPOIR cohort fulfilling ACR/EULAR 2010 criteria at baseline and having complete radiographic data at baseline and 10 years were considered in the present study. SDP was defined at 10 years as a significant increase of the Sharp/van der Heijde score, i.e., superior to the Smallest Detectable Change of 11.5 at 10 years. Three RA treatments were considered: glucocorticoids (GC), conventional synthetic and biologic Disease-Modifying Anti-Rheumatic Drugs (csDMARDs and bDMARDs), which posologies were standardized by the mean of dose quotients (DoseQ). Drug exposure was modelled with Weighted Cumulative Exposure (WCE) variables, considering the intensity of drug exposure defined as a weighted function of past doses, and was incorporated into a logistic regression model that also included baseline clinical, biological and radiological characteristics. The predictive performance of this WCE model was compared to models considering on the one hand only baseline characteristics (BSL model) and on the other, baseline characteristics and binary treatments exposure - in other terms, "ever exposed, yes or no" (BIT model).
Results: Overall, SDP at 10 years occurred in 85 (27.4%) patients. GC exposure was significantly associated with SDP in univariate analysis only, and therefore was not included in the final WCE model. In the final WCE model, the joint exposure to 1 DoseQ of csDMARD and 1 DoseQ of bDMARD during the 10-year follow-up was associated with a significant protective effect on SDP compared to patients receiving no treatment: OR=0.04 (95% CI: 0.002-0.72). Early csDMARD initiation was associated with a significantly lower risk of SDP compared to later initiation (Table 1).

Table 1. odd ratios for the association of patterns of drug regimen with 10-year radiographic progression

Exposure tested	Reference	OR (95%CI)
Treatments intakes during the last 10 years		
csDMARD & bDMARD for last 10 years	No treatment for last 10 years	0.04 (0.002-0.72)
Testing the interest of an early initiation of csDMARDs (not combined with bDMARD)		
csDMARD for last 10 years	csDMARD after month 3	0.79 (0.65-0.96)
	csDMARD after month 6	0.41 (0.19-0.86)
	csDMARD after year 1	0.13 (0.02-0.80)
Testing the interest of an early initiation of bDMARDs (in association with csDMARD)		
bDMARD after month 3	No treatment for last 10 years	0.04 (0.002-0.72)
bDMARD after month 6		0.04 (0.002-0.72)
bDMARD after year 1		0.04 (0.002-0.72)
bDMARD after year 2		0.04 (0.003-0.73)
bDMARD after year 3		0.05 (0.03-0.81)

Initiation of a bDMARD between the 3rd month and 3rd year of follow-up in combination with a csDMARD was significantly associated with a lower risk of SDP compared to no bDMARD treatment (Table 1).
The final WCE model was better at predicting SDP at 10 years compared to the BSL and BIT models, with AUC=0.92 (95% CI: 0.89-0.95) (Figure 1).

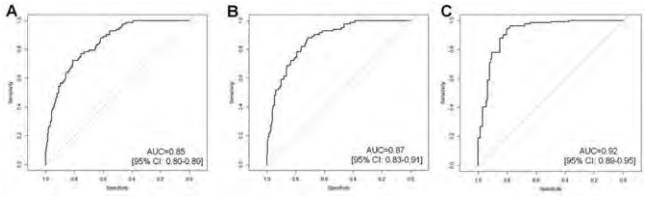


Figure 1. ROC curves of BSL model (A), BIT model (B) and WCE combined model (C) for 10-year radiographic progression

Conclusion: CsDMARDs and bDMARDs have a protective effect on radiographic progression at 10 years in RA patients. This study has shown the value of considering drug exposure in the study of RA prognosis, and modeling this exposure using WCE variables.
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THU0102 **DENDRITIC CELLS AS A PREDICTOR OF GOOD CLINICAL RESPONSE IN RHEUMATOID ARTHRITIS PATIENTS**

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Background: Dendritic cells (DCs) are known to contribute to the pathogenesis of rheumatoid arthritis (RA) through presentation of cartilage glycoprotein, production of proinflammatory cytokines and activation of Th1/Th17 responses. DCs are a heterogeneous population and can be divided into groups: myeloid (mDCs) and plasmacytoid (pDCs). DCs can induce both immune response and tolerance.
Objectives: To investigate the subpopulations of peripheral blood DCs (myeloid and plasmacytoid) in patients with early RA as a predictor of responsibility to disease-modifying antirheumatic drugs (DMARDs) treatment.
Methods: Fifty two patients with early RA (duration of the disease up to 12 months) were included in the study. All patients fullfield ACR/EULAR criteria (2010) and received methotrexate, leflunomide, sulfasalazine or their combination. Fifty five patients with osteoarthritis (OA) used as a control group. Analysis of the content of the B-lymphocytes, myeloid and plasmacytoid DCs was carried out by flow cytometry. B-lymphocytes, subtypes of peripheral blood DCs were characterized by the following phenotypes: myeloid DCs (CD3-CD14-CD19-HLA-DR + CD11c + CD123-), plasmacytoid DCs (CD3-CD14-CD19-HLA-DR + CD11c-CD123 +), B-lymphocytes (CD19 +). Analyses were performed before treatment and after 3 and 6 months.
Results: Patients with early RA are characterized by significant evaluation of the population of myeloid DCs in comparison of patients with osteoarthritis (26.6% vs 23.5, p=0.0007). Furthermore, the difference was found in the number of cells with the phenotype B-lymphocytes: 5.4% vs 3%, p = 0.0005). No significant differences were observed in the number of plasmocytoid DCs. After 3 and 6 month of observation we detected reducing amount of myeloid DCs 26.6% vs 21.1% vs 18.4% respectively. Also we revealed reducing B-cells in treatment (5.4% vs 3 % vs 2%). Disease activity according to DAS28 droped to low (4.32 to3.06, p=0.03). We also revealed a reliable negative correlation between both the activity of the disease and the B- cells (rS=-0.4, p=0.05, n=52) and myeloid DCS (rS=-0.6, p=0.0004, n=52). A reducing of the immune cells during the DMARDS therapy suggests that they are an attractive marker for good clinical response to therapy.
Conclusion: The data obtained confirm the determining role of myeloid DC and B lymphocytes in maintaining systemic inflammation in rheumatoid arthritis. In addition, these cells are a target of DMARDs therapy and a predictor of a good clinical response.
Disclosure of Interests: None declared
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THU0103 **COMPARISON OF BONE SCINTIGRAPHY AND FDG-PET/CT IN THE EVALUATION OF DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS: VALIDATION OF BONE SCINTIGRAPHY**

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Background: Clinical joint count assessment is important for detecting synovitis but its reliability is controversial
Objectives: This study assessed the correlation between bone scintigraphy and positron emission tomography (PET)-derived parameters in 28 joints with disease activity and compared the reliability of joint counts between bone scintigraphy and clinical assessment in rheumatoid arthritis (RA).
Methods: We enrolled 86 patients with active RA who underwent bone scintigraphy, fluorine-18-fluorodeoxyglucose (FDG) PET/CT and disease activity evaluation at the same time. This two-step study involved a development (n=67) and validation (n=19) group. Bone scintigraphy-derived joint assessment were compared with PET/CT derived and clinical joint assessment. Subsequently, we developed a disease activity score (DAS) using bone scintigraphy-positive joints and validated it in an independent group.
Results: The number of bone scintigraphy-positive joints in 28 joints was significantly correlated with the swollen (SJC)/ tender (TJC) joint counts and PET/CT derived joint counts. Intra- and inter-observer reliabilities of bone scintigraphy for the affected joint counts were excellent. Inter-observer reliability between nuclear medicine physicians and rheumatologists was good for SJC/TJC and PET/CT derived joint counts in 28 joints except shoulders. After multivariate analyses including erythrocyte sediment rate (ESR) and patients global assessment (PGA) in addition to bone scintigraphy-derived parameters, bone scintigraphy/DAS was derived as 0.056 × number of bone scintigraphy-positive joints in 28 joints + 0.012 × ESR + 0.030 × PGA. A significant correlation between bone scintigraphy/DAS and DAS28-ESR was confirmed in the validation group (p<0.001).
Conclusion: Bone scintigraphy-derived joint assessment significantly correlated with PET/CT derived joint counts. Bone scintigraphy could serve as a sensitive and reliable method for evaluating disease activity in RA patients.
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THU0104 THE GUT MICROBIOTA AND ITS RELEVANCE TO PERIPHERAL T REGULATORY CELLS AND T HELPER 17 IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a common autoimmune disorder with joint destruction and synovial inflammation characterized by abnormal immune responses to autoantigens. Our previous studies have demonstrated that impaired peripheral lymphocytes especially insufficiency of regulatory T cells (Tregs) played an important role in pathogenesis of RA[1 2]. Interestingly, the dysbiosis of gut microbiota triggers several types of autoimmune diseases through the imbalance of T lymphocyte subsets[3]. However, the detailed gut microbiota of RA patients and its correlation with Tregs and helper T cells 17 (Th17) are unclear up until now.
Objectives: To compare the difference of gut microbiota between RA and healthy controls (HCs), and to investigate the relevance of gut microbiota with circulating Tregs and Th17 in patients with RA.
Methods: From December 2018 to August 2019, a total of 205 diagnosed patients with RA and 199 age and sex-matched HCs were enrolled in this study. Stool of Every participant was collected for bacterial DNA extraction and 16S ribosomal RNA (rRNA) gene sequencing. The absolute numbers of Tregs and Th17 in PB of these individuals were measured by Flow Cytometer (FCM) combined with standard absolute counting beads. Data were expressed as mean ± standard deviation to the distribution. Independent-samples T test and Spearman rank correlation test. P value <0.05 were considered statistically significant.
Results: Patients with RA had a significantly difference of diversity and abundance of intestinal microbiota compared with those of HCs (P< 0.05). Detailedly, the abundance of Proteobacteria was significantly increased in RA patients (P< 0.05), and the abundance of Firmicutes, Fusobacteria and Verrucomicrobia were significantly reduced (P<0.05) at the level of Phylum (Figure 1). At the genus level, in the RA group, the abundance of Escherichia, Ruminococcus2 and Clostridium_sensu_stricto were significantly increased (P< 0.05), but the abundance of Lachnospiracea_incertae_sedis, Prevotella, Clostridium_XlVa, Roseburia, Dialister, Blautia, Megamonas and Gemmiger were significantly lower than the healthy controls (P< 0.05) (Figure 2). Moreover, Blautia, Anaerostipes and Ruminococcus2 have negative correlation with the absolute number of Tregs, and Cloacibacillus and Streptophyta have positive correlation with the absolute number of Th17.
Conclusion: Patients with RA had a dysbiosis of the gut microbiota in both diversity and abundance, which is closely related to the impaired peripheral lymphocyte subsets, that may be related to the pathogenesis of RA, which might provide a new idea for RA treatment.
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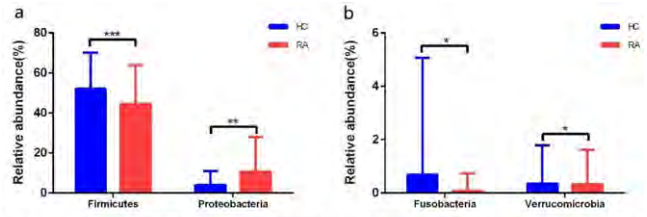


Figure1: The phylum-level profile for rheumatoid arthritis (RA) patients and healthy controls (HCs). Data were expressed as mean ± standard deviation to the distribution. Independent-samples T test was applied. (* P<0.05, ** P<0.01, *** P<0.001)

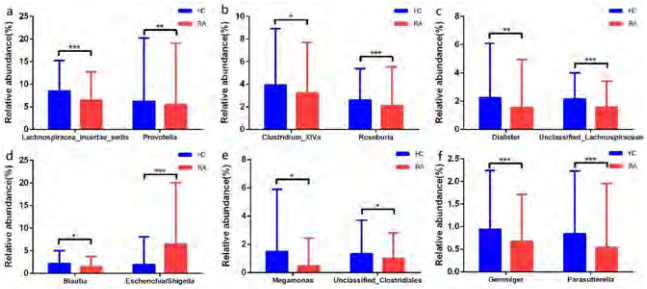


Figure2: The genus-level profile for rheumatoid arthritis (RA)patients and healthy controls (HCs). Data were expressed as mean ± standard deviation to the distribution. Independent-samples T test was applied. (* P<0.05, ** P<0.01, *** P<0.001)

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THU0105 ISOTOPE-LABELING-LC-MS-BASED METABOLIC PROFILING OF MULTIPLE SERUM SAMPLE SETS FOR THE DISCOVERY OF HIGH-CONFIDENCE RHEUMATOID ARTHRITIS BIOMARKERS

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Background: Early diagnosis of rheumatoid arthritis (RA) is hampered by suboptimal accuracy of currently available serological biomarkers. Metabolomics may reveal promising biomarker candidates associated with the biomolecular processes of RA. In this work, we applied a high-performance chemical isotope labeling (CIL) LC-MS technique for in-depth profiling of the amine/phenol-submetabolome in serum samples. To avoid false positives and obtain high-confidence biomarker candidates, we analyzed three independent sets of serum samples collected from RA patients and healthy controls to examine the common effects.
Objectives: We aimed to identify a metabolite signature with consistently high accuracy for RA.
Methods: Serum samples were taken from 3 RA cohorts, which comprised 50, 49, and 131 RA patients, respectively. Within each cohort, there were

sex/age-matched healthy controls: 50 in Cohort 1, 50 in Cohort 2, and 100 in Cohort 3. Among these 446 subjects, 75% were females and the average age was 52.5 years. Amine/phenol-containing metabolites were labeled by ^{12}C-dansyl chloride to improve the LC-MS detection. For each cohort, a pooled sample was prepared and labeled by ^{13}C-dansyl group to serve as the reference sample for relative quantification. Then the individual samples and the pooled sample were mixed 1:1. Finally, an LC-QTOF-MS platform analyzed the mixtures and output the intensity ratios of ^{12}C/^{13}C peak pairs.

Results: 1,149 amine/phenol-containing metabolites were commonly detected across the three sample sets. Among them, 134 were positively identified by our dansyl-labeling standard library, and 141 were matched to predicted retention times and mass values of dansyl-labeled human metabolites. Visualized by the partial least squares discriminant analysis (PLS-DA), the overall amine/phenol-submetabolome demonstrated clear and consistent differences between healthy controls and the RA groups, with cross-validation Q2 = 0.765, 0.745, 0.793, respectively. The selection of significant metabolites was conducted according to the fold change and false-discovery-rate-adjusted Welch's t-test. Cohort 1 demonstrated 85 metabolites having higher concentrations in the RA samples than the controls, and 89 metabolites with lowered concentrations. The numbers of increased/decreased metabolites in Cohort 2 and 3 were 87/26 and 90/53, respectively. Importantly, there were 59 significantly discriminatory metabolites commonly found in the three data sets (49 increased and 9 decreased). We picked the top three with the highest univariate classification performance to form a biomarker panel. We implemented the linear support vector machine (SVM) to build the classifier and the receiver operating characteristic (ROC) analysis to measure the performance. The area-under-the-curve (AUC) values (95% confidence interval) were 1.000 (1.000-1.000), 0.992 (0.967-1.000) and 0.902 (0.858-0.945) for the three cohorts, respectively. The results revealed the importance of examining multiple sample sets and even in the worst case (Cohort 3), our biomarker candidates could differentiate RA at 82.5% sensitivity and 82.5% specificity. Particularly, in Cohort 3, there were 30 RA patients negative for anti-cyclic citrullinated peptide and rheumatoid factor, and our metabolite panel demonstrated consistently high performance for differentiating these specific subjects from healthy controls.

Conclusion: Metabolites showing significant and consistent changes associated with RA have been identified with high discriminative power.

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THU0106 PREDICTORS OF FLARE IN RHEUMATOID ARTHRITIS PATIENTS WITH LOW DISEASE ACTIVITY

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Background: Low disease activity (LDA) in patients with rheumatoid arthritis (RA) are usually recognized as stable state. In according to most guidelines for RA, monotherapy of disease modifying anti-rheumatic drug (DAMRD) was recommended for RA patents with LDA. But some of patients with LDA suffer from flare in their disease course. Until now, we don't have enough data on factors that can predict flare in RA patients with LDA.

Objectives: The aim of this study is to evaluate predictor of flare in RA patient with LDA from long-term (3 year) cohort data.

Methods: Korean observational study network for arthritis (KORONA) registry is a nationwide Korean RA specific cohort registry that collecting data annually from 5,376 RA patients in 23 centers across South Korea. We include the data from 1, 801 RA patients with LDA (28 –joint disease activity score (DAS 28) < 3.2 at enrollment) who had consecutive data of DAS28 for 3 years. Flare was defined as an increase in DAS28 compared with baseline of >1.2 or >0.6 if concurrent DAS28 ≥3.2. Cox regression analysis was used to identify baseline predictors of flare.

Results: Among 1,801 RA patients, 673 patients (37.4%) experienced flare in 3 years. When we compare the baseline characteristics of both flare and non-flare group, more women and more non-adherent patients for medication were observed in flare group. Flare group had longer disease duration, lower EuroQol 5D score, higher health assessment questionnaire (HAQ) score, and higher erythrocyte sedimentation rate (ESR) than non-flare group at baseline. In multivariate analysis, physician's VAS, HAQ score, ESR, and poor adherence for medication were significant predictors of flare (Table 1).

Table 1. Multivariate analysis of prediction of flare with baseline variables

Measure	Hazard ratio	95% Confidence Interval	P-value
Female	1.130	0.906-1.409	0.280
Age	0.996	0.988-1.005	0.414
Physician's VAS	1.008	1.002-1.013	<0.01
Pain VAS	1.002	0.998-1.006	0.34
EQ5D	0.952	0.534-1.696	0.87
HAQ	1.407	1.109-1.786	<0.01
ESR	1.008	1.002-1.014	<0.01
Poor adherence	1.272	1.047-1.545	<0.05

VAS: Visual Analogue Scale; EQ5D: EuroQol 5D; HAQ: Health Assessment Questionnaire; ESR: Erythrocyte Sedimentation Rate

Conclusion: RA patient who have risk factors for flare, even though their disease activity was low, require more proactive treatment.

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THU0107 OBESITY PREDICTS RESPONSE TO NOT ALL BUT CERTAIN BIOLOGICAL / TARGETED DISEASE MODIFYING ANTI-RHEUMATIC DRUGS FOR RHEUMATOID ARTHRITIS - RESULTS FROM KANSAI CONSORTIUM FOR WELL-BEING OF RHEUMATIC DISEASE PATIENTS (ANSWER COHORT)

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Background: A number of previous reports suggested that obesity is one of the baseline factors indicates refractory to biologic disease-modifying antirheumatic drugs (bDMARDs). However, difference of the significant responses appears on obesity patients depending on each kind of drug is yet unclear. However, it is yet unclear how the significant responses on obesity patients vary on each kind of drug.

Objectives: To assess whether obesity affects clinical outcome in rheumatoid arthritis (RA) treated with each molecular-targeted agent including bDMARDs and tofacitinib.

Methods: In Kansai consortium for well-being of rheumatic disease patients (ANSWER) cohort, which was the real-world retrospective cohort of clinical database for rheumatic diseases, RA patients who initiated biological / targeted disease modifying anti-rheumatic drugs were included and consecutively followed. Obesity was defined as BMI over than 25, and patients were divided between

obese ("Ob") and non-obese ("non-Ob") patients. SDAI (simplified disease activity index) was compared between non-Ob and Ob at month 0, 3, 6, 9, 12 after the indicated drugs were administered. Using logistic regression analysis, odds ratio (OR) and their corresponding 95% confidence intervals (95% CIs) were further calculated to estimate achievement rate of SDAI remission defined as lower than 3.3 by obesity and other relevant clinical parameters. Once after the drugs were discontinued by any unfavorable reason, disease activities were no more scored and the Last Observation Carried Forward (LOCF) imputation method was used for SDAI at month 3 and thereafter.

Results: A total of 1936 patients met in the inclusion criteria were under the analysis. In each drug, SDAI remission rate (non-Ob, Ob, p-value by Chi-square test) at month 12 was as follows; Infliximab (IFX, n=135): 43%, 38%, NS (not significant); Etanercept (ETN, n=188): 44%, 19%, p=0.0122; Adalimumab (ADA, n=169): 50%, 56%, NS; Golimumab (GLM, n=315): 36%, 30%, NS; Certolizumab pegol (CZP, n=131): 33%, 56%, p=0.0287; Tocilizumab (TCZ, n=423): 41%, 29%, p=0.0456; Abatacept (ABT, n=144): 26%, 23%, NS; Tofacitinib (TOF, n=69): 27%, 23%, NS. In multivariate analysis to predict SDAI remission at month 12, obesity was an independent protective factor in CZP (OR: 0.29, 95% CIs: 0.10 – 0.83), but was an independent risk factor in TCZ (OR: 1.9, 95% CIs: 1.01 – 3.61) irrespective of age, sex, disease duration, SDAI at month 0 or number of previous bDMARDs. Any other drug including ETN did not show significant result between non -Ob and Ob in the multivariate analysis.

Conclusion: Obese patients were more resistant to TCZ but more effective in CZP than non-obese patients.

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, Speakers bureau: AbbVie, Asahi Kasei Pharma, Astellas Pharma, Bristol-Myers Squibb, Chugai Pharmaceutical, Eisai, Eli Lilly and Company, Janssen Pharmaceutical, Mitsubishi Tanabe Pharma, Novartis Pharma, Pfizer, Taisho Pharmaceutical, Takeda Pharmaceutical, and UCB Japan., Hiromu Ito: None declared, Koichiro Ohmura Grant/research support from: Astellas Pharma, AYUMI Pharmaceutical, Chugai Pharmaceutical, Daiichi Sankyo, Eisai, Japan Blood Products Organization, Mitsubishi Tanabe Pharma, Nippon Kayaku, Nippon Shinyaku, Sanofi, and Takeda Pharmaceutical., Speakers bureau: AbbVie, Actelion Pharmaceuticals Japan, Asahi Kasei Pharma, AYUMI Pharmaceutical, Bristol-Myers Squibb, Chugai Pharmaceutical, Eisai, Eli Lilly and Company, GlaxoSmithKline, Janssen Pharmaceutical, Mitsubishi Tanabe Pharma, Novartis Pharma, and Sanofi.

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THU0108 REAL-WORLD RADIOGRAPHIC PROGRESSION IN RA WITH BIOLOGIC DMARDS

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Background: As structural damage is irreversible and strongly associated with functional disability[1], it is an important outcome to be prevented in rheumatoid arthritis (RA). Acute phase markers, rheumatoid factor (RF) and anti-citrullinated protein (anti-CCP) positivity are important predictors of erosive disease[2]. Previous studies conducted in real life setting have divergent results regarding the role of disease activity in radiographic progression[3,4].

Objectives: To evaluate the impact of disease activity and biologic disease modifying anti-rheumatic drugs (bDMARDs) on radiographic progression of established RA in clinical practice in southern Brazilian public health system.

Methods: Longitudinal retrospective study including patients with RA (1987 ACR criteria) treated with bDMARDs and followed from 2015 to 2019. Clinical and demographic data were collected at baseline. Radiographs of hands and feet were performed yearly. X-rays were scored according to the van der Heijde-modified total Sharp method (vdH-mTSS) in known chronological order. Clinical relevant radiographic progression (CRRP) was defined as an increase ≥3 units on the score per year5.Demographic, clinical, and radiographic characteristics of RA patients with or without relevant progression were compared with Fisher exact and Mann-Whitney test.

Results: Seventy-five patients were included. The patients' characteristics are shown in table 1. Twenty three (30%) patients presented CRRP at any time point of the follow up (figure 1). Mean DAS28-ESR at baseline was higher in patients who progressed radiographically, than those who did not progress (4.8±1.1 vs 3.5±1.1; $p < 0.001$). No patient in remission at baseline presented with CRRP. Radiographic progression occurred in 15% of patients in low disease activity, 34% of patients in moderate disease activity and 57% of patients in high disease activity at baseline, depicting a linear relation between categories of disease activity and CRRP. RF, anti-CCP, disease duration, educational level, smoking status, total vdH-mTSS at baseline, number and duration of biologic DMARDs were not associated with CRRP. No single biologic DMARD was associated with worse radiological prognosis.

Table 1. Baseline characteristics and bDMARD treatment during 5 years of follow up

Characteristics	N = 75
Age, yrs, mean ± SD	58.1 ± 10.1
Female, n (%)	65 (86.6)
Disease duration, yrs, mean ± SD	16.2 ± 7.6
IgM RF positivity, n (%)	69 (92)
Anti-CCP positivity, n (%)	27 (75) *
DAS28-ESR, mean ± SD	4.2 ± 1.0
Educational level, n(%)	
Elementary school (≤ 8years)	49 (65)
Intermediate school (9-12 years)	23 (30,6)
University/college degree	3 (4)
Smoking	
Current or former	31 (41.3)
Never	44 (58,7)
vdH-mTSS, median (IQR)	21 (5-53)
Number of bDMARD, mean ± SD	2.4 ± 1.1
Duration of bDMARD, yrs, mean ± SD	7.4 ± 2.6
Methotrexate use, n, %	61 (81)
Biologic DMARD	184**
TNF inhibitors, n, %	106 (57.6)
Tocilizumab, n, %	30 (16.3)
Abatacept, n, %	25 (13.6)
Rituximab, n, %	23 (12.5)

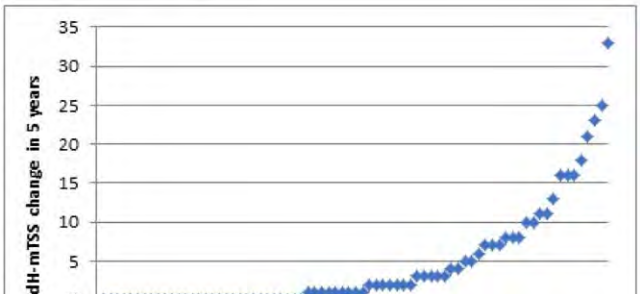
RF rheumatoid fator anti-CCP anti-citrullinated protein bDMARD biologic disease-modifying anti-rheumatic drug ESR erythrocyte sedimentation rate DAS28 disease activity in 28 joints vdH-mTSS van der Heijde-modified total Sharp score IQR interquartile range *information available from 36 patients **all bDMARD treatments

Conclusion: In contrast to controlled clinical trials, real-world studies have shown that patients with RA treated with bDMARD still develop radiological progression. We observed that despite prognostic factors, achievement of treatment target is the most important factor to prevent articular damage in RA.

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Figure 1. Cumulative probability plot of radiographic progression assessed by van der Heijde-modified total Sharp score (vdH-mTSS) in five years (n= 75)



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THU0109 DOES HIGH BASELINE LEVEL OF MATRIX METALLPROTEINASES 3 (MMP3) INDICATE MORE MTP5 JOINT EROSIONS IN EARLY RHEUMATOID ARTHRITIS PATIENTS? (THE 2-YEAR PROSPECTIVE ULTRASONOGRAPHIC STUDY)

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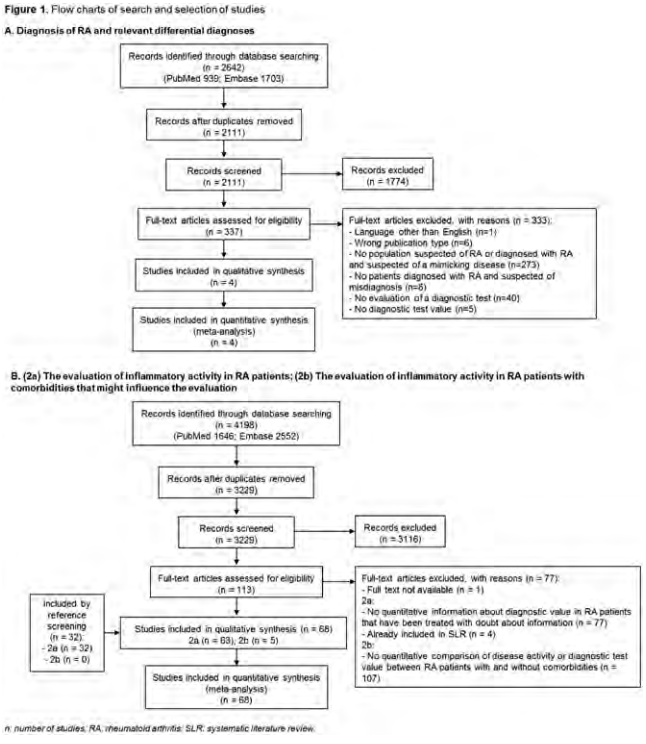
Background: The serum MMP3 level is considered biomarker which reflects local inflammation of joints and correlates with joint damage progression in early rheumatoid arthritis (1).
Objectives: To investigate the association of high baseline MMP3 serum levels with bone erosion finding at the level of typical location for rheumatoid arthritis (RA) in patients with early, treatment "naïve" RA, who has no radiographic visible erosions, using ultrasound method (US).
Methods: Sixty-three pts. (9 males and 54 females; mean age 53.4 yrs 21-81 ± 14.1) with early RA according to EULAR/ACR 2010 criteria and symptom duration of ≤12 months (mean duration of 3.8 months) had baseline serum MMP3 levels tested. Serum levels of soluble MMP3 were performed blindly, without knowledge of the US data at the basal visit only, using the recommended normal cut-off range (a level above normal was rated as positive). Patients had been DMARDs/glucocorticoid naïve, with no visible X-ray erosions at the study entry. The lateral, dorsal and posterior part of styloid, MCP2, MCP5 and MTP5 joints of both side, were analyzed for presence of bone erosion (yes/no), according to OMERACT US group definition, using high frequency linear probe by ESAOTE My Lab 70 machine at baseline visit and after 24 months.
Results: The 50 pts completed follow-up. 46 pts. had basal serum MMP3 level higher than normal (MMP3 +, mean value 185.1±241.0). US bone erosions were present in 55/63 (87.3%) pts, most often in MTP5 joints, both at the study entry and after 24 months of follow up (25 pts-39.6% and 32 pts-64% respectively). At baseline visit no significant difference was found between a group of MMP3+ and MMP3- pts. regarding to US bone erosion presence at the level of all analyzed joints (styloid process: 12 MMP3+/4 MMP3- pts.; p=0.836; MCP2: 14 MMP3+/6 MMP3- pts., p=0.713; MCP5:8 MMP3+/0 MMP3- pts, p=0.06; MTP5: 26 MMP3+/11 MMP3- pts, p=0.55). After 24 months, significant difference was found between a group of MMP3+ and negative pts for MTP5 US bone erosions finding (33 MMP3+/ 6 MMP3- pts, p=0.03) only, (styloid process:21 MMP3+/5 MMP3- pts, p=0.623; MCP2: 26 MMP3+/7 MMP3- pts, p=0.851, MCP5: 14 MMP3+/2 MMP3- pts, p=0.266).
Conclusion: In our group of RA patients without initial X-ray changes, the high baseline serum level of MMP3 was significantly correlated with new MTP5 bone erosions by US after 2-year of follow-up.
References: TCHETVERIKOV I, LARD LR, DEGROOT J*et al*: Matrix metalloproteinases-3, 8, 9 as markers of disease activity and joint damage progression in early rheumatoid arthritis.*Ann Rheum Dis* 2003;62:1094–99.

Disclosure of Interests: Slavica Prodanovic: None declared, Mirjana Sefik Bukilica: None declared, Jelena Colic: None declared, Srdjan Seric: None declared, Nemanja Damjanov Grant/research support from: from AbbVie, Pfizer, and Roche, Consultant of: AbbVie, Gedeon Richter, Merck, Novartis, Pfizer, and Roche, Speakers bureau: AbbVie, Gedeon Richter, Merck, Novartis, Pfizer, and Roche
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THU0110 DIAGNOSTIC ISSUES IN DIFFICULT-TO-TREAT RHEUMATOID ARTHRITIS: PRELIMINARY RESULTS OF A SYSTEMATIC LITERATURE REVIEW INFORMING THE 2020 EULAR RECOMMENDATIONS FOR THE MANAGEMENT OF DIFFICULT-TO-TREAT RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) patients treated according to European League Against Rheumatism (EULAR) recommendations failing ≥2 biological or targeted synthetic disease-modifying antirheumatic drugs (DMARDs) with a different mode of action who still have complaints which may be suggestive of active disease may be defined as suffering from 'difficult-to-treat RA'. Before switching to another DMARD in these patients, the diagnosis of RA and the presence of inflammatory activity should be verified to prevent possible over- and under treatment.
Objectives: To systematically summarise evidence in the literature on diagnostic issues regarding (mis-)diagnosis of RA and mimicking diseases, and assessment of inflammatory disease activity in difficult-to-treat RA patients, informing the 2020 EULAR recommendations for the management of difficult-to-treat RA.
Methods: A systematic literature search was performed: PubMed and Embase databases were searched up to December 2018. Relevant papers were selected and appraised (Figure 1).
Results: Regarding (mis-)diagnosis of RA and its differential diagnoses, four studies were selected (Figure 1a): one assessed the diagnosis of RA and three focused on coexisting mimicking diseases (fibromyalgia and bacterial infection). No diagnostic tests were replicated. For evaluation of inflammatory



activity in RA, and specifically the effect of comorbidities on assessing inflammatory activity, 63 and five studies, respectively, were included (Figure 1b). At patient level, ultrasonography (US) scores were related to composite indices (range of correlations (r): 0.25-0.70) and swollen joint counts (range r: 0.33-0.78). A multi-biomarker disease activity score (range r with composite indices: 0.41-0.52) and optical spectral transmission measures (range r with US: 0.54-0.64) were promising measures, but cut-offs are preliminary. At joint level, US was related to MRI (range of sensitivity 64-91% and specificity 60-94% for synovitis) and histology (range r: 0.52-0.65 for inflammation). Concomitant obesity and fibromyalgia may lead to overestimation of disease activity according to composite indices, US may be used to assess inflammatory activity in these patients.

Conclusion: This SLR highlights the gap of knowledge in the optimal confirmation of a (mis-)diagnosis of RA or diagnosis of mimicking diseases in difficult-to-treat RA patients. Current evidence for optimal assessment of inflammatory activity when there is doubt based on clinical assessment and composite indices is limited. Most studies reported correlations which are not directly useful in clinical practice to determine presence or absence of inflammatory activity. The evidence will be updated up to December 2019. Currently, US seems the most accurate measure to evaluate the presence of inflammation in difficult-to-treat RA patients, including those with concomitant obesity or fibromyalgia.

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THU0111 PHYSICIAN'S GLOBAL ASSESSMENT OF DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS: WHAT DO WE REALLY MEAN?

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Background: Physician's global assessment of disease activity (PhGA) is included in some scores of disease activity and, demonstrably, plays a major role upon treatment decisions in rheumatoid arthritis (RA) [1, 2, 3]. Therefore, understanding the reasons underlying the physician´s assessment is crucial.

Objectives: To understand the reasons underlying the physician´s assessment.

Methods: Cross-sectional study, including consecutive RA patients followed in a Tertiary Rheumatology Department. Socio-demographic (age and gender) and clinical data were collected through a standardized protocol, including 28 tender (TJ28) and swollen (SJC28) joints count, C-Reactive Protein (CRP), Erythrocyte Sedimentation Rate (ESR), Disease activity Score (DAS28-4v-CRP and DAS28-4v-ESR), PhGA and Patient Global Assessment of disease Activity (PGA) through a Visual Analogic Scale (VAS) 0-100mm, Health Assessment Questionnaire (HAQ), European Quality of Life-5 Dimensions (EQ-5D) and Hospital Anxiety and Depression Scale (HADS). Correlation between PhGA and other continuous variables was evaluated through Pearson´s Correlation Coefficient and variables with p<0.05 in univariate analysis were included in multivariable linear regression (stepwise model).

Results: 392 RA patients (80.6% female, 65.3±12.6 years) were included. PhGA was weakly correlated with CRP (r=0.23), TJC28 (r=0.35), PGA (r=0.26), HAQ (r=0.31) and EQ5D (r=-0.21). Moderate correlations were observed with SJC28 (r=0.45) and DAS-4V-CRP (r=0.48). In multivariable analysis, SJC28 (β=4.14, 95%CI:3.16-5.12), CRP (β=0.22; 95%CI: 0.02-0.03), HAQ (β=4.46, 95%CI:1.50-7.42) and PGA (β=0.08; 95%CI:0.00-0.16) remained as independent correlates of PhGA (R2=0.27, p<0,05).

Conclusion: In this study, PhGA was associated with SJC28, CRP, HAQ and PGA, suggesting that physicians adopt a comprehensive reading of the disease into account. However, a large proportion of the variance of PhGA remains unexplained. Given its driving role in treatment decisions, the need to standardize and better understand PhGA seems to deserve a closer attention.

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Disclosure of Interests: LILIANA SARAIVA: None declared, Luisa Brites: None declared, Ana Rita Cunha: None declared, Helena Assunção: None declared, Ana Rita Prata: None declared, Mariana Luis: None declared, Flavio Costa: None declared, Pedro Freitas: None declared, Marlene Sousa: None declared, José Antonio P. da Silva Grant/research support from: Pfizer, Abbvie, Consultant of: Pfizer, AbbVie, Roche, Lilly, Novartis, Catia Duarte: None declared

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THU0112 DIAGNOSTIC PERFORMANCE OF ANTI-CYCLIC CITRULLINATED PEPTIDE (CCP) 2 AND CCP3.1 ASSAYS IN EARLY RHEUMATOID ARTHRITIS

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Background: Anti-cyclic citrullinated peptide (CCP) antibodies are the most specific markers for rheumatoid arthritis (RA). Different generations of assays have been developed among which the anti-CCP2 and anti-CCP3 assays are most widely used.

Objectives: Since some differences between these assays have been reported it was our aim to compare their diagnostic performance and evaluate their usefulness for diagnostics of early RA.

Methods: The anti-CCP3.1 assay (Quanta Lite ® CCP3.1 IgG/IgA, Inova Diagnostics) was compared to anti-CCP2 IgG and IgA assays (EliA™ CCP, Thermo Fisher Scientific) employing sera of 184 early RA patients, 360 disease controls and 98 healthy subjects.

Results: Anti-CCP2 IgG and IgA assays showed high specificity versus healthy subjects (98.9%; 98%) and disease controls (98.8%; 99.4%). Sensitivity was 52.2% for the IgG and 30.4% for the IgA assay, respectively, resulting in high positive likelihood ratios (LR+) of 47.5 (IgG) and 50.7 (IgA). However, IgA antibodies did not show an added diagnostic value since all positive patients were also IgG positive. The anti-CCP3.1 assay was slightly more sensitive than the anti-CCP2 IgG assay (55.4%) but specificity was markedly lower and amounted to 95.9% versus healthy subjects and 90.8% versus disease controls resulting in a LR+ of only 6.0. Out of 360 disease controls 33 (9.2%) were found to be positive for CCP3.1 but among these only four (1.1%) were positive for anti-CCP2 IgG (and 2 of these also for anti-CCP2 IgA). The most common diagnosis of CCP3.1 positive control patients was osteoarthritis (12 patients); six patients suffered from spondyloarthropathies, two patients had reactive arthritis, 10 patients were diagnosed with an autoimmune rheumatic disease (AI RMD) and two patients had osteoporosis. However, at a cut-off of 60 AU/ml only nine disease controls remained positive (3 OA, 1 SpA, 4 AI RMD, 1 ReA) and 3 of them were also positive in the anti-CCP2 assay (ReA, SpA, SLE). When applying 60 AU/ml (high positive) as cut-off value at the early RA cohort, sensitivity (52.7%) became comparable to the anti-CCP2 assay and both specificity (97.5%) and LR+ (21.08) increased substantially.

Conclusion: When interpreting the results of anti-CCP assays disease specificity should be taken into account in order to reduce the risk of misclassification and a false positive diagnosis.

Table 1. Specificity, sensitivity and positive likelihood ratio (LR+) of CCP2 (IgG, IgA) and CCP3.1 assays.

	CCP3.1	CCP2 IgG	CCP2 IgA
Cut-off (U/ml)	20	10	10
Patients positive (n)	102	96	56
Specificity % (healthy subjects)	95.9	99.0	98.0
Specificity % (disease controls)	90.8	98.9	99.4
Sensitivity %	55.4	52.2	30.4
LR+ (healthy)	13.5	52.0	15.2
LR+ (disease controls)	6.0	47.5	50.7

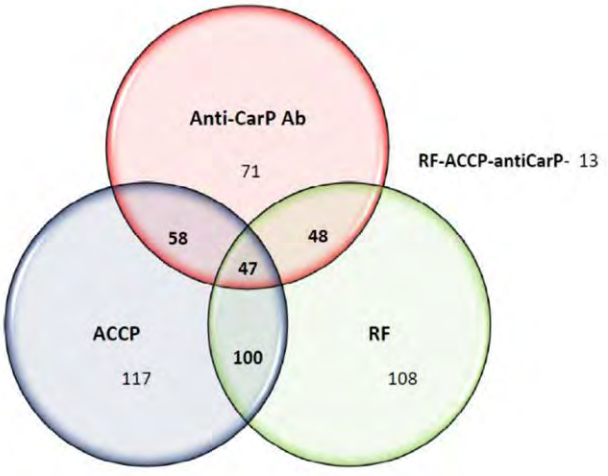
Disclosure of Interests: Daniela Sieghart Grant/research support from: Thermo Fisher Scientific, Speakers bureau: Thermo Fisher Scientific, Christian Konrad Employee of: Thermo Fisher Scientific, Sascha Swiniarski Employee of: Thermo Fisher Scientific, Helmuth Haslacher: None declared, Daniel Aletaha Grant/research support from: AbbVie, Novartis, Roche, Consultant of: AbbVie, Amgen, Celgene, Lilly, Medac, Merck, Novartis, Pfizer, Roche, Sandoz, Sanofi Genzyme, Speakers bureau: AbbVie, Celgene, Lilly, Merck, Novartis, Pfizer, Sanofi Genzyme, UCB, Günter Steiner Grant/research support from: Thermo Fisher Scientific, Speakers bureau: Thermo Fisher Scientific

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THU0113 **ANTI CARBAMYLATED PROTEIN ANTIBODY IN INDIAN POPULATION WITH RHEUMATOID ARTHRITIS – A BETTER PREDICTOR OF DISEASE OUTCOME**

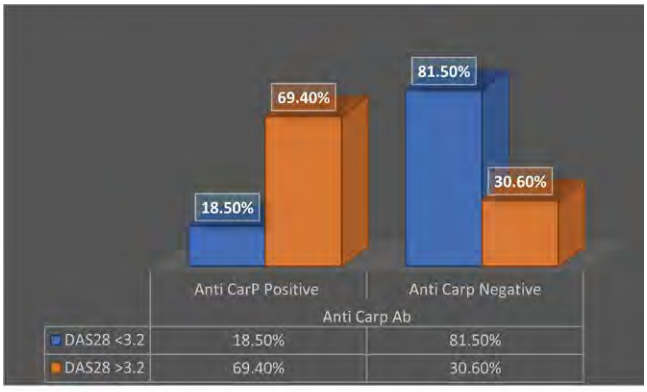
L. Sreekumar[1], M. Cb[2], M. Pillai[2], A. T. Ommen[2], T. C. Vishnu[3]. [1]*Amrita Institute of Medical Science, Kochi, India*; [2]*AIMS, Kochi, India*; [3]*Nairs Hospital, Kochi, India*

Background: While diagnosis of RA relies mainly on detection of RF and ACCP antibodies at present, anti carbamylated protein antibody which has strong association with severe joint damage and poorer disease outcome[1] can be found in even healthy individuals years before onset of symptoms of RA[2,3] thus enabling early initiation of DMARDs and reducing complications of RA.[4]
Objectives: Assess prevalence of anti-CarP Ab in RA patients in India and assess correlation between joint involvement, X-ray erosions and extra articular features between anti-CarP Ab positive and negative RA patients.
Methods: Cross-sectional study (2017-2019) conducted among 150 RA patients who met 2010 ACR/EULAR criteria in tertiary referral hospital. Tests for CRP, RF and ACCP were done, DAS28-CRP scores were calculated at presentation & X-ray images of hands and feet obtained.
Anti-CarP Ab was tested using ELISA. Cut-off level for positivity was defined using ROC curve as 13.48 U/mL, with specificity 92.73%, sensitivity 85.26%, PPV 95.29% and NPV 78.46%.
Results:



Venn diagram representing overlap of sero-markers

Venn diagram representing overlap of sero-markers
Study population had 18% males, 82% females, 72% RF+ cases (108), 78% ACCP+ cases (117) and 47.3% anti-CarP Ab+ cases (71).
48% of the 25 seronegative (RF-ACCP-) cases tested positive for anti-CarP Ab, indicating its ability in diagnosing more RA cases in conjunction with present markers.
Testing association between RF and anti-CarP Ab and between ACCP and anti-CarP Ab proved to be statistically insignificant showing that anti-CarP Ab is independent of the incumbent markers in diagnosing RA.
69.4% of RA patients with high disease activity (DAS >3.2) were positive for anti-CarP Ab and showed statistically significant association.



Association between DAS28 CRP and anti-CarP Ab

Association between DAS28 CRP and anti-CarP Ab
Also while 39 of 71 (54.9%) anti-CarP Ab positive RA cases had joint deformities and 23 of 71 (32.4%) of anti-CarP Ab positive cases had extra articular involvement and were statistically significant, 27 of 71 anti-CarP Ab positive cases showed joint erosions in X-ray but was not statistically significant.
In comparison, only extra articular involvement showed a statistical significance in ACCP positive patients whereas joint deformities and joint erosions on X-rays showed no correlation to ACCP.

		Joint Deformity				
		Absent	Present	Total	X^2	p value
anti-CarP antibody	Negative	50 63.3%	29 36.7%	79 100.0%	5.009	0.025
	Positive	32 45.1%	39 54.9%	71 100.0%		
Total		82	68	150		

		Extra articular features				
		Absent	Present	Total	X^2	p value
anti-CarP antibody	Negative	68 86.1%	11 13.9%	79 100.0%	7.278	0.007
	Positive	48 67.6%	23 32.4%	71 100.0%		
Total		116	34	150		

Conclusion: Anti-CarP antibody positivity is indicative of increased disease activity (DAS28-CRP score), joint deformities and extra articular involvement in RA patients. Aside from its presence demonstrated early in the course of RA through other studies, its ability in diagnosing RA cases in otherwise seronegative (RF and ACCP negative) population and the high sensitivity, specificity and diagnostic accuracy exhibited paves the way for its routine use as a diagnostic tool in conjunction with RF and ACCP for diagnosing RA and predicting disease outcome.

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THU0114 **CERTOLIZUMAB PEGOL IN PATIENTS WITH RHEUMATOID ARTHRITIS: POOLED EFFICACY ANALYSIS OF PHASE 3 CLINICAL TRIALS ACROSS BASELINE RHEUMATOID FACTOR QUARTILES**

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Background: The presence of rheumatoid factor (RF) in patients (pts) with rheumatoid arthritis (RA) is associated with higher disease activity,[1] and is regarded as a risk factor for more aggressive RA.[1] Most studies on anti-tumour necrosis factor (TNF) monoclonal antibodies such as infliximab, etanercept and adalimumab have shown better response in pts with negative versus positive and low versus high baseline RF titres.[2-3] Certolizumab pegol (CZP), a PEGylated, Fc-free anti-TNF, has shown rapid and sustained reduction in signs and symptoms of

moderate to severe RA, inhibition of radiographic progression and improvements in physical function in pts with an inadequate response to methotrexate (MTX).[4–7] The efficacy of CZP in pts with different baseline RF levels has not been studied.

Objectives: To assess the efficacy of CZP, as measured by Disease Activity Score 28-erythrocyte sedimentation rate (DAS28[ESR]), in pts with active RA across baseline RF levels.

Methods: In this post-hoc analysis, data were pooled from four clinical trials of CZP in RA: two global trials (RAPID 1, NCT00152386 and RAPID 2, NCT00175877), a Japanese trial (J-RAPID, NCT00791999) and a Chinese trial (RAPID-C, NCT02151851). Pts ≥18 years with adult onset RA for ≥6 months (defined by ACR 1987 criteria), who received MTX for ≥6 months (≥3 months for RAPID-C) prior to baseline, were randomised 1:1 to receive placebo (PBO) every two weeks (Q2W)/CZP 400 mg Q2W/CZP 200 mg Q2W (CZP 400 mg at Weeks [Wks] 0/2/4) plus MTX for at least 24 Wks. Complete study design and pt characteristics were reported previously.[4–7] Here we include only pts who received CZP 200 mg Q2W (CZP 400 mg at Wks 0/2/4). RF titres were measured by validated assays in local hospital laboratories. Pts were stratified into quartiles based on pooled baseline RF levels: <25.0, <78.5, <207.0 and ≥207.0 IU/mL. DAS28(ESR) categories were adopted to stratify pts: remission (REM), DAS28(ESR) <2.6; low disease activity (LDA), DAS28(ESR) ≤3.2. Missing values were imputed using last observation carried forward.

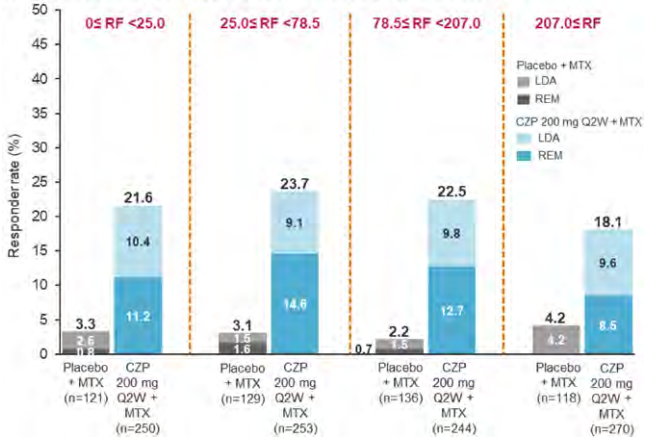
Results: Data were pooled from 1,017 and 504 pts in the CZP 200 mg Q2W and PBO Q2W groups, respectively. At baseline, mean [SD] DAS28(ESR) was similar with PBO vs CZP across RF quartiles (6.5 [0.9] – 7.0 [0.9] vs 6.6 [0.9] – 7.0 [0.9]). Compared with the PBO group, numerically higher DAS28(ESR) REM and LDA rates were observed for CZP 200 mg Q2W group at Wk 24 across RF quartiles (Figure 1). DAS28(ESR) REM and LDA responder rates increased to Wk 24 in pts treated with CZP. In general, LDA and REM rates were similar across RF quartiles at all timepoints (Figure 2).

Conclusion: Over 24 Wks of treatment, trends showed steady efficacy of CZP across baseline RF quartiles in pts with active RA. In this pooled post-hoc analysis, efficacy of CZP appeared to be consistent and independent of RF levels; observed efficacy may be related to the unique molecular structure of CZP. CZP treatment in association with MTX may be a feasible option in pts with RA regardless of baseline RF status.

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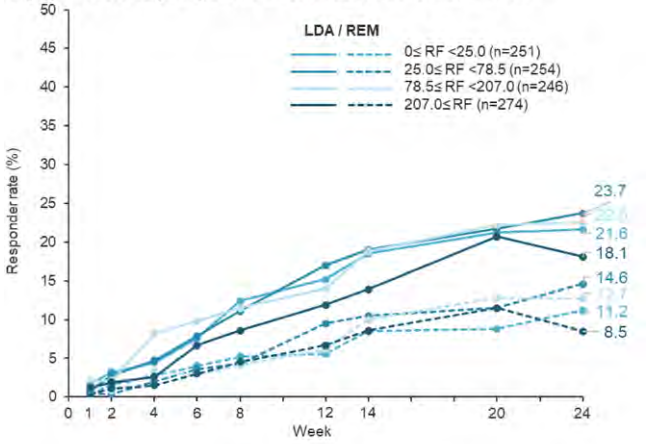
Figure 1. DAS28(ESR) LDA and REM rates over time for CZP



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Figure 2. DAS28(ESR) LDA and REM rates over time for CZP



Last observation carried forward. REM: DAS28(ESR) <2.6; LDA: DAS28(ESR) ≤3.2. CZP: certolizumab pegol; DAS28(ESR): Disease Activity Score 28 - erythrocyte sedimentation rate; LDA: low disease activity; MTX: methotrexate; Q2W: every two weeks; REM: remission; RF: rheumatoid factor.

Pharma Inc., AbbVie GK, Asahi Kasei Pharma Corporation, Nippon Kayaku Co., Ltd, Takeda Pharmaceutical Company Ltd, UCB Pharma, Shionogi & Co., Ltd., Mitsubishi-Tanabe Pharma Corp., Daiichi Sankyo Co., Ltd., Chugai Pharmaceutical Co. Ltd., Consultant of: Chugai Pharmaceutical Co Ltd, Astellas Pharma Inc., Eli Lilly Japan KK, Speakers bureau: AbbVie GK, Eisai Co., Ltd, Mitsubishi-Tanabe Pharma Corporation, Chugai Pharmaceutical Co Ltd, Bristol-Myers Squibb Company, AYUMI Pharmaceutical Corp., Eisai Co., Ltd, Daiichi Sankyo Co., Ltd., Gilead Sciences, Inc., Novartis Pharma K.K., Pfizer Japan Inc., Sanofi K.K., Dainippon Sumitomo Co., Ltd.

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THU0115 THE VALUE OF KL-6 AS A PREDICTIVE FACTOR OF ACUTE EXACERBATION IN PATIENTS WITH RHEUMATOID ARTHRITIS-ASSOCIATED INTERSTITIAL LUNG DISEASE.

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Background: Acute exacerbation (AE) is a life-threatening complication in connective tissue disease (CTD) associated interstitial lung disease (ILD) (CTD-ILD), including rheumatoid arthritis (RA). Although several risk factors for AE in CTD-ILD have been suggested, these are inconsistent. Krebs von den Lungen-6 (KL-6) is reported as a useful blood marker to detect severe CTD-ILD and RA-ILD, and serum KL-6 levels are significantly higher in patients with AE than in those without AE in RA-ILD patients [1]. However, the predictive value of KL-6 for AE in CTD-ILD or RA-ILD has not been completely confirmed.

Objectives: To investigate the predictive factors for AE including initial serum KL-6 levels at RA-ILD onset and sequential changes of KL-6. We also examined the causal relationship between AE and mortality of RA-ILD patients.

Methods: We retrospectively reviewed 115 patients with RA-ILD treated in our hospital between 2005 and 2019. Suspected drug-induced pneumonia cases or patients with other coexisting CTD were excluded. Cox regression analyses was used for univariate analysis to detect predictors of AE. Overall survival rate, respiratory-related deaths-free survival rate and AE-free survival rate were analyzed using the Kaplan-Meier method. $P < 0.05$ was considered statistically significant.

Results: Among 115 patients, 29 patients (25.2%) developed AE and 32 patients (27.8%) died. The median follow-up period (IQR) was 57 (25.0-91.5) months, 57.4% were female and the mean age at RA-ILD onset was 72.2 ± 7.9 years old throughout the whole cohort. Among the AE group, methotrexate (MTX), tumor necrosis factor α inhibitor (TNFi) and non TNFi biological-DMARDs were used at AE onset in 10.7%, 0.0%, and 3.6% of patients, respectively. There was a significant difference of serum KL-6 levels at AE onset between AE group and non-AE group (1081.9 ± 624.7 vs 556.1 ± 285.6 U/mL, $p < 0.001$). Initial serum KL-6 levels at RA-ILD onset in AE group were higher than those in non-AE group, without a significant difference (648.9 ± 325.7 vs 523.7 ± 276.8 U/mL, $p = 0.050$). The optimal cut-off level of initial serum KL-6 to predict AE was 551 U/mL according to ROC analysis. In univariate analysis, the following factors were significantly associated with AE; usual interstitial pneumonia (UIP) pattern on HRCT at AE onset (Hazard Ratio [HR]: 2.18; 95%

confidence interval [CI]: 1.02-4.61; p = 0.045), initial serum KL-6 > 551 U/mL at RA-ILD onset (HR: 2.46; 95%CI: 1.17-5.43; p = 0.018), increasing serum KL-6 levels > 10% before AE onset compared to the previous year (ΔKL-6 > 10%/year) (HR: 4.98; 95%CI: 2.17-11.84; p < 0.001). Initial serum KL-6 > 551 U/mL at RA-ILD onset and ΔKL-6 > 10%/year before AE were also significant prognostic factors for AE when we analyzed only in non-UIP patients (HR: 2.84; 95%CI: 1.15-7.35; p = 0.024, HR: 9.49; 95%CI: 3.02-36.25; p < 0.001, respectively). Conversely, median age at RA-ILD diagnosis, positive ratio of anti-CCP antibody, smoking habits, respiratory comorbidities, SDAI score, and therapeutics at both RA-ILD and AE onset had no significant associations with AE. Patients with initial serum KL-6 > 551 U/mL at RA-ILD onset and ΔKL-6 > 10%/year before AE had a significantly worse AE-free survival rate compared to others (p < 0.001). (Figure 1). Moreover, patients with AE had significantly lower overall survival rate (p < 0.001) and respiratory-related deaths-free survival rate (p < 0.001) than those without AE.

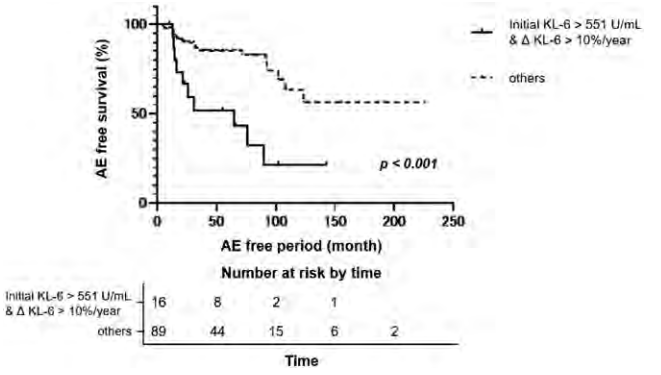


Figure 1. KL-6 was measured at RA-ILD onset. ΔKL-6 means the annual variation ratio of KL-6 before AE. The survival curve using the Kaplan Meier method (Log rank test).

Conclusion: Serum KL-6 levels at the disease onset and its sequential changes may be able to predict AE in the near future and support the early detection of AE in RA-ILD patients.

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Disclosure of Interests: Nozomi Tanaka: None declared, Keisuke Nishimura Speakers bureau: Mitsubishi Tanabe Pharma Corporation. Pfizer Inc. Kyowa Kirin Co., Ltd. Chugai Pharmaceutical Co., Ltd. ONO PHARMACEUTICAL CO., LTD. Japan Blood Products Organization. Kissei Pharmaceutical Co., Ltd. Astellas Pharma Inc. AYUMI Pharmaceutical Corporation. Eisai Co., Ltd. DAIICHI SANKYO COMPANY. Norvartis AG. Bayer AG. Sanofi K.K.
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THU0116 IS THE ROLE OF MEDICAL CONSULTATION IN RHEUMATOID ARTHRITIS A TIMELY TOPIC?

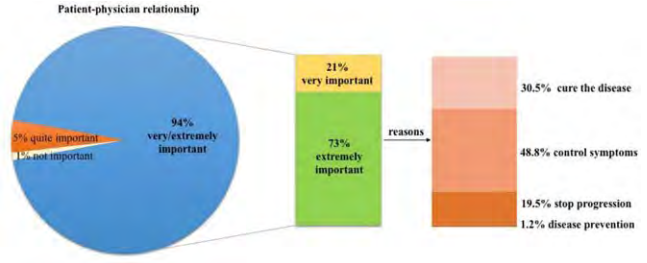
F. Ingegnoli[1,2], T. Ubiali[1,2], T. Schioppo[1,2], S. Ostuzzi[3], R. Caporali[1,2]. *[1]Clinical Rheumatology Unit, G Pini Hospital, Milan, Italy*; *[2]Università degli Studi di Milano, Dept of Clinical Sciences & Community Health, Milan, Italy*; *[3]ALOMAR Lombard Association for Rheumatic Diseases, Milan, Italy*

Background: Despite the treat-to-target recommendations and the efforts in dissecting factors that contribute to achieving disease control, the goal of remission in rheumatoid arthritis (RA) is accomplished in less than half of patients. Disease activity is assessed using composite indexes which are reliant on patient-reported outcomes, mainly the patient global assessment of disease activity (PGA). The debate on variables that can influence PGA is still open, and different internal and external factors had been taken into account: the origin of pain symptoms, psychosocial and lifestyle factors.

Objectives: To canvass the opinion of RA Italian patients concerning patient-perceived topics that matter most for future research.

Methods: A cross-sectional no-profit on-line anonymous survey was devised to evaluate opinions of the rheumatic diseases patients. In this sub-study we focused only on the data about RA patients. Patients were asked to rate the following topics: food/nutrition, air pollution, smoking, type of work, social participation, physical activity, emotional well-being/stress, alternative medicine, patient-physician relationship. Moreover, patients were inquired about why the topic was considered important (disease prevention, stop disease progression, control symptoms, cure the disease). The survey was disseminated between June and October 2019. Descriptive statistics were used to summarize the patient demographic, clinical data and survey results.

Results: 94% (82/87) of RA patients (81 female, median age 50 yrs) rated the patient-physician relationship as the main topic for future research (figure below). Likewise, intriguing results came from the reasons of previous patient rating: the patient-physician relationship was considered important for a better control of RA symptoms (48.8%), to cure the disease (30.5%), to stop disease progression (19.5%), and to prevent the disease (1.2%). These results were similar in all age groups.



Conclusion: These results highlight that the importance of medical consultation to patients and its impact on disease control should not be under-estimated. Administrative duties, time and economic constraints undermine the patient-physician relationship that is central to clinical care. The limited time spent for medical consultation is directly related to patient dissatisfaction, which in turn, may influence the patient's perception about the absence of disease activity and could be one of motives behind the worse evaluation of PGA.

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THU0117 PERSONS AT RISK OF RHEUMATOID ARTHRITIS OR AXIAL SPONDYLOARTHRITIS HAVE DIFFERENT PERCEPTIONS ON PREVENTIVE INTERVENTION THAN RHEUMATOLOGISTS

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Background: Persons at risk of developing rheumatoid arthritis (RA) may benefit from lifestyle[1] or pharmacological[2] intervention aimed at primary prevention. Although less studied, the same may apply to persons at increased risk of axial spondyloarthritis (axSpA)[3]. Patients' perceptions and physicians' views of risk and benefit have an important influence on patients' willingness to use treatment as previously shown in axSpA.

Objectives: Our aim was to investigate and compare the willingness of individuals at-risk of RA or axSpA and rheumatologists to initiate preventive intervention.

Methods: Individuals at risk of RA, defined as arthralgia and anti-citrullinated protein antibodies (ACPA; >10 kU/l) and / or rheumatoid factor (RF; >5 kU/l) without arthritis (Reade pre-RA cohort; n=100), healthy first degree relatives (FDR) of HLA-B27 positive axSpA patients (Amsterdam UMC pre-SpA cohort; n=38) and Dutch rheumatologists (n=49) completed a survey on preventive intervention in the at risk phase of RA (pre-RA cohort and rheumatologists) or axSpA (Pre-SpA cohort). The survey included questions on lifestyle intervention, disease perception and scenarios varying in disease risk, treatment effectiveness and side effects of hypothetical preventive medication[4].

Results: Overall participants depicted RA and axSpA to be a serious disease (RA: median VAS (0-10) 6.5, IQR 5-8; SpA: median VAS 6, IQR 4-8). Despite some concern about their increased risk, most persons did not expect to develop the disease (both: median VAS 3, IQR 1-5). Persons who considered RA to be a serious disease were more likely to start preventive intervention (OR 1.14, 95%CI 1.00;1.31). 100% of at risk patients were willing to change at least 1 of 13 lifestyle

components: i.e. smoking, alcohol consumption, exercise and diet and in total a medium number of 7 (pre-RA: IQR 4-10, pre-SpA: IQR 5-8) while 35% of rheumatologists gave lifestyle advice to ≥50% of at risk patients (most often smoking cessation).

At 30% disease risk, the willingness to use 100% effective preventive medication with no side effects was 53% (pre-RA), 55% (pre-SpA) and 74% (rheumatologists) which increased at 70% disease risk to 69% (pre-RA) and 92% (pre-SpA and rheumatologists). At 30% disease risk and minor side effects, willingness was 26% in pre-RA, 29% in pre-SpA and 31% by rheumatologists and at 70% disease risk 40%, 66% and 76% for pre-RA, pre-Spa and rheumatologists respectively. Differences between rheumatologists and persons at risk are shown in table 1. Of the rheumatologists 16% indicated that a 30% RA risk in 3 years was needed to start preventive therapy and another 16% preferred a 70% risk before starting medication.

Table 1. Willingness to use preventive medication

Disease risk	% of persons at risk for RA willing to use medication	% of person at risk for SpA willing to use medication	% of rheumatologist willing to use medication	Difference between rheumatologists and persons at risk for RA	Difference between rheumatologists and persons at risk for SpA
100% effective medication, no side effects					
30%	53%	55%	74%	p = 0.017	p = 0.076
70%	69%	92%	92%	p = 0.002	p = 0.964
100% effective medication, minor side effects					
30%	26%	29%	31%	p = 0.554	p = 0.866
70%	40%	66%	76%	p < 0.001	p = 0.320

Conclusion: Disease risk perception and willingness to start preventive intervention were comparable between pre-SpA and pre-RA patients. They seem willing to make several lifestyle changes to decrease disease risk and were generally willing to use medication in case of a clearly increased risk. Rheumatologists were overall more likely than at risk individuals to start preventive medication. Lifestyle advice was given less frequently by rheumatologists contrasting with individuals' high willingness to adjust lifestyle.

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Disclosure of Interests: Laurette van Boheemen: None declared, J.W. Bolt: None declared, Marieke ter Wee: None declared, Henriëtte de Jong: None declared, Marleen van de Sande Grant/research support from: Novartis, Eli Lilly, Boehringer Ingelheim, Janssen, Consultant of: Abbvie, Novartis, Eli Lilly, Speakers bureau: Novartis, MSD, Dirkjan van Schaardenburg: None declared

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THU0118 FREQUENT SELF-ASSESSMENTS PROMOTED TREAT-TO-TARGET FOR RA VIA EMPOWERING PATIENTS: A COHORT STUDY FROM CHINA BY SMART SYSTEM OF DISEASE MANAGEMENT (SSDM)

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Background: Treat-to-Target (T2T) strategy are critical for the treatment of RA, but Chinese rheumatologists can hardly provide patients with a complete assessment in the clinic due to limited time. According to DAS28 scores, disease activity of the cohort was divided into four groups: remission (Rem), low (LDA), moderate (MDA) and high (HDA) disease activity. T2T, achieving a DAS28 score lower than 2.6 (Rem) or below 3.2 (LDA), is the main management strategy recommended by ACR and EULAR.

Objectives: To evaluate the patterns of T2T and related influential factors among RA patients after applying SSDM with repeated self-assessment in the real world.

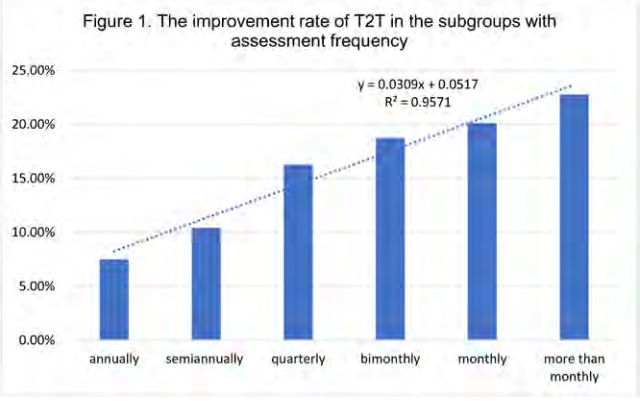
Methods: SSDM is a mobile application for disease management. Patients were trained to do DAS28 assessment with SSDM and required for repeating self-assessment after leaving the hospital. After entry by patients, data can be synchronized to the SSDM terminal of authorized rheumatologists. Based on the patients' data, rheumatologists will provide medical advices to them.

Results: From Jan 2015 to Jan 2020, 68,103 RA patients enrolled in SSDM. The mean age of 51.58±12.86 years old and median disease duration is 3.83 years. 52,355 patients performed self-assessment of DAS28, HAQ and morning stiffness duration totally for 114,792 times. Proportion of patients in Rem, LDA, MDA and HDA was 26%, 17%, 44% and 13% respectively at baseline. Among them, 5,488 RA patients from 219 hospitals across China were followed up for more than 12 months through SSDM.

The rate of T2T achievers were 50.20% (2,755/5,488) at baseline, and improved significantly to 65.14% (3,575/5,488) after 12 months follow up, p<0.05. Among T2T achievers at baseline, 77.20% (2,127/2,755) maintained T2T, 22.80% (628/2,755) relapsed. Of patients who didn't achieve T2T at baseline, only 56.75% (1,551/2,733) achieved T2T after 12 months follow up.

The frequency of self-assessment for DAS28 on T2T has been analyzed. Results indicated that the more frequent of the self-assessments being performed by patients, the higher improvement of T2T rate will be. The improvement rates of T2T in the subgroups which self-assessed with SSDM by annually, semiannually, quarterly, bimonthly, monthly and more frequent than monthly were 7.49%, 10.40%, 16.29%, 18.73%, 20.13% and 22.77% respectively. The improvement rate (y) of T2T was positively correlated with the frequency of self-assessment for DAS28(x) independently. The regression equation as "y = 0.0309x + 0.0517", r = 0.9785, p<0.01 (Figure 1).

Conclusion: Significant improvement was observed under applying SSDM through empowering RA patients. After proactive disease management via SSDM for more than 12 months, patients with DAS28<=3.2 score at baseline had a significantly higher retention rate of Rem disease activity. The patients who performed more frequent self-assessments had lower probability of relapse and higher rate of T2T. SSDM is a valuable tool for long term follow-up through empowering patients.



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Disclosure of Interests: None declared

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THU0119 COULD SYNOVITIS AND TENOSYNOVITIS DETECTED BY ULTRASOUND BE CONSIDERED A RISK FACTOR FOR SHORT-TERM FLARE IN RA PATIENTS IN CLINICAL REMISSION

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Background: The clinical value of ultrasound (US) detected synovitis and tenosynovitis as predictors of flares in RA patients in clinical remission is not clear.

Objectives: To investigate the value of US detected synovitis and tenosynovitis as risk factors for short term flare in RA patients in clinical remission.

Methods: Consecutive RA patients in clinical remission (DAS28 ERS < 2.6) for at least 3 months, underwent Power Doppler ultrasound (PDUS) examination of: 1st to 6th extensor compartments at the wrist, 2nd to 5th flexor, posterior tibial tendons and peroneals. Regarding joints, carpal joints, 1st to 5th MCP and 2nd to 5th interphalangeal proximal (IPP). Synovitis and tenosynovitis were defined according to OMERACT. Patients were followed for one year. Disease flare was defined as any increase of disease activity generating the need of change in therapy by the attending rheumatologist.
Results: Ninety patients were included. Patients´ characteristics are shown in the table. After one year of follow-up, 26 patients (29%) experienced a flare. At baseline 39%, 23% and 8% had US detected synovitis, tenosynovitis or both respectively. The presence of US detected tenosynovitis (RR: 4.9; 95% CI: 2.2-10.8), but not of US detected synovitis (RR: 1.3; 95% CI: 0.76-2.2), showed an increased risk of having a flare. In the multivariable analysis, and after adjusting by age, gender, disease duration, DAS28, DMARDs and biologics use, and the US detected synovitis, only subclinical tenosynovitis (OR: 9.8 95% CI: 2.5-39.1; p=0.001) and baseline DAS28 (OR: 5.7, 95% CI: 1.1-31.6; p= 0.047) were significantly associated with an increased risk of flare.
Conclusion: Subclinical tenosynovitis, but not synovitis, was associated with disease flare in patients with RA in clinical remission. This feature might have physio-pathological implications.
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Table 1. Demographic and clinical features from RA patients in clinical remission

Feature	Patients with flares (n=26)	Patients without flares (n= 64)	P value
Mean age (SD)	63.1 (12.6)	57.5 (13.2)	0.0679
Females, n (%)	54 (84)	24 (92)	0.316
Mean Disease duration years (SD)	5.5 (5.5)	8.4 (5.9)	0.0344
Positive Rheumatoid Factor, n (%)	16 (61.5)	40 (62.5)	0.802
Mean Erythrosedimentation rate (ESR)	18.3 (8)	14.1 (10.4)	0.0680
Mean DAS28 ESR (SD)	1.9 (0.5)	2.2 (0.3)	0.0091
Mean Swollen joint count (SS)	0.15 (0.4)	0.15 (0.4)	0.9806
Mean Patient's Global VAS (0-10) (SD)	1.4 (1.3)	1.1 (1.1)	0.2471
Mean tender joint count (SD)	0.2 (0.5)	0.2 (0.5)	0.9653
Treatment with DMARDs, n (%)	54 (81)	26 (100)	0.018
Treatment with biologics, n (%)	19 (30)	3 (11)	0.069

Disclosure of Interests: Johana Zacariaz H: None declared, martin brom: None declared, florencia mollerach: None declared, josefina marin: None declared, leandro ferreyra g: None declared, Javier Rosa Speakers bureau: ABBvie, Pfizer, BMS, Novartis, Janssen, Eli Lilly, enrique soriano Speakers bureau: Abbvie, Pfizer, BMS, Novartis, Janssen, Eli Lilly, UCB, Roche
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THU0120 OVERLAPPING SJOGREN'S SYNDROME AND ULTRASOUND REMISSION, FUNCTIONAL DISABILITY AND MANAGEMENT IN RHEUMATOID ARTHRITIS PATIENTS: A PROPENSITY SCORE MATCHED REAL-WORLD COHORT FROM 2009 TO 2019

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Background: Rheumatoid arthritis (RA) patients with Sjogren's syndrome (SS) are often referred to as more severe synovitis.
Objectives: We intend to clarify the impact of overlapping SS on ultrasound remission, functional ability improvement and clinical decision-making in RA patients in a real-world cohort from 2009 to 2019.
Methods: The medical records of RA patients in our medical center from 2009 to 2019 were reviewed. Cox proportional hazards models of ultrasound remission and health assessment questionnaire (HAQ) improvement were conducted in both the 1-to-1 nearest propensity score matched (PSM) and unmatched cohorts between those RA patients with SS (RA-SS) and without (RA-noSS) to correct critical confounders. Four kinds of PSM methods were used and the corresponding average treatment effect on the treated (ATT) was calculated to clarify the effect of overlapping SS on distinguishable characteristics or drug prescription in RA patients.
Results: A total of 1100 RA patients were included in the study, of which 133 (12.1%) overlapped with SS. Among 256 patients consisting of 128 RA-SS and 128 RA-noSS after 1-to-1 nearest PSM, overlapping SS was associated with a 44%, 32% lower probability of reaching ultrasound remission, no-functional disability in RA patients, respectively. More prevalent interstitial lung disease (ILD), leukopenia, hypergammaglobulinemia, rheumatoid factor (RF) positivity, higher erythrocyte sedimentation rate (ESR) and more hydroxychloroquine (HCQ) usage, less biologic disease-modifying anti-rheumatic drugs (bDMARDs) prescription were confirmed to be correlated with overlapping SS by the robust PSM.
Conclusion: Overlapping SS is associated with a lower probability of reaching ultrasound remission and functional activity improvement, higher prevalence of ILD, leukopenia and hypergammaglobulinemia in RA patients. Weaker interventions such as HCQ may be the mainstream of clinical decision making.

Table. Hazard Ratios for Ultrasound Remission/No Functional Disability Associated with Overlapping SS

	Unmatched cohort		Matched cohort	
	US remission	No functional disability	US remission	No functional disability
Unstratified	0.63 (0.51, 0.79)	0.60 (0.52, 0.70)	0.56 (0.42, 0.74)	0.68 (0.55, 0.83)
Stratified				
Gender	0.62 (0.50, 0.77)	0.63 (0.54, 0.74)	0.53 (0.40, 0.71)	0.66 (0.54, 0.80)
Age	0.63 (0.51, 0.78)	0.60 (0.52, 0.70)	0.54 (0.40, 0.72)	0.62 (0.50, 0.76)
RF	0.64 (0.52, 0.80)	0.63 (0.54, 0.73)	0.56 (0.42, 0.74)	0.68 (0.55, 0.83)
ACPA	0.63 (0.51, 0.79)	0.59 (0.50, 0.68)	0.57 (0.43, 0.76)	0.63 (0.51, 0.78)
Seropositivity	0.64 (0.52, 0.80)	0.63 (0.54, 0.74)	0.59 (0.45, 0.79)	0.75 (0.61, 0.92)
RA duration	0.64 (0.51, 0.79)	0.61 (0.52, 0.71)	0.58 (0.44, 0.77)	0.70 (0.57, 0.86)
BLDAS28CRP	0.64 (0.51, 0.80)	0.62 (0.53, 0.72)	0.54 (0.41, 0.72)	0.66 (0.54, 0.81)

Values are presented as total and stratified Hazard Ratio (95% CI) for ultrasound remission and no functional disability associated with overlapping SS in RA patients according to gender, age, RF/ACPA status, RA duration and DAS28-CRP at 1st visit. US remission refers to ultrasound GS<2 and PD=0. Unmatched cohort refers to whole sample (n=1100), matched cohort refers to propensity score matched (PSM) patients (n=256). The values are statistically significant at the level of 0.01.

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THURSDAY, 04 JUNE 2020

Rheumatoid arthritis - comorbidity and clinical aspects

THU0121 COMORBIDITIES AT DIAGNOSIS OF RHEUMATOID ARTHRITIS

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Background: Although many studies have reported an increased burden of comorbidities in patients with rheumatoid arthritis (RA), and their impact on RA outcomes, few studies have compared the pattern of comorbidities already at diagnosis of RA, in relation to the burden among matched control subjects. Only such a comparison can inform on which comorbidities are increased already before RA diagnosis, presumably due to overlapping causal factors, and which arise as a consequence of the RA disease or its treatment.
Objectives: The aim of this study was to investigate the pattern of common chronic conditions in patients with RA, overall and stratified by serological status, at the time of diagnosis, compared to a matched control group reflective of the general population.
Methods: This nationwide study included patients with a new-onset RA diagnosis, using data from the Swedish Rheumatology Quality register, from 2006 to 2015. We included 11,086 incident RA cases, of whom 62% were seropositive. From the Total Population Register, we identified 54,813 population controls, individually matched on age, sex and county of residence. Information about registered comorbidity diagnoses during the five years up until the RA diagnosis was retrieved from the Swedish National Patient Register. Information on dispersed drugs during the year up until the RA diagnosis was collected from the Prescribed Drug Register. Comorbidity diagnoses were grouped into 10 different categories (see table 1). Logistic regression was

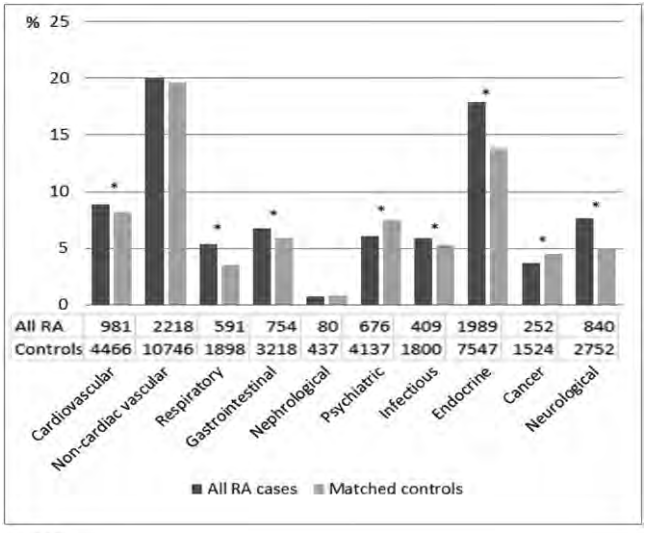
used to compare comorbidities between cases and controls, adjusted for the matching variables.

Table 1. Relative risk of comorbidities at RA diagnosis, overall and by serological status

	All RA		Seropos RA		Seroneg RA	
Comorbidities	OR*	95% CI	OR*	95% CI	OR*	95% CI
Cardiovascular	1.11	1.03–1.20	1.06	0.95–1.17	1.20	1.07–1.36
Non-cardiac vascular	1.03	0.98–1.09	1.03	0.96–1.10	1.06	0.97–1.16
Respiratory	1.58	1.44–1.74	1.74	1.54–1.96	1.35	1.15–1.59
Gastrointestinal	1.17	1.08–1.27	1.12	1.01–1.25	1.28	1.12–1.46
Psychiatric	0.87	0.82–0.92	0.87	0.80–0.93	0.96	0.87–1.06
Nephrological	0.90	0.71–1.15	0.89	0.63–1.25	0.96	0.68–1.36
Infectious	1.12	1.03–1.23	1.13	1.01–1.27	1.17	1.02–1.35
Endocrine	1.39	1.31–1.47	1.41	1.31–1.51	1.35	1.23–1.48
Cancer	0.88	0.79–0.97	0.81	0.71–0.93	0.93	0.80–1.10
Neurological	1.73	1.59–1.89	1.62	1.45–1.81	2.00	1.74–2.29

*All ORs are adjusted for sex and age, and cases with RA are compared to their individually matched control subjects.

Results: In seropositive as well as in seronegative RA, comorbidities within the respiratory (OR 1.58, 95% CI 1.44-1.74), gastrointestinal (OR 1.17, 95% CI 1.08-1.27), infectious (OR 1.12, 95% CI 1.03-1.23), endocrine (OR 1.39, 95% CI 1.31-1.47) and neurological (OR 1.73, 95% CI 1.59-1.89) categories were more common already at the time of RA diagnosis, compared to the matched population controls, as outlined in table 1. A history of cardiovascular disease was slightly increased among patients with seronegative RA (OR 1.20, 95% CI 1.07-1.36), and no increase was seen for non-cardiac vascular diseases. A history of psychiatric (OR 0.87, 95% CI 0.80-0.93) and cancer diagnoses (OR 0.81, 95% CI 0.71-0.93) was less common in seropositive RA vs. their matched controls. In terms of comorbidity burden, 15% of all RA patients had diagnoses from at least two of the ten comorbidity categories vs. 13% of the controls and 8% vs. 8% had diagnoses within three or more comorbidity categories.
Conclusion: This large nationwide study demonstrates a marked increase in several comorbidities, in particular respiratory, endocrine and neurological diseases, already at, and before, the diagnosis of RA compared with age and sex matched controls, while psychiatric diagnoses are less common. These findings are important for the interpretation of comorbidity studies in established RA.



* p < 0.05

Figure 1. Prevalence of comorbidities in Swedish patients with newly diagnosed RA compared to the matched controls* p < 0.05

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THU0122 EFFECT OF THE METABOLIC SYNDROME ON RENAL FUNCTION DECLINE IN FOUR RHEUMATIC DISEASES: AN 8-YEAR LONGITUDINAL ANALYSIS

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Background:
Objectives: To study the effect of the metabolic syndrome (MetS) on renal function decline in four rheumatic diseases.
Methods: Consecutive patients who fulfilled the ACR/SLICC criteria for systemic lupus erythematosus (SLE), EULAR/ACR criteria for rheumatoid arthritis (RA), ASAS criteria for spondyloarthritis (SpA) and the CASPAR criteria for psoriatic arthritis (PSA) were recruited in 2009/2010. At entry, patients recruited had measurement of body weight, height, waist circumference and blood pressure. MetS was defined by the updated joint consensus criteria, using the Asian criteria for central obesity, when ≥3 of the following were present: (1) waist ≥90cm in men or ≥80cm in women; (2) blood pressure ≥130/85mmHg or requiring therapy; (3) serum triglyceride level ≥1.7mmol/L; (4) serum HDL-chol ≤1.0mmol/L in men and 1.3mmol/L in women; and (5) fasting glucose ≥5.6mmol/L. Renal function of the participants was assessed by the 4-variable MDRD formula (eGFR). Patients were followed longitudinally for eGFR change. Change in eGFR was compared between those with and without the MetS at baseline. Regression analysis was performed for the effect of MetS on eGFR decline adjusted for other confounding factors.
Results: 1497 patients were studied (693 RA, 577 SLE, 121 SpA and 106 PSA). The age at entry was highest in RA (53.4±12.0 years) and lowest in SpA (39.0±11.9 years). Disease duration was longest in SLE (9.3±7.2 years) and shortest in PSA (3.6±3.2 years). MetS was present in 137 RA (20%), 85 SLE (15%), 13 SpA (11%) and 39 PSA (37%) patients. Patients were followed for 91.1±12.1 months. The mean decline of eGFR (ml/min/1.73m2) at last observation from baseline was 5.00±13.5 in RA, 4.16±11.6 in SpA, 3.95±12.3 in PSA and 8.93±16.4 in SLE (p=0.03; one-way ANOVA). The proportion of patients with eGFR decline by ≥10% was also greatest in SLE (41%) compared with RA (29%), SpA (24%) and PSA (25%) patients (p<0.001). Among patients with SLE, a significantly more profound drop in eGFR over 8 years was observed in patients with the MetS at baseline (-17.8±26%) than those without (-7.6±18%; p=0.002). The difference in last eGFR between patients with and without the MetS was significant after adjustment for baseline eGFR, age and sex (65.5±32.2 vs 88.4±24.4 ml/min/1.73m2; p<0.001). In a linear regression model, eGFR at last follow-up was significantly associated with the baseline eGFR (slope 0.72 SE 0.03; Beta 0.77; p<0.001), renal involvement (slope -4.36 SE 1.30; Beta -0.08; p=0.001) and the MetS (slope -6.88 SE 1.86; Beta -0.09; p<0.001). In patients with RA/SpA/PSA, eGFR also showed a greater trend of decline over time in those with MetS than without, but the difference did not reach statistical significance.
Conclusion: Among patients with common rheumatic diseases, SLE showed the greatest decline in renal function over time. The presence of MetS in SLE significantly accelerated renal function decline over time independent of the presence of renal disease. The MetS also unfavorably affected eGFR in patients with inflammatory arthritis. A more detailed analysis on the causes of eGFR decline in individual diseases and a longer period of follow-up of the renal function is needed.
Acknowledgments: NIL
Disclosure of Interests: None declared
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THU0123 DIABETES MELLITUS AND CARDIOVASCULAR RISK MANAGEMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS IN A LARGE INTERNATIONAL AUDIT

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Background: The cardiovascular disease (CVD) risk in patients with rheumatoid arthritis (RA) is comparable to that of patients with diabetes mellitus (DM). Although several studies have indicated high prevalences of glucose intolerance and DM in RA patients, little is known about how this affects their CVD risk.
Objectives: To examine indications for, and use of antihypertensive treatment (AntiHT) and lipid-lowering therapy (LLT) in RA patients with DM (RA-DM) and

RA patients without DM (RAwoDM). Further, to compare the prevalence of various types of CVD across RA-DM and RAwoDM.

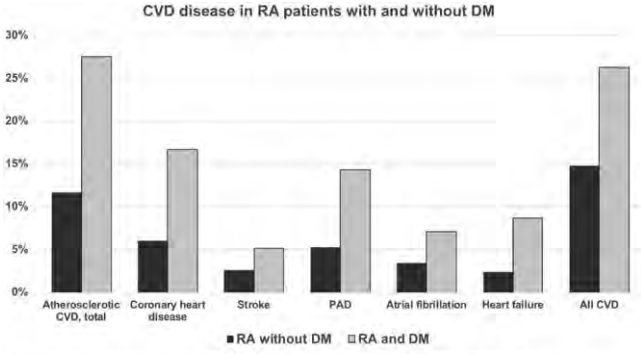
Methods: The cohort was derived from the **SU**rvey of cardiovascular disease **R**isk **F**actor in patients with **R**heumatoid **A**rthritis (SURF-RA), which was performed in 53 centres across 17 countries in 5 world regions (West and East Europe; North and Latin America; and Asia) from January 2014 to August 2019. Indication for AntiHT was defined as: 1) systolic/diastolic blood pressure (BP) ≥ 140/90 mm Hg, 2) self-reported hypertension, and/or 3) current use of AntiHT. Indication for LLT was defined according to European Society of Cardiology (ESC) guidelines (1), in which the Systematic Coronary Risk Evaluation (SCORE) is applied. SCORE risk estimates were multiplied by 1.5 according to EULAR recommendations. Target treatment targets for blood pressure and lipids were defined according to ESC guidelines applicable at the time when data were recorded.

Results: Presence of comorbid DM was available in 10 602 (73.1 %) of the 14 503 RA patients included in SURF-RA, of whom 75 and 1262 patients reported DM type 1 and type 2, respectively (total 1337 patients, 12.6 %). Although less often current smokers, RA-DM patients were more often previous smokers, male sex and had higher body mass index compared to RAwoDM (p<0.0001 for all). AntiHT (62.3 % vs 84.7 %) and LLT (100 % vs 47.2 %) were more frequently indicated in RA-DM than in RAwoDM patients (p <0.0001 for both). RA-DM were more likely than RAwoDM to receive AntiHT on indication (60.4% vs 57.6%, p<0.0001), while the difference in LLT use on indication was not significantly different (45.7 % vs 42.5%, p = 0.06). Moreover, RA-DM compared to RAwoDM patients had more often reached treatment goals when on AntiHT (60.7 % vs 54.1 %, p<0.0001) and LLT (62.8 % vs 48.9 %, p<0.0001). Finally, the risk of all recorded established CVD (coronary heart disease, stroke, peripheral artery disease and atrial fibrillation) was increased by a factor of 2 to 3 in RA-DM compared to RAwoDM (Figure).

Conclusion: The effect of RA and comorbid DM on CVD risk appears to be additive. While CVD preventive medications are more often indicated in RA-DM than in RAwoDM patients, they are also more likely to receive such therapy and to reach CVD preventive treatment goals. The latter finding may be due to more developed CVD preventive care in DM compared to RA patients. Improved CVD preventive systems for patients with RA are warranted.

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*CVD cardiovascular disease, RA rheumatoid arthritis, DM diabetes mellitus, PAD peripheral artery disease

Disclosure of Interests: Eirik Ikdahl: None declared, Silvia Rollefstad: None declared, Joe Sexton: None declared, Birgitte Nellemann: None declared, Georeg Kitas: None declared, Piet Van Riel: None declared, Cynthia S. Crowson Grant/research support from: Pfizer research grant, Ian Graham: None declared, Anne Grete Semb: None declared

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THU0124 FACTORS ASSOCIATED WITH THE RISK OF MAJOR ADVERSE CARDIOVASCULAR EVENT IN PATIENTS WITH RHEUMATOID ARTHRITIS: A NATIONWIDE, POPULATION-BASED, CASE-CONTROL STUDY

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Background: Few population-based studies have assessed factors associated with major adverse cardiovascular evet (MACE) among patients with rheumatoid arthritis (RA).

Objectives: The study aimed to assess risk factors of MACE in RA patients in Taiwan.

Methods: This study used the 2003–2013 Taiwanese National Health Insurance Research Database to identify 115,143 newly-diagnosed RA patients aged 20 years or more from 2004 to 2012. MACE was defined as having an inpatient visit with a diagnosis of myocardial infarction (ICD-9-CM 410.x except 410.2) with the receipt of coronary artery bass graft or percutaneous coronary intervcention/percutaneous transluminal coronary angioplasty, or having an inpatient visit with a diagnosis of ischemic stroke (ICD-9-CM 433-436 except 433.0 and 434.0). We firstly identified 108,319 RA patients who had no history of MACE before RA diagnosis date. From these patients, we identified 7,580 RA patients who developed MACE in the follow-up period and 100,739 who did not develop MACE in the follow-up periods. The index dates for MACE cases were the date of first inpatient visit for MACE. We finally selected 5,994 MACE cases and 23,97**6** non-MACE controls matching (1:4) for age, sex and disease duration. We examined the associations of MACE with comorbidities, use of biological and conventional synthetic disease modifying antirheumatic drugs (DMARDs), nonsteroidal anti-inflammation drug (NSAID), corticosteroid, antiplatelet agent, anticoagulant, statin and non-statin lipid lowering agents within one year before the index date using conditional logistic regression analyses with a full model and a parsinomious model (only considering the covariates with a p value <0.05 in the univarialbe analysis), shown as odds ratios (ORs) with 95% confidence intervals (CIs).

Results: We selected 5,994 MACE cases and 23,976 non-MACE controls. The mean ± SD age was 69.19±11.62 years and 18,925 (63.15%) subjectes were female. The mean ± SD disease duration was 3.44±2.21 years. Using multivariable conditional logistic regression analysis, the risk of MACE was associated with use of abatacept (OR, 0.12; 95% CI, 0.02–0.90), methotrexate (OR, 0.69; 95% CI, 0.62–0.76), ciclosporin (OR, 1.41; 95% CI, 1.06–1.86), NSAID (OR, 1.36; 95% CI, 1.27–1.45), antiplatelet agent (OR, 2.48; 95% CI, 2.32–2.64), non-statin lipid lowering agents (OR, 1.46; 95% CI, 1.28–1.65), and comorbidities including hypertension (OR, 1.23; 95% CI, 1.16–1.32), diabetes (OR, 1.28; 95% CI, 1.19–1.38), ischemic heart disease (OR, 1.22; 95% CI, 1.12–1.33) and chronic obstructive pulmonary disease (COPD) (OR, 1.13; 95% CI, 1.04–1.24) in the parsinomious model.

Conclusion: This population-based case-control study revealed that in newly-diagnosed RA patients, use of abatacept and methotrexate were associated with a decreased risk of MACE development, while use of ciclosporin, NSAID, antiplatelet agents and non-statin lipid lowering agents, and comorbidities including hypertension, diabetes, ischemic heart disease and COPD were associated with an increased risk of MACE development.

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Disclosure of Interests: None declared

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THU0125 IMPACT OF DISEASE ACTIVITY IN THE LEFT VENTRICULAR SYSTOLIC MYOCARDIAL FUNCTION OF PATIENTS WITH RHEUMATOID ARTHRITIS: A CASE-CONTROL STUDY

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Background: Patients with Rheumatoid Arthritis (RA) have higher incidence of cardiovascular diseases (CVD) compared to general population. There is controversy about the impact of RA disease activity on left ventricular systolic function (LVSF)[1]. LVSF may be assessed by conventional methods like left ventricular ejection fraction (LVEF) and myocardial shortening or by novel techniques evaluating myocardial strain such as speckle tracking echocardiography (STE).

Objectives: To assess the impact of RA disease activity on LVSF using ejection fraction and myocardial strain by STE.

Methods: Observational, cross-sectional study. RA patients aged 40-75 years that fulfilled the 2010 ACR/EULAR classification criteria and matched controls were included. Patients with a poor US window, history of previous CVD (ischemic heart disease, cerebrovascular accident or peripheral arterial disease) and pregnancy were excluded. Individuals were evaluated using two-dimensional speckle tracking echocardiography performed and reviewed by 2 certified echocardiographers. LVEF and myocardial strains (circumferential, longitudinal and

radial) were measured; differences were solved by consensus. Descriptive analysis was done with measures of central tendency and dispersion. Student-t and Mann-Whitney U tests were used for comparisons.

Results: A total of 140 subjects were included. Demographic and clinical characteristics are shown in Table 1. RA patients were divided in 2 groups, according to disease activity by DAS 28-CRP (remission or low activity and moderate or high activity). Echocardiographic comparisons between RA and controls and between the 2 groups in which RA patients were divided by disease activity are shown in Table 2. The LVEF was lower in RA subjects compared with controls (p= 0.022), however LVEF was normal (> 52% in men and >54% in women) in both groups. There was a significant difference in the circumferential strain (CS) between RA patients based on the disease activity by DAS 28-CRP (p= 0.006).

Table 1. Demographic and clinical characteristics.

	RA (n= 70)	Control (n= 70)	*P*
Female, n (%)	67 (95.7)	69 (98.6)	NS
Age, mean ± SD	52,4±6,7	52,0±6,1	NS
Type 2 Diabetes Mellitus, n (%)	9 (12.9)	7 (10)	NS
Hypertension, n (%)	14 (20)	16 (22.9)	NS
Dyslipidemia, n (%)	16 (22.9)	17 (24.3)	NS
Active smoking, n (%)	11 (10.9)	8 (16.3)	NS
Disease duration, years, median (q25 –q75)	8.0(3.0-15.0)	-	-
DAS-28-PCR, median (q25 –q75)	3.2(2.1-3.9)	-	-

Table 2. Echocardiographic findings

	LVEF	*P*	CS	*P*
RA, mean ± SD	63.0±4.3	**0.022**	-16.4±4.5	NS
Controls, mean ± SD	64.7±3.8		-16.2±4.1	
	LVEF	***P***	**CS**	***P***
Remission or low disease activity, median (q25 –q75)	64.0(60.0-66.0)	NS	-15.1(-17.2- -12.2)	**0.006**
Moderate and high diseases activity, median (q25 –q75)	63.0(60.0-66.0)		-18.1(-22.0- -13.9)	

LVEF*= Left ventricular ejection fraction*
CS*= Circumferential strain*

Conclusion: The decrease in the circumferential strain depends on the disease activity. Myocardial strain by speckle tracking echocardiography may detect early myocardial dysfunction in RA. It is important for the rheumatologist to establish an appropriate treatment in order to achieve the disease remission or a low disease activity, as there is an impact of the disease activity on the myocardial function.

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Disclosure of Interests: None declared

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THU0126 COMBINATION OF NON-DIPPING PROFILE WITH ELEVATION OF NIGHTTIME SYSTOLIC BLOOD PRESSURE IN PATIENTS WITH RHEUMATOID ARTHRITIS IS ASSOCIATED WITH HIGHER ARTERIAL STIFFNESS AND CARDIOVASCULAR RISK

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Background: Nocturnal hypertension (HTN) and non-dipping profile are important predictors of adverse cardiovascular (CV) outcomes. Their associations with subclinical vascular damage in rheumatoid arthritis (RA) are still a matter of investigation. It was shown that 10-year atherosclerotic CV disease risk (rASCVD) may be more accurate in CV risk prediction in RA than SCORE. Associations of impaired 24-h BP phenotypes with CV risk in RA are not well-studied yet.

Objectives: To assess dipping patterns and nighttime systolic blood pressure (SBPn) and their associations with arterial stiffness and CV risk assessed by rASCVD in patients with RA.

Methods: Study group included 90 patients with RA (females 78.7%, age 59.5±14.2 years, HTN 64%, median (med) HTN duration 6.4 years, RA duration – 7.2 years, seropositive RA 66%, mean DAS-28(CRP) 3.8±1.0) and control group (45 patients matched by gender, age and risk factors). All patients with HTN received antihypertensive therapy. Office BP was measured with a validated oscillometric device, 24-hour ABPM was performed with BPLab Vasotens, carotid-femoral PWV was assessed by applanation tonometry. 3 groups were formed after adjustment of dipping state by SBPn: dippers (G1), non-dippers with SBPn<120 mmHg (G2), non-dippers with SBPn≥120 (G3). CV risk in RA group was calculated as 10-year rASCVD. Risk≥7.5% was considered as high. p<0.05 was considered significant.

Results: Median rASCVD was 6.3%. Rate of BP control was 60% in RA and 66% in the controls (p=0.5). Patients with RA vs controls had higher mean SBPn (124±16 vs 110±8 mmHg, p=0.003), lower diurnal index (DI) (med 3.8 vs 8.1%, p=0.02), higher rate of night HTN (49.6 vs 12.2% (p=0.0002). The RA and control groups didn`t differ by dipping patterns, although RA patients more often had non-dipping profile (DI <10%): 83.9 vs 61.3%, (p=0.02). RA patients with SBPn ≥120 mmHg had higher age (63.7±12.5 vs 52.9±14.5 years), office SBP (143±17 vs 122±13 mmHg), HTN duration (med 5.4 vs 0.5 years), PWV (10.3±3.0 vs 7.9±2.5 m/s) and rASCVD (12 vs 3.4%), p<0.001 for trend. Analysis in hypertensive RA group confirmed significant differences in PWV (11.3±3.1 vs 9.1±3.2 m/s, p=0.02) and rASCVD (med 13.5 vs 10.5%, p=0.045). Patients with DI<10% had higher age (60.9±13.8 vs 54.3±11 years, p=0.04) and rASCVD (med 8.5 vs 3.1%, p=0.02). Patients with rASCVD ≥7.5% compared to <7.5% had higher SBPn (133±11 vs 112±8 mmHg), lower median DI (0 vs 6%), more often had masked HTN (43 vs 16%) and night HTN (48 vs 16%), p<0.01 for trend. SBPn significantly correlated with age (r=0.6), office SBP (r=0.5) and DBP (r=0.4), PWV (r=0.6), rASCVD (r=0.6); non-dipping pattern – with age (r=0.2), and rASCVD (r=0.3). After adjustment by SBPn, no differences were observed between G2 and G3. Patients in G3 vs G1 had higher PWV (10.4±3.1 vs 7.6±1.7 m/s, p=0.004), CRP (med 15.7 vs 7.8 mg/l, p=0.03), rASCVD (med 12.8 vs 3.1%) (p<0.001); in G3 vs G2 – higher PWV (10.8±3.1 vs 8.2±2.3 m/s), rASCVD (med 12.8 vs 2.7%) and ESR (med 45 vs 21 mm/h, p<0.01 for trend).

Conclusion: Patients with RA had higher incidence of non-dipping pattern and SBPn elevation. Combination of high SBPn and non-dipping was associated with higher arterial stiffness and CV risk – this may be mediated by inflammation. Higher CV risk was associated with masked and night HTN. This may help in defining indications for ABPM in this population.

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THU0127 ESTIMATED CARDIOVASCULAR RISK IN A LARGE COHORT OF RHEUMATOID ARTHRITIS PATIENTS FROM THE "CARDIOVASCULAR OBESITY AND RHEUMATIC DISEASE (CORDIS)" STUDY GROUP OF THE ITALIAN SOCIETY OF RHEUMATOLOGY.

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Background: Rheumatoid arthritis (RA) patients present high cardiovascular (CV) morbidity and mortality and EULAR recommends estimating their CV-risk [1]. The Systematic Coronary Risk Evaluation (SCORE) algorithm is suggested if National Guidelines are lack, but few data are available about different strategies.

Objectives: To estimate the 10-years CV-risk using different algorithms in RA compared to osteoarthritis (OA) patients, as control group.

Methods: A total of 1467 RA patients (78.3% female; mean age 59.8±11.5 years; mean disease duration 131±109 months), fulfilling the 2010 EULAR/ACR classification criteria, and 342 age and sex matched patients with OA (79.8% female; mean age 58.7±11.5 years) were enrolled in this multicentre cross-sectional study during 2019. Clinical and laboratory data were registered, and individual CV-risk was calculated using: SCORE chart, "Progetto Cuore" model (PCM), QRisk3, Reynolds Risk Scores (RRS) and Expanded Risk Score in RA (ERS-RA), as stated by suitable algorithms. Statistical analysis was performed using the Statistical System Graphpad Instat 8.0 (San Diego, CA-USA).

Results: In 46 (3%) RA patients a previous CV event was observed. Among traditional CV-risk factors, RA patients presented higher frequency of diabetes (9.9% vs 6.4%; p=0.04) and lower prevalence of dyslipidaemia (21.7% vs 32.5%; p<0.0001) compared to OA patients. Prevalence of hypertension was similar in both groups (40% vs 39.2%). Mean BMI (25.6±4.8 vs 26.6±4.4; p<0.0001) and prevalence of obesity (15% vs 21%; p=0.003) were significantly lower in RA patients. Finally, RA patients were more frequently smokers (20.4% vs 12.5% - p=0.002). 441 (30%) RA patients were in CDAI remission, 998 (68%) patients were on csDMARDs while a biologic agent was used in 617 (42%) patients. About 43% of RA patients were on a mean prednisone-dose of 4.5±3.5 mg/day. The 10-years CV-risk resulted 2 to 3-fold higher in RA compared to OA patients using the different algorithms. The QRisk3 estimated the highest CV risk in our cohort of patients, while the ERS-RA and RRS were significantly higher than PCM and SCORE.

Conclusion: Our study demonstrates a higher estimated CV-risk in RA compared to OA patients. The commonly used algorithms to estimate CV-risk in clinical practice perform differently, evaluating different traditional CV-risk factors and disease specific characteristic, as for QRisk3 or ERS-RA. Rheumatologist should impact on both traditional and RA related modifiable CV-risk factors.

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Disclosure of Interests: Fabio Cacciapaglia Speakers bureau: BMS; Roche; Pfizer; Abbvie, Matteo Piga: None declared, Gianluca Erre: None declared, Andreina Manfredi: None declared, Elena Bartoloni Bocci: None declared, Garifallia Sakellariou Speakers bureau: Abbvie, Novartis, MSD, Ombretta Viapiana: None declared, Sergio Colella: None declared, Anna Abbruzzese: None declared, Martina Dessì: None declared, Caterina Vacchi: None declared, Floriana Castagna: None declared, Giacomo Cafaro: None declared, Bianca Lucia Palermo: None declared, Alessandro GIollo: None declared, Marco Fornaro: None declared, Elisa Gremese Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Merck Sharp & Dohme, Novartis, Sanofi, UCB, Roche, Pfizer, Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Merck Sharp & Dohme, Novartis, Sanofi, UCB, Roche, Pfizer, Francesca Romana Spinelli Grant/research support from: Pfizer, Speakers bureau: Lilly, BMS, Celgene, Fabiola Atzeni: None declared

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THU0128 CAROTID ATHEROSCLEROSIS IN POSTMENOPAUSAL WOMEN WITH RHEUMATOID ARTHRITIS: A CASE CONTROL STUDY

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Background: Cardiovascular disease (CVD) is the primary cause of mortality in women in developed countries. CVD risk rises with age, yet for women there is a rapid increase that occurs after the onset of menopause (1). There has been found that there is four to five times atherosclerosis compared to premenopausal women. Adding to traditional CVD risk, rheumatoid arthritis (RA) patients have an increased CVD morbimortality because of the inflammatory disorder (2). To detect the burden of CVD, carotid ultrasound has been promoted to identify preclinical atherosclerosis.

Objectives: To determine the prevalence of carotid atherosclerosis and *carotid* intima-media thickness (cIMT) in postmenopausal patients with RA and compare them to matched controls.

Methods: Observational, cross-sectional study. RA patients aged 40-75 years that fulfilled 2010 ACR/EULAR criteria with post-menopause and matched controls (without RA) were included. Patients with history of previous atherosclerotic CVD, women who undergone menopause due to hysterectomy or cessation of periods other than by a natural cause, women on hormone replacement therapy and having irregular menses were excluded. Clinical history and carotid ultrasound were performed. Increased cIMT defined as ≥0.9 mm was measured using the two inner layers of the common carotid artery and carotid plaque as a focal narrowing ≥0.5 mm of the surrounding lumen. Descriptive analysis was done with frequencies (%), median (q25-q75). Comparisons with Chi-square and Mann Whitney-U test. Binary regression analysis was used to test association an increased cIMT with cardiovascular risk factors and RA diagnosis.

Results: A total of 139 women with established post-menopause were included. Baseline characteristics (Table 1). Right carotid atherosclerosis prevalence was found more than twice (19% vs 8%, p=0.01) and an increased cIMT was higher in postmenopausal RA patients (right 25% vs 10%, p=<0.001; left 31% vs 15%, p=<0.001) compared to controls (Table 2). Binary regression showed that the odds of having RA increases three times the risk of having ≥0.9 mm CIMT when adjusted to age, hypertension, dyslipidemia and active smoking OR 3.0, 95% CI (1.41-6.36) (p=0.004).

Table 1. Baseline characteristics

	RA (N=70)	Control (N= 69)	*p*
Age, median (q25-q75)	55.04 ± 5.381	56 6 ±.481	NS
Disease duration, year, median (q25-q75)	10.32 (4.5-15.3)		
Body mass index, median (q25-q75)	28.19 (25.36-31.84)	28.55 (26.57-31.18)	NS
Diabetes Mellitus, n (%)	8 (11.6)	14 (20)	NS
Hypertension, n (%)	19 (27.5)	26 (37.1)	NS
Dyslipidemia, n (%)	23 (32.9)	21 (30.4)	NS
Active smoking, n (%)	14 (20.3)	5 (7.1)	NS

Table 2. Carotid ultrasound findings

	RA (N= 70)	Controls (N=69)	*p*
Any plaque, n (%)	24 (34.3)	17 (24.6)	NS
Right CP, n (%)	19 (27.9)	8 (11.6)	**0.01**
Left CP, n (%)	17 (25)	13 (18.8)	NS
Any cIMT ≥0.9 mm, n (%)	38 (54.3)	19 (27.5)	**0.001**
Right carotid cIMT ≥0.9 mm, n (%)	25 (35.7)	10 (14.7	**<0.001**
Left carotid cIMT ≥0.9 mm, n (%)	31 (44.3)	15 (21.7)	**<0.001**
CP characteristics:			
Homogeneous n (%)	2 (2.8)	3 (4.3)	NS
Heterogeneous, n (%)	20 (28.6)	16 (23.2)	NS

CP: carotid plaque

Conclusion: Despite the increase in cardiovascular risk in postmenopausal women compared to the general population, women with RA have a higher risk compared to healthy women. Carrying out cardiovascular prevention and management in patients with RA is essential, especially in those who are in a stage of post-menopause.

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THU0129 SLEEP DISTURBANCE AND LOW INFLAMMATION PREDICT A PATTERN OF CHRONIC FATIGUE IN ACTIVELY TREATED PATIENTS WITH ESTABLISHED RA.

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Background: Fatigue is common among patients with rheumatoid arthritis (RA) and has major impact on the burden of disease. There is little knowledge regarding the factors predicting the longitudinal development of chronic fatigue.

Objectives: To identify baseline predictors for the development of chronic fatigue in patients with RA who initiate biological DMARD (bDMARD) treatment, and to compare disease courses across categories of fatigue for 12 months follow-up.

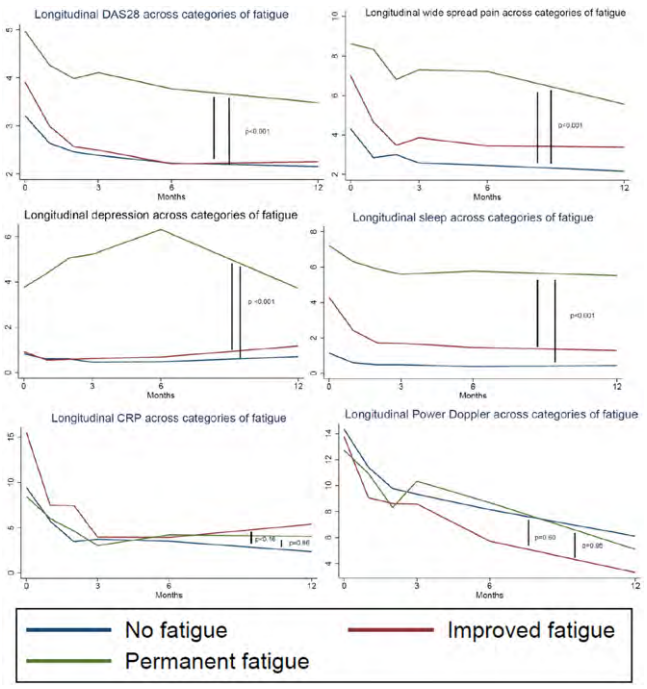
Methods: Different trajectories of fatigue were calculated from a cohort of 209 established RA patients initiating bDMARDs. Fatigue was assessed by use of the fatigue Numeric Rating Scale (0-10) from the Rheumatoid Arthritis Impact of Disease (RAID) questionnaire. The patients were assessed at 0, 1, 2, 3, 6 and 12 months. We defined three groups: no fatigue (≤3 at all visits), improved fatigue (>3 at baseline but ≤3 at follow-up) and chronic fatigue (≥ 4 at all visits). All patients had clinical/subjective assessments (28 tender/swollen joint count, assessor's/patient's global VAS, RAID score, widespread pain, pain catastrophizing, the Hospital Anxiety and Depression Scale and inflammatory markers (ESR, CRP and calprotectin (a major granulocyte protein sensitive for inflammation in RA patients)). All patients were assessed by ultrasound (grey scale (GS) and power Doppler (PD)) of 36 joints and 4 tendons with semi-quantitative scoring (0-3). Differences between groups at baseline was assessed by bivariate analyses, and logistic regression models adjusted for age and gender were used to explore baseline predictors of chronic vs improved fatigue. Trajectories of different groups were plotted as estimated marginal means in figures, and differences between groups assessed by mixed models with maximum likelihood random effects, adjusted for age and sex.

Results: Table 1 describes demographics and clinical factors of the three groups with significant differences shown in bold. Logistic regression with multivariate assessments found anti-CCP and low inflammation (calprotectin) to be predictors of chronic versus improved fatigue. Sleep disturbance was highly predictive of chronic fatigue. Figure 1 illustrates the trajectories for the three groups at all visits, showing the chronic fatigue group to have significantly higher DAS28, level of widespread pain, depression and sleep disturbance in contrast to no higher level of inflammation assessed by CRP and ultrasound PD.

Table 1.

	No fatigue	Improved fatigue	Chronic fatigue	No fatigue vs Improved fatigue	Improved fatigue vs chronic fatigue	No fatigue vs. chronic fatigue
	48	29	43	p	p	p
Age, mean (SD) years	51 (2)	48 (2)	54 (2)	0.28	0.09	0.28
Female gender (%)	35 (73)	24 (83)	38 (88)	0.40	0.50	0.09
Higher Education (%)	31 (65)	23 (79)	20 (47)	0.17	**0.01**	0.17
Anti-CCP positive (%)	29 (60)	20 (69)	36 (84)	0.72	**0.01**	**0.002**
RF positive (%)	27 (56)	17 (59)	30 (70)	0.76	0.11	0.15
Disease duration, mean (SD) years	7 (1)	8 (1)	11 (1)	0.81	0.11	0.03
RA disease activity						
DAS28CRP	3.2 (0.1)	3.9 (0.2)	4.7 (0.2)	**0.003**	**0.004**	**<0.001**
Swollen joints (28)	5.7 (0.7)	5.6 (1.0)	6.2 (0.7)	0.90	0.60	0.63
CRP mg/L mean (SD)	9.4 (2.4)	15.6 (4.1)	11.0 (2.6)	**0.02**	**0.02**	0.58
Calprotectin mg/L mean (SD)	1.6 (0.3)	2.0 (0.4)	1.5 (0.2)	0.44	0.20	0.92
Sum score PD mean (SD)	14.3 (1.8)	13.8 (2.5)	12.3 (1.9)	0.85	0.62	0.43
Sum score GS mean (SD)	31.6 (2.8)	29.3 (3.4)	28.2 (2.7)	0.61	0.81	0.39
Psychosocial factors						
RAID sleep (VAS 0-10)	1.2 (0.3)	4.3 (0.6)	6.7(0.4)	**<0.001**	**<0.001**	**<0.001**
RAID fatigue (VAS 0-10)	1.4 (0.2)	5.6 (0.3)	7.1 (0.3)	**<0.001**	**0.003**	**<0.001**
Widespread pain (0-25)	4.3 (0.4)	7.0 (0.8)	8.6 (0.7)	**0.001**	0.16	**<0.001**
HADS anxiety	1.5 (0.3)	1.4 (0.6)	3.4 (0.7)	0.26	0.58	0.10
HADS depression	0.8 (0.2)	0.9 (0.4)	3.0 (0.8)	0.98	0.36	**0.05**
Pain Catastrophizing (0-6)	1.0 (0.2)	2.5 (0.3)	2.9 (0.3)	**<0.001**	0.31	**<0.001**

Conclusion: Sleep disturbance is a modifiable factor presently found to predict chronic versus improved fatigue. Thus, attention should be given to RA patients with sleep problems to seek to avoid development of chronic fatigue. This issue should be explored in further studies.



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THU0130 PATTERNS OF COGNITIVE DECLINE IN RHEUMATOID ARTHRITIS: RESULTS OF CASE CONTROL STUDY NESTED IN A POPULATION-BASED COHORT

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Background: The risk of cognitive decline and dementia is of particular interest for patients exposed to prolonged inflammation. In rheumatoid arthritis (RA), the inflammatory mechanisms that are central to the disease's pathology share many features with those seen in Alzheimer's disease (AD). However, published reports on the strength and direction of the putative associations with cognitive decline and dementia in RA are conflicting and the potential impact of immunomodulation has not been fully established. This study reports on a case control analysis comparing the results of a cognitive test conducted in RA cases from a longitudinal population register with healthy controls. The relationship between test outcomes, disease characteristics, and treatment is examined.

Objectives:

- To characterise differences in cognitive function as assessed by a validated test battery between a group of patients with RA and a matched sample of healthy controls.
- To investigate disease and treatment related factors that might have an impact on the cognitive function of patients with RA.

Methods: A total of 38 people with RA were selected at random from subjects who had enrolled on the Norfolk Arthritis Register as part of the ICORA (Investigation of Cognition in RA) Study. The register is a large longitudinal inception cohort of patients recruited from both primary and secondary care. The study subjects were over 55 years old with a diagnosis of RA defined by the ACR criteria. Cognitive function was assessed using the Addenbrooke's Cognitive Examination III (ACE-III) battery. The ACE-III is a validated screening test for dementia that evaluates five cognitive domains (attention, memory, verbal fluency, language and visuospatial skills). A cut off value of 82 is indicative of cognitive

impairment. The ACE-III scores in the cases were compared with scores from 29 healthy population-based controls matched for age and sex.
Results: The mean age of the patient and control groups was 69 years. The RA patients had a mean disease duration of 9.8 years and had been taking DMARDs for 7.1 years. Among the patient group with RA, 14 (37%) scored below 82 compared with none in the group of healthy controls. The mean ACE-III scores of both groups are shown in the table below:

	Controls N=29	RA N=38
ACE-III Total	95.2 (3.7)	85.2 (7.4)
•Attention	17.7 (0.5)	16.5 (1.9)
•Memory	24.6 (1.9)	19.8 (4.0)
•Fluency	12 (1.4)	9.9 (2.6)
•Language	25.5 (0.8)	24.6 (1.7)
•Visuospatial	15.8 (0.5)	14.4 (1.5)

After adjusting for age, sex, BMI and smoking status, significant differences were seen in the ACE-III total (adjusted mean difference(SE)=8.67(1.77); p<0.001), memory (adjusted mean difference(SE)=4.16(1.03); p<0.001), fluency (adjusted mean difference(SE)=2.29(0.67); p=0.001) and visuospatial (adjusted mean difference(SE)=1.36(0.38); p<0.001). There was no difference in attention (p=0.19) or language (p=0.10).
Among the patients with RA there was no clear association between disease duration and ACE-III Total scores; however, there was a trend for increasing cognitive scores in those who had been taking DMARDs for longer (<5 years: mean ACE-III Total=84.1; 5-10 years: 85.0: 11-14 years: 85.4; >14 years: 89.6).
Conclusion: This study provides evidence to suggest that patients with established RA are at increased risk of cognitive decline when compared with healthy controls. The pattern of cognitive deficit, predominantly involving visuospatial and memory function, is consistent with an Alzheimer's disease profile. Our data suggest a potential role for DMARDs in reducing the rate of cognitive decline in patients with RA.
Disclosure of Interests: Tasuku Toyoda: None declared, Jacqueline Chipping: None declared, Jack Dainty: None declared, Stephen Jeffs: None declared, Michael Hornberger: None declared, Eneida Mioshi: None declared, Suzanne Verstappen Grant/research support from: BMS, Consultant of: Celltrion, Speakers bureau: Pfizer, Max Yates: None declared, Alex MacGregor: None declared
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THU0131 LOCALISATION OF RHEUMATOID LUNG NODULES IN PATIENTS WITH RHEUMATOID ARTHRITIS-RELATED INTERSTITIAL LUNG DISEASE: RIGHT OR LEFT?

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Background: The frequency of pulmonary rheumatoid nodules closely relates to the diagnostic modality and changes from <0.4% to 32% [1]. However, data regarding pulmonary rheumatoid nodules in RA-related interstitial lung disease (RA-ILD) is scarce.
Objectives: The aim of this study was to describe the general features and localisation of pulmonary rheumatoid nodules in RA-ILD patients followed up in a single tertiary center.
Methods: During January 2010 and March 2019, 826 RA patients had lung computerized tomography (CT) in Hacettepe University. Three radiologists re-evaluated lung CTs and 156/826 (18.8%) patients with had RA-ILD. Pulmonary nodules suggesting pulmonary rheumatoid nodules were identified by radiologist from lung CTs. In addition to demographic, clinical and laboratory data; number of the pulmonary rheumatoid nodules, size and localisation of the biggest nodule – named as dominant nodule-, type of ILD (UIP, NSIP and isolated airway disease (AD)) were recorded. p value less than 0.05 was considered as statistically significant.
Results: Of 156 patients, 68 (26, 38.2% male) patients (43.5%) had at least one pulmonary rheumatoid nodule. The mean (SD) follow-up duration was 167 (88) months for RA, and 72 (46) months for RA-ILD. Thirty patients had UIP (44.1%), 31 (45.6%) had NSIP and 7 (10.3%) had AD pattern. 35 (51.5%) of patients had exposed smoking (current or past). Rheumatoid factor and anti-CCP were positive in 60/68 (88.2%) and 33/45 (73.3%) patients, respectively. Median number of nodules was 3 (2-3). Median size of the dominant nodule was 6.8 (5.0-11.5) mm. While 41 (60.3%) of dominant nodules localised in right lung, 27 (39.7%) of dominant nodules localised in left lung (p=0.09). In addition, right inferior lobe (21, 39.9%) was the most common localisation and right middle lobe (7, 10.3%) was the least common localisation of dominant nodule (Figure 1).

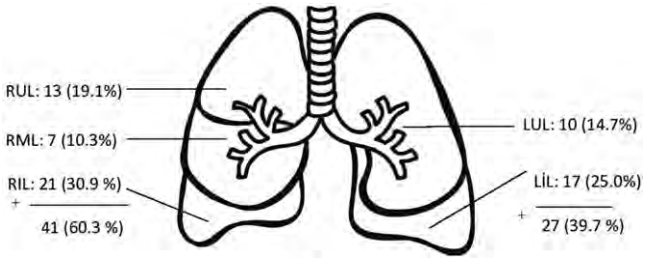


Figure 1. Localisation of dominant pulmonary rheumatoid nodules *LUL: Left upper lobe, LİL: Left inferior lobe, RIL: Right inferior lobe, RML: Right middle lobe, RUL: Right upper lobe*

Conclusion: We found a high prevalence of pulmonary rheumatoid nodules in RA-ILD patients and right inferior lobe was the most common localization of dominant nodules. Prospective studies are needed to determine how the presence and localization of pulmonary rheumatoid nodules affect the RA-ILD disease process.
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THU0132 ASSOCIATION OF RHEUMATOID ARTHRITIS AND DEMENTIA: A NATIONWIDE POPULATION-BASED STUDY

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Background: Rheumatoid arthritis (RA) and dementia have a mechanism that systemic inflammation is involved in the onset, and its relationship can be predicted, but still controversy about the relationship between them. According to the prior literature, rheumatoid arthritis has reduced the risk of progression to Alzheimer's disease (AD).
Objectives: To investigate the risk of dementia in RA patients based on Korean National Health Insurance Service (NHIS) claim database
Methods: We conducted a nationwide population-based study using a Korean NHIS consisted of 1 million individuals, who submitted medical care claims between 2002 and 2013. RA was identified using as the International Classification of Diseases code (ICD-10) M05 (seropositive RA) and dementia was defined as having a prescription of anti-dementia drugs with satisfying the AD (ICD 10 F00 or G30) or vascular dementia (VD, ICD 10 F1.0-1.3, F1.8 and F1.9) codes. The control groups were matched to the RA cohort by age and sex.
Results: Of the total 6,028 dementia patients, 100 were diagnosed with RA. In patients with RA over 65 years of age compared to age and sex-matched control group, the dementia risk was shown as whole dementia OR 1.011 (95% CI, 0.811-1.260), AD 1.043 (0.826-1.318), Vascular dementia (VD) 1.274 (0.745-2.177). The sub analysis was performed by dividing the Charlson comorbidities index (CCI) into more than three (moderate) and less than (mild) groups. The mild groups were whole dementia OR 0.851 (0.468-1.546), AD 0.776 (0.392-1.536), VD 0.917 (0.126-6.673), and in the moderate group, whole dementia OR 0.961 (0.750-1.231), AD 0.939 (0.717-0.7) 1.230) and VD 1.219 (0.692-2.149).

Conclusion: In conclusion, the risk of dementia in RA patents did not increase when compared to control group. Vascular dementia tended to increase in the RA group, but there was no statistical significance.

Table. Risk of dementia in RA patients

Outcomes	RA Yes/No, %	OR (95% CI) Model 1	Model 2	Model 3
All subjects				
Cognitive impairment	16.4/16.8	0.978(0.788-1.214)	0.976(0.786-1.211)	0.909(0.725-1.139)
Alzheimer dementia	14.1/14.0	1.006 (0.799-1.266)	1.004 (0.797-1.264)	0.940(0.740-1.194)
Vascular dementia	2.5/2.0	1.264(0.753-2.122)	1.257(0.749-2.111)	1.225(0.723-2.076)
Age < 65 years				
Cognitive impairment	8.8/16.8	0.479(0.146-1.577)	0.485(0.147-1.597)	0.831(0.458-1.508)
Alzheimer dementia	5.9/13.5	0.399(0.095-1.673)	0.402(0.096-1.687)	0.767(0.388-1.516)
Vascular dementia	2.9/2.7	1.200(0.161-8.942)	1.252(0.167-9.355)	0892(0123-6.3485)
Age ≥ 65 years				
Cognitive impairment	16.8/16.7	1.011 (0.811-1.260)	1.010 (0.810-1.259)	0.946(0.751-1.191)
Alzheimer dementia	14.6/14.0	1.043 (0.826-1.318)	1.044 (0.826-1.319)	0.981(0.770-1.251)
Vascular dementia	2.4/2.0	1.274(0.745-2.177)	1.263(0.739-2.159)	1.228(0.712-2.119)

Model 1: Crude(adjusted for age, sex)

Model 2: Adjusted for income and residence city size

Model 3: Adjusted for income, residence city size, comorbidity(hypertension, diabetes, dyslipidemia, mood disorder, cardiovascular disease, cerebrovascular disease, pulmonary disease, gastrointestinal disease, renal disease, connective tissue disoders, malignancy, HIV)

Disclosure of Interests: None declared
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THU0133 DIAGNOSES AND COMORBIDITIES IN PRE-RHEUMATOID ARTHRITIS: COMPARISON BETWEEN SEROPOSITIVE AND SERONEGATIVE PATIENTS AND MATCHED NON-RA SUBJECTS

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Background: Previous studies have suggested that comorbidities accumulate before the clinical diagnosis of RA, i.e., 'pre-RA' (1). Understanding patterns of diagnoses and comorbidities during the pre-RA period may provide new insights into pathogenesis.
Objectives: To elucidate diagnoses and comorbidities before the onset of clinically apparent RA compared to non-RA subjects, and for seropositive (RF and/or CCP positive) compared to seronegative (RF and CCP negative) patients with RA.
Methods: Adult residents of Olmsted County, Minnesota, with incident RA in 1999-2013 fulfilling the 1987 ACR classification criteria were identified by medical record review. Patients were age- and sex-matched 1:1 to non-RA controls from the same underlying population. The index date for each control corresponded to the incidence date of the matched RA patient. ICD9/10 diagnosis codes (≥2 codes ≥30 days apart prior to index date) were categorized using 161 chronic conditions identified by Clinical Classification Software. Logistic regression models adjusted for age and sex were used to estimate odds ratios (OR) and 95% confidence intervals (CI).

Table. Statistically significant associations between comorbidity categories and RA, adjusting for age and sex.

Comorbidity Category Description	Non-RA N (%)	RA N (%)	Odds Ratio (95% CI)
Polymyalgia	1 (0.2%)	30 (5%)	35.8 (7.51-643)
Systemic lupus erythematosus and connective tissue disorders	0 (0%)	15 (2.5%)	31.7 (4.25-4051)
Other respiratory disease	1 (0.2%)	6 (1.0%)	6.17 (1.03-118)
Hypertension with complications and secondary hypertension	2 (0.3%)	9 (1.5%)	4.57 (1.16-30.2)
Anemia (including pregnancy)	3 (0.5%)	11 (1.8%)	3.7 (1.15-16.4)
Other circulatory disease	4 (0.7%)	12 (2.0%)	3.03 (1.05-10.9)
Osteoarthritis	67 (11.3%)	138 (23.1%)	2.6 (1.87-3.67)
Other connective tissue disease	17 (2.9%)	35 (5.9%)	2.19 (1.21-4.12)
Fibromyalgia	16 (2.7%)	34 (5.7%)	2.19 (1.21-4.11)
Other nervous system disorders	43 (7.2%)	82 (13.7%)	2.04 (1.39-3.04)
Other upper respiratory disease	23 (3.9%)	41 (6.9%)	1.83 (1.09-3.14)
Asthma	37 (6.2%)	63 (10.6%)	1.78 (1.17-2.74)
Coronary atherosclerosis and other heart disease	44 (7.4%)	63 (10.6%)	1.56 (1.01-2.43)
Thyroid disorders	78 (13.1%)	107 (17.9%)	1.46 (1.06-2.02)

Results: The study included 597 RA patients (388 seropositive, 209 seronegative) and 594 controls. The median (range) age was 55 (19-91) years and 70% were female. The median (IQR) of total comorbidities at index was higher among RA patients at 3 (1-6) than controls at 2 (1-5) (p<.001). The median (IQR) of total comorbidities at index was higher in seronegative RA at 4 (2-7) compared to seropositive RA at 3 (1-5) (p=.001); the proportion with six or more was 37% vs. 24% respectively (p<.001). The Table shows the ORs (95% CI) for comorbidities with statistically significant associations with RA overall. The magnitude of the association between total comorbidities and RA peaked at 5+ comorbidities (OR 1.84; 95% CI 1.4-2.43). Spondylosis, intervertebral disc disorders, and back problems (OR 2.38; 95% CI 1.31-4.34); polymyalgia (OR 3.84; 95% CI 1.71-9.16); and systemic lupus erythematosus or other connective tissue disorders (OR 5.3; 95% CI 1.78-19.4) were more prevalent than among seronegative than seropositive patients.
Conclusion: The findings provide new insights about diagnoses and comorbidities preceding clinically apparent RA. Future studies of retrospective medical records for patients with particular comorbidities may provide new insights into the pathogenesis and clinical features of the transition from pre-RA to clinically overt RA, especially for seronegative disease.
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Disclosure of Interests: John M Davis III Grant/research support from: Research grants from Pfizer, Consultant of: Served on advisory boards for Abbvie and Sanofi-Genzyme, Elena Myasoedova: None declared, Tina Gunderson: None declared, Cynthia S. Crowson Grant/research support from: Pfizer research grant
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THU0134 COGNITIVE IMPAIRMENT IN RHEUMATOID ARTHRITIS

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Background: Increasing evidence suggests that systemic inflammation may be associated with an increased risk of developing cognitive dysfunction and Alzheimer's disease (AD). Some studies have found an association between rheumatoid arthritis (RA) and neurodegeneration with several finding increased incidence of mild cognitive impairment (MCI) in those with RA compared to healthy controls.
Objectives: This study aims to use preliminary data from the **R**h**e**umatoid arthriti**s**, medication and memory **st**udy (RESIST) to investigate the prevalence of MCI in a population of patients with RA and explore the relationship between MCI and specific demographic and clinical characteristics.
Methods: The Montreal Cognitive Assessment (MoCA) was used as a cognitive screening tool and was administered to subjects ≥55 years of age who had been diagnosed with RA according to the ACR/EULAR criteria. Demographic and clinical data was recorded at screening in face-to-face interviews and included age, gender, date of RA diagnosis and RA medication. RA disease activity score from 28 joints (DAS28), rheumatoid factor (RF) level, anti-cyclic citrullinated peptide (anti-CCP) level, erythrocyte sedimentation rate (ESR) were recorded. 260 participants completed both screening and baseline visits as part of the RESIST longitudinal study, MoCA scores from baseline were analysed for these participants. Statistical analysis was used to provide descriptive statistics and explore possible predictors of cognitive impairment.
Results: A total of 636 participants (mean age 68.1 yrs, female 67.5%) were screened between May 2018 and December 2019. The mean MoCA for screened participants was 25.4; 45.3% scored <26 in the MoCA and were considered to have mild cognitive impairment. Age was negatively correlated with MoCA score and was the only significant predictor of cognitive impairment. For each year of increase in age the MoCA score reduced by a mean of 0.08 points (p<0.05). There was little evidence of a difference in mean MoCA score by gender, RA medication, duration of disease, DAS28 score, ESR, anti-CCP or RF levels. The mean MoCA scores increased by 0.4 points between screening and baseline (P<0.001).
Conclusion: A large proportion of participants scored below the proposed cut-off for normal cognition in the MoCA suggesting a high prevalence of MCI in adults >55 years with moderately active RA. This provides further support for the

role of chronic inflammation in cognitive dysfunction and AD. Screening for MCI in rheumatology clinics might be clinically useful.

Demographics	Outcome
Age mean years (+/-SD) (n=633)	68.1 (8.01)
Gender (n=636)	429 (67.5)
Female n (%)	
RA Medication (n=636)	
csDMARD n (%)	368 (57.9)
TNFi n (%)	268 (42.1)
Duration of RA mean years (+/-SD) (n=484)	14.4 (13.9)
DAS28 mean (+/-SD) (n=306)	3.5 (2.04)
ESR mean (+/-SD) (n=501)	23.4 (22.0)
Anti-CCP (n=387)	
Positive n (%)	236 (61)
Rheumatoid Factor (n=377)	
Positive n (%)	277 (73.5)
MoCA Score points (n=636)	
≥26, n (%)	348 (54.7)
<26 n (%)	288 (45.3)
Subjective memory concerns (n=430)	
Yes n (%)	95 (22.1)
No n (%)	335 (77.9)

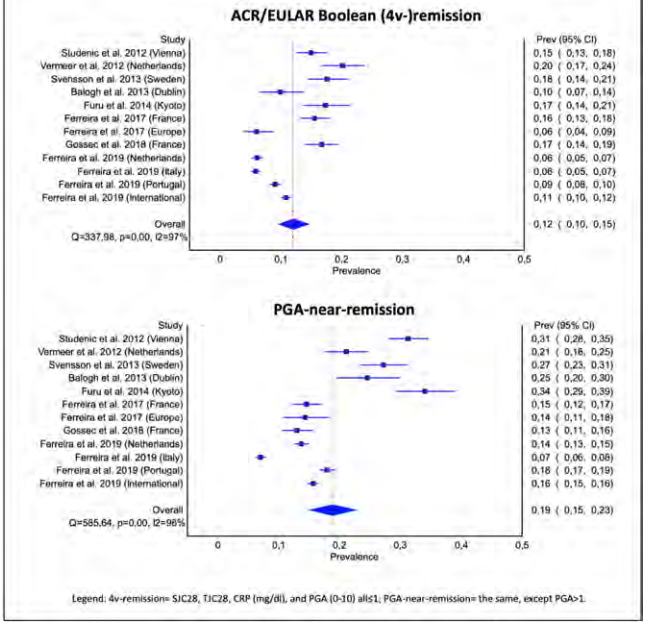
Disclosure of Interests: Christopher Edwards Grant/research support from: Abbvie, Biogen, Roche, Consultant of: Abbvie, Samsung, Speakers bureau: Abbvie, BMS, Biogen, Celgene, Fresenius, Gilead, Janssen, Lilly, Mundipharma, Pfizer, MSD, Novartis, Roche, Samsung, Sanofi, UCB
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THU0135 PATIENT GLOBAL ASSESSMENT LEVELS PRECLUDE THE MAJORITY OF RHEUMATOID ARTHRITIS PATIENTS OTHERWISE IN REMISSION, FROM REACHING THIS STATUS: SYSTEMATIC LITERATURE REVIEW AND META-ANALYSES INCLUDING 23,297 PATIENTS

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Background: Based on the American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) Boolean-based remission definition for rheumatoid arthritis (RA), the main reason for near-misses (failing Boolean remission solely due to one criterion >1) is a patient global assessment (PGA) >1/10.[1-3] The frequency of this PGA-near-remission status has not been well established.
Objectives: To synthesize the overall prevalence of ACR/EULAR Boolean-based remission and PGA-near-remission cross-sectionally in published studies, and to explore association with disease duration.
Methods: We systematically searched PubMed database (from 1/jan/2011 till 15/jan/2020) for "Rheumatoid arthritis" AND Boolean [OR synonyms] AND PGA [OR synonyms], and carried out a hand search of the references of the included studies. Two reviewers independently assessed the study inclusion and extracted the data (n (%) of patients in each remission status, mean (SD) disease duration, and country/city). Studies were excluded if any of the four Boolean criterion was not considered (e.g. C-Reactive Protein not assessed), or if only patients with low disease activity or remission were selected. If different time assessments were provided, we selected the 1y follow-up, as the most common. Random effects meta-analyses of proportions with double arcsine transformation were performed (also by disease duration subgroups) using MEDCALC®. Heterogeneity was assessed by I^2.
Results: From 41 studies identified, 8 studies concerning 12 subsamples were analysed (n=23,297 patients; of which 22% had ≤2 years mean disease duration). The overall prevalence of Boolean remission was 12% (95%CI: 10-15%, p<0.005) compared to 19% of PGA-near-remission (15-23%, p<0.005) (Figure 1). In patients with shorter disease duration, PGA-near-remission was more prevalent (14% vs 18%), but even more so in longer disease duration (11% vs 19%).

Figure 1 - Meta-analyses of prevalence of ACR/EULAR Boolean-based and PGA-near-remission in clinical cohorts



Conclusion: The overall prevalence of PGA-near-remission in patients with RA followed in clinical practice was 1/3 more prevalent than Boolean remission, a difference more pronounced in patients with established disease. Overall, over 61% of all RA patients otherwise in remission failed to satisfy the Boolean definition of remission solely due to a PGA>1. The use of PGA in the definition of treatment target exposes a substantial proportion of patients to the risk of overtreatment with immunosuppressive agents, while being deprived of the adjunctive therapy they probably need.
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THU0136 VERY ELDERLY ONSET RHEUMATOID ARTHRITIS (VEORA): CLINICAL AND THERAPEUTIC IMPLICATIONS AFTER 80 YEARS

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Background: There are differences in the characteristics of patients with Rheumatoid Arthritis (RA) depending on their age at onset with two traditional groups: YORA (young onset RA) and EORA (elderly onset RA). These aspects have not been studied in cases of very late onset (≥ 80 years)
Objectives: To describe the clinical characteristics, treatments and evolution at one year in "very elderly onset RA" (VEORA). Compare these characteristics with YORA (40-50 years) and EORA (60-70 years).
Methods: Retrospective and longitudinal study of RA patients from 2 spanish hospitals. From their databases, VEORA patients were identified and their clinical characteristics were analyzed at onset, treatments at diagnosis and in the first 12 months, as well as DAS28-ESR activity after 1 year. These variables were compared between cases belonging to one of the hospitals and 2 control

groups of YORA and EORA patients of the same center, matched by sex, diagnosis date ± 2 years, RF and / or ACPA status and presence of erosions in baseline Rx.

Results: A total of 2790 records of RA patients were analyzed, identifying 59 cases of onset in "very elderly" (2% of the total). Table 1 shows its clinical, analytical characteristics and treatments at diagnosis.

Table 1. Demographic and clinical data of the 59 VEORA patients

		n=59
	Female, n(%)	43 (73)
	Age at onset, years	83 ± 3
Comorbidity		
	Hypertension, n(%)	54 (92)
	Diabetes, n(%)	19 (32)
	CV disease	20 (34)
Clinical and analytical data at diagnosis		
	Acute onset, n(%)	26 (44)
	Polyarticular onset, n(%)	37 (63)
	Specific forms, n(%)	21 (36)
	Polymyalgia Rheumatica, n	16
	RS3PE, n	5
	Rheumatoid factor, n(%)	40 (68)
	ACPA, n(%)	24 (41)
	DAS28-ESR	5 (4,4-5,7)
	high activity, n(%)	32 (54)
First visit treatment		
	NSAIDs, n(%)	5 (9)
	Steroids, n(%)	55 (93)
	starting dose, mg/day*	10 (7,5-15)
	DMARD, n(%)	52 (88)
	Hidroxychloroquine	14 (24)
	Methotrexate	36 (61)
	starting dose, mg/week	10 (7,5-10)
	Combined therapy	5 (8)

Elderly patients (EORA and VEORA), compared with YORA, presented with higher frequency hypertension and CV disease, higher elevation in acute phase reactants at the onset and disease activity at diagnosis. VEORA patients, compared to EORA, showed a higher frequency of dyslipidemia (p = 0.04). There were also no significant differences between VEORA and EORA in the distribution and type of joints affected, time to diagnosis, acute phase reactants or disease activity at the onset. A higher frequency of special forms (such as PMR or RS3PE) was close to statistical significance in the VEORA group (p = 0.054).

Regarding initial treatment, both EORA and VEORA received steroidal treatment more frequently and a lower dose of Methotrexate during the first year. Biological treatments was also significantly higher in YORA (p=0,000). When comparing VEORA and EORA, differences related to the use of NSAIDs were found, lower in VEORA (p = 0.000), as well as in the maximum dose of Methotrexate reached in the next 12 months, higher in the EORA group (p = 0.01). No differences in adverse events with DMARDs were observed.

DAS28-ESR and the number of patients in remission or low activity at one year showed no differences between EORA and VEORA, or between these groups and that of younger patients.

Conclusion: There have been few differences in the comorbidity profile and clinical characteristics at the onset between VEORA and EORA patients. Despite the differences observed in its management (more conservative in EORA and VEORA vs YORA, and in VEORA vs EORA), we have not observed differences in DAS28-ESR activity after one year.

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THU0137 ASSESSING THE MULTIMORBID PROFILE (CIRS) IN RHEUMATOID ARTHRITIS. FIRST RESULTS.

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Background:

Objectives: To assess the presence and nature of multimorbidity in patients with rheumatoid arthritis (RA) and the impact of multimorbidity on disease activity.

Methods: The investigation enrolled 117 patients (mean age, 54.8±14.8 years) with RA according to the 2010 ACR/EULAR criteria, who had been examined and treated at the V.A. Nasonova Research Institute of Rheumatology in 2018–2019. The median disease duration was 5.0 [1.5; 9.5] years; the mean DAS28 score was 5.0±1.3. Documentation and anamnesis data were analyzed with emphasis on associated diseases. The Cumulative Illness Rating Scale (CIRS) was used to assess the profile of multimorbidity.

Results: The patients with RA had a high index of the spectrum of multimorbidity; concomitant diseases were detected in 96 (82%) cases.

The median number of diseases in one patient was 2 [1; 4], the mean total CIRS score was 6.7±3.3; the median value was 2.5 [1; 6]. The number of concomitant diseases diagnosed before using the CIRS was significantly lower (by 48%; p<0.01) than was found in the investigation conducted.

Chronic kidney disease that occurred in almost half (42.5%) of cases was most commonly undiagnosed in the cohort under study; on average, every three patients were not found to have signs of metabolic syndrome (hyperglycemia in 29%, hypercholesterolemia in 20%, obesity in 13.5%), chronic hypoxia (new-onset anemia verified in 24% of cases). In 12% of cases lung damages were not found before using the CIRS. There was a correlation of the quantitative equivalent of multimorbidity with the clinical and laboratory measures of RA activity, including the number of painful joints (r = 0.39; p<0.001), overall patient assessment (r=0.37; p=0.03), physician's global assessment of disease activity (r = 0.37; p < 0.01), DAS28 (r = 0.42; p<0.001), CDAI (r=0.37; p<0.001), SDAI (r=0.34; p< 0.001), HAQ (r=0.34; p<0.001). The total CIRS score did not differ in patients with early- and advanced- or end-stage RA: 6.6±3.5 and 6.7±3.3, respectively (p=0.9).

Conclusion: A systematic screening of multimorbidity should be carried out in all patients with RA. It is advisable to use the CIRS to estimate the prevalence of multimorbidity, its consequences and the risk factors for the development of multimorbidity in the long term.

Disclosure of Interests: None declared

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THU0138 AGEING IN RA PATIENTS DETERIORATED MODIFIED HEALTH ASSESSMENT QUESTIONNAIRE (MHAQ) OVER A 7-YEAR PERIOD INDEPENDENTLY FROM DISEASE ACTIVITY.

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Background: Recent advances of treatment for rheumatoid arthritis (RA) realizes us to set the treatment goal as remission. As the results, health assessment questionnaire (HAQ) has been also becoming better in these years. On the other hand, progress in ageing has been a major issue in Japan, including the patients with RA. which is thought as one of the factors affecting HAQ.

Objectives: To evaluate the impact of ageing on HAQ in RA patients.

Methods: The data of 208 RA patients used in this study was collected over a 7-year period from 2010 to 2017 as part of a prospective cohort study (TOMORROW Study: UMIN000003876) that included RA patients and age- and sex-matched volunteers recruited through mass media as controls. The data of RA patients included anthropometric, blood test data, disease activity score28-CRP (DAS28) and modified HAQ (mHAQ), together with baseline (BL) characteristics. The course of mHAQ for 7 years were analyzed by repeated measure ANOVA, and association between the changes of mHAQ at year-7 from BL (ΔmHAQ) and BL factors were analyzed by multiple regression analysis.

Results: Two hundred and eight RA patients (153 women; mean age 58.1 years) were enrolled in the present study. Modified HAQ decreased significantly over the 7-year study period in RA patients. When the patients were stratified into 3 groups (lower than 2.7, between 2.7 and 4.1, over 4.1) by DAS28 at BL, mHAQ of the patients with high disease activity (DAS28: over 4.1) at BL was significantly worse than other groups (p=0.018; repeated measure ANOVA). There was no interaction between time and 3 groups (p=0.118; repeated measure ANOVA). Multiple regression analysis with ΔmHAQ as the outcome variable and ACPA, age, BMI, CRP, DAS28, MMP-3 at BL as independent variables revealed that age (p=0.034) and DAS28 (p=0.042) were independently related with ΔmHAQ.

Conclusion: Ageing in RA patients impacted worsening of mHAQ over a 7-year period independently from disease activity. On assessing mHAQ in elderly RA patients, we must consider the age as well as the disease activity.

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THU0139 STATINS MODERATE THE EFFECT OF INFLAMMATION ON CORONARY PLAQUE PROGRESSION AND CARDIOVASCULAR DISEASE RISK IN RHEUMATOID ARTHRITIS

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Background: Cumulative inflammation correlates with coronary plaque increase and cardiovascular disease (CVD) events in rheumatoid arthritis (RA). Coronary plaque progression predicts CVD risk beyond baseline burden in general patients. Statins inhibit plaque progression and are effective for CVD prevention in general patients. Nevertheless, their impact on coronary plaque trajectory and CVD risk in RA are less clear.

Objectives: To explore if statin treatment may reduce CVD event risk, inhibit new plaque formation or promote the regression or protective calcification of prevalent atherosclerotic lesions in RA. We also evaluated whether statins moderate the effects of inflammation (CRP) on CVD risk and on coronary plaque progression.

Methods: One hundred-fifty patients underwent computed tomography angiography for coronary atherosclerosis evaluation (total, non-calcified, mixed/calcified plaque); 101 had repeat assessments within 6.9±0.3 years to evaluate plaque progression. CVD events were prospectively recorded, including cardiac death, myocardial infarction, unstable angina, revascularization, stroke, claudication, and heart failure hospitalization. Framingham-D'Agostino score assessed clinical risk. Plaque burden was measured as segment stenosis score (cumulative stenosis). Robust cox proportional hazards regression models evaluated the effects of time-varying statin use, log-transformed time-varying CRP (mg/dL) and their interaction on CVD risk controlling for Framingham-D'Agostino score, plaque burden and time-varying bDMARD use. Per-segment robust logistic regression assessed the effect of statin duration (years), log-transformed time-averaged CRP, and their interaction on likelihood of plaque formation in segments without plaque, and plaque regression or calcification in segments with non-calcified lesions. Models accounted for clustering of coronary segments within patients and controlled for Framingham-D'Agostino score, total prednisone dose, bDMARD duration, and time between scans.

Results: Sixteen patients incurred 19 CVD events. There was no main effect of current statin use on CVD risk (adjusted HR 1.10, 95% CI 0.33-3.67). However, there was an interaction between current statin use and time-varying CRP (p-interaction=0.030); higher time-varying CRP predicted greater CVD risk in patients not receiving statins (adjusted HR 2.78, 95% CI 1.01-7.65), but not current statin users (Figure 1A). Likewise, current statin use associated with lower CVD risk when patients had higher time-varying CRP (>0.5 mg/dL) but not when CRP was lower (<0.5 mg/dL, Figure 1B). Statin duration had no main effect on new plaque formation in segments without plaque at baseline (adjusted OR 1.13, 95% CI 0.95-1.05); however, statin use moderated the effect of time-averaged CRP on new plaque formation (p-interaction=0.030, Figure 2A). Time-averaged CRP associated with a higher likelihood of new plaque in patients receiving statins less than one year (adjusted OR 1.75, 95% CI 1.38-2.20) but not those treated for longer (adjusted OR 1.26, 95% CI 0.78-2.02). In segments with non-calcified plaque, longer statin duration predicted protective calcification (adjusted OR 1.28, 95% CI 1.07-1.53, Figure 2B).

Conclusion: In RA, statins moderated the effect of CRP on CVD event risk and new plaque formation in coronary segments without plaque. Longer statin duration was also associated with an increased likelihood of protective calcification of non-calcified plaque.

Figure 1. Time-varying cox proportional hazard models of the effect of **(A)** CRP stratified by statin use and **(B)** statin use stratified by CRP

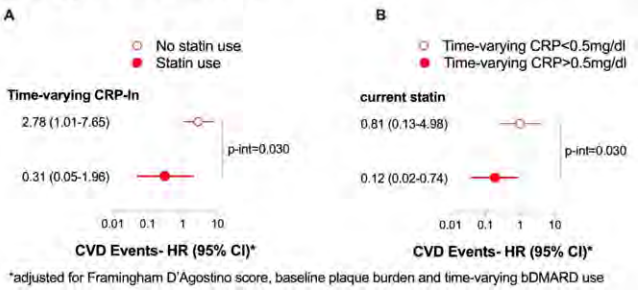
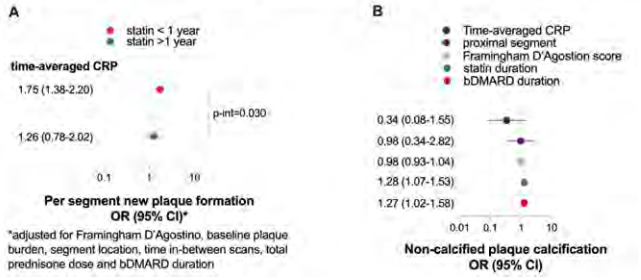


Figure 2. (A) statin duration moderates the effect of inflammation on new coronary plaque formation **(B)** Statins promote calcification of prevalent non-calcified lesions



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THU0140 COMORBIDITIES AMONG KOREAN WOMEN WITH RHEUMATOID ARTHRITIS IN CHILDBEARING YEARS: A NATIONWIDE POPULATION-BASED STUDY

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Background: Rheumatoid arthritis is a chronic systemic inflammatory disease known to be associated with many comorbidities. Many women with rheumatoid arthritis (RA) are diagnosed with the disease before completing childbearing, but the risk of comorbidities associated with RA among women in childbearing years is not known.

Objectives: We aimed to investigate the risk of comorbidities among Korean women with RA in childbearing years.

Methods: From National Health Insurance Service data of 2009-2016, containing inpatient and outpatient claim information for approximately 97% of the Korean population, we identified 20-44 year aged-women with RA and controls without rheumatic diseases such as RA, systemic lupus erythematosus, and ankylosing spondylitis. Prevalence of comorbidities including cancer (Ca), hypertension (HTN), hyperlipidemia (HLD), and diabetes mellitus (DM) were analyzed. The rheumatic diseases and comorbidities were defined by International Classification of Disease (ICD)-10 codes for disease classifications. The comorbidities associated with RA were defined by the ICD-10 codes presented after the RA diagnosis.

Results: Total 23,756 women with RA and 208,941 controls were identified. Women with RA had significantly higher prevalence of all comorbidities analyzed compared with the controls (49.92% vs 25.58%, p<0.001). In women with RA, Ca (OR 1.14), DM (OR 1.22), HTN (OR 1.56), and HLD (OR 2.44) occurred significantly more often compared with the controls (p<0.001).

Conclusion: During childbearing years, women with RA are more susceptible to comorbidities leading to a significant burden in this specific population of Korean women in childbearing years.

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Table 1. Risk of comorbidities associated with RA among Korean women in childbearing years during 2009-2016

	RA (n=23,756)		Controls (n=208,941)				
	n	(%)	n	(%)	p-value	OR	95% CI
Any comorbidities	10,859	(45.71)	53,423	(25.57)	<.0001	2.30	2.234-2.367
Ca	1,235	(5.20)	8,845	(4.23)	<.0001	1.14	1.072-1.217
DM	1,885	(7.93)	12,606	(6.03)	<.0001	1.22	1.155-1.285
HTN	3,274	(13.78)	17,052	(8.16)	<.0001	1.56	1.495-1.628
HLD	8,046	(33.87)	34,672	(16.60)	<.0001	2.44	2.367-2.516

RA, rheumatoid arthritis; Ca, cancer; DM, diabetes mellitus; HTN, hypertension; HLD, hyperlipidemia; OR, odds ratio; CI, confidence interval

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THU0141 A META-ANALYSIS FOR THE PREVALENCE AND RISK FACTORS OF SARCOPENIA IN RHEUMATOID ARTHRITIS

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Background: Sarcopenia is an essential issue in elderly or chronically ill subjects, and a recent surge of research on sarcopenia in patients with rheumatoid arthritis (RA) has emerged; however, the results remains controversial.
Objectives: To assess the prevalence and risk factors of sarcopenia in patients with RA.
Methods: We searched the studies investigating the prevalence and risk factors of sarcopenia in PubMed, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), AiritiLibrary, Chinese Electronic Periodicals Service (CEPS) and China National Knowledge Infrastructure (CNKI) Database from inception to October 5, 2019. Effects regarding prevalence and the associated risk factors were extracted and evaluated by random-effect model. Sensitivity analysis was performed for the effects.
Results: After searching, twenty studies containing 3,663 RA subjects were identified, and the pooled prevalence was 35%, among which the prevalence in male and female were 39.8% and 33.3% respectively. Twelve studies reported various risk factors, and therein which had been mentioned in more than two studies were included for meta-analysis, yielding age (odds ratio [OR] 1.168, 95% confidence interval [CI] 1.032-1.322, P =0.014), female (OR 4.438, 95% CI 1.857-10.605, P < 0.001), CRP (OR 1.797, 95% CI 1.422-2.272, P < 0.001), HAQ (OR 1.756, 95% CI 1.235-2.496, P=0.002) and RF seropositivity (OR 1.935, 95% CI 1.335-2.804, P < 0.001) were significantly associated with sarcopenia in subjects with RA. There was no alteration of the results after removal any of studies in sensitivity analysis.
Conclusion: Our meta-analysis demonstrated the prevalence and associated risk factors of sarcopenia in RA. More research was still warranted to clarify the relationship.
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THU0142 CHARACTERISTICS OF OSTEOPOROTICAL WOMEN IN A COHORT OF PATIENTS WITH RHEUMATOID ARTHRITIS.

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Background: The estimated prevalece of osteporosis in lumbar spine in women over 50 years is around 22.8% of the general population. In women with rheumatoid arthritis (RA), osteoporosis (OP) is more prevalent and begins at earlier ages.
Objectives: The aim of this study is to assess the effect of different risk factors in the development of OP in women with RA.
Methods: This is an observational study in women diagnosed of RA according ACR criteria 1987 and 2010, in order to know the influence of different clinical features in the development of OP. Between 2013 and 2109 we offer all women diagnosed of RA to participate in the study and perform an BMD (GE Lunar Prodigy®). SPSS25 was used for statistical analysis.
Results: We enrolled 295 women with RA. Mean age 62,4 (± 11,6) years old and average duration of the disease of 118,3 (±98,8) months. Table 1 shows the clinical features of the studied population. BMD was normal in 66 woman (22,4%), therefore 229 (77,6%) y 85 (28,8%) had BMD values less than -1 y -2.5, respectively in femoral neck and/or lumbar spine. Major risk fracture and hip risk fracture (FRAX DMO) was hight in 49,2 y 40,2% of the RA patients, of which almost 15% had a fracture [OR 7,6 (3,1-18,9) p<0,001], mainly women over 50 years old. We found osteoporosis in 85 women, with was associated, in bivariant analysis, at lower heigh, weight, BMI and older age. We didn't find association with RF, ACPA, smoking, vitamin D deficiency or biological therapy. Corticosteroids were associated with BMD <1 [OR 2.1 (1.2-3.6)] (p = 0.009)], as well as an increased risk of major and hip fracture [OR 4.9 (2, 6-9.4)] (p <0.001)]. Women with a previous fracture were eight times more likely to have a major fracture [OR 7.6 (3.1-18.9) p <0.001] and seven times more than a hip fracture [OR 6.9 (3.1- 15.2) p <0.001] than those without prior fracture. In the adjusted analysis, the OP (femoral neck and/or lumbar spine) was associated with lower weight and age along with the OP emory neck also with the RF level. However, the fracture was mainly related to BMI and OP femoral neck.

Table 1.

Clinical features	
Age RA, years (SD)	52,54 (13,21)
Height, cm (SD)	153,72 (7,54)
Weight, kg (SD)	70,04 (14,39)
Smokers, n (%)	33 (11,3)
OH-vit D2 <10pg/ml, n (%)	21 (7,8)
RF +, n (%)	219 (76,6)
ACPA +, n (%)	187 (65,4%)
Corticosteroids, n (%)	191 (64,7%)
Biologics treatment, n (%)	75 (25,4%)
MBD normal	66 (22,4%)
MBD lumbar spine CL <-1, n (%)	175 (59,3%)
MBD femoral neck <-1, n (%)	192 (65,8%)
MBD lumbar spine <-2,5, n (%)	60 (20,5%)
MBD femoral neck <-2,5, n (%)	55 (18,8%)
Fractures, n (%)	43 (14,7%)
Major risk fracture (FRAX), n (%)	125 (49,2%)
Femoral head risk fracture (FRAX), n (%)	102 (40,2%)

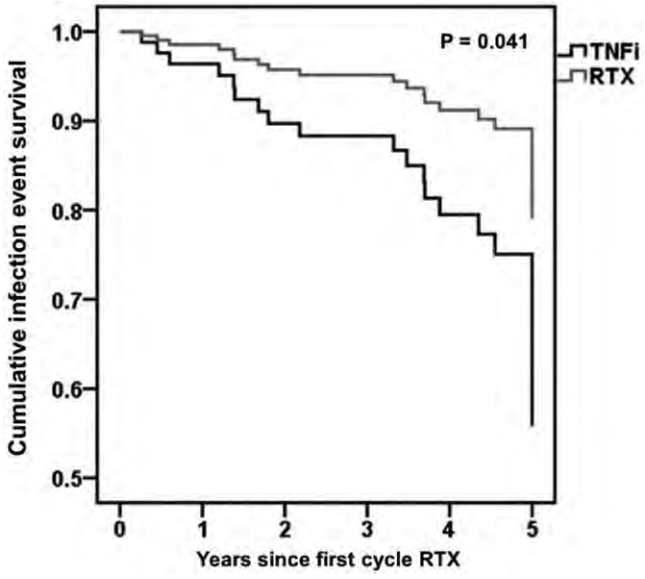
Conclusion: OP and fragility fractures occur earlier and higher in women with RA. BD T-score in femoral neck seems to be the best predictor of fracture.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.3293

THU0143 EFFECT OF RITUXIMAB OR TUMOUR NECROSIS FACTOR INHIBITORS ON LUNG INFECTION AND 5-YEAR SURVIVAL IN RHEUMATOID ARTHRITIS-ASSOCIATED BRONCHIECTASIS

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Background: Bronchiectasis (BR) is a significant pulmonary morbidity common in people with rheumatoid arthritis (RA). Patients with RA and bronchiectasis (RA-BR) often have severe arthritis but the use of biologics may be difficult in this group of patient due to concerns over safety. There is no data comparing the use of rituximab (RTX) and tumour necrosis factor inhibitors (TNFi) in RA-BR.
Objectives: To evaluate the effect of RTX in patients with RA-BR and compare 5-year respiratory survival between those treated with RTX and TNFi.
Methods: A retrospective observational cohort study of RA-BR was conducted in RTX or TNFi-treated RA patients from two UK centres over 10 years. BR was assessed using number of infective exacerbations/year. Respiratory survival was defined as time from therapy initiation to discontinuation either due to lung exacerbation or lung-related deaths.
Results: Of 800 RTX-treated RA patients, 68 had RA-BR (prevalence 8.5%). Post-RTX, new BR was diagnosed in 3/735 patients (incidence 0.4%). At 12 months post-Cycle 1 RTX, 21/68 (31%) patients had fewer exacerbations than the year pre-RTX, 36/68 (53%) remained stable and 11/68 (16%) had increased exacerbations. In multivariable analysis, a factor associated with increased risk of this initial exacerbation was pseudomonas colonisation [OR 7.23 (95% CI 1.28-40.80)] while older age reduced risk [OR 0.44 (95% CI 0.21-0.90) per 10 years of age]. The rates of exacerbation improved after Cycle 2 RTX and stabilised up to 5 cycles. Of patients who received ≥2 RTX cycles (n=60), increased exacerbations occurred in 7/60 (12%) and were associated with low IgG, aspergillosis and concurrent alpha-1-antitrypsin deficiency. Respiratory survival was compared between RA-BR patients treated with RTX (N=68) or TNFi (N=46). Most characteristics were matched but median (IQR) number of infective exacerbations/year in the previous 12 months pre-bDMARDs was higher in those treated with RTX than TNFi; 3.0 (1-4) and 0 (0-2) respectively. Overall, 8/68 (11.8%) patients discontinued RTX while 15/46 (32.6%) discontinued TNFi due to respiratory causes. The adjusted 5-year respiratory survival was better in RTX-treated compared to TNFi-treated RA-BR patients; HR 0.40 (95% CI 0.17–0.96); p=0.041.
Conclusion: The majority RA-BR patients had stable or improved pulmonary symptoms during RTX therapy over a prolonged follow-up period. In isolated cases, worsening of exacerbation after RTX therapy had definable causes. Despite a higher rate of exacerbations pre-biologic, rates of discontinuation due to adverse lung outcomes were better for RTX than a matched TNFi cohort. RTX appears to be an acceptable therapeutic choice for RA-BR if a biologic is needed.



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THU0144 DESCRIPTIVE ANALYSIS OF PREGNANCY, DELIVERY, AND LACTATION IN PATIENTS WITH RHEUMATOID ARTHRITIS FROM THE IORRA COHORT.

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Background: Rheumatoid Arthritis (RA) is common in women with reproductive age. For this reason, RA treatment during pregnancy and lactation is very important. In recent years, the use of biologic disease-modifying antirheumatic drugs (bDMARDs) has become common in RA treatment (1), treatment during pregnancy and lactation has changed drastically (2,3).
Objectives: To investigate the pregnancy, delivery and lactation status of RA patients and treatment during that period in daily practice.
Methods: The IORRA cohort is a large, single institute-based, observational cohort of RA patients established at Institute of Rheumatology, Tokyo Women's Medical University, in 2000. We identified female RA patients aged 20-49 years who answered 'pregnant' or 'delivered' in the IORRA survey in 2010-2016 and whose pregnancies were confirmed in the medical records. We examined the Disease Activity Score with 28 joint count (DAS28)-CRP, medication use situation, the outcome of pregnancy, and lactation in those patients.
Results: A total of 101 patients and 143 pregnancies were confirmed, of which 136 outcomes of pregnancy could be confirmed in the medical records. Among 136 confirmed pregnancy cases, there were 106 births and 30 miscarriages. Among 106 births, 4 cases (3.8%) were birth defects that could be confirmed in the medical records. The average age at pregnancy was 34.2±3.7 years and 36.1±3.3 years in delivered and miscarried cases, respectively. Miscarried cases were significantly older pregnancies (p=0.01). Of the 106 births, 65 birth weeks were confirmed, with an average of 37.9±1.8 weeks. The number of preterm delivery was 11 cases (16.9%). The average birth weight of 59 babies whose birth weight could be confirmed was 2699±517 g. There were 21 cases (35.6%) of low birth weight infants. The proportion of patients in DAS28-CRP remission was 73.1% before pregnancy, 61.6% during pregnancy, and 68.0% 1 year after delivery. Drugs used before pregnancy were glucocorticoid (48.8%), non-steroidal anti-inflammatory drugs (14.2%), conventional synthetic DMARDs (24.8%), and bDMARDs (48.0%). Etanercept accounted for 90% of bDMARDs. Among taking bDMARDs patients, 73.8% were discontinued after the pregnancy, and 26.2% were continued during pregnancy. Among those patients who continued bDMARDs, lactating patients were 12/26 (46.2%) cases after delivery, 10/30 (33.3%) cases in six months after delivery, and 7/36 (19.4%) cases in 1 year after delivery, respectively.
Conclusion: The actual situation of pregnancy, delivery, and lactation in RA patients was revealed. Especially, bDMARDs were used at relatively high rates in RA patients who wish to have a child.
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Disclosure of Interests: Moeko Ochiai: None declared, Eiichi Tanaka Consultant of: ET has received lecture fees or consulting fees from Abbvie, Asahi Kasei pharma co., Bristol Myers Squibb, Chugai Pharmaceutical, Daiichi Sankyo Co., Eisai Pharmaceutical, Janssen Pharmaceutical K.K., Nippon Kayaku, Pfizer, Takeda Pharmaceutical, Taisho Toyama Pharmaceutical Co., and UCB Pharma., Speakers bureau: ET has received lecture fees or consulting fees from Abbvie, Asahi Kasei pharma co., Bristol Myers Squibb, Chugai Pharmaceutical, Daiichi Sankyo Co., Eisai Pharmaceutical, Janssen Pharmaceutical K.K., Nippon Kayaku, Pfizer, Takeda Pharmaceutical, Taisho Toyama Pharmaceutical Co., and UCB Pharma., Eisuke Inoue Speakers bureau: EI has

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THU0145 INDICATIONS AND INCIDENCE OF TREATMENT WITH ANTIDEPRESSANTS IN PATIENTS WITH RHEUMATOID ARTHRITIS AND MATCHED CONTROLS

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Background: The incidence of depression is about 1.5-2 times higher in patients with rheumatoid arthritis (RA) versus controls. (1, 2) Previous data on treatment with antidepressants has pointed to an almost equal distribution of indications between depression and other indications. (3)

Objectives: To describe and compare indications and the incidence of treatment with antidepressants in patients with RA and matched controls.

Methods: The study involved an inception cohort of patients with incident RA ascertained from 1995 to 2002 according to the American College of Rheumatology 1987 classification criteria (4) and randomly drawn, population controls with the same age, sex, and area of residence (ratio 1:5). Indications on redeemed prescriptions were included in the Danish National Prescription Register from 2004 and we collected data on all prescriptions for antidepressants (Anatomical Therapeutic Classification code N06A) and counted person-years (PY) at risk from 01.01.2004 to 31.12.2017, death, or migration. The incidence of first treatment was evaluated as defined daily dose (DDD) for two definitions of exposure (DDD>0, DDD>178) within one calendar year together with the positive indication depression after one year of run-in.

Results: The current analyses involved 431 RA patients and 2167 controls (median age at inclusion: 59 years, 70% females; RA patients: 20% erosive, 74% rheumatoid factor positive). The most frequent indication for treatment with antidepressants was depression (Table 1).

Table 1. Indication on prescriptions for antidepressants, % (95% confidence interval (CI))

	Rheumatoid arthritis (n=6,955)	Controls (n=33,740)
Depressive disorders	62.3 (61.2-63.5)	62.7 (62.2-63.2)
Anxiety disorders	5.4 (4.9-6.0)	3.9 (3.7-4.1)
Nervous system medications	6.5 (5.9-7.1)	6.8 (6.6-7.1)
Other indications	0.2 (0.0-0.3)	0.2 (0.2-0.2)
No or missing indications	25.6 (24.6-26.7)	26.3 (25.9-26.8)

There were no significant differences in the incidence of treatment with the indication depression in patients versus controls **(Table 2)**.

Table 2. Incidence rate ratio for treatment with antidepressants

	DDD>0			DDD>178		
	Rheumatoid arthritis (Events/PY)	Controls (Events/PY)	Incidence rate ratio (95% CI)	Rheumatoid arthritis (Events/PY)	Controls (Events/PY)	Incidence rate ratio (95% CI)
Overall	98/3,720	471/19,229	1.08 (0.86-1.34)	73/3,893	339/20,338	1.13 (0.87-1.46)
Sex						
Females	79/2,616	354/13,460	1.15 (0.89-1.47)	61/2,753	264/14,299	1.20 (0.89-1.59)
Males	19/1,104	117/5,769	0.85 (0.49-1.39)	12/1,141	75/6,039	0.85 (0.42-1.57)
Age						
15-34	5/175	24/962	1.15 (0.34-3.07)	4/188	21/1,022	1.04 (0.26-3.07)
35-44	3/522	31/2,349	0.44 (0.85-1.40)	3/524	20/2,501	0.72 (0.14-2.42)
45-54	14/731	64/3,871	1.16 (0.60-2.09)	10/773	40/4,122	1.33 (0.59-2.71)
55-64	25/1,198	128/6,200	1.01 (0.63-1.56)	17/1,253	84/6,498	1.05 (0.58-1.78)
65-74	37/849	158/4,598	1.27 (0.86-1.82)	28/892	120/4,874	1.28 (0.81-1.94)
75+	14/246	66/1,248	1.08 (0.56-1.94)	11/265	54/1,321	1.02 (0.48-1.97)

Conclusion: The main indication for prescribing antidepressants in patients with RA was depression. Patients with RA were not exposed to antidepressants more often than controls. This could be due to prescription bias or reflect pertinent choice of treatment in patients with RA.

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THU0146 DAS28-REMISSION IS ASSOCIATED WITH AN INCREASE OF FINGER JOINT SPACE WIDTH IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The reduction of finger joint space width in patients with rheumatoid arthritis (RA) is associated with joint destruction. Anti-TNF treatment with certolizumab pegol is an effective therapy in RA-patients. The computer-assisted joint space analysis is a new computer based technique to measure joint space width on hand radiographs.

Objectives: The aim of this post-hoc analysis of the data set used in the RAPID 1 trial was to quantify finger joint space width of RA patients treated with Certolizumab pegol in Association to DAS28-remission.

Methods: The post-hoc analysis includes 297 patients. These patients were treated with certolizumab pegol 200 mg (every two weeks) plus methotrexate and certolizumab pegol 400 mg (every two weeks) plus methotrexate. All patients underwent x-rays of the hand at baseline and week 52 as well as the quantification

of finger joint space width of the metacarpal-phalangeal articulations (MCP) using the computer-assisted joint space analysis (Version 1.3.6; Sectra; Sweden). The joint space distance is expressed as mean joint space width of the MCP joints I to V (JSD-MCP total). Remission was defined with a Disease Activity Score 28 < 2.6.
Results: The group with DAS28-remission (DAS28 < 2.6) presented a significant joint space increase with 3.3 % for JSD-MCP total from 0.152 ± 0.033 cm (baseline) to 0.157 ± 0.033 cm (week 52) treated with certolizumab pegol 200 mg as well as with 3.9 % for JSD-MCP total from 0.152 ± 0.031 cm (baseline) to 0.158 ± 0.032 cm (week 52). For the patients without DAS28-remission (DAS28 > 2.6) under the treatment with certolizumab pegol 400 mg a non-significant change of JSD-MCP total from 0.145 ± 0.034 cm (baseline) to 0.144 ± 0.036 cm (week 52) was observed. A similar result was evaluated for the certolizumab pegol 200 mg group (JSD-MCP total: 0.146 ± 0.037 cm [baseline] to 0.143 ± 0.037 cm [week 52]).
Conclusion: The study highlights that patients treated with certolizumab pegol plus methotrexat and a DAS-Remission showed an increase of joint space width of the metacarpal-phalangeal articulations which is potentially associated with reparative effects of the cartilage under the anti-TNF treatment with certolizumab pegol.
References: N/A
Disclosure of Interests: Alexander Pfeil Grant/research support from: This study Investigator Initiated Study "Automatic assessment of joint space narrowing in rheumatoid arthritis based on the Post-hoc analysis" (number: IIS-2016-110818) is a part of the of the Investigator Initiated Study "The quantification of inflammatory related periarticular bone loss in certolizumab pegol treated patients with rheumatoid arthritis" (number: IIS-2014-101458) which is supported by UCB Pharma GmbH, Monheim, Germany., Anica Nussbaum: None declared, Diane Renz: None declared, Ansgar Malich: None declared, Joachim Böttcher: None declared, Peter Oelzner: None declared, Gunter Wolf: None declared
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THU0147 CARDIOVASCULAR RISK IN RHEUMATOID ARTHRITIS: DO WE ALREADY HAVE A SENSITIVE AND SPECIFIC INSTRUMENT?

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Background: Rheumatoid Arthritis (RA) is a chronic systemic inflammatory disorder with high cardiovascular (CV) risk due to both classic and specific disease risk factors. According to EULAR's recommendations, all patients should carry out an assessment of their CV risk, however, there are no specific evaluation algorithm's for RA.
Objectives: To assess the efficacy to predict CV risk in RA patients using the Systematic Coronary Risk Evaluation model (SCORE), Modified SCORE (mSCORE), Framingham Risk Score (FRS), Modified Framingham Risk Score (mFRS) and the American College of Cardiology/American Heart Association algorithm (ACC/AHA).
Methods: Cross-sectional observational study including patients fulfilling 2010 ACR/EULAR classification criteria for RA and followed in the Rheumatology Department at Guarda Local Health Unit. Clinical records were reviewed and sociodemographic, classic CV risk factors and disease related factors, previous history of CV events and current treatment were collected. Individual CV risk was calculated using aforementioned models. Patients were divided in two groups: group 1 (without CV event history) and group 2 (with a history of CV event). Discriminative capacity tests, sensitivity and specificity were asserted and the different models were compared.
Results: A total of 107 patients were included in the study and 10 suffered a CV event. Of 107 patients, 78% are women, the average age is 55.97± 6,78 and the average body mass index is 26,44± 4,43 kg/m^2 (Table 1). Models evaluated revealed reasonable discriminative capacity with areas under the curve between 0.73 and 0.88 (Figure 1). Regarding sensitivity and specificity we found that SCORE calculator fail to identified high risk in all patients with a CV event, however it presented a specificity of 94%. Others CV risk calculators showed the following sensitivities and specificities: mSCORE 63%, 88%; ACC/AHA 88%, 84%; FRS 63%, 88%; mFRS 88%, 76%.

Table 1. Patient characteristics

	Patients with RA (N=107)	*Patients with RA without CVD*	*Patients with RA with CVD (N=10)*	*p*
Age (years), mean±SD	56 ± 6,8	55,7 ± 6,9	58,5±5,6	0,240
Female, n(%)	83 (77,6)	79 (81,4)	4 (40)	0,003
Rheumatoid factor positivity, n(%)	36 (37,5)	33 (37,9)	3 (33,3)	0,787
Anti-CCP positivity, n (%)	34 (37)	29 (34,9)	5 (55,6)	0,226
Smoking, n (%)	4 (3,7)	3 (4,1)	1 (10)	0,031
BMI (weight(Kg)/height(m)2), mean±SD	26,4±4,4	26,2±4,4	29,7±4,1	0,040
Treatment with statins (%)	34	28	90	<0,001

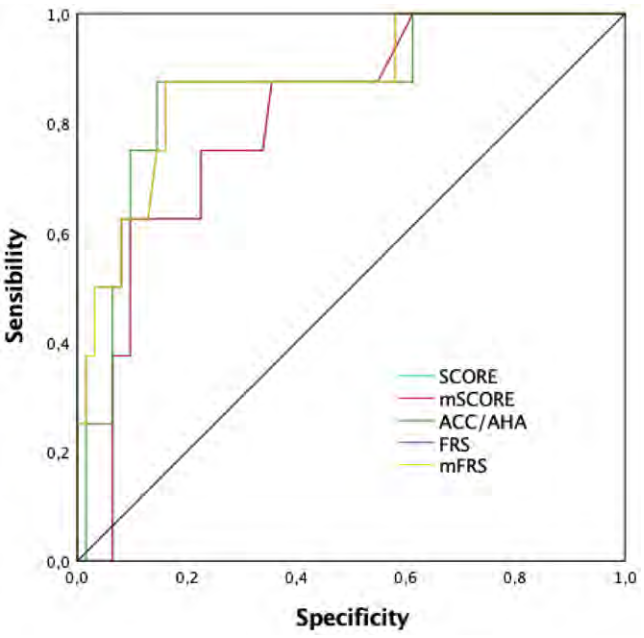


Figure 1. Receiver operating characteristic curves of the different risk prediction algorithms

Conclusion: The five models tested in this study have a relative discriminative capacity. SCORE did not identify any CV event, which may compromise its ability to assess the CV risk in this patients.
The most sensitive and specific model was the ACC/AHA, a very restricted model. When applying the multiplication factor of 1.5 recommended by EULAR, there is an improvement in sensitivity, however the specificity decreases.
This study proves the limitations of CV risk calculators designed for the general population when applied to patients with RA. In conclusion, CV risk assessment is extremely important and there is still no ideal calculator, which is both sensitive and specific, and easily applicable in a clinical context.
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THU0148 EFFICACY OF IL-1 INHIBITION ON RHEUMATOID ARTHRITIS AND TYPE 2 DIABETES, LONG-TERM FINDINGS FROM TRACK STUDY, A MULTICENTRE, OPEN-LABEL, RANDOMISED CONTROLLED TRIAL

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Background: The inflammatory contribution to type 2 diabetes (T2D) has suggested new therapeutic targets by using biologic DMARDs designed for rheumatoid arthritis (RA), and IL-1 would be a common pathogenic mediator, suggesting a possible common therapeutic target [1]. In TRACK study, a multicentre open-label, randomised controlled trial, anakinra, a human interleukin-1-receptor antagonist, showed to induce a significant improvement of metabolic alteration whereas TNFi did not show any significant improvement on that, after both 3 months and 6 months of therapy (crude difference of 0.93 of glycated haemoglobin, HbA1c% between groups) [2]. Concerning RA, a progressive reduction of disease activity was observed in both groups [2].
Objectives: Since TRACK study has been prematurely stopped for "early benefit" after 6 months of follow-up, in this work, we aimed at investigating how long lasted the improvement of HbA1c% and of RA disease activity, considering the original scheduled 24 months follow-up. We also assessed the rate of antidiabetic and anti-rheumatic therapies reduction and stoppage.
Methods: This study was designed as a multicentre, open-label, randomised controlled trial, enrolled participants, with RA and T2D, in 12 Italian Rheumatologic Units, between 2013 to 2016. Participants were randomised to anakinra or to a TNFi and the primary endpoint was the change in HbA1c% (EudraCT:

2012-005370-62; ClinicalTrial.gov: NCT02236481). In this further evaluation, we assessed how long lasted the improvement of HbA1c% and of RA disease activity, considering the original scheduled 24 months follow-up, and the rate of antidiabetic and anti-rheumatic drugs, mainly focusing on steroids, reduction and stoppage.

Results: In TRACK study, 39 participants with RA and T2D (age 62.72 ± 9.97, 74.4% female gender) were randomised to anakinra or to TNFi; the majority of participants had seropositive RA disease (rheumatoid factor and/or ACPA 70.2%) with active disease (DAS28: 5.54 ± 1.03; C-reactive protein 11.84 ±9.67 mg/L, respectively) and all participants had T2D (HbA1c%: 7.77 ±0.70, fasting plasma glucose: 139.13 ±42.17 mg). Considering the last available observation, a maintenance of reduced levels of HbA1c% was observed in anakinra-treated participants (Baseline: 7.73% ±0.67; 6 months: 6.70% ±0.67; last follow-up: 6.60% ±0.52). Paralleling with HbA1c%, a significant reduction of dosages of antidiabetic therapies was observed in anakinra-treated patients, with a percentage of patients who discontinued any anti-diabetic therapy. Conversely, an intensification of antidiabetic therapies was reported in TNFi-treated participants. Concerning RA, the clinical response was maintained during the whole follow-up, although a larger percentage of anakinra-treated participants discontinued the concomitant steroids therapy.

Conclusion: In this study, we observed the benefit of IL-1 inhibition in patients with RA and T2D, reaching the therapeutic targets of both diseases, which lasted longer than first 6 months of follow-up. Although the limitations due to open-label design and the necessity of further confirmatory studies, our results could suggest the concept that IL-1 inhibition may be considered a targeted therapeutic strategy for RA and T2D.

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THU0149 JAK KINASE INHIBITORS AND VARICELLA ZOSTER VIRUS INFECTION IN PATIENTS WITH RHEUMATOID ARTHRITIS. SYSTEMATIC REVIEW OF THE LITERATURE.

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Background:

Objectives: Objetive: To assess the incidence of Herpes Zoster (HZ) infection in patients with Rheumatoid Arthritis (RA) treated with JAKi.

Methods: Method: We conducted a systematic literature review searching in Medline, Embase and Cochrane. The final date was set on December 31, 2019, and only articles in English were included. See the following terms: rheumatoid arthritis, herpes zoster and the different JAK kinase inhibitors studied: tofacitinib, baricitinib, upadacitinib, filgotinib, peficitinib and decernotinib.

Conference abstract, case series and clinical practice records were excluded. Only phase II and phase III clinical trials were included, as well as extension studies, with the following criteria:

- Patients diagnosed with RA according to the American College of Rheumatology Criteria and /or EULAR criteria.
- Drugs evaluated: tofacitinib, baricitinib, upadacitinib, filgotinib, peficitinib or decernotinib, all of them compared with placebo.
- Safety data on HZ infection.

The search included a total of 2521 publications of which 504 were duplicated, leaving 2017. After screening by title and abstract 1874 studies that did not meet the criteria were eliminated and there were 143 fully reviewed. At the end 42 papers were included in the review.

The main objective of our study was the number of HZ infections depending on the doses of the drug administered, as well as with placebo.

Data collected from each study was: Author and year of publication of the study, study design and population included, number of patients treated, treatment administered and percentage of patients treated for HZ in each treatment arm.

Results: Results: In clinical trials of these drugs, a greater number of opportunistic infections due to varicella zoster virus have been identified compared to placebo, which leads to the appearance of HZ.

The role of different JAKs in the immune response may suggest differences in safety profiles between these drugs, which could have clinical implications. Therefore, we analyze the results separately for each JAKi.

Tofacitinib Of the 14 selected works, 4 are phase II, 8 phase III and 2 extension studies. We observe that the incidence of HZ ranges between 1% and 11%, the latter being the case of the Wollenhaupt extension study with a data collection period of nine and a half years. It is remarkable that in some of the studies included in this review there was no case of HZ and in others this information was not even collected.

Baricitinib Two phase II studies, 6 phase III studies and one extension study were analyzed, with an incidence of HZ between 1% and 9%, data similar to those obtained with tofacitinib.

Upadacitinib. An incidence of HZ between 1% and 4% was observed according to the 6 clinical trials (two phase II studies and four phase III studies) published as clinical product development.

Filgotinib Data similar to upadacitinib, with frequencies between 1% and 4% of HZ according to the studies (three phase II studies and one phase III study).

Peficitinib The incidence of HZ ranged between 4% and 7.5% (three phase II studies, two phase III studies, and one extension study).

Decernotinib There are only published three phase II trials, of short duration and with only four cases collected from HZ.

Conclusion: Conclusions: Opportunistic HZ infection have been reported between 1% and 11% in JAKi clinical trials. The results of the included studies seem to suggest that selective JAK1 inhibitors (Upadacitinib and Filgotinib) develop HZ as a treatment complication less frequently than other JAKi, but more studies are needed to support this conclusion.

Disclosure of Interests: Carmen Olga Sánchez Gonzalez: None declared, Juan Carlos Nieto Speakers bureau: Pfizer, Abbvie, MSD, Novartis, Janssen, Lilly, Nordic Pharma, BMS, Gebro, FAES Farma, Roche, Sanofi

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THU0150 INTERSTITIAL LUNG DISEASE RELATED TO RHEUMATOID ARTHRITIS. WHAT DO WE DON'T KNOW? THE LIRA STUDY (LUNG INVOLVEMENT IN RHEUMATOID ARTHRITIS).

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Background: Interstitial lung disease (ILD) is one of the more frequent and potentially severe extra-articular manifestation of rheumatoid arthritis (RA). ILD significantly decreases the survival and quality of life of patients and influences the treatment approach to the patient.

Despite its clinical relevance, the prevalence, incidence and survival of RA-ILD is unknown and supposed on the base of retrospective data or registry-based studies.

Objectives: For the first time, the Lung Involvement in Rheumatoid Arthritis (LIRA) study aims to investigate epidemiology, features and prognosis of RA-ILD patients in a prospective international multicentre study.

Methods: All RA patients referring to the involved centres will be evaluated every six months with a digital stethoscope and a software able to identify velcro crackles with a diagnostic accuracy of 83.9% (VECTOR). In fact, velcro crackles are virtually identified in all stages of fibrosing alveolitis like RA-ILD, and their search is as a simple and reliable method to screening patients to be undergone to high resolution computed tomography (HRCT).

For each patient, clinical and serological data are recorded at baseline and every six months; when velcro crackles or other conditions suspicious for ILD, such as cough or dyspnoea, are detected, a HRCT is requested to confirm ILD. Patients

with ILD periodically perform pulmonary function tests to monitor lung function evolution.

Results: At now, 205 RA patients have been enrolled (female/male 161/44, mean age 64.8±12.9 years, mean disease duration 14.2±8.9 years), anti-citrullinated peptides antibodies (ACPA) and rheumatoid factor (RF) were positive in 77.1% and 78.1%, respectively. The prevalence of ILD was 21% (43 patients). In other 13 patients the HRCT is ongoing; therefore, we could suppose up to a prevalence of 27.3%. Patients with ILD were symptomatic in 53.5% of cases (23 patients), they are more frequently males and were older than patients without ILD (mean age 73.2±7.4 and 62.7±13.2; p<0.0001, female/male ratio 139/23 vs 22/21; p<0.0001) without significant differences regarding disease duration, positivity for ACPA or RF.

Conclusion: The prevalence and the incidence of RA-ILD is still not well defined. Preliminary data of our study confirm a prevalence of ILD higher than 20%, patients are asymptomatic in almost the half of cases and more frequently males and elderly. Our study can help to define the clinical history of these patients, the possible association with clinical and serological features and the supposed role of some drugs.

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Disclosure of Interests: Marco Sebastiani: None declared, Caterina Vacchi: None declared, Giulia Cassone: None declared, Fabiola Atzeni: None declared, Martina Biggioggero: None declared, Antonio Carriero: None declared, Gian Luca Erre: None declared, Anna Laura Fedele: None declared, Federica Furini: None declared, Paola Tomietto: None declared, Vincenzo Venerito: None declared, Belén Atienza-Mateo: None declared, Giovanni Della Casa: None declared, Stefania Cerri: None declared, Gilda Sandri: None declared, Adalgisa Palermo: None declared, Elena Galli: None declared, Fabrizio Pancaldi: None declared, Miguel A González-Gay Grant/research support from: Pfizer, Abbvie, MSD, Speakers bureau: Pfizer, Abbvie, MSD, Carlo Salvarani: None declared, Andreina Manfredi: None declared

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THU0151 RISK OF MALIGNANCIES ASSOCIATED WITH CS DMARDS IN RHEUMATOID ARTHRITIS: COMPARISON WITH GENERAL POPULATION AND BIOLOGIC TREATED PATIENTS (ANALYSIS OF A NATIONAL CLAIM DATABASE)

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Background:

Objectives: To estimate the incidence rate of malignancies in csDMARD-treated RA patients and to compare it to that of general population and to biologic-treated RA patients

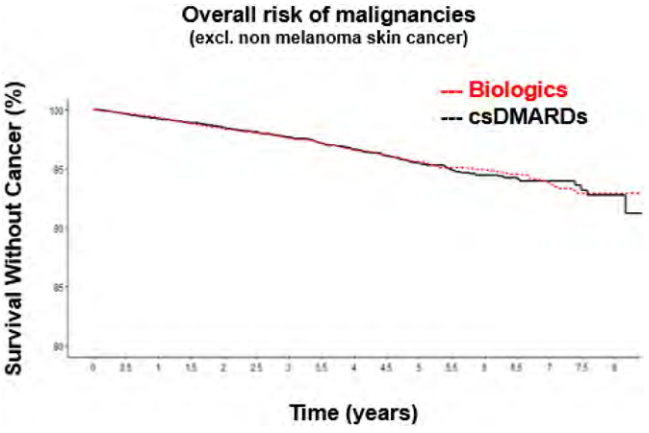
Methods: We conducted an historical cohort study within the national claim database that prospectively records individual health resource use of 86% of the French population (65 million inhabitants). RA adult patients were identified based on ICD-10 code (M05 or M06) between 2007-2016. Patients with previous cancer history were excluded. Treatment exposures were incident first use of any treatment: csDMARD (methotrexate, leflunomide, sulfasalazine, azathioprine, hydroxychloroquine) or biologics (anti-TNF, rituximab, abatacept, tocilizumab, ustekinumab, anakinra). To identify incident treatment periods, only patients who did not receive any treatment in the 1-year period before the index date were selected. Exposure was defined with a 90-day latency after treatment initiation and a 180-day carry-over period after drug discontinuation.

To compare the risk of malignancies between csDMARD-treated patients and general population, standardized incidence ratio (SIR [95%CI]) were calculated using FRANCIM ("France Cancer Incidence et Mortalité") estimations as reference.

To compare the risk of malignancies between csDMARD and biologics treated patients, a dynamically propensity score (including age, sex, year of first occurrence of RA code, date of treatment initiation, number of previous DMARDs, Charlson's comorbidity index, diagnosis of tobacco and/or alcohol-associated disorders, number of hospitalizations for RA, cumulative corticosteroid dose) was constructed using pooled logistic regression. Hazard Ratios (HRs) for risk of cancer were estimated using Cox proportional hazards model after dynamically propensity score matching. Exposure was considered as a time-dependent variable.

Results: Between 2007 and 2016, 83,706 RA patients exposed to csDMARD (n=63,837) and/or biologics (n=19,727) were identified.

As compared to the general population, csDMARDs treated patients had an increased risk of lung cancer (SIR=1.29 [1.14; 1.45]), invasive melanoma (SIR=1.52 [1.24; 1.86]) and a borderline increased risk of breast cancer (SIR=1.11 [1.01;1.22]). By contrast, they had a decreased risk of pancreatic cancer (SIR=0.68[0.51-0.9]) and liver cancer (SIR=0.43 [0.27; 0.67]). This later is due to a protopathic bias.



After propensity score matching, analyses the risk of malignancies between csDMARD and biologics treated patients were conducted on 19727 patients in each group (mean age: 51 ±14 yrs; female: 74.6%). Malignancies occurred in 435 patients exposed to biologics and 332 patients exposed to csDMARD. The overall risk of malignancies (figure), risk of solid cancer (excluding non-melanoma skin cancer), lymphoma, and other hematologic malignancies did not differ significantly between csDMARD and all biologics (table). Regarding organ specific cancer, no difference was observed. Results were similar for biologic in monotherapy or associated with csDMARD.

Type of malignancies	HR [95%CI] csDMARD (ref) vs. all biologics	p-value
All malignancies (excl. non-melanoma skin cancer)	**0.99 [0.86;1.14]**	p=0.9
Solid cancer (excl. non-melanoma skin cancer)	**0.95 [0.82;1.11]**	p=0.5
Lymphoma	**1.35 [0.72;2.53]**	p=0.3
Other hematologic malignancies	**1.18 [0.56;2.49]**	p=0.7

Conclusion: Using a large nationwide representative healthcare database, the overall risk of malignancies and the risk of organ-specific cancers and hematologic malignancies in biologic treated RA patients did not differ from that of patients treated with csDMARD. Compared to general population, patients treated with csDMARD had an increased risk of lung cancer and melanoma, but a decreased risk of pancreatic cancer.

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THU0152 THE ADVANTAGES OF DISTANCE BLOOD PRESSURE MONITORING IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Cardiovascular complications are very common in patients with rheumatoid arthritis (RA). The monitoring of the course of RA and comorbid conditions is the key aspect of the prevention of early mortality.

Objectives: To evaluate the effectiveness of the use of distance monitoring of blood pressure (BP) in patients with rheumatoid arthritis (RA) with comorbid arterial hypertension (AH).
Methods: 200 RA patients with AH (SBP – systolic 162.1 ± 7.3, DBP - diastolic 94.9 ± 9.2) are included in the trial, of which 8% are men. The average age was 54.0 ± 13.0. Patients were divided into 2 groups. Patients of group 1 (n=100) independently measured BP twice a day and entered the SBP and DBP results on self-control diaries in electronic form, or transmitted data from the tonometer via the installed mobile application. Pts of group 2 (n=100) were consulted on the first visit and in 3 months with further recommendations of monitoring and treatment of RA and AH.
Results: Activity on DAS 28 (CRP), pain on VAS (mm), level of cholesterol, age and prednisolone use significant moderate correlated ($p<0.01$) with the level of SBP. In 6 months the average level of SBP and DBP were 131.4 ± 8.2 and 82.6 ± 5.1 mm Hg in group 1 respectively. In group 1 80% of pts achieved target BP in comparison with 50% of pts in group 2. The frequency of prescribing of two-component and three-component antihypertensive therapy increased in 1.8 and 1.9 times in 1 group; in 1.4 and 1.3 times respectively.
Conclusion: Distance BP monitoring in patients with RA with the use of BP monitors with the function of remote data transmission lets to achieve target BP and hereby, reduce the incidence of adverse cardiovascular complications
Disclosure of Interests: None declared
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THU0153 TCZ MIGHT BE A RISK FACTOR FOR WORSENING OF ILD, PARTICULARLY OF CHRONIC ILD

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Background: Interstitial lung disease (ILD), frequent lung involvement, determine the prognosis of patients with RA. The presence of ILD also influences the selection of RA therapy. However, it is not fully elucidated what groups of RA-ILD patients worsen ILD.
Objectives: To identify the risk factors for worsening of ILD in RA patients under biological DMARD (bDAMARDs) therapy; particularly to determine whether types of bDMARDs are associated with exacerbation of ILD.
Methods: A retrospective cohort study was conducted. Subjects were consecutive 91 RA-ILD patients who received HR-CT examination at starting and during bDMARDs therapy. Clinical data were collected by reviewing.
ILD was diagnosed, when patients showed ground-glass opacity (GGO), consolidation, reticular pattern or honeycomb; the former two were acute and the latter two were chronic ILD lesions. The extent of each lesion was scored and recorded. When the score was increased, the lesion was judged as worsened. The incidence of exacerbation of ILD under an indicated agent was calculated as follows; the sum of (exposure period of the agent/exposure period of any agent) in patients with the exacerbation was divided by total exposure period of the agent.
Results: Subjects were 36 males and 55 females with a mean age of 66.8 years. At the entry, GGO, consolidation, reticular and honeycomb were found in16, 20, 63 and 17, respectively. Acute and chronic ILD were observed in 34 and 68, respectively. ILD worsened in 35 (38.5%). Between patients with and without ILD exacerbation, no differences were found in demographics (sex, age, disease duration, the positivity for anti-CCP ab and RF) and radiographic findings of pulmonary abnormalities. Disease activities at as 1st and sequential CT examinations were similar in both groups.
The incidences of the worsening of ILD varied according to bDMARDs (Fig 1). The incidence of total ILD worsening was high in TCZ compared to TNF and ABT. The incidence of acute ILD worsening was similar among the three groups. However, the worsening of chronic ILD was more frequently found in TCZ than other bDMARDs. The incidence of death by respiratory failure was similar in TNF, ABT, and TCZ (Fig. 2).

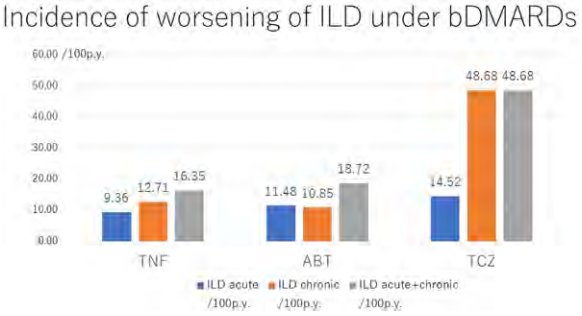


Fig. 1

Conclusion: TCZ might be a risk factor for exacerbation of ILD, particularly of chronic ILD.

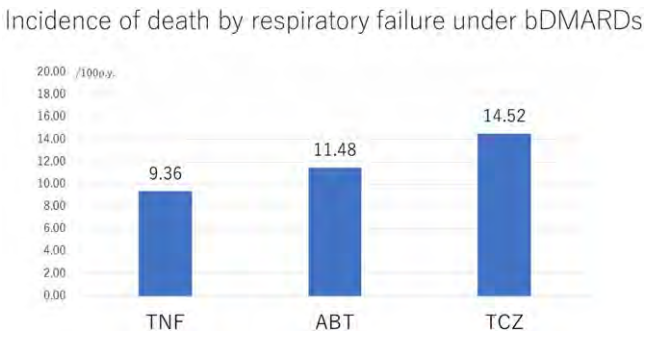


Fig. 2

Disclosure of Interests: None declared
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THU0154 PERCEPTIONS ABOUT INTERVENTIONS TO ENHANCE INFLUENZA VACCINE UPTAKE DIFFER BETWEEN VACCINATED AND UNVACCINATED RA/JIA PATIENTS

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Background: To optimize the control of vaccine preventable diseases, high immunization coverage rates must be achieved. Influenza vaccination rates among patients with rheumatoid arthritis (RA) and juvenile idiopathic arthritis (JIA) are suboptimal. Understanding patient preferences for interventions that may increase vaccine uptake is the first step to inform the development of specific strategies to enhance vaccine coverage in RA/JIA.
Objectives: To compare the perceptions of vaccinated and unvaccinated RA/JIA patients on a multi-modal intervention to enhance seasonal influenza vaccine coverage.
Methods: During the 2018-2019 influenza season, a multi-modal intervention was implemented at a large Canadian academic center. This consisted of (i) a letter sent from the Division of Rheumatology to patients addressing common misconceptions about flu vaccines and encouraging patients to plan for immunization; (ii) a nurse providing inactivated influenza vaccine at the rheumatology clinics for the first 7 weeks after the vaccine was released, and (iii) clinics posters specifically designed for rheumatic patients and rheumatologists to prompt a discussion on influenza prevention. Patients that were vaccinated on site completed a survey evaluating the relevance of the individual components of the intervention. After the intervention, during a scheduled rheumatology visit, RA/JIA patients were asked to complete a similar survey. We compared the responses from RA/JIA patients that were vaccinated at our institution, to those of patients that reported not having received the influenza vaccine in 2018-2019.
Results: During the intervention, 116 immunized RA/JIA patients completed the first survey. Forty RA/JIA patients not vaccinated during the 2018-2019 season completed the post-intervention survey. Both vaccinated and unvaccinated groups were mostly female (74.1% versus 87.2%), but vaccinated patients were older (50.8±19.4 versus: 40.5±14.9; 95% CI 3.7%,17%), and had shorter disease duration (10.1±9.3 versus 15.0±9.8; 95% CI -8.9%,-1.1%) than those not vaccinated. Unvaccinated patients were less likely than vaccinated patients to approve of the clinic's provision of influenza vaccine (98.2% versus 75%; 95% CI 12.8%, 43.5%). When asked about elements of the intervention, unvaccinated patients were less likely than vaccinated patients to consider posters (65.2% versus 38.9%; 95% CI 7.9%, 42.9%), letters (69.4% versus 35.3%; 95% CI 16.2%, 51.2%), or phone calls (58.0% versus 41.7%; 95% CI 2.1%, 33.5%) as good reminders.
Conclusion: Unvaccinated RA/JIA patients' opinions about interventions to increase vaccine uptake differ from vaccinated patients. Alternative, novel strategies to target vaccine hesitant RA/JIA patients are needed to optimize vaccine coverage.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.3429

THU0155 **SERUM MYOSTATIN IN PATIENTS WITH RHEUMATOID ARTHRITIS AND ITS CORRELATION WITH BODY COMPOSITIONS.**

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Background: Altered body composition is one of common findings in rheumatoid arthritis (RA), and it is estimated that up to two-thirds of patients may be affected loss of muscle mass and strength and concomitant increase in fat mass, so-called "rheumatoid cachexia". Despite great advances in the treatment of RA such as biologics and small molecule compounds, it appears that rheumatoid cachexia persists even after joint inflammation improves. Myostatin, a member of the transforming growth factor-beta superfamily, is a potent negative regulator of skeletal muscle growth and its inactivation can induce skeletal muscle hypertrophy, while its overexpression or systemic administration causes muscle atrophy. It enhances proteolysis and inhibits protein synthesis in skeletal muscle, and has generated increasing interest as a potential regulator of cachexic status such as patients with cancers, cardiac failure, and HIV infections.
Objectives: In this study, we investigated the possible role of myostatin for altered body compositions in patients with RA.
Methods: This was a cross-sectional study. Ninety-six RA patients who visited Niigata University Hospital between April to June 2017, were recruited in this study. Body composition was measured by bioelectrical impedance analysis with a tetrapolar impedance meter (InBody S-10, InBody Japan Inc, Tokyo, Japan) in each subject. The right femoral neck bone density was measured using the dual energy X-ray absorption method (DEXA). Serum myostatin level was measured by enzyme-linked immunosorbent assay with a commercially available kit (Quantikine ELISA GDF-8/ Myostatin Immunoassay, R&D systems, MN, USA). Patients' laboratory findings and disease activities were also measured, and the correlations between the titer of serum myostatin and these factors were analyzed by Spearman's correlation coefficient and stepwise multiple regression analysis. A p-value of <0.05 was taken to denote statistical significance.
Results: In Spearman's correlation coefficient analysis, serum myostatin level was positively correlated with skeletal muscle mass index and FFMI, and negatively correlated with percent body fat (%BF), fat mass index (FMI), right femoral neck bone density, swollen joint counts, ESR, and DAS28(4)-ESR. In stepwise multiple regression analysis, FFMI was selected as a positive independent variable (rho=0.3620, p=0.00019) and DAS28(4)-ESR as a negative independent variable (rho=-0.2298, p=0.0154) against serum myostatin levels, respectively. In 70 female patients in this study, %BF and FMI/FFMI ratio was significantly higher in patients with low FFMI group, compared to those with normal FFMI group.
Conclusion: Serum myostatin level was significantly correlated with body composition and disease activity in patients with RA. Patients with lower level of myostatin showed a trend of decreased skeletal muscle and increased body fat, suggesting serum myostatin as a possible biomarker for rheumatoid cachexia.
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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.1193

THU0156 **INCIDENT DIABETES ASSOCIATED WITH HYDROXYCHLOROQUINE, METHOTREXATE, BIOLOGICS AND CORTICOSTEROIDS IN RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS**

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Background: Rheumatoid arthritis (RA) is associated with greater risk of diabetes, the coexistence of RA and diabetes significantly increased risk of cardiovascular morbidity and mortality. For this reason, it is important to document the role of individual medications associated with RA in the diabetes development.
Objectives: We aim to evaluate the impact of antirheumatic drugs therapy on risk of developing diabetes in RA patients.
Methods: Electronic database searches of PubMed, EMBASE and Cochrane Library plus a hand search of conference proceedings were performed without language restrictions from inception to 14 October 2019. All study designs assessing the association between diabetes and antirheumatic agents in RA relative to a comparator group were included. The primary outcome was the association between treatments and diabetes. The secondary outcomes were their associations, stratified by dosage, exposure duration. Data were pooled using fixed-effects or random-effects meta-analysis according to I^2 and pooled hazard ratios (HRs) and 95% confidence intervals (CIs) was used as a summary statistic.
Results: Of 3961 identified articles, a total of 15 studies involving 552,019 patients with RA (11 for hydroxychloroquine, 7 for methotrexate, 6 for tumor necrosis factor inhibitors [TNFi], 8 for corticosteroids) were included. In pooled analysis, a reduced risk of diabetes was reported with hydroxychloroquine (meta-HR 0.61, 95%CI 0.56-0.66), methotrexate (meta-HR 0.81, 95%CI 0.75-0.87), TNFi (meta-HR 0.63, 95%CI 0.55-0.71), while corticosteroids increased the risk of developing diabetes in a dose-dependent manner (Any dose: meta-HR 1.46, 95% CI 1.39-1.53; <10 mg/day: meta-HR 1.30, 95% CI 1.13-1.51; ≥10 mg/day: meta-HR 2.25, 95% CI 1.88-2.70). Additionally, concomitant corticosteroids treatment with hydroxychloroquine appear to eliminate the excess diabetes risk from corticosteroids (meta-HR 0.64, 95% CI 0.51-0.79).
Conclusion: Our meta-analysis provides important evidence for the impact of antirheumatic drugs on diabetes in RA and may aid clinical decision-making by suggesting that hydroxychloroquine, methotrexate and TNFi decrease diabetes risk while corticosteroids increase such risk in RA. Large, prospective, well-designed studies are needed to explore the effects of such drugs on diabetes development in the RA patients with high-risk diabetes.
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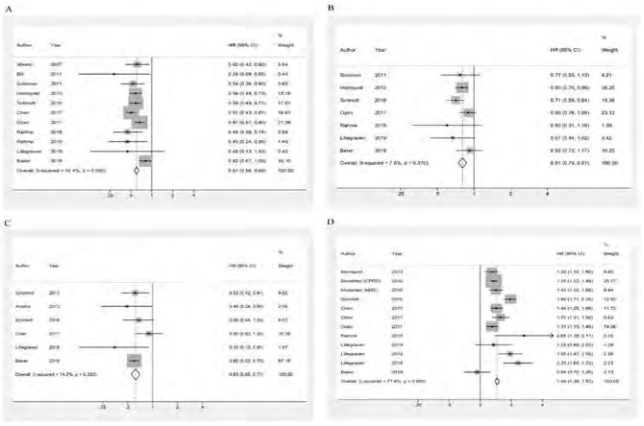


Figure 1. Meta-analysis of diabetes in patients with rheumatoid arthritis treated with (A) hydroxychloroquine; (B) methotrexate; (C) tumor necrosis factor inhibitors; or (D) corticosteroids. HR, hazard risk.

Disclosure of Interests: None declared
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THURSDAY, 04 JUNE 2020

Rheumatoid arthritis - biological DMARDs

THU0157 **'SWITCH ME IF YOU CAN' – REAL LIFE EXPERIENCE OF SWITCHING TO BIOSIMILAR DRUGS FROM GARTNAVEL GENERAL HOSPITAL, GLASGOW, UK**

M. A. Abdullah[1], S. Batool[1], S. Bawa[1]. [1]*Gartnavel General Hospital, Glasgow, United Kingdom*

Background: Rheumatology has entered the era of biosimilar drugs. Compared with the original approved biological drug, a biosimilar has highly similar physiochemical characteristics and biological activity[1]. There is also equivalent efficacy and no clinically meaningful differences in safety and immunogenicity[1]. Substantial cost savings can be made by starting both biological-naive patients and switching patients receiving original biological DMARDs (bDMARDs) to biosimilar DMARDs (bsDMARDs)[2]. We present our experience of switching to biosimilars at Gartnavel General Hospital, Glasgow, UK.
Objectives: To assess the adherence to bsDMARDs in patients switched from original bDMARDs and to identify factors affecting adherence

Methods: We identified 69 patients on etanercept and 101 patients on adalimumab who were switched to bsDMARDs. We used patient clinical records and DA28 scores held in our database to assess the response to treatment and identify patients who were switched back to original bDMARD. We also identified the reason for switching back to bDMARDs and any safety concerns were also analysed.
Results: Retention rate was 79.71% (55/69) in biosimilar etanercept and 90.10% (91/101) in biosimilar adalimumab group respectively. The overall failure rate was 20.29% (14/69) in biosimilar etanercept and 9.90% (10/101) in biosimilar adalimumab group. 15.94% (11/69) in biosimilar etanercept and 7.92% (8/101) in biosimilar adalimumab group were switched back to original bDMARD due to perceived disease flare. Control was regained in all these patients. Only 2 patients in each group (biosimilar etanercept – 2.9%, biosimilar adalimumab 1.98%) had clinically active disease requiring switch to bDMARD with different mechanism of action. 1 patient in biosimilar etanercept group had to stop biologic treatment due to cancer diagnosis.

Table. Reasons of switching back to bDMARD

Reason	biosimilar etanercept (11/69) 15.94%	biosimilar adalimumab (8/101) 7.92%
Difficulty using device	2	1
Anxiety	1	2
Felt worse on bsDMARD	0	1
Injection site pain and redness	1	1
Hair loss	0	1
Cough	0	1
Perceived disease flare	5	0
Recurrent infections	2	0
Not documented	0	1

Conclusion: Our study showed overall adherence was good (around 80%) in both switch groups with biosimilar adalimumab doing better than biosimilar etanercept patients. All patients who switched back to bDMARD regained control. Nocebo responses[3], such as subjective increase of disease activity and pain-related adverse events were identified as the main factors having a negative impact on adherence to bsDMARDs. No new safety signals were identified.
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Acknowledgments: Rheumatology department, Gartnavel General Hospital, Glasgow, UK
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.2561

THU0158 'ONE IS NOT ENOUGH' - RITUXIMAB SINGLE VS DOUBLE INFUSION PROTOCOL IN TREATMENT OF ESTABLISHED RHEUMATOID ARTHRITIS – REAL LIFE EXPERIENCE OF GARTNAVEL GENERAL HOSPITAL, GLASGOW, UK

S. Batool[1], M. A. Abdullah[1], K. Anderson[1], S. Bawa[1]. [1]*Gartnavel General Hospital, Glasgow, United Kingdom*

Background: Rituximab (RTX), chimeric anti-CD20 monoclonal antibody, is recommended as a treatment option for rheumatoid arthritis (RA) patients who had inadequate response or are intolerant to other DMARDs including at least one anti-TNF inhibitor[1]. The most cost-effective dosing and retreatment schedule remains to be defined. Based on series of case reports and observational studies, it is suggested that retreatment with RTX 1g single infusion provides similar clinical outcomes compared with 2 x 1g infusions[2]. We report our experience of using single infusion in treatment of established RA.
Objectives: Our unit adopted the single 1g infusion protocol in 2017. Patients were switched to RTX biosimilar – in September 2017. The aim of this study was to assess the effectiveness of single 1g infusion in maintaining the response in RA patients.
Methods: 80 established RA patients on RTX were identified using clinical records held on our database. 67.50% (54/80) were on single 1g infusion and 28.75% (23/80) were receiving 2 x 1g infusions. Flare and inadequate response were assessed by comparing DAS scores pre and post RTX treatment and clinical judgement. We also assessed the effectiveness of biosimilar RTX, and in switching to biosimilar RTX.
Results: RTX group: Overall retention rate was 57.41% (31/54) in single infusion retreatment group. 31.48% (17/54) flared and 76.47% (13/17) were switched back to 2 x 1g infusions with recapture of response in all patients. 1 patient continued single infusion due to recurrent cytopenia and 3 have not had retreatment yet. 11.11% (6/54) had secondary loss of effect (LOE). No flares were noted in 2 x 1g infusion group. 3.75% (3/80) had severe anaphylactic reaction needing to stop their treatment whereas 5% (4/80) experienced minor infusion reactions but managed to continue their treatment.
Switch group: 52 patients switched from RTX to biosimilar. 42 received single 1g infusion and 10 had 2x1g infusions. In single infusion group, 53.38% (22/42) maintained response, 33.33% (14/42) flared with recapture of response in 92.86% (13/14) on 2x1g infusions and secondary LOE in 11.90% (5/42). In 2x1g infusion group, 90% (9/10) maintained response whereas 10% (1/10) had secondary LOE.
Biosimilar RTX group: There were 25 patients on biosimilar RTX. 13/25 (52%) went onto single 1g infusion retreatment protocol. Of these, 3 (23.07%) had flare and 1 (7.69%) had secondary LOE. There were 6 (24%) primary response failures, 2 (8%) minor infusion reactions and 1 (4%) major infusion reaction in this group.
Conclusion: One third of patients in our cohort failed to respond to single infusion protocol. These results were reproducible in all groups – RTX, switch and biosimilar RTX single infusion group. Our study suggests clinicians and patients need to be vary in using single infusion protocol as there is significant risk of losing disease control.
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Acknowledgments: Rheumatology Department, Gartnavel General Hospital, Glasgow, UK
Disclosure of Interests: None declared
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THU0159 THE ADDITIONAL VALUE OF INTERLEUKIN-6 INHIBITORS ON PATIENT REPORTED OUTCOMES IN THE MANAGEMENT OF RHEUMATOID ARTHRITIS FAILURES TO A PREVIOUS ANTI-TUMOR NECROSIS FACTOR INHIBITOR: RETROSPECTIVE ANALYSIS FROM A LOCAL REGISTRY

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Background: To date the better strategy for the management of tumor necrosis factor inhibitor (TNFi) failures in rheumatoid arthritis (RA) is still under debate. At the same time, the patient's perspective is becoming increasingly important in the management of RA and the use of patient reported outcomes (PROs) is becoming more and more frequent in daily practice.
Objectives: To evaluate the additional value of PROs in the measure of comparative clinical response in a real-life local cohort of patients treated with different alternative mechanisms of action after the failure of a first-line TNFi.
Methods: Data were retrospectively extracted from the registry of the ASST Gaetano Pini-CTO Institute, which include all RA patients treated with biologic drugs between December 1999 and December 2019. The analysis was limited to patients who failed a first-line TNFi and the study population was stratified according to the prescribed second-line mechanism of action (MoA). In each treatment subgroup the 6- and 12-month clinical response was evaluated as the mean change from baseline of Clinical Disease Activity Index (CDAI) score, Patient Global Assessment (PGA), and pain VAS. The rates of patients achieving CDAI remission/low disease activity (LDA) and an acceptable level of pain (pain VAS ≤20) were also calculated. The comparison between treatment subgroups was performed by using the t-test and the Fischer's test for continuous and dichotomous variables, respectively.
Results: A total of 405 patients (192 treated with a second TNFi, 87 with interleukin-6 inhibitors [IL-6is], 70 with abatacept, and 56 with rituximab) were included in the study. In the overall population 352 patients (86.9%) were female, mean (±standard deviation) age was 55.7±13.1 years, mean disease duration 14.3±9.1 years, RF and ACPA were positive in 76.4% and 79.3% of patients, respectively. We observed a clear trend toward the superiority of IL-6is over TNFis in the 12-month mean change from baseline of CDAI score (-13.9 vs -9.2, p=0.06) and in remission/LDA rates (58.7 vs 45.1%; p=0.048). In the evaluation of PROs,

we found a statistically significant superiority of IL-6 over TNF inhibitors in the 12-month mean change from baseline of PGA (-34.5 vs -22.6%, p=0.02) and pain VAS (-35.4 vs -19.3%, p=0.01), and a significantly greater rate of acceptable pain level (42.1 vs 25.6%, p=0.01). No significant difference was observed in any of the evaluated items between a second TNFi and abatacept or rituximab.

Conclusion: In a RA cohort of real-life insufficient responders to a first TNFi, we observed an overall better clinical response to IL-6is compared to a second TNFi. This effect is much more evident in the measure of PROs rather than composite indices as a possible result of the involvement of IL-6 in the pathways leading to pain and fatigue development in RA.

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THU0160 THE EFFECT OF HLA-DRB1 RISK ALLELES ON THE CLINICAL EFFICACY AND SAFETY OF ABATACEPT IN SEROPOSITIVE, BIOLOGIC-NAÏVE PATIENTS WITH EARLY, MODERATE-TO-SEVERE RA TREATED WITH ABATACEPT OR ADALIMUMAB: DATA FROM THE OPEN-LABEL SWITCH PERIOD OF THE HEAD-TO-HEAD SINGLE-BLINDED 'EARLY AMPLE' TRIAL

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Background: Mechanistic differences between protein biologics are poorly understood. *HLA-DRB1* alleles containing the shared epitope (SE), which are strongly associated with RA, are present in 70–80% of anti-citrullinated protein antibody+ patients (pts) with RA.[1] Numerically higher efficacy responses with abatacept (ABA) vs adalimumab (ADA) were reported after 24 wks of treatment (Tx) in pts with early seropositive RA, specifically in SE+ pts.[2]

Objectives: To prospectively explore the relationship between *HLA-DRB1* SE genotype and the effects on disease activity after switching from ADA to ABA after completing 24 wks of initial Tx in biologic-naïve pts with early active RA.

Methods: This head-to-head exploratory trial (NCT02557100) enrolled seropositive (anti-cyclic citrullinated peptide 2+ and RF+) adults with early (≤12 mos of symptoms), moderate-to-severe RA (ACR/EULAR 2010 criteria). Pts were randomised 1:1 to SC ABA 125 mg/wk or SC ADA 40 mg every 2 wks (both with stable, oral MTX wkly) for 24 wks (single-blind period). At Wk 28, ADA-treated pts were switched to open-label (OL) ABA, following a 6-wk washout period (switch arm); ABA-treated pts continued treatment with ABA in an OL manner (non-switch arm). Pts were grouped by SE status based on *HLA-DRB1* genotype (–, no SE allele; +, ≥1 SE allele). Clinical efficacy was assessed to Wk 48 to determine the proportion of ACR20/50/70 responders and DAS28 (CRP) remitters in each arm. Safety was analysed throughout the trial and up to 8 wks post last dose.

Results: All 40 ABA-treated and 36/40 ADA-treated pts entered the OL ABA period; 3 (lost to follow up n=2, other n=1) and 1 (pt request to discontinue) pts, respectively, discontinued during the OL period. Baseline characteristics were balanced[2]; mean (SD) RA duration was 5.5 (2.6) mos. The greater efficacy responses seen with ABA vs ADA to Wk 24[2] were sustained at Wk 48 in the non-switch arm; in the switch arm, the efficacy responses generally increased over the OL period to Wk 48. Specifically, in both the overall population (Figure 1) and among SE+ pts (Figure 2), ACR20/50 response rates (RRs) and DAS28 (CRP) remission rates were similar between arms at Wk 48; ACR70 RR was still somewhat higher in the non-switch arm. Among SE– pts, ACR50 RRs were 56% in the non-switch arm vs 44% in the switch arm at Wk 24; at Wk 48, 56% of pts in the non-switch arm and 67% of pts in the switch arm achieved ACR50. However, data from the SE– subgroup must be interpreted with caution due to low pt numbers (n=9/arm). No new safety signals were identified.

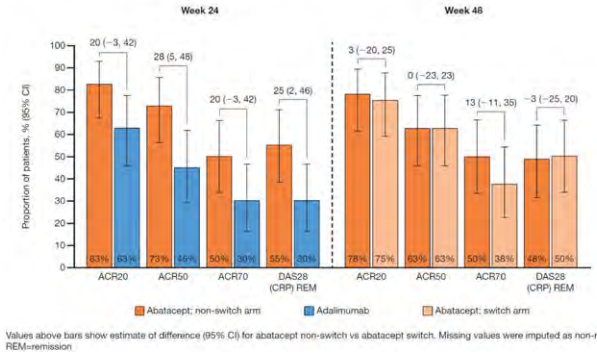
Conclusion: In this seropositive early RA population, particularly in the SE+ subgroup, a trend towards numerically higher and sustained efficacy responses by stringent definitions was seen in the abatacept non-switch arm at Wk 48; trends towards further improvement were observed in the adalimumab-to-abatacept switch arm.

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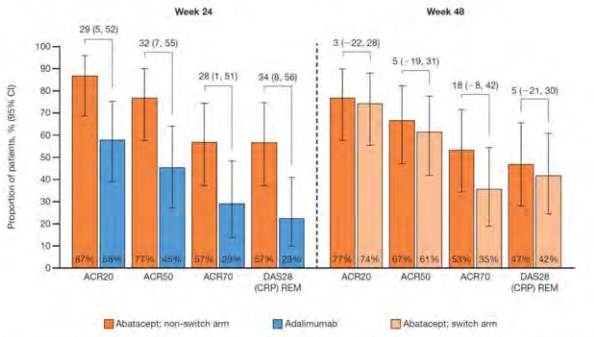
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Figure 1. Proportion of Patients With ACR Responses and DAS28 (CRP) Remission (<2.6) at Week 24 and Week 48



Values above bars show estimate of difference (95% CI) for abatacept non-switch vs abatacept switch. Missing values were imputed as non-responders
REM=remission

Figure 2. Proportion of SE+ Patients With ACR Responses and DAS28 (CRP) Remission (<2.6) at Week 24 and Week 48



Values above bars show estimate of difference (95% CI) for abatacept non-switch vs abatacept switch. Missing values were imputed as non-responders
REM=remission; SE=shared epitope

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THU0161 THE COMPARATIVE RISK OF HOSPITALIZED INFECTION IN RHEUMATOID ARTHRITIS PATIENTS INITIATING ABATACEPT OR TUMOR NECROSIS FACTOR INHIBITOR TREATMENT: A NATIONWIDE, POPULATION-BASED COHORT STUDY

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Background: Few population-based studies have compared the risks of hospitalized infection between patients with rheumatoid arthritis (RA) starting abatacept or TNFi treament.

Objectives: The study aimed to assess the relative risk of hospitalized infection in RA patients initiating TNFi treatment compared to those starting abatacept therapy.

Methods: The data source of this study was the 2003–2017 claims data from the Taiwanese National Health Insurance Research Database. First, we identified all RA patients who started their first biologic disease-modifying antirheumatic drug (DMARD)/targted-synthetic (ts) DMARD therapy. The index date was the first date of bDMARD/tsDMARD prescription. Subjects were followed up till the date of first hospitalization due to infection, 90 days after the last date of bDMARD/tsDMARD prescription, withdrawl from national health insurance or death, whichever came first. We calculated the incidences of hospitalized infection. We further matched abatacept users with TNFi users with a 1:4 ratio for age, sex and disease duration. A Cox regression analysis was used to examine the associations of covariates with the risk of hospitalized infection shown as hazard ratios (HRs) with 95% confidence interval (CIs). Covariates included age, sex, Charlson comorbidity index, a history of hospitaized infection within 5 years before the index date, prior RA-related medications within 6 months before the index date and concomitant RA-related medications. The relative risk of hospitalized infection in abatacept users compared to TNFi users were estimated after adjusting for covariates with a p-value < 0.05 in the univariable analysis.

Results: We identified 10,780 RA patiets who started their first bDMARD/tsDMARD treatment. Of them, 8,492 patients received TNFi treatment (etanercept n=4,390; adalimumab n=3,058; golimumab n=1,125), 614 patients were treated with tocilizumab, 278 patients were treated wtih rituximab, 737 patients were treated with abatacept, and 659 patients were treated wtih tofacitinib. The incidence rates (IRs) of hospitalized infection in patients treated with TNFi, tocilizumab, rituximab, abatacept and tofacitinib were 351, 407, 2,692, 260 and 0 per 10^5 years respectively. After matching (1:4) for age, sex and disease duration, we compared the risks of hospitalized infection between 728 abatacept users and 2,912 TNFi users. The IRs of hospitalized infection in patients treated with abatacept, TNFi, etanercept, adalimumab and golimumab were 262, 434, 331, 739 and 0 per 10^5 years respectivcely. After adjusting potential confounders, use of TNFi was not asssociated with a greater risk of hospitalized infection compared with abatacept use (HR, 2.14; 95% CI, 0.74–6.13; p = 0.159). However, the risk of hospitalized infection was higher in adalimumab users compared with abatacept users (HR, 3.24; 95% CI, 1.09–9.62; p = 0.035).

Conclusion: This nationwide, population-based, matched cohort study showed that among bDMARD/tsDMARD naïve RA patients, use of adalimumab, but not etanercept or golimumab, was associated with a greater risk of hospitalized infection compared with the risk associated with abatacept use.

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THU0162 LIKELIHOOD OF CLINICAL WORSENING AMONG RHEUMATOID ARTHRITIS PATIENTS WHO ACHIEVED A PARTIAL RESPONSE TO ADALIMUMAB AND WERE SUBSEQUENTLY SWITCHED TO SARILUMAB

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Background: Rheumatoid arthritis (RA) patients who achieve a response to therapy but fail to reach low disease activity (LDA) or remission (partial responders) may decline treatment changes for fear of clinical worsening and losing their achieved response. Little is known about the likelihood of worsening after switching therapy in partial responders, and this limits patients' ability to make informed treatment decisions.

Objectives: This post hoc analysis of the open-label extension (OLE) of MONARCH (NCT02332590) assesses the effects of switching from adalimumab to sarilumab in patients with RA who achieved a partial response to adalimumab but not remission or LDA.

Methods: MONARCH was a 24-week, head-to-head monotherapy trial comparing sarilumab with adalimumab. At study end, patients randomized to adalimumab were switched to sarilumab 200 mg q2w for the OLE. Partial responders to adalimumab were defined as patients who had improved more than the minimal clinically important difference (MCID) in the Clinical Disease Activity Index (CDAI) during MONARCH, but who continued to have moderate to high disease activity (CDAI >10) at OLE baseline (BL). MCID was defined as a CDAI decrease ≥12 from a BL CDAI >22 or ≥6 from a BL CDAI >10 to ≤22. Response following treatment switch was assessed by change in CDAI and other outcomes from OLE BL to OLE Week 24. The effect of switching was analyzed descriptively and categorized: worsening = CDAI increase ≥6; improvement = CDAI decrease ≥6; stable = CDAI absolute change <6. Patients randomized to sarilumab in MONARCH continued to receive sarilumab in the OLE and were included as a control group.

Results: Of 369 patients enrolled in MONARCH, 320 (87%) entered the OLE; 155 were switched from adalimumab to sarilumab, and of these, 91 were partial responders, who had a mean (SE) CDAI at OLE BL of 19.56 (0.86). Mean (SE) improvement in CDAI from OLE BL to OLE Week 24 in these patients was 7.37 (1.10). At OLE Week 24, only 6% of adalimumab partial responders had worsened after switching to sarilumab, while 57% had improved; the remaining 37% maintained stable disease activity. Analyses of other efficacy measures—patient and physician global assessments, disease activity score 28-joint erythrocyte sedimentation rate, and swollen and tender joint counts—demonstrated similar results: improvement was seen in 27–78% and worsening in 2–17%. No new safety signals emerged during the OLE. The adverse event profile among patients switching from adalimumab to sarilumab was consistent with the established safety profile of sarilumab.

Conclusion: Among adalimumab CDAI partial responders who switched to sarilumab, there was a low likelihood of clinical worsening, while more than half of such patients achieved clinically meaningful improvement. Similar results were observed for other efficacy measures. This small risk of worsening coupled with the substantial likelihood of improvement after switch may help alleviate patients' concerns around loss of response and help inform shared decision-making.

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THU0163 USE OF BIOLOGICAL AGENT IN MONOTHERAPY IN RHEUMATOID ARTHRITIS IN COMPARISON TO THE ASSOCIATIONS WITH D(ISEASE) M(ODIFIING) A(NTI) R(HEUMATIC) D(RUGS): REVIEW OF LITERATURE AND META-ANALYSIS OF RANDOMIZED TRIALS.

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Background: Biologic disease-modifying antirheumatic drugs (bDMARDs) extend the treatment choices for rheumatoid arthritis (RA) patients with suboptimal response or intolerance to conventional synthetic DMARDs (CsDMARDs). Currently, 9 biologic agents are approved in the RA treatment: and among them, three anti TNF agents are also approved in monotherapy (adalimumab, certolizumab and etanercept), but also abatacept, anakinra and tocilizumab. Registries of routine clinical practice treatment indicate that approximately one third of RA patients are being treated with a bDMARD in monotherapy and analyses from health care

claims suggest that when methotrexate (MTX) is prescribed in combination with a bDMARD, more than half of the patients do not collect the MTX prescription and overall patients seem to taper MTX intake over time. So it is important to evaluate the benefit and harm associated with use of biological agents as monotherapy, and not only the traditional combination therapy strategies.

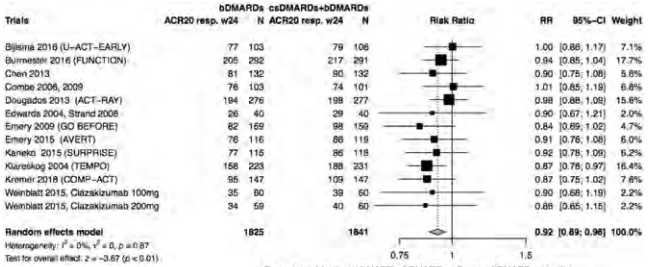
Objectives: To compare the efficacy and safety of the individual biological agents used in monotherapy in patients with RA than the combination therapy strategy with CsDMARD + bDMARD.

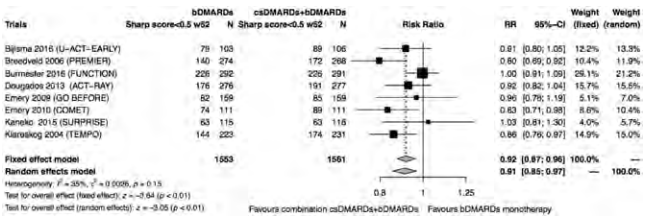
Methods: We used The Cochrane Central Register of Controlled Trials (CENTRAL), EMBASE, and MEDLINE in order to carry out our research, for published reports from inception of each database through December 2019. Search results were limited to randomised controlled trials (RCTs), with our two arms: biological agent in monotherapy and combination strategie (with any CsDMARDs). Major outcome was the ACR 20 reponse criteria at 24 week. The secondary outcomes were: the ACR 20 at 52 week, ACR 50, 70, 90 reponse criteria, the DAS 28 remission (with CRP and/or ESR), the score sharps modified non progressor, the proportion of patients who withdrawals the study due to adverse events, the proportion of patients who withdrawals the study due to lack of efficacy, the HAQ improvement > 0,22, CDAI and SDAI remission at week 24 and 52 if the data were available. The study of tolerance was also made. To estimate the relative efficacy of treatments whilst preserving the randomized comparisons within each trial, a Bayesian network meta-analysis was conducted in R (version 3.6.1) using fixed and random-effects.

Results: The systematic review identified 2566 citations. The analysis comprises 22 trials (6358 patients), including six biological agents approved for RA (abatacept, adalimumab, etanercept, golimumab, rituximab and tocilizumab) as well as two other molecules: Clazakizumab, a humanized monoclonal antibody that binds to the interleukin-6 (IL-6) cytokine and Anbainuo, recombinant human TNFRII:Fc fusion protein. No study satisfyies our search criteria for anakinra, certolizumab and infliximab. Compared to combination therapy with CsDMARD+bDMARD, bDMARD monotherapy has less probability to give a ACR20 response at 24 weeks (RR: 0,92 [0,89 – 0,96]) in fixed or random effect model and this result is similar at 52 weeks (RR: 0,94 [0,89 – 0,99]). For all other outcome mesures, we can see an increased of ACR50–70 and 90 responses, an improve of the DAS 28 remission score, an increase of the proportion of sharp's score non progressors (<0,5) as well as a decrease of withdrawals for inefficacy without increase of withdrawals for toxicity.

Conclusion: Evidence from this meta-analysis suggests that combinaison strategy with bDMARD+CsDMARD remains the most efficacious option, being more effective than the use of biologics in monotherapy. The interest from this point of view is to sensitize prescribers to the use of other CsDMARDs when there is a contraindication or intolerance to MTX, but also to make patients aware of the superiority of the association of biological agents with CsDMARDs.

figure





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THU0164

PERFUSE: A FRENCH PROSPECTIVE/ RETROSPECTIVE NON-INTERVENTIONAL COHORT STUDY OF INFLIXIMAB-NAIIVE AND TRANSITIONED PATIENTS RECEIVING INFLIXIMAB BIOSIMILAR SB2; AN INTERIM ANALYSIS

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Background: SB2 is approved in the EU as an infliximab (IFX) biosimilar, having demonstrated bioequivalence and similar efficacy, safety and immunogenicity as the reference. There is limited real-world evidence published on persistence, effectiveness or safety of SB2, in IFX-naiive patients or those transitioning from originator or another IFX biosimilar.

Objectives: PERFUSE is an ongoing non-interventional study of 1374 patients (500 with rheumatology diagnoses, 874 with gastroenterology diagnoses) receiving SB2 as routine therapy, with objectives to describe clinical characteristics, effectiveness, treatment persistence and safety in patients initiating SB2 and followed for 24 months at 21 specialist sites across France.

Methods: Adult patients eligible for inclusion in the rheumatology study cohorts have a diagnosis of Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA) or Ankylosing Spondylitis (AS) and initiated SB2 in routine clinical practice after September 2017, either as their first IFX or transitioning from treatment with IFX reference or another IFX biosimilar. Data are captured from patients' clinic records. Outcome measures include persistence on SB2, clinical characteristics at baseline (time of SB2 initiation), disease scores and Serious Adverse Events (SAEs).

Results: This 12-month interim analysis includes 500 patients (99 with RA, 62 with PsA and 339 with AS). M12 persistence on SB2 for IFX-naiive and transitioned patients combined was 73.8% (95% CI 61.5, 84.0), 76.2 % (95% CI 60.5, 87.9) and 71.5 % (95% CI 65.6, 76.9) in RA, PsA and AS respectively. In patients with prior IFX, no clinically meaningful difference in disease activity score from baseline to M12 was observed (Table 1). Low sample size precluded interpretation of disease score in the IFX-naiive cohort (not shown in Table 1). All

Table 1

	RA (N=99)		PsA (N=62)		AS (N=339)	
Age (mean, SD)	56.5 (13.8)		52.1 (12.9)		47.7 (12.5)	
Disease duration (mean, SD)	16.0 (9.4)		10.9 (10.7)		14.4 (11.8)	
Female (n) (%)	77 (77.8)		21 (33.9)		107 (31.6)	
IFX-Naiive (n) (%)	22 (22.2)		14 (22.6)		80 (23.6)	
Transitioned from Reference (n) (%)	37 (37.4)		24 (38.7)		111 (32.7)	
Transitioned from Biosimilar (n) (%)	40 (40.4)		24 (38.7)		148 (43.5)	
	SB2 Persistence at M12: n on SB2 at M12 (total n at M12), % (95% CI*)					
IFX-Naiive	5 (9)	55.6% (21.2, 86.3)	3 (7)	42.9% (9.9, 81.6)	21 (48)	43.8% (29.5, 58.8)
Transitioned from Reference	14 (22)	63.6% (40.7, 82.8)	15 (17)	88.2% (63.6, 98.5)	68 (87)	78.2% (68.0, 86.3)
Transitioned from Biosimilar	29 (34)	85.3% (68.9, 95.0)	14 (18)	77.8% (52.4, 93.6)	99 (128)	77.3% (69.1, 84.3)
Disease score in switched patients	**n**	**DAS-28 mean (95% CI)**	**n**	**DAS-28 mean (95% CI)**	**n**	**BASDAI mean (95% CI)**
Baseline	47	2.5 (2.2, 2.8)	19	2.2 (1.5, 2.8)	202	3.0 (2.7, 3.3)
M12	36	2.7 (2.3, 3.1)	14	2.0 (1.4, 2.6)	136	2.8 (2.5, 3.2)
Change from baseline at M12	26	0.5 (-0.1, 0.9)	9	0.0 (-0.7, 0.6)	125	0.1 (-0.2, 0.5)

* Clopper Pearson

7 reported SAEs are unrelated to SB2: prostate and breast carcinoma in the RA cohort; alcohol poisoning, nephrostomy, epistaxis, cutaneous lesion and malleolar fracture in the AS cohort.

Conclusion: This interim analysis indicates that patients with RA, AS or PsA can be successfully transitioned from originator or biosimilar IFX to SB2, without loss of disease control and with no safety concerns. The majority of transitioned patients continued SB2 treatment at M12 post-initiation. The PERFUSE study will provide ongoing, pertinent information about outcomes in these populations, helping to inform evidence-based treatment decisions.

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THU0165 PROSARA - A PROSPECTIVE, MULTICENTER, NON-INTERVENTIONAL STUDY TO EVALUATE THE SAFETY AND EFFECTIVENESS OF SARILUMAB FOR THE TREATMENT OF ACTIVE RHEUMATOID ARTHRITIS IN REGULAR CARE IN GERMANY

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Background: Blockade of IL-6 signaling by sarilumab has been demonstrated to be an effective treatment approach for rheumatoid arthritis. Due to strict inclusion and exclusion criteria, randomized controlled trials may not represent the heterogeneous RA patient population encountered in regular care.

Objectives: The current study investigated the safety and effectiveness of sarilumab in the treatment of RA in regular care in Germany.

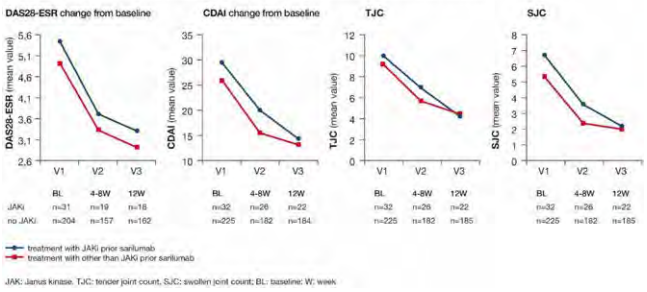
Methods: The prospective, observational, single-arm 24-months PROSARA study (SARILL08661) is currently running in Germany at 79 sites, aiming to include up to 750 RA patients treated with sarilumab. RA patients are selected at physician discretion and treated according to the label. Study objectives include the documentation of safety and various effectiveness outcomes. This interim analysis included patients with data available up to 12 weeks. All analyses are descriptive only.

Results: To date 348 patients were included in the study; of which 265 patients had post-baseline data. The mean age of the patients analyzed was 58.6 years (24-83); 76.3% are female. The mean disease duration was 10.3 years; comorbidities were present in 80.7% of patients. At baseline, 32.5% were biologic naïve. Most common pretreatment with b/ts DMARDs included TNF-inhibitors (TNFi, 56.2%), non-TNFi biologics (29.1%) or JAK-inhibitors (JAKi, 17.4%). At baseline, 49% received sarilumab as monotherapy and 29% in combination with conventional DMARDs (not specified for 22%). After 12 weeks of treatment with sarilumab, the mean DAS28-ESR decreased from 5.0±1.46 to 3.0±1.44 and CDAI from 26.7±13.79 to 13.6±11.4, respectively. DAS28-ESR remission/ low disease activity was achieved in 42.8% [n=77/180 patients with valid data on this parameter]/ 59.4% [n=107/180] of patients; 13.6% [n=28/206] and 49% [n=101/206] of patients reached CDAI remission and low disease activity. Boolean remission was observed in 9.5% [n=19/201] of patients at week 12. HAQ-DI improved from 1.3 at baseline to 1.1 at week 12 (n=195). The mean CDAI improvement was similar for autoantibody-positive (RF and/or ACPA; CDAI -12.5 at week 12) compared to -negative patients (CDAI -15.4 at week 12). Patients switching from JAKi to sarilumab (n=32), were more severely affected, had longer disease duration and received more prior treatments than patients switched from another compound. Of note, similar efficacy was observed among patients that switched from JAKi to sarilumab vs patients switched from other DMARDs; disease activity outcome measures including DAS28, CDAI, TJC, SJC and global assessments improved consistently (Figure 1).

Safety was consistent with the anticipated profile of IL-6-R-inhibition and no new safety signals occurred. Adverse events and serious adverse events were described in 33.9% and 6.3% of patients, respectively.

Conclusion: Sarilumab administered in regular care demonstrated rapid and clinically meaningful improvement in a general RA patient population including patients switching from JAKi. The safety profile was consistent with data reported from controlled clinical trials.

Figure 1. Effectiveness of sarilumab in patients switched from JAKi vs. patients switched from other DMARDs.



JAK: Janus kinase. TJC: tender joint count, SJC: swollen joint count; BL: baseline; W: week

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THU0166 HOW EFFECTIVE AND SAFE ARE BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS IN ELDERLY AND VERY ELDERLY PATIENTS WITH RHEUMATOID ARTHRITIS?

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Background: The proportion of elderly patients is increasing in the rheumatoid arthritis (RA) population. However, data on drug effectiveness and safety in these patients is scarce.

Objectives: To assess effectiveness and safety of biologic Disease-Modifying Antirheumatic Drugs (bDMARD) in elderly and very elderly RA patients.

Methods: Prospective cohort-study of RA patients registered at Reuma.pt starting a 1st bDMARD. Treatment persistence, EULAR response at 6 and 12 months, and adverse events (AE) were compared between adults (<65 years-old), elderly (65-74 years-old) and very elderly (≥ 75years-old).

Results: 2401 patients were included, of which 379 were elderly and 83 very elderly. Elderly and very elderly had higher disease activity at baseline and more comorbidities. Elderly patients started bDMARD later in the course of

RA (table 1). Crude and adjusted bDMARD treatment persistence was similar in the 3 groups (p=0.07, Graph). At 6/12 months, EULAR response was achieved by 81.6%/83.3%, 75.2%/68.5% and 82.6%/84.2% of adults, elderly and very elderly, respectively (table 2). Except for a lower response rate at 12 months in the elderly group, the EULAR response was comparable in the 3 groups. The same results were observed after adjustment for baseline characteristics, namely the chance of achieving EULAR response was not different in adults and very elderly (OR 0.78, 95% CI 0.19 to 3.2). Also, the variation of DAS, CDAI and SDAI at 6 months and 12 months were comparable in the 3 groups. AE were reported in 21%/22.5%/22.9% of adult/elderly/very elderly patients, respectively. The rate of AE per 100 patient-years was lower in adults when compared to elderly and very elderly (6.4, 13.5 and 14.7, respectively) (table 2). Also the rate of severe AE (SAE) was higher in very elderly (4.29 per 100 patient-years) when comparing to adults and elderly (1.03 and 1.94 respectively).

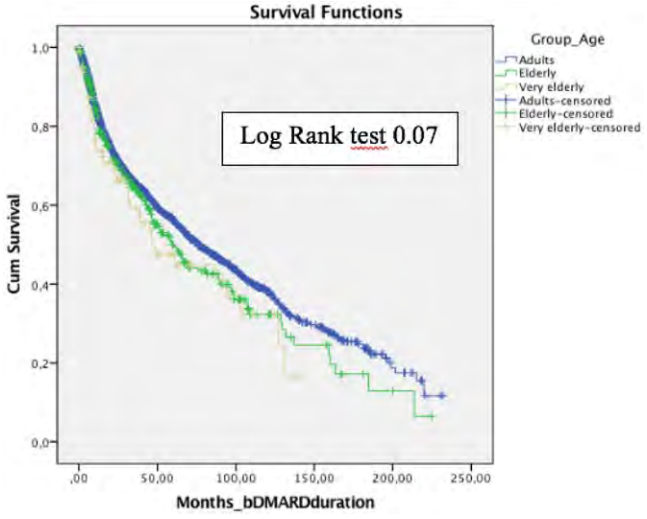
Table 1. Baseline characteristics. no:number; IQR:interquartile range; SD:standard desviation; DAS28-disease activity score 28 joints ESR; CV: cardiovascular; RF:Rheumatoid Factor; ACPA:anti-citrullinated protein antibodies

	Adults	Elderly	Very elderly	P value
Hypertension – no (%)	373 (26.7)	108 (42.4)	29 (47.5)	<0.01
Diabetes – no (%)	95 (6.8)	40 (15.7)	10 (16.4)	<0.01
CV disease – no (%)	93 (6.7)	24 (9.4)	10 (16.4)	<0.01
RF and/or ACPA positive – no (%)	1642 (73)	252 (72.8)	60 (74)	0.97
Years since diagnosis to 1st bDMARD -median (IQR)	7.4 (3.7-14)	9.9 (5-18)	5.2 (3-12.6)	<0.01
Baseline DAS28 mean ± SD	5.5 ± 1.3	5.7 ± 1.3	6 ± 1.4	0.02

Table 2. Efficacy of biologics at 6 (T6) and 12 month (T12) and safety

	Adults	Elderly	Very elderly	P value
Δ DAS T6 mean ± SD	-2 ± 1.4	-2 ± 1.9	-2.1 ± 1.4	0.9
EULAR responders T6 %	618 (81.6)	108 (75.2)	18 (81.8)	0.19
Δ DAS T12 mean ± SD	-2.1 ± 1.5	-1.8 ± 1.6	-2.6 ± 1.9	0.1
EULAR responders T12 – no (%)	538 (83.3)	84 (68.3)	16 (84.2)	<0.01
Patients with AE – no (%)	396 (21)	80 (22.5)	19 (22.9)	0.76
AE/ 100 patient-years	6.4	13.5	14.7	

Conclusion: The persistence on 1st bDMARD was similar in adults, elderly and very elderly RA patients. Though older patients have more comorbidities and more active disease at baseline, treatment with biologics was effective and with an acceptable safety profile. However, it is important to take into account the higher risk of AE and SAE in older patients. In conclusion, this study supports the use of bDMARD treatment in elderly and very elderly RA patients.



Graph – Persistence in bDMARD

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THU0167 ASSOCIATIONS BETWEEN RHEUMATOID ARTHRITIS DISEASE ACTIVITY AND PATIENT-REPORTED OUTCOMES IN SARILUMAB CLINICAL TRIALS

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Background: Sarilumab is a human interleukin (IL)-6 receptor inhibitor approved for the treatment of adults with moderately to severely active rheumatoid arthritis (RA). The relationship between disease activity (DA), sarilumab treatment, and improvements in patient-reported outcomes (PROs) has not been well-studied.

Objectives: Assess the association between DA and PROs in three sarilumab Phase 3 trials.

Methods: This post hoc analysis included patients from three trials: two placebo-controlled trials (MOBILITY; NCT01061736 and TARGET; NCT01709578) with sarilumab dose groups 150 mg and 200 mg q2w that were combined for this analysis; and MONARCH (NCT02332590) with sarilumab 200 mg versus adalimumab 40 mg q2w. Associations between PROs and DA were tested at Week 24. All statistics are descriptive.

Results: Sarilumab was generally associated with larger PRO improvement than placebo both in patients who did and patients who did not achieve DA thresholds (Table). Improvement was less pronounced in patients who did not achieve DA thresholds. In the active-comparator trial, PROs improved in both treatment groups, across all DA levels. There was no clear difference between sarilumab and adalimumab in PRO response. There was a consistent trend of positive but reduced PRO responses with increased DA level using multiple cut-points (data not shown).

Conclusion: Achieving lower DA was associated with increased PRO improvements. In patients who did not achieve DA thresholds, the improvements were more favorable with sarilumab than placebo. This may support the emerging concept that mechanisms other than inflammation may contribute to improvements in PROs, potentially mediated via IL-6 signaling.

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Disclosure of Interests: Mark C. Genovese Grant/research support from: Abbvie, Eli Lilly and Company, EMD Merck Serono, Galapagos, Genentech/Roche, Gilead Sciences, Inc., GSK, Novartis, Pfizer Inc., RPharm, Sanofi Genzyme, Consultant of: Abbvie, Eli Lilly and Company, EMD Merck Serono, Genentech/Roche, Gilead Sciences, Inc., GSK, Novartis, RPharm, Sanofi Genzyme, Gerd Rüdiger Burmester Consultant of: AbbVie Inc, Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB Pharma, Speakers bureau: AbbVie Inc, Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB Pharma, Laure Gossec Grant/research support from: Lilly, Mylan, Pfizer, Sandoz, Consultant of: AbbVie, Amgen, Biogen, Celgene, Janssen, Lilly, Novartis, Pfizer, Sandoz, Sanofi-Aventis, UCB, Hubert van Hoogstraten Shareholder of: Sanofi, Employee of: Sanofi, Amy Praestgaard Employee of: Sanofi Genzyme, Gregory St John Shareholder of: Regeneron Pharmaceuticals, Inc., Employee of: Regeneron Pharmaceuticals, Inc., Thomas Huizinga Grant/research support from: Ablynx, Bristol-Myers Squibb, Roche, Sanofi, Consultant of: Ablynx, Bristol-Myers Squibb, Roche, Sanofi, Daniel Aletaha Grant/research support from: AbbVie, Novartis, Roche, Consultant of: AbbVie, Amgen, Celgene, Lilly, Medac, Merck, Novartis, Pfizer, Roche, Sandoz, Sanofi Genzyme, Speakers bureau: AbbVie, Celgene, Lilly, Merck, Novartis, Pfizer, Sanofi Genzyme, UCB, Roy Fleischmann Grant/research support from: AbbVie, Akros, Amgen, AstraZeneca, Bristol-Myers Squibb, Boehringer, Ingelh-Centrexion, Eli Lilly, EMD Serono, Genentech, Gilead, Janssen, Merck, Nektar, Novartis, Pfizer, Regeneron Pharmaceuticals, Inc., Roche, Samsung, Sandoz, Sanofi Genzyme, Selecta, Taiho, UCB, Consultant of: AbbVie, ACEA, Amgen, Bristol-Myers Squibb, Eli Lilly, Gilead, GlaxoSmithKline, Novartis, Pfizer, Sanofi Genzyme, UCB
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Table. Median (interquartile range) change from baseline in PROs

	FACIT-fatigue (0–52)		Pain (VAS 0–100)		Sleep (VAS 0–100)	
MOBILITY[a]	Placebo	Sarilumab	Placebo	Sarilumab	Placebo	Sarilumab
DAS28-CRP <3.2	7.3 (14.0)	9.0 (13.0)	–36.0 (33.0)	–41.0 (37.0)	–17.0 (47.0)	–26.0 (46.0)
DAS28-CRP ≥3.2	4.3 (10.0)	7.5 (12.0)	–14.0 (35.0)	–18.5 (33.0)	–12.0 (35.0)	–14.5 (35.0)
CDAI ≤10	7.3 (13.0)	9.0 (13.0)	–37.0 (35.0)	–41.0 (39.0)	–17.0 (45.0)	–26.0 (44.0)
CDAI >10	4.3 (10.0)	8.0 (11.3)	–12.5 (34.0)	–22.0 (35.0)	–12.0 (33.5)	–14.0 (36.0)
SDAI ≤11	8.0 (13.0)	9.0 (13.0)	–37.0 (32.0)	–40.0 (38.0)	–24.0 (47.0)	–26.0 (45.0)
SDAI >11	4.0 (9.0)	8.0 (11.0)	–12.0 (34.0)	–22.0 (36.0)	–10.0 (34.0)	–16.0 (36.0)
TARGET[b]	Placebo	Sarilumab	Placebo	Sarilumab		
DAS28-CRP <3.2	16.0 (13.0)	14.0 (16.0)	–44.5 (28.5)	–53.0 (35.0)		
DAS28-CRP ≥3.2	7.0 (13.0)	8.5 (13.5)	–18.0 (38.0)	–27.5 (34.0)		
CDAI ≤10	14.0 (13.4)	14.0 (15.0)	–42.0 (32.0)	–52.0 (34.0)		
CDAI >10	6.0 (13.0)	9.0 (15.0)	–18.0 (38.0)	–28.0 (37.0)		
SDAI ≤11	15.0 (12.0)	14.0 (15.3)	–45.0 (30.0)	–52.5 (33.0)		
SDAI >11	6.0 (14.0)	8.9 (15.0)	–17.5 (38.0)	–27.0 (37.0)		
MONARCH[c]	Adalimumab	Sarilumab	Adalimumab	Sarilumab		
DAS28-CRP <3.2	10.0 (13.0)	11.0 (15.0)	–45.0 (23.0)	–42.0 (39.0)		
DAS28-CRP ≥3.2	7.0 (13.0)	5.0 (12.5)	–21.0 (30.0)	–20.5 (32.5)		
CDAI ≤10	10.0 (14.0)	11.0 (14.0)	–44.0 (25.0)	–42.0 (41.0)		
CDAI >10	7.0 (13.0)	7.0 (14.3)	–21.0 (31.0)	–28.5 (36.0)		

DA thresholds per trial protocols. [a]Placebo n = 398; sarilumab n = 799. [b]Placebo n = 181; sarilumab n = 365; sleep not assessed. [c]Adalimumab n = 185; sarilumab n = 184; SDAI and sleep not assessed.

THU0168

GESTATIONAL DESIRE AND CERTOLIZUMAB PEGOL IN PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATIC DISEASE. PRELIMINARY RESULTS OF THE GESTAMAD COHORT

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Background: The use of biological therapies during pregnancy has been contraindicated since the beginning of the use of these drugs. In recent years several studies have demonstrated the minimal-to-no transfer of certolizumab pegol (CZP) to the placenta and breast milk, which has allowed its approval for use in pregnancy and breastfeeding if clinically necessary. However, there are no studies evaluating the use of CZP during this period in real life or the characteristics of this subgroup of patients.

Objectives: To describe the profile of women of childbearing age diagnosed with chronic inflammatory rheumatic disease (CIRD): Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA) and axial Spondyloarthritis (axSpA), who initiate CZP by gestational desire using the GESTAMAD registry (multicenter study of women with chronic inflammatory rheumatic disease of childbearing age who are initiated on CPZ by gestational desire from the Madrid community).

Methods: Prospective multicenter study that aims to know the characteristics of women of childbearing age diagnosed with CIRD and gestational desire to which CZP is initiated for this reason. The comorbidities of the patients such as hypertension, diabetes and cardiovascular disease were collected. Disease activity was measured by DAS28 using CRP in RA and PsA and BASDAI in axSpA. The present study presents preliminary data from the initial cohort and will be followed prospectively for 24 months to assess the efficacy and safety of the drug during pre-conception, pregnancy and lactation.

Results: A total of 45 patients have been recruited in 6 Madrid hospitals from June to December 2019. Patients had a mean age of 35.9, (36.6 in RA, 35.2 in PA and 35.1 in SPA). Fifty-one percent had RA, 20.0 percent had PA and 28.8 percent had SPA. The mean disease duration for RA, PA and SPA was 9.5, 7.3 and 6.9 years, respectively. 48.9% of women were nulliparous. The abortion rate of patients diagnosed with spondyloarthropathy was upper of 25%. 33.3% of the patients had been treated with previous biologicals, with gestational desire/pregnancy being the reason for the change.

75.5% of the patients had been treated with synthetic disease modifying antirheumatic drugs (DMARD) previously. With regard to disease activity, the mean DAS 28 at the start of treatment was 4.5 in RA and 3.8 in PA and BASDAI 7.0 in axSPA.

In RA the highest values of CRP and ESR were found prior to initiation with CZP, but this difference was not statistically significant (p=0.644 and 0.605, respectively). 22.2% of patients had previous comorbidities.

Conclusion: The mean age of patients with gestational desire in CIRD is high. Women diagnosed with PsA and axSpA have a high rate of previous abortions, upper than 25%. The duration of the disease is equally long at the time of manifesting gestational desire. The use of treatments such as CZP, compatible with pregnancy and lactation would allow a better control of inflammatory joint disease in this period of life, encouraging patients not to postpone their gestational desire.

Disclosure of Interests: None declared

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THU0169

COMPARISON OF THE SYNOVIAL RESPONSE TO MECHANICAL STRESS AMONG PATIENTS WITH RHEUMATOID ARTHRITIS IN CLINICAL REMISSION ON METHOTREXATE OR ANTI-TNF

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Background: Physiologically, the joint synovium responds to physical activity according to the frequency and intensity of the efforts, producing slight effusion without detectable hyperemia. In patients with RA in remission, a similar response can be expected, since it is understood that the immune-mediated inflammatory component has been controlled physiopathologically. Our interest is to determine whether once clinical remission has been reached, treatment with MTX or antiTNF produces the same normalization of the synovial behaviour. Our interest is to determine whether once clinical remission has been reached, treatment with MTX or antiTNF produces the same normalization of the synovial behavior.

Objectives: The aim of the present study is to compare the synovial response to mechanical stress of patients with Rheumatoid Arthritis (RA) in remission treated with Methotrexate (MTX) or Etanercept (ETN).

Methods: Descriptive observational study. We included patients with RA in remission (DAS28<2.6) for at least 6 months on MTX or MTX and anti-TNF-alpha therapy (ETN). An ultrasound examination protocol was developed for the 2nd, 3rd and 4th MCP and non-dominant hand carpus for gray scale (GS) and power Doppler signal detection (sPD) according to EULAR/OMERACT definitions. Two ultrasound examinations were performed on each patient, before and 24 hours after starting a manual digital flexure exercise program against resistance measured by a handheld dynamometer CAMRY™ model EH101-17. Total synovitis scores in EG (0-12) and sPD (0-12) were compared.

Results: We included 37 patients on MTX treatment (median dose 15mg/week, range 7.5-25mg/week) and 16 patients on ETN treatment (median dose 50mg/week, range 25-50 mg/week). The baseline ultrasound score in the MTX treatment group was 1.6 SD 1.4 in EG and 2.2 SD 0.5 in PDs. After carrying out the controlled dynamometric effort, the score was 2.4 SD 1.9 in GS and 4.4 SD 1.5 in PDs (P<0.05 and P<0.001, respectively). In patients treated with TNEs, the basal score in GS was 1.3 SD 0.6 in GS and 0.6 SD

0.3 in PDs. After the controlled dynamometric effort, the score was 1.8 DE 0.9 in EG and 0.7 DE 0.4 in PDs (P=0.07 and P<0.001, respectively). In the group of patients treated with MTX, four subjects reported joint tenderness after physical effort.

Conclusion: Our observations are congruent with previous experiences in which it has been observed that physical stress translates into synovial changes detectable by ultrasonographic studies. Our results, although modest in patient volume, suggest that TNF-alpha activity is crucial in the development and maintenance of exercise-induced hyperemia. The clinical significance of our observation may be useful as a tool to predict the response to anti-TNF therapy in patients with RA, however specific methodological designs are needed for such associations.

Disclosure of Interests: None declared

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THU0170 BAFF CONTRIBUTES TO THE DEVELOPMENT OF IMMUNOGENICITY IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH TNF INHIBITORS

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Background: Immunogenicity related to treatment with TNF inhibitors (TNFi) is one of the causes for the decreased attainment of clinical response in patients with rheumatoid arthritis (RA)[1]. However, the involved mechanism is not entirely clear. The B-cell activating factor (BAFF) may play a role in the development of immunogenicity[2].

Objectives: To analyse the association between baseline serum BAFF concentration and the development of immunogenicity within 6 months (m) of TNFi treatment in patients with RA.

Methods: A total of 121 patients with RA initiated at standard doses of TNFi (infliximab (n=64), adalimumab (n=13), golimumab (n=11), certolizumab (n=33)) were included in this observational study and followed for 6m. Eleven (9%) received TNFi monotherapy, 92 (65%) TNFi+MTX (methotrexate) and 31 (26%) TNFi+csDMARDs other than MTX. A cohort of 68 untreated patients with early-RA and 20 healthy individuals (age- and sex-matched with the patients) were included as controls. Serum samples were obtained at baseline and 6m, up to 24h prior to TNFi administration. The baseline serum BAFF concentration was measured using ELISA. Drug and anti-drug antibody (ADA) levels were measured using sandwich and drug-sensitive bridging ELISA, respectively. Patients were stratified according to ADA development. Depending on data distribution, comparisons were conducted using unpaired t, Mann-Whitney U or Fisher's exact tests. The association between the development of ADA within 6m and clinical/serological variables was evaluated by uni- and multi-variable logistic regression. The presence of interactions with covariates (age, RF, ACPA, body mass index, baseline DAS28 and concomitant MTX dose) was tested, stratifying the results if this was significant (p<0.05). In case of no interaction, the model was later adjusted for these covariates.

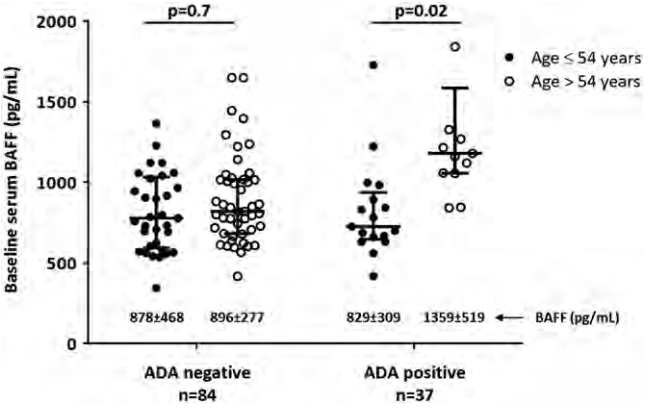
Results: Mean serum BAFF concentration in healthy controls (373±59 pg/mL) was significantly lower compared to patients with early RA (921±388 pg/mL) or established RA (936±407 pg/mL), (p<0.0001 for both). However, BAFF concentrations did not differ between early and established RA (p=0.9).

In this cohort, 37 (31%) patients developed ADA within 6m of treatment. These patients showed higher frequency of seropositivity (RF, p<0.05; ACPA<0.05), had higher baseline DAS28 (p<0.05), received lower dose of concomitant MTX (p<0.001) and had higher baseline BAFF concentration (p=0.06).The association between baseline BAFF concentration and ADA development was next investigated. The dose of concomitant MTX tended to interact on this association (p=0.06). A significant interaction was found between baseline BAFF concentration and age (Wald chi-square= 6.23; p=0.01); therefore, the results were stratified according to mean age (≤/>54yr). The results showed that baseline BAFF concentration was associated with ADA development only in older patients (OR=1.0, p=0.02); (shown in the figure). In addition, a significant Spearman correlation between baseline BAFF concentration and ADA levels at 6m was found in older patients (r=0.5, p<0.001).

Conclusion: Our results suggest that BAFF has a role in the development of immunogenicity. Nevertheless, this association depends on the age. In RA patients treated with TNFi, the development of ADA within 6m is associated with higher baseline BAFF concentration only in older patients but not in younger patients. The dose of concomitant MTX interacted on this association.

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[2] Bitoun S, et al. Ann Rheum Dis. 2018; 77: 1463-70.



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THU0171 EFFICACY OF ABATACEPT FOR SUPPRESSING RADIOGRAPHIC PROGRESSION OF CERVICAL LESIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS COMPARISON WITH METHOTREXATE TREATMENT; TWO YEARS OF FOLLOW-UP ~A MULTICENTER REGISTRY STUDY ~

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Background: Cervical lesions are known to occur at high frequency as a complication of rheumatoid arthritis (RA). Treatment with biological agents are more clinically effective than the DMARDs that were in use previously, in particular, with their efficacy in suppressing joint destruction having been emphasized. We reported the efficacy of infliximab, anti-tumor necrosis factor antibodies for suppressing the radiographic progression of RA cervical lesions at ACR2009, EULAR2010, 11, 12, 13, 14,16 and 18. However there is still few studies of efficacy of against RA cervical lesions of Abatacept (ABT) that inhibits T cell activation by binding to CD80/86.

Objectives: To evaluate the efficacy of ABT for suppressing the radiographic progression of RA cervical lesions comparison with MTX for 2 years.

Methods: We used ABT or MTX for treating Japanese patients with active RA who fulfilled the ACR criteria in 1987. The final study cohort of each 60 and 75 patients received continuous ABT and MTX treatment for at least 2 years. For evaluation of cervical lesions, the atlanto-dental interval (ADI), the space available for the spinal cord (SAC), and the Ranawat value were measured by plain lateral radiographs in the flexion position, at initiation and Year 1,2.

Results: In the patients receiving ABT (n=60) and MTX (n =75), the number of female were each 48(80%) and 52(69%) cases(p=0.160). The mean age was 67.7 ± 12.9 and 63.6 ± 11.0 years old (p=0.004); disease duration was 16.7 ± 14.2 and 8.0 ± 9.5 years (p<0.001) and the mean dose of MTX was 8.4 ± 3.6 and 8.2 ± 2.9 mg/w (p=0.804). Clinical findings related to RA were as follows; CRP 2.2± 2.1 and 1.7± 2.3 mg/dl(p=0.008); ESR 47.2 ± 23.4 and 31.9 ± 21.8mm/h(p<0.001); MMP3 253 ± 280 and 223 ± 350ng/ml(p=0.003); the number of RF-positive 57(95%) and 60(80%) cases(p=0.011); DAS28-ESR 5.13 ± 0.99 and 4.30 ± 1.38 (p<0.001); ADI 3.6 ± 2.1 and 2.6 ± 1.6mm(p=0.003); SAC 18.5 ± 2.8 and 20.8 ± 2.5mm(p<0.001) and Ranawat value 14.4 ± 1.9 and 16.0 ± 1.5mm (p<0.001). The

respective changes in cervical lesion parameters after 1 year were as follows: ADI: 0.20 ± 0.40 and 0.27 ± 0.45 mm (p = 0.367); SAC: –0.12 ± 0.32 and –0.17 ± 0.38 mm (p = 0.359); and Ranawat value: –0.15 ± 0.36 and –0.13 ± 0.34 mm (p = 0.783). The respective changes in cervical lesion parameters after 2 years were as follows: ADI: 0.35 ± 0.58 and 0.55 ± 0.70 mm (p = 0.099); SAC: –0.25 ± 0.47 and –0.45 ± 0.62 mm (p = 0.047); and Ranawat value: –0.23 ± 0.47 and –0.33 ± 0.55 mm (p = 0.293) in the patients receiving ABT and MTX (Fig. 1). The numbers of patients who did not showed progression in ADI, SAC and Ranawat value were each 42(70%) and 43(57%) cases(p=0.130); 46(77%) and 46(61%) cases(p=0.057) and 47(78%) and 53(71%) cases(p=0.313) after 2 years. Also the number who was able to suppress progression in all three parameters were each 42 cases (70%) receiving ABT and 43 cases (57%) receiving MTX (p=0.130) after 2 years (Fig. 2).

Conclusion: This study suggested that ABT treatment can be used to suppress the progression of RA cervical lesions more than MTX treatment.

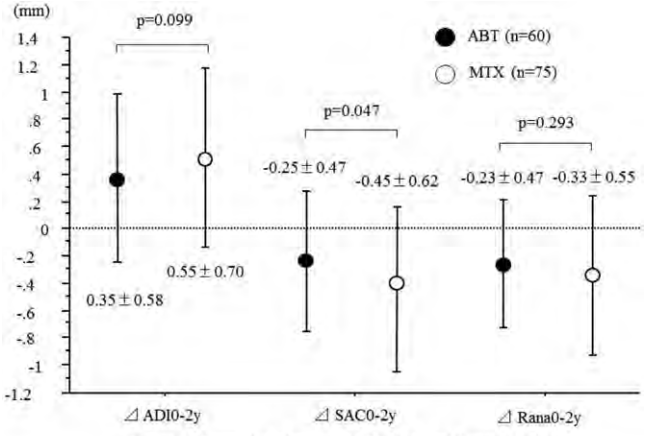


Figure 1 : Respective changes in ADI, SAC and Ranawat value from Year 0 to Year 2 in the ABT and MTX patients

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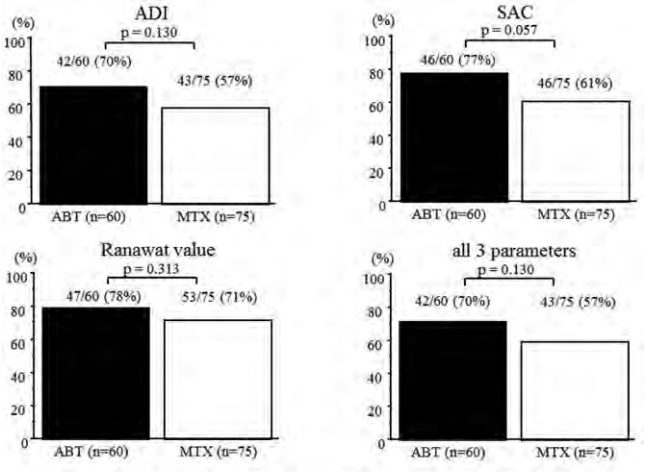


Figure 2 : The rate of patients who did not showed progression in ADI, SAC, Ranawat value and all three parameters after 2 years in the ABT and MTX patients

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THU0173

DIFFERENCES BETWEEN PATIENT-REPORTED AND PHYSICIAN-REPORTED ADVERSE DRUG REACTIONS ATTRIBUTED TO BDMARDS

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Background: Patient registries are a valuable tool to monitor a patient's health status. However, these systems operate primarily from the healthcare provider (HCP) perspective, which makes it difficult to collect detailed information on the nature, frequency and personal impact of adverse drug reactions (ADRs).

Objectives: Determining whether the distribution of patient-reported ADRs attributed to bDMARDs differs from ADR registrations by HCPs.

Methods: Patient reported ADRs were derived from the Dutch Biologic Monitor (DBM), a multi-centre cohort event monitoring system based on web-based questionnaires for bDMARD-using patients. ADR reports of the Dutch Rheumatic Arthritis Monitoring Registry (DREAM-RA) were used to outline the HCP perspective. ADR reports from foundation up to 31 October 2019 were coded according to MedDRA terminology. Fisher-Freeman-Halton test with Monte Carlo simulation was used to measure discrepancies between the distributions of High Level Group Terms (HLGT). The prevalence of the top 15 HLGTs were compared using Chi-Square Goodness-of-Fit tests.

Results: ADR reports of 404 DBM participants (1,977 ADRs) and 341 DREAM-RA patients (679 ADRs) were analysed. Patients and HCPs reported a different ADR distribution (p<.001). Administration site reactions were most frequently reported by patients, followed by infections and (epi)dermal conditions. HCPs most often reported (epi)dermal conditions, infections and general system disorders. Moreover, the distribution of ADRs that patients allegedly discussed with HCPs varied considerably from the distribution of HCP-reported ADRs (p<.001).

Table 1. Patient characteristics

	Dutch Biologic Monitor *n=404*	DREAM-RA *n=341*
Age, median (IQR), years	57.0 (49.0-65.0)	56.0 (46.0-65.0)
Female, n (%)	279 (73.5)	240 (70.4)
Indication for bDMARD therapy, n (%)		
Rheumatoid arthritis	299 (74.0)	381 (89.4)
Psoriatic arthritis	105 (26.0)	45 (10.6)
bDMARD use, n (%)		
Etanercept	164 (40.6)	152 (34.9)
Adalimumab	134 (33.2)	119 (44.6)
Tocilizumab	32 (7.9)	48 (14.1)
Other	100 (24.8)	107 (31.4)

Conclusion: Patients and HCPs report a different distribution of ADRs attributed to bDMARDs. Therefore, patient-reported ADRs should ideally be combined with HCP reports, as the combination of both perspectives gives a more complete picture of a patient's health status.

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THU0174

ANTI-IL-6 RECEPTOR ANTIBODY AMELIORATES DISEASE ACTIVITY OF RHEUMATOID ARTHRITIS PATIENTS WITH KNEE JOINT INVOLVEMENT -ANSWER COHORT STUDY-

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Background: It has been reported that rheumatoid arthritis (RA) patients who have large joint involvement associated with higher serological inflammatory markers and more functional disability[1]. Moreover, a previous report showed that these patients were more difficult to achieve clinical remission. However, it remains unclear which biologics are effective in the patients with RA who have large joint involvement.
Objectives: The aim of this study is to investigate the efficacy of anti-IL-6 receptor antibody (aIL-6) or TNF-inhibitor (TNFi) in the treatment of RA patients who have knee joint involvement.
Methods: We enrolled the 784 patients who visited our hospitals in 2003 to 2019 and were treated with aIL-6 or TNFi more than 12 weeks. We divided the patients into 2 groups with or without knee joint involvement for further analysis. Knee joint involvement was defined as the patients had at least one swelling joint of knee at baseline. We investigated the CDAI levels at baseline and 12 weeks after the initiation of biologics.
Results: Interestingly, the patients who had knee joint involvement with aIL-6 significantly ameliorated ΔCDAI (n=95, 15.0±10.8; mean±SD) compared to those with TNFi (n=148, 11.4±10.3) at 12 weeks (P=0.003). aIL-6 group consists of 95 tocilizumab treated patients. TNFi group includes 25 adalimumab, 25 certolizumab pegol, 14 etanercept, 54 golimumab and 30 infliximab treated patients. Baseline clinical characteristics of the 243 RA patients who had knee joint involvement were shown in Table 1. Mean ages, sex and disease durations were not significantly different between the two groups. Baseline CDAI levels of aIL-6 group (24.8±11.8) were slightly elevated compared to those of TNFi group (21.7 ±10.9). Multivariate analysis adjusted for age, gender and baseline CDAI levels revealed that aIL-6 significantly improved ΔCDAI levels compared to TNFi (P=0.04). By contrast, in the RA patients who had no swelling of knee joints, there was no significant difference of ΔCDAI improvement between aIL-6 group (n=156, 5.5±7.4) and TNFi group (n=385, 6.7±8.9).
Conclusion: Thus, these findings suggest that anti-IL-6 receptor antibody was more effective in the RA patients with knee joint involvement compared to TNF- inhibitor.
References:
[1] Burgers LE, et al.Ann Rheum Dis. 2018;77:e33.
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THU0175 REAL-WORLD EXPERIENCE OF SWITCHING FROM ORIGINATOR TO BIOSIMILAR RITUXIMAB IN RHEUMATOID ARTHRITIS

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Background: Pre-clinical and trial data confirm biosimilar rituximab (RTX-B) has equivalent physicochemical properties, function, efficacy and safety as originator (RTX-O)[1,2]. However, real-world data are lacking, including non-medical switch to RTX-B in patients established on RTX-O. Loss of response (LOR) has been observed following open-label switch to other biosimilars[3], and it is unclear how patients who develop LOR after switching should be managed.
Objectives: To describe our real-world experience of non-medical switch from RTX-O to RTX-B in RA and explore treatment strategies for patients developing LOR to RTX-B (switch back to RTX-O versus other b/tsDMARDs).
Methods: We conducted a retrospective observational study of RTX-treated RA patients in Leeds from May 2002–Jan 2020. From Oct 2017, all patients on

Table 1. Baseline clinical characteristics of 243 RA patients who had knee joint involvement

	aIL-6 group (n=95)	TNFi group (n=148)	p Value
Age (mean±SD)	60.7±15.2	61.9±14.4	0.58
Gender (female, %)	80.0	79.1	0.97
Duration (year)	9.3 ±10.3	8.4±10.5	0.56
DAS28ESR (mean±SD)	5.3±1.2	5.2 ±4.8	0.03
CDAI (mean ±SD)	24.8±11.8	21.7 ±10.9	0.04
MTX use, (%)	45.4	62.2	0.02
MTX dose (mg/day)	8.7 ±3.3	9.0 ±3.5	0.61
PSL use, (%)	44.3	45.6	0.74
PSL dose (mg/day)	5.5 ±3.5	5.1 ±2.9	0.55

Table 2. Distribution of patient-and HCP-reported ADRs

	Patient			HCP	p-value	
High Level Group Term	*Burden (1-5)*	*Reports (%)*	*HCP contact (%)*	*Reports (%)*	*All patient vs HCP reports*	*HCP contact vs HCP reports*
Administration site reactions	1.7	402 (20.3)	93 (11.1)	20 (2.9)	<.001	<.001
Infections - pathogen unspecified	2.9	229 (11.6)	130 (15.5)	93 (13.7)	0.153	0.344
Epidermal and dermal conditions	2.6	218 (11.0)	96 (11.4)	111 (16.3)	<.001	0.007
General system disorders NEC	2.8	175 (8.9)	82 (9.8)	52 (7.7)	0.382	0.172
Gastrointestinal signs and symptoms	2.4	81 (4.1)	17 (2.0)	29 (4.3)	0.824	0.015
Respiratory disorders NEC	2.4	77 (3.9)	33 (3.9)	26 (3.8)	1.0	1.0
Headaches	2.9	55 (2.8)	23 (2.7)	19 (2.8)	1.0	1.0
Joint disorders	3.3	55 (2.8)	32 (3.8)	3 (0.4)	0.093	0.006
Respiratory tract signs and symptoms	2.2	47 (2.4)	22 (2.6)	7 (1.0)	0.039	0.036
Skin appendage conditions	3.0	44 (2.2)	14 (1.7)	12 (1.8)	0.538	1.0
Musculoskeletal and connective tissue disorders NEC	3.1	40 (2.0)	16 (1.9)	4 (0.6)	0.009	0.039
Oral soft tissue conditions	2.4	33 (1.7)	12 (1.4)	7 (1.0)	0.277	0.644
Gastrointestinal motility and defaecation conditions	2.6	29 (1.5)	12 (1.4)	16 (2.4)	0.123	0.186
Ocular infections, irritations and inflammations	3.1	29 (1.5)	22 (2.6)	4 (0.6)	0.106	0.002
Therapeutic and nontherapeutic effects (excl toxicity)	2.9	27 (1.4)	16 (1.9)	3 (0.4)	0.057	0.010
Other	2.9	436 (22.1)	221 (26.3)	273 (40.2)	<.001	<.001

RTX-O were switched to RTX-B unless specified by treating clinician or informed consent not obtained. Demographic and clinical data were collected from electronic health records. Effectiveness was assessed by DAS28-CRP and RTX retention (using Kaplan-Meier method). Changes in treatment were based on clinician judgment.

Results: 944 patients with RA received ≥1 cycle of RTX in Leeds over the past 17 years. Of these, 358 required RTX re-treatment during the study period (Oct 2017–Jan 2020); 263 (73.5%) switched to RTX-B, whilst 95 (26.5%) remained on RTX-O (medical reason=46.3%; patient decision=53.7%). 256/263 patients on RTX-B with 4-month data were analysed. 201/256 (78.5%) were female, mean (SD) age 63.1 (12.4), 97.7% seropositive, 81.6% on csDMARD (62.9% methotrexate), 14.8% oral steroid, 58.6% had previous bDMARDs, and mean (SD) RTX-O cycles pre-switch was 6 (3.6). Total follow-up was 378 patient-years. Mean (SD) DAS28-CRP was 3.01 (1.17) 4 months post-last cycle RTX-O and 3.32 (1.31) post-switch to RTX-B (mean diff +0.30, 95% CI 0.004-0.60; p=0.047), with increase in VAS (+5.7, 95% CI 0.09-11.37; p=0.047), but not SJC, TJC or CRP. At last follow-up, 185/256 (72.3%) patients remained on RTX-B [median (range) RTX-B cycles 2 (1-4)]. RTX-B retention rate estimates were 79.4% and 71.3% at 12 and 18 months respectively. Following RTX-B discontinuation, 33/256 patients (12.8%) switched back to RTX-O [LOR=30 (11.7%), adverse effects (AEs)=3 (1.2%)], 13/256 (5.1%) started other b/tsDMARDs, and 25/256 (9.7%) stopped treatment (no longer indicated=7, deaths=7, loss to follow-up=6, patient choice=3, new contraindication=2). Of 46 patients with LOR/AE to RTX-B, 39 discontinued after cycle 1 (C1), 5 after C2 and 2 after C3. 31/33 patients switched back to RTX-O remained on treatment but follow-up was limited [mean (SD) 7.5 (5.2) months; 23/33 had 1 cycle only]. Compared with patients treated with other b/tsDMARDs, those switched back to RTX-O had more previous RTX-O cycles [mean (SD) 6.67 (3.28) versus 2.62 (2.10); p<0.0001]. Compared with patients who remained on RTX-B (n=185), those who discontinued for LOR/AE/death (n=53) had more previous bDMARDs (mean 1.26 vs 0.83; difference 0.43, 95% CI 0.10-0.77, p=0.01), but no differences in other clinical characteristics, treatment or B-cell numbers.

Conclusion: Our real-world single-centre experience of non-medical switch from RTX-O to RTX-B in RA showed approx. three quarters of patients remained on RTX-B and maintained stable disease activity. However, apparent LOR occurred in 16%. Of >10% switched back to RTX-O, the majority remained on treatment at short-term follow-up.

References:

[1] Lee at al, MAbs 2018.
[2] Shim et al, Rheumatology 2019.
[3] Tweehuysen et al, AR 2018.

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THU0176 OLOKIZUMAB IMPROVES PATIENT REPORTED OUTCOMES IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE RHEUMATOID ARTHRITIS INADEQUATELY CONTROLLED BY METHOTREXATE: RESULTS FROM THE DOUBLE-BLIND, RANDOMIZED CONTROLLED PHASE III STUDY (CREDO-1)

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Background: We previously reported positive efficacy and safety results of olokizumab (OKZ), an interleukin-6-inhibitor, in patients with Rheumatoid Arthritis (RA) inadequately controlled by methotrexate (MTX) (NCT02760368; CREDO-1)[1]. Here we present the patient reported outcomes (PRO) of CREDO-1 study.

Objectives: To assess the effect of OKZ treatment comparing to placebo (PBO) on quality of life, work productivity, and fatigue in patients with moderate to severe RA who have previously failed MTX therapy.

Methods: We compared PRO between three groups 1) subcutaneous injections of OKZ 64 mg every 2 weeks (q2w), 2) OKZ 64 mg every 4 weeks (q4w) and 3) PBO every q2w.

PRO included change from baseline in: Health Assessment Questionnaire-Disability Index (HAQ-DI); Patient's Global Assessment of Disease Activity (PtGA), Patient's Assessment of Arthritis Pain (Pain), Short Form-36 (SF-36) Physical (PCS) and Mental (MCS) components; European Quality of Life- Five-Dimension Questionnaire (EQ-5D), Functional Assessment of Chronic Illness Therapy-Fatigue Scale (FACIT-F) and Work Productivity Survey-Rheumatoid Arthritis (WPS-RA).

Results: 428 patients were enrolled and 396 completed the study. All PRO baseline characteristics were comparable across treatment arms: mean (SD) PtGA was 69.5 (15.5); Pain was 68.6 (17.5); HAQ-DI was 1.7 (0.5); SF-36 PCS was 32.1 (6.5); SF-36 MCS was 42.3 (10.0); EQ-5D was 40.3 (20.0) and FACIT-F was 26.8 (8.7).

Treatment with OKZ 64 mg q2w and 64 mg q4w resulted in significant improvement in PRO measures (Table 1). Improvements in all PRO measures observed at week 12 were persistent up to week 24.

Table 1. Changes from baseline at 12 week and 24 week for PRO measures

Score, LSM change from baseline (SE) LSM difference vs PBO 97.5% CI for LSM difference	**Week 12**		**Week 24**	
	OKZ q2w (n=143)	**OKZ q4w** (n=142)	**OKZ q2w** (n=143)	**OKZ q4w** (n=142)
PtGA	**-30.6** (1.72) -17.5 -23.0, -12.0	**-31.0** (1.73) -17.9 -23.4, -12.4	**-32.1** (1.92) -12.7 -18.8, -6.6	**-36.3** (1.96) -16.8 -23.0, -10.6
Pain	**-31.6** (1.82) -18.7 -24.6, -12.9	**-31.8** (1.83) -19.0 -24.8, -13.1	**-34.5** (2.05) -13.0 -19.5, -6.5	**-37.1** (2.08) -15.7 -22.3, -9.1
HAQ-DI†	**-0.54** (0.04) -0.34*** -0.47, -0.21	**-0.56** (0.04) -0.36*** -0.49, -0.23	**-0.55** (0.05) -0.27 -0.43, -0.12	**-0.65** (0.05) -0.37 -0.53, -0.22
SF-36 PCS	**6.72** (0.57) 4.53 2.72, 6.33	**6.03** (0.57) 3.84 2.01, 5.67	**7.84** (0.67) 4.30 2.19, 6.41	**8.73** (0.68) 5.20 3.04, 7.35
SF-36 MCS	**6.48** (0.73) 3.01 0.69, 5.33	**7.04** (0.73) 3.57 1.23, 5.92	**6.21** (0.79) 3.72 1.23, 6.22	**8.86** (0.80) 6.37 3.82, 8.92
EQ-5D Health Today Score	**19.7** (1.69) 12.2 6.8, 17.6	**18.7** (1.72) 11.2 5.8, 16.7	**20.9** (1.95) 12.6 6.5, 18.7	**23.6** (2.01) 15.3 8.9, 21.7
FACIT-F	**8.2** (0.67) 4.6 2.4, 6.8	**8.7** (0.68) 5.1 2.9, 7.3	**8.5** (0.80) 4.8 2.3, 7.3	**10.6** (0.81) 6.9 4.3, 9.5

†, secondary endpoint; *** P‹0.0001.

PRO changes were analyzed using ANCOVA model adjusted for the baseline value of the corresponding parameter. Missing data resulted from study withdrawal imputed based on the return to baseline assumption.

Mean improvements in both OKZ groups over PBO for PtGA, Pain, HAQ-DI, SF-36 PCS and MCS, and FACIT-F surpassed defined MCIDs for these measures. No notable differences in PRO measures were observed between the two dose regimens of OKZ.

Conclusion:

1. Treatment with OKZ over a 24-week period was associated with significant improvements in PRO in patients with moderate to severe RA.
2. There were no discernible differences between the two regimens of OKZ from patient's perspective.

References:

[1] Nasonov E.et al. Arthritis Rheumatol. 2019; 71 (suppl 10).

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Genentech/Roche, Gilead Sciences, Inc., GSK, Novartis, RPharm, Sanofi Genzyme
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THU0177

DURABILITY OF RESPONSE AMONG PATIENTS WITH RHEUMATOID ARTHRITIS INITIATING TOCILIZUMAB: DATA FROM THE US-BASED CORRONA RHEUMATOID ARTHRITIS REGISTRY

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Background: Understanding the durability of response to biologics and factors associated with failure to maintain response in a real-world setting can inform treatment decisions for patients with rheumatoid arthritis (RA).

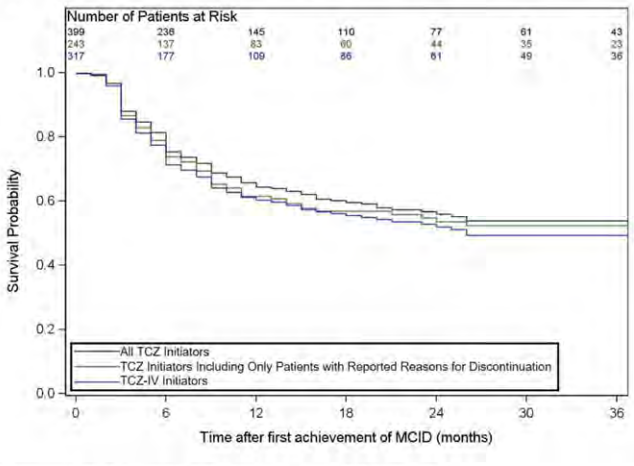
Objectives: To evaluate the durability of response and identify factors associated with decreased durability in US patients with RA initiating tocilizumab (TCZ) in routine clinical practice.

Methods: TCZ-naïve patients enrolled in the Corrona RA registry who initiated TCZ (subcutaneous [SC] or intravenous [IV]) after January 1, 2010 and had ≥1 follow-up visit were included. Durability of response was defined as maintaining continuous TCZ and: (a) a minimum clinically important difference (MCID) in clinical disease activity index (CDAI) (defined as an improvement in CDAI compared to baseline of: ≥2 if baseline CDAI ≤10; ≥6 if baseline >10 to ≤22; ≥11 if baseline >22) or (b) low disease activity (LDA; CDAI ≤10). Patient response was no longer durable upon the first: discontinuation of TCZ or failure to maintain MCID or LDA. Secondary analyses estimated durability after including only patients: (a) with reported reasons for discontinuation (patients with non-medical reasons for discontinuation [eg, insurance coverage] were censored) or (b) who initiated TCZ-IV. Durability was calculated with Kaplan-Meier survival analysis. Cox proportional hazards modeling identified factors associated with durability.

Results: A total of 1789 TCZ initiators (TCZ-IV, n=1284) were identified; 861, 483, and 298 patients were persistent and had follow-up visits at 1, 2, and 3 years, respectively. At baseline, the mean (SD) age was 58.5 (12.6) years, duration of RA was 12.0 (9.6) years and CDAI score was 23.2 (14.2). Most patients (93.4%) had prior biologic use and 67.4% had received ≥2 prior biologics. Among patients with follow-up data available at 1, 2 and 3 years, MCID in CDAI was achieved by 56.3% (261/464), 67.3% (183/272) and 69.8% (113/162), respectively. Overall, MCID durability remained above 50% after 36 months of follow-up, and the same is true when including only patients with reported reasons for discontinuation (**Fig 1**). For TCZ-IV initiators, median MCID durability was 26 months (**Fig 1**). For all MCID durability analyses, factors associated with reduced hazard of failure included increased duration of RA and higher baseline CDAI, while higher hazard of failure was associated with history of malignancy or diabetes (**Fig 2**). Among patients with follow-up data available, LDA was achieved in 53.7% (249/464), 60.3% (164/272) and 67.3% (109/162) at 1, 2 and 3 years, respectively. The overall median (95% CI) LDA durability was 13.0 (12.0, 20.0) months; when including only patients with reported reasons for discontinuation it was 13.0 (9.0, 29.0) months; among TCZ-IV initiators it was 13.0 (10.0, 19.0) months. Factors associated with an increased hazard of failing to maintain LDA included history of malignancy and, in contrast to MCID, higher baseline CDAI.

Conclusion: In this real-world RA population who initiated TCZ, most patients received ≥2 prior biologics. Median durability of response (MCID) was >3 years. Among factors associated with shorter durability of response, history of malignancy was significant in all analyses.

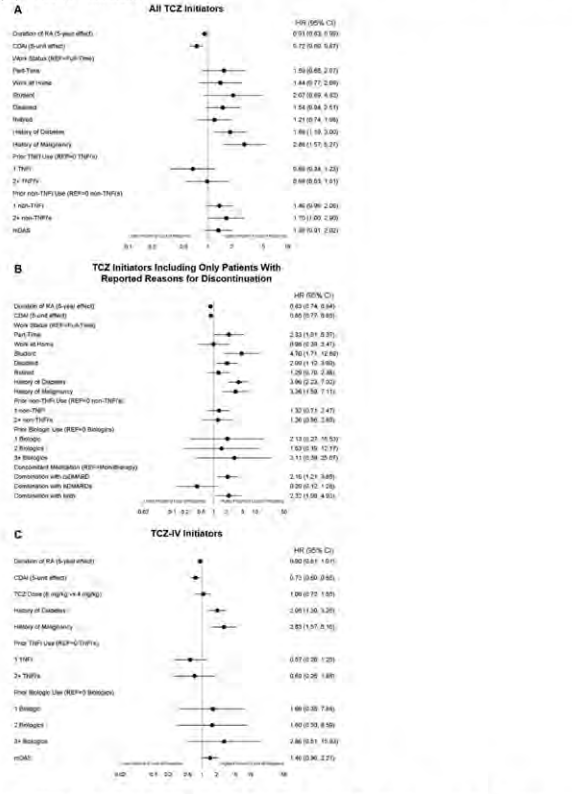
Figure 1. Kaplan-Meier Plots of MCID Durability of Response



IV, intravenous; MCID, minimum clinically important difference; TCZ, tocilizumab.

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Figure 2. Estimated Effects of Covariates on MCID Durability of Response Among (A) All TCZ Initiators, (B) Including Only Patients With Reported Reasons for Discontinuation and (C) TCZ-IV Initiators



bDMARD, biologic disease-modifying antirheumatic drug; CDAI, clinical disease activity index; csDMARD, conventional synthetic disease-modifying antirheumatic drug; IV, intravenous; MCID, minimum clinically important difference; mDAS, modified disease activity score; RA, rheumatoid arthritis; Ref, reference; TCZ, tocilizumab; TNFi, tumor necrosis factor inhibitor.

Disclosure of Interests: Dimitrios A Pappas: None declared, Taylor Blachley Employee of: Corrona, LLC, Jennie H. Best Shareholder of: Genentech, Inc., Employee of: Genentech, Inc., Steve Zlotnick Shareholder of: Genentech, Inc., Employee of: Genentech, Inc., William Reiss Shareholder of: Genentech, Inc., Employee of: Genentech, Inc., Kelechi Emeanuru Employee of: Corrona, LLC – employment, Joel M Kremer Shareholder of: May own stocks and opinions, Grant/research support from: Research and consulting fees from AbbVie Inc., Consultant of: AbbVie, Amgen, BMS, Genentech, Inc.,

Gilead, GSK, Lilly, Pfizer, Regeneron and Sanofi, Employee of: Corrona, LLC employee

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THU0178 PREDICTORS OF BIOLOGIC DISEASE MODIFYING ANTI-RHEUMATIC DRUG INITIATION AMONG PATIENTS WITH RHEUMATOID ARTHRITIS IN KOREA

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Background: Biological disease-modifying anti-rheumatic drugs (bDMARDs) have significantly improved clinical prospects for patients with rheumatoid arthritis (RA).

Objectives: To identify predictors of bDMARDs initiation in RA patients.

Methods: Using 2002-2016 Korea National Health Insurance Service database, we conducted a nested case-control study on RA patients. Four conventional DMARD (cDMARD) users were selected by risk set sampling per each bDMARD user, matched on the calendar year/month of RA diagnosis. Potential predictors were separately assessed for two periods, 1 year after RA diagnosis and 1 year prior to bDMARD initiation, by logistic regression analyses estimating odds ratio (OR) and 95% confidence interval (CI).

Results: The study included 27,940 cDMARD users and 6,985 bDMARD users. Younger age, initial use of a less potent cDMARD (sulfasalazine), corticosteroid use, and higher maximal methotrexate (MTX) dose during 1 year post-diagnosis were positive predictors for later bDMARD initiation, while male gender, initial use of a potent cDMARD (MTX, leflunomide, or tacrolimus), initial MTX dose of ≥10mg/wk, and initial cDMARD combination were negative predictors (Table 1). Use of non-MTX DMARDs (leflunomide, sulfasalazine, or tacrolimus), higher # of cDMARD used, subcutaneous administration of MTX, corticosteroid therapy, and higher maximal MTX dose were positive predictors of subsequent bDMARD. Although higher comorbidity score during 1 year before bDMARD initiation was a positive predictor, the effect was heterogenous by involved systems (Table 2).

Table 1. Predictors of bDMARD initiation among RA patients during 1-year post-diagnosis

Predictors	OR	(95% CI)	P-value
Age (/1 year)	0.977	(0.974-0.980)	<0.001
Sex (male vs. female)	0.850	(0.787-0.918)	<0.001
1st cDMARD at RA diagnosis (yes vs. no)			
Methotrexate	0.540	(0.476-0.614)	<0.001
Leflunomide	0.463	(0.388-0.552)	<0.001
Sulfasalazine	1.305	(1.197-1.424)	<0.001
Tacrolimus	0.181	(0.083-0.395)	<0.001
Initial MTX dose (≥10mg/week vs. <10mg/week)	0.539	(0.506-0.575)	<0.001
Initial cDMARD combination (yes vs. no)	0.621	(0.530-0.727)	<0.001
Subcutaneous MTX use (yes vs. no)	1.456	(1.156-1.834)	0.001
Maximal MTX dose (/1mg)	1.012	(1.008-1.016)	<0.001
Corticosteroids use (yes vs. no)	2.805	(2.345-3.355)	<0.001

Table 2. Predictors of bDMARD initiation among RA patients during 1-year prior to bDMARD initiation

Predictors	OR	(95% CI)	P-value
Age (/1 year)	0.970	(0.967-0.974)	<0.001
Non-MTX cDMARD use (yes vs. no)[1]			
Leflunomide	1.765	(1.573-1.980)	<0.001
Sulfasalazine	1.465	(1.297-1.654)	<0.001
Tacrolimus	2.070	(1.796-2.387)	<0.001
Subcutaneous MTX use (yes vs. no)	1.731	(1.577-1.900)	<0.001
Maximal MTX dose (/1mg)	2.568	(1.921-3.433)	<0.001
Glucocorticoid use (yes vs. no)	1.015	(1.010-1.021)	<0.001
Comorbidity index (/1 point)	1.124	(1.076-1.175)	<0.001
Individual comorbidities (yes vs. no)			
Stroke/ transient ischemic attack	0.764	(0.626-0.932)	0.008
Atrial fibrillation	0.666	(0.455-0.973)	0.036
Diabetes mellitus	1.208	(1.076-1.356)	0.001
Joint replacement therapy	1.788	(1.341-2.384)	<0.001
Hepatitis B infection	1.559	(1.238-1.964)	<0.001
Hepatitis C infection	2.117	(1.532-2.925)	<0.001
Chronic obstructive pulmonary disease	1.118	(1.012-1.234)	0.028

[1]MTX was excluded since all bDMARD initiators were required to use MTX before bDMARD initiation.

Conclusion: In this population-based nationwide study, we identified period-specific predictors of bDMARD initiation among RA patients in Korea. Overall, initial aggressive RA treatment after RA diagnosis were associated with less use of later bDMARD, while highly intensive therapy observed just before bDMARD initiation reflects refractory nature of RA during this period.

Disclosure of Interests: None declared

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THU0179 PERSISTENCE IN RHEUMATOID ARTHRITIS PATIENTS ON BIOSIMILAR AND BIO-ORIGINATOR ETANERCEPT: A POOLED ANALYSIS OF PAN-CANADIAN COHORTS

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Background: Biosimilar etanercept (ETA-B) was recently introduced in Canada but real-world data descriptions of drug persistence (and comparisons with the originator product, ETA-O) are still scarce.

Objectives: To describe and compare persistence of ETA-B and ETA-O in RA.

Methods: We used data from four ongoing, prospective cohorts in Canada: the Canadian Early Arthritis Cohort (CATCH), the Rheumatoid Arthritis Pharmacovigilance Program and Outcomes Research in Therapeutics (RAPPORT), the Early Undifferentiated Polyarthritis (EUPA) cohort, and the RHUMADATA® registry. We studied biologic-naïve and biologic-experienced RA adults initiating ETA-B or ETA-O between Jan. 2015 and Oct. 2019. Switchers from ETA-O to ETA-B (or vice-versa) were included. We assessed persistence of therapy in the first 12 or 24 months, measured as time from therapy initiation (time zero) to discontinuation. Individuals switching between products could contribute further person-time to the new exposure category. Multivariable Cox regression models were performed with each cohort dataset separately, following a common protocol. Model variables included age, sex, comorbidity, past biologic use, and disease duration. After testing for between-study heterogeneity (Higgin's I2), cohort-estimated hazard ratios (HR) were pooled using random effects meta-analysis.

Results: We identified 262 episodes of etanercept use (118 ETA-B and 144 ETA-O) from 250 RA patients. Sex, age, and other baseline characteristics across the four cohorts are shown in Table 1. Across cohorts, there was considerable variation in RA duration at the time of initiating ETA-B or ETA-O. In the pooled analysis, the HR for discontinuation at 24 months comparing ETA-B to ETA-O was 0.51 (95% confidence interval, CI: 0.26-0.98). The pooled analysis for therapy discontinuation at 12 months adjusted HR in this analysis was 0.82 (95% CI: 0.42-1.60).

Conclusion: Despite wide confidence intervals, the 24-month data suggested potential better persistence with ETA-B versus ETA-O, with a similar trend at 12 months. Some of the observed associations may be related to residual confounding (e.g. disease activity, time-dependent effects of concomitant medications) and/or survivorship bias (in patients transitioning from ETA-O to ETA-B).

Disclosure of Interests: Cristiano S Moura: None declared, Denis Choquette Grant/research support from: Rhumadata is supported by grants from Pfizer, Amgen, Abbvie, Gylead, BMS, Novartis, Sandoz, eli Lilly,, Consultant of: Pfizer, Amgen, Abbvie, Gylead, BMS, Novartis, Sandoz, eli Lilly,, Speakers bureau: Pfizer, Amgen, Abbvie, Gylead, BMS, Novartis, Sandoz, eli Lilly,, Louis Coupal: None declared, Orit Schieir: None declared, Marie-France Valois: None declared, Vivian Bykerk: None declared, Gilles Boire Grant/research support from: Merck Canada (Registry of biologices, Improvement of comorbidity surveillance)
Amgen Canada (CATCH, clinical nurse)
Abbvie (CATCH, clinical nurse)
Pfizer (CATCH, Registry of biologics, Clinical nurse)
Hoffman-LaRoche (CATCH)
UCB Canada (CATCH, Clinical nurse)
BMS (CATCH, Clinical nurse, Observational Study Protocol IM101664. SEROPOSITIVITY IN A LARGE CANADIAN OBSERVATIONAL COHORT)
Janssen (CATCH)

Table 1. Characteristics of studied patients according to their treatment episodes, biosimilar etanercept (ETA-B) or bio-originator etanercept (ETA-O).

Characteristic	EUPA		RAPPORT		RHUMADATA		CATCH	
	ETA-B	ETA-O	ETA-B	ETA-O	ETA-B	ETA-O	ETA-B	ETA-O
	N=19	N=27	N=32	N=30	N=39	N=52	N=28	N=35
Female sex, (%)	12 (63)	18 (67)	20 (63)	22 (73)	28 (72)	38 (73)	20 (71)	27 (77)
Mean age in years[1], SD	59 (13)	59 (16)	51 (15)	54 (15)	59 (15)	54 (15)	55 (12)	51 (13)
Current smoker, (%)	3 (17)	5 (21)	9 (32)	5 (19)	8 (21)	9 (17)	5 (18)	8 (23)
Cardiovascular disease, (%)	0 (0)	0 (0)	1 (3.1)	1 (3.3)	8 (21)	2 (4)	NA	NA
Diabetes, (%)	0 (0)	0 (0)	4 (13)	1 (3)	2 (5)	3 (6)	NA	NA
Hypertension, (%)	NA	NA	5 (16)	4 (13)	14 (36)	22 (42)	NA	NA
RA duration in years[1], SD	2 (3)	7 (13)	8 (6)	12 (15)	12 (12)	9 (9)	4 (4)	3 (3)
DAS-28[1]	2 (NA)	4 (2.8)	6 (1)	6 (1)	4 (2)	4 (1)	4.0 (2)	4 (2)
SDAI[1]	13 (14)	44 (5)	NA	NA	21 (15)	23 (8)	23 (14)	25 (16)
Past oral steroids, N(%)								
Past biologic, N(%)	15 (79)	17 (63)	6 (19)	4 (13)	29 (74)	31 (60)	9 (32)	13 (37)
Past non-biologic DMARD, N(%)	8 (42)	6 (22)	2 (6)	0 (0)	21 (54)	20 (38)	19 (68)	21 (60)
	19 (100)	27 (100)	30 (94)	26 (87)	39 (100)	52(100)	25 (89)	33 (94)

[1] At time zero or at the closest date before time zero. SD=standard deviation

Celgene (Clinical nurse)
Eli Lilly (Registry of biologics, Clinical nurse), Consultant of: Eli Lilly, Janssen, Novartis, Pfizer, Speakers bureau: Merck, BMS, Pfizer, Walter P Maksymowych Grant/research support from: Received research and/or educational grants from Abbvie, Novartis, Pfizer, UCB, Consultant of: WPM is Chief Medical Officer of CARE Arthritis Limited, has received consultant/participated in advisory boards for Abbvie, Boehringer, Celgene, Eli-Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, UCB, Speakers bureau: Received speaker fees from Abbvie, Janssen, Novartis, Pfizer, UCB., Sasha Bernatsky: None declared
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THU0180

RISK MODIFICATION OF TUBERCULOSIS INFECTION BY CHEMOPROPHYLAXIS AMONG PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING TNF INHIBITORS: A NATION-WIDE COHORT STUDY

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Background: Based on the benefit of chemoprophylaxis among patients receiving biologics [1], Health Insurance Review and Assessment (HIRA) service of Korea requires patients to undergo latent tuberculosis (LT) screening before initiation of any biologics and to receive chemoprophylaxis for positive LT.

Objectives: To assess the effect of chemoprophylaxis on tuberculosis infection (TI) risk among patients with rheumatoid arthritis (RA) receiving biologics in Korea

Methods: Using 2002-2016 Korea National Health Insurance database, we conducted a cohort study on RA patients initiating biologic drugs (TNF inhibitors, abatacept, tocilizumab) to compare TI risk between those who started isoniazid and/or rifampin within 1 year before biologics initiation (prophylaxis group) versus those who did not (non-prophylaxis group). TI was defined by ICD10 codes plus anti-tuberculosis medications as previously described [2]. Patients were followed-up from biologics initiation to censoring events (TI occurrence, death, biologics discontinuation, initiation of anti-tuberculosis drug due to non-TI cause, and end of database). To control >50 baseline confounders, we used propensity score (PS)-based fine stratification and weighting. A weighted Cox proportional hazards model estimated hazard ratios (HRs) and 95% confidence intervals (CIs).

Results: Before PS stratification (PSS) and weighting, we identified 2,250 and 7,259 RA patients for prophylaxis and non-prophylaxis group, respectively. Mean age was 57.6 years and 81.3% female. Three-fourths of patients in the prophylaxis group completed >70% of recommended treatment periods [3]. The incidence rate of TI per 100 person-years was 0.33 for prophylaxis group versus 0.57 for non-prophylaxis group. 28% of all TI cases (n=34) were extra-pulmonary with gastrointestinal (n=11) and miliary TI (n=9) being most common. The PSS-weighted HR (95% CI) of TI comparing prophylaxis versus non-prophylaxis group was 0.52 (0.32-0.86) (Table 1, Figure 1). Sensitivity analyses showed that the chemoprophylaxis was particularly effective for those with younger age (<65 years), male gender, or high comorbidity (≥ median value) (Table 1).

Table 1. Comparative risk of tuberculosis infection between prophylaxis versus non-prophylaxis group

		Crude			PSS-weighted	
		N	Events	PY	IR per 100 person-years	HR (95% CI)
Primary as-treated analysis[1]						
Total	P	2,250	18	5,532	0.33	0.52 (0.32-0.86)
	NP	7,259	100	17,503	0.64	
ITT analyses[1]						
1 year ITT	P	2,250	10	2,115	0.47	0.33 (0.17-0.64)
	NP	7,259	97	6,833	1.42	
2 year ITT	P	2,250	21	3,907	0.54	0.49 (0.31-0.78)
	NP	7,259	140	12,698	1.10	
4 year ITT	P	2,250	31	6,305	0.49	0.56 (0.38-0.82)
	NP	7,259	181	21,278	0.88	
Sensitivity Analyses						
Age <65 years	P	1,751	9	4,588	0.20	0.39 (0.19-0.78)
	NP	5,345	72	13,634	0.52	
Male	P	546	2	1,319	0.15	0.12 (0.03-0.50)
	NP	1,235	28	2,624	1.33	
Comorbidity score ≥3	P	824	6	1,908	0.31	0.34 (0.15-0.79)
	NP	2,668	52	6,129	0.94	

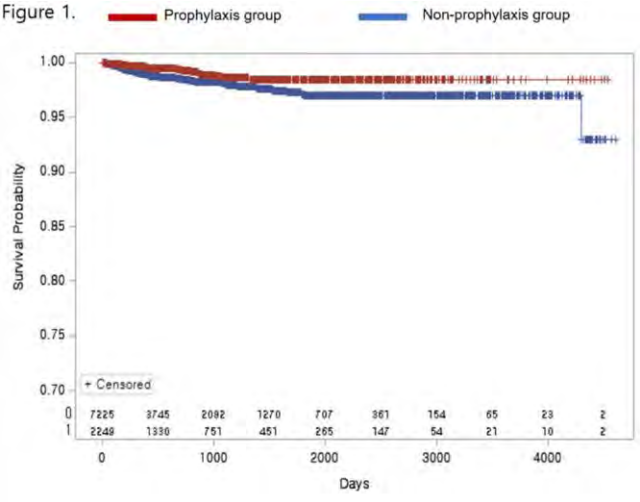
[1]As-treated analysis censored patients when they discontinued biologics use, while ITT analysis did not.
IR=incidence rate; ITT=intention-to-treat; HR=hazard ratio; PSS=propensity-score stratification; CI=confidence interval; PY=person-years; P=prophylaxis group; NP=non-prophylaxis group

Conclusion: We found 48% risk reduction of TI by chemo-prophylaxis among RA patients receiving biologics. Due to HIRA requirements, a majority of non-prophylaxis group were considered negative for LT by screening at biologics initiation [4]. These findings indicate that the risk of TI during bDMARD treatment is still high among RA patients who were negative for LT at baseline but did not undergo chemoprophylaxis, which is double the risk among RA patients who had LT and underwent chemoprophylaxis.

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Figure 1.



Disclosure of Interests: None declared
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THU0181 SOLUBLE VASCULAR BIOMARKERS IN RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDYLITIS: EFFECTS OF ONE-YEAR ANTI-TNF-A THERAPY

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Background: Rheumatoid arthritis (RA) and ankylosing spondylitis (AS) have been associated with inflammatory atherosclerosis, increased cardiovascular (CV) morbidity and mortality. Numerous proteins may serve as biomarkers of inflammatory atherosclerosis. The treatment of arthritis by tumour necrosis factor α (TNF-α) inhibitors may decrease the serum concentrations of these biomarkers.

Objectives: In this study we wished to determine circulating levels of oxidized LDL (oxLDL) - β2 glycoprotein I (β2GPI) complexes (AtherOx), anti-hsp60 antibodies, soluble urokinase plasminogen activator receptor (sUPAR) and N-terminal B-type natriuretic peptide (NT-proBNP) in sera of RA and AS patients. We also wished to assess the effects of anti-TNF treatment on these biomarkers.

Methods: Altogether 53 arthritis patients including 36 RA patients treated with either etanercept (ETN) or certolizumab pegol (CZP) and 17 AS patients treated with ETN were included in a 12-month follow-up study.Circulating oxLDL/β2gpI complexes, anti-human Hsp60 immunoglobulin G (IgG) levels and BNP_{8-29} fragment levels were assessed by ELISA. suPAR levels were assessed by suPARnostic® Quick Triage test. All laboratory assessments were performed at baseline, as well as 6 and 12 months after treatment initiation. Results were associated with DAS28, BASDAI, CRP.

Results: In the mixed cohort of 53 arthritis patients, the circulating levels of oxLDL/β2gpI significantly decreased after 12 months of anti-TNF therapy (0.20±0.11 U/ml) compared to baseline (0.24±0.10 U/ml; p=0.014). There was a tendency of non-significant decrease after 6 months (0.23±0.14 U/ml) versus baseline. Anti-Hsp60 antibody levels did not change after 6 months (158.6±138.6 AU/ml) and 12 months (167.3±143.3 AU/ml) compared to baseline (170.3±140.4 AU/ml). Among the patients, 21.2% had low, 36.4% "observe", 9.1% high and 33.3% critical suPAR levels. suPAR levels showed a tendency of non-significant decrease after 6 months (11.3±17.7 ng/ml) and 12 months (10.3±15.3 ng/ml) versus baseline (11.5±16.4 ng/ml). However, when the four serum level categories described above were considered, suPAR concentrations exerted significant decrease in RA patients with critical suPAR levels (>9ng/ml) (p=0.04). Similarly, BNP fragment levels showed only a tendency of decrease after 6 months (518.2±422.4 pmol/l) and 12 months (484.1±418.2 pmol/l) versus baseline (530.8±441.8 pmol/l). However, serum BNP levels at baseline and after 12 months were significantly increased in CCP positive compared to CCP negative RA patients (baseline: 670.6±323.0 versus 138.0±436.4 pmol/l; p=0.030 and 12 months: 652.9±283.2 versus 456.5±423.1 pmol/l; p=0.021), as well as in RF positive compared to RF negative RA patients (baseline: 680.6±381.6 versus 292.9±198.3 pmol/l; p=0.007 and 12 months: 668.9±346.5 versus 312.2±207.0 pmol/l; p=0.001).

Conclusion: One-year anti-TNF therapy significantly decreased circulating oxLDL/β2gpI complex levels. This therapy also decreased suPAR levels in patients with critically high suPAR. BNP fragment levels were associated with seropositivity in RA. These vascular biomarkers may reflect the effects of TNF inhibition on endothelial activation.

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THU0182 THE EFFECTIVENESS OF BIOLOGICAL AGENTS CONCOMITANT WITH TACROLIMUS IN RHEUMATOID ARTHRITIS

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Background: In Japan, oral tacrolimus (TAC) was approved for the treatment of RA in 2005 and the improvement of symptoms thorough the use concomitant with disease modifying antirheumatic drugs (DMARDs), including MTX has been reported[1 2]. On the other hand, the efficacy and tolerance of biological agents therapy concomitant with TAC are unknown.

Objectives: The objective of this study was to investigate the efficacy and tolerance of biological agents concomitant with TAC in Japanese patients with RA using retention rate analysis.

Methods: Total patients (n=2860) who underwent 5 biological agents (etanercept: ETN, adalimumab: ADA, golimumab:GLM, tocilizumab: TCZ, abatacept: ABT) treatment between 2003 and 2017 at Nagoya University Hospital and 12 other institutes (Tsurumai Biologics Communication Study Group) were enrolled[3]. In each biologics analysis, patients were divided into three groups: (1) concomitant only MTX (MTX group) (2) concomitant only TAC (TAC group) (3) others (others group). In TAC or MTX group, these drugs were only ones which concomitant with biologics. Kaplan-Meier analysis was used to estimate retention rate in each biologics group. To estimate the tolerance of concomitant biologics with TAC, cumulative hazard function in adverse events rate was performed in each biologics group. In both analyses, hazard ratios (HR) were assessed by Cox proportional hazards modeling adjusted for age, sex, disease duration and previously used biologics.

Results: In total 2860 patients, 142 patients (5.0%) administered each biologics concomitant with TAC (ETN: n=47, ADA: n=10 GLM: n=14, TCZ: n=27, ABT: n=49). Baseline characteristics of 142 patients were shown in table 1. Average dosages of TAC at starting were ETN: 2.2±0.7mg ADA: 2.4±1.0mg GLM: 1.9±1.0mg TCZ: 1.7±0.9mg ABT: 1.9±0.9mg. With comparison of retention rate between 3 groups in each biologics under analysis of cox proportional hazard modeling, in ETN and ABT analysis, the retention rate of TAC group was higher than others group (table 2, figure 1). Comparison of incidence of adverse event between 3 group using cumulative hazard function and cox proportional hazard modeling in ETN and ABT analysis. In ETN analysis, incident rate of other group was higher than TAC group. In ABT analysis, there was no significant difference between 3 gruops (figure 2).

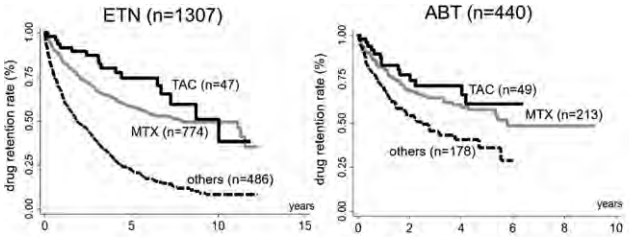


fig1: Comparison of retention rate with 3 groups (TAC, MTX, others) in ETN and ABT analysis
Adjusted confounder were baseline sex, age, disease duration, previously used biologic DMRADs

Table1

Baseline characteristic (n=142)		
age (years)		63 ± 3
gender	male	33 (23%)
	female	109 (77%)
disease duration (years)		12.0 ± 7.8
stage	1,2	34 (24%)
	3,4	108 (76%)
class	1,2	99 (70%)
	3,4	43 (30%)
naïve vs switch	naïve	71 (50%)
	switch	71 (50%)
corticosteroid use, no (%)	+	98 (75%)
	-	32 (25%)
corticosteroid dose (mg)		5.6 ± 3.2
DAS28-ESR		4.71 ± 1.55

Table 2

	HR (95%CI)/p-value									
n (MTX/TAC/others)	ETN		ADA		GLM		TCZ		ABT	
	(774/ 47/ 486)		(339/ 10/ 135)		(156/ 14/ 61)		(272/ 27/ 207)		(213/ 49/ 178)	
TAC vs others	**0.27 (0.16-0.45)**	***<0.001***	0.9 (0.37-2.20)	ns	0.46 (0.13-1.63)	ns	0.55 (0.24-1.31)	ns	**0.51 (0.26-0.97)**	***<0.05***
TAC vs MTX	0.65 (0.38-1.08)	ns	1.42 (0.61-3.31)	ns	0.83 (0.24-2.87)	ns	0.5 (0.21-1.17)	ns	0.74 (0.39-1.42)	ns
MTX vs others	**0.42 (0.35-0.50)**	***<0.001***	**0.9 (0.50-0.88)**	***<0.001***	**0.56 (0.33-0.96)**	***<0.05***	1.01 (0.78-1.57)	ns	**0.68 (0.46-0.99)**	***<0.05***

Bold italic: p<0.05 CI: confidence interval ns: not significant

Conclusion: We suspected that, in ETN and ABT treatment, combination therapy with TAC are subsequent options for treatment to RA patients, especially in whom MTX cannot be administration.

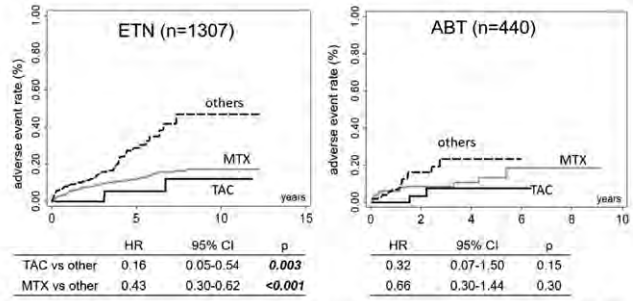


fig2: Incidence of adverse event using cox proportional hazard model in ETN and ABT analysis
Adjusted confounder were baseline sex, age, disease duration, previously used biologic DMRADs
Bold italic: p<0.05

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THU0183 ABATACEPT AND LOW GAMMA-GLOBULIN LEVELS: NO ASSOCIATION WITH INFECTIOUS RISK OR RA DISEASE ACTIVITY CONTROL

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Background: Abatacept (ABA) can induce decrease in gamma-globulins, but the long-term safety of such reduction is unknown. Moreover, it is suggested that such decrease is dissociated from disease activity response.

Objectives: To evaluate ABA-induced gamma-globulins reduction and its correlation with disease activity control and the risk of infection in rheumatoid arthritis(RA) patients.

Methods: This is a retrospective inception cohort of RA patients undergoing ABA for the first time in a large single tertiary cohort (2007 to 2019). Patients were evaluated regarding clinical and inflammatory data, total and specific (IgG, IgM, IgA) gamma-globulins assessed before, at 3 and 6 months, and then every 6 months up to discontinuation/censoring. The occurrence of severe or recurrent infections as cause of discontinuation of treatment was recorded. All patients were submitted to a systematic infectious screening protocol before and during treatment.

Results: One hundred seventy-nine RA patients were included. They were predominantly female (93%;n=167) and had a positive rheumatoid factor (RF, 84%; n=151). Median(range) age and disease duration were 55.1(17-81.3) and 14(1.6-39.8) years, respectively. ABA was used in median as the 3rd (1-8) bDMARD. Most patients (74.3%, n=134) had already used a TNFi previously and 34.1% (n=61) had failed to rituximab. Baseline DAS28 [median(range)] was 4.9 (2-8.62), CDAI 27(5-66), HAQ 1.5 (0-3), ESR 18(2-111), and CRP 8.1(0.1 -135.7). Levels of total gamma-globulins(TGG) were 1.2 (0.5-2.8g/dL), IgG 1,094(422-2,785mg/dL), IgM104(19-405 mg/dL), and IgA 324 (100-739mg/dL). Forty-five patients (25.1%) had low IgG before ABA, but only 8(4.5%) had IgG<600mg/dL and low TGG. At 3 months, remarkable decreases were observed in total gamma-globulin(1.2 *vs.*1.1g/dL), IgG(1,094*vs.*992mg/dL), IgM(104*vs.*93mg/dL), and IgA(324*vs.*302mg/dL), in comparison to baseline(p<0.05). Longitudinal measurements demonstrated that levels of gamma-globulins remained stable for subsequent evaluations(p>0.05). At baseline, TGG, IgG, IgM and IgA correlated positively to all disease activity parameters: DAS28(r=+0.33; r=+0.31;r=+0.24 and r=+0.37, respectively; p<0.02 for all), SDAI (r=+0.35; r=+0.37; r=+0.43; r=+0.34, respectively; p<0.04 for all), CDAI (r=+0.32; r=+0.29; r=+0.39; r=+0.31, respectively; p<0.03 for all, except IgA), swollen joints (r=+0.24; r=+0.23; p<0.01 only for TGG and IgG, respectively); tender joints (r=+0.18; r=+0.21; p<0.04 only for IgG and IgM respectively), ESR (r=+0.35; r=+0.24; r=+0.41; p<0.02 for TGG, IgG and IgA, respectively) and CRP (r=+0.20; r=+0.16; r=+0.27; p<0.05 for TGG, IgG and IgA, respectively). Longitudinally, most of these correlations were lost(p>0.05). Moreover, at 6 months, 25 patients (14%) achieved DAS28 ≤ 2.6 and 49 (27.4%) had low disease activity (DAS28 ≤ 3.2). Baseline or longitudinal measures of TTG and subtypes were similar among patients who responded and those who did not, regardless of the cut-off used(p>0.05. Only 14 patients (9.4%) had the medication discontinued due to infections: 3 due to recurrent infections and 11 to severe infections. One patient died. The frequencies of low IgG (under the normal limit of normality) at baseline and all time points(p>0.05) were similar among patients with and without severe/recurrent infections. None of these patients had low TGG or very low IgG(<600mg/dL) at baseline or during treatment and the levels of TGG and all subtypes were comparable at all time points (p>0.05).

Conclusion: This cohort of real-world RA patients shows that reduction in gamma-globulin levels induced by ABA is safe, non-progressive and not associated to a higher risk of infection, even in patients with low IgG or TGG. Additionally, it is not associated to clinical response.

Disclosure of Interests: None declared

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THU0184 PREVIOUSLY UNKNOWN GASTRO-INTESTINAL ADVERSE DRUG REACTIONS ATTRIBUTED TO ETANERCEPT

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Background: Although an increased risk of inflammatory bowel disease (IBD) during etanercept (ETN) use is included in the product information of ETN, no other gastro-intestinal (GI-)adverse drug reactions (ADRs) are described. This is in contrast with other TNFα-inhibitors such as adalimumab (ADA) and infliximab, as these are associated with various GI-ADRs such as nausea and abdominal pain.

Objectives: To identify the proportion and type of patient-reported and health care professional (HCP)-reported ETN associated GI-ADRs and compare these with ADA associated GI-ADRs.

Methods: Patient-reported data on ADRs attributed to biologics was collected from the Dutch Biologic Monitor (DBM) from 1 Jan 2017 until 1 Nov 2019. HCP reported data on ADRs attributed to biologics was collected from the Dutch rheumatic arthritis monitoring registry and the Dutch registry for spondyloarthritis from 22 Jun 2004 until 1 Nov 2019.

GI-ADRs were defined by MedDRA System Organ Class 'Gastrointestinal disorders'. All reported GI-ADRs attributed to ETN and ADA for patients with inflammatory rheumatic diseases (IRDs) were selected. Proportion of GI-ADRs for ETN and ADA in patient and HCP reports was defined as the number of patients with at least one GI-ADR per total number of patients using ETN or ADA. Patient-reported burden and actions taken after GI-ADRs were compared between ETN and ADA.

Results: We included 755 patients from the DBM using ETN (415) and ADA (358) for IRDs, of which 47 patients reported 60 GI-ADRs. The proportion of patient-reported GI-ADRs was 6.3% for ETN and 5.9% for ADA (Table 1). We included 1343 patients using ETN (804) or ADA (796) from the registries, with 43 HCP-reported GI-ADRs in 38 patients. The proportion of HCP-reported GI-ADRs was 1.6% for ETN, which was significantly lower than 3.4% for ADA (p=0.049). Patients experienced ETN associated GI-ADRs more burdensome than ADA associated GI-ADRs (p=0.05 using Mann-Whitney U) (Table 2). The ADR required action in 34% of patient-reported GI-ADRs attributed to ETN and 41% of GI-ADRs attributed to ADA, including biologic discontinuation. No hospitalisation following a GI-ADR was reported.

Table 1. Proportion of patient- and HCP-reported GI-ADRs attributed to ETN and ADA.

Patients	Proportion for ETN	Top 3	Proportion for ADA	Top 3	p-value*
DBM (n=755; 415 ETN, 358 ADA)	6.3% (26 pt)	1. Nausea: 6 2. Diarrhea: 5 3. Abdominal pain: 5	5.9% (21 pt)	1. Nausea: 8 2. diarrhea: 3 3. Oral aphthous ulcer: 2	0.9
Registries (n=1,343; 804 ETN, 796 ADA)	1.6% (13 pt)	1. diarrhoea: 6 2. Nausea: 2 3. Abdominal pain: 2	3.4% (25 pt)	1. Nausea: 7 2. Abdominal pain: 6 3. Diarrhoea: 5	0.049

*Differences between ETN and ADA were tested using Fisher's exact

Table 2. Actions following patient-reported GI-ADRs attributed to ETN and ADA in the DBM

	ETN (n=38)	ADA (n=22)
Mean burden score* ± SD	2.9 ± 1.0	2.5 ± 0.9
Contact HCP	23 (61%)	10 (45%)
Specialist doctor	10 (43%)	3 (30%)
General practitioner	10 (43%)	8 (80%)
Nurse	6 (26%)	2 (20%)
Other	7 (30%)	2 (20%)
Action of HCP		
Discontinuation	1 (4%)	1 (10%)
Dose adjustment	2 (9%)	1 (10%)
Treatment	4 (17%)	3 (30%)
Referral	3 (13%)	2 (20%)
Mentioned, no action	12 (52%)	5 (50%)
Other	3 (13%)	2 (20%)

*5 point Likert scale

Conclusion: Although GI-ADRs other than IBD are not included in the product information of ETN, they are often reported by both patients and HCPs. The type of patient-reported GI-ADRs attributed to ETN and ADA is comparable. However, patients regard GI-ADRs attributed to ETN as more burdensome.

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THU0186 CLINICAL EVALUATION OF THE IMMUNOGENICITY TO CT-P13 FOR SUBCUTANEOUS USE IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS: 1-YEAR CLINICAL RESULTS FROM A MULTICENTER, RANDOMIZED CONTROLLED PIVOTAL TRIAL

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Background: Novel subcutaneous infliximab (CT-P13 SC) was developed to augment the flexibility in therapeutic use of infliximab and noninferiority (NI) of CT-P13 SC versus CT-P13 intravenous (IV) was demonstrated for efficacy in patients with rheumatoid arthritis (RA) [1]. CT-P13 SC 120mg biweekly showed consistent higher therapeutic trough levels during the treatment period, which helps in maintaining efficacy over time. Since immunogenicity has clinical importance in patients using anti-TNF alpha agents and there is a general presumption that SC route is more immunogenic than IV route, this needs careful assessment.

Objectives: Immunogenicity assessment of CT-P13 SC with further impact analysis has been performed on the pivotal data set [1] to determine whether there was any correlation between the magnitude of anti-drug antibody (ADA) positivity and clinical outcomes in RA patients.

Methods: The immune response against CT-P13 in human serum was detected using an electrochemiluminescence (ECL) platform with an Affinity Capture Elution (ACE) step. An ADA ECL ACE assay showed ability to detect ADA at low levels in all samples regardless of residual drug in serum (25 ng/mL ADA in the presence of 80 μg/mL of CT-P13 in RA serum). To investigate the impact of ADA titer on PK, efficacy and safety, key clinical parameters were assessed by visit based ADA titer quartile. All patients who had 'Positive' ADA status result at each visit were included in the analysis and categorized into 4 groups using the 25th, 50th, 75th percentiles of ADA titer result, respectively.

Results: The four subgroups categorized by quartiles at each visit from week 22 to week 54 were: 1st (ADA titer ≤ 3), 2nd (3 < ADA titer ≤ 9), 3rd (9 < ADA

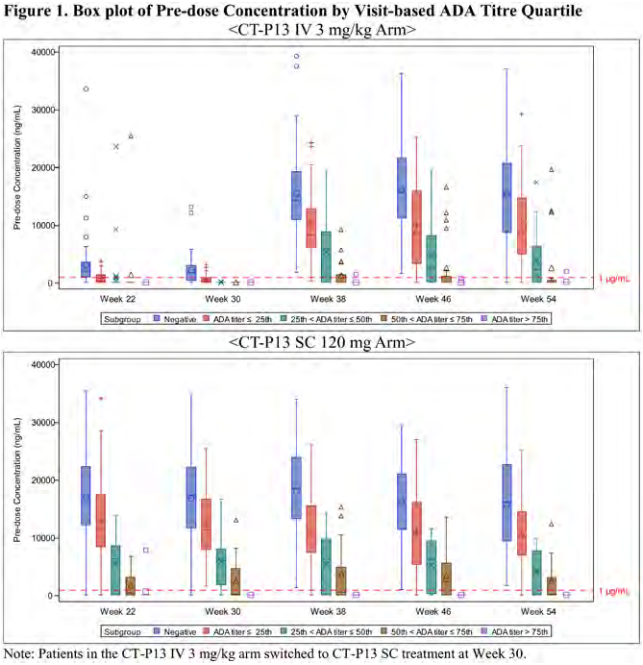
titer ≤ 27) and 4th (27 < ADA titer). There was a trend for pre-dose concentration to decrease as ADA titer increases for both CT-P13 SC and CT-P13 IV arms as expected (Figure 1). Patients in the 1st and 2nd subgroup maintained the sufficient therapeutic drug concentration level. Figure 2 shows the correlation between ADA titer and efficacy outcomes where the change from baseline of DAS28 (CRP) and the proportion of patients achieving ACR20 were lower in the 3rd and 4th subgroups. The ADA impact was especially apparent in the 4th subgroup where the mean pre-dose concentration of the patients was below the therapeutic drug concentration level (1 μg/mL), which led to worse efficacy outcomes in both arms, IV as well as SC. Nevertheless, no impact of ADA on safety profile in both arms was observed. A neutralizing antibody (NAb) method with enhanced drug tolerance but limited performance was also developed and clinical consequences of NAb titer in terms of PK, efficacy and safety were not different from the results with ADA.

Conclusion: The analysis of both ADA positivity and titer is clinically meaningful in the prediction of PK profile and clinical response. CT-P13 SC administration did not result in a greater incidence of ADA compared to the CT-P13 IV and there were no clinical differences depending on the formulation.

References:

[1] Westhovens R, et al. Annals of the Rheumatic Diseases 2019;78:1158-1159.

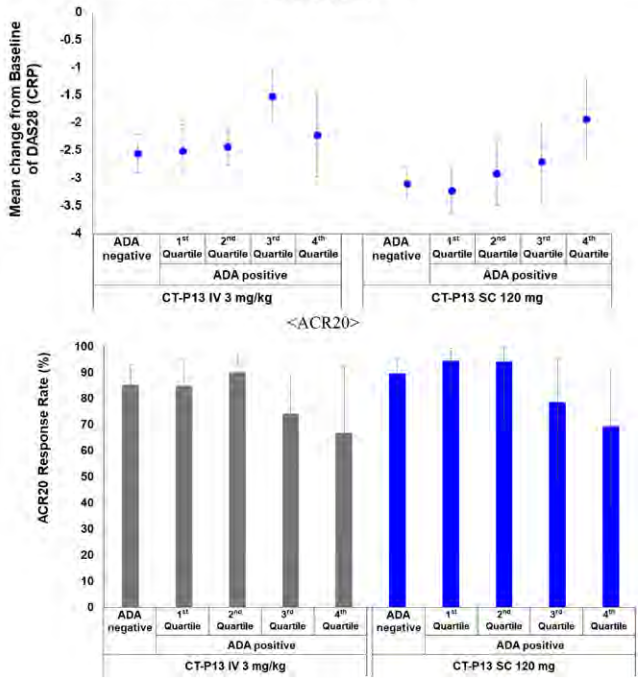
Figure 1. Box plot of Pre-dose Concentration by Visit-based ADA Titre Quartile



Note: Patients in the CT-P13 IV 3 mg/kg arm switched to CT-P13 SC treatment at Week 30.

Disclosure of Interests: Rene Westhovens Grant/research support from: Celltrion Inc, Galapagos, Gilead, Consultant of: Celltrion Inc, Galapagos, Gilead, Speakers bureau: Celltrion Inc, Galapagos, Gilead, DaeHyun Yoo Grant/research support from: Celltrion, Inc, Consultant of: Celltrion, Inc, Speakers bureau: Celltrion Healthcare, Inc, Piotr Wiland Grant/research support from: Celltrion, Inc, Speakers bureau: Novartis, Pfizer, Abbvie, Gedeon-Richter, Lilly, Roche, Sandoz, Marek Zawadzki Grant/research support from: Celltrion, Inc, Delina Ivanova Grant/research support from: Celltrion, Inc, Alfredo Berrocal Grant/research support from: Celltrion, Inc, Speakers bureau: Pfizer, Elias Chalouhi Grant/research support from: Celltrion, Inc, Éva Balázs Grant/research support from: Celltrion, Inc, Consultant of: Amgen, Sergii Shevchuk Grant/research support from: Celltrion, Inc, Sang Joon Lee Shareholder of: Celltrion, Inc, Employee of: Celltrion, Inc, Sung Hyun Kim Shareholder of: Celltrion, Inc, Employee of: Celltrion, Inc, JeeHye Suh Employee of: Celltrion, Inc, Chankyoung Hwang Employee of: Celltrion, Inc, Dae Seok Choi Shareholder of: Celltrion, Inc, Employee of: Celltrion, Inc

Figure 2. Mean Change from Baseline of DAS28 (CRP) and Proportion of ACR20 Responder at Week 30 by Visit-based ADA Titer Quartile



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THU0187

IMPACTS OF BODY MASS INDEX ON CLINICAL RESPONSE OF NOVEL SUBCUTANEOUS INFLIXIMAB (CT-P13 SC) IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS: 1-YEAR RESULTS FROM A PART 2 OF PHASE I/III RANDOMIZED CONTROLLED TRIAL

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Background: In the post-hoc analysis of PLANETRA, a Phase III randomized controlled trial (RCT), no significant association was found between body mass index (BMI) and clinical responses in rheumatoid arthritis (RA) patients using weight-based intravenous (IV) infliximab (3 mg/kg every 8 weeks)[1,2]. Since the subcutaneous (SC) formulation of CT-P13 which was approved from EMA after demonstrating non-inferiority compared to CT-P13 IV is a fixed-dose of 120 mg biweekly, it is meaningful to evaluate the impact of BMI on clinical response of CT-P13 SC[3,4].

Objectives: This report is to investigate post-hoc impact of BMI on clinical responses of CT-P13 SC 120 mg in Part 2 of a Phase I/III RCT in active RA patients throughout the 1-year treatment period.

Methods: A total of 165 patients who received at least one full dose of CT-P13 SC (after IV induction at Weeks 0 and 2) in the initial treatment stage before Week 30 and who had at least one efficacy evaluation result after Week 6 or thereafter were included in this analysis. Patients were categorized into 3 groups; under/normal weight (<25kg/m^2), overweight (≥25kg/m^2, <30kg/m^2), and obesity (≥30kg/m^2) based on the WHO BMI classification. Baseline characteristics, mean change from baseline in disease activity by DAS28 (CRP), remission (DAS28 [CRP]≤2.6) and low disease activity (LDA; 2.6<DAS28 [CRP]≤3.2), duration (week) of LDA, EULAR response, and ACR response were evaluated among the 3 BMI groups.

Results: In the under/normal weight (n=63), overweight (n=61), and obesity (n=41) groups, the mean±SD of age (years) (48.7±14.00, 51.5±10.93, 53.8±10.62) and the mean±SD of RA duration (years) (6.4±6.00, 8.2±9.27,

5.4±4.72) were comparable. At baseline, the rates of high disease activity (90.5%, 90.2%, 87.8%; DAS28 [CRP]>5.1) were similar among the groups. All other baseline and disease characteristics including gender, race, and other disease activity parameters were also comparable among the groups. The rate of remission or LDA (Figure 1), the mean change from baseline of DAS28 (CRP) (-3.3, -3.1, -3.3 at Week 54), duration of LDA up to Week 54 (26.2, 29.2, 27.9 weeks), and the good or moderate EULAR responder rates (84.1%, 80.3%, 90.2% at Week 54) were all comparable among the groups and there were no statistically significant differences (p-value>0.05). The ACR responder rates were also comparable among the groups except for the ACR70 at Weeks 2 and 6 which were obtained following 2 IV infusions in the IV dose loading phase. Absolute value of Pearson correlation coefficient was below 0.06 between BMI at screening and mean change from baseline in DAS28 (CRP) during CT-P13 SC treatment from Weeks 14 to 54, indicating that correlation between two measurements was weak and was not statistically significant (p-value>0.05) (Figure 2).

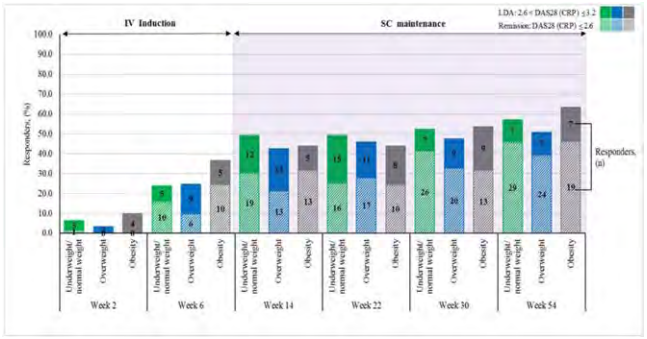
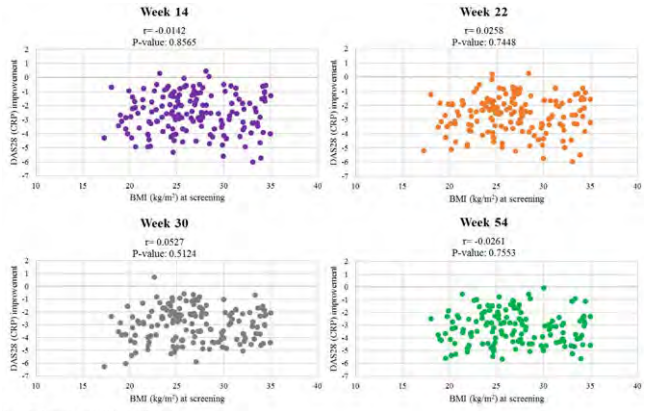


Figure 1. Remission or LDA Based on DAS28 (CRP)



1. r=Pearson correlation coefficient
2. P-value was obtained from t-test.

Figure 2. DAS28 (CRP) improvement

Conclusion: These post-hoc results showed that there was no impact of BMI on the clinical responses of CT-P13 SC 120 mg biweekly in RA patients. Therefore, CT-P13 SC 120 mg could be a reasonable therapeutic option regardless of BMI.

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[1] Yoo D.H., et al. Ann Rheum Dis, 2013;72:1613-20.
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[3] Westhovens R., et al. Ann Rheum Dis, 2019;78:A1158
[4] Westhovens R., et al. Arthritis Rheumatol. 2019;71 (suppl 10).

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THURSDAY, 04 JUNE 2020

Rheumatoid arthritis - non biologic treatment and small molecules

THU0188

EFFICACY OF FILGOTINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS WITH POOR PROGNOSTIC FACTORS: POST HOC ANALYSIS OF FINCH 3

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Background: Patients (pts) with rheumatoid arthritis (RA) with poor prognostic factors (PPF) are at risk for RA progression if disease activity is not rapidly controlled. In FINCH 3 (NCT02886728), filgotinib (FIL)—an oral, potent, selective JAK1 inhibitor—was effective relative to methotrexate monotherapy (MTX mono) in MTX-naïve patients with ≥1 PPF—erosions, seropositivity for rheumatoid factor (RF) or anti-cyclic citrullinated peptide (CCP), or hsCRP ≥4 mg/L.[1]

Objectives: This post hoc analysis examined FIL efficacy in FINCH 3 pts with multiple PPF.

Methods: The global, phase 3, double-blind, active-controlled FINCH 3 study randomised MTX-naïve pts with moderately to severely active RA 2:1:1:2 to oral FIL 200 mg once daily + MTX ≤20 mg weekly, FIL 100 mg + MTX, FIL 200 mg mono, or PBO + MTX up to week (W)52. This subgroup analysis included pts with all 4 of the following PPF at baseline (PPF pts): erosions, seropositivity for RF or anti-CCP, hsCRP ≥4 mg/L, and DAS(28)CRP >5.1. Comparisons were not adjusted for multiplicity.

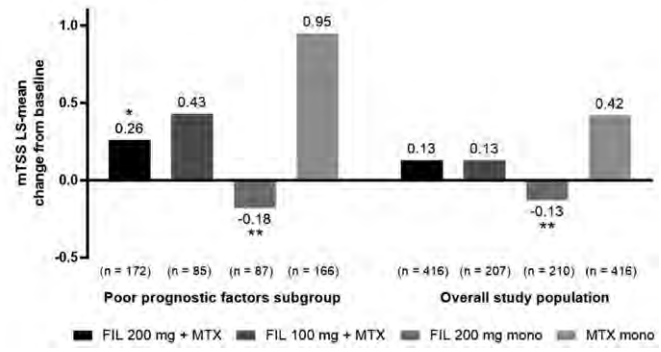
Results: Of 1249 pts randomised and treated in FINCH 3, 510 had all 4 PPF. At baseline, relative to the overall FINCH 3 population, PPF pts had longer mean disease duration (2.4 vs 2.2 years); higher mean hsCRP (27.9 vs 17.5 mg/L), mTSS (17.9 vs 13.3), DAS28(CRP) (6.3 vs 5.7), HAQ-DI (1.76 vs 1.56), CDAI (44.3 vs 39.8), and SDAI (47.1 vs 41.5); and greater frequency of seropositivity for RF (90.6% vs 67.9%), anti-CCP (92.4% vs 68.5%), or both (82.9% vs 59.6%). Efficacy in PPF pts was comparable to data from all FINCH 3 pts (**Table**, Figures 1–2). PPF pts receiving FIL 200 mg with or without MTX vs MTX mono had higher frequencies of ACR20/50/70 response and greater improvement in HAQ-DI at W24; responses were numerically greater for FIL 200 mg + MTX vs FIL 100 mg + MTX or FIL 200 mg mono (**Table**) and were evident by W12 (data not shown). Radiographic progression at W24 was lower in PPF pts receiving FIL 200 mg + MTX or FIL 200 mg mono vs MTX mono (Figure 1). Proportions of PPF pts receiving FIL 200 mg with or without MTX who achieved DAS28(CRP) <2.6, CDAI ≤2.8, SDAI ≤3.3, and Boolean remission at W24 (Figure 2) were larger vs pts receiving MTX mono and numerically greater vs pts receiving FIL 100 mg + MTX.

Table. Efficacy outcomes in patients with 4 PPF and all FINCH 3 patients at W24

	FIL 200 mg + MTX		FIL 100 mg + MTX		FIL 200 mg mono		MTX mono	
	PPF	All	PPF	All	PPF	All	PPF	All
n	172	416	85	207	87	210	166	416
ACR20, %	85.5*	81.0***	83.5	80.2*	81.6	78.1	74.7	71.4
ACR50, %	70.3***	61.5***	58.8	57.0**	59.8	58.1**	48.2	45.7
ACR70, %	54.1***	43.8***	37.6	40.1***	43.7*	40.0***	28.3	26.0
HAQ-DI[a]	−1.2***	−0.94***	−1.0*	−0.90**	−1.0*	−0.89*	−0.9	−0.79

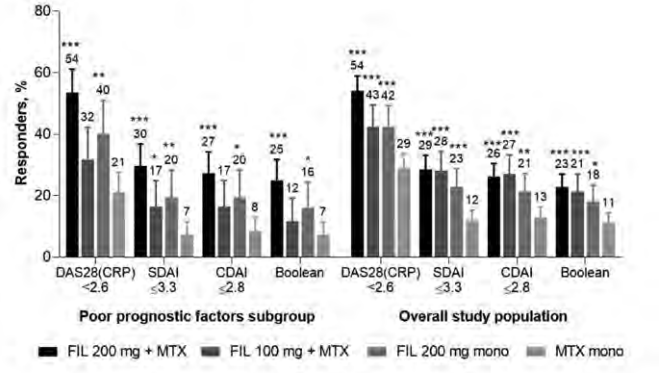
[a]Mean change from baseline.
*, p <0.05; **, p <0.01; ***, p <0.001 vs MTX mono, not adjusted for multiplicity.
FIL, filgotinib; mono, monotherapy; MTX, methotrexate; PPF, poor prognostic factors.

Figure 1. Change in mTSS from baseline at W24 in FINCH 3 patients with 4 poor prognostic factors and all FINCH 3 patients



Conclusion: FIL treatment provided rapid and deep disease control including higher rates of remission and other clinical outcomes, improved physical function, and less radiographic progression compared with MTX alone in MTX-naïve pts with RA with 4 PPF, a population at risk for severe progressive disease. In pts with 4 PPF, W24 remission rates following FIL 200 mg with or without MTX were higher vs MTX mono and numerically higher vs FIL 100 mg + MTX.

Figure 2. Rates of DAS28(CRP) <2.6, CDAI ≤2.8, SDAI ≤3.3, and Boolean remission at W24 in FINCH 3 patients with 4 PPF and all FINCH 3 patients



*, p <0.05; **, p <0.01; ***, p <0.001 vs MTX alone; not adjusted for multiplicity.

FIL, filgotinib; mono, monotherapy; MTX, methotrexate; PPF, poor prognostic factors; W, week.

References:

[1] Westhovens et al. *Ann Rheum Dis* 2019;78(Suppl2):259–60.

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, Consultant of: AbbVie; Gilead Sciences, Inc.; GSK; Novartis, Paul Bird Consultant of: AbbVie, Celgene Corporation, Eli Lilly, Janssen, Novartis, Pfizer – advisor, Speakers bureau: AbbVie, Celgene Corporation, Eli Lilly, Janssen, Novartis, Pfizer, Osvaldo Messina Speakers bureau: Amgen; Americas Health Foundation; Pfizer, Maya H Buch Grant/research support from: Pfizer, Roche, and UCB, Consultant of: Pfizer; AbbVie; Eli Lilly; Gilead Sciences, Inc.; Merck-Serono; Sandoz; and Sanofi, Beatrix Bartok Shareholder of: Gilead Sciences Inc., Employee of: Gilead Sciences Inc., Zhaoyu Yin Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Ying Guo Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Thijs Hendrikx Shareholder of: Galapagos (share/warrant holder), Employee of: Galapagos, Gerd Rüdiger Burmester Consultant of: AbbVie Inc, Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB Pharma, Speakers bureau: AbbVie Inc, Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB Pharma

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THU0189

EFFICACY AND SAFETY OF NINTEDANIB IN PATIENTS WITH AUTOIMMUNE DISEASE-RELATED INTERSTITIAL LUNG DISEASE TREATED WITH DMARDS AND/OR GLUCOCORTICOIDS AT BASELINE

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Background: In the INBUILD trial in patients with progressive fibrosing ILDs, nintedanib reduced the rate of decline in forced vital capacity (FVC) vs placebo over 52 weeks in the overall population and in the subgroup with autoimmune disease-related ILDs. Patients taking stable doses of medications to treat RA or CTD were eligible, but the protocol excluded enrolment of patients treated with azathioprine, cyclosporine, mycophenolate, tacrolimus, rituximab, cyclophosphamide, or oral glucocorticoids >20 mg/day.

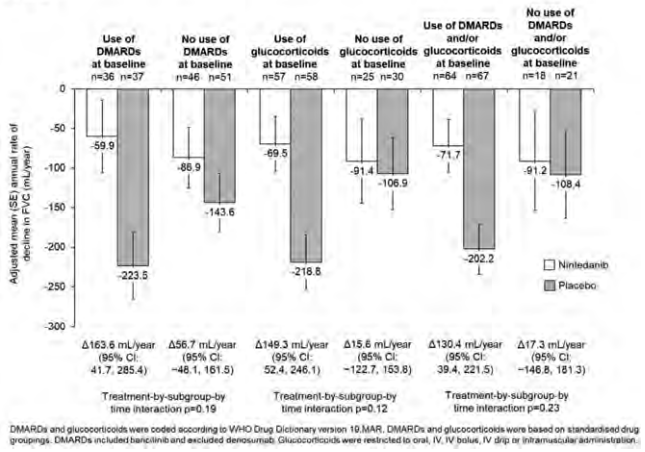
Objectives: Assess the influence of DMARDs and/or glucocorticoids at baseline on the efficacy and safety of nintedanib in patients with progressive autoimmune disease-related ILDs.

Methods: In patients with progressive autoimmune disease-related ILDs in the INBUILD trial, the rate of decline in FVC (mL/year) and adverse events (AEs) over 52 weeks of treatment (or until 28 days after last trial drug intake for patients who discontinued drug before week 52) were assessed in subgroups by use of DMARDs and/or glucocorticoids (any dose) at baseline (yes/no).

Results: 170 patients in the INBUILD trial (82 nintedanib, 88 placebo) had autoimmune disease-related ILDs (89 RA-ILD, 39 SSc-ILD, 19 MCTD-ILD, 23 other). The baseline characteristics of patients taking (n=131) and not taking (n=39) DMARDs and/or glucocorticoids are shown in the Table. All but 1 patient taking glucocorticoids at baseline was taking <20 mg/day. The mean (SE) annual rate of decline in FVC in the placebo group was numerically greater in patients taking vs not taking DMARDs and/or glucocorticoids at baseline (Figure). The effect of nintedanib vs placebo on reducing the rate of decline in FVC was numerically more pronounced in patients taking vs not taking DMARDs and/or glucocorticoids at baseline, but the treatment-by-subgroup-by-time interaction p-values did not indicate heterogeneity in the effect of nintedanib between subgroups (Figure). In patients taking vs not taking DMARDs and/or corticosteroids at baseline, respectively, diarrhoea was reported in 59.4% and 77.8% of patients treated with nintedanib and 28.4% and 23.8% of patients treated with placebo. Serious AEs were more frequent in patients taking vs not taking DMARDs and/or glucocorticoids at baseline in both the nintedanib (39.1% vs 16.7%) and placebo (35.8% vs 19.0%) groups.

Conclusion: In the INBUILD trial, the rate of FVC decline was numerically greater in placebo-treated patients who were taking DMARDs and/or glucocorticoids at baseline than in those who were not. The rate of FVC decline was slower in patients treated with nintedanib than placebo both in patients who were and were not taking DMARDs and/or glucocorticoids at baseline. Nintedanib had an acceptable safety profile both in patients who were and were not using DMARDs and/or glucocorticoids at baseline.

Figure.



DMARDs and glucocorticoids were coded according to WHO Drug Dictionary version 19 MAR. DMARDs and glucocorticoids were based on standardised drug groupings. DMARDs included baricitinib and excluded denosumab. Glucocorticoids were restricted to oral, IV, IV bolus, IV drip or intramuscular administration.

	DMARDs and/or glucocorticoids at baseline	
	Yes (n=131)	No (n=39)
Male, %	51.9	30.8
FVC, mL, mean (SD)	2372 (718)	2188 (619)
ILD diagnosis, %		
RA-ILD	60.3	25.6
SSc-ILD	15.3	48.7
MCTD-ILD	10.7	12.8
Other	13.7	12.8
Biologic DMARDs, %	15.3	–
Non-biologic DMARDs, %	46.6	–
Glucocorticoids, %	87.8	–

Most common biologic DMARDs, non-biologic DMARDs and glucocorticoids were abatacept (4.6%), hydroxychloroquine/hydroxychloroquine sulphate (19.8%) and prednisone (37.4%), respectively.

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THU0190

METHOTREXATE THERAPY IS NOT ASSOCIATED WITH AN INCREASED RISK OF LIVER FIBROSIS ASSESSED BY THE FIBROSIS-4 INDEX

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Background: Methotrexate (MTX) holds a unique place in the management of rheumatoid arthritis (RA) given its favorable balance between efficacy and safety. However, conflicting data still suggest a potential risk of MTX-induced long-term liver fibrosis. The fibrosis-4 (FIB-4) index was originally proposed as a simple and non-invasive marker of liver fibrosis in HIV/HCV co-infection. In patients with RA, FIB-4 values have been correlated to the amount of histologic liver lesions, suggesting that this index may be a valuable marker to diagnose liver disease in RA patients (1).

Objectives: To estimate the amount of scarring in the liver with the FIB-4 index in RA patients on maintenance therapy with MTX.

Methods: We performed a cross-sectional study including successive RA patients hospitalized in the Rheumatology department of Cochin Hospital for a 12-month period. Data on liver function, disease activity, hepatotoxic and cardiovascular risk factors were systematically collected. The FIB-4 index was calculated according the following formula: (age(years) × AST(U/L)/platelet (PLT) (109/L) × √ALT(U/L)). Using a lower cutoff value of 1.45, a FIB-4 score <1.45 had a negative predictive value of 90% for advanced fibrosis in the patient cohort in which this formula was first validated. In contrast, a FIB-4 >3.25 had a 97% specificity and a positive predictive value of 65% for advanced fibrosis (2).

Results: We included 170 patients with established RA: 141 (83%) were women, the mean age was 59+/-12 years and the mean disease duration was 15+/-11 years. Positive rheumatoid factors and anti-CCP antibodies were detected in 134 patients (79%). 102 patients (60%) were treated with methotrexate, with a mean dose of 10.0+/-8.4 mg/week, a mean treatment duration of 9.5+/-10.3 years and a cumulative dose of 5.3+/-5.1g. 23 patients (13.5%) received conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs) other than MTX, 112 (66%) corticosteroids (99 with a dose < 10 mg/day) and 85 targeted biologic DMARDs (bDMARDs) (50%). The mean FIB-4 value was 1.24+/-0.57, with 120 patients (71%) with value <1.45, 49 (29%) with values ranging from 1.45 to 3.25 and a single patient with FIB-4 >3.25. The FIB-4 was low and not significantly different between patients receiving MTX, patients previously treated with MTX and patients never treated with MTX (median 1.1, 1.25 and 1.18, respectively, p=0.709). This result was not modified after adjustment on treatments with other csDMARDs, corticosteroids, and bDMARDs. No correlation was observed between FIB-4 values and the cumulative dose of MTX (r=0.09, p=0.271). The FIB-4 index was low and similar between patients receiving cumulative MTX doses <5g, between 5 and 10g and 10g (Figure 1). The cumulative dose of MTX was not significantly higher in patients with a FIB-4 index >1.45 (median cumulative MTX dose 5.5g vs. 3.5g, p=0.302). No association was detected between the FIB-4 index and parameters of disease activity (DAS28, ESR and CRP levels), the body mass index, traditional cardiovascular risk factors and metabolic syndrome.

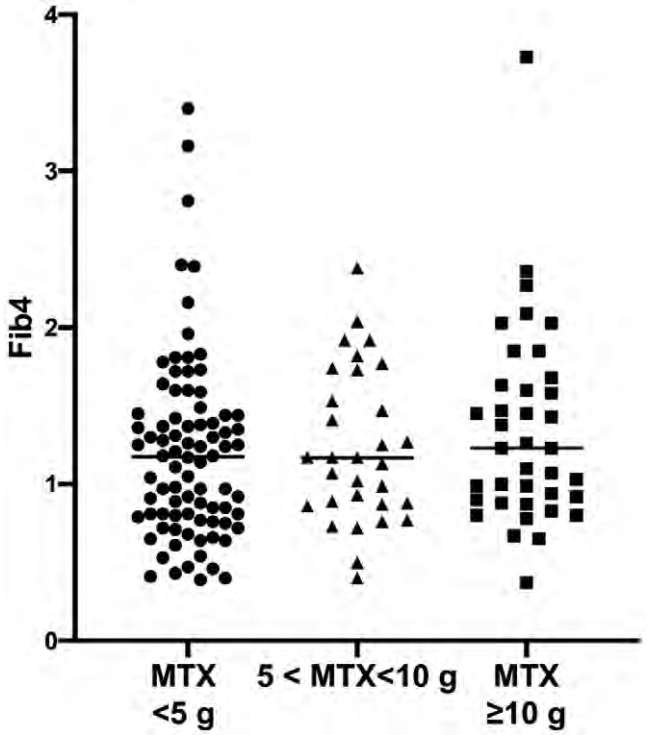


Figure 1. Fibrosis-4 index according to the cumulative dose of methotrexate in patients with rheumatoid arthritis

Conclusion: RA patients with long-term maintenance MTX therapy have low FIB-4 values suggesting that MTX is not associated with an increased risk of advanced liver fibrosis.

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[2] Sterling et al, Hepatology 2006

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THU0191 HAS THE DOSE OF METHOTREXATE IN RHEUMATOID ARTHRITIS BEEN OPTIMIZED BEFORE INITIATING BIOLOGICAL TREATMENT? RESULTS OF AN ALGERIAN MULTICENTER STUDY

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Background: Methotrexate (MTX) is the gold standard treatment for rheumatoid arthritis (RA). The international guidelines recommend optimizing its dose before the introduction of a biologic treatment in cases where it is well tolerated1.
Objectives: The objective of this study is to evaluate the dose of MTX before the initiation of biological treatment in RA patients with MTX ineffectiveness.
Methods: This is a multicenter, cross-sectional, prospective study including adults RA, over a period of 6 months (January-June 2019). We collected the following data: sex, age, comorbidities (diabetes, hypertension), rate of RF and ACPA, dose of MTX, rate of patients on corticosteroids, Disease Activity Score (DAS 28-vs), Health Assessment Questionnaire (HAQ) and SHARP Score.
Results: Number of patients: 239 (187 women / 52 men); average age: 48.3 years (19 - 81); average duration of the disease: 13.6 ± 8.2 years. Comorbidities: arterial hypertension (14,6 %) - diabetes (13 %),The RF were positive in 59.8%. The average value of ACPA is 228.76 ± 287.08 IU / L, positive in 73% case. The average DAS28vs is 4.77 ± 1.46 (0.77 - 12.26). The average modified SHARP 111.67 ± 98.16 (0-448), the average HAQ is 1.13 ± 0.82 (0 - 2.87). 86.7% of patients are under corticosteroids.Only 18.5% of patients had a dose of MTX between 20 and 25 mg / week. the remaining 82% of patients the average dose of MTX was 14 mg / week (10-18.5).
Conclusion: These results suggest that the dose of MTX was not optimized before the initiation of biotherapy in the majority of patients with RA.
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THU0192 UPADACITINIB TREATMENT AND THE ROUTINE ASSESSMENT OF PATIENT INDEX DATA 3 (RAPID3) AMONG PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Upadacitinib (UPA) is an oral reversible JAK inhibitor engineered for greater selectivity for JAK1 vs JAK2, JAK3, and TYK2, and is currently being assessed for the treatment of RA. RAPID3 is a pooled index of the three key patient-reported measures: patient global assessment, pain, and physical function.
Objectives: In this analysis we assessed the effect of UPA treatment on RAPID3 in the SELECT-BEYOND, SELECT-COMPARE, and SELECT-MONOTHERAPY trials.
Methods: In SELECT-BEYOND[1], bDMARD-IR pts received UPA 15 mg or 30 mg once daily (QD), or PBO for 12 wks while continuing stable csDMARD therapy. In SELECT-COMPARE[2], MTX-IR pts received UPA 15 mg QD, PBO, or ADA 40 mg every 2 wks for 12 wks while continuing MTX. In SELECT-MONOTHERAPY[3], pts received UPA monotherapy 15 mg or 30 mg QD, or continued MTX monotherapy (cMTX) for 14 wks. We assessed the least squares mean changes from baseline (BL) in RAPID3 and the proportion of pts reporting RAPID3 remission (≤3), low (LDA, >3 to ≤6), moderate (MDA, >6 to ≤12), and high disease activity (HDA, >12). Correlations between RAPID3 remission and remissions defined by CDAI, SDAI, and DAS28(CRP) were also assessed using Pearson correlation coefficients. Non-responder imputation was used for categorical endpoints, and last observation carried forward for continuous endpoints in pts who received rescue therapy in SELECT-COMPARE. Other continuous data are as observed. Data were analyzed descriptively.
Results: 498, 648, and 1629 pts were randomized in SELECT-BEYOND, -MONOTHERAPY, and -COMPARE, respectively. Numerically higher improvements from BL in RAPID3 were reported with UPA 15 mg and 30 mg treatment vs PBO in SELECT-BEYOND, and vs cMTX in SELECT-MONOTHERAPY (Table). UPA 15 mg QD was also associated with greater reductions from baseline in RAPID3 vs PBO and ADA in SELECT-COMPARE (Table). Of note, the improvements in RAPID3 with UPA and ADA exceeded the minimal clinically important difference (MCID = 3.8[4]). The proportions of pts achieving RAPID3 remission were numerically higher in the UPA 15 mg and 30 mg groups vs PBO and cMTX in SELECT-BEYOND and SELECT-MONOTHERAPY, respectively (Figure). In addition, the proportions of pts in RAPID3 HDA were lower with UPA vs PBO and cMTX in these trials. In SELECT-COMPARE, higher rates of RAPID3 remission, with fewer pts in HDA, were evident with UPA 15 mg treatment vs PBO and ADA (Figure). Correlations between RAPID3 and other remission endpoints were significant (p<0.001; r=0.35–0.75) in all three trials at both baseline and Wk 12/14.
Conclusion: UPA was associated with improvements in RAPID3, both as monotherapy and in combination, in MTX-IR (SELECT-COMPARE and SELECT-MONOTHERAPY) or bDMARD-IR (SELECT-BEYOND) pts. UPA treatment can result in improved patient-reported disease activity, pain, and physical function in RA.

Table. Change from baseline in RAPID3 at Wk 12 in SELECT-BEYOND and -COMPARE, and Wk 14 in SELECT-MONOTHERAPY

Phase III study	Group	N	Mean (SD) change from BL
SELECT-BEYOND (bDMARD-IR)	PBO	148	-3.5 (7.1)
	UPA 15 mg QD	159	-6.9 (6.7)
	UPA 30 mg QD	150	-7.4 (6.9)
SELECT-COMPARE (MTX-IR)	PBO	616	-4.2 (6.4)
	UPA 15 mg QD	613	-8.6 (6.6)
	ADA 40 mg EOW	307	-7.0 (6.1)
SELECT-MONOTHERAPY (MTX-IR)	cMTX	203	-3.5 (6.5)
	UPA 15 mg QD	201	-7.2 (7.1)
	UPA 30 mg QD	205	-8.5 (6.3)

ADA, adalimumab; bDMARD, biologic disease-modifying antirheumatic drug; BL, baseline; MTX, methotrexate; IR, inadequate response; PBO, placebo; QD, once daily; SD, standard deviation; UPA, upadacitinib

Disclosure of Interests: Martin Bergman Shareholder of: Johnson & Johnson – stockholder, Consultant of: AbbVie, BMS, Celgene Corporation, Genentech, Janssen, Merck, Novartis, Pfizer, Sanofi – consultant, Speakers bureau: AbbVie, Celgene Corporation, Novartis, Pfizer, Sanofi – speakers bureau, Yoshiya Tanaka Grant/research support from: Asahi-kasei, Astellas, Mitsubishi-Tanabe, Chugai, Takeda, Sanofi, Bristol-Myers, UCB, Daiichi-Sankyo, Eisai, Pfizer, and Ono, Consultant of: Abbvie, Astellas, Bristol-Myers Squibb, Eli Lilly, Pfizer, Speakers bureau: Daiichi-Sankyo, Astellas, Chugai, Eli Lilly, Pfizer, AbbVie, YL Biologics, Bristol-Myers, Takeda, Mitsubishi-Tanabe, Novartis, Eisai, Janssen, Sanofi, UCB, and Teijin, Gustavo Citera Grant/research support from: AbbVie, Amgen, Eli Lilly, Gema, Genzyme, Novartis and Pfizer Inc, Consultant of: AbbVie, Amgen, Eli Lilly, Gema, Genzyme, Novartis and Pfizer Inc, Sami Bahlas: None declared, Mira Ali Shareholder of: AbbVie, Employee of: AbbVie, Sebastian Meerwein Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Yanna Song Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Vibeke Strand Consultant of: AbbVie, Amgen, Biogen, Celltrion, Consortium of Rheumatology Researchers of North America,



Crescendo Bioscience, Eli Lilly, Genentech/Roche, GlaxoSmithKline, Hospira, Janssen, Merck, Novartis, Pfizer, Regeneron Pharmaceuticals, Inc., Sanofi, UCB

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THU0193

CLINICO-DEMOGRAPHIC, IMMUNOLOGIC AND SYNOVIAL HISTOLOGIC FEATURES INFLUENCING RESPONSE TO JAK-INHIBITORS IN RHEUMATOID ARTHRITIS: A MONOCENTRIC COHORT.

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Background: Janus kinase Inhibitors (JAKis) are approved for the treatment of Rheumatoid Arthritis (RA) in over 40 countries. The updated EULAR recommendations for RA treatment revised the preference of bDMARDs over tsDMARDs based on the new data related to JAKis long-term efficacy and safety. [1].

Objectives: To evaluate the efficacy and safety of JAKis molecules in an observational single center cohort of RA patients in a real life outpatient clinical setting.

Methods: 76 RA patients [mean age: 55.7±12.5 years, 64(84.2%) female, disease duration: 120.7±97.2 months, 43 (61.4%) seropositive (AB+) for ACPA and/or IgM-RF, 34(44.7%) with BMI ≥25.0 kg/m2] were followed after starting JAKis treatment monotherapy or in combination with conventional synthetic DMARDs (csDMARDs). At study entry, and every 3 months, the ACR/EULAR core data set variables were recorded for each patient. Clinical improvement and remission rate were evaluated according to Disease Activity Score (DAS) and Clinical Disease Activity Index (CDAI) and any therapy-related adverse effect was reported. Among the whole RA cohort, 20 patients underwent US-guided synovial tissue (ST) biopsy before JAKis treatment and classified using the Krenn score for the semiquantitative assessment of ST inflammation[2].

Results: Among the whole RA cohort who started JAKis [mean follow-up (FU) duration: 6.1±3.7 months], 22(28.9%) showed DAS-defined high disease activity. 54(71.1%) patients were previously treated with at least 1 csDMARD and 33(43.4%) were naive to biologic DMARDs (bDMARDs). Among RA previously exposed to b-DMARDs, 23(30.3%) were using anti-TNF and 14(18.4%) anti-IL6R, whereas 6(7.9%) patients received other bDMARD. In particular, 11(14.5%) patients were previously treated only with one bDMARD.

During the FU, 12(15.8%) patients discontinued JAKis [7 due to treatment failure and 5 to adverse events (1 anemia, 2 gastrointestinal intolerance, 2 H.Zoster infection)]. All RA who discontinued JAKis for incomplete or no-response were previously exposed to bDMARDs.

DAS Remission was achieved in 29 of 65(44.6%) patients during the FU, of whom 21(32.5%) achieved remission at 3 months. Similarly, 16(24.6%) patients reached CDAI remission of whom 12(18.5%) patients achieved remission at 3 months.

At baseline, there were no differences of DAS-remission rate based on age, gender, disease duration, BMI and high disease activity. Similarly, concomitant steroid and csDMARDs therapy did not impact on the rate of DAS and CDAI Remission. However, RA reaching DAS remission during FU had more likely a shorter disease duration (p=0.01) and were less previously exposed to bDMARDs (p=0.001) than patients not achieving DAS remission. Conversely, the DAS Remission rate was higher in AB+ (55.3%) than in AB- RA patients (27.3%, p=0.04).

Furthermore, bDMARDs naive RA showed higher probability to reach remission compared to bDMARD previously exposed RA [DAS remission: 66.7% vs 28.9%, respectively, p=0.003; OR(95%): 4.90 (1.69-14.3) and CDAI-remission: 37.0% vs 15.8%, p=0.05; OR(95%CIs): 3.12(0.97-10.10)], regardless to the type of the previous bDMARDs used. Finally, considering the baseline ST features, RA achieving clinical improvement did not differ in terms of Krenn score and micro-anatomical organization compared to RA not achieving the clinical improvement.

Conclusion: The efficacy rate of JAKis therapy is not influenced by BMI and baseline high disease activity. Previous exposure to bDMARDs impacts both on the clinical response and on the rate of JAKis therapy discontinuation. Therapy-related adverse effects mainly occurred in bDMARD previously exposed RA patients.

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Disclosure of Interests: Dario Bruno: None declared, Maria Rita Gigante: None declared, Luca Petricca: None declared, Anna Laura Fedele: None declared, Simone Perniola: None declared, Marco Gessi: None declared, Barbara Tolusso: None declared, Stefano Alivernini: None declared, Elisa Gremese Speakers bureau: Abbvie, BMS, Celgene, Jannsen, Lilly, MSD, Novartis, Pfizer, Sandoz, UCB

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THU0194

CHARACTERISATION OF DEPTH OF RESPONSE, INCLUDING 50% IMPROVEMENT IN ACR COMPONENTS AT WEEK 12 AND REMISSION AT WEEK 24, FOLLOWING TREATMENT WITH FILGOTINIB COMPARED WITH METHOTREXATE OR ADALIMUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The oral, potent, selective JAK1 inhibitor filgotinib (FIL) showed favorable efficacy at week (W)12 and W24 of treatment for rheumatoid arthritis (RA) compared with methotrexate (MTX) monotherapy (mono) in FINCH 3

(NCT02886728) and with placebo (PBO) or adalimumab (ADA) in FINCH 1 (NCT02889796).

Objectives: 50% clinical improvement from baseline at W12 is a key checkpoint for RA treatment.[1] These post hoc analyses evaluated FIL treatment effect on improvement in ACR components at W12 and remission at W24 in FINCH 3 and FINCH 1.

Methods: FINCH 3 and FINCH 1 were global, phase 3, double-blind studies in patients (pts) with active RA. In FINCH 3, MTX-naïve pts were randomised 2:1:1:2 to once-daily (QD) oral FIL 200 mg + weekly MTX, FIL 100 mg + MTX, FIL 200 mg mono + PBO, or PBO + MTX mono up to W52. In FINCH 1, pts with inadequate response to MTX (MTX-IR) on a background of stable MTX were randomised (3:3:2:3) to oral FIL 200 or 100 mg QD, subcutaneous ADA 40 mg Q2W, or PBO up to W52. Post hoc analyses evaluated proportions of pts with 50% improvement from baseline in each ACR component and in all 7 ACR components (ACR50c) at W12, and proportions of pts with ACR50c at W12 achieving clinical remission at W24. Comparisons between treatments were not adjusted for multiplicity; subgroup comparisons are descriptive.

Results: Analyses included 1249 pts in FINCH 3 and 1755 pts in FINCH 1. Greater proportions of pts receiving FIL 200 mg + MTX, FIL 100 mg + MTX, or FIL mono (FINCH 3) vs MTX mono (FINCH 3) or PBO + MTX (FINCH 1)—and numerically higher proportions of pts receiving FIL 200 mg + MTX vs FIL 100 mg + MTX (both studies) or ADA + MTX (FINCH 1)—achieved ACR50c and individual components at W12 (**Table**). Proportions of pts achieving CDAI ≤2.8 (Figure 1) or Boolean remission (Figure 2) at W24 were higher for pts with vs without ACR50c at W12 (Figures 1–2).

Table. Proportions of patients with 50% improvement in each ACR component and ACR50c at week 12

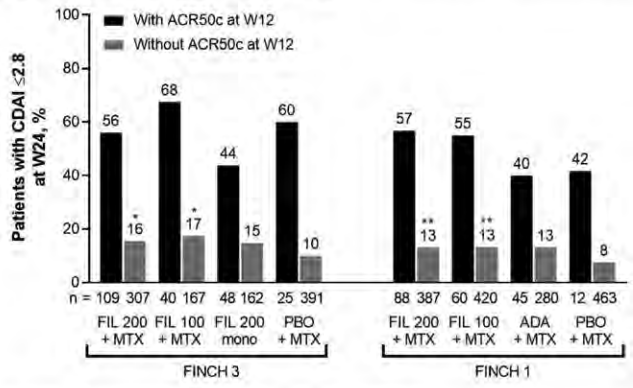
	ACR component							
	SJC66	TJC68	Pain	PGA	SGA	HAQ-DI	hsCRP	ACR50c
FINCH 3								
FIL 200 mg + MTX	82.2***	76.9***	59.2***	72.8***	56.5***	54.9***	59.1***	26.2***
FIL 100 mg + MTX	81.2***	74.4***	48.5*	68.1*	46.9**	49.5***	58.5***	19.3***
FIL 200 mg mono	82.9***	75.7***	47.6*	66.2*	47.1**	47.3**	59.5***	22.9***
MTX mono	67.1	59.6	39.2	58.4	35.6	35.6	33.7	6.0
FINCH 1								
FIL 200 mg + MTX	83.2$^{***,+}$	77.9$^{***,+}$	50.1$^{***,+}$	67.4***	48.2***	42.1$^{***,+}$	67.2$^{***,+++}$	18.5***
FIL 100 mg + MTX	77.9***	72.3***	45.1***	62.9***	43.2***	35.2***	55.0***	12.5***
ADA + MTX[a]	76.9	70.5	41.5	61.5	42.0	34.4	55.7	13.8
PBO + MTX	66.7	59.2	28.0	50.9	28.0	23.1	25.9	2.5

[a]Not formally compared vs PBO + MTX.

*, p <0.05; **, p <0.01; ***, p <0.001 vs MTX mono (FINCH 3) or PBO + MTX (FINCH 1); $^{+}$, p <0.05; $^{+++}$, p <0.001 vs ADA + MTX (FINCH 1); not adjusted for multiplicity.

ACR50c, 50% improvement from baseline in all ACR components; ADA, adalimumab; FIL, filgotinib; MTX, methotrexate; mono, monotherapy; PBO, placebo.

Figure 1. Proportions of patients with and without 50% improvement in all ACR components at week 12 who achieved CDAI remission at week 24

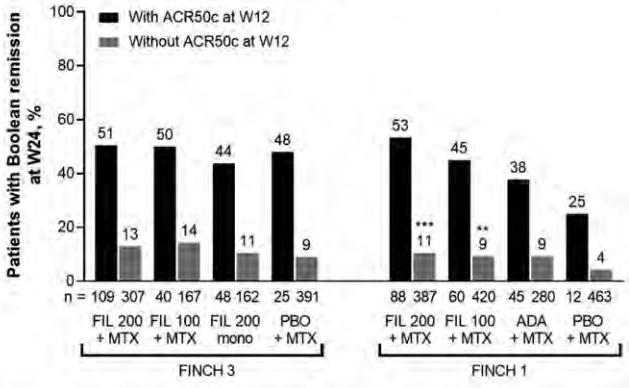


*, p <0.05; **, p <0.01 vs PBO + MTX; not adjusted for multiplicity.

ACR50c, 50% improvement from baseline in all ACR components; ADA, adalimumab; CDAI, Clinical Disease Activity Index; FIL, filgotinib; mono, monotherapy; MTX, methotrexate; PBO, placebo; W, week.

Conclusion: In MTX-naïve and MTX-IR pts with RA, FIL treatment was more effective vs MTX (FINCH 3) or PBO (FINCH 1) for achieving ACR50c at W12—a potential predictor of remission at W24. Proportions of pts achieving ACR50c at W12 were numerically higher for pts receiving FIL 200 mg + MTX vs FIL 100 mg + MTX (both studies) or ADA + MTX (FINCH 1).

Figure 2. Proportions of patients with and without 50% improvement in all ACR components at week 12 who achieved Boolean remission at week 24



*, p <0.05; **, p <0.01 vs PBO + MTX; not adjusted for multiplicity.

ACR50c, 50% improvement from baseline in all ACR components; ADA, adalimumab; FIL, filgotinib; mono, monotherapy; MTX, methotrexate; PBO, placebo; W, week.

References:

[1] Smolen JS, et al. *Ann Rheum Dis*. 2017;76:960–77.

Disclosure of Interests: Gerd Rüdiger Burmester Consultant of: AbbVie Inc, Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB Pharma, Speakers bureau: AbbVie Inc, Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB Pharma, Daniel Aletaha Grant/research support from: AbbVie, Novartis, Roche, Consultant of: AbbVie, Amgen, Celgene, Lilly, Medac, Merck, Novartis, Pfizer, Roche, Sandoz, Sanofi Genzyme, Speakers bureau: AbbVie, Celgene, Lilly, Merck, Novartis, Pfizer, Sanofi Genzyme, UCB, Janet Pope Grant/research support from: AbbVie, Bristol-Myers Squibb, Eli Lilly & Company, Merck, Roche, Seattle Genetics, UCB, Consultant of: AbbVie, Actelion, Amgen, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Eicos Sciences, Eli Lilly & Company, Emerald, Gilead Sciences, Inc., Janssen, Merck, Novartis, Pfizer, Roche, Sandoz, Sanofi, UCB, Speakers bureau: UCB, Yoshiya Tanaka Grant/research support from: Asahi-kasei, Astellas, Mitsubishi-Tanabe, Chugai, Takeda, Sanofi, Bristol-Myers, UCB, Daiichi-Sankyo, Eisai, Pfizer, and Ono, Consultant of: Abbvie, Astellas, Bristol-Myers Squibb, Eli Lilly, Pfizer, Speakers bureau: Daiichi-Sankyo, Astellas, Chugai, Eli Lilly, Pfizer, AbbVie, YL Biologics, Bristol-Myers, Takeda, Mitsubishi-Tanabe, Novartis, Eisai, Janssen, Sanofi, UCB, and Teijin, Patrick Durez Speakers bureau: AbbVie, Bristol-Myers Squibb, Celltrion, Eli Lilly, Pfizer, Sanofi, Antonio Gomez-Centeno: None declared, Alena Pechonkina Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Beatrix Bartok Shareholder of: Gilead Sciences Inc., Employee of: Gilead Sciences Inc., Franziska Matzkies Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Lei Ye Shareholder of: Gilead Sciences Inc., Employee of: Gilead Sciences Inc., Zhaoyu Yin Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Robin Besuyen Shareholder of: Galapagos, Employee of: Galapagos, William Rigby Grant/research support from: Bristol-Myers Squibb, Consultant of: AbbVie, Bristol-Myers Squibb, Genentech, Pfizer, Bernard Combe Grant/research support from: Novartis, Pfizer, Roche-Chugai, Consultant of: AbbVie; Gilead Sciences, Inc.; Janssen; Eli Lilly and Company; Pfizer; Roche-Chugai; Sanofi, Speakers bureau: Bristol-Myers Squibb; Gilead Sciences, Inc.; Eli Lilly and Company; Merck Sharp & Dohme; Pfizer; Roche-Chugai; UCB

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THU0195

INCIDENCE AND RISK OF VENOUS THROMBOEMBOLIC EVENTS AMONG PATIENTS WITH RHEUMATOID ARTHRITIS ENROLLED IN THE UPADACITINIB SELECT CLINICAL TRIAL PROGRAM

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Background: Patients (pts) with rheumatoid arthritis (RA) are at an increased risk for the development of venous thromboembolism (VTE, including pulmonary embolism [PE] and deep vein thrombosis [DVT]) vs the general population

(~2-fold increase).[1] Beyond RA, additional risk factors have been described, with prior history of VTE and obesity posing particular risk. VTE events have been observed in pts receiving JAK inhibitors, including upadacitinib (UPA).

Objectives: To describe the incidence of VTE in pts with RA receiving UPA relative to active comparators in the phase 3 clinical trial program and to evaluate potential risk factors.

Methods: Adjudicated events of treatment-emergent VTE were determined in pts receiving UPA in an integrated analysis (data cut-off, 30 Jun 2019) of five randomized phase 3 trials (SELECT-EARLY, SELECT-MONOTHERAPY, SELECT-NEXT, SELECT-COMPARE, and SELECT-BEYOND), of which 4 evaluated both the UPA 15 mg and 30 mg QD doses and 1 (SELECT-COMPARE) evaluated only UPA 15. Incidence of VTE was also determined in pts receiving adalimumab (ADA) + methotrexate (MTX) in SELECT-COMPARE and MTX monotherapy in SELECT-EARLY. Events are attributed to treatment received at time of event and are summarized per events/100 patient yrs. VTE risk factors were assessed using univariate Cox regression models.

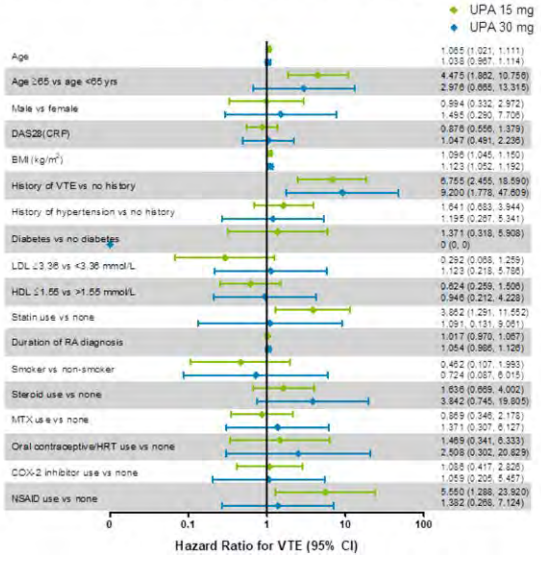
Results: A total of 35 VTE events were observed across treatment groups. The exposure-adjusted treatment-emergent event rates (E/100 PYs, 95% CI) of VTE were 0.5 (0.3, 0.7) for UPA 15, 0.3 (0.1, 0.7) for UPA 30, 0.5 (0.1, 1.3) for ADA + MTX, and 0.4 (0.1, 1.6) for MTX, with no pattern to event onset across treatments. Events of PE, DVT, or both PE and DVT were reported across treatment groups (**Table**). Pts who experienced VTE, across all treatment groups, on average, were older than pts who did not (62/59/58/61 yrs vs 54/55/54/53 yrs for UPA 15, UPA 30, ADA + MTX, and MTX, respectively). The mean body mass index (BMI) of pts with VTE tended to be higher (34–40 for pts with VTE vs 28-29 kg/m^2 for those without). Across UPA treatment groups, 135/2629 (UPA 15) and 62/1204 (UPA 30) pts had a prior history of VTE; of these pts, 5 (3.7%) and 2 (3.2%) experienced VTE on UPA 15 and UPA 30, respectively. Univariate Cox regression models identified BMI and prior history of VTE as factors associated with VTE in the UPA 15 and 30 mg groups (**Figure**). Age and NSAID use were shown to be associated with VTE risk among pts in the UPA 15 but not 30 mg group.

Table. Events of VTE Observed Across Treatment Groups

	UPA 15 mg QD[a] N=2629 (4565.8 PYs)	UPA 30 mg QD[b] N=1204 (2309.7 PYs)	ADA + MTX[c] N=579 (768.6 PYs)	MTX Monotherapy[d] N=314 (456.0 PYs)
Events, n	21	8	4	2
Patients, n	20	7	4	2
PE only	11	1	3	1
DVT only	5	2	1	0
PE + DVT	4	4	0	1

[a]From SELECT-EARLY, -MONOTHERAPY, -NEXT, -COMPARE, and -BEYOND.
[b]From SELECT-EARLY, -MONOTHERAPY, -NEXT, and -BEYOND.
[c]From SELECT-COMPARE.
[d]From SELECT-EARLY.
VTE, venous thromboembolism; PE, pulmonary embolism; DVT, deep vein thrombosis.

Figure: VTE Risk Factors in Patients Receiving UPA 15 or 30 mg QD Through Univariate Cox Regression



Conclusion: VTE event rates appeared balanced across UPA doses and active comparator groups in pts with RA. Risk factors for VTE events identified through univariate analyses in pts who received UPA included prior history of VTE and BMI, two factors previously known to be associated with VTE risk. One limitation is the small sample size, limiting the analysis to univariate. Continued follow-up of pts receiving UPA is ongoing to further contextualize the risk of VTE in the clinical trial program.

References:

[1] Kim SC, et al. *Arthritis Care Res* 2013;65:1600-7.

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THU0196

TOFACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS AND INDICATIVE OF DEPRESSION AND/OR ANXIETY: A POST HOC ANALYSIS OF PHASE 3 AND PHASE 3B/4 CLINICAL TRIALS

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Background: Depression/anxiety are common in RA pts. SF-36 MCS ≤38 can identify probable major depressive disorder and/or probable generalised anxiety disorder (pMDD/pGAD) in RA pts. Tofacitinib is an oral JAK inhibitor for the treatment of RA.

Objectives: To assess pMDD/pGAD prevalence in the tofacitinib RA program and efficacy by baseline (BL) pMDD/pGAD status.

Methods: Data from pts receiving tofacitinib, ADA, or PBO were pooled from 5 Phase (P)3 and 1 P3b/4 trials. Demographics/BL characteristics were reported by BL pMDD/pGAD (SF-36 MCS ≤38, presence; >38, absence). Month (M)3/6/9/12 SF-36 MCS change from BL (Δ) was estimated, and % with pMDD/pGAD reported. M3/6/12 efficacy outcomes compared tofacitinib-treated pts by BL pMDD/pGAD.

Results: BL pMDD/pGAD was seen in 44.5% (tofacitinib 5 mg BID), 39.8% (tofacitinib 10 mg BID), 45.4% (ADA 40 mg Q2W) and 39.1% (PBO) of pts. pMDD/pGAD pts had higher BL CRP and worse disability, fatigue, pain and sleep vs pts without. SF-36 MCS increases were greater for tofacitinib vs PBO/ADA (Fig 1a). The % of pts with BL pMDD/pGAD who continued to have pMDD/pGAD reduced over time, and was generally lower for tofacitinib vs PBO/ADA (Fig 1b). Regardless of BL pMDD/pGAD, efficacy was generally similar for tofacitinib 5 mg BID (Table) and 10 mg BID.

Conclusion: ~40% of RA pts had BL pMDD/pGAD. SF-36 MCS improvements were greater for tofacitinib vs PBO/ADA. With tofacitinib, % of pts with SF-36 MCS ≤38 reduced by ~60% at M12. Tofacitinib efficacy was similar in pts with/without BL pMDD/pGAD. Limitations include using SF-36 MCS to identify probable rather than confirmed MDD or GAD. Future research using gold standard psychiatric interviews to validate use of SF-36 MCS ≤38 is needed.

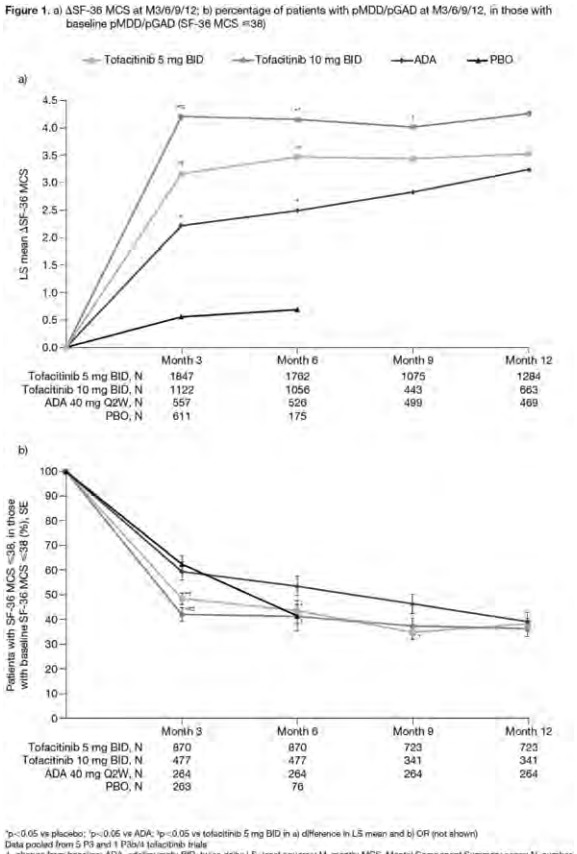


Table. M3/6/12 efficacy with tofacitinib 5 mg BID, by BL pMDD/pGAD[a]

	SF-36 MCS ≤38	SF-36 MCS >38	OR (95% CI)	P value
ACR20 (%)[b,c]				
M3	55.1	57.9	0.89 (0.74, 1.08)	0.2330
M6	61.7	62.8	0.96 (0.79, 1.16)	0.6511
M12	58.4	58.6	0.99 (0.80, 1.22)	0.9279
ACR50 (%)[b,c]				
M3	25.9	29.2	0.85 (0.70, 1.03)	0.1022
M6	36.0	38.0	0.92 (0.76, 1.11)	0.3724
M12	33.8	34.3	0.98 (0.80, 1.20)	0.8366
ACR70 (%)[b,c]				
M3	10.1	11.0	0.91 (0.69, 1.18)	0.4704
M6	16.5	16.5	1.00 (0.79, 1.26)	0.9901
M12	18.3	17.5	1.06 (0.83, 1.34)	0.6560
DAS28-4(ESR)<2.6 (%)[b,c]				
M3	5.4	7.4	0.72 (0.49, 1.05)	0.0872
M6	5.9	8.5	0.68 (0.49, 0.94)	0.0199*
M12	8.0	11.9	0.64 (0.47, 0.89)	0.0073**
ΔHAQ-DI, LS mean[c,d]	**SF-36 MCS ≤38**	**SF-36 MCS >38**	**Difference (95% CI)**	**P value**
M3	-0.41	-0.43	0.01 (-0.04, 0.06)	0.6008
M6	-0.49	-0.48	-0.01 (-0.06, 0.04)	0.6617
M12	-0.52	-0.52	-0.01 (-0.06, 0.05)	0.8475

*p<0.05; **p<0.01 Data pooled from 5 P3 and 1 P3b/4 tofacitinib trials [a]BL pMDD/pGAD = SF-36 MCS ≤38; [b]Logistic regression fit; [c]For PBO pts advancing to tofacitinib post-M3, only PBO data were included; [d]Mixed-effects linear model fit

Δ, change from baseline; ACR, American College of Rheumatology; BID, twice daily; BL, baseline; CI, confidence interval; DAS28-4(ESR), Disease Activity Score in 28 joints, erythrocyte sedimentation rate; HAQ-DI, Health Assessment Questionnaire-Disability Index; LS, least squares; M, month; MCS, Mental Component Summary score; OR, odds ratio; P, Phase; pGAD, probable generalised anxiety disorder; PBO, placebo; pMDD, probable major depressive disorder; pt, patient; RA, rheumatoid arthritis; SF-36, Short Form-36 health survey

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THU0197

SAFETY PROFILE OF UPADACITINIB UP TO 3 YEARS OF EXPOSURE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The safety and efficacy of upadacitinib (UPA), an oral JAK inhibitor, was evaluated in the phase 3 SELECT clinical program, which included 5 randomized, double-blind, controlled trials across a spectrum of rheumatoid arthritis (RA) patients (pts)[1-5].

Objectives: To describe the long-term integrated safety profile of UPA relative to active comparators in pts with RA treated in the SELECT program up to a cut-off date of 30 June 2019.

Methods: Treatment-emergent adverse events (TEAEs: AE onset ≥first dose and ≤30 days after last dose) were summarized for the following: methotrexate (MTX, 1 trial, mean exposure 76 wks); adalimumab (ADA, 1 trial, mean exposure 69 wks); pooled UPA 15 mg (5 trials, mean exposure 90 wks); pooled UPA 30 mg (4 trials, mean exposure 100 wks). TEAEs are reported as exposure-adjusted event rates (EAERs; events/100 patient years [E/100PYs]).

Results: 3833 pts received ≥1 dose of UPA 15 mg [n=2629, 4565.8 PYs] or 30 mg [n=1204, 2309.7 PYs] QD, with no option to switch doses. More than half of pts received UPA for ≥96 wks (median: UPA 15, 101.9 wks; UPA 30: 111.7 wks). The EAERs of overall SAEs and AEs leading to discontinuation on UPA 15 mg were comparable to MTX and ADA; rates on UPA 30 mg were numerically higher than UPA 15 mg (**Table**). The most common AEs (≥5 E/100 PYs) reported with UPA 15 mg were upper respiratory tract infection (URTI), nasopharyngitis, urinary tract infection (UTI), bronchitis, increased CPK, and increased ALT. For UPA 30 mg, the most common AEs reported were URTI, UTI, increased CPK, nasopharyngitis, bacterial bronchitis, and herpes zoster (HZ). Overall rates of serious infections and opportunistic infections were comparable between UPA 15 mg, MTX, and ADA groups but were higher on UPA 30 mg (**Figure**). Rates of HZ were higher in both UPA groups (30 mg higher than 15 mg) vs MTX and ADA. The majority of HZ cases were non-serious (96%) and involved a single dermatome (74%). Rates of VTE were comparable across treatment groups (0.3-0.5/100 PYs), as were rates of adjudicated MACE and malignancies (excluding NMSC). Rates of NMSC in UPA 15 mg and ADA were similar, with numerically higher rates on UPA 30 mg. SMR analysis demonstrated that the number of deaths in pts with RA exposed to UPA was not higher than what would be expected for the general population.

Conclusion: Through long-term follow-up, the integrated safety profile of UPA remained consistent with previous analyses, with no new signals identified.

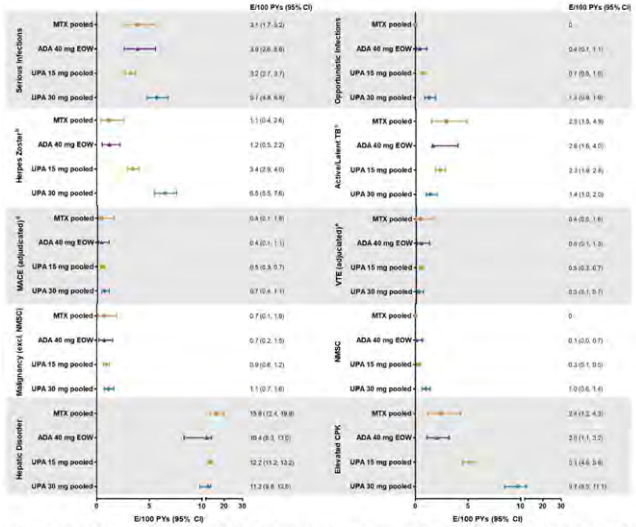
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Table. Overall TEAEs for UPA and Active Comparators (E/100 PYs [95% CI])

	MTX n=314 (456.0 PYs)	ADA 40 mg eow n=579 (768.6 PYs)	UPA 15 mg QD n=2629 (4565.8 PYs)	UPA 30 mg QD n=1204 (2309.7 PYs)
Any AE	271.7 (256.8, 287.3)	242.3 (231.4, 253.5)	247.7 (243.2, 252.3)	310.6 (303.5, 317.9)
Any SAE	12.7 (9.7, 16.4)	14.6 (12.0, 17.5)	12.9 (11.9, 14.0)	19.8 (18.0, 21.7)
Any AE leading to discontinuation	7.7 (5.3, 10.7)	8.2 (6.3, 10.5)	6.3 (5.6, 7.1)	10.0 (8.8, 11.4)
Deaths[a]	0.4 (0.1, 1.6)	0.8 (0.3, 1.7)	0.4 (0.2, 0.6)	0.7 (0.4, 1.1)

[a]Deaths included non-treatment emergent deaths: ADA, 1; UPA 15 mg, 3; UPA 30 mg, 3.

Figure. Overall AESIs in Patients Treated with Upadacitinib Compared to Active Controls[a]



MTX pooled: N=314, PYs=456.0; ADA 40 mg EOW: N=579, PYs=768.6; UPA 15 mg pooled: N=2629, PYs=4565.8; UPA 30 mg pooled: N=1204, PYs=2309.7
[a]Patients who switched from PBO, ADA, or MTX to UPA were included in the UPA analysis set from the start of UPA, while those who switched from upadacitinib to ADA were included in the ADA dataset from the start of ADA. There was no switch between UPA doses in any study. MTX monotherapy censored at time of rescue to combination therapy (either UPA + MTX or addition of csDMARD).
[b]Most HZ cases were non-serious (95.9%) and single dermatome (74.4%).
[c]There were 6 cases of active TB on UPA (0.1 E/100 PYs) and 1 on ADA.
[d]MACE was defined as CV death, non-fatal MI, and non-fatal stroke.
[e]VTE was defined as deep vein thrombosis and pulmonary embolism.
ADA, adalimumab; AE, adverse event; CPK, creatine phosphokinase; CV, cardiovascular; E, events; EOW, every other week; MACE, major adverse cardiovascular event; MI, myocardial infarction; MTX, methotrexate; NMSC, non-melanoma skin cancer; PBO, placebo, PYs, patient-years; QD, once daily; TB, tuberculosis; TEAE, treatment-emergent adverse event; UPA, upadacitinib; VTE, venous thromboembolism.

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THU0198 EFFICACY AND SAFETY OF FILGOTINIB FOR PATIENTS WITH RHEUMATOID ARTHRITIS WITH INADEQUATE RESPONSE TO METHOTREXATE: FINCH 1 52-WEEK RESULTS

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Background: Filgotinib (FIL) is an oral, potent, selective JAK1 inhibitor. FINCH 1 (NCT02889796) assessed FIL efficacy and safety in patients (pts) with rheumatoid arthritis (RA) with inadequate response to methotrexate (MTX-IR); primary outcome results at week (W)12 and W24 were previously reported.[1]
Objectives: To present FINCH 1 W52 results.
Methods: This global, phase 3, double-blind, active- and placebo (PBO)-controlled study randomised MTX-IR pts with active RA on a background of stable MTX 3:3:2:3 to oral FIL 200 mg or FIL 100 mg once daily, subcutaneous adalimumab (ADA) 40 mg every 2W, or PBO up to W52; pts receiving PBO at W24 were rerandomised to FIL 100 or 200 mg. Efficacy was assessed from clinical, radiographic, and pt-reported outcomes; W52 comparisons were not adjusted for multiplicity. Safety endpoints included adverse events (AEs) and laboratory abnormalities.
Results: Of 1755 treated pts, 1417 received study drug through W52. The majority (81.8%) were female, mean (standard deviation [SD]) RA duration was 7.8 (7.6) years, and baseline mean (SD) DAS28(CRP) was 5.7 (0.9). FIL efficacy was sustained through W52; 54%, 43%, and 46% of pts receiving FIL 200 and 100 mg and ADA, respectively, had W52 DAS28(CRP) <2.6 (nominal p for FIL 200 vs ADA = 0.024) (Figures 1–2, Table 1). FIL safety profile through W52 was consistent with W24 data. AEs of interest were infrequent and balanced among treatments (Table 2); 82 pts (4.7%) discontinued treatment due to AEs.

Table 1. Efficacy outcomes at week 52

	FIL 200 mg (n = 475)	FIL 100 mg (n = 480)	ADA (n = 325)
ACR20/50/70, %	78/62/44	76/59/38	74/59/39
DAS28(CRP) ≤3.2, %	66[+]	59	59
mTSS[a]	0.18[+++]	0.45	0.61
HAQ-DI[b]	–0.93[+]	–0.85	–0.85
SF-36 PCS[b]	12.0	11.5	12.4
FACIT-F[b]	11.9	12.2	11.7

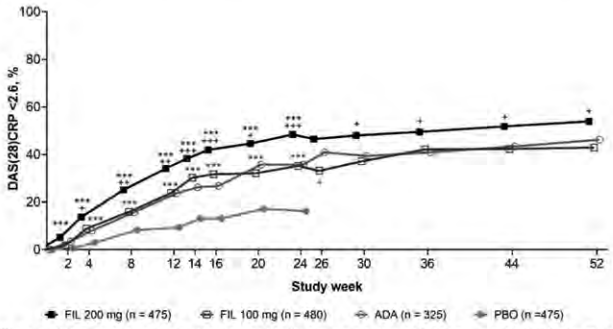
[a]Least squares mean change from baseline.
[b]Mean change from baseline.
[+]p <0.05, [+++]p <0.001 vs ADA; not adjusted for multiplicity.
ADA, adalimumab; FIL, filgotinib; mTSS, modified van der Heijde TSS.

Table 2. Treatment-emergent AEs through week 52

Event, n (%)	FIL 200 (n = 475)	FIL 100 mg (n = 480)	ADA (n = 325)
All AEs	352 (74.1)	350 (72.9)	239 (73.5)
Serious AEs	35 (7.4)	40 (8.3)	22 (6.8)
Infection	206 (43.4)	194 (40.4)	129 (39.7)
Serious infection	13 (2.7)	13 (2.7)	10 (3.1)
Herpes zoster	6 (1.3)	4 (0.8)	2 (0.6)
VTE	1 (0.2)	0	1 (0.3)
MACE (adjudicated)	0	2 (0.4)	1 (0.3)
Malignancy (excluding NMSC)	2 (0.4)	2 (0.4)	2 (0.6)
NMSC	1 (0.2)	1 (0.2)	0
Death	3 (0.6)	1 (0.2)	1 (0.3)

Data omitted for patients rerandomised from placebo to FIL.
ADA, adalimumab; AE, adverse event; FIL, filgotinib; MACE, major adverse cardiovascular event; NMSC, nonmelanoma skin cancer; VTE, venous thromboembolism.

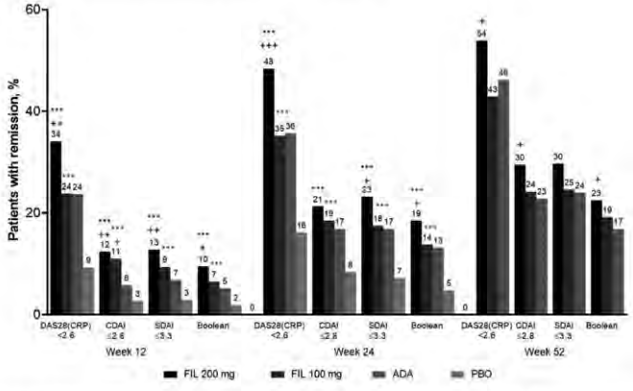
Figure 1. Proportion of patients with DAS28(CRP) <2.6 through week 52 with nonresponder imputation



***, p vs PBO <0.001, not adjusted for multiplicity except at week 12; *, p vs ADA <0.05, **, p vs ADA <0.01, +++, p vs ADA <0.001, not adjusted for multiplicity.
ADA, adalimumab; FIL, filgotinib; PBO, placebo.

Conclusion: Through W52, both FIL 200 and 100 mg showed sustained efficacy based on clinical and pt-reported outcomes and radiographic progression and were well tolerated in MTX-IR pts with RA, with faster onset and numerically greater efficacy for FIL 200 vs 100 mg.

Figure 2. Patients in remission at weeks 12, 24, and 52



***, p vs PBO <0.001, not adjusted for multiplicity except DAS28(CRP) at week 12; *, p vs ADA <0.05; **, p vs ADA <0.01; +++, p vs ADA <0.001; not adjusted for multiplicity.
ADA, adalimumab; FIL, filgotinib; PBO, placebo.

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THU0199

ABX464, A NOVEL DRUG IN THE FIELD OF INFLAMMATION, INCREASES MIR-124 AND MODULATES MACROPHAGES AND T-CELL FUNCTIONS.

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Background: ABX464 is a small oral molecule with a novel mode of action. It binds the Cap Binding Complex, involved in the biogenesis of RNAs and predominantly upregulates the expression of a microRNA miR-124 in PBMCs and T cells (1). miR-124 has been widely described for its anti-inflammatory properties, with many confirmed targets i.e. monocyte chemoattractant protein 1 (MCP-1, CXCL-1, SERPIN-E1, STAT-3, IL-6 receptor. It post-transcriptionally regulates the expression of MCP-1 in rheumatoid arthritis (RA) synoviocytes and decreases their proliferation (2). While miR-124 is decreased in synoviocytes of RA patients, its injection in joint improved arthritis in rats (3). miR-124 expression in macrophages leads to the induction and maintenance of anti-inflammatory M2 phenotype (4). Its effect in T cells remains controversial.

Objectives: (i) To assess the effect of ABX464 on miR-124 expression *in vitro* in macrophages and *in vivo* in patients; (ii) to assess the effect of ABX464

on arthritis in mice and (iii) to decipher the effect of ABX464 on human macrophages and T cells.

Methods: miR-124 was measured in human monocyte-derived macrophages (huMDM) treated with ABX464 for 4 days and in patients with ulcerative colitis included in a phase IIa RCT in blood and rectal biopsies at day 56 by TaqMan qPCR. Collagen-induced arthritis (CIA) was induced using usual protocol and ABX464 was given by gavage 2 weeks at 40 mg/kg after the 2nd injection of collagen and Freund adjuvant. HuMDM were exposed to 5 µM of ABX464 or DMSO (control) for 4 days, during a M1-polarization. Cytokines and chemokines were assessed in supernatants using both Proteome Profiler Array and Luminex. PBMCs were exposed to ABX464 (5 µM) for 6 days. Th1 (IFN-g+), Th17 (CCR6+IL-17+), Th2 (CRTH2+ IL-4+) and Tregs (CD25+CD125-/loFoxP3+) were assessed by flow cytometry. IL-6 receptor was assessed in CD4+ supernatant using ELISA.

Results: ABX464 increased miR-124 in vitro by 3.41 folds in huMDM (p=0.001) compared to DMSO. The phase IIa RCT conducted in 32 patients with moderate to severe active ulcerative colitis showed a good safety profile and significant clinical efficacy. A strong increase of miR-124 was observed both in blood and rectal biopsies of patients treated with ABX464 (637 and 7.69 folds respectively, compared to placebo, p<0.05). The use of ABX464 drastically decreased the incidence of arthritis from 52% (15/ 29 mice) to 10% (3/30 mice) in a CIA model. Macrophages treated with ABX464 produced significantly less MCP-1 (median decrease -67%, p=0.004), CXCL-1 (-18%, p=0.004) and SERPIN-E1 (-53%, p=0.004), as confirmed by the two technics (n=9). ABX464 significantly decreased Th17 (-56%, p=0.02), while increasing Th2 (+21%, p=0.01). IL-6 soluble receptor was significantly decreased in supernatant of PBMCs treated with ABX464 (-43%, p=0.04).

Conclusion: We demonstrated that ABX464 increases miR-124 both *in vitro* and in ulcerative colitis patients. *In vitro*, ABX464 decreased the expression of miR-124 target genes, that is MCP-1, CXCL-1, SERPIN-E1 in macrophages and decreases the number of Th17 as well as IL-6 soluble receptor in CD4+ T cells. A phase IIa RCT is currently ongoing in patients with rheumatoid arthritis and inadequate response to methotrexate and/or TNF-inhibitors (n=60). Results are expected during 2020 summer.

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THU0200 THE CHOICE OF BDMARD OR TSDMARD AS FIRST LINE THERAPY: DATA OF THE TARDIS-RA REGISTRY, A NATIONWIDE BELGIAN BIOLOGIC REGISTRY

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Background: The Tool for Administrative Reimbursement Drug Information Sharing (TARDIS) is an electronic platform combining data collection from all Belgian patients with Rheumatoid Arthritis (RA) on advanced therapy, together with a drug reimbursement request. Therapy choice after initial 2 classical synthetic DMARD failure is left to the treating rheumatologist in Belgium.

Objectives: To investigate first-line therapy choices for tumor necrosis factor inhibitor (TNFi) biologic (b) DMARDs, non-TNFi bDMARDs or targeted synthetic (ts) DMARDs via patient characteristics and initial treatment response in the TARDIS-RA registry.

Methods: All Belgian rheumatologist inserted patient data online when prescribing a b/tsDMARD. When data was entered for the first time, previous and current use of DMARD therapies was registered. Every next bDMARD or tsDMARD initiation, prolongation and discontinuation was registered electronically. First prolongation is 6 months for bDMARDs and 12 weeks for tsDMARDs, and yearly thereafter. Patients were selected for this analysis if they started a TNFi, non-TNFi or tsDMARD therapy between Jan 2018 and Jan 2019. Rituximab was excluded. Baseline characteristics of bionaive patients per therapy were compared with Mann-Whitney U or Chi^2 tests were appropriate. Regression analyses, adjusted for age, DAS28 baseline and disease duration, evaluated DAS28 change, remission (DAS28<2.6) and low disease activity (LDA, DAS28<3.2) between b/tsDMARDs at first TARDIS follow-up.

Results: In 2018, 1263 bionaive RA patients were included. Table 1 describes this population. Time until 1st follow-up differed between groups with 183 (181-184) days for bDMARD versus 84 (84-84) days for tsDMARD patients. Lineair regression showed an effect of therapy type on DAS28 change in bionaive patients (p=0.017). Logistic regression showed no difference per therapy for remission (p=0.090) nor low disease activity (p=0.123). Proportions of therapy prolongations at 1st follow up visit did not differ per therapy type.

Table 1. Baseline characteristics and treatment response of first-line TNFi, Non-TNFi or tsDMARDs

	TNFi	Non-TNFi	tsDMARD	p-value
Number patients	696 (57%)	293 (25%)	215 (18%)	
Age (years)	55, (45-64)	58, (51-68)	58, (49-66)	<0.001
Disease duration (years)	3, (1-7)	3, (1-9)	5, (2-13)	<0.001
DAS28 Baseline	4.8, (4.3-5.5)	5.1, (4.4-5.7)	4.7, (4.2-5.4)	0.010
DAS28 Change	2.2 (1.0-3.0)	2.2 (1.1-3.2)	1.9 (0.9-2.7)	0.014
Remission	296 (50%)	123 (49%)	78 (42%)	0.143
LDA	377 (64%)	153 (61%)	105 (56%)	0.196
Prolongation therapy	492 (82%)	219 (87%)	161 (86%)	0.158

Number given are median, (IQR) or number (proportion). TNFi = tumour necrosis factor inhibitor, ts= targeted synthetic, DAS = disease activity score, DAS28 change = DAS28 at 1st follow up visit minus DAS28 at baseline, remission = DAS28<2.6), LDA = low disease activity = DAS28<3.2), Prolongation = therapy was continued at 1st follow-up visit. Mann-Whitney U or Chi square tests were used where appropriate.

Conclusion: Initial therapy choices are partially driven by patient profile, although other factors such as patient preferences could not be verified. DAS28 change for tsDMARDs seemed less important versus bDMARDs, but can possibly be attributed to the preset evaluation moment being sooner for tsDMARDs versus bDMARDs aside of patient profile differences in age and disease duration. In contrast, proportion of remission, low disease activity and therapy prolongation did not differ by therapy.

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THU0201

LONG-TERM SAFETY AND EFFECTIVENESS OF UPADACITINIB OR ADALIMUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS AT 72 WEEKS FROM THE SELECT-COMPARE STUDY

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Background: In the SELECT-COMPARE study in rheumatoid arthritis (RA) patients with inadequate response to methotrexate (MTX), upadacitinib (UPA), a Janus Kinase (JAK) 1-selective inhibitor, showed significant improvements in treatment of signs and symptoms when compared to placebo (PBO) and adalimumab (ADA) up to 48 weeks.[1]

Objectives: To report safety and efficacy of UPA vs ADA up to 72 weeks in patients with RA from the ongoing long-term extension (LTE) of SELECT-COMPARE.

Methods: Patients were randomized to once daily (QD) UPA 15 mg, PBO, or ADA 40 mg every other week, with all patients continuing background MTX. The study was double-blind for 48 weeks. Between Weeks 14-26, patients were rescued (from PBO to UPA, UPA to ADA, or ADA to UPA) if there was <20% improvement in tender/swollen joint count at Weeks 14/18/22 or if Clinical Disease Activity Index (CDAI) was >10 at Week 26; all PBO patients who were not rescued were switched to UPA at Week 26. Patients continued UPA or ADA in a blinded manner until the last patient completed the Week 48 visit; patients received open-label treatment thereafter. Study visits occurred at Week 60, 72, and every 12 weeks thereafter. Treatment-emergent adverse events (TEAEs) per 100 patient years (PY) were summarized up to December 26, 2018. Efficacy was analyzed by randomized group.

Results: In total, 651, 651 and 327 patients were randomized at baseline to receive UPA, PBO, and ADA, respectively. Subsequently, 252 patients were switched from UPA to ADA, 159 were switched from ADA to UPA, and all PBO patients were switched to UPA. 1403 patients entered the LTE at Week 48 (UPA: 1091 [565 switched from PBO; 66 rescued from ADA; 460 on continued UPA]; ADA: 312 [110 rescued from UPA; 202 on continued ADA]). The cumulative exposures were 1396.7 and 515.1 PYs for UPA and ADA, respectively. UPA + MTX was generally well-tolerated as assessed by the frequency of AEs, including serious AEs, AEs leading to discontinuation of study drug, and AEs of special interest ([AESIs] including serious and opportunistic infections, malignancy, adjudicated major adverse cardiac events or venous thromboembolism; Figure 1). The event rates of AESIs were generally comparable between UPA + MTX and ADA + MTX, except for herpes zoster, lymphopenia, hepatic disorder, and CPK elevation, which were numerically higher with UPA + MTX. At both Weeks 60 and 72, significantly greater proportions of patient receiving UPA + MTX achieved ACR20/50/70 (P ≤.01/.001/.001), low disease activity (P ≤.001) and remission (P ≤.001) compared to those receiving ADA + MTX; Figure 2). Similarly, improvements in pain and function were significantly greater in the UPA vs ADA group through Week 72 (P ≤.01).

Conclusion: The safety profile for UPA + MTX was consistent with that reported previously and with the integrated Phase 3 safety analysis.[1,2] UPA + MTX maintained significantly higher levels of clinical response, including remission compared to ADA + MTX through Week 72.

References:

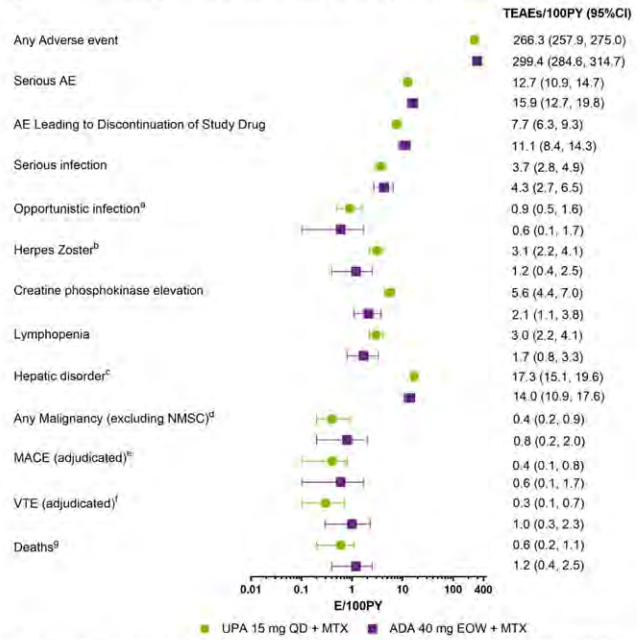
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Figure 1. Treatment-emergent adverse event summary; E/100PY (95% CI) in Patients (EAER)



UPA, upadacitinib; ADA, adalimumab; MTX, methotrexate; NMSC, non-melanoma skin cancer; MACE, major adverse cardiovascular event; VTE, Venous Thromboembolic Events.

[a]Opportunistic infections: UPA: 4 oral candidiasis, 4 esophageal candidiasis, 1 bronchopulmonary aspergillosis, 1 fungal pharyngitis, 1 herpes zoster disseminated; 1 meningitis Listeria, and 1 oral fungal infection; ADA: 3 oral candidiasis.

[b]Herpes zoster: majority of cases on UPA were nonserious and involved 1 or 2 dermatomes.

[c]Hepatic disorders: majority based on ALT/AST elevations.

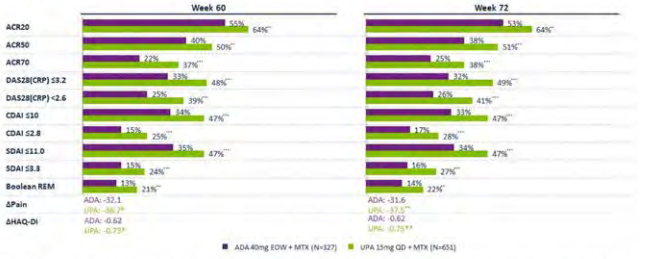
[d]Malignancies excluding NMSC: UPA: 1 laryngeal cancer, 1 endometrial adenocarcinoma, 1 malignant melanoma, 1 adenocarcinoma gastric, 1 adenocarcinoma of colon; ADA: 1 malignant melanoma, 1 colon cancer metastatic, 1 lung neoplasm malignant, 1 colon cancer metastatic.

[e]MACE (includes cardiovascular [CV] death, non-fatal myocardial infarction [MI], non-fatal stroke): UPA: 1 non-fatal stroke; 3 non-fatal MI, 1 CV death; ADA: 2 non-fatal stroke, 1 CV death.

[f]VTE: UPA, 1 deep vein thrombosis (DVT), 2 pts with pulmonary embolism (PE), 1 pt with DVT and PE; ADA: 4 pts with PE, 1 pts with DVT.

[g]Deaths (includes non-treatment emergent deaths): UPA: 2 deaths (undetermined/unknown), 1 cardiac failure, 1 sudden death, 1 arteriosclerosis coronary artery; 1 meningitis listeria, 1 acute respiratory distress syndrome, 1 lung carcinoma cell type unspecified Stage IV; ADA: 1 left ventricular failure; 1 cremocerebral injury; 1 colon cancer, 1 mixed connective tissue disease, 1 lung squamous cell carcinoma Stage IV, 1 undetermined death

Figure 2. Efficacy Endpoints



UPA, upadacitinib; ADA, adalimumab; ACR, American College of Rheumatology; DAS28(CRP), Disease Activity Score for 28-joints C-Reactive Protein; CDAI, clinical disease activity index; SDAI, Simplified Disease Activity Index; HAQ-DI, health assessment questionnaire-disability index; REM, remission

For patients who were rescued, non-responder imputation (NRI) was used for binary endpoints for rescue prior to Week 26 and last observation carried forward (LOCF) was used for continuous and binary endpoints for rescue at Week 26. For patients who prematurely discontinued the study drug at any time before/at Week 72, NRI was used for binary endpoints and observed case (OC) was used for continuous endpoints. No multiplicity adjustments were applied.

*, **, *** P ≤ .05, .01, and .001, respectively for UPA vs ADA

THU0202

INTEGRATED SAFETY ANALYSIS OF FILGOTINIB TREATMENT FOR RHEUMATOID ARTHRITIS FROM 7 CLINICAL TRIALS

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Background: Filgotinib (FIL), an oral, potent, selective JAK-1 inhibitor, provided statistically significant and clinically meaningful improvement in rheumatoid arthritis (RA) signs and symptoms, physical function, radiographic progression, and quality of life in a comprehensive clinical program of 4 phase 3 (FINCH 1–4; NCT02889796, NCT02873936, NCT02886728, NCT03025308) and 3 phase 2 (DARWIN 1–3; NCT01668641, NCT01894516, NCT02065700) trials in patients (pts) with early and biologic-refractory RA.[1–3]

Objectives: To assess long-term safety of FIL.

Methods: Treatment-emergent adverse events (TEAEs) from the FIL clinical program were integrated and presented for pts receiving FIL 200 mg or FIL 100 mg QD (including pts who transitioned to FIL from placebo [PBO], methotrexate [MTX], adalimumab [ADA], or another dose of FIL) as well as pts receiving PBO, MTX, and ADA across all 7 studies. Exposure-adjusted incidence rates (EAIRs) per 100 patient-years (PY) were calculated for adverse events (AEs) of interest per treatment. Incidence was total number of pts with events, and PY exposure was time between first and last doses. Major adverse cardiovascular events (MACE) and venous thromboembolism (VTE) were centrally adjudicated by an independent committee.

Results: Across the 7 trials, 4057 pts with RA (2227 pts FIL 200 mg; 1600 pts FIL 100 mg) received >1 dose of treatment for 5493 total PY of exposure (3079.2 PY FIL 200 mg; 1465.3 PY FIL 100 mg) (**Table**). EAIRs of serious AEs and TEAEs leading to death in pts receiving FIL were comparable to those for PBO, ADA, or MTX, with no dose-dependent effect (Figure 1). EAIR for herpes zoster (HZ), serious, and opportunistic infections are shown in Figure 2. EAIR for HZ were low overall, but numerically slightly higher for FIL relative to PBO, ADA, and similar to MTX. Serious infection EAIRs were comparable between pts receiving FIL 100 mg and ADA, and numerically slightly lower for FIL 200 mg and MTX. Rates of opportunistic infections (including active tuberculosis) were low overall; EAIR for FIL doses were comparable to placebo and numerically lower than ADA or MTX. Rates of MACE and VTE were numerically lower for FIL relative to PBO (Figure 1). Malignancies, including nonmelanoma skin cancer, were rare overall, and rates were low in pts receiving FIL (Figure 1).

Table. Total exposure to study treatments pooled from 7 studies

	Number of patients	Patient-years of exposure
FIL 200 mg	2227	3079.2
FIL 100 mg	1600	1465.3
ADA	325	290.1
MTX	416	356.2
PBO	781	302.4

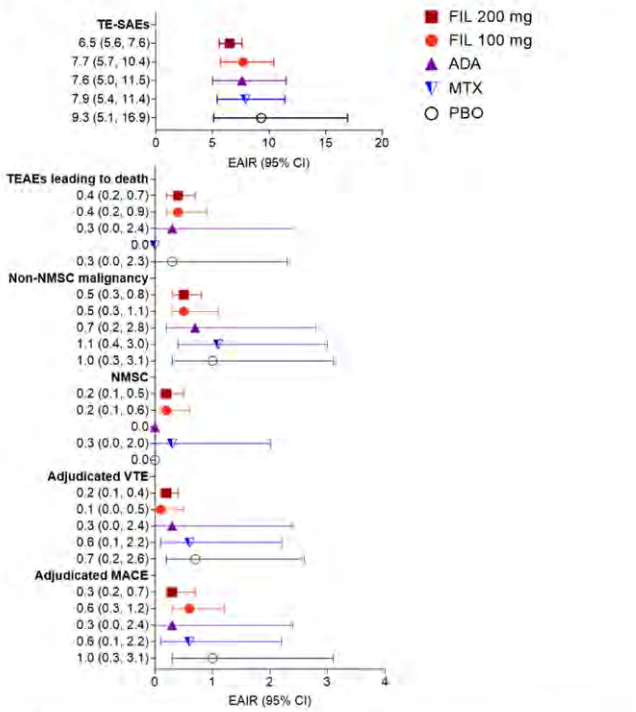
Patients could contribute to >1 treatment group.
ADA, adalimumab; FIL, filgotinib; MTX, methotrexate; PBO, placebo.

Conclusion: In this integrated analysis, FIL was well-tolerated, and no new safety concerns were identified. No clinically meaningful dose-dependent safety effects were observed. MACE and VTE were uncommon. Serious infections rates were low; HZ reactivation was infrequent. Safety results were consistent with selective JAK-1 inhibition and highlight the favourable safety and tolerability of FIL in patients with RA.

References:

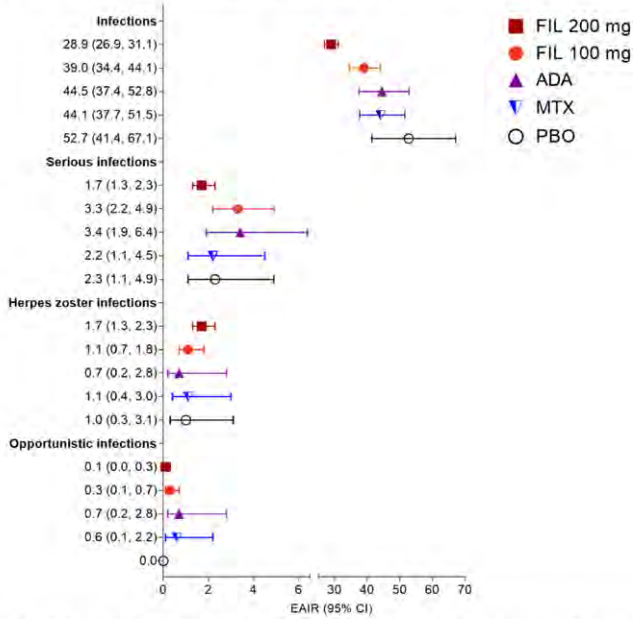
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Figure 1. Rates of TE-SAEs, deaths, malignancies, VTE, and MACE by treatment group per 100 patient-years



ADA, adalimumab; CI, confidence interval; EAIR, exposure-adjusted incidence rate; FIL, filgotinib; MACE, major adverse cardiovascular event; MTX, methotrexate; NMSC, nonmelanoma skin cancer; PBO, placebo; TEAE, treatment emergent adverse event; TE-SAE, treatment-emergent severe adverse event; VTE, venous thromboembolism.

Figure 2. Rates of infections by treatment group per 100 patient-years



ADA, adalimumab; CI, confidence interval; EAIR, exposure-adjusted incidence rate; FIL, filgotinib; MTX, methotrexate; PBO, placebo.

Disclosure of Interests: Mark C. Genovese Grant/research support from: Abbvie, Eli Lilly and Company, EMD Merck Serono, Galapagos, Genentech/Roche, Gilead Sciences, Inc., GSK, Novartis, Pfizer Inc., RPharm, Sanofi Genzyme, Consultant of: Abbvie, Eli Lilly and Company, EMD Merck Serono, Genentech/Roche, Gilead Sciences, Inc., GSK, Novartis, RPharm, Sanofi Genzyme, Kevin Winthrop Grant/research support from: Bristol-Myers Squibb, Consultant of: AbbVie, Bristol-Myers Squibb, Eli Lilly, Galapagos, Gilead, GSK, Pfizer Inc, Roche,

UCB, Yoshiya Tanaka Grant/research support from: Asahi-kasei, Astellas, Mitsubishi-Tanabe, Chugai, Takeda, Sanofi, Bristol-Myers, UCB, Daiichi-Sankyo, Eisai, Pfizer, and Ono, Consultant of: Abbvie, Astellas, Bristol-Myers Squibb, Eli Lilly, Pfizer, Speakers bureau: Daiichi-Sankyo, Astellas, Chugai, Eli Lilly, Pfizer, AbbVie, YL Biologics, Bristol-Myers, Takeda, Mitsubishi-Tanabe, Novartis, Eisai, Janssen, Sanofi, UCB, and Teijin, Tsutomu Takeuchi Grant/research support from: Eisai Co., Ltd, Astellas Pharma Inc., AbbVie GK, Asahi Kasei Pharma Corporation, Nippon Kayaku Co., Ltd, Takeda Pharmaceutical Company Ltd, UCB Pharma, Shionogi & Co., Ltd., Mitsubishi-Tanabe Pharma Corp., Daiichi Sankyo Co., Ltd., Chugai Pharmaceutical Co. Ltd., Consultant of: Chugai Pharmaceutical Co Ltd, Astellas Pharma Inc., Eli Lilly Japan KK, Speakers bureau: AbbVie GK, Eisai Co., Ltd, Mitsubishi-Tanabe Pharma Corporation, Chugai Pharmaceutical Co Ltd, Bristol-Myers Squibb Company, AYUMI Pharmaceutical Corp., Eisai Co., Ltd, Daiichi Sankyo Co., Ltd., Gilead Sciences, Inc., Novartis Pharma K.K., Pfizer Japan Inc., Sanofi K.K., Dainippon Sumitomo Co., Ltd., Alan Kivitz Shareholder of: AbbVie, Amgen, Gilead, GSK, Pfizer Inc, Sanofi, Consultant of: AbbVie, Boehringer Ingelheim,,Flexion, Genzyme, Gilead, Janssen, Novartis, Pfizer Inc, Regeneron, Sanofi, SUN Pharma Advanced Research, UCB, Paid instructor for: Celgene, Genzyme, Horizon, Merck, Novartis, Pfizer, Regeneron, Sanofi, Speakers bureau: AbbVie, Celgene, Flexion, Genzyme, Horizon, Merck, Novartis, Pfizer Inc, Regeneron, Sanofi, Franziska Matzkies Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Lei Ye Shareholder of: Gilead Sciences Inc., Employee of: Gilead Sciences Inc., Deyuan Jiang Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Ying Guo Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Beatrix Bartok Shareholder of: Gilead Sciences Inc., Employee of: Gilead Sciences Inc., Robin Besuyen Shareholder of: Galapagos, Employee of: Galapagos, Gerd Rüdiger Burmester Consultant of: AbbVie Inc, Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB Pharma, Speakers bureau: AbbVie Inc, Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB Pharma, Jacques-Eric Gottenberg Grant/research support from: BMS, Pfizer, Consultant of: BMS, Sanofi-Genzyme, UCB, Speakers bureau: Abbvie, Eli Lilly and Co., Roche, Sanofi-Genzyme, UCB

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THU0203

REAL WORLD EFFECTIVENESS OF BARICITINIB IN THE SWISS RHEUMATOID ARTHRITIS REGISTER (SCQM-RA)

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Background: Patients with rheumatoid arthritis (RA) intolerant or not responding adequately to conventional synthetic DMARD (csDMARD) usually receive biological DMARDs (bDMARDs) or targeted synthetic DMARDs (tsDMARDs) as 2nd line. Baricitinib (BARI), a once-daily oral selective Janus kinase inhibitor, is efficient in randomised controlled trials but still lacks evidence for effectiveness in real world settings.

Objectives: To characterise patients initiating treatment with BARI or other alternative bDMARDs, and to perform an analysis of drug maintenance.

Methods: This is an observational, prospective, cohort study, within the Swiss Clinical Quality Management (SCQM) register.

All treatment courses (TC) initiated between 2017-09-01 and 2019-10-01 were considered, comparing TC with BARI (BARI group) to TC with alternative bDMARDs, either TNF inhibitors (TNFi group) or other mode of action bDMARDs (OMA group), excluding rituximab.

Baseline characteristics were compared using ANOVA or $\chi 2$ tests. The crude drug maintenance was assessed by survival analysis (Kaplan-Meier). To correct for potential confounding factors, a Cox proportional hazard model was used. Missing values were imputed using multiple imputation with chained equations.

Results: During the study period, 979 TC were initiated (240 in BARI group, 461 in TNFi group and 278 in OMA group). BARI was prescribed to significantly older patients, with longer disease durations and more previous treatment failures (Table 1). Unadjusted drug maintenance was significantly shorter in the TNFi compared to the BARI group (log rank p = 0.019). After adjustment for potential confounding factors, the hazard of TNFi discontinuation remained higher than for BARI (Hazard Ratio (HR) 1.48 (95% CI = [1.05 – 2.09]; p = 0.02)). A similar trend was observed when comparing the OMA drugs to BARI, with a HR for discontinuation of 1.42 (95% CI = [0.98 – 2.05]; p = 0.06) (Figure 2). Covariates significantly associated with decreased drug maintenance were concomitant csDMARD and concomitant glucocorticoids (Figure 2).

Conclusion: In this preliminary analysis, baricitinib was prescribed to older patients, with longer disease durations, and more previous treatment failures compared to alternative bDMARDs. Baricitinib demonstrated a significantly higher drug maintenance than TNFi, while similar trend was observed in comparison to OMA drugs.

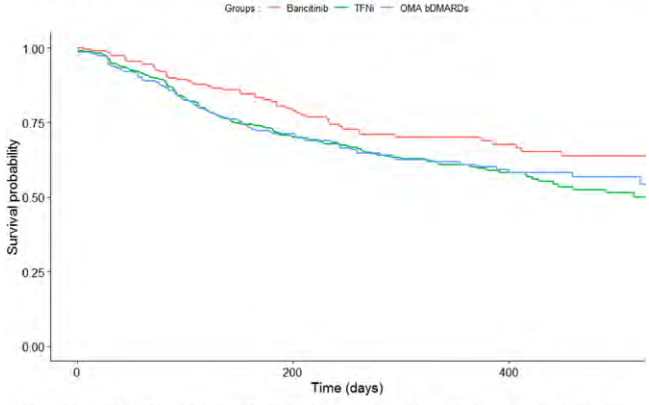
Conflict of interest: This analysis has been made possible by financial support of Eli Lilly (Suisse) SA to the Geneva University Hospitals (HUG).

Table 1. Baseline characteristics of studied population

Variable	Categories	Baricitinib (TC = 240; 240 patients) Mean (SD) Otherwise: n %	TNFi (TC = 461; 397 patients) Mean (SD) Otherwise: n %	OMA bDMARDs (TC = 278; 253 patients) Mean (SD) Otherwise: n %	P values
Concomitant csDMARD at baseline		45 %	54 %	46 %	**0.02**
Line of Therapy	1st	20 %	46 %	22 %	**<0.01**
	2nd	22 %	25 %	26 %	
	3rd	14 %	14 %	26 %	
	4th or later	43 %	16 %	27 %	
Gender (female)		80 %	71 %	74 %	**0.05**
Age		59 (13)	53 (14)	59 (13)	**<0.01**
Seropositivity (ACPA and/or RF)		75 %	71 %	79 %	**0.04**
HAQ-DI Score		0.9 (0.7)	0.7 (0.6)	0.8 (0.6)	**0.02**
Disease duration (years)		12 (10)	9 (10)	11 (9)	**<0.01**
CDAI baseline		19 (10)	15 (12)	19 (14)	0.09

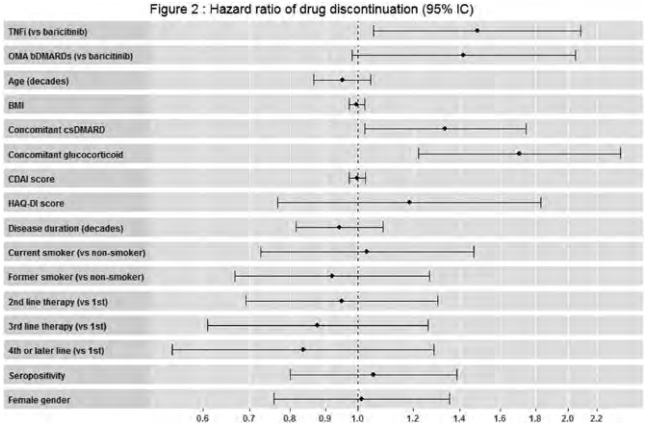
Legend
TC = Treatment Courses. SD = Standard Deviation. TNFi = TNF inhibitors. OMA bDMARDs = Other Mode of Action biological DMARDs. csDMARD = conventional synthetic DMARD. ACPA = Anti Citrullinated Peptide Antibodies. RF = Rheumatoid Factor. HAQ-DI= Health Assessment Questionnaire Disability Index. CDAI = Clinical Disease Activity Index.

Figure 1 : Multivariable Cox model of drug discontinuation by type of treatment



Adjusted for : age, gender, BMI, concomitant csDMARD, concomitant glucocorticoid, disease activity (CDAI), functional disability (HAQ-DI), disease duration, smoking status, line of therapy, and seropositivity (RF and/or ACPA). A cluster term accounted for patients with multiple TC.

Figure 2 : Hazard ratio of drug discontinuation (95% IC)



Disclosure of Interests: : Benoit GILBERT: None declared, Kim Lauper: None declared, Delphine Courvoisier: None declared, Clementine Perrier Shareholder of: Share of Eli Lilly Company, Employee of: I am currently an employee of Eli Lilly Suisse SA, Rudiger Muller Consultant of: AbbVie, Nordic, Sandoz, Axel Finckh Grant/research support from: Pfizer: Unrestricted research grant, Eli-Lilly: Unrestricted research grant, Consultant of: Sanofi, AB2BIO, Abbvie, Pfizer, MSD, Speakers bureau: Sanofi, Pfizer, Roche, Thermo Fisher Scientific
DOI: 10.1136/annrheumdis-2020-eular.1243

THU0204

A SUBGROUP ANALYSIS OF LOW DISEASE ACTIVITY AND REMISSION FROM PHASE 3 STUDY OF FILGOTINIB IN PATIENTS WITH INADEQUATE RESPONSE TO BIOLOGIC DMARDS

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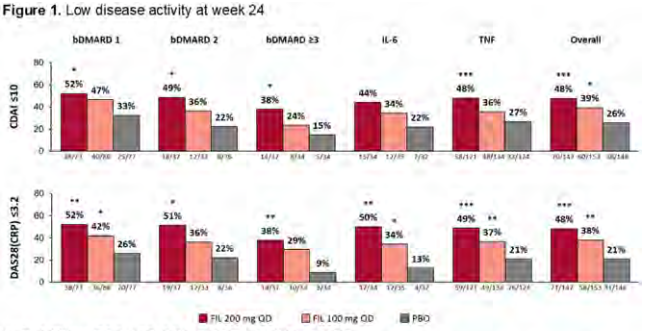
Background: Despite effective treatments, many patients (pts) with rheumatoid arthritis (RA) have inadequate responses to biologic DMARDs (bDMARD-IR), highlighting an unmet need. It is unclear whether prior bDMARD use affects efficacy of the oral, selective JAK-1 inhibitor filgotinib (FIL).
Objectives: To explore clinical response to FIL in bDMARD-IR pts stratified by mode of action (MOA) and number of prior bDMARDs.
Methods: The global, phase 3 FINCH-2 (NCT02873936) study treated 448 bDMARD-IR pts with active RA.[1] Pts were randomised 1:1:1 to once-daily FIL 200 mg, FIL 100 mg, or placebo (PBO) for 24 weeks. Efficacy was assessed by percent of pts achieving low disease activity (LDA) or remission at week (W)24 as measured by CDAI and DAS28(CRP) stratified by number and MOA of prior bDMARDs. Comparisons were not adjusted for multiplicity. Nonresponder imputation was used.
Results: In total, 448 bDMARD-IR pts were included, 105 with prior experience with ≥3 bDMARDs (**Table**). At W24, pts receiving FIL were in LDA at a higher proportion vs PBO, irrespective of number of prior bDMARDs or MOA (Figure 1). For pts receiving FIL 200 vs PBO, DAS28(CRP) ≤3.2 was achieved at W24 by 52% vs 26%, 51% vs 22%, and 38% vs 9% of pts with 1, 2, or ≥3 prior bDMARDs, respectively, and 49% vs 21% and 50% vs 13% of pts exposed to TNF or IL-6 inhibitors; for all subgroups, rates were significantly higher vs PBO (Figure 1). Delta between FIL 200 mg and PBO was maintained irrespective of number or type of prior bDMARDs. At W24, pts receiving FIL achieved remission at numerically higher rates vs PBO (Figure 2). For pts receiving FIL 200 mg vs PBO, DAS28(CRP) <2.6 was achieved at W24 by 36% vs 14%, 30% vs 14%, and 22% vs 6% of pts with 1, 2, and ≥3 prior bDMARDs, respectively, and 31% vs 14% and 29% vs 9% of pts exposed to TNF or IL-6 inhibitors (Figure 2). Delta between FIL 200 mg and PBO was maintained irrespective of number or type of prior bDMARDs. Treatment-emergent adverse events across subgroups were consistent with overall study population.

Table. Number and MOA of prior bDMARDs

	FIL 200 mg n = 147	FIL 100 mg n = 153	PBO n = 148	Total N = 448
Prior bDMARDs				
1	73 (49.7)	86 (56.2)	77 (52.0)	236 (52.7)
2	37 (25.2)	33 (21.6)	36 (24.3)	106 (23.7)
≥3	37 (25.2)	34 (22.2)	34 (23.0)	105 (23.4)
LOE ≥1 bDMARD	125 (85.0)	129 (84.3)	126 (85.1)	380 (84.8)
Intolerance ≥1 bDMARD	36 (24.5)	34 (22.2)	32 (21.6)	102 (22.8)
Prior TNFi	121 (82.3)	134 (87.6)	124 (83.8)	379 (84.6)
LOE ≥1 TNFi	97 (66.0)	113 (73.9)	103 (69.6)	313 (69.9)
Intolerance ≥1 TNFi	25 (17.0)	24 (15.7)	24 (16.2)	73 (16.3)
Prior non-TNFi	73 (49.7)	62 (40.5)	75 (50.7)	210 (46.9)
LOE ≥1 non-TNFi	52 (35.4)	43 (28.1)	56 (37.8)	151 (33.7)
Intolerance ≥1 non-TNFi	13 (8.8)	13 (8.5)	11 (7.4)	37 (8.3)
Prior IL-6i	34 (23.1)	35 (22.9)	32 (21.6)	101 (22.5)
LOE ≥1 IL-6i	25 (17.0)	22 (14.4)	21 (14.2)	68 (15.2)
Intolerance ≥1 IL-6i	5 (3.4)	10 (6.5)	5 (3.4)	20 (4.5)

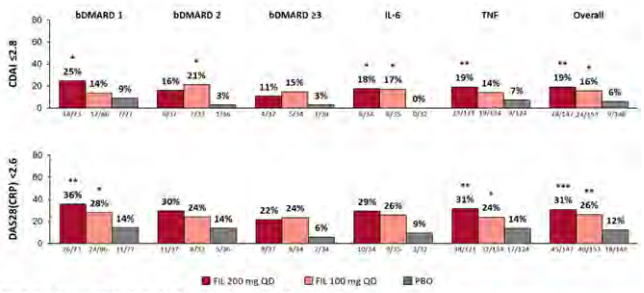
Data presented as n (%).
i, inhibitor; LOE, lack of efficacy.

Figure 1. Low disease activity at week 24



***P<0.001 vs PBO; **P<0.01 vs PBO; *P<0.05 vs PBO
bDMARD, biologic disease-modifying antirheumatic drug; CDAI, Clinical Disease Activity Index; DAS28(CRP), Disease Activity Score with C-reactive protein; FIL, filgotinib; IL, interleukin; PBO, placebo; QD, once-daily; TNF, tumour necrosis factor.

Figure 2. Remission at week 24



***P<0.001 vs PBO; **P<0.01 vs PBO; *P<0.05 vs PBO
bDMARD, biologic disease-modifying antirheumatic drug; CDAI, Clinical Disease Activity Index; DAS28(CRP), Disease Activity Score with C-reactive protein; FIL, filgotinib; IL, interleukin; PBO, placebo; QD, once-daily; TNF, tumour necrosis factor.

Conclusion: Treatment with FIL vs PBO led to higher rates of LDA and remission in pts with IR to IL-6 or TNF inhibition, or to 1, 2, or ≥3 prior bDMARDs, with a similar safety profile to the overall study population. A significantly higher proportion of pts overall receiving FIL 200 mg vs PBO were in LDA at W24. Improved efficacy of FIL vs PBO in pts who previously failed multiple bDMARDs indicates distinct benefits of selective JAK-1 inhibition with FIL.

References:

[1] Genovese, et al. *JAMA* 2019;322(4):315–25.

Disclosure of Interests: : Jacques-Eric Gottenberg Grant/research support from: BMS, Pfizer, Consultant of: BMS, Sanofi-Genzyme, UCB, Speakers bureau: Abbvie, Eli Lilly and Co., Roche, Sanofi-Genzyme, UCB, Maya H Buch Grant/research support from: Pfizer, Roche, and UCB, Consultant of: Pfizer; AbbVie; Eli Lilly; Gilead Sciences, Inc.; Merck-Serono; Sandoz; and Sanofi, Roberto Caporali Consultant of: AbbVie; Gilead Sciences, Inc.; Lilly; Merck Sharp & Dohme; Celgene; Bristol-Myers Squibb; Pfizer; UCB, Speakers bureau: Abbvie; Bristol-Myers Squibb; Celgene; Lilly; Gilead Sciences, Inc; MSD; Pfizer; Roche; UCB, Grace C. Wright Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Exagen, Eli Lilly, Myriad Autoimmune, Novartis, Pfizer, Regeneron Pharmaceuticals, Inc., Sanofi Genzyme, UCB, Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb, Exagen, Eli Lilly, Myriad Autoimmune, Novartis, Regeneron Pharmaceuticals, Inc., Sanofi Genzyme, UCB, Tsutomu Takeuchi Grant/research support from: Eisai Co., Ltd, Astellas Pharma Inc., AbbVie GK, Asahi Kasei Pharma Corporation, Nippon Kayaku Co., Ltd, Takeda Pharmaceutical Company Ltd, UCB Pharma, Shionogi & Co., Ltd., Mitsubishi-Tanabe Pharma Corp., Daiichi Sankyo Co., Ltd., Chugai Pharmaceutical Co. Ltd., Consultant of: Chugai Pharmaceutical Co Ltd, Astellas Pharma Inc., Eli Lilly Japan KK, Speakers bureau: AbbVie GK, Eisai Co., Ltd, Mitsubishi-Tanabe Pharma Corporation, Chugai Pharmaceutical Co Ltd, Bristol-Myers Squibb Company, AYUMI Pharmaceutical Corp., Eisai Co., Ltd, Daiichi Sankyo Co., Ltd., Gilead Sciences, Inc., Novartis Pharma K.K., Pfizer Japan Inc., Sanofi K.K., Dainippon Sumitomo Co., Ltd., Kenneth Kalunian Grant/research support from: Pfizer, Lupus Research Alliance, Sanford Consortium, Consultant of: Genentech, Nektar, BMS, Janssen, AstraZeneca, Biogen, Vielabio, Equillium, Eli Lilly, ILTOO, Abbvie, Amgen, Roche, Gilead, Alena Pechonkina Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Ying Guo Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Shangbang Rao Shareholder of: Gilead Sciences Inc., Employee of: Gilead Sciences Inc., YingMeei Tan Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Robin Besuyen Shareholder of: Galapagos, Employee of: Galapagos,

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THU0205 RESPONSE TO SMALL MOLECULES IS MOSTLY DRIVEN BY PATIENT GLOBAL ASSESSMENT OF DISEASE: A REAL WORLD OBSERVATION

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Background: Two Small molecules (Tofacitinib and Baricitinib) have been licensed in the UK for the use in rheumatoid arthritis. Their licensing came from several studies that showed good efficacy with baricitinib (1) study showing superior efficacy to adalimumab and tofacitinib showing non inferiority to TNF drugs (2). The response has also been shown in patient reported outcomes (find reference). Response when measure using the DAS score has two relatively subjective components (tender joints and patient global assessment) and two relatively objective components (Swollen joints and inflammatory markers)
Objectives: To determine in a real world setting if the response to small molecules is mostly due to a drop in subjective or objective components of the DAS score
Methods: A retrospective chart review was done on all new starters on small molecules in a district hospital in the North of England. Data were collected at baseline, three months and six months from October 2018 to date. Drop in the components of the DAS28 score was calculated and overall drop in DAS28 was modelled as the explanatory variable using linear regression modelling. This was the done Adjusting for age gender and duration of disease. Sensitivity of the model was examined using a logistic model of EULAR moderate/good response and using adjusted R squared estimates for linear model of improvement of the DAS28 score.
Results: 76 patients were included in the analysis from 85 starters on small molecules.61 (71.8 %) were on baricitinib and the baseline median DAS28 score was .5.97 (IQR 5.35,6.55)The median drop at three months in the DAS28 score was 2.42 (IQR 1.33,3.31). and at six months was 2.77 (IQR 2.01,3.83). There was numerical relative increased efficacy of baricitinib but this was not statistically significant (DAS drop at three months 2.54 IQR 1.73,3.09 vs 2.12 IQR 1.51,3.5). The relative contribution of the individual components of the DAS score to the drop ae in DAS are shown in table 1 below. Sensitivity analysis looking at predictors of a DAS drop of >0.6 confirmed this finding.

Table 1. Results of the adjusted linear regression models.

Component of DAS dropping at three months	Adjusted R squared at 3 months	Adjusted R squared at six months
Swollen Joints	0.12	0.05
Tender Joints	0.28	0.18
Patient global assessment	0.31	0.48
Erythrocyte sedimentation rate	0.04	0.17

Conclusion: In this real world observational study, there was a good response to both small molecules with numerical better response to baricitinib. Tender joint count and patient global response accounted for more of the drop in DAS28 than swollen joints and inflammatory markers. At six months the biggest contributor to response was patient global assessment. This shows that JAK inhibitors might mediate their response initially mostly through pain modulation then by inflammation as exposure to drug continues.
References:
[1] N Engl J Med. 2017 Feb 16;376(7):652-662
[2] N Engl J Med. 2014 Jun 19;370(25):2377-86
Disclosure of Interests: : Clerin Joseph: None declared, Syed Mujtaba Bilgrami Speakers bureau: Pfizer, Lesley Ottewell: None declared, Leanne Gray: None declared, William Mitchell: None declared, Fiona Wood: None declared, Marco Massarotti: None declared, Marwan Bukhari Speakers bureau: Bristol-Myers Squib, UCB celltech, Roche/Chugai, Pfizer, Abbvie, Merck, Mennarini, Sanofi-aventis, Eli-Lilly, Janssen, Amgen and Novartis.
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THU0206 A VERY EARLY (7-28 DAYS) RESPONSE ON JAK INHIBITOR TOFACITINIB IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS: EFFECT ON PAIN AND CENTRAL SENSITIZATION.

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Background: The presence of central sensitization (CS) significantly burdens the course of rheumatoid arthritis (RA). JAK inhibitors block intracellular signal pathways including the ones responsible for synthesis of mediators and cytokines causing pain and CS. The application of JAK inhibitors is supposed to relieve pain and reduce CS severity promptly.
Objectives: To evaluate JAK inhibitor effect on pain and signs of CS in patients with active RA 7 and 28 days after the start of therapy.
Methods: Study group included 39 patients with RA, their age was 50.9±11.1, 79.5% of women, 89.7% of RF "+", DAS28 5.8±0.6, receiving DMARDs (methotrexate 82.0% and leflunomide 18.0%), who were administered with tofacitinib 5 mg 2 times a day due to inefficiency or intolerance of genetically engineered biological drugs. There were assessed the pain severity using Brief pain inventory (BPI) questionnaire, the presence of neuropathic pain component (NPC) using PainDETECT questionnaire and signs of CS using Central Sensitisation Inventory (CSI) questionnaire at early time after tofacitinib administration.
Results: Patients initially experienced a severe pain – 5.72±2.21 according to the visual analogue scale (VAS), 53.8% had signs of central sensitization (CSI ≥ 40), 17.9% had NPC (PainDETECT ≥18). 7 days after tofacitinib intake there was statistically reliable reduction of pain severity – up to 4.37±2.2 (p=0.01), pain decrease of 29.4±17.9% (BPI), NCP – PainDETECT from 12.9±5.5 to 10.6±5.6 (p=0.047) and CS – CSI from 43.1±12.8 to 35.9±11.2 (p=0.01). The effect had increased after 28 days: pain level (VAS) was 2.84±1.57 (p=0.000), pain decrease of 43.6±29.6% (BPI), PainDETECT 29.8±12.4 (p=0.000), CSI 26.4±13.9 (p=0.000).
During this period there were no serious adverse reactions.
Conclusion: The application of JAK inhibitor tofacitinib allows to reach a fast analgesic effect, also due to impact on CS and NCP.
Source: National Registry patients with RA
Disclosure of Interests: : Andrey Karateev: None declared, Ekaterina Filatova: None declared, Elena Pogozheva: None declared, Vera Amirdzhanova: None declared, Evgeny Nasonov: None declared, Alexander Lila: None declared, V Mazurov: None declared, N Lapkina: None declared, Galina Lukina Speakers bureau: Novartis, Pfizer, UCB, Abbvie, Biocad, MSD, Roche, Tatiana Salnikova: None declared, Ruzana Samigullina: None declared, Diana Chakieva: None declared, Irina Marusenko: None declared, Olga Semagina: None declared, Marina Semchenkova: None declared
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THU0207 SUSTAINABILITY OF RESPONSE TO UPADACITINIB AS MONOTHERAPY OR IN COMBINATION AMONG PATIENTS WITH RHEUMATOID ARTHRITIS AND PRIOR INADEQUATE RESPONSE TO CONVENTIONAL SYNTHETIC DMARDS

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Background: The primary treatment goal for patients (pts) with rheumatoid arthritis (RA) is a state of sustained clinical remission (REM) or low disease activity (LDA).[1,2]
Objectives: To assess the long-term sustainability of responses to upadacitinib (UPA), a JAK inhibitor, with or without background csDMARD(s) in pts with RA.
Methods: Data are from two phase 3 randomized, controlled trials of UPA in RA pts with roughly similar baseline disease characteristics: SELECT-NEXT enrolled pts with an inadequate response (IR) to csDMARD(s) on background stable csDMARD(s) receiving UPA 15 mg or 30 mg once daily or placebo for 12 weeks (wks);

SELECT-MONOTHERAPY enrolled methotrexate (MTX)-IR pts receiving UPA 15 mg or 30 mg monotherapy or blinded MTX for 14 wks. After 12/14 wks, pts could enter a blinded long-term extension and receive UPA 15 mg or 30 mg for up to 5 years. This post hoc analysis evaluated clinical REM (CDAI ≤2.8; SDAI ≤3.3), LDA (CDAI≤10; SDAI≤11), and DAS28(CRP) <2.6/≤3.2 at first occurrence before Wk 84; additionally, these measures were evaluated at 3, 6, and 12 months after the first occurrence for the total number of pts randomized to UPA 15 mg. Sustainability of response was evaluated by Kaplan-Meier only for those pts who achieved REM/LDA and was defined as time to the earliest date of losing response at two consecutive visits or discontinuation of study drug. The predictive ability of time to clinical REM/LDA was assessed using Harrell's concordance (c)-index (for reference, an index ~ 0.5, indicates no ability to predict; an index of 1 or -1 would be a perfect prediction). The last follow up dates were 22 March, 2018 (SELECT-NEXT) and 25 May, 2019 (SELECT-MONOTHERAPY), when all pts had reached the Wk 84 visit.

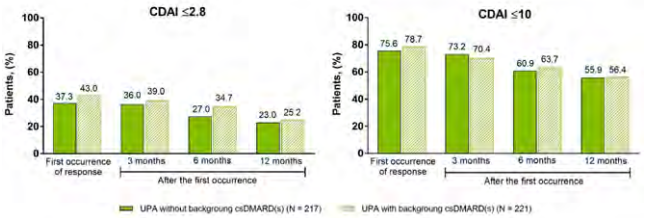
Results: Through Wk 84, the percent of treated pts achieving CDAI REM/LDA was 43%/79% for those receiving UPA 15 mg with background csDMARD(s) (SELECT-NEXT) and 37%/76% for those receiving UPA 15 mg without background csDMARD(s) (SELECT-MONOTHERAPY). 35%/25% of pts randomized to UPA 15 mg with background csDMARD(s) and 27%/23% of pts randomized to UPA 15 mg without background csDMARD(s) achieved sustained CDAI REM through 6/12 months after the first occurrence. 64%/56% of pts randomized to UPA 15 mg with background csDMARD(s) and 61%/56% of pts randomized to UPA 15 mg without background csDMARD(s) achieved sustained CDAI LDA through 6/12 months after the first occurrence (Figure 1). Time to initial clinical REM/LDA did not appear to be associated with sustained disease control. The c-indices (95%CI) for CDAI REM in the UPA 15 mg with background csDMARD(s) and UPA 15 mg without background csDMARD(s) groups were 0.541 (0.47, 0.62) and 0.568 (0.49, 0.65) and that of LDA were 0.521 (0.46, 0.58) and 0.498 (0.43, 0.56), respectively. Through last follow-up visit, 55% of pts receiving UPA 15 mg with background csDMARD(s) and 62% of pts receiving UPA 15 mg without background csDMARD(s) remained in CDAI REM while 72% and 70% of pts remained in CDAI LDA, respectively (Figure 2). Similar results were observed across other disease activity measures (SDAI REM/LDA and DAS28(CRP) <2.6/≤3.2).

Conclusion: More than a quarter and more than a half of pts with RA and prior IR to csDMARD(s) receiving UPA with or without background csDMARD therapy achieved sustained clinical REM and LDA, respectively, across disease activity measures. Sustainability of responses appeared comparable among pts receiving UPA with or without background csDMARDs through up to 84 wks.

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[2]ACR: Singh et al. Arthritis & Rheumatology Vol. 68, No. 1, January 2016, pp 1–26.

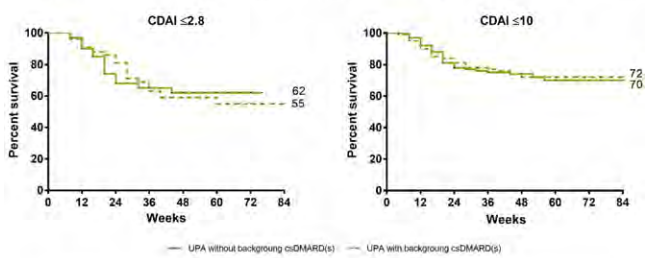
Figure 1. Proportion of patients sustaining CDAI remission or low disease activity at 3, 6, and 12 months after the first occurrence of response among the total randomized population



UPA, upadacitinib; csDMARD, conventional synthetic disease-modifying anti-rheumatic drugs; CDAI, Clinical Disease Activity Index; N, total number of patients randomized to UPA with or without background csDMARD(s).

Data for patients who maintained response through the cut-off (22 March, 2018 for SELECT-NEXT and 25 May, 2019 for SELECT-MONOTHERAPY , when all patients had reached Week 84 visit) were censored. Data are summarized, with no adjustments applied to account for between-study differences. Non-responder imputation was used for missing data.

Figure 2. Kaplan-Meier analysis of time to loss of CDAI remission or low disease activity after the first occurence of response



UPA, upadacitinib; csDMARD(s), conventional synthetic disease-modifying anti-rheumatic drugs; CDAI, Clinical Disease Activity Index; N, number of patients who had achieved CDAI remission or low disease activity.

Results are for patients who had achieved CDAI remission or low disease activity. UPA without backgroung csDMARD(s): CDAI ≤2.8, n = 81,CDAI ≤10, n = 164. UPA with backgroung csDMARD(s): CDAI ≤2.8: n = 95; CDAI ≤10, n = 174.

Data for patients who maintained response through the cut-off (22 March, 2018 for SELECT-NEXT and 25 May, 2019 for SELECT-MONOTHERAPY , when all patients had reached Week 84 visit) were censored. Data are summarized, with no adjustments applied to account for between-study differences. Non-responder imputation was used for missing data. Week 0 indicates the first occurrence of response.

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THU0208 AFFECTING COMMON BIOLOGICAL PROCESSES OR DISPARATE?: COMPARISON OF GENE-EXPRESSION MODIFICATION PROFILES AMONG TARGETING IL-6 AND TARGETING SPECIFIC JAK TREATMENTS.

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Background: After accumulation of evidences, it is recognized that inhibition of IL-6 signaling is one of the most established strategies for rheumatoid arthritis (RA) treatment. Tocilizumab (TCZ), an anti-IL6 receptor monoclonal antibody, is the pioneer which blocks IL-6 signaling by preventing IL-6 from binding to both membrane-bound and soluble receptors. Tofacitinib (TOF) inhibits Janus kinase (JAK) 1, JAK3 and, to a lesser extent, JAK2. Recently, Baricitinib (BAR), JAK 1 and JAK2 selective kinase inhibitor, were also approved to treat RA. These JAK inhibitors are known to inhibit cytokine signaling including interleukin (IL)-6. It is very important for clinicians to know whether these treatments affect common biological processes or disparate, because it will provide a rationale for switching each other if one of these treatments resulted in lack of efficacy.

Objectives: To compare the gene-expression modification profiles among TOF, BAR and TCZ treatments.

Methods: Total of 38 RA cases were analyzed, including TOF (n=15: 6-20mg/d), BAR (n=10: 2-4mg/d) and TCZ (n=13: 8mg/kg/4w or 163mg/2w) treatment groups. Peripheral blood was drawn at just before (pre) and 3 months after (post) these treatments. Total RNAs were then extracted with using PAXgene miRNA kit. After constructing single-stranded, strand-specific libraries, multiplex sequencing was done. After quantifying the expressions of transcripts, differentially expressed genes (DEGs) were selected by paired comparison (post vs. pre), setting thresholds at 2-fold change up/down and less than P=0.05 in paired T-test. And then, hierarchical clustering analysis and enrichment analysis using gene ontology (GO) terms were performed.

Results: From the comparison of post- vs. pre-treatment of TOF, BAR and TCZ, the 120 (up-regulated=25/down-regulated=95), 62 (up=20/down=42) and 193 (up=54/ down=139) genes were selected as DEGs respectively. It seems to be discrete depending on the treatment, because overlapped genes were only 1.0% in up-regulated and 5.7% in down-regulated genes. The hierarchical clustering with expression profiles of these DEGs showed major 4 clusters. 92.3% of TCZ and 70% of BAR cases were segregated into 1st and 3rd clusters respectively, while those of TOF cases fell into 2nd and 4th clusters. Disparate GO terms were enriched in each DEGs group. For example, genes relevant to viral defense including 'response to type I interferon (IFN)' were suppressed in TOF group. Meanwhile, down regulation of genes involved in phosphorylation process including 'IL-7 signaling' seemed to be significant in BAR group. It is noteworthy that terms related to wound healing such as 'platelet activation' were enriched in the down-regulated genes of TCZ group.

Conclusion: It is speculated that the downstream biological cascade for TOF, BAR and TCZ treatment might be shared, as IL-6 signaling is mediated by JAK1/JAK2/TYK2 activation. However, the influence of these treatments over the transcriptome in the peripheral blood seems to be disparate. Enrichment analysis using GO terms also indicated that different biological processes were involved in the effect of each treatment. Our findings will support a rationale for switching each other if one of these treatments resulted in lack of efficacy. An increased risk of herpes zoster by a treatment with JAK inhibitors has been well recognized. It makes sense because IFN signaling is also mediated by JAK/STAT pathway. On the other hand, we have experienced a case with exacerbation of skin ulcer during TCZ treatment despite the activity of RA was absolutely under control. It is accounted for by the suppression of genes involved in wound healing after TCZ treatment.

Disclosure of Interests: : Yoshinobu Koyama Grant/research support from: Eli-Lilly and Mochida., Speakers bureau: BMS, Ayumi, Chugai, Ono, Mitsubishi Tanabe, Abbvie and Eisai., Yoshiharu Sato: None declared, Moe Sakamoto: None declared, Hiroshi Iijima: None declared, Toshie Higuchi: None declared

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THU0209 UPTAKE OF JANUS KINASE INHIBITORS FOR MANAGEMENT OF RHEUMATOID ARTHRITIS IN AUSTRALIA

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Background: JAK inhibitors (JAKi) are oral tsDMARDs with a different mode of action (MOA) to both oral cs- and parenteral bDMARDs. In Australia the cost of b/tsDMARDs for treatment of RA is subsidized if the patient has documented high levels of clinical/laboratory disease activity and has not responded to a pre-specified combination of csDMARDs, including MTX. Once eligible for subsidy the clinician can prescribe the b/tsDMARD deemed most clinically appropriate.

Objectives: To determine the patterns of use and reasons for initiation and discontinuation of JAKi in real-world rheumatology practice in Australia.

Methods: Deidentified clinical data were sourced from the OPAL dataset, which is collected in a custom-built electronic medical record at the time of the consultation[1] by 94 rheumatologists in Australia, representing one third of Australian clinical rheumatologists. Data from patients >18 years with a diagnosis of RA who commenced a b/tsDMARD between Jan-2007 and Sept-2019 were included in the analysis. Tableau® was used to display data on medication initiation and cessation dates, and reasons for starting and stopping b/tsDMARDs, which is recorded at the time of the decision.

Results: At Sept 2019, there were 45,317 patients with RA in the data set, with 27% prescribed b/tsDMARDs. Of patients currently on treatment at Sept 2019, 53% were receiving a TNFi and 21% a JAKi, with the remainder receiving tocilizumab, abatacept or rituximab. Of patients who commenced their current treatment after JAKi's become available in Sept 2015, 46% were treated with a TNFi, and 32% were treated with a JAKi. Tofacitinib (TOF) has been the most prescribed b/tsDMARD since Sept 2015 with 22% of all initiations; however, since baricitinib (BARI) became available in Sept 2018, it has taken over as the preferred JAKi with 24% of new initiations compared to 14% for TOF. From Sept 2018-Sept 2019 etanercept and adalimumab were the most commonly prescribed agents in first line, followed by TOF then BARI; however, BARI was the most prescribed agent in lines 2-6+ (figure 1). The main clinician-listed reason for choice of TOF was MOA in 54%, efficacy compared with alternatives in 30%, mode of administration in 7%, efficacy as monotherapy in 7%, and safety in 1%. BARI was chosen for MOA in 35%, efficacy compared with alternatives in 38%, mode of administration in 12%, efficacy as monotherapy in 12%, and safety in 1%. The main reasons for stopping TOF were lack of efficacy (34%), better alternative (25%) and adverse reaction (13%); those for BARI were lack of efficacy (35%) and adverse reaction (25%) which is consistent with the rates observed in the first 12-months of clinical experience with TOF, and better alternative (12%). Patient non-adherence was listed in 1% and 2% of cessations for TOF and BARI, respectively. 45% of patients discontinuing a JAKi in first line switched to a TNFi in second line, and 40% switched to another JAKi, citing lack of efficacy, adverse reaction, and better alternative as the reason for switching.

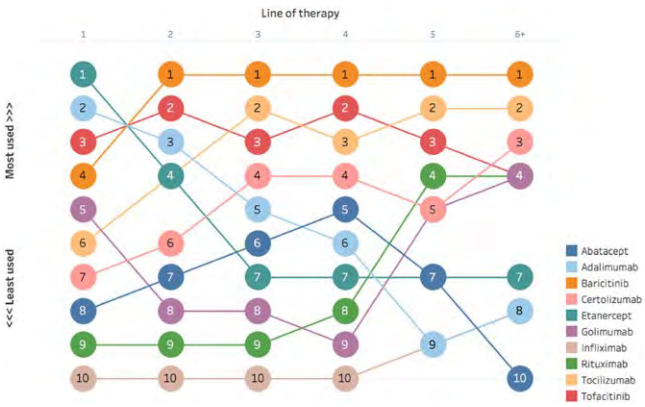


Figure 1. Rank of new initiations by line of therapy (Sept 2018-Sept 2019)

Conclusion: There has been significant and sustained uptake of JAKi for the management of RA in Australia. MOA and perceived efficacy rate much higher than mode of administration for clinicians when selecting a JAKi. Clinical outcomes and persistence following JAKi cycling requires further investigation.

References: Littlejohn GO, Tymms KE, Smith T, Griffiths HT. Using big data from real-world Australian rheumatology encounters to enhance clinical care and research. Clin Exp Rheum Nov 2019

Disclosure of Interests: None declared

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THU0210 EARLY DISCONTINUATION OF TOFACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS CO-TREATED WITH RIFAMPIN FOR LATENT TUBERCULOSIS: RESULTS FROM THE REAL-WORLD DATA

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Background: Rheumatoid arthritis (RA) patients need to undergo screening and receive treatment for latent tuberculosis infection (LTBI) before starting tofacitinib, which is primarily metabolized by cytochrome P450 (CYP) 3A4. Among chemoprophylactic agents, rifampin is known to be a potent CYP3A4 inducer; therefore, it is expected to decrease the efficacy of tofacitinib. However, tofacitinib and rifampin have been co-administered practically because of the short duration of chemoprophylaxis.

Objectives: The aim of this study was to determine the efficacy of tofacitinib on co-administration with rifampin.

Methods: Biologic-naïve RA patients treated with tofacitinib were selected, and electronic medical reports were reviewed retrospectively. All patients underwent screening for LTBI before starting tofacitinib, and patients with positive results were treated to prevent progression to active tuberculosis. To evaluate the efficacy of tofacitinib with or without rifampin, the discontinuation rates of tofacitinib were examined during the first 6 months. Kaplan–Meier analysis was used to construct cumulative discontinuation curves, and comparisons were performed using the log-rank test.

Results: Among 81 patients who started tofacitinib, 21 (25.9%) were LTBI-positive and 18 (22.2%) were administered rifampin concomitantly with tofacitinib. The median follow-up time was 6 months in both patients who received rifampin (interquartile range [IQR] 2.21, 6.00) and those who did not receive rifampin (IQR 5.97, 6.00) (p = 0.083). There were no significant differences between patients who received rifampin and those who did not receive rifampin in all baseline characteristics, except the swollen joint count (3.00 [1.75, 5.25] vs. 5.00 [4.00, 7.00]; p = 0.025), at the time of starting tofacitinib. In patients who received rifampin at the time of starting tofacitinib, the mean duration of co-administration was 47.00 ± 23.54 days (median 56; IQR 28.75, 59.00). During follow-up, 14 of the 81 patients (17.3%) discontinued tofacitinib. As shown in the Figures 1 and 2, the discontinuation rate of tofacitinib within the first 6 months was significantly higher among patients who received rifampin for LTBI than among those who did not receive rifampin (lack of efficacy: 24.7% vs. 5.1%, p = 0.008; all causes: 38.9% vs. 11.2%, p = 0.002). Seven patients discontinued tofacitinib because of

uncontrolled RA activity, and rifampin had been administered concomitantly in four of these seven patients. Of the four patients, three stopped taking tofacitinib in the middle of LTBI treatment, and the DAS28-ESR scores of these patients were higher at discontinuation than at baseline.

Conclusion: Discontinuation rates were higher in RA patients who started tofacitinib during chemoprophylaxis involving rifampin than in those who did not receive rifampin. Physicians should be aware that the efficacy of tofacitinib could be decreased by the chemoprophylactic regimen for tuberculosis.

Figure 1. Discontinuation rates of tofacitinib owing to lack of efficacy within 6 months

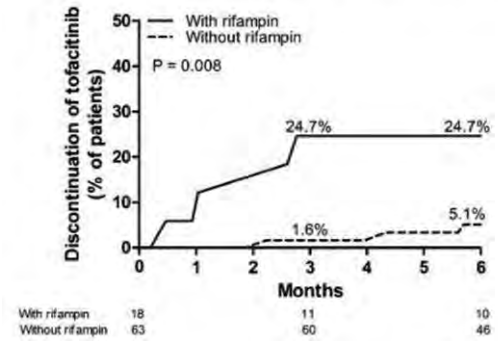
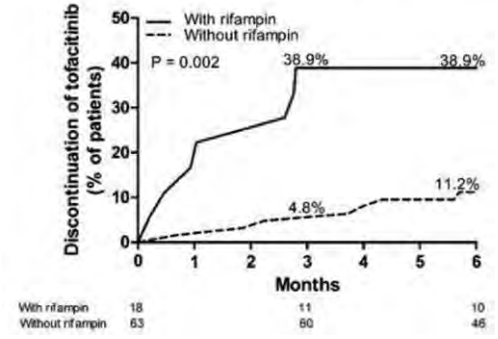


Figure 2. Discontinuation rates of tofacitinib owing to all causes within 6 months



Disclosure of Interests: None declared

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THU0211

RADIOGRAPHIC OUTCOMES IN PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING UPADACITINIB AS MONOTHERAPY OR IN COMBINATION WITH METHOTREXATE: RESULTS AT 2 YEARS FROM THE SELECT-COMPARE AND SELECT-EARLY STUDIES

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Background: For patients with rheumatoid arthritis (RA), long-term prevention of structural joint damage is a key treatment goal.[1] In the SELECT-EARLY and SELECT-COMPARE trials, upadacitinib (UPA), an oral JAK inhibitor, inhibited the progression of structural joint damage at 6 months and 1 year when used either as monotherapy or in combination with methotrexate (MTX) in patients (pts) with active RA.[2]

Objectives: To describe the radiographic progression up to 2 years (96 wks) among pts with RA receiving UPA either as monotherapy or in combination with MTX.

Methods: Both the SELECT-EARLY and SELECT-COMPARE phase 3, randomized controlled trials enrolled pts at high risk for progressive structural damage with baseline (BL) erosive joint damage and/or seropositivity.[3,4] In SELECT-EARLY, MTX-naïve pts (N=945) were randomized to UPA 15 mg or 30 mg once daily (QD) or MTX monotherapy. In SELECT-COMPARE, pts with an inadequate response to MTX (N=1629) were randomized to UPA 15 mg, placebo (PBO), or adalimumab (ADA) 40 mg every other wk, with all pts continuing background MTX; at wk 26, all pts receiving PBO were switched to UPA 15 mg, regardless of response. In both trials, mean changes from BL in modified Total Sharp Score (mTSS), joint space narrowing, and joint erosion as well as the proportion of pts with no radiographic progression (change in mTSS ≤0) were evaluated based on X-rays taken at wks 24/26, 48, and 96 for those patients in whom wk 96 X-rays were available. Data are reported as observed (AO).

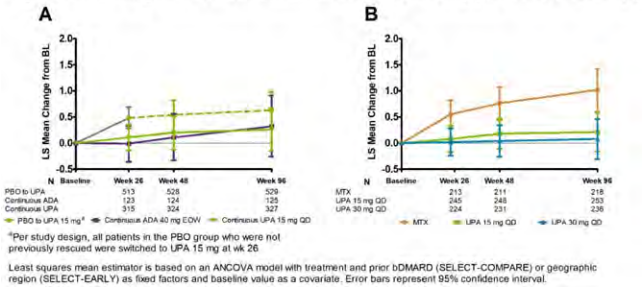
Results: BL demographics have been reported previously.[3,4] In the SELECT-EARLY study, at wk 96 UPA monotherapy (15 mg and 30 mg doses) significantly inhibited radiographic progression compared with MTX as measured by mean change in mTSS and by the proportion of patients with no radiographic progression (Figures 1 and 2). When patients who were rescued (MTX added to UPA or UPA added to MTX) were removed from the analysis, changes in mTSS from baseline remained similar. By the same measures, in SELECT-COMPARE, the degree of inhibition of structural progression observed was comparable between UPA and ADA. Following the switch of all PBO patients to UPA, the rate of progression slowed and was comparable to that observed in pts receiving UPA from BL. Among pts from both studies that had no radiographic progression at wk 24/26, >90% remained without radiographic progression at wk 48 and 96.

Conclusion: UPA was effective in inhibiting the progression of structural joint damage through 2 years both in MTX-naïve patients receiving UPA monotherapy and MTX-inadequate responder patients receiving UPA in combination with MTX.

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[3] Fleischmann, et al. *Arthritis Rheumatol* 2019;71(11):1788-1800.
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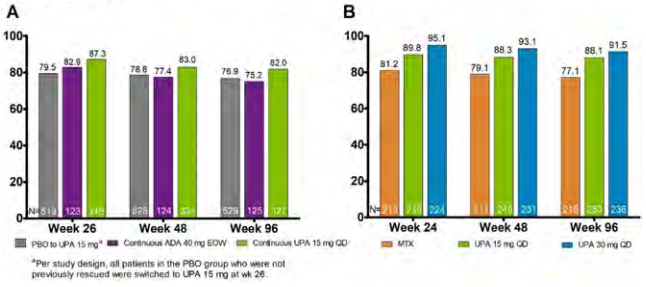
Figure 1. Mean Change in mTSS from Baseline in SELECT-COMPARE (A) and SELECT-EARLY (B)



[a]Per study design, all patients in the PBO group who were not previously rescued were switched to UPA 15 mg at wk 26

Least squares mean estimator is based on an ANCOVA model with treatment and prior bDMARD (SELECT-COMPARE) or geographic region (SELECT-EARLY) as fixed factors and baseline value as a covariate. Error bars represent 95% confidence interval.

Figure 2. Proportion of Patients with No Radiographic Progression in SELECT-COMPARE (A) and SELECT-EARLY (B)



[a]Per study design, all patients in the PBO group who were not previously rescued were switched to UPA 15 mg at wk 26.

Disclosure of Interests: : Charles Peterfy Consultant of: AbbVie, Acerta, Amgen, AstraZeneca, Bristol Myers Squibb, Centrexion, Daiichi Sankyo, Five Prime Therapeutics, Genentech, Gilead, Hoffman-La Roche, Janssen, Lilly USA, MedImmune, Merck, Myriad, Novartis, Plexxikon, Pfizer, Sanofi, Salix Santarus, Samsung, Samumed, Setpoint, Sorrento, UCB, Vorso, Employee of: founder and CEO of Spire Sciences, which provides imaging services to multiple pharmaceutical companies, Speakers bureau: Amgen, Vibeke Strand Consultant of: AbbVie, Amgen, Biogen, Celltrion, Consortium of Rheumatology Researchers of North America, Crescendo Bioscience, Eli Lilly, Genentech/Roche, GlaxoSmith-Kline, Hospira, Janssen, Merck, Novartis, Pfizer, Regeneron Pharmaceuticals, Inc., Sanofi, UCB, Mark C. Genovese Grant/research support from: Abbvie, Eli Lilly and Company, EMD Merck Serono, Galapagos, Genentech/Roche, Gilead Sciences, Inc., GSK, Novartis, Pfizer Inc., RPharm, Sanofi Genzyme, Consultant of: Abbvie, Eli Lilly and Company, EMD Merck Serono, Genentech/Roche, Gilead Sciences, Inc., GSK, Novartis, RPharm, Sanofi Genzyme, Alan

Friedman Shareholder of: AbbVie Inc, Employee of: AbbVie Inc, Jose Jeffrey Enejosa Shareholder of: AbbVie, Employee of: AbbVie, Stephen Hall Grant/research support from: Abbvie, UCB, Janssen, Merck, Eduardo Mysler Grant/research support from: AbbVie, Amgen, Bristol Myers Squibb, Roche, Eli Lilly, Novartis, Janssen, Sanofi, and Pfizer., Speakers bureau: AbbVie, Amgen, Bristol Myers Squibb, Roche, Eli Lilly, Novartis, Janssen, Sanofi, and Pfizer, Patrick Durez Speakers bureau: AbbVie, Bristol-Myers Squibb, Celltrion, Eli Lilly, Pfizer, Sanofi, Xenofon Baraliakos Grant/research support from: Grant/research support from: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB and Werfen, Consultant of: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB and Werfen, Speakers bureau: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB and Werfen, Tim Shaw Shareholder of: AbbVie, Employee of: AbbVie, Yanna Song Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Yihan Li Shareholder of: AbbVie, Employee of: AbbVie, In-Ho Song Shareholder of: AbbVie Inc., Employee of: AbbVie Inc.

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THU0212 FIRST LINE TREATMENT WITH CONVENTIONAL SYNTHETIC DISEASE MODIFYING ANTIRHEUMATIC DRUGS IN RHEUMATOID ARTHRITIS: A MULTINATIONAL POPULATION-BASED COHORT FROM 14 REAL WORLD HEALTHCARE DATABASES AND 9 COUNTRIES - REALITY VERSUS GUIDELINES

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Background: Treatment guidelines recommend early initiation of csDMARDs following diagnosis of rheumatoid arthritis (RA), with methotrexate (MTX) as first-line therapy. Scarce evidence exists on adherence to this guidance

Objectives: To characterize first-line csDMARD treatment during the first year following an RA diagnosis.

Methods: 14 real world databases (3 Primary care, 6 primary/secondary care records, 5 claims) from 9 countries were included, all mapped to the OMOP common data model.

Patients were included on the earliest event of: 1st diagnosis of RA or 1st DMARD prescription with an RA diagnosis within 30 days. Patients were >18 years-old, required 1+ year pre-index data, and at least 1-year follow-up. Study period covered 2000-2018. Previous users of DMARDs or non-RA inflammatory arthritis history were excluded. Only MTX, Hydroxychloroquine (HCQ), Sulfasalazine (SSZ) and Leflunomide (LEF) were available in all databases.

Results: We identified 323,547 eligible participants. Large variation was observed internationally (Figure 1). MTX as first-line monotherapy ranged from 33.3% to 74.5%, and in combination with HCQ from 2.1% to 6.7%. Three additional csDMARDs were used as first-line: HCQ in 10.1% to 30.2%, SSZ in 0.9% to 28.7%, and LEF in 1.8% to 15.2%.

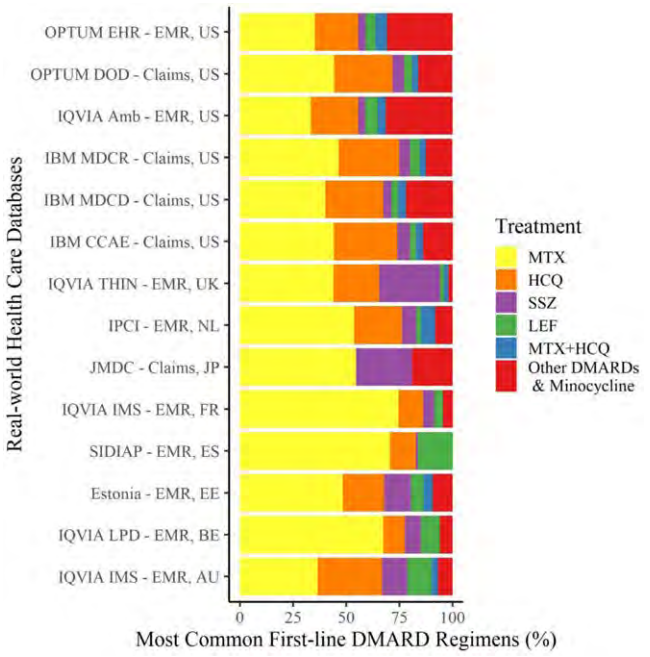


Figure 1. First line csDMARD treatment during 1yr from first observed RA diagnosis

Conclusion: We report wide heterogeneity of first-line csDMARDs regimens internationally. Despite recommendations for MTX to be first line therapy, data suggest that a large proportion of patients receive alternative csDMARD.

Disclosure of Interests: : Anthony G Sena Shareholder of: J&J shares, Grant/research support from: Full-time employment salary from Janssen, Consultant of: Full-time employment salary from Janssen, Employee of: Janssen employee, Paid instructor for: Janssen employee, Speakers bureau: Janssen employee, Denis Granados: None declared, Nigel Hughes Shareholder of: J&J shares, Grant/research support from: Full-time employment salary from Janssen, Consultant of: Janssen employee, Employee of: Janssen employee, Paid instructor for: Janssen employee, Speakers bureau: Janssen employee, WALID FAKHOURI Shareholder of: E Lilly Shares, Employee of: Eli Lilly and Company, Antje Hottgenroth Shareholder of: Eli Lilly shares, Employee of: Lilly Deutschland GmbH, Raivo Kolde: None declared, Sulev Reisberg: None declared, Carmen Olga Torre: None declared, Talita Duarte-Salles: None declared, Yesika Díaz: None declared, Jose Felipe Golib-Dzib Grant/research support from: Full-time employment salary from Janssen, Employee of: Yes, Janssen employee, Paid instructor for: Janssen Employee, Speakers bureau: Janssen Employee, Emily S. Brouwer Shareholder of: J&J shares, Takeda shares, Grant/research support from: Full-time employment salary from Janssen, Consultant of: Janssen employee, Employee of: Janssen employee, Paid instructor for: Janssen Employee, Speakers bureau: Janssen Employee, Edward Burn: None declared, Jennifer Lane: None declared, David Vizcaya Employee of: Bayer, Sara Bruce Wirta Employee of: Janssen-Cilag Sweden AB, Marcel de Wilde: None declared, Katia Verhamme: None declared, Peter Rijnbeek: None declared, Elke Theander Employee of: Janssen-Cilag Sweden AB, Katerina Chatzidionysiou Consultant of: AbbVie, Pfizer, Lilly., Daniel Prieto-Alhambra Grant/research support from: Professor Prieto-Alhambra has received research Grants from AMGEN, UCB Biopharma and Les Laboratoires Servier, Consultant of: DPA's department has received fees for consultancy services from UCB Biopharma, Speakers bureau: DPA's department has received fees for speaker and advisory board membership services from Amgen, Patrick Ryan: None declared

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THU0213 UPADACITINIB AS MONOTHERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS AND PRIOR INADEQUATE RESPONSE TO METHOTREXATE: RESULTS AT 84 WEEKS FROM THE SELECT-MONOTHERAPY STUDY

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Background: In the SELECT-MONOTHERAPY trial, upadacitinib (UPA), an oral JAK inhibitor, demonstrated significantly greater efficacy compared to continuing methotrexate (MTX) when used as monotherapy over 14 weeks (wks) in patients (pts) with rheumatoid arthritis (RA) and prior inadequate response to MTX.[1]

Objectives: To describe the long-term safety and efficacy of UPA monotherapy in an ongoing long-term extension (LTE) of the SELECT-MONOTHERAPY trial.

Methods: Pts on stable MTX were randomized to either continue MTX (cMTX, given as blinded study drug) or switch to once-daily (QD) UPA 15 (UPA15) or 30 (UPA30) mg monotherapy for 14 wks. From Wk14, pts could enter a blinded LTE and continue to receive UPA15 or UPA30; pts randomized to cMTX were switched to UPA15 or UPA30 per pre-specified assignment at baseline. Treatment-emergent adverse events (TEAEs) per 100 pt yrs (PYs) of exposure are summarized up to a cut-off data of 5 February 2019, when all pts had reached Wk84. Efficacy outcomes through Wk84 are reported as observed and using non-responder imputation.

Results: Of 648 pts randomized, 598 (92%) completed 14 wks and entered the LTE on blinded UPA. By the cut-off date, 20% in total had discontinued due to the following: AE (6%), consent withdrawal (4%), lost to follow-up (2%), lack of efficacy (1%), or other reasons (7%). Cumulative exposures were 421.5 and 425.9 PYs for UPA15 and UPA30, respectively. The most frequently reported TEAEs were urinary tract infection, creatine phosphokinase (CPK) increase, upper respiratory tract infection, nasopharyngitis, worsening of RA, bronchitis, herpes zoster (HZ), and alanine aminotransferase increase; the most common serious AE was pneumonia. Events of HZ, hepatic disorder, and CPK elevations were higher among pts receiving UPA30, while rates of serious infection and malignancy appeared comparable between doses (**Figure**). Most HZ events involved 1-2 dermatomes, with a single disseminated cutaneous event (UPA30) and none with CNS involvement. Five patients experienced MACE, and there were 5 VTE events (UPA15: 4; UPA30: 1). All MACE and VTE events occurred in pts with underlying risk factors. Pts continuing to receive UPA15 and UPA30 achieved stringent endpoints at Week 84 (**Table**). Pts who switched from cMTX to UPA15 or UPA30 demonstrated comparable efficacy responses to those initially randomized to UPA.

Conclusion: The adverse event profile associated with long-term exposure to UPA15 or 30 as monotherapy was consistent with an integrated analysis of UPA safety across the entire phase 3 program, with no new safety signals identified. Further, UPA15 or 30 monotherapy resulted in continued and sustained improvements in RA signs and symptoms through 84 wks.

References:

[1] Smolen, et al. *Lancet* 2019;393(10188):2303-11.

Figure. Treatment-emergent Adverse Events Through ≥84 Weeks (E/100 PYs, 95% CI).

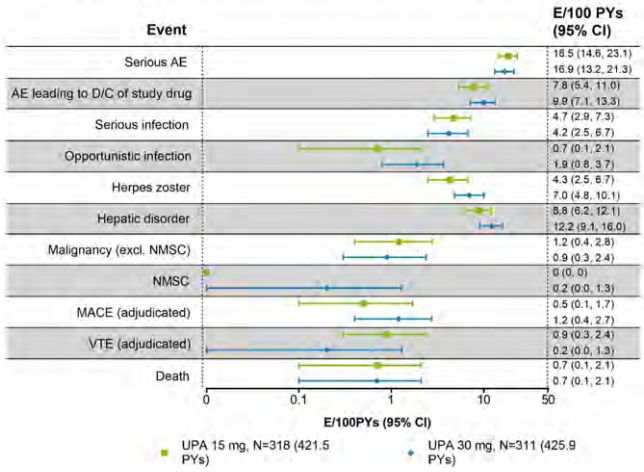


Table. Proportion of Patients at Week 84

Parameter (%)	cMTX→UPA 15 mg n=108		cMTX→UPA 30 mg n=108		UPA 15 mg n=217		UPA 30 mg n=215	
	AO	NRI	AO	NRI	AO	NRI	AO	NRI
ACR20/50/70	86/71/49	67/56/39	90/68/50	66/51/38	88/71/54	65/53/41	96/78/66	74/62/52
DAS28(CRP) ≤3.2/<2.6	80/56	64/44	79/63	62/49	76/60	57/46	85/77	67/61
CDAI ≤10/≤2.8	78/38	62/30	85/29	65/22	74/34	55/25	85/49	67/39
Boolean Remission	27	22	23	18	26	20	41	33

AO, as observed; NRI, non-responder imputation.

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THU0214 LONG-TERM EFFECTIVENESS OF METHOTREXATE WITH STEP DOWN GLUCOCORTICOID BRIDGING (COBRA SLIM) VERSUS OTHER CONVENTIONAL DMARD REGIMENS AS INITIAL RA THERAPY: 5-YEAR OUTCOMES OF THE CARERA TRIAL.

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Background: The treat-to-target Care in Early Rheumatoid Arthritis (CareRA) trial demonstrated that remission induction with csDMARD combinations and step-down glucocorticoids (GCs) was not superior over methotrexate (MTX) monotherapy with step-down GCs (Cobra Slim) in RA patients with a high-risk profile (1). Moreover, Cobra Slim showed benefit over a tight step-up with MTX in monotherapy (TSU) in RA patients with a low-risk profile.

Objectives: To compare the long term outcomes up to 5 years of different initial intensive treatment strategies in participants of the CareRA-plus study.

Methods: In the CareRA trial, patients with DMARD naïve early RA were stratified in a high- or low-risk group based upon the presence of serummarkers, disease activity and erosive status. High-risk patients were randomised to Cobra Classic (MTX+sulphasalazine with highly dosed GC remission induction scheme), Cobra Avant-Garde (MTX+leflunomide with moderately dosed GC scheme) or Cobra Slim. Low-risk patients were randomised to Cobra Slim or TSU. Patients completing this trial were eligible for the CareRA-plus observational study. Here, patients were evaluated 6-monthly over 3 years. Therapy adaptation was left to the treating physician. Efficacy was assessed by DAS28-CRP and HAQ and compared between the originally allocated treatment arms. The 5-year evolution

from CareRA baseline of DAS28-CRP and HAQ was assessed via linear mixed models. All adverse events (AEs), considered to be clinically relevant by investigators, and DMARD/GCs therapy were registered.

Results: Of 322 eligible patients, 252 (78%) were included in CareRA-plus, of which 203 (81%) completed the study. Characteristics and outcomes at the CareRA closing visit (year 2) did not differ between patients entering CareRA-plus or not. DAS28-CRP<2.6 at year 5 in high-risk patients was 72%, 77% and 64% in the Classic, Slim and Avant-Garde group respectively (p=0.403). In the longitudinal analyses, all treatment arms in the high-risk group had comparable DAS28-CRP (p=0.921) and HAQ scores over time (p=0.540). In the low-risk population, 83% of patients in the Slim and 82% in the TSU arm had DAS28-CRP<2.6 at year 5 (p=0.945). Low-risk patients starting Cobra-Slim had lower DAS28-CRP scores over 5 years than those receiving TSU (p= 0.002). HAQ score over time did not differ (p=0.129). In high-risk patients, the total numbers of AEs throughout CareRA-plus, were 70 in 36 Classic, 95 in 48 Slim and 80 in 36 Avant-Garde patients (p=0.182). In the low-risk group there were 18 AEs in 10 Slim and 36 in 17 TSU patients (p=0.048). During the 5-year study, biologics were initiated in 22% of all patients: 23% of Classic, 23% of Slim high-risk, 25% of Avant-Garde, 17% of Slim low-risk, and 15% of TSU patients. At the year 5 visit, 71%, 61% and 50% of high-risk patients were on csDMARD monotherapy (mostly MTX) in Classic, Slim and Avant-Garde respectively. Of the low-risk group, 65% in COBRA-Slim and 62% in TSU were taking a single csDMARD. At the year 5 visit, 9% of all participants received chronic oral GC therapy (>3 months).

Conclusion: All intensive treatment strategies resulted in excellent long-term clinical outcomes. Initial Cobra Slim therapy showed comparable 5-year effectiveness as Cobra Classic and Avant-Garde in high-risk early RA patients and better efficacy and safety than conservative step up treatment in low-risk patients.

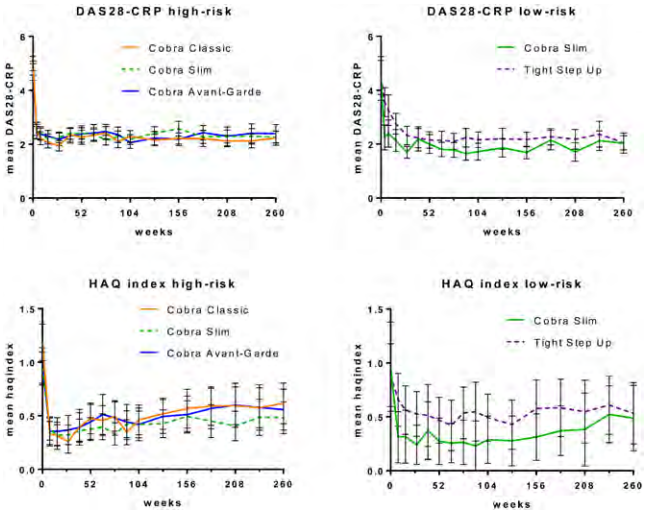


Figure 1. Mean disease activity by DAS28-CRP or mean functionality by HAQ index scores for high-risk or low-risk patients.

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THU0215 WHOLE BLOOD TRANSCRIPTIONAL CHANGES FOLLOWING SELECTIVE INHIBITION OF JANUS KINASE 1 (JAK1) BY FILGOTINIB IN ADULTS WITH MODERATELY-TO-SEVERELY ACTIVE RHEUMATOID ARTHRITIS WITH PRIOR INADEQUATE RESPONSE TO METHOTREXATE (FINCH1)

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Background: Filgotinib (FIL), an oral selective JAK1 inhibitor, has shown efficacy and safety in multiple phase 3 studies in adults with moderately-to-severely active rheumatoid arthritis (RA). We have previously described the molecular response to FIL in large-scale RNA sequencing studies of gene expression in other RA populations[1-3] and herein conducted a similar study in RA patients (pts) with prior inadequate response to methotrexate (MTX; FINCH1).

Objectives: Identify RA-associated gene transcripts and biological pathways that are altered in response to FIL treatment.

Methods: RA pts who had an inadequate response to MTX were enrolled in FINCH1 (ClinicalTrials.gov NCT02889796) and randomized to receive either a stable dose of MTX with placebo (PBO+MTX), adalimumab (ADA+MTX), or one of two doses of FIL (FIL 100mg+MTX, FIL 200mg+MTX) once daily (QD). Whole blood samples were collected from pts using PAXgene tubes at baseline, week 4, and week 12. RNA from these samples was extracted and sequenced on the Illumina HiSeq 2500 platform following globin RNA depletion. Correlations between baseline gene expression and disease measurements were performed using Spearman's rank partial correlation with covariates. Differentially expressed genes (DEGs) were identified using voom-limma. Pathway analysis was performed on v6.1 of the Molecular Signature Database using single sample gene set enrichment analysis (GSEA) with the focus on immune signaling pathways from the Kyoto Encyclopedia of Genes and Genomes (KEGG). A false-discovery rate of 5% was applied for all analyses.

Results: Differential gene expression analyses comparing baseline samples with after-treatment samples revealed more rapid transcriptional kinetics for FIL-treated pts compared to ADA+MTX-treated pts. No significant DEGs were observed in PBO-treated pts. More significant DEGs were observed in the FIL 200mg+MTX arm compared to the FIL 100mg+MTX arm, consistent with the superior clinical efficacy of the FIL 200mg dosage. As with other FIL clinical trial RNA-seq studies and consistent with the selective MoA of FIL, JAK-STAT pathway-induced genes SOCS2 and CISH were significantly downregulated across both FIL treatment arms and timepoints, but not in the ADA+MTX arm. RA disease activity associated genes[2-3] FAM20A and METTL7B were significantly reduced at both 4 and 12 weeks only in the FIL 200mg+MTX arm. While no significant changes in KEGG immune signaling pathways were observed in the PBO+MTX arm, a dose-dependent effect on pathway modulation was observed in the FIL arms. The most prominently down-regulated KEGG pathways included JAK-STAT signaling and leukocyte transendothelial migration.

Conclusion: More rapid and sustained changes of transcriptional activity were observed in the whole blood transcriptional profile of RA pts following FIL 200mg+MTX compared to ADA+MTX treatment. Dose-dependent changes were observed in FIL-treated pts, most notably in the KEGG JAK-STAT signaling pathway. These observations confirm an inhibition of JAK-STAT signaling by FIL and are consistent with the observed clinical efficacy of FIL in these pts.

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THU0216 PERIPHERAL PROTEIN BIOMARKER CHANGES FOLLOWING SELECTIVE INHIBITION OF JANUS KINASE 1 (JAK1) BY FILGOTINIB IN METHOTREXATE NAÏVE ADULTS WITH MODERATELY-TO-SEVERELY ACTIVE RHEUMATOID ARTHRITIS (FINCH3)

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Background: Filgotinib (FIL), an oral selective JAK1 inhibitor, has shown efficacy and safety in multiple phase 3 studies in adults with moderately-to-severely active rheumatoid arthritis (RA), including those who are naïve to methotrexate (MTX) therapy (FINCH3; NCT02886728).
Objectives: A longitudinal study of protein biomarkers related to JAK signaling[1], bone biology[2], immune cell migration[2], and inflammation[2] was conducted in FINCH3 pts to identify disease relevant biomarkers that are altered by FIL vs MTX.
Methods: MTX-naive RA pts enrolled in FINCH3 received a stable dose of MTX (MTX mono), FIL200mg monotherapy (FIL200mg mono) or one of two doses of FIL once daily with MTX (FIL100mg+MTX, FIL200mg+MTX). Up to 27 disease relevant biomarkers were evaluated. Baseline (BL) correlation between biomarkers and clinical response measures were analyzed by Spearman Rank. Multiscale bootstrap resampling was used to evaluate significant intra-cluster biomarker membership. Mean changes in biomarker levels from BL to wks 4, 12 and 24 were compared between arms using MTX-adjusted estimates from a linear mixed effects model, adjusted for age, sex, race and BL biomarker level. A false discovery rate of 5% was applied for all analyses.
Results: At BL, distinct clusters (CL) of biomarkers differentiated by JAK signaling were identified. The strongest intra-group correlations were in biomarkers upstream of JAK2 signaling (CL1; Rho range 0.88–0.98) and cytokines associated with JAK1 signaling (CL2; Rho range 0.72–0.77). Within MTX-naïve RA pts, there were significant BL correlations between 15 biomarkers and clinical measures. The strongest associations observed were between DAS28CRP and IL6, CXCL10, TNFRI, YKL-40, and CXCL13 (Rho >0.3).
Relative to MTX mono, 23 biomarkers exhibited significant *early responses* to treatment (any arm, wk 4). The strongest treatment effect observed at wk 4 was a reduction by FIL+MTX (regardless of dose) and FIL200mg mono for CXCL13 (FIL100mg+MTX: -28.2%; FIL200mg+MTX: -40%; FIL200mg: -34%). This reduction was sustained in each arm through 24 wks, with the greatest reduction by FIL200mg+MTX (-37.8%). Dose differences were observed relative to FIL100mg+MTX, where FIL200mg+MTX led to an *early* (wk 4) and significantly greater reduction of 9 biomarkers. There was a significant dose difference as a *delayed* response (wk 24) with a greater reduction by FIL200mg+MTX for 8 biomarkers.
FIL200mg mono produced a greater effect on 18 biomarkers vs MTX mono, remaining significant through wk 24. The greatest effect in FIL200mg mono were reductions by wk 24 in CTX1 (-29.1%), CXCL13 (-33.2%), and IL6 (-29.5%), all of which were biomarkers associated with DAS28CRP at BL. Effects observed at any time point were largely similar between FIL200mg as a mono or in combination with MTX. Four biomarkers were uniquely different between FIL200mg mono and FIL200mg+MTX arms by wk 24: greater increase of MMP7 and decrease of GMCSF in FIL200mg+MTX; greater decrease of TRACP5B and ICAM1 in FIL200mg alone.
Conclusion: Treatment through 24 weeks with FIL200mg (mono or with MTX) reduced many of the disease-relevant biomarkers tested; markers related to JAK signaling[1], bone biology[2], inflammation[2], and immune cell migration[2] in the MTX-naïve RA setting. Changes were significantly reduced relative to MTX mono at wk 4, supporting the rapid onset of FIL clinical efficacy. The current study identified significant reductions of RA-associated disease markers that were unique to FIL mono, supporting the FIL mechanisms of action in the treatment of RA.
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THU0217 UPADACITINIB MONOTHERAPY IN METHOTREXATE-NAÏVE PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS AT 72 WEEKS FROM SELECT-EARLY

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Background: Upadacitinib (UPA), an oral JAK inhibitor, demonstrated significant improvements in signs, symptoms, and structural inhibition as monotherapy vs methotrexate (MTX) in a randomized, controlled trial (RCT) of MTX-naive RA patients (pts) through 48 weeks (wks).[1]
Objectives: To present the safety and effectiveness of UPA through 72 wks in an ongoing long-term extension (LTE) of the SELECT-EARLY RCT.
Methods: SELECT-EARLY included 2 study periods: (1) a 48-wk double-blind, active comparator-controlled, with pts randomized to UPA monotherapy 15 or 30 mg once daily or MTX (titrated to 20 mg/wk by Wk8); (2) an LTE, up to 4 years. Pts received open-label treatment once the last pt reached Wk48. Rescue therapy was added (MTX, for UPA groups; UPA, for MTX group) to pts not achieving CDAI remission (≤2.8) at Wk26. Non-responder imputation (NRI) was used for missing data as well as for pts receiving rescue therapy. Treatment-emergent adverse events (TEAEs) are summarized per 100 pt yrs (PY) through the cut-off date of 21 Feb 2019, when all pts had reached Wk72. Data are censored at the time of MTX or UPA addition among rescued patients.
Results: Of 945 pts randomized and treated, 781 (83%) completed Period 1. Of these, 775 entered the LTE, including 57 rescued pts (MTX, 33; UPA 15 mg, 17; UPA 30 mg, 7). A total of 52 (7%) pts discontinued during the LTE through the cut-off date (primary reasons: AEs [n=16, 2.1%]; consent withdrawal [n=12, 1.5%]; lost to follow-up [n=10, 1.3%]). Cumulative exposures to monotherapy with MTX, UPA 15 mg, and UPA 30 mg were 350.6, 389.5, and 383.9 PYs, respectively. Both UPA 15 mg and 30 mg as monotherapy was associated with continued statistically significant improvements in disease activity measures vs MTX monotherapy through 72 wks (**Table**). The safety profiles of the UPA 15 and 30 mg groups were comparable for total TEAEs and numerically higher than MTX. Serious TEAEs and TEAEs leading to discontinuation of study drug were comparable across all groups (**Figure**). Most AEs of special interest were comparable across MTX and UPA groups, with the exception of higher rates of herpes zoster, opportunistic infections, and elevated creatine phosphokinase among the UPA groups. Two pts receiving MTX monotherapy experienced a venous thromboembolic event, with one event reported on UPA 30 mg and none on UPA 15 mg. There were 12 deaths (including 3 non-treatment-emergent) due to varied causes.

Table. Proportion of Patients at Week 72 (NRI)

Parameter (%)	MTX Monotherapy	UPA 15 mg QD Monotherapy	UPA 30 mg QD Monotherapy
ACR20/50/70	50/39/26	71***/62***/47***	72***/67***/54***
DAS28(CRP) ≤3.2/<2.6	38/28	63***/52***	69***/61***
CDAI ≤10/≤2.8	42/19	60***/35***	69***/44***
Boolean Remission	13	29***	33***

***, *P* <0.001 for differences between MTX and UPA 15 and UPA 30 mg groups.
MTX, methotrexate; UPA, upadacitinib; QD, once daily; ACR, American College of Rheumatology; DAS28(CRP), 28-joint disease activity index based on C-reactive protein; CDAI, clinical disease activity index.

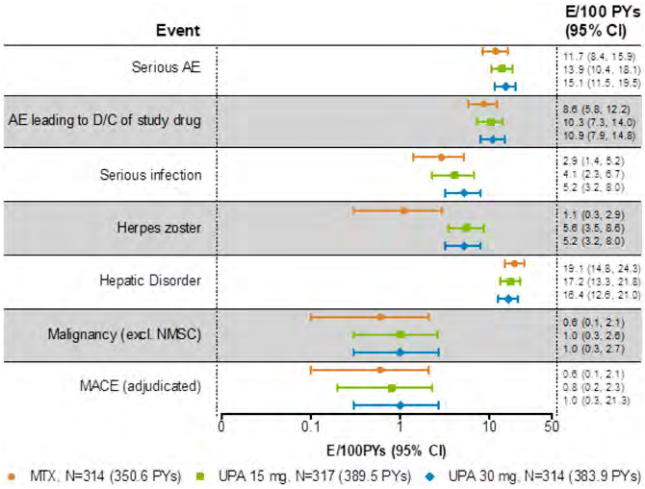


Figure. Treatment-emergent Adverse Events Through ≥72 Weeks (E/100 PYs, 95% CI).

Conclusion: Long-term UPA monotherapy was associated with continued improvements in RA signs and symptoms vs MTX monotherapy through 72 wks, and only a small proportion of pts required MTX addition at Wk26. Through 72 wks of treatment, the safety profile of UPA monotherapy remained consistent with data reported through 48 wks.[1]

References:

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THU0218 INCIDENCE AND RISK FACTORS FOR HERPES ZOSTER IN RHEUMATOID ARTHRITIS PATIENTS RECEIVING UPADACITINIB

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Background: Upadacitinib (UPA) is an oral JAK inhibitor approved for the treatment of rheumatoid arthritis (RA). The background rate of herpes zoster (HZ) in patients (pts) with RA is around 0.98/100 person years (PY)[1]. Pts with RA receiving JAK inhibitors have been reported to have an increased risk of HZ.

Objectives: To evaluate the incidence and risk factors for HZ in pts with RA receiving UPA relative to active comparators in the Phase 3 clinical trial program.

Methods: The incidence rate of HZ was determined in pts receiving UPA (as monotherapy [mono] or combination therapy) in five randomized Phase 3 trials (SELECT-EARLY, SELECT-MONOTHERAPY, SELECT-NEXT, SELECT-COMPARE, and SELECT-BEYOND), of which 4 evaluated both the UPA 15 and 30 mg once-daily (QD) doses and 1 trial (SELECT-COMPARE) evaluated only the 15 mg QD dose. Incidence of HZ was also determined in pts receiving adalimumab (ADA) + methotrexate (MTX) in SELECT-COMPARE and MTX mono in SELECT-EARLY. Risk factors for HZ were assessed using univariate and multivariate Cox regression models. Data cut-off was 30 June 2019.

Results: Overall, 2629 pts who received UPA 15 mg QD (4565.8 patient-years [PY]), 1204 pts who received UPA 30 mg QD (2309.7 PY), 579 pts who received ADA + MTX (768.6 PY), and 314 pts who received MTX mono (456.0 PY) were analyzed. Fewer than 5% of pts across the treatment groups reported prior HZ vaccination. HZ (n/100 PY [95% CI]) occurred in 142 pts (3.1 [2.6–3.7]) with UPA 15 mg, 126 pts (5.5 [4.5–6.5]) with UPA 30 mg, 8 pts (1.0 [0.4–2.1]) with ADA + MTX, and 5 pts (1.1 [0.4–2.6]) with MTX mono. Most of the HZ cases (~71%) with UPA (**Table**) and all cases with ADA + MTX and MTX mono involved a single dermatome. Ophthalmic involvement was seen in 6 (4.2%) and 3 (2.4%) cases in the UPA 15 and 30 mg groups, respectively, and unilateral involvement with multiple dermatomes was seen in 26 (18.3%) and 23 (18.3%) cases. There was a single case of HZ meningitis reported in a Japanese pt on UPA 30 mg. In multivariate analyses, prior history of HZ and Asian region were associated with an increased risk of HZ in both the UPA groups (p≤0.01; **Figure**). In addition, pts ≥65 years old had increased risk of HZ in the 15 mg group.

Conclusion: HZ events in pts with RA receiving UPA were more common in the 30 mg vs 15 mg group, and in both UPA groups compared with the ADA + MTX and MTX groups.

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Table. Summary of extent of involvement in pts with HZ

Categories, n (%)[a]	Any UPA 15 mg QD (N=2629)	Any UPA 30 mg QD (N=1204)
Total patients with ≥1 HZ event	142 (5.4)	126 (10.5)
Single dermatome	101 (71.1)	89 (70.6)
Ophthalmic involvement	6 (4.2)	3 (2.4)
HZ Oticus (Ramsay Hunt Syndrome)	2 (1.4)	1 (0.8)
Multidermatomal (unilateral)[b]	26 (18.3)	23 (18.3)
Disseminated, cutaneous only (no CNS involvement)[c]	7 (4.9)	8 (6.3)
Disseminated with CNS or visceral involvement	0	1 (0.8)[d]
Missing	8 (5.6)	5 (4.0)

[a]Pts may fall into >1 category; [b]≤2 adjacent dermatomes; [c]≥3 dermatomes, unilateral nonadjacent dermatomes, or bilateral dermatomes; [d]HZ meningitis

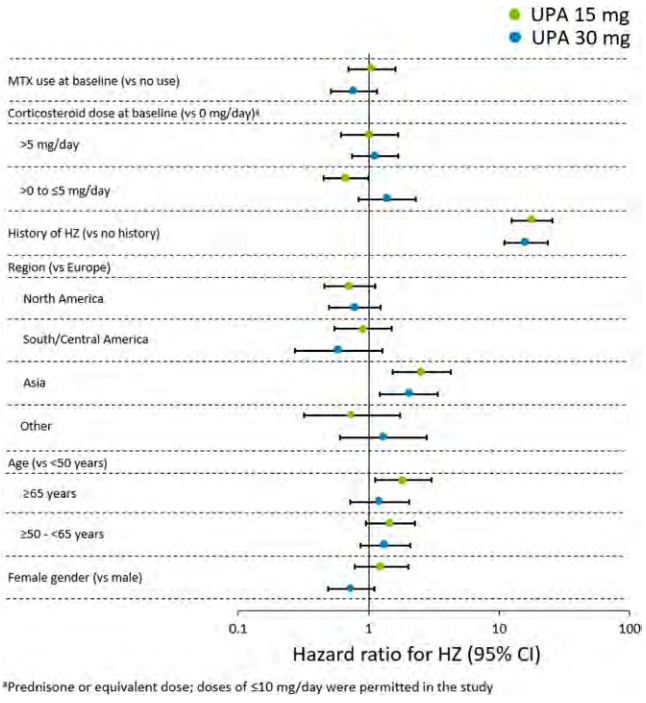


Figure. Multivariable-adjusted risk factors for HZ in pts receiving UPA

Disclosure of Interests: : Kevin Winthrop Grant/research support from: Bristol-Myers Squibb, Consultant of: AbbVie, Bristol-Myers Squibb, Eli Lilly, Galapagos, Gilead, GSK, Pfizer Inc, Roche, UCB, Peter Nash Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Gilead, Janssen, MSD, Novartis, Pfizer Inc, Roche, Sanofi, UCB, Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, MSD, Novartis, Pfizer Inc, Roche, Sanofi, UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, MSD, Novartis, Pfizer Inc, Roche, Sanofi, UCB, Kunihiro Yamaoka Speakers bureau: AbbVie GK, Astellas Pharma Inc., Bristol-Myers Squibb, Chugai Pharmaceutical Co. Ltd, Mitsubishi-Tanabe Pharma Corporation, Pfizer Japan Inc., and Takeda Pharmaceutical Company Ltd, Eduardo Mysler Grant/research support from: AbbVie, Lilly, Pfizer, Roche, BMS, Sandoz, Amgen, and Janssen., Consultant of: AbbVie, Lilly, Pfizer, Roche, BMS, Sandoz, Amgen, and Janssen., Leonard Calabrese Consultant of: AbbVie, GSK, Bristol-Myers Squibb, Genentech, Janssen, Novartis, Sanofi, Horizon,

Crescendo, and Gilead, Speakers bureau: Sanofi, Horizon, Crescendo, Novartis, Genentech, Janssen, and AbbVie, Nasser Khan Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Jose Jeffrey Enejosa Shareholder of: AbbVie, Employee of: AbbVie, Yanna Song Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Jessica Suboticki Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Jeffrey R. Curtis Grant/research support from: Abbvie, Amgen, BMS, Corrona, Crescendo, Janssen, Pfizer, Regeneron/Sanofi, and UCB, Consultant of: AbbVie, Amgen, BMS, Corrona, Crescendo, Janssen, Pfizer, Sanofi/Regeneron, and UCB

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THU0219 **FIRST-INHUMAN STUDY OF SAFETY, PHARMACOKINETICS AND PHARMACODYNAMICS OF IRAK1/4 INHIBITOR R835 IN HEALTHY SUBJECTS**

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Background: Toll-Like Receptors (TLR) and Interleukin-1 Receptors (IL-1R) play a critical role in the innate immune response as microbial and tissue damage sensors, providing a bridge between the innate and adaptive immunity. Interleukin receptor associated kinases (IRAK) 1 and 4 are serine/threonine kinases that are essential for signaling downstream of most TLRs and IL-1Rs and the resulting production of pro-inflammatory cytokines. Suppression of TLR and IL-1R signaling through inhibition of IRAK1/4 kinases is a promising therapeutic approach for the treatment of inflammatory and autoimmune diseases. We have identified a potent and selective IRAK1/4 inhibitor (R835) that showed dose-dependent inhibition of lipopolysaccharide (LPS, a TLR4 agonist), and IL-1β induced serum cytokines in mice. R835 prevented disease onset and progression in multiple rodent models of inflammatory diseases, including arthritis and lupus models.

Objectives: The aim of this FIH study was to characterize the safety, pharmacokinetics (PK) and pharmacodynamics (PD) of R835 after single or multiple dose oral administrations.

Methods: This study was a randomized, placebo-controlled, double-blind Phase 1 study in healthy subjects in three parts: single ascending doses (20 mg-1920 mg, Part A) with food effect in a separate cohort (480 mg), multiple ascending doses (120 mg and 960 mg, BID, Part B) with a caffeine interaction (960 mg cohort), and an intravenous LPS challenge test at 240 mg oral dose of R835 (Part C).

Results: Single doses of up to 480 mg R835 in organic solution, single doses of up to 1920 mg R835 as capsule, multiple doses of 120 mg R835 Q12H (organic solution), and 960 mg R835 Q12H (capsule) were safe and well tolerated. All R835 related adverse events (AEs) were mild in intensity and reversible, and mostly associated with the higher doses of R835 in the organic solution. The most common AEs were headache and gastrointestinal disturbance. The PK of R835 was linear and dose proportional in exposure over the dose range studied. A nominal level of accumulation in plasma achieved rapidly upon repeated BID administrations with steady-state essentially attained in 2 days. A high-fat meal with the capsule formulation resulted in slow rate of absorption but had no effect on the extent of absorption. There was no effect of R835 on metabolism of caffeine (P450 CYP1A2 prototype substrate). In the LPS challenge test, R835 profoundly inhibited the acute release of cytokines, including TNF-α, IL-6, IL-8, MIP1α and MIP1β, but had no impact on CRP release.

Conclusion: R835 was well tolerated after single or multiple dose administrations. The most common AEs were headache and gastrointestinal disturbance. For both of the formulations tested, the PK of R835 was linear and exposure was dose proportional with rapid steady-state attainment following BID administration. There was no drug-drug interaction by use of caffeine as the protype substrate. R835 inhibited the LPS induced release of cytokines in the serum, including TNF-α, IL-6, IL-8, MIP1α and MIP1β, mirroring preclinical data in mice. The desirable PK and safety profile combined with proof of mechanism, as demonstrated by inhibition of cytokine release, support progression of R835 into Phase II clinical development as an agent for the treatment of inflammatory and autoimmune diseases.

Disclosure of Interests: : Lucy Yan Shareholder of: Amgen, Rigel, Employee of: Amgen, Rigel, Sandra Tong Shareholder of: Rigel, Employee of: Rigel, Anthony Absalom: None declared, Izaak den Daas: None declared, Gary Park Shareholder of: Rigel Pharmaceuticals, Employee of: Rigel Pharmaceuticals, Vanessa Taylor Shareholder of: Rigel Pharmaceuticals, Employee of: Rigel Pharmaceuticals, Donna Chow Shareholder of: Rigel, Employee of: Rigel, Meng Lee Shareholder of: Rigel, Employee of: Rigel, Hanzhe Zheng Shareholder of: Rigel, Employee of: Rigel, Andrew Chow Shareholder of: Rigel, Employee of: Rigel

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THURSDAY, 04 JUNE 2020

SLE, Sjögren's and APS - etiology, pathogenesis and animal models

THU0220 **AUTOPHAGY IN SJOGREN'S SYNDROME SALIVARY GLAND EPITHELIAL CELLS (SGECS) IS ASSOCIATED WITH THE SEVERITY OF INFLAMMATION AND EPITHELIAL CELLS ACTIVATION.**

S. Colafrancesco[1], C. Barbati[1], V. Iannizzotto[2], L. Mastromanno[1], S. Nayar[2], E. Pipi[2], A. Gattamelata[1], F. Ciccia[3], C. Alessandri[1], F. Barone[2], F. Conti[1], R. Priori[1]. [1]*Sapienza University of Rome, Dipartimento di Scienze Cliniche Internistiche Anestesiologiche e Cardiovascolari, Rome, Italy*; [2]*University of Birmingham, Institute of Inflammation and Ageing, Birmingham, United Kingdom*; [3]*Università Degli Studi Della Campania L. Vanvitelli, Napoli, Italy*

Background: Sjögren's Syndrome (SS) is characterized by chronic inflammation supported by intrinsic activation of salivary gland epithelial cells (SGECs). Eventually, apoptosis of SGECs ensues, which leads to salivary gland dysfunction and exposition of autoantigens. Autophagy is a stress coping mechanisms of cells implicated in both survival and exposition of autoantigens, and is thereby plausibly implicated in the pathogenesis of SS. At present, the exact relationship between apoptosis and autophagy in SS SGECs is unclear, as is the link between these mechanisms and SGECs activation.

Objectives: To explore autophagy in SGECs from patients with SS and to evaluate its relationship with apoptosis and SGECs activation.

Methods: Consecutive patients with suspected SS referring to our "Sjogren Clinic" were enrolled, and minor salivary gland (MSG) biopsies were collected for: (1) SGECs culture, (2) PCR analysis, (3) IFI analysis. In SGECs cultures, the expression of autophagy (LC3II), apoptosis (annexin V/PI) and adhesion molecules (ICAM) was investigated by flow cytometry (results expressed as mean % ± SD). The expression of the autophagy gene MAP1LC3II was evaluated by PCR (expressed as 2^deltaCT normalized to GADPH) on both MSG sections and MSG acinar and ductal epithelium samples obtained by laser capture microdissection. Tissue expression of LC3II was evaluated by IFI on SS MSG.

Results: Primary SGECs cultures were established from 14 MSG obtained for diagnostic purposes (SS n=8, Sicca n=6). These cells exhibited an inverse correlation between apoptosis and autophagy (p=0.007, r=-0.784), with lower levels of apoptosis (19.7±6.5 vs 24.5±8.5, p=ns) and higher levels of autophagy (59.7±13.1 vs 54.19±19.4, p=ns) in SS compared to Sicca. In SS, MAP1LC3 was positively correlated with Focus Score (p=0.021 r=0.478); however, PCR studies did not reveal significant differences in MAP1LC3 expression between SS (n=26) and Sicca (n=15) (0.024±0.010 vs 0.022±0.008, p=ns). Ductal SGECs (n=4) isolated by laser microdissection of MSG revealed a higher expression of MAP1LC3 (0.005±0.0005 vs 0.003±0.0008; p=0.057) compared to normal acinar epithelium (n=5); a major expression of LC3II in ducts was confirmed by IFI (Image).

In SS, a higher expression of ICAM compared to sicca was observed (11.1±3.8 vs 6.9±6.9, p=0.006) and autophagy and apoptosis showed a trend of positive and negative correlation with this molecule, respectively (p=0.683 r=0.118 and p=0.106 r=-0.446).

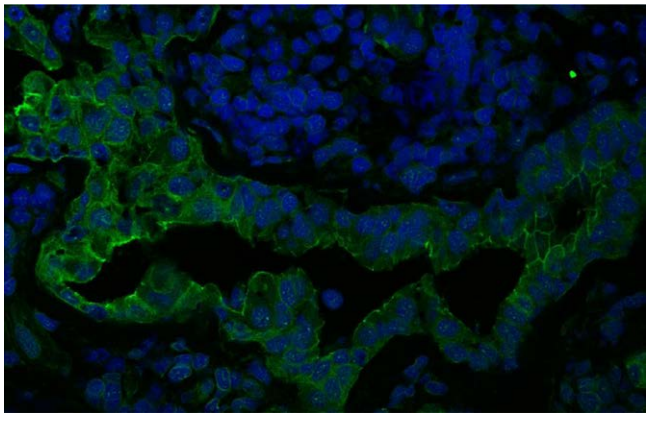


Figure. LC3-II staining in SS MSG [LC3-II+ (*green*) and Hoechst stain (*blue*); 60x magnification].

Conclusion: In SS, autophagy is upregulated in SGECs and inversely correlated with apoptosis, thus supporting a role of this process in cells' death prevention during inflammatory process. Indeed, the degree of msg inflammation is correlated more with the activation of autophagy than apoptosis. Interesting, in SS, SGECs autophagy is mainly observed at ductal level and is correlated with

higher expression of adhesion molecules suggesting a link between this pathway and changes in SGECs immune phenotype.

Disclosure of Interests: : Serena Colafrancesco: None declared, cristiana barbati: None declared, Valentina Iannizzotto: None declared, Linda Mastromanno: None declared, Saba Nayar: None declared, Elena Pipi: None declared, angelica gattamelata: None declared, francesco ciccia Grant/research support from: pfizer, novartis, roche, Consultant of: pfizer, novartis, lilly, abbvie, Speakers bureau: pfizer, novartis, lilly, abbvie, cristiano alessandri Grant/research support from: Pfizer, Francesca Barone: None declared, fabrizio conti Speakers bureau: BMS, Lilly, Abbvie, Pfizer, Sanofi, Roberta Priori: None declared

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THU0221 EVIDENCE FOR A PATHOGENIC ROLE OF EXTRA-FOLLICULAR, IL-10 PRODUCING CCR6+B-HELPER T-CELLS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: IL-10 plays a key role in systemic lupus erythematosus (SLE) pathogenesis, promoting B-cell response. IL10 is mainly secreted by regulatory T-cells, but follicular helper T-cells (T_{FH}), also produce it. We previously identified a subset of $CCR6^+IL\text{-}7R^+$T-cells in human tonsils providing IL-10-dependent B-cell help. These $CCR6^+$T-cells were able to produce IL-10, inducing IgG production.

Objectives: to investigate a possible role of $CD4^+CCR6^+IL7R^+$T-cells in SLE pathogenesis.

Methods: 37 patients fulfilling the ACR criteria for SLE have been included. Disease activity was assessed by 2k-SLEDAI. PBMC were analyzed by flow cytometry, using specific lineage markers. $CCR6^+IL7R^+$T-cells purified from total PBMC of SLE patients or healthy donors (HD) were co-cultured with autologous $CD20^+$B-cells. IL-10, Il-17, total IgG and anti-dsDNA antibodies titers in patients serum and culture supernatants were assessed by ELISA. Embedded sections of lymph nodes from 8 SLE patients were analyzed by immunofluorescence (IF).

Results: IL10 levels were significantly higher in SLE patients (Fig 1A). $CD4^+CCR6^+IL7R^+$T-cells were significantly increased in SLE, in particular in those with higher disease activity and higher IL10 levels. $CD4^+CCR6^+IL7R^+$T-cells levels associated with anti-dsDNA positivity. $CCR6^+IL7R^+$T-cells of SLE patients induced production of IgG and anti-dsDNA IgG (in anti-dsDNA + patients) from autologous B-cells, providing spontaneous help for autoantibody production *ex vivo* (Fig 1B-C). The IF study of lymph nodes of SLE patients showed that IL-10-producing $CCR6^+$T-cells were highly abundant and co-localized with B-cells at follicle margins.

Conclusion: our study revealed a novel population of extra-follicular B-helper T-cells, which produce IL-10 and could play a prominent pathogenic role in SLE. Further studies will clarify if this potentially pathogenic cell population might represent a possible future therapeutic target.

References:

[1] Facciotti F. J Allergy Clin Immunol. 2016; Geginat J. Semin Immunol. 2019; Tsokos GC. Nat Rev Rheumatol. 2019

Tab 1: SLE patients characteristics

	(n=37)
Demographics	
Female/Male, n	37/5
Age, years, median (IQR)	44 (38-49)
Disease duration, years, median (IQR)	19 (11-26)
Lab tests	
ANA	86%
*anti-dsDNA (%)	46%
medium/high titre	41%
Disease activity and clinical manifestations	
SLEDAI-2K, median (min-max)	3.5 (0-24)
Moderate/high activity	19%
Ongoing therapy	
Prednisone dose mg/day, median (IQR)	7,5 mg (2,5 – 20)
hydroxychloroquine	78%
Immunosuppressants	87%

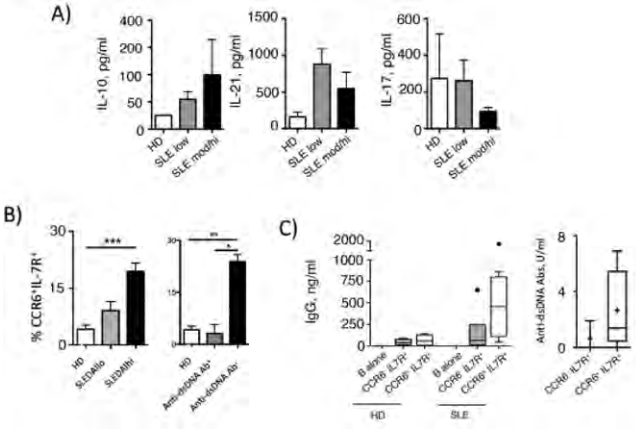


Fig 1

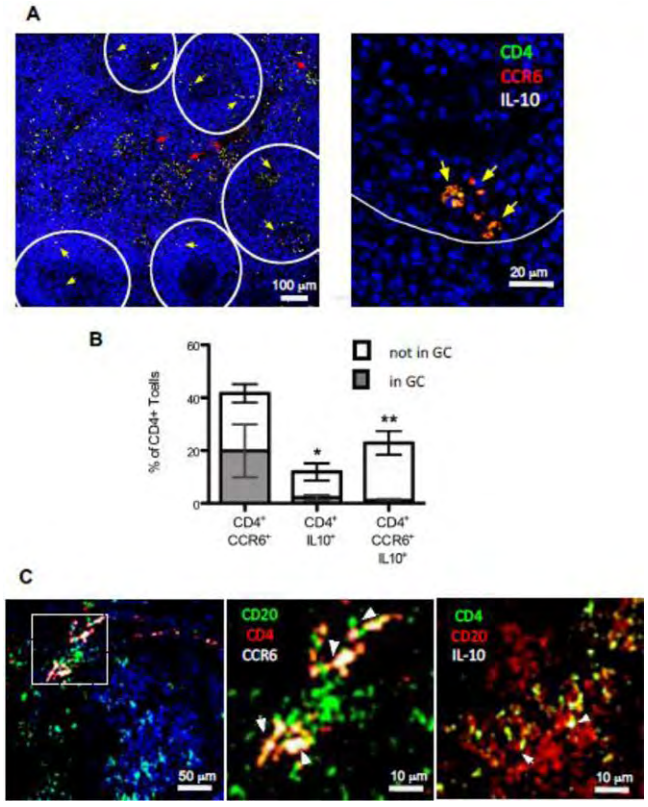


Fig 2

Disclosure of Interests: : Maria Gerosa: None declared, Federica Facciotti: None declared, Paola Larghi: None declared, Roberto Bosotti: None declared, Chiara Vasco: None declared, Nicola Gagliani: None declared, Chiara Cordiglieri: None declared, Elsa Rottoli: None declared, Alessandra Emiliana Penatti: None declared, Lorenza Maria Argolini: None declared, Bhavna Karnani: None declared, Yasushi Kobayashi: None declared, Mauro Bombaci: None declared, Jan Piet Van Hamburg: None declared, Roberta Gualtierotti: None declared, Stefano Gatti: None declared, Sara Torretta: None declared, Lorenzo Pignataro: None declared, Sander W. Tas: None declared, Roberto Caporali Consultant of: AbbVie; Gilead Sciences, Inc.; Lilly; Merck Sharp & Dohme; Celgene; Bristol-Myers Squibb; Pfizer; UCB, Speakers bureau: Abbvie; Bristol-Myers Squibb; Celgene; Lilly; Gilead Sciences, Inc; MSD; Pfizer; Roche; UCB, Sergio Abrignani: None declared, Massimiliano Pagani: None declared, Fabio Grassi: None declared, Pier Luigi Meroni: None declared, Richard Flavell: None declared, Jens Geginat: None declared

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THU0222

B CELL MODULATORY VARIANT TNF RECEPTOR DOMAINS (VTDS) IDENTIFIED BY DIRECTED EVOLUTION TO INHIBIT BAFF AND APRIL, ALONE OR COMBINED WITH VARIANT IG DOMAINS (VIGD™) THAT INHIBIT T CELL COSTIMULATION, FOR THE TREATMENT OF SEVERE AUTOIMMUNE AND/OR INFLAMMATORY DISEASE

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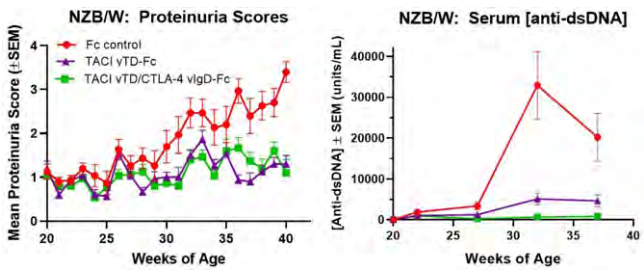
Background: BAFF and APRIL are TNF superfamily members that bind both TACI and BCMA on B cells; BAFF also binds BAFF-R. Together, BAFF and APRIL support B cell development, differentiation, and survival. Their co-neutralization dramatically reduces B cell function, including antibody production, whereas inhibition of either BAFF or APRIL alone mediates relatively modest effects.

Objectives: While CTLA-4-based therapeutics that block T cell costimulation provide safe and moderately effective T cell inhibition in many disease settings, and while B cell targeting therapies have demonstrated promising therapeutic potential, we postulate that improved, combined BAFF and APRIL inhibition, either alone or coupled with inhibition of T cell costimulation, will provide more effective and durable relief from severe B cell-related autoimmune diseases like SLE.

Methods: We used our directed evolution platform to identify variant domains of the TNF family receptors TACI or BCMA that exhibit enhanced affinity for BAFF and APRIL as compared to their wild-type (WT) counterparts. These variant TACI or BCMA domains (vTD), alone or together with platform-derived CTLA-4 domains (vIgD), were fused to a modified human IgG1 Fc lacking effector function, yielding a panel of immunomodulatory molecules: TACI vTD-Fc, BCMA vTD-Fc, TACI vTD/CTLA-4 vIgD-Fc, & BCMA vTD/CTLA-4 vIgD-Fc. All were evaluated for functional activity: 1) *in vitro* in primary human B cell & MLR assays and in a Jurkat/NF-kB reporter cell line expressing TACI, and 2) *in vivo* in standard immunization models, and in the bm12-induced and NZB/NZW spontaneous mouse models of lupus.

Results: The novel engineered TACI vTD-Fc or BCMA vTD-Fc fusion proteins significantly inhibited BAFF- and APRIL-mediated signaling *in vitro* in TACI$^+$ Jurkat cells. TACI (or BCMA) vTD/CTLA-4 vIgD-Fc proteins also attenuated T cell activation in primary human lymphocyte assays. When administered to mice, these molecules rapidly and potently reduced key B and T cell subsets, including plasma cells, follicular T helper cells, germinal center cells, & memory T cells. Treatment with TACI vTD-Fc or TACI vTD/CTLA-4 vIgD-Fc proteins also significantly reduced titers of antigen-specific antibodies in immunized mice more so than abatacept or WT TACI-Fc, and potently suppressed anti-dsDNA autoantibodies, blood urea nitrogen levels, proteinuria, and renal immune complex deposition in the bm12 & NZB/W lupus models.

Conclusion: Directed evolution of TNFR and IgSF domains has successfully facilitated the development of Fc fusion proteins containing TACI or BCMA vTDs, with or without fusion to CTLA-4 vIgDs. These novel immunomodulators consistently demonstrate potent immunosuppressive activity and efficacy *in vitro* and *in vivo*, appearing superior to existing and/or approved immunomodulators like belimumab, abatacept, or atacicept. Such biologics may therefore be attractive candidates for the treatment of serious autoimmune diseases, particularly B cell-related diseases such as SLE, Sjogren's syndrome, etc.



Disclosure of Interests: : Stacey R. Dillon Shareholder of: Shareholder of Alpine Immune Sciences, Inc., Employee of: Employee of Alpine Immune Sciences, Inc., Lawrence S. Evans Shareholder of: Shareholder of Alpine Immune Sciences, Inc., Employee of: Employee of Alpine Immune Sciences, Inc., Mark W. Rixon Shareholder of: Shareholder of Alpine Immune Sciences, Inc., Employee of: Employee of Alpine Immune Sciences, Inc., Joe Kuijper Shareholder of: Shareholder of Alpine Immune Sciences, Inc., Employee of: Employee of Alpine Immune Sciences, Inc., Dan Demonte Shareholder of: Shareholder of Alpine Immune Sciences, Inc., Employee of: Employee of Alpine Immune Sciences, Inc., Katherine E. Lewis Shareholder of: Shareholder of Alpine Immune Sciences, Inc., Employee of: Employee of Alpine Immune Sciences, Inc., Steve Levin Shareholder of: Shareholder of Alpine Immune Sciences, Inc., Employee of: Employee of Alpine Immune Sciences, Inc., Kayla Kleist Shareholder of: Shareholder of Alpine Immune Sciences, Inc., Employee of: Employee of Alpine Immune Sciences, Inc., Sherri Mudri Shareholder of: Shareholder of Alpine Immune Sciences, Inc., Employee of: Employee of Alpine Immune Sciences, Inc., Susan Bort Shareholder of: Shareholder of Alpine Immune Sciences, Inc., Employee of: Employee of Alpine Immune Sciences, Inc., Janhavi Bhandari Shareholder of: Shareholder of Alpine Immune Sciences, Inc., Employee of: Employee of Alpine Immune Sciences, Inc., Fariha Ahmed-Qadri Shareholder of: Shareholder of Alpine Immune Sciences, Inc., Employee of: Employee of Alpine Immune Sciences, Inc., Jing Yang Shareholder of: Alpine Immune Sciences, Inc., Employee of: Alpine Immune Sciences, Inc., Michelle A. Seaberg Shareholder of: Shareholder of Alpine Immune Sciences, Inc., Employee of: Employee of Alpine Immune Sciences, Inc., Rachel Wang Shareholder of: Shareholder of Alpine Immune Sciences, Inc., Employee of: Employee of Alpine Immune Sciences, Inc., Russell Sanderson Shareholder of: Alpine Immune Sciences, Inc., Employee of: Alpine Immune Sciences, Inc., Martin F. Wolfson Shareholder of: Shareholder of Alpine Immune Sciences, Inc., Employee of: Employee of Alpine Immune Sciences, Inc., Jan Hillson Shareholder of: Alpine Immune Sciences, Inc., Employee of: Alpine Immune Sciences, Inc., Stanford L. Peng Shareholder of: Alpine Immune Sciences, Inc., Employee of: CMO and President of Alpine Immune Sciences, Inc., Kristine M. Swiderek Shareholder of: Shareholder of Alpine Immune Sciences, Inc., Employee of: Employee of Alpine Immune Sciences, Inc.
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THU0223

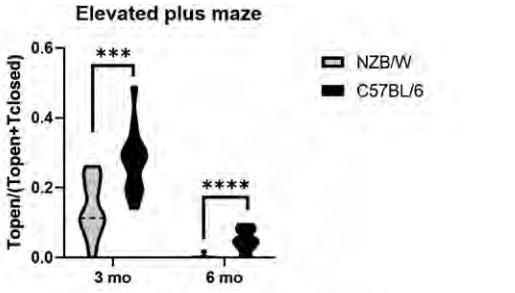
THE NEUROPSYCHIATRIC PHENOTYPE OF NZB/W LUPUS-PRONE MOUSE MODEL AT PRE-NEPHRITIC AND NEPHRITIC STAGES OF THE DISEASE: MURINE MODEL RECAPITULATES HUMAN DISEASE

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Background: The pathogenesis of neuropsychiatric lupus (NPSLE) remains ill-defined due to limited access to tissue and the diversity and complexity of clinical manifestations with most evidence deriving from animal studies in MLR/lpr lupus-prone mouse.

Objectives: To phenotype and characterize the neuropsychiatric disease in New Zealand Black/White (NZB/W) F1 strain; a spontaneous lupus prone mouse which is characterized by systemic autoimmunity.

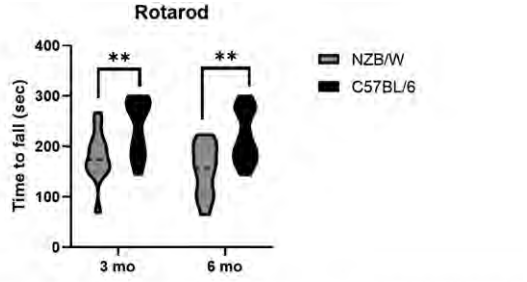
Methods: Mice were tested in a comprehensive behavioral test battery to assess possible effects on general depressive-like disorders, anxiety, cognitive function and motor performance/coordination. The following tests were conducted in the same order for all subjects (All females, NZB/W strain n=13 and C57BL/6 n=14) at 3 and 6 months of age: Open field, Novel object recognition (NOR), Novel object location (NOL), Elevated plus maze (EPM), Rotarod, Tail suspension test (TST), Prepulse inhibition (PPI), and Sucrose preference test (SPT). For comparisons, statistical significance was indicated as a two-sided P<0.05.



Graph 1. Elevated plus maze (EPM) evaluates anxiety-like phenotype. NZB/W mice exhibit anxiety-like phenotype at 3 months of age (P < 0.001, unpaired t-test) and at 6 months of age (P < 0.0001, unpaired t-test). NZB/W mice become more anxious over the course of the disease (3 mo. versus 6 mo. P<0.001, paired t-test)

Results: NZB/W mice at 3 months and 6 months of age exhibit depressive-like disorder as assessed by SPT and TST (P <0.05 and <0.0001, respectively). Anxiety-like phenotype was evident in lupus-prone mice at both time points based on EPM test (Graph 1). Open-field test revealed decreased locomotor activity and rotarod (Graph 2) showed impaired motor coordination in 3 month-old and 6 month-old NZB/W mice (P<0.001 and <0.01, respectively). NZB/W mice exhibit cognitive dysfunction at 3 and 6 months of age based on NOR test (P<0.05). No differences in cognitive function was observed between the two groups (P=0.11). Prepulse inhibition test revealed decreased sensorimotor gating in 3 month-old NZB/W mice, a difference not reaching statistical significance (P=.078). It was not possible to interpret correctly the PPI at second time point (6 months of age) due to age-related hearing loss in B6 at 6 month-old. NZB/W become more anxious over the course of the disease as assessed by EPM (3 mo. versus 6 mo. P<0.001, paired t-test, Graph 1).

Conclusion: The NZB/W lupus-prone strain exhibit depressive-like behavior, anxiety, cognitive impairment and motor disturbances both at early and late stages of the disease. This polygenic murine model may be more suitable for investigating the autoimmunity-mediated neuroinflammation in human SLE.



Graph 2. Rotarod performance demonstrates impaired motor coordination in NZB/W F1 strain both at 3 and 6 months of age (P < 0.01, unpaired t-test).

Disclosure of Interests: : None declared
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THU0224 SKIN PROTEOME INVESTIGATION IN CUTANEOUS LUPUS ERYTHEMATOSUS (CLE) REVEALS NOVEL UNIQUE DISEASE PATHWAYS

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Background: Cutaneous lupus erythematosus (CLE) is an autoimmune disease. It can be limited to the skin or be one of manifestations of systemic LE (SLE). The typical histopathologic pattern in CLE/SLE is interface dermatitis, which can also be observed in dermatomyositis (DM). While LE may affect any organ system, DM most commonly affect muscles and skin.

Objectives: The aim of this study was to investigate the whole proteome of skin inflammatory foci in the cohort of CLE and DM patients in a comparatory, hypothesis-free manner and identify disease-unique molecular mechanisms.

Methods: CLE (n=6), DM (n=5) patients and controls (n=6) were recruited at diagnosis or disease exacerbation. Skin biopsies were acquired, examined by a pathologist and selected inflammatory foci were laser micro-dissected. The total protein content was analyzed by mass-spectrometry, further analysis was performed by string-db.org platform. Certain proteomic findings were confirmed by immunohistochemistry (IHC).

Results: CLE infiltrates were more protein rich in comparison to DM lesions. There ratio of 5x upregulated proteins in LE/DM was 60, while ratio for DM/LE was 13. Our results confirmed high abundance of (IFN)-regulated proteins both in CLE and DM, including: IFIT, MX and OAS families. Proteins expressed differentially in CLE covered complement proteins (C1b), including membrane attack complex (MAC) (C5, C6, C7, C8A and B) and complement regulators (CFHR1, CFHR2, CFHR5), as well as regulators of coagulation: thrombospondin 2 (THBS2), thrombin (F2), fibrinogen (F12) and annexin A3 (ANXA3). Importantly, we identified interleukin (IL) -16 as the only detectable and highly abundant cytokine in the CLE lesions and confirmed this finding by IHC.

Conclusion: Conclusions Our data confirm evidence on IFN-regulated processes in CLE/SLE. Importantly, we identified IL-16 as a novel cytokine most strongly upregulated locally in the skin lesions. Moreover, we identified activation of MAC, complement regulating proteins as well as involvement of coagulation/fibrinolysis system. The study brings information on novel pathways involved in the inflammatory foci of the skin lesions in CLE patients. Our findings are of interest in further search of new therapeutic targets.

Disclosure of Interests: : Timothy Niewold: None declared, Karin Popovic-Silwerfeldt: None declared, Julia Lehman: None declared, Alexander Meves: None declared, Cristine Charlesworth: None declared, Benjamin Madden: None declared, Aliisa Hayry: None declared, Aleksandra Antovic: None declared, Ingrid E. Lundberg Grant/research support from: Bristol Meyer Squibb, Corbus Pharmaceuticals, Inc and Astra Zeneca, Marie Wahren-Herlenius: None declared, Elisabet Svenungsson: None declared, Vilija Oke: None declared
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THU0225 INTEGRATIVE PLASMA METABOLOME AND TRANSCRIPTOME ANALYSIS REVEALED THE IMPORTANCE OF HISTIDINE HOMEOSTASIS IN SLE PATHOGENESIS WITH POTENTIAL FOR IMPROVED SLE PATIENTS STRATIFICATION

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Background: Recently, immunometabolism has gathered attention of many immunologists. It has been widely recognized that metabolic reprogramming in each immune cell brings different effects on different cells and is important for regulating their functions. Along with the progress of statistical genetics, serum metabolites were shown to be under genetic regulations1). Metabolic changes are now considered not only to be mere phenotypes of cells but also to be key factors for controlling immune cell differentiation, proliferation and function through regulating gene expressions eventually. Although genome-wide association studies have brought deep insights into SLE pathogenesis, the precise pathway from genome to metabolome has been largely unknown, and vice versa.

Objectives: The aim of this study is to investigate metabolomic regulation in SLE in relation to gene expressions by integrating plasma metabolome data and transcriptome data.

Methods: We collected plasma samples from patients with SLE (n=57) who met the 1997 American College of Rheumatology criteria for SLE. Gender- and age-matched healthy controls (HCs) (n=56) were recruited. Metabolic profiles focusing on 39 amino acids were analyzed with liquid chromatography (LC)-mass spectrometry. Transcriptome data of SLE patients were obtained from our RNA-sequencing data of each immune cell subset (total 19 subsets). Whole-genome sequencing was also performed.

Results: Our previous experiment showed that about 160 peaks were detected from comprehensive LC-TOFMS and amino acids were useful for distinguishing SLE patients from HCs. Both partial least squares discriminant analysis (PLS-DA) and random forest, a machine learning algorithm, revealed the importance of histidine (His), one of the essential amino acids, to classify SLE patients from HCs, whose plasma level was lower in SLE patients. In addition, inverse correlation between His level and titer of ds-DNA as well as damage index (SDI) was detected. His level was correlated neither with PSL dosage nor with type I interferon (IFN) signature. Receiver operating characteristic (ROC) analysis showed the best predictability for SLE with the combination of specific amino acids including His. Our transcriptome analysis has revealed the significance of oxidative phosphorylation (OXPHOS) in B cells for SLE pathogenesis. Interestingly, OXPHOS signature was inversely correlated with His level in SLE B cells.

Conclusion: His may be an important factor for SLE pathogenesis especially in B cells independently from IFN signal. SLC15A4, a transporter of His on lysosome, is one of the SLE GWAS SNPs and has been reported to play an

important role in IFN production in B cells through regulation of TLR7/9 activation 2). We also identified that SLE patients with risk allele of SLC15A4 had tendency to show higher plasma His level, indicating His homeostasis could become a novel treatment target for SLE. Moreover, the inverse correlation of His level to SDI as well as OXPHOS signature suggests that His might play a key role for promoting organ damages in SLE.

References:

[1] *Nat Genet.* 2017;49:568. 2) *Immunity*. 2014;41:375. 3) *Semin Arthritis Rheum.* 2019;48:1142

Disclosure of Interests: : Yukiko Iwasaki: None declared, Yusuke Takeshima: None declared, Masahiro Nakano: None declared, Mineto Ota: None declared, Yasuo Nagafuchi: None declared, Akari Suzuki: None declared, Yuta Kochi: None declared, Tomohisa Okamura: None declared, Takaho Endo: None declared, Ichiro Miki: None declared, Kazuhiro Sakurada: None declared, Kazuhiko Yamamoto Grant/research support from: Astellas, BMS, MitsubishiTanabe, Pfizer, Ayumi, Takeda, Chugai, Eisai, Taisho Toyama, UCB, and ImmunoFuture, Keishi Fujio Grant/research support from: Astellas, BMS, MitsubishiTanabe, Pfizer, Ayumi, Takeda, Chugai, Eisai, Taisho Toyama, Eli Lilly, Sanofi, and UCB

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THU0226 MESENCHYMAL STEM CELL TRANSPLANTATION AMELIORATES EXPERIMENTAL SJÖGREN'S SYNDROME BY DOWNREGUALTING MDSCS VIA COX2/PGE2 PATHWAY

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Background: Although mesenchymal stem cells (MSCs) transplantation have been demonstrated to be an effective therapeutic approach to treat experimental Sjögren's syndrome (ESS)[1], the specific underlying mechanisms remain to be elucidated. Myeloid-derived suppressor cells (MDSCs) were significantly increased with decreased suppressive capacity during disease development in ESS[2-3]. However, the therapeutic effects and mechanisms by which MSCs regulating MDSCs in SS still remain unknown.

Objectives: Here we aim to explore whether regulation of MDSCs was responsible for the beneficial effects of MSC transplantation on SS.

Methods: The MSCs were infused intonon-obese diabetic (NOD) mice via the tail vein. The histological features of submandibular glands, lung, saliva flow rate were evaluated. The number and immune-suppressive activity of MDSCs, the subsets of MDSCs, polymorphonuclear MDSCs (PMN-MDSCs) and monocytic-MDSCs (M-MDSCs) in NOD mice were determined. The bone marrow cells under MDSCs differentiation conditions were co-cultured with or without MSCs. The COX2 inhibitor NS-398, anti-TGF-β1, or anti-IFN-β antibodies were added to coculture medium of MSCs and MDSCs induced from bone marrow cells respectively.

Results: We found that MDSCs in bone marrow and peripheral blood increased in ESS mice. MSC transplantation ameliorated SS-like syndrome and down-regulated the percentages of MDSCs, PMN-MDSCs and M-MDSCs and promoted their suppressive ability in ESS mice significantly (Figure 1). In vitro, MSCs could down-regulate the differentiation and up-regulate the suppressive ability of MDSCs. Mechanistically, MSCs inhibited the differentiation of MDSCs and PMN-MDSCs via secreting prostaglandin E2, and inhibited the differentiation of M-MDSCs by secreting interferon-β (Figure 2).

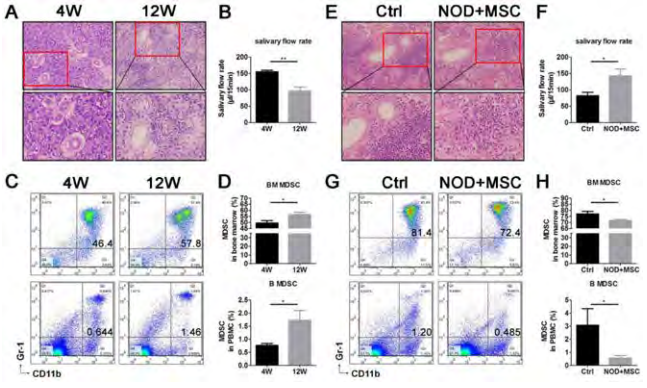


Figure 1. MSCs ameliorated SS symptoms and decreased MDSCs in NOD mice.

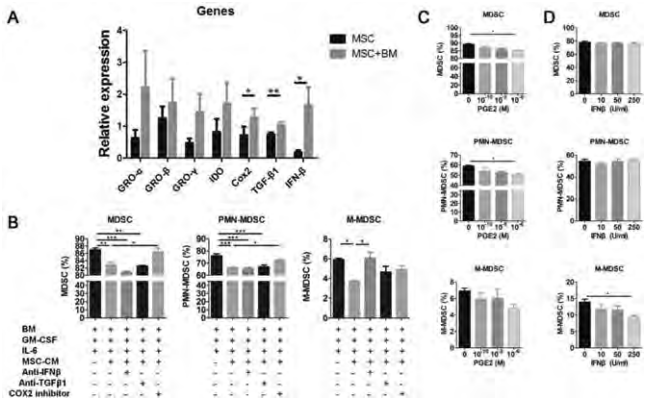


Figure 2. MSCs inhibited the differentiation of PMN-MDSCs and M-MDSCs by COX2/PGE2 and IFN-β respectively.

Conclusion: Our findings suggested that MSCs alleviated SS-like symptoms by suppressing the aberrant accumulation and improving the suppressive function of MDSCs in ESS mice via COX2/PGE2 pathway.

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Disclosure of Interests: None declared

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THU0227 CAFFEINE INTAKE MODULATES DISEASE ACTIVITY AND CYTOKINES LEVELS IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease mainly affecting women of childbearing age. The interplay between genetic and environmental factors may contribute to disease pathogenesis[1]. At today, no robust data are available about the possible contribute of diet in SLE. Caffeine, one of the most widely consumed products in the world, seems to interact with multiple components of the immune system by acting as a non-specific phosphodiesterase inhibitor[2]. *In vitro* dose-dependent treatment with caffeine seems to down-regulate mRNA levels of key inflammation-related genes and similarly reduce levels of different pro-inflammatory cytokines[3].

Objectives: We evaluated the impact of caffeine consumption on SLE-related disease phenotype and activity, in terms of clinimetric assessment and cytokines levels.

Methods: We performed a cross-sectional study, enrolling consecutive patients and reporting their clinical and laboratory data. Disease activity was assessed by SLE Disease Activity Index 2000 (SLEDAI-2k)[4]. Caffeine intake was evaluated by a 7-day food frequency questionnaire, including all the main sources of caffeine. As previously reported, patients were divided in four groups according to the daily caffeine intake: <29.1 mg/day (group 1), 29.2-153.7 mg/day (group 2), 153.8-376.5 mg/day (group 3) and >376.6 mg/day (group 4)[5]. At the end of questionnaire filling, blood samples were collected from each patient to assess cytokines levels. These were assessed by using a panel by Bio-Plex assays to measure the levels of IL-6, IL-10, IL-17, IL-27, IFN-γ, IFN-α and Blys.

Results: We enrolled 89 SLE patients (F/M 87/2, median age 46 years, IQR 14; median disease duration 144 months, IQR 150). The median intake of caffeine was 195 mg/day (IQR 160.5). At the time of the enrollment, 8 patients (8.9%) referred a caffeine intake < 29.1 mg/day (group 1), 27 patients (30.3%) between 29.2 and 153.7 mg/day (group 2), 45 patients (51%) between 153.8

and 376.5 mg/day (group 3) and 9 patients (10.1%) >376.6 mg/day (group 4). A negative correlation between the levels of caffeine and disease activity, evaluated with SLEDAI-2K, was observed (p=0.01, r=-0.26). By comparing the four groups, a significant higher prevalence of lupus nephritis, neuropsychiatric involvement, haematological manifestations, hypocomplementemia and anti-dsDNA positivity was observed in patients with less intake of caffeine (figure 1 A-E). Furthermore, patients with less intake of caffeine showed a significant more frequent use of glucocorticoids [group 4: 22.2%, *versus* group 1 (50.0%, p=0.0001), group 2 (55.5%, p=0.0001), group 3 (40.0%, p=0.009)]. Moving on cytokines analysis, a negative correlation between daily caffeine consumption and serum level of IFNγ was found (p=0.03, r=-0.2) (figure 2A); furthermore, patients with more caffeine intake showed significant lower levels of IFNα (p=0.02, figure 2B), IL-17 (p=0.01, figure 2C) and IL-6 (p=0.003, figure 2D).

Conclusion: This is the first report demonstrating the impact of caffeine on SLE disease activity status, as demonstrated by the inverse correlation between its intake and both SLEDAI-2k values and cytokines levels. Moreover, in our cohort, patients with less caffeine consumption seems to have a more severe disease phenotype, especially in terms of renal and neuropsychiatric involvement. Our results seem to suggest a possible immunoregulatory dose-dependent effect of caffeine, through the modulation of serum cytokine levels, as already suggested by *in vitro* analysis.

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Figure 1. Prevalence of lupus nephritis (A), neuropsychiatric involvement (B), haematological manifestations (C), hypocomplementemia (D) and anti-dsDNA positivity (E) in the four groups

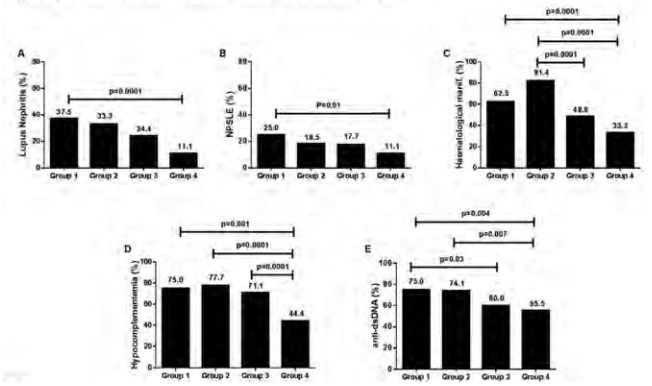
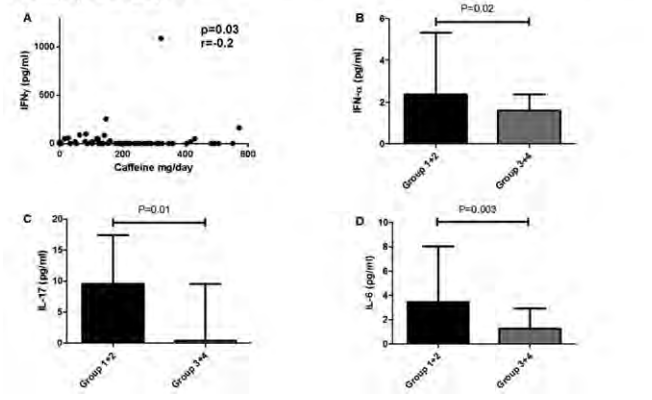


Figure 2. Correlation between daily caffeine intake and IFNγ serum level (A); IFN-α (B), IL-17 (C) and IL-6 (D) serum levels in group 1+2 and group 3+4



Disclosure of Interests: Valeria Orefice: None declared, Fulvia Ceccarelli: None declared, cristiana barbati: None declared, Ramona Lucchetti: None declared, Giulio Olivieri: None declared, enrica cipriano: None declared, Francesco Natalucci: None declared, Carlo Perricone: None declared, Francesca Romana Spinelli Grant/research support from: Pfizer, Consultant of: Novartis, Gilead, Lilly, Sanofi, Celgene, Speakers bureau: Lilly, cristiano alessandri Grant/research support from: Pfizer, Guido Valesini: None declared, Fabrizio Conti Speakers bureau: BMS, Lilly, Abbvie, Pfizer, Sanofi

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THU0228

PROTECTIVE EFFECT OF LEFLUNOMIDE ON THE SALIVARY SECRETION OF SUBMANDIBULAR GLAND IN THE NOD MOUSE

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Background: A study of 15 PSS patients showed that leflunomide had no significant effect on the decrease of salivary flow rate and the formation of lymphocytic infiltrates in salivary glands [1]. However, due to the small number of samples included in this study and the small size of human salivary gland biopsies, the therapeutic effect of leflunomide may be underestimated. At present, there is no further study on this issue, the effect of leflunomide on Sjogren's syndrome is still not clear.

Objectives: To investigate the therapeutic effect of leflunomide on salivary gland secretion dysfunction in the NOD mice with Sjogren's syndrome.

Methods: The NOD mice were randomly divided into four groups: preventive drug group, preventive control group, therapeutic drug group, and therapeutic control group. Salivary flow rate was measured after pilocarpine stimulation; After hematoxylin and eosin staining, the average number and area of infiltrating lesions were compared; The percentage of $CD3^+$ T, $CD4^+$ T, $CD8^+$ T, $CD44^+$ $CD62L^-$ $CD4^+$ T, $CD19^+$ B, and $CD138^+$ B cells in submandibular gland and spleen were detected by flow cytometry; The levels of serum inflammatory factors TNF-a, IL-17A and IL-6 were detected by CBA method.

Results: The salivary flow rate (t = -5.81, P<0.001; z =-3.61,P<0.05), the number of infiltrating foci(t=3.95,P<0.01; t=4.94,P<0.001)and the average area of infiltrating foci(t=3.18.61,P<0.05; z=2.35,P<0.05)in the treatment groups were significantly ameliorated. $CD4^+$ T cells(t=2.39 P<0.05; t´=3.82 P<0.01)and $CD44^+CD62L^-CD4^+$ T cells(t´=3.53,P<0.05; t´=3.36,P<0.05) in the submandibular gland were significantly decreased. $CD3^+T$(t=6.08, P<0.001; t=2.76,P<0.05),$CD4^+T$(t´=3.73,P<0.05; t=2.39, P<0.05), $CD19^+B$(t=5.88,P<0.001; t´=4.23, P<0.01) and $CD138^+B$ (t=4.30, P<0.001; t=4.46, P<0.01) cells in the spleen were also significantly decreased. In addition, the serum IL-17A of the treatment group reduced to lower level(t=4.15,p<0.01;t=3.36,p<0.01),and the TNF-a level of the preventive drug group decreased(t=4.56; p<0.001).

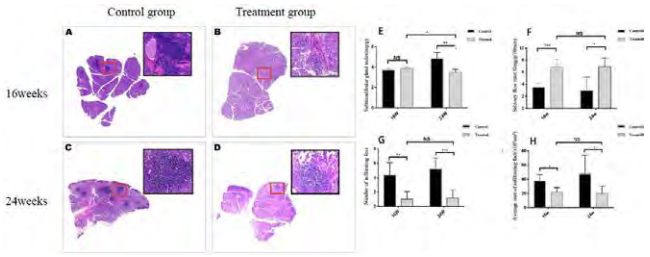


Figure 1. Leflunomide reduced lymphocyte infiltration and improved salivary gland function in NOD mice. A-D: Histology of the submandibular glands of NOD mice in control and treated groups. E-H: The comparison of the submandibular gland index, salivary flow rate, number of infiltrating foci and average area of the submandibular gland, between the control and treated groups. (mean±SD; n=7 per group; * P<0.05, ** P<0.01, *** P<0.001).

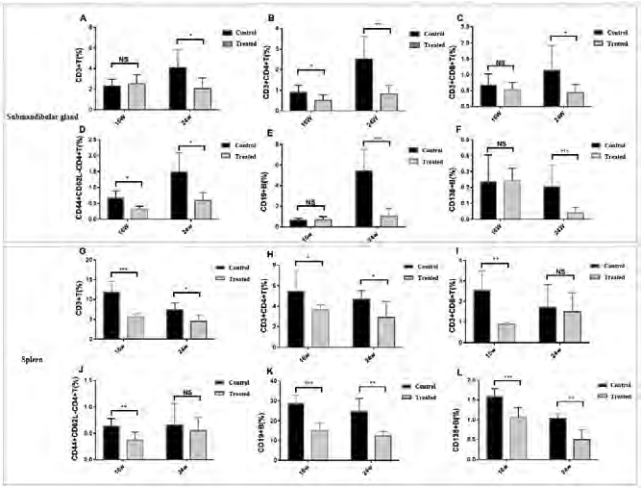


Figure 2. Changes of lymphocyte subsets in submandibular gland and spleen A-L: Frequencies of CD3+ T cells, CD4+ T cells, CD8+ T cells, CD44+ CD62L-CD4+T cells, CD19+ T cells

and CD138+ B cells in the SMG tissues and the spleen collected from treated group and control group. (mean±SD; n=7 per group; * P<0.05, ** P<0.01, *** P<0.001).

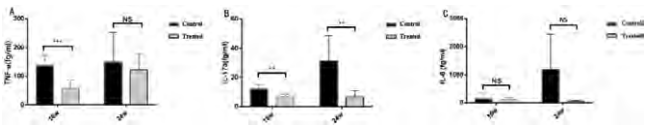


Figure 3. The proinflammatory cytokine levels of TNF-α, IL-17, and IL-6 in the serum samples from the treated and control group. (mean±SD; n=7 per group; * P<0.05, ** P<0.01, *** P<0.001).

Conclusion: Leflunomide may prevent and improve salivary gland hypofunction and inhibit immune activation in NOD mice, providing a theoretical basis for evaluating leflunomide in the treatment of Sjogren's syndrome.

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THU0229 HSA-MIR-513C-3P OVEREXPRESSION DECREASES XBP-1S CORRELATING WITH INCREASED INFLAMMATION AND AUTOANTIBODIES IN SALIVARY GLANDS FROM SJÖGREN'S SYNDROME PATIENTS

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Background: Endoplasmic reticulum (ER) stress and the Unfolded Protein Response (UPR) are linked to inflammation in a variety of human pathologies including autoimmune diseases. Salivary glands (SG) from Sjögren's syndrome (SS) patients have high levels of IFN-gamma among other cytokines, which trigger or exacerbate protein unfolding or misfolding, inducing ER stress. In this study, we focused on the IRE1α/XBP-1 pathway of the UPR, whose transcription factor is XBP-1s, which induces genes linked to regulation of the secretory pathway. We recently found that SG of SS patients have reduced levels of XBP-1s transcripts associated with an increased DNA methylation of XBP-1 promoter [1]. We postulate that other epigenetic mechanisms, such as miRNAs, could coexist with promoter DNA hyper-methylation to regulate XBP-1s expression.

Objectives: Due to hsa-miR-513c-3p overexpression has been reported in SG from SS patients [2] and that XBP-1 is a predicted target of hsa-miR-513c-3p, the aim of this study was to evaluate whether mRNA levels of XBP-1s is modulated by hsa-miR-513c-3p and also if IFN-gamma modify the expression hsa-miR-513c-3p and XBP-1s.

Methods: SG biopsies from 16 SS-patients with low and high focus score and 5 controls were analyzed. hsa-miR-513c-3p levels were measured by Taqman miRNA assays, whereas XBP-1s mRNA levels were determined by qRT-PCR. Additionally, *in vitro* assays using IFN-gamma and chemically synthesized hsa-miR-513c-3p mimics and inhibitors were performed to study its effect on XBP-1s expression.

Results: By Taqman assays we validated the overexpression of hsa-miR-513c-3p in SG from 8 SS patients with low (p=0.03) and 8 SS-patients with high (p=0.003) focus score, compared with SG from 5 controls. In the same samples, a decrease of XBP-1s transcript levels was observed in SG from SS-patients with low (p=0.002) and high (p=0.026) focus score. XBP1s transcript levels were negatively correlated with hsa-miR-513c-3p (r=-0.47, p=0.014), Ro (r=-0.73, p=0.0009), ANA (r=-0.7, p=0.0033) and focus score (r=-0.72, p=0.001). Stimulation of 3D-acini with 1 ng/mL IFN-gamma increase the hsa-miR-513c-3p levels (p=0.014) and decrease the XBP-1s transcript levels (p=0.027). A negative correlation was found between hsa-miR-513c-3p and XBP-1s transcript levels in 3D-acini stimulated with IFN-gamma (r=-0.87, p=0.0001). The XBP-1s transcript levels were decreased in HSG cells transfected with hsa-miR-513c-3p mimic and increased in HSG cells transfected with the miRNA inhibitor.

Conclusion: IFN-gamma-induced upregulation of hsa-miR-513c-3p is consistent with the presence of STAT1-binding elements in its promoter region. Our findings suggest that the combined action of miRNAs and DNA methylation modulated by IFN-gamma could explain the altered expression of XBP-1s, a key transcription factor involved in cellular proteostasis, affecting secretory function in LSG from SS-patients. Our results confirm previous correlations found between XBP-1s protein levels and clinical parameters of SS-patients, suggesting an association of XBP-1s with inflammation and impaired SG function.

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Disclosure of Interests: : None declared

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THU0230 IGG1 ANTIBODIES AGAINST PHOSPHORYLCHOLINE ARE NEGATIVELY ASSOCIATED WITH DISEASE ACTIVITY, DISEASE DAMAGE, CARDIOVASCULAR DISEASE AND ATHEROSCLEROSIS IN SLE: POTENTIAL UNDERLYING MECHANISMS.

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Background: Phosphorylcholine (PC) is an important component in cellular membranes and in lipoproteins that is exposed and recognized by the immune system, when cells undergo apoptosis or lipoproteins like LDL undergo oxidation. PC is also exposed in some microorganisms including nematodes and bacteria (non-self). We reported that IgM anti-PC is associated with protection in atherosclerosis, SLE, RA and other chronic inflammatory conditions.[1] We also reported potential underlying protective mechanisms: 1: increase in clearance of human dead cells,[2] 2: inhibition of uptake of oxLDL in macrophages, 3: inhibition of cell death.[1] 4: anti-inflammatory; 5: promotion of polarization of T regulatory cells in SLE-patients´ T cells from a low level and also in plaque T cells.[3] We generated in-house fully human IgG1 anti-PC clones for experimental studies to study anti-PC properties in humans. In contrast to mice, anti-PC are not germ-line encoded with a dominant clone. [4]

Objectives: We here study IgG1 and IgG2 anti-PC, with focus on atherosclerosis and SLE and properties of fully human IgG1 clones, in relation to SLE.

Methods: We determined anti-PC by ELISA in 116 SLE-patients and 110 age- and sex-matched controls. For functional studies, we used three in-house generated, fully human monoclonal IgG1 anti-PC (A01, D05, E01). Apoptosis was induced in Jurkat T-cells and pre-incubated with A01, D05, E01 or isotype control IgG1 and effects on efferocytosis by human macrophages studied. Anti-PC peptide/protein characterization was determined using a proteomics de novo sequencing approach.

Results: IgG1 but not IgG2 anti-PC levels were higher among SLE patients (p=0.02). IgG1 anti-PC was negatively associated with SLICC and SLEDAI (OR: 2,978 CI: 0.876-10.098, OR: 5.108 CI 1.3 20.067 respectively) and negatively associated with CVD, atherosclerotic plaques and echolucent (potentially vulnerable plaques) but the association for the two former was not significant after controlling for confounders. D05 had maximum effect on macrophage efferocytosis efficiency, followed by A01 and E01. The monoclonal antibodies showed differential binding specificity to PC and PC associated neo-epitopes. Peptide analysis showed difference in the CDR3 region of the three anti-PC IgG1 clones which are crucial for recognition of PC on apoptotic cell surface and other neo-epitopes.

Conclusion: Anti-PC IgG1 is negatively associated with disease activity, and disease damage in SLE, but the negative association with CVD is also dependent on confounding risk factors. One potential underlying mechanism could be increased clearance of dead cells.

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THU0231 IL-2 DRIVES THE CONVERSION OF T FOLLICULAR HELPER TO T FOLLICULAR REGULATORY CELLS THROUGH EPIGENETIC MODIFICATION IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is a complex polygenic autoimmune disease characterized by immune-system aberrations. Among several types of immune cells, T follicular helper (Tfh) cells promote autoantibody production, whereas T follicular regulatory (Tfr) cells suppress Tfh-mediated antibody responses. (1)

Objectives: To identify the characteristics of Tfr cells and to elucidate the mechanisms of conversion of Tfh cells to Tfr cells, we probed the phenotype of T helper cells in patients with SLE and underlying epigenetic modifications by cytokine-induced signal transducer and activators of transcription (STAT) family factors.

Methods: Peripheral blood mononuclear cells from SLE patients (n=44) and healthy donors (HD; n=26) were analyzed by flow cytometry. Memory Tfh cells were sorted and cultured under stimulation with T cell receptor and various cytokines. Expression of characteristic markers and phosphorylation of STATs (p-STATs) were analyzed by flow cytometry and quantitation PCR. Histone modifications were evaluated by chromatin immunoprecipitation.

Results: The proportion of $CXCR5^+FoxP3^+$ Tfr cells in $CD4^+$ T cells tended to increase (2.1% vs 1.7%, p=0.17); however, that of $CD4^+CD45RA^-FoxP3^{hi}$ activated Tfr cells in Tfr cells was decreased (4.8% vs 7.1%, p<0.05), while $CD4^+CD45RA^-FoxP3^{low}$ non-suppressive Tfr cells was increased (50.1% vs 38.2%, p<0.01) in SLE compared to HD. The percentage of PD-1^{hi} activated Tfh cells was significantly higher in SLE compared to HD (15.7% vs 5.9%, p<0.01). Furthermore, active patients had a higher ratio of activated Tfh/Tfr cells compared to inactive patients. In vitro study showed that IL-2, but not other cytokines such as TGF-β1, IL-12, IL-27, and IL-35, induced the conversion of memory Tfh cells to functional Tfr cells characterized by $CXCR5^+$B-$cl6^+Foxp3^{hi}pSTAT3^+$ $pSTAT5^+$ cells. The loci of *FOXP3* at STAT binding sites were marked by bivalent histone modifications. After IL-2 stimulation, STAT5 directly bound on FOXP3 gene loci accompanied by suppressing H3K27me3. Finally, we found that serum level of IL-2 was decreased in SLE and that stimulation with IL-2 suppressed the generation of $CD38^+CD27^+$B cells by ex vivo coculture assay using Tfh cells and B cells isolated from human blood.

Conclusion: Our findings indicated that the regulatory function of Tfr cells is impaired due to the low ability of IL-2 production and that IL-2 restores the function of Tfr cells through conversion of Tfh cells to Tfr cells in SLE. Thus, the reinstatement of the balance between Tfh and Tfr cells will provide important therapeutic approaches for SLE.

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Disclosure of Interests: : He Hao: None declared, Shingo Nakayamada Grant/research support from: Mitsubishi-Tanabe, Takeda, Novartis and MSD, Speakers bureau: Bristol-Myers, Sanofi, Abbvie, Eisai, Eli Lilly, Chugai, Asahi-kasei and Pfizer, Yamagata Kaoru: None declared, Naoaki Ohkubo: None declared, Shigeru Iwata: None declared, Yoshiya Tanaka Grant/research support from: Asahi-kasei, Astellas, Mitsubishi-Tanabe, Chugai, Takeda, Sanofi, Bristol-Myers, UCB, Daiichi-Sankyo, Eisai, Pfizer, and Ono, Consultant of: Abbvie, Astellas, Bristol-Myers Squibb, Eli Lilly, Pfizer, Speakers bureau: Daiichi-Sankyo, Astellas, Chugai, Eli Lilly, Pfizer, AbbVie, YL Biologics, Bristol-Myers, Takeda, Mitsubishi-Tanabe, Novartis, Eisai, Janssen, Sanofi, UCB, and Teijin

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THU0232 INTERFERON SIGNATURE IN LUPUS KIDNEY IS CORRELATED WITH REMISSION WITHIN 56 WEEKS

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Background: Activation of the type I interferon (IFN) pathway has been implicated in the initiation of systemic lupus erythematosus(SLE) and most SLE patients show increased expression of IFN-regulated genes in peripheral blood mononuclear cells or whole blood. However, the IFN signature in lupus kidney is not well examined especially at single cell resolution.

Objectives: To clarify the significance of the IFN signature in lupus kidney at single cell resolution

Methods: 18 lupus kidney (LN) and 34 transplanted kidney (KTx) samples were included in the study. Residual frozen kidney biopsies were collected after clinical diagnosis. The tissue from one donor was split into two. One portion was used for total RNA-Seq (tRNA-Seq) by SMARTer Stranded Total RNA-Seq Kit v2 - Pico Input Mammalian (Takara/Clontech). The rest was used for single nucleus RNA-Seq (snRNA-Seq) using Chromium Single Cell 3' Reagent Kits v3 (10x Genomics) (7 LN and 17 KTx). For the tRNA-Seq, the sequence reads were aligned to Ensembl genome annotation (Ens93) by STAR and the aligned reads were counted by htseq. IFN score of tRNA-Seq was calculated using the reported method [1] per each module (M1.2, M3.4 and M5.12). For the snRNA-Seq, the sequenced reads were processed on the standard pipeline of CellRanger (10x Genomics) and the data was visualized using Seurat. IFN score of snRNA-Seq was computed by the method reported by Arazi A, *et al* [2].

Clinical outcomes of LN were examined on the medical records retrospectively and the clinical remission in 56 weeks for LN was defined as a urinary protein/creatinine ratio less than 0.5 g/gCr.

Results: 11 LN had clinical remission and 7 LN showed non remitted disease within 56 weeks after the biopsy. There were no statistical significance co-variants such as age, gender and WHO class in pathology. IFN score of M1.2, M3.4 and M5.12 were significantly increased in LN with remission within 56 weeks (median 0.773 vs 0.659, 0.595 vs 0.243 and 0.415 vs 0.100: p-value 0.03, 0.01 and 0.02 [Wilcox rank-test]) in tRNA-Seq. In the snRNA-Seq, the lupus kidney with low IFN score showed restricted IFN signature in the endothelial cells mainly, which can be detected even in the controls, but those with high IFN score indicated broadly spread IFN signature among all of the cell types.

Conclusion: LN with high IFN score in kidney tissue is correlated with remission within 56 weeks. LN with low IFN score showed IFN signature restricted to endothelial cells but those with a higher IFN score revealed broadly affected cell types with IFN signature. These results suggest that the IFN signature of LN may start from endothelial cells and then spread to the whole kidney.

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THU0233

ANTIBODIES AGAINST COMMENSAL STREPTOCOCCAL SPECIFIC PROTEIN (SSP) AND MITOCHONDRIAL IMMUNO- DOMINANT PROTEIN(MIP) IN DIAGNOSIS OF SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) AND OTHER SYSTEMIC AUTOIMMUNE DISEASES

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Background: Streptococcal infection has well known to cause rheumatic fever with various presentations similar to SLE. Besides, both streptococcal-blood stream infection and SLE had aggravated neutrophil extracellular traps (NETs) formation. Previously, we did report a streptococcal induced endocarditis rat model, and identified layers of neutrophil extracellular traps (NETs). According to our findings, specific immunoglobulin G (IgG) could bridge bacteria to host and these IgGs are required to induce the formation of NETs. Whether oral commensal bacteria could induce pathogenic antibodies which promote NET formation remained unknown.
Objectives: So we aimed to search for novel autoantibodies in SLE through antibody repertoire screening which recognize whole proteins derived from *Streptococcus mutans*, and investigated to find cross-reactive antibodies presented in the serum of lupus patients and do the correlation between serum MPO(myeloperoxidase)-DNA, a marker of NETosis.
Methods: The streptoccocal specific protein (SSP) was identified through LC-MS and by a proteomics survey. We then purified the target protein in streptococci with expression vector, and antibody level will be detected quantitatively. We recruited patients with SLE, other systemic autoimmune diseases (AIDs) patients to elucidate the performance of this biomarker. Besides, we pursued the Basic Local Alignment Search Tool (BLAST) and searched for cross-reactive autoantigens.
Results: 79 lupus patients and 95 patients with other systemic autoimmune disease were enrolled. By using cut-off value 1.06(set according to area under the receiver operating characteristic
curve) of anti-SSP o.d. value (174 samples), 27 of 79 (34.2%) SLE patients have positive results while only 7/95 (7.4%) was detected in control group. The specificity and sensitivity of the anti-SSP for diagnosis of SLE was 92.6% and 34.2% respectively. According to BLAST and B cell–epitope prediction algorithms, The P32-55 epitopes were identified and we synthesized a highly immunogenic and surface-accessible epitope related protein. We named the protein to be MIP (mitochondrial immuno-dominant protein.) Most of the sera from SLE patients could recognize MIP and anti-MIP correlated with serum MPO-DNA(r=0.41, p=0.039).
Conclusion: The novel anti-SSP antibody against commensal streptococcal specific protein can differentiate SLE and other AIDs. Further investigation to determinate whether the anti-SSP antibody or the associated immune-complex could induce or aggravate NETs formation is warranted.
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Disclosure of Interests: : Che-Hao Hsu: None declared, Chiau-Jing Jung: None declared, Yu-Min Kuo Speakers bureau: Novartis, Pfizer, Rothe, Janssen, Abbvie, UCB, Chugai, Bristol Myers Squibb, Amgen and Astellas
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THU0234

INFLUENCE OF THE SPLICING MACHINERY DYSREGULATION ON THE PATHOGENESIS OF LUPUS AND THE KIDNEY INVOLVEMENT

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Background:
Objectives: The aim of this study was to evaluate whether alterations in the splicing machinery of immune cells from Systemic Lupus Erythematosus (SLE) patients could influence the development and activity of the disease and the kidney involvement.
Methods: The study was conducted in 41 SLE patients and 34 healthy donors (HD). Monocytes, lymphocytes and neutrophils were purified by immunomagnetic selection. Then, selected elements of the splicing machinery and a set of genes related to inflammation, renal and cardiovascular disease (including interleukins, adipocytokines, chemokines, and oxidative stress markers, among others) were evaluated using a microfluidic qPCR array (Fluidigm). Besides, the inflammatory profile in plasma, including the analysis of 27 proteins, was evaluated by using the Bioplex assay. In parallel, an extensive clinical/serological evaluation was performed; comprising disease activity and cardiovascular and renal involvement along with autoantibodies, complement factors, and acute phase reactants. Correlation and association studies and logistic models among those clinical and analytical parameters were developed. Mechanistic in vitro studies were carried out by incubation of HD-leukocytes with anti-dsDNA-IgG purified from SLE patients and changes promoted in both, splicing machinery and leukocyte inflammatory profile, were assessed.
Results: A significantly altered expression of spliceosome components was found in all the leukocyte subsets: 27, 12 and 11 components were differentially expressed in monocytes, lymphocytes and neutrophils, respectively, in SLE patient's vs HD. In parallel, a number of genes codifying for proteins involved in inflammation, fatty acid metabolism, oxidative stress and migration were found altered and correlations with spliceosome components were further identified. Besides, those statistical analyses demonstrated multiple links among altered spliceosome components and the clinical profile of these patients, such as the activity of the disease (SLEDAI), the occurrence of obstetric complications and the presence of arterial hypertension. Logistic regression and ROC curve analyses identified a signature composed in each leukocyte subset by 3 altered spliceosome components that could differentiate between SLE and HDs. Remarkably, the levels of a high number of those altered components were associated to the presence of lupus nephritis (LN). Moreover, ROC curve analyses allowed to identify several cell-specific spliceosome components as potential biomarkers of renal disease. In patients with LN we could also identify a distinctive inflammatory profile in plasma in relation to patients without renal involvement, which further correlated with the altered expression of a number of spliceosome components in each leukocyte subset. Lastly, the in vitro treatment of HD leukocytes with anti-dsDNA promoted the alteration of several spliceosome components found also altered in vivo in SLE lymphocytes, monocytes and neutrophils.
Conclusion: 1)The splicing machinery is greatly altered in leukocytes from SLE patients, regulated, at least partially, by anti-dsDNA antibodies and closely related to the activity of the disease, including obstetrical complications, hypertension and lupus nephritis. 2)Specific components of the spliceosome in SLE leukocytes subsets might be used as potential biomarkers to typify the disease, particularly kidney involvement.
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THU0235

VITAMIN D AND INTERFERON SIGNATURE GENE EXPRESSION IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Vitamin D deficiency is more prevalent in patients with systemic lupus eythematosus (SLE) as a result of sun avoidance.[1] The potential negative impact of vitamin D deficiency on SLE disease activity has been shown in a number of studies.[2] The expression of the interferon signature genes in SLE correlates positively with disease activity, and these genes are thought to mediate the clinical manifestations of the disease.[3]
Objectives: The aim of this study was to establish whether a relationship exists between serum 25-hydroxyvitamin D level and the interferon signature gene expression in whole blood of SLE patients.
Methods: Informed consent was obtained from 92 SLE patients who were over the age of 18 and who fulfilled the SLICC classification criteria for SLE. The patients were interviewed and blood samples were taken. SLE disease activity was measured by SLE disease activity index-2K (SLEDAI-2K). RNA extraction was performed from whole blood. QuantiGene Plex technology

was used to measure the expression of 12 interferon signature genes in the extracted RNA. The study was approved by the University Research Ethics Committee.

Results: 92.4% of the cohort studied were female. 58.7% were receiving vitamin D3 supplementation at a mean dose of 1031IU daily. 27.2% had vitamin D insufficiency (25-hydroxyvitamin D 21-29ng/ml) and 15.2% were vitamin D deficient (25-hydroxyvitamin D <20ng/ml). Mean serum 25-hydroxyvitamin D was 30.75ng/ml (standard deviation 9.53ng/ml). Median SLEDAI-2K was 4 (range 0-12). Serum 25-hydroxyvitamin D had a significant negative correlation with body mass index (BMI) (R=-0.258, p=0.006) but there was no significant negative correlation with SLEDAI-2K or with the expression of the interferon signature genes. The expression of most interferon signatures genes measured (IFI35, OAS1, MX1, IFITM1, STAT2, IFIT3, IFIT1, STAT1, SOCS1) had a significant positive correlation with SLEDAI-2K.

Conclusion: This study did not show a significant relationship between serum vitamin D level and disease activity. In keeping with this, there was no significant negative correlation between serum 25-hydroxyvitamin D and interferon signature gene expression. Further prospective studies and randomised controlled trials are required to study this relationship in greater depth.

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THU0236 EFFICACY AND SAFETY OF NON-MITOGENIC ANTICD3 ANTIBODY ADMINISTRATION IN THE TREATMENT OF LUPUS-PRONE MICE

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Background: Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease characterized by the production of autoantibody and systemic tissue damages including glomerulonephritis. Immune responses mediated by autoreactive T-cells, as well as by autoantibody, is involved in the development and progression of end-organ damages[1]. Biologic agents which manipulate T-cell function such as CTLA4-Ig and anti-CD40L have been revisited and tried to treat human SLE, however, both of them failed to demonstrate efficacy.

A mouse specific anti-CD3ε mAb, clone 145-2C11 (2C11) is known to be immunosuppressive by down-modulation of TCR and depletion of T-cells[2]. Administration of Fc-deleted 145-2C11 $F(ab')_2$ to lupus-prone mice was reported to reduce lymphadenopathy and prolong survival, but had no significant effect on anti-DNA antibody titer[3]. The mechanisms by which 2C11 ameliorates lupus are still unclear.

In this study, we used non-mitogenic Fc-modified silent 145-2c11 (2C11S), which disables interaction between target cells and Fc receptor-bearing cells, abolishes antibody directed cytotoxicity, and has longer half-life than $F(ab')_2$. 2C11S is expected to exert its effect in safe and stable as compared with functional parent-2C11 (2C11P) antibody.

Objectives: The purpose of our study is to clarify the difference between 2C11S and 2C11P and to examine their therapeutic effects against murine lupus-prone (NZB/W F1) mice.

Methods: 20 μg of 2C11P (absolute antibody), 2C11S (absolute antibody), or isotype control immunoglobulin G1 κ (IC)(BioLegend) were administered intraperitoneally to C57BL6 mice. The difference of their action on T-cells were evaluated in a time series from peripheral blood. Plasma cytokine levels were measured within 24 hours after antibody administration.

In NZB/W F1 mice from weeks 10 or 20, 2C11P, 2C11S, and IC were administered (100 μg / week, 4 times, intraperitoneally). Plasma anti-dsDNA antibody titer, spleen and kidney blood cell subpopulation, and histology of renal tissue were evaluated before and/or after treatment.

Results: Duration of reduced TCR expression in 2C11S group was approximately twice as long as that in 2C11P group, and the levels of plasma TNF-α was not increased in 2C11S group while significant increase was observed in 2C11P group (IC; mean 48.3 ± SD 16.7 pg/ml, 2C11S; 57.9 ± 6.12, 2C11P; 168 ± 50.6, IC VS 2C11S; p>0.99, IC VS 2C11P; p=0.03, ANOVA).

In NZB/W F1 mice, the number of follicular helper T (Tfh) cells in spleen significantly decreased in 2C11S group (IC; median $9.0*10^4$ [interquartile range $8.5*10^4$], 2C11S; $1.8*10^4$ [$1.0*10^4$], 2C11P; $1.0*10^5$ [$9.4*10^4$], IC VS 2C11S; p=0.03, IC VS 2C11P; p>0.99, Kruskal-Wallis). The number of germinal center B (GCB) cells in spleen also decreased in 2C11S group (IC; $1.2*10^5$ [$1.7*10^5$], 2C11S; $9.0*10^3$ [$2.3*10^4$], 2C11P; $8.0*10^4$ [$2.3*10^5$], IC VS 2C11S; p=0.03, IC VS 2C11P; p>0.99). The number of infiltrating $CD4^+$T-cells in kidney significantly reduced in 2C11S group (IC; $3.4*10^3$ [$1.0*10^4$], 2C11S; $6.4*10^2$ [$8.8*10^2$], 2C11P; $1.2*10^3$ [$4.4*10^3$], IC VS 2C11S; p=0.048, IC VS 2C11P; p=0.23). In addition, the rate of increase in anti-dsDNA IgG titers significantly decreased in 2C11S group (IC; 2.3 [1.3], 2C11S; 0.9 [1.0], 2C11P; 1.3 [1.4], IC VS 2C11S; p=0.03, IC VS 2C11P; p=0.24). Finally, glomerular hypercellularity was markedly alleviated only in 2C11S group (IC; 4.4*10 [8.4], 2C11S; 3.8*10 [1.1], 2C11P; 3.9*10 [8.2], IC VS 2C11S; p=0.02, IC VS 2C11P; p=0.57).

Conclusion: 2C11S did not induce cytokine release with maintaining longer effect on TCR down-modulation. 2C11S reduced autoantibody production by suppressing GCB differentiation, possibly through down-regulation of Tfh cell number. Consequently, 2C11S ameliorated lupus nephritis. On the other hand, 2C11P did not show therapeutic effect.

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THU0237 UNCOVERING DIFFERENCES BETWEEN THE SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) AND HEALTHY IMMUNOMES USING MULTI-PARAMETRIC INTERROGATION

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Background: Systemic lupus erythematosus (SLE) is a complex, systemic autoimmune disease that interferes with the balance between regulation and immunity, resulting in immune system dysfunction. Disease course is unpredictable due to alternating remissions and flares[1].

Disease activity and treatment response are measured with composite scores such as the SLE Disease Activity Index (SLEDAI)[2]. However, disease heterogeneity can impede reliable patient assessments. Mechanistic insights into SLE are required for better assessment.

Current studies are mainly descriptive, and a complex disease like SLE is best interrogated with multi-parametric, holistic approaches such as mass cytometry (CyTOF).

Objectives: (1)To characterise immune signatures of newly diagnosed SLE patients and in the process:

a.Study the roles of B and T cells in SLE

b.Gain a holistic understanding of the adaptive immune response

(2)To compare immunological profiles of newly diagnosed SLE patients with age-matched healthy controls

We hypothesise that significant differences exist between immunomes of newly diagnosed SLE and healthy subjects.

Methods: Peripheral blood mononuclear cells (PBMCs) of 5 SLE subjects (median age 125 months) were tested with CyTOF. Data was uploaded to an online analytical platform, the Extended Polydimensional Immunome Characterization (EPIC) discovery tool, for comparison with 51 age-matched controls in its database.

Subsequently, normalization and FlowSOM (Flow cytometry analysis by Self-Organising Maps) clustering to 50 nodes were performed with 37 functionally and phenotypically important immune markers. The Mann-Whitney U test identified significantly different cluster frequencies.

Results: Correspondence analysis comparing global differences in cluster frequencies showed segregation of SLE subjects away from healthy controls. Multiple significant differences were identified ($p < 0.05$). Notably, a memory $CD4^+CD152^+PD1^+$ T cell subset ($CD4^+CD152^+PD1^+CD45RO^+CD25^-FoxP3^-$) was enriched in SLE (median: 2.17%, interquartile range: 1.66 to 7.74% of CD45+ PBMCs) versus control (1.34%, 1.06 - 1.58%; p = 0.00267). Expression

of these known checkpoint inhibitors (PD1, CD152) could be important for SLE immunopathogenesis.

Secondly, the innate lymphoid cell 2 (ILC2) subset ($Lin^-CD7^+CD25^+CD127^+GATA3^+$) was markedly depressed in SLE (0.11%, 0.1 - 0.255%) versus control (0.41%, 0.25 - 0.55%; p = 0.0293). ILC2s protect epithelial integrity; a reduction suggests impaired protective roles in SLE.

Supervised cell frequencies from bivariate analysis correlate strongly with unsupervised cell frequencies, validating these results (Pearson's correlation coefficient r = 0.9926, p < 0.001 ($CD4^+CD152^+PD1^+CD45RO^+CD25^-FoxP3^-$); r = 0.8863, p < 0.05 (ILC2)).

Conclusion: With a multi-parametric, unbiased approach comparing SLE subjects to a large database of age-matched healthy controls, we identified two immune subsets of potential immunopathogenic importance. With this information, the CyTOF panel can be redesigned to probe more specifically into the SLE immunome, facilitating disease-specific interrogation.

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THU0238 ASSOCIATION OF SYSTEMIC DISEASES OF CONNECTIVE TISSUE (SDCT) AND GERONTOLOGICAL PROCESSES

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Background: The approach from the point of view of the evolutionary perspective of finding targets for therapeutic effects among the components of the cellular destruction system is critical both in the treatment of rheumatological diseases and in gerontology.

Objectives: To identify the relationships between the pathways of cell death in synovial fluid (SF) of people of different age groups with SDCT.

Methods: : SF was analyzed in patients of two age groups. Group N 1 of patients: 10 SLE (43±2.3 years), 13 RA (45±1.6 years), 7 SSD (35±1.8 years) and 8 donors (42±2.7 years, postmortem). Group N 2 (age) of patients: 9 SLE (69±1.8 years), 10 RA (65±1.6 years), 5 SSD (65±0.7 years) and 9 donors (66±2.3 years, postmortem). SF treated with 0.1% Triton-x-100, resuspended in 0.1% citrate buffer (pH = 7.4) and centrifuged at 25000 g for 30 minutes. The supernatant has been used in the experiment. The activity of adenosine monophosphate-activated protein kinase (AMPK) was evaluated by Western blotting. The level of p53 protein was analyzed by the enzyme immunoassay method using ELISA kit (eBioscience, (USA). The content of 8-hydroxy-2-deoxyguanosine (8-OH-dG) was evaluated using the EIA Kit (USA). Quantitative determination of cytochrome C (Cyt c) was carried using the ELISA kit. Active forms of oxygen free radicals (AFRF) were registered by EPR.

Results: : An interaction was established between the pathways of cell death in SDCT (mostly distinctive in SLE), age-related changes and clinical manifestations of the autoimmune process were established. The severity of cell death types depends on the nosological form of SDCT (tab.1).

TAB.1. SOME MARKERS OF AUTOPHAGY, APOPTOSIS AND NECROSIS IN SF OF DONORS AND PATIENTS WITH SDCT (M±m): AMPK (cond.unit/mg protein), ATP-ase (nM Pi /min•mg protein), AFRF (unit/mg protein); Cyt c, p 53, 8-OH-dG - (ng/ml)

Group N1	AMPK	ATP-ase	AFRF	Cyt c	p 53	8-OH-dG
Donor (8)	1,3± 0,2	3,7±0,3	9,7±2,3	10,4±0,3	0,7±0,1	9,5±0,8
SLE (10)	9,4±0,3***	10,3±0,3*	44,9±3,6**	40,1±2,9*	1,7±0,1*	28,9±1,4**
RA (13)	7,3±0,2***	9,7±0,5*	32,8±4,6**	29,3 ±3,7*	1,5±0,06*	23,8±0,9*
SSD (7)	4,3±0,2*	5,9±0,4	17,8+4,3*	18,9±3,7*	0,9±0,1	23,7±0,8*
Group N2	**AMPK**	**ATP-ase**	**AFRF**	**Cyt c**	**p 53**	**8-OH-dG**
Donor (9)	3,7± 0,4	0,9±0,2	24,8±5,1	15,2±3,4	1,3±0,2	18,3±0,2
SLE (9)	18,2±0,2***	4,2±0,3**	64,6±3,1**	52,8±3,9*	3,4±0,1*	44,8±0,7*
RA (10)	17,0±0,4***	4,0±0,2**	54,9±1,6*	44,3 ±3,3*	3,2±0,3*	42,2±0,4*
SSD (5)	9,8±0,3**	2,8±0,2*	38,8±4,4*	38,6±2,9*	2,9±0,1*	30,7±0,3*

Notes: difference with the control norm: * - p <0.05; ** - p <0.01; *** - p <0.001

Autophagy (especially in the case of SLE, as well as RA) is directly involved in the formation of the immune response and the inflammatory process. During aging, as well as during SDCT, there is a sharp increase in the activity of AMPK (intracellular energy sensor), expression of apoptosis inductors increases and also the acid-base balance shifts, the number of active forms of oxygen radicals increases, ox-red changes, the components of cellular destruction are activated, the activity of the cytokine system of the organism is disturbed (cytokines - regulators of apoptosis), the expression of chaperones decreases and immuno-oxygenase homeostasis shifts. Inhibition of the genetically determined process of cell death, apoptosis, underlies the development of autoimmune diseases, immunepro-liferative pathology (carcinogenesis) and gerontological changes.

Conclusion: The chaperone-mediated induction of the immune response as a signaling mechanism of autophagy, supposedly, is a common central link and a molecular switch that causes both the development of autoimmune diseases of connective tissue and geron-tological processes.

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THU0239 DYNAMIC TEMPORAL CHANGES IN CLINICAL DISEASE ACTIVITY AND GUT MICROBIOTA REPRESENTATION OF A PATHOBIONT LINKED TO LUPUS NEPHRITIS

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Background: From a cross-sectional cohort, we have identified a candidate human gut anaerobic pathobiont, *Ruminococcus gnavus* (RG) of the family *Lachnospiraceae* that was linked to active Lupus nephritis (LN)(1). Based on 16S rRNA amplicon analysis, LN patients displayed increased fecal RG abundance, concordant with serum IgG anti-RG antibody responses that appeared intertwined with anti-dsDNA responses implicated in renal pathogenesis. Indeed, monocolonization of germ-free mice is reported to result in generalized inflammation and expansions of Th17 cells. However, RG at low levels are also prevalent in healthy adults, and the temporal dynamics of RG representation within Lupus microbiota ecosystems have not been investigated. Also, genomic sequences of few RG strains have been reported, and these vary greatly in genome structure, gene representation and sequence, which may have broad implications for adaptation to a host with systemic inflammation and/or factors that contribute to immune activation in a susceptible host.

Objectives: To investigate the relationships between *in vivo* RG expansions and disease activity that often wax and wane overtime, we initiated longitudinal studies in Lupus patients and controls. As representation of RG strains alone might alter pathogenic potential, we also sought to characterize RG strains from active LN patients.

Methods: From our cohort, patients were characterized for demographics, clinical disease activity, and serologies including standard autoantibody and complement levels, and anti-bacterial responses of interest. High throughput 16S rRNA amplicon libraries from fecal samples were analyzed using QIIME 2 and DADA2 (1). Also, individual RG colonies were isolated and subjected to whole genome sequencing. Species and strains were then assigned in part based on multi-locus sequence typing and reference guided genomic assemblies.

Results: 16S rRNA analysis of 34 samples, at 2-4 timepoints from 14 SLE patients, documented highly conserved patterns of gut community representation overtime in 10/14 patients, based in part on unsupervised hierarchical cluster analysis. Notably, independent of vacillations in clinical disease activity of up to 8 SLEDAI points, conserved microbiome phylogenetic abundance/composition was documented at a family level, and the level of amplicon sequence variants that approximate identification of individual species. In pilot studies, from two active lupus nephritis patients hundreds of fecal bacterial colonies were isolated, with initial assignments by 16S rRNA sequence. From highly redundant whole genome sequence analysis, these Lupus-patient fecal colonies were found to distribute into only four distinct RG strains, which differed from reported strains.

Conclusion: Our findings suggest that many Lupus patients have little or no detectable perturbations in representation of the *Lachnospiraceae* family or abundance of RG species overtime. Moreover, this seeming microbiota stability was documented even in patients with dramatic changes in disease activity. However, these approaches are inadequate to detect shifts between RG strains. In pilot studies we have isolated and characterized the genomes of four unique RG strains from active LN patients, which include variations in gene content and sequence that may have implications for the host-commensal relationship and immune activation. Broadening of these studies to larger number of SLE patients and healthy subjects, with metagenomic surveys of strain representation in genomic shotgun libraries are currently in progress, in coordination with

murine colonization testing for immune modulatory properties of individual strains.

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THU0240 SELECTIVE DEPLETION OF AUTOREACTIVE B CELLS USING A PEPTIDE VACCINATION APPROACH

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Background: B cell depletion is currently approved or being tested in clinical trials for the treatment of many autoimmune diseases including rheumatoid arthritis, myositis, systemic sclerosis, and lupus. We previously demonstrated that the heavy chain variable regions (V_H) of anti-DNA antibodies contain epitopes that can bind MHC class I molecules.[1] Vaccination of autoimmune-prone NZB/NZWF1 mice with plasmid DNA vectors carrying minigenes that encode such epitopes induced $CD8^+$ cytotoxic T lymphocytes (CTL) that killed anti-DNA antibody-producing B cells, reduced serum anti-DNA antibody levels, retarded the development of nephritis, and improved survival.[1] Treatment with peptides alone did not induce such $CD8^+$ T-cells, as we and others have reported impaired CD8+ regulatory and CTL responses in mice and humans.[2,3] Here, we asked if we could overcome such impairment using synthetic oligodeoxynuleotides containing unmethylated cytidine-phosphate-guanosine dinucletides (CpG-ODN) that can enhance innate and adaptive immunity.
Objectives: To determine if peptides representing MHC class I binding epitopes in the autoantibody V_H regions conjugated to CpG-ODN will elicit $CD8^+$ CTLs that will ablate autoantibody-producing B cells, reduce serum autoantibody levels, and retard the development of autoimmune disease.
Methods: We first sceeened V_H regions of anti-dsDNA and other autoantibodies for MHC class I-binding epitopes uisng various bioinformatic approaches, and then verified the binding using cellular binding approaches. We immunized lupus-prone (NZB/NZW F1) mice that develop lupus that mimics human lupus with CpG-ODN or a control ODN, and assessed CTL responses. We then treated these mice with CpG-ODN conjugated to MHC class I-binding VH epitopes. We monitored lupus mice for proteinuria, serum anti-dsDNA antibodies, and survival.
Results: Immunization with CpG-ODN corrected the impairment in peptide-specific CTL responses in lupus-prone mice. The CpG-ODN conjugated with MHC class I-binding, anti-dsDNA antibody V_H-derived epitopes induced potent peptide-specific CTL responses against autoreactive B cells that expressed the respectie epitopes, and against B cells from diseased lupus-prone mice. The animals treated with CpG-ODN-peotde conjugates had reduced serum anti-DNA antibody levels and proteinuria, significantly delayed development of nephritis, and improved survival as compared to animals injected with a control ODN.
Conclusion: Seletive ablation of autoreactive B cells by CTLs induced by peptide vaccines conjugated to CpG-ODN represents a novel approach to treat autoantibody-mediated diseases.

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THU0241 ALTERATIONS OF THE FECAL MICROBIOTA ASSOCIATED WITH EXACERBATION OF LUPUS ACTIVITY BY HCMV PP65 422-439 IMMUNIZATION IN NZB/W F1 MICE

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Background: Systemic lupus erythematosus (SLE) is a multifactorial disease. Gut microbiota is an important environmental factor for SLE[1]. The perturbation of gut microbiota is often observed at onset or during the disease course. The fragment of HCMV phosphoprotein $65_{422-439}$ ($HCMVpp65_{422-439}$) containing B cell epitopes has been reported to elicit humoral immunity and accelerate the autoimmune response in murine lupus[2,3]. However, little is there to know about the interplay between viral trigger for SLE and the change of gut microbiota during lupus progression.
Objectives: By using a murine lupus model with NZB/W F1, we investigated the differential alteration in gut microbiota associated with the progression of lupus disease in $HCMVpp65_{422-439}$ immunized mice and control mice.
Methods: Ten weeks-old NZB/W F1 mice were given or not given an intraperitoneal injection of 100-μg $HCMVpp65_{422-439}$ peptide biweekly for four times. Fecal samples, urine and blood of mice were collected once every two weeks followed by 16S rRNA genes sequencing and ELISA tests. The pathological investigation of renal tissue from sacrificed mice was conducted at 24 weeks of mice age. Statistical analysis for dynamics and alteration of the gut microbiota as well as functional prediction of bacterial communities related to the progression of lupus-like activity was performed.
Results: $HCMVpp65_{422-439}$ immunization results in the onset of lupus-like activities in NZB/W F1 mice with a higher titer of anti-dsDNA antibody, creatinine and proteinuria, and severe glomerular damage (figure 1). Also, higher diversity and increased family abundance of several bacterial species were observed in $HCMVpp65_{422-439}$ immunized mice (Table 1 and Figure 2a). The predicted metagenomic taxonomic profile in NZB/W F1 mice showed statistically significant enrichment of flagellar assembly, bacterial motility, and chemotaxis (Figure 2b). Spearman's correlation analysis revealed that a significant association between the increased relative family abundance for *Saccharimonadaceae, Marinifilaceae, Desulfovibrionaceae,* and *Rikenellaceae* and $HCMVpp65_{422-439}$ induced lupus-like activity in NZB/W F1 mice (Figure 2c).

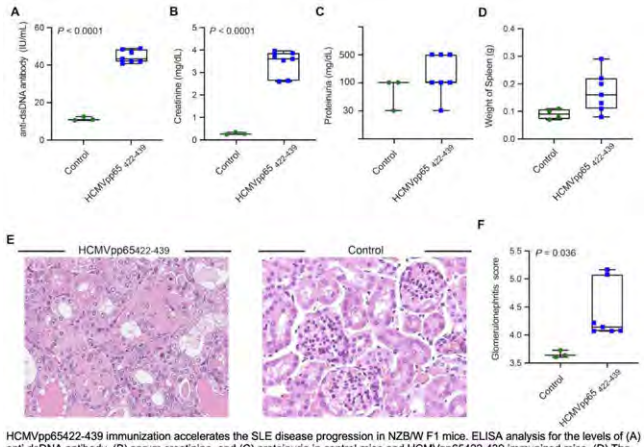
Table 1. Significant test of microbial community structure between two groups

	MRPP		Adonis		Anosim	
Groups	E-Δ	P	R^2	P	R	P
Pre-disease vs. Control	0.43	0.1	0.77	0.1	1	0.112
Pre-disease vs. $HCMVpp65_{422-439}$	0.52	0.007	0.55	0.009	0.97	0.01
Control vs. $HCMVpp65_{422-439}$	0.45	0.013	0.35	0.014	0.58	0.019

Conclusion: Our results demonstrated that $HCMVpp65_{422-439}$ immunization induced the change in gut microbiota composition and suggested the association of gut microbiota alteration with lupus-like activity in NZB/W F1 mice.

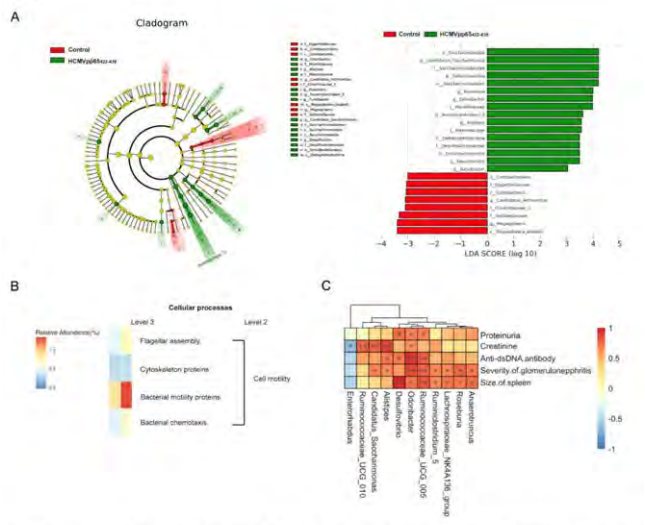
References:
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Figure 1



HCMVpp65422-439 immunization accelerates the SLE disease progression in NZB/W F1 mice. ELISA analysis for the levels of (A) anti-dsDNA antibody, (B) serum creatinine, and (C) proteinuria in control mice and HCMVpp65422-439 immunized mice. (D) The representative photograph and diagram shows the size of spleen collected from both groups. (E) Hematoxylin and eosin staining of the glomerular from control mice and HCMVpp65422-439 immunized mice. (F) The glomerulonephritis score of renal lesions from control and immunized mice.

Figure 2



(A) LEfSe was conducted to determine the features of different abundances between groups and the effect size of features were accessed by LDA. Significant difference are shown (LDA>3). (B) Metagenomic taxonomic profile to predict the functional profile of microbial communities in HCMVpp65$_{422-439}$ groups by phylogenetic reconstruction of unobserved states (PICRUSt). (C) Spearman's rank correlation between the relative abundance of altered microbial genera and the lupus activity in NZB/W F1 mice. These results are shown as heatmap diagram with the color of each correlation test, which is corresponding to the Spearman rho value: "++" represents the P value < 0.05 and "++" represents the P value < 0.01.

Disclosure of Interests: : None declared
DOI: 10.1136/annrheumdis-2020-eular.1846

THU0242 **REGULATORY ROLE OF TRANSCRIPTION FACTOR BLIMP-1 IN SJÖGREN'S SYNDROME**

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Background: The pathogenesis of primary sjögren's syndrome (pSS) is multifactorial. Self-antigen-driven responses perform a vital function in the development of autoimmune diseases [1]. B cells, only 20-25% of total infiltrating cells in labial glands, are the cellular basis for spontaneous antibody production [2]. Genome-wide association studies (GWAS) have identified Blimp-1 as a susceptibility gene for autoimmune diseases and played an important role in the pathogenesis of autoimmune diseases [3].
Objectives: To investigate the expression and effect of B lymphocyte induced maturation protein 1 (Blimp-1) in pSS and the correlation of Blimp-1 with B cell subsets and clinical features.
Methods: The PRDM1 mRNA expression in B lymphocyte and labial gland were examined by RT-PCR. The levels of B cell subsets were examined by flow cytometry. Hematoxylin-eosin (HE) staining and immunohistochemistry (IHC) were used to examine the invasion degree of lymph cell and Blimp-1 distribution, respectively. The correlation of PRDM1 mRNA with B cell subsets and clinical indicators were also analyzed.
Results: The levels of PRDM1 mRNA expression of B cells were significantly higher in SS than in healthy controls (HC) and which were also significantly higher in the high immunoglobulin (Ig) group than that in normal Ig group

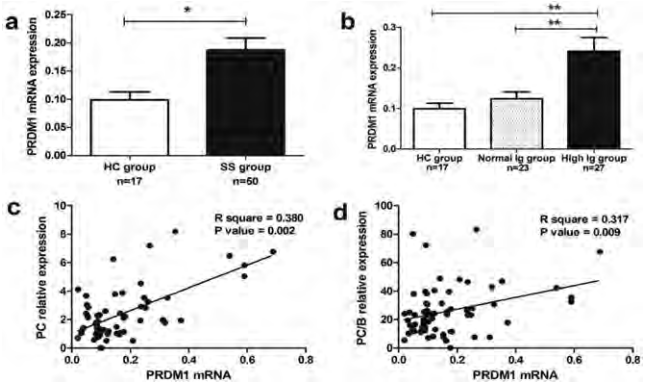


Fig. 1 (a-b) RT-PCR showed that PRDM1 mRNA expression in SS patients and HC. (c-d) Correlation between PRDM1 mRNA expression and PC and PC/B.

(*P*<0.02, Fig. 1a-b). The number of CD19+B cells and CD138+ plasma cells(PC) have increased while the CD27+ cells decreased in SS(*P*<0.05). The percentage of PC and PC/B is positively correlated with PRDM1 mRNA(*r*=0.380, *P*=0.002; *r*=0.317, *P*=0.009, Fig. 1c-d). Blimp-1 expression level showed a positive correlation with invasion degree of lymph cell in histology (Fig. 2a-c), Ig levels and ESSDAI score and an inverse correlation with the glucocorticoids usage (Fig. 3c).

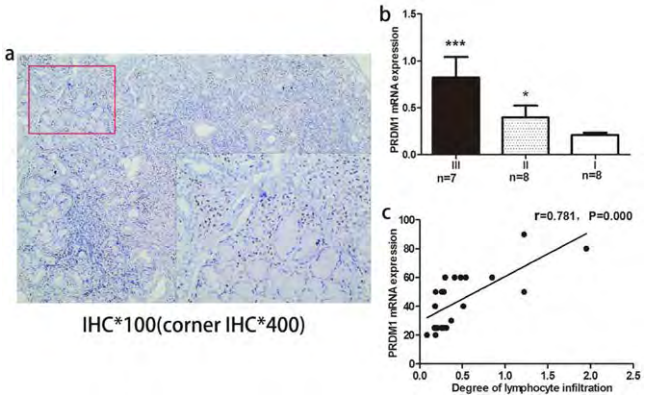


Fig. 2 (a) Expression of Blimp-1 in labial glands of sjögren's syndrome. (b) PRDM1 mRNA levels in different invasion degree of lymph cell group. (c) Correlation between PRDM1 mRNA expression and invasion degree of lymph cell. *p<0.05, ***p<0.001.

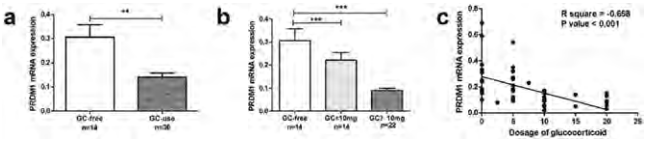


Fig. 3 (a-b) RT-PCR showed that PRDM1 mRNA expression in different usage of glucocorticoids. (c) Correlation between PRDM1 mRNA expression and different glucocorticoid usage. **p<0.01, ***p<0.001.

Conclusion: Blimp-1 displayed high expression in SS, which could affect pSS disease activity. SS activity is suppressed by glucocorticoid which might be through inhibition of Blimp-1.
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Table 1. Clinical characteristics of pSS and HC.

	HC(n=17)	pSS(n=50)
Sex (Male/Female)	0/17	0/50
Age(x±*s*)	45.24±18.55	46.8±11.05
Xerostomia(positive/negative)	0/17	43/7
Keratoconjunctivitis sicca	0/17	35/15
Arthralgia	0/17	32/18
Fatigue	0/17	18/32
ESSDAI(x±*s*)	-	2.78±1.61 (0~7)
ESSPRI(x±*s*)	-	3.3±1.39 (1~6)
ANA(positive/negative)	-	49/1
SSA	-	49/1
SSB	-	18/32

pSS: primary sjögren 's syndrome; HC: Healthy controls; ESSDAI: The European League Against Rheumatism Sjögren's Syndrome Disease Activity Index; ESSPRI: EULAR Sjögren's Syndrome Patient Reported Index.** P<0.01,*** P<0.001.

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THU0243 **HSA_CIRC_0123190 FUNCTIONS AS A COMPETITIVE ENDOGENOUS RNA TO REGULATE APLNR EXPRESSION BY SPONGING HSA-MIR-483-3P IN LUPUS NEPHRITIS**

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Background: Lupus nephritis (LN) is one of the most severe complications of systemic lupus erythematosus (SLE). Circular RNAs(circRNAs) can act as competitive endogenous RNAs (ceRNAs) to regulate gene transcription, which is involved in mechanism of many diseases, such as, autoimmunity diseases. However, the role of circRNA in lupus nephritis has been rarely reported.
Objectives: In this study, we aim to investigate the clinical value of circRNAs and explore the mechanism of circRNA involvement in the pathogenesis of LN.
Methods: Renal tissues from three untreated LN patients and three normal controls (NCs) were used to identify differently expressed circRNAs by RNA sequencing (RNA-seq). Validated assays were used by quantitative reverse transcription polymerase chain reaction (qRT-PCR). Correlation analysis and receiver operating characteristic (ROC) curve were used to reveal the clinical value of selected circRNA, miRNA and mRNA. The interactions between circRNA and miRNA, or miRNA and mRNA were further determined by luciferase reporter assay. The degrees of renal fibrosis between the two groups were compared by Masson-trichome staining and immunohistochemistry staining.
Results: 159 circRNAs were significantly dysregulated in LN patients compared with NC group. The expression of hsa_circ_0123190 was significantly decreased in renal tissues of patients with LN (p=0.014), as same as the sequencing results. The area under the ROC curve of hsa_circ_0123190 in renal tissues was 0.820. Bio-informatic analysis and luciferase reporter assay illustrated that hsa_circ_0123190 can act as a sponge for hsa-miR-483-3p which was also validated to interact with APLNR mRNA. APLNR mRNA expression was positively related with chronicity index (CI) of LN (R^2=0.452, p=0.033). Finally, the factors of renal fibrosis, especially TGF-β (p=0.018), were more pronounced in the LN group.
Conclusion: Hsa_circ_0123190 could function as a ceRNA to regulate APLNR expression involved in renal fibrosis by sponging hsa-miR-483-3p in LN
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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.4025

THURSDAY, 04 JUNE 2020

SLE, Sjögren's and APS - clinical aspects (other than treatment)

THU0244 **3 YEAR FOLLOW UP OF AN AT-RISK CONNECTIVE TISSUE DISEASE COHORT: ANALYSIS OF CLINICAL, GENE EXPRESSION AND FLOW CYTOMETRIC BIOMARKERS**

S. U. Hassan[1], Z. Wigston[1], A. Psarras[1], K. Dutton[1], M. Y. MD Yusof[1], E. Vital[1]. [1]*University of Leeds, Leeds, United Kingdom*

Background: We previously reported results from the first 118 "At-Risk" of autoimmune connective tissue disease (AI-CTD) individuals (i.e. ANA positivity, non-specific symptoms of ≤1 year and treatment naïve). At 1 year, 16% progressed to meet classification criteria for an AI-CTD. This was predicted by high baseline interferon (IFN) Score B and family history of RMD[1].
However, some may have progressed at later time points, or had clinically significant disease despite not meeting diagnostic criteria. Longer term outcomes, baseline and follow up flow cytometry biomarkers were never reported.
Objectives:
(i)Describe detailed analysis of 3-year follow-up data of the At-Risk cohort
(ii)Evaluate flow cytometric biomarkers as predictors of these outcomes
(iii)Analyse follow up biomarkers
Methods: We conducted a prospective observational longitudinal study of At-Risk individuals in Leeds (n=150). Patients were assessed at baseline, then annually for 3 years. Depending on diagnostic criteria and need for therapy, patients were grouped as follows:
1. Absolute non-progressors (no clinical diagnostic criteria)
2. Undifferentiated CTD (U-CTD) (≥1 clinical criteria at baseline persisting at follow-up but not meeting criteria). This group was subdivided into those who required treatment with an immunosuppressant (IS) excluding antimalarials and those who did not
3. Year 1 progressors (meeting criteria for an RMD by 1 year)
4. Late progressors (meeting criteria for AI-CTD beyond 1 year follow-up).

Bloods were analysed at baseline and 1 year for two IFN-stimulated gene expression scores previously described[2], monocytes and subsets of B and T cells using flow cytometry. Association between clinical criteria, biomarkers at baseline and long term outcomes were tested using ANOVA.
Results: 3 year follow up data was available in 147/150 patients. Outcomes were: Absolute non-progressors: 63/147 (43%); U-CTD: 54/147 (37%); Year 1 progressors: 21/147 (14%) [SLE=18; pSS=3]; Late progressors (in years 1-2): 9/147 (6%) [SLE=7; pSS=2]. None progressed or required IS initiation beyond the first 2 years of follow-up. In U-CTD group, 7/54 (13%) were prescribed an IS. This work describes a larger group of 36/147 (24%) At-Risk individuals who developed clinically significant disease (CSD: progressors or need for IS) versus clinically non-significant disease (CNSD: absolute non-progressors or UCTD not needing IS). Analysis of baseline biomarkers between CSD and CNSD confirmed a significant difference in IFN Score B (mean difference -0.74, p = 0.027), but not IFN Score A (mean difference -0.68, p = 0.15). In flow cytometry analysis, there was also a significant difference in percentage monocytes (mean difference -4.09, p = 0.004) but no other subset. Absence of clinical criteria at baseline did not predict clinical outcome, and no one clinical criterion had greater predictive value.
In follow up samples we noted a significant reduction in expression of IFN Score B in both groups, regardless of whether they received antimalarials or IS therapy.
Conclusion: Here we report findings of a larger group of 24% At-Risk individuals who developed CSD (progressors and patients who did not meet criteria but needed IS therapy). These results provide a more complex picture of IFN activity in the initiation of SLE than previously suspected. First, we confirm that a specific subset of ISGs rather than a classic IFN signature predicts progression. Second, the reduction in IFN-Score-B in both groups suggests that IFN Score B activity is a transient phenomenon, playing a greater role in disease initiation than in disease maintenance.
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Disclosure of Interests: Sabih-Ul Hassan: None declared, Zoe Wigston: None declared, Antonios Psarras: None declared, Katie Dutton: None declared, Md Yuzaiful Md Yusof: None declared, Edward Vital Grant/research support from: AstraZeneca, Roche/Genentech, and Sandoz, Consultant of: AstraZeneca, GSK, Roche/Genentech, and Sandoz, Speakers bureau: Becton Dickinson and GSK
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THU0245 **PENALIZED REGRESSION ANALYSIS IDENTIFIES CRITERIA AND NON-CRITERIA FEATURES THAT MAY INCREASE THE ACCURACY OF EXISTING SETS OF CRITERIA FOR CLASSIFYING SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)**

C. Adamichou[1], I. Genitsaridi[1], D. Nikolopoulos[2], A. Bortoluzzi[3], A. Fanouriakis[2], E. Kalogiannaki[1], E. Papastefanakis[1], I. Gergianaki[1], P. Sidiropoulos[1], D. Boumpas[2], G. Bertsias[1]. [1]*University of Crete Medical School, Iraklio, Greece*; [2]*National and Kapodistrian University of Athens, Athens, Greece*; [3]*University of Ferrara, Ferrara, Italy*

Background: The ACR-1997, SLICC-2012 and EULAR/ACR-2019 classification criteria have high sensitivity and specificity for SLE, yet they classify non-overlapping groups of patients suggesting that they can be supplemented with additional features to improve their diagnostic performance.
Objectives: To identify criteria and non-criteria manifestations that are significantly associated with SLE in clinical practice and can be used to complement the existing sets of classification criteria.
Methods: Individual items from all three classification criteria (ACR-1997, SLICC-2012, EULAR/ACR-2019) and non-criteria features were analyzed in a randomly selected sample of 800 adults diagnosed with SLE or control rheumatologic diseases (1:1 ratio). The classification performance of each set of criteria was analyzed in combination with complementary features; multivariable least absolute shrinkage and selection operator (LASSO) logistic regression was performed for feature selection. We calculated the diagnostic odds ratio (DOR) of the criteria and the additional features retained in each model.
Results: The EULAR/ACR-2019 and SLICC-2012 criteria have increased accuracy for SLE classification as compared to the ACR-1997 criteria (univariate DOR: 243.2 and 157.3 *versus* 78.8, respectively). In multivariable regression based on the ACR-1997 criteria, inclusion of additional features such as maculopapular rash, alopecia and hypocomplementemia significantly enhanced the model predictive capacity (area under the curve [AUC]: 0.95 *versus* 0.87 of the ACR-1997 criteria alone). Similar analysis based on the SLICC-2012 and EULAR/ACR-2019 criteria identified photosensitivity as an additional criterion significantly associated with SLE (multivariable DOR: 5.4 and 9.4, respectively). Accordingly, models including photosensitivity had superior predictive capacity over the criteria-only models (AUC: 0.94 *versus* 0.91 for SLICC-2012, 0.96 *versus* 0.91 for EULAR/ACR-2019). Furthermore, non-criteria features including Raynaud's/livedo reticularis, anti-RNP antibodies, splenomegaly and myocarditis were independently associated with SLE thus enhancing further the predictive capacity of criteria-based models.
Conclusion: We identified a number of criteria and non-criteria features which can be used in combination with the existing sets of criteria to increase classification of SLE patients in clinical practice. Photosensitivity could be considered as an additional feature to improve sensitivity of the recent classification criteria.
Disclosure of Interests: Christina Adamichou: None declared, Irini Genitsaridi: None declared, Dionysis Nikolopoulos: None declared, Alessandra Bortoluzzi: None declared, Antonis Fanouriakis Paid instructor for: Paid instructor for Enorasis, Amgen, Speakers bureau: Paid speaker for Roche, Genesis Pharma, Mylan, Eleni Kalogiannaki: None declared, Emmanouil Papastefanakis: None declared, Irini Gergianaki: None declared, Prodromos Sidiropoulos: None declared, Dimitrios Boumpas: None declared, George Bertsias Grant/research support from: GSK, Consultant of: Novartis
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THU0246 DIAGNOSTIC CLUSTER PROFILING OF PATIENTS IN A REAL-WORLD DATA SET WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Previous systemic lupus erythematosus (SLE) studies have identified potential clusters of SLE clinical manifestations post diagnosis.
Objectives: To describe the presentation of SLE at diagnosis across different cohorts of patients and describe management and outcomes after diagnosis within clusters.
Methods: Cross-sectional study of 263 rheumatologists in the US and EU5. Data were collected from the Adelphi Real World 2015 Lupus Disease Specific Programme. Rheumatologists completed patient record forms (PRFs) for the next 5 prospectively consulting SLE patients; these patients completed patient self-completion (PSC) forms describing how SLE affected them. PRF data includes patient's characteristics and management history. PSCs focused on similar data collection, including patient reported outcome measures on the humanistic burden. Age at diagnosis, symptoms at diagnosis, organ involvement at diagnosis, and severity at diagnosis were used as covariates in a latent cluster analysis.
Results: Data were extracted from 1376 PRFs. Cluster analysis resulted in up to 6 clusters, and disease understanding led to the selection of a 4-cluster solution. Cluster 1 displayed the mildest disease, characterised by joint involvement, while cluster 2 displayed more skin involvement in conjunction with joint. Cluster 3 were characterised by renal involvement and cluster 4 had skin and joint involvement, but also high constitutional and haematological involvement at diagnosis (Table 1).

Table 1 Cluster analysis

		Clusters				
Organ involvement at diagnosis, n (%)	**Overall** (n=1304)	**1** (n=210)	**2** (n=493)	**3** (n=162)	**4** (n=439)	**p-value**
Musculoskeletal	1145 (87.8)	174 (82.9)	444 (90.1)	134 (82.7)	393 (89.5)	0.0065
Mucocutaneous	898 (68.9)	5 (2.4)	397 (80.5)	95 (58.6)	401 (91.3)	<0.0001
Neuropsychiatric	87 (6.7)	19 (9.0)	9 (1.8)	16 (9.9)	43 (9.8)	<0.0001
Cardiorespiratory	176 (13.5)	36 (17.1)	14 (2.8)	22 (13.6)	104 (23.7)	<0.0001
Gastrointestinal	44 (3.4)	8 (3.0)	14 (2.8)	8 (4.9)	14 (3.2)	0.6115
Opthalmic	47 (3.6)	0	20 (4.1)	10 (6.2)	17 (3.9)	0.0102
Renal	213 (16.6)	15 (7.1)	9 (1.8)	162 (100)	27 (6.2)	<0.0001
Constitutional	425 (32.6)	45 (21.4)	89 (18.1)	55 (34.0)	236 (53.8)	<0.0001
Haematological	452 (34.7)	64 (30.5)	22 (4.5)	80 (49.4(	286 (65.1)	<0.0001
Severity at diagnosis, n (%)						
Mild	209 (16.0)	55 (26.2)	99 (20.1)	1 (0.6)	54 (12.3)	<0.0001
Moderate	806 (61.8)	122 (58.1)	324 (65.7)	75 (46.3)	285 (64.9)	
Severe	289 (22.2)	33 (15.7)	70 (14.2)	86 (53.1)	100 (22.8)	

Significant between-cluster differences were observed when comparing outcomes; cluster 4 have been diagnosed longest (mean weeks diagnosed 354.6 v. 1: 232.6, 2: 228.7, 3: 338.2, p<0.0001). Cluster 3 consulted more in the last 12 months (mean number of visits 7.9 vs. 1: 5.7, 2: 6.3, 4: 7.6).
Significant differences were also observed between clusters in relation to current treatment proportions: corticosteroid (highest cluster 3: 78.4%), immunosuppressant (highest cluster 3: 75.3%), biologic DMARD (highest cluster 4: 17.8%) and antidepressant (highest cluster 4: 4.1%).
Conclusion: This study demonstrates the heterogeneity of SLE at diagnosis and highlights four distinct presentations of the disease at diagnosis. Significant proportions of patients present with advanced disease, these clusters go on to present the greatest burden demonstrating the need for better diagnostic tools and novel earlier intervention.
Study funded by Johnson and Johnson.
Disclosure of Interests: Zahi Touma Consultant of: Consultant for Janssen, Ben Hoskin Consultant of: Consultant for Janssen, Christian Atkinson Consultant of: Consultant for Janssen, David Bell Consultant of: Janssen, Olivia Massey Consultant of: Janssen, Jennifer H. Lofland Employee of: Janssen, Pamela Berry Employee of: Janssen, Chetan Karyekar Shareholder of: Johnson & Johnson, Consultant of: Janssen, Employee of: Janssen Global Services, LLC. Previously, Novartis, Bristol-Myers Squibb, and Abbott Labs., Karen Costenbader Grant/research support from: Merck, Consultant of: Astra-Zeneca
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THU0247 FREQUENCY AND PREDICTORS OF THE LUPUS LOW DISEASE ACTIVITY STATE IN CHINESE PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: AN OBSERVATIONAL COHORT STUDY

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Background: As a consensus-based definition of minimally acceptable disease activity in systemic lupus erythematosus (SLE), Lupus Low Disease Activity State (LLDAS) has been well-validated and widely accepted. However, no data about the time to LLDAS in Asian ethnicity has been reported so far.
Objectives: To estimate the time to LLDAS and the predictors of time to LLDAS in our prospective observational cohort of Chinese patients with SLE.
Methods: Patients were from Peking University First Hospital SLE cohort and those having not fulfilled LLDAS at enrolment were included in this study. The time to LLDAS and annual cumulative probabilities of LLDAS achievement were estimated by the Kaplan-Meier approach. The predictors of time to LLDAS were identified by univariate and multivariable Cox proportional hazards.
Results: A total of 574 patients with SLE were included and 435 (75.8%) of them achieved LLDAS during a median 4.2 years of follow-up. The median time to LLDAS was 19.0 months and the cumulative probabilities at 1, 2, 3, 5 and 10 years were 19.8%, 57.6%, 72.0%, 85.1% and 98.0%, respectively. In multivariable Cox models, older age at disease onset, treatment-naïve and hydroxychloroquine prescription were found to be independent predictors of shorter time to LLDAS, after adjusted by daily prednisone dose, SLE Disease Activity Index 2000 and physician's global assessment. Finally, we developed a matrix model based on the identified independent predictors to present the time to LLDAS in patients with respective characteristics.
Conclusion: Our study proved that LLDAS is attainable as an early treatment target for SLE in Chinese patients. The older age at disease onset, treatment-naïve and hydroxychloroquine prescription were independent predictors of shorter time to LLDAS.

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Table 1 Baseline variables associated with LLDAS achievement based on multivariable Cox models

Characteristics	Model 1		Model 2		Model 3	
	HR (95% CI)	*p* value	HR (95% CI)	*p* value	HR (95% CI)	*p* value
Age at disease onset, years	1.010 (1.003-1.016)	0.005	1.009 (1.002-1.016)	0.010	1.010 (1.003-1.017)	0.004
Treatment-naïve	1.346 (1.105-1.641)	0.003	1.425 (1.161-1.749)	0.001	1.484 (1.204-1.830)	<0.001
Nephritis	0.776 (0.641-0.939)	0.009	1.066 (0.820-1.385)	0.634	0.925 (0.737-1.160)	0.498
SLEDAI			0.968 (0.950-0.987)	0.001		
PGA					0.685 (0.551-0.853)	0.001
Daily prednisone (or equivalent) dose, mg/d			1.003 (0.998-1.007)	0.266	1.005 (0.999-1.010)	0.093
HCQ	1.638 (1.263-2.123)	<0.001	1.713 (1.318-2.225)	<0.001	1.664 (1.284-2.157)	<0.001

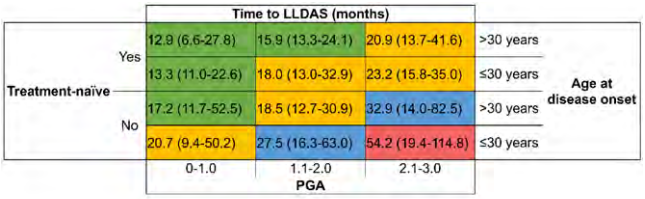


Figure 1 Matrix model for time to LLDAS.

Disclosure of Interests: None declared

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THU0248 GLOMERULAR AND TUBULOINTERSTITIAL LESIONS IN PER-PROTOCOL REPEAT BUT NOT BASELINE KIDNEY BIOPSY PORTEND RELAPSE AND LONG-TERM RENAL FUNCTION IMPAIRMENT, RESPECTIVELY, IN INCIDENT CASES OF PROLIFERATIVE LUPUS NEPHRITIS

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Background: In patients with lupus nephritis (LN), clinical response to treatment and renal histopathology have been shown to be discordant. No clinical or laboratory markers have to date been shown to reliably portend renal prognosis, in particular renal function impairment.

Objectives: To investigate whether per-protocol repeat renal biopsies are predictive of LN relapses and long-term impairment of renal function.

Methods: Forty-two patients with an incident biopsy-proven active proliferative (class III/IV ± V) LN from the LN database of the Université catholique de Louvain were included in the present retrospective study. Per-protocol repeat kidney biopsies were performed in all patients after a median time of 24.3 (IQR: 21.3–26.2) months. The NIH activity index (AI) and chronicity index (CI) scores were assessed in both baseline and repeat biopsies. We defined acute glomerular lesions as cellular proliferation, fibrinoid necrosis or karyorrhexis, cellular crescents, hyaline thrombi or wire loops, and leucocyte infiltration, and chronic glomerular lesions as glomerular sclerosis and fibrous crescents, in alignment with the NIH activity and chronicity indices. Similarly, we defined acute tubulointerstitial lesions as mononuclear cell infiltration and chronic tubulointerstitial lesions as interstitial fibrosis and tubular atrophy.

Results: Despite a moderate correlation between urinary protein/creatinine (U-P/C) ratios and AI scores at repeat biopsy (r=0.48; P=0.001), ten patients (23.8%) with U-P/C ratios <1.0 g/g still had a high degree of histological activity (AI score >3). High AI scores in repeat (but not baseline) kidney biopsies were associated with an increased probability and/or shorter time to renal relapse (N=11) following the repeat biopsy (HR: 1.2; 95% CI: 1.1–1.3; P=0.007), independently of proteinuria levels. This association remained significant for the NIH activity index items within the glomerular but not the tubulointerstitial compartment of the kidney biopsies. High NIH CI scores in repeat (but not baseline) kidney biopsies were associated with a sustained increase in serum creatinine levels corresponding to ≥120% of the baseline value (HR: 1.8; 95% CI: 1.1–2.9; P=0.016) through a median follow-up time of 131.5 (IQR: 73.8–178.2) months, being the case also for acute and chronic tubulointerstitial lesions in repeat but not baseline kidney biopsies.

Conclusion: Our results highlight the usefulness of per-protocol repeat biopsies as an integral part of the treatment evaluation, also in patients who have shown adequate clinical response. Glomerular lesions consistent with active renal disease portend LN relapses, while tubulointerstitial lesions consistent with active disease and chronic damage portent long-term renal function impairment.

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THU0249 CLINICAL FEATURES AND RENAL PROGNOSIS IN LUPUS NEPHRITIS PATIENTS UNDERGOING A REPEATED BIOPSY: RESULTS OF 103 RE-BIOPSIES IN 438 PATIENTS

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Background: Indications to repeat renal biopsy (RB) in lupus nephritis (LN) are not unanimously acknowledged.

Objectives: To evaluate the renal outcome of patients with LN undergoing a second RB.

Methods: We retrospectively analyzed prospectively collected data of patients with LN followed up in four Italian referral centres for systemic lupus eryhtematosus. Serological and clinical information were retrieved according to a shared database. RB were classified according to ISN/RPS 2003 classification; chronicity (CI) and activity indexes (AI) were defined according to Austin et al. The primary renal outcome was renal failure, defined as serum creatinine (SCr)>1.0mg/dL with eGFR<60ml/min. Non-parametric tests were used for statistics. Patients repeating RB due to renal remission were excluded from the analysis.

Results: Four-hundred and thirty-eight patients were recruited. One-hundred and three patients repeated RB after 6.1±4.7 (mean± SD) years from the first due to: protocol biopsy due to renal remission (Group 1, n=8); proteinuric flare (Group 2, n=51); worsened renal function (Group 3, n=26); partial renal response (Group 4 n=18). Patients undergoing a second RB were younger (p<0.001), had lower serum C3 at LN diagnosis (p<0.001) and displayed more frequently class IV and higher AI at first RB (p=0.0038 and p=0.043, respectively). At the end of follow-up, patients who repeated RB had more frequently renal failure (p=0.003). At the second RB, the histological class was unchanged in 55% of patients. CI increased at second RB compared to the first (3.6±2.4 vs.1.7±1.7; p<0.001). Overall, 26 out of 103 patients (25%) developed renal failure: 0 from group 1, 10 from group 2, 14 from group 3, 2 from group 4 (p<0.001). Uncontrolled hypertension at LN diagnosis, increased SCr and increased proteinuria at second RB predicted renal failure (Table).

Conclusion: Patients undergoing a repeated RB had more aggressive clinical and histological features already at first RB and developed renal failure more frequently. Among baseline features, uncontrolled hypertension had the strongest association with renal failure, thus suggesting that control of blood pressure since early stages is highly advisable.

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Table . Comparison of patients undergoing 2nd RB according to development of renal failure

	Renal failure (n=26)	No renal failure (n=69)*	p
Total FU (years), mean (SD)	21 (10.4)	16.5 (9.39)	0.002
SCr (mg/dl) at 2° RB, mean (SD)	1.7 (1)	0.98 (0.35)	0.001
Proteinuria (g/24h) at 2° RB, mean (SD)	4.7 (3.9)	2.99 (2.63)	0.022
Class IV and IV+V at 2° RB, %	76.9	54.5	0.07
Hypertension at onset, %	84.6	32.4	<0.001
HCQ intake at 2° RB, %	9.5	52	<0.001
Glucocorticoids at 2° RB %	84	87	ns
Immunosuppressants at 2° RB %	40	58	ns
AI at onset, mean (SD)	7.14 (3.95)	7.02 (3.86)	ns
AI at 2° RB, mean (SD)	5.37 (4.12)	4.02 (3.71)	ns
CI at onset, mean (SD)	2.05 (1.88)	1.56 (1.64)	ns
CI at 2° RB, mean (SD)	3.87 (3.08)	3.52 (2.16)	ns
Years between 2° RB and end of FU, mean (SD)	14.1 (10.5)	9.3 (8.84)	ns

*Group 1 excluded

RB, renal biopsy; AI, activity index; CI, chronicity index; SCr serum creatinine; FU, follow-up; SD, standard deviation.

Disclosure of Interests: Mariele Gatto Speakers bureau: GSK, Francesca Saccon: None declared, Francesca Radice: None declared, Paolo Gilles Vercelloni: None declared, Renato Alberto Sinico: None declared, Giulia Frontini: None declared, Valentina Binda: None declared, Piergiorgio Messa: None declared, Federico Alberici: None declared, Gabriella Moroni: None declared, Andrea Doria Consultant of: GSK, Pfizer, Abbvie, Novartis, Ely Lilly, Speakers bureau: UCB pharma, GSK, Pfizer, Janssen, Abbvie, Novartis, Ely Lilly, BMS

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THU0250 URINE AND SERUM S100 PROTEINS ASSOCIATE WITH LUPUS NEPHRITIS AND RESPONSE TO TREATMENT

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Background: Systemic lupus erythematosus (SLE) is a systemic autoimmune/inflammatory disease. Approximately 30% of SLE patients develop lupus nephritis (LN) that affects treatment and prognosis. Easily accessible biomarkers do not exist to reliably predict renal disease[1]. Recently, calcium-binding S100 proteins have been suggested as biomarkers in systemic inflammatory conditions, including SLE[2,3].

Objectives: The MASTERPLANS Consortium aims to identify indicators of treatment responses in SLE. This study tested the applicability of S100 proteins in serum and urine as biomarkers for disease activity and response to treatment with rituximab in LN.

Methods: S100A8/A9 and S100A12 proteins were quantified in the serum and urine of 243 SLE patients from the BILAG-BR study and 48 matched controls using MSD technology to determine whether they perform as biomarkers for active LN (n=85 SLE patients) and/or may be used to predict response to treatment with rituximab. Renal disease activity and response to treatment was based on BILAG-BR scores and changes in response to treatment[4,5].

Results: Serum S100A12 (p<0.001), and serum and urine S100A8/A9 (p<0.001) are elevated in SLE patients. While serum and urine S100 levels do not correlate with global SLE disease activity (SLEDAI), levels in urine and urine/serum ratios are elevated in SLE patients with active LN (S100A8/A9: urine p>0.005, urine/serum p<0.05; S100A12: urine p<0.05, serum/urine p<0.005). S100 proteins perform better as biomarkers for active LN involvement in SLE patients positive for anti-dsDNA antibodies. Lastly, binary logistic regression and AUC analysis suggests the combination of serum S100A8/A9 and S100A12 to predict response to RTX treatment in LN after 6 months.

Conclusion: Findings from this study show promise for clinical application of S100 proteins to predict active renal disease in SLE and response to treatment with rituximab. Significantly overlapping values between groups currently prohibit the definition of cut-off values and prospective studies are required to validate findings.

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Acknowledgments: Clinical information and serum/urine samples from SLE patients were provided by BILAG-BR centres.

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THU0251 IMMUNOPHENOTYPIC CLUSTERS OF SLE PATIENTS REVEAL SUBGROUPS WITH SEVERE DISEASE RESISTANT TO CONVENTIONAL THERAPY

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Background: Biomarkers to predict response to rituximab include plasmablasts and, in the current MASTERPLANS consortium, Sm/U1RNP antibodies and high expression of IFN Score B (a subset of interferon-stimulated genes that predict more clinical outcomes than a classic interferon signature). The relationships amongst these biomarkers and their association with response to conventional therapies are less well described.

Objectives: To analyse the inter-relationships amongst immune biomarkers in two independent SLE cohorts in association with disease activity and stage of therapeutic pathway.

Methods: CONVAS is a cohort of unselected SLE patients; data available include current and historic disease activity, use of biologic therapy, flow cytometry, gene expression (IFN Score A and IFN Score B), and immunoprecipitation for autoantibodies (n=91). BILAG-BR is a British registry study for SLE patients commencing biologics; data available include current and historic disease activity, gene expression (IFN Score A and IFN Score B) and immunoprecipitation for autoantibodies (n=112). In both cohorts, biologics were only prescribed to patients with active disease (BILAG 1 x A or 2 x B) and failure of either cyclophosphamide or mycophenolate. Given the mixture of continuous and categorical variables, data were clustered using Gower distance and Partitioning Around Medioids. K was chosen using silhouette coefficient and clusters visualised with t-Distributed Stochastic Neighbor Embedding (t-SNE).

Results: There were 6 clusters. In rituximab-naïve patients:

1. Sm/U1RNP+, Ro60-, highest IFN Score A, low $CD4^+$ T cells, low NK cells, high plasmablasts
2. Sm/U1RNP-, Ro60+, medium IFN Score A, low $CD4^+$ T cells, high NK cells, high plasmablasts
3. Sm/U1RNP-, Ro60-, lowest IFN Score A, high $CD4^+$ T cells, low NK cells, low plasmablasts

Other antibody subtypes and flow cytometric markers did not improve the accuracy of clustering. In rituximab-treated patients, 3 equivalent clusters for antibody subtypes and IFN Score A were observed but differentiated due to flow cytometry findings, as expected after rituximab treatment. Overall, the patients in the cluster defined by Sm/U1RNP antibodies and high IFN Score A were notable for a higher rate of prior disease activity in the renal, neurological and general BILAG domains (Table 1).

Table 1 : Clinical features in unselected SLE patients (CONVAS)

System affected (ever)	Sm/U1RNP & high IFN Score A (n=27)	Other (n=92)	*p* value
General	14/27 (52%)	24/92 (26%)	0.02
Mucocutaneous	23/27 (85%)	73/92 (79%)	0.50
Neuro	10/27 (37%)	17/92 (19%)	0.04
MSK	25/27 (93%)	83/92 (90%)	0.71
Cardiorespiratory	9/27 (33%)	20/92 (22%)	0.22
Renal	12/27 (44%)	15/92 (16%)	0.005
Haematology	25/27 (93%)	67/92 (73%)	0.03

Analysis of autoantibody status and interferon scores only in BILAG-BR confirmed similar clustering. Across both cohorts, the prevalence of the Sm/U1RNP and high IFN Score A cluster was associated with inadequate response to conventional immunosuppressive treatment (Table 2).

Table 2 : Prevalence according to stage of therapy

Treatment group	Sm/U1RNP & high IFN Score A	Other	*p* value
Antimalarial or conventional IS-treated (CONVAS) (n=90)	16/90 (17.8%)	74/90 (82%)	0.02
Conventional IS inadequate response, Previous rituximab (CONVAS) (n=38)	14/38 (36.8%)	24/38 (63.2%)	
Conventional IS inadequate response, starting rituximab (BILAG-BR) (n=163)	51/163 (31.2%)	112/163 (68.7%)	N/A

Conclusion: A cluster of 23% of unselected SLE patients had more severe immune abnormalities, more severe clinical disease activity and were less likely to be maintained on conventional therapies, with twice as many requiring biologic therapy. Other data in MASTERPLANS have demonstrated that Sm/U1RNP antibodies and IFN Scores predict better response to rituximab. This subgroup of patients may therefore be more appropriate for first-line biologic therapy.

Disclosure of Interests: Antonios Psarras: None declared, Danyang Li: None declared, Adewonuola Alase: None declared, Zoe Wigston: None declared, Ian Bruce Grant/research support from: Genzyme, Sanofi, GSK, UCB, Consultant of: Eli Lilly, AstraZeneca, Iltoo, Merck Serono, Neil McHugh: None declared, Edward Vital Grant/research support from: AstraZeneca, Roche/Genentech, and Sandoz, Consultant of: AstraZeneca, GSK, Roche/Genentech, and Sandoz, Speakers bureau: Becton Dickinson and GSK

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THU0252 CORRELATION BETWEEN DISEASE ACTIVITY AND MENTAL HEALTH IN SLE PATIENTS: A CROSS-SECTION STUDY WITH SELF-ASSESSMENTS BASED ON SMART SYSTEM OF DISEASE MANAGEMENT (SSDM) MOBILE TOOLS

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Background: WHO survey showed that the prevalence of anxiety and depression in Chinese population and Chinese patients with chronic diseases were between 3.1% - 4.2% and 3.1% - 7.3%, respectively. SLEDAI-2K and Hospital Anxiety and Depression Scale (HADS) are commonly used to evaluate SLE patients' disease activity and mental health. All the Assessments were mainly performed by health professionals (HCPs) with paper questionnaire previously. SSDM is a novel smart disease management tool that allows patients to do self-assessments on SLEDAI-2K and HADS by mobile App.

Objectives: To investigate the prevalence of anxiety and depression in Chinese patients with SLE and to analyze the potential association between disease activity of SLE and mental health.

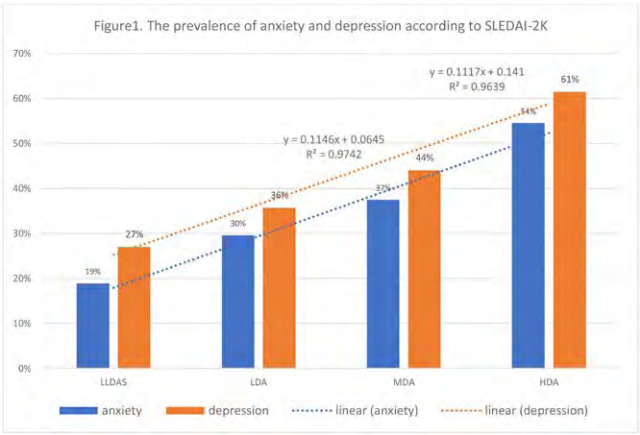
Methods: Under the guidance and training by HCPs, SLE patients downloaded SSDM and performed self-assessments bundle of SLEDAI-2K and HADS with SSDM. SLEDAI-2K <=4, 5-9, 10-14 and >=15 are defined SLE inactive, low (LDA), moderate (MDA) and high (HDA) disease activity, respectively. SLEDAI-2K score <= 4 is set as the main criteria for Lupus Low Disease Activity State (LLDAS) and achievement of T2T. HADS score >=8 can be diagnosed with anxiety or depression.

Results: From June 2016 to Jan 2020, 3,332 SLE patients (199 male, 3,133 female) with a mean age of 36.34 ± 12.80 (10-91) years and the median disease duration of 3.43 years from 216 hospitals performed bundle self-assessments for 4,967 times in total. According to the HADS and SLEDAI-2K Assessment results, the prevalence of anxiety and depression in all patients was 36.7% and 39.3% respectively, which was significantly higher than that in the WHO survey in Chinese population and chronic disease patients. The proportion of patients achieved and failed on LLDAS was 53% and 47%, respectively. The prevalence of anxiety (A) and depression (D) was 19% and 27% among LLDAS achievers; 41% and 47% among LLDAS failures, respectively (pA<0.01, pD<0.01).

According to SLEDAI-2K, in LLDAS, LDA, MDA and HDA subgroups, the prevalence of anxiety and depression was 19%, 30%, 37%, 54% and 27%, 36%, 44%, 61%, respectively. The correlation coefficients of anxiety (A) and depression (D) with SLEDAI-2K were rA=0.9957 and rD=0.9819. It suggested that with the increase of disease activity, the proportion of SLE patients with anxiety and depression increased significantly. (Figure 1)

Conclusion: Conclusion: Higher prevalence of anxiety and depression were Associated with higher levels of disease activity in SLE patients. SSDM is an effective mobile interface to monitor and study entanglement of disease activity and mental health in SLE patients, which build a foundation for proactive interventions physically and mentally in future.

References:



Acknowledgments: SSDM was developed by Shanghai Gothic Internet Technology Co., Ltd.

Disclosure of Interests: None declared

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THU0253 FATIGUE AND PAIN REMAIN PROMINENT AND IMPACTFUL IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): A CROSS-SECTIONAL SURVEY OF SLE PATIENTS IN THE UNITED STATES

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Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune inflammatory condition impacting multiple organ systems.[1,2] SLE affects approximately 1.5 million Americans, disproportionately females of reproductive age, and is more prevalent in non-Caucasian populations.[3] Fatigue and pain are some of the most prominent symptoms of SLE, contributing to the heavy disease burden and disruption to daily life.[4] This study aimed to further understand the burden of SLE. Lilly worked with the Lupus Foundation of America (LFA) and Evidera to develop the SLE-UPDATE (Understanding Preferences, Disease Activity and Treatment Expectations) survey.

Objectives: To understand the patient-perceived symptom burden of SLE, in particular pain and fatigue, within the current landscape of therapeutic options. This study also focused on current treatment patterns in SLE patients.

Methods: This was a cross-sectional, non-interventional, online survey study conducted in partnership with the LFA. English-speaking United States patients aged ≥18 years with a self-reported diagnosis of SLE completed the survey following online screening and informed consent. Descriptive data are presented by means (standard deviation [SD]) for continuous measures, and frequency (n, %) for dichotomous measures. Demographic, clinical, and patient-reported outcomes were collected including the FACIT-Fatigue (range 0-52, higher scores

indicate less fatigue), Pain Numerical Rating Scale (NRS) (0 [none] to 10 [worst imaginable]), Worst Joint Pain NRS (0 [none] to 10 [worst imaginable]), and the LupusPRO, a validated, lupus-specific quality of life (QoL) instrument (range 0-100, higher scores indicate better QoL).

Results: A total of 500 patients with SLE completed the survey. Patients were predominantly female (75%), white/Caucasian (76%), with a mean age of 42.6 years and mean disease duration of 11.1 years.

Most patients with SLE rated their overall condition as either good (38%) or fair (31%), with 8% rating poor and 7% excellent. Current non-biologic prescription medication use included: antimalarials 42%, corticosteroids 33%, immunosuppressants 33%, nonsteroidal anti-inflammatory drugs (NSAID) 32%, other analgesics 15% and 10% were using tofacitinib. Biologic therapies were being used by only 19%, including intravenous (IV) Benlysta (37%), *subcutaneous* (SC) Benlysta (25%), rituximab (17%), and 22% were using other biologics. Fatigue was the most commonly reported symptom (69%), with 40% of patients ranking fatigue as their most bothersome SLE symptom. Forty eight percent of patients with current fatigue rated the severity as moderate and 33% as severe. The mean (SD) FACIT-Fatigue score was 22.9 (12.0). The next most commonly reported symptoms were joint stiffness (57%), sleep problems (55%), joint pain/swelling (53%), and muscle pain (52%). Sixty percent of patients reported experiencing pain all or most of the time over the past seven days. A total of 30% of patients with current joint pain/swelling rated it as severe, and 24% of patients with current joint stiffness rated it as severe. The mean scores for Worst pain NRS and Worst Joint Pain NRS were both 5.8 out of 10.

The LupusPRO domains indicated by respondents as the most impacted by SLE were Emotional Health, Pain/Vitality, and Lupus Medications.

Conclusion: Fatigue, followed by pain and joint stiffness, were the most common patient-reported symptoms contributing to the overall SLE disease burden. Further research could highlight the efforts required to address the inadequacies in treatment and management of pain and fatigue in this patient population.

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THU0254 ARTICULAR INVOLVEMENT, STEROID TREATMENT AND FIBROMYALGIA ARE THE MAIN DETERMINANTS OF PATIENT-PHYSICIAN DISCORDANCE IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Remission or the lowest possible disease activity are the main targets in the management of Systemic Lupus Erythematosus (SLE). Anyway, conflicting data are present in the literature regarding the correlation between physician-driven definitions and patient perception of the disease. The discordance between patient and physician perspectives may have a negative impact on disease outcomes.

Objectives: The aim of this study was to identify the main determinants of patient-physician discordance in the evaluation of SLE and health status.

Methods: This is a cross-sectional study that enrolls patients with a diagnosis of SLE (ACR 1997 criteria). For each patient, demographics, comorbidities, treatment, clinical and laboratory data were collected. Disease activity was evaluated with the SELENA-SLEDAI score and organ damage with the SLICC/DI. Patients included have been categorized according to the following categories: remission, on or off treatment[1], low disease activity (LLDAS)[2] and active disease status. At enrollment, each patient completed the following PROs: SF-36, FACIT-Fatigue, LIT and SLAQ. We defined a SLAQ score<6, corresponding to the 25° percentile of our cohort, as the cut-off value to define a low disease activity state according to the patient self-evaluation.

Results: We enrolled 259 consecutive adult SLE patients (93.05% female, 97.2% Caucasian, mean age 45.33±13.14 years, median disease duration 14 years (IQR 6-21)). 208/259 patients satisfied the definition of LLDAS and among them 171 were in remission; 51/259 patients were active. No significant differences emerged as for the results of PROs between groups. Considering the subgroup of 208 patients in LLDAS, we identified 56 patients with a subjective condition of low disease activity (SLAQ<6) and we defined them as "concordant"; the remaining 152 patients in LLDAS presented a subjective active disease (SLAQ≥6) and we defined them as "discordant". Comparing these two groups, we found that "discordant" patients had more frequently ongoing and past joint involvement (p<0.05) and a concomitant diagnosis of fibromyalgia (p<0.01); finally, they were more frequently on glucocorticoid therapy (p<0.01). "Discordant" patients showed a significantly worse quality of life, evaluated by all PROs (p<0.0001) (Tab 1).

Table 1. Determinants of patient-physician discordance

	Discordant patients (152/208)	Concordant patients (56/208)	p-value
Age at enrollment (years)	47.7±13.1	44.3±10.8	**ns**
Disease duration (years)	15.5±10.2	13.8±9.2	**ns**
SLICC-DI	1.3±1.7	0.9±1.7	**ns**
Ongoing joint involvement (% of patients)	10.5%	0	**p<0.05**
Past joint involvement (% of patients)	70.9%	55.3%	**p<0.05**
GC therapy (% of patients)	50%	28.6%	**p<0.01**
GC daily dose (mg of prednisone)	1.6±1.9	1.1±1.9	**p=0.06**
Fibromyalgia (% of patients)	15.8%	1.8%	**p<0.01**
PCS	54.7±14.1	65.8±20.4	**p<0.0001**
MCS	54±14.5	64.3±17.7	**p<0.0001**
LIT	28.4±20.4	14±16.8	**p<0.0001**
FACIT	35.3±10.1	47.3±3.6	**p<0.0001**

Conclusion: Articular involvement, fibromyalgia and ongoing glucocorticoid treatment, even at low dose, are the major determinants of patient-physician discordance in SLE, determining a negative patient perception of health status.

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THU0255 AUTOANTIBODY PROFILE AND ETHNICITY: RISK FACTORS FOR ACCELERATED DEVELOPMENT OF LUPUS NEPHRITIS

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Background: Systemic Lupus Erythematosus (SLE) is a multisystem autoimmune disease. African ancestry is associated with an increased risk of Lupus Nephritis (LN). Anti-DNA autoantibodies play a major role in the development of LN and anti-Ro antibodies have also been implicated. McCarty et al suggested that women of African ancestry with the unusual autoantibody combination of anti-Sm, Ro & RNP antibodies (AB) were at increased risk of developing LN (1).

Objectives: Our aim was to determine the correlation between autoantibody profile: Sm, Ro and RNP as a combination in the development of LN in patients with African ancestry. We investigated time to the development of LN from SLE onset.

Methods: A retrospective case-control study was conducted at Guys and St Thomas NHS Trust, London, United Kingdom.

75 patients with confirmed LN meeting the ACR classification criteria for SLE and Nephritis, were included: African (n=35), Caucasian (n=22) and Asian (n=17) ancestry. LN patients with the combination of Sm, Ro and RNP antibodies (Group 1) were compared to LN patients without this autoantibody combination (Group 2). Demographic data, pathology results and laboratory findings were collected. Anonymised data was analyzed using Statistical Package for Social Sciences (SPSS). Left censorship bias was reduced by use of a database of confirmed LN in our cohort of patients. Research and Development Office approval was obtained for this study.

Results: There were 66 (88%) females and 9 (12%) males. The median age in Group 1 was 39 years (range 18-60), while in group 2 the median age was 45 years (range 24-64).

We stratified our population based on their antibody status: Of the 75 (100%) patients, 32 (42.6%) patients had the combination of Sm, Ro & RNP antibodies (Group 1) while the remaining 43 (57.4%) patients did not (Group 2).

In Group 1, regardless of ethnicity, 29 (90.6%) patients developed LN within 5 years or less from the onset of SLE symptoms, while the remaining 3 (9.4%) developed LN after 5 years. In contrast, in Group 2, 24 (55.8%) patients developed LN within 5 years or less while 19 (44.2%) developed LN after 5 years. (P value = 0.002)

Further stratification was based on ethnicity and antibody (AB) status to investigate the time to develop LN from SLE symptom onset: African ancestry with positive AB, African with negative AB, Asian with positive AB, Caucasian with positive AB and Asian & Caucasian with negative Ab. Analysis showed that of 29 (38.7%) African ethnicity patients with the autoantibody combination, 19 (65.5%), developed LN within 5 years. In comparison, 46 (61.3%) patients, independent of ethnicity and AB status, developed LN after 5 years (P value = 0.01).

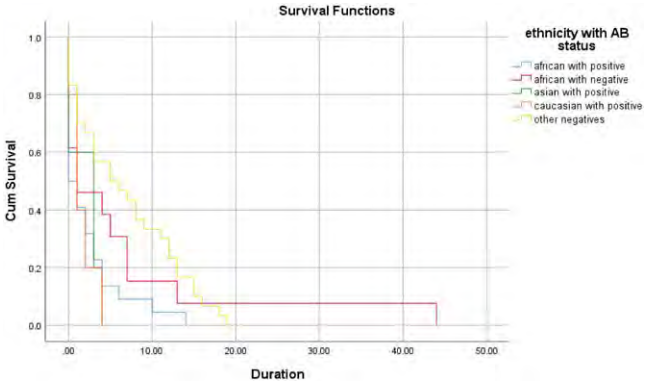
Conclusion: Patients with the unusual autoantibody combination of Sm, Ro & RNP developed LN significantly earlier than patients who did not have this combination. This autoantibody combination was significantly over represented in the African ancestry patients. Our data suggests that African ancestry patients with this autoantibody combination are at increased risk of developing LN soon after SLE symptom onset and merit close monitoring for the development of renal disease.

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Table 1.1 Ethnicity with Autoantibody status showing the rate of progression into Lupus Nephritis.

		Duration of LN onset		Total
		Less than 5 years after SLE onset	More than 5 years after SLE onset	
Ethnicity with AB status	African with positive	19	3	22
	African with negative	9	4	13
	Asian with positive	5	0	5
	Caucasian with positive	5	0	5
	Other negatives	15	15	30
Total		53	22	75



Graph 1. Ethnicity with Autoantibody status showing the rate of progression into Lupus Nephritis (P value= 0.01)

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THU0256 CARDIAC INVOLVEMENT IN NEWLY DIAGNOSED SPANISH PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: DATA FROM THE RELES COHORT

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Background: Cardiac involvement is one of the most important causes of disability and mortality in patients with systemic lupus erythematosus (SLE). Transthoracic echocardiography (TTE) is a sensitive and specific technique in detecting cardiac abnormalities, particularly mild pericarditis, valvular lesions and myocardial dysfunction in SLE.

Objectives: Using data of patients from the inception cohort Registro Español de Lupus Eritematoso Sistémico (RELES), we aimed to analyse the echocardiographic features of cardiac involvement of systemic lupus erythematosus (SLE).

Methods: Prospective observational study on a multicenter Spanish inception cohort. Patients with SLE, diagnosed by the American College of Rheumatology (ACR) criteria, since January 2009, who had at least one TTE performed were selected. Demographic data, diagnostic criteria, follow-ups, treatments and SLEDAI were analyzed.

Results: We included 289 patients diagnosed with SLE with TTE performed. The mean age was 40.5 ± 1.9 years, of which 86.9% (251) were women and 82.4% (238) Caucasian. The ACR score at diagnosis was 4.98 ± 0.1. Most frequent SLE manifestations were arthritis (59.2%), photosensitivity (49.5%), malar rash (39.1%) and serositis (31.1%). The main immunological findings were: ANA (97.6%), anti-DNA (66.4%), hypocomplementemia (58.7%), antiphospholipid antibodies (31.5%). One third (31.5%) of the TTE performed were pathological. Of these, 13.8% had pericardial effusion, 13.3% valvulopathy, 6.5% myocardial dysfunction, 5.2% pulmonary hypertension and 3.2% myocardiopathy. Regarding valvulopathies, 9,5% presented valvular dysfunction, 3.2% valvular thickening and 0.6% vegetation. The most frequently injured valve was the mitral (9.1%), followed by the aortic (2.8%). The majority of patients (88.26%) were asymptomatic at the time of TTE. However, patients with pathological TTE had more dyspnea than those in the normal TTE group (24.7% vs. 5.8%, p<0.001). Presenting a pathological TTE was associated with higher SLICC score (p<0.001), greater number of admissions (p<0.001) and mortality (p=0.002). A higher SLEDAI was also associated with higher mortality (p<0.001).

Conclusion: Cardiac involvement in SLE is not only related to damage accrual but can also be an early manifestation (beyond pericarditis), especially in active SLE. TTE assessment should be considered as a part of routine examination for SLE due to the high prevalence of heart disease even in asymptomatic patients.

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THU0257 ESTIMATED 10-YEARS CARDIOVASCULAR RISK IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: PRELIMINARY RESULTS FROM THE "CARDIOVASCULAR OBESITY AND RHEUMATIC DISEASE (CORDIS)" STUDY GROUP OF THE ITALIAN SOCIETY OF RHEUMATOLOGY.

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Background: Systemic lupus erythematosus (SLE) patients are at high risk for CV events, and EULAR recommends assessing the 10-year CV-risk using the Systematic Coronary Risk Evaluation (SCORE) [1]. The QRISK3, another score to assess CV-risk in UK population, considers different factors among which also SLE. The Progetto Cuore score (PCS) is validated to estimate CV risk in Italian people and largely replicates the SCORE project [2].
Objectives: This cross-sectional study aimed to estimate CV-risk using SCORE, QRISK3 and, for the first time, PCS in a multicentric cohort of Italian SLE patients.
Methods: During 2019 we evaluated 173 SLE patients (87.7% female; age 40±16 years; disease duration 138±105 months), fulfilling the 1997 ACR classification criteria. Clinical and laboratory data were registered, and individual CV-risk was calculated using suitable algorithms for the SCORE, QRISK3 and PCS. Statistical analysis was performed using Graphpad Instat 8.0 (San Diego, CA-USA).
Results: In 13 (7%) SLE patients a previous CV event was recorded. Hypertension was present in 60 (37.5%) and diabetes in 27 (16.9%) patients. Mean total cholesterol was 184±39 mg/dL, HDLc 58±18 mg/dL, LDLc 124±37 mg/dL, triglycerides 105±63 mg/dL; dyslipidaemia was reported in 58 (36.2%) patients and 29 (18.1%) were on statin. Mean BMI was 24.9±5.3 Kg/sm, 60 (37.5%) and 23 (14.3%) patients were overweight and obese, while 25 (15.6%) patients were smokers. 87 (54.3%) SLE patients had a SLEDAI<4, 91% of patients were taken HCQ and 65% were on prednisone (mean dose 5.4±5.9 mg/day), but only 7.5% took >7.5 mg/day. The CV-risk of SLE patients according to SCORE, QRISK3 and PCS was 1.1±2.1%, 10.5±12.3% and 3.7±5.4%, respectively. Stratifying patients at low, moderate or high CV risk according to the PCS and SCORE a double proportion of patients was at moderate (8% vs 3.9%) or high (1.9% vs 0.9%) CV risk (p=0.03). Finally, CV-risk according to QRISK3 was higher than 20% (high risk) in 32/160 (20%) patients.
Conclusion: This multicentre study demonstrated that the mean estimated CV-risk in SLE patients is globally low using the SCORE, QRISK3 and PCS. The PCS seems to better intercept those patients at moderate/high risk, at least in Italian SLE patients, while QRISK3 predicts the highest CV risk. The lack of disease-specific CV-risk factors (such as autoantibodies profile or organ involvement) probably account for the underestimation of CV risk using the SCORE and PCS.
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[2] ARD 2019;0:1–2. **doi:**10.1136/annrheumdis-2019-215715
Disclosure of Interests: Fabio Cacciapaglia Speakers bureau: BMS; Roche; Pfizer; Abbvie, Andreina Manfredi: None declared, Gianluca Erre: None declared, Elena Bartoloni Bocci: None declared, Garifallia Sakellariou Speakers bureau: Abbvie, Novartis, MSD, Ombretta Viapiana: None declared, Sergio Colella: None declared, Anna Abbruzzese: None declared, Marco Fornaro: None declared, Giacomo Cafaro: None declared, Maria Antonietta Fenu: None declared, Bianca Lucia Palermo: None declared, Martina Dessì: None declared, Adalgisa Palermo: None declared, Alessandro Giollo: None declared, Elisa Gremese Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Merck Sharp & Dohme, Novartis, Sanofi, UCB, Roche, Pfizer, Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Merck Sharp & Dohme, Novartis, Sanofi, UCB, Roche, Pfizer, Francesca Romana Spinelli Grant/research support from: Pfizer, Speakers bureau: Lilly, BMS, Celgene, Fabiola Atzeni: None declared, Matteo Piga: None declared
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THU0258 SJOGREN'S SYNDROME WITH AND WITHOUT AND AUTOIMMUNE THYROIDITIS: IS THERE ANY DIFFERENCE?

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Background: Sjögren's syndrome (SS) is a systemic autoimmune disease mainly affecting exocrine glands and characterized by a progressive lymphocytic infiltration of salivary and lacrimal glands with consequent loss of function and development of sicca symptoms. Autoimmune thyroiditis (AT) is the most frequent autoimmune disease associated with SS and detectable in about 10 - 30% of cases[1]. Interestingly, patients with concomitant SS and AT seem to display a more attenuated phenotype compared to patients with solely SS. It is also noteworthy that up to 30% of patients with AT experience sicca symptoms without a clear diagnosis SS[2]. At the light of these evidences, it is unclear whether SS and AT represent two distinct nosological entities or different expressions of the same pathology.
Objectives: Aim of this study is to evaluate the prevalence of AT in a large monocentric cohort of patients with SS and to define its clinical and laboratory characteristics compared to isolated SS.
Methods: Consecutive patients with SS (AECG criteria) referring to our "Sjögren Clinic" (Sapienza University of Rome) were enrolled and divided in two groups: SS with AT (group 1) and SS without AT (group 2). Group 1 was further divided in two subgroups depending on the presence (1a) or absence (1b) of anti Ro/SSA antibodies. The following clinical and laboratory data were retrospectively collected for all patients: concomitant celiac disease, arthralgia, lung involvement, purpura, lymphoma, presence of ANA, anti-Ro/SSA, anti-La/SSB, rheumatoid factor, cryoglobulins, leukopenia and hypergammaglobulinaemia. These characteristics were compared between the following groups: group 1, group 2, group 1a and 1b. For statistic Chi Square and Fisher's test analysis were performed.
Results: Six-hundred and three SS patients were enrolled (group 1 n=135; group 2 n=381; group 1a n=96; group 1b n=39). The prevalence of AT was 135/603 (22.3%). When comparing SS patients with or without AT (group 1 vs group 2) the frequency of rheumatoid factor was significantly higher in group 2 compared to group 1 (p=0.006). No case of lymphoma was recorded in group 1 while 14 cases of lymphoma were ascertained in group 2 (p=0,08). Conversely, celiac disease was higher in group 1 compared to group 2 (p=0.01). No other differences between these groups were identified. Stratifying SS patients with AT according to the presence (group 1a) or not (group 1b) of anti Ro/SSA antibodies, ANA, rheumatoid factor and hypergammaglobulinemia were significantly more positive in group 1a compared to group 1b (p=0.0002, p=0.002, p=0.02, respectively); no clinical differences were identified.
Conclusion: In this study, we confirm the presence of a less aggressive disease in patients with SS and AT compared to solely SS. The higher prevalence of rheumatoid factor and lymphoma occurrence in SS without AT, strictly suggest a more severe phenotype in this subset. Although is known that in SS patients with anti Ro/SSA+ antibodies and RF there is a more aggressive disease, in SS with AT the presence or absence of such autoantibodies do not seems to associate with any difference in clinical severity. Follow up studies are presently being carried out in order to provide conformation of a less sever phenotype and a better disease outcome in patients with associated SS and AT.
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THU0259 LYMPHOMAS IN ANTICENTROMERE ANTIBODY POSITIVE PRIMARY SJOGREN'S SYNDROME

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Background: Patients with primary Sjogren's syndrome (pSS) are at high risk of lymphoma. Signs of lymphomas in ACA+pSS were not widely reported, the descriptions were single [1, 2]. According to pSS treatment recommendations [3, 4, 5, 6], glandular forms require only symptomatic treatment, in the absence of systemic manifestations systemic therapy is not required.
Objectives: to evaluate the incidence of lymphomas in ACA+pSS; to compare clinical and laboratory manifestations in 2 groups of ACA+pSS: with and without lymphomas.
Methods: we examined 119 ACA+pSS patients. We evaluated both glandular and systemic manifestations. We diagnosed lymphomas based on study of biopsy specimens of affected organs.
Results: MALT-lymphomas diagnosed in 19 (16%) ACA+pSS patients. Persistent enlargement of parotid salivary glands, decreased C4-complement, decreased CD19+cells in peripheral blood, cryoglobulinemic vasculitis, lymphoid infiltration of minor salivary glands (MSG) more than 200 cells in focus, severe xerostomia and xerophthalmia more often detected in patients with ACA+pSS+lymphomas. RF and antiRo were found in only 25% of patients with lymphomas and its

frequency did not differ between groups. Only 20% of patients with lymphoma had monoclonal immunoglobulins secretion and its frequency also did not differ between groups. Anemia, leukopenia, thrombocytopenia, increased ESR, hypergammaglobulinemia, increased levels of immunoglobulins were found in the study groups with the same frequency. There were no differences in the frequency of detection of recurrent parotitis, lymphadenopathy, Raynaud phenomenon, arthritis/arthralgia, pleuritis/pericarditis, neuropathy, nephritis, hypergammaglobulinemic purpura.

Conclusion: in the present study in patients with lymphomas, the course of pSS was characterized by minimal systemic manifestations and low immunological activity, but severe glandular manifestations with the development of late stage damages of salivary and lacrimal glands, severe lymphoid infiltration of MSG, which led to the frequent occurrence of MALT-lymphomas. Thus, in patients with pSS, regardless of the type of detected antibodies (antiRo/La, ACA, RF or others), regardless of the presence or absence of systemic manifestations, damage of salivary and lacrimal gland progresses, which in some cases leads to the development of lymphomas, therefore, therapy that can prevent this complication should be initiated immediately after diagnosis of pSS is confirmed. The signs of lymphoproliferation detected in the present study should be evaluated in all ACA+pSS patients for early diagnosis of lymphoma.

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THU0260 GLUCOCORTICOID DOSE IS AN INDEPENDENT PREDICTOR OF MORTALITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS HOSPITALIZED FOR INFECTION

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Background: Infection is an important cause of mortality and morbidity in patients with systemic lupus erythematosus (SLE) and a common cause for hospitalization. Glucocorticoids (GC) may contribute to increased mortality.

Objectives: We performed a 10-year retrospective study of SLE patients hospitalized for infection, and the clinical predictors of mortality, especially GC dose, in these patients.

Methods: Diagnosis codes for SLE were obtained from the electronic medical records for hospitalized patients from 2005 to 2015. Chart review was performed to ascertain the indication for hospitalization. The first hospitalization for infection (if any) was used as the index admission. Demographic and clinical characteristics, infection site and immunosuppressive drugs over the past month were abstracted. Multivariable logistic regression was used to determine predictors of all-cause mortality at 1 year.

Results: Diagnosis codes were obtained for 768 unique SLE patients with 3660 hospitalization episodes over 10 years, of which 689 had a physician diagnosis of SLE on chart review. Of these, 250 (36%) had an index admission for infection. 243/250 (97.2%) fulfilled the ACR 1997 criteria for SLE and were studied further (Figure 1). Median (IQR) age was 45.1 (37.3, 56) years, 86% were female, 72% were Chinese, median (IQR) disease duration was 9 (4, 17) years. 53 (21.8%) patients had chronic kidney disease (CKD), 34 (14%) had diabetes mellitus (DM) and 12 (4.9%) had cancer. 231 (95.1%) patients were on immunosuppressive drugs and 210 (86.4%) were on GC. The median (IQR) GC dose was 8 (5, 15) mg oral prednisolone equivalent per day. The median (IQR) Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) score was 4 (1, 10). The most common organism was Escherichia coli, followed by Staphylococcus aureus and Salmonella enteritidis. The respiratory tract was the most common site of infection. 27.9% of patients who had blood cultures performed had bacteremia. There were 11 (4.5%) ICU admissions, 6 (2.5%) patients died in hospital and 1-year all-cause mortality was 13 (5.3%). SLEDAI had only a weak positive correlation with GC dose [R^2 = 0.039/Pearson's correlation = 0.197, p = 0.004)] (Figure 2). Increased age (odds ratio (OR) 1.07, 95% CI 1.02-1.12, p = 0.005), average daily GC dose (OR 1.05, 95% CI 1.02-1.09, p = 0.002), bone infections (OR 42.24, 95% CI 2.76-646.8, p = 0.007) and CKD (OR 4.78, 95% CI 1.06-21.54, p = 0.04) were independent predictors of 1-year mortality, after adjusting for gender, SLEDAI, DM, and cancer (Table 1).

Table 1. Predictors of mortality

Factors	Univariable Odds Ratio (95% CI)	P-value	Multivariable Odds Ratio (95% CI)	P-value
Age at admission (years)	1.04 (1.005, 1.07)	0.02	**1.07 (1.02,1.12)**	**0.005**
Average dose of oral prednisolone (mg/day)	1.04 (1.01, 1.06)	0.006	**1.05 (1.02,1.09)**	**0.002**
Gender (female vs male)	3.52 (1.22, 10.12)	0.02	0.37 (0.07, 2.10)	0.26
Disease duration > 10 years	1.27 (0.49, 3.33)	0.62		
Positive blood culture	0.54 (0.17, 1.75)	0.30		
Site of infection	1 (reference)	0.17		0.06
Gastrointestinal				
Respiratory	1.09 (0.28, 4.29)	0.90	0.71 (0.09, 5.57)	0.74
Renal	0.27 (0.03, 2.48)	0.25	0.44 (0.03, 5.94)	0.54
Skin, Gynecological, Other	0.94 (0.25, 3.51)	0.93	1.04 (0.16, 6.74)	0.96
Bone	11.75 (1.29, 107.1)	0.03	**42.24 (2.76, 646.8)**	**0.007**
Primary Bacteremia	0.00 (0.00, 0.00)	0.99	0.00 (0.00, 0.00)	0.99
SLEDAI score ≥4	1.23 (0.47, 3.21)	0.66	0.65 (0.15, 2.74)	0.56
Diabetes Mellitus	0.46 (0.14, 1.50)	0.20	1.61 (0.31, 8.3)	0.57
Chronic Kidney Disease	0.30 (0.11, 0.78)	0.01	**4.78 (1.06, 21.54)**	**0.04**
Cancer	0.18 (0.04, 0.77)	0.02	3.52 (0.25, 48.82)	0.35

Conclusion: Higher dose of oral GC was an independent predictor of mortality, even after adjusting for disease activity. It is important to prescribe the minimum effective dose of GC in SLE patients with infection, especially in older patients with CKD and bone infection.

Figure 1. Selection of cases

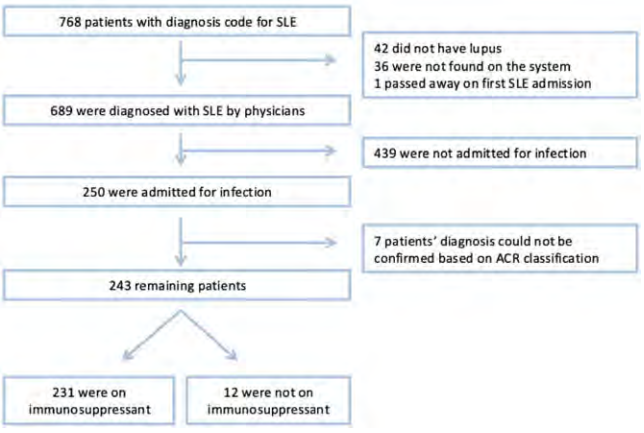
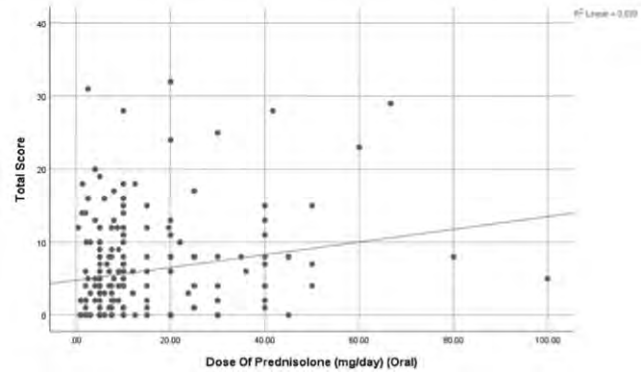


Figure 2. Relationship between SLEDAI score and glucocorticoid dose



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THU0261 NEW 2019 SLE EULAR/ACR CLASSIFICATION CRITERIA ARE VALID FOR IDENTIFYING SLE AMONG PATIENTS ADMITTED FOR PERICARDIAL EFFUSION

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Background: The new 2019 SLE European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) classification criteria for systemic lupus erythematosus (SLE) have been recently published. Seritis is a prominent -often inaugural- feature of active SLE. Low titers of antinuclear antibodies (ANA) have been frequently reported in patients with idiopathic pericarditis. Of note, ANA positivity at a titer ≥1/80 is now mandatory as an entry criterion in the 2019 SLE EULAR/ACR classification criteria.
Objectives: Although classification criteria have theoretically no individual diagnostic purpose, we aimed at testing this new criteria set in unselected patients with pericardial effusion
Methods: In a retrospective study performed in the Department of Internal Medicine, University Paris Diderot, a French competence centre for rare systemic autoimmune diseases (AID), all consecutive adult patients hospitalized from January 2009 to January 2019 for pericardial effusion were reviewed. Clinical and biological data collected at time of the diagnosis of pericardial effusion were analyzed. The characteristics of the patients are listed in Table 1. Three sets of lupus criteria (SLE ACR-1997, SLE SLICC and 2019 SLE EULAR/ACR criteria) were applied in all ANA-positive patients
Results: Over a 10-year period, 137 patients were admitted for pericardial effusion. Search for ANA was systematically performed at diagnosis in all but 8 (n=129) and measured at a titer ≥ 1:80 on Hep-2 cells in 49 patients (38%) that were eventually separated in three groups: 17 (34.7%) patients with a final diagnosis of SLE based on senior clinician judgement, 6 (12.2%) patients with a final diagnosis of autoimmune disease (AID) other than SLE (primary Sjögren's syndrome (n=2), undifferentiated connective-tissue disease (n=2) and systemic sclerosis (n=2)) and 26 (53.1%) patients with a diagnosis of idiopathic pericarditis after exclusion of malignancy, tuberculosis and systemic inflammatory diseases with a median 12.3 [1.6-29.8] months follow-up
The 2019 SLE EULAR/ ACR criteria were met in 100% of patients with SLE, 33.3% of patients with non-SLE AID and 11.5% of patients with idiopathic pericarditis. Thus this new set of criteria for SLE offered a higher sensitivity (100%) but a lower specificity (84.38%) as compared to the former criteria, for the diagnosis of SLE in patients with pericardial effusion. Interestingly, the 2019 SLE EULAR/ACR classification score was higher in SLE patients (median: 30 [11-45]) as compared to non-SLE AID (median: 8 [6-12], p=0.0006) and idiopathic pericarditis patients (median: 6 [5-12], p< 0.00001). Moreover, the 2019 classification set score strongly correlated with the SLEDAI activity score [6] as shown Figure S1 (R^2 =0.8105, p<0.00001). Setting the 2019 SLE EULAR/ACR classification threshold score >12 (out of a theoretical maximum of 51) instead of ≥10 increased the specificity of 2019 SLE EULAR/ ACR criteria from 84.38% to 100%. Overall, in patients with pericardial effusion and positive ANA, the diagnosis of SLE could be ruled out when 2019 SLE EULAR/ACR criteria score was < 10 and confirmed when the score was > 12.
Conclusion: This study shows that the new 2019 SLE EULAR/ACR criteria for SLE are helpful in clinical practice for the diagnosis of SLE in patients admitted for pericardial effusion
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THU0262 LEVELS OF OSTEOCALCIN AND PROCOLLAGEN TYPE I C-TERMINAL PROPEPTIDE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS, THEIR ASSOCIATION WITH BONE MINERAL DENSITY AND LEVEL OF INTERLEUKIN-6

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Background: Osteoporosis and fractures associated with it are considered to be one of the most severe complications of systemic lupus erythematosus (SLE). The role of a systemic inflammatory process, vitamin D deficiency, hypogonadism and peculiarities of disease treatment in reduced bone mineral density (BMD) is being discussed. Even though the frequency of osteoporosis in patients with SLE is being studied extensively by scientists from different countries, data on the peculiarities of bone tissue metabolism and the factors that provoke disorders of bone remodeling in such individuals are quite limited. The association between markers of bone tissue metabolism and BMD, and how they change during an inflammatory process is poorly studied.
Objectives: The objective of our research is to study the levels of osteocalcin (OC) and procollagen type I C-terminal propeptide (PICP) in patients with systemic lupus erythematosus and to estimate their association with BMD and inflammatory activity based on the levels of interleukin-6 (IL-6).
Methods: A total of 58 women with SLE (the average age was 45.11 ± 1.03 years old) and 29 individuals from the control group (the average age was 46.79 ± 2.30 years old) were examined. The diagnosis of SLE was established on the basis of 2019 EULAR/ACR classification criteria for SLE. Levels of IL-6, OC and PICP in serum were determined by enzyme immunoassay. Changes in BMD of the lumbar spine at the level of L1-L4 and the proximal femur were determined by dual-energy X-ray absorptiometry. In postmenopausal women, the diagnosis of osteoporosis was established by the T-score ≤ -2.5 SD. Osteopenia met T-score from -1 to -2.5 SD. In women of reproductive age, the Z-score was used to determine BMD. Values of the Z-score ≤ -2.0 SD were considered as "below expected range for age".
Results: The average OC level in serum of practically healthy individuals equaled 17.64 ± 0,59 ng/ml, and in patients with SLE it was 13.96 ± 0.40 ng/ml, i.e. it was 20.9% lower. The average PICP level in the control group equaled 107.8 ± 4.28 ng/ml, in the main group it was 92.9 ± 5.01 ng/ml, i.e. 16% lower. Overall, the decrease in the bone turnover markers (PICP and/or OC) was noticed in 28 patients with SLE (48.3%) and only in 4 practically healthy individuals (13.8%).
In women with decreased bone turnover markers, the T-score of the lumbar spine and hip was 2.3-2.6 times lower ($p < 0.05$) than in the group with adequate levels of bone turnover markers. Z-score was also lower among patients with decreased levels of OC and PICP. In this group, the average BMD level was 0.81 ± 0.05 g/cm^2 and was 13.8% lower than in the group of patients with no signs of bone tissue metabolism disorder – 0.94 ± 0.02 g/cm^2. Among the group of women with signs of suppression of biosynthetic processes in bone tissue, there were twice more individuals with decreased BMD. In patients with critically high levels of IL-6 (above 20.0 ng/L), OC level was lower than in patients with high (12.5-20.0 ng/L) and adequate (< 12.5 ng/L) levels of IL-6 (by 17.3 and 19% respectively). The proportion of individuals with low OC levels increased from 31.2% in the last group to 70.6% among patients with critically high levels of IL-6.
PICP level was also lower (38.1% and 39.7% respectively) in case of critically high IL-6 levels compared to its high and adequate levels. The proportion of individuals with low PICP levels increased from 6.3% in the group with adequate IL-6 level to 58.8% in the group with critically high IL-6 level.
Conclusion: Women with SLE have bone tissue metabolism disorder in the form of decreased bone turnover markers (procollagen type I C-terminal propeptide and osteocalcin) associated with the inflammatory activity. In the group of patients with the signs of suppression of biosynthetic processes in the bone tissue, there were more individuals with decreased BMD.
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THU0263 LUNG INVOLVEMENT IN PRIMARY SJÖGREN SYNDROME – AN UNDER-DIAGNOSED ENTITY

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Background: Interstitial lung disease (ILD) represents a frequent extra-glandular manifestation of primary Sjögren's Syndrome (pSS). Limited published data regarding phenotyping and treatment exists. Advances in managing specific ILD phenotypes have not been comprehensively explored in patients with coexisting pSS.
Objectives: This retrospective study aimed to phenotype lung diseases occurring in a well-described pSS cohort and describe treatment course and outcomes.
Methods: Between April 2018 and September 2019, all pSS patients attending our Outpatient clinic were screened for possible lung involvement. Clinical, laboratory and computer tomography (CT) findings were analysed. Patients were classified according to CT findings into 5 groups: usual interstitial pneumonia

(UIP), non-specific interstitial pneumonia (NSIP), desquamative interstitial pneumonia (DIP), combined pulmonary fibrosis and emphysema (CPFE) and unspecific-ILD.

Results: Lung involvement was confirmed in 24/240 patients (10%). Clinically manifest pSS occurred later in patients with ILD vs. non-ILD (53.2 [42.0-61.7] *vs.* 62.3 [55.6-68.8] years; p=0.0016). The commonest phenotype was UIP n=10 (41%), followed by NSIP n=7 (29%), DIP n=2 (8%), CPFE n=2 (8%) and unspecific-ILD n=3 (13%). Forced vital capacity (FVC) and carbon monoxide diffusion capacity (D_{LCO}) appeared lower in UIP and DIP, without reaching a significant difference. Treatment focused universally on intensified immunosuppression, with 12/24 patients (50%) receiving cyclophosphamide. No anti-fibrotic treatments were used. Follow-up was median 13.2 [7.9-72.3] months, during which 6/24 (25%) patients exhibited a further decline in FVC. No deaths occurred.

Conclusion: Lung involvement in pSS is heterogeneous. Better phenotyping and tailored treatment may improve outcomes and requires further evaluation in larger prospective studies.

Disclosure of Interests: None declared

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THU0264 MYELOID MALIGNANCIES, SYSTEMIC AUTOIMMUNE DISEASES AND CARDIOVASCULAR RISK: AN UNDER-REPORTED ASSOCIATION?

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Background: The association between systemic autoimmune diseases (ADs) and lymphoproliferative malignancies is well established; nonetheless, few studies have investigated the prevalence and prognostic impact of myeloid malignancies on systemic autoimmune conditions.

Objectives: To investigate the frequency of myeloid malignancies (i.e myelodysplastic syndrome (MDS) and chronic, either Philadelphia-positive or Philadelphia-negative, myeloproliferative disorders (MPNs)) in patients with ADs and their influence on the ADs clinical course and vice-versa.

Methods: A retrospective systematic search through the electronic health records of the patients admitted at our Rheumatology University Hospital from 2009 and 2019 was performed to select those presenting with ADs and MDS or MPNs. To refine the search the ICD-9-CM diagnosis codes for MDS/MPNs were utilized. Medical charts of eligible patients were retrieved and data were collected with regard to demographics, type of AD, AD duration, prior treatments, serum laboratory indices, bone marrow aspiration and biopsy data. Categorical variables were compared using chi square test and Fisher's test; continuous variables were compared using Student's t-test. A 2-tailed value of p <0.05 was taken to indicate statistical significance.

Results: Out of the medical records of 5040 patients, we identified 51 patients (31 F: 20 M, mean age: 61 years (15)) with AD and myeloid malignancies: 17/51 with AD and MDS and 34/51 with AD and MPNs. No demographic differences were observed in the two subgroups. Regarding MDS, anaemia was the most common haematologic presenting finding (15/17, 88%), while the most common diagnosis was refractory anemia with excess of blasts (RAEB I/II) (5/17, 29%) followed by sideroblastic anemia (2/17, 12%). In the MPNs subgroup, 12/34 patients (35%) had a diagnosis of chronic myeloid leukemia (CML), 9/34 (26%) had a myelofibrosis (MF), 7/34 (21%) had an essential thrombocythemia (ET) and 6/34 (18%) had a polycythemia vera (PV). The JAK2 V617F mutation was detected in 100%, 57%, and 66% of PV, ET, and MF patients. Regarding the temporal appearance of myeloid malignancy, MDS occurred concurrently (9/17) or followed (7/17) the diagnosis of ADs in the vast majority of the cases whereas MPNs generally preceded the diagnosis of ADs (19/34). In MDS the most commonly diagnosed ADs were seronegative arthritis (5/17, 29 %), large and small vessel vasculitis (4/17, 23%) and Systemic Lupus Erythematosus (3/17, 17%). In patients with MPNs the diagnosis of rheumatoid arthritis (2/9, 22%), and antiphospholipid syndrome (3/9, 33%) were often associated with MF, whereas anti-Ro52 (TRIM21) positive systemic connective tissue disorders (4/7, 57%) were more frequently detected in ET. Cardiovascular events were observed in 14/51 (27%): 4/17 (23%) in MDS, 3/12 (25%) in CML and 7/22 (32%) in Philadelphia-negative MPNs. The latter seven cardiovascular events were all observed in patients presenting JAK2 V617F mutation (p=0.05).

Conclusion: Our study is limited by its retrospective design. However, our results documented that the frequency of MDS and MPNs in ADs is not negligible and might be considered in the assessment of cardiovascular risk in systemic autoimmunity. Moreover, it has been reported that, under viral infection, TRIM21 is up-regulated by activation of the IFN/JAK/STAT pathway; interestingly, anti-Ro52 (TRIM21) were over-represented in MPN, where the JAK/STAT signal is hyper activated. This could explain also our observation that frequently the onset of ADs follows the diagnosis of MPN.

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THU0265 THYMIC STROMAL LYMPHOPOIETIN (TSLP) AS A BIOMARKER OF PRIMARY SJÖGREN'S SYNDROME (PSS) AND RELATED LYMPHOMA: VALIDATION IN INDEPENDENT COHORTS

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Background: Thymic stromal lymphopoietin (TSLP) has been implicated in primary Sjögren's syndrome (pSS) and related B-cell lymphoproliferation/lymphoma (NHL) by tissue studies on salivary glands (SG) (1). It resulted significantly higher in the serum of pSS patients compared to non-pSS sicca and to healthy subjects, with the highest levels found in NHL.

Objectives: The purpose of this work was to confirm that serum TSLP is elevated in pSS by the study of independent cohorts.

Methods: Serum TSLP levels were measured by ELISA in 91 pSS patients (F=86, 94.5%; mean age 57.2 years, 25-80) from the Udine cohort (cohort 1, UD), Italy. One additional multicentre cohort (cohort 2) from the Italian SS Study Group (GRISS) was studied, including 125 pSS patients from the Universities of Roma (RO), L'Aquila (L'AQ), Pisa (PI) and Perugia (PG). pSS patients with active NHL (n=12 in cohort 1; n=1 in cohort 2) were excluded from comparative analyses to avoid bias. Secondly, additional serum samples from pSS-related NHL in stable and complete remission, from both cohort 1 and 2, were analysed in a separate subgroup (n = 12). Thirdly, a preliminary evaluation of serum TSLP was performed in pSS patients from a different geographical area (University of Athens, Greece; cohort 3).

Results: Cohort 2 included 125 pSS patients (F=114, 91.2%; mean age 58.1 years, 23-84): 124 benign, 1 with NHL. In this cohort, serum TSLP levels were confirmed to be high (mean 30.26 pg/mL, 0.41-95.21) and comparable to cohort 1 (mean 33.81 pg/mL, 0-140.8; p=ns). No difference was found by the separate analysis of pSS from each single Centres (RO n=49, mean 33.21, 1.4-95.21; L'AQ n=34, mean 38.6, 16.31-85.11; PI n=28, mean 20.23, 0.41-56.67; PG n=13, mean 19.39, 1.03-68.38; p=ns), and vs cohort 1 (p=ns). The only patient in cohort 2 with NHL showed serum TSLP of 160.91 pg/mL, comparable to the mean TSLP in the 12 UD pSS-NHL (151.96 pg/mL). Importantly, in pSS-related NHL in stable remission, serum TSLP resulted undetectable (7/13) or detectable at very low levels (6/13) (mean 10.46, 0-38.5), and significantly lower than in benign pSS patients from the two cohorts (n=203, mean 31.48, 0-140.8; p=0.0022). Metachronous samples from one patient, at the stage of NHL activity and then at NHL remission, showed a decrease in TSLP from 128.04 pg/mL to undetectable levels. Finally, TSLP levels were increased also in the Greek cohort (mean 54.9, 26.72-78.95), and significantly higher than the two Italian cohorts (p=0.0085 and p<0.0001, vs cohort 1 and 2, respectively).

Conclusion: Serum TSLP levels are increased in pSS, as herein confirmed in independent cohorts. TSLP might be important in the disease pathophysiology and mirrors the course of pSS-related B-cell lymphoproliferation itself. It may thus represent a novel important biomarker.

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THU0266 RESILIENCE IN WOMEN WITH PRIMARY SJÖGREN'S SYNDROME

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Background: Resilience is the ability to react positively to stressful life events, a multidimensional feature that varies in relation to context, time, age, sex, culture and personal experience, appearing among the most important traits in patients suffering from rheumatic diseases[1]. Several studies focus on patients with RA and SLE and the role of resilience in the respective clinical manifestations, as well as in the development of anxiety and depression[2,3]. Conversely, the data available regarding patients with primary Sjögren's Syndrome (pSS) are limited.
Objectives: To assess, in women with pSS (classified according to the criteria of Vitali et al.[4]), the relationship between resilience and anxiety, depression, health, fatigue, physical activity and quality of life in relation to disease activity and duration and in consideration of demographic, job and cultural characteristics.
Methods: 74 female patients with pSS afferent to the dedicated clinic of the University Hospital Policlinico Umberto I of Rome were recruited. Resilience was assessed by administering the Italian validated version of the Resilience Scale (RS-14)[5] consisting of 14 items, each of which is assigned a score from 1 to 7, with a range from 14 to 98. Higher scores relate to greater resilience. ESSDAI (EULAR Sjögren's syndrome disease activity index), ESSPRI (EULAR Sjogren's Syndrome Patient Reported Index), SSDDI (Sjogren's Syndrome Disease Damage Index) were assessed and EuroQol / GH EQ VAS (visual analogue scale), HADS (Hospital Anxiety and Depression Scale), SF-12 (Short-form 12 health survey), FAS (Fatigue Assesment Scale), IPAQ (International Physical Activity Questionnaire), FACIT-F (Functional Assessment of Chronic Illness Therapy – Fatigue) questionnaires were submitted. Educational qualifications and job were also considered. The statistical analysis was carried out by means of Spearman's correlation.
Results: No relationship was found between resilience, systemic disease activity, disease duration, patient-reported symptoms and damage. Furthermore, no apparent link was found between socio-demographic characteristics, employment and resilience. Conversely, an inverse relationship was found between resilience and mood disorders (p=0.0379), with greater resilience associated with a better perception of quality of life (p=0.0232) and general health (p=0.0002), mainly mental (p=0.0001) than physical (p=0.0035), as well as less fatigue (p=0.0079) and more phyisically active lifestyle (p=0.0012)
Conclusion: For the first time, the role of resilience in women with pSS in relation to their disease and other individual parameters was assessed. The most resilient patients are less depressed and show better perception of their health. Greater resilience tends to correlate with less anxiety, physical and mental fatigue and a more active lyfestile, while there was no relation between resilience value, active disease and socio-demographic features.
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THU0267 SERUM IGG2 LEVELS PREDICT VERY LONG-TERM PROTECTION FOLLOWING PNEUMOCOCCAL VACCINE IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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Background: Systemic lupus erythematosus (SLE) patients are at increased risk for *Streptococcus pneumoniae* infection. Although pneumococcal vaccination is an attractive method to prevent invasive pneumococcal infection, vaccination coverage remains dramatically low in SLE. Moreover, the efficacy of vaccination may be reduced in SLE patients and sequential pneumococcal vaccination using new conjugated pneumococcal vaccines in combination with 23-valent pneumococcal polysaccharide vaccine (PPV23) is now advocated. However, limited study directly addressed the immune efficacy of such prime-and-boost strategy in SLE
Objectives: We aimed to measure the immunological efficacy of the sequential pneumococcal vaccination using PCV13 in combination with PPV23 and identify factors associated with long-term immune protection following vaccination in SLE.
Methods: SLE patients received PCV13 vaccine followed by PPSV23 vaccine 8 weeks later. Immune protection, defined by an antigen-specific IgG concentration ≥ 1.3 µg/mL for at least 70% of 7 pneumococcal serotypes (4, 6B, 9V, 14, 18C, 19F, 23F), was assessed at baseline, 2 months, 12 months, and 36 months, defining very long-term protection.
Results: 21 (40[25-75] years; 85.7% female) SLE patients received the sequential PCV13/PPV23 vaccines. Only 10 (47.6%) showed a sustained immune protection against pneumococcal infection 36 months after PCV13 shot (very long-term protected, VLTP). Eleven patients had no long-term protection (NLTP) with a seroconversion that never (n=6) or only transiently (n=5) occurred. SLE disease features, treatment received and immunological characteristic did not differ between VLTP and NLTP patients except for a lower serum IgG2 levels in NLTP (1.45 [1.30, 1.82] vs 3.30 [2.92, 4.44] g/L, p<0.001). Noteworthy the ROC curve showed that the serum IgG2 level before vaccination (AUC 0.95 [95% CI: 0.84-1]; p=0.004) was predictive for very long-term protection. A baseline serum IgG2 level of 2.125µg/ml or more showed a sensitivity of 100% and a specificity of 90.9% for very long-term protection
Conclusion: The benefit of sequential PCV13/PPV23 vaccination in SLE is limited. Baseline IgG2 serum level before vaccination is strongly indicative of very long term protection following vaccination
Disclosure of Interests: None declared

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THU0268 NEURO-DEVELOPMENTAL OUTCOME IN CHILDREN BORN TO MOTHERS WITH SLE AND APS

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Background: Systemic Lupus erythematosus and antiphospholipid disease are very common autoimmune diseases in women at reproductive age.
Objectives: Evaluate the neuro-developmental outcome in children born to mothers with SLE or APS and to assess and characterize memory impairment in children's born to mother with systemic lupus erythematosus or APS using children's memory scale and the relation between tetrahydrobiopterin concentration range of children with developmental and neurological disorders.
Methods: Women attending rheumatology clinics University of Asyut, SLE patients were eligible if they met the American College of Rheumatology (ACR) criteria for SLE and APL prior to pregnancy, and had at least one live birth following SLE diagnosis. Maternal history Data collected using a structured format that included medical and obstetric history. A detailed history of medication exposures and the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) during pregnancy was obtained. Offspring history Medical and developmental histories of the offspring including antenatal, delivery, prenatal and pediatric histories, as child's cognitive, physical or social maturity compared with established age-appropriate norms. Speech or hearing delays, diagnosis of attention- deficit hyperactivity disorder (ADHD), or any special educational needs (eg, occupational or speech therapy, behavioral counseling) was recorded. Assessment and characterization of memory impairment using children's memory scale by neurologists. Tetrahydrobiopterin was measured by ELISA compared to children born to control healthy subjects of the same age and sex.
Results: Data on 38 mothers and 60 offspring were analysed: ADHD was reported for 15 of 60 (25%) offspring. Recent memory delay was detected in 93% (14/15) Speech delay 40% (6/15). Maternal APS history was significantly associated with increased use special educational need among offsprings, including after adjustment for lupus anticoagulant (LA) positivity (39.4% for delays age >2 years; p<0.05). Anticardiolipin and anti-BETA2GP1 were not detected to be associated with delays. Recent memory delay was associated with increased Tetrahydrobiopterin level (P=0.01).

Conclusion: The prevalence of neurodevelopmental abnormalities in children born to mothers with SLE or APS seems to be higher than normal population and more educational attention is important in these children, and need long-term follow-up.

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THU0269 CLINICAL COMPARISON OF NEW CRITERIA FOR SYSTEMIC LUPUS ERYTHEMATOSUS IN A COLOMBIAN COHORT

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Background: Due to heterogeneity of the disease, there has been several classification criteria for Systemic Lupus Erythematosus (SLE). These have considered the knowledge obtained through the years and have strived for increased sensibility and specificity. Recently, both EULAR and ACR have proposed new criteria for disease classification that mandate a positive ANA result to apply the criteria.

Objectives: To compare the 2019 EULAR/ACR classification criteria (1) with the Systemic Lupus International Collaborating Clinics (SLICC) 2012 classification criteria (2) and the American College of Rheumatology (ACR) 1997 classification criteria in a Colombian cohort (3).

Methods: A cross-section retrospective study was done with data collected between 2014 and 2018 from a population diagnosed with SLE by a group of rheumatology in an autoimmunity referral centre and followed for one year. The new 2019 EULAR/ACR classification criteria were applied to the information collected from the clinical records. Three sets of criteria were compared using Cohen´s kappa coefficient and concordance was evaluated

Results: We obtained information for 480 patients, in this analysis were mostly females (96%). Anti-nuclear antibody (ANA) results were available for 95% of the patients. According to SLICC classification criteria the diagnosis of SLE was definite in 92% of patients, 81% by ACR 1997 and 89% using ACR/EULAR 2019. The sensibility was 93% and 97% for ACR/EULAR 2019 and SLICC 2012, and the specificity was 67% and 48% respectively. The concordance analysis between the two sets of criteria showed agreement of 92% (kappa 0.52 p <0.001) in the whole group.

Conclusion: We found good agreement between SLICC 2012 criteria and EULAR/ACR 2019 classification criteria. In contrast with previous studies, where the new criteria had a sensitivity of 96.1% and specificity of 93.4%, in our cohort the sensitivity was maintained in 93% but the specificity decreased to 67%. A possible explanation could be the ANA negativity that was seen in 5% of the patients and would force to discard patients with false negative results. Despite this, the agreement of the criteria is good and should continue to be applied in our population, without abandoning the expert's clinical criteria.

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THU0270 ONLINE INTERACTION AND FREQUENT SELF-ASSESSMENTS PROMOTED TREAT-TO-TARGET FOR SLE VIA EMPOWERING PATIENTS: A COHORT STUDY FROM CHINA BY SMART SYSTEM OF DISEASE MANAGEMENT (SSDM)

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Background: Treating to target (T2T) is routine in RA, but no comparable standard has been defined for SLE. In 2015, the definition of Lupus Low Disease Activity State (LLDAS) was generated by Asia-Pacific Lupus Collaboration, and the preliminary validation demonstrated its attainment to be associated with improved outcomes in SLE. A SLEDAI-2K score lower than 4 is the main criteria for LLDAS. SSDM is an interactive mobile disease management application, including application systems for both the doctors and patients.

Objectives: To evaluate the patterns of T2T and related influential factors among SLE patients after applying SSDM in real world.

Methods: Patients were trained to master SSDM by healthcare professionals in clinics. The first assessment for SLEDAI-2K was performed as the baseline. Patients were required to perform repeated self-assessments after leaving the clinics. The data is synchronized to the SSDM of authorized rheumatologists. Based on the patients' data, rheumatologists will provide medical advices to the patients.

Results: From July 2015 to Jan 2020, 32,559 SLE patients enrolled in SSDM. The mean age is 36.35 years old and median disease duration is 3.85 years. Among them 1,937 SLE patients from 134 hospitals across China were followed up for more than 12 months, and the demographics were summarized in table 1.

Table 1.

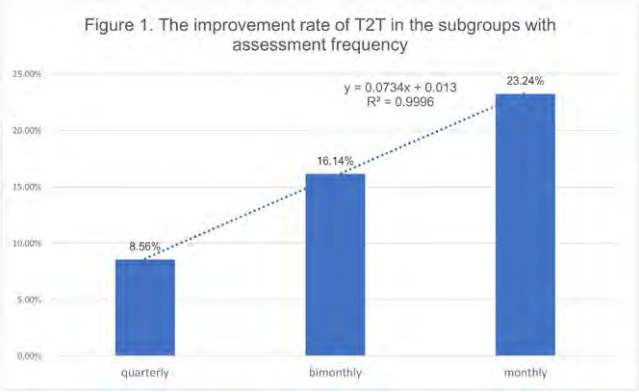
Baseline\Final follow-up	n	%	x <= 4	%	5 <= x <= 9	%	10 <= x <= 14	%	15 <= x	%
x <= 4	1040	53.69%	820	78.85%	135	12.98%	50	4.81%	35	3.37%
5 <= x <= 9	357	18.43%	230	64.43%	60	16.81%	32	8.96%	35	9.80%
10 <= x <= 14	222	11.46%	120	54.05%	38	17.12%	40	18.02%	24	10.81%
15 <= x	318	16.42%	156	49.06%	49	15.41%	47	14.78%	66	20.75%
Total	1937	100%	1326	68.46%	282	14.56%	169	8.72%	160	8.26%

The ratio of T2T achievers was 53.69% (1,040/1,937) at the baseline and improved significantly to 68.46% (1,326/1,937) after a 12-month follow-up, p<0.01. Among T2T achievers at the baseline, 78.85% (820/1,040) maintained T2T, and 21.15% (220/1,040) relapsed. Of patients who didn't achieve T2T at baseline, 56.41% (506/897) of the patients achieve T2T after 12-month follow-up.

The impact of the online interaction and the frequency of self-assessment for SLEDAI-2K on T2T has been analyzed. Compared with 1,475 patients who didn't interact online with their physicians through SSDM, 462 patients with online interaction achieved higher rate of T2T improvement (19.48% vs 13.29%, p<0.05). The more frequent of the self-assessments being performed by patients, the higher improvement of T2T rate will be. The improvement rates of T2T in the subgroups which self-assessed with SSDM by quarterly, bimonthly and monthly were 8.56%, 16.14% and 23.24% respectively. The improvement rate (y) of T2T was positively correlated with the frequency of self-assessment for SLEDAI-2K(x) independently, r = 0.9998. (Figure 1)

Conclusion: After proactive disease management via SSDM for more than 12 months, the rate of T2T in SLE patients increased significantly. Online interaction between patients and physicians contributed in promoting T2T improvement rate. The patients who performed more self-assessments through SSDM had higher probability of T2T achievement. SSDM is a valuable tool for long term SLE follow-up through empowering patients.

References:



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THU0271 PERFORMANCE OF THE EULAR/ACR 2019 CLASSIFICATION CRITERIA FOR SYSTEMIC LUPUS ERYTHEMATOSUS IN EARLY DISEASE, ACROSS SEXES AND ETHNICITIES

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Background: EULAR/ACR 2019 SLE Classification Criteria were validated in an international cohort.
Objectives: To evaluate performance characteristics of SLE classification systems in sex, race/ethnicity, and disease duration subsets.
Methods: Sensitivity and specificity of the EULAR/ACR 2019, SLICC 2012 and ACR 1982/1997 criteria were evaluated in the validation cohort.
Results: The cohort consisted of female (n=1098), male (n=172), Asian (n=118), Black (n=68), Hispanic (n=124) and White (n=941) patients; and patients with an SLE duration of 1-3 years (n=196), 3-5 years (n=157), and ≥5 years (n=879). Among patients with 1-3 years disease duration, the EULAR/ACR criteria had better sensitivity than the ACR criteria (97% (95%CI 92-99%) vs 81% (95%CI 72-88%). The new criteria performed well in men (sensitivity 93%, specificity 96%) and women (sensitivity 97%, specificity 94%). The new criteria had better sensitivity than the ACR criteria in White (95% vs 83%), Hispanic (100% vs 86%) and Asian patients (97% vs 77%).
Conclusion: The EULAR/ACR 2019 criteria perform well in patients with early disease, and across sexes and ethnicities.
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THU0272 BASEMENT MEMBRANE SEROLOGICAL MARKERS OF COLLAGEN TYPE IV AND LAMININ REMODELING ARE DIFFERENTIALLY EXPRESSED IN SLE

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Background: Collagen type IV and laminin are the main constituents of basement membranes (BMs). Epitopes on these molecules are targeted in various autoimmune diseases, systemic lupus erythematosus (SLE) in particular. Accelerated large vessel disease is a well-recognized cause of premature cardiovascular morbidity and mortality in SLE. Novel tools for quantification of soluble MMP-derived fragments of collagen type IV (C4M) and laminin (LG1M) have emerged as promising biomarkers for BM remodeling in atherosclerosis.

Objectives: To study serum levels of collagen type IV and laminin metabolites in patients with SLE and in healthy controls. And to search for associations with disease activity, organ damage and cardiovascular comorbidity.

Methods: One hundred and six SLE patients without and 20 with previous CVD events were included (1). One hundred and twenty male and female blood donors aged 20-65 years served as healthy reference. Disease activity (SLEDAI) and damage (SLICC) scores were calculated. Coronary artery calcification (CAC) was studied by CT scan and expressed as Agatston score. Carotid intima-media thickness (IMT) was measured by ultrasound (LOGIQ E9, GE Healthcare). In either subgroup atherosclerosis was defined as Agatston > 99 U and/or IMT>1 mm and/or presence of plaque. C4M and LG1M were measured by competitive ELISAs (2).

Results: Patient characteristics are presented in Table 1. Overall, C4M and LG1M were significantly increased in the entire SLE cohort vs. healthy controls (35.7 ± 17.5 vs. 22.3 ± 9.4 ng/mL, p<0.0001 and 20.9 ± 21.1 vs. 9.7 ± 8.0 ng/mL, p<0.0001, respectively) (Fig 1). Highly significant positive correlations were detected between C4M and LG1M in the entire SLE cohort and in the healthy control group (Fig 2).In terms of CVD and atherosclerosis LG1M was significantly higher in SLE patients with manifest CVD vs. those without (34.47 ± 41.22 vs. 18.34 ± 13.55, p=0.0015) and in those with atherosclerosis by imaging (25.53 ± 28.12 vs 17.53 ± 13.35, p=0.036). There were no associations between C4M and CVD or atherosclerosis. There was a weak association between LG1M and SLICC (r=0.22, p=0.01), but not with SLEDAI. Details on associations with other CVD risk factors and specific organ involvement will be presented.

Table 1 Characteristics for SLE patients with and without CVD

Patients characteristics	All (126)	SLE + CVD (20)	SLE without CVD (106)	p
Females, no. (%)	113 (89)	18 (90)	95 (89)	0.95
Age, yrs., mean ± SD	50.6± 14.4	54.8 ± 15.3	46.8± 14.1	0.15
Disease duration, yrs., mean ± SD	13.9 ± 9.3	19.0± 11.3	13.0± 11.3	0.007
SLEDAI, median, range	4 (0-14)	4 (0-10)	4 (0-14)	0.717
SLICC, median, range	1 (0-11)	3 (1-11)	1 (0-10)	0.0001
Atherosclerosis, no. (%)	53 (42)	14 (70)	39 (37)	0.0006
LG1M (ng/ml), mean ± SD	20.9± 21.2	34.5± 41.2	18.3 ± 13.6	0.0015
C4M (ng/ml), mean ± SD	35.7 ± 17.5	38.1± 20.6	35.3± 16.9	0.518

Conclusion: Serological levels of collagen type IV and laminin biomarkers were elevated and interrelated in an unstratified SLE population. Moreover, LG1M but not C4M was significantly elevated in SLE patients with previous CVD events and in those with atherosclerosis by imaging. These findings indicate that LG1M may serve as a serological marker for SLE-related large vessel disease. However, additional extravascular sites of increased basement membrane remodeling may contribute to the abnormal biomarker pattern.

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Kay SD and Genovese F contributed equally to this work.

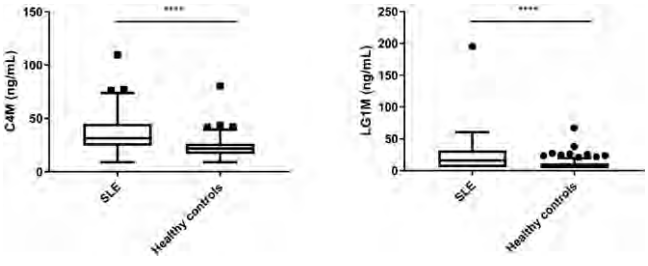


Figure 1. Levels of C4M and LG1M in serum of patients with SLE and healthy controls; graphs are presented as box and whiskers plot (in the style of Tukey). Statistical significance: ****p<0.0001.

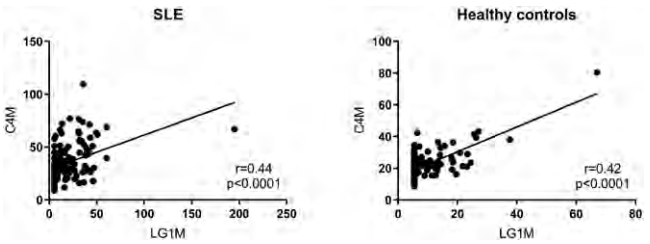


Figure 2. Correlation plots (Spearman r) of C4M and LG1M in SLE patients and healthy controls.

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THU0273

DISEASE ACTIVITY IS IMPORTANT RISK FACTORS FOR MATERNAL AND FETAL OUTCOMES DURING PREGNANCY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) primarily affects women of childbearing age and disease activity frequently increase during pregnancy. Patient with SLE still have markedly higher risk for obstetric complications, despite discussing reproductive planning with physicians and choosing a suitable time for pregnancy.

Objectives: This study aimed to examine the frequency and risk factors of complications occurring during pregnancy for women with SLE and compare with the general obstetric population.

Methods: The medical records of patients with SLE and age-matched controls at Ajou University Hospital between January 1999 and June 2019 were collected and retrospectively analyzed. Clinical features and pregnancy complications for all pregnancy-related admissions for women with and without SLE were compared. Multivariate logistic regression analysis was performed to obtain the predictor of maternal and fetal adverse outcomes.

Results: During this period, we analyzed 163 pregnancies in patients with SLE and 596 pregnancies in general population. Of these, except for body mass index (BMI), no other significant differences regarding demographic characteristics were noted between the groups. Lupus patients delivered significantly earlier(37 weeks + 0 days vs. 37 weeks + 6 days, p<0.001) and experienced more stillbirth (odds ratio (OR) 12.8), pre-eclampsia (OR 4.2), preterm labor (OR 2.6), emergency cesarean section (OR 2.5) and intrauterine growth retardation (odds ratio: 2.4) than age-matched controls. Using logistic regression, thrombocytopenia, low complement levels, high proteinuria, anti-ds DNA antibody positivity and high SLE Disease Activity Index (SLEDAI) were associated with maternal and fetal complications, whereas high cumulative steroid dose after SLE onset, high median steroid dose during pregnancy and history of cyclophosphamide treatment were only correlated with maternal complications. The area under the curve for SLEDAI score of adverse pregnancy outcome was 0.726 (95% CI 0.65-0.81) and cumulative steroid dose after SLE onset and median steroid dose during pregnancy for maternal outcome were 0.658 (95% confidence interval (CI) 0.55-0.76) and 0.750 (95% CI 0.65-0.85). The optimal cut-off value for SLEDAI was 4 and cumulative and median steroid dose were 2750mg and 6mg, respectively.

Conclusion: Pregnant women with SLE have a higher risk of adverse pregnancy outcomes. Pregnancies should be delayed until disease activity is well controls (SLEDAI<4) for longer than 6 months.

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THU0274 RENAL CHARACTERISTICS AND OUTCOME OF LUPUS NEPHRITIS ACCORDING TO ITS TIME OF ONSET

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Background: Lupus nephritis (LN) usually develops within 5 years of systemic lupus erythematosus (SLE) onset. It is unclear whether the course and outcome of LN differ between patients who initially had LN at SLE onset (initial-onset LN) and those who developed LN within 5 years after SLE onset (early-onset LN).
Objectives: To compare clinical characteristics and renal outcomes between SLE patients with initial-onset LN and SLE patients with early-onset LN.
Methods: SLE patients with biopsy-proven LN were retrospectively reviewed. The clinical parameters and renal outcomes were compared between initial-onset LN and early-onset LN groups. We used Cox regression analysis to estimate risk of worse renal outcome, according to the onset time of LN.
Results: Of the total 136 LN patients, 92 (67.6%) and 44 (32.4%) patients were classified into the initial-onset and early-onset LN groups, respectively. The initial-onset LN group had higher prevalences of impaired renal function (34.8% vs. 11.4%, p=0.004) and microscopic hematuria (73.9% vs. 54.5%, p=0.024), and higher urine protein/creatinine ratio (4626.1 [2180.0–6788.3] vs. 2410.0 [1265.0–5168.5] mg/g, p=0.006) at LN diagnosis. Renal relapse (46.3% vs 25.7%, p=0.039) and progression to chronic kidney disease (CKD) or end-stage renal disease (ESRD) were more common (24.4% vs. 8.3%, p=0.042) in the initial-onset LN group. In the multivariable Cox regression analysis, initial-onset LN group had higher risk of renal relapse (adjusted hazard ratio [HR] 2.938, 95% confidence interval [95% CI] 1.344–6.426, p=0.007) and progression to CKD or ESRD (adjusted HR 4.642, 95% CI 1.107–19.458, p=0.036), compared with early-onset LN group.
Conclusion: Patients with LN at SLE onset may have more severe renal presentations and worse renal outcome than those who develop LN within 5 years.
References: Not applicable

Table. Hazard ratios for renal relapse and progression to CKD/ESRD according to onset time of LN

	Univariable analysis		Multivariable analysis[a]	
	HR (95% CI)	p	HR (95% CI)	p
Renal relapse				
Early-onset LN	1.000 (reference)		1.000 (reference)	
Initial-onset LN	2.734 (1.315–5.686)	0.007	2.938 (1.344–6.426)	0.007
Progression to CKD/ESRD				
Early-onset LN	1.000 (reference)		1.000 (reference)	
Initial-onset LN	4.201 (1.249–14.132)	0.020	4.642 (1.107–19.458)	0.036

[a]Adjusted for age, ISN/RPS class, activity index, chronicity index, GFR, UPCR, hematuria and use of HCQ
LN, lupus nephritis; CKD, chronic kidney disease; ESRD, end-stage renal disease; ISN/RPS, International Society of Nephrology/Renal Pathology Society (ISN/RPS); GFR, glomerular filtration rate; UPCR, urine protein/creatinine ratio; HCQ, hydroxychloroquine; HR, hazard ratio; CI, confidence interval

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THU0275 SEVERE PREECLAMPSIA RELATED TO ANTIPHOSPHOLIPID SYNDROME: AN EUROPEAN STUDY OF 40 WOMEN

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Background: One of the 3 features of obstetrical antiphospholipid syndrome (APS) is severe preeclampsia (PE). Its time of occurrence, the associated risk of thromboses and systemic lupus erythematosus (SLE) have not been reported yet.
Objectives: We analyzed severe PE in a series of women with APS.
Methods: We retrospectively collected data of female patients from 5 French internal medicine and 1 Italian rheumatology units. Inclusion criteria were: a severe PE/eclampsia(1), that occurred before 34 weeks of gestation (WG) in patients who met the APS classification criteria(2).
Results: 40 patients were enrolled (Table 1). Because of known APS/positive aPL/previous obstetrical complications, 23(57.5%) patients were treated during the index PE: 4 with low dose aspirin (LDA), 4 with low molecular weight heparin (LMWH), and 15 with a combination of both. 7 patients were also treated with hydroxychloroquine, 8 with corticosteroids and 3 with immunosuppressants. 17(42.5%) patients received no treatment. 24(60%) live births were observed. During a follow-up period of 3 years, 26(65%) patients had at least 1 new pregnancy, with a total of 38 pregnancies which resulted in 33(86.8%) live births. 57.5% pregnancies who resulted in live births occurred without any maternal or fetal complications. All 26 patients who had at least 1 pregnancy after index PE were treated with LDA; LMWH was given at prophylactic and therapeutic dosage in 13(50%) patients, respectively. No patient experienced 3 consecutive miscarriages.

Table 1. 40 APS patients with severe PE

Overall features (n, %)	
Patients	40 (100)
Age at PE, (median, IQR)	30.5 (27-33)
PE term, WG (median, IQR)	25.5 (23-29)
Live births	24 (60)
Birth term, WG (median, IQR)	25.5 (23.7-30.3)
Associated SLE	12 (30)
Maternal complications (n, %)	25 (62.5)
HELLP	18 (45)
E	6 (15)
CAPS	3 (7.5)
Placental abruptions	3 (7.5)
Fetal complications (n, %)	31 (77.5)
IUGR	18 (45)
IUFD	11 (2.5)
Preterm delivery	22 (55)
Obstetrical history (n, %)	
Primiparous	21 (52.5)
Index PE before APS	12 (30)
Thrombosis (n, %)	
Thrombosis before PE index	14 (35.0)
Thrombosis after PE index	2 (5.0)
Abs at APS diagnosis (n, %)	
aPL triple positivity	21 (52.5)
IgG/IgM anti-cardiolipin	34 (85.0)
IgG/IgM anti-β2GPI	25 (62.5)
LAC	33 (82.5)

Legend to Table 1: PE: preeclampsia; APS: antiphospholipid syndrome; IQR: interquartile range; WG: weeks of gestation; SLE: systemic lupus erythematosus; HELLP: Hemolysis, elevated liver enzymes, low platelet; E: eclampsia; CAPS: catastrophic APS; IUGR: intrauterine growth restriction; IUFD: intrauterine fetal death; CHB: congenital atrioventricular block; aPL: antiphospholipid antibodies; LAC: lupus anticoagulant.

Conclusion: Among the APS criteria, "3 consecutive miscarriages criterion" was not found. The majority of patients also experienced thrombosis and SLE before the index PE.
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THU0276 HIGH HYDROXYCHLOROQUINE EXPOSURE IS ASSOCIATED WITH ABNORMAL STRAIN IMAGING IN LUPUS PATIENTS WITH END-STAGE RENAL DISEASE

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Background: Hydroxychloroquine (HCQ) cardiotoxicity remains an underrecognized condition. Diagnosis ultimately relies on invasive endomyocardial biopsy (EMB) and non-invasive screening methods are warranted. Strain imaging is a novel tool to detect early subclinical left ventricular (LV) dysfunction and may have a role in screening for HCQ cardiotoxicity (1). Strain measures systolic deformation indices that when decreased can predict cardiovascular outcomes more accurately than LV ejection fraction (2).
Objectives: We assessed whether high HCQ cardiotoxicity risk is associated with a specific strain pattern in a group of patients with SLE and end-stage renal disease (ESRD).
Methods: This was a retrospective study in a tertiary care center in New York on a group of patients with an established diagnosis of SLE, ESRD and cardiomyopathy on the index echocardiogram followed between years 2003 and 2019. The patients were stratified into two groups: high risk HCQ toxicity group was defined as either cumulative HCQ dose ≥1000g and/or an endomyocardial biopsy confirming HCQ toxicity. Low/moderate risk group was defined as a cumulative dose of HCQ <1000g. Clinical, demographic, electrocardiographic and echocardiographic strain parameters were compared between the groups.
Results: A total of 16 patients were included. Two patients had EMB consistent with HCQ induced toxicity and 3 patients had cumulative HCQ doses ≥1000g. There were no significant differences in the baseline demographic characteristics between the two groups. Compared to patients with low/moderate risk, patients in the high risk group had a lower heart rate at the time of the echocardiogram (69 vs 87 beats per minute, p=0.08) and a higher frequency of LV hypertrophy (40% vs 9.1%, p=0.2). Strain analysis showed that both groups had compromised LV global longitudinal strain (GLS) and global cross-sectional strain (GCS). However, compared to the low/moderate risk group, the high risk group had a weaker LV GLS (-12.3% vs -14.9%, p=0.27).

Characteristics overall and stratified by HCQ risk group

	Characteristic	Overall (n=16)	Low/Moderate HCQ Risk(n=11)	High HCQ Risk and/or Positive EMB (n=5)	P value
Demographics	Age, years	47.5 (36.5,60.7)	50.0 (33.9,60.5)	42.5 (42.7,61.0)	0.95
	Female, n(%)	14 (87.5)	9 (90)	5 (83.3)	0.99
Clinical Features	SLE duration, years	7.4 (4.3,17.5)	5.5 (3.5,13.2)	15.6 (11.6,19.3)	0.15
	HCQ cumulative dose, g	422.8 (224.2,422.8)	285.4 (110.8,523.6)	1140 (1006,1625.4)	0.005
	HCQ therapy duration, years	3.4 (2.5, 8.9)	3.2 (1.5,5.1)	7.8 (6.8,11.6)	0.06
	HCQ daily dose, mg/d	226 (200,394.9)	200 (179.4,253.7)	400 (389.8,400)	0.007
	Hypertension, n (%)	14 (87.5)	10 (90.9)	4 (80.0)	0.99
	Diabetes, n (%)	3 (18.8)	2 (18.8)	1 (20.0)	0.99
	CAD, n (%)	3 (18.8)	2 (18.8)	1 (20)	0.99
Echocardiogram	EF, %	55 (42.5,60)	55 (40,60)	55 (55,70)	0.45
	LA size, cm	3.8 (3.4,4.3)	3.8 (3.4,4.2)	4.3 (3.4,4.9)	0.30
	LVEDD, cm	4.9 (4.4, 5.5)	4.8 (4.2,5.5)	5.0 (4.9,5.4)	0.43
	E/E'	12.3 (8.8,16.3)	12 (8.8,14.9)	16.9 (4.9,21.8)	0.43
	Moderate-severe LV hypertrophy, n(%)	3 (18.7)	1 (9.1)	2 (40.0)	0.20
Strain echocardiography	GLS, %	-13.9 (-16.7,-12.3)	-14.9 (-16.7,-12.9)	-12.3 (-15.4,-12.2)	0.27
	Base/Apex Ratio	0.8 (0.7,0.9)	0.76 (0.68,0.86)	0.76 (0.66,0.83)	0.95
	GCS, %	-20.2 (-21.7,-17)	-19.7 (-20.5,18.0)	-21.7 (-23.9,-20.9)	0.16
	RV GLS, %	-20.19 (-22.1,-17.5)	-20.2 (-22.3,-17.1)	-19.8 (-22.1,-17.5)	0.99

Conclusion: We report an association of higher HCQ cardiotoxicity risk and impaired strain in a set of SLE ESRD patients. Standard echo measures did not differentiate between high and low/moderate risk patients. Although the findings did not reach statistical significance, given the small sample size, results are still suggestive of a possible utility of strain echocardiography for detection of early HCQ toxicity.

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Disclosure of Interests: None declared
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THU0277 THE EXPRESSION OF IFNA, INFB AND INFΓ AND SERUM LEVELS OF THOSE CYTOKINES IN SJÖGREN'S SYNDROME PATIENTS

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Background: In the pathogensis of autoimmune mediated diseases, such as Sjögren's syndrome (SS), interferons (IFN) and IFN pathway activation play a vital role.
Objectives: We planned to assess IFNα, INFβ and INFγ expression and IFNs serum levels in SS patients and correlation of these parameters with: autoantibodies specific for SS, serum concentration of C3, C4 component of complement (C3, C4), rheumatoid factor (RF), gammaglobulins, focus score (FS) and eye dryness symptoms.
Methods: Whole blood RNA was isolated from 77 SS patients [F91%vsM9%]; mean age 49,69±15.36; SS diagnosis according to EULAR/ACR 2016 criteria. The analysis of INFα, - β and - γ expression levels was based on validated TaqMan probes by ΔCT methods. Serum concentrations of rheumatoid factor (RF), C3- and C4 complement components (mg/dL) and gammaglobulins (g/dL), were assessed. Anti-Ro/SSA and/or anti-La/SSB autoantibodies were assessed by semiquantitative immunoblotting evaluation. The eye dryness and keratoconjunctivitis sicca were confirmed with Schirmer's test (score of less than 5 mm/5') and the ocular staining score (OSS) using lissamine green and fluorescein staining. The biopsy of minor salivary gland was performed with the histopathological evaluation of FS. The study was approved by the Bioethics Committee. Differences between groups of patients were determined using non-parametric Mann-Whitney U test or Kruskall-Wallis test with Dunn's post hoc. Correlations were determined using non-parametric Spearman test. The level of statistical significance was set at $p < 0.05$.
Results: IFNβ had the highest expression levels among IFNs and IFNβ serum concentrations were higher than those of IFNα and -γ. In cases with high IFNβ serum concentration lower IFNβ expression was observed. There was a highly significant correlation between IFNα and IFNβ expression (r =0.6;p=0.001). IFNβ expression (p=0.059) was higher in the group of younger (<45 y.o.) patients (n= 23; 29.9%) as compared to the group of older individuals (at least 45 y.o.). In patients with SS-A / Ro antibodies with strong antigen binding affinity (3) IFN β expression and IFNβ serum levels were highest of all IFNs. The presence of anti La/SS-B antibodies was associated with the increased IFNβ expression while not with the increased IFNβ serum concentration. In terms of IFNα expression and protein level, RF(+)patients had average higher values compared to RF(-) patients. The average mRNA level of IFNα was about 3 times lower in patients with low C3 serum concentration compared to patients with normal C3 serum concentration values. IFNβ mRNA level was 2.5 times lower in patients with low Schirmer's test (<5mm/5') in comparison to patients with Schirmer's test>5mm/5'; Schirmer's test <5mm/5' was associated with higher IFNβ serum concentration.
Conclusion: Type I IFN signature predominates in the peripheral blood of studied patients. Presented results confirmed the pivotal role of type I IFN in the disease process. The serum concentration of IFNβ and the expression of IFNβ were the highest values of those parameters for cytokines assessed in this study. A positive correlation between IFNα and IFNβ mRNA levels has been observed.
Disclosure of Interests: None declared
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THU0278 NAILFOLD CAPILLAROSCOPY IN SJÖGREN'S SYNDROME: A SYSTEMATIC LITERATURE REVIEW AND STANDARDISED INTERPRETATION

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Background: Sjögren Syndrome (SS) is a rheumatic connective tissue disease in which vascular involvement (e.g. Raynaud's phenomenon) may occur. No systematic review exists elucidating on the role of nailfold capillaroscopy in SS.
Objectives: To give a standardised overview of capillaroscopic changes and clinical associations in SS.
Methods: The literature was searched through in three databases by two reviewers. All published original studies which assess patients with SS by capillaroscopy were revised. A quality assessment was applied, based on sample size, population description, presence of a control group, presence of instrumental specifications and/or standardly applied capillaroscopic methodology, presence of clear descriptions of capillaroscopic parameters and based on the used statistical analysis. The capillaroscopic findings were described in a EULAR consented standardised way (1). Significant associations of capillaroscopic parameters in SS-patients with clinical and laboratory variables were also reported.
Results: The literature search resulted in 826 hits. Based on title and abstract screening 519 original studies were retained and of these, 12 full texts described an assessment by nailfold capillaroscopy in SS. Six studies (four case-control studies and two case-series) were retained after performing a critical quality assessment (fig 1). EULAR standardised description (table 1) attested conclusive results for capillary 'morphology', suggesting a not higher prevalence of abnormal shapes in SS than in healthy (2,3). Concerning clinical associations, capillary density was associated with Raynaud in two studies and with interstitial lung disease in one study (2-4). No association between serologic features (anti-nuclear antibodies, anti-SSA, anti-SSB and anti-RF) and capillaroscopic parameters were found (2,5).

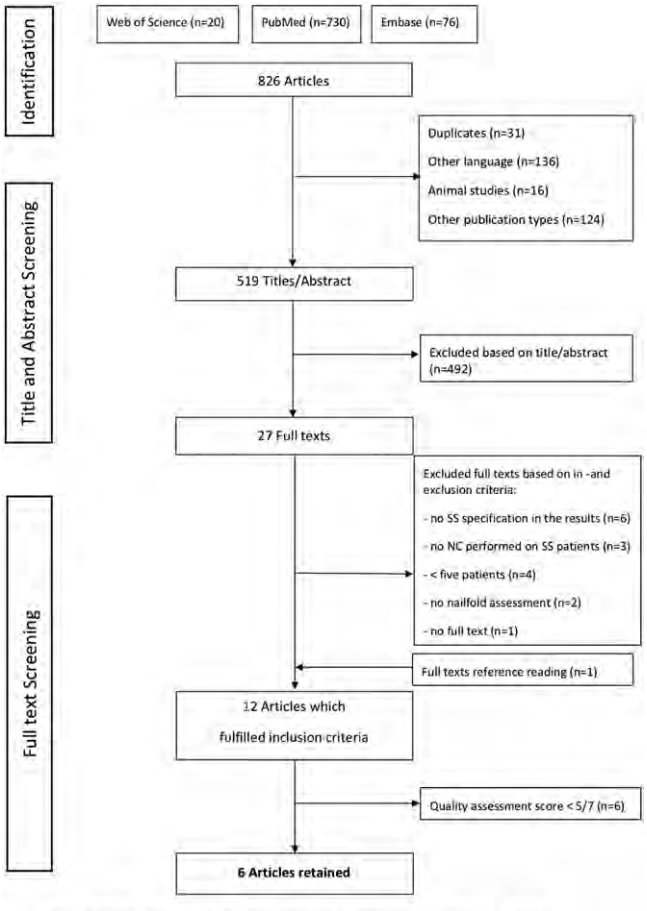


Fig 1. Flowchart of the search strategy about nailfold capillaroscopy in Sjögren Syndrome

Conclusion: A small number of studies have investigated the role of nailfold capillaroscopy in SS. Prospective follow up studies with standard evaluation and capillaroscopy in SS are warranted.

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Table 1. Standardised description of capillaroscopic characteristics in Sjögren's Syndrome vs Healthy Legend. Only studies mentioning p-values were considered in this table. *Tektonidou et al. did not report differences between healthy controls and the SS group as a whole, but rather reported differences between healthy controls and subgroups of patients with/without Raynaud's and with/without centromere antibodies.

Assessment	Parameter	Significant	Not significant	Conclusion
Quantitative	**Density**	1 study [2]	1 study [3]	Not conclusive
	Dimension	0 studies	0 studies	Not conclusive
	Dilation	0 studies	1 study [2]	
	Giant			
	Normal morphology	0 studies	0 studies	Not conclusive
		0 studies	1 study [3]	
	Hairpin shaped	0 studies	1 study [3]	
	Tortuosity			
	Crossing			
	Abnormal morphology	0 studies	2 studies [2,3]	**Equal absence of abnormal morphology in SS vs healthy controls**
	Haemorrhages	0 studies	2 studies [2,3]	Not conclusive*
Semi quantitative		0 studies	0 studies	No data
Qualitative	Normal	0 studies	1 study [3]	Not conclusive*
	Non specific abnormalities	0 studies	1 study [3]	Not conclusive*
	Scleroderma pattern	0 studies	0 studies	No data

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THU0279

PREVALENCE AND RISK FACTORS OF HERPES ZOSTER REACTIVATION IN PATIENTS WITH BIOPSY PROVEN LUPUS NEPHRITIS UNDERGOING IMMUNOSUPPRESSIVE THERAPIES

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Background: Herpes zoster (HZ) reactivation is fairly common in patients with systemic lupus erythematosus (SLE). However, there is a paucity of studies that reported the risk factors of HZ reactivation in well-defined subsets of SLE patients.
Objectives: To study the prevalence of HZ reactivation in patients with active biopsy confirmed lupus nephritis (LN) undergoing immunosuppressive therapies.
Methods: Patients who had biopsy proven active LN that was treated with immunosuppressive regimens in our unit between 2003 and 2018 were retrospectively reviewed for the occurrence of HZ reactivation within 2 years' therapies. HZ was a clinical diagnosis based on history and physical signs by attending physicians. The following were collected: age and SLE duration at renal biopsy, sex, SLE disease activity scores, maximum daily dose and total duration of high-dose prednisolone and other immunosuppressive drugs in the induction period, maintenance therapies, laboratory parameters at renal biopsy and 6 months post-therapy that included lupus serology, albumin, globulin, immunoglobulin levels (IgG/A/M) and white cell counts (lymphocyte and neutrophil), histological classes of LN and clinical response at 6 month and 2 years. The incidence of HZ reactivation within 2 years of active LN treatment and the total prevalence of HZ infection over time until last follow-up was calculated. Risk factors for HZ reactivation were studied by logistic regression.
Results: 251 patients with 311 episodes of active LN were studied (92% women; age 34.2±14.2 years at first renal biopsy). The distribution of histological classes (WHO or ISN/RPS) was: class III/IV±V (69%), I/II/V/VI (31%). First-time renal disease occurred in 61% of patients. Induction treatment regimens were: prednisolone in combination with CYC (17%), azathioprine (11%), MMF (42%), tacrolimus (25%). Within 2 years of immunosuppressive therapies, 55 (18%) episodes of LN were complicated by HZ infection. The incidence of HZ reactivation was 8.84/100 patient-year. The median time for HZ reactivation since LN treatment was 11 months. 28 patients had HZ infection occurring longer than 2 years post-therapy, giving an overall prevalence of 3.24/100 patient-years. The distribution of HZ lesions was: head and neck region (15%), lower limbs (27%), trunk (55%) and upper limbs (4%). Fourteen episodes of HZ (25%) were treated by intravenous anti-viral drugs while others were treated at out-patient settings

with oral acyclovir. Secondary bacterial infection occurred in 9% of the episodes. Disseminated disease or mortality was not reported in any patients. Significant post-herpetic neuralgia developed in 9% of the episodes. Patients with HZ reactivation were more likely to have first-time renal disease (76% vs 58%; p=0.02) and a shorter SLE duration at LN (31.4±50 vs 62.7±72 months; p=0.02) than those without HZ. A trend of higher SLEDAI score, higher anti-dsDNA titer, lower C3 and albumin level but higher rate of refractory renal disease was also observed in HZ-infected patients. Other clinical parameters such as histological classes of LN, neutrophil, lymphocyte counts and immunoglobulin levels at baseline and 6 months post-therapy were not significantly different between HZ-infected and control patients. HZ-infected patients had been treated with a significantly higher dose of prednisolone (0.72±0.40 vs 0.63±0.24 mg/kg/day) as induction therapy. Dosages of other immunosuppressive drugs were not associated with HZ reactivation. Logistic regression revealed first-time renal disease (OR 2.25[1.08-4.71]; p=0.003), peak MMF daily dose (OR 1.24[1.10-3.07]; p=0.02) and cumulative CYC dose (OR 1.14[1.01-1.28]; p=0.04) during induction therapy were significantly associated with HZ within 2 years.

Conclusion: HZ reactivation is fairly common in LN patients undergoing immunosuppressive therapies but unpredictable from histological and laboratory parameters. Higher doses of prednisolone, MMF and CYC were associated with a higher risk of HZ reactivation within 2 years.

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Disclosure of Interests: None declared

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THU0280 IMPACT ON PHYSICIAN GLOBAL ASSESSMENT ON REMISSION RATES IN SLE. ANALYSIS FROM A GERMAN SLE-COHORT.

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Background: Defining remission for SLE as a suitable target for a treat to target (T2T) approach has been a major challenge in the past years. A few years back, four definitions of remission were presented by the international DORIS task force.[1] Parameters included in the definition are clinical activity (cSLEDAI), steroid dose, immunosuppressive therapy, serology and physician global assessment (PGA). In particular the PGA, its threshold and general utility have been and still are discussed controversially.

Objectives: It was our aim to evaluate the added value of PGA in remission assessment.

Methods: In this monocentric cross-sectional study, patients with SLE according to the 1997 American College of Rheumatology (ACR) criteria were enrolled and assessed between September 2016 and December 2017. Two different definitions of remission were applied. The internationally accepted DORIS remission and a modified DORIS remission excluding PGA. Factors influencing PGA were assessed in the entire cohort. Regression analyses were used to assess differences between patients in DORIS and modified DORIS remission.

Results: A total of 233 patients were included (87.6% female). 98 patients (41.9%) fulfilled any of the four DORIS remission definitions, while 154 patients (66.1%) were in any modified remission in which PGA was excluded. In general, PGA rating was associated with disease activity (clinical SLEDAI; p=<0.0001), depression (Center for Epidemiological Studies Depression Scale; p=0.049), pain reported by the patient (numeric rating scale; p=<0.0001) and hypocomplementemia (p=<0.0001). Damage (SLICC damage index, SDI) did not influence PGA (p=0.98). Both, DORIS and modified DORIS remission were associated with lower damage (p=0.026; p=0.003), lower pain on NRS (p=0.001; p=0.013), normal complement (p=0.0005; p=0.005) and better illness perception (p=0.006; p=0.023). Patients in modified DORIS remission had a tendency for more immunosuppressive therapy (p=0.046).

Conclusion: Exclusion of PGA in remission assessment led to an increased number of patients in remission. Clinical parameters and factors associated with DORIS remission vs. modified DORIS remission were similar, hence the added value of PGA in our cohort regarding remission assessment is questionable. The use and especially the correct threshold of PGA for remission still has to be discussed.

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THU0281 EXPLORING THE GENETIC DIVERSITY OF STAPHYLOCOCCUS AUREUS IN PATIENTS AFFECTED BY SYSTEMIC LUPUS ERYTHEMATOSUS: ASSOCIATION WITH DISEASE-RELATED FEATURES AND ACTIVITY

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Background: Infective factors play a central role in autoimmune diseases pathogenesis. It is possible to speculate that the host genotype could interact with genetic background of infective agents. We previously evaluated a large SLE cohort, observing the association between the *S. Aureus* (SA) carriage status and presence of a more active disease in terms of autoantibodies positivity.

Objectives: We evaluated epidemiological, molecular characterization, genetic diversity and evolution of SA isolated from SLE patients by means of phylogenetic analysis.

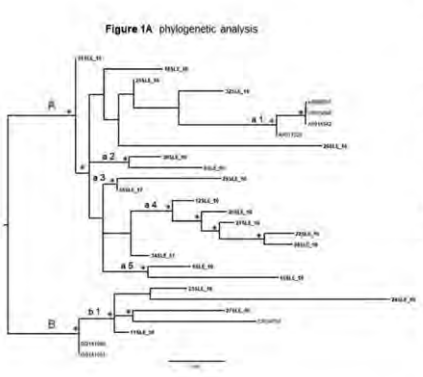
Methods: Consecutive SLE patients (ACR 1997 criteria) were enrolled: clinical/laboratory data were collected and nasal swab for SA identification was performed. On the basis of translation elongation factor (*tuf*) gene, a phylogenetic analysis was performed to investigate phylogenetic relationships and to assess significant clades in patients with persistent carriage status (nasal swab positive in two consecutive evaluation, performed 1 week apart). The first dataset was composed by seven SA tuf gene isolated from non-SLE individuals from different countries (downloaded from the GenBank database, https://www.ncbi.nlm.nih.gov/nucleotide/) and tuf gene SA collected from SLE patients enrolled in the present study.

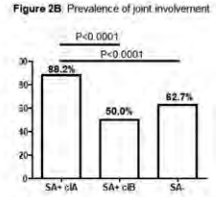
Results: We enrolled 118 patients (M/F 10/198; median age 45.5 years, IQR 13,2; median disease duration 120 months, IQR 144). Skin involvement is the most frequent disease manifestation (86 patients, 72.9%), followed by joint involvement (78 patients, 66.1%). Twenty-four patients (20.3%) were SA carriers (SA+), three of them resulted MRSA. SA+ patients showed a significantly higher prevalence of joint involvement (79.2% *versus* 62.7%, P=0.01) and anti-dsDNA positivity (75.0% *versus* 55.3%, P=0.004). Moreover, SA+ SLE showed a more active disease, in terms of SLEDAI-2k values [SA+: median 2 (IQR 3.75) *versus* SA-: median 0 (IQR 2), P=0.04). The phylogenetic analysis has been restricted on the 21 non-MRSA SA+ patients. The maximum likelihood phylogenetic tree of the first dataset revealed a statistically supported larger clade (A, N=17) and a smaller one (B, N=4; figure 1A). SLE patients located in the clade A showed a significantly higher prevalence of joint involvement (88.2%) in comparison with clade B (50.0%, P<0.0001) and SA- (62.7%, P<0.0001, figure 2B). Moreover, haematological manifestations were significantly more frequent in clade A patients (64.7%) compared with B (50.0%, P=0.004, figure 2C).

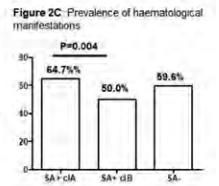
Conclusion: The results of the present study confirmed the association between SA carriage status and disease activity, in terms of SLEDAI-2k values and anti-dsDNA positivity. The phylogenetic analysis on *tuf* gene show a clustering of *SA+* patients in two major clade (A and B). Interestingly the *tuf* genotype of clade A is significantly associated with a specific disease phenotype, characterized by joint involvement and positivity for anti-dsDNA. These findings support the hypothesis that bacterial genetic variants may be associated with specific disease features.

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THU0282 EPIDEMIOLOGY OF CUTANEOUS INVOLVEMENT IN SJÖGREN'S SYNDROME: DATA FROM THREE FRENCH POPULATIONS OF PSS (TEARS, ASSESS, DIAPSS)

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Background: Cutaneous involvement is common during primary Sjogren's Syndrome (pSS) but prevalence and characteristics are difficult to establish precisely because of the limited number of patients studied in most cohorts, the variability of the disorders evaluated in each cohort, the rarity of some of them, and the heterogeneity of evaluations from previous studies (1).
Objectives: To determine the prevalence and significance of dermatological disorders in primary Sjogren Syndrome.
Methods: ~~We use 2 French cohorts (ASSESS, in which prevalence of skin disorders in 395 pSS patients was evaluated, and diapSS in which 91 consecutive pSS patients had an examination by a dermatologist) and baseline data of the TEARS randomized trial (110 patients with recent or active pSS, treated with rituximab or placebo, and evaluated for skin dryness using a visual analogue scale out of 100).~~
Results: Skin manifestations included in the ESSDAI were rare in the ASSESS cohort (n=16/395, 4.1%, mainly purpuras; only 3 had high activity) but associated with activity in the other ESSDAI domains (peripheral neurological (p<0.001), muscular (p=0.01), hematological (p=0.017) and biological (p=0.017)), history of arthritis (p=0.008), splenomegaly (p=0.024) and higher gamma globulin level (p=0.008)) (Table). Compared to pSS patients not receiving a dermatological consultation, the pSS patients who had a dermatological consultation had significantly more dermatological involvement outside ESSDAI score [42% (29/69) versus 19.6% (11/56); p=0.008]. The TEARS study showed a high prevalence of cutaneous dryness (VAS>50; 48.2%) and that these dry skin patients had higher pain VAS (61.5+/-28.2 vs 46.8+/-27.0; p=0.003) and drought (79.4+/-15.2 vs 62.5+/-21.7; p<0.0001).

	Cutaneous involvement	No Cutaneous involvement	Total	p values*
Muscular	3/16 (18.8)	10/373 (2.7)	13/389 (3.3)	0.001
Peripheral nervous system PNS	4/16 (25)	34/373 (9.1)	38/389 (9.8)	0.00001
Biological	8/16 (50)	138/371 (37.2)	146/387 (37.7)	0.017
Hematologic	7/16 (43.8)	55/373 (14.7)	62/389 (15.9)	0.017
History of arthritis	12/16 (75)	154/374 (41.2)	166/390 (42.6)	0.008
History of splenomegaly	2/16 (12.5)	10/3762.7)	12/392 (3.1)	0.024
History of lymphoma	0/16 (0)	18/379 (4.7)	18/395 (4.6)	0.372
Mean (SD) ESSDAI score	14.5 (6.8)	4.4 (5.1)		0.00001
Mean (SD) ESSDAI score after excluding the points awarded by skin manifestations	8.1 (6.2)	4.4 (5.1)		0.014
Gammaglobulin levels (mean +/- SD)	23.1 +/-7.3	18.5 +/-8.1	-	0.006

Conclusion: The most common skin disorder is dryness, which is associated with a higher level of pain and overall subjective dryness. ESSDAI skin activity is rare, associated with hypergammaglobulinemia and ESSDAI activity. Systematic dermatological examination is informative for non-specific pSS lesions
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THU0283 DISTINCT CLINICAL FEATURES OF LATE–ONSET SYSTEMIC LUPUS ERYTHEMATOSUS AMONG MALAYSIAN MULTI-ETHNIC COHORT

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Background: Systemic Lupus Erythematosus (SLE) commonly affects young women in their reproductive age group. However, there is an increase prevalence of late-onset SLE, parallel to the higher life expectancies among general populations worldwide. It has been reported that up to 25% SLE populations have a later onset of disease and their disease expression and course may be different.
Objectives: To determine the clinical features and outcomes of late-onset SLE patients in a multi-ethnic Malaysian cohort.
Methods: Medical records of SLE patients who attended regular follow-up clinics in Universiti Kebangsaan Malaysia Medical Centre (UKMMC) from 2011 until June 2019 were reviewed. Late-onset SLE was defined as the onset of SLE symptoms or diagnosis after the age of 50 years old. Information on their socio-demographics and disease characteristics were obtained from the clinical records. Disease damage was assessed using the SLICC/ACR (Systemic Lupus International Collaborating Clinics/American College of Rheumatology) Damage Index (SDI) scores. The disease characteristics and autoantibody profiles were compared between late-onset and younger onset patients. Damage accrual at disease onset and at 5 years was obtained and compared between the two groups.
Results: A total of 429 patients were included and majority of them were Malays (n= 225, 52.4%) followed by Chinese (n=180, 42), Indian (n=21, 4.9%) and others (n=3,0.7%). This multi-ethnic SLE cohort was consisted of predominantyly female patients (n=372,86.7%) with disease duration of 9.9 years ± 6.8 years. A total of 13.8% (n=59) had late onset SLE with mean onset of disease at 58.1 ± 6.3 years while younger group was 27.2 ± 9.4 years. The commonest system involvement among the late-onset group was haematological manifestation (69.5%).Compared to the younger-onset SLE, late-onset SLE occurred significantly higher among the Chinese (66.1%) as compared to Malay (32.3%), Indians and other ethnics (1.7%), p<0.01. Patients with late-onset SLE also had significantly less musculoskeletal (37.3% vs 62.4%) and renal (23.7% vs 71.1%), p<0.001 and tend to have less muco-cutanoues manifestations (28.8 vs 42.4%, p=0.06). Meanwhile, pulmonary involvement was more common among the late onset SLE patients (11.9% vs 0.8%, p<0.001). Extractable nuclear antigen (ENA) results were available in 197 patients and patients with late-onset SLE had significantly higher rate of anti-RO positive (63% vs 3.9%), p=0.01. Otherwise, no significant difference in the other autoantibodies expressions including anti-La, anti-Sm, anti-RNP, anti-ribosomal P and anti-phospholipid antibodies. Patients with late-onset SLE tend to have more damage accrual at 5 years as compared to the younger age group (p=0.07). The mortality in the late onset group was 13.6% (n=8) as compared to 2.7% (n=10) in the younger age group, p=0.01. Majority of the cause of death in the later onset SLE was infection (87.5%) while in the younger age group was infection and active disease (90%).
Conclusion: Late onset SLE occurs more commonly among Chinese ethnics in Malaysia and Malaysian SLE patients with late onset of the disease have distinct clinical manifestations. Damage accrual at 5 years tend to be higher in the late-onset group and the mortality is significantly higher with the major cause of death is infection. The different disease expression and outcome in late onset SLE suggest different factors in influencing the disease course and hence further studies including their genetic profiles are warranted.
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THU0284 PREVALENCE OF NEUROPSYCHIATRIC LUPUS IN PSYCHOSIS PATIENTS WITH A POSITIVE ANTINUCLEAR ANTIBODY

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Background: Psychosis is a rare manifestation of Neuropsychiatric Systemic Lupus Erythematosus (NPSLE). Patients with SLE may have Psychosis as part of their initial presentation of disease[1]. Current guidelines do not make a recommendation regarding the use of Antinuclear Antibody (ANA) in the assessment of patients with psychosis[2]. There is limited evidence assessing the utility of ANA testing in this setting.

Objectives: Primary objective: Determine the prevalence of NPSLE in patients admitted to a mental health service with a diagnosis of a psychosis, who have had a positive antinuclear antibody test.

Secondary objectives: Determine the frequency and proportion of positive ANA testing in this patient group. Determine the pattern and titres of positive ANAs. Determine the subsequent investigation, referral and diagnosis of patients with positive ANAs.

Methods: Retrospective chart review of patients admitted to a mental health service of two metropolitan tertiary referral centres, Prince of Wales Hospital (POWH) and Royal Prince Alfred Hospital (RPAH), with a diagnosis of psychosis who had been tested for ANA. Patients were identified using their electronically entered diagnosis based on the International Classification of Disease[3] codes. Assessment of patient data for SLE used the 2019 ACR/EULAR classification criteria[4]. Decisions regarding attribution of psychosis related events to SLE follows the criteria used by Bortoluzzi et al[5].

Results: Between 1st of January 2010 and 31st of March 2018 there were 5585 (POWH) and 4620 (RPAH) mental health admission with an ICD diagnosis of psychosis representing 2451 and 2315 individual patients. 449/2451 (18%) and 462/2315 (20%) patients were tested for ANA. 78/449 (17%) and 57/462 (12%) were positive. Discharge data was available for all patients and long-term follow up data was completed for 53/78 (81% - POWH) patients and 50/57 (88% - RPAH). The mean follow-up time 43 ± 23 months and 51 ± 29 months respectively.

At discharge there were four patients who met 2019 ACR/EULAR for SLE. Of these, two patients met criteria for NPSLE. One was diagnosed clinically and treated specifically for NPSLE with intravenous methylprednisolone and rituximab.

There were no additional diagnoses of SLE or NPSLE clinically or by criteria found in the available follow up data. Hence the overall prevalence of NPSLE in patients admitted with psychosis was 1.3%, 95%CI [0,6.9%] and 1.8%, 95%CI [0,9.4%] respectively.

Conclusion: The prevalence of neuropsychiatric lupus in patients with psychosis and a positive ANA was 1/78 and 1/57 a two tertiary referral centres. This study expands significantly on the limited evidence available as to the expected outcomes of a positive ANA test in a patient with psychosis.

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THU0285 ANALYSIS OF THE RELATIONSHIP BETWEEN ORGAN DAMAGE AND QUALITY OF LIFE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease that can not only cause systemic symptoms, such as fever and arthritis, but can also damage important organs, such as those of the central nervous system and the kidneys. Prevention of irreversible organ damage is important for better prognosis [1]. Additionally, the importance of maintaining the quality of life (QOL) of patients has recently been emphasized. However, only a few studies have examined the relationship between irreversible organ damage and patient QOL.

Objectives: To assess the relationship between organ damage and QOL, and to survey which organs have more significant effects on QOL.

Methods: We conducted a questionnaire-based survey of 183 patients with SLE at Kyoto University Hospital from September to December 2019. We used the SLICC/ACR Damage Index (SDI) to evaluate organ damage [2]. The following five scales were employed to evaluate QOL: the physical (PCS) and mental component summary (MCS) of the Medical Outcome Study (MOS) 36-Item Short-Form Health Survey version 2.0 (SF-36v2) [3], health (HRQOL) and non-health-related QOL (N-HRQOL) of LupusPRO [4], and SLE Symptom Checklist (SSC) [5].

Results: Linear regression analysis showed significant correlation between the SDI score and all QOL scales except for N-HRQOL, suggesting negative effects of organ damage on QOL (Table 1). Next, we analysed whether there was a significant difference in the SF-36 score between those who were positive and negative for each SDI item (41 in total), using the Wilcoxon rank sum test. Muscle atrophy or weakness ($p = 3.0\times10^{-10}$), osteoporosis with fracture or vertebral collapse ($p = 9.7\times10^{-8}$), claudication ($p = 7.4\times10^{-5}$), and cognitive impairment or major psychosis ($p = 9.9\times10^{-5}$) significantly correlated ($p < 1.2\times10^{-3}$) with PCS, and scarring chronic alopecia ($p = 3.4\times10^{-4}$) with MCS (Table 2). In addition, the five SDI items significantly correlated with the remaining three QOL scales (HRQOL, N-HRQOL, and SSC; $p < 0.05$).

Table 1. Relationship between the SDI score and QOL

	SF-36		LupusPRO		SSC
	PCS	MCS	HRQOL	N-HRQOL	
p-value	$<2.0\times10^{-16}$	1.7×10^{-3}	2.2×10^{-11}	0.23	1.9×10^{-8}

Table 2. Relationship between each SDI item and the SF-36 score ($p < 1.2\times10-3$)

SDI item	PCS score		*p*-value
	Positive (Median (IQR))	Negative (Median (IQR))	
Muscle atrophy/weakness	33 (19-45)	50 (43-54)	3.0×10^{-10}
Osteoporosis with fracture/vertebral collapse	24 (12-32)	49 (38-54)	9.7×10^{-8}
Claudication	31 (19-35)	49 (38-54)	7.4×10^{-5}
Cognitive impairment/psychosis	27 (17-33)	49 (38-54)	9.9×10^{-5}
SDI item	MCS score		*p*-value
	Positive (Median (IQR))	Negative (Median (IQR))	
Scarring chronic alopecia	42 (29-51)	49 (39-54)	3.4×10^{-4}

Conclusion: We demonstrated that organ damage has negative effects on patient QOL, indicating the importance of preventing irreversible organ damage for maintaining QOL. Moreover, muscle atrophy/weakness, osteoporosis with fracture/vertebral collapse, claudication, cognitive impairment/major psychosis, and scarring chronic alopecia significantly correlated with QOL deterioration, suggesting that these items should be examined with special care in clinical practice.

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THU0286 THE SYSTEMIC LUPUS INTERNATIONAL COLLABORATING CLINICS (SLICC) FRAILTY INDEX (SLICC-FI) PREDICTS DAMAGE ACCRUAL IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) PATIENTS. DATA FROM A MULTI-ETHNIC, MULTI-CENTER US LUPUS COHORT

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Background: The Systemic Lupus International Collaborating Clinics (SLICC) Frailty Index (SLICC-FI) has been developed as a predictor of outcomes in SLE patients[1-3]. It combines disease activity, damage, comorbidities and health-related quality of life measures.
Objectives: To evaluate the SLICC-FI as a predictor of damage accrual in systemic lupus erythematosus (SLE) patients.
Methods: Patients from a multi-ethnic, multi-center US lupus cohort were included. Damage was ascertained with the SLICC/American College of Rheumatology (ACR) damage index (SDI) at last visit. The first visit in which the SLICC-FI could be derived was considered as the baseline visit. Univariable and multivariable Poisson regression models were performed to determine the association between the baseline SLICC-FI and last SDI, adjusted for sex, age at diagnosis, ethnicity, insurance, prednisone daily dose, antimalarial and immunosuppressive drug use at baseline. Age and gender were included a priori in the multivariable model, the other variables were included if they had a p<0.10 in the univariable models.
Results: Of the 503 patients included, 454 (90.3%) were female with mean (SD) age 37.1 (12.5) years at diagnosis; 174 (34.6%) were African-American, 144 (28.6%) were Caucasians, 86 (17.1%) Hispanics (Texas), and 99 (19.7%) were Hispanics (Puerto Rico). The mean (SD) baseline SLICC-FI was 0.26 (0.06). The final mean (SD) SDI score was 1.9 (2.2). Higher SLICC-FI scores at baseline predicted greater damage accrual in the univariable analysis [Estimate=5.058, (SE=0.498); p<0.0001]. The SLICC-FI remained associated with damage accrual in the multivariable model, after adjustment for possible confounders [Estimate= 3.561 (SE=0.538); p<0.0001].
Conclusion: The SLICC-FI predicts damage accrual in SLE patients from a multi-ethnic cohort, supporting the importance of this index in the evaluation of SLE patients, combining several aspects of the disease.
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THU0287 EVALUATION OF PREDICTIVE FACTORS OF WORSE PROGNOSIS IN LUPUS NEPHRITIS: FOCUS ON NEW PATHOGENETIC PATHWAYS

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Background: cytokine dysregulation plays an important role in the pathogenesis of Lupus Nephritis (LN) representing an attractive field of research aiming to find new pathways for new targeted therapies. IL-17, IL-23 axis seems to have a great influence in the development of LN.
Objectives: to evaluate the strongest prognostic factors in a cohort of patient with LN focusing on of the impact of IL-17, IL 23 axis as new pathogenetic pathway on renal outcome.
Methods: 91 patients with active LN at disease onset or disease flare were enrolled. Laboratory, immunological and disease activity data were collected at the baseline and at 6(T6),12(T12),24(T24) months and at the last follow-up(FU). 84 renal biopsies were evaluated according to ISN/RPS classification, assessing the activity and chronicity indexes and the active interstitial infiltrate using the BANFF score system. Baseline serum levels of IL-17 and IL-23 were assessed by ELISA in 37 patients.
Results: among the 84 renal biopsies evaluated 77% belonged to class III and IV according to ISN/RPS; 41,8% of patients had an active interstitial infiltrate<5%, 35.2% between 5% and 25% and 15,4% above 25%. Regarding immunological data 35,2% of patients revealed a seropositivity for antiphospholipid antibodies(APL+). The median serum level of IL-17 and IL-23 were 0.12±0.15 pg/ml and 27.7±9.12 pg/ml respectively. Using the ROC curves analysis we found a cut off value of 25.89 pg/ml for IL-23 for remission at T6. Among the 10 patients with a IL-23 level above this cut-off none achieved remission at T6 and the univariate analysis shows that a serum level of IL-23 above the defined cut-off was associated with an active interstitial infiltrate>5% at renal biopsy and with the development of persistent proteinuria. The analysis of IL-17 could not let us to find a cut off value for renal damage progression since a too much high number of patients had a null value. Nevertheless patients with more elevated serum levels of IL-17 at the baseline showed more elevated level of interstitial infiltrate at renal biopsy and a worse renal outcome overall. Finally we conducted an univariate and multivariate analysis for each renal outcome considered. We found that an inflammatory interstitial infiltrate>5% at renal biopsy and APL+ were associated with worse renal outcome in terms of early and persistent remission, chronic damage, persistent proteinuria, and renal flare both in univariate and multivariate analysis. Higher serum level of IL-23 was associated with persistent proteinuria, renal flare and tended to be associated to chronic renal damage and persistent renal activity.
Conclusion: interstitial inflammatory infiltrate and APL+ represent in our study the strongest predictors of worse renal outcome. An higher serum level of IL-23 was found to be a negative prognostic factor pointed out the possibility to consider the IL-17-IL 23 axis as a biomarkers of a more aggressive renal disease.
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THU0288 CANCER RISK IN PATIENTS WITH CUTANEOUS LUPUS ERYTHEMATOSUS AND SYSTEMIC LUPUS ERYTHEMATOSUS COMPARED TO THE GENERAL POPULATION: A DANISH NATIONWIDE COHORT STUDY

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Background: Research suggesting an elevated risk of cancer among patients with Systemic Lupus Erythematosus (SLE) has increased in recent years. Yet, the size of the overall cancer risk and the risk of respective cancer sites varies. Research examining the cancer risk of Cutaneous Lupus Erythematosus (CLE) patients remains limited. Therefore, in order to further guide and monitor patients with SLE and CLE, additional research estimating the risk of cancer is needed.

Objectives: To determine if patients with SLE or CLE have an increased risk of cancer compared to the general population, and furthermore to identify specific cancer types associated with increased risk.
Methods: This was an observational cohort study of 3424 SLE and 1886 CLE patients identified in The Danish National Patient Register (DNPR) from 1st January 1995 to 31st December 2014. The cohorts were followed up for cancer by linkage to The Danish Cancer Registry (DCR). Based on the age, sex, and calendar specific cancer rates from Denmark, standardized incidence ratios (SIRs) were calculated for the SLE and CLE groups, respectively.
Results: The SLE and CLE cohorts were followed for 27,676 and 13,048 person years, each group's average duration of follow-up being 8.1 and 6.9 years, respectively. Compared to the general population, the SIRs for the overall cancer (except non-melanoma skin cancer) risk was 1.45 (95%CI 1.30 to 1.62) in the SLE group and 1.35 (95%CI 1.15 to 1.58) in the CLE group. Both CLE and SLE patients had increased risks of hematological, pancreas and lung cancers. Liver, tongue/mouth/pharynx, non-melanoma skin cancer, oesophagus and meninges cancers were only increased in the SLE group.

Table 1. SIR for overall cancer in Danish SLE patients according to gender, time since diagnosis and age

Overall cancer except NMSC	Observed no. cancers	Expected no. cancers	PYRS	SIR (95% CI)
All	308	212.0	27,676	1.45 (1.30 to 1.62)
Female	246	170.0	23,925	1.45 (1.27 to 1.64)
Male	62	42.0	3751	1.48 (1.13 to 1.89)
Time since SLE diagnosis				
< 1 year	52	20.3	3213	2.56 (1.91 to 3.36)
1 to 4 years	103	70.3	10,270	1.47 (1.20 to 1.78)
4 to 9 years	83	64.4	8163	1.29 (1.03 to 1.60)
10+ years	70	57.0	6030	1.23 (0.96 to 1.55)
Age at SLE diagnosis				
< 40 years	11	9.0	7201	1.23 (0.61 to 2.20)
40 to 60 years	94	67.0	12,309	1.41 (1.14 to 1.73)
60+ years	203	137.0	8166	1.49 (1.29 to 1.71)

SLE = Systemic lupus erythematosus, NMSC = Non-melanoma skin cancer, PYRS = Person years, SIR = Standardized Incidence Ratio, CI = Confidence Interval

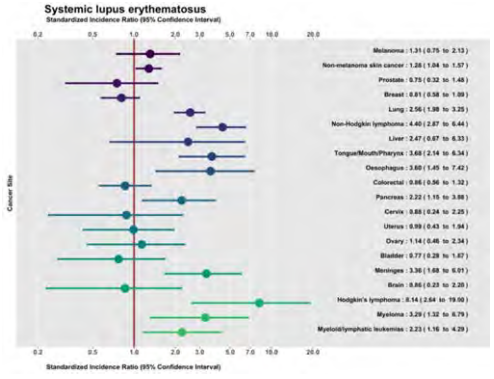
Table 2. SIR for overall cancer in Danish CLE patients according to gender, time since diagnosis and age

Overall cancer except NMSC	Observed no. cancers	Expected no. cancers	PYRS	SIR (95% CI)
All	155	114.7	13,048	1.35 (1.15 to 1.58)
Female	119	87.5	10,092	1.36 (1.13 to 1.63)
Male	36	27.2	2956	1.32 (0.93 to 1.83)
Time since CLE diagnosis				
< 1 year	29	12.8	1681	2.26 (1.51 to 3.24)
1 to 4 years	53	40.2	4955	1.32 (0.99 to 1.72)
4 to 9 years	41	34.2	3797	1.20 (0.86 to 1.63)
10+ years	32	27.4	2615	1.17 (0.80 to 1.65)
Age at CLE diagnosis				
< 40 years	6	2.9	2369	2.04 (0.75 to 4.43)
40 to 60 years	49	31.4	5962	1.56 (1.15 to 2.06)
60+ years	100	80.3	4717	1.24 (1.01 to 1.51)

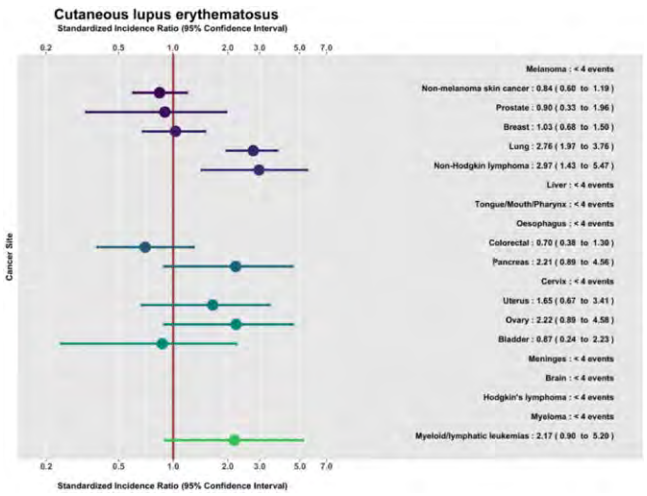
CLE = Cutaneous lupus erythematosus, NMSC = Non-melanoma skin cancer, PYRS = Person years, SIR = Standardized Incidence Ratio, CI = Confidence Interval

Graphs

SLE cancer sites: Standardized incidence ratios and corresponding 95% confidence intervals



CLE cancer sites: Standardized incidence ratios and corresponding 95% confidence intervals



Conclusion: The risk of overall cancer was significantly increased in patients with SLE and CLE. Hematological, pancreas and lung cancers were elevated in both groups, while certain virus-associated cancers and other sites were increased only among SLE patients. Awareness of cancer in patients with SLE and CLE should be considered, especially of symptoms from high-risk sites.
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THURSDAY, 04 JUNE 2020

Vasculitis

THU0289

PREDICTORS AND SEVERITY OF POST-THROMBOTIC SYNDROME IN VASCULAR BEHÇET'S DISEASE: RETROSPECTIVE MULTICENTER STUDY

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Background: Postthrombotic syndrome(PTS) defines chronic manifestations of venous insufficiency following deep vein thrombosis(DVT).It is the most frequent and disabling complication of DVT.
Objectives: Aim of the study is to describe clinical characteristics and predictors of PTS,severe PTS among Behçet's disease(BD)patients with known low extremity DVT.Also,to depict venous Doppler ultrasonography(US)findings and its association with the clinical characteristic and treatments.
Methods: This retrospective multicenter study included 205(166men,39women;mean age 39±9.5 years)BD patients with DVT history.The Villalta scale was used to assess the presence and severity of PTS.Doppler US of bilateral legs are performed within 1 week of clinical evaluation.Total number of vessels with reflux,thrombi,recanalization and collaterals were calculated and presented as scores.
Results: Of 205 BD patients with known DVT history; 127(62%) had PTS and 18% had severe PTS diagnosed by Villalta scale.(Table 1)

Table 1. Demographic and Clinical Characteristics of Patients

	Entire Study Population (n:205)	PTS present (n:127)	PTS absent (n:78)	P value
Sex(male,%)	166,81%	101,79.5%	65,83.3%	.584
History of smoking,%	105,52%	64,51.2%	41,53.2%	.895
BMI(n:198)	26.2±4.6	26.7±5	25.6±3.8	.123
Disease duration,years	9(5-15)	10(5-16)	8(5-13)	.205
DVT following time years	6(3-11)	7(3-11.5)	5(3-9)	.179
Current age	39±9.5	40.5±9.6	36.8±8.8	**.012**
Number of vascular events	1(1-2)	1(1-2)	1(1-2)	.723
VeinesQoL total	82±16.3	75.8±14	92.2±14.6	**<.001**
VeinesQoL symptom	37.5±9	34.4±8.3	42.6±7.7	**<.001**
Doppler Findings				
Iliofemoral thrombi	41,26.5%	32,35%	9,17%	**.014**
Bilateral involvement	62,43.4%	45,49%	17,33%	**.080**

All median values presented with interquartileranges(IQR)

Table 2 summarize multivariate logistic regression analyses for the risk of having PTS-moderate/severePTS.

Table 2. Multivariate Regression Analysis of presence of PTS

	Odds Ratio(with 95%CI)	P
Current age	1.05(1.01-1.10)	.048
BSAS	1.06(1.04-1.10)	.000
Bilateral Doppler USG involvement	2.81(1.18-6.67)	.019
Iliofemoral thrombi	2.74(1.02-7.38)	.045
Moderate/severe PTS		
	Odds Ratio	p
Body mass index	1.09(1.001-1.19)	.048
IS	0.10 (0.02-0.05)	.005

Severe PTS patients had increased reflux(p=.027) compared to mild group and decreased recanalization scores(p=.013)compared to moderate group(Figure1) Patients treated with AC+IS had increased recanalization(p:.078),collateral scores compared patients treated with only ISs(p=.004)(Figure2)

Conclusion: After an acuteDVT,BD patients faced with high risk of having PTS,-severe PTS.ISs decreases the risk of having PTS.Our results also suggest that AC treatment may decrease severity of PTS by increasing recanalization of thrombi.

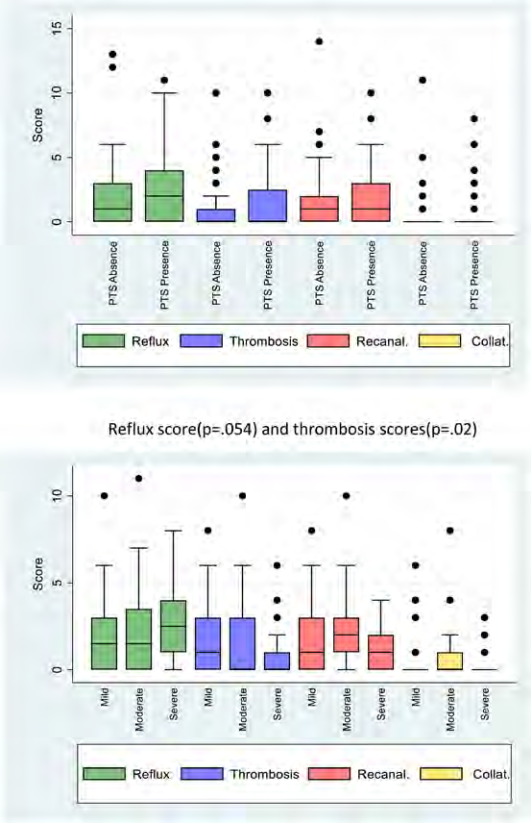


Figure 1. US scores for PTS absent and present groupReflux score(p=.054) and thrombosis scores(p=.02)

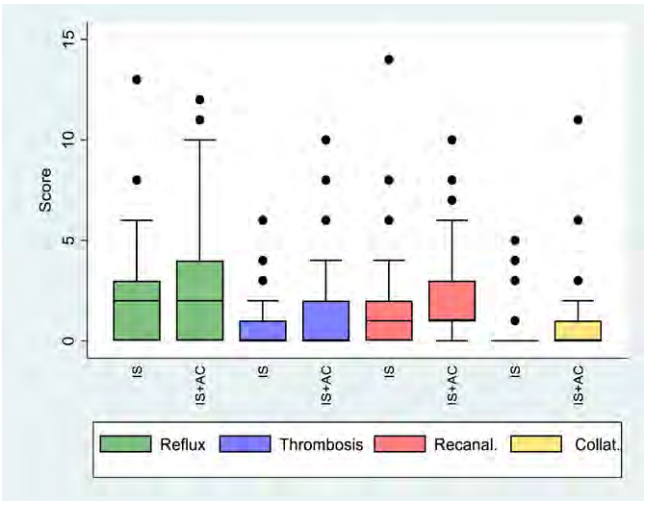


Figure 2. US scores for treatment groups

References:

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THU0290

THE EARLIER IMMUNOSUPPRESIVE TREATMENT MAY PREVENT MAJOR ORGAN INVOLVEMENT IN BEHCET DISEASE

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Background: Immunosuppressive(IS) agents are used for the treatment and prevention of major organ involvement in Behçet's disease.

Objectives: We aimed to investigate the rate of new major organ involvement development in patients under IS treatment for any reason during follow-up,and to compare the rate with patients never receiving IS treatments.

Methods: Data were collected retrospectively from files of patients who had a minimum follow-up duration of 6 months and were diagnosed with Behçet's disease according to the ISG criteria.Major organ manifestations were defined as ocular, vascular, neurologic, and gastrointestinal involvement.ISs were defined as azathioprine,cyclophosphamide, corticosteroids,interferon alfa,TNF inhibitors and cyclosporine.

Results: 640 patients were included in the study,of which 354 (55%) were male.The median age at diagnosis was 28(IQR: 23-35); the median follow-up duration was 5.75 (IQR: 3-8.91) years.Erythema nodosum was more common in females, but uveitis and vascular involvement were more prevalent among male patients (Table 1).198 (31%) patients had uveitis, 163 (26%) patients had vascular involvement, 63 (10%) patients had neurological involvement and 11(2%) patients had gastrointestinal involvement.The distribution of these 241 vascular events is displayed in Figure 1. 324 (51%) patients were not receiving any immunosuppressives when they developed their first major organ involvement.On the other hand, a total number of 348 (53%) patients were started on immunosuppressives [324 (51%) for major organ involvement, 24 (3%) for mucocutaneous involvement].38 (11%) of these patients developed a different major organ involvement (Table 2) under ISs. 23 of these 38 patients were on Azathioprine; eight were on Cyclophosphamide and Azathioprine, three were on interferon-alfa.Among patients receiving IS for any reason, 91 (28%) experienced relapses in the same organ.

Conclusion: During follow-up in our tertiary rheumatology center, about 40 % of patients receiving immunosuppressives, either experienced a new and different organ manifestation or had a relapse in the same organ.Our results suggest that earlier and more aggressive treatment may be necessary for the treatment of patients with BD to prevent both relapses and new major organ involvement in daily practice.

Table 1. Organ involvement among genders*

	Male (n= 354)	Female (n = 286)	p	All patients (n=640)
Oral ulcer	350 (99)	277 (99)	0.699	632 (99)
Genital ulcer	268 (76)	226 (81)	0.091	498 (78)
Erythema Nodosum	166 (47)	173 (62)	**<0.001**	343 (54)
Pathergy	191 (64)	145 (60)	0.433	341 (54)
Arthritis	59 (17)	55 (20)	0.308	114 (18)
Family history	70 (20)	74 (27)	0.051	144 (23)
Uveitis	130 (37)	68 (25)	**0.001**	198 (31)
Gastrointestinal	7 (2)	4 (1)	0.763	11 (2)
Vascular	124 (35)	37 (13)	**<0.001**	163 (26)
Neurologic	36 (10)	27 (10)	0.851	63 (10)
Parenchyma	14 (4)	17 (6)	0.220	31 (5)
Venous Sinus Thrombosis	18 (5)	10 (4)	0.356	28 (4)

* Values denote the number (%) of patients

Table 2. Distribution of major organ involvement developed in patients under and without immunosuppressive treatments

	No immunosuppressives (n= 302)	While on immunosuppressives (n= 38)
Vascular	99 (31)	16 (5)
Uveitis	150 (46)	9 (3)
Neurological	28 (9)	7 (2)
Gastrointestinal	4 (1)	3 (1)
Others†	21 (6)	3 (1)

* Values denote the number (%) of patients
†Simultaneous involvement of more than one organ

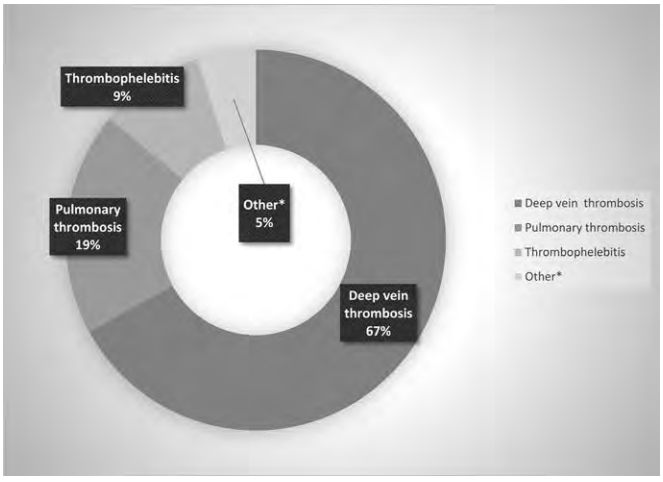


Figure 1. Distribution of vascular events*

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THU0291 IS GIANT CELL ARTERITIS REALLY GIANT CELL ARTERITIS? A HISTOLOGICAL REVIEW OF TEMPORAL ARTERY BIOPSIES FROM A UK DISTRICT GENERAL HOSPITAL

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Background: Despite the advent of newer imaging techniques, temporal artery biopsy (TAB) retains a key role in the diagnosis of giant cell arteritis (GCA). The classical histological description of GCA is that of granulomatous lesions characterized by a transmural inflammatory infiltrate[1]. Giant cells are typically noted in the internal elastic lamina. Vascular remodeling and structural changes are also frequently described, with intimal hyperplasia or fragmentation, fibrosis and calcifications[1].

Objectives: To identify the type and location of the inflammatory lesions in TAB-positive cases of GCA.
Methods: We conducted a retrospective analysis of all TABs undertaken at our unit between 2011- 2018 with clinical record review. TABs were performed by vascular, ophthalmology and ENT teams.
Results: 379 TABs were reviewed of which 68 (17.9%) were reported as positive and 10 (2.6%) were equivocal (presence of fragmentation and intimal thickening). Of the TAB-positive cases, 43 (63.2%) were greater than 1cm in keeping with the British Society for Rheumatology guidance and 65 (95.6%) were biopsies in patients on corticosteroids at the time of procedure. The following tables demonstrate the frequency of the type and location of the inflammatory lesions detected in TAB-positive cases of GCA.

Type of inflammatory lesion	Frequency
Chronic inflammatory infiltrate (lymphocytes, macrophages, plasma cells)	66
Giant cells	41
Intimal thickening	22
Intimal fragmentation	33
Location of inflammatory infiltrate	Frequency
Full thickness	32
Intima only	7
Intima and Media only	3
Media only	7
Media and Adventitia only	8
Adventitia only	4
Intima and Adventitia only	3
Not recorded	4

Conclusion: Only 60% of our TAB-positive biopsies had giant cells present. Although perhaps surprisingly low, this finding is similar to other studies [1,2]. It emphasises the need to review the body of a report as well the conclusion. Other non-giant cell features present in positive reported biopsies may suggest a less certain diagnosis and prompt clinical review. There was considerable variablity in the style of reporting. With no standardised scoring system in place, the variable spectrum of inflammation and differences in reporting, there is the potential for inconsistencies amongst pathologists in interpreting and recording TAB results. Consistent reporting templates and close collaboration between rheumatologists and pathologists is needed to help correlate clinical, laboratory and imaging findings.

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THU0292 THE PERFORMANCE OF THE SUGGESTED EXPANSION OF THE 1990 ACR CRITERIA WITH THE ORIGINAL ACR 1990 CRITERIA IN GIANT CELL ARTERITIS PATIENTS

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Background: The ACR Giant Cell Arteritis (GCA) criteria from 1990 includes items of clinical findings and biopsy results (1). Since that time better imaging modalities as ultrasound (US), magnetic resonance imaging (MRI) and positron emission tomography (PET) have challenged the former gold standard status of biopsy diagnosing GCA (2). In 2017 suggested expansion of the ACR criteria was proposed including these imaging modalities and a more nuanced set of clinical features (3).
Objectives: To test the sensitivity of the suggested expanded GCA criteria against the original ACR 1990 criteria in a retrospective cohort of patients diagnosed with GCA.
Methods: We included all patients diagnosed with GCA in our rheumatology clinic between 2006 and 2018 in Agder County in Southern Norway.

A predefined protocol was used when reviewing the medical records in GCA patients at the time of diagnosis. Data collected included the separate items for the original and the suggested expansion of the ACR 1990 criteria. We calculated the sensitivity of both criteria sets and recorded the frequency and absolute numbers of the single criteria items as shown in table 1.

Table 1. Comparing the original with the proposed expansion of the ACR 1990 criteria

	Original Criteria	N	Suggested expansion Criteria	n	N
Criterion 1	Age ≥ 50 yrs	77	Age ≥ 50 yrs	77	77
Criterion 2	New onset of or new type of localized pain in the head	48	New onset of or new type of localized pain in the head	48	61
			Visual symptoms	14	
			Sight loss	2	
			PMR	22	
			Constitutional symptoms	2	
			Tongue claudication	5	
			Jaw claudication	16	
Criterion 3	Abnormal temporal artery palpation tenderness, decreased pulse	26	Abnormal of extracranial arteries tenderness to palpation, decreased pulse	26	30
			Bruits over arteries	6	
Criterion 4	ESR > 50 mm/h	62	ESR > 50 mm/h	62	72
			CRP > 10 mg/l	72	
Criterion 5	Abnormal artery biopsy	22/37	Abnormal artery biopsy	22/37	68
			US	61/69	
			MRI	6/10	
			F-FDG PET	4/4	

Results: A total of 77 patients (22 men and 55 Women) with a diagnosis of GCA were identified. Mean age was 69.2 years. The table below shows the absolute number of patients fulfilling the separate criteria for the ACR 1990 and the suggested expansion criteria. Patients were usually not exposed to all submodalities of criterion 5. The denominator for item 5 in the table displays the number of assessments performed for biopsy and the separate imaging modalities.

The number of patients fulfilling the original ACR 1990 criteria was 51 (66.2%) and for the suggested expansion criteria 75 (97.4%). All patients fulfilled the age criterion. For the original ACR 1990 criteria, 62.3% met criterion 2, 33.8% criterion 3, 80.5% criterion 4 and 28.6% criterion 5, whereas for the suggested expansion criteria the percentages was 79.2%, 39.0%, 93.5% and 88.3% respectively.

Conclusion: The proposed expansion of the ACR 1990 criteria had a much higher sensitivity (97.4%) than the original criteria (66.2%) tested in a clinical cohort of GCA patients. The single most important parameter increasing sensitivity was US examination however also new clinical features and C-reactive protein measurement contributed to increase the sensitivity.

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THU0293

PREDICTORS OF LONG-TERM THERAPY WITH GLUCOCORTICOID IN POLYMYALGIA RHEUMATICA

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Background: Polymyalgia rheumatica (PMR) is a common inflammatory condition of elderly persons. Clinical symptoms respond to low-dose glucocorticoids (GC), but treatment is often required for several years. 2015 EULAR/ACR recommendations[1)] recommend considering early introduction of methotrexate (MTX) in addition to GC, particularly in patients at a high risk for relapse and/or prolonged therapy. However, risk factors for prolonged therapy are not clear yet.

Objectives: We investigated predictive factors which corresponded to the long-term GC therapy.

Methods: This was a retrospective study in a single general hospital in Japan. We reviewed the medical records of the Japanese patients with PMR between April 2011 and January 2020. Diagnosis of PMR was based on Bird's criteria or 2012 EULAR/ACR Classification Criteria[2)]. All patients were treated with prednisolone (PSL), according to the BSR and BHPR guidelines[3)], for more than 6 months. Patients treated with MTX and accompanied by the giant cell arteritis were excluded from this study. Relapse was defined as the reappearance of symptoms associated with elevated C-reactive protein (CRP) levels in patients receiving GC that required an increase in GC dose. Remission was defined as the absence of clinical symptoms and normal CRP with discontinuation of GC. We compared the clinical findings, laboratory data at baseline and clinical course between those who achieved remission within 2 years (early-remission group) and those who required GC therapy for more than 2 years (long-therapy group). Comparisons between groups were made using Student's t-test and chi-square test (IBM SSPE statistics version 26). This study was approved by the ethics committee of Tokyo Medical University (T2019-0079).

Results: As of January 2020, 89 patients have been treated with PSL for more than 6 months. 50 patients have achieved a remission, 29 were undergoing treatment, and 10 have transferred to other hospitals or died (Table 1). The median time required for the patients to achieve remission was 16 months (Interquartile Range 12-21). After one-year GC therapy, remission was achieved in 14% (11/77), 66% (41/62) after 2-year, 84% (47/56) after 3-year, and 91.0% (49/54) after 4-years. Forty-one patients, who achieved remission within 2 years, were included in the early-remission group. Twenty-one were included in the long therapy group (Table 1). There were no differences in sex, age at onset, body mass index, clinical features, and serum albumin at diagnosis. Serum CRP of long-therapy group was significantly higher than those of the early-remission group (Table 2). Mean relapse times in the full follow-up times were 0.4 in the early-remission group and 3.1 in the long-therapy group. Multivariate logistic regression analysis showed that history of relapse till 6 months was significant predictors of the long-term GC therapy (odds ratio, 6.48; 95%CI 1.44-29.12).

Conclusion: The remission rates of our study are lower than those of the previous reports. We have tapered GC gradually according to the BSR and BHPR guidelines[3)]. However, some patients need the long-term therapy for more than 2 years. We might consider additional MTX therapy in patients who experience a relapse during the first six months.

Table 1 Summary of patients with diagnosis with PMR
GC therapy more than 6 months

		Duration of GC therapy	
		less than 2 years	more than 2 years
Remission	n=50	41	9
Under treatment	n=29	19	10
Changing hospital or death	n=10	8	2
Patients included in the analysis		Early-remission n=41	Long-treatment n=21

PMR, polymyalgia rheumatica; GC, glucocorticoid

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Table 2 Clinical findings in patients of 2 groups

		Early-remission n=41		Long-therapy n=21		p
Demographic, clinical, and laboratory findings at diagnosis						
Woman	n (%)	20	(48.8)	12	(57.1)	0.5
Age: years	mean (SD)	74.2	(7.8)	73.7	(5.8)	0.8
Body weight, kg	mean (SD)	55.3	(11.18)	52.1	(9.23)	0.3
Body mass index, kg/m^2	mean (SD)	22.7	(4.03)	20.7	(3.10)	0.06
Fever	n (%)	10	(24.4)	7	(33.3)	0.5
Body weight loss	n (%)	13	(31.7)	10	(47.6)	0.2
Peripheral edema	n (%)	16	(39.0)	10	(47.6)	0.3
Serum C-reactive protein, mg/dL	mean (SD)	6.4	(4.17)	8.8	(4.06)	0.03
Serum albumin, mg/dL	mean (SD)	3.2	(0.47)	3.2	(0.57)	0.7
Treatment and clinical course						
Starting dose of PSL: mg/day	mean (SD)	12.6	(4.09)	14.5	(3.94)	0.1
mg/kg/day	mean (SD)	0.24	(0.084)	0.28	(0.079)	0.1
Mean duration of GC treatment	month (SD)	14.2	(4.59)	43.4	(21.98)	<0.01
Achieving remission	n (%)	41	(100)	9	(42.9)	
Relapse: times	mean (SD)	0.4	(0.70)	3.1	(2.06)	<0.01
Relapse till 6 months	n (%)	3	(7.3)	8	(38.1)	<0.01

PSL, prednisolone; GC, glucocorticoid; SD, standard deviation

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THU0294 THE DIFFERENCES IN THE CLINICAL SPECTRUM OF CRYOGLOBULINEMIC VASCULITIS BETWEEN SJÖGREN'S SYNDROME AND HCV HEPATITIS

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Background: Cryoglobulinemic vasculitis (CV) is a serious complication of Sjögren's syndrome (SS) and is closely associated with type II IgMk cryoglobulins. CV has been well documented in HCV patients without SS, and shares common features with CV in SS. So far, few studies have described the clinical picture of CV in HCV negative SS, but the number of studied patients was rather small and CV was not well defined. To better describe the clinical spectrum of CV in SS and explore the differences compared to HCV-related CV, a large cohort of well characterized patients is required.
Objectives: To study the clinical phenotype of CV in HCV-negative SS patients, in a large cohort of well characterized patients, after applying stringent classification CV criteria and in comparison with the classical CV of HCV patients.
Methods: From a total cohort of 1997 consecutive SS patients who fulfill the 2016 EULAR/ACR criteria and are followed up in 5 clinical centers ([Universities of **U**dine, **P**isa and **A**thens, **H**arokopio and **I**oannina, (**UPAHI)**], those who fulfil the 2011 classification criteria for CV were identified and compared with matched HCV-CV patients according to age and gender. Glandular, extra-glandular manifestations and serologic features were compared between the 2 CV groups. Statistical analysis for categorical variables was performed by Fisher exact or chi-square tests and for continuous variables with t test or Mann-Whitney accordingly.
Results: Among the 1083 SS patients who have been evaluated for cryoglobulins, 114 (9,8%) were found positive. Seventy-one (6,5%) SS patients met the 2011 CV criteria while 44 patients presented with type II IgMk cryoglobulinemia without CV. Sixty nine of 71 (97%) SS related CV patients were females and 2 of 71 (3%) males. Forty eight of 71 (68%) had SS disease onset >35 and <65 years old while 14/71 (19,7%) and 9/71 (12,7%) had SS disease onset <35 and >65 years old respectively. The most common clinical manifestations of CV among SS patients were purpura (90%) followed by arthralgias (70%), fatigue (59%), Raynaud's phenomenon (48%), lymphadenopathy (31%), peripheral neuropathy (22,3%), vasculitic ulcer (11,3%) and glomerulonephritis (11,3%). Interestingly, almost 50% of SS related CV patients developed lymphoma and displayed high frequency of strong predictors including purpura, low C4 complement (88,6%) and salivary gland enlargement (SGE). Compared to HCV-CV patients, SS-CV patients had higher frequency of sicca manifestations, SGE, fatigue, arthritis, Raynaud's phenomenon, lymphadenopathy, type II IgMk cryoglobulins and lymphoma.
Conclusion: The prevalence of cryoglobulinemia and CV among SS patients is about 10% and 6-7% respectively. SS-CV patients are mainly middle-aged females with purpura as the main clinical manifestation, and up to one half of them may develop lymphoma, which is rarer in HCV-CV. Compared to HCV-CV patients, SS patients with CV have more frequently sicca symptoms, SGE and type II IgMk cryoglobulins.
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THU0295 LOW IMMUNOGENICITY IN PATIENTS WITH GIANT CELL ARTERITIS TREATED WITH TOCILIZUMAB: 3-YEAR RESULTS FROM THE RANDOMIZED CONTROLLED PORTION AND OPEN-LABEL FOLLOW-UP OF A PHASE 3 TRIAL

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Background: Tocilizumab (TCZ) has low immunogenicity in patients with rheumatoid arthritis.[1] The risk for immunogenicity remains to be determined in patients with giant cell arteritis (GCA) treated with TCZ. TCZ administered subcutaneously every week (QW) or every other week (Q2W) with 26-week prednisone tapering was superior to placebo (PBO) plus 26-week (PBO+26) or 52-week (PBO+52) prednisone tapering for the achievement of sustained remission in patients with GCA in the 52-week, double-blind part 1 of the GiACTA trial.[2] Part 2 was a 2-year open-label, long-term follow-up in which patients were treated at the investigators' discretion; part 2 treatment could include initiation/termination of TCZ QW with or without glucocorticoids or methotrexate.
Objectives: To investigate immunogenicity of TCZ QW and Q2W regimens in patients with GCA in combination with a 26-week prednisone taper regimen versus PBO+26 or PBO+52 over the course of the GiACTA study in the randomized controlled part 1 and long-term follow-up part 2.
Methods: In parts 1 and 2 combined, anti–TCZ antibodies (ADA) and corresponding pharmacokinetic (PK) parameters were assessed in serum samples taken at scheduled times at weeks 0, 8, 24, 36, 52, 76, 100, 136, and 156 or at early withdrawal. Additional assessments were made for patients who interrupted blinded TCZ treatment for ≥4 weeks in part 1 and those who withdrew from the study because of anaphylaxis/hypersensitivity. All samples were tested by screening assay, and samples that were ADA positive were further analyzed by a confirmation assay to verify specificity. If the confirmation assay was positive, 2 additional tests were performed to characterize the detected ADA: a neutralizing assay to test the neutralizing potential of ADAs and an assay to determine whether the detected ADA were of the IgE isotype. Proportions of patients in whom ADA developed were summarized for the safety population.
Results: Among evaluable patients (had baseline and ≥1 postbaseline ADA assessments and received ≥1 dose of study treatment) in part 1, ADA developed in 1 of 95 (1.1%) and 3 of 46 (6.5%) patients after TCZ QW and Q2W dosing, respectively. One of 49 (2.0%) and 1 of 47 (2.1%) in the PBO+26 and PBO+52 groups, respectively, tested positive for ADA but had not received TCZ and were considered false positives. In parts 1 and 2 combined, among 199 patients who received ≥1 dose of TCZ, 193 (97%) were evaluable (Table); TCZ-induced ADA developed in 13 of these patients (6.7%) postbaseline (4 during part 1, 9 during part 2). Of these 13 patients, 8 (4.1%) had ADA with neutralizing potential and 1 (0.5%) had IgE ADA. Most TCZ-induced ADA were transient. There was no clear impact of TCZ-induced ADA on TCZ PK (Figure). No patients with TCZ-induced ADA experienced anaphylaxis, hypersensitivity reactions, or injection site reactions, and none withdrew because of lack of efficacy
Conclusion: In patients with GCA, treatment-induced ADA developed in a minority of patients and had no impact on TCZ PK, efficacy, or safety. The

Table. Immunogenicity in Patients Who Received TCZ (part 1 + part 2)

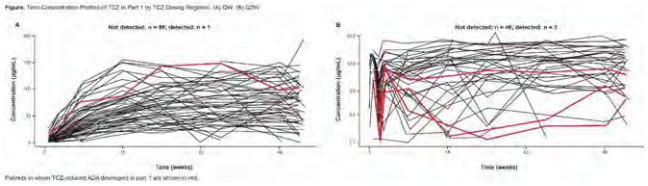
	Patients Who Received TCZ N = 199
Baseline	
Evaluable patients	194 (97.5)
Positive screening assay	12 (6.0)
Positive confirmation assay	6 (3.0)
Postbaseline	
Evaluable patients	193 (97.0)
Treatment-induced ADA	13 (6.7)
Characterizaton of ADA	
Neutralizing potential	8 (4.1)
IgE	1 (0.5)

Data are number (%) of patients based on N at baseline and on number of evaluable patients postbaseline.

immunogenicity of subcutaneous TCZ treatment was low, consistent with that observed in patients with RA.

References:

[1] Burmester GR et al. *Ann Rheum Dis* 2017;76:1078-85.
[2] Stone JH et al. *N Engl J Med* 2017;377:317-28.



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THU0296 PROTEIN PROFILING IN INDIVIDUALS BEFORE ONSET OF ANCA-ASSOCIATED VASCULITIS

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Background: Etiology and pathogenesis of ANCA-associated vasculitis (AAV) is multifactorial and understanding of the processes leading from a healthy immune system to autoimmunity and on to debut of symptoms in AAV is rudimentary.

Objectives: To identify inflammatory proteins related to the early processes preceding AAV development, and potential novel biomarkers, using large-scale protein analyses

Methods: The Swedish National Patient Register of in-patient carevand the Swedish Cause of Death Register with discharge diagnosis from ICD-9 and-10 for AAV were co-analysed with the registers of 4 different blood biobanks to identify AAV individuals with available samples predating onset of symptom. Of the pre-AAV cases 86 (36 male, 50 female; mean age (SD); 51.9 (16.9) years) were identified with at least one plasma or serum sample (28 plasma, and 100 serum) pre-dating symptom onset (mean (SD); -4.3 (3.1) years), and 14 had 2-3 samples. Serum and plasma control samples matched for sex, age and sampling date were identified (n=198; 82 male, 116 female; mean age (SD); 51.9±15.9 years). The samples were analysed for levels of 92 proteins using proximity extension assay (OLINK inflammation panel, SciLifeLab, Uppsala, Sweden). Data were analysed using routine statistical methods, random forest and Partial Least square-discriminant analysis (PLS-DA).

Results: As previously described for the assay significant difference between plasma and serum samples were observed both in pre-AAV individuals and controls. In pre-AAV plasma samples significantly increased concentrations of interleukin (IL)-2, chemokine ligand (CCL)-4, fibroblast growth factor (FGF)21, IL-4 and CCL20 were found closer to symptom onset, (<5 years) than later (> 5 years) and compared with controls. In serum tumor necrosis factor receptor superfamily member (TNFRSF)9, CXCL9, osteoprotegerin and vascular endothelial growth factor-A were significantly increased <5 years before onset vs. later (>5 years) and compared with controls. PLS-DA score scattered plot separated the pre-AAV individuals from healthy controls (R^2=0.26), with significantly increased levels of CCL23, CXCL5, and matrix metalloproteinases-1 (MMP-1), *transforming growth factor*-ß, orosomucoid, en-rage (S100A12) and IL-7 and decreased FGF-19 level in serum. Binary logistic regression analyses comparing tertiles for these proteins confirmed significantly increased odds ratios for disease development of CCL23, CXCL5 and MMP-1. The findings were confirmed in random forest analysis where these factors were among the 20 most discriminatory factors between pre-symptomatic AAV and controls.

Conclusion: In serum samples collected years before symptom onset of AAV, proteins involved in immune system activation were increased, suggesting that the inflammatory process is initiated long before clinical manifestations of the disease appear. These findings propose the elevated proteins as novel biomarkers for disease progression.

References:

[1] Watts et al. Ann Rheum Dis 2007;66:222-22

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THU0297 SERIOUS INFECTIONS IN 134 PATIENTS WITH GIANT CELL ARTERITIS WITH TOCILIZUMAB IN CLINICAL PRACTICE. FREQUENCY, TYPE AND CLINICAL ASSOCIATIONS

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Background: Infections are the most common adverse event of Tocilizumab (TCZ) in Giant Cell Arteritis (GCA). In GiACTA study **(1),** serious infections were observed in 7% (9.6/100 patient-years) of patients who received TCZ weekly. Randomized clinical trials (RCTs) are conducted under highly standardized design excluding some real-world patients. Therefore, adverse events may be underestimated in RCTs. In our series of real-life, serious infections occurred in 11.9% (10.6/100 patient-years) **(2).**

Objectives: In a wide series of GCA of clinical practice treated with TCZ, we assess the frequency, type and predisposing factors of serious infections.

Methods: Multicenter study of 134 patients diagnosed with GCA, all of them refractory to conventional therapy, treated with TCZ. Serious infection was considered when a life-threatening infection, fatal, or requiring hospitalization occurred, intravenous antibiotics were required, or the infectious process led to persistent or significant disability.

Results: 16 of 134 (11.9%, 10.6/100 patient-years) patients developed serious infections during follow-up. The most frequent infections were pneumonia (n=4), urinary tract infection (n=4), and facial herpes zoster (n=2). At TCZ onset, serious infections were more frequent in older patients (74.3±9.6 vs 72.9±8.7 years), with a longer GCA evolution (20 [4.3-45.6] vs 13 [5-29.3] months), with visual manifestations (43.75% vs 17.8%) and a higher dose of prednisone at TCZ onset (30.4±15.5 vs 21.1±16.1 mg/day) (TABLE). Presence of comorbidities were similar in both groups. 13 of the 16 patients who had infections received a dose of prednisone greater than 15 mg/day (16.3/100 patient-years) compared to 3 patients under treatment with less than 15 mg/day of prednisone (4.2/100 patient-years).

Conclusion: The age, GCA duration, ocular involvement and the dose of glucocorticoids, at TCZ onset, seem to be predisposing factors related to an increased risk of developing serious infections in GCA patients.

TABLE

	SERIOUS INFECTIONS (n=16)	WITHOUT SERIOUS INFECTIONS (n=118)	p
BASAL FEATURES AT TCZ ONSET			
GENERAL FEATURES			
Age, years, mean± SD	74.3±9.6	72.9±8.7	0.552
Sex, female/male n(%)	13/3	88/30	0.760
Time from GCA diagnosis to TCZ onset (months), median [IQR]	20[4.3-45.6]	13[5-29.3]	0.604
COMORBIDITIES			
Hypertension, n(%)	9(56)	86(73)	0.551
Diabetes, n(%)	3(19)	39(33)	0.677
Chronic kidney disease, n(%)	3(19)	27(23)	0.512
CLINICAL FEATURES OF GCA			
PMR, n(%)	9(56.25)	64(54.2)	0.879
Aortitis, n(%)	5(31.25)	53(45)	0.301
Visual manifestations, n(%)	7(43.75)	21(17.8)	**0.017**
CORTICOSTEROIDS AT TCZ ONSET			
Prednisone dose mg/d, mean (SD)	30.4±15.5	21.1±16.1	**0.031**

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[1] Stone JH, et al. N Engl J Med. 2017; 377:317-28.

[2] Calderón-Goercke M et al. Semin Arthritis Rheum 2019 Aug;49(1): 126-135.

Disclosure of Interests: Monica Calderón-Goercke: None declared, D. Prieto-Peña: None declared, Santos Castañeda: None declared, Clara Moriano: None declared, Elena Becerra-Fernández: None declared, Marcelino Revenga: None declared, Noelia Alvarez-Rivas: None declared, Carles Galisteo: None declared, Águeda Prior-Español: None declared, E. Galindez: None declared, Cristina Hidalgo: None declared, Sara Manrique Arija: None declared, Eugenio de Miguel Grant/research support from: Yes (Abbvie, Novartis, Pfizer), Consultant of: Yes (Abbvie, Novartis, Pfizer), Paid instructor for: yes (AbbVie, Novartis, Pfizer, MSD, BMS, UCB, Roche, Grunental, Janssen, Sanofi), Speakers bureau: yes (AbbVie, Novartis, Pfizer, MSD, BMS, UCB, Roche, Grunental, Janssen, Sanofi), Eva Salgado-Pérez: None declared, Vicente Aldasoro Speakers bureau: Roche, Abbvie, MSD, UCB, Pfizer, Menarini, Grunenthal, Gebro, Novartis, Janssen, Ignacio Villa-Blanco Consultant of: UCB, Speakers bureau: Novartis, MSD, Lilly, Susana Romero-Yuste: None declared, J. Narváez: None declared, Catalina Gomez-Arango: None declared, Eva Perez-Pampín: None declared, Rafael Melero: None declared, Francisca Sivera: None declared, Carlos Fernández-Díaz Speakers bureau: Brystol Meyers Squibb, Alejandro Olive: None declared, María Álvarez del Buergo: None declared, Luisa Marena Rojas: None declared, Carlos Fernández-López: None declared, Francisco Navarro: None declared, Enrique Raya: None declared, Beatriz Arca: None declared, Roser Solans-Laqué: None declared, Arantxa Conesa: None declared, Carlos Vázquez: None declared, Jose Andrés Román-Ivorra: None declared, Pau Lluch: None declared, Paloma Vela-Casasempere: None declared, Carmen Torres-Martín: None declared, Juan Carlos Nieto Speakers bureau: Pfizer, Abbvie, MSD, Novartis, Janssen, Lilly, Nordic Pharma, BMS, Gebro, FAES Farma, Roche, Sanofi, Carmen Ordas-Calvo: None declared, Cristina Luna-Gomez: None declared, Francisco J. Toyos Sáenz de Miera: None declared, Nagore Fernández-Llanio: None declared, Antonio García: None declared, Carmen González-Vela: None declared, Javier García-Fernández: None declared, Patricia Vicente-Gómez: None declared, Ángel García-Manzanares: None declared, Norberto Ortego: None declared, Francisco Ortiz-Sanjuán: None declared, Montserrat Corteguera: None declared, J. Luis Hernández: None declared, Miguel A González-Gay Grant/research support from: Pfizer, Abbvie, MSD, Speakers bureau: Pfizer, Abbvie, MSD, Ricardo Blanco Grant/research support from: AbbVie, MSD, and Roche, Speakers bureau: AbbVie, Pfizer, Roche, Bristol-Myers, Janssen, and MSD

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THU0298 SWITCH OR SWAP STRATEGY IN TAKAYASU ARTERITIS PATIENTS FAILING TNFA INHIBITORS?

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Background: biologic drugs (bDMARD), especially anti-TNFα (TNFi), are used in refractory TA patients. Up to 60% of patients are eventually switched to a different bDMARD because of inefficacy. No data are available on which strategy (switch or swap) is more efficient in this setting.

Objectives: to evaluate whether switch or swap strategy can be more effective in TA patients failing TNFis.

Methods: TA patients treated with bDMARDs after TNFi failure were identified from 3 referral centres. Patients were classified as "switch" if treated with a different TNFi (infliximab, IFX, etanercept, ETN, golimumab, GOL, adalimumab, ADA) or "swap" if treated with a non-TNFi bDMARD (tocilizumab, TCZ, ustekinumab, USK). Baseline features and disease outcome (number of patients with NIH score <2, steroid dose reduction (SDR), disease relapses and vascular interventions) at month 6 and month 12 after 2nd bDMARD introduction were analyzed. Non parametric tests were used.

Results: 24 TA patients were identified. TNFi (IFX= 13; ADA= 8; ETN= 1; GOL= 2) was withheld after a median of 19 (8.5; 38) months (in 9 patients <12 months) for inefficacy in 19 (79%) patients and side effects in 5 (21%) patients. 11 (46%) patients were switched and 13 (54%) patients were swapped (12 to TCZ, 1 to USK). Baseline features at 2nd bDMARD start are summarized in Table 1. 2nd bDMARD retention at month 6 was comparable between switch (8, 73%) and swap (10, 77%) patients, p=1. Reasons for discontinuation were: inefficacy in 5 patients, allergic reaction in 1 switch patient. 5 (45%) switch and 6 (46%) swap patients had a NIH<2 (p=1). Median SDR was similar: 3.75(0-19.69) in swap and 4.37(1.87-10) mg daily in switch, p=0.829. Also at month 12, 2nd bDMARD retention was comparable: 7 (64%) switch vs 7 (54%) swap, p=0.210. Discontinuation reason was inefficacy in all cases. 6 (54%) switch and 4 (30%) swap patients had a NIH<2 (p=0.222). Median SDR from baseline was 3.75(0.62-7.5) in switch and 1.25 (0-6.25) in swap,p=0.620. 12 patients experienced a relapse within the first year: 10 (77%) swap and 2 (18%) switch patients, p=0.074. 3 patients underwent vascular interventions within the first year: 2 (18%) switch and 1 (8%) swap patient, p=0.576.

Table 1. Disease features of switch and swap TA patients at 2nd bDMARD start.

	Switch (11 patients)	Swap (13 patients)	p value
Age (years)	39 (31-54)	37 (32-46)	0.613
Sex (female,%)	82	100	0.199
Numano			
-*I*	2	1	
-*IIa*	2	2	
-*IIb*	1	1	
-*III*	1	1	
-*IV*	0	2	
-*V*	5	6	
Disease duration (years)	4 (2 -6)	3 (2 – 8)	0.743
Previous csDMARD (%)	91	100	0.458
TNFi duration (months)	25 (9 – 27)	16 (9 – 44)	0.813
Steroid dose (mg daily)	15 (8.75 – 22.5)	15 (10 – 25)	0.726
Current csDMARD, n(%)	10 (91)	9 (70)	0.327
- Methotrexate	6	6	
- Azathioprine	1	2	
- Sirolimus	1	0	
- Salazopyrin	0	1	
- Cyclophosphamide	1	0	
- Mycofenolate	1	0	
NIH ≥2 (%)	73	61	0.679
CRP (mg/L)	34 (14 – 73)	24 (10 – 45)	0.604
ESR (mm/1h)	43 (35 – 56)	51 (35 – 68)	0.729

Conclusion: our retrospective study suggests that in first-line TNFi failure TA patients both switch and swap strategies are seemingly effective.

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THU0299

MYOCARDIAL INVOLVEMENT IN TAKAYASU ARTERITIS PATIENTS ASSESSED BY MAGNETIC RESONANCE IMAGING AND ITS RELATION WITH DISEASE ACTIVITY

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Background: Cardiac involvement in Takayasu arteritis(TA) is the major cause of morbidity and mortality. [1] Cardiovascular magnetic resonance (CMR) is an excellent modality for the assessment of myocardial involvement. Studies have shown subclinical myocardial scarring in 25-27% of patients.[2,3] There is no such study from India.

Objectives: To evaluate the prevalence of myocardial involvement in TA, as detected by CMR and its correlation with disease activity score (ITAS 2010 and ITAS-A).

Methods: Patients classified as Takayasu arteritis according to Sharma et al. criteria [4] were included after an informed consent. Demographic, clinical, laboratory data were documented in the predesigned proforma. CMR was done on a dedicated CMR machine. Disease activity was recorded by ITAS2010 and ITAS-A.[5] Ethical clearance has been obtained from the ethics committee of the institute (INT/IEC/2018/001538).

Results: In the present study, 37 TA patients were included. Mean(±SD) age was 29 ±11 years. Female to male ratio was 3:1. The most frequent presenting symptom was upper limb claudication (49%), and vessel involved was left subclavian and descending thoracic aorta(75% each). Of the total cohort, 65% had hypertension, 35% had dyslipidemia and 19% had valvular involvement. Five patients (14%) had myocardial involvement as detected by CMR. Three (8%) patients had late gadolinium enhancement(LGE) on CMR suggestive of myocardial fibrosis. In the current study, both the CMR and echocardiography performed equally in detecting various valvular heart disease, whereas only CMR had detected subclinical myocardial fibrosis in two patients. Details of different risk factors and relation with disease activity provided in table 1.

Conclusion: To the best of our knowledge, this is the largest cohort on CMR in TA. Prevalence of subclinical myocardial involvement in Indian patients was much less(8% vs 25-27%) compared to the previous studies. The higher percentage of LGE detected by the earlier studies may be a reflection of cumulative damage with increasing age, prolonged hypertension, and disease duration. Myocardial involvement trend towards early age of onset, less disease duration, lack of classical risk factors, and more with disease activity. Judicious use of CMR may help in detecting subclinical myocardial involvement.

Table 1. Relation of different risk factors with myocardial heart disease.

Parameters	MHD - (n=32)	MHD + (n=5)	p
Disease duration>5 yr	13(41)	2(40)	0.98
Age at onset<18 yr	7(22)	3(60)	0.07
BMI>23kg/m^2	19(59)	1(20)	0.1
Hb<12gm/dl	16(50)	2(40)	0.68
Platelets>450x 10^9/L	4(13)	0(0)	0.40
ESR>20 mm in 1st hour	28(88)	4(80)	0.65
CRP>10 mg/dl	16(50)	4(80)	0.21
Cholesterol>200 mg/dl	10(31)	1(20)	0.61
LDL>130 mg/dl	9(28)	0(0)	0.17
BNP>125 pg/ml	11(34)	3(60)	0.27
ITAS2010-Active	17(53)	3(60)	0.77
ITAS-A-Active	11(34)	3(60)	0.27

[MHD: myocardial heart disease]

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THU0300

RISK FACTORS FOR COMPLICATIONS AND REFRACTORY COURSE IN PATIENTS WITH ANCA-ASSOCIATED SYSTEMIC VASCULITIS

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Background: ANCA-associated systemic vasculitis (AAV) is characterized by a high incidence of complications and high mortality. The most significant complications during the first 3 years of the disease are infectious and cardiovascular. Development of chronic kidney disease also impairs the prognosis of AAV. Refractory to induction therapy can significantly increase the severity of organ lesions in patients with AAV.

Objectives: The aim of this study was to determine risk factors for complications and refractory course in patients with AAV.

Methods: Patients with granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA) were observed during the first 3 years of the disease and included in this study between 2010 and 2018. Most common infectious complications requiring inpatient treatment were pneumonia, mycosis, sepsis, purulent arthritis, purulent otitis media. Cardiovascular complications included pulmonary thromboembolism, myocardial infarction, ischemic stroke, venous thrombosis.

Results: In total 209 (165 [79%] female and mean age 51.8 ± 13.2 years) AAV patients (94 GPA; 46 MPA; and 69 EGPA) were included in the analysis. Risk factors for infectious complications were BVAS level at the beginning of induction therapy > 25 (OR – 2.92, 95% CI (1.53;5.45) p<0.001), usage of prednisone in doses more than 60 mg / day at the induction of remission (OR – 2.76, 95% CI (1.45;5.29) p=0.003), usage of prednisone in doses ≥ 10 mg / day after 6 months of induction therapy (OR – 2.60, 95% CI (1.38;4.93) p=0.003), ANCA-PR3 positivity (OR – 2.25, 95% CI (1.13;4.46) p=0.017) and presence of diabetes mellitus in the AAV onset (OR – 1.77, 95% CI (1.14;3.45) p=0.038). Patients with AAV had following risk factors for cardiovascular complications: male (OR – 2.28, 95% CI (1.33;3.88) p=0.002), BVAS level > 25 (OR – 2.1, 95% CI (1.11;3.16) p=0.008) and presence of coronary artery disease in the AAV onset (OR – 2.2, 95% CI (1.18;4.10) p=0.015). ANCA positivity (OR – 5.62, 95% CI (2.1;14.9) p<0.001), presence of rapidly progressive glomerulonephritis in the first 3 months from onset AAV (OR – 5.02, 95% CI (3.42;7.35) p<0.001) and over 60 years of age (OR – 2.17, 95% CI (1.38;3.44) p=0.001) were risk factors of development of chronic kidney disease. Risk factors for refractory to induction therapy in patients with AAV were ANCA-PR3 positivity (OR – 3.13, 95% CI (1.63;6.02) p<0.001), BVAS level > 25 (OR – 2.63, 95% CI (1.74;4.34) p<0.001), initiation of therapy after 4 months from the onset of clinical manifestations (OR – 2.17, 95% CI (1.26;3.91) p=0.005). We additionally defined that identification of pathological phenotypes of alpha-1-antitrypsin was risk factors for refractory course in patients with GPA manifestations (OR – 2.66, 95% CI (1.12;6.33) p=0.048).

Conclusion: Our study has shown that high disease activity, ANCA positivity and comorbid pathology increase risk of serious complications. Early administration of immunosuppressive therapy, adequate steroid dosing and use of risk factors for complications and refractory course in clinical practice can significantly improve the prognosis of AAV.

Disclosure of Interests: None declared

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THU0301 OUTPATIENT REFERRAL WITH A POSITIVE ANCA? A SINGLE-CENTRE EVALUATION OF THE IMPACT OF IMPLEMENTING THE 2017 REVISED INTERNATIONAL CONSENSUS ON ANCA TESTING FROM 1547 NEW PATIENT REFERRALS

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Background: Anti-neutrophil cytoplasmic antibodies (ANCAs) are valuable laboratory markers used in the detection of medium and small-vessel vasculitis: granulomatosis with polyangiitis, eosinophilic granulomatosis with polyangiitis and microscopic polyangiitis. Historically, and in our own centre, ANCAs are screened for using indirect immunofluorescence (IIF) with antigen-specific immunoassays being performed on IIF-ANCA positive results. While highly sensitive, IIF has a low specificity compared to antigen-specific immune-assay for MPO and PR3. Anecdotally, positive IIF ANCA results often trigger rheumatology referrals. A 2017 International consensus statement has recommended ten clinical indications for requesting ANCA, and suggested high quality immunoassays are the preferred screening method, without the categorical need for IIF.

Objectives: This service evaluation explores the local impact and implications of adopting the 2017 International Consensus on ANCA testing by evaluating new patient referrals to a single UK rheumatology centre.

Methods: New out-patient referrals to a single consultant rheumatologist at one UK centre were collected over 40-months (2016-19) and prospectively coded by referral indication from the clinical letter prior to clinical assessment. Data collected included: anonymised baseline demographics, referral source, key features for referral, and diagnosis following assessment. Referral text was coded using clinical reasoning theory, to identify up to four 'key-features' of the referral, typed by the clinician as free text. This included clinical findings, suspected diagnosis, ANCA testing (MPO/PR3 status), other autoantibodies, arthralgia, synovitis, or other important features (e.g. rash, Raynaud's phenomenon). Diagnosis at the visit was coded against established rheumatological diagnoses. We retrospectively identified any patient where ANCA/ MPO/PR3 formed a key part of the referral, using electronic text search tools.

Results: A total of 1748 referrals were seen, 177 (10.1%) were excluded due to incomplete data. This left 1547 for analysis, of these 18 (1.2%) had been referred with an ANCA IIF positive result as a key component for the referral. The 18 ANCA positive were predominantly female (16/18) and had a mean age of 49 (SD 16.6). The majority of referrals were initiated primary care (16/18); the remaining referrals were from haematology and ophthalmology. The majority (17/18, 94%) tested negative for MPO and PR3, 1/18 (6%) was PR3 antibody positive (known inflammatory bowel disease). Retrospectively, none of the ANCA requests would have met the 2017 gating criteria for testing. In total 13/18 patients were given an additional diagnosis: Fibromyalgia 6 (28%); Soft tissue rheumatism 4 (22%); undifferentiated inflammatory arthritis 1; reactive arthritis 1; biomechanical joint pain 1; probable connective tissue disease 1.

Conclusion: This service evaluation shows that routine outpatient referrals with positive IIF ANCA represent a small but significant proportion of referrals to our centre (1.2%). The vast majority of these would be filtered out with a gating strategy. This evaluation demonstrates the low specificity of IIF ANCA without any suggestive clinical symptoms. By adopting MPO/PR3 immune-assays as the primary screening method, the vast majority of these referrals (17/18, 94%) would have tested 'negative', reducing uncertainty for patients and primary care clinicians. None of these patients were diagnosed with vasculitis. These data support adoption of the 2017 Consensus Statement across our, and other units, to reduce unnecessary referrals, uncertainty, and cost. Our electronic requesting system allows for the introduction of an ANCA gating strategy. These data can be used to educate primary care teams regarding indications and interpretation of ANCA testing.

References:

[1] Broeders S, Goletti S, Tomasi J, et alRevised 2017 international consensus on ANCA testing in small vessel vasculitis. Annals of the Rheumatic Diseases 2019;78:e113.

Disclosure of Interests: None declared

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THU0302 HEAD-TO-HEAD COMPARISON OF 18F-FDG-PET/CT AND ULTRASOUND OF THE TEMPORAL ARTERY

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Background: For the diagnosis of giant cell arteritis (GCA) several diagnostic tools do exist such as ^{18}F-FDG-PET/CT (PET) with excellent diagnostic accuracy for the larger vessels and ultrasound for the temporal arteries (TA). Recent data propose that PET is able to detect vasculitis in vessels as small as the TA (1). Comparison of PET, ultrasound (US) and histology of the TA on a segment level has not been done.

Objectives: To describe diagnostic accuracy of PET of the TA in a vasculitis university clinic and to analyse strength and limitations of PET by comparing ^{18}F-FDG uptake to US and histology results on a segment level.

Methods: We analysed patients, included in our ethical board approved local prospective GCA cohort having received a PET in between 2015 and 2019 because of suspected GCA.

PET of the TA was performed using time-of flight technique and was scored 'vasculitis' if tracer uptake was higher than in the surrounding tissue. Standard uptake value (SUV) measurement in the trunk (T), parietal branch (PB) and frontal branch (FB) of the TA was recorded. US was performed for each branch.

Results: From 37 consecutively recruited patients, GCA was confirmed in 19 patients and excluded in 18 patients which served as controls (Table 1). PET of the TA showed vasculitis in 12/19 GCA patients and in 1/18 controls. Median SUV_{max} of all vasculitic FB (n=18) was 2.91, 2.20 for the T (n=14) and 2.34 for the PB (n=5).

Table 1. Patient characteristics. Data are expressed as number (%) or median (interquartile range)

	GCA (n=19) (51%)	Control (n=18) (49%)	P-value
Female	11 (57)	9 (50)	0.64
Median age (years) at PET	73 (64-78)	62.5 (57-71.75)	0.04
Amaurosis fugax/Loss of vision	9 (47)	9 (50)	>0.99
New onset headache	13 (68)	11 (61)	0.74
Jaw claudication	7 (37)	3 (16)	0.38
Scalp tenderness/ pathological TA	7 (37)	6 (33)	0.54
Proximal muscle pain	11 (58)	8 (44)	0.29
Fever	1 (5)	5 (28)	0.06
Median Erythrocyte sedimentation rate (mm/h)	73 (48-90)	50 (28.5 - 68.5)	0.06
Median C-reactive protein (mg/L)	66 (29-105)	46 (13-133)	0.57

16 of the 19 GCA patients received US of the TA and 9 showed vasculitic findings. From the control group 2 patients showed vasculitic findings. Most often vasculitic findings were localized in the FB (n=16), followed by the T (n=13) and the PB (n=13).

In the 16 patients that received US, diagnostic sensitivity and specificity of temporal PET for GCA within the TA was 56% and 94% and of US 56% and 89%, respectively.

Whereas US detects vasculitis in comparable frequencies in all TA branches, PET recorded vasculitis less often in the PB (only 4 of the 13 in US vasculitic PB). Indeed, the median diameter of all PET positive TA branches, measured in the US, was higher (2.00mm) compared to PET negative branches (1.50mm). Vasculitis was confirmed histologically in 9 of the 13 biopsied patients. Only 2/9 patients showed vasculitis in the preceding PET in the biopsied branch.

Conclusion: High diagnostic accuracy for temporal arteries supports PET as an 'all-in-one' exam for GCA. A limitation might be the vessel diameter, as sensitivity of PET for vasculitis of the small parietal branch is low. Thus, in cases with high suspicion of GCA despite a negative PET, US of the TA and or biopsy might enhance diagnostic sensitivity.

References:

[1] Nielsen et al. Simple dichotomous assessment of cranial artery inflammation by conventional 18F-FDG PET/CT shows high accuracy for the diagnosis of giant cell arteritis: a case-control study. *Eur J Nucl Med Mol Imaging*. 2019;46(1):184-193. **doi:**10.1007/s00259-018-4106-0

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THU0303 TREATMENT OF GIANT CELL ARTERITIS WITH TOCILIZUMAB IN CLINICAL PRACTICE IN SWEDEN

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Background: Giant cell arteritis (GCA) is the most common form of systemic vasculitis in adults. GCA is often associated with comorbidities related to the disease itself or caused by its treatment, here: mainly glucocorticosteroids. Since 2017, tocilizumab (TCZ) is approved for the treatment of GCA, but its uptake and treatment outcomes in clinical practice remain to be characterized.
Objectives: To describe characteristics of GCA patients treated with tocilizumab (TCZ) in clinical practice, to evaluate the use of prednisolone up until and following TCZ treatment start, and to describe the TCZ treatment duration.
Methods: We linked together the Swedish Rheumatology Quality Register (SRQ), the national Prescribed Drug register, and national Patient register, covering data from July 2009 until July 2019. Through these linkages, we identified GCA patients treated with TCZ including start and discontinuation, their comorbidities and use of other medications. TCZ treatment durations were evaluated through survival probability curves.
Results: We identified 468 patients with GCA treated with TCZ, before and after its formal approval for GCA, Table 1. Over calendar time, the proportion who started TCZ as first ever bDMARD increased, as did the mean age at start of TCZ. The pattern of co-morbidities and health care utilisation demonstrated substantial burden from, e.g., diabetes and infections (Table). Patients starting treatment with TCZ were characterized by an increasing average dose of prednisolone during the last 1.5 years before TCZ start. Thereafter, prednisolone use declined substantially, from a mean of 15 mg/day in the six months before the start of TCZ to 6 mg/day 1 year after its start (Figure 1). Analysis of the duration of TCZ treatment (from start until discontinuation) suggested that at one year, two thirds of patients were still on treatment (Figure 2).

Table. Swedish GCA patients starting treatment with tocilizumab July 2009 - Nov 2019.

	July 2009 -July 2015	July 2016 - July 2017	July 2017 -July 2018	July 2018 - Nov 2019
Patients	89	140	140	99
Female	64%	77%	73%	71%
Age, mean (sd)	67 (7.9)	68 (8.8)	69 (8)	70 (7.8)
Previous use of bDMARDs	27%	21%	11%	11%
Hospitalisations most recent 5 years, mean (sd)	3.9 (4.2)	3.2 (2.6)	2.9 (2.5)	3.3 (3)
Co-morbidities, most recent 5 years:				
Chronic obstructive pulmonary disease	6%	2%	4%	3%
Ischemic heart disease	12%	7%	14%	11%
Diabetes mellitus, type 1&2	34%	26%	26%	26%
Fractures (any location)	15%	14%	11%	10%
Knee/hip replacement	7%	10%	7%	8%
Myocardial infarction	2%	1%	4%	3%
Stroke	2%	4%	2%	5%
Hospitalisation listing infection	39%	40%	39%	37%

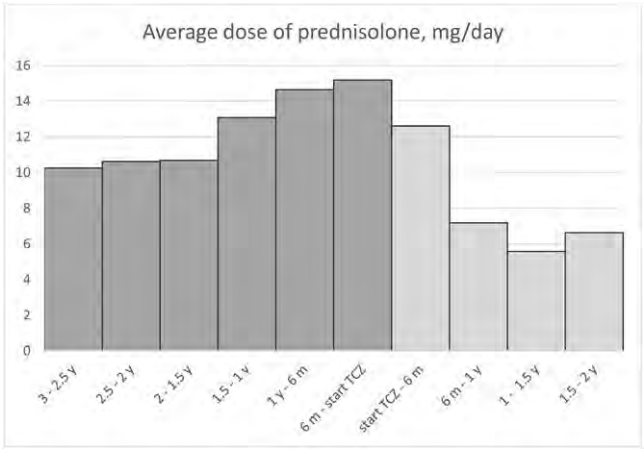


Figure 1. Average daily dose of prednisolone before and after* start of tocilizumab, based on cumulative dose every 6 months.*The average daily dose of prednisolone after the start of TCZ is calculated only among patients who were still on treatment at the end of each period (351 patients in the first 6 months, 251 in 6m-1y, 161 in 1 – 1.5 y, 95 in 1.5 – 2y).

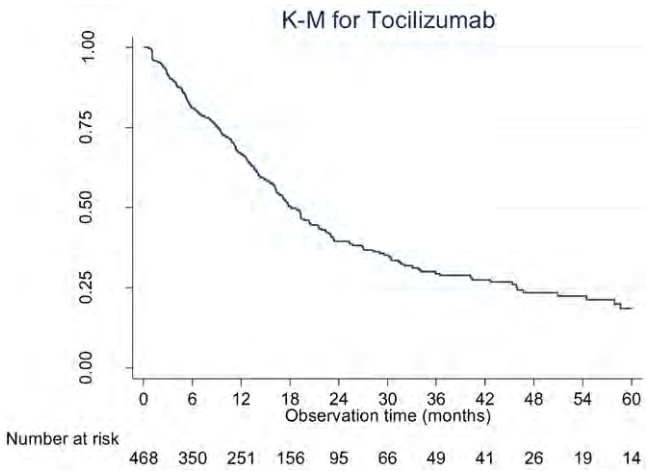


Figure 2. Kaplan-Meier curve for tocilizumab in GCA by time since treatment start.

Conclusion: Patients treated with TCZ for GCA in clinical practice are characterized by a significant burden of co-morbidities, many of which may be related to prolonged use of glucocorticosteroids. This study confirms a marked reduction in the use of oral prednisolone following treatment with TCZ, and demonstrates that in a majority of patients in clinical practice, treatment with TCZ for GCA is extended beyond one year. Future analyses will evaluate the association of these observed treatment patterns with the level of GCA disease control, co-morbidities and quality of life, over time.
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THU0304

CLINICAL PRACTICE VARIATION BETWEEN ACADEMIC AND NON-ACADEMIC CENTERS IN THE MANAGEMENT OF ANCA ASSOCIATED VASCULITIS IN THE NETHERLANDS

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Background: ANCA associated vasculitis (AAV) is a complex, rare systemic autoimmune disease with an estimated prevalence of 5-18 patients per 100.000 individuals worldwide. Managing a low prevalent disease can be challenging which is reflected in clinical practice variation.
Objectives: This study investigated clinical practice variation of the care for AAV patients in the Netherlands.
Methods: In a nationwide online survey, AAV patients were selected from academic and non-academic centers. Within centers, patients were eligible when they had a confirmed diagnosis of microscopic polyangiitis (MPA), granulomatosis with polyangiitis (GPA) or eosinophilic granulomatosis with polyangiitis (eGPA) according to the treating physician. There were no exclusion criteria. In each center a comparable number of patients was included. Data capture encompassed a wide set of variables on diagnosis, management and outcomes.

Results: From December 2018 to November 2019, 230 AAV patients were recruited in 6 non-academic and 3 academic hospitals (120 vs 110 patients respectively). Differences in clinical diagnoses (GPA, MPA and eGPA) were observed between non-academic and academic centers (p=0.05), which was mainly caused by a higher number of MPA patients in non-academic centers. The year of diagnosis was comparable (median 2013 [2009-2016], p=0.150). The median follow up since diagnosis was 4.8 years [1.8-9.6] with a median in-hospital time-to-diagnosis of 13 days [2-50]. Patients were diagnosed at a mean age of 63 years (±11.18) in non-academic centers and 53 years (±16.92) in academic centers (p<0.001). Besides steroids, oral cyclophosphamide was the most preferred drug (54%) for induction therapy, whereas rituximab was given significantly more often as (part of the) induction therapy in patients treated in academic centers compared to patients in non-academic centers (27% vs 8%, p<0.001). In non-academic centers pneumocystis pneumonia (PCP) prophylaxis was prescribed significantly less (76% vs 91%, p=0.003). Also, screening for Staphylococcus aureus carriership was significantly less (17% vs 68%, p<0.001). With respect to mortality and co-morbidity, 22 patients (10%) died, 100 patients (44%) had at least one infection and 24 patients (10%) suffered from at least one malignancy. We observed no significant differences on these endpoints between academic and non-academic centers.

Conclusion: The present study highlights important practice variation in the management of AAV between academic and non-academic hospitals in the Netherlands. A high proportion of patients is treated with oral cyclophosphamide as induction therapy while rituximab is increasingly used in academic centers. Rates of mortality, infections and malignancies were not different. Altogether, this study raises awareness into the variation of management for AAV patients and allows the identification of areas for improvement of clinical care for Dutch AAV patients.

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THU0305 PREVALENCE AND CLINICAL OUTCOME OF INTERSTITIAL LUNG DISEASE IN ANCA ASSOCIATED VASCULITIS

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Background: Lung involvement is frequent in ANCA-associated vasculitis (AAV). Classical lung manifestations consist of capillaritis with lung haemorrhage, inflammatory infiltrates and nodules. Interstitial lung disease (ILD) is increasingly recognized among patients with AAV. However, little is known concerning risk factors and clinical course of these patients.

Objectives: The aim of our study was to characterize the prevalence and clinical course of ILD in patients with AAV.

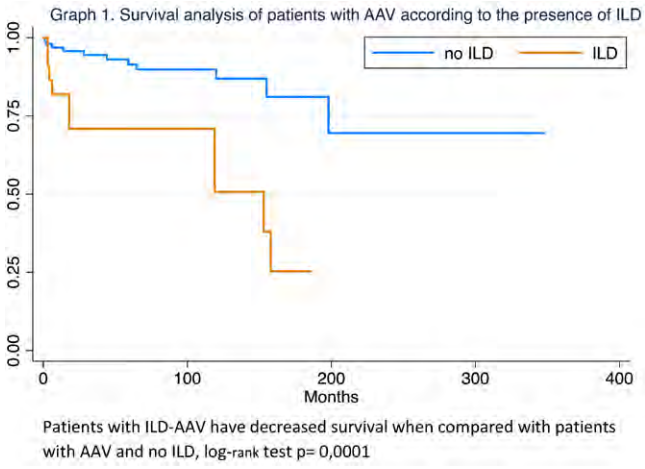
Methods: We have performed a clinical retrospective single-centre observational analysis (1990-2019) of all patients with the diagnosis of microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA) diagnosed according to 2018 Draft Classification Criteria for GPA and MPA[1]. Demographic, clinical and immunologic data were reviewed. Radiologic pattern of ILD were assessed by high-resolution-CT. Main outcome evaluated was overall-all survival.

Results: The study population consisted of 123 patients, 56% female, aged 59.3±18.2 years old at the time of diagnosis. Clinical diagnosis was of MPA in 54% of patients and GPA in 46%. While 108 (88%) ANCA positive patients had PR3 (n=25) or MPO (n=83), 15 (12%) patients had negative or atypical ANCA. Any lung involvement was present in 82 (71%) and ILD was identified in 24 (20%) of all patients. ILD pattern was of usual interstitial pneumonia (UIP) in 12 patients, non-specified interstitial pneumonia (NSIP) in 9 and chronic organizing pneumonia (OP) in 3. There was an association between the presence of ILD and ANCA specificity: MPO were present in 100% of patients with UIP and in 75% of patients with NSIP/OP (p=0.017). Bronchiectasis were more prevalent among patients with ILD (19/24; p<0.001). During the median follow-up time period of 68 (23-126) months, mortality was of 42% among patients with ILD-AAV compared with 11% in no ILD-AAV (log-rank p=0.0001). On the multivariate Cox regression model, ILD was an independent predictor of mortality HR 2.95 (95%CI 1.09-7.96; p=0.033).

Conclusion: ILD is a frequent manifestation of MPA and GPA patients. The presence of ILD, particularly UIP, is associated with ANCA-MPO and is a predictor of mortality. Therefore, a better management of fibrotic lung involvement in AAV is warranted.

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[1] Robson JC, Grayson PC, Ponte C, et al. Draft classification criteria for the ANCA associated vasculitides. Ann Rheum Dis 2018;77 (suppl 2):60-1.



Disclosure of Interests: João Fernandes Serodio: None declared, José Hernández-Rodríguez: None declared, Georgina Espígol-Frigolé: None declared, Marco Alba: None declared, Javier Marco-Hernández: None declared, Marcelo Sánchez: None declared, Fernanda Hernández-González: None declared, Jacobo Sellarés: None declared, Maria C. Cid Grant/research support from: Kiniksa Pharmaceuticals, Consultant of: Janssen, Abbvie, Roche, GSK, Speakers bureau: Vifor, Sergio Prieto-González: None declared

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THU0306 ROLE OF 18-FDG PET/CT IN DIAGNOSIS AND FOLLOW UP OF LARGE VESSELS VASCULITIS

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Background: 18-FDG PET/CT is a functional imaging method which allows to identify inflammation of vessel walls. The use of PET in large vessels vasculitis(LVV) at disease onset and during follow up is still debate either to confirm clinical remission either to drive the therapy choice. American Society of Nuclear Cardiology (ASNC) recently advanced recommendations aimed to standardize the application of PET in LVV(1).

Objectives: The aim of our study was to assess the clinical role of PET performed in patients affected by LVV at the diagnosis and during the follow up.

Methods: We retrospectively evaluated PET/CT of 49 patients affected by clinically active LVV according to LVV visual grading (LVG, grading 0-3) and measured the standardized uptake value(SUV) of large vessels. 38 (77,6%) patients were affected by Giant Cells Arteritis and 11(22,4%) by Takayasu Arteritis. 32(65.3%) patients repeated the imaging after a mean follow-up of 11.5±5.4 months.

All baseline (T0) and follow up (T1) clinical data of disease activity were collected. Patients were treated according to EULAR LVV management recommendations(2). T0 PET/CT study was performed in patients with a clinically active disease defined by suggestive symptoms/signs and/or high inflammatory markers. The mean disease duration before T1 PET/CT examination was 4 months. T0 PET was performed in 25/49 patients(52%) at the diagnosis of

LVV, whereas in 24/49(48%) patients with already diagnosed but active LVV disease.

Results: Baseline PET was positive in 21 patients(42.9%). According to ASNC recommendations, 19 patients (38.8%) presented a LVG=3, 2(4.0%) a LVG=2, 6(12.2%) LVG=1 and 22 (44.9%) LVG=0. Patients performing PET at disease onset(75%) had higher LVG score than patients performing PET during the disease course (25%),p=0,002. At T0, aortic, carotid, axillary and subclavian SUV did not correlate with inflammatory markers.

Follow up PET/CT studies were performed in 32 patients, 13 (40.6%) with a clinically active disease despite therapy, while 19(59.4%) in clinical remission.

Follow up PET was still positive in 8 patients (25%) with a LVG=3, 10 (31.2%) patients presented LVG=1 and 14 (43.8%) LVG=0. T1 PET/CT study showed a significant reduction of SUV values in descending aorta, left and right subclavian arteries, and left and right axillary arteries when compared with first PET/CT study. According to LVG, 12 patients with active PET/CT study at T0 (19 pts) presented a reduction of LVG from score 2 and 3 to grade 1 or 0 (64.2%) at second PET/CT study. Only 3 patients presented an increased LVG score at T1, while in the other 17 patients T1 PET confirmed the previous score. No significant difference was found between LVG scores according with clinical characteristics, but among 8 patients presenting an active T1 PET, 4(50%) were in clinical remission.

Conclusion: The use of ASNC recommendations for FDG PET/CT in LVV enables to confirm a metabolically active disease in 40% of patients and in 75% of patients at disease onset, suggesting that post-posing the exam could lead to underrate the real extension of disease. Our data, even if limited, suggest that PET/CT could be crucial in management of patients in clinical remission, detecting patients with still metabolically active LVV. Further prospective studies are necessary to evaluate the role of PET/CT in driving therapeutic strategies.

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THU0307 RESPONSE OF BEHÇET'S REFRACTORY ORAL AND/OR GENITAL ULCERS TO APREMILAST IN COMBINATION VS MONOTHERAPY. NATIONAL MULTICENTER STUDY OF 51 CASES OF CLINICAL PRACTICE

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Background: Apremilast (APR) has demonstrated efficacy in the treatment of oral and/or genital aphthous ulcers in Behçet´s disease (BD). Combination of APR to other disease-modifying anti-rheumatic drugs (DMARDs) has not been assessed.

Objectives: To compare the efficacy and safety of APR in monotherapy or combined with DMARDs in refractory BD.

Methods: National multicenter open-label study on 51 BD patients with oral and/or genital ulcers refractory to conventional treatment.

Results: We included 51 patients (35 women/16 men), mean age 44.7±13.2 years. Before APR, all patients had received several systemic conventional drugs. The main clinical symptoms for starting APR were oral (n=19) and genital (2) aphthous ulcers or both (30).

Excluding corticosteroids, colchicine or NSAIDs, APR was given at standard dose of 30 mg twice daily in monotherapy (n=31), or combined with conventional DMARDs in 16 cases (6 azathioprine, 5 methotrexate, 4 hydroxychloroquine, 4 sulfasalazine, 1 dapsone) or with biologic DMARDs in 4 (2 tocilizumab, 1 adalimumab, 1 infliximab). There were not found statistically significant differences in demographic features, previous therapy, clinical manifestations or reported adverse effects.

After a median follow-up of 6 [3-12] months, most of the patients experienced improvement of the orogenital ulcers in both groups (89.8% in the first 2 weeks), without statistically significant differences. **(TABLE)**

Conclusion: APR leads to a rapid and maintained improvement in most patients with refractory BD orogenital ulcers. APR seems as effective and safe in monotherapy as combined.

TABLE:

	Week 1-2		Week 4		Month 6		Month 12		Month 24	
Outcome of oral and/or genital ulcers n, (%)	**C n=19**	**M n=30**	**C n=19**	**M n=26**	**C n=12**	**M n=17**	**C n=7**	**M n=6**	**C n=1**	**M n=1**
Complete resolution	8 (42.1)	11 (36.7)	12 (63.2)	20 (77)	7 (58.4)	14 (82.4)	3 (42.8)	3 (50)	1 (100)	1 (100)
Partial resolution	9 (47.4)	16 (53.4)	7 (36.8)	3 (11.5)	5 (41.6)	2 (11.7)	4 (57.2)	3 (50)	0	0
No response	2 (10.5)	3 (9.9)	0	3 (11.5)	0	1 (5.9)	0	0	0	0
p value	0.9		0.1		0.1		0.8		0.7	

Abbreviations: C= combined; M= monotherapy; n= available data.

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THU0308 COMPARISON OF CHILDHOOD-ONSET VERSUS ADULT-ONSET TAKAYASU ARTERITIS: A STUDY OF 141 PATIENTS FROM TURKEY

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Background: Childhood-onset Takayasu Arteritis (c-TAK) may differ from adult-onset Takayasu Arteritis (a-TAK) in clinical maaifestations and treatment.
Objectives: To compare c-TAK with a-TAK patients for vascular involvement, disease activity, damage, and treatment.
Methods: Patient charts from two tertiary-care centers of a pediatric and adult clinic were reviewed. Adult patients diagnosed before the age of 18 were included in the c-TAK group. The activity was assessed with the physician's global assessment (PGA) and Indian Takayasu Clinical Activity Score (ITAS). The damage was evaluated with Takayasu Arteritis Damage Score (TADS) and Vasculitis Damage Index (VDI).
Results: Twenty four c-TAK and 121 a-TAK patients were compared. 21 (88%) of the c-TAK group and 104 (89%) of the a-TAK group were female. Age at symptom onset was 14 (IQR: 9-15) for c-TAK and 30 (IQR: 24-43) for a-TAK patients. Diagnostic delay in months was shorter for c-TAK patients [c-TAK: 3 (1-10) vs. a-TAK: 12 (5-58)]. Follow-up duration was similar [53 months (IQR: 16-131) vs. 68 (IQR: 30-102), p=0.763].
ITAS was comparable for c-TAK and a-TAK patients on the first visit [14 (SD: 7) vs. 13 (SD: 5), p=0.362, respectively]. However, the PGA score was higher in the c-TAK group compared to the a-TAK group [9 (IQR 7-10) vs. 7 (IQR 6-8), p<0.001].
14 (64%) of c-TAK patients and 10 (9%) of a-TAK patients received pulse glucocorticoids, p= 0.002. Cumulative glucocorticoid dose was 10 grams (IQR: 6-13) for c-TAK patients and 7 grams (IQR: 4-12) for a-TAK patients (p=0.128).
After diagnosis, children had more vascular interventions than the adults did [9 (38%) vs. 20 (18%), p=0.031, respectively].
Rates of achieving at least one remission were lower for c-TAK patients [c-TAK: 12 (50 %) vs. a-TAK: 94 (82%), p=0.001]. c-TAK patients had a PGA score of 6 (IQR 3-8), the PGA score in a-TAK patients was 1 (IQR 1-3), p<0.001. Still, ITAS was similar for both groups [c-TAK: 1 (IQR 0-3) vs. a-TAK: 0 (IQR 0-2), p= 0.579]. 9 (38%) of c-TAK patients had at least one relapse, and the 43 (38%) of a-TAK patients had at least one relapse (p=0.960).
TADS was similar [c-TAK: 8 (IQR 4-12), a-TAK: 8 (IQR 6-10), p=0.919]. However, VDI of the a-TAK patients was higher than the c-TAK patients [c-TAK: 4 (IQR 2-5), a-TAK: 5 (IQR 3-7), p=0.017]. Glucocorticoid related damage was higher in a-TAK patients (Diabetes: 8% vs. 4%, avascular necrosis: 6% vs. 0, and cataracts: 11% vs. 0)
Conclusion: Aorta involvement, biologic agent use, and vascular interventions were more common in c-TAK patients. However, cumulative damage was not increased for c-TAK patients which may be partly explained by more common corticosteroid related side-effects in adults.

Table 1. Baseline symptoms, physical examination findings*

	c-TAK (n= 24)	a-TAK (n= 117)	p
SYMPTOMS			
Stroke	1 (4)	8 (7)	1
Carotidynia	0	19 (16)	0.044
Upper Extremity Claudication	5 (21)	72 (62)	<0.001
Hypertension	13 (54)	22 (19)	<0.001
Pulse loss (Radial)	8/23 (35)	62 (58)	0.043
BRUIT			
Subclavian	8 (35)	62 (57)	0.054
Renal	9 (39)	15 (14)	0.014
Abdominal Aorta	11 (48)	9 (8)	<0.001

*Values denote the number (%) of patients

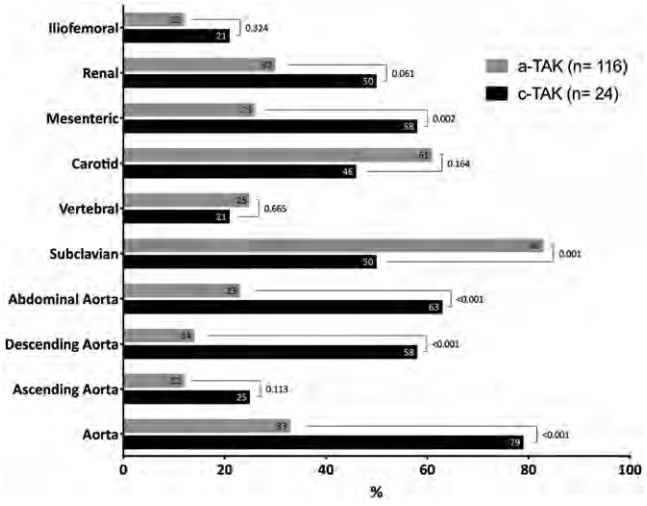


Figure 1. Comparison of involved arteries** Numbers in bars represent percentage of patients in each group

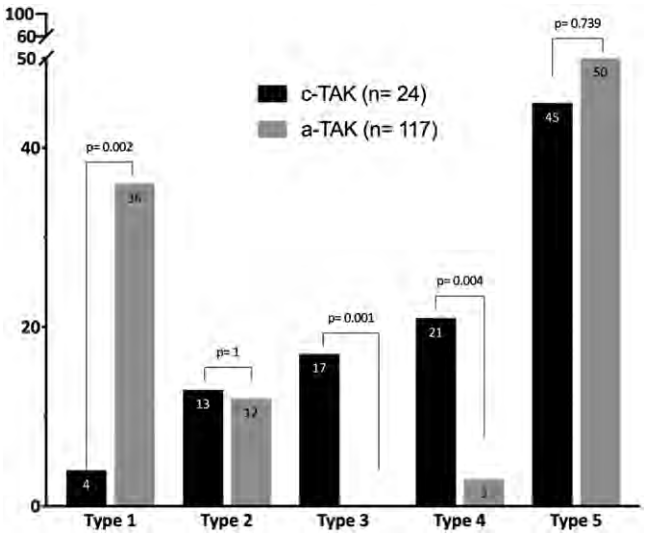


Figure 2. Angiographic classification types according to Hata** Numbers in bars represent percentage of patients in each group. Type 2a and Type 2b are combined. a-TAK group had no patient with Type 3 disease

Table 2. Medical treatment*

	First Treatment			Treated Ever		
	c-TAK (n=22)	a-TAK (n=115)	p	c-TAK (n=24)	a-TAK (n=114)	p
Methotrexate	5 (23)	69 (60)	0.001	12 (50)	76 (67)	0.123
Azathioprine	8 (36)	38 (33)	0.763	21 (88)	79 (69)	0.070
Leflunomide	0	1 (1)	1	3 (13)	35 (31)	0.070
Cyclophosphamide†	6 (27)	6 (5)	0.004	12 (50)	10 (9)	<0.001
Biologics				10 (42)	16 (14)	0.004
Anti-TNF	-	-	-	4 (17)	18 (16)	-
Tocilizumab	-	-	-	7 (29)	4 (4)	-

*Values denote the number (%) of patients.

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THU0309

UNILATERAL TEMPORAL ARTERY BIOPSY IS SUFFICIENT FOR DIAGNOSING GIANT CELL ARTERITIS IF THE SERUM C-REACTIVE PROTEIN LEVEL IS 10 MG/DL OR HIGHER

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Background: Temporal artery biopsy (TAB) is the gold standard for diagnosing giant cell arteritis (GCA). However, previous studies have reported that the discordance rate of TAB is 3-45%, *i.e.*, in unliteral TAB, GCA may be overlooked in one in five patients, approximately. Evidence as to whether bilateral TAB should be performed initially or one-sided TAB is sufficient for diagnosing GCA is lacking.
Objectives: To investigate the predictors of patients with GCA in whom one-sided TAB is sufficient.
Methods: The present study was a cross-sectional, single center study conducted from April 1, 2011 to July 31, 2019 at Tokyo Metropolitan Tama Medical Center. Of all consecutive GCA cases for which bilateral TAB was performed, bilaterally positive cases and unilaterally positive cases were extracted as bilateral positive group (BPG) and unilateral positive group (UPG), respectively. GCA was defined in accordance with the classification criteria of the 1990 American College of Rheumatology, and GCA was diagnosed if no other etiology was found within six months after beginning of high-dose glucocorticoid treatment. Demographic, clinical and laboratory data were obtained from the medical records, and the BPG and the UPG were compared statistically in each variable. Statistical significance was defined as $p < 0.05$.
Results: During study, 264 biopsies were performed for 145 cases, who suspected GCA and underwent TAB. The pathological positivity rate was 26.1% (68 / 264 biopsies). Of these, 53 cases had final diagnosis of GCA, in which 43 cases were biopsy proven GCA. Thirty-seven biopsy proven GCA with bilateral TAB

were enrolled; 64.9% women; mean (SD) age 75 (8.9) years; median [IQR] TAB length 17.5 [13.0,20.0] mm; headache 54.1%; jaw claudication 45.9%; scalp tenderness 16.2%; temporal artery (TA) tenderness 32.4%; TA engorgement 32.4%; TA pulse abnormality 5.4%; visual symptoms 2.7%; a fever of 38.5°C or higher 40.5%; shoulder girdle pain 48.6%; imaging of aortitis or arteritis 40.5%; median [IQR] white blood cell 9,100 [7200, 12050] /µl; median [IQR] platelet cell 37.5 [27.0, 46.3] $\times 10^4$ /µl; median [IQR] C-reactive protein (CRP) 10.1 [3.9, 16.5] mg/dL; erythrocyte sedimentation rate [IQR] 105 [66, 129] mm/h. Thirty-one in 37 cases were positive bilaterally while 6 in 37 cases were positive unilaterally; and the discordance rate was 16.2%. The median sample length after formalin fixation was 19.0 mm for the BPG and 14.5 mm for the UPG ($p = 0.171$). The parameters above were compared between UPG and BPG. Of these, only the serum CRP value (mg/dL) differed statistically between groups, and the median value of the two groups was 10.6 and 6.5, respectively (median test: $p = 0.031$). To predict BPG, in whom unilateral TAB is sufficient for diagnosing GCA, the cut-off value of serum CRP with a specificity of 100% and a sensitivity of 61.3% was set at 9.3 mg/dL (ROC analysis: AUC 0.726).

Conclusion: When the serum CRP level is 10 mg/dL or higher in GCA suspected patients, an unilateral TAB alone was sufficient for an accurate diagnosis.

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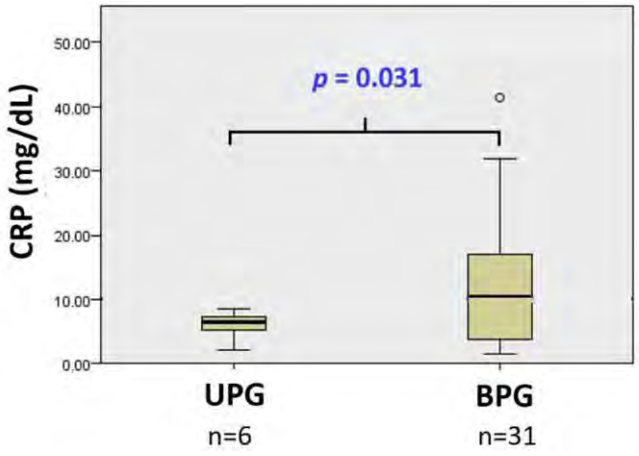


Figure. Comparison of median CRP levels between unilaterally positive group and bilaterally positive group.

Disclosure of Interests: None declared

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THU0310 CASE–CONTROL SEROPREVALENCE STUDY ON THE ASSOCIATION BETWEEN BARTONELLA INFECTION AND ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY-ASSOCIATED VASCULITIS

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Background: Bartonellosis is an emerging anthropozoonosis caused by infection with intracellular Gram-negative *Bartonella* species. It leads to necrotizing granulomas and endothelial damage and causes acute and chronic human diseases, such as cat scratch disease, bacillary angiomatosis and endocarditis. Endocarditis due to *Bartonella henselae* and *B. quintana* is reported to produce anti-neutrophil cytoplasmic antibodies (ANCAs) that disappear with effective antimicrobial treatment.

Objectives: Hypothesizing a role for *Bartonella* infection in ANCA-associated vasculitis (AAV), which also includes granulomatous and vascular inflammation, we studied the seroprevalence of 5 *Bartonella* species in patients with AAV.

Methods: The study used plasma samples from patients with granulomatosis with polyangiitis and microscopic polyangiitis that were enrolled in the Rituximab for AAV (RAVE) trial and from healthy controls living in the United States. Western blot assays were used for serological testing of infection with *B. quintana*, *B. henselae* Houston-1, *B. elizabethae*, *B. vinsonii* subsp. *berkhoffii* and *B. alsatica*. The associations of positive serology results and AAV were expressed as odds ratios (OR). Clinical characteristics of seropositive and seronegative patients, assessed by the BVAS/WG instrument, were compared. These comparisons were done for 9 organ systems; in case they showed differences with $P<0.10$, the corresponding organ system-specific clinical features were also analyzed. Statistical analysis was performed using Fisher's exact test or Student's t-test, as appropriate.

Results: We analyzed blood samples of 187 patients with AAV (collected at start of the trial) and of 127 controls. There were no significant differences between the cases and controls for mean age (P=0.148) and proportion of males (P=0.36). *Bartonella* spp. serological testing was positive for 112 (60%) cases and 40 (31%) controls (OR 3.25 [95% CI 2.02–5.22], P<0.001). Significant associations were also found within subsets of PR3-AAV (OR 4.00 [95% CI 2.37–6.76], P<0.001), MPO-AAV (OR 2.18 [95% CI 1.17–4.06], P=0.017), newly-diagnosed (OR 3.89 [95% CI 2.21–6.86], P<0.001) and relapsing disease (OR 2.86 [95% CI 1.65–4.98], P<0.001). Species-specific positive serological testing was found in particular against *B. henselae* (cases: 27%, controls: 0.8%; OR 39.93 [95% CI 5.42–293.90]; P<0.001). Compared to AAV patients without seropositivity for *Bartonella* spp., AAV patients testing seropositive for *Bartonella* spp. had significantly more bloody nasal discharge (P=0.046), sinus involvement (P=0.035) and conjunctivitis/episcleritis (P=0.016).

Conclusion: This study reveals higher seroprevalence of *Bartonella*, especially *B. henselae*, in patients with AAV than in healthy controls. Although cross-reactivity of *Bartonella* with other microorganisms cannot be excluded, these results may support an etiopathogenic role of *Bartonella* infection in AAV that deserves further investigation.

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THU0311 CERTOLIZUMAB THERAPY IN REFRACTORY UVEITIS DUE TO IMMUNE-MEDIATED INFLAMMATORY DISEASES (IMID). MULTICENTER STUDY OF 39 PATIENTS

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Background: Infliximab and adalimumab therapy has significantly improved the prognosis of patients with non-infectious refractory uveitis. However, there is not enough evidence for the use of other anti-TNF drugs such as Certolizumab Pegol (CZP).

Objectives: To evaluate the efficacy and safety of CZP in uveitis secondary to Immune-Mediated Inflammatory Diseases (IMID).

Methods: Multicenter study of 39 patients with uveitis due to IMID refractory to glucocorticoids and conventional immunosuppressants. Efficacy of CZP was evaluated with the following ocular parameters: best corrected visual acuity (BCVA), anterior chamber cells, macular thickness and presence of retinal vasculitis. Efficacy of CZP was compared between baseline, 1st week, 1st and 6th month, and 1st and 2nd year. Statistical analysis was performed with the STATISTICA software (Statsoft Inc. Tulsa, Oklahoma, USA).

Results: 39 patients/56 affected eyes (18 men/21 women) with a mean age of 40.5±11.9 years were studied. IMIDs included were: spondyloarthritis (n=17), psoriatic arthritis (6), Crohn (3), JIA (2), Behçet (2), reactive arthritis (2), rheumatoid arthritis (1), relapsing polychondritis (1), pars planitis (1), Birdshot (1) and idiopathic uveitis (3). Uveitis pattern was as follows: anterior (n=30), posterior (4), panuveitis (3) and intermediate (2).

Previous CZP, patients received: oral prednisone (n=18) methylprednisolone bolus (1), methotrexate (22), azathioprine (10), cyclosporine (4), leflunomide (2), mycophenolate mofetil (2) and cyclophosphamide (1). 77% of patients had received previous biological therapy, with a mean of 1.6±1.2 biological drugs per patient. Gestational desire was the reason for prescribing CZP in 8 patients. CZP was administered in monotherapy in 16 patients and in the remaining 23 patients combined with conventional immunosuppressants.

After a median follow-up of 24 [6-36] months, most of the ocular variables analysed showed a rapid and significantly sustained improvement (**Table**). CZP was discontinued in 11 patients for the following reasons: remission (n=1), insufficient response of ocular symptoms (n=1) and limited response of extraocular manifestations (n=9). No serious adverse effects were reported.

Conclusion: CZP seems to be effective and safe in patients with refractory uveitis due to IMID.

Table

	Baseline	1st week	1st Month	6th Month	1st year	2nd year
BCVA (mean±SD)	0.77±0.29	0.77±0.30*	0.82±0.29*	0.85±0.26*	0.86±0.27*	0.88±0.23*
Tyndall (median [IQR])	0 [0-2]	0 [0-2]	0 [0-1]*	0 [0-0]*	0 [0-0]*	0 [0-0]*
OCT (mean±SD)	355±61.5	-	284.1±40.4*	-	224.8±121.1*	-
Retinal Vasculitis (eyes affected, %)	2 (3.6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

*p<0.05

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THU0312 AUTOLOGOUS NON-MYELOABLATIVE HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR REFRACTORY TAKAYASU ARTERITIS: A RETROSPECTIVE MULTICENTRE CASE-SERIES FROM THE AUTOIMMUNE DISEASES WORKING PARTY (ADWP) OF THE EUROPEAN SOCIETY FOR BLOOD AND MARROW TRANSPLANTATION (EBMT)

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Background: Takayasu arteritis (TAK) is a chronic granulomatous large-vessel vasculitis, characterized by arterial thickening and fibrosis leading to stenosis and vascular occlusions. More than 10-20% of patients are refractory to conventional immunosuppressive therapy. Autologous hematopoietic stem cell transplantation (AHSCT) has emerged as a promising treatment option in severely affected and refractory patients with various autoimmune diseases and vasculitis, particularly ANCA-positive vasculitis and Behçet's disease.

Objectives: This study, approved by the ADWP, aims to evaluate the use and outcome of AHSCT in adult TAK patients.

Methods: This is a retrospective survey of patients reported to the EBMT registry between 1998 and 2019, who received AHSCT primarily for TAK. Clinical and laboratory data, including data on diagnosis, previous lines of therapy, transplant regimen, treatment-related mortality, as well as data regarding course of disease and treatment were recorded.

Results: Data from six adult patients treated with AHSCT between 2003 and 2019 for refractory Takayasu have been identified. Median (ranges) follow-up was 9.9 (1-14) years. Five patients were female (83%), median age was 25 (9-39) years at diagnosis and 28 (22-41) years at HSCT. All patients were pretreated with a median of 6 (4-8) lines of therapy, including systemic steroids (6 patients), methotrexate (5 patients), cyclophosphamide, mycophenolate mofetil or infliximab (4 patients), tocilizumab or etanercept (2 patients), and other biologic or conventional-synthetic DMARDs. Conditioning included cyclophosphamide and rabbit anti-thymocyte globulin in all patients. At six months post-transplantation, remission was obtained in all cases, which persisted at 12 months in 5 cases. Four patients reactivated TAK at a median time of 27 (7-52) months after AHSCT, and 3 resumed disease-modifying therapy. At last follow-up, all patients were alive, 2 patients were in remission (off-therapy), 2 patients improved compared to baseline, and 2 patients were in complete and partial remission, respectively, under immunosuppressive treatment.

Conclusion: This small retrospective series demonstrates that AHSCT has the potential to provide significant clinical responses in TAK patients who had been unresponsive to previous immunosuppressive therapy, with an acceptable safety profile.

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THU0313 DISEASE PATTERN AND TIME TO DIAGNOSIS IN A FAST-TRACK GIANT CELL ARTERITIS CLINIC USING ULTRASOUND AS PRIMARY DIAGNOSTIC TOOL

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Background: Giant Cell Arteritis (GCA) is a vasculitis predominantly affecting the large vessels from aorta and its proximal branches and extra-cranial arteries. Precise and fast diagnosis is important in order to initiate proper treatment and avoid ischaemic events, e.g. irreversible visual loss. Unnecessary and prolonged glucocorticoid treatment is also unwanted due to its significant side effects. Therefore, immediate diagnosis of GCA is recommended, and the primary diagnostic tool, according to EULAR recommendation, is vascular ultrasound (US)[1]. In 2018, a GCA Fast-Track Clinic (FTC) was implemented in our department covering a population of approximately 900.000. Patients even with a low á-priori suspicion of GCA were accepted. It is the aim to have patients seen within one office day.

Objectives: In this retrospective study, to describe clinical data from patients seen in the FTC in a 1-year period from September 1st, 2018 and to investigate the time required for making a diagnosis, and to which extent US as the primary diagnostic tool was adequate for making the final diagnosis.

Methods: All patients, irrespective of clinical presentation, had US of bilateral temporal-, facial-, axillary and common carotid arteries done (exam time 30 min.). All US were done by ultrasonographers with experience and training in vascular US. Immediately after the initial US, patients were seen by a senior registrar in rheumatology at our out-patient clinic. The senior registrar was aware of the conclusion of the US. Decisions on further diagnostic procedures were solely up to this rheumatologist. From electronic patient report files, all patients' clinical- and US-findings as well as results from other diagnostic procedures (temporal artery biopsy (TAB) and positron emission tomography computed tomography (PET-CT)) were evaluated. Furthermore, final diagnosis and fulfilment of ACR1990 classification criteria for temporal arteritis at three months was noted, as was the number of days required for diagnosis.

Results: A total of 120 patients were seen in the FTC and had a vascular US done. Demographic and clinical data are seen in table 1. Of 120 patients, 42 (35%) had a clinical diagnosis of GCA at three months and 42% fulfilled ACR1990 criteria for temporal arteritis. Based on US alone, 36% of patients had GCA. A

diagnosis or exclusion of GCA were done on median 1 day (in 55% of patients). However, in cases where further diagnostics (TAB and PET-CT) were necessary, the time for diagnosis increased substantially. See table 2 for data on waiting time from referral, diagnoses and time required for diagnosis.

Table 1

Demographic and clinical data (n=120)	
Females	72%
Age (years)	74 (46-98)
Symptom duration (days)	16 (1-180)
New onset headache	72%
Jaw claudication	21%
Temporal artery abnormality	33%
Visual symptoms	42%
Visual loss (permanent visual loss)	18% (19%)
Constitutional symptoms	32%
Fever	11%
Weight loss	18%
Polymyalgia symptoms	33%
Glucocorticoid therapy	68%
Duration of glucocorticoid (days)	3 (1->365)
Haemoglobin (mmol/L)	8.0 (5.0-10.0)
C-reactive protein (mg/L)	22 (0-290)
Sedimentation rate (mm/hr)	38 (2-146)

Values are percentage, median (range)

Table 2

Office days from referral to visit	1 (0-20)
Days for diagnosis/exclusion of GCA	1 (1-46)
GCA clinical diagnosis	35%
GCA ACR1990 criteria	42%
Nr. of US (% w. GCA)	120 (36%)
Nr. of PET-CT (% w. GCA)	44 (23%)
Nr. of TAB (% w. GCA)	34 (21%)
Polymyalgia diagnosis	17%
Arthritis diagnosis	5%
Other diagnosis	17%

Conclusion: In this newly established GCA FTC, fast and precise diagnosis of GCA or exclusion of this was possible in majority of patients referred, even though referral criteria were liberal. In 55% of patients, further diagnostic procedures were considered unnecessary, and a diagnosis on day 1 could be established based on US, clinical findings and existing paraclinical data.

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THU0314 RELAPSES AND LONG-TERM REMISSION IN LARGE VESSEL GIANT CELL ARTERITIS IN NORTHERN ITALY: CHARACTERISTICS AND PREDICTORS IN A LONG-TERM FOLLOW-UP STUDY

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Background: Previous studies evaluated clinical relapses and long-term remission mainly in patients with biopsy-proven GCA and/or patients satisfying the ACR 1990 criteria for GCA classification. Also, radiological involvement was unfrequently used to define relapses and monitor disease activity in patients with LV-GCA

Objectives: To evaluate characteristics and predictors of relapses and long-term remission in an Italian cohort of patients with large-vessel (LV) giant cell arteritis (GCA).

Methods: We evaluated 87 consecutive patients with LV-GCA followed up at the Rheumatology Unit of Reggio Emilia Hospital (Italy) for at least 2 years. Patients with relapses and long-term remission were compared to those without. A comparison group of 34 patients with biopsy proven GCA without LV vasculitis (LVV) at diagnosis was considered for comparison.

Results: 37 patients (42.5%) experienced one or more relapses. Nineteen (37.2%) of the 51 relapses were experienced during the first year after diagnosis. The majority of relapses occurred with doses of prednisone (PDN) ≤ 10 mg/day (74.5%). Polymyalgia rheumatica (PMR) (41.2%) and worsening at imaging of LVV (39.2%) were the most frequently observed relapsing manifestations. The total cumulative prednisone dose was significantly higher (p = 0.0001) and the total duration of PDN treatment longer (p = 0.0001) in relapsing patients compared to those without relapses. Relapsing patients had at diagnosis more frequently fever ≥ 38°C (p = 0.03) and visual manifestations (p = 0.03), and less frequently long-term remission (p = 0.003). In the multivariate model fever ≥ 38 °C (HR 3.22, 95%CI:1.43-7.27),duration of PDN treatment (HR 1.01, 95%CI: 1.00-1.02) and total cumulative PDN dose (HR 1.20, 95%CI: 1.09-1.33) were significantly associated with an increased risk of relapses, while aortic arch involvement at imaging at diagnosis (HR 0.22, 95%CI: 0.09-0.55) and long-term remission (HR 0.30, 95%CI: 0.12-0.75) with a reduced risk. 37 patients (42.5%) experienced long-term remission. PMR and disease relapses were less frequently observed (p = 0.003 for both), and the total cumulative prednisone dose was lower (p = 0.005) in patients with long-term remission compared to those without. In the multivariate model the presence of relapses (HR 0.33, 95%CI: 0.14-0.78) and the total cumulative PDN dose (HR 0.89, 95%CI: 0.83-0.96) were significantly negatively associated with long-term remission.

Conclusion: In our cohort of patients with LV GCA we identified predictors of a relapsing course and long-term remission, which were observed in around half of the patients.

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THU0315 THE CLINICAL RELEVANCE OF SERUM IMMUNE COMPLEXES IN ANCA-ASSOCIATED VASCULITIS

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Background: AAV is an autoimmune disease characterized by systemic vasculitis and pauci-immune-type crescentic glomerulonephritis (CGN) with ANCA production[1)]. Several authors have reported cases of ANCA-associated CGN with definite IC deposits[2)3)], however, the clinical significance of IC in patients with ANCA-associated CGN remains unclear.

Objectives: To investigate the clinical relevance of serum immune complexes (ICs) in ANCA-associated vasculitis (AAV) patients.

Methods: We developed a novel proteomic strategy for identifying and profiling antigens in immune complexes in the serum of microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA) patients. The serum was collected from the cohort of Japan Research Committee of the Ministry of Health Labour, Welfare for Intractable Vasculitis (JPVAS) before treatment and 6 months after initiation of treatment. The serum from healthy individuals was used for control samples. The Baseline data of each patient was collected with demographic information, laboratory data, disease activity according to the Birmingham Vasculitis Activity Score (BVAS) 2003, disease severity, and imaging data.

Results: We were able to examine 91 AAV patients (52 MPA patients and 39 GPA patients) with 82.4% for MPO-ANCA positive and 20.9% for PR3-ANCA positive. Almost half of the patients was female (56.0%). The median age was 70 years [interquartile range (IQR): 64-77]. The median BVAS was 17 (IQR: 12-23). We identified autoantigen of EGF-containing fibulin-like extracellular matrix protein 1 (EFEMP1) in 43 of MPA (82.6%) and 16 of GPA (41.0%) at baseline. After 6 months of treatment, no cases of EFEMP1 were identified in MPA and GPA. The clinical features of EFEMP1 positive in AAV patients were higher age at onset (p <0.01), less ear, nose and throat symptoms at initiation of treatment (p <0.05), higher serum Cr at initiation of treatment (p <0.01), higher vasculitis damage index (VDI) renal component at 12 months and 24 months after initiation of treatment (both p <0.05).

Conclusion: Our findings indicate that an autoantigen as immune complexes of EFEMP1 were involved in the pathogenesis of AAV patients and may predict renal prognosis.

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Table. Comparison with and without EFEMP1 (all cases)

group	EFEMP1 positive (n=59)	EFEMP1 negative (n=32)	**p-value
Sex(%male)	27/59 (45.8%)	13/32 (40.6%)	0.665
Age, years	74 (66-78)	68 (60-71)	0.003
WBC(/ml)	8270 (7325-12725)	9150 (7325-11700)	0.280
Cr(mg/dl)	1.4 (0.9-3.8)	0.8 (0.6-1.5)	0.005
CRP(mg/dl)	7.0 (2.3-12.5)	7.6 (4.0-11.0)	0.566
MPA(%)	43/59 (72.9%)	9/32 (28.1%)	<0.001
GPA(%)	16/59 (27.1%)	23/32 (71.9%)	<0.001
MPO-ANCA positive	54/59 (91.5%)	24/32 (65.6%)	0.003
PR3-ANCA positive*	7/56 (12.5%)	12/32 (37.5%)	0.012
BVAS total	15 (12-20)	20 (12-25)	0.087
BVAS renal positive	53/59 (89.8%)	26/32 (81.3%)	0.332
BVAS chest positive	16/59 (27.1%)	14/32 (43.4%)	0.161
BVAS ENT positive	17/59 (28.8%)	18/32 (56.3%)	0.014
BVAS systemic positive	40/59 (67.8%)	24/32 (75.0%)	0.631
VDI renal 6 months	1 (0-2)	0 (0-1)	0.053
VDI renal 12 months	1 (0-2)	0 (0-1)	0.007
VDI renal 24 months	1 (0-2)	0 (0-1)	0.012

IQR interquartile range. Values are median(IQR) or n(%), *missing data, **Wilcoxon signed-rank test/Fisher's exact test

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THU0316 VALIDATION OF ACR/EULAR PROVISIONAL CLASSIFICATION CRITERIA FOR ANCA-ASSOCIATED VASCULITIS IN A LATIN-AMERICAN TERTIARY CENTER

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Background: There is lack studies about performance of new criteria set for ANCA-Associated Vasculitis (AAV) in Latin-America.

Objectives: To validate the new classification criteria for AAV in a real-life cohort of patients with these conditions.

Methods: We performed a review of medical records from January 1990 to December 2019 at Hospital Nacional Guillermo Almenara Irigoyen from Peru. AAV was diagnosed by experienced rheumatologists based on the ACR 1990 criteria, Chapel Hill 2012 consensus, EMEA criteria and their experience and clinical acumen. Granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA) were diagnosed. Renal limited vasculitis was considered as MPA. To evaluate the performance of the new criteria, we classified all patients using "former criteria set" (including the 1990 ACR criteria for GPA and EGPA and the 1994 Chapel Hill Consensus Conference for MPA) and the EMEA (European Medicines Agency) criteria set. At the same time, we classified all patients using the ACR/EULAR Provisional criteria (new criteria set). The values for sensitivity, specificity and level of agreement (using Cohen's kappa) of all sets of criteria were calculated using the clinical diagnosis as gold standard.

Results: Two hundred twelve patients were identified; 12 of them were excluded (eight did not have ANCA and four had incomplete data). Female/male ratio was 1.9:1 [130 (65%)/70 (35%)] and their mean (SD) age at diagnosis was 59.3 (12.6) years. One hundred fifty-four (77%) had MPA, 41 (20.5%) GPA and 5 (2.5%) EGPA. One hundred ninety-six patients had ANCA-IIF results [p-ANCA: 131 (66.8%), c-ANCA: 43 (21.9%), negative-ANCA: 22 (11.3%)] and 190 patients had ANCA-ELISA results [MPO: 129 (67.9%), PR3: 37 (19.5%), negative-ANCA: 24 (12.6%)]. Type of diagnosis according to criteria set used is depicted in Table 1. The new criteria set had better agreement (kappa: 0.653) than the EMEA criteria (kappa: 0.506) and the former criteria set (kappa: 0.305). Performance of the criteria sets is depicted in Table 2.

Table 1. Type of AAV according to criteria set used.

TYPE OF AAV	Clinical diagnosis	Former criteria	New criteria	EMEA criteria
MPA, n (%)	154 (77)	76 (38)	137 (68.5)	110 (56.0)
GPA, n (%)	41 (20.5)	30 (15)	39 (19.5)	39 (19.5)
EGPA, n (%)	5 (2.5)	2 (1)	4 (2)	2 (1.0)
Not classifiable, n (%)	NA	92 (46)	20 (10)	44 (22.0)
PAN				5 (2.5)

PAN: Polyarteritis nodosa. NA: Not applicable.

Table 2. Performance of the different criteria sets in AAV patients.

DIAGNOSIS	CRITERIA SET	SE	SP	Kappa
MPA	Former	49.4	100.0	0.309
	EMEA	69.9	93.9	0.471
	New	87.0	93.5	0.713
GPA	Former	68.3	98.7	0.744
	EMEA	92.7	99.4	0.938
	New	80.5	96.2	0.781
EGPA	Former	40.0	100.0	0.565
	EMEA	40.0	100.0	0.565
	New	60.0	99.5	0.659

SE: Sensitivity. SP: Specificity.

Conclusion: The ACR/EULAR Provisional Criteria for AAV have better agreement with the clinical diagnosis of AAV in Latin-American patients from a real-life cohort.

Disclosure of Interests: Victor Pimentel-Quiroz: None declared, Alfredo Sánchez-Torres: None declared, Cristina Reategui Sokolova: None declared, Rocío Violeta Gamboa Cárdenas Grant/research support from: Pfizer, César Sánchez-Schwartz: None declared, Mariela Medina Chinchon: None declared, Francisco Zevallos Miranda: None declared, Erika Noriega: None declared, Jose Alfaro Lozano Speakers bureau: Lilly, Jorge-M Cucho-V: None declared, Zoila Rodriguez Bellido: None declared, Cesar Pastor Asurza: None declared, Eduardo Acevedo-Vásquez: None declared, Risto Perich Campos Consultant of: Pfizer, Speakers bureau: Pfizer, Graciela S Alarcon: None declared, Manuel F. Ugarte-Gil Grant/research support from: Jannsen, Pfizer

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THU0317 EXPANDED DOUBLE NEGATIVE T CELLS IN PATIENTS WITH ANTINEUTROPHIL CYTOPLASMIC AUTOANTIBODY ASSOCIATED VASCULITIS PRODUCE CYTOKINES AND INDUCE RENAL DAMAGE

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Background: Antineutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis (AAV) are recognized as a small-vessel vasculitis of autoimmune origin characterized by inflammation and the presence of circulating ANCA with the major target antigens identified as proteinase 3 (PR3) and myeloperoxidase (MPO). A very minor T cell subpopulation which lacks both CD4 and CD8 markers, known as CD4-CD8- double negative (DN) represents less than 5% of the total peripheral blood (PB) T cells in healthy individuals and plays a vital role in the pathogenesis of autoimmune disorders.
Objectives: To investigate whether DN T cells and cytokine (IFN-γ, IL-4 and IL-17) are involved in the pathogenesis of AAV and to verify whether DN T cells are associated with kidney damage.
Methods: Nineteen healthy controls (HCs) and 40 active patients with AAV were enrolled in this study. Peripheral blood mononuclear cells from AAV patients and controls were isolated by magnetic bead separation, and phenotypic characterisation of mononuclear cells were determined via flow cytometry. The diagnostic value for DN T subsets was evaluated by the areas under the receiver operating characteristic curves (AUC).
Results: The percentage (p<0.001) and absolute numbers (p=0.028) of DN T cells were found to be significantly higher in patients with AAV as compared with controls. Less the percentage of DN T cells from patients with AAV were of CD62L+CD45RO+ (p=0.024) phenotype than was found in HCs, and the percentage of CD62L-CD45RO- (p=0.043) was higher. The percentage of DN T cells expressing IFN-γ (p=0.032), IL-4 (p=0.039) and IL-17 (p=0.042) increased in AAV patients. In AAV with renal damage, the percentage of DN T cells was expanded (p=0.016) than those patients without renal damage. After conventional methylprednisolone treatment, the percentage of DN T cells in patients with remission was significantly lower than those active patients (p=0.028). The ROC curve analysis showed that the ratios of CD4+ T cells to DN T cells and CD8+ T cells to DN T cells were useful in diagnosing AAV patients. The AUCs were 0.967 (95% confidence interval [CI] 0.922-1.000; p<0.001) and 0.879 (95%CI 0.789-0.969; p<0.001), respectively.
Conclusion: DN T cells represent a inflammatory T cell subset that produces inflammatory cytokines (IFN-γ, IL-4 and IL-17) in AAV patients. Suppression of DN T cells may be new specific treatment in autoimmune disorder such as AAV.
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Disclosure of Interests: None declared
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THU0318 PATTERNS OF CLINICAL PRESENTATION IN TAKAYASU'S ARTERITIS

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Background: Takayasu's arteritis (TAK) is a clinically heterogenous disease. Patterns of clinical presentation in TAK at diagnosis have not been well described, and a "triphasic pattern" of constitutional symptoms evolving into vascular inflammation and fibrosis has been reported but never systematically evaluated.
Objectives: To describe patterns of clinical presentation in TAK at diagnosis and evaluate the presence of an antecedent triphasic disease pattern in patients with TAK who presented with a major ischemic event at diagnosis.
Methods: Patients with TAK were prospectively recruited from the National Institutes of Health (NIH) and the Vasculitis Clinical Research Consortium (VCRC). All patients fulfilled the 1990 American College of Rheumatology (ACR) Classification Criteria for TAK. Based on clinical presentation at diagnosis, patients were divided into five groups from the different stages of the triphasic pattern of disease as follows: 1) constitutional symptoms (phase I), 2) carotidynia (phase II), 3) other vascular-associated symptoms (phase II), 4) major ischemic event (phase III) defined as CVA or TIA, retinal ischemia, MI, renovascular hypertension, or mesenteric ischemia, or 5) asymptomatic. Phase II was divided into two separate groups because patients with carotidynia reportedly have a higher rate of relapsing disease.
Associated clinical characteristics were evaluated in each group and differences among groups were assessed by chi square test and Kruskal-Wallis test, as appropriate. Preceding symptoms were also assessed to determine the presence of a triphasic disease pattern.
Results: A total of 275 patients with TAK were included (VCRC=208; NIH=67). Similar heterogeneity of clinical presentation was identified in each cohort: constitutional symptoms (8%), carotidynia (13-15%), other vascular symptoms (43-47%), major ischemic event (28-30%), and asymptomatic (2-6%). Frequency of male gender was more common in patients who presented with constitutional symptoms or were asymptomatic at diagnosis (p<0.01). Patients who presented with constitutional symptoms and major ischemic events were youngest at diagnosis. Patients in the asymptomatic group were oldest at diagnosis and often were not treated (p<0.01). Involvement of the abdominal vasculature was associated with major ischemic events and asymptomatic presentations. Major ischemic events after diagnosis were infrequent in the groups who did not present with a major ischemic event, occurring in 10-20% cases. Relapse (p<0.01) and recurrent pharyngitis preceding diagnosis (p<0.01) was most frequent in patients who presented with carotidynia.
A total of 79 patients [VCRC=59 patients, NIH=20 patients] presented with a major ischemic event. The majority of these patients (53%) reported symptoms of active disease prior to the major ischemic event. Few patients (19%) who presented with a major ischemic event reported a triphasic pattern of disease.
Conclusion: There is heterogeneity in clinical presentation at the time of diagnosis in TAK and this heterogeneity can be used to group patients according to pattern of disease presentation. Patients do not necessarily progress sequentially through phases of disease, but the majority of patients presenting with a major ischemic event report some preceding symptoms. Data from this study demonstrate distinct subgroups within TAK and supports the concept that TAK is possibly a heterogenous collection of multiple diseases.
References: N/A

Disclosure of Interests: None declared
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THU0319 DEVELOPMENT AND OUTCOME OF AORTIC COMPLICATIONS DURING TOCILIZUMAB TREATMENT OF GCA AND HISTOPATHOLOGIC EVIDENCE OF RESIDUAL INFLAMMATION-A CASE SERIES.

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Background: Giant cell arteritis (GCA) may affect the aorta and the large aortic branches and lead to dissections and aortic aneurysms. Tocilizumab (TCZ) treatment has the capacity to control aortic inflammation as has been demonstrated by CRP normalization and imaging data. However, limited data are available on the histopathological findings obtained from patients who underwent surgery because of aortic complications during TCZ treatment.
Objectives: We report on 5 patients with aortitis who were treated with TCZ and developed aortic complications.
Methods: We describe a retrospective case series of patients with GCA treated with TCZ, who presented in our clinic between 2011 and 2019. Three patients underwent surgery. Histopathologic examination was performed in specimen from all of them.

Results: Five female patients were diagnosed with GCA (4/5) or Takaysu arteritis (1/5) involving the aorta, all them diagnosed by MR angiography and/or FDG PET CT scan. Three patients (one with aortic aneurysm, one with dissection) underwent surgery after having been treated with TCZ for seven weeks, nine months and four years, respectively. Imaging before surgery showed remission on MRI and/or PET-CT in all cases. At the time of surgery, all patients showed normalized CRP and ESR values. Histopathological evaluation of the aortic wall revealed infiltrates, consisting predominantly of CD3+CD4+ T cells. Enlargement of pre-existing aneuryms was observed in the other two patients 10 weeks and 4 months after discontinuation of TCZ, respectively. Both patients were not eligible for surgical intervention and died during follow-up.

Conclusion: Our case series suggests that during treatment with TCZ, regular imaging is necessary in this patient population to detect development of structural changes such as aneurysms or dissections. Despite treatment, residual inflammation might persist which could contribute to eventual aortic complications.

Disclosure of Interests: Andrea Rubbert-Roth Consultant of: Abbvie, BMS, Chugai, Pfizer, Roche, Janssen, Lilly, Sanofi, Amgen, Novartis, Peter Karl Bode: None declared, Thomas Langenegger: None declared, Claudia Pfofe: None declared, Thomas Neumann: None declared, Olaf Chan-Hi Kim: None declared, Johannes von Kempis Consultant of: Roche

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THU0320 RENAL TRANSPLANTATION DUE TO RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS (RPGN) AND SYSTEMIC AUTOIMMUNE DISORDERS. STUDY OF 42 PATIENTS FROM A SINGLE CENTER.

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Background: Rapidly Progressive Glomerulonephritis (RPGN) is characterized by a rapid and severe decline in kidney function that may lead to a kidney transplantation. RPGN is classified in three groups: **a)** Type I or associated to anti-glomerular basement membrane antibodies (RPGN-GBMa), **b)** Type II or associated to immunocomplexes (RGPN-immunocomplexes), and **c)** Type III or pauci-immune (RPGN-pauci-immune). RPGN can be primary, without extra-renal involvement (RPGN-renal-limited), or secondary to systemic autoimmune disorders (RPGN-SAD), infectious diseases or drugs. Kidney transplantation in RPGN-SAD may be associated to a worse outcome.

Objectives: To assess **a**) clinical features of the three types of RPGN, **b)** comparison of post-transplant survival and graft survival between these three types.

Methods: We studied three groups of patients according to renal biopsy: **a)** RPGN-GBMa (n = 11), **b)** RPGN-immunocomplexes (n = 2) and c) RPGN-pauci-immune (n=29). All these patients were transplanted in a single reference University Hospital. The main outcome variables were **a)** graft survival up to 15 years and patient survival up to 30 years and **b)** evolution of renal function (serum creatinine and proteinuria) in the first 5 years of follow-up.

Results: We included a total of 42 patients with renal transplant due to RPGN, mean age at diagnosis 44.87±17.01 years (48.53±17.45 at the time of the transplant). No significant differences at baseline were observed between the three RPGN groups regarding sex, age and cardiovascular risk factors. Renal biopsy had been performed in the 42 patients with RPGN: type I or RPGN-GBMa (n=11, 26.2%), type II or RPGN-immunocomplexes (n=2, 4.8%) and type III or RPGN-pauci-immune (n=29, 69.0%).

It was also reported the presence or absence of systemic autoimmune disorders (31% RPGN-SAD and 69% RPGN-renal-limited). According to the presentation and the clinical characteristics of the patients, another classification has been established: **a)** type I (18.2% (n = 2) Goodpasture-syndrome), **b)** type II (100% renal-limited), **c)** type III (13.8% (n = 4) granulomatosis with polyangiitis) and 20.70% (n = 6) microscopic polyangiitis. The evolution of serum creatinine and the proteinuria after the transplant is shown in TABLE 1 **and 1.1**. Neither differences were found in terms of graft and patient survival between the 3 groups (Figures 1 and 2).

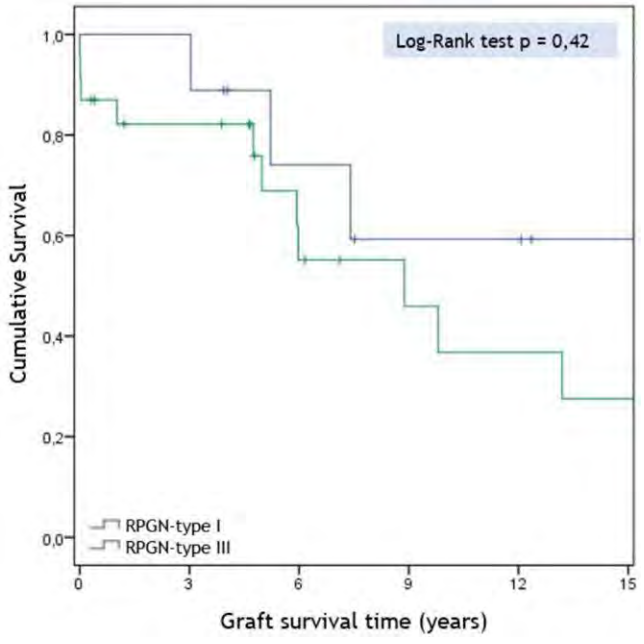


Figure 1. Graft survival.

TABLE 1.

	1 Month			6 Months			1 Year		
Serum Creatinine mg/dL	RPGN-type I	RPGN-type II	RPGN-type III	RPGN-type I	RPGN-type II	RPGN-type III	RPGN-type I	RPGN-type II	RPGN-type III
N	11	2	26	10	2	22	10	2	22
Mean±SD	1.78±0.8	3.85±.4.03	1.64±0.67	1.59±0.73	1.45±0.77	1.99±1.31	1.55±0.62	1.50±0.70	1.77±1.10
Proteinuria mg/24 h	RPGN-type I	RPGN-type II	RPGN-type III	RPGN-type I	RPGN-type II	RPGN-type III	RPGN-type I	RPGN-type II	RPGN-type III
N	9	2	23	10	1	19	10	ND	19
Mean±SD	470.00±566.85	400.00±565.68	408.22±449.00	611.87±832.20*	797.00±556.29*	362.98±323.38*	656.10±1206.68	ND	282.54±272.35

*p<0.05

TABLE 1.1

	3 Years			5 Years		
Serum Creatinine mg/dL	RPGN-type I	RPGN-type II	RPGN-type III	RPGN-type I	RPGN-type II	RPGN-type III
N	11	2	20	8	2	18
Mean±SD	1.64±0.74	1.70±0.69	1.85±1.34	1.55±0.86	1.60±0.84	1.72±0.82
Proteinuria mg/24 h	RPGN-type I	RPGN-type II	RPGN-type III	RPGN-type I	RPGN-type II	RPGN-type III
N	11	2	17	8	2	16
Mean±SD	510.79±832.90	272.57±291.20	340.65±344.17	238.23±311.19	443.88±300.87	579.26±1114.5

*p<0.05

Conclusion: Our study has shown similar graft and patient survival as well as renal outcome in renal transplant due to the three types of RPGN. Renal transplantation could be the best option for patients with end stage renal disease due to RPGN regardless of systemic manifestations.

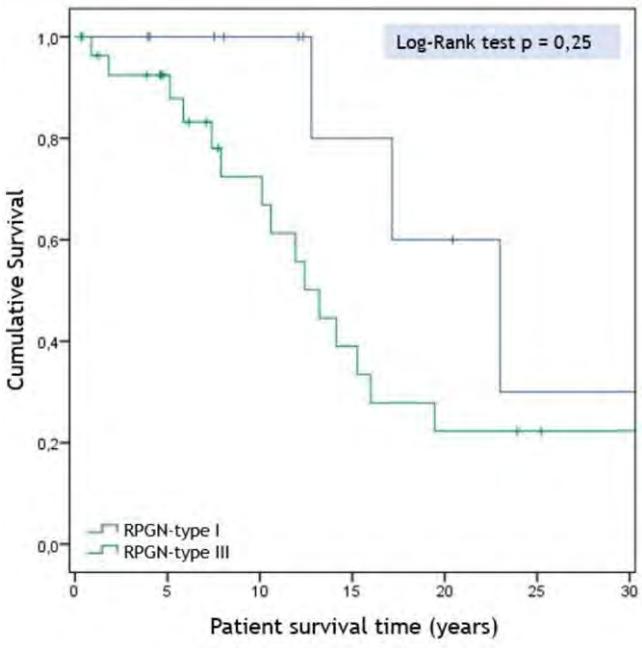


Figure 2. Patient survival.

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THU0321 URINARY T CELLS IDENTIFY ACTIVE RENAL ANCA ASSOCIATED VASCULITIS

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Background: ANCA-associated vasculitis (AAV) causes necrotizing crescentic glomerulonephritis (NCGN) which is a major contributor to morbidity and mortality in AAV. Since therapy relies on cytotoxic agents with potentially severe adverse effects, a reliable non-invasive biomarker of disease activity is needed to determine the right balance between over- and undertreatment. Using the urine space as a window into the local inflammatory milieu of the kidney, quantification of urinary leukocytes using flow cytometry has become an upcoming marker of various other inflammatory kidney diseases. As recent studies have illuminated the emerging role of T regulatory (Treg) and Th17 cells in the pathogenesis of AAV, these could represent a viable non-invasive biomarker more closely displaying the underlying pathogenic processes than metabolites or epiphenomena of inflammation.

Objectives: To quantify urinary T cells in active renal AAV and asses their biomarker characteristics.

Methods: Using flow cytometry, T-lymphocytes and their subsets were quantified in peripheral blood and urine samples from patients with active AAV with or without NCGN, in stable remission with previous NCGN and healthy controls. Concentrations of urinary soluble metabolites and cytokines (Monocyte-attracting protein 1 (MCP-1), sCD163, sCD25 and C5a) were measured using Multiplex analysis. Results were verified in a separate validation cohort.

Results: Patients with renal active AAV (n = 30) showed significantly higher urinary cell counts of total T cells, CD4+, CD8+, Treg and Th17 subsets than disease (n = 21) and healthy controls (n = 8). Patients with active renal AAV also showed a significantly higher percentage of Tregs in urine than in blood. While Tregs allowed a robust discrimination between active renal AAV and disease controls (receiver operator characteristics (ROC): area under the curve (AUC) 0.93, sensitivity 79%, specificity 95%) quantification of all T cells proved to be slightly more accurate (ROC: AUC 0.95, sensitivity 92%, specificity 95%). Soluble markers showed a slightly inferior discrimination (MCP-1 ROC: AUC 0.90, sensitivity 60%, specificity 100%, sCD163 ROC: AUC 0.92, sensitivity 96%, specificity 85%) while sCD25 and C5a were far less accurate.

Conclusion: Urinary T cells are significantly elevated in active renal AAV and the increased frequency of Tregs in urine suggests active migration into inflamed glomeruli and thereby the urine rather than mere bleeding of ruptured capillaries. These cells show great potential for a non-invasive biomarker close to the local inflammatory milieu. Particularly the total count of urinary T cells showed slightly superior biomarker characteristics than previously established soluble markers. Further studies are needed to confirm these results and show potential prognostic value of these cellular markers.

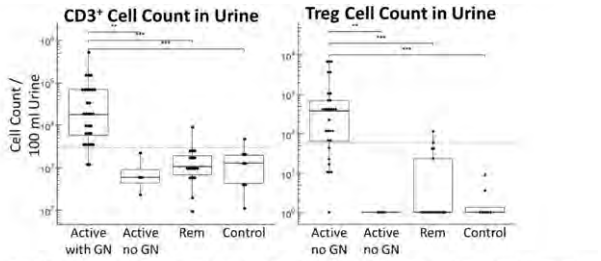


Fig. 1 Boxplots of urinary T cells in ANCA associated vasculitis, dotted line indicates optimal cut-off to determine renal disease activity Kruskal-Wallis with post-hoc Dunn's, p-value summary: * = 0.05 – 0.01 ** = 0.01 – 0.001, *** ≤ 0.001
GN: glomerulonephritis, Rem: stable remission with previous GN

Disclosure of Interests: None declared

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THU0322 EFFECTIVENESS OF COMBINED LOCAL COLCHICINE AND STEROIDS IN ORAL ULCERS OF BEHÇET'S DISEASE

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Background: Behçet's disease (BD) is a chronic, multi-system vasculitic disease. It is characterized with relapsing episodes of oro-genital ulcers accompanied by cutaneous lesions, ocular symptoms, arthropathy, vascular thrombosis, central nervous system, gastrointestinal & cardiopulmonary involvements. Oral ulcers are frequently the first disease manifestationOral and genital ulcers cause pain and interfere with the quality of life. They may lead to difficulty in swallowing and walking. Most of them can be managed with topical glucocorticoids. Up till now there is no study discussed the effect of combined local therapy on oral ulcers in BD.[1,2]

Objectives: To evaluate the effectiveness of combined local therapy (colchicine, steroid, antibiotic and anesthetic) on oral ulcers in BD

Methods: This study included 44 Patients who had Behçet's disease (according to International Study Group criteria) with active oral ulcers (at least three times in the previous 12-month period) Patients were excluded if they had active major organ involvement in the last 6 months. Patients with depilating diseases also were excluded.

Patients were randomly divided into two equal groups; group I received combined local therapy (lidocaine HCL 2.0% gel mixed with grinded tablet of 5 mg prednisone and grinded tablet of 0.6 mg colchicine). Group II received combine local therapy (lidocaine HCL 2.0% gel mixed with grinded tablet of 5 mg prednisone). Local treatments were applied to the lesions 3 times per day until healing of the ulcer (advised not to eat or drink for 30 minutes after application). All other topical medications were stopped during this study.

All patients were assessed with Oral ulcer severity score (OUSS), Behçet's Disease Quality of Life score (BD-QoL), Medical Outcomes Study Questionnaire Short Form 36 Health Survey (SF-36) at baseline and after 24 weeks.

Results: Thirty eight patients had completed this study; (20 in Group I & 18 in Group II). There were no significant differences between the 2 groups in both demographic data &educational status. At baseline there was no significant difference between both groups regarding all assessment measures. There was significant improvement ($P<0.05$) in both groups regarding OUSS, BD-QoL, SF-36 after 24 weeks. There was significant better improvement

(P<0.05) in group I than in group II in all assessment measures (except ulcer free periods and sites). The results of the study are summarized in table 1 & figure 1.

Table 1. A comparison of the individual ulcer characteristics in both groups at baseline and after 24 weeks

Ulcer characteristics	Group I baseline	Group II baseline	Group I after 24 weeks	Group II after 24 weeks
Number	13.6 ±3.5	12.9 ±2.3	8.2 ±1.5*¶	10.3 ±1.7*
Size	11.8 ±3.3	12.5 ±2.4	7.6 ±1.8*¶	9.6 ±1.2*
Duration	6.7 ±1.1	6.6 ±1.7	4.5 ±1.9*¶	5.5 ±1.3*
Ulcer-free period	4.7 ±0.9	5.1 ±1.5	5.7 ±1.1*	5.9 ±0.7*
Pain	8.7 ±1.2	8.6 ±1.4	5.3 ±1.5*¶	6.7 ±1.1*
Site	4.9 ±0.8	5.1 ±1.2	3.8 ±0.6*	4.2 ±0.9*

***Significant improvement after 24 weeks of the study**
¶ Significant difference between the two studied groups

Conclusion: Combined local therapy (colchicine, steroid, antibiotic and anesthetic) is an effective method in management of oral ulcers in BD.

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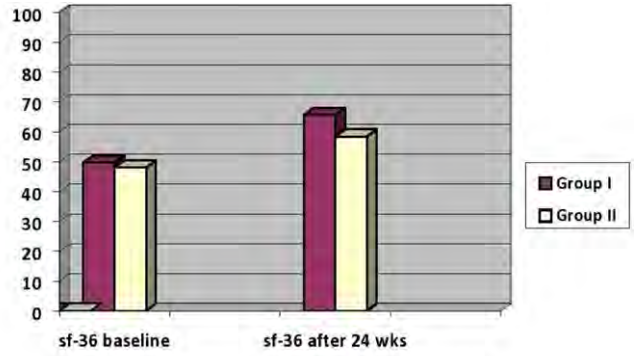


Figure 1: SF-36 (Total score) at baseline and after 24 weeks in both groups

Disclosure of Interests: None declared
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THU0323 MYELOID BIOMARKERS IN GIANT CELL ARTERITIS AND POLYMYALGIA RHEUMATICA – TWO INDEPENDENT COHORTS

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Background: Giant cell arteritis (GCA) commonly overlaps with polymyalgia rheumatica (PMR). The incidence of GCA among PMR patients is between 16 and 21%, and both diseases are treated with long-term glucocorticoids (GCs). Patients with GCA suffer from inflammation of their large-sized arteries, whereas PMR is characterized by synovial inflammation. A key question for every physician dealing with a PMR patient is whether or not the patient also has GCA. Symptoms of GCA are often non-specific and difficult to identify. Compared to healthy controls (HCs), newly-diagnosed GCA and PMR patients display a change in leukocyte composition with a shift towards the myeloid lineage, evidenced by elevated monocyte and neutrophil counts. Persistence of this myeloid bias (during and after treatment) is in congruence with mounting evidence that GCs do not sufficiently suppress the vascular/synovial inflammation, contributing to a relapsing disease course. Yet, it may be difficult to readily identify the myeloid bias in the blood, and therefore easily detectable biomarkers are required to monitor this myeloid bias in GCA and PMR patients.

Objectives: The first objective of this study is to identify disease specific biomarkers for GCA and for PMR using myeloid serum/plasma markers. Next, we assessed whether (a profile of) these markers could be used to reflect the persistent myeloid profile.

Methods: Biomarkers were measured in two independent cohorts: Groningen, the Netherlands (GPS cohort) and Aarhus Denmark (Aarhus cohort). Both cohorts included treatment-naive GCA and PMR patients, supplemented with age- and sex matched HCs (Table 1). Along with the GPS cohort, age-matched inflammatory controls were included. GCA-lookalike patients were added in the measurements for the Aarhus cohort. All patients started treatment with GCs, and follow-up samples were measured at 8 weeks for GCA patients. All measurements were performed by ELISA: sCD206, calprotectin, A1AT and elastase in serum samples, whereas PR3 and MPO were measured in plasma samples.

Table 1. Baseline characteristics of the two cohorts

	GPS cohort			Aarhus Cohort				
	GCA	PMR	HC	Infection	GCA	PMR	HC	GCA-lookalike
N	48	39	50	16	52	25	20	18
PET-CT: positive/ negative/ not done	32 5 11	0 29 10	NA	NA	48 4 0	0 25 0	NA	0 13 5
CRP, median (mg/L)	52	35	2	70	74	35	1	54

Results: Analyses of biomarkers in the two cohorts had mostly equivalent results. Compared to HCs, levels of sCD206, calprotectin, PR3 and A1AT were elevated in GCA, PMR and infection/GCA-lookalike patients. GCA patients had higher levels of sCD206 than PMR patients, but only in the Aarhus cohort this reached statistical significance (Aarhus: p=0.02, GPS: p=0.17). Treatment with GCs substantially affected the biomarker levels: in GCA patients of both cohorts, calprotectin and A1AT levels dropped, sCD206 levels remained high (unchanged), and elastase and PR3 levels increased. Next, we assessed whether the biomarkers correlated with inflammation and the myeloid bias in the GPS cohort. Particularly in GCA patients, A1AT levels correlated with inflammatory marker CRP. Elastase correlated significantly with neutrophil counts in both GCA (R=0.42) and PMR (R=0.57). Calprotectin correlated with neutrophil counts in both GCA and PMR, and with monocyte counts in GCA.

Conclusion: This is one of the first studies in GCA and PMR patients to study biomarkers in two independent cohorts. We consistently showed elevated levels of monocyte/macrophage and neutrophil products in both cohorts. Levels of sCD206 may help in discriminating GCA from PMR patients. The myeloid bias may be monitored using a combination of calprotectin and elastase levels. Additionally, sCD206 or calprotectin may serve as tissue inflammation markers under the cover of GC treatment, a notion to be further investigated using follow-up imaging data.

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THU0324 CYTOMEGALOVIRUS REACTIVATION AND HIGH INITIAL SERUM CREATININE ARE SIGNIFICANT PROGNOSTIC FACTORS FOR SUBSEQUENT SEVERE INFECTIONS IN PATIENTS WITH ANCA-ASSOCIATED VASCULITIS

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Background: There are several reports that cytomegalovirus (CMV) reactivation resulted in more co-infections affecting survival in rheumatic disease, and CMV reactivation can lead to infections in granulomatosis with polyangiitis patients by inducing CD4+CD28- T cell and depressing naïve T cell populations.[1-4] Despite this evidence, the prognostic value of CMV reactivation for severe infections in patients with connective tissue disease are still unknown.

Objectives: The aim of this study was to examine prognostic factors for severe infection during the early phase of treatment, especially in CMV reactivation, in patients with antineutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis (AAV) who received initial high dose corticosteroid therapy (prednisolone > 0.8mg/kg/day).

Methods: We analyzed the data of 88 consecutive hospitalized patients newly diagnosed with AAV at our hospital from January 2006 to March 2019 in this retrospective cohort study. There were 32 patients with CMV reactivation during remission induction therapy compared to 56 patients without CMV reactivation. CMV reactivation was defined by the detection of CMV pp65 antigen in blood samples, and CMV positive cells ≥ 5 per 3.0×10^5 polymorphonuclear neutrophils (PMNs). The variable for severe infections within 180 days with a p value < 0.1 in univariate analysis were selected for multivariate analysis using the Cox regression model. The positive predictive value (PPV) and positive likelihood ratio (PLR) of CMV reactivation for subsequent severe infections were also analyzed.

Results: Patients with CMV reactivation, compared to those without, had a higher prevalence of MPO-ANCA, renal manifestation and renal impairment at diagnosis, received hemodialysis (HD), higher revised five factor score (FFS), older age, higher Birmingham Vasculitis Activity Score at diagnosis, and higher initial doses of corticosteroids (CS) at baseline. Revised FFS ≥ 2, renal involvement, high initial serum creatinine (≥ 1.5 mg/dl) at diagnosis, received HD, and CMV reactivation were associated with severe infections in the univariate analysis, although receiving cyclophosphamide or rituximab was not. Among these variables, CMV reactivation (Hazard ratio [HR] 3.50; 95% confidence interval [CI]: 1.22-10.10; p = 0.02) and high initial serum creatinine at diagnosis (HR 8.09; 95%CI: 2.00-32.73; p < 0.01) were independent risk factors for severe infections within 180 days. (Table 1) The PPV and PLR of CMV reactivation for subsequent severe infections were 35% and 1.91. When including higher initial serum creatinine, PPV and PLR for subsequent severe infections was 67% and 7.26.

Table 1. Cox regression analysis for severe infections within 180 days.

	Univariate analysis		Multivariate analysis	
Potential prognostic factors	HR (95% CI)	P value	HR (95% CI)	P value
Age ≥ 65	1.36 (0.48-3.71)	0.580		
Male	1.23 (0.50-3.04)	0.648		
Past history of lung disease	0.39 (0.11-1.36)	0.140		
Past history of diabetes mellitus	0.64 (0.15-2.77)	0.550		
Lung involvement	1.76 (0.67-4.62)	0.254		
Renal involvement†	3.68 (1.22-11.10)	0.021		
Serum Cr ≥ 1.5 at diagnosis	9.50 (3.40-26.49)	< 0.001	8.09 (2.00-32.73)	0.003
Hemodialysis	4.85 (1.73-13.54)	0.003	0.96 (0.31-2.97)	0.950
BVAS ≥ 20	1.50 (0.59-3.81)	0.393		
Revised FFS ≥ 2	4.40 (1.28-15.13)	0.018	0.83 (0.16-4.27)	0.818
MPSL pulse therapy	1.16 (0.47-2.86)	0.746		
Received CYC or RTX	1.54 (0.55-4.27)	0.409		
CMV reactivation	5.10 (1.93-13.48)	0.001	3.50 (1.22-10.06)	0.020

† "Renal involvement" was excluded in the multivariate analysis to avoid multicollinearity.

Conclusion: Our study shows that there should be focus on subsequent severe infections when CMV reactivation is detected during early phase of treatment, especially in renal-impaired patients with ANCA-associated vasculitis.

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Disclosure of Interests: Daisuke Waki Speakers bureau: Mitsubishi Tanabe Pharma, AbbVie Inc, eisai Co,. Ltd, ONO PHARMACEUTICAL CO., LTD,, Keisuke Nishimura Speakers bureau: Mitsubishi Tanabe Pharma Corporation. Pfizer Inc. Kyowa Kirin Co., Ltd. Chugai Pharmaceutical Co., Ltd. ONO PHARMACEUTICAL CO., LTD. Japan Blood Products Organization. Kissei Pharmaceutical Co., Ltd. Astellas Pharma Inc. AYUMI Pharmaceutical Corporation. Eisai Co., Ltd. DAIICHI SANKYO COMPANY. Norvartis AG. Bayer AG. Sanofi K.K.
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THU0325 REDUCED OF TREG CELLS ASSOCIATED WITH THE DISEASE ACTIVITY OF ANCA-ASSOCIATED VASCULITIS

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Background: Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a group of autoimmune disease that can cause systemic organ damage, characterized with the presence of abnormal antibodies (ANCAs) in the circulation and the small- and medium-vessel vasculitis[1].However,the etiology of AAV remained unclear. Several observations have showed that the breakdown of immune tolerance caused by many complex interactions was involved in the pathogenesis of AAV[2].It has been confirmed that the disorder of the CD4+T cell,especially the imbalance of Th17 and Treg cells can destroy the immune tolerance and cause many autoimmune disease[3]. But the relationship between the Th17/Treg and AAV is unknown.

Objectives: We investigated the absolute numbers of CD4+T subsets cells in peripheral blood of patients with AAV and healthy adults,and then compared them in different disease activity of AAV to explore the role of CD4+T subsets cells in the pathogenesis and development of AAV.

Methods: 49 patients with AAV,hospitalized at the Second Hospital of Shanxi Medical University from the May 2016 to the November 2019 were enrolled, and 31 age and gender-matched healthy adults were anticipated as controls.According to BVAS, the patients were divided into disease-activity group (BVAS≥15, n=27) and non-disease-activity group (BVAS<15, n=22). The absolute numbers of CD4+T subsets cells including Th17 and Tregs in peripheral blood of these individuals were detected by flow cytometry.We analyzed whether there was difference of CD4+T subsets between the patients and healthy controls,and between disease-activity group and non-disease-activity group.

Results: There was significant decreased level of Treg cells in the patients with AAV compared with healthy controls,especially in the disease-activity group. The absolute numbers of Treg cells was decreased in the patients with AAV compared with healthy controls (P<0.001) leading to a higher Th17/Treg ratio in the patients (P<0.01).Similarly,the absolute number of Treg cells was decreased in the disease- activity group (P<0.01) compared with the non-disease-activity group, and the absolute number of Treg cells was significant negative correlation with the disease activity indexes such as BVAS (r=-0.342,P=0.016), erythrocyte sedimentation rate(ESR) (r=-0.315,P=0.027) and C-reactive protein(CRP) (r=-0.305,P=0.033). But there was no statistically significant in the absolute number of Th17 cells between the patients and healthy controls, and between disease-activity group and non-disease-activity group.

Conclusion: The results we investigated here suggested that the decreased number of Treg cells failed to control autoimmune inflammatory response and maintain immune tolerance, and the disease activity of AAV was associated with the reduced number of Treg cells.

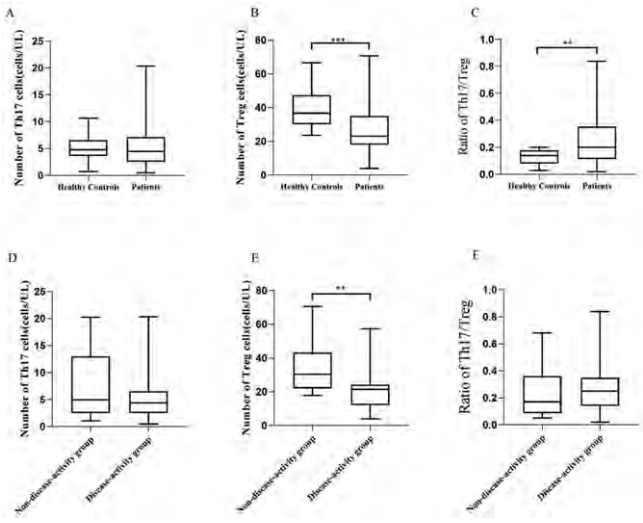


Figure 1. (A-C) Characteristics of the absolute number of Th17 cells and Treg cells in peripheral blood of healthy controls (n=31) and the patients with AAV (n=49). There was significant decreased level of Treg cells in the patients with AAV compared with healthy controls leading to a higher Th17/Treg ratio in the patients with AAV. (D-F) The absolute number of Treg cells was decreased in the disease- activity group (n=27) compared with the non-disease-activity group (n=21). The absolute number of Th17 cells and Treg cells was detected by flow cytometry. Statistical analyses were performed by the Mann-Whitney U test. *p<0.05,**p<0.01, ***p<0.001.

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THU0326 **TOFACITINIB IN THE TREATMENT OF SEVERE AND REFRACTORY BEHÇET'S DISEASE: A SINGLE-CENTRE EXPERIENCE IN CHINA**

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Background: Small-molecule JAK inhibitors have succeeded in the treatment of rheumatoid arthritis, psoriasis, and inflammatory bowel disease[1]. Tofacitinib is under investigation for various autoimmune diseases [2], but its effectiveness on Behçet's disease(BD) has not been demonstrated.
Objectives: We aimed to investigate the efficacy and safety of Tofacitinib in the treatment of severe and refractory BD.
Methods: We retrospectively analyzed the efficacy and safety profile of Tofacitinib in treating severe and refractory BD patients in our hospital from 2017 to 2020.
Results: Thirteen BD patients (7 males and 6 females) were enrolled, with a mean age and median course of 40.6±14.7 years and 84 months (60, 132). Vascular/cardiac, gastrointestinal, and articular involvement were presented in 5, 6, and 2 patients, respectively. Three patients had multiple arterial stenosis or occlusion, two presented with aortic root dilation with aortic valve regurgitation, and one experienced perivalvular leakage (PVL). All the six patients with gastrointestinal involvement had multiple episodes of ileocecal and colon ulcers, intestinal bleed, and three had anastomotic ulcers or leaks.
All the patients had received high-dose glucocorticoids and immunosuppressants before tofacitinib therapy, they displayed poor response with evidence of disease progression; furthermore, three patients with gastrointestinal involvement and one patient with polyarthritis had failed anti-TNF antibody treatment. They were then treated with Tofacitinib, 5mg twice daily, with background glucocorticoids and immunosuppressants, for a median of 6 months (range 4 to 19).
After a median follow-up of 7 (5, 19) months, the ESR and CRP level decreased significantly (21(8, 50) mm/h vs 8(3, 19.5) mm/h, P<0.01, and 25(5.85, 49.5) mg/L vs 1.89(0.44, 6.65) mg/L, P<0.01, respectively). All patients with vascular/cardiac and articular involvement achieved clinical improvement. Vascular lesions of three patients were radiologically stable, no progressive aneurysm or PVL was observed. Two patients with intestinal ulcers revealed complete mucosal healing; the other three had sustained elevation of ESR and CRP, active mucosal ulcers, recurrent bleeding, or fistula formation. The dose of corticosteroids was tapered in six cases (46.2%), furthermore, the number of immunosuppressants lessened in seven cases. However, two patients had herpes zoster infection during follow up, while being treated with five to six immunosuppressants in addition to Tofacitinib for refractory intestinal ulcers.
Conclusion: Our study suggests that Tofacitinib is effective for the treatment of vascular and articular BD; given the limited data, its therapeutic effect on gastrointestinal BD could not be validated. We have to be cautious of infectious risk for severely immunocompromised patients. Further large-scale prospective studies are warranted to confirm the therapeutic potential of JAK inhibitors in BD patients.
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THURSDAY, 04 JUNE 2020

Scleroderma, myositis and related syndromes

THU0327 **EFFECT OF IMMUNOSUPPRESSIVE MEDICATION ON GASTRO-INTESTINAL INVOLVEMENT IN SYSTEMIC SCLEROSIS PATIENTS STRATIFIED FOR DISEASE DURATION.**

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Background: Gastrointestinal tract (GIT) involvement is associated with high morbidity in systemic sclerosis (SSc) but the data on its impact from unselected and well characterized SSc cohorts are scarce. Currently, the effect of immunosuppressive (IS) treatment on GIT involvement is largely unknown.
Objectives: To evaluate the severity and worsening of GIT involvement in two prospective SSc cohorts. To assess factors associated with severity of GIT involvement, stratified for disease duration. To evaluate effect of IS treatment on worsening of GIT involvement.
Methods: All SSc patients fulfilling the 2013 SSc classification criteria from two SSc cohorts were evaluated. Incident SSc was defined as disease duration since first symptom non-Raynaud < 24 months at first presentation. GIT involvement was assessed by the UCLA GIT 2.0 score at baseline and after one year to assess worsening of GIT involvement. Worsening was defined as change > minimal clinical important difference for total score and for each of the seven subdomains. GIT involvement was defined as present if the patients reported symptoms resulting in a score of ≥0.01 and was segregated into mild ≥0.01 (<0.5 or for fecal incontinence and distention/bloating <1.01), moderate (≥0.5 or for fecal incontinence and distention/bloating ≥1.01) or severe GI symptoms (> 1.01 or for distension/bloating > 1.61 or for fecal soiling > 2.01). Logistic regression was applied to identify risk factors associated with GIT involvement at baseline. The effect of IS treatment on worsening on each of the subdomains after one year was evaluated with logistic regression, with adjustment for baseline disease duration and severity.
Results: In total, 834 SSc patients were included; 236 (28%) had incident disease (table 1). Incident cases (IC) showed comparable severity of GIT involvement compared to non-incident cases (NIC) except for significantly less severe reflux and distension/bloating (figure 1). Logistic regression showed female sex (OR 8.5(1.1-36.01)) and smoking (OR 2.9(1.2-7.3)) to be associated with GIT severity at baseline in IC; in NIC anti-centromere antibody (OR 1.7(1.3-2.2)) was additionally associated with GIT severity. The use of IS at baseline did not associate with GI severity at baseline. In total n = 685 (82% never had IS treatment (83% NIC, 81% IC); of these 258 (38%) started with IS after baseline assessment (52% IC, 32% NIC, p =0.02). When comparing change of GIT involvement after one year between those who started IS and those who did not, worsening of GI symptoms occurred more frequently in patients who started IS treatment (figure 2), but notably, patients in this group were also more frequently anti-topoisomerase positive, had ILD, and diffuse disease subset compared to the patients without IS treatment; age and sex were comparable. In the logistic regression with adjustment for disease duration and severity, there were no significant associations between IS treatment and worsening on GIT involvement.
Conclusion: Regardless disease duration, about 1/3 of all SSc patients had moderate-severe GIT involvement. Disease duration and treatment initiation with IS did not have a significant influence on worsening of GIT involvement.
Table:

Baseline characteristics

	Non-inception cohort (n=598)	Inception cohort (n=236)
Female, n(%)	504 (85)	180 (76)
Age, mean(SD)	55 (13)	56 (14)
Disease duration non Raynaud-Phenomenon, median (IQR)	8.8 (4.8-14.4)	0.7 (0.3-1.2)
Diffuse cutaneous subset, n(%)	119 (20)	67 (28)
Interstitial lung disease, n(%)	233 (39)	71 (30)
Anti-centromere, n(%)	296 (50)	96 (41)
Immunosuppresive treatment at baseline, n(%)	102 (17)	44 (19))
Duration of treatment at baseline in years, mean (SD)	4.1 (4.8)	1.2 (2.9)
Methotrexate, n(%)	54 (9)	24 (10)
Mycophenolate mofetil, n(%)	25 (4)	13 (6)
Hydroxycholoquine, n(%)	20 (3)	7 (3)
Cyclofosfamide, n(%)	1 (1)	10 (4)
Azathioprine, n(%)	11 (2)	2 (1)
Corticosteroids, n(%)	58 (10)	27 (11)

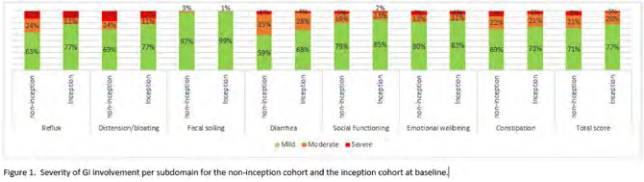


Figure 1. Severity of GI involvement per subdomain for the non-inception cohort and the inception cohort at baseline.

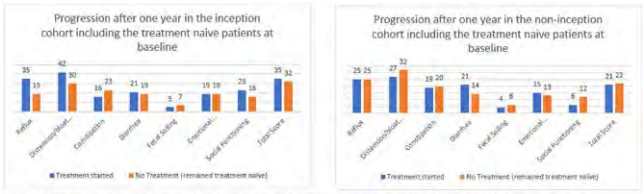


Figure 2. Percentage of progressors in inception cohort versus percentage of progressors in non-inception cohort after one year of follow-up stratified for immunosuppressive treatment (n=250 non-inception cohort, n=106 inception cohort).

Acknowledgments: NA

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THU0328 SAFETY AND EFFICACY OF SUBCUTANEOUS TOCILIZUMAB IN SYSTEMIC SCLEROSIS: RESULTS FROM THE OPEN-LABEL PERIOD OF THE PHASE 3 FOCUSSCED TRIAL

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Background: The anti–interleukin-6 (IL-6) receptor-α antibody tocilizumab (TCZ) demonstrated skin score improvement and forced vital capacity (FVC) preservation in patients with systemic sclerosis (SSc) in a phase 2 randomized controlled trial.[1,2] Data from the 48-week, double-blind (DB), placebo (PBO)-controlled period of the focuSSced phase 3 trial were previously presented,[3] and open-label (OL) data up to week 96 are presented herein.

Objectives: To assess the long-term safety and efficacy of TCZ in SSc patients.

Methods: Adult patients with active SSc (≤60-month duration, modified Rodnan skin score [mRSS] 10-35, and elevated acute-phase reactants) treated with PBO or TCZ in the DB period received OL TCZ 162 mg SC weekly from weeks 48 to 96 in the OL period (PBO→OL TCZ and TCZ→OL TCZ, respectively). Exploratory analysis of data up to week 96 included no formal statistical analyses. Changes in mRSS and percent predicted FVC (ppFVC) were assessed.

Results: Overall, 92/105 TCZ (88%) and 89/107 PBO (83%) patients entered the OL TCZ treatment period at week 48, and 85/105 TCZ→OL TCZ (81%) and 82/107 PBO→OL TCZ (77%) patients completed treatment up to week 96. Continued decline in mRSS was observed in the OL period for PBO→OL TCZ and TCZ→OL TCZ patients (Table). Change in ppFVC for patients who switched from PBO to TCZ (PBO→OL TCZ) was comparable between weeks 48 and 96 (OL period) to the change in patients who received TCZ from BL to week 48 in the DB period (Table). Rates (95% CI) of serious adverse events from weeks 48 to 96 were 15.8 (8.6, 26.5) per 100 PY for TCZ→OL TCZ patients, 14.8 (7.9, 25.3) per 100 PY for PBO→OL TCZ patients, and 15.4 (11.0, 20.9) for all TCZ exposure over 96 weeks (n = 193). Rates (95% CI) of serious infections were 2.3 (0.3, 8.1) per 100 PY for TCZ→OL TCZ patients, 3.4 (0.7, 10.0) per 100 PY for PBO→OL TCZ patients, and 3.0 (1.3, 5.9) for all TCZ exposure over 96 weeks. One death occurred during the OL period in each arm.

Conclusion: Although OL data have to be interpreted with caution, results from OL TCZ treatment show numeric improvements in mRSS and FVC preservation similar to those of the DB period, with a beneficial effect on trajectory of FVC decline in patients who switched from PBO to TCZ. Long-term safety results were consistent with the known safety profile of TCZ, and no new or unexpected events were observed.

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Disclosure of Interests: Dinesh Khanna Shareholder of: Eicos, Grant/research support from: NIH NIAID, NIH NIAMS, Consultant of: Acceleron, Actelion, Bayer, BMS, Boehringer-Ingelheim, Corbus, Galapagos, Genentech/Roche, GSK, Mitsubishi Tanabi, Sanofi-Aventis/Genzyme, UCB Pharma, Celia J. F. Lin Employee of: Genentech, Helen Spotswood Shareholder of: Roche Products Ltd, Employee of: Roche Products Ltd, Jeff Siegel Employee of: Genentech, Daniel Furst Grant/research support from: AbbVie, Actelion, Amgen, BMS, Corbus Pharmaceuticals, the National Institutes of Health, Novartis, Pfizer, and Roche/Genentech, Consultant of: AbbVie, Actelion, Amgen, BMS, Cytori Therapeutics, Corbus Pharmaceuticals, the National Institutes of Health, Novartis, Pfizer, and Roche/Genentech, Speakers bureau: CMC Connect (McCann Health Company), Christopher Denton Grant/research support from: GlaxoSmithKline, CSL Behring, and Inventiva, Consultant of: Medscape, Roche-Genentech, Actelion, GlaxoSmithKline, Sanofi Aventis, Inventiva, CSL Behring, Boehringer Ingelheim, Corbus Pharmaceuticals, Acceleron, Curzion and Bayer

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THU0329 SAFETY, TARGET ENGAGEMENT, AND INITIAL EFFICACY OF AVID200, A FIRST-IN-CLASS POTENT AND ISOFORM-SELECTIVE INHIBITOR OF TGF-BETA 1 AND 3, IN PATIENTS WITH DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS (DCSSC): A PHASE 1 DOSE ESCALATION STUDY

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Background: AVID200 is a novel, potent TGF-beta receptor ectodomain-based trap designed to selectively neutralize TGF-beta 1 and 3. These two isoforms have been implicated as central mediators of the pathogenesis of systemic sclerosis (SSc). AVID200 avoids inhibition of TGF-beta 2, the isoform that supports normal cardiac function and hematopoiesis.

Objectives: This first-in-human study (AVID200-01; NCT03831438) is a Phase 1, open label, multicenter, cohort dose-escalation trial designed to evaluate safety, tolerability, pharmacokinetic (PK) profile, pharmacodynamic (PD) effects, target engagement, and preliminary efficacy in patients with diffuse cutaneous SSc (dcSSc).

Methods: Eligible patients must have dcSSc of <5 years (y) duration and a modified Rodnan Skin Score (MRSS) ≥15. AVID200 at dose levels of 1, 3, 9, or 15 mg/kg IV is administered every 2 weeks (Q2W) for 6 weeks (3 doses). Patients tolerating dosing and who have not experienced disease worsening during the initial Treatment Period may receive up to 6 additional doses Q2W (Extension Period). The ability of AVID200 to selectively sequester its target is assessed in plasma by TGF-beta quantification per ELISA and a cell-based functional readout. Expression of biomarkers of TGF-beta inhibition and genes correlating with MRSS are assessed.

Table. Change in Efficacy From Baseline

	Baseline to Week 48		Baseline to Week 96		Week 48 to Week 96	
	PBO	TCZ	PBO→OL TCZ	TCZ→OL TCZ	PBO→OL TCZ	TCZ→OL TCZ
mRSS, mean (95% CI)[a]	–5.3 (–6.9, –3.7) n = 92	–6.7 (–8.0, –5.4) n = 97	–8.4 (–10.0, –6.8) n = 83	–9.6 (–10.9, –8.4) n = 85	–2.5 (–3.3, –1.6) n = 82	–2.3 (–3.2, –1.5) n = 85
ppFVC, mean (95% CI) [median]	–4.1 (–5.8, –2.4) [–3.9] n = 92	–0.2 (–1.6, 1.2) [–0.7] n = 94	–3.3 (–5.1, –1.5) [–3.1] n = 79	–0.5 (–2.4, 1.3) [–1.4] n = 84	0.6 (–0.7, 1.9) [0.3] n = 78	–0.3 (–1.7, 1.1) [0.0] n = 82
Decline in ppFVC ≥10%, n/N (%)[a]	15/91 (16.5)	5/93 (5.4)	14/79 (17.7)	11/84 (13.1)	NA	NA
Improvement in ppFVC, n/N (%)[a]	26/91 (28.6)	43/93 (46.2)	22/79 (27.8)	35/84 (41.7)	NA	NA

[a]Observed data. NA, not assessed.

Results: The first 2 dose cohorts have completed treatment: male/female 3 each, median age 61y (range 45-70), median MRSS at baseline 31 (range 23-39). Recruitment into cohort 3 is complete. AVID200 was well tolerated with no dose limiting toxicities or serious adverse events (SAEs). AEs, all considered possibly related, included single cases of Grade 1 dizziness and CPK elevation, and Grade 2 anemia. All patients demonstrated a decline in MRSS at 6 weeks by 3, 4, and 9 points in Cohort 1, and 2, 8, and 9 points in Cohort 2. Four of 6 patients demonstrated continued decrease in MRSS 12 weeks after the last dose, with all patients showing a decline in MRSS relative to baseline at this timepoint by 7, 6, and 7 points in Cohort 1 and 4, 8, and 13 points in Cohort 2. AVID200 in plasma engaged endogenous activated TGF-beta and potently neutralized signaling from exogenous TGF-beta 1 and 3, but not TGF-beta 2, across the treatment period. PD effects in skin biopsies, including expression of markers of SSc activity, TGF-beta activity, and myofibroblast-associated genes were assessed. Five of 6 patients showed decreased expression of PD biomarker genes, THBS1 and MS4A4A, comparing end of treatment biopsies to baseline, and all patients showed a decline in SERPINE1 expression, a marker gene for TGF-beta activity. Clustering of RNA-seq expression data showed close coregulation of COMP, THBS1, SERPINE1, LOXL, COL10A1, COL11A1, COL12A1, CTGF, and CDH11, suggesting that blocking TGF-beta inhibits this group of profibrotic genes. Single-cell sequencing data show that expression of these genes is upregulated by subsets of SSc fibroblasts.

Conclusion: AVID200 at doses of 1 and 3 mg/kg was well-tolerated in this first study in dcSSc patients. Evidence of anti-fibrotic effects as indicated by rapid, persistent and clinically meaningful declines in MRSS was observed in all patients, as well as AVID200 target engagement and modulation. Recruitment into additional dose and extension cohorts is ongoing. Together, these clinical data support selective TGF-beta 1 and 3 inhibition by AVID200 as a promising therapeutic approach for dcSSc.

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THU0330

EFFECTS OF NINTEDANIB IN PATIENTS WITH SYSTEMIC SCLEROSIS-ASSOCIATED ILD (SSC-ILD) AND DIFFERING EXTENTS OF SKIN FIBROSIS: FURTHER ANALYSES OF THE SENSCIS TRIAL

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Background: In the SENSCIS trial, nintedanib reduced the progression of SSc-ILD compared with placebo, as shown by a significantly lower rate of decline in forced vital capacity (FVC) over 52 weeks. There was no significant difference between treatment groups in change in modified Rodnan skin score (mRSS) at week 52. An mRSS of 18–25 has been proposed as an upper cut-off to enrich a cohort for skin-progressive patients. Progression of skin fibrosis has been associated with later progression of ILD.

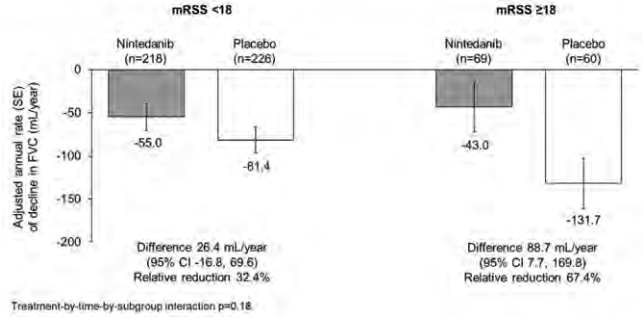
Objectives: To assess the effects of nintedanib on the rate of FVC decline and change in mRSS in the SENSCIS trial in subgroups by mRSS <18 and ≥18 at baseline.

Methods: Patients with SSc-ILD with onset of first non-Raynaud symptom <7 years before screening and ≥10% fibrosis of the lungs on a high-resolution computed tomography scan were randomised to receive nintedanib or placebo. We analysed the rate of decline in FVC (ml/year) over 52 weeks and the change from baseline in mRSS at week 52 in subgroups by mRSS (<18; ≥18) at baseline.

Results: In the nintedanib and placebo groups, respectively, 219/288 (76.0%) and 226/288 (78.5%) patients had mRSS <18 at baseline. Compared with those with mRSS <18, patients with mRSS ≥18 had a lower mean FVC % predicted (68.3% vs 73.7%) and greater proportions were taking mycophenolate at baseline (58.1% vs 45.6%), were anti-topoisomerase I antibody positive (67.4% vs 58.7%) and had diffuse cutaneous SSc (100% vs 37.8%). The mean (SE) annual rate of decline in FVC in the placebo group was numerically greater in patients who had mRSS ≥18 than mRSS <18 at baseline (-131.7 [29.2] mL/year vs -81.4 [15.4] mL/year). The effect of nintedanib vs placebo on reducing the annual rate of decline in FVC was numerically more pronounced in patients with mRSS ≥18 (difference: 88.7 mL/year [95% CI 7.7, 169.8]) than mRSS <18 (difference: 26.4 mL/year (95% CI -16.8, 69.6) at baseline, but statistical testing did not indicate heterogeneity in the treatment effect of nintedanib between subgroups (p=0.18 for treatment-by-time-by-subgroup interaction) (Figure). In the nintedanib and placebo groups, respectively, changes in mRSS at week 52 were -2.2 (0.3) and -2.1 (0.3) (difference -0.1 [95% CI -1.0, 0.7]) in patients with mRSS <18 at baseline and -2.1 (0.7) and -1.6 (0.7) (difference -0.6 [95% CI -2.1, 1.0]) in patients with mRSS ≥18 at baseline (p=0.62 for treatment-by-visit-by-subgroup interaction).

Conclusion: In the placebo group of the SENSCIS trial, the rate of decline in FVC over 52 weeks was numerically greater in patients with mRSS ≥18 than <18 at baseline, while reductions in mRSS were similar. A lower rate of FVC decline was observed in patients treated with nintedanib than placebo both in patients with mRSS ≥18 and <18 at baseline.

Figure. Rate of decline in FVC over 52 weeks in subgroups by mRSS <18 and ≥18 at baseline in the SENSCIS trial



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THU0331 INTERSTITIAL LUNG DISEASE IN SYSTEMIC SCLEROSIS: DECLINE IN FORCED VITAL CAPACITY DOES NOT PREDICT FURTHER PROGRESSION IN THE FOLLOWING PERIOD

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Background: In systemic sclerosis (SSc) patients with interstitial lung disease (ILD) approximately 30% show progressive ILD. It is unknown whether a progressive ILD period is followed by further lung function decline. In clinical practice, treatment is frequently initiated after observation of lung function decline over 6-12 months and lung function stabilization at follow up is often interpreted as treatment effect.

Objectives: Assess the predictive ability of lung function decline over 12 months for further deterioration adjusted for known risk factors for ILD and treatment in two large and well characterized SSc cohorts.

Methods: Patients with SSc-ILD by HRCT, fulfilling SSc classification criteria, from the Oslo and Zurich University Hospital were included. The first period with three consecutive annual forced vital capacity (FVC) measurements (i.e. at 0, 12 and 24 months, +/- 3 months) was used. Lung function decline was assessed by absolute changes in FVC% predicted. Moderately progressive ILD was defined as FVC decline of >5-<10% and significantly progressive ILD as FVC decline ≥10% in 12 months. Candidate predictors by experts (including SSc subtype, autoantibodies, disease duration, baseline and FVC decline in the first period, extent of lung and skin (mRSS) fibrosis, CRP, reflux, tendon friction rubs, O2 desaturation, dyspnea) for FVC decline in the second period were tested using logistic regression analysis. Treatment included low dose corticosteroids, mycophenolate mofetil; and other immunosuppressive treatment (cyclophosphamide, Rituximab and Tocilizumab).

Results: In total, 240 SSc-ILD patients met the inclusion criteria (table). Of these 69 (29%) SSc-ILD patients showed progressive ILD in the first 12 months period; 34 (14%) with moderate (5-10%) and 35 (15%) with significant FVC decline (≥10%). Independent of FVC changes in the first period, 77 (32%) showed progressive ILD in the second period; 44 (18%) moderate and 33 (14%) significant FVC decline. Only 21 (9%) SSc-ILD patients had two progressive periods, and 115 (48%) were stable in the two 12 month's periods; all independent of treatment. In multivariable logistic regression, progressive ILD in the first period (moderate, significant or combined FVC decline) was not predictive for progression in the following period. Of all applied risk factors, only mRSS was significantly predictive for further FVC decline, also when adjusted for age, gender and treatment (OR 1.03, 95%CI 1.00-1.08, p=0.035).

Conclusion: Decline of FVC in one 12 months period did not predict further ILD progression in the following 12 months independent of treatment. These results have important clinical implications. Firstly, a decline of lung function in one period seems not to be the right indicator for initiating treatment. Secondly, stabilization of lung function under treatment initiated after ILD progression cannot necessarily be interpreted as a treatment response on the individual patient level.

Table:

		First period	Both periods	
	SSc-ILD (n=240)	**ILD progression (n=69)**	**ILD progression (n=21)**	**Stable ILD (n=115)**
Age, years (SD)	48 (14.7)	49 (13.8)	50 (14.3)	46 (15.3)
Male, n (%)	57 (24)	18 (26)	5 (24)	27 (24)
Disease duration yrs, mean (SD)	10.2 (11.4)	9.8 (10.2)	8.8 (11.0)	10.8 (12.3)
Disease duration <3 years, n (%)	68 (28)	22 (32)	8 (38)	29 (25)
Diffuse cutaneous SSc, n (%)	95 (40)	30 (44)	11 (52)	43 (27)
Anti-topoisomerase I Ab, n (%)	84 (35)	27 (40)	9 (43)	42 (37)
mRSS, mean (SD)	10 (9.3)	11 (10.2)	16 (13.0)	8 (8.3)
CRPml, mean (SD)	3.6 (7.2)	3.3 (6.2)	4.4 (9.1)	3.1 (5.1)
GERD, n (%)	148 (62)	44 (64)	15 (74)	70 (61)
FVC % predicted	90 (20.3)	90 (21.9)	92 (21.7)	89 (19.3)
DL_{CO} % predicted	64 (17.9)	64 (16.6)	70 (11.3)	65 (17.5)
Lung fibrosis >20%, n (%)	55 (23)	16 (23)	4 (19)	27 (24)
Mycophenolate Mofetil, n (%)	47 (20)	15 (22)	5 (24)	23 (20)
Other immunosuppression, n (%)	79 (33)	22 (32)	9 (43)	42 (37)
Corticosteroids, n (%)	62 (26)	18 (26)	8 (38)	28 (24)

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THU0332 ULTRASONOGRAPHIC EVALUATION FOR SALIVARY GLAND INVOLVEMENT IN SYSTEMIC SCLEROSIS

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Background: While salivary gland ultrasound (SGUS) has widely used for evaluating Sjögren's syndrome, information on SGUS findings of systemic sclerosis (SSc) is limited.

Objectives: We aimed to evaluate the salivary gland involvement in patients with SSc using SGUS.

Methods: We consecutively included patients with SSc fulfilling American College of Rheumatology/European League against Rheumatism (ACR/EULAR) 2013 classification criteria, primary Sjögren's syndrome (pSS) fulfilling ACR/EULAR 2016 classification criteria, and idiopathic sicca syndrome. All patients underwent SGUS examination using the Outcome Measures in Rheumatology (OMERACT) definition of a SGUS scoring system. The hyperechoic bands using 0-3 scoring system (none/<25% of the parenchyma/25-50% />50%) and intraglandular power Doppler signal (PDS) were assessed. Hocevar scoring system (0-48) comprising parenchymal echogenicity, homogeneity, hypoechoic areas, hyperechogenic reflections, and clearness of posterior borders were also evaluated.

Results: A total of 147 patients were included in the study: SSc (n=59), pSS (n=56), and idiopathic sicca syndrome (n=32). The proportion of the highest OMERACT grades among the four glands≥ 2 were significantly higher in SSc

(54.2%) and pSS (62.5%) than idiopathic sicca syndrome (3.1%). Total OMERACT SGUS scores, total fibrosis scores, Hocevar score were significantly higher in SSc and pSS compared to idiopathic sicca syndrome (Table 1). The proportion of the highest fibrosis grades among the four glands ≥2 were significantly higher in SSc (79.7%) than pSS (62.5%) and idiopathic sicca syndrome (46.9%). There were no significant differences in PDS among 3 groups. Twenty-one patients (65.6%) of 32 SSc patients with OMERACT grade ≥2 were anti-centromere antibody (ACA)-positive compared with 9/27 (33.3%) SSc patients with scores of 0–1. The positivity of anti-Ro-60/SSA were also significantly higher in SSc patients with SGUS grade ≥2 (37.5%) than those with SGUS scores of 0–1 (3.7%). In SSc group, there was no significant difference in auto-antibody profile and organ involvement between patients with fibrosis scores ≥2 and those with scores 0-1.

Table 1. Characteristics of the study population included in the study

	SSc (n =59)	pSS (n =56)	Idiopathic sicca syndrome (n =32)	*P*- value (SSc vs pSS)	*P*- value (SSc vs idiopathic sicca)	*P*- value (pSS vs idiopathic sicca)
Age, mean (SD), years	54.8 (12.1)	60.5 (11.9)	62 (11.2)	**0.013**	**0.006**	0.559
Female, n (%)	53 (89.8)	56 (100)	28 (87.5)	**0.028**	0.737	**0.015**
Anti-Ro-60/SSA, n (%)	13 (22.0)	39 (69.6)	7 (21.9)	**<0.001**	0.986	**<0.001**
ACA, n (%)	30 (30.8)	8 (14.3)	2 (6.3)	**<0.001**	**<0.001**	0.238
Anti-topoisomerase, n (%)	16 (27.1)	0 (0)	0 (0)	**<0.001**	**<0.001**	1.000
Max OMERACT US grade ≥ 2, n (%)	32 (54.2)	35 (62.5)	1 (3.1)	0.369	**<0.001**	**<0.001**
Total SGUS scores, median (IQR)	4.0 (6)	7.0 (8)	0 (1)	0.231	**<0.001**	**<0.001**
Max fibrosis US grade ≥ 2, n (%)	47 (79.7)	35 (62.5)	15 (46.9)	**0.042**	**0.004**	0.263
Total fibrosis scores, median (IQR)	6 (3)	6 (6)	4 (4)	0.674	**< 0.001**	**0.006**
PDS sum scores of four salivary glands, median (IQR)	2 (5)	0 (4)	0 (2)	0.131	0.152	1.000

Conclusion: Based on OMERACT definitions for SGUS, more than half of the patients with SSc, especially those with ACA, had salivary gland involvement. Salivary glandular fibrosis is more prominent in patients with SSc than those with pSS and idiopathic sicca syndrome.

References:

[1] Jousse-Joulin S, et al. Video clip assessment of a salivary gland ultrasound scoring system in Sjogren's syndrome using consensual definitions: an OMERACT ultrasound working group reliability exercise. Ann Rheum Dis. 2019;78(7):967-73.

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THU0333 CARDIOVASCULAR COMORBIDITIES ARE COMMON IN RHEUMATOID ARTHRITIS PATIENTS WHO PRACTICE LESS PHYSICAL ACTIVITY AND WHO HAVE WORSE FUNCTIONAL CAPACITY.

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Background: Patients with rheumatoid arthritis have more cardiovascular comorbidities which contributes to hospitalization and mortality.

Objectives: This study aims to investigate whether there is an association between cardiovascular comorbidities in RA with subgroup of patients and clinical findings of the disease

Methods: This study is a cross-sectional part of Rheumatoid Arthritis in Real Life (REAL), which is a multicenter prospective study conducted in Brazil, involving 13 centers specialized in the care of patients with RA. All subjects met the ARA (1987) or ACR/EULAR (2010) RA classification criteria. Subjects were submitted to clinical interview with physical exam and review of medical records. A sample of 1116 patients was selected for convenience. The association between cardiovascular comorbidities (systemic arterial hypertension (HA), diabetes mellitus (DM) type2, dyslipidemia, stroke and heart failure), the clinical characteristics and laboratory parameters of RA was evaluated through chi-square hypothesis tests, Student`s t-test, Fischer exact test, correlations test and ANOVA. Also, correction Bonferoni test was used for multiple comparisons. Differences were considered statistically significant only when $p \leq 0.05$.

Results: 89% of the patients were female, with a mean age of 58 years. 62% of patients with RA had comorbidities, with HA the most prevalent. There were statistically significant association between cardiovascular comorbidities with age (61.71±9.69years old vs 53.03±12.10) (p <0.001), lower educational level (n=282±66.5vs 143±33,5) (p <0.001), lower physical activity (n=132±73.3 vs 48±26.7) (p <0.001), disease duration (18.5±9.75 years vs 14.4±8.61) (p <0.001), positive anti-CCP test (60.5% vs 39.5%) (p = 0.027), high clinical disease activity index CDAI) (65.9%vs 34.1%) (p <0.001), DAS28VHS (3.72±1.46 vs 3.45±1.58) (p = 0.008) and HAQ score (1.00±0.76) vs 0.83±0.77 (p <0.001).

Conclusion: The frequency of cardiovascular comorbidities is high in RA patients and is associated with age, disease duration and positive anti-CCP test. It is also important to see that these comorbidities are more common in patients with lower frequency of physical activity and lower functional capacity, higher disease activity score and lower level of education. Better control of disease activity and extensive information to patients about the importance of exercise should be parallel objectives in RA.

Disclosure of Interests: Ivanio Pereira Grant/research support from: Has received consulting fees, speaking fees and supporting for internationals congresses from Roche, Pfizer, UCB Pharma, Eli-Lilly, Abbvie and Janssen, Consultant of: Has received consulting fees, speaking fees and supporting for internationals congresses from Roche, Pfizer, UCB Pharma, Eli-Lilly, Abbvie and Janssen, Paid instructor for: Has received consulting fees, speaking fees and supporting for internationals congresses from Roche, Pfizer, UCB Pharma, Eli-Lilly, Abbvie and Janssen, Speakers bureau: Has received consulting fees, speaking fees and supporting for internationals congresses from Roche, Pfizer, UCB Pharma, Eli-Lilly, Abbvie and Janssen, Gabriela Ribas: None declared, G Castro: None declared, Geraldo Castelar Grant/research support from:: Has received consulting fees from AbbVie, Bristol-Myers Squibb, Eli Lilly, Glaxosmithkline, Janssen, Pfizer, Sanofi Genzyme and Roche, Consultant of:: Has received consulting fees from AbbVie, Bristol-Myers Squibb, Eli Lilly, Glaxosmithkline, Janssen, Pfizer, Sanofi Genzyme and Roche, Paid instructor for:: Has received consulting fees from AbbVie, Bristol-Myers Squibb, Eli Lilly, Glaxosmithkline, Janssen, Pfizer, Sanofi Genzyme and Roche, Speakers bureau:: Has received consulting fees from AbbVie, Bristol-Myers Squibb, Eli Lilly, Glaxosmithkline, Janssen, Pfizer, Sanofi Genzyme and Roche, Ana Beatriz Vargas-Santos Grant/research support from: Has received supporting for international medical events from AbbVie and Janssen, Cleandro Albuquerque Grant/research support from: Has received personal fees and/or non-financial support from Pfizer, AbbVie, AstraZeneca, Janssen, Bristol-Myers Squibb, Roche, Novartis and UCB, Consultant of: Has received personal fees and/or non-financial support from Pfizer, AbbVie, AstraZeneca, Janssen, Bristol-Myers Squibb, Roche, Novartis and UCB, Paid instructor for: Has received personal fees and/or non-financial support from Pfizer, AbbVie, AstraZeneca, Janssen, Bristol-Myers Squibb, Roche, Novartis and UCB, Speakers bureau: Has received personal fees and/or non-financial support from Pfizer, AbbVie, AstraZeneca, Janssen, Bristol-Myers Squibb, Roche, Novartis and UCB, Ana Paula Gomides Consultant of: Abvvie, Manoel Bertolo Grant/research support from: Has participated in clinical and/or experimental studies related to this work and sponsored by Roche; has delivered speeches at events related to this work and sponsored by AbbVie and Pfizer, Paid instructor for: Has participated in clinical and/or experimental studies related to this work and sponsored by Roche; has delivered speeches at events related to this work and sponsored by AbbVie and Pfizer, Speakers bureau: Has participated in clinical and/or experimental studies related to this work and sponsored by Roche; has delivered speeches at events related to this work and sponsored by AbbVie and Pfizer, Paulo Louzada Jr Grant/research support from: Has received supporting for internationals congresses from Bristol-Myers Squibb, UCB and consulting fees from Pfizer, Paid instructor for: Has received supporting for internationals congresses from Bristol-Myers Squibb, UCB and consulting fees from Pfizer, Speakers bureau: Has received supporting for internationals congresses from Bristol-Myers Squibb, UCB and consulting fees from Pfizer, Rina Giorgi: None declared, Maria Fernanda Guimarães: None declared, Sebastião Radominsky Grant/research support from: Has received consulting and speaking fees from Abbvie, Janssen, Pfizer, Roche and UCB, Consultant of: Has received

consulting and speaking fees from Abbvie, Janssen, Pfizer, Roche and UCB, Paid instructor for: Has received consulting and speaking fees from Abbvie, Janssen, Pfizer, Roche and UCB, Speakers bureau: Has received consulting and speaking fees from Abbvie, Janssen, Pfizer, Roche and UCB, Karina Bonfiglioli Consultant of: Roche, Abbvie, Pfizer, Janssen and BMS, Maria de Fátima Sauma: None declared, Claiton Brenol: None declared, Evandro Coutinho: None declared, Licia Mota Grant/research support from: Has received personal or institutional support from AbbVie, Janssen, Pfizer and Roche; has delivered speeches at events related to this work and sponsored by AbbVie, Janssen, Pfizer, Roche and UCB., Speakers bureau: Has received personal or institutional support from AbbVie, Janssen, Pfizer and Roche; has delivered speeches at events related to this work and sponsored by AbbVie, Janssen, Pfizer, Roche and UCB.

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THU0334 LASER SPECKLE CONTRAST ANALYSIS FOR MEASUREMENT OF PERIPHERAL BLOOD PERFUSION IN SYSTEMIC SCLEROSIS PATIENTS: CAN IT PREDICT FUTURE ISCHEMIC DIGITAL TROPHIC LESIONS?

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Background: Vasculopathy is a hallmark of systemic sclerosis (SSc). Laser speckle contrast analysis (LASCA) is a research tool to assess peripheral blood perfusion (PBP) (1). At this moment, its reliability has been attested in SSc patients, but its predictive value for future ischemic digital trophic lesions (DTL) is unknown (1).

Objectives: To investigate in an unselected, prospective SSc cohort if baseline LASCA PBP measurements can discriminate between patients who will develop ischemic DTL (iDTL) and those who will not.

Methods: Patients (fulfilling 2013 ACR/EULAR criteria and/or 2001 LeRoy and Medsger criteria) were recruited during the period of December 2017 to September 2018. LASCA was performed at baseline, in standardized conditions (1). Regions of interest (ROIs) (diameter 1 cm) were outlined at the 2nd-5th fingertip both volar and dorsal. The 'average PBP' of these ROIs was calculated (expressed in arbitrary perfusion units [PU]). A monthly telephone survey was conducted for 1 year to investigate DTL occurrence. DTL were considered 'ischemic' if not related to calcinosis. Logistic regression and ROC analysis were used to assess if average PBP is predictive of future iDTL.

Results: Of the 106 patients with complete follow-up (92 women [86,8%]; 18 limited SSc [17,0%], 82 limited cutaneous SSc [77,4%], 6 diffuse cutaneous SSc [5,7%]), 29 patients (27,4%) had a DTL history. Forty-nine patients (46,2%) were on vasodilator therapy. Only 7 patients developed at least 1 iDTL during follow-up (6,6%) (Figure 1a). Performing univariate logistic regression (ULR), average PBP was not predictive for future iDTL (Table 1). Of note, analyzing only the patients not taking vasodilators, average PBP in the 'iDTL group' (n = 3) was median 46,8 PU (min. 45,6 - max. 68,8) vs. median 141,4 PU (min. 24,4 - max. 269,5) in the 'no iDTL group' (n = 54) (Figure 1b). In this subgroup, all 3 patients who developed iDTL (100%) had an average PBP ≤ 70 PU whereas only 9 of the 54 patients without iDTL development (16,7%) had such PBP values.

Table 1. Results of ULR

Variable	Summary statistics		ULR			
	iDTL cases (n = 7)	Non-iDTL cases (n = 99)	Parameter	OR (95% CI)	p	ROC AUC (95% CI)
Average PBP (PU) mean (+/- SD)	123,0 (74,6)	142,9 (61,9)	**Average PBP (linear)**	0,995 (0,982-1,007)	0,418	0,597 (0,352-0,843)

Conclusion: In this pilot study with an unselected day-to-day SSc population, where patients were allowed to continue vasodilators, there was an unexpected low iDTL incidence, undermining the power of our study. Even though, the observations in the subgroup of patients not taking vasodilators deserve future investigation to assess whether low PBP values, as measured by LASCA, are associated with a higher iDTL incidence.

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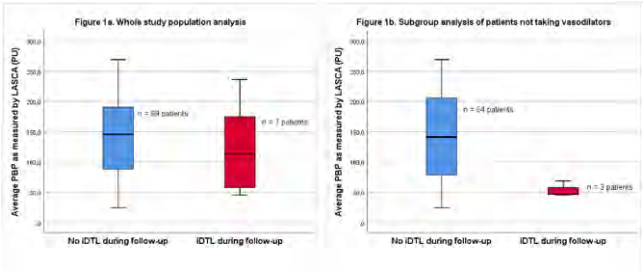


Figure 1. Distribution of 'average PBP' as measured by LASCA for 'no iDTL group' and 'iDTL group'

Disclosure of Interests: Claire Debusschere: None declared, Amber Vanhaecke: None declared, Maurizio Cutolo Grant/research support from: Bristol-Myers Squibb, Actelion, Celgene, Consultant of: Bristol-Myers Squibb, Speakers bureau: Sigma-Alpha, Ellen Deschepper: None declared, Vanessa Smith Grant/research support from: The affiliated company received grants from Research Foundation - Flanders (FWO), Belgian Fund for Scientific Research in Rheumatic diseases (FWRO), Boehringer Ingelheim Pharma GmbH & Co and Janssen-Cilag NV, Consultant of: Boehringer-Ingelheim Pharma GmbH & Co, Speakers bureau: Actelion Pharmaceuticals Ltd, Boehringer-Ingelheim Pharma GmbH & Co and UCB Biopharma Sprl

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THU0335 IS CARDIOVASCULAR RISK IN INFLAMMATORY MYOPATHIES UNDERESTIMATED?

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Background: Inflammatory myopathies (IIM) comprise a heterogeneous group of rare connective tissue diseases (CTD) which can occur in any age group and in association with other autoimmune CTD. Extramuscular manifestations, including cardiac involvement, are common and may occur in the absence of muscle symptoms.

The link between inflammation and atherosclerosis has been well established in other immune-mediated diseases suggesting that atherosclerosis in these conditions is driven by disease activity rather than traditional cardiovascular (CV) risk factors. Large observational studies have identified atherosclerotic cardiovascular events (CVE) as one of the leading causes in mortality in IIM but to date there are no specific recommendations for patients with IIM beyond the general guidelines for management of CV risk in the general population.

A systematic review of the literature available was carried out, identifying six observational studies based on data collected from local or national healthcare databases. All six studies showed an increased incidence of MI and/or stroke compared to the general population, with a suggestion in some of them that this incidence was particularly high in the first few years after disease onset.

Objectives: To establish if the incidence of atherosclerotic CVE in an IIM cohort is higher than expected when compared to QRISK2 predicted risk, and if so to determine if this risk is influenced by disease duration, gender, disease phenotype or ethnicity.

Methods: Patients referred to the Myositis clinic at King's College Hospital (KCH) were identified, excluding patients with Inclusion Body Myositis, overlap diagnoses with other CTD or prior atherosclerotic CVE. Only patients fulfilling ACR/EULAR criteria for IIM and under follow up at KCH (Denmark Hill site) were included in the study. Retrospective data was gathered by reviewing electronic patient records.

Results: 327 patients were identified through the Myositis Departmental database. After applying exclusion criteria the final dataset consisted of 159 patients (114 female, 71.7%), including dermatomyositis (82 patients), polymyositis (49 patients), Clinically Amyopathic Dermatomyositis (7 patients), anti-synthetase syndrome (12 patients) and necrotizing myopathy (9 patients). 81 patients were white (50.9%). Mean age of entry in the study was 49.1 years (SD 15.2) for women and 49.7 years (SD 12.2) for men. The mean follow up time was 2.61 years with a median time of 2.78 years (IQR 1.64-2.85). The mean disease duration was 6.77 years for the whole cohort with a median time of 4.61 years (IQR 2.43-9.07).

The incidence rate of atherosclerotic CVE was 16.3/1000 patient-years (95% CI: 8.8-30.3), twice as high as expected by QRISK2. Analysis showed statistical difference with males (RR=6.49, p=0.002) and white patients (RR=5.04, p=0.02) although the statistical significance for white ethnicity was lost after adjusting for age and gender. Statistical analysis showed association between disease duration and higher incidence of atherosclerotic CVE, with a rate reduction of 0.7 per year from disease onset (p=0.01) after adjusting for age and gender.

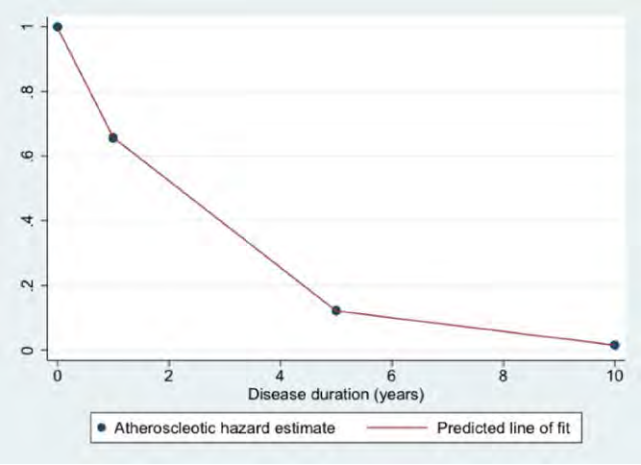


Fig. 1. Atherosclerotic risk by disease duration

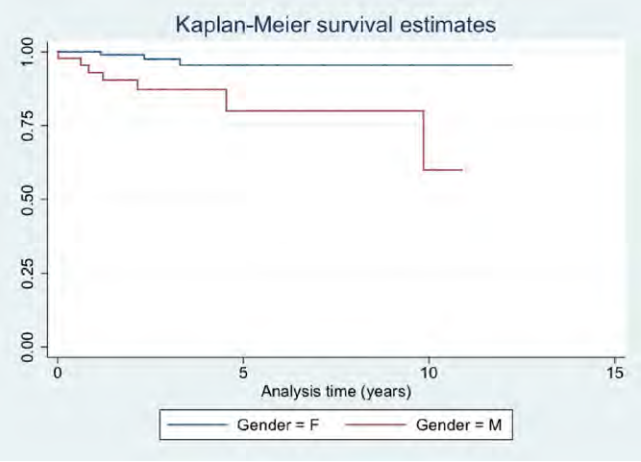


Fig. 2. Kaplan-Meier survival plot to atherosclerotic event

Conclusion: Our results suggest that atherosclerotic cardiovascular risk in inflammatory myopathies is underestimated, particularly early on the disease. Based on our results we would recommend a low threshold for primary prevention of atherosclerosis including the use of statins particularly for the first year after diagnosis.

Disclosure of Interests: None declared

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THU0336 IMMUNE CHECKPOINT INHIBITOR-RELATED MYOSITIS: A RETROSPECTIVE COHORT STUDY

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Background: Myositis is a rare immune checkpoint inhibitor (ICI)-related adverse event frequently associated with myasthenia gravis (MG) and myocarditis (MC) leading to mortality rates up to 52%.[1]

Objectives: To characterize the presentation, course and outcomes of patients with ICI-related myositis alone or with overlap syndrome (myositis with MG or MC or both).

Methods: We retrospectively identified a cohort of patients treated with ICI at MD Anderson Cancer Center between 2016 and 2019. Suspected myositis was identified using International Classification of Disease version 10 codes and confirmed by electronic medical record review of muscle enzymes, pathology, and other tests, when available. Patients with myositis alone or with overlap syndrome were compared using Fischer's exact tests and t tests.

Results: During the study period 8,636 patients received ICI, of which 31 (0.36%) were diagnosed with myositis: 14 (45%) with myositis alone and 17 (55%) with overlap (MG in 5, MC in 4, MG and MC in 8). Twenty patients received programmed death-1 (PD-1) or programmed death-ligand-1 (PDL-1) inhibitors, and 10 received combination PD-1/PDL-1 inhibitor with a cytotoxic T-lymphocyte associated antigen 4 (CTLA-4) inhibitor. One patient received single agent CTLA-4 inhibitor (excluded from pooled data). For the entire cohort the median age at diagnosis was 69 years (range: 40-95 years); the most common presenting symptoms were fatigue in 27 (90%) patients, weakness in 24 (80%), and myalgia in 23 (77%); median CK was 2,236 U/L (range: 23-19,794 U/L). For treatment, 22 of 30 (73%) patients received at least one therapy in addition to steroids: plasmapheresis in 15 (50%) patients, intravenous immune globulin (IVIG) in 12 (40%), biologics in 9 (30%) (rituximab in 6, infliximab in 5, tocilizumab in 3), tacrolimus in 6 (20%), and mycophenolate mofetil in 4 (13%). Median length of exposure to steroids was 47 days (range: 1-250 days). Five (17%) patients were rechallenged with ICI after myositis resolution (3 with myositis alone, 2 with overlap), of which 1 (20%) patient experienced a myositis flare. Twenty-five (83%) patients were not rechallenged on ICI and 3 (12%) of those patients had a flare. Differences between patients with myositis alone compared to those with overlap are shown in Table 1. Patients with overlap more often received a second therapy, specifically plasmapheresis and IVIG, had longer hospitalizations and greater symptom burden at discharge. Overall death between groups was similar; however death attributed to the adverse event occurred only in those with overlap.

Table 1. Myositis alone vs. Overlap

	Myositis alone (N=13)	**Overlap** (N=17)	*P* value
	N(%)/median days [range]		
Time to symptom onset	42 [10-161]	22 [9-149]	0.234
Initial steroid dose (mg/kg day)	1.7	1.8	0.187
Second therapy	7 (54)	15 (88)	0.049
Plasmapheresis	3 (23)	12 (71)	0.025
IVIG	1 (8)	11 (65)	0.002
Outcomes			
Hospitalization length	5 [2-50]	24 [7-92]	0.019
Respiratory failure	0 (0)	13 (76)	
Symptoms at discharge			0.047
Improved	8 (62)	6 (35)	
Resolved	3 (23)	1 (6)	
Death			
Overall	8 (62)	12 (71)	0.706
Adverse event	0 (0)	7 (41)	

Conclusion: Our results represent the largest cohort of ICI-related myositis to date. Patients with overlap syndrome are treated more aggressively and have worse outcomes than those with myositis alone. Prospective studies are warranted to determine risk factors for developing myositis or overlap syndrome and to determine optimal treatment.

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Disclosure of Interests: None declared

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THU0337 THE EFFECTIVENESS OF PLASMA EXCHANGE THERAPY FOR ANTI-MDA5 ANTIBODY-POSITIVE REFRACTORY INTERSTITIAL LUNG DISEASE

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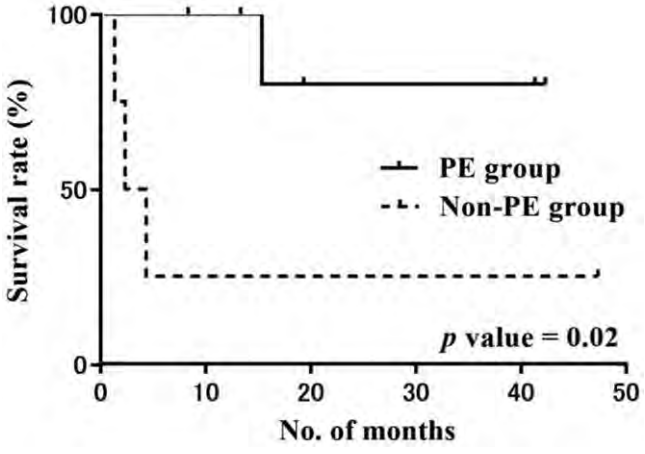
Background: This is an extended report of our study [1]. Anti-melanoma differentiation-associated gene 5 (MDA5) antibodies, which are closely related to interstitial lung disease (ILD) with or without rapid progression, are a type of myositis-specific autoantibody. Since rapid progressive-ILD (RP-ILD) with anti-MDA5 antibodies is refractory and fatal, intensive immunosuppressive therapy with combination calcineurin inhibitor, and intravenous pulse cyclophosphamide was developed, and was shown to improve patient survival and prognosis [2]. However, 20–30% of cases were still fatal, and several additional

therapies have been reported e.g. tofacitinib [3] and plasma exchange therapy (PE) [1, 4, 5].

Objectives: We evaluated the effect of plasma exchange (PE) on survival in patients with refractory RP-ILD who were positive for anti-MDA5 antibodies.

Methods: Among 167 patients newly diagnosed with PM/DM, clinically amyopathic DM, or cancer associated myositis from 2008 to 2019 at our hospital, 12 were diagnosed with refractory RP-ILD and were positive for anti-MDA5 antibodies. PE was used as an adjunct to standard therapy and consisted of fresh frozen plasma as replacement solution. The primary outcome was non-disease-specific mortality. anti-MDA5 antibody titres were measured by ELISA using the MESACUP anti-MDA5 test in 155 patients whose serum was frozen and stored at the time of diagnosis.

Results: Anti-MDA5 antibodies were detected in 35 patients, of whom 26 were diagnosed with RP-ILD and 11 were refractory to intensive immunosuppressive therapy. Seven patients received PE (PE group) and four did not (non-PE group). The 1-year survival rate of the PE group was higher than that of the non-PE group (100% and 25%, respectively, P = 0.011). Regarding adverse events associated with PE, two patients had anaphylactic shock, one had high fever due to fresh frozen plasma allergy and one had a catheter infection. All adverse events resolved with appropriate treatment.



Conclusion: We evaluated the association between 1-year survival rate and PE for refractory RP-ILD in patients positive for anti-MDA5 antibodies. Intensive immunosuppressive therapy improved the survival rate in RP-ILD patients with anti-MDA5 antibodies, but 20-30% of cases were still fatal. PE could be administered to patients with active infectious disease who were immunocompromised by intensive immunosuppressive therapy. PE may be considered in refractory RP-ILD patients positive for anti-MDA5 antibodies.

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Disclosure of Interests: None declared

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THU0338 THE CIRCULATING CD19-POSITIVE LYMPHOCYTES IN PATIENTS WITH SYSTEMIC SCLEROSIS: MODULATION WITHIN A YEAR AFTER THE INITIATION OF RITUXIMAB THERAPY

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Background: Significant disorders of B-cell homeostasis have been detected in systemic sclerosis (SSc) [1,2]. The improvement of the disease with anti-CD20 monoclonal antibody rituximab (RTM) has been shown in SSc [3]. There are limited data on change in circulating B lymphocytes count after RTM treatment in patients with SSc.

Objectives: to investigate the modulations in absolute and relative numbers of circulating CD19-positive B lymphocytes (B-lymph) in patients with SSc within a year after the initiation of RTM therapy.

Methods: 71 pts with SSc were included in the prospective study. Mean age was 46±13 yrs., 83% were women, 59% had diffuse subset. Duration of SSC from the first non-Raynaud`s symptom was 5.6 ± 4.4 yrs. All pts received low doses of glucocorticoids and 45% -immunosuppressive medications. The average follow-up of patients was 13.2 ± 2.0 (11-18) months. The mean dose of RTM for the period of follow up was 1.43 ± 0.60 grams, 48 patients received < 2 g of RTM (group 1, mean of 1.1 ± 0.1 g) and 23 patients received ≥ 2 grams of RTM (group 2, mean dose of 2.2 ± 0.6 g). Peripheral blood CD19-positive cell count was obtained by flow cytometry in patients and in 20 healthy persons, comparable in sex and age. Data are presented as the percentage (P %) and absolute number (AN) of B-lymph per ml of blood. In patients, the number of B-lymph was determined before (n=67 pts), within first month after the first introduction of RTM (n=66), 6 months later (n=34) and at the end of the study (n=71)

Results: At baseline, the AN and P% of B-lymph in pts did not differ from the healthy control. In pts with short disease duration (≤ 3 yrs.) the number of B-lymph before treatment with RTM was the higher (compared with longer duration > 3 yrs) those who was ill ≥3 yrs.) and there was negative correlation between B-lymph count and duration of the disease (R - 0.36, p=0.003 for AN and R - 0.48, p=0.001 for P %). The number of B-lymph was significantly lower in patients receiving cyclophosphamide (Cyc) before being started with RTM. There was a negative correlation between the AN of B-lymph and the cumulative dose of Cyc (R -0.293, p=0.016). In 1 month after the initiation of RTM a complete depletion of B-lymph was observed in all pts and in six months it persisted in 79% of cases, the rest began to repopulate (15%) or reached a normal levels (6%). At the end of the follow up the number of B-lymph was significantly lower than before treatment and a complete (n=41 pts) or partial (n=23) depletion of B-lymph remained, and only in 7 (10%) pts the count of this cells was normalized. We revealed a negative correlation between the AN of B-lymph and the cumulative dose of RTM (R-0.237, p=0.048). Higher doses of RTM in group 2 induced a more significant depletion than in group 1. Change in forced vital capacity and diffusing capacity of the lung (% predicted) during follow up were less pronounced for pts in group 1 compared with group 2 (ΔFVC 2,4% and 7,5% p=0,01; ΔDLCO -0,35% and 5,05%, p=0,001, respectively).

Conclusion: RTM may be more effective at the early stage of the disease, when the level of B-lymph is the highest. In SSc, the repopulation of B-lymph after depletion with RTM develops slowly. There were a more significant depletion of B-lymph and a more pronounced improvement in pulmonary function with the higher dose of RTM to compare with the lower one. This results indicate the option of a flexible dosing regimen of RTM.

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Disclosure of Interests: None declared

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THU0339 THE INFLUENCE OF SKIN CALCINOSIS ON THE PROGNOSIS OF DIGITAL ULCERS IN PATIENTS WITH SSC.

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Background: Digital ulcers (DUs) are one of the main burdens in patients with systemic sclerosis (SSc) as they have a major impact on quality of life and prognosis. Some DUs are associated with the presence of subcutaneous calcinosis (SC) that may worsen their management, and the prognosis of these DUs is still not well defined.

Objectives: To define the characteristics of SSc patients with DUs related to SC and analyze the impact on prognosis and on healing time.

Methods: We prospectively collected data from DUs of the hands evaluated in our dedicated wound-care outpatient clinic from October 2018 to August 2019. Fifty-five patients were enrolled (50 females, 18 with limited-SSc and 37 with diffuse-SSc, mean age 62.3±17.2 years). For every DU we collected: presence/absence of calcinosis, pathogenesis (spontaneous, post-traumatic), area of DU, location (fingertip, periungual area, metacarpophalangeal, proximal/distal interphalangeal-PIP/DIP), VAS-pain at the baseline and after two weeks, local signs of infection (edema, redness), deep wound swab results and time to the healing. Additionally, we calculated the wound-bed score (WBS), at the baseline and we correlated the total score with the time of healing. All the ulcers were managed with weekly treatment following a definite protocol: wound cleansing, disinfection, mechanic debridement, application of antiseptic dressing.

Results: Out of 98 DUs evaluated, 24 (24.5%) were associated with SC. Patients with SC were older than those without calcinosis (67.1+-16.9 vs 59.4+-16.9 p<0.05) and were more frequently affected by lc-SSc (18 – 75% vs 6 – 25% p<0.001). There were no significant differences between the mean areas of DUs (SC 22mm^2 vs non-calcinosis 30.8mm^2) neither in the localization of the ulcers: fingertip (14-61% vs 34-49.3%), periungual area (4-17.4% vs 16-23.2%), PIP (2-9% vs 13-18.9%), DIP (2-9% vs 9-13%) and MCP (1-4% vs 4-5.8%). The VAS-pain was not statistically different at the baseline (6.0 for SC vs 5.4), neither after 2 weeks (3.8 vs 3.2). Although the presence of local signs of infection was similar (5-20.8% vs 14-18.9%), the positivity for the wound swab was higher in SC compared with those without calcinosis (6-26.1% vs 9-11.5%; p=0.05).

All the DUs treated in our outpatient clinic healed but those with SC required more weeks (10.4±7.9 vs. 7.13±5.7; p=0.03). The WBS was similar in the two groups (8.96+-0.46 in SC vs 9.43+-0.33) and was negatively correlated with the time of healing (r=-0.24, p=0.02).

Conclusion: Although DUs with calcinosis have a different pathogenesis compared to those without SC, the location, dimensions and DU-related pain are similar in both groups. Despite these aspects, DUs associated with calcinosis are more prone to be infected and require more time to heal; the WBS may represent a simple, easy-calculated score to predict the time for DUs healing. The presence of calcinosis may represent a negative prognostic factor in the management of SSc-DUs.

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THU0340 DURATION AND SYSTEMIC SCLEROSIS SUBTYPE ARE ASSOCIATED WITH DIFFERENT GUT MICROBIOME PROFILES

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Background: A growing body of evidence suggests that the gut microbiota plays a significant role in the development of autoimmune diseases. Altered microbiota composition was associated with gastrointestinal and extraintestinal features in systemic sclerosis (SSc) patients.

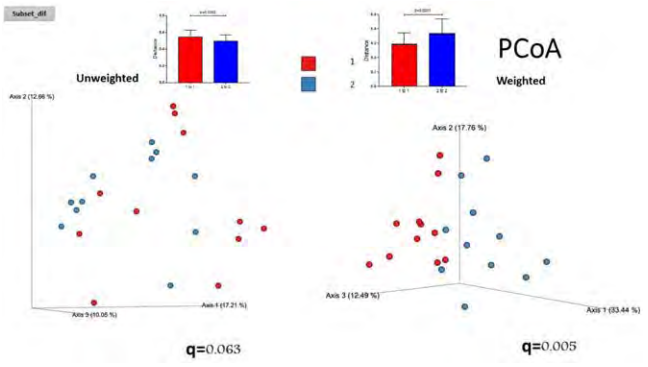
Objectives: To look for differences in gut microbiota between SSc patients regarding disease duration, disease subset and occurrence of digital ulcers (DU).

Methods: SSc patients seen at our center were recruited in a prospective study. The exclusion criteria included antibiotic or probiotic treatment during the month prior to recruitment, recent hospitalization, BMI>30, diabetes mellitus or concomitant inflammatory bowel disease. Fecal samples were processed and 16S rRNA gene sequences were analyzed using the QIIME2 packageWeighted (quantitative) and unweighted (qualitative) UniFrac distances, alpha diversity for richness and homogeneity, taxa plots for species and phyla and ANCOM analyses were performed.

Results: During July 2018-May 2019, 26 SSc patients (mean age [SD] 53[12.7] years) and disease duration 8.8 [7.1] years) fulfilled the criteria and were willing to participate in the study. Thirteen patients had diffuse SSc, 16 patients had active DU, 8 patients had Raynaud's phenomenon only without DU, 2 patients had past DU. The microbiota was significantly more similar between patients without active DU compared to those with active DU (P=0.024), but species richness did not differ. Patients with SSc duration less than 6 years had significantly different microbiota compared to long-lasting SSc (unweighted PCoA – q=0.031). Significant variations concerning quantitative and qualitative UniFrac distances (q=0.063, q=0.005) and species richness (q=0.009) were found among patients with diffuse compared to limited SSc. Limited SSc was associated with greater species richness. Taxa plot analysis revealed higher relative abundance of Firmicutes in diffuse disease and of Actinobacteria and Bacteroidetes in limited SSc.

Conclusion: Disease duration, disease subset and active DU were associated with shifts in the microbiome of SSc patients. The impact of these changes on disease progression needs further elucidation.

Figure:



Disclosure of Interests: Yolanda Braun-Moscovici: None declared, Shira Ben Simon: None declared, Katya Dolnikov: None declared, Sami Giryes: None declared, Doron Markovits: None declared, Yonit Tavor: None declared, Kohava Toledano: None declared, Alexandra Balbir-Gurman Consultant of: Novartis, Omry Koren: None declared

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THU0341 DIGITAL ARTERY VOLUME INDEX (DAVIX©) PREDICTS THE ONSET OF FUTURE DIGITAL ULCERS IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Neointima proliferation is a key pathologic feature of Systemic Sclerosis (SSc), causing arterial vessel narrowing and being the recognised culprit pathological lesion in Digital Ulcers (DUs), pulmonary artery hypertension and renal crisis. Nevertheless, there are no validated imaging techniques to assess the severity of vascular involvement in SSc. Digital Artery Volume index (DAVIX ©) is an MRI **Time of flight angiography** based quantitative score of digital arteries flow, without the need to administer contrast.

Objectives: To determine the value of DAVIX in predicting the onset of digital ulcers (DUs), the worsening of patient reported outcomes (PROs) and clinical parameters in SSc patients.

Methods: We enrolled 91 consecutive patients affected by Raynaud's phenomenon, 63 of which fulfilled the 2013 ACR/EULAR classification criteria for SSc and 28 had a score <9. The data collected included: pulmonary function tests (PFTs), nailfold capillaroscopy, modified Rodnan Skin Score (mRSS), and Scleroderma Health Assessment Questionnaire Disability Index (sHAQ-DI). DAVIX of the dominant hand was calculated as % mean of the 4 fingers, employing IAG proprietary algorithm. The distribution was analysed with D'Agostino-Pearson normality test. Medians were compared by Mann-Whitney-Wilcoxon test, correlation with clinical parameters was performed using Spearman's or Pearson test, as appropriate (Prism 7).

Results: 78/91 patients were females and median disease duration was 4 years (IQR1.91-9). Complete historical and prospective follow-up data were available for 68 patients. DAVIX© correlated with mRSS (r=-0.258, p=0.017), DLCO% (r=0.338, p=0.008) and capillaroscopy pattern (r=-0.388, p=0.001). In patients with DUs, DAVIX© showed a stronger correlation with DLCO% (r=0.786, p=0.048). DAVIX© predicted the worsening of HAQ-DI (r=-0.295, p=0.029), sHAQ (r =-0.333, p=0.029) and VAS pain (r=-0.269, p=0.038) independently of the presence of DUs. In the context of DU, 7 patients had DUs at baseline (5 with a positive history for DUs). 12 patients developed DUs within 12 months, 3 of them had DUs at baseline. 38 patients did not have either previous or current DUs, neither did they develop new DUs within 12 months. DAVIX of patients

with current DUs was 3-fold lower than DAVIX of patients without DUs (0.18 vs 0.63 p=0.0093). Further, DAVIX of patients with positive history of DUs was 50% lower than in patient with a negative history (median 0.34 vs 0.64, p=0.0052). In patients without current DUs, DAVIX of patients who developed new DUs within 12 months of follow-up was 3-fold lower than in patients who didn't develop DU (0.21 vs 0.65, p=0.0156). ROC curve analysis indicated that DAVIX threshold <0.49 conferred a 4 times higher risk of developing new DUs (67%) compared to overall risk of our population 17.6%.

Conclusion: Outcome measures of vascular involvement in SSc are scanty. We demonstrated that DAVIX© is a promising and feasible surrogate outcome measure of neointima proliferation in SSc and a useful imaging biomarker of vascular disease activity. The predictive value of DAVIX for the future onset of DU could be employed as a useful stratification tool in clinical trials. The value of DAVIX in predicting the worsening of PROs and clinical parameters in overall patients, may offer insights on the role of vascular disease activity in the overall progression of SSc.

References:

[1] Lettieri G, Abignano G, *et al* Digital artery volume index: the first objective, automated, non-invasive imaging diagnostic of macrovascular involvement in ssc. *Annals Rheum Dis* 2018

Disclosure of Interests: Klodian Gjeloshi: None declared, Fiammetta Danzo: None declared, Giovanni Lettieri: None declared, Giuseppina Abignano: None declared, Mark Hinton: None declared, Anne-Maree Dean: None declared, Giovanna CUOMO: None declared, Olga Kubassova Shareholder of: IAG, Image Analysis Group, Consultant of: Novartis, Takeda, Lilly, Employee of: IAG, Image Analysis Group, Francesco Del Galdo: None declared

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THU0342 DECLINE IN SUBCLINICAL SYSTEMIC SCLEROSIS PRIMARY HEART INVOLVEMENT ASSOCIATES WITH POOR PROGNOSTIC FACTORS AND ACTIVE INTERSTITIAL LUNG DISEASE

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Background: Primary systemic sclerosis heart involvement (pSSc-HI) is described in the majority of SSc patients when sensitive methods such as cardiovascular magnetic resonance (CMR) are used [1]. The natural history of these subclinical findings are unknown.

Objectives: To evaluate for interval change in subclinical pSSc-HI, the association between change in CMR abnormalities and disease phenotype and whether disease modifying antirheumatic (DMARD) and/or vasodilator treatment influence the CMR course.

Methods: SSc patients, fulfilling the 2013 ACR/EULAR criteria, with no cardiovascular (CV) disease, diabetes and no more than 2 CV risk factors had two CMRs performed (V1 & V2; minimum 1 year apart). A 3T CMR with late gadolinium enhancement (LGE), T1 mapping for extracellular volume (ECV of diffuse fibrosis) quantification and stress perfusion was undertaken.

Results: 31 SSc patients were evaluated, with median (IQR) follow up (between the 2 CMR scans) of 33 (17, 37) months. Median (IQR) age was 52 (47,60), 32% had diffuse cutaneous SSc, 52% interstitial lung disease (ILD), 29% Scl70+.

4/31 patients had a non-ischaemic LGE pattern suggesting focal fibrosis at V1, with no change in the pattern, distribution, or median (IQR) LGE scar mass between V1 and V2 [1.88 (1.01, 6.34) vs 1.70 (1.21, 4.18)]. At V2, 2 additional patients showed focal fibrosis, of which one had an episode of clinically diagnosed myocarditis. No significant change in ECV, T1 native, myocardial perfusion reserve (MPR) or left ventricle (LV) volumes and function were noted at V2 compared with V1 (p>0.01).

SSc patients with either increase in pre-existing LGE scar mass (n=1) or new fibrosis were all dcSSc, with ILD, 2 Scl70+. A reduction in forced vital capacity and total lung capacity associated with a reduction in LV ejection fraction (LVEF) (rho=0.413, p=0.021; rho-0.335, p=0.07) and MPR (rho=0.543, p=0.007; rho=0.627, p=0.002).

Patients receiving DMARD treatment had higher baseline LV end-diastolic volume compared to those with no DMARD treatment [mean (SD) 78 (19) vs 69 (10), p=0.167]. A decrease in LV stroke volume and an increase in T1 native at V1 vs V2 was noted for those on DMARD [mean (SD) 49 (8) vs 46 (8), p =0.023; 1208 (65) vs 1265 (56), p=0.008 respectively] (Figure 1). No significant change in CMR measures in those receiving vasodilator or angiotensin-converting-enzyme inhibitor treatment was noted (p>0.01).

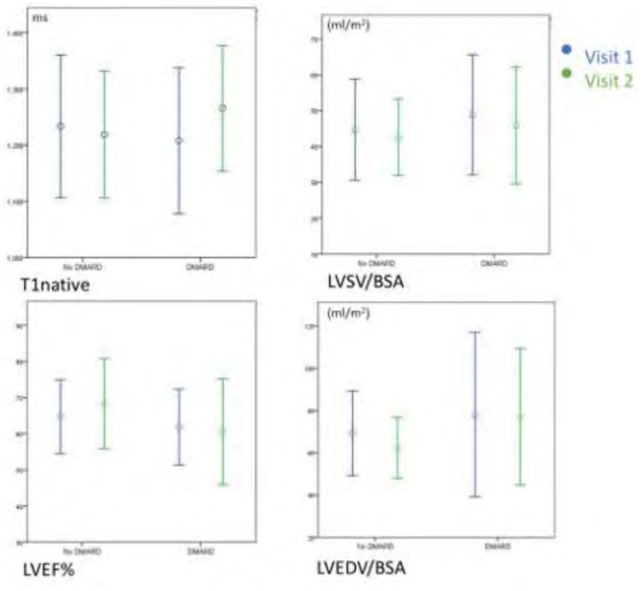


Figure 1. Mean (SD) of T1 native, LVSV/BSA, LVEF, and LVEDV/BSA at V1 compared to V2 in those with and without DMARD treatment.BSA, body surface area; DMARD, disease modifying antirheumatic drugs; EDV, end-diastolic volume; SV, stroke volume; LV left ventricular; EF, ejection fraction.

Conclusion: This first, pilot longitudinal study of CMR-defined subclinical pSSc-HI suggests largely stable appearances with follow-up. Progression of new focal fibrosis and decline in LV function and MPR, where observed, associated with poor prognostic factors of SSc and ILD progression. Consistent with this, individuals on DMARD appeared to show interval decline. Larger longitudinal studies are warranted to confirm these findings and inform on utility of CMR monitoring of subclinical pSSc-HI in poor prognosis SSc.

References:

[1] Ntusi NA et al, J Cardiovasc Magn Reson. 2014

Disclosure of Interests: Raluca-Bianca Dumitru: None declared, Lesley Anne Bissell: None declared, Bara Erhayiem: None declared, Graham Fent: None declared, Ananth Kidambi: None declared, Giuseppina Abignano: None declared, John Greenwood: None declared, John Biglands: None declared, Francesco Del Galdo: None declared, Sven Plein: None declared, Maya H Buch Grant/research support from: Pfizer, Roche, and UCB, Consultant of: Pfizer; AbbVie; Eli Lilly; Gilead Sciences, Inc.; Merck-Serono; Sandoz; and Sanofi

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THU0343 AUTOANTIBODIES CAN PARTLY PREDICT SEVERITY OF DAMAGE BUT NOT EXTENT IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOSITIS

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Background: Patients with idiopathic inflammatory myopathies (IIM) might suffer from irreversible damage once inflammation has decreased. Autoantibodies are found in up to 80% of patients with IIM and are coupled with specific clinical features. Whether autoantibodies can be used as biomarkers to predict patterns of damage in IIM remains unknown.

Objectives: To investigate the association between autoantibodies and organ damage in patients with IIM using longitudinal national register data.

Methods: Data were retrieved from the electronic Swedish Rheumatology Quality Register (SRQ). Patients (n=302) with a clinical diagnosis of IIM (2017

EULAR/ACR criteria) were included. Autoantibody status was tested by either line blot or RNA- and protein immunoprecipitation; HMGCR and FHL-1 autoantibodies were tested by ELISA. Patients were grouped into six categories of autoantibodies (Table 1). The *Myositis Damage Index* (MDI) score was applied to measure organ damage using both components (*extent* and *severity*) as a continuous variable and were analyzed using generalized estimating equations (GEE). A categorical variable for each time point of MDI assessment since diagnosis was created to adjust for time (Table 2). A base model which included autoantibody group and time was fit. Other potential predictors included age at diagnosis, sex, disease duration from diagnosis to inclusion to SRQ, arthritis, Raynaud, mechanics' hands and heart involvement at registry; core set measures at each MDI time point allowing multiple longitudinal observations were also tested.

Table 1. ***Clinical diagnosis and autoantibody groups.***

Diagnosis	N (%)
Polymyositis	119 (38)
Dermatomyositis (DM)	99 (33)
Inclusion body myositis	35 (12)
Amyopathic DM	9 (3)
Juvenile DM	8 (3)
Low probability myositis	32 (11)
Autoantibody	286 (%)
Antisynthetase (AS)	74 (26)
Necrotizing myopathy NM)	20 (7)
DM- specific	44 (15)
FHL-1	18 (6)
Associated antibodies AA)	50 (18)
Negative to any	80 (28)

AS: Jo1, PL7, PL12, EJ, OJ; **NM**: SRP, HMGCR; **DM-specific**: TIF1γ, Mi2, MDA5, SAE; **AA**: Ro52, PmScl, U1RNP, KU.

Table 2. Predictors of damage severity and extent.

	Estimate	**P value**
Severity		
Time#	0.20	NS
Autoantibody group[1]		
Negative	*reference*	--
Antisynthetase	-0.6	NS
IMNM	1.6	NS
DM- specific	-2.6	**
FHL-1	0.4	NS
Associated	0.7	NS
MMT score[1]	-0.1	***
Extent		
Time#	0.33	NS
CK, mkat/L[2]	-0.006	*

 # Time from diagnosis to MDI. *<0.05<0.01***<0.001**
1. Adjusted for gender + disease duration + time.
2. Adjusted for disease duration + time.

Results: Mean age at diagnosis was 54 years (SD 16), 205 were female (68%), median disease duration was 4 months (IQR 1-39). Clinical diagnosis and the autoantibody groups are shown in Table 1. The median time from diagnosis to the first MDI assessment was 2.2 years (IQR 1.2 – 5.5), 227 patients had a second MDI assessment at median 4.5 years (3.3-8.6 years) and 114 patients had a third assessment at 7.8 (5.8-9.9) years. *Severity of damage:* Only the DM-specific autoantibodies (P = 0.01) and manual muscle test score (MMT) (P = 0.007) were independent negative predictors; disease duration was a positive predictor (P = 0.01). *Extent of damage*: Autoantibodies were not significant predictors; creatine kinase (CK) levels were negative predictors (P = 0.01) (Table 2).

Conclusion: Presence of DM-specific autoantibodies, a high MMT score over time and short disease duration seem to predict less damage severity whereas high CK levels seem to predict of less extent of damage. These findings indicate that some myositis specific autoantibodies may serve as predictors of damage along with other clinical measures.

References:

[1] Sultan SM, et al. Interrater reliability and aspects of validity of the myositis damage index. Annals of the Rheumatic Diseases. 2011;70:1272-6.

Disclosure of Interests: Fabricio Espinosa-Ortega: None declared, Marie Holmqvist: None declared, Maryam Dastmalchi: None declared, Andrew Mammen: None declared, Ingrid E. Lundberg Grant/research support from: Bristol Meyer Squibb, Corbus Pharmaceuticals, Inc and Astra Zeneca, Helene Alexanderson: None declared

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THU0344 CLINICAL AND HISTOLOGICAL SPECTRUM OF ANTI-MI2 DERMATOMYOSITIS: A MULTICENTRE RETROSPECTIVE COHORT

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Background: Dermatomyositis (DM) shows a wide clinical spectrum that seems to be different based on the type of autoantibody status. Furthermore, less is known regarding to the histopathology of different serological subsets of DM

Objectives: The aim of our study was to investigate clinical and histopathological hallmarks in adult DM patients positive for anti-Mi2 (Mi2+) antibody compared to DM patients negative for anti-Mi2 (Mi2-)

Methods: All clinical data of adult DM patients admitted in three tertiary Rheumatology Units, who fulfilled EULAR/ACR 2017 classification criteria[1], were included in this study. Overlap syndrome and antisynthetase syndrome were exclusion criterion. Serum samples were tested in the local reference laboratories using line immunoassays methods for Myositis specific and associated antibodies. Histopathological study was carried out from muscle biopsies performed for diagnostic purpose in outpatient clinic of Bari (Italy) University. Quantitative analysis was performed for myofiber and capillary features, whereas semi-quantitative analysis (score from 0 to 3) was performed for inflammatory cells infiltrate, both at endomysial and perimysial sites

Results: A total of 95 DM patients, followed for a median (IQR) follow-up of 28 (9-85) months, were analyzed. Of these, 23 (24.2%) patients (87% female, mean age at onset 55.4±16.2 years) were anti-Mi2+, while 72 (75.8%) patients were Mi2- (72.2% female, mean age at onset 55.2±17 years). All Mi2+ patients showed muscle involvement. Moreover, Mi2+ DM showed higher levels of serum creatine kinase (CK) at onset compared to Mi2- (CK (IQR): 2649 UI/l (1130-6000) vs 575 UI/l (164-1617), p<0.001). Prevalence of interstitial lung disease (ILD) was lower in Mi2+ patients (8.7% vs 30.6%, p=0.05), and no case of rapidly progressive ILD (RP-ILD) was found. Survival analysis at 5-years follow-up highlighted good survival for Mi2+ patients, but not different from Mi2- (95.7% vs 83.1%, p=0.151). Multivariate analysis showed that age at onset (HR:1.07), RP-ILD (HR:36.2) and cancer associated myositis (HR:6.1) correlated with a poor prognosis. Finally, a total of 26 biopsies (12 Mi2+ and 14 Mi2-) were included into the histological analysis showing higher prevalence of necrotic/degenerating myofibers (median (IQR) 2.6 (0.7-11)% vs 0.6 (0.4-1.1)%, p=0.009) and sarcoplasmic deposit of membrane attack complex (MAC) (median (IQR) 0.2 (0-1.2)% vs (0(0-0)%,p=0.009) in Mi2+ patients. In addition, the endomysial macrophage score was higher in Mi-2+ patients (median 1.5 (0.25-2) vs (0.5 (0-1), p=0.031)

Conclusion: Mi2+ patients represent a specific DM subset with higher muscle damage, sarcoplasmic MAC deposits and endomysial macrophages infiltration as histological hallmarks

References:

[1] Ann Rheum Dis. 2017 Dec;76(12):1955-1964

Disclosure of Interests: Marco Fornaro: None declared, Francesco Girolamo: None declared, Lorenzo Cavagna: None declared, Franco Franceschini: None declared, margherita giannini: None declared, Giovanni Zanframundo: None declared, Micaela Fredi: None declared, Marilin Tampoia: None declared, Angela Amati: None declared, Luigi Serlenga: None declared, Anna Lia: None declared, Liala Moschetti: None declared, Dario Dabbicco: None declared, Laura Coladonato: None declared, Florenzo Iannone Consultant of: Speaker and consulting fees from AbbVie, Eli Lilly, Novartis, Pfizer, Roche, Sanofi, UCB, MSD, Speakers bureau: Speaker and consulting fees from AbbVie, Eli Lilly, Novartis, Pfizer, Roche, Sanofi, UCB, MSD

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THU0345 **EFFECT OF THE LONG-TERM RITUXIMAB TREATMENT ON B-LYMPHOCYTES AND ANTINUCLEAR AUTOANTIBODY LEVEL IN PATIENTS WITH SYSTEMIC SCLEROSIS**

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Background: Anti-B-cell therapy is seen as a promising therapeutic option for systemic sclerosis (SSc). The study of antinuclear antibody levels during treatment with rituximab (RTX) in patients (pts) with SSc could have theoretical and practical interest.
Objectives: To assess the changes in ANA, anti-topoisomerase-1 (Scl-70) levels and B-lymphocytes (B-lymph) count during RTX therapy during prospective observation.
Methods: This prospective study included 88 pts with SSc, 83% of them had interstitial lung disease and 75% had positive Scl-70 autoantibody. The mean age was 47 yrs (17-71), female-73 pts (83%), the diffuse cutaneous subset of the disease had 50 pts (57%). The mean disease duration was 5,9±4,8 yrs. The mean follow-up period was 27 months (12-42). The cumulative mean dose of RTX was 2,9±1,1grams. All patients received prednisolone at a dose of 11,7±4,4 mg, immunosuppressants received 42% of them. Patients were divided into groups depending on the duration of the disease: group 1 (n=33) - up to 3 yrs, group 2 (n=25) - from 3 to 6 yrs, group 3 (n=30) - more than 6 years (6-18yrs). The results are presented in the form of mean values, median, upper and lower quartiles.
Results: Parallel to clinical improvement in most patients (96%) we found positive changes in many parameters at the end of the study compared to the baseline. The Rodnan skin score decreased from 11,21±9,33 to 6,19±4,74 (p<0,001). The disease activity index (EScSG-AI) decreased from 2,9±1,74 to 1,36±1,15 (p<0,001). Forced vital capacity, % predicted, increased from 76,35±19,65 to 84,37±21,04 (p<0,001). Diffusing capacity for carbon monoxide, % predicted, increased from 45,56±17,72 to 47,62±16,96 (p<0,019). The dose of prednisolone decreased from 11,7±4,4 to 9,2±3,2 mg (p<0,001). The absolute number of B-lymph decreased from 0,224±0,19 to 0,0175±0,058 (p<0,001). The pts of the group 1 showed the highest values of B-lymph at baseline and level of B-lymph decreased from 0,326±0,22 to 0,008±0,01 (Δ 0,318) at the end of the study. In group 2 depletion was less pronounced (from 0,197±0,14 to 0,026±0,07 (Δ 0,171) and the lowest depletion was observed in group 3 (from 0,151±0,16 to 0,019±0,07 (Δ 0,131), p<0,001 for all groups. An initially positive ANA was found in 92% of pts (range 1/320-1/1280). During observation, the number of pts with high (1/640-1/1280) ANA titers decreased from 70 to 41 (p<0,001), and the average level of ANA decreased by 30-40% in all groups. At baseline 63 pts (75%), had positive Scl-70 with equal levels in all groups. At the end of the study level of Scl-70 decreased from 125,02±89,12 to 108,6±86,89 units/ml (p<0,007). A negative correlation was found between the duration of the disease and ANA (r = -0,54; p<0,003) and Scl-70 (r = -0,44; p<0,017).
Conclusion: In our study a clinical improvement was shown in most pts at the long-term complex therapy, including RTM. We found a significant decrease in the absolute number of B-lymph, as well as decrease of ANA and Scl-70 levels. Initially pts with a short duration of the disease had a higher level of B-lymph and in these pts depletion was more pronounced, compared to those with a longer duration of the disease. However, the level of Scl-70 and ANA decreased both to those who started RTX therapy at an early stage of the disease (<3yrs) and to those who had a long disease duration.
Disclosure of Interests: None declared
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THU0346 **SARC-F PERFORMANCE FOR SARCOPENIA SCREENING IN PATIENTS WITH SYSTEMIC SCLEROSIS**

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Background: Because the method of diagnosing sarcopenia is complex and is considered to be difficult to introduce into routine practice, the European Working Group on Sarcopenia in Older People's (EWGSOP) recommends use of the SARC-F questionnaire as a way to introduce assessment and treatment of sarcopenia into clinical practice[1]. Only recently, some studies have focused their attention on the presence of sarcopenia in systemic sclerosis (SSc) and there is no data about the performance of SARC-F in this population.
Objectives: To test the diagnostic properties of the SARC-F questionnaire for sarcopenia screening in SSc patients.
Methods: Cross-sectional study, including 94 SSc patients assessed by clinical evaluation, laboratory and pulmonary function tests. Sarcopenia was evaluated using the EWGSOP diagnostic criteria updated in 2019 (EWGSOP2): dual-energy X-ray absorptiometry, handgrip strength, and short physical performance battery (SPPB)[1]. Participants also completed the SARC-F questionnaire. The questionnaires' performances were evaluated through receiver operating characteristic (ROC) curves and standard measures of diagnostic accuracy were computed using the EWGSOP2 criteria as the gold standard for diagnosis of sarcopenia.
Results: Sarcopenia was identified in 15 (15,9%) SSc patients by the EWGSOP2 criteria. Area under the ROC curve of SARC-F screening for sarcopenia was 0.588 (95% confidence interval (CI) 0.482, 0.688) (figure 1). The results of sensitivity, specificity, positive likelihood ratio (PLR) and negative likelihood ratio (NLR) with the EWGSOP2 criteria as the reference standard were 35.71 [95% CI, 12.76-64.86], 81.01 (95% CI, 70.62-88.97), 1.88 (95% CI, 0.81-4.35) and 0.79 (95% CI, 0.53-1.19), respectively. The optimal cut-off point of SARC-F in our sample was ≥ 4 (Youden index: 0.21), the same cut-off point recommended in the literature[2,3]. Only 6 (40%) out of the 15 participants with sarcopenia were identified by the SARC-F questionnaire in our population. However, the SARC-F properly identified 4 out of 5 patients who had severe sarcopenia.
Conclusion: This is the first study to evaluate the performance of SARC-F questionnaire for sarcopenia screening in patients with SSc. Although it appropriately identifies severe cases of sarcopenia, the SARC-F alone may not be an adequate screening tool in high-risk populations, such as SSc, that may benefit from early intervention and treatment.
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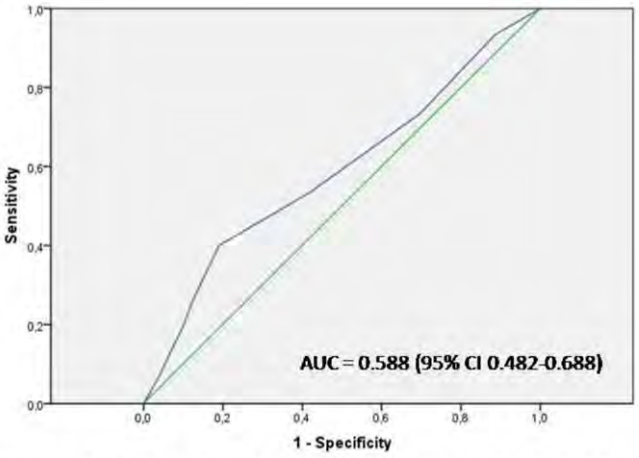


Figure 1. Receiver operating characteristic (ROC) curve analyze of SARC-F screening for sarcopenia (n=94). Discrimination was quantified using the area under the curve (AUC). The optimal cut-off point of SARC-F was ≥ 4.

Disclosure of Interests: Vanessa Hax: None declared, Rafaela Santo: None declared, Leonardo Santos: None declared, Mirian Farinon: None declared, Marianne de Oliveira: None declared, Guilherme Levi Três: None declared, Andrese Aline Gasparin: None declared, M Bredemeier: None declared, Ricardo Xavier Consultant of: AbbVie, Pfizer, Novartis, Janssen, Eli Lilly, Roche, Rafael Mendonça da Silva Chakr: None declared
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THU0347 **CLINICAL DESCRIPTION OF A COHORT OF PATIENTS WITH SCLEROTIC-TYPE CHRONIC GRAFT-VERSUS-HOST DISEASE TREATED IN A MULTIDISCIPLINARY PRACTICE**

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Background: Graft versus host disease is the most frequent complication after allogeneic transplantation of hematopoietic progenitors. Its chronic form usually involves a multisystemic syndrome that reflects a complex immune response with varying degrees of inflammation, immune dysregulation and fibrosis, responsible for the characteristic clinical manifestations of the disease. Joint, muscular and fascial involvement represents one of the areas, often unnoticed or poorly evaluated, that negatively impacts the physical function and quality of life of these patients.
Objectives: Describe the presence of musculoskeletal manifestations and their clinical characteristics in patients with chronic GVHD (cGVHD) evaluated in a multidisciplinary consultation
Methods: Descriptive and retrospective observational study to detail the initial presence and during the follow-up of diagnostic and nonspecific musculoskeletal manifestations of cGVHD in a cohort of 103 patients included in the database. The clinical characteristics of 68 patients with a defined diagnosis of sclerotic cGVHD are described. Demographic variables are collected along with clinical conditions about transplant and in a systematic way the assessment according to diagnostic criteria of the American National Institute of Health 2015 highlighting: range of motion scale and photographic range of motion (P-ROM) scale in shoulders, elbows, hands and ankles; and laboratory data: presence of eosinophilia and autoantibodies. Descriptive and frequency statistical analysis was done using Microsoft Office Excel 2007.
Results: Sixty-eight(66%)patients meet diagnostic criteria for sclerotic cGVHD during follow-up. Forty-five(66.2%) women and 23(33.8%) men, with a mean age of 54.5 years (range 10-78), Acute myeloid leukemia was the reason for transplant in 20(29, 4%) followed by non-Hodgkin lymphoma in 15 (16.2%). In 40(58.7%) patients it was performed from a related donor and with reduced intensity conditioning in 43(63.2%). Only in one patient the source of hematopoietic progenitors was bone marrow (rest peripheral blood). The average time from transplant to the first visit was 29.5 months (range 4 -168). Twelve(17.64%) patients presented isolated joint/fascial involvement without objective skin involvement (Table 1)

Table 1. Clinical features of the sclerotic joint/fascial chronic GVHD cohort (N= 68)

Unspecific musculoskeletal symptoms:	46 (67.6%)
-Artromyalgia	39(57.3%)
-Edema	13(19%)
-Stiffness	4(5.8%)
Fasciitis/contractures	28(41.2%)/43(63,2%)
Restricted ROM[1]	
-Mild/Moderate/Severe	34(50%)/14(20.2%)/4(5.8%)
Impaired mobility	
-Shoulders	26(38.2%)
-Elbows	21(30.8%)
-Wrist/fingers	29(42.6%)
-Ankles	21(30.6%)
Sclerodermatous involvement	
-Superficial /deep	6(8.8%)/7(10.3%)
-Mixed (sclerodermiform + lichenoid)	20(29.4%)
-Overlapping skin sclerosis	13(19.2)
NIH [1]Global Score	25(36.7%)/7(10.3%)/1(1.5%)
-Mild/Moderate/Severe	
Eosinophilia	21 (30.8%)
Autoantibodies	14 (20.6%)

[1]ROM (range of motion) [2]NIH: National Institute of Health

Conclusion: Joint involvement secondary to sclerosis is very common in our cohort, mainly of the dorsal wrist flexion with deleterious repercussion on physical function. It needs to be recognized and evaluated early with validated scales. The search for new biomarkers associated with fibrosis, the use of advanced imaging techniques and the multidisciplinary approach can help improve the prognosis of patients with cGVHD.
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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.3386

THU0348 ALTERED IMMUNE RECOGNITION OF SPECIFIC GUT BACTERIA BY IMMUNOGLOBULINS IN EARLY SYSTEMIC SCLEROSIS

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Background: Gastrointestinal tract (GIT) involvement is highly prevalent in systemic sclerosis (SSc) and associates with GIT symptoms that are present early and progress over time. Changes in gut microbiota are often reported in inflammatory disease settings but whether GIT symptoms associate with altered immune recognition of specific gut bacteria in early SSc is unknown.
Objectives: Here, we profiled Ig coating patterns of gut bacteria in early disease from two well-characterized SSc cohorts to determine if the pattern and extent of bacterial immunoglobulin (Ig) coating differs in early SSc.
Methods: We collected fecal material from early SSc patients (<36 months from time of diagnosis) at Oslo and Lund University Hospitals and from healthy age and gender matched controls (HC). To assess whether adaptive immunity was triggered against gut microbiota in early disease, we sorted and sequenced IgA, IgM and IgG coated bacteria from fecal samples by flow cytometry and performed 16s rRNA sequencing to compare the relative Ig coating of early SSc patients to HC. Data was resolved to the family level, rarefied to 5101 reads and converted to relative abundance. Taxonomic profiles, relative abundance, IgA, IgM and IgG coating patterns and extent of Ig coating were assessed. Unadjusted p-values <0.05 were defined as significant.
Results: We included 50 SSc patients (26 from Oslo, 24 from Lund) with early SSc and 9 gender and age matched HC. Mean age of SSc patients at time of inclusion was 53 years, mean time since diagnosis was 13 months; 82% were female, 61% had limited cutaneous SSc and 43% were anti-centromere antibody positive. In all, 82% were treatment naïve while 18% had received either cyclophosphomide or mycophenolate mofetil immunosuppressants. We found increased relative abundance of IgA coated Desulfovibrionaceae in both SSc cohorts compared to HC and increased IgM and IgG coating of Veillonellaceae and Streptococcaceae (Figure 1). All of these bacteria have previously been associated with other autoimmune diseases or pro-inflammatory status; Desulfovibrionaceae to immune activation in the gut, and Veillonellaceae and Streptococcaceae to other chronic inflammatory and fibrotic conditions. While abundance of IgA coated Desulfovibrionaceae was higher in cyclophosphomide or mycophenolate mofetil-treated SSc patients than untreated patients, Veillonellaceae and Streptococcaceae were not affected by treatment. A lower abundance of IgA and IgM coated Akkermansiaceae; and IgM and IgG coated Bifidobacteriaceae was detected in treated compared to treatment naïve early SSc patients (Figure 2).

Figure 1: Phylogenetic tree of gut bacteria based on the 16S rRNA gene sequence showing relative abundance of IgA, IgM and IgG coated gut bacteria an the Lund (SWE) and Oslo (NOR) early SSc cohorts compared to healthy controls (HC) with high abundant gut bacteria in orange and low abundant gur bacteria in green

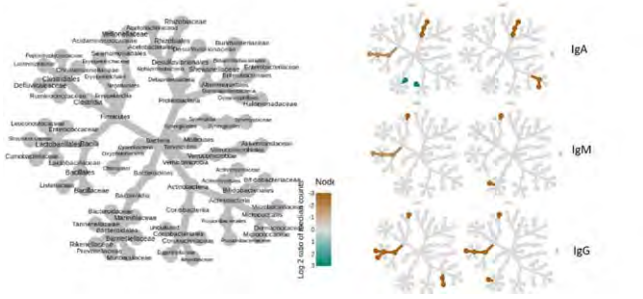
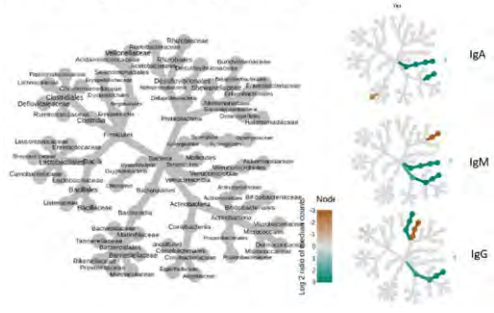


Figure 2: Phylogenetic tree of gut bacteria based on the 16S rRNA gene sequence showing relative abundance of IgA, IgM and IgG coated gut bacteria in treated (yes) and untreated (no) SSc patients with early disease with high abundant gut bacteria in orange and low abundant gur bacteria in green



Conclusion: We find the pattern and extent of Ig coating to inflammatory-associated gut bacteria differs between treatment-naïve, early SSc patients treated with cyclophosphomide or mycophenolate mofetil and HC which suggests

immunosuppressive treatments may modify gut microbiota in SSc. Overall these findings support the involvement of altered immune recognition of specific gut bacteria in early SSc.

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THU0349 THE RELATIONSHIP BETWEEN DISEASE ACTIVITY AND SEVERITY IN SYSTEMIC SCLEROSIS: A PROSPECTIVE ANALYSIS OF 278 PATIENTS

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Background: Evaluating disease activity and severity in systemic sclerosis (SSc) is crucial to define the patients who are candidate for treatment options.

Objectives: We aimed to investigate the relationship between disease activity and severity in SSc in a large cohort.

Methods: This is a cross-sectional prospective analysis of 278 (253 females) patients fulfilling ACR/EULAR (2013) classification criteria for SSc. Disease activity and severity were calculated seperately for cutaneous subsets (EscSG and Medsger). The patients were grouped as inactive if EscSG score=0, mildly active if EscSG score>0<3, active if EscSG score≥3.

Results: The mean age, duration of Raynaud's and non-Raynaud features were 48.5±13.1, 12.1±9.8 and 8.3±7.5 years respectively. Characteristics of the SSc patients were summarized in table-1.

Table-1: Characteristics of SSc patients

	All patients n=278(%)
ANA	223(80.2),
anti-centromer	128(46.0)
anti -Scl70	39(14.0)
Anti-RNApol3	29/165(17.6)
limited cutaneous pattern	143 (51.4)
diffuse cutaneous pattern	135(48.6)
digital ulcers	101(36.3)
Synovitis	56(20.1)
flexion contractures	81(29.1)
Myositis	40(14.4)
lung involvement	140(50.4)
PAH	9(3.2)
GIS inolvement	166(59.2)
renal crisis	8(2.9)
İmmunosuppressives	173(62.2)
Steroids	156(56.1)
specific vasodilatory drugs	47(16.9)

Ninety-three (34%) and 151(54%) patients were evaluated as having active and mildly active disease. Only 34(12%) patients had inactive disease. The patients with diffuse cutaneous involvement (dcSSc) who were active had higher modified Rodnan Skin score(mRSS) and severity scores of general, skin and joint-tendon involvements; the patients who had mildly active disease also had higher scores of mRSS and severity scores of skin compared to those with inactive disease (table-2).The patients with limited cutaneous involvement (lcSSc) who were assessed as having active disease had higher mRSS and higher severity scores of general, skin, peripheral vascular, lung, joint-tendon and gastrointestinal involvements; the patients who had mildly active disease also had higher scores of mRSS and severity scores of skin, lung, joint-tendon and gastrointestinal involvements compared to those with inactive disease (table-2).

Table-2: Severity scores of dcSSc and lcSSc patient groups according to activity of disease.

	dcSSc				lcSSc			
	inactive n=7	mildly active n=72	active n=64	*p	inactive n=27	mildly active n=79	active n=29	*p
mRSS	7,0±3,6*	16,3±7,6**	20,4±8,4*	<0.001	4,0±4,1*	7,9±5,1**	9,9±7,5*	<0.001
Severity Score								
General	1,0±1,6	0,4±0,7*	0,8±0,8*	0.004	0,4±0,6*	0,4±0,6	0,7±0,7*	0.004
PVI	1,5±0,6	1,8±0,8	2,1±0,9	NS	1,3±0,6*	1,6±0,7**	2,1±0,9*	<0.001
Skin	0,8±0,4*	1,7±0,7**	1,8±0,7*	0.001	0,7±0,5*	1,1±0,4**	1,2±0,6*	<0.001
Joint/tendon	0,5±0,8*	1,5±1,0	1,9±1,3*	0.023	0,3±0,7*	1,0±1,0	1,2±1,1*	0.003
Myositis	0,3±0,8	0,2±0,4	0,2±0,5	NS	0,1±0,6	0,1±0,4	0,2±0,5	NS
GIS	0,3±0,5	0,7±0,6	0,7±0,6	NS	0,3±0,5*	0,6±0,5**	0,7±0,5*	0.005
Lung	1,0±0,63	1,3±1,1	1,6±1,4	NS	0,3±0,7*	1,2±1,0**	1,5±1,1*	<0,001
Heart	0,2±0,4	0,1±0,6	0,1±0,5	NS	0,0±0,0	0,1±0,5	0,04±0,2	NS
Renal	0,0±0,0	0,0±0,0	0,9±0,46	NS	0,0±0,0	0,1±0,6	0,0±0,0	NS

**when inactive and mildly active group compared; p=0.005 for mRSS, p=0.036 for skin severity in dcSSc; p=0.005 for mRSS, p=0.012 for skin, p=0.004 for joint/tendon, p=0.021 for GIS and p<0,001 for lung severity.
**when active and mildly active group compared p=0.004 for PVI severity.

Conclusion: One third of our cohort was found to have active disease despite treatment and only 12% had inactive disease. Skin involvement and severity of different organs were shown to be higher in patients with active disease in both cutaneous subsets, together with severity of lung, peripheral vascular and gastrointestinal involvements in active lcSSc. LcSSc and dcSSc patients who had mildly active disease also had severe disease similar to those with active patients. Disease activity and severity should be assessed as separate measurements to highlight the course of the disease and may guide to the management of patients with SSc.

Disclosure of Interests: None declared

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THU0350 LOGOPEDIC TESTING IN SSC PATIENTS REVEALS HIGH FREQUENCY OF OROPHARYNGEAL DYSFUNCTION: A MONOCENTRIC EXPERIENCE

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Background: Up to 98% of patients with systemic sclerosis (SSc) show involvement of the gastrointestinal system (GI) [1]. While meteorism, heartburn and GI dysmotility are very common and accessible to pharmacologic treatment on an evidence based level [1–3], checking for oropharyngeal dysfunction is usually not part of the standard diagnostic algorithm. However, in a survey of the German Network for Systemic Sclerosis (DNSS) patients reported coughing and/or a sore voice in up to 78% [1]. As impairment in speaking or swallowing for example does not only substantially reduce quality of life, it can also be very stigmatizing. In addition, the usual prokinetic therapy of GI-involvement, e.g. metoclopramide, does not appear to improve these symptoms. As the first step to approach this problem is the qualitative and quantitative description, we evaluated the oropharyngeal function in our cohort of SSc patients by detailed logopedic assessment.

Objectives: To evaluate the frequency and type of oropharyngeal dysfunction, e.g. swallowing or speaking, in patients with SSc and to elucidate the correlating and associated factors, e.g. disease duration or modified Rodnan Skin Score.

Methods: After obtaining written consent, oropharyngeal function using a standardized assessment protocol was evaluated in patients with SSc fulfilling the ACR/EULAR criteria by a speech therapist. Furthermore, we investigated whether oropharyngeal dysfunction is associated with patients' characteristics. In addition, all patients received instruction for a training program to treat their individual oropharyngeal dysfunction.

Results: 37 patients with d/lSSc were assessed for eligibility. 34 patients met the inclusion criteria (3 patients did not speak German) and written consent was obtained.

Oropharyngeal dysfunction (impairment of speaking, swallowing, breathing or oropharyngeal muscle function) was found in 29 of 34 (85%) of both l/dSSc patients. Neither the subtype of SSc, disease duration nor mRSS were significantly correlated with oropharyngeal dysfunction in general. Only GI involvement in general was associated with oropharyngeal dysfunction.

After logopedic therapy, 28 of the 34 (82%) patients with oropharyngeal dysfunction reported a benefit after 3 days of training and were motivated to continue logopedic training at home.

Oropharyngeal dysfunction	Present (n=29)	absent (n=5)	p-values (x^2-test)
dcSSc	8	0	0,027
lcSSc	22	4	0,027
disease duration (mean)	12,7 y	12 y	0,462
mRSS<4	9	2	0,322
mRSS>4	20	3	0,322
Raynauds syndrom	29	5	0,673
digital ulcers	19	2	0,812
lung fibrosis	11	2	0,596
eosophageal dilatation	15	2	0,566
eosophageal dysmotility	19	0	0,015
GI-involvement	23	1	0,007

Conclusion: Logopedic assessment revealed a high incidence of oropharyngeal dysfunction in our cohort of SSc patients. Oropharyngeal dysfunction was not associated with disease duration, skin- or lung-involvement or dcSSc/lcSSc differentiation. A logopedic training program seems to be of benefit for this currently not pharmacologically treatable problem.

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THU0351 MUSCLE INVOLVEMENT IN PATIENTS WITH SYSTEMIC SCLEROSIS AND ANTI-PM/SCL+ ANTIBODIES IS ASSOCIATED WITH CARDIAC AND PULMONARY INVOLVEMENT. ANALYSIS OF THE MULTICENTRE EUSTAR COHORT.

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Background: Anti-PM/Scl antibodies positivity has been associated with frequent skeletal muscle involvement in patients with Systemic Sclerosis (SSc) in different studies, including the EUSTAR cohort (1). Moreover, although myositis has been previously associated with heart involvement in SSc patients (2), this issue has never been explored among anti-PM/Scl+ patients.

Objectives: To evaluate the cardiac involvement in anti-PM/Scl patients with SSc in the large multicentre EUSTAR database, with focus on the subgroup of patients with muscle involvement.

Methods: Patients from the EUSTAR database were included when the item anti-PM/Scl was fulfilled in at least one visit.

Results: Anti-PM/Scl status was available in 7,353 SSc patients from EUSTAR database: 295 were anti-PM/Scl+. After exclusion of 151 patients with multiple autoantibody positivity, 144 anti-PM/Scl + patients were compared with 7,058 anti-PM/Scl- patients. Among them, 3,120 (44.2%) were positive for ACA, 2,361 (33.5%) for anti-Topo I and 274 (3.88%) for anti-RNAP3.

Regarding the specific cardiac outcomes, in the anti-PM/Scl+ as compared to the anti-PM/Scl- group, a decreased rate of elevated sPAP at ECHO was recorded (12.8% vs 25.0%, p:0.001), while no differences were observed in the frequency of conduction blocks (26.2% vs 23.7%, p:0.526), abnormal diastolic function (33.9% vs 36.4%, p:0.582), pericardial effusion (10.2% vs 10.9%, p:1.000) and LVEF ≤50% (4.76% vs 6.11%, p:0.818). In multivariate analysis, adjusted for age at disease onset, sex, and disease duration, the negative association of anti-PM/Scl with elevated sPAP was not confirmed (p:0.061).

When comparing anti-PM/Scl+ patients with (n=47) and without (n=87) CK elevation, the former group had a higher frequency of conduction blocks (43.2% vs 17.5%, p:0.005; OR 95% CI 3.47, 1.51-7.97) and left ventricular dysfunction, both diastolic (45.6% vs 27.2%, p:0.050; OR 95% CI 2.25, 1.05-4.81) and systolic (LVEF ≤50% 13.3% vs 0%, p:0.018; OR 95% CI 16.8, 0.87-324). Moreover, anti-PM/Scl+ patients with CK elevation had significantly increased rate of lung fibrosis on HRCT (p:0.045), intestinal symptoms (p:0.017), joint contractures (p:0.045) and tendon friction rubs (p:0.034).

Conclusion: In the largest series of anti-PM/Scl positive SSc patients so far reported, muscle involvement in anti-PM/Scl+ patients (defined as increased serum CK) seems to represent a marker of a more severe disease phenotype, including a higher frequency of cardio-pulmonary involvement.

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THU0352 DIAGNOSTIC PERFORMANCES OF HAND ULTRASOUND PARAMETERS AND THEIR IMPACT ON THE 2013 ACR/EULAR CLASSIFICATION CRITERIA FOR SYSTEMIC SCLEROSIS.

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Background: Recent studies have highlighted that ultrasound (US) examination could offer a better assessment of hand manifestations of systemic sclerosis (SSc). Indeed, US allows a simultaneous evaluation of vascular, fibrotic and inflammatory hand features of the disease. Power Doppler US can especially explore macrovascular involvement characterized by an obliteration of digital arteries or ulnar arteries. Ulnar artery occlusion (UAO) is especially frequent in SSc patients and could be a relevant marker of the severity of SSc-associated vasculopathy. Among other hand manifestations of SSc, US evaluation can notably explore tenosynovial involvement such as fibrotic tenosynovitis (TS), which is considered to be SSc-specific.

Objectives: This study aims to assess the diagnostic performances of these hand US parameters for the diagnosis of SSc.

Methods: 244 patients with suspected SSc were consecutively included. They all had US evaluation assessing the presence of fibrotic TS and UAO. The final diagnosis of SSc was based on the evaluation of an expert, independently from US results and from any pre-established classification criteria.

Results: 166 patients were finally diagnosed as SSc. 62 SSc and 8 non-SSc patients had UAO (uni or bilateral) (p=0.001). 23 SSc patients and 1 non-SSc patient had US fibrotic TS (p=0.007). A US SSc-pattern (presence of UAO and/or fibrotic TS) was reported in 73 SSc patients and 9 non-SSc patients (p<0.001). UAO had an area under ROC curve (AUC) for the diagnosis of SSc of 0.618 (95%CI 0.539-0.697); with Se= 0.373 (0.304-0.449) and spe=0.862

(0.751-0.928). The presence of a US fibrotic TS had an AUC of 0.561 (0.480-0.643); with Se= 0.139 (0.094-0.199) and spe=0.983 (0.909-0.997). The US-SSc pattern had a AUC of 0.641 (0.563-0.695), with Se=0.440 (0.367-0.516) and spe=0.845 (0.731-0.916). When used as a diagnostic tool, the original 2013 classification criteria had an AUC of 0.982 (0.969-0.996) with Se= 0.946 (0.900-0.971) and spe=0.931 (0.836-0.973). Including UAO and fibrotic TS in this classification had few impact (AUC of 0.979 (0.962-0.996) with Se= 0.940 (0.893-0.967) and and spe=0.931 (0.836-0.973)) but allows the substitution of some items (such as capillaroscopy) by US parameters with similar performances for diagnosis.

Conclusion: The use of hand US parameters may help to refine the diagnostic strategy of SSc and their inclusion in addition with the items of the ACR/EULAR classification could be discussed.

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THU0353 ENDOCAN AND CIRCULATING PROGENITOR CELLS IN SYSTEMIC SCLEROSIS: ASSOCIATION WITH PULMONARY HYPERTENSION

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Background: Systemic sclerosis (SSc) is characterized by early vascular involvement and by varying degrees of fibrosis in skin, lungs, and other tissues. Vascular manifestations include Raynaud's phenomenon, digital ulcers, and pulmonary hypertension (PAH). The prevalence of PAH is 7.85–13% in SSc and it is the second most common cause of mortality in SSc. Circulating CD34+ cell number is associated to cardiovascular health status in several chronic conditions, including inflammatory disease. CD34+ cell number was found inconstantly reduced in SSc. Endocan is a proteoglycan expressed by endothelial cells likely interacting with white blood cells, recently suggested as a marker of vascular stress.

Objectives: to evaluate CD34+ cell number and endocan as a markers od cardiovascular involvement in SSc.

Methods: Standard transthoracic echocardiography, Rodnan skin score were performed. Vitamin D levels, CD34+ cell number, markers of inflammation, red blood cells distribution width (RDW) and Endocan plasma levels were also determined.

Results: 37 female SSc patients (11 diffuse/26 limited) and 35 matched healthy controls (HC) were enrolled. CD34+ cell count was lower as compared to controls (2.3±0.73 vs 2.9±0.6; p<0.001), CRP and ESR were significantly higher in SSc patients than controls. Vitamin D3 was lower in SSc patients with respect to controls (18±4.5 vs 27.26±10.98; p<0.001), Rodnan skin score was 28.89±10.24. Endocan was two times greater than controls and serum endocan levels were higher in patients with diffuse Ssc as compared with limited ones. We found no correlation between Endocan and: Rodnan skin score, ESR, fibrinogen; we found a trend of correlation between Endocan and Vitamin D levels (r= -0.315), RDW (r= 0.310), CRP (r= 0.310), but statistical significance was not reached likely due to the small sample size. We found an association of PAPs with Endocan levels (rho= 0.442, p<0.01) and CD34+ count (-0.349, p<0.05. A significant correlation was also found between Endocan and CD34+ cell number (rho= -0.605, p<0.01).

Conclusion: In our study population, we found a significant correlation between CD34+ cell number and Endocan plasma levels and PAPs; Endocan and CD34+ progenitor cells might be suggested as potential marker of pulmonary arterial hypertension in SSc patients.

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THU0354 CHARACTERIZATION OF ANTI-MYOSITIS ANTIBODY RELATED MYOPATHIES. DESCRIPTIVE STUDY IN A MULTICENTRIC COHORT.

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Background: Idiopathic inflammatory myopathies (IIM) are a group of rare diseases consisting on immune-mediated muscle damage. About 40 to 60% show specific-myositis antibodies; aditionally, 20-40% can show myositis-related (non-specific) antibodies. The profile of antibodies can help to divide patients into subgroups with more homogeneous clinical characteristics and prognosis.

Objectives: This study characterizes patients with IIM with specific or related anti-myositis antibodies, in five hospitals in the Alicante health area.

Methods: This is an observational study, carried out in five hospitals with a reference population of 1.083.463 people. Patients with positive anti-myositis antibodies between October 2015 and May 2018 were selected from the database of the Clinical Laboratory of the University Hospital of Alicante. We considered the following antiboides: anti-myositis specific antibodies (anti-TIF1y, anti-MDA5, anti-Mi-2, anti-PmScl75, anti-PMScl100, anti-NXP2, anti-SRP), anti-synthetase antibodies (anti-PL7, anti-PL12, anti-Jo1, anti-OJ), myositis-related antibodies (anti-Ro52, anti-Ku). Clinical records were examined, identifying those patients with a diagnosis of IIM acording to their clinician, rheumatologist. Epidemiological and clinical data were obtained.

Results: 291 patients with positive anti-myositis antibodies were identified. Among them, 40 patients had a diagnosis of IIM. Median age was 59.5 (IQR 41.5, 70) years and 68% were women. Within the subgroups, the most frequent diagnosis were dermatomyositis (n=22; 55%) and polimyositis (n=9; 22%). The most common antibody detected was anti-TIF-y among specific antibodies, and anti-Jo-1 among the anti-synthetase antibodies. The most common extramuscular feature was skin involvement. The presence of interstitial lung disease was reported in about one third of patients, being UIP the most commong pattern. Regarding treatment, the use of steroids was generalized; methotrexate was the most used inmunosupresant agent. Eight patients had a cancer related myopathy.

	DM (N=22)	PM (n=9)	DMJ (N=3)	IMNM (n=1)	AS (n=5)
Age, median (IQR)	65,5(46, 76)	57(34, 66)	15,7 (14, 18)	83 (-)	61(56, 64)
Female n(%)	15(68,2)	6(66,6)	2(66,6)	1(100)	3(60)
Muscular feat. n(%)	16(77,7)	9(100)	1(33,3)	1(100)	5(100)
ILD n(%)	1(4,5)	3(33,3)	0	0	5(100)
Disfagia n(%)	3(13,6)	1(11,1)	0	0	0
Skin feat n(%)	17(77,3)	0	2(66,6)	0	1(20)
arthritis n(%)	1(4,5)	0	2(66,6)	0	4(80)
Raynaud n(%)	4(19)	1(11,1)	0	0	1(20)
Calcinosis n(%)	1(4,5)	1(11,1)	(66,6)	0	0
Puffy hands n (%)	2(9)	0	0	0	2(40)
Sicca synd n(%)	3(13,6)	1(11,1)	0	0	0
Cáncer n(%)	7(31,8)	1(11,1)	0	0	0
Ck máx(UI/l), median (IQR)	432(171, 706)	809(350, 1653)	-	-	665(396, 2300)

Conclusion: This register allows us to characterise patients with inflammatory myositis in our area. It is important to make multicentric and prospective registers in infrequent diseases such as IIM in order to have more detailed and representative information about clinical and socio-demographic characteristic as well as prognostic data from these patients.

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THU0355 **PARAMETRIC CARDIAC MAGNETIC RESONANCE IMAGING IDENTIFIES ARRHYTHMOGENIC SUBSTRATES IN SYSTEMIC SCLEROSIS PATIENTS**

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Background: Cardiac involvement in systemic sclerosis (SSc) accounts for 26-36% of deaths. This most frequently manifests as ventricular rhythm disturbances (VRDs), eventually culminating in sudden cardiac death. However, no specific guidelines exist for implantation of cardioverter defibrillators (ICD) in SSc patients. Parametric cardiovascular magnetic resonance (CMR) indices of myocardial oedema and fibrosis like native T1/T2 mapping have been shown to be associated with prognosis in SSc patients with acute cardiac events and normal echocardiograms. However, their relationship with arrhythmogenicity per se has not been previously investigated in SSc.

Objectives: To investigate the relationship between parametric CMR indices and arrhythmogenicity in SSc patients.

Methods: 84 consecutive SSc patients (80% diffuse-cutaneous SSc) from eight European centers presenting with cardiac symptoms were examined using a 1.5 T CMR system. 24h Holter recordings were obtained within a month of the CMR scan. The presence of VRDs was defined as any type of premature ventricular contraction (PVC) in couples, triplets, bigeminism, trigeminism, quadrigeminism and non-sustained ventricular tachycardia, as well as having >30 PVCs per hour. Logistic regression analysis was used to evaluate the relationship between VRD occurrence and native T1/T2 mapping as well as myocardial extracellular volume fraction (ECV).

Results: Mean age in the cohort was 55 (13) years and 78 (93%) patients were female. Of these, 67 (80%) experienced at least one type of VRDs. Each 10 ms increase of native T1-mapping was associated with a higher occurrence of VRDs [odds ratio (95% confidence interval): 1.21 (1.08-1.36), p=0.001]. Similarly, a 1% increase in ECV conferred an increased probability of experiencing VRDs [1.25 (1.01-1.53), p=0.037]. Lastly, a 1ms unit increase in T2-mapping also led to increased probability of having experienced VRDs [1.09 (1.01-1.19), p=0.035].

Conclusion: Parametric CMR indices are associated with arrhythmogenicity in SSc patients with cardiac symptoms and should be investigated further in larger studies for their clinical utility in selecting high-risk SSc patients for ICD implantation.

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THU0356 **DISEASE ACTIVITY ASSESSMENT IN SYSTEMIC SCLEROSIS PATIENTS BASED ON THE CURRENTLY AVAILABLE ACTIVITY INDICES AND THE PHYSICIAN GLOBAL ASSESSMENT**

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Background: Disease activity assessment is crucial in defining the appropriate therapy and to monitor the efficacy of treatment in systemic sclerosis.

Objectives: We aimed to test the performance of the 'old' European Scleroderma Trials and Research Group (EUSTAR) Activity Index (old-AI) (1), the 'new' EUSTAR activity index (new-AI) (2), and the scleroderma activity index derived from the old-AI (Pecs-AI) (3). We compared the three indices to the disease activity based on the physician's global assessment (PGA). We also assessed the correlations with the change in modified Rodnan Skin Score (MRSS), FVC and arthritis after one year follow-up.

Methods: We evaluated 77 patients (50 diffuse /dcSSc/ and 27 limited cutaneous SSc /lcSSc/ patients) from a single tertiary clinical center. Cohort enrichment was performed to increase the number of patients with early disease and dcSSc. Seventy-two patients were re-evaluated after one year. Nine patients had overlap syndromes: rheumatoid arthritis (n=3), Sjögren syndrome (n=2), polymyositis (n=2), and mixed connective tissue disease (n=2). The overall disease activity was evaluated using both composite indices (old-AI, Pecs-AI, new-AI) and the PGA of disease activity, based on the blinded evaluation of a single physician (LV). In addition to the minimal essential data from the EUSTAR database we also performed detailed assessment of the musculoskeletal involvement evaluating measures of hand function, DAS28 scores, and the Clinical Disease Activity Index (CDAI) (4).

Results: Three times more patients with active disease were identified by the new-AI compared to the old-AI at baseline investigation (n=37, 48.7%, vs. n=11, 14.3%). Two patients (18%) with active disease based on the old-AI were missed by the new-AI. Pecs-AI index identified 15 patients (19.5%) with active disease (cut-off >2.75 points). Active disease was equally frequent in dcSSc and lcSSc patients based on old-AI, but was more frequent in dcSSc patients based on the new-AI in the whole cohort, and also after excluding overlap cases.

Patients with active disease based on the old-AI had more frequently rheumatoid factor (6/9, vs. 12/45, p=0.047), and DLCO<70% (11/11, vs. 36/65, p<0.01). Active disease based on the new-AI was associated with current cyclophosphamide treatment (9/37, vs.2/39, p=0.023), and diabetes mellitus (7/30, vs. 0/39, p<0.01). The PGA correlated moderately at both baseline and one year follow-up examination with the old-AI (rho: 0.519, and rho: 0.692, respectively, p<0.001), the new-AI (rho: 0.401, and rho: 0.429, respectively, p<0.001), and the Pecs-AI (rho: 0.425, and rho: 0.593, respectively, p<0.001).

CDAI correlated significantly with the old-AI (rho: 0.345, and rho: 0.283, respectively, p<0.05) and the Pecs-AI (rho: 0.363, and rho: 0.324, respectively, p<0.05) at both the baseline and one-year follow-up investigations, but showed no consistent correlation to the new-AI or PGA.

Conclusion: The two validated disease activity indices indentify different patient groups. Joint involvement is potentially underrepresented in the new EUSTAR activity index. Active disease is also present in lcSSc and should be assessed regularly in these patients.

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THU0357 **NAILFOLD CAPILLARY MICROSCOPY HAS LIMITED PROGNOSTIC VALUE IN PREDICTING FUTURE DEVELOPMENT OF CONNECTIVE TISSUE DISEASE IN CHILDREN WITH RAYNAUD'S PHENOMENON.**

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Background: For adults with Raynaud's phenomenon (RP), nailfold capillary microscopy (NCM) is established to be an effective method for differentiating between PRP and SRP (1,2). Although Raynaud's phenomenon (RP) is very common in childhood, studies on diagnostic methods to differentiate between primary RP (PRP) and secondary RP (SRP) at a young age are scarce (3,4).
Objectives: The general aim of this study was to determine the prognostic value of nailfold capillary microscopy (NCM) in addition to antinuclear antibodies (ANAs) for later development of connective tissue diseases (CTD) in children with RP.
Methods: This was a case-control study, in which 83 patients diagnosed with RP and having undergone NCM in childhood were retrospectively included. Based on whether they were diagnosed with a connective tissue disease (CTD) during follow-up, they were classified as PRP or SRP. PRP and SRP patients were compared on demographics, NCM and ANA positivity. Variables associated with SRP were included in a multivariate logistic regression model. Predictive values were calculated for NCM, ANA positivity and the combination of NCM and ANA positivity.
Results: At the time of the baseline NCM, the mean age of the RP patients was 15.4±2.3 years. Averagely 6.4±3.2 years after the baseline NCM, 65 of the 83 patients were classified as PRP and 18 as SRP. The most common CTDs were MCTD and undifferentiated CTD. ANA positivity was associated with SRP ($p<0.001$). Of the NCM parameters, only capillary loss was associated with SRP ($p=0.01$). Abnormal numbers of dilated capillaries, giant capillaries and haemorrhages were not significantly associated with SRP. In a multivariate logistic regression model, only ANA positivity was predictive for SRP (OR 11.19, CI 3.07-40.79). ANA alone had a sensitivity of 66.7% and a specificity of 85.9% for SRP. ANA combined with capillary loss had a sensitivity of 33.3% and a specificity of 96.8%.
Conclusion: This study demonstrates that childhood RP is primary in most cases. Whereas RP in adulthood is most strongly associated with SSc, children with RP seem to be at risk of developing other CTDs with less apparent NCM abnormalities. Dilated capillaries, giant capillaries and haemorrhages on NCM are not associated with the spectrum of CTDs that children are at risk for, and do not differentiate between primary and secondary RP. Although capillary loss on NCM is associated with SRP, capillary loss may add little to the predictive value of serology. To clarify which NCM parameters are helpful for early detection of SSc-like CTDs, additional research is required.
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THU0358 **NEGATIVE CHANGES OF BODY COMPOSITION IN MYOSITIS PATIENTS AND THEIR ASSOCIATION WITH DISEASE SPECIFIC CHARACTERISTICS, PHYSICAL ACTIVITY AND NUTRITIONAL STATUS.**

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Background: Skeletal muscle, pulmonary and articular involvement in idiopathic inflammatory myopathies (IIM) limit the mobility/self-sufficiency of patients, and can have a negative impact on body composition.
Objectives: The aim was to assess body composition and physical activity of IIM patients and healthy controls (HC) and the association with selected inflammatory cytokines/chemokines and laboratory markers of nutrition and lipid metabolism.
Methods: 54 patients with IIM (45 females; mean age 57.7; disease duration 5.8 years; polymyositis (PM, 22) / dermatomyositis (DM, 25) / necrotizing myopathy (IMNM, 7)) and 54 age-/sex-matched HC (45 females, mean age 57.7) without rheumatic/tumor diseases were included. PM/DM patients fulfilled Bohan/Peter criteria for PM/DM. We assessed body composition (densitometry: iDXA Lunar, bioelectric impedance: BIA2000-M), physical activity (Human Activity Profile, HAP questionnaire), serum levels of 27 cytokines/chemokines (commercial multiplex ELISA kit, Bio-Rad Laboratories) and serum levels of selected parameters of nutrition and lipidogram. Disease activity (MITAX and MYOACT activity score) and muscle involvement (manual muscle testing, MMT-8, and functional index 2, FI2) were evaluated. Data are presented as mean±SD.
Results: Compared to HC, patients with IIM had a trend towards significantly increased body fat % (BF%; iDXA: 39.9±7.1 vs. 42.4±7.1 %, $p=0.077$), but significantly decreased lean body mass (LBM; iDXA: 45.6±8.1 vs. 40.6±7.2 kg, $p=0.001$; BIA: 52.6±8.8 vs. 48.7±9.0 kg, $p=0.023$), increased extracellular mass/body cell mass (ECM/BCM) ratio (1.06±0.15 vs. 1.44±0.42, $p<0.001$), reflecting deteriorated nutritional status and predisposition for physical activity, and significantly lower bone mineral density (BMD: 1.2±0.1 vs. 1.1±0.1 g/cm^2, $p<0.001$). Disease duration negatively correlated with BMD and LBM-BIA. Disease activity (MITAX, MYOACT) positively correlated with LBM (by BIA and DXA), similarly as with basal metabolic rate (BMR), and fat free mass (FFM). CRP was positively associated with BF% (BIA and DXA). Higher BF%-DEXA was associated with worse physical endurance (FI2) and worse ability to perform physical activity (HAP). MMT-8 score negatively correlated with ECM/BCM ratio. Serum levels of several inflammatory cytokines/chemokines (specifically IL-1ra, MCP, IL-10) and markers of nutrition (specifically albumin, C3-, C4-complement, cholinesterase, amylase, insulin and C-peptide, vitamin-D, orosomucoid), and lipid metabolism (specifically triglycerides, high-density lipoprotein, apolipoprotein A and B, atherogenic index of plasma) were significantly associated with alterations of body composition in IIM patients. ($p<0.05$ for all correlations)
Conclusion: Compared to healthy age-/sex-matched individuals we found significant negative changes in body composition of our IIM patients associated with their disease activity and duration, inflammatory status, skeletal muscle involvement, and physical activity. These data could reflect their impaired nutritional status and predispositions for physical exercise, aerobic fitness and performance.
Serum levels of certain inflammatory cytokines/chemokines and markers of nutrition and lipid metabolism were associated with alterations of body composition in IIM patients. This might further support the role of systemic inflammation and nutritional status on the negative changes in body composition of IIM patients.
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THU0359 **GENDER IMPACT ON LOWER URINARY TRACT INVOLVEMENT IN SYSTEMIC SCLEROSIS PATIENTS**

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Background: Lower urinary tract symptoms (LUTS) are an underdiagnosed but frequent manifestation in systemic sclerosis (SSc) [**1**]. LUTS pathogenesis in SSc is undetermined, mainly involving dysautonomia, fibrosis and a possible antibody-mediated damage [**2**]. Divergently from general population, female sex and advanced age are not reported to significantly impact LUTS in SSc [**2**].

Objectives: To evaluate the potential influence of gender and hormone-related factors in LUTS prevalence and severity among SSc patients (Pts).

Methods: A population of 42 SSc Pts and 50 age- and sex-matched healthy subjects (HSs) was evaluated. SSc diagnosis was based on 2013 ACR/EULAR criteria. Demographic data, medications interfering with pelvic floor dynamics and general comorbidities commonly associated with LUTS – diabetes mellitus, chronic heart failure, chronic obstructive pulmonary disease, peripheral neuropathy, pelvic organ prolapse, fecal incontinence – were recorded. Validated self-reported questionnaires derived from the International Conference on Incontinence were used to assess prevalence and severity of LUTS, namely of urinary incontinence (UI) and overactive bladder (OAB) [**3**]. Data were analysed using non-parametric tests. A p value <0.05 and a confidence interval (CI) of 95% were considered statistically significant.

Results: There were no significant differences in main demographic data between SSc Pts and HSs. Specifically, median age was 61 years (IQR 21-85) *vs* 57 years (IQR 28-93) and female prevalence 83% *vs* 84% in SSc Pts *vs* HSs, respectively. Amongst the female population, 83% of SSc Pts *vs* 84% of HSs was in post-menopausal state, with a median of 1 (IQR 0-3) *vs* 1 (IQR 0-4) pregnancy by natural route, respectively. No woman of the study had received hormone replacement therapy or local hormonal therapies prior to the study. Similarly, there were not any significant differences in analysed comorbidities, while ongoing treatment was significantly different between the two populations, SSc patients more frequently receiving calcium channel blockers and glucocorticoids than healthy subjects (p< 0.001). In SSc Pts, statistically significant correlation was observed between stress UI and sex, with an increased female-to-male ratio (p< 0.005), but any significant difference was observed in US distribution depending on parity and menopausal state, nor on other analysed variables. Interestingly, female dominance has not resulted as a significant predictive factor for LUTS prevalence or severity in SSc Pts. In fact, in the regression analysis, SSc disease was the only significant predictor for LUTS (OR 3.45, 95% CI 1.41-7.95; p< 0.01), independently of other analysed variables, particularly of gender and hormone-related factors.

Conclusion: This study confirms the absence of pathogenic female-gender participation in LUTS prevalence among SSc Pts. However, consistently with findings on general population, a significant increased prevalence of urinary symptoms, particularly of stress UI, in SSc female Pts has emerged [**4**]. It is therefore conceivable that hormonal factors may act as a catalytic circumstance rather than pathogenic players in LUTS progression during SSc disease.

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THU0360 EFFICACY OF A SELF-TREATMENT PROTOCOL FOR FACE AND TEMPOROMANDIBULAR JOINTS REHABILITATION IN SYSTEMIC SCLEROSIS (SSC)

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Background: In SSc, skin involvement of the face is frequent and extremely disabling, resulting in limited mouth opening, an altered dentition, difficulty in teeth care, as well as having a strong impact on the emotional and psychological well-being, thus impairing quality of life.

Objectives: to evaluate the efficacy of a self-treatment protocol (created by AMURR A Multidisciplinary Association of Rheumatological Rehabilitation) for face and tempomandibular joints (TMJs) rehabilitation with two devices used in the dental field.

Methods: 40 SSc patients (37 female and 3 male) with a mouth opening ≤ 40 mm, were recruited and randomized in two groups of treatment: Group 1 (20 patients: mean age 50,650 yrs ± 13,937 SD, mean disease duraton 10,45 yrs ± 7,877 SD, opening mouth 32,250 mm ± 5,590 SD) treated with a home self-treatment protocol consisting of 23 exercises carried out at home in front of a mirror, 22/23 exercises were performed once a day, one of these using a device to obtain uniform stretching of the buccal rhyme, another one usingused three times a day to reduce tension of muscles of the TMJs, facilitating the mouth opening; group 2 (20 patients: mean age 58,05 yrs ± 18,103 SD, mean disease duration 17,4 yrs ± 15,017 SD, opening mouth 34,950 mm ± 5,753) without physical rehabilitation, only drugs as treatments of SSc and its complications. All patients underwent a baseline (T0) and 45 days (T1) clinimetric assessment by self-assessment of quality of life with SF-36 (Short-Form 36 Health Survey), of the degree of disability of the mouth with MHISS (of the Mouth Handicap in Systemic Sclerosis scale), Muscle pain evaluated by numerical rating scale (NRS) of the temporomandibular joint with TMD (Temporo mandibular Disorders), evaluation of mouth opening and ROM of the cervical spine. Statistical analysis was performed using the t-test or the Mann-Whitney test for assessing changes in all measurement scales between treatment groups.

Results: The protocol of home physiotherapy exercises resulted in a statistically significant improvement in the treated group compared to group 2 both for mouth opening (T0: 32,250 ± 5,590, T1: 35,650 ± 6,046) vs (T0: 34,950 ± 5,753 T1: 34,300 ± 6,001) (p<0.001), cervical flexion (T0: 2,950 ± 1,939 T1: 1.700 ± 1,525) vs (T0: 4,450 ± 2,282 T1:4,075 ± 2,238) (p<0.01), cervical extension (T0: 17,025 ± 1,895 T1: 17,625 ± 1,605) vs (T0: 17,050 ± 2,089 T1: 16,525 ± 3,110) (p<0.05), cervical right lateral flexion (T0: 14,075 ± 2,386 T1:13,400 ± 2,431) vs (T0: 14,200 ± 1,765 T1: 14,425 ± 1,742) (p<0.01), cervical right rotation (T0: 14,200 ± 3,416 T1:13,750 ± 3,206) vs (T0: 14,900 ± 1,683 T1: 15,550 ± 2,188) (p<0.01), cervical left rotation (T0: 14,725 ±3,640 T1:14,450 ± 3,710) vs (T0: 15,900 ± 2,614 T1: 16,450 ± 2,964) (p<0.05), mouth disability at MHISS (T0: 19,100 ± 10,356 T1: 16,000 ± 9,989) vs (T0: 20,950 ± 9,950, T1: 21,100 ± 10,775) (p<0.01).

Conclusion: The use of the home exercises protocol associated with the two devices has shown a significant improvement of the disability linked to skin involvement of the face. This highlights the fundamental role that home rehabilitation self therapy has in practice. These data will need to be confirmed in a larger cohort of patients

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THU0361 EPIDEMIOLOGIC VARIATION ON SCLERODERMA RENAL CRISIS AND CLINICAL FEATURES VARIATION ON SYSTEMIC SCLEROSIS PATIENTS OVER TIME: DATA FROM RESCLE REGISTRY.

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Background: Scleroderma renal crisis (SRC) prevalence is decreasing. However, no Systemic Sclerosis (SSc) patient's registry has evaluated that decrease over time. No treatment have been able to prevent SRC development.
Objectives: Primary objective: to identify SRC prevalence in 2 periods in the RESCLE (Registro de ESCLErodermia) registry. Secondary objective: to idenfy which features could justify that change on SRC prevalence.
Methods: Up to December 2018, 1937 SSc patients were included by 31 referral centers in RESCLE registry. SRC prevalence and incidence in diagnosed patients before and after 2003 was determined. Clinical characteristics of diagnosed patients in each period of time were analysed to identify differences between them.
Results: Out of 1937 SSc, 43 (2.2%) developed SRC. Prevalence of SRC before and after 2003 was 3.5% and 1.08%. SRC Incidence: Graphic 1. Significant differences between Pre-2003 vs. Post-2003 SSc cohorts were found in univariate analysis: Table 1 and 2.

Table 1. Univariate analysis

	Pre-2003(%)	Post-2003(%)
Demographic data		
lcSSc	63	59
dcSSc	28	15
ssSSc	6.4	14
Early SSc	1.1	3.3
Very early SSc	1.9	9.6
Age at SSc dx	49.1(±15.2)y	55.0(±15.6)y
Time from SSc dx to SRC	1.1(0.2-4.3)y	0.6(0.1-1.5)y
ACR/EULAR 2013 criteria	99	86
Comorbidities		
Smoked	20	37
Arterial hypertension	35	29
Diagnostic procedures		
PAPs >40mmHg by Echocardiography	38	25
Not-sclerodermal pattern at VCS	8.9	19
Lupus anticoagulant	12	4.8
Prognostic features		
Overall mortality	29	11
ILD-related death	10	1.6

Conclusion: SRC Prevalence and Incidence has decreased. Prevalence is three-fold in diagnosed SSc cohort pre-2003 than in post-2003. The post-2003 cohort showed lesser prevalence of dcSSc subtype, earlier SSc diagnosis, less organic involvement and more intensive treatment than pre-2003 cohort. All these findings could explain the decline in the SRC prevalence.
Figure:

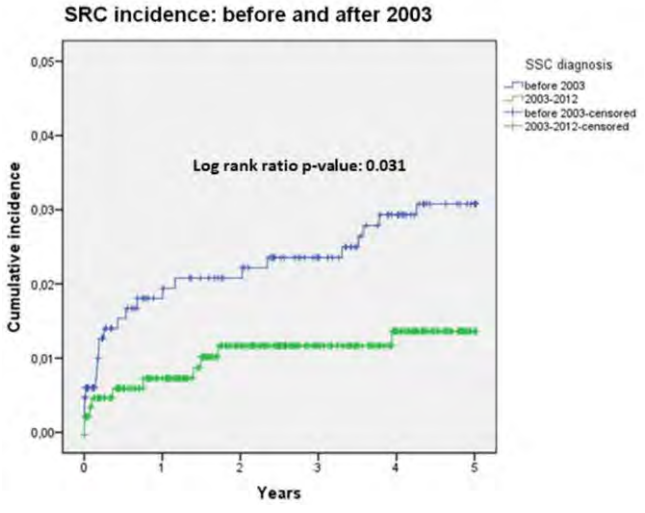


Table 2. Univariate analysis

	Pre-2003 (%)	Post-2003 (%)
Clinical data		
Skin sclerosis (as 1st symptom)	7.2	4.1
Digital ulcers	49	31
Telangiectasia	66	52
Acroosteolysis	12	4.6
Calcinosis	29	14
Joint contractures	28	13
ILD	49	37
Cardiac conduction alteration	20	27
Left diastolic dysfunction	41	32
Peripheral neuropathy	13	6.1
Sicca syndrome	37	24
Treatment features		
Calcium channel blockers	23	40
Specific vasodilators	2.1	14
Prostaglandin	0.99	3.4
Angiotensin system inhibitors	5.1	16
Corticosteroids	11	20
Immunosuppressant	3	15

y: years old; lcSSc: limited cutaneous SSc; dcSSc: diffuse cutaneous SSc; ssSSc: sine scleroderma SSc; ILD: Interstitial lung disease; PAPs: systolic Pulmonary Arterial Pressure; VCS: Video-capillaroscopy; dx: diagnosis

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THU0362 PREDICTORS OF MORTALITY IN SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is known as the most severe connective tissue disorder, and to be associated with a high mortality risk. Moreover, there is a great variability of mortality rate in the literature.
Objectives: To determine the mortality rate and its predictors in systemic sclerosis in a long-term follow- up of a bi-centric cohort of SSc patients
Methods: We have carried out a retrospective observational study by systematically analysing the medical records of patients diagnosed with SSc in Toulouse University Hospital and Ducuing Hospital. We included patients over 18 years old, whose diagnosis was made after 01/01/2000 and who met the classification criteria for the American College of Rheumatology (ACR) /EULAR 2013, and with at least one follow-up visit after the inclusion visit. Patients were followed until 30/05/2018. We quantified mortality as Standardized Mortality Ratio (SMR) and percentage mortality at 1, 3, 5, 10 and 15 years of disease. For comparison, we used the mortality rate for the population in the French Region of Occitanie in 2016, using data from the French National Statistical Agency. We determined a single primary cause of death (SSc or non-SSc related) and evaluated predictors of mortality using multivariable Cox regression.
Results: We included 375 patients (292 females), 63 (15.2%) patients with diffuse cutaneous SSc, 279 (76.7%) with limited cutaneous SSc and 33 (8.1%) with sine scleroderma SSc. During the study period 6 patients were lost to follow-up and 69 died (18.4%). The SMR ratio was 1.85 (95% CI 1.45-2.34). The overall survival rates were 97.5% at 1 year, 93.4% at 3 years, 87.1% at 5 years, 77.9% at 10 years and 61.3% at 15 years. Among the 69 deaths recorded 46.4% were SSc related deaths, 53.6% were non-related. Among the SSc related deaths, three main causes were identified: interstitial lung disease (ILD) (34.4%), pulmonary hypertension (31.2%) and digestive tract involvement (18.8%). Among the causes of SSc non-related deaths, cardiovascular

disorders (37.8%) and various infections (35.1%) largely distanced those from cancer (13.5%). Four significant independent predictive factors were identified using multivariable Cox regression: carbon monoxide diffusing *capacity* (*DLCO*) < 70% (HR=3.01; p=0.0053), *C-reactive protein (*CRP) >5 mg/l (HR=2.13; p=0.0174), cardiac involvement (HR=2.86; p=0.0012) and the fact of being male (HR=3.25; p=0.0004) (Table 1). The same four factors were identified as predictive of mortality at 5 and 10 years in multivariable Cox regression (Table 2).

Table 1. Multivariate analyses of mortality prognosis factors

	HR	IC95	p
Sex: Male	3.25	1.69-6.22	0.0004
DLCO <70%	3.1	1.40-6.88	0.0053
Cardiac involvement	2.86	1.52-5.41	0.0012
CRP >5 mg/l	2.13	1.14-5.41	0.0174

Table 2. Multivariate analyses of mortality prognosis factors at 5 and 10 years

	At 5 years			At 10 years		
	HR	95% CI	p	HR	95% CI	p
Sex: Male	2.131	0.99-4.58	0.0526	3.42	1.75-6.67	0.0003
DLCO <70%	5.489	1.61-18.60	0.0063	4.54	1.74-1.85	0.002
Cardiac involvement	2.893	1.30-6.41	0.0089	3.18	1.62-6.24	0.0008
CRP >5 mg/l	3.283	1.42-7.53	0.005	2.37	1.23-6.46	0.01

Conclusion: Our results confirm that SSc is a devastating condition as reflected by a pooled SMR of 1.85. The two principal causes of SSc-related death remain PH and ILD. However, SSc non-related death are represented mainly by cardiovascular diseases. This work identified sex (male), DLCO <70%, cardiac involvement and CRP> 5mg/l as independent predictors of mortality. With the emergence of new therapies, these important observations should help refine the monitoring and management to prolong these patients' survival.

Disclosure of Interests: None declared

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THU0363 EFFECTS OF NINTEDANIB IN PATIENTS WITH SYSTEMIC SCLEROSIS-ASSOCIATED ILD (SSC-ILD) AND NORMAL VERSUS ELEVATED C-REACTIVE PROTEIN (CRP) AT BASELINE: ANALYSES FROM THE SENSCIS TRIAL

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Background: In the SENSCIS trial in patients with SSc-ILD, nintedanib reduced the rate of decline in forced vital capacity (FVC) over 52 weeks. Elevated CRP is a marker of an inflammatory phenotype and has been associated with a greater rate of decline in FVC and higher mortality in patients with SSc.

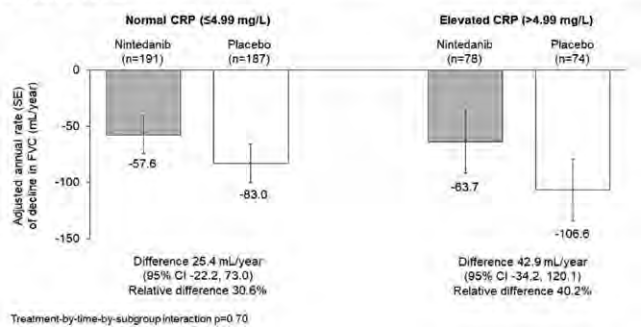
Objectives: To assess the effects of nintedanib in subgroups by CRP at baseline in the SENSCIS trial.

Methods: Patients with SSc-ILD with onset of first non-Raynaud symptom <7 years and ≥10% fibrosis of the lungs on HRCT were randomised to receive nintedanib or placebo. We analysed the rate of decline in FVC (mL/year) over 52 weeks, the proportion of patients with an absolute increase in FVC ≥3% predicted (proposed as the minimal clinically important difference for improvement in FVC in patients with SSc-ILD), and absolute change from baseline in mRSS at week 52 in subgroups with normal vs elevated high-sensitivity CRP (≤4.99 vs >4.99 mg/L) at baseline.

Results: Of patients with available data, 78/270 (28.9%) and 74/261 (28.4%) in the nintedanib and placebo groups, respectively, had CRP >4.99 mg/L at baseline. Compared with patients with lower CRP, those with CRP >4.99 mg/L included a similar proportion of patients who were ATA-positive (61.8% vs 60.2%, respectively), a greater proportion with diffuse cutaneous SSc (63.2% vs 49.3%) and had a higher mean mRSS (13.7 vs 10.2) and lower mean FVC % predicted (68.6% vs 73.9%). The adjusted annual rate of decline in FVC in the placebo group was numerically greater in patients with CRP >4.99 than ≤4.99 mg/L at baseline (-106.6 [SE 27.6] vs -83.0 [17.1] mL/year). The effect of nintedanib vs placebo on reducing the rate of decline in FVC was numerically more pronounced in patients with CRP >4.99 than ≤4.99 mg/L at baseline but the treatment-by-time-by-subgroup interaction p-value did not indicate heterogeneity in the effect of nintedanib between subgroups (p=0.70) (Figure). In the nintedanib and placebo groups, respectively, the proportions of patients with an absolute increase in FVC ≥3% predicted at week 52 were 20.4% and 15.0% in those with CRP ≤4.99 mg/L and 24.4% and 14.9% in those with CRP >4.99 mg/L at baseline (treatment-by-subgroup interaction p=0.59); adjusted mean changes in mRSS at week 52 were -2.2 (SE 0.3) and -2.1 (0.3) in those with CRP ≤4.99 mg/L (difference -0.1 [95% CI -1.0, 0.8]) and -2.3 (0.5) and -1.0 (0.5) in those with CRP >4.99 mg/L at baseline (difference -1.2 [-2.7, 0.2]; treatment-by-visit-by-subgroup interaction p=0.20).

Conclusion: In the SENSCIS trial, the rate of decline in FVC over 52 weeks in the placebo group was numerically greater in patients with elevated CRP at baseline. Nintedanib reduced the rate of decline in FVC both in patients with normal and elevated CRP at baseline, with a numerically greater effect in patients with elevated CRP.

Figure. Rate of decline in FVC (mL/year) over 52 weeks in subgroups by CRP at baseline in the SENSCIS trial



Disclosure of Interests: Gabriela Riemekasten Consultant of: Cell Trend GmbH, Janssen, Actelion, Boehringer Ingelheim, Speakers bureau: Actelion, Novartis, Janssen, Roche, GlaxoSmithKline, Boehringer Ingelheim, Pfizer, Patricia Carreira Grant/research support from: Actelion, Roche, MSD, Consultant of: GlaxoSmithKline, VivaCell Biotechnology, Emerald Health Pharmaceuticals, Boehringer Ingelheim, Roche, Speakers bureau: Actelion, GlaxoSmithKline, Roche, Lesley Ann Saketkoo Grant/research support from: Corbus Pharmaceuticals, United Therapeutics, Consultant of: Boehringer Ingelheim, Eicos Sciences, Speakers bureau: Boehringer Ingelheim, Martin Aringer Consultant of: Boehringer Ingelheim, Roche, Speakers bureau: Boehringer Ingelheim, Roche, Lorinda Chung Grant/research support from: United Therapeutics, Boehringer Ingelheim, Consultant of: Bristol-Myers Squibb, Boehringer Ingelheim, Mitsubishi Tanabe, Eicos Sciences, Janet Pope Grant/research support from: AbbVie, Bristol-Myers Squibb, Eli Lilly & Company, Merck, Roche, Seattle Genetics, UCB, Consultant of: AbbVie, Actelion, Amgen, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Eicos Sciences, Eli Lilly & Company, Emerald, Gilead Sciences, Inc., Janssen, Merck, Novartis, Pfizer, Roche, Sandoz, Sanofi, UCB, Speakers bureau: UCB, Corinna Miede Employee of: Employee of Boehringer Ingelheim, Susanne Stowasser Employee of: Employee of Boehringer Ingelheim, Martina Gahlemann Employee of: Employee of Boehringer Ingelheim, Margarida Alves Employee of: Employee of Boehringer Ingelheim, Dinesh Khanna Shareholder of: Eicos Sciences, Inc./Civi Biopharma, Inc., Grant/research support from: Dr Khanna was supported by NIH/NIAMS K24AR063120, Consultant of: Acceleron,

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THU0364 SYSTEMIC SCLEROSIS OVERLAP AND NON-OVERLAP SYNDROMES SHARE SIMILAR CLINICAL CHARACTERISTICS BUT DRAMATICALLY DIFFERENT TREATMENT.

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Background: Overlap between systemic sclerosis (SSc) and another auto-immune systemic disease (AISD) in the same patient seems to be more frequent than each disease's prevalence would explain.
Objectives: Our aim was to investigate for overlap syndrome from 2 French cohorts of SSc patients and to compare their characteristics with non-overlap SSc.
Methods: Our study was retrospective observational and bicentric. Patients responding to the 2013 ACR-EULAR scleroderma classification criteria for SSc were screened for concomitant AISD. Patients satisfying 2010 ACR-EULAR diagnostic criteria for rheumatoid arthritis (RA) and/or 2016 ACR-EULAR classification criteria for Sjögren's syndrome (SgS) and/or 2012 SLICC systemic lupus erythematosus (SLE) classification criteria were included in our study. Patient, disease, and treatment characteristics were retrospectively retrieved from medical records and were compared to a SSc cohort.
Results: A population of 534 SSc patients was studied. Thirty-four (6.4%) patients were identified as having overlap syndrome. There was 21 (3.9%) patients with RA, 14 (2.6%) with GSS and 4 (0.7%) with SLE (5 patients had 2 AISD). Diagnosis of RA, SLE or SgS was made after diagnosis of SSc for 22 (65%) patients, concomitantly for 10 patients (29%), and before for 2 (6%) patients. Interestingly, two patients with SSc/RA overlap were tested ACPA-positive 2 and 5 years before the first arthritis, respectively. Patients with SSc/RA were severe with 81% of them having erosive disease and despite treatment, only 48% (10/21) patients achieved RA remission (DAS28-CRP < 2.6) at the time of their last visit. Disease duration was longer in patients with SSc overlap syndrome compared to non-overlap patients (15.5 ± 10.6 years *vs.* 9.5 ± 8, p < 0.001). Proportion of limited cutaneous SSc was similar in overlap and non-overlap groups (70.6% *vs.* 75.5%, respectively, p = NS), as was the positivity for anti-centromeres antibodies (50% *vs.* 43.2%, respectively, p = NS). The disease phenotype of SSc overlap syndrome was similar to the one of non-overlap SSc in terms of prevalence of pulmonary arterial hypertension, interstitial lung disease, digital ulcer and mortality. With respect to treatments, patients with overlap were more likely to receive glucocorticoids (85.3% *vs.* 45%, p < 0.001), immunosuppressive drugs (82.4% *vs.* 49.2%, p < 0.001) and biologic DMARD (bDMARD, 52.9 % *vs.* 3.8%, p < 0.001). The most prescribed bDMARDs in the overlap population was tocilizumab (40.6%), TNF-alpha inhibitor (29.4%) and rituximab (26.5%) (p < 0.001 for all comparison *vs.* non-overlap SSc).
Conclusion: We found a prevalence of overlap syndrome higher than 5% among SSc patients. While SSc overlap and non-overlap share common characteristics, overlap patients are more likely to receive glucocorticoids and biologics such as anti-TNF. These overlap should be searched actively (eg, screening for ACPA) since some treatment used for other autoimmune diseases such as glucocorticoids or TNF-alpha inhibitor may be harmful in SSc.
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THU0365 INCREASED HSP90 IN MUSCLE TISSUE AND PLASMA ASSOCIATES WITH DISEASE ACTIVITY AND SKELETAL MUSCLE INVOLVEMENT IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

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Background: Heat shock proteins (Hsps) are chaperones playing important roles in skeletal muscle physiology, adaptation to exercise or stress, and activation of inflammatory cells
Objectives: The aim of our study was to assess Hsp90 expression in muscle biopsies and plasma of patients with idiopathic inflammatory myopathies (IIM) and to characterize its association with IIM-related features.
Methods: Total of 277 patients with IIM (198 females, 79 males; mean age 54.8; disease duration 4.1 years; DM, 104/PM, 108/CADM, 31/IMNM, 25) and 157 healthy individuals (92 females, 65 males; mean age 47.0) were included in plasma analysis. Muscle biopsy samples (PM, DM, IMNM, myodystrophy, myasthenia gravis) were stained for Hsp90α (Thermo Fisher Scientific, USA) and Hsp90β (Abcam, UK). Plasma Hsp90 was measured by ELISA kit (eBioscience, Vienna, Austria). The cytokines/chemokines were analysed by using Bio-Plex Pro™ human Cytokine 27-plex Assay (BIO-RAD, California, USA.Data are presented as median(IQR).
Results: In muscle biopsies, Hsp90 expression of both subunits (alpha and beta) was higher in IIM than in controls. Increased Hsp90 was detected in perifascicular degenerating and regenerating fibers, inflammatory cells (DM, PM), and necrotic and regenerating fibers (IMNM). Plasma Hsp90 levels were increased in IIM patients compared to healthy controls (55.9 (46.9 – 62.5)vs 9.76(7.5 – 13.8), p<0.0001), and in individual subgroups of IIM vs. healthy controls (DM-22.01(14.1 – 41.2), PM-19.7(14.3 – 42.2), CADM-18.9(11.7 – 29.7), IMNM-19.6(16.3 – 45.5), p<0.0001 for all). Hsp90 was higher in males compared to females (p=0.040) and in patients with ILD (p=0.003), cardiac involvement (p=0.004), dysphagia (p=0.018) and presence of anti-Ro52 (p=0.036). Hsp90 levels in all patients positively correlated with muscle enzymes (Tab.1). Hsp90 was associated with disease activity and skeletal muscle involvement (Tab.1). Out of all clinical parameters listed in above-mentioned univariate analysis, in multiple regression analysis Hsp90 levels in IIM patients were significantly affected by muscle enzymes only (p<0.0001, β=0.345). Furthermore, Hsp90 positively correlated with some crucial cytokines involved in pathogenesis of myositis (Tab. 1).

Tab. 1.

Clinical parameters	Spearman's r	p – value
LDH; AST; ALT	0.554; 0.383; 0.181	< 0.0001; < 0.0001; 0.003
PtDGA; PhDGA; MITAX; MYOACT	0.223; 0.217; 0.175; 0.159	< 0.001; < 0.001; 0.004; 0.012
Pulmonary disease activity	0.201	0.001
Muscle disease activity	0.146	0.018
MMT8, total score; m. biceps brachii; m. gluteus maximus; m. iliopsoas	-0.126; -0.125; -0.159; -0.143	0.042; 0.043; 0.011; 0.023
MDI – Myositis damage index – severity	0.150	0.041
Current Prednisone equivalent dose	0.183	0.006
Cytokines: IL-1b; IL-2; IL-4; IL-6; IFN-γ	0.188; 0.269; 0.190; 0.182; 0.229	0.002; < 0.0001; 0.002; 0.003; < 0.0001

Conclusion: We demonstrate increased Hsp90 expression in IIM muscle biopsy samples, specifically in inflammatory cells, degenerating, regenerating and/or necrotic fibers. Increased Hsp90 plasma levels in IIM patients are associated with disease activity and damage, and with the involvement of proximal skeletal muscles, heart and lungs.
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THU0366

SYSTEMATIC CORONARY RISK EVALUATION (SCORE) MISCLASSIFIES CARDIOVASCULAR RISK IN ANTISYNTHETASE SYNDROME: RESULTS OF THE PILOT MULTICENTRIC STUDY RI.CAR.D.A.

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Background: Antisynthetase Syndrom (ASyS) is an autoimmune overlap disease characterized by antiaminoacyl-tRNA-synthetase (anti-ARS) antibodies and the classic triad of arthritis, myositis and interstitial lung disease (ILD) (1). Markers of cardiovascular (CV) or cerebrovascular (CVB) risk have never been examined in ASyS.
Objectives: Aim of this study (RIsk of CARdiovascular Disease in ASyS: RI. CAR.D.A.) was to test the ability of an established traditional CV risk prediction score (Systematic Coronary Risk Evaluation-SCORE) and its EULAR modified version (mSCORE) to identify ASyS patients at high CV risk. Moreover, we sought to examine for the first time associations of CV surrogate markers with clinical and immunological ASyS parameters.
Methods: SCORE/mSCORE and the gold standard marker of aortic stiffness (carotid-femoral pulse wave velocity-cfPWV) were examined in patients with ASyS and healthy controls in a multicenter setting (6 Rheumatology Centers). Moreover, sonography of the common- (CCA), internal- (ICA) and external- (ECA) carotid arteries was performed in subsets of both groups, evaluating carotid intima-media-thickness (cIMT), plaques and duplex-sonographic indices of CBV risk such as the resistance- (RI) and pulsatility-index (PI).

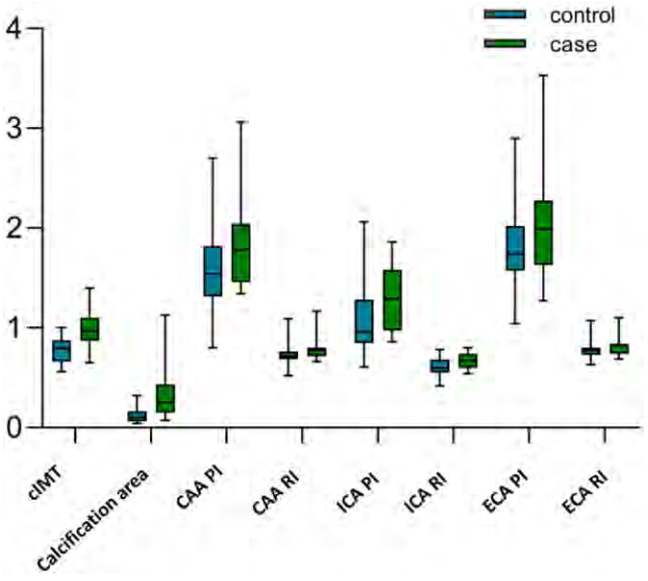


Figure 1. Carotid Doppler surrogate markers of cardiovascular and cerebrovascular risk in controls and ASyS (case). *cIMT* Carotid intima media thickness; *CAA* (common-), *ICA* (internal), *ECA* (external) carotid artery; *RI* resistance index; *PI* pulsatility index. (all; $p < 0.05$)

Results: We recruited 66 ASyS patients with different anti-ARS and 88 controls. According to mSCORE *5/50 (10%)* of the patients had high CV risk. However, cfPWV and carotid sonography (CS) revealed an increased CV risk in *21.2%* and subclinical carotid arteriosclerosis (plaques and/or cIMT>0.9 mm) (SCA) in *85.7%* of the patients respectively. ROC analyses showed similarly poor diagnostic performances of SCORE/mSCORE in comparison to cfPWV *(>10 m/s)* and SAC by areas under the curve (AUC) of *0.56 (95%CI=0.39-0.73)* and *0.63 (95%CI=0.3-0.96),* respectively. cfPWV and SCA were higher in ASyS patients compared to controls (*padj=0.021* and *p=0.003*, respectively). cfPWV and cIMT correlated in the patient group significantly with age (*r=0.679; p<0.001 and r=0.664; p<0.001,* respectively*).* Moreover, cfPWV correlated with BMI (*padj=0.001)* and diabetes *(padj=0.043)*. ACC-RI and ACC-PI showed significant associations with a marker of myositis activity [creatine phosphokinase (CPK): *r=0.629*; *p=0.012* and *r=0.574*; *p=0.032*, respectively]. Finally, ACI-RI and ACI-PI values were higher in patients with ILD (both; *p=0.039*).
Conclusion: This is the first report of higher aortic stiffness and SCA in ASyS patients compared to controls. Active myositis and presence of ILD were associated with higher CVB risk parameters. Furthermore, SCORE/mSCORE performed poorly in identifying patients at high CV risk and carotid arteriosclerosis compared to cfPWV and CS respectively. Thus, cfPWV and CS could improve CV and CBV screening in ASyS patients.
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Disclosure of Interests: None declared
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THU0367

INCIDENCE AND PREVALENCE OF SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE IN FLANDERS: A 12-YEARS COLLABORATIVE MULTICENTER PROSPECTIVE COHORT STUDY.

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Background: Systemic sclerosis-associated interstitial lung disease (SSc-ILD) is the main cause of death in SSc and accounts for up to 30-35% of SSc-mortality (1-2). All SSc cases, irrespective of the extent of the skin disease, should be evaluated for ILD (3). The epidemiology of SSc-ILD in Belgium is unknown. In literature, the prevalence of ILD in SSc varies between 19% and 52%. However, different criteria were used to diagnose ILD (4). In 2008, Goh et al. proposed a flow diagram to diagnose SSc-ILD based on chest high-resolution CT-scan (HRCT) and pulmonary function tests (PFTs). Their categorization into limited or extensive ILD has prognostic value (5).
Objectives: To determine the prevalence and incidence rate of SSc-ILD in Flanders.
Methods: Up to 12-year follow-up data of consecutive SSc patients were obtained by 2 Flemish expert centres (University Hospitals Ghent and Leuven). Patients fulfilling the LeRoy and/or ACR-EULAR classification criteria were included consecutively in the prospective cohort (6). Patients received HRCT at baseline and on indication thereafter, as well as yearly PFT. All HRCTs were centrally analyzed (Ghent) and patients were categorized according to the Goh criteria as without ILD, with limited ILD (limILD) or with extensive ILD (extILD) (5).
Results: Between 2006 and 2018, 797 SSc patients (557 Ghent/240 Leuven; 22% limited SSc (LSSc)/59% limited cutaneous SSc (LcSSc)/19% diffuse cutaneous SSc (DcSSc)) had baseline HRCT and PFT. The baseline characteristics are depicted in the table. The mean age (SD) was 53 +/-15 years and the majority of patients was female (76%).
272 SSc patients had ILD at baseline, implicating a baseline prevalence of 34% (272/797). The baseline prevalences were 35% and 55% for the LcSSc and DcSSc subgroups respectively. During a median follow-up of 39 months (IQR: 11-79 months), 44 patients were diagnosed with incidental SSc-ILD, resulting in an incidence rate of 21,0/1000 person-years (PY), 95% CI:15,2-28,1. The incidence rates were 21,7/1000 PY, 95%CI: 14,3-31,6 and 43.9/1000PY, 95%CI: 22.7-76.8 for the LcSSc and DcSSc subgroups respectively.

Table. Baseline characteristics

	SSc (n=797)	LcSSc (n=470)	DcSSc (n=149)
age (years) °	53+/-15	54+/-15	54+/-14
♂/♀ *	193(24%)/604(76%)	109(23%)/361(77%)	58(39%)/91(61%)
Disease Duration (months) #	for 718: 22 (5-72)	for 443: 25 (5-80)	for 145: 16 (7-52)
LSSc/LcSSc/DcSSc *	178(22%)/470(59%)/ 149(19%)		
follow-up (months) #	39 (11-79)	38.5 (9.75-81)	44 (17.5-78)
Anti-centromere antibodies§	252/538 (47%)	163/317 (51%)	19/108 (18%)
Anti-topoisomerasel antibodies§	119/519 (23%)	66/297 (22%)	45/112 (40%)
ILD at baseline, *	272 (34%)	163 (35%)	82 (55%)
*LimILD, **	*230 (29%)*	*139 (30%)*	*67 (45%)*
*ExtILD, **	*42 (5%)*	*24 (5%)*	*15 (10%)*
New ILD during follow-up, §	*44/525*	*27/307*	*12/67*

°: mean +/- standard deviation, *: number of patients (percent), #: median (interquartile range), §= number of patients/total number of patients with available data (%)

Conclusion: In an unselected cohort of SSc patients, a third of the patients has ILD at baseline which is in line with previous prevalence reports. Importantly, this is the first study reporting incidence rates of SSc-ILD.

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THU0368 RAPID SKIN THICKNESS PROGRESSION RATE IS ASSOCIATED WITH HIGH INCIDENCE RATE OF CARDIOPULMONARY INVOLVEMENT AND MORTALITY IN PATIENTS WITH EARLY DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS (DCSSC)

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Background: There has been no prior inception cohort study regarding the incidence rate of cardiopulmonary involvement in patients with early dcSSc comparing among different groups of skin thickness progression rate.

Objectives: The aims of this study were to compare differences in early dcSSc patients, which were classified into 3 subgroups; (a) rapid skin progression [RPsp], (b) intermediate skin progression [IMsp], and (c) slow skin progression [SLsp]; regarding: (1) clinical characteristics,(2) incidence rate of left ventricular ejection fraction (LVEF) < 50 %, interstitial lung disease (ILD),and pulmonary hypertension (PH). In addition, to compare mortality rate between skin improved and non-improved skin group.

Methods: We used an inception cohort of early dcSSc patients seen at the Rheumatology clinic, Maharaj Nakorn Chiang Mai Hospital, between January 2010 and December 2017. All patients were assessed for demographic data, clinical manifestations, modified Rodnan Skin Score (mRSS) and underwent echocardiography, and HRCT at the study entry and then annually.

Results: One hundred and two dcSSc patients (55 females and 89 anti-Scl 70 antibody positivity) with a mean±SD age of 53.2 ± 8.8 years and mean disease duration of 11.2 ± 8.7 months were enrolled, during a mean observation period of 54.0 ± 24.0 months. Mean±SD of baseline mRSS was 21.9 ± 9.1. Patients were classified into 3 groups: (a) 41 (40.2 %) patients with RPsp; (b) 37 (36.3 %) IMsp and; (c) 24 (23.5 %) SLsp. At enrollment, the RPsp group had significantly differences in clinical manifestations compared to IMSp and SLsp group as the followings: mean disease duration (5.4 ± 2.3 vs. 11.5 ± 6.1 and 20.7 ± 10.3 months, p < 0.001), anti-Scl 70 antibody- positive (95.1 % vs. 75.7 % and 91.7 %, p= 0.035), mRSS (26.4 ± 7.9 vs. 22.1 ± 8.4 and 13.8 ± 6.5, p < 0.001), dry mouth (48.8 % vs. 37.8 % and 8.3 %, p= 0.005), LVEF < 50 % (26.8 % vs. 21.6 % and 0, p= 0.010), pericardial effusion (0 vs. 10.8 % and 0, p= 0.018), arrhythmia (7.3 % vs. 29.7 % and 8.3 %, p= 0.018), muscle weakness (26.8 % vs. 27.0 % and 0, p= 0.009), creatine kinase ≥ 500 U/L (34.1 % vs. 18.9 % and 4.2 %, p= 0.016, and NT-proBNP (935.7 ± 2300.3 vs. 746.4 ± 1385.2 and 164.0 ± 225.3 ng/L, p= 0.001). During the observation period, the RPsp group had a significantly higher incidence rate of LVEF < 50 % compared with the SLsp group (6.06 vs. 0 per 100 person-years, incidence rate ratio= 21.27, p= 0.001). The RPsp group had a significantly higher incidence of ILD compared with the SLsp group (69.69 vs. 34.66 per 100 person-years, incidence rate ratio= 2.01, p= 0.012). Skin non-improved group had higher mortality rate compared with the skin improved group (28.6 % vs. 5.9 %, p= 0.004).

Conclusion: Our study cohort found that early dcSSc patients with rapid skin progression had higher incidence rate of LVEF < 50 % and ILD compared to those with slow skin progression. In addition, skin non-improved patients had significantly higher mortality rates than those with skin improved.

Disclosure of Interests: None declared

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THU0369 EVALUATION OF DIFFERENT CLASSIFICATION CRITERIA IN SYSTEMIC SCLEROSIS IN A TURKISH COHORT: THE IMPORTANCE OF NON-SKIN MANIFESTATIONS, SEROLOGY AND CAPILLAROSCOPY

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Background: Proximal scleroderma is the major criterion in both 1980 and 2013 classification criteria for sytemic scleroris (SSc). ACR(1980) criteria included digital lesions and bibasiler fibrozis, nonetheless ACR/EULAR(2013) criteria based on a scoring system including digital lesions, telangiectasia, abnormal nailfold video-capillaroscopy(NVC), PAH, Raynaud's and specific autoantibodies.

Objectives: We aimed to implement both criteria in a Turkish SSc kohort to evaluate the contribution of non-skin manifestations, NVC and autoantibodies.

Methods: A consecutive hundred and thirty-nine (125 females) SSc patients diagnosed and evaluated by the same experts (YY, MI) with relevant NVC records and at least 6 months follow-up were included into the study. Classificaiton criteria were used retrospectively using a preformed database.

Results: Characteristics of the SSc patients were summarized in table-1. The mean age, duration of Raynaud's and non-Raynaud symptoms were 47.1±11.9, 8.9±7.9 and 5.7±5.8 years, respectively. Diffuse and limited cutaneous disease were diagnosed in 62(44.6%) and 60(43.2%) patients respectively. Asclerodermic disease was present in 17(12.2%) patients. ANA, anti-centromere and anti-Scl70(+) positivity was 80.5%, 18.0% and 37.4%, respectively.

Twelve patients (8.6%) could not be classified as SSc by both criteria; 5 with Raynaud's+specific antibodies (2 anti-centromere+, 2 anti-Scl70+), 4 with Raynaud's+puffy hands+NC abnormalities, 2 with Raynaud's+telangiectasia and a patient with Raynaud's+sclerodactyly. Nineteen (13.7%) patients could not be classified as SSc according to ACR (1980) can be classsified according to ACR/EULAR (2013) (table-1 and -2).

The sensitivity for ACR/EULAR (2013) and ACR (1980) criteria were found to be 91,4% vs 75,5%; 98.4% vs 96.8% in diffuse cutaneous SSc, 98.3% vs 68.3% in limited cutaneous SSc and 47.1 vs 23.5% in asclerodermic SSc, respectively.

Table 1. The sensitivity for ACR (1980) and ACR/EULAR (2013) classification criteriain SSc

	ACR/EULAR (2013) +	ACR/EULAR (2013)-	*total*
ACR (1980)+	**108**	**0**	**108**
ACR (1980)-	**19**	**12**	**31**
total	**127**	**12**	**139**

Table 2. SSc patients fulfilling ACR (1980) and/or ACR/EULAR (2013) criteria

ACR/EULAR (2013) *ACR (1980)*	Classified n=127	Not classified n=12
+Prox scleroderma **+**	87	
+Puffy hands	29	4
+Sclerodactyly +	112	1
+Digital ulcers + +Pitting scars	62 72	
+Telangiectasia	86	2
+Nailfold capillaroscopy	97	4
Normal	9	
Early	17	3
Active	40	
Late	50	1
+PAH	12	
+Interstitial lung Disease +	60	
+Raynaud's	120	12
+SSc- specific antibodies	79	5

Conclusion: The sensitivity of ACR/EULAR (2013) criteria was shown to be higher than ACR (1980) criteria in our Turkish SSc cohort with established cases.

Although in diffuse cutaneous subgroup, the sensitivity was >%96 for both criteria, in limited cutaneous subgroup, the sensitivity was preserved for ACR/EULAR(2013) while apparently decreased for ACR(1980) criteria (<%70). The sensitivity for both of the two sets were lowest in the asclerodermic group. In SSc patients with limited or no skin involvement, non-skin manifestations, NVC findings and spcific serology should be carefully sought. Some of these patients could not be classified by the current criteria.

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THURSDAY, 04 JUNE 2020

Spondyloarthritis - treatment

THU0370 CLUSTER-RANDOMIZED PRAGMATIC CLINICAL TRIAL EVALUATING THE POTENTIAL BENEFIT OF A TIGHT-CONTROL AND TREAT-TO-TARGET STRATEGY IN AXIAL SPONDYLOARTHRITIS: THE RESULTS OF THE TICOSPA TRIAL.

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Background: Current recommendations for axial spondyloarthritis (axSpA) management include tight control and treat-to-target (TC) strategies, but no study has evaluated its potential benefit

Objectives: To evaluate the benefit of TC strategies in comparison to usual care (UC) in patients with axSpA.

Methods: *Study design:* Pragmatic, prospective, cluster-randomized controlled (2 arms), one-year trial (NCT03043846). *Centers*: 18 axSpA expert centers randomly allocated (1:1) to the treatment arm: TC vs. UC. *Patients*: axSpA diagnosis and ASAS criteria, non-optimally treated with NSAIDs, bDMARD-naïve, and ASDAS > 2.1 at inclusion. *Study treatment*: a) TC arm: the strategy was pre-specified by the scientific committee based on current axSpA recommendations and aiming at a target (ASDAS <2.1); visits every 4w; b) UC arm: treatment decisions were at the rheumatologist's discretion with visits every 12w. *Outcomes:* the % of patients with a significant (>30%) improvement in the ASAS-HI score over one-year follow-up was the main outcome. Other outcomes (disease activity, quality of life, treatment, …) over follow-up were evaluated (Table 1). The number/type of adverse events were collected. *Statistical analysis*: this was an intention-to-treat analysis. To take into account the cluster-randomization design, for all outcomes, two models were performed: first a two-level mixed model with 2 random effects was used to estimate the % of responders/the change of the outcome over follow-up (i.e. mod1); in a second step, the imbalanced variables observed at baseline were included in the model (i.e.mod2). Cost-effectiveness was assessed by estimating the (baseline- and cluster-adjusted) incremental cost per quality-adjusted life-year (QALY) gained for TC vs. UC.

	Estimated outcomes at week 48		Cluster-adjusted (mod1)	Cluster and imbalance-adjusted (mod2)
	TC	UC		
ASDAS LDA*	76.5%	59.5%	<0.01	0.03
ASDAS ID	25.9%	18.7%	-	-
ASDAS CII	61.2%	46.0%	<0.01	0.02
ASDAS MI	16.5%	14.9%	-	-
ASAS40	52.3%	34.7%	<0.01	0.01
ASAS20	94.9%	85.9%	<0.01	0.03
BASDAI 50	79.0%	43.8%	0.01	0.03
Physician Global (0-10)	2.0 (0.2)	1.8 (0.2)	-	-
CRP (mg/L)	3.9(1.4)	3.5 (1.5)	-	-
BASG (0-10)	2.6 (0.5)	3.4 (0.5)	0.09	-
BASFI (0-10)	1.7(0.5)	2.4 (0.5)	-	-
ASAS HI SMD	47.3%	36.1%	-	-
EQ5D	0.7(0.1)	0.8(0.1)	0.02	-
ASAS-NSAID score	1.5(2.2)	- 4.9 (2.9)	-	-

Results: 160 patients were included (80 in TC and 80 in UC). Mean age was 37.9(11.0) years with a disease duration of 3.7(6.2) years, 51.2% were males. A radiographic damage of the SI-joints, a (ever) positive MRI sacroiliitis and HLA-B27+ were seen in 46.9%, 81.9% and 75.0% patients respectively. Mean ASDAS at inclusion was 3.0 (0.7) and mean ASASHI was 8.6 (3.7). 72 patients per group attended the one-year visit. Although 47.3% vs. 36.1% patients in the TC and UC arms achieved a significant improvement in ASASHI at the one-year visit, the difference was not statistically significant, with either model. Across all other outcomes a trend was observed in favor of the TC arm (Table 1). The number of bDMARDs was significantly higher in TC arm (56.2% vs. 27.2%). The number of infections was comparable in both groups (15 vs. 16 in the TC and UC, respectively), with only 2 severe infections occurring in the UC arm. From a societal perspective, TC resulted in an additional 0.04 QALY and saved €265 when compared to UC and a 67% probability of being cost-effective at a cost-effectiveness threshold of €20,000 per QALY.

Conclusion: In this setting of SpA expert centers, UC resulted in a good outcome in a substantial number of patients but the TC was not superior for the primary outcome despite a greater number of bDMARDs prescription. Nevertheless, a general trend in favor of the tight control was observed, with a comparable safety profile and was found to be favorable from a societal health economic perspective.

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THU0371 HIGH INTENSITY EXERCISE HAS COMPARABLE 3-MONTH EFFECTIVENESS TO TNF-INHIBITORS ON DISEASE ACTIVITY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS. POST-HOC ANALYSES OF DATA FROM (THE ESPA TRIAL.)

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Background: We have previously reported that a supervised 12-week high intensity cardiorespiratory and strengthening exercise programme reduced disease activity in patients with axial spondyloarthritis (axSpA), in an assessor blinded randomized controlled trial (ESpA)(1). There were no reports of disease flare, and the programme was deemed safe. It is of interest to compare the treatment response of the programme vs. the response to treatment with a biologic immune-modulating TNFalpha-inhibitor (TNFi).

Objectives: To compare 3-month change in disease activity following an exercise programme vs. treatment with a TNFi, in patients with axSpA.

Methods: Post-hoc comparison between participants in the intervention group in the ESpA and patients from NOR-DMARD, a longitudinal observational study, who commenced treatment with a TNFi (2).The inclusion criteria of ESpA were a diagnosis of axSpA, age 18-70 years and baseline BASDAI >3.5. Patients fulfilling these criteria were selected from NOR-DMARD. Data was collected at baseline and 3 months. The primary outcome was defined as ASDAS, and BASDAI scores, and secondary outcomes were BASDAI sub-scores and C-reactive protein (CRP). Baseline values were compared in bivariate analyses. Responses at 3 months were compared between the groups using ANCOVA models adjusted for age, gender and baseline values. The standardised mean difference in 3-month response between the exercise and TNFi groups was estimated by dividing the difference in change at 3-months by the standard deviation (SD) of change.

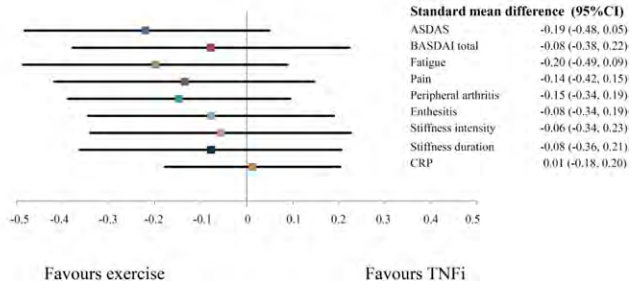
Results: Fifty patients were randomised to the exercise intervention in the ESpA study, mean age (SD) 45.2 (0.6), 25 males (50%). 344 patients in the NORDMARD study were eligible for the current analyses, mean age (SD) 39.6 (1.5), 150 males (43.6 %). Baseline demographics and estimated marginal means for disease activity at - months are presented in table 1. The standard mean differences are presented in Figure 1. There were no significant differences in change in disease activity at 3-months between patients participating in ESpA and patients starting a TNFi.

Table 1

Number	Baseline TNFi Mean(SE)	Baseline Exercise Mean(SE)	3 months TNFi EMM (SE)	3 months Exercise EMM(SE)	Adjusted β for comparison at 3- months (95% CI)	p
Primary outcomes						
ASDAS	3.16 (0.05)	2.45 (0.12)	2.13 (0.06)	1.88 (0.15)	-0.25 (0.56,0.05)	0.11
BASDAI total	5.92 (0.08)	4.94 (0.22)	3.89 (0.12)	3.72 (0.32)	-0.18 (-0.85,0.50)	0.61
BASDAI subscores						
Fatigue	6.60 (0.11)	5.8 (0.25)	4.63 (0.14)	4.06 (0.39)	-0.57 (-1.39,0.25)	0.17
Pain	6.48 (0.11)	5.8 (0.27)	4.29 (0.15)	3.89 (0.39)	-0.39 (-1.21,0.42)	0.35
Peripheral arthritis	4.41 (0.15)	3.76 (0.31)	3.10 (0.13)	2.64 (0.35)	-0.45 (-1.18,0.29)	0.23
Enthesitis	5.41 (0.13)	4.46 (0.33)	3.54 (0.14)	3.30 (0.39)	-0.24 (-1.06,0.58)	0.57
Stiffness intensity	6.75 (0.11)	5.42 (0.30)	4.01 (0.14)	3.86 (0.37)	-0.16 (-0.95,0.63)	0.70
Stiffness duration	6.66 (0.15)	4.32 (0.35)	4.17 (0.15)	3.93 (0.41)	-0.24 (-1.11,0.63)	0.59
Soluble biomarker						
CRP	7.94 (0.72)	4.12 (0.71)	3.81 (0.38)	3.95 (0.95)	0.13 (-1.88, 2.15)	0.90

Adjusted β derived from ANCOVA models adjusted for age, gender and baseline values. Disease activity at 3 months was the dependent variable in the models. EMM: Estimated marginal means.

Figure 1 Standard mean difference in change in disease outcomes at 3 months



Conclusion: High intensity exercise has comparable 3-month effectiveness to TNF-inhibitors, in patients with axSpA. This confirms the important role of high-intensity exercise in the treatment of axSpA.

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THU0372 EFFECTIVENESS OF STEROID INJECTION FOR HAND PSORIATIC DACTYLITIS: RESULTS FROM A MULTICENTRE PROSPECTIVE OBSERVATIONAL STUDY.

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Background: Dactylitis is a common feature of PsA, occurring in 16 to 49% of PsA patients, mostly in early disease.

Objectives: To assess the effectiveness of steroid injection (local treatment, LT) into the digital flexor tendon sheath for the treatment of active dactylitis in PsA patients as compared to systemic treatment (ST) alone.

Methods: 73 hand dactylitis were assessed in a prospective observational study by the Leeds Dactylitis Index basic (LDI-b) score and evaluated for pain (VAS pain), *functional impairment (VAS-FI).* In accordance with EULAR and GRAPPA recommendations, steroid *injection* was proposed to all patients. Patients who refused LT were treated with oral NSAIDs. The patients of the two groups continued baseline therapy with csDMARDs or corticosteroids. The clinical outcomes were measured at baseline, 1 month (T1) and 3 months (T3) by assessors blinded to this study.

Results: The reduction of VAS-pain, VAS-FI and LDI-b values was statistically significant higher in the LT group as compared to the ST group, both at T1 (p <0.001, p<0.001 and p=0.008, respectively) and at T3 (p<0.001, p<0.001 and p<0.001, respectively) (see Table 1). A clinically meaningful treatment response was observed at T1 in 33 (87%) digits in LT group and in 6 (17%) digits in ST group (p < 0.001). At T3, clinical response improved significantly in both the groups, with significant difference (see Table 2). In both the groups, no local and systemic adverse events were observed during the follow up period.

Table 2. Percentage of Significant response and Remission of dactylitis.

		T1 1 month	T3 3 months
Significant response, n (%)	LT	33 (86.8%)	36 (94.7%)
	ST	6 (17.1%)	11 (31.4%)
	p value	**< 0.001**	**< 0.001**
Remission n (%)	LT	1 (2.8%)	7 (18.4%)
	ST	0 (0%)	0 (0%)
	p value	ns	**0.012**

Values are presented as number of dactylitic fingers achieving response/remission. p values < 0.05 were considered statistically significant.

Conclusion: For the first time, we show the effectiveness of steroid injection into the digital *flexor tendon sheath* in improving clinical aspects and symptoms of hand psoriatic dactylitis.

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THU0373 SECUKINUMAB DOSE ESCALATION ON ACR RESPONSES IN ANTI-TUMOUR NECROSIS FACTOR NAÏVE PATIENTS WITH PSORIATIC ARTHRITIS: 2-YEAR DATA FROM THE PHASE 3 FUTURE 4 AND FUTURE 5 STUDIES

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Background: Secukinumab (SEC) 150 and 300 mg doses are approved for the treatment of psoriatic arthritis (PsA). SEC 300 mg is the recommended dose for patients (pts) with concomitant moderate-to-severe plaque psoriasis or who are anti-tumour necrosis factor (TNF) inadequate responders. An increase from

Table 1. Variation of clinical parameters during follow up.

		T0 baseline	T1 1 month	T3 3 months	T0 vs T1 95% CI	T0 vs T3 95% CI
VAS - PAIN	LT	6.89±1.93	1.97±1.62	1.34±1.48	4.92 (**4.17; 5.67**)	**5.55 (4.76; 6.32)**
	ST	6.03±2.43	5.49±2.53	5.0±2.65	0.54 (-0.23;1.32)	1.03 (-0.02; 2.07)
	Mean differences (95% CI)	0.87 (-1.89; 0.16)	**3.51 (2.53; 4.49)**	**3.66 (2.67; 4.65)**		
VAS - FI	LT	7.87±1.53	2.76±1.87	1.68±1.54	**5.11 (4.49; 5.72)**	**6.18 (5.52; 6.84)**
	ST	6.89±1.92	6.14±2.25	5.74±2.63	**0.74 (0.23; 1.26)**	**1.14 (0.32; 1.97)**
	Mean differences (95%CI)	0.98 **(-1,79; 0,17)**	**3.38 (2.42; 4.34)**	**4.05 (3.06; 5.05)**		
Finger circumference (cm)	LT	7.17±0.57	6.61±0.59	6.55±0.54	**0.56 (0.46; 0.65)**	**0.62 (0.52; 0.73)**
	ST	7.05±0.80	6.90±0.89	6.88±0.91	**0.15 (0.06; 0.25)**	**0.17 (0.07; 0.27)**
	Mean differences (95%CI)	0.12 (-0.44; 0.21)	0.29 (-0.07– 0.69)	0.33 (-0.02 -0.68)		
LDI-b	LT	12.31±0.03	9.91±7.15	1.25±4.35	**8.40 (5.73;11.06)**	**11.05 (8.22; 13.89)**
	ST	14.97±11.07	9.88±10.98	10.04±11.09	**5.10 (1.63; 8.55)**	**4.93 (1.54; 8.32)**
	Mean differences (95%CI)	2.67 (-1.82; 7.16)	**5.97 (1.58; 10.35)**	**8.79 (4.74;12.83)**		

VAS, visual analogue scale; VAS-FI, Visual analogue scale for functional impairment; LDI-b, Leed's dactylitic index basic; LT, local treatment group; ST, systemic treatment group.

150 mg to 300 mg has been reported to be beneficial in some patients with a suboptimal response to SEC 150 mg.[1] Here, we present a post hoc analysis in anti-TNF naïve pts who escalated from SEC 150 to 300 mg dose in two Phase 3 studies, FUTURE 4 (NCT02294227) and FUTURE 5 (NCT02404350).

Objectives: To evaluate the clinical efficacy on joints following dose escalation from SEC 150 to 300 mg on ACR responses in anti-TNF naïve pts with PsA.

Methods: Study design, patient inclusion and exclusion criteria of the FUTURE 4 and FUTURE 5 studies have been reported previously.[1–3] In FUTURE 4, 341 pts were randomised in a 1:1:1 ratio to SEC 150 mg with loading dose (LD), SEC 150 mg without LD, or placebo. In FUTURE 5, 996 pts were randomised in a 2:2:2:3 ratio to SEC 300 mg with LD, SEC 150 mg with LD, SEC 150 mg without LD or placebo. Following a protocol amendment, pts were allowed to escalate from 150 mg to the 300 mg dose, in the event of suboptimal response based on investigator's judgment, starting at Week 36 in FUTURE 4 and at Week 52 in FUTURE 5. ACR responses in anti-TNF naïve pts were evaluated pre- and up to 32 and 40 weeks post-escalation, in FUTURE 4 and FUTURE 5, respectively: pts were grouped into four ranges based on their response: no (<20); low (≥20 to <50); moderate (≥50 to <70); high (≥70) ACR responses. Data presented are as observed in the Sankey-style overlay plot.

Results: Dose escalation from SEC 150 to 300 mg occurred in 136 pts in FUTURE 4 and in 236 pts in FUTURE 5. The proportion of ACR responders increased and the proportion of non-responders decreased in anti-TNF naïve pts who escalated from SEC 150 to 300 mg in the two studies. The proportion of anti-TNF naïve pts with a response ≥ACR50 increased from 20% to 41% in FUTURE 4 and 28% to 46% in FUTURE 5, post dose escalation. The ACR responses in anti-TNF naïve pts up to 40 weeks after escalation from SEC 150 to 300 mg are presented in the Sankey-style overlay (Figure).

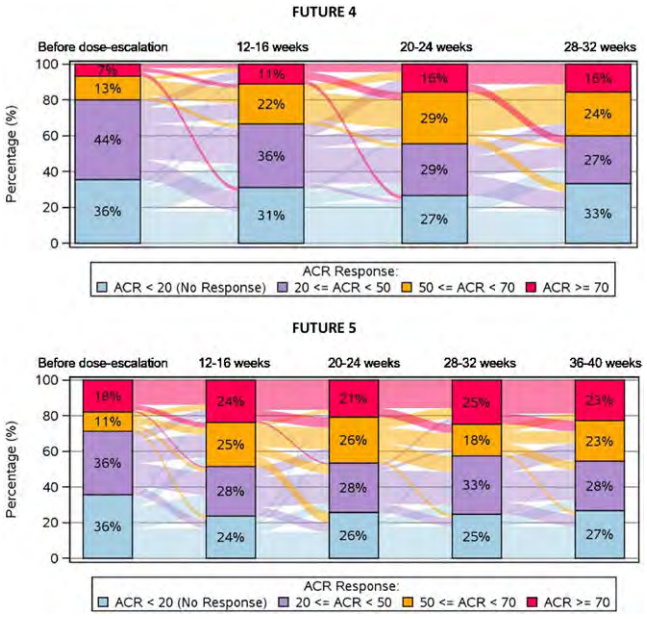


Figure. ACR Response bar chart with Sankey-style overlays up to 40 weeks, after dose escalation from SEC 150 mg to 300 mg, in anti-TNF naïve pts in FUTURE 4 and 5

Conclusion: The proportion of ACR responders increased within 12-16 weeks and was sustained up to 40 weeks following dose escalation in anti-TNF naïve pts with PsA. These results suggest that dose escalation from SEC 150 to 300 mg may be beneficial in anti-TNF naïve pts with a suboptimal response on SEC 150 mg.

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THU0374

NONSTEROIDAL ANTI-INFLAMMATORY DRUG-SPARING EFFECT OF SECUKINUMAB IN PATIENTS WITH ANKYLOSING SPONDYLITIS: 4-YEAR RESULTS FROM THE MEASURE 2, 3 AND 4 PHASE 3 TRIALS

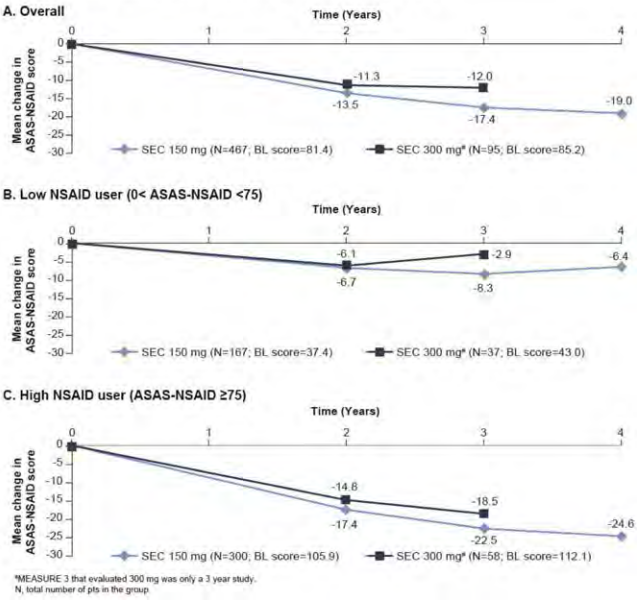
M. Dougados[1], U. Kiltz[2,3], A. Kivitz[4], K. Pavelka[5], S. Rohrer[6], S. Mccreddin[7], E. Quebe-Fehling[6], B. Porter[8], Z. Talloczy[8]. *[1]Université de Paris, Hôpital Cochin, Department of Rheumatology, Paris, France*; *[2]Rheumazentrum Ruhrgebiet, Herne, Germany*; *[3]Ruhr University, Bochum, Germany*; *[4]Altoona Center for Clinical Research, Duncansville, United States of America*; *[5]Institute of Rheumatology, Department of Rheumatology, Prague, Czech Republic*; *[6]Novartis Pharma AG, Basel, Switzerland*; *[7]Novartis Ireland Ltd., Dublin, Ireland*; *[8]Novartis Pharmaceutical Corporation, East Hanover, United States of America*

Background: Nonsteroidal anti-inflammatory drugs (NSAIDs) are effective in reducing pain and stiffness in ankylosing spondylitis (AS) patients (pts).[1] However, continuous use of NSAIDs may lead to gastrointestinal, cardiovascular and renal toxicity.[2] Therefore, reduction in NSAID intake is desirable in AS pts.

Objectives: To evaluate the long-term effect of secukinumab (SEC) on NSAID intake in AS pts pooled from the 3 SEC trials (MEASURE [M] 2-4).

Methods: NSAID intake was evaluated prospectively using the Assessment of SpondyloArthritis International Society (ASAS)-NSAID score.[3] The score was determined by type of NSAID, daily dose, and weights from frequency of intake, as well as % of time use in period. An ASAS-NSAID score of '0' indicates no NSAID intake. Pts with ASAS-NSAID score >0 at baseline (BL) were analysed. SEC dose groups were defined as Any 150 or 300 mg, as defined for pooled safety analyses for SEC. Pts with initial placebo treatment (up to 24 weeks) were included in their respective post-Week 24 SEC dose groups to analyse ASAS-NSAID score at Year (Y) 2 (M2-4), Y3 (M2-3) and Y4 (M2) from BL. From the ASAS-NSAID score at BL, the mean change in ASAS-NSAID score, proportion of pts achieving 50% reduction, and the proportion of pts with score <10 were evaluated for each dose at Y2, 3 and 4. Based on the distribution of ASAS-NSAID scores at BL, 2 subgroups were evaluated: (i) <75 (low user); (ii) ≥75 (high user).

Figure: Mean change from baseline in ASAS-NSAID score



Results: Overall, 562 pts (SEC: 150 mg, N=467; 300 mg, N=95) were analysed. The mean ASAS-NSAID score decreased with time in both dose groups. Greater improvements were observed in high NSAID users and with longer treatment exposure (Figure). Proportion of pts who achieved 50% reduction in ASAS-NSAID score increased with time in both SEC 150 and 300 mg groups. Proportion of pts with clinically meaningful reduction of ASAS-NSAID score <10 increased with time in both dose groups and in both low and high NSAID users (Table).

Table

	Time (years)	NSAID intake					
		Low (<0 ASAS-NSAID <75)		High (ASAS-NSAID ≥75)		Overall	
		SEC 150 mg (N=167)	SEC 300 mg# (N=37)	SEC 150 mg (N=300)	SEC 300 mg# (N=58)	SEC 150 mg (N=467)	SEC 300 mg# (N=95)
Proportion of pts who achieved 50% reduction from BL in ASAS-NSAID score, % (n/m)*	2	25 (38/154)	18 (6/33)	19 (50/267)	14 (7/49)	21 (88/421)	16 (13/82)
	3	23 (13/56)	21 (7/33)	26 (26/100)	17 (8/46)	25 (39/156)	19 (15/79)
	4	29 (7/24)	-	26 (14/54)	-	27 (21/78)	-
Proportion of pts with ASAS-NSAID score <10, % (n/m)*	2	39 (60/154)	33 (11/33)	12 (33/267)	12 (6/49)	22 (93/421)	21 (17/82)
	3	34 (19/56)	33 (11/33)	17 (17/100)	13 (6/46)	23 (36/156)	22 (17/79)
	4	38 (9/24)	-	20 (11/54)	-	26 (20/78)	-

*Observed data. #MEASURE 3 that evaluated 300 mg was only a 3 year study. N, total number of pts in the group; n, number of pts with response; m, number of evaluable pts

Conclusion: SEC provided sustained improvement in ASAS-NSAID score in AS pts and was associated with clinically relevant NSAID-sparing effect in AS pts, when used to measure NSAID intake up to 4 years of treatment. Overall, SEC provided long-term NSAID-sparing effects in both high and low NSAID users.

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THU0375 IMPROVEMENTS IN GLOBAL FUNCTIONING AND HEALTH-RELATED QUALITY OF LIFE AND THEIR ASSOCIATION WITH DISEASE ACTIVITY AND FUNCTIONAL IMPROVEMENT IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS TREATED WITH UPADACITINIB: RESULTS FROM THE SELECT-AXIS 1 TRIAL

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Background: Upadacitinib (UPA) has been shown to be effective in patients with active ankylosing spondylitis (AS) [1]. However, improvements in global functioning and health-related quality of life (HRQoL) in these patients, and their relationship with established clinical response measures have not been fully characterized.

Objectives: To evaluate the effect of UPA on the Assessment of SpondyloArthritis international Society Health Index (ASAS HI) and Ankylosing Spondylitis Quality of Life (ASQoL) questionnaire and quantify incremental improvements in ASAS HI and ASQoL response in patients achieving established AS disease activity and physical function improvements at Week (Wk) 14.

Methods: This was a post-hoc analysis of the SELECT-AXIS 1 trial [1]. Patients received either UPA 15 mg once daily or placebo (PBO) for 14 wks. Mean change in ASAS HI and ASQoL from baseline (BL) to Wks 4, 8 and 14 for UPA and PBO were calculated and UPA vs PBO responses were compared. Changes in ASAS HI and ASQoL above the minimum clinically important difference (MCID ≥3-point improvement for both measures) and ASAS HI 'good health state' (ASAS HI score ≤5) at Wk 14 were determined. Changes from BL in ASAS HI and ASQoL were assessed within the combined UPA and PBO group reaching established improvement thresholds across AS clinical response measures (ASAS response criteria, ASDAS improvement criteria, and BASFI MCID) at Wk 14. Mean ASAS HI and ASQoL changes across groups within each measure and magnitude of ASAS HI and ASQoL change between responders and non-responders were compared.

Results: UPA treatment resulted in significant improvement from BL in ASAS HI and ASQoL at Wk 14 with more patients achieving a MCID and ASAS HI good health state vs PBO (Table). Significant improvements were observed earlier for ASAS HI than for ASQoL, starting at Wk 4. At Wk 14, achievement of clinical improvement thresholds was associated with increasing improvements in both ASAS HI and ASQoL scores (Figures 1 and 2). The magnitude of improvement between the best and worst response categories was greater for ASAS HI than ASQoL: 43-fold vs 7-fold for ASAS response, 5-fold vs 3.8-fold for ASDAS improvement, and 34-fold vs 10.4-fold for BASFI MCID achievement.

Table. ASAS HI and ASQoL Outcomes at Week 14

	ASAS HI		ASQoL	
Outcome	**UPA** (n=93)	**PBO** (n=94)	**UPA** (n=93)	**PBO** (n=94)
LSM change from baseline	-2.8[a]	-1.4	-4.2[a]	-2.7
Achievement of MCID (≥3-point improvement)[c], n/N (%)	38/85 (44.7)[b]	24/89 (27.0)	51/83 (61.4)[b]	37/86 (43.0)
ASAS HI good health state (ASAS HI score ≤5)[d], n/N (%)	33/74 (44.6)[b]	15/71 (21.1)	NA	NA

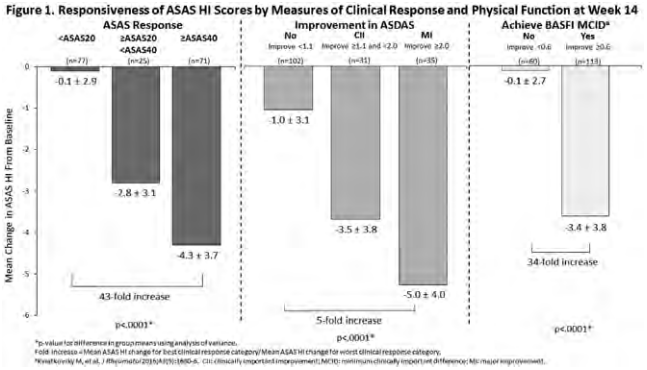
[a]p<0.05 vs PBO based on mixed-effects model for repeated measures
[b]p<0.05 vs PBO based on Cochran-Mantel-Haenszel test with non-responder imputation
[c]In patients with ASAS HI/ASQoL score ≥3 at baseline
[d]In patients with ASAS HI >5 at baseline
LSM, least squares mean; NA, not applicable

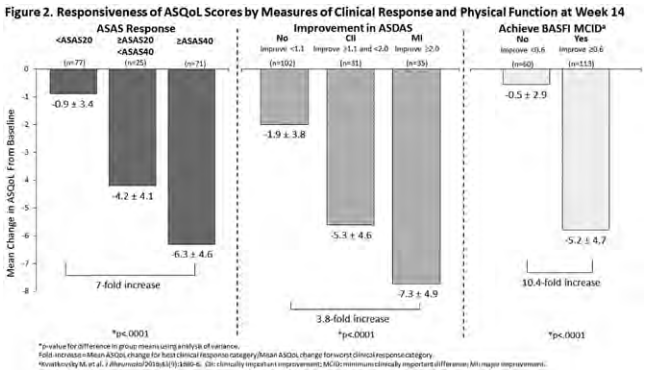
Conclusion: UPA treatment in patients with active AS resulted in clinically meaningful improvements vs PBO in global functioning and HRQoL as measured by ASAS HI and ASQoL, with both measures showing discriminatory ability. Earlier UPA vs PBO response and greater magnitude of change across known clinical response groups suggests that ASAS HI may demonstrate greater responsiveness and ability to capture improvements in AS disease activity and physical function achieved with treatment.

References:

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Figure 1. Responsiveness of ASAS HI Scores by Measures of Clinical Response and Physical Function at Week 14





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Disclosure of Interests: Uta Kiltz Grant/research support from: AbbVie, Amgen, Biogen, Novartis, Pfizer, Consultant of: AbbVie, Biocad, Eli Lilly and Company, Grünenthal, Janssen, Novartis, Pfizer, UCB, Speakers bureau: AbbVie, MSD, Novartis, Pfizer, Roche, UCB, Joachim Sieper Consultant of: AbbVie, Boehringer Ingelheim, Eli Lilly and Company, Janssen, Merck, Novartis, Pfizer, Roche, and UCB Pharma, Speakers bureau: AbbVie, Boehringer Ingelheim, Eli Lilly and Company, Janssen, Merck, Novartis, Pfizer, Roche, and UCB Pharma, Atul Deodhar Grant/research support from: AbbVie, Eli Lilly, GSK, Novartis, Pfizer, UCB, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myer Squibb (BMS), Eli Lilly, GSK, Janssen, Novartis, Pfizer, UCB, Speakers bureau: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myer Squibb (BMS), Eli Lilly, GSK, Janssen, Novartis, Pfizer, UCB, Patrick Zueger Shareholder of: AbbVie, Employee of: AbbVie, In-Ho Song Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Naijun Chen Shareholder of: AbbVie Inc, Employee of: AbbVie Inc, Désirée van der Heijde Consultant of: AbbVie, Amgen, Astellas, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Cyxone, Daiichi, Eisai, Eli-Lilly, Galapagos, Gilead Sciences, Inc., Glaxo-Smith-Kline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB Pharma; Director of Imaging Rheumatology BV

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THU0376 THE EFFECT OF 8 YEARS OF TNF-A BLOCKING THERAPY ON BONE MINERAL DENSITY IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Ankylosing spondylitis (AS) is a chronic inflammatory disease that mainly affects the axial skeleton. Bone loss reflected by low bone mineral density (BMD) is a common feature of AS and can already be observed at early stages of the disease. A recent cohort study of 135 AS patients reported 7.2% improvement in lumbar spine BMD and 2.2% improvement in hip BMD after 4 years of tumor necrosis factor-alpha (TNF-α) blocking therapy.[1]

Objectives: To assess the effect of 8 years of TNF-α blocking therapy on BMD of the lumbar spine and hip in AS patients.

Methods: Included in this study were consecutive AS outpatients from the Groningen-Leeuwarden Axial SpA (GLAS) cohort who received TNF-α blocking therapy for at least 8 years. A maximum of one switch to another TNF-α inhibitor was allowed. Patients were excluded when they used bisphosphonates at baseline or during follow-up. BMD of the lumbar spine (anterior-posterior projection L1-L4) (LS-BMD) and hip (total proximal femur) (hip-BMD) was measured at baseline, 1 year, 2 years and then bi-annually using dual-energy X-ray absorptiometry (Hologic QDR Discovery (UMCG) or Hologic QDR Delphi (MCL), Waltman, MA, USA). Z-scores, the number of SD from the normal mean corrected for age and gender, were calculated using the NHANES reference database. Low BMD was defined as lumbar spine and/or hip BMD Z-score ≤1. Generalized estimating equations were used to analyze BMD over time within subjects. Pairwise contrast were used to compare baseline and follow-up visits. P values <0.05 were considered statistically significant.

Results: In total, 131 AS patients were included; 73% were male, 83% HLA-B27+, mean age was 41.3 ± 10.8 years, median symptom duration 14 years (IQR 7-24), median CRP levels 13 mg/L (IQR 6-22), and 28% had poor vitamin 25(OH) D3 status (<50) at baseline. 27% of patients switched to a second TNF-α inhibitor during follow-up and disease activity improved significantly during treatment: mean $ASDAS_{CRP}$ 3.8 ± 0.8 at baseline and 2.1 ± 0.9 after 8 years (P<0.001). At baseline, low BMD at the lumbar spine and hip was present in 34% and 19% patients, respectively. Both LS-BMD and hip BMD Z-scores were significantly improved during TNF-α blocking therapy at all follow-up visits compared to baseline. Significant improvement compared to the previous time point was found up to and including 4 years for the lumbar spine and up to and including 2 years for the hip. Thereafter, flattening of improvement was observed. Median percentage of improvement in absolute BMD after 8 years of TNF-α blocking therapy compared to baseline was 7.1% (IQR 0.8-13.5) for the lumbar spine and 1.6% (IQR -3.5-5.5) for the hip (Figure 1).

Conclusion: In AS patients with established disease, both lumbar spine and hip BMD improved significantly at group level during 8 years of TNF-α blocking therapy. This effect was most pronounced in the lumbar spine, which corresponds to the disease process in AS. Main improvements in lumbar spine BMD were observed during the first 4 years of treatment.

References:

[1] Beek et al. J Bone Miner Res. 2019; jun;34(6):1041-8

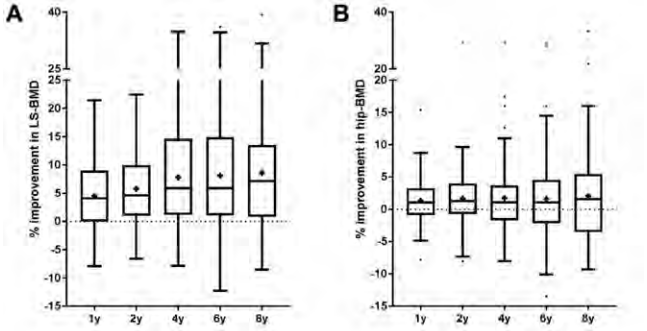


Figure 1. Percentage improvement during 8 years of TNF-α blocking therapy on LS-BMD (A) and hip-BMD (B) in patients with AS (n=131). Box-and-whisker plots (Tukey): boxes indicate medians with interquartile ranges, + indicates mean; whiskers indicate 1.5 times interquartile distances; • indicate outliers.

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THU0377 IMPACT OF FILGOTINIB ON STRUCTURAL LESIONS IN THE SACROILIAC JOINTS AT 12 WEEKS IN PATIENTS WITH ACTIVE AXIAL SPONDYLOARTHRITIS: MAGNETIC RESONANCE IMAGING DATA FROM THE DOUBLE-BLIND, RANDOMIZED TORTUGA TRIAL

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Background: Filgotinib, an oral selective Janus kinase (JAK) 1 inhibitor, reduced disease activity and improved symptoms and inflammation of the sacroiliac joint (SIJ) and spine in patients with active axial ankylosing spondylitis (AxSpA) in the Phase 2 TORTUGA trial (NCT03117270).[1] The effects of JAK inhibitors on structural lesions in active AxSpA are unknown and optimal methods for image analysis of structural disease progression are not established.

Objectives: The aim of this post hoc analysis was to evaluate the effects of filgotinib on magnetic resonance imaging (MRI) measures of structural changes in the SIJ in patients from the TORTUGA trial, as assessed by Spondyloarthritis Research Consortium of Canada (SPARCC) SIJ Structural Scores (SSS).

Methods: TORTUGA was a multicenter, double-blind, randomized trial of 116 patients with active AxSpA treated with filgotinib 200 mg (n=58) or placebo (n=58) once daily for 12 weeks. MRI was conducted at baseline and Week 12 (or early discontinuation visit). MRIs were re-evaluated post hoc by two independent experts (blinded to time point and assigned treatment) to determine SPARCC SSS; inter-reader discrepancies were resolved by an independent adjudicator. Observed changes from baseline were evaluated using analysis of covariance

with factors for treatment, baseline value, and randomization stratification. Least-squares mean changes from baseline and between-group differences with 95% confidence intervals were calculated.

Results: MRI scans from 87 patients with an evaluable MRI at baseline and Week 12 (or early termination visit) were re-evaluated (48 filgotinib, 39 placebo). Erosion scores decreased in the filgotinib group and increased in the placebo group (p=0.02 for between-group difference; Table 1; Figure 1a). Backfill scores increased in the filgotinib group but not in the placebo group (p=0.005; Table 1; Figure 1b). There was no statistically significant between-group difference in SSS total ankylosis (p=0.46) or fat lesion (p=0.17) changes from baseline (Table 1).

Table 1. Summary of Spondyloarthritis Research Consortium of Canada Sacroiliac Joint Structural Scores.

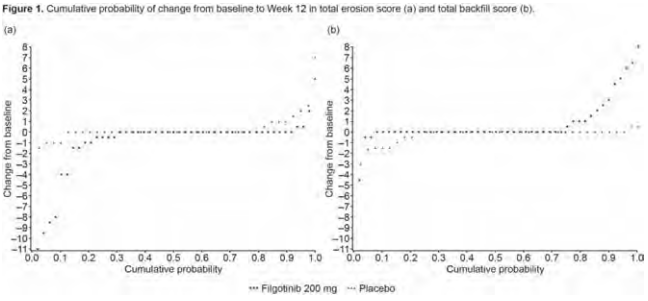
Score	Mean (SD) BL score	LSM change from BL (95% CI) at Week 12	LSM group difference at Week 12 (95% CI)
Erosion			
FIL 200 mg	3.38 (5.34)	–0.46 (–1.31, 0.40)	–1.01 (–1.87, –0.16)
PBO	2.62 (3.76)	0.56 (–0.31, 1.42)	[p=0.02]
Backfill			
FIL 200 mg	1.02 (1.99)	0.76 (0.07, 1.45)	1.02 (0.32, 1.72)
PBO	1.35 (2.59)	–0.26 (–0.97, 0.45)	[p=0.005]
Fat metaplasia			
FIL 200 mg	4.19 (6.06)	0.37 (–0.23, 0.97)	0.43 (–0.18, 1.03)
PBO	4.35 (5.44)	–0.06 (–0.67, 0.56)	[p=0.17]
Ankylosis			
FIL 200 mg	9.58 (8.15)	0.14 (–0.02, 0.30)	0.06 (–0.10, 0.22)
PBO	9.83 (8.45)	0.08 (–0.08, 0.25)	[p=0.46]

BL, baseline; CI, confidence interval; FIL, filgotinib; LSM, least-squares mean; PBO, placebo; SD, standard deviation

Conclusion: In addition to previously reported decreases in SPARCC inflammation, filgotinib was associated with significant reduction in SIJ erosion scores and increase in backfill scores at Week 12 of the TORTUGA trial, versus placebo. Long-term effects are to be determined.

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THU0378 DO COMORBIDITIES DECREASE THE FIRST TNF-INHIBITOR RETENTION AND TREATMENT RESPONSE IN AXIAL SPONDYLOARTHRITIS PATIENTS? DATA FROM TURKBIO

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Background: The frequency of comorbidities has increased in spondyloarthritis patients compared to the general population. The effect of comorbidities on tumour necrosis factor alpha inhibitor (TNFi) drug retention and treatment response has not been well evaluated.

Objectives: The purpose of this study to assess the impact of comorbidities on the first TNFi drug survival and treatment response in patients with axial spondyloarthritis (axSpA) registered in the **TURKBIO** database.

Methods: In this study, the frequency of comorbidities, disease activity scores at baseline and month 6 and drug retention were recorded in AxSpA patients iniating first TNFi treatment between 2011 and 2019. Kaplan Meier plot and log rank tests were used for drug survival analysis. Cox regression analysis with HR was performed to evaluate the correlation between comorbidities and drug survival.

Results: There were 2428 patients with AxSpA (39.3% female) who used their first TNFi during the study period. Among them, a total of 770 (31%) had at least one comorbid disease. Hypertension was the most common comorbidity (9.7%), followed by the affective disorders (8%) and chronic lung disease (5.8%). The baseline characteristics of patients are shown in Table 1. The presence of any comorbidity did not impact the first TNFi retention (Figure 1). When comorbidities were analysed seperately, we found that only history of cerebrovascular event was negatively associated with drug retention rate (HR: 6.9, p:0.008). There was no statistically significant difference in Bath AS Disease Activity Index 50% (BASDAI50) response between patients with and without comorbidity at 6 months. Less axSpA patients with comorbidity achieved a ASDAS score ≤ 2.1 compared to patients without comorbidity at 6 months.

Table 1. Baseline Characteristics of Patients

Radiographic Spondyloarthritis, n (%)	2318 (95.5)
Female, n(%)	954 (39.3)
Age, year	42.2±11.8
Age at diagnosis, years	32.5± 11.3
Age at initial TNFi, years	39.4 ± 11.1
Symptom duration, years	9.7± 7.5
Time to initial TNFi, years	7±6.8
HLA-B27- positivity, n (%)	1144 (47.1)
Smokers, n (%)	1068 (44)
Baseline BASDAI	35.5±22.2
Baseline ASDAS-CRP	2.8±1.1
Baseline CRP (mg/L)	15.7±24.4
VAS global patient	46.6±28.7

-Quantitative variables are presented as mean ± SD, and qualitative variables are presented as frequency and percentage

-ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score using C-reactive protein VAS, visual analogue scale

Conclusion: The results of this study demonstrated that the presence of previous cerebrovascular event decreased the first TNFi survival in patients with axSpA. It also suggested that comorbidities might decrease TNFi treatment response.

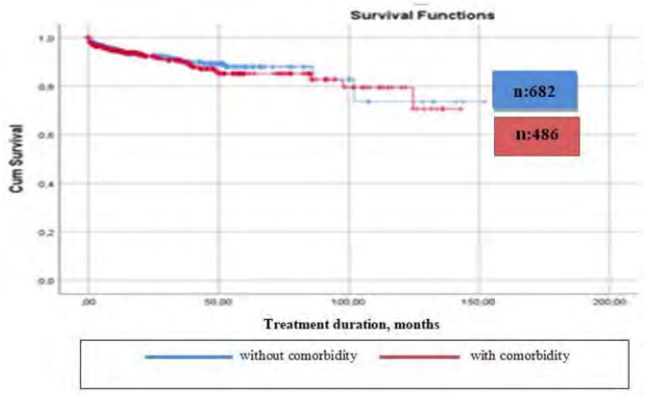


Figure 1. Drug survival of initial TNFi in AxSpA patients (p=0.56).

Disclosure of Interests: None declared
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THU0379 REDUCTION OF ANTERIOR UVEITIS FLARES IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS FOLLOWING ONE YEAR OF TREATMENT WITH CERTOLIZUMAB PEGOL: 48-WEEK INTERIM RESULTS FROM A 96-WEEK OPEN-LABEL STUDY

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Background: Acute anterior uveitis (AAU), inflammation of the anterior uveal tract, is reported in up to 40% of patients (pts) with axial spondyloarthritis (axSpA).[1] AAU is associated with significant clinical burden; symptoms include blurred vision, photophobia and pain.[2] Previous studies have shown that TNF inhibitors (TNFi) can reduce AAU flare incidence in pts with radiographic axSpA,[3-5] but few have focused on pts across the full axSpA spectrum.

Objectives: To analyse the impact of certolizumab pegol (CZP) treatment on AAU in pts with active radiographic and non-radiographic axSpA and a recent history of AAU.

Methods: C-VIEW (NCT03020992) is an ongoing multicentre, open-label, phase 4 study. Pts had active axSpA according to the ASAS classification, a history of recurrent AAU (≥2 AAU flares in total and ≥1 AAU flare in the year prior to study entry), were HLA-B27 positive, and were eligible for TNFi treatment (previous failure of ≥2 NSAIDs, biologic naïve or had failed ≤1 TNFi). Pts received CZP 400 mg at Weeks (Wks) 0/2/4, then 200 mg every two wks (Q2W) to Wk 96. The primary variable was incidence of AAU flares compared to historic rates. A pre-specified interim analysis compared AAU incidence in the 48 wks prior to CZP treatment with the 48 wks of treatment, using Poisson regression adjusted for possible within-pt correlations, with period (pre- and post-baseline) and axSpA disease duration as covariates. Incidence rates (IR) were calculated based on the number of cases/pts at risk over 48 wks. Observed data are reported.

Results: Of 115 enrolled pts, 89 initiated CZP treatment; 85 completed Wk 48. Baseline characteristics are shown in the Table. The 48-wk interim analysis revealed significantly fewer AAU flares/pt during CZP treatment vs before treatment (Figure; Poisson-adjusted IR: 0.2 vs 1.5, p<0.001). The number of pts experiencing 1 and ≥2 AAU flares (64.0% and 31.5% respectively) substantially reduced during CZP treatment (12.4% and 2.2%). After 48 wks CZP treatment, disease activity improved substantially (mean ± SD Ankylosing Spondylitis Disease Activity Score [ASDAS]: 2.0 ± 0.9; Bath Ankylosing Spondylitis Disease Activity Index [BASDAI]: 3.3 ± 2.1), with 31.4% pts achieving ASAS partial remission and 29.1% ASDAS major improvement. No new safety signals were identified.

Table. Baseline characteristics

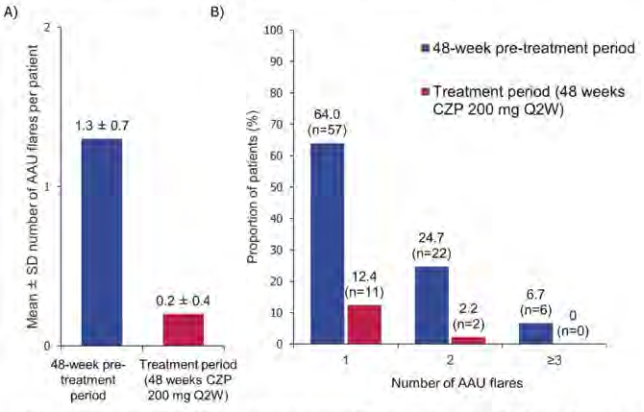
	CZP 200 mg Q2W (N=89)
Age (years), mean ± SD	46.5 ± 11.2
Male, n (%)	56 (62.9)
Racial group, n (%)	
Caucasian	87 (97.8)
Other	2 (2.2)
Diagnosis, n (%)	
Radiographic axSpA	76 (85.4)
Non-radiographic axSpA	13 (14.6)
Duration of axSpA (years), mean ± SD	8.6 ± 8.4
Time since onset of first uveitis flare (years), mean ± SD	9.9 ± 9.0
ASDAS, mean ± SD	3.5 ± 0.9
BASDAI, mean ± SD	6.5 ± 1.5

Conclusion: In this open-label study, AAU flare rate significantly reduced in axSpA pts with a history of recurrent AAU during the first 48 wks of CZP. Pts also experienced substantial improvements in axSpA disease activity.

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Figure: (A) Mean number of acute anterior uveitis flares experienced by patients in C-VIEW and (B) proportion of patients experiencing 1, 2 or ≥3 acute anterior uveitis flares



AAU: acute anterior uveitis; CZP: certolizumab pegol; Q2W: every 2 weeks; SD: standard deviation.

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THU0380 SECUKINUMAB IS FREQUENTLY PREFERRED IN MULTI ANTI-TNF RESISTANCE SPONDYLOARTHRITIS PATIENTS: HUR-BIO REAL LIFE RESULTS

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Background: Anti-TNF agents have been used for the last two decades. However, targeting interleukin-17 (secukinumab (SEC)) is a relatively novel treatment

option for spondyloarthritis (SpA). Therefore, SEC is frequently preferred after multi anti-TNF agents, in real life.

Objectives: The objective of this study was to assess the retention rate and response of SEC in anti-TNF naïve and anti-TNF resistance patients in real life experience.

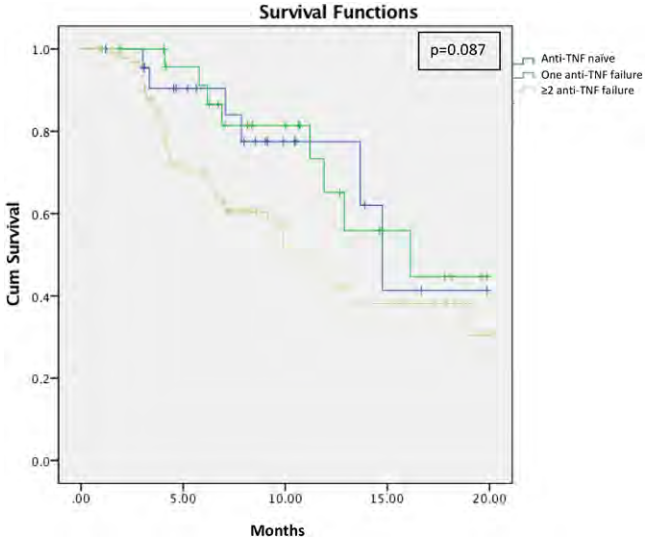


Figure. Secukinumab survival in anti-TNF naïve, one anti-TNF failure and ≥2 anti-TNF failure patients

Methods: HUR-BIO is a monocentric database of biologics including 2886 SpA patients, since 2005. SEC is approved at May 2018 in Turkey and 147 patients have used SEC by January 2020. Demographic and clinical data were obtained from HUR-BIO registry. SpA patients were classified as ankylosing spondylitis (AS) and non-radiographic SpA (nrAxSpA). Response and retention rate of SEC were determined regarding to anti-TNF naïve vs anti-TNF resistance patients. Kaplan-Meier analysis was used to estimate SEC retention rates.

Results: In total, 147 axial SpA patients (96 (65.3%) AS and 51 (34.7%) nrAxSpA) were analyzed. Overall, 23/147 (15.7%) patients were anti-TNF naïve, 27 (18.4%) patients were 1 anti-TNF failure and 97 (65.9%) patients were ≥2 anti-TNF failure. Baseline characteristics of patients and the main causes of discontinuation of anti-TNF agents were shown in table. Median duration of SEC usage was 7.9 (min-max, 3.0-19.8) months in AS and 6.7 (min-max, 3.0-19.8) months in nrAxSpA group (p=0.365). SEC survival at 12 months was similar between AS and nrAxSpA patients (56% vs %52, p=0.315) (not shown).SEC survival was similar among anti-TNF naïve, one anti-TNF failure and ≥2 anti-TNF failure patients (Figure). BASDAI 50 response was reached in 61.5% of anti-TNF naïve, 42.1% of one anti-TNF failure and 43.2% of ≥2 anti-TNF failure patients at the last control (p=0.452). Patients who used ≤ 1 anti-TNF agent had a higher drug survival rate (%69 vs %46, p=0.027) at 1 year, in comparison with patients who used > 1 anti-TNF agents before SEC(not shown).

Table. Baseline characteristics of patients and the main causes of discontinuation of anti-TNF agents

	Anti-TNF naive, n=23	One anti-TNF failure, n=27	≥2 anti-TNF failure, n=97	p
Age, years, mean±SD	46.0 ± 11.2	42.4 ± 8.4	44.3 ±9.9	0.611
Female, n (%)	7 (30.4)	15 (55.6)	61 (62.9)	0.019
Disease duration, months, median (min-max)	72 (12-408)	102 (12-300)	120 (12-396)	0.054
Disease duration ≥5 years, n (%)	12 (52.2)	18 (66.7)	72 (74.2)	0.112
Secukinumab indications				<0.0001
-Anti-TNF inefficacy, n (%)	-	9 (33.4)	80 (82.5)	
-Anti-TNF adverse event, n (%)	-	10 (37.0)	16 (16.5)	
-Others, n (%)	-	8 (29.6)	1 (1.0)	
History of smoking, n (%)	14 (60.9)	17 (63.0)	54 (55.7)	0.754
History of uveitis, n (%)	5 (21.7)	7 (25.9)	10 (10.3)	0.081
Baseline BASDAI	54 (10-96)	54.5 (0-88)	60 (0-100)	0.307
Baseline BASFI	53 (10-78)	38 (0-94)	55 (0-100)	0.142
Baseline back pain VAS	55 (0-100)	50 (0-100)	70 (0-100)	0.113
ESR, mm/h, median (min-max)	21 (2-120)	24.5 (2-107)	20 (2-84)	0.621
CRP, mg/dL, median (min-max)	0.7 (0.1-8.4)	1.3 (0.1-10.4)	0.7 (0.1-30.8)	0.439
Syndesmophytes on X-ray, n (%)	8 (66.7)*	8 (47.1)	16 (22.9)*	0.019

*p=0.007

Conclusion: For SpA, SEC is a relatively new player in biological era. When SEC launched for new treatment option, it is preferred mostly (almost 2/3) in multi anti-TNF resistance patients. Moreover, those difficult patients' (usually female) treatment response and retention rate were not satisfactory than biological naïve patients.

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THU0381 MANAGEMENT OF CARDIOVASCULAR COMORBIDITY IN PSORIATIC ARTHRITIS IN THE ROUTINE CLINICAL PRACTICE: A COMPARATIVE STUDY OF METHOTREXATE OR APREMILAST AS MONOTHERAPY AND COMBINED

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Background: The presence of cardiovascular disease in psoriatic arthritis (PsA) is of particular concern, as it is considered the leading cause of mortality in PsA. Thus, it is essential to recognize those appropriate therapies that could target this comorbidity, reducing the risk of cardiovascular disease and metabolic alterations.

Objectives: To evaluate the efficacy of methotrexate (MTX) and apremilast as monotherapies or in combination, in the clinical manifestations of the disease and the reduction of cardiovascular risk factors in PsA.

Methods: Prospective longitudinal study in 30 PsA patients diagnosed according to CASPAR criteria: 10 patients were treated with MTX (12 ± 2,58 mg/week), 10 patients with apremilast (60 mg/day) and 10 were treated with combined therapy for 6 months, recruited in the routine clinical practice at the Reina Sofia Hospital of Cordoba and University Hospital of Jaen, Spain. Clinical and analytical parameters were collected at baseline and after 6 months of treatment: lipid profile (cholesterol, HDL, LDL, TG, ApoA and ApoB), glucose and insulin, body surface area (BSA) affected by psoriasis, number of tender and swollen joints, DAS28, DAPSA, VAS, CRP and ESR.

The presence of cardiometabolic risk factors such as metabolic syndrome (MetSyn) was evaluated according to National Cholesterol Education Program (NCEP) adult treatment panel III (ATP III) criteria, meeting 3 of the following characteristics: abdominal obesity (men (>102 cm); women (>88 cm), TG > 150 mg/dL, HDL (men (<40 mg/dL); women (<50 mg/dL), blood pressure > 130/85 mmHg, glucose levels > 110 mg/dL). Insulin resistance (HOMA-IR > 2,5), body mass index (BMI), ApoB/ApoA ratio, atherogenic index (AI) and SCORE (age, gender, cholesterol, HDL, smoking habit and diabetes) were also studied.

Results: Apremilast or MTX monotherapies caused a moderate reduction of the clinical inflammatory markers (CRP and ESR) and disease activity (VAS, DAPSA and DAS28) after 6 months of treatment. On the other hand, while apremilast significantly reduced the affected BSA, MTX had no significant effect. All those parameters were more significantly reduced after the combined treatment (MTX+ apremilast).

Apremilast monotherapy significantly improved alterations in the lipid profile (reducing cholesterol and LDL levels, ApoB/ApoA ratio and AI), insulin resistance and decreased BMI, thus reducing the number of patients with MetSyn. MTX monotherapy treatment had no positive effect on these parameters. None of the treatments had significant effects on SCORE values.

The beneficial effects of apremilast on the lipid profile were mitigated after the combination with MTX. Nevertheless, the number of patients with MetSyn decreased even more after the combined therapy of MTX with apremilast compared to apremilast monotherapy.

Conclusion: 1) In patients with moderate disease activity, treatment with apremilast monotherapy might have some advantages compared to the MTX monotherapy, since it can decrease the percentage of BSA with psoriasis, the lipid profile alteration, IR and weight, thus improving the cardiovascular risk profile. 2) Combined therapy (MTX+ apremilast) can induce a deeper reduction in the disease activity compared to the monotherapies, maintaining, in turn, the positive effects of apremilast on the cardiovascular risk.

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THU0382 ARTICULAR MANIFESTATIONS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES TREATED WITH ANTI-TNFA

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Background: Articular manifestations are the most frequent extra-digestive manifestations of Inflammatory Bowel Disease (IBD). Anti-TNF have proved to be as effective on articular symptoms as on IBD's ones, but have been suspected to induce paradoxical articular manifestations.

Objectives: The aims of this study were to describe the frequency, the type and the management of all articular manifestations occurring in patients treated with anti-TNF for IBD and to look for factors associated with their occurrence.

Methods: In this retrospective monocentric study, we included all patients who received an anti-TNF for an IBD in our tertiary hospital referent for inflammatory rheumatic and bowel diseases. We searched for all incident articular manifestations occurring during treatment with anti-TNF, including new or recurrent articular manifestations. Characteristics of patients with paradoxical articular manifestations (defined as inflammatory articular symptoms occurring while IBD was in remission, without immunization against anti-TNF) were compared to that of patients without articular manifestations to identify factors associated with their occurrence.

Results: Through a systematic search of all IBD patients seen in our tertiary hospital between February 2013 and May 2017, we identified 442 patients (36.2±15 years, 50.5% men) who had ever received an anti-TNF for IBD: Crohn's disease (n=277), ulcerative colitis (154) and undetermined colitis (n=11). 74 (16.7%) had already a history of inflammatory articular manifestations including 37 patients with a diagnosis of spondyloarthritis (SpA) made before anti-TNF's beginning.

Among them, 115 (26%) patients developed a new articular manifestation after a mean of 20 (±22) months of treatment: mechanical in 56 (12.6%) and inflammatory in 59 (13.3%). Within patients with new inflammatory articular manifestations: 39% were paradoxical, 27% were concomitant of an IBD flare, 27% were associated to an immunization against anti-TNF, 3% were induced lupus, 2% were chondrocalcinosis and 2% were polymyalgia rheumatic. Articular manifestations associated to an immunization were linked to a loss of efficiency of the treatment for 62%, with (42%) or without (20%) associated digestive symptoms and 38% were due to delayed hypersensitivity reaction. Among paradoxical articular manifestations, 83% were new articular symptoms, including 35% of SpA de novo, and 17% were recurrence of known articular manifestations. The only predictive factor of paradoxical articular manifestation was a previous diagnosis of SpA (21.7% vs 6.8%; p=0.02). Paradoxical manifestations improved in 17 patients despite continuation of anti-TNF, methotrexate was added in 2 and anti-TNF was discontinued in only 4 patients.

Conclusion: Inflammatory articular manifestations occurred in about 13% of patients treated with anti-TNF for IBD. More than a quarter were linked to an immunization against anti-TNF, which has to be searched in this situation. Less than half of them (39%) were paradoxical. In most of cases, they were transitory and did not require anti-TNF's discontinuation. The only predictive factor of paradoxical articular manifestations was having a history of SpA.

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THU0383 GENDER DIFFERENCES IN NONRADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: FROM CLINICAL CHARACTERISTICS TO EFFECTIVENESS OF TNF INHIBITORS

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Background: While a male predominance is found in radiographic axial spondyloarthritis (r-axSpA), an equal male to female distribution was repeatedly reported for the nonradiographic disease form (nr-axSpA). Some important differences in clinical manifestations and response to treatment with tumor necrosis factor inhibitors (TNFi) between the sexes have been delineated for r-axSpA. It remains unclear, whether comparable sex differences can be assumed for nr-axSpA. Indeed, existing data on gender differences in nr-axSpA is limited to subgroups and is particularly scarce regarding effectiveness of treatment.

Objectives: To investigate sex differences with regard to demographics, clinical manifestations and response to TNFi in nr-axSpA after exclusion of patients with co-morbid fibromyalgia (FM).

Methods: Response to a first TNFi was assessed in 85 women and 78 men with nr-axSpA and without concomitant FM in the Swiss Clinical Quality Management Cohort. The primary outcome was the proportion of patients achieving a 40% improvement in the Assessment of Spondyloarthritis international Society criteria (ASAS40) at 1 year. Additional response outcomes were evaluated as secondary outcomes. Patients having discontinued TNFi were considered non-responders. Logistic regression analyses were adjusted for baseline differences (Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Maastricht ankylosing spondylitis enthesitis score (MASES), diagnostic delay, body mass index (BMI)).

Results: Baseline characteristics of women and men are shown in Table 1. Significant differences were restricted to diagnostic delay, BASDAI, MASES and BMI. An ASAS40 response was achieved by 17% of women and 38% of men (OR 0.34, 95% CI 0.12; 0.93, p=0.02). A lower response rate in women was confirmed in the adjusted analysis (OR 0.19, 95% CI 0.05; 0.62, p=0.009) as well as for the other outcomes assessed (Table 2).

Table 1. Baseline characteristics of women and men with nr-axSpA starting a first TNFi (after exclusion of patients with co-morbid FM).

Parameter	N	Men	Women	p
	163	**N = 78**	**N = 85**	
Age, years	163	35.6±10.8	39.1±11.4	0.10
Age at onset, years	162	27.9±8.6	28.1±8.5	0.66
Diagnostic delay, years	**162**	**4.1±7.6**	**7.8±9.9**	**0.005**
HLA-B27 positive, %	149	75.7	68.0	0.36
Prior MRI sacroiliitis, %	154	70.8	68.3	0.86
BASDAI	**148**	**5.3±2.0**	**6.3±1.6**	**0.003**
ASDAS	140	3.3±1.0	3.4±0.7	0.29
Elevated CRP, %	154	42.5	38.3	0.62
BASFI	148	3.6±2.4	3.8±2.5	0.54
BASMI	141	1.2±1.1	1.4±1.2	0.42
EQ-5D	141	54.8±22.8	55.8±18.3	0.79
Peripheral arthritis,%	159	41.6	52.4	0.20
Enthesitis, %	158	80.5	85.2	0.53
MASES	**157**	**2.3±2.5**	**3.9±3.3**	**0.002**
csDMARDs ever, %	163	34.6	42.4	0.34
Taking NSAIDs, %	150	92.9	86.2	0.29
Current smoking, %	139	28.3	22.8	0.55
BMI	**160**	**25.9±4.2**	**24.0±4.4**	**<0.001**

Table 2. Response rates of women versus men after 1 year of treatment with a first TNFi.

			Unadjusted analyses			Adjusted analyses		
Outcome	Women %	Men %	OR	95% CI	P	OR	95% CI	P
ASAS40	17	38	0.34	0.12; 0.93	0.02	0.19	0.05; 0.62	0.009
BASDAI50	23	50	0.30	0.11; 0.77	0.007	0.19	0.05; 0.58	0.005
ASDAS improv. ≥1.1	28	58	0.29	0.10; 0.78	0.008	0.26	0.08; 0.75	0.02
ASDAS <2.1	27	49	0.39	0.15; 1.00	0.03	0.18	0.04; 0.65	0.01
ASDAS improv. ≥2	4	26	0.13	0.01; 0.68	0.005	0.04	0.00; 0.27	0.003
ASDAS <1.3	8	29	0.23	0.05; 0.82	0.01	0.07	0.01; 0.39	0.005

Conclusion: Despite only few sex differences in patient characteristics in nr-axSpA, response rates to TNFi are significantly lower in women than in men.

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THU0384 IMPACT OF IXEKIZUMAB ON WORK PRODUCTIVITY IN NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS PATIENTS: RESULTS FROM THE COAST-X TRIAL AT 52 WEEKS

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Background: Patients with non-radiographic axial spondyloarthritis (nr-axSpA) experience impairments in health-related quality of life comparable to those seen in ankylosing spondylitis, including impacts on work productivity. Ixekizumab (IXE) is a high-affinity monoclonal antibody that selectively targets interleukin-17A and effectively treats axial spondyloarthritis.[1,2,3]

Objectives: This analysis evaluated the effect of IXE treatment for 52 weeks on work productivity and activity impairment as measured by absenteeism, presenteeism, overall work impairment, and activity impairment in patients with active nr-axSpA.

Methods: COAST-X (NCT02757352) was a phase 3, multicenter, randomized, double-blind, placebo-controlled, parallel-group outpatient study investigating the efficacy and safety of 80 mg IXE every 2 weeks (Q2W) and every 4 weeks (Q4W) compared to placebo (PBO) in 303 patients naïve to biologic disease-modifying anti-rheumatic drugs with active nr-axSpA during a 52-week treatment period. From Weeks 16 through 44, if patients' disease activity required escalation of treatment at investigator discretion, patients were switched to open-label IXE Q2W or subsequent tumor necrosis factor inhibitor treatment. Analysis was performed for the intent-to-treat population, which included data up to the time of biologic switching. Patients who switched to open-label IXE were considered non-responders. Changes from baseline in work productivity were measured for patients reporting full- or part-time work at Weeks 16 and 52 with the Work Productivity and Activity Impairment (WPAI) Questionnaire for Spondyloarthritis and analyzed with an analysis of covariance model including treatment, geographic region, screening magnetic resonance imaging and C-reactive protein level status, and baseline value as factors. Missing data was imputed using the modified baseline observation carried forward.

Results: A majority of patients (63.5–65.7%) reported part-time or full-time paid work at baseline, with baseline scores for presenteeism and overall work activity slightly higher for patients in the PBO arm (p<0.05). Patients treated with IXE Q4W had significantly greater improvement than PBO in activity impairment at Weeks 16 (p=0.003) and 52 (p=0.004), presenteeism at Weeks 16 (p=0.007) and 52 (p=0.003), and overall work impairment at Weeks 16 (p=0.014) and 52 (p=0.005; Figure). Patients treated with IXE Q2W had significantly greater improvement than PBO in activity impairment at Weeks 16 (p=0.007) and 52 (p=0.006; Figure). Patients treated with either IXE regimen had numeric improvements in all WPAI measures compared to those receiving PBO at Weeks 16 and 52 (Figure).

Conclusion: Patients with nr-axSpA treated with either IXE regimen had significant improvements in activity impairment compared to PBO. Patients receiving IXE Q4W also had significant improvements in presenteeism and overall work impairment.

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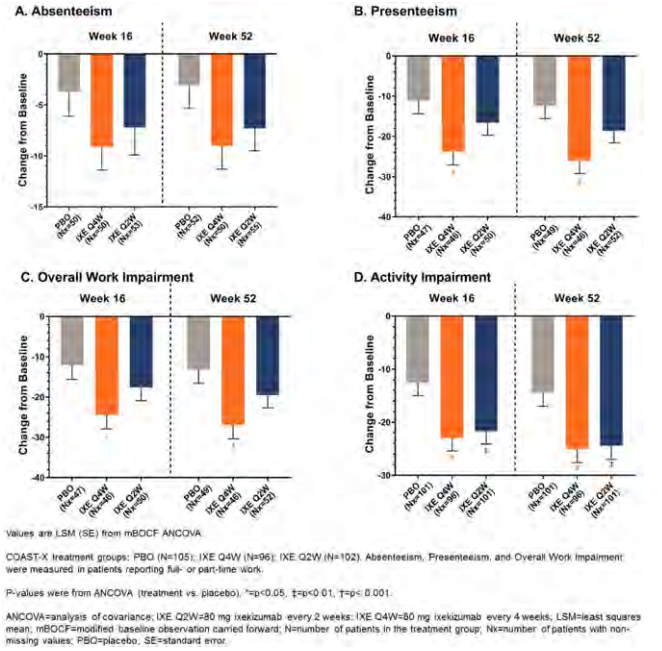


Figure. Changes from baseline in A) Absenteeism, B) Presenteeism, C) Overall Work Impairment, and D) Activity Impairment.

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THU0385 SAFETY OF TOFACITINIB THERAPY IN HBSAG CARRIERS WITH ANKYLOSING SPONDYLITIS: A PROSPECTIVE STUDY

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Background: Targeted synthetic DMARDs (ts-DMARDs) are becoming more available and affordable in developing countries, where the prevalence of hepatitis B virus (HBV) infection is still an important public health issue. The safety of ts-DMARDs therapy in terms of the reactivation of hepatitis B virus (HBV) infection need more concern. Rare data from a prospective study focus on the use of ts-DMARDs in patients with concurrent ankylosing spondylitis (AS) and HBV infection were available by now.

Objectives: To evaluate the influence of tofacitinib on reactivation of HBV infection in HBsAg carriers with AS.

Methods: In this 52 weeks observation, HBsAg carriers with active AS (BASDAI ≥ 4) despite failed treatment with at least two NSAIDs and sulfasalazine (for patients with persistent peripheral arthritis) were studied. Patients must be positive for HBsAg and have a normal liver function prior to study.

All patients received therapy with tofacitinib (5mg twice daily). Entecavir were prescribed preventively regardless of individual viral load. Pre-existing NSAIDs and sulfasalazine were allowed. Liver enzymes (AST/ALT) and HBV viral load were monitored every 4 weeks. Increased viral load and abnormal liver function were managed according to expert opinion.

Results: Eleven patients (9 male) were recruited. Eight patients had a baseline viral load >2000 copy/ml (group 1), and the other 3 patients had a viral load ≤ 2000 copy/ml (group 2). Two patients from group 1 discontinued tofacitinib at week 12 due to ineffectiveness, and both continued taking Entecavir for another 3 months after the discontinuation of tofacitinib.

One patients (male, 26 years old) from group 1 underwent a mild increase of both ALT and AST (67 and 56 IU/L, respectively) at week 16, but no elevated viral load (2.1e3 copies/ml, baseline 2.8e3) or a HBV YMDD mutant was found. The tofacitinib treatment continued. After prescription of polyene phosphatidyl choline, the liver enzyme of this patient decreased to normal range in 4 weeks and remained normal throughout the study.

No reactivation of hepatitis B was observed in patients from group 2.

Conclusion: Tofacitinib treatment may be a safe and effective option for HBsAg carriers with AS refractory to traditional treatment. Prophylaxis strategy with effective anti-viral drugs is recommended.

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Disclosure of Interests: None declared

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THU0386 PREDICTORS OF MAINTENANCE OF SECUKINUMAB TREATMENT IN A MULTICENTER COHORT OF 561 SPONDYLARTHRITIS

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Objectives: Secukinumab (SEC) is an interleukin-17 inhibitor used to treat patients with axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA). Drug maintenance is often used as a proxy for treatment effectiveness and safety in real life settings. We aim to assess SEC maintenance in routine clinical practice and to identify survival predictors associated.

Methods: We conducted a retrospective, longitudinal, observational, multicenter study including all patients (pts) with axSpA or PsA who received at least 1 injection of SEC between July 2016 and October 2019. We collected patient's demographics and clinic characteristics, SEC date of initiation and dosage and dosage modification of SEC, previous biologic Disease-modifying antirheumatic drugs (bDMARDs) and concomitant treatments. Date and reasons of discontinuation – i.e., lack of efficacy, safety issue, sustained remission or others – were collected. Several potential maintenance predictors were tested: age, gender, disease (axSpA or PsA), smoking status, bDMARDs history and concomitant treatment. Among patients with non-radiographic axSpA (nr-axSpA), evidence of MRI sacroiliitis or elevated CRP were also assessed as potential maintenance predictors. Drug maintenance was analyzed by the Kaplan-Meier method and adjusted for baseline factors were estimated by log rank analysis.

Results: The main characteristics of the 561 pts included were the following: 363 (64.7%) axSpA, 198 (35.3%) PsA, 329 (58.6%) female, mean age 45,6 +/- 12 years, 221 (39.4%) smokers, 175 (31.2%) radiographic sacroiliitis, 259 (46.2%) MRI sacroiliitis, 198 (35.3%) elevated CRP, 247 (44.0%) HLA B27 positive, mean BASDAI 48,3 +/- 26.8%. SEC was associated to methotrexate (MTX) in 139 pts (24.8%) and was the first line bDMARD in 55 pts (9.8%). The median drug maintenance (MDM) of SEC was 79 weeks (wk) [73-84]. At 52 wk, 245 pts (60%) SpA were still treated with SEC. During the 3-year follow-up, 264 pts discontinued SEC: 180 (68.2%) pts for lack of effectiveness, 47 (17.8%) for adverse events, 14 (5.3%) for others and 23 (8.7%). SEC prescription as first line bDMARD was associated with longer survival versus second line or more: 111 wk [83-138] vs. 69 wk [57-80] (p=0. 017) (figure 1). MDM was not significantly different depending on gender, MTX combo, elevated CRP, axSpA vs PsA and smoking status. Among the nr-axSpA pts, MRI sacroiliitis or elevated CRP did not modify SEC maintenance (p=0.68) (figure 2).

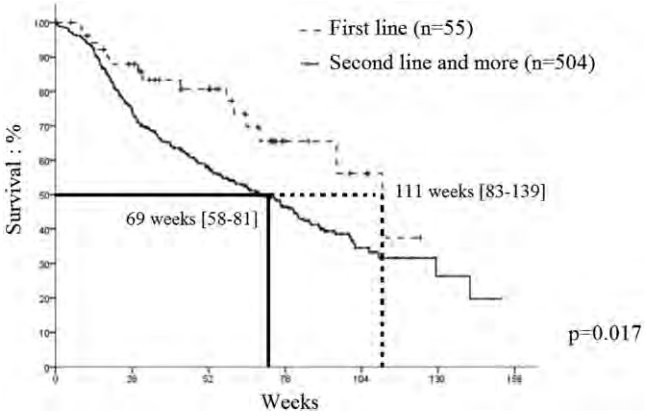


Figure 1. Secukinumab maintenance according to therapeutic line

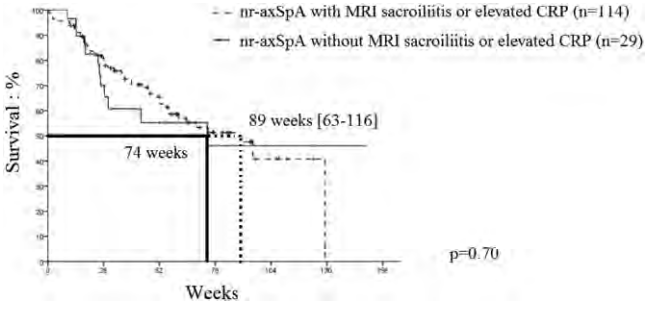


Figure 2. Secukinumab maintenance in nr-axSpA population

Conclusion: In routine clinical practice, SEC median maintenance was 79 weeks. Fist line administration was the only independent factor associated with improved SEC retention. Lack of effectiveness was the most common reason of discontinuation.

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Ingelheim, Celgene, Lilly, Janssen, Medac MSD France, Nordic Pharma, Novartis, Pfizer, Roche, Sanofi Aventis, SOBI and UCB, Guy Baudens: None declared, Pascal Claudepierre Speakers bureau: Janssen, Novartis, Lilly, Corinne Miceli Richard: None declared, Philippe Dieudé: None declared, Jean-Hugues Salmon Speakers bureau: Novartis, Janssen, Jérémie SELLAM: None declared, Eric Houvenagel Speakers bureau: Janssen, Novartis, Marie-Hélène Guyot: None declared, Chi Duc Nguyen: None declared, Xavier Deprez Speakers bureau: Novartis, Janssen, Isabelle CHARY VALCKENAERE: None declared, Pierre Lafforgue Speakers bureau: Novartis, Janssen, Damien LOEUILLE: None declared, Christophe Richez Consultant of: Abbvie, Amgen, Mylan, Pfizer, Sandoz and UCB., Rene-Marc Flipo Speakers bureau: Novartis, Janssen, Lilly, Thao Pham Speakers bureau: Novartis, Janssen, Lilly

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THU0387 THE IMPACT OF TREATMENT WITH A BIOLOGICAL DISEASE-MODIFYING ANTIRHEUMATIC DRUG ON SPINAL MOBILITY AND ITS CORRELATION WITH DISEASE ACTIVITY IN PATIENTS WITH SPONDYLOARTHRITIS

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Background: Bath Ankylosing Spondylitis Metrology Index (BASMI) is an instrument developed to assess spinal and hip mobility. The relationship between BASMI and disease activity is not always linear and, above all, the data that correlate the variation in BASMI values (ΔBASMI) with the variation in disease activity scores and response to treatment are not unanimous.

Objectives: Explore the effect of biological disease-modifying antirheumatic drugs (bDMARD) in spine mobility (as assessed by BASMI) and the associations between ΔBASMI and disease activity.

Methods: Observational retrospective study was performed including consecutive patients with the diagnosis of Spondyloarthritis (SpA) followed at our Rheumatology Department. Demographic, clinical, including Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), BASMI, Ankylosing Spondylitis Disease Activity Score with erythrocyte sedimentation rate and C-reactive protein (ASDAS ESR and ASDAS CRP, respectively), and laboratorial data were collected from our national database at baseline, 6 and 12 months after initiation of a bDMARD. The variation of each parameter was calculated as the difference between the levels recorded at 6 and 12 months and the reference level and presented in the form of Δ. Statistical analysis was performed using SPSS 23.0. Correlations between variables were studied using Spearman correlation analysis and comparison between groups was performed using Wilcoxon and Kruskal-Wallis tests.

Results: Median age of patients (n=178) was 42 years old [34, 50], 92 (51.7%) were males with a median disease duration of 4.9 [1.0, 10.3] years. One hundred and twenty-six patients (70.8%) had Ankylosing Spondylitis, 15 (8.4%) Inflammatory Bowel Disease related SPA and 30 (16.9%) Undifferentiated SpA. Fifty four (30.3%) patients were taking glucocorticoids and regarding conventional synthetic disease-modifying anti-rheumatic drugs use before starting the bDMARD: Sulfasalazine (52, 29.2%), Methotrexate (31, 17.4%) and Leflunomide (3, 1.7%). Regarding the bDMARD, only one patient started Secukinumab and the others a Tumor necrosis factor inhibitor (TNFi) [Golimumab (n= 64, 36.0%), Adalimumab (n=36, 20.2%), Infliximab (n= 35, 19.7%), Etanercept (n= 32, 18.0%) and Certolizumab (n= 10, 5.6%)].

The majority of the patients had very high disease activity at baseline (86.0%, n=153); median ESR was 29 mm/h [15, 47], median CRP was 13.7 mg/L, [6.60, 27.3], median ASDAS CRP was 7.6 [6.0, 9.0] and median BASMI was 8.0 [7-0, 9.0]. After 6 and 12 months of treatment, mean ESR, CRP, ASDAS-CRP and BASMI were significantly lower than mean baseline values (p<0.01), with median ASDAS-CRP at 12 months of 2.20 [1.50, 2.90] and median ΔBASMI of -4.10 [-5.50, -2.40].

BASMI at baseline showed a moderate correlation with ASDAS CRP (r=0.468, p<0.01), BASDAI (r=0.496, p<0.01) and patient visual analogic scale (VAS) (r=0.563, p<0.01). No correlations were found between BASMI and CRP, ESR, physician VAS or the consumption of nonsteroidal anti inflammatory drugs at baseline.

A significant positive correlation was found between ΔBASMI and ΔASDAS at 6 months and 12 months (r=0.243, p=0.02; r=0.286; p<0.01) and also between ΔBASMI and ΔBASDAI at 6 and 12 months (r=0.183, p=0.04; r=0.291, p=0.02). No correlations were found between ΔBASMI and ΔCRP or ΔESR. No differences were observed in ΔBASMI, regarding the bDMARD of choice.

Conclusion: In our cohort, starting a bDMARD improved BASMI scores through a 12 month period and there was a correlation between the variation of BASMI and disease activity improvement. As such, a TNFi may retard the progression of spinal mobility dysfunction in SpA patients. We cannot draw conclusions regarding differences between TNFi and interleukin 17 inhibitors and further work is needed to clarify possible differences in their impact in improving spine mobility.

Disclosure of Interests: Salomé Garcia: None declared, Bruno Miguel Fernandes: None declared, Sara Ganhão: None declared, Maria Rato: None declared, Filipe Pinheiro: None declared, Georgina Terroso: None declared, Miguel Bernardes Speakers bureau: Abbvie, Amgen, Biogen, Eli-Lilly, Glaxo-Smith-Kline, Pfizer, Janssen, Novartis, Lúcia Costa: None declared

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THU0388 UVEITIS IN AXIAL SPONDYLOARTHRITIS: FREQUENCY AND RELATIONSHIP TO BIOLOGICAL THERAPY. SINGLE CENTER UNIVERSITY STUDY OF 255 PATIENTS

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Background: Uveitis is one of the most frequent extra articular manifestation of spondyloarthritis (SpA). Biological therapy, especially monoclonal TNF inhibitors, may be useful to prevent and to treat uveitis. However, other biologics had been related to paradoxical uveitis.

Objectives: Our aim was to assess a) the epidemiological and clinical features of uveitis associated to SpA and b) its relationship with biological treatment used in SpA.

Methods: An observational study of patients who developed uveitis form a cohort of 255 consecutive unselected patients with axial SpA (axSpA) classified according to the ASAS criteria. They were divided into: a) ankylosing spondylitis (AS) according to New York modified criteria (n= 193) b) non-radiographic axSpA (nr-axSpA) (n= 62). All these patients were followed in a single reference University Hospital.

Results: We studied 255 patients with axSpA (151 men/104 women); mean age 37.8±10.6 years. In 36 (31 in AS; 5 in nr-axSpA) (14.2%) patients at least one episode of uveitis was observed after a follow-up 12.4±4.5 years. The mean age at onset of uveitis was 45.7±14.2 years. The diagnosis of uveitis preceded SpA diagnosis in 5 patients, but most of them occurred after a median of 6 [2-15] years of follow-up. Pattern of uveitis was anterior and acute in all cases, and unilateral in 83%. Median of anterior chamber cells was 1 [1-2] cells. Comparison of baseline characteristics and clinical features between patients who developed uveitis and those who did not is shown in table. Almost all patients who developed uveitis were HLAB27 positive. In these patients a lower frequency of enthesitis and inflammatory bowel disease was observed.

Table.

	Uveitis N= 36	Non uveitis N= 219	p
Baseline general features			
Age, years (mean±SD)	45.7 ± 14.2	44.7 ± 12.1	0.49
Sex, n (m/w) (%)	21/15 (58.3/41.7)	130/89 (59.4/40.6)	0.91
HLAB27, positive n (%)	35 (97.2)	130 (59.4)	0.00
Anti-TNF, n			
Adalimumab	3	53	0.06
Certolizumab	1	4	0.79
Golimumab	1	11	0.87
Infliximab	1	29	0.13
Etanercept	0	12	0.31
Disease Characteristics			
Follow-up of AxSpa, year (mean±SD)	13.64 ± 7.6	12.16 ± 9.73	0.33
AS, n (%)	31 (86.1)	162 (74.0)	0.12
nr-AxSp, n (%)	5 (13.9)	57 (26.0)	0.12
Peripheral arthritis, n (%)	9 (25.0)	67 (30.6)	0.49
Hip affection, n (%)	3 (8.3)	15 (6.8)	0.97
Enthesitis, n (%)	9 (25.0)	81 (37.0)	0.16
Dactylitis, n (%)	2 (5.5)	14 (6.4)	0.85
Psoriasis, n (%)	4 (11.1)	24 (11.0)	0.79
Inflammatory bowel disease, n (%)	1 (2.8)	15 (6.8)	0.57
Family history, n (%)	12 (33.3)	58 (26.5)	0.39

6 patients with uveitis received anti-TNF therapy and suffered from 7 episodes of uveitis after 5.6±4 years of treatment, meanwhile only 1 out of the 3 patients who were treated with anti IL-17 did a single episode of uveitis after 4.2±1.9 of follow-up. Patients treated with secukinumab developed 2.72 episodes of uveitis/100 patients/year, meanwhile those who received monoclonal anti TNF presented 2.53 episodes/100 patients / year.

Conclusion: The most frequent clinical pattern of uveitis was acute unilateral anterior. Almost all of them were HLA B27 positive. No differences were found in cumulative incidence between secukinumab and monoclonal anti-TNF.

Disclosure of Interests: Iñigo González-Mazón: None declared, Lara Sanchez-Bilbao Grant/research support from: Pfizer, Javier Rueda-Gotor: None declared, David Martinez-Lopez: None declared, Miguel A González-Gay Grant/research support from: Pfizer, Abbvie, MSD, Speakers bureau: Pfizer, Abbvie, MSD, Ricardo Blanco Grant/research support from: AbbVie, MSD, and Roche, Speakers bureau: AbbVie, Pfizer, Roche, Bristol-Myers, Janssen, and MSD
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THU0389 OBESITY IS A STRONG PREDICTOR OF WORSE CLINICAL OUTCOMES AND TREATMENT RESPONSES TO BIOLOGICS IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Obesity population are rising rapidly and have become a major health issue. Studies have shown that obesity is a low-grade inflammatory status characterized by increase in proinflammatory cytokines.
Objectives: To examine the impact of overweight or obesity on disease activity and treatment responses to biologics in patients with ankylosing spondylitis (AS) in a real-world setting.
Methods: Body mass index (BMI) is available in 1013 patients from the Chinese Ankylosing Spondylitis Imaging Cohort (CASPIC). Differences in clinical outcomes (such as BASDAI, ASDAS, BASFI, and ASAS HI) and treatment responses to biologics (ΔBASDAI and ΔASDAS) over 3, 6, 9, and 12 months are assessed between BMI categories (normal weight BMI <24 kg/m2; overweight BMI=24-28 kg/m2; obesity BMI ≥28 kg/m2) using Kruskal-Wallis test. The association between BMI and clinical characteristics and treatment responses to biologics was determined, and multivariate median regression analyses were conducted to adjust for confounders (such as age, gender, smoke, and HLA-B27).
Results: Among 1013 patients with AS, overweight accounts for 33%, while obesity for 12.4%. There were significant differences between patients who were obese or overweight and those with a normal weight regarding clinical outcomes (BASDAI: 2.90/2.56 vs 2.21; ASDAS-CRP: 2.20/1.99 vs 1.81; BASFI: 2.13/1.69 vs 1.38; ASAS HI: 6.87/5.29 vs 5.12 and BASMI: 2.35/1.76 vs 1.62; all P<0.05). After adjusting for age, gender, smoke, and HLA-B27, obesity remained associated with higher disease activity (BASDAI: β=0.55, P=0.005; ASDAS-CRP: β=0.40, P<0.001), poorer functional capacity (BASFI: β=0.58, P=0.001), worse health index (ASAS HI: β=1.92, P<0.001) and metrology index (BASMI: β=0.71, P=0.013). For TNFi users, BMI was found to be negatively correlated with changes in disease activity (ΔBASDAI and ΔASDAS) in the multivariate regression model (all P<0.05), and overweight and obese patients showed an unsatisfactory reduction in disease activity during 3-month, 6-month, 9-month, and 12-month follow-up period, compared to normal weight patients (all P<0.05).
Conclusion: Overweight or obesity impacts greatly on clinical outcomes and treatment responses to biologics in patients with ankylosing spondylitis, which argues strongly for obesity management to become central to prevention and treatment strategies in patients with AS.

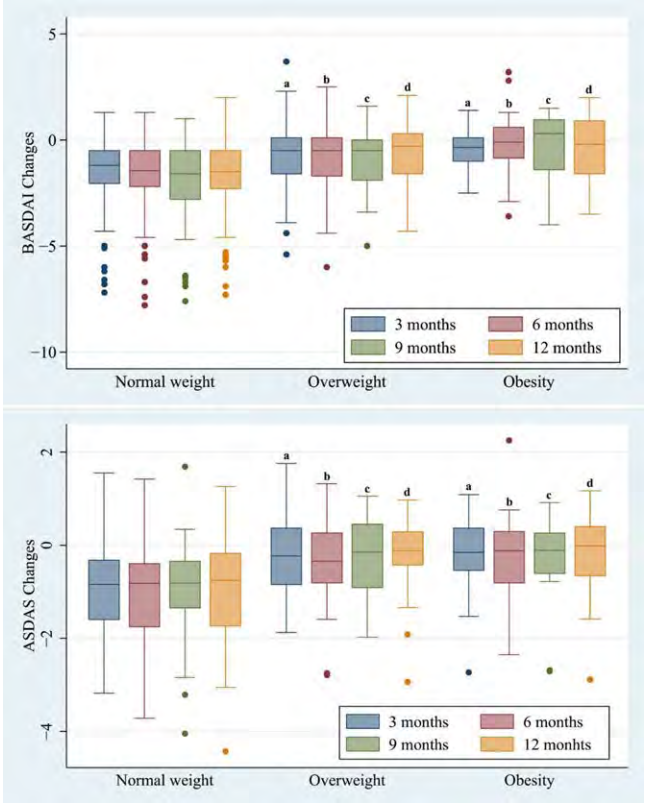


Figure 1. Changes of disease activity for TNFi users during 3-, 6-, 9- and 12-month follow-up according to BMI categories. a: vs. normal weight, P<0.05 in 3 months; b: vs. normal weight, P<0.05 in 6 months; c: vs. normal weight, P<0.05 in 9 months; d: vs. normal weight, P<0.05 in 12 months.

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[1] Maachi M, Pieroni L, Bruckert E, et al. Systemic low-grade inflammation is related to both circulating and adipose tissue TNFalpha, leptin and IL-6 levels in obese women. Int J Obes Relat Metab Disord 2004;28:993–7.

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THU0390 THE INFLUENCE OF OBESITY ON RETENTION AND TREATMENT RESPONSE OF SECUKINUMAB IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: REAL LIFE DATA FROM THE TURKBIO REGISTRY

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Background: Axial spondyloarthritis (axSpA) is a chronic, inflammatory disease that primarily affects the axial skeleton. Secukinumab is a human monoclonal antibody that binds to the protein interleukin (IL)-17A. Although some studies showed that obesity had a negative effect on the efficacy of tumor necrosis factor

Table 1

	(BMI <25) (n=33)	(BMI 25-30) (n=63)	(BMI ≥ 30) (n=39)	P	All patients (n=185)
Age (years)	40.2±11.3	45.7±11.7	50.0±10.6	**0.002** *	45.2±11
Male Gender n (%)	25 (75.8)	34 (54.0)	16 (41.1)	**0.012** **	104 (56.2)
HLA-B27 (+) n (%)	14 (73.6)	37 (84.0)	11 (44.0)	**0.013** **	76 (64.3)
Prior Naive/1/≥2 bDMARD n (%)	12 (36.3)/9 (27.3)/12 (36.3)	17 (26.9)/13 (20.6)/33 (52.4)	10 (25.6)/14 (35.8)/27 (69.2)	0.302	56 (30.3)/ 49 (26,5)/ 80 (43,2)
ASAS20 response¶	13 (61.9)/11 (57.9)/4 (57.1)	19 (48.7)/16 (59.3)/8 (42.1)	11 (40.7)/7 (29.1)/3 (50.0)	0.345/0.073/0.886	59 (518)/47 (49.5)/20 (42.6)
ASAS40 response¶	9 (42.9)/7 (36.8)/3 (42.9)	15 (39.5)/10 (37)/1 (5.3)	6 (24)/5 (20,8)/3 (50.0)	0.334/0.386/0.012	40 (35.0)/29 (30.5)/11 (23.4)
BASDAI50 response ¶	10 (47.6)/9 (47.4)/4 (57.1)	15 (39.5)/11 (40.5)/3 (15.8)	9 (34.6)/5 (21.7)/3 (50.0)	0.634/0.192/0.077	48 (42.1)/37 (38.9)/16 (34.0)
ASDAS-CII ¶	3 (14.3)/5 (26.3)/1 (14.3)	6 (17.6)/8 (30.8)/5 (27.8)	6 (23.1)/5 (21.7)/2 (33.3)	0.237/0.162/0.531	23 (21.4)/22 (23.6)/11 (23.9)
ASDAS-MI ¶	5 (23.8)/3 (15.8)/0 (0)	8 (23.5)/6 (23.1)/2 (11.1	1 (3.8)/1 (4.3)/1 (16.7)	0.237/0.162/0.531	18 (16.8)/18 (19.3)/8 (17.4)

§; Mean±SD. ¶; at 3/6/12 Months, n (%),*One-way ANOVA test, ** Pearson Chi-Sqaure Test

alpha inhibitor (TNFα -i) treatment in AS patients (1), no data is available for secukinumab.
Objectives: To evaluate the effect of obesity on the treatment response and drug survival of secukinumab in patients with axSpA.
Methods: We performed an observational cohort study based on the TURKBIO between 2018-2020. A total of 185 patients were included in the study. The patients were divided into three groups as obese (BMI≥30 kg/m^2), overweight (BMI:25-30 kg/m^2), and normal (BMI<25 kg/m^2). Disease activity was evaluated at baseline and 3, 6 and 12 months of secukinumab therapy. Clinical response was evaluated as achievement of BASDAI50, ASAS20/40, and ASDAS-Clinical and improvement (CII and MI) rates.
Results: 185 axSpA patients were identified in the registry; 135 (72%) had available BMI data. Thirty nine (28.8%) patients were obese. The mean age of obese patients was higher (p=0.002). The frequency of HLA-B27 and male gender was lower in obese group (p=0.012 and p=0.013, respectively). There was no significant difference between groups in terms of clinical response parameters at 3, 6 and 12 months (Table 1). Drug retention rates were higher in biologic naive patients(p=0.007) (Figure 1).

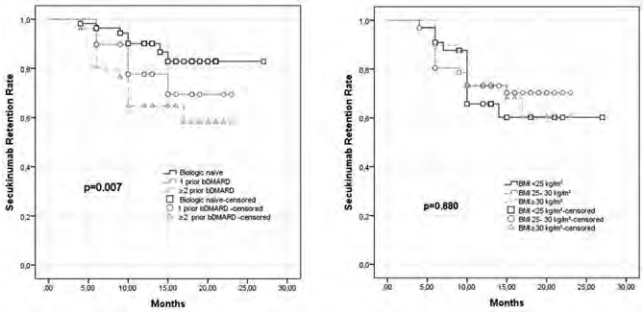


Figure 1

Conclusion: This study demonstrated that obesity had no impact on the efficacy and retention of secukinumab treatment in patients diagnosed with axSpA. The drug survival was found to be higher among biologic-naive axSpA patients compared to biologic-experienced.
References:
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Disclosure of Interests: None declared
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THU0391 THE INFLUENCE OF OBESITY ON TREATMENT RESPONSE TO BIOLOGIC AGENTS IN ANKYLOSING SPONDYLITIS

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Background: Obesity can be a factor that affects response to tumor necrosis factor inhibitors (TNFi). Few studies have investigated the impact of obesity on the response to TNFi in patients with ankylosing spondylitis (AS).
Objectives: The aim of our study was to investigate the impact of different body mass index (BMI) categories on TNFi response in patients with AS.
Methods: Patients with AS from the Korean College of Rheumatology Biologics (KOBIO) registry were included in the current study. Patients who started a first TNFi after recruitment, and had available BMI data as well as a baseline and follow-up visit at 1 year (±6 months) were included. Patients with a BMI <18.5 were excluded. Patients were categorized according to BMI: normal (BMI 18.5 to <25), overweight (BMI 25–30), and obese (BMI >30). We evaluated the proportion of patients achieving the 40% improvement in ASAS criteria (ASAS40), as well as Ankylosing Spondylitis Disease Activity Score (ASDAS) improvement status at 1 year.
Results: A total of 1003 AS patients starting a first TNFi were considered in the current study (696 patients of normal weight, 267 patients with overweight, and 40 obese patients). After at 1 year follow-up visit, obese individuals were significantly higher ASDAS-CRP levels but were not significantly lower ASDAS major improvement in comparison to patients of normal weight.
Conclusion: Obesity is associated with significantly higher ASDAS-CRP at follow-up visit in patients with AS.
Disclosure of Interests: None declared
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THU0392 PATIENT JOURNEY TO DIAGNOSIS OF ANKYLOSING SPONDYLITIS AND ITS TREATMENT PATTERNS ACROSS CENTRAL EASTERN EUROPE AND THE UNITED STATES

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Background: Long delays in the diagnosis of ankylosing spondylitis (AS) and in receiving advanced therapies signify a critical unmet need. Little is known about delays or treatment patterns in Central Eastern European (CEE) countries.
Objectives: To describe patient time to diagnosis of and its treatment patterns in CEE and the US.
Methods: Data were collected via a cross-sectional survey of rheumatologists in Czech Republic, Poland, Russia, Ukraine (Sept–Dec 2019) and US (Jun–Aug 2018) via physician-completed patient record forms. In consecutive patients with a physician-reported diagnosis of AS, rheumatologists recorded patient demographics, clinical features, time to first consultation and diagnosis and treatment history. Data were compared for CEE vs US using t-test for independent samples (continuous outcomes) and Fisher's exact test (categorical outcomes). Low rates of HLA-B27 and sacroiliitis at diagnosis may reflect combining non-radiographic axial spondyloarthritis under the diagnosis of AS in real-world practice.
Results: 209 physicians (121 CEE; 88 US) provided data for 1363 patients (876 CEE; 487 US). While some demographic differences existed between regions, estimated prevalence of HLA-B27 in patients with AS was the same between US and CEE. Not all patients were stated to have sacroiliitis at diagnosis (Table 1). Time to first consultation and time to diagnosis were longer in CEE, with more patients experiencing a delay due to another condition initially being diagnosed (Table 2). At diagnosis a similar proportion of patients in CEE and US were prescribed NSAIDs, with higher use of csDMARDs in CEE. bDMARDs were more commonly prescribed at diagnosis in the US, with increased usage continuing after diagnosis (Figure 1).

Table 1. Patient demographic and clinical characteristics

	CEE (n=876)	US (n=487)	P value*
Demographic characteristics			
Age, mean (SD)	45.4 (12.7)	46.4 (14.1)	0.21 (TT)
Male, n (%)	6319 (72.0)	344 (70.6)	0.62 (FE)
BMI, mean (SD)	25.9 (4.1)	27.4 (4.5)	<0.01 (TT)
Full time employment, n (%)	460 (53.9)	342 (70.8)	<0.01 (FE)
Caucasian, n (%)	853 (97.4)	393 (80.7)	<0.01 (FE)
Clinical features at diagnosis			
HLA-B27 positive, n (%)	592 (67.6)	329 (67.6)	1.00 (FE)
Inflammatory back pain, n (%)	712 (82.0)	369 (76.7)	0.02 (FE)
Sacroiliitis identified by X-ray, n (%)	598 (68.9)	272 (56.5)	<0.01 (FE)
Back pain >3 months, n (%)	427 (49.2)	225 (46.8)	0.46 (FE)
Physician perceived severity, n (%)			0.02 (FE)
- Mild	69 (8.7)	20 (5.1)	
- Moderate	414 (52.1)	233 (59.1)	
- Severe	312 (39.2)	141 (35.8)	

*Statistical test legend: TT=t-test; FE=Fisher's Exact.

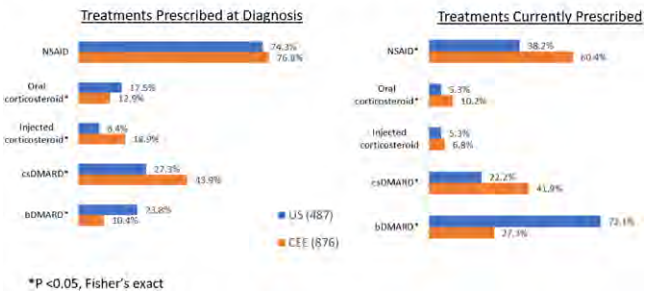
Table 2. Patient diagnosis journey

	CEE (n=876)	US (n=487)	P value*
Time from first symptoms to first consultation$^{\alpha}$, mean months (SD)	27.7 (53.7)	18.5 (57.1)	0.02 (TT)
Time from first consultation$^{\alpha}$ to diagnosis, mean months (SD)	17.8 (48.6)	6.0 (13.2)	0.02 (TT)
Reasons for delay$^{\beta}$, n (%)			
- Other condition initially diagnosed	108 (33.3)	9 (11.8)	<0.01 (FE)
- Waiting for referral to correct HCP	69 (21.3)	22 (28.9)	0.17 (FE)
- Needed test conducting to confirm diagnosis	100 (30.9)	21 (27.6)	0.68 (FE)

*Statistical test legend: TT=t-test; FE=Fisher's exact; $^{\alpha}$ First consultation with any healthcare professional about AS symptoms; $^{\beta}$Delay defined as >3 months from first consultation to diagnosis.

Conclusion: Time to diagnosis was three times longer in CEE vs the US. Despite similar prescription of NSAIDs at diagnosis in US and CEE, a greater proportion of patients currently received NSAIDs and csDMARDs in CEE, while bDMARD use in the US was greater. This suggests different treatment approaches and differences in medication access across the regions.

Figure 1: Treatments prescribed at diagnosis and currently in CEE and US



*P <0.05, Fisher's exact

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THU0393 INFLAMMATORY BOWEL DISEASES AMONG SECUKINUMAB-TREATED PATIENTS: 24 CASES FROM THE MISSIL REGISTRY

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Background: An alert regarding about the tolerance of Interleukin 17 (IL-17) inhibitors has been issued from data of randomized controlled trials showing cases of de novo inflammatory bowel diseases (IBD). In a recent analysis of pooled data from 21 clinical trials, cases of IBD events (including Crohn's disease (CD), ulcerative colitis (UC) and inflammatory bowel disease unclassified (IBDU)) were uncommon (1). Yet, real-world data are lacking.

Objectives: To describe real-world data about patients treated by IL-17 inhibitors developing new onset IBD (CD or UC).

Methods: A French national registry called MISSIL was started in February 2018 to collect the cases of patients treated by IL-17 inhibitors developing new onset IBD. This registry is conducted by rheumatologist, dermatologist and gastroenterologist learned societies specialized on immune-mediated inflammatory diseases. In France, secukinumab (SEK) has been granted market authorization since June 2016 and ixekizumab since April 2018.

Results: 24 cases under SEK were reported between February 2018 and January 2020: 3 patients with psoriasis and 21 patients with spondylwoarthritis. There were 20 patients with new onset CD and 4 with UC. Mean age was 51.7 ± 15.7 years old and 12/24 were female; 10 presented an axial spondyloarthritis, 5 a peripheral spondyloarthritis and 6 both,13/17 were HLA-B27 positive,7/19 had a radiographic sacroiliitis and 11/17 a MRI sacroiliitis. Only 2 were biological Disease-modifying antirheumatic drug (bDMARD)-naïve. Crohn's disease was mainly located at the ileum, colon and rectum. The median time to onset of symptoms was 2 (1-6) months. The main symptoms were diarrhea, nausea and vomiting and loss of weight. Median CRP at the onset of symptoms was 68 mg/L (41-140.5); 21 patients underwent biopsies, 12 were in favor of CD. IL-17 inhibitors were consistently stopped. Patients were treated by corticosteroids (16/24), mesalazine (7/24), methotrexate (3/24), thiopurines (2/24), infliximab (9/243), adalimumab (3/24), golimumab (2/24), ustekinumab (5/24). The evolution was favorable under treatment with complete resolution (4/24), improvement (11/24) or stabilization (5/24). 3 patients worsened under treatment and 1 died (massive myocardial infarction).

Conclusion: IBD flare in patients treated with IL-17 inhibitors are rare and lead to discuss the potential iatrogenic role of IL-17 inhibitor drugs. Further cases are needed to better characterize this complication. A case-control study will be conducted to identify patients at risk to develop IBD under IL-17 inhibitor.

References:

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THU0394 COMPARISON OF TREATMENT RETENTION OF SECUKINUMAB AND TNF-INHIBITORS IN PSORIATIC ARTHRITIS. OBSERVATIONAL DATA FROM A NORDIC COLLABORATION.

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Background: A head-to-head trial (EXCEED) has indicated similar effectiveness of secukinumab (SEC) and the tumor necrosis factor inhibitor (TNFi) adalimumab (ADA) in psoriatic arthritis (PsA). In the clinical setting, treatment retention serves as a combined measure of overall effectiveness and tolerability.

Objectives: To explore baseline patient characteristics, and compare treatment retention rates for SEC and each of etanercept (ETN), infliximab (IFX), golimumab (GOL), certolizimab (CZP) and ADA in PsA.

Methods: Patients starting SEC or any TNFi in 2015-2018, in the 5 Nordic countries, were identified in clinical rheumatology registers. Data were pooled for analysis and stratified by 1st, 2nd and ≥3rd line of treatment. One year treatment retention was compared by crude Kaplan-Meier curves and a proportional hazard model for risk of discontinuation, censored at 1 year and adjusted for sex, age, country and baseline CRP, patient global and use of csDMARD, with ADA as reference.

Results: In total, 6062 patients with PsA were included, contributing 8172 treatment starts (table 1). SEC was mainly used as 2nd or ≥3rd line treatment. The survival curves and 1-year treatment retention rates, stratified by line of treatment, were similar for SEC compared to the TNFis, with some differences between the different TNFi (fig 1, table 2). Adjusted hazard ratios (HR) also indicated similar risk of SEC withdrawal compared to ADA (table 2).

Table 1. Patient characteristics at treatment start

	1st line		2nd line		≥3rd line	
	SEC N=164	TNFi N=3808	SEC N=273	TNFi N=1767	SEC N=767	TNFi N=1393
Females	48%	47%	44%	42%	36%	39%
Age, years	52 (13)	49 (13)	50 (12)	50 (13)	52 (12)	51 (12)
Disease duration, years	12 (10)	10 (10)	13 (10)	13 (10)	16 (10)	16 (10)
Swollen joint count 28	3 (4)	2 (3)	2 (3)	2 (3)	3 (4)	2 (3)
CRP, mg/L	10 (18)	10 (17)	7 (11)	9 (17)	13 (22)	11 (20)
Patient global score	57 (24)	58 (24)	60 (25)	59 (26)	68 (23)	65 (24)
Concomitant therapy						
csDMARD	30%	60%	41%	57%	49%	53%
Methotrexate	24%	49%	31%	48%	40%	44%
Sulphasalazine	2%	9%	5%	5%	4%	6%

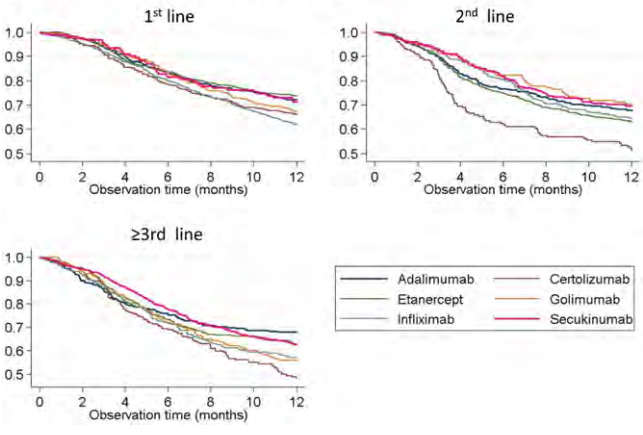
Numbers are mean (SD) unless noted otherwise

Table 2. One year treatment retention and hazard of discontinuation for SEC and TNFi

Line of treatment	Drug	N	1 year treatment retention % (95% CI)	Adjusted HR (95% CI) for discontinuation
1st line	ADA	569	73 (69-76)	Ref
	CZP	273	66 (60-72)	1.2 (0.9-1.6)
	ETN	1747	73 (71-75)	0.9 (0.7-1.1)
	GOL	212	67 (60-73)	1.2 (0.9-1.7)
	IFX	1007	62 (59-65)	1.4 (1.1-1.7)
	SEC	164	72 (63-78)	1.0 (0.7-1.4)
2nd line	ADA	415	69 (63-73)	Ref
	CZP	176	51 (43-58)	1.6 (1.2-2.2)
	ETN	701	63 (59-66)	1.2 (0.9-1.5)
	GOL	151	69 (61-76)	0.9 (0.6-1.2)
	IFX	324	65 (59-70)	1.0 (0.8-1.4)
	SEC	273	69 (62-74)	0.9 (0.7-1.2)
≥3rd line	ADA	346	67 (62-72)	Ref
	CZP	221	49 (42-56)	1.5 (1.2-2.0)
	ETN	372	62 (57-67)	1.1 (0.9-1.5)
	GOL	206	56 (49-63)	1.3 (1.0-1.8)
	IFX	248	57 (50-63)	1.3 (1.0-1.8)
	SEC	767	63 (59-67)	1.0 (0.8-1.3)

Conclusion: In this large study of bDMARD treatment of PsA in clinical practice, SEC was most often used as 2nd or ≥3rd line treatment, and the treatment retention of SEC was comparable with that of TNFi. Further analyses, taking into account other comorbidities, channeling and effectiveness will be presented.

Figure 1. Treatment retention for secukinumab and TNFi, stratified by 1st, 2nd and ≥3rd line of treatment.



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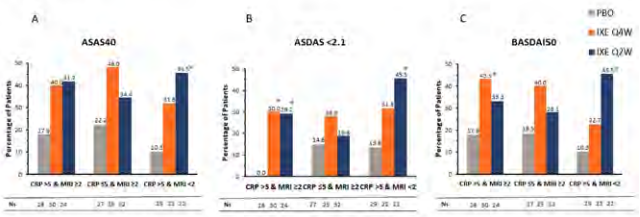
THU0395 EFFICACY OF IXEKIZUMAB ON DISEASE ACTIVITY AND QUALITY OF LIFE IN PATIENTS WITH ACTIVE NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS AND OBJECTIVE SIGNS OF INFLAMMATION, STRATIFIED BY BASELINE CRP/SACROILIAC JOINT MRI STATUS

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Background: Ixekizumab (IXE), a high-affinity anti-interleukin-17A monoclonal antibody, is effective in patients (pts) with active non-radiographic axial spondyloarthritis (nr-axSpA), who had elevated C-reactive protein (CRP) and/or active sacroiliitis on magnetic resonance imaging (MRI).[1]
Objectives: To determine if disease activity and patient-reported outcomes at Week 16 were similar between groups after stratifying pts by CRP/sacroiliac joint (SIJ) MRI status at baseline.
Methods: COAST-X (NCT02757352) included pts with active nr-axSpA and objective signs of inflammation, i.e. presence of sacroiliitis on MRI (Assessment of Spondyloarthritis International Society [ASAS]/ Outcome Measures in Rheumatology criteria) or elevation of serum CRP (>5.0 mg/L). Pts were randomized 1:1:1 to receive subcutaneous 80 mg IXE every 4 weeks (Q4W) or Q2W, or placebo (PBO). Depending on the baseline values of CRP and MRI SIJ (Spondyloarthritis Research Consortium of Canada [SPARCC] score), pts in the intent-to-treat population (N=239) were divided into 3 subgroups (CRP >5 and MRI ≥2; CRP ≤5 and MRI ≥2; CRP >5 and MRI <2). Logistic regression analysis with treatment, subgroup, and treatment-by-subgroup interaction was used to detect treatment group differences in ASAS40, Ankylosing Spondylitis Disease Activity Score (ASDAS) <2.1 (low disease activity), and Bath Ankylosing Spondylitis Disease Activity Index 50 (BASDAI50) responses at Week 16. Analysis of covariance model with baseline value, treatment, subgroup, and treatment-by-subgroup interaction was used to detect the treatment group difference in change from baseline in Short Form-36 physical component score (SF-36 PCS).
Results: The proportion of pts achieving ASAS40 (primary endpoint), ASDAS <2.1, and BASDAI50 (secondary endpoints) was higher in IXE treatment groups compared to PBO at Week 16 (Figure 1). The response rates in IXE-treated subjects were higher in all subgroups (CRP >5 and MRI ≥2; CRP ≤5 and MRI ≥2; CRP >5 and MRI <2) without consistent differences in efficacy between the subgroups. Similarly, pts in the IXE groups showed improvement in SF-36 PCS scores (secondary endpoint) versus pts on PBO at Week 16 (Figure 2).

Conclusion: Pts with active nr-axSpA and objective signs of inflammation at baseline who were treated with IXE showed an overall improvement in the signs and symptoms of the disease. The efficacy was not different between pts with both elevated CRP and active sacroiliitis on MRI and pts with either elevated CRP or active sacroiliitis on MRI.

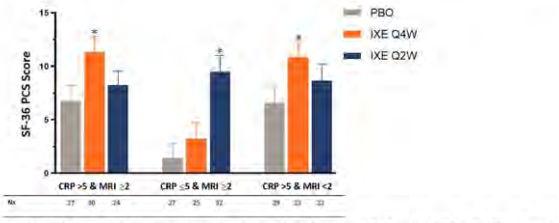
Figure 1: Disease Activity and Patient-Reported Outcomes (NRI) at Week 16 by Baseline CRP and MRI SIJ SPARCC Score



* p<0.05, as compared to PBO. Data from ITT population in 3 subgroups, N=239. Baseline CRP is defined as the last CRP value prior to first study injection.

Abbreviations: ASAS40, Assessment of Spondyloarthritis International Society 40; ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI50, Bath Ankylosing Spondylitis Disease Activity Index 50; CRP, C-reactive protein; ITT, intent-to-treat; IXE Q4W, ixekizumab every 4 weeks; IXE Q2W, ixekizumab every two weeks; MRI, magnetic resonance imaging; N, number of patients in the analysis population; NRI, non-responder imputation; Ns, number of patients in each subgroup; PBO, placebo; SIJ, sacroiliac joints; SPARCC, Spondyloarthritis Research Consortium of Canada Score.

Figure 2: Change from Baseline in SF-36 PCS Score at Week 16 by Baseline CRP and MRI SIJ SPARCC Score



* p<0.05, as compared to PBO. mBOCF data provided as least square mean ± standard error from ITT population in 3 subgroups, N=239. Baseline CRP is defined as the last CRP value prior to first study injection.

Abbreviations: CRP, C-reactive protein; ITT, intent-to-treat; IXE Q4W, ixekizumab every 4 weeks; IXE Q2W, ixekizumab every 2 weeks; mBOCF, modified baseline observation carried forward; MRI, magnetic resonance imaging; N, number of patients in the analysis population; Ns, number of patients in each subgroup; PBO, placebo; SF-36 PCS, Short Form-36 physical component score; SIJ, sacroiliac joints; SPARCC, Spondyloarthritis Research Consortium of Canada Score.

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THU0396 IMPACT OF IXEKIZUMAB ON WORK PRODUCTIVITY IN PATIENTS WITH ANKYLOSING SPONDYLITIS: RESULTS FROM THE COAST-V AND COAST-W TRIALS AT 52 WEEKS

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Background: Patients with ankylosing spondylitis (AS) are burdened with decreased work productivity.[1] Ixekizumab (IXE), a high-affinity monoclonal antibody selectively targeting interleukin-17A, has been shown to improve disease signs and symptoms in 2 phase 3 trials assessing patients with active AS.[2, 3]

Objectives: This study investigated the effect of IXE treatment for 52 weeks on work productivity and activity impairment as measured by absenteeism, presenteeism, overall work impairment, and activity impairment in patients with active AS.

Methods: COAST-V (NCT02696785) and COAST-W (NCT02696798) were phase 3, multicenter, randomized, double-blind, placebo (PBO)-controlled (COAST-V active-controlled with adalimumab) trials investigating the efficacy of IXE every 4 weeks (Q4W) and every 2 weeks (Q2W) in 341 patients with active AS naïve to biologic disease-modifying antirheumatic drugs (bDMARDs; COAST-V) and in 316 patients who were inadequate responders or intolerant to 1 or 2 tumor necrosis factor inhibitors (TNFi; COAST-W). Patients receiving PBO were switched to IXE Q4W or Q2W at Week 16; patients receiving adalimumab (ADA) were switched to IXE Q4W or Q2W at Week 20. Data for IXE Q4W and Q2W were combined for PBO/IXE and ADA/IXE groups. Changes from baseline in work productivity were measured for those reporting full- or part-time work at Weeks 16 and 52 with the Work Productivity and Activity Impairment (WPAI) Questionnaire for Spondyloarthritis.

Results: Compared to bDMARD-naïve patients (COAST-V), TNFi-experienced patients (COAST-W) were slightly older, had longer disease duration, reported less paid employment, and had greater scores for impaired work productivity, signifying more severe baseline disease. At Week 16, bDMARD-naïve patients treated with IXE Q4W or Q2W had significant improvements in activity impairment compared to placebo ($p<0.01$); TNFi-experienced patients treated with IXE Q4W or Q2W had significant improvements in presenteeism ($p<0.05$) and overall work impairment ($p<0.05$; Figure). TNFi-experienced patients treated with IXE Q2W also had significant improvement in activity impairment at Week 16 ($p<0.05$; Figure). Improvements were sustained through Week 52 (Figure).

Conclusion: Both bDMARD-naïve and TNFi-experienced patients with AS receiving IXE had greater improvements in aspects of work productivity compared to placebo. Improvements were sustained through Week 52.

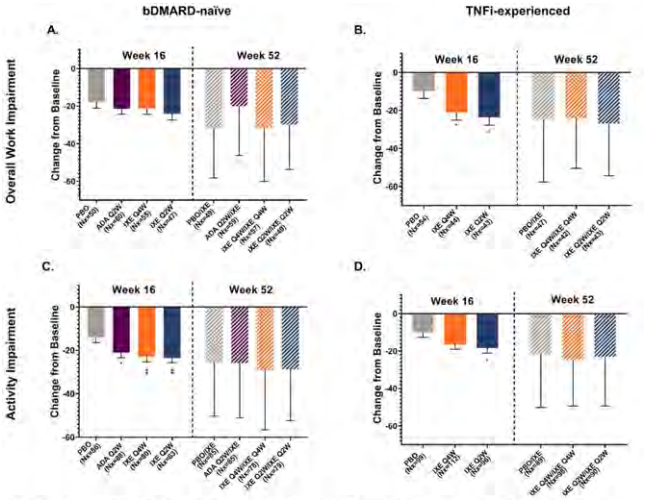
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For Week 16, values are LSM (SE) from ANCOVA with missing data imputed via mBOCF. For Week 52, values are mean (SD) with missing data imputed via mBOCF.

At Week 16, patients receiving placebo (COAST-V, COAST-W) or were switched to IXE Q4W or Q2W. At Week 20, patients receiving ADA (COAST-V) were switched to IXE Q4W or Q2W. Data for IXE Q4W and IXE Q2W were combined for the PBO/IXE and ADA/IXE groups.

COAST-V treatment groups: PBO (N=87) → PBO/IXE (N=86); ADA Q2W (N=90) → ADA Q2W/IXE (N=86); IXE Q4W (N=81) → IXE Q4W/IXE Q4W (N=78); IXE Q2W (N=83) → IXE Q2W/IXE Q2W (N=79).

COAST-W treatment groups: PBO (N=104) → PBO/IXE (N=93); IXE Q4W (N=114) → IXE Q4W/IXE Q4W (N=98); IXE Q2W (N=95) → IXE Q2W/IXE Q2W (N=90).

Absenteeism, Presenteeism, and Overall Work Impairment were measured in patients reporting full- or part-time work.

P-values were from ANCOVA (treatment vs. placebo) for Weeks 0-16. *=p<0.05, ‡=p<0.01, †=p<0.001.

ADA Q2W=40 mg adalimumab every 2 weeks; bDMARD=biological disease-modifying anti-rheumatic drug; IXE Q2W=80 mg ixekizumab every 2 weeks; IXE Q4W=80 mg ixekizumab every 4 weeks; LSM=least squares mean; mBOCF=modified baseline observation carried forward; N=number of patients in the treatment group; Na=number of patients with non-missing values. PBO=placebo; SD=standard deviation; SE=standard error; TNFi=tumor necrosis factor inhibitor

Figure. Changes from baseline in Overall Work Impairment in A) bDMARD-naïve (COAST-V) and B) TNFi-experienced (COAST-W) patients and Activity Impairment in C) bDMARD-naïve and D) TNFi-experienced patients.

THU0397

SYMPTOMS OF PERIPHERAL ARTHRITIS ARE SIGNIFICANTLY IMPROVED IN PATIENTS WITH ANKYLOSING SPONDYLITIS TREATED WITH SECUKINUMAB

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Background: Ankylosing spondylitis (AS) is a chronic inflammatory disease of the axial skeleton associated with pain, stiffness, and disability.[1] Up to 66% of patients (pts) with AS may also have peripheral involvement, including swollen and tender joints (STJs),[2,3] which are associated with worse overall disease activity.[4] A previous analysis showed that secukinumab, a selective inhibitor of interleukin 17A, led to significant improvements in efficacy outcomes vs placebo, regardless of peripheral joint involvement.[3] However, the effect of secukinumab on symptoms of peripheral arthritis in pts with AS was not assessed.

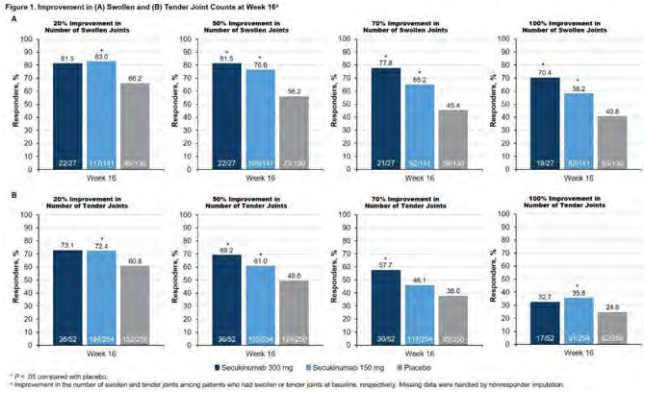
Objectives: The objective of this analysis was to assess changes in peripheral symptoms in pts with AS treated with secukinumab vs placebo.

Methods: Data from pts with active AS and peripheral symptoms who were enrolled in MEASURE 1 (NCT01358175), 2 (NCT01649375), 3 (NCT02008916), and 4 (NCT02159053) were pooled in this post hoc, hypothesis-generating analysis. No adjustments for multiple comparisons were made. Pts with peripheral symptoms were identified by the presence of STJs, based on 44-joint counts at baseline (BL). Pts received subcutaneous (SC) secukinumab every 4 weeks at doses of 300 mg with an intravenous (IV) loading dose (MEASURE 3 only), 150 mg with an IV or SC loading dose, or placebo. Treatment response through Week 16 was assessed based on the proportions of pts who achieved improvements of 20%, 50%, 70%, or 100% in the number of swollen and number of tender joints and improvements in the BASDAI score for question 3 and Patient Global Assessment (PGA). Changes in the number of swollen and number of tender joints were assessed in pts with swollen or tender joints at BL, respectively.

Results: This pooled analysis included 560 pts with AS and STJs at BL (Table). At Week 16, treatment with secukinumab led to significantly greater proportions of pts achieving reductions in the number of swollen (Fig 1A) or tender (Fig 1B) joints compared with placebo; the treatment effect was more pronounced in reduction of swollen joints. Furthermore, a greater proportion of secukinumab-treated pts achieved complete resolution of swollen or tender joints vs placebo (Fig 1). Secukinumab also led to significant improvements in peripheral pain/swelling (Fig 2A) and disease activity (Fig 2B) vs placebo, as assessed using BASDAI question 3 and the PGA, respectively.

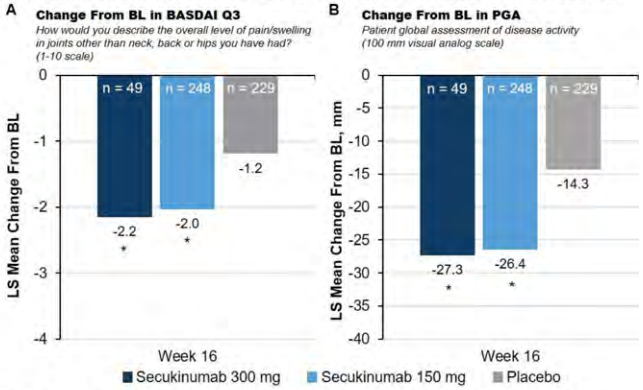
Table. Patient Characteristics at Baseline

	Secukinumab		Placebo (n = 252)
	300 mg (n = 52)	150 mg (n = 256)	
Age, mean, y	43.6	43.7	44.9
Time since diagnosis, mean, y	5.6	7.2	7.3
Male, %	63.5	62.1	57.5
PGA of Disease Activity, mean, mm	73.4	71.7	70.1
BASDAI question 3, mean	6.3	6.6	6.4
Swollen 44-joint count, mean	1.9	2.6	2.5
Tender 44-joint count, mean	7.1	7.8	7.9



* P < .05 compared with placebo.
† Improvement in the number of swollen and tender joints among patients who had swollen or tender joints at baseline, respectively. Missing data were handled by nonresponder imputation.

Figure 2. Change From Baseline in (A) BASDAI Question 3 and (B) Patient Global Assessment at Week 16 in Patients With Peripheral Swollen or Tender Joints at Baseline[a]



BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BL, baseline; LS, least squares; PGA, Patient Global Assessment; Q, question
* *P* < .05 compared with placebo.
[a] LS mean and *P* value are from mixed-effect model repeated measures analysis, with treatment, visit, and TNF-α inhibitor status as factors, baseline and weight as covariates, and treatment by visit and baseline by visit as interaction terms.

Conclusion: In parallel with its previously reported efficacy in axial symptoms,[3] secukinumab led to significant improvements in symptoms of peripheral arthritis in pts with AS. Significant improvements were seen in both tender and swollen joints.

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THU0398 DRUG RETENTION RATES AND TREATMENT OUTCOMES IN 1860 AXIAL SPONDYLOARTHRITIS PATIENTS TREATED WITH SECUKINUMAB IN ROUTINE CLINICAL PRACTICE IN 13 EUROPEAN COUNTRIES IN THE EUROSPA RESEARCH COLLABORATION NETWORK

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Background: To determine the real-life 6- and 12-month secukinumab effectiveness in Europe overall, as well as stratified by prior biologic disease-modifying anti-rheumatic drug (bDMARD)/targeted synthetic (ts)DMARD use.

Objectives: Real-life data from axSpA patients treated with secukinumab from 13 countries in the European Spondyloarthritis (EuroSpA) Research Collaboration Network were pooled. We calculated proportions of patients achieving Bath Ankylosing Spondylitis Disease Activity Score (BASDAI) <2/<4 and Ankylosing Spondylitis Disease Activity Score (ASDAS) <1.3/<2.1 at 6 and 12 months, including with LUNDEX adjustments (crude value adjusted for drug retention). Retention rates were compared between b/tsDMARD naïve, 1 prior and ≥2 prior b/tsDMARD users with Kaplan-Meier analyses with log rank test and disease states by Chi-square test.

Methods: A total of 1860 axSpA patients were included (Table 1). Overall 6/12-month secukinumab retention rates were 82%/72% and higher in bionaïve patients (Table 2, Figure). Significant differences in retention rates in-between the registries were found. Inactive disease/low-disease-activity (LDA) were achieved more often in bionaïve patients (Table 2).

Table 1

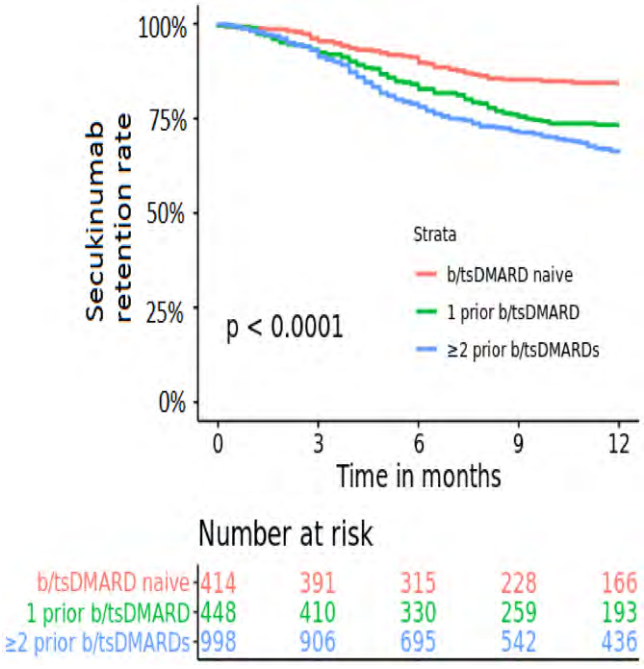
	All patients (n=1860)	b/tsDMARD naïve (n=414)	1 prior b/tsDMARD (n=448)	≥2 prior b/tsDMARDs (n=998)
Age (years), mean (SD)	47 (12)	45 (12)	47 (12)	48 (12)
Men, %	57%	68%	58%	49%
Years since diagnosis, mean (SD)	10 (9)	8 (9)	10 (9)	11 (9)
Current smokers, %	25 %	27%	25%	23%
Patient's global (0-100), median (IQR)	70 (50-81)	80 (60-90)	64 (50-80)	70 (50-82)
Physician's global (0-100), median (IQR)	45 (25-63)	64 (43-78)	45 (22-60)	40 (20-58)
C reactive protein (mg/L), median (IQR)	8 (3-25)	15 (5-31)	7 (3-25)	6 (2-22)
Erythrocyte sedimentation rate (mm/h), median (IQR)	22 (9-44)	30 (14-44)	24 (8-45)	18 (8-42)
Pain (0-100), median (IQR)	70 (50-81)	80 (65-90)	65 (49-80)	70 (50-80)
BASDAI, median (IQR)	6.2 (4.6-7.6)	6.8 (5.2-8.0)	5.9 (4.2-7.2)	6.1 (4.4-7.6)
BASFI, median (IQR)	5.5 (3.2-7.3)	6.1 (3.2-7.6)	4.8 (2.8-6.8)	5.5 (3.3-7.2)
ASDAS, median (IQR)	3.6 (2.9-4.3)	4.2 (3.5-4.8)	3.5 (2.7-4.2)	3.5 (2.8-4.2)

Table 2

	Months	All patients (n=1860)	b/tsDMARD naïve (n=414)	1 prior b/tsDMARD (n=448)	≥2 prior b/tsDMARDs (n=998)	p-value*
Secukinumab retention rate, % (95%CI)	6	82% (80-84%)	90% (87-93%)	83% (79-86%)	78% (76-81%)	0.001
	12	72% (69-74%)	84% (81-88%)	73% (69-78%)	66% (63-69%)	<0.001
BASDAI <2, %						
Crude	6	26	37	35	18	<0.001
LUNDEX adjusted		21	34	28	13	<0.001
Crude	12	25	41	29	18	<0.001
LUNDEX adjusted		16	31	18	11	<0.001
BASDAI <4, %						
Crude	6	51	71	60	40	<0.001
LUNDEX adjusted		40	65	47	30	<0.001
Crude	12	51	76	56	39	<0.001
LUNDEX adjusted		32	57	36	23	<0.001
ASDAS <1.3, %						
Crude	6	9	13	13	6	0.001
LUNDEX adjusted		7	12	11	5	<0.001
Crude	12	11	18	15	7	0.002
LUNDEX adjusted		7	13	9	4	0.002
ASDAS <2.1, %						
Crude	6	24	32	26	20	0.002
LUNDEX adjusted		19	29	21	15	<0.001
Crude	12	27	44	27	21	<0.001
LUNDEX adjusted		17	33	17	12	<0.001

*Comparisons between b/tsDMARD naïve, 1 prior and ≥2 prior b/tsDMARD users were performed with Kaplan-Meier with log-rank test or Chi-Square test, as appropriate

Conclusion: In this real-life study of 1860 patients with axSpA in 13 European countries secukinumab retention was high and significantly higher for bionaïve patients. Overall, a higher proportion of bionaïve than previous b/tsDMARD users achieved inactive disease/LDA.



Figure

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THU0399

HOW DO TNF-ALPHA-INHIBITORS IN MEDICAL HISTORY AFFECT PATIENT REPORTED OUTCOMES AND RETENTION IN ANKYLOSING SPONDYLITIS PATIENTS TREATED WITH SECUKINUMAB IN REAL WORLD? - GERMAN AQUILA STUDY

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Background: Secukinumab (SEC), a fully human monoclonal antibody that selectively inhibits interleukin 17A, is approved for treatment of patients with ankylosing spondylitis (AS). However, there is lack of real-world evidence on SEC treatment outcomes, disease activity, physical functioning and on its retention, especially in anti-tumor necrosis factor (anti-TNF) naïve patients and patients pretreated with different anti-TNFs in medical history.[1]

Objectives: The aim of this interim analysis is to evaluate SEC treatment outcomes on disease activity, physical functioning and retention rates in AS patients stratified by number of anti-TNFs (naive, 1 or ≥2) in medical history.

Methods: AQUILA is an ongoing, multi-center, non-interventional study. AS and psoriatic arthritis patients treated with SEC in daily practice are enrolled and observed from baseline (BL, d0 or d1 of study start) up to week 52 according to clinical routine. Real-world effectiveness of SEC was assessed prospectively and analyzed as observed. Here, we report interim results of SEC effectiveness on different treatment outcomes in AS patients by means of validated questionnaires such as patient´s global assessment (PGA), Bath Ankylosing Disease Activity Index (BASDAI), and Assessment of Spondyloarthritis Health Index (ASAS-HI). In addition, retention rates (time from study inclusion until premature SEC treatment discontinuation) were assessed through Kaplan-Meier plots. This interim analysis focuses on *anti-TNF naïve* and AS patients treated with *1 anti-TNF* or *≥2 anti-TNFs* in medical history. Wilcoxon tests were conducted to show significant differences between the subgroups.

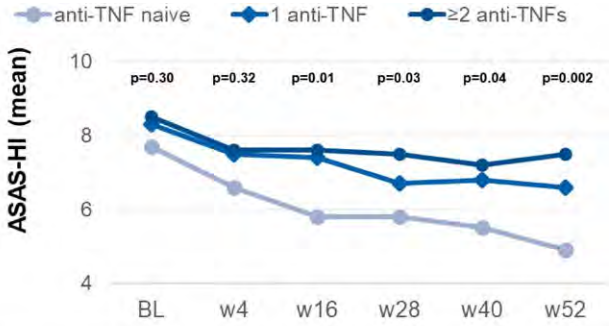
Results: At BL, 311 AS patients were included; 72 (23.2%) of them received SEC already for more than 1 day up to more than 6 months before BL. Most AS patients were anti-TNF-experienced (71.1%): 82 (26.4%) and 139 (44.7%) AS patients had 1 or ≥2 prior anti-TNF treatments, respectively. BL scores for PGA, BASDAI and ASAS-HI were similar between the different anti-TNF subgroups. Constant improvement was shown in all parameters from BL up to week 52, irrespective of prior anti-TNF treatment (PGA-*anti-TNF naïve*: 5.9 to 3.5, PGA-*1 anti-TNF:* 6.1 to 4.2 and PGA-*≥2 anti-TNFs:* 6.7 to 5.1; BASDAI-*anti-TNF naïve*: 5.3 to 3.4, BASDAI-*1 anti-TNF:* 5.5 to 3.7 and BASDAI-*≥2 anti-TNFs:* 5.7 to 4.7). However, overall better improvement was observed in *anti-TNF naïve* patients, as seen by the example of ASAS-HI (Fig. 1). Between 30% and 40% of patients prematurely discontinued SEC treatment in the subgroups *1 anti-TNF* and *≥2 anti-TNFs*, respectively, while only about 20% did so in the *anti-TNF naïve* AS patients (Fig. 2).

Conclusion: SEC has shown to improve disease activity, physical functioning and QoL in anti-TNF-naïve and pretreated AS patients in a real-world setting. The benefits of SEC were numerically more distinct in anti-TNF-naïve patients. Moreover, SEC demonstrated high retention rate, particularly in anti-TNF-naïve patients, thereby confirming previously reported real-world data on SEC from EuroSpA research collaboration network.[2]

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Disclosure of Interests: Uta Kiltz Grant/research support from: AbbVie, Amgen, Biogen, Novartis, Pfizer, Consultant of: AbbVie, Biocad, Eli Lilly and Company, Grünenthal, Janssen, Novartis, Pfizer, UCB, Speakers bureau: AbbVie, MSD, Novartis, Pfizer, Roche, UCB, Jan Brandt-Juergens: None declared, Peter Kästner Consultant of: Chugai, Novartis, Elke Riechers Grant/research support from: AbbVie, Chugai, Lilly, Janssen, Novartis, Pfizer, Roche, UCB, Consultant of: AbbVie, Chugai, Novartis, UCB, Daniel Peterlik Employee of: Novartis Pharma GmbH, Hans-Peter Tony Consultant of: AbbVie, Astra-Zeneca, BMS, Chugai, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, Sanofi
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anti-TNF naive	n=79	n=69	n=75	n=60	n=59	n=56
1 anti-TNF	n=72	n=53	n=64	n=58	n=52	n=41
≥2 anti-TNFs	n=123	n=89	n=114	n=83	n=65	n=59

Figure 1. Change of health in AS patients treated with SEC stratified by anti-TNF pretreatment

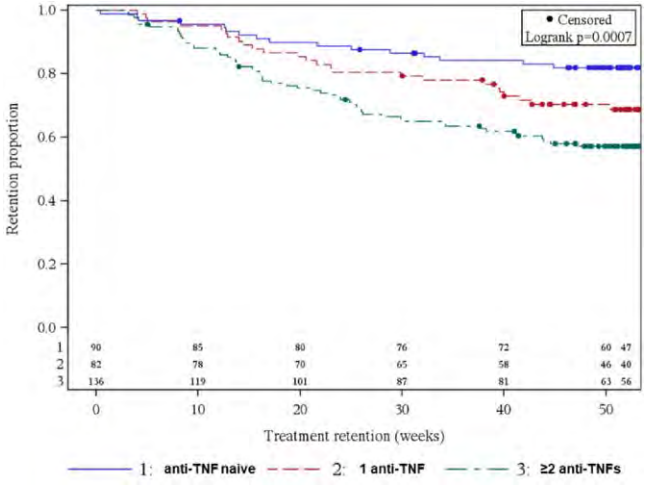


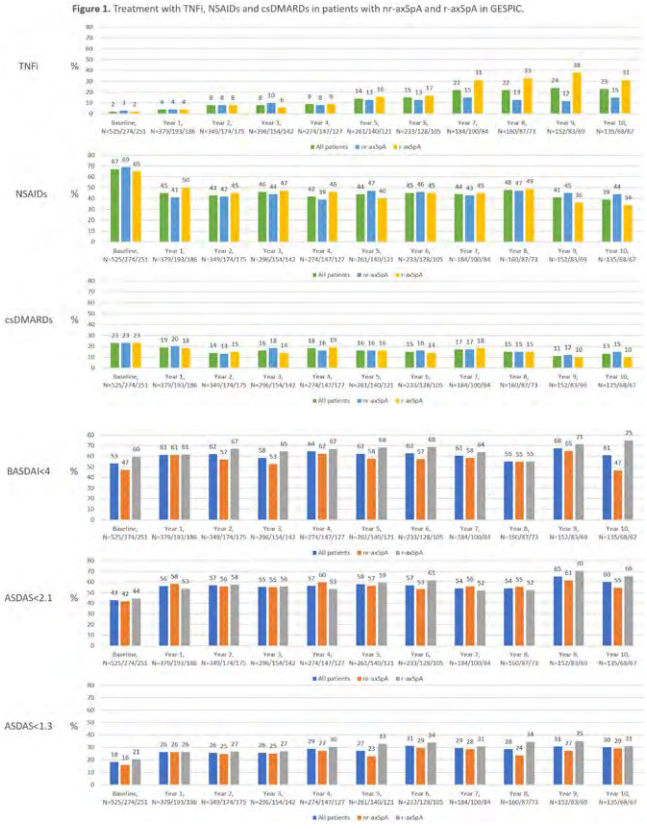
Figure 2. SEC treatment retention depending on anti-TNF pretreatment (Kaplan-Meier plot)

THU0400

CLINICAL COURSE OF EARLY AXIAL SPONDYLOARTHRITIS OVER TEN YEARS: LONG-TERM RESULTS FROM THE GERMAN SPONDYLOARTHRITIS INCEPTION COHORT

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Background: Previous studies showed that patients with non-radiographic and radiographic axial spondyloarthritis (nr- and r-axSpA) have similar disease burden and similar response to anti-inflammatory therapy given similar level of inflammatory activity. Only little is known, however, about long-term disease course in patients with early axSpA.
Objectives: To investigate the long-term (up to 10 years) clinical course of patients with early axSpA.
Methods: In total, 525 patients with early axSpA (r-axSpA with symptom duration ≤10 years and nr-axSpA with symptom duration ≤5 years) from the German Spondyloarthritis Inception Cohort (GESPIC) were included. The final patient classification was based on central reading results in 458 patients with available pelvic X-rays, and on local rheumatologist judgement in 67 patients. A total of 251 patients were finally classified as r-axSpA and 274 as nr-axSpA. Clinical evaluation, which included disease activity (BASDAI, C-reactive protein – CRP, ASDAS) as well as therapy recording, was performed at baseline and every 6 months thereafter until year 2 and annually thereafter till year 10. Treatment was conducted at the discretion of the local rheumatologist.
Results: Since the cohort has started prior to introduction of TNF inhibitors (TNFi), only 2% patients received TNFi at baseline that increased to 23% at year 10 (15% in nr-axSpA and 31% in r-axSpA) – Figure 1. The use of NSAIDs and csDMARDs decreased in both groups (Figure 1), while use of systemic steroids did not change substantially (9% at baseline, 8% at year 10). The proportion of patients with low disease activity according to BASDAI (<4) was higher in r-axSpA as compared to nr-axSpA at almost all time points, while the proportion of patients with low disease activity according to ASDAS (<2.1), as well as with ASDAS inactive disease (<1.3) was similar between nr-axSpA and r-axSpA (Figure 2). In the group of patients who completed year 10 (n=134 in total, 68 with nr-axSpA, 67 with r-axSpA) the same trends in therapy and disease activity were observed.
Conclusion: Patients with nr-axSpA and r-axSpA showed a similar disease course in terms of disease activity on the group level. The drop-out rate in this observational cohort was overall high, but comparable between groups. The lower proportion of patients with nr-axSpA being treated with TNFi might reflect a later introduction of TNFi for this indication.



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Disclosure of Interests: Denis Poddubnyy Grant/research support from: AbbVie, MSD, Novartis, and Pfizer, Consultant of: AbbVie, Bristol-Myers Squibb, Eli Lilly, MSD, Novartis, Pfizer, Roche, UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, MSD, Novartis, Pfizer, Roche, UCB, Valeria Rios Rodriguez Consultant of: Abbvie, Novartis, Murat Torgutalp: None declared, Maryna Verba: None declared, Johanna Callhoff: None declared, Mikhail Protopopov Consultant of: Novartis, Fabian Proft Grant/research support from: Novartis Pharma GmbH, Consultant of: Consultancy / speaker fees from: Abbvie, BMS, Celgene, Lilly, MSD, Novartis, Pfizer, Roche, UCB, Speakers bureau: Consultancy / speaker fees from: Abbvie, BMS, Celgene, Lilly, MSD, Novartis, Pfizer, Roche, UCB, Judith Rademacher: None declared, Hildrun Haibel Consultant of: Abbvie, Jansen, MSD, and Novartis, Speakers bureau: Abbvie, Jansen, MSD, and Novartis, Joachim Sieper Consultant of: AbbVie, Boehringer Ingelheim, Eli Lilly and Company, Janssen, Merck, Novartis, Pfizer, Roche, and UCB Pharma, Speakers bureau: AbbVie, Boehringer Ingelheim, Eli Lilly and Company, Janssen, Merck, Novartis, Pfizer, Roche, and UCB Pharma, Martin Rudwaleit Consultant of: AbbVie, BMS, Celgene, Janssen, Eli Lilly, MSD, Novartis, Pfizer, Roche, UCB Pharma
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THU0401

IMPACT OF BODY COMPOSITION MEASURES ON THE RESPONSE TO BIOLOGICAL DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Data on the impact of body weight and body mass index (BMI) on the response to biological disease-modifying anti-rheumatic drugs (bDMARDs) in axial spondyloarthritis (axSpA) including ankylosing spondylitis (AS) are still contradictory. Data on the impact of different components of the body composition on the treatment response are lacking.

Objectives: To investigate the impact of body composition on the response to biological disease-modifying anti-rheumatic drugs (bDMARD) in patients with AS after 6 months of treatment.

Methods: Patients with AS (radiographic axSpA), fulfilling the modified New York criteria and starting a bDMARD therapy were recruited between 2015 and 2019 in an extension of the prospective German Spondyloarthritis Inception Cohort (GESPIC-AS). All patients were required to be candidates for bDMARD therapy at baseline with high disease activity (BASDAI >=4 and/or ASDAS >=2.1) despite previous treatment with nonsteroidal anti-inflammatory drugs. Disease activity measures (BASDAI, CRP, ASDAS), as well as body composition parameters were assessed at baseline and after 6 months of bDMARD treatment. Body composition was assessed by the bioelectrical impedance analysis (BIA). Weight, body mass index (BMI), fat mass index (FMI), fat free mass index (FFMI), skeletal muscle mass value (SMM), visceral adipose tissue (VAT), total body water (TBW), and extracellular water (ECW) values were collected. The primary measure of the treatment response was ASDAS change at month 6 as compared to baseline.

Results: A total of 129 patients with AS were included in this cohort. BIA was performed in 77 patients. There were 71.4% males, and 85.7% were HLA-B27 positive. At baseline, BASDAI was 5.4±1.4, CRP was 12.8±16.5 mg/l, and ASDAS - 3.0±1.0. The baseline BMI was 25.0±4.3 kg/m^2. A total of 75 patients were treated with TNFi, 2 patients received an IL-17 inhibitor.

A higher BMI at baseline was associated with a worse response to bDMARD therapy that was attributable to both, the fat mass as reflected by FMI and to the fat-free mass reflected by FFMI, but not to SMM or VAT or water components – Table. This effect was independent of age, sex, symptom duration, HLA-B27 status and ASDAS at baseline.

Conclusion: Both fat mass and fat free mass have an impact on the response to bDMARDs after 6 months of treatment in patients with AS. Interestingly, skeletal muscle mass, visceral fat as well as water components showed no association with treatment response.

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Disclosure of Interests: : Valeria Rios Rodriguez Consultant of: Abbvie, Novartis, Mikhail Protopopov Consultant of: Novartis, Fabian Proft Grant/research support from: Novartis Pharma GmbH, Consultant of: Consultancy / speaker fees from: Abbvie, BMS, Celgene, Lilly, MSD, Novartis, Pfizer, Roche, UCB, Speakers bureau: Consultancy / speaker fees from: Abbvie, BMS, Celgene, Lilly, MSD, Novartis, Pfizer, Roche, UCB, Judith Rademacher: None declared, Burkhard Muche: None declared, Anne Katrin Weber: None declared, Susanne Lüders: None declared, Hildrun Haibel Consultant of: Abbvie, Jansen, MSD, and Novartis, Speakers bureau: Abbvie, Jansen, MSD, and Novartis, Maryna Verba: None declared, Joachim Sieper Consultant of: AbbVie, Boehringer Ingelheim, Eli Lilly and Company, Janssen, Merck, Novartis, Pfizer, Roche, and UCB Pharma, Speakers bureau: AbbVie, Boehringer Ingelheim, Eli Lilly and Company, Janssen, Merck, Novartis, Pfizer, Roche, and UCB Pharma, Denis Poddubnyy Grant/research support from: AbbVie, MSD, Novartis, and Pfizer, Consultant of: AbbVie, Bristol-Myers Squibb, Eli Lilly, MSD, Novartis, Pfizer, Roche, UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, MSD, Novartis, Pfizer, Roche, UCB

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THU0402

SERUM MARKERS OF BONE RESORPTION, FORMATION, AND MINERALIZATION DURING 8 YEARS OF TNF-A BLOCKING THERAPY IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Ankylosing spondylitis (AS) is a chronic inflammatory disease, characterized by both excessive bone formation and bone loss. The bone turnover marker (BTM) bone-specific alkaline phosphatase (BALP) plays a central role in bone mineralization. Our previous study demonstrated that 3 years of TNF-α blocking therapy results in a significant increase in BALP.[1] However, longer follow-up is needed to investigate whether BALP stays elevated during TNF-α blocking therapy and also to explore the course of other BTM, osteocalcin (OC), procollagen type 1 N-terminal peptide (PINP) and serum type 1 collagen C-telopeptide (sCTX) in AS.

Objectives: To evaluate serum markers of bone resorption, formation, and mineralization during 8 years of TNF-α blocking therapy in AS patients.

Methods: Included were consecutive AS outpatients from the University Medical Center Groningen (UMCG) attending the Groningen-Leeuwarden Axial SpA (GLAS) cohort and who were treated with a maximum of 2 TNF-α blockers for at least 8 years. Patients were excluded when they used bisphosphonates at baseline or during follow-up. Data for a specific visit was coded as missing when patients either had experienced a fracture or received systemic corticosteroids within 1 year of that particular visit. Clinical and laboratory measurements were performed at baseline (before start of TNF-α blocking therapy), 3 and 6 months as well as 1, 2, 4, 6 and 8 years. Markers of bone formation OC, PINP and BALP, and marker of bone resorption sCTX were measured in serum. Z-scores of BTM were calculated using matched 10-years-cohorts of a Dutch reference group to correct for the normal influence that age and gender have on bone turnover. Serum levels of 25-hydroxyvitamin D (25(OH)D3) were assessed yearly. Generalized estimating equations were used to analyze BTM Z-scores over time within patients. Simple contrast was used to compare follow-up visits to baseline. P-values <0.05 were considered statistically significant.

Results: In total, 37 AS patients were analyzed; 62% were male, 86% HLA-B27+, mean age was 38.6 ± 10.4 years, median symptom duration 14 years (IQR 10-25), median CRP 13 mg/L (IQR 6-25), and 30% had low vitamin 25(OH)D3 status (<50) at baseline. 35% of patients switched to a second TNF-α inhibitor during follow-up. $ASDAS_{CRP}$ improved significantly during treatment, from mean 3.8 ± 0.9 at baseline to 1.9 ± 0.9 after 8 years of follow-up (P<0.001). 25(OH)D3 levels were stable at group level, median 58 nmol/L (IQR 45-70) at baseline and 60 nmol/L (IQR 50-70) after 8 years. Bone regulation marker OC Z-score was

Table. Univariable and multivariable linear regression analysis of the association between response to bDMARD treatment (change in the ASDAS score after 6 months) and body composition parameters in patients with AS (n=77)

Variables	Univariable	Multivariable analysis*						
	Analysis ß (95%CI)	Model 1 ß (95%CI)	Model 2 ß (95%CI)	Model 3 ß (95%CI)	Model 4 ß (95%CI)	Model 5 ß (95%CI)	Model 6 ß (95%CI)	Model 7 ß (95%CI)
BMI, kg/m2	-0.016 (-0.063; 0.031)	-0.043 (-0.079; -0.006)	-	-	-	-	-	-
FMI, kg/m2	-0.024 (-0.103; 0.054)	-	-0.065 (-0.128; -0.003)	-	-	-	-	-
FMMI,kg/m2	-0.010 (-0.133; 0.112)	-	-	-0.138 (-0.253; -0.022)	-	-	-	-
SMM, kg	0.026 (-0.020; - 0.071)	-	-	-	0.012 (-0.044; 0.069)	-	-	-
VAT, liters	0.069 (-0.099; 0.238)	-	-	-	-	-0.095 (-0.248; 0.057)	-	-
TBW, liters	0.020 (-0.016; 0.056)	-	-	-	-	-	0.007 (-0.036; 0.051)	-
ECW, liters	0.054 (-0.43; 0.150)	-	-	-	-	-	-	0.005 (-0.98; 0.107)

*Adjusted for age, sex, HLA-B27 status, symptom duration, and ASDAS at baseline.

BMI: Body Mass Index; FMI: Fat Mass Index; SMM: Skeletal Muscle mass; VAT: Visceral Adipose Tissue; AS: ankylosing spondylitis; bDMARD: biological disease-modifying anti-rheumatic drug; CI: 95% confidence interval.

found to be significantly increased only after 3 months of TNF-α blocking therapy compared to baseline. No significant changes during follow-up were found for collagen resorption marker sCTX Z-score. Collagen formation marker PINP Z-score was significantly increased after 3 and 6 months as well as 2 years of TNF-α blocking therapy. Bone mineralization marker BALP Z-score was significantly increased at all time points up to and including 2 years and returned to baseline levels during 4 to 8 years of TNF-α blocking therapy (Figure 1).

Conclusion: In this subgroup of AS patients with established and active disease responding to TNF-α blocking therapy, we observed that the bone turnover balance favored bone formation during the first years of TNF-α blocking therapy, which corresponds to previously reported improvement in bone mineral density, especially at the lumbar spine.[1] New finding of our study is that after 8 years of treatment, markers of bone resorption, formation, and mineralization were all comparable to baseline values.

References:

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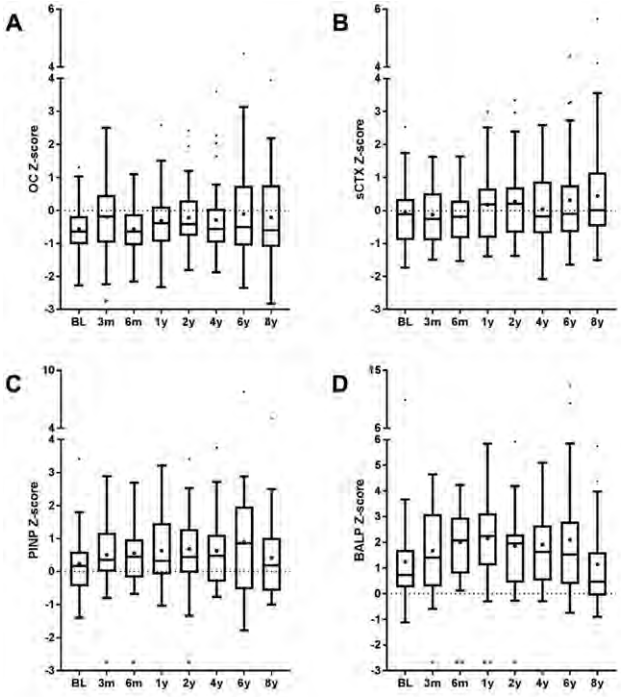


Figure 1. The effect of 8 years of TNF-α blocking therapy on bone formation markers OC (A), sCTX (B), PINP (C) and BALP (D) in patients with AS (n=37). Z-scores were calculated to correct for the effect of age and gender on bone turnover. Box-and-whisker plots (Tukey): boxes indicate medians with interquartile ranges, ● indicates mean; whiskers indicate 1.5 times interquartile distances; • indicate outliers. * indicate p-value of <0.05 and ** indicate p-value of <0.01.

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THU0403 THE EFFECT OF SPINAL STABILIZATION EXERCISES ON SPINAL CURVES DIAGNOSED WITH ANKYLOSING SPONDYLITIS

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Background: Postural deformities can cause changes in spinal curvatures patients with ankylosing spondylitis. In these patients, preventive and therapeutic approaches are needed for spinal deformities (1). Positive effects of the spinal stabilization exercises are manifested in reducing pain, maintaining mobility, improving posture, increasing aerobic capacity and improving quality of life (2).

Objectives: The aim of this study is to investigate the effect of stabilization exercises on spinal curvatures in s ankylosing spondylitis patients.

Methods: Twenty-eight ankylosing spondylitis patients (25 females, 3 males) with a mean age of 30.87 ± 9.13 years were included in the stabilization exercises program. The patients performed spinal stabilization exercises two days a week for six weeks. Stabilization training includes training of deep muscles providing diaphragmatic breathing, neutral spine position control training and local motor control, and motor control training of global muscles, dynamic stabilization exercises and strengthening training. Thoracic kyphosis and lumbar lordosis curvature of patients in an upright position were evaluated with Spinal Mouse (SM) device before and after therapy program. The SM device is a reliable, valid, safe, quick method that can be used in the clinics and researches of the adults with no side effects.

Results: At the end of 6 weeks of treatment, there was a decrease in the total curvature degree of the thoracic vertebrae in the sagittal axis (**p=0.026**). No significant difference was found in the lumbal region (p= 0.109).

Table 1. Differences of Total Curve Degrees

	Pre-Exercises Program Mean ± SD	Post-Exercises Program Mean ± SD	z	p
Thoracal Total Curve Degrees	43.50±8.11	42.57±7.70	-2.232	***0.026**
Lumbal Total Curve Degrees	-26.42±8.46	-23.77±7.15	-1.604	0.109

*p<0.05, SD: Standart Deviation

Conclusion: Stabilization exercises are effective in reducing thoracic kyphosis in patients with ankylosing spondylitis patients. The use of these exercises in treatment programs will contribute significantly to improving spinal alignment and preventing postural deformities.

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Disclosure of Interests: : None declared

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THURSDAY, 04 JUNE 2020

Crystal diseases, metabolic bone diseases other than osteoporosis

THU0404 INFLUENCE OF URATE TRANSPORTOSOME FOR HYPERURICEMIA AND GOUT

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Background: Gouty arthritis, caused by a persistent increase in serum uric acid level, can be caused by underexcretion of uric acid by uric transporters; however, the effects of allelic variants of urate transportosome are yet to be fully determined.

Objectives: In this study we investigated the effects of 10 genes of urate transportosome in a cohort of patients with primary hyperuricemia and gout.

Methods: The cohort consisted of 114 hyperuricemic individuals; 207 gout patients; and 274 normouricemic controls.

Results: We identified 39 non-synonymous allelic variants in the 10 genes of urate transportosome in hyperuricemia/gout cohort. For 22 variants, a European MAF <0.0001 is documented. From the total of 39 identified variants we selected 23 variants for functional characterization based on a) finding of a newly identified variant, b) MAF variant was significantly different in the group of patients with hyperuricemia/gout, c) with high probability, in silico predictions showed devastating influence of variant on protein function.

Conclusion: Although further analyzes are needed to elucidate the contribution of urate transportosome to urate homeostasis, our results clearly show that ABCG2 transporter analysis has significant clinical potential. Of the identified non-synonymous allelic variants of the urate transportosome, rs2231142 (p.Q141K) in the ABCG2 gene, proved to be the most clinically significant on the age onset (P < 0.0002, Kruskal-Wallis test).

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Disclosure of Interests: : Blanka Stiburkova: None declared, Katerina Pavelcova: None declared, Jana Bohata: None declared, Marketa Pavlikova: None declared, Tappei Takada: None declared, Yu Toyoda: None declared, Lenka Hasikova: None declared, Jakub Zavada Speakers bureau: Abbvie, UCB, Sanofi, Elli-Lilly, Novartis, Zentiva, Accord, Karel Pavelka Consultant of: Abbvie, MSD, BMS, Egis, Roche, UCB, Medac, Pfizer, Biogen, Speakers bureau: Abbvie, MSD, BMS, Egis, Roche, UCB, Medac, Pfizer, Biogen
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THU0405 SERUM METABOLIC PROFILING ANALYSIS OF GOUT PATIENTS BASED ON UHPLC-Q-TOF/MS

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Background: Gout is a common kind of inflammatory arthritis with metabolic disorders. The detailed pathogenesis of gout remains largely unknown. Metabolomics has become an important tool in detecting the new pathogenesis and biomarkers. However, few studies have focused on the serum metabolic profiling of gout.
Objectives: The study aims to investigate the metabolic profiling of gout patients with ultra-performance liquid chromatograph quadrupole time-of-flight mass spectrometry (UPLC-Q-TOF-MS), and explore the potential pathological mechanisms and biomarkers.
Methods: Serum samples from 31 gout patients and 31 healthy controls were analyzed by UPLC-Q-TOF-MS. Principal components analysis (PCA), orthogonal partial least squares-discriminant analysis (OPLS-DA) and Hierarchical clustering analysis were performed to detect different compounds between the two groups. Receiver operating characteristic (ROC) curve analysis and pathway analysis of the different metabolites were conducted.
Results: A total of 9192 compounds were detected, of which 138 significantly different compounds were selected, according to the criteria of (Variable importance in projection (VIP)>3, P<0.05). Eventually, 96 reliable metabolites matched the HMDB database were confirmed. ROC curve results showed that the area under the curve (AUC) value of 4-hydroxytriazolam for gout was 0.933 (CI95%: 0.875-0.992), yielding a highest AUC value, with the sensitivity of 83.9% and specificity of 93.5%. The pathway analysis results indicated that the significantly different metabolites were mainly involved in “primary bile acid biosynthesis”, “purine metabolism” and “glycerophospholipid metabolism”.
Conclusion: The serum metabolic profiling in gout patients were significantly different from healthy subjects. 4-hydroxytriazolam was the potential biomarkers. Primary bile acid biosynthesis may be a novel metabolic pathway of gout.

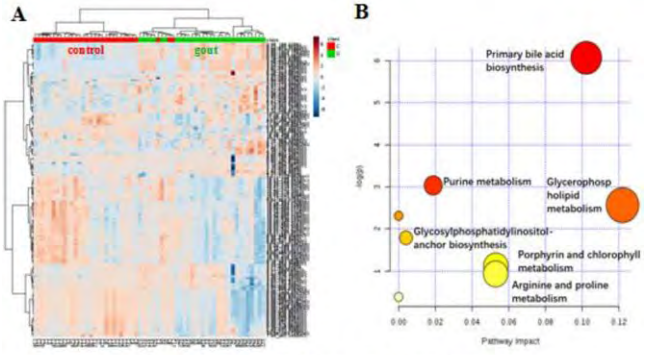


Figure.1 A: Hierarchical clustering analysis of the significantly different compounds. B: Pathway analysis of the significantly different metabolites.

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Disclosure of Interests: : None declared
DOI: 10.1136/annrheumdis-2020-eular.5963

THU0406 IDENTIFICATION OF INTRACELLULAR VACUOLES IN SYNOVIAL FLUID WITH CALCIUM PYROPHOSPHATE AND MONOSODIUM URATE CRYSTALS

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Background: Synovial fluid analysis using polarized microscopy is the gold standard for the diagnosis of crystal-related arthritis. In our experience, we have noted that, when calcium pyrophosphate (CPP) crystals are observed, they sometimes appear within intracellular vacuoles. However, this phenomenon is not seen in those samples containing monosodium urate (MSU) crystals. This finding has been scantly reported in the literature, but may be useful in clinical practice to ensure accurate crystal identification.
Objectives: Our study aims to assess whether the presence of vacuoles contributes to identifying the type of crystal, and also to gauge the frequency of their presentation.
Methods: We conducted an observational study in a rheumatology unit between February and June of 2019. Synovial fluids containing CPP or MSU crystals, obtained in daily clinical practice, were consecutively included for analysis. Two observers simultaneously analyzed the presence of vacuoles by ordinary light and phase contrast microscopy in less than 24 hours after their extraction, using a microscope equipped with two viewing stations. The primary study variable was to determine whether CPP and MSU crystals are seen inside intracellular vacuoles, and to calculate the frequency of this finding for each type of crystal, estimating their 95% confidence interval (95% CI) and comparing rates using Fisher’s exact test.
Results: Twenty-one samples were obtained. Data is given in the Table. MSU crystals were present in 7 (33.3%) and CPP crystals in 14 (66.6%). Interestingly, none of the MSU samples showed crystal-containing vacuoles (95% CI 0-35.4%). On the contrary, cytoplasmic vacuoles containing crystals were present in all of the CPP samples (95% CI 78.5-100%). The findings were confirmed by phase-contrast microscopy. Differences were statistically significant (p<0.001).

Table.

SAMPLES ACCORDING TO TYPE OF MICROCRYSTAL (n=21)	SAMPLES WITH VACUOLS (UNDER ORDINARY LIGHT)	SAMPLES WITH VACUOLS (UNDER PHASE CONTRAST)
CPP (14; 66.6%)	14 (100%) *(95%CI 78.5-100%)*	14 (100%) *(95%CI 78.5-100%)*
MSU (7; 33.3%)	0 (0%) *(95%CI 0-35.4%)*	0 (0%) *(95%CI 0-35.4%)*

Conclusion: The presence of vacuoles may be a useful and easy way to differentiate MSU and CPP crystals when performing synovial fluid microscopy in clinical practice, since it appears to be a distinctive feature in CPP crystal fluids.
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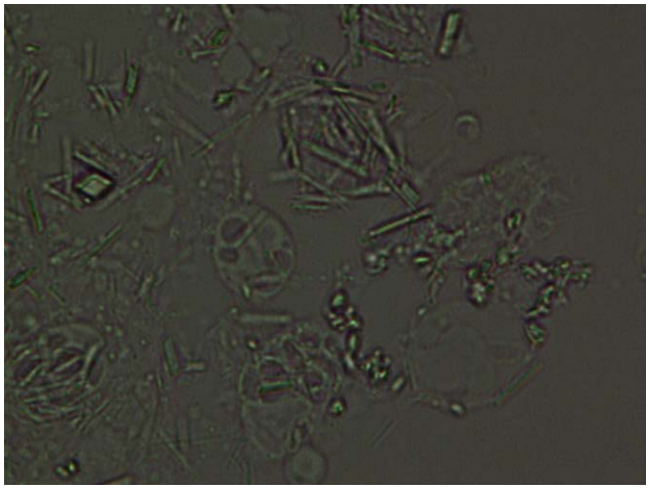


Image 1. Microscopy with ordinary light. Cells with cytoplasmic vacuoles are observed, as well as abundant intra and extracellular CPP crystals.

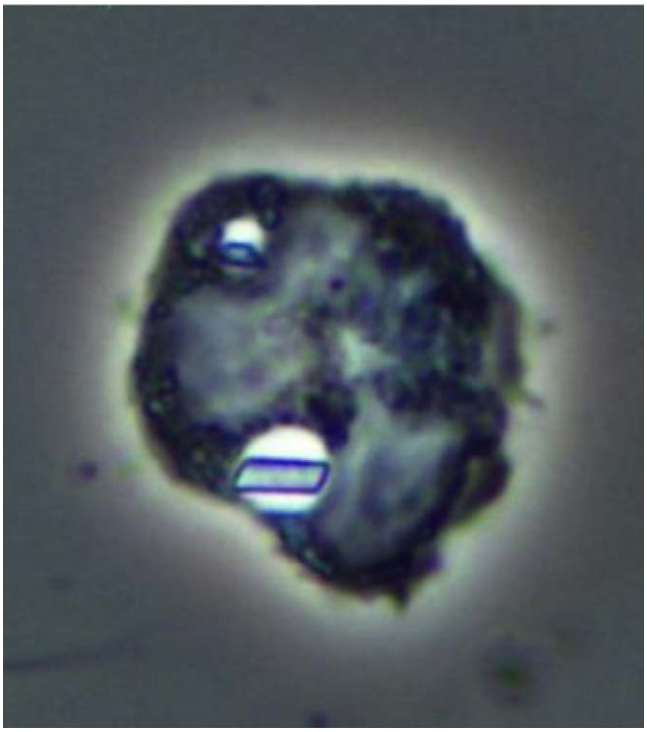


Image 2. Microscopy with phase contrast technique. Cells with intracellular vacuoles are observed inside which have microcrystals with parallelepiped morphology, compatible with CPP.

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THU0407 THE VALUE OF SONOGRAPHY IN THE INTERCRITICAL PHASE OF GOUT

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Background: Disease remission is the goal of therapy for many chronic rheumatic diseases. In 2016, provisional gout remission criteria were proposed (1). To the best of our knowledge, no studies have compared ultrasound (US) findings in gouty patients with and without remission.
Objectives: To determine the prevalence of US pathologic findings in patients with gout fulfilling and not fulfilling the provisional remission criteria and to investigate the value of the US findings as predictors of a gouty flare within 6 months.
Methods: Patients with a diagnosis of gout according to the 2015 classification criteria (2) were recruited in this prospective, monocentric study. The following clinical information was recorded at baseline and after 6 months: number of gouty flares in the preceding 6 months, number of subcutaneous tophi, current serum urate level, and patient reported outcomes (pain visual analogue scale and patient global assessment visual analogue scale). Bilateral US assessment of the following anatomical areas was performed (3): elbow, wrist, II metacarpophalangeal joint, knee, ankle and I metatarsophalangeal joint. US evidence of tophi, aggregates, double contour sign and synovitis were recorded according to the correspondent OMERACT definitions.
Results: Forty-nine patients with gout were consecutively enrolled. The remission criteria were satisfied in 9 (18.4%) patients. Monosodium urate (MSU) deposits and findings of synovitis were observed by US less frequently in patients in remission (55.6% and 22.2%), compared with those not fulfilling the criteria (100.0% and 72.5%) (p values<0.01). The US MSU total score was 1.0; 0.0–2.0 (median and inter-quartile range) for patients in remission, compared with 6.0; 5.0–7.0 for those not fulfilling the criteria (p<0.01). US synovitis total score was significantly correlated with patient global assessment (R=0.55, p<0.01), patient pain (R=0.51, p<0.01) and number of gouty attacks in the previous 6 months (R=0.36, p=0.03), whereas MSU total score was associated with the number of gouty attacks in the previous 6 months (R=0.49, p<0.01), the number of subcutaneous tophi (R=0.45, p<0.01), patient pain (R=0.41, p=0.01), patient global assessment (R=0.41, p<0.01). At logistic regression analysis, the presence of subcutaneous tophi (OR=2.8, p=0.02), CRP level (OR=6.5, p=0.04) and US synovitis score (OR=2.0, p=0.04) and were predictors of subsequent development of gouty flare within 6 months.
Conclusion: This study provides new insights into the inter-critical phase of gout, highlighting the clinical relevance of US synovitis as a predictor of subsequent development of gouty flare and joint pain. Despite MSU deposits are still detectable in patients satisfying the 2016 provisional remission criteria for gout, the remission is associated with less US detected MSU deposits.
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Disclosure of Interests: : Edoardo Cipolletta: None declared, Andrea Di Matteo Grant/research support from: the publication was conducted while Dr. Di Matteo was an ARTICULUM fellow, Giada Brunori: None declared, Antonella Moretti: None declared, Walter Grassi Speakers bureau: Prof. Grassi reports personal fees from AbbVie, personal fees from Celgene, personal fees from Grünenthal, personal fees from Pfizer, personal fees from Union Chimique Belge Pharma, outside the submitted work., Emilio Filippucci Speakers bureau: Dr. Filippucci reports personal fees from AbbVie, personal fees from Bristol-Myers Squibb, personal fees from Celgene, personal fees from Roche, personal fees from Union Chimique Belge Pharma, personal fees from Pfizer, outside the submitted work.
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THU0408 EFFECT OF NEW-ONSET GOUT ON KIDNEY TRANSPLANT OUTCOMES: A RETROSPECTIVE COHORT ANALYSIS OF THE UNITED STATES RENAL DATA SYSTEM

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Background: Gout is a frequent comorbidity in kidney transplant (KT) recipients. However, assessing the independent effect of gout on KT outcomes is difficult because of multiple confounders (e.g., temporal changes in estimated glomerular filtration rate [eGFR], cyclosporine or tacrolimus dose, urate-lowering medication use) that obscure a clear picture of gout's potential impact.
Objectives: This investigation assessed if the development of new-onset gout after KT was an independent risk factor for loss of graft function, as assessed by the need for maintenance hemodialysis following KT.
Methods: This retrospective cohort study analyzed data on patients in the United States Renal Data System (USRDS) who received a primary KT between 1/1/2008 and 12/31/2015. The date of transplantation was the 'index' date. Eligible patients were required to have ≥24 months of Medicare coverage and no prior history of gout, defined as ≥1 claim with a gout diagnosis code in the 24 months prior to the index date. All patients were also required to have ≥12 months of coverage post index. Patients who died, experienced graft failure, or returned to dialysis <12 months post index were excluded. Because the first year following transplant is associated with the highest frequency of rejections, we evaluated subjects beginning 1 year after transplant. The exposure of interest was new-onset gout, defined as the presence of ≥2 claims for gout post index, and the primary endpoint was return to dialysis >12 months post index. Baseline time-invariant confounders included recipient and donor demographics and clinical characteristics at index. Time-varying confounders included body mass index (BMI) adjusted tacrolimus and cyclosporine dose, eGFR, and urate-lowering medication use post index. Patients who died or lost Medicare coverage >12 months post index were censored; all patients remaining at the end of the study period (12/31/2016) were also censored. A marginal structural model (MSM) was fitted to determine the relative risk of new-onset gout on return to dialysis, while controlling for both time-invariant and time-varying confounders.
Results: 18,525 of 466,589 KT recipients in the USRDS met study eligibility. Within the observation period, 1,399 (7.6%) developed new-onset gout and 1,420 (7.7%) returned to dialysis >12 months post index. Median time from index to new-onset gout and from index to return to dialysis was 16.2 months (IQR: 33.4) and 32.8 months (IQR: 28.4), respectively. Adjusting for baseline time-invariant and time-varying confounders via the MSM showed new-onset gout was associated with a 51% increased risk of return to dialysis >12 months post index (RR: 1.51, 95% CI: 1.03, 2.20).

Conclusion: New-onset gout was independently associated with a 51% increased risk of return to dialysis >12 months after primary KT compared to a control cohort without gout. To our knowledge, this is the first observation of this outcome in an appropriately controlled cohort study of KT recipients with gout. Results from this analysis may have important implications for the monitoring and management of new-onset gout in the kidney transplant population.

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Disclosure of Interests: : Justin Li: None declared, David Yin: None declared, Zheng Wang: None declared, Mark Brigham: None declared, Brian LaMoreaux Shareholder of: Horizon Therapeutics, Employee of: Horizon Therapeutics, Jeffrey Kent Shareholder of: Horizon Therapeutics, Employee of: Horizon Therapeutics, Megan Francis-Sedlak Shareholder of: Horizon Therapeutics, Employee of: Horizon Therapeutics, Richard Johnson Shareholder of: Colorado Research Partners LLC, XORTX Therapeutics, Consultant of: Horizon Therapeutics, Eli Lilly, Speakers bureau: Horizon Therapeutics, Nandini Hadker: None declared, Kevin Francis: None declared, Herman Sanchez: None declared, Gavin Miyasato: None declared
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THU0409 A RANDOMIZED, PHASE 2 STUDY EVALUATING THE EFFICACY AND SAFETY OF ANAKINRA IN DIFFICULT-TO-TREAT ACUTE GOUTY ARTHRITIS: THE ANAGO STUDY

K. Saag[1], A. So[2], P. Khanna[3], R. Keenan[4], S. Ohlman[5], T. Kullenberg[5], L. Osterling Koskinen[5], M. H. Pillinger[6], R. Terkeltaub[7]. [1]*Uni Alabama, Birmingham, United States of America*; [2]*Uni Lausanne, Lausanne, Switzerland*; [3]*Uni Michigan, Ann Arbor, United States of America*; [4]*Duke Uni School Med, Durham, United States of America*; [5]*Sobi, Stockholm, Sweden*; [6]*New York Uni School Med, New York, United States of America*; [7]*Uni California San Diego, La Jolla, United States of America*

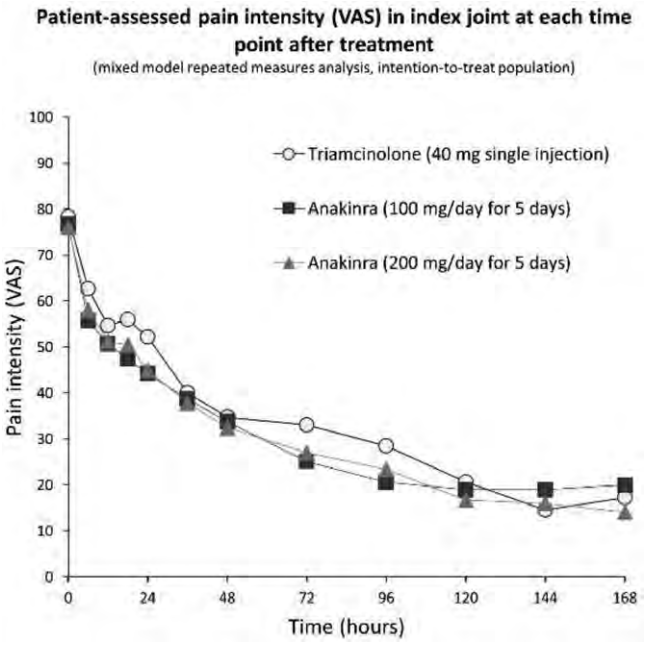
Background: In gout, urate crystals deposited in and around joints trigger episodes of acute arthritis, mediated by the proinflammatory cytokine IL-1β. In uncontrolled studies, the IL-1 receptor antagonist anakinra appears effective in reducing pain and signs of acute flares in patients with difficult-to-treat gout. However, confirmatory, adequately-powered, prospective trials are lacking. The 'anaGO-study' (anakinra in gout) was a multi-center, randomized, double-blind, double-dummy, phase 2 study investigating the efficacy and safety of anakinra in acute gout (NCT03002974).

Objectives: The primary objective was to evaluate the efficacy of two regimens of anakinra (100 or 200 mg daily s.c. injections for 5 days) compared to triamcinolone (single i.m. injection 40 mg) with respect to patient-assessed pain intensity. The primary endpoint was change in pain intensity from baseline to 24-72 hours (average of 24, 48 and 72 hours) in the most affected joint measured on a visual analogue scale (0-100 VAS). Secondary outcomes included: time to onset of effect, time to response, time to pain resolution, time to rescue medication use, patient's and physician's assessments of global response, clinical signs, inflammatory biomarkers and safety.

Methods: Patients were recruited who had acute gout based on ACR/EULAR 2015 gout classification criteria, and were unsuitable for anti-inflammatory therapy with NSAIDs and colchicine due to contraindication, intolerance or inefficacy. Patients were randomized to each group in a 1:1:1 ratio and stratified by urate-lowering therapy use (yes/no) and BMI (<30.0 or ≥30.0 kg/m^2).

Results: 165 patients were randomized; 110 to anakinra (56 to 100 mg/day, 54 to 200 mg/day) and 55 to triamcinolone; 108 and 53 were included in the primary analysis, respectively. The median (range) age was 55 (25-83) years, 87% were male, mean disease duration was 8.7 years and mean number of self-reported flares during the past year was 4.5. The pain intensity, from baseline to 24-72 hours, decreased in both treatment groups; mean (95% CI) change was -39.4 (-46.8, -32.0) for triamcinolone and -41.2 (-46.3, -36.2) for anakinra. The 100 mg and 200 mg doses of anakinra were comparably effective in decreasing pain (100 mg/day: -41.8 [-48.9, -34.8] and 200 mg/day: -40.7 [-47.9, -33.4]). Mean (95% CI) difference in pain reduction between anakinra and triamcinolone treatment groups was -1.8 (-10.8, 7.1) (p-value = 0.688 for primary endpoint). The majority of secondary efficacy endpoints were numerically in favor of anakinra, and in most instances also statistically significant, in comparison to triamcinolone, e.g. physician's assessment of clinical signs at 72 hours and patient's and physician's assessment of global response at Day 8. No unexpected safety findings were identified in any of the treatment groups.

Conclusion: Anakinra and triamcinolone reduced patient-assessed gout flare pain to similar degrees in patients for whom conventional therapy was ineffective or contraindicated. Both doses of anakinra showed comparable efficacy in pain reduction. The majority of secondary efficacy endpoints favored anakinra. Anakinra was shown to be an additional option for use during acute gout flares.



Disclosure of Interests: : Kenneth Saag Grant/research support from: Horizon, Sobi, Shanton, Grant/research support from: Horizon Pharma, Sobi, Shanton, Consultant of: Horizon and Sobi, Consultant of: Horizon Pharma, Amgen, Radius, LG-Pharma, Takeda, Sobi, Atom, Arthrosi, Alexander So Consultant of: Sobi, Grünenthal, Puja Khanna Grant/research support from: Dyve, Selecta, Sobi, Consultant of: Sobi, Horizon, Robert Keenan Consultant of: Sobi, Selecta, Horizon, Sven Ohlman Shareholder of: Sobi, Employee of: Former employee of Sobi, Torbjörn Kullenberg Shareholder of: Sobi, Employee of: Former employee of Sobi, Lisa Osterling Koskinen Shareholder of: Sobi, Employee of: Sobi, Michael H. Pillinger Grant/research support from: Horizon, Hikma, Consultant of: Sobi, Horizon, Robert Terkeltaub Consultant of: Sobi, Selecta, Horizon, Astra-Zeneca
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THU0410 COMPANION IMMUNOSUPPRESSION WITH AZATHIOPRINE INCREASES THE FREQUENCY OF PERSISTENT RESPONSIVENESS TO PEGLOTICASE IN PATIENTS WITH CHRONIC REFRACTORY GOUT

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Background: Pegloticase is a mammalian recombinant uricase coupled to monomethoxy polyethylene glycol that is approved in the US for treatment of patients with chronic refractory gout and causes profound reductions in serum urate. However, treatment with pegloticase is limited by the induction of anti-drug antibodies and loss of responsiveness in nearly half of treated patients.

Objectives: The goal of this study was to determine whether co-therapy with azathioprine (AZA) would increase the frequency of chronic refractory gout patients who had persistent urate lowering from pegloticase therapy.

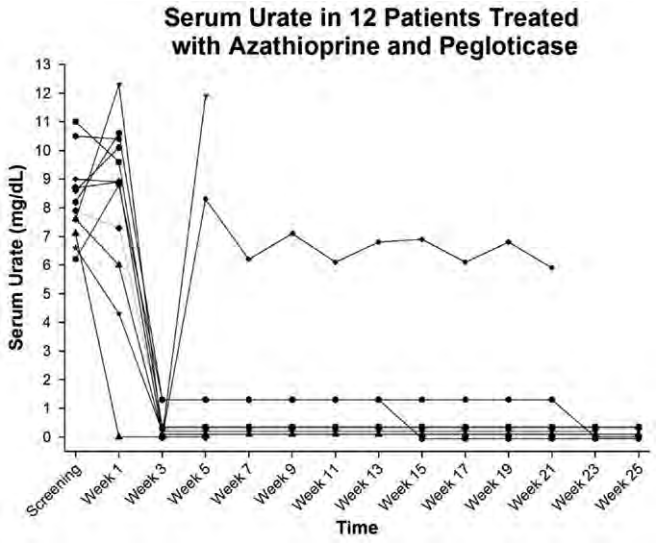
Methods: This open label multicenter study enrolled subjects with chronic gout who failed to lower serum urate to <6 mg/dL despite medically indicated doses of urate lowering therapy (NCT02598596). Patients were screened for adequate levels of the AZA metabolizing enzyme thiopurine methyl transferase and then started on daily oral AZA 1.25 mg/kg for 1 week and then 2.5 mg/kg for

the remainder of the trial. Blood levels of AZA metabolites 6-thioguanine and 6-methylmercaptopurine were measured biweekly. After receiving 2 weeks of AZA, patients were started on pegloticase (8 mg IV) and were treated biweekly for 24 weeks. The primary endpoint was the persistent lowering of serum urate to <6 mg/dL at the last three consecutive study visits. Patients who had an increase in serum urate to >6 mg/dL while on therapy did not receive additional pegloticase. All patients received infusion prophylaxis with hydrocortisone as well as gout flare prophylaxis.

Results: To date, 12 patients have been enrolled. All patients were male, 75% white and 25% African American. Mean age was 62.4 ± 14.7 years, the mean BMI was 31.1 ± 4.5 and the mean duration of gout was 13.8 ± 9.2 years. At baseline, all patients had visible tophi; 58.3% suffered from gout flares; 81.8% had hypertension; 45.5% had dyslipidemia and 9.0% had coronary artery disease. Of the 12 patients, 6 have completed the full course of treatment with persistent urate lowering and 2 remain on treatment also with persistent urate lowering (figure). 2 patients lost the urate lowering effect, both after 2 doses of pegloticase, and did not receive additional therapy. 1 patient experienced an infusion reaction during the first dose (1 infusion reaction in 90 infusions [1.1%] in the entire trial to date) and 1 subject had subjective symptoms of AZA intolerance with no laboratory abnormalities; these subjects discontinued the study and were not evaluable for the endpoint. No adverse events related to AZA were reported and gout flares were noted in 6 subjects (mean 1.5 flares/patient with flares).

Conclusion: AZA can be used safely in subjects with chronic refractory gout and appears to increase the frequency of subjects experiencing long term lowering of serum urate.

References:



Disclosure of Interests: : Hope Rainey: None declared, Herbert S.B. Baraf Grant/research support from: Horizon; Gilead Sciences, Inc.; Pfizer; Janssen; AbbVie, Consultant of: Horizon; Gilead Sciences, Inc.; Merck; AbbVie, Speakers bureau: Horizon, Anthony Yeo Employee of: Horizon, Peter Lipsky Consultant of: Horizon Therapeutics

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THU0411 STRUCTURED CARDIOVASCULAR ASSESSMENT INCLUDING CAROTID ULTRASOUND IN GOUT: ANALYSIS OF SUBSEQUENT EVENTS IN THE FOLLOW UP

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Background: Gout is an independent cardiovascular (CV) risk factor. This excess of morbidity and mortality requires optimal management, especially in high-risk individuals. So, the inclusion of subclinical atherosclerosis screening by carotid ultrasound in the initial evaluation may help to accurately stratify the CV risk. However, longitudinal outcomes using this technique are not available in gout.

Objectives: To analyze the new CV events occurred in patients with gout after structured CV assessment incorporating carotid ultrasound.

Methods: Retrospective analysis of an inception cohort of new patients with crystal-proven gout. At baseline, a structured CV assessment was performed considering age, gender, traditional risk factors, CV and renal disease, laboratory data, SCORE and Framingham risk tools and carotid ultrasound; according to 2013 ESC guidelines, CV risk was stratified as low, moderate, high or very high. The cohort includes 356 patients, mean aged 64 years (SD 14.0) mostly males (86.0%), 21.8% with tophaceous gout and mean serum urate at diagnosis of 8.2mg/dL (SD 1.8). The CV risk stratification was: low in 20 (5.6%), moderate in 47 (13.2%), high in 34 (9.6%), and very high risk in 242 (68.0%). Major CV events (coronary disease (CD), heart failure (HF), stroke, peripheral artery disease (PAD) and CV death) were recorded during the follow-up by electronic case reports review. A binary composite endpoint of "new major CV event" was used. The incidence after inclusion in the cohort was estimated. To evaluate potential baseline predictors (clinical and gout-related) of CV events, a Cox regression model was built.

Results: Mean follow-up in the cohort was 41.5 months (SD 16.8). Forty new major CV events have been identified (incidence 3.25%/patient-year), distributed as follows: HF 1.46 (n=18), CV death 0.65 (n=8), CD 0.49 (n=6), stroke 0.33 (n=4), and PAD 0.33%/patient-year (n=4). Per risk stratification, the incidence of a new event was 0.16%/patient-year in the high-risk group and 3.01%/patient-year in the very high-risk, while no events occurred in low and moderate groups. The table shows the univariate and multivariate analysis of baseline variables. An independent association and a trend towards significance were noted for age and to be classified at a very high CV risk at baseline, respectively.

	Univariate regression		Multivariate regression	
	HR (95%CI)	*P*	HR (95%CI)	*P*
Age	1.07 (1.04-1.11)	<0.001	1.04 (1.00-1.08)	0.031
Female gender	3.27 (1.68-6.33)	<0.001	1.24 (0.55-2.81)	0.605
Body mass index	1.00 (0.94-1.06)	0.863	-	-
Glomerular filtration rate	0.98 (0.97-0.99)	<0.001	1.00 (0.99-1.01)	0.766
Very high CV risk at baseline	9.54 (2.30-39.64)	0.002	4.11 (0.89-19.02)	0.070
Serum urate at diagnosis	1.19 (1.00-1.42)	0.052	1.12 (0.94-1.33)	0.227
ULT at diagnosis	0.81 (0.29-2.27)	0.688	-	-
Tophi	1.33 (0.66-2.66)	0.422	-	-
Years since first flare	1.00 (0.97-1.03)	0.772	-	-
Number of flares suffered	0.99 (0.97-1.00)	0.255	-	-
Number of involved joints	1.00 (0.89-1.12)	0.976	-	-
Joint pattern at presentation				
-Monoarticular	1.00(ref)	-	1.00(ref)	-
-Oligoarticular	1.86 (0.91-3.80)	0.089	1.35 (0.65-2.82)	0.421
-Polyarticular	2.75 (1.05-7.22)	0.039	1.34 (0.48-3.76)	0.579

HR: Hazard ratio; 95%CI: 95% confidence interval.

Conclusion: First longitudinal study assessing the use of subclinical atherosclerosis screening as part of CV risk assessment in new patients with gout. Those classified at the very high-risk group presented the majority of events, being HF the most frequent. Age, and likely to be classified as very high risk, independently predicted a new CV event during follow-up, data that may be of interest in terms of management of the patient with gout at the time of diagnosis.

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THU0412 EFFECT OF METFORMIN ON CLINICAL GOUT OUTCOMES IN GOUT PATIENTS WITH DIABETES MELLITUS

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Background: Gout and diabetes mellitus type 2 (DM) are frequently co-existing. Metformin is the first choice of treatment for patients with DM type 2, and might – based on previous studies - have beneficial clinical effects on gout through a putative anti-inflammatory as well as serum uric acid (SUA) lowering effect. [1,2,3]

Objectives: To investigate the anti-inflammatory and SUA lowering effect of metformin in patients with gout starting uric acid lowering treatment (ULT).

Methods: Patients with clinical diagnosis of gout, a first outpatient visit between January 2010 and March 2018 and a follow-up of at least 6 months were included in a retrospective cohort study, conducted in two rheumatology centres in the Netherlands. From this cohort patients with DM starting ULT were selected. Patients with metformin use were compared to patients using other or no antidiabetic medication (control group). Metformin use was defined as use ≥80% of the time during the first six months after initiation of ULT. To evaluate the anti-inflammatory effect, the differences in incidence density (ID) of gout flares in the first six months after starting ULT was measured and analysed using Poisson regression. To evaluate the SUA lowering effect, the difference in baseline SUA, proportion of patients reaching target serum uric acid (SUA < 0.36 mmol/l) at six months follow up, and ULT dosage at time of reaching this target were analysed. All analyses included correction for confounding.

Results: Of 2108 gout patients, 309 patients who started ULT also had DM, with 155 in the metformin group and 154 in the control group (table 1). ID of flares was 2.8 and 3.3 per patient year in the control and metformin group respectively, resulting in an incidence rate ratio of 0.93 (95% CI 0.75 – 1.15). SUA levels at baseline were similar, between the two groups (Table 1, p=0.31). At six months 46.1% and 57.4% reached target SUA in the control and metformin group respectively, odds ratio of 1.30 (95%CI 0.80 – 2.08). No difference was found in allopurinol dose at time of reaching target SUA between the groups (1.14 mg, 95% CI -38.89 – 41.19).

Table 1. Baseline patient, disease and treatment characteristics

	Metformin (n = 155)	Control (n = 154)
Age (years)	70.9 (+/- 13.3)*	75.3 (+/- 14.5)*
Males, n (%)	72.9	64.3
BMI (kg/m^2)	30.1 (+/- 5.8)**	30.5 (+/- 6.6)**
Comorbidities		
Hypertension (%)	65.8	64.3
Hypercholesterolemia (%)	20.0	18.2
Serum uric acid baseline (mmol/L)	0.53 (+/- 0.14)	0.54 (+/- 0.13)
Renal function, eGFR (ml/min/1.73m^2)	60.0 (+/- 21.0)*	50.0 (+/- 34.0)*
Co-medication		
Diuretics (%)	67.7	60.4
Insulin (%)	19.4	23.4
Tophi (%)	34.2	33.8
Erosive gout (%)	17.4	18.2
Type of ULT (% allopurinol)	98.1	98.7
Start dose allopurinol (mg/day)	108 (+/- 49.4)	105 (+/- 54.5)

* = significant difference between 2 groups, p < 0.05

** = > 50% of data is missing

Conclusion: In contrast to a previous report[1], in this study in patients with DM and gout and starting ULT, metformin does not have a clinically relevant added anti-inflammatory or urate lowering effect.

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THU0413 KEY ROLE OF THE CLINICAL NURSE SPECIALIST IN PATIENTS WITH GOUT: RESULTS OF A QUALITY-OF-CARE SURVEY

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Background: Gout is the most common nontraumatic arthritis. With a prevalence in Spain of 2.4% and an increasing incidence, many gout patients are treated in Rheumatology. Different comorbidities complicate the management of this disease that not only attacks joints, but also induces kidney damage and accelerated atherosclerosis. This, together with a poor adherence to urate-lowering therapies and a suboptimal management, justifies its relevant morbidity and mortality, with high socioeconomic impact. Some studies suggest enhancing the role of the Clinical Nurse Specialist (CNS) in the care of gout to combat therapeutic failure

Objectives: To determine the factors that affect the perceived quality and satisfaction of gout patients treated in Rheumatology with CNS support and identify areas for improvement

Methods: In 2018, we implemented the following nurse-supported visit protocol

- 1st (rheumatologist and nurse; face-to-face): clinical history, joint examination, vital signs, anthropometrics, start of treatment, comorbidities management, health promotion
- 2nd (nurse; telephone, after analytical results): 1 month after 1st visit. Targeted questions (adherence, side effects, attacks, blood pressure, lifestyle habits) and therapeutic adjustment
- 3rd (rheumatologist and nurse; face-to-face): at 3-6 months. Targeted questions, joint examination, vital signs, anthropometrics, therapeutic adjustment, health promotion
- 4th (rheumatologist and nurse; face-to-face): at 12 months. Targeted questions, examination, therapeutic adjustment, health promotion. Subsequently, semi-annual/annual appointments in Rheumatology or Primary Care, according to patient complexity and gout control

We applied a treat-to-target strategy (serum uric acid <5-6 mg/dl), facilitating patient access to us in case of attack, side effects or doubts. We conducted a cross-sectional observational study with demographic data and questions about care aspects included in a survey. We invite to respond anonymously and voluntarily to patients with a follow-up of ≥6 months

Results: 44 surveys were obtained between August 2019 and January 2020. 95% male, 55% with an age range of 46-60 years; 41% >60 years. 68% considered the referral time to our Department reasonable; excessively long for 14%. All respondents were satisfied with the face-to-face nurse-supported consultation, and 93% considered the telephone CNS consultation to be good. 57% were not able to remember the name of the CNS, compared to 27% who did not know the rheumatologist name. 91% considered that the time to solve doubts and for explanations was enough. 46% considered the availability of CNS/rheumatologist as good, and 37% as excellent. The global satisfaction was good in 48% and excellent in 43%

Conclusion: We found a high global satisfaction in gout patients followed in our Department. They valued very positively the role of CNS in the face-to-face and telephone consultations, as well as the staff availability, their dedication to answer questions and offer explanations. We must remember our names to patients and optimize referral to our Department. Exploring patients' opinions is essential. It improves communication, adherence and attention offered, and allows to provide them a better experience in their relationship with the Department

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THU0414 ORDINARY LIGHT MICROSCOPY IS ABLE TO IDENTIFY MOST CRYSTAL-CONTAINING SYNOVIAL FLUIDS

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Background: Optical microscopy remains the gold standard for the diagnosis of crystal arthropathies. The complete protocol consists of three phases. In the first stage, microscopy with simple light provides information on the morphology of the crystal. The second stage, polarized light, allows detecting the intensity of the birefringence. Finally, with the first-order red compensator, the type of elongation is detected, positive for calcium pyrophosphate (CPP) crystals and negative for

monosodium urate (MSU) crystals. Finally, with the obtained data, the presence and type of crystals is concluded.
Objectives: Analyze the validity and agreement of each stage of microscopy regarding the conclusion, emphasizing ordinary light microscopy.
Methods: Fifty consecutive samples of synovial fluid obtained in routine clinical practice were independently analyzed under the compensated polarized microscope by 5 observers blinded to clinical data (250 observations in total). Each observer recorded the presence and type of crystals at each stage and reached a conclusion after gathering all the information. To estimate the diagnostic yield of each microscope stage, sensitivity, specificity and positive and negative predictive values, as well as the accuracy (number of correct observations/number of total observations), were calculated; also, the total weighted kappa was used to assess the degree of agreement with the complete protocol.
Results: Main results of the study are shown in Table 1. Regarding diagnostic yield, ordinary light microscopy showed excellent sensitivity, specificity and predictive values, similar to the results noted with simple and compensated polarized microscopy.

Table 1. In parentheses, 95% confidence intervals.

	Accuracy	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Kappa
Ordinary light	96.8% (93.8-98.4)	97.2% (93.1-98.9)	96.2% (90.7-98.5)	97.2% (93.1-98.9)	96.2% (90.7-98.5)	0.954 (0.919-0.989)
Simple polarized light	92.0% (88.0-94.8)	84.1% (76.8-89.5)	100% (97.0-100)	100% (96.5-100)	86.1% (79.5-90.8)	0.874 (0.821-0.927)
Compensated polarized light	97.6 % (94.9-98.9)	95.5% (89.8-98.0)	99.3% (96.1-99.9)	99.1% (94.8-99.8)	96.5% (92.1-98.5)	0.962 (0.933-0.992)

Diagnoses established by ordinary light microscopy matched conclusions (accuracy) in 242/250 (96.8%) observations. Discrepant cases were crystals missed under ordinary light in 4 cases (3 MSU, 1 CPP), and 4 samples with CPP crystals initially seen but later concluded their absence. Interestingly, lowest accuracy was seen with simple polarization; CPP crystals were not detected in 20 out of 93 observations with CPP (21.5%). The accuracy of compensated polarized light was similar to ordinary light. On 5 occasions no crystals were seen but finally they were present (1 MSU, 4 CPP); on the contrary, CPP was registered in one observation but the conclusion indicated no crystals.
Regarding agreement with the complete protocol, the kappa with simple light is 0.954, similar to compensated polarized light (0.962), while simple polarized light showed the lowest agreement (0.874).
Conclusion: Ordinary light microscopy is enough to correctly reach the majority of diagnoses, with a very high degree of agreement with the complete protocol. Results were comparable to using a compensated polarized microscopy. Thus, if a microscope with polarizer and first-order compensator was not available, using ordinary light would be enough on most occasions. Polarized light microscopy better identifies MSU crystals, but over 20% of CPP crystals were missed at this stage, reinforcing the value of the ordinary light microscopy.
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THU0415 MELTING OF TOPHI WITH LOCAL STEROIDS IN CHRONIC TOPHACEOUS GOUT: AN OBSERVATIONAL STUDY

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Background: Chronic tophaceous gout is usually difficult to treat with urate lowering therapy (ULT) [1]. Faster resolution of tophi has been seen with use of pegloticase [2], but this drug is costly and not widely available. Local steroid use is recommended in acute gouty arthritis but its role in reduction of tophi has not been studied. This study was aimed to see the effect of local steroids in tophi resolution.
Objectives: To study the change in size of gouty tophi with local steroid injection compared to conventional treatment.
Methods: Four crystal proven chronic tophaceous gout patients with multiple tophi were screened and enrolled in the study after taking informed consent. Total 12 tophi in 4 patients were imaged by using Duel Energy Computed Scan (DECT) for their size and volume. All 4 patients were treated with ULT as per recommended dose to achieve target serum uric acid (SUV) level. Six tophi were treated with local steroids injection (methylprednisolone acetate) at two months interval till complete resolution of tophi. Dose of steroid varied from 10 mg to 40 mg depending upon tophi size but subsequent repeat doses were same in each tophi. Six tophi not treated with local steroid served as internal control in the same patients. All 4 patients were followed up regularly in out-patient department to monitor treatment response and local side effects if any.
Results: All 4 patients achieved target SUV (<356 µmol/L) at three months of follow up. Six tophi which were treated with local steroids injection clinically had marked reduction in size at 7-12 months of follow up [Table-1], while other 6 tophi which served as internal control had no clinically significant change in size and volume of tophi. DECT was repeated in the same settings to confirm the clinical findings. DECT revealed near complete resolution of 5 tophi [Image-1], and 50% reduction in size of one tophi. Six tophi which were not treated with local steroid had no significant reduction in size in DECT as well. Only side effect noted was skin discoloration in 5 out of 6 injected sites, none of the tophi had infection.
Conclusion: Interestingly this is the first such study to document the use of local steroid in tophi. Thus intralesional steroids can be alternative to pegloticase or surgery where faster dissolution of tophi is required. This observation needs to be explored in large number of patients to calculate the total dose requirement of steroid as per volume and urate burden of tophi. Possible explanation of melting tophi with steroids is breaking down outer fibrous layer of tophi by local steroids which might be acting as barrier in dissolution of urate crystals with ULT.
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Table 1.

	Age/sex	Total Tophi	Treated Tophi	Outcome of treated tophi	Internal control tophi	Duration in months
Case 1	22/M	2	1	Near complete resolution	No Change	7
Case 2	45/F	1	1	Complete resolution	NA	8
Case 3	58/M	5	2	Near complete resolution	No change	12
Case 4	24/M	4	2	Completely resolved=1, 50% size reduction=1	No change	12

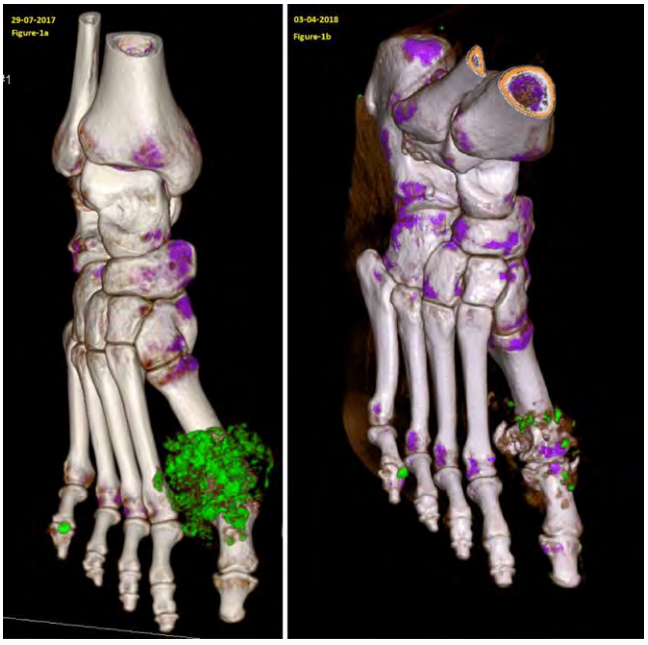


Figure 1 a: DECT of Rt foot shows urate crystal deposition at 1st MTP joint and 5th toe. Figure1b: DECT after 7 months of steroid injection in Rt 1st MTP joint tophi shows almost complete resolution but no change in 5th toe tophi (served as internal control).

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THU0416

PEGLOTICASE RESPONSE IMPROVEMENT BY CO-TREATMENT WITH METHOTREXATE: RESULTS FROM THE MIRROR OPEN-LABEL CLINICAL TRIAL IN PATIENTS WITH UNCONTROLLED GOUT

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Background: Gout is a painful inflammatory arthritis caused by persistently elevated serum uric acid (sUA) levels. Pegloticase, an infused recombinant PEGylated uricase, rapidly lowers sUA levels by converting uric acid to allantoin, a water-soluble molecule that is readily excreted by the kidneys. In the phase 3 clinical trials, 42% of patients[1] dosed with pegloticase every two weeks maintained sUA levels below 6.0 mg/dL during months 3 and 6 of pegloticase treatment. The loss of pegloticase efficacy has been attributed to the development of anti-drug antibodies (ADAs)[1-3] and these ADAs have been associated with infusion reactions (IRs).[1,2] Case reports[4] and prospective case series[5, 6] indicate that methotrexate (MTX) may allow patients to attain more complete therapeutic benefits, presumably through attenuation of pegloticase immunogenicity. The current study prospectively examines the efficacy and safety of MTX-pegloticase co-therapy in patients with uncontrolled gout.

Objectives: To assess efficacy and safety of concomitant pegloticase and MTX therapy in patients with uncontrolled gout.

Methods: Adult patients with uncontrolled gout who were beginning pegloticase therapy were considered for enrollment in this ongoing multicenter, open-label, efficacy and safety study of pegloticase with MTX co-treatment (NCT03635957). Patients were administered oral MTX (15 mg/week) and folate (1 mg/day) 4 weeks prior to the first pegloticase infusion (Day 1) and throughout the pegloticase treatment period. Blood was drawn prior to each infusion to measure sUA level, monitor clinical parameters, and examine for ADA development. All patients followed typical IR prophylaxis protocols (fexofenadine one day before and the morning of each infusion and acetaminophen and IV corticosteroid the morning of each infusion). Patients also received gout flare prophylaxis with either NSAIDs, colchicine or prednisone initiated at least 1 week prior to Day 1. The primary study outcome was the proportion of responders, defined as sUA <6 mg/dL for at least 80% of the time during month 6 (weeks 20, 22, and 24). All analyses were performed on a modified intent-to-treat population, defined as patients who received ≥1 pegloticase infusion.

Results: A total of 17 patients were screened and 14 patients (all men, average age: 49.3 ± 8.7 years) were enrolled. On Day 1, mean sUA was 9.2 ± 2.5 mg/dL and 12 of the 14 patients had visible tophi. At the 6 months timepoint, 11/14 (78.6%, 95%CI 49.2-95.3%) met the responder definition, with 3 patients discontinuing after meeting stopping rules (pre-infusion sUA values greater than 6 mg/dL at 2 consecutive scheduled visits). All patients tolerated MTX. One serious AE of bacterial sepsis occurred (resolved). AEs that occurred in >1 patient during the co-treatment period were: diarrhea and upper respiratory tract infection in 3 patients each, sinusitis, muscle strain, and hypertension in 2 patients each. Gout flares occurred in 12/14 (85.7%) patients. No new safety concerns were identified.

Conclusion: An increased proportion of patients maintained therapeutic response at 6 months when treated concomitantly with MTX and pegloticase (78.6%) when compared to the previously reported 42% using pegloticase alone.[1] These results support and reflect the improved response rates demonstrated in two prior case series.[5,6] A definitive randomized double-blinded trial evaluating pegloticase with MTX vs. pegloticase with placebo is ongoing.

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THU0417

READMISSION RISK AND QUALITY OF CARE IN PATIENTS PRESENTING TO THE EMERGENCY DEPARTMENT WITH GOUT FLARES

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Background: Gout is the most common form of inflammatory arthritis and its economic burden is substantial, with estimates for the overall cost exceeding $20 billion (US) annually. Contributing to the economic burden are hospital admissions and iatrogenic events associated with pharmacotherapy. Identification of modifiable risk factors would be an important contribution to clinical practice.

Objectives: The aim of this study was to identify opportunities for enhancing gout care in patients presenting to the Emergency Department (ED) with gout flares.

Methods: This retrospective cohort study used data from electronic medical records (EMR) at a large community hospital. All consecutive patients visiting the medical center ED with a primary diagnosis of gout from 1/1/2016 to 7/1/2019 were included. Patients were then followed for 90 days to determine whether they were readmitted to the ED for any reason. A chart review identified whether they were on appropriate medications in terms of gout flare management. All data were summarized using descriptive statistics. A multiple logistic regression was constructed to identify risk factors for ED utilization within 90 days of the index visit.

Results: A total of 214 patients were included in the analysis. Most patients were male (79%), mean age was 59.4 ± 15.6 years, and mean Charlson comorbidity index was 0.5 ± 1.14. The most common medications prescribed during the ED visit included NSAIDs (41.6%), opioids (28%), corticosteroids (26.6%), and colchicine (21%). Allopurinol and febuxostat were initiated in the ED in 4.7% and 0.9%, respectively. Discharge medications for the management of gout included NSAIDs (37%), corticosteroids (34.6%), opioids (23.8%), colchicine (14%), febuxostat (7%), and allopurinol (6.5%). Of the patients sent home with an opioid, 40% were newly prescribed. An anti-inflammatory medication was not prescribed in 29.6% of patients discharged from the ED. Readmission within 90 days was recorded in 16.8% of patients. Of these readmissions, 33.3% were gout-related and 11.1% were cardiac related.

After adjusting for age and comorbidity index, patients receiving colchicine were 2.8 times more likely (OR, 2.81; 95% CI, 1.12 to 7.02; p=0.027) to return to the ED within 90 days. The most common cause of readmission in this subset was gout-related (54.5%).

Conclusion: Nearly 30% of patients were discharged from the ED without an anti-inflammatory medication, whereas initiation of urate lowering therapy was rare. Opiates were used frequently, but the indication was uncertain. Only 5.6% of subjects revisited the ED for gout-related diagnoses in the subsequent 3 months. Colchicine prescription was associated with an increased risk of gout-related ED utilization within 90 days. Treatment of gout in the ED is sub-optimal and often does not follow established guidelines.

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THU0418

CAROTID ATHEROSCLEROSIS AND SONOGRAPHIC SIGNS OF URATE CRYSTAL DEPOSITS IN GOUT: AN ASSOCIATION STUDY

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Background: Carotid subclinical atherosclerosis is prevalent in patients with gout, although poorly predicted by cardiovascular risk assessment tools. Gout itself is deemed to contribute to its development. However, a previous report did not show an association between clinical characteristics of gout and the presence of subclinical atherosclerosis [1].

Objectives: To explore the association between sonographic signs of urate crystal deposits and carotid atherosclerosis.
Methods: Consecutive new patients with crystal-proven gout attended in a tertiary Rheumatology unit were eligible for the study. It included musculoskeletal and carotid ultrasound assessment, performed by a trained sonographer blinded to clinical data. Patients were examined during intercritical periods; flare prophylaxis with low-dose colchicine or other agents was permitted, but patients under urate-lowering treatment were excluded. The musculoskeletal scans evaluated wrists, 2nd MCPs and 1st MTPs joints, and triceps and patellar tendons, for the presence of signs suggestive of urate crystal deposits (double contour, hyperechoic aggregates, and tophi), following OMERACT definitions. Also, local power-Doppler (PD) signal was registered and graded as 0 to 3. The sum of locations showing crystal deposits or positive PD signal (≥1) was estimated in order to assess crystal and inflammatory burden, respectively. Carotid arteries were scanned for increased intima-media thickness (IMT) and presence of atheroma plaques, according to Mannheim consensus. The association analysis was done by logistic regression, considering increased IMT or atheroma plaques as the dependent variables.
Results: Eighty-eight new patients with gout were enrolled, mean aged 62.0 years (SD 14.5), 89.8% males. Mean gout duration was 5.9 years (SD 9.0), clinical tophi were observed in 16.1% of patients and mean serum urate level at diagnosis was 8.4 mg/dl (SD 1.5). All participants showed at least one sonographic sign of crystal deposits at the examined locations, with a mean sum of 9.4 (SD 4.0). Regarding individual signs, their mean (SD) sum was as follows: 4.6 (2.1) for tophi, 3.9 (2.8) for aggregates and 0.9 (1.0) for double contour. The mean sum of locations with positive PD signal was 1.1 (SD 1.0). Regarding carotid scans, increased IMT was seen in 26 patients (30.6%) and atheroma plaques in 51 (58.0%). Table 1 shows the results of the association analysis. Positive PD signal was significantly associated with the presence of atheroma plaques, while tophi showed a trend with both increased IMT and atheroma plaques.

Table 1. Results of the association analysis by simple logistic regression.

	Increased IMT		Atheroma plaques	
Sum of locations with:	OR (95%CI)	p	OR (95%CI)	p
Deposits	1.08 (0.96-1.22)	0.187	1.07 (0.96-1.19)	0.246
Double-contour	1.04 (0.65-1.65)	0.873	0.93 (0.60-1.42)	0.722
Hyperechoic aggregates	1.05 (0.89-1.24)	0.558	1.03 (0.88-1.20)	0.701
Tophi	1.23 (0.97-1.55)	0.091	1.22 (0.99-1.51)	0.068
Positive power-Doppler	0.78 (0.47-1.28)	0.320	1.73 (1.06-2.82)	**0.028**

IMT: intima-media thickness; OR: odds ratio; 95%CI: 95% confidence interval.

Conclusion: Sonographic deposits were consistently observed in new patients with gout. Crystal and inflammatory load, here shown as tophi and positive PD signal, seem associated with carotid atherosclerosis. This new finding may contribute to understanding the complex relationship between gout and atherosclerosis.
References:
[1] Ann Rheum Dis. 2017;76:1263.
Disclosure of Interests: : Irene Calabuig: None declared, Agustín Martínez-Sanchis: None declared, Mariano Andrés Grant/research support from: Grünenthal, Consultant of: Grünenthal, Menarini, Speakers bureau: Grünenthal, Horizon
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THU0419 BIOLOGICS IN THE TREATMENT OF CALCIUM PYROPHOSPHATE DEPOSITION DISEASE. A SYSTEMATIC LITERATURE REVIEW

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Background: Only few case reports and case series have analysed the efficacy of IL-1 inhibitors in the treatment of calcium pyrophosphate deposition disease (CPPD), reporting conflicting results.
Objectives: The main aim of this systematic literature review (SLR) was to summarize the evidence in the use of biological therapies in CPPD.
Methods: PRISMA-IPD guidelines were used for this review. Published articles reporting the use of TNFα and/or IL-1 inhibitors in the treatment of CPPD were reviewed. We performed a SLR using PubMed, Embase and Cochrane databases. The search resulted in 83 articles; 11 were further evaluated in the SLR.
Results: Seventy-six patients were included: 2 received infliximab, whereas 74 anakinra. The main data of included studies are reported in table 1.

Table 1. Studies evaluating biological therapies in patients with CPPD.

Authors	*Year of publication*	*Population of interest*	*Number of CPPD patients*	*Diagnostic criteria*	*Clinical presentation*
McGonagle D. et al.	2008	CPPD	1	SFA	Chronic
Announ N. et al.	2009	CPPD	1	SFA	Acute
Couderc M. et al.	2012	CPPD	3	Imaging	Acute and chronic
Diamantopoulos A.P. et al.	2012	CPPD	1	SFA	Chronic
Moltó A. et al.	2012	CPPD	5	SFA	Acute and chronic
Ottaviani S. et al.	2013	CPPD	16	SFA and/or imaging	Acute
Verhoeven F. et al.	2013	G and CPPD	2	NR	Acute and chronic
Bruges-Armas J. et al.	2014	CPPD	2	NR	Chronic
Aouba A. et al.	2015	G, CPPD and HADD	1	Imaging	Acute
Desmarais J. et al.	2018	G, CPPD	11	SFA and/or imaging	Acute
Thomas M. et al.	2018	CPPD	32	SFA and/or imaging	Acute

Legend. **G**: gout, **HADD**: hydroxyapatite deposition disease, **NR**: not reported, **SFA**: synovial fluid analysis

Sixty-seven (88.2%) patients presented with an acute CPPD (mean disease duration: 2.7±6.9 months; polyarticular involvement in 61.2%, oligoarticular in 31.3% and monoarticular in 7.5%), whereas 9 (11.8%) patients with a chronic CPPD (mean disease duration: 130.1±133.6 months; polyarticular involvement in 66.7% and oligoarticular in 33.3%).
Anakinra was used in refractory disease (85.1%) or in patients with contraindications to standard treatments such as colchicine, oral glucocorticoids and/or non-steroidal anti-inflammatory drugs (23.0%). Clinical response to anakinra was reported in table 2.

Table 2. Efficacy of anakinra in the treatment of CPPD

	Acute CPPD (n=67)	*Chronic CPPD (n=7)*
Clinical efficacy (%)	54 (80.6)	3 (42.9)
Pre TJC	6.3±2.4	3.8±2.4
Post TJC	1.2±0.6	1.3±1.5
Mean reduction	*5.1±2.3* *	*2.5±1.9* +
Pre SJC	4.8±2.2	3.8±2.4
Post SJC	1.1±0.6	1.3±1.5
Mean reduction	*3.7±2.2* *	*2.5±1.9* +
Pre VAS pain (0-100 mm)	68.5±9.5	/
Post VAS pain (0-100 mm)	24.2±10.4	/
Mean reduction	*44.2±10.9* *	/
Pre CRP (mg/l)	40.9±50.9	50.0±66.5
Post CRP (mg/l)	22.2±8.6	3.2±2.5
Mean reduction	*18.6±54.1* *	*46.7±64.0* +

Legend. CRP: C-reactive protein, **SJC**: swollen joint count, **TJC**: tender joint count, **VAS**: visual analogue scale. + p values were not calculated because of a too small sample size. * p values were <0.01

Duration of anakinra treatment prior to complete resolution of symptoms was associated with the clinical phenotype of chronic CPPD (Rpb: 0.67, p<0.01) and with disease duration (R: 0.49, p<0.01). In 47 out of 57 (82.5%) responders, complete resolution of symptoms was observed within 4 days after the first injection of anakinra. Adverse events were reported in 4.1% of the cases: local skin reaction at the injection site, skin rash on the back and bacterial pneumonia.
Conclusion: This SLR provides evidence in favour of the use of anakinra as a therapeutic option in patients with CPPD, especially in acute refractory CPPD or when standard treatments are contraindicated.
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fees from Union Chimique Belge Pharma, personal fees from Pfizer, outside the submitted work.

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THU0420 ULTRASOUND SHOWS GREAT ACCURACY FOR THE DIAGNOSIS OF CRYSTAL ARTHRITIS IN PATIENTS WITH RECENT-ONSET SYNOVITIS

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Background: The value of ultrasound (US) in the diagnosis of crystal arthropathy, such as gout or calcium pyrophosphate deposition disease (CPPD), in patients with recent onset synovitis has been evaluated only by a few studies.

Objectives: To investigate, in patients with acute arthritis, the accuracy of US for the diagnosis of crystal arthropathy.

Methods: Consecutive patients with recent onset (<6 weeks) acute arthritis were enrolled. The US examinations were performed a rheumatologist blinded to clinical data. Calcium pyrophosphate and monosodium urate crystal deposits were identified in the joint affected by synovitis (target joint), as well as in the classic sites for gout and CPPD (set of joint) (Table 1), according to the OMERACT definitions.

Table 1. Anatomical targets of ultrasound examination

	Gout	CPPD	Both
Wrist	Radiocarpal j Intercarpal j	Triangular FC complex Scapho-lunate ligament	/
Hand	DC in the II MCPj HC	Deposits within the II MCPj HC	II MCPj
Knee	Popliteal groove DC in the femoral condyle's HC	Meniscal FC Deposits within the femoral condyles' HC	Supra-patellar recesses
Hip	DC in the femoral head's HC	Deposits within the femoral head's HC Acetabular FC	Hip j
Foot	DC in the I MTPj HC	Deposits within I MTPj HC	I MTPj

Legend. **DC**: double contour, **FC**: fibrocartilage, **HC**: hyaline cartilage, **MCPj**: metacarpophalangeal joint, **MTPj**: metatarsophalangeal joint, **j**: joint.

The diagnostic accuracy of US and synovial fluid analysis (SFA) was evaluated taking the classification criteria for gout and CPPD as gold standard (1,2). Moreover, the US and SFA results were compared in the joints in which the SFA was performed.

Results: One-hundred and four patients were enrolled: 22 CPPD patients, 23 with gout and 59 disease controls. Table 2 reports the diagnostic accuracy of US and SFA, using the classification criteria as gold standard.

Table 2. Diagnostic accuracy of US and SFA

	Sensitivity	*Specificity*	*Positive LHR*	*Negative LHR*
US (target joint)				
Crystal arthritis	0.84 (0.7-0.93)	0.91 (0.8-0.97)	9.5 (4.1-22)	0.2 (0.1-0.3)
CPPD	0.91 (0.71-0.99)	0.91 (0.80-0.97)	10.2 (4.4-23.8)	0.1 (0-0.4)
Gout	0.83 (0.61-0.97)	0.91 (0.80-0.97)	9.1 (3.9-21.4)	0.2 (0.1-0.5)
US (set of joints)				
Crystal arthritis	0.96 (0.85-0.99)	0.87 (0.76-0.95)	7.6 (3.8-15.3)	0.1 (0-0.2)
CPPD	1 (0.85-1)	0.88 (0.76-0.95)	8 (4-16)	0 (0-0.2)
Gout	0.91 (0.72-0.99)	0.88 (0.76-0.95)	7.3 (3.6-14.8)	0.1 (0-0.4)
SFA				
Crystal arthritis	0.9 (0.77-0.97)	1 (0.94-1)	/	0.1 (0-0.2)
CPPD	0.90 (0.7-0.99)	1.0 (0.94-1)	/	0.1 (0-0.3)
Gout	0.91 (0.71-0.99)	1 (0.94-1)	/	0.1 (0-0.3)

Legend. **LHR**: likelihood ratio

SFA was performed in 67 knees (64.4%), 10 wrists (9.6%), 10 ankles (9.6%), 5 I MTP joints (4.8%), 5 hips (4.8%), 4 elbows (3.8%), 4 shoulders (3.8%).

The total agreement between US and SFA was excellent (93.8% in CPPD and 90.2% in gout). SFA positive/US negative results occurred in 1 patient with CPPD (1.2%) and in 4 patients with gout (4.9%). On the contrary, US positive/SFA negative results occurred in 4 patients with CPPD (4.9%) and in 4 patients with gout (4.9%).

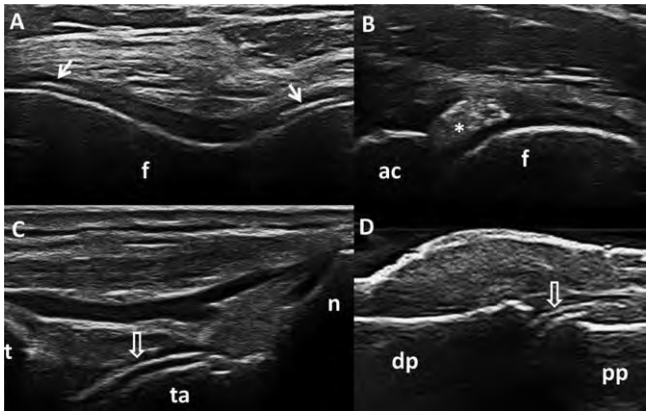


Figure 1 provides a pictorial evidence of the US appearance of crystal deposits. A: anterior suprapatellar transverse scan of the femoral condylar HC. HC calcifications (arrows) B: anterior longitudinal scan of the hip. FC calcification (asterisk) C: anterior longitudinal scan of the ankle. DC sign (void arrow) .D: dorsal longitudinal scan of distal interphalangeal joint. DC sign (void arrow).

Conclusion: US is useful for the diagnosis of gout and CPPD in patients with acute synovitis. Extending the US evaluation to the joints which are most commonly involved in gout and in CPPD, other than those affected by synovitis, increases the sensitivity of US.

References:

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THU0421 TUMOR-INDUCED OSTEOMALACIA: DATA FROM A MONOCENTRIC EXPERIENCE ON 16 PATIENTS

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Background: Tumor-induced osteomalacia (TIO) is a rare paraneoplastic syndrome due to a phosphaturic tumor, which overproduces fibroblast growth factor-23 (FGF-23), causing hyperphosphaturia, hypophosphoremia, low $1,25(OH)_2VitD_3$ and osteomalacia. Locating the tumor is critical, because lesions are typically small, benign mesenchymal tumors, anywhere in the body; the delay between onset of symptoms and diagnosis ranges from 2.5–28 years. Surgical removal is the only effective therapeutic approach.

Objectives: To retrospectively evaluate patients affected by TIO, investigating clinical management and disease outcome.

Methods: We retrospectively collected data of patients affected by TIO referred to a tertiary Rheumatology Center between Sep 2000 and Jan 2020.

Results: We included 16 patients with a definite diagnosis of TIO, mean age±standard deviation 62.4±14.6 yrs, 56.2% females, mean age at symptoms onset 48.0±14.3 yrs (53.8±13.1 at diagnosis). Mean diagnostic delay between symptoms onset and tumor detection was 6.8±6.4 yrs. All patients complained bone pain, muscle weakness, and fractures before diagnosis of TIO. Biochemical findings were: mean serum Phosphorus (PS) 1.4±0.4 mg/dL (reference range (RR) 2.5-4.6), mean serum Calcium 9.4±0.7 mg/dL (RR 8.4-10.2), mean serum $1,25(OH)_2VitD_3$ 30.5±23.4 ng/L (RR 25-86). Intact-FGF-23 was dosed in 9 patients, always resulting elevated: mean 396.6±707.3 pg/mL (RR 25-45). PTH was increased in 30% of cases, while serum alkaline phosphatase was increased in 87.5%. 24h-Urine Phosphorus (PU) was increased in only 13% of patients, but, when renal phosphate

wasting by tubular reabsorption of phosphate (TRP) was calculated, PU resulted increased in all.
Tumor was localized in all cases (Fig.1) and were localized in bone and soft tissue, by using functional imaging, followed by anatomical techniques. Before the introduction in routinely practice of ^{68}Ga-DOTATATE-PET-CT in 2013, Octreoscan-SPECT/CT and ^{18}F FDG-PET were used as imaging modalities. Since 2013, diagnostic delay consistently reduced, from 8.6±8.3 yrs (7 patients) to 4.5±2.6 yrs (9 patients), confirming higher diagnostic accuracy of ^{68}Ga-DOTATATE-PET-CT.

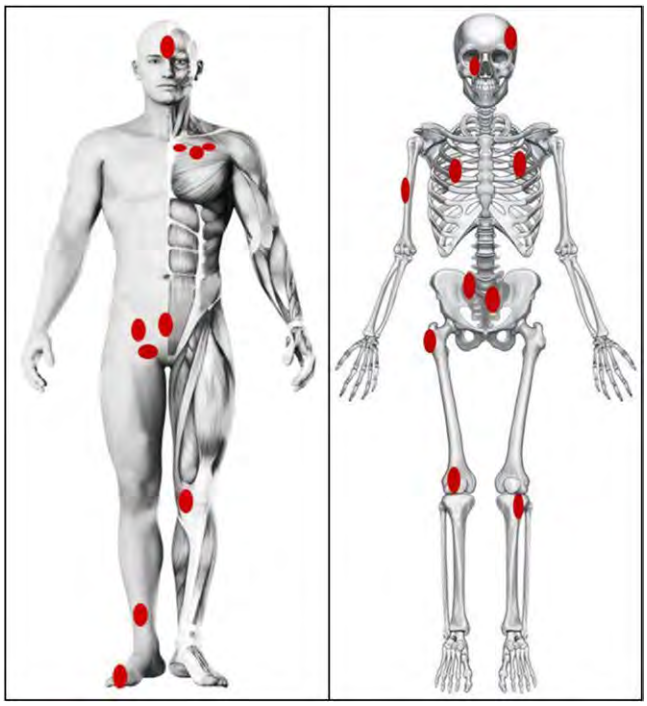


Figure 1.

13 patients underwent surgery; in two cases surgery was not possible due to tumor location, so pharmacological support with phosphate supplements and calcitriol was started; a patient underwent to TC-guided radiofrequency ablation. After surgery, 7 patients experienced a complete remission, 3 had a persistence of the disease, and 3 an overtime relapse, even after a long-standing normalization of PS (6 years). After surgical tumor removal, PS significantly increased in few days (from 1.36±0.39 to 2.9±1.1, p=0.0001), while iFGF-23 levels tended to rapidly decreased (from 396.6±707.3 to 62.8±78.4). Before the introduction of ^{68}Ga-DOTATATE-PET-CT, 6 patients underwent to imaging-guided closed biopsy to confirm tumor localization; by using ^{68}Ga-DOTATATE-PET-CT only 2 subjects had closed biopsy. Furthermore, in our population only patients who had biopsy to detect the lesion (7 patients) had relapses compared to patients who did not.
Conclusion: To our knowledge, this is the widest European cohort of patients affected by TIO reported in the last two decades. We confirm an important delay between symptoms onset and diagnosis. To locate tumor, a stepwise approach is recommended, starting with a thorough medical history and physical examination, followed by functional imaging, preferring ^{68}Ga-DOTATATE-PET-CT. Tumor biopsy is not recommended due to the potential cell spilling. Surgery is considered the only definitive treatment, aiming to a wider excision. Active surveillance is always needed, due to the possible relapses, even after a long period of complete clinical and biochemical remission.
Disclosure of Interests: : Chiara Crotti: None declared, Francesca Bartoli: None declared, Maria Manara Consultant of: Consultant and/or speaker for Eli-Lilly, MSD, Sanofi-Genzyme, Novartis, Alfa Wasserman and Cellgene, Speakers bureau: Consultant and/or speaker for Eli-Lilly, MSD, Sanofi-Genzyme, Novartis, Alfa Wasserman and Cellgene, Primo Andrea Daolio: None declared, Francesca Zucchi: None declared, Roberto Caporali Consultant of: AbbVie; Gilead Sciences, Inc.; Lilly; Merck Sharp & Dohme; Celgene; Bristol-Myers Squibb; Pfizer; UCB, Speakers bureau: Abbvie; Bristol-Myers Squibb; Celgene; Lilly; Gilead Sciences, Inc; MSD; Pfizer; Roche; UCB, Luigi Sinigaglia: None declared, Massimo Varenna: None declared
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THU0422 CALCIUM PYROPHOSPHATE CRYSTAL DEPOSITION WITHIN TOPHUS LOBULE: A FREQUENT ASSOCIATION OBSERVED IN LONG-TIME COURSE TOPHI

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Background: Calcium pyrophosphate (CPP) crystals and monosodium urate (MSU) crystals are frequently found in the same synovial fluids of gouty patients suggesting an interaction in crystal formation and deposition. This association has never been reported in tophus.
Objectives: we aimed to describe the prevalence of CPP crystal deposition in tophus and to determine the associated risk factors.
Methods: 22 tophi consecutively harvested were fixed in 4% paraformaldehyde and embedded in paraffin. 5-µm thick sections were analyzed by compensated polarized microscopy (CPM) after hematoxylin and eosin staining. Characterization of CPP crystals were performed by scan electronic microscopy (SEM) and Fourier transform infrared (FTIR) spectroscopy. Clinical characteristics were compared between patients having tophus with CPP deposition and patients having tophus without CPP crystals.
Results: All tophi appeared multi-lobulated depositions of MSU crystals separated by fibrous tissue and surrounded by a foreign giant cell reaction. CPP crystals were identified in few lobules of 5 tophi (22.7%) harvested from 3 great toes, 1 elbow bursa and 1 finger of 5 patients. CPP crystals formed aggregate deposition within the lobule of MSU crystals. Both monoclinic and triclinic CPP crystal phases were identified by CPM, SEM and FTIR. Tophi were harvested from 22 male gouty patients with a mean age of 50.8 (28-66) years and a mean BMI of 24.2 kg/m2 (18.9-29.4). Mean serum urate level (SUL) was 499 ± 107 µmol/L. 59% of patients had chronic renal disease stage 2 or 3, 40.9% dyslipidemia, 22.7% type 2 diabetes mellitus, 13.6% hypertension and 50% obesity. Patients with tophi containing CPP deposition were older (61.2 [56-66] vs 47.8 [28-64] years, p=0.009) and had a longer gout duration (19 [10-31] vs 9 [3-20] years, p= 0.007) and tophus duration (11.4 [8-16] vs 4.5 [1-9] years, p< 0.0001) than patients with tophi alone. Tophi did not display calcification on radiographies performed before surgery. However, the density of tophi containing CPP crystal deposition was higher than the density of tophi without CPP crystals (51 [25-100] vs 21.5% [0-40], p=0.009). The proportion of bone erosion and gout arthropathy was similar between the two groups. Similarly, no difference was observed for SUL (467 ± 43 vs 509 ± 109 µmol/L), estimated glomerular filtration rate (76.6 ± 11.9 vs 74.9 ± 15.7 ml/min/1.73m2) and prevalence of comorbidities. Interestingly, no calcification was detected on knee and wrist radiographies of patients with tophi containing CPP deposition.
Conclusion: These results reported for the first time, in a small sample size, that CPP crystal deposition occurred within tophus lobules. They suggested that long-time course tophi might act as a facilitating agent of CPP nucleation. This hypothesis needs specific confirmation studies
Disclosure of Interests: : None declared
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THU0423 ADHERENCE TO URATE-LOWERING THERAPY IN PATIENTS WITH SEVERE GOUT WHO RECEIVED CANAKINUMAB FOLLOWING A 5-YEAR RETROSPECTIVE ANALYSIS

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Background: The adherence to lowering therapy for gout is low, including in chronic severe gout. Whether interleukin 1 inhibitors may contribute to better adherence is unknown.
Objectives: To compare adherence to urate-lowering therapy in patients with severe gout who received canakinumab versus patients who received standard anti-inflammatory therapy (NSAIDs, glucorticoids, colchicine).
Methods: Of the 513 patients with gout observed at the V.A. Nasonova Research Institute of Rheumatology, Moscow from 2013 to 2014 y 247 patients with the most severe gout, requiring regular symptomatic treatment, were selected. Of these, 25 patients (3 (12%) women and 22 (88%) men), the average age of 54.5 ± 12.7 g, received (at least 1) canakinumab injection of 150 mg subcutaneously as a symptomatic therapy, the remaining 222 patients (men) mean age

51.9 ± 11.4 g. received standard anti-inflammatory therapy (colchicine (55% of patients), glucorticoids (5%), NSAIDs (40%), or a combination of these (3%). On average, after 4,8 ± 1.7 years, a comparative analysis of adherence to reducing therapy was carried out, as well as the need for anti-inflammatory therapy and assessment of adherence according to the Score compliance on the scale of the Moriscy-Green patients who received and did not receive canakinumab.

Results: Evaluation was available in 180 patients (16 who received canakinumab and 164 who received standard anti-inflammatory therapy) who were initially given reducible therapy. 11 patients died (2 patients (8%) who received canakinumab and 9 (4%) patients on standard anti-inflammatory therapy), 56 patients (7 (28%) and 49 (22%), respectively) were not available for observation. Adherence to urate-lowering therapy was better in patients who received canakinumab (see table 1).

Table 1. Score compliance on the scale of the Moriscy-Green

Adherence to therapy	Patients receiving canakinumab, (n %)	Patients receiving standard anti-inflammatory therapy, (n %)	p=
High (> 4 points)	14 (87)	83 (51)	0,07
Moderate (3 points)	2 (13)	46 (28)	0,13
Low (2 and <points)	0	35 (21)	0,03

The likelihood of maintaining the target uric acid level when taking urate-lowering drugs in patients who previously received canakinumab was higher (12 patients (75%) who received canakinumab and 32 (20%) patients received standard anti-inflammatory therapy (p = 0.005).

During the year preceding the analysis, there were no acute attacks of arthritis in 12 (75%) patients who received canakinumab and 46 (28%) patients received standard anti-inflammatory therapy (p = 0.002).

132 patients who previously received regular anti-inflammatory therapy and received standard anti-inflammatory therapy and 1 patient (1 attack) (p = 0.005) who previously received canakinumab took anti-inflammatory drugs over the past year due to the development of exacerbations (an average of 3 seizures per year): NSAIDs (54%) or colchicine (46%).

Conclusion: Therapy with interleukin 1 Kanakinumab may contribute to a better adherence to lowering therapy and isidentified with a lesser need for symptomatic therapy with long-term follow-up.

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THU0424

SHORT-TERM ADHERENCE OF URATE-LOWERING AGENTS WILL NOT IMPROVE END-STAGE RENAL DISEASE AND MORTALITY

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Background: Gout is the most common inflammatory arthritis worldwide with a diverse spectrum of clinical manifestations. Many studies indicated that gout is associated with hypertension, metabolic syndrome, chronic kidney disease and ischaemic heart diseases.

Objectives: This study investigated the association between the compliance of urate-lowering agents (ULA) compliance and progression end-stage renal disease (ESRD) and all-cause mortality.

Methods: We identified 53,917 patients with incident gout from 2002 to 2012. We followed up these patients till 31DEC2015. The primary data source was the National Health Insurance database of Taiwan. Proportion of days covered (PDC) was used to measure medication adherence. Patients with PDC≧80% more than two years defined adherence to ULA. Cox proportional hazards model was used to estimate difference and hazard ratios (HRs) for ESRD and all-cause mortality.

Results: A total of 53,917 patients were included (figure 1). Patient with urate-lowering agent PDC≧80% more than 2 years were 2,371. After propensity score matched 1:4 with age, sex and comorbidities, PDC <80% were 9,484 matched cohort (Table 1). The mean follow-up duration is 12.30±2.45 years in PDC≧80% group and 9.52±3.46 years in PDC <80%. During follow-up, ESRD was detected in 1,349 patients (306 with PDC≧80% and 1,043 with PDC <80%) and all-cause mortality was found 3,430 patients (842 with PDC≧80% and 2,588 with PDC <80%). This matching showed no difference in ESRD (HR, 0.91; 95% CI, 0.80-1.03) and all-cause mortality (HR, 0.96; 95% CI, 0.88-1.03) (Table 2).

Table 1. Baseline characteristic of adherence and non-adherence of urate-lowering agent among patients with gout in matched and unmatched cohort

	Unmatched Cohort			Propensity-score Matched Cohort		
Variable	PDC≧80% N=2371^	PDC<80% N=51546^	P	PDC≧80% N=2371^	PDC<80% N=9484^	P
Age (years) (mean ± standard deviation)	59.96±13.44	51.52±15.61	<0.0001	59.96±13.44	60.23±13.41	0.3755
follow-up duration (years) (mean ± standard deviation)				12.30±2.45	9.52±3.46	
Gender			0.3098			0.2855
Male	1929(81.36%)	42358(82.18%)		1929(81.36%)	7624(80.39%)	
Female	442(18.64%)	9188(17.82%)		442(18.64%)	1860(19.61%)	
Comorbidities						
Hypertension	406(17.12%)	3695(7.17%)	1.71E-71	406(17.12%)	1571(16.56%)	0.5138
Diabetes Mellitus	276(11.64%)	2367(4.59%)	1.78E-54	276(11.64%)	1080(11.39%)	0.7291
Ischemic heart disease	109(4.60%)	988(1.92%)	1.58E-19	109(4.60%)	444(4.68%)	0.8617
Cerebrovascular disease	113(4.77%)	891(1.73%)	1.05E-26	113(4.77%)	481(5.07%)	0.5416
Peripheral arterial disease	20(0.84%)	170(0.33%)	3.67E-05	20(0.84%)	74(0.78%)	0.7561
Congestive heart failure	81(3.42%)	606(1.18%)	1.88E-21	81(3.42%)	286(3.02%)	0.3137
Anemia	182(7.68%)	1559(3.02%)	5.22E-36	182(7.68%)	769(8.11%)	0.4882
CKD	266(11.22%)	1978(3.84%)	2.61E-69	266(11.22%)	963(10.15%)	0.1281

Table 2. hazard ratio of ESRD and all-cause mortality in patients with gout

Outcome	Hazard ratio (95% Confidence interval)
ESRD	
ULA adherence level	
PDC<80%	Reference
PDC≧80%	0.91 (0.80-1.03)
All-cause mortality	
ULA adherence level	
PDC<80%	Reference
PDC≧80%	0.96 (0.88-1.03)

PDC= Proportion of days covered

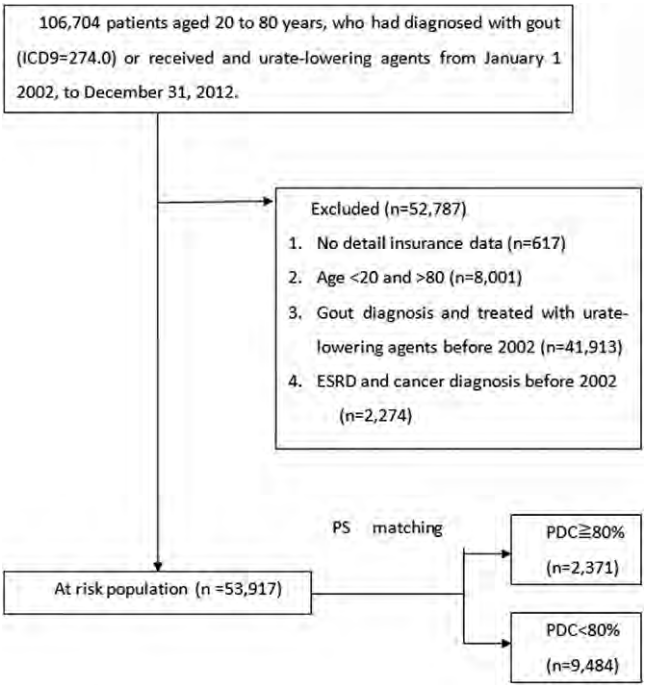


Figure 1. Flow chart for study design

Conclusion: Gout patients with/without two years adherence of urate-lowering agents does not have an impact on ESRD and all-cause mortality.
References: Nil
Disclosure of Interests: : None declared
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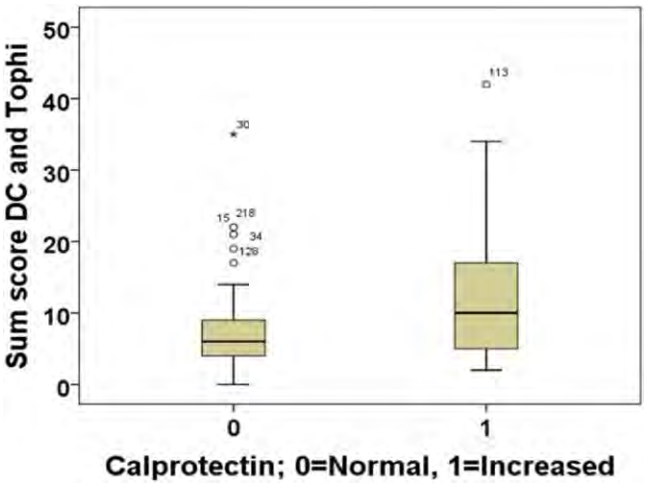
THU0425 ULTRASOUND DETECTED URATE CRYSTALS DEPOSITIONS ARE ASSOCIATED WITH ELEVATED CALPROTECTIN AND CRP INDICATING SUBCLINICAL INFLAMMATION; BASELINE RESULTS FROM THE NOR-GOUT STUDY

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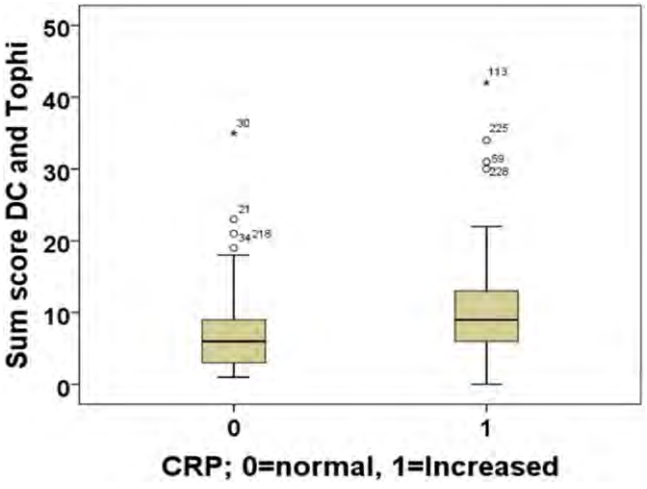
Background: Ultrasound detects depositions of monosodium urate (MSU) crystals in gout patients. The OMERACT ultrasound group has developed definitions for elementary lesions in gout including the double contour (DC) sign (depositions of crystals on the surface of cartilage) and tophus (larger hypoechoic aggregation of crystals, usually well delineated). Calprotectin is a major granulocyte protein found to be sensitive to reflect the level of inflammation in several immunological diseases. There may be an association between low grade inflammation and co-morbidity (including cardio-vascular pathology) in gout patients.
Objectives: To explore whether the extent of depositions (e.g. DC and tophi) was associated with inflammation in gout patients.
Methods: The baseline data from NOR-GOUT, a prospective observational study of patients with crystal-proven gout with increased serum urate levels (>360 µmol/L), were presently used. All patients had an extensive ultrasound examination(GE E9 machine, grey scale 15MHz) to assess MSU depositions (DC and tophi) with bilateral assessment of radiocarpal joint, MCP 2, insertion of triceps and quadriceps, proximal and distal patellar and the Achilles tendon, cartilage of distal femur (maximal flexed knee), the talar cartilage of tibiotalar joint and MTP 1 joint. The degree of elementary lesions was semi-quantitatively scored 0-3 (0=none, 1=possible, 2=certain, 3=major deposits). Total sum scores of DC and tophi were calculated and the associations with calprotectin (plasma assessed by ELISA (Calpro), normal levels <910 µg/L) as well as C-reactive protein (CRP, assessed as a routine at our laboratory, normal levels <4mg/L) were explored. Correlations were performed by use of Spearman and differences between groups were investigated by Mann-Whitney tests.
Results: A total of 111 patients who had calprotectin assessed were included in the study (92% men, mean (SD) age 54.5 (14.5) years, disease duration 7.1 (6.6) years) when initiating MSU lowering treatment. The mean (SD) sum sore DC and tophi was 9.1 (7.8), calprotectin 780 (500) µg/L, CRP 7 (15) mg/L, serum urate (SUA) 505 (87) µmol/L, creatinine 96 (18) µmol/l and eGFR 79 (20) ml/min/1.73m^2. Table 1 shows significant correlations between sum sore DC/tophi and calprotectin, CRP, SUA, creatinine and eGFR. Increased calprotectin levels (≥910 µg/L) were found in 28% and increased CRP (≥ 4 mg/L) in 39%. Patients with increased vs normal levels of calprotectin had significantly higher levels of DC/tophi depositions (mean (SD) 13.0 (10.4) vs 7.4 (5.8), p=0.01), and similar was found for CRP (11.4 (9.5) vs 7.6 (6.2), p=0.033) (illustrated in table 2).
Conclusion: In gout patients, higher load of MSU depositions was associated with increased inflammatory markers. This indicates that the amount of depositions is associated with higher inflammatory activity, which could have systemic implications.

	Sum score DC and tophi	Calprotectin	CRP	SUA	Creatinine
Calprotectin	0.31*				
CRP	0.29*	0.65**			
SUA	0.31**	0.22*	0.19		
Creatinine	0.34**	0.25*	0.15	0.36**	
eGFR	-0.38**	-0.27*	-0.21*	-0.18	-0.86**

*p≤0.05, **p≤0.001



Disclosure of Interests: : Hilde Berner Hammer Consultant of: Has received fees as consultant from Roche, AbbVie and Novartis., Speakers bureau: Has received fees for speaking from AbbVie, BMS, Pfizer, UCB, Roche, MSD and Novartis, Gro Jensen: None declared, Lars Karoliussen: None declared, Lene Terslev Speakers bureau: LT declares speakers fees from Roche, MSD, BMS, Pfizer, AbbVie, Novartis, and Janssen., Espen Andre Haavardsholm Grant/research support from: Research funding from Pfizer, UCB, Roche, MSD and AbbVie, Consultant of: Pfizer, Speakers bureau: Pfizer, UCB, Roche, and AbbVie,, Tore K. Kvien Grant/research support from: Received grants from Abbvie, Hospira/Pfizer, MSD and Roche (not relevant for this abstract)., Consultant of: Have received personal fees from Abbvie, Biogen, BMS, Celltrion, Eli Lily, Hospira/Pfizer, MSD, Novartis, Orion Pharma, Roche, Sandoz, UCB, Sanofi and Mylan (not relevant for this abstract)., Paid instructor for: Have received personal fees from Abbvie, Biogen, BMS, Celltrion, Eli Lily, Hospira/Pfizer, MSD, Novartis, Orion Pharma, Roche, Sandoz, UCB, Sanofi and Mylan (not relevant for this abstract)., Speakers bureau: Have received personal fees from Abbvie, Biogen, BMS, Celltrion, Eli Lily, Hospira/Pfizer, MSD, Novartis, Orion Pharma, Roche, Sandoz, UCB, Sanofi and Mylan (not relevant for this abstract)., Till Uhlig Consultant of: Lilly, Pfizer, Speakers bureau: Grünenthal, Novartis



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THU0426 CLINICAL CHARACTERISTIC OF INFECTIOUS ULCERATION OVER TOPHI

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Background: Infection in ulceration over tophi is the leading cause of sepsis in patients with gout, which is the main indication for surgery. Additionally,

patients with infection will significantly prolonged wound closure time compared with those without infection. Investigation of infection in ulceration over tophi will improve our understanding of this critical issue.

Objectives: To describe the microbiological profile in ulceration over tophi, antibiotic susceptibility patterns of causative agents, and to study the prediction of infection in ulceration over tophi among patients with gout.

Methods: Patients with ulceration over tophi were prospectively enrolled. The clinical characteristics were recorded and microbiological specimens were taken on admission. Specimens were cultured for aerobic and anaerobic bacteria, and antibiotic susceptibility testing was performed for the culture isolates. Patients were divided into 2 groups according to having infectious ulceration or not and the potential risk factors for infectious ulceration over tophi were examined using univariate and multivariate logistic regression analyses.

Results: A total of 82 patients were included for analysis. 46 pathogens were isolated from 39 (47.6%) patients, among which the top 3 were *Staphylococcus aureus* (43.5%), *Pseudomonas aeruginosa* (17.4%) and *Enterococcus faecalis* (13.0%). Overall, the Gram-positive bacilli were more sensitive to gentamicin (81.5%), amikacin (88.9%), trimethoprim/sulfamethoxazole (92.6%), nitrofurantoin (96.3%), linezolid (100.0%), teicoplanin (100.0%) and vancomycin (100.0%) whereas penicillin, oxacillin and ampicillin were 66.7% to 77.8% resistant. The Gram-negative bacilli were more sensitive to amikacin (84.2%), cefoperazone/sulbactam (84.2%) and meropenem (89.5%) whereas ampicillin, amoxicillin/clavulanate, cefotaxime, cefazolin, piperacillin, trimethoprim/sulfamethoxazole and tetracycline were 68.4% to 100% resistant. Patients with infection had a higher rate of smoking history and type 2 diabetes, with higher levels of erythrocyte sedimentation rate, C-reactive protein and leucocyte, and lower level of albumin. In stepwise logistic regression analysis, type 2 diabetes (adjusted OR 5.064; 95% CI = 1.430 to 17.928) and albumin level (adjusted OR 0.855; 95% CI = 0.782 to 0.935) were independent predictors of infection in ulceration over tophi.

Conclusion: Infection is common in ulceration over tophi. Different antibiotic susceptibility patterns were observed in Gram-positive bacilli and Gram-negative bacilli. Type 2 diabetes and low albumin level were associated with an increased risk of infection in ulceration over tophi. The data in this study will be beneficial for tailoring infection control measures in a way that improves outcomes of ulceration over tophi.

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Table 1. Bacteria isolated from initial ulceration specimens taken on the first admission.

Bacteria	Number* (n = 46)	Proportion (%)
Gram-positive bacilli	**27**	**58.7**
Staphylococcus aureus	20	**43.5**
Enterococcus faecalis	6	**13.0**
Streptococcus mutans	1	**2.2**
Gram-negative bacilli	19	**41.3**
Pseudomonas aeruginosa	8	**17.4**
Klebsiella pneumonia	4	**8.7**
Enterobacter cloacae	3	**6.5**
Escherichia coli	2	**4.3**
Acinetobacter baumannii	2	**4.3**

* Number of ulceration

Disclosure of Interests: : None declared
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THU0427 SHOULD FEBUXOSTAT-RESISTANCE BE ADDED TO CRITERIA FOR REFRACTORY GOUT? A PRELIMINARY STUDY

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Background: Refractory gout manifests as recurrent flares, chronic arthritis and progressive tophaceous deposits. Febuxostat is a widely-used potent serum urate-lowering reagent, but some gout patients cannot achieve target serum uric acid (sUA) after they used this reagent.

Objectives: To determine whether febuxostat-resistance should be a criterion for refractory gout, characteristics of gout patients who were resistance to febuxostat or allopurinol were compared.

Methods: This study was performed from December 2015 to December 2019. Medical records of gout patients who met the 2015 gout classification criteria [1] and undertook febuxostat (febuxostat group) or allopurinol (allopurinol group) urate-lowing therapy (ULT) were assessed. Dose of ULT was adjusted till sUA was below 6 mg/dL and 5 mg/dL for patients with urate deposition. We screened gout patients who had contraindication or history of failure to normalize sUA for≥ 3 months of treatment with the maximum medically appropriate febuxostat (febuxostat-resistance) or allopurinol (allopurinol-resistance) dose as defined by physicians. Furthermore, these screened patients met the traditional criteria of refractory gout except therapeutic reaction [2].Demography and clinical characteristics were recorded. Features between febuxostat-resistance and allopurinol-resistance patients were compared.

Results: (1) Of 683 gout patients who were included, 516 and 167 of them used febuxostat or allopurinol. (2) Age (41.92±11.58 vs. 42.26±9.41 years), Male gender (97.50% vs. 97.01%), duration of gout (5.78±4.74 vs. 5.05±4.72 years) and sUA (6.30±2.50 vs. 6.67±2.14 mg/dL) were similar between febuxostat group and allopurinol group (P>0.05). (3) Dose of febuxostat or allopurinol were 47.28mg/day and 178.24mg/day. (4) Sixteen patients were febuxostat-resistance, while 6 patients were allopurinol-resistance. Prevalence rates of treatment resistance were comparable between groups (3.10% vs. 3.59%, P>0.05). (5) Some parameters were different between resistance patients and non-resistance patients in both groups (Table 1, P<0.05). However, characteristics of febuxostat-resistance and allopurinol-resistance patients were similar (P>0.05).

Table 1 Characteristics of gout patients in febuxostat group and allopurinol group

Parameters	Febuxostat Group		Allopurinol Group	
	Non-resistance (n=500)	Resistance (n=16)	Non-resistance (n=161)	Resistance (n=6)
Age (year)	41.93±11.65	41.67±9.58	42.22±13.33	44.50±16.98
Male Gender (%)	97.40	100.00	96.89	100.00
BMI (kg/m^2)	25.44±3.46	26.22±3.47	25.86±3.97	25.60±6.42
Duration of gout (years)	5.75±4.76	7.00±3.97*	4.96±4.73	7.75±2.62*
Flares in previous 18 months (times)	1.31±0.44	3.67±0.70*	1.13±0.24	3.25±0.50*
Presence of Tophi (%)	23.80	100.00*	14.90	100.00*
Presence of Complication (%)	35.8	100.00*	31.06	100.00*
sUA (mg/dL)	6.21±2.47	9.13±1.24*	6.42±2.32	10.15±3.55*
SCr (μmol/L)	100.67±15.03	163.96±29.41*	96.93±22.91	133.75±31.60*
ESR (mm/L)	24.59±19.28	42.83±21.13*	27.49±24.10	56.50±28.12*
CRP (mg/L)	18.92±18.59	28.81±23.85*	23.12±22.63	32.28±23.64*

*P<0.05 compared with non-resistance patients in the same group.
BMI body mass index, *sUA* serum uric acid, *SCr* serum creatinine, *ESR* erythrocyte sedimentation rate, *CRP* C-reactive protein

Conclusion: Febuxostat-resistance is a potential criterion for refractory gout, because febuxostat-resistance patients shares similar characteristics of patients with refractory gout.

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Disclosure of Interests: : None declared
DOI: 10.1136/annrheumdis-2020-eular.1270

THU0429 THE ASSOCIATION OF SERUM VITAMIN A, VITAMIN E, AND FOLATE WITH HYPERURICEMIA: AN ANALYSIS OF POPULATION-BASED NATIONALLY REPRESENTATIVE DATA

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Background: Hyperuricemia is an important risk factor for gout as well as hypertension, type 2 diabetes and renal impairment. Although previous studies investigated the association of questionnaire-based micronutrient intake with serum uric acid levels, limited data on serum micronutrients levels in relation to the risk of hyperuricemia especially in Asian population.

Objectives: This study aimed to evaluate the association of serum vitamin A, vitamin E and folate level with hyperuricemia in the Korean general population.
Methods: The present study included 6023 participants (2722 men and 3301 women) aged ≥19 years with available data on serum vitamin A, vitamin E, folate and serum uric acid. General characteristics of participants were compared using the Chi-square test and Student's t test. The association between serum vitamin A, E and folate and serum uric acid levels were evaluated using general linear regression model. Multivariate logistic regression analyses were performed to estimate the effects of these micronutrients on hyperuricemia.
Results: Serum uric acid levels were increased from the lowest quintile of vitamin A levels to the highest quintile after adjustment for covariates ($P_{trend} < 0.001$ in both sexes). In addition, dose-dependent relationship was observed between vitamin A levels and the risk of hyperuricemia in fully-adjusted analyses ($P_{trend} < 0.001$ in both sexes). However, neither serum vitamin E nor serum folate was associated with hyperuricemia across analyses models.
Conclusion: This study suggested that vitamin A could be a risk factor of hyperuricemia and further studies are warranted to elucidate underlying mechanism of the observed findings.
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Disclosure of Interests: : None declared
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THU0430 RENAL URATE DEPOSITION: SUMMARY OF PUBLISHED EVIDENCE

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Background: Gout is the most common inflammatory arthropathy in U.S. adults. Although the severity of this debilitating disease is often defined by the presence of tophi in the joints, systemic deposition of urate in major organ systems including the renal parenchyma is not as well established. Urate is primarily cleared through the kidneys and patients with gout often have concomitant renal disease along with other comorbidities such diabetes, coronary artery disease, and hypertension; however, a causal role between these entities has not yet been carefully established. We hypothesize that urate deposits serve as a trigger in the inflammatory nidus to propogate subclinical tissue damage that results in the chronicity of the disease. This could potentially explain its independent role in the development and progression of chronic kidney disease in gout patients.
Objectives: To review the published literature for evidence of urate deposition in the renal parenchyma in patients with gout and summarize the histopathology and imaging findings.
Methods: PubMed (from 1940 to 2020) was used to identify reports of autopsy, pathology and radiology imaging demonstrating urate deposition within the native renal parenchyma in patients with gout. Key words included: gout nephropathy, chronic urate nephropathy, renal tophi, gouty kidney, autopsy findings in gout, and renal imaging in gout. The reference lists from these publications were also used to identify additional articles. Literature referencing urate nephrolithiasis and renal transplants were excluded from the study.
Results: There were 25 articles documenting renal parenchymal urate deposition in gout patients confirmed by autopsy, biopsy and/or radiology imaging in native kidneys. Among the 19 articles examining urate deposition by autopsy and/or biopsy, 100% found urate deposition in the collecting ducts and adjacent medullary interstitium. Based on these findings, the most commonly proposed mechanism for urate deposition is urate crystal precipitation in the collecting ducts with eventual desquamation of the collecting duct walls from inflammation and/or tubular obstruction with subsequent extrusion of crystals into the medullary interstitium. 89% of reports documented inflammatory cells and/or tubulointerstitial fibrosis adjacent to the renal urate deposits. 68% reported cortical thinning or scarring. In addition, 74% of included publications reported renal vascular pathology including arteriosclerosis, glomerosclerosis and nephrosclerosis. There were 6 imaging articles that all reported abnormal renal ultrasound findings with hyperechogenic renal medullas that were attributed to urate deposition.
Conclusion: There is a growing body of literature documenting urate deposition in the renal parenchyma in gout patients based on autopsy, pathology and imaging findings. Inflammation and fibrosis adjacent to regions of urate deposition and vascular changes were common. Given the strong association of gout with renal disease, there is a critical need to elucidate the mechanism by which urate impairs the renal tissue. Thus dedicated investigation is key to determine the prevalence and clinical significance of urate deposition in the kidneys of gout patients.
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Disclosure of Interests: : Puja Khanna Grant/research support from: Dyve, Selecta, Sobi, Consultant of: Sobi, Horizon, Brad Marder Employee of: Horizon Therapeutics, Brian LaMoreaux Shareholder of: Horizon Therapeutics, Employee of: Horizon Therapeutics, Ada Kumar Shareholder of: Horizon Therapeutics, Employee of: Horizon Therapeutics
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THU0431 PEGLOTICASE RESPONSE RATE IN UNCONTROLLED GOUT PATIENTS CO-TREATED WITH METHOTREXATE: EXPERIENCE IN A COMMUNITY RHEUMATOLOGY PRACTICE

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Background: Pegloticase is an infused biologic approved to treat uncontrolled gout. The drug is highly effective, but patients can develop anti-drug antibodies that interfere with efficacy.[1] Randomized clinical trials have shown that 42% of patients treated with bi-weekly pegloticase had a serum uric acid (sUA) below 6.0 mg/dl at 3 and 6 months.[2] Mild-to-moderate immunomodulation has been shown to lower the prevalence of anti-drug antibody formation in patients with other autoimmune diseases (rheumatoid arthritis, Crohn's disease, juvenile idiopathic arthritis).[3] Cases published in the literature suggest that low-to-moderate doses of methotrexate[4,5] or azathioprine[6] may also attenuate anti-pegloticase antibody formation in uncontrolled gout patients. Therefore, immunomodulation may allow patients to remain on pegloticase therapy longer and achieve a more complete therapeutic response.
Objectives: To examine pegloticase treatment response in patients co-treated with methotrexate.
Methods: This retrospective chart review included patients from a single community rheumatology practice who began pegloticase (8 mg every 2 weeks) therapy between January 2017 and September 2019 and were co-treated with methotrexate. Unless contraindicated, methotrexate co-treatment with pegloticase is now standard in this practice and all patients undergo close monitoring of laboratory parameters including serum uric acid level (sUA), blood counts, and liver function tests (LFTs). To maximize the number of cases, patients administered methotrexate in any form were included. Collected data included demographic information, laboratory values, methotrexate treatment parameters (timing with respect to pegloticase therapy, dose, route), pegloticase response parameters (number of infusions, duration of therapy), and adverse events. Main outcome measures included the number of pegloticase infusions administered (responder defined as ≥12 infusions administered) and therapy duration.
Results: Ten patients (9 male) were included. All patients had visible tophi and average patient age was 52.3 ± 13.5 years. Nine patients began subcutaneous methotrexate (25 mg weekly) an average of 19.9 ± 7.0 days (range: 14 to 35 days) before the first pegloticase infusion. The remaining patient began oral methotrexate (12.5 mg weekly) 14 days after the first pegloticase infusion. Eight of 10 patients (80%) were considered responders, receiving an average of 15.5 ± 3.8 pegloticase infusions (range: 12-21 infusions) over 31.8 ± 9.5 weeks (range: 22.1 to 48.3 weeks). In these 8 responders, mean sUA was 0.2 ± 0.0 mg/dL immediately prior to the last pegloticase infusion. All 10 patients had an initial, rapid decrease in sUA, but two patients discontinued treatment before infusion 12. One patient had increased sUA with a mild infusion reaction, and one patient was lost to follow-up after infusion 5. No new safety concerns emerged. A gout flare occurred in 1 patient and was treated with prednisone. LFT and blood cell parameters were stable over the study period, except in two patients. One had a mild, transient LFT elevation that resolved without treatment, one had an LFT elevation and pancytopenia that improved with methotrexate discontinuation and transfusion, respectively. This patient remained on pegloticase and continued as a responder.
Conclusion: This case series suggests that methotrexate, when used as a co-therapy with pegloticase, allows more patients to complete therapy and to achieve the full therapeutic response. No new safety concerns emerged.
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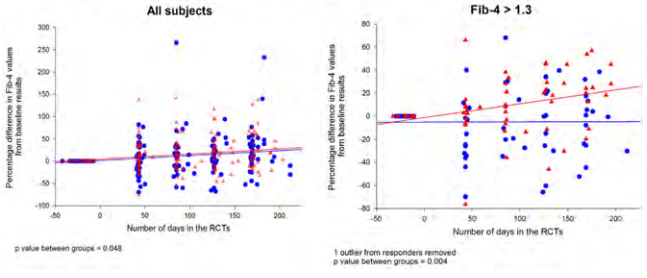
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Disclosure of Interests: : John Albert Consultant of: Horizon Therapeutics, Speakers bureau: Horizon Therapeutics, Tony Hosey Shareholder of: Horizon Therapeutics, Employee of: Horizon Therapeutics, Brian LaMoreaux Shareholder of: Horizon Therapeutics, Employee of: Horizon Therapeutics
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THU0433 TREATMENT WITH PEGLOTICASE IMPROVES HEPATIC FIBROSIS ESTIMATED BY FIBROSIS-4 INDEX IN SUBJECTS WITH CHRONIC REFRACTORY GOUT

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Background: Hyperuricemia is associated with non-alcoholic fatty liver disease (NAFLD)[1,2], but the relationship to fibrosis remains uncertain[3]. Moreover, it is not known whether lowering serum urate will affect the course of NAFLD. The availability of data from two randomized trials of pegloticase, a pegylated recombinant mammalian uricase, that profoundly decreases serum urate afforded the opportunity to test the hypothesis that lowering urate might improve NAFLD.
Objectives: To determine whether treatment of chronic refractory gout patients with pegloticase was associated with improvement in NAFLD determined by Fibrosis 4 index (Fib4).
Methods: Databases from patients with chronic refractory gout who participated in two randomized 6 month clinical trials (RCTs) of pegloticase were analyzed[4]. Sub-sets who had persistent urate lowering to levels <1 mg/dL in response to biweekly pegloticase (Responders, n=36) were compared to those who received placebo (n=43). Since liver biopsy information was not available on these subjects, we relied on Fib4, a validated non-invasive estimate of liver fibrosis in a variety of liver diseases[5,6] calculated from measurements of AST, ALT, platelet count and age (Age x AST/platelets x √ALT). A Fib4 value of 1.3 is an indication that further evaluation of liver disease is warranted.
Results: At baseline, the mean Fib4 values were 1.40 ± 0.86 in pegloticase responders and 1.04 ± 0.53 in subjects receiving placebo. As shown in figure 1, subjects receiving placebo exhibited a change of 0.26 ± 0.41 in the Fib4 score over the six months of the RCTs compared with 0.13 ± 0.62 in the pegloticase responders (p=0.048; by linear regression). When only the subjects with a Fib4 value > 1.3 were considered, a significant difference in the change in the Fib4 values over the 6 months of the trial between pegloticase responders and those receiving placebo was also observed (-0.15 ± 0.67 vs 0.37 ± 0.42, p=0.004, by linear regression). The correlations between serum urate area under the curve (AUC) over the 6 months of the trial and the change in Fib4 value was r_s=0.33, p=0.0.0004 (Spearman rank-order correlation coefficient). Finally, multiple linear regression analysis indicated serum urate AUC (as a surrogate measure for group) is the main contributor to the change in Fib4 (p=0.018 by linear regression).

Figure 1. Impact of Pegloticase Therapy on NAFLD Estimated by Fibrosis-4 Index



Conclusion: The data are consistent with the conclusion that persistent lowering of serum urate had a significant impact on Fib4 levels, implying a possible effect on the course of NAFLD. The results support a more complete analysis involving biopsy examination of the impact of urate on liver inflammation and fibrosis.
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Disclosure of Interests: : Naomi Schlesinger Grant/research support from: Pfizer, Amgen, Consultant of: Novartis, Horizon Therapeutics, Selecta Biosciences, Olatec, IFM Therapeutics, Mallinckrodt Pharmaceuticals, Anthony Yeo Employee of: Horizon Therapeutics, Peter Lipsky Consultant of: Horizon Therapeutics
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THU0434 LEFLUNOMIDE CO-THERAPY WITH PEGLOTICASE IN UNCONTROLLED GOUT

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Background: Pegloticase is a PEGylated biologic for uncontrolled gout that has well-established efficacy. However, anti-drug antibody (ADA) development causes many patients to discontinue treatment before receiving the full therapeutic course.[1] ADAs bind to the pegloticase molecule, leading to reduced therapeutic efficacy and discontinuation of therapy.[2] Emerging data indicates that co-treatment with pegloticase and immunomodulating agents may prevent ADA development, allowing more patients to receive a full course of treatment. Prior case reports describe the results of pegloticase treatment with methotrexate, azathioprine or cyclosporine[3-6]; however, the literature does not contain information on the use of leflunomide with pegloticase.
Objectives: To evaluate overall pegloticase responder rate in uncontrolled gout patients co-treated with leflunomide.
Methods: This retrospective study was conducted in a rheumatology practice where an immunomodulatory agent is typically used in conjunction with pegloticase. Patients co-treated with oral leflunomide (20 mg/day) and pegloticase (8 mg/infusion) were included. Extracted data included demographics, gout characteristics, pegloticase therapy parameters (serum uric acid [sUA], number of infusions), leflunomide therapy parameters (timing with respect to the first pegloticase infusion, dose, route), adverse events (e.g., gout flare, infusion reactions), and safety information (clinical laboratory parameters). Prior to each infusion all patients were administered a standard prophylaxis regimen of fexofenadine the night before and day of infusion, solumedrol day of infusion. The primary outcome was the proportion of pegloticase responders, defined as those receiving ≥12 infusions.
Results: At data collection, 10 patients (5 male, 72.7 ± 12.5 years old, baseline sUA = 6.59 ± 3.15 mg/dL) had been co-treated with pegloticase and leflunomide. 4 patients (40%) received ≥12 infusions of pegloticase; 2 patients began treatment but were lost to follow-up, though neither of these patients experienced a rise in sUA during therapy. Of the 6 patients described, 4 met the primary outcome for a responder and 2 were lost to follow-up, resulting in 4/6 or 66% response rate. The 4 remaining patients had not reached their 12th infusion at time of data cutoff and were ongoing with a mean of 8.0 ± 1.6 infusions (range: 6-10 infusions). No new safety concerns emerged. One patient had 3 gout flares during treatment and 1 patient required emergency care because of loss of consciousness and wooziness prior to pegloticase infusion due to pre-medication with solumedrol. No clinically meaningful laboratory value changes occurred, with the exception of a mild and transient ALT rise in 1 patient.
Conclusion: Preliminary evidence suggests that low-to-moderate immunomodulation can minimize or prevent ADA formation against pegloticase and increase the number of patients fully benefitting from pegloticase. No prior studies have examined the effect of leflunomide on pegloticase responder rates. The current study indicates that oral leflunomide may be a viable immunomodulator for patients with uncontrolled gout undergoing pegloticase therapy.
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THU0435 CALCIUM PYROPHOSPHATE DIHYDRATE (CPPD) CRYSTALS BUT NOT BASIC CALCIUM PHOSPHATE (BCP) CRYSTALS INDUCE SYNDECAN-4 EXPRESSION IN CARTILAGE

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Background: Chondrocalcinosis is a painful rheumatic condition caused by the deposition of calcium pyrophosphate dihydrate crystals (CPPD) in joint tissues, and especially in cartilage. It is known that CPPD crystals cause inflammation and degenerative changes in joint, but the underlying mechanisms remain poorly understood. In particular, nothing is known about how these crystals regulates transmembrane heparan sulphate proteoglycans (HSPGs). Our attention focused on one family of HSPGs called syndecans as they have important roles both as adhesion molecules, by mediating chondrocyte-extracellular matrix interactions, and as modulators of intracellular signaling triggered by cytokines and growth factors.
Objectives: The aim of this study was to evaluate how CPPD crystals modulates syndecan expression in chondrocytes and in cartilage, and how this modulation can be ultimately linked to cartilage damage during chondrocylcinosis.
Methods: Murine chondrocitic ATDC5 cells were stimulated with 0,1 ng/ml CPPD crystals or with 0,1 ng/ml basic-calcium phosphate crystals (BCP), a family of calcium-containing crystals found in other rheumatic conditions such as osteoarthritis (OA). Cytotoxicity was evaluated by lactate dehydrogenase (LDH) release in the supernatant at 30 minutes, and 3, 6, 24 hours after stimulation. At the same time-points, mRNA expression levels of syndecans (Synd-1, -2, -3, -4) and of matrix-degrading enzymes (Mmp-3, -9, -13; Adamts-4, -5) was analysed by qRT-PCR. Finally, Syndecan-4 protein expression was studied by immunohistochemistry (IHC) in cartilage samples of patients with chondrocalcinosis and in samples of patients with severe OA without chondrocalcinosis as control.
Results: LDH assay revealed no increased cytotoxicity by CPPD or BCP at any time-point. qRT-PCR indicated that CPPD crystals but not BCP crystals induced Synd-2 and -3 upregulation at 30 minutes after stimulation and Synd-4 upregulation at 3 hours, while no modulation of syndecans was seen at later time-points. CPPD also induced Adamts-4 expression at 3 hours after stimulation, and Mmp-9 expression at 3 and 6 hours. The expression of the other matrix-degrading enzymes was not affected. Human chondrocalcinosis cartilage exhibited enhanced Synd-4 expression compared to severe OA cartilage containing BCP calcification. Interestingly, Synd-4 expression was observed in the extracellular matrix but not on cell membrane, suggesting that maybe Synd-4 undergoes shedding (Figure 1).



Figure 1. Representative Synd-4 IHC in control patients (Ctrl, severe OA) and chondrocalcinosis patients (CPPD). Note increased Synd-4 expression in extracellular matrix of CPPD patients compared to Ctrl ones.

Conclusion: BCP and CPPD crystals seem to trigger differential effects in terms of modulation of syndecans in chondrocitic cells. CPPD crystals induce Synd-4 and Adamts-4 and Mmp-9 which are not induced by BCP crystals. It remains to be clarified whether the two events are interlinked. In particular, further studies are required to investigate if Adamts-4 and Mmp-9 are involved in Synd-4 shedding or if vice versa Synd-4 regulates Adamts-4 and Mmp-9 activation and downstream cartilage breakdown in chondrocalcinosis.
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THU0436 ASSESSMENT OF CARDIOVASCULAR RISK LEVELS IN CPPD VERSUS RA AND GOUT, AND RISK-FLUCTUATION ANALYSIS BASED ON CALCULATOR TYPE: ATP III AND REYNOLDS RISK SCORE

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Background: Cardiovascular risk in CPPD patients is not so well evaluated as in other rheumatic diseases, and optimal risk calculators for patients with *calcium pyrophosphate* crystal deposition disease have not yet been studied.
Objectives: To assess CVR and compare stratification results using ATP III and Reynolds Risk Score (RRS) calculators in CPPD, RA and gout patients versus the control subjects.
Methods: The case-control study included 168 patients aged 18 - 80 years old, with 42 participants in each subgroup – CPPD, gout, RA patients and healthy volunteers, matched by gender (10 males and 32 females) and age (mean age 54 years). CPPD diagnosis was based on McCarty 1961 y criteria, RA – following ACR/EULAR 2010 y criteria, and gout - ACR/EULAR 2015 criteria. CPPD and gout diagnosis was crystal- verified in all cases. Exclusion criteria were as follows: diabetes mellitus and eGFR<60 ml/min/1.73m^2. The following data was collected for all patients: anthropometric parameters, BP, lab tests, including serum glucose level, creatinine, total cholesterol (TC), HDLp, CRP; CVR was assessed using ATP III and RRS scales. Statistica 12.0 package was used for statistical data processing.
Results: Both groups were comparable in terms of anthropometric parameters, rates of individual indicators and factors did not differ, except for family history of cardiovascular disease, systolic BP, HDLp, hsCRP (see Table).

Table 1. Risk factors and CVR stratification by ATP III and RRS in CPPD, RA, gout and control group.

	CPPD (n=42)	RA (n=42)	Gout (n=42)	Control (n=42)
Smoking, n (%)	11 (26,2)	12 (28,6)	8 (19,0)	12 (28,6)
Systolic BP, mmHg, M±SD	124±14$^{*/**}$	138±17$^{\#\#}$	144±26$^{\#\#\#}$	127±16
TC, mg/dl, M±SD	261.9±64.2	244.1±77.5	249.3±62.7	244.1±52.6
HDLp, mg/dl, M±SD	63.2±20.2$^{*/**}$	49.2±16.5$^{\#\#}$	52.0±9.7$^{\#\#\#}$	58.1±16.4
hsCRP, mg/l, Me [25-75th percentiles]	3.8 [1,0;12,4] $^{*/**/***}$	8,6 [4.1;20.6] $^{\#\#}$	8.5 [4.1;2.9] $^{\#\#\#}$	1,5[0.8;2.6]
hsCRP ≥5 mg/l, n (%)	18 (43)$^{*/**/***}$	27 (64)$^{\#\#}$	29 (69)$^{\#\#\#}$	3 (7)
Family history of CVD, n %	6 (14)$^{*/***}$	16 (38)$^{\#}$	4 (10) $^{\#\#\#}$	17 (40)
High and very high CVR levels, ATP III scale (>10%), n (%)	5 (12)	9 (21)	7 (17)	8 (19)
High and very high CVR levels, RRS scale (>10%), n (%)	9 (21)	14 (33)	12 (29)	7 (17)

*p<0.05 between CPPD and RA, **p<0.05 between CPPD and gout, ***p<0.05 between CPPD and controls, $^{\#}$p<0.05 between RA and gout, $^{\#\#}$p<0.05 between RA and controls, $^{\#\#\#}$p<0.05 between gout and controls.

Based on ATP III risk calculation the number of CPPD patients with high and very high CVR was 5 (12%) patients and was close to that in RA (9(21%)), gout (7 (17%)) and the control group (8 (19%)). Mean CRP levels and number of pts with CRP ≥5 mg/l were significantly lower in CPPD and control group pts, than in RA and gout, however CRP ≥5 mg/l levels were documented almost in half of CPPD pts (43%) and only in 7% of pts from the control group (p<0.05).
Although CVR calculations based on RRS scale yielded similar results, and all groups remained comparable, nevertheless, the number of pts with high and very high CVR increased in each group, except for the control. There were no meaningful differences in between the groups in TC levels, however HDLp was significantly higher in CPPD pts (p<0.05), than in RA and gout, and in the control group pts vs RA pts (p<0.05).
Conclusion: CPPD associated cardiovascular risk is considerably high and comparable to CVR levels in RA and gout. Given that RRS based CVR calculation resulted in increased number of patients with high and very high risks in all groups, except for the control group, it can be suggested that use of calculators including CRP is appropriate not only in RA pts, but also in microcrystal deposition arthritis, associated with inflammation, therefore prospective studies on larger samples are deemed necessary.
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THU0437 SPECIFIC COMORBIDITIES ENHANCE MONOSODIUM URATE CRYSTAL DEPOSITION IN GOUT: A MULTICENTRE DUAL-ENERGY COMPUTED TOMOGRAPHY STUDY

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Background: The reasons explaining why some patients exhibit higher monosodium urate (MSU) crystal burdens than others remain largely unknown. While MSU crystal formation is enhanced by certain factors in vitro such as pH, temperature, and other ion concentrations, it is currently unknown whether comorbidities and clinical features are associated with increased MSU deposition in vivo.
Objectives: To determine which factors are associated with the burden of MSU crystal deposition quantified by dual-energy CT (DECT) in urate lowering therapy (ULT)-naive gout patients.
Methods: In this multicenter cross-sectional study, DECT scans of knees and feet were prospectively obtained from ULT-naive, or not taking any ULT for more than a year, gout patients. Demographic, clinical (including gout

history and comorbidities), and biological data were collected, and their association with DECT MSU crystal volume was analyzed using bivariate and multivariate analyses. A second bivariate analysis was performed by splitting the dataset depending on an arbitrary threshold of DECT MSU volume (1 cm3).

Results: A total of 125 gout patients were included, of whom 91 underwent both DECT scans of knees and feet. In bivariate analysis, age (p=0.03), symptom duration (p=0.003), subcutaneous tophi (p=0.004), hypertension (p=0.02), diabetes mellitus (p=0.05), and chronic heart failure (p=0.03) were associated with the total DECT volume of MSU crystal deposition. In multivariate analysis, factors associated with DECT MSU volumes ≥1 cm3 were gout duration (OR for each 10-year increase 3.15 [1.60;7.63]), diabetes mellitus (OR 4.75 [1.58;15.63]), and chronic heart failure (OR 7.82 [2.29;31.38]). The model performance was good with an AUC of 0.816.

Conclusion: Specific comorbidities, particularly chronic heart failure, diabetes mellitus, and hypertension, are more strongly associated with increased MSU crystal deposition in knees and feet than gout duration, regardless of serum urate level.

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THU0438 INADEQUATE CARE FOR PATIENTS HOSPITALISED WITH GOUT: EVIDENCE THAT EULAR GUIDANCE IS NOT UTILISED

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Background: Hospitalisations due to gout have increased over the last decade, in direct contrast to declining admissions for other inflammatory arthritides including RA [1]. Gout is a treatable condition with recently published EULAR guidelines [2, 3]. Admissions could be avoided with effective use of urate-lowering therapies (ULT).

Objectives: We hypothesised that the majority of patients attending hospital with acute gout attacks would not be on ULT. Furthermore, we hypothesised that the majority of patients would not be provided with a plan for ULT commencement and/or uptitration on discharge, leaving them at risk of further hospitalisations.

Methods: We retrospectively analysed electronic health records for all patients presenting acutely with a primary admission diagnosis of gout (ICD-10 code: M10) at two hospitals in London, UK, from January – December 2017. Analyses of in-hospital gout management were performed for these patients, including to ascertain the number and proportion of patients who: i) had a known history of gout; ii) were receiving ULT at time of attendance; iii) were provided with a discharge plan for ULT commencement and/or uptitration.

Results: Over a 12-month period, there were 234 emergency attendances for gout in 225 individuals. 80% were male, with a mean age of 58 years. 70/234 (30%) attendances resulted in admission to hospital (mean length of stay: 2 days; range: 0-31 days). 211 patients had routinely captured clinical data available for further analysis. 90/211 (43%) patients had prior diagnoses of gout, of whom 38% were on ULT at presentation (32 allopurinol, 2 febuxostat). 38% of patients were discharged with a plan for ULT commencement and/or uptitration. 20 patients re-presented to hospital with acute gout within 12 months (17/20 were not receiving ULT).

Conclusion: Most patients hospitalised with gout were not receiving ULT, even those with a prior history of gout attacks. Few were provided with a ULT plan, leaving them at risk of re-admission to hospital. Hospital admissions are unpleasant for patients and incur a high economic burden for health services; if they are to be prevented, there must be a concerted effort to implement and follow gout management guidelines to ensure patients receive ULT at appropriate doses.

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THU0439 EFFICACY AND SAFETY OF ANAKINRA IN THE TREATMENT OF RECURRENT GOUT FLARES: RESULTS FROM THE EXTENSION PHASE OF THE ANAGO STUDY

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Background: The anaGO (anakinra in gout) study was a multi-center, randomized, double-blind, double-dummy, phase 2 study investigating the efficacy and safety of anakinra for recurrent gout flares. Results from subsequent flares (extension phase) are presented in relation to the previously reported results from the 1st flare (flare at study enrollment).

Objectives: The objective of the extension phase was to evaluate the efficacy, safety and immunogenicity of two anakinra regimens (100 or 200 mg daily s.c. injections for 5 days) compared to triamcinolone (single i.m. injection 40 mg) for subsequent flares after initial study enrollment flare. The primary endpoint of the study was change in patient-assessed flare pain intensity from baseline to 24-72 hours (average of 24, 48 and 72 hours) in the most affected joint measured on a visual analogue scale (0-100 VAS). Secondary endpoints included: patient's and physician's assessments of global response, anti-drug antibodies (ADA) and safety.

Methods: The study included patients with acute gout (ACR/EULAR 2015 gout classification criteria) unsuitable for anti-inflammatory therapy with NSAIDs and colchicine due to contraindication, intolerance or inefficacy. Patients were eligible for treatment of subsequent flares for up to 2 years. Each patient received the same treatment for all flares, starying with the flare at enrollment.

Results: 161 patients were treated for 1 flare, 61 patients for 2 flares, 31 patients for 3, and 20 patients for 4 or more flares with 1 patient treated for 9 flares. In total, 300 flares were treated in the full study; anakinra 100 mg and 200 mg, 107 and 106 flares, respectively; and triamcinolone, 87 flares. Both anakinra doses and triamcinolone provided a clinical meaningful reduction in patient-assessed pain intensity in both the 1st and subsequent flares. Mean changes in pain intensity from baseline to 24–72 hours for total anakinra and triamcinolone were: 1st flare -41.2 and -39.4; 2nd flare -33.9 and -31.1; 3rd flare -31.8 and -51.2, respectively. Mean differences in pain reduction between anakinra and triamcinolone treatment groups were (negative value favors anakinra): 1st flare -1.8, 2nd flare -2.8 3rd flare 19.4. The majority of secondary endpoints favored anakinra, including patient's and physician's global assessement of response and physician's assessement of the joint. No unexpected safety findings during subsequent flares were identified. 21 patients (19.6%) developed ADA to anakinra in low titers at some time point; 7 (6.5%) had pre-existing ADA at baseline and 12 (11.2%) developed treatment induced ADA. 2 patients had pre-existing ADA to triamcinolone at baseline. 4 patients on anakinra (3.7%) developed neutralizing antibodies (NAbs). Pre-dose 72 hour anakinra serum concentrations were in similar range for ADA+ and ADA- patients. Presence of ADA was not associated with adverse events or had an impact on pain reduction.

Conclusion: The efficacy and safety of anakinra and triamcinolone in subsequent flares were similar to the findings from 1st flare in patients with acute gout. Patient-assessed pain in the 1st and 2nd flare was reduced to similar degrees in all treatment groups, but to a larger extent in the 3rd flare in the small triamcinolone group. Secondary endpoints were in favor of anakinra across flares 1 to 3. The overall incidence of ADA and NAb was low also after repeated anakinra dosing and did not appear to impact exposure, efficacy or safety. In conclusion, anakinra was shown to be an option in the treatment of recurrent gout flares in patients for whom conventional therapy is unsuitable.

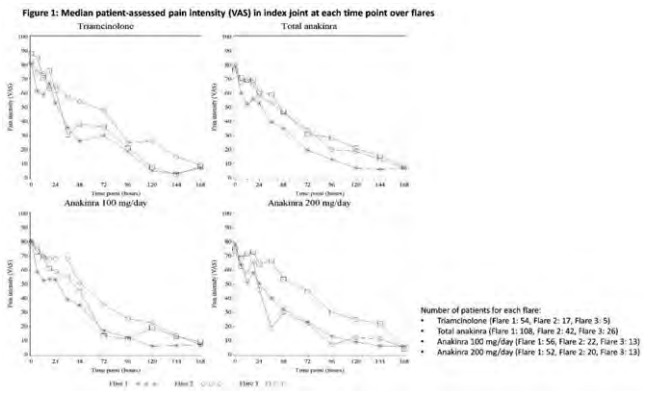
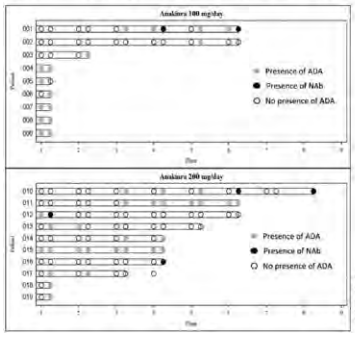


Figure 2: Presence of anti-drug antibodies and neutralizing antibodies over time



ADA, anakinra anti-drug antibodies; NAb, anakinra neutralizing anti-drug antibodies; bars indicate number of flares with 2 timepoints for each flare, flare baseline and flare post baseline; gray bullets indicate presence of ADA at that timepoint; filled bullets indicate presence of NAb at that timepoint; empty bullets indicate absence of NAb/ADA at that timepoint.

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THU0440 LOW DOSE COLCHICINE COMBINED WITH SPORADIC INTRAMUSCULAR INJECTIONS OF BETAMETHASONE – EFFICIENT AND SUSTAINED TREATMENT OF ACUTE GOUTY ARTHRITIS

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Background: Gouty arthritis is a common, potentially disabling and increasingly prevalent disease [1]. The main goals of treatment are to treat acute arthritis, decrease uric acid (UA) levels and prevent occurrence of further attacks. According to 2016 updated EULAR evidence-based recommendations for the management of gout, the most common and efficient options include prescription of colchicine (up to 6 mg during the first day) and intra-articular injections of glucocorticoids (GC) [2]. First option often causes diarrhea, the latter is extremely traumatic and painful in this group of patients.

Objectives: The aim of this study was to determine the efficacy of sustainability of anti-inflammatory effect of combination of low dose colchicine with sporadic intramuscular injections of betamethasone in the treatment of acute gouty arthritis.

Methods: 41 treatment naïve patients with acute gouty arthritis (27 male /65,9 %/, 14 female /34,1 %/, mean age 55,9 ± 13,7 years, mean disease duration 5,9 ± 4,4 years) were recruited in the study. On the first visit all the patients were prescribed 1.5 mg of colchicine per day and 2 intramuscular injections of betamethasone preparation (7mg-1ml) with an interval of 4 days. On the second visit (30th day) daily dose of colchicine was decreased to 1.0 mg, urate-lowering therapy (ULT) was begun. 21 patients (51,2%) received febuxostat 80 mg/day, 20 patients (48,8%) – allopurinol 100-150 mg/day.

Routine investigation included accurate collection of disease history, objective examination with determining the disease activity (Gout Activity Score /GAS/) and visual analogue scale (VAS patient), CBC, CRP, measurement of serum UA and creatinine level, urinalysis and other examinations [4]. GAS, VAS, CRP and uric acid were measured 3 times: at baseline, on 30th and 60th day of follow-up period.

Results: Investigation had shown the following results at baseline: sUA_1- 9,2 ± 1,5 mg/dl, CRP_1- 24,3 ± 21,5 mg/L, VAS_1- 8,3 ± 1,3 cm, GAS_1 6,3 ± 0,7. All enrolled patients completed 60 days of treatment. Preparations were well tolerated, no serious adverse events occurred: mild dyspepsia was observed in 4 (9,8%) patients, mild hypertension – in 7 (17,1%), 10 (24,4%) patients had transient diarrhea. Only in 14 out of 41 patients (34,1 %) there was a necessity to add NSAIDs to the main scheme of treatment.

On the second visit (30th day) all investigated measures with exception for UA (sUA_2 - 8,8 ± 1,9 mg/dl, p>0.05) had shown significantly lower results: CRP_2- 4,9±3,5 mg/dl, VAS_2 – 4,2±1,2 cm, GAS_2- 4,9 ± 0,7 (p<0.001).

On the third visit (60th day) the following results were obtained: sUA_3- 4,7 ± 1,3 mg/dl, CRP_3 - 3,5±2,0 mg/L, VAS_3 - 3,3±2,1 cm, GAS_3 - 3,7±0,9. All the measures were significantly lower than at baseline (p<0,001).

During all the follow-up period recurrent attacks of arthritis were observed in 6 patients (14,6%), particularly, only 2 patients experienced arthritis after the prescription of ULT.

Conclusion: Low dose colchicine in combination with sporadic (1-2) intramuscular injections of betamethasone can present as an efficient, non-traumatic, safe and cost-effective option for the treatment of acute gouty arthritis. Moreover, according to results of our study, anti-inflammatory effect was stable even after the prescription of ULT.

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THU0441 DIAGNOSTIC ACCURACY OF THE NIJMENGEN SCORE FOR GOUTY ARTHRITIS IN PATIENTS HOSPITALIZED FOR ACUTE MONOARTHRITIS

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Background: The gold-standard for diagnosis of gout is the identification of monosodium urate (MSU) crystal in joint fluid. However, the sensitivity, specificity, and reproducibility of such analysis are not excellent, and joint aspiration is sometimes difficult, or impossible. The Nijmengen score is an easy-to-use rule without joint fluid analysis with excellent validity, in primary as well as in secondary care (1, 2). However, it's validity as not been evaluated in the particular situation of patients whose acute arthritis necessitates hospitalization.

Objectives: The objective of the present study was to assess diagnosis performances of the score in patients hospitalized for acute monoarthritis.

Methods: *Inclusion*: all patients hospitalized for acute monoarthritis in the rheumatology department of the Dijon University Hospital between 2016 and 2019. *Assessment*: 1- clinical examination by an experimented rheumatologist; 2- joint aspiration and synovial fluid analysis following aspiration; 3- ultrasound (US) examination of the knees, first metatarso-phalangeal joints, and arthritic joint by a trained rheumatologist; 4- dual-energy computed tomography (DECT) of the arthritic joint; 5- Nijmengen score (cutoff scores of ≥ 8 needed for diagnosis of gout, and ≤ 4 to rule out gout) and ACR/EULAR 2015 classification criteria (3) (cut-off score of ≥ 8 needed for diagnosis of gout). *Analysis*: positive and negative predictive values, and ROC curve analysis of the Nijmengen score, using as gold-standard on one hand the results of the MSU crystal research, on the other hand those of the ACR/EULAR criteria.

Results: A total of 39 patients were included (mean age = 69.8 ± 15 years, 74.4 % males, mean BMI = 27.5 ± 4.6 Kg/m2, mean serum uric acid = 354.6 ± 117.5 µmol/l). The affected joints were the knee (n = 31), ankle (n = 3), hip (n = 2), wrist (n = 2), shoulder (n = 1). Joint fluid analysis revealed MSU crystal in 11 patients. The ACR/EULAR was ≥ 8 in 15 patients. The Nijmengen score was ≥ 8 in 11 patients, including 5 with MSU crystal on joint fluid analysis and 9 with an ACR/EULAR score ≥ 8. The Nijmengen score was ≤ 4 in 15 patients, including 14 with no MSU crystal on joint fluid analysis and 14 with an ACR/EULAR score < 8. The positive predictive values of a Nijmengen score ≥ 8 were 45 % (joint fluid analysis as gold standard) and 81.8 % (ACR/EULAR). The negative predictive values of a Nijmengen score ≤ 4 were 93.3 % (joint fluid analysis and ACR/EULAR as gold standard). On ROC curve analyses, the areas under the curve were 0.763 (95% CI = 0.612 – 0.914) using joint fluid analysis as gold standard (figure 1) and 0.908 (95% CI = 0.814 – 1.0) using the ACR/EULAR score as gold standard (figure 2).

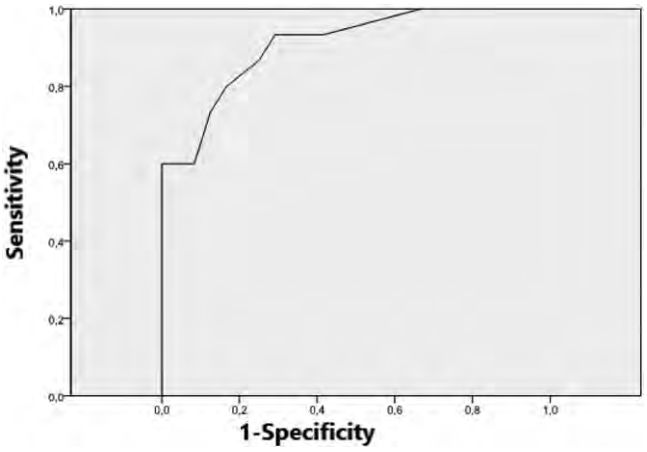


Fig. 1 ROC curve (fluid analysis as gold standard)

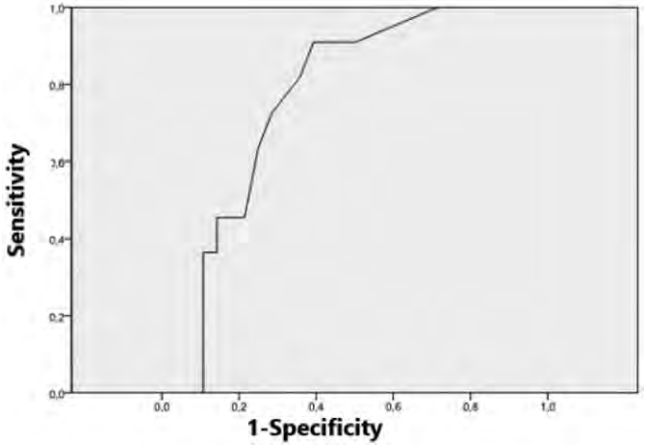


Fig. 2 Roc curve (ACR/EULAR as gold standard)

Conclusion: Although having been developed for use in primary-care, the Nijmengen score appears to be useful in patients hospitalized for acute monoarthritis in a rheumatology unit.

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THU0442 GOUT AND HEART FAILURE IN THE US: A NATIONAL PERSPECTIVE

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Background: Heart failure (HF) is the eighth leading cause of death in the US, with a 38% increase in the number of deaths due to HF from 2011 to 2017 (1). Gout and hyperuricemia have previously been recognized as significant risk factors for heart failure (2), but there is little nationwide data on the clinical and economic consequences of these comorbidities.

Objectives: To study heart failure hospitalizations in patients with gout in the United States (US) and estimate their clinical and economic impact.

Methods: The Nationwide Inpatient Sample (NIS) is a stratified random sample of all US community hospitals. It is the only US national hospital database with information on all patients, regardless of payer, including persons covered by Medicare, Medicaid, private insurance, and the uninsured. We examined all inpatient hospitalizations in the NIS in 2017, the most recent year of available data, with a primary or secondary diagnosis of gout and heart failure. Over 69,800 ICD 10 diagnoses were collapsed into a smaller number of clinically meaningful categories, consistent with the CDC Clinical Classification Software.

Results: There were 35.8 million all-cause hospitalizations in patients in the US in 2017. Of these, 351,735 hospitalizations occurred for acute and/or chronic heart failure in patients with gout. These patients had a mean age of 73.3 years (95% confidence intervals 73.1 – 73.5 years) and were more likely to be male (63.4%). The average length of hospitalization was 6.1 days (95% confidence intervals 6.0 to 6.2 days) with a case fatality rate of 3.5% (95% confidence intervals 3.4% – 3.7%). The average cost of each hospitalization was $63,992 (95% confidence intervals $61,908 - $66,075), with a total annual national cost estimate of $22.8 billion (95% confidence intervals $21.7 billion - $24.0 billion).

Conclusion: While gout and hyperuricemia have long been recognized as potential risk factors for heart failure, the aging of the US population is projected to significantly increase the burden of illness and costs of care of these comorbidities (1). This calls for an increased awareness and management of serious co-morbid conditions in patients with gout.

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THU0443 SEASONAL VARIATIONS AND ASSOCIATED FACTORS OF GOUT ATTACKS: A PROSPECTIVE MULTICENTER STUDY IN SOUTH KOREA

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Background: Gout shows a seasonal variation that widely differs among geographic areas, and we previously reported a seasonal effect on gout in Korea. However, we had no information regarding changes in diet and had only limited laboratory data because this was a retrospective study in patients receiving a urate-lowering therapy. Therefore, we designed this prospective study to elucidate the seasonality and associated factors of gout attacks in Korea.

Objectives: To evaluate the seasonality and associated factors of the incidence of gout attacks in Korea.

Methods: We prospectively enrolled patients with gout attacks who were treated at nine rheumatology clinics between January 2015 and July 2018 and followed them for 1-year. Demographic data, clinical and laboratory features, and meteorological data including seasonality were collected.

Results: Two hundred-five patients (males, 94.1%) were enrolled. The proportion of patients with initial gout attacks was 46.8% (n = 96). The mean age, body mass index, attack duration, and serum uric acid level at enrollment were 50.5 years, 26.1, 10.2 days, and 7.3 mg/dL, respectively. Gout attacks were most common during spring (43.4%, $P < 0.001$) and in March (23.4 %, $P < 0.001$). A similar pattern of seasonality was observed in the group with initial gout attacks. Alcohol was the most common provoking factor (39.0%), particularly during summer (50.0%). The mean diurnal temperature change on the day of the attack was highest in the spring (10.3°C), followed by winter (9.1°C), summer (8.1°C), and fall (8.0°C) ($P = 0.027$). The mean change in humidity between the 2 consecutive days (the day before and the day of the attack) was significantly different among the seasons (3.4%, spring; 0.2%, summer; 0.4%, fall; -3.9%, winter; $P = 0.015$). One hundred twenty-five (61%) patients completed 1-year follow-up (51% in the

initial attack group). During the follow-up period, 51 gout flares developed (18 in the initial attack group). No significant seasonal variation in the follow-up flares was found.

Conclusion: In this prospective study, the most common season and month of gout attacks in Korea were spring and March, respectively. Alcohol was the most common provoking factor, particularly during summer. Diurnal temperature changes on the day of the attack and humidity changes from the day before the attack to the day of the attack were associated with gout attack in our cohort.

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THU0444 INCIDENCE OF ACUTE GOUT FLARE IN PATIENTS INITIATED ON INTRAVENOUS BUMETANIDE FOR ACUTE CONGESTIVE HEART FAILURE EXACERBATION

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Background: Heart failure is a prevalent and ever-increasing public health concern associated with significant morbidity, mortality, and financial burden. Therefore, identifying any factors that worsen the outcome of patients with heart failure is crucial to the nation's medical and financial health.

One of the major comorbidities associated with heart failure is gout. Gout is a clinical syndrome of joint inflammation resulting from the deposition of monosodium urate crystals, causing painful and swollen arthritis. Acute gout flares in the context of acute heart failure (AHF) exacerbations result in longer lengths of stay and form an independent risk factor for increased readmissions or death[1]. The use of loop diuretics in treating patients with AHF exacerbations may cause new onset of gouty arthritis or recurrence of established gout by increasing serum uric acid levels. Uric acid alone is implicated as an independent predictor of mortality in patients with chronic heart failure[2].

Objectives: In this study, we aim to better characterize the incidence of acute gout flares in patients being treated with intravenous bumetanide for AHF exacerbations.

Methods: This single-center retrospective cohort study included adult patients within an urban tertiary-care center hospital between 5 August 2016 and 30 June 2018. Chart review was performed to identify 130 patients who were hospitalized for AHF exacerbations, received intravenous (IV) bumetanide, and developed an acute gout flare for a total of 176 cases (Figure 1).

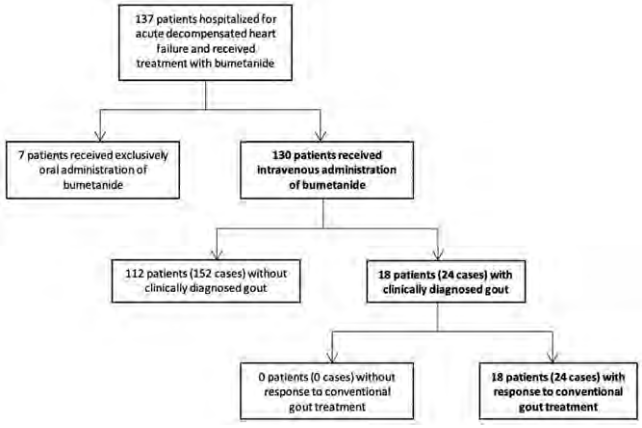


Figure 1 Patient Selection

Patients were identified as having an acute gout flare if the primary treating physician(s) documented a clinical picture congruous with acute gout (e.g., onset of a painful, swollen, or erythematous joint) and administered conventional treatment for acute gout including non-steroidal anti-inflammatory agents (NSAIDs), steroids, colchicine, urate-lowering therapies, and/or intra-articular joint injection with symptomatic improvement.

Results: The annualized incidence of acute gout while receiving IV bumetanide for a heart failure exacerbation is 7.17%.

There was no statistical difference in age, gender, race, or BMI among patients who developed acute gout compared with those who did not develop acute gout while receiving IV bumetanide.

An acute gout flare that occurred during treatment of AHF with IV bumetanide increased hospital length of stay (LOS) by 3 days (mean LOS 15.2 days in those who had acute gout, mean LOS 11.6 days in those who did not [p-value 0.277]).

Patients who received allopurinol during their hospitalization for AHF exacerbation had lower 30-day readmission rates for any cause (p-value 0.017, Table 4). There was no reduction in the 30-day readmission rate in patients who received colchicine without allopurinol during their hospitalization for AHF exacerbation. Those with a history of gout had higher readmission rates than those without a history of gout (p-value 0.007).

Conclusion: Gout is known to be a weighty contributor to patients' morbidity and mortality in heart failure, and the occurrence of acute gout flare in AHF exacerbations may be precipitated by the use of loop diuretics. We show that the use of IV bumetanide in patients hospitalized for AHF exacerbations is associated with a 7.17% yearly incidence of acute gout flares. Furthermore, patients with a history of gout were found to have higher readmission rates, and those who received allopurinol during their hospitalization had lower readmission rates.

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THU0445 PREVALENCE AND INFLUENCE OF DISEASE DURATION IN THE AMOUNT OF ARTICULAR AND PERIARTICULAR DEPOSITS OF MONOSODIUM URATE (MSU) CRYSTALS IN NON-TREATED GOUTY ARTHRITIS PATIENTS

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Background: Monosodium urate crystals deposition arthritis (Gout) is the most prevalent inflammatory arthropathy in our society. The use of muskuloskeletal ultrasound (MSUS) is emerging as a diagnostic method of patients with gout, mainly in the past few years.

Objectives: Our objective is to establish the prevalence of articular and periarticular ultrasound lesions in patients with known or recent gout diagnosis without urate-lowering therapy (ULT) as well as to analyze the influence of disease duration on these findings.

Methods: Observational, cross-sectional and descriptive study, including patients with diagnosis of Gout (fulfilling the ACR / EULAR Classification Criteria 2015) between September and November 2019 in our Rheumatology service of a tertiary center. Demographic and clinical records were collected (table 1) and MSUS was performed on each patient systematically by two rheumatologists, exploring a total of 20 structures (8 tendons and 12 joints). Suggestive images of MSU crystals deposition were defined following the OMERACT 2015 ultrasound elementary lesions definitions. Deposits included lesions as tophus, hyperechoic aggregates (HA) and double contour (DC).

Table 1. Demographic and laboratory data

Features	Patients (n=38)	%
Sex	Men 34 Women 4	89,5 10,5
Age (years)	Mean ±SD 60±14,43	
Comorbidities	Arterial hypertension18 Mellitus diabetes 4 Dyslipidemia 13 Smoking 7 Alcohol 14	47,4 10,5 34,2 18,4 36,8
BMI (Kg/m2)	Mean±SD 27,3±4,23	
Blood urate levels (mg/dL)	Mean±SD 8,2±1,74	
Blood creatinine levels (mg/dL)	Mean±SD 1,09±0,75	

Results: A total of 38 patients were included, 34 men (89.5%) and 4 women (10.5). Twenty seven (71.1%) presented MSU crystals in synovial fluid samples, while rest of them (28.9%) met 2015 ACR / EULAR Clasiffication Criteria for Gout. Disease duration (since onset of symptoms) was less than 6 months in 20 patients (52.6%) and longer than 6 months in 18 (47.36%). Thirty seven patients (97.36%) presented some type of MSU deposits on the explored areas. One hundred and thirty (17,10%), out of 760 explored locations, had MSU deposits. Patients with disease duration less than 6 months had 56 locations with deposits (43.07%), while those with a symptomathology longer than 6 months had 74 locations with deposits (56.92%). Left knee was the most frequent location of UMS deposits (78.95%). Out of the 145 MSUS images with elementary lesions due to MSU crystal deposits, 28 were tophi (19.31%), 33 HA (22.75) and 84 DC (57.93%). Out of the total images with deposits (DC, HA and tophi), DC in the left

knee was the most frequent (21.38%), followed by DC in right knee (17.24%) and DC in 1st MTP (10.24%).

Conclusion: Almost 100% of patients with recently diagnosed gout without ULT, presented on at least one of the scanned locations MSUS images suggestive by MSU crystals deposition. Most of MSU crystals deposits were on knees and 1st MTP. Patients with non-treated longer than 6 months of disease duration gout had a greater number of MSU crystals deposit locations detected by MSUS. The presence of tophi and HA was statistically higher in patients with disease duration longer than 6 months (table 2).

Table 2. MSU crystals median locations and MSUS images in both groups

	<6months (n,%)	>6months (n,%)	p value
Deposits locations	56 (43,07)	74 (56,92)	0,075[1]
MSUS images with deposits -Tophi	8 (28,57) 0 (0-0)	20 (71,43) 0 (0-1)	0,018[1]
Median, IR () - HA Median, IR () -	7 (21,21) 0 (0-0) 39	26 (78,79) 0 (0-1)	0,023[1]
DC Median, IR ()	(46,43) 0,5 (0-1)	45 (53,57) 0 (0-2)	0,853[1]

[1]Mann-Whitney U test comparing medians between both groups IR: interquartile range

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THU0446 SUCCESSFUL TREATMENT OF GOUT IS FREQUENT IN CLINICAL PRACTICE WHEN APPLYING A TREAT-TO-TARGET STRATEGY: RESULTS FROM THE NOR-GOUT STUDY

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Background: International EULAR and ACR recommendations support lifestyle changes, diet and urate lowering therapy (ULT) in gout. Treat-to-target ULT is often not performed, resulting in insufficient treatment of gout. We studied how many patients achieved the recommended treatment target of <360 µmol/l for serum urate (SUA) when a treat-to-target approach was applied in clinical practice, and which factors predicted reaching this target.

Objectives: We studied how many patients achieved the recommended treatment target of <360 µmol/l for serum urate (SUA) when a treat-to-target approach was applied in clinical practice, and which factors predicted reaching this target.

Methods: 211 patients with crystal proven gout were included into the prospective, observational NOR-Gout study if they recently had a gout flare as well as insufficiently treated serum urate SUA >360 µmol/l).

The intervention consisted of individual verbal information on lifestyle, including factors related to physical activity, diet and the importance of drug adherence. ULT (mainly allopurinol) was initiated and escalated monthly according to EULAR recommendations. Patients were during the first year seen by physician and nurse every three months with additional visits after month 1 and month 2, with further visits monthly as necessary until the treatment target of SUA <360 µmol/l (or <300 if tophi) was met.

Baseline age was 53.6 (SD 12.2) years, disease duration 7.8 years (SD 7.6), BMI 28.8 (SD 4.5) kg/m^2, 95.3% were males. Baseline SUA was 500 (77) µmol/l and 16.6% had subcutaneous tophi. Assessments included questions on frequency of alcohol use, and application of the self-efficacy scales for symptoms (SES, range 10-100) as well as the beliefs in medicines questionnaire (BMQ), which included a scale for general overuse of medicines (range 4-16).

186/211 (88.2%) patients completed the visit for the primary SUA endpoint at 12 months.

Results: SUA continuously declined over 12 months and the frequency of responders increased (table 1):

Table 1. Responders and SUA levels during the treat-to-target intervention

Month	Month 0	1	2	3	6	9	12
% n Responders	0	21.3 43/202	48.7	69.3	86.7	81.9	85.5
SUA<360	0/211		94/193	131/189	151/187	136/166	159/186
SUA µmol/l (mean, SD)	500 (78)	413 (77)	371 (64)	341 (61)	327 (59)	316 (56)	311 (49)

At 12 months 87.6% (163/186) of patients used allopurinol and 13.4% (23/186) febuxostat with mean daily doses of 289 mg (range 100-900) and 59 (20-120) mg, respectively.

Reaching the treatment target of SUA after 12 months was bivariately related to work status, alcohol use, and beliefs in general overuse of medicines. In multivariable analyses in the final model also adjusted for baseline SUA, several variables predicted reaching the SUA target of <360 µmol/l: age (per 10 years) (OR 1.5; 95% CI 1.06 – 1.96, p=0.026), alcohol use no more than monthly vs. at least weekly (OR 6.9, 95% CI 1.90 – 25.2, p=0.003), self-efficacy for symptoms (per 10 units) (OR1.31; 95% CI 1.00 – 1.63; p=0.05), and low belief that medicines are generally overused (per decreasing unit) (OR 1.30; 1.04 – 1.62, p=0.019).

Conclusion: Most patients (85.5%) with recent gout flare und increased SUA reached the target SUA after 12 months. A good treatment result was predicted by increasing age,

less frequent alcohol use, when patients believed they could cope with symptoms and when they did not believe that drugs are generally overused.

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THU0447 HOME-MONITORING GOUT FLARES WITH A SMARTPHONE APP – RESULTS OF A FEASIBILITY STUDY

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Background: Gout flares are considered a key clinical and research outcome in gout. Early treatment of gout flares increases patient well-being and warrants timely notification of the treating clinician.

Objectives: To test the feasibility of a smartphone app to home-monitor gout flares real-time for both patients with a suspicion of and established gout.

Methods: Thirty patients were recruited during their visit at the outpatient rheumatology clinic. Inclusion criteria were age ≥ 18 years, smartphone possession, established gout (crystal proven) or a clinical suspicion of gout and at least one flare reported in the last three months.

A straight-forward query app was used to incorporate an adapted version of the 2017 four-criteria gout flare definition.[1] For 90 consecutive days the app asked patients to report their current pain score on an 11-points scale as screening question. Scoring pain below 4 terminated the query, otherwise the app posed the remaining criteria: does the patient experience warm and/or swollen joints and are symptoms regarded as a gout flare. Responses were transmitted in real-time to the dashboard and the clinician was alerted via email if predefined conditions were met. End of study evaluation consisted of the number of generated alerts, duration of (possible) flares and actions taken. Patient feasibility was assessed by measuring app attrition and using a questionnaire based on the Technology Acceptance Model. [2] All constructs were analysed using descriptive statistics.

Results: All 30 recruited patients finished the trial. Three minor, resolvable technical issues were reported. Seventeen participants never missed a question. In total 110 responses (4.1%) were missed with three participants responsible for

66 missings. 90% of the participants rated app usability good to excellent and 70% would recommend the app to other patients.

Twelve out of thirty patients generated a total amount of 174 alerts where four patients with a suspicion of gout were responsible for 148 alerts (85%). These patients scored three out of four criteria as they had warm, swollen and painful joints but, after consultation with the clinician, their symptoms were not regarded as a gout flare.

The 174 alerts belonged to 23 (possible) flares with a median duration of 5 days [IQR 3,5 – 7,5]. Twenty-one pro-active telephone calls were made which resulted in four visits to the clinic within 48 hours. Clinical guidance over the phone consisted of checking in on patient's symptoms, giving advice and ten medication adjustments.

Conclusion: This prospective study shows feasibility of a smartphone app for home-monitoring gout flares for patients because of high usability scores and low attrition rates. The app has added value for gout care because it enables clinicians to act on flares as they occur. The next step is to further implement the app whilst perpetuating investigation into the added value for patients and clinical practice alike.

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THU0448 NO DIFFERENCE IN GOUT FLARES AFTER INITIATION OF URATE LOWERING THERAPY BETWEEN ONCE OR TWICE DAILY 0.5 MG COLCHICINE PROPHYLAXIS

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Background: Initiation of urate lowering therapy (ULT) is associated with an increase in gout flares[1]. Therefore, guidelines advice prophylactic therapy during the first six months of ULT[2]. Colchicine 0.5-1 mg/day is recommended. Whether 1 mg/day colchicine is superior to 0.5 mg/day is unknown.

Objectives: To examine the difference in gout flares in the first six months after initiation of ULT between 0.5 and 1.0 mg/day colchicine prophylaxis.

Methods: Patients with clinical diagnosis of gout, a first outpatient visit between January 2010 and March 2018 and a follow-up of at least 6 months were included in a retrospective cohort study, conducted in two rheumatology centres in the Netherlands. Within this cohort, patients starting ULT and colchicine prophylaxis were selected. Difference in gout flare incidence density (ID) in the first six months after start of ULT between colchicine 0.5 and 1.0 mg/day was analysed using Poisson regression, corrected for confounders. Secondary analyses included the proportion of patients reaching a target of serum urate acid (SUA) of < 0.36 mmol/l within the first six months.

Results: Of 2108 gout patients, 379 patients started ULT and used colchicine prophylaxis (table 1). ID of flares was 2.8 and 2.6 per patient year on colchicine 1.0 and 0.5 mg/day respectively, resulting in an incidence rate ratio of 1.05 (95% CI 0.86 – 1.27). Within the first six months 68% in the colchicine 1mg/day and 63% in the colchicine 0.5 mg/day reached their target (difference 5%, 95% CI -0.08 – 0.18).

Table 1. Baseline patient, disease and treatment characteristics

	Colchicine prophylaxis	
	0,5 mg/day (n=275)	**1 mg/day (n=104)**
Men, no. (%)	226 (82%)	88 (85%)
Age, years	67.3 (58.8-76.3)	65.3* (54.4-71.9)
BMI, kg/m^2	29.0 (26.1-32.1)	29.5 (27.9-31.6)
Comorbidity no. (%)		
Hypertension	146 (53%)	54 (52%)
Diabetes Mellitus	66 (24%)	24 (23%)
Hypercholesterolemia	43 (16%)	15 (14%)
Renal insufficiency	56 (20%)	18 (17%)
Crystal-confirmed diagnosis, no. (%)	197 (72%)	77 (74%)
Serum urate acid at start ULT (mmol/l), mean ± SD	0.51 ± 0.11	0.50 ± 0.11
ULT medication, no. (%)		
Allopurinol	272 (99%)	103 (99%)
Benzbromaron	2 (0.6%)	
Febuxostat	1 (0.4%)	1 (1%)

*Compared to colchicine 0,5 mg/day, P<0.05.
**No SD possible, n = 1.

Conclusion: Use of 1 mg/day colchicine is not superior to 0.5 mg/day as prophylaxis for ULT induced gout flares. For generalisability it should be noted that flare rates were not very high, probably due to the background ULT being characterised by a "start low, go slow" approach. In this context colchicine 0.5 mg/day is sufficient as prophylaxis.

References:

[1] Seth R et al. J Rheumatol 2014;92;42-47.

[2] Richette P et al. Ann Rheum Dis 2017;76:29–42.

Disclosure of Interests: : Frouwke Veenstra: None declared, L.M. Verhoef: None declared, Lieke Nieboer: None declared, Alfons den Broeder: None declared, Wing-Yee Kwok: None declared, Inger Meek: None declared, Frank van den Hoogen: None declared, Noortje van Herwaarden: None declared, Marcel Flendrie Grant/research support from: M. Flendrie has received grants from Menarini and Grunenthal., Consultant of: M. Flendrie has received consultancy fees from Menarini and Grunenthal.

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THU0450 OPTIMISTIC STATUS ASSOCIATES WITH COMPLIANCE TO URATE-LOWERING THERAPY IN GOUT PATIENTS

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Background: Compliance to urate-lowering therapy (ULT) is poor in gout patients, which contributes to increased frequency of acute gout attacks, deposition of tophi and urate nephropathy [1]. Optimistic status is probably a potential and considerable factor affecting compliance to ULT in gout patients.

Objectives: To compare optimistic status between gout patients and healthy controls, and also between gout patients with good and poor compliance. Relationship between optimistic status and compliance to ULT, sUA target achievement of gout patients were assessed as well.

Methods: This was a monocentric and observational study which was performed from August 2018 to December 2019. Adult patients who met the 2015 gout classification criteria were included in this study. The healthy controls were individuals who were free of gout, hyperuricemia and other rheumatic diseases from the physical examination center of our hospital. Demographic data, including age, gender and education were collected from all individuals. Serum uric acid (sUA) were collected from gout patients at enrollment and again after 3 months. Disease duration of gout, visual analogue scale (VAS) of pain were also assessed for gout patients at enrollment. Compliance to ULT was measured using the medication possession ratio (MPR) in the following 3 months. Poor compliance was defined as MPR<0.8 and good compliance was defined as MPR≥0.8. All subjects completed the life orientation test-revised (LOT-R) for optimistic status assessment.

Results: Five hundred and thirty gout patients and 307 healthy controls matched by age (41.4±12.3 vs. 42.1±9.3 years), gender (male 97.1% vs. 95.1%) and education (college graduated 54.2% vs. 58.0%) were included in this study. Of the 530 gout patients, the mean disease duration was 5.7±4.9 years, and 292 (55.1%) patients' MPR were lower than 0.8. There was no statistic difference in LOT-R between gout patients and healthy controls (19.0±2.4 vs. 19.2±2.5, P>0.05) (Table 1). Gout patients with poor compliance (MPR<0.8) had higher level of sUA (525.5±138.0 vs. 471.2±152.5 μmol/L, P<0.05), followup sUA (450.1±154.5 vs. 361.6±120.0 μmol/L, P<0.05) and higher LOT-R (19.6±2.6 vs. 17.8±1.7, P<0.05) than those with good compliance (MPR≥0.8). Of the 292 gout patients with poor compliance, there were only 83 (28.4%) patients achieved sUA target after 3 months, and their LOT-R were significantly lower than

those did not achieve sUA target (18.8±2.1 vs. 19.6±2.4, P<0.05). Finally, LOT-R correlated positively with sUA (r=0.131, P<0.05) and followup sUA (r=0.09, P<0.05), but negatively with MPR (r=-0.473, P<0.05) of gout patients (Table 2).

Table 1 Demographic and optimistic status of gout patients and healthy controls

Variables	Gout patients (*n*=530)	Controls (*n*=307)	P
Age (years)	41.4±12.3	42.1±9.3	0.116
Male gender, n (%)	511 (96.4)	292 (95.1)	0.368
College graduated, n (%)	287 (54.2)	178 (58.0)	0.312
LOT-R	19.0±2.4	19.2±2.5	0.189

LOT-R: life orientation test-revised

Table 2 Correlation analysis between LOT-R and clinical variables in gout patients

Variables	LOT-R	
	r	P
Age	0	0.994
Disease duration	-0.058	0.182
VAS	0.034	0.432
sUA	0.131	0.003*
Followup sUA	0.126	0.016*
MPR	-0.393	<0.001*

LOT-R: life orientation test-revised, *VAS:* visual analogue scale, *sUA:* serum uric acid, *MPR:* medication possession ratio
*P<0.05

Conclusion: Gout patients share similar optimistic status to healthy controls. However, optimistic status relates to compliance to ULT and sUA target achievement of gout patients.

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[1] Harrold L R, Andrade S E, Briesacher B A, et al. Adherence with urate-lowering therapies for the treatment of gout. Arthritis research & therapy 2009, 11(2):R46.

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THURSDAY, 04 JUNE 2020

Basic and translational pain science

THU0451

CELL-MATRIX ADHESION OF BONE MARROW STROMAL CELLS IN MODIC TYPE 1 CHANGES IS INCREASED AND RELATES TO INCREASED EXPRESSION OF INTEGRIN B1

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Background: Modic type 1 changes (MC1) are vertebral bone marrow lesions associated with non-specific low back pain (LBP). The pathophysiology of MC1 includes inflammation, fibrosis, and high bone turnover. Bone marrow stromal cells (BMSCs) are key regulators of these processes: BMSCs contribute to inflammation by regulating myelopoiesis/osteoclastogenesis; BMSCs can differentiate into osteoblasts contributing to high bone turnover, and BMSCs can differentiate into pro-fibrotic myofibroblasts.

Objectives: To identify dysregulated biological processes in MC1 BMSCs contributing to the pathobiology of MC1.

Methods: Bone marrow aspirates were obtained from LBP patients with MC1 undergoing lumbar spinal fusion. Aspirates were taken prior to screw insertion. From each patient, a MC1 and a healthy control (HC) aspirate from the adjacent vertebral body was collected. BMSCs were isolated by plastic adherence and expanded. RNA from BMSCs passage 3 was sequenced (n=3+3) (Illumina Novaseq) and gene ontology of significantly dysregulated genes (p-value < 0.05) was analyzed. Specificity and rate of BMSC matrix adhesion were quantified: BMSCs (n=8+8) were seeded on fibronectin-coated, collagen-I-coated, and non-coated plastic dishes. BMSC adhesion was evaluated from 15min to 30min (Δ 30min - 15min). Percentage of adherent cells of MC1 and HC BMSC was compared with paired t-test. In order to identify integrins responsible for dysregulated cell-matrix adhesion, gene expression of 15 relevant integrins was measured by quantitative real-time PCR (qPCR). Normalized expressions were compared between MC1 and HC BMSC with paired t-test. Integrin β1 protein level was semi quantitatively analyzed by Western Blot (n = 5+5) and normalized to β-Actin expression.

Results: By RNA sequencing, 154 genes were differentially expressed between MC1 and HC BMSCs (p-value ≤ 0.01; $\log_2$-ratio ≥ 0.5). Gene ontology enrichment analysis revealed an overrepresentation of the biological process "cell-matrix adhesion" among all significantly regulated genes (p-value < 9.3e-13). A change in cell adhesion was corroborated with adhesion assay. Binding (Δ 30min - 15min) to collagen I (MC1+16%, HC +10%, p-value = 0.10), fibronectin (MC1+17%, HC +6%, p-value = 0.03), and non-coated surface (MC1+46%, HC +35%, p-value = 0.05) was increased in MC1 (Figure 1). Integrin gene expression analysis revealed significant upregulation of integrin beta-1 gene (*ITGB1)* in MC1 vs. HC (fold change = 1.24, p-value = 0.047), whereas there was no significant difference between the other integrins tested. On protein level, integrin β1 was upregulated in MC1 in four out of five patients (Figure 2).

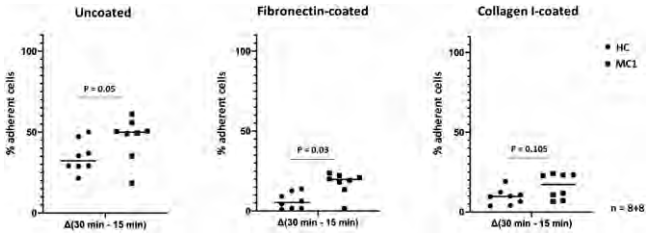


Figure 1. Adhesion assay.

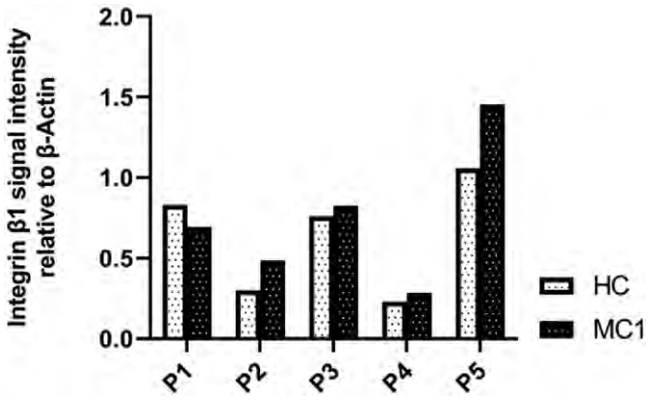


Figure 2. Western Blot analysis.

Conclusion: Adhesion of BMSCs to matrix and integrin β1 expression are increased in MC1. Integrin β1 is essential for cell-matrix adhesion and an important contributor to the initiation and progression of tissue fibrosis, a hallmark of MC1. Therefore, BMSCs and integrin β1 might be relevant novel targets for the treatment of MC1.

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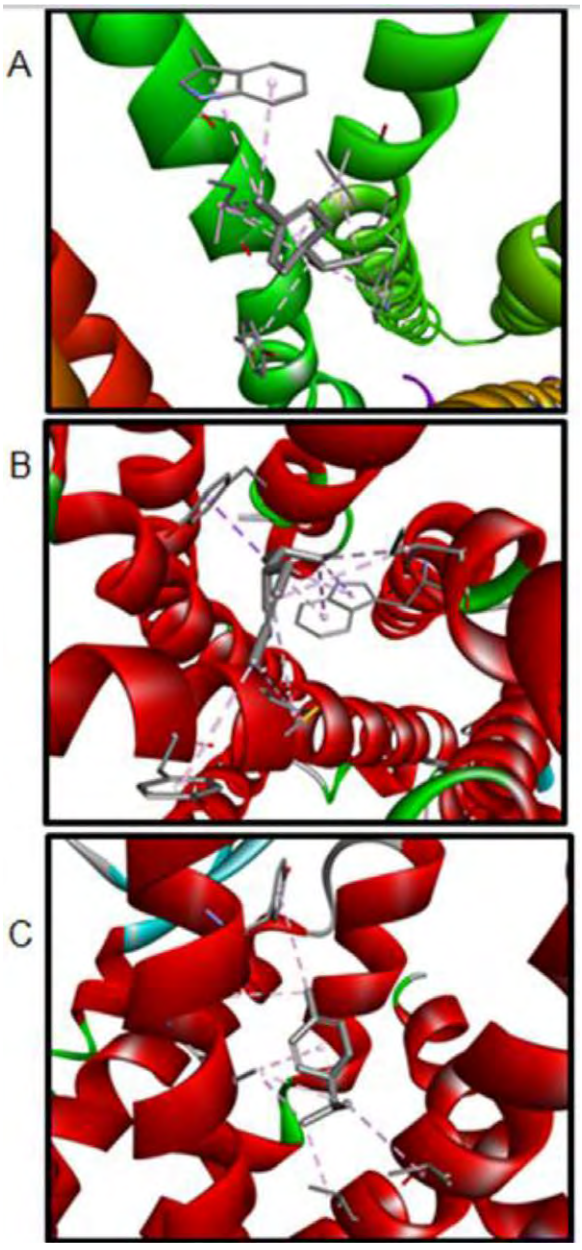


Figure 1. Graphical 3D representation of the binding modes of α-phellandrene with opioid receptors: A - Mu; B - Kappa; C – Delta

THU0452 **ANTINOCICEPTIVE EFFECT OF A-PHELLANDRENE IN CHRONIC PAIN: IN SILICO PHARMACOKINETIC, MOLECULAR DOCKING AND IN VIVO EVALUATION**

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Background: The pharmacological approaches of chronic pain are a challenge in the clinical context. Currently, only palliative treatments are performed. The α-phellandrene (α-phel) is a cyclic monoterpene found in essential oils of aromatic plants, which presents several biological activities, such as antinociceptive, antihyperalgesic and immunostimulant.1,2

Objectives: This study aimed to investigate the action of α-phellandrene in chronic pain through *in silico* and *in vivo* approaches, aiming to develop a new therapeutic option for painful conditions, reducing analgesic doses and side effects.

Methods: The pharmacokinetic analysis of α-phel was performed by PreADMET online server. The software ACD/ChemSketch 14.0 was used to optimize the 3D structure of α-phel. Molecular docking was performed with the software AutoDock Tools 1.5.6 to evaluate the pharmacodynamics interactions of α-phel and opioid receptors.

The mechanism of action of α-phel in chronic pain was analyzed *in vivo*. Ethics Committee of UFPI approved this project (protocol nº 305/17). Female Swiss mice (25-30 g) underwent partial sciatic nerve ligation surgery to induce neuropathy. The neuropathic mice (N=6) were pre-treated with Naloxone (2 mg/kg, i.p.) or Saline (10 mL/kg, p.o.). After 20 minutes, they were treated with α-phel (6,25 mg/kg, p.o.) or morphine (5 mg/kg, i.p.) and evaluated by Von Frey test.

Results: The predicted pharmacokinetic parameters (Table 1) suggest good intestinal absorption and good permeability. Plasma protein binding is elevated, however, it is reversible and technological alternatives, such as carrier systems, can improve it. The α-phel does not inhibit CYP3A4, it indicates a minimal possibility of interactions with others drugs and adverse reactions.

Table 1. Pharmacokinetic parameters of α-phel

ID	VALUE
BBB	7.17054
Buffer_solubility_mg_L	1227.08
Caco2	23.4164
CYP_2C19 and 2C9_inhibition	Inhibitor
CYP_2D6_inhibition_substrate	Non
CYP_3A4_inhibition	Non
CYP_3A4_substrate	Weakly
HIA	100.00000
MDCK	267.707
Pgp_inhibition	Non
Plasma_Protein_Binding	90.00000
Pure_water_solubility	141.466

The structure of α-phel binding opioid receptors is shown in Figure 1. The lowest ligand-receptor binding energies were, respectively: -6.0 kca/mol, -6.6 kcal/mol and -7.4 kcal/mol for the interaction of α-phel with Mu, Kappa and Delta receptors. It indicates that α-phel has high affinity for all three opioid receptors, binding in a strong and stable way.

The analgesic potential of the substance was tested *in vivo* as well. It was observed that Naloxone, an opioid antagonist, significantly reversed the effect of α-phel, indicating that it displays antinociceptive and antihyperalgesic activity through opioid system.

Conclusion: The monoterpene α-phel presents antinociceptive activity and reduces the sensitivity in chronic pain through the activation of opioid receptors.

Thus, *in vivo* and *in silico* results indicate that α-phel is an analgesic opioid agonist. This work may guide further preclinical studies, since α-phel may be an important strategy to treat chronic pain, with fewer side effects, dependence and tolerance than conventional drugs.

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Disclosure of Interests: : None declared

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THURSDAY, 04 JUNE 2020

Pain in rheumatic diseases, including fibromyalgia _

THU0453 **THIRD OCCIPITAL NERVE RADIO-FREQUENCY UNDER FLUOROSCOPIC GUIDANCE IN MANAGEMENT OF CERVICOGENIC HEADACHE IN RHEUMATOID ARTHRITIS**

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Background: Rheumatoid arthritis is a common type of autoimmune arthritis characterized by chronic inflammation. Cervical spine is often affected specially in long lasting disease

Objectives: Evaluate efficacy of Third occipital nerve Radiofrequency under fluoroscopic guidance to treat refractory cervicogenic headache in RA patients.

Methods: The current study was revised and approved from the local ethical committee of Faculty of Medicine; Assiut University, then registered in the clinical trials under the number of NCT03852355. Inclusion criteria included, Patients who fulfilled the American College of Rheumatology (ACR) (2010) criteria for RA and suffering

from upper neck pain and/or headache due to bilateral 3rd occipital nerve involvement, excluding other local cervical spine pathologies was confirmed by MRI and previously failed conservative treatment for at least three months prior to enrollment. Sixty adult patients were randomly assigned to one of the two studied groups Group 1 (RF, n = 30), received bilateral Third occipital nerve Radiofrequency under fluoroscopic guidance or Group 2 (control group, n = 30), received oral prednisolone 10 mg/day. The two groups were then followed-up with neck disability index (NDI), nocturnal neck pain VAS score and headache score every two weeks for three months. Sleep disturbance, sleep disability index were reassessed six months post intervention. Post interventional assessment was done by pain physician who were kept blind to the grouping process.

Results: Neck disability index (1ry outcome), Nocturnal pain VAS, and severity of headache showed significant differences during the whole post-interventional study period. The patients in RF group demonstrated significant improvement of pain in comparison to baseline value over the whole six months with p-value < 0.001 as regard to the fore-mentioned three parameters. On the other aspect, the control group patients showed significant improvement in comparison to its baseline value after the 2nd, 12th and 24th weeks only as follows: (0.001,0.003, 0.003 for the NDI) (p values of 0.02,0.01, 0.01 for the nocturnal pain VAS), (0.001 0.009, 0.005 for the headache VAS severity.

Conclusion: Radiofrequency of 3rd occipital nerve is effective in treatment of refractory cervicogenic headache in RA.

Disclosure of Interests: : None declared

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THU0454 SOMATIC SYMPTOMS IN FIBROMYALGIA AND THEIR CORRELATION WITH DRUG TREATMENT

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Background: Drug treatment in fibromyalgia (FM) is often disappointingly ineffective, and there are currently very few data to support therapeutic choices towards a personalized medicine approach.

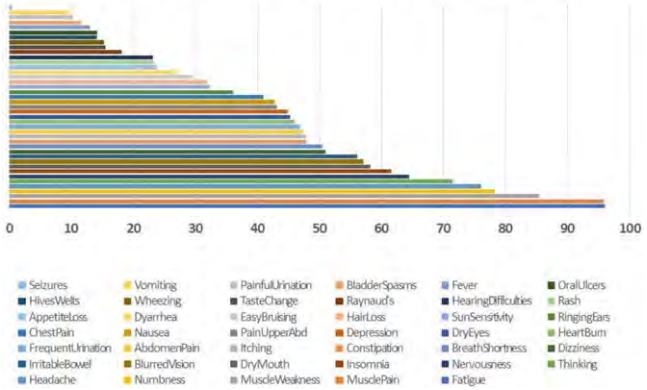
Objectives: To evaluate the prevalence of selected somatic symptoms in FM, and to study their relationship with drug treatments.

Methods: The study population consisted of 526 patients (471 F 55 M, mean age 47.31±11.33 yrs) affected by FM not associated with other rheumatic diseases. All patients were required to compile a questionnaire reporting the presence of 42 somatic symptoms -as suggested (1) – in the last 7 days. Drug usage was assessed by interview.

Results: On average, patients reported the presence of 17.04±6.68 symptoms (range 4-35), with ample variations in the prevalence of different symptoms (Fig. 1), ranging from over 95% (fatigue and muscle pain) to less than 10 %, seizures being reported by only 2 patients (0.4%). 31.1% of patients were not taking any drug for their FM. The most frequently used drugs were analgesics (ANA, 41.7%) followed by benzodiazepines (BD, 29.1%), SSRIs (16%), gabapentinoids (GABA, 14,4%), and NSRI (14.3%) (Fig. 2). Different drugs were associated with a different spectrum of somatic symptoms: as compared to non users, BD users reported a significantly higher (p< 0.05 by chi-square test) prevalence of irritable bowel (65.4% vs 52.3%), fatigue (98.7% vs 94.9%), thinking difficulties (78.4% vs 68.5%), muscle weakness (94.1% vs 81.7%), abdominal pain (55.6% vs 43.9%), insomnia (73.9% vs 56.6%), depression (63.4 % vs 37.2%), constipation (60.1% vs 42.9%), pain in upper abdomen (50.3% vs 40.2%), nausea (53.6% vs 38.3%), nervousness (71.9% vs 61.5%), chest pain (49.0 vs 37.75), blurred vision (65.4% vs 53.6%), dry mouth (72.5% vs 52.3%), itching (56.2% vs 44.5%), vomiting (13.7% vs 7.8%), taste change (22.2% vs 12.7%), dry eyes (55.6% vs 41.0%), breath shortness (56.9% vs 47.7%), appetite loss (33.3% vs 19.7%), painful urination (15.0% vs 8.4%), and bladder spasms (18.3% vs 8.6%). NRSI users reported a significantly higher prevalence of thinking difficulties, constipation, blurred vision, dry mouth, wheezing, dry eyes, easy bruising. Among GABA users, there was a higher prevalence of thinking difficulties, numbness, insomnia, constipation, nausea, dry mouth, dry eyes, appetite loss, sun sensitivity, easy bruising, and bladder spasms. In no cases a higher prevalence of symptoms was recorded in drug non users vs users.

Conclusion: The usage of different drugs in FM is associated with different somatic symptoms. The higher prevalence of symptoms in drug users as compared to non users raises serious questions concerning the opportunity or the appropriateness of drug selection in FM.

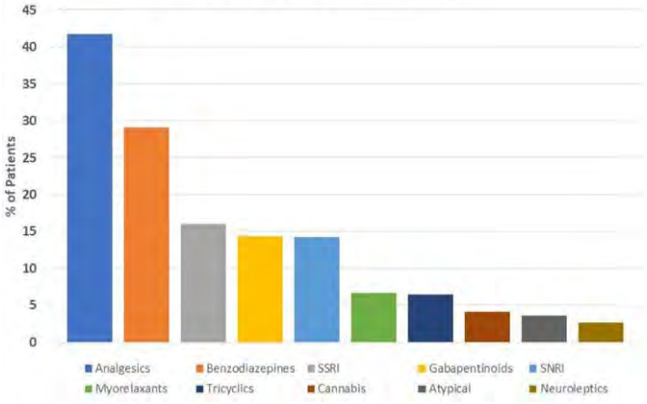
Figure 1. Prevalence of Somatic Symptoms in The Population (%)



References:

[1] Wolfe F., et al. Arthritis Care Res (Hoboken). 2010 May;62(5):600-10

Figure 2. Drug Usage in The Population



Disclosure of Interests: : None declared

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THU0455 DIFFERENCES IN PSYCHIATRIC COMORBIDITIES AND LIFE ADVERSITIES BETWEEN PATIENTS WITH RHEUMATOID ARTHRITIS ASSOCIATED WITH FIBROMYALGIA AND PATIENTS WITH PRIMARY FIBROMYALGIA

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Background: Patients with rheumatic arthritis (RA) continue to report significant pain despite apparent disease control by immunosuppressive drugs (1), leading to the hypothesis that central sensitisation (CS) plays a role in the chronic musculo-skeletal pain defining fibromyalgia (FM).

Objectives: The aim of our study was to evaluate the differences in psychiatric comorbidities and life adversities between patients with AR+FM and patients with primary FM (PFM).

Methods: In a observational cross- sectional study patients with PFM and AR+FM were consecutively recruited. The inclusion criteria were an age of 18-70 years; a diagnosis of RA according to the 2010 ACR classification criteria and FM according to the 1990 ACR criteria and 2016 ACR criteria. Lifetime diagnoses of major depression disorder (MDD), panic disorder (PD) and post-traumatic stress disorder (PTSD), three of the most frequently described psychiatric disorders among FM patients, were made with the Structured Clinical Interview for DSM-5. Depressive symptoms were measured using the Zung Self-rating Depression Scale (ZSDS). Childhood trauma was measured using the short form of the Childhood Trauma Questionnaire (CTQ) and stressful events were assessed

using the Paykel's Interview for Recent Life Events. Pain was assessed using a visual analogue scale (VAS). The Fibromyalgia Impact Questionnaire (FIQ) was also used.

Results: Seventy-seven patients were originally screened, but seven were excluded because of current depressive episode or having a ZSDS of ≥60 or categorized as minimizers of childhood maltreatment at CTQ. The final analysis therefore involved 70 patients, all Caucasians: 30 with PFM and 40 with AR+FM. All patients with PFM and 38 (95%) of the 40 with AR+FM were treated for FM symptoms (antidepressants, pregabalin). The lifetime rates of MDD were significantly higher in PFM vs AR+FM (76.7 % and 40% respectively, p =0.003), as well as the rates of PD (50 % and 15% respectively, p =0.003), whereas there was no difference in PTSD rates. The PFM patients reported significantly higher levels of physical (p=0.020) and sexual abuse (p=0.011) and physical neglect (p<0.001), whereas there was no between-group difference in the levels of emotional abuse (p=0.912) and neglect (p=0.542); consistently, the proportion of sexually abused (p=0.005) or physically neglected patients was also higher in the PFM group (p=0.023). The rates of emotional neglect were high in both groups, without any significant difference between them. The vast majority of AR+FM patients (90%) said that only event occurring in the year preceding the onset of FM was RA, whereas the PFM patients mainly reported non-physical events (36%, particularly the ending of a relationship, or working or financial problems) or no event at all (40%), (p<0.001). Binary logistic regression used to identify the factors predicting association of PFM/AR+FM status, showed an association with lifetime major depression, life events preceding the development of FM, and BMI (p<0.05 at all).

Conclusion: PFM and SFM differ in psychiatric co-morbidities and environmental adversities, suggesting that the putative common pathogenetic condition of CS may develop through different pathways.

References:

[1] McWilliams DF, Walsh DA. BMC Musculoskelet Disord 2016; 17, 337.

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THU0456 THE "JOINT CRITERIA" FOR FIBROMYALGIA DIAGNOSIS IN RHEUMATOID ARTHRITIS PATIENTS: RELIABILITY COMPARED TO THE 2010 ACR CLASSIFICATION CRITERIA FOR FIBROMYALGIA

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Background: A significant proportion of rheumatoid arthritis (RA) patients have concomitant fibromyalgia (FM) (1). Associated FM diagnosis in RA patients can determine worse treatment outcomes compared to patients without FM (1). A difference between tender joint count (TJC) and swollen joint count (SJC) ≥7, also named the "joint criteria" was proposed as being diagnostic for FM in patients with RA. The "joint criteria" were validated against the 1990 ACR Classification Criteria for FM and are easy to apply to patients with RA (2). Since then, the 2010 ACR Classification criteria for FM, which include somatic symptoms besides pain sensitivity, were developed and validated.

Objectives: We aimed to determine the reliability of the joint criteria for fibromyalgia in RA compared to the ACR 2010 Classification Criteria for FM and to compare RA patients diagnosed with FM (FRA) to those without FM in terms of clinical variables.

Methods: We performed a cross-sectional study on RA patients who presented in our department during a 3 months period. Tender joint count (TJC), swollen joint count (SJC), patient global assessment of disease activity (PGA) were determined. DAS28 scores were calculated using CRP. We applied the 2010 ACR Classification Criteria and the joint criteria for FM diagnosis. Kappa agreement coefficient was used to determine the reliability of the joint criteria against the 2010 ACR Classification Criteria for FM in patients with RA. Differences between groups were assessed using Mann-Whitney U test for numerical data or Chi square test for ordinal data.

Results: We included 100 consecutive RA patients, 84% female, with a mean age of 57.3(12) years and mean disease duration of 14(9) years. Twenty-four patients (24%) had associated FM according to the ACR 2010 Classification Criteria and 22 (22%) patients satisfied the joint criteria for associated FM. The level of agreement between the joint criteria and the ACR 2010 classification criteria for FM was kappa=0.66, p< 0.001, with a sensitivity of 70% and a specificity of 93%. FRA patients had similar demographic and disease characteristics compared to RA patients. Patients with FRA according to the joint criteria had significantly higher PGA, DAS28, and HAQ scores, but similar CRP values and SJC compared to RA patients (Table 1).

Table 1 Demographic and clinical data of FRA and RA patients

Variable	FRA n=22	RA n=78	p-value
Age (years)	60 (10.7)	59 (12.2)	0.093
Disease Duration (years)	13.3 (13)	12.2 (7.5)	0.589
ACPA seropositivity(%)	69	55	0.1
SJC	2(4)	2(4)	0.7
CRP (g/dl)	12.8(14.2)	8.1(13.7)	0.06
DAS28CRP	4 (1.7)	3.5 (1.2)	0.009
HAQ	1.75 (0.5)	1 (0.7)	<0.001
PGA (mm)	70(11)	44(23)	<0.001

Data are expressed as mean (SD) or median (IQR)

FRA- Fibromyalgic Rheumatoid Arthritis; RA- Rheumatoid Arthritis;

ACPA- Anti- citrullinated Protein Antibodies; CRP- C-reactive Protein; SJC- Swollen Joint Count;

DAS28CRP- Disease Activity Score; HAQ- Health Assessment Questionnaire; PGA- Patient Global Assessment

Conclusion: The joint criteria are diagnostic for FM in RA patients with moderate reliability compared to the ACR 2010 Classification criteria. When diagnosed with the joint criteria, FRA patients have higher disease activity scores despite having similar clinical and laboratory inflammatory markers compared to RA patients.

References:

[1] Wolfe F, Michaud K. Severe rheumatoid arthritis (RA), worse outcomes, comorbid illness, and sociodemographic disadvantage characterize RA patients with fibromyalgia. J Rheumatol. 2004;31(4):695–700.

[2] Pollard LC, Kingsley GH, Choy EH, Scott DL. Fibromyalgic rheumatoid arthritis and disease assessment. Rheumatology 2010;49(5):924–8.

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THU0457 LONGITUDINAL ASSOCIATION OF SEDENTARY TIME AND PHYSICAL ACTIVITY WITH SLEEP QUALITY IN WOMEN WITH FIBROMYALGIA: THE AL-ÁNDALUS PROJECT

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Background: Sleep disturbances are common in fibromyalgia, and influences quality of life. Recent literature has suggested that non-pharmacological treatments (e.g., physical exercise and cognitive behavioural therapy) may help to improve sleep quality (SQ) and the management of fibromyalgia[1]. In this regard, sedentary time (ST) and physical activity (PA) intensity levels could play a role on SQ in this population[2]. However, evidence is scarce and mainly based on cross-sectional data.

Objectives: This study aimed to examine the longitudinal associations (2- and 5-year follow-up) of ST and PA intensity levels with SQ in women with fibromyalgia.

Methods: In this prospective cohort study, women diagnosed with fibromyalgia (age: 51.4±7.6 years) with completed data were included at baseline (*n*=409), at 2-year follow-up (*n*=214) and at 5-year follow-up (*n*=218). Sedentary time and PA intensity levels (light and moderate-to-vigorous [MVPA]) were assessed using triaxial accelerometers worn for consecutive 7 days. The percentage of time spent in different behaviours was calculated (e.g., (ST/accelerometer wear time) × 100). The SQ global score was calculated as a sum of all components (score

ranges from 0 to 21 where higher values indicate worse SQ) of the Pittsburgh Sleep Quality Index. Linear regressions were performed to analyse the association of changes in ST and PA over time (predictor variables) with SQ at 2- and 5-years follow-up (dependent variables) while considering baseline SQ, age, fat percentage, marital status, educational level, sleep or relaxation medication, and regular menstruation as confounders.

Results: Overall, after adjusting for confounders, non-statistical significant associations were found between changes in ST and PA intensity levels from baseline to 2-years follow-up with SQ at 2-year follow-up (P>0.05); except for the change in MVPA from baseline to 2-years follow-up, which showed evidence of statistical significance (B=-0.207; P=0.059). Regarding the 5-year follow-up, we did not observe either any association between changes in ST or PA intensity levels from baseline to 5-year follow-up with SQ at 5-year follow-up (P>0.05).

Conclusion: The main findings suggest that neither ST nor PA intensity levels over time predict SQ at 2- and 5-year follow-up in women with fibromyalgia. Future PA-counselling randomised controlled trials might shed more light on the role that ST and PA could play on SQ.

References:

[1] Macfarlane GJ, et al. *Ann Rheum Dis,* 2017; 76(2):318–328.

[2] Borges-Cosic M, et al. *Scand J Med Sci Sports* 2019; 29:266–274.

Acknowledgments: This study was supported by the Spanish Ministry of Economy and Competitiveness (I+D+i DEP2010-15639; I+D+I DEP2013-40908-R) and the Spanish Ministry of Education, Culture and Sport (FPU15/00002).

Disclosure of Interests: : None declared

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THU0458 HIGH PREVALENCE OF JOINT HYPERMOBILITY IN INFLAMMATORY BOWEL DISEASE PATIENTS WITH PAIN UNRESPONSIVE TO BOWEL-TARGETED THERAPY

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Background: Musculoskeletal manifestations occur in 20-50% of patients (pts) with inflammatory bowel disease (IBD). A substantial number of patients complain of non-inflammatory musculoskeletal pain.

Objectives: To assess the incidence of joint hypermobility (JHM), benign joint hypermobility syndrome (BJHS) among patients with inflammatory bowel disease (IBD) examined in the inter-disciplinary rheumatology service at a tertiary referral center and the impact on IBD manifestations and outcome.

Methods: Medical records of 180 consecutive IBD pts referred to the inter-disciplinary clinic were retrospectively reviewed. Data regarding age, gender, diagnosis, disease duration, clinical and laboratory features, previous and current therapy, Harvey-Brandshaw Index were entered into a database and analyzed. Beighton's scoring of ≥4/9 was used to define patients with JHM. The 1998 Brighton's criteria were used to identify patients with BJHS. Outcome was defined as improvement of joint pain. The statistical methods used included descriptive statistics, T test, Spearman's correlation and multiple logistic regression analysis.

Results: Forty-six patients (mean(SD) age 36.2(12.4), disease duration 13.9(8.8) years) out of 180 IBD patients (mean(SD) age 40.4(14.3), disease duration 15.7(9.1) years) fulfilled the criteria for JHM. Twelve patients had active inflammatory joint disease (2 with axial involvement, 10 with peripheral joint disease and 2 with axial and peripheral joint involvement). The other 32 answered both major criteria for BJHS. The median Beighton scoring was 7 (range 5-9). Most of them were on biological treatment. Patients with JHM suffered frequently of arthralgia and abdominal pain, in spite of endoscopic remission and normal levels of calprotectin and inflammatory markers (p=0.02, r=0.17). JHM and BJHS were associated with poorer outcome (p=0.004, r=0.2). In a multiple logistic regression analysis, only JHM reached borderline significance for predicting worse outcome.

Conclusion: Joint and abdominal pain did not improve with immunomodulatory therapy in IBD patients with JHM. JHM may have a negative impact on achievement of clinical remission, in a significant subset of IBD patients. Rheumatologists and gastroenterologists should be aware of this.

Disclosure of Interests: : Haya Zidany: None declared, Matti Waterman: None declared, Kohava Toledano: None declared, Yehuda Chowers: None declared, Doron Markovits: None declared, Amir Karban: None declared, Alexandra Balbir-Gurman Consultant of: Novartis, Yolanda Braun-Moscovici: None declared

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THU0459 CHRONIC MUSCULOSKELETAL PAIN AND CHRONIC WIDESPREAD PAIN IN CHILE: PREVALENCE AND ASSOCIATED FACTORS

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Background: Chronic musculoskeletal pain (CMP) is a key cause of health loss worldwide. Cultural factors may affect pain processing and it is key to have more information regarding CMP epidemiology in Latin America.

Objectives: We aimed to determine the prevalence of CMP and Chronic Widespread Pain (CWP) in Chile and to explore risk factors.

Methods: We used data recollected in the 2017 Chilean National Health Survey. Using COPCORD we defined CMP as non-traumatic pain for more than three months. CWP was defined by the presence of CMP in five body regions. Associations between CMP and CWP and risk factors was investigated through univariate and multivariate logistic regression models.

Results: After excluding subjects with missing information our final sample was 4045 subjects. CMP was present in 21,8% (95% CI 19,6%, 24,1%) and CWP in 4.2% (95% CI 3,3%, 5,1%). Significant risk factors for CMP in multivariate analysis were older age, female gender, lower educational level, and depressive symptoms. Protective factors for CMP were not being married and moderate alcohol consumption. CWP shared risk factors with CMP. (Table 1)

Conclusion: We found a high prevalence for CMP and CWP similar to values previously described. Female gender, older age, depressive symptoms and diabetes were the main risk factors associated with chronic pain, while moderate alcohol consumption was found to be protective.

References: x

Disclosure of Interests: : None declared

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THU0460 PHYSICAL FITNESS AND QUALITY OF LIFE IN WOMEN WITH FIBROMYALGIA: LONGITUDINAL ANALYSES FROM THE AL-ÁNDALUS PROJECT

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Background: Optimizing the highly deteriorated quality of life (QoL) of patients with fibromyalgia is one of the main goals in the management of the disease[1]. Physical fitness has been identified as a powerful marker of health that is positively related to QoL in this population [2], although previous evidence is mainly based on cross-sectional data.

Objectives: This study aimed to examine the longitudinal associations (2- and 5-year follow-up) between physical fitness and QoL in women with fibromyalgia.

Methods: In this prospective cohort study, women diagnosed with fibromyalgia (age: 51.3±7.6 years) with completed data were included at baseline (n=441), at 2-year follow-up (n=220) and at 5-year follow-up (n=227). The Senior Fitness Tests battery was used to assess physical fitness components and a standardized global fitness index was calculated. The eight dimensions plus the two physical and mental component summaries of the Short-Form health survey-36 questionnaire were used to assess QoL. To examine whether changes in fitness predicted QoL at follow-up, multiple linear regression models were built. The bidirectionallity of the associations (whether changes in QoL predicted fitness at follow-up) was also tested. Outcome values at baseline and age, fat percentage, analgesic consumption, educational level, and occupational status at follow-up were entered as potential confounders in all analyses.

Results: Changes in fitness were associated with physical function (β=0.160), physical role (β=0.275), bodily pain (β=0.271), general health (β=0.144), and

physical component summary (β=0.276) at 2-year follow-up (all, *P*<0.05) and with changes in physical role (β=0.215) and physical component summary (β=0.135) at 5-year follow-up (all, *P*<0.05). Changes in physical function (β=0.165), physical role (β=0.230), bodily pain (β=0.230), general health (β=0.130) and physical summary component (β=0.251) were associated with fitness at 2-year follow-up (all, *P*<0.05). Changes in all dimensions of QoL (β rating from 0.113 to 0.198), as well as the physical (β=0.174) and mental (β=0.164) summary components were associated with fitness at 5-year follow-up (all, *P*<0.05).

Conclusion: Increasing levels of physical fitness over time predicts future QoL in women with fibromyalgia, especially for physical domains at 2-year follow-up. In addition, increasing QoL across all domains over time predicts future global fitness at 2- and, specially, 5-year follow-up. Future research is warranted to determine the clinical relevance of the bidirectional association between physical fitness and QoL in fibromyalgia.

References:

[1] Macfarlane GJ, et al. Ann Rheum Dis, 2018; 76(2), 318-328.

[2] Álvarez-Gallardo IC, et al. 2019;99:1481–1494.

Acknowledgments: This study was supported by the Spanish Ministry of Economy and Competitiveness (I+D+i DEP2010-15639; I+D+I DEP2013-40908-R; BES-2014-067612) and the Spanish Ministry of Education (FPU14/FPU 15/00002)

Disclosure of Interests: : None declared

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THU0461

THE COMPARATIVE EFFICACY OF NON-PHARMACOLOGICAL INTERVENTIONS FOR FIBROMYALGIA: A SYSTEMATIC REVIEW WITH BAYESIAN NETWORK META-ANALYSIS

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Background: Non-pharmacological interventions are recommended as first-line treatment options in the management of fibromyalgia (FM)[1]. However, whether one intervention is more effective than another for specific patient-centred outcomes in FM is unknown.

Objectives: To compare the relative efficacy of non-pharmacological interventions on FM impact questionnaire (FIQ), pain, fatigue, sleep and depression in people with FM.

Methods: A Bayesian network meta-analysis was conducted. Randomised controlled trials (RCTs) assessing any non-pharmacological intervention versus usual care, placebo or active controls in patients with FM aged >16 years were searched for in seven databases. A common comparator was identified between interventions to develop a network (Figure 1). Standardised mean difference (SMD) and 95% credible interval (CrI) was estimated between interventions. Direct and indirect evidence were pooled using the random effect model. Modified Cochrane's tool was used to assess risk of bias.

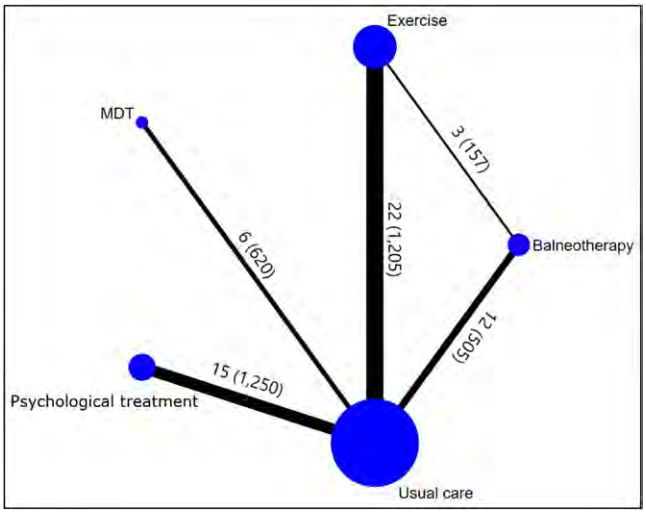


Figure 1. Network map of different interventions evaluating FIQ

Table 1. Results from logistic regression models, univariate and multivariate, for CMP and CWP,

	Models for CMP				Models for CWP			
	Uniivariate		Multivariate		Univariate		Multivariate	
	OR	**CI**	**OR**	**LCI**	**OR**	**CI**	**OR**	**LCI**
Age (x 10 years)	1.29	[1.2 - 1.38]	1.33	[1.19 - 1.48]	1.29	[1.2 - 1.38]	1.37	[1.15 - 1.63]
Sex (females)	1.97	[1.48 - 2.63]	1.86	[1.34 - 2.6]	1.97	[1.48 - 2.63]	2.83	[1.54 - 5.21]
Marital status								
married/ cohabiting	1.00	-	1.00	-	1.00	-	1.00	-
annulled/separated/divorced	0.95	[0.62 - 1.46]	0.61	[0.38 - 0.99]	0.95	[0.62 - 1.46]	0.60	[0.3 - 1.17]
widower	0.92	[0.63 - 1.35]	0.41	[0.26 - 0.64]	0.92	[0.63 - 1.35]	0.51	[0.26 - 0.97]
Single	0.48	[0.35 - 0.67]	0.73	[0.5 - 1.06]	0.48	[0.35 - 0.67]	0.67	[0.35 - 1.26]
Education								
> 12 years	1.00	-	1.00	-	1.00	-	1.00	-
9 - 12 years	1.79	[1.22 - 2.61]	1.59	[1.06 - 2.39]	1.79	[1.22 - 2.61]	1.08	[0.51 - 2.31]
< 9 years	2.44	[1.67 - 3.59]	1.42	[0.92 - 2.19]	2.44	[1.67 - 3.59]	0.87	[0.39 - 1.95]
Ocupation								
working for salary	1.00	-	1.00	-	1.00	-	1.00	-
loking for work	0.93	[0.45 - 1.92]	1.18	[0.54 - 2.61]	0.93	[0.45 - 1.92]	0.50	[0.1 - 2.48]
working without salary	1.67	[1.2 - 2.33]	1.04	[0.71 - 1.53]	1.67	[1.2 - 2.33]	1.27	[0.69 - 2.36]
Not working	1.00	[0.72 - 1.38]	0.96	[0.65 - 1.42]	1.00	[0.72 - 1.38]	1.05	[0.61 - 1.79]
Depresive symptoms	2.41	[1.71 - 3.39]	2.21	[1.53 - 3.18]	2.41	[1.71 - 3.39]	2.05	[1.28 - 3.29]
Diabetes	1.97	[1.39 - 2.78]	1.30	[0.88 - 1.91]	1.97	[1.39 - 2.78]	2.11	[1.28 - 3.49]
Alcohol consumption*								
abstemious	1.00	-	1.00	-	1.00	-	1.00	-
mild consumption	0.79	[0.6 - 1.04]	1.04	[0.76 - 1.41]	0.79	[0.6 - 1.04]	0.49	[0.29 - 0.81]
moderate consumption	0.17	[0.07 - 0.44]	0.19	[0.07 - 0.55]	0.17	[0.07 - 0.44]	0.10	[0.01 - 0.92]
severe consumption	1.50	[0.53 - 4.26]	2.28	[0.82 - 6.34]	1.50	[0.53 - 4.26]	3.97	[0.91 - 17.28]
Physical Activity**	0.57	[0.39 - 0.82]	0.92	[0.62 - 1.37]	0.57	[0.39 - 0.82]	0.87	[0.4 - 1.9]
Tobacco consumption***	0.97	[0.72 - 1.29]	1.30	[0.94 - 1.81]	0.97	[0.72 - 1.29]	1.92	[1.13 - 3.28]
BMI (kg/m^2)								
<20	0.45	[0.19 - 1.08]	0.41	[0.16 - 1.07]	0.45	[0.19 - 1.08]	0.57	[0.14 - 2.37]
20 -<25	1.00	-	1.00	-	1.00	-	1.00	-
25 - <30	1.01	[0.69 - 1.48]	0.80	[0.55 - 1.18]	1.01	[0.69 - 1.48]	0.56	[0.32 - 1.01]
30- <35	1.02	[0.68 - 1.54]	0.78	[0.51 - 1.19]	1.02	[0.68 - 1.54]	0.88	[0.47 - 1.67]
>=35	1.72	[1.1 - 2.71]	1.16	[0.72 - 1.88]	1.72	[1.1 - 2.71]	1.07	[0.5 - 2.28]

* Abstemious last 12 months/ mild consumption: <20gr/day for women and <40gr/d for men/ moderate consumption: >=20 and <40rg/d for women, and >=40 and <60 for men/ severe: >=40 gr/d for women and >=60gr/d for men./ ** Practice of sports or physical activity during on the last month, outside of work schedule, for 30 minutes or longer each time/ *** Current consumption

Results: 78 studies (n = 5,639 participants) met the inclusion criteria. There was a high risk of bias on blinding and most trials had small sample size (n<50). While multidisciplinary treatment (MDT) was the best for improving pain [-1.28 (-1.84, -0.72)], sleep [-1.14 (-2.38, 0.07)] and depression [-1.20 (-1.99, -0.46)], balneotherapy and exercise were the most effective treatments for FIQ [-1.06 (1.51, -0.61)] and fatigue [-0.75 (-1.35, -0.25)], respectively (Figure 2).

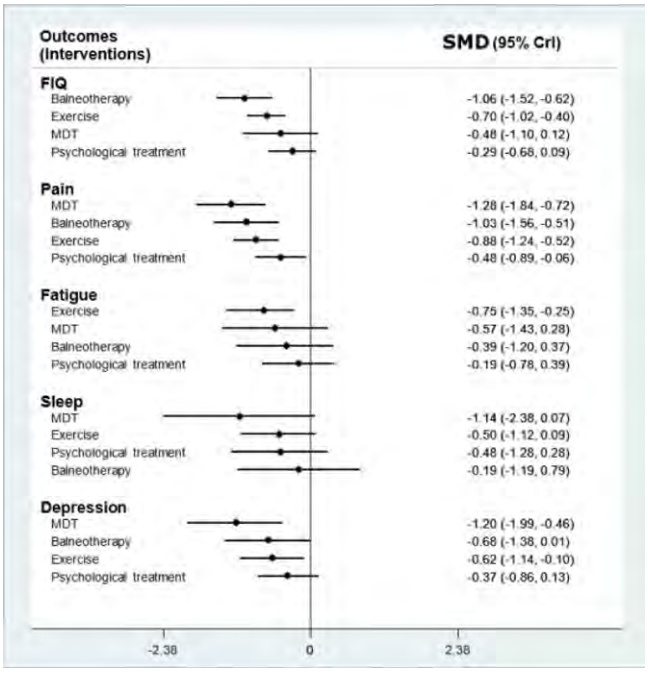


Figure 2. Standardised mean difference (SMD) versus usual care in descending order for different outcomes

Data from 47 exercise trials (n = 3,271 participants) were analysed to examine comparative efficacy of different exercise types. Strengthening showed the greatest benefits for FIQ [-0.76 (-1.39, -0.15)], pain [-0.94 (-1.58, -0.29)] and depression [-0.83 (-1.53, -0.14)], whereas aerobic exercise was the best for fatigue [-0.98 (-2.33, 0.18)] and sleep [-0.96 (-2.08, 0.13)] (Table 1).

Table 1. Relative effect size between types of exercises

FIQ					
Aerobic	**-0.58**	-0.09	0.18	0.12	**-0.57**
	(-1.13, -0.03)	(-0.55, 0.36)	(-0.44, 0.80)	(-0.36, 0.57)	**(-0.95, -0.24)**
-0.60	Flexibility	0.49	0.76	0.70	0.004
(-1.36, 0.18)		(-0.23, 1.20)	(-0.07, 1.58)	(-0.04, 1.41)	(-0.67, 0.64)
-0.10	0.49	Mind-body	0.27	0.20	**-0.49**
(-0.74, 0.53)	(-0.50, 1.49)		(-0.37, 0.91)	(-0.24, 0.65)	**(-0.85, -0.15)**
0.05	0.65	0.16	Mixed	-0.06	**-0.69**
(-0.59, 0.70)	(-0.35, 1.63)	(-0.53, 0.85)		(-0.73, 0.59)	**(-1.06, -0.34)**
0.21	0.80	0.31	-0.06	Strengthening	**-0.76**
(-0.42, 0.84)	(-0.19, 1.79)	(-0.41, 1.02)	(-0.73, 0.59)		**(-1.39, -0.15)**
-0.73	-0.13	**-0.62**	**-0.78**	**-0.94**	Usual care
(-1.16, -0.30)	(-1.02, 0.74)	**(-1.15, -0.11)**	**(-1.31, -0.26)**	**(-1.58, -0.29)**	
Pain					

Data are standard mean difference (95% credible intervel) between exercises, pairwised from the top left to the bottom right. The negative value indicates that the first exercise is more effective than the second exercise. For example, aerobic is better than flexibility for FIQ -0.58 (-1.13, -0.13), but not pain -0.60 (-1.36, 0.18).

Conclusion: Several non-pharmacological interventions are beneficial for FM. However, the effect size varies between interventions and outcomes. All types of exercises are effective for FIQ and pain apart from flexibility exercise. The results of this study may be used to guide the selection of the most effective non-pharmacological interventions according to the predominant symptom in individual patients.

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Disclosure of Interests: : None declared
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THU0462 CHARACTERIZATION OF PATIENTS WITH FIBROMYALGIA AFFECTS WITH OR WITHOUT JOINT HYPERLAXITY SYNDROME

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Background: The prevalence of joint hypermobility (JH) and Joint Hypermobility Syndrome (JHS) in patients with fibromyalgia (FM) is considerable and is much more than can be explained at random(1). Some authors propose that FM and JHS share a common pathophysiological mechanism is some patients. Currently it is accepted that Ehlers-Danlos Syndrome Hypermobility subtype (EDSh) and JHS are the same entity. We regard the subgroup of FM patients with JHS a different subtype of FM, even phenotypically similar to EDSh.

Objectives: Determine the possible differences between both groups according to their body composition, bone metabolism and clinical findings.

Methods: Our study is observational, descriptive, transverse cohort study in which we included 86 women with fibromyalgia recruited at the Fibromyalgia and Chronic Fatigue Unit at Parc Salut-Mar in Barcelona, Spain. The patients were grouped according to the presence or absence of JHS, following the Brighton Criteria. Diverse clinical data was collected: Pain Visual Analogue Scale (PVAS), time from pain onset, time from diagnosis, somatic symptoms, state of mind, presence of a FM trigger, concurrent medication, anxiety, quality of life, disease impact, anthropometric data, Bioelectrical Impedance Analysis (BIA), bone density test (BMD) and bone metabolism data in blood samples.

Results: 51 patients were included in the FM group and 35 patients in the FM-JHS group. We did not find differences between groups PVAS; time from pain onset; somatic symptoms using the Psychiatric Disorder and Somatic Pathology Scale (TOPYPS); nor Fibromyalgia Impact Questionnaire (FIQ). Both groups scored similarly on SF-36 Health Questionnaire. The use of opioids was more common in the FM group (p<0,001). Anxiety disorder (AnD) was present in a greater proportion of FM-JHS (p<0,001). We found the Body Mass Index and Muscle Mass (MM) to be less in the FM-JHS group (p=0.001 and p=0.008, respectively). Obesity and fat mass (FatM) were more frequent in the FM group. The FatM and less MM correlated with less quality of life on the SF-36 scale. There was less bone mass (BM) in the FM-JHS group (p=0.005). We found an inverse correlation between the Beighton score and the MM and BM in the FM-JHS group. The FM-JHS group also had less bone mineral density (BMD) at total hip DXA, with significant differences p=0.038. The BM by Bioelectrical Impedance Analysis (BIA) had a positive correlation on the BMD by DXA. The optimum point, capable of distinguishing between normal DXA and osteopenia/osteoporosis was 2,325kg with a specificity of 86% and sensibility of 52%. Vitamin D deficiency/insufficiency was found in 62/84 (73,8%) without significant differences between groups (p>0,05)

Conclusion: Our work revealed that FM patients with JHS are different from FM without JHS, by manifesting differences in certain clinical, anthropometric, and bone metabolism features.

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Disclosure of Interests: : None declared
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THU0463 EFFICACY AND SAFETY OF NERIDRONATE IN BONE EDEMA SYNDROME

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Background: Bone Marrow Edema Syndrome (BMES) is a severely disabling pain syndrome without a definite treatment and refers to transient clinical conditions with unknown pathogenic mechanism, such as transient osteoporosis of the hip (TOH), regional migratory osteoporosis (RMO), and reflex sympathetic dystrophy (RSD). Magnetic resonance imaging is used for the early diagnosis and monitoring the progression of the disease. Early differentiation from other aggressive conditions with long-term sequelae is essential in order to avoid unnecessary treatment.

Objectives: Aim of this monocentric trial was to test the efficacy and the safety of the amino-bisphosphonate neridronate in patients with BMES administered in two different regimens.

Methods: 192 patients with BMES secondary to osteoarthritis localized to knee, hip, wrist or foot were randomly assigned to I.V. infusion of 100 mg neridronate given four times over 10 days (Group A, 72 subjects) or alternatively to I.V. infusions of 100 mg every 21 days over 3 months (Group B, 120 subjects). At baseline and after 180 days we performed an MRI. We assessed a 0-100 mm pain VAS in each patient, too. Outcomes were to evaluate the MRI changes and the VAS changes. A control group (35 patients) was enrolled too, treated conservatively with NSAIDs and articular rest.
Results: we observed a significant improvement in MRI with the resolution of bone marrow lesions present at the baseline ($p<0.01$), without a significant difference between Group A and Group B. Visual analogue scale (VAS) score decreased significantly during the study in both groups ($p<0.05$) without a significant difference between the two treatment groups ($p>0.1$). Both groups showed a significant clinical and radiologic improvement compared with control group ($p<0.001$).
Conclusion: In patients with BMES, the infusions of neridronate 100 mg every 21 days over 3 months or alternately every 3 days over 10 days are associated with clinically relevant and persistent benefits without significant differences between the two treatment-schedules. These results provide conclusive evidence that the use of bisphosphonates, at appropriate doses, is the treatment of choice BMES.
Disclosure of Interests: : None declared
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THU0464 USE OF BENZODIAZEPINES AND ANTIDEPRESSANTS IN PATIENTS WHO ATTEND A RHEUMATOLOGY CLINIC

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Background: During the last decades, anxiolytics and antidepressants (ADP) have been among the most prescribed therapies in all developed countries (1). In Spain a prevalence of use of 11.4% was communicated (2), slightly over the European average (3,4). They have potential addiction problems and side effects.
Objectives: The objective of this study was to evaluate the prevalence of anxiolytics and antidepressants among patients who attend a Rheumatology consult, as well as the indication for them.
Methods: Patients who were referred for the first time to the Rheumatology consult were included. Demographical data, reason for referral and final diagnosis were recorded. Regarding the treatment with ADP or/and benzodiazepines (BDZ), their duration and the indication for the prescription were recorded. Sample size was estimated for a 0.05% alpha risk. Descriptive, univariate and multivariate analyses (ANOVA) were performed in order to study the prevalence of these treatments, and their associations with demographical or clinical characteristics. The study was approved by the Hospital Universitario de Elche Ethics Committee.
Results: 350 patients were included (women 77.1%, men 22.9%), mean age 58.1 yo. 40% were occupied and 31.4% were unemployed. The majority were married or lived with a couple (71.4%). Most of them had been referred for musculoskeletal pain (73.4%). More than a third (39.4%) were on BZD and/or ADP: 107 patients were on BZD (30.6%), 68 were on ADP (19.4%), and 47 (13.4%) were on both. The most frequent reasons for their prescription were anxiety, depression and insomnia. The final diagnosis in the clinic was a non-inflammatory condition in 53.1%, and inflammatory in 18%. In the univariate analyses, the use of BZD/ADP was not associated with civil status, but it was associated with female sex ($p<0.001$), unemployment ($p<0.001$) and non-inflammatory final diagnosis ($p<0.001$). In the multivariate analyses, the use of BZD and/or ADP was associated with female sex ($p=0.002$ [RR 3.4, CI 95% 1.6-7.4]) and non-inflammatory final diagnosis, specifically fibromyalgia ($p= 0.007$ [RR 16.1, CI 95% 2.2-120.7]).
Conclusion: The use of anxiolytics and antidepressants is frequent in the patients referred to the Rheumatology clinic, and it's associated to female sex and non-inflammatory conditions, over all fibromyalgia.
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THU0465 SERUM LEVEL OF ADRENOCORTICOTROPHIC HORMONE IS A CONTRIBUTING HORMONE OF METABOLIC SYNDROME IN NEWLY DIAGNOSED FIBROMYALGIA

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Background: Evidence of components of metabolic syndrome including. Obesity dyslipidemia, abnormal glucose tolerance rate and hypertension are associated with fibromyalgia. Adrenocorticotrophic hormone (ACTH) is reported to be significantly higher in fibromyalgia patients, and it causes obesity, high blood pressure.
Objectives: This study aimed to assess the serum level of ACTH as a contributing as well as a discriminator hormone in newly diagnosed fibromyalgia women presented with variable components of metabolic syndrome.
Methods: This cross-sectional study comprised 100 women with newly diagnosis fibromyalgia and 30 apparent healthy women served as control from Kurdistan region-Iraq. Clinical data including the score of fibromyalgia impact questionnaire-revised (FIQR), tender point, body mass index, waist circumference, blood pressure and fasting serum levels of glucose and lipid profile, and ACTH level. The score of metabolic syndrome was calculated using the formula:

$$\frac{2\times waist}{height}+\frac{serum\,glucose}{5.6}+\frac{Serum triglyceride}{1.7}+\frac{Systolic\,blood\,pressure}{130}-\frac{serum\,high density\,lipoprotein}{1.02 or\,1.28\,(male or female)}$$

Results: Compared to the controls, the Fibromyalgia women displayed significantly higher values of waist circumference (88.9 ± 5.7cm versus 87.1 ± 2.7cm, $p=0.019$), systolic blood pressure (136.1 ±13.5mmHg versus 131.4 ± 7.1, $p=0.014$), metabolic syndrome score (3.10 ±0.25 versus 3.03±0.19, $p=0.039$), and serum ACTH levels (16.66 ± 3.23pg/ml versus 14.42 ± 2.18pg/ml. $p<0.001$). Serum ACTH levels significantly and inversely correlated with the total score of the FIQR ($r = - 0.320$. $p=0.001$) and number of tender points ($r= - 0.374$, $p<0.001$). Metabolic syndrome score is significantly and inversely correlated with the total FIQR score ($r = - 0.296$, $p=0.003$). Multivariable regression analysis using showed that serum level of ACTH is a significant ($p=$ predictor of 19.7% of fibromyalgia patients (Figure 1), and it is a significant ($p=0.007$) discriminator of tender points as the area under the curve is 0.325($_{95\%}$ C.I.: 0.212-0.438) (Figure 2).

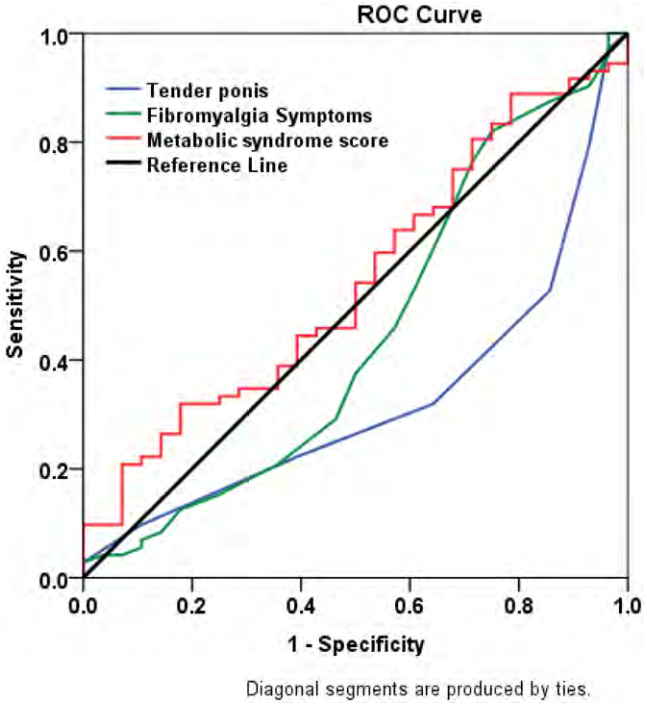


Figure 2. serum level of ACTH (cutoff level ≥14.5pg/ml, sensitivity=72%, specificity=50%) as a discriminator of the tender points (AUC $_{95\%\ C.I.}$: 0.325[0.212-0.438], $p=0.007$), score of

fibromyalgia symptoms (AUC $_{95\% C.I}$: 0.474[0.313-0.581], p=0.409), and metabolic syndrome score (AUC $_{95\% C.I}$: 0.546[0.423-0.668], p=0.480)

Conclusion: Fibromyalgia women responded to the stress of pain by increasing the serum level of ACTH which effectively improves the clinical feature of fibromyalgia symptoms, but at the same time elevates the score of metabolic syndrome. Therefore, assessment of serum level of ACTH can serve as a predictor and discriminator of fibromyalgia comorbidity.

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THU0466 EARLY DIAGNOSIS IS ASSOCIATED WITH LESS DISEASE SEVERITY AND BETTER OUTCOME IN FIBROMYALGIA SYNDROME: A TRICENTRIC PROSPECTIVE ANALYSIS OF A COHORT OF 370 PATIENTS

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Background: Delayed diagnosis of fibromyalgia (FM) has been reported to be associated with more economic burden, healthcare utilization and worse response to treatment[1,2]. However, its impact on the patients' symptomatology and disease severity is still underestimated.

Objectives: to evaluate the effect of diagnostic delay (DD) on FM severity and disease assessment parameters.

Methods: in this cross sectional study, 370 FM patients were prospectively interviewed. Information about DD, widespread pain index (WPI), symptom severity scale (SSS), total severity scale (SSS+WPI) and number of tender points were collected. We proposed to classify our patients into 3 categories; early diagnosis (ED ≤ 2 years; 83 patients), late diagnosis (LD: >2-7 years; 198) and very late diagnosis (VLD >7 years; 89 patients).

Results: the mean age of patients was 33.9 (±9.8) and 79.4 % were female. The mean for DD was 5.6 (±3.6) while the means for SSS, total scale and tender points were 7.8 (±1.6), 16.46 (±4.1), 14.31 (±2.3) respectively. A significant correlation has been found for DD with SSS (r = 0.14), total scale (r = 0.37) and tender points (r = 0.16) but not with WPI (r = 0.059).

Comparing the three categories, the mean for SSS was 7.54 (±1.6), 7.73 (±1.4) and 8.25 (±1.7) in the groups of ED, LD and VLD respectively (P =0.008) while the mean for the total scale was 15 (±3.8), 15.95 (±3.8) and 18.96 (±4.4) respectively (P = 0.000) and the mean for tender points was 13.7 (±2.3), 14.35 (±2.1) and 14.77 (±2.8) respectively (P = 0.011). The mean for WPI did not significantly differ as it was 7.45 (±2.8), 7.8 (±3.6) and 7.18 (±4.8) in the groups of ED, LD and VLD respectively (P = 0.415).

Conclusion: early diagnosis of FM is associated with low SSS, total severity scale and tender points reflecting a better outcome and a less disease severity.

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Disclosure of Interests: : None declared

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THU0467 CONCEPTS AND PERCEPTIONS ABOUT FIBROMYALGIA DIAGNOSIS, MONITORING AND TREATMENT AMONG COLOMBIAN RHEUMATOLOGISTS, PHYSIATRIST AND PAIN PHYSICIAN

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Background: Fibromyalgia is a chronic disease characterized by the presence of widespread and persistent musculoskeletal pain associated with a variety of symptoms. The concepts and perceptions around diagnosis and treatment of fibromyalgia among physicians are not objectively known. The purpose of this study is to obtain objective data through a survey and describe the concepts and perceptions about the diagnosis, treatment and treatment of fibromyalgia among colombian rheumatologists, physiatrist and pain physicians

Objectives: The main purpose of this study is to obtain objective data on this subject and describe the concepts and perceptions about the diagnosis, treatment and monitoring of FM among colombian rheumatologists, physiatrist and pain physicians.

Methods: Cross-sectional study. Through a focus group in which two rheumatologists and one expert in qualitative research methods participated, a survey was designed to evaluated the perceptions and concepts that rheumatologists, physiatrist and pain physicians have on the diagnosis and treatment of fibromyalgia. The survey was self-applied anonymously through the internet.

Results: Survey applied to 139 rheumatologists, 99 physiatrist and 81 pain physicians. 35 rheumatologists (25.2 %), 17 physiatrist (17.1 %) and 58 pain physicians (71.6 %) consider that there is not enough evidence to recognize fibromyalgia as a disease. 45 rheumatologists (32.4 %), 86 physiatrist (86 %) and 73 pain physicians (90.1 %) consider that the 1990 ACR (American college of Rheumatology) criteria are not sufficient to diagnose fibromyalgia, despite the fact more than 90% of them use the criteria as a tool to approach the diagnosis when suspecting fibromyalgia. The most formulated medications for managing fibromyalgia are antidepressants and is used by more than 80% of the respondents, followed by antiepileptics in pain physician (88.9%) but less than physiatrists and rheumatologists (66.6 % and 64.7 % respectively), and analgesic much more for pain physician and physiatry and less for rheumatologists (84 %, 75.7 % and 26.6 % respectively). All respondents consider that the patient with fibromyalgia should have a multidisciplinary approach. Most doctors of the three specialties believe that physiatrist should be the leaders of interdisciplinary management in the treatment of fibromyalgia patients.

Conclusion: We present objective information on the perceptions of fibromyalgia among a group of Colombian rheumatologists, physiatrist and pain physician, documenting a frequent use of the ACR 1990 classification criteria. As regards treatment, a high percentage use of antidepressants and antiepileptic. Most believe that physiatrist should be the leaders of interdisciplinary management in the treatment of fibromyalgia patients.

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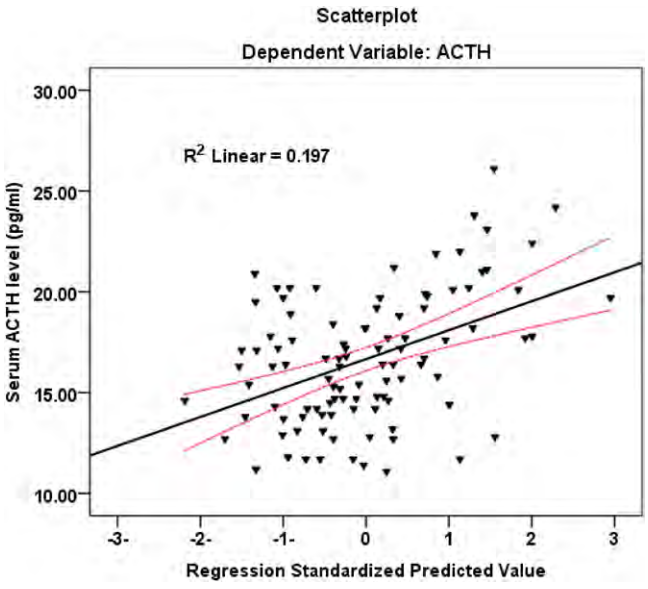


Figure 1. Multivariable regression analysis with *posthoc* ANOVA test showed significant correlations between serum level adrenocorticotrophic hormone as a dependent variable with the score s of fibromyalgia impact questionnaire and metabolic syndrome, and the number of tender points. R=0.443, F=7.777, P<0.001, prediction 19.7%),

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THU0468 EFFICACY AND SAFETY OF INTRA-ARTICULAR THERAPIES IN RHEUMATIC AND MUSCULOSKELETAL DISEASES: AN OVERVIEW OF SYSTEMATIC REVIEWS INFORMING THE 2020 EULAR RECOMMENDATIONS FOR INTRA-ARTICULAR THERAPIES INCLUDING SYNOVIORTHESIS

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Background: Intra-articular therapy (IAT) is subject to wide variability and there are gaps in the evidence on its efficacy and safety.
Objectives: To assess the efficacy and safety of frequently used IATs to inform a EULAR Taskforce.
Methods: We performed an overview of systematic reviews (SR) of randomised clinical trials (RCT) assessing efficacy and safety of IAT in adults with RMDs. MEDLINE was searched until January 2019. SRs were assessed with the AMSTAR-2 tool. Critically low-confidence SRs were excluded.
Results: Of 159 articles identified, 42 were reviewed in detail and 15 met the inclusion criteria (146 RCTs). The populations included were mainly knee osteoarthritis (OA) in 10 SRs, rheumatoid arthritis (RA) in 3, hip and temporo-mandibular (TM) OA and shoulder adhesive capsulitis in 1 SR each.
In knee OA, Hyaluronic Acid (HA) showed a modest benefit over placebo for pain and function but with unclear clinical significance in some studies. Platelet rich plasma (PRP) showed a small effect over HA only for function. Mesenchymal stem cells (MSC) performed better than PRP and HA for some outcomes, however, in studies with high risk of bias. Intra-articular Glucocorticoids (GC) were better than placebo (PBO) for pain and function.
More adverse events (AE) were seen in the PRP group compared with HA and for HA compared with PBO including serious AE each in 1 SR on knee OA.
Results for other included diseases are shown in table 1.
Conclusion: Most of the SRs assessed had results of low confidence. HA and GC showed a small, short term benefit in knee arthritis in OA and RA compared to PBO. High risk of bias prevents conclusions on the efficacy of PRP and MSC in knee OA. More AE were reported in PRP and HA treated groups.

Disclosure of Interests: : Sebastian C Rodriguez-García Speakers bureau: Novartis Farmaceutica, S.A., Merck Sharp & Dohme España, S.A., Sanofi Aventis, UCB Pharma, Raul Castellanos-Moreira Speakers bureau: Lilly, MSD, Sanofi, UCB, Jacqueline Uson Jaeger: None declared, Esperanza Naredo: None declared, Loreto Carmona Grant/research support from: Novartis Farmaceutica, SA, Pfizer, S.L.U., Merck Sharp & Dohme España, S.A., Roche Farma, S.A, Sanofi Aventis, AbbVie Spain, S.L.U., and Laboratorios Gebro Pharma, SA (All trhough institution)
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THU0469 QUANTIFYING THE PLACEBO EFFECT AFTER INTRA-ARTICULAR INJECTIONS: IMPLICATIONS FOR TRIALS AND PRACTICE

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Background: In recent years, diverse compounds for intra-articular administration were brought into the market with a subsequent significant and heterogeneous literature production. Understanding the efficacy of intra-articular therapies (IAT) on pain implies bearing in mind the related placebo (PBO) effect. To date, most studies analyzing it were focused on the compound being administered rather than the route of administration.
Objectives: We aimed at evaluating the size of the PBO effect after intra-articular injections.
Methods: We conducted an overview of systematic reviews (SRs) including randomized-controlled trials (RCTs) of frequently used IAT. SRs with a saline solution PBO arm and high-confidence results according to the AMSTAR-2 tool were selected for analysis.
Data on the change in pain in the PBO arms from baseline to 3-6 and 12-16 weeks after the IA procedure was extracted. The standardized mean differences (SMD) from baseline were calculated as the ratio between the size of the intervention effect in each study and the variability observed in that study. A meta-analysis was then performed using an inverse-variance random-effects model in Review Manager 5.3. The overall effect sizes obtained refer to versions of the SMD, which corresponds to the Hedges' (adjusted) g. e.g. a "g" of 1 indicates the two groups being compared differ by 1 standard deviation and so on.
Results: Two SR were included comprising 50 RCTs, 44 not meeting inclusion criteria were excluded so pain, measured by visual analogue scale (VAS) and Lequesne index, was retrieved from 6 RCT.
At 3-6 weeks, an SMD [95%CI] = 0.74 [0.47-1.00] was found. One study showing too large an effect was excluded after conducting sensitivity analysis resulting in a significant reduction of heterogeneity with an SMD = 0.62 [0.45-0.79] (Fig.1).
At 12-16 weeks, we found a SMD = 0.33 [0.13-0.52] (Fig.2)

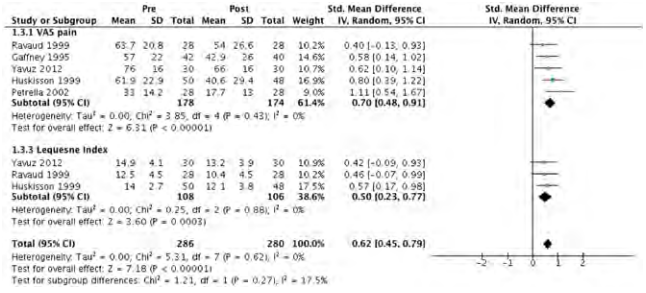


Figure 1. Forest plot for intra-articular PBO effect at 3-6 weeks after injection.

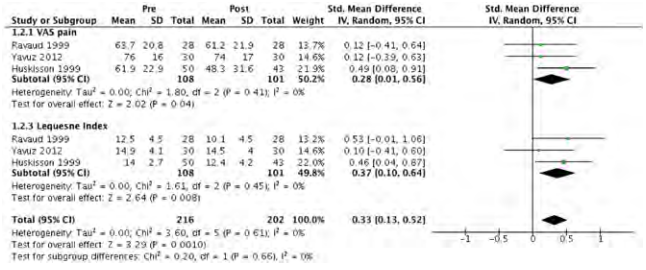


Figure 2. Forest plot for intra-articular PBO effect at 12-16 weeks after injection.

Using the interpretation suggested by Cohen[1], our results would confirm a moderate to large effect of IA saline (PBO) at 3-6 weeks with a subsequent reduction to a small but persistent effect at 12-16 weeks.

Conclusion: Our results showed a moderate to large short-term effect of intra-articular PBO that persisted on the mid-term although reduced. Based on these findings we suggest this effect should be considered when assessing the efficacy of IAT in RCTs and also in clinical practice where it could be maximized as well.

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Disclosure of Interests: : Sebastian C Rodriguez-García Speakers bureau: Novartis Farmaceutica, S.A., Merck Sharp & Dohme España, S.A., Sanofi Aventis, UCB Pharma, Raul Castellanos-Moreira Speakers bureau: Lilly, MSD, Sanofi, UCB, Jacqueline Uson Jaeger: None declared, Esperanza Naredo: None declared, Loreto Carmona Grant/research support from: Novartis Farmaceutica, SA, Pfizer, S.L.U., Merck Sharp & Dohme España, S.A., Roche Farma, S.A, Sanofi Aventis, AbbVie Spain, S.L.U., and Laboratorios Gebro Pharma, SA (All trhough institution)
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THU0470 EFFECT OF LAND AND WATER-BASED EXERCISE ON PHYSICAL FUNCTION IN WOMEN WITH FIBROMYALGIA: PRELIMINARY FINDINGS FROM THE AL-ÁNDALUS RANDOMISED CONTROL TRIAL

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Background: Previous evidence has shown physical function (PF) improvements after physical exercise programs in fibromyalgia[1]. However, research comparing the efficacy of land vs. water-based programs is scarce.
Objectives: This study aimed at comparing the effects of two exercise interventions (land- and water-based) on PF in patients with fibromyalgia.
Methods: A total of 262 women were initially randomized and 152 (age:50.6 ±7.7 years) completed all the assessments with an attendance ≥70% (control n=62, land-based n=48, water-based n=42). The intervention groups trained three non-consecutive days/week (60 min/session) during 24 weeks. Every session consisted of exercises focused on improving cardiorespiratory fitness, muscle strength, and flexibility. Physical function components were assessed with the Functional Senior Fitness Test battery, and a standardized global PF index was calculated. Pre-, post- and re-test (12-week detraining) assessments were conducted. Groups did not differ in sex, sociodemographic characteristics, disease duration, drugs intake, and body mass index. Analysis of covariance was used to test the differences in changes from baseline (post-test vs. pre-test and re-test vs. pre-test) between groups using age, pain sensitivity, and baseline outcomes values as covariates.
Results: Land- and water-based exercise groups improved lower body strength (mean difference; 95% confidence interval=2.8; 1.8, 3.8 and 1.7; 0.6, 2.8, respectively), upper body strength (4.8; 2.8, 6.8 and 3.5; 1.4, 5.6, respectively), and agility (-0.8; -1.2, -0.4 and -0.4; -0.8, -0.0, respectively) compared to the control group (all, P≤0.033). Additionally, land-based exercise group improved lower body flexibility and cardiorespiratory fitness compared to both the control (6.4; 2.8, 9.9 and 55.0; 31.0, 79.2, respectively) and water-based (5.4; 1.7, 9.2 and 37.5; 11.4, 63.6, respectively) groups (all, P≤0.002). Global PF improved in the land-based compared to the control group (0.4; 0.2, 0.5, P<0.001) and the water-based group (0.2; 0.0, 0.4, P=0.019). After the detraining period, land- and water-based groups maintained improvements in upper body strength (3.1; 1.2, 5.0 and 2.2; 0.1, 4.2, respectively) compared to the control group (all, P≤0.032). Land-based exercise group maintained improvements in lower body flexibility (5.1; 1.5, 8.8), lower body strength (1.7; 0.8, 2.6), agility (-0.6; -1.0, -0.3) and cardiorespiratory fitness (31.0; 6.8, 55.2) compared to control group (all, P≤0.007), and agility (-0.5; -0.9, -0.1) and cardiorespiratory fitness (40.2; 11.7, 68.7) compared to the water-based group (all, P≤0.014). The improvements in global PF were maintained in the land-based group compared to the control group (0.1; 0.0, 0.3, P=0.049).
Conclusion: Land- and water-based exercise interventions are overall effective to improve PF in patients with fibromyalgia. However, the land-based exercise intervention presented greater effectiveness compared to the water-based exercise intervention. Improvements were overall sustained in the land-based group after a 12-week detraining period.

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Disclosure of Interests: : None declared
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THU0471 VITAMIN D SUPPLEMENTATION; IS IT EFFECTIVE IN FIBROMYALGIA PATIENTS?

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Background: Fibromyalgia syndrome (FMS) is a chronic pain syndrome which presented by easy fatigability, widespread body pain, anxiety and tenderness points on specific anatomic regions. Fibromyalgia may be risk factor for vitamin D deficiency because of pain, poor mobility, or depression, potentially leading to less time of sun exposure or high rates of adiposity leading to decreased synthesis of vitamin D & there are conflicting results on the role of vitamin D in improving chronic nonspecific musculoskeletal pains[1, 2].
Objectives: Assessment of the effectiveness of vitamin D supplements as adjuvant therapy in functional status, quality of life and psychological status in fibromyalgia patients with vitamin D insufficiency.
Methods: One hundred adult patients of primary FMS (according to the 2010 ACR criteria for FMS) associated with vitamin D insufficiency (21-29 ng/mL) were selected to participate in this study. Patients with secondary FMS were excluded; also we excluded patients with any psychiatric disorders and patients who had other chronic diseases interfering with calcium, phosphorus, and vitamin D metabolism. After written consent; the patients were randomly divided into 2 equal groups; group

Table 1. Summary of SR. P: population; C: comparation; H: High, M: Moderate; L: Low confidence; MA: meta-analysis; SOC: standard of care; PRO: patient reported outcomes; ROM: range of motion; MPA: methylprednisolone acetate; TA/TH: triamcinolone acetonide/ hexacetonide; MW: molecular weight; YR: Yttrium synoviorthesis *Same SR assessed knee arthritis in OA and RA separately

SR	P	C	AMSTAR2	Efficacy	Safety
Newberry	**knee OA**	HA vs PBO; HA; Lavage	**H**	**MA**. **HA better than PBO** in function in older patients (small effect).	No diff in AE
Juni		GC vs Sham; PBO; SOC	**H**	**MA**. **GC better** in pain and function until 6w. No diff at 12-24w.	No diff in AE
Pas		MSC vs PBO; PRP; HA	**M**	**No MA**. **MSC better** in pain, PRO, MRI, etc High risk of bias.	No diff in AE
Trojian		HA vs PBO; GC	**M**	**NMA**. **HA better vs GC or PBO** in WOMAC pain, stiffness, function and OARSI criteria.	No diff in AE
Gallagher		HA vs PBO	**M**	**No MA**. **No diff** in joint space width. High risk of bias.	Not reported
Samson		HA vs Glucosamine; Chondroitin; Lavage	**M**	**MA**. **HA better** in pain (small effect), unclear clinical benefit	**MA. More AE with HA. SAE in 3/1002 knees with HA** (severe swelling, hypersensitivity reaction)
Di		PRP vs HA	**L**	**No MA**. **PRP better** only in WOMAC function.	**More AE with PRP** (p<0.05) SAE in 2 knees with HA (severe swelling)
Silvinato*		MPA vs TA; TH	**L**	**MA**. **MPA better vs TA in pain until w6** No diff. in pain or function at 12w.	No diff in AE
Trigkilidas		HA vs PBO; GC	**L**	**No MA**. **HA (small effect) better in mild-moderate OA**	No diff in AE
Lo		HA vs PBO	**L**	**No MA**. **HA (small effect) better in pain. (publication bias).** High heterogeneity	No diff in AE
De Souza	**TM OA**	HA vs GC	**M**	**HA better in pain at w24**	Not reported
Figueiredo	**Hip OA**	HA vs GC; PBO; PRP; Anaesthetics	**L**	**MA**. **No diff** in HA vs comparators in pain and OARSI criteria	No diff in AE
Lee	**Shoulder capsulitis**	HA vs SOC	**M**	**No MA**. **No diff** in HA vs SOC.	No diff in AE
Heuft	**RA (knee)**	YR vs PBO; GC	**M**	**No MA.** YR better vs PBO, TH better vs YR in ROM and knee circumference. **SR inconclusive**	Not reported
Silvinato*		MPA vs TA; TH	**L**	**MA**. **No diff** in pain or function.	No diff in AE
Saito		HA vs PBO	**L**	**MA**. **HA better in global effectiveness, pain and inflammation.**	No diff in AE

I received duloxetine (60 mg once daily for 6 months) plus 50,000 unit oral cholecalciferol weekly for 8 weeks then monthly for 16 weeks. Group II received duloxetine (60 mg once daily for 6 months) plus placebo. The patients were assessed at baseline and after 6 months of treatment by measuring serum levels of 25(OH)D, Fibromyalgia Impact Questionnaire (FIQ), Medical Outcomes Study Questionnaire Short Form 36 Health Survey (SF-36) & Hospital Anxiety and Depression Scale (HADS).
Results: Eighty six patients completed this study. There was no significant difference between all groups in demographic data, educational status and all baseline variants except serum levels of 25(OH) D. After 6 months; there was significant improvement (P<0.05) in group I in serum levels of 25(OH) D. There was significant improvement (P<0.05) after 6 months in FIQ, SF-36 and HADS in both groups. There was significant better improvement (P<0.05) in group I than in group II in FIQ, SF-36 and HADS. The results of the study are summarized in table 1.

Table 1. Pre- and post-treatment assessment measures of the patient groups

assessment measures	Baseline	Baseline	After 6 months	After 6 months
	Group I	Group II	Group I	Group II
25(OH)D	25.3 ± 4.9 ng/ml	26.8 + 5.3 ng/ml	36.8 + 3.9 ng/ml	25.6 ± 3.4 ng/ml
FIQ	47.5±5.4	46.7±6.7	27.5±6.1	38.5±7.3
SF-36 (Total score)	47.6±10.4	47.0±9.9	61.0±5.8	54.8±5.3
HAD anxiety	8.2±0.6	8.4±0.3	7.1±0.7	7.5±1.4
HADS depression	8.6±0.3	8.6±0.9	7.3±0.8	7.7±1.4

Conclusion: Vitamin D supplement is effective as an adjuvant therapy in improving functional status, quality of life and psychological status in fibromyalgia patients with vitamin D insufficiency.
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Disclosure of Interests: : None declared
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THU0472 CATHEPSIN S GENE EXPRESSION MEASURED IN THE PERIPHERAL BLOOD OF OSTEOARTHRITIC PATIENTS PRIOR TO SURGERY AS A BIOMARKER OF POST-OPERATIVE PAIN DEVELOPMENT

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Background: Osteoarthritis (OA) is a chronic rheumatic disease, which involves pain, limited inflammation, and local destruction of the knee joint. OA pain is a major clinical symptom, which limits working capacity and denotes an important indication for joint replacement in the end-stage OA. In spite of significant number of positive outcomes, chronic postoperative pain represents a major adverse consequence of surgery, which is observed in 10-40% of OA patients. Therefore, identification of patients potentially capable of developing chronic postoperative pain prior to surgery could significantly improve therapy outcome. Recently we hypothesized that genes related to pain sensitization whose expression is upregulated in about 10-40% of the examined end-stage OA patient cohort might be responsible for postoperative pain. Retrospective analysis of gene expression in the peripheral blood of end-stage OA patients before joint replacement surgery revealed that expression of cathepsins S and K, caspase 3, and MMP-9 genes might be associated with postoperative pain development [Ann Rheum Dis,78, suppl 2:A520].
Objectives: To examine the validity of our hypothesis in the prospective study.
Methods: We examined peripheral blood of 26 healthy volunteers (average age 55±8.3 years old) and 40 end-stage OA patients (average age 56.5±8.9 years old) undergoing joint replacement surgery. Patients were examined before and 6 months after surgery. Pain was assessed prior to surgery using VAS index and neuropathic pain questionnaires DN4 and PainDETECT. Functional activity was evaluated by WOMAC. After surgery pain indices according to VAS of 30% and higher were considered. MMP-9 and caspase 3 protein levels were quantified by ELISA. Total RNA isolated from whole blood was used in expression studies for caspase 3; metalloproteinase (MMP)-9; cathepsins K and S genes. These were performed with quantitative real-time RT-PCR.
Results: Out of 40 patients pain complaints were obtained from 9 patients (22,5%) after 6 months' post-surgery. Prior to surgery all the examined genes were significantly upregulated in the patients who developed post-operative pain compared to healthy controls and those subjects who did not develop pain after surgery. However, no difference in the levels of the examined pain-related and functional indices in patients, who developed pain or not, was noted before surgery. ROC curve analyses confirmed significant associations (p<0.05) between expressions of the examined genes prior to surgery with the likelihood of pain development after surgery. The cut-off values for the examined gene expressions were 11.34 for cathepsin S (sensitivity of 0.89 and specificity of 0.76), 10.11 for caspase 3 (sensitivity of 0.86 and specificity of 0.65), 10.09 for cathepsin K (sensitivity of 0.86 and specificity of 0.78). Moreover, among the examined genes cathepsin S expression was the most informative predictor of postoperative pain development [AUC= 0.857, 95%CI (0.708-1.000)].
Conclusion: High cathepsin S gene expression in the peripheral blood of the end-stage OA patients measured prior to joint replacement surgery could serve an important biomarker of post-operative pain development.
Disclosure of Interests: : None declared
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THU0473 IS PAIN INTENSITY ASSOCIATED WITH EARLY MORTALITY IN PATIENTS WITH PSORIATIC ARTHRITIS?

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Background: Studies regarding excess mortality among patients with psoriatic arthritis (PsA) are conflicting due to the heterogenous nature of the disease. Thus, identifying risk factors for mortality is crucial, but few studies have examined these in PsA. Presence of chronic pain can cause excess mortality and since pain is prevalent among patients with PsA this association should be explored.
Objectives: To investigate whether higher cumulative pain intensity is associated with an excess mortality ratio in patients with PsA.
Methods: A nested case-control study was performed using data from the national Danish healthcare registers and the DANBIO rheumatology register. Cases were patients who died while followed in routine care. Cases were matched on sex, year of birth and calendar period of DANBIO entry with up to five controls. The main exposure of interest was the mean pain intensity (all causes) reported during the time followed in routine rheumatology practice. The pain intensity was measured on a visual analogue scale (VAS) ranging from 0 (no pain) to 100 (worst imaginable pain). Conditional logistic regression was used to calculate the odds of mortality per 5 unit increase in VAS pain while adjusting for inflammatory markers.
Results: The Danbio PsA cohort consisted of 8019 patients. In total, 266 cases, i.e. PsA patients who died during the observational period, were identified and matched with 1198 controls (4.5 controls per case). Increasing pain intensity was associated with increased odds of mortality (OR 1.05, 95%CI 1.01 to 1.09) in the crude model, but the association disappeared when adjusting for age, sex, calendar time, socioeconomic status, average c-reactive protein and swollen joint count during the observation period (OR 0.98, 95%CI 0.93-1.03).
Age, average CRP, biological DMARD use, glucocorticoid use, and comorbidities (see table) increased the odds of mortality.

Table regression estimates from fully adjusted model

	Odds Ratio	95% CI
Age	2,73	1,60-4,68
C-reactive protein	1,05	1,03-1,07
Swollen joint count	1,08	0,97-1,22
Health assessment questionnaire	1,25	0,84-1,86
bDMARD use	2,62	1,51-4,57
cDMARD use	0,69	0,46-1,03
Glucocorticoid use	3,90	2,51-6,05
Chronic obstructive pulmonary disease	2,19	1,20-4,02
Diabetes mellitus	2,65	1,62-4,31
Cancer	6,15	3,88-9,76
Cardiovascular disease	2,61	1,71-3,97

Conclusion: These results indicate that experienced pain in itself is not associated with excess mortality. Age, recent glucocorticoid use, biological DMARD

use, chronic pulmonary disease, diabetes, cancer and cardiovascular disease were all associated with an increased mortality.

Disclosure of Interests: : None declared

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THU0474 NEUROPATHIC SYMPTOMS IN ITALIAN PATIENTS WITH FIBROMYALGIA: RESULTS FROM A NATIONAL ON-LINE SURVEY

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Background: Fibromyalgia (FM) is the second most frequent disorder in rheumatic patients. Other than widespread pain, fatigue, sleep disturbance and cognitive impairments, patients complain also symptoms of suspected neuropathic origin, like burning pain, thermal sensitive skin, hyperalgesia, pins and needles sensations. Recent studies highlighted the presence of small- fibers pathology (SFP) and/or large-nerve fibers involvement in about 50% of FM patients, which could be the cause of neuropathic pain.

Objectives: The aim of the study was to investigate the prevalence of neuropathic pain and symptoms indicative for the presence of SFP in Italian FM patients, studying the association with clinical variables.

Methods: An on-line survey was designed according to the Checklist for Reporting Results of Internet E-Surveys guidelines (CHERRIES) and Strengthening the Reporting of Observational Studies in Epidemiology (STROBE). The on-line Survey Monkey® platform was adopted to collect data. We calculated a-priori minimum number of 800 responders.

We administered the survey by involving 7 FM patients' associations distributed nationwide between July and September 2019. We explored demographic and clinical variables including pain and stiffness intensity, symptoms duration, and counting of painful sites. Neuropathic Pain Symptoms Inventory (NPSI) and Fibromyalgia Impact Questionnaire (FIQ) were administered. To study the presence of symptoms indicative of potential SFP we asked for the presence of 8 signs and symptoms reported in literature as characteristics of SFPs. Two groups of FM patients were considered: those positive (FM+) to the Fibromyalgia Research Criteria (FRC) (Wolfe et al., 2011), and those complaining typical FM symptoms but not fulfilling the FRC (FM-).

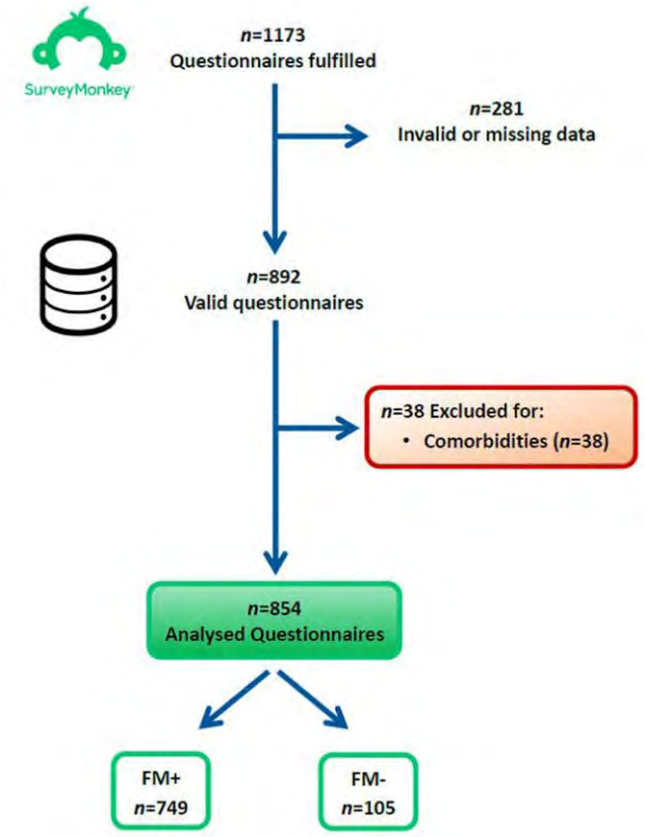
Results: The survey was correctly completed by 76% of participants (892/1173). A total sample of 854 patients (749 in FM+ and 105 in FM-) was analyzed after the exclusion of subjects with major comorbidities. The mean NPSI score was significantly higher in FM+ (56.3/100) respect to FM- (34.2/100). NPSI score was ≥50/100 in 62.4% of FM+ patients and in 21.0% of FM-. More than 3 symptoms indicative for SFP were found in 51% of FM+ patients and in 15.2% of FM-. Dry eyes/mouth, allodynia and changed pattern of sweating on body were the 3 most frequently reported symptoms. We found statistically significant strong associations (p<0.001) for the NPSI score with disability (*rho*=0.53) and pain (*rho*=0.63), and a moderate correlation with stiffness levels (*rho*=0.45) and counting of painful sites (*rho*=0.33). Symptoms indicative for SFP were significantly correlated (p<0.001) with all clinical variables with low grade of association (Cramer's V or *rho*<0.30). Although the higher prevalence of neuropathic pain and symptoms potentially indicative for SFPs, electromyography and electroneurography were performed in 40%-44% of cases, and skin biopsy in 1%-2% of the sample, as well as the assumption of gabapentinoids (12.6% in FM+ and 18% in FM-).

Conclusion: This findings highlight the importance of neuropathic pain symptoms identification, since we found a high prevalence and a strong correlation with clinical variables in our cohort of FM patients. The assessment of the neuropathic dimension of pain through self-administered questionnaire should be part of the routine clinical practice.

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Figure 1. Enrollment process flow-chart



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THU0475 THE EFFICACY OF ORAL GLUCOCORTICOSTEROIDS FOR PAIN IN RHEUMATOID ARTHRITIS: A PRELIMINARY REPORT OF A META-ANALYSIS

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Background: Glucocorticosteroids (GCs) are used to provide rapid relief of symptoms in people with active RA. Their use is recommended by most RA management guidelines and systematic reviews, although the magnitude of their benefit above placebo is uncertain. Persistent pain remains a problem in RA, even despite optimal immunomodulatory management. Systemic GC use may be associated with important adverse events.

Objectives: To quantify the specific effects of oral GCs for RA pain.

Methods: A systematic literature review was performed for RCTs using GCs in RA compared to inactive treatment. Trials were included whether or not participants received DMARD treatments, so long as a specific effect could be assigned to GCs. Medline, Embase and Cochrane databases were searched until November 2019 and 2 reviewers independently assessed titles, abstracts and full texts. Data for pain were synthesized in a meta-analysis. This study is part of a wider review (PROSPERO CRD42019111562).

For subgroup analyses, follow up time points of 0-3 months, >3 - 6 months and >6 months were selected to address duration of effect. Individual studies could contribute to each of the 3 follow up subgroups.

Meta-analysis was performed on standardized mean differences (SMDs, bodily pain data) and mean differences (MDs, 100mm VASpain only) of change from baseline (sd), using the Meta and Metafor packages in R. Heterogeneity was quantified using I^2 and tau statistics. Bias was assessed with a funnel plot and Eggers test.

Results: 15983 papers, 470 abstracts and 152 full texts were assessed. Pain data from 12 RCTs were suitable for the meta-analyses. The most common pain metric was the 100mm VASpain (9 trials).

Study populations ranged from n=12 to n=350 participants, 50% to 71% were female with mean ages from 43 to 66 years. Baseline scores for VASpain ranged from to 34 to 66 mm. Means were reported for DAS28 (from 4.9 to 5.8), ESR (25 to 60mm) and CRP (5 to 27mg/L).

Data synthesis at the reported primary time point/end point showed a statistically significant reduction in bodily pain in participants treated with GCs; SMD = -0.36 (10 studies, 1377 participants, 95% CI, -0.59 to -0.14, p=0.002) with significant heterogeneity (I^2 = 66%, tau = 0.27, p<0.01). The Funnel plot suggested asymmetry, favouring GCs (Eggers p = 0.007).

Subgroup analyses were used to investigate the time course of specific effects on pain. Efficacy displayed time-related decreases after initiation. From 0-3 months SMD= -0.56 (95% CI, -0.76 to -0.36, p<0.001, 9 studies, 936 participants, I^2 = 43%, Eggers p= 0.002). Efficacy was lower at >3 - 6 months (SMD= -0.32, 95%CI -0.52 to -0.11, p=0.002, 3 studies, 382 participants, I^2 =0%, Eggers p=0.75) and further reduced at >6 months (SMD= -0.07, 95%CI, -0.23 to 0.08, p=0.357, 4 studies, 665 participants, I^2 = 7%, Eggers p=0.43).

For trial data collected during concomitant oral GC dosage, mean difference (MDs) in 100mm VASpain was -14mm (95% CI, -20mm to -9mm) greater improvement in GC than control in the 0-3 month period (8 studies, 1047 participants, I^2 = 70%). For later follow ups, MDs at >3 to 6 months were -6mm (95% CI, -11mm to -1mm, 3 studies, 537 participants), and -1mm (95% CI, -6mm to 4mm, 3 studies, 369 participants) at >6 months.

Conclusion: Oral GCs have efficacy for pain in RA but the mean effect is of borderline clinical importance, and greatest shortly after steroids are commenced. GCs were usually used alongside other treatments as part of a combination. Future research might determine who might gain most benefit from systemic GCs, and improve other treatments to reduce the burden of pain.

Acknowledgments: Dr Douglas Grindley for help devising search strategy

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THURSDAY, 04 JUNE 2020

Back pain, mechanical musculoskeletal problems, local soft tissue disorders

THU0476 **GLYCOSAMINOGLYCAN REMODELLING OF LUMBAR INTERVERTEBRAL DISCS IN ELITE ROWERS THROUGHOUT THEIR ANNUAL TRAINING CYCLE**

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Background: To assess the glycosaminoglycan (GAG) content of lumbar intervertebral discs (IVD) in elite rowers (ER) at different stages of their annual training cycle and compared to healthy volunteers (HV) using GAG chemical exchange saturation transfer (gagCEST).

Objectives: Does GAG content of IVDs differs between ER in different stages of the training cycle from HV?

Methods: 205 lumbar IVD of 21 ER (23 ±3 years, 9 female, 11 male) and 25 HV (27 ±2 years, 13 female, 12 male) were prospectively examined with 3T magnetic resonance imaging (MRI). Standard T2 weighted (T2w) sequences were used for morphological grading according to the Pfirrmann classification. GAG content of the nucleus pulposus (NP) and annulus fibrosus was determined with gagCEST in non-degenerated discs according to Pfirrmann. ER were examined during the peak of their competition preparation (T0) and 6 months later during the peak of their post-competition recovery period (T1).

Results: At T0 we found significantly higher gagCEST values in ER (A) compared to HV (C) (NP: 4.26 ±2.37% vs. 3.38 ±1.72%, p<0.05; confidence interval (CI) 0.32%/1.44%; AF: 2.75 ±1.7% vs.1.961 ±1.23%, p<0.01; CI 0.4%/1.2%). At T1 gagCEST values in ER (B) decreased and illustrated no significant difference compared to HV (C) (NP: 3.55 ± 2.31%, p = 0.531, CI 0.038%/0.73%; AF: 2.31 ±1.57%, p = 0.073, CI 0.03%/0.74%).

Conclusion: Compared to HV lumbar IVD of ER show significantly higher gagCEST values during the peak of their competition preparation and similar values during the recovery period, indicating a GAG remodelling effect by training.

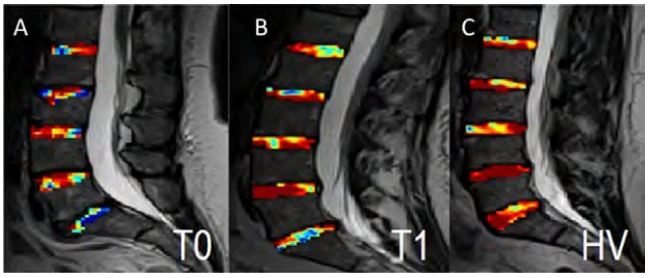


Figure 1. Comparison of gagCEST values of lumbar IVD between ER (A, T0; B, T1) and HV.

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Lilly Deutschland GmbH
Novartis Pharma GmbH Pfizer Deutschland GmbH
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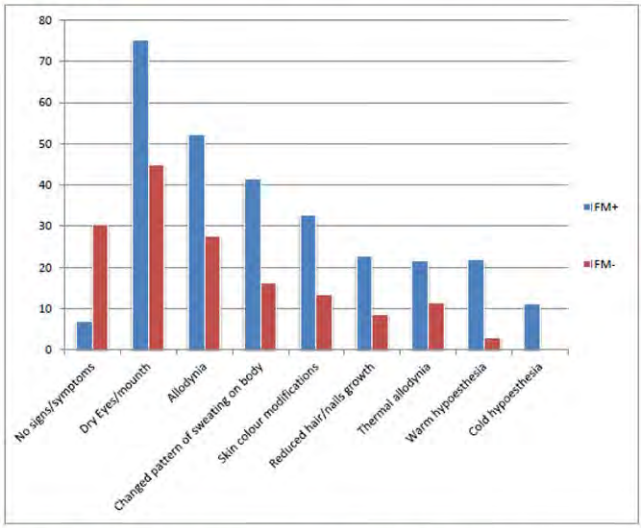
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THURSDAY, 04 JUNE 2020

Pain in rheumatic diseases, including fibromyalgia

THU0477 **SURAL NERVE SIZE IN FIBROMYALGIA SYNDROME**

Figure 2. Prevalence ad distribution of sing/symptoms indicative for the presence of small-fiber pathology



Values reported in percentage. All between-groups differences were statistically significant ($p<0.01$)

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Background: The pathophysiology of fibromyalgia syndrome (FM) still needs to be fully clarified. In addition to the central sensitization mechanisms, some evidence suggests an involvement of the peripheral nervous system, mainly intended as small fibers neuropathy. The sural nerve showed some alterations, in terms of increasead cross-sectional area (CSA), in the course of small fibers neuropathy.
Objectives: To evaluate sural nerve CSA and factors associated with increased CSA in FM patients.
Methods: A cross sectional evaluation was conducted in consecutive FM patients according to the 2016 American College of Rheumatology criteria. Demographic, clinimetric parameters (in particular the revised Fibromyalgia Impact Questionnaire [FIQR] to assess the severity of the disease and the PainDetect Questionnaire [PDQ] to evaluate neuropathic pain features) and the sural nerve dimensions measured by ultrasound were recorded for each patient. The size of the sural nerve was described in terms of the mean cross-sectional area (CSA) measured bilaterally. CSA was measured at the leg level, 14 cm from the apex of the lateral malleolus, where the sural nerve is detectable as a structure adjacent to the small saphenous vein in the distal portion of the leg. The ultrasound examination was performed with a MyLab Class C (Esaote S.p.A., Genoa, Italy) equipped with a 6-18 MHz multifrequency broad band probe. CSA was compared with demographic and clinimetric parameters through one-way analysis of variance (ANOVA). A multiple regression was also conducted using CSA as dependent variable, with age, body mass index (BMI), disease duration, FIQR and PDQ as independent variables.
Results: The study involved 110 FM patients (105 women and five men), with a mean age of 50.7 (±11.1) years and a mean disease duration of 5.8 (±5.2) years. Sural nerve CSA showed a statistically significant increase in patients with higher PDQ scores (p=0.0096) and, even more significantly, in overweight or obese subjects (p <0.001). The multiple regression analysis, using CSA as dependent variable, confirmed that the PDQ score (p=0.0049) and the body mass index (p<0.0001) are the only two independent variables associated with CSA size (Table 1).

Table 1. Multiple regression analysis of the independent variables related to the mean cross-sectional area (dependent variable) of sural nerve.

Indipendent variables	Coefficient	Standard error	t	p	$r_{partial}$	$r_{semipartial}$
Constant	-0.2551					
BMI	0.07592	0.01847	4.111	0.0001	0.3739	0.3462
Disease duration	-0.02492	0.02092	-1.191	0.2364	-0.1160	0.1003
Age	0.002455	0.009833	0.250	0.8033	0.02448	0.02103
FIQR	0.0001376	0.006862	0.0201	0.9840	0.001966	0.001689
PDQ	0.05272	0.01997	2.639	0.0096	0.2506	0.2223

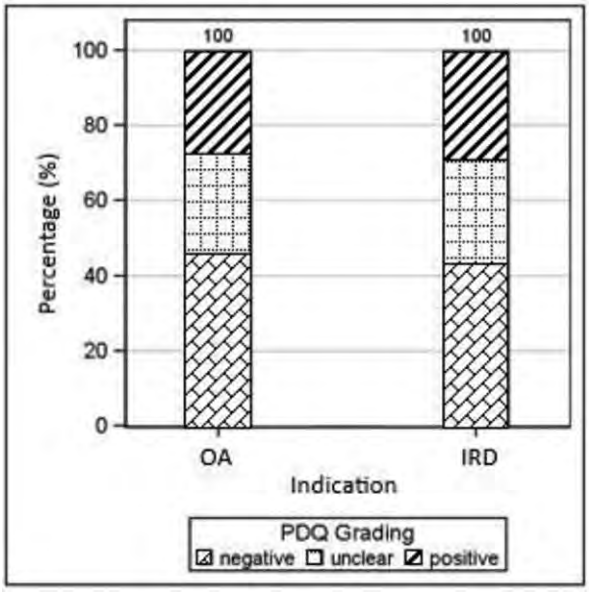
Abbreviations: BMI=Body Mass Index; FIQR=revised Fibromyalgia Impact Questionnaire; PDQ=PainDetect Questionnaire

Conclusion: Increased sural nerve CSA is associated with neuropathic like pain features and BMI. Overweight and obesity appear to be associated with an FM phenotype with greater peripheral involvement than normal-weight subjects. Sural nerve ultrasound, an easy to perform examination, could be a useful tool to identify this kind of patients.
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Disclosure of Interests: : None declared
DOI: 10.1136/annrheumdis-2020-eular.2461

THU0478 IS NEUROPATHIC PAIN IN INFLAMMATORY RHEUMATIC DISORDERS AN UNDERESTIMATED PROBLEM? RESULTS FROM THE GERMAN PAINDETECT DATABASE

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Background: The aim of the study was to investigate the impact and relevance of neuropathic pain in inflammatory rheumatic disorders (IRD) and osteoarthritis (OA).
Objectives: Pain is one of the main symptoms in patients with IRD and OA. To enhance a mechanistic based treatment of pain the differentiation between nociceptive and neuropathic pain via screening tools (e.g. painDETECT questionaire) might possibly be helpful. The goal of the study was to investigate (1) if neuropathic pain is a significant burden for patients with IRD and (2) if pain patterns differs from degenerative joint diseases such as OA in over 9.000 patients in each group.
Methods: painDETECT is a questionnaire that has been evaluated and used in numerous clinical trials to detect neuropathic pain in various diseases. The collected data is centrally managed and evaluated. In total (end of 2019) 395.984 patients have been documented. Out of the painDETECT database 9256 patients with IRD and 9436 patients with OA were extracted, analyzed and compared on their neuropathic pain pattern (screening was performed using the painDETECT-questionaire., PDQ). Secondary parameters were: intensity of pain, functional status, depression, chronicity and sleep disorder. Patients had been recruited from general practitioners (GPs), Rheumatologists, Orthopedics and Neurologists from 862 office-based physicians into the painDETECT-database. This project is an open label registry study in Germany.
Results: The median PDQ-score of patients with inflammatory rheumatic disorders adds up to 14,2 (1-38) and of OA patients to 13,8. 28.7% of inflammatory rheumatic disorders and 27.2% of OA-patients showed signs for neuropathic pain by positive PDQ. The difference was according to this high patient numbers statistically significant (P=0.0015). VAS-Score, Depressions-Score, Chronicity -Score and Functional -Score showed no clinically relevant differences between these two groups.
Conclusion: Nearly one third of patients with IRD as well as patients with OA showed neuropathic pain components by using PDQ. Despite increasingly better disease control through more effective therapies, pain still remains a major burden for many patients and has a profound impact on their quality of life. The present data indicate a surprisingly high symptoms of neuropathic pain even in IRD patients and should be considered in the management of our patients. A new documentation system for Rheumatologists (RheumaAssist) could help to address these questions.



Percentage of PDQ-categories (negative/unclear/positive) for patients with inflammatory rheumatic disorders (IRD) or Arthrosis (OA)
Acknowledgments: This investigation was supported within a grant of Pfizer Deutschland GmbH.
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GmbH Roche Pharma Rheumazentrum Rhein-Ruhr Sanofi-Genzyme Deutschland GmbH Swedish Orphan Biovitrum GmbH UCB Pharma GmbH, Speakers bureau: AMGEN GmbH AbbVie Deutschland GmbH & Co. KG Biogen GmbHBristol-Myers Squibb Celgene GmbH Chugai Pharma arketing Ltd. / Chugai Europe GmbHHexal Pharma Janssen-CilagGmbH Johnson & Johnson Deutschland GmbHLilly Deutschland GmbH / Lilly Europe / Lilly Global Novartis Pharma GmbH Pfizer Deutschland GmbH Roche Pharma Rheumazentrum Rhein-Ruhr Sanofi-Genzyme Deutschland GmbH Swedish Orphan Biovitrum GmbH UCB Pharma GmbH, Rainer Freynhagen Consultant of: AOP Orphan Pharma, Grünenthal, Lilly, Merck, Mitsubishi Tanabe Pharma, Pfizer, Scilex Pharmaceutics, Speakers bureau: AOP Orphan Pharma, Grünenthal, Lilly, Merck, Mitsubishi Tanabe Pharma, Pfizer, Scilex Pharmaceutics, Thomas Tölle Consultant of: AOP Orphan, Almiral Hermal, Bionest Partners, Benkitt Renkiser, Grünenthal, Hexal, Indivior, Kaia Health, Lilly, Medscape Mundipharma, MSD, Novartis, Pfizer, Recordati Pharma, Sanofi-Aventis, and TAD Pharma, Speakers bureau: AOP Orphan, Almiral Hermal, Bionest Partners, Benkitt Renkiser, Grünenthal, Hexal, Indivior, Kaia Health, Lilly, Medscape Mundipharma, MSD, Novartis, Pfizer, Recordati Pharma, Sanofi-Aventis, and TAD Pharma, Michael Hammer Consultant of: Abbvie, Pfizer, Medac and Janssen, Speakers bureau: Abbvie, Pfizer, Medac and Janssen, Christoph Baerwald Consultant of: CGB received speaker or consulting fees from AbbVie, Paid instructor for: CGB received speaker or consulting fees from AbbVie, Speakers bureau: CGB received speaker or consulting fees from AbbVie, Jochen Walter Consultant of: Pfizer, Speakers bureau: AbbVie, Frauenhofer Institut, Gilead, Janssen-Cilag, Medac, Novartis, Pfizer, Ralf Schröder Shareholder of: Pfizer Pharma GmbH, Employee of: Pfizer Pharma GmbH, Matthias Schneider Grant/research support from: GSK, UCB, Abbvie, Consultant of: Abbvie, Alexion, Astra Zeneca, BMS, Boehringer Ingelheim, Gilead, Lilly, Sanofi, UCB, Speakers bureau: Abbvie, Astra Zeneca, BMS, Chugai, GSK, Lilly, Pfizer, Sanofi, Ralf Baron Consultant of: RB received speaker or consulting fees from AbbVie, Paid instructor for: RB received speaker or consulting fees from AbbVie, Speakers bureau: RB received speaker or consulting fees from AbbVie

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THU0479 ASSOCIATION BETWEEN CENTRAL SENSITIZATION AND CLINICAL AND ULTRASONOGRAPHIC PARAMETERS IN INFLAMMATORY ARTHRITIDES

G. Adami[1], E. Gerratana[2], A. Giollo[1], C. Benini[1], E. Vantaggiato[1], D. Rotta[1], L. Idolazzi[1], D. Gatti[1], M. Rossini[1], A. Fassio[1]. [1]*University of Verona, Verona, Italy*; [2]*University of Messina, Messina, Italy*

Background: Central sensitization (CS) is an important feature of patients with chronic pain, especially rheumatoid arthritis (RA) and psoriatic arthritis (PsA) patients. CS might interfere with the clinical evaluation of inflammation. Central Sensitization Inventory (CSI) is a validated instrument for assessing central sensitization.

Objectives: We seek to investigate the inference of central sensitization (assessed with the CSI) on clinical (disease activity scores) and ultrasound parameters (US 7-joints score) in RA and PsA patients.

Methods: We conducted a cross-sectional analysis on patients with an established diagnosis of RA or polyarticular PsA. Demographic, anamnestic and clinical parameters were collected. Disease activity was measured with SDAI in RA patients and with DAPSA in PsA patients. The presence and severity of synovitis was measured with the US 7-joints score. Exclusion criteria included: diagnosis of fibromyalgia, depression and patients with PsA with enthesitis predominant and/or spondylitis subtypes. Differences between variables were analysed with t-test and ANOVA for multiple comparisons. Correlation between continuous variables was analysed with Pearson correlation. CSI was analysed either as positive\negative (threshold 40 points) or divided in four categories, i.e., subclinical (≤29), mild (30-39), moderate (40-49), severe (50-59) and extreme (≥60).

Results: We enrolled 42 patients in the study. Descriptive characteristics of the study population are presented in table 1. We found no difference in clinical parameters between diseases, sex or age. Women had a higher CSI score compared to men (mean 39.3 vs 26.7 p=0.005). We found a correlation between CSI score and DAPSA (r^2 0.39, p =0.001), number of tender joints (r^2 0.13, p=0.02) and HAQ (r^2 0.47, p<0.001) (Figure 1) while we found no correlation between CSI score and SDAI or other clinical parameters. We found a significant difference in DAPSA, tender joints count and HAQ between CSI categories (ANOVA p=0.01, p=0.02 and p<0.001 respectively). US 7-joints score was associated with SDAI (r^2 0.33, p=0.03), number of swollen joints (r^2 0.28, p=0.002) and disease duration (r^2 0.35, p<0.001) but not with DAPSA or tender joints.

Table 1. Descriptive characteristics of the study population

Age (mean, SD in years)		55.9 (12.3)
BMI		25.9 (3.9)
CSI questionnaire score (mean)		35 (16)
CSI categories (n, %)	**Subclinical**	18 (42.9%)
	Mild	9 (21.4%)
	Moderate	8 (19.0%)
	Severe	4 (9.5%)
	Extreme	3 (7.1%)
Diagnosis (n, %)	**PsA 52.4%**	9 men 13 women
	RA 47.6%	2 men 18 women
CSI score in PsA (mean, SD)		34.4 (16.5)
CSI score in RA (mean, SD)		34.8 (15.5)
CRP (median, IQR in mg/L)		1.85 (1.0-4.6)
Tender joints (mean, SD)		2 (2)
Swollen joints (mean, SD)		1 (2)
SDAI categories (n, %)	**Remission**	4 (20.0%)
	Low disease activity	8 (40.0%)
	Moderate disease activity	7 (35.0%)
	Severe disease activity	1 (5.0%)
DAPSA categories (n, %)	**Remission**	6 (33.3%)
	Low disease activity	4 (22.2%)
	Moderate disease activity	7 (38.9%)
	Severe disease activity	1 (5.6%)
US 7-joints score (mean, SD)		6 (7)
HAQ (mean, SD)		0.6 (0.6)
Prednisone equivalent (mean, SD in mg/day)		1.47 (3.2)
Biological DMARD (n, %)	**No**	15 (35.7%)
	Yes	27 (64.3%)
Conventional DMARD (n, %)	**No**	13 (31.0%)
	Yes	29 (69.0%)

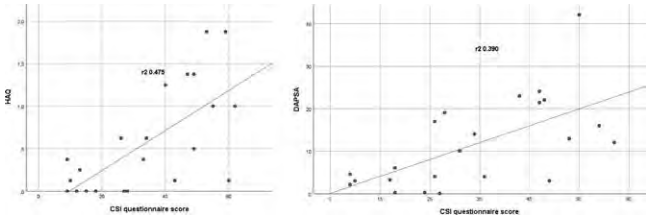


Figure 1. Correlation between DAPSA score and CSI score and between HAQ and CSI score

Conclusion: We found an association between CS and sex, functional disability, tender joints count and disease activity score in PsA patients while there was no correlation between RA disease activity and central sensitization. US 7-joints score was associated with swollen joints count, disease duration and disease activity in RA patients but not in PsA patients. In PsA patients, DAPSA might be more influenced by central sensitization, especially in female individuals.

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THU0480 EXPERIENCE USING DIFFERENT CRITERIA OF FIBROMYALGIA IN PATIENTS WITH ANKYLOSING SPONDYLITIS: 1990 AMERICAN COLLEGE OF RHEUMATOLOGY CLASSIFICATION CRITERIA VS. NEW

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Background: Fibromyalgia (FM) is a very frequent condition in patients with diseases associated with pain syndrome, such as rheumatoid arthritis (RA), ankylosing spondylitis (AS) and other chronic rheumatic diseases. FM, RA and AS has different clinical characteristics, but can share symptoms such as pain, fatigue and sleep disturbance that leads to delay in appropriation correct diagnosis [1]. For today well known many different criteria for FM: 1990 American College of Rheumatology (ACR) classification criteria, modified 2010 ACR diagnostic criteria, 2016 Fibromyalgia Diagnostic Criteria and new AAPT Diagnostic Criteria for

Fibromyalgia. According to the literature, prevalence FM in AS patients can reach from 12.6 to 28.5%, but prevalence estimates should be interpreted with care as no data that the criteria for FM have been validated for use in patients with AS and other chronic inflammatory arthritis [1, 2]. The lack of appropriate information needs further investigation for better identification FM.

Objectives: The aim of our study was to compare the presence of FM by 1990 ACR classification criteria, modified 2010 ACR diagnostic criteria, 2016 Fibromyalgia Diagnostic Criteria and new criteria FM 2019 - AAPT Diagnostic Criteria for Fibromyalgia in AS patients.

Methods: One hundred and thirteen AS patients (19 women and 94 men) with mean age (M ± SD) 42.3±10.94 years were enrolled in the study. Diagnosis AS was established according to modified New York criteria. For FM detection were used 1990 ACR classification criteria, modified 2010 ACR diagnostic criteria, 2016 Fibromyalgia Diagnostic Criteria and AAPT Diagnostic Criteria for Fibromyalgia. All patients were asked to complete self-reported disease-related questionnaires for patients with AS.

Results: According 1990 ACR criteria, FM met in 26 patients (23%). 38.1% patients were positively screened for FM due to modified 2010 ACR diagnostic criteria, and in 31.9% patients according 2016 Fibromyalgia Diagnostic Criteria, and in 41.6% patients due to AAPT Diagnostic Criteria for Fibromyalgia. All new criteria correlated with 1990 ACR classification criteria with p<0,01: r=0.654, r=0.664, r=0.520, concordantly. Using the ROC analysis, we evaluated the sensitivity and specificity of different FM criteria in patients with AS. Our results showed high diagnostic value of all new criteria, but the most sensitive for detection FM in patients with AS were the modified 2010 ACR diagnostic criteria with sensitivity of 96% and specificity of 79%.

Conclusion: Our study results confirmed very high prevalence FM in patients with AS.The most sensitive tool for detection FM in patients with AS were the modified 2010 ACR diagnostic criteria with sensitivity of 96% and specificity of 79%.The similar percentages of FM due to different classification criteria might be a good sign in context of the validity of these criteria for AS patient.

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Disclosure of Interests: : None declared

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THURSDAY, 04 JUNE 2020

Back pain, mechanical musculoskeletal problems, local soft tissue disorders

THU0481 THE PREVALENCE OF CHRONIC MUSCULOSKELETAL PAIN IN PATIENTS WITH ULCERATIVE COLITIS IN COMPARISON TO CONTROLS FROM THE GENERAL POPULATION: A CROSS-SECTIONAL STUDY

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Background: Musculoskeletal symptoms are common in patients with ulcerative colitis (UC) but the knowledge of the prevalence of chronic regional pain (ChRP) and chronic widespread pain (ChWP) in patients with UC is scarce.

Objectives: To compare the prevalence of ChRP, ChWP and chronic pain in different body locations in patients with UC with controls from the general population and to investigate if disease activity in UC is related to chronic pain.

Methods: From a national inflammatory bowel disease (IBD) Register (SWIBREG), all living patients with a confirmed UC diagnosis, aged 20-74 years (n=1134), who were residents in two counties in Northern Sweden were posted a validated questionnaire. Persons from the general population from a previous study (1) using the same questionnaires was used as controls (n=3867). The questionnaire comprises demography, history of pain and body localisation of pain. The disease activity of UC was measured by Patient- Simple Clinical Colitis Activity Index (P-SCCAI). ChRP and ChWP was defined as having pain for at least three months the last year. ChWP was defined as having pain on both left and right side of the body and both above and below the waist, and in the axial part of the body.

Results: The response rate for the patients with UC was 49.0% and for the controls 62.7%. The patients were older than the controls (mean age 52.8 vs 46.5 years; p<0.001) but there was no difference in gender (men 50.5% vs 46.7%; p=0.086). The reported prevalence of any chronic pain, ChRP and ChWP was higher in patients with UC versus controls (54.4% vs 39.5%; p<0.001; 32.5% vs 24.2%; p<0.001 and 19.4% vs 12.5%; p<0.001). The differences for reported chronic pain (any pain) was seen in all age groups. The patients with UC reported significantly more pain in the regions "lower back", "hip/upper leg" and "lower leg/foot" compared to controls (Table). The patients with P-SSCAI >5 (n=121) reported more ChWP than patients with P-SSCAI <5 (n=426) (46.3% vs 12.7%; p<0.001) and controls (46.3% vs 12.5%; p<0.001) with significant differences compared to controls in all body regions. No significant difference in ChWP was found between patients with P-SSCAI <5 and controls (12.7% vs 12.5%; p=0.917). There was a slightly higher prevalence of reported any chronic pain between patients with P-SSCAI <5 and controls (46.5% vs 39.5%; p=0.007).

Table. The prevalence of reported chronic musculoskeletal pain in different body regions in patients with ulcerative colitis and controls.

Body region	Ulcerative colitis (n = 556)	Controls (n = 2425)	P-value
Anterior chest	32 (5.8 %)	115 (4.7 %)	0.2
Neck	119 (21.4 %)	460 (19.0 %)	0.3
Dorsal chest	63 (11.3 %)	236 (9.7 %)	0.3
Lower back	168 (30.2 %)	557 (23.0 %)	0.0008
Shoulder/upper arm	126 (22.7 %)	482 (20.0 %)	0.2
Elbow/lower arm/hand	103 (18.5 %)	405 (16.7 %)	0.4
Hip/upper leg	113 (20.3 %)	319 (13.1 %)	<0.0001
Knee	95 (17.1 %)	335 (13.8 %)	0.07
Lower leg/foot	97 (17.4 %)	300 (12.4 %)	0.003

Conclusion: Patients with UC reported more chronic pain than controls from the general population, especially from the lower back and hip region. Higher UC disease activity was associated with more pain in all body regions.

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Disclosure of Interests: : Nina Pettersson: None declared, Fredrik Kragsbjerg: None declared, Arvid Hamrin: None declared, Stefan Bergman: None declared, Helena Forsblad-d'Elia Grant/research support from: Unrestricted grant from Novartis., Consultant of: Advisory Board Fees from Sandoz, Novartis, and Abbvie, Pontus Karling: None declared

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THURSDAY, 04 JUNE 2020

Pain in rheumatic diseases, including fibromyalgia

THU0482 PAIN CATASTROPHIZING AND DISEASE PERCEPTION DIFFERS BETWEEN NORWEGIAN AND FINNISH OUTPATIENT CLINIC PSORIATIC ARTHRITIS PATIENTS DESPITE COMPARABLE OUTCOMES ON OBJECTIVE MEASURES OF DISEASE

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Background: Pain catastrophizing (the tendency to describe a pain experience in more exaggerated terms than the average person, to ruminate on it more, or to feel more helpless about it), has been associated with reduced likelihood of achieving remission in rheumatoid arthritis patients (1). Cultural and societal differences between countries may have an impact on outcome such as patients' perceptions of disease.

Objectives: To compare patient pain catastrophizing, patient perception of disease, objective measures of disease and treatment in psoriatic arthritis (PsA) patients between a Norwegian and a Finnish outpatient clinic. Further, to explore for associations with pain catastrophizing.

Methods: All PsA patients followed at the outpatient clinics are routinely monitored using a structured medical support system (GoTreatIT® Rheuma). Data collection, done in 2018-19 is listed in the table.

Patients reported their pain catastrophizing answering the two questions, "When I feel pain it is terrible and I feel it is never going to get any better. When I feel pain, I can't stand it anymore." Each question is scored 0-6 and mean value of both is calculated. Pain catastrophizing was defined if mean score ≥4.

Categorical variables were presented as numbers (%) and continuous variables as mean (SD) and associates explored using univariate and multivariate analysis.
Results: A total of 302 Finnish and 363 Norwegian PsA patients were examined. Pain catastrophizing was reported significantly less commonly among the Finnish as compared to the Norwegian PsA clinic patients, both expressed as mean (SD) values (1.48 (1.42) vs 2.05 (1.42), p<0.001) and proportions of patients having a score ≥4 (7.6% (n=23) vs 12.5% (n=45), p=0.043, respectively). As shown in the table the Finnish patients had significantly more years of education, shorter disease duration and less pain and fatigue than the Norwegian patients. For the other features, no significant differences between the two cohorts were found.

	Finland (n=302)	Norway (n=363)	P
Age, years	54.0 (13.3)	54.7 (12.5)	0.49
Females	153 (50.7%)	181 (49.9%)	0.84
BMI. Kg/m2	28.8 (5.6)	28.1(5.1)	0.06
Current smoking	44 (14.6%)	51 (14.1%)	0.86
Education, years	13.6 (3.5)	12.7 (3.8)	0.001
Disease duration, years	4.7 (4.3)	9.9 (8.9)	<0.001
CRP, mg/L	4.3 (6.8)	4.0 (8.8)	0.69
MDglobal assessment, VAS 0-100 mm	6.84 (1.29)	5.71 (8.50)	0.19
28 swollen joint count	0.48 (1.35)	0.31 (1.16)	0.14
28 tender joint count	1.01 (2.83)	1.37 (2.80)	0.14
DAPSA	9.66 (8.95)	11.33 (9.60)	0.06
Pain, VAS 0-100 mm	30.73 (25.92)	35.55 (25.76)	0.023
Fatigue, VAS 0-100 mm	29.96 (29.24)	42.56 (31.94)	<0.001
MHAQ, 0-3	0.39 (0.44)	0.43 (0.41)	0.24
Body surface area for psoriasis	2.45 (8.15)	2.66 (6.15)	0.17
Current b-tsDMARDs	121 (40.1%)	139 (38.3%)	0.64

In univariate analyses female gender, higher BMI, less years of education, Dr. global, tender joint count, DAPSA, pain, fatigue, MHAQ and psoriasis body surface area were found to be associated with more pain catastrophizing.
In multivariate analysis (mandatory adjusting for age, gender, BMI, years of education and disease duration) fewer years of education, higher scores for pain, fatigue and MHAQ and being patient at the Norwegian center were independently associated with more pain catastrophizing.
Conclusion: Our data indicate that cultural differences across countries may have a significant impact on outcomes that reflecting patients' perceptions of disease. This may have an implication when merging heterogeneous databases across countries.
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Disclosure of Interests: : Glenn Haugeberg: None declared, Inger Johanne Widding Hansen: None declared, Hilde Berner Hammer: None declared, Arthur Kavanaugh Grant/research support from: Abbott, Amgen, AstraZeneca, BMS, Celgene Corporation, Centocor-Janssen, Pfizer, Roche, UCB – grant/research support, Brigitte Michelsen: None declared, Kirsi Paalanen: None declared, Tuulikki Sokka-Isler: None declared
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THURSDAY, 04 JUNE 2020

Back pain, mechanical musculoskeletal problems, local soft tissue disorders

THU0483 **ASSOCIATION OF CENTRAL SENSITIZATION AND ATTENTION DEFICIT IN MEDICAL STUDENTS WITH CHRONIC BACK PAIN**

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Background: Back pain is one of the most common health complaints among university students. A subset of people suffering from chronic back pain exhibit features of increased pain sensitivity and altered pain processing, suggesting central sensitization (CS) to pain[1]. The mechanisms behind these processes are, to date, not fully understood[2]. Evidence shows that in chronic pain, cognitive factors could contribute to the occurrence of central pain sensitization[3,4].
Objectives: To assess the association between CS and features of adult Attention Deficit Hyperactivity Disorder (ADHD) in medical students suffering from chronic back pain.
Methods: Data was collected from medical students during the academic year 2018-2019 at Suez Canal University using an online survey. The survey included a section on self-reported musculoskeletal pain including back pain lasting more than 3 months in the neck, upper back and lower back, part (A) of the central sensitization inventory (CSI) and the Adult Attention Deficit Hyperactivity Disorder Self-Report Scale (ASRS-v 1.1). Associations between CSI and ASRS-v 1.1 in students with back pain was assessed using Spearman's correlation. Linear regression was used to estimate cross-sectional associations adjusted for age and gender.
Results: Two hundred and thirty students completed the survey, 93 (40.4%) had back pain for more than 3 months. Students with back pain had significantly higher CS and attention deficit according to CSI (P<0.01), and the ASRS-v 1.1 scores (P=0.09). Correlation results showed a strong positive association between CS and ADHD in students with back pain (correlation coefficient = 0.41, P<0.001). This association remained significant after adjusting for age and gender (P<0.001).
Conclusion: Results of this study suggest that in students suffering from chronic back pain, features of attention deficit are associated with elevated CS. The direction of the association requires further study and may provide novel insights into the interaction between CS and cognitive factors.
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Disclosure of Interests: : None declared
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THURSDAY, 04 JUNE 2020

Pain in rheumatic diseases, including fibromyalgia

THU0484 **FIBROMYALGIA AND MULTIPLE SWITCHING OF BIOLOGICS IN SPONDYLOARTHRITIS**

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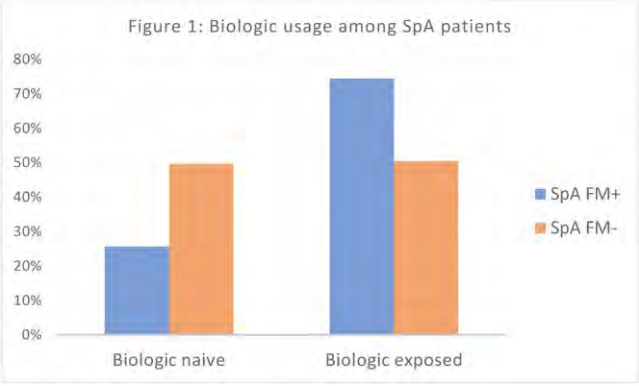
Background: Fibromyalgia (FM) is a condition characterized by chronic widespread pain, tender points, fatigue and disturbed sleep rhythm. Some of these symptoms such as fatigue, tender points and diffuse pain seen in patients with spondylarthritis (SpA). Moreover, FM and SpA can coexist creating a diagnostic challenge, particularly in early disease course and influence clinical disease activity assessment.
Objectives: With this cross-sectional study, we aim to estimate the prevalence of FM in SpA and to elaborate its effect on biological treatments.
Methods: FM was identified according to the ACR 2010 diagnostic criteria. SpA patients identified according to rheumatologist using various SpA subsets criteria. A review of the electronic medical files for SpA patients attending the rheumatology outpatient clinic and infusion unit at a major tertiary hospital during the period from June to December 2018 were included. Patients' demographics, socioeconomics, disease characteristics, activity, HLA status and abnormal MRI sacroiliac were explored. Regarding SpA medications, number, frequency and dose of DMARDs and biological agents were obtained.
Continuous variables were reported by their mean and standard deviation (SD) and qualitative variables by frequency and percentage. Statistical significance was set at p <0.05. Statistical analysis was performed using SPSS version 23.
Results: Of the 305 enrolled SpA patients, 43 (14.1%) had FM. Females represents 57.4% of the patients, mean age was 44.07 ± 11.85 years. Arab ethnicity represents most of our cohort 84.9%, the majority were Emirati 64.6%. Smokers were 8.2% and ex-smokers were 3.3%. Axial SpA represents 38.4% while peripheral SpA 61.6% of our cohort according to ASAS classification.
HLA B27 tested in a sample of 180 patients; it was positive in only 17.8%. CRP found to be elevated in 20.3% of the patients at baseline. Abnormal MRI SIJ bone marrow edema changes were found in 10.8%, while other SIJ changes was seen in additional 20.6%. The prevalence of FM showed no statistically significant difference between axial and peripheral SpA. Patients SpA and FM have longer disease duration than SpA alone, P= 0.034. Table.1 show demographics, socioeconomics and clinical data of our cohort.
Regarding medication, the use of biologics among SpA patients with FM is more frequent than SpA patients without FM (74.4% vs 51.5 % respectively), P= 0.005.

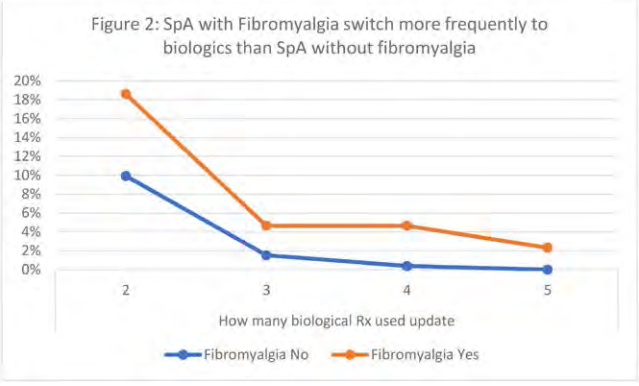
Interestingly, the likelihood ratio testing showed that SpA patient with Fibromyalgia switch more frequently to another biologics than SpA without fibromyalgia, P= 0.015.

Cramer's V test showed that there is a high statistically significant (P= 0.002) and very strong association (> 0.25) between presence of Fibromyalgia and multiple switching of biologics in SpA.

There was no difference in the exposure to prednisolone nor conventional DMARDs between SpA patients with or without FM, P= 0.64 & 1 respectively.

Gender, Female, n (%)	175 (57.4)
Age, mean ± SD (min- max), years	44.07 ± 11.85 (18- 78)
Type of A, n (%)	117 (38.4)
Axial	188 (61.6)
Peripheral	
Fibromyalgia, n (%)	43 (14.1)
FM in axial SpA	18 (41.9)
FM in Peripheral SpA	25 (58.1)
SpA Disease duration (months)	107.7± 50.4
FM+, mean ±SD	86± 57.9
FM-, mean ±SD	
Elevated CRP, n (%)	62 (20.3)
HLA B27 in 180 patients, n (%)	32 (17.8)
Positive	148 (82.2)
Negative	
Abnormal MRI SIJ, n (%)	92 (30.2)
Bone marrow edema	33 (10.8)
Subchondral sclerosis	21 (6.9)
Fatty transformation of bone marrow	5 (1.6)
Erosion	2 (0.7)
Number of conventional DMARDs ever tired, n (%)	81 (26.6)
None	166 (54.4)
One	46 (15.1)
Two	12 (3.9)
Three	
Frequency of DMARDs usage, n, (%)	224 (73.4)
Conventional DMARDs	56 (18.4)
Prednisolone	164 (53.8)
Biologic DNARDs	





Conclusion: FM coexistence with SpA might impact clinical evaluation of disease activity and possibly negatively affect self-measurement of treatment response. In our study, SPA patients exposed to more biologics if they have coexisting FM; Moreover, they are more frequent switchers among biologics including TNFi and IL17i.

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THURSDAY, 04 JUNE 2020

Back pain, mechanical musculoskeletal problems, local soft tissue disorders

THU0485 THE EFFECT OF PERINEURAL INJECTION THERAPY IN PERIARTHRITIS SHOULDER

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Background: Primary adhesive capsulitis of the shoulder is a common pathology of the glenohumeral joint characterized by shoulder pain and progressive restriction of the range of motion,its treatment options either medication, local injection, physiotherapy, hydrodistension, manipulation under anesthesia, arthroscopic and open capsular release[1].

Subcutaneous prolotherapy injections can reduce vascular endothelial growth factor levels and restore effective repair processes so induce apoptosis of proliferating peptidergic noceffectors and neovessels and inhibit TRPV1 receptors resulting to reduction of pain[2,3].

Objectives: To assess the effectiveness of perineural injection therapy in management of pain and physical function in Primary adhesive capsulitis of the shoulder.

Methods: One hundred patients with primary adhesive capsulitis in the freezing stage were selected in this study according to the classification of Hannafin and Chiaia and had restriction of passive motion of greater than 30°in 2 or more planes of movement. Patients with previous corticosteroid injection or previous surgery in the affected shoulder, secondary adhesive capsulitis including inflammatory or infectious arthritis,previous fracture, rotator cuff lesions were excluded from this study.

Ptients were randomly devided into two equal groups; Group I received 6 weekly subcutaneous injections of 0.5-1 ml of buffered dextrose 5% in each chronic constriction injury points and tender points at shoulder and along course of suprascapular, supraclavicular, axillary, musculocutanous and radial nerves. Group II received oral NSAIDs and muscle relaxants for 6 weeks. All patients in both groups received the same stretching and exercise therapy during the period of treatment. All procedures were done after informed consent. Assessments were performed at baseline, at the end of the treatment and after three and six months using visual analog scale (VAS) for pain, range of mvement measurements by goniometer, Shoulder Pain and Disability Index (SPADI) & the Western Ontario Rotator Cuff (WORC) Index.

Results: Patients in Group I had more rapid relief of pain and better functional improvement compared with group II ($p<0.05$). There was significant improvement in both groups ($p<0.05$) after 3 and 6 months with significant difference between the 2 groups indicated that better results in perineural group. Results were summarized in table 1.

Table 1. Pre- and post-treatment clinical measurement of the patient groups

	Baseline GI	Baseline GII	After end of treatment GI	After end of treatment GII	After 3ms GI	After 3ms GII	After 6ms GI	After 6ms GII
VAS	8.7±0.9	8.4±1.0	5.0±1.5*¶	5.7±1.1*	4.4±1.5*¶	5.1±1.6*	3.8±1.2*¶	4.9±1.3*
SPADI	80.4±9.8	78.9±10.7	41.5±10.2*¶	50.4±8.8*	35.8±7.5*¶	46.6±7.9*	32.6±10.2*¶	44.5±8.7*
WORC	28.5±10.6	26.5±11.5	60.4±9.8*¶	55.9±10.5*	67.9±9.7*¶	57.3±10.3*	71.5±12.3*¶	60.1±9.6*

*significant improvement after treatment
¶ **significant difference between the two studied groups**

Conclusion: Perineural injection therapy is an effective modality in management of pain and physical function of Primary adhesive capsulitis of the shoulder.

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Disclosure of Interests: : None declared
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THU0486 2019 FRENCH GUIDELINES AND CARE PATHWAY ABOUT LOW BACK PAIN MANAGEMENT IN ADULTS

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Background: Low back pain (LBP) is a frequent, disabling symptom, for which the risk of chronicity is increased by heterogeneous care. Developing and implementing recommendations is likely to improve LBP management.
Objectives: To develop French guidelines and care pathway on the management of LBP, coordinated by the French National Authority for Health (FNAH) and based on previous international guidelines in addition to update literature.
Methods: A compilation report was constituted on the basis of a systematic review of guidelines between January 2013 and December 2018, and systematic reviews and meta-analysis in the field of LBP between January 2015 and December 2018. This report summarized the state-of-the-art for each predefined area of the guideline. A panel of experts including patients' representatives and 19 health professionals involved in LBP management was constituted to elaborate the guideline based on the compilation report. A care pathway was constituted to identify the trajectory and the different steps followed by a patient with LBP. Then, the compilation report and the preliminary guidelines were submitted to 24 academic institutions and stakeholders for feedback. Based on the preliminary guideline and the responses of academic institutions and stakeholders, the final recommendations were drawn up by the expert panel. The guideline was finally submitted to an independent committee of the FNAH for final validation. For each area of the guidelines, agreement between experts of the working group was evaluated through the RAND/UCLA method.
Results: The initial literature search identified 572 references of recent international guidelines or systematic reviews about LBP. After selection, the compilation report included 101 references. The compilation report was submitted to the expert group during 3 different meetings to reach a consensus on different topics. Thirty-one preliminary recommendations and a care pathway (divided in two parts to facilitate its use and readability) were drafted and submitted to academic institutions and stakeholders. Having considered their comments, final recommendations and care pathway were written. The final guideline was validated by the FNAH. Then, the consensus of the expert panel was assessed about all the final guidelines separately: 32 recommendations (including the care pathway) were evaluated as appropriate; none were evaluated uncertain or inappropriate. Strong approval was obtained for 27 of them (including the care pathway) and weak for 5 of them.
Conclusion: This new LBP guideline was based on recent scientific evidence. It introduced several concepts, including the need to identify low back pain at risk of chronicity, in order to provide quicker intensive management if necessary. This guideline should be updated in 5 years' time, in order to keep it in line with ongoing scientific evidence.
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THU0487 DIAGNOSTIC DILEMMA: WHICH CLINICAL TEST IS MOST ACCURATE FOR DIAGNOSING SUPRASPINATUS MUSCLE TEARS AND TENDINOSIS?

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Background: Supraspinatus tears and tendinosis are the most common pathology that cause shoulder pain to approximately half of the patients presenting clinically.[1]
Objectives: To investigate the diagnostic accuracy of five clinical tests in the diagnosis of supraspinatus tears and tendinosis compared with magnetic resonance imaging (MRI).
Methods: A total of 116 painful shoulders of 106 consecutive patients were examined. Patients were assessed using the most commonly used special clinical tests including the Jobe test (empty can), Neer test, drop arm test, Hawkins test and full can tests to identify supraspinatus tears and tendinosis. A visual analogue scale (VAS) was used for pain detection, and the Shoulder Pain and Disability Index (SPADI) questionnaire was administered. MRI examinations were performed on 1.5 Tesla MR system and images were assessed by a blinded radiologist. The primary outcomes were to determine the sensitivity, specificity, and accuracy of the five clinical tests, and to establish their correlation with MRI for supraspinatus tears and tendinosis.
Results: The mean age was 55.10 ± 10.20 years, and 32.08% of the patients were female. The Hawkins test had a higher sensitivity and accuracy in tears (sensitivity 89.66%, accuracy 56.03%, respectively) and higher sensitivity in tendinosis (79.07%). The drop arm test had a lower sensitivity but higher specificity in both tendinosis and tears (sensitivity 0%, 12.07%, respectively, and specificity 87.67%, 96.5%, respectively
Conclusion: The Hawkins test was the most sensitive in both supraspinatus tendinosis and tears compared with MRI findings.
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[1] Yamaguchi K, Ditsios K, Middleton WD, Hildebolt CF, Galatz LM, Teefey SA,The demographic and morphological features of rotator cuff disease. A comparison of asymptomatic and symptomatic shoulders. J Bone Joint Surg Am, 2006. 88(8): p. 1699-704.
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THU0488 PSYCHIATRIC SYMPTOMS, TEMPERAMENT PROFILE, STRESS PERCEPTION AND SLEEP QUALITY IN THE PATIENTS WITH CHRONIC SHOULDER PAIN: RELATIONSHIP WITH PAIN, DISABILITY, AND FUNCTIONAL CAPACITY

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Background: Shoulder pain is very common in general population. Psychiatric symptoms and poor sleep quality related with chronic pain and disability may be present in these patients.
Objectives: The aim of this study was to investigate the psychiatric symptoms, perceived stress, temperament profile and sleep disturbance in the patients with chronic shoulder pain (CSP) and also to evaluate the relationship with pain, disability, and functional capacity.
Methods: We prospectively evaluated 150 patients (M/F=41/109) (60.46±10.59 years) who have had shoulder pain for at least 3 months and 120 healthy controls (M/F=35/85) (58.35±8.52 years). Pain was evaluated with Visual Analog Scale (VAS), disability with Shoulder Disability Questionnaire (SDQ), functionality with The University of California-Los Angeles (UCLA) Shoulder Scale and range of shoulder motion, temperament profiles with TEMPS-A, stress perception with Perceived stress scale (PSS), psychiatric symptoms with Symptom Checklist-90-R (SCL-90R), Rosenberg self esteem with Self-Esteem Scale (RSES) and sleep disturbance with Pittsburgh sleep quality index (PSQI).
Results: The mean VAS pain score, SDQ score, and UCLA score of the patients with shoulder pain were 4.34±1.79, 61.98±26.88, and 58.90±17.78, respectively. SCL-90-R total and all subscale scores except interpersonal sensitivity, psychoticism, paranoid, and phobia were significantly higher in the patient group than the control group ($p<0.05$). Also PSQI total and sleep quality and latency subscale scores were significantly higher in the patient group ($p<0.05$). There was no significant difference between the patient and control groups in terms of RSES and PSS. The study identified 28 depressive temperament in the patient group which was statistically different from the control group ($p<0.05$). There were no significant differences between two groups in terms of cyclothymic, irritable, anxious, and hyperthymic temperaments ($p>0.05$). When the patient group is evaluated according to functionality, the patients having fair/poor shoulder function had more psychiatric symptoms except hostility, poor sleep quality, decreased self-esteem and increased stress perception. Also, anxious and depressive temperaments were found more common in the patients with fair/poor shoulder function. Psychiatric symptoms (somatization, obsessive-compulsive, interpersonal-sensitivity, depression and anxiety) and total PSQI were positively correlated with SDQ ($p<0.05$). There was positive correlation between PSS and SDQ ($p>0.05$). SCL90R total score, subscale of depression and anxiety, total PSQI and PSS were significantly correlated with VAS score ($p<0.05$).

Conclusion: We found psychiatric symptoms such as obsessive-compulsive besides somatization, anxiety, depression, hostility and sleep disturbances higher in the patients with CSP. Additionally, psychiatric symptoms, anxious and depressive temperaments were more common in the patients with fair/poor shoulder function. Self-esteem was not related with the pain. All these findings indicate the importance of psychological health in the patients with CSP. In order to reach treatment goals, psychiatric symptoms and temperament profiles of these patients also should be considered.

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THU0489 HIP INVOLVEMENT IN DIFFUSE IDIOPATHIC SKELETAL HYPEROSTOSIS (DISH): CROSS-SECTIONAL STUDY

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Background: In DISH or Forestier-Rotés disease, hip involvement is often misdiagnosed as hip osteoarthritis, especially when it is the initial manifestation of the disease or in patients with scarce vertebral signs. At present, a correct identification of this entity may suppose considerable therapeutic implications[1].
Objectives: The purpose of this study was to assess the prevalence and characteristics of hip involvement in our cohort of patients with DISH and evaluate the association of this extra-spinal manifestation with the variables studied.
Methods: We carried out a cross-sectional study in DISH patients who met Resnick and / or Utsinger classification criteria. We collected demographic, anthropometric, clinical and imaging data. Hip involvement was defined as the characteristic irregular bony excrescences above acetabulum. The cohort was divided between patients with and without hip involvement. A univariate descriptive analysis was performed with means and standard deviations, absolute frequencies and percentages. The normality of the data was checked using the Shapiro-Willis test. The bivariate analysis, for the qualitative variables, the χ^2 test or Fisher's exact test were identified. For the quantitative variables, the Student's t-test was used if the data followed a normal distribution, and otherwise using the Mann-Whitney U test.
Results: Of the 58 patients included, 67.2% were male. The median age was 69.4 years (44-89). The average time of disease evolution was 14.8 (+9.3) years. Although the most frequent initial symptom was thoraco-lumbar pain (39.7%), hip complaints were initially present in 13.8%. 22,6% of patients did not fulfil Resnick classification criteria. Hip involvement was identified in 53.4% and a 61,3% the cartilage space were preserved. In the bivariate analysis, hip involvement was associated with female sex, a reduction in the intermaleolar distance (IM) and the presence of certain enthesopathies (greater trochanter, superior iliac spines and distal patellar entheses). The acetabular ossifications were significantly related to the mixed pattern compared to the other possible phenotypes of the disease.
Conclusion: Hip involvement has been described in more than 50% of our patients. We found out that it was associated with female sex and a more broad ossification phenotype (mixed pattern). The measurement of IM distance could be useful for the clinical evaluation of this condition. Ossifications of other pelvic ring entheses were more observed in association with acetabular hyperostosis than other peripheral insertions.

References:

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THU0490 DEEP FRICTION MASSAGE VERSUS LOCAL STEROID INJECTION FOR TREATMENT OF PLANTAR FASCIITIS: A RANDOMIZED CONTROLLED TRIAL

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Background: Deep friction massage (DFM) has long been proven to be effective in the treatment of some tendinopathies.
Objectives: to evaluate the efficacy of DFM in the treatment of plantar fasciitis (PF) in comparison with local steroid injection.
Methods: In this randomized controlled trial, 60 patients with PF were selected from those attending the rheumatology and rehabilitation outpatient clinic and then randomized to receive either 40 mg triamcinolone local injection (group I: 30 patients; 41 heals) using the medial approach or to receive seven sessions of deep transverse friction massage (10 min each) every other day (group II: 30 patients; 36 heels). The outcome measures were the pain and function assessment by visual analog scale and foot function index, respectively, at 2 and 6 weeks of follow-up.
Results: Demographic data showed a statistically insignificant difference in age, female to male ratio, and BMI in both groups. The mean age was 39.42 years in group I and 41.32 years in group II (P=0.86). The female to male ratio was 3: 1 in group I and 2.75: 1 in group II, and the mean BMI was 32.41 in group I and 33.31 in group II (P=0.51). At 2 and 6 weeks of follow-up, DFM led to less improvement in pain and function compared with local steroid injection (P=0.001 and 0.002, respectively, at both time points of follow-up).
Conclusion: This study revealed that DFM is not effective as a single modality in treatment of PF. Further large-scale studies are needed to support this observation.

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THU0491 HYALURONIC ACID INJECTION IN PLANTER FASCIITIS: CAN WE USE?

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Background: Plantar fasciitis is the most common cause of hind foot pain. Treatment is aimed at pain reduction and maintaining or improving function. Several types of injected materials are used including corticosteroids, hyaluronic acid and Platelet-rich plasma.
Objectives: The aim of this study was to evaluate the efficacy of hyaluronic acid injection in comparison to corticosteroid injection for the treatment of degenerative plantar fasciitis.
Methods: This study included forty patients with degenerative plantar fasciitis diagnosed according to clinical examination and ultrasound findings. They were divided into two groups. Group one included twenty patients who were injected with Methylprednisolone (MP). Group two included another twenty patients who were injected with hyaluronic acid (HA). Clinical assessment was done including morning heel pain, localized heel tenderness, patient assessment of heel pain using the numerical rating scale (NRS), Functional assessment using the Manchester-Oxford foot questionnaire (MOXFQ) and musculoskeletal ultrasound assessment including planter fascia thickness, echogenicity, power Doppler signals, erosions and calcification.
Patients were injected and a follow up was done at two and six weeks for each group.
Results: The two groups MP &HA showed no significant baseline differences in clinical and sonographic variables, while they both significantly improved from baseline after two &six weeks injection (P<0.001).The MP group achieved a significant improvement in NRS, MOXFQ, plantar fascial thickness and echogenicity in the first follow up after two weeks better than the second follow up after six weeks (P<0.001). The HA group achieved significant improvement in NRS, MOXFQ, plantar fascial thickness and echogenicity in the second follow up after six weeks better than the first follow up after two weeks (P<0.001).
Over all, MP group had significant improvement clinically and sonographically than HA group after two weeks (P<0.001), while HA group had significant improvement clinically and sonographically in comparison with MP group after six weeks.
Conclusion: Our study supports the use of a single injection of hyaluronic acid as therapy for plantar fasciitis in preference to methylprednisolone acetate injections, while MP offers short term improvement (after two weeks). HA injection offers better therapeutic advantages in the intermediate-term follow up (after six weeks). Moreover, it has a longer duration of action and enables better tissue healing and can therefore be used as an effective alternative treatment for plantar fasciitis.

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THU0492 MAGNETIC RESONANCE IMAGING OF THE SACROILIAC JOINTS IN PATIENTS WITH HYPERMOBILITY: A RETROSPECTIVE COHORT STUDY

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Background: The incidence of inflammatory and structural lesions on magnetic resonance imaging of sacroiliac joints (MRI SIJs) in patients with hypermobility related disorders has not been fully investigated. Hypermobile patients are more susceptible to pelvic instability and biomechanical stress of the SIJs, leading to MRI SIJ changes

similar to those occurring in spondyloarthritis (SpA). Patients with hypermobility and suspected SpA pose a unique challenge owing to the high prevalence of back pain in the hypermobility cohort and the absence of spinal restriction on clinical examination.
Objectives: In this study, we aim to investigate the incidence of MRI SIJ lesions in patients with hypermobility.
Methods: We performed a retrospective study of all patients with a confirmed diagnosis of hypermobility related disorders (including hypermobility syndrome, hypermobility spectrum disorders and Ehlers-Danlos Syndromes) referred for an MRI lumbar spine and SIJ between 2011 and 2019 to investigate long-standing back pain. MRIs were examined by a musculoskeletal (MSK) radiologist with more than 25 years of experience, who was blinded to the clinical outcome of the patients. MRI SIJs were assessed for the presence of bone marrow oedema, subchondral sclerosis, erosion, fatty change, enthesitis, ankylosis, joint fluid and capsulitis.
Results: 51 patients with confirmed hypermobility related disorders were referred for MRI SIJ and lumbar spine between 2011 and 2019. 3 patients demonstrated clinical features in keeping with a diagnosis of SpA and were excluded from the study. 15/48 (31.3%) of patients with hypermobility and back pain (but no clinical picture of SpA) were found to have inflammatory and/or structural lesions on MRI SIJ. The most frequent lesions were small foci of bone marrow oedema (16.6%) followed by subchondral sclerosis (12.5%) and fatty change (10.4%). The incidence of erosions was 4.2%.
Conclusion: There is a relatively high incidence of inflammatory and structural lesions on MRI SIJ of patients with hypermobility. The presence of hypermobility should be taken into consideration when interpreting MRI changes in patients with suspected SpA. Further research into long-term outcomes of MRI SIJs in patients with hypermobility and back pain is required to establish the clinical significance of these findings.
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THU0493 IMPACT OF AGE, GENDER AND EDUCATION LEVEL ON THE CHOICE OF TREATMENT METHOD FOR BACK PAIN AMONG PEOPLE OVER 50 YEARS OF AGE

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Background: According to data collected by the Statistics Poland in 2014, lower back pain is the second most common complaint reported by people over the age of 60 and occurs in about 40% of them. Another 29% of respondents suffer from pain in other spine sections. Treatment of such a common condition can be a challenge due to the multitude of causes of pain, accompanying diseases and the patient's approach to his own health.
Objectives: The aim of the study was to investigate whether factors such as gender, age, level of education and pain severity affect self-chosen methods of treating back pain.
Methods: A survey was conducted on students of Pomeranian Universities Of The Third Age. There were collected socio-demographic characteristics of the participants, features of back pain and detailed information on analgesic methods, including drugs, ointments, exercises and physiotherapy treatments (laser, cryotherapy, hydromassage, ultrasound, heat treatments and other). The responses of participants over the age of 50 were included in the analysis. The answers were divided into groups by age (younger - 50–69 years and older - over 70 years), sex, level of education (lower, medium and higher) and intensity of pain assessed on the VAS scale (<6 and ≥6). The collected data were compared in these groups.
Results: 546 answers were received. 291 respondents were 50-69 years old, 255 aged 70-90 and more, 86% (471) of participants were women. 43% of respondents had secondary education and the same number had higher education. Over 90% (494) declared that they have suffered from back pain. Most of them described pain as chronic (56%), the median pain intensity assessed on the VAS scale was 6 [1-10], and the mean pain intensity was 5.89 ± 1.79. 82.6% of respondents declared doing physical exercises to relieve back pain, 75.9% were using physiotherapy, 60.7% were taking analgesic drugs and 54.3% were using ointments, gels, patches and other local analgesic methods. The higher pain severity was observed in group of females (5.74 vs. 5.61, p=0.002) and people with lower education level (6.52) than in other groups (5.89 and 5.68, p=0.005). Analgesic drugs were taken more often by younger people (66.9% vs. 53.7%, p=0.003), women (62.5% vs. 49.2%, p=0.042), people of lower education level group (80.6% vs. 62.2% secondary education group vs. 52.5% higher education group, p<0.001) and by people with pain severity ≥6 (81.5% vs. 68.9%, p<0.001). Analgesic gels, ointments, patches and other pharmaceuticals were used more often only in group with higher pain severity (62.9% vs. 43.4%, p<0.001). Performing exercises to relieve pain was more often declared by women (84.4% vs. 70.8%, p=0.003) and people with higher education (85.1% vs. 81.3% secondary education group vs. 79.1% lower education group, p<0.001). The study showed that only in groups with varying intensity of pain there was a significant difference in the frequency of using physiotherapy treatments - 68.9% in group with pain severity <6 vs. 81.5% with pain severity ≥6 (p<0.001).
Conclusion: 1. The severity of pain has the greatest impact on the choice of back pain relief method, but this is not the only important factor.
2. People with lower levels of education and men less often perform physical exercises for treatment regardless of the severity of back pain.
3. In the treatment of back pain, attention should be given to recommending the patient an appropriate analgesic method, which will be easily used and more effective.
References:
Population aged 60+. Demographic structure and health. 2016. Statistics Poland.
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THU0494 BACK PAIN, SPINE OSTEOARTHRITIS AND 'CANDIDATE GENES' POLYMORPHISM

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Background: Low back pain (LBP) and spine osteoarthritis are among the leading health-related causes of disability and reduction in patient quality of life. More recent work suggested that the factors that lead to disc degeneration may have important genetic components. Genetic predisposition has been confirmed by recent findings of associations between degeneration and gene polymorphisms of matrix macromolecules.
Objectives: Evaluation of genetic polymorphisms of genes collagen 1A1 (COL1A1), interleikin 1β (IL-1β), interleikin 6 (IL-6), vitamin D receptor (VDR) in patients with LBP, associated with spine osteoarthritis.
Methods: We examined 33 patients (men-17, women-16, middle age 28, 7±3,77) with LBP end onset, verified by magnetic resonance imaging (MRI) and 15 controls was carried out. Assessed the intensity of pain syndrome on visual analog scale (VAS, mm) and the nature of its current (IASP, 1994). Polymerase chain reaction and restriction fragments length polymorphism was used to detect the polymorphism of COL1A1 (rs 1800012), IL-1 (rs 1143627), IL-6 (rs 1800795), VDR (rs 1544410).
Results: The severity of the pain (VAS) average was 60 mm, all the patients revealed chronic option currents pain syndrome. In 86 % of patients detected changes disc in the form of protrusions and hernias, 17 % of patients had a characteristic reducing the height of the intervertebral disc of lower height disc and osteophytes, arthritis facet joints identified in 20 % of patients in 34% of patients diagnosed changes type Modic II. In 83% of patients with LBP identified homozygous variant allele (GG) Col1A1 gene. The absence of T-alleles in the gene IL 1β in the group of patients was associated with severity of the disease. Carriage of allele in heterozygous AG found in 54% of patients of the main group and was not observed in the control that requires further accumulation of facts. Identified association GG-genotype of IL-6 clinical and instrumental signs of the syndrome Modic-II.
Conclusion: These findings may be the reason for the patient-specific approach to diagnosing and treatment of back pain. It proves the necessity of research of genetic polymorphisms in patients with spine osteoarthritis.
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THURSDAY, 04 JUNE 2020

Basic and translational science in paediatric rheumatology

THU0495 NOVEL UNDERSTANDING OF THE PATHOGENESIS OF JUVENILE IDIOPATHIC ARTHRITIS: FOCUS ON MESENCHYMAL STEM CELLS IMPAIRMENT, SENESCENCE AND IMMUNOREGULATORY FUNCTION

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Background: Juvenile idiopathic arthritis (JIA) is a well-known chronic rheumatic disease of childhood characterised by progressive joint destruction and severe systemic complications.
Immune cells are known to trigger the pathophysiological cascade in JIA, but there is little information regarding the contribution made by Mesenchymal stem cells (MSCs). These cells are able to modulate the immune response and decrease the level of pro-inflammatory cytokines. With addition of regenerative property it makes MSCs potential candidates for clinical application as immunosuppressants in treatment of autoimmune diseases.
Objectives: To investigate MSCs proliferation, viability and immunomodulatory function in JIA and healthy children.
Methods: MSCs were separated from peripheral blood (PB) and synovial fluid (SF) of JIA patients and healthy controls. Cell proliferation rate was counted by Population doublings per day (PDD) during 9 days, in the last of which alamarBlue™ assays were performed to assess cell viability. Due to measure senescence MSCs were stained with SA-β-galactosidase. Immunofluorescence was used to examine the expression of p16, p21, p53. Oxidative stress was measured with DCFH-DA. Cell cycle analysis was evaluated with Propidium Iodide and analysed by Accuri® C6 Flow Cytometer.
Commercially-available bone marrow mesenchymal stem cells (BM-MSCs) were treated with graded concentrations of pro-inflammatory cytokines (0.1-100 ng/ml) with following examination of cell viability. Mixed lymphocyte reactions (MLR) were performed to measure MSC immunomodulatory ability *in vitro*.
Results: The growth kinetics of JIA-MSCs were different from healthy controls. JIA-MSCs divided slowly and appeared disorganised with large cytoplasm and loads of outgrowth. They demonstrated a decrease in cell proliferation (negative PDD) and metabolic activity. Difference in growth kinetics and metabolic activity were found inside the JIA PB group with some evidence of response following biological treatment. Thus, PB-MSCs from patients treated with TNFi and anti-IL6 medications had notably higher cell proliferation and metabolic activity against JIA patients received other therapy. Considering this difference, it was hypothesised that cytokines obtained in a high amount in PB and SF of JIA patients may influence MSCs viability. To prove this BM-MSCs were treated with cytokines and demonstrated a dose-dependent decrease in metabolic activity significantly after TNFα and IL1, no significantly after treatment with IL6. Both BM-MSCs treated with cytokines and JIA-MSCs displayed high level of reactive oxygen species.
Cell cycle analysis revealed that JIA-MSCs were arrested in G0/G1 phase with low number of mitotic cells. In addition, the number of senescence-associated SA-β-gal-positive cells was notably higher in JIA-MSCs. Furthermore, JIA-MSCs expressed high level of immunofluorescence for p16, p21 and p53 which played an important role in regulating the senescence progress of MSCs.
Results of MLR showed the ability of BM-MSCs to decrease the percentage of activated T-helpers, T-suppressors, B-cells and natural killers proliferation, while JIA-MSCs lost this property.
Conclusion: Taken together current research has demonstrated that under the influence of proinflammatory cytokines JIA-MSCs suffered from oxidative stress and disruption of metabolic activity acquire senescent morphology, shorten of telomere length, arrest in G0 phase of cell cycle and finally loss of immune regulation. We are continuing our research to determine the mechanisms that are responsible for the impaired phenotype with the aim of identifying new therapeutic strategies for the treatment of JIA.
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THU0496 APPLICATION OF SYSTEMS BIOLOGY-BASED IN SILICO TOOLS TO OPTIMIZE TREATMENT STRATEGY IN STILL'S DISEASE

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Background: Systemic Juvenile Idiopathic Arthritis (sJIA) and Adult Onset Still's Disease (AOSD) are manifestations of an autoinflammatory disorder with complex pathophysiology and significant morbidity, together also termed Still's disease.
Objectives: To investigate the optimal treat-to-target strategy for Still's disease by in silico models based on systems biology.
Methods: Molecular characteristics of Still's disease and data on biological inhibitors of interleukin (IL)-1 (anakinra, canakinumab), IL-6 (tocilizumab, sarilumab), glucocorticoids as well as conventional disease-modifying anti-rheumatic drugs (DMARDs, methotrexate) were used to construct in silico mechanisms of action (MoA) models by means of Therapeutic Performance Mapping System technology (TPMS). TPMS combines artificial neuronal networks (ANN), sampling-based methods and artificial intelligence. The models were validated with publicly available expression data from sJIA patients (Fig.1).

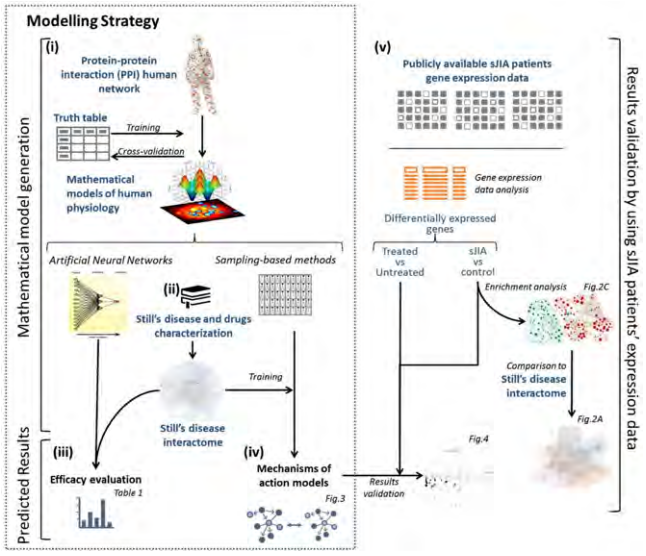


Figure 1. Schematic TPMS approach used to evaluate the Still's disease treatments efficacy and their MoA

Results: Biologicals demonstrated more pathophysiology-directed efficiency than non-biological drugs. IL-1 blockade mainly acts on the innate immune system, while IL-6 signaling blockade has a weaker activity on the innate immunity and rather affects the adaptive immunity (Table 1). The MoA models showed that the IL-1β inhibitor canakinumab is more efficient than the IL-6 receptor inhibiting antibody tocilizumab in the autoinflammatory/systemic phases of Still's disease. MoA models reproduced 67% of the information obtained from expression data (Fig.2).

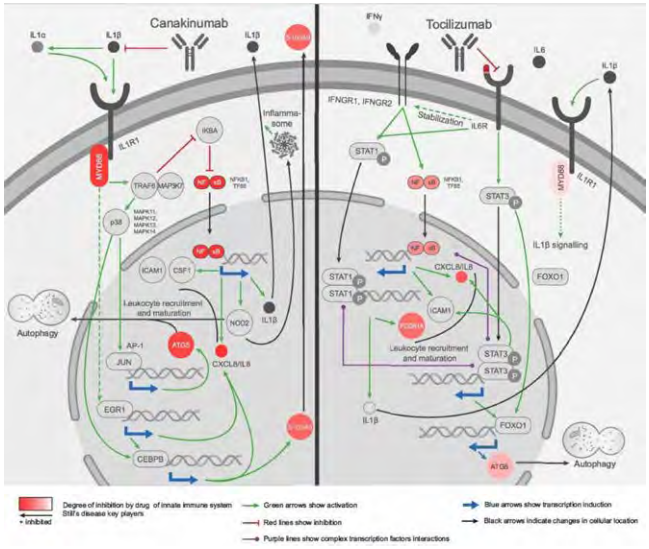


Figure 2. Systems biology-based MoA models of canakinumab and tocilizumab focused on innate immune system modulation. Canakinumab preferably modulates NF-κB, IL-8 (CXCL8), MyD88, S100A9 and ATG5, which are involved in processes of general innate immune inflammation, neutrophil recruitment, activation and autophagy, whereas tocilizumab preferably modulates FCGR1, which is involved in neutrophil activation

Conclusion: Systems biology-based modelling supported the preferred use of biologics as immunomodulatory treatment strategy for Still's disease. This further encourages early IL-1β blockade in initial autoinflammatory/systemic phases of Still's Disease to prevent the development of disease or drug-related complications. Further studies are needed to determine the optimal timeframe of the window of opportunity for canakinumab treatment.

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THURSDAY, 04 JUNE 2020

Paediatric rheumatology

THU0497

MAINTENANCE OF MINIMAL DISEASE ACTIVITY OR INACTIVE DISEASE STATUS AND PATIENT-REPORTED OUTCOMES IN INDIVIDUAL PAEDIATRIC PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS TREATED WITH SUBCUTANEOUS ABATACEPT

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Background: Maintenance of clinical response over time has been shown in individual patients (pts) with polyarticular-course juvenile idiopathic arthritis (pJIA) treated with SC abatacept (ABA).[1] It is unknown whether each individual pt with sustained efficacy also consistently maintains the previously reported shorter-term benefits on patient-reported outcomes (PROs)[2,3] over time.
Objectives: Investigate whether combined efficacy and stringent, optimal PRO responses to ABA treatment are maintained by individual pts with pJIA over time.
Methods: In this analysis of the intent-to-treat population, pts in two age cohorts (2–5 and 6–17 yrs) who achieved clinical response to weekly SC ABA (10–<25 kg [50 mg], 25–<50 kg [87.5 mg], ≥50 kg [125 mg]) at Mo 4 (time point of primary pharmacokinetic endpoint[4]) were followed for 2 yrs. Stringent efficacy outcomes (Juvenile Arthritis Disease Activity Score 27 [JADAS27] minimal disease activity [MDA; ≤3.8] and inactive disease [ID; ≤1] status) were combined with optimal PRO endpoints (childhood [C]HAQ-DI=0, Parental Global Assessment [PaGA] ≤1 and Pain visual analogue scale [VAS] <35). Combined efficacy and PRO responses were analysed at Mos 4, 13 and 21.
Results: 219 pts entered the study (46 [21.0%] 2–5 yrs; 173 [79.0%] 6–17 yrs); a subgroup of these pts achieved a clinical response at Mo 4 (Table 1). Many pts who achieved JADAS27 MDA or JADAS27 ID combined with optimal PROs at Mo 4 sustained their response at Mo 13, and at both Mo 13 and Mo 21 in the 2–5-yr and 6–17-yr cohorts (Table 1). Across the cohorts, 33–88% of pts maintained a combined JADAS27 MDA with optimal PRO responses through Mo 21. Where estimable, median times to combined efficacy and specific optimal PRO responses were consistent across the cohorts (Table 2; Figs 1, 2).

Table 1. Proportion of pts with combined efficacy and optimal PRO responses at Mos 4, 13 and 21

Endpoint	Responders at Mo 4		Responders at Mos 4 and 13*		Responders at Mos 4, 13 and 21*	
	2–5 yrs (n=46)	6–17 yrs (n=173)	2–5 yrs	6–17 yrs	2–5 yrs	6–17 yrs
JADAS27 MDA and CHAQ-DI=0	9 (20)	34 (20)	5/9 (56)	25/34 (74)	3/9 (33)	16/34 (47)
JADAS27 MDA and PaGA ≤1	8 (17)	14 (8)	8/8 (100)	7/14 (50)	7/8 (88)	5/14 (36)
JADAS27 MDA and Pain VAS <35 mm	28 (61)	70 (41)	25/28 (89)	58/70 (83)	21/28 (75)	43/70 (61)
JADAS27 ID and CHAQ-DI=0	7 (15)	20 (12)	2/7 (29)	13/20 (65)	1/7 (14)	9/20 (45)
JADAS27 ID and PaGA ≤1	6 (13)	10 (6)	4/6 (67)	4/10 (40)	4/6 (67)	4/10 (40)
JADAS27 ID and Pain VAS <35 mm	17 (37)	31 (18)	10/17 (59)	22/31 (71)	8/17 (47)	17/31 (55)

Data are n (%) or n/N (%). *% based on n of pts who achieved response at Mo 4 (denominator)

Table 2. Kaplan–Meier estimates for median (95% CI) times (mos) to achieving combined efficacy and optimal PRO responses

Endpoint	2–5 yrs	6–17 yrs
JADAS27 MDA and CHAQ-DI=0	21.5 (6.8, NE)	21.5 (13.1, 24.4)
JADAS27 MDA and PaGA ≤1	NE (15.9, NE)	24.6 (24.3, NE)
JADAS27 MDA and Pain VAS <35 mm	2.8 (1.9, 2.9)	3.8 (3.7, 6.6)
JADAS27 ID and CHAQ-DI=0	NE (18.4, NE)	24.4 (18.7, NE)
JADAS27 ID and PaGA ≤1	NE (21.3, NE)	24.6 (24.3, NE)
JADAS27 ID and Pain VAS <35 mm	3.8 (3.8, 10.3)	13.2 (10.3, 15.9)

NE=not estimable

Conclusion: Many individuals with pJIA who achieved stringent efficacy and PRO measures with weekly SC abatacept by Mo 4 sustained them over 2 years. Time to achieve combined efficacy and Pain VAS <35 response was shorter than that for PaGA ≤1 and CHAQ-DI=0.

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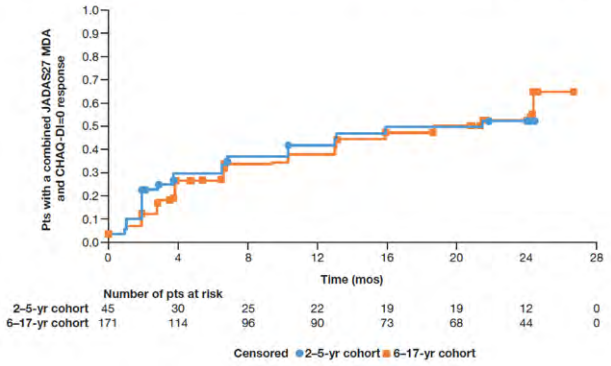
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Table 1. Summary of ANN scores. A) Global Still's disease evaluation. B) Immune system component. ANN scores mean the probability of the resulted relationship is true positive: +++ correspond to values >78% (p-value<0.05); ++ correspond to values > 59% (p-values<0.15) and; + correspond to values > 38% (p-value<0.25)

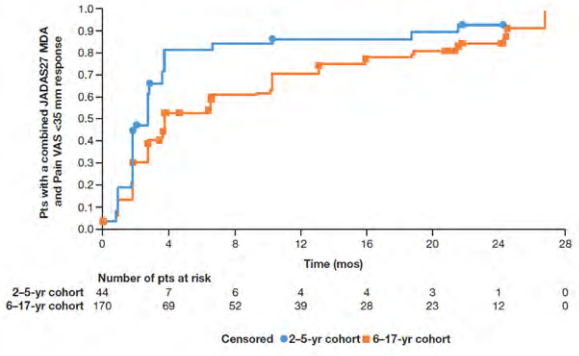
A) Still's disease molecular definition		Biologics				Non-biologics	
		Anakinra	Canakinumab	Sarilumab	Tocilizumab	Methotrexate	Prednisone
Still's disease		+++ (81%)	+++ (86%)	+++ (85%)	+++ (85%)	- (5%)	++ (70%)
Systemic profile		+++ (80%)	+++ (88%)	+++ (85%)	+++ (85%)	- (4%)	++ (70%)
Rheumatic profile		+++ (87%)	+++ (92%)	+++ (81%)	+++ (81%)	- (9%)	++ (64%)
B) Immune system components		Biologics				Non-biologics	
		Anakinra	Canakinumab	Sarilumab	Tocilizumab	Methotrexate	Prednisone
Innate immune system deregulation		++ (71%)	++ (71%)	+ (55%)	+ (55%)	- (10%)	++ (65%)
Adaptive immune system	T-cell response activation	+ (45%)	- (37%)	++ (71%)	++ (71%)	- (25%)	+ (47%)
	Defective immune regulation	- (19%)	- (37%)	+ (47%)	+ (47%)	- (15%)	+ (50%)

Figure 1. Kaplan–Meier Estimates of a Combined JADAS27 MDA and CHAQ-DI=0 Response by Age Cohort



Number of pts with the event of this combined response at baseline: 1
Pts without combined JADAS27 MDA and CHAQ-DI=0 response were censored at the date of the last combined JADAS27 MDA and CHAQ-DI=0 response assessment
N at Mo 0 is number of treated pts with combined JADAS27 MDA and CHAQ-DI=0 response assessments at Day 1
Pts who had the event of this combined response at baseline were excluded from the analysis
CHAQ-DI=Childhood HAQ-DI; JADAS27=Juvenile Arthritis Disease Activity Score 27; MDA=minimal disease activity; pt=patient

Figure 2. Kaplan–Meier Estimates of a Combined JADAS27 MDA and Pain VAS <35 mm Response by Age Cohort



Number of pts with the event of this combined response at baseline: 3
Pts without combined JADAS27 MDA and Pain VAS <35 mm response were censored at the date of the last combined JADAS27 MDA and Pain VAS <35 mm response assessment
N at Mo 0 is number of treated pts with combined JADAS27 MDA and Pain VAS <35 mm response assessments at Day 1
Pts who had the event of this combined response at baseline were excluded from the analysis
JADAS27=Juvenile Arthritis Disease Activity Score 27; MDA=minimal disease activity; pt=patient; VAS=visual analogue scale

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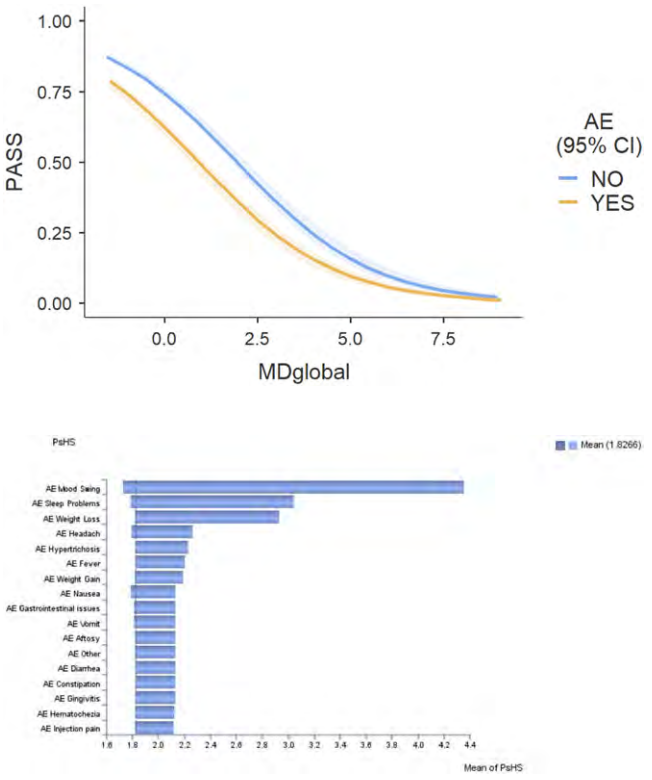
PATIENT-REPORTED TREATMENT BURDEN AND ITS IMPACT ON QUALITY OF LIFE IN JUVENILE IDIOPATHIC ARTHRITIS: RESULTS FROM THE PHARMACHILD REGISTRY

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Background: Juvenile Idiopathic Arthritis (JIA) patients experience impaired health and wellbeing due to multiple causes of physical and psychosocial distress, including treatment burden. Despite emerging evidence of its relevance [1], the contribution of treatment adverse events to patient-reported outcomes (PROs) in JIA has been poorly explored.
Objectives: To evaluate and rank the impact of patient-reported adverse events (AEs) on overall wellbeing, health-related quality of life (HRQoL), school problems and self-reported medication adherence using data from Pharmachild, a large international JIA pharmacovigilance registry.
Methods: Registry entries on 5340 prospective visits of 2251 patients enrolled till December 2018 were analyzed; all included patients were treated with at least one DMARDS or Biologic agent at the time of visit. In the Juvenile Arthritis Multidimensional Assessment Report (JAMAR), patients and parents compiled a checklist of treatments, side effects, self-reported adherence, administration difficulties and disease-related school problems occurred in the previous 4 weeks. Evaluated outcomes included patient acceptable symptom state (PASS), VAS-measured patient assessment of overall wellbeing (PGA) and HRQoL, assessed through the physical health (PhH) and psychosocial health (PsH) subscales. The relationships between AEs and PROs were tested through generalized linear models, accounting for disease activity and symptoms levels. Bayesian Networks were used to explore the causal effects of specific AEs on outcomes to disentangle the confounding role of disease status.
Results: AEs were reported in 22.9% of visits. For similar levels of physician global assessment (MD global), patient-assessed disease activity, pain and function, patients reporting AEs had worse PGA, PsH, and lower probability of reaching PASS (fig. 1, all p-values <0.001). The impact of AEs on PGA was small but not trivial (effect size η^2 0.031) and appears to be mediated by effects on PsH and school problems (p <0.001). Non-linear regression modelling revealed a significant moderating effect of MD global levels < 2.5 on the relationship between AEs and PGA (p 0.003), indicating that the impact of AEs is higher for lower disease activity states. AEs predicted self-reported medication adherence (p<0.001), even when adjusted for the number of administered treatments. In the Bayesian network model, mood swing and sleep problems emerged as the most influential items affecting PsH, (respectively, total effect 2.62 and 1.25, both p< 0.001). Fig. 2 shows the total standardized effect of specific AEs on mean PsH levels. Nausea had the highest impact on treatment adherence (total effect -0.0541, p <0.001), being the only AE directly linked to drug refusal.
Conclusion: AEs have a measurable effect on the wellbeing and psychosocial health of JIA patients, particularly when disease activity is low, and significantly affect school activity and medication adherence. Mood swings and sleep problems show the strongest influence on HRQoL. Addressing AEs appears important to reduce disease impact, improve patients' satisfaction and therapeutic compliance.

References: :

[1] Weitzman, Elissa R., et al. Journal of patient-reported outcomes 2.1 (2018): 1.



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THU0499 IS THERE A DIFFERENT PRESENTATION OF JUVENILE SYSTEMIC DIFFUSE AND LIMITED SUBSET? DATA FROM THE JUVENILE SCLERODERMA INCEPTION COHORT. WWW.JUVENILE-SCLEORDERMA.COM

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Background: Juvenile systemic scleroderma (jSSc) is an orphan disease with a prevalence of 3 per 1 000 000 children. There are limited data regarding the clinical presentation of jSSc. The Juvenile Systemic Scleroderma Inception Cohort (JSSIC) is the largest multinational registry that prospectively collects information about jSSc patients.

Objectives: Evaluation of the jSSc patients at the time of inclusion in the JSSIC.

Methods: Patients were included in the JSSIC if they fulfilled the adult ACR/EULAR classification criteria for systemic scleroderma, if they presented the first non-Raynaud symptom before 16 years of age and if they were younger than 18 years of age at time of inclusion. Patients' characteristics at time of inclusion were evaluated.

Results: Until 15th of December 2019 hundred fifty patients were included, 83% of them being Caucasian and 80% female. The majority had the diffuse subtype (72%) and 17% of all jSSc had overlap features. The mean age of first presentation of Raynaud´s phenomenon was 9.8 years in the diffuse subtype (djSSc) and 10.7 years in the limited subtype (ljSSc) (p=.197). The mean age at first non-Raynaud's symptoms was 10.0 years in the djSSc and 11.2 years in the ljSSc (p=0.247). Mean disease duration at time of inclusion was 3.4 years in the djSSc and 2.4 years in the ljSSc group.

Significant differences were found between the groups regarding mean modified Rodnan skin score, 18.2 in the djSSc vs 6.2 in the ljSSc (p=0.02); presence of Gottron´s papulae (djSSc 30% vs ljSSc 13%, p=0.43);presence of teleangiectasia (djSSc 42% vs 18% ljSS, p=0.01); history of ulceration (djSSc 42% vs 18% ljSSc,p=0.008); 6 Minute walk test below the 10th percentile (djSSc 85% vs ljSSc 54%, p=0.044), total pulmonary involvement (djSSc 49% vs ljSSc 31%, p=0.045), cardiac involvement (ljSSc 17% vs djSSc 3%, p=0.002). djSSc patients had significantly worse scores for Physician Global Assessment of disease activity compared to ljSSc patients (VAS 0-100) (40 vs 15) (p=0.001) and for Physician Global Assessment of disease damage (VAS 0-100) (36 vs 17) (p=0.001).

There were no statistically significant differences in the other presentations. Pulmonary hypertension occurred in approximately 6% in both groups. No systemic hypertension or renal crisis was reported. ANA positivity was 90% in both groups. Anti-Scl70 was positive in 35% in djSSc and 36% in the ljSSc group. Anticentromere positivity occurred in 3% in the djSSc and 7% in the ljSSc group.

Conclusion: In this unique large cohort of jSSc patients there were significant differences between djSSc and ljSSc patients at time of inclusion into the cohort regarding skin, vascular, pulmonary and cardiac involvement. According to the physician global scores the djSSc patients had a significantly more severe disease. Interestingly the antibody profile was similar in both scleroderma phenotypes.

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THU0500

PHYSICAL ACTIVITY AND SCREEN-BASED MEDIA USE IN ADOLESCENTS WITH JUVENILE IDIOPATHIC ARTHRITIS - DATA FROM A GERMAN INCEPTION COHORT

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Background: Insufficient physical activity (PA) and screen-based media use (SBM) are different aspects of sedentary behavior (SB), independently and inversely related to health and wellbeing. Recent research indicates that adolescents with chronic conditions are at least as likely at risk of being physically inactive or accumulating high levels of screen-based SB when compared with their healthy peers [1].
Objectives: Since PA and SBM have not yet been (sufficiently) evaluated in young patients with juvenile idiopathic arthritis (JIA), our aim was to i) quantify the daily SBM use of adolescents with JIA, ii) measure the frequency of their weekly PA, and iii) compare both aspects of SB with those of age- and sex-matched controls from the general population during the course of the disease.
Methods: Data from JIA patients and controls enrolled in the inception cohort study ICON were analyzed. Young people, such as friends and mates, served as the peer group. Patients and peers aged 13 and over were followed prospectively and questioned about their weekly PA frequency and SBM use at a two-year interval. Data from young people for whom at least two questionnaires were available were analyzed using linear mixed models.
Results: Data from 209 patients with JIA (63% female, 28% rheumatoid factor negative polyarthritis) and 138 peers (55% female) were included in the analysis. At baseline (T1), 51% of the patients were treated with a DMARD, 58% at follow-up (T2). The proportion of adolescents being physically active at most twice a week was substantially higher in patients than in controls (T1: 59% vs. 43%; T2: 54% vs. 42%). In patients, the total daily screen time was 3.5±2.6 hours at T1 and 3.6±2.5h at T2, respectively. In comparison, a value about 0.5h less was found in the controls both at T1 and T2. Both groups increasingly spent time on mobile phones during the observation period. At T1 (66% vs. 45%) and T2 (60% vs. 45%), the proportion of physically inactive girls was significantly higher than that of boys. Conversely, boys reported higher levels of SBM than girls. Patients with high SBM consumption (>3h/day) showed a significantly lower PedsQLTM psychosocial functioning (OR 0.94; 95%CI: 0.89-0.99) and a significantly higher cJADAS-10 score (OR 1.34; 95%CI: 1.07-1.67) than those who did not exceed the national recommendations on SBM use.

Sedentary behaviors	Baseline		2-year follow-up	
	JIA N=209 (%)	CG N=138 (%)	JIA N=209 (%)	CG N=138 (%)
TV/videos				
At most 2h/day	85.4	89.0	86.2	93.4
At least 3h/day	14.6	11.0	13.7	6.6
Computer/Internet				
At most 2h/day	76.9	83.1	72.1	74.6
At least 3h/day	23.0	16.9	27.8	25.4
Gaming consoles				
At most 2h/day	93.5	98.5	92.5	96.2
At least 3h/day	6.5	1.5	7.5	3.8
Total screen time				
At most 2h/day	40.0	45.1	41.5	39.5
At least 5h/day	26.2	15.8	31.3	20.9
Physical activity frequency				
At most 2 times/week	58.9	43.4	54.4	42.3
At least 3 times/week	41.1	56.6	45.6	57.7

Conclusion: Although adolescents with JIA tend to become more physically active during the course of disease, on average they remain more inactive and spend significantly more time on SBM than their peers. Given that high SBM use was associated with lower self-reported psychosocial quality of life and higher disease activity, it is important to develop sustainable and effective interventions to reduce sedentary behaviors in this population.

References:
[1] Elmesmari R et al. Accelerometer measured levels of moderate-to-vigorous intensity physical activity and sedentary time in children and adolescents with chronic disease: A systematic review and meta-analysis. PLoS One 2017;12:e0179429.

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THU0501 EARLY DIAGNOSIS OF THE AUTOIMMUNE LYMPHOPROLIFERATIVE SYNDROME (ALPS) IN PATIENTS WITH UNDEFINED AUTOINFLAMMATORY OR AUTOIMMUNE DISORDERS: THE PRACTICAL ROLE OF A FLOW CYTOMETRY PANEL

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Background: ALPS is a rare disorder due to a defective apoptotic mechanism leading to abnormal lymphoproliferation and autoimmunity. The disease is difficult to identify in the early phase when it may be misdiagnosed. Elevated TCR alpha-beta CD4-CD8- lymphocytes (double negative T lymphocytes DNT) together with hyperIgG, high levels of IL10, Il18, vitamin B12 and soluble Fas ligand have been suggested as the main ALPS hallmarks (1). Therefore, a specific flow cytometry panel (DNT cells, ratio of CD25+CD3+ to HLA–DR+CD3+ cells, increased B220+ T-cells, and decreased CD27+ memory B cells) has been proposed to serve as a diagnostic screen for ALPS (2).

Objectives: To evaluate the usefulness of a specific lymphocyte flow cytometry panel in the early identification of ALPS/ALPS-like disorders in a cohort of patients with undefined autoinflammatory or autoimmune disorders.

Methods: The clinical data of patients referred to the pediatric Rheumatology Unit of the Istituto Giannina Gaslini Hospital for a suspicion of autoimmune or autoinflammatory condition from October 2015 to April 2018, were retrospectively analyzed. Data on clinical manifestations, laboratory workup, genetic analysis and treatment were collected. Flow cytometry was included among the screening panel: DNT, CD25+CD3+, HLA–DR+CD3+ cells, B220+ T-cells, and CD27+ memory B cells were included. A statistical analysis was performed: data were analyzed with an univariate logistic regression analysis, to identify the most significant variables associated with ALPS. These variables were then included in a multivariate analysis to select a set of clinical and laboratory parameters, each of them associated with a significant probability to be associated with ALPS independently from other variables.

Results: 475 patients were retrospectively analized. 211 patients not fulfilling the inclusion criteria were excluded. The patients were classified as follows: i) Autoimmune disease 26 pts (10 SLE; 3 MCTD; 6 jDM; 5 Behçet; 1 SjS; 1 Kawasaki) ii) Juvenile Idiopathic Arthritis 35 pts iii) Monogenic systemic autoinflammatory disease (MSAID) 27 pts (17 FMF; 3 MKD; 1 TRAPS; 4 DADA2; 2 SAVI) iv) PFAPA 100 pts v) Systemic Undefined Recurrent Fever 45 pts vi) Undetermined-SAID 15 pts vii) ALPS/ ALPS probable 16 pts. The flow cytometry panel showed, as expected, an elevation of DNT in all ALPS patients. Among the other parameters, CD3CD25+/CD3HLADR+, and B220+ T cells, were significatively altered in 75% of ALPS patients. Conversely, B CD27+ did not differentiate ALPS from the other subgroups. The multivariate analysis revealed 5 clinical/laboratory parameters that showed the higher independent association to ALPS in the cohort of patients. Splenomegaly, female gender, elevated DNT, arthralgia and elevated alfabeta+B220+ lymphocytes were positively and significantly associated to ALPS.

Conclusion: The use of the specific flow cytometry panel, comprehensive of DNT, B220+, HLA-DR and CD25, in patients with undefined autoinflammatory or autoimmune disorders may identify a subgroup of patients with ALPS.

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[1] Joao B. Oliveira et al. Blood 2010; 116 (14): e35–e40.

[2] Lenardo MJ et al. *Immunity*. 2010;32(3):291–295.

Disclosure of Interests: Caterina Matucci Cerinic: None declared, Leonardo Oliveira Mendonca: None declared, maurizio miano: None declared, paola terrnaova: None declared, federica casabona: None declared, Marta Bustaffa: None declared, Francesca Bovis: None declared, Roberta Caorsi: None declared, Stefano Volpi: None declared, Angelo Ravelli: None declared, Carlo Dufour: None declared, Marco Gattorno Consultant of: Sobi, Novartis, Speakers bureau: Sobi, Novartis

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THU0502 EFFICACY AND SAFETY OF SECUKINUMAB TREATMENT IN JUVENILE IDIOPATHIC ARTHRITIS PATIENTS

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Background: Anti-IL-17A biologic drug secukinumab (SEC) proved to be effective for treatment of psoriatic arthritis. However data about its efficacy in juvenile idiopathic arthritis (JIA) are restricted to off-label experience.

Objectives: To evaluate the effectiveness and safety of SEC in JIA patients in the National Medical Research Center of Children`s health, Moscow, Russia.

Methods: 25 patients started SEC therapy from 12/2017 to 11/2019 in single-center prospective study. 3 patients withdrew treatment: two patients (8%) due to AE (1 - allergy followed by MAS after first injection and 1 – leukopenia) and one patient (4%) – after 10 months of treatment due to secondary inefficacy. Among others, 14 patients which were successfully treated for 6 months or longer were included into analysis. At the baseline, information was collected on the characteristics of the onset of the disease, previous therapy and its success. Patients were monitored at least 1 time per year. At each visit, clinical and laboratory characteristics of JIA severity were assessed. Response to therapy was assessed using the ACRPedi 30/50/70/90 criteria, the C.Wallace criteria for inactive disease (WID) and clinical remission. AEs were assessed at each visit.

Results: Among 14 patients received SEC for at least 6 months, 7 (50%) have enthesitis-related arthritis, one (7.1%) – persistent oligoarthritis, 4 (28.6%) – RF-negative polyarthritis, 2 (14.3%) – psoriatic arthritis. 6 patients (42.9%) were HLA-B27 positive. Median age of JIA onset was 8.8 (IQR 5:11), age at SEC initiation – 14 (9.9:16.1), disease duration before SEC start – 3.3 (2.7:5.8). 7 (50%) were biologics-naïve, 2 (14.3%) were previously treated with anti-TNF drug, 5 (35.7%) have 2 or more different biologics in anamnesis.

SEC demonstrated high efficacy after the first injection resulting in JADAS-71 decreasing in all patients by median 4.3 (1.6:7.1) points and 7/7/5/2 patients (50%/50%/35.7%/14.3%) achieved ACR Pedi 30/50/70/90 response.

After 6 months of treatment, WID was achieved by 7 (50%) patients, JADAS-71 decreased from baseline level 15.2 (12.7:20.5) to 0.8 (0:4.2) points, and 14/13/11/9 patients (100%/92.9%/78.6%/64.3%) achieved ACR Pedi 30/50/70/90 response. One patients who had active uveitis at SEC initiation remained with subactive uveitis; one patient with uveitis remission had not flare episodes during follow-up period. One patient (7.1%) had successfully treated evaluation of transaminases after 4-th injection.

Conclusion: Secukinumab showed high effectiveness and safety in children with JIA and can be further used both as a first-line drug in JIA associated with HLA-B27, and as an alternative drug for the ineffectiveness of the standard treatment regimen with biologics. No serious adverse events were registered during follow-up period.

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THU0503 PLUTO TRIAL: SENSITIVITY ANALYSES OF SRI4 RESPONSE WITH BELIMUMAB VS PLACEBO IN PAEDIATRIC PATIENTS WITH CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS (CSLE)

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Background: Belimumab (BEL) is the first treatment approved in children ≥5 years of age with cSLE. This recent approval was based on favourable results of the PLUTO trial, evaluating efficacy and safety of intravenous (IV) BEL, plus standard SLE therapy (SST), vs placebo (PBO), in children with cSLE.[1]
Objectives: To evaluate the SLE Responder Index 4 (SRI4) sensitivity of response for the comparison of BEL vs PBO at Week (Wk) 52.
Methods: In PLUTO (NCT01649765; GSK study BEL114055), an ongoing Phase 2, randomised, PBO-controlled, double-blind study, patients (pts) 5–17 years of age with active cSLE were randomised to monthly BEL 10 mg/kg IV, or PBO, plus SST, for 52 weeks. The primary efficacy endpoint was the SRI4 response rate at Wk 52. Pre-specified sensitivity analyses supporting the primary efficacy endpoint for the intention-to-treat (ITT) population included unadjusted, last observation carried forward (LOCF), completer responses, and response using SLE Disease Activity Index (SLEDAI) 2K proteinuria scoring rule (4-point score for proteinuria >0.5 g/24 h), all at Wk 52. Completers were pts who completed 52 weeks of treatment. Any pts who withdrew or received protocol-prohibited medication or a dose of allowable medication that resulted in treatment failure prior to the Wk 52 visit had missing data handled using LOCF (missing values imputed using the last previous non-missing value). Statistics are descriptive.
Results: Overall, 93 pts were randomised (BEL, n=53; PBO, n=40). Majority (94.6%) of pts were female, mean (standard deviation [SD]) age was 14.0 (2.49) years and mean (SD) disease duration was 2.4 (1.93) years. By Wk 52, numerically more BEL (52.8%) than PBO (43.6%) pts were SRI4 responders; difference vs PBO 9.24; odds ratio (OR; 95% confidence interval [CI]) vs PBO 1.49 (0.64, 3.46). For each sensitivity analysis (unadjusted, LOCF, completer, and SLEDAI 2K responses) the odds of being a responder at Wk 52 were higher for pts receiving BEL vs PBO (Table).

Table. Sensitivity analyses: SRI4 response at Wk 52

	PBO (n=40)	BEL (n=53)
Unadjusted response (ITT), n*	39	53
n (%)	17 (43.6)	28 (52.8)
Observed difference vs PBO	9.24	
OR (95% CI)† vs PBO	1.45 (0.63, 3.33)	
LOCF response (ITT), n*	39	53
n (%)	18 (46.2)	30 (56.6)
Observed difference vs PBO	10.45	
OR (95% CI)‡ vs PBO	1.51 (0.65, 3.52)	
Completer response (completers), n*	30	45
n (%)	17 (56.7)	27 (60.0)
Observed difference vs PBO	3.33	
OR (95% CI)‡ vs PBO	1.16 (0.44, 3.09)	
Response using SLEDAI 2K (ITT), n*	39	53
n (%)	17 (43.6)	28 (52.8)
Observed difference vs PBO	9.24	
OR (95% CI)‡ vs PBO	1.49 (0.64, 3.46)	

*One pt was excluded because they did not have a baseline Safety of Estrogens in Lupus National Assessment (SELENA)-SLEDAI assessment; †calculated from a logistic regression model for the comparison between BEL and PBO without adjustment for any covariates; ‡calculated from a logistic regression model for the comparison between BEL and PBO with covariates treatment group, baseline age (5–11 years vs 12–17 years), and baseline SELENA-SLEDAI score (≤12 vs ≥13)

Conclusion: The results of the SRI4 primary efficacy endpoint sensitivity analyses further support a favourable effect for BEL vs PBO.
References:
[1] Brunner HI, *et al*. *Arthritis Rheumatol.* 2018;70(59): 3224–5, Abst. 2867
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THU0504 EARLY JOINT REPLACEMENT IN JIA: TREND OVER TIME AND FACTORS INFLUENCING IMPLANT SURVIVAL

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Background: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic condition in childhood. New therapies acting on specific targets have led to a significant improvement in the management of JIA. However, when medical therapy fails, total joint replacement represents the standard treatment to obtain pain relief and improve functional outcomes.
Objectives: To describe early prosthesis in a JIA cohort followed in a tertiary referral hospital and to analyze any possible factors influencing implant survival, including surgical improvements over time.
Methods: This is a monocentric retrospective cohort study; patients were enrolled from January 1992 to June 2019. All patients who underwent total joint replacement and were followed in our institute were included.
Results: Eighty-five patients met the inclusion criteria, with a median follow-up of 17.2 years. The total number of replaced joints over 27 years was 198 (Figure 1). Clinical features and implant data are reported in Table 1.

Table 1. Patients' clinical features and implants data

Total number of patients/ implants	85/198
JIA categories	16 Oligoarticular 37 Polyyarticular (7 RF postive) 24 Systemic 8 other
Age at first arthroplasty median (mean+SD; range)	22.7 y (25.1±6.9;14.3-46.5)
Disease duration at I arthroplasty median (mean+SD; range)	17.4 y (18.6±8.1;1.88-43.7)
Location of arthroplasty	121 Hips 66 Knees 11 Ankles
Type of arthroplasty	156 Regular 6 Custom 31 Hybrid implant 5 unknown
Arthroplasty complications	8 Intraoperative fracture 3 Infections 14 Aseptic mobilization
Revisions	13 (9 hips, 4 knees)

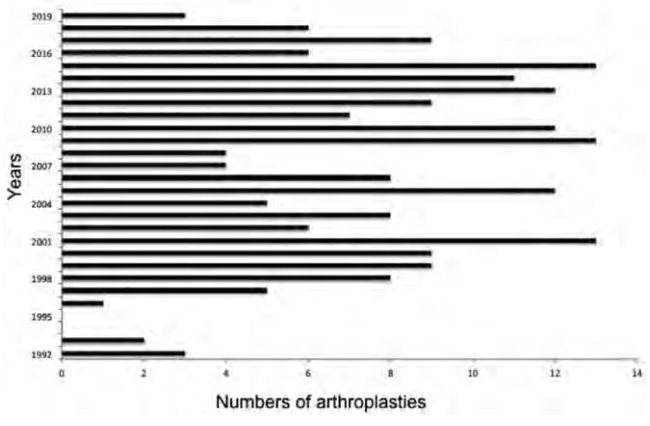


Figure 1. Numbers of arthroplasties performed for each year.

We grouped all arthroplasties by the year of surgical procedure: before 2000 (group A; 28 implants), between 2000 and 2010 (group B; 94 implants) and after 2010 (group C; 76 implants).
A significant difference of age at arthroplasty was found between group A and group B (21.93 y vs 26.82; p = 0.03) and between group A and group C (21.93 y vs 27.81 y; p = 0.00).

The same upward trend was found with regard to disease duration before arthroplasty: a significant difference between group A and group B (16.98 y vs 21.66 y; p = 0.03) and between group A and group C (16.98 y vs 22.93 y; p= 0.00).
The rate of implant survival at 5, 10 and 15 years were comparable (from 84% to 89%); whereas 50% of eligible implants lasted 20 years or more (Figure 2).

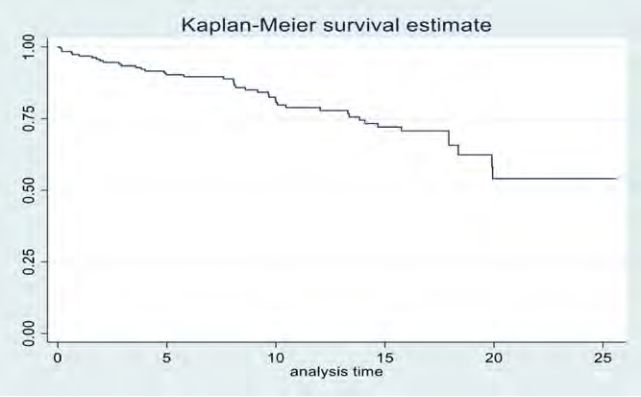


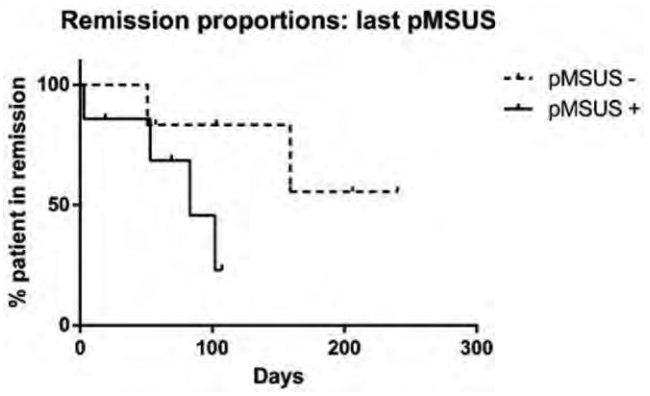
Figure 2. Kaplan Meier survival curve of implants.

The year of surgery was found to be significantly related to implant survival [Hazard Ratio (HR) 1.001, confidence interval (CI) 1.0001-1.0006; p< 0.001] as well as the presence of complications (HR 3.69, CI 1.82-7.48; p < 0.001) in multivariate analysis. Furthermore, prostheses of polyarticular RF-neg patients had more possibilities to last longer than those of S-JIA patients (HR 0.23, CI 0.09-0.53; p= 0.00) as well as implants of all polyarticular JIA (RF-pos and neg together) (p < 0.001).
Conclusion: We observed an upward trend of both age at arthroplasty and disease duration before the first arthroplasty over time. JIA category, year of implants and the presence of complications significantly affected implant survival. Future researches should assess functional outcome and survival of implants according to medical therapy and different surgical approaches.
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THU0505 MUSCULOSKELETAL ULTRASOUND MONITORING DURING MTX TAPERING IN JIA: A PROSPECTIVE BLINDED COHORT STUDY

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Background: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in children. Musculoskeletal ultrasound (MSUS) is a reliable tool in the assessment of chronic inflammatory arthropathies. MSUS in JIA has demonstrated a higher sensitivity for detecting synovitis and tenosynovitis as compared to physical examination. The occurrence of subclinical synovitis (Sub-S: MSUS+/ physical examination -) seems more frequent in wrist and foot joints; the clinical significance of Sub-S in real-life practice is still debated. Methotrexate (MTX) is the most widely used first-line DMARD in JIA therapy. Weekly treatment with MTX leads to clinical remission (CR) in 50-70% of patients. After a variable period of CR (usually 6-18 months), MTX is discontinued. Relapse rate after MTX suspension ranges between 40-50%; no predictors of disease flare have been identified so far.
Objectives: We designed a cohort study in order to explore if MSUS monitoring during MTX tapering was able to predict disease flare.
Methods: JIA patients in CR (as defined by the JADAS score) for at least 12 months were enrolled in the study. Patients at first attempt of suspension (G1) were tapered as follows: 1 week of suspension every 3 weeks for 3 months + 1 dose every 2 weeks for 3 months; if CR persisted, MTX was stopped. Patients who had a previous flare during/after MTX tapering (G2) had a similar tapering schedule but the step with 1 MTX dose every 2 weeks lasted 6 months. All patients underwent a complete MSUS of 48 joints every 3 months; clinicians who performed physical examinations and follow-up were blinded to US findings for the entire study period.
Results: 18 consecutive patients were enrolled between April 2018 and September 2019; patients had prevalently oligoJIA (55.5%) and RF- polyJIA (22.2%). Patients had been treated with MTX for 24.7 months (17.7–48.3), CR had been achieved 4.2 months after MTX start; 61.1% were at their first attempt of MTX tapering (G1). *Baseline MSUS:* at T0 MSUS detected 9/18 patients (50.0%) with Sub-S (MSUS+). Affected sites at T0 were distributed as follows: 4 MCP joints, 9 MTP joints, 1 f-IP joints, 11 knees. No significant differences resulted in comparing demographic and baseline disease features between MSUS- and MSUS+ patients at T0. *Follow-up MSUS*: 14 patients (77.8%) completed the entire study protocol, 4 patients are still ongoing. 7 patients relapsed: 42.9% during tapering, 1 of them relapsed during a VZV infection and was excluded from further analysis. We considered as T_{last}-MSUS the last available MSUS before relapse or final MSUS (i.e. three months after MTX withdrawal) for not-relapsed subjects.
At T_{last} 8 patients had at least 1 Sub-S. Sub-S per patient at T_{last} were more than Sub-S at T0 (2.85 vs 0.53 p=0.03) but the presence of Sub-S was not related with disease flare (50.0 vs 44.4% p=1). MSUS found 27 Sub-S of the small joints (sMSUS): 88.9% were in the feet, they had an OMERACT grading of 1. sMSUS+ patients were older (8.7 vs 3.9, p=0.002) therefore a weight-induced sub-S not related with JIA could be presumed.
Kaplan-Meier curves were analyzed comparing MSUS results at T0 and T_{last}, both considering all Sub-S and excluding small feet joints (pMSUS). The best performance was achieved with MSUS at T_{last} and pMSUS (figure below, p=0.11).



Conclusion: •Sub-S are present in 50% of patients in clinical remission >12 months.
•Sub-S in older patients interest often feet small joints; these Sub-S may be of mechanical origin and are not associated with disease flare.
•Sub-S increase during MTX tapering.
Further patients must be enrolled to understand if Sub-S excluding feet small joints may predict disease flare.
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THU0506 LONG-TERM EFFECTIVENESS AND SAFETY OF CANAKINUMAB AS A SECOND BIOLOGIC AFTER TOCILIZUMAB IN CHILDREN WITH EARLY AND LATE JIA WITH ACTIVE SYSTEMIC FEATURES

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Background: Canakinumab (CAN) is often used as second biologics in juvenile idiopathic arthritis with active systemic features (sJIA). However, there are little information about its long-term efficacy and safety.
Objectives: To evaluate the long-term effectiveness and safety of CAN as a second biologics after tocilizumab (TOC) in sJIA patients depending on the duration of the disease.

Methods: Thirty-one patients were enrolled in this study: the group of early sJIA (with duration shorter than 2 years, 19 patients) and the group of late sJIA (with duration longer than 2 years, 12 patients). At the baseline, information was collected on the characteristics of the onset of the disease, previous therapy and its success. At each visit at least 1 time per year clinical and laboratory characteristics of sJIA severity were assessed. Response to therapy was assessed using the ACRPedi 30/50/70/90 criteria and the C.Wallace criteria for inactive disease (WID) and clinical remission.

Results: The most common reason for withdrawal of previous TOC was secondary ineffectiveness (22 cases, 71%); in 6 cases (19.4%) allergic reaction was observed; in two cases (6.5%) primary non-effectiveness appeared; and in one case (3.2%) there was marked infusion reaction.

At CAN initiation, sJIA activity was as follows: 15 (12: 23) for JADAS-71; 45 (36.5: 72) and 58 (45: 81) for physician's and patient's global assessment VAS; and 0.25 (0: 0.62) for the CHAQ disability index.

After 12-month treatment, 22 (71%) patients reached WID: 21 on CAN therapy and 1 – after CAN withdrawal due to administrative reason and stable WID. ACR50/70/90 response was achieved by 84.2%/84.2%/64.7% patients in early arthritis group and in 83.3%/75%/75% patients in late arthritis group (p=0.792).

However, 42.1% of patients with early sJIA achieved remission in the first 1.5 years without any further relapse during all the studied period and only 16.7% of patients with late arthritis (p=0.239). In multivariable analysis, it was found that age of sJIA onset (OR (2.5-97.5 CI) 0.353 (0.13 - 0.72), p=0.015), number of joints with active arthritis at sJIA onset (2.308 (1.26-5.73), p=0.025), and JADAS-71 at sJIA onset (0.664 (0.44-0.88), p=0.016) were associated with successful treatment with rapid achievement of stable remission.

During the 76.7 patient-years follow-up period, 18 of 31 (58.1%) patients were able to achieve a stable clinical remission and 27 (87.1%) – WID. Two patients have achieved successfully drug-off remission. Serious adverse event (SAE) was reported in one (3.2%) patient (enteritis).

Conclusion: Long-term canakinumab therapy proved to be effective and safe as a second biologics after tocilizumab for any duration of the disease. However, patients with early arthritis are more likely to quickly achieve stable remission without further relapse. Younger onset of sJIA with polyarthritis involvement and low disease activity are predictors of rapid and stable remission.

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THU0507 ASSOCIATION BETWEEN JUVENILE IDIOPATHIC ARTHRITIS AND AUTISM

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Background: Juvenile Idiopathic Arthritis (JIA) is a heterogenous group of autoimmune disorders characterised by chronic joint inflammation, diagnosed in around 1 in 1,000 children and young people (CYP) under the age of 16. Autistic Spectrum Condition (ASC) is a neurodevelopmental condition characterised by differences in social communication and sensory perception, as well as restricted interests and repetitive behaviours. Recent estimates from the Centers for Disease Control and Prevention (CDC) suggest that 1.68% of CYP are diagnosed with ASC, with males being more likely to be diagnosed (sex ratio of 4:1) [1]. The causes of both JIA and ASC are complex interactions between genetic and environmental factors. There appears to be some evidence that ASC may be associated with certain parental autoimmune conditions [2], although research into any association between JIA and ASC is sparse with the exception of a review of clinical database information [3].

Objectives: In this parent-led study, the association between JIA and ASC was explored in order to determine if children with JIA, or children who do not themselves have JIA but have at least one first-degree relative with JIA (FDR), are more likely to be diagnosed with ASC.

Methods: Parents of CYP with JIA were invited to complete an online survey, giving details of each member of their family including diagnosis status for JIA and ASC, and age of diagnoses. A total of 247 responses were collated, representing 558 CYP. Overall, 202 CYP were diagnosed with JIA from 197 families. The eldest child with JIA from each family was selected (total 197; 66 male and 131 female) and the rate of ASC was compared against the general population using Fisher's exact tests.

Results: Children with JIA themselves and FDR children were significantly more likely to be diagnosed with ASC.

Group	Odds Ratio (95% CI)	p-value	
JIA children overall	6.107 (1.760, 21.190)	0.0020	**
FDR children overall	7.009 (2.033, 24.160)	0.0006	***

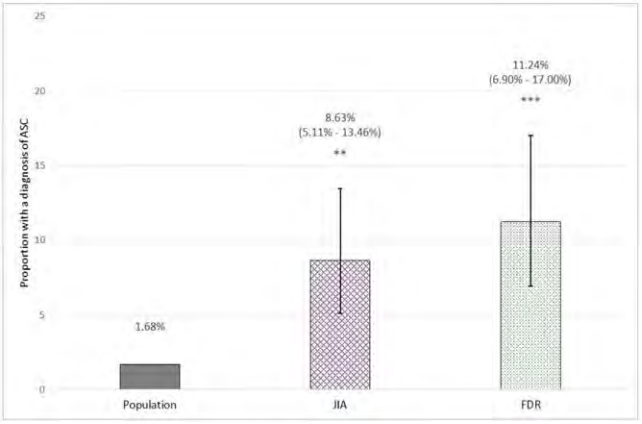


Figure 1. Proportion of children diagnosed with ASC in the general population (CDC estimates), JIA group and FDR group. Error bar indicates 95% CI. Significance indicated compared to population.

Conclusion: Individuals with JIA and family members of individuals with JIA are more likely to be diagnosed with ASC. The results remained unchanged in a sensitivity analysis in which JIA children who had another sibling with JIA were excluded in order to minimise the risk that these results were affected by selecting the eldest child with JIA.

It is possible that we are underestimating the association between JIA and ASC in this study. The majority of children sampled were from the United Kingdom and Ireland; however, we chose to utilise the most recent CDC estimates for ASC prevalence, as the most recent estimates from the UK were from 2006 and longitudinal data suggests that ASC prevalence continues to increase, likely due to changes in diagnostic criteria and improved recognition of the condition. When using the UK prevalence estimates, JIA children and FDR children remain significantly more likely to be diagnosed with ASC than the general population as a whole.

Future research should focus on confirming these findings in larger, population-based samples.

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THU0508 LARGE VESSEL VASCULITIS IN A COHORT OF CHILDREN WITH RESISTANT KAWASAKI DISEASE IN SINGAPORE

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Background: Kawasaki Disease (KD) is one of the most common systemic vasculitidies in children today. IVIG is the mainstay of treatment, however, about 1/5 of patients do not respond resulting in an increased risk of Coronary Artery Abnormalities (CAA) [1].

Objectives: To describe a cohort of infants and young children with resistant Kawasaki Disease (rKD) who were noted to have prolonged difficult courses with resultant CAA and ultimately diagnosed with Aortitis.
Methods: Demographic, clinical manifestations and imaging data were collected from children seen in Rheumatology clinic with a diagnosis of rKD and aortitis. Nonparametric descriptive statistics were used to describe the data.
Results: Between 2010-2018, 63 out of 417 KD referrals were diagnosed with rKD. 7 children had prolonged time to CRP normalisation, prolonged admission or recurrence of symptoms (Table 2). All patients underwent Magnetic Resonance Angiography (MRA) and were found to have evidence of large vessel arteritis consisting of wall irregularity, thickness and contrast enhancement.

Table 1

ID	Age at diagnosis (mo)	Number of clinical KD signs**	BCG site inflammation	Lowest Hemoglobin g/DL	Highest WBC 10 (9)L	#Highest Platelet 10 (9)L	Highest CRP mg/L	Lowest Albumin g/L	Maximum ALT U/L	Maximum AST U/L
A	31	3	0	NA	NA	NA	NA	NA	NA	NA
B	7	4	0	9.5	37.3	875.0	206.0	21.0	36.0	32.0
C	4	4	1	9.8	43.2	918.0	130.0	22.0	44.0	52.0
D	3.5	4	1	9.2	42.4	1715.0	181.4	18.0	61.0	99.0
E	5	4	1	6.7	17.6	1413.0	148.2	27.0	20.0	24.0
F	2	3	0	6.4	35.6	959.0	212.1	15.0	8.0	19.0
G	24	NA	NA	8.6	21.9	1002.0	181.4	27.0	17.0	30.0

5 patients were male; All were Singaporean Chinese except for G who was from the Philippines; A & G were treated in an outside facility/separate service initially and some data was not available; # Blood test results were generally taken at the same time apart from the platelet count; **Only D presented with lymphadenitis.

Table 2

ID	TIme to CRP normalization (weeks)	Number of IVIG given	Steroids	Time to abnormal echo (weeks)	Time to aneurysm development (weeks)	Other outcomes
A	*	2	oral only	4	4	1st IVIG given 3 weeks after symptom onset
B	*	2	IV/PO	2	2	deceased, MI secondary to thrombus
C	2	1	IV/PO	1.1	0	treated with Infliximab and then Methotrexate,
D	5	1	IV/PO	0.3	2	post infliximab psoriasis, treated with Infliximab and then Methotrexate, multiple infections in hospital; BCG reactivation while on Infliximab
E	9	2	no	1.4	2.7	UTI, AIHA, lost to follow up
F	3	3	IV/PO	0.71	2.5	post Infliximab psoriasis, multiple infections in hospital
G	7	2	oral only	7	0	lost to follow up

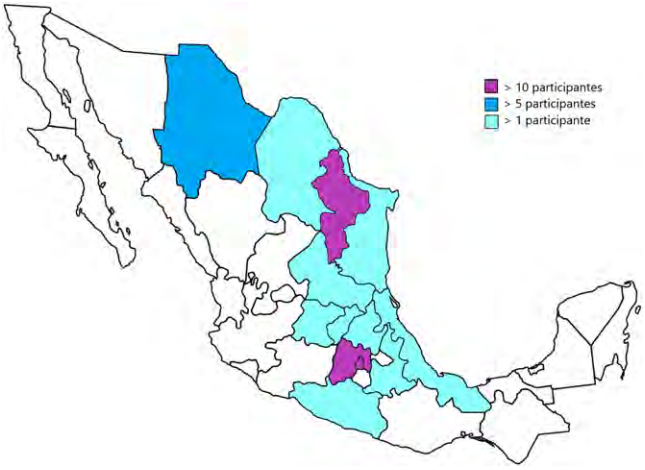
*patients A & B had recurrent KD episodes interspersed with short periods of symptom resolution

Conclusion: While transthoracic echocardiograms remain imaging investigation of choice, for children with recalcitrant or recrudescent KD, especially in the setting of delayed CRP resolution of >2 weeks; an MRA should be considered.
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THU0509 IMPACT OF PEDIATRIC RHEUMATIC DISEASES ON MEXICAN CAREGIVERS.

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Background: Pediatric rheumatic diseases (PRD) have an important impact on different aspects of the patients' and caregivers' life, such as physical, emotional, economic, and social. Some studies have shown that parents of patients with PRD have important impact but there is a lack of information of this topic from Latinamerican countries.
Objectives: The aim of this study is to describe and analyze the impact of juvenile idiopathic arthritis (JIA), juvenile systemic lupus erythematosus (JSLE), and juvenile dermatomyositis (JDM) on Mexican primary caregivers.
Methods: This is a multicenter cross-sectional study conducted in third-level reference pediatric hospitals in Mexico from December 2018 to November 2019. We included primary caregivers of pediatric patients with JIA, JSLE, and JDM that were treated in participant centers.
CAREGIVERS questionnaire, a validated multiassesment tool to measure the impact of PRD on caregivers, was applied to the participants. Collection of social, demographic, and clinical data was also performed and correlated with questionnaire results.
Results: A total of 200 primary caregivers participates in the study (109 JIA, 28 JDM, and 63 JSLE), aged 38 (IQR 32 – 46), mostly women (84.5%), from 6 centers, representing 13/32 Mexican states (Figure). One third (78) had a remunerated job, 123 (61.5%) had a relationship, 77 (38.5%) reached high school or higher, and 131 (65.5%) spends more than one hour to get to the center. Patients cared aged 12 (IQR 9 – 16), mostly women (67%), 87 (43.5%) with active disease, 43 (21.5%) with any disability, 94% and 29% treated with DMARD and biologics, respectively.
Feelings of worry and sadness predominant at diagnosis that decreased over time (42.5% and 28.5% vs 9.5% and 31.5%, respectively) and changed for peace (44%). Concerns about disabilities were more frequent on JIA group (34%), while pain and economic issues in JSLE (47% and 30%, respectively. Most of the caregivers feel anxiety about the future of their patients (148, 74%), regardless of the diagnosis. Participants reported that the way they spend the time, social life, and personal health worsened since diagnosis (49.5%, 32%, and 34.5%, respectively), especially in those with JSLE (60%, 39%, 46%). In 126 (63%) participants the economic situation worsened, 129 (64.5%) borrowed money (76% in JSLE, P = .03), 63 (31.5%) had problems to buy medications, and 48.5% have had problems at work. In 25 (12.5%), the family relationship was affected after diagnosis, however, the main supportive network reported were family members.
Conclusion: This work described the main impacted areas in life of primary caregivers of patients with PRD, showing a perspective of the burden of the disease.
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THU0510 CHOREA AND CARDITIS: AN UNEXPECTED COMBINATION. THE NEW FACE OF ACUTE RHEUMATIC FEVER

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Background: Acute Rheumatic Fever (ARF) is an immunomediated multisystem disease that occurs about 2-5 weeks after Group A Streptococcus Pyogenes beta-hemolytic (GAS) pharyngitis. After a negative peak in the 1980s, following the introduction of antibiotic prophylaxis, the disease is currently recovering. Rheumatic carditis is one of the most worrying aspects as it is still one of the major causes of cardiovascular death in the young-adult population. However, if diagnosed early and treated, sequelae with aortic and mitral valve involvement can be prevented.
Objectives: The aim of our study is a description of Acute Rheumatic Fever in all its manifestations in a cohort of pediatric patients belonging to the Azienda Ospedaliera Universitaria Integrata of Verona.
Methods: A retrospective analysis was conducted collecting all the cases of ARF, diagnosed by Jones's criteria, related to Pediatric Rheumatology and Pediatric Cardiology of Verona from January 2005 to December 2019. Demographic and clinical data were collected for all patients such as clinical presentation, disease evolution and cardiac involvement.
Results: 73 patients were analyzed, of whom 53 had an acute onset of ARF and 20 received a diagnosis of previous ARF due to indolent carditis. The prevalent age at the time of diagnosis in both groups was between 5 and 14 years of age. Among patients with acute onset, carditis was the most frequent major manifestation (94.3%), followed by polyarthritis (41.5%), chorea (24.5%) and erythema marginatum (7.5%). Only in one patient we could observe subcutaneous nodules (1.8%). Regarding the minor manifestations, the increase in inflammation markers was present in 83% of cases and fever was present in 75.5%, followed by arthralgia (58.4%) and prolonged of PR interval to ECG (9.4%). Carditis was also present in all 13 patients who presented chorea. Clinically, previously unknown heart murmur occurred in 28 patients. Therefore, the mismatch between cardiac objectivity and carditis finding is clear: infact, compared to an important finding of carditis (50 patients) only slightly more than half of the patients (28 patients) showed an evident clinic finding. Finally, no correlation was found between the levels of the antistreptolysin O titer and the severity of heart damage. Patients with early diagnosis of carditis were treated at onset with corticosteroid therapy according to the American Heart Association scheme and did not show valvular cardiac outcomes. A patient who received a late diagnosis of carditis currently presents a significant and permanent cardiac damage despite adequate steroid treatment undertaken at the time of diagnosis.
Conclusion: The description of this cohort of pediatric patients shows that the ARF has not disappeared in industrialized countries. Treatment of streptococcal infection (primary prophylaxis) plays a key role in preventing ARF. Of great impact is the prevalence of carditis which is present in 94.3% of patients. Early diagnosis is therefore of primary importance and the subsequent follow-up path, consisting of periodic therapy with penicillin (secondary prophylaxis) and periodic cardiological checks, greatly affects children's quality of life. Chorea, unlike what has been described in the literature, occurred simultaneously with the cardiac process, while the cutaneous manifestations (subcutaneous nodules and erythema marginatum), once pathognomonic of the rheumatic disease, are today of rare observation.
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THU0511 THE RISK FACTORS OF HIP OSTEOARTHRITIS IN JIA PATIENTS: THE DATA FROM A SINGLE CENTER RETROSPECTIVE CONTINUOUS STUDY

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Background: Hip osteoarthritis (HOA) is a severe irreversible complication of patients with juvenile idiopathic arthritis (JIA) leads to intensive pain, disability and required total hip arthroplasty (THA) in childhood or in the young adults.
Objectives: the aim of our study was to evaluate risk factors of HOA in JIA patients.
Methods: we analyzed 753 patients with JIA for last 10 years. In each patient we observed if the HOA developed or no. We evaluated the main clinical JIA measurements, such a JIA category, CRP, ESR, WBC, PLT, active joints, initial or delayed hip involvement, ANA, HLA B27, onset age, JIA duration, time before HOA and before THA, bone metabolic markers, treatment, particularly glucocorticosteroids (GCS), their cumulative doses, route of administration (oral, intra-articular, pulse therapy). HOA was confirmed with radiological assessment (MRI and CT). For comparison analysis used nonparamentric statistics. Each possible variable was evaluated with univariate regression analysis and further multiple regression analysis was applied.
Results: the comparative study between 2 groups shown in the table 1. HOA was detected in 48 (6.4%), in oligoarthritis-0%, in polyarthritis - 4.9%, in psoriatic arthritis - 5.0%, in enthesitis-related arthritis -11.8%, in systemic arthritis 19% (p=0.0000001), THA was performed in 16 (2.1%). Hip involvement at onset of JIA was similar in both groups (49.5% vs 41.7%, p=0.367).

Table 1. Characteristics of JIA patients, depends on HOA development.

Parameter	HOA (n=48)	No HOA (n=705)	p
Onset age, y	8.0 (4.0; 12.5)	5.9 (3.0; 10.7)	0.045
HLA B27, n (%)	13/25 (52.0)	88/283 (31.1)	0.033
JIA duration, y	7.5 (3.2; 12.1)	4.2 (1.8; 7.2)	0.00007
CRP, mg\l	2.8 (0.8; 20.9)	1.3 (0; 7.1)	0.006
Active joints, n	11.0 (6.0; 27.0)	6.0 (3.0; 12.0)	0.000001
Oral GCS, n(%)	21 (43.8)	131/704 (18.6)	0.00003
GCS pulse-therapy, n (%)	21 (43.8)	114/702 (16.2)	0.000002
GCS, cumulative doses, mg	5000 (3000; 16000)	2000 (1000; 4000)	0.001
Biologics, n (%)	43 (89.6)	308 (43.7)	0.0000001
Remission, n (%)	24 (50.0)	461 (65.4)	0.03
Time, before remission, y	7.4 (3.9; 12.3)	3.0 (1.4; 6.2)	0.0000001
Alkaline phosphatase, U\l	129.3 (84; 244)	223 (147; 386)	0.00001
Delayed hip involvement, n (%)	28 (58.3)	24/87 (27.6)	0.00004

We calculated cut-off and OR of variables, associated with HOA development (table 2). After selection of 26 clinically meaningful and statistical significant risk factors only 22 pass the univariate regression analysis. In multiple regression analysis the main independent risk factors of HOA development were: HLA b27 (p=0.001), oral GCS/pulse therapy GCS (p=0.03) and alkaline phosphatase≤165 U/l (p=0.00006).

Table 2. Cutt-offs, odds ratio for HOA risk factors in JIA patients.

Parameter	*Se*	*Sp*	OR (95%CI)	p
Active joints > 4	89,6	42,0	6,2 (2,4-15,9)	0,000002
Alkaline phosphatase ≤ 165 U/l	65,9	70,8	4,7 (2,4-9,2)	0,000001
GCS > 2700 mg	82,6	58,1	6,6 (2,1-20,6)	0,0004
Time before remission>5 years	66,7	78,9	7,5 (3,1-18,0)	0,0000001
Time before biologics >7,8 years	44,2	86,7	5,2 (2,6-10,2)	0,0000001

Conclusion: the main risk factors of HOA were increased inflammatory activity, systemic arthritis, HLA B27, systemic corticosteroids, delayed remission and biologics, decreased bone metabolism. Delayed hip involvement underline the possible non-inflammatory mechanism of HOA, such as avascular necrosis.
Disclosure of Interests: None declared
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THU0512 HEALTH RISK BEHAVIORS IN ADOLESCENTS WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA) IN THE COURSE OF DISEASE: RESULTS OF THE GERMAN MULTICENTER INCEPTION COHORT (ICON)

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Background: Health risk behaviors (HRB) are defined as specific forms of behavior associated with increased susceptibility to a specific disease or ill health on the basis of epidemiological or social data. The social implications of HRB include being able to use them as a way to gain respect and acceptance from peers, establishing independence from parents, or providing a subjective feeling of maturity and adequate stress management [1].
Objectives: Since chronically ill adolescents such as those suffering from JIA can develop a HRB that is challenging for optimal care the aim of this study was to compare the frequency of HRB in adolescents with JIA and their peers, and to determine whether they change during the course of disease.
Methods: Patients ≤ 16 years of age with recently diagnosed JIA (< 12 months) were enrolled in the inception cohort of patients with newly diagnosed JIA (ICON), an ongoing prospective observational, controlled multicenter study

started in 2010. Patients from the age of 13 who were questioned about their health behavior and followed up for at least 2 years were selected. HRB were quantified and compared with those of subjects from the general population after matching for age and sex. Data from 2-year follow-up (FU) were used to analyze correlates of multiple risk behavior defined as involvement in two or more risky behaviors.

Results: A total of 209 adolescents with JIA (63% female, mean age at baseline 14.4±0.9, mean disease duration 2.6±2.0) and 138 healthy peers (55% female, mean age 14.5±1.0) were included. At baseline, 51% of patients were treated with a DMARD, 21% with a biologic (FU: 59% and 38%). The most common JIA category was rheumatoid factor negative polyarthritis (28%). While at baseline 20% of patients and 4% of controls did not engage in regular physical activity, the proportion at follow-up amounted to 16% and 10%, respectively (OR 3.69; 95%CI: 1.01-13.50). In both groups the proportion of regular smokers, alcohol consumers and drug users increased during the observation period. Significant group differences were found in terms of alcohol consumption and smoking habits, but not in relation to illicit and legal drugs (see table). Patients stated significantly more often that they had not used a condom during their last sexual intercourse (28% vs. 19% controls, p<0.05). Multiple risk behavior was associated with PedsQL™ total score (OR 0.96; 95%CI: 0.92-0.99) and disease duration (OR 0.75; 95%CI: 0.57-0.98).

Forms of HRB	Baseline		2-year follow-up	
	JIA N=209 (%)	CG N=138 (%)	JIA N=209 (%)	CG N=138 (%)
Inactivity/smoking/alcohol consumption				
Physical activity <1/week	20.3	3.7	16.2	9.5
Active ≤2/week	58.9	43.4	54.4	42.3
Regular smokers	2.4	0.7	7.8	2.2
Regular alcohol consumers	3.8	3.6	15.8	23.2
Drug use				
12-month prevalence	1.9	1.4	8.1	8.0
Multiple consumers	0.5	0.0	4.8	3.6
Sexual intercourse				
Lifetime prevalence	3.3	1.4	25.2	23.2
No condom use during last sexual intercourse	28.6	50.0	28.0	19.4

Conclusion: Although adolescents with JIA became more physically active during the course of the disease, they are as likely, or more likely, to take risky behaviors than their healthy peers, except for alcohol consumption. In order to achieve optimal outcomes, addressing emotional wellbeing and providing mandatory anticipatory guidance appears to be warranted in this population.

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THU0513 MEDICATION BURDEN IN YOUNG ADULTS WITH JUVENILE IDIOPATHIC ARTHRITIS – RESULTS OF AN OBSERVATIONAL COHORT STUDY

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Background: Juvenile idiopathic arthritis (JIA) often persists into adulthood, and many young adults with JIA still need antirheumatic medication. Rheumatologists prescribe DMARDs and glucocorticoids, but are not always aware of other medications taken by patients concurrently. Self-reported medication use was used to obtain information on drug exposure of young adults with JIA.

Objectives: To evaluate medication use in a large cohort of young adults with JIA ever treated with DMARDs.

Methods: Patients ever treated with DMARDs and prospectively observed in the JIA biologic registry JuMBO were asked about their drug consumption at each JuMBO visit. In addition, patients reported their current health status in terms of disease activity and pain (scored on numerical rating scales 0-10), functional ability (by HAQ) and quality of life (by SF-36). The Anatomical Therapeutic Chemical Classification System for medicinal products (ATC) was used to classify self-reported medication use. Local therapies, with the exception of ophthalmological drugs, and cough and cold remedies were not included.

Results: A total of 1,306 young adults (68% female) with JIA and a mean disease duration of 13.6±6 years (ys) were included in the analysis. The majority of them were classified as polyarticular-onset JIA (35.6%), 20.5% as enthesitis-related arthritis.

At the last follow-up (FU), the patients´ mean age was 23.1±4.1 ys. They had received a mean of 2.6±1.4 DMARDs, 79% were ever treated with biologics. At FU, patients used on average 1.9±1.8 drugs. About one in five patients (296, 22.7%) reported no medication use at all, 367 (28.1%) reported only DMARD use. The most frequently reported drugs were DMARDs (64%), NSAIDs (48%), glucocorticoids (19%), followed by analgesics (10.6%), drugs for acid-related disorders (6.9%) and anti-infectives for systemic use (6.1%). Antidepressant drug use reported 3.4% and antihypertensive drug use 3.1% of the patients. Women used significantly more frequently NSAIDs, glucocorticoids, non-opioid analgesics and thyroid medication. There were 178 (14%) patients who received at least 3 other medications in addition to DMARDs. This patient group frequently reported the use of pain medication (74% NSAIDs, 23% non-opioid analgesics, 20% opioid drugs) and antidepressants (16%) and had been treated late with bDMARDs (7.4±4.9 ys after symptom onset). There were significant differences in drug usage between patients with various JIA categories (table). Moreover, the use of glucocorticoids, antihypertensives and antidepressants in adulthood (adjusted by propensity scores) increased with longer time from symptom onset to bDMARD start.

Table. Self-reported medication use in patients with different JIA categories at the last JuMBO FU

	Sys JIA	OA, pers.	OA, ext.	RF- PA	RF+ PA	ERA	PsA	Other arthritis	P value
	N= 66	N=117	N=227	N=350	N=115	N=268	N=116	N=47	
Drugs per patient, mean	2.7±2.2	1.3±1.6	2.2±2.0	1.8±1.8	2.7±2.0	1.5±1.5	1.9±1.7	1.7±1.8	<0.001
Drugs, in %									
DMARDs	68	45	74	60	87	60	62	57	<0.001
bDMARDs	59	32	64	48	73	53	53	47	<0.001
sDMARDs	27	25	34	28	46	21	29	23	<0.001
Glucocorticoids	32	10	23	19	35	10	19	17	<0.001
NSAIDs	36	36	52	48	55	44	55	55	0.008
Drugs for acid related disorders	6	3	8	7	7	6	8	15	0.314
Analgesics	12	6	11	13	14	8	10	11	0.198
Opioids	9	2	4	4	4	2	2	4	0.181
Antiinfectives	9	4	7	7	3	6	7	6	0.641
Antidepressants	6	3	5	3	1	5	3	0	0.319
Antihypertensives	11	1	3	3	5	2	3	6	0.005
Antithrombotics	5	1	1	1	4	0.4	0	0	0.027

Conclusion: Self-reported medication use adds important information when assessing the long-term outcome of JIA. About 15% of JIA patients ever exposed to DMARDs, especially those with late start of bDMARD therapy, have a high medication or disease burden in young adulthood.

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THU0514 BIOLOGICAL THERAPY IN JUVENILE PSORIATIC ARTHRITIS – 15 YEARS OF SINGLE CENTER EXPERIENCE

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Background: Juvenile psoriatic arthritis (JPsA) is one of the clinical variants of juvenile idiopathic arthritis (JIA), which is often characterized by an unfavorable course, refractory to therapy, requiring the prescription of Biological agents (BA).
Objectives: analysis of BA use in patients with JPsA and therapy survival, switching to another line of BA.
Methods: the retrospective cohort study included 1095 JIA patients who received BA and were observed in our clinic from 2004 to 2019. All cases of new onset psoriasis were collected; clinical features of disease onset and course, exposure to Methotrexate (MTX) and BA, presence of ANA, HLA B27 were studied.
Results: among 1095 JIA patients who received BA over the past 15 years, a separate cohort of patients with JPsA for analysis was allocated. We identified 50 pts (57% female) aged 2-18 years (Me 13.3) at the time of initiation of therapy. All patients met the JPsA classification criteria, the average age of arthritis onset was 7.4±5.3 years (ME 6.75). However, cutaneous psoriasis occurred only in 68 %(34 pts), with manifestation at the age of 10±5 years. In 25 of 34 pts (73.5%) the development of psoriasis was preceded by joint manifestations in an average of 5±3.9 (ME 3) years. 6 pts from 1095 (0.65%) developed psoriasis under BA therapy: infliximab - 2 cases (0.62/100PY), adalimumab - 3 (0.15/100PY), abatacept -1 (0.31/100PY). 2/6 pts was ANA+, 3/6 – HLA B27+. Average age of disease onset was 9.8±7.8 years; BA exposure before psoriasis was 2.7±1.1 years and in 3.6±1.3 (ME 4) after the onset of arthritis. Therapy was continued in 4/6 pts; switched from infliximab to adalimumab in 2. Serious comorbid pathology was associated with JPsA in 7 pts (type 1 diabetes mellitus – 2 pts; Down syndrome; endogenous mental illness (schizophrenia); oligophrenia; ovaries polycystic; acute lymphoblastic leukemia in a state of incomplete remission). The clinical picture of the disease was represented by polyarthritis in 84%, oligoarthritis in 8%, the same number of patients 8% had an axial lesion. Sacroiliitis was detected in 20 patients (40%), dactylitis in 21 (42%), and uveitis in 10 (20%). HLA B27 was detected in 16/35 pts (45%), 32% pts were ANA-positive. The duration of the disease at the time of application of the first BA was 5±4 (Me 3.75) years. In 49 patients, BA was used in combination with methotrexate. The total number of BA courses switching included was 80 (infliximab-19, adalimumab-22, etanercept-27, golimumab-4, abatacept-5, tocilizumab-2, rituximab-1). 49% of patients have experience of using >2 BA (16 pts-2 BA, 4 pts-3 BA, 1 pt - 5 BA). Primary/secondary inefficiency (18/35; 51%), adverse events (8/35; 23%), organizational difficulties in market access mostly after the age of 18 (7/35; 20%), and remission (2/35; 6%) were the reasons for the withdrawn of BA. Among the serious adverse events, multiple sclerosis was registered after 6 years of abatacept using (the relationship with the drug used has not been proven), pregnancy in the 3rd year of adalimumab use (interruption at 16 weeks); serious local reaction after etanercept using– 1; infusion reactions (1-rituximab, 2-infliximab); uveitis de novo (2- etanercept).
Conclusion: JPsA is one of the most severe variants of JIA, characterized by a high proportion of serious comorbid conditions, the development of refractoriness and adverse events of BA therapy (including uveitis, multiple sclerosis), requiring switching to line 2 and 3 with a limited choice of BA with pediatric indications. Special study requires the manifestation of psoriasis de novo mainly developed during TNF-monoclonal antibodies therapy.
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THU0515 SYSTEMIC LUPUS ERYTHEMATOSUS IN CHILDHOOD AND ADOLESCENCE - UPDATE FROM THE NATIONAL PEDIATRIC RHEUMATOLOGY DATABASE

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Background: Systemic lupus erythematosus (SLE) is a clinically heterogeneous disease, which begins in childhood and adolescence in 15 - 20% of cases. Since 2004, data on SLE have been collected by means of a disease-specific questionnaire as part of the National pediatric rheumatology database (NPRD) in Germany. Since 2014, kidney biopsy results have been recorded to further specify kidney involvement.
Objectives: Evaluation of clinical signs and symptoms, outcome and laboratory data of patients with juvenile systemic lupus erythematosus from a large database in Germany.
Methods: Data from patients with SLE recorded in the NPRD in 2017 were considered for the analysis. In addition to age, sex, onset of disease, the criteria that led to the diagnosis, various laboratory parameters, organ involvement (current, ever) and therapy (current, last 12 months), current disease activity (numerical rating scale 0-10, NRS) and ECLAM (score 0-10) were recorded. Patient-reported outcomes included global assessments of overall-wellbeing and fatigue (NRS 0-10) and functional ability (CHAQ).
Results: 196 patients (86% female) with a median age of 16 years were documented. Criteria most frequently met at diagnosis included “antinuclear antibodies” (88%), followed by “anti-ds-DNA-Ab” (66%), “butterfly erythema” (42%) and “arthritis” (41%). A positive family history was found in 10% of patients.
At documentation, 85% of patients received disease-modifying anti-rheumatic drugs, most frequently hydroxychloroquine (73%), followed by mycophenolate mofetil (32%) and azathioprine (17%). Systemic glucocorticoids obtained 52% of patients, 12% ≥ 0.2 mg/kg/day. Biologics (rituximab 2%) and cyclophosphamide i.v. (3%) were rarely administered during the last 12 months. Disease activity was reported as 1.0 (NRS, median, IQR 0 - 9), ECLAM as 1.0 (median, range 0 - 10). In the laboratory, leukopenia < 3500/µl was found in 9% of patients, lymphopenia < 1500/µl in 47% and erythrocyte sedimentation rate (ESR) > 25 mm in 15% of patients. Mean CHAQ was 0.24, and 86% of patients had a CHAQ score < 0.5. Mean patient`s global assessment of overall-wellbeing was 1.5, while the mean fatigue score was 2.86 (18% NRS score 7-10).
The following organ involvement was ever present: general symptoms 84%, skin/mucosa 72%, joints 73%, thyroid 15%, muscle 25%, lungs 17% and CNS 30%. In 45/190 (24%) patients, a kidney involvement was stated. In 34 patients (75%) a kidney biopsy was performed and histology yielded the following results: Class 1: 6.7%, Class 2: 16.7%, Class 3: 40.0%, Class 4: 23.3%, Class 5: 13.3%.
Conclusion: The most common clinical symptoms documented in juvenile SLE patients were skin and joint involvement. In the course of the disease, a quarter of the patients developed kidney involvement, mostly proliferative nephritis. Apparently, azathioprine is increasingly being replaced by mycophenolate mofetil, biologicals have hardly been used so far. Although functional outcome and overall-wellbeing of jSLE patients was good, fatigue was a concern for some patients.
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THU0516 FIFTEEN CASES OF 3 NLR FAMILY MEMBERS (NLRP3, NLRP12 AND NLRC4) RELATED INFLAMMASOMOPATHIES IN A SINGLE CENTER OF CHINA

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Background: There are four members in NLR family, NLRP3, NLRC4, NLRP1, and NLRP12, the mutations of which can lead to autoinflammatory diseases, while little reports describe those diseases in Chinese population.
Objectives: To report several cases of NLR-related autoinflammatory diseases in our center and to compare the differences of the presentations of CAPS between Chinese and western patients.
Methods: This study was undertaken at Peking Union Medical College Hospital (PUMCH) between 2012 and 2019. Demographic data, clinical presentations and genetic results were collected.
Results: 15 patients had been diagnosed as NLR-related autoinflammatory diseases in our center, including 11 CAPS, 1 FCAS4 and 3 NLRP12-AD patients.
We found 10 NLRP3 mutations, 3 NLRP12 mutations and 1 NLRC4 mutation. There are 3 novel mutations: NLRP3 c.1311G>T, NLRP3 c.1711G>A, and NLRC4 c.514G>A.
The major symptoms of those diseases are similar, such as recurrent episodes of fever associated with rash. And some may suffer from arthritis/arthralgia, uveitis, sensorineural deafness, symptoms of central neural systems (CNS).
On the other hand, different inflammasomopathies have unique characteristics. Symptoms of FCAS1, the mildest CAPS disorder, including rash and fever with/without arthritis/arthralgia, usually develop in the first year of life. The onset age of MWS is later (8m to 5y), and those patients were more likely to develop arthritis/arthralgia, eye involvement, hearing loss and symptoms of CNS. NOMID was the most severe type, and was presented with chronic urticarial-like rash shortly after birth, as well as severe CNS manifestations and musculoskeletal involvement. One of our NOMID patients had clubbing fingers, which was not reported before. The onset age of NLRP12-AD ranges from 6m to 5y and the presentation is similar to MWS while the FCAS4 patient presented with rash and fever, like FCAS1.

For laboratory examinations, all patients had raised inflammatory markers like ESR or CRP. Most of those patients had increased cytokines, including IL-1β, IL-6 as well as TNF-α. Leukocytosis and thrombocytosis were also observed in most patients, while anemia was mostly found in patients diagnosed as NOMID.

We also compared the clinical manifestations of CAPS between Chinese and western patients. The frequency of fever in Chinese is much higher than that in western population, while less Chinese patients suffered from ocular manifestations. Besides, Chinese patients seem to exhibit higher frequencies of severe symptoms, either CNS symptoms, or musculoskeletal symptoms, albeit with insignificant difference.

	Chinese	Western	p value
n	26	136	
Gender Ratio	15:11	69:67	0.518
Fever	25/26 (96%)	108 (79%)	0.002
Rash	24/26 (92%)	132 (97%)	0.397
Triggered by cold	3/26 (12%)	34 (25%)	0.076
Ocular manifestations	10/26 (38%)	97 (71%)	0.001
Hearing loss	9/26 (35%)	56 (41%)	0.535
Neurological symptoms	15/26 (58%)	55 (40%)	0.105
Severe	4/11 (36%)	16 (12%)	0.141
Musculoskeletal manifestations	18/26 (69%)	117 (86%)	0.093
Severe	3/11 (27%)	6 (4%)	0.137
Increased CRP/ESR	25/26 (96%)	NA	

Conclusion: We reported a case series of NLR-related autoinflammatory disease and found some novel mutated alleles and clinical phenotypes, which expanded our knowledge to those diseases. By comparing clinical manifestations of CAPS patients in China and in western countries, it seems that the symptoms in different populations are not identical.

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THURSDAY, 04 JUNE 2020

Diagnostics and imaging procedures

THU0517 THE ROLE OF ULTRASOUND-DEFINED SYNOVITIS GRADE I IN PATIENTS PRESENTING WITH INFLAMMATORY ARTHRALGIA, A RETROSPECTIVE STUDY

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Background: Musculoeskeletal ultrasound (MSUS) is frequently used in several rheumatology units to detect subclinical inflammation in patients with joint symptoms suspected for progression to inflammatory arthritis (IA). Synovitis grade I (EULAR-OMERACT combined score) is known to be a casual finding in healthy individuals, but studies headed to unravel its possible role on rheumatic diseases are sparse.

Objectives: To investigate the correlation between synovitis grade I, and the diagnosis of IA made after a year follow-up period since MSUS findings, in patients of an MSUS-specialized unit of a Rheumatology Department.

Methods: We conducted a descriptive, retrospective and unicentric study. 30 patients were selected from the MSUS-specialized unit of our Rheumatology Department from July-18 to January-19. Patients presenting synovitis grade 0 (exclusively), 2 and/or 3 on combined score were excluded. Data collection at baseline included age, sex, immunological profile and previous physical examination to the MSUS findings, as well as the diagnosis made by the rheumatologist in 1-year visit follow-up: dividing the patient sample into two groups: those who were diagnosed with IA and those not. Non-parametric statistical tests for comparing means were used.

Results: The mean age was 51,6 years and 70% were females. 6 (20%) patients were diagnosed with inflammatory arthritis after a year follow-up: 2 (4,8%) psoriatic arthritis, 1 (3,3%) undifferentiated arthritis, 1 (3,3%) rheumatoid arthritis, 1 (3,3%) Sjögren's syndrome. Non-inflammatory arthropathies were also found 24 (80%), of which, 12 (40%) were non-specific arthralgias and 8 (19%) osteoarthritis.

In the group of patients who did not developed an IA the mean C-reactive protein (CPR) value was 3,12 mg/L and erythrocyte sedimentation rate (ESR) was 8,2 mm; all of them were rheumatoid factor (RF) positive and ACPA-negative except one patient. 5 (31,3%) patients presented low antinuclear antibodies (ANAs) levels. In those who HLA B-27 and Cw6 were tested (4,25%); both were negative except for one that was HLA B-27 positive. The median number of swollen and painful joint count was 0, and the mean of joints with MSUS involvement was 3,5; the mean involved metacarpophalangeal (MCP) joints was 1,83; proximal interphalangeal (PIP) joints was 1,48 and distal interphalangeal (DIP) joints 0,21.

Among the group of patients that developed an IA the mean of CPR and ESR was 9,27 mg/L and 14,17 mm respectively; 2 (33%) patients were RF- positive, and 1 ACPA-positive. ANAs were positive in 3 cases (50%). The median of swollen joint count was 2 and for painful joint count was 0, the median of joints with MSUS involvement was 4,5. The mean of MSUS involvement was for MCP, PIP and DIP joints: 1,67, 2 and 0. Comparing the means of CPR values in the two groups with Student's t-test we obtained a statistically significant difference (p=0,023). No other significant differences were found.

Conclusion: Despite the limitations and possible statistical bias, the presence of MSUS-defined synovitis grade I and elevated CRP levels could be related to further diagnoses of inflammatory arthropathy. Besides, the absence of synovitis in DIP joints might have a diagnostic role. Normal physical exploration and normal levels of CRP might suggest low MSUS value. However, further research is needed to clarify the role of MSUS-defined synovitis grade I.

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THU0518 ACCURACY OF DUAL-ENERGY COMPUTED TOMOGRAPHY FOR THE DETECTION OF BONE MARROW EDEMA IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: An important applications of the Dual energy computed tomography DECT in the field of musculoskeletal radiology is the detection of bone marrow edema (BME), using a post-processing software to remove calcium in trabecular bone by using a "virtual non-calcium (VNCa)" subtraction process DECT have been successfully employed in the evaluation of the extent of BME in patients with sacroiliitis (1)

Objectives: The aims of this study were i)to evaluate the discriminating capacity of DECT versus MRI in the detection of BME of the sacroiliac joints in patients with axial-SpA and to define the optimal cutoff; ii) to define of inter-observer agreement between radiologists

Methods: All patients underwent a pelvic DECT examination, within 30 days of the MRI imaging, (Somatom Force; Siemens Healthineers, Enlangen, Germany). Each exam was evaluated by two operators: an experienced radiologist and a radiologist in training. The dedicated software also allows the precise calculation of the attenuation values in the region of interest (ROI). On the reformatted color-coded dual-energy virtual non-calcium images bone marrow signal is depicted in green and corresponding to high signal intensity on T2-weighted fat suppression MR images (Fig. 1). With the consent of the two operators, three ROIs were manually positioned for each side of the sacroiliac joints in the subchondral region of

the proximal, middle and distal thirds of each joint head, respectively. The inter-observer agreement analysis was carried out in the semi-quantitative evaluation of the scores assigned in CT. The accuracy of DECT for the detection of BME compared to MRI was analyzed using the Receiver Operating Characteristics (ROC) curve method

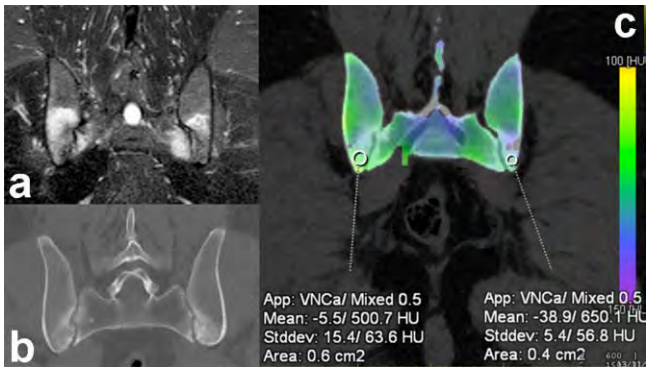


Figure 1. *Patient with SpA A. Short tau inversion recovery MR image demonstrating extensive BME in both iliac and sacral subchondral bone, indicating active sacroiliitis. B. CT Semicoronal multiplanar reformatted grayscale image shows signs of structural change. C. Semicoronal multiplanar reformatted color-coded dual-energy* VNCa *image reveals bone marrow signal involving both sacroiliac joints, corresponds to* BME *on the MR image*

Results: 56 axial-SpA patients have been evaluated, 30 males and 26 females, a mean age of 48.6 ± 12.3 years, a mean disease duration of 5.5 ± 2.9 years, a mean C-reactive protein level of 3.0 ± 2.5 mg/dl. The inter-rater agreement of readers showed a high statistical significance greater than 0.80, in particular the weighted kappa is 0.815, with a standard error of 0.04 and a 95% variability coefficient between 0.73 and 0.89. Sensitivity, specificity, and positive likelihood ratio in the identification of BME at DECT were 95.8%, 83.3% and 6.67, respectively. The differences in mean CT number (HU) among the four levels of edema category were significant (p<0.0001). The AUC was 0.905 in the differentiation of the presence of BME from no edema (Fig. 2). A cutoff value of –14.8 HU yielded overall sensitivity of 82.86% and specificity of 90.48%, with an LR+ of 8.70, in the detection of BME

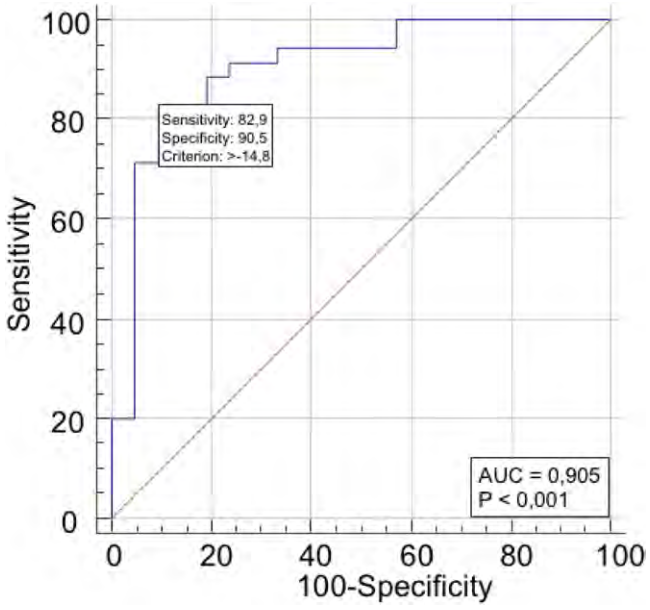


Figure 2. Graph shows ROC curves from CT numbers (in Hounsfield units) derived from DECT images in the detection of sacroiliitis with and without BME. AUC was 0.905

Conclusion: We confirm the potential of DECT for the detection of BME of the sacroiliac joints in patients affected by SpA. This new method appears to be very useful, not only in the diagnostic phase, but also for the monitoring of patients.

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THU0519 OPTIMAL USE OF CONTRAST ENHANCED MRI FOR CLINICAL TRIALS OF INFLAMMATORY DISEASES: RETROSPECTIVE ANALYSIS OF DATA FROM A PHASE IIB STUDY OF BARICITINIB IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS

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Background: Magnetic resonance imaging (MRI) was used to confirm dose selection in a phase IIb clinical trial of baricitinib in patients with active rheumatoid arthritis (RA) on background methotrexate therapy (NCT01185353).[1] MRI data were retrospectively assessed for consistency, timing of post-contrast sequences following intravenous (IV) Gadolinium (Gd), and readability. Data were re-analyzed using a novel quantitative computer-aided methodology to extract the continuous volume of inflammatory changes.[2]
Objectives: The objective was to examine how image quality and timing of the post-contrast MRI sequence can impact MRI-based exploratory endpoints in RA clinical trials when using novel computer-aided analysis tools.
Methods: A total of 154 patients with definitive radiographic erosion had an MRI of the hand and wrist at baseline and at weeks 12 and 24. Three-dimensional T1-w fat-suppressed MRI sequences before and after IV Gd contrast were performed with dedicated coils. Due to the limited field of view, the coils were re-positioned during the image acquisition between the metacarpophalangeal (MCP) and finger joints and the wrist, following IV Gd injection, which introduced a time delay of the post-contrast sequences in the two anatomies in all patients.
Digital Imaging and Communications in Medicine (DICOM) headers of the MRIs were automatically assessed; the distribution of the time delay in minutes from Gd injection to post-contrast scan acquisition was calculated and the image quality and suitability for reading were evaluated (Figure 1). The time delays across MRI acquisitions at baseline and weeks 12 and 24 were also compared. Quality scores were assigned for each image using visual image quality assessment by an experienced reader blinded to treatment regimen, patient visits, and time after Gd. The images were categorized by quality based on total score. The reader used a proprietary software, to pre-define regions of interest (ROI) around the wrist and MCP joints (MCP-2 to MCP-5) in all three timepoints as a batch, avoiding adjacent blood vessels and possible artifacts. From these ROIs, the normalized volume of inflammation (NormI) was calculated in each joint relative to a standardized ROI in the thenar muscle. Quantitative Total Volume of Inflammation (QVI) was extracted automatically from all ROIs by counting the pixels that were enhanced two standard deviations above the intensity level of the normal muscle, allowing differentiation of areas with low-to-high inflammation.
Results: The timing of post-contrast images from Gd injection was closely linked to image quality. In up to 10% of MRI data, the delay from Gd injection to scan acquisition caused significant variation in signal intensities. This led to a perceived increase in enhanced synovial volume due to the known effusion effects of the contrast media over time, which did not correspond to real size of the underlying synovial volume and pathology (Figure 2).
Conclusion: The acquisition of MRIs in RA trials should be done in a methodical and systematic manner, where the quality of MRI scans and the correct timing of post-contrast sequences are optimized. The incorporation of unacceptable quality data will impact the interpretation of RA clinical trial data, especially when novel computer-assisted quantitative analysis methods for post-processing are used. Incorrect timing and inconsistency in image quality can be prevented by using coils covering the whole hand and/or a dynamic contrast-enhance (DCE)-MRI sequence immediately following IV Gd injection to ensure correct timing of the post-contrast MRI sequence.

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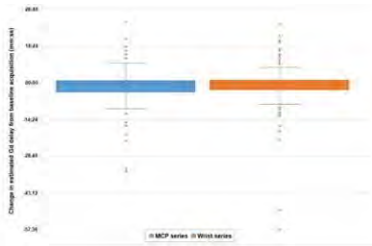


Figure 1. Changes in Gd delay between pre-contrast image and post-contrast image measured in all images using automated workflow of DICOM header checks
Abbreviations: DICOM, Digital Imaging and Communications in Medicine; Gd, gadolinium; MCP, metacarpophalangeal

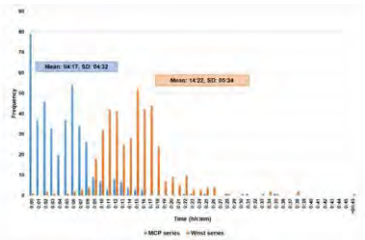


Figure 2. Distribution of the delay from Gd injection to scan acquisition for all post-contrast magnetic resonance images
The number of series with a Gd delay greater than Q3+1.5×IQR (outliers with a significantly longer than expected Gd delay) was 11 (3%) for the MCP series and 17 (4%) for the wrist series.
Abbreviations: IQR, interquartile range; MCP, metacarpophalangeal; SD, standard deviation

Disclosure of Interests:
Mikael Boesen Consultant of: AbbVie, AstraZeneca, Eli Lilly, Esaote, Glenmark, Novartis, Pfizer, UCB, Paid instructor for: IAG, Image Analysis Group, AbbVie, Eli Lilly, AstraZeneca, esaote, Glenmark, Novartis, Pfizer, UCB (scientific advisor)., Speakers bureau: Eli Lilly, Esaote, Novartis, Pfizer, UCB, Mark Hinton: None declared, Javier Gonzalez-Zabaleta: None declared, Scott Beattie Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Douglas Schlichting Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Terence Rooney Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Olga Kubassova Shareholder of: IAG, Image Analysis Group, Consultant of: Novartis, Takeda, Lilly, Employee of: IAG, Image Analysis Group
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THU0520 DIFFUSE ENTHESITIS AND LOW-GRADE INFLAMMATION IN PATIENTS WITH METABOLIC SYNDROME: A CLINICAL AND ULTRASOUND STUDY.

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Background: Metabolic syndrome (MS) is a clinical condition characterized by central obesity and additional factors such dyslipidemia, hypertension, raised fasting plasma. Scanty observations describe the association of MS with musculoskeletal conditions, such as enthesopathies and diffuse idiopathic hyperostosis syndrome (DISH). Musculoskeletal ultrasound (US) has been applied to the study of entheses, but the real prevalence and characteristics of entheseal involvement in MS has yet to be clarified.
Objectives: The aim of our work was to study the US-defined entheseal changes in MS, to correlates the US enthesitis scores to clinical characteristics, and to define a relation between MS-related enthesitis and the presence of concurrent DISH
Methods: Sixty consecutive outpatients (24 males, 36 females, mean age 60 years), all fullfilling International Diabetes Foundation (IDF) criteria for MS, were also evaluated with multi-site bilateral US entheseal examination. Each patient underwent power Doppler (PD) US examination of twelve entheseal sites, using Esaote MyLab Twice with 6–18 MHz transducer. Enthesitis was defined on the basis of OMERACT's filter. Inflammatory and structural changes were scored as a whole when present (score 1) or absent (score 0). The sum of entheses with inflammatory and structural damage was defined as "global inflammatory score" (GIs) and "global structural damage score" (GSDs) for each patient. The Leeds Enthesitis Index (LEI) was also applied, and a spinal radiography was obtained for each patient to research concurrent signs of DISH satisfying Resnick and Niwayama criteria.
Results: Patients showed moderate overweight (mean BMI 29) and a diagnosis of type 2 diabetes was present in 24 (40%). A low-grade inflammatory state was demonstrated in MS (mean CRP 0,58 md/dL, mean ESR 21,9 mm/h). A high prevalence of US-defined enthesitis was noted in 52 patients (86%) and 127/720 entheses (17,6%). PD signals, were reported in 11 patients (18%) and 11/720 entheses (1,52%), and they were associated to clinical symptoms expressed as LEI (p=0,0138). Erosions, although rare (0.3% of entheses), were more frequent in males (p= 0.001). Moreover, in 57 patients (95%) and 217 entheses (30%) structural damages were found. A correlation was found between GIs and GSDs and both BMI (p=0.0233 and p=0.0068 respectively), LEI (p=0.03 and p=0.0099 respectively), and type 2 diabetes (p=0.0248 and p=0.0156 respectively). In 28 patients (46%) a concurrent diagnosis of DISH was made. In multivariate regression analysis the best predictors for DISH were higher levels of CRP (p=0,038) and older age (p<0,0001). DISH correlated with older age (p<0,0001), CRP and ESR (p= 0,0428 p=0,0069 respectively) and US global scores for enthesitis (p=0,0312 for GIs, p=0,0071 for GSDs).
Conclusion: This is the first study where diffuse enthesitis and entheseal structural damage are demonstrated with high prevalences in MS, comparable or also higher than those reported for SpA-related enthesitis. Our data, obtained using the most recent OMERACT's definition for US-detected enthesitis (proposed for SpA), also suggest a low specificity of this definition, in consideration of the high prevalence of MS-associated enthesitis. Moreover PD was associated to entheseal pain expressed as LEI. Both GIs and GSDs showed a correlation with overweight and type 2 diabetes. As secondary result, this study demonstrated that almost half of patients with MS could have a concurrent diagnosis of DISH. Patients with DISH were older, with higher levels of inflammation, and higher scores of US-defined enthesitis. Our results suggest that MS and DISH could be strictly related; diffuse enthesitis with a low-grade inflammatory state should be regarded as potential factor of progression from MS towards a conclamed DISH.
Disclosure of Interests: None declared
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THU0521 EVALUATION OF LIVER FIBROSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS UNDER METHOTREXATE TREATMENT. UTILITY OF FIBROSCAN AND BIOMARKERS IN ROUTINE CLINICAL PRACTICE.

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Background: Despite therapeutic advances in recent years, methotrexate (MTX) remains the gold standard for the treatment of rheumatoid arthritis (RA). Among the side effects that have been blamed on it are liver fibrosis (LF) and cirrhosis, although late studies have failed to show such a relation[1,2]. The only validated test in the diagnosis of LF is biopsy. Given the relevance of MTX in the treatment of RA, it is important to evaluate non-invasive diagnostic options for LF such as transitional elastography (FibroScan, FS).
Objectives: To evaluate the percentage of LF in RA patients treated with MTX. Secondly, to assess the correlation between altered liver function, RA activity, and LF. To determine whether dose and/or duration of treatment with MTX may affect the development of LF in such patients.
Methods: We did a prospective study between February 2019 and January 2020. Patients affected of RA treated with MTX were included. Patients with basal liver disease (hepatitis B, hepatitis C and steatohepatitis), alcohol consumption, type I diabetes mellitus, chronic renal failure, heart failure, obesity and concomitant treatment with leflunomide or antiretrovirals were excluded. Demographic, clinical, analytical and therapeutic variables were collected. Liver fibrosis was assessed by FS in kilopascals (kpa) and using the APRI score. RA activity was assessed by DAS28 score. Continuous variables are described with mean and standard deviation (SD), and qualitative variables are shown with absolute value and percentage. Spearman's and Mann-Whitney's U tests were used for the bivariate analysis.
Results: Fifty patients were included (Table 1 and 2). Of these, 38 were women (76%) with mean age of 61.8 years (SD 11.7) and mean RA evolution time of 13.7 years (SD 8.2). The mean DAS28 at the visit was 2.39 (SD 1.1). The FS showed an average of 4.8 kpa (SD 2). The mean duration of treatment with MTX was 85.8 months (SD 93.3) and that of AD-MTX was 5414.6mg (SD 5011). Patients were divided into those with DA-MTX greater than 4000mg (21, 42%) and less than 4000mg (29, 58%) and no significant differences were found in terms of LF in FS (p 0.637) or APRI scale (p 0.806). No significant differences were found in terms of treatment duration either. Six patients (12%) had elevated aspartate aminotransferase (AST) and 9 (18%) had elevated alanine aminotransferase (ALT). No significant difference was found in FS values in relation to ALT, but it was with elevated AST (p 0.021). Similarly, differences were found in APRI based on AST (p 0.045). Metabolic syndrome was collected in 4 patients (8%) without significant differences with FS or APRI values. There were no significant differences in LF depending on gamma-glutamyl transpeptidase (GGT) values.
Conclusion: FS and APRI score are useful for the determination of LF in RA patients treated with MTX. There is no evidence of a relationship between AD-MTX and LF by FS or APRI. AST values may be related to the presence of fibrosis as determined by FS or APRI. and the presence of the metabolic syndrome are not.

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THU0522 DIFFERENCES IN MUSCLE PROPERTIES IN GCA PATIENTS COMPARED TO HEALTHY CONTROLS AS ASSESSED BY QUANTITATIVE MRI

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Background: Giant cell arteritis (GCA) is a systemic inflammatory vasculitis that often presents with headaches and visual symptoms. It is a medical emergency as it can lead to permanent sight loss. Prompt treatment with high doses of glucocorticoid therapy are often required. However, it has been shown that GCA patients on glucocorticoid therapy develop muscle weakness, known as glucocorticoid induced myopathy (1).
Quantitative MRI may be sensitive to detect the differences in muscle parameters between newly diagnosed GCA patients compared to healthy controls. MRI T2 is sensitive to fluid related to physiological changes at the molecular level, and is regarded as an indirect measure of muscle inflammation (2). MRI muscle fat fraction (FF) is useful for identifying myosteatosis (3). Diffusion tensor imaging (DTI) is sensitive to changes in muscle microstructure and may be useful in identifying changes to muscle fibres (4).
Objectives: To obtain preliminary estimates of the extent to which quantitative MRI-based measurements of muscle T2, FF, DTI and volume differ between newly diagnosed GCA patients and healthy controls (HC) and how the muscle changes over 3- and 6-month intervals following glucocorticoid therapy.
Methods: MRI of the mid-thigh were acquired using Dixon imaging to assess FF, Stimulated Echo Acquisition Mode echo planar imaging (STEAM-EPI) to measure diffusion, and a fat-suppressed multi-echo spin-echo to measure T2. Regions of interest were drawn around the quadriceps and hamstrings. All participants had knee extension and flexion torque measured on an isokinetic dynamometer, and isometric dynamometer to measure grip strength.
Results: 20 GCA patients (68.2±8.3 years, 14/20 female, mean ESR 26.9mm/h, mean CRP 39.6mg/L) were enrolled within 14 days of starting glucocorticoids: 15 returned at 3 months (mean ESR 17mm/h, mean CRP 5.7mg/L); 8 returned at 6 months (mean ESR 18mm/h, mean CRP 6mg/L). 20 directly age- and gender-matched HC also were recruited. T2 and FF were higher and muscle volume lower in the GCA patients at baseline compared to HC (fig. 1 and 2). Within the hamstrings, the mean differences between GCA patients and HC for T2, FF and muscle volume were 2.2ms (95% CI 1, 4; p=0.09), 3.8% (95% 2, 5; p<0.001), and -166cm3 (95% CI 110, 210; p<0.001) respectively. There was no substantive difference in mean diffusivity or fractional anisotropy. Results in the quadriceps followed a similar trend. Following glucocorticoid treatment, there were no substantive changes in MRI measurements. Knee flexion/extension and handgrip strength were lower in the GCA patients at baseline compared to HC, with differences of -5.3Nm (95% CI -32.6, -7.4; p=0.003) and -4.4Nm (95% CI -56.7, -1.3; p=0.04) for flexion and extension respectively. Muscle strength did not change following glucocorticoid treatment.

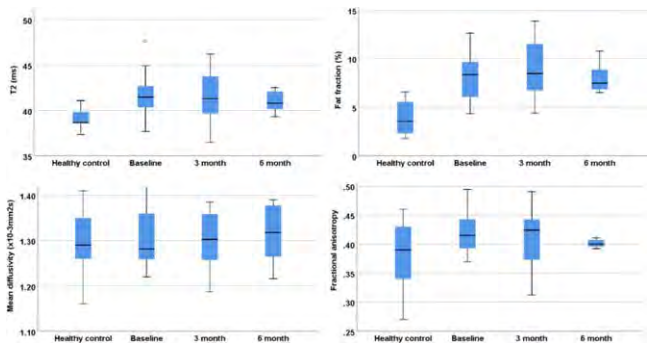


Figure 1. Quantitative MRI measurements of GCA patients and healthy controls in the hamstrings.

Conclusion: This pilot study suggests for the first time that muscle health may be affected in newly diagnosed GCA patients compared to age and gender matched HC, as demonstrated by higher T2 and FF, and lower muscle volume and muscle strength. These preliminary results show that muscle changes may occur in the early stages of GCA and persist throughout the disease duration. If these findings are confirmed, it will be important to consider interventions to improve muscle health in the treatment pathway for GCA.

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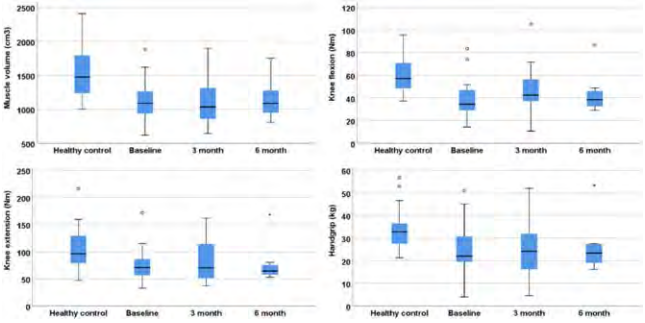


Figure 2. Quantitative muscle volume and muscle strength measurements of GCA patients and healthy controls.

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THU0523 CLINICAL UTILITY OF TESTING CONVENTIONAL AND NON-CONVENTIONAL ANTI-PHOSPHOLIPID ANTIBODIES IN SUSPECTED OBSTETRIC ANTI-PHOSPHOLIPID SYNDROME

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Background: Anti-phospholipid syndrome (APS) is an important cause for recurrent pregnancy losses (RPL). Conventional APS antibodies (aPLs) like lupus anti-coagulant (LA), anti-cardiolipin(ACL) and anti-beta 2 glycoprotein I (anti-β2 GP I) are not present in significant number of obstetric APS(OAPS) patients, leading to a state described as " sero-negative" OAPS (SNOAPS). Recent literature shows non-conventional aPLs like Anti phosphatidylserine-prothrombin complex (Anti-PSPT) and Anti-Annexin V (Anti-Ann V) can be positive in up to 50% of SNOAPS patients
Objectives: Testing the performance of conventional and non-conventional aPLs in suspected OAPS patients (obstetric events as defined in the Sydney classification criteria for APS)
Methods: We performed a retrospective chart review of 101 patients who underwent combined testing for non-conventional aPLs for suspected OAPS from May 2016 to November 2019 at our department. Patients were categorized into OAPS cases (n=50, median age 31 years) and controls (n=51, median age 30 years) based on their fulfillment of clinical definition of OAPS events defined by Sydney criteria. Conventional aPLs were tested by methods adapted in Sydney criteria and Anti PSPT /Anti Ann V were tested by commercial ELISA. The sample size(n=101) has 95% confidence interval with a margin of error of 10% for the objective of the study.

Results: 36 cases (72%) were 'sero-positive' & 14 cases (28%) were truly 'sero-negative' for conventional aPLs. 5 (35.7%) of the SNOAPS patients were positive for Ant-PSPT and/or Anti AnnV antibodies. Performance of the various aPLs in suspected OAPS is displayed in Table 1 & Figure 1.

Table 1 showing the performance of the various conventional and non-conventional APLs in suspected obstetric APS cases

Antibody	Sensitivity	Specificity	Likelihood Ratio(+)	Likelihood Ratio (-)	Positive Predictive Value	Negative Predictive Value	Accuracy	Youden's Index
LA	50%	94.1 %	8.5	0.5	89.3%	65.7%	72.3%	44.1%
ACL	32%	98%	16.3	0.7	94.1%	59.5 %	65.3%	30 %
anti β2 GP I IgM	38.4%	91.4 %	4.5	0.7	83.3%	57.1 %	63.5%	29.8%
anti β2 GP I IgG	24%	96.1 %	6.1	0.8	85.7%	56.3%	60.4%	20.1%
Anti PSPT	28%	96.1 %	7.1	0.7	87.5%	57.6 %	62.4%	24.1%
Anti AnnV	28%	98 %	14.3	0.7	93.3%	58.1%	63.4%	26%
Conventional APLs	72%	88.2%	6.1	0.3	85.7%	76.3 %	79.8%	60.2%
Non-conventional APLS	38%	94.1%	6.4	0.7	86.4%	60.7 %	66.3%	32.1%
All APLs	82%	86.3%	6.00	0.20	85.4%	83 %	84.2%	68.3%

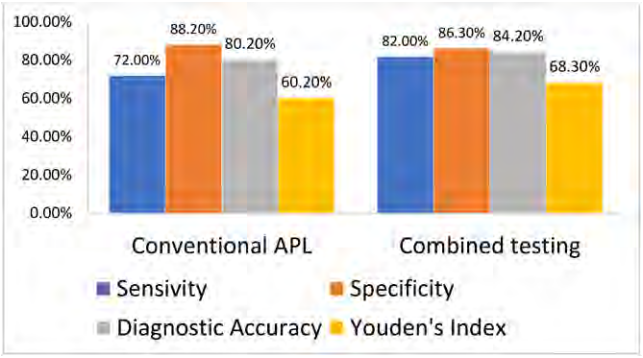


Figure 1 showing the comparative diagnostic performance of Conventional aPL testing vs Combined testing along with non-conventional aPLs in suspected obstetric APS scenario

Conclusion: In a delicate situation like RPL, performance of non-conventional aPLs on their own, though not as sensitive as conventional aPLs, still demonstrate better specificity. Non-conventional APLs can newly identify 1/3rd of SNOAPS as APS. The real value of testing Anti PSPT & Anti Ann V in RPL, is combined testing with conventional aPLs wherein they improve the sensitivity and accuracy of diagnosis of OAPS by 10% & 4.4 % respectively, with only 1.9% drop in specificity. Non-conventional aPLs should be tested in SNOAPS.

Disclosure of Interests: None declared

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THU0524

FACTORS EXPLAINING PATIENT PERSPECTIVE IN PSORIASIS AND PSORIATIC ARTHRITIS (PSA): THE ROLE OF INFLAMMATION AND STRUCTURAL DAMAGE DETECTED BY ULTRASOUND (THE ECHOPRO STUDY)

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Background: Patient reported outcomes (PROs) reflect patients' opinion on disease activity, impact of disease, quality of life (QoL) and are essential in the assessment of PsA patients. PROs may be influenced by several factors other than disease activity and severity. Ultrasound (US) is an objective tool to evaluate joint inflammation and structural damage in PsA.

Objectives: This cross-sectional study aimed at evaluating the role of US-detected inflammation (synovitis, tenosynovitis, enthesitis) and structural damage (erosions, enthesophytes, osteophytes, cortical irregularities), to explain PROs in PsA and to compare that to psoriasis (PsO) patients with and without musculoskeletal (MSK) symptoms.

Methods: PsA (CASPAR criteria) [1], PsO with MSK symptoms without fulfilling CASPAR criteria (symptoPsO) and PsO with no MSK symptoms (asymptoPsO) were included. Socio-demographic characteristics, comorbidities, disease duration and treatment were collected. All patients underwent to: a) dermatological and rheumatologic assessment: PsO severity, swollen joint count (SJC), tender JC (TJC), number of dactylitis and enthesitis; b) US evaluation of joints, tendons and entheses according to OMERACT definitions[2], (figure 1); c) PROs assessement: fatigue, disability (HAQ) and QoL (SF36). Variables were compared across groups (chi square or one-way ANOVA test). Correlations were evaluated using Spearman's test.

Results: 208 patients (76 PsA, 64 symptoPsO and 68 asymptoPsO) with similar socio-demographic characteristics and PsO duration were included (table 1). Except for enthesophytes, all US changes were significantly higher in PsA, followed by symptoPsO patients.

Table 1. Characteristics of the patients:

	PsA N= 76	SymptoPsO N=64	AsymptoPsO N=68	p
Females, N (%)	33 (43.4)	39 (55.7)	23 (37.1)	NS
Age	55.58 ± 12.71	52.16 ± 15.61	50.03 ± 14.66	NS
Psoriasis duration	18.76 ± 13.37	19.47 ± 15.98	15.03 ± 12.29	NS
PASI	0 (0; 36)	3 (0; 16)	5.5 (0; 22.1)	<0.001
68 TJC	4 (0; 30)	2 (0; 23)	0	<0.001
66 SJC	0 (0; 23)	0 (0; 3)	0	<0.001
Number of enthesitis	3 (0; 13)	2 (0; 13)	0	<0.001
Number of dactylitis	0 (0; 5)	0	0	NS
Fibromyalgia, N (%)	6 (7.9)	4 (5.7)	0	NS
N of joints with US synovitis	1 (0; 32)	0 (0; 7)	0 (0; 6)	0.001
N of US enthesitis	0 (0; 11)	0 (0; 2)	0 (0; 2)	<0.001
N of US tenosynovitis	0 (0; 7)	0 (0; 1)	0 (0; 1)	0.005
N of joints with US osthephytes/cortical irregularities	2 (0; 22)	1 (0; 25)	1 (0; 21)	0.027
N of joints with US erosions	0 (0; 4)	0 (0; 2)	0 (0; 2)	0.016
N of US entheses with enthesopthytes/calcifications	3 (0; 9)	2 (0; 10)	1 (0; 8)	NS
N of US enthesis with erosions	0 (0; 5)	0 (0; 1)	0 (0; 2)	0.001
Fatigue (0-10)	4.91 ± 3.08	3.46 ± 3.40	2.57 ± 2.86	<0.001
HAQ (0-3)	1 (0; 2)	0 (0; 2)	0 (0; 1)	<0.001
SF36 PF	61.31 ± 30.08	77.46 ± 25.02	89.35 ± 19.25	<0.001

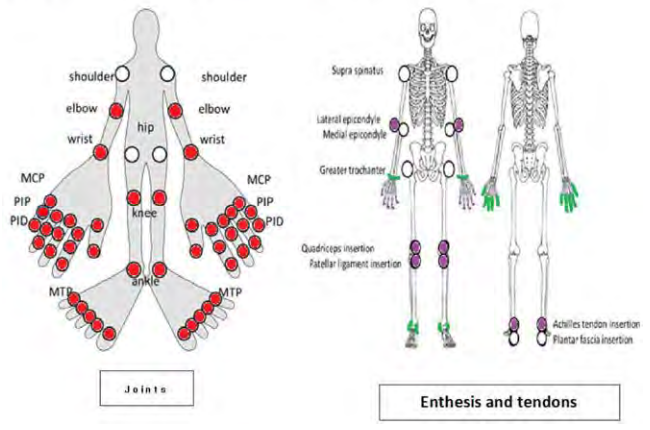
Across all 3 groups, all PROs correlated mainly with demographic variables, comorbidities, TJC, clinical enthesitis, skin severity, depression and fibromyalgia points (r=0.24-0.72). SymptoPsO and PsA reported similar scores of fatigue and impact on most QoL domains, significantly higher than asymptoPsO. HAQ correlated with total number of joints with US irregularities/osteophytes in PsA (r= 0.23; p=0.05), and SF36 physical function with both US inflammatory and damage variables in all three groups (r=0.24-0.34).

Conclusion: Quality of life, disability and fatigue were more impaired in PsA and symptoPsO patients than asymptoPsO. In all groups, PROs seem to be mostly associated with socio-demographic characteristics and comorbidities rather than objective measures such as US changes or clinical variables.

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Figure 1. Anatomical sites of US evaluation: joints, enthesis and tendons



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THU0525 DIAGNOSTIC PERFORMANCE OF MAGNETIC RESONANCE IMAGING FOR DETECTING SUBCHONDRAL BONE EROSION OF SACROILIAC JOINTS IN PATIENTS WITH SUSPECTED SPONDYLOARTHRITIS

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Background: The utility of structural lesions of sacroiliac joints (SIJ) for the early diagnosis of spondyloarthritis (SpA) has been well established by previous reports [1]. Computed tomography (CT) is usually the preferred modality to assess structural changes.
Objectives: The aim of this study was to evaluate the performance of magnetic resonance imaging (MRI) for detecting subchondral bone erosions of SIJ in patients with suspected SpA. SIJ CT findings were considered as the gold standard when interpreting results.
Methods: A cross-sectional prospective monocentric study included consecutive patients aged over 16 and consulting for symptoms suggestive of SpA from February 2014 to February 2017. Patients with a confirmed sacroiliitis on pelvic radiograph were not included. Eligible patients underwent CT and MRI of SIJ. Imaging findings were assessed consensually by 2 experimented musculoskeletal radiologists, blinded to the clinical and laboratory data. Erosion was defined as resorption or destruction of the subchondral bone. The sensitivity, specificity, positive and negative predictive values of MRI for detecting SIJ erosions were determined with CT results as gold standard.
Results: Fifty-four patients were enrolled: 13 men and 41 women. The average age at inclusion was 39.4 ± 11 years [17-59], and the average age at onset of symptoms was 35.6 ± 10.6 years [16-55]. Cervical, thoracic, lumbar and buttock pain were noted respectively in 46.3%,37%, 92.6%, and 57.4% of the studied patients. Sacroiliac compression test, distraction provocative test, sacral thrust test, Gaenslen's test, Faber's test (Patrick) and Mennel's test were respectively positive in 23, 18, 24, 12, 28, and 17 patients. HLA B27 typing was positive in 23.4% of patients. Erosions were detected by CT scan in 30 patients. MRI showed erosions in 18 of them. A significant association was found between CT and MRI results (p=0.000), and between the presence of erosions and the diagnosis of SpA (p= 0.05 for CT and p= 0.012 for MRI). Sensitivity, specificity, positive and negative predictive values of MRI for detecting subchondral erosions were respectively estimated at 60%, 100%, 100% and 66.7%.
Conclusion: Erosions of SIJ appear in early stages of SpA and have been reported in 60-90% of patients with axial SpA after mean symptom duration of 2.5 years[2, 3], hence the importance of the detection of these structural lesions. In our study, despite its moderate sensitivity, MRI showed an excellent specificity for detecting subchondral bone erosions.

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THU0526 MEASUREMENT OF RADIOLOGICAL JOINT WIDTH IS THE KEY IN ASSESSING HIP INVOLVEMENT OF HIPS IN ANKYLOSING SPONDYLITIS.

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Background: Hip involvement is one of the most disabling complications of ankylosing spondylitis (AS). Frequently, arthroplasty is necessary by the time symptoms appear.
Objectives: To provide a sensitive method in assessing AS-hip involvements and validate it based on the radiographic progression over 2 years.
Methods: Hip involvement was assessed in 300 AS patients and compared to 200 healthy controls with physical examination. Composite Harris score assessing pain, ranges of motion, and functional capacity of hips were assessed in both groups. Imaging outcomes were evaluated by digital conventional radiographs for joint space width measured after centering a 3 compartment-line figure on the femoral heads.
Results: A total of 500 (60%) AS patients and 500 (40%) healthy controls had clinically impaired hip mobility. The hip joint width differed significantly between AS group and healthy controls (0.93±0.54, range 5.41-0.35vs 4.83±0.74, range 6.72-3.56, P<0.0001). Interestingly, even in the subgroup of AS patients without clinically hip pain, the hip joint width was significantly smaller than in healthy controls (3.29±0.66, range 5.4-2.1 vs 4.83±0.74, range 6.72-3.56, P<0.0001). We then evaluated the MRI images of the same 300 subjects. First, we evaluated the 200 control subjects to establish a threshold. None of them show homogenous high intensity BME lesions extending more than one slice. we examine the MRI of the 300 AS patients. Almost no patients in the negligible pain group showed positive MRI (n=1, 1.2%). Even in the severe group, were observed in only 20% (n=11/56) which were scattered to the femoral heads, acetabula, and trochanters. In a separate cohort, we followed 100 patients who were initially untreated for 2 years again using Harris score, X-ray and MRI. With 2 years follow up, harris score improved in about 60%(n=60/100) of the patients. Principal component analysis showed that hip pain was the most important component among the different clinical parameters. Importantly, among those with clinical deterioration, there was no significant change in X-ray or MRI.
Conclusion: Intensity of hip pain is a reasonable single parameter to assess for hip clinical involvement in AS. The higher the hip pain, the narrower the hip joint width. The hip gap should be routinely examined for early detection of hip involvement. Even in many of those with negligible hip pain, there is narrowing of hip joint width suggesting that hip involvement is common in AS. Hip disease progresses very slowly over 2 years.

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Table1 AS group characteristics

AS group	Age	Sex	Duration (M)	Harris score	BASDAI	BASFI	BASMI	PO	CRP mg/dl	ESR MM/H	HLA-B27	joint width(mm)
Number	300	300	300	300	300	300	300	300	265	279	287	300
Median	27	1	48	77	5.8	36	1	0	1.27	22	1	1.75
Mean	29.94	0.74	67.38	71.83	5.69	37.48	1.26	0.03	2.85	25.10	0.92	1.95
Std. Deviation	10.52	0.44	63.39	8.84	1.58	18.78	1.58	1.25	4.98	19.53	0.27	0.94

Table2 Health control characteristics

Health control	Age	Sex	harris score	joint width(mm)
Number of values	200	200	200	200
Median	27.00	1.00	100.00	4.76
Mean	29.94	0.74	94.90	4.85
Std. Deviation	10.45	0.44	6.59	0.74

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Disclosure of Interests: Qing Han: None declared, Zhaohui Zheng: None declared, Kui Zhang: None declared, Zheng Yu: None declared, Fengfan Yang: None declared, Qiang Liang: None declared, Ping Zhu: None declared, Xenofon Baraliakos Grant/research support from: Grant/research support from: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB and Werfen, Consultant of: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB and Werfen, Speakers bureau: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB and Werfen
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THU0527 FREQUENCY AND ANATOMIC DISTRIBUTION OF MAGNETIC RESONANCE IMAGING LESIONS IN THE SACRO-ILIAC JOINTS OF HEALTHY SUBJECTS AND PATIENTS WITH SPONDYLOARTHRITIS

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Background: Lesions detected by magnetic resonance imaging (MRI) of the sacroiliac joints are critical to the diagnosis of non-radiographic axial spondyloarthritis (1). However, some lesions, such as bone marrow edema (BME), usually observed in patients with spondyloarthritis may be encountered in other conditions. BME have been described in patients with non-specific back pain, healthy subjects, women with postpartum and in athletes (2). Moreover, it has recently been shown that structural lesions of the sacroiliac joint, such as erosions and fat metaplasia, may be present in healthy subjects (3).
Objectives: To evaluate and compare the frequency and location of lesions (BME, subchondral condensation, fat metaplasia, erosions and ankylosis) on MRIs of the sacroiliac joint of healthy individuals and patients with spondyloarthritis.
Methods: This is a retrospective study conducted at the University Hospital of Besançon including 200 patients, each having received an MRI of the sacroiliac joints in coronal section and in T1 and Semicoronal short tau inversion recovery sequences. Two experienced readers evaluated the whole set of images to detect erosions, subchondral condensation, fat metaplasia, BME and ankylosis according to the definitions established by the Assessment of SpondyloArthritis MRI working group. We subdivided a sacroiliac joint into three segments, upper, medium and lower along the cranio-caudal axis. Within the middle segment, we retained 3 portions: anterior, intermediate, posterior along the ventro-dorsal axis. Overall, one sacroiliac joint contained five quadrants on the iliac side and five quadrants on the sacral side.
Results: Collected MRI of 200 patients (62% female), 96 patients had spondyloarthritis (mean age 37.4±11.8 years, 48% HLA-B27+), 104 subjects were unaffected by the disease (mean age 39.9±11.6 years, 11% HLA-B27+). Of the 96 spondyloarthritis patients, 62 (65%) had inflammatory buttock pain compared to 26 (25%) in the group without spondyloarthritis. BME was seen in 62 (65%) patients with spondyloarthritis mainly in the iliac quadrant of the intermediate middle segment and in 21 (20%) patients without spondyloarthritis predominantly in the antero-middle quadrant. There were equal BME in women and men with spondyloarthritis. Subchondral condensation occurred in 45% of patients without spondyloarthritis, mostly in the antero-middle quadrant and in 36% of patients with spondyloarthritis. Fat metaplasia was present in 35% of spondyloarthritis patients and in 23% of control patients. Erosions were seen in 31% of healthy patients and in 61% of patients with spondyloarthritis.
Conclusion: In this large retrospective cohort, we observed a significant frequency of inflammatory but also structural lesions on MRIs of sacroiliacs joints from healthy patients, which could lead to the misdiagnosis of spondyloarthritis. Fine identification of the location of these lesions is crucial to avoid erroneous diagnosis.
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THU0528 NAILFOLD VIDEOCAPILLAROSCOPY REPORTING IN CLINICAL RESEARCH: INTERNATIONAL DELPHI BASED CONSENSUS

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Background: Nailfold capillaroscopy (NVC), a non-invasive technique to assess microcirculation, is increasingly being incorporated into rheumatology routine clinical practice. Currently, the degree of description of NVC methods varies amongst research studies, making interpretation and comparison between studies challenging. In this field, an unmet need is the standardization of items to be reported in research studies using NVC.
Objectives: To perform a Delphi consensus on minimum reporting standards in methodology for clinical research, based on the items derived from a systematic review focused on this topic.
Methods: The systematic review of the literature on NVC methodology relating to rheumatic diseases was performed according to PRISMA guidelines (PROSPERO CRD42018104660) to July 22nd 2018 using MEDLINE, Embase, Scopus. Then, a three-step web-based Delphi consensus was performed in between members of the EULAR study group on microcirculation in rheumatic diseases and the Scleroderma Clinical Trials Consortium. Participants were asked to rate each item from 1 (not appropriate) to 9 (completely appropriate).
Results: In total, 3491 references were retrieved in the initial search strategy, 2862 were excluded as duplicates or after title/abstract screening. 632 articles were retrieved for full paper review of which 319 fulfilled the inclusion criteria. Regarding patient preparation before the exam, data were scarce: 38% reported acclimatization, 5% to avoid caffeine and smoking, 3% to wash hands and 2% to avoid manicure. Concerning the device description: 90% reported type of instrument, 77% brand/model, 72% magnification, 46% oil use, 40% room temperature and 35% software for image analysis. As regards to examination details: 76% which fingers examined, 75% number of fingers examined, 15% operator experience, 13% reason for finger exclusion, 9% number of images, 8% quality check of the images and 3% time spent for the exam. Then, a three-round Delphi consensus on the selected items was completed by 80 participants internationally, from 31 countries located in Australia, Asia, Europe, North and South America. Some items reached the agreement at the second round (85 participants), and other items were suggested as important to consider in a future research agenda (e.g. temperature for acclimatization, the impact of smoking, allergies at the application of the oil to the nailbed, significance of pericapillary edema, methods of reporting hemorrhages, ramified and giant capillaries). The final agreement results are reported below:

PATIENT PREPARATION	1-3	4-6	7-9	Median (rating 1-9)
Patients should undergo a period of acclimatization	4	8	73	8
Patients should be asked to remove nail polish prior to procedure	10	14	61	9
Patients should be asked to remove artificial or gel nails prior to procedure	9	13	63	9
Patients should be asked to avoid manicure prior to procedure	0	10	75	9
Patients should be asked about their job and hobbies	4	10	71	9
Patients should be asked about their sport and physical activities (*i.e.* outdoor/indoor activities)	10	14	61	8
Patients should be asked about their dominant hand	6	14	65	8
Patients should be asked about specific medications (*i.e.* beta-adrenergic blockers, vasodilators, anticoagulants and antihypertensive drugs) and other agents with vasoactive effects (*i.e.* cannabis, cocaine, amphetamines)	2	6	77	9
Patients should be asked about their comorbidities	5	3	77	9
Patients should be asked about recent finger trauma, nail biting (onychophagy) and/or habit of self-injuring the cuticles	2	4	79	9
Patients should be asked to provide a detailed description of digital colour changes (to ascertain the diagnosis of Raynaud's phenomenon)	2	9	74	9
Specify whether the exam is performed during a Raynaud's attack	13	15	57	8
Patients should be asked about their age	3	8	74	9
Patients should be asked about history of digital ulcers	6	5	69	9
Capillaroscopy should not be performed during RP attack	13	12	55	8
DEVICE DESCRIPTION				
The make and model of the nailfold capillaroscopy device should be reported	1	12	72	9
Details of magnification should be reported	0	2	83	9
The use of automated grid should be reported	0	10	75	8
The use of oil should be reported	14	13	58	8
Details of computer software for image analysis should be reported	8	11	66	9
EXAMINATION DETAILS				
Details of experience or qualification of personnel responsible for image acquisition and interpretation should be reported	9	16	60	8
In case of more than one examiner, training for each examiner should be specified	10	15	60	8
The number of fingers examined should be reported	1	0	84	9
It should be reported which fingers have been examined	2	2	81	9
Each finger should be analyzed and reported separately or together based on the study design	18	17	50	7
Images of each finger should be coded, numbered and stored in order to allow comparative/prospective studies	2	14	69	8
Reasons for finger exclusion should be reported	2	6	77	9
Number of images collected at each nailfold should be reported	6	17	62	8
Details of image quality (and missing data) should be reported	2	15	68	8
Details of global condition of the hands (e.g. flexion contractures) should be reported	6	15	64	8
Details on image reading (e.g. blind reading) should be reported	7	8	70	9
Report the overall pattern (i.e. normal: stereotype normal and non-specific abnormalities versus abnormal: scleroderma patterns	1	8	76	9
Report the validated scleroderma patterns (i.e. early, active, late or scleroderma-like)	0	8	77	9

Conclusion: On the basis of the available literature the description of NVC methods was highly heterogeneous and individual published studies differed markedly. These practical suggestions developed using a Delphi process among international participants provide a guidance to improve and to standardize the NVC methodology in future clinical research studies.

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THU0529 CAPILLAROSCOPIC ALTERATIONS IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

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Background: Nailfold capillaroscopy (NFC) is a useful, noninvasive, widely available diagnostic tool in rheumatology practice. We commonly use it to describe patterns of abnormalities in systemic sclerosis however we have enough data which proves NFC usefulness for monitoring idiopathic inflammatory myopathies (IIM) considering it as diagnostic tool, monitoring of disease activity and treatment efficiency. Despite evident clinical relevance of NFC in IIM patients we still do not have clear capillaroscopic images for IIM definition.

Objectives: That's why, the goal of our research was aimed to analyze capillaroscopic peculiarities among IIM patients and find possible associations with clinical and activity data.

Methods: 69 patients with IIM were examined and 47 IIM patients with capillaroscopic alterations were included in the study, 26 patients with dermatomyositis (DM) and 21 patients with polymyositis (PM) according to the Targoff Criteria (1997). NFC we performed using *Dino*-Lite CapillaryScope with 200 magnification. We assessed nailfold capillary density (NCD), presence of microhemorrhages, giant, dilated and ramified capillaries, scleroderma patterns (defined as an early, active or late pattern) and neovascular pattern (defined as an active and late scleroderma patterns). To asses disease activity we use Manual Muscle Testing 8 (MMT8), Health Assessment Questionnaire (HAQ), Myositis Disease Activity Assessment Tool (MDAAT), Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI), physician's VAS, patient's VAS, serum muscle enzymes levels. We divided patients into 4 groups: 1st group – 17 DM patients with active disease (8 of them with newly onset disease), 2nd group included 9 DM patients with inactive disease, 3rd group – 11 PM patients with active disease (5 of them with newly onset disease) and 4th group included 10 PM patients with inactive disease.

Results: The most common finding was low NCD, 70% of all patients had NCD lower than 6 per 1 mm. NCD for the 1st group was 4,4±1,12, 2nd group – 6,0±1,0, 3rd group – 5,8±1,1, 4th group – 9,2±2,1 ($F=26,27$, $p<0,001$). Hemorrhages were significantly more common among DM patients and active disease and were observed among 47,1% ($p=0,036$, $\chi 2=8,574$) with no significant difference with regard to the disease onset. Analyzing scleroderma patterns, among 1st group of patients – 17,6% had early, 47,1% – active, 35,3% – late pattern, in the 2nd group – 66,7% had early pattern, in the 3rd group – 27,3% patients with early and 18,2% with active pattern and in the 4th group – 50% of patients presented with early pattern ($p=0,001$, $\chi 2=31,87$). Neovascular pattern was found significantly more often among patients with active DM ($p=0,001$) with no regard to the disease onset. No statistically significant difference in giant and ramified capillaries distribution was found.

Conclusion: According to our results, we can admit that the most common capillaroscopic finding was decreased NCD, which were significantly lower among patients with active DM, the same as microhemorrhages and neovascular scleroderma pattern. This data suggests that NCD, microhemorrhages and neovascular scleroderma pattern could be consider as biomarkers of DM activity but not PM, therefore more detailed research with larger numbers of patients are required.

Disclosure of Interests: None declared

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THU0530 HIGHLY-SENSITIVE CARDIAC TROPONIN I AND BETA-2-GLYCOPROTEIN-I IGA ANTIBODIES INFORM THE UTILITY OF SCREENING AND FOLLOW-UP NON-INVASIVE CORONARY ATHEROSCLEROSIS EVALUATION AND OPTIMIZE CARDIOVASCULAR RISK ASSESSMENT IN RHEUMATOID ARTHRITIS

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Background: Occult coronary atherosclerosis burden predicts mid-term cardiovascular disease (CVD) events in rheumatoid arthritis (RA) above and beyond Framingham D'Agostino cardiac risk score (FRS-DA). Highly-sensitive cardiac troponin I (hs-cTnI) levels in blood associate with coronary plaque burden and event risk in RA. Moreover, IgA antibodies against beta2-glycoprotein-1 (a-b2GPI-IgA)- an atherosclerotic plaque antigen- in RA promote coronary plaque progression and moderate the effect of inflammation on CVD events. It is currently unclear when to recommend a screening, non-invasive coronary atherosclerosis evaluation in asymptomatic RA patients and whether such an assessment should be repeated.

Objectives: To explore whether either biomarker alone or their combination improved prediction of plaque presence on an initial coronary CT angiogram (CCTA) beyond FRS-DA score; to evaluate whether either biomarker predicted progression to extensive or obstructive plaque on a follow-up evaluation.

Methods: One hundred fifty RA patients underwent a baseline CCTA; 101 had repeat evaluation within 6.9±0.3 years. Hs-cTnI and a-b2GPI-IgA were assessed at baseline; the latter were confirmed 12 weeks later, if positive. Lesions rendering greater than 50% luminal stenosis were considered obstructive. Extensive plaque was defined as >5 coronary segments with plaque, or stenosis score>5, or coronary artery calcium score (CAC)>100. The diagnostic accuracy of FRS-DA alone vs. with hs-cTnI or a-b2GPI-IgA individually or combined for plaque or CAC at baseline was evaluated as area under the curve (AUC). Improvement

in prediction accuracy between constructs was further assessed as integrated discrimination improvement (IDI). Similar AUC and IDI constructs evaluated the transition to obstructive or extensive atherosclerosis at follow-up in patients with baseline non-extensive or non-obstructive disease.

Results: High hs-cTnI (>1.5pg/ml) added to FRS-DA increased AUC from 0.717 to 0.731 (Figure 1A) and improved prediction accuracy for baseline plaque [IDI=0.041 (SE)=0.017, p=0.015]. In contrast, a-b2GPI-IgA did not [IDI=0.005 (0.006), p=0.47] and the combination offered no added benefit to the hs-cTnI model alone. Similar observations were made for CAC. Presence of a-b2GPI-IgA independently associated with coronary plaque progression (IRR=1.67 [95%CI 1.04-2.67]), whereas hs-cTnI did not. Likewise, a-b2GPI-IgA associated with transition to extensive or obstructive disease independently of FRS-DA (OR=13.48 [95%CI 2.09-86.99]). Notably, 71.4% of a-b2GPI-IgA positive patients with high hs-cTnI progressed to extensive or obstructive disease compared to 7.7% of a-b2GPI-IgA negative subjects with high hs-cTnI (p=0.008). Addition of a-b2GPI-IgA to FRS-DA in patients with prevalent non-extensive non-obstructive plaque increased AUC from 0.785 to 0.900 (Figure 1B) and significantly improved the prediction for development of obstructive or extensive atherosclerosis at follow-up [0.387, (0.13), p=0.003].

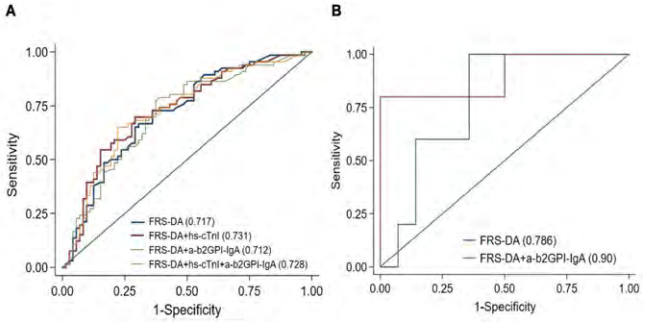


Figure 1. (A) Diagnostic accuracy for prediction of occult coronary atherosclerosis at baseline. FRS-DA alone is the base model followed by addition of hs-cTnI or a-b2GPI-IgA individually or combined. **(B)** Diagnostic accuracy for progression from non-obstructive and non-extensive plaque at baseline to obstructive or extensive atherosclerosis at follow-up.

Conclusion: High hs-cTnI improved the risk of baseline plaque presence beyond clinical risk score and may trigger an initial non-invasive coronary atherosclerosis evaluation. A-b2GPI-IgA presence may justify a follow-up evaluation in patients with non-extensive, non-obstructive plaque at baseline.

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THU0531 A PROSPECTIVE STUDY EVALUATING THE ROLE OF 68GA-RGD2 PET/CT ANGIOGENESIS IMAGING IN ASSESSING DISEASE ACTIVITY AND TREATMENT RESPONSE IN RHEUMATOID ARTHRITIS AND ITS COMPARISON WITH DAS28

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Background: PET/CT imaging of synovial angiogenesis using ^{68}Ga-RGD (cyclic tripeptide agent targeting $\alpha_v\beta_3$ integrin) to study disease activity in rheumatoid arthritis (RA) has been demonstrated earlier in a few patients. However, post treatment changes in disease activity on ^{68}Ga-RGD$_2$ PET/CT imaging have not been adequately assessed.

Objectives: To compare the performance of ^{68}Ga-RGD$_2$ PET/CT with disease activity score (DAS) 28 in assessing disease activity and treatment response in RA.

Methods: Thirty patients (24F, 6M) aged 43±12 years with clinically diagnosed RA were prospectively studied. After calculation of DAS28 by a rheumatologist, all 30 patients underwent ^{68}Ga-RGD$_2$ PET/CT scan. Of these, 27 patients underwent a second ^{68}Ga-RGD$_2$ PET/CT scan and clinical assessment after at least 3 months of treatment. Total body and regional images of the upper limbs were acquired and interpreted by two nuclear medicine physicians blinded to the clinical findings. Joints showing focally increased tracer uptake compared to the background were considered positive and joints showing uptake equal to or less than background were considered negative. Data of 30 patients were used for inter-observer and inter-modality agreement calculations. Changes in PET parameters and DAS28 were compared in 27 patients to assess treatment response.

Results: Out of 1560 joints examined in the initial scan, 394 were positive on PET/CT compared to 348 on clinical evaluation. Inter-observer agreement between nuclear medicine physicians was excellent (Cohen's kappa 0.92, p<0.05) and inter-modality agreement between PET and clinical examination was moderate (Cohen's kappa 0.55, p<0.05). The DAS28 and SUVmax values (highest and average) of 27 patients showed significant reduction on follow-up compared to the initial evaluation. There was significant correlation between percentage change in DAS28 and percentage change in scan parameters like PET positive joint counts (0.689, p<0.001), average SUVmax (0.712, p<0.001) and highest SUVmax values (0.558, p=0.003) of scan-positive joints in 27 patients. Additional advantages of ^{68}Ga-RGD$_2$ PET/CT included objective assessment, whole body evaluation of all small and large joints, and greater reproducibility.

Conclusion: ^{68}Ga-RGD$_2$ PET/CT is a promising tool for objective assessment of disease activity and treatment response in patients with RA.

Table 1. Clinical and PET parameters of the patients

Parameter	Initial data (n=27) Mean (SD)/Median (IQR)	Follow-up data (n=27) Mean (SD)/Median (IQR)
TJC(28)	10 (5-13)	3 (2-4)
SJC(28)	6 (3-7)	1 (0-2)
ESR	25 (20-41)	24 (18-35)
PtGA	6.0 (5.0-6.0)	3.0 (2.0-4.0)
DAS28(3)	5.14 (0.85)	3.74 (0.88)
DAS28(4)	5.60 (0.90)	3.80 (0.96)
PET positive Joints	12 (7-8)	4 (2-9)
aSUVmax	2.08 (1.68-2.52)	1.79 (1.00-2.06)
hSUVmax	3.45 (2.71-4.70)	3.34 (1.95-4.25)

TJC/SJC: tender/swollen joint counts; ESR: erythrocyte sedimentation rate; PtGA: patients global assessment scale; DAS: disease activity score; aSUVmax/hSUVmax: average/highest SUVmax (maximum standardized uptake value); SD: standard deviation; IQR: interquartile range

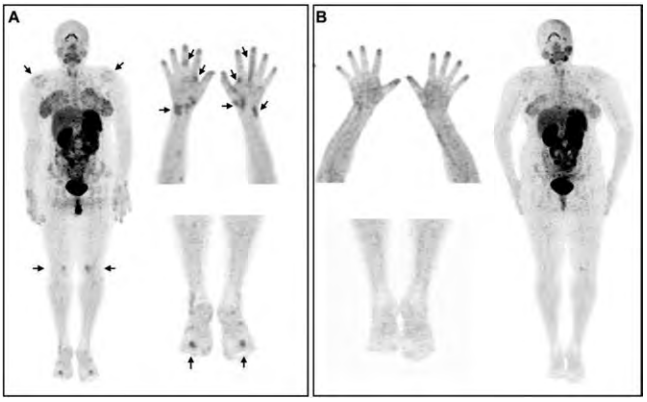


Figure 1. ^{68}Ga-RGD$_2$ PET scan of a 26-year female RA patient on treatment. **A.** Initial scan shows increased tracer uptake in multiple joints of upper and lower limbs and tendon sheaths of hands and ankle region (arrows); DAS28 was 4.56 (moderate disease activity) and ESR 12 mm/1st hour. **B**. Follow-up scan after 4 months shows resolution of tracer activity in the previously involved joints with only a mild focus persisting in the left knee joint; DAS28 was 1.73 (clinical remission according to ARA) and ESR 08 mm/1st hour.

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THU0532 SEMIQUANTITATIVE ANALYSIS OF BONE SCINTIGRAPHY TO PREDICT SPINAL PROGRESSION IN EARLY AXIAL SPONDYLOARTHRITIS: A PILOT STUDY

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Background: Axial spondyloarthritis (axSpA) is a chronic inflammatory disease that typically affects the axial joint and enthesis. Abnormal hyperplasia of osteoblasts in the vertebral corner is the underlying pathogenesis of syndesmophyte

formation. Therefore, detecting abnormal osteoblast hyperactivity in the axial joints of patients with axSpA might be an attractive imaging modality to detect potential of spinal structural progression. Bone scintigraphy is used to evaluate the sites of active bone formation by detecting osteoblast activities and visualizing the whole skeleton at once. Therefore, bone scintigraphy is a theoretically ideal imaging modality to predict abnormal bone growth of axial joints in patients with axSpA.

Objectives: To investigate whether bone scintigraphy with semiquantitative analysis in patients with early axial spondyloarthritis (axSpA) has prognostic value for predicting spinal structural progression of these patients after 2 years.

Methods: The records of 53 patients with early axSpA who underwent baseline bone scintigraphy were reviewed retrospectively. The sacroiliac joint to sacrum (SIS) ratio of bone scintigraphy was measured for semiquantitative analysis, and modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) and syndesmophyte growth were calculated at baseline and after 2 years. Receiver operating characteristic (ROC) curve analysis was used to determine the cutoff for the SIS ratio of bone scintigraphy. To identify factors associated with significant spinal structural progression, univariate and multivariate logistic regression analyses were performed. Significant progression of spinal structural damage over 2 years was defined as an increase of mSASSS of at least 2 units for 2 years or new syndesmophyte growth/bridging of pre-existing syndesmophytes.

Results: Multivariate regression analysis revealed obesity (P = 0.023), current smoking status (P = 0.012), and high SIS ratio of bone scintigraphy (P = 0.015) as independent predictors for worsening mSASSS by at least 2 units over 2 years. For new syndesmophyte growth/bridging of pre-existing syndesmophytes over 2 years, current smoking (P = 0.013), high SIS ratio of bone scintigraphy (P = 0.025), and pre-existing syndesmophyte (P = 0.036) were independent predictors.

Conclusion: Semiquantitative analysis of bone scintigraphy (high SIS ratio) in patients with early axSpA may be useful for identifying patients at high risk for spinal structural progression after 2 years.

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THU0533 A SINGLE MRI DIXON SEQUENCE TO ASSESS DISEASE ACTIVITY AND CARTILAGE IN EARLY RHEUMATOID HANDS: ONE SEQUENCE TO ASSESS THEM ALL?

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Background: OMERACT recommends three "core set" MRI sequences with an optional cartilage-dedicated sequence to perform Rheumatoid Arthritis (RA) MRI scoring (RAMRIS) (1). Dixon method allows the production of four different images from a single MRI sequence.

Objectives: To test a short MRI protocol based on a single Dixon sequence to assess disease activity and cartilage in hands of patients with early RA.

Methods: Twenty-four patients (16 women, mean age 45.7 years old) with early DMARD-naive RA meeting the ACR/EULAR 2010 criteria were prospectively included. Both hands of each patient were imaged with MRI including contrast-enhanced T1-weighted Dixon and OMERACT "core set" MRI sequences and with conventional radiography.

Two musculoskeletal radiologists (R1 and R2) separately assessed disease activity according to RAMRIS scoring system based on the Dixon images (contrast-enhanced T1-weighted Dixon water-only images to score synovitis, tenosynovitis and osteitis and contrast-enhanced T1-weighted Dixon fat-only images to score erosions) and the three OMERACT "core set" MRI sequences (contrast-enhanced fat-saturated T1-weighted images to score synovitis and tenosynovitis, fat-saturated T2-weighted images to score osteitis and T1-weighted images without contrast-material injection to score erosions).

One radiologist (R1) separately measured the thickness of the cartilage in the joints corresponding to those assessed by the Sharp/van der Heijde modified scoring method on contrast-enhanced T1-weighted Dixon out-of-phase images and radiographs (2).

RAMRIS scoring and measurement of the cartilage thickness were repeated by R1 to assess intra-observer agreement. Statistical analysis was based on intra-class correlation coefficients (ICC) with 95% confidence interval to assess inter-technique, intra-observer and inter-observer agreement. The strength of agreement was interpreted as follows: ≤0, poor; 0.01-0.20, slight; 0.21-0.40, fair; 0.41-0.60, moderate; 0.61-0.80, substantial and ≥0.81, excellent.

Results: Agreement between total RAMRIS scores obtained with the Dixon water- and fat-only images and total RAMRIS scores obtained with the OMERACT sequences was excellent for R1 (0.94; 0.86-0.97) and R2 (0.91; 0.81-0.96). Intra-observer agreement was excellent with Dixon images (0.97; 0.92-0.98) and OMERACT sequences (0.96; 0.90-0.98). Inter-observer agreement was excellent with Dixon images (0.92; 0.82-0.96) and OMERACT sequences (0.93; 0.85-0.97).

Agreement between the measures of cartilage thickness on the Dixon out-of-phase images and the measures of cartilage thickness on radiographs was substantial (0.71; 0.66-0.75). Intra-observer agreement was excellent with Dixon out-of-phase images (0.94; 0.93-0.95) and radiographs (0.93; 0.92-0.94).

Conclusion: An MRI protocol based on a single contrast-enhanced T1-weighted Dixon sequence allows reproducible RAMRIS scoring and measurement of the cartilage thickness. Further studies should be performed to evaluate the value of a short MRI protocol based on the Dixon method to monitor disease activity including cartilage loss in treated RA patients.

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Disclosure of Interests: Thomas Kirchgesner: None declared, Maria Stoenoiu: None declared, Nicolas Michoux: None declared, Patrick Durez Speakers bureau: AbbVie, Bristol-Myers Squibb, Celltrion, Eli Lilly, Pfizer, Sanofi, Bruno Vande Berg: None declared

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THU0534 LUNG ULTRASOUND IN PATIENTS WITH SECONDARY INTERSTITIAL LUNG DISEASES

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Background: Currently, lung ultrasound (LUS) is increasingly used in rheumatology.

Objectives: To evaluate the relationship between lung ultrasound and pulmonary function and disease activity in patients with rheumatic diseases with secondary lung involvement.

Methods: Thirty patients with rheumatic diseases were included in the study, who, according to the data of the high-resolution RCT of lungs (64-slice CT system Philips Diamond Select Brilliance), showed interstitial lung involvement as a type of nonspecific interstitial pneumonia. In 4 patients, mixed connective tissue disease (MCTD) was diagnosed, 20 had systemic vasculitis (SV), and 6 had rheumatoid arthritis (RA). The mean age of the patients was 56,55 ± 10,59, the duration of the disease was 2,3 ± 1,2 years. All patients underwent a standard clinical examination, the following indices and scales were used to assess the activity of the underlying disease: VDI damage index, Bermingham systemic vasculitis activity scale (BVAS), RA activity scale (DAS 28-CRP). The functional state of the lungs was assessed using spirometry, bodipletismography, gas diffusion "single breath". LUS was carried out for the evaluation of the location and number of B-lines on both right and left hemithoraces using commercially available echographic equipment with a 5-12 MHz linear transducer (Accuvix A30, Samsung Medison).

Results: Most patients had an average number of B-lines 24,5[11,5;34,0]. There were no significant differences in the number of B-lines between groups of patients of different nosologies. The total number of B-lines correlated with the index of activity of systemic vasculitis BVAS ($p<0,05$; $r=0,83$). There were no statistically significant correlations with clinical manifestations of pulmonary involvement.

Conclusion: Lung ultrasound may be useful in screening secondary lung involvement in patients with rheumatic diseases with high activity.

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THU0535 ARE THERE DISCRIMINATING FEATURES BETWEEN "SCLERODERMA" AND "SCLERODERMA-LIKE" CAPILLAROSCOPIC PATTERN?

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Background: The "scleroderma" type capillaroscopic pattern is a diagnostic criterion of the EULAR/ACR scoring system for systemic sclerosis (SSc). In addition, the validated staging system of Cutolo et al. is used that categorizes the capillaroscopic changes into an "early", "active" and "late" phase. A "scleroderma-like" capillaroscopic pattern can also be observed in a number of rheumatic diseases, i.e., dermatomyositis (DM), systemic lupus erythematosus (SLE), undifferentiated connective tissue diseases, overlap syndromes, and rheumatoid arthritis (RA).
Objectives: To evaluate the categories "early", "active" and "late" in "scleroderma-like" pattern in rheumatic diseases different from SSc and to assess the presence of discriminating features between "scleroderma" and "scleroderma-like" capillaroscopic pattern.
Methods: 544 capillaroscopic images that showed a "scleroderma" and "scleroderma-like" pattern have been analysed from the following groups: 405 images from 42 SSc patients, 66 images from 4 patients with DM, 37 images from 9 RA patients and 36 images from 5 SLE patients.
Results: 30 of the images obtained from SSc patients demonstrated an "early" phase capillaroscopic pattern, 284 an "active" phase, and 29 a "late" phase. In 62 images, neoangiogenesis could be observed in images from an "active" phase capillaroscopic pattern that could be classified as "active-to late stage of transition". Among the 66 images from DM patients, 43 capillaroscopic pictures revealed an "active" phase and 23 - neoangiogenic capillaries with giant capillary loops, capillary loss and derangement ("active neoangiogenic" pattern). An "early" and "late" phase capillaroscopic pattern was not present in this group. The images from SLE patients (n=36) could be classified into the following groups: 3 images "early" phase, 29 images "active" phase, and 4 images with neoangiogenesis during the active phase. A "late" phase capillaroscopic pattern was not observed. In the group of capillaroscopic pictures from RA patients (n=37), an "early" phase changes could be observed in 11 images (8 out of 9 patients) and an "active" phase in 3 images (2 patients). 23 of the images from RA patients demonstrated evidence of neoangiogenesis associated with mild capillary derangement, moderate capillary loss, and single giant capillaries ("advanced neoangiogenic" pattern).
Conclusion: In conclusion, an "early" phase "scleroderma" pattern is present in RA and SLE patients, but obviously not in DM patients. An "active" phase "scleroderma" pattern was found in all three patients groups other that SSc i.e., DM, SLE and RA. In DM, profound neoangiogenesis is also a characteristic finding. In RA, advanced neoangiogenesis with moderate devascularization and single giant capillaries could also be documented. A classic "late" phase "scleroderma" pattern was found only in SSc patients and was not observed in other rheumatic diseases i.e., SLE, RA, DM. The results of the current study suggest presence of differences between "scleroderma" and "scleroderma-like" capillaroscopic pattern that may reflect different pathogenic mechanisms of microvascular damage.
Disclosure of Interests: Sevdalina Lambova: None declared, Ulf Müller-Ladner Speakers bureau: Biogen
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THU0536 ASSOCIATION BETWEEN OVERWEIGHT/OBESITY AND DISEASE ACTIVITY ON BONE SCINTIGRAPHY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: In previous studies, obesity is highly prevalent in patients diagnosed with rheumatoid arthritis and it is positively associated with disease activity[1]. Although Tc-99m-labeled bone scintigraphy has been widely performed to evaluate the disease activity of the joints involved in this disease[2]; the effect of body mass index (BMI) on the results of bone scintigraphy is yet to be accessed.
Objectives: In the present study, we evaluated the relationship between BMI and uptake intensity of the joints that was measured using bone scintigraphy in patients with rheumatoid arthritis.
Methods: A total of 80 patients (21 men and 59 women; mean age 56±14 years) with rheumatoid arthritis who underwent Tc-99m methylene diphosphonate bone scintigraphy before treatment were enrolled in this study. Data were collected for baseline BMI and disease activity score for the 28 joints using erythrocyte sedimentation rate (DAS28-ESR) of these patients. Uptake intensity of these 28 joints was automatically measured for each patient using an in-house software, expressed as joint uptake-to-background normal bone uptake ratio (joint uptake ratio). The correlation of BMI with DAS28-ESR and joint uptake ratio on bone scintigraphy was assessed.
Results: Mean BMI of the enrolled patients was 24.4±3.7 kg/m^2 and 50 patients (62.5%) were classified as overweight/obesity. BMI was significantly positively correlated with the sum of 28 joint uptake ratios on bone scintigraphy ($p=0.021$, correlation coefficient=0.358) as well as DAS28-ESR ($p=0.030$). Patients with overweight/obesity (39.2±9.5) had significantly higher values of the sum of 28 joint uptake ratios than the other patients (33.9±9.5; $p=0.025$). In correlation analysis with each joint uptake ratio of 28 joints, BMI more significantly positively correlated with uptake ratios of shoulder, elbow, and knee joints than those in wrist and hand joints. In subgroup analysis of patients having low (DAS28-ESR ≤3.2) and high (DAS28-ESR >3.2) disease activity, BMI still showed significant positive correlation with the sum of 28 joint uptake ratio on bone scintigraphy in both subgroups ($p<0.05$ for all).
Conclusion: The Baseline BMI in patients with rheumatoid arthritis had significant positive correlation with joint uptake intensity measured on bone scintigraphy, especially for large joints. The results of our study might provide an evidence that supports an association between BMI and disease activity of rheumatoid arthritis.
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THU0537 VALIDITY AND DIAGNOSTIC PERFORMANCE OF FLUORESCENCE OPTICAL IMAGING MEASURING SYNOVITIS IN HAND OSTEOARTHRITIS. RESULTS FROM THE NOR-HAND STUDY.

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Background: Fluorescence Optical Imaging (FOI) demonstrates enhanced microcirculation in finger joints as a sign of inflammation.
Objectives: We wanted to assess the validity and diagnostic performance of FOI measuring synovitis, comparing it with Magnetic Resonance Imaging (MRI)- and ultrasound-detected synovitis in persons with hand osteoarthritis (OA).
Methods: Two hundred and twenty-one participants (88% female, age (SD) 60.6 (6.2) years) with hand OA from the Nor-Hand study underwent FOI and grey scale (GS) and power Doppler (PD) ultrasound of the bilateral hands and contrast-enhanced MRI of the dominant hand. The FOI scan was performed after the administration of an intravenous fluorescence dye (indocyanine green, ICG) and 360 images (1/second) were produced in 6 minutes. One reader scored the bilateral distal interphalangeal (DIP), proximal interphalangeal (PIP), metacarpophalangeal (MCP) and first carpometacarpal (CMC-1) joints for FOI enhancement, blinded for clinical information and other imaging data. Images were scored according to the 'FOI activity score' (FOIAS) where four out of 360 images are assessed, defined as phase 1, 2, and 3, based on the inflow and washing out of the fluorescence dye, and a composite image (Prima Vista Mode; PVM) of the 240 first images. Two readers evaluated separately the severity of

MRI-defined synovitis (grade 0-3) in the DIP, PIP, MCP and CMC-1 joints of the dominant hand and the severity of GS synovitis (grade 0-3) and PD activity (grade 0-3) in the same joints of the hands bilaterally. Spearman's rho was calculated for correlations between sum scores of all joints for FOI, MRI and ultrasound and sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV) and area under the curve (AUC) for FOI using MRI and ultrasound as reference.

Results: Despite frequent MRI and ultrasound findings in the CMC-1 joint, no FOI enhancement was detected in the thumb base, and CMC-1 was excluded from the analyses. FOI had poor to fair correlations with MRI and GS synovitis and PD activity. The strongest correlation with MRI was found for PVM in the PIP joints with Spearman's rho of 0.32, while the DIP joints had consistently the weakest correlations ranging from 0 to 0.14 (Figure 1). None of the FOI phases or PVM demonstrated both good sensitivity and specificity, and AUC remained low with both MRI and GS synovitis as a reference (table 1). The NPVs of FOI were consistently higher when GS synovitis was used as reference rather than MRI, due to higher frequency of low degree MRI-defined synovitis. However, when changing cut-off for MRI synovitis as reference from grade 1 to grade 2 the diagnostic performance of FOI increased to the level of GS synovitis. The diagnostic performance for FOI was similar with both GS synovitis and PD activity as reference.

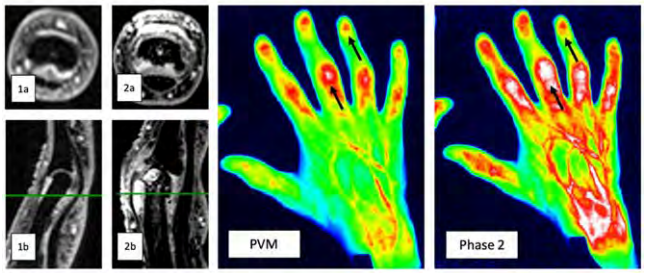
Table 1. Diagnostic performance of FOI measuring synovitis in hand OA using MRI and GS synovitis as reference

FOI	Reference	Sensitivity	Specifisity	PPV	NPV	AUC
PVM	MRI	0.48	0.72	0.61	0.61	0.61
Phase 1		0.02	0.99	0.61	0.53	0.50
Phase 2		0.58	0.62	0.58	0.62	0.60
Phase 3		0.24	0.90	0.67	0.57	0.57
PVM	GS	0.59	0.64	0.17	0.93	0.62
Phase 1		0.02	0.99	0.28	0.89	0.51
Phase 2		0.69	0.56	0.17	0.94	0.63
Phase 3		0.23	0.86	0.17	0.90	0.56

FOI; Fluorescence optical imaging, PVM; Prima Vista Mode, GS; Grey scale, PVM; Prima Vista Mode, PPV; Positive Predictive Value, NPV; Negative Predictive Value, AUC; Area under the curve

Conclusion: FOI sum scores showed poor to fair correlations with MRI- and ultrasound-detected synovitis in persons with hand OA. These findings might be explained by the low-grade inflammation with minor vascularization in the majority of inflamed joints. None of the FOI phases or PVM demonstrated both good sensitivity and specificity and the method was not able to detect CMC-1 synovitis.

Figure 1: MRI synovitis grade 2 in DIP 4 (1a-1b) and grade 3 in PIP 3 (2a-2b) compared with FOI Phase 2 and FOI PVM with good agreement in PIP joint and poor agreement in DIP joint.



MRI; Magnetic resonance imaging, FOI; Fluorescence optical imaging, PVM; Prima Vista Mode, DIP; distal interphalangeal joint, PIP; proximal interphalangeal joint

Disclosure of Interests:

Øystein Maugesten: None declared, Alexander Mathiessen: None declared, Hilde Berner Hammer Consultant of: Has received fees as consultant from Roche, AbbVie and Novartis., Speakers bureau: Has received fees for speaking from AbbVie, BMS, Pfizer, UCB, Roche, MSD and Novartis, Tore K. Kvien Grant/research support from: Received grants from Abbvie, Hospira/Pfizer, MSD and Roche (not relevant for this abstract)., Consultant of: Have received personal fees from Abbvie, Biogen, BMS, Celltrion, Eli Lily, Hospira/Pfizer, MSD, Novartis, Orion Pharma, Roche, Sandoz, UCB, Sanofi and Mylan (not relevant for this abstract)., Paid instructor for: Have received personal fees from Abbvie, Biogen, BMS, Celltrion, Eli Lily, Hospira/Pfizer, MSD, Novartis, Orion Pharma, Roche, Sandoz, UCB, Sanofi and Mylan (not relevant for this abstract)., Speakers bureau: Have received personal fees from Abbvie, Biogen, BMS, Celltrion, Eli Lily, Hospira/Pfizer, MSD, Novartis, Orion Pharma, Roche, Sandoz, UCB, Sanofi and Mylan (not relevant for this abstract)., Sigrid Valen Hestetun: None declared, Till Uhlig: None declared, Sarah Ohrndorf: None declared, Ida K. Haugen: None declared

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THU0538 IN PSORIATIC ARTHRITIS PATIENTS CONSIDERED IN REMISSION BY THEIR RHEUMATOLOGIST, CAN DISCORDANCE IN DISEASE ACTIVITY ASSESSMENT BETWEEN PATIENT AND RHEUMATOLOGIST BE EXPLAINED BY RESIDUAL INFLAMMATION AS MEASURED BY ULTRASONOGRAPHIC EXAMINATION?

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Background: Psoriatic arthritis (PsA) is a heterogeneous disease and its assessment is sometimes difficult. Perception of disease activity by patient and physician is frequently discordant in patients in clinical remission. Ultrasound (US) is an imaging technique, which can detect inflammation in PsA.

Objectives: The aim of our study was to assess whether persistence of disease activity evaluated by the patient, considered in remission by his rheumatologist, was associated with inflammation measured by US.

Methods: We performed a transversal monocentric study. PsA patients were included if they met the CASPAR criteria and were considered in remission by their rheumatologist. Demographic data, characteristics of the disease and treatments were collected. Discordance was defined by a difference between patient's and rheumatologist's global assessment ≥30/100 on a Visual Analogic Scale. An US examination was performed on 50 joints, 28 tendons and 14 entheses by an independent investigator. Synovial or tendon sheath hypertrophy and PD signal were evaluated on a semi-quantitative scale, B Mode and PD signal abnormalities on entheses were searched, according to the EULAR-OMERACT scoring system. US remission was defined by no power Doppler (PD) signal on joints, tendons and entheses and minimal US activity by maximum one PD signal on the same sites. Univariate and multivariate analyses were performed to evaluate factors associated with US abnormalities.

Results: Sixty-two PsA patients were included. 40.3% were women, the mean (SD) age was 55 (14) years, 42% were in US remission and 71% in minimal US activity (Table 1), 19.4% had ≥1 PD synovitis and 88.7% had a B mode synovitis, 95.2% had a B mode abnormality on entheses and 51.6% had ≥1 PD signal on entheses. Thirty nine percent had a discordant disease activity assessment with their rheumatologist. In univariate analysis, discordance was not associated with US remission (OR=1.71 (95%CI 0.61-4.83), p=0.224) or US minimal disease activity (OR=0.99 (95%CI 0.32-3.05), p=0.602). In multivariate analysis, US remission was independently associated with female gender (OR=3.94 (95%CI 1.20-12.9), p=0.024) and younger age (OR=0.95 (95%CI 0.91-0.99), p=0.027). Minimal US activity was associated with history of enthesis lesion (OR=11.26 (95%CI 1.34-94.93), p=0.026) and age (OR=0.95 (95%CI 0.90-1), p=0.044).

Table 1. Ultrasound characteristics of the 62 PsA patients.

	N (%)
Ultrasound remission	26 (41.9)
Ultrasound minimal disease activity	44 (71)
Patients with ≥1 grey scale synovitis	55 (88.7)
Patients with ≥1 Power Doppler synovitis	12 (19.4)
Patients with ≥1 grey scale tenosynovitis	15 (24.2)
Patients with ≥1 Power Doppler tenosynovitis	1 (1.6)
Patients with ≥1 grey scale enthesitis lesion (thickness, hypo echogenicity, calcification, enthesophyte, erosion, bursitis)	59 (95.2)
Patients with ≥1 Power Doppler enthesitis	32 (51.6)

Conclusion: Our study showed persistent inflammation evaluated by US in PsA patients considered in remission by their rheumatologist. However, prevalence of residual inflammation evaluated by US was not higher in patients with self-assessment of their disease discordant from their rheumatologist.

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THU0539

IMPACT OF BODY MASS INDEX ON THE AGREEMENT BETWEEN ULTRASOUND- AND CLINICAL ASSESSMENTS OF DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS: MULTICENTRE AND CROSS-SECTIONAL STUDY

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Background: Clinical assessment of swollen joint count (SJC) in rheumatoid arthritis (RA) might be affected by obesity in terms of obesity-related excess adipose tissue.
Objectives: To compare the level of agreement between synovitis evaluated by Power Doppler ultrasound (PDUS) and clinical examination (SJC as component of SDAI) in obese (O) (i.e. Body Mass Index (BMI) >30) versus non-obese (NO) (BMI≤30) RA patients.
Methods: RA patients ≥18 years fulfilling 2010 ACR-EULAR criteria were included in the cross-sectional multicentre (13 centres) French observational RABODI study (ClinicalTrials.gov Identifier: NCT03004651). Clinical synovitis was evaluated on 44 joints. ESR and CRP were collected and SDAI, DAS28, DAS were calculated. A standard US examination on 44 joints was performed by an independent investigator blinded to clinical data. US synovitis was defined by a synovial hypertrophy ≥1 and PD signal≥1 on a semi-quantitative scale according to the EULAR-OMERACT scoring system. Levels of agreement between number of synovitis defined by PDUS and clinical examination were compared in O versus NO patients using Chi2 test, and Kappas (k) and ORs were calculated. A patient was considered "discordant" if ≥1 joint was discordantly classified by PDUS and clinical examination. SDAI was calculated and compared, with SJC defined either by clinical examination or PDUS.
Results: 121 patients were included: mean (SD) age of 58.5 (12.7) years, mean disease duration of 11.1 (9.7) years. 81% were female, 84.3% anti-CCP positive, 63.6% had erosive disease. Mean SDAI was 12.6 (±10.2). 53 (43.8%) had a BMI >30 and 68 (56.2%) ≤30. 59 (48.7%) and 62 (51.2%) had a SDAI≤11 and >11, respectively. The 2 groups were comparable, except for weight (mean (SD) 65.4 (13.5) vs 96.7 (14.7) kg, p< 0.001), some comorbidities (diabetes, asthma and fibromyalgia more frequent in O patients), tender joint count (mean 4.04 (±5.23) in NO vs 7.38 (±8.64) in O, p=0.021). Mean number of SJC was 2.4 (3.3), and PDUS 6.7 (±6.3). Levels of agreement between clinical and PDUS findings were comparable in O vs. NO patients regarding SDAI and other scores (Table). Patients with ≥3 discordant joints were numerically higher in O patients compared to NO (26/53 (49.1%) vs 22/68 (32.4%), p=0.062). At the joint level, discordance was higher in O patients in MCP4 (p=0.057), wrist (p=0.089).

Table. Level of agreement between PDUS synovitis and SJC in obese versus normally weighted RA patients

Score with PDUS vs. SJC		BMI ≤ 30 N=68	BMI > 30 N=53	OR (95%CI)	P*
SDAI	Non-Discordant (ND)	63	46	**1.92 (0.57-6.42)**	**0.28**
	Discordant (D)	5	7		
	Kappa	**0.85**	**0.73**		
DAS28	ND	62	47	**1.32 (0.4-4.35)**	**0.64**
	D	6	6		
	Kappa	**0.81**	**0.77**		
DAS44	ND	63	52	**0.24 (0.03-2.14)**	**0.23**
	D	5	1		
	Kappa	**0.83**	**0.96**		
≥1 synovitis	ND	51	35	**1.54 (0.7-3.4)**	**0.28**
	D	17	18		
	Kappa	**0.50**	**0.32**		

Conclusion: In RA patients, despite a perceived higher difficulty to clinically detect SJ in O patients, the discrepancy between clinically- and PDUS defined synovitis was not significantly higher than in NO patients, and did not impact the extend of the definition of disease activity level.

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THU0540

A PHASE 2B STUDY OF INTRAVENOUSLY (IV) ADMINISTERED TC 99M TILMANOCEPT TO DETERMINE DIFFERENTIAL UPTAKE, REPRODUCIBILITY OVER TIME AND IMAGE STABILITY IN HEALTHY SUBJECTS AND IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA) ON STABLE TREATMENT

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Background: At present, there are no reliable noninvasive means to directly monitor disease activity in RA patients. Activated macrophages are a critical component of the inflammatory etiology of RA due to their role in prolonged RA joint inflammation and destruction through the release of pro-inflammatory cytokines and chemokines. Tc 99m tilmanocept is a radiopharmaceutical imaging agent that binds with high affinity to the macrophage mannose receptor CD206 that resides on activated macrophages. Previous clinical trials demonstrated safety and tolerability of Tc 99m tilmanocept, as well as a determination of optimal clinical dose and timeframe for RA imaging.
Objectives: The current phase 2b study aims to evaluate reproducibility and stability of imaging and will assess quantitative Tc 99m tilmanocept uptake cut points that reliably enable discrimination between joints of healthy people and RA patients.
Methods: The analysis cohort contained 18 healthy controls (HC) clinically free of inflammatory joint disease and 12 subjects with clinically diagnosed RA who are on stable anti-inflammatory and/or anti-rheumatic therapy. Each subject received a 150-mcg dose of tilmanocept radiolabeled with 10 mCi of Tc 99m in a 3mL IV injection. Injection was followed by planar imaging at 60 and 180 minutes for both HC and RA subjects on study Day 0 and repeated in RA subjects on Day 8. Images were quantitatively assessed to detect localization within synovial spaces of bilateral hands and wrists by determining average pixel intensity in each region of interest relative to average pixel intensity in a joint-specific reference region.
Results: Data obtained from the interim analysis support the hypothesis that Tc 99m tilmanocept imaging can provide robust quantitative imaging in HC and RA subjects. Repeat images within and between days demonstrate root mean squared differences that are approximately 10% or less of the observed localization of Tc 99m tilmanocept. Qualitatively, images of HC indicated no disease-related site-specific localization, whereas localization is present in RA subjects at levels expected given the difference in macrophage number and density in different pathotypes of RA. Notably, images from patients with active RA exhibit the same localization patterns on images taken in a test-retest fashion on the same day as well as in subjects with images acquired on Day 0 and Day 8 (see Figure 1). These results show low imaging readout variability, enabling reliable quantification of joints with RA-involved macrophage-mediated inflammation. Analysis of the HC and RA images was used to determine initial quantitative "cut-points" to differentiate between joints with and without the inflammation typically seen in RA.



Figure 1. Tilmanocept consistently localizes in areas of macrophage-driven inflammation, demonstrating low variability. RA patients exhibit reproducible localization over a 1-week period. Typical of healthy subjects, no evidence of inflammation-related Tc 99m tilmanocept uptake was observed in the healthy control. Images on the right show same patient imaged on 2 different days.

Conclusion: Tc 99m tilmanocept imaging of the joints in healthy subjects as well as in patients with active RA under stable treatment is reproducible and stable over time. The results confirmed that the signal in joints of healthy subjects and RA patients can be quantified and used to establish cut points to distinguish inflamed and non-inflamed joints on a joint-by-joint basis. These results provide the foundation for a noninvasive, objective method to monitor activity in macrophage-driven inflammation in joints of patients with RA.

Disclosure of Interests: Ayah Hussein Employee of: Currently employed by Navidea Biopharmaceuticals, David Ralph Consultant of: Previous consultant for Navidea Biopharmaceuticals, Employee of: Currently employed by Navidea Biopharmaceuticals, Beth Potter Employee of: Currently employed by Navidea Biopharmaceuticals, Bonnie Abbruzzese Employee of: Currently employed by Navidea Biopharmaceuticals, Rachael Hershey Employee of: Currently employed by Navidea Biopharmaceuticals, Katherine Repp Employee of: Previously employed by Navidea Biopharmaceuticals, Haya Shakhtra Employee of: Currently employed by Navidea Biopharmaceuticals, Mehak Goel Employee of: Currently employed by Navidea Biopharmaceuticals, Madison Palmer Employee of: Currently employed by Navidea Biopharmaceuticals, Allison Kissling Employee of: Previously employed by Navidea Biopharmaceuticals, Carley Hartings Employee of: Previously employed by Navidea Biopharmaceuticals, Michael Blue Employee of: Currently employed by Navidea Biopharmaceuticals, Michael Rosol Employee of: Currently employed by Navidea Biopharmaceuticals

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THU0541 ANATOMICAL LOCATION OF SACROILIAC JOINT MRI LESIONS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS, POSTPARTUM WOMEN, PATIENTS WITH DISC HERNIATION, CLEANING STAFF, RUNNERS AND HEALTHY PERSONS

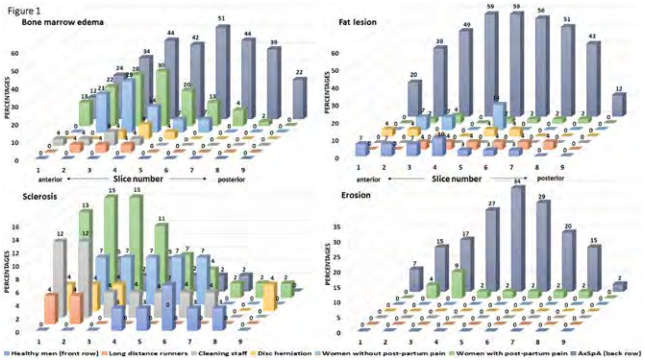
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Background: Bone marrow edema (BME) on sacroiliac joint (SIJ) MRI is central in the Assessment of SpondyloArthritis International Society classification criteria for axial spondyloarthritis (axSpA). However, BME can be seen in other conditions and healthy persons. The presence of structural lesions may contribute to diagnosing axSpA.

Objectives: To investigate the location and distribution of SIJ MRI lesions in patients with axSpA and disc herniation, women with and without post-partum pain (PPP), cleaning staff, runners, and healthy persons.

Methods: In a prospective cross-sectional study of 204 participants, MRI of the SIJs was evaluated by two readers. MRI images were scored according to the SPARCC SIJ Inflammation[1] and Structural (SSS)[2] lesion definitions. Based on concordant reads, lesions were analysed according to location (unilateral/bilateral SIJ, upper/lower sacral/iliac quadrant/joint half, anterior (slice1-3)/central (slice 4-6)/posterior (slice 7-9) SIJ sections.

Results: BME was present in nearly all groups, in all quadrants, and primarily in the anterior SIJ section (Figure 1), but rarely as a bilateral feature, except in axSpA and women with PPP (Table 1). Fat lesion (FAT) was mainly found in axSpA, in all slices, and mostly bilaterally in the sacrum. In the other groups FAT was primarily located in the anterior and central SIJ sections. Sclerosis was only seen in the ilium, and was present in most groups, particularly in women with PPP, often bilaterally. Erosion was only seen in women with PPP (mostly unilaterally) and in axSpA (mainly bilaterally in the ilium). Backfill and ankylosis were only seen in axSpA.



Conclusion: Typical locations of common SIJ lesions in axSpA and non-axSpA were reported. In non-axSpA, except women with PPP, bilateral as well as posterior lesions were rare, while backfill and ankylosis were absent.

References:

[1] Maksymowych et al, *Arthritis Rheum, 2005*

[2] Maksymowych et al, *J of Rheumatol,* 2015

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Table 1. Participant characteristics and distribution of lesions – unilaterally/bilaterally in iliac/sacral quadrants

			AxSpA	Women with post-partum pain	Women without post-partum pain	Disc herniation	Cleaning staff	Long distance runners	Healthy men
Number of participants			41	46	14	25	26	23	29
Age			30.9 (6.4)	32.6 (3.3)*	33.1 (4.1)	35.2 (5.7)**	39.1 (4.6)***	32.7 (6.2)	30.9 (6.4)
Male sex			63	0***	0***	44	0***	78	100***
Low back pain VAS (0-10)			3.8 (2.8)	5.5 (2.4)**	0.4 (0.7)***	5.5 (2.4)*	0.8 (1.8)***	0.2 (0.5)***	0.1 (0.3)***
HLA-B27 positive			81	11***	7***	0***	0***	4***	14***
C-Reactive Protein >3 mg/l			59	17***	21**	20**	15**	17**	3***
	Quadrant:		**UNI / BI**	**UNI / BI**	**UNI / BI**	**UNI / BI**	**UNI / BI**	**UNI / BI**	**UNI / BI**
BME	Ilium	Upper	27 / 7	11 / 9	0 / 0	0 / 0	0 / 4	0 / 0	0 / 0
		Lower	22 / 17	15 / 13	21 / 0	0 / 0	0 / 4	4 / 0	0 / 0
	Sacrum	Upper	29 / 22	17 / 9	29 / 0	4 / 0	4 / 0	0 / 0	0 / 0
		Lower	24 / 20	9 / 9	4 / 0	4 / 0	0 / 0	0 / 0	0 / 0
FAT	Ilium	Upper	20 / 17	2 / 0	7 / 0	4 / 0	0 / 0	0 / 0	0 / 7
		Lower	17 / 29	0 / 0	7 / 0	4 / 0	0 / 0	0 / 0	0 / 3
	Sacrum	Upper	22 / 44	2 / 4	0 / 7	0 / 4	0 / 0	4 / 0	3 / 3
		Lower	17 / 42	2 / 2	4 / 7	0 / 0	0 / 0	4 / 0	3 / 3
Sclerosis	Ilium	Upper	5 / 2	4 / 4	0 / 7	4 / 4	4 /4	0 / 0	3 / 7
		Lower	0 / 0	9 / 9	7 / 0	0 / 4	15 / 0	4 / 0	0 / 0
	Sacrum	Upper	0 / 0	0 / 0	0 / 0	0 / 0	0 / 0	0 / 0	0 / 0
		Lower	0 / 0	0 / 0	0 / 0	0 / 0	0 / 0	0 / 0	0 / 0
Erosion	Ilium	Upper	22 / 24	4 / 0	0 / 0	0 / 0	0 / 0	0 / 0	0 / 0
		Lower	17 / 24	2 / 2	0 / 0	0 / 0	0 / 0	0 / 0	0 / 0
	Sacrum	Upper	10 / 5	2 / 0	0 / 0	0 / 0	0 / 0	0 / 0	0 / 0
		Lower	22 / 2	2 / 2	0 / 0	0 / 0	0 / 0	0 / 0	0 / 0

Values are % or mean (SD)

Mann-Whitney test was applied, tests are patients with axSpA compared with all other groups. P<0.05*; p<0.01**; p<0.001***

BI: bilateral; BME: Bone marrow edema; FAT: fat lesion; HLA-B27: Human Leukocyte Antigen B27;UNI: unilateral; VAS: Visual Analogue scale

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THU0542 THE IMPACT OF GLUCOCORTICOID INITIATION ON THE DIAGNOSTIC ACCURACY OF ULTRASOUND IN GIANT CELL ARTERITIS: EXPERIENCES FROM A DISTRICT GENERAL HOSPITAL IN THE UK

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Background: Temporal and axillary artery ultrasound (US) has been recommended by EULAR as the first-line investigation in patients with suspected giant cell arteritis (GCA).[1] US is reported as having a 77% sensitivity and 96% specificity for GCA.[1] However, these figures have largely been derived from studies carried out in specialist centres where US was performed rapidly following the onset of symptoms. When performed by highly experienced sonographers, halos can still be detected on US weeks after initiation of glucocorticoid treatment.[2] Little is known about the relationship between the dose and duration of glucocorticoid and diagnostic accuracy of US in real-world experience.
Objectives: We evaluated the impact of glucocorticoid initiation on the diagnostic accuracy of US in patients with suspected GCA in routine clinical practice in a district general hospital.
Methods: This is a single-centre retrospective study of all temporal and axillary artery US performed since its inception in November 2015 until October 2019. Patients who were aged ≥50 years and assessed by a rheumatologist were included in the study. US was performed by either a musculoskeletal consultant radiologist, musculoskeletal sonographer or vascular sonographer. US was considered positive for GCA when a halo, occlusion or stenosis was seen. Patients' medical records and investigation results were reviewed in a systematic manner. The reference standard for GCA was the final clinical diagnosis after a minimum of 3-month rheumatology follow up.
Results: 311 US performed on 305 patients were included. 62% of the scans were requested by rheumatologists, the rest by ophthalmologists and general physicians. 57 of these episodes had a final clinical diagnosis of GCA. US had an overall sensitivity of 39% and specificity of 100% for GCA. Overall positive and negative predictive values were 100% and 88%, respectively. Sensitivity was 31% for US done in the first 2 years (n=160) which was lower than sensitivity of 45% in the latter 2 years (n=151) (p=0.2663). Specificity remained the same in the two periods. When performed on patients who were not on any glucocorticoids, US had a sensitivity of 89% which was significantly higher than sensitivity of 29% in those who had been treated with any dose or duration of steroids (p=0.0007).
Compared to US-negative GCA patients, US-positive GCA patients are older and more likely to have jaw claudication (Table 1).

Table 1 Characteristics of patients with a final clinical diagnosis of GCA

	All GCA (n=57)	US positive (n=22)	US negative (n=35)	*p*-value
Age, mean years	74	78	72	**0.01**
Sex, no of females	41 (72%)	13 (59%)	27 (77%)	0.15
Any head pain present, no of patients	49 (86%)	18 (82%)	31 (89%)	0.50
Jaw claudication, no of patients	26 (46%)	15 (68%)	14 (40%)	**0.04**
Ocular ischaemia, no of patients	8 (14%)	3 (14%)	5 (14%)	0.94
ESR, mm/hour,* mean	67	66	68	0.78
CRP, mg/L,* mean	85	85	84	0.96
Days of high-dose glucocorticoid pre-US, mean	5	4	6	0.11

* ESR was determined in n=55 patients and CRP in n=53 patients. ESR and CRP were measured before initiation of high-dose steroid treatment.

Table 2 Diagnostic accuracy of US stratified by duration of high dose glucocorticoid* pre-scan

Steroid duration	n	Sensitivity, %	Specificity, %	PPV, %	NPV, %
0-1 day	154	71	100	100	97
2-3 days	34†	22	100	100	77
4-5 days	32†	33	100	100	79
6-7 days	18	13	100	100	59
>7 days	41	33	100	100	72

*>30mg of oral prednisone or equivalent
†included episodes when patients were treated with intravenous methylprednisone

Conclusion: US has an 89% sensitivity and 100% specificity for GCA when performed before initiation of glucocorticoid. Its sensitivity rapidly decreases within a day of starting high dose steroid but up to one-third of GCA cases can still be detected after over 1 week of treatment.
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Disclosure of Interests None declared
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THU0544 MULTIMODAL PHOTOACOUSTIC/ULTRASONIC IMAGING SYSTEM: A NEW IMAGING METHOD FOR EVALUATING RA

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Background: Photoacoustic imaging (PAI), a new imaging technique which can be integrating with ultrasound (US) imaging, has shown potential in visualizing small joints. We have developed a multimodal photoacoustic/ultrasound (PA/US) imaging system, equipped with a handheld probe, which can provide dual-wavelength PA/US imaging to identify the micro-vessels of the inflamed articular regions and measure the oxygenation level of human inflamed synovium.
Objectives: To validate the potential value for RA of the imaging system.
Methods: A total of 32 RA patients received PA/US examination on seven small joints (MCP2, MCP3, PIP2, PIP3, MTP2, MTP5, and wrist of the clinically dominant side). The 0-3 score was used to semi-quantify the PA and PD signals of the inflammatory articular lesions, and the sums of PA and PD scores (PA-sum and PD-sum) were utilized. The relative oxygen saturation (SO2) values of the inflamed regions were measured by calculating the ratio of PA signals at the wavelength of 750nm and 830nm. All the patients were classified to 3 PA+SO2 patterns (Pattern 1: no or minimal PA signals; Pattern 2: evident PA signals and hyperoxia; Pattern 3: evident PA signals and hypoxia). The correlations between imaging scores and laboratory data, as well as clinical scoring systems were assessed.
Results: A total of 32 patients of RA were recruited aged from 25-71 years-old were examined. PD-sum had moderate correlation with the clinical scores (r=0.529, 0.546, 0.490, 0.493 for DAS28ESR, DAS28CRP, SDAI, CDAI), moderate correlations with TJC (r=0.575) and SJC (r=0.491), fair correlation with VAS (r=0.239), poor correlation with PGA (r=0.153), and moderate correlation with EGA (r=0.457). The PA-sum had substantial correlations with the clinical scores (r= 0.699, 0.746, 0.723, 0.736 for DAS28ESR, DAS28CRP, SDAI, CDAI), substantial correlations with TJC (r=0.787) and SJC (r=0.694), moderate correlations with VAS (r=0.544) and PGA (r=0.529), and substantial correlation with EGA (r=0.708).
Ten patients were classified as Pattern 1, 12 as Pattern 2, 9 as Pattern 3. The PA+ SO2 patterns presented substantial correlations with the clinical scores (DAS28ESR r=0.690, DAS28CRP r=0.782, SDAI r=0.805, CDAI r=0.799, SJC r=647, TJC r=0.676, respectively), substantial correlation with VAS (r=0.714), and moderate correlation with PGA (r=0.476) and EGA (r=0.502). Significant differences between those who were classified as hypoxia and hyperoxia with evident PA signals, were detected in VAS (p=0.020) and PGA (p=0.026).
Conclusion: The PA-sum scores and the PA+SO2 patterns can be utilized as objective imaging parameters reflecting the disease activity of RA. PAI may serve as a supplement to conventional US examinations for RA patients.
References:
[1] Backhaus, M., et al., Evaluation of a novel 7-joint ultrasound score in daily rheumatologic practice: a pilot project. Arthritis Rheum, 2009. 61(9): p. 1194-201.
[2] Colebatch, A.N., et al., EULAR recommendations for the use of imaging of the joints in the clinical management of rheumatoid arthritis. Ann Rheum Dis, 2013. 72(6): p. 804-14.

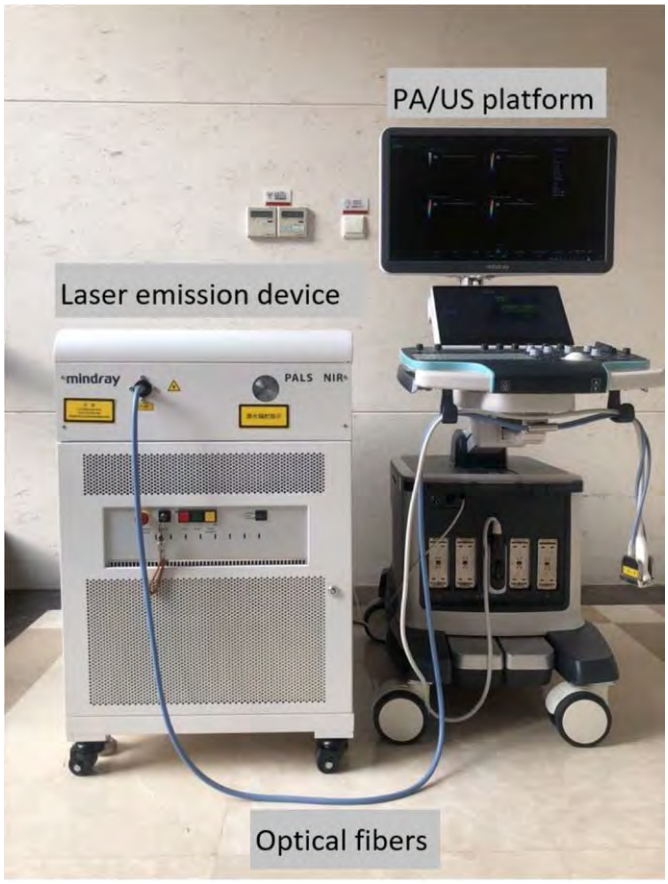


Figure 1. the photo of the multimodal PA/US imaging system

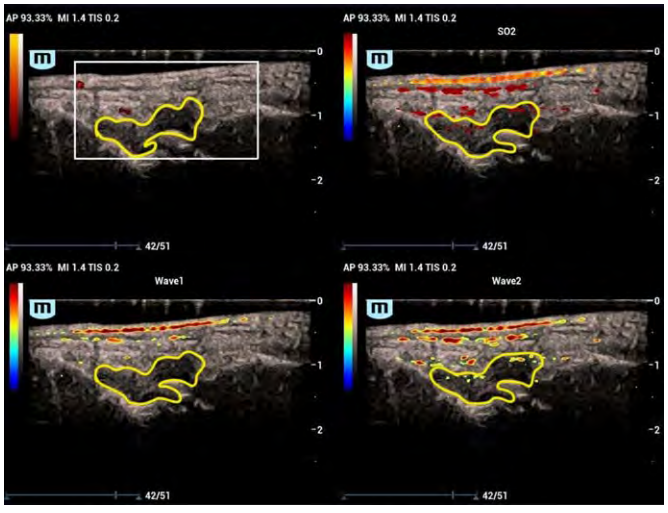


Figure 2. an example of the PA/US imaging

Disclosure of Interests: Chenyang Zhao: None declared, Qian Wang: None declared, Xixi Tao: None declared, Chen Yu: None declared, Sirui Liu: None declared, Mengtao Li: None declared, Xinping Tian: None declared, Zhenhong Qi: None declared, Jianchu Li: None declared, Fang Yang: None declared, Lei Zhu: None declared, Xiaofeng Zeng Consultant of: MSD Pharmaceuticals, Meng Yang: None declared, Yuxin Jiang: None declared

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THURSDAY, 04 JUNE 2020

Public health, health services research, and health economics

THU0545

THE ASSOCIATION OF RHEUMATOID ARTHRITIS WITH HEALTH CARE COSTS FROM THE PAYERS PERSPECTIVE FROM 2001-2015

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Background: Costing studies require long-term follow-up data ideally within a homogenous payment structure without multiple potential insurers. We examined trends in associated costs of rheumatoid arthritis from the public payer's perspective over time.

Objectives: The purpose of this study was to measure the population RA associated direct and indirect health care costs using statistical attribution methods among a population with identical health care coverage.

Methods: The study was matched longitudinal study of patients with algorithm defined RA residing in Ontario Canada with an RA diagnosis from 2001-2016 (n=104,933). Cases were matched 1:1 during the year of first diagnosis to 2 distinct control groups without RA. Control group 1 were matched on year of birth, and sex (underlying costs). Control group 2 were matched on year of birth, sex, and medical history. Medical history was measured using The John Hopkins Expanded Diagnostic Clusters, a tool that categorizes people with similar conditions based upon their use of healthcare services (physician visits, hospitalizations, emergency department visits, ambulatory care). After matching, healthcare costs were reported in 2015 Canadian Dollars (CAD) overall and by cost sub-category by exposure group and calendar year before versus after RA diagnosis. RA-associated costs were measured as the difference in costs among RA patients and their corresponding matched comparators.

Results: At the year of diagnosis, RA cases were predominantly female (70%, n=72,873), mean year of birth 1950, (SD=17.7, Range=1910-2000), with mean year of diagnosis 2006, (SD=6.3, Range=2001-2016). RA patients experienced inceased indirect cost acquisition compared to the direct costs of RA alone. The health care costs of RA patients were identical to age/sex/medical history matched controls yet rising up until 2 years before RA diagnosis where they diverged from age/sex/disease matched controls $3,585/ptyr compared to $3,352/ptyr. The costs of RA patients were highest $8,468 CAD/ptyr ($888,572,644 total) in the year of diagnosis declining to a steady state by 2 years post diagnosis $7,867/ptyr with a slight increase in costs by 8 years post diagnosis $8,035/ptyr in (Figure 1). Differences age/sex matched controls were detectable throughout the study time period even up to 19-years pre-diagnosis. In the year of diagnosis, the direct costs of RA were $4046/ptyr (8468-4422), while the indirect costs of RA were $1254/ptyr ($4422-$3168) and the underlying age-sex specific costs were $3,168/ptyr. Our analysis suggest that both the direct and inflammatory costs of RA are growing over time compared to matched controls (Figure 1) by year 8 the direct joint-related costs of RA were 2528 (8035-5507) the indirect costs were 1,144 (5507-4363) and the age/sex underlying costs were 4,363.

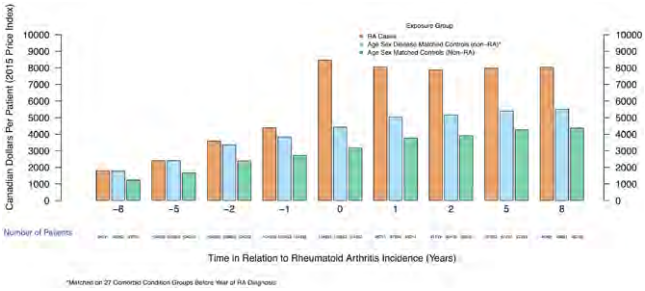


Figure 1. Annual Per-Patient Total Health Care Costs Over Time Grouped by Exposure Before and After Rheumatoid Arthritis Diagnosis

Conclusion: The costs of RA have grown over time with medications representing a smaller than expected portion of total costs but a large increase in costs relative to matched controls. These results indicate that the direct costs of RA are decreasing over time compared to matched controls at 8 years post diagnosis

and that over time, the indirect associated portion of costs remains almost constant, showing that over time the costs of indirectly related issues are becoming a larger proportion of total costs. Methodological advancements in costing attribution over time could contribute to understanding the patterns in health care resource usage among populations with chronic diseases.

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THU0546 HEALTHCARE COSTS OF NOT ACHIEVING REMISSION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Guidelines recommend sustained remission as a treatment goal for patients with rheumatoid arthritis (RA). However, only one-third of patients are known to achieve this goal with current treatments. A few studies have evaluated the impact of remission in a real-world setting, but evidence is limited to the elderly population.

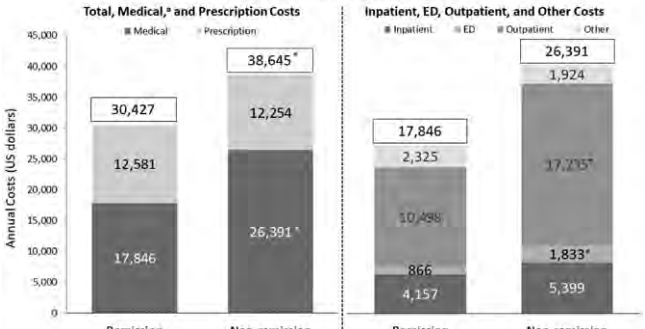
Objectives: To understand the impact of remission on healthcare costs by comparing overall and RA-related direct healthcare costs and resource use in patients with RA who maintain vs those who do not maintain remission using a real-world database.

Methods: Data for this retrospective cohort study were derived from Optum electronic health records linked to claims from commercial and Medicare Advantage health plans in the United States. Patients with ≥2 diagnoses for RA, ≥1 Disease Activity Score 28 (DAS28-CRP/ESR) or Routine Assessment of Patient Index Data 3 (RAPID3) measurement, and continuous medical and pharmacy coverage 6 months before and 1 year after the index date were included. Two cohorts were created: remission and non-remission. Remission was defined as DAS28 <2.6 or RAPID3 ≤3.0. In the remission cohort, the index date was defined as the first date remission was achieved. In the non-remission cohort, the index date was defined as the first date of DAS28 or RAPID3 measurement. Outcomes were all-cause and RA-related total, medical, and prescription costs; healthcare resource use (number of inpatient, emergency department [ED], outpatient, and other visits); and number of prescriptions within 1 year of index date. A weighted generalized linear model and binomial regression were used to estimate adjusted annual direct costs and healthcare resource use, respectively. Confounding between cohorts due to age, sex, race and comorbidities using the Elixhauser index was controlled for in the models.

Results: A total of 335 patients with RA (remission cohort: 125; non-remission cohort: 210) met the study inclusion criteria. Annual all-cause total direct costs in the remission cohort were significantly less than in the non-remission cohort ($30,427 vs $38,645, respectively; cost ratio (CR)=0.79; 95% CI: 0.63, 0.99). All-cause medical costs were significantly lower in the remission cohort than in the non-remission cohort (Figure 1); furthermore, among all-cause medical costs, outpatient visit costs were significantly lower in the remission than in the non-remission cohort. All-cause resource use (mean number of visits) was less in the remission vs non-remission cohort: inpatient (0.23 vs 0.63; visit ratio (VR)=0.36; 95% CI: 0.19, 0.70), ED (0.36 vs 0.77; VR=0.47; 95% CI: 0.30, 0.74), and outpatient visits (20.7 vs 28.5; VR=0.73; 95% CI: 0.62, 0.86). Annual RA-related total direct costs were similar in both cohorts (Figure 2); however, RA-related medical costs were numerically lower in the remission vs non-remission cohort ($8,594 vs $10,002, respectively; CR=0.86; 95% CI: 0.59, 1.25). RA-related resource use (mean number of visits) was less in the remission vs non-remission cohort: inpatient (0.15 vs 0.22; VR=0.67; 95% CI: 0.35, 1.30), ED (0.04 vs 0.13; VR=0.31; 95% CI: 0.10, 0.95), and outpatient visits (5.4 vs 7.4; VR=0.72; 95% CI: 0.58, 0.91).

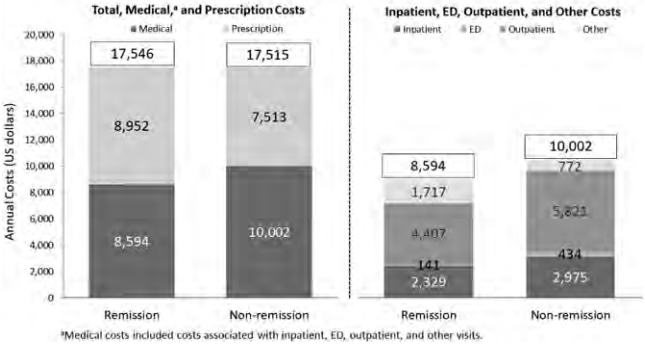
Conclusion: Significant economic burden was associated with patients who did not maintain remission compared with those who maintained remission. Although outpatient visits were the driver of medical costs in both groups studied in this analysis, the contribution of outpatient visits was greater among those who did not maintain remission.

Figure 1. Annual All-Cause Direct Costs



*p<0.05; [a]Medical costs included costs associated with inpatient, ED, outpatient, and other visits.

Figure 2. Annual RA-Related Direct Costs



[a]Medical costs included costs associated with inpatient, ED, outpatient, and other visits.

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THU0547 ESTIMATION OF THE IMPACT OF A STRATEGY TO OPTIMIZE COSTS ON NATIONAL HEALTH-CARE SYSTEM IN PATIENTS WITH RHEUMATOID ARTHRITIS: A DIRECT COST ANALYSIS

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Background: Rheumatoid arthritis (RA) is a disease associated with a high and increasing direct cost to the health-care resources. It is estimated that about 250,000 persons may have RA in Colombia. The characteristic joint damage and disability associated to RA increase slowly over many years (10–20 years).

Objectives: To assess the development of RA in Colombian-population over the next five-years and to estimate the impact of a strategy to reduce direct-costs on the national health-care system.

Methods: We use a population-based approach of epidemiological type to analyze the development of the disease over time. We design a continuous mathematical model for the transmission and evolution of RA in a population. The description of a biological phenomenon (disease), by differential equations is called mathematical modeling and allows us not only to study and analyze the dynamics of the disease, but also to predict its future development. The system is formed by eight ordinary differential-equations, explaining the influence of the epidemiological parameters considered in the evolution of RA. This mathematical modeling-approach has been extensively used to study the dynamical behavior of diseases in populations from an epidemiological point of view. The parameters of the mathematical-model are estimated using real-data from RA-prevalence. Total population was divided into eight groups as follows: general population, prevalent (at risk), pre-clinical (asymptomatic), symptomatic (tender/swollen joints), diagnosed without treatment (fulfilling classification-criteria), starting early treatment (before two years of symptoms), starting late treatment (after two years of symptoms), and chronic RA patients (disease duration more than 2 years). Numerical simulations allow to explain the RA-epidemiology and predict the disease over the next five-years.
Results: In the next five-years there will be 129,000 new RA-patients in Colombia, with an estimated cost on the national health-care system of about $4125 million (USD). The analysis of the proposed mathematical model allows us to recommend an action-strategy to optimize and reduce direct-costs. The strategy is related to the implementation of the optimal clinical-diagnosis of RA and starting timely-treatment of patients with the most effective approaches available. Applying this strategy would allow the health-care system to reduce about 20% of its direct costs over the next five-years, reducing costs from $4125 million to $3337 million with estimated savings of $789 million. Figure 1

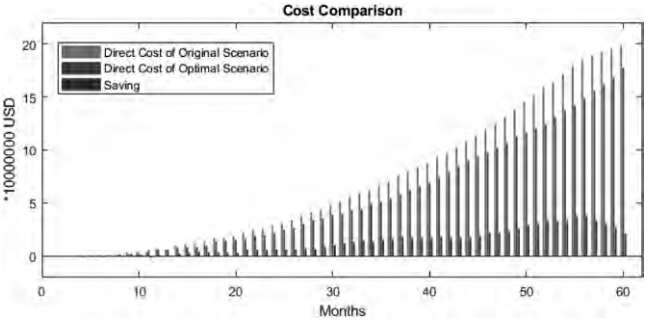


Figure 1 Comparison of direct-costs associated to rheumatoid arthritis over time

Conclusion: We investigated the development of RA over the next five-years and were able to predict the number of new patients. The impact of the implementation of a strategy based on optimal-diagnosis and timely-treatment may reduce about 20% of its direct costs over the next five-years.
Disclosure of Interests: None declared
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THU0548 THE ECONOMIC BURDEN OF ANKYLOSING SPONDYLITIS IN SPAIN. RESULTS OF THE SPANISH ATLAS 2017

M. Merino[1], O. Braçe[2], A. González[1], Á. Hidalgo-Vega[1,3], M. Garrido-Cumbrera[2,4], J. Gratacos-Masmitja[5,6]on behalf of Atlas Working Group. *[1]Fundación Weber, Madrid, Spain*; *[2]Health & Territory Research (HTR), Universidad de Sevilla, Seville, Spain*; *[3]Universidad de Castilla-La Mancha, Toledo, Spain*; *[4]Spanish Federation of Spondyloarthritis Associations (CEADE), Madrid, Spain*; *[5]Hospital Universitari Parc Taulí, Sabadell, Spain*; *[6]I[3]PT, UAB, Barcelona, Spain*

Background: Ankylosing Spondylitis (AS) is a disease associated with a high number of comorbidities, chronic pain, functional disability, and resource consumption.
Objectives: This study aimed to estimate the burden of disease for patients diagnosed with AS in Spain.
Methods: Data from 578 unselected patients with AS were collected in 2016 for the Spanish Atlas of Axial Spondyloarthritis via an online survey. The estimated costs were: Direct Health Care Costs (borne by the National Health System, NHS) and Direct Non-Health Care Costs (borne by patients) were estimated with the bottom-up method, multiplying the resource consumption by the unit price of each resource. Indirect Costs (labour productivity losses) were estimated using the human capital method. Costs were compared between levels of disease activity using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score (<4 or low inflammation versus ≥4 or high inflammation) and risk of mental distress using the 12-item General Health Questionnaire (GHQ-12) score (<3 or low risk versus ≥3 or high risk).
Results: The average annual cost per patient with AS in 2015 amounted to €11,462.3 (± 13,745.5) per patient. Direct Health Care Cost meant an annual average of €6,999.8 (± 9,216.8) per patient, to which an annual average of €611.3 (± 1,276.5) per patient associated with Direct Non-Health Care Cost borne by patients must be added. Pharmacological treatment accounted for the largest percentage of the costs borne by the NHS (64.6%), while for patients most of the cost was attributed to rehabilitative therapies and/or physical activity (91%). The average annual Indirect Costs derived from labour productivity losses were €3,851.2 (± 8,484.0) per patient, mainly associated to absenteeism. All categories showed statistically significant differences (p<0.05) between BASDAI groups (<4 vs ≥4) except for the Direct Non-Healthcare Cost, showing a progressive rise in cost from low to high inflammation. Regarding the 12-item General Health Questionnaire (GHQ-12), all categories showed statistically significant differences between GHQ-12 (<3 vs ≥3), with higher costs associated with higher risk of poor mental health (Table 1).

Table 1. Average annual costs per patient according to BASDAI and GHQ-12 groups (in Euros, 2015)

	N	Direct Health Costs	Direct Non-Health Costs	Indirect Costs	Total Cost
BASDAI					
<4	91	**7,592.0***	557.3	**2,426.5***	**10,575.8***
≥4	376	**9,706.9***	768.0	**5,104.8***	**15,579.7***
Psychological distress (GHQ-12)					
<3	146	**8,146.8***	**493.6***	**3,927.2***	**12,567.6***
≥3	260	**9,772.9***	**807.2***	**4,512.3***	**15,092.5***
Total	578	6,999.8	611.3	3,851.2	11,462.3

* p <0.05

Conclusion: Direct Health Care Costs, and those attributed to pharmacological treatment in particular, accounted for the largest component of the cost associated with AS. However, a significant proportion of the overall costs can be further attributed to labour productivity losses.
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Disclosure of Interests: María Merino: None declared, Olta Braçe: None declared, Almudena González: None declared, Álvaro Hidalgo-Vega: None declared, Marco Garrido-Cumbrera: None declared, Jordi Gratacos-Masmitja Grant/research support from: a grant from Pfizzer to study implementation of multidisciplinary units to manage PSA in SPAIN, Consultant of: Pfizzer, MSD, ABBVIE, Janssen, Amgen, BMS, Novartis, Lilly, Speakers bureau: Pfizzer, MSD, ABBVIE, Janssen, Amgen, BMS, Novartis, Lilly
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THU0549 COST-EFFECTIVENESS OF DIAGNOSING AXIAL SPONDYLOARTHRITIS IN THE NETHERLANDS

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Background: In order to facilitate diagnosis of axial spondyloarthritis (axSpA) in clinical practice, three diagnostic algorithms have been published: the original Berlin algorithm (BER), and modifications 1 (M1) and 2 (M2). These mainly differed mainly in the position and definition of inflammatory back pain (Figure). BER was the most specific of these algorithms, while M2 was most sensitive, and the latter was accepted as the algorithm of choice. However, it is unknown to what extent it is acceptable, in terms of costs and effects, to increase sensitivity (i.e. reducing underdiagnosis and undertreatment) at the expense of specificity (i.e. increasing overdiagnosis and overtreatment).

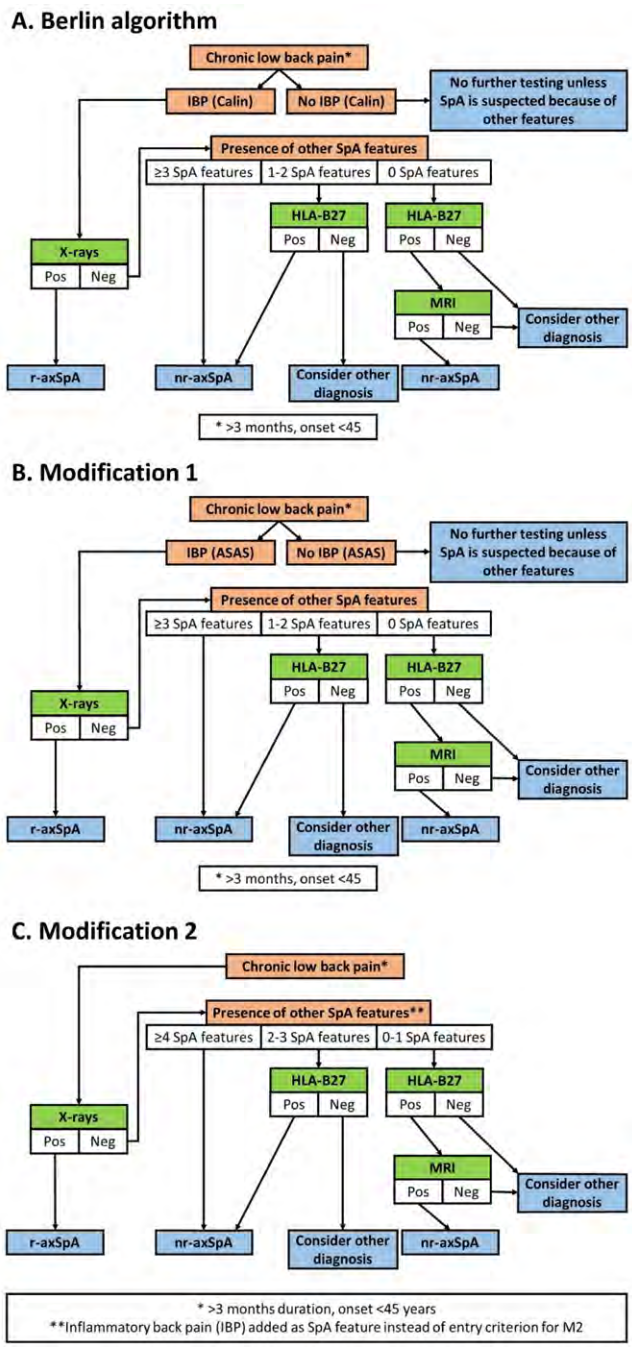


Figure. Flowchart of the Berlin algorithm (A), and Modifications 1 (B) and 2 (C)

Objectives: To compare lifetime cost-effectiveness of currently available diagnostic algorithms for axSpA in the Netherlands.
Methods: A cost-effectiveness model was developed to estimate costs, quality adjusted life years (QALYs) and net monetary benefit (NMB) of different diagnostic algorithms for axSpA among patients with chronic low back pain (CLBP) referred to a rheumatologist, over a 60-year time horizon. The model combined a decision-tree (diagnostic process) with a state-transition model (long-term treatment). For the diagnostic process, patient-level data from an observational cohort of referred CLBP patients (SPondyloArthritis Caught Early, SPACE) were used. In the state-transition model, both axSpA and CLBP were modelled using three health states each, based on disease activity and treatment (including up to three sequential biologicals) (for axSpA), or disease severity (for CLBP). Three available diagnostic algorithms (BER, M1, M2) were compared. To estimate the impact of uncertainty on results, probabilistic sensitivity analyses were conducted. For all analyses, both a societal perspective (including all healthcare, informal and work-related costs) and a healthcare perspective (only including healthcare costs) were adopted. Results were expressed as incremental cost-utility ratio (ICUR) and incremental NMB (iNMB).
Results: From a societal perspective, algorithm M2 resulted in more QALYs and lowest costs per patient (24.23 QALY; €157,274), thus dominating BER and M1 (Table). From a healthcare perspective, BER had lowest costs, but M2 was still considered cost-effective at €3,250/QALY (Table). At a willingness-to-pay (WTP) threshold of €20,000 per one QALY gained, the probability of M2 being most cost-effective was 94%, compared to 5% for M1 and 1% for BER. Compared to the most cost-effective algorithm (M2), an additional €7,500 could be spent per patient to achieve perfect diagnosis while remaining cost-effective.

Table. Base-case deterministic cost-utility results of comparisons between diagnostic algorithms

Perspective	Algorithm	SE/SP	Cost, €	QALY	iCost, €	iQALY	ICUR, €/QALY	iNMB, €*
Societal	M2	51% / 88%	157,274	24.23	-	-	-	-
	M1	73% / 82%	158,236	24.15	962	-0.08	Dominated by M2	-2,583
	Berlin	80% / 85%	159,295	23.96	2,021	-0.27	Dominated by M2	-7,479
Healthcare	Berlin	51% / 88%	91,755	23.96	-	-	-	-
	M2	73% / 82%	92,642	24.23	887	0.27	3,250	4,571
	M1	80% / 85%	92,710	24.15	67	-0.08	Dominated by M2	-1,688

*Calculated using a WTP threshold of €20,000/QALY. iCost, incremental cost; iQALY, incremental QALY; SE, sensitivity; SP, specificity.

Conclusion: The relative increase in sensitivity of M2 at the expense of specificity when compared to the original BER algorithm is acceptable in terms of costs and effects from both societal and healthcare perspectives. A considerably more expensive diagnostic algorithm with better accuracy than M2 would still be considered good value for money. It is worthy to invest in more accurate diagnosis in axSpA.
Disclosure of Interests: Casper Webers: None declared, Sabine Grimm: None declared, Astrid van Tubergen Consultant of: Novartis, Floris A. van Gaalen: None declared, Désirée van der Heijde Consultant of: AbbVie, Amgen, Astellas, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Cyxone, Daiichi, Eisai, Eli-Lilly, Galapagos, Gilead Sciences, Inc., Glaxo-Smith-Kline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB Pharma; Director of Imaging Rheumatology BV, Manuela Joore: None declared, Annelies Boonen Grant/research support from: AbbVie, Consultant of: Galapagos, Lilly (all paid to the department)
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THU0550

HEALTH CARE UTILIZATION AND COSTS IN ADULTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN THE UNITED KINGDOM: A REAL-WORLD OBSERVATIONAL RETROSPECTIVE COHORT STUDY

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Background: There is limited real-world evidence demonstrating the long-term direct costs associated with systemic lupus erythematosus (SLE) in the United Kingdom (UK).
Objectives: To describe health care resource utilization and costs in adults with SLE in the UK over time and document costs by disease severity and type of encounter, including primary care, hospitalizations, outpatient visits, and prescription drugs.
Methods: Patients aged ≥18 years with SLE were identified in the linked Clinical Practice Research Datalink – Hospital Episode Statistics database from January 1, 2005, to December 31, 2017. Patients were required to have data from ≥12 months before and after the index date, defined as the date of earliest diagnosis available in the data set. Patients were classified as having mild, moderate, or severe disease using an adapted claims-based algorithm.[1] Costs were calculated in 2017 UK pounds from the UK national health care system perspective. We estimated all-cause health care costs and incremental costs associated with each year of follow-up compared with a baseline year (3 years before index) using each patient as his or her own control and adjusting for age, sex, disease severity, and comorbid conditions.

Results: Of the 802 patients identified, 369 (46.0%) had mild SLE, 345 (43.0%) had moderate SLE, and 88 (11.0%) had severe SLE. The mean all-cause cost increased in the 3 years before diagnosis and, in the first year after diagnosis, amounted to £7532 (standard deviation [SD] £9634). This cost varied by disease severity: mild SLE, £5221 (£8064); moderate SLE, £8323 (£9846); and severe SLE, £14,125 (£11,267) (Figure 1). Adjusted total mean annual increase in costs per patient in the overall study population was £4476 (95% confidence interval £3809–5143) greater in the year of diagnosis compared with the baseline year (P<0.0001), adjusted for age, sex, disease severity, and comorbid conditions. Primary care utilization was the leading component of costs during the first year after diagnosis, followed by prescriptions, outpatient care, and inpatient care (Figure 2). Information on biologic use in hospitals is unavailable in these data.

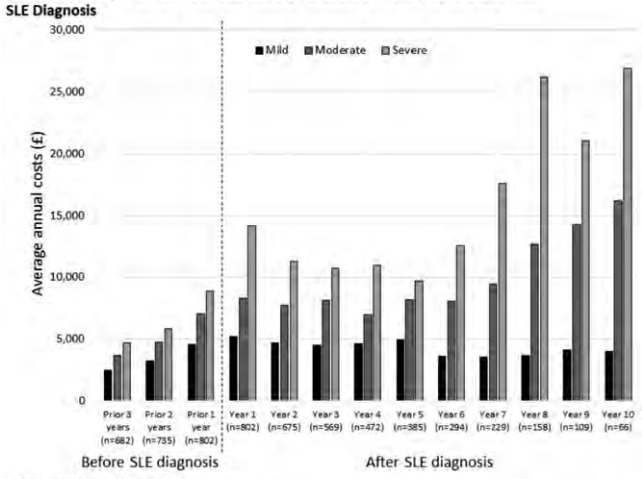
Conclusion: The direct costs of health care for patients with SLE in the UK are substantial and persist over the years after diagnosis. Patients with moderate or severe SLE have higher all-cause costs over time compared with patients with mild SLE. Earlier diagnosis and treatment may reduce disease severity and occurrence of comorbidities, and the associated high health care costs.

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[1] Garris C, et al. *J Med Econ*. 2013;16:667–677.

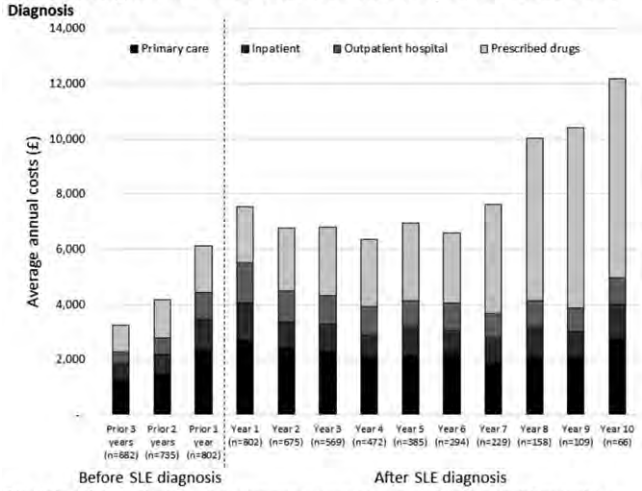
[2] Department of Health. NHS reference costs 2017/18. https://improvement.nhs.uk/resources/reference-costs/#rc1718; 2018 [accessed May 11, 2019].

Figure 1. Average Annual Total SLE Costs by Disease Severity, Before and After SLE Diagnosis



SLE, systemic lupus erythematosus.
SLE disease severity was classified as mild, moderate, or severe using an adapted claims-based algorithm[1] that uses SLE-related conditions and medications.

Figure 2. Average Annual Total SLE Costs by Utilization Category, Before and After SLE Diagnosis



NHS, National Health Service; SLE, systemic lupus erythematosus. To account for inflation and variations in pricing over time, 2017 unit costs were applied to all years as per the NHS Reference Costs.[2] Costs were estimated using a health system perspective and included direct medical resource use only. Other costs, such as out-of-pocket expenditure by patients, privately insured spending, and costs of informal and formal caregiving, were not captured.

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THU0551 SOCIAL CARE USE IN PEOPLE WITH CHRONIC PAIN IN THE UNITED KINGDOM

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Background: Chronic pain is a common and disabling health problem and those affected may need support with their activities of daily living (ADLs). Currently there are no data quantifying how much social care support people with chronic pain need.

Objectives: To describe formal and informal social care use in people with chronic pain

Methods: Between June-July 2019, previous participants of the *Cloudy with a Chance of Pain* study were invited to take part in an online survey, adapted from a validated Personal Social Services Research Unit interview survey. It collected data on whether participants with chronic pain needed help with ADLs, how frequently help was needed and who provided it (formal and informal social care). Additional data was collected on demographics, employment status, pain diagnosis, and comorbidities. Descriptive statistics described the burden of social care need and multivariable logistic regression identified factors associated with social care need.

Results: There were 981 respondents; 791 (81%) were female, median age 59 years (table 1). In the last month 527(61%) respondents reported needing help with ADLs. Over three-quarters of help was provided informally by family and friends (408 (77%)). For 309 (59%) respondents, help was needed at least daily. In the multivariable logistic regression model, needing help was lower with older age, (OR (95% CI) 0.96 (0.94-0.98), but higher in female gender (OR (95% CI) 1.96 (1.27-3.01), fibromyalgia (OR(95% CI) 2.75(2.53-5.54)), osteoarthritis (OR (95% CI) 1.56 (1.11-2.19)) and multi-morbidity OR (95% CI) 2.13 (1.51-3.01)). Compared to full-time work, respondents who were retired or unable to work were also significantly more likely to need help with ADLs, respective OR (95% CI) 2.16 (1.21-3.84) and 6.98 (3.72-13.08).

Table 1.

	All respondents n=981	Need help[$] *n=527*	No help[$] *n=337*	Missing
Age med (IQR)	59 (50-66)	57 (47-64)	61 (52-68)	5
Female n (%)	791 (81)	452 (86)	251 (74)	11
Employment status *n (%)*	134 (14)	54 (10)	70 (21)	1
FT	169 (17)	79 (15)	69 (20)	
PT	50 (5)	26 (5)	19 (6)	
Self-employed	7 (0.7)	4 (0.8)	2 (0.6)	
Student	23 (2)	12 (2)	10 (3)	
Homemaker	360 (37)	151 (29)	143 (42)	
Retired	221 (23)	188 (36)	21 (6)	
Unable to work	16 (1.6)	12 (2)	3 (0.9)	
Unemployed				
Diagnosis reported *n (%)*[*]	929 (95)	516 (98)	313 (93)	11
Osteoarthritis	482 (49)	269 (51)	160 (47)	
Fibromyalgia	265 (27)	207 (39)	40 (12)	
Rheumatoid arthritis	205 (21)	115 (22)	73 (22)	
Arthritis (type not specified)	128 (15)	73 (14)	55 (16)	
Ankylosing Spondylitis	56 (6)	33 (6)	23 (7)	
Gout	18 (2)	13 (2)	5 (1)	
Migraine/chronic headache	115 (13)	82 (16)	33 (10)	
Neuropathic pain	155 (18)	120 (23)	35 (10)	
Other (inc Psoriatic arthritis, hypermobility)	272 (29)	209 (39)	63 (19)	
Any MSk diagnosis *n (%)*	828 (95)	460 (87)	279 (83)	64
Multi-morbidity[∞] *n (%)*	712 (82)	473 (90)	54 (36)	0

med - median, IQR - interquartile range, MSk – musculoskeletal

[$] 117 respondents did not answer the question about whether they did or did not need help with ADLs

*some participants reported more than one diagnosis for their pain

includes MSK diseases above and the following chronic diseases listed in questionnaire: angina, heart attack, stroke, COPD, diabetes, cancer, parkinson's, multiple sclerosis, depression, other (participants asked to specify)

Conclusion: A high proportion of people with chronic pain needed support with ADLs; for more than half, on a daily or more frequent basis. Interestingly, younger patients were more likely to need help which may reflect responder

bias (younger patients with severe pain potentially more likely to respond than those with milder pain). The majority of support was provided informally, and this could be for a number of reasons. For example, lack of awareness/not meeting eligibility/unable to afford formal social care, or preference to be cared for by familiar persons. This should be explored in future research. These results demonstrate the burden of social care may be significantly greater than government and social care organisations are aware, with important implications for policy and planning.

Disclosure of Interests: Jenny Humphreys: None declared, Katy Dempsey: None declared, Ollie Phelan: None declared, Laura Boothman: None declared, Louise Cook: None declared, William Dixon Consultant of: Bayer and Google

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THU0552 SWITCH TO BIOSIMILAR ADALIMUMAB - IS IT COST EFFECTIVE?

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Background: Since the introduction of anti-TNF biosimilars in routine clinical practice, there has been a drive to implement the switch program for all biosimilars at the point of availability. First adalimumab biosimilar was granted marketing authorisation by the EMA in March 2017. Our Trust was aligned to NHS England strategy which required adoption of biosimilar within three months for new patients and one year for switchers. This could help deliver significant savings to the NHS whilst achieving similar clinical outcomes.

Objectives: We report our early experience of introducing adalimumab biosimilar (SB5).

Methods: A list of all patients prescribed adlimumab was extracted through our database. A 'switch' letter was drafted and sent to all patients including Imraldi information sheet. Patients were given the opportunity to contact nurse helpline for information or if disease control worsened/adverse effects developed. We reviewed all relevant records and collected data on any adverse events and disease outcome on either side of the switch. Patients were reviewed as originally planned by their respective clinicians.

Results: 198 patients were identified established on adalimumab. All had switched by October 2019 to Imraldi. Mean age of switchers was 48 (range 16-83 years). Gender distribution was equal (99 each). 35 (17%) were Asian, two Afro-Caribbean, four other and the remaining 157 (80%) were White Caucasian. 54 (27%) had RA, 81 (41%) PsA, 57 (29%) AS and six had JIA. Coprescribed DMARDs included methotrexate (n=53, 27%), sulfasalazine (n=15, 7.5%), hydroxychloroquine (n=14, 7%) and leflunomide in two individuals. 83 (42%) participants were prescribed adalimumab monotherapy.

Prior to switch, median DAS28 for RA group was 2.28 (0.57 – 6.29). Median BASDAI and spinal VAS for AS cohort was 3.3 (0.8 – 8.8) and 3.0 (0 – 9) respectively. Tender and swollen joint components for PsARC were median three (0-8 tender, 0-6 swollen) in PsA group. Only 30% of the patients had been reviewed face-to-face following the switch. Their respective median disease activity indices were not significantly different from pre-switch assessments. Fifteen (7.5%) patients switched back to the originator for following reasons; injection site reaction (n=7), loss of disease control (n=7) and inability to use the new device (n=1).

Conclusion: Our experience of switching adalimumab patients has been reasonably successful. All were happy to switch after receiving a letter and having the opportunity to contact if necessary. Substantial annual cost savings of over £300,000 have been projected for this financial year. At group level there were no major differences in disease outcomes and 90% reported no issues. However, just under 10% of those reviewed have decided to return to the originator within three months of switch with loss of efficacy and thereby confidence in the drug. We support the routine switching from originator to biosimilar adalimumab however close monitoring is required certainly in the first few weeks of dose administration.

Disclosure of Interests: Julie Begum: None declared, Muhammad Khurram Nisar Grant/research support from: Muhammad Nisar undertakes clinical trials and received support (including attendance at conferences, speaker fees and honoraria) from Roche, Chugai, MSD, Abbvie, Pfizer, BMS, Celgene, Novartis and UCB, Consultant of: Muhammad Nisar undertakes clinical trials and received support (including attendance at conferences, speaker fees and honoraria) from Roche, Chugai, MSD, Abbvie, Pfizer, BMS, Celgene, Novartis and UCB, Speakers bureau: Muhammad Nisar undertakes clinical trials and received support (including attendance at conferences, speaker fees and honoraria) from Roche, Chugai, MSD, Abbvie, Pfizer, BMS, Celgene, Novartis and UCB

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THU0553 A HEALTH ECONOMIC ANALYSIS OF THE USE OF COLOUR DOPPLER ULTRASONOGRAPHY AS THE PRIMARY DIAGNOSTIC MODALITY IN PATIENTS WITH SUSPECTED GIANT CELL ARTERITIS

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Background: EULAR has recommended ultrasonography (US) as first imaging modality for diagnosis of Giant Cell Arteritis (GCA)[1]. For patients with a high pre-test probability who have a negative scan, the recommendation is to use another diagnostic modality like temporal artery biopsy (TAB) to make a diagnosis[1]. We know that a fast-track pathway incorporating US, results in better clinical outcomes[2]; but there are little data on the health-economics of this approach. Since 2017, we have used ultrasonography as the primary diagnostic modality for suspected GCA. In patients with a high pre-test probability with a negative ultrasonography, we perform a temporal artery biopsy.

Objectives: To compare the cost of investigating GCA using first-line US and second-line TAB the use of TAB only. To compare the cost per definite diagnosis of GCA.

Methods: Number of cases from 2007-2009 and 2017-2019 were calculated by the number of TAB performed and number of referrals to hospital GCA clinic, respectively. Costs of the procedure were calculated as per the nationally agreed tariff by the United Kingdom National Health Service. For ease of comparison, we used the 2018/19 tariff (£1284/TAB; £51 for US)

Results: In 2007-2009, 162 cases were referred to clinic and had a TAB, of which 86 were positive. No cases had US. The 2018/19 corrected cost was £208008; the cost per positive diagnosis was £2418.70 (Table 1).

Table 1. Numbers of cases investigated for suspected GCA by TAB or US and the costs corrected to 2018/19 UK NHS tariff.

Years	No of referrals	No of TAB	No of US	No of patients with GCA	Total cost	Cost of making 1 positive diagnosis
2007-09	162	162	0	86	£208008	£2418.70
2017-19	419	69	416	142	£109812	£773.32

In 2017-2019, 419 patients were referred to the GCA clinic, 416 of whom had US for diagnosis. 3 individuals had a TAB as the first diagnostic modality and 66 others were referred for a TAB because of a high pre-test probability and negative US. The 2018/19 corrected cost of this pathway was £109812 and the cost per positive diagnosis was £773.32 (Table 1).

If all cases in 2017-2019 had a TAB for suspected GCA, the 2018/19 corrected cost would have been £537996. The estimated 2018/19 corrected savings in our center was £142728/year. The estimated 2018/19 corrected savings per definite diagnosis of GCA has dropped by £1645.37 (Table 1).

Conclusion: The EULAR recommendation of using first-line US for diagnosis of GCA followed by a TAB in cases with uncertain diagnosis after US, is highly cost-effective in the UK, resulting in cost savings of >£140K per year.

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Disclosure of Interests: None declared

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THU0554 COMORBIDITY AND HEALTH CARE UTILIZATION IN PERSONS WITH SJÖGREN'S SYNDROME: A CLAIMS DATA ANALYSIS

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Background: Sjögren's syndrome (SS) can affect numerous organs, including the muscles, the peripheral nervous system, kidneys and lungs. Epidemiological studies assessing comorbidity and health care utilization are needed to improve health care for this multifaceted disease.

Objectives: To capture comorbidity and medication of persons with SS in a population-based cohort in comparison to matched controls.

Methods: Individuals with an outpatient diagnosis of M35.0 (ICD-10) in ≥2 quarters of a year or an inpatient diagnosis of M35.0 were identified in a German

statutory health insurance fund covering 7.2 million people. Persons in rheumatologic care were grouped by incident or prevalent diagnosis and by co-existing autoimmune disease (sSS) or primary (p)SS and compared to age- and sex-matched controls regarding comorbidity (ICD-10), medical prescriptions, hospitalization and inability to work in the previous year.

Results: In 2018, 7,374 persons (0.1%) had incident and 53,917 persons (0.73%) prevalent SS diagnosis, and 5,920 (11%) were in rheumatologic care. Of these (90% female, mean age 66 years), 3,431 (58%) had further autoimmune disease (sSS), mostly rheumatoid arthritis (80%) and systemic lupus erythematosus (13%). Compared to controls, frequent comorbid conditions in SS were hypertension, osteoarthritis, osteoporosis and depression (table 1). Systemic antirheumatic drugs were prescribed in 31% (pSS) and 66% (sSS) while < 4% received topical therapies. Glucocorticoids (7% controls/34% pSS/59% sSS), NSAIDs (28%/41%/45%), opioids (9%/15%/22%), analgesics (19%/30%/36%) and antidepressants (14%/21%/22%) were more frequently prescribed in SS than in controls, and also hospitalization (21%/32%/39%) and inability to work in persons <65 years (41%/48%/44%, median days 17/24/31) were more frequent in pSS and sSS than in controls.

Table 1 Comorbidity claims diagnoses (%) in persons with Sjögren`s syndrome and controls

	Controls	pSS	sSS
N	*29,910*	*2,489*	*3,431*
Age in years, mean	66.0	65.2	66.6
Female, %	88.9	89.1	90.1
Keratoconjunctivitis sicca	0.5	27.9	28.3
Interstitial kidney disease	7.6	12.8	17.0
Lung involvement	0.0	1.2	1.4
Myopathy	0.0	2.4	3.0
Polyneuropathy	6.1	12.5	15.7
Hypertension	51.5	54.8	63.0
Osteoarthritis	21.9	39.9	46.9
Osteoporosis	10.3	26.6	38.1
Fibromyalgia	1.1	10.8	11.2
Depression	17.8	30.1	32.3
Hypothyroidism	12.8	20.8	19.9
Solid Tumour	8.8	10.3	9.9
Metastatic Cancer	1.1	1.2	1.8

Conclusion: SS claims diagnosis is associated with substantial comorbidity and frequent prescription of anti-inflammatory drugs, analgesics and antidepressants. The individual and societal burden of SS shows that, in addition to effective treatment strategies, intensive attention to comorbidities is important in this disease.

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Disclosure of Interests: Katinka Albrecht: None declared, Thomas Dörner Grant/research support from: Janssen, Novartis, Roche, UCB, Consultant of: Abbvie, Celgene, Eli Lilly, Roche, Janssen, EMD, Speakers bureau: Eli Lilly, Roche, Samsung, Janssen, Imke Redeker: None declared, Kirsten Karberg: None declared, Ursula Marschall: None declared, Angela Zink Speakers bureau: AbbVie, Amgen, BMS, Gilead, Hexal, Janssen, Lilly, MSD, Pfizer, Roche, Sanofi Aventis, UCB, Johanna Callhoff: None declared

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THU0555

HEALTHCARE COSTS IN PATIENTS WITH RHEUMATOID ARTHRITIS SWITCHING FROM THEIR FIRST CONVENTIONAL SYNTHETIC DISEASE-MODIFYING ANTIRHEUMATIC DRUG TO ANOTHER DISEASE-MODIFYING ANTIRHEUMATIC DRUG REGIMEN

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Background: EULAR and ACR guidelines recommend a treat-to-target approach for rheumatoid arthritis (RA). For patients failing their first conventional synthetic disease-modifying antirheumatic drug (csDMARD), EULAR recommends switching to or adding another DMARD. Understanding treatment patterns, durability, and healthcare costs associated with treatments initiated after first csDMARD can help optimize treatment for these patients.

Objectives: To describe real-world healthcare costs among patients with RA who failed their first csDMARD.

Methods: The study included adults with ≥2 RA claims ≥30 days apart in a large US health claims database, who started a csDMARD regimen as the first DMARD then switched to or added another DMARD (index date [ID], 1/1/2012–3/31/2017). All patients had continuous enrollment 1-year before and ≥1 year after ID. Treatment duration was defined as number of days from initial treatment fill until loss of treatment persistence. Unadjusted mean total annualized per-patient-per-year (PPPY) healthcare costs while on treatment were compared via analysis of variance. A generalized linear model with gamma distribution and log link was used to compare total costs adjusted for pre-index costs, patient characteristics, and type of initiated treatment.

Results: The study involved 7,816 patients (median age of 54 yrs, 74% female). Mean (standard deviation) duration of index therapy was 14.0 (12.6) months for patients overall (9.2 [10.1] for monotherapy vs 16.9 [13.1] for combination therapy, $P < .0001$).

Prior to switching, the unadjusted mean PPPY healthcare costs totaled $12,923: $13,923 for monotherapy vs $12,317 ($P = .0009$) for combination therapy. Once switched, patients accrued unadjusted mean PPPY on-treatment healthcare costs of $30,742: $28,757 on monotherapy vs $31,943 ($P = .0003$) on combination therapy. Figure 1 details pre- and post-ID unadjusted costs by index therapy.

Patients on non-TNFi bDMARD monotherapy had higher adjusted total healthcare cost (cost ratio [CR] = 1.58, $P = .0052$) than the total cost on JAKi monotherapy, whereas csDMARD monotherapy (CR = 0.28, $P < .0001$) and csDMARD + csDMARD(s) (CR = 0.26, $P < .0001$) had lower total cost than the cost on JAKi monotherapy. Other factors impacting costs included baseline Charlson Comorbidity Index (CCI) = 2 or ≥3 vs CCI = 1 (CR = 1.14 and 1.25, respectively; both $P < .0001$), baseline total (medical + pharmacy) healthcare costs (CR = 1.24, $P < .0001$), and baseline opioid use (CR = 1.11, $P < .0001$, Figure 2).

Figure 1. Unadjusted mean healthcare costs PPPY (US dollars) among csDMARD patients switching to or adding on another DMARD treatment.

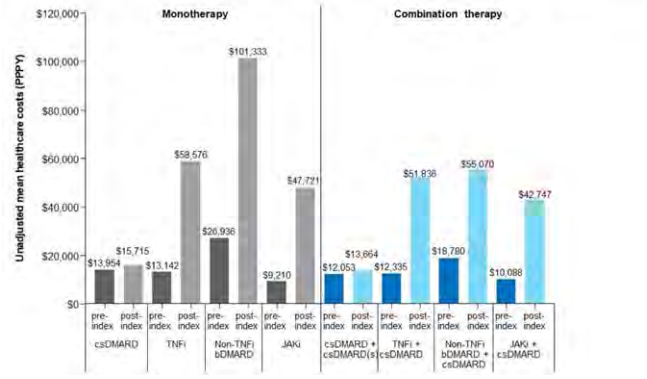
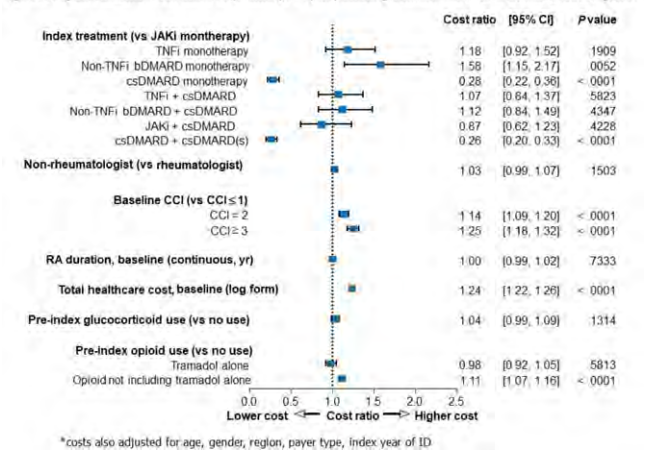


Figure 2. Adjusted healthcare cost model for patients (N = 7,816) switching from first csDMARD to another DMARD regimen.*



*costs also adjusted for age, gender, region, payer type, index year of ID

Conclusion: Real-world data demonstrate short durability of available treatments initiated after first csDMARD. Among the initiated treatments, lowest total healthcare costs were associated with csDMARD, followed by JAKi, then TNFi, and finally non-TNFi bDMARD.

Disclosure of Interests: Robin K Dore Grant/research support from: AbbVie, Amgen, Biogen, Bristol-Myers Squibb, Eli Lilly and Co., Gilead Sciences, Inc., GlaxoSmithKline, Myriad, Novartis, Pfizer, Radius, Regeneron, Sanofi, and UCB., Consultant of: AbbVie, Amgen, Biogen, Bristol-Myers Squibb, Eli Lilly and Co., Gilead Sciences, Inc., GlaxoSmithKline, Myriad, Novartis,

Pfizer, Radius, Regeneron, Sanofi, and UCB., Jenya Antonova Employee of: Gilead Sciences. Inc., Lawrence Chang Consultant of: Gilead Sciences, Inc., Magdaliz Gorritz Consultant of: Gilead Sciences, Inc., Xin Wang Consultant of: Gilead Sciences, Inc., Mark C. Genovese Grant/research support from: Abbvie, Eli Lilly and Company, EMD Merck Serono, Galapagos, Genentech/Roche, Gilead Sciences, Inc., GSK, Novartis, Pfizer Inc., RPharm, Sanofi Genzyme, Consultant of: Abbvie, Eli Lilly and Company, EMD Merck Serono, Genentech/Roche, Gilead Sciences, Inc., GSK, Novartis, RPharm, Sanofi Genzyme

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THU0556 MISSING DATA AND MULTIPLE IMPUTATION IN RHEUMATOID ARTHRITIS REGISTRIES USING SEQUENTIAL RANDOM FOREST METHOD

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Background: Missing data in clinical epidemiological researches violate the intention to treat principle,
reduce statistical power and can induce bias if they are related to patient's response to treatment. In multiple imputation (MI), covariates are included in the imputation equation to predict the values of missing data.
Objectives: To find the best approach to estimate and impute the missing values in Kuwait Registry for Rheumatic Diseases (KRRD) patients data.
Methods: A number of methods were implemented for dealing with missing data. These included *Multivariate imputation by chained equations* (MICE), *K-Nearest Neighbors* (KNN), *Bayesian Principal Component Analysis* (BPCA), *EM with Bootstrapping* (Amelia II), *Sequential Random Forest* (MissForest) and mean imputation. Choosing the best imputation method was
judged by the minimum scores of *Root Mean Square Error* (RMSE), *Mean Absolute Error* (MAE) and
Kolmogorov–Smirnov D test statistic (KS) between the imputed datapoints and the original datapoints that were subsequently sat to missing.
Results: A total of 1,685 rheumatoid arthritis (RA) patients and 10,613 hospital visits were included in the registry. Among them, we found a number of variables that had missing values exceeding 5% of the total values. These included duration of RA (13.0%), smoking history (26.3%), rheumatoid factor (7.93%), anti-citrullinated peptide antibodies (20.5%), anti-nuclear antibodies (20.4%), sicca symptoms (19.2%), family history of a rheumatic disease (28.5%), steroid therapy (5.94%), ESR (5.16%), CRP (22.9%) and SDAI (38.0%), The results showed that among the methods used, MissForest gave the highest level of accuracy to estimate the missing values. It had the least imputation errors for both continuous and categorical variables at each frequency of missingness and it had the smallest prediction differences when the models used imputed laboratory values. In both data sets, MICE had the second least imputation errors and prediction differences, followed by KNN and mean imputation.
Conclusion: MissForest is a highly accurate method of imputation for missing data in KRRD and outperforms other common imputation techniques in terms of imputation error and maintenance of predictive ability with imputed values in clinical predictive models. This approach can be used in registries to improve the accuracy of data, including the ones for rheumatoid arthritis patients.

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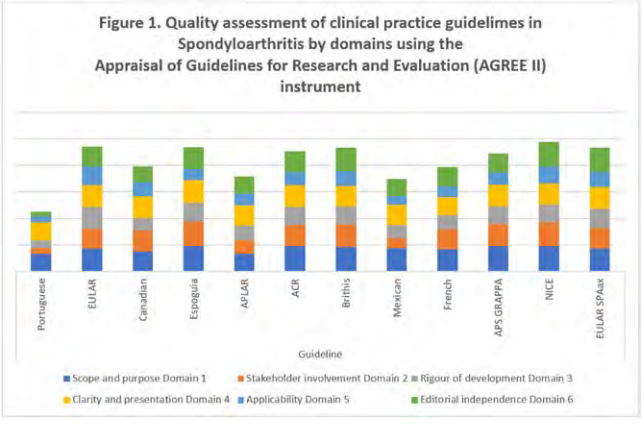
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THU0557 QUALITY ASSESSMENT OF CLINICAL PRACTICE GUIDELINES IN AXIAL AND PERIPHERAL SPONDYLOARTHRITIS: A SYSTEMATIC APPRAISAL

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Background: Clinical practice guidelines (CPG) in spondyloarthritis (SpA) serves as a tool for rheumatologists, health-care providers and patients in the selection of appropriate treatment framework in common clinical scenarios guiding decision-making processes. However, the quality of these guidelines has not yet been evaluated systematically in the field.
Objectives: The aim of the study was to evaluate the quality of the CPG available for the treatment of axial and peripheral SpA.
Methods: A systematic and scientific literature search between 2014 and 2019 was performed in order to identify and select CPG focused on the treatment of axial and peripheral SpA. The authors systematically searched the main guideline databases and guideline developer websites completing the search in PUBMED/MEDLINE and EMBASE. Four independent reviewers with methodological and clinical expertise in the field of SpA, assessed the eligible guidelines using the Appraisal of Guidelines for Research and Evaluation (AGREE II) instrument. Their degree of agreement was evaluated with the intra-class correlation coefficient (ICC). The statistical analyses as done using the R psych package.
Results: Twelve CPG were selected for evaluation. The scores for each of the AGREE II domains were: scope and purpose 86% (range: 67–99%); stakeholder involvement 71% (range: 22–93%); rigour of development 61% (range: 29–82%); clarity and presentation 79% (range: 68–86%); applicability 48% (range: 21–71%); and editorial independence 72% (range: 19–92%). Most of the appraised guidelines could be recommended (n=12) or recommended with limitations (n=12) for use in clinical practice. The overall agreement among reviewers was moderate (ICC: 0.40; 95% CI 0.16 to 0.82). The CPG with the best quality assessment using the AGREE II instrument was the NICE guideline developed by the National Institute for Health and Care Excellence. A slightly higher quality assessment of CPG developed by research agencies or guideline developers was observed, in comparison to those developed by scientific societies. Figure 1. .ssessment cientific societies.eld of ocieties and XXXXXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX
Conclusion: Quality assessment of guidelines for the treatment of axial and peripheral SpA is good with an average of 69%. However, a cut-off point has not been clearly established. Measures should be taken to assure that CPGs are based on the best available evidence and rigorously developed and reported. Additional efforts are needed to provide high-quality guidelines that serve as a useful and reliable instrument for clinical decision-making process in the field of SpA.



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THU0558 ANTI-CCP NEGATIVE PATIENTS WITH NEW MUSCULOSKELETAL SYMPTOMS: IMPROVING REFERRALS FROM PRIMARY CARE

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Background: The presence of anti-cyclic citrullinated peptide antibodies (anti-CCP antibodies) is associated with progression to inflammatory arthritis (IA) [1]; however, most patients attending primary care with a new non-specific musculoskeletal (MSK) complaint and no clinical synovitis have a negative result for this test (CCP-). Considering that only a small proportion of these individuals will be diagnosed with an IA within the next 12 months, predicting disease progression in these patients appears to be more challenging.
Objectives: To investigate factors that could be associated with disease progression in patients testing CCP- in order to optimise primary care referrals to Rheumatology.
Methods: A prospective observational study recruiting patients over 16 years old with a new MSK complaint and no clinical synovitis was conducted. Patients recruited from primary care centres across the UK from July 2007 until November 2018 were included in this analysis. Those testing negative for the anti-CCP2 assay (initially phadia, later bioplex) were sent questionnaires 1 year later, and GPs were contacted in November 2019 to confirm their disease status.
Results: 7521 eligible patients were recruited from primary care. 7290 (97%) of them were CCP- and 5678 returned the questionnaire after 1 year. 239 patients (4.2%) of these CCP- reported progression to IA; however, this diagnosis was only confirmed in 53 of them (0.93%). In another 38 patients, the IA diagnosis could not be confirmed and therefore they were not included in the analysis. 21 patients progressed to rheumatoid arthritis (RA), 13 to spondyloarthritis, 11 to polymyalgia rheumatica (requiring disease-modifying anti-rheumatic drugs), 3 to polymyositis, 3 to systemic lupus erythematosus and 2 to systemic sclerosis. Table 1 describes the most troublesome joints and table 2 other concomitant MSK diagnoses of the non-progressors/ progressors; and among the last ones, the RA group. Multivariable analysis showed that pain in specific joints was associated with development of IA within the following 12 months: hand odds ratio (OR) 2.1 [95%CI (1.09-4.16), p=0.027], knee OR 2.0 [95%CI (1.13-3.91), p=0.02], and shoulder OR 1.8 [95%CI (1.02-3.45), p=0.043). Smoking exposure, having a first degree relative with RA and gender were not predictive for progression. Older age showed only a slightly higher risk for IA [OR 1.04, 95%CI (1.01-1.06) p=0.001].

Table 1. Characteristics, troublesome joints of the participants

	NON-PROGRESSORS (n=5588)	PROGRESSORS (n=52)	RA progressors (n=21)
Female %	72	58	57
Mean age y.o.	53 (16-91)	60 (30-82)	60 (30-82)
FDR with RA %	38	33	33
Ever Smoked %	38	43	40
Neck pain %	30	29	14
Shoulder pain %	41	58	52
Elbow pain %	29	38	29
Wrist pain %	38	46	48
Hand pain %	53	71	76
Thumb pain %	36	48	57
Back pain %	33	25	24
Hip pain %	36	29	19
Knee pain %	55	71	62
Ankle pain %	30	23	24
Foot pain %	34	40	33

Table 2. Concomitant MSK diagnosis

	NON-PROGRESSORS (n=5588)	PROGRESSORS (n=52)	RA progressors (n=21)
Carpal tunnel syndrome%	13	17	30
Rotator cuff %	12	19	20
Trigger finger %	5	4	0
Tennis elbow %	15	10	5
Osteoarthritis %	18	25	20

Conclusion: In CCP- patients without clinical synovitis, hand, knee and shoulder pain should be investigated more carefully as these involve a higher risk of progression to IA. Patient reported outcomes regarding rheumatic diseases are not reliable; the distribution of joint pain seems to be a more useful tool than the family history when assessing the need for referral to Rheumatology.
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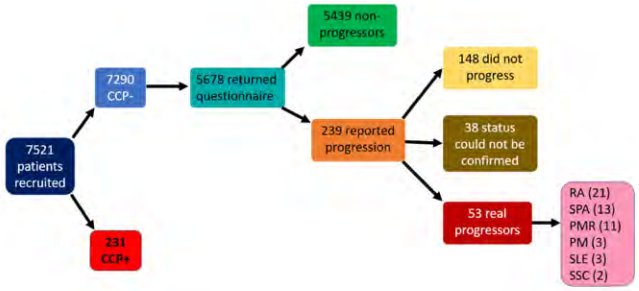


Figure 1. Study participants and outcome

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THU0559 IMPLEMENTATION OF A TRIAGE SYSTEM IN A HOSPITAL WITH HIGH DEMAND FOR CARE

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Background: Our hospital has 4 Rheumatologists and is in charge of 425.000 inhabitants (1 rheumatologist per 106.250 inhabitants). In November 2017, there were 503 referrals from primary care waiting for a first visit with the rheumatologist. Given the impossibility of covering this number of waiting patients through normal operation, it was decided to implement a rapid access polyclinic that started in December of 2017.
Objectives: To evaluate the effectiveness of a triage system in a center with high demand for care.
Methods: Patients referred by the general practitioner were evaluated by a senior rheumatologist in a 10-minute consultation using a predefined interrogation, expanded case-by-case based on the criteria of each rheumatologist. According to the results of the interview, the situation of the patient was categorized into: urgent, normal rheumatology control or control in primary care. For urgent consultations, an early control polyclinic was created to evaluate these patients within the following 15 days. The usual consultations entered into the usual scheduling system. The pathologies that were considered to require control in primary care were assigned to a coordination polyclinic where the patients were evaluated by an internist, in charge of confirming the diagnosis, educating the patient, and, if applicable, refer to primary care. No patient was discharged immediately after the triage. We report the data of the first 136 patients.
Results: The waiting time was reduced from a median of 275 days (IQR 66-591) to 46.5 (23-140). Refer to table 1 for full results. In 52.2% of referred patients the suspicion of a chronic autoimmune or inflammatory disease was described in the referral note. In these patients, when comparing with patients whose referral notes did not refer to an inflammatory or autoimmune disease, the waiting time for triage was significantly shorter, the percentage of patients who were discharged from rheumatology was significantly lower, and the percentage of patients in whom a chronic autoimmune or inflammatory disease was confirmed in the first control was significantly higher.

Table 1

	All patients	Only those with suspected autoimmune or chronic inflammatory disease in referral note	Patients referred for other reasons (fibromyalgia, arthralgia, myalgia, osteoporosis, etc.)	p
Number (%)	136 (100)	71 (52.2)	65 (47.8)	NA
Age,mean years (SD)	51.8 (16.3)	50.7 (16.4)	53.1 (16.2)	NS
Men, n (%)	24 (17.6)	15 (21.1)	9 (13.8)	NS
Time between referral and triage, median days (IQR)	46.5 (23-140)	34 (15.5-124.5)	54 (28-441)	0,017
Triage resolution				
Urgent control, n (%)	92 (67.6)	55 (77.5)	37 (56.9)	0,011
Normal Control, n (%)	25 (18.4)	12 (16.9)	13 (20)	NS
Primary care coordination, n (%)	19 (14)	4 (5.6)	15 (23.1)	0,003
Time between triage and first control, median days (IQR)	21 (14-42)	21 (12.5-41)	26 (21-42)	NS
First control resolution, n (%)	96 (70.6)	54 (76.1)	42 (64.6)	NS
Diagnosis confirmation, n (%)	37 (38.5)	26 (48.1)	11 (16.9)	0,028
Continue control, n (%)	41 (42.7)	26 (48.1)	15 (23.1)	NS
Discharge to primary care, n (%)	18 (18.8)	2 (3.7)	16 (24.6)	<0,001

SD: standard deviation; n: number; IQR: Interquartile range

Conclusion: We consider this strategy as successful in reducing care times and identifying patients who require an early start of treatment and close control. Referral notes from primary care were generally adequate to identify patients who required to continue rheumatologist control.

References: None.

Disclosure of Interests: Sebastian Ibáñez Consultant of: Novartis, Paid instructor for: Bristol Myers, Speakers bureau: Abbvie, Francisca Valenzuela: None declared, Oriela Martinez: None declared, Omar Valenzuela Consultant of: Bristol Myers, Paid instructor for: Bristol Myers, Speakers bureau: Bristol Myers, Abbvie, Francisco Silva Consultant of: Roche, Speakers bureau: Roche, María José Villar: None declared, María Paz Poblete: None declared, Claudia Mardones: None declared

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THU0560 PRIMARY CARE PHYSICIAN PERSPECTIVES ON DELAYS IN DIAGNOSIS OF AXIAL SPONDYLOARTHRITIS: A QUALITATIVE STUDY

S. H. Liu[1], K. Lapane[1], D. Shridharmurthy[1], S. Khan[1], K. Ferrucci[1], C. Dubé[1], E. Yi[2], J. Kay[1,3]. [1]*University of Massachusetts Medical School, Population and Quantitative Health Sciences, Worcester, United States of America*; [2]*Novartis Pharmaceuticals Corporation, HE&OR and Medical Access, US Clinical Development and Medical Affairs, East Hanover, United States of America*; [3]*University of Massachusetts Medical School, Medicine, WORCESTER, United States of America*

Background: The average delay in diagnosis for patients with any form of spondyloarthritis (SpA) ranges from 7 to 10 years [1–5]. In axial spondyloarthritis (axSpA), a subgroup of SpA, it is 5 to 14 years [4, 6, 7]. Factors that contribute to this delay include the lack of diagnostic criteria for axSpA and the difficulty in distinguishing inflammatory back pain (IBP), a key symptom of axSpA, from other highly prevalent forms of low back pain [8–10]. This impedes timely referral of these patients to rheumatologic care and initiation of appropriate treatment.

Objectives: Describe understanding of, attitudes towards, and practices regarding axSpA among primary care physicians.

Methods: We recruited 18 primary care physicians practicing in the United States as part of a larger qualitative study: the **Sp**ondylo**A**rthritis **S**creening and **E**arly **D**etection (SpA-SED) Study. We used purposive sampling with a goal of including an equal number of family medicine and internal medicine physicians who were balanced by gender. Physicians provided informed consent to participate in an in-depth interview (up to 60 minutes), conducted in person (n = 3) or over the phone (n = 15), between February and May 2019. The interview guide was developed by a multidisciplinary team, with input from rheumatologists. Topics included the physicians' approaches to evaluating back pain, their awareness about axSpA, their differential diagnosis of axSpA, the laboratory tests and imaging studies ordered when axSpA is suspected, their referral patterns for patients with presumed axSpA, their thoughts about factors contributing to diagnostic delay in axSpA, and their opinions about an Inflammatory Back Pain Assessment – ASAS criteria screening tool [5].

Results: Barriers to early diagnosis included patient factors (eg, multiple complaints, back pain not being the chief complaint), disease characteristics (eg, slow rate of disease progression), physician characteristics (eg, lack of rapport between patients and their primary care physicians), and structural/system issues (eg, lack of time). Most physicians reported that they would perform laboratory tests before referring a patient to a rheumatologist.

Conclusion: Primary care physicians were surprised to learn of the average delay to axSpA diagnosis, considered that this lengthy delay was problematic, and agreed that improvements are needed in screening for and early detection of axSpA. Physicians believed that there would be a role for using a screening tool in the primary care setting to improve diagnostic delay, but that evidence to support its implementation is needed.

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THU0561 PREDICTING LIVER TOXICITY CAUSED BY CONVENTIONAL SYNTHETIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS

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Background: Routine laboratory testing is recommended for early identification of toxicity during conventional synthetic disease modifying antirheumatic drug (csDMARD) treatment. Based on expert consensus, testing is recommended every 2–4 weeks for the first 3 moths and quarterly thereafter (1).

Objectives: In addition to evaluating the incidence of alanine transaminase (ALT) elevations in rheumatoid arthritis (RA) patients initiated on 1–2 csDMARDs, we aimed to distinguish patterns in ALT levels to develop a model for identifying patients at high risk for liver toxicity.

Methods: We identified RA patients who were initiated a new csDMARD course at the rheumatology clinic of Turku University Hospital in 2013–2019. Baseline and follow-up safety monitoring results were drawn from the electronic health record (EHR) data. Data on diagnoses and csDMARD initiation/cessation dates were manually confirmed from the EHR.

As the primary endpoint, we used ALT-elevations of more than twice the upper limit of reference range (women ≥ 70 U/l, men ≥ 100 U/l) within 6 months after treatment initiation. Intergroup differences were tested using Mann-Whitney test for continuous variables and the chi-square test or Fisher's exact test (n<5) for categorical variables. Associations between different

characteristics and the primary endpoint were tested using Cox proportional hazards regression.

Results: We identified 2851 RA patients of whom 1017 initiated a new csDMARD course requiring laboratory monitoring. Of these, 860 patients (58.9 years, 68% women, 65% seropositive) were included in the analyses after excluding patients with missing laboratory results (n=148) or elevated ALT at baseline (n=9). Of the 860 patients, 220 initiated two csDMARDs simultaneously [99% sulfasalazine (SSZ) and methotrexate (MTX)]. Primary endpoint was reached in 55 of 860 (6.4%) patients, including 10 who initiated two csDMARDS. Of these 55 patients, primary endpoint was reached in 40 of 55 (73%) patients during first three follow-up tests. In 31 of 55 (56%) patients, including 3 initiators of 2 csDMARDs, elevated ALT led to csDMARD cessation during the first 6 months. In Cox proportional hazards model with age, sex, seropositivity, baseline ALT, and csDMARDs as the explanatory variables, only baseline ALT level [hazard ratio 1.56 per 1 SD increase, 95% confidence interval (CI) 1.30–1.88, p<0.001] was associated with incident ALT-elevations. Survival according to normalized baseline ALT is shown in Figure, where normalized ALT value of 1.0 refers to the upper limit of reference range (women 35 U/l, men 50 U/l).

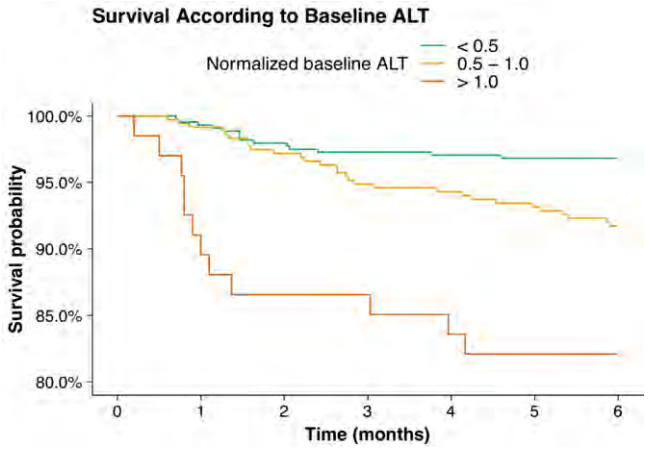


Table. Multivariable Cox proportional hazards model including the results of the first follow-up laboratory test. Only values before occurrence of primary endpoint were used (n=843).

Characteristic	Hazard ratio (95% CI)	P Value
Age (per year)	1.00 (0.98-1.02)	0.78
Sex (male)	0.50 (0.21-1.15)	0.10
Seronegativity	0.88 (0.44-1.75)	0.71
Baseline ALT*	1.72 (1.32-2.25)	<0.001
ALT / t (per 1 SD increase / 30 days) [§]	1.33 (1.17-1.52)	<0.001
Methotrexate	0.58 (0.22-1.52)	0.27
Sulfasalazine	0.95 (0.38-2.35)	0.91
Azathioprine	2.30 (0.48-11.13)	0.30
Leflunomide	1.08 (0.23-5.16)	0.92

*Normalized ALT according to sex-specific reference range; [§]Rate of change from baseline to 1st follow-up test

Conclusion: Most incident ALT elevations can be predicted before the first csDMARD dose. Patients with elevated ALT at baseline or a rising trend at first follow-up are at high risk for liver toxicity and benefit from frequent testing.

References:

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Disclosure of Interests: Laura Kuusalo Consultant of: Gilead, Pfizer Finland, Speakers bureau: Abbvie, Orion, Pfizer Finland, Novartis, Sanofi, Mikko Venäläinen: None declared, Sofia Saranpää: None declared, Heidi Kirjala: None declared, Laura Elo: None declared, Laura Pirilä Consultant of: Novartis, MSD Finland, Roche, Bristol-Myers-Squibb, Pfizer Finland, Sanofi, Abbvie, Eli Lilly Finland, UCB Pharma, Janssen-Cilag, Mylan, Sandoz, Boerhinger-Ingelheim, Paid instructor for: Boehringer-Ingelheim, MSD Finland, Speakers bureau: Boehringer-Ingelheim, Pfizer Finland

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THU0562 ECONOMIC IMPACT ASSOCIATED WITH COMPLICATIONS OF WOMEN IN REPRODUCTIVE AGE LIVING WITH INFLAMMATORY IMMUNE-MEDIATED DISEASES (PSO, PSA, RA, AXSPA) IN SPAIN

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Background: Cost of the complications that may appear during reproductive age in women living with inflammatory immune-mediated diseases have scarcely been studied.

Objectives: To obtain an expert consensus in the use of resources associated to complications of women in reproductive age living with immune-mediated diseases: psoriasis (PSO), psoriatic arthritis (PsA), rheumatoid arthritis (RA) and axial spondyloarthritis (axSpA) and estimate an economic impact.

Methods: A cost-analysis was developed to estimate the impact associated with the complications of women of reproductive age with PSO, PsA, RA and axSpA. The analysis considered the complications during fertility and conception (preconception consultation and assisted reproduction), in pregnancy (miscarriage in the first trimester, late abortion in the second trimester, preeclampsia, delayed or restricted intrauterine growth and threat of premature delivery) and in the postpartum (admissions in neonatology of premature infants).

An online questionnaire was designed for the validation of the inputs used in the cost-analysis. Subsequently, the questionnaire was sent to a multidisciplinary panel composed of, rheumatologist, gynecologists, neonatologists and dermatologist. A consensus meeting was carried out to validate and agree the parameters used in the analysis.

Unitary cost for resources (€,2019) were obtained from national local databases. The perspective of analysis was the National Healthcare System and the time horizon was one year.

Results: During fertility and conception, an annual cost per patient of € 229 was estimated for a preconception consultation in a patient with PSO, of € 3,642 for a preconception consultation in patients with PsA, RA and axSpA and € 4,339 for assisted reproduction.

Women with complications in pregnancy had an annual cost per patient of € 1,214 for a miscarriage in the first trimester, € 4,419 for a late abortion in the second trimester, € 11,251 for preeclampsia € 3,183 for delayed or restricted intrauterine growth and € 12,122 for the threat of premature delivery.

In the postpartum complications, an annual cost per patient of € 120,364, € 44,709 and € 5,507 were estimated associated with admissions in neonatology of premature infants of <28 weeks, from 28 to 32 weeks and from 33 to 37 weeks, respectively.

Conclusion: This modeling provides insight on the economic burden of complications associated with women in reproductive age for immune-mediated diseases (PSO, PsA, RA, axSpA). Individualization of treatment, additional and close monitoring may reduce the risk and burden of these complications.

Disclosure of Interests: Julia Martínez-Barrio Consultant of: UCB Pharma, Olga Villar Consultant of: UCB Pharma, Oníca Armijo Consultant of: UCB Pharma, María Castellanos Consultant of: UCB Pharma, Natalia Marín Huarte Consultant of: UCB Pharma, María Mareque Consultant of: UCB Pharma, Miguel Angel Casado Consultant of: UCB Pharma, Nuria Martínez Consultant of: UCB Pharma

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THU0563 IMMUNOGENICITY AND SAFETY OF 23-VALENT PNEUMOCOCCAL VACCINE IN PATIENTS WITH ANKYLOSING SPONDYLITIS (PRELIMINARY RESULTS).

N. Muravyeva[1], B. Belov[1], G. Tarasova[1], M. Cherkasova[1], G. Lukina[1]. [1]*V.A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Background: For the treatment of patients with ankylosing spondylitis (AS), biological drugs are widely used, which can effectively control the activity of the disease and radically change the prognosis. However, the use of these drugs is associated with an increasing risk of infections, some of which can probably be prevented by vaccination.

Objectives: The aim of the study was to evaluate the immunogenicity and safety of the 23-valent pneumococcal vaccine (PPV-23) in patients with AS.

Methods: The study included 18 patients with AS: 14 men, 4 women, age 38.7±11.5 years, duration of the disease 16.2±10.8 years. 5 patients had a history of more than 2 episodes of lower respiratory tract infections (pneumonia, bronchitis). At the time of inclusion in the study in 89% of patients, activity of

diseases was assessed as high (median BASDAI was 5.1 [4; 6.2]). All patients received non-steroidal anti-inflammatory drugs, 6 patients - sulfasalazine, 4 - methotrexate, 1 - glucocorticoids, 1 – etanercept. PPV-23 was administered in an amount of 1 dose (0.5 ml) subcutaneously against the background of therapy. In 14 patients vaccination was performed before the appointment of secukinumab; 2 of them continued to take methotrexate, 3 - sulfasalazine. The level of antibodies to pneumococcal capsular polysaccharide was determined using the EIA PCP IgG kit (TestLine Clinical Diagnostics s.r.o., Czech Republic) before vaccination, 1 and 3 months after vaccination. The duration of follow-up was 6.7±4.9 months.

Results: The dynamics of the concentration of antibodies to pneumococcal capsular polysaccharide is presented in the table.

Table. Concentration of pneumococcal antibodies in patients with AS, U/ml, Me [25; 75 percentile]

1 visit (initial)	2 visit (after 1 month)	3 visit (after 1 month)
78.2 [35.2; 246.3]	246.7 [148.6; 266.1]*	261.1 [214.1; 273,4]**

*p=0.04 **p=0.008

After 1 and 3 months after vaccination, the concentration of antibodies to pneumococcal capsular polysaccharide was significantly higher than the baseline values. None of the patients had lower respiratory tract infections. There was no exacerbation of disease. 83% of patients did not have any adverse effects of vaccination. Reactions at the injection site (pain, swelling and hyperemia of the skin up to 2 cm in diameter), resolved independently after 3-5 days, were noted in 2 patients. One patient registered a severe local reaction (infiltration and hyperemia of the skin up to 8 cm in diameter, pain in the arm), accompanied by low-grade fever for 2 days, which required the appointment of antihistamine drugs.

Conclusion: Preliminary results indicate satisfactory immunogenicity and safety of the PPV-23 in patients with AS. Further research is needed to better assess the immunogenicity, efficacy and safety of the vaccine.

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THU0564 PARTICIPANT ENGAGEMENT IN AN ARTHRITISPOWER REAL-WORLD STUDY TO CAPTURE SMARTWATCH AND PATIENT-REPORTED OUTCOME DATA AMONG RHEUMATOID ARTHRITIS PATIENTS

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Background: Clear characterization of how different types of patient-generated data reflect patient experience is needed to guide integration of electronic patient-reported outcome (ePRO) measures and biometrics in generating real-word evidence (RWE) related to rheumatoid arthritis (RA).

Objectives: To characterize the level of participant (pt) engagement/adherence and data completeness in an ongoing study of 250 RA pts enrolled in the Digital Tracking of Arthritis Longitudinally (DIGITAL) study[1] of the ArthritisPower real-world registry.

Methods: ArthritisPower pts with RA were invited to join a digital RWE study with 14-day lead-in and 12-week main study period. In the lead-in, pts were required to electronically complete: a) two daily single-item Pain and Fatigue numeric rating scales and b) longer weekly sets of ePROs. Successful completers of the lead-in were mailed a smartwatch (Fitbit Versa) and study materials. The smartwatch collected activity, heart rate, and sleep duration/quality biosensor data; a study-specific customization of the ArthritisPower mobile application collected ePROs. The main study period included automated and manual reminders/prompts about completing ePROs, wearing the smartwatch and regularly syncing it. Study coordinators monitored pt data and contacted pts via email, text and/or phone to resolve adherence issues during the conduct of the study based on pre-determined rules triggering pt contact. Rules were based chiefly on consecutive spans of missing data. Pts were considered adherent in giving complete data for each week if providing (1) daily ePROs for ≥5 of 7 days/week, (2) weekly ePROs and (3) ≥80% of synced activity data for ≥5 of 7 days/week. Composite adherence for the first month of the main study period required meeting >70% weekly adherence parameters during the first 30 days, ie completing daily ePROs for ≥5 of 7 days/week, weekly ePROs ≥3 of 4 weeks and ≥80% of synced activity data for ≥5 of 7 days/week.

Results: As of December 2019, 170 ArthritisPower members enrolled and completed at least 30 days of the main study period; 92.9% female with mean (SD) age 52.5 (10.7) and 10.5 (10.4) years since diagnosis. The overall conversion rate from initial interest to successful completion of the lead-in period was 49.0%. Pts who advanced to the main study were significantly more likely than those who did not to be currently employed (52.9% vs. 41.8%, p=0.038) and be on biologic DMARD monotherapy (64.7% vs. 47.5%, p=0.001). Overall, daily ePRO data had the lowest adherence with 70.0% of pts providing >70% of the requested data consistently across the first 30 days of the main study period (Figure 1). Composite adherence was met by 66.5% of pts. The most common time of day to provide ePRO data was morning, in the hours around scheduled app and email notifications at 10 a.m. in pt's local time zone. Activity data had the highest adherence and persistence, with 92.9% of pts providing 80% or more of activity data for each 24-hour period in the first 30 days (Figures 1 & 2). Observed weekly adherence did not decline over time. Of 5100 possible person days in the study at day 30, we observed 643 days (91.0% of actual to maximum possible total patient days) where activity data was provided for at least 80% of the 24-hour period.

Conclusion: RWE studies involving passive data collection in RA require pt-centric implementation and design to minimize pt burden, promote longitudinal engagement and maximize adherence. Passive data capture via activity trackers such as smartwatches, along with regular contact such as automated reminders, may facilitate greater pt adherence in providing longitudinal data for clinical trials.

References:

[1] Nowell WB, et al. JMIR Res Protoc. 2019;8(9):e14665.

Figure 1. Completeness of Data in Lead-in and Main Study Period, Month 1 (N=170)

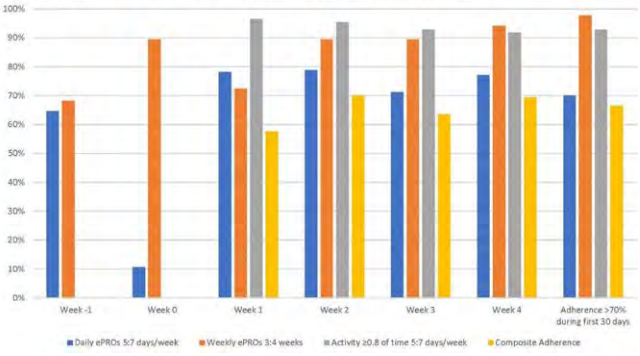
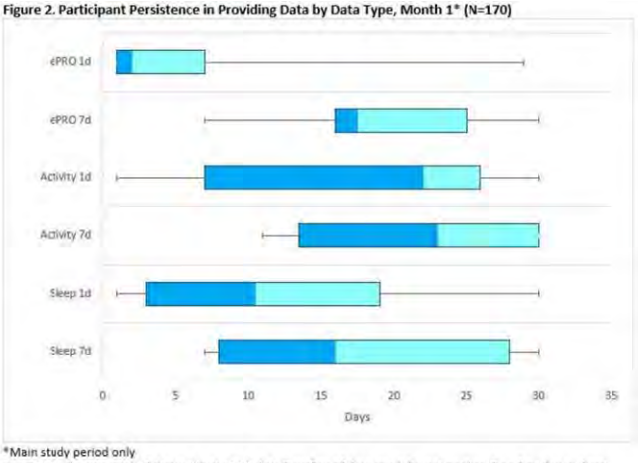


Figure 2. Participant Persistence in Providing Data by Data Type, Month 1* (N=170)



*Main study period only

- ePRO 1d: Days until 1st day without ePRO data (number of days until the patient has their first day without daily or weekly ePRO data)
- ePRO 7d: Days until 7 consecutive days without ePRO data (first occurrence of 7 days with no PRO)
- Activity 1d: Days until 1st day without activity data
- Activity 7d: Days until 7 consecutive days without activity data
- Sleep 1d: Days until 1st day without sleep data
- Sleep 7d: Days until 7 consecutive days without sleep data

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declared, Kelly Gavigan: None declared, Shilpa Venkatachalam: None declared, Laura Stradford: None declared, Jessica Boles: None declared, Justin Owensby: None declared, Cassie Clinton: None declared, Ilya Lipkovich Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Amy Calvin Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Virginia S. Haynes Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company
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THU0565 **RESEARCHERS' PERSPECTIVES ON ADHERENCE INTERVENTION RESEARCH AND OUTCOMES IN RHEUMATOLOGY: AN INTERNATIONAL QUALITATIVE STUDY**

S. Salmasi[1], A. Kelly[2], S. J. Bartlett[3], M. De Wit[4], L. March[5], A. Tong[5], P. Tugwell[6], K. Tymms[2], S. Verstappen[7], M. De Vera[1]on behalf of OMERACT-Adherence Working Group. *[1]University of British Columbia, Vancouver, Canada*; *[2]The Australian National University, Canberra, Australia*; *[3]McGill University, Montréal, Canada*; *[4]OMERACT Patient Research Partner, Amsterdam, Netherlands*; *[5]The University of Sydney, Camperdown, Australia*; *[6]University of Ottawa, Ottawa, Canada*; *[7]The University of Manchester, Manchester, United Kingdom*

Background: Medication non-adherence is a significant problem among patients with rheumatic diseases. Research on adherence interventions in rheumatology is limited and disappointing, with studies using heterogeneous outcomes. Understanding these limitations is needed to inform the design of better interventions and research studies.
Objectives: To describe researchers' perspectives and experiences on adherence intervention research and outcomes in rheumatology.
Methods: Semi-structured interviews using video conference were conducted with researchers who had been an investigator on an adherence study of any design in the past 10 years. Interviews were recorded and transcribed verbatim. Participants were asked about their experiences with conducting adherence research and perspectives on introduction of a core domain set of outcomes for adherence intervention trials in rheumatology. Data collection and thematic analysis were conducted iteratively, until saturation.
Results: We interviewed 13 researchers from seven countries (Australia, Belgium, Canada, Netherland, Thailand, UK, and USA). A majority worked in academia (75%), specialized in epidemiology and/or health services research (62%) and had led between 2-5 adherence studies in the past five years (62%).
Three themes were identified: **1)** challenges in designing, conducting and evaluating adherence studies; **2)** current outcomes in adherence intervention studies and their relevance; and **3)** implementing a core domain set of outcomes for adherence intervention studies.
Major challenges in conducting adherence research included inconsistent adherence terminology and measurement. Participants noted a lack of guidance on outcome selection and measurement when evaluating the effectiveness of an adherence intervention and indicated their preference for research to report adherence, intervention-specific, and health-related outcomes. Finally, implementing a core domain set of outcomes was thought to be challenging but valuable in strengthening the evidence (by facilitating meta-analysis), and improving clinical outcomes (by informing clinicians about the effectiveness of interventions).
Conclusion: Adherence research in rheumatology has been hindered by lack of standardization and guidance on terminology, measurement and outcome selection. Our findings form the basis for recommendations for improving the design, conduct and evaluation of adherence intervention studies in rheumatology, particularly for developing a core domain set of outcomes to improve consistency and facilitate comparisons.

Table 1. Themes and representative quotations.

Theme 1: Challenges in designing, conducting and evaluating studies of adherence interventions
"…the people you often most want in your sample are the people who are non-adherent and often the people who are non-adherent are the people who are hardest to recruit."
"Long term the issue has been about measurements because people confuse and conflate various aspects of medication adherence.
Theme 2: Current outcomes in adherence intervention studies and their relevance
"you have a whole range of outcomes…psychological outcomes…there's measures of health care utilization and things like attendance at hospital, nurse appointments and duration, things like times off work,, and also all the relevant clinical outcomes."
Theme 3: Implementing a core domain set of outcomes for adherence intervention studies
"…will make trials more comparable and increase the likelihood that you'd be able to combine efforts internationally"

Disclosure of Interests: Shahrzad Salmasi: None declared, Ayano Kelly: None declared, Susan J. Bartlett Consultant of: Pfizer, UCB, Lilly, Novartis, Merck, Janssen, Abbvie, Speakers bureau: Pfizer, UCB, Lilly, Novartis, Merck, Janssen, Abbvie, Maarten de Wit Grant/research support from: Dr. de Wit reports personal fees from Ely Lilly, 2019, personal fees from Celgene, 2019, personal fees from Pfizer, 2019, personal fees from Janssen-Cilag, 2017, outside the submitted work., Consultant of: Dr. de Wit reports personal fees from Ely Lilly, 2019, personal fees from Celgene, 2019, personal fees from Pfizer, 2019, personal fees from Janssen-Cilag, 2017, outside the submitted work., Speakers bureau: Dr. de Wit reports personal fees from Ely Lilly, 2019, personal fees from Celgene, 2019, personal fees from Pfizer, 2019, personal fees from Janssen-Cilag, 2017, outside the submitted work., Lyn March: None declared, Allison Tong: None declared, Peter Tugwell: None declared, Kathleen Tymms: None declared, Suzanne Verstappen Grant/research support from: BMS, Consultant of: Celltrion, Speakers bureau: Pfizer, Mary De Vera: None declared
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THURSDAY, 04 JUNE 2020

Rehabilitation

THU0566 **THE EFFECT OF KINESIO-TAPING ON CHRONIC NONSPECIFIC LOW BACK PAIN: PRELIMINARY RESULTS OF A DOUBLE BLINDED RANDOMIZED CLINICAL TRIAL.**

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Background: The technique of Kinesio-Taping is a method of adhesive bandage exerting traction on the skin which would favorably influence the muscular and articular systems by reducing the pressure exerted on the subcutaneous mechanoreceptors thus reducing pain and muscle tension.
Objectives: The aim of this study is to assess the effectiveness of Kinesio-Taping in the short and medium term on pain and function in patients with chronic nonspecific low back pain compared to a placebo.
Methods: We conducted a double-blind, two-arm randomized clinical trial. The study should include a total of 70 patients randomized into 2 groups: Kinesio-Taping (n = 35) and control group (n = 35). To this date we have included 46 patients. All patients receives four I-shaped adhesive strips arranged in a star-like shape and applied to the most painful region of the lower back with a tension between 25% to 30% in the taping group. The placebo group received a taping procedure with no tension. Taping is applied three times (at baseline, fourth and eighth day). Patients are assessed at baseline, on day 14 and at 4 weeks by the Arabic version of the Oswestry Physical and Functional Disability Index (ODI) which is the primary outcome. The secondary outcomes are the assessment of pain and functional disability according to the visual analog scale (VAS) evaluated on a scale of 0 to 10, as well as Rolland-Morris score.
Results: Both groups were comparable at baseline concerning the demographical and clinical characteristics (P > 0.05) (table 1). The result of repeated measures ANOVA showed a significant change in ODI score and in VAS for pain and functional disability as well as Rolland-Morris score in both groups. Using the ANCOVA, controlling for pre-test scores, a significant difference was found between the two groups (table 2).

Table 1. Clinical characteristics of study population.

	Taping groupe (n=22)	Placebo groupe (n=24)	*p* value
Age	42±8,32	40±9,56	0,618
Female gender	21	18	0,098
Prolonged standing position	14	16	0,829
Heavy load carrying	15	16	0,913
Walking aid	0	2	0,490
Comorbidities	8	6	0,403
Body mass index	27±3,68	28±7,02	0,501
ODI of baseline	36±18,82	31±12,65	0,329

Conclusion: Our clinical trial offers preliminary evidence on the superiority of Kinesio-Taping in the treatment chronic back pain compared to placebo concerning the reduction of pain and disability. Thus, it can be used as a complementary method in chronic non-specific low back pain.

Table 2. Primary and secondary outcomes in the Kinesio-Taping and placebo group.

	Taping groupe (n=22)				Placebo groupe (n=24)				ANCOVA
	Baseline	Day 12	4 weeks	*p* value	Baseline	Day 12	4 weeks	*p* value	
ODI	36±18,82	24±19,83	24±19,32	<0,001	31±12,65	28±13,32	29±13,24	0,03	<0,001
VAS of pain	7±1,3	3,9±2,2	4,6±2,2	<0,001	6,5±1,2	5,5±2,2	5,7±2,2	0,008	<0,001
VAS of functional disability	6,7±1,5	4±2,8	4,4±2,5	<0,001	5,9±2,3	5,2±2,2	5,3±2,2	0,003	<0,001
Rolland Morris	7,4±4,6	5,2±4,7	5,3±4,6	<0,001	8,4±4,8	7,6±4,2	7,3±4,1	0,05	0,06

ODI: Owestry Disability Index **VAS:** visual analog scale

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.2979

THU0567 HIP ABDUCTORS STRENGTH AND TRUNK, PELVIS, HIP AND KNEE FRONTAL PLANE KINEMATICS ANALYSIS DURING SINGLE-LEG SQUAT IN INDIVIDUALS WITH AND WITHOUT PATELLOFEMORAL OSTEOARTHRITIS

C. Carvalho[1], G. Keppe Pisani[1], A. Felipe Martinez[1], L. Mancini[1], F. Viadanna Serrão[1], P. Regina Mendes Da Silva Serrão[1]. [1]*Federal University of São Carlos, Physical Therapy, São Carlos, Brazil*

Background: Previous studies have observed that individuals with patellofemoral pain (PFP) have decreased hip abduction torque, as well as increased hip adduction and knee abduction during activities with uniltateral weight bearing[1,2]. Considering that, a significant number of patients with patellofemoral osteoarthritis (PFOA) have a previous history of PFP[3], it is speculated that the mechanical causes of PFP and PFOA may be similar. However, although alterations in hip muscle strength and lower limb kinematics during various functional activities have been reported in patients with PFP, they have not been explored in subjects with PFOA.
Objectives: The objectives of this study were to compare the hip eccentric abductors torque and the trunk, pelvis, hip, and knee frontal plane kinematics in subjects with and without PFOA isolated during the single-leg squat.
Methods: This is a cross-sectional study. The volunteers were divided into two groups: control group (CG - healthy individuals) and PFOA group (PFOAG - individuals with PFOA grade II or III). Eccentric peak torque of the hip abductors was evaluated using an isokinetic dynamometer Biodex Multi-Joint System 3, at angular speed of 30°/s. Trunk, pelvis, hip and knee kinematics were recorded during the single-leg squat using a 6-camera, 3-dimensional motion-analysis system (Vicon Motion Systems, Nexus System 2.1.1 and 3D Motion Monitor). The t-test Student was used to compare the variables between the groups. The significance level was set at 5% for all analyses ($p \leq 0.05$).
Results: The CG was composed by 12 participants (41.7% women). PFOA had 9 participants (44.4% women). Age ($p = 0.1$), height ($p = 0.9$) and body mass ($p = 0.2$) showed homogeneity between groups. Regardind body mass index, the OAPFG showed higher values ($p = 0.02$). PFOAG showed greater increased hip adduction than CG ($p = 0.05$) (Table 1). However, there were no differences among groups for trunk lean, contralateral pelvic elevation and knee abduction ($p > 0.05$). PFOAG showed lower hip abductor torque compared with the CG ($p = 0.006$).

Table 1 – Values of joint angles during single-leg squatting and hip abductors torque (normalized by body mass) in PFOA and healthy individuals

	PFOAG	CG	*p* value
Contralateral trunk lean (°)	4.7±1.3	4.8±1.1	0.94
Contralateral pelvic elevation (°)	1.4±1.2	2.6±1.0	0.45
Hip adduction (°)	14.9±2.2	8.9±1.6	0.05*
Knee abduction (°)	22.8±3.8	19.4±3.3	0.51
Hip eccentric abdutor torque (Nm/kg·100)	166.5±24.9	204±27.7	0.006*

PFOAG: patellofemoral osteoarthritis group; CG: control group *Statistical difference between groups

Conclusion: PFOA individuals showed greater hip adduction and lower hip abductors torque than the CG. Thus, it is suggested that muscle weakness may excessively influence hip adduction. Hip adduction is the main component of the knee valgus in the frontal plane. So, excessive dynamic valgus results in an increase Q-angle and, consequently, an increase in the lateral forces acting on the patella, causing greater stress on the lateral patellofemoral joint, which may contribute to disease progression. Therefore, we suggest that the hip abductor strengthening should be considered when treating individuals with PFOA.
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THU0568 EFFECTIVENESS OF FOOT ORTHOSIS TO PROMOTE PHYSICAL ACTIVITY FOR PATIENTS WITH CONCURRENT RHEUMATOID ARTHRITIS AND SARCOPENIA

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Background: Sarcopenia is a progressive systemic skeletal muscle disorder associated with an increased likelihood of adverse outcomes including physical disability, falls, and mortality. The muscle mass of patients with rheumatoid arthritis (RA) is lower than that of age-matched healthy individuals, and a high prevalence rate of sarcopenia has been reported[1)]. In particular, foot deformities may increase the prevalence rate of sarcopenia because of inactivity due to foot pain on walking. Treatment with a foot orthosis (FO) can reportedly reduce pain[2)]; however, whether a FO can resolve inactivity and sarcopenia is unclear.
Objectives: To elucidate the effectiveness of a FO on physical activity and sarcopenia in patients with RA.
Methods: Thirty patients with RA with foot deformities were enrolled from April 2017 to December 2019. Sarcopenia was diagnosed using the algorithm of the European Working Group on Sarcopenia in Older People, and the cut-off values of the Asian Working Group for Sarcopenia were applied. We also collected the clinical variables of patients with concurrent RA and sarcopenia who continued to use a FO for 6 months. The primary outcome was physical activity determined by the International Physical Activity Questionnaire. The secondary outcomes were foot pain measured with a visual analog scale; activities of daily living (ADL) measured with the Health Assessment Questionnaire; and body mass index, body fat percentage, and the skeletal muscle mass index measured with a body composition device. The clinical variables were compared between baseline and 6 months after continuous treatment with a FO.
Results: The prevalence rate of sarcopenia was 76.6% (23/30), and nine patients with RA continued to use the FO for 6 months. Table 1 shows outcomes at baseline and after 6 months of treatment with a FO. The only clinical variable that showed a significant difference was foot pain. Physical activities, ADL, and body compositions were maintained after 6 months.

Table 1. Outcomes of 6-month treatment with FO

	Baseline	6 months	p value
Physical activity	132 (66, 594)	594 (396, 2376)	0.07
IPAQ	0 (0, 0)	0 (0, 0)	1.00
Walking, MET-min/week	0 (0, 0)	0 (0, 0)	0.32
Moderate, MET-min/week			
Vigorous, MET-min/week			
Foot pain	4.6 (3.1, 7.4)	2.8 (1.1, 4.7)	0.02
VAS score			
ADL	1.5 (1.1, 2.3)	1.1 (0.9, 1.5)	0.07
HAQ			
Body composition	21.4 (20.7, 22.7)	20.7 (19.3, 22.1)	0.89
BMI, kg/m^2	31.1 (24.2, 37.6)	32.9 (26.3, 36.5)	0.82
BFP, %	5.2 (4.8, 5.3)	5.2 (5.0, 5.2)	0.61
SMI, kg/m^2			

IPAQ: International Physical Activity Questionnaire, VAS: visual analog scale, ADL: activities of daily living, HAQ: Health Assessment Questionnaire, BMI: body mass index, BFP: body fat percentage, SMI: skeletal muscle mass index
Data are presented as median (lower quartile, upper quartile)

Conclusion: The prevalence rate of sarcopenia in patients with RA with foot deformities was much higher than previous reported[1)]. However, 6 months of treatment with a FO not only reduced foot pain but also maintained physical activity and muscle mass. Physical therapy has recently been recommended for patients with inflammatory arthritis. physical activity and muscle mass of patients with RA and concurrent foot deformities may be increased by combining physical therapy with orthotic treatment.

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THU0569 PHYSICAL ACTIVITY IN AXIAL SPONDYLOARTHRITIS AND RHEUMATOID ARTHRITIS: A CROSS-SECTIONAL STUDY IN A SOUTH-EAST ASIAN COHORT

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Background: Axial spondyloarthritis (AxSpA) and rheumatoid arthritis (RA) are two common rheumatic diseases that can result in joint damage and deformities, leading to reduced physical function and quality of life. Physical activity (PA) and exercise have been shown to improve general well-being and reduce cardiovascular risk in patients with AxSpA and RA, and are part of the non-pharmacological management in the EULAR guidelines. Despite this, PA levels are reduced in AxSpA and RA patients[1,2]. In addition, it has also been reported that Asians have lower levels of PA[3].

Objectives: This study aims to examine the patterns of PA in a multi-ethnic Asian cohort.

Methods: This was a cross-sectional study conducted between May 2016 and Jan 2017. Consecutive patients with AxSpA and RA were recruited at an outpatient rheumatology clinic at Singapore General Hospital, the largest tertiary hospital in Singapore. Controls were based on a previous cross-sectional study[4]. PA was assessed using the Global Physical Activity Questionnaires (GPAQ) developed by the world health organization (WHO)[5].

Results: 74 AxSpA and 69 RA patients were recruited and compared to 886 controls. AxSpA patients were younger (median age [IQR], 37.0 [26.3] years) and predominantly male (75.7%), while RA patients were the oldest (median age [IQR], 59.0 [16.5] years) and predominantly female (81.2%). BMI was similar between all three groups. RA patients had more comorbidities (such as hypertension, hyperlipidemia, diabetes mellitus) compared to AxSpA patients and controls.

All three groups had similar proportion of participants meeting WHO recommendations for PA (AxSpA = 77.0%, RA = 79.7%, controls = 83.1%, p=0.35) and median (IQR) time (95% CI) of PA per day [60 (107.1) vs 57.9 (122.9) vs 51.4 (94.3), p=0.93). More AxSpA patients had a high level of sedentary activity compared to RA or controls (AxSpA = 56.8%, RA = 23.2%, controls = 7.2%, p < 0.01). When comparing AxSpA and RA patients with inactive disease or in remission versus active disease, levels of PA did not differ between the 2 groups (p=0.33).

Conclusion: Levels of PA did not differ significant between AxSpA and RA patients compared to the general population, and disease activity levels did not affect the level of PA in patients with AxSpA and RA. Of note was that patients with AxSpA and RA demonstrated higher levels of sedentary activity compared to the general population. Improving PA and decreasing sedentary activity could reduce the cardiovascular risk, especially in patients with RA.

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THU0570 EXPERTS' VIEWS ON THE IMPACT OF REHABILITATION FOR PATIENTS WITH RHEUMATOID ARTHRITIS IN AUSTRIA

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Background: Rehabilitation methods and standards for patients with rheumatoid arthritis (RA) have significantly changed due to more efficient medication improving the course of the disease. Therefore, physical activity, participation, disease management and patient education are most important goals in rehabilitation of patients with RA.

Objectives: Aim of this study was to evaluate the significance and impact of rehabilitation methods according to the subjective attitudes and views of experts and professionals in the field of RA. Opinions of members of the task force (TF) "Rehabilitation" of the Austrian Society of Rheumatology (ÖGR) were compared to the estimation of the other members of the ÖGR.

Methods: All members of the ÖGR were invited to participate in an online survey to rate the impact of rehabilitation for patients with RA between 0 (no impact) and 10 (high impact). Besides sociodemographic and experience related data about the experts and professionals, two main issues were investigated: (1) Impact of rehabilitation related to specific interventions (2) Impact of rehabilitation methods for patients with RA according to different disease and treatment points.

Results: 129 members (50% male, 50% female) of the ÖGR participated in the online survey. 12 persons were members of the TF "Rehabilitation" of the ÖGR. 11 (8.6%) respondents were general physicians, 66 (51.6%) specialists in internal medicine with further expertise in rheumatology, 15 (11.5%) specialists in internal medicine, 14 (10.9%) specialists for physical medicine with further expertise in rheumatology, 2 (1.6%) specialists in orthopaedics, 13 (10.2%) health professionals and 7 (5.5%) persons were from other profession categories such as researchers for example. The majority of respondents (80%) worked already

more than five years with patients with RA in a stationary setting. Results of the online survey demonstrate that the ranking of the impact of specific rehabilitation interventions did only marginally differ between the two person groups: Both groups ranked the importance of occupational and physical therapy the highest. Only the subjective importance of splints and assistive technologies was higher assessed by the general members of the ÖGR. Further, the ranking about the estimated impact of rehabilitation methods for patients with RA was very similar between the two person groups: The importance of rehabilitation for patients with functionality restrictions and for patients with RA in the first years of their disease was ranked the highest by both groups.

Conclusion: Results of the online survey demonstrate that ratings related to the impact of rehabilitation interventions for RA patients do only slightly differ between the investigated member groups of the ÖGR. Finally, the results indicate that rehabilitation methods for RA patients and rehabilitation related knowledge are well accepted and successfully transferred into disease management of patients with RA by professionals and experts in rheumatology in Austria.

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THU0571 EFFICIENCY OF COMPLEX REHABILITATION PROGRAM IN PATIENTS WITH OSTEOARTHRITIS

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Background: Rehabilitation techniques and nonpharmacologic therapies help to relieve pain and improve functional status in patients with osteoarthritis (OA) in addition to drug treatment [1–4].

Objectives: To evaluate the efficiency of 12-month complex rehabilitation program in patients with OA.

Methods: 50 patients with OA of hand, knee and ankle joints (76% females, age of 48 to 69 years, disease duration of 2 to 15 years) were included and randomized into 2 groups. All patients received non-steroidal anti-inflammatory drugs and chondroprotectors in standard doses. 26 study group patients underwent 12-months complex rehabilitation program: laser therapy of 12 to 15 min (infrared laser radiation, wavelength of 0,89 micrometers, pulse frequency of 1200 to1500 Hz) for hand, knee and ankle joints, 3 courses for 10 sessions with a mean interval of 3,3 months; 45-min dynamic exercises using gym apparatus Enraf-Nonius under the supervision of a trainer 3 times a week; 45-min exercises for hands 3 times a week; 45-min occupational therapy, 10 sessions; wrist, ankle and knee orthoses, education program (3 daily 90-min studies); balance training on the COBS-platform 3 times a week. 24 patients received only drug therapy (control). Tender and swollen joint count, joint pain on 100-mm VAS, Lequesne index, WOMAC, hand grip strength, the average powers of knee extension and ankle flexion by EN-TreeM movement analysis, symmetry index (SI) and load distribution on the COBS-platform in the different modes were evaluated at baseline and at 12 months.

Results: After 12 month in the study group tender joint count decreased by 56,2% (p<0,01), swollen joint count – by 67,3% (p<0,01), pain on VAS - by 54,7% (p<0,01), Lequesne index – by 2,3 times (p<0,01), WOMAC – by 1,8 times (p<0,01). The grip strength of a more affected hand enhanced by 41,3% (p<0,05), of a less affected – by 43,4% (p<0,05). The average extension power of a weaker knee increased by 57,3% (p<0,01), of a stronger – by 44,2% (p<0,05). The average flexion power of a more affected ankle joint elevated by 34,9% (p<0,05), of a less affected – by 48,2% (p<0,05). The pressure on the COBS-platform of the extremity with more affected joint of the patients with OA of knee joints increased by 11,7% (p<0,05), SI – by 12,9% (p<0,05) in the mode «habitual stand». The load on the limb with more affected joint elevated by 13,2% (p<0,05), SI – by 25% (p<0,05) in the mode «get up and sit down». The pressure on the COBS-platform of the extremity with more affected joint of the patients with OA of ankle joints was enhanced by 14,3% (p<0,05), SI – by 18,2% (p<0,05) in the mode «habitual stand». The load on the limb with more affected joint was elevated by 12,8% (p<0,05), SI – by 20,1% (p<0,05) in the mode «tiptoe bounce (do not leave ground)». In the study group there were statistically significant differences from the control group in all parameters (p<0,05).

Conclusion: 12-month complex rehabilitation program relieves pain, improves functional ability, power of motion, balance and load distribution in patients with OA.

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THU0572 THE ROLE OF PRESSURE PAIN THRESHOLD IN A REHABILITATIVE APPROACH TO ANALYZE PAIN PROCESSING MECHANISM IN HAND OSTEOARTHRITIS PATIENTS: A PILOT STUDY.

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Background: The hand pain experienced by patients with hand osteoarthritis (OA) is often accompanied by hypersensitivity and sings of peripheral and central sensitization[1]. The European League Against Rheumatism (EULAR) published a systematic literature review that summarized the current non-pharmacological, pharmacological and surgical approaches for the management of hand OA[2]. The identified review did not consider interventions that specifically targeted reducing pain sensitivity. A reliable method to assess the presence of hypersensitivity is the pressure pain threshold (PPT)[3]. During the rehabilitation management considering the pain mechanism involved could be an important factor to address more effective treatments[4].

Objectives: The aim of the present study was to investigate the role of pain processing mechanism in patients with hand OA through PPT and using a specific functional Magnetic Resonance Imaging (fMRI).

Methods: 20 patients with hand OA and 20 healthy controls, aged 50 to 90 years, were recruited. Pressure pain threshold (PPT) was assessed bilaterally over the hand, on the C5-C6 zigoapophyseal joint, median, ulnar, radial nerves, and anterior tibial muscle by a blinded assessor respect to the condition of the subjects[3]. In five participants for each group, PPT over the hand was assessed neurophysiologically by advanced modalities including functional MRI to analyze the pain mechanisms related to hand OA[5].

Results: The results showed that PPTs were significantly lower over the hand and the median, ulnar, radial nerves (P<0.05), but not over the C5-C6 zigoapophyseal joint and anterior tibial (P>0.05) in OA patients as compared to healthy controls. Both groups demonstrated activation of the thalamus, frontal and somatosensory cortex area during PPT over the hand, although the total brain area activated in OA patients was greater than in control participants.

Conclusion: Patients with hand OA shown features of altered pain mechanism that were evident both in PPTs measures than using functional MRI. PPT is a useful marker in detecting pain sensitivity in hand OA and could be used in future pain studies to evaluate pain modulation strategies.

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THU0573 YOGA LEADS TO SUSTAINED IMPROVEMENT IN FATIGUE AND MOOD IN RHEUMATOID ARTHRITIS: PRELIMINARY RESULTS OF A RANDOMIZED CONTROLLED TRIAL

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Background: Rheumatoid arthritis (RA) patients experience reduced health-related quality of life (HRQOL). Previous studies suggest that yoga, a mind-body practice, can improve physical and mental health but it has not been extensively studied in RA.

Objectives: To investigate the effect of yoga on HRQOL and secondary on fatigue, anxiety, depression and disease activity in RA patients

Methods: 43 RA patients (mean (SD) age 55 (10) years, median (IQR) disease duration 5 (3,8) years, 93% female), stable on standard pharmacological treatment and DAS28CRP < 5.1 were randomly assigned to 12 weeks yoga intervention (2x/week 90 min; n=22) or arthritis-related educational lectures control (1x/week 60 min; n=21). Yoga based on „Yoga in daily life system" included asanas, relaxation, pranayama and meditation. Study evaluations at baseline, post-intervention and 3-month follow-up included The Short Form-36 (SF-36) scores for Physical Component Summary (PCS) and Mental Component Summary (MCS), Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), Hospital Anxiety and Depression scale (HADS) and Disease Activity Score-28CRP (DAS28CRP) questionnaires. Data were presented as change from baseline to each time point. Between group differences were analyzed using the t-test for normally and Mann-Whitney U test for non-normally distributed variables. P values <0.05 were considered statistically significant.

Results: 35 patients (17 = intervention, 18 = control group) completed the trial period. Significant improvement in FACIT-F (p=0.013), HADS anxiety (p=0.047) and HADS depression (p=0.004) was found in yoga group compared to control at post-intervention and maintained at follow-up (p=0.025, p=0.02 and p=0.045, respectively). There was no significant difference found between groups for SF-36 MCS, PCS and DAS28CRP at all time points (all p>0.05). No serious adverse events were observed during trial period.

Conclusion: Although no change in SF-36 scores and disease activity was observed, yoga practice produced significant and sustained improvement in fatigue and mood which strongly account for decreased life quality in RA. Despite limitations our findings suggest that yoga may be of benefit in management of RA patients.

Table. Changes in outcomes

	N= 37 (postintervention)			N= 35 (follow-up)	
Variables	**Baseline mean (SD)**	**Change from baseline (95%CI)**	**Difference between groups (95%CI, p-value)**	**Change from baseline (95%CI)**	**Difference between groups (95%CI, p-value)**
FACIT-F (0-52)	Yoga 33.89 (10.77)	4.18 (-0.26,8.61)	**6.66** (1.53,11.78) **p= 0.013**	3.29 (-1.23,7.82)	**6.63** (0.85,12.4) **p=0.025**
	Control 35.37 (9.3)	-2.17 (-5.58,1.25)		-3.33 (-7.27,0.61)	
HADS-A (0-21)	Yoga 7.39 (3.72)	-1.94 (-3.28,-0.6)	**-1.83** (-3.64,-0.024) **p= 0.047**	-2.24 (-3.63,-0.84)	**-2.4** (-4.4,-0.04) **p=0.02**
	Control 6.89 (2.86)	0.056 (-1.39,1.51)		0.17 (-1.38,1.71)	
HADS-D (0-21)	Yoga 5.11 (3.03)	-1.06 (-1.92,-0.2)	**-1.73** (-2.88,-0.58) **p= 0.004**	-0.2 (-1.1,0.63)	**-1.18** (-2.33,-0.03) **p=0.045**
	Control 5.0 (1.82)	0.83 (-0.06,1.72)		0.94 (0.12,1.77)	
SF-36:MCS (0-100)	Yoga 49.49 (11.99)	2.97 (-4.15,10.09)	3.86 (-4.66,12.33) p= 0.366	1.25 (-3.62,6.12)	1.7 (-5.09,8.49) p=0.618
	Control 49.71 (8.99)	-1.59 (-7.51,4.33)		-0.45 (-5.56,4.65)	
SF-36:PCS (0-100)	Yoga 52.57 (10.11)	0.44 (-3.13,4.02)	1.61 (-3.31,6.53) p= 0.511	-1.54 (-5.44,2.35)	-1.9 (-6.98,3.18) p=0.453
	Control 48.30 (9.76)	-1.16 (-4.81,2.48)		0.35 (-3.21,3.92)	
DAS28CRP	Yoga 2.32 (0.81)	-0.0024 (-0.42,0.42)	0.093 (-0.44,0.63) p=0.724	0.11 (-0.43,0.66)	0.66 (0.02,1.3) p=0.092
	Control 2.91 (0.84)	-0.096 (-0.45,0.26)		-0.54 (-0.92,-0.17)	

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THU0574 PHYSICAL ACTIVITY IN PEOPLE WITH AXIAL SPONDYLOARTHRITIS AND THE IMPACT OF ATTITUDE, BARRIERS AND FACILITATORS.

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Background: Barriers such as high disease activity, fatigue, pain, stiffness, physical exertion and lack of time all have a negative impact on physical activity level in people with axial Spondyloarthritis (axSpA), while more time is a facilitator (1, 2). In addition, an intrinsic drive to exercise is an important motivator, guided by personal interest and enjoyment in exercise (1). There is a need for a better understanding of the impact of barriers, facilitators and attitudes on level of physical activity.

Objectives: To study the association between self-reported level of physical activity and self-perceived health, attitudes, barriers and facilitators to physical activity in people with axSpA.

Methods: In 2018, members with axSpA from the Danish Patient Association for Spondyloarthritis were invited to participate in an on-line survey. The questionnaire included diagnosis, socio-demographics, self-perceived health (poor, fair or good), level of physical activity (≤ 1 day/week, 2-3 days/week or 4-7 days/week) overall attitude (I do not care and I do not know, it's ok or I like physical activity), barriers and facilitators toward physical activity (range 8-56, low to high disagreement). A logistic regression analysis was applied to study associations between level of physical activity (dependent variable) and attitudes, barriers, facilitators and self-perceived health (independent variables).

Results: 445/972 members (46%) completed the questionnaire. Median age was 56 years (range 22-85), 241 (54%) were men. 23% were physically active for at least 30 minutes on a moderate intensity level ≤ 1 day/week, 36% 2-3 days/week and 41% 4-7 days/week. Responders who were physically active ≥ 2 days/week had more positive attitudes to physical activity (p< 0.001), disagreed more often to suggested barriers (p<0.001), and had better self-perceived health (p<0.003) compared with those who reported a low physical activity level (≤ 1 day/week). In the regression analysis, positive attitudes (OR 14.21, 95%CI 3.34 - 60.53) and a higher disagreement with barriers for physical activity (OR 1.12, 95%CI 1.07 - 1.17) were associated with high level of physical activity.

Conclusion: The overall attitude and experienced barriers towards physical activity have a strong impact on the level of physical activity in people with axSpA. To support lifestyle changes, health professionals need to discuss the impact of barriers and attitudes to physical activity with their clients.

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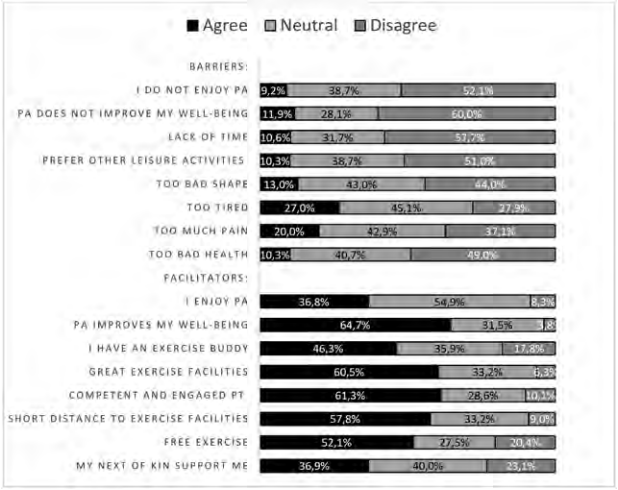


Figure 1. Percentage agreement with barriers and facilitators for physical activity. PA: Physical activity, PT: Physiotherapist

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THU0575 **THE EFFECT OF PREOPERATIVE PHYSICAL ACTIVITY ON KNEE AND HIP ARTHROPLASTY OUTCOME IN PATIENTS WITH OSTEOARTHRITIS**

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Background: Joint replacement is a therapeutic option increasingly widespread among osteoarthritis (OA) patients. Besides improving operating techniques and postoperative management, it is important to pursue the best preoperative conditions in order to achieve the desired result. As physical activity (PA) potentially acts on the preoperative predictors, knowing the effect of leisure and occupational PA should be of great interest to obtain a positive outcome.
Objectives: To investigate the influence of preoperative PA on the clinical outcomes of total hip arthroplasty (THA) and total knee arthroplasty (TKA) in OA patients.
Methods: Data from the Knee and Hip OsteoArthritis Long-term Assessment (KHOALA) cohort (1), a multi-regional French cohort of 878 patients with symptomatic hip and/or knee OA, were analysed. We included in our study patients undergoing THA or TKA during a 7-year-follow-up period. The level of total and leisure-time preoperative PA was measured with the Modifiable Activity Questionnaire (MAQ). Outcomes were measured one year after surgery. For the primary endpoint, quality of life (QoL) was measured with the OsteoArthritis Knee and Hip Quality Of Life questionnaire (OAKHQOL). For secondary endpoints, QoL was measured with Short Form 36 (SF-36), pain with the Visual Analogue Scale (VAS), function with the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and with walking distance. The population characteristics were described using frequency or mean and standard deviation (SD), depending on the distribution of the variable. Association between exposures and outcomes was calculated with a multivariate linear analysis with backward selection, adjusting for confounders (age, sex, body mass index, site of joint replacement, polyarticular OA, OA duration, comorbidities, radiological grade of OA, inclusion centre, rehabilitation after surgery, previous joint issues, instruction level). A p-value <0.05 was set as statistically significant.
Results: 150 patients were included. 58.7% underwent TKA and 41.3% THA. The mean age at the time of surgery was 66.6 years (±7.7 SD). The majority of patients were female (75%), overweight (mean BMI 29.63 kg/m2, ±5.5 SD) and had polyarticular OA (60%). 53% of patients met the World Health Organization recommendations on PA before surgery. For the primary endpoint, a high preoperative total PA was associated with a better relationship with the partner ($\beta = 0.55$, $p = 0.02$) one year after surgery. As for secondary endpoints, a high two-year preoperative total PA was associated with an impaired SF-36 Mental Component Summary score ($\beta = -0.87$, $p = 0.02$), but a longer walking distance ($\beta = 442.81$, $p < 0.01$). Leisure-time PA also showed a positive impact on walking distance ($\beta = 76.25$, $p = 0.02$), but a negative one on social functioning in SF-36 ($\beta = -0.47$, $p = 0.01$). No statistically significant association between preoperative PA and pain nor WOMAC was found.
Conclusion: In this cohort study, the preoperative level of PA demonstrated a heterogeneous effect on the various aspects of QoL one year after THA and TKA in OA patients. Preoperative PA was directly associated with gain of function, measured as walking distance, after surgery. Considering the increasing prevalence of OA and the crucial role of PA on health, further studies on this relevant topic are needed.
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Education

THU0576 **EMPOWERING PEOPLE WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES TO BE AT THE HEART OF MEDICAL EDUCATION: A EULAR SCHOOL OF RHEUMATOLOGY INITIATIVE**

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Background: The earliest examples of active patient involvement in teaching are interventions in which the patient was teaching students how to conduct physical examinations. Over the last two decades, educators have used the expertise of patients to enrich the education of undergraduate physicians and health professionals (HP) in several ways, mainly asking people to outline their own stories. Early patient involvement also aims to sensitise students to pursue a holistic approach and ultimately to build a trustful physician-patient relationship. Most studies report that high patient involvement brings benefits to both learners and patients. Learners report higher satisfaction. Patients report raised self-esteem and empowerment, new insights into their problems and deeper understanding of the physician-patient relationship.
Objectives: To develop a novel educational framework within the EULAR School of Rheumatology for people with rheumatic and musculoskeletal diseases (RMDs) who are willing to be involved in teaching undergraduate physicians and HPs (Patient Education Partners, PEPs).
Methods: A multidisciplinary working group including people with RMDs, 1 Rheumatologist, 1 HP in rheumatology and 1 educationalist was established. The project was developed through a questionnaire launched in May 2019, to patient associations across Europe, 2 face to face meetings and online teleconferences.
Results: Patient associations from 23 European countries responded to the questionnaire and in 10 of them (43%), there have been programmes running for up to 31 years which involve patients with RMDs in undergraduate education. To some extent, 485 people with RMDs have been trained over the years across Europe. However, there are different country and disease-specific types of training and a lack of standardised training for patients involved in these programs. The patient associations from countries that do not have the programme would be interested in taking part, if such initiative were to be developed. The topics that people would like to cover when teaching medical and other health professions students are: disease specific factors, doctor-patient communication, personal history and physical examination, the importance of education and work to the individual, the importance of disease self-management. A subsequent mapping of European countries was undertaken to identify best practice examples of existing programmes: Germany, Denmark, Belgium, Ireland and the UK were included. From these foundations, we developed a new on-line Course, to equip patients with a basic medical knowledge about their disease and effective communication strategies.
Conclusion: We established a European framework to train people with RMDs who were willing to be involved in teaching undergraduate physicians and HPs. This will allow them to gain confidence and effective communication skills to share their lived experience and become PEPs. The content of the course is currently being developed and all EULAR pillars are involved. Participation in this training course, particularly by people from countries that do not yet engage patients in undergraduate education, may facilitate the implementation of such initiatives, and ultimately improve the training of physicians and HPs across Europe.
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THU0577 **INFLUENCE OF THE ROUTE OF ADMINISTRATION ON SAFETY AND ADHERENCE PRACTICES OF RHEUMATOID PATIENTS TREATED BY JAK-INHIBITORS AND OTHER DMARDS. AN ETHNOGRAPHIC STUDY FOR AN APP-BASED EDUCATION TOOL.**

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Background: JAKi (JAK inhibitors) seem simpler of use than injected biologic agents due to their oral administration route. Safety and adherence issues remain and may need to modify patients' counseling.
Objectives: To understand the influence of the DMARDs' route of administration on these issues for both patients and physicians in order to update the Hiboot® education tool (ref1).
Methods: Hiboot® is a free smartphone application developed by the French Society of Rheumatology to enhance the patient's safety, adherence to treatment, self-assessment and to give periodic counseling messages (ref1). This ethnographic study involved i)18 patients with rheumatoid arthritis (RA) recruited by 3 rheumatologists considering diversity of clinical and sociological profiles. The panel included i) 14 women and 4 men, median age 56 years-old, median disease duration 10 years. Four patients were treated by methotrexate (MTX) monotherapy, 5 with MTX-bDMARDs or MTX-JAKi combo, 1 by bDMARDs monotherapy, 8 by JAKi monotherapy; ii) 9 rheumatologists with hospital or mixed hospital-private practice from 6 cities in France.
The interviews were conducted by 2 anthropologists using in-depth semi directive and biographical methods (enough to reach saturation), registered and transcribed. The semi-directive interviews dealt with: i) the patient history with RA and its treatments, ii) the daily medication management, iii) the evolution of patients' perceptions and knowledge over time.
Results: For patients, adherence and safety behaviors were guided by their representations of 3 risks: disease-related, treatment-related, physician-related. When the disease-related risk was perceived greater than the treatment-related risk, patients tended to report better adherence. Beliefs on efficacy and safety depended more on the patient's experience with RA over time (severity, activity, control) than on the route of administration (oral vs sub-cutaneous). However, patients treated with JAKi needed to update their lay knowledge and skills regarding their daily constraints and medication management.
For rheumatologists, JAKi were considered a promising therapeutic option, but rarely prescribed so far due to a lack of personal experience. Owing to their recent introduction on the market (~2 years in France), JAKi were prescribed to patients with longer disease duration and after several DMARDs lines. The rheumatologists' conservative attitude towards JAK-i depended on risk perceptions similar to the patients': disease-related, treatment-related and patient-related i.e their perception of patients' abilities to manage their care (presumed skills, autonomy…).
This study confirms the importance of patients' beliefs of the balance between medication necessity and risks regarding safety and adherence (ref2) which are shared with the rheumatologists. This study unexpectedly emphasized a doctor-related risk in patients as well as a patient-related risk in rheumatologists. One limitation is a bias in the recruitment of patients with long-standing RA.
Conclusion: Rheumatologist-patient collaboration needs a shared vision of medication risks, independently of the route of administration. However new skills are needed for patients treated with JAKi. This qualitative study will serve to modify the Hiboot application to include the JAKi issues such as the reminders or daily life management.
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THU0578 ONLINE CME IMPROVES CLINICAL DECISION-MAKING IN THE MANAGEMENT OF PATIENTS WITH PSORIATIC DISEASE

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Background: Psoriatic arthritis can be a challenging condition for rheumatologists to manage.
Objectives: We assessed whether an online, virtual patient simulation (VPS) activity could improve the performance of rheumatologists in ordering appropriate tests, tailoring treatment options and selecting an evidence-based treatment for patients with PsA.
Methods: This CME-certified VPS consisted of 2 patient cases presented in a platform that allowed physicians to assess the patients and complete open-field entries, choosing from an extensive database of diagnostic and treatment options reflecting the scope and depth of actual practice. After each decision, learners received clinical guidance (CG) based on current evidence and faculty recommendations. Clinical decisions were compared pre- and post-CG using a 2-tailed paired t-test to determine *P* values (*P*<.05 is significant). Rationales for clinical decisions were collected in real time. Data were collected between 28 February 2019 and 16 May 2019 and reported here as % relative improvement, *P* value.
Results: Case 1 (n=48 rheumatologists):
45 yr old female patient diagnosed with PSO 5 years ago. Current treatment with MTX 15mg & folic acid once weekly plus ibuprofen. Experiencing nausea and increasing skin lesions. Recently showing signs and symptoms of PsA.
Statistically significant changes were observed for:
•Ordering appropriate tests to evaluate the patient (chemistry panel, 11%, *P*=.04; full blood count [FBC], 10%, *P*=.04; IFNγ release assay for TB, 22%, *P*=.01; liver function tests [LFTs],13%, *P*=.02; rheumatology consult, 19%, *P*=.01 and viral hepatitis panel, 52%, *P*<.001)
•Tailoring treatment options based on individual patient characteristics and available evidence (discontinue MTX [46%]and folic acid [140%], both *P*<.001; order patient education, 24%, *P*=.006; guidance on lifestyle changes, 20%, *P*=.01; preventative vaccines prior to ant-TNF therapy, 38%, *P*=.002 and a followup appointment at an appropriate timescale, 26%, *P*=.006)
•Selecting an evidence-based therapy for a patient newly diagnosed with PsA while on MTX therapy (adalimumab, 138%, *P*<.001)
Case 2 (n=116 rheumatologists):
55 yr old male who has had PSO for 9 years. Developed joint symptoms 1 year ago. Diagnosed with PsA & treated with MTX/folic acid. Elevated liver enzymes noted after 9 months; treatment switched to adalimumab. Skin lesions much improved but ongoing issues with pain and stiffness in hands. Current medications are citalopram, adalimumab, simvastatin and triamcinolone for skin flares.
Statistically significant changes were observed for:
•Ordering appropriate tests to evaluate the patient (C-reactive protein [9%], erythrocyte sedimentation rate [9%] and FBC [17%], all P<.01; Beck depression inventory [51%], BSAxPGA [21%], chemistry panel [15%], Global QoL 13%], Leeds enthesitis index [25%], LFTs [32%], PGA [21%], RAPID3 [63%], total BSA [137%]and X-ray of hands and feet [27%], all *P*<.001)
•Tailoring treatment options based on individual patient characteristics and available evidence (discontinue biologic DMARD [67%], order patient education [22%], physical therapy [31%] and occupational therapy 27%], preventative vaccines [35%], psychosocial counselling [31%] and a follow-up appointment at an appropriate timescale [32%], all *P*<.001)
•Selecting an evidence-based therapy for a patient with inadequate control of PsA on adalimumab (secukinumab, 152%, *P*<.001; ixekizumab, 167%, *P*=.01)
Conclusion: These results demonstrate the success of immersive, online VPS education that engages physicians in a practical learning experience in improving their performance in managing patients with PsA.
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Disclosure of Interests: Elaine Bell: None declared, Alice B Gottlieb Grant/research support from:: Research grants, consultation fees, or speaker honoraria for lectures from: Pfizer, AbbVie, BMS, Lilly, MSD, Novartis, Roche, Sanofi, Sandoz, Nordic, Celltrion and UCB., Consultant of:: Research grants, consultation fees, or speaker honoraria for lectures from: Pfizer, AbbVie, BMS, Lilly, MSD, Novartis, Roche, Sanofi, Sandoz, Nordic, Celltrion and UCB., Speakers bureau:: Research grants, consultation fees, or speaker honoraria for lectures from: Pfizer, AbbVie, BMS, Lilly, MSD, Novartis, Roche, Sanofi, Sandoz, Nordic, Celltrion and UCB., Philip J Mease Grant/research support from: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Eli Lilly, Novartis, Pfizer, Sun Pharmaceutical, UCB – grant/research support, Consultant of: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Eli Lilly, Novartis, Pfizer, Sun Pharmaceutical, UCB – consultant, Speakers bureau: Abbott, Amgen, Biogen Idec, BMS, Eli Lilly, Genentech, Janssen, Pfizer, UCB – speakers bureau, Gwen Littman: None declared, Mark Via: None declared
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THU0579 "EVOLVING THE MANAGEMENT OF RA" PROGRAMME: EDUCATIONAL TOOLS TO SUPPORT DAILY PRACTICE

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Background: The eRA (evolving the management of RA) programme was initiated in Europe to provide practical educational tools that address unmet needs in the management of rheumatoid arthritis (RA). Several eRA tools – covering early access to care, management of comorbidities, treat-to-target strategies, and patient empowerment – are available to the rheumatology community. Through ongoing activities, the eRA Steering Committee (SC) identified a need for tools on non-pharmacological management of RA.

Objectives: To improve accessibility to eRA tools for rheumatology professionals; to review the evidence base of non-pharmacological interventions to create new eRA resources that may support management decisions.

Methods: A web platform providing information on eRA programme and tools was developed in 2019. The platform collects survey-based metrics to quantify perception of eRA and use of eRA tools in clinical practice. Platform and tools are translated to further support access and use across Europe.

To address unmet needs in non-pharmacological patient management, the eRA SC reviewed the core literature on agreed priority interventions, including physical activity, diet, patient education and self-management, psychosocial interventions, occupational therapy and orthotics, hand exercises, and hydrotherapy/balneotherapy. Available evidence for each intervention was assessed and graded according to the Oxford Centre for Evidence-based Medicine Levels of Evidence.

Results: The eRA web platform is now live in 3 countries (www.evolvingthemanagementofRA.com), hosting translated copies of the eRA tools, with additional countries launching throughout 2020.

From a review of core literature on non-pharmacological interventions, the eRA SC determined that strong evidence exists to support use of physical activity, patient education and self-management, psychosocial interventions, and occupational therapy and orthotics. Evidence was lacking or conflicting for diet and nutrition, hand exercises, and balneotherapy/hydrotherapy. A set of educational slides was produced by the eRA SC to summarise the evidence (Fig. 1) and provide top-line guidance on use of interventions in practice that should engage relevant members of the multi-disciplinary team. These slides are available through eRA dissemination activities.

Conclusion: The eRA programme content is now freely available to health care professionals in several countries on a web platform, supported by translations of the eRA tools. An additional slide set on non-pharmacological management serves to further increase the practical guidance of this programme's educational offering.

Intervention	Strength*	Evidence summary
Physical activity	strong evidence	Resistance and/or aerobic exercise has positive effects on several outcomes (e.g. strength, function) Some types of physical activity present with inconsistent evidence (e.g. Tai Chi, yoga) regarding their effects on outcomes
Occupational therapy interventions and orthotics	limited evidence	Occupational therapy interventions have positive effects on function Podiatry interventions have positive effects on pain, but evidence is inconsistent regarding effects on function Wrist splints may have positive effects on pain, but there is insufficient evidence regarding their effects on function
Patient education and self-management interventions	strong evidence	Patient education has positive effects on coping ability (e.g. with pain) and adherence (e.g. to supportive interventions) For education, there is inconsistent evidence regarding the long-term benefits and effects on self-efficacy For self-management programmes, there is inconsistent evidence regarding effects on function
Psychosocial interventions	limited evidence	Psychosocial interventions have positive effects on many outcomes when used as an adjunct to pharmacological management, but evidence is inconsistent regarding long-term effects Cognitive-behaviour therapy has positive effects on depression and fatigue
Hand exercises	additional evidence needed	Additional high-quality evidence is required before findings can translate into daily practice in RA management
Nutrition and diet	additional evidence needed	Additional high-quality evidence is required before findings can translate into daily practice in RA management NOTE: Healthy diet and weight control are supported by EULAR recommendations and national guidelines should be followed
Balneotherapy / hydrotherapy	additional evidence needed	Additional high-quality evidence is required before findings can translate into daily practice in RA management

*Available evidence for each intervention was assessed and graded according to the Oxford Centre for Evidence-based Medicine Levels of Evidence.

Fig. 1. Summary of evidence for non-pharmacological interventions

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THU0580 EULAR TASK FORCE ON GENDER EQUITY IN ACADEMIC RHEUMATOLOGY: PRELIMINARY SURVEY FINDINGS

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Background: Women represent an increasing proportion of the overall rheumatology workforce, but are underrepresented in academic rheumatology, especially in leadership roles [1].

Objectives: The EULAR Task Force on Gender Equity in Academic Rheumatology has been convened to establish the extent of the unmet need for support of female rheumatologists, health professionals and non-clinical scientists in academic rheumatology and develop a framework to address this through EULAR and EMEUNET.

Methods: To investigate gender equity in academic rheumatology, an anonymous web-based survey was targeted at the membership of EULAR and Emerging EULAR Network (EMEUNET) and their wider networks. The survey was developed based on a narrative literature review [1], best practice from The Association of Women in Rheumatology, a survey of task force members and face-to-face task force discussions. Personal experiences were explored and 24 potential interventions to aid career advancement were ranked. Statistics were descriptive with significance testing for male/female responses compared using chi-squared/t-tests. The level of significance was set at $p<0.001$.

Results: A total of 301 respondents from 24 countries fully completed the survey. By profession, 290 (86.4%) were rheumatologists, 19 (6.3%) health professionals, and 22 (7.3%) non-clinical scientists. By gender, 217 (72.1%) were women, 83 (27.6%) men, and 1 (0.3%) third gender. By age, 203 (67.5%) were 40 or under. By ethnicity, 30 (10.0%) identified themselves as ethnic minority. A high proportion of respondents reported having experienced gender discrimination (47.2% total: 58.1% for women and 18.1% for men) and sexual harassment (26.2%: 31.8% and 10.8% respectively) (Figure 1). Chi-squared tests on the numbers on which these proportions were based showed

statistically significant differences between women and men in having experienced gender discrimination (X2=36.959 (df=1), p <0.001) and sexual harassment (X2=12.633 (df=1), p <0.001). The highest-ranked interventions for career advancement regardless of respondents' gender included: leadership skills training; speaking/presentation/communication skills training; information on training/career pathways; effective career planning training; support on grant writing applications; and high-impact scientific writing master-classes (Figure 2). Only 8 of 24 proposed interventions showed a significantly higher ranking (p<0.001) by female respondents and these typically related to promotion of female role models and gender-balance in committees, editorial boards and research funding (Figure 2).

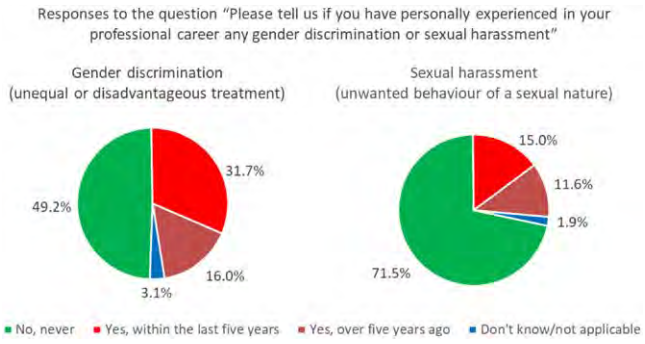


Figure 1. Perceived gender discrimination and sexual harassment, 301 responses



Figure 2. Mean perceived utility of potential interventions for career advancement by gender and statistically significant gender differences (p<.001), 300 responses

Conclusion: The results of the survey will inform the development of task force policy proposals for interventions to support career advancement among EULAR and EMEUNET members. The identified interventions have potential to support career advancement of all rheumatologists, health professionals and non-clinical scientists regardless of gender.

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THU0581 USE OF EHEALTH BY PATIENTS WITH RHEUMATOID ARTHRITIS: AN OBSERVATIONAL, CROSS SECTIONAL, MULTICENTER STUDY

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Background: The use of eHealth tools (internet, mobile applications, connected devices) in chronic diseases and in the field of rheumatoid arthritis (RA) is growing (1). eHealth may improve the overall care of patients suffering from chronic diseases (2,3).

Objectives: The main objective of this study was to describe the use of eHealth by RA patients in France. The secondary objectives were to identify differences in demographic and disease characteristics between patients using eHealth tools or not. We also assessed patients' expectations about digital devices.

Methods: We conducted a cross-sectional, multicenter study. Patients with RA according to the ACR / EULAR 2010 criteria were recruited in 5 university hospitals (Bordeaux, Clermont-Ferrand, Limoges, Montpellier and Toulouse). Patients completed an anonymous self-questionnaire including demographic data, assessment about the use of eHealth (access, support, frequency of use, type of use, reason for use). The treating rheumatologist of the patient filled in an independent medical questionnaire collecting the disease characteristics, the activity of RA and the treatments. Data were collected from December 2018 to July 2019.

Results: The questionnaires were completed by 575 patients, with an average age of 62±13 years, 78% of whom were women. 473 (82%) patients had access to eHealth through a computer (n=402, 86%), a tablet (n=188, 40%) and/or a smartphone (n=221, 47%). Among them, 36% (170/473) used internet for health in general and 29% (134/473) specifically for RA. Regarding the use of eHealth for RA, all patients used it to learn about their disease and 66% (89/134) as a tool to help monitoring RA. Most of them (n=87/125, 70%) had a paper medical record, 24/125 patients (19%) used a digital tool (spreadsheet n=10, 8% and / or mobile application n=9, 7% and / or website n=5, 4%) and 31/125 patients

(25%) did not use any tool to monitor their RA. Few patients (16/126, 13%) used numeric reminders for their treatments. A specific application for RA was used by 27/127 patients (21%) using eHealth. Age, level of study, employment, treatment, comorbidities, membership of a patient association group and patient education program were associated with the use of eHealth for RA in univariate analysis. In multivariate analysis, membership of patient's association (OR: 5.8 [3.0-11.2]), bDMARDs use (OR: 0.6 [0.4-1]) and comorbidities (OR: 0.7 [0.6-0.8]) remained associated with eHealth use for RA. According to the patients, recommendation by a doctor (n=225/330, 68%), ease of use (n=105/330, 32%) and data security (n=69/330, 21%) were the factors that would favor the use of eHealth.

Conclusion: To date, few patients used eHealth for their disease. The use of a reliable and validated eHealth tool in RA could therefore be promoted by rheumatologist and might optimize the therapeutic adherence.

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THU0582 EFFECTIVE MANAGEMENT OF REFRACTORY GOUT: EFFECT OF ONLINE CONTINUING EDUCATION ON RHEUMATOLOGISTS' KNOWLEDGE

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Background: Gout is a chronic condition with a considerable effect on patient health and quality of life. Despite the availability of multiple pharmacologic treatments and evidence-based management guidelines, treatment targets are often not achieved in patients with gout. Identification and optimal management of patients with severe or refractory gout is specially challenging.

Objectives: The objective of this study was to determine if an online, continuing education activity could improve knowledge of rheumatologists regarding strategies to ensure effective and safe use of urate-lowering therapies in the management of patients with refractory gout.

Methods: Educational design included an online, 30-minute, video-based discussion among two faculty experts with synchronized slides. Educational effectiveness was assessed with a repeated-pairs pre-/post-assessment study design using 3 knowledge questions and 1 confidence question, in which each individual served as his/her own control. A chi-squared test assessed differences from pre- to post-assessment. P values <.05 are statistically significant. Cramer's V was used to calculate the effect size (<0.06 modest effect; 0.06-0.15 noticeable effect; 0.16-0.26 considerable effect; >0.26 extensive effect). The activity launched May 1, 2019, with data collected through December 30, 2019.

Results: The analysis set consisted of responses from rheumatologists (n=300) who answered all assessment questions during the study period. Analysis of pre- vs post-intervention responses demonstrated a significant improvement in overall knowledge of rheumatologists with considerable educational impact (V = .201, P<.001). Average correct responses increased from 54% pre to 74% post education. Specific areas of improvement in knowledge include:

•Optimal strategies for reducing the risk for immunogenicity associated with the use of pegloticase in patients with refractory gout (40% pre, 73% post; P<.001; V = .326)

•Serum uric acid targets to optimize management of the patient with severe or refractory gout (45% pre, 57% post; P<.05; V = .120)

•Selection of pegloticase for rapid decreases in tophi and serum uric acid in patients with refractory gout (77% pre, 91% post; P<.001; V = .187)

Post-education, 32% of rheumatologists were more confident in their ability to manage patients with refractory gout.

Conclusion: This study demonstrated the success of online, 30-minute, video-based discussion among two faculty experts with synchronized slides on improving the knowledge of rheumatologists regarding appropriate management of patients with refractory gout.

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THU0583 STRATEGIES FOR ASSESSMENT OF COMPETENCES DURING RHEUMATOLOGY TRAINING ACROSS EUROPE: RESULTS OF A QUALITATIVE STUDY.

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Background: In order to become a rheumatologist, trainees must successfully complete a rheumatology training program. Both the content and the assessments within these programs are regulated by national authorities, and therefore a wide heterogeneity between countries is expected.

Objectives: To gain insight into current methods and practices for the assessment of competences during rheumatology training, and to explore the underlying priorities and rationales for competence assessment across EULAR countries.

Methods: We used a qualitative approach through online focus groups of rheumatology trainers and trainees, separately. The study included five countries - Denmark, The Netherlands, Slovenia, Spain and United Kingdom. A summary of current practices of assessment of competences was developed, modified and validated during the focus groups. A prioritising method (9 diamond technique) was then used to identify key assessment priorities.

Results: Overall, 26 participants (12 trainers, 14 trainees), participated in 9 online focus groups (2 per country, except Slovenia), totalling 12 hours of online discussion. Strong nationally (Netherlands, UK) or institutionally (Spain, Slovenia, Denmark) standardised approaches were described. Current practices were described as follows: two countries only provide national summative assessments (Slovenia, UK), while all were providing formative assessments regularly at varying frequencies. All groups identified providing frequent formative feedback to trainees for developmental purposes as the highest priority (figure 1). Most discussions identified a need for improvement, particularly in developing streamlined approaches to portfolios that remain close to clinical practice, protecting time for quality observation and feedback, and adopting systematic approaches to incorporating teamwork and professionalism into assessment systems.

Joint group priority order (n=26)	Trainers priority order (n=12)	Trainees priority order (n=14)
1. Getting and giving regular feedback on real life practice is most important to learning (regular feedback).	1. regular feedback	1. regular feedback
2. As well as service provision, the main priority is to make sure trainees succeed in their training to time, to agreed standards (service, timely).	4. portfolio driven	2. service, timely
3. Being assessed on conducting effective clinical examinations across a suitable range of cases is vital (effective in clinic).	2. service, timely	3. effective in clinic
4. A trainee portfolio drives the trainee and trainer to sample across practice for both developmental and qualifying purposes (portfolio driven).	3. effective in clinic	5. regular skills
5. Skills such as injections or ultrasound should be assessed regularly throughout training (regular skills).	7. functions in teams	6. prevent failure
6. Once trainees get to this stage, every help should be available to prevent failure (prevent failure).	5. regular skills	7. functions in teams
7. How a trainee functions in teams is an important aspect of becoming fit to practice (functions in teams).	6. prevent failure	4. portfolio driven
8. Rigorous rheumatological knowledge tests are the best way to assess future rheumatologists (knowledge tests).	8. knowledge tests	8. knowledge tests
9. A professional attitude will emerge in time anyway and is impossible to assess, so best to leave this alone (professional attitudes emerge).	9. professional attitudes emerge	9. professional attitudes emerge

Figure 1. Priorities on assessment of competences for all participants and stratified by trainees and trainers.

Conclusion: This paper presents a clearer picture of the current practice on the assessment of competences in rheumatology in key countries and the underlying rationale of trainers' and trainees' priorities. This work informed the EULAR Points-to-Consider for the assessment of competences in rheumatology training across Europe.
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THU0584 CASE-BASED ONLINE EDUCATION SIGNIFICANTLY INCREASES CLINICIAN COMPETENCE IN ASSESSING SSC-ILD DISEASE PROGRESSION AND IMPLEMENTING APPROPRIATE THERAPY

C. Rohani-Montez[1], M. Calle[1], C. Allen[1], C. Denton[2]. [1]*Medscape Education Global, London, United Kingdom*; [2]*Royal Free Campus, University College London, London, United Kingdom*

Background: Due to the heterogeneity in both the initial manifestations of systemic sclerosis (SSc) and progression with SSc-associated interstitial lung disease (SSc-ILD), diagnosis and prognosis can be challenging in clinical practice. Clinicians need expert case-based guidance on how best to monitor patients with SSc and the treatment implications.
Objectives: This study was conducted to determine whether online case-based independent medical education could improve rheumatologists' and pulmonologists' competence in evaluating and monitoring SSc-ILD progression and initiating the right treatments when progression is identified.
Methods: Rheumatologists and pulmonologists participated in two comprehensive online case studies, using a 'test then teach' approach and completed all pre- and post-questions.[1] The effects of the education on knowledge and competence were assessed using a 3-question, repeated pairs, pre-assessment/post-assessment study design. For all questions combined, the chi-square test assessed differences from pre- to post-assessment. P values <.05 are statistically significant. The activity launched on September 24, 2019, and data were collected through December 9, 2019.
Results: Overall significant improvements were seen after participation for both rheumatologists (average correct response rate of 65% at pre-assessment vs 97% at post-assessment; P<.001, N=89), and pulmonologists (average correct response rate of 64% at pre-assessment vs 95% at post-assessment; P<.001, N=71). Specifically, significant improvements were observed in clinicians' competence in assessing response to therapy and monitoring for disease progression; and managing evidence of disease worsening (figure).

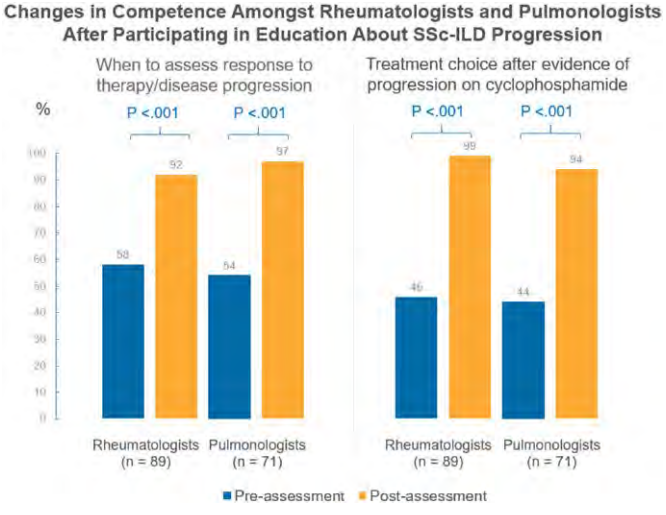


Figure.

After participating in the activity, 54% of rheumatologists and 51% of pulmonologists had measurable improved confidence related to communicating with patients with SSc-ILD about the possibility of disease progression.
Given that only around half of clinicians provided correct responses at baseline, it will be important to continue to reinforce these learnings in ongoing education.
Conclusion: This study demonstrates the success of online, case-based education in improving rheumatologists' and pulmonologists' competence in managing patients with SSc-ILD. This could lead to earlier changes in therapeutic approach for those with signs of progression and result in improved overall outcomes for these patients.
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THU0585 ONLINE EDUCATION YIELDS SIGNIFICANT GAINS IN RHEUMATOLOGISTS' KNOWLEDGE OF THE JAK INHIBITORS MODE OF ACTION AND CLINICAL TRIAL DATA

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Background: Physicians face challenges staying up-to-date with the latest research and accessing the ever-growing field of knowledge is time-consuming. Online education can make these clinician's tasks more efficient and less time-consuming.
Objectives: This study assessed whether the online CME accredited round-table-discussion with title "*Meet the JAKs: Understanding the Role of Janus Kinase Inhibition in RA*" improves physicians' understanding mechanism of action (MOA) of current and emerging Janus kinase (JAK) inhibitors and rationale for their development in rheumatoid arthritis (RA).
Methods: Rheumatologists participated in an online CME activity (https://www.medscape.org/viewarticle/913625) consisting of a 30-minute video discussion between 2 experts with accompanying slides. Educational effect was assessed using a 4-question repeated pairs, pre-/post-assessment. A chi-square test was used to determine if a statistically significant improvement (P <.05 significance level) existed in the number of correct responses from the pretest and posttest scores. Cramer's V was used to estimate the level of impact of the education. The CME activity launched on June 4, 2019, and the data were collected through September 3, 2019.
Results: A total of 107 rheumatologists completed the pre- and post activity assessments. Overall the activity had a signficiant impact (P <.001) on rheumatologists' knowledge of JAK inhibitors and related
clinical trial data with a Cramer's V value of 0.319 indicating an extensive educational impact. The average percentage of correct responses rose from 47% pre-activity to 78% post-activity. The repeated pairs analysis (each individual learner tracked pre- and post-education) showed that 34% of learners improved their knowledge and 44% reinforced their knowledge. The change in percentage of correct responses from pre- to post-assessment achieved statistical significance for all 3 questions presented: (1) understanding the MOA of JAK inhibitors vs biologics (64% at baseline rising to 82% post acivity; P <0.01), (2) understanding the specificity of different JAK inhibitors (49% at baseline rising to 85% post acivity; P <.001), (3) knowledge of clinical trial outcomes with JAK inhibitors (29% at baseline rising to 67% post acivity; P <.001) and (4) 60% of rheumatologists gained confidence in their ability to describe the MOA of current and emerging JAK inhibitors.
Conclusion: This online CME activity significantly improved rheumatologists' understanding of JAK inhibitors mode of action. However, there is clearly room for further improving physicians' knowledge of clinical trial outcomes with these agents, since one third of rheumatologists provided incorrect answers to question 3 post-activity) and this topic can be further addressed in future education.
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THU0586 **ESTABLISHING THE KEY COMPONENTS OF A EULAR PORTFOLIO FOR TRAINING IN RHEUMATOLOGY: A EULAR SCHOOL OF RHEUMATOLOGY INITIATIVE**

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Background: In clinical training, a portfolio is expected to stimulate learning and encourage critical reflection. Some, but not all, European countries use a portfolio in rheumatology training, and their scope varies widely. A EULAR portfolio for Rheumatology trainees could contribute to improve overall training, raise educational standards, foster the setting of common goals and harmonize rheumatology training across countries.
Objectives: Develop key components that should be included in a EULAR portfolio of Rheumatology.
Methods: A working group (WG) composed of 9 rheumatologists and 1 educationalist was established. A systematic literature review (SLR) was conducted in November 2018, according to the PIM structure: Population: trainees; Instrument of interest: portfolio; Measurement of properties of interest: content portfolio. A survey was disseminated among the WG group and WG members of the EMerging EUlar NETwork (EMEUNET), inquiring about the content and structure of existing national portfolios. Portfolio materials of selected countries were reviewed. Last, the WG elected the key components of the portfolio.
Results: 13/2,034 articles were included in the SLR (12 high/1 moderate risk of bias). Information on direct observation of procedural skills (DOPS) (9/13), personal reflections (8/13), learning goals (5/13) and multisource feedback (5/13) were most often included in the portfolio. Twenty-five respondents filled out the survey (response rate ≈ 50%). Reflective writing (n=7), learning goals (n=4) and feedback (n=4) were considered the most useful components of a portfolio. About half indicated that a portfolio was a bureaucratic burden; 4 respondents mentioned lack of feedback by supervisors as a barrier. Portfolio materials of 7 European countries were reviewed. Several portfolios (Germany, Italy, Greece and Spain) were logbooks, i.e. a record of clinical activities. Other portfolios (UK, Denmark, The Netherlands) also included information on workplace-based assessments, learning goals, and personal reflections. The proposed key components of the portfolio are included in Table 1.

Table 1. Key components of the EULAR portfolio of Rheumatology.

Key component	Content
Curriculum vitae	Personal record of achievements, experiences, knowledge and skills
Personal Development Plan	Learning goals and action plan
Clinical work	Information on managing patients (e.g. rheumatoid arthritis)
	Skills (e.g. joint aspiration)
	Assessments (summative and formative)
	Personal reflections
Professional behaviour	Multisource feedback
	Personal reflections
Education	Continuing professional development, list of formal and non-formal learning activities
	Assessments (e.g. teaching assessment, evidence based medicine assignment)
	Personal reflections
Research	List of abstracts, published articles
	Information on research funding, scholarships, bursaries, academic posts

Conclusion: This initiative resulted in the establishment of a list of key components to be included in a EULAR portfolio of Rheumatology. Assessment forms for each key portfolio component are currently being developed. Portfolio implementation, particularly in countries that do not use it yet, may contribute significantly to promote a higher standard of patient care across Europe.
Disclosure of Interests: Marloes van Onna: None declared, Sofia Ramiro Grant/research support from: MSD, Consultant of: Abbvie, Lilly, Novartis, Sanofi Genzyme, Speakers bureau: Lilly, MSD, Novartis, Catherine Haines: None declared, M. Holland-Fischer: None declared, José Antonio P. da Silva Grant/research support from: Pfizer, Abbvie, Consultant of: Pfizer, AbbVie, Roche, Lilly, Novartis, Jean Dudler: None declared, Christopher Edwards Grant/research support from: Abbvie, Biogen, Roche, Consultant of: Abbvie, Samsung, Speakers bureau: Abbvie, BMS, Biogen, Celgene, Fresenius, Gilead, Janssen, Lilly, Mundipharma, Pfizer, MSD, Novartis, Roche, Samsung, Sanofi, UCB,
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Educational cases

THU0587 **TB OR NOT TB? THIS IS THE QUESTION. CASE REPORT OF AN EXTRAPULMONARY TUBERCULOUS ARTHRITIS.**

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Background: Tuberculous (TB) arthritis consists of 1-3% of all TB cases, whereas TB tenosynovitis & bursitis account for 1%. Primarily it involves large joints but occasionally smaller non-weight-bearing joints. Diagnosis is usually delayed due to lack of awareness, radiographic findings & constitutional or pulmonary involvement.
Objectives: We aim to increase rheumatologists awareness to detect possible TB etiology for arthritis & tenosynovitis.
Methods: Our case is a 32 years old male complaining of polyarthritis of wrists, MCPs, ankle joints 4 months prior to presentation. Patient was referred as diagnosed rheumatoid patient resistant to treatment based on clinical presentation & laboratory investigation. His lab. was as follows; ESR 76 mm/hr, CRP 56.6 mg/L, RF 181.8 IU/ml, Serum creat 0.8 mg/dL, SGOT 20 SGPT 22, FBS 94, Uric acid 5.4, Hepatitis & HIV negative. CBC showing Hb 14.1 g/dL, TLC 7030/ml & platelets 289000/ml. There was no history of genitourinary, gastrointestinal manifestations, oral/genital ulcers, ophthalmological, mucocutaneous, cardiac, pulmonary, hepatic nor renal manifestations. The treatment at time of presentation was Methotrexare 25mg/week IM injection, Leflunamide 20mg/d & low dose steroids, prednisolone 5mg/d. Patient was referred to our department to assess activity, perform musculoskeletal ultrasound to the various involved joints. Hence, expected by referring physician to shift from DMARDs to biologic treatment.
Results: MSUS study following eular guidlines showed active synovitis in both radiocarpal & midcarpal joints bilaterally grade II by doppler signal (figure 1). Other active synovitis in multiple MCPs as well as tenosynovitis of Peroneus longus and brevis bilaterally was detected (figure 1). The swelling aound the ankle was alarming though the other swollen joints seemed to be consistent with a case of RA in activity. This swelling revealed a well-defined hypoechoic heterogeneous cystic fluid collection with posterior through-transmission (figure 2) & hyperechoic hyperemic wall on PD imaging opposite medial malleolous of right fibula. The laboratory investigations prior to shifting patient had to included TB tests, tuberculin test and PCR following the positive result that we found in the skin test. Aspiration was performed from the cystic swelling and sent for clinical pathology analysis. Thick yellowish fluid aspirate on cytology revealed moderately cellular mainly of PMN cells, neutrophils, nuclear debris in proteinaceous background no atypical or malignant cells were found. As regards bacteriology no pus with no growth (both aerobic & anerobic). These results warranted us to perform a culture for atypical bacteria and revealed growth of mycobacterium tuberculosis. AntiTB therapy was started for 9 months in the form of 2 months of isoniazid (INH) and rifampicin (RIF), pyrazinamide (PZA) and ethambutol (EMB) followed by 7 months of INH and RIF. Excision of the synovial cyst was done on the spot.

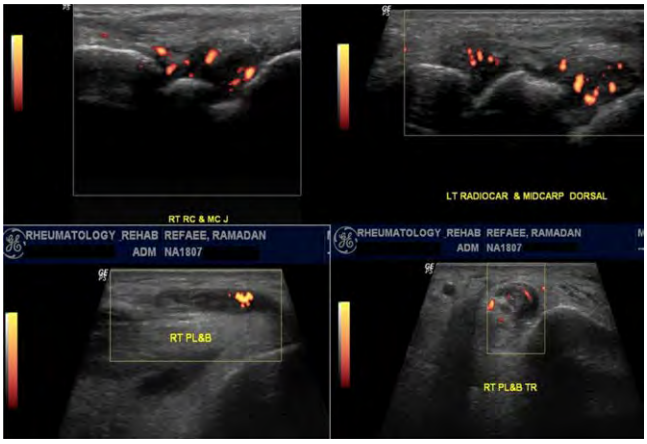


Figure 1.

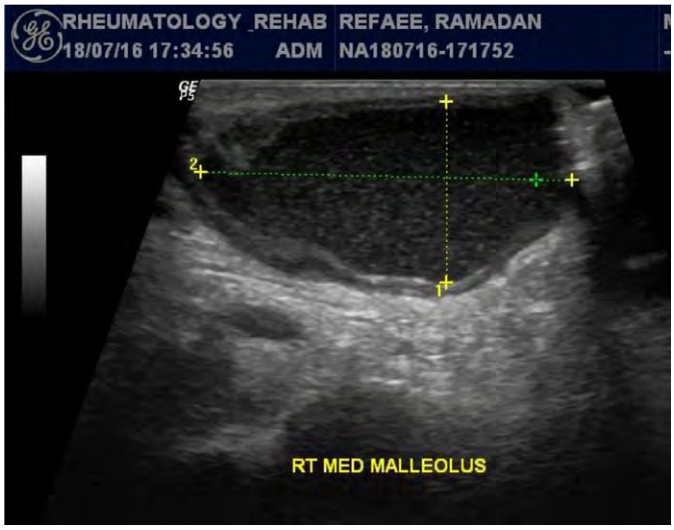


Figure 2.

Conclusion: Extrapulmonary TB is usually diagnosed late due to a reduced diagnostic suspicion. A variant of 8 - 60% of TB cases are +ve for RF & 7–39% +ve for ACPA. Musculoskeletal manifestations occur in approximately 1-3% of TB cases. Of these, spondylitis and arthritis are the most frequent, whereas bursitis and tenosynovitis are exceptional. Extraarticular cystic masses occur in tuberculous arthritis. Mixture of septic tuberculous arthritis and Poncet's disease is rare but documented.

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THU0588 TAKAYASU'S ARTERITIS PRESENTING WITH UNILATERAL DIGITAL CLUBBING IN A 23 YEAR-OLD MALE

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Background: Takayasu Arteritis is a chronic, large vessel arteritis that commonly involves the aorta and its major branches, mostly the ascending/descending aorta, subclavian arteries, and carotids [1].

Herein, we report a case of a 23 year-old medically free Indian male who presented to our hospital in acute distress complaining of cough, hemoptysis and shortness of breath for one week as well as intermittent fever and fatigue for five months. He presented with a BP of 140/100 mmHg as well was both systolic and early diastolic murmurs in the mitral and aortic areas, respectively. He also had a paraumbilical bruit and unilateral clubbing in the left hand with digital ischemia of the left index finger. Doppler ultrasound of the left arm showed monophasic flow pattern with low velocity in left distal radial, distal ulnar, and all digital arteries, except the second digital arteries; low velocity in the median artery; and no flow in the lateral artery of second digit (Figure 1). Computed tomography angiogram (CT Angio) (Figure 2) of the chest, abdomen, and pelvis showed fusiform aneurysm dilatation of the thoracic aorta extending into the right braciocephalic and subclavian arteries as well as the right common carotid artery.

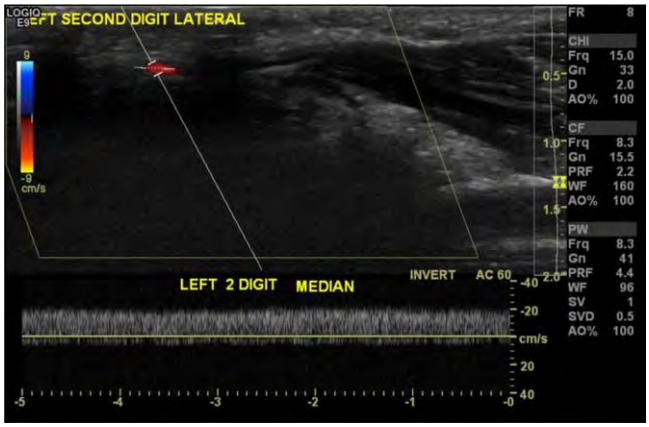


Figure 1.



Acknowledgments

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Figure 2.

Unilateral clubbing in patients with TA occurs as a result of subclavian artery stenosis that leads to tissue ischemia and hypoxia [2-4]. In turn, the bone marrow release megakaryocytes, which enter the systemic circulation when an A-V shunt exists [5]. Platelet-derived growth factor (PDGF) (release from megakaryocytes) and vascular endothelial growth factor (VEGF) levels are highly expressed in the connective tissues of nail beds, leading to its proliferation and platelets clumps' accumulation [6, 7].

Objectives: To report the fourth case worldwide and third case of an adult, respectively, with Takayasu's arteritis who presents with unilateral clubbing.

Methods: Our patient was started on pulse steroid therapy of methylprednisolone 1 gram IV od for 5 days and later switched to prednisolone 20 mg po BID. He also received methotrexate 10 mg PO once weekly and rituximab 750 mg IV stat; another dose of rituximab was given two weeks later.

Results: His clubbing has significantly improved within 2 weeks of starting immunosuppressive therapy. He was discharged with follow up on methotrexate 12.5 mg PO once weekly and prednisilone 20 mg PO OD (to be tapered). Clubbing improved by a rate of 60% two weeks following discharge in two weeks.

Conclusion: In all four cases of Takayasu arteries presenting with unilateral clubbing, patients' clinical condition including presence of clubbing improved after initiation of immunosuppressive therapy.

References:

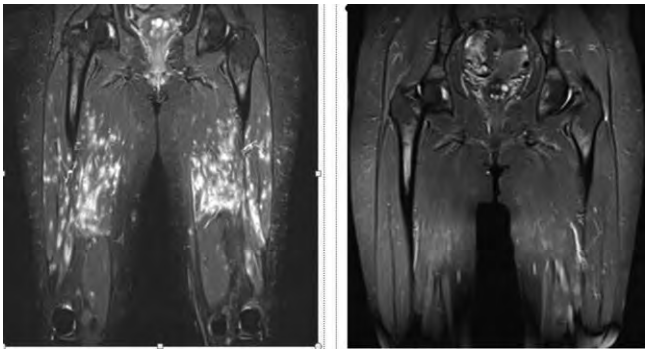
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Disclosure of Interests: None declared
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THU0589 'KU FEVER': A CASE REPORT

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Background: Anti-Ku antibodies have been associated with various connective tissue diseases, including myositis, arthritis, interstitial lung disease and glomerulonephritis [1].
Objectives: We present a case of a woman initially diagnosed with biopsy proven Kikuchi-Fujimoto disease who later developed a rapidly progressive myositis in association with anti-Ku antibodies.
Methods: A 47 year-old woman, originally from Myanmar, presented with lymphadenopathy, myalgia, fatigue, livedo reticularis and low-grade fever for the previous 6 months. This was initially diagnosed as a viral infection. Her myalgia progressed with proximal muscle weakness in both legs and associated rise in creatine kinase levels to 349U/L (normal range 25-200). She also developed dyspnoea, an erythematous rash, mouth ulcers and unintentional weight loss.
Blood tests show a lymphopenia and progressively rising CK, with a maximum level of 516 U/L. MRI whole body confirmed a widespread diffuse myositis in her upper and lower limbs, with an unusual 'speckled' pattern. High resolution CT Chest was normal. C3 0.40 g/l (normal range 0.75-1.65) and C4 0.12 g/l (0.14-0.54) were low, with a positive ANA (1:160) and Ro-60 antibody. dsDNA, antiphospholipid screen and virology screens were all negative. Extended myositis panel revealed positive anti-Ku antibodies. Axillary lymph node biopsy confirmed necrotising lymphadenitis, consistent with Kikuchi-Fujimoto disease.
Results: She was initially treated with low dose Prednisolone and Hydroxychloroquine, with a limited response. Due to progressive myositis, pulsed IV Methylprednisolone 1g was provided over 3 days and mycophenolate mofetil (MMF) was started.
An inpatient stay was needed after developing an axillary node abscess and a chest infection. This was treated with intravenous antibiotics and repeated aspirations. Due to progressive myositis on a background of sepsis, intravenous immunoglobulin (IVIG) was administered over 5 days. Our patient made a good recovery, with normalization of CK levels and resolution of the myositis noted on repeat MRI scan. She remains on MMF as maintenance therapy.



Conclusion: Anti Ku antibodies appear to be associated with 2 spectrums of disease – elevated CK levels with interstitial lung disease and renal disease associated with anti-dsDNA antibodies [1] To our knowledge this is the first report in association with Kikuchi-Fujimoto disease. The combination of MMF and IVIG appears to have been effective treatment and her renal function remains stable, although we are monitoring the patient carefully for the possible development of interstitial lung disease.
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Disclosure of Interests: None declared
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THU0590 WHEN RARE IS EVEN RARER: A COMPLEX CASE OF BEHCET DISEASE

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Background: Behcet disease is a rare inflammatory disorder with the unique ability to affect vessels of any size. The disease could be associated to thrombosis in both the venous and arterial compartment, and often aneurysms. In particular, the presence of aneurysms of the pulmonary artery is rarely, if ever, seen in conditions other than Behcet. Cardiac involvement, albeit uncommon, is also described and associated to a severe prognosis. The treatment is based on immunosuppressants, meanwhile the use of anticoagulants -especially when aneurysms are present- is debated.
Objectives: To describe a complex case of Behcet disease.
Methods: We report the case of a 45 years old man of Chinese origin who presented to A&E with fever and acute dyspnea. Blood test revealed raised ESR and CRP and raised neutrophil count. Chest X rays showed bilateral opacities suggesting pneumonia. The patient did not improve over the course of antibiotics. Later on, he presented with an episode of hemoptysis and worsening dyspnea, so he was admitted to the Intensive Care Unit. CT showed bilateral pulmonary thromboembolism and aneurysm of the pulmonary artery. Echocardiogram and cardio-MRI revealed a large, mobile thrombus within the right atrium. Extensive work-up for infections and cancer was unrevealing. ANA, ENA and ANCA antibodies were negative. On the basis of a past medical history of recurrent oral ulcers and papulopustular skin lesions that patient admitted on questioning, a diagnosis of Behcet disease was suspected. In keeping with that, HLA-B51 turned out positive. The patient was promptly started on IV steroid pulses followed by Cyclophosphamide 1 gr IV monthly for six months, then on IV anti-TNF alpha Infliximab. He was also commenced on low molecular weight heparin (LMWH) and subsequently direct factor Xa inhibitor Apixaban.
Results: The patient improved significantly with progressive regression of the pulmonary CT changes. He was discharged and able to get back to his daily life activities. After 2 years and a half of treatment, the aneurysm was stable and the intracardiac thrombus completely cleared.
Conclusion: This case is of particular interest because of the concomitant presence of two rare vascular complications of Behcet disease-intracardiac thrombosis (<1-2%, less than 100 cases described worldwide) and pulmonary artery aneurysm (1-2%). Prompt introduction of immunosuppressant therapy was associated with a favorable outcome with no recurrence. We could speculate that, to some extent, the concomitant use of anticoagulants may have contributed to the complete resolution of the intracardiac thrombosis.
Disclosure of Interests : MARIA DI CICCO: None declared, oscar massimiliano epis Consultant of: yes, Speakers bureau: yes, Cinzia Casu: None declared, Antonella Adinolfi: None declared, Luisa Alvaro: None declared, Valeria Campanella: None declared, Michel Chevallard: None declared, Marina Muscarà: None declared, Mariaeva Romano: None declared, Emanuela Schito: None declared, Nicola Ughi: None declared, Elisa Verduci: None declared, Davide Antonio Filippini: None declared
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THU0591 CENTRAL NERVOUS SYSTEM VASCULITIS IN WHIPPLE DISEASE: A CASE REPORT

A. Giollo[1], C. Zivelonghi[2], D. Cardellini[2], G. M. Schiavi[2], G. Vattemi[2], O. Viapiana[1], M. Rossini[1]. [1]*University of Verona, Rheumatology Section, Department of Medicine, Verona, Italy*; [2]*University of Verona, Department of Neuroscience, Biomedicine and Movement Sciences, Verona, Italy*

Background: Whipple disease (WD) is a rare systemic infection with possible involvement of the central nervous system (CNS). The neurological manifestations of the disease are various and can mimic any neurologic condition.
Objectives: To describe the severe neurological complications occurred in a patient with WD misdiagnosed as a chronic inflammatory immune-mediated disorder.
Methods: Case report
Results: A 46-year-old woman developed acute right-sided hemiparesis and dysarthria. She had a 10-year history of ill-defined rheumatic condition (defined as seronegative rheumatoid arthritis, spondyloarthritis, and adult onset Still's disease) presenting with polyarthritis, episodic fever > 38°C and rash of unclear etiology poorly responsive to different immunotherapies including methotrexate, anti-IL6 and anti-IL1 inhibitors. Brain MRI demonstrated multiple anterior circulation infarctions and stenosis of the bilateral M1 segments of the middle cerebral artery on MR angiography. Black blood sequences revealed contrast enhancement of the vessel walls consistent with vasculitis (Figure 1). Cerebrospinal fluid (CSF) analysis was unrevealing, including PCR for viruses and bacteria. A working diagnosis of primary CNS vasculitis and progressive neurologic deterioration with abnormal behavior and altered mental status prompted the

initiation of intravenous (IV) methylprednisolone followed by cyclophosphamide without significant improvement. Re-evaluation of the long-standing history of joint symptoms unresponsive to immunotherapy, along with recurrent fevers and chronic diarrhea raised the suspicion of unrecognized Whipple's disease. PCR for Tropheryma Whippleii was positive in stool, urine, blood and CSF, and duodenal mucosal biopsies confirmed the diagnosis. A combination of ceftriaxone, doxycycline, and hydroxychloroquine was initiated. Three days later the patient developed periocular burning pain and cutaneous vesicles consistent with shingles. Varicella-zoster virus DNA was detected in CSF and IV acyclovir was started. At 3 months follow-up neurologic examination was unremarkable except for a slightly fatuous behavior.

Conclusion: Recognition of rare manifestations of WD is important to avoid diagnostic delay and inappropriate, potentially harmful treatments.

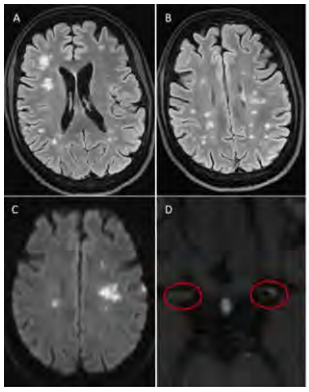


Figure. Brain MRI with FLAIR sequences revealing hyper intense lesions in the subcortical white matter of both hemispheres (A, B). C, DWI sequences showing several recent ischemic lesions bilaterally with prominent involvement of the left frontal lobe. D, black blood sequences documenting enhancement and thickening of the wall vessel of both MCAs (red circles).

Disclosure of Interests: Alessandro Giollo: None declared, Cecilia Zivelonghi: None declared, Davide Cardellini: None declared, Gian Marco Schiavi: None declared, Gaetano Vattemi: None declared, Ombretta Viapiana: None declared, Maurizio Rossini Speakers bureau: AbbVie, Abiogen, Amgen, BMS, Eli-Lilly, Novartis, Pfizer, Sanofi, Sandoz and UCB

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THU0592

INSIDIOUS CORONARY ARTERY DISEASE IN A YOUNG PATIENT WITH POLYARTERITIS NODOSA: A CASE REPORT AND REVIEW OF LITERATURE

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Background: Polyarteritis nodosa (PAN) is a systemic necrotizing vasculitis that typically affects medium-sized muscular arteries, with occasional involvement of small muscular arteries[1]. Although overt myocardial infarction is uncommon, myocardial ischemia may result from narrowing or occlusion of the coronary arteries[2].

Objectives: Herein, we report a case with 7-year's history of PAN and unstable angina pectoris due to coronary occlusions of the three main arteries. We also reviewed the literatures regarding coronary artery involvement in PAN.

Methods: A 22-year-old Chinese man who presented with chest pain lasting for a few minutes and then subsiding spontaneously for 1 month was admitted to our hospital. He was diagnosed as PAN 7 years ago and during 7-years' follow-up, he has been in stable condition, without any discomfort or abnormal laboratory findings. In December 2019, he suffered from chest distress accompanied by retrosternal pain, with frequency of about 2-3 times a week. His symptoms were gradually aggravating with dyspnea at night.

Results: Coronary computed tomography angiography showed diffuse coronary stenosis (Fig. 1). Further coronary angiography revealed a slight plaque infiltration of the left main coronary artery, and occlusion of all the three major coronary arteries, as well as multiple coronary aneurysms. 95% stenosis of the obtuse margin branch artery was also found and a stent was then implanted (Fig. 2). Prednisone 50mg/day and methotrexate 15mg/week were reinitiated, in combination with anti-anginal medications including aspirin and statin.



Fig. 1 Coronary computed tomography angiography found diffuse coronary stenosis.

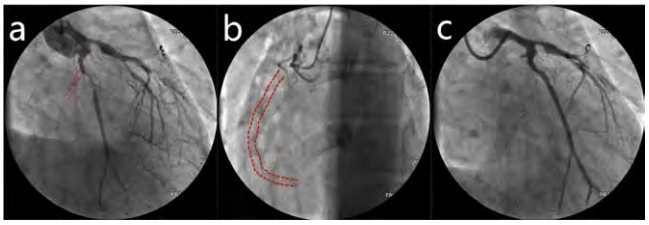


Fig. 2 Coronary angiography. (a) A 50% stenosis followed by aneurysmal change of the proximal end of left anterior descending (LAD) artery, and totally occluded from the middle segment; A aneurysmal change of the initial part of left circumflex artery (LCX) and then totally occluded (dotted line); A 95% stenosis obtuse margin branch. (b) A totally occluded right coronary artery (dotted line). (c) Final appearance of the LCX after stent implantation.

After we reviewed all the English literatures reporting cardiac involvements in adults with PAN from 1990 to 2019, a total of 34 patients from 32 articles were identified. 25 (73.5%) patients were admitted to hospital due to acute coronary syndromes manifesting as chest pain or dyspnea. Coronary stenosis or occlusions were most common on imaging or autopsy. Most of the patients had more than one vessel involved, of whom 7 patients showed evidence of triple vessel lesions. Aneurysm was also common in these patients, especially multiple aneurysms. Spontaneous coronary artery dissections were rare in PAN patients. Most patients received glucocorticoid, and/or immunosuppressant therapy, including cyclophosphamide and azathioprine, with or without invasive operations. 15 patients died from cardiopulmonary arrest, the most frequent cause being death, and 15 patients were stable without symptoms after treatment.

Conclusion: We report a young PAN patient with insidious stenosis of three main coronary arteries under the circumstance of stable disease activity for years. This reminds us of the necessity of assessing heart, probably other organs as well, in PAN patients even though their acute phase reactants in serum are normal. But how often to do the screening and which screening examination should be done, remain to be further investigated.

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Disclosure of Interests: None declared
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THU0593 LIBMAN SACKS ENDOCARDITIS COMPLICATED WITH CEREBRAL EMBOLISM REVEALING SYSTEMIC LUPUS ERYTHEMATOSUS: A CASE REPORT

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Background: Libman Sacks endocarditis (LS) is an uncommon sterile endocarditis mostly associated with malignancies. It can also complicate the evolution of systemic lupus erythematosus (SLE) in 1 out of 10 patients after many years of evolution of the disease.
Objectives: To raise awareness of the possible rare complications of LS in SLE
Methods: We report a case of a complicated Libman sacks endocarditis revealing the diagnosis of SLE.
Results: A 53 years old female patient with history of hypertension was admitted to the rheumatology department for polyarthritis since 2 months with fatigue and dyspnea. On physical examination, she had no fever nor cutaneous lesions, her pulse rate was accelerated to 112 per minute and there was no heart murmur. Musculoskeletal examination revealed the presence of arthritis of little joints of the hands and bilateral arthritis of the knees. Biological results showed an accelerated sedimentation rate of 49 mm the first hour, elevated c-reactive protein of 79 mg/l, anemia and lymphopenia. Renal and hepatic functions were both normal. Transthoracic cardiac echocardiography showed no valvulopathy but a 5mm sessile vegetation on the mitral valve. To rule out infectious endocarditis, blood cultures came out negative, serological tests for brucella, parvovirus B19, coxiella brunettii, mononucleosis, were also negative. Culture of knee joint fluid for common bacteria and polymerase chain reaction tests for tuberculosis were also negative. The patient presented rapidly with agitation, cerebellar ataxia, and unilateral paresis. CT-scan showed the presence of ischemic lesions in the lenticular nucleus and the semiovale centers. Lumbar punction showed no abnormalities. She was prescribed large spectrum antibiotics and anti coagulants but with persistant worsening of her neurological state. She was then transferred to the intensive care unit. Antinuclear antibodies, came out by then positive 1:3200 with an homogenous fluorescence and with positive anti nucleosome anti bodies. The diagnosis of LS endocarditis associated with SLE complicated with brain embolisms was confirmed with delay.
Conclusion: LS endocarditis is not common but when it presents it is often associated with high morbidity and mortality. Health care professionals should consider LS diagnosis in patients with underlying SLE and should be aware of the risk of embolisation. Tests to rule out infectious disease may delay initiation of appropriate treatement leading to severe prognosis. The treatment of LS endocarditis is still not well codified.
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THU0594 A CASE OF TAKAYASU'S ARTERITIS IN A PATIENT WITH TUBERCULOUS LYMPHADENITIS

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Background: Takayasu's arteritis (TA) is a large vessel vasculitis that principally affects the aorta and its main branches. The incidence has been reported at between 1.2 – 2.3 cases per million per year, more commonly in the Asian population. The age of onset is typically between tenth and fourth decade; between 80 and 90 percent of the cases are female.
The relationship between Mycobacterium Tuberculosis (mTB) and TA has long been considered; both demonstrate chronic inflammatory changes on histological examination and some granuloma formation in arterial walls. There is increasing evidence implicating mTB in the pathogenesis of TA through molecular mimicry between the mycobacterium heat shock protein -65 (mHSP-65) and the human homologue HSP -60 (hHSP-60). However, no definitive link between the two diseases has been explained.
Objectives: Case presentation.
Results: A 23-year-old lady was referred to our outpatient rheumatology clinic with a twelve-month history of persistently enlarged cervical lymph nodes on the left side for which she had received six months of anti-Tuberculosis medication. She had been referred to the respiratory physicians who had diagnosed presumed Tuberculous Lymphadenitis, with caseating granulomas demonstrated on biopsy, positive acid-fast bacilli smear but a negative culture. The patient had been initiated six months of anti-Tuberculosis medication; however, her lymphadenopathy showed no improvement. More recently she described a five-month history of weakness, paraesthesia and claudication symptoms in her left upper limb with episodes of dizziness and blurred vision, episodes occurring 2-3 times per day and lasting between a few minutes to a few hours.
Her examination at this presentation revealed an unrecordable blood pressure in the left upper limb and 104/67mmHg in the right. There was significant tender lymphadenopathy of the left cervical lymph nodes and diminished pulses in the left upper limb. Right sided pulses were normal. The rest of her examination was normal.
Investigations at presentation revealed elevated inflammatory markers with C-reactive protein (CRP) of 116mg/dL and erythrocyte sedimentation rate (ESR) of 128mm/h. Complete blood count (CBC) found her to be anaemic with a haemoglobin of 100g/L, with a mean cell volume of 71.3fl, and have elevated platelet count of 649x 109/L. Recent computerized tomography scan with contrast of the thorax demonstrated features consistent with Takayasu Arteritis. Marked left subclavian stenosis was found on magnetic resonance imaging. High dose prednisolone at 60mg once daily along with Azathioprine 2mg/kg/day was started with a follow up appointment in two weeks.
Conclusion: There is increasing evidence implicating mTB in the development of TA and a few cases recognising this link have been reported. We report a case of TA in a patient recently diagnosed and treated for Tuberculous lymphadenitis who then developed symptoms of TA. There should be a low threshold for suspecting a diagnosis of Takayasu's arteritis in patients previously or actively infected with Mycobacterium Tuberculosis. Further research exploring the relationship between mTB and TA is required.
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THU0595 SUCCESSFUL COMBINED IMMUNE-MODULATING THERAPY OF IN UTERO MYOCARDITIS AS THE MANIFESTATION OF NEONATAL LUPUS IN A RO/SS-A ANTIBODY EXPOSED NEWBORN

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Background: Congenital heart block (CHB) occurs in 2-5% of pregnancies due to maternal Ro/SSA and/or anti-La/SSB antibodies, and has a recurrence rate of 12-20% in the following pregnancy. The highest risk for CHB of the foetus is in the gestational age between 16- and 28-weeks. Without immunotherapy, this autoantibody mediated disorder comes with substantial mortality with a rate of 15-30%. Ro/SSA and/or anti-La/SSB antibodies attack the atrioventricular node with the subsequent inflammation and fibrosis. In addition, other cardiac manifestations

are known such as endocardial fibroelastosis, dilated cardiomyopathy, and valvular insufficiency. The early clinical diagnosis in utero is essential to be specified due to myocardial tissue damages can be reversible. In the prevention and in the confirmed cardiac involvement the first line therapies are chloroquine, dexamethasone and intravenous immunoglobulins, and also a regular foetal echocardiography is of essential importance.

Objectives: Main objective of this report is description of successful treatment of an anti-SS-A antibody exposed foetus with cardiac manifestation.

Methods: Case report of a 25-year-old pregnant woman and her baby. The mother was diagnosed with Sjogren's syndrome in 2013. In previous case history there were two late foetal deaths at the 23rd and 33rd gestational age in 2016 and 2017, respectively as a consequence of foetal bradycardia. During her 2nd pregnancy the mother received chloroquine and azathioprine. At present she was admitted to our Institute in October 2019 at 23rd weeks of gestation without any compliant and any abnormality of pregnancy. Foetal development was normal. Mother received azathioprine and chloroquine from the beginning of pregnancy and dexamethasone from the 16th weeks of gestation. Foetal echocardiography was performed at the 16th gestational week, and every week thereafter. Reflective areas, reflecting oedema and inflammation, appeared at 24th gestational week, localised to the left atrium.

Results: The case was referred, and the combo therapy was completed with 1 mg/maternal kg intravenous immune globulin, dexamethasone dose was increased to 4 mg for a week, then decreased to 2 mg. Intratect was given every 2nd week. Progression was stopped as according to control foetal echocardiography after the 2nd infusion. After 4th IVIG the involved area of myocarditis decreased significantly, localised to anterior wall of left atrium and the atrial primum septum. However, at 32nd g. week pericardial fluid was visualised in maximum 9 mm width without signs of pericardial tamponade.

At the end of last December, the baby was born at the 35th gestational week with 50 cm and 2570 g and no signs of any congenital anomaly. Pericardial fluid was 4 mm maximum. Her development is normal.

Conclusion: Neonatal lupus with various cardiac manifestations may develop in anti-SS-A antibody exposed babies. Therefore, these pregnancies require stringent gynaecologic and cardiologic controls. Although congenital heart block is the most frequent complication developing between the 18-28th gestational weeks, other manifestations also may occur. High dose intravenous immune globulin therapy can be effective even after failure to combined traditional immune suppressant therapy.

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Disclosure of Interests: Emese Kiss Consultant of: EK has received consultancy fees from Egis., Ágnes Szappanos: None declared

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THU0596 ABNORMAL RIGHT VENTRICLE RESERVE ON EXERCISE PREDICTS PULMONARY HYPERTENSION IN MIXED CONNECTIVE TISSUE DISEASE: A CASE REPORT

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Background: Pulmonary hypertension is one of the most common complications in patients with mixed connective tissue disease (MCTD). Patients are usually at the late stage and have irreversible right heart dysfunction when diagnosed as pulmonary hypertension with the rest echocardiography. Early detection of right heart dysfunction before pulmonary hypertension is essential to ensure that patients receive timely and appropriate treatment for this progressive disease. We aimed to use exercise stress echocardiography to detect early right heart dysfunction in patients with CTD and without pulmonary hypertension.

Objectives: To present a clinical case of MCTD with normal right ventricular (RV) function at resting but presenting RV dysfunction on exercise, who developed pulmonary hypertension after one-year follow-up.

Methods: Case report. The patient was subject to the treadmill exercise stress echocardiography. The autoantibodies including anti-nRNP/Sm, anti-Ro-52, and antinuclear antibody (ANA) were detected. The patient was followed-up to one year.

Results: A 31-year-old female patient was admitted to our department in 2018, with a history of MCTD for five years. Autoantibodies testing revealed that the patient was positive for anti-nRNP/Sm (+++), anti-Ro-52 (+++), and ANA (1:3200). Echocardiography revealed no obvious cardiac dysfunction. However, the velocity of tricuspid valve regurgitation was 3.0m/s following treadmill exercise stress. The patient was followed-up to one year. Then, she developed occult pulmonary hypertension with the velocity of tricuspid valve regurgitation of 3.3m/s following treadmill exercise stress. Accordingly, MTX and prednisone were switched to MTX, prednisone, hydroxychloroquine (HCQ) and beraprost.

Conclusion: This study showed that treadmill exercise echocardiography could detect right heart dysfunction early before diagnosed as pulmonary hypertension with rest echocardiography in patients with MCTD in its early stage.

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THU0597 CORNEAL MELT - DON'T ALWAYS BLAME RHEUMATOID ARTHRITIS

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Background: Corneal melt is a rare inflammatory disease of the peripheral cornea; it may lead to perforation of the globe and visual failure. Corneal melt can be a manifestation of systemic vasculitis in patients with RA and other conditions, such as cancer. Without early and aggressive treatment it may be associated with a poor visual outcome and a high mortality. It has been reported in patients with stable RA.

Objectives: A case report in a patient with long standing but well controlled Rheumatoid Arthritis (RA) and metastatic disease.

Methods: A 75 year old male with a background of sero positive Rheumatoid Arthritis for more than 10 years presented to the Eye Casualty with a two week history of a painful left red eye. His other medical history was significant for Stage IIB poorly differentiated cancer of the left lower lobe. Left lower lobectomy with a patch of diaphragm resected. Intratumoural lymphovascular invasion noted. He completed Adjuvant Carboplatin/Vinorelbine chemotherapy September, 2017. He had DVT proximal left leg 22nd of September, 2017. Follow up CT in 2018 demonstrated a right renal upper pole lesion for which he was awaiting biopsy with?metastatic lung disease vs primary renal carcinoma. His RA was well controlled on Methotrexate 10mg weekly. He had been treated by the ophthalmology team for left marginal Keratitis for the prior 2 months with steroid eye drops without significant improvement. On presentation to ED, he described sharp eye pain, waking him from the sleep, associated with watery discharge and photophobia. Examination showed corneal melt in left eye involving 25% of inferior portion of the cornea and spastic entropion with injecting eye lashes. He had no active joints and there were no other signs of vasculitis. CRP was 4.1. He had a negative ANA and ANCA; viral swabs were negative. He was admitted under the medical team. Intravenous Methyl Prednisolone was started. The patient felt better after 5 days of Methyl Prednisolone. Left temporary tarsorrhaphy was done by Ophthalmology. Cyclophosphamide was initiated after discussion with Oncologist pending the result of the renal biopsy. Patient was discharged after 5 days of admission in the hospital

Results: The renal biopsy was positive for metastatic Squamous cell carcinoma of lung. Cyclophosphamide was withdrawn and he was started on Carboplatin/Gemcitabine. The corneal melt improved with complete resolution of his visual symptoms.

Conclusion: In this case, although the history of RA was felt by the ophthalmology team to be the most likely association with the corneal melt, we would argue the oncological diagnoses were likely the driving force behind the presentation.

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Disclosure of Interests: None declared

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THU0598 A CASE REPORT ON A RARE PRESENTATION OF GOUT INVOLVING THE PATELLAR TENDON

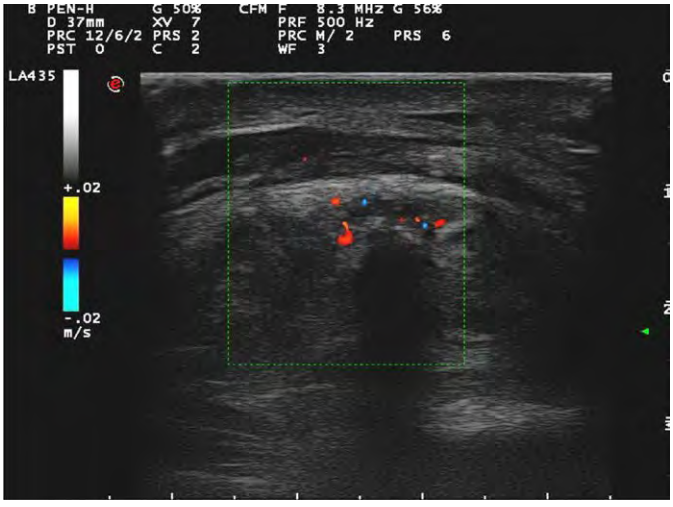
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Background: Gout is an inflammatory arthropathy associated with long-standing hyperuricemia. The first metatarsophalangeal joint is the most commonly involved joint, although gout is often polyarticular. Involvement of tendons has been described, but is rare. We report a case of gout involving the inferior portion of the patellar tendon.
Objectives: A Case report to highlight a rare presentation of gout.
Methods: A 50 year old male presented to the Rheumatology emergency clinic with severe right knee pain, unable to weight bear. He had been recently diagnosed with Sero negative Inflammatory Arthritis and treated with Methotrexate for 4 months. He had presented one week previously to the general medical team on call with similar but less severe pain. He was discharged on steroids, which were of no significant benefit. The pain progressively worsened to the extent that he was not able to bear weight on the right knee. He denied pain or swelling of any other joint.
On examination of his right knee, it was extremely tender, slightly erythematous with increased local temperature. There was no arthritis in any other joint and there were no tophi. Joint aspiration was attempted but there was no fluid.
He was admitted with query Septic arthritis and started on intravenous antibiotics. Uric acid level was 583u/l. US of the knee showed small fluid in the pre patellar bursa.Orthopaedic team was involved and he was taken to the operation theatre. Knee joint was aspirated which was negative for crystals and there was no growth on cultures.
He ultimately had an MRI of his right knee which showed significant soft tissue oedema and abnormality in the patellar tendon.



MRI of Rt knee showing marked soft tissue edema (arrow)

MRI of Rt knee showing marked soft tissue edema (arrow)
Targeted US of the knee done by a consultant rheumatologist showed significant changes in the inferior portion of the patellar tendon consistent with infiltration. The external tendon boundaries were normal. It was thought to be likely that these represented gouty tophi.



USG of the rt knee showing infiltrates in the inferior portion
of patellar tendon with increased Doppler flow
He went on to have a patellar tendon biopsy which has shown changes consistent with gout.
He was started on Colchicine 0.5mg bd leaving the hospital and Allopurinol was started two weeks later.
Results: He was seen in the clinic as follow up with complete resolution of his pain. Methotrexate was stopped. He has reported no flares and Allopurinol is being titrated up to achieve serum uric acid concentration <300u/l.
Conclusion: The most important finding in this case report is that interstitial gouty tophi of the patellar tendon, can cause debilitating symptoms and can prove difficult to diagnose and treat.
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THU0599 PULMONARY ARTERY ANEURYSM, BUDD CHIARI SYNDROME, INTRACARDIAC AND INFERIOR VENA CAVA THROMBOSES: AN UNUSUAL CASE OF BEHÇET'S DISEASE

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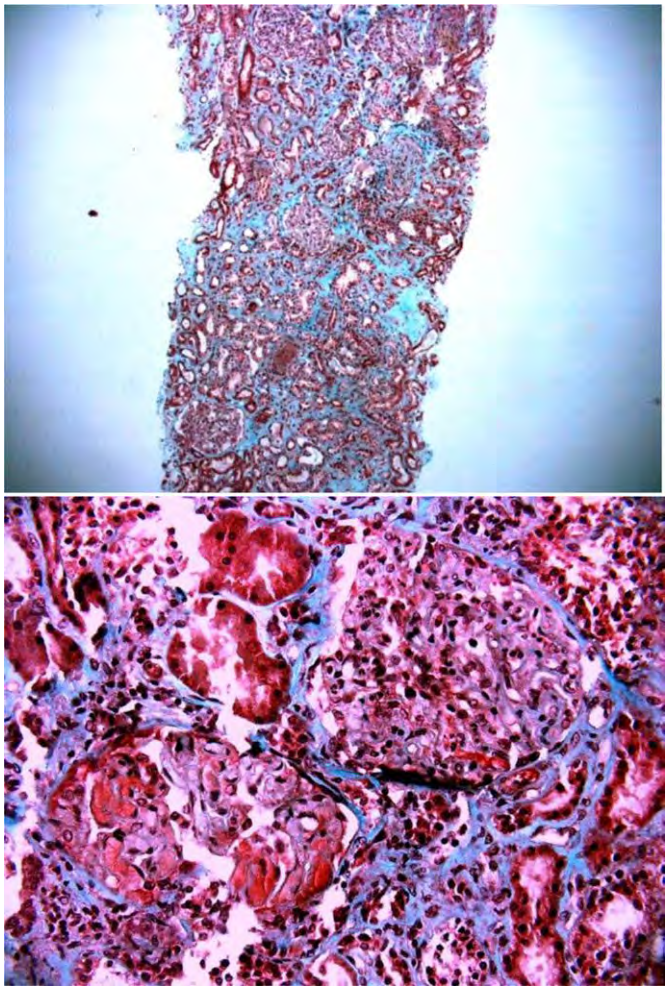
Background: *Behçet's disease (BD) or "Silk Road" disease is a rare multisystemic inflammatory disease of unknown etiology.* Vascular involvement manifested as thrombosis, arterial aneurysm, and occlusion can carry a high mortality risk. BD can be a diagnostic conundrum with its broad array of clinical presentations.
Objectives: Identifying vasculo-Behçet's disease and its management.
Methods: A 25-year-old man born in Malaysia and known for cirrhosis due to idiopathic Budd Chiari syndrome presented to the emergency room with a transient ischemic attack. An inferior vena cava (IVC) occlusive thrombus and a patent foramen ovale (PFO) were discovered. Thrombolysis, angioplasty, PFO closure, and a transjugular intrahepatic portosystemic shunt (TIPS) procedure were performed. The following year, the patient experienced numerous IVC and TIPS-associated thromboses as well as a right atrial thrombus attached to his PFO closure device, all of which were refractory to anticoagulation. A few months later, the patient suffered from an acute right anterior cerebral artery stroke, with no etiology uncovered at the time. It was later determined that the patient had experienced years of recurrent oral and genital aphthae, thereby prompting a strong clinical suspicion of BD. Six months later, after only one appointment at the rheumatology clinic during which he was prescribed colchicine, the patient presented to the hospital with hemoptysis. A computed tomography (CT) pulmonary angiogram revealed a right lower lobar pulmonary arterial aneurysm with a peripheral thrombus, a right bronchial artery dilatation, and pulmonary emboli. The patient declined anticoagulation and was sent home. Two months later, he returned to the hospital, this time with hematemesis. A repeat CT pulmonary angiogram was performed and showed an increasing pulmonary emboli burden and an enlarging aneurysm. A thrombophilia workup was negative.
Results: A diagnosis of BD with pulmonary aneurysms was made and treatment was initiated with methylprednisolone pulses and monthly intravenous cyclophosphamide as recommended by the European League Against Rheumatism. A month later, there was radiological evidence of significant improvement in the burden of pulmonary emboli, an interval decrease in the aneurysm's diameter, and resolution of the right atrial thrombus.
Conclusion: *BD with vascular involvement or vasculo-Behçet's disease can affect small, medium, and large vessels of both the venous and arterial vasculatures and is thought to originate from vessel wall inflammation.* Thrombi in vasculo-Behçet's disease are typically quite adherent to the vessel walls and tend not to embolize. In this case, pulmonary arterial thrombosis burden was significantly decreased after immunosuppression alone, favoring a diagnosis of in situ thrombosis rather then thromboembolism. Moreover, pulmonary artery aneurysm, Budd-Chiari syndrome, and vena cava thrombosis, which are quite uncommon and carry the highest mortality risk in vasculo-Behçet's, were all present in this case. Early recognition can be life-saving as immunosuppression is the first-line therapy rather than anticoagulation, which carries a significant risk of pulmonary hemorrhage in the presence of a pulmonary artery aneurysm.

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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.6668

THU0600 A CASE OF SYSTEMIC SCLEROSIS COMPLICATED BY RENAL CRISIS: POTENTIAL ETIOPATHOGENETIC ROLE OF CYTOMEGALOVIRUS AND TREATMENT

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Background: Scleroderma renal crisis (SRC) is a rare complication of systemic sclerosis (SSc), which can be triggered by viruses, such as Cytomegalovirus (CMV). SRC presents as a new-onset accelerated-phase hypertension with/without rapidly progressive renal failure.
Objectives: Here we describe the case of a patient developing SSc complicated by the appearance of SRC after a recent episode of acute Cytomegalovirus infection.
Methods: A 66-year-old male was referred to our Scleroderma Unit in March 2019. He presented with widespread skin rash, exertional dyspnoea and peripheral oedemas. He reported a myocarditis due to CMV occurred in October 2018. Antibodies anti-CMV IgM were detected in his serum. The patient developed a progressive cutaneous involvement characterized by diffuse oedema, sclerosis and melanoderma. Subsequently, Raynaud's phenomenon, puffy hands and pitting scars occurred. Laboratory tests showed positive ANA in a titer of 1:640 in a nucleolar staining pattern. Additionally, persistence of anti-CMV IgM was found. Skin biopsy showed scleroderma-like finding. Nailfold capillaroscopy revealed a SSc pattern. Chest high resolution computed tomography displayed basal interstitial thickening and subpleuric ground-glass opacities. Therefore, the patient was diagnosed with SSc. Three weeks later he developed severe hypertension and a rapid, progressive renal impairment. Serum creatinine increased (up to 4.15 mg/dl), glomerular filtration rate impaired (25 ml/min). Renal biopsy (picture A, B) revealed acute thrombotic microangiopathy. A diagnosis of thrombotic thrombocytopenic purpura was excluded. The patient was diagnosed with SRC and we started therapy with ACE-inhibitor and loop diuretic. Even if the dosage of ACE-inhibitor was increased up to the maximum tolerate dose, his renal function did not improve and the blood pressure control was inadequate. Consequently, the patient underwent plasma exchange (PEx) sessions. Two weeks later there was an improvement of renal function and blood pressure normalized. Six months later the disease was controlled: glomerular filtration rate was 41 ml/min and blood pressure was within the normal range. The patient was treated with ACE-inhibitor and underwent fortnightly apheretic sessions. Treatment for scleroderma vasculopathy is ongoing.
Results: Viral infections may be responsible for SSc. A brief interval between an acute viral infection and the onset of SSc may suggest CMV as a possible trigger for the disease. Similarly, other infectious agents could be involved in the multistep and multifactorial mechanism of SSc. This case sheds light on the potential and intriguing role of CMV in SSc. Moreover, it leads us to hypothesize a CMV possible direct role in sclerodermal kidney damage. Use of ACE-inhibitor significantly reduced the mortality rate due to this complication. Exact therapeutic mechanism of PEx in the treatment of SSc is unclear.
Conclusion: In our case the integrated ACE-inhibitor-PEx approach has showed effectiveness and safety in the management of SRC.
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Disclosure of Interests: None declared
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THU0601 REFRACTORY ACUTE CORONARY SYNDROME AND CARDIOGENIC SHOCK AS ATYPICAL ONSET OF EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS

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Background: Eosinophilic Granulomatosis with Polyangiitis (EGPA) is an ANCA-associated vasculitis, characterized by eosinophilic infiltration in tissues, intravascular and extravascular granuloma formation. It is a rare disease, affecting between 0 and 4 per million population per year. The cardiac involvement occurs in 15-60% of EGPA patients (generally ANCA-negative); it is often insidious, underestimated and it has a poor prognosis. The disease usually shows a prodromal phase characterized by asthma and allergic manifestations.
Objectives: We report the case of a young patient with acute coronary syndrome (ACS) complicated by cardiogenic shock as the first manifestation of EGPA.
Methods: A 36 year old Indian male patient, with a previous history of asthma, rhinitis, Raynaud syndrome and allergy to ketoprofen, presented to the emergency department with a complaint of chest pain and dyspnea. Cardiac troponin was elevated and he was admitted to intensive care unit with a diagnosis of ACS. The patient conditions rapidly deteriorated due to acute cardiogenic shock and an urgent coronary angiogram was performed. An occlusion of the left main coronary artery was treated with angioplasty and two drug-eluting stents. Echocardiography showed severe left ventricular dysfunction requiring inotropic and intra-aortic balloon pump support. A mild dermatitis after salicylic acid administration resolved with intravenous hydrocortisone 1 g. The thrombophilia

screening was negative, as well as cardiovascular risk factors. Over the next days, the clinical conditions rapidly improved with recovery of normal ventricular function on discharge. However, two weeks later he was readmitted with recurrent mandibular and chest pain. Troponin levels were elevated and fluctuated, suggesting recurrent ischemic events. Repeated ECG during angina crisis showed ischemic alterations in different coronary territories. The coronary angiogram detected coronary vasospasm of the circumflex artery, reversible after nitroglycerin (Figure 1). Nitroglycerin and calcium channel blockers were initiated, but did not resolve the vasospastic angina crisis, occurring daily. Laboratory tests revealed eosinophilia (4390 cells/mcl), increased C reactive protein (9.4 mg/l) and positive antinuclear antibodies (1:320). The other serological and immunological tests were negative, including MPO-ANCA and PR3-ANCA. An abdomen and chest CT scan was negative.

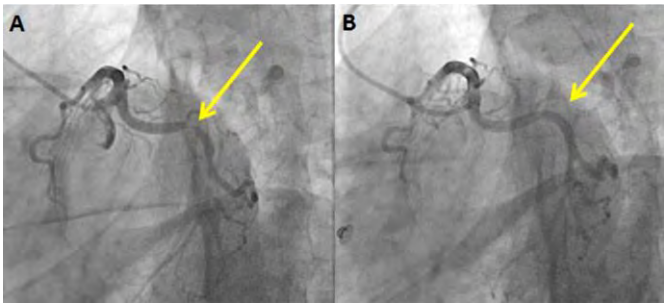


Figure 1. Coronary angiogram showing coronary vasospasm in the left circumflex artery (panel A, yellow arrow), reversible after nytroglicerin infusion (panel B, yellow arrow)

Results: The eosinophilia and the history of asthma rose the suspect of EGPA vasculitis. The patient was treated with intravenous methylprednisolone 250 mg once daily for 3 days, followed by oral prednisone 1 mg/kg/day, with rapid and complete resolution of the recurrent angina episodes. Intravenous cyclophosphamide 10 mg/kg was administered every 2 weeks for 2 times, then 12 mg/kg every 4 weeks. Oral corticosteroid was tapered, with the persistence of a complete remission of the symptoms, after 2 months of immunosuppressive therapy.

Conclusion: Coronary involvement in EGPA can mimic atherosclerotic artery disease and can be life threatening, if not promptly recognized. An accurate medical history and complete serological and immunological tests are crucial to detect an atypical onset of EGPA, prompting early immunosuppressive therapy which is pivotal for the patient survival.

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THU0602 EXTENDED BONE HYDATIDOSIS IN THE HIP AND FEMUR WITH EXTENSION TO THE SOFT PARTS: A CASE REPORT

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Background: Osseous hydatid cyst is an uncommon disease with weak response to treatment.hydatid disease should be included in the differential diagnosis of cystic lesions of bone in endemic regions. Bone cysts account for only 0.5 to 2.5% of all hydatid cysts in humans.

Objectives: To report a case of osseous hydatid disease extended on hip and femur

Methods: We report a case of osseous hydatid disease

Results: A 49 YEAR OLD BRICKLAYER, with no past-medical history and no animal contact, was admitted to our department for a left hip pain. the patient was apyretic and in a good general health condition. He had a very painful walk. the mobilility of the left hip joint was very painful and restricted.

The pelvis X-rays showed osteolytic lesions in the ischiopubic branch and in the left femur and proximal extremity of the tibia.

The C-Reactive protein value, the protein electrophoresis were normal. tumor markers test was negative.

An ultrasound of the hip showed a low abondance intra-articular effusion. The Pelvic MRI showed multilocular appearance extending over the bone and muscle with breach of the bone cortex of the femur very suggesting of the diagnosis of a bony and muscular echinococcosis.

NO other localization of hydatidosis were detected, body ct scan was normal

Conclusion: Hydatid disease occurs worldwide and mainly associated with sheep farming. The liver and lungs are the most common locations. Bone cysts are uncommon but severe. Although immunofluorescent assays are useful, the final diagnosis depends on histology. The treatment is almost surgery. Recurrence is common

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THU0603 IGG4-RELATED SINGLE-ORGAN DISEASE: IMMUNOSUPPRESSION NEEDED AFTER COMPLETE RESECTION? A CASE REPORT AN BRIEF LITERATURE REVIEW.

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Background: IgG4-related disease (IgG4-RD) is a polymorphic autoimmune disease leading to tumourous swelling and/or fibrosis of affected organs. Riedel's thyroiditis is – besides chronic periaortitis, Mikulicz Syndrome and many others – an organ manifestation of IgG4-RD that has been thought to be an independent disease for a long time. About 40% of patients have single organ IgG4-RD while the others suffer from multisystemic disease [1].

Objectives: Glucocorticoids, sometimes combined with other immunosuppressives are the standard treatment of IgG4-RD, in some situations (e.g. mechanical complications or suspected malignancy) surgery may be necessary but little is known about the management of fully resected single-organ IgG4-RD [1].

Methods: We report a case of single-organ IgG4-RD (Riedel's thyroiditis) after complete resection and perform a brief review of the literature to guide clinical management in this situation.

Results: A woman (51 y) with pre-existing Hashimoto's thyroiditis (thyroid peroxidase antibody positive) developed a rapidly growing struma with very firm consistency (not allowing fine needle biopsy). Besides slightly increased C-reactive protein (5,3 mg/l) there was no laboratory sign suggestive for IgG4-RD (normal serum IgG4, complement, eosinophils and IgE). Within 4 months the patient suffered from hoarseness and progredient dyspnea. Surgical thyroidectomy was performed and histopathology revealed IgG4-related Riedel's thyroiditis with extensive (storiform) fibrosis, a dense lymphoplasmacytic infiltrate, obliterative phlebitis, eosinophilia and 13 IgG4-positive plasma cells per high power field.

After referral to our department a comprehensive work-up showed no signs of other manifestations of IgG4-RD. Treatment with glucocorticoids is clearly recommended for patients with symptomatic IgG4-RD in an international consensus statement, whereas "watchful waiting" may be appropriate in some cases of asymptomatic or mild disease. While some highly fibrotic lesions may not respond well to glucocorticoids and may require surgical intervention, no clear guidance is available for the management of fully resected single organ IgG4-RD [2].

A brief review of the literature revealed that few cases of single-organ IgG4-RD remaining in remission after resection without medical treatment have been reported e.g. IgG4-related cholecystitis, autoimmune-pancreatitis, tumours of the intestinal tract, lung, thymus, meninges, paravertebral space and others [3–9].

After discussion of the options with the patient no systemic immunosuppression was given under close follow up without signs of relapse in clinical examinations, laboratory or imaging during the first 6 months.

Conclusion: Limited evidence from case reports suggests that a "watchful waiting" strategy without systemic immunosuppressive treatment may be reasonable in some cases of single-organ IgG4-RD after the affected organ was completely resected (e.g. due to mechanical complications or suspected malignoma). However, close follow-up monitoring should be applied due to the risk of relapse or development of new organ manifestations.

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Disclosure of Interests: Jan Schirmer: None declared, Marcus Seeger: None declared, Dominik Schulte Paid instructor for: Ferring, Speakers bureau: Amgen, Astra Zeneca, Braun, Fresenius, Ipsen, Johnson & Johnson, Lilly, MSD, Novartis, Novo Nordisk, Sanofi, Matthias Laudes Speakers bureau: Roche, Sanofi, Chugai, Stefan Schreiber Consultant of: AbbVie, Arena, BMS, Biogen, Celltrion, Celgene, IMAB, Gilead, MSD, Mylan, Pfizer, Fresenius, Janssen, Takeda, Theravance, provention Bio, Protagonist and Falk, Bimba F. Hoyer: None declared

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THU0604 UNDIAGNOSED RHEUMATIC DISEASE IN NEWLY PRESENTING MGUS PATIENT

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Background: Monoclonal gammopathy of undetermined significance (MGUS) is considered to be a premalignant condition with on average of 1% annual risk of progression to multiple myeloma or other lymphoproliferative disorders [1]. Numerous studies have highlighted a common feature of autoimmune inflammatory diseases is non-specific hypergammaglobulinaemia which can be associated with monoclonal gammopathy [2, 3]. We looked at a population of 3.6 million where patients with MGUS was referred to haematology network for evaluation.

Objectives: Our hypothesis was that undiagnosed rheumatic diseases were being referred to haematology rather than rheumatology erroneously.

Methods: The Haematological Malignancy Research Network (HMRN) ethics approval (REC 04/01/1205/69) from Leeds West Research Ethics Committee. The HMRN that comprises a population-based cohort of patients newly diagnosed by a single integrated haemato-pathology laboratory in two adjacent UK Cancer Networks (population 3.6 million). The database includes prognostic factors, sequential treatment/response history and socio-demographic details which are recorded to clinical trial standards. 255 patients were screened in this study. We looked at a range of autoimmune/innate immune conditions diagnosed after MGUS.

Results: In the 255 patients cohort group, the average age at the diagnosis of MGUS was 70.23 ± 11.95 years (median 70.2 years), with more subjects being male (n=145, 56.9%). Mean duration of follow up was 2570 days. 10 out of the 255 patients progressed onto multiple myeloma.

Diagnosed rheumatic disease was found in 48 patients (18.8%). None of the patient in this group has disease progression to multiple myeloma. In this group, 37 patients (14.5%) presented the rheumatic disease before their MGUS diagnosis and 11 (4.3%) were diagnosed after their MGUS referral. Interestingly, among the 11, more males(n=8, 72.7%) have their rheumatic disease diagnosed after MGUS.

Those 11 cases included crohn's disease (1), polymyalgia rheumatica (2), immune thrombocytopenia (2), autoimmune hepatitis (2), Schnitzler's syndrome (1), giant cell arteritis (1), rheumatoid arthritis (2).

Conclusion: Approaching 1 in 20 cases of MGUS have an underlying inflammatory disease that may often be non-specifically driving antibody production including monoclonal band formation. When diagnosing MGUS, clinicians should be aware of the potential underlying autoimmune rheumatic conditions.

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THU0605 AN ATYPICAL CASE OF PONCET DISEASE

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Background: Poncet disease (PD) is defined as an inflammatory rheumatism associated with visceral tuberculosis without direct bacteriological involvement of the joints [1]. It is classified as a parainfectious rather than a reactive arthritis [2].

Objectives: Here by a first case of PD who presented with sterile arthritis and tuberculous spondylodiscitis.

Methods: We report a case of a 40-year-old women who presented with polyarthritis in 2014. On physical examination, she had synovitis in both wrists, the metacarpophalangeal joints and the fifth proximal interphalangeal joint of the right hand. Her serum was negative for Rheumatoid Factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) antibody. Her C-reactive protein (CRP) was 24,5mg/l. Ultrasound revealed tenosynovitis of the superficial and deep flexor tendons on both hands with Doppler signal. The Magnetic resonance imaging (MRI) of the hands showed active synovitis in the wrists mainly in the distal radioulnar joint, erosions in the ulnar styloid as well as edematous infiltration of the soft tissue of the hands. Since she fulfilled the new ACR/EULAR 2010 criteria for RA, a diagnosis of rheumatoid arthritis (RA) was made and the patient was put on Methotrexate (MTX) 15 mg/week/po in January 2015. Eight months later, the patient developed high temperature 38°c and lumbar stiffness. A chest CT performed as part of the etiologic investigation didn't show pulmonary manifestations but revealed a lytic vertebrae lesion. Lumbar spine MRI showed prevertebral edema and soft tissue enhancement with abnormal marrow signal in L2 and L3 which was concerning for infectious etiology. MTX was stopped. A CT-guided core needle biopsy concluded to a tuberculous spondylodiscitis. The patient was initiated on an antituberculous-therapy (ATT) for 15 months. The course was marked by the reoccurrence of low back pain. MRI of the spine was then performed and revealed persistence of spondylodiscitis and multiple abscesses at the levels of L2-L3. The ATT was resumed.

Results: The patient received four drugs for 4 months, followed by isoniazid and rifampicin for 1 year. At follow up, the patient responded well to treatment with complete resolution of symptoms without sequelae. She did not present neither polyarthritis nor synovitis. Moreover, she sustained a negative CRP (2mg/dl). Ultrasound control of the wrists did not show synovitis or tenosynovitis Doppler signal. Similarly, a disappearance of effusion as well as synovitis was noted on the MRI at follow up.

Conclusion: We report a unique case of Poncet disease with tubercular spondylodiscitis. It is important to recognize PD in a patient presenting with polyarthritis in order to avoid unnecessary long-term disease-modifying antirheumatic treatment. Future research is indicated to understand the etiopathogenesis of Poncet's disease and to educate clinicians as to the importance of maintaining a high index of suspicion about this rare, yet potentially easily treatable disease.

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THU0606 RHEUMATOID ARTHRITIS INDUCED BY ALPHA-INTERFERON THERAPY: A RARE CASE PRESENTATION

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Background: Interferon-α (IFN-α) is known for its antiviral and antiproliferative effects, used mainly for the treatment of chronic hepatitis C infection [1]. Immunomodulatory effects have been reported in patients treated with IFN-α, including hematological, immunological, rheumatological and dermatological disorders [2]. In fact, IFN-α may lead to the induction or exacerbation of autoimmune diseases such as psoriasis, systemic lupus erythematosus, and rarely rheumatoid arthritis (RA).

Objectives: We report the case of a Caucasian who developed anticyclic citrullinated peptide antibody (anti-CCP)-positive RA following treatment of chronic hepatitis C infection with pegylated IFN-α2a.

Methods: A 57-year-old women was diagnosed of chronic hepatitis C infection after detection of abnormal liver function. She has a genotype Ib with a high viral load: RNA was 100,000 UI/ml. Liver histology showed advanced fibrosis and portal fibrosis (A3 F4 according to metavir score). A history of blood transfusion was found. The patient was placed on a 24-week course of PEGylated -IFN-α2a 180 µg weekly and a 1000 mg daily dose of ribavirin. After

two months of antiviral treatment, she developed symmetrical polyarthritis, with pain and edema in the wrists, elbows, shoulders and metacarpophalangeal joints, associated with prolonged morning stiffness. The musculoskeletal examination was notable for active synovitis of the proximal phalangeal joints, metacarpophalangeal joints, wrists, elbows. Distal interphalangeal joints were spared. She had no musculoskeletal symptoms prior to antiviral therapy. Review of systems was otherwise unremarkable. X-ray showed no remarkable findings. Ultrasonography of the hands revealed diffuse synovitis as well as tenosynovitis of the ulnar extensor tendons in both wrists. Laboratory results revealed a normal C-reactive protein, elevated liver enzymes: ALAT (alanin-aminotransferase) 119,ASAT (aspartat-aminotransferase) 66, Gamma-GT 203 and undetectable cryoglobulins. Anti-CCP was 21 IU/ml (negative < 20 IU/ml), antinuclear antibodies were positive 1280 (negative<160), rheumatoid factor was 192 (normal < 30 IU/ml).

A diagnosis of rheumatoid arthritis (RA) was made on the basis of clinical and ultra-sonographic evidence as well as Rheumatoid Factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) antibody positivity. Moreover, an autoimmune thyroiditis was found that evolved into hypothyroidism treated with thyroxine.

Results: The patient developed a sustained virological response as evidenced by persistent undetectable HCV RNA and normal aminotransferase activities. Upon completion of a 12-week course of antiviral therapy, The rheumatoid syndrome disappeared after cessation of IFN therapy. By that time, antinuclear antibodies were in a titre of 1 /180, rheumatoid factor and Anti-CCP were negative.

Conclusion: The present case suggests that biological agents, affecting the cytokine network, may work as triggering factors for the development of RA in previously predisposed individuals. Screening for RF and anti-CCP may be considered before treating with IFN. In addition, a close surveillance for the occurrence of autoimmune phenomena during and after treatment should be worthy, for early diagnosis and adequate clinical management.

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THURSDAY, 04 JUNE 2020

HPR Measuring health (development and measurement properties of PROs, tests, devices)

THU0607-HPR COMPARISON OF THE PATIENT REPORTED PHYSICAL ACTIVITY LEVEL ACCORDING TO KINESIOPHOBIA PRESENCE IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: Many factors such as poor functional or emotional status might play a role in participating physical activity for people with rheumatic diseases. There is a lack for evidence regarding to the effect of kinesiophobia presence on the physical activity levels of axSpA patients.

Objectives: The primary objective was to compare the patient reported physical activity levels in axSpA patients with kinesiophobia and those without. Evaluating disease related and physical characteristics, quality of life and emotional status according to presence of kinesiophobia were also aimed.

Methods: One-hundred forty-eight consecutive axSpA patient were allocated to Kinesiophobia+ group (n: 90, 66% males) or Kinesiophobia- group (n: 58, 64% males). The presence of kinesiophobia was defined as having a score of >37 in Tampa Scale for Kinesiophobia. All patients were evaluated regarding to physical characteristics (age, body-mass index), functional status (Bath Ankylosing Spondylitis Functional Index), disease activity (Bath Ankylosing Spondylitis Disease Activity Index), spinal mobility (Bath Ankylosing Spondylitis Metrology Index), patient reported physical activity (International Physical Activity Questionnaire Short Form), emotional status (Hospital Anxiety and Depression Scale), and quality of life (Assessment of SpondyloArthritis International Society Health Index).

Results: Physical characteristics and spinal mobility were similar in patients with and without kinesiophobia (p>0.05, Table). Disease activity, function, quality of life, depression and anxiety scores were poorer in Kinesiophobia+ group compared to Kinesiophobia- group (p<0.05, Table). Patient reported physical activity level was found to be lower in patients with kinesiophobia (p<0.05, Table).

Table. Comparison of groups according to kinesiophobia presence

	Kinesiophobia+ Group (n: 90) Median (IQR 25/75)	Kinesiophobia- Group (n: 58) Median (IQR 25/75)	p*
Physical Characteristics			
Age (years)	41.0 (37.0/52.0)	44.0 (36.0/53.0)	0.850
Body-Mass Index (kg/m^2)	26.8 (24.6/30.1)	26.0 (22.7/29.0)	0.364
Disease Related Characteristics			
BASDAI (score)	2.7 (1.3/4.6)	1.8 (0.6/3.5)	**0.036**
BASMI (score)	3.3 (1.9/5.0)	2.7 (1.6/3.5)	0.114
BASFI (score)	2.5 (1.2/4.4)	1.2 (0.5/2.7)	**0.003**
Patient Reported Physical Activity Level			
IPAQ (MET/week)	505.5 (169.0/1653.0)	858.0 (330.0/2772.0)	**0.042**
Quality of Life			
ASAS-HI (score)	7.0 (5.0/9.1)	4.0 (2.0/7.9)	**0.001**
Emotional Status			
HAD Anxiety (score)	7.0 (4.0/9.0)	5.0 (3.0/8.0)	**0.006**
HAD Depression (score)	7.0 (4.0/10.0)	3.0 (1.0/7.0)	**0.001**
Fear of Movement			
TAMPA (score)	41.0 (39.0/44.0)	34.0 (31.0/36.0)	**p<0.001**

*Mann-Whitney U Test, IQR 25/75: Interquartile range 25/75, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, BASMI: Bath Ankylosing Spondylitis Metrology Index, BASFI: Bath Ankylosing Spondylitis Functional Index, IPAQ: International Physical Activity Questionnaire Short Form, HAD: Hospital Anxiety and Depression Scale, ASAS-HI: Assessment of SpondyloArthritis International Society Health Index, TAMPA: The Tampa Scale for Kinesiophobia, p<0.05.

Conclusion: It seems that the presence of kinesiophobia may have a negative impact on patient reported physical activity level, and disease related parameters. However, it is also possible that kinesiophobia might occur as result of poor disease activity or disability. Strategies such as patient education should be included in axSpA management for preventing kinesiophobia development or improving kinesiophobia related consequences.

Disclosure of Interests: None declared

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THU0608-HPR VALIDITY OF SIX MINUTE STEPPER TEST IN EVALUATION OF FUNCTIONAL EXERCISE CAPACITY IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: In most patients with ankylosing spondylitis (AS), exercise capacity decreases due to pulmonary dysfunction, chest wall restriction and peripheral muscle weakness. The six-minute walk test (6MWT) is a validated simple field, hence frequently used to evaluate exercise capacity. However, 6MWT has some limitations, especially the fact that it requires a corridor of at least 30 meters long to perform this test which can limit its use in some centers. Shorter corridors force patients to turn more frequently, slowing down the pace of walking that reduces potential walking distance. To overcome technical and spatial limitations, 6-minute stepper test (6MST) has been proposed to evaluate exercise capacity. In the literature 6MST has been suggested for a variety of diseases. Since, it requires only a limited amount of space and equipment and is feasible, easy to perform, well tolerated.

Objectives: In the literature, there is no study in which 6MST is used to evaluate exercise capacities of patients with AS. Therefore, the aim of this study was to evaluate validity of 6MST in AS population in comparison to 6MWT.

Methods: 6MWT and 6MST were performed in 51 patients with AS (52.26±13.33 years, 30F/21M). Demographic and clinical characteristics were recorded. Functional exercise capacity was evaluated using 6MWT and 6MST. The total distance of 6MWT was compared to the total number of steps of 6MST. Before, during and after 6MWT and 6MST, heart rate (HR), oxygen saturation (SpO_2), breathing frequency (BF), blood pressure (BP), dyspnea and fatigue were assessed using modified Borg scale.

Results: The number of steps on the 6MST was significantly correlated with the distance of the 6MWT (r=0.61, p<0.0001). Dyspnea (p=0.04) and leg fatigue (p<0.0001) was significantly higher in 6MST than in 6MWT. HR, SpO_2, BF, BP and fatigue were similar in both 6MST and 6MWT.

Conclusion: The 6MST is a valid test to evaluate exercise capacity in patients with AS. It is also an appropriate alternative to the 6MWT for determining exercise capacity when the 6MWT is not feasible due to technical restrictions. The 6MST can be proposed as a new exercise capacity evaluation tool in AS, as it is valid, reliable, portable and inexpensive.

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THU0609-HPR RESPONSIVENESS OF THE DISABILITIES OF THE ARM, SHOULDER AND HAND (DASH) AND THE UPPER EXTREMITY FUNCTIONAL INDEX (UEFI) IN PATIENTS WITH POSTTRAUMATIC ELBOW STIFFNESS

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Background: There are many patient-rated outcome measures to assess the subjective component of function in musculoskeletal disorders of elbow. The first step of functional assessment is to select the instrument, which is sufficiently responsive. Although the disabilities of the arm, shoulder and hand (DASH) and the upper extremity functional index (UEFI) are widely used in reporting outcomes in upper extremity function, the responsiveness of these two scales has not been investigated in elbow disorders.

Objectives: This study aimed to compare and report the responsiveness of the DASH and the UEFI in patients with posttraumatic elbow stiffness.

Methods: Fifty-seven patients with posttraumatic elbow stiffness (32 women; mean age, 44.54 ± 6.51 years) were included. All patients completed the DASH and UEFI at baseline and after a six-week intervention, which was a structured exercise program. Patients who improved (much improved and slightly improved) and those who unimproved were defined using a 5-point global rating chance scale (GROC). Responsiveness was assessed using effect size and standardized response mean (SRM). ES has observed the mean change scores divided by the standard deviation of the initial score. SRM was calculated for the improved group and the unimproved group, dividing the mean change scores by the standard deviation of mean change scores. Similar to effect size, SRM values and ES values of 0.20, 0.50 and 0.80 were considered small, moderate or large, respectively.

Results: Forty-eight patients (84.21%) were classified improved and 9 patients (15.79%) were classified unimproved according to the GROC. Effect sizes and SRMs were large (greater than 1.00) for participants who were “much improved” or “slightly improved” on the GROC for both the DASH and UEFI. For groups of participants who improved on the GROC, effect sizes and SRMS were ranged from 1.87 to 2.09 and 2.13 to 2.56 for the DASH, and 1.59 to 2.16 and 1.65 to 2.29 for the UEFI, respectively (Table 1).

Table 1. Mean baseline scores, change scores, effect size and standardized response mean for improved and unimproved patients

Global Rating of Change	Improved (n=48)		Unimproved (n=9)
	Much Improved (n=27)	Slightly Improved (n=21)	No Change (n=9)
	Mean (SD)	Mean (SD)	Mean (SD)
The disabilities of the arm, shoulder and hand			
Baseline	43.41 (14.22)	42.66 (13.41)	44.21 (7.24)
After 6-week	13.65 (11.60)	17.51 (8.91)	39.72 (6.81)
Change	-29.75 (11.61)	-25.14 (11.77)	-4.48 (3.26)
ES	2.09	1.87	0.61
SRM	2.56	2.13	1.37
The upper extremity functional index			
Baseline	42.00 (10.15)	42.76 (15.75)	39.75 (9.85)
After 6-week	64.00 (10.53)	67.47 (11.47)	47.00 (5.39)
Change	22.00 (9.60)	24.71 (14.96)	7.25 (6.47)
ES	2.16	1.56	0.73
SRM	2.29	1.65	1.12

Abbreviations: ES, Effect Size; SD, Standard Deviation; SRM, Standardised Response Mean.

Conclusion: These findings showed that for patients receiving physiotherapy for the management of elbow stiffness, both the DASH and the UEFI are similarly responsive to change in symptoms and disability and similarly able to discriminate between patients who improved or unimproved.

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THU0610-HPR PREDICTION EQUATION FOR MUSCLE MASS OVERESTIMATES MUSCLE MASS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid Arthritis (RA) is a chronic, progressive, inflammatory autoimmune disease characterized by systemic manifestations. Often is observed in RA patients changes in body composition, such as reduced muscle mass (sarcopenia) with stable or increased fat mass (FM) [1]. Total-body skeletal muscle mass (SMM), specifically appendicular skeletal muscle, is a key diagnostic feature for the assessment of geriatric syndromes associated with skeletal muscle wasting, such as sarcopenia [2]. Estimation of SMM can be accomplished by a variety of methods, but the majority that considered the gold standard for this purpose are high cost. Due high cost, this methods are unfeasible in population studies and increases the difficulty of use in different clinical contexts. Predictive equations have been developed for estimation of whole-body skeletal muscle mass on the basis of anthropometric data, which can be collected in a more affordable manner, in an attempt to make SMM calculation easier and enable its use in epidemiological research and in clinical settings [3]. However, these equations were not developed for RA populations.

Objectives: To compare the anthropometric equation that estimate SMM with body composition measurements derived from DXA in RA patients.

Methods: Ninety patients diagnosed with RA according to ACR/EULAR criteria were recruited. Body composition was assessed by total body dual-energy x-ray absorptiometry (DXA) for measurement of appendicular lean mass index (ALMI, kg/m2). The prediction equation for muscle mass proposed by Lee et al (variables included: body weight, height, age, sex and race) was used to generate estimates of SMM, stratified by BMI. Frequency analysis, independent student’s t test and intraclass correlation coefficients (ICC) were performed. Statistical significance was considered as $p<0.05$

Results: Of the 90 patients analyzed, most were women (86.7%; 78/91), with mean age of 56.5±7.3 and median disease duration time of 8.5 (3-18) years. The mean of BMI was 27.39±5.14. Thirty (33.3%) RA patients had normal weight, forty patients (44.4%) were overweight and twenty patients (22.2%) were obese. In normal weight patients, just like overweight and obese patients, the estimates of SMM obtained by Lee equation were higher than those obtained by DXA measurements(Obese: Lee 10.66±1.19 vs DXA 7.10±0.73; Overweight: Lee 8.63±0.99 vs DXA 6.57±0.82; Normal weight: Lee 7.14±0.85vs DXA 6.03±0.71; $p<0.05$). The Lee equation estimates showed ICC of 0.78 (0.66 - 0.85) with DXA measurements. When stratified by BMI, Lee equation showed ICC of 0.87 (0.72 - 0.94) for normal weight, 0.83 (0.68 - 0.91) for overweight and 0.77 (0.42 - 0.90) for obese with DXA.

Conclusion: The muscle mass index by Lee equation overestimates the muscle mass in overweight or obese RA patients compared to DXA. Thus, sarcopenic RA patients may be wrongly classified as normal by the equation. This is probably related to the obese cachexia that these patients often present. More studies are necessary to analysis to better prediction equations for muscle mass in RA patients.

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THU0611-HPR MEASUREMENT OF MINIMAL DISEASE ACTIVITY IN PSORIATIC ARTHRITIS USING PROMIS-PHYSICAL FUNCTION OR THE HEALTH ASSESSMENT QUESTIONNAIRE-DISABILITY INDEX

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Background: Minimal disease activity (MDA) is a treat-to-target strategy (T2T) objective in psoriatic arthritis (PsA). MDA criteria, include physical function, traditionally assessed via the Health-Assessment Questionnaire Disability Index (HAQ-DI). It is of interest to assess the performance of more current physical function instruments such as the Patient-Reported Outcomes Measurement Information System-Physical Function Profile (PROMIS-PF).
Objectives: To assess the interchangeability of the HAQ-DI with the PROMIS-PF in the calculation of MDA in PsA.
Methods: Longitudinal PsA data were collected including HAQ-DI and PROMIS-PF in a PsA cohort. MDA definitions were built substituting the HAQ-DI criterion with the PROMIS-PF short form 4a (PROMIS-PF4a) or with the PROMIS-PF computer adaptive test (PROMIS-PF Bank). We assessed agreement/accuracy between HAQ-DI based and PROMIS-PF based MDA definitions at each visit and longitudinally through the kappa statistic/ROC curve analysis.
Results: One hundred participants contributed 352 observations with up to five visits. Mean (SD) age was 52 (12) years, 60% were female, and 43% were in MDA at baseline. Kappa statistic for PROMIS-PF based MDA reflected almost perfect agreement with HAQ-DI MDA: kappa=0.94 (95% CI 0.90-0.97) for MDA PROMIS-PF Bank, and kappa=0.90 (95% CI 0.80-0.95) for MDA PROMIS-PF4a. Higher longitudinal agreement was seen between MDA HAQ-DI and MDA PROMIS-PF Bank versus MDA PROMIS-PF4a between consecutive visits: kappa ranged between 0.81-0.94 versus 0.72-0.84, respectively (Table 1). Area under ROC curve for predicting MDA HAQ-DI was 0.97 for MDA PROMIS-PF Bank and 0.95 for MDA PROMIS-PF4a (Figure 1).

Table 1. Agreement between HAQ-DI based MDA and PROMIS-PF based MDA definitions at each visit and longitudinally

Agreement		Visit 1	Visit 2	Visit 3	Visit 4
MDA HAQ-DI and	Kappa	0.91	0.93	0.92	0.83
MDA PROMIS-PF4a	95% CI	(0.80-0.98)	(0.82-1.00)	(0.80-1.00)	(0.66-0.96)
	N	86	81	72	58
MDA HAQ-DI and	Kappa	0.91	0.98	0.94	0.93
MDA PROMIS-PF4a	95% CI	(0.81-0.98)	(0.90-1.00)	(0.84-1.00)	(0.82-1.00)
	N	86	82	73	58
Longitudinal agreement		Visit 1 to visit 2	Visit 2 to visit 3	Visit 3 to visit 4	N/A
MDA HAQ-DI state change with	Kappa	0.75	0.84	0.72	N/A
MDA PROMIS-PF4a state change	95% CI	(0.47-0.95)	(0.58-1.00)	(0.37-0.94)	
	N	71	67	51	
MDA HAQ-DI state change with MDA	Kappa	0.81	0.94	0.84	N/A
PROMIS-PF Bank state change	95% CI	(0.49-1.00)	(0.75-1.00)	(0.48-1.00)	
	N	72	68	52	

*Bias corrected 95% CI were calculated using bootstrapping with 2000 repetitions of individual patients.
^MDA state changes are defined as transitions in the respective MDA state between designated consecutive visits.
Abbreviations: CI confidence interval; N number of observations; HAQ-DI Heath Assessment Questionnaire-Disability Index; PROMIS-PF4a Patient Reported Outcomes Measurement Information System Physical Function form 4a; PROMIS-PF Bank Patient Reported Outcomes Measurement Information System Physical Function Bank administered as a computer adaptive test; MDA HAQ-DI Minimal disease activity includes the HAQ-DI ≤0.5 criterion; MDA PROMIS-PF4a includes the PROMIS-PF4a ≥41.3 criterion; MDA PROMIS-PF Bank includes the PROMIS-PF CAT ≥41.3 criterion.

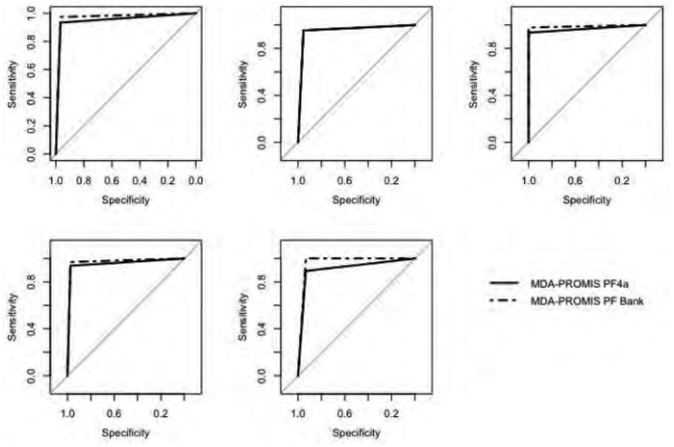


Figure 1. Areas under receiver operative characteristic curve to predict HAQ-DI based MDA using MDA PROMIS-PF4a or MDA PROMIS-PF Bank at each visit and overall using all observations (from left to right: visit 1, 2, 3, 4, and overall across visits)

Conclusion: Excellent agreement was seen between HAQ-DI and PROMIS-based MDA definitions statically and longitudinally. The PROMIS-PF Bank and PROMIS-PF4a are accurate replacements for the HAQ-DI in calculating MDA state in PsA.
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THU0612-HPR DOES PAIN AND COMORBIDITY BURDEN PREDICT FRAILTY IN PATIENTS WITH KNEE-OSTEOARTHRITIS? FINDINGS FROM THE RESEARCH ON OSTEOARTHRITIS AGAINST FRAILTY (ROAF) STUDY.

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Background: Pain and comorbidity burden has been suggested to act as a stressor during aging, potentially accelerating declines in health and functioning in patients with osteoarthritis of the knee (KNEE-OA) (1,2).
Objectives: The aims of the present research were to assess *(i)* the prevalence of frailty and *(ii)* its potential associated factors in a cohort of adult patients with KNEE-OA.
Methods: Patients fulfilling the clinical American College of Rheumatology knee-OA criteria were assessed according to the Survey of Health, Ageing and Retirement in Europe Frailty Instrument (SHARE-FI), and classified as frail, pre-frail, or non-frail. The clinical evaluation included the following items: Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain subscale (3) and Medical Outcomes Study Short Form-36 (SF-36). Evaluation of the comorbidities burden was performed with the modified Rheumatic Disease Comorbidity Index (mRDCI). Radiographic knee OA was defined according to Kellgren/Lawrence (KL) grades. Chi-square, analysis of variance (ANOVA), and multinomial logistic regression analyses were used to test the prognostic value of frailty for the outcomes of interest.

Table 1. Multinomial logistic regression analyses:c oefficients, standard errors and Wald statistic.

Variable	Coefficient	Std. Error	Wald	P
Age, yrs	-0.17872	0.065399	4.4682	0.0534
Gender	-0.087304	0.73366	0.01416	0.9053
BMI, Kg/m^2	-0.096320	0.081124	1.4097	0.2351
Pain duration from diagnosis, yrs	0.13065	0.069051	3.5801	0.0585
Educational level, yrs	0.066913	0.080301	0.6944	0.4047
Kellgren/Lawrence grades	0.62074	0.50629	1.5032	0.2202
mRDCI	-0.60277	0.18993	10.0714	0.0015
SF36-MCS	0.028143	0.020074	1.9655	0.1609
SF36-PCS	-0.00070260	0.025118	0.0007824	0.9777
WOMAC Pain subscale	-0.29129	0.081619	12.7373	0.0004
Constant	*17.42518*	*5.73269*	*9.2393*	*0.0024*

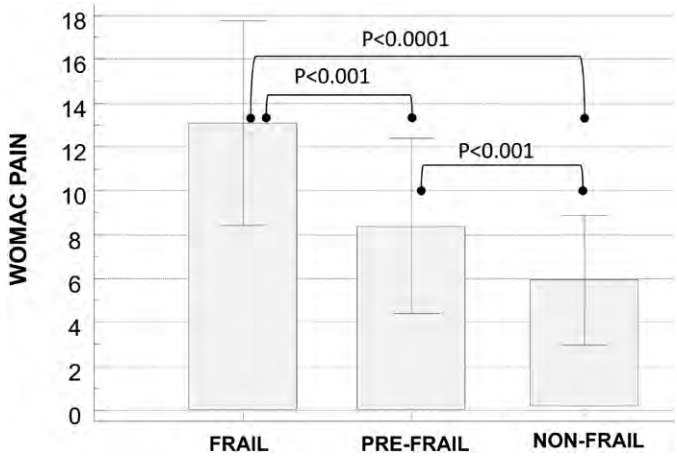


Figure 1. Distribution of the WOMAC-Pain scores according to the frailty categories by SHARE-FI, and p-values for comparison (ANOVA test)

Conclusion: Frailty or pre-frailty are common in KNEE-OA. The main factors associated with frailty were pain and comorbidity burden. Implementation of the frailty assessment into the routine rheumatological practice could represent a major advance in KNEE-OA care. Further studies are needed to identify the physiological mechanisms underpinning these associations.

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THU0613-HPR ADAPTATION AND VALIDATION OF THE MINI OSTEOARTHRITIS KNEE AND HIP QUALITY OF LIFE (MINI-OAKHQOL) QUESTIONNAIRE IN TURKISH POPULATION

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Background: The 20-item Mini-OAKHQOL was derived from the 40-item OAKHQOL questionnaire which was developed to assess the quality of life in subjects with osteoarthritis of the lower limbs. It has 5 subscales containing physical activities, mental health, pain, social support, social functioning; and two independent items addressing sex life and professional life (1). The Mini-OAKHQOL's good psychometric properties have recently been shown and validation studies have been done in several populations (1,2).

Objectives: We aimed to investigate the validity and reliability of the Turkish version of the Mini-OAKHQOL in patients with knee and hip osteoarthritis.

Methods: Patients diagnosed with knee or hip osteoarthritis clinically and radiologically were included in the study. Demographic data were noted. The French version of Mini-OAKHQOL was used for translation and adaptation. Translation-back translation methodology was applied and cross-cultural adaptation of the Mini-OAKHQOL into Turkish was done. Face and content validities were evaluated by cognitive information interviews with patients and expert committee. Internal consistency of the scale was made with Cronbach alpha coefficient. Convergent validity was evaluated by the correlations of Mini-OAKHQOL with Nothingam Health Profile (NHP), subscales of Short form 36 (SF-36), and VAS of the quality of life. The relations of the Mini-OAKHQOL with age, BMI, disease duration, VAS of the pain, WOMAC, and Lequesne Index were assessed for divergent validity. P <0.05 was considered significant.

Results: Seventy-three patients (63 female, 10 male) with the mean age of 57.22 (SD: 9.91) years were recruited. The main site of the symptomatic lower limb osteoarthritis was knee in 44, hip in 25, and both in 4 patients. The mean BMI was 31.69 (SD: 11.06) and the median disease duration was 36 months (IQR: 12–72). Turkish version of Mini- OAKHQOL had a good face and content validity. Cronbach's alpha coefficients of the subscales for internal consistency were 0.927, 0.841, 0.867, 0.771, and 0.677. Physical activities, mental health, pain dimensions of Mini-OAKHQOL had moderate to high correlations with Nottingham Health Profile and the physical functioning, physical role limitations, energy/fatigue, social functioning, pain, and general health subscales of SF-36 (rho between 0.484-0.748). The social function subscale of Mini-OAKHQOL had mild significant correlations with emotional well-being (rho: 0.239) and general health (rho: 0.315) subscales of SF36. The subscales of Mini-OAKHQOL had no correlation with disease duration, BMI, and age; and had generally moderate correlations with VAS-pain, Lequesne Index, and the WOMAC subscales. These data show good convergent and divergent validities of Mini-OAKHQOL.

Conclusion: The Turkish version of the Mini-OAKHQOL is a valid and reliable instrument to assess the quality of life in patients with knee/hip osteoarthritis. In addition, it is a simple, accurate, disease-specific, and not time-consuming self-report instrument.

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THU0614-HPR ASSESSING THE EFFECT OF INTERVENTIONS FOR AXIAL SPONDYLOARTHRITIS ACCORDING TO THE ENDORSED ASAS/OMERACT CORE OUTCOME SET: A META-RESEARCH STUDY OF TRIALS INCLUDED IN COCHRANE REVIEWS

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Background: The Assessment of SpondyloArthritis international Society (ASAS) has defined separate core sets for: i) symptom-modifying anti-rheumatic drugs (SM-ARD), ii) clinical record keeping, and iii) disease-controlling anti-rheumatic therapy (DC-ART). These all include the following domains: 'physical function', 'pain', 'spinal mobility', 'spinal stiffness' and 'patient global assessment' (PGA). The core set for clinical record keeping further includes the domains 'peripheral joints' and 'acute phase reactants', and the core set for DC-ART further includes the domains 'fatigue', 'spine/hip radiographs'.

Objectives: To assess the effect of interventions for each of the 9 axSpA core domains.

Methods: We investigated the efficacy across all interventions included in Cochrane reviews according to the core outcome set for axSpA, as reported in these eligible axSpA trials. We combined data using the standardized mean difference (SMD) to meta-analyze outcomes involving similar constructs. By meta-regression analysis, we examined the effect for each of the nine separate SMD measures on the primary endpoint across all trials.

Results: Among 85 articles screened, we included 43 trials with 63 randomized comparisons. Mean (SD) number of core outcomes domains measured for SM-ARD trials was 4.2 (1.7). 6 trials assessed all 5 proposed domains. Mean (SD) for number of core outcome domains for DC-ART trials was 5.8 (1.7). Unfortunately, no trials assessed all 9 domains. 8 trials were judged to have high risk of selective outcome reporting. The most responsible core domains for achieving success in meeting the primary objective per trial were pain; OR (95% CI) 5.19 (2.28, 11.77) and PGA; OR (95% CI) 1.87 (1.14, 3.07).

Conclusion: Overall outcome reporting was good for SM-ARD trials, and poor for DC-ART trials. None of the DC-ART trials assessed all 9 domains. Outcome-reporting bias and 'missing data' should be reduced by implementing the endorsed ASAS/OMERACT outcome domains in all clinical trials. Our findings suggest that PGA and pain likely provide a holistic assessment of disease beyond "objective measures" of spinal inflammation.

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Musculoskeletal Statistics Unit, The Parker Institute is grateful for the financial support received from public and private foundations, companies and private individuals over the years. The Parker Institute is supported by a core grant from the Oak Foundation; The Oak Foundation is a group of philanthropic organizations that, since its establishment in 1983, has given grants to not-for-profit organizations around the world.., Consultant of: Dr. Christensen reports non-financial support from Board membership, grants from Consultancy (AbbVie, Amgen, Axellus A/S, Biogen, Bristol-Myers Squibb, Cambridge Weight Plan, Celgene, Eli Lilly, Hospira, MSD, Norpharma, Novartis, Orkla Health, Pfizer, Roche, Sobi, Takeda), personal fees from Employment (Research Unit for Musculoskeletal Function and Physiotherapy, Institute of Sports Science and Clinical Biomechanics, University of Southern Denmark), non-financial support from Expert testimony, grants from Grants/grants pending (Axellus A/S, AbbVie, Cambridge Weight Plan, Janssen, MSD, Mundipharma, Novartis, and Roche), grants from Payment for lectures including service on speakers bureaus (Abbott, Amgen, Axellus, Bayer HealthCare Pharmaceuticals, Biogen Idec, Bristol-Myers Squibb, Cambridge Weight Plan, Ipsen, Janssen, Laboratoires Expanscience, MSD, Mundipharma, Norpharma, Novartis, Pfizer, Roche, Rottapharm-Madaus, Sobi, and Wyeth), grants from Payment for manuscript preparation (Axellus, Bristol-Myers Squibb, and Cambridge Weight Plan, Aleris-Hamlet (via Norpharma)), non-financial support from Patents (planned, pending or issued), non-financial support from Royalties, grants from Payment for development of educational presentations (Bristol-Myers Squibb, MSD, Pfizer), non-financial support from Stock/stock options, grants from Travel/accommodations/meeting expenses unrelated to activities listed (Abbott, AbbVie, Axellus, Biogen, Bristol-Myers Squibb, Cambridge Weight Plan, Celgene, Laboratoires Expanscience, Norpharma, Novartis, Pfizer, Roche, Rottapharm-Madaus, and Wyeth), non-financial support from Other (err on the side of full disclosure), outside the submitted work; and I am involved in many health-care initiatives and research that could benefit from wide uptake of this publication (including Cochrane, OMERACT, IDEOM, RADS, and the GRADE Working Group).

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THU0615-HPR FORCE-TIME CURVE ANALYSIS OF HANDGRIP STRENGTH IN PATIENTS WITH FIBROMYALGIA: COMPARISON WITH HEALTHY SUBJECTS

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Background: Factors associated with handgrip strength (HGs), in female with fibromyalgia (FM), use of force-time (FeT) curve to assess peak force, area under the curve (AUC), and variability of the time to reach maximum plateau of the curves (Fig.1) (1) to identify the impact of FM patients versus healthy controls have not been extensively studied.

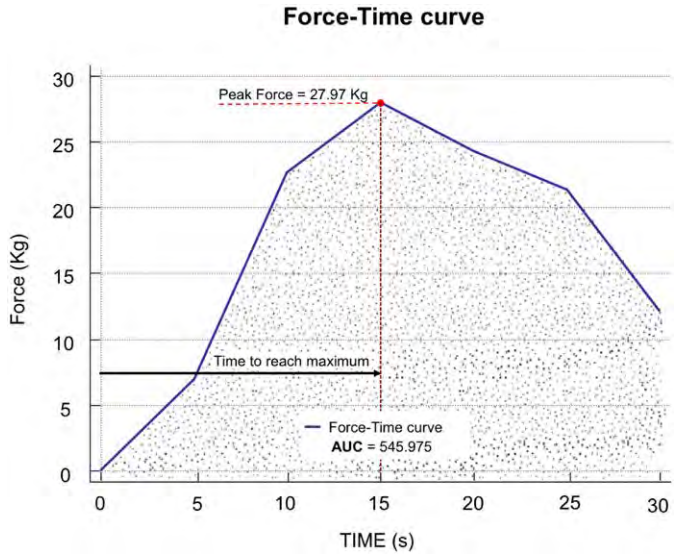


Figure 1. Force–time (FeT) curve showing the method of calculation of the various force attributes.

Objectives: The aim of the study was to compare the HGs of FM with healthy subjects and to evaluate the relationship between curve characteristics and FM disease severity (2,3).
Methods: One hundred and ten women (mean age 53.8±12.4 years; range 18 to 80) were included and compared with 111, age and BMI matched, female healthy controls. HGs was measured with an electronic device, while demographic and clinical characteristics of the subjects were obtained by the Revised version of the Fibromyalgia impact questionnaire (FIQR) and Fibromyalgia Activity Score (FAS). The patient opinion of their symptoms state (PASS) was evaluated as external criterion. The HGs threshold that best discriminates between the presence and absence of FM, as well as between moderate and severe FM, was determined using the receiver operating characteristic (ROC) curves analyses. Multivariate regression procedure was used in order to assess the relative contribution of the covariates on the HGs.
Results: HGs-AUC and peak force levels were lower in patients with FM than healthy women (median 342.7 vs 496.5; and in Kg median was 13.9 vs 19.9, respectively; both at significant level of p<0.001) and in women with severe FM compared with those with mild-moderate FM (p<0.0001). The time to reach maximum plateau of the curves was significantly higher in patients with FM than healthy women (15.5 vs 11.8 sec; p>0.001). ROC analyses revealed that the HGs peak force threshold that best discriminated between the presence and absence of FM was 14.2 kg (AUC 0.801; p<0.001), whereas the HGs peak force threshold that best discriminate between PASS was 16.3 kg (AUC 0.834; p<0.001). A negative correlation was found between FIQR and FAS scores and peak force, AUC in patients with FM (all at p< 0.001). Furthermore, a correlation was observed between widespread pain index (WPI) and peak force, AUC (both at p<0.0001), and of the time to reach maximum plateau of the curves (P=0.04) in patients with FM. Factors significantly associated with HGs-AUC in multivariate analysis were WPI and FIQR (both at p<0.001).
Conclusion: HGs is reduced in woman FM patients and is inversely related to FM severity and symptomatology. The FeT curve gave more information about grip in the FM and could be used as a complementary tool in the assessment and monitoring of FM. Further research on male FM patients is needed to confirm or contrast these findings.

Table 6. Correlations between HGs curve characteristics and questionnaires studied through the Spearman's rho correlation coefficients (rho).

	FIQR	FAS	HGs peak force levels	Time to reach maximum plateau of the curves	HGs-AUC
WPI	0.732 <0.0001	0.823 <0.0001	-0.612 <0.0001	-0.195 0.0415	-0.615 <0.0001
FIQR		0.761 <0.0001	-0.576 <0.0001	-0.054 0.5768	-0.592 <0.0001
FAS			-0.577 <0.0001	-0.167 0.0813	-0.588 <0.0001
HGs peak force levels				-0.151 0.0249	0.991 <0.0001
Time to reach maximum plateau of the curves					-0.135 0.0456

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THU0616-HPR EXPIRATORY FLOW ACCELERATOR (EFA) IN SYSTEMIC SCLEROSIS PATIENTS WITH MUCUS HYPERSECRETION, PRODUCTIVE COUGH AND DYSPNOEA: PRELIMINARY RESULTS FROM A HOME-BASED AIRWAY CLEARANCE TECHNIQUE DAILY PROGRAM

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Background: Systemic sclerosis (SSc) is a chronic disease with frequent lung involvement. As mucociliary clearance is impaired, mucus retention and frequent pulmonary infections, increase morbidity and mortality (1).
Airway clearance techniques (ACT) enhance removal of mucus from the airways. Expiratory flow accelerator (EFA) is a new technology that promotes deep and gentle drainage of the bronchial secretions, through the Venturi effect. No respiratory effort is required and no negative pressure is generated, avoiding risk of bronchial collapse (2).
Objectives: The aim of this study was to describe the effectiveness of EFA in improving pulmonary symptoms in SSc patients.
Methods: SSc patients with daily productive cough, frequent pulmonary exacerbations, exertional dyspnea and/or reduced physical activity were selected. All of them underwent a home-based ACT program with EFA. A Respiratory Physiotherapist (RT) trained each patient to use the device 3 times a day, 15 minutes each session. Every subject compiled the Saint George's Respiratory Questionnaire (SGRQ) and scleroderma Health Assessment Questionnaire (SHAQ) at baseline, 30, 90 and 180 days from the beginning. Statistical analysis has been carried out with General linear model for repeated measures. A value of p<0.05 was considered statistically significant.
Results: 8 patients were enrolled (M:F=1:7), median age 54 (IC95% 46-69) years. Interstitial lung disease affected the majority of them (7/8). SGRQ total score and SHAQ domain for respiratory symptoms decreased over time

(p= 0.003 and p= 0.005). In particular, there was an improvement in two SGRQ domains: activities (p= 0.013) and symptoms (p= 0.005) (fig.1).

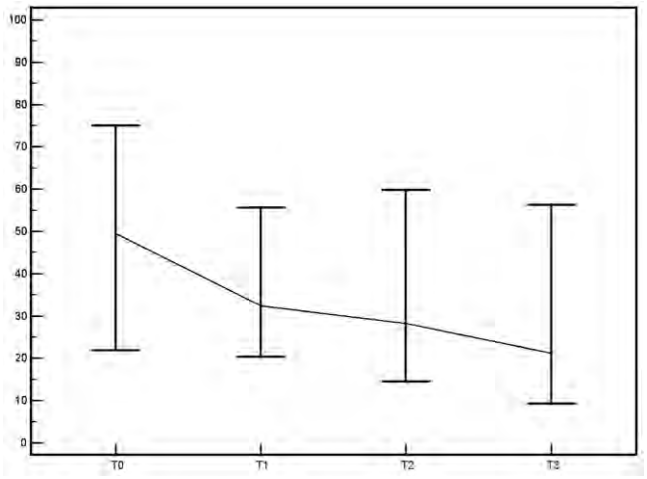


Figure 1

Conclusion: This is the first study to investigate the effect of EFA technology on airway clearance in SSc patients. The observations suggest the importance of a daily ACT program with EFA in improving respiratory symptoms. This technology appear to be extremely promising in SS patient management as it is well tolerated and it has the potential to slow down the pulmonary disease progression by limiting bronchial infections.

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THU0617-HPR TOWARDS A UNIVERSAL DEFINITION OF DISEASE ACTIVITY SCORES THRESHOLDS

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Background: For rheumatologists monitoring patients with various diseases and dealing with multiple scores with different maximum values (9 for RA-DAS, 6.4 for AS-DAS and 60 for PMR-AS) and values thresholds to characterize the different levels of disease activity (low, intermediate and high) can be a tedious task. The same problematic could arise in other specialty than rheumatology. Normalization of these scores seems to be necessary to facilitate daily clinical practice (1).

Objectives: To indentify and standardize scores of activity of inflammatory diseases.

Methods: We conducted a literature review on activity criteria using both a manual approach and the BIBOT software (2) published in English between 1.1.1975 and 31.12.2018. Within all extracted disease activity scores, we selected those with cut off values in four classes (remission, low, moderate and high disease activity). We used a linear interpolation to map all these disease activity scores to our new score, the AS-135, and developed a smart-phone application to perform the conversion automatically.

Results: 1068 articles were analyzed by BIBOT, 86 were excluded on the basis of the language used for their writing and 11 were excluded on the basis of their publication date. 599 were selected based on their titles, abstracts and keywords. 108 activity criteria from various fields (rheumatology, dermatology, gastroenterology, psychiatry, neurology and pneumology) were identified, but it is in rheumatology that we find separation into four classes. 10 scores met our inclusion criteria and were implemented in the Android app. These are: DAS28 (ESR), DAS28 (CRP), SDAI, ASDAS (ESR), ASDAS (CRP), ESSDAI, SLE-DAI-2K, DAPSA, PMR-AS (ESR) and PMR-AS (CRP). We built the AS135 score modification for each selected score using a linear interpolation of the existing criteria. It was defined on the interval [0,10] and values 1, 3 and 5 were used as thresholds. These arbitrary thresholds are then associated with the thresholds of the existing criteria and an interpolation can be calculated, allowing the conversion of the existing criteria into AS135 criterion. We have finally created a mobile application that allows each user to obtain both the original value of the activity criterion.



Conclusion: We have created a mobile application that allows any user to obtain in a simple way the level of disease activity, whatever the criterion used to describe it, since the application returns, in addition to the value of the activity criterion calculated from data returned by the physician, the transformation of this value into AS135 criterion and its interpretation in terms of level of activity of the pathology. The application is now available for Android devices and we plan to start developing a version for iOS devices.

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Disclosure of Interests: None declared

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THU0618-HPR PSYCHOSOCIAL CHANGES IN RHEUMATIC DISEASE: A NURSING LED CROSS-SECTIONAL STUDY

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Background: Nursing management in Rheumatic Diseases (RD) is focused on global patient care. Starting from basic knowledge of diagnostic and therapeutic management, nurses can assess the impact of RD on patients' quality of life not only at the physical level, but also at the psychological, social, and emotional levels.

Objectives: To evaluate psycosocial changes in RD patients through nursing-led Patient-Reported Outcomes

Methods: We performed a cross-sectional study of 100 RD patients compared with 100 healthy volunteers matched for age, sex and BMI. Specialist nurses invited patients and volunteers to complete questionnaires on quality of life through seven domains (anxiety, depression, fatigue, sleep disturbance, pain interference, physical functions and satisfaction with participation in social

roles) of the Patient-Reported Outcomes Measurement Information System (PROMIS).

Results: Among 100 RD patients, 52 (52%) had a diagnosis of Rheumatoid Arthritis; 17 (17%) had a diagnosis of axial spondylorthritis (Ankylosing Spondylitis and Psoriatic Artritis); 25 (25%) had connectivitis (i.e. Lupus, Systemic Sclerosis, Sjögren Syndrome), and finally 6 (6%) had vasculitis. Median disease duration was 7±5 years. Just under half (43%) of RD patients had active disease measured by specific disease activity index. As shown in table 1, no significant difference highlight between the two groups with regard to anthropompetric and demographic characteristics. We found that patients report significantly greater psychosocial changes than healthy controls. More specifically, as shown in figure 1A, mean T score for anxiety, depression, fatigue and sleep disturbances were significantly higher in the RD patients than in healthy controls (56 ± 9 vs 48 ± 8 p<0.001; 52 ± 9 vs 46 ± 8 p <0.001; 58 ± 8vs 48 ± 8 p <0.001; 52 ± 10 vs 44 ± 8 p <0.001) respectively. Moreover, also in the social dimension in terms of pain interference, physical functions and satisfaction with participation in social roles, patients showed a median T score worse than healthy controls (Fig.1B).

Table 1

		Patients (N=100)	Healthy (N=100)	*p*
	Age (years)	52.5±11	51±18	
Demographic and Anthropometric				
ns	Gender n male (%)	43 (43)	47 (47)	
ns	BMI (Kg/m2)	25.1±4	27.8±4	
ns	Smoke n (%)	52 (52)	46 (46)	
ns	Marital Status n not married (%)	42(42)	41 (41)	
ns	Occupation n yes (%)	31 (31)	35 (35)	
ns	Education level n degree (%)	54 (54)	64 (64)	
ns	Rheumatoid Arthritis	52 (52)	-	
	Axial Spondylorthritis	17 (17)	-	
	Connectivitis	25 (25)	-	
	Vasculitis	6 (6)	-	
	Disease duration (years)	7.1±5.18	-	
	Disease Activity n yes (%)	43 (43)	-	
	Medications n (% patients)		-	
	NSAID	7 (7)	-	
	Steroids	26 (26)	-	
	Biological Treatment	54 (54)	-	
	Methotrexate	34 (34)	-	

Continuous variables are shown as mean ± standard deviation. Categorical variables are presented as number and proportion. The overall p-value was calculated by the Mann–Whitney non-parametric test for independent samples and by Chi-square test as appropriate

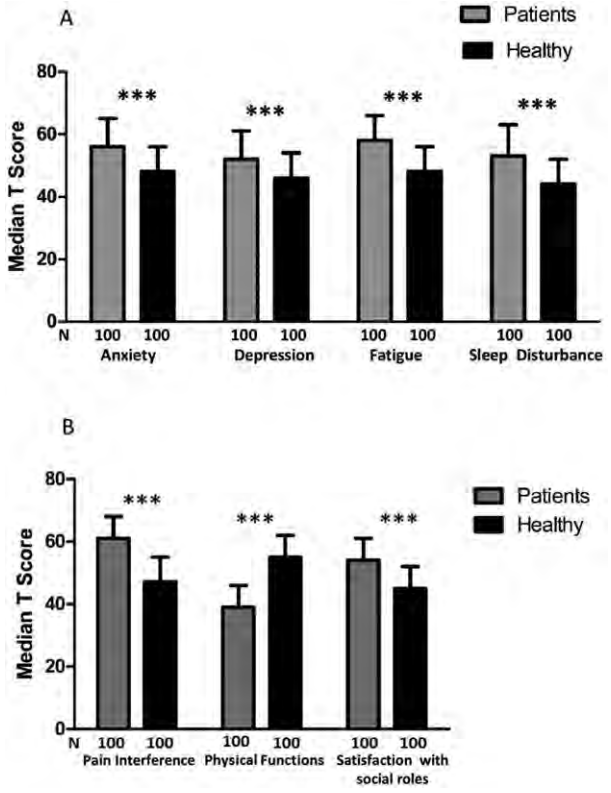


Figure 1. Median T Score stratified by study group. Data are shown as mean and standard deviation. The overall p-value wascalculated by the Mann–Whitney non-parametric test for independent samples.

Conclusion: This exploratory study highlights the need to adopt validated questionnaires in clinical practice, and demonstrates that PROMIS is a valid, objective, and standardized instrument that can help nursing staff to better define the consequences of the disease in a patient's daily life.

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Disclosure of Interests: None declared

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THU0619-HPR PREVALENCE OF DISTAL INTERPHALANGEAL JOINT ULTRASONOGRAPHY FEATURES IN PSORIATIC ARTHRITIS, SKIN PSORIASIS, OSTEOARTHRITIS AND HEALTHY INDIVIDUALS: A CROSS-SECTIONAL STUDY

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Background: Distal interphalangeal (DIP) joint involvement is a feature of both psoriatic arthritis (PsA) and hand osteoarthritis (OA), and nail-changes are features seen both in PsA and nail psoriasis patients without joint involvement (PsO). In both PsA and OA, ultrasonography (US) is used to quantify DIP joint inflammation.

Objectives: To explore disease-specific US-detected characteristics in the DIP-joints and extensor tendon entheses in patients with DIP-joint OA, PsA, PsO with nail involvement, and healthy controls (HC).

Methods: In PsA, PsO, OA and HC US examination of DIP joints 2-5 and the extensor tendon were performed. The US images were scored for DIP joint grey-scale synovitis, DIP joint Doppler, osteophytes and erosions (grade 0-3) and presence/absence of enthesitis and peritendonitis of the extensor tendon according to OMERACT standards. Prevalences were calculated on all included fingers (i.e. four fingers per participant), and differences in prevalences were tested using Chi-square statistics.

Results: Fifty PsA patients (44% females; mean age: 55y), 13 PsO patients (38% females; mean age 54y), 12 OA patients (100% females, mean age 71y), and 29 HC (52% females, mean age 48y) participated. The prevalences across the diagnosis groups are shown in figure 1, and the distribution of US outcomes was significantly different (highest Chi-square P-value: 0.0127). The PsA group had the largest prevalence of extensor tendon enthesitis (45.5%), peritendonitis (15%), and DIP joint erosions (11%), but also exhibited a considerable prevalence of osteophytes (46%). In the PsO group, the most marked findings were synovitis (33%) and enthesitis (35%). The OA group had the largest prevalence of DIP joint synovitis (67%) and osteophytes (88%) but also 25% prevalence of enthesitis. 24% of the HC group had a grade 1 synovitis.

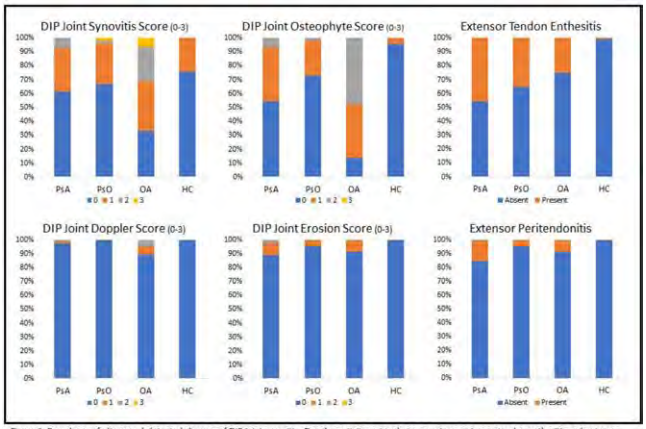


Figure 1: Prevalence of ultrasound detected changes of DIP-joint synovitis, Doppler activity, osteophytes, erosions, extensor tendon enthesitis and extensor peritendonitis in patients with psoriatic arthritis (PsA), skin psoriasis (PsO), osteoarthritis (OA) and healthy controls (HC).

Conclusion: This cross-sectional study found significant patterns of US findings distributed dependent on the underlying condition. PsA patients were mainly differentiated by the presence of extensor tendon enthesitis and peritendonitis. A high prevalence of enthesitis and synovitis was seen in patients

with DIP joint OA. The high prevalence of enthesitis in PsO is consistent with a preclinical phase of PsA in this group.

Disclosure of Interests: Jørgen Guldberg-Møller Speakers bureau: Novartis, Ely Lilly, AbbVie, BK Ultrasound, Marius Henriksen: None declared, Mikael Boesen Speakers bureau: Image Analysis Group, AbbVie, AstraZeneca, Eli Lilly, Esaote, Glenmark, Novartis, Pfizer, UCB, Lene Dreyer: None declared, Karen Ellegaard: None declared, Marie Skougaard: None declared, Christine Ballegaard: None declared, Ai Lyn Tan: None declared, Richard Wakefield Speakers bureau: Novartis, Janssen, GE, Lars Erik Kristensen Consultant of: UCB Pharma (Advisory Board), Sannofi (Advisory Board), Abbvie (Advisory Board), Biogen (Advisory Board), Speakers bureau: AbbVie, Amgen, Biogen, Bristol-Myers Squibb,Celgene, Eli Lilly, Gilead, Forward Pharma, Janssen Pharmaceuticals, MSD, Novartis, Pfizer, and UCB Pharma
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THU0620-HPR MEASUREMENT OF LOW DISEASE ACTIVITY USING THE CLINICAL DISEASE ACTIVITY INDEX (CDAI) VERSUS THE DISEASE ACTIVITY SCORE 28 (DAS 28): IMPACT OF INFLAMMATION MARKERS ON THE COMPARATIVE EFFECTIVENESS OF BIOLOGICS FOR THE TREATMENT OF RHEUMATOID ARTHRITIS

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Background: Biologics for the treatment of rheumatoid arthritis (RA) have different modes of action to target auto-inflammatory processes causing the signs and symptoms of the disease. Different biologics may thus have different effects on inflammatory markers. For instance, previous studies have shown that the interleukin-6-inhibitor tocilizumab (TOC) decreases the level of acute phase reactants (APRs) [1]. Such direct effects on inflammatory markers may lead to an overestimation of clinical response if disease activity is measured via scores including inflammatory markers, such as the Disease Activity Score 28 (DAS 28). The detected changes in disease activity may not adequately reflect the clinical improvement of signs and symptoms.

Objectives: In our study, we compared biologics with each other using two different disease activity scores: the DAS 28 including APRs and the clinical disease activity index (CDAI) excluding APRs. The aim of this study was to assess whether the use of the two different scores affects comparative effectiveness studies on biologics for the treatment of RA.

Methods: We compared results on the comparative effectiveness of biologics using the corresponding thresholds for low disease activity (LDA) for the DAS 28 (< 3.2) and the CDAI (≤ 10). We performed two separate network meta-analyses (NMAs) after a thorough step-by-step evaluation of the similarity, homogeneity and consistency assumptions of the patient populations and the study data.
Our study formed part of a systematic review (including NMAs) that was largely based on clinical study reports and re-analyses of LDA using individual patient data provided by sponsors for studies conducted up to 2017. Thus, the analyses include hitherto unknown data on LDA analysed by means of the CDAI, especially data from older studies. An extensive comparison of DAS 28 and CDAI in different patient populations was possible.

Results: For all analysed patient populations, comparisons of TOC versus other biologics yielded remarkable results: advantages for TOC were found in NMAs using the DAS 28, which were not confirmed in NMAs using the CDAI. For methotrexate (MTX)-naïve patients, using the DAS 28, TOC showed a greater benefit than abatacept (ABA), certolizumab pegol (CZP), and etanercept (ETA), which was not confirmed by the CDAI. In contrast, TOC showed less benefit than adalimumab (ADA) and ETA. For patients after MTX failure and using the DAS 28, TOC showed a greater benefit than ABA, ADA, anakinra (ANA), ETA, golimumab (GOL), and infliximab (INF). With the exception of ANA, these advantages were not confirmed by the CDAI. Similar differences between DAS 28 and CDAI were shown in patients treated with biologics in monotherapy or after failure of biologics.

Conclusion: In comparative effectiveness studies of biologics, the assessment of LDA using the DAS 28 instead of the CDAI leads to a consistent overestimation of the benefit of TOC in all patient populations, regardless of pre-treatment or combined therapy with MTX. The inclusion of APRs in disease activity scores may thus introduce bias. A score excluding inflammatory markers should therefore be used to ensure valid results.

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Disclosure of Interests: Kirsten Janke: None declared, Katharina Biester: None declared, Dietmar Krause Grant/research support from: Pfizer and AbbVie (Abbott), Bernd Richter: None declared, Christoph Schürmann: None declared, Katharina Hirsch: None declared, Beate Wieseler: None declared
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THU0621-HPR SARC-F SCALE ON SCREENING SARCOPENIA AND PHYSICAL FUNCTION IN PATIENTS WITH KNEE OSTEOARTRITIS

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Background: Sarcopenia has been defined as a loss of muscle mass and consequently of muscle function. In patients affected by osteoarthritis (OA) a more likely and accelerated development of sarcopenia has been reported. The SARC-F is a simple sarcopenia screening tool includes five assessment items: strength, assistance walking, rising from a chair, climbing stairs, and falls. SARC-F ≥ 4 is defined as sarcopenia.

Objectives: The present study aimed to examine the utility of SARC-F in the patients with knee osteoarthritis.

Methods: Patients with radiographic and clinic evidence of tibiofemoral OA (Kellgren-Lawrence score ≥2) were included. Sarcopenia were identified using the SARC-F scale. Patients with a total score 4 and higher than 4 were classified as having sarcopenia. Patients were assessed by The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), four-meter walking test, hand grip test, shortened version of the falls efficacy scale-international (the short FES-I) and EuroQol- 5 Dimension (EQ-5D). A multiple linear regression model was used to identify independent predictors of SARC-F.

Results: A total 76 patients with median age 61 ranged 55 to 78 years old (72.4% female) were screened in this study (Table 1). Of the sample, 38.1% of patients were sarcopenic as a SARC-F (Figure 1). Through multiple regression analyses, SARC-F scores was significantly associated with four-meter walking test, hand grip, WOMAC-Function, EQ-5D and short FES-I describing between 57% and 63% of the variance (adjusted R^2) (Table 2). Also, poor physical performance and grip strength were associated with SARC-F ≥ 4 independently (P<0.005).

Table 1. Summary Table of Characteristics of sarcopenic vs non-sarcopenic patients with knee OA

Measures	Sarcopenic patients with knee OA (n:47) Sarc-F≥4	Non-Sarcopenic patients with knee OA (n:29) Sarc-F<4	p value$^{\varphi}$
Age, mean(SD)	62.7(6.9)	59.3 (6.9)	0.294
BMI, mean(SD)	27.84 (9.56)	28.54 (8.38)	0.327
WOMAC, mean(SD)	43.52 (10.83)	28.06 (14.9)	0.001*
GRADE (K-L) med (min-max)	3(2-4)	2(2-4)	0.008*
Hand Grip, mean(SD)	20 33 (4.89)	28.22 (7.13)	0.001*
4 m Walking Test, mean(SD)	11.88 (4.24)	9.55 (4.30)	0.001*
EQ-5D, mean(SD)	9.41 (1.52)	7. 13 (1.75)	0.001*
EQ-5D-VAS, mean(SD)	44.31 (14.12)	66.90 (16.25)	0.001*
Short FES-I, mean(SD)	18. 06 (9.45)	9.04 (5.32)	0.001*
Number of falls the past year, mean(SD)	4.01 (1.24)	3.14 (2.74)	0.674

φMann Whitney U test; *p< 0.05; BMI, Body mass index; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index EQ-5D, EuroQol-5 Dimension; FES-I, Falls Efficacy Scale-International

Table 2. Multiple linear regression analysis for SARC-F

	β	t	P value	95% Confidence Interval (lower-upper bound)
Walking Speed	0.11	1.20	0.23	-0.31/ 0.12
Hand Grip	-0.35	-1.73	0.04	-0.20 / 0.01
WOMAC-Function	0.26	2.31	0.01	0.00 / 0.05
Short FES-I	0.18	1.96	0.01	0.04 / 0.01
EQ-5D	0.22	2.29	0.02	0.02 / 0.39
EQ-5D VAS	-0.24	-2.73	0.001	-0.04 / -0.00
$R^2 = 0.61$				

WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index, EQ-5D, EuroQol-5 Dimension; FES-I, Falls Efficacy Scale-International

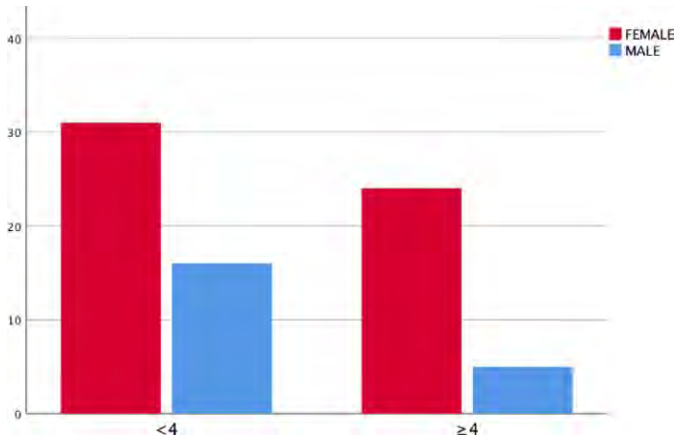


Figure 1. Sarcopenic vs non-sarcopenic patients according to sex

Conclusion: In this study, sarcopenia defined by the SARC-F questionnaire has a predictive value of clinical characteristics of patients to predict sarcopenia parameters and poor physical performance in patients with knee OA.

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THU0622-HPR PATIENTS' SATISFACTIONS TO TUMOUR NECROSIS FACTOR INHIBITORS FOR MANAGEMENT OF ANKYLOSING SPONDYLITIS IN KOREA; RESULTS FROM A MULTICENTERED, OBSERVATIONAL, AND CROSS-SECTIONAL STUDY

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Background: An experience of particular treatment is one of the characteristics impacting on patients' decisions to continue, discontinue, or alter their medical treatments.[1] Reports on patients' treatment satisfaction would be weighty when selecting an optimal treatment reflecting the patient's perspective.

Objectives: We aimed to evaluate the treatment satisfaction of ankylosing spondylitis (AS) patients treated with tumor necrosis factor inhibitors (TNF-Is) and identify the factors associated with satisfaction in Korea.

Methods: The study was conducted from July to November in 2018 at 4 hospitals representative in treating AS in Korea. Patients aged≥19, diagnosed as AS based on 'Modified New York criteria 1984', and treated with current TNF-Is and same type of device for≥3 months were included. We used 'Treatment Satisfaction Questionnaire For Medication (TSQM)' which is consisted of 4 domains; effectiveness, side effects, convenience, and global satisfaction. Scores (0 ~ 100) of satisfaction indicate the higher the better. Multivariable linear regressions with 95% of statistical significance level was performed to identify related factors.

Results: Enrolled 497 patients (85.3% male, 40.3 years old) were prevalent with AS for mean 10 years and indicated average 3.1 in Bath AS Disease Activity Index (BASDAI). Adalimumab (39.6%) was the most commonly used, followed by etanercept (23.5%), infliximab (21.9%) and golimumab (14.9%). TNF-Is were prescribed at low, regular, and high dose for 24.9%, 70.5% and 4.7% of patients and as subcutaneous with pen type, syringe type, and intravenous injection for 50.9%, 26.8% and 22.3% of patients, respectively. Conventional disease-modifying antirheumatic drugs(cDMARDs) and steroids were concomitantly used for 5.4% and 8.3% of patients, respectively.

Average score of TSQM was the lowest in convenience amongst 4 domains; 72.2 in effectiveness, 96.9 in side effects, 67.6 in convenience, and 71.4 in global satisfaction. Negative associations were shown between BASDAI and all domains of TSQM. Patients who prescribed TNF-Is at high dose were more satisfied to effectiveness while they were less satisfied to side-effect, as against patients prescribed it at low dose. TNF-Is, use of cDMARDs and steroids were not significantly associated with treatment satisfaction (Fig. 1).

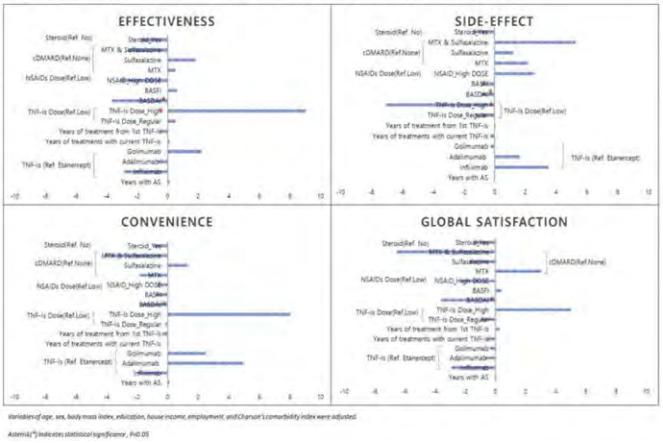
Conclusion: AS patients treated with TNF-Is in Korea were quite satisfied with their treatments. Since the worst satisfaction in the convenience domain was presented amongst 4 domains, more convenient treatment options may be required to enhance the entire satisfaction of patients. With the result of a negative association between disease activity and satisfaction, this study strengthened the previous studies reporting the positive relationship between health improvement and satisfaction.[2]

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Figure 1. Related factors with treatment satisfaction measured by TSQM



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THU0623-HPR REVISION AND VALIDATION OF THE GERMAN VERSION OF THE SYSTEMIC SCLEROSIS QUALITY OF LIFE QUESTIONNAIRE (SSCQOL) WITH MOKKEN SCALE ANALYSIS

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In the validation study, German-speaking SSc patients included in the Swiss *MANagement Of Systemic Sclerosis (MANOSS)* cross-sectional study completed the revised (polytomous) SScQoL. Mokken model was used to test the construct validity of the scale including its subscales. The scalability (*H* coefficient) values of ≥ $^{0}.^{50}$ are considered "strong", $^{0}.^{49}$ to $^{0}.^{40}$ "moderate" and $^{0}.^{39}$

to $^{0}.^{30}$ "weak" scales, while values of $<^{0}.^{30}$ are not considered as unidimensional. Internal consistency (reliability) was assessed using Cronbach's α.

The validation sample comprised ^{79} patients ($^{74}.^{7}$% female) with a median age of ^{61} (IQR: ^{49} to ^{71}) and disease duration of ^{8} (IQR: ^{4} to ^{13}) years. Table ^{1} presents the results of validation with Mokken model. The construct validity of the revised German SScQoL was confirmed in all subscales and the global scale. The scalability (*H* coefficients) were all above $^{0}.^{50}$ suggesting a robust unidimensional scale. Internal consistency was high (Cronbach's α = $^{0}.^{97}$).

Background: The Systemic Sclerosis Quality of Life Questionnaire (SScQoL) has been validated in six European languages.[1] Previous adaptation into German revealed issues with the dichotomous response structure in 10 items necessitating a review of the tool and further psychometric testing with patients in German speaking countries.

Objectives: The aim of this study was to assess the German version of the SScQoL, extend the response structure and test its construct validity using Mokken scale analysis.

Methods: This was a mixed methods study involving cognitive debriefing and survey methods. The expert committee extended the response structure of the 10 items from dichotomous to polytomous (4-point) responses: 'always', 'usually', 'sometimes' and 'never'. In cognitive debriefing, a small convenience sample of patients with SSc completed the new version while 'thinking aloud' and commented on relevance of the items and the response structure.

Results: In cognitive debriefing, six patients with SSc completed the new German SScQoL and reported problems with the remaining dichotomous items. These were subsequently converted into polytomous 4-point response structure by the expert committee.

Conclusion: The German SScQoL has been revised into polytomous item structure and shown to be a valid and reliable measure of health-related quality of life in SSc. Further cross-cultural validity tests are required to assess its measurement equivalence with other SScQoL versions and thus enable multinational comparisons.

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Table 1. Mokken scale analysis of the revised German SScQoL

Subscale (items)	Scalability (H)	Standard error
Function (6)	0.664	0.048
Emotional (13)	0.652	0.060
Sleep (2)	0.798	0.061
Social (6)	0.692	0.053
Pain (2)	0.960	0.029
Global scale (29)	0.623	0.062

Table legend: scalability $H \geq 0.50$ = strong, 0.49 to 0.40 = moderate, 0.39 to 0.30 = weak, while values of <0.30 are not considered as unidimensional.

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THU0624-HPR COMPARISON OF WRIST PROPRIOCEPTION, GRIP STRENGTH AND PINCH STRENGTH IN PATIENTS WITH PSORIATIC ARTHRITIS AND RHEUMATOID ARTHRITIS: PRELIMINARY STUDY

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Background: Hand articular damage occurs in rheumatoid arthritis (RA) and functional ability deteriorates as the disease progresses. Limitation of hand motion, oedema, pain etc. factors contribute to reduce grip strength, pinch strength and joint position sense; this problems contribute to function and disability. Following RA, affecting grip and pinch strength (1) and joint position sense (2) was reported former research. But there is a little knowledge about disabilitiy of hand functions in psoriatic arthritis (PsA).

Objectives: To compare joint position sense, grip strength and pinch strength in patient with PsA and RA.

Methods: In our cross sectional study, 23 RA patients [Mean age; 52.7±12.6, Women:20(87.0%)] who were classified according to the ACR 2010 criteria and 19 PsA patients [Mean age 53.5±12.6, Women:14 (%73.7)] who were classified according to the CASPAR criteria were included.It was recorded demographic and clinical data of patients. Wrist position sense was evaluated by goniometric re-position error test (in 30◦ wrist extansion, 3 repeat). Grip strenght was examined using a hand dynamometer (Lafayette Proffessional Hand Dynamometer, USA) and pinch strength (two point, three point, lateral) was evaluated by pinchmeter (Lafayette,USA).

Results: Patients were similar in terms of age, gender, disease duration, morning stiffness duration, pain of hand joints, number of tender and swallen joints and disease activity (p>0.05). RA patients had longer disease duration (p=0.004) and lower ESR levels (p=0.046) compared to PsA. Grip and pinch strength were found similar in both dominant and non-dominant side between RA and PsA patients (Table 1). Wrist joint position error was higher in PsA group in non-dominant side (p=0.011).

Table 1. Comparison of Groups for Grip and Pinch Strength and Joint Position Sense

Variables	RA (n=23) Median(IQR)	PsA (n=19) Median(IQR)	p*
Grip Strength	20(14/25)	25(20/29)	0.109
Dominant	20(14/25)	21(15/26)	0.404
Non-dominant			
Pinch Strength	3.1(2.2/3.8)	3(2.2/3.4)	0.810
Dominant	3(2.3/4.0)	3.4(2.5/4.20)	0.471
2 Point	3.4(3.0/4.2)	3.5(2.6/4.5)	0.840
3 Point	3(1.9/3.7)	3(2.4/3.7)	0.714
Lateral	2.8(2.3/3.8)	3.1(2.3/4.2)	0.723
Nondominant	2.9(2.5/4.0)	3.2(2.4/4.2)	0.561
2 Point			
3 Point			
Lateral			
Joint Position Error	6(5/7)	7(5/9)	0.234
Dominant	6(3/8)	8(6/11)	**0.011**
Non-dominant			

Data have shown as median (interquartile range 25-75) *Mann Whitney-U Test

Conclusion: Our study showed that patients with PsA had hand impairment as much as RA patients. We think, hand assessment in patients with PsA rehabilitation programme is essential for clinicians. There is need future studies including asymptomatic healthy group to interpret of results in detailed.

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Disclosure of Interests: None declared

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THU0625-HPR ELECTRONIC PATIENT-REPORTED OUTCOMES: A SURVEY ABOUT ACCEPTANCE, USAGE AND BARRIERS AMONG GERMAN RHEUMATOLOGISTS

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Background: The use of patient-reported outcomes (PROs) allows for patient-centered, measurable and transparent care. Electronic PROs (ePROs) have many benefits and hold great potential to improve current usage of PROs;

yet, limited evidence exists regarding acceptance, usage and barriers among rheumatologists.

Objectives: This study aimed to evaluate the current level of acceptance, usage, and barriers among German rheumatologists regarding the utilization of ePROs. The importance of different ePRO features for rheumatologists was investigated. Additionally, the most frequently used PROs for patients with rheumatoid arthritis (RA) were identified

Methods: Data was collected via an online survey consisting of 18 questions. The survey was completed by members of the Working Group Young Rheumatologists of the German Society for Rheumatology (Deutsche Gesellschaft für Rheumatologie (DGRh)) at the annual 2019 DGRh conference. Only members currently working in clinical rheumatology were eligible to complete the survey.

Results: A total of 119 rheumatologists completed the survey. 90% reported collecting PROs in routine practice and 25.5% already used ePROs. 44.3% were planning to switch to ePROs in the near future.The main reason for collecting PROs was for clinical decision making (66.4%), followed by research (39.5%), reimbursement (23.5%), internal quality management (21.9%) and patient satisfaction (16.8%). The most commonly cited reason for not switching to ePROs was the unawareness of suitable software solutions (figure 1).Respondents were asked to rate the features for ePROs on a scale of 0-100 (0 = unimportant, 100 = important). The most important features were automatic score calculation and display (score: 77.5), as well as the simple data transfer to medical reports (76.9) (table 1). When asked about PROs in RA, the respondents listed pain, morning stiffness and physician global assessment (PGA) as the most frequently used PROs (figure 2).

Table 1. Ratings for features of ePRO on a scale of 0-100 (0 = unimportant, 100 = important))

Question	mean	SD
How important would the graphic display be to you for ePROs?	63.5	31.19
How important would the automatic score calculation and display of ePROs be to you?	77.5	27.64
How important would the simple transfer of the ePROs in medical report be to you?	76.9	30.07
How important would an automatic alarm of yourself be for you if a critical threshold is exceeded by an ePRO?	51.65	33.5
How important would an automatic alarm of the patient be for you if a critical threshold is exceeded by an ePRO?	34.55	30.61

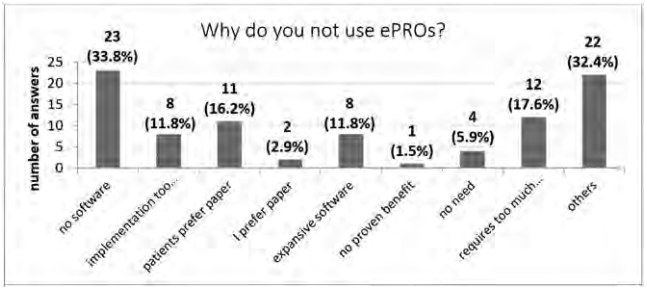


Figure 1. Reasons why ePROs are currently not used (multiple answers were possible for question)

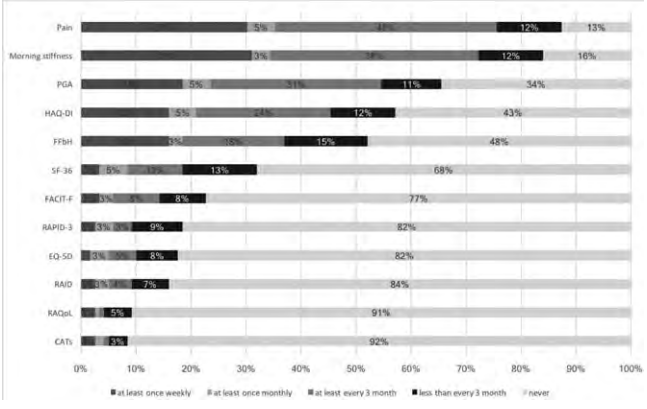


Figure 2. PROs being used in clinical practice and their respective frequency

Conclusion: The potential of ePROs is widely seen, and there is a great interest in ePROs. Despite this, a minority of physicians only uses ePROs, and the main reason for not implementing was cited as the unawareness of suitable software solutions.

Developers, patients and rheumatologists should work closely together to help realize the full potential of ePROs and ensure a seamless integration into clinical practice.

Disclosure of Interests: Martin Krusche Consultant of: Sanofi, Novartis and Medac, Speakers bureau: Roche/Chugai, Novartis, Sobi,, Philipp Klemm Consultant of: Lilly, Medac, Manuel Grahammer Shareholder of: MG is MD and shareholder of Abaton GmbH, Johanna Mucke: None declared, Diana Vossen Consultant of: Medac, Novartis, Abvie, Speakers bureau: Abvie, BMS, Arnd Kleyer Consultant of: Lilly, Gilead, Novartis,Abbvie, Speakers bureau: Novartis, Lilly, Philipp Sewerin Grant/research support from: AbbVie Deutschland GmbH & Co. KG
Bristol-Myers Squibb Celgene GmbH
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Rheumazentrum Rhein-Ruhr, Consultant of: AMGEN GmbH AbbVie Deutschland GmbH & Co. KG Biogen GmbHBristol-Myers Squibb Celgene GmbH Chugai Pharma arketing Ltd. / Chugai Europe GmbHHexal Pharma Janssen-CilagGmbH Johnson & Johnson Deutschland GmbHLilly Deutschland GmbH / Lilly Europe / Lilly Global Novartis Pharma GmbH Pfizer Deutschland GmbH Roche Pharma Rheumazentrum Rhein-Ruhr Sanofi-Genzyme Deutschland GmbH Swedish Orphan Biovitrum GmbH UCB Pharma GmbH, Speakers bureau: AMGEN GmbH AbbVie Deutschland GmbH & Co. KG Biogen GmbHBristol-Myers Squibb Celgene GmbH Chugai Pharma arketing Ltd. / Chugai Europe GmbHHexal Pharma Janssen-CilagGmbH Johnson & Johnson Deutschland GmbHLilly Deutschland GmbH / Lilly Europe / Lilly Global Novartis Pharma GmbH Pfizer Deutschland GmbH Roche Pharma Rheumazentrum Rhein-Ruhr Sanofi-Genzyme Deutschland GmbH Swedish Orphan Biovitrum GmbH UCB Pharma GmbH, Johannes Knitza Grant/research support from: Research Grant: Novartis
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THU0626-HPR IMPORTANCE OF A SYSTEMATIC COGNITIVE ASSESSMENT: IMPLEMENTATION OF A COGNITIVE EVALUATION AND REHABILITATION CLINIC IN RHEUMATIC PATIENTS

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Background: Cognition is the ability to learn, process and remember information to be used later.(1) Cognitive impairment reflects a decrease in one or more cognitive domains: memory, language, reasoning, among others. (2) It has been reported in rheumatic diseases such as systemic lupus erythematosus, rheumatoid arthritis, fibromyalgia, and it is frequently found in young patients during the first years of their illness correlating the disease progression.(3) This condition can lead to anxiety and depression, compromising the quality of life. Given the lack of consensus regarding the best test to diagnose cognitive impairment, multiple tools have been used to address this problem.

Objectives: To describe the systematical assessment in a Cognitive Evaluation and Rehabilitation Clinic in rheumatic patients from a University Hospital in Mexico.

Methods: Observational and descriptive study. A multidisciplinary team met for 6 months to establish the structure a Cognitive Evaluation and Rehabilitation Clinic in a University Hospital in Mexico (Figure 1). As a pilot group we included outpatients from a Rheumatology clinic, referred

Table 1. Demographic characteristics

	N=21
Age, mean (SD)	43.62 (14.68)
Female, n (%)	14 (66.66)
Years of education, mean (SD)	15.24 (2.70)
Psychiatric disorder	
Depression, n (%)	4 (19.04)
Rheumatic diagnosis	
Systemic lupus erythematosus, n (%)	13 (61.90)
Rheumatoid arthritis, n (%)	3 (14.30)
Others, n (%)	5 (23.80)

by their physician (Table 1). The following psychological tests were used: Montreal Cognitive Assessment (MoCA) and Neurobehavioral Cognitive Status Examination (NCSE). After results (Table 2), the team decided to extend the evaluation with Automated Neuropsychological Assessment Metrics (ANAM), Wechsler Adult Intelligence Scale (WAIS-IV) and International Neuropsychiatric Interview (MINI) (Figure 2). Statistical analysis was performed with SPSS v.24, descriptive statistic were used with measures of central frequency trend.

Table 2. Comparison of MoCA and NCSE results.

	MoCA N=21	NCSE N=21
Total score, mean (SD)	24.24 (3.49)	*38.52 (1.69)*
Level of cognitive impairment		
Normal, n (%)	7 (33.3)	17 (81)
Mild, n (%)	**13 (61.9)**	**1 (4.8)**
Moderate, n (%)	**1(4.8)**	**3 (14.2)**
Severe, n (%)	0 (0)	0 (0)

MoCA, Montreal Cognitive Assessment; NCSE, Neurobehavioral Cognitive Status Examination.

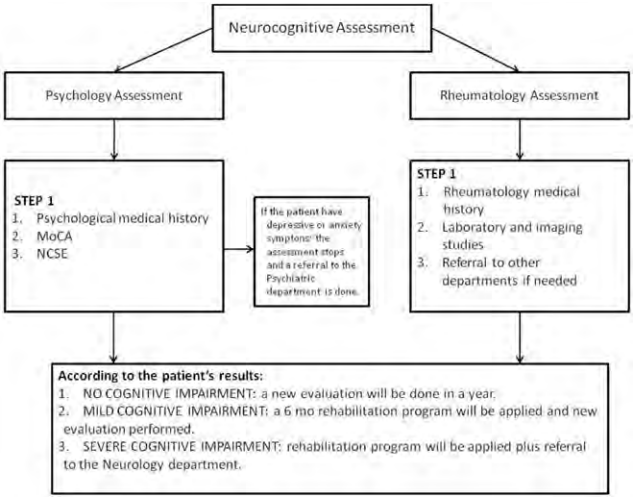


Figure 1. Pilot program of the Neurocognitive Assessment

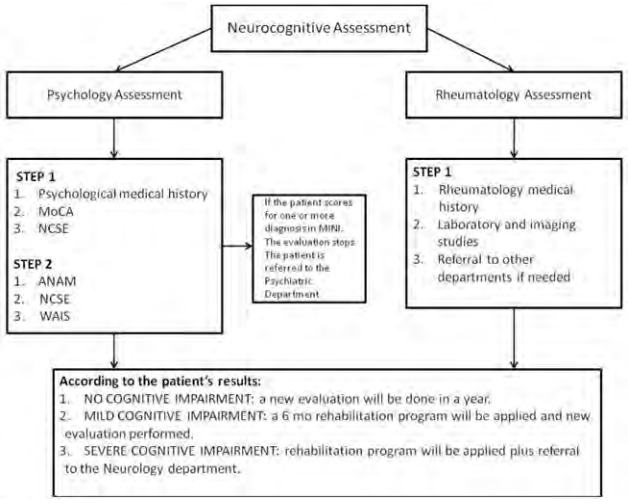


Figure 2. Final Program of the Neurocognitive Assessment

Results: We evaluated 21 patients (66% females) with an average age of 43.62 years (SD 14.6) (Table 1). The total number of patients with cognitive impairment was 15 (71%), 14 (66%) diagnosed with MoCA, 6 (28%) with NCSE and a coincidence of both tests in 4 (19%) patients (Table 2).

Conclusion: A high percentage of patients with cognitive impairment was found, also a discrepancy between the MoCA and NCSE results. We realized those tests were not enough to get a detail cognitive functioning, for this reason it was decided to make a more extensive evaluation adding ANAM, WAIS-IV and MINI. Neuropsychological evaluation should be performed as part of a multidisciplinary management for the patient and the rheumatologist should be aware of this manifestation and the importance of cognitive testing.

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THU0627-HPR JOINT INVOLVEMENT SIGNIFICANTLY INFLUENCES QUALITY OF LIFE OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Joint involvement is one of the most common features observed in Systemic Lupus Erythematosus (SLE), potentially involving up to 90% of patients [1]. Several patients' reported outcomes (PROs) have been employed to measure Quality of life (QoL) in SLE patients, but frequently not specifically developed for SLE patients. More recently, the LupusQoL has been validated, a disease specific questionnaire[2,3].

Objectives: We focused at assessing the relationship between musculoskeletal manifestations and QoL in a large SLE cohort, by using the LupusQoL.

Methods: SLE patients with a clinical history of joint involvement (arthralgia/arthritis – group A) were enrolled in the present study. SLE diagnosis was performed according to the revised 1997 ACR criteria. As a control group, we enrolled SLE patients without history of joint involvement (group B).Disease activity was assessed by the SLE Disease Activity Index-2000 (SLEDAI-2k). The activity of joint involvement was assessed by using the disease activity score on 28 joints ($DAS28_{ESR}$). The LupusQoL was administered to the enrolled patients (Group A and Group B). It consists of 34 items referring to eight domains: physical health (PH), pain (P), planning (PL), intimate relationships (IR), burden to others (BO), emotional health (EH), body image (BI) and fatigue (F).

Results: Group A included 110 patients [M/F 8/102; median age 49 years (IQR 13), median disease duration 156 months (IQR 216)], while group B included 58 patients [M/F 11/47; median age 40 years (IQR 15), median disease duration 84 months (IQR 108)]. Group A showed a significantly lower disease duration and mean age in comparison with group B (P< 0.001 for both comparisons). As represented in figure 1, group A showed significantly lower values in all LupusQoL domains except for "burden to others" domain. Moreover, we observed an inverse correlation between $DAS28_{ESR}$ and all the LupusQoL domains in group A patients [PH (r=-0.5, P>0.0001), P (r=-0.5, P<0.0001), PL (r=-0.5, P<0.0001), IR (r=-0.2, P=0.006), BO (r=-0.4, P=0.0004), EH (r=-0.3, P=0.0009), BI (r=-0.4, P=0.001), F (r=-0.4, P<0.0001)]. Conversely, SLEDAI-2k values inversely correlated only with PL (r=-0.3, P=0.006), IR (r=-0.25, P=0.02), EH (r=-0.3, P=0.02).

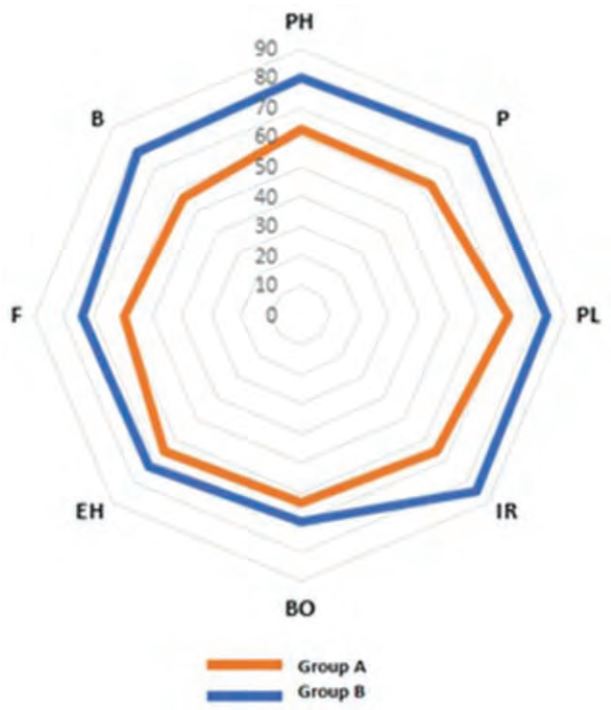


Figure 1.

Conclusion: In the present study, by using a disease specific PRO, we found a poorer QoL in SLE patients with joint involvement in comparison with those without this manifestation. Moreover,$DAS28_{ESR}$ significantly correlated with all LupusQol domains, differently from SLEDAI-2k, suggesting the need to evaluate joint involvement with a specific activity index.

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	Group (A)	Group (B)	p
PH	80,38 ± 21,43	62,88 ± 23.28	< 0.0001
P	82,36 ± 25.08	62,30± 26.02	< 0.0001
PL	83,04 ± 27.82	70,58± 29.45	0.001
IR	84,49± 25.99	65,36± 36.33	0.0005
BO	69,58 ± 28.46	63,45± 28.95	0.129
EH	71,98 ± 24.69	64,69± 23.05	0.0169
F	73,69 ± 24.29	59,78±26.06	0.0004
B	78,14 ± 24.61	56,28±30.14	<0.0001

Disclosure of Interests: Francesco Natalucci: None declared, Fulvia Ceccarelli: None declared, enrica cipriano: None declared, Giulio Olivieri: None declared, Carlo Perricone: None declared, Francesca Romana Spinelli Grant/research support from: Pfizer, Consultant of: Novartis, Gilead, Lilly, Sanofi, Celgene, Speakers bureau: Lilly, Simona Truglia: None declared, Francesca Miranda: None declared, cristiano alessandri Grant/research support from: Pfizer, fabrizio conti Speakers bureau: BMS, Lilly, Abbvie, Pfizer, Sanofi, Guido Valesini: None declared
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THU0628-HPR SSCENTRY: A PERSONAL DISEASE DIARY APP FOR SYSTEMIC SCLEROSIS PATIENTS

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Background: Systemic Sclerosis (SSc) is a connective tissue disease characterized by severe alterations in the microvasculature and progressive fibrosis of the skin and internal organs [1]. Management of SSc is not easy, for both patients and physicians [2]. Symptoms are manifold and have a significant impact on patient's daily autonomy and psychological well-being.

Objectives: SScEntry (SSc data Entry tool; Figure 1) is a solution conceived to assist SSc patients in monitoring their disease, as a kind of "sentry". The core idea is to provide patients with a personal diary to annotate and track the onset, evolution and resolution of symptoms as well as any changes in their general health condition, through an app for iOS and Android smartphones and tablets.

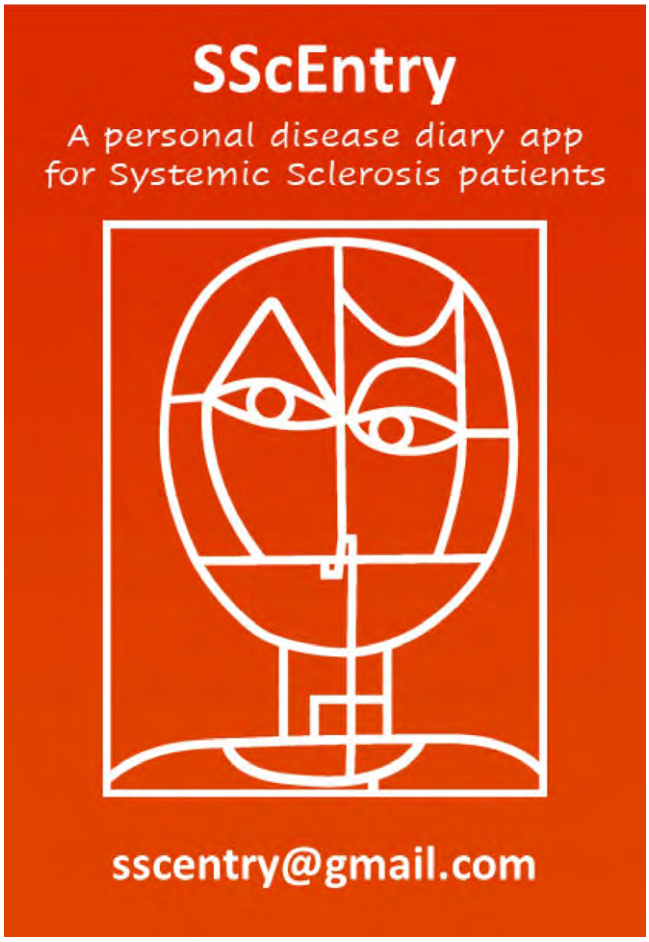


Figure 1. SScEntry logo.

Methods: SScEntry is a smartphone/tablet app designed by rheumatology and computer science engineering specialists in close partnership [3]. A carefully designed user interface (UI), inspired to a social network wall, allows annotating the evolution of symptoms by means of standard clinical investigation methods such as scientifically validated questionnaires. The UI facilitates data collection through speech-based interaction as well as touch and gestures optimized for patients with finger skin lesions and joints impairments. User engagement over the course of time is fostered by: follow-up reminders to update information on the evolution of past events and periodic questionnaires for general health assessment; the integration of symptom photos taken with on-device camera and health data collected from wearable devices; gamification features. Privacy and security have been a primary design concern, with app access protection and full on-device data encryption; no personal data transmission occurs without explicit user consent. SScEntry generates a disease activity summary report, for displaying to the physician during visit or emailing/printing.

Results: SScEntry is ready for Android and iOS smartphones and tablets. All planned features have been implemented (Figure 2). Currently supported languages are English and Italian. Areas of interest include vascular, cutaneous, articular, visceral (gastro-intestinal and cardio-pulmonary) as well as relationship, sexual and working life.



Figure 2. SScEntry features.

Conclusion: Novel Narrative-based Medicine approaches are getting increasing attention to enhance the mutual understanding between patient and physician, reinforcing the therapeutic adherence at the core of healthcare. This is particularly important with chronic and disabling diseases like SSc. Involving patients in disease management with SScEntry will increase their compliance and confidence, with benefits on psychological well-being. Expected benefits for rheumatologists include better evaluation of target therapy and outcomes, as no data on disease activity is lost during the patient clinical history.

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Disclosure of Interests: Emanuela Praino: None declared, Floriano Scioscia: None declared, Crescenzio Scioscia: None declared, Giuseppe Loseto: None declared, Filippo Gramegna: None declared, Saverio Ieva: None declared, Agnese Pinto: None declared, Michele Ruta: None declared, Eugenio Di Sciascio: None declared, Giovanni Lapadula: None declared, Florenzo Iannone Consultant of: Speaker and consulting fees from AbbVie, Eli Lilly, Novartis, Pfizer, Roche, Sanofi, UCB, MSD, Speakers bureau: Speaker and consulting fees from AbbVie, Eli Lilly, Novartis, Pfizer, Roche, Sanofi, UCB, MSD

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THU0629-HPR COULD THE ASAS HEALTH INDEX BE A USEFUL INSTRUMENT IN ASSESSING PATIENTS WITH PSORIATIC ARTHRITIS?

I. Morante Bolado[1], E. Aurrecoechea[1], I. Villa-Blanco[1], M. Santos Gómez[1], L. Riancho-Zarrabeitia[1], J. L. Martín-Varillas[1], R. Queiró Silva[2]. [1]*Sierrallana Hospital, Torrelavega, Spain*; [2]*Central University Hospital of Asturias, Oviedo, Spain*

Background: At present, there is a growing tendency to use instruments that capture, in the best possible way, the impact that the spondyloarthritides (SpA) generate on patients´ lives. For that purpose, tools such as the Psoriatic Arthritis Impact of Disease (PsAID), for psoriatic arthritis (PsA), and the Assessment of SpondyloArthritis international Society-Health Index (ASAS-HI), for SpA, have been recently developed and validated. However, the performance of the ASAS-HI to assess the impact of disease in psoriatic arthritis is barely known.

Objectives: To determine the possible application of ASAS HI to assess PsA by comparing its results to other PsA measurement tools.

Methods: In this observational, cross-sectional study, 89 consecutive patients with PsA (CASPAR criteria) were included. The convergent validity of ASAS-HI (Spearman's rho) and its discriminative validity (ROC curves) was analyzed against other PsA measures (DAPSA and PsAID).

Results: ASAS HI showed a high convergent validity both against DAPSA (rho 0.78, p <0.0001) and PsAID (rho 0.80, p <0.0001). PsAID and DAPSA also showed high convergent validity (rho 0.79, p <0.0001). ASAS HI showed a high discriminative capacity for both DAPSA remission [optimal criterion ≤ 2, area under the ROC curve 0.92 (95%CI: 0.85-0.97), sensitivity 73%, specificity 94%, p < 0.0001] (fig 1) and DAPSA low activity state [optimal criterion ≤ 10.6, area under the ROC curve 0.87 (95%CI: 5-10.6), sensitivity 93%, specificity 61%, p < 0.0001]. PsAID also demonstrated a high discriminative capacity for DAPSA remission [optimal criterion ≤ 0.8, area under the ROC curve 0.94 (95%CI: 0.55-0.95), sensitivity 76%, specificity 100%, p < 0.0001] and DAPSA low activity [optimal criteria ≤ 4.9, area under the ROC curve 0.83 (95%CI: 3.4-5.2), sensitivity 92%, specificity 61%, p < 0.0001].

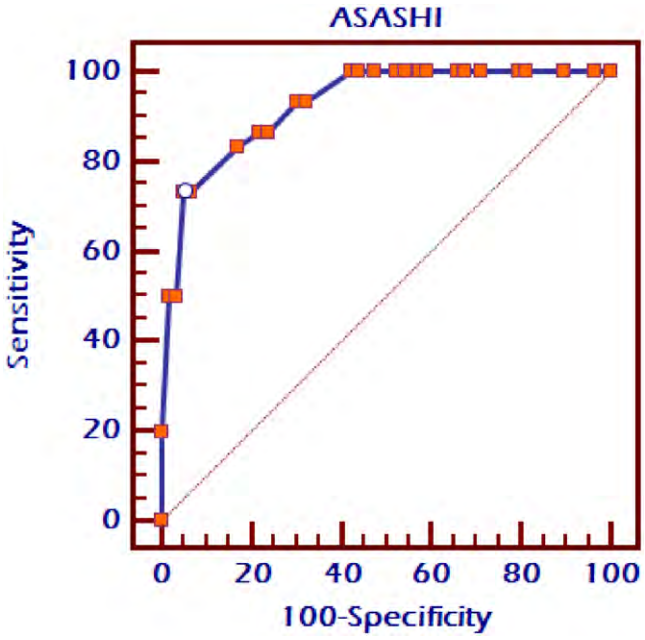


Figure 1. ROC curve analysis between DAPSA remission and ASAS HI

Conclusion: ASAS HI could be used as an appropriate tool in the assessment of patients with PsA.

Disclosure of Interests: Isla Morante Bolado: None declared, Elena Aurrecoechea: None declared, Ignacio Villa-Blanco Consultant of: UCB, Speakers bureau: Novartis, MSD, Lilly, Montserrat Santos Gómez: None declared, Leyre Riancho-Zarrabeitia Grant/research support from: Yes, Speakers bureau: Yes, José Luis Martín-Varillas Grant/research support from: AbbVie, Pfizer, Janssen and Celgene, Speakers bureau: Pfizer and Lilly, Rubén Queiró Silva: None declared

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THU0630-HPR ADVERSE EVENTS, ADVERSE REACTIONS AND MEDICATION-RELATED PROBLEMS ASSOCIATED WITH THE USE OF MEDICINES IN REUMATOID ARTHRITIS

W. Rivero[1], P. Rodriguez[1], M. Cabrera[2], P. Santos-Moreno[3]. [1]*Biomab - Center for Rheumatoid Arthritis, Pharmaceutical Chemist, Bogota, Colombia*; [2]*Biomab - Center for Rheumatoid Arthritis, Data Administration, Bogota, Colombia*; [3]*Biomab - Center for Rheumatoid Arthritis, Rheumatology, Bogota, Colombia*

Background: According to the Third Consensus of Granada of the WHO an adverse event (AE) is an unfortunate situation/event that occurs during the pharmacological treatment of a disease and that may not necessarily be related to the use of one or more medications. An adverse reaction (AR) is an unfortunate situation/event that is directly related to the use of a medicine. A medication-related problem (MRP) is an unexpected result in the treatment with a certain medication, resulting in the appearance of adverse events/reactions.

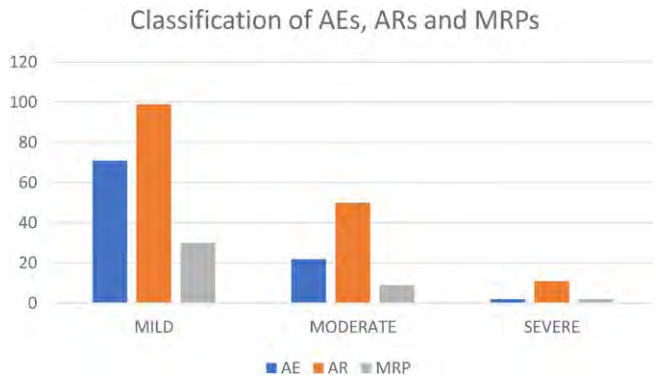
Objectives: Determine and analyze the incidence of adverse events, adverse reactions and medication-related problems in patients treated for rheumatoid arthritis.

Methods: Of a large cohort of approximately 6,000 patients with rheumatoid arthritis (RA) in a specialized center, between 2018 and 2019 pharmaceutical chemist intervention was performed on those patients who reported AEs, ARs and MRPs during their treatment. These reports were made by the treating doctors, the pharmaceutical chemist and directly by the patients to the treating institution. Interaction between medications, adherence to them, patient lifestyles during pharmacotherapy, sociodemographic variables and support relative networks were monitored and investigated. The severity of the events and reactions was evaluated using the Dader method of therapeutic drug monitoring, Morisky Green test to measure adherence and the variables of the Naranjo algorithm in order to characterize them as AEs, ARs or MRPs and determine level of damage

GENDER				TYPE OF EVENT/REACTION			Men
44	15%	convDMARDs	178	BIOLOGICS	118		Women
252	85%	Cardiovascular	5	Cardiovascular	23	p< 0.05	**AGE**
		Dermatological	37	Dermatological	55	p< 0.05	Betw 20 and 40 yo
74	25%	Digestive	84	Digestive	9	p< 0.05	Betw 45 and 50 yo
68	23%	Inflamatory	23	Inflamatory	16		Betw 51 and 70 yo
33	11%	Non-adherence	15	Non-adherence	8		Betw 70 and 79 yo
107	36%	Neurological	8	Neurological	0	p< 0.05	Betw 80 and 99 yo
14	5%	Respiratory	6	Respiratory	7		**TYPE OF THERAPY**
		convDMARDs	181	61%	Biologics	115	39%
CAUSALITY			Probable	236	79%	Possible	46
16%	Unlikely	14	5%				

to the patient. The cases were analyzed in the pharmacovigilance committee of institution and their causality is defined giving solution to the cases and their follow-up according to relevance.

Results: The analysis yielded a cohort of RA 296 patients (44 men-15%, 252 women-85%) who reported AEs, Ars and MRPs. 181 patients (61%) in management with conventional DMARDS and 115 patients (39%) in biological therapy were identified. The highest incidence occurs in ages between 70 and 79 years (36% of cases); more commonly in women (85% of cases); more commonly using convDMARDs (61% of cases), all this being statistically significant ($p < 0.05$). The classification resulted in 66 (22%) AEs, 117 (40%) ARs and 35 (12%) MRPs. The reported causality was probable in 236 cases (79%), possible 46 cases (16%), unlikely: 14 cases (5%) according to the classification of the Naranjo algorithm.



Conclusion: The range of population where AEs, ARs and MRPs most occur are in people over 70 years old; are more common in women and in those who are in conventional DMARDs therapy. The most common AEs, Ars and MRPs with conventional therapy are digestive disorders and in case of biological therapy are dermatological reactions with a mainly probable causality. More studies are needed to clarify these results.

References:

[1] Third Consensus of Granada on Drug Related Problems (DRP) and Negative Outcomes associated with Medication (NOM). Ars Pharm 2007; 48 (1): 5-17

Acknowledgments: This project was carried out by the scientific direction and the pharmacy of Biomab - Center for Rheumatoid Arthritis

Disclosure of Interests: Wilberto Rivero: None declared, Pedro Rodriguez: None declared, Michael Cabrera: None declared, Pedro Santos-Moreno Grant/research support from: I have received research grants from Abbvie, Biopas-UCB, Janssen, Novartis, Pfizer., Speakers bureau: I have been a speaker for Abbvie, Biopas-UCB, Janssen, Lilly, Novartis, Pfizer, Roche, Sanofi.

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THU0631-HPR EARLY ARTHRITIS GLOBAL ASSESSMENT: WHAT DIFFERENCES EXIST BETWEEN PATIENTS AND PHYSICIANS?

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[1]Madrid, Hospital de la Princesa, Madrid, Spain; *[2]Hospital de la Princesa, Madrid, Spain*; *[3]Hospital de La Princesa, Madrid, Spain*

Background: In recent years there is a growing interest in the assessment of rheumatoid arthritis through patient reported outcomes measures (PROMs). Nonetheless, discrepancies in the disease global disease assessment reported by patients (PtGA) or physicians (PhGA) have been previously described.

Objectives: Our aim was to evaluate differences between PtGA and PhGA and their predictors in an early arthritis cohort.

Methods: Cross-sectional study analyzing data from the baseline visit of patients included in the PEARL study (Princess Early Arthritis Register Longitudinal Study) in which demographic, laboratory and clinical characteristics including PtGA and PhGA (0-100 mm) are systematically collected.

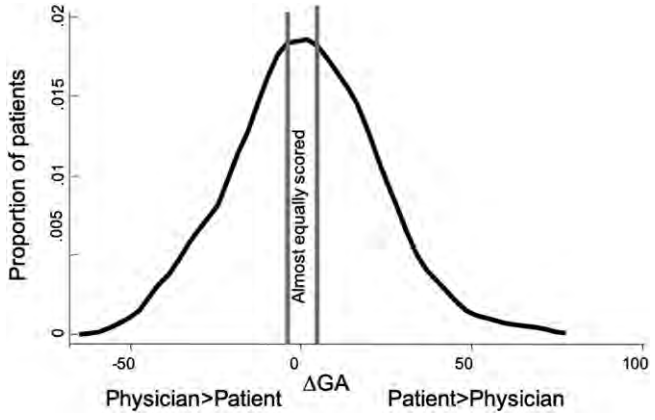
The main variable was the difference between PtGA and PhGA (ΔGA). The descriptive analysis was performed using the Kruskal-Wallis, Mann-Whitney or Pearson correlation tests as appropriate.

A multivariate linear regression model was developed with ΔGA as a dependent variable. All those predictors available at the baseline visit reaching a $p < 0.15$ in the univariate analysis were included in the initial model. The final one was obtained through the progressive elimination of those variables not showing an improvement in the model as assessed by the adjusted R^2 parameter considering those that had a $p > 0.15$. To categorize the dependent variable, differences between PtGA and PhGA were considered relevant when greater than 5 points.

Results: 530 patients were included, 422 (79.6%) were women with a mean age of 55.3 +/- 16 years, 21.2% current smokers, 54% and 50.4% rheumatoid factor and anti-CCP positive respectively. A 43.3% had moderate activity and 33.6% high, measured by DAS28-VSG.

The median of ΔGA was 4, (interquartile range; -10 to 18; see figure 1). In 22% of the cases patients and physicians scored the same, in 46.5% the patients' scores were higher and physicians' were so in 31.5% of the cases.

The variables that explained ΔGA after adjusting the multivariate model were pain [β=0.36 (95%CI 0.28 to 0.44)], number of swollen joints [β= -3.19 (95%CI -3.7 to -2.7)] and ESR [β=-0.11 (95%CI -0.2 to -0.03)]. Pain had a greater influence on patients' opinion while the number of swollen joints and ESR were more relevant for physicians. Other variables such as race, marital status, profession, sex, smoking, seropositivity or disease activity were not relevant in the prediction of ΔGA.



Conclusion: In our cohort, disagreements between PtGA and PhGA were observed. Patients scored higher based on painful perception and physicians did so relying on objective evidence of inflammation.

Disclosure of Interests: Cristina Valero: None declared, Sebastian C Rodriguez-García Speakers bureau: Novartis Farmaceutica, S.A., Merck Sharp & Dohme España, S.A., Sanofi Aventis, UCB Pharma, Noelia García Castañeda: None declared, Juan Pablo Baldivieso: None declared, Esther Patiño: None declared, Ana Ortiz: None declared, Isidoro González-Álvaro Grant/research support from: Roche Laboratories, Consultant of: Lilly, Sanofi, Paid instructor for: Lilly, Speakers bureau: Abbvie, MSD, Roche, Lilly

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THU0632-HPR DETERMINANTS OF HAPPINESS AND QUALITY OF LIFE IN PEOPLE WITH SYSTEMIC SCLEROSIS: A STRUCTURAL EQUATION MODELLING APPROACH

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Background: In recent years more attention has been given to patients reported outcomes (PROs). Systemic sclerosis (SSc) is no exception. As there is no effective treatment or cure to SSc, it is important to recognize the relevance to patients of the different features of the disease to improve quality and enjoyment of life: the ultimate targets of therapy. Remarkably lacking in PROs is the evaluation of the overall perspective of subjective well being, equivalent to 'happiness' or "positive psychological dimensions".

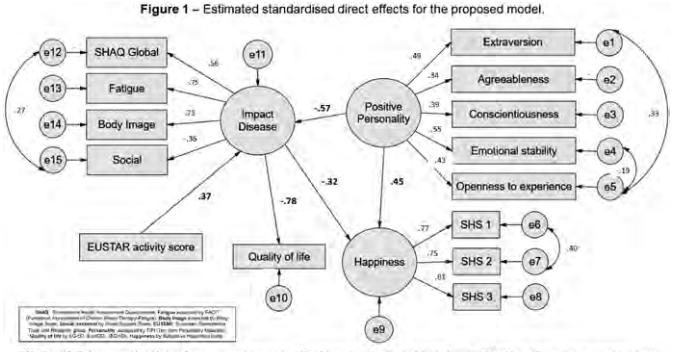
Objectives: To examine the determinants of happiness and quality of life (QoL) in patients with SSc with emphasis on disease activity, disease impact and personality traits.

Methods: This is an observational, cross-sectional and multicenter study from six rheumatology clinics in Portugal. A total of 113 patients with SSc with a complete set of data on disease activity, disease impact, personality, quality of life and happiness were included.

Structural equation modelling (latent variable structural model) was used to estimate the association between the variables using a maximum likelihood estimation with Satorra-Bentler's correction and performed with STATA® 15.0. Two hypotheses were pursued: H1 – Disease activity and impact of disease are negatively associated to overall QoL and happiness; H2 – 'Positive' personality traits are related to happiness both directly and indirectly through perceived disease impact.

Results: Results obtained in the structural equation measurement model indicated a good fit [$\chi 2/df=1.44$; CFI=0.93; TLI=0.90; RMSEA=0.06] and supported all driving hypotheses (Figure 1). Happiness was positively related to 'positive' personality (β=0.45, p=0.01) and, to a lesser extent, negatively related with impact of disease (β=-0.32; p=0.01). This impact, in turn, was positively related to EUSTAR activity score (β=0.37; p<0.001) and mitigated by 'positive' personality traits (β=-0.57; p<0.001). Impact of disease had a much stronger relation with QoL than with happiness (β=-0.78, p<0.001). Quality of life and happiness had no statistically significant relationship.

Figure 1 – Estimated standardised direct effects for the proposed model.



Conclusion: Optimization of Qol and happiness in people with SSc requires effective control of the disease process. Personality and its effects upon the patient´s perception of the disease impact, seems to play a pivotal mediating role in these relations and should deserve paramount attention if happiness and enjoyment of life is taken as the ultimate goal of health care.

Disclosure of Interests: Tânia Santiago: None declared, Eduardo Santos: None declared, Ana Catarina Duarte: None declared, Patrícia Martins: None declared, Marlene Sousa: None declared, Franscisca Guimarães: None declared, Soraia Azevedo: None declared, Raquel Ferreira: None declared, Miguel Guerra: None declared, Ana Cordeiro Consultant of: Ana Cordeiro has acted as a consultant for Roche, Speakers bureau: Ana Cordeiro has received speaker fees from Boehringer Ingelheim, Lilly, and Vitoria, Inês Cordeiro: None declared, Sofia Pimenta: None declared, Patrícia Pinto: None declared, Maria Joao Salvador: None declared, José Antonio P. da Silva Grant/research support from: Pfizer, Abbvie, Consultant of: Pfizer, AbbVie, Roche, Lilly, Novartis

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THU0633-HPR CORE MUSCLE ENDURANCE IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: It is stated that the muscles responsible for spinal stability around the trunk show long-term activity at low intensity in daily life, therefore, endurance insufficiency can cause loss of functionality and spinal stabilization and may induce pain (1).

Objectives: The primary purpose of this study was to compare the core muscle endurance of individuals with AS with the core muscle endurance of healthy individuals. The secondary aim of the study was to examine the association between core muscle endurance and balance, disease activity, spinal mobility, functional status, physical activity level and fatigue in individuals with AS.

Methods: The research is a cross-sectional study. 41 patients with AS and 40 healthy controls were included in the study. The core muscle endurance of both groups was assessed with trunk extension test, trunk flexion test, right and left side plank tests (2). In addition, in the AS group relationship between core endurance and balance, thoracic kyphosis angle, disease activity, functionality, spinal mobility, physical activity and fatigue was examined. Balance was evaluated with BIODEX Balance Systems and thoracic kyphosis angle was evaluated with a digital inclinometer. Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Metrology Index (BASMI), International Physical Activity Questionnaire (IPAQ), Fatigue Severity Scale (FSS) were used to assess disease activity, functionality, spinal mobility, physical activity and fatigue respectively.

Results: Significant differences were found between AS group and control group in core endurance were summarized in Table 1. Additionally, significant relationships were observed between core endurance and all the assessed parameters except thoracic kyphosis angle (p<0.05), (Table 2).

Table 1. Comparision of Core Endurance between AS and Control Groups

	AS Group (n=41) Median (IQR)	Control Group (n=40) Median (IQR)	*P*
Trunk Extensor Test (sec)	44.0 (12.0–77.5)	98.25 (63.75-120.0)	**<0.001**
Trunk Flexor Test (sec)	41.0 (15.0–66.0)	93.0 (55.85-120.0)	**<0.001**
Dominant Side Plank Test (sec)	29.0 (9.8–62.0)	43.27 (28.57–68.25)	**0.046**
Non-Dominat Side Plank Test (sec)	32.0 (10.0–61.32)	41.25 (25.0- 62.37)	0.092

p>0.05, Mann-Whitney U Test; AS: Ankylosing Spondylitis, IQR: Interquartile Range sec: seconds

Table.2 Association between core endurance and other parameters

	Trunk Extensor Test	Trunk Flexor Test	Dominant Side Plank Test	Non-Dominant Side Plank Test
Pain (VAS)	**-0.535***	**-0.339***	**-0.369***	-0.203
Stiffness (VAS)	**-0.496***	-0.234	**-0.377***	0.224
Overall Stability Index	**-0.480***	**-0.488***	**-0.725***	**-0.702***
BASFI	**-0.505***	**-0.441***	**-0.562***	**-0.574***
BASMI	**-0.587***	**-0.390***	**-0.613***	**-0.501***
BASDAI	**-0.468***	-0.202	**-0.433***	**-0.345***
Kyphosis Angle(°)	-0.262	-0.287	-0.215	-0.258
IPAQ	**-0.354***	**-0.355***	**-0.523***	**-0.451***
FSS	**-0.545***	**-0.445***	**-0.542***	**-0.502***

*: Spearman's Correlation Coefficient (rho), p<0.05; VAS: Visual Analog Scale, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, BASFI: Bath Ankylosing Spondylitis Functional Index, BASMI: Bath Ankylosing Spondylitis Metrology Index, IPAQ:International Physical Activity Questionnaire, FSS: Fatigue Severity Scale

Conclusion: Core muscle endurance is lower in patients with AS and it is in relation with many factors regarding the disease. The use of these tests may provide additional information about the patients' situation for clinicians.

References:
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THU0634-HPR KNEE EXTENSOR MUSCLE STEADINESS IN RELATION TO MAXIMAL TORQUE AND PHYSICAL FUNCTIONING IN PATIENTS WITH KNEE OSTEOARTHRITIS

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Background: Osteoarthritis (OA) of the knee is characterized by knee pain and limitations in daily activities. Muscle weakness is associated with these characteristics, quantified as maximal voluntary muscle torque (MVT). The quality of muscle contraction is presented by fluctuations observed on a torque-time curve and the extent of these fluctuations is referred to as muscle steadiness. Whether muscle steadiness is associated with maximal muscle torque and consequently with pain and activity limitations is unknown.
Objectives: To determine the association of knee extensor muscle steadiness with MVT and to explore the association of muscle steadiness with physical functioning in subjects with knee OA.
Methods: Baseline data of 172 patients out of 177 patients with knee OA, who participated in the VIDEX trial (trial registration number, NL47786.048.14), were used for this study. Maximal voluntary knee extension torque (MVT) was assessed using an isokinetic dynamometer. Torque-time curve data were processed into (i) coefficient of magnitude of torque variance (CV) in percentage (%), (ii) frequency of torque variance as peak power frequency (PPF) in Hertz (Hz) and (iii) MVT in Newton meters (Nm). Physical functioning was assessed using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) questionnaire, the Get-Up & Go (GUG) test, the 6-minute walk test (6MWT) and the Stair climb up & down test. Correlation and Regression analyses were performed to determine associations. Sex, age, BMI, KL-grade, knee alignment and pain were considered as potential confounders.
Results: Lower CV and PPF, reflecting better muscle steadiness, were significantly associated ($p< 0.01$ and $p<0.05$, respectively) with higher MVT, but associations were weak. Regression analyses showed a significant association of lower CV with better physical functioning on the WOMAC ($p<0.05$), also after correction for relevant confounders. The association with WOMAC was confounded by pain, but not by sex, age and BMI. No associations of CV with the GUG test, the 6MWT and the Stair climb up & down test were found. PPF was not significantly associated with physical functioning.
Conclusion: This is the first explorative study of muscle steadiness in relation to physical functioning in knee OA patients. Muscle steadiness is, to some extent, related to better physical functioning, but this is not consistent across all measures of physical functioning in this study. There seems to be some relationship, but it is weak and needs further exploration. No previous studies comparing clinical scores to muscle steadiness in knee OA were found to compare our results. Studies on muscle steadiness are needed to improve our understanding on this aspect of muscle torque.
References: N/A
Disclosure of Interests: Anuja Satam: None declared, Marike van der Leeden: None declared, Arjan de Zwart: None declared, Simon Verberne: None declared, Jim Schrijvers: None declared, Joost Dekker: None declared, WIllem Lems Grant/research support from: Pfizer, Consultant of: Lilly, Pfizer, Jaap Haarlaar: None declared, Martin van der Esch: None declared
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THU0635-HPR PREVALENCE AND CLINICAL CHARACTERISTICS OF NEOPLASIA AMONG A COHORT OF PATIENTS WITH SYSTEMIC SCLEROSIS

J. L. Tandaipan Jaime[1], E. Riera Alonso[1], N. Gimenez Gomez[2], G. Ghio[1], L. Berbel Arcobe[1], S. Martinez Pardo[1]. *[1]Hospital Universitari Mutua Terrassa, Rheumatology, Terrassa, Spain*; *[2]Hospital Universitari Mutua Terrassa, Research Support Department, Terrassa, Spain*

Background: Patients with Systemic Sclerosis (SSc) have increased risk of malignancy compared to general population. The specific risk factors and underlying physiopathological mechanisms are still unknown, although some studies suggest that a relationship between malignancies and certain antibodies can exist. Lung, breast and hematological cancers are the most frequently seen among these patients.
Objectives: To describe the prevalence of malignancies in a cohort of SSc patients and analyze the epidemiological, clinical and immunological characteristics
Methods: A retrospective observational study was conducted at a tertiary-level university hospital, including a cohort of patients with SSc (ACR/EURLAR 2013 criteria). The main variable was neoplasia prevalence and also, malignancy type, age, evolution of the SSc at the time of diagnosis and mortality were collected. Regarding SSc, demographic data, clinical and immunological characteristics, organ involvement, capillaroscopy findings and presence of other autoimmune diseases were collected.
Results: A 15% of the 98 patients with SSc presented malignancies (80% women). The mean age at the time of diagnosis was 57±15 years old (table 1). The frequency of cancer was: 40% breast, 13% colon, 7% ovary and lung. 2 patients died (1 breast, 1 lung). The limited subtype (lSSc) was the most frequent (80%) and 33% showed overlap syndrome (26% Sjögren syndrome). Regarding clinical manifestations: 67% had telangiectasia, 33% pitting scars, joint and digestive involvement. Most frequently seen antibodies were: 67% anti centromere (ACA) and 20% anti topoisomerase (ATA). None of the patients presented anti-ARN polimerase III (ARN-pol), and 13% had none of them (triple negative). Active and early capillaroscopy patterns were seen in a 46% and 27%. SSc and cancer were diagnosed in less than 5 years difference among a 33% of the cohort. A relationship between age and cancer was detected (p=0,042). Patients with neoplasia were a mean of 10 years older than those without malignancies (IC95%: 1-19 years)

Table 1.

	SSc with neoplasia n= 15(%)	SSc without neoplasia n= 83(%)
Female	12 (80)	76 (92)
Mean age*(n; DE)	57(15)	52(17)
Pre-scleroderma	1 (7)	11 (13)
Limited	12 (80)	54 (65)
Diffuse	2 (13)	12 (15)
SINE	0	6 (7)
Overlap syndrome	5 (33)	14 (17)
Sjögren	4 (27)	10 (12)
MCTD	1 (7)	2 (2)
Rheumatoid Arthritis	1 (7)	3 (4)
Myositis	1 (7)	0
Clinical manifestations		
Telangiectasia	10 (67)	41 (49)
Pitting Scars	5 (33)	11 (13)
Joint	5 (33)	27 (33)
Digestive	5 (33)	33 (40)
Digital ulcers	4 (27)	11 (13)
Calcinosis	4 (27)	12 (14)
ILD	3 (20)	16 (19)
PAH	3 (20)	8 (10)
Cardiac	3 (20)	4 (5)
Muscular	2 (13)	3 (4)
Puffy Fingers	2 (13)	24 (29)
Renal	0	2(2)
Antibodies		
ACA	10 (67)	46 (55)
ATA	3 (20)	12 (14)
Anti-ARN	0	4 (5)
Triple negative	2 (13)	23 (28)
Capillaroscopy		
Early	4 (27)	19 (23)
Active	7 (46)	39 (47)
Late	0	3 (4)
Treatment		
Calcium antagonists	11 (73)	52 (63)
PPIs	7 (46)	33 (40)
Corticosteroids	8 (53)	24 (29)
DMARD	5 (33)	26 (31)

*P<0,05 test t-student
MCTD (Mixed Connective Tissue Disease), ILD (Interstitial Lung Disease), PAH (Pulmonary Artery Hypertension), Triple negative (anti ARN, ACA and ATA negative antibodies), PPI (Proton Pump Inhibitor), ACE inhibitors (Angiotensin Converting Enzyme inhibitors), ARBs (Angiotensin II Receptor Blockers), DMARD (Disease-Modifying Anti-Rheumatic Drugs).

Conclusion: Our study showed a similar prevalence of the most frequent neoplasia among patients with SSc compared to general population (around 15%). This prevalence is similar to other series. The only epidemiological factor related to neoplasia was the age; a major proportion of lSSc was detected but without statistical significance. In a third of the patients there were less than 5 years

of difference between cancer and SSc diagnosis. No association was found between neoplasia and certain antibodies. We recommend further studies to evaluate the relationship between SSc and cancer.

Disclosure of Interests: None declared

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THU0636-HPR REMS TECHNOLOGY APPLIED TO RHEUMATIC DISEASE

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Background: Many Rheumatic disease such as rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, systemic lupus erythematosus, dermatomyositis/polymyositis and vasculitis are characterised by osteoporosis and fragility fractures. Inflammatory cytokines, steroid treatment, immobilization and reduced physical activity due to joint pain and muscle weakness are considered the major risk factors for the development of low bone mineral density in these diseases.Many evidences have highlighted the role of pro-inflammatory cytokines (TNF-a, IL-1, IL-6, IL-7, IL17) in bone homeostasis regulation.Chronic inflammation is often characterized by an imbalance between bone formation and resorption, with a clear prevalence of osteoclastogenesis which is a strong determinant in rheumatic diseases bone loss.

Objectives: The aim of this study is to evaluate the REMS (Radiofrequency Echographic Multi-Spectrometry) technology in rheumatologic patients, compared to DEXA currently recognised as the gold standard for the evaluation of bone mineral density.

Methods: Twenty female patients (mean age 60.6 ±14.41 years) with different rheumatologic diseases were considered. Each patient underwent a lumbar spine and hip examination performed by DEXA and REMS technology. In particular, after a quality control to assess that both the exams were performed correctly, 18 lumbar and 20 femoral exams (DEXA vs REMS) were compared.

Results: As Expected the exams performed show a good diagnostic match (>60%LS and >85% FEMORE). The tests that didn't show diagnostic concordance were those affected by arthrosis processes (greater on the Spine). The REMS T-score values were lower than those obtained with the DXA method.

Conclusion: These results show how REMS technology can discriminate patients with osteoporosis as much as DEXA technology. The REMS technology can be a diagnostic option especially in patients with rheumatologic diseases that cause alterations in the spine reducing the diagnostic sensitivity of DXA technology.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.6500

THU0637-HPR THE ASSOCIATION BETWEEN THE RECALL PERIOD AND THE AMOUNT OF INFORMATION ABOUT REPORTED ADVERSE DRUG REACTIONS BY PATIENTS USING BIOLOGICALS

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Background: In order to monitor the safety of medicines pharmacovigilance, it is important that patients report their adverse drug reactions (ADRs). Theoretically, the quality of the reported information might be affected by the elapsed time between the onset of the ADR and the moment of reporting. Real-life evidence demonstrating a negative relationship between this recall period and the quality of reported ADRs is however lacking.

Objectives: To assess the effect of recall period on the amount of information that patients report about their ADR (information density) in patients using a biologic for an immune-mediated inflammatory disease (IMID).

Methods: The Dutch Biologic Monitor is a multi-center cohort ADR monitoring system collecting data on reported ADRs by patients using a biologic for an IMID. Per patient, every first unique reported ADR between 1 February 2017 and 1 September 2019 was eligible. ADR reports were selected by stratified random sampling based on length of recall period and biologic. The recall period was defined by the number of days between the onset and reporting date of the ADR. The amount of information in an ADR report (information density) was determined based on eleven domains: specification, location, frequency, time-to-onset, course, causality, cause or consequence, health care professional (HCP) visits, HCP action, patient action and ADR burden. Information density was calculated by the number of reported domains divided by the number of domains deemed relevant in the ADR report. The association between the information density of the ADR reports and different recall periods was compared using a one-way ANOVA test. One-way ANOVA and independent t-tests were used to assess the impact of gender, age, type biologic and burden of the ADR on the information density of the reported ADRs.

Results: Out of 1109 reported ADRs by 531 IMID patients, we included 402 ADR reports of 294 patients (55%) (see table 1). Included reports were equally divided over seven different recall periods: 0-1, 1-2, 2-4, 4-8, 8-12, 12-26 and 26-52 weeks. Results have shown no association between the information density in patient-reported ADRs and the length of recall period (p=0.805) (figure 1). However, the proportion of reported information about HCP visits for the ADR increased with increasing recall period: 0-1 week (14%), 1-2 weeks (24%), 2-4 weeks (34%), 4-8 weeks (40%), 8-12 weeks (48%), 12-26 weeks (50%) and 26-52 weeks (46%).

Table 1. Characteristics of included patients with adverse drug reactions

Characteristics (N=294)	N (%)
Gender (female)	202 (69%)
Age (years) (mean ± SD)	53 ± 13
Smoking	59 (20%)
BMI (kg/m^2) (mean ± SD)	25.7 ± 5.3
Reported ARDs (mean ± SD)	1.4 ± 0.8
Indication	
Rheumatoid arthritis	129 (44%)
Psoriatic arthritis	51 (17%)
Axial spondyloarthritis	43 (15%)
Crohn's disease	42 (14%)
Other indications	29 (10%)
Biologic	
Adalimumab	97 (33%)
Etanercept	72 (24%)
Infliximab	27 (9%)
Tocilizumab	16 (5%)
Secukinumab	15 (5%)
Rituximab	14 (5%)
Other biologics	53 (18%)

Female patients reported more information about their ADR (p=0.002), whereas the patient's age was not associated with information density (p=0.221). Etanercept (ETA) users report significantly more information than adalimumab (ADA) users (p=0.019). The number of patients using other biologics was too low for further analysis. A higher ADR burden tended (p=0.120) to result in more reported ADR information (figure 2).

Conclusion: The length of recall period did not affect the amount of information that patients report about their ADR(s). The recall period was longer for patients reporting information about their HCP visit. Furthermore, female patients tend to report more information about their ADR than male patients and ETA-users tend to report more than ADA-users.

Figure 1: No effect of length of recall period on information density in patient-reported ADRs

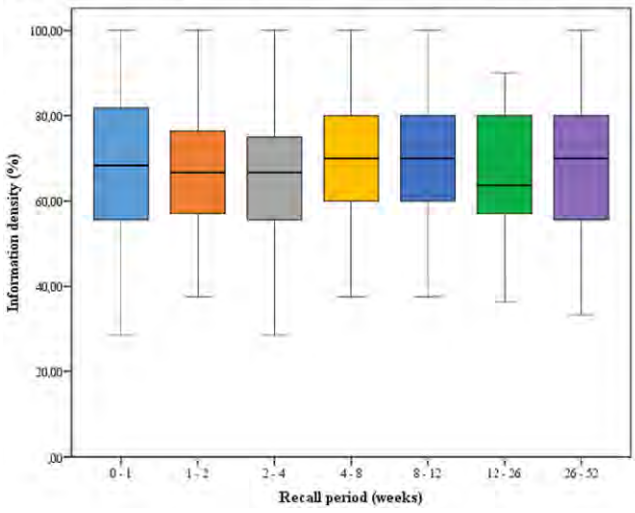
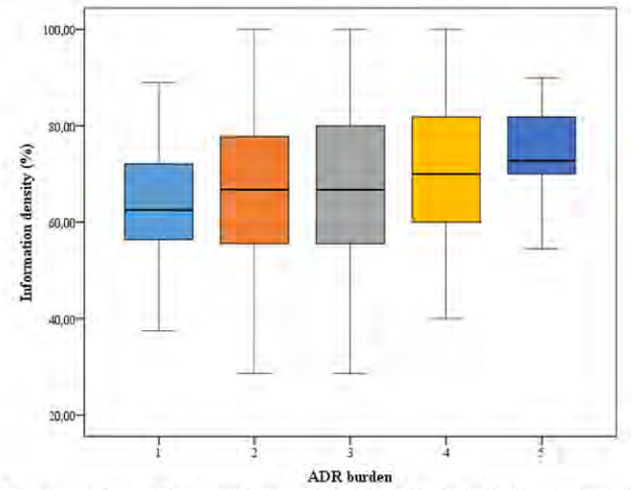


Figure 2: The effect of ADR burden on information density in patient-reported ADRs



Patients reported their ADR burden on a 5-point scale, ranging from 1 (no burden) to 5 (very high burden)

Disclosure of Interests: Alexandra Laurijssen: None declared, Jette van Lint: None declared, Bart van den Bemt Grant/research support from: UCB, Pfizer and Abbvie, Consultant of: Delivered consultancy work for UCB, Novartis and Pfizer, Speakers bureau: Pfizer, AbbVie, UCB, Biogen and Sandoz., Lilian Beijer: None declared, Naomi Jessurun: None declared

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THU0638-HPR PHYSICAL ACTIVITY LEVELS OF RADIOGRAPHIC AND NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS PATIENTS

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Background: It is known that cardiovascular disease risk is increased in chronic inflammatory diseases. Additionally, regular exercise is one of the main components of the management of patients with axial spondyloarthritis (axSpA). However, it was reported that axSpA patients do not meet recommended physical activity levels. It is still unknown, whether the disease subgroups of axSpA play a role in participating in physical activity.

Objectives: To compare the physical activity levels among radiographic, non-radiographic axSpA patients, and healthy controls.

Methods: Thirty-three patients with radiographic axSpA (23 [70%] male), 33 patients with non-radiographic axSpA (23 [70%] male) and 33 age and sex matched healthy controls (23 male [70%]) were included in the study. axSpA patients were assessed regarding to disease activity (Bath Ankylosing Spondylitis Disease Activity Index; BASDAI), functional status (Bath Ankylosing Spondylitis Functional Index; BASFI), spinal mobility (Bath Ankylosing Spondylitis Metrology Index; BASMI). Physical activity level of all subjects was measured by using an accelerometer (Actigraph wGT3X-BT) which was worn on the waist for seven consecutive days.

Results: The groups were similar in terms of physical characteristics (age and body mass index) (p>0.05). Disease related characteristics (BASMI, BASFI, BASDAI) were comparable between radiographic and non-radiographic axSpA patients (p>0.05). Radiographic axSpA patients showed lesser physical activity compared to non-radiographic axSpA patients and healthy controls (p<0.05, Table 1). There is no difference between non-radiographic axSpA patients and healthy controls regarding the physical activity levels (p>0.05).

Table 1. Comparison of Groups

	Radiographic axSpA (n: 33) Median (IQR 25/75)	Non-radiographic axSpA (n: 33) Median (IQR 25/75)	Healthy Controls (n:33) Median (IQR 25/75)	p
Physical Characteristics				
Age (years)	41.0 (32.0/46.0)	37.0 (32.0/40.0)	33.0 (28.0/41.0)	0.093*
BMI (kg/m^2)	26.0 (22.9/29.6)	26.3 (25.4/28.7)	24.8 (22.3/26.9)	0.064*
Disease Related Characteristics				
BASMI (score)	2.1 (1.5/3.9)	1.5 (1.1/2.0)	NA	0.051**
BASFI (score)	2.4 (0.7/3.9)	1.2 (0.6/2.9)	NA	0.267**
BASDAI (score)	3.6 (1.6/5.8)	2.4 (1.4/5.4)	NA	0.519**
Physical Activity Level				
Light Physical Activity (min)	2198.0 (1377.0/2658.0)	2576.0[#] (1858.0/3690,0)	2200.0 (1846.0/2762.0)	**0.015***
Medium Physical Activity (min)	188.0 (109.0/304.0)	264.0 (216.0/446.0)	363.0 (267.0/491.0) [##]	**p<0.001***
Vigorous Physical Activity (min)	0.0 (0.0/0.1)	2.0 (0.0/12.0)	4.0 (0.0/19.0)[##]	**0.009***
Total Step Count (n)	42481.0 (33651.0/57047.0)	62872.0 (53075.0/80160.0) [#]	69710.0 (59943.0/85894.0) [##]	**p<0.001***

*Kruskal-Wallis Test, **Mann-Whitney U Test, [#]: difference between radiographic axSpA and non-radiographic axSpA, [##]: difference between radiographic axSpA and healthy controls, IQR 25/75: Interquartile range 25/75, BMI: Body Mass Index, BASMI: Bath Ankylosing Spondylitis Metrology Index, BASFI: Bath Ankylosing Spondylitis Functional Index, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, NA: Not Applicable, p<0.05.

Conclusion: The results of the present study suggest that radiographic damage in axSpA may alter the physical activity levels. Every effort should be taken to increase physical activity levels in axSpA patients, especially in radiographic cases.

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Disclosure of Interests: None declared

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THU0639-HPR GOUT DISEASE ACTIVITY SCORE – FURTHER EVALUATION OF CONSTRUCT AND CONVERGENT VALIDITY

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Background: A new instrument for measuring of disease activity in gout is a 4-variable gout disease activity score (GAS), announced in 2016 (1). GAS calculates self-reported number of attacks in the last year, patient visual analogue scale (VAS) for gout severity, serum uric acid level (mg/dL) and the number of tophi, and has shown good psychometric properties (1).

Objectives: to test GAS in patients with gout and to evaluate its construct and convergent validity

Methods: 74 patients with gout were evaluated successively, as they entered the Institute of Rheumatology in Belgrade. Construct validity was assessed by associationos between GAS and SF-36, using Spearman's rank correlation coefficients. Convergent validity was evaluated by testing the ability of the GAS score to distinguish between patients grouped by perceived disease severity, perceived general health and physicians perceived disease severity by using Kruskal–Wallis one-way analysis of variance. Computer statistic program SPSS 20.0 was used for data evaluation.

Results: For the construct validity, significant correlations were found between GAS and SF-36 subscales, specially for Body pain (r=-0.725), Physical functioning (r=-0.684) and Physical limitations (r=-0.563), whereas Social functioning, Mental health, and Vitality were less affected. Correlation between GAS and Physical component scale of the SF-36 was the most prominent (r=-0.780). For the convergent validity, significant differences in GAS scores were found between patients grouped by perceived general health (p<0,01) and perceived disease severity (p<0,01), and by doctors perceived disease severity (p<0,01), demonstrating the ability of the GAS to distinguish between subgroups of patients.

Conclusion: GAS has shown good psyshometric properties in Serbian cohort of patients and has proved to be valid and reliable tool for use in clinical practice.

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Table 1. Characteristics of the examined patients

Patient characteristics	Mean	Std deviation	95% Confidence Interval
Age (yrs)	59,27	10,22	56,90-61,51
Disease duration (yrs)	8,75	7,72	7,01-10,49
Number of attacks/last year	3,89	3,74	3,08-4,71
Weight (kg)	91,44	(17,14)	86,52-96,37
Height (cm)	176,73	(7,95)	174,45-179-02
Body Mass Index (kg/m2)	29,14	(4,1)	27,96-30,32
Waist circumference (cm)	102,69	9,56	100,35-105,05
Systolic blood pressure	135,44	14,48	130,43-140,50
Diastolic blood pressure	86.74	9.86	82,31-89,22
Serum urate level (µmol/ L)	485,6	102,09	449,94-521,20
	No	%	
Male	71	95,9	
Monoarthritis	29	39,2	
Olygoarthritis	31	42,1	
Polyarthritis	14	18,9	
Presence of tophi	17	23	

Disclosure of Interests: None declared
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THURSDAY, 04 JUNE 2020

HPR Professional education, training and competencies

THU0640-HPR GENDER DISPARITY IN AUTHORSHIP OF CLINICAL PRACTICE GUIDELINES IN RHEUMATOLOGY

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Background: Women are generally less represented as first author among original medical researches and clinical guidelines. Indeed, women are first authors in only 30% of clinical guidelines published in high impact medical journals. It is not known if a comparable underrepresentation occurs also in rheumatologic guidelines.
Objectives: The aim of the present analysis is to evaluate the representation of female authors in rheumatological guidelines over a period of time between 2004 and 2019.
Methods: We searched PubMed for guidelines published in English in the rheumatological field from 1st January 2004 to 1st January 2019. Gender of each author (man or woman) was identified by use of a minimum of two resources (i.e., author's name and an internet search to identify the author's photograph or gender pronoun).
Results: We found 366 guidelines published between 2004 and 2019 (Table 1: stratified by year of publication and Table 2: stratified by disease). Overall, the proportion of female first authors was 32.0% (95% CI, 28.0% - 35%). After stratification by year of publication the percentage of female first authors was lower in past years compared to recent years. The percentage of female first author increased substantially over the time (Figure 1).

Table 1. Percentage of female and male first author of rheumatological guidelines stratified by years

Years	% FEMALE	%MALE
2004 (n=14)	**21.4**	**78.6**
2005 (n=21)	**23.8**	**76.2**
2006 (n=25)	**32.0**	**68.0**
2007 (n=32)	**37.5**	**62.5**
2008 (n=43)	**20.9**	**79.1**
2009 (n=18)	**33.3**	**66.7**
2010 (n=15)	**6.7**	**93.3**
2011 (n=27)	**25.9**	**74.1**
2012 (n=27)	**25.9**	**74.1**
2013 (n=20)	**48.3**	**51.7**
2014 (n=20)	**25,0**	**75,0**
2015 (n=13)	**46,2**	**53,8**
2016 (n=20)	**45,0**	**55,0**
2017 (n=29)	**51,7**	**48,3**
2018 (n=22)	**40,9**	**59,1**

Table 2. Percentage of female and male first author of rheumatological guidelines stratified by disease

Disease	% FEMALE	% MALE
Osteoarthritis (n=34)	**26.5**	**73.5**
Rheumatoid arthritis (n=96)	**18.8**	**81.2**
Fibromyalgia (n=30)	**20**	**80**
Lupus erythematosus (n=29)	**34.5**	**65.5**
Psoriatic arthritis and Spondyloarthritis (n=73)	**23.3**	**76.7**
Sjogren syndrome (n=5)	**40**	**60**
Gout (n=19)	**10.5**	**89.5**
Systemic sclerosis (n=18)	**16.7**	**83.3**
Polymyalgia and Giant cells' arteritis (n=12)	**0**	**100**
Osteoporosis (n=26)	**30.8**	**69.2**
ANCA associated vasculitides (n=14)	**21.4**	**78.6**
Polymyositis and Dermatomyositis (n=6)	**50**	**50**
Behcet's disease (n=4)	**25**	**75**



Figure 1. Temporal trend of the percentage of first author gender from 2004 to 2019 (male in blue, female in pink)

Conclusion: We found a prevalence of male as first authors of guidelines in the rheumatological field published between January 2004 and January 2019. The EULAR Task Force on Gender Equity in Academic Rheumatology (EULAR GEAR) has been recently established, making an important first step toward gender equity in the authorship of guidelines in the rheumatological fields. Indeed, in the last 15 years we have witnessed an increase in female representativeness. Notwithstanding, efforts should be made to improve the representation of female authors nationally and internationally.
Disclosure of Interests: Giovanni Adami: None declared, Ombretta Viapiana: None declared, Elisabetta Vantaggiato: None declared, Camilla Benini: None declared, Denise Rotta: None declared, Davide Gatti Speakers bureau: Davide Gatti reports personal fees from Abiogen, Amgen, Janssen-Cilag, Mundipharma, outside the submitted work., Maurizio Rossini Speakers bureau: AbbVie, Abiogen, Amgen, BMS, Eli-Lilly, Novartis, Pfizer, Sanofi, Sandoz and UCB
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THU0641-HPR ILLITERACY IS NOT AN OBSTACLE FOR ASSIMILATION OF A PATIENT EDUCATION SESSION ON METHOTREXATE SELF-INJECTION IN RA PATIENTS A PROSPECTIVE PILOT STUDY

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Background: Patient education for RA patients has been shown to improve adherence and self-management of this chronic disease.
Objectives: To assess the impact of illiteracy on assimilation of a patient education session on methotrexate self-injection in RA patients.
Methods: Prospective pilot study that included 27 consecutive patients (81.5% female, mean age 44.4 years, illiteracy rate 40.7%) with RA (median duration of progression of 4 years, mean delay in referral for specialist of 6 months, median duration of methotrexate use of 1 year). The patients benefited from an individual patient education session to learn how to self-inject with methotrexate

subcutaneously. The patient education session was supervised by a nurse and a rheumatologist. A 10-question dichotomous questionnaire was then administered to patients to assess the level of uptake of messages passed during the patient education session. The prevalence of correct answers was compared between illiterate and non-illiterate patients.

Results: The mean duration of patient education session is 13 min.

Table I illustrates the results of the correct responses prevalence and the comparison of correct response rates between illiterate and non-illiterate patients.

Table 1. Prevalence of correct responses and comparison of correct response rates between illiterate and non-illiterate patients.

Questions	N=27	Illiterate		P
		Yes (N=11)	No (N=16)	
1.Do I always have to self-inject on the same day of the week? (%)	96,3	90,9	100	NS
2.Should Methotrexate be protected from light and away from children? (%)	96,3	100	93,7	NS
3.Can I self-inject anywhere on my thigh and belly 5 cm from the navel? (%)	85,2	100	75	NS
4.Is it important to change the injection sites? (%)	70,4	72,7	68,75	NS
5.Do I need to pinch the skin before self-injection? (%)	92,6	100	87,5	NS
6.Can I always use the same needle for each injection? (%)	81,5	90,9	75	NS
7.Do I have to wear gloves to inject Methotrexate? (%)	81,5	90,9	75	NS
8.Do I have to apply an antiseptic product (alcohol, Betadine) to the injection site before self-injecting? (%)	88,9	90,9	87,5	NS
9.Can I use the rest of the MTX ampoule for the next injection? (%)	74,1	81,8	68,7	NS
10.Do I tell my doctor if I have side effects? (%)	100	100	100	NS

Conclusion: This study suggests that illiteracy does not affect the assimilation of information given during a patient education session. These preliminary results should encourage the development of patient education programs in our context where illiteracy rate is high.

Disclosure of Interests: None declared

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THU0642-HPR EVOLUTION OF THE PERCEPTIONS OF RA PATIENTS AFTER EDUCATION PATIENT SESSION TEACHING METHOTREXATE SELF-INJECTION A PROSPECTIVE PILOT STUDY

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Background: Methotrexate is a gold standard for treatment of RA. In our context, RA patients prefer to be injected by paramedics rather than self-injecting. This can be explained by patients' bad perceptions of self-injection or lack of information. Appropriate self-injection education can therefore be an important element in overcoming these obstacles and improving disease self-management.

Objectives: Compare the RA patients' perceptions on methotrexate self-injection before and after a patient education session.

Methods: Prospective pilot study that included 27 consecutive patients (81.5% female, mean age 44.4 years, illiteracy rate 40.7%) with RA (median duration of progression of 4 years, mean delay in referral for specialist of 6 months, median duration of methotrexate use of 1 year). The patients benefited from an individual patient education session to learn how to self-inject with methotrexate subcutaneously. The patient education session was supervised by a nurse and a rheumatologist with a control a week later. Perceptions of the reluctance to self-inject and the difficulties encountered by patients were assessed before the patient education session, after the 1st and 2nd self-injection of methotrexate using a 10 mm visual analog scale. Patients also reported their level of satisfaction (10 mm VAS) after the 1st and 2nd self-injection.

Results: The mean duration of patient education session is 13 min.

Table I compares the evolution of the degrees of reluctance to self-injection, the difficulties encountered, and the satisfaction experienced by the patients.

Table 1. Evolution of RA patients' perceptions on the methotrexate self-injection. (N = 27)

	Before	After the 1st self-injection	After the 2end self-injection	p
VAS reluctance (0-10mm)	6,5 ± 3,6	2,2 ± 2,9	1,0 ± 2,3	<0,0001
VAS difficulty (0-10mm)	7,5 ± 2,6	2,5 ± 2,7	1,0 ± 1,9	<0,0001
VAS satisfaction (0-10mm)	-	8,9 ± 1,8	9,5 ± 1,5	0,002

Conclusion: This study suggests the effectiveness of a methotrexate self-injection patient education session in RA patients. It also highlights the value of patient education in rheumatologic care. A large-scale study is necessary to better interpret and complete these preliminary results from this pilot study.

Disclosure of Interests: None declared

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THU0643-HPR PHYSIOTHERAPISTS' ADHERENCE TO OSTEOARTHRITIS CLINICAL GUIDELINES: A NATIONAL ITALIAN SURVEY.

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Background: Osteoarthritis (OA) is the most prevalent joint disease in the world, and one of the top causes of disability [1]. OARSI and EULAR guidelines recommend non-surgical interventions as first-line interventions for OA [2]. Despite this, only less than 40% of people suffering from OA receive the recommended intervention [3].

Objectives: The aim of this study is to investigate to what extent a population of Italian physiotherapists adhere to the OA-guidelines in their clinical practice.

Methods: A quantitative web-based cross-sectional survey was developed according to the Checklist for Reporting Results of Internet E-Survey. The questionnaire was realised in Italy by a panel of physiotherapists, based on the EULAR, OARSI and NICE OA-guidelines. The questionnaire was delivered using REDCap through the Italian Association of Physiotherapists and the University of Genoa newsletters. The questionnaire was divided into two sections. The first section included 24 statements adapted from the aforementioned guidelines. Participants were asked to express their statement agreement on a scale from 1 (completely disagree) to 5 (completely agree). Participants who partially or totally agreed (score 4-5) were considered to agree with the statements. We defined a ≥ 70% agreement with a statement as consensus. In the second section, a clinical vignette was presented, illustrating an OA clinical case. Participants had to select, from a list of clinical options, how they would manage this case. Participants were classified as 'Delivering', 'Partially delivering' and 'Non-delivering' the recommended intervention, depending on the recommended or not-recommended interventions chosen.

Results: 812 physiotherapists (age: 36±13,59; 48% women) completed the survey between 26 November 2019 and 9 January 2020. The consensus was achieved for 12 sentences (52%) out of 23 (Fig. 1). All the statements focussed on exercise, education, and surgical referral received > 70% of agreement, whereas no consensus was reached for the statements on the clinical diagnostic criteria, for the use of glucosamine or chondroitin products and for the use of topic NSAIDs. In the second section, 20% of the analysed physiotherapists would deliver an intervention in line with OA guidelines and a 20% would carry out an intervention that is partially in line with OA guidelines. Conversely, the 40% of the participants of this survey would include at least a not-recommended intervention, considered, therefore, as 'non-delivering' the recommended intervention (Fig. 2).

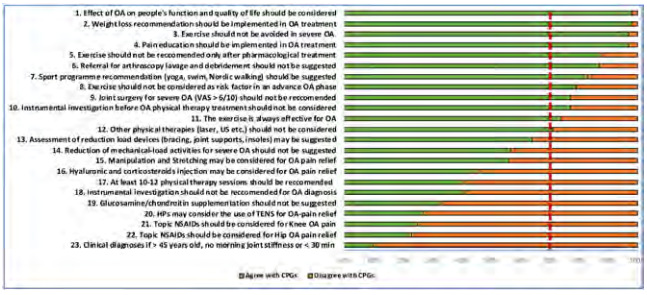


Figure 1. Agreement to Clinical Guidelines (%)

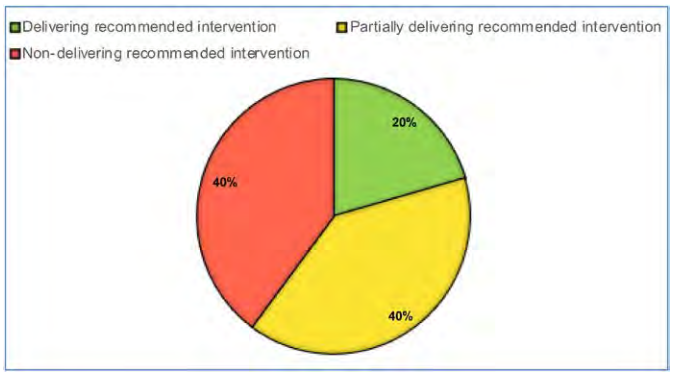


Figure 2. Adherence to Clinical Guidelines (%) reported in the Clinical Vignette

Conclusion: Our findings reveal an overall sub-optimal adherence to OA-guidelines in a sample of Italian physiotherapists. Italian physiotherapists appear to be aware of the importance of exercise and education for patients suffering from OA. Instead, a sub-optimal level of knowledge was found regarding the criteria for OA clinical diagnosis and on the role of other non-surgical interventions in the management of OA. These results identified some gaps between evidence and clinical practice, which may lead to an incorrect management of patients suffering from OA.

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THU0644-HPR TRENDS IN DIAGNOSIS AND TREATMENT OF FIBROMYALGIA AMONG MEXICAN PHYSICIANS.

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Background: Fibromyalgia (FM) is a disease characterized by widespread pain which affects 2-8% of the population. Previous studies have shown lack of awareness of classification criteria and accompanying symptoms of FM, as well as heterogeneity in the management of these patients among both rheumatologist and non-rheumatologist physicians.

Objectives: The objective of this study was to explore the trends in diagnosis and management of fibromyalgia among general practitioners, family physicians, psychiatrists, neurologists and rheumatologists in northeastern Mexico

Methods: We designed an online survey to yield data on perception of FM, knowledge of existing classification criteria including the ACR 1990, ACR 2010, ACR 2010 modified and AATP classification criteria, as well as pharmacologic and nonpharmacologic therapy for the treatment of FM. Participants should have finished their residence at least in 2019. General practitioners, family physicians, psychiatrists, neurologists and rheumatologists were included.

Results: A total of 236 participants were included, most of the participants were general practitioners, 149 (59.3%). Other specialties included were rheumatologists 21 (8.9%), neurologists 18 (7.6%), psychiatrists 8 (3.4%), and family physicians 49 (20.8%). FM was considered a clinical entity by 208 (88.1%) participants. Participants' characteristics are shown in Table 1. Twenty-eight (11.9%) participants didn't know any classification criteria for FM, and 38 (16.1%) participants answered that they didn't use any classification criteria to make a formal diagnosis of FM. The 1990 ACR classification criteria was used the most, 62 (26.3%); closely followed by the 2010 modified ACR classification criteria, 61 (25.8%). A total of 101 (42.8%) participants made a formal diagnosis of FM in the previous year and 179 (75.8%) referred the patient to another specialist. Most patients were referred to a rheumatologist, 126 (53.4%). One-hundred and fifty-eight (66.9%) participants believe rheumatologist should be the main care providers for patients with FM.

Table 1. Participants' characteristics.

Variable	
Age, median (25p-75p)	33 (27-38)
Women, n (%)	203 (86)
Rheumatologists, n (%)	21 (8.9)
General practitioners, n (%)	140 (59.3)
Public practice, n (%)	113 (47.9)
Public and private practice, n (%)	51 (21.6)
< 5 years of practice, n (%)	100 (42.4)
> 15 years of practice, n (%)	30 (12.7)

Conclusion: A total of 88.1% of physicians know at least one classification criteria for the diagnosis of FM. In Mexico, rheumatologists are considered the main care providers for patients with FM. Regarding therapies with level 1A evidence for efficacy in the treatment of FM, only cognitive behavioral therapy and patient education were used by more than 50% of physicians. Serotonin-norepinephrine reuptake inhibitor and tricyclic antidepressants (both of which have level 1A evidence) were only used by 20.8 and 29.2%, respectively.

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Table 2. Pharmacologic and non-pharmacologic treatment of fibromyalgia among physicians.

Variable	n (%)
Exercise (any kind), n (%)	91 (38.6)
Aerobic exercise (aerobic), n (%)	86 (36.4)
Cognitive behavioral therapy, n (%)	127 (53.8)
Patient education, n (%)	142 (60.2)
Gabapentinoids, n (%)	107 (45.3)
Tricyclic antidepressants, n (%)	69 (29.2)
Selective serotonin reuptake inhibitors, n (%)	121 (51.3)
Serotonin-norepinephrine reuptake inhibitor, n (%)	49 (20.8)
Muscle relaxers, n (%)	85 (36)
NSAID, n (%)	137 (58.1)
Opioids, n (%)	27 (11.4)
Mindfulness, n (%)	42 (17.8)

Disclosure of Interests: None declared

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THU0645-HPR ULTRASOUND EDUCATION FOR RHEUMATOLOGIST IN RUSSIA: REALITIES AND WHAT IS NEEDED TO IMPROVE.

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Background: Musculoskeletal ultrasonography (MSUS) is a valuable imaging modality for the practicing rheumatologist. In everyday practice, physical examination is limited by its sensitivity and subjectivity of assessment. MSUS is inexpensive, available, and allows repeat examination as soon as necessary. Thus, MSUS has become the "third eye" of the rheumatologist, in that it allows more detailed examination of muscles, bones, and joints, just as the stethoscope provides further details about the respiratory and cardiovascular systems. Most ultrasound examinations in Russia, including abdominal and vascular sonography, echocardiography, are conducted by trained physician - radiologist, called "ultrasonography specialists". Nevertheless, it is very difficult to perform MSUS, mainly because standardized ultrasound protocols fore same region are different for various diseases and often do not provide physicians with the information they need, and also may been mistake. The conduct of MSUS by rheumatologists themselves is limited to the need for 4-month radiology (ultrasound) certification. However, the number of rheumatologists conducting MSUS themselves is increasing. Training week small group courses are provided by VA Nasonova Research Institute of Rheumatology for the practicing rheumatologist and other physicians.

Objectives: We analyzed the training and awareness of the rheumatologists and radiologists in MSUS, as well as their commitment for participation in our courses.

Methods: We studied a one and a half-year period, from June 2018 to December 2019. During this time, 57 applications were submitted to participate in the courses. All participants who arrived were tested before starting the course. Test included 40 general questions about MSUS. Test results as well as commitment to training were analyzed in two groups: rheumatologists and radiologists. Non-parametric statistics were used for data processing.
Results: Among 57 applications submitted for the courses, 26 were from rheumatologists and 31 from radiologists, but the courses were attended by 13 rheumatologists and 26 radiologists (68%). Thus, commitment was reliably higher in radiologists (84%) than in rheumatologists (50%). Fisher's methods show high statistically significance (X^2 = 7,51, p = 0,006). Although the test focused on ultrasound, it was surprise for us that the median percentage of correct answers was higher in rheumatologists - 64 (54; 80)%, than radiologists ("ultrasonography specialists") 48 (40; 62)%. Difference also were significantly (p = 0,04).
Conclusion: Thus, despite better preparedness of rheumatologist, motivation to study MSUS prevails among radiologists. It is necessary to actively introduce MSUS into general rheumatologic educational programs in order to motivate rheumatologists to study MSUS. Changes in professional standard will also encourage wide use of MSUS by rheumatologists.
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THU0646-HPR EXPLORING THE ROLE OF NURSE IN RHEUMATIC CARE AND FEASIBILITY OF ENHANCING TREAT TO TARGET STRATEGIES IN JAPAN.

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Background: The role of rheumatology nurses is considered important for the implementation of T2T [1]. For nurses' contribution to implementation of the T2T strategy, it is necessary to explore the nurses' opinion on their roles in real clinical practice.
Objectives: The aim of this study is to evaluate what is required for nurses to implement T2T in real clinical practice in Japan.
Methods: Registered nurses engaged in rheumatic care in clinical practice in Japan were enrolled. Focus group interviews were conducted exploring 'What is necessary for RA nurses to implement T2T'using semi-structured interviews. Data analysis was used with Krippendorff's content analysis method.
Results: 24 nurses (all females) from 10 hospitals were enrolled in this study. The results of the qualitative analysis were categorized in 10 main categories, derived from 37 subcategories based on 64 different codes: (1) provide basic knowledge of RA, (2) provide knowledge of RA drugs, (3) provide knowledge and skills of self-monitoring, (4) enhance self-efficacy and support self-management, (5) support decision-making, (6) psychological and social support, (7) understand the diversity and feelings of patients and their families, (8) support based on individual needs, (9) ensure continuing educational opportunities for nurses to enable the provision of high quality care, (10) collaborate with multidisciplinary teams.
These categories are mostly covered in the contents of the 2018 updated EULAR recommendations for the role of nurses except "evidence-based rheumatic care", "telehealth" and "comprehensive participation in disease management".
Conclusion: These findings indicate the areas of exploration including further educational and training needs, attitudes and the professional scope for nurses to extend their roles to provide greater value to patient care.
In Japan, evidence-based RA nursing and telehealth systems have not yet been established. In addition, therapeutic intervention by nurses and nurse-led clinic are not permitted. Our results might reflect this situation and possibly elucidates the gap between EULAR's evidence-based recommendations and opinions of Japanese nurses working in daily clinical practice. As evidence-based nursing is considered to be crucial from both cost-effectiveness and improvement of patients QOL, this result also might shed light on what we need for future better rheumatic nursing in Japan.
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THU0647-HPR SHARED DECISION MAKING AMONGST RHEUMATOLOGISTS IN TRAINING IN THE NETHERLANDS: WHERE DO WE STAND?

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Background: The training curriculum for rheumatologists in training in the Netherlands describes competences and entrusted professional activities (EPA) to monitor the progress in learning. However, this training program does not discuss training of Shared Decision Making. As the basis for shared care and patient participation is made during these years, the question arises how rheumatologist in training think about Shared Decision Making and how they use this in daily practice.
Objectives: Inventory of vision, experience and self-evaluation of skills related to Shared Decision Making amongst rheumatologists in training in the Netherlands in order to identify barriers in the implementation of Shared Decision Making in daily practice.
Methods: Qualitative data was collected from on online survey amongst rheumatologists in training who were registered in January 2018 by the Dutch Society of Rheumatology.
Results: Forty-two rheumatologists in training from various years of training responded (60%). Respondents think that Shared Decision Making is important. A third applies Shared Decision Making on a regular basis in daily practice. Self rating of skills for Shared Decision Making varies from sufficient to good. However, respondents are uncertain about their performance due to a lack of feedback and unclearness of the concept. They indicate that Shared Decision Making is not possible for all patients and find it difficult to assess whether the patient has a clear understanding of the options. Patient's preferences are discussed only by 33% of the doctors on a regular basis when starting new treatment.
Conclusion: Rheumatologists in training agree on the importance of Shared Decision Making, but are uncertain about their performance. Unclearness of the concept is described as a known barrier in literature[1,2] and is frequently mentioned by respondents. Rheumatologist in training indicate that not all patients are fit for Shared Decision Making. Regarding the limited training on the subject this could also be a misjudgment of patients preferences and lack of experience how to deal with different patient types. There is a clear plea for more training and feedback on the subject. Training should be integrated in the curriculum focusing on how to assess patients preferences and how to apply Shared Decision Making also for patients who indicate to leave decisions up to their doctor.
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THU0648-HPR STUDY OF PAIN ATTITUDES & BELIEFS BETWEEN RHEUMATOLOGISTS, PHYSICAL THERAPISTS AND PATIENTS FOR FIBROMYALGIA- A CROSS-SECTIONAL SURVEY

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Background: Attitudes and beliefs about pain determine the interpersonal interaction in evaluation and treatment of a chronic painful condition like fibromyalgia in a multidisciplinary healthcare system. Two distinct dimensions for pain attitudes and beliefs were identified as Biomedical and Behavioral. The former utilized a pathoanatomical model whereas the latter incorporated the psychosocial factors into clinical presentations.
Objectives: The study aimed to evaluate the pain attitudes and beliefs amongst rhematologists, physical therapists and fibromyalgia patients and to compare the biomedical and behavioral dimensions between the three groups in study population of fibromyalgia syndrome (FMS).
Methods: A nation-wide cross-sectional survey (online and direct interviews) was conducted between 2010-16 to identify first group- 18 (16 male, 2 female) rheumatologists (snowball sampling), and second group- 122 (44 male, 78 female) physical therapists (purposive sampling), both with previous experience of treating adults with fibromyalgia. Also 188 patients with FMS were also studied from outpatient departments of tertiary care hospitals as the third group. All participants filled the Pain Attitudes and Beliefs (PABS) scale and the scores were analysed to identify the two dimensions descriptively in percentiles, and their between-group comparisons were done using Chi-Square test at 95% confidence interval using SPSS version 22 for Windows software.
Results: There was an overall predominance of biomedical dimension for FMS reported in all three groups, with rheumatologists being most prevalent (76.8%), followed by patients (65.6%) and then by physical therapists (54.12)%. Between-group comparisons were significant (p<.05) for all 6 analyses.
Conclusion: Biomedical dimension was predominantly reported by rhematologists, physical therapists and patients for chronic pain in FMS and this necessitates further research on development and implementation of educational interventions in this part of the world.
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THU0649-HPR ASSESSMENT OF THE EFFECTIVENESS OF THE EDUCATIONAL PROGRAM FOR PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Effective therapy of rheumatoid arthritis (RA) is impossible without the active and competent participation of the patient in this process, which requires educational programs based on the real needs of the patient
Objectives: The purpose of the study was to develop an educational program for patients with RA and evaluate its effectiveness
Methods: The study included 65 patients with RA. 35 patients of the main group were trained in the educational program. Of these, 30 patients made up the control group. The educational program consisted of 4 daily classes of 90 minutes. Initially and after 6 months, the indices DAS28, HAQ, RAPID3 were determined using the MDHAQ questionnaire
Results: After 6 months after training in the main group, the DAS28 index decreased by 1.28 ± 0.28 points (p <0.05), HAQ - by 0.65 ± 0.39 (55.2%) (p <0.01), RAPID3 - by 4.87 ± 0.82 (45.6%) (p <0.01), anxiety level - by 0.78 ± 0.28 (52.1%) (p < 0.05), depression - by 0.76 ± 0.54 (43.4%) (p <0.05), fatigue - by 2.96 ± 1.21 points (42.3%) (p <0, 05), sleep improved by 0.85 ± 0.34 (52.3%) (p <0.05). 6 months after participating in the educational program, a good response to treatment according to DAS28 according to EULAR criteria was significantly more often recorded (54.5% versus 29.0% in the control group (p <0.05), and the number of patients noted improvement well-being increased by 9 times (p <0.01). The dynamics in the control group was less pronounced, which determined statistically significant differences between groups for most indicators (p <0.05)
Conclusion: The educational program improves functional capabilities, psychological status, helps control the activity of the disease and improves the quality of life of patients with RA
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THU0650-HPR THE USE OF GAMIFICATION TO MOTIVATE HEALTH PROFESSIONALS IN RHEUMATOLOGY TO PARTICIPATE IN BLENDED LEARNING.

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Background: Blended learning is an increasingly popular learning supplement for traditional classroom-based courses in medical education. Once implemented, many factors influence its success. This was demonstrated by Shivetts et al., who concluded that student motivation plays a major role. In particular, if a learner is not self-motivated, e-learning may not represent the best learning environment.[1] However, gamification methods are known to enhance motivation in medical education and, if used correctly, can overcome this deficit.[2] For this purpose, a quiz duel was created and used as a blended learning approach for health professional training in rheumatology. We hypothesize that the use of the quiz duel gamification technique improves learners' motivation to successfully complete their blended learning course.
Objectives: To investigate the potential of gamification methods in motivating health professionals to answer multiple choice questions (MCQs) in a pilot blended learning scenario.
Methods: Four hundred and sixty MCQs were developed in accordance with the learning objectives of a certified training course and integrated into a learning management system (LMS). As a gamification technique, a duel mode was created. Course participants had access via an individual user account and used personal smartphones. After each answer was provided, the learners received corrective and explanatory feedback, as well as information on how the duel opponent answered. Incorrectly answered MCQs were repeated in further duels.
Information on the number of MCQs answered (1), days learned (2), and learning time spent (3) was collected and analyzed. Each day on which at least one MCQ was answered counted as a learning day per user. The learning time was calculated with 1.5 min per MCQ answered. Analysis was performed over a 15-week period (08/19–12/19).
The training event ("RFAplus") was organized by the Rheumatologische Fortbildungsakademie GmbH and took place on three weekends in intervals of four weeks in Germany. The LMS used was Humeo (Humeo GmbH). All users agreed to the terms and conditions of use and data protection before participating in the blended learning intervention.
Results: Nineteen female health professionals in rheumatology participated in the study. The mean age of participants was 43.5 years (range, 21–60 years). The 460 MCQs were answered 20,397 times, with 1039 MCQs per

user (range, 247-1839 MCQs) during the 15-week period (105 days). Each MCQ was answered 2.33 times. In total, there were 1167 learning days, with 60.8 days per user (range, 15-95 days). The users spent 30,596 min (509.9 h) answering the MCQs, resulting in 1,610 min (or 26.8 h) per user. Furthermore, each user answered 17.5 MCQs and spent an average of 26 min per learning day.

Conclusion: Blended learning is an interactive method to potentially extend learning time over several weeks. However, the success of this technique lies in motivating the participants to continue learning after the event. A quiz duel as a gamification technique proved to be effective in motivating participants to learn daily. In our study, learners spent an average of 27 h, i.e., almost half of the total attendance time of 60 h, learning. Correspondingly, this technique could also replace parts of lengthy face-to-face courses in an attempt to save costs in the future. Information drawn from the MCQs could potentially serve as promising learning analytics.

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THU0651-HPR ONLINE EDUCATION YIELDS SIGNIFICANT GAINS IN RHEUMATOLOGISTS' KNOWLEDGE OF THE ROLE OF ENTHESITIS IN THE DIAGNOSIS AND MANAGEMENT OF PSA

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Background: Physicians face challenges staying up-to-date with the latest research and accessing the ever-growing field of knowledge is time-consuming. Online education can make these clinician's tasks more efficient and less time-consuming.

Objectives: As part of a larger curriculum, we developed an online CME activity titled: "Enthesitis in Psoriatic Arthritis: Disease, Diagnosis and Decisions." The goal of this study was to assess whether this online CME accredited video discussion improves physicians' understanding of the role of enthesitis in the diagnosis and management of patients with psoriatic arthritis (PsA) in clinical practice.

Methods: Rheumatologists participated in an online CME activity (https://www.medscape.org/viewarticle/910671) consisting of a 30-minute video discussion between 2 experts with accompanying slides. Educational effect was assessed using a 4-question repeated pairs, pre-/post-assessment. A chi-square test was used to determine if a statistically significant improvement (P <.05 significance level) existed in the number of correct responses from the pretest and posttest scores. Cramer's V was used to estimate the level of impact of the education. The CME activity launched on March 28, 2019, and the data were collected through June 7, 2019.

Results: A total of 145 rheumatologists completed the pre- and post activity assessments. Overall the activity had a signficiant impact (P <.0001) on rheumatologists' knowledge of the role of enthesitis in the diagnosis and management of PsA, with a Cramer's V value of 0.153 indicating a noticeble educational impact. The average percentage of correct responses rose from 54% pre-activity to 69% post-activity. A repeated pairs analysis showed that 22% of rheumatologists improved their knowledge and 47% reinforced their knowledge, respectively. The change in percentage of correct responses from pre- to post-assessment for all questions are shown in table. Almost 40% of rheumatologists had a measurable improvement in confidence in their ability to evaluate the presence of enthesitis according to a clinical exam or ultrasound.

Table. Impact of education on rheumatologists' knowledge of enthesitis

Question #	Question topic	Aggregated data		Linked Learner Results[a]	
		Average % of correct responses Pre- vs. Post-education	P-value	% Improved[b] learners Pre- vs. Post-education	% Reinforced[c] learners Pre- vs. Post-education
1.	Immunopathology of PsA	75% vs 84%	.0579	12%	72%
2.	Prevalence of enthesitis in patients with PsA	44% vs 68%	<.0001	33%	34%
3.	Clinical trial outcomes in patients with enthesitis	43% vs 56%	.0345	22%	34%

[a]Each individual learner tracked pre and post-education
[b]Incorrect answer pre-education, Correct answer post-education
[c]Correct answer pre-education, Correct answer post-education

Conclusion: This online CME activity significantly improved rheumatologists' understanding of role of enthesitis in the diagnosis and management of PsA. However, there is clearly room for further improving physicians' knowledge of clinical trial outcomes with biologics in patients with enthesitis, since 44% of rheumatologists provided incorrect answers to question 3 post-education. This topic can be addressed in future education.

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THU0652-HPR ONLINE EDUCATION YIELDS SIGNIFICANT GAINS IN RHEUMATOLOGISTS' KNOWLEDGE OF BIOLOGICS AND BIOSIMILARS BUT A SUBSTANTIAL GAP REMAINS

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Background: Biologics are complex proteins which have revolutionized the treatment of many serious diseases. Due to their complexity and manufacturing which involves living organisms, it is not possible to create identical versions of reference biologics, but it is possible to create biosimilar drugs. Biosimilars have the potential to yield high cost savings and expand treatment options to meet the growing demand for biological therapies.

Objectives: This study assessed whether the online CME-accredited round-table-discussion titled "Understanding Biologics: from protein to clinical practice" improved physicians' understanding of the inherent variability of biologics and what similarity means in the context of biologics as well as the analytical assessment of quality that applies to both biologics and biosimilars.

Methods: Rheumatologists participated in an online CME activity (www.medscape.org/viewarticle/900121) consisting of a 30-minute video discussion between 4 experts with accompanying slides. Educational effect was assessed using a 4-question repeated pairs, pre-/post-assessment. A chi-square test was used to determine if a statistically significant improvement (P <.05 significance level) existed in the number of pre-/post-test correct responses. Cramer's V was used to estimate the level of impact of the education. The CME activity launched on 22 Aug 2018, and the data were collected through 9 Oct 2018.

Results: A total of 622 rheumatologists participated in the educational activity, and 87 completed the pre- and postassessment. Overall the activity had a signficiant impact (P <.001) on rheumatologists' understanding of the inherent variability of biologics and the regulatory requirements for approval of a biosimilar. The Cramer's V value of 0.186 indicates a considerable effect of the education. The average perecentage of correct responses rose from 33% pre-activity to 51% post-activity. A linked learning assessment (individual responses matched pre- and post-education) showed that 25% of learners improved their knowledge and 26% reinforced their knowledge. The change in percentage of correct responses from pre- to post-assessment achieved statistical significance (P <.05) in 2 of the 3 questions presented: (i) understanding the type of studies needed to demonstrate comparability of a biosimilar to an originator (11% at baseline; 45% post activity), (ii) understanding the type of variability considered acceptable for a biologic (46% at baseline; 63% post activity). However, no knowledge gain was observed regarding basic analytic attributes evaluated to ensure batch to batch consistency (37% at baseline; 38% post activity). Almost 45% of rheumatologists gained confidence in their ability to describe the regulatory requirements for approval of a biosimilar.

Conclusion: This online CME activity significantly improved rheumatologists' understanding of the inherent variability of complex biologic medicines and the role of analytical studies in the regulatory approval of biosimilars. However, there is room for further improving physicians' knowledge, especially of basic analytics of biologics and biosimilars.

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THU0653-HPR BARRIERS FOR THE UPTAKE OF EULAR POSTGRADUATE EDUCATION FOR HEALTH PROFESSIONALS IN RHEUMATOLOGY IN EASTERN EUROPEAN COUNTRIES: RESULTS FROM 3 NATIONAL SURVEYS

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Background: Health professionals play an important role in the care for people with rheumatic and musculoskeletal diseases. In order to improve and maintain the quality of their work, appropriate professional education is needed. EULAR has developed several educational products and activities specifically targeted at Health Professionals in Rheumatology (HPR), but particularly in Eastern European countries, their uptake is limited. The overarching aim of a EULAR project (named HEE4ALL: Health professionals Education in Eastern European countries for All) is to develop and execute implementation strategies for EULAR educational activities in 3 eastern European countries.

Objectives: The aim of the present analysis was to identify barriers and facilitators for the uptake of EULAR educational activities among HPR in Eastern European countries.

Methods: First, a questionnaire was sent to representatives of national health professionals' or patients' organization in 17 Eastern European countries, in order to determine their eligibility to participate in the implementation project. Eligibility criteria were: Having a national HPR organization; Willing and able to compose a team with HPR, Patients, and Rheumatologists; and Interested to participate in the project. Selected countries (minimum 3) were requested to set up a national implementation team, and conduct a national, electronic survey among HPR on anticipated barriers and needs regarding educational activities. The survey included the following elements: a. characteristics of the responding HPRs; b. Familiarity with EULAR educational offerings; c. Anticipated barriers and facilitators (score 0=no barrier at all to10 very important barrier); d. Ability to pay for the HPR online course.

Results: Representatives from 10/17 Eastern European countries responded to the first questionnaire, with 3 countries meeting the selection criteria: Hungary, Serbia and Turkey. Subsequently, 216 (H:106, S:42 and T:68) HPR completed the 3 national surveys. In all 3 countries, the majority of the respondents was female (93.1%), and nurse (70.8%) or physical therapist (19.0). Familiarity with EULAR educational offerings was poor, with the lowest proportions of HPR being familiar with postgraduate face-to-face courses (13.9%), educational visits (19.0%) and the EULAR online course for HPR (25.0%). The highest ranked barriers in all 3 countries included the costs of EULAR annual congress, the costs of the EULAR HPR online course and a lack of mastery of English language.The maximum amount of money HPR were able to pay for the EULAR online course was on average €66, €29 and €83 in Hungary, Serbia and Turkey, respectively.

Conclusion: Based on a survey in 3 Eastern European countries, it appears that familiarity with EULAR educational offerings is suboptimal. However, when HPR are aware of the educational offerings, their costs and a lack of mastery of the English language seem to be the most important barriers for participation. Based on these results, the 3 national teams developed implementation plans during a 2-day meeting (October 2019). The implementation plans are now executed and a process and effect evaluation is planned by November, 2020.

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Poster Presentations

FRIDAY, 05 JUNE 2020

Innate immunity in rheumatic diseases

FRI0001 NEUTROPHILS IN GRANULOMATOSIS WITH POLYANGIITIS DISPLAY FEATURES OF PYROPTOSIS

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Background: Granulomatosis with polyangiitis (GPA) is characterized by extravascular necrotizing granulomatous inflammation and systemic ANCA – associated (AAV) vasculitis with neutrophils as a key player in the pathogenesis (1). We and others have shown that neutrophil-related cell death mechanisms contribute to chronic inflammatory processes in AAV (2, 3). Recently, another form of inflammatory cell death primarily described in monocytes called pyroptosis was also discovered in neutrophils (4). A cardinal feature of pyroptosis is the activation of the NLRP3 inflammasome, a sensor of different pathogen- and damage-associated molecular patterns (PAMP, DAMP), following caspase-1-mediated processing and secretion of IL-1beta (5).
Objectives: The aim of this study was to investigate, if neutrophils from GPA patients express pyroptosis-related components NLRP3, active caspase 1 and cleaved IL-1beta.
Methods: Polymorphonuclear leukocytes (PMN) were isolated from peripheral blood of GPA patients and healthy controls (HC) (n = 10 each). Expression of NLRP3, inactive/active caspase 1 and active IL-1beta was determined by western blot. In addition, peripheral blood mononuclear cells (PBMC) were isolated from GPA and HC. mRNA expression of *nlrp3* and *il1b* was determined by qPCR. To exclude false-positive results by contamination with monocytes we performed flow cytometry analysis of whole blood samples with markers CD3, CD14, CD15, CD66b and NLRP3.
Results: PMN from GPA patients showed markedly increased expression of NLRP3, active caspase 1 and active IL-1beta compared to HC. In contrast, there was no difference between GPA and HC on the mRNA level of neither *nlrp3* nor *il1b* in PBMC. In addition, we confirmed by flow cytometry increased expression of NLRP3 in PMN from GPA, but not in monocytes.
Conclusion: Here we provide evidence, that neutrophils from GPA undergo pyroptosis, demonstrated by increased NLRP3, active caspase 1 expression as well as IL-1beta processing. Neutrophils are present in high numbers at the site of granulomatous lesions of inflamed tissue in GPA and IL-1beta is increased in GPA sera (2). Therefore, neutrophils represent a potential source of IL-1beta in GPA. Given the fact that GPA-associated features such as massive release of necrosis-related DAMP or microbial agents such as *Staphylococcus aureus* (6) can activate the NLRP3-inflammasome, we identified here a potential relevant mechanism of neutrophils contributing to chronic inflammation of GPA.
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FRI0002 S100A11 (CALGIZZARIN) IS RELEASED DURING NEUTROPHIL EXTRACELLULAR TRAPS FORMATION AND STIMULATES RELEASE OF IL-6 AND TNF IN RHEUMATOID ARTHRITIS

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Background: S100A11 protein, a member of S100 family, has been associated with several autoimmune inflammatory conditions such as rheumatoid arthritis (RA). Although the pathogenesis of autoimmune diseases is not fully understood, the formation of neutrophil extracellular traps (NETs) seems to play a certain role. Recent data indicate that S100A8/A9 is released via NETosis and can further augment inflammatory responses.
Objectives: The aim of our study was to examine the association of S100A11 with NETs in RA.
Methods: To assess the expression of S100A11 by neutrophils of RA synovial tissue (n=8), immunofluorescence staining of S100A11 and myeloperoxidase (MPO) was performed. The levels of S100A11 and MPO in RA synovial fluid (n=23) were measured by ELISAs (RayBiotech and Abcam), and the activity of peptidyl arginine deiminases (PADs) was measured by an in-house immunoassay. NETosis was induced by adding phorbol 12-myristate 13-acetate (PMA) to neutrophils from RA patients (n=7). Release of NETs was visualised by immunocytochemistry (n=7) and the presence of S100A11 in supernatants was analysed by ELISA (RayBiotech). Neutrophils purified from healthy donors (n=5) were stimulated by S100A11 and the release of cytokines TNF and IL-6 was measured by ELISA (RayBiotech).
Results: S100A11 was expressed by synovial tissue neutrophils of the RA patients (n=8). The levels of S100A11 in the synovial fluid of RA patients (n=23) correlated with the levels of a NETosis marker MPO (r=0.562, p=0.005) and with PADs activity (r=0.690, p<0.001), which affects NETs immunogenicity. Neutrophils treated with LPS (n=7) did not up-regulate the secretion of S100A11 compared to unstimulated controls (0.23±0.05 vs. 0.29±0.07 ng/ml; p=ns). However, the release of S100A11 was markedly up-regulated in PMA-stimulated neutrophils undergoing NETosis compared to untreated controls (1.16±0.17 vs. 0.29±0.07 ng/ml; p<0.001). Moreover, diphenyleneiodoinum treatment abolished PMA-induced S100A11 secretion. By immunofluorescence staining (n=8) we demonstrated that neutrophils activated by PMA release NETs containing S100A11 protein. In addition, extracellular S100A11 augmented the inflammatory response of neutrophils from healthy donors (n=5) via IL-6 and TNF in comparison with unstimulated cells (0.39±0.11 vs. 0.05±0.01 pg/ml; p<0.05 and 0.31±0.06 vs. 0.09±0.03 pg/ml; p<0.05).
Conclusion: Here we show for the first time that release of S100A11 by neutrophils is dependent on NETosis. Moreover, extracellular S100A11 augments the inflammatory response by inducing TNF and IL-6 secretion in neutrophils.
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Disclosure of Interests: Adela Navratilova: None declared, Viktor Becvar: None declared, Jiří Baloun: None declared, Dres Damgaard: None declared, Claus Henrik Nielsen: None declared, Karel Pavelka Consultant of: Abbvie, MSD, BMS, Egis, Roche, UCB, Medac, Pfizer, Biogen, Speakers bureau: Abbvie, MSD, BMS, Egis, Roche, UCB, Medac, Pfizer, Biogen, Jiří Vencovský: None declared, Ladislav Šenolt: None declared, Lucie Andres Cerezo: None declared, David Veigl: None declared
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FRI0003 ELEVATED HISTONE H4 IN NEUTROPHIL EXTRACELLULAR TRAPS PROMOTES MACROPHAGE ACTIVATION IN BEHÇET'S DISEASE

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Background: Neutrophil-released neutrophil extracellular traps (NETs) are upregulated and promote autoinflammation and thrombosis in Behçet's disease (BD), a multi-system inflammatory disease with unknown etiology [1,2]. However, whether NETs promote macrophage activation in BD remains unclear.
Objectives: To investigate the potential role of NETs in promoting aberrant macrophage activation in BD.

Methods: We quantified NETs by measuring dsDNA using ELISA and immunofluorescence. Macrophages were stimulated with BD- and healthy controls (HC)-derived NETs, and IL-8 and TNF-α production were measured by ELISA. NETs-stimulated macrophages were incubated with naive $CD4^+$ T cells, and Th1 cell differentiation was examined on day 7 by flow cytometry. Histones H1, H2A, H2B, H3, H4, S100A8 and neutrophil elastase in NETs were analyzed by western blot. Macrophages were stimulated with anti-Histone 4 antibody-treated NETs, and IL-8 production was measured by ELISA.
Results: Circulating NETs (2336±534 ng/ml vs. 1472±549 ng/ml, *P*=0.0008) and neutrophil-derived NETs (909.2±485.2 ng/ml vs. 582.4±199.2 ng/ml, *P*=0.0108) were significantly higher in BD patients compared with those in HC. BD NETs stimulated macrophages to produce a higher level of IL-8 (17±4 ng/ml vs. 13±4 ng/ml, *P*=0.0474) and TNF-α (166±61 pg/ml vs. 102±48 pg/ml, *P*=0.0132) than HC NETs. Moreover, BD NETs promoted macrophages to facilitate Th1 differentiation than HC NETs (33±10% vs. 24±7%, *P*=0.0398). Western blot analysis revealed more Histone H4 (289076 (144365, 544038) IOD values vs. 42121 (6958, 129625) IOD values, *P*=0.0286), but not Histones H1, H2A, H2B, H3, S100A8 or neutrophil elastase in BD NETs compared to HC NETs. Importantly, neutralizing Histone H4 abrogated the BD NETs-stimulated IL-8 overproduction by macrophages (9.99±2.07 ng/ml vs. 13.95±2.91 ng/ml, *P*=0.021).
Conclusion: BD NETs promoted macrophages activation, which might be mediated by a higher level of Histone H4.
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FRI0004 SURFACE AMP DEAMINASE 2 AS A NOVEL REGULATOR MODIFYING THE EXTRACELLULAR ATP-ADENOSINE BALANCE THAT IS DIFFERENTIALLY EXPRESSED IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Adenosine and its nucleotides represent crucial immunomodulators in the extracellular environment. ATP and ADP are released from stressed cells in states of inflammation, whereas adenosine serves as a key anti-inflammatory mediator[1]. The ectonucleotidases CD39 and CD73 are responsible for the sequential catabolism of ATP to adenosine via AMP, thereby promoting an anti-inflammatory milieu induced by the "adenosine halo". Great importance has been attributed to these enzymes in the pathogenesis of autoimmune diseases such as rheumatoid arthritis (RA) and as targets in cancer therapy[2 3]. AMPD2 mediates AMP deamination to IMP, thus constituting an ambiguous mediator both enhancing the degradation of inflammatory ATP and reducing the formation of protective adenosine. Here, we postulate that this pathway is also present on the cell surface of immune cells and modified under inflammatory conditions.
Objectives: Therefore, we analysed surface AMPD2 expression and its modulation on distinct cell lines and primary immune cells.
Methods: Firstly, AMPD2 surface expression was verified by immunoprecipitation from membrane fractions isolated from cell lines (HEK293 and HMEC1) and CD14+ monocytes analysed by western blot and mass spectrometry. In addition, surface biotinylation of the aforementioned cells was performed. Also, AMPD2 surface expression was evaluated by flow cytometry, analysing both cell lines (HEK293, HMEC1, THP1, and Jurkat) and primary human immune cells from healthy donors and patients with RA.
Secondly, co-expression of surface AMPD2, CD39 and CD73 on PBMCs was analysed by flow cytometry directly after isolation as well as after a 24h culture period. Moreover, surface expression was assessed after immunostimulation and Golgi transport inhibition.
Results: AMPD2 surface expression was confirmed by western blot and mass spectrometry of (i) precipitated AMPD2 from membrane fractions and (ii) biotinylated surface molecules in HEK293 and HMEC1 as well as CD14+ monocytes. Surface expression was reduced after AMPD2 knockdown in HEK293. Flow cytometric analysis further verified AMPD2 surface expression and revealed a significant decrease after Golgi transport inhibition (p<0.01). TLR

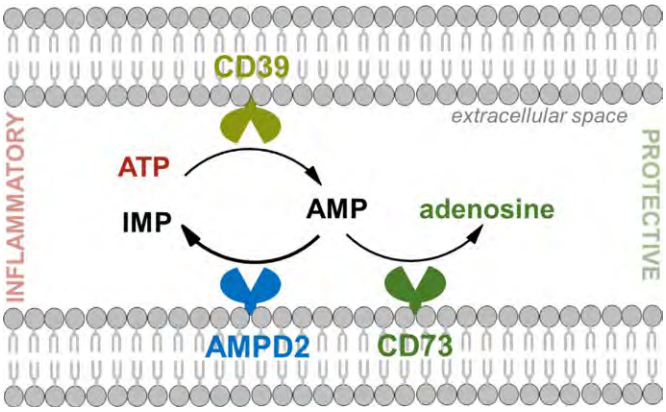


Figure 1. Surface AMPD2 as a novel regulator of the extracellular ATP-adenosine balance.

stimulation strongly enhanced the surface expression of AMPD2 and CD39 on monocytes (p<0.05), whereas dexamethasone at high therapeutic doses inversely affected AMPD2 surface expression on lymphocytes and monocytes (p<0.01). Analysis of AMPD2 surface expression on PBMCs from RA patients revealed higher expression levels compared to sex- and age-matched healthy controls (p<0.05).
Conclusion: We demonstrate AMPD2 surface expression on immune cells for the first time. Hence, we reveal a novel regulator of the extracellular ATP-adenosine balance that is differentially expressed in RA patients compared to healthy controls. The extracellular conversion of AMP into IMP may constitute a shunt-like mechanism adding to the CD39-CD73 system controlling immunomodulation.
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FRI0005 DIVERSITY OF ANTI-CITRULLINATED PROTEIN ANTIBODY COMPOSITIONS INFLUENCE SYNOVIAL FIBROBLAST REACTIVITY

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Background: Anti-citrullinated protein antibodies (ACPAs) play an important role in rheumatoid arthritis (RA) pathogenesis. We hypothesized that the effect of these antibodies is mediated by their binding to synovial fibroblasts and inducing an increased mobility of fibroblasts[1].
Objectives: In our study, we analyzed and compared fibroblast modulation by ACPA pools obtained from different patients or by a set of monoclonal ACPAs with different fine specificity that were obtained from different tissue sites.
Methods: Synovial fibroblasts were isolated from RA patients synovial tissue biopsies. Individual polyclonal ACPA and control IgGs were purified from sera of four ACPA-positive RA patients by affinity purification on protein G and CCP-2 columns. Monoclonal antibodies were derived from memory B cell isolated from blood2, synovial fluid or bronchoalveolar lavage of RA patients. Whole antibodies and F(ab')2 fragments were tested in fibroblast migration using IncuCyte live-cell analysis. Blocking experiments were performed with soluble citrullinated proteins in SF migration. Cross-reactivity of the antibodies to citrullinated and acetylated epitopes was tested using PAD inhibitors (Cl-amidine and GSK199),

histone acetyltransferases (anacardic acid) and deacetylases (trichostatin A). Binding patterns of monoclonal ACPAs, both whole and F(ab')2 fragments were analyzed in synovial biopsies obtained from both healthy donors and RA patients.

Results: Three out of four tested individual ACPA were able to promote fibroblast migration. Five out of nine tested monoclonal ACPAs stimulated fibroblast migration. One of these antibodies, clone 1325:01B09 is characterized by cross-reactivity to citrullinated, homocitrullinated and acetylated targets. The effect of 1325:01B09 on fibroblast migration was completely abolished by Cl-amidine or by pre-incubating the antibody with citrullinated fibrinogen or histone but not citrullinated enolase or vimentin. Despite the cross-reactivity to acetylated epitopes, neither anacardic acid nor trichostatin A could modulate the 1325:01B09 effect on fibroblast migration. F(ab')2 fragments of this antibody stimulated fibroblast migration and labelled podoplanin-positive fibroblasts in inflamed RA synovium similarly to the intact antibody, indicating an Fc-independent effect.

Conclusion: The effect on fibroblast mobility was likely to be mediated by binding to citrullinated epitopes but not through Fc receptors. Detection of fibroblast modulating ACPAs in majority of RA patients indicated that fibroblasts might be key cellular targets in disease pathogenesis, although individual variability might exist in the composition of ACPA cellular targets.

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FRI0006 ASSESSING PRO-INFLAMMATORY PROPERTIES OF H-FERRITIN BY EX VIVO AND IN VITRO OBSERVATIONS

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Background: The concept of 'hyperferritinemic syndrome' has recently been proposed, suggesting high levels of ferritin as pathogenic pro-inflammatory mediator [1] Ferritin is an intracellular iron storage protein, comprising 24 subunits, heavy (H) and light (L) based on molecular weight. The H-/L subunits ratio may be different in tissues, since the ferritin enriched in L subunits (L-ferritin) and the ferritin enriched in H subunits (H-ferritin) may be observed in different tissues, according to pathophysiologic status [1].

Objectives: We aimed to assess the presence of H- and L-ferritin as well as of CD68/H-ferritin and CD68/L-ferritin in bone marrow (BM) biopsies of adult macrophage activation syndrome (MAS) patients. In the same patients, we matched the findings of BM biopsies with sera to identify the main represented subunits of ferritin. Furthermore, we evaluated effects of ferritin, L-ferritin, and H-ferritin on human monocytes, assessing pro- and anti-inflammatory cytokines, and expression of NLRP3 inflammasome. Finally, we checked the ability of monocytes, which were treated with ferritin, to stimulate or not the proliferation of peripheral blood mononuclear cells (PBMCs).

Methods: Immunofluorescence analysis was performed to investigate the tissue presence of L- and H-ferritin in BM biopsies as well as of CD68/H-ferritin and CD68/L-ferritin. Liquid chromatography mass spectrometry (LC-MS/MS) based proteomics was performed to identify L- and H-ferritin in sera proteins. Human monocytes were cultured with M-CSF for 7 days and, after that, treated with ferritin, H-ferritin, and L-ferritin at 10nM, for 120 and 240 minutes. After stimulation, IL-1β, IL-6, IL-10, IL-12, IFN-γ, TGF-β, TNF, and VEGF were assessed by RT-PCR and, in case of positive finding, evaluated by western blot. NLRP3 inflammasome was also assessed. Finally, the proliferation of PBMCs when co-cultured with ferritin-treated monocytes was tested by a specific proliferation assay.

Results: Immunofluorescence showed an increased H-ferritin expression in the BMs of MAS patients, whereas L-ferritin did not. Conversely, LC-MS/MS identified that the L-ferritin was the dominant form, after stringent probability matching. *In vitro*, H-Ferritin induced a significant increased expression of IL-1β, IL-6, IL-12, and TNF after 240 minutes. Ferritin also induced a significant increased expression of IL-1β, IL-6, IL-12, and TNF after 240 minutes. Effects on pro-inflammatory cytokines were more marked with H-ferritin than ferritin. Conversely, no significant effects were retrieved analysing IFN-γ, IL-10, TGF-β, and VEGF after 240 minutes, after ferritin and H-ferritin stimulation. Furthermore, both ferritin and H-ferritin induced a direct effect on NLRP3 inflammasome. Finally, monocytes, which were treated with H-ferritin, stimulated the proliferation of co-cultured PBMCs.

Conclusion: In our work, results showed the presence of H-ferritin and CD68/H-ferritin cells in BM biopsies of MAS patients, by immunofluorescence. Conversely, LC-MS/MS identified L-ferritin in sera proteins of those patients. Furthermore, pro-inflammatory effects of ferritin and, particularly, of H-ferritin on human monocytes were observed *in vitro*, increasing pro-inflammatory cytokines and NLRP3 inflammosome. Finally, H-ferritin-treated monocytes stimulated the proliferation of co-cultured PBMCs.

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FRI0007 MOSPD2: A NOVEL THERAPEUTIC TARGET FOR THE TREATMENT OF RHEUMATOID ARTHRITIS

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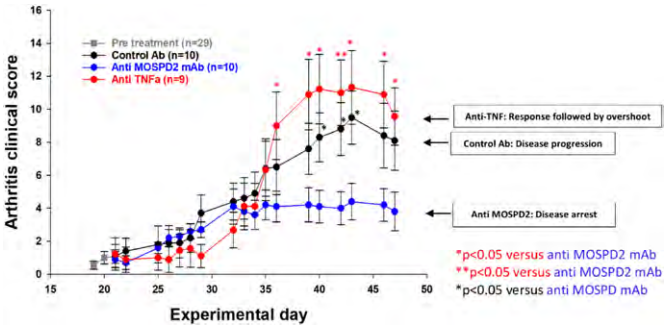
Background: Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease with an unknown etiology that affects the joints. B and T lymphocytes are major drivers of arthritis, mediated through their secretion of antibodies against self-antigens and the production of pro-inflammatory cytokines. Nevertheless, innate immune cells play an important role in disease progression, and recruitment of blood monocytes/macrophages was highly correlated with tissue damage in RA patients[1,2]. Once infiltrated into the joint, monocytes can produce proinflammatory cytokines and chemokines that further escalate the inflammatory process and tissue damage. Consistent with that, genetic and pharmacological intervention targeting CCR2 and CCR5, chemokine receptors which are abundantly expressed on monocytes, was shown to reduce disease severity in multiple preclinical models of RA[3]. Blocking monocyte migration in RA can be therefore an attractive therapeutic approach, if implied in a manner that can overcome the redundancy of chemokine receptors and ligands.

Motile sperm domain-containing protein 2 (MOSPD2) is a 518 amino acids single-pass membrane protein to which no function was ascribed up until recently. Assessment of MOSPD2 in immune cell subsets showed it is expressed by monocytes and neutrophils. We previously discovered that MOSPD2 regulates human monocyte and neutrophil migration in a chemokine-agnostic manner[4].

Objectives: Using anti MOSPD2 mAbs, the role of MOSPD2 in mouse monocyte migration in-vitro and RA progression in mice was assessed.

Methods: In-vitro, MCP-1 and SDF-1 chemokines were used to induce migration of mouse splenic monocytes through a trans-well plate in the presence of anti MOSPD2 mAbs. In-vivo, DBA-1 mice were injected with type II collagen on days 0 and 21 to induce arthritis. Mice were then treated twice a week with anti MOSPD2 mAb, anti TNF-α or an isotype control antibody until study end (day 42). Animals were monitored for arthritis score, and upon sacrifice, hind limb joints were examined for pathology.

Results: Anti MOSPD2 mAbs significantly inhibited migration of mouse monocytes in-vitro. Treatment with anti MOSPD2 mAb after disease was already initiated, limited disease progression and significantly ameliorated clinical manifestation at the climax phase of the disease by more than 50% compared with isotype control and anti TNF-α treatment. Pathological examination revealed that treatment with anti MOSPD2 mAb reduced pannus formation and joint inflammation.



Conclusion: The results further support the involvement of monocytes in RA pathogenesis and highlight the key role MOSPD2 plays in this disease. Accordingly, targeting of monocyte migration using anti MOSPD2 mAbs may hold promise as a treatment for various chronic inflammatory diseases, including RA.

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Disclosure of Interests: None declared

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FRI0008 IGM ANTIBODIES AGAINST MALONDIALDEHYDE AND PHOSPHORYLCHOLINE IN DIFFERENT SYSTEMIC RHEUMATIC DISEASES

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Background: IgM antibodies against phosphorylcholine (anti-PC) and malondialdehyde (anti-MDA) may have protective properties in both atherosclerosis and rheumatic disease, especially anti-PC. Low levels of IgM anti-PC is associated with SLE itself and also with atherosclerotic plaques[1] and with being a non-responder to biologics in RA.[1] We determined mechanisms by which anti-PC (and to some extent anti-MDA) could be protective: 1: anti-inflammatory; 2: inhibition of uptake of oxLDL in macrophages, 3: inhibition of cell death.[1] 4: increase in clearance of human dead cells,[2] 5: anti-PC promotes polarization of T regulatory cells in SLE-patients´ T cells from a low level and also in cells from atherosclerotic plaques.[3]

Objectives: To compare systemic rheumatic diseases in relation to natural anti-PC and anti-MDA, to develop novel classifications but also potential treatment against rheumatic disease. We here determine anti-PC and anti-MDA in different systemic rheumatic conditions and study there potential role properties.

Methods: Anti-PC and anti-MDA was measured using ELISA in patients with SLE (374), RA (354), Mixed connective tissue disease (MCTD, 77), Systemic sclerosis (SSc, 331), Sjögren's syndrome (SjS, 324), primary antiphospholipid syndrome (PAPs, 65), undifferentiated connective tissue disease (UCTD, 118) and 515 matched healthy controls (HC). Cardiovascular score (CV) was broadly defined based on clinical disease symptoms. Anti-PC and anti-MDA peptide/protein characterization were compared using a proteomics de novo sequencing approach. anti-MDA and anti-PC were extracted from total IgM. The proportion of Treg cells was determined by flow cytometry.

Results: The maximal difference between cases and controls was shown for MCTD: significantly lower IgM Anti-PC but not anti-MDA among patients (median 49.3RU/ml vs 70.4 in healthy controls, p(t-test)=0.0037). IgM low levels were more prevalent in MCTD, SLE, SjS, SSc and UCTD. IgM anti-PC variable region profiles were different from and more homologous than anti-MDA. Anti-PC but not anti-MDA were significantly negatively correlated with CV in the whole patient group. In contrast to IgM anti-PC, anti-MDA did not promote polarization of Tregs.

Conclusion: Anti-PC is decreased in MCTD and also in SLE, SjS and SSc but not in other studied diseases. Anti-PC may thus differentiate between these. In contrast, anti-MDA did not show these differences between diseases studied. Anti-PC level is negatively correlated with CV in the patient group cohort. In contrast to anti-PC, anti-MDA did not promote Treg polarization. These findings could have both diagnostic and therapeutic implications, one possibility being active or passive immunization with PC in some rheumatic conditions.

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Acknowledgments: Preciseads Clinical Consortium

Disclosure of Interests: Divya Thiagarajan: None declared, Susanna Lundström: None declared, Roman Zubarev: None declared, jitong Sun: None declared, Marta Alarcon-Riquelme: None declared, Johan Frostegård Grant/research support from: Unconditional competitive grant from Amgen, related only to PCSK9, not the topic of this abstract

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FRI0009 IMMUNO-PHENOTYPIC ANALYSIS OF PERIPHERAL BLOOD MONONUCLEAR CELLS IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH E6011, A HUMANIZED ANTI-FRACTALKINE MONOCLONAL ANTIBODY

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Background: Fractalkine (FKN) and its solo receptor CX3CR1 are deeply involved in the pathogenesis of rheumatoid arthritis (RA). FKN is expressed on vascular endothelium, while CX3CR1 is expressed on peripheral blood leukocytes such as monocytes, macrophages, NK cells, effector $CD8^+$ T cells and a minor fraction of $CD4^+$ T cells. E6011, a novel humanized anti-FKN monoclonal antibody (mAb), is under clinical development in RA.

Objectives: In order to continuously assess the E6011 pharmacodynamics by monitoring the alteration of peripheral blood immune cells, including CX3CR1-expressed cell populations, a series of multi-color flow cytometry (FCM) was conducted before and during the course of the E6011 treatment of active RA patients in phase 2 clinical trial.

Methods: Immuno-phenotypic changes were explored by FCM during the E6011 administration in 190 Japanese RA patients with inadequate response to MTX (NCT02960438). Patient's peripheral blood were drawn into fixative tube (CytoChex® BCT, Streck) at each clinics and thereafter transported to the FCM facility at KAN Research Institute, Inc. within 30 hours after the blood collection to operate the FCM analysis by standardized method. Immuno-phenotyping was carried out by multi colors flow cytometry (BD FACSCantoII™, BD LSRFortessa™, BD Biosciences).

Results: Based on these determined conditions, CX3CR1 expression on monocytes, NK cells and a part of $CD8^+$ and $CD4^+$ T cells were confirmed in this method. Interestingly, during the E6011 treatment, the proportion of $CD16^+$ monocytes, which highly express CX3CR1 within whole monocytes, were significantly decreased at 2 week after initial treatment from the baseline (E6011: $p < 0.001$, placebo: $p > 0.48$) and sustained up to 24 week, while that of $CD16^-$ monocytes were increased. The reduction of the frequency of $CX3CR1^+$ cells in NK cells, $CD4^+$ and $CD8^+$ T cells were not observed, but in some certain populations like CX3CR1-expressed $CD56^+CD16^+$ NK cells and terminal differentiated effector $CD8^+$ T cells, the frequency of $CX3CR1^+$ cells in these populations tended to increase from the baseline at 2 week and kept increasing up to 24 week by the E6011 treatment.

Conclusion: E6011 significantly decreased the proportion of $CD16^+$ monocytes in whole monocytes. Our results indicated that the reduction of $CD16^+$ monocytes after initial treatment might be a sensitive marker of E6011 in peripheral blood,

possibly reflecting mechanism of action of E6011, since the $CD16^+$ monocytes highly express CX3CR1.

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Disclosure of Interests: Tomohiro Yamada Employee of: KAN Research Institute, Inc,, Jungo Kakuta Employee of: KAN Research Institute, Inc., Eri Fusaoka-Nishioka Employee of: KAN Research Institute, Inc., Jun-ichi Ito Employee of: EISAI, Nobuyuki Yasuda Employee of: KAN Research Institute, Inc., Tetsu Kawano: None declared, Toshio Imai: None declared

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FRI0010 GM-CSFR PATHWAY IS IMPLICATED IN PATHOGENIC INFLAMMATORY MECHANISMS IN GIANT CELL ARTERITIS

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Background: Giant Cell Arteritis (GCA) is characterized by inflammation of large and medium arteries. Classic symptoms include headaches, malaise and, in severe cases, blindness and aortic aneurysms. Corticosteroids (CS) are the first line of treatment. Relapsing disease patients undergo multiple courses of CS therapy increasing their CS exposure and toxicity. A significant unmet need for disease-modifying CS-sparing therapy remains in GCA as the efficacy of current treatment options, including tocilizumab have limitations.

We have previously reported elevated expression of granulocyte-macrophage colony stimulating factor (GM-CSF) pathway transcriptomic signature in GCA vessels. GM-CSF may contribute to underlying disease mechanisms by regulating inflammatory macrophages, dendritic cells (DCs) and T helper (T_H1/T_H17) cells which are involved in GCA pathogenesis. GM-CSF produced by T cells[1] can promote polarization of inflammatory macrophages[2] and recruitment and differentiation of monocytes into inflammatory DCs[2] that can in turn recruit T cells and stimulate T_H1/T_H17 differentiation creating a feedback loop. GM-CSF may also exert direct effects on angiogenesis[3] and vessel wall remodeling[4].

Objectives: To demonstrate the contributing role of GM-CSF pathway to inflammation in GCA arteries.

Methods: Immunostaining was used to examine expression of GM-CSF and GM-CSF-Rα proteins in temporal artery biopsies (TABs) from GCA and controls (patients with suspected but not confirmed GCA and a negative TAB). Costaining with cell markers such as CD31, CD3, and CD68 allowed visualization of cells expressing GM-CSF and GM-CSF-Rα. Expression of GM-CSF pathway molecules such as phospho-JAK2 and PU.1 proteins was detected by immunohistochemical staining of GCA and control TABs. *Ex vivo* cultured GCA arteries treated (10 each) with mavrilimumab (anti-GM-CSF-Rα) or placebo for 5 days were assayed for gene expression by qPCR, and culture supernatants were analyzed by ELISA.

Results: Endothelial cells and macrophages were the main cell types expressing GM-CSF and GM-CSF-Rα. Increased expression of phospho-JAK2 (activated signaling molecule) and nuclear-localized PU.1 (transcription factor) in GCA TABs compared to controls indicated the presence of active GM-CSF signaling pathway in GCA.

Inhibition of PU.1 mRNA expression in *ex vivo* cultures of GCA arteries treated with mavrilimumab indicated blockade of GM-CSFR signaling pathway. Mavrilimumab induced decrease in mRNA expression of key cell type markers including DC and macrophage activation markers CD83 and HLA-DRA, monocyte markers CD14 and CD16, T cell marker CD3ε, and B cell marker CD20 in these GCA artery cultures. Expression of inflammatory T_H1/T_H17 factors IFNγ (mRNA), TNFα, CXCL10 (IFNγ-stimulated chemokine) and IL-6 (mRNA and protein) was also inhibited by mavrilimumab in GCA artery cultures.

Conclusion: Increased GM-CSF, GM-CSF-Rα, and downstream pathway-associated protein levels in GCA biopsies were consistent with previously-observed increased transcriptome signature. Expression of genes associated with inflammatory cells was suppressed by mavrilimumab in cultured GCA arteries. These data implicate the GM-CSF pathway in GCA pathophysiology and increase confidence in rationale for targeting the GM-CSF pathway in GCA.

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Disclosure of Interests: Maria C. Cid Grant/research support from: Kiniksa Pharmaceuticals, Consultant of: Janssen, Abbvie, Roche, GSK, Speakers bureau: Vifor, Sujatha Muralidharan Shareholder of: Kiniksa, Employee of: Kiniksa, Marc Corbera-Bellalta: None declared, Georgina Espigol-Frigole Consultant of: Roche and Janssen, Javier Marco Hernandez: None declared, Amanda Denuc: None declared, Roberto Rios-Garces: None declared, Nekane Terrades-Garcia: None declared, John F. Paolini Shareholder of: Kiniksa, Employee of: Kiniksa, Annalisa D'Andrea Shareholder of: Kiniksa, Employee of: Kiniksa

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FRI0011 DEVELOPMENT OF A HIGH-DIMENSIONAL FLOW CYTOMETRY PANEL TO ANALYSE NATURAL KILLER CELLS IN SLE

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Background: Natural Killer (NK) cells are an innate immune cell type that has somewhat been overlooked in the context of systemic lupus erythematosus (SLE). SLE patients display a reduced number of NK cells with an activated phenotype and increased capacity to produce IFN-γ, decreased antibody-dependent cellular cytotoxicity (ADCC), and altered natural cytotoxicity (1). NK cell activation is determined by the integration of input from a myriad of activating and inhibitory receptors. Previously, using Nanostring® gene expression technologies, we found our SLE cohort showed decreased gene expression of a number of these receptors (KLRC2, KLRC1, KLRB1, KLRF1, KLRG1, PRF1 and IL2RB) leading us to explore NK cells in SLE in more depth.

Objectives: Our aim was to develop a high-dimensional flow cytometry panel to characterise dysregulation of NK cell in SLE, with particular reference to the activating and inhibitory receptors found to be dysregulated in SLE at the gene expression level.

Methods: Markers for NK panel were selected to include canonical phenotyping/functional molecules of NK cells with a particular emphasis on receptors found to be lower in our SLE cohort's gene expression findings. NK panel was designed to minimise spectral overlap, expression and co-expression of markers was taken into consideration. Antibodies were titrated, and voltages optimised to achieve the best separation index for each of the antibodies. The 24-marker panel was run on 52 SLE patients of various disease manifestations, treatments and disease severity. 20 healthy controls were also run for comparison.

Results: A 24-marker flow cytometry panel including 19 NK cell antigens was optimised, including basic phenotype (CD3/CD56/CD16/NKp46) and NK differentiation markers (CD57/CD94), activating and inhibitory receptors (NKG2A/NKG2C/NKG2D), costimulatory receptors (CD244/CD226), transcription factors (Eomes/Tbet) and effector molecules (granzyme/perforin). Immunophenotypic high-parameter analysis of SLE and control samples is in progress and results will be presented.

Conclusion: Our development of a high-dimensional immunophenotypic panel allows identification of changes in NK cells in SLE including antigen expression levels, subset percentages and potentially of novel subsets. This panel will be used to investigate NK cell changes with disease course/activity, therapeutic response, and to discover potential drug targets for SLE.

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Staff Specialists' TESL and Trust Fund Committee

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FRI0012

THERAPEUTIC VALUE OF CURCUMIN ON INITIATION AND DEVELOPMENT OF INFLAMMATION IN TAKAYASU'S ARTERITIS CAUSED BY HSP65-MEDIATED CCL2 OVEREXPRESSION

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Background: Takayasu's arteritis (TA) is a chronic inflammatory disease characterized with macrophages infiltration. During active stage, aorta adventitial fibroblasts (AAFs) proliferate excessively and produce numerous pro-inflammatory factors in the adventitia, which is the main target of TA therapy. Monocyte chemokine CCL2 may contribute to the infiltration of macrophages in TA arteries [1] but whether with relationship with HSP65, an antigen of Mycobacterium tuberculosis (M. TB) which might involve in the pathogenesis of TA [2] and activate AAFs to produce inflammatory factors, has not been reported. The treatment of TA is full of difficulties and contradictions [3]. Curcumin is a traditional Chinese medicine with anti-inflammatory effect [4], whether it is effective on TA and the underlying mechanism remains unclear.

Objectives: To explore the mechanism of TA inflammation triggered by M. TB associated antigen HSP65 activating AAFs, as well as the therapeutic value of curcumin in the initiation and development of TA.

Methods: We first verified high HSP65 expression in aortic adventitia of TA patients by IHC. mRNA-seq was used to profile DEGs between AAFs stimulated by HSP65 with or without pretreated with curcumin, and AAFs without any treatment. Then the key chemokine CCL2 screened by mRNA-seq was detected in the adventitia of TA aorta, and its correlation with HSP65 expression was analyzed by double-labelled IF. Subsequently, we explored how HSP65 affected the production of inflammatory factors by AAFs at cellular level and its related signal pathway. Simultaneously, we explored whether curcumin could hinder this process. and verified the effect of curcumin on serum CCL2 level in patients with TA. Finally, serum CCL2 and other inflammation indicators of TA patients at baseline and after 3 months treatment by curcumin were determined.

Results: HSP65 was highly expressed in the adventitia of TA arteries. DEGs analysis showed a key role of CCL2. The expression of CCL2 in adventitia of TA arteries was significantly higher than healthy subjects, and was correlated with HSP65. HSP65 facilitated the production of CCL2, IL-6 and IL-1β by AAFs via activating TLR4-JAK2/AKT/STAT3 pathway, among which the change of CCL2 was the most remarkable. Curcumin reversed the upregulation of CCL2 induced by HSP65 in vitro, which was more obvious than that of MTX and tofacitinib. Finally, curcumin significantly downregulated the level of serum CCL2 of TA patients.

Conclusion: HSP65 initiates and promotes inflammation of TA by upregulated CCL2 in AAFs through JAK/AKT/STAT3 pathway, while curcumin can reverse this process and slow down the initiation and development of TA.

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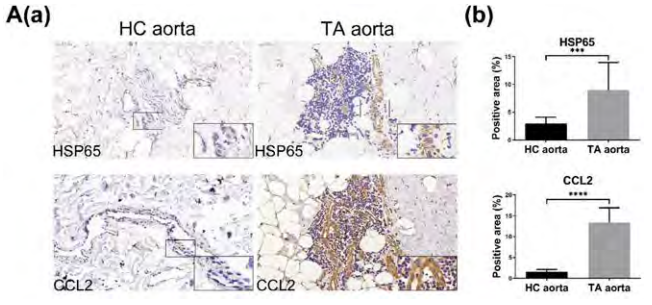


Figure A. High expression of HSP65 and CCL2 in aortic adventitia of TA patients (n=8) than that of healthy controls (n=6).

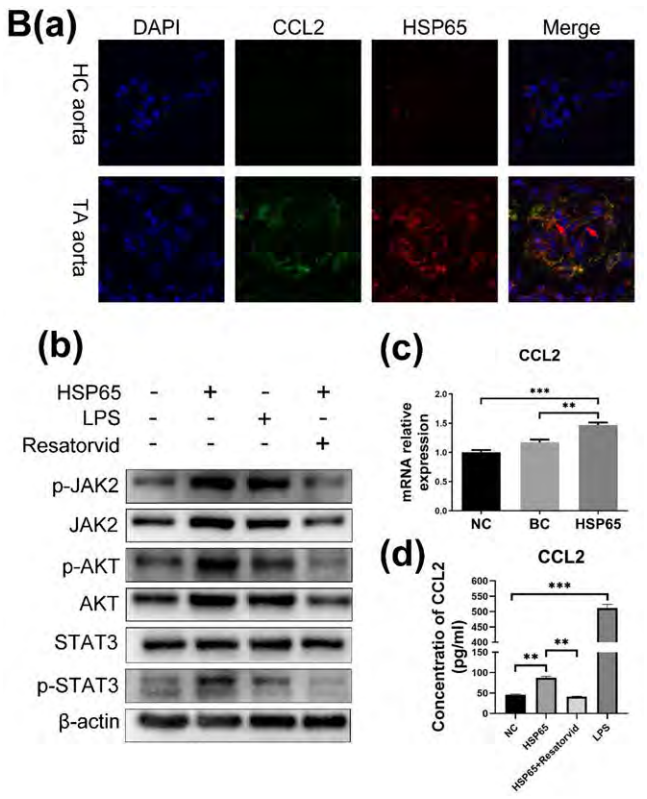


Figure B. HSP65 increased production of CCL2 in AAFs through TLR4/JAK2-STAT3 pathway.

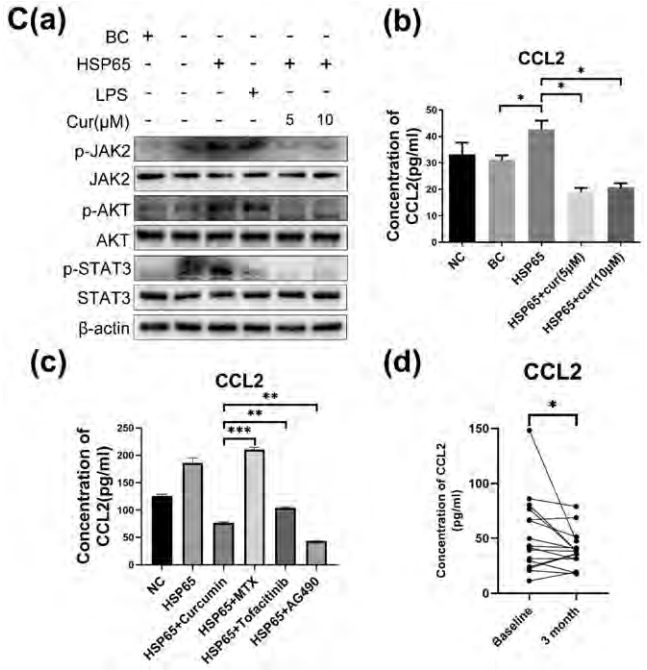


Figure C. Curcumin reversed inflammatory response initiated by HSP65 via inhibiting JAK2/AKT/STAT3 signal pathway in AAFs and significantly reduced serum CCL2 concentration of TA patients.

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Disclosure of Interests: None declared

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FRI0014

A PUTATIVE ROLE OF IGF-1R ON THE PATHOGENESIS OF GOUT THROUGH BINDING TO TRANSCRIPTION FACTORS

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Background: Recent studies showed that SNPs on IGF-1/IGF-1R were highly associated with hyperuricemia and gout [1,2]. It was shown that the IGF-1/IGF-1R signaling pathway played a role in regulating the serum urate level. By modulating the uric acid transporters, IGF-1/IGF-1R influenced the resorption and secretion of uric acid. However, we demonstrated that the increased activation of IGF1R could activate the mTOR pathway, leading to a higher inflammatory response upon pathogen stimulation [3]. This finding indicates that IGF-1/IGF1-R has a role in inflammation, which could results in gout. The IGF-1/IGF-1R pathway may have an overall influence on both urate transporters and inflammatory pathways. it was shown that IGF-1R was not only expressed on the cell surface, but could also internalize into the nucleus and recruit RNA polymerase, regulating the expression of other transcription factors[4]. These transcription factors have been shown to regulate inflammation and have been predicted to bind promoter regions of urate transporters [5]

Objectives: To unveil how the IGF-1/IGF1-R associates with hyperuricemia and gout by studying the IGF-1R SNP rs6598541.

Methods: To assess the influence of the SNP to IGF1-R, the protein expression of IGF-1R on the cell surface was identified by flow cytometry in different genotypes. Additionally, we measured the in vitro immune response of PBMCs with different genotypes upon exposure to MSU and/or LPS. To estimate the overall influence of the SNP on the immune response, we analyzed the SNP's function on transcription factors.

Results: We observed an enhanced inflammatory response in the homozygous genotype with the risk alleles upon LPS and/or MSU stimulation, indicative of a higher risk for gout. However, the IGF-1R surface expression level was comparable between different genotypes. Furthermore, in epigenetic analysis, we found that rs6598541 located in an enhancer region, which is bound by c-FOS, c-JUN and other transcription factors. In recent years, c-FOS and c-JUN have been shown to regulate inflammatory responses.

Conclusion: The risk allele of rs6598541 is associated with a higher inflammatory response, which might be the key factor for gout. Because of the location of the SNP, it might explain the function of IGF-1R in gout, and the pathogenesis might be modulated through transcription factors. According to the recent study, intracellular IGF-1R could act as a transcription factor regulating other transcription factors expression, like c-JUN. Additionally, c-JUN has been shown to regulate inflammatory responses. It is tempting to speculate that IGF-1R regulates transcription factors expression and leads to an overall immune responses, which influence the risk of gout.

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FRI0015

PHENOTYPE AND FUNCTION OF THE PERIPHERAL BLOOD DENDRITIC CELLS OF PSORIASIS PATIENTS WITH AND WITHOUT ARTHRITIS

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Background: Psoriasis is a frequent skin disease that can appear with an arthritic manifestation in approximately 30% of the cases [1]. The underlying excessive immune reaction caused by pro-inflammatory cytokines can be triggered by several risk factors [2]. Various subgroups of Dendritic cells (DCs) in the skin play a crucial role in the induction of the dermal inflammatory response [3].

Objectives: As the role of peripheral blood DCs remains unknown and the cause of an arthritic manifestation is still not completely understood [4], this project aimed to detect differences in phenotype or function of peripheral blood DCs in psoriatic patients with or without arthritis.

Methods: We analyzed peripheral blood cells of 60 psoriasis patients with and without arthritis. Different DC subpopulations were detected by flow cytometry. Monocyte-derived DCs were cultured with or without Lipopolysaccharides to gain immature (iDC) and mature (mDC) cells. The DC phenotype was determined by staining with CD80, CD83, CD86, CD206, CCR7, CD1a, HLA-DR, CD40, GPN-MB, DC209 and CD14. Their T-cell stimulatory capability was analyzed by co-incubation with Carboxyfluorescein succinimidyl ester stained lymphocytes and the quantification of CD4+ T-lymphocytes afterwards. To measure the migration capacity DCs were seated into transwell chambers with a semipermeable membrane and partly supplemented with Macrophage Inflammatory Protein 3 Beta (Mip3b). Migrated cells were detected by flow cytometry. Measured cell counts were normalized to cell counts without Mip3b stimulation.

Results: Comparing the factor of increase of migrated mDC counts due to mip3b stimulation, we detected a significant lower rate in samples of patients with arthritis (PsA) compared to those of patients without (Ps). Assays of mDCs without mip3b stimulation showed a significant higher count of migrated cells in the samples of the arthritic group [Figure 1]. Cell counts with Mip3b stimulation did vary slightly in the groups. The DC subpopulations and the expression of analyzed cell surface proteins did not show significant differences. The amounts of stimulated T-Lymphocytes did not differ significantly.

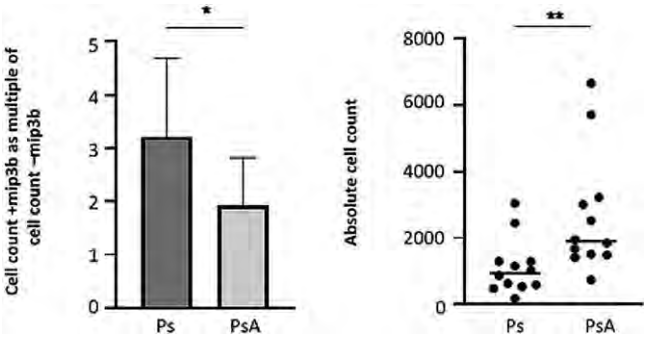


Figure 1. Migration essay showing mDCs following Mip3b (+miß3b) as multiples of mDCs without stimulation (-mip3b). The factor of increase is significantly lower in patients with arthritis (PsA) compared to patients without (Ps). Absolute counts of migrated mDCs without Mip3b are significantly higher in the arthritic group. Cell counts with stimulation do not differ significantly (data not shown). N=24, p<0.05

Conclusion: CCL19 (Mip3b) is a potent ligand to the CCR7 receptor inducing migration of DCs towards the lymphatic node [5]. The CCR7 amounts on the DC surface did not differ significantly in the groups. The mDCs without CCL19 stimulation migrated in higher amounts in samples of arthritic patients. Cell counts of stimulated DCs showed only slight differences. These results could be generated by a different appearance of the DCs of arthritic patients that might facilitate migration. Further experiments focusing on this aspect should be performed. A possible effect of disruptive factors (age, sex, medication…) needs to be clarified.

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Ann-Christin Pecher: None declared, Daniela Dörfel: None declared, Jörg Henes Grant/research support from: Novartis, Roche-Chugai, Consultant of: Novartis, Roche, Celgene, Pfizer, Abbvie, Sanofi, Boehringer-Ingelheim,
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FRI0016 R835, A NOVEL IRAK1/4 DUAL INHIBITOR IN CLINICAL DEVELOPMENT, BLOCKS TOLL-LIKE RECEPTOR 4 (TLR4) SIGNALING IN HUMAN AND MOUSE

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Background: Toll-Like Receptors (TLR) and Interleukin-1 Receptors (IL-1R) play a critical role in the innate immune response as microbial sensors, providing a bridge between the innate and adaptive immunity (1). Interleukin receptor associated kinases (IRAK) 1 and 4 are serine/threonine kinases that are essential for signaling downstream of most TLRs and IL-1Rs and the resulting production of pro-inflammatory cytokines (2). Suppression of TLR and IL-1R signaling through inhibition of IRAK1/4 kinases is a promising therapeutic approach for the treatment of inflammatory and autoimmune diseases.
Objectives: The aim of the study was to characterize the effects of R835, a novel small molecule inhibitor of IRAK1/4, on TLR4 signaling.
Methods: R835 was identified in cell-based assays measuring cytokine production induced by LPS (TLR4 ligand). Inhibition of IRAK1 and IRAK4 kinases by R835 was confirmed in biochemical assays and cell lysates. The ability of R835 to inhibit TLR4 signaling was further evaluated in human and mouse whole blood assays. R835 was tested in a mouse model of LPS-induced cytokine release. Mice were pre-treated orally with vehicle or R835 prior to challenge with LPS and serum cytokine levels were monitored over a 24-hour period.
Results: We have identified R835, a selective small molecule inhibitor of IRAK1 and IRAK4. R835 blocked LPS/TLR4 signaling and the resulting production of proinflammatory cytokines in both human and mouse cells and whole blood. R835 suppressed serum cytokine elevation in mice challenged with LPS.
Conclusion: Our study demonstrates that R835, through inhibition of IRAK1/4 kinase activity, blocks LPS-induced cytokine production in vitro and in vivo. In a recent phase 1 study, R835 substantially reduced the increase of serum cytokines after an intravenous LPS challenge in healthy volunteers. Importantly, this shows that the pharmacological inhibition of IRAK1/4 pathway by R835 in humans mirrors the results obtained in mice. To our knowledge, R835 is the first dual IRAK1/4 inhibitor to enter clinical development and demonstrate inhibition of TLR4-induced cytokines in both mice and humans. R835 is a promising clinical candidate that will allow the exploration of IRAK1/4 inhibition in the treatment of cytokine-driven rheumatic and autoimmune diseases.
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Disclosure of Interests: Chrystelle Lamagna Shareholder of: Rigel Pharmaceuticals, Employee of: Rigel Pharmaceuticals, Caroline Gundel Shareholder of: Shareholder of Rigel Pharmaceuticals, Employee of: Employee of Rigel Pharmaceuticals, Meagan Chan Shareholder of: Rigel Pharmaceuticals, Employee of: Rigel Pharmaceuticals, Chi Young Shareholder of: Rigel Pharmaceuticals, Employee of: Rigel Pharmaceuticals, Sylvia Braselmann Shareholder of: Shareholder of Rigel Pharmaceuticals, Employee of: Employee of Rigel Pharmaceuticals, Roy Frances Shareholder of: Rigel Pharmaceuticals, Employee of: Rigel Pharmaceuticals, Sothy Yi Shareholder of: Rigel Pharmaceuticals, Employee of: Rigel Pharmaceuticals, Yan Chen Shareholder of: Rigel Pharmaceuticals, Employee of: Rigel Pharmaceuticals, Gary Park Shareholder of: Rigel Pharmaceuticals, Employee of: Rigel Pharmaceuticals, Lu Chou Shareholder of: Rigel Pharmaceuticals, Employee of: Rigel Pharmaceuticals, Esteban Masuda Shareholder of: Rigel Pharmaceuticals, Employee of: Rigel Pharmaceuticals, Vanessa Taylor Shareholder of: Rigel Pharmaceuticals, Employee of: Rigel Pharmaceuticals
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FRI0017 ACTIVATION OF TOLL-LIKE RECEPTORS IN PERIPHERAL BLOOD MONONUCLEAR CELLS OF TAKAYASU ARTERITIS PATIENTS

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Background: The activation of self-specific T cells is essential in pathogenesis of Takayasu arteritis (TAK). Dendritic cell (DC) plays an indispensable role as the only antigen presenting cell for initial T cell, and Toll-like receptors (TLRs) are common source of activation signals for DCs. Then we speculate that there are activation of TLRs in TAK patients.
Objectives: To investigate the activation of TLRs in TAK patients.
Methods: Twenty-seven TAK patients were enrolled during April to October in 2019, with diagnosis met the 1990 criteria of American College of Rheumatology. Patient were divided into groups by the disease activity and medication history. Disease activity was assessed by the 1994 NIH criteria. Quantitative Real-time Polymerase Chain Reaction (RT-qPCR) was used to analyze the mRNA relative abundance of 28 target genes in peripheral blood mononuclear cells (PBMCs). Differences between groups and correlation between any two genes were analyzed.
Results: The demographic data and clinical features of TAK patients were shown in Table 1. (1) Compared with health control (HC) group, mRNA abundance of *TLR2, TLR4, P50, P65, IκBα, CTLA4, CD3,* and *BCL6* in untreated TAK group was upregulated (<0.05), whereas mRNA abundance of *CD40* was downregulated (p <0.05). (2) Compared with HC group, mRNA abundance of *TLR2, TLR4, IκBα, PD-1 and BCL6* in treated TAK group was upregulated (p <0.05), whereas mRNA abundance of *LAG3, CD40* and *TCR* was downregulated (p <0.05). (3) Compared with untreated TAK group, mRNA abundance of *P50, P65, CD28, CTLA4, TLR2, TLR4, IκBα, PD-1 and RORC* was upregulated in treated TAK group (p <0.05). (4) Compared with non-active treated TAK group, mRNA abundance of *p50, CD28, TCR, GATA3, RORC and FOXP3* was upregulated in nonactive treated TAK group (p <0.05). BCL6 showed correlation with the TLRs-NFκB pathway. (Figure 1~2, Table 2)

Table 1. Demographic data and clinical features of patients with TAK

								Prednisone	
	Age (year)	Gender (male/ female)	Disease duration* (months)	ESR (mm/h)	hs-CRP* (mg/L)	Interleukin 6 (pg/mL)	TNFα(pg/ mL)	used/ non-used	Dosage (mg/d)
Treated (*n*=20)	39.37±9.27	1/19	43 (12, 103)	14.60±8.94	1 (0.55, 5.625)	2.1 (2, 3.95)	7.56±4.39	18/2	10 (10, 32.5)
Active (*n*=11)	39.30±7.889	1/10	118 (16, 166.5)	16.82±10.81	5.63 (1.49, 8.33)	3.15 (2.025, 5.775)	8.42±5.57	10/1	10 (10, 15)
Nonactive (*n*=9)	39.44±10.59	0/9	40 (12, 44)	11.89±4.61	0.84 (0.31, 1)	2 (2, 2.4)	6.60±2.11	8/1	8.75 (6.875, 16.25)
P value	0.89	—	0.16	0.34	0.02	0.08	0.65	—	0.37
Untreated (*n*=7)									
Active (*n*=4)									
1	31	M	—	91	140.72	—	—	—	0
2	25	F	—	19	11.28	6.3	5.2	—	0
3	23	M	—	71	77.36	6.3	6.2	—	0
4	29	F	—	127	113.62	22.2	8.4	—	0
Nonactive (*n*=3)									
5	34	F	—	7	0.34	2	4.3	—	0
6	27	F	—	14	0.16	25.7	4	—	0
7	38	F	—	5	0.32	3	4	—	0

* median (min, max)

Table 2. Genes expressed abnormally in PBMCs of TAK patients

	Abnormally expressed in untreated TAK		Abnormally expressed in treated TAK		Influenced by treatment		Associated with the TAK activity	
	upregulated	downregulated	upregulated	downregulated	upregulated	downregulated	Upregulated	downregulated
Genes associated with the TLRs-NFκB pathway	*TLR2, TLR4, p50, p65, IκBα*	—	*TLR2, TLR4, IκBα*	—	—	*p50, p65*	*p50*	—
Positive and negative costimulatory molecules and their ligands	*CTLA4*	*CD40*	*PD-1*	*CD40, LAG3*	—	*CD28, CTLA4*	*CD28*	—
Genes associated with the activation or differentiation of T cell or B cell	*CD3, BCL6*	—	*BCL6*	*TCR*	—	*CD3, TCR, RORC*	*TCR, GATA3, RORC, FOXP3*	—

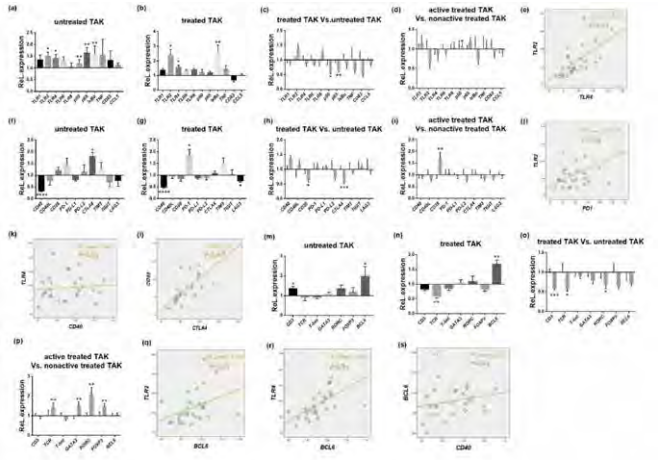


Figure 1. mRNA abundance of genes in PBMCs in TAK patients analyzed by qPCR

(a)~(e) Partial genes associated with TLRs-NFκB pathway. **(f)~(l)** Partial genes associated with the TLRs-NFκB pathway or costimulatory molecules. **(m)~(s)** Partial genes associated with the activation or differentiation of T cell or B cell. **(a)(f)(m)** Compare the untreated TAK group with the HC group whose data normalized to one. **(b)(g)(n)** Compare the treated TAK group with the HC group whose data normalized to one. **(c)(h)(o)** Compare the untreated TAK group with the treated TAK group whose data normalized to one. **(d)(i)(p)** Compare the active untreated TAK group with the nonactive treated TAK group whose data normalized to one. **(e)(j)~(l)(r)** Pearson correlation test, n=27 (all TAK patients enrolled). **(q)(s)** Spearman correlation test, n=27 (all TAK patients enrolled). Data are mean ± SEM. Untreated TAK group, n=7. Treated TAK group, n=20. Active untreated TAK group, n=9. Nonactive treated TAK group, n=11. HC group, n=11. *, $P<0.05$. **, $P<0.01$. ***, $P<0.001$. ****, $P<0.0001$.

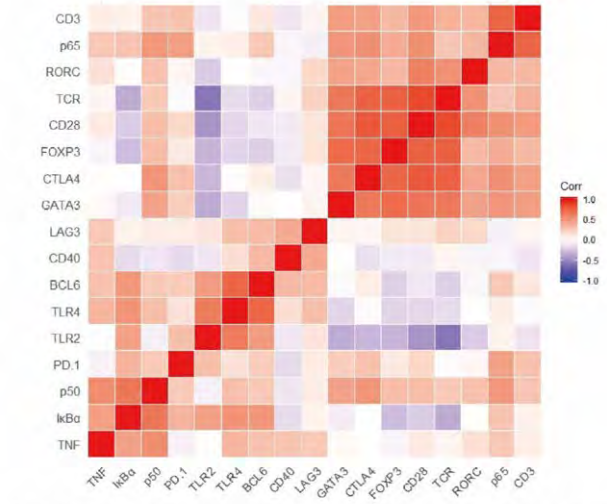


Figure 2 Correlation between any two genes expressed abnormally in PBMCs in TAK patients

Cluster Analysis by the result of Spearman correlation test. n=27 (all TAK patients enrolled).

Conclusion: TLRs-NFκB pathway may be activated in TAK patients, with upregulation of *BCL6*, and there may be deficiency of *CD40*. *TLR2, TLR4, PD-1, LAG3, CD40* and *BCL6* may play roles in the pathogenesis of TAK. *p50, CD28, TCR, GATA3, RCRC* and *FOXP3* may be related to the disease activity of TAK.

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FRIDAY, 05 JUNE 2020

Rheumatoid arthritis - prognosis, predictors and outcome

FRI0018

USING SELF-REPORTED OUTCOMES TO DETECT NEW-ONSET FLARE IN A REAL-WORLD STUDY OF PARTICIPANTS WITH RHEUMATOID ARTHRITIS - INTERIM RESULTS FROM THE DIGITAL TRACKING OF ARTHRITIS LONGITUDINALLY (DIGITAL) STUDY

V. S. Haynes[1], J. Curtis[2], F. Xie[2], I. Lipkovich[1], H. Zhao[2], C. L. Kannowski[1], J. L. Poon[1], K. Gavigan[3], D. Curtis[3], S. K. Nolot[1], W. B. Nowell[3]. [1]*Eli Lilly and Company, Indianapolis, United States of America*; [2]*University of Alabama at Birmingham, Birmingham, United States of America*; [3]*Global Healthy Living Foundation, Upper Nyack, United States of America*

Background: Patients with rheumatoid arthritis (RA) experience fluctuating symptoms, increased pain, decreased function and variable quality of life; such changes often occur between visits to clinicians. Digital Tracking of Arthritis Longitudinally (DIGITAL) study[2] is evaluating the use of electronically captured patient-reported outcomes (ePRO) and passive data collection from a Fitbit device to identify disease worsening in a real-world study of participants (pts) with RA.

Objectives: Evaluate agreement between self-reported new-onset flare and ePROs in an interim analysis from DIGITAL using a classification model.

Methods: Members of the ArthritisPower registry with RA were invited to participate in DIGITAL. Pts who successfully completed a two-week Lead-in period entered the Main Study in which they wore a smartwatch and provided daily (pain and fatigue numeric rating scales (NRS)) and weekly ePROs, including the OMERACT RA Flare Questionnaire (FLARE) and PROMIS measures. This interim analysis is of ePRO data from pts who completed at least 30 days of the Main Study. A "Yes" response to the FLARE item, "Are you having a flare now?" identified flare. For modeling association between new-onset flare and ePRO, the dataset was split into training (the first 30 days of the Main Study) and test data (Day 31 and following). Within each dataset, repeated binary outcomes (Flare/No Flare) per pt were defined each week. To focus on new-onset flare, within each dataset, outcomes for patient weeks for which flare was present in the previous week were excluded.

Candidate variables for the model included baseline and current FLARE score (0-50 scale) and each of its 5 items, daily pain, daily fatigue, and several PROMIS weekly instruments and their lagged values (last week or last 6 days for daily). 'Baseline' was calculated in non-flare weeks. Training data was used for logistic regression model selection combining clinical expertise with backward elimination. Performance of the final model was evaluated using test data.

Results: The training data was composed of outcomes from 128 pts who reported 388 weekly flare assessments as no flare or onset flare over 2800 days during the first month of the Main Study. Of pts in the training dataset, 92.2% were female, 87.5% white, with mean age (SD) 52.7 (11.0) and years since RA diagnosis 10.4 (10.3); 62.5% were on a biologic. Among those in the training dataset, 58 flare outcomes occurred in 50 (39.1%) unique pts.

The test data comprised outcomes from 123 pts who reported 442 weekly flare assessments as no flare or onset flare over 3366 days in which 64 flare outcomes occurred, and primarily included continued observations from pts who contributed to the training dataset.

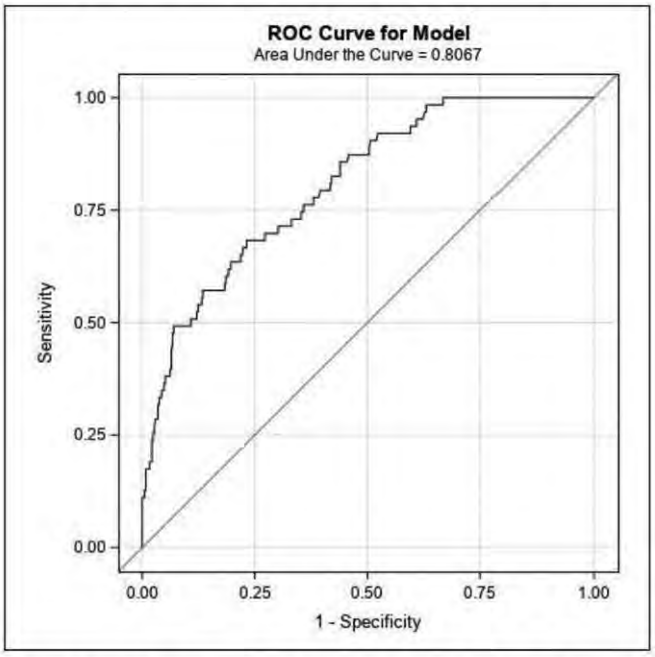
The best-performing model to classify flare in training data included the current and baseline FLARE instrument activity question (i.e. "Considering how active your rheumatoid arthritis has been, how much difficulty have you had when taking part in activities such as work, family life, social events that are typical for you during the last week"), current daily pain, and baseline daily pain average and standard deviation. In test data, this model had an area under the receiver operator curve of 0.81 (Figure). At a cut point requiring specificity to be ≥0.80, sensitivity to detect flare was 0.62 and overall accuracy was 0.78.

Conclusion: New-onset flare is common among RA patients, and the FLARE instrument and daily pain scores appear effective to classify it. Evaluation of passive data as a proxy for self-reported new-onset flare is ongoing.

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Figure. Performance of Flare Classification Using Best Fit Model*



*Model using current and prior week single-item for "difficulty taking part in work, family life and social events" from the FLARE instrument, and current daily pain and baseline daily pain average and standard deviation.

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FRI0019

MRI INFLAMMATION, DISEASE ACTIVITY AND FUNCTIONAL IMPAIRMENT ARE MORE EFFECTIVELY REDUCED BY ESCALATION TO BIOLOGICS COMPARED TO CSDMARD-ESCALATION IN RHEUMATOID ARTHRITIS PATIENTS IN CLINICAL REMISSION FOLLOWING A TREAT-TO-TARGET STRATEGY: SECONDARY ANALYSES OF THE IMAGINE-RA TRIAL

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Background: The effect of different treatment escalations on MRI inflammation in rheumatoid arthritis (RA) patients following an MRI treat-to-target (T2T) strategy has not previously been investigated.

Objectives: To compare the effect of different treatment escalations on MRI inflammation, physical function and disease activity in RA patients in clinical remission, following an MRI T2T strategy.

Methods: One hundred RA patients in clinical remission (DAS28-CRP<3.2 and no swollen joints), on conventional synthetic (cs) DMARDs following an MRI T2T strategy targeting DAS28-CRP≤3.2, no swollen joints plus absence of MRI osteitis, were followed for 2 years with clinical and MRI (wrist and 2nd-5th MCP joints) evaluation every 4 months[1]. If target was not met, a predefined treatment escalation algorithm dictated: First: increase in csDMARDs (A), second: adding a TNF inhibitor (TNFi) (B), third and onwards: switch between biologics (C). If target was met, no change in baseline csDMARDs was done (D). Outcomes were assessed 4 months after treatment change. MRIs were evaluated with known chronology by one experienced reader. Repeated measures mixed linear models were used to express estimates of group differences on predefined co-primary outcomes (MRI osteitis, HAQ) and key secondary outcomes (MRI combined inflammation, Simplified Disease Activity Index (SDAI)).

Results: Escalation to first TNFi (B) or to 2nd or later biologic (C) compared to csDMARDs (A) was consistently more effective on all outcomes (e.g. in group B osteitis was reduced with 1.8 units more than A) (Table). Unchanged (D) compared to escalation in csDMARD (A) treatment did not differ, except for HAQ-score. Escalation to a 2nd or later biologics (C) compared to the first TNFi (B) was more effective suppressing MRI inflammation. Escalation to TNFi treatment (B) or to 2nd or later biologic (C) compared to unchanged treatment (D) was more effective on all outcomes except from HAQ-score (no difference between groups).

Conclusion: T2T-based treatment escalations to biologics compared to csDMARD-escalations more effectively improved MRI inflammation, physical function and disease activity. Further optimization of the treatment in RA patients in clinical remission may improve long-term outcomes.

References:

[1] Møller-Bisgaard et al. JAMA 2019

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Comparisons of treatment escalations[1]
A: Increment in csDMARD mono/combination therapy (n=73)); B: Switch from csDMARD combination therapy to TNFi (n=39); C: Switch from TNFi to 2nd biologic/switch between biologics (n=21); D: No change in csDMARDs from baseline (n=58)

	A vs B	A vs C	A vs D	B vs C	B vs D	C vs D
Outcomes						
Primary						
MRI	1.8 (1.0; 2.6) p<.0001	3.6 (2.3; 4.8) p<.0001	0.3 (−0.3; 1.0) p=.32	1.8 (0.8; 2.9) p=.0006	−1.4 (−2.4; −0.5) p=.0045	−3.3 (−4.6; −1.9) p<.0001
Osteitis						
HAQ	0.081 (0.033; 0.13) p=.0011	0.091 (0.031; 0.15) p=.0032	0.054 (0.014; 0.095) p=.0091	0.0092 (−0.051; 0.070) p=.77	−0.027 (−0.082; 0.028) p=.33	−0.037 (−0.10; 0.031) p=.29
Key secondary						
MRI combined inflammation[a]	2.5 (0.9; 4.1) p=.0018	5.4 (3.1; 7.7) p<.0001	0.4 (−0.9; 1.8) p=.52	2.9 (0.8; 4.9) p=.0064	−2.1 (−4.0; −0.2) p=.032	−5.0 (−7.5; −2.4) p=.0002
SDAI	2.7 (1.9; 3.5) p<.0001	2.4 (1.4; 3.4) p<.0001	0.5 (−0.2; 1.2) p=.14	−0.3 (−1.3; 0.7) p=.60	−2.2 (−3.1; −1.3) p<.0001	−1.9 (−3.0; 0.8) p=.0006

[1] Estimates of group differences (least squares means (95% CI)).
[a] Sum score of synovitis, osteitis and tenosynovitis

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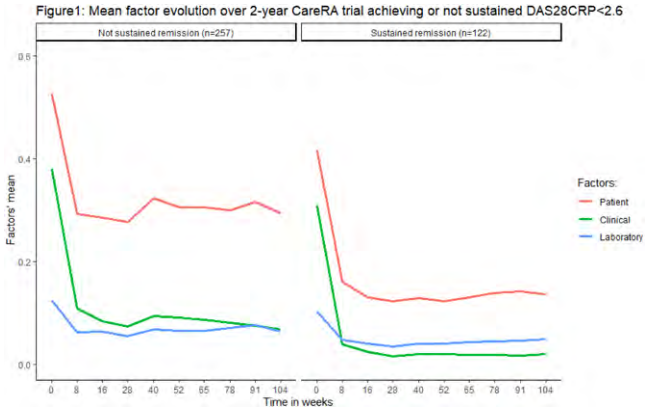
FRI0020 CLINICAL TREATMENT RESPONSE STILL DOES NOT MATCH PATIENT REPORTED IMPROVEMENT, EVEN IN EARLY RHEUMATOID ARTHRITIS

S. Pazmino[1], A. Lovik[2], A. Boonen[3], D. De Cock[1], V. Stouten[1], J. Joly[4], D. Bertrand[1], R. Westhovens[1,4], P. Verschueren[1,4] on behalf of CareRA Study Group. [1]*KU Leuven, Development and Regeneration, Leuven, Belgium*; [2]*KU Leuven, Leuven Biostatistics, Leuven, Belgium*; [3]*Maastricht UMC, Maastricht, Netherlands*; [4]*University Hospitals Leuven, Rheumatology, Leuven, Belgium*

Background: Commonly used disease activity scores in rheumatoid arthritis (RA) include one patient reported outcome (PRO) -the patient's global health assessment (PGA). Exploratory factor analysis (EFA) was performed on data from the 2 year Care in early Rheumatoid Arthritis (CareRA) trial to explain the evolution of disease burden extracting 3 factors.[1]
Objectives: To assess the evolution and relative responsiveness over time of clinical, laboratory and patient assessments included in composite scores, together with other PROs like pain, fatigue and functionality in patients with early RA (≤1 year) treated to target (T2T) within the CareRA trial.
Methods: DMARD naïve patients with early RA (n=379) were included, randomized to remission induction with COBRA-like treatment schemes (n=332) or MTX monotherapy (n=47) and T2T.
Components of disease activity scores (swollen/tender joint count (S/TJC), C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR), and physician (PhGH) or patient (PGA) global health assessment), pain and fatigue (both on 0-100 scale) and HAQ were recorded at every visit.
Missing data was handled with multiple imputation (n=15). Clustering was removed with multiple outputation (n=1000), then each of the 15 000 datasets was analyzed by EFA with principal component extraction and oblimin rotation. The analyses were combined after re-ordering the factors by maximizing factor congruence. The 3 extracted factors and their individual components (with their loadings) were: 1. Patient containing PGA (0.87), pain (0.86), fatigue (0.90) and HAQ (0.5) 2.Clinical with SJC (0.92), TJC (0.89) and PhGH (0.76) and 3.Laboratory with CRP(0.87) and ESR (0.78).[1](Pazmino, ACR 2019 abstract, Table 3)
Afterwards, variables were first normalized to a 0-1 scale, then multiplied -weighted- by the factor loadings previously obtained.[1] For each Patient, Clinical and Laboratory severity score, the weighted variables belonging to each score were summed together and then re-scaled to 0-1 (higher values suggest more burden).
The percentage (%) improvement from baseline to week 104 and the area under the curve (AUC) across time points were calculated per factor.
Differences in % improvement and AUC were compared between patients not achieving and achieving early and sustained (week 16 to 104) disease activity score remission (DAS28CRP <2.6) with ANOVA. Bonferroni correction was used for multiple testing.
Results: Severity scores of Patient, Clinical and Laboratory factors improved rapidly over time (Figure 1). In patients achieving sustained remission (n=122), Patient, Clinical and Laboratory scores improved 56%, 90% and 27% respectively. In patients not achieving sustained remission (n=257) the improvement was 32%, 78% and 9% respectively (p<0.001 only for clinical improvement).
Patients in CareRA who achieved sustained remission had an AUC of 15.1, 3.4 and 4.7 in Patient, Clinical and Laboratory scores respectively, compared to 32.3, 10.0, and 7.2 in participants not achieving sustained remission (p<0.001 for all comparisons).
Conclusion: Patient, Clinical and Laboratory severity scores improved rapidly over time in patients achieving rapid and sustained disease control. However, overall, Patient burden seemed not to improve to the same extent as Clinical burden. Patient's unmet needs in terms of pain, fatigue, functionality and overall well-being should thus be given more attention, even in patients in sustained remission.

References:

[1] Pazmino S, *et al.* Including Pain, Fatigue and Functionality Regularly in the Assessment of Patients with Early Rheumatoid Arthritis Separately Adds to the Evaluation of Disease Status [abstract]. ACR. 2019.



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FRI0021 SHOULD WE USE GLUCOCORTICOID IN EARLY RHEUMATOID ARTHRITIS?: RESULTS AT 5 YEARS FROM THE ERA LOUVAIN BRUSSELS COHORT

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Background: The EULAR recommendations, updated in 2016, propose the initiation of glucocorticoid (GC) therapy in combination with cDMARDs background therapy for every patient with early rheumatoid arthritis (ERA).[1]
Objectives: The aim of this study is to evaluate the proportion of patients with ERA who have been treated with GC in daily practice, to analyse the baseline characteristics of these patients, and to assess the clinical benefit and side effects of GC during 5 years of follow-up.
Methods: We included patients with ERA from the UCLouvain Brussels cohort who met the ACR/EULAR 2010 classification criteria and were naïve to cDMARDs. Treatments were initiated based on the decision of a senior rheumatologist. We retrospectively collected patient characteristics prior to the introduction of cDMARDs with or without GC. Efficiency and serious adverse events were analysed at 6 months, 1 year, 3 years and 5 years.
Results: Data from 474 eligible ERA patients were collected. The average age of the population is 48.9 years. 70.5% of the patients are women. 27.3% are smokers and 68.8% are positive for anti-citrullinated protein antibody (ACPA).
178 patients (37.7 %) initiated GC compared to 294 patients (62.3%) who received only NSAIDs and/or analgesics in combination with cDMARDs.
At baseline, the elevation of CRP is the main factor that favors the initiation of GC (CRP 2.9 vs 2.0 mg/dl, p = 0.015) followed by smoking habits (34.2% vs 23.3%, p = 0.018), the absence of ACPA (37.2% vs 27.6%, p = 0.037), the prescription of methotrexate as a monotherapy (70.6% vs 50.5%, p <0.001), and the age (50.6 vs 48.0, p = 0.050). Other parameters such as swollen joint count, tender joint count, DAS28-CRP, HAQ or baseline erosion were similar between groups.

5 years follow-up of DAS28-CRP, HAQ or VAS pain values did not differ between the two groups (Fig 1A).

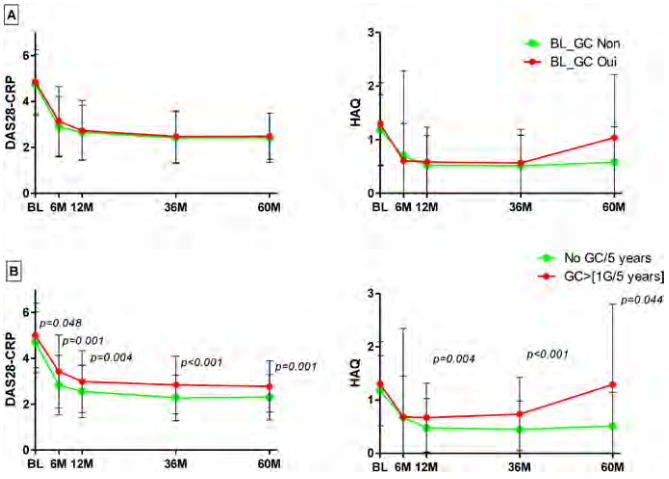


Figure 1. Comparison of DAS28-CRP and HAQ scores evolution. **(A)** in two groups of patients: treated with GC (BL-GC Yes) or without GC (BL_GC No) in combination with cDMARDs as first line treatment. **(B)** in two groups of patients: never treated with GC during 5 years follow-up (No GC/ 5 years) and those who received a high cumulative dose of GC ≥ 1 g/5years (GC>[1G/5years]).

Interestingly, patients not exposed at baseline to GC showed a higher remission rate (DAS28-CRP< 2.6) of 48.4% vs 44.3% at 6 months.

We also analysed a subgroup of patients (n=139) who received a cumulative dose of more than 1 g of prednisolone during the 5 years period. We confirmed the baseline differences for CRP, smoking habits, age and found in this subgroup more males (36.7% vs 28.2%, p=0.021) and higher DAS-28CRP values (5.0 vs 4.7, p=0.048).

During the 5 years follow up, DAS-28CRP, VAS pain and HAQ remained significantly higher leading to a higher number of bioDMARDs prescribed in this group (Fig 1B).

More severe infections were reported in this subgroup (11.5% vs 4.2%). Bone densitometry values, number of fractures, and cardiovascular profiles were similar between groups.

Conclusion: In our ERA cohort, initiation of GC treatment does not add additional benefit for the short and long-term control of the disease.

GC were more prescribed in seronegative RA patients with higher level of inflammation and we confirm that patients exposed to higher cumulative doses of GC are at higher risk to develop severe infections.

Further studies are needed to support that GC induction therapy should not be offered to all ERA patients.

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[1] Smolen JS, Landewé R, Bijlsma J, et al., EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. Ann Rheum Dis. 2017 Jun;76(6):960-977.

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FRI0022 THE ANALYSIS OF THE INVOLVEMENT OF TRANSFORMING-GROWTH INTERACTING FACTOR POLYMORPHISMS IN THE BONE METABOLISM OF RHEUMATOID ARTHRITIS

H. Tan[1], L. Zhang[1], B. Yang[1], L. Zhou[1] on behalf of All authors have declared that no competing interests exist. The data and material analysed in the current study are available from the corresponding author on reasonable request..

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Background: Rheumatoid arthritis (RA) is an autoimmune disease that mainly invades synovial membranes and further damage to articular cartilage and bone. The abnormal activation of transforming-growth factor β (TGF-β) in the subchondral bone is related to the onset of RA joint cartilage degeneration and transforming-growth interacting factor (TGIF) is a negative regulator of TGF-β signaling, while there is no literature addressing the relationship between TGIF polymorphisms and the bone metabolism of RA.

Objectives: The aim of the study was to comprehensively explore the possible association for single nucleotide polymorphisms (SNPs) in the TGIF gene with serum bone metabolism markers and RA susceptibility.

Methods: Three SNPs within the TGIF gene were genotyped in 155 RA patients and 168 healthy controls by high resolution melting (HRM) analysis in a case-control study. The serum levels of osteocalcin, bone alkaline phosphatase (BALP) and β type I collagen-crosslinked C telopeptide (β-CTX) were detected by electrochemical luminescence in 108 RA patients randomly selected from RA patients group.

Results: Genotypes and alleles frequency analysis showed rs7362020 was associated with bone erosion in RA (P=0.012, P=0.003, respectively) and individuals carrying T allele for rs7362020 showed a decreased RA risk (OR=0.59, 95% CI = 0.42-0.84; P= 0.003). In the gender-specific analysis, rs73620203 polymorphism was associated with bone erosion of female RA patients (P values of the distribution of genotypes and alleles were 0.022 and 0.006, respectively). In addition, RA patients with CC, CT and TT genotypes at rs73620203 locus had statistically significant differences in serum osteocalcin and BALP (P=0.006, P=0.037, respectively) and the serum levels in TT genotype RA patients were significantly lower than CC and CT genotype RA patients. The serum levels of β-CTX in rs85440 AA genotype male RA patients were significantly higher than female RA patients (P=0.001), while the serum levels of osteocalcin and BALP in genotype AA, AG and GG female and male RA patients were not significantly different (P all>0.05).

Conclusion: Our study provided the first evidence that rs73620203 is associated with bone erosion of RA and provided new insight into the relationship between three SNPs within TGIF gene and regulation of bone metabolism in RA patients of different genders.

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FRI0023 TREATING EARLY AND INTENSIVELY IS ASSOCIATED WITH LOWER FATIGUE LEVELS ON THE LONG TERM, EVEN IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS CONSIDERED TO HAVE A FAVOURABLE RISK PROFILE

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Background: Fatigue is reported in up to 90% of patients with established Rheumatoid Arthritis (RA). Fatigue has a large impact on patient`s life and is perceived difficult to manage in many patients. The early disease course could constitute a window of opportunity to tackle fatigue.

Objectives: To explore that, if RA can be controlled rapidly, complaints of fatigue could be less in the long run, even in patients considered at low risk to develop a severe disease course.

Methods: Patients with a low risk profile recruited in the 2-year pragmatic Care in Early Rheumatoid Arthritis (CareRA) trial were used in this analysis. This low risk profile was based on the absence of erosions, rheumatoid factor, anti-citrullinated protein bodies or low disease activity status. The low-risk group was randomised to either a tight step-up starting with 15mg MTX weekly in monotherapy (MTX-TSU) or COBRA Slim, consisting of 15 mg MTX weekly and a prednisone step-down scheme starting at 30 mg. Fatigue was measured by the multi-dimensional fatigue inventory (MFI), a self-report instrument consisting of 20 questions with a Likert scale from 1-5 as answer. These 20 questions can be subdivided in five subscales (0-20) of four questions (higher scores indicating higher fatigue levels): general fatigue, mental fatigue, physical fatigue, reduced activity and reduced motivation. General fatigue means the general feeling of being tired. Mental fatigue implicates concentration and memory problems. Physical fatigue implicates a lack of energy and strength. Reduced activity means that patients can do less activities for example on one day. Reduced motivation means that patients don't want to plan or do things due to lack of motivation. MFI was obtained at baseline, at week 16, week 52 and week 104. Cobra Slim was compared with MTX-TSU by Mann-Whitney-U test. The 5 domains of the MFI of the two groups were compared by a generalized estimating equation (GEE) over 2 years adjusting for baseline MFI domain score and DAS28.

Results: Of the 90 patients recruited in the low-risk group, 80 (89%) patients completed the MFI at baseline. Randomisation was successful resulting in similar baseline characteristics and MFI levels between Cobra Slim (n=38) and MTX-TSU (n=42). After 2 years of treatment, DAS28CRP levels (Slim 1.9 ±0.8 - MTX-TSU 2.2 ±1.0, p=0.253) and DAS28CRP remission (Slim 81.5% - MTX-TSU 77.1%, p=0.677) did not differ between patients. However, general (Slim 9.8 ±4.1 – MTX-TSU 13.1 ±4.0, p=0.005) and mental (Slim 6.8 ±2.7 - MTX-TSU 10.0 ±4.9, p=0.022) fatigue levels on the MFI were lower in the Cobra Slim group at week 104. GEE analysis confirmed that groups differed in the general (p=0.026) and mental (p=0.013) fatigue scale over 2 years (Figure 1).

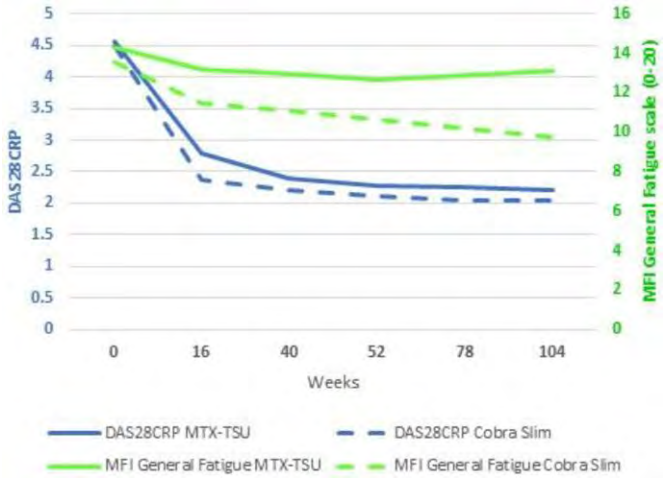


Figure 1. DAS28CRP and MFI General Fatigue score over 2 years between groups

Conclusion: Patients treated intensively have lower fatigue levels over 2 years compared to patients treated more conservatively, even if disease activity became similar in the two groups over time. This underlines the importance of initiating an optimal intensive treatment even in so called low-risk patients. Moreover, our results show that fatigue is a heterogeneous concept, with different interactions between treatment and type of fatigue. Although our study was limited by a small sample size, the data clearly shows how to improve fatigue levels significantly in early RA.

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FRI0024

HOW OFTEN DOES REACHING TARGET MISS THE MARK? LONGITUDINAL PATTERNS OF REMISSION IN REAL-WORLD EARLY RHEUMATOID ARTHRITIS PATIENTS

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Background: Early diagnosis and rapid initiation of DMARDs following a treat-to-target approach have made remission a realizable goal for many with RA. Yet, some patients are unable to sustain remission over time.

Objectives: To describe longitudinal patterns of remission and identify predictors of sustained vs transient remission in real-world early RA patients.

Methods: Data were from the Canadian Early Arthritis Cohort (CATCH), a prospective study of early RA patients (symptoms < 1 year) treated in rheumatology clinics across Canada from 2007- 2019. The sample was limited to patients with active disease at enrolment who later reached remission (SDAI<=3.3) and were followed for 12-24 months thereafter. Patients were classified as in sustained remission (Pattern 1) or transient remission with transient remission patients divided into those who transitioned from REM to LDA only (Pattern 2) and those who transitioned from REM to MDA or HDA (Pattern 3), over FU. Multi-adjusted multinomial regression was used to identify predictors of transient remission patterns.

Results: The study included 1,419 (46%) CATCH participants that reached remission. At enrolment, most (70%) were female, mean(sd) SDAI was high (27(15)) and 92% were treated with csDMARDs. Only 47% remained in sustained remission by 12-months and, only 40% by 24 months (Pattern 1) (Figure). Among patients with transient remission patterns, transitions to LDA only (Pattern 2) were more common than to MDA/HDA over FU (Pattern 3) (Fig 1). Older age, female sex, smoking, higher comorbidity index and positive serology, were significantly associated with transient remission patterns (Table). There were also borderline significant associations between transient remission patterns and longer time to remission, lack of early MTX treatment and reducing treatment after remission (Table).

Table. Adjusted Multinomial Regression Results of Predictors of Transient Remission Patterns over 24-Month Follow Up

	Pattern 2 vs, Pattern 1 OR (95% CI)	Pattern 3 vs. Pattern 1 OR (95% CI)
Age	1.01 (1.00, 1.02)	1.01 (0.99, 1.02)
Women vs Men	**1.78 (1.33, 2.39)**	**1.63 (1.09, 2.44)**
Current smoker	**1.57 (1.09, 2.28)**	1.53 (0.95, 2.47)
RDCI at baseline	1.11 (0.99, 1.25)	**1.30 (1.13, 1.50)**
Seropositive	**1.38 (1.03, 1.85)**	1.21 (0.81, 1.80)
MTX first 3 months	1.18 (0.85, 1.63)	0.76 (0.51, 1.12)
Time to remission (months)	1.01 (1.00, 1.01)	1.01 (1.00, 1.02)
Treatment reduction after REM vs. No Change	1.33 (0.96, 1.86)	1.01 (0.99, 1.02)

Pattern 1: Sustained REM
Pattern 2: Transient REM: Transitions to LDA only
Pattern 3: Transient REM: Transitions to MDA/HDA
RDCI: Rheumatic Disease Comorbidity Index (range 0-9)
Treatment reduction: Change from biologic or JAK to csDMARD(s) OR reduction in number of csDMARDs OR change from MTX +/- csDMARDs to non-MTX csDMARD

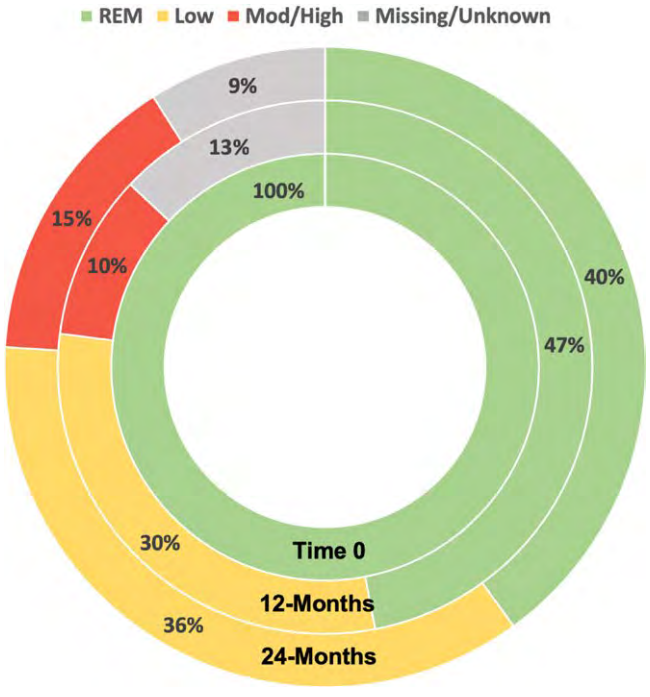


Figure. Distribution of Disease Activity States over 12-24 After First Achieving SDAI REM

Conclusion: Results of this large longitudinal analysis of real-world data suggests that < 50% of patients that reach remission sustain remission for 12-24months. Closer monitoring of patients with prognostic indicators for transient remission and additional research focusing on why remission is lost may help improve the rates of sustained remission.

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Amgen Canada (CATCH, clinical nurse)
Abbvie (CATCH, clinical nurse)
Pfizer (CATCH, Registry of biologics, Clinical nurse)
Hoffman-LaRoche (CATCH)
UCB Canada (CATCH, Clinical nurse)
BMS (CATCH, Clinical nurse, Observational Study Protocol IM101664. SERO-POSITIVITY IN A LARGE CANADIAN OBSERVATIONAL COHORT)
Janssen (CATCH)
Celgene (Clinical nurse)
Eli Lilly (Registry of biologics, Clinical nurse), Consultant of: Eli Lilly, Janssen, Novartis, Pfizer, Speakers bureau: Merck, BMS, Pfizer, Carol Hitchon Grant/research support from: UCB Canada; Pfizer Canada, Edward Keystone Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, F. Hoffmann-La Roche Inc, Gilead, Janssen Inc, Lilly Pharmaceuticals, Pfizer Pharmaceuticals, Sanofi-Aventis, Consultant of: AbbVie, Amgen, AstraZeneca Pharma, Biotest, Bristol-Myers Squibb Company, Celltrion, Crescendo Bioscience, F. Hoffmann-La Roche Inc, Genentech Inc, Gilead, Janssen Inc, Lilly Pharmaceuticals, Merck, Pfizer Pharmaceuticals, Sandoz, UCB., Speakers bureau: Amgen, AbbVie, Bristol-Myers Squibb Canada, F. Hoffmann-La Roche Inc., Janssen Inc., Merck, Pfizer Pharmaceuticals, Sanofi Genzyme, UCB, Janet Pope Grant/research support from: AbbVie, Bristol-Myers Squibb, Eli Lilly & Company, Merck, Roche, Seattle Genetics, UCB, Consultant of: AbbVie, Actelion, Amgen, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Eicos Sciences, Eli Lilly & Company, Emerald, Gilead Sciences, Inc., Janssen, Merck, Novartis, Pfizer, Roche, Sandoz, Sanofi, UCB, Speakers bureau: UCB, Carter Thorne Consultant of: Abbvie, Centocor, Janssen, Lilly, Medexus/Medac, Pfizer, Speakers bureau: Medexus/Medac, Diane Tin: None declared, Vivian Bykerk: None declared

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FRI0025 CIRCADIAN RHYTHMS OF ENDOTHELIAL NITRIC OXIDE SYNTHASE PRODUCTION IN FEMALES WITH RHEUMATOID ARTHRITIS AND ARTERIAL HYPERTENSION DEPENDING ON NOS3 T786C GENE POLYMORPHISM

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Background: One of the most common comorbidity in patients with rheumatoid arthritis (RA) is arterial hypertension (AH), with incidence ranging from 20 to 60%. Mechanisms of this comorbidity arises a lot of interest. In our previous study was established the association of *T786C NOS3* (rs2070744) gene polymorphism with AH in females with RA in the Ukrainian population [1].
Objectives: So next, we were aiming to investigate daily fluctuation of endothelial nitric oxide synthase (NOS3) in RA patients with AH depending on *NOS3 T786C* gene polymorphism.
Methods: In the study were enrolled 173 females with RA aged 43.7 ± 7.35 years (Mean ± SD) and 34 age-matched healthy women without joint diseases and autoimmune diseases (control). Serum NOS3 level was determined at 08:00 and 20:00 using Cloud-Clone Corp kits (USA). *NOS3 T-786C* polymorphism was determined by Real-Time PCR (Bio-Rad iCycler IQ5) using SNP-express kit. Study was carried out in compliance with bioethical standards and provisions of the WHO, Helsinki Declaration of the General Assembly of the World Medical Association (1989).
Results: Among enrolled patients prevailed individuals with more than 5 years disease history, II-III radiographic stage (80.9 %), and were seropositive for anti-cyclic citrullinated peptide (80.6%). There were 114 (66%) normotensive patients and 59 (34%) patients with AH (13% - I stage, 20.8% - II stage). The daily fluctuation of NOS3 serum level was established in the control group. The evening NOS3 level was higher in 1.3 times, than the morning level ($p<0.001$). In RA patients the similar fluctuations of NOS3 level was registered, but the daily NOS3 production was lower, than in control. Diurnal variation of NOS3 level depended on comorbid AH and *NOS3 T-786C* genotype. In *CC* genotype NOS3 levels at 08:00 and at 20:00 were lower in 1.2-1.3 times ($p<0.05$) than in *TT* and *TC* genotypes. In patients with RA and AH the lowest diurnal variation of NOS3 level was in *CC* genotype. The decrease of evening NOS3 production was strong associated with comorbid AH (OR 3.78; 95% CI 1.96-7.28).
Conclusion: Circadian rhythms of NOS3 production in females with RA and AH depend on *NOS3 T786C* gene polymorphism. The depression of NOS3 production in the evening can be predictor of comorbid AH in females with RA.

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FRI0026 PROTEOMICS ANALYSIS COMPARING THE MODE OF ACTION OF UPADACITINIB AND ADALIMUMAB HEAD TO HEAD IN RA IDENTIFIES NOVEL, DISCRETE EARLY IMMUNE PATHWAY MODULATION IN THE SELECT-COMPARE PHASE 3 STUDY

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Background: Upadacitinib (UPA), an oral JAK1 selective inhibitor, showed greater efficacy compared to adalimumab (ADA) in patients with active rheumatoid arthritis (RA) despite treatment with methotrexate (MTX) in the SELECT-COMPARE phase 3 study[1]. The regulatory immune networks affected by JAK1 inhibition compared with TNF-blockade have not been explored previously in a head-to-head trial.
Objectives: To infer the relative immunological pathway modulation of UPA compared with ADA in patients with RA via the evaluation of a pre-defined set of plasma proteins associated with inflammation.
Methods: Patients from the SELECT-COMPARE studies were randomly selected (PBO, n=100; UPA 15 mg QD, n=100; ADA 40 mg EOW, N = 100). The levels of 184 inflammation related proteins were analyzed using the Olink® platform; change from baseline in protein levels were expressed as Log2 Fold Change; a Repeated Measure Mixed Linear Model identified proteins differentially modulated by UPA and ADA compared to PBO, and between Responders (R defined as achieving Low Disease Activity [LDA] based on CDAI [≤ 10] at week 12) and Non Responders (NR defined as not achieving LDA at week 12) for the UPA and ADA groups. Pathway analysis were performed with Ingenuity® Pathway Analysis (Qiagen Inc.); selection criteria: mean $|Log2\ FC| \geq 0.1$ AND a FDR ≤ 0.05 → n = 88 out of 184 proteins; the top 10% pathways based on Z score for the ADA and UPA groups, and each visit (Week 2 and Week 8) were selected for comparison.
Results: Both UPA and ADA inhibited protein biomarkers (pBM) associated with Neutrophil / Macrophage biology. However, UPA preferentially inhibited pBM associated with T cells and ADA preferentially inhibited pBM associated with M1 or 'inflammatory' Macrophages. The pathways implicated *in silico* by these pBM changes in response to UPA and ADA tended to be similar except for T cell activity related pathways that were preferentially modulated by UPA.
In the ADA group, clinical response was mainly associated with lower levels of pBMs such as IL6, TNFRSF1A, MMP10, IL2RA, PLAUR, CCL2, TNFRSF10C, and SERPINE1, suggesting that control of these pathways may be important for response to ADA in RA.
In the UPA treated group, clinical response was mainly associated with slightly higher levels of the pBM IL17A, IL17C, CCL11, CCL20, and TIMP4.
Analysis of the reciprocal changes in the above showed that IL6, TNFRSF1A, IL2RA, NPPB, and SERPINE1 were downregulated similarly in UPA R and NR patients. By comparison, IL17A was modestly upregulated similarly in ADA R and

NR patients; CCL20 was downregulated similarly in ADA R and NR patients; and IL17C, IL22RA1, TIMP4, and CCL11 were not modulated by ADA. Finally, taken together, among the 184 inflammation-related pBM tested, none were associated with clinical response for both ADA and UPA.

Conclusion: We detected common but also discrete alterations in pBMs upon exposure to ADA and UPA overall and further distinctions when we examined pathway changes associated with achievement of a low disease clinical status achieved by each patient population. Whereas both drugs exhibit inhibition of macrophages and granulocyte associated pathways, ADA appears to preferentially affect M1 macrophages and UPA appears to preferentially affect T cells. This modulatory pattern by UPA is consistent with its broad cytokine receptor inhibition profile compared with highly specific TNF inhibition and could account at least in part, for the greater efficacy of UPA over ADA in the SELECT-COMPARE study.

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FRI0027 INTENSIVE THERAPY IMPROVES SUBCLINICAL SYNOVITIS AND REDUCE FLARE IN RHEUMATOID ARTHRITIS PATIENTS ACHIEVED TREATMENT TARGET

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Background: Subclinical synovitis has been confirmed to be associated with the subsequent bone erosion and flare in rheumatoid arthritis (RA) patients who have already achieved clinical remission. But whether intensive therapy can improve the subclinical synovitis and reduce flare remains controversial.

Objectives: We designed an 1-year open-labelled, randomized and controlled clinical trial to elucidate if intensive therapy can improve the subclinical synovitis and reduce clinical relapse.

Methods: RA patients in clinical remission/low disease activity (defined by DAS28-CRP<3.2), however with subclinical synovitis [power Doppler (PD)≥1 and/or gray scale (GS)≥2 on ultrasound] were randomized into either maintenance or intensive treatment group. The rate of relapse [defined by DAS28(CRP) increased by at least 0.6 and >3.2] in 12 months was taken as the primary outcome. The improvement of PD and GS synovitis at 3, 6, 9 and 12 months were taken as secondary outcomes.

Results: 108 patients with 54 in each group were enrolled. Patients in maintenance group were older [59.5(19.4-77.5) vs. 51.8 (22.1-73.0), p=0.009] with lower baseline PD score [0(0-4) vs. 1(0-11), p=0.021] than intensive treatment group. The relapse rate was significantly higher in maintenance group than in intensive group [24.1% (13/54) vs. 9.1% (5/54), p=0.039] in one year. The intensive therapy is the single independent protective factor for relapse [OR=0.284 (0.081-0.998), p=0.049]. For 26 patients in maintenance group and 38 in intensive group with PD score≥1, their age and baseline PD were comparable. The relapse rate was also higher in maintenance group than in intensive group, although the difference was statistically insignificant [23.1% (6/26) vs. 7.9% (3/38), p=0.164].

Both maintain and intensive therapy could improve GS and PD scores (Table 1). However, at 12 month, both GS and PD score improvement were significantly better in intensive group than in maintenance group (Table 2).

Table 2. The improvement of GS and PD scores at each follow up time point between the maintenance and intensive therapy group.

Patients with GS≥2				Patients with PD≥1			
Change of GS against baseline	maintenance group(n=54)	Intensive group(n=54)	P	Change of PD against baseline	maintenance group (n=26)	Intensive group(n=38)	P
3m	1(-10-12)	1(-11-13)	0.815	3m	1(-4-3)	1(-3-7)	0.499
6m	1(-14-21)	2(-14-19)	0.330	6m	1(-7-4)	1(-1-8)	0.099
9m	3(-3-16)	4(-2-26)	0.266	9m	1(0-3)	1.5(1-11)	0.256
12m	2(-7-19)	3.5(-4-26)	**0.048**	12m	1(-2-2)	1(-1-11)	**0.020**

Conclusion: For RA patients who have already achieved treatment target, intensive therapy can alleviate the subclinical synovitis better than maintenance therapy and reduce the relapse.

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FRI0028 JAK2 MUTATION MAY PREDICT RESPONSE AND GUIDE FIRST LINE TREATMENT IN RHEUMATOID ARTHRITIS

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Background: JAK2 mutation found to be associated with the myeloproiferative disorders [1] with possibility of measurement in blood by PCR [2] . There are many interesting parallels between the CTDs and MPDs [3] . STAT4 is activated by the JAK members as JAK2 in response to IL and TNF, with subsequent down-stream signaling for autoimmunity [4] . JAK inhibitors are medications function by inhibiting activity of Janus kinase enzymes and have therapeutic application in treatment of cancer and rheumatoid arthritis [5] .

Objectives: Impact of pretreatment JAK2 mutation on response to first line csDMARDS in RA.

Methods: 76 newly diagnosed RA patients and 50 matched controls were included. Pretreatment JAK2 mutation was measured in serum by PCR with TNF-α and IL 6 were assessed by ELISA in patients and controls. All patients started treatment by conventional synthetic DMARDs (including methotrexate). Response assessment at 3rd month was evaluated by DAS28 and ACR response criteria. JAK2 mutation was correlated with different clinical and laboratory parameters of patients.

Results: 62 females (81.6%) and 14 males (18.4%) with age mean ± SD; (48.8 ± 7.3). Pretreatment JAK2 mutation, TNF-α and IL 6 were significantly high in patients. JAK2 mutation was detected in 39 (51.3%) patients while 37 (48.7%) patients were JAK2 non mutant. Mutant JAK2 was significantly associated with severity of disease assessed by DAS28; 14 (70%) of patients with DAS28 (≤2.6) were non mutant JAK2 versus sex (30%)

Table 1. The improvement of GS and PD scores at each follow up time point in the maintenance and intensive therapy group.

Patients with GS≥2					Patients with PD≥1				
GS	maintenance group(n=54)	P (against baseline)	Intensive group(n=54)	P (against baseline)	PD	maintenance group (n=26)	P (against baseline)	Intensive group(n=38)	P (against baseline)
Baseline	5(1–24)	–	5.5(0–28)	–	Baseline	2(1–4)	–	1.5(1–11)	–
3m	4(0–16)	**0.031**	5(0–28)	0.233	3m	0(0–6)	**0.006**	1(0–10)	**0.001**
6m	4(0–17)	**0.025**	4(0–17)	**0.014**	6m	1(0–9)	**0.006**	0(0–4)	**<0.001**
9m	2(0–21)	**<0.001**	2(0–12)	**<0.001**	9m	0(0–2)	**0.001**	0(0–3)	**<0.001**
12m	3(0–23)	**0.002**	2(0–11)	**<0.001**	12m	0(0–6)	**0.001**	0(0–4)	**<0.001**

patients mutant JAK2 while 13 (76.5%) of patients with DAS28 (>5.1) were mutant JAK2 versus four (23.5%) patients non mutant JAK2 (P 0.03), table1**. JAK2 mutation found to be significantly correlated with ACR 20, 50 and 70 response criteria; 40% of patients with non mutant JAK2 showed ACR 70 versus 17.9% in mutant group, 35.1% of patients with non mutant JAK2 showed ACR 50 versus 30.8% in mutant group while 24.3% of patients with non mutant JAK2 showed ACR 20 versus 51.3% in mutant group (P 0.02),** table1**. JAK2 mutation was associated with high pretreatment TNFα (mean±SD; 41.7±39.5 in mutant versus 24.3±23.04 pg/ml in non mutant group) with P (0.04), while no significant relation between JAK2 mutation and pretreatment IL6 level.**

Conclusion: Adult SLE with pretreatment JAK2 mutation significantly showed high disease activity, high pretreatment TNFα level and poor response to 1st line csDMARDs including MTX so they could get benefit with introduction of JAK inhibitors as first line mono or in combination with csDMARDS especially those with moderate to severe active RA.

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Table 1. JAK2 mutation with disease activity and response criteria.

DAS28	Non Mutant JAK2	Mutant JAK2	X	P
Remission (≤ 2.6)	14 (70%)	6 (30%)	8.6	0.03
Low disease activity (≤ 3.2)	13 (54.2%)	11 (45.8%)		
Moderate disease activity (3.2 - 5.1)	6 (40%)	9 (60%)		
Sever disease activity (>5.1)	4 (23.5%)	13 (76.5%)		
ACR	**Non Mutant JAK2**	**Mutant JAK2**		
ACR 20	9 (24.3%)	20 (51.3%)	7.0	0.02
ACR 50	13 (35.1%)	12 (30.8%)		
ACR 70	15 (40.5%)	7 (17.9%)		

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FRI0029

EFFECTIVENESS OF A NURSE LED TREAT TO TARGET (T2T) MODEL IN ACHIEVING REMISSION FOR EARLY RHEUMATOID ARTHRITIS PATIENTS IN A REAL-WORLD SETTING

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Background: Rheumatoid Arthritis (RA) is a chronic, inflammatory and systemic autoimmune disease, affecting multiple joints particularly small joints in hands and feet.[1] For the past two decades, there has been significant change in approach for the diagnosis and treatment of RA. Now early diagnosis and aggressive management of RA is considered key role for preventing permanent damage to joints.[2] Treat to Target (T2T) strategy has been proven to be very effective in achieving pre-decided outcome either clinical remission (CR) or low disease activity(LDA).[3]

Objectives: To assess the outcome of nurse led T2T strategy in Early RA patients within first 2 years of treatment.

Methods: This was Observational Prospective Study, based on data collected in our ANP led Early Inflammatory Arthritis clinic. All patients diagnosed with inflammatory arthritis were managed following a T2T protocol. Every patient had predefined target set according to co-morbidities, preexisting osteoarthritis and duration of disease. Patients were followed up at varying intervals depending on clinical need until the steroid free target was achieved or for up to 2 years. Clinical Disease Activity Index (CDAI) tool was used to assess disease activity.

Data collected included age, gender, diagnosis, Rheumatoid factor and/or Anti CCP positivity, erosions on x ray at the time of diagnosis and Health Assessment Questionnaire (HAQ-DI). For this analysis, only patients meeting the 2010 ACR/EULAR criteria[4] for the diagnosis of RA were included.

The primary analysis in this study was the proportion of patients who achieved CR or LDA using different DMARDs used alone or in combination and the clinical determinants of this outcome.

Results: Out of 417 patients with Early Inflammatory Arthritis, 300 met criteria for RA. 27 were lost to follow up (3 deaths) and 44 remained on the T2T pathway. For the 229 patients completing the pathway, mean age was 43.25 years (SD 9.405), Female gender 146 (63.75%), Anti CCP positive in 160 (69.86%), Rheumatoid Factor (RF) positive in 154 (67.24%), Both RF and Anti CCP positive 141 (61.57%), CDAI at baseline was 22.65 (SD 22.19) and Mean HAQ-DI at presentation 1.19 (SD 0.629). There were 18.34% (42) of patients who had erosive changes on x-ray at presentation.). Outcome of T2T strategy showed that 151 (65.93%) achieved clinical remission and 78(34.06%) achieved low disease activity

Conclusion: Remission in patients who were less than 40 years of age was 100% as opposed to 49% above the age of 40 years. This difference was found to be statistically significant with a p value of <0.05 (Table 1).

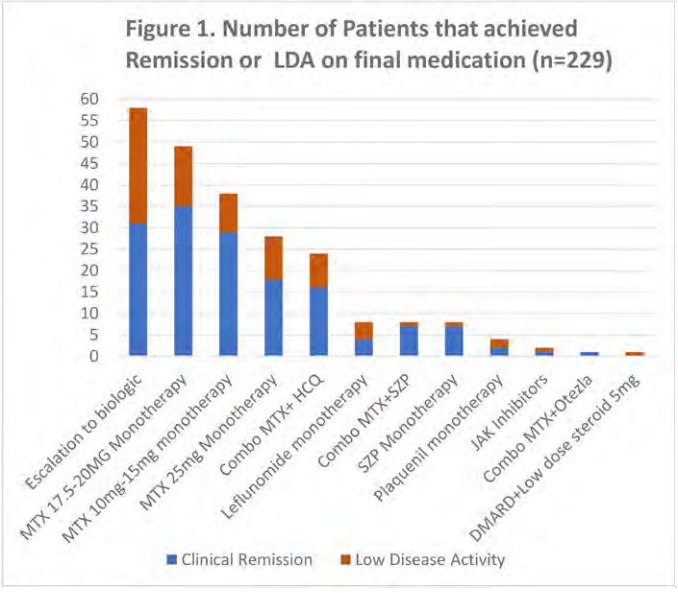
Table 1. Treat to target outcomes with analysed variables.

Group Characters	Remission n (%)	Low disease activity n (%)	Total	P value
Female	92 (63.01)	54 (36.99)	146	0.215
Male	59 (71.08)	24 (28.92)	83	
RF +	103 (66.88)	51 (33.12)	154	0.666
RF -	48 (64)	27 (36)	75	
CCP +	105 (65.63)	55 (34.37)	160	0.760
CCP -	44 (67.79)	21 (32.31)	65	
< 40 years	76 (100)	0 (0)	76	**0.000**
>40 years	75 (49.02)	78 (50.98)	153	

Further to this, Methotrexate monotherapy was the dominant DMARD used to achieve remission and/or low disease activity in more than 50 % of the RA patients (Figure 1).

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FRI0030

MORE THAN HALF OF NEWLY DIAGNOSED RA PATIENTS ARE NOT CONVINCED OF THE NECESSITY OF RA MEDICINES: ASSOCIATIONS WITH RA CHARACTERISTICS, SYMPTOMS, AND FUNCTION IN THE CANADIAN EARLY ARTHRITIS COHORT (CATCH)

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Background: Although DMARDs are essential for early aggressive control of RA to reduce symptoms and disability, medication adherence is variable. Beliefs about the necessity of medications and safety concerns predict adherence and are modifiable.
Objectives: To examine associations among RA medication necessity beliefs and concerns, sociodemographics, RA characteristics, symptom level and function in newly diagnosed RA patients.
Methods: Baseline data were analyzed from participants in the Canadian Early Arthritis Cohort (CATCH) who enrolled between 2017-2020 and completed the Beliefs about Medicine Questionnaire (BMQ) and PROMIS-29. All met ACR1987 or 2010 ACR/EULAR criteria and had active RA at enrollment. BMQ Necessity (N) and Concerns (C) scores were classified as **high** (≥20) or **low** (<20) and categorized into: Accepting (↑N ↓C); Ambivalent (↑N↑C); Sceptical (↓N↑C); and 4) Indifferent (↓N↓C). Groups were compared using ANOVA and chi-square tests.
Results: The 362 patients were mostly white (83%) women (66%) with a mean (SD) age of 56 (15), symptom duration of 6 (3) months, and 32% were obese (BMI≥30). More than half (56%) were DMARD-naive or minimally exposed. Mean N and C scores were similar between men and women; 54% were classified as **Indifferent**, 31% **Accepting**, 9% **Ambivalent,** and 6% **Sceptical**.
As compared to those classified as **Accepting**, more **Indifferent participants** smoked, had a healthy weight, lower TJCs, and trend for lower CDAI (Table). Groups were similar by sociodemographics, symptom duration, and DMARD/steroid use, except fewer **Indifferent** patients received MTX. **Indifferent** patients had statistically and meaningfully lower patient global, depression, anxiety, fatigue and pain interference, and higher function and participation scores (Table).
Conclusion: Many new RA patients had low medication necessity beliefs and concerns, and only 31% had high necessity beliefs and low concerns around diagnosis. Lifestyle and lower CDAI, TJCs, symptoms and functional impacts were associated with RA medication indifference. Identifying medication indifference can prompt discussions about medication beliefs/concerns to facilitate shared decision-making and adherence.

Mean (SD) or N (%)	Accepting	Ambivalent	Sceptical	Indifferent	SIG
N (%)	112 (31%)	34 (9%)	21 (6%)	195 (54%)	--
Age	57 (15)	57 (14)	56 (12)	55 (15)	0.518
Women	68 (62%)	21 (62%)	14 (70%)	127 (69%)	0.605
Minority	13 (12%)	8 (24%)	2 (10%)	36 (20%)	0.173
Education > HS	69 (62%)	21 (62%)	12 (57%)	119 (61%)	0.862
Currently smoking	**10 (9%)**	**10 (30%)**	**4 (20%)**	**30 (17%)**	**.010**
Former smoker	**50 (47%)**	**13 (39%)**	**12 (60%)**	**62 (35%)**	
Never smoked	**47 (44%)**	**10 (30%)**	**4 (20%)**	**87 (49%)**	
Healthy BMI (<25)	**8 (28%)**	**22 (22%)**	**6 (33%)**	**67 (41%)**	**.036**
Overweight (25-30)	**12 (41%)**	**47 (46%)**	**6 (33%)**	**46 (28%)**	
Obese (30+)	**9 (31%)**	**33 (32%)**	**6 (33%)**	**52 (32%)**	
Symptom duration (m)	5.3 (2.8)	5.1 (2.9)	5.1 (3.2)	5.8 (3.0)	0.411
Tender joint (0-28)	**9 (7)$_a$**	**8 (6)$_{a,b}$**	**8 (6)$_{a,b}$**	**7 (6)$_b$**	**0.032**
Swollen joint (0-28	8 (6)	7 (5)	8 (5)	6 (5)	0.203
CDAI	**26.8 (12.5)$_a$**	**28.0 (14.8)$_{a,b}$**	**26.9 (11.6)$_{a,b}$**	**22.9 (12.5)$_b$**	**0.011**
Methotrexate	**91 (81%)**	**24 (71%)**	**15 (71%)**	**130 (67%)**	**0.057**
Non-MTX DMARDs	60 (54%)	20 (59%)	12 (57%)	105 (54%)	0.943
Oral steroids	37 (33%)	10 (29%)	8 (38%)	46 (24%)	0.222
Parenteral steroids	39 (35%)	11 (32%)	6 (29%)	59 (30%)	0.852

	BMQ Classification								
	Accepting (High N Low C)		Ambivalent (High N High C)		Sceptical (Low N High C)		Indifferent (Low N Low C)		SIG
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Patient Global (0-10)	5.2$_a$	2.7	6.0$_b$	2.9	5.8$_a$	2.6	4.4$_b$	2.6	**<0.0001**
Pain (0-10) V0	5.8$_a$	2.8	7.0$_b$	2.8	5.9$_{a,b}$	2.8	5.2$_a$	2.8	**0.0013**
PHQ8 Depression	7.3$_a$	5.6	11.8$_b$	7.4	7.5$_{a,c}$	6.6	5.4$_c$	5.0	**0.0051**
PROMIS-29									
Physical Function	39.4$_a$	7.7	37.4$_a$	7.1	38.4$_a$	8.3	42.4$_b$	7.9	**0.0001**
Depression	51.9$_a$	9.6	57.9$_b$	11.5	56.9$_b$	9.3	49.6$_c$	9.3	**<0.0001**
Anxiety	58.5$_a$	9.5	52.5$_b$	9.6	58.4$_a$	8.6	50.7$_b$	9.7	**<0.0001**
Fatigue	55.7$_a$	10.2	57.7$_a$	10.4	54.9$_{a,b}$	12.3	51.8$_b$	10.9	**0.0018**
Sleep Disturbance	53.0$_a$	8.8	54.5$_a$	6.7	55.4$_a$	6.8	53.0$_a$	9.0	0.5367
Participation	41.8$_a$	10.0	40.6$_a$	10.2	40.8$_{a,b}$	8.1	44.2$_b$	9.6	**0.0553**
Pain Interference	62.1$_a$	7.8	64.1$_a$	8.1	62.2$_{a,b}$	8.5	58.9$_b$	8.8	**0.0004**

Note: Values in the same row with differing subscripts are significantly different (p< 0.05).

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FRI0031

OBSERVATIONS ON BIOMARKERS IN VERY EARLY RHEUMATOID ARTHRITIS CONSECUTIVELY RECRUITED OVER 20 YEARS, FROM BASELINE PRESENTATION TO FIVE-YEAR OUTCOMES

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Background: Since July 1998, the Early Undifferentiated PolyArthritis (EUPA) cohort recruited consecutive adults with recent-onset immune-mediated polyarthritis[1,2]. Patients were treated aiming at 0 swollen joint.
Objectives: To analyze the impact of biomarkers over 20 years on baseline variables, treatments, comorbidities and outcomes over the first 5 years of follow up.
Methods: Variables and Outcomes were collected over 5 years in consecutive patients fulfilling RA criteria, grouped according to date of inclusion (Period 1: 1998-2004; Period 2: 2005-2010; Period 3: 2011-2018). Comparisons of baseline characteristics, treatment, and outcomes over 5 years between the 3 Periods were previously presented (ACR 2018 and 2019). Erosive damage was scored according to Sharp/van der Heijde; erosive status was defined as ≥5 Erosion units. We now present observed associations between the presence of baseline prognostic biomarkers (anti-CCP2 (ACPA), RF, anti-Sa, and erosive status) with concomitant and subsequent disease activity levels, radiographic scores, comorbidities and impact of treatment. False discovery rate correction was used to adjust p-values for multiple comparisons.
Results: 753 patients were included: 247, 263 and 243 in Periods 1, 2 and 3, respectively. Variables at baseline. No biomarkers, including erosive status, were associated with demographics or disease activity. Erosive disease was more prevalent in ACPA+ (19.9% vs 13.9%, p=0.0417). Current smoking decreased by period (20.6, 17.2, 8.6%; p=0.02) in ACPA negatives only, remaining stable among ACPA+ (25.3, 20.9, 18.8%, NS). All comorbidities were significantly more present in ACPA negatives vs positives (RR between 1.55 and 1.99). Prevalence of cardiovascular (CV; 44.8, 55.0, 60.0%; p=0.036) and cancer (4.1, 7.1, 13.1%;

p=0.02) comorbidities increased over time in ACPA negatives and remained stable in ACPA+ (CV: 33.0, 30.8, 40.7, NS; cancer: 3.0, 4.4, 6.2, NS). RF positivity decreased by period (47.8, 36.9, 36.7%, p=0.03), but ACPA+ remained stable (40.8, 35, 35.4% NS).

Outcomes over 5 years of follow up.

There was no link between the presence of any biomarker and subsequent disease activity scores. Positive ACPA, RF and anti-Sa at baseline predicted development of more erosive status (RR = 1.50; 1.37 and 1.52, all p<0.001). 68% reached DAS28 remission overall (70.3% in ACPA negatives, 65.2% in ACPA+). Independent of ACPA status, remission rates increased between Periods 1 vs 2 (RR = 1.14, p=0.04) and 1 vs 3 (RR=1.13, p=0.055), but not between 2 vs 3. CV comorbidities among ACPA+ increased significantly more over time vs ACPA negatives (+8.9% vs +4.1%; RR = 1.18, p=0.03). Erosion scores increased significantly more in ACPA+ treated with DMARDs only vs receiving a biologic (ΔSharp: 3.98 vs 3.11, p= 0.026; ΔErosions: 2.58 vs 1.83, p= 0.02). By period, erosive status decreased significantly (Periods 2 vs 1: RR= 0.65, p=0.002; 3 vs 1: RR=0.42, p=0.002; 3 vs 2: RR=0.64, p=0.007), both in ACPA+ and negatives.

Conclusion: In this cohort of recent onset RA recruited over 20 years, we observed a constant drift towards RF-negative arthritis at baseline with decreasing smoking rates and increasing comorbidities in seronegative patients. Positive antibodies were associated more cardiovascular comorbidities accrual. Autoantibody positive (especially ACPA+) patients developed more erosive disease and had better erosion outcomes with biologic treatments. Irrespective of the presence or absence of biomarkers, marked improvements in control of disease activity and in remission rates occured over each period.

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Janssen (CATCH)
Celgene (Clinical nurse)
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FRI0032

REGIONAL AND WIDESPREAD PATTERNS OF NON-ARTICULAR PAIN ARE COMMON AT RA DIAGNOSIS AND CONTRIBUTE TO POOR OUTCOMES AT 12 MONTHS: A PROSPECTIVE STUDY OF PAIN PATTERNS IN CANADIANS WITH RA

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Background: Persistent pain can occur in early RA patients, despite improvement in synovitis and may be due to coexisting non-articular pain (NAP). Though NAP is often attributed to fibromyalgia and widespread NAP, regional NAP syndromes may be more common and under-recognized.

Objectives: To describe patterns of NAP, predictors of persistent NAP and impact on outcomes in the first year following early RA diagnosis.

Methods: Data were from participants enrolled in the Canadian Early Arthritis Cohort (CATCH) between *2017-2019* who completed 0,6,12-month evaluations with patient-reported outcomes [PROs] and clinical data available. We used the McGill Body Pain Diagram (BPD) to classify patients as experiencing no NAP, regional (RP:1-2 regions) or widespread NAP (WP:3-5 regions). Multinomial regression was used to identify baseline predictors of persistent RP and WP at 12-months. Multi-adjusted GEE with linear and logit links were used to estimate time-varying associations of NAP patterns with outcomes updated at each time point.

Results: Study included 421 participants: 66% were female, with a mean(sd) age 56 (14); 72% were seropositive and 90% were treated with MTX ± csDMARDs as initial therapy. NAP at baseline was common (55%), with majority (62%) reporting regional NAP. NAP prevalence was 33% at 12 months (Figure). Female sex and baseline depressive symptoms were independent predictors of widespread NAP at 12 months while poorer function and lack of early MTX treatment independently predicted regional NAP, at 12 mos. Regional and widespread NAP were associated with lower likelihood of remission in adjusted models that accounted for changes in NAP and remission over time (Table).

Conclusion: NAP is commonly reported in early RA pts seen in real world settings. Regional NAP was more common than WSP at all time-points, but both NAP patterns were associated lower odds of achieving remission targets by 12 months. These data support considering the role of NAP when assessing RA treatment efficacy during clinical visits and warrant different treatment approaches to reduce symptoms in RA patients receiving target-based care.

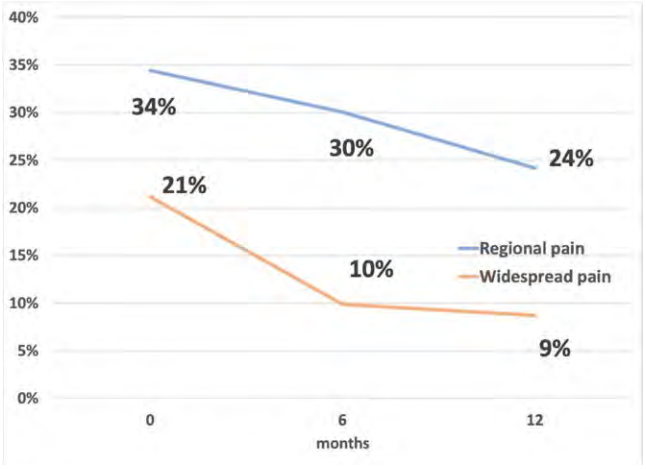


Figure. Point prevalence of regional and widespread NAP at baseline, 6 and 12 months.

Table. Results of Multi-Adjusted GEE Logistic Regression showing Regional and Widespread NAP is associated with a reduced likelihood of achieving Stringent Remission Targets

	Boolean Remission Outcome		SDAI Remission Outcome	
Disease stage and Clinical Disease Activity	Age/sex adjusted OR (95% CI)	Fully Adjusted	Age/sex adjusted OR (95% CI)	Fully Adjusted
NAP Pattern by Body Pain Diagram				
Regional vs No NAP	**0.34 (0.18, 0.66)**	**0.41 (0.20, 0.83)**	**0.41 (0.23, 0.71)**	**0.55 (0.30, 1.00)**
Widespread vs No NAP	**0.21 (0.07, 0.67)**	**0.27 (0.08, 0.85)**	**0.23 (0.09, 0.61)**	**0.29 (0.11, 0.80)**
Age	NI	1.01 (0.98, 1.04)	NI	1.01 (0.98, 1.03)
Women vs Men	NI	0.76 (0.41, 1.42)	NI	0.69 (0.37, 1.27)
RDCI[ϕ] at baseline	NI	0.91 (0.73, 1.14)	NI	0.90 (0.74, 1.10)
Symptom duration	NI	0.96 (0.86, 1.08)	NI	1.00 (0.90, 1.10)
Seronegative vs ACPA+/RF+	NI	1.15 (0.60, 2.19)	NI	1.43 (0.79, 2.60)
MTX in first 3 months	NI	1.51 (0.73, 3.13)	NI	1.20 (0.64, 2.24)
Oral Steroids in first 3 months	NI	0.53 (0.25, 1.10)	NI	**0.44 (0.22, 0.87)**

[ϕ] *RDCI = rheumatic disease comorbidity index*

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Eli Lilly (Registry of biologics, Clinical nurse), Consultant of: Eli Lilly, Janssen, Novartis, Pfizer, Speakers bureau: Merck, BMS, Pfizer, Glen Hazlewood: None declared, Carol Hitchon Grant/research support from: UCB Canada; Pfizer Canada, Edward Keystone Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, F. Hoffmann-La Roche Inc, Gilead, Janssen Inc, Lilly Pharmaceuticals, Pfizer Pharmaceuticals, Sanofi-Aventis, Consultant of: AbbVie, Amgen, AstraZeneca Pharma, Biotest, Bristol-Myers Squibb Company, Celltrion, Crescendo Bioscience, F. Hoffmann-La Roche Inc, Genentech Inc, Gilead, Janssen Inc, Lilly
Pharmaceuticals, Merck, Pfizer Pharmaceuticals, Sandoz, UCB., Speakers bureau: Amgen, AbbVie, Bristol-Myers Squibb Canada, F. Hoffmann-La Roche Inc., Janssen Inc., Merck, Pfizer Pharmaceuticals, Sanofi Genzyme, UCB, Diane Tin: None declared, Carter Thorne Consultant of: Abbvie, Centocor, Janssen, Lilly, Medexus/Medac, Pfizer, Speakers bureau: Medexus/Medac, Janet Pope Grant/research support from: AbbVie, Bristol-Myers Squibb, Eli Lilly & Company, Merck, Roche, Seattle Genetics, UCB, Consultant of: AbbVie, Actelion, Amgen, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Eicos Sciences, Eli Lilly & Company, Emerald, Gilead Sciences, Inc., Janssen, Merck, Novartis, Pfizer, Roche, Sandoz, Sanofi, UCB, Speakers bureau: UCB, Susan J. Bartlett Consultant of: Pfizer, UCB, Lilly, Novartis, Merck, Janssen, Abbvie, Speakers bureau: Pfizer, UCB, Lilly, Novartis, Merck, Janssen, Abbvie
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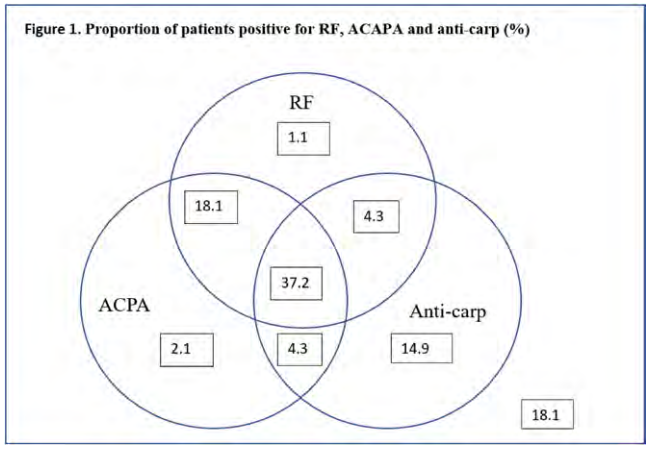
FRI0033

ANTI-CARBAMYLATED PROTEIN POSITIVITY PREDICTS DAS28-REMISSION AT 12 MONTHS IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS: RESULTS FROM THE SINGAPORE EARLY ARTHRITIS COHORT

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Background: Anti-carbamylated protein antibody (anti-carp) positivity has been associated with poorer outcomes in Western cohorts of early rheumatoid arthritis; however, it is unknown if this applies to Asians.
Objectives: We determined whether anti-carp predicted DAS28-remission, disability and radiographic progression in a multi-ethnic Asian ERA cohort.
Methods: Patients with physician diagnosed ERA (symptom duration ≤1 year) were recruited from the Singapore Early Arthritis Cohort (n= 317) by convenience sampling. Serum anti-carp was measured cross-sectionally using a commercial ELISA (SincereBio). The test was repeated in 40 healthy individuals to establish the optimal sensitivity and specificity for the diagnosis of RA via a receiver operating curve. Disease activity (DAS28-ESR or DAS28-CRP) was recorded at baseline, 3, 6 and 12 months. Two independent accessors quantified the radiographic damage at baseline and at follow-up using the modified Sharp van der Heijde score (mSS). We used multivariable logistic regression to determine whether anti-carp predicted the following outcomes; (i) DAS-28 remission at 12 months, (ii) any disability (mHAQ>0) at 12 months and (iii) radiographic progression (any increase in the mSS). In each regression model, we chose covariates known to influence the dependent variable in our cohort or from literature.
Results: One hundred patients were recruited, of mean age (SD) 49.8 (12.5) years, median (IQR) disease duration 10.2 (6.9-15.1) weeks at cohort entry and baseline median DAS-28 4.5 (2.9-5.9) (Table 1). The anti-carp assay was performed after a median (IQR) disease duration of 2.24 (1.82-3.14) years. 93 patients had baseline hand radiographs and 66 had follow-up hand radiographs after ≥ 12 months. Receiver operating characteristics curve yielded optimal sensitivity (95%) and specificity (60%) for the diagnosis of RA at 1.60OD. Therefore, 60 patients were anti-carp positive and 35 patients (37.2%) were positive for RF, ACPA and anti-carp (Figure 1). Anti-carp positivity independently predicted DAS28-remission at 12 months (OR 3.41, 95% CI 1.08-10.7, p=0.04) (Table 2). Anti-carp positivity did not predict disability at 12 months (OR 0.61, 95% CI 0.18-2.07, p=0.43) or radiographic progression (OR 0.23, 95% CI 0.03-2.03, p=0.18).

Figure 1. Proportion of patients positive for RF, ACAPA and anti-carp (%)



Conclusion: Contrary to previous studies done on Western cohorts where anti-carp predicted worse outcomes, anti-carp positivity predicted DAS28-remission at 12 months in our multi-ethnic Asian cohort. This suggests that different genetic and environmental determinants account for anti-carp expression in patients with RA.
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Table 1. Predictors of DAS28-remission at 12 months

			Univariable Logistic Regression		*Multivariable Logistic Regression*		
Variable		*N (%)*	OR	*p*	OR (CI)	*SE*	*p*
Anti-carp		60 (60)	3.0 (1.31–6.88)	0.01	3.41 (1.08–10.7)	1.99	0.04
Serology	RF and ACPA negative	31 (33.0)	Ref				
	Either RF or ACPA positive	11 (11.7)	0.99 (0.25–3.93)	0.99	1.10 (0.17–7.04)	1.04	0.92
	RF and ACPA positive	52 (55.3)	1.12 (0.45–2.75)	0.80	0.89 (0.28–2.81)	0.52	0.84
Baseline DAS28	Remission	17 (17.4)	Ref				
	Low DA	10 (10.2)	0.50 (0.05–4.67)	0.54	0.13 (0.01–1.67)	0.17	0.12
	Mod DA	32 (32.7)	0.29 (0.05–1.65)	0.16	0.10 (0.02–0.68)	0.10	0.02
	High DA	39 (39.8)	0.18 (0.04–0.90)	0.04	0.06 (0.01–0.41)	0.06	<0.01
Combination csDMARDs or biologic DMARD		74 (74)	1.13 (0.46–2.76)	0.80	1.97 (0.58–6.67)	1.23	0.28
Radiographic damage at baseline		11 (20)	1.79 (0.65–4.95)	0.26	1.27 (0.33-4.95)	0.88	0.73
Tertiary education		23 (38.3)	0.77 (0.34-1.77)	0.54	0.42 (0.12-1.45)	0.27	0.17
Ethnicity	Chinese	42 (70)	Ref				
	Malay	39 (68.4)	0.61 (0.22-1.71)	0.35	0.56 (0.14-2.25)	0.40	0.41
	Indian	8 (13.3)	0.60 (0.20-1.77)	0.35	0.79 (0.20-3.13)	0.56	0.74
Females		46 (76.7)	0.43 (0.17-1.11)	0.08	0.48 (0.13-1.85)	0.33	0.29

Chapter of Rheumatologists, Singapore. Dr Lahiri does not personally receive any remuneration.
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FRI0034 GLUCOCORTICOID TREATMENT IS ASSOCIATED WITH LOWER EXTREMITY MUSCLE WASTING IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Short-term (up to 3-4 months) glucocorticoids combined with methotrexate is recommended for initial therapy of active rheumatoid arthritis (RA) patients by EULAR, considering the long-term safety of glucocorticoids such as higher cardiovascular risk. However, in real-world clinical practice, glucocorticoids are widely used even up to 70% in refractory RA patients. Glucocorticoids can pharmacologically lead to enhancement of lipogenesis and muscle degradation. On the other hand, their anti-inflammatory effect can indirectly mitigate fat deposition and muscle catabolism. The overall effect of glucocorticoid therapy on body composition (BC) in RA patients remain elusive until now.
Objectives: To investigate the characteristics of disease indicators, body mass index (BMI) and BC in RA patients with previous glucocorticoid treatment in a cross-sectional study.
Methods: Consecutive RA patients were recruited and clinical data including disease activity, function and radiographic assessment were collected. BC including fat and muscle mass and their distributions was assessed by bioelectric impedance analysis. Multivariate multinomial logistic regression analysis was performed to identify the association of disease characteristics, BMI and BC with previous glucocorticoids treatment in RA patients, following the step-forward selection rule that variables were included in the equation when the *P* value was <0.05 or removed when the *P* value was >0.10.
Results: (1) There were 620 RA patients recruited, the mean age was 49.5±12.8 years old, and the median disease duration was 48 months (IQR 23-108 months) with 82.3% female. There were 107 (17.3%) patients with treatment naïve (without previous glucocorticoids or DMARDs therapy for six months before enrollment), 333 (53.7%) with previous glucocorticoid therapy with or without previous DMARDs therapy, and 180 (29.0%) with previous DMARDs therapy only. (2) For disease characteristics aspect, there were significant differences in all core disease activity indicators, functional indicator, and radiographic assessment indicators among three subgroups. Compared with those with treatment naïve, RA patients with previous glucocorticoid therapy had lower disease activity indicators including 28TJC, 28SJC, PtGA, PrGA, PainVAS, ESR, CRP, DAS28-CRP, SDAI and CDAI, and lower HAQ-DI and lower rate of functional limitation (all *P*<0.0167). While compared with those with previous DMARDs therapy only, RA patients with previous glucocorticoid therapy had higher disease activity indicators including 28TJC, 28SJC, PtGA, PrGA, PainVAS, DAS28-CRP, SDAI and CDAI (all *P*<0.0167). (3) For BMI and BC aspects, there were significant differences in lower fat-free mass and lower muscle indicators among three subgroups. Compared with those with previous DMARDs therapy only, RA patients with previous glucocorticoid therapy showed lower fat-free mass and lower muscle indicators including appendicular muscle mass especially in both lower extremities (all *P*<0.0167). There was no difference in BMI and fat indicators among three groups. (4) Multivariate multinomial logistic regression analysis showed that compared with previous DMARDs therapy only, previous glucocorticoid therapy was positively associated with DAS28-CRP (*OR*=1.289, 95%*CI*: 1.119-1.484, *P*<0.001), and negatively associated with lower extremity muscle mass (*OR*=0.907, 95%*CI*: 0.840-0.979, *P*=0.013).
Conclusion: Previous glucocorticoid treatment is associated with lower extremity muscle wasting. Further prospective study is needed to confirm their relationship.
References: None.
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FRI0035 THE CHALLENGE OF ASSESSING WELL-BEING IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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Background: Advances in therapeutics and treatment strategies for Rheumatoid Arthritis (RA) have improved clinical outcomes. Although these advances also impact the well-being as shown in many patient-reported outcomes, still a sizeable number of patients in clinical remission report a reduced well-being.
Objectives: To explore factors that contribute to well-being in patients with early RA.
Methods: Patients from the 2-year pragmatic treat-to-target Care in Early Rheumatoid Arthritis (CareRA) trial were included. Patients were treated intensively, with a combination of csDMARDs and glucocorticoid remission induction schemes, except one group treated with MTX monotherapy.
Eight different validated questionnaires including the Arthritis Self-Efficacy Scale (ASES), the multidimensional Fatigue Inventory (MFI), the Pittsburgh Sleep Quality Index (PSQI) the Revised Illness Perception Questionnaire (IPQ-R), the Utrecht Coping List (UCL), the Short Form 36 (SF-36), RA Quality of Life questionnaire (RA-QOL) and the Social Support List (SSL) were taken. Questionnaires were obtained at baseline, at week 16, 52 and 104 except for the IPQ and UCL, which were only taken at baseline and week 16.
Three patients` groups were created including all patients, patients in remission (DAS28crp < 2.6) and not in remission. Regression models were constructed to define well-being at week 16, 52 and 104. The Patient Global Assessment (PGA) on a Visual Analogue Scale 0-100 (VAS) was chosen as a proxy for well-being (score 0-100). As predictors, all subscales of the 8 validated questionnaires, summing to 84 variables, with and without the VAS for Pain (VAS-Pain) were used in 18 models (3 patient groups, 3 time points, with/without VAS-Pain) in total. Data reduction used forward, backward and stepwise selection based on the Aikake information criteria. Data was checked for influential observations by Cook's distance and for multicollinearity by variance inflation factors (threshold = 5). Influential observations were removed one observation every time. Highly correlated variables were deleted by backward selection (α=5%). Missing data was handled by multiple imputation using CART with 15 iterations.
Results: In total, 379 patients were included. Table 1 gives the number of variables and the associated R^2. In the 9 models defining well-being without VAS-Pain, 53 variables were used at least once. Most common variables were bodily pain (n=8) and social function (n=5) of the SF-36, and positive emotions (n=4) of the SSL. In the 9 models with VAS-Pain, 31 variables were used at least once. Most common variables were vitality (n=3) and social function (n=3) of the SF-36, and identity (n=3) of the IPQ-R. Model content was heterogenous regarding patient population and time.

R^2 and number of variables in each model of well-being

	All patients		Patients in remission		Patients not in remission	
	R^2	#	R^2	#	R^2	#
week 16	52%	13	39%	7	53%	6
week 16 with VAS-Pain	78%	4	69%	6	80%	5
week 52	44%	8	44%	7	57%	12
week 52 with VAS-Pain	84%	5	84%	6	92%	2
week 104	40%	13	39%	8	62%	10
week 104 with VAS-Pain	81%	7	82%	4	86%	11

R^2 = coefficient of determination, the proportion of the variance in the dependent variable that is predictable from the independent variable(s). # = number of variables selected in regression model

Conclusion: Well-being is apparently difficult to define uniformly as many factors contribute to it. As already known, well-being, defined by PGA, and VAS-Pain are highly associated, even in patients in remission where pain levels should be theoretically lower. Other well-being definitions could lead to different results and should be further explored.
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FRI0036

VALIDATION OF RISK SCORES FOR PREDICTING PROGRESSION IN INDIVIDUALS "AT RISK OF RHEUMATOID ARTHRITIS"

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Background: Composite scores for risk of progression were described in 2015 in a cohort of 100 anti-cyclic citrullinated peptide (anti-CCP) + individuals at risk of developing Inflammatory Arthritis (IA) (1). The first score, designed for primary care, was based on anti-CCP and rheumatoid factor (RF) titres, small joints tenderness and early morning stiffness (EMS). A second score developed for secondary care added power Doppler presence (PD+) and/or at least one allele positive for the shared epitope (SE+).
Objectives: To validate previous data by scoring risk factors in a new cohort of 394 individuals.
Methods: Individuals at risk of developing IA selected by a positive anti-CCP test and a new musculoskeletal symptom have been followed in a single-centre prospective observational cohort since 2008. The previous risk score was derived from 100 patients. With the same recruitment and follow-up pathways, the next 394 consecutive participants were studied (full data were available for 373 patients for secondary care model). Participants followed for less than 10 weeks without progression were excluded.
Results: Participants from both cohorts were similar in terms of age and sex. Although the mean time to progression is comparable, there were significantly more participants with a high titre anti-CCP test in the 2015 cohort (Table 1).

Table 1. Patients characteristics

Score	2015	2020
N	100	394
Percentage of progression n/N	50/100 (50%)	82/413 (19.9%)
Mean of follow-up before progression to IA (Months (SD))	15.35 (15.27)	13.50 (12.62)
Mean follow-up of non progressors (Months (SD))	39.7 (15.82)	27.6 (19.75)
Mean follow-up duration: all participants (Months (SD))	27.7(19.36)	24.8 (19.38)
High CCP titre	83%	65%
Women	72%	72%
Smoker ever	72%	50%
Age (Mean (SD))	51.2 (11.9)	50.2 (13.474)

Cox multivariable analysis showed similar Hazard Ratios (HR) of progression in both groups (Table 2) confirming the high predictive value of high CCP/RF titre, early morning stiffness duration, power doppler presence and shared epitope. High risk of progression individuals identified by the secondary score were eight times more likely to develop IA (HR = 8.290, CI = 3.763-18.264, p<0.001), 50% of them had progressed at 2 years (Figure 1).

Table 2. Multivariable Cox regression analysis of time to progression to inflammatory arthritis.

	2015 (n=98)			2020 (n=394)		
Primary care model	**HR**	**p-value**	**CI**	**HR**	**p-value**	**CI**
High anti-CCP or RF titre	4.86	0.031	1.16–20.43	4.96	<0.001	1.445–3.526
EMS≥30min	1.86	0.039	1.03–3.37	2.26	<0.001	1.445–3.526
Small Joints Tenderness	1.42	0.252	0.78–2.57	1.30	0.249	0.832–2.035
	2015 (n=98)			**2020 (n=373)**		
Secondary care model	**HR**	**p-value**	**CI**	**HR**	**p-value**	**CI**
High anti-CCP or RF titre	3.04	0.147	0.68–13.6	3.92	0.001	1.790–8.567
EMS≥30min	1.56	0.167	0.83–2.92	2.10	0.002	1.314–3.357
Small Joints Tenderness	1.54	0.178	0.82–2.88	1.34	0.216	0.843–2.135
PD signal	1.92	0.033	1.06–3.50	2.35	0.001	1.424–3.887
Shared epitope	1.57	0.272	0.70–3.49	2.33	0.003	1.333–4.059

Conclusion: These data from a new large cohort confirm the validity previous Leeds Risk Scores for Primary and Secondary care, and the fidelity of the risk factors over time to predict progression.
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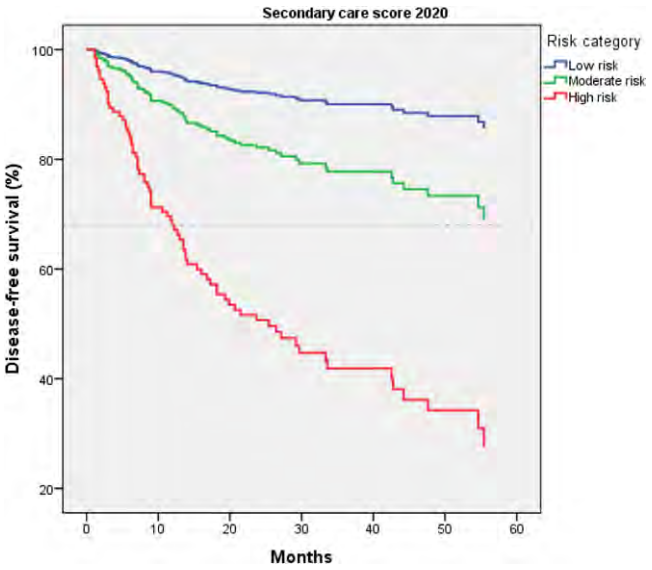


Figure 1. Probability of IA free survival according to categories of risk in the secondary care model.

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FRI0037

ALL-CAUSE MORTALITY IN EARLY RHEUMATOID ARTHRITIS PREDICTED BY HEALTH ASSESSMENT QUESTIONNAIRE AT ONE YEAR

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Background: Patients with RA are at greater risk of mortality than the general population. Higher HAQ disability has been associated with hospitalizations and mortality in established RA; whether HAQ disability predicts mortality in early RA (ERA) is unknown.
Objectives: The objective of this study is to analyze how well the HAQ can predict future mortality in patients with early RA.
Methods: Data were from adult early RA patients (symptoms <1 year) enrolled in the Canadian Early Arthritis Cohort (CATCH) between 2007 and 2017; who initiated treatment with 1 or more DMARDs and had completed HAQ data at baseline and 1 year. Descriptive statistics, t-tests and chi-square tests were used to summarize and compare baseline patient characteristics including sociodemographic variables, RA characteristics and comorbidities amongst deceased and non-deceased patients. Discrete-time proportional hazards models were used to estimate crude and multi-adjusted associations between HAQ at baseline and 1 year, respectively, with all-cause mortality in each year of follow up.
Results: This study included 1724 patients with early RA; mean age was 55 years and 72% were female. In 10 years of follow up, 62 deaths (2.4%) occurred. Deceased patients had higher HAQ scores and DAS28 scores at baseline and at 1 year versus the non-deceased group. Age, male sex, lower education, smoking, more comorbidities, higher baseline disease activity and steroid use were associated with mortality in unadjusted survival models (Table 1). Contrary to HAQ at baseline, the association between all-cause mortality and HAQ at 1 year

remained significant even after adjusting for age, gender, comorbidities, disease activity, smoking, education, seropositivity, symptom duration and steroid use in adjusted survival models (Table 2).

Table 1. Unadjusted survival model: Association of each variable with all-cause mortality

Baseline Variable	Unadjusted Hazard OR	95% CI
Socio-Demographic		
Age (years)	1.10	1.07 – 1.13
Female	0.37	0.22 – 0.62
Caucasian (white or European)	1.01	0.46 – 2.24
Aboriginal	1.71	0.61 – 4.76
Education > high school degree	0.48	0.28 – 0.82
Current Smoker	1.81	1.01 – 3.24
Rheumatic Disease Comorbidity Index (0-9)	1.60	1.36 – 1.87
RA Characteristics		
Symptom duration (months)	0.99	0.91 – 1.08
Seropositivity in first year	1.11	0.55 – 2.23
DAS28 ESR or CRP if ESR is missing	1.26	1.06 – 1.51
Oral Steroid use	1.75	1.03 – 2.98

Table 2. Multivariable discrete-time survival models: HAQ baseline vs 1 year

Model	Model 1: Crude (Time + HAQ-DI)		Model 2: Adjusted for age + sex		Model 3: Adjusted for Model 2 + DAS28 + RDCI		Model 4: Adjusted for Model 3 + education, smoking, seropositivity, symptom duration and oral steroids use		Model 5: Adjusted for Model 3 + smoking, symptom duration only	
HAQ-DI (0-3) (at baseline)	1.46	1.02 – 2.09	1.37	0.96 – 1.95	1.25	0.81 – 1.94	1.32	0.85 – 2.04	1.30	0.84 – 2.00
HAQ-DI (0-3) (at 1 year)	2.58	1.78 – 3.72	2.40	1.63 – 3.52	1.75	1.10 – 2.77	1.87	1.16 – 3.02	1.73	1.09 – 2.74

*Hazard OR, 95% CI

~HAQ-DI: (Health Assessment Questionnaire Disability Index); RDCI: Rheumatic Disease Comorbidity Index; DAS28: Disease Activity Score

Conclusion: Higher HAQ at 1 year was significantly associated with all-cause mortality in a large early RA cohort suggesting that poorer disease control and function in the first year of RA contributes to higher mortality.

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FRI0038

THE RELATIONSHIP BETWEEN ABATACEPT EXPOSURE AND EFFICACY MEASURES IN EARLY MTX-NAIVE ANTI-CITRULLINATED PROTEIN ANTIBODY-POSITIVE PATIENTS WITH RA DURING THE DE-ESCALATION PERIOD OF A PHASE IIIB STUDY

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Background: Although EULAR/ACR guidelines suggest tapering biologic treatment for RA following sustained remission in patients (pts), specific de-escalation (DE) regimens are not defined. The Phase IIIb Assessing Very Early Rheumatoid arthritis Treatment (AVERT)-2 trial (NCT02504268) is evaluating SC abatacept (ABA) + MTX versus ABA placebo (PBO) + MTX in Anti-Citrullinated Protein Antibody (ACPA)-positive pts with early (ACR/EULAR 2010 criteria; disease duration ≤6 mths), active RA (SDAI >11). AVERT-2 was designed to investigate achievement of SDAI remission and a clinically meaningful dose DE strategy among pts in sustained remission who completed induction with ABA + MTX. In moderately to severely active RA and JIA patients, a relationship between ABA Cmin and efficacy was observed. Therefore, this analysis in very early RA patients, reports on the pharmacokinetics (PK) and immunogenicity of ABA and the maintenance of remission during the DE period of AVERT-2.

Objectives: To assess the relationship between changes in ABA exposure and the maintenance of remission and the effect of immunogenicity on exposure during the DE period of AVERT-2.

Methods: Pts received blinded SC ABA (125 mg once wkly [QW]) + MTX or ABA PBO + MTX induction treatment for 56 wks. Pts who completed induction with ABA + MTX and had sustained SDAI remission (≤3.3 at Wks 40 and 52) were re-randomized 1:1:1 to ABA QW + MTX for 48 wks (Arm C), ABA every other wk (EOW) + MTX for 24 wks followed by ABA PBO + MTX for 24 wks (Arm D), or ABA QW + MTX PBO for 48 wks (Arm E) in the DE period. ABA trough (Cmin) and anti-drug antibody (ADA) samples were collected in all subjects during the DE period. Serum ABA concentrations and ADA were measured using a validated enzyme immunoassay method and an electrochemiluminescence assay, respectively. Efficacy endpoints included change from DE Day 1 in SDAI score, HAQ-DI score, Physician's Global Assessment (PhGA), and tender (TJC) and swollen (SJC) joint counts. The relationship between ABA Cmin and efficacy endpoints were assessed. Additionally, the impact of immunogenicity on ABA Cmin was explored.

Results: Mean ABA Cmin values remained stable throughout the DE period for subjects in Arms C and E. ABA Cmin values decreased by ~50% in subjects in Arm D for the first 24 weeks from the start of DE and were ~0 for weeks 24-48 consistent with the change in the frequency of ABA dosing from EOW to ABA withdrawal (Figure 1 top).

The incidence of immunogenicity appeared to increase upon withdrawal of ABA in Arm D. ADA formation did not appear to affect ABA Cmin, as ABA Cmin remained consistent between pts with and without ADA.

Upon withdrawal of ABA in Arm D, there appeared to be an increase in the mean change from baseline (Day 1 of DE) in SDAI over time, which followed a similar time course as the washout of ABA (Figure 1 bottom). Similar results were observed for other efficacy endpoints such as HAQ-DI, PhGA, TJC, and SJC.

Conclusion: The PK data in these early onset, MTX-naive, ACPA+ RA pts correlated well with the maintenance of remission in Arms A and E. Tapering of ABA from EOW to MTX only in Arm D results in a corresponding decrease in ABA Cmin, an increase in positive antibody response, and loss of remission.

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Disclosure of Interests: Yash Gandhi Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Sean Connolly Shareholder of: Bristol-Myers

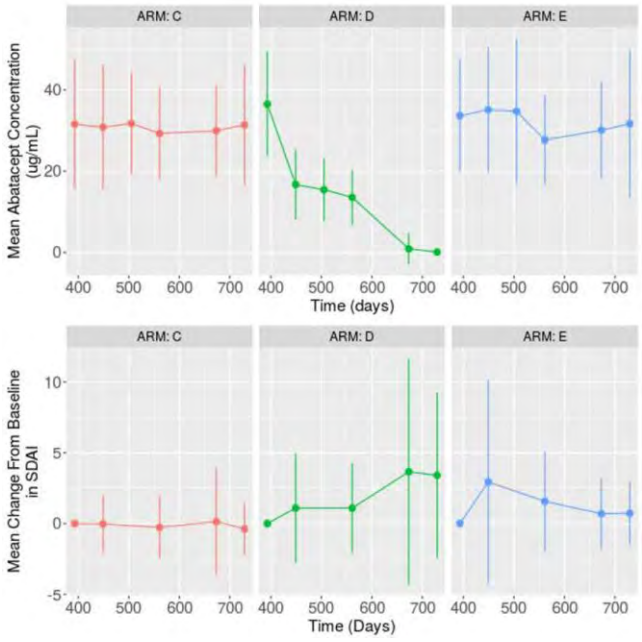


Figure 1: Mean (SD) ABA Cmin values (top) and Mean Change From Baseline in SDAI (bottom) in Subjects in DE Arm C (ABA QW + MTX), D (ABA EOW + MTX followed by ABA placebo + MTX), and E (ABA QW + MTX placebo)

Squibb, Employee of: Bristol-Myers Squibb, Kuan-Hsiang Gary Huang Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Robert Wong Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Shannon Chilewski Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Bindu Murthy Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb

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FRI0039 LUNG ULTRASOUND UTILITY IN INTERSTITIAL LUNG DISEASE DETECTION IN RHEUMATOID ARTHRITIS

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Background:
Objectives: To analyze the diagnostic utility of lung ultrasound (US) to detect interstitial lung disease (ILD) in Rheumatoid arthritis (RA) patients comparing with high-resolution computed tomography (HRCT).
Methods: Study design: We performed a cross-sectional, observational study in patients with RA-ILD (cases) controlled with a gruop of RA patients without ILD (controls) paired by sex, age and time of disease evolution.
Protocol: Patients were selected between May and September 2019. Patients were interwied by two rheumathologist for the protocolized collection of clinical data. The patients were assessed using HRCT, Pulmonary Function Test (PFT) and lung US.. The rheumatology who performed the lung US were blinded to patients clinical data. Variables: (1) B-lines number; (2) evaluation of the lung- ultrasound score already described: L. Gargani, Gutiérrez comprehensivo, Gutiérrez reducido and Mohhammadi;(3)pleural irregularities; (4) A pattern US lost;(5). Other variables included demographic, clinical-analytical, therapeutic and ILD-type description. Statistical analysis: descriptive, bivariant analysis. We applied Pearson's correlation coefficient between B-lines, PFT and clinical variable.Furthermore, to establish the cut-off point of the US B-lines number for detecting the presence of significant AR-ILD in relation to HRCT, we used the receiver operating characteristic (ROC) curve analysis. A logistic regression analysis was performed to identify the intercostal spaces (IV: B-lines number in each space) wich were *independently associated with ILD (DV: ILD in HRCT).*
Results: 71 patients were included, 37 (52,1%) with ILD-RA and 34 (47,95) RA controls. The main characteristics are shown in Table 1. RA-ILD presented more B-lines number than control without ILD (median ICR] 91.0 [31.0-149.0] vs 6.5 [1.5-30.5]; p=<0.001) and more pleural irregularities (PI) [PI-median(ICR) 41.0 (5.0-57.5) vs 2.5 (0.0-7.2); p<0,001]. Furthermore, RA-ILD showed a negative correlation between B-lines and DLCO(r =-0.337, p=0.048)and positive with DAS28 (r =0.347, p=0.035). Regarding US score, we found that the detection of 32.5 B-lines in 72 intercostal spaces, had a *Sensitivity of 75.7%, Specifity=79.4%*, PPV= 80% and NPV=75%,whilst in reduced score of 10 intercostal spaces, the detection of 5.5 B-lines had a sensivity= 62.2%,Specifity= 91.3%, PPV=88.4%, NPV=69.5%. In multivariate analysis, the intercostal spaces which showed independent association with ILD were 3rd right anterior axillary space(OR [IC 95%] 19.0 [1.3-27.5]), 8th right posterior axillary space (OR [IC 95%] 0.04 [0.0-0.6]), 8th right subescapular space (OR [IC 95%] 16.5 [1.8-45.5]),9th right paravertebral space (OR [IC 95%] 7.11 [1.0-37.1]) and 2nd left clavicular middle space(OR [IC 95%] 21.9 [1,26-37.8]).
Conclusion: Lung Ultrasoud could be a useful tool for interstitial lung disease diagnosis associated with Rheumatoid Artrithis. A 10 space reduced score showed a similar total predictive capacity than 72-space score

References:

VARIABLE	RA-ILD n=37	RA n=34	P-VALUE
Epidemiological Characteristics			0
Age in years, mean (±SD)	70,5 (9.1)	70.6 (7.5)	0.970
Sex, male, (%)	20(54.1)	18(52.9)	0.920
Body Mass Index, mean, (±SD)	27.5 (3.0)	29.2 (4.2)	0.106
Clinical-analytical characteristics			
Smoking			0.899
Smokers,n (%)	4(11.8)	4(10.8)	
RA evolution time, months, median , (p75-p25)	172.5 (100.4-234.4)	134.5 (106.5-211.9)	0.304
ILD evolution time, median, (p75-p25)	42.8 (21.3-101.3)	-	-
Rheumatoid Factor (RF)+ (>10), n (%)	35(94.6)	27 (79,4)	0.055
RF (>60)	28(77.8)	18 (52,9)	0.029
ACPA+ (>20), n (%)	34(91.9)	26 (76,5)	0.073
ACPA (>340), n (%)	26 (72.2)	11(32.4)	0.001
Erosive, n (%)	22 (59.5)	19 (55.9)	0.761
Clinical manifestation			
DAS28,mean (±SD)	3.1 (1.2)	2.7 (0.9)	0.151
Remision-LDA, n (%)	21 (56.8)	24(72.7)	0.164
Mild-High activity actividad, n (%)	16 (43.2)	9 (27.3)	0.164
HAQ, mean (±DE)	1.1 (0.6)	0,7 (0.6)	0.021
Tratamient			
sDMARs, n (%)	32 (86.5)	34 (100)	0.026
bDMARs, n (%)	11 (29.7)	11 (32.4)	0.811
Metotrexate, n (%)	19 (51.4)	28 (82.4)	0.060
Leflunomide, n (%)	4 (10.8)	4 (11.8)	0.899
Sulfasalazine, n (%)	5 (13.5)	2 (5.9)	0.281
Hidroxicloroquine, n (%)	4 (10.8)	2 (5.9)	0.456
Micofenolate, n (%)	4 (10.8)	0 (0.0)	0.048
Infliximab, n (%)	0 (0.0)	3 (8.8)	0.065
Etanercept, n (%)	3 (8.1)	4 (11.8)	0.606
Adalimumab, n (%)	0 (0.0)	1 (2.9)	0.293
Golimumab, n (%)	1 (2.7)	1 (2.9)	0.952
Certolizumab, n (%)	0 (0.0)	1 (2.9)	0.293
Tocilizumab, n (%)	2 (5.4)	0 (0.0)	0.169
Abatacept, n (%)	4 (10.8)	0 (0.0)	0.048
Rituximab, n (%)	1 (2.7)	0 (0.0)	0.334

Disclosure of Interests: None declared

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FRI0040 MULTI-VARIATE APPROACH INCLUDING SEROLOGY AND GENETICS FOR AN IMPROVED IDENTIFICATION OF PATIENTS AT RISK OF DEVELOPING RA

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Background: First-degree relatives of rheumatoid arthritis (RA) patients (FDR-RA) have a 3 - 5-fold increased prevalence of the disease [1]. RA development is triggered by an interaction between genetic and environmental factors. As the field is moving towards prevention in pre-clinical stages of RA, it is key to identify individuals with imminent RA, prior to onset of symptoms, which will presumably rely on both the measurement of autoantibodies and genetic risk markers.
Objectives: Assemble a pattern of serologic biomarkers in combination with genetics to improve the identification of individuals at high risk to develop RA.

Methods: The cohort included 827 serum samples from 601 individuals, followed within the Swiss multicenter cohort study SCREEN-RA of FDR [2]. FDR-RA were categorized into four groups according to the presence of symptoms and systemic autoimmunity associated with RA; 1: asymptomatic FDR-RA without anti-CCP or symptoms, 416 (69%); 2: FDR-RA with clinically suspect arthralgia (CSA) [3] or with signs of arthritis, without anti-CCP, 72 (12%); 3: FDR-RAs with no signs of arthritis, positive anti-CCP test, 55 (9%); 4: FDR with signs of arthritis or CSA, positive anti-CCP-test, 58 (10%).

Serum samples were analyzed for the presence of anti-CCP (IgG, IgA), RF (IgM, IgA) and anti-RA33 (IgM, IgA, IgG) using the EliA™ instrument platform (Phadia AB, Uppsala, Sweden).

Genetic measurements were performed using the AmpliSeq™ technology on the Ion GeneStudio™ instruments (Thermo Fisher Scientific, Carlsbad, USA), covered variants were analyzed using an algorithm focusing on the identification of RA patients.

Results: The overall prevalence of biomarkers, considering results above cutoff values, was 1% for anti-CCP IgG and IgA, 10% and 2% for RF IgM and RF IgA, respectively, and 6-15% for all three anti-RA33 isotypes. Several individuals had multiple positive serology tests (Fig 1): 3.6% (22) were positive for 2 tests and 1% (6) were positive for 3 or more tests. Among the 28 individuals positive for ≥2 tests, 17 (61%) were symptomatic.

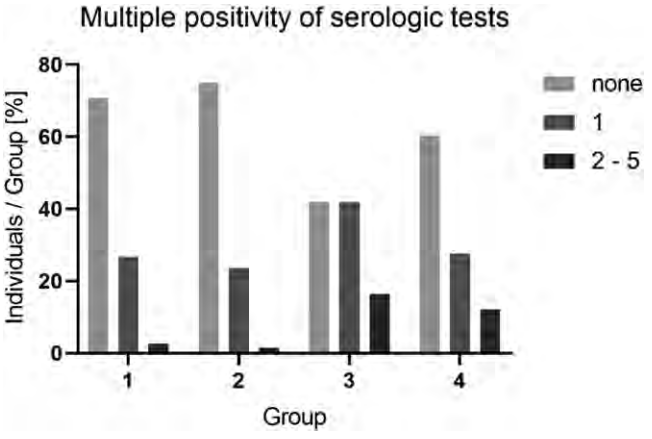


Figure 1. Distribution of positive serology within the different groups. No positivity (none), positive for one (1), equal or more than 2 (2-5) of the serologic tests.

Nine of 604 FDR-RA subsequently developed classifiable RA and were positive for serologic biomarkers before date of RA diagnosis (Table 1). The RA converters had a mean age of 39 years (24-75 yrs) and an average follow-up time within the study of 3.6 years (1-7 yrs).

Table 1. Biomarker status of subsequent RA converters before date of diagnosis.

RA converters	CCP IgG	CCP IgA	RF IgM	RF IgA	RA33 total
1	+	+	+	+	+
2	+	–	+	+	–
3	–	–	+	–	+
4	–	–	+	–	–
5	–	–	+	–	–
6	–	–	–	–	+
7	–	–	–	–	+
8	–	–	–	–	–
9	–	–	–	–	–

Using an algorithm to analyze the RA-associated genetic SNPs, we could highlight 48 FDR-RA (8%) with an increased genetic risk to develop RA. 15 out of 48 individuals (31%) at high genetic risk reported CSA, and 12 out of 48 individuals (25%) displayed signs of systemic autoimmunity associated with RA.

Conclusion: When looking at FDR it could help to not only include anti-CCP autoantibody testing but also additional biomarkers like RF and anti-RA33. Furthermore, looking at the genetic risk factors could give additional information. The combination with the multi-variate profile could even improve the early diagnosis of these patients.

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[1] Kuo et al. Rheumatology 2017; 56:928933
[2] Finckh et al. Ann Rheum Dis 2011; 70: S3–282
[3] van Steenbergen HW, et al. Ann Rheum Dis 2017; 76:491–496

Disclosure of Interests: Maresa Grundhuber Grant/research support from: Thermo Fisher Scientific, Employee of: Thermo Fisher Scientific, Isabel Gehring Grant/research support from: Thermo Fisher Scientific, Employee of: Thermo Fisher Scientific, Céline Lamacchia Grant/research support from: Thermo Fisher Scientific partially supported this study, Pascale Roux-Lombard: None declared, Michael Nissen Grant/research support from: Abbvie, Consultant of: Novartis, Lilly, Abbvie, Celgene and Pfizer, Speakers bureau: Novartis, Lilly, Abbvie, Celgene and Pfizer, Ulrich Walker Grant/research support from: Ulrich Walker has received an unrestricted research grant from Abbvie, Consultant of: Ulrich Walker has act as a consultant for Abbvie, Actelion, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, MSD, Novartis, Pfizer, Phadia, Roche, Sandoz, Sanofi, and ThermoFisher, Paid instructor for: Abbvie, Novartis, and Roche, Speakers bureau: Abbvie, Actelion, Bristol-Myers Squibb, Celgene, MSD, Novartis, Pfizer, Phadia, Roche, Sandoz, and ThermoFisher, Burkhard Moeller: None declared, Diego Kyburz Grant/research support from: Abbvie, Roche, Consultant of: Abbvie, BMS, Novartis, Pfizer, Roche, UCB, Gilead, Sanofi, Speakers bureau: Pfizer, BMS, Novartis, Abbvie, Adrian Ciurea Consultant of: Consulting and/or speaking fees from AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Merck Sharp & Dohme, Novartis and Pfizer., Maryam Poorafshar Grant/research support from: Thermo Fisher Scientific, Employee of: Thermo Fisher Scientific, Axel Finckh Grant/research support from: Pfizer: Unrestricted research grant, Eli-Lilly: Unrestricted research grant, Consultant of: Sanofi, AB2BIO, Abbvie, Pfizer, MSD, Speakers bureau: Sanofi, Pfizer, Roche, Thermo Fisher Scientific
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FRI0041

ULTRASOUND-DETECTED SYNOVITIS AMONG INDIVIDUALS AT RISK OF RHEUMATOID ARTHRITIS INCREASES THE RISK OF DEVELOPING CLINICAL ARTHRITIS

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Background: During the transition to rheumatoid arthritis (RA) patients pass through several phases. In the preclinical phase, the presence of anti citrullinated protein antibodies (ACPA) can be detected [1]. A set of clinical characteristics for patients with arthralgia who are at risk of progression to RA was established (clinically suspected arthralgia; CSA) [2]. Ultrasound (US) is more sensitive diagnostic tool in detecting synovitis than clinical assessment and was recommended to use in diagnostics of RA.

Objectives: To test if ultrasound-detected synovitis among patients at risk of progression to RA increases the risk of developing clinical arthritis (CA) in the future.

Methods: ACPA+ individuals with arthralgia and/or those fulfilling CSA criteria were enrolled into the study and were assessed in 3 months interval (routine clinical investigation with laboratory tests, 68-joint count, US assessment). Tender and swollen joint counts were provided by an independent investigator. Sonographer was blinded to all clinical and laboratory data. CA was defined as clinically swollen and tender joint. All US assessments were provided by a single experienced investigator. Thirty joints US score was assessed bilaterally in wrist, MCP I-V, PIP II-V (dorsal and palmar approach), MTP II-V (dorsal approach), ankle (dorsal, medial and lateral approach). US synovitis was defined according the EULAR-OMERACT and scored separately in gray-scale (GS) 0-3 (zero to severe synovitis) and Power Doppler (PD) 0-3 (zero to high activity). Scores were calculated as sum scores. For the statistical analysis, we used GraphPad Prism 8.0.0 software (Wilcoxon-Mann-Whitney test), and relative risk ratio (RR).

Results: 93 patients were enrolled into the study (95% female). 58 patients were ACPA+ (all of them RF+), 35 were ACPA- (10 of them RF+). Of ACPA+ individuals, 100% fulfilled the CSA criteria, all seronegative individuals met the CSA criteria. At baseline, GS≥1 was detected in 69 patients (74%), PD≥1 was in 26 (28 %) patients. Single erosion was found by US in 1 patient (0,9%) at baseline. 14 patients (15%) developed CA within 30 months, 77% of them till month 10 from the baseline. No statistical difference in US synovitis score was found between ACPA+ vs. ACPA- and CSA+ vs. CSA- groups at baseline. RR to develop CA at the joint level in patients with GS≥1 at baseline was 1.37 (95% CI 0.99-1.89; p<0.05), with PD≥1 the RR was 2.5 (95% CI 1.3-4.8; p<0.05), in GS≥2 RR was 3.8 (95% CI 2.6-5.6; p<0.0001), in PD≥2 RR was 5.3 (95% CI 2.4-11.7; p<0.0001). US-detected synovitis preceded clinical finding of arthritis by 3 months (SD 1.2).

Conclusion: US-detected synovitis in patients at risk of RA further increases the risk of developing clinical arthritis in the future. US detected synovitis in joints appear about 3 months prior synovitis detected by routine clinical assessment.

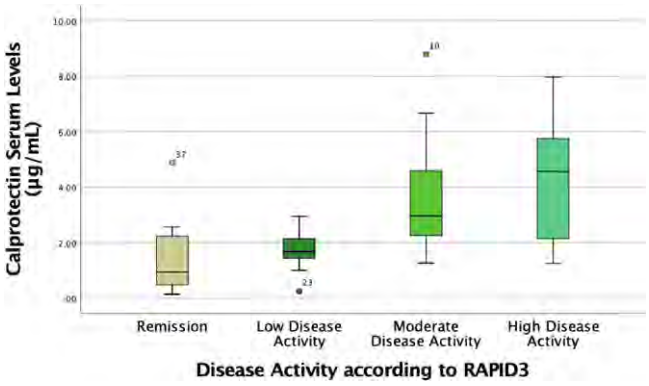
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[2] van Steenbergen HW, Aletaha D, Beaart-van de Voorde LJJ, et al. EULAR definition of arthralgia suspicious for progression to rheumatoid arthritis. Annals of the Rheumatic Diseases 2017;76:491-6.
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Disclosure of Interests: Petra Hanova: None declared, Klára Prajzlerová: None declared, Nora Petrovská: None declared, Monika Gregová Consultant of: Novartis, Abbvie, Paid instructor for: Novartis, Speakers bureau: Novartis, Abbvie, MSD, Heřman Mann: None declared, Karel Pavelka Consultant of: Abbvie, MSD, BMS, Egis, Roche, UCB, Medac, Pfizer, Biogen, Speakers bureau: Abbvie, MSD, BMS, Egis, Roche, UCB, Medac, Pfizer, Biogen, Jiří Vencovský: None declared, Ladislav Šenolt: None declared, Mária Filková: None declared
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FRI0042 DISCREPANCIES BETWEEN RAPID3 AND DAS28 IN RHEUMATOID ARTHRITIS PATIENTS IN REMISSION OR LOW DISEASE ACTIVITY RECEIVING TNF INHIBITORS: WHAT IS THE ROLE OF THE INFLAMMATION BIOMARKERS?

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Background: Patients and Rheumatologist often differ in their perception of RA disease activity. Remission or low disease activity should be the treatment target in RA, patients should be included in treatment decisions.
Objectives: To identify factors influencing patient's self-reported disease activity by RAPID3 test.
Methods: 47 RA patients in remission or low disease activity by DAS28ESR (DAS28ESR ≤ 3.2) receiving TNFi (etanercept, adalimumab and infliximab) stratified their disease activity by RAPID3, then two patients' groups were defined: *target group* (RAPID3 with remission 0-3 or low disease activity 3.1-6), *non-target group* (RAPID3 with moderate 6.1-12 or high disease activity >12). Demographic data, disease duration, autoantibody status, radiological data, concomitant csDMARD therapy was collected. Laboratory measurements included CRP, ESR, calprotectin serum levels, TNFi trough serum levels, and antidrug antibodies (enzyme-linked immunosorbent assay (ELISA) test kit (Calprolab™ Calpro AS, Oslo, Norway, and Promonitor®, Progenika SA, Spain, respectively) according to the manufacturers' protocol. Pearson´s correlations coefficients were used to identify variables correlating with RAPID3 score. Mixed-effects analyses of covariance (ANCOVAs) models were used to identify factors influencing RAPID3 score.
Results: Patients in "*target group"* have shown a significant lower TJC, pain by VAS 0-10mm, and calprotectin serum levels, but higher TNFi serum trough levels in comparison to "*non-target group*". When patients were classified according to RAPID 3 categories, patients in "*remission*" have shown lower calprotectin serum levels than those classified as in "*high disease activity*" (0.94 (4.88-0.14) vs. 4.57 (7.97-1.25), *p*=0.001, respectively). Accordingly, when classified according to pain by VAS 0-10mm, patients with low levels of pain had lower calprotectin serum levels vs. those with severe pain (1.43 (6.33-10.14) vs. 5.16 (8.80-1.25), *p*=0.009, respectively). When distributed according to PGA (1=very good, 2=good, 3=regular, 4=bad, 5=very bad) patients in "*very good*" group had lower mean of calprotectin serum levels than those in "*very bad*" group (0.94 (4.88-0.14) vs. 4.57 (7.97-1.25), *p*=0.001, respectively). PGA and Pain VAS have shown a strong correlation with RAPID 3 (R^2 0.978, and 0.834, *p*=0.001, respectively), while calprotectin and TNFi serum trough levels showed a moderate correlation (R^2 0.311, and 0.372, *p*=0.005, respectively). The multivariate adjusted analysis showed a significant association between Pain and RAPID3 (p<0.001) according to the different covariates (age, gender, anti-CCP positivity, time in remission, SJC, TJC, DAS28ESR). In addition, calprotectin and TNFi trough serum levels were associated with RAPID 3 (p<0.005). Backward selection of variables did not substantially modify the association between RAPID 3 and pain, calprotectin and TNFi trough serum levels.
Conclusion: 61.7% of RA patients undergoing TNFi classified as in remission or low disease activity by DAS28ESR, self-reported their disease activity as moderate or high by RAPID3. The most significant factor influencing patient's perception of disease activity is pain (pain VAS and TJC). However, inflammation markers (calprotectin, TNFi serum trough levels) remain statistically significant after fully adjustment by different confounders. Thus, therapies improving these three domains will have a larger impact in patient´s perception of disease activity.

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Disclosure of Interests: Jose Inciarte-Mundo Employee of: Eli Lilly, Speakers bureau: Abbvie, Eli Lilly, BMS, Roche and Pfizer, Rosa Morlà Speakers bureau: Abbvie, Eli Lilly, BMS, Roche and Pfizer, Beatriz Frade-Sosa: None declared, Julio Ramírez Speakers bureau: Abbvie, Eli Lilly, BMS, Roche, Novartis and Pfizer, Raul Castellanos-Moreira Speakers bureau: Lilly, MSD, Sanofi, UCB, Virginia Ruiz Speakers bureau: Lilly, Pfizer, Juan de Dios Cañete: None declared, José Gomez Puerta Speakers bureau: Abbvie, Eli Lilly, BMS, Roche and Pfizer, Raimón Sanmartí Speakers bureau: Abbvie, Eli Lilly, BMS, Roche and Pfizer
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FRI0043 JOINT SPACE NARROWING PRECEDES EROSIVE RADIOGRAPHIC DAMAGE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized through symmetric polyarthritis leading to joint destruction over time in many patients. Radiographic damage is an important outcome in RA clinical trials, most commonly assessed by conventional radiographs and quantified/reported by the modified total Sharp van der Heijde Score (mTSS). The mTSS is assessing erosive (ERO) changes as well as joint space narrowing (JSN; reflecting cartilage wasting) in the small joints of the hands and feet. While erosions are the hallmarks of RA, loss of cartilage has been reported to be highly relevant for functional limitations in RA. The sequence of occurrence of these events is not completely understood.
Objectives: To investigate the time to radiographic progression and assess potential differences between time-to-JSN progression and time-to-ERO progression.
Methods: Radiographs of RA patients from a large prospective clinical routine cohort were scored using the mTSS by one experienced reader (G.S.) unaware of the aim of this project. Time-to-JSN and time-to-ERO was estimated using survival analyses utilizing the Kaplan-Meier estimator. In additional analyses, patients were stratified based on JSN and/or ERO damage at baseline. Further, potential predictors (demographics, csDMARD/bDMARD treatment/combination therapy) of time-to-ERO and time-to-JSN were evaluated using Cox-regression techniques. All statistical analyses were conducted using SAS v9.4 (Cary, New York, USA).
Results: We assessed 798 patients longitudinally for radiographic progression. JSN occurred significantly earlier than erosions (p<0.001, Figure 1). After stratification for baseline damage (Figure 2), these differences remained significant with a shorter time-to-JSN in patients without any baseline ERO or JSN (n=44, p=0.008), patients with JSN but no ERO at baseline (n=200, p<0.001), and patients with baseline ERO and JSN (n=536, p<0.001). Only in the small group of patients with isolated erosions (without JSN) at baseline there was no difference in time-to-progression of ERO vs. JSN (n=18, p=0.241). Overall, shorter time to progression of ERO was significantly predicted by positivity for rheumatoid factor or anti-citrullinated peptide antibodies (CCP; p<0.003), as well as by erosions at baseline (p<0.001) in Cox regression. In contrast, seropositivity for neither RF nor CCP was associated with shorter time to JSN progression (p=0.226); however, baseline concomitant JSN and ERO damage did show to be a significant predictor (p<0.001).

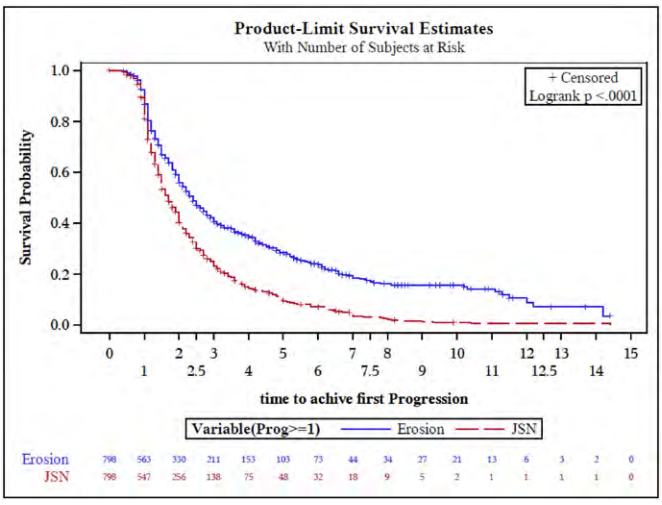


Figure 1. Time to joint space narrowing and time to erosive damage (n=798).

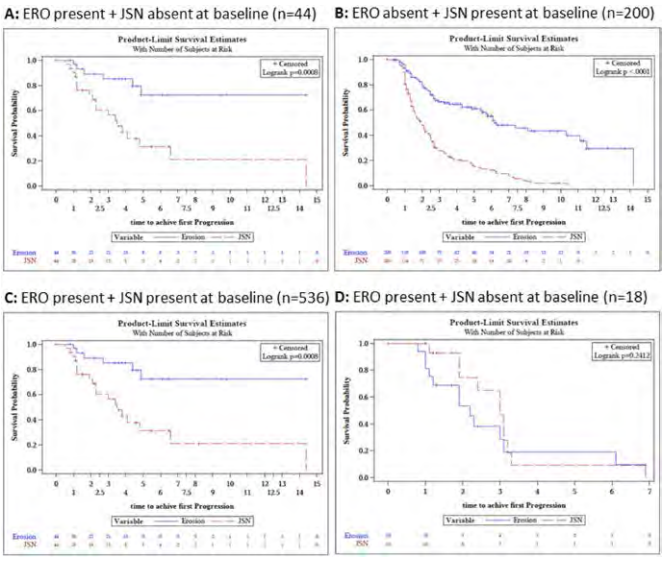


Figure 2. Time to JSN/ERO stratified by presence or absence of ERO/JSN at baseline.

Conclusion: We identified a significantly shorter time to progression of JSN compared to ERO in this longitudinal cohort of RA patients. JSN remains an important radiographic outcome, as it is strongly associated with impairment of physical function. This calls for a stronger focus on cartilage damage in RA, and a stronger consideration of JSN in routine evaluation of RA radiographs in clinical practice.

Disclosure of Interests: Andreas Kerschbaumer Paid instructor for: Celgene, Speakers bureau: Andreas Kerschbaumer has received lecture fees from Bristol-Myers Squibb, Gilead, Merck Sharp and Dohme and Pfizer., Farideh Alasti: None declared, Gabriela Supp: None declared, Josef S. Smolen Grant/research support from: AbbVie, Eli Lilly, Janssen, Merck Sharp & Dohme, Pfizer, Roche – grant/research support, Consultant of: AbbVie, Amgen Inc., AstraZeneca, Astro, Celgene Corporation, Celtrion, Eli Lilly, Glaxo, ILTOO, Janssen, Medimmune, Merck Sharp & Dohme, Novartis, Pfizer, Roche, Samsung, Sanofi, UCB – consultant, Speakers bureau: AbbVie, Amgen Inc., AstraZeneca, Astro, Celgene Corporation, Celtrion, Eli Lilly, Glaxo, ILTOO, Janssen, Medimmune, Merck Sharp & Dohme, Novartis, Pfizer, Roche, Samsung, Sanofi, UCB – speaker, Daniel Aletaha Grant/research support from: AbbVie, Novartis, Roche, Consultant of: AbbVie, Amgen, Celgene, Lilly, Medac, Merck, Novartis, Pfizer, Roche, Sandoz, Sanofi Genzyme, Speakers bureau: AbbVie, Celgene, Lilly, Merck, Novartis, Pfizer, Sanofi Genzyme, UCB

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FRI0044

ROBUST ANALYSES FOR RADIOGRAPHIC PROGRESSION IN RHEUMATOID ARTHRITIS

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Background: Reducing structural damage is an important treatment goal for rheumatoid arthritis (RA). Demonstrating a clinically meaningful, statistically significant difference in radiographic progression (assessed by van der Heijde modified total Sharp score, mTSS) is a common objective in trials for RA treatments. Complete collection of radiographic data is challenging, especially in long term follow-up and pediatric studies. Therefore, scores for individual joints or entire patients are regularly missing. A frequently used analysis method for mTSS is the analysis of covariance model, in which missing data are imputed using linear extrapolation (ANCOVA+LE). However, other ways to deal with missing information have also been proposed.

Objectives: To evaluate robust analysis methods for mTSS data.

Methods: Simulated data were used to compare a random coefficient model (RC) without imputation, ANCOVA+LE and ANCOVA with last observation carry forward imputation (LOCF).

A log-normal distribution was used to generate baseline patient level data to simulate a 2-arm clinical trial using baseline mTSS and rate of change in mTSS from recently completed trials. Changes in mTSS (12, 28 and 44 week timepoints) were generated under linear, concave quadratic (fast progression then slow progression), and convex quadratic (slow progression then fast progression) assumptions, with the proportion of change forced to be 0 (a proportion of simulated patients do not have progression). A monotone missing pattern was assumed to generate a data set with missing data (the 'observed' dataset).

ANCOVA analyses were performed using baseline and treatment as predictors. The RC model was applied using baseline, treatment, time, and time-by-treatment interactions as fixed effect and time as a random effect. Bias (difference between average of simulation sample mean and true value, the smaller the better), root mean square error (RMSE, a measure of variation among simulation samples, the smaller the better), power and type I error rate were compared between methods.

Results: The random coefficient model provided better or at least similar results in bias, RMSE, power and type I error rate as ANCOVA+LE under evaluated scenarios (Table 1).

Progression assumption	Simulation parameters (Number of simulations = 500; common sample size=300, baseline mTSS=~11.7)	Model	Bias	Power	RMSE
Linear	p_{pbo} = 0.6, r_{pbo} = 0.065 p_{trt} = 0.68 r_{pbo} = 0.046 Δ_{wk44} = −0.49	ANCOVA + Full	0.002	0.924	0.140
		ANCOVA + LE	0.003	0.866	0.155
		ANCOVA+LOCF	0.154	0.844	0.190
		RC + FULL	0.001	0.92	0.139
		RC + OBS	−0.002	0.872	0.156
Concave	p_{pbo} = 0.6, r_{pbo} = −0.0009, q_{pbo} = 0.11 p_{trt} = 0.68, r_{trt} = −0.0011, q_{trt} = 0.093 Δ_{wk44} = −0.611	ANCOVA + Full	0.002	0.982	0.141
		ANCOVA + LE	−0.002	0.926	0.180
		ANCOVA+LOCF	0.188	0.94	0.222
		RC + FULL	0.002	0.978	0.141
		RC + OBS	−0.005	0.924	0.174
Convex	p_{pbo} =0.6, r_{pbo} = 0.0037, q_{pbo} =−0.09 p_{trt} = 0.68, r_{trt} = 0.003, q_{trt} = −0.1 Δ_{wk44} = −0.83	ANCOVA + Full	0.003	1	0.139
		ANCOVA + LE	0.343	0.948	0.368
		ANCOVA+LOCF	0.391	0.974	0.405
		RC + FULL	−0.004	1	0.140
		RC + OBS	0.199	0.988	0.249

Abbreviations: FULL = complete dataset with no missing values trt = active treatment, OBS = the 'observed' dataset, pbo = placebo, p= proportion of patients with no progression, r = linear progression rate (mTSS units per week), q = quadratic term coefficient. Δ = active treatment progression – placebo r

Conclusion: RC is a robust analysis method for mTSS. We recommend its use in primary analyses, especially for long-term extension and pediatric studies with a higher likelihood of missing data. This method can also provide reference for time points when no data are collected via estimated slope. ANCOVA+LE can be used for sensitivity analysis.

References: None.

Disclosure of Interests: Robert B.M. Landewé Consultant of: AbbVie; AstraZeneca; Bristol-Myers Squibb; Eli Lilly & Co.; Galapagos NV; Novartis; Pfizer; UCB Pharma, Luna Sun Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Yun-Fei Chen Shareholder of: Own shares in Eli Lilly and Company., Employee of: Employee of Eli Lilly and Company, Douglas Schlichting

Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Désirée van der Heijde Consultant of: AbbVie, Amgen, Astellas, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Cyxone, Daiichi, Eisai, Eli-Lilly, Galapagos, Gilead Sciences, Inc., Glaxo-Smith-Kline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB Pharma; Director of Imaging Rheumatology BV

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FRI0045 DISEASE ACTIVITY TRAJECTORIES FOR EARLY AND ESTABLISHED RHEUMATOID ARTHRITIS: DATA FROM THE OBRI REGISTRY

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Background: Description of disease activity status in patients with rheumatoid arthritis (RA) at fixed points in time modelled as continuous (e.g. number of swollen joints counts), dichotomous variable (e.g. remission or low disease status using composite measures) do not reflect the patient's disease course in chronic and relapsing RA.

Objectives: We proposed to describe the longitudinal disease activity trajectories for patients with early and established RA over two years' follow-up in routine clinical care.

Methods: RA patients enrolled in the Ontario Best Practices Research Initiative (OBRI) with available DAS28-ESR over two years of follow-up were included. Using a latent growth curve modelling (LCGM), subgroups of patients following distinct pattern of DAS28-ESR change over time were identified. Fit statistics and model selection was based on Bayesian information criterion (BIC).

Results: A total of 1273 patients were included, 454 (36%) with early RA and 819 (64%) with established RA. At baseline, patients with early RA were significantly younger (57.3 vs. 59.1 years) and with higher DAS28-ESR (4.6 vs. 4.3), and were less likely to have an erosion (25.0% vs. 59.7%), to be RF-positive (70.3% vs. 76.8%), and to use biologic DMARDs (7.0% vs. 29.2%).

In patients with early RA (Figure 1A), three subgroups of patients were identified by LCGM with a better fit (BIC: -3070.84). Almost 88% patients with moderate disease activity reached remission (group 1: 48.4%) or low disease status (group 2: 39.3%) after two years, while 12% of patients with high disease profile remained in a moderate state (group 3).

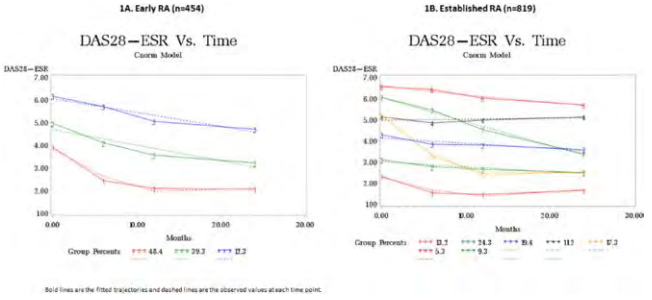


Figure 1. Observed and fitted trajectories from the latent growth curve analysis in patients with early and established RA.

In patients with established RA (Figure 1B), seven subgroup of patients were identified by LCGM with a better fit (BIC: -5378.13). After two years' follow-up, 37.5% of patients in remission or low disease state at baseline remained or reached to remission (group 1 and 2, respectively). Two groups of patients with high disease activity at baseline had an improvment after two years (17.3% reached remission and 9.3% reached moderate state; group 5 and 7, respectively). 16.5% of patients with high disease activity at baseline remained in high disease status after two years (group 4 and 6). 19.4% of patients with moderate activity at baseline remained in a moderate state after two years (group 3).

Conclusion: Disease course is different between early and established RA. While 70% of early RA patients with moderate or high disease profiles reached remission, only 17% of established patients with high disease activity achieved remission after two years of follow-up. These findings suggest the potential effects of receiving early treatment and health care. The impact of sociodemographic, clinical and medication profile on disease course will be examined as future work for this study.

Disclosure of Interests: Mohammad Movahedi Consultant of: Allergan, Angela Cesta: None declared, Xiuying Li: None declared, Claire Bombardier Grant/research support from: Dr Bombardier reports sources of funding for Ontario Best Practice Research Initiative Research grants from Abbvie, Janssen, Amgen, Medexus, Merck, Pfizer, and Novartis outside of the submitted work. Consulting Agreements: Abbvie, Covance, Janssen, Merck, Pfizer, Sanofi and Novartis outside of the submitted work. Advisory Board Membership: Hospira, Sandoz, Merck, Pfizer and Novartis outside of the submitted work.

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FRI0046 PHARMACOGENOMICS-DRIVEN INDIVIDUALIZED PREDICTION OF TREATMENT RESPONSE TO METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS: A MACHINE LEARNING APPROACH

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Background: Methotrexate (MTX) is the most common anchor drug for rheumatoid arthritis (RA), but the risk of missing the opportunity for early effective treatment with alternative medications is substantial given the delayed onset of MTX action and 30-40% inadequate response rate. There is a compelling need to accurately predicting MTX response prior to treatment initiation, which allows for effectively identifying patients at RA onset who are likely to respond to MTX.

Objectives: To test the ability of machine learning approaches with clinical and genomic biomarkers to predict MTX response with replications in independent samples.

Methods: Age, sex, clinical, serological and genome-wide association study (GWAS) data on patients with early RA of European ancestry from 647 patients (336 recruited in United Kingdom [UK]; 307 recruited across Europe; 70% female; 72% rheumatoid factor [RF] positive; mean age 54 years; mean baseline Disease Activity Score with 28-joint count [DAS28] 5.65) of the PhArmacogenetics of Methotrexate in RA (PAMERA) consortium was used in this study. The genomics data comprised 160 genome-wide significant single nucleotide polymorphisms (SNPs) with $p<1\times10\text{-}5$ associated with risk of RA and MTX metabolism. DAS28 score was available at baseline and 3-month follow-up visit. Response to MTX monotherapy at the dose of ≥15 mg/week was defined as good or moderate by the EULAR response criteria at 3 months' follow up visit. Supervised machine-learning methods were trained with 5-repeats and 10-fold cross-validation using data from PAMERA's 336 UK patients. Class imbalance (higher % of MTX responders) in training was accounted by using simulated minority oversampling technique. Prediction performance was validated in PAMERA's 307 European patients (not used in training).

Results: Age, sex, RF positivity and baseline DAS28 data predicted MTX response with 58% accuracy of UK and European patients ($p = 0.7$). However, supervised machine-learning methods that combined demographics, RF positivity, baseline DAS28 and genomic SNPs predicted EULAR response at 3 months with area under the receiver operating curve (AUC) of 0.83 ($p = 0.051$) in UK patients, and achieved prediction accuracies (fraction of correctly predicted outcomes) of 76.2% ($p = 0.054$) in the European patients, with sensitivity of 72% and specificity of 77%. The addition of genomic data improved the predictive accuracies of MTX response by 19% and achieved cross-site replication. Baseline DAS28 scores and following SNPs rs12446816, rs13385025, rs113798271, and rs2372536 were among the top predictors of MTX response.

Conclusion: Pharmacogenomic biomarkers combined with DAS28 scores predicted MTX response in patients with early RA more reliably than using demographics and DAS28 scores alone. Using pharmacogenomics biomarkers for identification of MTX responders at early stages of RA may help to guide effective RA treatment choices, including timely escalation of RA therapies. Further studies on personalized prediction of response to MTX and other anti-rheumatic treatments are warranted to optimize control of RA disease and improve outcomes in patients with RA.

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FRI0047

STRATEGIES REGARDING GOAL SETTING AND SELF-MANAGEMENT IN DIFFICULT-TO-TREAT RHEUMATOID ARTHRITIS: PRELIMINARY RESULTS OF A SYSTEMATIC LITERATURE REVIEW INFORMING THE 2020 EULAR RECOMMENDATIONS FOR THE MANAGEMENT OF DIFFICULT-TO-TREAT RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) patients treated according to European League Against Rheumatism (EULAR) recommendations failing ≥2 biological or targeted synthetic disease-modifying antirheumatic drugs with a different mode of action who still have complaints which may be suggestive of active disease and for whom management is perceived as problematic by patient and/or rheumatologist have been defined as suffering from 'difficult-to-treat RA'. A mismatch in goal setting between patient and health care professional, and suboptimal self-management may contribute to this disease state, while specific management recommendations regarding these factors are currently lacking.[1]

Objectives: To systematically summarise evidence in the literature on the identification and optimisation of a mismatch in goal setting and suboptimal self-management in difficult-to-treat RA patients, informing the 2020 EULAR recommendations for the management of difficult-to-treat RA.

Methods: A systematic literature review (SLR) was performed: PubMed, Embase and Cochrane databases were searched up to December 2018. Relevant papers were selected and appraised. Effect sizes were extracted or calculated.

Results: Three studies were selected on the identification and four on the optimisation of a mismatch in goal setting (Figure 1). No accurate measures were found to identify a mismatch in goal setting, but patients expressed a desire to take their quality of life goals more explicitly into account. Education was found to improve goal setting (4 of 4 studies, effect size not calculable).

Five studies were selected on the identification and 31 on the optimisation of suboptimal self-management (Figure 1). Although formal evaluations in high quality studies were lacking, the Arthritis Self-Efficacy Score was found to be the most reliable tool to identify suboptimal self-management. Patients were found to desire more education on nutrition, the disease and the diagnostic process to be able to improve self-management. Self-management programs, educational and psychological interventions were found to improve self-management (Table 1).

Table 1: Effect sizes of studies on the optimisation of self-management

Outcome	Type of intervention	Benefit of intervention compared to control[1] in *n* of *n* selected studies	Studies with effect size (*n*)	Effect size per study[2]
Self-efficacy	Self-management programs	12/13	6	0.18–0.39; 0.23–0.67; 0.37; 0.43–0.53; 0.49;[3] 7.52–8.25
	Education	6/6	3	0.05–0.17; 0.22–0.59; 1.23
	Psychological	2/2	2	0.20–0.35; 0.45
Anxiety	Psychological	1/2	1	0.17[3]
Depressive symptoms	Psychological	1/2	1	0.15–0.33[3]
RA knowledge	Education	3/3	2	0.34–0.47; 0.84

n: number of studies; RA: rheumatoid arthritis.

1. Mostly usual care or wait list; 2. If different outcome measures were used the range in effect sizes over these measures is reported; 3. Pooled effect size, reported in systematic literature review.

Conclusion: In difficult-to-treat RA patients, limited evidence was found on a mismatch in goal setting and suboptimal self-management, especially regarding their identification. Non-pharmacological interventions were found to improve goal setting and self-management.

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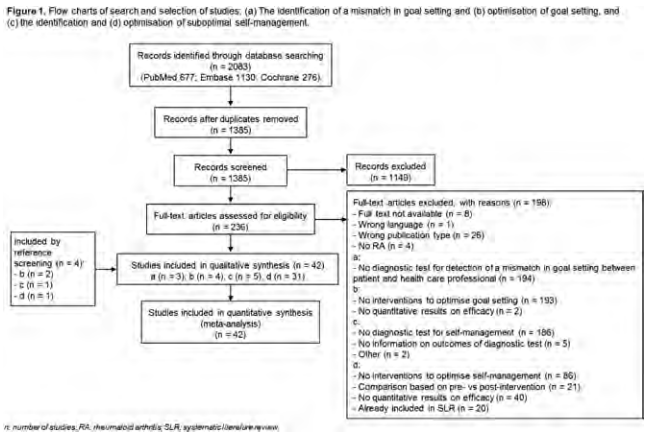


Figure 1. Flow charts of search and selection of studies: (a) The identification of a mismatch in goal setting and (b) optimisation of goal setting, and (c) the identification and (d) optimisation of suboptimal self-management.

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FRI0048

NUMBER NEEDED TO TREAT TO ACHIEVE MINIMUM CLINICALLY SIGNIFICANT DIFFERENCES IN PATIENT-REPORTED OUTCOMES IN PATIENTS TREATED WITH BARICITINIB

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Background: Baricitinib (BARI) provided rapid and sustained improvements in patient-reported outcomes (PROs) in randomized, controlled trials (RCTs) in patients (pts) with active rheumatoid arthritis (RA) and inadequate responses (IR) to methotrexate (MTX) (RA-BEAM; NCT01710358)[1,2] and biologic DMARDs (bDMARD-IR; RA-BEACON; NCT01721044)[3,4].

Objectives: To determine the number needed to treat (NNT) to report improvements ≥minimum clinically important differences (MCIDs) in multiple PROs at Week (Wk) 12 after treatment with BARI 4-mg in RA-BEAM and BARI 2-mg or BARI 4-mg in RA-BEACON. NNTs ≤10 vs placebo (PBO) are considered clinically meaningful.

Methods: Evaluated PROs with respective MCID definitions included Patient Global Assessment of Disease Activity (PtGA, 0-100 mm visual analog scale [VAS], MCID ≥10 mm), pain (0-100 mm VAS, MCID ≥10 mm), physical function (Health Assessment Questionnaire-Disability Index, MCID ≥0.22 points), fatigue (Functional Assessment of Chronic Illness Therapy-Fatigue [FACIT-F], MCID≥4.0), and health-related quality of life (SF-36 physical component summary [PCS: MCID ≥2.5] and domain scores: physical function [PF], role physical [RP], bodily pain [BP], general health [GH], vitality [VT], social functioning [SF], role emotional [RE], mental health [MH], MCID ≥5.0).[5] The percentages of pts reporting improvements ≥MCID were determined at Wk 12. NNTs were calculated as 1/difference in response rates between BARI 2-mg or 4-mg and PBO.

Results: At Wk 12, percentages of pts reporting clinically meaningful improvements were greater and statistically different from PBO ($p<0.01$) with BARI 2-mg and 4-mg across most PROs in both RCTs. Most NNTs were ≤10. (Figure)

Conclusion: Across different populations, MTX-IR and bDMARD-IR pts with active RA reported clinically meaningful improvements in PROs after BARI treatment. The NNTs in these analyses indicate that <10 pts need to be treated with BARI 2- or 4-mg to report a clinically meaningful benefit.

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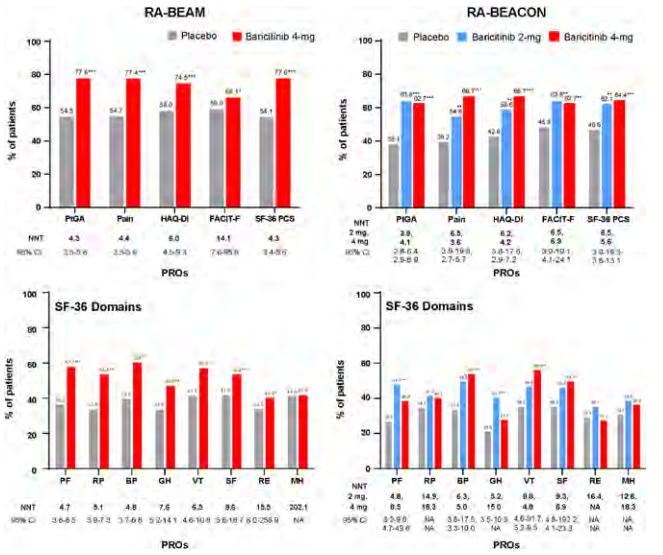


Figure. Percentages of patients reporting improvements ≥MCID with baricitinib vs placebo and associated NNTs for baricitinib in RA-BEAM and RA-BEACON. *p<0.05; **p<0.01; ***p<0.001. Abbreviations: BP, bodily pain; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; GH, general health; HAQ-DI, Health Assessment Questionnaire-Disability Index; MCID, minimum clinically important difference; MH, mental health; NA, not applicable (ie, difference between treatment and placebo is not statistically significant, confidence interval of NNT is not calculated); NNT, numbers needed to treat; Pain, Patient's assessment of pain; PCS, physical component score; PF, physical function; PtGA, Patient's Global Assessment of Disease Activity; RE, role emotional; RP, role physical; SF-36, Short Form-36; SF, social functioning; VT, vitality

Disclosure of Interests: Vibeke Strand Consultant of: AbbVie, Amgen, Biogen, Celltrion, Consortium of Rheumatology Researchers of North America, Crescendo Bioscience, Eli Lilly, Genentech/Roche, GlaxoSmithKline, Hospira, Janssen, Merck, Novartis, Pfizer, Regeneron Pharmaceuticals, Inc., Sanofi, UCB, Luna Sun Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Jorge Ross Terres Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Carol L. Kannowski Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company

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FRIDAY, 05 JUNE 2020

Rheumatoid arthritis - comorbidity and clinical aspects

FRI0049 RHEUMATOID ARTHRITIS ASSOCIATED INTERSTITIAL LUNG DISEASE: TOBACCO AND OTHER RISK FACTORS

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Background: Among the risk factors associated with the development of interstitial lung disease (ILD) in patients with rheumatoid arthritis (RA) are: male sex, old age, erosive RA, rheumatoid nodules, smoking and high levels of rheumatoid factor (RF) and anticitrullinated protein antibody (ACPA). The factors of poor prognosis include: HRCT (High Resolution Computed Tomography) pattern of usual interstitial pneumonia (NIU) with altered baseline functional tests (forced vital capacity FVC <60%, diffusion capacity of the lung for carbon monoxide DLCO<40%).

RA associated UIP (RA-UIP) has an appearance that is identical to idiopathic UIP (idiopathic pulmonary fibrosis [IPF]) on HRCT.

Objectives: To analyze different risk factors and poor prognosis in a cohort of patients with ILD-RA.

To assess the degree of association between tobacco (smokers, ex-smokers and non-smokers) and altered baseline functional respiratory tests (FRT) (FVC <80% and DLCO <40%) with HRCT patterns.

Methods: Descriptive study of 57 patients treated in our Hospital (1/1/2018 until 12/31/2019) with a diagnosis of RA (ACR 2010 criteria) and secondary ILD.

The most recent American Thoracic Society (ATS)/European Respiratory Society (ERS)/Japanese Respiratory Society (JRS)/Latin American Thoracic Society (ALAT) guidelines define three HRCT (High Resolution Computed Tomography) patterns of fibrosing lung disease in the setting of idiopathic pulmonary fibrosis (IPF): definite UIP (traction bronchiectasis and honeycombing), possible UIP and inconsistent with UIP. The distinction between definite UIP and possible UIP in these to the presence or absence of honeycombing. Approved by the Ethics Committee.

Quantitative variables are expressed as mean (SD) and dichotomous variables as percentages (%). The association between tobacco-UIP and FVC-UIP was studied using two Chi-square tests and the DLCO-UIP relationship with an exact Fisher test. Statistical analysis with SPSS version 21.

Results: 21 men and 36 women were included, with a mean age of 69 ± 10 years (mean ± SD), history of smoking (smokers 14%, non-smokers 43%, ex-smokers 42%). 83% were positive RF and 70% positive ACPA. Regarding the HRCT findings: 29 (50%) had a inconsistent with UIP pattern and 28 (49%) had an UIP pattern (45% defined, 3% possible). Of the UIP patients, 14 (50%) had a smoking relationship (35% ex-smokers, 25% smokers) and 15 were male (53%). Of the sample analyzed, 8% (5 patients) have died, all ex-smoking men, the UIP pattern being the most frequent found (4 UIP, 1 inconsistent with UIP).

No statistical association was observed between patients with exposure to tobacco and the UIP pattern (p = 0.438), nor among patients with baseline FVC <80% and UIP (p = 0.432) and also among patients with baseline DLCO <40% and UIP pattern (p = 0.459).

Conclusion: Our results, in general, do not match what is published in the literature. Male sex, smoking exposure and fibrosing pattern (UIP) represent a worse prognosis for patients with ILD-RA. However, more studies are required to determine more precisely how these risk factors affect the disease.

Disclosure of Interests: None declared

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FRI0050 EFFICACY OF ATORVASTATIN VERSUS COLCHICINE IN DECREASING BIOMARKERS OF MYOCARDIAL DAMAGE IN PATIENTS WITH SEVERE RHEUMATOID ARTHRITIS

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Background: Patients with rheumatoid arthritis (RA) have been associated to higher morbidity and mortality due to cardiovascular events. The impact of atorvastatin and colchicine in reducing these complications has been evaluated without comparative studies of these drugs in RA patients. We assess whether atorvastatin is superior to colchicine in cardiovascular risk markers (high-sensitivity troponin I (hs-cTnI), echocardiographic abnormalities and inflammatory cytokine) in patients with RA

Objectives: The primary objective was to compare the initial and final levels of hs-cTnI with both treatments. Secondary objectives: Describe initial echocardiographic abnormalities, compare changes in these alterations with treatment, evaluate factors associated with a higher level of hs-cTnI and echocardiographic abnormalities, compare changes in serum levels of inflammatory cytokines (TNF, IL 8, IL 1β, IL 6, IL 10, IL 12p70) and values of lipid profile

Methods: Prospective randomized pilot study, blinded for cardiologist and rheumatologist, with patients with RA and severe disease activity (DAS 28> 5.1), without known heart disease, kidney disease or previous use of atorvastatin and / or colchicine. Patients were assigned according to randomization in two groups: atorvastatin 40 mg/day or colchicine with an initial dose of 0.75 mg/day titled according to tolerance up to a maximum dose of 1.5 mg/day, both were received for four weeks. NCT04056039

Results: Recruitment of September 2018 to August 2019, 60 participants had undergone randomization (30 in each group) with a median age 48. The duration of follow-up from randomization was 28 days in each group. Participants were followed by weekly telephone contact to assess of adherence treatment. A detected value of hs-cTnI was found in all patients, initial value in the atorvastatin group: Median 1ng /L, IQR 1-2 and final: Median 1ng /L, IQR 1-3 vs initial value in the colchicine group: 1ng /L, IQR 1-2 and final: 1ng /L, IQR1-2 p = 0.67. Echocardiographic abnormalities in 46 patients (76.66%); 63.33% diastolic dysfunction, 15% tricuspid regurgitation and 11.66% left ventricular hypertrophy.

There were changes in initial and final diastolic dysfunction in the atorvastatin group from 19 to 9 vs colchicine 19 to 12 p = 0.05, 95% CI 0.49-0.82. Correlation of initial hs-cTnI with age p <0.001 and rheumatoid factor p = 0.02; correlation of diastolic dysfunction and age p <0.001. There was a greater decrease in the

level of tumor necrosis factor (TNF) and IL 1β in the atorvastatin group, however, decrease was higher in IL6 and IL12p70 in the colchicine group. Mild diarrhea was reported as the most frequent adverse effect in the atorvastatin group of 3.33% and colchicine of 23.33% p = 0.010. There was a statistically significant decrease in cholesterol and LDL-cholesterol levels in favor of treatment with atorvastatin

Conclusion: We do not observe substantial differences in decrease in hs-cTnI with atorvastatin and colchicine, a prospective study of 222 patients is required to avoid β-type error. Echocardiographic abnormalities in 76% of patients showed a greater decrease in diastolic dysfunction in the atorvastatin group, as well as lower cholesterol and LDL-cholesterol levels, thus, as a tendency to falling of TNF and IL 1β in this group

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FRI0051 RHEUMATOID ARTHRITIS PATIENTS WITH HIGH DISEASE ACTIVITY AND TREATED WITH HIGH DOSE GLUCOCORTICOID FREQUENTLY FALL: NINE YEARS OF THE TOMORROW STUDY

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Background: Falling is a multicausal phenomenon resulting from complex interactions between intrinsic and extrinsic or environmental factors. Patients with rheumatoid arthritis (RA) who have muscle weakness and stiff or painful joints might be at increased risk of falling. However, little is known about the exact properties of risk factors for falling in patients with RA. Recently, the disease activity of RA has been more satisfactorily controlled by the "treat-to-target" strategy, including the use of biologics. Given this new era, it is important to accurately estimate the incidence of falling in patients with RA and to elucidate contributing risk factors.

Objectives: The objective of this study was to evaluate the incidence of falling and associated risk factors in 208 patients with RA and in age- and sex-matched 205 controls (Co) who participated in the TOMORROW (TOtal Management Of Risk factors in Rheumatoid arthritis patients to lOW er morbidity and mortality) study, a 10-year cohort study that started in 2010 in Japan. This research was conducted using TOMORROW study data for 9 years.

Methods: We evaluated the incidence of falling by self-administered questionnaire every year and confirmed them by medical records. We also collected information about general health status, body composition including bone mineral density, lean body mass, fat mass and laboratory data. We compared the frequency of the incidence of falling in RA patients and Co for 9 years and analyzed risk factors for falling.

Results: A total of 157 patients with RA (mean age: 57.1 ± 12.5 years, female: 84.7%, mean disease duration 13.9 ± 12.0 years) and 169 Co (mean age: 57.6 ± 12.5 years, female: 84.0%) completed 9 years observation. The rate of individuals who fell did not differ between two groups (RA: 66.9%, Co: 59.2%, p=0.19). However, number of falls was higher in RA than Co (0.35 vs 0.21/person-year, p=0.03). Multivariate logistic regression analysis adjusted for age, sex and BMI, revealed that RA was not a risk factor for the incidence of falling (OR: 1.36, 95%CI: 0.8-2.32, p=0.26) and the history of falling was a risk factor for the incidence of falling (OR: 3.27, 95%CI: 1.78-7.0, p<0.001). Multivariate linear regression analysis adjusted for age, sex and BMI, revealed that mHAQ (β=0.17, p=0.04), mean DAS28-CRP over 9 years (β=0.19, p=0.02) and mean dosage of glucocorticoid over 9 years (β=0.18, p=0.03) were the risk factors for number of falls (table 1).

Table 1. Multivariate linear regression analysis of risk factors associated with number of falls sustained by patients RA.

		RA	N=157
	Number of falls	β	p
At the entry	Anti-CCP antibody (U/mL)	0.016	0.835
	RF (IU/ml)	0.020	0.803
	History of falling	0.103	0.201
	DAS28-CRP	0.078	0.333
	mHAQ	0.169	0.039
	Dose of GC (mg/day)	0.028	0.723
9 years	Average DAS28-CRP	0.185	0.024
	Average dose of GC (mg/day)	0.179	0.025

RA, rheumatoid arthritis; CCP, cyclic citrullinated peptide; RF, Rheumatoid factor; DAS28-CRP, disease activity score 28 with C-reactive protein; mHAQ, modified Health Assessment Questionnaire; GC, glucocorticoid.

Conclusion: There was no difference in the incidence of falling between RA and Co. However, number of falls was significantly higher in RA group. High disease activity and higher dosage of glucocorticoid were the risk factors for number of falls among RA patients.

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FRI0052 INFLUENCE OF RHEUMATOID ARTHRITIS ON THE CLINICAL AND BIOLOGICAL PROFILE OF TYPE-2 DIABETES MELLITUS

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Background: Type-2 diabetes and rheumatoid arthritis (RA) are two chronic diseases characterized by tissue inflammation and insulin resistance. To date, no data have evaluated the influence of RA-induced joint and systemic inflammation on the course of type-2 diabetes.

Objectives: To study the impact of RA on type-2 diabetes

Methods: Observational, multicenter, cross-sectional usual-care study, including 7 rheumatology centers. This study included over a 24-month period consecutive patients with type-2 diabetes and RA, fulfilling the 2010 ACR / EULAR criteria, and diabetic controls with osteoarthritis (OA). The following data were collected: demographics, disease activity and severity indices, current treatment for RA and diabetes, history and complications of diabetes. A systematic blood test was performed, assessing inflammatory (CRP levels) and metabolic (fasting glycemia and insulin levels, HbA1c) parameters. The HOMA2%B (insulin secretion) and HOMA2%S (tissue insulin sensitivity) indices (HOMA calculator, © Diabetes Trials Unit, University of Oxford) were used to assess insulin resistance. Ra and OA

patients were compared using parametric tests after adjusting for age and BMI. A multivariate logistic regression was performed ti identify factors independently associated with insulin resistance.

Results: We included 122 RA patients (74% women, mean age 64+/-11 years, mean disease duration 15+/-11 11 years, 75% with positive ACPA antibodies and 64% with erosive disease) and 54 controls with OA. 64% of RA patients were treated with oral corticosteroids <10 mg/day, 65% received methotrexate and 53% received targeted biological therapies.

The characteristics of type-2 diabetes in the 54 OA patients corresponded to severe insulin-resistant diabetes: age> 65 years, high BMI> 30 kg/m^2, mean HbA1c 7.3%+/-11 1.3%, 30% of insulin requirement, high frequency of other cardiovascular risk factors, macroangiopathy found in almost half of patients and biological criteria of insulin resistance (elevation of HOMA2%B and decrease of HOMA2%S).

RA patients with type-2 diabetes had a younger age (64+/-11 years vs. 68+/-12 years, p=0.031) and lower BMI (27.7+/-11 5.5 vs. 31.5+/-11 6.3, p<0.001). These patients also had severe diabetes (HbA1c 7.0%+/-11 1.2%, 29% of insulin requirement, 43% of macroangiopathy) with an insulin resistance profile identical to OA controls. After adjusting for age and BMI, RA patients had a significantly increased insulin secretion compared to OA patients (HOMA2%B: 83.1+/-11 65.2 vs. 49.3+/-11 25.7, p=0.023) as well as a significant reduction of insulin sensitivity (HOMA2%S: 61.1+/-11 31.6 vs. 92.9+/-11 68.1, p=0.016). This insulin resistance was associated with the inflammatory activity of RA, with a negative correlation between the HOMA2%S and the DAS28 (r=-0.28, p=0.027). The multivariate logistic regression confirmed the independent association between the HOMA2%S index and DAS28 (OR: 3.93, 95% CI 1.02-15.06), as well as high blood pressure (OR: 1.29, 95% CI 0.33-1.99 CI).

Conclusion: RA patients with type-2 diabetes displayed severe, poorly controlled diabetes, highlighting the burden of comorbidities associated with RA. The clinical-biological profile of diabetic RA patients was severe insulin-resistant diabetes, with a biological profile of insulin resistance linked to the inflammatory activity of the disease. These findings may have therapeutic implications, with the potential targeting of insulin resistance through the treatment of joint and systemic inflammation.

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FRI0053 PROLIFERATIVE SYNOVITIS, AN ULTRASOUND PATTERN ASSOCIATED WITH ACPA POSITIVE RHEUMATOID ARTHRITIS

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Background: Seronegative (sero-) and seropositive (sero+) Rheumatoid Arthritis (RA) have different genetic, immunopathological and vascular morphology features, but no previous studies have analyzed if US characteristics differ between sero+ or sero- RA. Our preliminary studies suggest that sero+ RA is associated with an expansive synovitis pattern that we have called "proliferative synovitis" (PS)

Objectives: To analyze potential differences between patients with RA according to their autoantibody status by using ultrasonography (US). We aimed to assess whether PS is associated with ACPA+ pts

Methods: We collected clinical, epidemiological data and bilateral carpal and hand US images of pts with RA. Synovial hypertrophy (SH), Power Doppler signal (PD) and total score (sum of scores of SH and PD) in wrist and hand (1-5 metacarpophalangeal) were assessed. We evaluated the presence of PS, defined as expansive synovial growth encompassing the concepts of synovial SH grade II and III. We performed synovial biopsies of a subgroup of pts using arthroscopy or US guided in order to see immunohistochemistry differences between "proliferative" and "flat" (non-proliferative) synovitis. Serum levels of angiogenic and inflammatory biomarkers were performed

Results: Two hundred and five RA patients were collected. Overall, 173 (84.8%) pts were sero+ for RF (68.7%) or ACPA (74.6%), general characteristics are summarized in Table. No significant differences between sero+ and sero- pts in terms of disease activity or therapy were found. PS was present in 55.5% of sero+ pts (55.3% in RF+ and 58.2% in ACPA+ pts) and 16.1% of sero- pts (p=0.0001). Globally, 101 pts (49.2%) had PS. Ninety-six (95.0%) were RF or ACPA positive. Only 5 pts with sero- RA had PS (p=0.001). In the univariate analysis, significantly more pts with PS had erosive disease (72.3% vs 35.0% p=0.0001), higher US scores (p=0.0001) and more of them were taking conventional synthetic Disease-modifying anti-rheumatic drugs (csDMARD) (81.8% vs 69.6% p=0.05). No differences regarding disease activity were found.

In the multivariate analysis erosions [OR 4.90 CI 95% (2.17-11.07) p=0.0001] and ACPA [OR 3.5 CI 95% (1.39-10.7) p=0.09] but not RF status [OR 0.74 CI 95% (0.31-1.71) p=0.483] were independently associated with the presence of PS.

We immunostained synovial biopsies from 23 pts with PS (13 pts) or non-PS (10 pts). PS was significantly associated with higher density of vessels (p=0.042) and a strong trend to a higher density of B, T, Mast cells and macrophages (figure 1). Significantly higher serum levels of angiogenic (Activin A, bFGF, IL18, IL20, PIGF, SDF-1 and VEGF-D) and pro-inflammatory (IL23) cytokines were found in patients with PS (figure 2).

Conclusion: The presence of "proliferative Synovitis" was significantly associated with ACPA and erosive disease in patients with RA. PS pattern also was associated with higher density of synovial vessels and higher serum levels of angiogenic and inflammatory mediators

Table.

	Total US pattern p value			
	N=205	Proliferative (N=101)	Non proliferative (N=104)	
Female, n (%)	162 (79.4)	79 (78.2)	83 (80.6)	0.57
Age, mean (SD) years	57.1 (± 14,1)	56.3 (± 12.0)	58.0 (± 15.9)	0.40
Current Smoker, n (%)	47 (26.9)	22 (25.6)	25 (28.1)	0.73
Disease duration, mean (SD) months	113.3 (± 105.7)	127.7 (± 111.1)	99.3 (± 99.3)	0.05
Erosion, n (%)	108 (53.7)	73 (72.3)	35 (35.0)	0.00
ACPA, n (%)	153 (75.4)	89 (89)	64 (62.1)	0.00
RF, n (%)	99 (68.3)	78 (78)	63 (61.2)	0.01
DAS 28–CRP, mean (SD)	2.55 (±1.03)	2.66 (±1.04)	2.44 (±1.02)	0.17
GC, n (%)	99 (49.3)	45 (45.5)	54 (52.9)	0.32
cDMARDs, n (%)	152 (75.6)	81 (81.8)	71 (69.6)	0.05
bDMARD, n (%)	69 (34.3)	35 (35.4)	34 (33.3)	0.76
Total US score	14.9 (± 11.5)	18.8 (± 11.8)	11.1 (± 9.9)	0.00

*ACPA anti-citrullinated protein antibodies, RF rheumatoid factor, DAS28-CRP Disease Activity Score 28-joint count, CRP C-reactive protein, GC glucocorticoids, bDMARD biological disease-modifying antirheumatic drugs

Figure 1. Synovial cells density in 23 patients with RA.

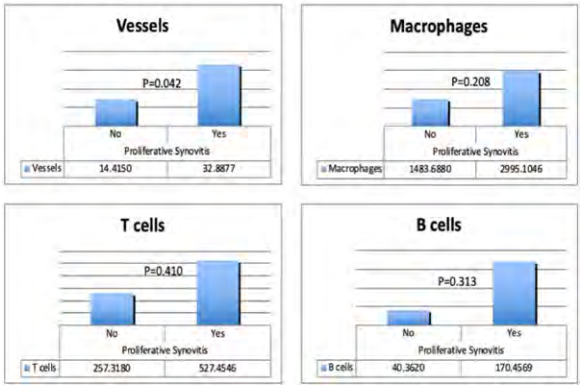
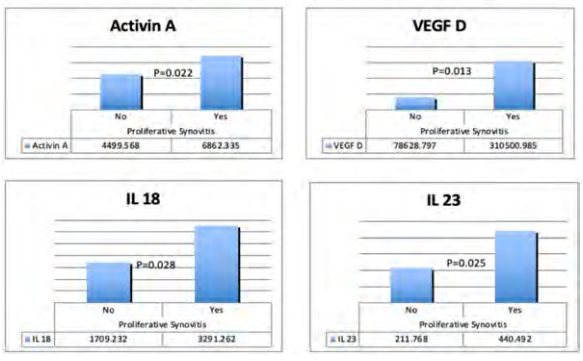


Figure 2. Serum levels of angiogenic and inflammatoy biomarkers in patients with RA.



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FRI0054 CHANGES IN DEPRESSIVE SYMPTOMS IN RHEUMATOID ARTHRITIS (RA) PATIENTS DURING TOCILIZUMAB (TCZ) THERAPY: THE GERMAN NONINTERVENTIONAL ARATA STUDY

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Background: Depression is a common comorbidity in patients with RA and influences perception of disease activity and quality of life. We have previously reported that mean depression scores improved during TCZ therapy in conjunction with reductions in disease activity.[1]

Objectives: To evaluate individual changes in depressive symptoms over 52 weeks in RA patients initiating treatment with TCZ.

Methods: We analyzed data from a large German multicenter observational study of patients with active RA who initiated TCZ therapy during routine clinical care (ML29087 ARATA study; NCT02251860). The Beck Depression Inventory-II (BDI-II), a self-report questionnaire for depression screening that has been validated in RA, was used to assess symptoms of depression. Patients were classified by baseline BDI-II scores into depression categories of no (BDI-II<14), mild (BDI-II 14-19), moderate (BDI-II 20-28), and severe depression (BDI-II≥29).[2] Individual changes in BDI-II scores between baseline and week 52 were assessed. Erythrocyte sedimentation rate was used as the acute phase reactant in Disease Activity Score-28 joints (DAS28) assessments.

Results: Of 1155 patients enrolled from 108 clinical centers in Germany between May 2014 and July 2018, 474 completed the BDI-II at baseline (BDI-II cohort); baseline characteristics were similar to those of patients who did not complete the BDI-II. Approximately half of patients in the BDI-II cohort had BDI-II scores indicating no depression (248; 52.3%); the remaining patients had mild (87; 18.4%), moderate (84; 17.7%), or severe (55; 11.6%) depression. The mean (SD) baseline characteristics of the BDI-II cohort were 55.5 (12.5) yrs of age, 75.7% female, 10.6 (9.2) yrs RA duration, 4.9 (1.2) DAS28, and 24.3 (10.2) Clinical Disease Activity Index (CDAI). Baseline DAS28 and CDAI scores were similar among different depression subgroups, but patients with severe depression were more likely to be female (87.3% vs 70.6% for no depression) and had higher levels of anxiety, suicidal ideation, fatigue, pain, and sleep disturbance than patients with no or milder depression.

A total of 229 of the 474 patients (48.3%) in the BDI-II cohort completed the BDI-II at both baseline and week 52. At 52 weeks, the depression category of approximately half of patients with depressive symptoms at baseline changed to a lower level or no depression (Figure 1). Moderate to large improvements in BDI-II from baseline (>10 points) were reported by 33.3% to 38.5% of patients with baseline depressive symptoms (Figure 2).

Conclusion: At 52 weeks after initiating TCZ, the depressive disease burden was reduced. Future analyses with a representative patient cohort will be aimed at exploring whether improvements in depression occur independent of reductions in disease activity.

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Figure 1. Flow analysis of change in depression category for RA patients with completed BDI-II questionnaires at baseline and week 52 (n=229)

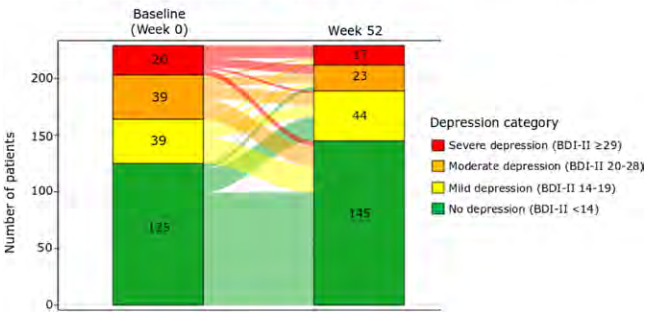
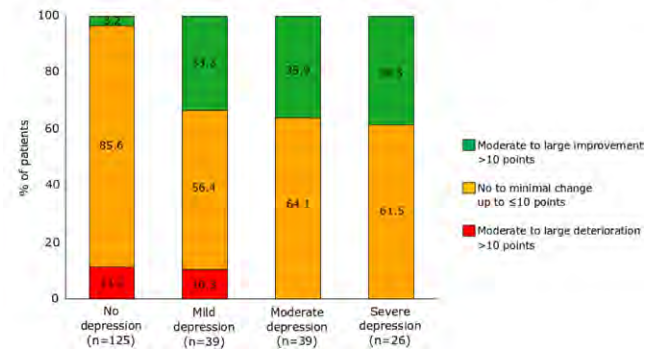


Figure 2. Improvement or deterioration of BDI-II scores over 52 weeks by BDI-II subgroup at baseline



FRI0055 PREVALENCE OF CLINICALLY LATENT TUBERCULOSIS IN RHEUMATOID ARTHRITIS – A RETROSPECTIVE CLINICOPATHOLOGIC STUDY OF 161 AUTOPSY PATIENTS

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Background: The risk of tuberculosis (**TB**) is higher in rheumatoid arthritis (**RA**) than in the general population.

Objectives: The **aim** of this study was to determine the prevalence and histological characteristics of post-primary inactive or active **TB** in **RA**, to appraise the involvement of different organs, and to statistically assess the relationship between inactive and active **TB** in **RA**.

Methods: At the National Institute of Rheumatology **9475** patients died between 1969 and 1992; among them **161** with **RA** and all of them were autopsied.

RA was confirmed clinically according to the criteria of the **ARA**.

TB was detected at autopsy and specified histologically, retrospectively reviewing all available clinical and pathological reports.

Demographics of different patient cohorts were compared with the Student t-probe. The relationship between inactive **TB** and active **TB** with miliary dissemination was analyzed with χ^2-test.

Results: Post-primary **TB** was associated with **RA** in **21** (**13.04%**) of 161 patients. Post-primary **TB** was localized to the lung. **Twelve** (57.14%) of 21 **TB** were histologically only fibrous, pigmented (antracothic) tuberculotic scars (**fTB**), and **9** (42.86%) of 21 revealed a fibrocaseous tubercle (**fcTB**). **One** of 12 **fTB** and **5** of 9

fcTB were associated with disseminated (miliary) tuberculosis (**mTB**) in **6** (3.7% of 161; 28.57% of 21) **RA** patients with **fTB** or **fcTB**.
Demographics, onset and duration of disease of **161 RA patients with TB**, **fTB**, **fcTB**, or **mTB** are summarized in Table.

Sex	Number of autopsies	Mean age in years at death ±SD	Range of age (in years)	Mean age at onset of disease ± SD	Disease duration (in years) ±SD
RA patients (total)	161	65.32±12.95	16–88	50.83±16.96	14.43±10.51
without TB	140 of 161	64.77±13.28	16–88	50.22±16.99	14.36±10.13
with TB	21 of 161	69.00±9.70	50–84	54.19±16.39	14.81±12.41
with fibrous TB	12 of 21	70.92±8.48	59–84	52.33±16.01	18.58±12.76
with fibrocaseous TB	9 of 21	66.44±10.59	50–80	56.67±16.55	9.78±9.91
with miliary TB	6 of 21	68.33±11.09	50–82	58.67±8.24	9.67±4.85

The **mean age** of **RA** patients was **higher with TB**, **fTB**, **fcTB** or **mTB** in comparison to **total population** or to the patients **without TB**, but the difference was only significant between patient cohorts with **fTB** and **RA** patients **without TB** (70.92 years versus 64.77, **p <0.043**).
There was a definitely shorter duration of **RA** in patients with **fcTB** or **mTB** compared to the **total population**.
Proliferative or exudative epithelioid granulomatous **mTB** involved different organs, such as lung in 5, liver in 3, spleen in 2, lymph nodes in 2, adrenal gland in 1, synovial membrane in 1, vertebrae in 1 and pituitary gland in 1of 6 **RA** patients with active **mTB**.
There was a significant correlation between: **TB** and **mTB** (c=1, χ^2=33.96, p<0.00000001), **TB** and **fTB** (c=1, χ^2=78.36, p<0.00000001), **TB** and **fcTB** (c=1, χ^2=55.69, p<0.00000001), or **fcTB** and **mTB** (c=0.99, χ^2=56.89, p<0.000001). The link between **fTB** and **mTB** was not significant (c=0.45, χ^2=0.007, p<0.9333 – NS).
Conclusion: TB, fTB, fcTB, or mTB complicated **RA in both sexes,** and a**t any time in the course of the disease.**
The mean age at death was higher in all forms of **TB**. Significant difference was only in mean age of **fTB** compared to the patients' cohort without **TB**. Fibrocaseous tubercle or miliary dissemination of tuberculosis reduced definitely the survival time (and disease duration) of aged **RA** patients.
Post-primary **TB** especially **fcTB** (mostly in the lungs) represents a high risk of miliary dissemination in **RA**. In our autopsy material **mTB** was the consequence of endogenous exacerbation of **TB** (and was not due to an exogenous reinfection), based on the high values of Youle's association coefficients between **TB** or **fcTB** and **mTB**.
The **mTB** may be considered as a terminal phenomenon, because of the limited numbers of granulomas involving only a few organs. The exudative character – beside proliferative epithelioid granulomas – must be regarded as histological evidence of impaired immune reactivity, an unfavorable prognostic sign in elderly patients, forecasting the possible fatal outcome of **RA** associated **TB**.
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FRI0056 LUNG COMPROMISE SCREENING IN PATIENTS WITH EARLY RA. A MULTICENTRIC CROSS SECTIONAL STUDY

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Background: Rheumatoid arthritis (RA) affects 0.4-1.3% of general population (1). It can affect lungs in different ways, with interstitial lung disease (ILD) as the most severe. Clinically evident ILD has been reported in 10-42% of patients, with a great impact in prognosis (2).
Objectives: To identify the prevalence of lung involvement in early rheumatoid arthritis patients (ERA) without previous known lung disease and describe the association between high resolution computed tomography (HRCT), lung functional tests (LFT) and clinical findings.
Methods: Cross sectional multicentric study. We included ERA patients (1 year or less since diagnose) consecutively. Patients with previous RA related lung disease or biologic/targeted synthetic Dmard treatment were excluded. HRCT, immunological tests (rheumatoid factor, anti-CCP, ANA), LFT and clinical evaluation were performed.
Results: We included 74 patients, 63 (85,1%) woman, mean (SD) of 47 (17,7) years. Thirty-seven patients (50%) were current or former smokers. Abnormal findings in HRCT were found in 62 patients (88,6%): ILD in 6 (8,6%), airway involvement in 40 (70%) and emphysema in 7 (10%). Ten patients (13,5%) had abnormal auscultation (2 sibilances, 2 roncus, and 6 crackles). Six patients (8,1%) had digital clubbing. Regarding immunological tests, 54/61 (88,5%) patients were positive for Anti CCP, and 53/61 (86,9%) were positive for FR. We compared features of patients with findings related to RA in HRCT (interstitial and/or airway) with those without them. We found no differences in the mean (SD) of DAS-28 [4,74 (1,38) vs 4,32 (1,39); p= 0,27]. The prevalence of anti- CCP was not higher in patients with abnormal HRCT [38/44 (86,3%) vs 16/17 (94,1%); p=0,39]. Patients with abnormal HRCT were older [median (IQR) 50,5 years (44,5-59,5) vs 43 years (32-51); p=0,008) and showed higher VSG values [mean (SD) 39,09 (24,03) vs 27,38 (17,6); p= 0,043]. Abnormal physical examination or dyspnea (class 2 mMRC or higher) was significantly associated with HRCT abnormalities [26 (50%) vs 3 (13,6%); p=0.003) and the presence of ILD on HRCT was significantly associated with crackles on the auscultation [4/68(6,25%) vs 2/6 (33,33%); p 0,023].
Conclusion: This study shows a high prevalence of lung involvement in ERA patients of less 1 year from diagnosis. Also, we showed a significant association between HRCT and physical examination findings. This data highlights the importance of the clinical examination in Rheumatoid Arthritis patients. More studies with bigger samples and longitudinal follow up are needed to confirm and complete our results.
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FRI0057 A MODEL FOR QUANTIFYING THE EFFECT OF INFLAMMATION ON CARDIOVASCULAR DISEASE RISK PREDICTION IN RA PATIENTS

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Background: Patients with rheumatoid arthritis (RA) are at increased risk for cardiovascular disease (CVD)[1]. Quantifying the effect of inflammation on CVD risk is important because rheumatologists can reduce inflammation with effective RA medications. A new score has been developed for predicting the risk for a CVD event (MI, stroke or CV death) in RA patients. It combines serological measures of inflammation (the multi-biomarker disease activity [MBDA] score, a measure of RA disease activity; and three individual biomarkers [TNF-RI, MMP-3 and leptin]), with age and four conventional CVD risk factors (smoking, hypertension, diabetes and history of a high- risk CVD condition)[2]. To gain insight into the potential effect that treating inflammation may have on the CVD risk score, it would be useful to know how the score is affected by the level of inflammation.
Objectives: Explore the quantitative contribution of inflammation to CVD risk score in individual RA patients.
Methods: To quantify the effect of inflammation on the CVD risk score across a range of MBDA scores, a commercial dataset of 177,486 RA patients with ≥2 MBDA tests between October 2010 and June 2019 was split 2:1 into training and validation datasets. Curves showing variation in the CVD risk score across the spectrum of all possible MBDA scores (1-100) were generated for canonical patient types differing in the number of conventional risk factors (0 to 4) and age (45, 55, 65, 75, 85 years). To generate these curves, the contributions of TNF-RI, MMP-3 and leptin to the CVD risk score were treated in aggregate (denoted the molecular score) and estimated using a linear regression model of the difference in molecular scores vs. the difference in MBDA scores. This model for the molecular score was fit in the training dataset, then in the full dataset, with dataset (training or validation) and the interaction between dataset and change in MBDA score included as additional predictor variables. The method was considered validated if the F-test for the interaction variable was not significant at the 0.05 level.
Results: The model for estimating the molecular score from the MBDA scores was validated and shown to fit the data well (Figure 1). The estimated molecular

score was applied to the CVD risk score algorithm to generate curves that show how CVD risk score varies with MBDA score for several distinct patient types. These curves demonstrate that the predicted 3-year CVD risk increases continuously and markedly with increasing level of inflammation, as represented by the MBDA score (Figure 2). Age and the number of conventional risk factors also affected the predicted CVD risk, with older patients (Figure 2a) and those with more conventional risk factors (Figure 2b) being at higher risk for a CVD event.

Conclusion: The level of CVD risk predicted by a new prognostic test for RA patients depends not only on conventional risk factors, which are relatively time invariant, but also varies greatly due to inflammation, which can potentially be reduced with RA treatment.

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Figure 1: Predicted versus observed molecular score in the validation dataset (N=59,162). The model derived to determine predicted molecular scores (denoted m) was: mref + β(MBDA – MBDAref), where MBDAref and mref are fixed reference values and β is the coefficient estimated in the training dataset. The dashed line represents predicted molecular score = observed molecular score.

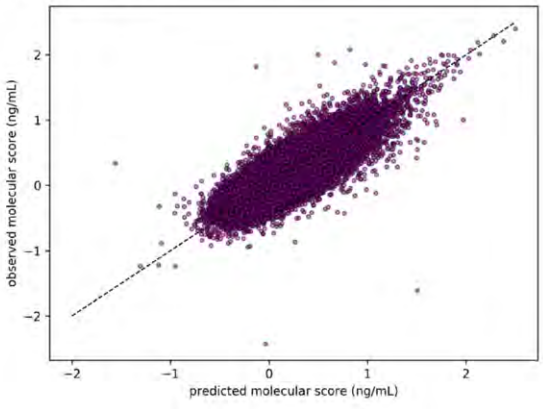
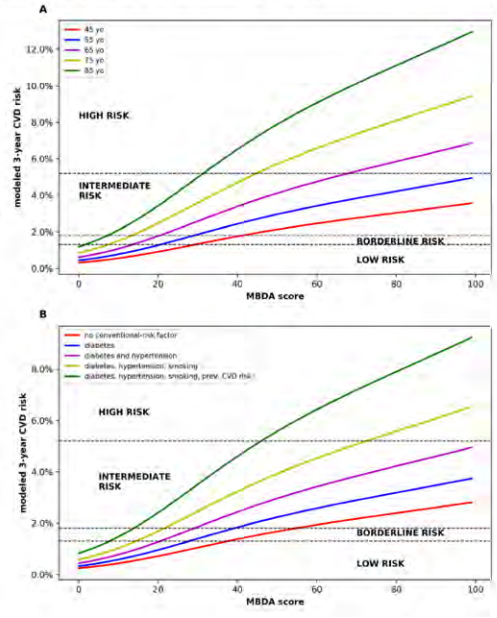


Figure 2: Relationship between inflammation and predicted CVD risk. A) Predicted 3-year CVD risk by MBDA score for hypothetical patients having diabetes, hypertension and the indicated ages. B) Predicted 3-year CVD risk by MBDA score for hypothetical 55-year old patients having 0 to 4 conventional risk factors, as indicated. Curves were derived using the CVD risk prediction algorithm across the range of all possible MBDA scores with molecular scores assigned by the model described above. For these CVD risk curves, MBDAref was fixed at 39 (the median MBDA score in the validation dataset), and mref was fixed at 0.07 (the median molecular score observed in patients with an MBDA score of 39).



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FRI0058

THE IMPORTANCE OF SPECKLE TRACKING ECHOCARDIOGRAPHY IN THE EVALUATION OF CARDIAC FUNCTIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is an inflammatory disease that includes chronic, progressive joint arthritis and also has multi-systemic involvement. It is known that the acceleration of many cardiovascular diseases causing mortality and morbidity, especially atherosclerosis and heart failure, is increased in RA patients.

Objectives: In this study, it was aimed to analyze the layer-specific (endocardial, transmural and epicardial) strain values obtained by speckle tracking echocardiography method in the determination of subclinical cardiac dysfunction in RA patients and to determine the correlation between anti cyclic citrullized peptide (Anti-CCP) titers, disease activity score (DAS-28), disease duration and strain values.

Methods: This study was performed with 63 RA patients and 31 healthy participants. The patients were grouped as <5 years, 5-10 years and >10 years according to their disease duration. DAS28-CRP was used to determine disease activation. The standard assessment included complete serum concentration of C-reactive protein, Anti-CCP, Romatoid faktör (RF), N-terminal pro b-type natriuretic peptide (NT-proBNP) and homocysteine. Endocardial, transmural and epicardial strain values were analyzed by M-mode, 2D, tissue doppler and speckle tracking echocardiography.

Results: When the groups were compared in terms of laboratory data, NT-proBNP value of RA patients was higher than the control group (p=0.044), homocysteine level was similar (p>0.05). When the groups were compared in terms of conventional echocardiographic parameters, ejection fraction of the control group was similar (p>0.05). E/A and E/E' ratios were found to be significantly different (p<0.001, p=0.015). When the groups were compared in GLS values obtained by speckle tracking echocardiography, endocardium, transmural and epicardium GLS values were lower in RA patients (p<0.05) (Table 1). As the disease duration increased, GLS values were found to be worse (p<0.05). There was a significant correlation between RA disease activity scores level and LV GLS value, increasing levels of disease activity was associated with worse LV GLS (r=0.583, p<0.01 and r=0.681, p<0.01 ve r=0.689, p<0.01 for endocardium, transmural and epicardium respectively. There was a significant correlation between anti-CCP, RF and LV GLS value, higher Anti-CCP and RF titers were associated with worse LV GLS (r=0.467, p<0.01 and r=0.509, p<0.01 and r=0.551, p<0.01) for endocardium, transmural and epicardium respectively.

Table 1. Comparison of layer-specific GLS values of groups

	<5	5-10	>10	Control	p
GLS endocardium Mean ± SD	-23,98±1,84	-23,29±1,59	-21,71±1,93	-24,95±0,73	ɣ: 0,000 β: 0,000 ρ: 0,001
GLS transmural Mean ± SD	-21,78±1,71	-21,20±1,66	-19,85±1,50	-22,98±1,17	ɣ: 0,001 δ: 0,020 †: 0,017 ρ: 0,001 β: 0,000
GLS epicardium Mean ± SD	-20,05±2,02	-19,23±1,77	-17,98±1,38	-20,83±0,70	δ: 0,023 β: 0,000 ɣ: 0,000 ρ: 0,001

SS: Standard Deviation, ϰ: 1-2, δ: 2-3, β: 3-4, ɣ: 1-3, †: 1-4, ρ: 2-4, GLS: Global longitudinal strain

Conclusion: The layer-specific global longitudinal strain values obtained by speckle tracking echocardiography were found to be decreased in RA patients. This study, which has been shown to decrease strain values before the reduction

of ejection fraction values obtained by conventional methods, may be a guide for the clinician in early detection of cardiac dysfunction in RA patients with high DAS-28 score, long disease duration, high Anti-CCP and high RF titers.

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FRI0059 SARCOPENIA IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Sarcopenia is defined as the decrease in strength, mass and function of muscles and may be related with aging, chronic inflammation or malnutrition. Proinflammatory cytokines may be associated with development of sarcopenia.

Objectives: The aim of this study was to evaluate sarcopenia in patients with Rheumatoid Arthritis (RA).

Methods: One hundred patients with RA (30 Male/70 Female) and 100 healthy controls (30 Male/70 Female) were included in this cross sectional study. According to The European Working Group on Sarcopenia in Older People (EWGSOP2) 2018, three parameters; muscle strength, muscle mass and physical performance, which are evaluated by hand grip strength, Body Impedance Analyzer (BIA) and 6 meters gait speed test, respectively, are used to diagnose sarcopenia. Patients with arthritis in dominant hand joints and ankle joints were excluded. Sarcopenia is defined as the decrease of strength and mass of muscles. On the other hand patients with low muscle strength but normal muscle mass are defined as probable sarcopenia.

Results: The mean age was 58.52±10.95 for patients and 56.62±10.08 for controls (p=0.203). Frequency of probable sarcopenia was 35 (35.0%) in RA and 9 (9.0%) in control group (p<0.001). Results of hand grip and 6 meters gait speed tests were lower in RA patients (p=0.002 and p<0.001 respectively). Frequency of probable sarcopenia was higher in females, older patients and patients with longer disease duration. Disease activity and Health Assessment Questionnaire scores were higher in patients with probable sarcopenia compared with patients with no sarcopenia (p<0.05) (Table 1). In multivariate regression analysis; age, gender and DAS28 ESR/CRP were associated with hand grip strength (p<0.001, R^2=0.62) (Table 2).

Table 1. Factors associated with sarcopenia in rheumatoid arthritis

Rheumatoid arthritis group	No sarcopenia (n=65)	Probable Sarcopenia (n=35)	p-value
Sex, n (%)			
Male	24 (36.9)	6 (17.1)	**0.04**[a]
Female	41 (63.1)	29 (82.9)	
Age*	55.00 (25.00–82.00)	63.00 (24.00–82.00)	**0.004**[b]
Disease duration (year)*	4.00 (1.00–37.00)	8.00 (1.00–41.00)	**0.037**[b]
DAS28 CRP*	2.13 (1.08–4.69)	2.55 (1.54–5.56)	**0.010**[b]
DAS28 ESR (mean±SD)	2.63±0.94	3.36±1.00	**<0.001**[c]
CDAI*	5 (0–25)	9 (0–29)	**0.012**[b]
SDAI*	5.09 (0.04–26.04)	9.8 (0.39–31.7)	**0.006**[b]
HAQ*	0.15 (0–1.05)	0.4 (0–19.5)	**<0.001**[b]

[a]Pearson Chi-Square, [b]Mann-Whitney U Test, [c]Independent Samples t-Test. *Variables given as median (minimum-maximum) DAS: Disease activity score ESR:Erythrocyte sedimentation rate, CRP:C-reactive protein, CDAI: Clinical Disease Activity Index, SDAI: Simplified Disease Activity Index, HAQ: Health Assessmnet Questionnaire

Table 2. Multivariate analysis for hand grip test in patients with rheumatoid arthritis

	Unstandardized Coefficients		95% CI		Standardized Coefficients	
	B	Std.Error	Lower	Upper	Beta	p-value
Constant	53.65	3.89	45.93	61.37	–	**<0.001**
Gender	–13.06	1.41	–15.86	–10.26	–0.60	**<0.001**
DAS28 CRP	–3.21	0.70	–4.61	–1.82	–0.29	**<0.001**
Age	–0.22	0.06	–0.33	–0.10	–0.23	**<0.001**

DAS: Disease activity score CRP:C-reactive protein

Conclusion: Loss of muscle strength in patients with RA may be seen frequently. Longer disease duration and higher disease activity should lead to development of sarcopenia due to chronic inflammation. Sarcopenia potentially effects patients' social lives and daily functions and conceive decrease quality of life. Physicians should be aware of development of sarcopenia during the course of the disease, and take into account the preservative and preventive methods against to sarcopenia including exercise and control of disease activity.

Acknowledgments: None to declare

Disclosure of Interests: None declared

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FRI0060 EVALUATION OF THE CARDIOVASCULAR RISK IN WOMEN WITH RHEUMATOID ARTHRITIS WITH DUPLEX STUDY OF THE CAROTID AND FEMORAL ARTERIES

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Background: The increasing of the cardiovascular disease (CVD) in patients with rheumatoid arthritis (RA) is well know, even with the absence of traditional coronary risk factors. The ultrasound – duplex scan (USD) is a non invasive technique able to early detect atherosclerotic changes in the blood vessel, that gives the possibly to retard the development of symptomatic CVD.

Objectives: To evaluate the cardiovascular (CVS) risk in patients with RA classificated as low risk by Framingham Score (FS), before and after the EULAR 1.5 multiplication factor and stratify with the carotid and femoral USD (intima-media thickness - IMT and atherosclerotic plaques - AP)

Methods: Thirty-five female patients with RA and low CVS risk by FS and 35 healthy women with low CVS risk by FS (control group) were enrolled for the study. All of them submitted to carotid and femoral USD

Results: The groups were homogenous by age and CVS comorbidities -Table 1. Mean age in the diagnosis was 44.57 years, mean disease duration was 12.11 years and mean disease activity was Disease Activity Score 28: 1,91 and Clinical Disease Activity Score: 6.176. In the RA patients group 46% showed changes in the carotid and/or femoral USD compared with 14% of the control group (p = 0,004) –Graphic 1. The USD with abnormalities in RA group 31% of the carotid USD and 81% of the femoral USD (p= 0,005) showed IMT and/or AP. After EULAR 1.5 multiplication factor, 66% remained low CVS risk. Where 35% of the RA patients showed changes in the carotid and/or femoral USD compared with 14% of the control group (p=0,07)

Conclusion: The USD is able to early detect the CVD, special attention should be given to the femoral arteries, that are frequently affected. The Eular criteria is also effective and should be used in the clinical practice

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	AR	Control	Value-P
Age - Mean	58.54	55.14	0.064
Systemic Arterial Hypertension	31.42	20.00	0.274
Diabetes Mellitus (DM)	5.71	11.42	0.238
Dyslipidemia (DLP)	25.71	20.00	0.569
Total Cholesterol	196.11	183.54	0.134
Low Density Lipoprotein (LDL)	115.05	108.08	0.348
High-Density Lipoprotein Cholesterol (HDL)	57.94	52.57	0.109
Smoking	5.71	2.08	0.380

Table 1. Group characteris-

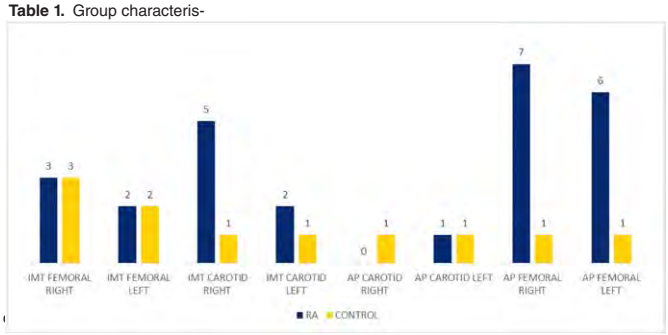


Figure 1. USD abnormalities

IMT - intima-media thickness; AP atherosclerotic plaques
Disclosure of Interests: None declared
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FRI0061

THE ADVERSE OBSTETRIC OUTCOMES WHEN RHEUMATOID ARTHRITIS IS CONTROLLED DURING PREGNANCY: IS THE DISEASE ITSELF A PROBLEM? DATA FROM A CASE-CONTROL COHORT OF 190 PREGNANCIES AT A MULTI-NATIONALITY SPECIALIZED CENTER IN QATAR

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Background: Rheumatoid arthritis is implicated in causing adverse pregnancy outcomes including high rates of prematurity and low birth weight. But little is known about the impact of the disease when it's controlled as most of the information is extracted from retrospective data.
Objectives: To examine the adverse obstetric outcomes after controlling disease during pregnancy. We also took into account many confounders that might affect the outcome.
Methods: This is an ongoing Case-Control Prospective Cohort. It is implemented in a tertiary center where cases are recruited from a single specialized pregnancy and rheumatic disease clinic to ensure standardized management. These cases were fulfilling the ACR 2010 classification criteria for rheumatoid arthritis. Disease activity was measured using CDAI once before pregnancy and once in each trimester. We excluded subjects with chronic morbidities or twin pregnancy. Data were collected in pre-specified data sheets. Routine blood tests in addition to C-reactive protein were obtained. Cases were recruited at different disease activity stages, but treatment was escalated to reach remission as possible by the third trimester. Data were analyzed using SPSS software for descriptive and comparative analyses.
Results: Since 2017 we have recruited 215 subjects. A total of 190 completed pregnancies were analyzed in this report (114 controls and 76 cases). Five subjects were excluded as their disease was not controlled by 27 weeks of gestation. Baseline characteristics of age, baseline BMI and anemia were similar. Exposure to passive smoking was significantly higher in the control group. There was no statistical difference in the incidence of gestational diabetes, pre-eclampsia and infections. Rates of abortions and cesarean sections were significantly higher in the cases group. The incidence of PROM & low birth weight was not statistically different. Three cases of IUFD were reported among controls versus none in the cases (Table 1). Prematurity rate was numerically higher in the control group but did not reach a statistical difference. Congenital anomalies and NICU admission rates were comparable between the groups. But the incidence of neonatal morbidities was significantly higher in the control group (p. value 0.006), but the majority of morbidities were due to jaundice that resolved with phototherapy. we have evaluated the incidence of group B streptococcal Agalactae as a possible contributor to morbidities but it was similar between the groups. All cases were on DMARDs during pregnancy. Hydroxychloroquine was the most commonly used (55%) followed by sulfasalazine (40%). Steroid was used for variable duration in pregnancy in 23 cases. In most of them, it was tapered and stopped by the end of pregnancy. Biologics were used in 15 cases with few adverse outcomes including: abortion (1 case), PROM (1), maternal UTI (1), repeated URT infection (1) and neonatal bronchiolitis (1).

Table 1. Birth Outcomes

Birth Outcome	Cases (n)	Controls (n)	*P.value*
Abortion	9	1	0.001
IUFD	0	3	0.18
PROM	1	8	0.09
Cesarean	20	17	0.02
LBW	6	8	0.68
Premature	8	25	0.74

Conclusion: From this ongoing cohort we conclude that controlled RA during pregnancy carries low risk of adverse obstetric outcomes in spite the regular use of DMARDs. Although these results are reassuring, further regression models are required after recruiting more subjects.
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Disclosure of Interests: None declared
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FRI0062

THE USE OF A COMORBIDITY INDEX FOR PREDICTING CLINICAL RESPONSE IN RHEUMATOID ARTHRITIS PATIENTS RECEIVING THEIR FIRST BIOLOGICAL AGENT

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Background: Several studies in Rheumatoid arthritis (RA) have suggested that a greater number of comorbidities is associated with worse functional status and disease activity measures. However, it is useful to use a composite comorbidity index, such as Rheumatic Disease Comorbidity Index (RDCI) that is validated for the use in patients with rheumatic diseases, to better understand the overall role of comorbidities in treatment outcomes.
Objectives: To evaluate the impact of comorbidities on 12-month clinical response in a cohort of patients with RA treated with a first-line biologic disease-modifying antirheumatic drug (bDMARD), by using the RDCI.
Methods: Observational retrospective study was performed including consecutive patients with the diagnosis of RA followed at our Rheumatology Department. The prevalence of comorbidities was computed, and patients were stratified according to RDCI for evaluating its role in clinical response disease activity at baseline and follow up (6 and 12 months). Correlations between variables were studied using Spearman correlation analysis, comparison between groups was performed using Kruskal-Wallis and Chi-square. A multivariate logistic regression model was developed to examine the role of RDCI along with other baseline factors as potential predictor of achieving remission, low disease activity (LDA), and EULAR good/moderate response. Statistical analyses were performed using SPSS statistical software, version 23.0.
Results: A total of 251 patients were included: 83.7% (n=210) females, mean age of 58 (± 11.10) years old, with a median disease duration of 16.11 years [10.79 - 23.04]. The majority exhibited a very high or high disease activity at

baseline (median DAS28 3V 5.48 [4.70 – 6.19]) and 90% (n=226) of them were concomitantly using corticosteroids and/or other disease-modifying anti-rheumatic drugs (129 with methotrexate (MTX), 96 with leflunomide and 35 with sulfasalazine). The most frequently reported comorbidities were cardiovascular disorders (37.5%), osteoporosis (7.6%) and depression (6.8%). The median RDCI score was 1.0 [0.0 – 2.0] and the majority of patients (63.6%) carried at least one comorbidity. When comparing baseline demographic and clinical characteristics of the 4 subgroups, stratified according to RDCI score (RDCI=0, 1, 2, or ≥3), we found statistically significant differences in age, age at diagnosis, sex and the prescribed anti-TNF agent (p<0.05). There was a progressive increase in the mean age as the RDCI score increased between the subgroups.

RDCI strongly correlates with the number of comorbidities (NC) (r=0.764, p<0.01). NC was weakly correlated with patient and physician global assessment of disease activity (pVAS and phVAS) (r=0.183, p<0.01 and r=0.196, p=0.019, respectively), DAS28 3V (r=0.192, p=0.046) and HAQ-DI (r=0.301, p<0.01) at 6 months. Moreover, RDCI poorly correlated with CRP (r=0.192, p=0.01), pVAS (r=0.183, p=0.02) and HAQ-DI (r=0.202, p<0.01). Weaker correlations were also found at 12 months: NC with pVAS (r= 0.196, p=0.02), DAS28 3V (r=0.216, p=0.01) and HAQ-DI (r=0.187, p=0.04); RDCI with phVAS (r= 0.196, p=0.04).

The 12-month DAS28 remission rate was 37.8% (n=95); 6.7% (n=17) achieved EULAR good response and 54.4% (n=137) a moderate EULAR response. RDCI was not an independent predictor of DAS remission (OR 0.794, 95% CI 0.561-1.125, p = 0.194) nor it was of EULAR good/moderate response (OR 0,720, 95% CI 0.430- 1.206, p= 0.212).

Conclusion: Although our data point to a weak association between morbidities, assessed by the RDCI, and response to a first bDMARD, it is important to consider this simple and useful tool in future prospective and broader studies, since information bias regarding comorbidities may have been responsible for our results.

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FRI0063 LEVEL OF N-TERMINAL FRAGMENT OF BRAIN NATRIURETIC PEPTIDE PROGENITOR AND ATHEROSCLEROTIC DAMAGE OF BRACHIOCEPHALIC ARTERIES IN PATIENTS WITH EARLY AND LONG-STANDING ACTIVE RHEUMATOID ARTHRITIS

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Background: The high prognostic significance of the N-terminal fragment of the B-type natriuretic peptide (NT-proBNP) concentration in the development of cardiovascular diseases (CVD) was identified for rheumatoid arthritis (RA) patients (pts) and general population.

Objectives: To investigate the significance of NT-proBNP levels in pts with early untreated and long-standing RA with high disease activity; to identify potential relationship of NT-pro-BNP levels with atherosclerotic lesion of the brachiocephalic arteries (BCA), traditional risk factors and inflammatory markers.

Methods: A total of 227 RA pts (76%females, 24%males, 55 [46;61]years old, moderate to high activity (DAS28-5,3[4,6;6,3], SDAI–27(22;35), positive for ACCP (73%)/RF (87%),) were enrolled in the study: 136 pts with early RA (disease duration ≤12 months) and 91 pts with long-standing RA (>12 months). All early RA pts were not treated with glucocorticoids and disease-modifying anti-rheumatic drugs (DMARDs). Long-standing RA pts already developed the lack of efficacy/resistance and/or intolerance of DMARDs. Lack of efficacy of 3 or more DMARDs was established in 46% of pts, intolerance to previous DMARDs therapy - in 54% pts. 73% were receiving methotrexate, 21% - leflunomide, 7% - sulfasalazine, 46% glucocorticoids. Pts with early and long-standing RA were comparable in terms of age, sex, body mass index and RA activity rates (DAS28, SDAI, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels). High incidence of traditional risk factors was found in early and long-standing RA pts: the incidence rate of arterial hypertension (58%vs68%), overweight (58%vs61%), smoking (27%vs17%), DM type 2 (4%vs7%) were not significantly different. Pts with congestive heart failure were not include in the study. The control group consisted of 20 healthy donors, matched to pts by age and sex. Serum levels of NT-proBNP (pg/mL) were measured using electrochemiluminescence test Elecsys proBNP II (Roche Diagnostics, Switzerland). NT-proBNP levels > 125,0 pg/mL were considered as elevated. The BCA intima-media thickness (IMT) was assessed by duplex ultrasound scanning. Atherosclerotic lesion of BCA was documented in the presence of plaque (IMT≥1,2mm).

Results: The NT-proBNP levels were significantly higher in RA pts than in the control group (median 92,1 (48,2-164,7) pg/mL vs 55,3 (36,6-67,3) pg/mL, p<0.05). Pts with early RA had higher NT-proBNP levels (118,9 (60,2-201,3) pg/ml) than pts with long-standing RA (73,4 (43,0-114,3) pg/ml, p<0,001). Elevated NT-proBNP concentrations were found in 71 (52%) early RA pts vs 21 (23%) pts with long- standing RA (p<0,01). Atherosclerotic lesion of the BCA was detected in 73 (54%) pts with early RA and in 37 (41%) pts with long- standing RA (p>0,05). The NT-proBNP levels correlated with age (r=0,51, p<0,001), CRP (0,23, p=0,001) and IMT of BCA (r=0,46, p=0,03) in RA pts. Aforementioned correlations were significantly remained for both groups of RA pts. Association between IMT of BCA and CRP concentrations was not found.

Conclusion: NT-pro-BNP levels are higher in pts with active RA than in control subjects. Early untreated RA pts had a higher NT-proBNP levels than pts with disease duration >12 months and resistance or intolerance of DMARDs. The increased concentration NT-pro-BNP (>125pg/ml) were found in half of pts with early untreated RA and every fourth pts with long-standing active RA. NT-proBNP concentration correlated with CRP level in pts with active RA. Correlation between NT-pro-BNP concentrations and IMT of BCA may be indicative of possible impact of this biomarker on atherosclerotic damage of BCA in pts with early and long-standing active RA.

Disclosure of Interests: None declared

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FRI0064 SAFETY OF LOW DOSE METHOTREXATE (MTX) AND TUBERCULOSIS (TB)

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Background: Increased awareness of the importance of MTX in rheumatic disease is leading to more MTX use in patients from TB-endemic areas. Current management guidelines for rheumatic disease address TB in the context of biologics but not MTX use.

Objectives: To systematically review the published literature on TB rates with MTX ≤30 mg per week.

Methods: We searched CINAHL, Embase, Global, MEDLINE and World of Science databases (Jan 1990 to May 2018) for terms including 'methotrexate' and 'tuberculosis'. We also searched citations from review articles. Titles, abstracts or full manuscripts of the 4707 reports identified were screened independently by 2 reviewers to identify studies reporting TB in patients taking MTX. Study quality was assessed using the McGill Mixed Methods Appraisal Tool (MMAT). Data was extracted on TB incidence (new TB diagnosis vs reactivation of latent TB), and outcomes (pulmonary, dissemination, death) and safety of isoniazid, INH. Descriptive summaries are presented on studies providing outcomes in patients taking MTX ≤30 mg per week.

Results: After removing duplicates and studies not meeting criteria or providing sufficient information, 31 studies were included (8 cohort, 7 case-control, 1 clinical trial, 15 case reports/case series). Only 27% of articles reported data from low to moderate human development index countries. Studies were of moderate quality. Seven case control studies were heterogeneous but most demonstrated a modest increased risk of TB with MTX (Table). Five cohort studies reported TB incidence rates in rheumatic disease (treated with MTX +/- biologics) ranging from 102-367.9/100,000 patient-years. These rates were generally higher than comparator general population rates. Two cohort studies of MTX in RA (without biologic) reported cumulative TB incidence in Maldova (12 TB cases in 44 RA patients, 27%) and in China (9/114, 7.9%). Other cohort studies generated rates of overt infection (143/100,000 patient years in Spain, higher if co-prescribed with corticosteroids and other immunosuppressants in South Africa), and latent TB rates detection (16/922 RA screened, 1.7%, in Canada). When reported, rates of extra-pulmonary TB were higher than comparator general population rates. One clinical trial (China), 2 cohorts (Japan, USA) and 2 case-series (Belgium, USA) evaluated safety of INH and MTX. Isoniazid-related hepatotoxicity and neutropenia were generally more common when taken with MTX, but were usually reversible.

Conclusion: Despite a paucity of high-quality data, this review confirms that TB screening and clinical surveillance are needed in patients from TB-endemic areas who are prescribed MTX, particularly with co-administration of corticosteroids or other immunosuppressants. Isoniazid, if monitored, appears safe and prevents TB reactivation.

References:

Table. Case control studies

Region (Year)	Diagnosis	TB with MTX	TB without MTX	Odds Ratio
Mexico (1999)	Mixed (4 RA)	1/6	5/75	2.76
Japan (2004)	RA	3/47	17/154	0.56
Canada (2009)	RA	29/483	21/1046	3.12
Brazil (2010)	Lupus	2/3	1/57	112
Taiwan (2012)	Psoriasis	33/144	464/2341	1.2
Taiwan (2015)	JIA	4/357	4/1026	2.90
South Africa (2017)	RA	0/134	0/18	NA

JIA=juvenile idiopathic arthritis

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FRI0065 CLINICAL FEATURES OF METHOTREXATE ASSOCIATED LYMPHOPROLIFERATIVE DISORDER IN RHEUMATOID ARTHRITIS PATIENTS AND INFLUENCE OF CD8 POSITIVE LYMPHOCYTE INFILTRATION

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Background: Lymphoproliferative disorders (LPD) that develop in rheumatoid arthritis (RA) patients treated with MTX (MTX-LPD) is one of the important complications for RA patients. We have previously epidemiologically demonstrated an association between MTX and the development of LPD in RA patients [1)]. MTX-LPD has varied pathologies including various clinical symptom and histological finding. Therefore, we need more information about MTX-LPD. In addition, it is one of the characteristics for MTX-LPD that spontaneous regression (SR) after MTX discontinuation. However, the mechanism of SR is not clarified.

Objectives: We collect the information such as clinical symptom and histological finding of MTX-LPD with RA patients, and clarify the clinical features of MTX-LPD. In addition, we investigated the difference between SR cases and cases that treated with chemotherapy after MTX discontinuation (CTx cases).

Methods: We enrolled 90 MTX-LPD patients from Kagawa Prefecture, Japan between June 2005 and December 2019. Patients were diagnosed according to American College of Rheumatology (ACR) 1987 classification criteria or ACR/European League Against Rheumatism (EULAR) 2010 classification criteria, and treated with disease modifying antirheumatic drugs (DMARDs) including MTX. We collected as follow information; age, gender, duration of RA, laboratory data (lymphocyte counts and sIL-2R) and treatment of MTX-LPD. In addition, we divided 16 MTX-LPD cases diagnosed histological into two groups (SR:CTx group; n=10:6), and analyzed the histological findings (CD4, CD8, CD163 and CD47) using the staining in immunohistochemistry (IHC) between the two groups. Each positive cell analyzed using virtual viewer soft ImageScope.

Results: Characteristics of 90 MTX-LPD patients are as follow; mean age 66.5±11.2 years,63 female, duration of RA 18.5±19.4 years. 65 patients (72.2%) were spontaneously improved by discontinuing MTX. 58 patients (64.4%) were proven MTX-LPD histologically. In these patients, diffuse large B-cell lymphoma (DLBCL) was the most frequent histological type of MTX-LPD (56.9%). Infiltration of CD8 positive lymphocyte in the lesion was significant less in the SR cases than in the CTx cases (Figure 1). However, CD4, CD163 and CD47 positive cells had no significant difference between two groups.

Conclusion: We revealed clinical features of MTX-LPD with RA patients. In addition, CD8 positive lymphocytes are involved in tumor immunity. In this study, we suggested that the extent of CD8 positive lymphocyte infiltration may predict SR of MTX-LPD. Further study is necessary on revealing the mechanism of SR in MTX-LPD.

References:

[1] Kameda T. et al. Arthritis Care Res (Hoboken). 2014 Sep;66(9):1302-9.

Disclosure of Interests: None declared

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Figure 1. CD8 positive lymphocytes in the specimen of lesion using the staining in immunohistochemistry (IHC) between SR and CTxgroup.

FRI0066 SUBCLINICAL CORONARY CALCIFICATION ASSOCIATED WITH LONG-TERM CARDIOVASCULAR OUTCOMES IN RHEUMATOID ARTHRITIS

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Background: Large, multicenter studies established the strong prognostic value of coronary artery calcium (CAC) scoring in asymptomatic individuals. Increasing CAC score is an independent predictor of worsening cardiovascular disease event risk in general patients. The prognostic significance of higher CAC score strata in the long-term cardiovascular risk in rheumatoid arthritis (RA) is unknown.

Objectives: To evaluate the long-term cardiovascular event risk across CAC strata in a prospective, single center cohort of established RA patients without symptoms or prior diagnosis of cardiovascular disease.

Methods: One hundred-fifty patients underwent computed tomography angiography for coronary atherosclerosis evaluation. CAC score was measured according to Agatston. CVD events were prospectively recorded, including cardiac death, myocardial infarction, unstable angina, revascularization, stroke, claudication, and heart failure hospitalization over 6.0±2.4 years of follow-up. Unadjusted, robust Cox proportional hazards regression models evaluated CVD event risk across higher CAC strata (CAC=1-99, CAC=100-399 and CAC≥400) compared to CAC=0. Additional multivariable robust Cox regression models with time-varying covariates evaluated the impact of log transformed CAC or different CAC thresholds (CAC>0 vs. CAC=0, CAC≥100 vs. CAC<100 and CAC≥400 vs. CAC<400)

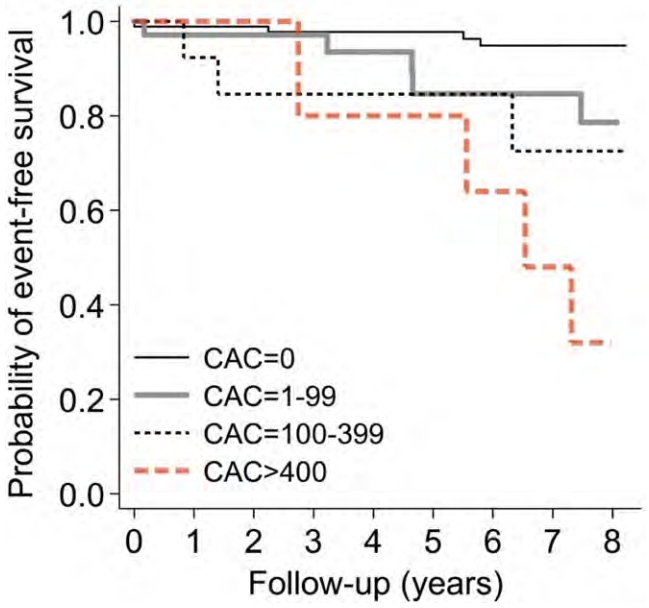


Figure 1. Increasing CAC scores associated with higher cardiovascular event risk in RA

on future CVD events. Models were controlled for Framingham-D'Agostino clinical risk score, time-varying current bDMARD use and time-varying CRP.
Results: Sixteen patients incurred 19 events, for a total of 2.1 (95% CI 1.3-3.3) events/100 patient-years. Increasing HR for cardiovascular events was observed for ascending CAC strata; 3.87 (1.03-14.48), 6.31 (1.38-28.91) and 16.98 (4.50-64.10) for CAC=1-99, CAC=100-399 and CAC≥400 respectively compared to CAC=0 (figure 1). In fully adjusted models, CAC score associated with future event risk independently of Framingham D'Agostino score, time-varying bDMARD use and time-varying CRP (HR=1.31 [95%CI 1.04-1.66]). CAC thresholds ≥100 (vs. <100) and CAC≥400 (vs. <400) in fully adjusted models similarly constituted independent predictors of long-term cardiovascular events (Figure 2).

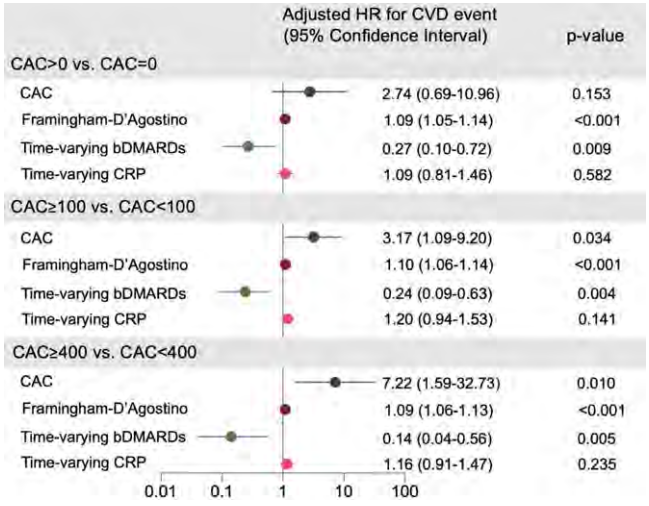


Figure 2. Impact of different CAC thresholds on cardiovascular event risk in RA

Conclusion: Increasing CAC scores are strong, independent predictors of long-term cardiovascular events in RA patients without symptoms or prior diagnosis of cardiovascular disease.
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FRI0067 ALL-CAUSE AND CAUSE-SPECIFIC MORTALITY OF PATIENTS WITH RHEUMATOID ARTHRITIS IN KOREA: A NATION-WIDE POPULATION-BASED STUDY

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease associated with excess mortality.
Objectives: To compare all-cause and cause-specific mortality between RA patients versus general population, using a nationally representative cohort from Korea National Health Insurance Service database (KNHIS).
Methods: Patients with RA aged ≥ 40 years were identified from 2010-2016 KNHIS database and their annual cohorts were constructed per each calendar year. RA patients of each cohort were required to have prevalent RA on January 1st of the given calendar year. The KNHIS were linked with Korea national mortality data to obtain cause of death information and to estimate expected deaths of RA patients in reference to mortality data of the general population in Korea. Standardized mortality ratio (SMR) with a 95% confidence interval (CI) was calculated to compare mortality of RA patients and general population.
Results: A total of 6,404 deaths occurred among 79,440 RA patients during 2011-2016 period, showing all-cause SMR (95% CI) of 1.45 (1.42-1.49) compared to general population. The SMR was 1.72 (1.59-1.85) for biologics users and 1.43 (1.39-1.46) for non-users, versus general population. The annual SMR of RA patients showed a growing trend of mortality over time particularly among biologics users (Table 1). The SMRs for common causes of death among RA patients showed approximately tripled risk of dying due to pulmonary and infectious causes compared to general population (Table 2). There was approximately 20% increased risk of cardiovascular deaths but 8% decreased risk of cancer-related deaths among RA patients compared to general population (Table 2).

Table 1. Annual all-cause SMR of RA patients compared to 2010 general population

Calendar year[1]	RA patients	Biologics users	Biologics non-users
2011	1.00 (0.92–1.07)	1.13 (0.87–1.39)	0.98 (0.90–1.06)
2012	1.13 (1.06–1.21)	0.98 (0.75–1.22)	1.15 (1.07–1.23)
2013	1.22 (1.14–1.30)	1.29 (1.04–1.54)	1.21 (1.13–1.29)
2014	1.30 (1.23–1.38)	1.53 (1.26–1.79)	1.28 (1.20–1.36)
2015	1.45 (1.38–1.53)	1.81 (1.53–2.09)	1.41 (1.33–1.50)
2016	1.45 (1.37–1.52)	1.94 (1.66–2.22)	1.39 (1.31–1.47)

CI, confidence interval; RA, rheumatoid arthritis; SMR, standardized mortality ratio
[1]2010 data were used to identify RA diagnosis dates but were not included for SMR estimation since diagnosis dates of RA were unclear for those who had RA in 2010.

Table 2. Cause-specific SMR comparing RA patients versus general population

Cause of death	RA patients	Biologics users	Biologics non-users
Infection	3.12 (2.93–3.13)	4.12 (3.36–4.88)	3.03 (2.83–3.23)
Cancer	0.92 (0.87–0.97)	0.98 (0.81–1.14)	0.91 (0.85–0.96)
Respiratory[1]	3.14 (2.97–3.32)	4.64 (3.89–5.38)	3.01 (2.83–3.19)
Cardiovascular[2]	1.18 (1.12–1.25)	1.26 (1.03–1.50)	1.18 (1.11–1.25)

CI, confidence interval; RA, rheumatoid arthritis; SMR, standardized mortality ratio
[1]Includes pulmonary infections and chronic lung diseases (J00-J98, U04); [2]Includes atherosclerotic and non-atherosclerotic deaths (I00-I99).

Conclusion: The all-cause mortality of RA patients during 2011-2016 was overall 45% greater than that of general Korean population, which increased annually over the study period. The increased mortality was more prominent among biologics users than non-users. The risk of infectious and respiratory deaths were tripled among RA patients compared to general population.
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[1] Sokka T, et al. Mortality in rheumatoid arthritis: 2008 update. Clin Exp Rheumatol. 2008;26(5 Suppl 51):S35-61.
Acknowledgments: None
Disclosure of Interests: None declared
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FRI0068 LIPID PROFILE AND BONE MINERAL DENSITY IN PATIENTS WITH RHEUMATOID ARTHRITIS: IS THERE AN ADDED RISK OF OSTEOPOROSIS?

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Background: Bone is a target in many inflammatory rheumatic diseases such as rheumatoid arthritis (RA). It has been supposed that an atherogenic lipid profile could be associated with lower bone mineral density (BMD) and vertebral fractures (VF).
Objectives: We aimed to evaluate the relationship between the lipid profile, BMD and the presence of VF in RA patients.
Methods: A cross sectional study was conducted in a population of 169 established RA. In each subject we evaluated the body mass index (BMI), tobacco use, alcohol consumption, presence of diabetes and high blood pression, lipid profile (total cholesterol (TC), High density lipoprotein cholesterol (HDLc), low density lipoprotein cholesterol (LDLc), triglycerides (TG), and VF. RA characteristics were also assessed (disease duration, disease activity score (DAS), auto antibodies, corticosteroid intake, and secondary sjogren's syndrome). BMD was measured by dual energy X-ray absorptiometry (DXA) in lumbar spine and femoral neck. Logistic and linear regression were performed with SPSS 20, both BMD and VF were assessed as dependent variables.
Results: The mean age was 55.5±11.9 years, with a female predominance (152 women). The average BMI was 26.79 ± 5.36. We had 24.3 % of hypertensive patients and 16.6 % of diabetics. The average lipid concentrations were 4.39±1 mmol/L for TC, 1.293±0.36 mmol/L for HDLc, 2.74±0.80 mmol/L for LDLc and 1.25±0.62 mmol/L for TG. At the linear regression there was no correlation between plasma lipid concentrations and BMD, whether at the lumbar spine or the femoral neck. However we found a significant correlation between VF and high TC concentrations (p=0.043, OR: 2.864, 95% IC [1.036-7.922]). At the multivariate regression, high TC levels were still associated with VF, adjusted in BMI, age and the duration of corticosteroid use (p=0.006, OR: 6.07, 95%

CI[1.69- 21.77]). The same finding was observed between high concentrations of HDLc and the prevalence of VF adjusted in the same variables (p=0.006, OR: 197.01, 95% CI [4.64-8363.51]).
Conclusion: Although there was no relation between lipid plasma levels and BMD in our population. There was a significant association between high concentrations of TC, HDLc and the prevalence of VF.
Disclosure of Interests: None declared
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FRI0069 EFFECTS OF ADALIMUMAB ADDED TO TREAT-TO-TARGET STRATEGY WITH METHOTREXATE AND INTRA-ARTICULAR TRIAMCINOLONE ON LIPIDS IN EARLY- AND TREATMENT NAÏVE RHEUMATOID PATIENTS: SECONDARY ANALYSES FROM THE MULTICENTER DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED OPERA TRIAL

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Background: Systemic inflammation in rheumatoid arthritis (RA) is associated with reduced serum lipid levels (LL) and treatment with disease modifying antirheumatic drugs has been associated with increased serum LL [1]. It is unclear whether the changes in serum LL reported in association with adalimumab (ADA) treatment are due to suppressed inflammation or the ADA treatment *per se*.
Objectives: The primary objective was to compare the effect of ADA + methotrexate (MTX) to placebo (PBO) + MTX on changes in low density lipoprotein cholesterol (LDL-C) from baseline to month 12 in patients with early- and treatment naïve RA. Secondary objectives were to compare the treatment groups on changes in total cholesterol (TC), high density lipoprotein cholesterol (HDL-C), triglycerides, very low density lipoprotein cholesterol (VLDL-C) and non-HDL-C (=TC – HDL-C).
Methods: We present secondary analyses from the OPERA trial, which was an investigator-initiated, multicenter double-blind, placebo-controlled, treat-to-target trial of 180 early and treatment naïve RA patients, who were randomized (1:1) to oral MTX 20 mg once a week in combination with either PBO or ADA 40 mg SC EOW [2]. Any swollen joint was injected with triamcinolone hexacetonide. Lipid profiles of each patient were assessed at baseline and 12 months. All randomized patients with available LDL-C at baseline were included in Intention To Treat (ITT) analysis. Sensitivity analyses were performed on the Per Protocol (PP) and the ITT population with baseline observations carried forward (BOCF). All analyses were based on repeated measurements using mixed linear models.
Results: In total, 174 patients (97% of the original OPERA trial population) were included in ITT analysis (ADA n=86; PBO n=88) and 156 patients (ADA n=78; PBO n=78) completed the study with LDL-C measurements at both baseline and 12 months (PP). At baseline mean LDL-C was 2.9 mmol/L (SD 0.9) with 63 (36.2%) patients having an LDL-C above 3.0 mmol/L. There was no significant difference in LDL-C change between ADA+MTX and PBO+MTX groups after 12 months. A nearly statistically significant between-group difference in TC change was found. Other changes in LL were comparable across the two groups. Results in ITT, PP and ITT with BOCF populations were similar.

Table. Change in primary and secondary outcomes in the ITT analysis

	Adalimumab (n=86)		Placebo (n=88)		Difference between means	(95% CI)	*P* value
	Mean	SE	Mean	SE			
Δ LDL-C*, mmol/L	0.26	0.08	0.07	0.08	0.18	(-0.05; 0.42)	0.12
Δ TC, mmol/L	0.49	0.10	0.22	0.10	0.27	(-0.002; 0.54)	0.052
Δ HDL-C, mmol/L	0.27	0.04	0.23	0.04	0.05	(-0.06; 0.15)	0.38
Δ TG, mmol/L	-0.07	0.07	-0.18	0.07	0.11	(-0.08; 0.29)	0.25
Δ VLDL-C, mmol/L	-0.03	0.03	-0.07	0.03	0.03	(-0.05; 0.12)	0.43
Δ non-HDL-C, mmol/L	0.22	0.09	0.00	0.09	0.22	(-0.02; 0.46)	0.07
Δ LDL-C, Sensitivity Analyses							
Per Protocol	0.27	0.08	0.08	0.08	0.19	(-0.04; 0.42)	0.11
BOCF	0.26	0.08	0.08	0.08	0.18	(-0.03; 0.40)	0.10

Δ = 12 months - baseline. *Primary outcome. ITT: Intention To Treat. BOCF: Baseline Observation Carried Forward. LDL-C: low-density lipoprotein cholesterol. TC: total cholesterol. HDL-C: high-density lipoprotein cholesterol. TG: triglycerides. VLDL-C: very-low-density lipoprotein cholesterol. non-HDL-C = TC – HDL-C.

References:
[1] England BR *et al., Bmj* 2018;**361**:k1036
[2] Hørslev-Petersen K *et al.*, *Ann Rheum Dis* 2014;**73**:654–61
Disclosure of Interests: Dzenan Masic: None declared, Kristian Stengaard-Pedersen: None declared, Brian Bridal Løgstrup: None declared, Kim Hørslev-Petersen Grant/research support from: Pfizer (Travel expences), Merete L. Hetland Grant/research support from: BMS, MSD, AbbVie, Roche, Novartis, Biogen and Pfizer, Consultant of: Eli Lilly, Speakers bureau: Orion Pharma, Biogen, Pfizer, CellTrion, Merck and Samsung Bioepis, Peter Junker: None declared, Mikkel Østergaard Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Merck, and Novartis, Consultant of: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo Nordisk, Orion, Pfizer, Regeneron, Roche, Sandoz, Sanofi, and UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo Nordisk, Orion, Pfizer, Regeneron, Roche, Sandoz, Sanofi, and UCB, Christian Ammitzbøl: None declared, Sören Möller: None declared, Robin Christensen: None declared, Torkell Ellingsen: None declared
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FRI0070 PREGNANCY AND OFFSPRING OUTCOME IN RA FEMALE PATIENTS- A BOW BETWEEN CENTURIES

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Background: Clinical and preclinical rheumatoid arthritis (RA) may negatively impact several pregnancy and offspring outcome parameters [1,2].
Objectives: Assessing pregnancy and offspring outcome in RA patients and controls.
Methods: RA pregnant patients (G1) were prospectively recruited. Demographic data, disease activity scores, immunology and obstetric/offspring outcome parameters were recorded. The same parameters were retrospectively collected (interview) in RA patients who delivered children before RA onset (G2) and in healthy subjects (C). Ethical committee approval for the study was obtained and all participants signed informed consents.
Results: Table 1 presents demographic and disease related data. Table 2 shows the outcome parameters in the 3 groups. G1 delivered babies between the years 2008-2019. CsDMARDs were stopped by the majority of patients in the 1st trimester of pregnancy; 2 patients continued low dose corticosteroids throughout pregnancy (Fig 1). G2 and C delivered the babies between the years 1963 and 2000.

Table 1.

Parameter	G1	G2	C
Subjects^	22	27	36
Disease duration (y±SD)	5.92±6.14	-	-
Disease activity*			
T1-R/LDA/HDA^	9/15/5	-	-
T2- R/LDA/HDA^	15/6/8		
T3- R/LDA/HDA^	18/6/5		
RF + (%)	86.36	92.59	-
ACPA + (%)	36.36	62.96	-
Contraception^	0	3	5
Fertility treatment^	1	1	1

^- number, y- years, SD- standard deviation, R-remission, LDA-low disease activity, HDA-high disease activity, * DAS 28 3 variables, T-trimester

Overall, RA pregnant patients were older at conception, had a lower number of pregnancies/deliveries and a higher rate of spontaneous abortions and 'C' sections compared to G2 and C. Time to pregnancy (TTP) was increased in G1 when compared to G2 and C. Both G1 and G2 newborns were smaller for their gestational age versus C, the majority of them still being in the normal range. All these aforementioned parameters showed statistical significance. Number of premature deliveries and pregnancy/offspring pathology events showed a low frequency and no difference was identified between groups when comparing them.

Table 2.

Parameter	G 1	G 2	C	p G1 vs G2	p G1 vs C	p G2 vs C
Pregnancies ^¶	29	70	88	<0.0001	<0.05	<0.05
Children/mother^	1.31	2.59	2.14	-	-	-
Age at conception y¶	34;6	23;4.5	23;6.5	<0.0001	<0.0001	<0.05
m;IQR (min-max)	(28 -44)	(17-38)	(16- 39)			
TTP >12 months (%)£	37.93	48.57	30.68	<0.0001	<0.05	>0.05
Births ^¶	28	53	67	<0.0001	<0.0001	>0.05
Spontaneous abortions^£	10	14	22	<0.0001	<0.0001	>0.05
Stillbirths^	0	1	0	-	-	-
'C 'section delivery£ (%)	21.42	1.85	1.51	<0.0001	<0.0001	>0.05
Premature delivery £ (%)	7.14	5.66	3.07	>0.05	>0.05	>0.05
Eclampsia (%)	3.57	0	0	-	-	-
Birth weight g (mean ± SD) ¶	2950±461	3250±652	3500±463	<0.05	<0.0001	<0.05
Birth weight < 2500g (%)	7.14	13.33	1.49	-	-	-
Malformations^	0	0	1	-	-	-
Transfer to NICU^	0	1	1	-	-	-
Other child pathologies^	2 (autism)	0	0	-	-	-

^- number, y- years, g-gram, NICU- newborn intensive care unit, ¶ Mann Whitney U test, £ Fisher's exact test, m-median

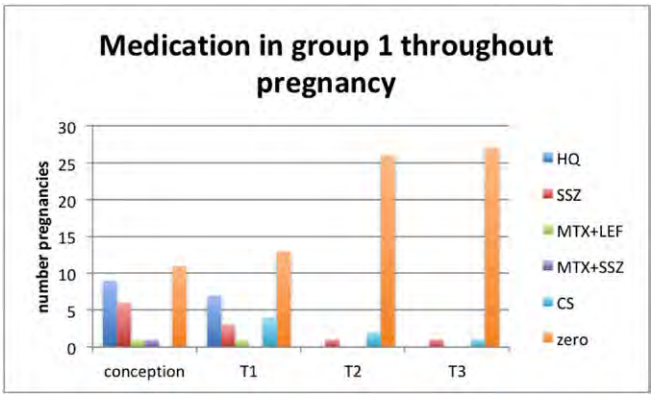


Fig 1:

Conclusion: Current pregnancy management guidelines implementations in RA assure a good pregnancy course in patients that have achieved remission and LDA status. RA patients show lower fertility and more miscarriages in comparison to both preclinical RA and general population. Newborns from RA mothers are healthy and show a normal gestational age/weight at delivery, yet smaller family sizes were observed. Preclinical RA does not influence fertility, pregnancy outcome and family size. Newborns belonging to G1 and G2 are smaller in comparison to general population but true hypotrophy is a rare event.

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Disclosure of Interests: None declared

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FRI0071 ANALYSIS OF DATA GAPS IN RHEUMATOID ARTHRITIS

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Background: Although ideally Recommendations for the management of rheumatoid arthritis (RA) should be supported by the highest level of evidence, many of which are based on "expert opinion". This means that there are knowledge gaps to which a part of the research efforts in this disease should be directed.

Objectives:

1.- Analyze the causes of the low level of evidence in some of the recommendations on diagnosis and management of RA in the main published documents

2.- Identify the knowledge gaps that justify said low level of evidence

3.- Design actions to respond to the knowledge gaps identified.

Methods: Qualitative study. A group of six experts in systematic review of the literature was selected. Fourteen documents of national and international recommendations on RA (EULAR, ACR and SER) of the last 5 years were analyzed by a peer review. They selected recommendations with low level of evidence (Oxford 4 and 5) / grade of recommendation (C and D), and classified by areas (diagnosis, monitoring, treatment, others) and then possible causes of low level of evidence were analyzed. These were submitted to a Delphi to select the 10 recommendations in which participants considered it more critical to obtain quality evidence. Subsequently, actions were proposed to improve the levels of evidence in general and, through the PICOS structure (population, intervention, comparator, study design) specific studies were proposed to respond to the issues raised in these 10 recommendations

Results: 185 recommendations were found that had a low level of evidence / grade of recommendation, most related to the treatment of RA. The two most frequent causes of this low level of evidence and / or the degree of recommendation were the absence of studies and an incorrect classification of the level of evidence and / or degree of recommendation. In addition, other reasons and methodological barriers were found for which nine critical recommendations were finally selected for which new PICOs were developed with which to propose targeted research projects

Conclusion: It is necessary to improve the methodological approach in the RA recommendations guidelines to correct errors and fill gaps with appropriate studies.

Table 1. Actions to increase the level of evidence / recommendation.

#	Action
1	Prioritization of research towards knowledge gaps with the design and development of specific studies
2	Increase knowledge of experts in the methodology of consensus documents (including RSL, formulation of recommendations, etc.)
3	Supervision of the entire process by expert methodologists, to ensure a correct allocation of the levels of evidence and degree of recommendation
4	Review and select those topics that are really of interest and should be reviewed and can be answered
5	Expert opinion should never become a recommendation, but will be included in the text that accompanies that recommendation.
6	Clear syntax will be used and short recommendations will be made
7	Establishment and application of homogeneous criteria to formulate recommendations

Key words: Rheumatoid arthritis, recommendations, data gaps

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FRI0072 DISCONTINUATION OF DMARD USE IN RHEUMATOID ARTHRITIS PATIENTS WITH LUNG DISEASE

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Background: Pulmonary manifestations such as interstitial lung disease (ILD) and chronic obstructive pulmonary disease (COPD) are frequent extra-articular features that carry a poor prognosis in Rheumatoid Arthritis (RA). Little data is available on how RA patients (pts) with pulmonary disease are managed in real-world settings.

Objectives: To assess treatment patterns and DMARD discontinuation in RA patients with comorbid lung disease in comparison with other RA patients.
Methods: The study included RA Patients enrolled in the Forward Databank with ≥1 year observation after 2000 initiating a DMARD. Forward is a large longitudinal rheumatic disease registry in the US. RA patients' diagnoses were rheumatologist-confirmed, and every 6 months participants completed comprehensive questionnaires regarding symptoms, disease outcomes, medications, and clinical events. Lung disease (LD+) was defined as at least one of the following: emphysema, asthma, bronchitis, COPD, pleural effusion, fibrosis of the lung, "RA lung", or ILD, the later classified by ICD9 codes (England 2019). DMARDs were categorized hierarchically into four groups: csDMARDs, TNFi and NTNFi (bDMARDs), and tsDMARDs. Percentage of patients who initiated different DMARDs were reported for pts with LD+/LD-. Discontinuation was analyzed by Kaplan Meier (KM) curves, log-ranks tests, and Cox regression models using time-varying covariates. Best models were created using backward selection models (10% probability of removal) and pre-defined clinical models.
Results: Of the 21,525 eligible RA patients, 13.8% had LD+ at the time they initiated a DMARD (follow-up: 69,597 pt-yrs (median 1.9 yrs/pt)). LD+ patients tended to have more severe RA outcomes and comorbidities. MTX-monotherapy (48% vs 44%, p<0.001) and NTNFi were initiated more frequently in LD+ pts with lower use of TNFi (Figure). DMARD discontinuation rates were higher among LD+ patients for all DMARD groups, but KM curves were only significantly different for csDMARDs and TNFi. Different HRs for LD+ were found depending on the model used ranging from 1.18 to 1.28, and all models revealed an increased risk of discontinuation for LD+ patients. Compared to csDMARDs, TNFi were more often discontinued (Table). Other variables associated with an increased risk of discontinuation included: HAQ, Rheumatoid Disease (RD) comorbidity index, pain, prior bDMARDs, and csDMARDs.
Conclusion: Different DMARD treatment patterns were found for LD+ patients, who tended to initiate more csDMARD and NTNFi and less likely to initiate a TNFi. LD+ patients were at a higher risk of discontinuation irrespectively of the DMARD treatment, but with greater risk for TNF users.
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Figure. DMARD treatment initiators by disease group

Table. Cox models for DMARD discontinuation by stepwise (removal probability 10%) and clinical models including DMARD treatment.

Model of DMARD persistence*	Model 1- Stepwise-Without drugs	Model 2 – Stepwise	Model 3 - Clinical
LD+ vs LD–	1.18 (1.08 - 1.29)	1.28 (1.13 - 1.45)	1.20 (1.08 - 1.34)
TNF vs csDmard		1.32 (1.08 - 1.63)	1.22 (1.04 - 1.44)
NTNF vs csDmard		1.13 (0.83 - 1.52)	1.13 (0.90 - 1.41)
tsDmard vs csDmard		1.30 (0.65 - 2.60)	1.02 (0.64 - 1.62)

*Best models searched/Clinical adjusted for LD+/LD-, DMARDs, age, sex, education, HAQ disability, RD comorbidity index, smoking, pain, glucocorticoids, year of entry, prior bDMARDs and csDMARDs counts and MRC breath scale.

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FRI0073 SEROLOGICAL PREDICTORS OF THE SEVERITY OF RHEUMATOID ARTHRITIS RELATED INTERSTITIAL LUNG DISEASE

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Background: The most common extra-articular manifestation of rheumatoid arthritis(RA) is interstitial lung disease (ILD). Although pulmonary manifestations in RA encompass the main airway, parenchyma, vasculature and pleura, ILD in particular, is associated with reduced survival. Up to 10% of RA patients suffer from clinically significant ILD while a substantial proportion have abnormal CT chest findings despite being asymptomatic.There are various biochemical and serological markers to predict the severity of the joints in RA. However, the clinical and laboratory determinants of RA related ILD (RA-ILD) are not well defined owing to the paucity of research data in this regard.
Objectives: The main objective of this study is to determine the correlation between the rheumatoid factor (RF) serotypes and the severity of RA-ILD based on computer tomography (CT) findings.
Methods: We recruited a total of 100 RA patients who were tested for IgA RF, IgG RF and IgM RF and had high resolution CT chest performed. Participants were aged above 18 years, met the 2010 ACR/EULAR RA criteria, had RA for more than 6 months, were non-smokers, not pregnant and had no known chronic lung disease or lung malignancy based on their medical records. Seventy-two patients had ILD changes on HRCT of the chest and were included in this study. The CT images were scored based on a scoring system proposed by Kazerooni et al. Ground glass opacities represented the alveolar findings whereas honeycombing and septal thickening were the interstitial findings. The ground glass and fibrosis scores were on a scale of 0-5, with higher scores for greater involvement of the lobes. For each subject, the maximum ground glass and fibrosis scores were 25, respectively.
Results: The frequency of RF positivity was comparable across the 3 serotypes (83.33-84.72%). The correlation between the clinical variables and the CT scores are listed in Table 1.We found that the the CT scores for ground glass showed significant positive correlation with disease duration (p=0.047)and IgA RF levels (p<0.050)whereas the fibrosis scores had significant relationship with multiple clinical covariates i.e age (p=0.004), disease duration (p=0.042), IgA RF levels (p<0.050), IgG RF levels (p=0.041) and anti-CCP levels (p=0.006). On multivariate analysis, only IgA RF levels remained significantly (p<0.05, standardized beta coefficient =0.604) associated with the ground glass scores. As for the fibrosis scores, IgA RF levels and age were independent predictors based on multivariate analysis after adjusting for confounders, with p scores of <0.05 and 0.02, respectively.

Table 1. Correlation of CT scores with clinical covariates and antibodies

Parameters	Ground glass		Fibrosis	
	r	p value	*r*	p value
Age	0.229	0.053	0.334	**0.004**
Disease duration	0.235	**0.047**	0.240	**0.042**
Total MSS	0.058	0.628	0.224	0.145
Cumulative Methotrexate dose	0.039	0.748	0.098	0.413
Ig A	0.608	**<0.05**	0.576	**<0.05**
Ig M	0.053	0.660	0.019	0.873
Ig G	0.183	0.124	0.241	**0.041**
Anti CCP	0.117	0.328	0.319	**0.006**

Conclusion: The IgA RF was the only serotype which was independently associated with the severity of RA-ILD.
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Disclosure of Interests: Sakthiswary Rajalingham Speakers bureau: Pfizer (500USD), Syahrul Sazliyana Shaharir: None declared, Radhika Sridharan: None declared
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FRI0074 UNDERLYING PROBLEMS AND IMPACT OF DIFFICULT-TO-TREAT RHEUMATOID ARTHRITIS: PRELIMINARY RESULTS OF A CROSS-SECTIONAL CASE-CONTROL STUDY

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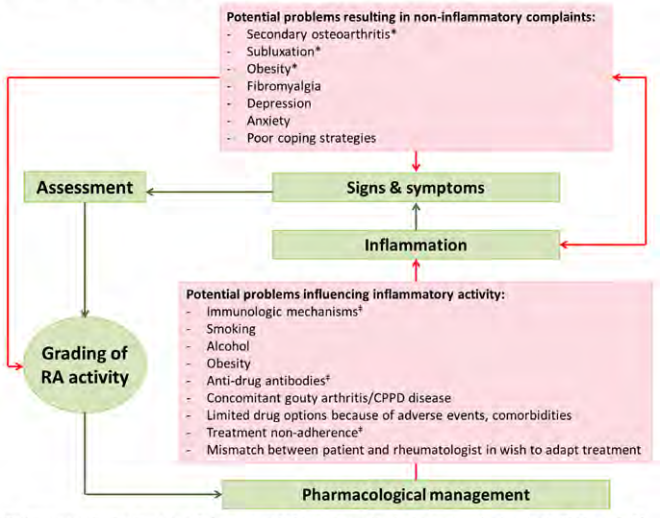
Background: Difficult-to-treat (D2T) RA is defined here by signs and symptoms, suggestive of active/progressive RA, which are perceived as problematic by rheumatologist and/or patient, and are present despite treatment according to EULAR recommendations including ≥2 b/tsDMARDs with different mechanisms of action.[1] Its treatment is generally based on trial-and-error and challenged by several underlying problems (Figure 1),[2-4] of which the exact impact is unknown.
Objectives: To obtain insight into the potential problems underlying D2T RA and into its impact.
Methods: Consecutive RA patients fulfilling the 2010 ACR/EULAR classification criteria, treated according to current standard of care for ≥1 year, are being enrolled, and categorised as D2T or not (controls). Potential problems underlying D2T RA (Figure 1) and its impact on quality of life and physical functioning were assessed and compared between the two patient groups.
Results: In this preliminary analysis, 45 patients are classified as having D2T RA and 100 are controls (Table 1). Fibromyalgia (33 vs 9%), depression (18 vs 4%), a mismatch between patient and rheumatologist in wish to adapt treatment (51 vs 15%) and DMARD discontinuation because of adverse events (96 vs 57%), were statistically significantly more frequent in D2T RA patients than in controls. Higher levels of threatening illness perception and helplessness, and more comorbidities according to EULAR domains were found in D2T RA patients (Figure 2). Other potential problems did not differ statistically significantly.

Table 1. Patient characteristics

	D2T RA (n=45)	Control RA (n=100)	p-value
Demographics			
Age‡	60.9 (10.8)	64.5 (10.9)	0.06[1]
Female, %	76	72	0.66[2]
Disease characteristics			
Disease duration, years	17.0 (10.0-27.5)	14.0 (8.0-24.0)	0.18[3]
RF positivity, %	76	65	0.21[2]
ACPA positivity, %	71	65	0.47[2]
DAS28-ESR	4.0 (3.4-5.7)	2.5 (1.8-3.3)	<0.001[3]
Drugs			
Number of previous DMARDs	7 (5-10)	2 (1-4)	<0.001[3]
Number of current DMARDs	2 (1-2)	1 (1-2)	0.03[3]
Current conventional synthetic DMARDs, %	74	86	0.07[2]
Current biological DMARDs, %	57	39	0.06[2]
Current targeted synthetic DMARDs, %	22	0	<0.001[2]
Glucocorticoid therapy, %	53	16	<0.001[2]
Dose, mg/day prednisone or equivalent daily, in users	7.5 (5.0-13.8)	5.0 (5.0-7.5)	0.03[3]

ACPA: anti-citrullinated protein antibodies; D2T: difficult-to-treat; DAS28-ESR: disease activity score assessing 28 joints using erythrocyte sedimentation rate; DMARD: disease-modifying antirheumatic drug; mg: milligram; n: number; RF: rheumatoid factor.
Numbers are median (interquartile range), unless stated otherwise; ‡ mean (standard deviation).
Differences between groups were analysed using: 1. Independent T-test; 2. Chi-square Test; 3. Mann-Whitney U Test.

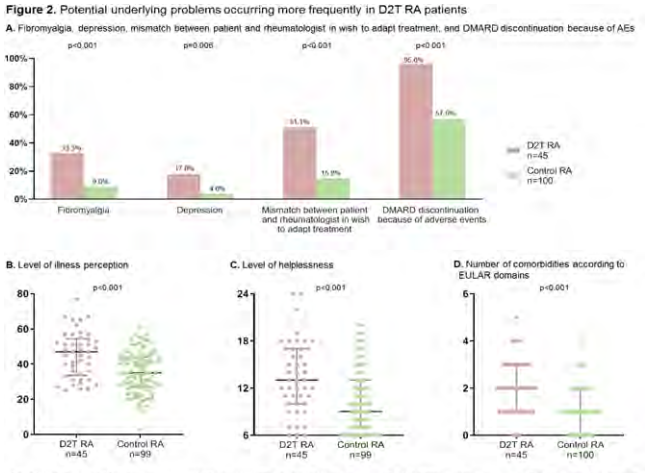
Figure 1. The management cycle of D2T RA, including potential problems underlying the disease state



The drug management cycle is shown in green. Factors in pink, which influence (red arrows) the ideal drug management cycle and lead to difficulty in grading RA activity or drug effectiveness. All these factors may in different grades in individual patients contribute to D2T RA.
CPPD: calcium pyrophosphate deposition; D2T: difficult-to-treat; RA: rheumatoid arthritis. * Factors that might also hamper proper grading of disease activity. ‡ Factors have not yet been determined. Adapted from: de Hair MJH *et al. Rheumatology* 2017;57:1135–44.

Quality of life and physical functioning were significantly lower in D2T RA patients than in controls (median (IQR) EQ-5D 2.6 (1.8-3.0) vs 1.6 (1.4-2.2) and HAQ 1.8 (1.3-2.1) vs 1.0 (0.5-1.4), p<0.001).
Conclusion: This first prospective study describing a cohort of D2T RA patients shows higher occurrences of potential underlying problems and a higher clinical impact. These should be recognised in daily practice and taken into account before considering another DMARD switch. More detailed research on disease state (biomarkers, radiographic damage) and use of medication (drug levels and in-depth interviews on treatment non-adherence) will follow.
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Figure 2. Potential underlying problems occurring more frequently in D2T RA patients



AEs: adverse events; D2T: difficult-to-treat; DMARDs: disease-modifying antirheumatic drugs; EULAR: European League Against Rheumatism; RA: rheumatoid arthritis. Fibromyalgia according to ACR 2010 criteria. Depression according to Hamilton anxiety and depression scale (0-21, score >10 reflects probable depression). Level of illness perception according to Illness Perception Questionnaire (0-60, higher score reflects more threatening view of illness). Level of helplessness according to Illness Cognition Questionnaire for chronic diseases (6-24, higher score reflects higher level of helplessness). EULAR comorbidity domains (0-6): cardiovascular disease, malignancies, infections, gastrointestinal disease, osteoporosis, depression.
B-D: Dark lines represent median values. Whiskers represent interquartile ranges (25^{th}–75^{th}). Differences between groups were analysed using: A. Chi-square Test; B-D. Mann-Whitney U Test.

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FRI0075

DECREASED RISKS OF HOSPITALIZED INFECTION UNDER TARGETED THERAPIES VS METHOTREXATE IN ELDERLY AND OLDER ELDERLY PATIENTS COMPARED TO YOUNGER PATIENTS WITH RHEUMATOID ARTHRITIS USING JAPANESE HEALTH INSURANCE DATABASE

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Background: Recently, vital prognosis has been improved in patients with rheumatoid arthritis (RA)[1]. In elderly patients, it is difficult to establish a treatment strategy due to multi-morbidities and treatment-related risks. Since older age is a significant risk factor of serious infections, one of the primary concerns during treatment of RA, rheumatologists should always strike a balance between efficacy and safety of the immunosuppressive treatment. However, infection data under the targeted therapy (TT) in elderly patients is still limited to date.
Objectives: To compare the risk of hospitalized infection (HI) under the TT among young, elderly, and older elderly patients with RA using the Japanese health insurance database.
Methods: This retrospective longitudinal population-based study was conducted using claims data in Japan provided by Medical Data Vision Co., Ltd. We defined individuals as RA cases if they met all of the following: 1) having at least one ICD10 code (M05x, M06x except for M061, or M08x except for M081 and M082); 2) having at least one prescription of disease-modifying antirheumatic drugs (DMARDs) including methotrexate (MTX) and TT (biological DMARDs and Janus kinase inhibitors) between April 2008 and September 2018; and 3)

16 years old or older. We define the month patients met the above all criteria for the first time in this database as the index month. We excluded patients who were prescribed any DMARDs during the first 12 months from MTX users and those with prescription of any TT during the first 12 months from TT users (i.e., prevalent users). Among the study population, we divided patients into 3 groups according to their age at the index month; young group (16-64), elderly group (65-74), and older elderly group (>=75). The observation started from the index month and ended at 36 months later, the last month of the exposure of DMARDs, the month of loss of follow-up, or September 2019, whichever came first. HI was defined by ICD10 code with one prescription of predefined drugs for each infection during hospitalizations. Some of HIs were defined by ICD10 code alone.

Results: In this study, 8269, 6454, 5745 patients with RA were included in the young, elderly, and older elderly groups, respectively. The incidence rate (IR) of HI (/100 patient-years [PY]) [95%CI] was 3.4 [3.1-3.7] in the young group, 5.8 [5.3-6.3] in the elderly group, and 12.0 [11.2-12.8] in the older elderly group. IR rate (IRR) of HI (reference: the young group) was 1.7 [1.5-1.9] in the elderly group and 3.6 [3.2-4.0] in the older elderly group. In the young group, the IRR of HI in TT users vs MTX users was significantly elevated (1.8 [1.5-2.1]), whereas, those of the elderly and the older elderly groups were significantly decreased (IRR 0.8 [0.7-0.9] for elderly; 0.6 [0.5-0.7] for older elderly). Concomitant use of immunosuppressive DMARDs or prednisolone >=10mg/day with TT became less frequent with aging.

Conclusion: The elderly and older elderly patients had significantly higher risks of HI compared to the young. The risk of HI under the TT compared to MTX was decreased in the elderly patients, probably due to adjusting for treatment by attending physicians.

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FRI0076 RELATIONSHIP BETWEEN DEPRESSION, LEARNED HELPLESSNESS, DISABILITY AND DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid Arthritis (RA) has been associated with depression by up to 46% (1)

Within the universe of manifestations of depression is learned helplessness (LH) LH is defined as an inadequate perception of the disease, generating feelings of defenselessness, loss of self-esteem, pessimism, and negativity. This leads to passivity, surrendering to fate, and thoughts that nothing within their power can change their situation, this condition produces a rapid deterioration which prevents responding adaptively to a traumatic situation, increasing the frequency of anxiety and depression. (2)

Objectives: To assess the relationship between depression, LH, disability and disease activity among patients with RA

Methods: Descriptive observational study included RA patients diagnosed according to ACR / EULAR 2010 randomly recruited between June and September 2019 at University Hospital "Dr. José Eleuterio González" in Monterrey, México.

Beck Depression Inventory (BDI) and Rheumatology Attitude Index (RAI) were applied for measure depression and LH, to measure disability Health Assessment Questionnaire (HAQ-DI) was applied. CDAI and DAS28-PCR scales were used for measure disease activity.

Descriptive analysis was carried out with measures of central tendency and dispersion. Spearman correlation were used for comparisons, according to the distribution of the variables. A p <0.05 was considered statistically significant.

Results: A total of 177 patients were included, demographic and clinic features are presented in table 1. Prevalence of LH was 94.5% (167/177); 60% (100/167) mild levels (9-15) and 33% (67/167) high levels (>15). A significant correlation was found between higher levels of dysfunctionality and BDI and higher levels of LH (rho = 0.338; p = 0.001). There was a positive association when measuring CDAI (rho = 0.235; p = 0.002) BDI (rho=0.278 P=<0.001) and DAS28-PCR (rho=0.166; p=0.027) with higher levels of LH. There was no association found between other variables as gender, years of diagnosis of RA, years of study or presence of comorbidities like fibromyalgia or osteoarthritis.

Table 1. Demographic and clinical characteristics of the patients. HAQ-DI Health Assessment Questionnaire RAI Rheumatology attitude index, DAS28-PCR Disease Activity Score CDAI Clinical disease activity index BDI Beck Depression Inventory

Demographics	n = 177
Gender	
Female n, %	165 (93.3%).
Male n, %	12 (6.8%)
Age (mean), SD.	52.16 (12.8)
Years of study (average), SD.	8.3 (3.6)
Years with RA (mean), SD.	8.2 (8.0)
RAI (mean), SD	13.83 (3.9)
HAQ-DI (mean), SD	0.67 (0.77)
CDAI (mean), SD	12.0 (11.4)
DAS28-PCR (mean), SD	2.4 (0.6)
BDI (mean), DE	9.30 (9.7)
LH, n (%)	168/177 (94.5%)
	High levels 108/177 (61%)
	Low levels 60/177 (33%)

Conclusion: In this study the prevalence of LH was high >90%, mainly in mild levels. Dysfunctionality seems to be the factor most associated with the presence of depression and LH.

Rheumatologist should consider the high levels of LH, to assess patients in order to obtain a better outcome.

Table 2. Correlation between learned helplessness and clinical variables LH Learned Helplessness HAQ-DI Health Assessment Questionnaire RAI Rheumatology Attitude Index DAS28-PCR Disease Activity Score CDAI Clinical Disease Activity Index BDI Beck Depression Inventory

	rho	p
LH –HAQ-DI	0.338	<0.001
LH-CDAI	0.235	0.002
LH-DAS28PCR	0.166	0.027
LH-BDI	0.278	<0.001

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FRI0077 THE PREVALENCE OF DEPRESSION AND ANXIETY IN PATIENTS WITH RHEUMATOID AND PSORIATIC ARTHRITIS AND ITS CONTRIBUTORY FACTORS

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Background: Rheumatoid Arthritis (RA) and Psoriatic arthritis (PsA) are both chronic, progressive inflammatory arthritis that can cause significant disability and morbidity. Depression in RA has been associated with higher levels of disease activity, pain, fatigue, work disability, lower treatment compliance and increased suicidal risk and mortality [1]. PsA patients suffer from psoriasis and joint involvement; hence have greater odds of depression by 2.1 times compared with RA [2].

Objectives: To compare the prevalence rates of depression and anxiety and its associated factors between RA and PsA patients in Hospital Putrajaya.

Methods: A cross sectional survey using the Hospital Anxiety and Depression Scale (HADS) questionnaire were distributed to 300 patients who attended rheumatology outpatient clinic from February – April 2019. The HADS was categorized into 3 groups based on their scores 0-7 (Normal); 8-10 (Borderline); and 11-21 (Abnormal). Data on patient demographics and components of disease assessment scores were recorded. Disease activity was assessed using DAS 28-CRP for all patients. Additional evaluation using Bath Ankylosing Spondylitis Disease Activity Score (BASDAI) and body surface area (BSA) were done for PsA patients. P value of < 0.05 was taken as significant.

Results: In total, 205 RA and 73 PsA patients were eligible for analysis. Majority of the patients were female, Malay and married for both groups. The mean age group for RA and PsA were 56.2 ± 11.9 years and 51.0 ± 14.6 years. The mean duration of disease for RA were 8 ± 10 years; while for PsA were 6 ± 11 years. The prevalence rates of depression and anxiety for RA were 8.3% and 13.7%; and PsA were 9.6% and 17.8% respectively. Borderline scores for depression occurred in 16.1% of RA patients and 12.3% for PsA. Twenty percent of RA patients (n=41) and twenty-four percent of PsA patients (n=18) scored borderline for anxiety. The significant positive correlations with depression and anxiety in RA include high disease activity scores (r = 0.27; r = 0.31), number of tender joints (r = 0.26; r = 0.24) and pain (r = 0.29; r = 0.27). Higher number of swollen joints significantly correlated with depression (r = 0.16) but not with anxiety. RA patients with Ischaemic Heart Disease (IHD) ± heart failure have higher depression scores (p < 0.05). As for PsA group, high BASDAI score (anxiety: r = 0.34, depression: r = 0.26) and psoriasis involving head and neck region (p < 0.05) were significant associated factors. Age was inversely correlated with anxiety in the PsA group.

Conclusion: There is higher prevalence of anxiety in both RA and PsA as compared to depression. Higher disease activity scores were associated with depression and anxiety in both RA and PsA with axial involvement.

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FRI0078 SERUM IRISIN LEVEL IN RHEUMATOID ARTHRITIS PATIENTS: ITS RELATIONSHIP TO DISEASE ACTIVITY AND CARDIOVASCULAR MANIFESTATIONS

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Background: Active Rheumatoid Arthritis (RA) is associated with considerable changes in body composition, lipids, adipokines and insulin sensitivity. RA is an independent risk factor for CVD. The mechanisms leading to synovial inflammation are similar to those found in unstable atherosclerotic plaque. Irisin is a metabolic hormone and a novel adipomyokine related to insulin resistance and endothelial functions (1).

Objectives: To investigate the relationship between serum irisin levels, disease activity and cardiovascular risk in RA patients, and to test its performance in predicting subclinical atherosclerosis in RA patients.

Methods: 60 RA patients fulfilling the 2010 ACR/EULAR RA Classification Criteria and 30 healthy controls were recruited for serological testing of irisin levels. BMI was calculated. Waist/hip ratio was measured. RA disease activity was assessed by DAS28-ESR. Disability was assessed by HAQ-DI in its Arabic version. Serum ESR, CRP, glycated hemoglobin (HbA1c), lipid profile (serum level of cholesterol, triglyceride, HDL, LDL and cholesterol/ LDL ratio), insulin levels were measured in all patients and controls. Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) was used to calculate insulin resistance. Carotid intimal medial thickness (C-IMT), an indicator of atherosclerosis, was measured by carotid doppler ultrasonography. Echocardiography was performed to assess cardiac abnormalities. Our RA patients were classified twice; first, according to cardiovascular abnormalities and second, according to cut-off values of DAS28.

Results: Serum irisin levels were significantly lower in RA patients (9.84 ± 10.56)ng/ml compared to controls (20.48±13.82)ng/ml (p<0.001). BMI values were significantly higher in all patients than controls (P= 0.035), while waist/hip ratio in female patients only were significantly higher (P= 0.007).We found a negative correlation between serum irisin and DAS28-ESR (r = -0.455, P-value 0.005)& HAQ-DI (r = -0.309, P-value 0.016). There was a negative correlation between serum irisin level and parameters of cardiovascular risk including anthropometric measurements (BMI and waist/hip ratio), HOMA-IR (r=–0.371, p=0.009) and C-IMT (r=–0.511, p<0.001). No correlation could be detected between irisin and lipid profile. The frequency of cardiovascular (CV) involvement in RA patients was 45% (27 patients) (11.6 % with echocardiographic abnormalities and 40% having increased C-IMT). Patients with CV involvement showed lower serum irisin level, increased disease activity assessed by DAS28 and increased disease disability assessed by HAQ-DI with statistically significant difference (P < 0.001, P < 0.05 and P < 0.001 respectively). Classifying the patients based on cut-off values of DAS28 into 3 groups (low disease activity, moderate and high disease activity), we found a statistically significant difference between the irisin levels of the 3 groups, being lowest among highly active patients (P= 0.014). c-IMT values were significantly higher in highly active patients (P= 0.04). Assessing the biomarker's performance as an independent indicator of subclinical atherosclerosis in RA patients using ROC curve, it showed an excellent ability (AUC 0.8, P <0.001). As regarding its ability to differentiate patients with high disease activity, it showed a very good performance (AUC 0.73, P <0.001).

Conclusion: In RA patients, serum irisin level was significantly lower and perform better than traditional yardsticks in identifying disease activity. It may act as an independent indicator of subclinical atherosclerosis in RA patients. Serum irisin level may be responsible for increased cardiovascular risk in those patients.

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Disclosure of Interests: None declared

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FRI0079 CHARACTERISTICS OF DIFFICULT-TO-TREAT RHEUMATOID ARTHRITIS

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Background: Despite remarkable progress in therapy, not a few patients with rheumatoid arthritis (RA) have not achieved treatment target. Various factors can be ascribed to difficult-to-treat RA, however, little is known about their characteristics.

Objectives: To clarify characteristics of patients with difficult-to-treat RA in real-world.

Methods: We reviewed all consecutive RA patients in Keio University Hospital between 2016 and 2017 and collected medical information. We defined patients in moderate disease activity and high disease activity according to disease activity score for 28 joints (DAS28) at the last visit despite more than one year treatment for RA as difficult-to-treat RA and analyzed their clinical characteristics.

Results: A total of 1693 patients with RA were enrolled in the analysis. The mean age at the last visit was 64 years old, female was 83%, and the mean disease duration was 11.9 years. Rheumatoid factor and anti-cyclic citrullinated peptide were positive for 76% and 75% of the patients, respectively. The current treatment were conventional synthetic disease modifying anti-rheumatic drugs in 73%, biologic agents or janus kinase (JAK) inhibitors in 57%, and glucocorticoids in 13%. Disease activity according to DAS28 was remission in 65%, low disease activity in 21%, and moderate/high disease activity in 14%, which was defined as difficult-to-treat RA. Characteristics of difficult-to-treat RA were the mean age of 70 years old, female of 89%, and the mean disease duration of 14.8 years. The current treatments were conventional synthetic disease modifying anti-rheumatic drugs alone in 40.7%, biologic agents or JAK inhibitors in 55.8%, and glucocorticoids in 29.0%. The causes of difficult-to-treat RA were unresponsiveness to several biologic agents and/or JAK inhibitors in 22.9%, comorbidities in 33.8%, and personal reasons in 39.8% (costs in 35.9%, low adherence in 4.3%, concerns about possible adverse reaction of drugs in 54.3% and high patient global assessment in 5.4%). Patient characteristics were significantly different between the causes; age at RA onset (51 vs 61 vs 51 years, p<0.001), current age (65 vs 77 vs 66 years, p<0.001), estimated glomerular

filtration rate (75 vs 61 vs 73 mL/min/1.73m2, p<0.001), tender joint count (3.4 vs 1.6 vs 2.1, p=0.005), swollen joint count (3.1 vs 1.6 vs 2.9, p=0.003), evaluator global assessment (21 vs 14 vs 16 mm, p=0.03), health assessment questionnaire-disability index (1.3 vs 1.3 vs 0.9, p=0.005), a history of serious infection (28 vs 41 vs 13%, p<0.001) and rheumatic disease comorbidity index (1.2 vs 2.2 vs 0.9, p<0.001).

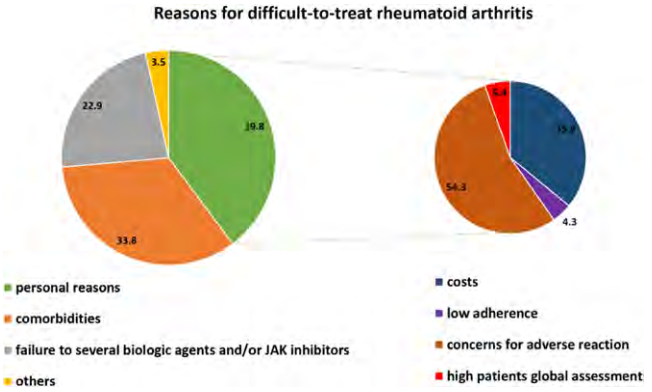
Conclusion: There are still 14% of patients with RA were difficult-to-treat in real world in spite of intensive treatment. Their characteristics are distinct by the cause of difficulty to treat, suggesting the approach to difficult-to-treat RA should be personalized.

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FRI0080 CLINICAL CHARACTERISTICS OF PATIENTS WITH ELDERLY-ONSET RHEUMATOID ARTHRITIS (EORA)

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Background: The onset of rheumatoid arthritis (RA) occurs usually between 35-50 years of age. Since the general population is ageing, beginning of RA in older age is more common. The term *elderly onset of rheumatoid arthritis* (EORA) describes the disease with onset at age over 60. The term *younger-onset rheumatoid arthritis* (YORA) refers to the disease with typical, earlier onset. Observational studies indicate, that substantial differences do occur between the two RA subtypes (EORA and YORA).

Objectives: The goal of the study was to analyze the course of disease and treatment in EORA in comparison to YORA patients.

Methods: The study was conducted in consecutive RA patients, treated in the Department of Rheumatology and Connective Tissue Diseases, Medical University of Lublin, Poland. The study group consisted of 113 patients (93 women, 20 men), with the mean (SD) age 59.4 (19.0), disease duration 12.9 (10.3) years.

The cut off between EORA and YORA was set at 60 years of age. There were 63 (55.8%) EORA and 50 (44.2%) YORA patients. Demographic and clinical information was obtained through structured interview, review of medical records and laboratory tests. Disease activity was assessed based on joint counts and Disease Activity Score of 28 joints (DAS28).

Results: In patients with EORA vs YORA, the mean (SD) age was 73.64 (6,6) vs 41.5 (13.7) (p<0.001), the age of RA diagnosis 65.0 (4.2) vs 23.3 (4.8) (p<0.001), RA duration 8.6 (5.4) vs 18.3 (12.3) years (p<0.001).

The group of patients with EORA compared with YORA, was characterized by: significantly higher number of men [respectively 16 (25.4%) vs 4 (8.0%)], unfavorable metabolic parameters [higher body mass index (BMI): 26.0 (5.8) vs 23.4 (4.1) kg/m^2 (p=0.04); serum uric acid: 5.7 (1.5) vs 4.4 (1.6) mg/dl (p=0.001)], as well as unfavorable parameters of RA activity [higher DAS28: 4.4 (1.5) vs 3.2 (1.6) (p<0.001); higher tender joints count (TJC): 6.1 (6.2) vs 3.2 (3.7) (p=0.01); higher erythrocyte sedimentation rate (ESR) 45.9 (30.3) vs 24.1 (25.6) (p<0.001) and white blood cell count (WBC): 8.3 (2.7) vs 7.0 (2.4) x10^3/ml (p=0.01)]. At the time of assessment, remission or low disease activity was achieved in significantly fewer EORA vs YORA patients [15 (23.8%) vs 25 (50%) (p=0.007)].

In EORA patients methotrexate was used as the first disease modifying drug (DMARD) more often [54 (85.7%) vs 26 (52%) (p<0.001)], the use of biological DMARDs was less common [5 (7.9%) vs 23 (46.0%) (p<0.001)], as well as glucocorticoids (GC) [49 (77.8%) vs 47 (94.0%) (p=0.04)]. Significantly more patients with EORA than YORA, were affected by concomitant diseases [62 (98.4%) vs 41 (82%) (p=0.007)].

The prevalence of joint erosions, extra-articular manifestations and antibodies typical for RA (rheumatoid factor, RF-IgM and/or anti-citrullinated peptide, ACPA) did not differ significantly between the groups.

Conclusion: In our study group, EORA patients were characterized by higher proportion of men, higher inflammatory parameters and higher disease activity, in comparison with YORA. In patients with EORA we also found unfavorable metabolic parameters and higher incidence of concomitant diseases, which could affect the method of treatment (less common use of GC and biological DMARDs).

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FRI0081 WERE FRAIL RA PATIENTS AT YOUNGER AGE MORE LONELY, DEPRESSED OR ANXIOUS THAN NON-FRAIL RA PATIENTS?

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Background: Frailty is a state that reflects reduced reserve and resistance to stressors among elderly persons. A preceding study showed that 38 out of 90 (42%) RA patients aged ≥ 55 years who visited our outpatient clinic were frail. Presence of frailty was not age-dependent. Patients were mainly classified as frail because of positive answers on single items that report on depressive feelings (73.7%), anxiety (57.9%), missing people around (65.8%) and emptiness (63.2%) [1]. It is unclear whether frailty is a cause, consequence or comorbidity of poor psycho-emotional health. Alternatively, they could also be congruent conditions. Exploring whether poor psycho-emotional health might be a longitudinal predictor of frailty, might shed light upon the relation between frailty and psycho-emotional health.

Objectives: In this mixed qualitative / quantitative study, we assessed whether older frail RA patients were already more lonely, depressed, and/or anxious than non-frail RA patients at 40 years.

Methods: All 90 RA patients who participated in our previous study on frailty in 2017 were invited for the current study. Participants were invited to rate validated multidimensional questionnaires on depression and anxiety (Geriatric Depression Scale (GDS) and Hospital Anxiety and Depression Scale (HADS)), loneliness (de Jong Gierveld loneliness scale) social support (Social Support List) for their current situation, but also retrospectively for their situation at the age of 40. Current frailty was assessed by the Groningen Frailty Indicator (GFI).

Semi-structured interviews took place in an age-stratified sample to explore how the diagnosis of RA has influenced patients' life. Items of questionnaires were compared using the chi-square test. Interviews were annotated by two independent readers. Codes were taxonomically organized and linked to themes using NVivo 12.

Results: 32 (36%) of the 90 invited patients participated and 28 completed all psycho-emotional questionnaires. Twelve out of 32 patients (37.5%) were classified as frail by the GFI. On the GDS at current age, 6/12 frail patients had signs of depression compared to 2/17 non-frail patients (p=0.04) (Table 1). More frail patients had signs of an anxiety disorder on the HADS, both at current age and age 40 (age 40: 7/11 frail patients versus 0/0 non-frail patients, p<0.01; Table 1). Results on the individual level were more blurred: 3 (42%) out of 7 frail patients were anxious at age 40, but not at current age. The loneliness, social support and HADS depression questionnaires showed no difference between frail and non-frail patients, both at current age and age 40. A stratified sample of 10/32 (31%) patients were interviewed of which 5 (50%) were frail on the GFI. Frail patients more often expressed anxious feelings at current age. Since the diagnosis of RA, frail patients worried more about the future, i.e. about the progression of RA. Non-frail patients tended to be more optimistic. In the interviews, patients expressed not having feelings of depression and anxiety at age 40.

Table 1. Number of frail and non-frail patients per questionnaire at current age and age 40.

Questionnaire	Frail	Non-frail	Total	p-value
GDS now				
No depression	6	15	21	0.04
Depression	6	2	8	
GDS age 40				
No depression	9	17	26	0.06
Depression	3	0	3	
HADS anxiety now				
No indication anxiety	6	17	23	0.01
Indication anxiety	5	0	5	
HADS anxiety age 40				
No indication anxiety	4	17	21	<0.01
Indication anxiety	7	0	7	

Conclusion: Although it is difficult to disentangle the causal conundrum between psycho-emotional health and frailty, frail patients were on a group level more anxious at younger age on the HADS in our study. Psychiatric symptomatology might be misinterpreted for frailty at current age. Limitations of our study include a high chance on amplified memory bias.

References:

[1] Cleutjens et al. Ann Rheum Dis 2018;77(Suppl 2):577.

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FRI0082 SLEEP PROBLEMS IN EARLY RHEUMATOID ARTHRITIS

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Background: It is well known that patients with established RA suffer from problems with sleep quality[1]. There are however few, if any, studies on sleep quality among newly diagnosed patients.

Objectives: To investigate the sleep quality among patients newly diagnosed with RA.

Methods: We used the Swedish study Epidemiological Investigation of RA (EIRA) including patients at the time of diagnosis, based on the 1987 ACR criteria during 2008-2016. At 1 and 3 years after diagnosis, the patients were sent a questionnaire in which they were asked to rate their sleep quality on 10 different questions. We then calculated 6 different sleep components consisting of insomnia, non-restorative sleep, sleep problems, general quality of sleep, if poor sleep affected the health and if they were getting enough sleep[2].

Sleep problems were defined as mostly or always having problems with either of the following: falling asleep, many awakenings with difficulties to go back to sleep, waking up early or having disturbed/restless sleep. Insomnia was defined as answering mostly or always on either problem with falling asleep, many awakenings with difficulties to go back to sleep or waking up early, in combination with mostly or always being tired during the day.

Having problems with non-restorative sleep was defined as mostly or always having trouble waking up or not feeling well rested when waking up. We defined having problem with not getting enough sleep, sleep quality affecting the health and poor sleep quality as reporting any of the two highest scores on the corresponding questions.

We then calculated the proportion of people experiencing no problems at 1 or 3 years after RA diagnosis, developing problems, improving or always having problems with their sleep.

Results: We identified 1483 patients with data at either one or both time points. The mean age was 59 years (IQR 19), and 1063 (72%) were women. At 1 year, 36% of the patients reported having at least one type of sleep problem, after 3 years, this figure was 29%. Over 20% of the patients reported having "Rather big" or "Very big" problems with sleep after one year (Table 1) and 31% had problems at one or both time points (Table 2). Disturbed sleep was a problem for their health in 20% of the patients and 11% reported having "poor" or "very poor" sleep quality at both times. Insomnia was experienced by 118 (10%) patients at 1 year and 112 (11%) at 3 years.

Table 1. Sleep problems at 1 and 3 years after diagnosis of RA.

	1 year	3 years
Insomnia	118 (9%)	112 (11%)
Not getting enough sleep	102 (8%)	113 (11%)
Problems with sleep in general	270 (22%)	231 (22%)
Sleep quality affecting health	238 (19%)	197 (19%)
Poor sleep quality	218 (17%)	209 (20%)
Problem with non-restorative sleep	218 (17%)	154 (14%)

Table 2. Individuals experiencing no problems, developing problems, improving or always having problems with their sleep at 1 and 3 years after diagnosis of RA.

	No problems at any time point	Improved	Developed problems	Problems at both 1 and 3 years
Insomnia	702 (85%)	43 (5%)	46 (6%)	39 (5%)
Not getting enough sleep	719 (86%)	36 (4%)	47 (6%)	34 (4%)
Problems with sleep in general	576 (69%)	81 (10%)	78 (9%)	103 (12%)
Sleep quality affecting health	616 (74%)	65 (8%)	70 (8%)	85 (10%)
Poor sleep quality	623 (74%)	57 (7%)	66 (8%)	91 (11%)
Problem with non-restorative sleep	654 (78%)	71 (8%)	46 (5%)	67 (8%)

Conclusion: In a population-based early RA cohort receiving today's standard care, 30% of the patients reported some type of sleep problem during the first 3 years. Although this is a lower rate than has been reported in established RA, this is a significant proportion of RA patients, and these findings warrant further studies to closer identify the course of sleep problems and the factors influencing it such as pain.

References:

[1] Bourguignon C et al PMID 14596374

[2] Akerstedt T et al PMID 18484368

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FRI0083 GLUCOCORTICOID USE IS ASSOCIATED WITH DETERIORATION OF MUSCLE QUALITY AND FUNCTION: FROM THE CHIKARA STUDY

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Background: We previously reported that glucocorticoid (GC) use was an independent risk factor for developing sarcopenia in patients with rheumatoid arthritis (RA)1. On the other hand, sarcopenia was not associated with deterioration of muscle function (dynapenia)2.
Objectives: Factors associated with deterioration of muscle quality and function were prospectively investigated.
Methods: Muscle quality and function were examined by measuring power, speed, and balance in standing-up motion using an exercise functional analysis device (BM-220, Tanita, Japan) at baseline and at 2-year follow-up in the prospective, observational CHIKARA study. Associations between changes in these parameters (Δ muscle quality, Δ muscle function) and body composition, disease activity, treatment, physical function, and history of falls and fractures were investigated by univariate and multivariate analyses.
Results: Eighty-one RA patients completed the survey. Their average age was 66 years, disease duration was 5.3 years, the simplified disease activity index (SDAI) was 5.3, and the modified Health Assessment Questionnaire (mHAQ) was 0.25 at baseline. Of the patients, 12.3% used GCs at an average dose of 3.08 mg/day over 2 years. The average GC dose was negatively correlated with changes in muscle quality (r=-0.25, p=0.03), power (r=-0.23, p=0.04), and speed (r=-0.24, p=0.03). The SDAI at baseline was negatively correlated with power (r=-0.23, p=0.04) and speed (r=-0.22, p=0.05) (Table 1). No factor was associated with the mHAQ and a history of falls. No independent factor was identified on multiple regression analysis.

Table 1. Associations between changes in muscle quality and function and body composition, disease activity, treatment, physical function, and history of falls and fractures

	Δ muscle quality		Δ muscle function					
			power		speed		balance	
	r	p	r	p	r	p	r	p
age, years	-0.21	0.063	-0.11	0.337	-0.23	0.041	0.18	0.105
GC dose, mg/day	-0.25	0.025	-0.23	0.041	-0.24	0.032	-0.02	0.883
CRP, mg/dl	0.01	0.910	0.03	0.781	0.03	0.799	0.20	0.067
MMP-3, ng/ml	-0.25	0.022	-0.13	0.249	-0.17	0.134	0.02	0.847
DAS28ESR	-0.09	0.441	-0.05	0.665	-0.09	0.435	0.01	0.961
SDAI	-0.14	0.216	-0.23	0.041	-0.22	0.048	0.01	0.917
mHAQ	-0.13	0.248	-0.04	0.728	-0.06	0.578	-0.06	0.585
SMI, kg/m^2	0.03	0.764	<0.01	0.998	0.03	0.761	0.24	0.034
BMR, kcal/day	0.05	0.278	0.01	0.96	0.11	0.322	0.18	0.111
fall	0.07	0.531	0.12	0.286	0.02	0.871	-0.02	0.852
fracture	<0.01	0.973	<0.01	0.989	-0.05	0.677	-0.19	0.097

Δ, changes from baseline; GC, glucocorticoid; CRP, C-reactive protein; MMP-3, matrix metalloproteinase 3; DAS, Disease Activity Score; ESR, erythrocyte sedimentation rate; SDAI, simplified disease activity index; mHAQ, modified Health Assessment Questionnaire; SMI, skeletal muscle index; BMR, basal metabolic rate.

Conclusion: GC use was associated with deterioration in muscle quality and function, as well as sarcopenia development. GC use adversely affected muscle mass, quality, and function. In addition, since high disease activity led to low exercise function, disease activity control is important to prevent deterioration of exercise function.
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FRIDAY, 05 JUNE 2020

Rheumatoid arthritis - biological DMARDs

FRI0084

SAFETY, PHARMACOKINETICS, PHARMACODYNAMICS, IMMUNOGENICITY, AND PRELIMINARY EFFICACY OF ROZIBAFUSP ALFA IN SUBJECTS WITH RHEUMATOID ARTHRITIS: INTERIM ANALYSIS OF A PHASE 1B RANDOMIZED, PLACEBO-CONTROLLED, MULTIPLE ASCENDING DOSE CLINICAL TRIAL

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Background: Autoimmune diseases, including systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA), are associated with autoantibody production and dysregulated T- and B-cell responses. Rozibafusp alfa (AMG 570) is a first-in-class bispecific antibody-peptide conjugate targeting T- and B-cell activity through inhibition of ICOSL and BAFF and is currently in phase 2 clinical development for the treatment of SLE.
Objectives: This interim analysis of a phase 1b study (NCT03156023) reports the safety, pharmacokinetics (PK), pharmacodynamics (PD), immunogenicity, and preliminary efficacy of rozibafusp alfa in subjects with RA.
Methods: Subjects (N~34; age 18–75 years) with active RA, defined as a disease activity score (DAS28-CRP) >2.6, were randomized 3:1 to receive rozibafusp alfa or placebo subcutaneously every 2 weeks for 10 weeks (6 doses), with 24 weeks of follow-up. Subjects were divided into 4 cohorts to study 4 ascending doses of rozibafusp alfa. All subjects were maintained on a stable dose of methotrexate. The primary endpoint was the subject incidence of treatment-emergent adverse events (TEAEs). Additional assessments included serum PK profiles, PD (eg, ICOSL receptor occupancy [RO], changes in peripheral blood B cells), incidence of anti-rozibafusp alfa antibodies, and Patient and Physician Global Assessments (PtGA and PhGA) of disease activity.
Results: As of June 5, 2019, 34 subjects were enrolled and included in this interim analysis. Rozibafusp alfa was generally well tolerated. TEAEs occurred in 92.3% and 87.5% of subjects receiving rozibafusp alfa and placebo, respectively. Most of these events were of grade ≤2 severity. The most common TEAE was upper respiratory infection (23.1%) for subjects receiving rozibafusp alfa and nasopharyngitis (37.5%) for subjects receiving placebo. No treatment-related AEs were of grade ≥3 severity and occurred in >2 subjects. Rozibafusp alfa demonstrated a nonlinear PK profile with greater than a dose-proportional increase in concentration across evaluated doses. The terminal half-life of rozibafusp alfa ranged from 5 to 11 days, with longer half-lives at higher dose levels. ICOSL RO on circulating B-cells was dose-related and reversible; upon multiple dosing, >90% mean RO was observed in cohorts 3 and 4. Treatment with rozibafusp alfa reduced the percentage of naïve B-cells and increased the percentage of memory B-cells in all cohorts. As of March 22, 2019, 2 of 18 (11.1%) rozibafusp alfa-treated subjects developed anti-rozibafusp alfa antibodies with no correlation to safety or AEs. Preliminary analysis of disease-related activity showed a trend for greater numerical improvement from baseline in PtGA and PhGA with rozibafusp alfa vs. placebo in cohorts 3 and 4.
Conclusion: This interim analysis is the first to report the safety and tolerability of multiple ascending doses of rozibafusp alfa in RA subjects, with preliminary efficacy findings observed in the highest dose cohorts. PK/PD analysis demonstrated nonlinear, target-mediated disposition consistent with cell surface target interaction and PD activity consistent with dual ICOSL/BAFF neutralization. These findings informed the design and dose selection of an ongoing phase 2, randomized, placebo-controlled study to assess the efficacy and safety of rozibafusp alfa in subjects with active SLE and inadequate responses to standard of care therapy.
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Amgen Inc., Employee of: Employee of Amgen Inc., Vishala Chindalore Grant/research support from: Nektar Therapeutics for conducted studies, Speakers bureau: > 5 years ago, Stanley Cohen Grant/research support from: Grant and research support from Amgen, AbbVie, Pfizer, Genentech, and Lilly, Consultant of: Consultant for Amgen, AbbVie, Pfizer, Genentech and Lilly, Alan Kivitz Shareholder of: AbbVie, Amgen, Gilead, GSK, Pfizer Inc, Sanofi, Consultant of: AbbVie, Boehringer Ingelheim,,Flexion, Genzyme, Gilead, Janssen, Novartis, Pfizer Inc, Regeneron, Sanofi, SUN Pharma Advanced Research, UCB, Paid instructor for: Celgene, Genzyme, Horizon, Merck, Novartis, Pfizer, Regeneron, Sanofi, Speakers bureau: AbbVie, Celgene, Flexion, Genzyme, Horizon, Merck, Novartis, Pfizer Inc, Regeneron, Sanofi, Maximilian Posch: None declared, Barbara Sullivan Shareholder of: Shareholder of Amgen Inc., Employee of: Former employee of Amgen Inc. Current employee of Ultragenyx, Jane Parnes Shareholder of: Stockholder of Amgen Inc., Employee of: Employee of Amgen Inc.

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FRI0085 RETENTION RATE OF ADALIMUMAB AND ABP 501 IN THE TREATMENT OF A LARGE COHORT OF PATIENTS WITH INFLAMMATORY ARTHRITIS: A REAL LIFE RETROSPECTIVE ANALYSIS

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Background: The recent introduction of ABP 501, an adalimumab biosimilar, in treatment of rheumatic diseases was supported by a comprehensive comparability exercise with its originator. On the other hand observational studies comparing adalimumab and ABP 501 in inflammatory arthritis are still lacking.

Objectives: To compare the clinical outcomes of the treatment with adalimumab, both originator and biosimilar, in a large cohort of patients affected by autoimmune arthritis in a real life setting.

Methods: We retrospectively analysed the baseline characteristics and the retention rate in a cohort of patients who received at least a course of adalimumab (originator or biosimilar ABP 501) in eight Rheumatology Units from January 2003 to January 2020. We stratified the study population according to biosimilar use. Descriptive data are presented by medians (interquartile range [IQR]) for continuous data or as numbers (percentages) for categorical data. Drug survival distribution curves were computed by the Kaplan-Meier method and compared by a stratified log-rank test. P values ≤0.05 were considered statistically significant.

Results: 764 patients (53.4% female, median age 55 [44-65] years, median disease duration 60 [25-149] months) treated with adalimumab were included in the analysis. 308 (40.3%) were affect by rheumatoid arthritis, 244 (31.9%) by psoriatic arthritis, and 212 (27.7%) by axial spondylarthritis. 558 (73%) were treated with adalimumab originator and 206 (27%) with ABP 501. Among the biosimilars 60 (29.1%) patients were naïve to adalimumab treatment. The overall 6-month retentions rate was 93.1%. The 6-month retention rate for adalimumab and ABP 501 were 93.3% and 91.2% respectively, without significant differences between the groups (p=0.541). Patients switching from originator to biosimilar showed and overall higher treatment survival when compared to naive (6-month retention rate 95% vs 90-4%), although it was not significant (p=0.179).

Conclusion: In our retrospective study adalimumab originator and its biosimilar ABP 501 showed the same effectiveness. Patients switching from originator to biosimilar showed an higher retention rate when compared to naive.

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FRI0086 DISEASE ACTIVITY MEASURES AND OTHER POTENTIAL PREDICTORS OF SUCCESSFUL TNF INHIBITORS TAPERING IN RA PATIENTS

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Background: Biologic therapy (BT) resulted in a substantial improvement of outcomes in Rheumatoid Arthritis (RA). However, it is also associated with higher costs, adverse events and patient´s request to dose reduction and drug holidays. Although clinical practice guidelines suggest consider tapering biologics after sustained remission, the optimal approach for de-escalation remains unknown.

Objectives: i) to identify potential features associated with long-term successful TNF inhibitors (TNFi) tapering (Tap) in RA patients (pts), including the possible predictive value of different disease activity measures (DAS28, SDAI, CDAI). ii) to describe long-term outcome in relation to dose reduction of BT.

Methods: Observational prospective study of 91 RA pts who started a first TNFi between 2000-2014 and in whom tapering (dose down-titrated or interval widen) was applied after achieving sustained remission/Low disease activity. Demographic, clinical and analytical data were collected at biologic initiation. Disease activity was measured using DAS28, SDAI and CDAI at de-escalation start and at 6 (6 m), 12 (12 m), 18 (18 m) and 24 months (24 m) follow-up. Tap failure (primary outcome) was defined as reinstatement of full dose, escalation to the previous dose level or discontinuation due to secondary inefficacy. Tap status (Tap failure/success) was also assessed at each studied time point. Mann–Whitney U test and Fisher's exact test were used to test statistical differences. Logistic regression analysis was used to identify predictors of tap failure at 12 and 24 m.

Results: Of the 91 cases included (mean age 53 ±12.5 years, 74% women), eleven (12%) experienced Tap failure at the 12 m mark. At 24 m, 18 pts (20%) failed to taper, while 74 (80%) succeeded. At 12 and 24 m no significant differences were found in baseline and pre-Tap characteristics between those who experienced tap failure and those who succeeded (Table 1). In the univariate analysis, at the 12 m mark, there were no factors related to tapering; however, at 24 m, a longer time from TNFi start to achievement of remission was identified as a predictor of Tap failure (OR=1.64, p=0.02); this feature remained associated with failed Tap at 24 m in the multivariate analysis (OR=1.75, p=0.02). Neither of the three disease activity indices measured at Tap initiation predicted long-term tap failure.

Conclusion: In our cohort of RA patients on tapered TNFi, time from TNFi start to achievement of remission seemed to determine successful tapering of biological treatment. However, disease activity scores measured at dose reduction initiation were not predictive of successful de-escalation strategies.

table

Baseline Characteristics	Pts who presented a tap failure at 24 m (n=18)	Pts who presented a successful tap at 24 m (n=73)	Total population (n=91)	P value
Age at TNFi start (years)	48.4 (13.2)	54 (12.1)	53 (12.5)	P=0.06
Sex (female) n (%)	13 (72)	54 (74)	67 (74)	P=1.00
Non smokers, n (%)	7 (41)	41 (58)	48 (54)	P=0.28
BMI, m (SD)	25.3 (4.8)	25.5 (4.2)	25.5 (4.3)	P=0.75
RF +, n (%)	15 (83)	59 (81)	74 (81)	P=1.00
CCP, + n (%)	13 (72)	58 (82)	71 (80)	P=0.51
Monotherapy, n (%)	3 (17)	8 (11)	11 (12)	P=0.45
Disease duration, m (SD)	8.8 (6.6)	10.2 (7.1)	9.9 (7)	P=0.36
DAS28 at TNFi start, m (SD)	4.7 (1.3)	4.7 (1.1)	4.7 (1.2)	P=0.71
CDAI at TNFi start, m (SD)	25.2 (23.5)	22.5 (12.3)	23.1 (15.1)	P=0.64
SDAI at TNFi start, m (SD)	23.4 (13.7)	22.1 (12.4)	22.3 (12.6)	P=0.9
Pre-Tap Characteristics:				
DAS28 at Tap initiation, m (SD)	2.3 (0.7)	2.4 (0.7)	2.4 (0.7)	P=0.83
CDAI at Tap initiation, m (SD)	3.6 (3)	3.5 (4.2)	3.5 (4)	P=0.47
SDAI at Tap initiation, m (SD)	4.4 (3)	3.8 (4.2)	3.9 (3.9)	P=0.17
Time from TNFi start to achievement of remission	1.9 (1.6)	1.1 (1)	1.3 (1.2)	P=0.08
Time from achievement of remission to tapering	2.2 (2.5)	2.5 (2.6)	2.4 (2.5)	P=0.46

m, mean; SD, standard deviation

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FRI0087 DURABILITY OF CERTOLIZUMAB PEGOL IN PATIENTS WITH RHEUMATOID ARTHRITIS OR PSORIASIS OVER THREE YEARS: AN ANALYSIS OF POOLED CLINICAL TRIAL DATA

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Background: Durability over time varies according to the safety, tolerability and efficacy of a drug.[1] However, durability may vary between patient (pt) subgroups,[1,2] and physicians should consider pt characteristics when making treatment decisions. Certolizumab pegol (CZP) is an anti-tumour necrosis factor (anti-TNF) agent approved for the treatment of chronic inflammatory diseases, including rheumatoid arthritis (RA) and plaque psoriasis (PSO).[3] However, little is known about the impact of pt baseline characteristics on long-term CZP durability.

Objectives: To investigate the durability of CZP and reasons for discontinuation over 3 years (yrs) in subgroups of pts with RA or PSO using pooled clinical trial data.

Methods: 27 RA and 3 PSO clinical trials were pooled for indication-specific analyses. Kaplan-Meier curves were calculated to estimate CZP durability for pt subgroups by age, gender, disease duration, prior anti-TNF use and geographic region. Reasons for CZP discontinuation were investigated.

Results: 6927 RA and 1112 PSO pts were included; mean ages were 53.0 yrs (standard deviation [SD]: 12.2 yrs) and 45.4 (13.0) yrs, respectively. 79.3% RA pts were female (of all patients, 19.4% were women of childbearing age [18–<45 yrs; WoCBA]) compared with 33.5% (15.2% WoCBA) in PSO. Mean disease durations were 6.4 (6.9) yrs for RA and 18.4 (12.3) yrs for PSO. 18.5% RA and 13.3% PSO pts had prior anti-TNF use. Maximum CZP exposure was ~8 yrs for RA and ~3 yrs for PSO. At 1 yr, 63.4% of RA pts remained on CZP vs 80.3% PSO pts, decreasing to 49.2% RA pts and 70.1% PSO pts at 3 yrs (Table 1). Reasons for discontinuation, at any time during the trials, included lack of efficacy (RA 13.5%; PSO 1.8%), adverse events (RA 11.9%; PSO 8.1%), consent withdrawn (RA 6.7%; PSO 6.7%), lost to follow-up (RA 1.8%; PSO 4.3%), protocol violation (RA 1.7%; PSO 0.3%) and other (RA 9.2%; PSO 8.7%). In RA pts, CZP durability was lower in the elderly and in pts with disease duration <1 yr. In PSO, durability was lower in pts with disease duration <1 yr or prior anti-TNF use. Durability was lower in WoCBA pts than male pts aged 18–<45 yrs for both indications. CZP durability was lower in Western Europe and North America compared to other regions.

Conclusion: Overall, CZP durability was similar to that reported for other anti-TNFs with some differences between indication and subgroups.[1] Factors influencing durability included age, disease duration and geographic region. Gender differences were observed in the 18–45 yrs age group, however, both male and female CZP durability was higher than in older RA pts.

Table 1. CZP durability at 3 years,[a] by patient subgroup

% patients	RA	PSO
All	49.2	70.1
Age, yrs		
18–<45	52.1	66.3
45–<65	49.4	68.3
≥65	43.3	69.4
Gender		
Female	49.3	64.1
Male	48.2	69.2
WoCBA	51.1	62.0
Male aged 18–<45 yrs	56.5	68.3
Prior anti-TNF use		
Yes	49.3	60.1
No	49.6	68.5
Disease duration, yrs		
<1	43.2	39.6
1–<5	52.6	63.6
5–<10	51.4	64.4
≥10	48.7	69.7
Region		
Asia-Pacific	58.5	
Central Europe	61.5	78.8
Eastern Europe	54.2	
Latin America	57.1	
N America	36.6	53.9
W Europe	33.8	67.7
Rest of the world	66.3	

[a] For PSO, the 3 year analysis was calculated with Week 144 data. CZP: certolizumab pegol; N: North; PSO: psoriasis; RA: rheumatoid arthritis; TNF: tumour necrosis factor; W: Western; yrs: years.

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[1] Neovius M. Ann Rheum Dis 2015;74:354–60; **2.** Lie E. Ann Rheum Dis 2015;74:970–8; **3.** EMA. CIMZIA SmPC 2019. Available at: https://www.ema.europa.eu [Last accessed 09/01/20].

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FRI0088 CHANGE IN SERUM BILIRUBIN SUGGESTS TREATMENT RESPONSE IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH MOLECULAR-TARGETED AGENTS

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Background: Bilirubin is an antioxidant with anti-inflammatory properties. In previous reports, serum bilirubin levels were correlated with disease activity of autoimmune diseases including rheumatoid arthritis (RA). Various molecular-targeted

agents have been developed for RA, and targets, such as IL-6 and TNFα, are associated with liver function. However, the association between serum bilirubin and treatment response in RA patients treated with molecular-targeted agents is still unknown.

Objectives: We aimed to evaluate the role of serum bilirubin in the prediction of the early treatment response in RA patients who initiated molecular-targeted agents.

Methods: We retrospectively recruited biologic naïve RA patients (n=292) with moderate-to-high disease activity from a tertiary hospital between Jan 2013 and Dec 2019. Patients with viral hepatitis, drug-induced hepatitis, or alcoholic liver disease were excluded. Molecular-targeted agents included tocilizumab (TCZ, n=40), adalimumab (ADA, n=59), etanercept (ETN, n=66), golimumab (GOL, n=60), abatacept (ABA, n=31), and tofacitinib (TOF, n=36). Clinical and laboratory data were collected from electronic medical records. Patients were categorised into an increased bilirubin group (higher serum bilirubin at 3 months than at baseline) and decreased bilirubin group (equal or lower serum bilirubin at 3 months than at baseline). At 6 months of treatment, good response (defined as a DAS28 score ≤3.2) was evaluated. Multivariate logistic regression analysis and multiple linear regression analysis were used to evaluate the association between serum bilirubin and treatment response. The variables included in the multiple logistic and linear regression analyses were age, female sex, rheumatoid factor, prednisolone, DMARDs, baseline liver enzymes, baseline DAS28 score, and components.

Results: The mean serum bilirubin level at baseline was 4.7±1.8 mg/L. After 6 months of treatment, 180 (61.6%) patients achieved good responses. The mean serum bilirubin levels at 3 and 6 months were 5.3±2.3 and 5.5±2.2 mg/L, respectively. At 6 months, a good response was more frequent in the increased bilirubin group than in the decreased bilirubin group (71.2% [99/139] vs. 52.9% [81/153], p=0.001). In multivariate logistic regression analysis, the ORs among good responders at 6 months were 1.221 (95% CI 1.014–1.471, p=0.036) for baseline serum bilirubin and 1.377 (95% CI 1.146–1.654, p=0.001) for the change in serum bilirubin at 3 months. According to target agents, the mean changes in serum bilirubin from baseline to 6 months were 1.9±2.5 for TCZ, 1.0±1.5 for ADA, 0.7±1.9 for ETN, 0.6±2.2 for GOL, 0.3±1.2 for ABA, and 0.4±2.2 for TOF (Figure 1). Among the target agents, TCZ showed a significant increase in the mean serum bilirubin level at 3 and 6 months from baseline. In multiple linear regression analysis performed on TCZ, the change in bilirubin at 3 months was associated with the DAS28 score at 6 months (β=−0.349, p=0.020).

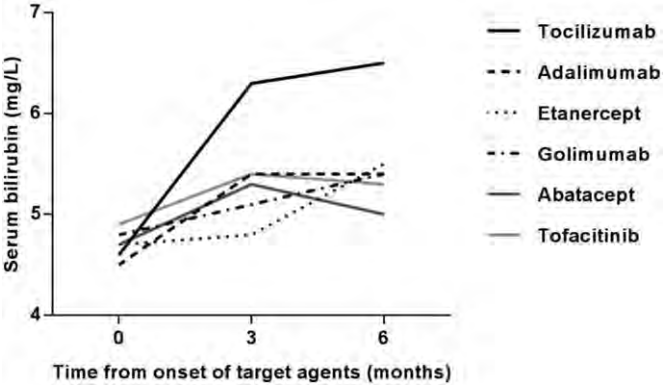


Figure 1. Change in serum bilirubin during treatment with molecular-targeted agents in rheumatoid arthritis patients

Conclusion: High baseline serum bilirubin and an increase in serum bilirubin during treatment are helpful to predict a good response to molecular-targeted agents, especially TCZ.

Disclosure of Interests: None declared

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FRI0089

COMPARATIVE EFFICACY (ACR 20) OF TOCILIZUMAB TO OTHER TARGETED IMMUNE MODULATORS (TIM) FOR RHEUMATOID ARTHRITIS: A NETWORK META-ANALYSIS (NMA)

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Background: Clinical trial and real-world evidence have both firmly established efficacy and safety of intravenous (IV) and subcutaneous (SC) tocilizumab, both as monotherapy or in combination with a conventional disease modifying antirheumatic drug (cDMARD). However, tocilizumab's relative efficacy to the new Janus kinase (JAK) inhibitor class of therapies is less certain, given the lack of head-to-head trials.

Objectives: To evaluate the relative efficacy of: 1) combination tocilizumab plus cDMARD to other TIMs plus a cDMARD in TIM-naïve or mixed (<20% TIM-experienced) adults with moderate to severe RA; 2) tocilizumab monotherapy to other TIM monotherapies in TIM-naïve or mixed adults with moderate to severe RA. Efficacy was defined as achievement of an ACR20 response or better at 24 weeks.

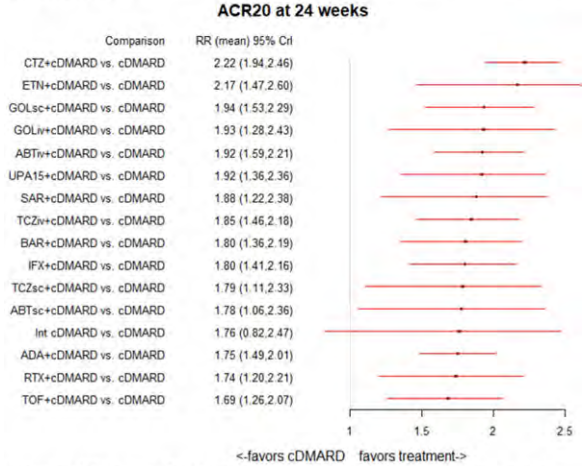
Methods: Randomized controlled trials (RCTs) were selected from a recent systematic literature review conducted by the Institute for Clinical and Economic Review (ICER), as well as from a trial for upadacitinib (SELECT-COMPARE, NCT02629159), which was not included in the ICER 2017 report. Treatments included JAK inhibitors (upadacitinib, baricitinib, and tofacitinib), tumor necrosis factor alpha inhibitors (TNFi; adalimumab, certolizumab pegol, etanercept, golimumab, and infliximab), and other non-TNFis (rituximab, sarilumab, tocilizumab, and abatacept). A Bayesian NMA was performed in OpenBUGS and R to evaluate comparative efficacy using a random effects model for combination therapy and fixed effects model for monotherapy. Model selection was based on deviance information criterion. Forest plots of relative risks (RR) are presented.

Results: In combination therapy analysis, a total of 35 studies were included with a pooled study population of 17,508 patients. Study populations were predominantly female (mean 79%, range 39-95%), and had a baseline mean age of 52 years (range 47-58), mean disease duration of 8 years (range 2-12), and mean DAS28 score of 6 (range 5-7). When compared to cDMARD, all TIMs were 1.69 to 2.22 times more likely to achieve an ACR20 response or better at 24 Weeks (statistically significant) (Figure 1). In pair-wise comparison, tocilizumab IV and SC did not differ from all other TIMs, including JAK inhibitors (no statistically significant difference).

In monotherapy analysis, a total of 5 studies were included with a pooled study population of 1,189 patients. Study populations were predominantly female (mean 82%, range 75-90%), had a baseline mean age of 53 years (range 51-54), mean disease duration of 6 years (range 2-9), and mean DAS28 score of 6 (range 5-7). When compared to cDMARD, all TIMs were 1.65 to 1.84 times more likely to achieve ACR20 response or better (statistically significant) (Figure 2). In pair-wise comparison, tocilizumab IV was associated with a greater likelihood of achieving an ACR20 response or better compared to adalimumab (RR=1.10, 95% credible interval (CrI) = 1.03,1.29).

Conclusion: Results of this NMA demonstrate similar efficacy (ACR20 at week 24) between tocilizumab (IV and SC) and other TIMs, including new JAK inhibitors, when used in combination with a cDMARD among TIM-naïve/mixed patient populations. Tocilizumab IV monotherapy had more favorable efficacy than adalimumab monotherapy. Patients unable to tolerate cDMARDs may experience additional value from tocilizumab compared to adalimumab.

Figure 1. ACR20 at 24 weeks (combination therapy)—Compared to cDMARD all TIMs, in combination with cDMARDs, were 1.69 to 2.22 times more likely to achieve an ACR20 response*

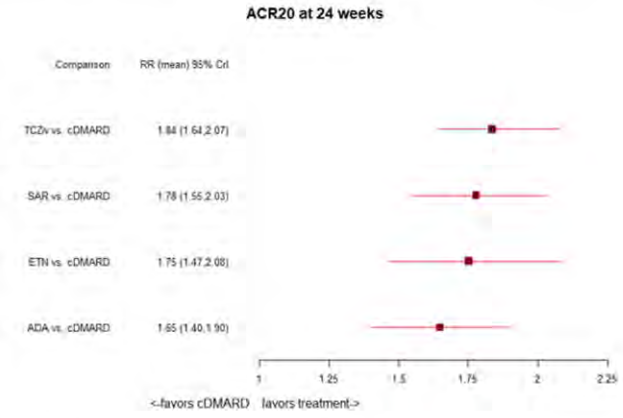


Abbreviations- ABT: Abatacept, ADA: Adalimumab, BAR: Baricitinib, cDMARD: Conventional Disease-modifying Antirheumatic Drugs, CrI: credible interval, CTZ: Certolizumab pegol, ETN: Etanercept, GOL: Golimumab, IFX: Infliximab, Int: Intensive, iv: intravenous, RTX: Rituximab, SAR: Sarilumab, sc: subcutaneous, TOF: Tofacitinib, TCZ: Tocilizumab, UPA: Upadacitinib

* Statistically significant; 95% CrIs do not overlap with 1

cDMARDs are defined as systemic agents with broad immunomodulatory effects like methotrexate, leflunomide, hydroxychloroquine, and sulfasalazine.

Figure 2. ACR20 at 24 weeks (monotherapy)- Compared to cDMARD all TIMs given as monotherapy were 1.65 to 1.84 times more likely to achieve ACR20 response*



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FRI0090

MAINTENANCE OF CLINICAL RESPONSE WITH ABATACEPT IN COMBINATION WITH MTX IN INDIVIDUAL PATIENTS WITH EARLY RA WHO ARE MTX-NAÏVE AND ANTI-CITRULLINATED PROTEIN ANTIBODY (ACPA)+: RESULTS FROM THE INDUCTION PERIOD OF AVERT-2, A RANDOMISED PHASE IIIB STUDY

P. Emery[1], Y. Tanaka[2], V. Bykerk[3], C. Bingham[4], T. Huizinga[5], G. Citera[6], K. H. G. Huang[7], S. Connolly[7], Y. Elbez[8], R. Wong[7], K. Lozenski[7], R. Fleischmann[9]. [1]*LIRMM, University of Leeds, NIHR BRC LTHT, Leeds, United Kingdom*; [2]*University of Occupational and Environmental Health, Kitakyushu, Japan*; [3]*Hospital for Special Surgery, New York, United States of America*; [4]*Johns Hopkins University, Baltimore, United States of America*; [5]*Leiden University Medical Center, Leiden, Netherlands*; [6]*Instituto de Rehabilitación Psicofísica, Buenos Aires, Argentina*; [7]*Bristol-Myers Squibb, Princeton, United States of America*; [8]*Excelya, Boulogne-Billancourt, France*; [9]*University of Texas, Dallas, United States of America*

Background: In the 56-wk induction period (IP) of the Phase IIIb Assessing Very Early RA Treatment (AVERT)-2 trial (NCT02504268), more patients (pts) achieved SDAI remission (≤3.3) with abatacept (ABA) + MTX vs ABA placebo (PBO) + MTX at IP Wk 52.[1] It is unknown whether each individual pt within a treatment (Tx) group achieves and sustains the same efficacy endpoints at all time points during the IP.
Objectives: To investigate whether ABA effectiveness is sustained by individual pts who achieved SDAI remission (≤3.3), SDAI low disease activity (LDA; >3.3–11), DAS28 (CRP) <2.6, ACR50/70 response or Boolean remission at IP Wk 24 (AVERT-2 primary endpoint) and both Wks 40 and 52 (Wks 40/52).
Methods: Pts were randomised 3:2 to blinded SC ABA (125 mg/wk) + MTX or ABA PBO + MTX induction Tx for 56 wks. Key inclusion criteria: age ≥18 yrs; RA diagnosis (ACR/EULAR 2010 criteria); RA duration ≤6 mos; SDAI >11; ACPA+; CRP >3 mg/L or ESR ≥28 mm/h; TJC ≥3 and SJC ≥3; DMARD naïve. Response rates were investigated by Tx arm in the cohort 1 analysis population (all randomised pts treated in the IP [intent-to-treat analysis]).
Results: Of randomised cohort 1, 752 pts were treated during the IP: 451 with ABA + MTX and 301 with ABA PBO + MTX. Baseline characteristics were similar across Tx arms.[1] Stringent SDAI remission endpoint at IP Wk 24 was achieved by 22% of ABA + MTX-treated pts; of these, 56% sustained SDAI remission at IP Wks 40/52 (Table). A similar proportion of ABA + MTX-treated pts achieved (17%) and sustained (58%) Boolean remission at IP Wks 24 and 40/52. At IP Wk 24, 42% of ABA + MTX-treated pts achieved DAS28 (CRP) <2.6 and 74% sustained DAS28 (CRP) <2.6 to IP Wks 40/52; a high proportion of patients sustained ACR50/70 responses at IP Wks 40/52 (83% and 79%, respectively). A lower proportion of pts sustained SDAI LDA to IP Wks 40/52 vs other endpoints (Table). Most efficacy endpoints were achieved by fewer pts who received ABA PBO + MTX than ABA + MTX (Table); among responders in this Tx group, fewer sustained remission at Wks 40/52, which correlates with a higher proportion of pts sustaining SDAI LDA at Wks 40/52 with ABA PBO + MTX than ABA + MTX.
Conclusion: The majority of individual pts with RA who achieved clinically stringent endpoints such as SDAI remission, DAS28 (CRP) <2.6 or Boolean remission, as well as clinically meaningful endpoints such as ACR50/70 at IP Wk 24 with weekly SC abatacept, sustained their responses to Wks 40/52. The high proportion of patients achieving early stringent remission and response to SC abatacept by individual pts may be indicative of sustained efficacy over time.
References:
[1] Emery P, et al. ACR 2018; San Diego, USA: Poster 563.

Table. Proportion of Pts With Response at IP Wk 24 Who Also Achieved Remission at Wks 40/52

	Responders at IP Wk 24, n (%)		Responders at IP Wk 24 and Wks 40/52, n/N (%)	
Endpoint	ABA + MTX (n=451)	ABA PBO + MTX (n=301)	ABA + MTX*	ABA PBO + MTX*
SDAI remission (≤3.3)	100 (22)	40 (13)	56/100 (56)	17/40 (43)
SDAI low disease activity (>3.3–11)	167 (37)	82 (27)	46/167 (28)	32/82 (39)
DAS28 (CRP) <2.6	188 (42)	78 (26)	139/188 (74)	43/78 (55)
ACR50 response†	260 (58)	125 (42)	215/260 (83)	92/125 (74)
ACR70 response†	156 (35)	66 (22)	123/156 (79)	42/66 (64)
Boolean remission	76 (17)	29 (10)	44/76 (58)	8/29 (28)

*% based on number of pts within each Tx group who achieved response at IP Wk 24 (denominator); †Response at IP Wks 24 and 52

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FRI0091

A STUDY OF THERAPEUTIC PREFERENCES IN RHEUMATOID ARTHRITIS AFTER FAILURE OF A FIRST-LINE STRATEGY INCLUDING METHOTREXATE, USING THE DISCRETE CHOICE EXPERIMENTS METHODOLOGY

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Background: Therapeutic decisions in patients with rheumatoid arthritis (RA) who have an inadequate response to methotrexate (MTX-IR) are complex. European guidelines position at the same level all biological disease-modifying anti-rheumatic drugs (bDMARDs) and targeted synthetic DMARDs (tsDMARDs) for the treatment of RA[1,2]. Furthermore, therapeutic decisions, or physician preferences, may be influenced by many factors related to patients and/or physicians.

Objectives: To describe the therapeutic preferences of physicians involved in the management of RA after failure of a first-line strategy (including MTX) and the influence of predefined factors on these preferences.

Methods: We planned to include 216 rheumatologists experienced in the management of RA in this cross-sectional multicenter study. A total of 64 hypothetical clinical cases (vignettes) were developed from a random combination of the following parameters: presence or absence of poor prognostic factors 1) RA-related autoantibodies, 2) structural damage progression on X-ray, 3) high or moderate disease activity, and presence or absence of a history of 4) infection, 5) pulmonary involvement, and 6) cardiovascular disease. Each participant was asked to complete 8 vignettes and were asked to choose the most and least appropriate therapeutic option (best-worst [BW] scaling method) from 3 of the following: replacing MTX by another conventional (c) sDMARD; adding one or more csDMARDs to MTX; adding a bDMARD (TNF inhibitor [TNFi], tocilizumab [TCZ], abatacept [ABA] or rituximab [RTX]). Each vignette was completed 10 times per participant. Physician preferences were assessed using discrete choice experiments methodology. Therapeutic option preference was expressed using a score – one point incremented when considered most appropriate; or removed when considered least appropriate. The therapeutic score was standardized for each vignette, ranging from -1 (more often chosen as the least appropriate) to +1 (more often chosen as the most appropriate). A normalized Best-to-Worst (BW) Score was then computed. The multiplication of vignettes and therapeutic options were used to elicit participants' preferences without directly asking them to state their preferred options[3,4,5]. Statistical analyses were carried out using SAS (version 9.4), or R (version 3.5.1).

Results: A total of 211 French rheumatologists were recruited. Half of them had a hospital-only activity, 25% office-only activity and the rest had mixed activity. Each vignette was assessed by between 20 and 28 rheumatologists with a 94% completion rate. TNF inhibitors were the strategy of choice in 80% of the vignettes. ABA was the second preferred strategy in 75% of the vignettes; except in the 20% of patients with a history of infection and pulmonary comorbidity where it was the first choice. TCZ was chosen as a third strategy. All other strategies were associated with a negative BW score. Factors related to the prescribing physician appear to have no or only a limited impact on therapeutic decisions.

Conclusion: This study provides information on the prescription habits of French rheumatologists in MTX-IR patients in RA, and reveals a conservative trend with TNFi the main therapeutic choice and ABA for patients with pulmonary involvement or high risk of infection. The study should be repeated in the future to include new therapeutic options.

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FRI0092 LONG-TERM SAFETY AND EFFICACY OF SARILUMAB OVER 5 YEARS IN PATIENTS WITH RHEUMATOID ARTHRITIS REFRACTORY TO TUMOR NECROSIS FACTOR INHIBITORS

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Background: Sarilumab is a human IL-6 receptor (IL-6R) inhibitor approved for the treatment of adults with moderate to severely active rheumatoid arthritis (RA). In the TARGET study (NCT01709578), sarilumab plus conventional synthetic disease-modifying antirheumatic drugs (DMARDs) significantly improved signs and symptoms of RA and physical function versus placebo in patients refractory to tumor necrosis factor (TNF) inhibitors.

Objectives: Here we report the long-term safety and efficacy of subcutaneous (SC) sarilumab over 5 years in patients who continued treatment in the open-label extension study (OLE), EXTEND (NCT01146652).

Methods: Patients who received double-blind placebo, sarilumab 150 mg, or sarilumab 200 mg every 2 weeks (q2w) in the 24-week randomized controlled trial (RCT) were eligible to receive open-label sarilumab 200 mg q2w in the OLE, with dose reduction to 150 mg q2w permitted to manage laboratory abnormalities or per investigator's discretion. Safety outcomes are presented for the OLE population for the follow-up from RCT baseline through OLE cut-off date. Efficacy assessments included Clinical Disease Activity Index (CDAI) score and the proportion of responders (CDAI ≤10 and ≤2.8) over time.

Results: Of the 546 patients randomized in the RCT, 454 (83%) entered and were treated with sarilumab 200 mg in the OLE (original placebo group n = 156; sarilumab 150 mg n = 145; sarilumab 200 mg n = 153). Demographics and disease characteristics at OLE baseline were similar across groups (mean age 53.2 years; 81% female; mean RA duration [SD] 11.8 years [8.9]). At the time of data cut-off (January 15, 2019), 199/546 (36%) patients had discontinued: 100 (18%), 68 (13%), and 27 (5%) due to treatment-emergent adverse events (AEs), other reasons, and lack of efficacy, respectively. Cumulative exposure to sarilumab through the RCT and OLE (n=521) was 1654.8 patient-years (PY), and 268 patients (51%) had ≥4 years' exposure. The rates per 100 PY of AEs, serious AEs, AEs leading to discontinuation, and AEs leading to death were 160.4, 10.2, 8.1, and 0.3, respectively. The most common AEs were neutropenia and injection site erythema (15.3 and 11.9 per 100 PY). Absolute neutrophil count <1000 cells/mm^3 (Grade 3–4 neutropenia) was observed in 74 patients (14.2%) and normalized on treatment in 48 (9.2%). Alanine aminotransferase >3× the upper limit of normal was observed in 46 patients (8.8%) and normalized on treatment in 25 (4.8%). Infections and serious infections occurred at rates of 57.8 and 3.9 per 100 PY, respectively. Clinical efficacy was sustained through 5 years of the OLE (Table). At OLE Week 240 (n = 95) mean change (SD) in CDAI from RCT baseline was –31.2 (14.6).

Table. Proportion of responders*

	Original RCT group		
	Placebo +DMARD (n=156)	**Sarilumab 150 mg +DMARD (n=145)**	**Sarilumab 200 mg +DMARD (n=153)**
CDAI ≤2.8, n (%)			
OLE baseline	21 (13)	26 (18)	23 (15)
After 192 weeks' follow-up	17 (11)	28 (19)	28 (18)
CDAI ≤10, n (%)			
OLE baseline	62 (40)	75 (52)	76 (50)
After 192 weeks' follow-up	57 (37)	61 (42)	66 (43)

*Nonresponder imputation

Conclusion: The safety profile of sarilumab was consistent with results of Phase 3 trials, IL-6R inhibition, and SC administration, and no new safety signals were identified over 5 years of follow-up in patients with RA refractory to TNF inhibitors. Clinical efficacy was sustained through 5 years' follow-up.

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Shareholder of: Sanofi Genzyme, Employee of: Sanofi Genzyme, Henry Leher Shareholder of: Regeneron Pharmaceuticals, Inc., Employee of: Regeneron Pharmaceuticals, Inc., Amy Praestgaard Employee of: Sanofi Genzyme, Gerd Rüdiger Burmester Consultant of: AbbVie Inc, Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB Pharma, Speakers bureau: AbbVie Inc, Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB Pharma

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FRI0093 FACTORS ASSOCIATED WITH REFRACTORY RHEUMATOID ARTHRITIS (RRA) ACCORDING TO THREE AVAILABLE DEFINITIONS: TWO CROSS-SECTIONAL ANALYSES IN A LARGE ITALIAN MONOCENTRIC COHORT

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Background: Three definitions of refractory rheumatoid arthritis (RRA) have been proposed: Buch's (B-RRA), i.e. failure of ≥1 anti-cytokine and ≥1 cell-targeted bDMARD [1]; Kearsley-Fleet's (KF-RRA), i.e. exposure to ≥3 bDMARDs classes [2]; De Hair's (DH-RRA), i.e. signs and/or symptoms of RA activity and failure of ≥1 csDMARD and ≥2 bDMARDs [3].

Objectives: To evaluate the rate of RRA according to the three definitions in a monocentric cohort with two cross-sectional analyses in 2012 and 2019. We investigated also the major determinants of each definition. Secondary objective was to evaluate the most frequent treatments in RRA patients.

Methods: Patients affected by RA followed at Padova University Hospital were included at two different time points. In the 2012 cohort patients on bDMARDs on 31st December 2012 and in the 2019 cohort patients on b/target synthetic DMARDs (tsDMARD) on 1st March 2019. Factors independently associated with RRA definitions were tested with multivariable regression analysis, including all variables achieving a p<0.10 in the univariate analysis.

Results: We included 260 patients in the 2012 cohort and 571 in the 2019 cohort. Rate of RRA in 2012 cohort was: 23 (8.8%) B-RRA, 57 (21.9%) KF-RRA and 12 (4.6%) DH-RRA; rate of RRA in 2019 cohort was: 165 (28.9%) B-RRA, 96 (16.8%) KF-RRA and 57 (10%) DH-RRA. Following multivariate regression analysis, in the 2012 cohort a significant association was found between number of bDMARDs treatment and all RRA definitions [Tab.1]. Also in the 2019 cohort the variable associated with all RRA definitions was the number of bDMARDs treatment [Tab.2]. Both in 2012 and 2019, IL6-inhibitors were more frequently prescribed in RRA patients; instead TNF inhibitors were less frequently prescribed in RRA.

Conclusion: Rate of RRA in the 2019 cohort was 10-30% which is higher compared to the 2012 cohort. This might be explained by the fact that RRA definitions are mainly affected by the number of bDMARDs. Thus, an accurate RRA definition should consider not only the number of treatments but also the current disease activity.

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Table 1. Factors associated with three definitions of RRA in the 2012 cohort, multivariate analysis

Characteristics		OR (95% C.I.)	p value
	B-RRA		
CRP	per mg/L increase	0,81 (0,68-0,95)	0,011
HAQ	per unit increase	3,28 (0,85-12,54)	0,84
Combination with any csDMARD		4,61 (0,65-32,59)	0,124
bDMARD treatment duration	per year increase	0,58 (0,52-1,03)	0,114
No bDMARDs		91,0 (7,87-1055,58)	<0,001
Model constant			0,009
	KF-RRA		
PDN	per mg increase	1,49 (0,87-2,56)	0,144
DAS28	per unit increase	4,22 (1,4-12,71)	0,011
No bDMARDs		- (0-0)	0,99
Model constant			0,989
	DH-RRA		
Combination with any csDMARD		6,24 (0,69-56,61)	0,614
Comorbidity		12,82 (0,46-1122,91)	0,065
No bDMARDs	per unit increase	6,25 (2,75-121,39)	0,003
Model constant			0,002

B-RRA refractory RA according to Buch, *KF-RRA* refractory RA according to Kearsley-Fleet, *DH-RRA* refractory RA according to De Hair

Table 2. Factors associated with three definitions of RRA in the 2019 cohort, multivariate analysis

Characteristics		OR (95% C.I.)	p value
	B-RRA		
No. bDMARDs		18.77 (11.06;31.85)	p<0.001
PDN daily dose	per 5 mg increase	2.15 (1.17;2.15)	0.014
Model Constant			p<0.001
	KF-RRA		
BMI	per 5 unit increase	0.61 (0.35;1.05)	0.072
No. bDMARDs		8.69 (5.16;14.64)	p<0.001
bDMARD treatment start year	per year increase	0.92 (0.84;1.01)	0.087
Model Constant			0.069
	DH-RRA		
No. bDMARDs		3.9 (2.67;5.71)	p<0.001
bDMARD treatment start year	per year increase	0.91 (0.83;0.99)	0.026
DAS28	per 0.6 unit increase	5.55 (3.34;9.23)	p<0.001
RX progression		2.7 (1.21;6.03)	0.015
Model Constant			0.04

B-RRA refractory rheumatoid arthritis according to Buch, *KF-RRA* refractory rheumatoid arthritis according to Kearsley-Fleet, *DH-RRA* refractory rheumatoid arthritis according to De Hair, *RX progression* (mTSS ≥0,5 over the last 24 months)

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FRI0094 SIGNIFICANT IMPROVEMENT OF NT-PROBNP LEVELS IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH TOCILIZUMAB AND TOFACITINIB

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Background: N-terminal pro-brain natriuretic peptide (NT-proBNP) is a recognized predictor of congestive heart failure (CHF) and cardiovascular death. Rheumatoid arthritis (RA) patients (pts) were shown to have higher NT-proBNP concentrations than in general population, but it remains unclear, whether NT-proBNP levels are related to RA duration, activity or treatment.

Objectives: To investigate the effect of interleukin 6 receptor inhibitor - tocilizumab (TCZ) and JAK inhibitor - tofacitinib (TOFA) on NT-proBNP levels in RA pts during a 12-month (m) follow-up period.

Methods: The study enrolled 60pts (50women/10men) with the lack of efficacy/resistance and/or intolerance of basic anti-inflammatory drugs (DMARDs); median age was 55[42;61] years, median disease duration 55[29;120]m, with moderate to high activity (DAS28-5,1[4,6;6,1], serum positivity for rheumatoid factor (RF)(85%)/ anti-cyclic citrullinated peptide antibodies (ACCP)(80%). The study did not include RA pts with CHF and clinically overt cardiovascular disease (CVD). Twenty nine RA pts received TCZ(8mg/kg) every 4 weeks: 61% received TCZ in combination with methotrexate (MTX), 35% - with low-dose glucocorticoids (GCs). Thirty one RA pts were prescribed oral TOFA at 5 mg BID with dose escalation to 10 mg BID in 8 (26%)pts. TOFA was used in combination with MTX in 90% pts, with GCs – in 29% pts. Pts treated with TCZ and TOFA were comparable in terms of age, sex, body mass index. RA activity rates (DAS28, SDAI, ESR, CRP) were higher in pts on TCZ -therapy compared with pts treated with TOFA. Echocardiography data and NT-proBNP levels using electrochemiluminescence method Elecsys proBNP II (Roche Diagnostics, Switzerland) were obtained at baseline and after 12m.

Results: Significant positive changes in major disease activity, clinical and laboratory parameters were found in RA pts after 12 m of TCZ infusion and TOFA intake: remission (DAS28<2,6) was achieved in 54% and 39% pts, low activity levels (DAS28<3,2) – in 46% and 51% pts, respectively.

The NT-proBNP levels were significantly higher in RA pts than in the control group (median 69,1 (37,9;105,8) pg/mL vs 55,3 (36,6;67,3) pg/mL, $p<0.05$).

Six pts (10%) (three in each pts group) had NT-proBNP levels over 125pg/ml, but were asymptomatic and had unremarkable echocardiography.

There was a good correlation between NT-proBNP level at baseline with age (r=0,55, $p<0,001$), SDAI (r=0,5, h=0,01), ACCP (r=0,23, $p=0,01$).

Decrease of median NT-proBNP levels was documented after 12m of TCZ therapy (81,5[43,0;102,0]vs41,6[25,4;64,2]pg/ml ($p<0,01$) and after 12m TOFA therapy (66,1[30,5;105,0]vs16,8 [5,0;81,0]pg/ml, $p=0,001$).

After 12m of TCZ correlations of ΔNT-proBNP were established with ΔESR (R=0,43;p<0,05], ΔCRP (R=0,46;p<0,05], ΔEe left ventricle (LV) (r=0,88,p=0,03).

In the group of pts treated with TOFA ΔNT-proBNP level significantly correlated with the percentage change in DAS 28 (r=0,41,p=0,038), there was no direct correlation with changes in the parameters of the LV diastolic function.

Conclusion: TCZ and TOFA treatment for 12 m reduced NT-proBNP levels in RA pts without clinically manifest CVD and CHF. Falling NT-proBNP concentrations are associated with positive dynamics of RA activity (DAS 28) and inflammatory markers (CRP, ESR), therefore allowing to suggest that increased NT-proBNP levels should be considered as a component of disease activity. Correlation between ΔNT-proBNP and ΔEeLF may be indicative as possible impact of these biomarkers on the LV diastolic function's development in RA pts.

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FRI0095 SARILUMAB IMPROVED PATIENT-PERCEIVED IMPACT OF RHEUMATOID ARTHRITIS WHATEVER THE BASELINE DISEASE ACTIVITY: FIRST RESULTS FROM AN INTERVENTIONAL NON CONTROLLED STUDY: SARIPRO, IN MODERATE AND SEVERE RHEUMATOID ARTHRITIS PATIENTS

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Background: Sarilumab, an anti-IL-6R antibody, is approved for the treatment of moderate to severe RA and shown efficacy on disease activity and patient-reported outcomes (PROs). Detailed analyses of drug efficacy from the patient point of view is important. SariPRO is a pragmatic interventional study close to the daily practice.

Objectives: To assess the effectiveness of sarilumab on several PROs using the RAID (Rheumatoid Arthritis Impact of Disease) score.

Methods: The SariPRO study (NCT 03449758) was a French multicenter interventional study assessing the effects of sarilumab 200 mg on PROs in patients with moderately to severely active RA with an inadequate response or intolerance to conventional synthetic or biologic DMARDs. The primary endpoint was change in total RAID score from baseline to week 24 (RAID ranges 0-10 where 10 is maximal impact). Changes from baseline for RAID, DAS28-ESR and CDAI according to baseline disease activity were analyzed as secondary outcomes. Safety was assessed by monitoring adverse events (AE). All statistical analyses were descriptive, 95% CI was given when appropriate.

Results: 84 patients were included in 31 centers and 62 were evaluable and analyzed for effectiveness. They had similar characteristics to the 84 patients at baseline and were as expected for an RA population initiating a biologic: mean (SD) age: 59.9 (12.4) years, 71.0% female, disease duration 9.7 (10.3) years, rheumatoid factor positivity 82.5%, ACPA positivity 86.4%, and DAS28=4.9 (11). Total RAID score decreased significantly from 5.7 (2.0) at baseline to 3.3 (2.5) at W24; mean change was -2.4 [95% CI: -3.0; -1.8]. Furthermore, this improvement was noted both for highly and less active patients at baseline: for patients with DAS28-ESR < 5.1 (n=31), mean change was -1.56 [-2.28; -0.83] and for patients with DAS28-ESR≥5.1 (n=27), mean change was -1.98 [-2.91; -1.05]. Changes in DAS28-ESR and CDAI were significant (-2.8 [-3.2; -2.4] and -15.2 [-18.5; -11.8], respectively). AEs were consistent with the safety profile of anti-IL-6R antibodies and with results from RCTs (data not shown).

Conclusion: In this real world study, treatment with sarilumab during 24 weeks in RA patients led to an improvement in the total RAID score irrespective of baseline levels of disease activity. This is the first time RAID score is used as the primary endpoint in a study.

References:

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FRI0096 CLINICAL BENEFITS REPORTED IN AMPLE TRIAL OBSERVED IN A REAL-WORLD (RW) COHORT OF US RHEUMATOID ARTHRITIS (RA) PATIENTS

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Background: Efficacy observed in controlled trials may not reflect RW effectiveness, given documented differences in patient populations and management.[1]

Objectives: This study aimed to assess disease measures over time as measured in a trial setting (AMPLE) and in a separate RW observational setting, both among patients with RA treated with abatacept.

Methods: The RW cohort comprised retrospective patient-level data abstracted by 31 community rheumatologists for adult RA patients treated with abatacept who had an anti-cyclic citrullinated peptide-2 titer ≥250 AU/mL. AMPLE was a phase III, randomized controlled trial of RA patients treated with abatacept that assessed disease measures over a 2-year follow-up. Data included demographics, treatments, labs, and disease measures (tender and swollen joint counts (TJC, SJC), C-reactive protein (CRP), American College of Rheumatology-20 (ACR20) and ACR50 at baseline and 3 and 6 months) and were summarized descriptively. Disease measures were evaluated across AMPLE and RW cohorts.

Results: Of the 291 RW patients and 318 AMPLE patients, the majority were female (70%, 81%), white (72%, 81%), and RF-positive (91%, 76%), respectively (Table 1). The mean ages at abatacept initiation were 54.7 and 51.4 years

Table 1: Patient Characteristics.

	RW cohort (n=291)	AMPLE cohort (n=318)
Female (n, %)	205 (70%)	259 (81%)
White (n, %)	209 (72%)	257 (81%
Age at abatacept initiation, years (mean, SD)	54.7 (14.8)	51.4 (12.6)
RF-positive* (n, %)	249 (91%)	240 (76%)
Concomitant medications (n, %)		
Corticosteroids†	132 (45%)	207 (65%)
Methotrexate	179 (62%)	318 (100%)
Prior biologic use (n, %)	241 (83%)	0 (0%)
Route of administration (n, %)		
Intravenous	183 (63%)	0 (0%)
Subcutaneous	108 (37%)	318 (100%)

LEGEND: *among 274 with known RF status; †corticosteroids in AMPLE cohort at any time in the 2-year study period

old in RW and AMPLE, respectively. Concomitant corticosteroids (45%, 65%) and methotrexate (62%, 100%) were common in RW and AMPLE, respectively. All patients in AMPLE were biologic naïve, whereas 83% of RW patients had prior biologic use. AMPLE administered abatacept subcutaneously (SC), while 37% of RW patients received abatacept SC. Patients had median SJC and TJC of 6 and 8 in RW and 13 and 22 in AMPLE at abatacept initiation, respectively (Table 2). SJC (TJC) improved a median of 65% (60%) and 68% (66%) at 3 months and 75% (67%) and 76% (75%) at 6 months in RW and AMPLE, respectively (Fig 1). The majority of patients achieved ACR20 at 3 months (79% and 60%) and 6 months (88% and 66%) in RW and AMPLE, respectively, while 58% and 32% achieved ACR50 at 3 months and 67% and 45% at 6 months, respectively (Fig 2).

Table 2. Changes in Disease Activity.

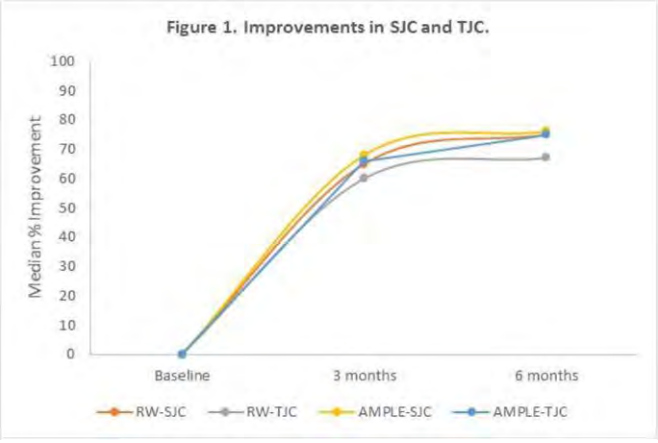
	RW cohort (n=291)	AMPLE cohort (n=318)
SJC (median)		
Baseline value	6	13
3-month value	2	4
6-month value	1	3
TJC (median)		
Baseline value	8	22
3-month value	3	7
6-month value	2	5
CRP, mg/dL (mean)		
Baseline value	1.08	1.6
3-month value	0.47	0.8
6-month value	0.30	0.8
ACR20 achieved (n, %)		
3-month value	194 (79%)	191 (60%)
6-month value	78 (88%)	209 (66%)
ACR50 achieved (n, %)		
3-month value	144 (58%)	103 (32%)
6-month value	60 (67%)	144 (45%)

LEGEND: values soonest after 3 months and value between 6-9 months used for RW cohort; values at days 85 and 197 used for AMPLE cohort.

Conclusion: Despite differences in patient characteristics, improvements in SJC and TJC, as well as high rates of ACR20 and ACR50, were observed in both trial setting and RW settings. These improvements in disease activity were observed at similar magnitudes in both settings, demonstrating that trial efficacy is achievable in RW clinical practice with abatacept treatment.

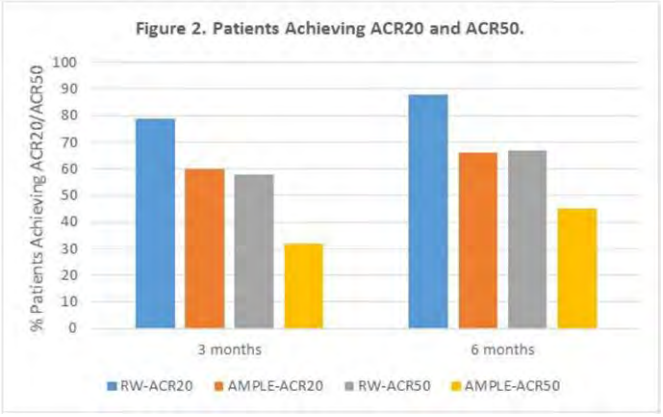
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FRI0097

EFFECTS OF BIOLOGICAL DISEASE-MODIFYING ANTI-RHEUMATIC DRUG TREATMENT ON PHYSICAL ACTIVITY, MUSCLE POWER, AGILITY AND INHIBITION OF FALL IN PATIENTS WITH RHEUMATOID ARTHRITIS -THE 2-YEAR RESULTS

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Background: Treatment with biological DMARDs (bDMARDs) rapidly improves signs and symptoms in patients with rheumatoid arthritis (RA). The efficacy of these bDMARDs was evaluated using composite measures or biomarkers used in daily clinical practice or clinical studies. Although a rapid improvement in composite measures or biomarkers is important in the treatment of RA, the primary goal of treatment is improvement of long-term health-related quality of life (HR-QOL) [1]. HR-QOL is evaluated based on physical functions (PF) such as muscle power and agility. We reported the 1-year results of our study presented at EULAR 2019 [2]. The present study was conducted to investigate the 2-year results of our study by including more patents than those included in the previous one.

Objectives: This study was aimed at investigating the efficacy of bDMARDs with respect to PF and fall risk in RA patients.

Methods: At our institute, in addition to routine rheumatology evaluation, periodic evaluation of physical function is performed by staff members in our rehabilitation center in RA patients in whom the first bDMARD treatment was initiated in Oct. 2015–Feb. 2018. In total, 41 cases were registered in this study. Evaluation of PF included evaluation of muscle power [grasping power (GP) and knee extension power (KEP)]; agility [time up and go test (TUG) and 10-m walking time (10 mW)]; and a questionnaire using modified HAQ, portable fall risk index [3], and the 25-question geriatric locomotive function scale (locomo25) [4] at baseline (BL), which implies the time at the initiation of bDMARD treatment, i.e., 1, 3, 6, 12, and 24 months. Disease activity of RA was evaluated at the same time points. Although 2 years had elapsed from BL in 37 patients, 13 patients dropped out from the evaluation of physical function owing to cessation of bDMARD treatment, rejection of evaluation for physical function, or major joint surgery performed in a patient. The results of 24 patients who completed the evaluation at 24 months were investigated in this study.

Results: Baseline characteristics of the 24 patients were as follows: mean age 60.8 years, RA duration 12.3 years, mean SDAI 19.0, and mean CRP level 2.1 mg/dl. The bDMARDs used in the study were abatacept in 7 patients, adalimumab in 4 patients, tocilizumab in 4 patients, golimumab in 4 patients, etanercept in 3 patients, certolizumab in 1 patient, and an infliximab biosimilar in 1 patients. Data are presented as mean values at BL and at 1, 3, 6, 12, and 24 months (Fig.1). SDAI and CRP levels were significantly improved at and after 1 month. GP and KEP were significantly improved at and after 3 and 6 months. TUG and 10 mW results were significantly improved at and after 3 and 6 months. Modified HAQ results were significantly improved at and after 3 months. Locomo25 scores were significantly improved at and after 1 month. Portable fall risk index values were significantly improved at and after 12 months.

Fig1. Change of Mean Values and P-value during bDMARDs Treatment in RA Patients

	Baseline	1 month	3 months	6 months	12 months	24 months
SDAI	19.0 (Cont.)	9.8 (<0.01)	6.7 (<0.01)	6.3 (<0.01)	5.5 (<0.01)	4.7 (<0.01)
CRP (mg/dl)	2.1 (Cont.)	0.7 (<0.01)	0.8 (<0.01)	0.7 (<0.01)	0.4 (<0.01)	0.1 (<0.01)
Grasping Power (kg)	11.9 (Cont.)	13.2 (0.08)	14.4(<0.01)	15.4 (<0.01)	16.6 (<0.01)	18.3 (<0.01)
KEP (N/kg)	3.0 (Cont.)	3.1 (0.11)	3.3 (0.08)	3.5 (<0.01)	3.7 (<0.01)	3.9 (<0.01)
TUG (second)	9.1 (Cont.)	8.2 (0.055)	8.2 (<0.05)	7.4 (<0.01)	7.6 (<0.05)	7.5 (<0.01)
10mW (second)	8.0 (Cont.)	7.5 (0.0503)	7.4 (0.26)	6.8 (<0.01)	6.8 (<0.01)	6.9 (<0.01)
mHAQ	0.48 (Cont.)	0.40 (0.12)	0.24 (<0.01)	0.26 (<0.01)	0.20 (<0.01)	0.22 (<0.05)
Locomo25	29.1 (Cont.)	21.1 (0.02)	18.4 (<0.01)	18.9 (<0.01)	16.0 (<0.01)	15.0 (<0.01)
Fall risk index	8.5 (Cont.)	8.4 (0.61)	7.8 (0.13)	8.0 (0.25)	7.1 (<0.01)	7.2 (<0.05)

Data is expressed as mean (p-value). P-value was caluculated using Wilcoxon signed-rank test between baseline and each month.
SDAI: simplified disease activity index, KEP: knee extention power, TUG: timed up and go test, 10mW: 10m walking time, mHAQ: modified health assessment questionnaire

Conclusion: Although there was a rapid improvement in the signs and symptoms of RA after the initiation of bDMARD treatment, improvement in PF was slightly delayed. Significant improvement of muscle power and agility was achieved after 3–6 months onward. Inhibition of fall risk was achieved at and after 12 months after the initiation of bDMARD treatment. These results suggest that physiotherapy plays a vital role in RA patients who undergo treatment with bDMARDs to gain more rapid improvement of PF.

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Disclosure of Interests: Yuji Hirano Speakers bureau: Tanabe-Mitsubishi, Pfizer, Eisai, Abbie, Chugai, Bristol-Meyers, Jansen, Astellas, UCB, Eli-Lilly, Asahikasei, Daiichi-Sankyo, Amgen, Ayako Morisaka: None declared, Hironobu Kosugiyama: None declared, Shiori Inuzuka: None declared, Takeshi Kamiya: None declared, Hiroyuki Mori: None declared, Naohito Morishima: None declared, Tomoji Ishikawa: None declared

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FRI0098 ASSOCIATION BETWEEN THE SEROLOGIC STATUS OF ISOTYPE-SPECIFIC AUTOANTIBODIES AND THERAPEUTIC EFFICACY IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH ABATACEPT: A PROSPECTIVE ULTRASOUND COHORT STUDY IN JAPAN

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Background: The presence of anti-cyclic citrullinated protein antibodies (ACPA) and anti-carbamylated protein (anti-CarP) antibody is specific for rheumatoid arthritis (RA). Recently, it was reported that the serological status of ACPA is associated with the therapeutic response of the T-cell co-stimulation blocker abatacept (1, 2). However, it is currently unclear whether the serological status of each isotype levels of these autoantibodies before treatment introduction or the changes during treatment are associated with the therapeutic response of abatacept.

Objectives: To evaluate longitudinal changes in the isotypes of ACPA and anti-CarP in RA patients treated with abatacept, and associations between the baseline serological status/ these changes and clinical response/ ultrasonographic response.

Methods: This study is part of an ongoing non-randomized multicenter prospective cohort study of patients with active RA who received biological or targeted DMARD therapy at 13 participating rheumatology centers from the Kyushu region of Japan since June 2013 (3). As of the present report, we enrolled 43 consecutive Japanese patients with active RA who have introduced treatment with abatacept and had finished the first 12-month observation period. We evaluated disease activity by clinical composite measure and ultrasound score at baseline, 3, 6, 9 and 12 months. In ultrasound of bilateral hands from 22 sites, the findings obtained by gray-scale (GS) and power Doppler (PD) assessments were graded on a semi-quantitative scale from 0 to 3 and the sum of GS or PD scores was used as the total GS or PD score. The serum levels of IgG/IgM/IgA-type of ACPA and anti-CarP were measured by the ELISA method in Leiden University Medical Center. We evaluated the association between serologic status of autoantibodies and clinical /ultrasonographic therapeutic efficacy.

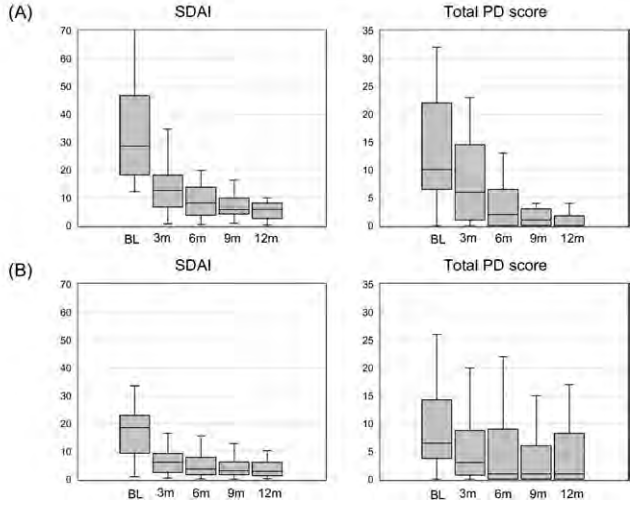
Results: The median age was 72 years, and the disease duration was 54 months. Methotrexate was concomitant in 22 (51%). Sixteen (37%) patients had a history of previous use of biological DMARDs. Nineteen (44%) and 23 (54%) patients achieved SDAI remission and PD remission (total PD score =0) at 12 months, respectively. The serum levels of all isotypes of ACPA/anti-CarP significantly decreased at 12 months from baseline. The reduction of IgM-ACPA level significantly correlated with the reduction of SDAI (rs=0.33, p=0.031) and total PD score (rs=0.49, p=0.0007). Both clinical and ultrasonographic therapeutic responses were better in patients with the detectable IgM-ACPA at baseline than in patients without that (Figure): the reduction of SDAI (p=0.0078) and that of total PD score (p=0.0079) were significantly larger in the former than in the latter. All isotype of anti-CarP did not associate with therapeutic response.

Conclusion: Treatment of abatacept induced to the reduction of the autoantibody levels. The IgM-ACPA level at baseline and the change in IgM-ACPA associated with both clinical and ultrasonographic therapeutic response in patients treated with abatacept. IgM-ACPA, compared with usual IgG-ACPA, better reflects the treatment response of abatcept in patients with RA

References:

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Figure 1. Clinical and ultrasonographic response in patients with the detectable IgM-ACPA at baseline (A) than in patients without that (B).



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FRI0099 THE IMPACT OF BIOLOGICAL DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS ON THE COURSE OF RHEUMATOID ARTHRITIS-ASSOCIATED LUNG DISEASE

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Background: Pulmonary involvement is one of the frequent extra-articular manifestations of rheumatoid arthritis (RA) (1). Biological disease-modifying anti-rheumatic drugs (bDMARDs) are effectively used in the treatment of musculoskeletal findings of RA but their effect on RA-associated lung disease is unclear.

Objectives: The aim of this retrospective study is to evaluate and compare different bDMARD treatments used in RA patients with RA-associated lung disease.

Methods: All RA patients who received bDMARDs between 2008 and 2018 in a single rheumatology centre and had thorax high-resolution computed tomography (HRCT) were reviewed for the findings of lung involvement. Patients with positive finding were included in the study. Following the biologic treatment, whether there was a progression/regression in lung involvement was evaluated by comparing the baseline and the latest thorax HRCT findings. Clinical and laboratory data were collected from medical records.

Results: A total of 40 patients (mean age:62.4 years; 72.5% women) were included in the study. Clinical and demographic characteristics of patients are summarized in Table 1. During the mean 107.43 ± 65 months follow-up period, HRCT findings remained stable in 31 patients (76%) and improved in one (2.5%), while 7 patients (17.5%) had progress in their lung involvement. When patients with and without progress were compared, lung involvement at the diagnosis of RA and the presence of respiratory symptoms at bDMARDs initation was found to be more frequent in the first group (p=0.023 and p=0.020, respectively). Mean ESH values at bDMARDs initation were also higher in patients who had progress (p=0.006). There was no significant difference between the groups in the age, sex, type of bDMARDs used or other baseline laboratory data. Logistic regression analysis showed that lung involvement at the diagnosis of RA was a significiant independent risk factor for the progress (OR: 11.0, 95% CI=1.48-81.60). There was no statistically difference on progression of HRCT findings between patients received TNFi (n=22) and non-TNFi biologics (n=18), (p=1.00). The mean drug survival of first bDMARD also was not statistically different between groups (40.83±21.6 months in non-TNFi group and 42.23±40.50 months in TNFi group (p=0.90)). 5/18 (%27.8) patients in the non-TNFi group and 1/22 (%4.5) in TNFi group had died during the follow-up (p=0.14)

Table 1. Demographic and clinic characteristics of the patients at the Initiation of BDMARDs.

Characteristics	N=40
Male/Female, n	11/29
Age at bDMARDs initiation, years (mean±SD)	56,51±10.53
Age at the diagnosis, years (mean±SD)	49,38±11,7
Disease duration at bDMARDs initiation, years (mean±SD)	7,15±5,53
Past or current smoker, n (%)	21/40 (52.5)
RF positivity, n (%)	29/40 (72.5)
ACPA positivity, n (%)	35/39 (89.7)
Anti-SSA positivity n (%)	3/9 (33.3)
Patients with Sjögren's syndrome, n (%)	5/10 (50)
ESR at bDMARDs initiation, (mm/h)	38,37 ± 22,2
CRP at bDMARDs initiation, (mg/l)	16,08 ± 14,54
DAS28 at bDMARDs initiation	3,68 ± 1,1
Respiratory symptom at bDMARDs initation, n(%)	12/40 (30)
Lung involvement at the diagnosis, n (%)	8/25 (24,2)
Concomitant steroid, n (%)	37/40 (92.5)
Concomitant MTX, n (%)	16/40 (40)
Concomitant other csDMARDs, n (%)	31/40 (%77,5)
Initiated bDMARDs, TNFi/nonTNFi, n	22/18
RA-lung involvement type based on HRCT findings, n (%)	
-Rheumatoid nodulosis	17 (42.5)
-ILD-ground-glass opacity	12 (30)
-ILD-honeycombing	11 (27.5)

Conclusion: This study showed that the impact of TNFi and non-TNFi biologic treatments on the course of RA-assosiated lung involvement is similar. It also suggested that lung involvement at the diagnosis of RA was a significiant risk factor for the progress of the pulmonary disease.

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[1] Turesson C, O'Fallon WM, Crowson CS, Gabriel SE, Matteson EL. Extraarticular disease manifestations in rheumatoid arthritis: incidence trends and risk factors over 46 years. Ann Rheum Dis. 2003;62(8):722–7

Disclosure of Interests: None declared

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FRI0100

COMPARISON OF PATIENTS (PTS) WITH RHEUMATOID ARTHRITIS (RA) AMONG DISEASE ACTIVITY CATEGORIES AFTER 6 MONTHS OF TREATMENT WITH A TUMOUR NECROSIS FACTOR INHIBITOR (TNFI): RESULTS FROM THE CORRONA® RA REGISTRY

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Background: Targeting remission (REM) or low disease activity (LDA) is a widely accepted treatment strategy for RA. However, there are limited data on the proportion of pts who achieve these targets, or remain in moderate (MDA) or high disease activity (HDA) following advanced therapy.

Objectives: To estimate the proportion of RA pts in disease activity states (REM, LDA, MDA, and HDA) who were biologic-naïve at initiation and had continuous treatment with a TNFi for 6–12 months in the Corrona RA registry.

Methods: Eligible pts were aged ≥18 years, biologic-naïve, initiated TNFi treatment between January 1, 2010 and July 31, 2019, and had continuous use of a TNFi for 6–12 months. Disease activity was defined based on Clinical Disease Activity Index (CDAI) at the visit closest to 6-month follow-up: REM, ≤2.8; LDA, >2.8–10; MDA, >10–22; and HDA, >22. Disease characteristics, disease activity measures, and pt-reported outcomes (PROs) were reported at TNFi initiation and at the 6-month follow-up visit.

Results: 2586 biologic-naïve pts who initiated a TNFi and had continuous use for 6–12 months were included. At TNFi initiation, 167 (6%) were in REM, 479 (19%) had LDA, 907 (35%) had MDA, and 1033 (40%) had HDA. After 6–12 months of treatment, 563 (21.8%) were in REM, 923 (35.7%) had LDA, 674 (26.1%) had MDA, and 426 (16.5%) had HDA. Pts with HDA/MDA at 6–12 months were more likely to have a history of hypertension (32.7% HDA; 34.0% MDA; vs 23.6% REM) and had higher mean body mass index (BMI) (30.9 HDA; 31.1 MDA; vs 29.0 REM) at baseline compared with pts in REM. Disease activity measures and PROs were worse in pts with MDA and HDA vs LDA and REM after 6–12 months (Table). Pt Global Assessment was higher than Physician Global Assessment across all groups.

Conclusion: While 57.4% of pts who initiated a TNFi experienced a favorable outcome, >40% required additional or alternative intervention to achieve REM/LDA. Pts who remained in MDA/HDA continued to have an inadequate response to TNFi (as measured by disease activity measures and PROs) after 6–12 months of treatment compared with those who achieved REM/LDA.

Table. Summary of disease activity measures and PROs in previously biologic-naïve pts at the 6–12-month follow-up visit, stratified by disease activity category at the 6–12-month follow-up visit

Characteristics at 6–12 months, mean (standard deviation)	Disease activity category at 6–12 months			
	REM (n=563)	LDA (n=923)	MDA (n=674)	HDA (n=426)
CDAI	1.2 (0.8)	6.2 (2.1)	15.4 (3.4)	32.7 (9.2)
Tender joint count (28)	0.1 (0.3)	1.0 (1.3)	4.3 (3.3)	13.4 (7.0)
Swollen joint count (28)	0.1 (0.3)	1.1 (1.6)	4.0 (3.6)	9.1 (5.9)
C-reactive protein	6.4 (22.7)	7.0 (10.6)	11.1 (19.9)	12.6 (22.1)
Modified health assessment questionnaire	0.1 (0.2)	0.3 (0.4)	0.5 (0.5)	0.8 (0.5)
Pt global assessment	6.6 (6.8)	28.6 (20.9)	43.7 (25.7)	58.0 (22.7)
Physician global assessment	3.6 (4.3)	12.1 (10.4)	27.4 (15.9)	44.9 (19.8)
Pt pain assessment	8.7 (11.0)	30.3 (23.5)	46.1 (27.0)	59.9 (24.4)
Pt fatigue assessment	15.7 (19.2)	34.5 (26.6)	48.3 (28.0)	59.4 (27.5)
Morning stiffness (min)	16.5 (36.5)	55.4 (146.3)	96.9 (197.5)	143.6 (260.0)

Disclosure of Interests: Joel M Kremer Shareholder of: May own stocks and opinions, Grant/research support from: Research and consulting fees from AbbVie Inc., Consultant of: AbbVie, Amgen, BMS, Genentech, Inc., Gilead, GSK, Lilly, Pfizer, Regeneron and Sanofi, Employee of: Corrona, LLC employee, Anne Winkler Consultant of: AbbVie, Pfizer, and Novratis, Speakers bureau: AbbVie, Janssen, Sanofi, Genentech, Celgene, Eli Lilly, and Novartis., Laura Anatale-Tardiff Employee of: Corrona, LLC employee, Robert McLean Employee of: Corrona, LLC, Ying Shan Employee of: Corrona, LLC employee, Page Moore Employee of: Corrona, LLC employee, Namita Tundia Shareholder of: May own stocks and options, Employee of: AbbVie employee, Jessica Subotički Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., John Tesser Consultant of: Sanofi/Regeneron, Speakers bureau: Sanofi/Regeneron

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FRI0101

EFFECTS OF IL6 INHIBITORS ON THE INCIDENCE OF MAJOR ADVERSE CARDIOVASCULAR EVENTS IN RHEUMATOID ARTHRITIS PATIENTS: A SYSTEMATIC REVIEW WITH META ANALYSIS

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Background: Rheumatoid arthritis (RA) is associated with a 2 fold increased risk of cardiovascular events (CVE) and mortality when compared to the general population. The systemic inflammation in RA seems to play a pivotal role by creating endothelial dysfunction and thus accelerating atherosclerosis. This long lasting inflammatory process potentiates the effects of additional classical cardiovascular risk factors. Since the 2000s, numerous therapeutic advances, in particular biologics, allow better control of this inflammation. Among these, IL6 inhibitors (IL6i) are known to provide rapid and sustained improvements in clinical, biological and radiographic outcomes. However, an increase in circulating lipid concentrations in patients treated with IL6i is usual. This raises the question of the risk -to -benefit ratio of IL6i.
Objectives: The purpose of this systematic literature review and meta-analysis was to evaluate the impact of IL6i on the incidence of major adverse cardiovascular events in RA patients in comparison with TNFalpha inhibitors (TNFi), non TNFi bDMARDs or csDMARDS.
Methods: A systematic literature search of MEDLINE (via PubMed), EMBASE and the Cochrane Library databases until February 2019 was performed. Included studies were observational studies or randomized controlled trials having reported relevant confirmed CVEs (death from CVE, myocardial infarction, heart failure and stroke) in patients with RA treated with IL6i, and a suitable control group. A meta-analysis of the relative risk for each CVE in RA patients treated with IL6i compared to patients in the control groups was performed. A random effect model was applied in case of substantial heterogeneity.
Results: Of 6869 studies, 23 randomized controlled trials and 6 controlled cohorts could be included. IL6i were significantly associated with a reduction in the risk of myocardial infarction in comparison with TNFi (OR, 0.73; 95% CI [0.56 to 0.96]). No other significant effects were observed with regard to the risks of stroke, heart failure (HF), and death from CVE in comparison with csDMARDs, TNFi, or non-TNFi bDMARDs (table 1).

Table 1. Pooled relative risks of cardiovascular events in RA patients treated with IL-6 inhibitors and respective control groups

	Cs DMARDS	TNFi	Non TNFi bDMARDS
Myocardial infarction	1.44 [0.50;4.17]	0.73 [0.56; 0.96]	0.81 [0.48; 1.36]
Stroke	1.08 [0.40; 2.91]	1.20 [0.82; 1.77]	0.73 [0.39; 1.37]
Heart failure	0.17 [0.01; 4.08]	1.51 [0.61; 3.70]	1.19 [0.71; 1.98]
Cardiovascular death	1.59 [0.62; 4.11]	1.13 [0.72; 1.78]	NA

Our findings of a potentially protective effect of IL6i use on the risk of MI are reassuring. Although several beneficial effects might be involved, like the effective control of systemic inflammation, the anti-arrhythmia effect or the improvement of endothelial and left ventricle dysfunction, a potential indication bias with a decreased likelihood to prescribe these drugs in patients with high cardiovascular risk cannot be excluded.
Conclusion: This review of the literature with meta-analysis provides reassuring results about the association between use of IL6i and CVE in RA patients. Data from long-term observational studies is however needful to confirm and ascertain this result.
Disclosure of Interests: None declared
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FRI0102

SERUM TNFA LEVELS AT 24 HOURS AFTER FIRST ADMINISTRATION OF CERTOLIZUMAB PEGOL PREDICT EFFECTIVENESS AT WEEK 12 IN PATIENTS WITH RHEUMATOID ARTHRITIS FROM TSUBAME STUDY (UMIN ID:0002381)

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Background: To increase the remission rate of rheumatoid arthritis (RA), it is necessary to determine the efficacy of the tumor necrosis factor (TNF) inhibitor as early as possible. Moreover, the response to certolizumab pegol (CZP) at 12 weeks has been reported to predict its long-term efficacy.
Objectives: As part of a prospective single-center observational study (TSUBAME study), we prospectively enrolled patients to be treated with CZP in our institution to evaluate its effectiveness and safety starting at 24 hours after the first dose in clinical settings, while recording blood CZP concentrations and biomarkers over time to examine their correlation with clinical effects.
Methods: One hundred patients with RA and inadequate response to MTX who received CZP were enrolled in the TSUBAME study. The changes in serum TNFα, IL-6, and CZP levels at 24 hours after first administration of CZP were measured, and the correlation between serum biomarkers and clinical response was determined.
Results: At 24 hours after CZP initiation, significant improvement was observed in the disease activity (baseline and 24 h: 5.4 ± 1.3, 5.0 ± 1.3, respectively, $p < 0.01$), which was maintained until week 12. (baseline and 12 w: 5.4 ± 1.3, 3.3 ± 1.4, respectively, $p < 0.01$). Serum TNFα and IL-6 levels significantly decreased at 24 hours after first administration of CZP compared to baseline. No correlation was found between TNFα and IL-6 levels at baseline and the clinical response. According to univariate analysis, low serum TNFα and IL-6 levels and high CZP levels at 24 hours were associated with DAS28 (ESR) remission at 12 weeks. According to multivariate analysis, low serum TNFα levels at 24 hours were significantly associated with DAS28 (ESR) remission at 12 weeks (OR 0.05, 95%CI 0.01, 0.75, $p = 0.03$). Based on these findings, an ROC curve was created using remission according to the DAS28 (ESR) at week 12 as a dependent variable and TNFα concentration at 24 hours as an independent variable, resulting in a cut-off value of 0.76 pg/ml. From this result, the TNFα concentration at 24 hours was divided into 2 groups according to this cut-off, and the rates of remission according to the DAS28 (ESR) at week 12 were compared. In the group with TNFα concentration at 24 hours below the cut-off value, the rate of remission according to the DAS28 (ESR) at week 12 was significantly higher than in the group with TNFα concentration at 24 hours above the cut-off value (below the cut-off: above the cut-off = 56.3%: 21.6%, $p < 0.001$). Between the group that achieved remission according to the DAS28(ESR) and the group that did not achieve remission at week 12, there was almost no difference in the distribution of TNFα concentrations at baseline; however, the distribution of TNFα concentrations at 24 hours was lower in the group that achieved remission.
Conclusion: CZP was effective where serum TNFα was strongly neutralized within 24 hours. These results suggest that low serum TNFα levels at 24 hours after first administration of CZP may predict the effectiveness of CZP. To increase the remission rate in RA, it is necessary to determine the effectiveness of the molecular targeted drugs used at an early point, in addition to how rapid the onset of action is. CZP is extremely fast-acting, and its effectiveness can be predicted as early as 24 hours after the first dose, suggesting that it may be possible to determine the effectiveness early.
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Disclosure of Interests: Yusuke Miyazaki Grant/research support from: Astellas Pharma Inc and UCB S.A., Kazuhisa Nakano: None declared, Shingo Nakayamada Grant/research support from: Mitsubishi-Tanabe, Takeda, Novartis and MSD, Speakers bureau: Bristol-Myers, Sanofi, Abbvie, Eisai, Eli Lilly, Chugai, Asahi-kasei and Pfizer, Satoshi Kubo: None declared, Shigeru Iwata: None declared, Kentaro Hanami: None declared, Shunsuke Fukuyo: None declared, Ippei Miyagawa: None declared, Ayako Yamaguchi: None declared, Akio Kawabe: None declared, SAITO KAZUYOSHI: None declared, Yoshiya Tanaka Grant/research support from: Asahi-kasei, Astellas, Mitsubishi-Tanabe, Chugai, Takeda, Sanofi, Bristol-Myers, UCB, Daiichi-Sankyo, Eisai, Pfizer, and Ono, Consultant of: Abbvie, Astellas, Bristol-Myers Squibb, Eli Lilly, Pfizer, Speakers bureau: Daiichi-Sankyo, Astellas, Chugai, Eli Lilly, Pfizer, AbbVie, YL Biologics, Bristol-Myers, Takeda, Mitsubishi-Tanabe, Novartis, Eisai, Janssen, Sanofi, UCB, and Teijin
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FRI0103

ASSOCIATION BETWEEN SEROPOSITIVITY AND DISCONTINUATION OF INFLIXIMAB IN RHEUMATOID ARTHRITIS

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Background: Infliximab is still a widely used biologic agent in treatment of rheumatoid arthritis (RA). Because infliximab is expensive and can have adverse events, identification of factors that predict an adequate response to this treatment has been investigated.
Objectives: In this study, we investigated the association between rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA) status and

the discontinuation of infliximab therapy due to adverse events or insufficient response in bio-naïve patients with RA.

Methods: This study included patients enrolled in the Tsurumai Biologic Communication Registry in Japan. A crude comparison of infliximab discontinuation between seropositive and seronegative patients was using Kaplan-Meier analysis and log-rank test. We evaluated the associations between the specified baseline characteristics and discontinuation of infliximab therapy using Cox proportional hazard regression. We could not perform simultaneous assessments of the impact of RF and ACPA seropositivity on clinical efficacy becasue of collinearity.

Results: Baseline characteristics of the patients included in this study are shown in Table 1 and the crude comparison between RF and ACPA status is shown in Figure 1. RF and ACPA seropositivity was significantly predictive of discontinuation of infliximab therapy after adjusting for baseline characteristics, including age, sex, stage, class, disease activity at baseline, and prednisolone use (Table 2). The hazard ratio was 1.99 (95% confidence interval 1.25, 3.18) for RF and 2.73 (95% confidence interval 1.24, 6.02) for ACPA.

Table 1. Characteristics of RA patients at baseline by RF and ACPA status

	RF (n = 344; 985 patient-years)			ACPA (n = 250; 824 patient-years)		
	RF positive	RF negative		ACPA positive	ACPA negative	
	(n = 263)	(n = 81)	*P*†	(n = 211)	(n = 39)	*P*†
Age, years (SD)	55.7 (12.3)	54.6 (13.9)	0.48	55.4 (12.3)	49.7 (14.3)	0.01
Female, no. (%)	205 (78.2)	66 (81.5)	0.64	170 (80.6)	28 (71.8)	0.28
DAS28ESR (SD)	5.50 (1.33)	4.95 (1.51)	0.005	5.54 (1.28)	4.61 (1.82)	0.0005
Stage I+II/III+IV, no. (%)	81/174 (31.8/68.2)	25/50 (33.3/66.7)	0.78	61/139 (30.5/69.5)	15/20 (42.9/57.1)	0.17
Class I+II/III+IV, no. (%)	155/102 (60.3/39.7)	52/22 (70.3/29.7)	0.14	126/72 (63.6/36.4)	23/12 (65.7/34.3)	0.85
Current MTX treatment, %	100	100	1	100	100	1
MTX dose, mg/week (SD) ‡	7.56 (2.16)	7.80 (2.22)	0.4	7.82 (2.20)	7.31 (2.66)	0.22
Current PSL treatment, no. (%)	141 (68.1)	37 (56.1)	0.077	128 (67.4)	19 (55.9)	0.24
PSL dose, mg/day (SD) ‡	3.98 (3.91)	2.70 (2.74)	0.01	3.73 (3.78)	2.63 (2.85)	0.11
BMI, kg/m^2 (SD)	22.6 (3.88)	21.3 (4.22)	0.1	22.0 (4.10)	22.5 (3.33)	0.68

Data are presented as mean, unless otherwise stated. SD: standard deviation

† Chi-square test for categorical variables and t-test for continuous variables.

‡ MTX dose and PSL dose were mean value in patients with concomitant MTX and PSL treatment, respectively.

Table 2. Cox proportional hazard regression for infliximab therapy due to adverse event and insufficient response

Model including RF status (n = 226)			Model including ACPA status (n = 182)		
Variable	HR (95% CI)	*P*	Variable	HR (95% CI)	*P*
RF positive	1.99 (1.25-3.18)	0.0037	ACPA positive	2.73 (1.24-6.02)	0.012
Age at baseline	0.99 (0.98-1.01)	0.43	Age at baseline	0.99 (0.98-1.01)	0.36
Sex (referent: male)	1.21 (0.76-1.94)	0.41	Sex (referent: male)	0.99 (0.60-1.62)	0.96
Prednisolone use	1.03 (0.71-1.49)	0.85	Prednisolone use	1.02 (0.67-1.56)	0.92
Stage III + IV (referent: I + II)	1.01 (0.99-1.03)	0.17	Stage III + IV (referent: I + II)	1.01 (0.98-1.03)	0.54
Class III + IV (referent: I + II)	0.99 (0.98-1.02)	0.73	Class III + IV (referent: I + II)	0.99 (0.97-1.01)	0.55
DAS28ESR at baseline	0.95 (0.83-1.10)	0.54	DAS28ESR at baseline	0.99 (0.84-1.18)	0.97

Conclusion: RF and ACPA seropositivity in bio-naïve patients with RA correlated with a higher rate of infliximab discontinuation due to adverse events or ineffectiveness.

Disclosure of Interests:

Yoshikazu Ogawa: None declared, Nobunori Takahashi Speakers bureau: AbbVie, Asahi Kasei, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eisai, Eli Lilly, Janssen, Mitsubishi Tanabe, Ono, Pfizer, Takeda, and UCB Japan, Toshihisa Kojima Grant/research support from: Chugai, Eli Lilly, Astellas, Abbvie, and Novartis, Consultant of: AbbVie, Speakers bureau: AbbVie, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eli Lilly, Janssen, Mitsubishi Tanabe, Pfizer, and Takeda, Naoki Ishiguro Grant/research support from: AbbVie, Asahi Kasei, Astellas, Chugai, Daiichi-Sankyo, Eisai, Kaken, Mitsubishi Tanabe, Otsuka, Pfizer, Takeda, and Zimmer Biomet, Consultant of: Ono, Speakers bureau: Astellas, Bristol-Myers Squibb, Daiichi-Sankyo, Eli Lilly, Pfizer, and Taisho Toyama

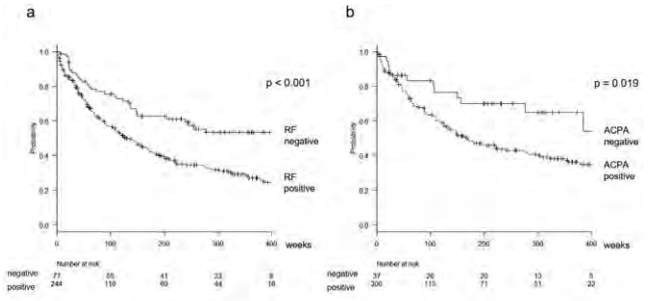


Fig. 1 Kaplan-Meier survival curve and log-rank test.
(a) Discontinuation of infliximab therapy, stratified by RF status. (b) Discontinuation of infliximab therapy, stratified by ACPA status

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FRI0104

PERSISTENCE OF TOCILIZUMAB THERAPY AMONG PATIENTS WITH RHEUMATOID ARTHRITIS: DATA FROM THE US-BASED CORRONA RHEUMATOID ARTHRITIS REGISTRY

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Background: Understanding the persistence of biologic therapies and factors associated with discontinuation can help inform treatment decisions for patients with rheumatoid arthritis (RA).

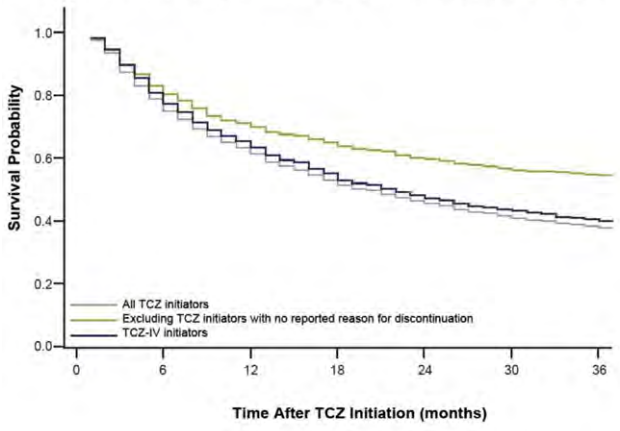
Objectives: To evaluate the persistence of tocilizumab (TCZ) therapy and identify factors associated with its discontinuation among US patients with RA in routine clinical practice.

Methods: Eligible participants were TCZ-naïve patients enrolled in the Corrona RA registry who initiated TCZ after January 1, 2010 and had ≥ 1 follow-up visit. Persistence of therapy was defined as maintaining continuous TCZ treatment with no interruptions; patients were considered no longer persistent upon the first discontinuation of TCZ. Persistence was calculated using Kaplan-Meier survival analysis for the overall population; secondary analyses evaluated persistence excluding patients who stopped TCZ with no reported reason for discontinuation (patients with non-medical reasons for discontinuation [eg, insurance] were censored) and in only those patients who initiated intravenous (IV) TCZ. Cox proportional hazards modeling was used to identify factors associated with persistence.

Results: A total of 1789 TCZ initiators were included; 81.0% were female, 85.0% were white and 75.4% were overweight or obese. The mean (SD) age was 58.5 (12.6) years and mean (SD) disease duration was 12.0 (9.6) years. Most patients (93.4%) had prior biologic use and 67.4% had received ≥ 2 prior biologics. Overall, 28.8% initiated TCZ as monotherapy. Among all TCZ initiators, the median (95% CI) duration of persistence was 20 (18 to 22) months (Fig 1). Factors associated with an increased hazard of TCZ discontinuation included smoking and higher baseline CDAI, whereas prior tumor necrosis factor inhibitor (TNFi) use was associated with a reduced hazard (Fig 2A). After excluding patients with no reported reason for discontinuation (remaining n = 1303), the median (95% CI) duration of persistence was 46 (38 to 55) months (Fig 1); smoking, use of 1 prior non-TNFi and higher baseline patient pain score were associated with an increased hazard of discontinuation (Fig 2B). Among the 1284 patients who initiated TCZ IV, median (95% CI) duration of persistence was 22 (19 to 25) months (Fig 1); smoking, lack of insurance and higher baseline patient fatigue score were associated with an increased hazard of discontinuation, whereas use of 1 prior TNFi was associated with a decreased hazard (Fig 2C).

Conclusion: In this real-world population of US patients with RA, TCZ was most frequently initiated after an inadequate response to ≥ 2 biologics. Overall median duration of persistence was approximately 20 months and was higher (46 months) when patients with no reported reason for TCZ discontinuation were excluded. As expected, factors indicative of higher baseline disease activity were associated with shorter persistence.

Figure 1. Persistence of TCZ Therapy Among All TCZ Initiators, TCZ Initiators Excluding Those With No Reported Reason for Discontinuation and TCZ-IV Initiators

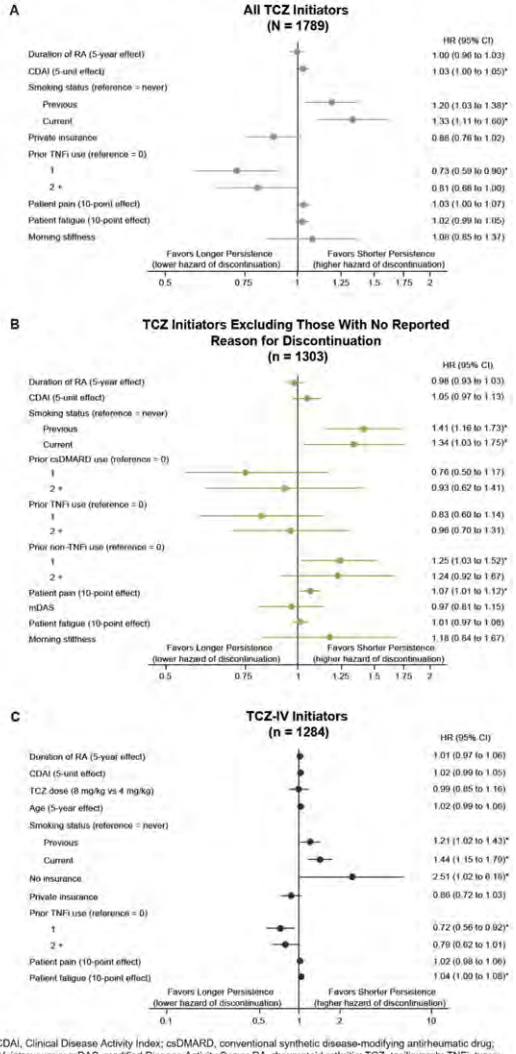


Number of Patients at Risk

1789	1245	861	636	483	378	298
1303	947	663	516	399	318	257
1284	921	644	482	376	307	244

IV, intravenous; TCZ, tocilizumab.

Figure 2. Estimated Effects of Covariates on Duration of TCZ Persistence Among **(A)** All TCZ Initiators, **(B)** TCZ Initiators Excluding Those With No Reported Reason for Discontinuation and **(C)** TCZ-IV Initiators



CDAI, Clinical Disease Activity Index; csDMARD, conventional synthetic disease-modifying antirheumatic drug; IV, intravenous; mDAS, modified Disease Activity Score; RA, rheumatoid arthritis; TCZ, tocilizumab; TNFi, tumor necrosis factor inhibitor. * $P < 0.05$

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Disclosure of Interests: Dimitrios A Pappas: None declared, Taylor Blachley Employee of: Corrona, LLC, Jennie H. Best Shareholder of: Genentech, Inc., Employee of: Genentech, Inc., Steve Zlotnick Shareholder of: Genentech, Inc., Employee of: Genentech, Inc., Kelechi Emeanuru Employee of: Corrona, LLC – employment, Joel M Kremer Shareholder of: May own stocks and opinions, Grant/research support from: Research and consulting fees from AbbVie Inc., Consultant of: AbbVie, Amgen, BMS, Genentech, Inc., Gilead, GSK, Lilly, Pfizer, Regeneron and Sanofi, Employee of: Corrona, LLC employee

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FRI0105

EVALUATION OF CXCL13 AND ICAM1 SERUM LEVELS AS PREDICTORS OF CLINICAL RESPONSE TO ABATACEPT IN RHEUMATOID ARTHRITIS.

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Background: Soluble intercellular adhesion molecule 1 (ICAM1) and C-X-C motif chemokine 13 (CXCL13) were described as differentially associated with two major subtypes of synovitis in rheumatoid arthritis (RA). Raised serum levels of ICAM1 (which is upregulated in synovial fibroblasts in response to TNFα), and of CXCL13 (which is expressed by synovial follicular dendritic cells and activated mature antigen-experienced T-helper cells), are associated with a myeloid or lymphoid synovial phenotype, respectively (1). It has been suggested that a preferential clinical response to anti-TNFα, as compared to anti-IL-6R monotherapy, can be predicted by measuring these two biomarkers (2). No information is available on the possible utility of these biomarkers in RA patients treated with abatacept (ABA), a T-cell co-stimulation blocker.

Objectives: To analyze the effect of ABA on ICAM1 and CXCL13 serum levels in RA and to verify whether they predict the response to the drug.

Methods: 63 RA patients [F/M=51/12; median (10^{th}-90^{th} percentile) age=60 (41-72) years; CRP-DAS28=4.6 (3.3-5.8); ACPA positive: 86%], before and after 6 months of treatment with ABA + methotrexate and 22 sex and age-matched healthy controls (HC) were evaluated. Serum ICAM1 and CXCL13 levels were dosed by commercial ELISA (Life Technologies and R&D). Response to treatment was defined with the EULAR criteria.

Results: CXCL13 serum levels were higher in RA at baseline than in HC [136 (42-325) vs 32 (19-57) pg/ml, p<0.01], while no difference was observed in ICAM1 [186 (125-276) vs 184 (153-246) ng/ml, p=0.9]; positive correlations between ICAM1 and CRP (r:0.28; p=0.03) and CXCL13 levels and CRP (r:0.40; p<0.01) and CRP-DAS28 values (r:0.27, p=0.05) were found. After therapy with ABA, a reduction of CXCL13 was observed [136 (42-325) vs 94 (29-319) pg/ml, p<0.01], both in responders [n: 37: 151 (57-462) vs 97 (26-329) pg/ml; p<0.01] and non-responders (n: 14: 142 (68-293) vs 89 (42-198) pg/ml; p=0.01]. Not significant variation of ICAM1 serum levels was found in the entire cohort [186 (125-276) vs 190 (113-252) ng/ml, p=0.06]. However, a significant decrease was observed in non-responders [222 (169-302) vs 186 (110-233) ng/ml, p=0.02]. At baseline, no significant difference was found among patients seropositive for ACPA if compared with the negative ones [ACPA+ vs ACPA- for ICAM1 [187 (123-280) vs 177 (134-258) ng/ml; p=0.7] and for CXCL13 [143 (42-368) vs 113 (56-270) pg/ml; p=0.4]].

Conclusion: Our results confirmed that CXCL13 serum levels are directly correlated with disease activity and demonstrated that ABA therapy induces their reduction. These findings suggest that the co-stimulation blockade at central level and/or in the synovium lead to a reduced production of CXCL13. We could not demonstrate that CXCL13 levels predict the clinical response to ABA in this cohort of patients.

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[1] Rosengren S, Rheumatology 2011;2.Dennis G, Arthritis Res Ther 2014

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FRI0106

RISK FACTORS FOR SERIOUS INFECTIONS IN PATIENTS WITH RA INITIATING TREATMENT WITH BIOLOGIC DMARDS: A REAL-WORLD POPULATION-BASED OBSERVATIONAL STUDY

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Background: Patients with RA are at increased risk of infection compared with the general population, but it is unclear whether this is due to the underlying disease or to immunosuppressive medications used to manage the disease.[1] Some biologic DMARDs (bDMARDs) have been associated with an increased risk of serious infection.[2] A large cohort study found no increased risk of serious infection in patients initiating abatacept compared with patients initiating other bDMARDs.[3] It is clinically important to identify which patients are at a higher risk of infections at the time of initiating treatment with a bDMARD. However, studies that assess risk factors for infection and derive corresponding risk scores of infection, especially at the time of bDMARD treatment initiation, are lacking or based on too few patients.[4]

Objectives: To identify the risk factors for serious infections among patients with RA initiating treatment with a bDMARD in a real-world observational setting.

Methods: The Truven MarketScan® Commercial and Supplemental Medicare databases were used to identify patients diagnosed with RA who initiated treatment with a bDMARD between January 2007 and December 2015. Patients were followed from treatment initiation until the occurrence of a serious infection requiring hospitalisation, the end of enrolment or 31 December 2015, whichever came first. The Cox proportional hazards model was used to estimate the hazard ratios (HRs) of serious infection associated with baseline risk factors including demographics, the presence of co-morbidities, prior hospitalised infections and medications. An infection risk score was developed using the independent risk factors found to be significant in the model.

Results: The study cohort included 84,308 patients initiating treatment with a bDMARD, mainly etanercept (36.7%), adalimumab (29.3%), infliximab (12.4%), rituximab (7.3%) and abatacept (6.8%). During a mean follow-up of 6.6 months, 1724 patients were hospitalised for a serious infection (incidence rate 3.7/100 persons per year). The baseline risk factors significantly and independently associated with serious infections were age, prior hospitalisation for infection, hypertension, diabetes, lymphoma, asthma, chronic obstructive pulmonary disease, cardiovascular disease, other autoimmune disease, corticosteroid use and antibiotic use. The infection risk score, with a possible range of 0 to 15, had a mean (SD) value of 2.6 (1.9) with range 0–12.5. The HR (95% CI) of serious infection was 1.43 (1.40–1.45) for every unit increase in the risk score. Relative to patients with a score of 0, the HR (95% CI) of serious infection for a risk score of 5 was 5.9 (5.3–6.5), and for a risk score of 10 was 34.5 (28.5–41.6).

Conclusion: In this large, real-world cohort of patients with RA who were initiating treatment with a bDMARD, several patient characteristics were found to independently predict the subsequent risk of serious infection. The risk score, based on easily available patient characteristics, can be a simple and useful tool for the clinician to identify patients at higher risk of infection at the time of bDMARD initiation for the treatment of RA.

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FRI0107

EFFECTIVENESS OF ABATACEPT ON CLINICAL DISEASE ACTIVITY AND RADIOGRAPHIC PROGRESSION IN RHEUMATOID ARTHRITIS PATIENTS IN DAILY CLINICAL PRACTICE IN JAPAN: COMPARISONS ACCORDING TO ACPA STATUS

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Background: The clinical effectiveness of abatacept (ABA) in rheumatoid arthritis (RA) patients has been reported to be higher when the patients' anti-cyclic citrullinated peptide antibody (ACPA) status is positive. The report from the ORA registry demonstrated that the ACPA positivity was associated with a better response to ABA [1]. In a sub-analysis of the AMPLE trial, patients with very high ACPA titers who were treated with ABA had a statistically significant response compared to patients with lower titers [2]. However, these studies did not demonstrate the data regarding the structural progression.

Objectives: This study aimed to evaluate the effectiveness of ABA on the clinical disease activity as well as the radiographic progression in patients with RA in the clinical settings.

Methods: All eligible patients were registered in the TBCR, a Japanese multicenter registry system for RA patients treated with biologics [3]. The present study included 553 consecutive patients whose ACPA data were obtained, treated with ABA and observed for longer than 52 weeks. We primarily compared the status of disease activity (SDAI) and radiographic progression (van der Heijde modified total Sharp score: mTSS) between ACPA-positive [ACPA (+)] and ACPA-negative [ACPA (-)] RA patients. The ACPA positive was defined as ≥13.5 U/ml of anti-CCP antibody.

Results: Number of cases was 446/ 107 [ACPA (+)/ ACPA (-)], respectively. Baseline characteristics between groups were quite similar; mean age was 68.0/ 67.3 years, rate of methotrexate (MTX) use rate was 41.2/ 50.0%, rate of bio-naive was 28.0/ 31.8%, and mean SDAI score was 22.2/ 20.8. Significant difference was observed in mean change in SDAI score from baseline to 52 weeks between the ACPA (+) and ACPA (-) group (-13.4 vs -9.9, p = 0.027) (Figure 1A). Proportion of patents that achieved low disease activity (LDA; SDAI ≤11) at 52 weeks was significantly higher in the ACPA (+) group compared to the ACPA (-) group (72.1 vs 56.0%, p < 0.01) (Figure 1B). In univariate and multivariate logistic regression analysis, ACPA positivity was an independent predictor for achievement of LDA at 52 weeks (Table). There observed no significant difference between ACPA (+) and ACPA (-) group in the proportion of patients that achieved structural remission (ΔmTSS ≤0.5) at 52 weeks (66.2 vs 62.1%) (Figure 2A) as well as mean change in mTSS (1.66 vs 1.17), erosion score (0.60 vs 0.53), and joint narrowing (JSN) score (1.06 vs 0.64) (Figure 2B).

Figure 1

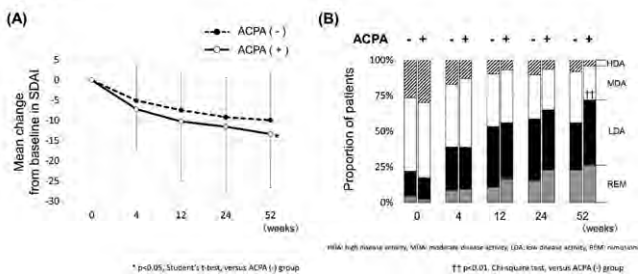
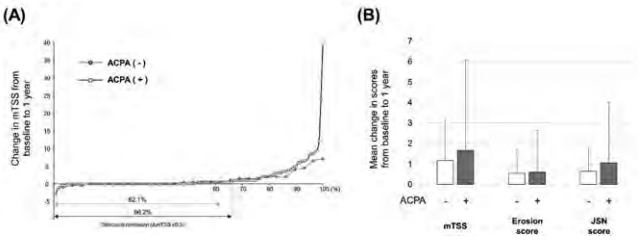


Table.

	Univariate		Multivariate	
Variables	OR (95%CI)	p-value	adjusted OR (95%CI)	p-value
Age	0.99 (0.98-1.01)	0.439	1.00 (0.97-1.02)	0.749
male (vs female)	1.12 (0.70-1.80)	0.634	0.79 (0.40-1.58)	0.511
disease duration	0.99 (0.97-1.00)	0.053	0.99 (0.97-1.01)	0.468
Biologics-naïve	1.23 (0.81-1.85)	0.335	1.18 (0.67-2.08)	0.575
Concomitant MTX use	1.12 (0.75-1.69)	0.585	1.14 (0.66-1.95)	0.649
Concomitant PSL use	0.82 (0.55-1.23)	0.329	0.97 (0.58-1.64)	0.923
SDAI @baseline	0.96 (0.94-0.97)	***<0.001***	0.96 (0.94-0.98)	***<0.001***
mHAQ @baseline	0.50 (0.36-0.69)	***<0.001***	0.57 (0.38-0.86)	***0.008***
ACPA positive	2.03 (1.29-3.17)	***0.002***	2.61 (1.36-5.00)	***0.004***
			Bold italic, p<0.05	

Figure 2



Conclusion: Consistent with previous reports, the ACPA-positive group demonstrated significantly higher LDA achievement rate at 52 weeks and indeed the ACPA positivity was significantly associated with LDA achievement in multivariate analysis. However, the ACPA-negative group demonstrated quite similar transition of SDAI score and LDA achievement rate except at 52 weeks compared with the ACPA-positive group. Additionally, there was no significant difference in the structural progression at 52 weeks between the groups. ABA treatment

may be considered not only in the ACPA-positive RA patients but also in the ACPA-negative patients in the clinical practice.

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FRI0108 ASSOCIATION BETWEEN CHANGES IN C-REACTIVE PROTEIN AT WEEK 12 AND PATIENT-REPORTED OUTCOMES AT WEEK 24 WITH SARILUMAB THERAPY ACROSS THREE PIVOTAL PHASE 3 STUDIES

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Background: Evaluation of early response to rheumatoid arthritis (RA) therapy at 12 weeks after initiation is recommended in treatment guidelines. C-reactive protein (CRP) response at 12 weeks on therapy may indicate favorable longer-term patient-reported outcomes (PROs).

Objectives: To describe the association between CRP response at Week 12 and PROs at Week 24 with sarilumab therapy across three pivotal studies.

Methods: The analysis included patients with RA who took part in MOBILITY (NCT01061736), TARGET (NCT01709578), or MONARCH (NCT02332590) and were treated with sarilumab 200 mg every 2 weeks (q2w) or adalimumab 40 mg q2w (MONARCH only). Patients who achieved a CRP response at Week 12 (defined as serum CRP ≤3 mg/L) were evaluated for PROs at Week 24. Response for PROs was defined as change from baseline visual analog scale score ≥10 for pain, sleep, and morning stiffness and an increase of ≥4 for FACIT-Fatigue score. Odds ratios (ORs) and 95% confidence intervals (CIs) were generated for the likelihood of achieving PRO responses at Week 24.

Results: The proportions of patients achieving a CRP response at Week 12 were 78% (MOBILITY), 74% (TARGET), 80% (MONARCH, sarilumab), and 36% (MONARCH, adalimumab). Of these, 71.4% (MOBILITY; OR 3.78, 95% CI 2.31–6.18), 71.5% (TARGET; OR 2.86, 95% CI 1.44–5.65), 79.7% (MONARCH, sarilumab; OR 4.40, 95% CI 2.04–9.47), and 79.7% (MONARCH, adalimumab; OR 2.76, 95% CI 1.36–5.61) reported pain score responses at Week 24. Fatigue responses at Week 24 among Week 12 CRP responders were 66.6% (MOBILITY; OR 2.74, 95% CI 1.69–4.45), 59.9% (TARGET; OR 3.18, 95% CI 1.58–6.42), 73.0% (MONARCH, sarilumab; OR 4.78, 95% CI 2.21–10.33), and 64.1% (MONARCH, adalimumab; OR 1.64, 95% CI 0.88–3.06). Sleep was evaluated in MOBILITY only, and 58.2% of those achieving Week 12 CRP responses reported sleep score responses at Week 24 (OR 3.51, 95% CI 2.10–5.87). Morning stiffness responses (evaluated in TARGET and MONARCH only) at Week 24 among patients with Week 12 CRP responses were 71.5% (TARGET; OR 3.70, 95% CI 1.86–7.39), 81.1% (MONARCH, sarilumab; OR 5.36, 95% CI 2.47–11.63), and 75.0% (MONARCH, adalimumab; OR 2.42, 95% CI 1.24–4.72).

Conclusion: Achievement of a CRP response at Week 12 in patients with RA treated with sarilumab 200 mg q2w or adalimumab 40 mg q2w was associated with improvements at Week 24 in PROs for pain, fatigue, sleep, and morning stiffness. Among patients with RA, CRP responses at 12 weeks on treatment predict favorable longer-term PRO improvements.

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FRI0109 TEMPORAL CHANGES IN LUNG NODULES DETECTED IN INDIVIDUALS WITH RHEUMATOID ARTHRITIS WITH BIOLOGIC DMARD TREATMENTS

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Background: Lung nodules in rheumatoid arthritis (RA), patients impose diagnostic and therapeutic challenges due to unpredictable outcome of these nodules. biologic (b) disease-modifying anti-rheumatic drugs (bDMARDs) are important therapeutic agents used in treatment of RA. There is hesitation about use of conventional synthetic DMARDs (csDMARD) and bDMARDs due to increased risk of nodules although their association remains unclear. There are scarce data on lung nodules observed in RA patients and systematic studies are needed.

Objectives: The aim of this study is to evaluate effects of biologic treatments and conventional synthetic DMARDS on pulmonary nodules observed in rheumatoid arthritis patients.

Methods: Electronic health records of RA patients who had had thorax computed tomography (CT) confirmed lung nodules in the last 5 years were retrospectively evaluated. Pre-treatment and post-treatment follow up CT images were meticulously examined for the number, size, attenuation, calcification, and cavitary formation. Demographic features, smoking status, disease characteristics and used medications were retrieved from file records. Clinical and laboratory findings, demographic features, treatment and follow-up duration, number of solid and cavitary nodules were compared between groups.

Results: There were 21 patients in both biologic (11 females, mean age; 59.7±8.4) and csDMARD (12 females, mean age; 71.4±8.3) treated groups. There was no difference in frequency of nodule types and sizes between csDMARD and bDMARDs groups **(table)** despite csDMARD users were remarkably older. Administered biologic treatments were anti-TNF-alpha in 8, tofacitinib in 7, rituximab in 4, and abatacept in 2 patients. The most common types of nodules were solid and cavitary nodules, observed in 17 and 8 patients, respectively in biologic users. Calcific nodules were present in three patients, and ground glass nodules were observed in a single patient. Nodules were multiple in 12 patients and solitary in 9 patients. Calcific and ground glass nodules were all solitary in our study. Cavitary and solid nodules were concurrent in five patients. Median follow duration was 14(5-55) months. Progression was observed in small number of patients; three patients in receiving aTNFα, and one in rituximab **(figure)** and one in abatacept users. Interestingly none of patients receiving tofacitinib did not show progression. There was no difference regarding number of patients who progressed with either csDMARD or bDMARDs. None of the nodules showed malignant transformation within the observation period.

Conclusion: In conclusion, risk of progression in lung nodules with biologic treatments is seem to be low, at least not more than csDMARD in short term and any malignant transformation was not observed in our study.

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Table. Changes in nodule characteristics with respect to treatment groups.

	csDMARD	bDMARDs
SOLID NODULES		
Pre-treatment		
Total number of nodules, n	72	54
Post-treatment		
Completely diminished, n	5	14
Regressed, n	5	12
Stable, n	33	20
Enlarged, n	23	4
Cavitary transformation	6	4
De novo solid nodules	26	7
CAVITARY NODULES		
Pre-treatment		
Total number of nodules	10	16
Post-treatment		
Completely diminished, n	0	1
Regressed	0	5
Stable	4	8
Enlarged, n	6	2
Newly formed cavitary nodules	6	9**

*number less than calculated due to cavitation, **de novo 5 nodules, 4 transformation from solid nodules

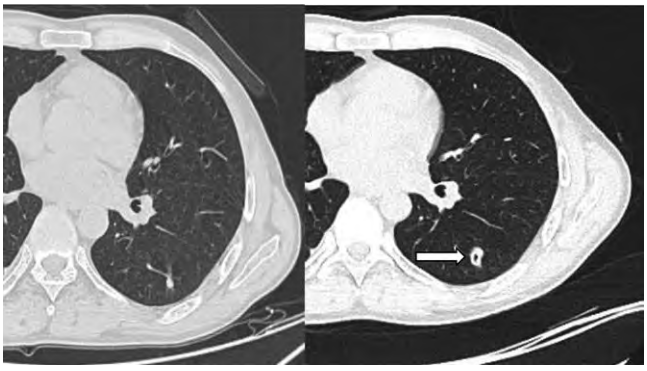


Figure. Nodule progression in a patient receiving rituximab (white arrow)

Disclosure of Interests: None declared

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FRI0110

TAPERING TOWARDS DMARD-FREE REMISSION IN ESTABLISHED RHEUMATOID ARTHRITIS: 2 YEAR RESULTS OF THE TARA TRIAL

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Background: In rheumatoid arthritis (RA) disease outcomes have improved enormously in the last decades. Due to early initiation of therapy, a treat-to-target approach and a growing arsenal of disease-modifying antirheumatic drugs (DMARDs) and biologics, RA patients are in sustained remission more often. This raises the subsequent questions whether treatment should be continued, tapered or stopped. Although DMARD free remission (DFR) is nowadays achievable for increasing numbers of RA patients, the optimal tapering approach still needs to be defined.

Objectives: To evaluate the 2-year clinical effectiveness of two gradual tapering strategies, namely tapering the csDMARD first followed by the TNF-inhibitor, or tapering the TNF-inhibitor first followed by the csDMARD.

Methods: In this multicenter single-blinded randomised controlled trial RA patients with controlled disease for at least 3 consecutive months, defined as a DAS≤2.4 and a swollen joint count (SJC) ≤1, which was achieved with csDMARDs and a TNF-inhibitor were included. Eligible patients were randomised into gradual tapering csDMARDs followed by the TNF-inhibitor, or vice versa. Medication was tapered in three steps over the course of 6 months. After 12 months, the other DMARD was tapered. Gradual tapering was done by cutting the dosage into half, a quarter and thereafter it was stopped. In case of a flare (DAS44>2.4 or SJC>1) the previous effective dose was restarted and tapering was not initiated any further throughout the whole study period. The primary outcome for the clinical effectiveness was the number of patients with a disease flare, defined as DAS44>2.4 and/or SJC>1. Secondary outcomes were DFR, disease activity, quality of life and functional ability. Outcomes were calculated in an intention-to-treat analysis, using all available data.

Results: A total of 189 patients were randomly assigned to tapering the csDMARD first or tapering the TNF-inhibitor first. The cumulative flare rate, after 24 months, for tapering the csDMARD first was 61% (95% CI, 50% - 69%) and for tapering the TNF-inhibitor first was 62% (95% CI, 50%-70%) (p=0.35)(figure 1). The cumulative flare rate differed the most between both groups between 12 and 18 months of follow-up (figure 1). Figure 2 shows an overview of how gradual tapering took place and which medication patients were using at different time points(figure 2). This was indicated for both tapering arms, and for the first and second year (figure 2). For the second year, tapering status was only indicated for the patients who actually tapered medication, so who stayed flare-free in the first year. Patients that tapered their csDMARD first were more often able to completely taper their csDMARD (n=30), and subsequently they also had a higher chance of reaching DFR(n=15) (table 1). However, mean DAS and mean HAQ over time and after 2 years did not differ between both tapering arms (table 1).

Table 1. Baseline characteristics and results after 24 months.

	Tapering csDMARD first (n=94)	Tapering TNF-inhibitor first (n=95)
Baseline (T0)		
Age (years), mean (sd)	55.9 (14.1)	57.2 (10.6)
Gender, female, n(%)	66 (71)	58 (61)
Symptom duration (years), median (IQR)	6.0 (4.3-8.5)	6.3 (4.1-8.9)
ACPA positive, n(%)	61 (72)	65 (75)
RF positive, n(%)	49 (57)	56 (64)
2-year follow-up (T24)		
Cumulative flare, n(%)	57 (61)	59 (62)
DMARD free remission, n(%)	15 (16)	8 (8)
Tapered, n(%)	30 (32)	20 (21)
DAS, mean (sd)	1.39 (0.67)	1.30 (0.70)
ΔDAS (T24-T0), mean (sd)	0.41 (0.55)	0.33 (0.77)
HAQ-DI, mean (sd)	0.62 (0.53)	0.52 (0.51)
ΔHAQ-DI (T24-T0), mean (sd)	0.074 (0.40)	0.058 (0.31)

Conclusion: The order in which tapering and stopping medication was performed was not superior to each other based on flare rates, DAS and HAQ. However, patients who tapered their csDMARD first could more often completely taper off their medication and, therefore, also reached DFR more often.

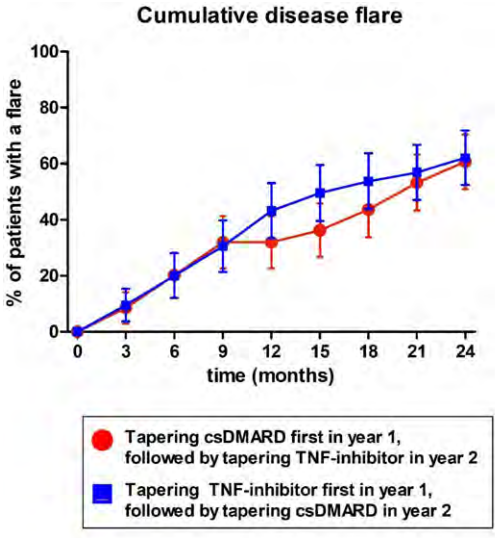


Figure 1 Cumulative flare rate over time. csDMARDs; conventional synthetic disease-modifying antirheumatic drug, TNF-inhibitor; tumor necrosis factor inhibitor.

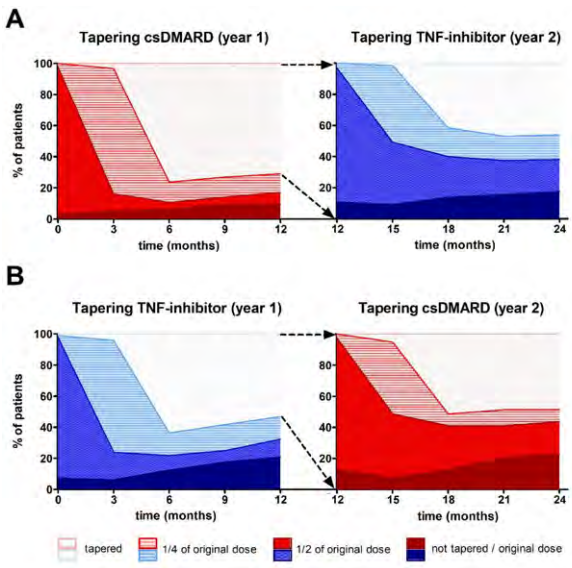


Figure 2 Overview of gradual tapering per time point.
Numbers indicate percentages of patients. Every 3 months the TNF-inhibitor or csDMARD was tapered until after 6 months the drug could be stopped. In case of a flare, defined as DAS>2.4 and/or SJC>1, patients were set back at their previous effective dose. No further tapering was allowed after having a flare. For the second year (T12 - T24), only tapering status was shown for patients who - according to protocol - should have tapered their medication in the second year. csDMARD; conventional synthetic disease modifying antirheumatic drug.

Disclosure of Interests: None declared
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FRI0111

TOCILIZUMAB MAY INDUCE SECONDARY HYPOGAMMAGLOBULINAEMIA. A RETROSPECTIVE CASE SERIES OF 42 PATIENTS

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Background: Tocilizumab (TCZ) is a recombinant humanized, anti-human monoclonal antibody of the immunoglobulin $G1_k$ subclass directed against soluble and membrane-bound interleukin 6 receptors (IL-6R) [1].
Interleukin-6 (IL-6) has a pleiotropic effect on inflammation, immune response, and hematopoiesis. When it was first identified, it was named as B-cell-stimulating factor 2 (BSF-2) according to its ability to induce immunoglobulin production in Epstein-Barr virus-transformed B-cell lines or in Staphylococcus aureus Cowan 1-stimulated B cells [2-4].
Nowadays, it is known that IL-6 controls the survival, population expansion and maturation of B cells and plasmablasts. In that way, the regulation of Blimp-1 by STAT3 is linked to antibody secretion and is associated with long-lived plasma cells that produce large amounts of immunoglobulin. Furthermore, the ability of IL-6 to promote humoral immunity has been linked to its effects on follicular helper T cells where they promote B cell proliferation and immunoglobulin class switching [5].
Objectives: Hypogammaglobulinaemia is a known complication of some immunosuppressive drugs, not previously described in patients who received therapy with monoclonal antibody against the IL-6R. We aimed to analyzed the prevalence of hypogammaglobulinaemia in our series of patients treated with tocilizumab after a carefully diagnostic workup which ruled out other causes and analyzed whether is associated with a higher risk of infection.
Methods: We conducted a retrospective review from 2010 to 2019 of forty-two patients affected with a rheumatic disease and treated with TCZ at our centre. In those patients in whom we had no record of immunoglobulin levels, we determined them in the blood analysis performed by usual clinical practice.
Results: 42 patients were identified, from whom 38 had rheumatoid arthritis. A 31% had immunoglobulin levels prior to starting treatment with TCZ but no one had hypogammaglobulinaemia. 2 patients were excluded due to their underlying disease could justify the IgG level abnormalities. During the treatment's follow-up, we identified that a 30% of the patients (12/40) had hypogammaglobulinaemia. Of those patients in whom immunoglobulin levels had been determined prior to starting treatment with TCZ, a 36.3% of them (4/11) developed hypogammaglobulinaemia during the follow-up. From the series, we observed a statistical significance tendency (p=0.0057) for infection risk in those patients with hypogammaglobulinaemia in contrast to those with normal IgG level (41.5% vs 14.3%, respectively).
Conclusion: Secondary hypogammaglobulinaemia may occurs in patients receiving anti-IL6 agents such as tocilizumab and this could be associated with an increasing infection risk. The prevalence is not precisely known, in part because measurement of IgG prior to or during the treatment has not been a standard of care. No medical data have been previously disclosed about this possible adverse effect of anti-interleukin-6 agents. Nevertheless, ideally randomized trials are needed to assess this initial hypothesis.
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Disclosure of Interests: Francisco Vílchez-Oya: None declared, Ana Pros: None declared, Irene Carrión Barberà Grant/research support from: I received a grant from the Spanish Rheumatology Foundation (FER) and laboratories KERN PHARMA for a brief stay abroad., Juan Antonio Meraz Ostiz: None declared, Tarek Carlos Salman Monte: None declared, Carolina Perez-Garcia: None declared
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FRI0112

RISK OF MALIGNANCY WITH NON-TNFI BIOLOGIC OR TOFACITINIB THERAPY IN RHEUMATOID ARTHRITIS: A META-ANALYSIS OF OBSERVATIONAL STUDIES

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Background: With an increasing usage of non-TNFi biologics and tofacitinib, it is crucial to understand the comparative safety of these agents regarding malignancies risk.
Objectives: We aim to assess the risk of developing cancer in patients with RA exposed to non- TNF inhibitors (TNFi) biologics or tofacitinib therapy.
Methods: Systematical search of PubMed, EMBASE and Cochrane Library plus a hand search of conference proceedings were performed for observational studies that reported cancer incidence in patients with RA treated with biologics or tofacitinib with active comparator of conventional DMARDs (csDMARDs) or TNFi. The pooled relative risk (RR) and 95% confidence interval (CI) were calculated with fix-effects or random-effects model.
Results: Of 2,819 identified articles, a total of 10 studies involving over 323,361 patients and 1,179,263 patient-years of follow-up were included. Pooled analysis showed there was no increased risk of developing cancer in general or specific cancer types in RA patients receiving treatment with rituximab (pooled RR 1.13, 95% CI 0.80-1.59), tocilizumab (pooled RR 0.96, 95% CI 0.83-1.11), or tofacitinib (pooled RR 0.97, 95% CI 0.66-1.43), compared with those receiving csDMARDs or TNFi. However, abatacept usage in RA was associated with a slightly increased overall cancer risk (pooled RR 1.13, 95% CI 1.02-1.24) and non-melanoma skin cancer (pooled RR 1.26, 95% CI 1.09-1.45), relative to csDMARDs or TNFi.
Conclusion: Compared with csDMARDs or TNFi, there was no increased risk of malignancies among RA patients treated with non-TNFi biologics or tofacitinib, with exception of abatacept associated with slightly increased total cancer and specific caner types. Extended researches are required to confirm the findings in a real-world context.
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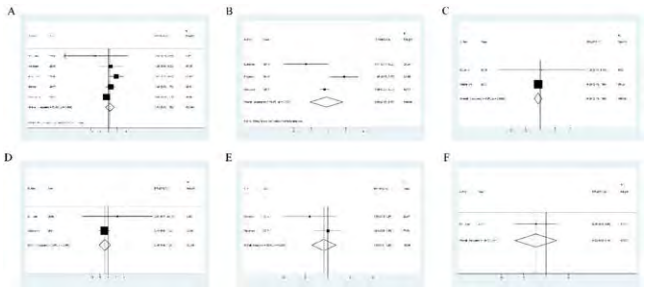


Figure 1. Relative risk of developing cancer between rituximab and csDMARDs. (A) any cancer; (B) all cancer types excluding NMSC; (C) solid tumors; (D) hematological cancer; (E) NMSC; or (F) melanoma. csDMARDs: conventional synthetic disease-modifying antirheumatic drugs. NMSC: non-melanoma skin cancer.

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FRI0113

THE BASELINE SOLUBLE GP130 IS ASSOCIATED WITH THE RESPONSE OF RHEUMATOID ARTHRITIS PATIENTS TO SARILUMAB

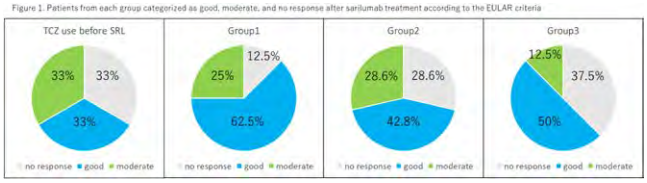
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Background: IL-6 contributes significantly to the chronic inflammatory process of rheumatoid arthritis (RA). Sarilumab (SRL), a human anti-human IL-6 receptor alpha monoclonal antibody that blocks the signaling originated by the IL-6/IL-6R complex like tocilizumab,is an effective treatment. However, predictors of the response to sarilumab are still required.
Objectives: We aimed to combine IL-6, soluble IL-6R (sIL-6R) and gp130 (sgp130) levels to identify groups of sarilumab responses.
Methods: This research is a retrospective study. a total of 32 RA patients with SRL therapy in our department from February 1 in 2018 to December 31 in 2019 were included. Serum and clinical data from 32 RA patients were collected before treatment and until the last visit. Follow-up period was up to one year after starting SRL treatment. Serum were tested for IL-6 (Human IL-6 Quantikine ELISA Kit, R&D systems), sIL-6R (Human soluble IL-6R alpha Quantikine ELISA Kit, R&D systems) and sgp130 (Human soluble gp130 Quantikine ELISA Kit, R&D systems), using specific ELISAs according to the manufacturer's instructions. Hierarchical cluster analysis (JMP14.3.0) was used to establish the relationship between IL-6, sIL-6R and sgp130. We evaluated the efficacy of SRL treatment on the last visit using European League Against Rheumatism (EULAR) response criteria in the groups of patients. The other statistical analyses were performed with EZR 1.41, and p Values less than 0.05 were considered significant.
Results: The median age of patients was 70.5 (IQR: 66.5-74.3) years and the median of disease duration was 7.3 (1.7-15.3) years. Nine (28.1%) patients were biologics and Jakinibs naive. the median follow-up periods were 24 (12-26) weeks. The baseline DAS28 was median 4.39 (3.77 - 5.43), and CDAI was 21.1 (11.7-29.5). When comparing responders and non-responders, there were no significant differences in any of the baseline parameters and cytokines. Four statistical significant clusters of RA patients (i.e., Group1, Group2, Group3 and tocilizumab use group before SRL) were defined by serum concentrations of IL-6, sIL-6R and spg130 at baseline. The levels of IL-6 expressed as median in Group1 patients were 25.6 (14.4–72.2) pg/ml, in Group2 5.9 (3.3–11.3) pg/ml, and in Group3 70.2 (45.4–86.1) pg/ml ($p < 0.002$, significant difference only between Group2 and Group3). The levels of sIL-6R expressed as median in Group1 patients were 38.7 (34.7-45.1) ng/ml, in Group2 35.1 (24.8-41.9) ng/ml, and in Group3 35.7 (34.2-39.8) ng/ml ($p = 0.5477$). The levels of sgp130 expressed as median in Group1 patients were 272.6 (263.0-277.2) ng/ml, in Group2 223.1 (221.0-228.0) ng/ml, and in Group3 204.6 (192.0-207.6) ng/ml ($p < 0.00003$, significant difference between the three groups respectively). There were no significant differences in any of the baseline clinical features and laboratory findings between the three groups. Out of the 8 patients in Group1 had a good or moderate response to SRL. Conversely, the percentage of patients with no response to SRL was higher in Group3 than in Group1 and Group2.
Conclusion: RA patients could be easily stratified prior to the rapeutic intervention with sgp130 related to the IL-6 signal reguration. Group1 patients, who had the best response to SRL, had the highest level of sgp130.

Table 1. Comparison of baseline serum IL-6, sIL-6R and sgp130 of each groups of patients

	TCZ use before SRL		Group 1	Group 2	Group 3	P value
	n=3		N=9	N=8	N=9	
IL-6, pg/mL	69.8, 77.6, 592.6	Median [IQR]	25.6 [14.4-72.2]	5.9 [3.3-11.3]	70.2 [45.4-86.1]	<0.002 c
sIL-6R, ng/mL	390.5, 413.2, 481.7	Median [IQR]	38.7 [34.7-45.1]	35.1 [24.8-41.9]	35.7 [34.2-39.8]	0.547
sgp130, ng/mL	205.6, 219.2, 239.8	Median [IQR]	273 [263-277]	223 [221-228]	205 [192-208]	<0.001 abc

*a, b and c mean that statically significant difference between subgroups as a: group1 vs. 2, b: group 1 vs. 3, c: group 2 vs. 3.



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FRI0114

EFFICACY OF LEVILIMAB, NOVEL MONOCLONAL ANTI-IL-6 RECEPTOR ANTIBODY, IN COMBINATION WITH METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS: 1-YEAR RESULTS OF PHASE 2 AURORA STUDY

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Background: Previously, 12-week results of phase 2 clinical study of levilimab (LVL) in patients with active rheumatoid arthritis (RA) have been reported[1]. The study has met the primary endpoint at W12 confirming that treatment with LVL 162 mg SC + methotrexate (MTX) either QW or Q2W is superior to MTX alone in patients with RA and inadequate response to methotrexate (MTX-IR). Here we report 1-year efficacy and safety data in QW and Q2W arm of the study.
Objectives: This study was aimed to assess the efficacy and safety of 2 dosing regimens of LVL in active MTX-IR RA subjects.
Methods: This multicenter double-blind placebo-controlled study (NCT03455842) enrolled 105 MTX-IR subjects with active RA (ACR2010). The study design is outlined on Figure 1. Secondary endpoints for the open-label period included ACR20/50/70, LDA, remission rates, and DAS28-CRP(4), among others. The safety was evaluated up to W56.

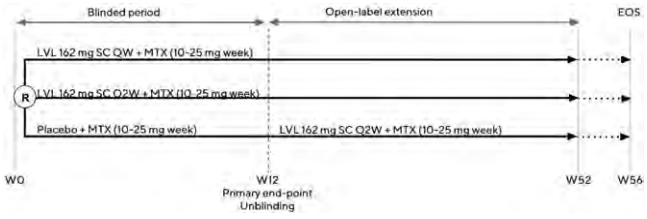


Figure 1. Study design

Results: At W12 ACR20 was reached by 77.1% and 57.1% of subjects of QW and Q2W arms respectively. Within open-label (OLE) period further increase in clinical response degree was observed up to W52, more pronounced in ACR50 and even more in ACR70 / RA LDA and Remission rates (Table 1). Figure 1 summarizes the dynamic of DAS28-CRP(4) change throughout the study. QW regimen showed better efficacy results.

Table 1. Efficacy results (full analysis set), n (%).

	QW + MTX (n = 35)	Q2W + MTX (n = 35)	p-value
ACR20 W12	27 (77.1)	20 (57.1)	0.07
W52	32 (91.4)	25 (71.4)	**0.03**
ACR50 W12	18 (51.4)	11 (31.4)	0.09
W52	26 (74.3)	23 (65.7)	0.43
ACR70 W12	10 (28.6)	7 (20.0)	0.40
W52	23 (65.7)	16 (45.7)	0.09
LDA (DAS28 <3.2) W12	20 (57.1)	10 (28.6)	**0.02**
W52	29 (82.9)	24 (68.6)	0.16
EULAR Remission W24	4 (11.4)	2 (5.7)	0.67
W52	10 (28.6)	10 (28.6)	1.00

Table 2 shows the main safety endpoints for the entire study (W0 – W56). The most common treatment related AEs (registered >5% of subjects) were laboratory abnormalities (neutrophil count decrease, ALT / AST increase, blood cholesterol/triglycerides increased). SAE occurred within the blinded study period were reported previously[1]. During OLE, starting from W12, four new serious AE (SAEs) were reported: 3 in LVL QW arm: haemorrhage (gr.3, unrelated), vaginal cyst (gr.3, unrelated) and keratitis (gr.2, unrelated); 1 in LVL Q2W arm: myocardial ischemia with cardiovascular insufficiency (gr.5, unrelated).

Table 2. Safety results (full analysis set, W0 – W56), n (%).

	QW + MTX (n = 35)	Q2W + MTX (n = 35)
Any TEAEs/SAEs	34 (97.1)	29 (82.9)
Any SAEs	4 (11.4)	2 (5.7)
Any gr. 3-4 AEs	16 (45.7)	12 (34.3)
Gr. 3-4 neutropenia	4 (11.4)	5 (14.3)
AEs of special interest *(ALT / AST high; Leucopenia / Neutropenia; Infections; Cholesterol/triglycerides high)*	28 (80.0)	26 (74.3)
Treatment discontinuation due to AE	0	4 (11.3)
Deaths	0	2 (5.7) (unrelated)

Conclusion: Within 1 year of treatment LVL + MTX showed sustained efficacy, with continuous clinical improvement in MTX-IR subjects with active RA. The safety profile of LVL was consistent with other IL6R inhibitors. LVL QW regimen was shown to be safe with better efficacy in terms of time and magnitude and was selected for phase 3 confirmatory clinical study.

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[1] http://dx.doi.org/10.1136/annrheumdis-2019-eular.7220

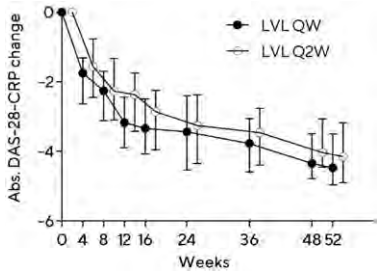


Figure 2. Absolute DAS-28-CRP(4) change (median ± IQR, full analysis set)

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FRIDAY, 05 JUNE 2020

Rheumatoid arthritis - non biologic treatment and small molecules

FRI0115

FILGOTINIB PROVIDED RAPID AND SUSTAINED IMPROVEMENTS IN FUNCTIONAL STATUS, PAIN, AND HEALTH-RELATED QUALITY OF LIFE, AND REDUCED FATIGUE OVER TIME IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO ARE METHOTREXATE-NAÏVE: RESULTS FROM THE FINCH 3 STUDY

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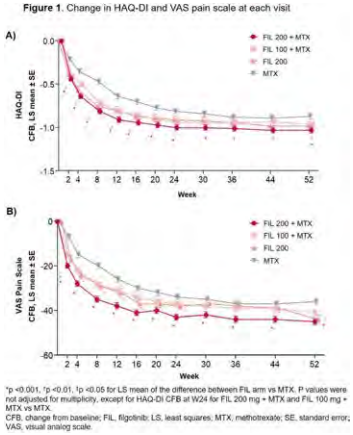
Background: In the FINCH 3 study, filgotinib (FIL)—a potent, selective, oral small molecule Janus kinase 1 inhibitor[1]—in combination with methotrexate (MTX), demonstrated significant improvements in the signs and symptoms of rheumatoid arthritis (RA) vs MTX alone in patients (pts) who were MTX-naïve.[2] For pts with RA, rapid control of pain and fatigue along with maintenance of physical function and health-related quality of life (HRQoL) are important outcomes of their care.[3] Thus, patient-reported outcomes (PROs) can provide physicians with evidence to guide treatment decisions beyond the guideline-recommended treatment targets of reducing immune inflammation to prevent joint damage, physical disability, and mortality.[4]

Objectives: To evaluate the rate and magnitude of change in PROs assessing functional status, pain, HRQoL, and fatigue from FINCH 3.

Methods: In the FINCH 3 study (NCT02886728), pts with active RA who were MTX-naïve received FIL 200 mg daily + MTX, FIL 100 mg + MTX, FIL 200 mg (+ placebo [PBO]), or MTX (+ PBO) for up to 52 weeks. PROs were recorded prospectively and included HAQ-DI (functional status) and VAS pain scale (day 1, week [W]2, W4, W8, W12, W16, W20, W24, W30, W36, W44, W52), SF-36 (HRQoL), and FACIT-Fatigue (day 1, W4, W12, W24, W36, W52). The least squares mean of the change from baseline (CFB) at each time point up to W52 and p values (each FIL arm vs MTX) were analysed using a mixed-effects model for repeated measures. For HAQ-DI, the proportion of pts who achieved the minimum clinically important difference (MCID; reduction ≥0.22) between each FIL arm and MTX was analysed using logistic regression analysis. P values for the comparisons of PROs were not adjusted for multiplicity, except for HAQ-DI CFB at W24 for FIL 200 mg + MTX and FIL 100 mg + MTX vs MTX.

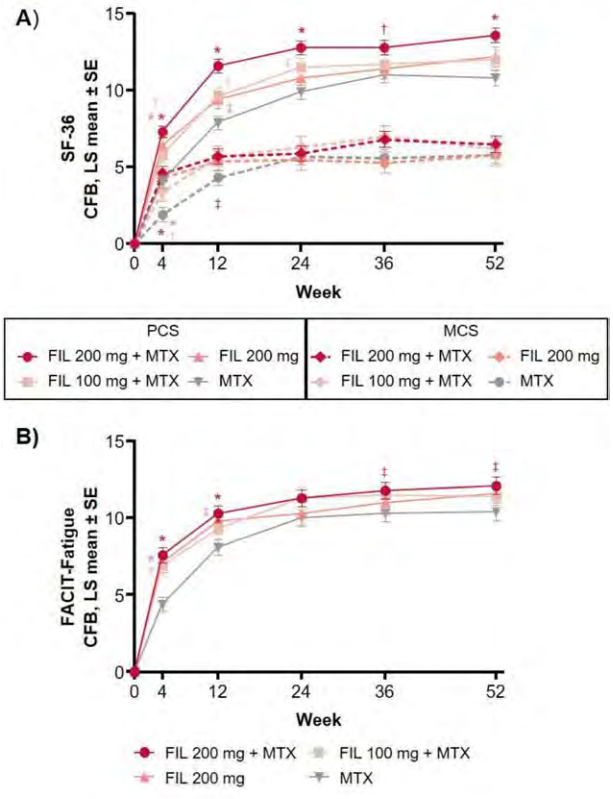
Results: Of the 1249 pts randomised and treated (FIL 200 mg + MTX, n = 416; FIL 100 mg + MTX, n = 207; FIL 200 mg, n = 210; MTX, n = 416), 1025 (82.1%) completed the study. Compared with MTX alone, a nominally significantly greater CFB in functional status and pain from W2 to W24 was observed in all FIL arms; the benefit was sustained from W30 to W52 (Fig 1). By W2, a nominally significantly greater proportion of pts achieved the HAQ-DI MCID or greater (≥0.22) in all FIL arms (FIL 200 mg + MTX: 61.9%, p <0.001; FIL 100 mg + MTX: 58.5%, p <0.001; FIL 200 mg: 53.9%, p = 0.004) compared with MTX (42.2%). By W8, ≥72% of pts in all FIL arms vs 63% of pts in the MTX arm achieved the HAQ-DI MCID; a numerically greater proportion of pts in FIL arms vs MTX achieved HAQ-DI MCID through W52. SF-36 physical component summary and FACIT-Fatigue scores were nominally significantly improved with FIL treatment vs MTX alone at various time points (Fig 2**A, B**). Improvements in SF-36 mental component summary scores were nominally significant for pts in all FIL arms vs MTX alone as early as W4, and the CFB reached at W12 for FIL arms was generally sustained up to W52 (Fig 2**A**).

Figure 1. Change in HAQ-DI and VAS pain scale at each visit



*p <0.001, †p <0.01, ‡p <0.05 for LS mean of the difference between FIL arm vs MTX. P values were not adjusted for multiplicity, except for HAQ-DI CFB at W24 for FIL 200 mg + MTX and FIL 100 mg + MTX vs MTX.
CFB, change from baseline; FIL, filgotinib; LS, least squares; MTX, methotrexate; SE, standard error; VAS, visual analog scale.

Figure 2. Change in SF-36 and FACIT-Fatigue at each visit



*p <0.001, †p <0.01, ‡p <0.05 for LS mean of the difference between FIL arm vs MTX. P values were not adjusted for multiplicity.
CFB, change from baseline; FIL, filgotinib; LS, least squares; MCS, mental component score; MTX, methotrexate; PCS, physical component score; SE, standard error.

Conclusion: For pts with moderate to severe RA who were MTX-naïve, FIL—with or without concomitant MTX—led to more rapid and sustained improvements in functional status, pain, fatigue, and HRQoL, compared with MTX alone.

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FRI0116

COMPARABLE EFFICACY AND SAFETY OF TWO REGIMENS OF RHEUMATOID ARTHRITIS TREATMENT WITH TOFACITINIB: DATA FROM RUSSIAN NATIONAL REGISTRY

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Background: Current EULAR and national guidelines recommend use of synthetic target drug Tofacitinib (TOFA) for active rheumatoid arthritis (RA) treatment in case of resistance or intolerance to metotrexate (MTX) or other conventional DMARDs. Two treatment regimens are approved: TOFA mono-therapy and combination with conventional DMARD, preferably with MTX.

Objectives: Aim of presented study was to compare efficacy and safety of TOFA given in two regimens: as mono-therapy and in combination with MTX.

Methods: We analyzed data from Russian national registry of RA. 450 patients (pts) treated with TOFA in dose 10 mg daily have been enrolled in this investigation. Among them 169 pts have composed TOFA mono-therapy group (mono) and 281 pts treated with TOFA plus MTX have been included in combo-therapy group (combo). Period of treatment varied from 6 months to 3 years and even more. Treatment efficacy was evaluated on the basis of clinical and laboratory indices of RA activity: CDAI, SDAI, DAS28, HAQ, GPA (general pain assessment), TJC, SJC, CRP, ESR monthly during first 6 months, than in 1,2,3 years and after 3 year period of treatment.

Results: There were no significant differences in pts demographic characteristic and disease longevity and/or severity in two separated groups. Majority of baseline indices were identical in these groups aside from SDAI, CRP (were higher in combo-group) and HAQ (was higher in mono-group). Pts monitoring have shown dramatically decrease of all used indices during the first several months of therapy in both groups. Moreover all clinical and laboratory parameters after 6-months treatment were comparable in mono- and combo- groups. Positive dynamics remained during further 3-year period in both groups. Significant differences between baseline and ultimate data after 3 year course therapy were revealed in CDAI, SDAI, DAS28, HAQ, GPA, TJC, SJC, CRP, ESR in both groups. In particular DAS28 index decreased from 5.38±0.08 to 2.88±0.07 ($p<0.05$) in mono-group and from 5.54±0.09 to 3.40±0.21 ($p<0.05$) in combo-group. Along with this comparing of endpoints in two analyzed groups have shown that levels of CDAI, SDAI, GPA were significant higher in combo-group than in mono-group ($p<0.05$). Adverse effects were registered in 4.73% pts from mono-group and in 4.98% pts from combo-group ($p>0.05$). Spectrum of adverse reactions was similar in compared groups: respiratory infection (in 2.96% and 3.36% cases respectively) and herpes infection (in 0.59% and 0.71% cases, respectively) were registered predominantly.

Conclusion: Data gained from National RA registry have demonstrated that treatment with TOFA in mono-therapy regimen has the comparable efficacy with regimen of combined therapy, included MTX and TOFA. Safety of both regimens can be qualified as good. Obtained results confirm high efficacy and safety of target therapy with TOFA and prove the recommendation for use it in different regimens – mono-therapy or combination with MTX.

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FRI0117

INCIDENCE RATE OF HERPES ZOSTER IN RHEUMATOID ARTHRITIS PATIENTS UNDER TOFACITINIB: REAL-LIFE DATA FROM TURKEY – HURBIO REGISTRY

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Background: Tofacitinib (TOF) is an orally administered Janus Kinase (JAK) inhibitor and is commonly used in rheumatoid arthritis. There is a heterogeneity among numbers reported from different continents about herpes zoster (HZ) incidence rate (1-3). However, data about HZ risk in our country, which stands like a bridge between Asia and Europe, is lacking.
Objectives: To assess the real-life incidence of herpes zoster in RA patients under tofacitinib.
Methods: We analyzed all patients who had at least 1 control visit under tofacitinib and registered to HURBIO database. We calculated incidence rate by dividing the number of patients with herpes zoster to total follow-up years, then multiplied by 100 (per 100 patient-years).
Results: A total of 204 (174 (85.4%) female) patients were recruited. Mean age was 53.2±12.5 years. Mean disease duration was 11.5±8.1 years. Rheumatoid factor and anti-CCP antibodies were positive in 135/198 (68.1 %) and 115/171 (67.2 %) patients, respectively. Median follow-up while receiving TOF was 11.6 (IQR:5.2-26.2) months. Combination with DMARDs was used in 83.3% of patients. 55.5% of patients was biologic-naive. Eleven (5.3%, incidence rate: 3.9 (2.3-8.5; % 95 CI) per 100 patient-years) patients had zona zoster. Ten of these patients was female, median age was 59 (IQR; 52-69) and 4 of them was older than 65 years-old. Rheumatoid factor was positive in 9 patients. Only 1 of these patients had diabetes. Median follow-up of these patients under TOF was 8.1(IQR: 6-25) months. Ten of these patients had concomitant DMARDs (9 hydroxycholoroquine, 4 methotrexate, 2 leflunomide; according to last follow-up visit) and 9 of them received concomitant steroids (med(IQR); 4 (1-8) mg- at equivalant methyl-prednisolon dose). Eight of them was biologic-naive. Tofacitinib was discontinued in 4 of these patients.
Conclusion: In this real-life data from Turkey, we found a HZ incidence rate similar to that reported from USA and global data; however, we found a lower incidence rate that reported from Japan (Figure 1).

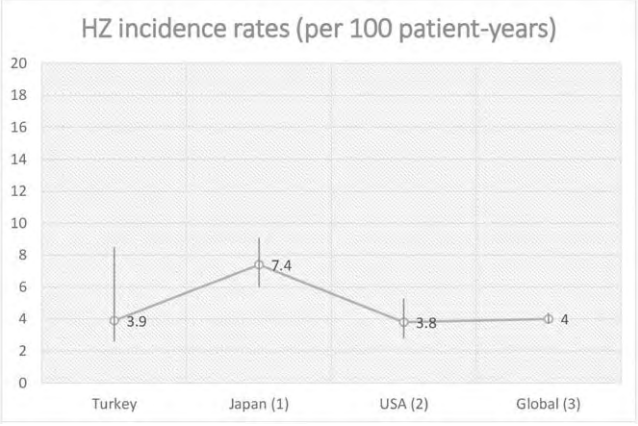


Figure 1. Reported herpes zoster incidence rates across different countries (numbers in paranthesis indicate reference number)

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FRI0118

RISK OF LIVER FIBROSIS ON TRANSIENT ELASTOGRAPHY IN PATIENTS WITH RHEUMATIC DISEASE UNDER LONG-TERM METHOTREXATE TREATMENT

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Background: Methotrexate (MTX) is a cornerstone drug for the treatment of rheumatic disease and low doses of MTX are both tolerable and safe, with monitored toxicity, assessed via the liver function test. However, there is still controversy regarding the risk of liver fibrosis with long-term use of MTX. Transient elastography is commonly used to assess and monitor fibrosis progression in patients with chronic liver disease.
Objectives: The present study aims to investigate liver fibrosis using transient elastography and related factors in patients with rheumatic disease receiving long-term MTX.
Methods: The present retrospective, longitudinal, cross-sectional study included patients with an autoimmune disease who are taking cumulative MTX dosed over 7 g, and who had liver fibrosis upon examination using transient elastography. Liver fibrosis was defined as liver stiffness, valued over 7.2 kPa. Logistic regression analysis was performed to identify factors associated with liver fibrosis, and receiver operating characteristics analysis was used to determine the predictive value of each factor.
Results: We included 83 patients with autoimmune disease, with a median MTX cumulative dose of 11.6 (range 7.3-16.0) g. Sixty-eight patients (81.9%) had rheumatoid arthritis (RA), and 13 patients (15.7%) had Takayasu arteritis. The median MTX exposure duration was 18 (range 9-31) years. The median liver stiffness value was 4 (range 1.8-10.2) kPa. Five patients (6%) showed liver fibrosis (3 patients; RA, 2 patients; Takayasu arteritis). In the linear regression analysis, cumulative MTX dose showed a tendency towards a positive correlation with increasing liver stiffness value ($r2 = 0.039$, $p = 0.074$). In the logistic regression analysis, cumulative MTX dose was associated with a higher risk of liver fibrosis (OR: 1.734, 95% CI: 1.060–2.837, $p = 0.029$). In addition, cumulative MTX dose had an area under the curve (AUC) of 0.813 (95% CI 0.695-0.930) and a sensitivity of 80% and specificity of 71.8% at a cut-off value of 12.7 g.
Conclusion: Liver fibrosis was observed in 6% of patients with long-term MTX use and higher cumulative MTX doses increased the risk of liver fibrosis. Thus, transient elastography should be considered in patients exposed to high cumulative doses of MTX.

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FRI0119

TITLE USE OF JAK INHIBITORS IN THE TREATMENT OF RA PATIENTS IN THE ROMANIAN REGISTRY OF RHEUMATIC DISEASES

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Background: JAK inhibitors are the newest therapeutic class available in Romania for the treatment of rheumatoid arthritis (RA). Both available JAK inhibitors (baricitinib and tofacitinib) are fully reimbursed.
Objectives: Efficacy and safety data for JAK inhibitors, derived from the Romanian Registry of Rheumatic Diseases (RRBR).

Methods: cohort retrospective study, the data being gathered from RRBR, which includes all the patients treated with biologics and targeted synthetic DMARDs in the country. Inclusion criteria: at least one treatment course of JAK inhibitors, until end of 2019. The collected data: demographic and disease characteristics, efficacy parameters (DAS28) and safety data (exposure to JAK inhibitors in person-years (PY) and reported adverse events (AE).
Results: the RA cohort treated with JAK inhibitors included 416 patients (7.6% of all RA patients registered in RRBR) exposed to baricitinib (306 pts) or tofacitinib (110 pts) for 66255 PY. The mean age was 57.91 years, 365 (88%) women, 41 (10%) smokers, mean RA duration 11.32 years, 316 (76%) RF positive, 254 (61%) ACPA positive, 356 (85.5%) patients associate a synthetic DMARD, 76 (18%) use steroids (66% <7.5mg prednisone/day); 268 (65%) patients have cardiovascular comorbidities, 84 pts (20%) have modified lipid profile, 89 patients (21.4%) have latent TB, 86 (20.7%) have resolved HBV infection state. JAK inhibitors were the first treatment option for 178 patients (43%), all other patients have been exposed previously to at least one TNF-inhibitor or a biologic with another mode of action, being insufficient responders, as follows: 96 patients – to 1 biologic, 80 patients – to 2 biologics, 30 patients – to 3 biologics, 23 patients – to 4 biologics, 8 patients – to 5 biologics and 1 patient - to 7 molecules before the JAK inhibitors start. Of all patients exposed to JAK inhibitors, 252 (60.5%) patients have continued the therapy since the start summarising 61481PY of exposure. The efficacy parameters reported to this category revealed a mean DAS28 score of 3.08, significantly lower compared to 6 months before (4.77). Regardless the number of biologic agents used before starting a JAK inhibitor, there is no significant difference in DAS28 score when comparing it with DAS28 efficacy of the first treatment option scenario (3.10 vs 2.94, p>0.05). Steroid use, the presence of RF or disease duration have no influence on the efficacy DAS28. On contrary, the ACPA positivity subgroup has a significantly lower DAS28 score, compared to ACPA negativity (3.18 vs 3.82, p<0.05); smoker status has a significantly higher DAS28 compared to non-smokers (3.58 vs 2.94, p<0.05). A total number of 46 AEs were reported for a total exposure of 66255PY. Infections were the most frequently reported AE (0.04/100PY, with 27 events); 6 cases of herpes zoster infection (0.009/100PY, all mild); 3 MACE (0.004/100PY). There were 3 severe adverse events (0.004/100PY) (1 hepatitis non-viral, 2 MACE) with one fatal (acute myocardial infarction).
Conclusion: JAK inhibitors represent a safe and efficacious treatment option for patients with active RA.
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FRI0120 ORAL GLUCOCORTICOID USE IS ASSOCIATED WITH HYPERTENSION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Oral glucocorticoids (GC) are frequently prescribed to patients with rheumatoid arthritis (RA), however GC use is associated with a number of potential side effects. Hypertension is cited as a possible side effect, but few studies have specifically investigated GC-associated hypertension in patients with RA with conflicting results.
Objectives: The aim of this study was to determine whether GCs were associated with an increased risk of incident hypertension in a cohort of patients with RA.
Methods: A retrospective cohort of patients with incident RA and no hypertension at RA diagnosis were identified from UK primary care electronic health records (Clinical Practice Research Datalink). GC prescriptions were used to determine time-varying GC use and dose, categorised as: no use, >0–4.9 mg/day, 5–7.4 mg/day, 7.5–14.9 mg/day, ≥15mg/day. A 3-month risk attribution model was used where patients continued to remain at risk for 3 months after the end of prescriptions. Hypertension was identified if a patient had either: 1) 2 consecutive systolic blood pressure (BP) measurements >140mmHg within a year, 2) 2 consecutive diastolic BP measurements >90mmHg within a year or 3) antihypertensive prescriptions on at least two occasions and a Read code for hypertension. Unadjusted and adjusted Cox proportional hazards (PH) regression models were fitted to determine if there was an association between GC use and hypertension. Models were adjusted for baseline age, gender, baseline body mass index, baseline ever smoking, time-varying synthetic disease-modifying anti-rheumatic drug use, time-varying non-steroidal anti-inflammatory drug use and baseline Charlson comorbidity index.
Results: There were 17,760 patients with incident RA and no hypertension. The cohort had a mean age of 56.3 ± 12.7 years and were predominantly female (68%). 7,421 (42%) were prescribed GCs during follow-up. There were 6,243 cases of incident hypertension over 97547 person years (pyrs) of follow-up, giving an incident rate of 64.1 per 1000 pyrs. Of those 1321 cases were in those exposed to GCs and 4922 were in those unexposed, giving incident rates of 87.6 per 1000 pyrs and 59.7 per 1000 pyrs, respectively. The adjusted Cox PH model indicated that recent GC use was associated with a 17% increased hazard of hypertension (hazard ratio: 1.17 (95% CI 1.10 to 1.24)). When categorised by dose, the adjusted model indicated only doses above 7.5mg were significantly associated with hypertension (Table 1).

Table 1. Unadjusted and adjusted Cox proportional hazards regression model results

		Unadjusted HR (95% CI)	Age and gender adjusted HR (95% CI)	Fully adjusted* HR (95% CI)
Recent GC use		1.44 (1.35 to 1.53)	1.23 (1.16 to 1.31)	1.17 (1.10 to 1.24)
Recent GC dose	No GC use	Reference	Reference	Reference
	>0 – 4.9mg	1.35 (1.21 to 1.53)	1.13 (1.01 to 1.28)	1.10 (0.98 to 1.24)
	5mg – 7.4mg	1.40 (1.22 to 1.60)	1.11 (0.97 to 1.27)	1.07 (0.93 to 1.23)
	7.5mg – 14.9mg	1.44 (1.33 to 1.57)	1.26 (1.16 to 1.38)	1.18 (1.08 to 1.29)
	15mg and over	1.60 (1.40 to 1.84)	1.45 (1.27 to 1.66)	1.36 (1.18 to 1.56)

* Adjusted for: Baseline age, gender, baseline body mass index, baseline ever smoking, synthetic disease-modifying anti-rheumatic drug use (time-varying), non-steroidal anti-inflammatory drug use (time-varying) and baseline Charlson comorbidity index.

Conclusion: In this large cohort of patients with RA and without hypertension, recent GC use was associated with incident hypertension. In particular doses ≥7.5mg were associated with hypertension while the association with lower doses was inconclusive. Clinicians need to consider cardiovascular risk when prescribing GCs and ensure BP is regularly monitored.
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FRI0121 STEROID-SPARING EFFECT OF JAK INHIBITORS IN RHEUMATOID ARTHRITIS PATIENTS FOLLOWED UP IN A REAL LIFE SETTING

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Background: Glucocorticoids (GCs) are a milestone of Rheumatoid Arthritis (RA) treatment; EULAR recommendations on the management of medium to high dose glucocorticoids remind to evaluate comorbidities and risk factors for adverse events when planning GCs treatment. Tofacitinib and Baricitinib are Janus kinases inhibitors (JAKi) registered for RA treatment. About 60% of patients enrolled in randomized clinical trials with JAKi were co-treated with GCs; however, little is known about tapering and percentage of withdrawal both in clinical trials and real life.
Objectives: To evaluate the steroid-sparing effect of JAKi in patients with RA.
Methods: We prospectively enrolled consecutive adult patients with RA starting JAKi. At baseline and after 4, 12 and 24 weeks we calculated C-Reactive Protein based Disease Activity score 28 ($DAS28_{CRP}$). Daily dose of GCs was recorded at each visit as prednisone (PDN)-equivalent dose. Data are expressed as median (IQR). Continuous variables were compared by Mann Whitney test while dichotomous ones by Chi-square test. P values < 0.05 were considered statistically significant.
Results: Between January 2018 and January 2020, 108 patients started JAKi: 67 patients Baricitinib, 41 patients Tofacitinib. The analysis was restricted to 64 RA patients (50 female, 14 male) who had at least 6 months of follow-up. Table 1 shows the demographic, clinical and clinimetric characteristics of the cohort.

Patients treated with baricitinib and tofacitinib were comparable for age, disease duration, PDN dose and previous number of csDMARDS and bDMARDS; 30 patients (47.6%) were treated with JAKi in monotherapy. At baseline, the median daily PDN dose was 5 (7.25) mg; after 4, 12 and 24 weeks the median daily dose significant decreased to 5 (6.25) mg, 2.5 (5) mg and 0 (5) mg, respectively (p<0.0001). The percentage of patients treated with GC decreased from 81.5% to 63.5% at week 4, and to 48.4% at week 12 and 24. After 4, 12 and 24 weeks we detected a significant reduction of DAS28 (p<0.00001 compared to baseline). A similar percentage of patients who withdrew PDN compared to those who were still on PDN achieved remission after 12 and 24 months. Similarly, the reduction in DAS28 was comparable between the two groups at week 4 [4.8 (4.2) in those who withdrew vs 4.1 (1) in those who did not] at week 12 [4.8(1.6) for both] and at week 24 [3.7 (1.4) in those who withdrew vs 2.3 (0.7) in those who did not].

Table 1. Demographic, clinic and clinimetric characteristics of the 64 patients

	Baricitinib= 41	Tofacitinib=23	P value
Female:male	33:8	17:6	P=ns
Age, median (IQR), years	58 (15)	66 (14.5)	P=ns
Disease duration, median (IQR), months	144 (144)	150 (120)	P=ns
N° of previous csDMARDS	3 (3)	3 (1)	P= ns
N° of previous bDMARDs	2 (3)	1 (3)	P= ns
$DAS28_{CRP}$ at baseline	4.7 (1.6)	4.8 (2)	P=ns
PDN dose at baseline, median (IQR), mg	5 (7.5)	5 (5)	P=ns
PDN dose at 4 weeks, median (IQR), mg	5 (7.5)	5 (5)	P=ns
PDN dose at 12 weeks, median (IQR), mg	2 (5)	2.5 (4.7)	P=ns
PDN dose at 24 weeks, median (IQR), mg	0 (5)	2.5 (0)	P=ns

IQR: interquartile range; $DAS28_{CRP}$: Disease Activity Score 28 using C-Reactive Protein, csDMARDS: conventional synthetic Disease Modyfing anti-rheumatics drugs, bDMARDS: biotheconological Disease Modifying anti-rheumatics drugs PDN= prednisone

Conclusion: The rapid reduction of disease activity determined by JAK inhibitors allows a fast tapering of PDN, as suggested by the last EULAR recommendations for the management of RA.

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FRI0122 EFFICACY AND PATIENT-REPORTED OUTCOME MEASURES FROM A TWO-PART MULTICENTER, PLACEBO-CONTROLLED, RANDOMIZED WITHDRAWAL TRIAL OF REPOSITORY CORTICOTROPIN INJECTION FOR PERSISTENTLY ACTIVE RHEUMATOID ARTHRITIS

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Background: Repository corticotropin injection (RCI) is a naturally sourced complex mixture of adrenocorticotropic hormone analogs and other pituitary peptides approved for short-term adjunctive treatment of rheumatoid arthritis (RA).
Objectives: This two-part, international, multicenter, placebo (PBO)-controlled study assessed the efficacy of RCI in persistently active RA patients (pts) using clinical and patient-reported outcome measures (PROMs) (ClinicalTrials.gov NCT02919761).
Methods: Adults ≥18 years with persistently active RA (DAS28-ESR >3.2) despite disease-modifying anti-rheumatic drug and glucocorticoid use received open-label RCI (80 U) subcutaneously 2x/week (BIW) for 12 weeks (Part 1). Pts with DAS28-ESR <3.2 at Week (W) 12 entered the double-blind maintenance phase (Part 2) and were randomized to 80 U RCI or PBO BIW through W24. Efficacy endpoints included the proportion of pts who achieved DAS28-ESR <3.2 at W12 (primary) and maintained it through W24 (secondary). Mean changes from baseline (BL) were assessed for select PROMs (exploratory): Patient Global Assessment of Pain (PGAP); Patient Global Assessment of Disease Activity (PGADA); Health Assessment Questionnaire Disability Index (HAQ-DI); Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) scale; and Work Productivity and Activity Impairment (WPAI) questionnaire. Analyses used the modified intent-to-treat population (mITT-P; pts who received ≥1 dose of study drug and contributed any efficacy data).
Results: In the mITT-P (N=259), 62.9% (p<0.0001) achieved DAS28-ESR <3.2 at W12 (mean BL DAS28-ESR=6.3). In Part 2 (RCI, n=77; PBO, n=76), more RCI-treated pts maintained DAS28-ESR <3.2 at W24 (62.3%, p=0.035) vs. PBO (43.4%). Clinically significant improvements in PROMs from BL were observed through W12 and sustained to W24 (Table 1), with mean changes exceeding the reported minimal clinically important difference thresholds (MCIDs) for each.
Conclusion: RCI for persistently active RA resulted in clinically significant improvements in efficacy endpoints and PROMs for up to 6 months in pts who continued and discontinued RCI after 3 months of initial therapy.

References:

Table 1. PROMs From the 12-week Double-blind Withdrawal Phase, mITT-P

PROM (Score range) [MCID]	Baseline, Mean (SD)		Mean Change From Baseline (SD)							
			Week 12		Week 16		Week 20		Week 24	
	RCI	PBO	RCI	PBO	RCI	PBO	RCI	PBO	RCI	PBO
PGAP (0-100) [10]	65.7 (18.7)	62.8 (21.0)	−46.8 (23.4)	−45.8 (23.2)	−43.6 (26.1)	−41.2 (25.7)	−45.9 (23.7)	−42.8 (24.7)	−43.8 (23.9)	−40.7 (25.2)
PGADA (0-100) [10]	68.0 (16.6)	61.4 (20.0)	−48.1 (20.9)	−41.9 (24.5)	−44.5 (25.3)	−39.5 (26.5)	−48.5* (21.5)	−39.9 (27.7)	−45.9 (24.6)	−39.3 (28.2)
FACIT-F (0-52) [4]	22.7 (7.7)	22.6 (9.0)	−10.1 (8.1)	−10.2 (8.9)	−8.7 (8.2)	−8.6 (9.1)	−10.1 (7.8)	−10.5 (9.7)	−9.4 (7.9)	−10.5 (9.2)
WPAI (% due to RA) [N/A]										
Work time missed	19.9 (20.8)	31.9 (33.5)	−13.6 (25.4)	−20.7 (31.8)	−7.44 (35.3)	−15.7 (28.7)	−5.7 (26.5)	−14.2 (34.6)	−13.8 (24.9)	−9.2 (32.0)
Impairment while working	46.8 (25.8)	55.3 (30.7)	−34.7 (25.5)	−33.1 (24.3)	−31.3 (25.3)	−31.7 (32.7)	−27.2 (25.2)	−47.3 (28.7)	−30.0 (25.8)	−40.0 (28.3)
Overall work impairment	54.7 (28.9)	61.9 (33.4)	−36.9 (33.4)	−30.4 (26.9)	−33.4 (31.5)	−35.1 (40.2)	−23.6 (26.5)	−43.8 (34.3)	−32.7 (30.1)	−32.4 (28.8)
Activity impairment	64.9 (22.8)	61.1 (24.1)	−39.9 (24.3)	−37.2 (28.6)	−34.5 (25.8)	−30.0 (30.0)	−38.3 (23.8)	−37.7 (24.9)	−36.0 (24.9)	−37.9 (27.1)
HAQ-DI (0-3) [0.22]	1.7 (0.5)	1.7 (0.6)	−1.0 (0.6)	−1.0 (0.6)	−0.9 (0.5)	−0.9 (0.7)	−1.0 (0.6)	−1.0 (0.6)	−0.9 (0.6)	−1.0 (0.6)

*p<0.05 vs. PBO by 2-sample *t* test.

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FRI0123 SAFETY PROFILE OF BARICITINIB FOR THE TREATMENT OF RHEUMATOID ARTHRITIS UP TO 8.4 YEARS: AN UPDATED INTEGRATED SAFETY ANALYSIS

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Background: Baricitinib (bari) is an oral selective inhibitor of Janus kinase (JAK) 1 and 2, approved for the treatment of moderately to severely active rheumatoid arthritis (RA) in adults.

Objectives: Here we update the drug's safety profile with data up to 8.4 years of treatment.
Methods: Long-term safety of bari was assessed from 9 completed randomized trials (5 Ph3, 3 Ph2, 1 Ph 1b) and 1 ongoing long-term extension (LTE) study. Incidence rates (IR) per 100 patient-years (PY) were calculated for all patients with RA treated with ≥1 dose of bari through 1-Sep-2019 (All-Bari-RA analysis set). IRs for deep vein thrombosis (DVT), pulmonary embolism (PE), and DVT and/or PE (DVT/PE) were also calculated for groups of patients while receiving bari 2mg or bari 4mg within All-Bari-RA. Major adverse cardiovascular events (MACE) were adjudicated in 5 phase 3 studies and the LTE.
Results: 3770 pts received bari for 13,148 PY, with a median and maximum exposure of 4.2 and 8.4 years, respectively. Overall IRs per 100 PY were: for any treatment-emergent adverse event (AE)(25.8); serious AE (including death) (7.2); temporary interruption due to AE (9.5); permanent discontinuation due to AE (4.8); death (0.52); serious infection (2.7); opportunistic infection (0.44) (excluding tuberculosis [TB], including multidermatomal herpes zoster [HZ]); TB (0.15); HZ (3.0); MACE (0.50); DVT (0.31); PE (0.24); DVT/PE (0.45); malignancies excluding non-melanoma skin cancer (NMSC) (0.90); NMSC (0.33); lymphoma (0.06); and gastrointestinal perforation (0.04). Incidence rates (IR)[95% confidence intervals] for patients while receiving bari 2mg (N=1077) and bari 4mg (N=3400) were DVT 2mg (0.38) [0.18, 0.73] and 4mg (0.30) [0.21, 0.43]; PE 2mg (0.26) [0.09, 0.56] and 4mg (0.25) [0.16, 0.36]; and DVT/PE 2mg (0.47) [0.23, 0.84] and 4mg (0.46) [0.34, 0.61]. IRs for death tended to increase in later time intervals (beyond 192 weeks). No particular cause of death contributed to this increase. For all other safety topics of interest, across 48-week treatment intervals, IRs remained stable over time. Across safety topics, IRs were consistent with previous analyses[1,2].
Conclusion: In this update with 3,021 additional PY of exposure, bari maintained a safety profile similar to that previously reported,[1,2] with no increase of IRs across safety topics through exposures up to 8.4 years.
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Table.

	n/NAR	IR
Treatment emergent AE	3391/3770	25.8
Serious AE (including death)	940/3770	7.2
Temporary d/c due to AE	1241/3647	9.5
Permanent d/c due to AE	644/3770	4.8
Death	69/3770	0.52
Serious infection	344/3770	2.7
Opportunistic infection (excluding tuberculosis, including multidermatomal herpes zoster)	59/3770	0.44
Herpes zoster	384/3770	3.0
Tuberculosis	20/3770	0.15
Major adverse cardiovascular events*	63/3251	0.50
DVT	41/3770	0.31
PE	32/3770	0.24
DVT and/or PE	60/3770	0.45
Malignancies excluding NMSC	120/3770	0.90
NMSC	44/3770	0.33
Lymphoma	8/3770	0.06
Gastrointestinal perforation	6/3770	0.04

*studies with positive adjudication. AE=adverse event; D/C= discontinuation; DVT=deep vein thrombosis; IR=incidence rate; NAR=number of patients at risk; NMSC=non-melanoma skin cancer; PE=pulmonary embolism

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FRI0124

EFFICACY AND SAFETY OF BARICITINIB AND TOFACITINIB IN RHEUMATOID ARTHRITIS: DATA FROM REAL-WORLD

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Background: Oral targeted synthetic disease modifying anti-rheumatic drugs (DMARDs) including baricitinib and tofacitinib (JAKi), are the latest addition to the therapeutic options for rheumatoid arthritis (RA).
Objectives: To assess and compare the efficacy and safety of Baricitinib and Tofacitinib in RA patients in real life.
Methods: An observational longitudinal retrospective study was performed including RA patients who fulfilled the ACR/EULAR 2010 criteria and initiated treatment with Baricitinib or Tofacitinib from September 2017 to January 2020. Demographic, clinical and laboratory parameters and adverse events were collected. Infection was considered severe if it implied hospitalization. Statistical analysis was performed with R software (3.6.1) which consist in Bayesian lineal regression models including monotonic effect and Kaplan-Meier survival curves.
Results: 98 patients were included. Basal characteristics are exposed in table 1.

Table 1. Basal characteristics

	Baricitinib n=32	Tofacitinib n= 66
Female sex	96,88%	84,85%
Age	53,2 (13,1)	55,4 (13,4)
Disease evolution (years)	12,6 (9,1)	14,4 (8,6)
Monotherapy	14 (21,21%)	20 (30,3%)
DMARD		
Metotrexate	13 (40,63%)	24 (36,36%)
Leflunomide	4 (12,5%)	10 (15,15%)
Hydroxychloroquine	1 (3,7%)	2 (3,03%)
Glucocorticoids	22 (68,75%)	48 (72,73%)
First indication	6 (18,75%)	22 (33,33%)
After bDMARD failure	24 (75%)	44 (66,67%)

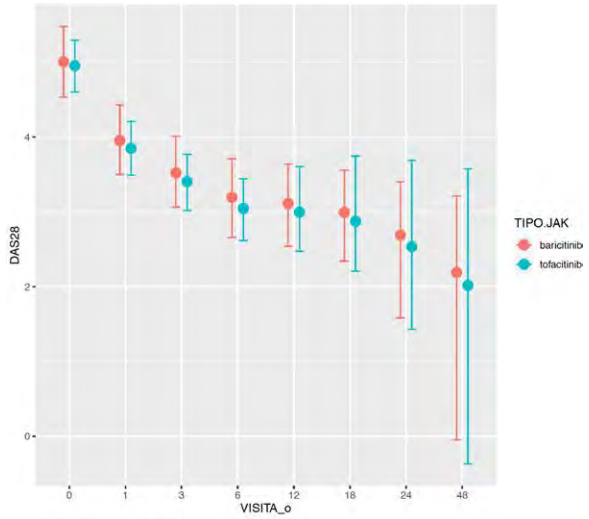
In both groups, a significative reduction of disease activity scores was noted (graphics 1 and 2).
Any difference between both treatments was detected in terms of efficacy even in first line, after bDMARD failure, in monotherapy nor combined therapy. Safety data are exposed in table 2 and neither was detected any statistical difference. In 2 of the cases of herpes zoster infection developed postherpetc neuralgia. Definitive discontinuation was registered in 23 cases (23,45%) accounting 6 (6,12%) for intolerance symptoms such as dizziness, nausea or headache (4 with Tofacitinib and 2 in Baricitinib group).

Table 2. Safety data

	Baricitinib n=32	Tofacitinib n=66
Temporary interruption	24 (75%)	50 (75,75%)
Adverse reaction	8 (25 %)	17 (25.75%)
Infections	22 (68,75%)	46 (69,69%)
Serious infections	3 (9,37%)	5 (7,57%)
Herpes Zoster	2 (6,25%)	2 (3,03%)
Permanent discontinuation	9 (28,13%)	14 (28,2%)
Intolerance	2 (6,25)	8 (12,12%)
Primary failure	1 (3,13%)	2 (3,03%)
Secondary failure	5 (15,63%)	3 (4,54%)
Infections	1 (3,13)	1 (1,51%)
Drug survival	23 (71,87%)	52 (78,78%)

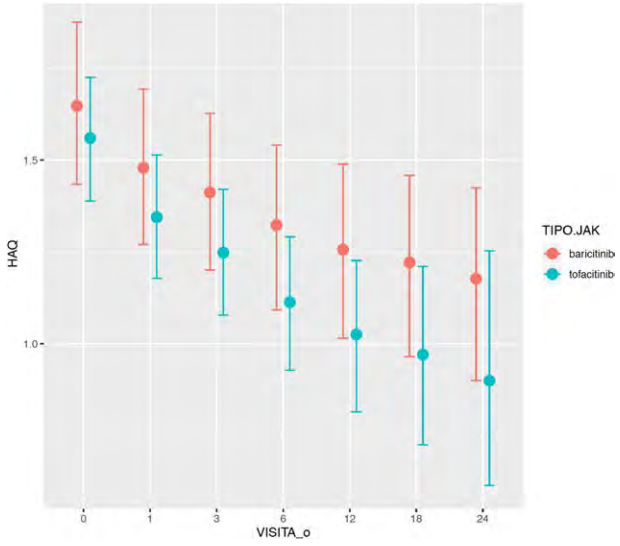
Survival analysis did not showed any difference between groups.

Conclusion: Baricitinib and Tofacitinib are both comparable in terms of efficacy and safety in real world conditions.



Graphic 2. Evolution of HAQ

Graphic 1. Evolution of DAS28



Graphic 2. Evolution of HAQ

Disclosure of Interests: None declared
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FRI0125

IMPACT OF RAMADAN DIURNAL INTERMITTENT FASTING ON CHRONIC MEDICATIONS INTAKE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Fasting during Ramadan, the ninth month of Islamic calendar, requires the abstinence from food and drink from sunrise to sunset [1]. Muslims are allowed to consume two major meals per day, one shortly before dawn (Suhoor) and the other immediately after sunset (Iftar). Although some previous investigations have reported a beneficent impact of fasting on rheumatic diseases' activity [1,2], very few studies have dealt with the possible impact of intermittent fasting on chronic medications intake.
Objectives: The objective of this study was to assess the impact of Ramadan intermittent fasting on adherence and tolerance of Disease-Modifying Anti-Rheumatic Drugs (DMARDs) in patients with rheumatoid arthritis (RA).
Methods: This is a prospective monocentric study including patients with rheumatoid arthritis (RA) who fasted Ramadan 2019. Each patient was evaluated during 2 visits: 6 months before starting Ramadan fasting and after fasting at least 7 days. The following parameters were assessed: compliance with treatments, tolerability and timing of intake (Iftar meal, evening, Suhoor meal).
Results: Thirty-six patients were enrolled: 7 men and 29 women. The average age of patients was 57.5 years ± 10.9 [39-79] and the mean disease duration was 6.7 years ± 3.3 [1-13]. Biological agents, methotrexate (MTX), Salazopyrin (SLZ) and Leflunomide (LFN) were respectively prescribed in 8, 22, 4 and 4 patients.
Ramadan fasting did not affect either compliance with biological agents or tolerance. No additional side effects have been reported during this period.
The compliance to MTX was comparable before and during fasting in 68.4% of cases. It was impaired by fasting in the rest with a full stop in 26.3% of patients. MTX was taken away from meals (as recommended) by 42.8% of patients. The timing of drug intake was the Iftar meal in 21.4% of patients, the Suhoor meal in 14.3% of patients and the evening in 64.3% of patients.
Except 1 patient, adherence to SLZ was adequate during Ramadan fasting. It was taken with the 2 major meals in 50% of cases and during the evening in 50% of cases.
Patients under LFN did not report any discontinuation.
The reported reasons of discontinuations of Conventional Synthetic Disease-Modifying Anti-Rheumatic Drugs (csDMARDs) were: objective adverse effects (25%), apprehension of gastrointestinal adverse effects (25%) and lack of time between the two major meals (50%) (since they were advised to take MTX away from meals).
Regarding the tolerance, gastrointestinal side effects of MTX were reported to be more frequent during Ramadan by 20% of patients, fewer by 13.3% of patients and unchanged by the rest of the patients. The gastrointestinal tolerance of SLZ and LFN was similar before and during Ramadan fasting.
Conclusion: Even if the tolerability of chronic medications was not impaired by Ramadan fasting in the majority of patients, adherence to conventional DMARDs was reported to be reduced by more than a quarter of patients, mainly because of a lack of time between the two major meals. Physicians should be aware of the impact of Ramadan fasting on chronic drugs intake because they have a crucial role in helping patients with RA adjust medications safely.
References:
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FRI0126

POOR ADHERENCE TO METHOTREXATE IS ASSOCIATED WITH PERSISTENT DISEASE ACTIVITY DURING FOLLOW-UP FOR RHEUMATOID ARTHRITIS

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Objectives: Although methotrexate (MTX) is the cornerstone therapy in patients with rheumatoid arthritis (RA), adherence to MTX in these patients is typically suboptimal. Thus, we investigated the proportion of RA patients who were adherent to MTX and whether non-adherence to MTX affected the clinical outcome in these patients during follow-up.
Methods: We enrolled 331 RA patients from a single tertiary center. Data were collected at the time of enrollment and then annually for 4 consecutive years. Adherence was defined by the proportion of days covered at 1 year. Patients were divided into two groups: patients who took more than 80% of MTX and those who did not. Univariate and multivariate analyses were performed to identify the association between drug compliance and clinical outcome.
Results: Of the 331 RA patients, 8.7% had taken less than 80% of MTX during the follow-up period. Non-adherent patients had lower EuroQol-5D scores (P=0.013) and higher RAPID3 scores (P=0.004) at baseline than adherent patients. Leflunomide was more commonly prescribed to adherent patients than non-adherent patients (P=0.012). Non-adherent patients had a higher mean Disease Activity Score 28 (DAS28)-erythrocyte sedimentation rate score (P=0.001), higher mean DAS28-C-reactive protein (CRP) score (P=0.001), and higher mean rate of tender and swollen joints (P=0.003 and P=0.002, respectively) than adherent patients. In the multivariate analysis, poor MTX adherence was significantly associated with a higher mean DAS28-CRP score (odds ratio, 0.270; 95% confidence interval, 0.165–0.444; P<0.001).

Conclusion: Adherence to MTX can affect disease activity during follow-up in Korean patients with RA. Our results provide a rationale for patient education to maintain good drug adherence in RA patients, to control disease activity.
Disclosure of Interests: None declared
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FRI0127

SUPPRESSION OF RADIOGRAPHIC PROGRESSION AFTER GRADUAL METHOTREXATE TAPERING IN PATIENTS WITH RHEUMATOID ARTHRITIS PATIENTS MAINTAINING LOW DISEASE ACTIVITY - PROSPECTIVE MULTICENTER STUDY-

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Background: Many studies have been reported to reduce/discontinue Biologics in the treatment of rheumatoid arthritis (RA). In contrast, study for tapering methotrexate (MTX) has been limited (1,2).
Objectives: We prospectively examined whether bone destruction will progress at 48 weeks after tapering or discontinuing MTX (UMIN000028875).
Methods: The subjects were RA patients who have maintained low disease activity or lower for 24 weeks or more in DAS28-CRP after MTX administration. Patients having PDUS Grade 2 or 3 per site by bilateral hand ultrasonography (26 area) were excluded in this study owing to risk for joint destruction. The joint destruction was evaluated by the joint X-ray evaluation by modified total Sharp scoring (mTSS) at 1 year after the start of tapering MTX. Evaluation of clinical disease activities, severe adverse events, the continuation rate during MTX tapering were also evaluated. According to tapering response, prognostic factor for good response for tapering, joint destruction was determined. Predictors for successful tapering MTX and progression of bone destruction were determined. Statistical analysis was performed by t-test or Wilcoxon rank sum test using SAS .13.2 software.
Results: The subjects were 79 (16 males, 63 females). Age average 60.9 years, disease duration 4 years 4 months, MTX dose 8.43 mg / w, DAS28-CRP 1.52, DMARDs (24.3%), ACPA 192.7 U / ml (70.5%), RF 55.6 IU / ml (65.4%).MTX was tapered from an average of 8.43 mg / w before study to 5.46 mg / w one year later. In the treatment evaluation, DAS28-CRP increased from 1.52 to 1.84. 89.7% of subjects did not progress joint damage. Other disease activities significantly increased (Table 1). The one-year continuation rate was 78.2%. Since tapering effects were varied widely, we divided patients into three groups; Flared group (N=14, initial MTX dose 8.71mg/w, final MTX dose 8.42mg/w), Low response group (N=31, final MTX reduction rate< 50%, initial MTX dose 8.93mg/w, final MTX dose 6.22mg/w), High response group (N=34, final MTX reduction rate≥ 50%, initial MTX dose 8.5mg/w, final MTX dose 3.15mg/w)(Table 2).Higher RF value at baseline and higher MTX dose at 3M, 6M were predictors of whether a subject was in Low response group or High Response group. Higher RF value and mTSS at baseline and higher MTX dose at 6M were predictors whether a subject was in Flared group or High response group. Lower age was predictor of whether a subject was in Flared group or Low responder group. Finally, mean ΔmTSS /y in Flared group (0.36) was not significantly higher than in low response group (0.07) and in high response group (0.01).

Table 1

	0M	12M	P
RF	47.7 ± 70.1	59.1 ± 72.5	NS
CRP	0.15 ± 0.18	0.30 ± 0.73	NS
ESR	18.60 ± 14.28	21.47 ± 18.08	NS
DAS28-E	2.1 ± 0.65	2.46 ± 0.84	0.002*
DAS28-C	1.53 ± 0.34	1.83 ± 0.70	0.001*
CDAI	2.03 ± 1.78	3.77 ± 4.08	0.0002*
SDAI	2.20 ± 1.79	3.86 ± 3.67	<.0001*
SJC	0.55 ± 0.73	1.01 ± 1.26	0.0041*
TJC	0.10 ± 0.34	0.38 ± 1.96	0.0128*
MMP3	52.70 ± 30.14	58.75 ± 43.20	NS
HAQ-DI	0.14 ± 0.35	0.22 ± 0.42	0.0165*

* significant: Pairs test, Average(SD)

Table 2. Predictors for successful tapering MTX and progression of bone destruction

	Flared group (F)(n = 14)	Low reduced group(L) (n = 31)	High reduced group (H)(N = 34)	P value
sex (F:M)	4:10	5:26	7:27	N.S
Age(years)	54.6 (10.1)*	62.3 (10.8)*	61 (13.0)	0.05*(F vs L)
Duration(M)	56.8(32.7)	60.3 (50.9)	47.5 (37.3)	N.S
LDA (M)	30.2(28.1)	29.8 (24.8)	26.1 (23.0)	N.S
MTX dose(mg/w) baseline	8.71(2.3)	8.93 (2.2)	8.5 (2.7)	N.S
0M	6 (2.4)	6.71 (2.0)	5.88 (2.2)	N.S
3M	6.43 (2.5)	6.64 (1.9)*	5.62 (1.8)*	0.05**(L vs H)
6M	7.28 (2.2)*	6.52 (1.8)*	4.59 (1.8)*	<.0001* (F vs H) 0.0001* (L vs H)
12M	8.42 (1.9)*	6.22 (1.7)*	3.15 (1.7)*	<.0001* (F vs H,L vs H) 0.0002* (F vs L)
GSS 0M	1.71 (2.6)	2.87 (3.3)	1.68 (2.2)	N.S
PDS 0M	0.43 (1.1)	0.87 (1.6)	0.41 (1.0)	N.S
PSL(mg/dl) 0M	0.15 (0.5)	0.41 (1.3)	0.76 (1.2)	N.S
CCP(U/ml) 0M	133.1 (205.3)	210 (371.6)	179 (308.9)	N.S
RF (IU/ml) 0M	44.2 (38.5)*	75.1 (99.5)*	24.1 (27.5)*	0.003* (F vs H) 0.006* (L vs H)
DAS28-CRP 0M	1.47 (0.2)	1.6 (0.4)	1.51 (0.3)	N.S
DAS28-CRP 12M	2.76 (1.0)*	1.67 (0.5)*	1.58 (0.4)*	<.0001* (F vs L,H)
mTSS 0M	16.6 (7.2)*	15.7 (14.3)	11.2 (9.1)*	0.005**(F vs H)
mTSS/y 0M	4.36 (2.3)	3.42 (4.6)	4.89 (5.8)	N.S
ΔmTSS/y	0.36 (0.63)*	0.07 (0.4)	0.01 (0.09)*	0.05*(F vs L,H)

*t-test ** Willcoxon rank sum test

Conclusion: Patients with MTX-administered low disease activity and finger joint echo PDUS grade 1 satisfy almost no joint destruction even after MTX reduction. For tapering, predictors may be helpful for maintaining patient's satisfaction.
References:
[1] Baker KF, Skelton AJ, Lendrem DW et al. Predicting drug-free remission in rheumatoid arthritis: A prospective interventional cohort study. J. Autoimmunity. 2019;105: 102298.
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Disclosure of Interests: None declared
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FRI0128

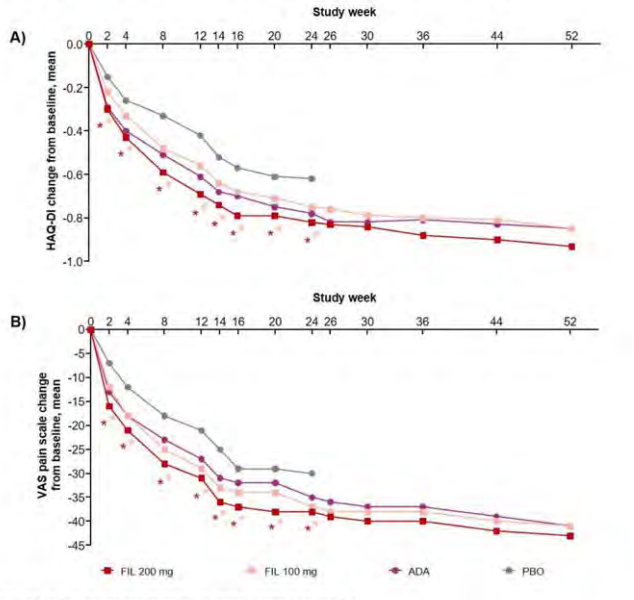
FILGOTINIB PROVIDED RAPID AND SUSTAINED IMPROVEMENTS IN FUNCTIONAL STATUS, PAIN, HEALTH-RELATED QUALITY OF LIFE, AND FATIGUE IN PATIENTS WITH RHEUMATOID ARTHRITIS AND INADEQUATE RESPONSE TO METHOTREXATE: RESULTS FROM THE FINCH 1 STUDY

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Background: In the FINCH 1 study, filgotinib (FIL)—an oral, potent, selective Janus kinase 1 inhibitor—in combination with methotrexate (MTX) provided significant improvements in the signs and symptoms of rheumatoid arthritis (RA) in patients (pts) with inadequate response to MTX.[1] While EULAR guidelines recommend a treat-to-target approach focusing on reducing inflammation to prevent joint damage, physical disability, and mortality, pts consider control of pain and fatigue, along with maintenance of physical function and health-related quality of life (HRQoL), to be important aspects for their care.[2,3]
Objectives: To evaluate the rate and magnitude of change in patient-reported outcomes (PROs) from FINCH 1.
Methods: In the FINCH 1 study (NCT02889796), pts with active RA received oral FIL 200 mg + MTX, FIL 100 mg + MTX, PBO + MTX, or subcutaneous adalimumab (ADA) 40 mg + MTX for up to 52 weeks (W); pts receiving PBO at W24 were rerandomised 1:1 to FIL 100 or 200 mg. PROs included the HAQ-DI and VAS pain scale, SF-36, and FACIT-Fatigue questionnaire. The change from baseline (CFB) at each time point was assessed up to W52 for each treatment group. The mixed-effects model for repeated measures was used to compare each FIL group with PBO for the CFB at each time point through W24. The logistic regression model was used to compare each FIL group with PBO for the proportion of pts achieving the minimum clinically important difference (MCID) of ≥0.22 reduction in CFB in HAQ-DI at each time point through W24.
Results: Of 1755 pts randomised and treated (475 FIL 200 mg + MTX; 480 FIL 100 mg + MTX; 325 ADA + MTX; and 475 PBO + MTX), 1417 (80.7%) received study drug through W52. As early as W2 through W24, pts receiving either dose of FIL experienced nominally significantly greater (p <0.001) CFB in HAQ-DI and VAS pain scale than those receiving PBO; CFB improvements were maintained through W52 (Fig 1**A, B**). At W2, compared with PBO (40.2%), a nominally significantly greater proportion of pts achieved the HAQ-DI MCID in both the FIL 200 (52.5%; p <0.001) and 100 mg (46.7%; p = 0.043) groups. This benefit vs PBO was maintained up to W24 and the proportion of pts who achieved a HAQ-DI reduction of ≥0.22 remained ≥75.8% in the FIL 200 mg group and ≥71.5% in the FIL 100 mg group from W12 through W52. FIL provided nominally significantly greater improvement in HRQoL vs PBO at W4

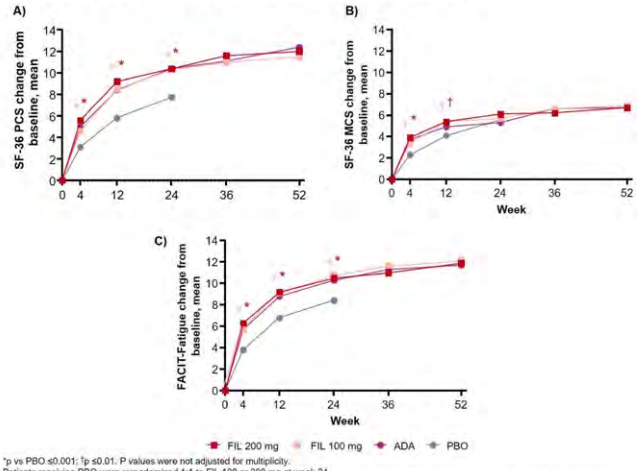
and W12 for both the CFB of the SF-36 Physical Component Summary (PCS) ($p < 0.001$) and Mental Component Summary (MCS) ($p \leq 0.006$); nominal significance was also seen at W24 for CFB of SF-36 PCS (Fig 2**A, B**). By W4, pts receiving either dose of FIL reported a nominally significantly greater mean CFB in FACIT-Fatigue scores vs PBO ($p < 0.001$); significance was maintained through W24 and improvement in reported fatigue continued through W52 in the FIL groups (Fig 2**C**). In general, CFB for HAQ-DI, VAS pain scale, and FACIT-Fatigue observed for the FIL groups was higher or comparable to ADA at various time points (Fig 1, 2).

Figure 1. Change from baseline in A) HAQ-DI and B) VAS pain scale at each visit



*p vs PBO <0.001, not adjusted for multiplicity except at week 12 for HAQ-DI.
Patients receiving PBO were rerandomized 1:1 to FIL 100 or 200 mg at week 24.
ADA, adalimumab; FIL, filgotinib; HAQ-DI, Health Assessment Questionnaire Disability Index; PBO, placebo; VAS, visual analog scale

Figure 2. Change from baseline in SF-36 A) PCS and B) MCS and C) FACIT-Fatigue



*p vs PBO ≤0.001; †p ≤0.01. P values were not adjusted for multiplicity.
Patients receiving PBO were rerandomized 1:1 to FIL 100 or 200 mg at week 24.
ADA, adalimumab; FACIT, Functional Assessment of Chronic Illness Therapy; FIL, filgotinib; MCS, mental component summary; PBO, placebo; PCS, physical component summary; SF-36; Short-Form 36.

Conclusion: Both doses of FIL provided rapid and sustained improvements in functional status, pain, HRQoL, and fatigue compared with PBO for pts with RA and inadequate response to MTX throughout the 52-week period.

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FRI0129

DEVELOPMENT OF A PREDICTION MODEL FOR MAXIMUM METHOTREXATE (MTX) DOSE WITHOUT HEPATOTOXICITY USING AN INDEX OF ERYTHROCYTE MTX-POLYGLUTAMATE (MTXPG) LEVELS SPECULATED BY CLINICAL AND GENETIC MARKERS

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Background: MTX is transported into cells and retained long after polyglutamation. MTXPG level can predict response and possibly adverse effects of MTX. We reported erythrocyte MTXPG concentrations efficiently discriminated patients with and without hepatotoxicity[1]. We also developed genetic and clinical prediction models for efficacy and hepatotoxicity of MTX[2]. In the present study, we firstly investigated the effects of clinical and secondly genetic variables on the concentration of total MTXPG and determined oral maximum MTX dose without hepatotoxicity using these variables.

Objectives: To develop a prediction model for maximum MTX dose without hepatotoxicity.

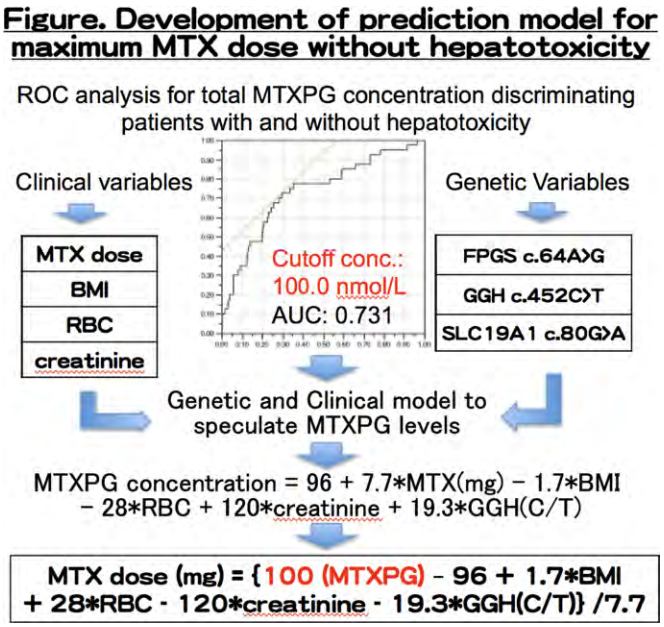
Methods: Concentrations of erythrocyte MTX-PG (PG1 to PG4) were detected by LC-MS/MS and calculated total MTXPG as sum of them. MTX-PGn levels were measured in 265 RA patients including 40 patients with elevated AST or ALT (≥ 60 U/L; 1.5 times of upper limits) and the 6 SNPs of 6 gens related to MTXPG metabolism were identified by RT-PCR.

Results: Total concentrations of MTXPG were 141.3 ± 86.5 and 87.6 ± 47.8 nmol/L (mean±SD) in 40 RA patients with hepatotoxicity and 225 patients without, respectively ($p<0.0001$). By ROC analysis, the two groups were most efficiently discriminated with cutoff concentration of 100.0 nmol/L (AUC 0.731). Next, genetic and clinical model to speculate the MTXPG concentration was established by multivariate analysis using 4 clinical and 3 genetic variables which were selected from 20 clinical and 6 genetic variables by univariate analysis ($p<0.1$). Finally, a speculation model for MTXPG concentration by 4 clinical variables (MTX dose, BMI, RBC count, and creatinine) and one genetic variable (GGH c.452C>T) was developed (Figure). When MTXPG concentration of 100 nmol/L was applied to the model, maximum MTX dose without hepatotoxicity was calculated for each patient as **MTX dose (mg) = {100 (MTXPG) – 96 + 1.7*BMI + 28*RBC - 120*creatinine - 19.3*GGH(C/T)} / 7.7**. Real dose of oral MTX exceeded the calculated dose in 23 of 40 patients (57.5%) with hepatotoxicity, whereas it exceeded in 95 of 223 patients (42.6%) without hepatotoxicity (OR 1.82, $p=0.081$).

Conclusion: Maximum MTX dose without hepatotoxicity was speculated by several clinical and genetic markers without measurement of erythrocyte MTX-PG concentrations.

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Disclosure of Interests: Shunichi Kumagai Grant/research support from: Astellas, Chugai, Mitsubishi Tanabe Co.Ltds, Consultant of: Sysmex Co.Ltd, Speakers bureau: many companies, Soshi Takahashi: None declared, Miho Takahashi: None declared, Toshiharu Saito: None declared, Katsuyuki Yoshida: None declared, Motoko Katayama: None declared, Saki Mukohara: None declared, Norihiko Amano: None declared, Akira Onishi Speakers bureau: AO received a speaker fee from Chugai, Ono Pharmaceutical, Eli Lilly, Mitsubishi-Tanabe, Asahi-Kasei, and Takeda, Masakazu Shinohara: None declared, Saori Hatachi: None declared

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FRI0130

A SYSTEMATIC REVIEW OF NATURAL SUPPLEMENTS IN THE TREATMENT OF RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic autoimmune condition affecting almost 1% of the general population (1). Pharmacological management has been the mainstay of treatment for RA and includes DMARDs and biologics. Despite these therapies, anywhere from 28-90% of patients with RA use complementary and alternative medicine (2). These non-pharmacological therapies range from dietary interventions to supplements to nonprescription therapies.

Objectives: To determine the efficacy of non-pharmacological, orally-ingested interventions on clinically-relevant endpoints in patients with rheumatoid arthritis.

Methods: We systematically reviewed EMBASE and MEDLINE electronical databases from inception until Feb 23, 2019 for relevant articles. Only randomized controlled trials (RCTs) which assessed oral, non-pharmacological interventions (e.g. diets, vitamins, oils, herbal remedies, fatty acids, supplements, etc.) in adult patients with RA, that presented clinically-relevant outcomes (defined as pain, fatigue, disability, joint counts, and/or disease indices) were included.

Clinical outcome data was extracted by two independent authors as difference from baseline measurement. Therapies with at least 3 RCTs which presented data on the same clinical outcome were meta-analyzed using a pooled random effects model using RevMan 5.

Results: A total of 4423 unique articles were independently assessed by two authors, of which 72 articles met our inclusion criteria. Thirteen different interventions were studied more than once, and six interventions had clinical outcomes reported in at least 3 trials. However, only vitamin D and fatty acids met criteria for meta-analysis.

Pooled random effects models suggested vitamin D supplementation improved HAQ scores from baseline (mean difference = -0.10, 95% confidence interval (CI) = -0.17 to -0.02; p=0.01) but had no effect on DAS28 scores (Table 1).

Table 1. Mean differences from baseline of various clinical outcomes in RA patients taking vitamin D or fatty acid supplementation compared to control group.

Clinical Outcome	Total Patients	Mean Difference (95% CI)	P-value
Vitamin D			
HAQ	573	-0.10 (-0.17 to -0.02)	0.01
DAS28	174	-0.30 (-0.71 to 0.11)	0.15
Fatty Acids			
TJC	661	-2.05 (-2.83 to -1.27)	0.04
SJC	582	-0.35 (-0.96 to 0.26)	0.26
RAI	234	-1.82 (-4.69 to 1.05)	0.21
Pain	756	-0.61 (-1.02 to -0.20)	0.004
Patient Global	484	-0.26 (-0.59 to 0.07)	0.12
Physician Global	382	-1.08 (-1.98 to -0.18)	0.02
HAQ	277	-0.13 (-0.18 to -0.09)	<0.001
DAS28	543	-0.19 (-0.36 to -0.01)	0.03

Fatty acid supplementation improved total joint counts, pain, physician global assessment scores, HAQ, and DAS28 from baseline (Table 1). There were significantly more patients who achieved ACR20 criteria (Relative Risk Ratio = 2.73, 95% CI 1.62-4.58; p<0.001) (Figure 1).

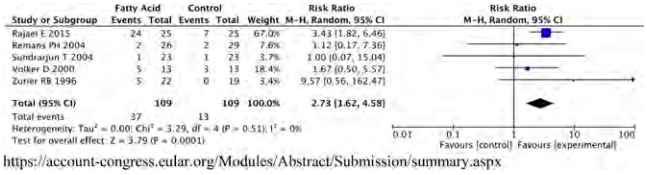


Figure 1. Forest plot of studies in which RA patients taking fatty acids achieved ACR20 criteria. https://account-congress.eular.org/Modules/Abstract/Submission/summary.aspx

Conclusion: From our meta-analysis, vitamin D and fatty acids supplementation showed statistically significant improvement in some clinical outcomes in patients with RA; however, the degree of improvement is unlikely to be clinically significant. Overall, many trials were of low quality and had high risks of bias including inadequate reporting of data. Further clinical trials that are well-designed and fully powered are still needed to confirm the efficacy of many supplements and diets in RA.

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FRI0131

SUSTAINABILITY OF RESPONSE BETWEEN UPADACITINIB AND ADALIMUMAB AMONG PATIENTS WITH RHEUMATOID ARTHRITIS AND PRIOR INADEQUATE RESPONSE TO METHOTREXATE

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Background: The primary treatment goal for patients (pts) with rheumatoid arthritis (RA) is a state of sustained clinical remission (REM) or low disease activity (LDA).[1,2]

Objectives: To assess the long-term sustainability of response to upadacitinib (UPA), a JAK inhibitor, and adalimumab (ADA), both with background methotrexate (MTX), among pts with RA and prior inadequate response to MTX.

Methods: In the phase 3, randomized, placebo (PBO) and active-controlled SELECT-COMPARE trial, pts on stable background MTX received UPA 15 mg once daily, PBO, or ADA 40 mg every other week. Pts not achieving 20% improvements in tender/swollen joint counts (Weeks 14-22) or LDA (CDAI ≤10 at Week 26) were rescued from UPA to ADA or PBO/ADA to UPA; all non-rescued PBO pts were switched to UPA at Week 26. This post hoc analysis evaluated clinical REM (CDAI ≤2.8; SDAI ≤3.3), LDA (CDAI≤10; SDAI≤11), and DAS28(CRP) <2.6/≤3.2 at first occurrence before Week 72 or prior to treatment switch; additionally, these measures were evaluated at 3, 6, and 12 months after the first occurrence for the total number of pts randomized to UPA (n=651) or ADA (n=327). Sustainability of response was evaluated by Kaplan-Meier only for those pts who achieved REM/LDA and was defined as time to the earliest date of losing response at two consecutive visits, discontinuation of study drug, or losing response at the time of rescue. The predictive ability of time to clinical REM/LDA was assessed using Harrell's concordance (c)-index (for reference, an index ~ 0.5, indicates no ability to predict; an index of 1 or -1 would be a perfect prediction). The date of the last follow up was 6 July, 2018, when all pts had reached the Week 72 visit.

Results: Through Week 72, a significantly higher proportion of pts receiving UPA + MTX vs ADA + MTX achieved CDAI REM (41% vs 31%, p=.0035) as well as CDAI LDA (70% vs 59%, p=.0007). 26%/22% of pts randomized to UPA + MTX and 16%/14% of pts randomized to ADA + MTX achieved sustained CDAI REM at 6/12 months after the first occurrence. Additionally, 49%/46% of pts randomized to UPA + MTX and 36%/34% of pts randomized to ADA + MTX achieved sustained CDAI LDA at 6/12 months after the first occurrence (Figure 1). Time to initial clinical REM/LDA did not appear to be associated with sustained disease control. The c-indices (95% CI) for CDAI REM in the UPA +MTX and ADA + MTX groups were 0.528 (0.48, 0.58) and 0.510 (0.43, 0.59) and that of LDA were 0.601 (0.56, 0.64) and 0.555 (0.50, 0.61), respectively. Through last follow-up visit, 51% of UPA + MTX pts and 45% of ADA + MTX pts remained in CDAI REM while 65% of UPA + MTX pts and 58% of ADA + MTX pts remained in CDAI LDA, respectively (Figure 2). Similar results were observed across other disease activity measures (SDAI REM/LDA and DAS28(CRP) <2.6/≤3.2).

Conclusion: A significantly greater proportion of pts with RA and prior inadequate response to MTX receiving UPA + MTX vs ADA + MTX achieved clinical REM or LDA across disease activity measures. REM and LDA were sustained through Week 72 in both treatment arms, with numerically higher proportions retaining response among UPA-treated pts.

References:

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Figure 1. Proportion of patients sustaining CDAI remission or low disease activity at 3, 6, and 12 months after the first occurrence of response among the total randomized population

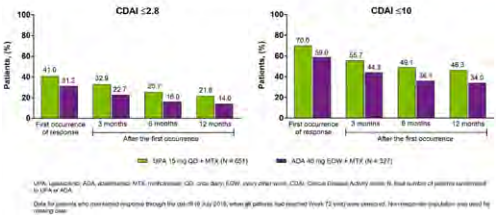
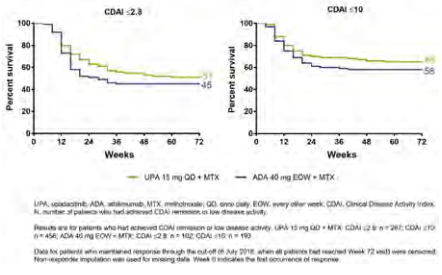


Figure 2. Kaplan-Meier analysis of time to loss of CDAI remission or low disease activity after the first occurrence of response



Disclosure of Interests:

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FRI0132 EFFICACY AND SAFETY OF SWITCHING JAKINIBS IN RHEUMATOID ARTHRITIS

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Background: Different Jakinibs (JAKi) have shown efficacy in rheumatoid arthritis (RA) but in an important proportion of patients, insufficient response leads to therapy withdrawal. The different JAKi show variable selectivity for the four Jak isoforms (Jak1,2,3 y Tyk2) but there are no clinical trials analyzing the response to a JAKi after the suspension of another JAKi and therefore, observational data may be useful in this regard.

Objectives: To describe efficacy and safety of the second JAKi in patients with suspension of the first due to failure or side effects.

Methods: Spanish observational multicentric study. Data were retrospectively obtained from medical records of 28 patients with RA sequentially treated with baricitinib o tofacitinib in any order.

Results: We identified 28 patients with RA treated with baricitinib and tofacitinib. Patient´s characteristics are summarized in Table 1. Half of the patients received tofacitinib first, and the other half baricitinib as the first JAKi. Mean survival for the first JAKi was 7,6 ± 6,1 months. The reason for withdrawal was inefficacy in 17 cases (61%) and adverse effects in 11 (39%). Mean follow-up after starting on the second JAKi was 9,6 ± 5,6 [3-19] months. Disease activity data along follow-up are depicted in Table 2. Survival on the second JAKi was 82% at 3, 76% at 6, and 62% at 12 months when 13 of the 21 patients maintained the therapy. In all 8 patients who discontinued the second JAKi, the reason was inefficacy. The treatment suspension rate was similar among patients discontinuing the first JAKi for inefficacy (n=5, 29,4%) or for adverse effects (n=3; 27,3%).

Table1. Baseline Charateristics.

	N 28
Clinical characteristics	
Female	24 (86%)
Age*	61.2 ± 13.2
ACPA (+)	19 (67,9%)
Erosions	13 (46,4%)
Extra-articular manifestations	8 (28,6%)
TJC*	10,8 ± 5,4
SJC *	7,4 ± 4,6
DAS28-CPR*	5,4 ± 0,91
High disease activity	71,5%
Moderate disease activity	23,8%
Low disease activity	4,7%
Previous treatment	
bDMARD	24 (86%)
Nº of previous bDMARDs *	3,9±2,2
iTNF	75%
No-iTNF	67,9%

(*) Mean ± SD

Tabla 2. Treatment results during the follow-up period.

	Baseline (n 28)	3 m (n 28)	6 m (n 25)	12 m (n 21)
TJC	10,8±5,4	3,8±3,3	4,23±2,5	1,9±1,5
SJC	7,2±4,6	1,8±1,7	1,7±2	0,7±1
CPR mg/dL	1±0,6	0,54±0,48	0,64±0,9	0,33±0,24
DAS28CPR	5,4±0,91	3,29±0,97	3,15±1,2	2,15±0,6
Prednisone mg	7,2±4,2	6,8±3,5	5,3±2,5	3,1±2,1

Conclusion: Our data show that therapy with a second JAKi is a safe and efficacious option after discontinuation of the first JAKi due to either inefficacy or side effects. The response rate to the second JAKi is similar in patients with inefficacy or side effects which suggests that failure to the first does not reduce the chance of response to the second.

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FRI0133 RELATIONSHIP BETWEEN MELATONIN SERUM LEVELS AND THE EFFICACY OF SELECTIVE SEROTONIN REUPTAKE INHIBITOR PAROXETINE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Numerous clinical and epidemiological studies have established that there is a close relationship between inflammation, chronic pain and psycho-emotional disorders in rheumatoid arthritis [1, 2]. The common pathogenetic mechanism is manifested in the defect of melatonin mediation and cytokine stimulation [3]. Therefore, features of the use of selective serotonin reuptake inhibitors is relevant.

Objectives: To study the relationship between serum melatonin level and the efficacy of selective serotonin reuptake inhibitor paroxetine in patients with RA.

Methods: A total of 127 RA patients and 71 healthy volunteers were examined. The following information was collected for each patient: medical history data, physical examination results, serum melatonin levels. RA patients were randomly categorized into two treatment groups – 63 and 64 patients. The basic treatment for patients of both groups included nonsteroidal anti-inflammatory drugs, glucocorticoids (equivalent to 10 mg of prednisolone), and disease-modifying antirheumatic drugs (methotrexate, leflunomide or sulfasalazine). To evaluate the effectiveness of treatment, patients of both groups were further divided into three subgroups depending on the serum melatonin level (low level corresponds to 25 percentile, medium - 25-75, high - 75 percentile). First group received paroxetine 20 mg once a day for 12 weeks in addition to the basic treatment. Effectiveness of the treatment was evaluated according to the ACR/EULAR criteria.

Results: The mean baseline plasma melatonin levels in RA patients were significantly higher than in the healthy volunteers (26.1±32.7 vs 13.6±4.6 pg/mL at 8 am and 11.5±15.5 vs 3.6±4.6 pg/mL at 20 pm (p<0,001), respectively). A good response to basic treatment was observed in groups with medium and high serum melatonin levels, who received paroxetine (p<0.05). However, patients who did not receive paroxetine gave best response to treatment in group with low serum melatonin levels (p<0.05).

Conclusion: Obtained data suggest that the high level of serum melatonin is one of the predictors of resistance for basic RA treatment. The proposed scheme of treatment with addition of paroxetine demonstrated high efficacy concerning the main manifestations of the disease in RA patients with high melatonin serum level. This study demonstrates the possible influence of serotoninergic interactions on the melatoninergic system and their contribution to the pathogenesis of RA.

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FRI0134 EFFECT OF JAK INHIBITORS ON PAIN AND QUALITY OF LIFE IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Pain control is considered a treatment priority from most patients with Rheumatoid Arthritis (RA). Despite the treat to target approach, residual pain is commonly reported by patients with RA. Treatment with JAK inhibitors (JAKi) has been associated to a rapid control of pain.

Objectives: To investigate the effect of JAKi on pain and quality of life in a mono-centric real-life clinical setting.

Methods: Patients candidate to baricitinib or tofacitinib were evaluated at baseline and after 12 and 24 weeks of treatment. Disease activity was assessed by Disease Activity Score (DAS)28 with C reactive protein (CRP). A reduction of ≥ 50% of pain visual-analogue scale (VAS) 0-100 mm was recorded as "very much improved, substantially improved" (1). Pain VAS score ≤ 10 mm was considered "no/limited pain" (2). Patients' satisfaction was assessed by the Patient Acceptable Symptom State question (3). Data were expressed as mean (SD) or median (interquartile range) according to the variables' distribution. Mann Witney test was use and p values <0.05 were considered statistically significant.

Results: Overall 108 patients started a JAK inhibitor (baricitinib n=67, tofacitinib n=41). Eighty-four patients (baricitinib n=51; tofacitinib n=33) were followed-up for at least 3 months and were included in the analysis. Table 1 summarizes demographic and clinical characteristic of the cohort. After 12 and 24 weeks of treatment we detected a significant reduction of DAS28 compared with baseline [from 4.7 (1.5) to 3.2 (1.7) 2.9 (1.5) and 2.7 (1.1), respectively; p<0.001; p<0.00001 and p<0.00001). At week 4, 27% and 51.8% of patients achieved remission and low disease activity, respectively; the percentages increase to 32.1% and 60.7% at week 12 and 42.2% and 70.3% at week 24. When evaluating the extent of reduction of the single items included in the DAS28 composite index we found that number of tender (TJ) and swollen joints (SJ) decreased from 9 (7.8) to 5 (3.5) to 4 (5) and 1 (3) at week 4, 2 (4) and 1 (3) at week 12, and 2 (4) and 1 (3) at week 24, respectively (p<0.00001 for all); the median reduction of TJC and SJC at week 4, 12 and 24 was 60%, 77% and 88%, and 81%, 86% and 100%, respectively. GH decreased from 70(30) to 40(40) at week 4, 40(30) at week 12 and 37(40) at week 24 (p<0.00001) with a median reduction of 37.5%, 44% and 46%. C reactive protein decreased by 54.5% at week 4, 47% at week 12 and 55% at week 24. VAS pain was significantly reduced at week 4, 12 and 24 [from 70(25) to 40(40,)30(40) at the three timepoints, p<0.00001] decreasing by 37.5%, 50% and 54%, respectively. A substantial reduction (≥50%) in VAS pain was reported by 41.3%, 54.4% and 53.9% of patients after 4, 12 and 24 weeks, respectively. Limited/no pain was reported by 21.3%, 24.7% and 36.5% at weeks 4, 12 and 24, respectively. Overall, 81.8% of patients achieved the PASS after a median time of 10 (7-15) days.

Conclusion: JAK inhibitors baricitinib and tofacitinib induce a rapid improvement of disease activity driven both by pain and inflammation control. Even if no/limited pain was described only by one third of the patients, most of them reported a rapid and sustained reduction of pain accounting for the achievement of a satisfactory health condition.

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	Baricitinib (n=51)	Tofacitinib (n=33)	P
F:M	43: 8	26:7	ns
Age, mean (SD)	59±12	60±12	ns
Disease duration, mean (SD)	163±101	170±112	ns
Baseline DAS28(PCR), median (IQR)	4.7 (4-5.6)	4.7 (4.3-5.4)	ns
Concomitant methotrexate, n (%)	27 (52.9)	8 (24.2)	<0.001
Daily prednisone dose, median (IQR)	5 (2.5-9.5)	5 (1.88-9.9)	ns
N° of previous csDMRADs, median (IQR)	3 (1-4)	2.5 (2-3)	ns
N° of previous bDMRADs, median (IQR)	2 (1-4)	1 (0-2.5)	ns

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FRI0135

PREDICTORS FOR SHORT-TERM CLINICAL EFFECTIVENESS OF BARICITINIB IN RHEUMATOID ARTHRITIS PATIENTS IN ROUTINE CLINICAL PRACTICE: DATA FROM A JAPANESE MULTICENTER REGISTRY

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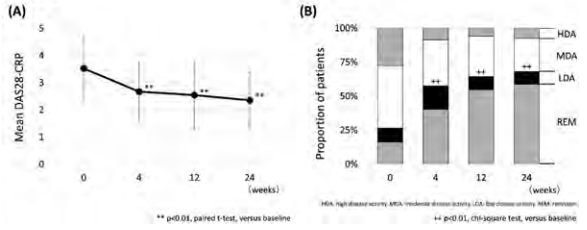
Background: Baricitinib is considered as a specific JAK1/2 inhibitor. While a number of randomized controlled trials have reported on the clinical efficacy and safety profile of baricitinib in rheumatoid arthritis (RA) patients, clinical data for RA patients in routine clinical practice are scarce.

Objectives: This study aimed to evaluate the short-term effectiveness and safety profiles of baricitinib and explore factors associated with improved short-term effectiveness in patients with RA in clinical settings.

Methods: A total of 113 consecutive RA patients who had been treated with baricitinib were registered in the TBCR, a Japanese multicenter registry for RA patients treated with biologics or JAK inhibitors (targeted DMARDs) [3], and followed for at least 24 weeks. Univariate and multivariate logistic regression analysis was used to study predictive factors for achievement of low disease activity (LDA) at 24 weeks.

Results: Mean age was 66.1 years, mean RA disease duration was 14.0 years, 71.1% had a history of use targeted DMARDs, and 48.3% and 40.0% were receiving concomitant methotrexate (MTX) and oral prednisone, respectively. Mean DAS28-CRP significantly decreased from 3.55 at baseline to 2.32 at 24 weeks (Figure 1A). At 24 weeks, 68.2% and 64.1% of patients achieved LDA and moderate or good response, respectively (Figure 1B). Multivariate logistic regression analysis revealed that no previous targeted DMARD use and lower DAS28-CRP score at baseline were independently associated with achievement of LDA at 24 weeks (Table). While the percent change in DAS28-CRP was similar regardless of whether patients used concomitant MTX (Figure 2A), patietns with previous use of targeted DMARDs (Switch group) showed lower percent improvement in DAS28-CRP compared to targeted DMARDs-naïve patients (Naïve group) (Figure 2B). The overall retention rate for baricitinib was 86.5% at 24 weeks, as estimated by Kaplan-Meier analysis. The discontinuation rate due to adverse events was 6.5% at 24 weeks. In the present study cohort, seven patients developed herpes zoster, with an incidence rate of 8.4 per 100 patient-years. All seven patients were treated with antiviral agents for herpes zoster and restarted baricitinib treatment.

Figure 1



Table

	Univariate		Multivariate	
variables	OR (95%CI)	p-value	adjusted OR (95%CI)	p-value
Male	1.17 (0.43-3.16)	0.755		
Age, <65 years	1.46 (0.62-3.44)	0.388		
Disease duration, <10 years	1.41 (0.61-3.23)	0.419		
ACPA positive	1.56 (0.51-4.80)	0.433		
no previous biological DMARDs	4.67 (1.49-14.66)	***0.008***	33.4 (2.53-442.62)	***0.008***
concomitant MTX	0.860 (0.40-2.02)	0.789		
concomitant PSL	0.24 (0.10-0.56)	***0.001***		
DAS28-CRP@baseline	0.55 (0.38-0.80)	***0.002***	0.28 (0.13-0.62)	***0.002***
mHAQ@baseline	0.27 (0.09-0.77)	***0.015***		

Bold italic, p<0.05

Conclusion:

In this study, we demonstrated the short-term clinical effectiveness and safety profile of baricitinib in Japanese RA patients in the 'real-world' setting. To the best of our knowledge, this study is the first to report the clinical outcomes of baricitinib in routine clinical practice in Japan. Baricitinib significantly improved disease activity, with an expected safety profile. We observed some interesting features regarding the effectiveness of baricitinib. Baricitinib was significantly more effective when used as a first-line targeted DMARD and may play a key role in the modern treatment strategy for RA, although careful observation is necessary for possible complications and AEs including herpes zoster.

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FRI0136

PERIPHERAL PROTEIN BIOMARKER CHANGES FOLLOWING SELECTIVE INHIBITION OF JANUS KINASE 1 (JAK1) BY FILGOTINIB IN ADULTS WITH MODERATELY-TO-SEVERELY ACTIVE RHEUMATOID ARTHRITIS WITH PRIOR INADEQUATE RESPONSE TO METHOTREXATE (FINCH1)

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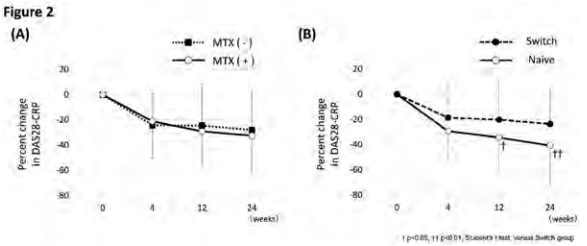
Background: Filgotinib (FIL), an oral selective Janus kinase 1 (JAK1) inhibitor has shown efficacy and safety in multiple phase 3 studies in adults with moderately-to-severely active rheumatoid arthritis (RA), including those with prior inadequate response to methotrexate (MTX) therapy (FINCH1; NCT02889796).

Objectives: A longitudinal study of protein biomarkers related to JAK signaling[1], bone biology[2], immune cell migration[2], and inflammation[2] was conducted to identify RA-associated markers altered by FIL vs MTX or adalimumab (ADA).

Methods: FINCH1 RA patients (pts) were randomized to receive either a stable dose of MTX with placebo (PBO+MTX), ADA+MTX, and either FIL100mg+MTX or FIL200mg+MTX, once daily. Plasma, serum, and urine samples were taken from a subset of pts (~548) at baseline (BL) and weeks (wks) 4 and 12. Twenty-six pre-defined cytokines (biomarkers) were evaluated using ELISA. BL correlation between biomarkers and clinical response measures (DAS-28CRP, SJC28, TJC28, CDAI, Patient Assessment and FACIT), were analyzed by Spearman Rank. Multiscale bootstrap resampling evaluated significant intra-cluster biomarker membership. Mean changes in biomarker levels from BL to wks 4 and 12 were compared between arms using PBO-adjusted estimates from a linear mixed effects model. A 5% false-discovery rate was applied for all analyses.

Results: At BL, distinct biomarker-based pt clusters (CL) were identified. The strongest intra-group correlations were in bone-cartilage resorption/inflammation (CL1; Rho range 0.37–0.88) and JAK activity (CL2; Rho range 0.41–0.71). Individual BL cytokine levels were significantly associated with DAS28CRP, with unique biomarkers specific to various subcomponents of the score. Eleven biomarkers were associated with DAS28CRP, while 5, 3, and 2 were associated with CDAI, SJC28, and TJC28, respectively. The magnitude of FIL-associated treatment effects was time- and dose-dependent. Significant biomarker changes from BL were observed in FIL pts, relative to PBO+MTX pts. FIL100mg+MTX led to a significant change in 8 biomarkers by either 4 or 12 wks of treatment; FIL200mg+MTX significantly changed these and an additional 4 biomarkers by either time point. The greatest effect of FIL200mg+MTX was at 12 wks for CXCL13 (-38.4%) and IL6 (-53.7%). All treatment arms led to significant reductions in TNFα relative to PBO+MTX. FIL200mg+MTX treatment led to larger reductions of TNFα than ADA+MTX treatment at both wk4 (-24.7% vs -17.9%)

Figure 2



and wk12 (-20.5% vs -12.2%), although the differences were not statistically significant.
FIL and ADA caused differential patterns of cytokine response at either wks 4 or 12. Of 12 biomarkers with a significant FIL200mg+MTX treatment effect, there was a significantly larger reduction in TNFSF13B and CTX1 relative to ADA+MTX at 12 wks. Of 8 biomarkers with FIL100mg+MTX effects, only 2 (CXCL10 at wk 4; CXCL13 at wks 4 and 12) had significant differences from ADA+MTX. Relative either to FIL200mg+MTX or FIL100mg+MTX, and despite the same direction of effect, ADA+MTX led to a significantly larger reduction in CCL2, CXCL10, CCL4, and CXCL13.
Conclusion: Compared with PBO, 12 wks of FIL treatment significantly reduced cytokines associated with JAK activity[1], bone biology[2], inflammation[2], and immune cell migration[2] in MTX-IR pts. The effects were largely FIL dose-dependent; most cytokines exhibited similar effects regardless of treatment arms, but differential changes between FIL+MTX and ADA+MTX were observed, supportive of the different mechanisms of action of these therapies.
References:
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Disclosure of Interests: Peter C. Taylor Grant/research support from: Celgene, Eli Lilly and Company, Galapagos, and Gilead, Consultant of: AbbVie, Biogen, Eli Lilly and Company, Fresenius, Galapagos, Gilead, GlaxoSmithKline, Janssen, Nordic Pharma, Pfizer Roche, and UCB, Emon Elboudwarej Shareholder of: Gilead Sciences Inc., Employee of: Gilead Sciences Inc., Bryan Downie Shareholder of: Gilead Sciences Inc., Employee of: Gilead Sciences Inc., Jinfeng Liu Shareholder of: Gilead Sciences Inc., Roche, Employee of: Gilead Sciences Inc., Rachael E. Hawtin Shareholder of: Gilead Sciences Inc., Employee of: Gilead Sciences Inc., Amer M. Mirza Shareholder of: Gilead Sciences Inc., Employee of: Gilead Sciences Inc.
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FRI0137 DISCONTINUATION OF BARICITINIB AFTER ACHIEVING LOW DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS IN CLINICAL PRACTICE; A MULTICENTER OBSERVATIONAL STUDY.

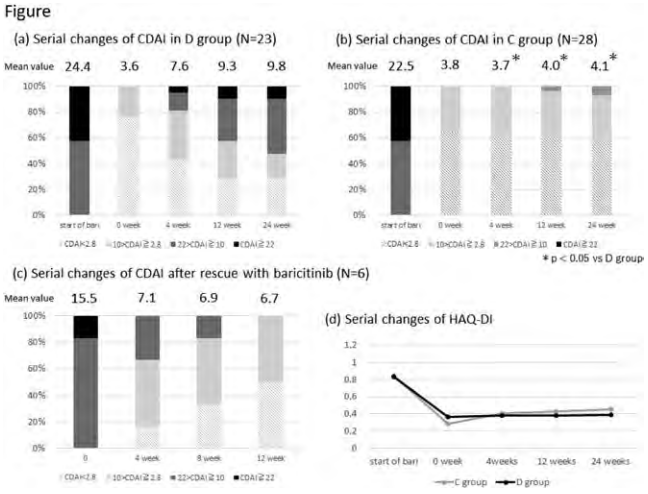
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Background: Baricitinib (bari) is an oral Janus kinase (JAK) 1/JAK2 selective inhibitor that has shown good efficacy in patients with RA and adequate response to conventional synthetic DMARDs in some clinical trials [1,2]. However, concerning the high cost and long-term safety related to the inhibition of particular molecules, we would like to discontinue bari after achieving long low disease activity (LDA).
Objectives: To evaluate the clinical outcomes in patients with RA who discontinued bari after achieving LDA for 24 weeks in real-world multicenter clinical data.
Methods: Japanese 67 patients with RA who show an inadequate response to csDMARDs or bDMARDs were scheduled to receive bari 4 or 2 mg/day once daily dose as a monotherapy or in combination with other csDMARDs. We included 51 patients who achieved and maintained LDA at least for 24 weeks after baricitinib therapy. They were allowed to decrease baricitinib after discontinuation of prednisolone. Bari was either discontinued or continued after study enrolment. The decision of discontinuation and continuation of baricitinib was determined based on patient-physician decision making with informed consent. We divided patients into two groups: a discontinuation group (D group; n = 23) and a continuation group (C group; n = 28). We evaluated the proportion of patients who remained LDA for 24 weeks in both groups. Clinical outcomes including Clinical Disease Activity Index (CDAI), and HAQ-DI were compared between both groups. The last observational carried forward method was used for patients who could not discontinue baricitinib due to flare before 24 weeks. In D group, patients were treated with re-initiation of bari or initiation of the other DMARDs in the event of flare. We investigated the serial changes of patients treated with re-initiation of bari in CDAI after flare.
Results: The baseline characteristics of the patients are summarized in Table. The titer of RF was lower in D group than that in C group. There were no significant differences in any other items. Ten of 23 (43.4%) in D group remained bari-free without disease activity flare. Serial changes of CDAI were summarized in Figure. CDAI in D group significantly increased from 3.6 at baseline to 9.8 at last observation. LDA rates in C group were 92.9% at last observation. CDAI in C group did not change throughout the follow-up period. CDAI at last observation was higher in D group than that in C group. HAQ-DI in D group changed from 0.28 at baseline to 0.45 at last observation. There was no significant change in HAQ-DI between both groups (P = 0.28). In D group, rescue by re-administration of bari or other DMARDs induced improvement, reducing CDAI from 15.5 at disease flare to 6.8. Especially, all patients treated with re-initiation of bari resulted in re-introduction of LDA in this study.

Table. Characteristics of patients at baricitinib initiation

	D group (n=23)	C group (n=28)	p-value
Age (years)	66.9 (8.6)	67.9 (12.7)	0.31
Gender, female, n (%)	6 (73.9)	24 (85.7)	0.49
Disease duration (years)	7.6 (10.3)	8.3 (9.9)	0.37
Prior use of biologics, n (0/1/2/≥3)	(21/2/0/0)	(17/6/4/1)	------
MTX (mg/w)	5.5 (3.8)	4.9 (4.3)	0.62
PSL (mg/d)	1.4 (1.9)	0.9 (0.9)	0.51
RF, U/ml	99 (141)	187 (214)	0.04
ACPA, U/ml	135 (173)	194 (214)	0.11
CDAI	24.4 (9.2)	22.5 (9.7)	0.36
HAQ-DI	0.83 (0.49)	0.83 (0.52)	0.98

Figure



Conclusion: It was possible to discontinue bari without flare in about 43% of patients with RA. Overall the patients treated with re-initiation of bari could result in re-introduction of LDA without deterioration of HAQ-DI.
References:
[1] Tanaka Y et al. Mod Rheumatol. 2018;28:583-91
[2] Tanaka Y et al. Mod Rheumatol. 2018;28:20-9

Disclosure of Interests: Eiji Torikai: None declared, Yuji Hirano Speakers bureau: Tanabe-Mitsubishi, Pfizer, Eisai, Abbie, Chugai, Bristol-Meyers, Jansen, Astellas, UCB, Eli-Lilly, Asahikasei, Daiichi-Sankyo, Amgen, Daisuke Suzuki: None declared, Yasuhide Kanayama: None declared
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FRI0138 THE IMPACT OF UPADACITINIB VERSUS METHOTREXATE OR ADALIMUMAB ON INDIVIDUAL AND COMPOSITE DISEASE MEASURES IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: In Phase 3 trials, upadacitinib (UPA), an oral JAK1-selective inhibitor, has been assessed as monotherapy vs MTX (SELECT-EARLY[1]) and in combination with MTX vs adalimumab + MTX (ADA; SELECT-COMPARE[2]) in RA pts who were MTX naïve or with inadequate responses to MTX (MTX-IR), respectively.

Objectives: In this analysis we assessed individual and composite measures of disease activity in SELECT-EARLY and SELECT-COMPARE.

Methods: In SELECT-EARLY, MTX-naïve pts received UPA 15 mg or 30 mg monotherapy once daily (QD), or MTX monotherapy, for 12 wks. In SELECT-COMPARE, MTX-IR pts on stable background MTX received UPA 15 mg QD, PBO, or ADA 40 mg every 2 wks for 12 wks. For this analysis, responses at Wk 12 were defined as ≥50% improvement in the 7 components of the ACR response criteria. Among ACR50 responders, the proportions of pts with ≥50% improvement in all 7 components of the ACR criteria was assessed. The proportion of pts achieving TJC68=0 and SJC66=0 was also determined. All analyses were based on observed data without imputation.

Results: 947 pts were randomized in SELECT-EARLY, and 1629 pts in SELECT-COMPARE. Mean time since RA diagnosis was 2.7 years in SELECT-EARLY (median 6 months) and 8.2 years in SELECT-COMPARE; mean DAS28(CRP) was 5.9 and 5.8, respectively. In SELECT-EARLY, significantly more MTX-naïve pts receiving UPA 15 mg or 30 mg monotherapy achieved ≥50% improvements in all ACR components at Wk 12 compared with MTX (Figure 1**a,** Figure 1**b**). In SELECT-COMPARE, significantly more MTX-IR pts on UPA 15 mg + MTX achieved ≥50% improvement in the ACR components vs PBO (all components) and ADA + MTX (all components except SJC and PhGA). Among pts with ACR50 responses at Wk 12, approximately half of the MTX-naïve pts on UPA 15 mg and 30 mg in SELECT-EARLY had ≥50% improvements in all 5 remaining ACR components (pain, PtGA, PhGA, HAQ-DI, hsCRP) compared with 28% with MTX. Corresponding proportions in MTX-IR pts in SELECT-COMPARE were 34% for UPA 15 mg + MTX, 28% for ADA + MTX, and 17% for PBO. UPA treatment also significantly increased the proportions of pts achieving both TJC68=0 and SJC66=0 vs PBO or MTX, and SJC66=0 vs ADA + MTX (Figure 1**a,** Figure 1**b**).

Conclusion: In MTX-naïve and MTX-IR pts, treatment responses at 12 wks occurred in significantly higher proportions of pts receiving UPA monotherapy vs MTX and UPA + MTX vs PBO for all 7 components of the ACR response criteria, and for 5 of 7 ACR components for UPA + MTX vs ADA + MTX. Favorable outcomes with UPA treatment were evident both in composite and individual parameters.

References:

[1] van Vollenhoven R, et al. Arthritis Rheumatol 2018;70(Suppl. 10): Abstract 891

[2] Fleischmann R, et al. Arthritis Rheumatol 2018;70(Suppl. 10): Abstract 890

Figure 1a. Proportions of pts achieving 50% improvements in core components of the ACR score at Wk 12

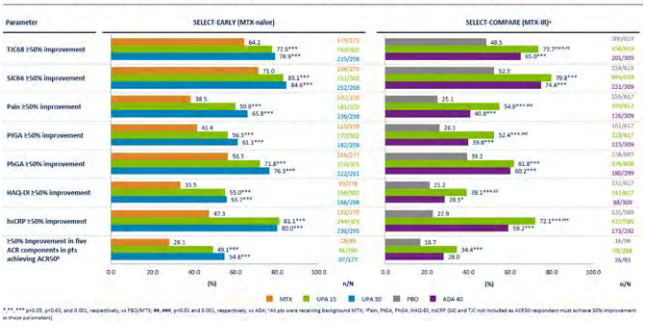
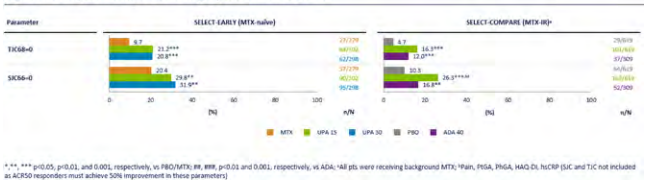


Figure 1b. Proportion of pts achieving 0 joint counts at Wk 12



Disclosure of Interests: Ronald van Vollenhoven Grant/research support from: AbbVie, Arthrogen, Bristol-Myers Squibb, GlaxoSmithKline, Lilly, Pfizer, and UCB, Consultant of: AbbVie, AstraZeneca, Biotest, Bristol-Myers Squibb, Celgene, GSK, Janssen, Lilly, Medac, Merck, Novartis, Pfizer, Roche, and UCB, Andrew Ostor Consultant of: MSD, Pfizer, Lilly, Abbvie, Novartis, Roche, Gilead and BMS, Speakers bureau: MSD, Pfizer, Lilly, Abbvie, Novartis, Roche, Gilead and BMS, Eduardo Mysler Grant/research support from: AbbVie, Amgen, Bristol Myers Squibb, Roche, Eli Lilly, Novartis, Janssen, Sanofi, and Pfizer., Speakers bureau: AbbVie, Amgen, Bristol Myers Squibb, Roche, Eli Lilly, Novartis, Janssen, Sanofi, and Pfizer, Nemanja Damjanov Grant/research support from: from AbbVie, Pfizer, and Roche, Consultant of: AbbVie, Gedeon Richter, Merck, Novartis, Pfizer, and Roche, Speakers bureau: AbbVie, Gedeon Richter, Merck, Novartis, Pfizer, and Roche, In-Ho Song Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Yanna Song Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Jessica Suboticki Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Vibeke Strand Consultant of: AbbVie, Amgen, Biogen, Celltrion, Consortium of Rheumatology Researchers of North America, Crescendo Bioscience, Eli Lilly, Genentech/Roche, GlaxoSmithKline, Hospira, Janssen, Merck, Novartis, Pfizer, Regeneron Pharmaceuticals, Inc., Sanofi, UCB

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FRI0139

FILGOTINIB PROVIDED RAPID AND SUSTAINED RELIEF OF PAIN AND FATIGUE AND IMPROVED HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH RHEUMATOID ARTHRITIS AND INADEQUATE RESPONSE TO BIOLOGIC DMARDS: RESULTS FROM THE FINCH 2 STUDY

D. Walker[1], T. Takeuchi[2], B. Bartok[3], S. Rao[3], I. H. Lee[3], R. Besuyen[4], J. E. Gottenberg[5], M. C. Genovese[6]. [1]*Northumbria Healthcare Trust, North Shields, United Kingdom*; [2]*Keio Univ School of Medicine, Tokyo, Japan*; [3]*Gilead Sciences, Inc., Foster City, CA, United States of America*; [4]*Galapagos BV, Leiden, Netherlands*; [5]*Strasbourg Univ Hospital, Strasbourg, France*; [6]*Stanford Univ, Stanford, CA, United States of America*

Background: EULAR guidelines recommend a treat-to-target approach focusing on reducing inflammation to prevent joint damage, physical disability, and mortality.[1] However, patients consider reduction in pain and fatigue, along with maintenance of physical function, and improvement in health-related quality of life (HRQoL) important areas for improvement with RA treatment.[2] In the FINCH 2 study, filgotinib (FIL)—a potent, selective, oral small molecule Janus kinase 1 inhibitor—in combination with conventional synthetic (cs)DMARD therapy significantly improved the signs and symptoms of rheumatoid arthritis (RA) in patients with an inadequate response to a biologic (b)DMARD compared with placebo (PBO).[3] In addition, patients experienced significant improvements in HAQ-DI at week (W)12 and W24 with FIL 100 mg ($p < 0.001$, $p = 0.003$) or 200 mg ($p < 0.001$ for both) compared with PBO.[3]

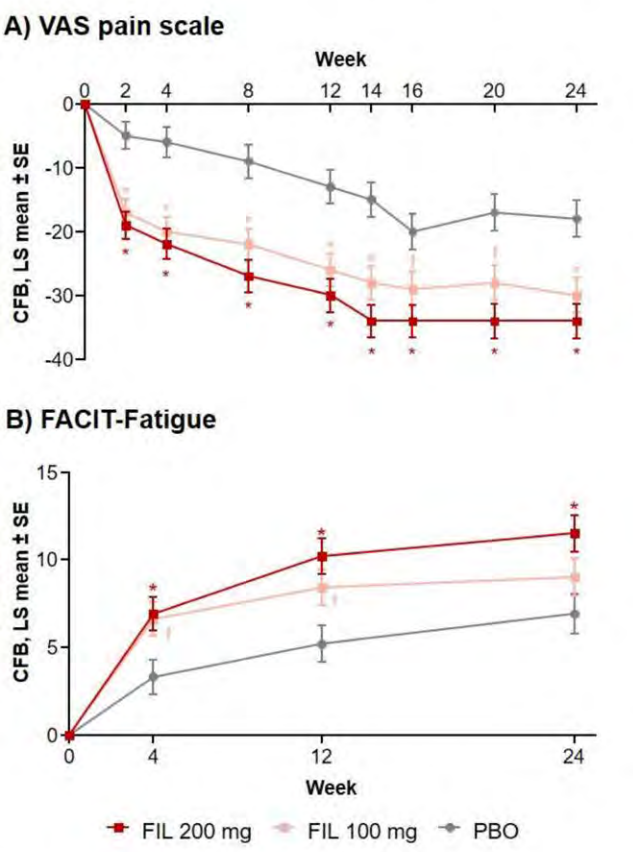
Objectives: To evaluate the rate and magnitude of change in patient-reported outcomes (PROs) from FINCH 2 assessing pain, HRQoL, and fatigue.

Methods: Patients in this double-blind, randomised study (NCT02873936) received FIL 200 mg, FIL 100 mg, or PBO while continuing csDMARD therapy. PROs were collected prospectively on day 1 and at the W2, W4, W8, W12, W14, W16, W20, and W24 visits for assessment of pain (VAS pain scale) and on day 1 and at W4, W12, and W24 for assessment of fatigue (FACIT-Fatigue) and HRQoL (SF-36). Changes from baseline for each PRO at each time point up to W24 were analysed longitudinally using a mixed-effects model for repeated measures. P values for the difference between each FIL arm and PBO at each time point were calculated.

Results: Among the 448 patients randomised and treated (FIL 200 mg, n = 147; FIL 100 mg, n = 153; PBO, n = 148) 381 (85.0%) completed the study. Baseline mean (SD) VAS pain scale was 67 (21.0), SF-36 physical component summary (PCS) was 31.1 (7.89), SF-36 mental component summary (MCS) was 44.3 (11.6), and FACIT-Fatigue score was 24.4 (11.6); baseline values did not vary between treatment groups. Significantly greater improvements in VAS pain scores began at W2 and were maintained through W24 for patients who received either dose of FIL vs PBO (Fig 1**A**). FIL also significantly improved patients' fatigue at W4, W12, and W24 compared with PBO for those receiving 200 mg doses, and at W4 and W12 for those receiving 100 mg doses (Fig 1**B**). HRQoL related to physical functioning (SF-36 PCS) was

significantly enhanced at W4, W12, and W24 with both doses of FIL as compared with PBO (Fig 2**A**). Improvements to mental-health-related QoL (SF-36 MCS) were reported for FIL as early as W4 and maintained through W24, with statistically significant improvements at W4 and W12 for FIL 200 mg vs PBO (Fig 2**B**).

Figure 1. Change in patients' pain and fatigue at each visit



*p ≤0.001, †p <0.01 for LS mean difference between the FIL arm vs PBO.
CFB, change from baseline; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; FIL, filgotinib; LS, least squares; PBO, placebo; SE, standard error; VAS, visual analog scale.

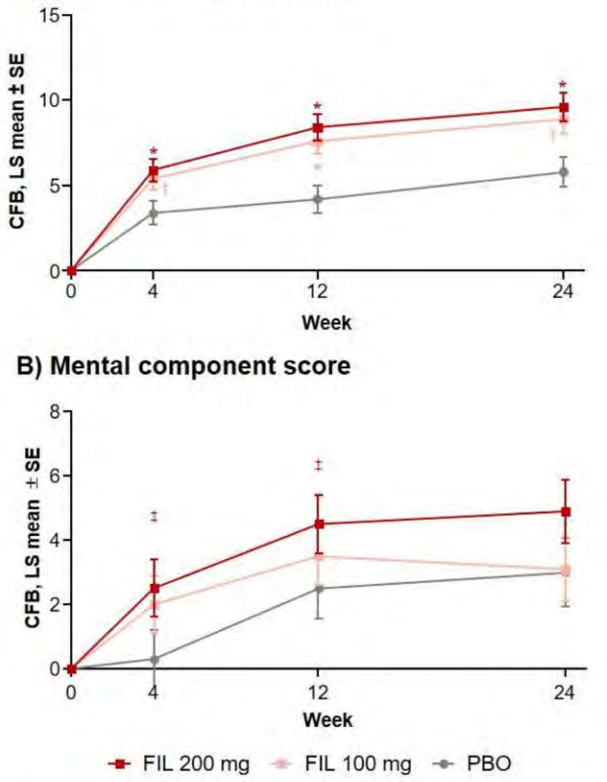
Conclusion: In a patient population with refractory disease that had inadequate response to prior bDMARDs and had significant disease at baseline, FIL treatment—coadministered with csDMARD therapy—was able to provide rapid and sustained improvements in key measures of pain, HRQoL, and fatigue as reported by patients.

References:

[1] Smolen, et al. *Ann Rheum Dis*. 2017;76:960–77.
[2] Fautrel, et al. *Rheumatol Int*. 2018;38:935–47.
[3] Genovese, et al. *JAMA*. 2019;322(4):315–25.

Disclosure of Interests: David Walker Grant/research support from: Gilead, Consultant of: Gilead, Lilly, Pfizer, Roche, Speakers bureau: Lilly, Pfizer, Roche, Tsutomu Takeuchi Grant/research support from: AbbVie, Asahikasei Pharma Corp., Astellas Pharma, Inc., Chugai Pharmaceutical Co, Ltd., Daiichi Sankyo Co., Ltd., Eisai Co., Ltd., Mitsubishi-Tanabe Pharma Corp., Nipponkayaku Co. Ltd., Shionogi & Co., Ltd., Takeda Pharmaceutical Co., Ltd., UCB Japan, Consultant of: Astellas Pharma, Inc., Chugai Pharmaceutical Co, Ltd., Eli Lilly Japan,, Speakers bureau: Abbvie, AYUMI Pharmaceutical Corp., Bristol-Myers Squibb, Chugai Pharmaceutical Co, Ltd., Daiichi Sankyo Co., Ltd., Eisai Co., Ltd., Eli Lilly Japan, Gilead Sciences, Inc., Mitsubishi-Tanabe Pharma Corp., Novartis Pharma K.K., Pfizer Japan Inc., Sanofi K.K., Dainippon Sumitomo Co., Ltd, Beatrix Bartok Shareholder of: Gilead Sciences Inc., Employee of: Gilead Sciences Inc., Shangbang Rao Shareholder of: Gilead Sciences Inc., Employee of: Gilead Sciences Inc., I-Heng Lee Shareholder of: Gilead Sciences Inc., Employee of: Gilead Sciences Inc., Robin Besuyen Shareholder of: Galapagos, Employee of: Galapagos, Jacques-Eric Gottenberg Grant/research support from: BMS, Pfizer, Consultant of: BMS, Sanofi-Genzyme, UCB, Speakers bureau: Abbvie, Eli Lilly and Co., Roche, Sanofi-Genzyme, UCB, Mark C. Genovese Grant/research support from: Abbvie, Eli Lilly and Company, EMD Merck Serono, Galapagos, Genentech/Roche, Gilead Sciences, Inc., GSK, Novartis, Pfizer Inc., RPharm, Sanofi Genzyme, Consultant of: Abbvie, Eli Lilly and Company, EMD Merck Serono, Genentech/Roche, Gilead Sciences, Inc., GSK, Novartis, RPharm, Sanofi Genzyme

Figure 2. Change in SF-36 at each visit



*p ≤0.001, †p <0.01, ‡p <0.05 for LS mean difference between the FIL arm vs PBO.
CFB, change from baseline; FIL, filgotinib; LS, least squares; PBO, placebo; SE, standard error; SF-36, Short-Form 36.

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FRI0140

IMPACT OF BASELINE DEMOGRAPHICS AND DISEASE ACTIVITY ON OUTCOMES IN PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING UPADACITINIB

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Background: Upadacitinib (UPA), an oral selective JAK1 inhibitor, has demonstrated favorable efficacy and acceptable safety in five Phase 3 global studies in patients with moderately to severely active rheumatoid arthritis (RA).[1–5]

Objectives: This analysis reports the efficacy and safety of UPA in predefined RA patient subgroups based on differences in baseline demographics and disease activity.

Methods: Data were pooled from three pivotal, double-blind, PBO-controlled, multicenter, Phase 3 studies in patients with RA who had an inadequate response(IR) to conventional synthetic DMARDs (csDMARD-IR: SELECT-NEXT [N=661]), MTX(MTX-IR; SELECT-COMPARE[N=1629]), or biologic DMARDs(bDMARD-IR: SELECT-BEYOND[N=498]). Two integrated analysis sets were evaluated: one comparing UPA 15 mg QD vs PBO(SELECT-NEXT, SELECT-COMPARE, SELECT-BEYOND) and the other comparing UPA 15 mg QD and UPA 30 mg QD vs PBO(SELECT-NEXT, SELECT-BEYOND). All patients received background treatment with csDMARDs. The proportion of patients achieving ACR20 and DAS28(CRP) ≤3.2 at Week 12 was evaluated by predefined baseline demographics and disease activity measure groups, including age, sex, weight, BMI, race, geographic region, duration of RA, RF, and ACPA status, and level of high sensitivity CRP. Non-responder imputation was used for missing data. Subgroup analyses for safety were performed for age, race, sex, weight, BMI, and Asian region.

Results: Across the three Phase 3 studies, 1036, 384, and 1041 patients received UPA 15 mg QD, UPA 30 mg QD or PBO, respectively. The demographic and baseline disease characteristics in the two integrated analysis sets were balanced across treatment groups. ACR20 and DAS28 ≤3.2 response rates at Week 12 were consistently higher with UPA 15 mg and UPA 30 mg vs PBO across the evaluated demographic and baseline disease characteristics(Figure 1**a,** Figure 1**b**). The efficacy of UPA 15 mg QD was generally similar to that observed with UPA 30 mg QD. At 12 weeks, the proportion of patients with treatment-emergent AEs, serious AEs, severe AEs, and AEs leading to discontinuation were generally comparable across different age, sex, race, weight, and BMI groups. Compared with the global population, patients receiving UPA in the Asian region had a higher rate of CPK elevations(UPA 30 mg only) and herpes zoster; herpes zoster also has been observed to be higher in the Asian region with other JAK inhibitors.[6,7]

Conclusion: In this analysis of pooled integrated efficacy data in csDMARD-IR or bDMARD-IR patients with RA, UPA 15 mg or 30 mg QD in combination with csDMARDs improved efficacy outcomes at Week 12 when compared with PBO across all predefined subgroups evaluated.

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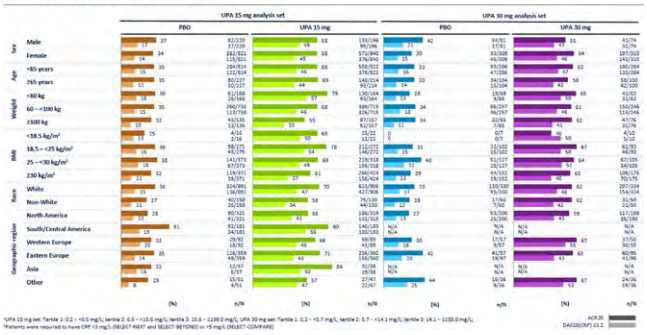
[6] Winthrop KL, et al. Arthritis Rheum 2014;66:2675-84;

[7] Winthrop KL, et al. ACR 2016 [Abstract 3027]

Figure 1a. Proportions of patients in each subgroup achieving ACR20 or DAS28(CRP) ≤3.2 at Week 12



Figure 1a. Proportions of patients in each subgroup achieving ACR20 or DAS28(CRP) ≤3.2 at Week 12



Disclosure of Interests: Michael Weinblatt Grant/research support from: Amgen, Bristol-Myers Squibb, Crescendo, Lily, Sanofi/Regeneron, Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Crescendo, Gilead, Horizon, Lily, Pfizer, Roche, Eduardo Mysler Grant/research support from: AbbVie, Amgen, Bristol Myers Squibb, Roche, Eli Lilly, Novartis, Janssen, Sanofi, and Pfizer., Speakers bureau: AbbVie, Amgen, Bristol Myers Squibb, Roche, Eli Lilly, Novartis, Janssen, Sanofi, and Pfizer, Andrew Ostor Consultant of: MSD, Pfizer, Lilly, Abbvie, Novartis, Roche, Gilead and BMS, Speakers bureau: MSD, Pfizer, Lilly, Abbvie, Novartis, Roche, Gilead and BMS, Aaron Broadwell Grant/research support from: Janssen Research & Development, LLC, Janssen, Eli Lilly, Consultant of: AbbVie, Amgen, AstraZeneca, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, Sandoz, Speakers bureau: AbbVie, Amgen, Celgene, GSK, Horizon, Janssen, Mallinckrodt, Novartis, Pfizer, Radius, Sanofi-Regeneron, UCB, Sławomir Jeka Grant/research support from: AbbVie, Pfizer, Roche, Novartis, MSD, Sandoz, Eli Lilly, Egis, UCB, Celgene, Speakers bureau: AbbVie, Pfizer, Roche, Novartis, MSD, Sandoz, Eli Lilly, Egis, UCB, Celgene, Kendall Dunlap Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Jessica Suboticki Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Jeffrey Enejosa Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Barbara Hendrickson Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Sheng Zhong Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Katya Cherny Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Grace Wright Consultant of: AbbVie, Amgen, BMS, Exagen, Janssen, Lilly, Medac, Myriad Autoimmune, Novartis, Pfizer, Sanofi Genzyme Regeneron, and UCB, Speakers bureau: AbbVie, Amgen, BMS, Exagen, Lilly, Medical Education Resource, Myriad Autoimmune, Novartis, Sanofi Genzyme Regeneron, UCB, and Vindico

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FRI0141

CHARACTERIZATION OF SERIOUS INFECTIONS WITH UPADACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Upadacitinib (UPA) is a selective and reversible Janus kinase (JAK) inhibitor with an approved dose of 15 mg once daily (QD) for the treatment of rheumatoid arthritis (RA). Patients (pts) receiving JAK inhibitors have been reported to be at increased risk of developing serious infection events (SIE) and opportunistic infections (OI).

Objectives: To evaluate the incidence of SIEs and OIs in pts with RA receiving UPA and active comparators in the Phase 3 SELECT clinical trial program.

Methods: The exposure-adjusted event rate (EAER) per 100 patient-years (E/100 PY) of SIEs and OIs was determined in pts receiving UPA in five randomized Phase 3 trials (SELECT-EARLY, SELECT-MONOTHERAPY, SELECT-NEXT, SELECT-COMPARE, and SELECT-BEYOND), of which four evaluated both UPA 15 mg and 30 mg QD doses and one (SELECT-COMPARE) evaluated only UPA 15 mg QD. Incidences of SIEs and OIs were also determined in pts receiving adalimumab (ADA) + methotrexate (MTX) in SELECT-COMPARE and MTX monotherapy in SELECT-EARLY. Data were analyzed descriptively, with no statistical comparisons between groups or doses. Risk factors for SIEs were

determined using a univariate Cox regression model. The data cut-off was June 30, 2019.

Results: Overall, 2629 pts who received UPA 15 mg, 1204 pts who received UPA 30 mg, 579 pts who received ADA + MTX, and 314 pts who received MTX monotherapy were included in this analysis. The EAERs (E/100 PYs [95% CI]) of SIEs were 3.2 (2.7–3.7) in the UPA 15 mg group, 5.7 (4.8–6.8) in the UPA 30 mg group, 3.9 (2.6–5.6) in pts receiving ADA + MTX, and 3.1 (1.7–5.2) in pts receiving MTX monotherapy. Pneumonia was the most common SIE, with EAERs (E/100 PYs [95% CI]) of 0.7 (0.5–1.0), 1.3 (0.9–1.9), 0.7 (0.2–1.5), and 0.7 (0.1–1.9) in the UPA 15 mg, UPA 30 mg, ADA + MTX, and MTX monotherapy groups, respectively. Rates of OIs (including oral candidiasis and disseminated herpes zoster [HZ]) (E/100 PYs [95% CI]) were 0.7 (0.5–1.0), 1.3 (0.9–1.9), 0.4 (0.1–1.1), and 0 (0–0) in the UPA 15 mg, UPA 30 mg, ADA + MTX, and MTX monotherapy groups, respectively. Oral candidiasis was the most frequent OI with EAERs (E/100 PYs [95% CI]) of 0.4 (0.2–0.6) in the UPA 15 mg group, 0.6 (0.3–1.0) in the UPA 30 mg group, 0.4 (0.1–1.1) in the ADA + MTX group, and 0 (0–0) in the MTX monotherapy group. Serious adverse events of HZ were only reported in the UPA groups (0.2 E/100 PYs [95% CI: 0.1–0.3] and 0.6 E/100 PYs [95% CI: 0.4–1.1] in the UPA 15 mg and 30 mg groups, respectively). Overall, there were 3 (4 coded events), 3, 1, and 0 pts who had active tuberculosis events in the UPA 15 mg, UPA 30 mg, ADA + MTX, and MTX monotherapy groups, respectively. Risk factors for SIEs are shown in the Figure. For both UPA doses, age ≥75 years and smoking were noted to have hazard ratios >1.

Conclusion: The incidence rate of SIEs and OIs was higher in the UPA 30 mg group than the UPA 15 mg group. SIEs observed with UPA 15 mg were similar to that seen with ADA although the rates of HZ were higher on UPA. Pts with RA who are ≥75 years old and/or smokers may be at higher risk than other pts with RA for SIEs while receiving UPA.

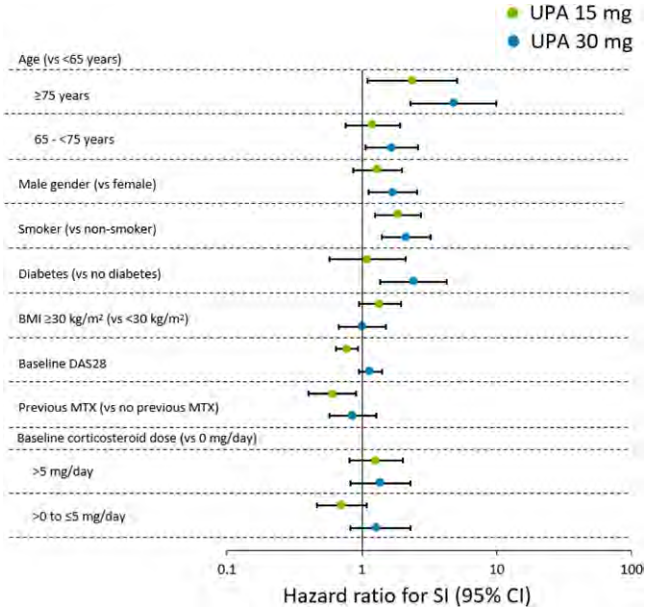


Figure. Univariate analysis of SIE risk factors

Disclosure of Interests: Kevin Winthrop Grant/research support from: Bristol-Myers Squibb, Consultant of: AbbVie, Bristol-Myers Squibb, Eli Lilly, Galapagos, Gilead, GSK, Pfizer Inc, Roche, UCB, Leonard Calabrese Consultant of: AbbVie, GSK, Bristol-Myers Squibb, Genentech, Janssen, Novartis, Sanofi, Horizon, Crescendo, and Gilead, Speakers bureau: Sanofi, Horizon, Crescendo, Novartis, Genentech, Janssen, and AbbVie, Filip van den Bosch Consultant of: AbbVie, Celgene Corporation, Eli Lilly, Galapagos, Janssen, Novartis, Pfizer, and UCB, Speakers bureau: AbbVie, Celgene Corporation, Eli Lilly, Galapagos, Janssen, Novartis, Pfizer, and UCB, Kunihiro Yamaoka Speakers bureau: AbbVie GK, Astellas Pharma Inc., Bristol-Myers Squibb, Chugai Pharmaceutical Co. Ltd, Mitsubishi-Tanabe Pharma Corporation, Pfizer Japan Inc., and Takeda Pharmaceutical Company Ltd, Carlo Selmi Grant/research support from: AbbVie, Janssen, MSD, Novartis, Pfizer, Celgene, and Leo Pharma, Consultant of: Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, Roche, and Sanofi-Regeneron, Speakers bureau: AbbVie, Aesku, Alfa-Wassermann, Bristol-Myers Squibb, Biogen, Celgene, Eli-Lilly, Grifols, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi-Genzyme, UCB Pharma, Yanna Song Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Barbara Hendrickson Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Ivan Lagunes-Galindo Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Iain McInnes Grant/research support from: Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Janssen, and UCB, Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Gilead, Janssen, Novartis, Pfizer, and UCB

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FRI0143

THE EFFICACY AND COST-EFFECTIVENESS OF HYDROXYCHLOROQUINE, SULFASALAZINE, METHOTREXATE TRIPLE THERAPY IN PREVENTING RELAPSE OF RHEUMATOID ARTHRITIS

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Background: TNFα inhibitors (TNFi) is effective for rheumatoid arthritis (RA) patients refractory to conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs), but because of high cost, the discontinuation is common that often lead to disease relapse.

Objectives: To investigate, among RA patients refractory to csDMARDs but achieved therapy target after treated with TNFi and methotrexate (MTX), if the combination therapy of csDMARDs is more effective in reducing disease relapse than MTX monotherapy, and more cost-effective than continuing the treatment with TNFi and MTX.

Methods: In this multi-center, outcome assessment blinded, randomized, superiority clinical trial, RA patients who failed to csDMARDs treatment (DAS28(CRP)>3.2) received MTX plus TNFi for 12 weeks first (induction therapy). Then patients achieving low disease activity [LDA, DAS28(CRP)<3.2] were randomized into three groups in 1:1:1 ratio: (A) maintaining TNFi + MTX for 60 weeks; (B) adding hydroxychloroquine (HCQ) and sulfasalazine (SSZ) for 12 weeks and then removing TNFi but continuing HCQ and SSZ for 48 weeks; and (C) maintaining TNFi + MTX for 12 weeks and then removing TNFi but continuing MTX only for 48 weeks. The primary outcome is disease relapse [DAS28(CRP) increased by at least 0.6 and >3.2] in 60 weeks. Secondary outcomes include the incremental cost effectiveness ratio (incremental cost per reducing 1% relapse rate); adverse events and radiology progression.

Results: 117 patients were enrolled for induction therapy. 67 patients achieved LDA after 12 weeks of induction therapy and were randomized with 21, 24 and 22 patients into each group, respectively. Male [OR=0.046 (0.005-0.451), p=0.008] and less baseline tender joint count [OR=0.825 (0.710-0.958), p=0.012] were independent predictive factors for LDA achievement. The relapse rate in 60 weeks was comparable between group A and B [33.3% (7/21) vs. 37.5% (9/24), p>0.05], while both significantly lower than that of group C [77.3% (17/22), p<0.01, p<0.01, respectively]. The adverse events and modified Sharp score progression were both comparable among the three groups. The incremental cost effectiveness ratio of group A is higher than group B (1315.7 yuan vs 101.5 yuan).

Conclusion: For RA patients refractory to csDMARDs but achieved therapy target after treated with TNFi and MTX, the triple therapy of MTX+HCQ+SSZ is as effective as and more cost-effective than TNFi maintain therapy in reducing disease relapse. Both strategies are more effective than MTX monotherapy.

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FRIDAY, 05 JUNE 2020

SLE, Sjögren's and APS - clinical aspects (other than treatment)

FRI0144 SEROLOGICAL EVOLUTION IN PATIENTS WITH POSITIVE ANTIPHOSPHOLIPID ANTIBODIES- A RETROSPECTIVE STUDY OF CHINESE COHORT

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Background: Antiphospholipid antibodies (aPLs) and thromobotic/obestetric events are the characteristics the antiphospholipid syndrome. The titers of aPL sometimes may decrease and become negative during the follow-up period. Whether the negativization being related with a lower risk of thrombotic events, allowing for withdrawal of anti-coagulant therapy is controversial. And the factors associated with each aPL negativization are still unknown.

Objectives: To explore the clinical and serological course of patients with positive aPLs, and the factors and therapeutic implications associated with aPL negativization.

Methods: Patients with a persistent positive aPL serology according to established criteria between 1997 and 2018 were included. The test of Lupus anticoagulant (LA), anti-cardiolipid antibody (aCL) and anti-β2 glycoprotein I (anti-β2GP1) were following the International Society on Thrombosis and Haemostasis guidelines.The patients were classified as aPL negativization if the following aPL tests became negative, on two or more occasions at least 12 weeks apart. Titer more than 40RU/ml was defined as moderate to high titer for aCL and anti-β2GP1. For patients receiving warfarin, the results of LA were counted only when INR<1.5.

Results: The baseline characteristics of 93 patients were shown in Table 1. After a mean follow-up of 45.0 (45.0) months, the percentage of aPL negativization was 10.8% (9/83), 26.1% (18/69), 24.5% (13/53) for LA, aCL and anti-β2GP1 respectively (Figure 1). Patients with triple aPL positivity at baseline were associated with persistently positive serology for all the three aPLs. Multivariate analysis confirmed that double positive of two methods (dVRRT and SCT) was the only independent protective factor for LA negativization (OR 0.055; 95%CI: 0.006-0.545; p=0.013). SLE, moderate to high titer of aCL and number of baseline aPL positivity were independently associated with aCL negativization (OR 18.2; 95%CI: 1.45-228; p=0.025, for SLE; OR 0.217; 95%CI: 0.053-0.888; p=0.034, for moderate to high titer of aCL; OR 0.198; 95%CI: 0.057-0.689; p=0.011, for number of baseline aPL positivity). Moderate to high titer of anti-β2GP1 and number of baseline aPL positivity were independently protective factors for anti-β2GP1 negativization (OR 0.168; 95%CI: 0.032-0.872; p=0.034, for moderate to high titer of anti-β2GP1; OR 0.243; 95%CI: 0.073-0.813; p=0.022, for number of baseline aPL positivity). Unfortunately, we didn't find any relationship between aPL persistent positivity and further thrombosis/pregnancy morbidity due to limited events.

Table 1. The baseline characteristics of aPL positive patients

baseline characteristics	n=93
Female, n(%)	82.0 (88.2)
Age, mean±SD	33.7±13.8
Disease duriation, median(IQR)	68.0 (85.0)
Follow-up period, median(IQR)	45.0 (45.0)
Thrombotic events, n(%)	29.0 (31.2)
Obstetric events, n(%) (n=82)	25.0 (26.9)
Non-criteria manifestiations, n(%)	45.0 (48.4)
SLE, n(%)	62.0 (66.7)
Number of aPL positivity, median(IQR)	2.00 (1.00)
aPL triple positivity, n(%)	40.0 (43.0)

Conclusion: The proportion of aCL and anti-β2GP1 negativization are higher than LA. The number of positive antibodies and higher antibody load are associated with persistently positive serology. Patients with SLE were easier to get aCL negativization.

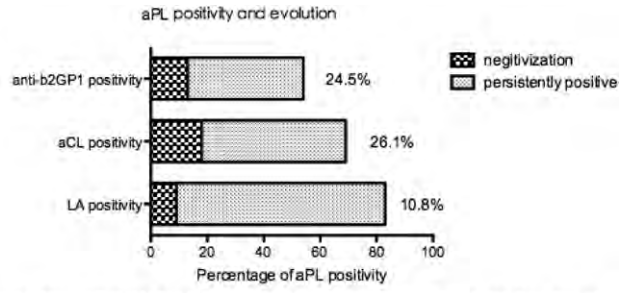


Figure 1 The positivity of aPLs at baseline and the serological evolution during the follow-up.

Disclosure of Interests: None declared
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FRI0145 FOLLOW-UP OF A MONOCENTRIC COHORT OF SERONEGATIVE ANTIPHOSPHOLIPID SYNDROME

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Background: Seronegative antiphospholipid syndrome (SN-APS) is the term proposed to describe patients with clinical signs highly suggestive of APS but persistently negative for conventional antiphospholipid antibodies (aPL) assays. Therefore, new antigenic targets or different methodological approaches have been investigated to detect aPL in SN-APS [1].

Objectives: The aim of this study was to describe the clinical follow-up of a monocentric cohort of SN-APS patients.

Methods: The study included all consecutive SN-APS patients examined from 2014 to 2018. In all patients other possible causes of thrombosis or obstetric morbidity were ruled out. APL were investigated through two tests: 1. anti-cardiolipin/vimentin antibodies (aCL/Vim) by enzyme-linked immunosorbent assay (ELISA) 2. anti-cardiolipin antibodies (aCL) by thin-layer chromatography (TLC)-immunostaining.

Results: We enrolled 121 patients (all Caucasian except one Asian and one Hispanic women). Clinical and demographic characteristics are reported in Table 1.

Table 1. Clinical and demographic characteristics

Features	SN-APS n= 121 (%)
Male/Female	14/107
Mean age in years (from-to)	42.58 (16-78)
PAPS/SAPS	78/43 (64.5/35.5)
SLE	28 (23.1)
Others autoimmune diseases	15 (12.4)
Pregnancy morbidity	56/107 (52.3)
Spontaneous abortions	49 (45.8)
Normal fetus deaths	22 (20.6)
Premature births	7 (6.54)
Thrombosis	72 (59.5)
Arterial thrombosis	36 (29.8)
Venous thrombosis	48 (39.7)
Recurrent thrombosis	28 (23.1)
Thrombosis + Pregnancy morbidity	8 (6.6)
Non-criteria APS features	45 (37.2)
Livedo reticularis	18 (14.9)
Thrombocytopenia	12 (9.9)
Migraine	19 (15.7)
Seizures	5 (4)
Others	11 (9)
Cardiovascular risk factors	50 (41.3)
Hypercholesterolemia	8 (6.6)
Smoking	22 (18.2)
Hypertension	22 (18.2)
OC/HRT	7 (5.8)
Diabetes	4 (3.3)

Sixty-nine out 121 patients (57%) resulted positive for at least one non-conventional test in two occasions more than 12 weeks apart (Figure 1). The agreement between first and second test resulted respectively of K=0,703 e K=0,655 (Cohen's K test). Figure 2 shows the prevalence of aCL (TLC-immunostaining) and aCL/Vim. We found a significant correlation between aCL (by TLC-immunostaining) and aCL/Vim (p = 0.027), brain MRI ischemic changes (p = 0.012) and age (p = 0.023). ACL/Vim was significantly correlated with livedo reticularis (p = 0.015).

Patients with double positivity showed a higher prevalence of mixed thrombotic and obstetrical features than patients with single positivity (p < 0.001, likelihood positive ratio 8.2).

Non-conventional aPL positivity better supported the diagnosis of APS and, following the therapeutic changes implemented, in a median follow up of 41 months (IQR 39.5) only 3 cases of recurrent thrombosis (2 cases of arterial thrombosis during treatment with antiaggregant therapy and one case of venous thrombosis in treatment with new oral anticoagulant therapy) were observed. During the follow-up, 35 patients with obstetric morbidity who resulted positive for the tests had 20 pregnancies; 12 of them (60%) experienced a good outcome under conventional treatment for classical APS.

Conclusion: The results demonstrate that new methods – TLC-immunostaining – or new antigens - CL/Vim – allow to detect aPL in so-called "SN-APS" patients and, consequently, to prescribe the most appropriate therapy.

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Fig.1 The prevalence of autoantibodies in SN-APS

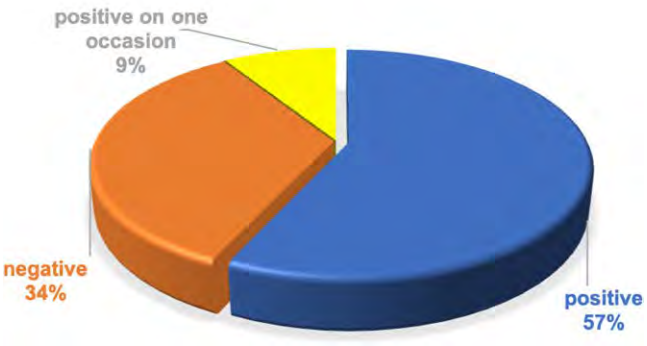
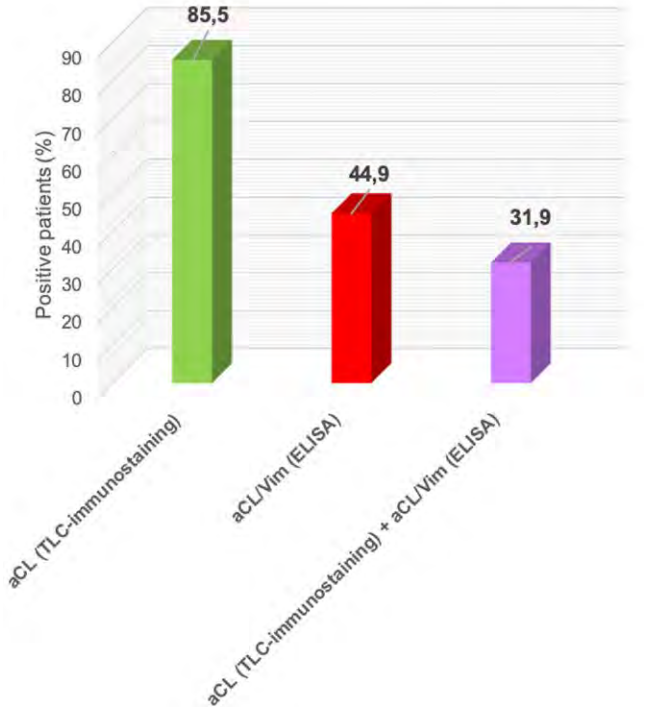


Fig.2 The percentage of SN-APS positive for more than one test



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FRI0146 SLICC/ACR DAMAGE INDEX IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME WITH AND WITHOUT SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: The role of antiphospholipid syndrome (APS) as a cause of chronic organ damage in patients with systemic lupus erythematosus (SLE) is important. While acute disease manifestations of APS are well known, information on the long-term prognosis and damage in affected patients is still very limited.

Objectives: To assess the severity of organ damage in patients with APS without SLE and with concomitant SLE, as well as the feature of irreversible damage to internal organs in patients with primary APS during a dynamic observation using SLICC/ACR Damage Index (SDI).

Methods: The study included 195 patients (41 men and 154 women) who were observed at the Institute of Rheumatology from 2007 to June 2018 with a diagnosis of SLE and APS. The study inclusion criteria were: a follow-up period of at least 3 years with the study of serological markers of APS for previous years, the possibility of dynamic monitoring of patients, patient consent. Patients were divided into 3 groups, depending on presence of APS: group I -SLE with APS (n=99 with average age 34.6 [25-44), group II - SLE without APS (n=45; 33.5[26-42]) and group III - 45 (average age 37.7 [27-46]) patients with primary APS (PAPS) diagnosed according to international diagnostic criteria, without signs of any disease. In all three groups organ damage was assessed using SDI. SDI 1-2 points corresponded to moderate damage, more than 2 points - to severe.

Results: A linear increase in irreversible organ damage was noted over 10 years of follow-up. At the time of inclusion in the study, the average SDI was significantly higher in the SLE + APS group than in the SLE group: 1.32 versus 0 when included ($p < 0.0001$). A direct correlation was found between the age of patients and the value of SDI both in the group I ($p=0.004$, $r=0.284$) and in the group II ($p=0.04$, $r=0.281$) when included in the study. There was a direct correlation between the activity of the disease on the SLEDAI at the end of the study and the value of SDI ($p=0.03$, $r=0.41$) in the group II. The number of patients by the 10th year of follow-up remained in group I were 44 of 99, in group II - 24 of 51 and in group III - 14 of 45. SDI was more than 2 points in 39 (89%) of 44 patients in group I, in 12 (50%) of 24 in group II and 9 (65%) of 14 in Group III ($p=0.0002$ OR=13; 95% CI 2,4-70). 5 years after the start of the observation average SDI in group I and II was 2.5 and 1.3 ($p < 0.0001$) and after 10 years - 2.8 and 1.9 ($p = 0.0008$) accordingly. An increase of total SDI occurred primarily due to damage to peripheral vessels due to the large number of thromboses (in 55% of patients) in the group II. Using step-by-step multiple logistic regressions in the study groups only APS was an independent predictor of increased SDI. The most common cause of an increase in SDI in the PAPS group was damage to peripheral vessels (64%) as a result of a high frequency of venous thrombosis, followed by damage to the neuropsychiatric system (55%) and the cardiovascular system (40%).

Conclusion: APS is an independent predictor of increased SDI. The determination of irreversible organ damage in patients with PAPS using SDI allows us to assess the functional disorders of organs and systems and can be used in clinical practice in these patients.

Disclosure of Interests: None declared
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FRI0147 PREVALENCE OF COMORBIDITIES IN ANTIPHOSPHOLIPID SYNDROME VERSUS RHEUMATOID ARTHRITIS: A MULTICENTRE, AGE- AND SEX-MATCHED STUDY

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Background: Comorbidities in rheumatic diseases (RDs) have been associated with increased morbidity and mortality. Evidence on prevalence of comorbidities in antiphospholipid syndrome (APS) and its difference from high comorbidity burden RDs is limited.

Objectives: To compare the prevalence of common comorbidities between APS [primary (PAPS) and Systemic lupus erythematosus (SLE)-APS] and Rheumatoid arthritis (RA) patients.

Methods: 326 APS patients from the Greek registry (237 women, mean age 48.7±13.4 years, 161 PAPS) were matched 1:2 for age and sex with 652 RA patients from Greek RA Registry. Prevalence of cardiovascular (CV) risk factors, stroke, coronary artery disease (CAD), osteoporosis, diabetes mellitus (DM), Chronic obstructive pulmonary disease (COPD), depression and neoplasms were compared between APS and RA using logistic regression analysis.

Results: Regarding CV burden, hyperlipidemia and obesity (BMI≥30) were comparable while hypertension, smoking, CAD and stroke were more prevalent in APS compared to RA patients (Table 1). Osteoporosis and depression were more frequent in APS while DM, COPD and neoplasms were comparable between two groups. Comparison of APS subgroups to 1:2 matched RA patients revealed that smoking and stroke were more prevalent in PAPS and SLE-APS vs RA. Hypertension, CAD and osteoporosis were more prevalent only in SLE-APS vs. RA while DM was less prevalent in PAPS vs. RA patients.

Table 1. Comparison of comorbidities between Antiphospholipid syndrome (APS) vs. matched Rheumatoid Arthritis (RA) patients and between primary APS (PAPS) or Systemic Lupus Erythematosus-APS (SLE-APS) vs matched RA patients

	APS	RA	OR*	PAPS	RA	OR	SLE-APS	RA	OR
n (%)	326	652		161	322		165	330	
Hypertension	97 (29.8)	136 (21)	1.61 (1.19-2.18)	40 (25)	75 (23.3)	1.09 (0.70-1.69)	57 (34.6)	61 (18.5)	2.33 (1.52-3.56)
Smoking	175 (53.7)	264 (40.5)	1.70 (1.30-2.22)	87 (54)	142 (44)	1.49 (1.02-2.18)	88 (53.3)	122 (37)	1.95 (1.33-2.85)
Hyperlipidemia	79 (24.2)	135 (20.7)	1.23 (0.89-1.68)	40 (24.8)	62 (19.3)	1.39 (0.88-2.18)	39 (23.6)	73 (22)	1.09 (0.70-1.70)
Obesity	48 (20.5)	105 (19.5)	1.06 (0.73-1.56)	20 (17)	51 (19)	0.86 (0.49-1.52)	28 (24)	54 (19.7)	1.28 (0.76-2.15)
Stroke±	66 (20.3)	9 (1.4)	13.8 (6.5-29.1)	36 (22.4)	4 (1.2)	19.9 (6.6-59.9)	30 (18.2)	5 (1.5)	7.8 (2.7-22.6)
Coronary disease±	16 (4.9)	13 (2)	3.14 (1.17-8.45)	2 (1.2)	7 (2.2)	0.46 (0.04-4.77)	14 (8.5)	6 (1.8)	10.9 (2.7-44.3)
Osteoporosis×	66 (20.3)	92 (14)	1.45 (1.01-2.06)	19 (11.8)	42 (13)	0.96 (0.54-1.73)	47 (28.5)	50 (15)	1.91 (1.20-3.05)
Diabetes×	18 (5.5)	58 (9)	0.58 (0.33-1.01)	5 (3)	29 (9)	0.34 (0.13-0.89)	13 (8)	29 (9)	0.88 (0.44-1.79)
COPD≠	11 (3.4)	14 (2.2)	1.26 (0.56-2.84)	3 (1.9)	6 (2)	0.96 (0.23-4.0)	8 (5)	8 (2.4)	1.28 (0.44-3.72)
Depression#	53 (16.3)	66 (10)	1.70 (1.15-2.53)	23 (14)	30 (9.3)	1.69 (0.93-3.05)	30 (18.2)	36 (10.9)	1.65 (0.96-2.84)
Neoplasms˅	14 (4.3)	27 (4.1)	1.05 (0.54-2.06)	5 (3)	12 (3.7)	0.84 (0.28-2.52)	9 (5.5)	15 (4.6)	1.31 (0.55-3.1)

* OR: Odds ratio, crude or adjusted for:
± age, sex, smoking, hypertension, hyperlipidemia, BMI, corticosteroid (Cs) duration
× Cs duration
≠ smoking, Cs duration
sex, disease duration, Cs duration
˅ age, disease duration

Conclusion: Comorbidity burden in APS (PAPS and SLE-APS) is comparable or even higher to that in RA, entailing a high level of diligence for CV risk prevention, awareness for depression and corticosteroid exposure minimization.

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FRI0148 SEROLOGICAL PROFILES IN PRIMARY SJÖGREN SYNDROME, SJOGRENSER PROJECT

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Objectives: Primary Sjögren´s Syndrome (pSS) is characterized by hyperactivity of the B cell, with the consequent production of autoantibodies. The presence of anti-Ro and anti-La has been associated with extraglandular manifestations and lymphoma development. The aim of this study is to evaluate the frequency of different serological profiles in patients of SJOGRENSER registry and to assess whether the combination of antibodies and serological markers are associated with the development of systemic disease and the systemic illness and/or the development of systemic disease and complications.

Methods: SJOGRENSER is a transversal multicenter study with pSS patients (patients who meet 2002 pSS classification criteria); it is collected demographic, clinical, serological data and the activity index: ESSDAI and ESSPRI. It was established three serological profiles: 1. ANA/Ro+ with La/RF-; 2. ANA/Ro/La+ with RF-; 3. ANA/Ro/La/RF+. A descriptive analysis was done, with means and standard deviations, frequencies and proportions. Student t for quantitative variables and Chi2 for qualitative ones were performed to evaluate differences between groups, it was considered a p <0.05 as significant. The association was analyzed by multinominal analysis.

Results: Four hundred and thirty-seven patients were included, the most frequent serological patterns observed were: ANA/Ro/La/RF+ 221 patients (50.5%), ANA/Ro/La+ 61 patients (13.9%) and ANA/Ro+ 60 patients(13.7%). There were only two patients with ANA/La +. The ESSDAI score was significantly associated with the profile ANA/Ro/La/RF+ (6 vs 4, p=0.007) and the group with the ANA/Ro/La+ profile reached an ESSDAI<5 (79%, p=0.043) (Table 1).

Table 1. Serological markers associated with the development of systemic disease

Involvement	Profile 1 ANA + Anti-Ro + Anti-La - RF – n=60 Nº (%)	Profile 2 ANA + Anti-Ro + Anti-La + RF – n= 61 Nº (%)	Profile3 ANA + Anti-Ro + Anti-La + RF + n= 221 Nº(%)	p
ESSDAI index	4	4	6	0.007
ESSDAI<5	44 (73.3)	48 (78.7)	139 (63.2)	0.043
ESSPRI index	6.1	5.3	5.0	0.007
Constitutional syndrome	5 (8.3)	9 (14.8)	51 (23.1)	0.023
Lymphadenopathy	8 (13.3)	9 (14.8)	37 (16.7)	0.790
Glandular	14 (23.3)	16 (26.2)	87 (39.4)	0.024
Articular	49 (81.7)	40 (65.6)	187 (84.6)	0.004
Lung	3 (5.0)	4 (6.6)	29 (13.2)	0.100
Kidney	0 (0)	5 (8.2)	31 (14.1)	0.006
Peripheral nervous system	5 (8.3)	6 (9.8)	18 (8.2)	0.918
Central nervous system	4 (6.7)	7 (11.5)	13 (5.9)	0.320
Hematological	24 (40.0)	26 (42.6)	147 (66.5)	<0.001
Biologic	5 (8.3)	4 (6.6)	26 (11.8)	0.428
Lymphoma	1 (1.7)	2 (3.3)	3 (1.4)	0.598

In contrast to the ESSPRI index was lower significantly associated with the profile ANA/Ro/La/RF+ and higher in the ANA/Ro+ (5 vs 6.1, p=0.007). The presence of antiLa and/or RF to the profile ANA/Ro+ rises the percentage of patients with constitutional syndrome, glandular, kidney and hematological affectation with statistically significant differences. The percentage of patients with articular involvement it was similar in the profiles ANA/Ro+ and ANA/Ro/La/RF +.

The multinomial analysis showed that the profile ANA/Ro/La/RF+ was associated with higher ESSDAI values (OR=1.09 (1.01-1.17)). The hematological involvement was associated with the profiles ANA/Ro/La/FR+ (OR= 2.76 (1.46-5.22)). Higher scoring of ESSPRI was associated with the profile ANA/Ro+ (OR=0.79 (0.69-0.91)).

Conclusion: The most frequent serological profile was ANA/Ro/La/RF+ and it was associated with higher ESSDAI score. The presence of antiLa and/or RF with an ANA/Ro+ increased the presence of systemic involvement. The ANA/Ro+ profile was associated with a higher level of ESSPRI.

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FRI0149 THE CLINICAL FEATURES OF SJÖGREN'S SYNDROME PATIENTS WITH EARLY AND LATE DISEASE ONSET

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Background: Sjögren's syndrome (SS) affects mainly individuals of the 4th or 5th decade of life, although patients with early (≤35 years old) or late (≥65 years old) disease onset have been described in the literature. The clinical spectrum of the disease extends from mild dryness to severe systemic vasculitis and lymphoproliferative disorders. The phenotypic diversity of SS is defined by many factors, including age, since many parameters related to age may affect the clinical expression of the disease. Few studies have been conducted to study the effect of age on the clinical phenotype of SS, though with limited number of patients. Large and well-defined groups of SS are required to address such questions.
Objectives: To study the clinical phenotype of SS patients with early and late disease onset and to explore the association of age with lymphoma development in a unified multicenter cohort.
Methods: From a total cohort of 1997 consecutive SS patients who fulfill the 2016 EULAR/ACR criteria and are followed up in 5 clinical centers ([Universities of **U**dine, **P**isa and **A**thens, **H**arokopio and **I**oannina, (**UPAHI)**], those with either early (≤35 years) or late (≥65 years) disease onset were identified and matched according to gender and disease duration with middle aged controls whose disease onset was at the 4th or 5th decade of life. Glandular manifestations, extra-glandular manifestations, serologic characteristics and histologic features were compared between the 2 age groups and the middle-aged control groups. Statistical analysis for categorical variables was performed by Fisher exact or chi-square tests and for continuous variables with t test or Mann-Whitney accordingly.
Results: Three hundred seventy-nine (19%) SS patients with early and 293 (15%) with late disease onset were identified and compared with 353 and 285 middle aged SS controls respectively. The median disease duration of patients with early onset was 12 years (range:0-68) and for those with late disease onset was 5 years (range: 0-27). SS patients with early disease onset had statistically significant higher frequency of Raynaud's phenomenon, lymphadenopathy, hypergammaglobulinemia, anti-Ro/SSA, anti-La/SSB, rheumatoid factor, salivary gland enlargement, low C4 complement levels, leukopenia and lymphoma (10,3% vs 5,7%, p= 0.03, OR= 1,91, 95% CI: 1,11-3,27) while SS patients with late disease onset had more frequently dry mouth, interstitial lung disease and lymphoma (6,8% vs 2,1%, p=0,01, OR= 3,4. 95%CI: 1,35-1,81).
Conclusion: In a multicenter cohort of 1997 consecutive SS patients, those with early and late disease onset comprise more than one third of the total SS population. Patients with early disease onset, exhibit robust B cell responses with traditional risk factors for lymphoma as opposed to patients with late disease onset. Both age groups have increased lymphoma prevalence but presumably for different reasons, since late onset patients lack classical predictors of lymphoma. Therefore, these predictors deserve further study in different disease subsets.
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FRI0150 USEFULNESS OF SALIVARY GLAND ULTRASONOGRAPHY IN THE ASSESSMENT OF SALIVARY GLAND ACTIVITY AND DAMAGE IN PRIMARY SJÖGREN'S SYNDROME: A SINGLE CENTER EXPERIENCE

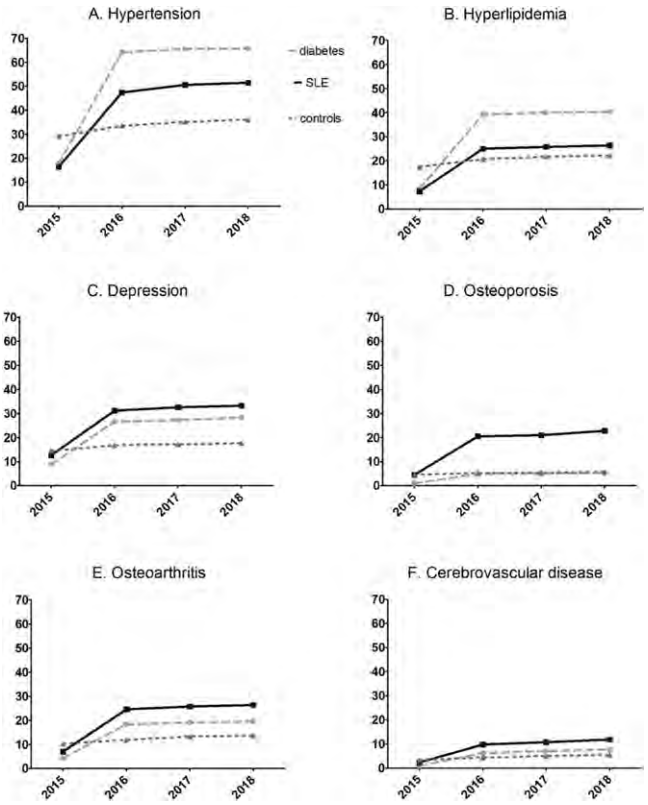
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Background: Salivary gland ultrasonography (SGUS) has an emerging role in the diagnosis of primary Sjögren's syndrome (pSS); however, it is still an open issue whether distinct sonographic abnormalities may indicate reversible glandular activity or irreversible disease-induced damage.
Objectives: to assess the association between SGUS abnormalities, salivary gland disease activity and loss of function in pSS patients over a long-term follow-up.
Methods: Patients with pSS fulfilling the AECG 2002 criteria were included in this observational study. Both parotid and submandibular glands were examined at the time of the study inclusion and during the follow-up. SGUS findings (i.e gland size, echogenicity, homogeneity, hyperechoic bands, number and location of the hypoechoic/anechoic areas, number of lymph nodes, calcification, posterior border visibility) were defined according to previous studies and monitored over the time. Patients demographics, clinical, histological and laboratory data were routinely collected. ESSDAI and ESSPRI were used to asses disease activity and PROs.
Results: We included 419 (402 F:17M) pSS patients: 206/419 at the diagnosis and 213/419 with a median disease duration of 7 (IQR 4-11) years. SGUS examination was repeated in 81/206 and in 108/213 patients, after a median follow-up of 30 (IQR 12-42) months, respectively. Noteworthy, 18/419 pSS patients were treated with rituximab (RTX) during the study period. The overall SGUS score correlated directly with the minor salivary focus score (r=0.366, p=0.000) and with the ESSDAI (r=0.482, p=0.000); the parotid inhomogeneity score correlated directly with the glandular domain of the ESSDAI (r=0.530, p=0.000). The unstimulated salivary flow rate (USFR) correlated inversely with the overall SGUS score (r=-257, p=0.000) and with the presence of hyperechoic bands in both the parotid (r=-210, p=0.03) and the submandibular glands (r=-316, p=0.000). When compared to patients with an established pSS, newly diagnosed patients presented less frequently a gross inhomogeneity in their parotid glands (30/206, 14.6% vs 53/213, 24.9%, p=0.01) and less hyperechoic bands in both their parotid (33/206, 16% vs 61/213, 29%, p=0.001) and submandibular glands (53/206, 26% vs 110/213, 52%, p=0.001). However, over a median 30 month-follow-up we did not observe any significant change neither in the number of hypo-anechoic areas nor in the inhomogeneity score in both newly diagnosed patients and in those with an established disease. Out of the 18 pSS patients treated with RTX, 14 (78%) presented at the baseline a moderate to gross inhomogeneity in their glands: no changes in the number of hypo-anechoic areas were observed also in these patients with the exception of a variation in the number of intra-parotid lymph nodes.
Conclusion: SGUS abnormalities appeared to be associated to both salivary gland disease activity and damage. Namely, the presence of hyperechoic bands significantly correlated with salivary loss function. Diffuse-scattered hypoechoic areas did not change over a median 30-month followed-up indicating that additional studies are required to better elucidate the correlation between SGUS abnormalities and the corresponding histopathologic lesions.
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FRI0151 COMORBIDITY IN INCIDENT SYSTEMIC LUPUS ERYTHEMATOSUS: ANALYSIS OF A CLAIMS DATA COHORT

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Background: Systemic lupus erythematosus (SLE) targets many tissues including heart, kidney, bone and brain, causing a variety of comorbidities. Epidemiological studies assessing comorbidity in SLE facilitate earlier detection to limit its progression.
Objectives: To analyze comorbidities in individuals with an incident diagnosis of systemic lupus erythematosus (SLE) in claims data in comparison to matched controls.
Methods: Individuals with ≥2 outpatient or 1 inpatient SLE diagnosis (M32.1, M32.8, M32.9, ICD10) in 2016-2018 and no diagnosis in 2015 or 2014 were identified in a German statutory health insurance fund covering 7.2 million people > 18 years old. Comorbidities defined by the Elixhauser index, medical prescriptions, hospitalization and sick leave were analyzed in the year prior to diagnosis and during a two year follow-up in comparison to age and sex-matched controls without related autoimmune diseases (1:10). To account for detection bias, a second age and sex-matched control group with incident diabetes mellitus (E10-14) was drawn (1:5). To consider diagnostic uncertainty, two sensitivity analyses were performed, namely (i) excluding cases with ICD diagnosis of Sjögren's syndrome, mixed connective tissue disease, systemic sclerosis and tubulointerstitial nephritis and (ii) excluding cases without any prescription of antimalarials.
Results: A total of 559 persons were included (87% female, mean age 55 years). The mean Elixhauser score increased from 1.1 in 2015 to 4.2 in the index year and to 4.5 in the 2nd year after diagnosis. Hypertension (47%), depression (31%), hyperlipidemia (25%), osteoarthritis (25%) and osteoporosis (21%) were among the most frequent comorbidities in the index year. Drug prescriptions (mean 9.7, Δ+6.3), among these glucocorticoids (56%), HCQ (50%) and azathioprine (13%), and hospitalization (40%, Δ+26%) increased in the 1st year after the SLE diagnosis. The increase in comorbidity diagnoses was low in controls without related autoimmune disease, while controls with incident diabetes showed a more pronounced increase in cardiovascular risk factors and and a lesser increase in osteoporosis and cerebrovascular disease (figure 1). Comparable results were found in the sensitivity analyses, where patients with HCQ were younger and had less general comorbidity.
Figure 1. Comorbidity claims in persons with incident systemic lupus erythematosus in 2016 (N=559, M32.1,8,9) and age and sex-matched controls (N=5,590 without related autoimmune disease, N=2,795 with incident diabetes, E10-14)



Conclusion: Cardiovascular, bone and neurologic comorbidities are frequently detected already at the time of diagnosing SLE. High numbers of medical prescriptions and hospitalization following SLE diagnosis reflect the comprehensive disease burden. Differences to controls without autoimmune disease are overestimated by detection bias.

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FRI0152 PULMONARY HYPERTENSION IN NEWLY DIAGNOSED SPANISH PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: DATA FROM THE RELES COHORT

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Background: Systemic lupus erythematosus (SLE) is a systemic autoimmune disease characterized by multiorgan involvement. Pulmonary hypertension (PH) is an uncommon manifestation with high morbidity and mortality whose characteristics, prevalence and evolution in SLE are not completely defined.

Objectives: Using data of patients from the inception cohort Registro Español de Lupus Eritematoso Sistémico (RELES), we aimed to to identify the factors associated with pulmonary hypertension (PH) in systemic lupus erythematosus (SLE).

Methods: Prospective observational study on a multicenter Spanish inception cohort. Patients with SLE, diagnosed by the American College of Rheumatology (ACR) criteria, since January 2009, who had at least one transthoracic echocardiogram (TTE) performed were selected. Demographic data, diagnostic criteria, follow-ups, treatments and SLEDAI were analyzed.

Results: Of 289 patients diagnosed with SLE with TTE performed, 15 (5.2%) patients were identified to have PH. Mean age was 56,9±7,7 years, of which 93,3% (14) were women and 80% (12) Caucasian. The ACR score at diagnosis was 4.66. Mean SLEDAI was 15. Only 5 patients had dyspnea at the time of diagnosis. Mean pulmonary arterial systolic pressure was 49.2±5.6 mmHg. Among the PH, 4 patients had pericarditis (26.6%), 3 (20%) valvulopathies (1 antiphospholipid syndrome), 1 patient pulmonary embolism and 1 shrinking lung. Multivariable analysis indicated that pericarditis (odds ratio (OR)=2.53), and valvulopathies (OR 8.96) were independently associated with the development of PH in SLE. Having PH was associated with older age at diagnosis (p<0.001), more dyspnea (p<0.001), higher ESR (p=0.007), more serositis (p<0.001), higher SLEDAI (p=0.011), higher SLICC (p <0.001), higher number of admissions (p=0.006) and higher mortality (p=0.003).

Conclusion: PH in SLE is a serious comorbidity with high mortality. In the RELES cohort it was associated with increased disease activity, pericarditis and valvulopathies. Performing TTE in patients with SLE may favor early diagnosis and treatment.

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FRI0153 ULTRA HIGH-RESOLUTION ULTRASOUND (UHFUS) OF LABIAL SALIVARY GLANDS: POTENTIAL APPLICATIONS IN PRIMARY SJÖGREN'S SYNDROME

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Background: Major salivary gland ultrasonography has an established role in diagnosis and assessment of pSS. Nowadays, however, interest is also growing in last-generation ultra high resolution ultrasound (UHFUS) transducers, which can produce frequencies up to 70 MHz and achieve tissue resolution up to 30 µm, opening up new possibilities for the study labial salivary glands (LSG).

Objectives: To investigate the usefulness of UHFUS in LSG ultrasound-guided biopsy and preoperative planning.

Methods: Consecutive patients undergoing a LSG for clinically suspected pSS were included in this study from January 2018 to December 2019. UHFUS of LSG was performed by using VEVO MD, equipped with a 70 MHz probe, scanning first the central compartment of the inferior lip, and then both peripheral compartments. The following parameters were evaluated: distribution of the glands, parenchymal inhomogeneity (score 0-3, from normal to evident), and fibrosis. UHFUS imaging was used to help locate the LSG for the US-guided biopsy. The same expert pathologist calculated the surface area of gland sections examined, the LSG focus score (FS), the number of foci and evaluated the presence of ectopic germinal centers (GCs). Consecutive patients that had undergone a traditional LSG biopsy from December 2016 to December 2017 were included as controls.

Results: We included a total of 249 patients with suspected pSS: 137 undergoing the UHFUS-guided LSGs and 112 the traditional LSG biopsy procedure. No demographic differences were observed between the two groups. No differences were also observed in the distribution of the final diagnosis. A diagnosis of pSS according the ACR 2016 criteria was made in 60/137 (43.8%) and 36/112 (32.1%) patients, respectively whereas a diagnosis of no-SS sicca was made in 44/137 (32.1%) and in 43/112 (38.4%) patients; the remaining diagnosis included secondary SS (4/137, 3% and 9/112, 8%) and undifferentiated connective tissue disease (UCTD) (29/137, 21.2%, and 24/112, 21.4%). With respect to no-SS sicca controls and UCTD patients, pSS patients presented higher UHFUS inhomogeneity scores in both central and peripheral labial compartments (p=0.001). There were no complications from the HUFUS-guided LSG biopsy. The mean glandular surface area obtained was significantly higher than the area obtained by traditional LSG biopsy procedure (7.4 ±4.0 mm^2 vs 6.3±3.7 mm^2, p=0.02) thus facilitating the assessment of the FS. Interestingly, the latter showed a good correlation with the UHFUS inhomogeneity (r=0.509**, p=0.000).

Conclusion: UHFUS of LSG appeared feasible and sensitive in pSS, potentially offering unique advantages in LSG ultrasound-guided biopsy.
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FRI0154 **SHOULD BE OLDER PATIENTS TESTED FOR ANTIPHOSPHOLIPID ANTIBODIES? 695 CASES FROM THE RETROSPECTIVE SERIES HIBISCUS**

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Background: Although guidelines do not recommend antiphospholipid antibodies testing after 60 yo, recent data reported late onset antiphospholipid syndrome (APS).
Objectives: To comparatively analyse the clinical, laboratory features and outcomes in 695 cases with primary APS between patients older and younger than 70 yo.
Methods: we have performed an international study within the framework of the International Registry of primary APS patients treated with Hydroxychloroquine, HIBISCUS (an ongoing retrospective and prospective register launched in 2016). 28 centres from 17 countries participate. Data about late onset APS were analysed in 695 patients and were obtained from a standardized form registered in the database containing 66 items with respect to demographics, clinical and biological features.
Results: Arterial events and especially stroke represented the main initial and recurrent clinical manifestation in 40 primary APS patients older than 70 yo. There were not statistically significant differences with respect to cardiovascular risk factors between the two groups of patients. A significant male predominance, a familial APS history, a higher prevalence of triple positivity, lower complement levels, and anticardiolipin antibodies (aCL) IgA isotype were found in older patients. Low anticoagulation regimens were safe and efficient, with a low relapse rate in older patients.
Conclusion: we suggest that the detection of aPL antibodies should be included into the initial screening panel tests in elderly with thrombotic events, especially arterial, in particular those with recurrent stroke and familial APS.
Our study further suggests that lower intensity anticoagulation regimens could be a therapeutic option in older APS patients, as no differences in outcomes and relapse rate were found between patients with high and low intensity anticoagulation regimens.
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FRI0155 **A MULTICENTER "AT-RISK" COHORT FOR THE DISCOVERY OF ENVIRONMENTAL, CLINICAL AND MOLECULAR PREDICTORS FOR THE TRANSITION INTO SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)**

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Background: SLE onset is preceded by a preclinical phase evidenced by the presence of anti-nuclear and other autoantibodies (autoAbs), which however, have low predictive value for development of clinical SLE.
Objectives: To define the subgroup of autoAbs-positive individuals who are at high risk for progression into SLE by integrating environmental, clinical/serological, genetic and transcriptome data.
Methods: A multicenter, across five European countries, inception cohort of autoAbs-positive individuals or first-degree relatives (FDRs) of SLE patients who are monitored prospectively over five years for possible transition to SLE according to the classification criteria. Structured data collection on demographics, family and medical history, clinical (criteria and selected non-criteria manifestations) and serological parameters, use of medications, hydroxyvitamin D levels and lifestyle (tobacco, alcohol use, physical activity, adherence to Mediterranean diet). Blood samples are stored for RNA-sequencing and genotyping.
Results: A total 254 at-risk individuals (93% women, 99% Caucasians, aged [mean ± standard deviation] 36 ± 12 years) have been included and enrolment/monitoring is still ongoing. Forty individuals (16%) have FDR with SLE and 88 individuals (35%) have FDR with another autoimmune disorder. The frequency of active and past use of tobacco was 28% and 20%, respectively. Sedentary lifestyle (moving only for necessary chores or outdoor activity 1-2 times/week) was reported by 54% and adherence to the Mediterranean diet was low (3.4 ± 2.3, maximum score: 9). At enrolment, individuals had 1.9 ± 1.1 ACR-1997 classification criteria, with anti-nuclear antibodies (ANA) being the most frequent (88%), followed by synovitis (39%), photosensitivity (33%) and immunologic disorder (30%) (Table 1). During follow-up of 15.2 ± 7.2 months, a total 15 individuals (5.9%) have progressed into classified SLE, including cases with severe hematological and neurological disease.

Table 1. Baseline characteristics of the at-risk for SLE cohort

	N (%) or mean ± SD
ACR 1997 classification criteria	1.9 ± 1.1
Malar rash	68 (27%)
Discoid rash	29 (11%)
Photosensitivity	83 (33%)
Mucosal ulcers	49 (19%)
Synovitis	100 (39%)
Serositis	30 (12%)
Renal disorder	28 (11%)
Neurologic disorder	31 (12%)
Hematologic disorder	58 (23%)
Immunologic disorder	77 (30%)
ANA	222 (88%)
SLICC 2012 classification criteria	
Clinical criteria	1.0 ± 0.9
Immunological criteria	1.3 ± 0.9

Conclusion: Among individuals with positive autoAbs or FDRs with SLE, the short-term risk for transition into clinical SLE is low. Following the study completion, clinical and lifestyle data will be combined with blood transcriptome to define a high-risk subgroup of individuals for progression into SLE.
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FRI0156 **WORK PARTICIPATION IN PATIENTS WITH SYSTEMATIC LUPUS ERYTHEMATOSUS: A SYSTEMATIC REVIEW**

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Background: The treatment of systemic lupus erythematosus (SLE) has improved over the last decades, however, absenteeism and work disability numbers remain higher than those observed in the general population (1). SLE has its onset between the ages of 20 and 40 years, and has a major burden on the lives of patients, both mentally and financially. A recent online survey amongst 2070 European SLE patients revealed that 69.5% of patients had their careers affected due to SLE (2).
Objectives: To determine the magnitude of absenteeism and work disability in patients with SLE and to investigate the factors that might affect work participation in these patients in order to develop interventions to reduce the impact of the burden in the future.
Methods: A systematic literature search was performed to identify published articles reporting on the prevalence of work related burden, as well as the relation of having SLE on employment status, sick leave and/or presenteeism. Full-text original articles (all languages) published before April 2019 were identified by literature search performed in MEDLINE, Cochrane, Embase and CINAHL.
Results: In total, 2057 non-duplicate citations were screened after database searching and snowballing. Finally, 81 articles were included; most studies (n=59) had a cross-sectional design and the remaining 22 studies had a longitudinal design. Only 15 longitudinal cohort studies reported on associations, 6 studies described a longitudinal prediction model, 2 studies reported on associations and described a prediction model, and 3 studies had a longitudinal design but only reported on prevalences over time. In total, 3500 working patients were included in the studies reporting on associations or describing a longitudinal prediction model. In the association studies, the most frequently used outcome measures were respectively being employed/probability of being employed and work loss/job cessation. Other studies used loss of days from (non)workforce activities/sick leave days, work disability, productivity loss or work entry. Most associations with work outcome were found for demographic variables and two or three disease variables, like Systemic Lupus Activity Questionnaire (SLAQ) score and depressive symptoms. This was also the case in the prediction studies. Most studies did not assess work related variables as possible predictors for work outcome.
Conclusion: A large heterogeneity was found in type of study design and outcome measures, which limits comparison with other studies. More longitudinal studies are needed to truly assess the impact of SLE on work participation, and to identify factors that could be influenced during interventions, in order to encourage work participation of these patients.
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FRI0157 **EPSTEIN BARR VIRUS BLOOD REPLICATION INCREASES DURING ACTIVE SYSTEMIC LUPUS ERYTHEMATOSUS**

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Background: A role for Epstein Barr Virus (EBV) infection in Systemic Lupus Erythematosus (SLE) pathogenesis is highly suspected. The frequency of EBV seroprevalence and DNA detection in peripheral blood mononuclear cells are increased in SLE patients compared to healthy controls.
Objectives: To analyse the relationship between EBV blood replication and SLE disease activity.
Methods: Monocentric, observational and retrospective study of SLE patients (ACR or SLICC criteria) who have had a blood EBV DNA assessment using Polymerase Chain Reaction (artus® EBV Virus QS-RGQ assay) between 2012 and 2018. Exclusion criteria were: organ or bone marrow transplant, absence of EBV seroconversion and insufficient data. SLE clinical features, the Safety of Estrogens in Lupus Erythematosus National Assessment–Systemic Lupus Erythematosus Disease Activity Index (SELENA-SLEDAI) flare index (SFI) and therapeutic regimen on the day of EBV DNA load assessment were recorded. A SELENA-SLEDAI score > 4 defined an active SLE. A blood EBV DNA load ≥125 IU/mL was defined as elevated.
Results: A total of 105 patients (98 women and 7 men) were included in the study. At inclusion, median (quartiles) age and SLE duration were 34 (23.5-43) and 7 (2-14) years old, respectively. Treatment were hydroxychloroquine (HCQ) (n = 67; 64%), prednisone (n = 66; 63%) with an average (±Standard Deviation) dose of 11.3 (±16) mg/day and an immunosuppressant (n = 42; 40%). According to SFI, 57 SLE patients were experiencing a flare at the time of EBV assessment; flares were classified as severe and mild/moderate in 38 (36%) and 19 (18%) SLE patients, respectively. According to the SELENA-SLEDAI score, 60 patients (57%) were deemed active and 45 (43%) inactive. Main clinical manifestations were arthritis in 32 (30%) patients, constitutional symptoms (fever, weight loss, anorexia or lymphadenopathy) in 31 (30%), cutaneous involvement in 23 (22%), glomerulonephritis in 19 (18%), cytopenia in 14 (13%), neuropsychiatric involvement in 13 (12%) and serositis in 10 (16%). Blood EBV DNA was elevated in 54 (90%) of the 60 patients with active lupus versus 6 (13%) of the 45 patients with inactive SLE ($p < 10^{-4}$). It was increased in 34 (89%) of the 38 patients with severe flare, in 17 (89%) of the 19 patients with a mild/moderate flare ($p = 1$) and in 8 (17%) of the 48 patients without flare ($p < 10^{-4}$ vs severe flare and $p < 10^{-4}$ vs mild/moderate flare). EBV DNA load correlated with SELENA-SLEDAI score ($r=0.58$; $p<0.0001$). Elevated blood EBV DNA was not associated with HCQ, prednisone or immunosuppressant intakes. Eighteen patients with active SLE had a second assessment of blood EBV DNA load. For these patients, the median [range] of viral load was significantly higher during periods of active SLE (236 [0-2680] IU/mL) compared with periods with lower SELENA-SLEDAI score (0 [0-1537] IU/mL, $p<10^{-4}$ in paired analysis).
Conclusion: Blood EBV viral load is dramatically increased in active phase of SLE, independently of the treatment. We were unable to demonstrate whether the replication of EBV was the cause or the consequence or just an epiphenomenon of the disease activity. Further studies are needed to study whether EBV viral load is linked with Interferons secretion or B lymphocyte activation.
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FRI0158 **CLINICAL AND IMAGING FEATURES OF ARTICULAR MANIFESTATIONS IN PRIMARY SJÖGREN'S SYNDROME: SIMILARITIES AND DIFFERENCES ACCORDING TO THE TIME OF ONSET**

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Background: Articular manifestations (AMs) are observed in a large proportion of patients with primary Sjögren's syndrome (pSS) and can occur at the time of pSS diagnosis or during the disease course. Although in the majority of cases AMs are mild and self-limiting, some patients may experience chronic polyarthritis requiring treatment with DMARDs. However to date no specific discriminating biomarkers have been identified. Magnetic resonance imaging (MRI) can help assessing the extent of articular involvement and guide the treatment.
Objectives: To describe clinical and serological features of patients with pSS developing articular involvement along with the MRI findings of affected joints.
Methods: Clinical records were retrospectively evaluated and MRI was performed to evaluate AMs. Disease activity was assessed with the EULAR SS disease activity index (ESSDAI) and its clinical version without the biological domain (ClinESSDAI). Patient-reported symptoms were assessed with the EULAR SS Patient Reported Index (ESSPRI). MRI features were described according to the OMERACT rheumatoid arthritis (RA) MRI scoring system. Values are displayed

as mean ± standard error of the mean or number and percentages. Patients were tested for autoantibodies such as anti-cyclic citrullinated peptide, anti-citrullinated α enolase and anti-carbamylated proteins with commercially available ELISA kits.

Results: 45 pSS patients were included. 29 patients (64%) displayed AMs at pSS onset while 15 (36%) at a later stage (6.7±1 years after pSS diagnosis). Besides AMs, at the time of pSS diagnosis the two cohorts were comparable with regard to other ESSDAI domains. Interestingly, all patients with anti-SSA and anti-/SSB had AMs at the time of pSS diagnosis (p=0.05) while those developing AMs in the disease course were more likely single positive for anti-SSA (p=0.04). When comparing the clinical and serological features of both groups of patients at the time of overt AMs (Tables 1-2), patients that displayed AMs in the course of the disease have a significantly higher ESSPRI compared to patients that display AMs at pSS onset. With regard to MRI, 80% of patients with AM displayed signs of synovitis, 59% bone erosions, 59% joint space narrowing and 50% bone marrow oedema. To note, 60% of patients displaying AMs at pSS onset show bone marrow oedema while this is present in only 27% of patients developing AMs at a later stage (p<0.05). Anti-cyclic citrullinated peptide, anti-citrullinated α enolase, anti-carbamylated proteins were undetectable in all patients.

Conclusion: Our results confirm the relevance of AMs in pSS, particularly because of the high prevalence of RA-like MRI features. MRI assessment in patients with pSS is advisable to identify more severe AMs in the spectrum of pSS disease and guide the therapeutic approach.

Table 1. Clinical and serological features at the time of overt AMs. Categoric variables

	All AMs (N=44)		AMs at pSS onset (n=29)		AMs in the course of disease (N=15)		
	N	%	N	%	N	%	p value
ESSDAI domains							
Constitutional	3	7	3	10	0	0	0.54
Lymphadenopathy	15	34	7	24	8	53	0.09
Glandular	9	20	5	17	4	27	0.46
Articular	44	100	29	100	15	100	na
Cutaneous	6	14	2	7	4	27	0.15
Pulmonary	6	14	5	17	1	7	0.65
Renal	0	0	0	0	0	0	na
Muscular	0	0	0	0	0	0	na
PNS	6	14	4	14	2	13	1
CNS	1	2	0	0	1	7	0.34
Hematological	10	23	8	28	2	13	0.45
Biological	5	11	1	3	4	27	**0.04**
Morning stiffness	44	100	29	100	15	100	na
Small joints	29	66	17	59	12	80	0.31
Large joints	3	7	2	7	1	7	1
Both	12	27	10	34	2	13	0.17

Table 2. Clinical and serological features at the time of overt AMs. Continuous variables

	All AMs (N=44)	AMs at pSS onset (n=29)	AMs in the course of disease (N=15)	p value
	MEAN±SEM	MEAN±SEM	MEAN±SEM	
Years from pSS diagnosis	2.3±0.6	0	6.7±1	na
VAS pain	8.4±0.3	7.7±0.4	9.7±0.15	**0.001**
VAS dryness	7±0.4	5.6±0.5	7.5±0.6	**0.02**
VAS fatigue	6.3±0.4	6.3±0.5	8.5±0.7	**0.02**
ESSPRI	7.2±0.3	6.5±0.4	8.6±0.4	**0.001**
ESSDAI	18±1.6	16.8±1.8	20.2±3	0.32
ClinESSDAI	17.5±1.6	16.4±1.8	19.6±3	0.35
N of involved joints	5.5±4	6.3±0.8	4±0.5	0.06

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FRI0159

EROSIVE ARTHRITIS IN SYSTEMIC LUPUS ERYTHEMATOSUS: APPLICATION OF CLUSTER ANALYSIS

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Background: Systemic Lupus Erythematosus (SLE) related arthritis has been traditionally defined non-erosive and then considered a minor manifestation. Thanks to the application of more sensitive imaging techniques, such as ultrasonography (US), erosive damage has been identified in up to 40% of SLE patients with joint involvement, suggesting the need for more appropriate treatment (1). Antibodies directed against citrullinated and carbamilated proteins (ACPA and anti-CarP, respectively) have been associated with erosive damage and then proposed as biomarkers for this more aggressive phenotype (2).

Objectives: Here, we evaluated a large SLE cohort with joint involvement by using cluster analysis, in order to identify the disease phenotype associated with erosive arthritis.

Methods: For this analysis, we enrolled consecutive SLE patients (ACR 1997 criteria) with a clinical history of joint involvement (arthritis/arthralgia). Clinical and laboratory data were collected in a standardized computerized electronically filled form, including demographics, past medical history with the date of diagnosis, co-morbidities, previous and concomitant treatments, serological status. The presence of rheumatoid factor (RF), ACPA and anti-CarP was investigated by ELISA test. Erosive damage was assessed by ultrasonography at level of metacarpophalangeal, proximal interphalangeal and metatarsophalangeal joints (MyLab Eight Exp, Esaote, Florence, Italy). Data have been analysed by hierarchic cluster analysis (SPSS program, IBM).

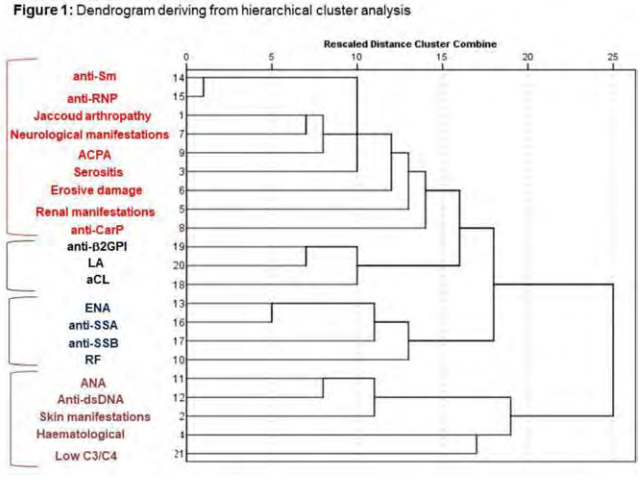
Results: We enrolled 203 patients [M/F 12/191, median age 46.0 years (IQR 18); median disease duration 120.0 months (IQR 108)]. Erosive damage was identified in 53 patients (26.1%), all of them referring at least one episode of arthritis during disease course. Moving on autoantibodies status, RF was positive in 29.5%, anti-CarP in 28.5% and ACPA in 11.2%. The univariate analysis demonstrated a significant association between US-detected erosive damage and anti-CarP (p=0.01), ACPA (p=0.03), and renal manifestations (p=0.03). In Figure 1 we reported the dendrogram obtained from cluster analysis, allowing the identification of four cluster. Positivity for ACPA, anti-CarP, erosive damage, Jaccoud's arthropathy and renal manifestations were allocated in the same cluster. Interestingly, RF resulted allocated in a different cluster, including ENA, anti-SSA and anti-SSB antibodies.

Conclusion: The application of cluster analysis allowed the identification of a specific SLE phenotype, characterized by erosive damage, renal manifestations and positivity for anti-CarP and ACPA. We could speculate about the presence of a shared pathogenic mechanism, involving NETosis, contributing to nephritis and erosive arthritis.

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Figure 1: Dendrogram deriving from hierarchical cluster analysis



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FRI0160

THE CORRELATION BETWEEN PREGNANCY, DISEASE ACTIVITY AND ADVERSE PREGNANCY OUTCOMES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Patients with systemic lupus erythematosus (SLE) can present with acute disease flares/exacerbations during pregnancy and postpartum period.[1] These flares can cause adverse pregnancy outcomes (APO).
Objectives: In this study, our pregnant SLE cohort, which was under medical surveillance of both our Rheumatology and Gynecology and Obstetrics departments was analyzed. We intended to determine the effects of pregnancy on disease activity and the correlation between disease flares and adverse pregnancy outcomes.
Methods: 168 pregnancy data involving 136 patients with SLE meeting the ACR criteria were examined. Cumulative clinical, laboratory and serological parameters were described and disease activity and flares were calculated using SLEDAI-2K disease activity index during preconceptional six month period, during all trimesters of pregnancy, and during postpartum six month period. Patients with low lupus disease activity scores (LLDAS) during each of these periods were identified. Fetal/neonatal death, premature birth due to preeclampsia, eclampsia or HELLP syndrome, neonates small for gestational age were determined as adverse pregnancy outcomes. Relationship of APO with disease activity was studied and patients with APO were compared to patients without APO.
Results: Mean SLEDAI-2K scores was 1.3±2.2 (0-16) during preconceptional six month period, 1.3±2.6 (0-16) during conception period, 1.7±3.2 (0-22) during first trimester, 1.4±2.7 (0-16) during second trimester, 1.5±3.3 (0-20) during third trimester and 3.5±5.4 (0-26) during postpartum six month period. Mean postpartum six month period SLEDAI-2K score was higher compared to the mean pregnancy SLEDAI-2K score ($p<0.05$). LLDAS was sustained in 79% of all pregnancies. 19% of pregnancies resulted in flares. 42% of these flares were severe and 58% were mild or moderate. 49% of severe flares occurred during the postpartum six month period and this percentage was significantly higher compared to each trimester ($p<0.05$). Most of the flares during pregnancy and postpartum period had mucocutaneous (37%), renal(35%) and hematological(25%) involvement.
APO was observed in 34% of pregnancies (n=57). APO (+) group was characterized by significantly longer disease duration and higher disease activity in all periods compared to APO (-) group (142±70 vs 170±88 months, $p<0.05$). In APO (-) group, the proportion of patients with severe disease activity during all pregnancy periods and postpartum period was significantly low (%18 vs 35, $p<0.05$), while the proportion of patients with sustained LLDAS was much higher (%88 vs 70).
Conclusion: Postpartum six-month period appears to have the highest risk for disease flares during SLE pregnancies. Disease activity during pregnancy increases the risk of APO. Patients with sustained LLDAS have significantly lower APO rates. In order to achieve a positive pregnancy outcome and lower maternal morbidity, regular follow up of patients during pregnancy and postpartum period by Rheumatology and Gynecology and Obstetrics Departments is necessary.
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FRI0161

PHENOTYPIC DIFFERENCES BETWEEN SJÖGREN'S SYNDROME PATIENTS WITH LOW AND HIGH-GRADE INFLAMMATION BASED ON SALIVARY GLAND FOCUS SCORE

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Background: Sjögren's syndrome (SS) is characterized by the presence of lymphocytic infiltration around the ductal epithelium of the salivary and lachrymal glands. The periepithelial inflammatory lesions and the enclosed B cell component are responsible for the glandular and extraglandular manifestations of the disease. Previous studies have shown that the severity of inflammation observed within the salivary glands is correlated with the occurrence of extraglandular manifestations. However, in these studies either the number of patients is small or the SS criteria are not well defined. To explore the association between the degree of inflammation within the salivary glands and the phenotype of the disease, large and well characterized cohorts of SS patients is required.
Objectives: To compare the phenotypic features of SS patients with low and high degree of inflammation within the minor salivary glands as reflected by the focus score (FS).
Methods: From a total cohort of 1723 consecutive SS patients who fulfill the 2016 EULAR/ACR criteria and are followed up in 4 clinical centers ([Universities of **P**isa, **A**thens, **H**arokopio and **I**oannina, (**PAHI**)], those who had performed a lip biopsy and the focused score was available, were classified into low grade (FS<3) or high grade (FS≥3). Glandular (dry mouth, dry eyes, parotid gland enlargement) and extra-glandular manifestations (Raynaud's phenomenon, arthralgias/myalgias, arthritis, palpable purpura, liver involvement, kidney involvement, lung involvement, neurologic involvement, long standing lymphadenopathy and lymphoma) as well as serologic features (ANA, RF, anti-Ro/SSA, anti-La/SSB) were compared between the 2 groups. Statistical analysis for categorical variables was performed by Fisher exact or chi-square tests and for continuous variables with t test or Mann-Whitney accordingly.
Results: Eight hundred and eight minor salivary gland biopsies were available and evaluated based on focus score at the initial evaluation of SS patients, of whom 753 had low grade (FS<3) and 153 high grade (≥3) inflammation. The median disease duration after SS diagnosis was not statistically significant different for the 2 groups (median: 4 years, range: 0-36 years). SS patients with high grade inflammation displayed higher prevalence of salivary gland enlargement (SGE) (40% vs 25%, p=0,0002), long standing lymphadenopathy (22% vs 14%, p=0,02), ANA (97% vs 88%, p=0,0001), anti-La/SSB (52% vs 32%, p<0,0001), RF (61,5% vs 48%, p=0,003), peripheral neuropathy (PN) (5,3% vs 1,5, p=0,01) and of lymphoma (26% vs 8%, p<0,0001, OR=4,142, 95%CI=2,65 to 6,47) compared to those with low grade inflammation.
Conclusion: SS patients with FS ≥3 at the initial evaluation, display higher prevalence of lymphoma as well as higher B cell hyperactivity and certain clinical manifestations (SGE, PNS, lymphadenopathy) that constitute risk factors for lymphoma development.
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FRI0162

COMPARISON OF MUSCULOSKELETAL INVOLVEMENT OF WRIST AND HAND BY MRI IN TWO SYSTEMIC LUPUS ERYTHEMATOSUS GROUPS: HAND ARTHRITIS AND HAND ARTHRALGIA

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Background: Articular involvement can reach up to 95% within the multisystemic manifestations of SLE. Originally, a non-erosive pattern of articular inflammation was described, but the emergence of more sensitive imaging techniques, such as Magnetic Resonance Imaging (MRI), show synovitis (S), erosions (E), bone marrow edema (BME) and tenosynovitis (TS) in patients with systemic lupus erythematosus (SLE). Nowadays, a specific validated pattern of articular involvement associated with this disease does not yet exist, although it has begun to be studied (1,2).

Objectives: To asses the extent of structural joint involvement in proximal interphalangeal joints (PIP), hand and wrist: E, BME, S, TS and peritendinitis (PT) by MRI, in patients diagnosed with SLE with hand arthritis or arthralgia.
Methods: All patients with SLE who manifested hand pain and/or swelling in the prior 6 months were consecutively included in the study. They were divided into two groups: arthritis or arthralgia, according to the physical examination by an expert rheumatologist. All patients underwent an MRI with contrast injection on their non-dominant hand. The images obtained were evaluated following RAMRIS criteria extended to PIP and Tenosinovitys score for RA by two expert musculoskeletal radiologists, blind to the groups.
Results: 32 patients were included: arthritis: n = 13, arthralgia: n = 19, with a mean age of 50.91 ± 13.37 years and a disease evolution time of 10.21 ± 8.26 years. The average SLEDAI score 6.30 ± 3.40 for the arthritis groups and 3.79 ± 2.14 for the arthralgia group. The average SLICC score was 0.23 ± 0.42 in the arthritis group and 0.1 ± 0.31 in the arthralgia group. E was found in 7 patients with arthritis (53.84%) (15.38% in PIP, 0% in hand and 53.84% in wrist) and in 13 patients with arthralgia (68.42%) (0% in PIP, 10.52% in hand and 68.42% in wrist). BME was observed in 4 patients with arthritis (30.76%) (7.69% in PIP, 0% in hand and 30.76% in wrist) and in 5 patients with arthralgia (26.31%) (5.26% in PIP, 10, 52% in hand and 15.78% in wrist). S was observed in 12 patients with arthritis (92.30%) (61.58 in PIP, 76.92% in hand and 84.61% in wrist) and in 8 patients with arthralgia (42.10%) (31.57% in PIP, 36.84% in hand and 36.84% in wrist). TS was observed in 6 patients with arthritis (46.15%) (38.46% in flexor tendons and 23.07% in extensor tendons) and in 8 patients with arthralgia (42.10%) (31.57% in flexor tendons and 21.05 % in extensor tendons). PT was found in 6 patients with arthritis (23.07%) and in no patient with arthralgia (0%)
Conclusion: MRI allows us to diagnose musculoskeletal involvement in SLE, morphologically similar to rheumatoid arthritis (erosion, bone marrow edema, synovitis and tenosynovitis), which usually are underestimated on plain radiography. This study also shows the important erosive burden of arthritis in SLE, which has not been well characterised yet. In addition, it demonstrates the underestimation of physical examination to diagnose active inflammatory damage, such as subclinical synovitis, in patients with inflammatory arthralgias.
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FRI0163 ANTIPHOSPHOLIPID PATTERNS PREDICT THE RISK OF THROMBOSIS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: It is well known that Lupus anticoagulant (LAC) positivity is more strongly associated with both arterial and venous thrombosis than either anticardiolipin (aCL) or anti-β2glycoprotein (aB2GPI) antibodies (1). An unanswered question is the contribution of which combinations of positive aPLs to thrombosis risk.
Objectives: We aimed to evaluate which aPL combinations increase the risk of future thrombosis in patients with Systemic Lupus Erythematosus (SLE).
Methods: This prospective analysis included SLE patients who had been tested for all 3 aPLs in Hopkins Lupus Cohort. We constructed a dataset with one record per month of follow up for each patient. Rates of thrombosis for each aPL or each combination of aPL were calculated as the number of thromboses divided by the number of person months at risk and the results are converted to rates per 1000 person-years.
Results: There were 805 patients with a complete profile of 7 aPLs with a total of 73417 person months of follow up. LAC was the most predictive of any [3.47 (1.96, 6.14) p<0.0001], venous [4.3 (1.99, 9.25) p=0.0002], and arterial [3.37 (1.51, 7.53) p= 0.0029] thrombosis. In individual models, aB2GPI positivity was a significant risk factor for any [1.90 (1.16, 3.13) p=0.0113] and venous [2.3(1.23, 4.61) p=0.0103] thrombosis. When we looked at patients who were LAC positive, and asked if having another positive aPL increase the risk ratio for any/venous/arterial thrombosis, we found that having aB2GPI IgA appeared to add significant risk to any [1.68 (1.01, 2.79) p=0.044], and venous [2.01 (1.02, 3.97) p=0.043] thrombosis among those with or without LAC (Table 1).

Table 1. Additive effect of other aPLs adjusting for LAC

	ANY thrombosis		VENOUS thrombosis		ARTERIAL thrombosis	
	age adjusted RR 95%(CI)	P-value	age adjusted RR 95%(CI)	p-value	age adjusted RR 95%(CI)	p-value
Model 1: LAC + aCL-G						
LAC (+) vs (-)	3.78 (2.08, 6.85)	<.0001	5.03 (2.25, 11.24)	<.0001	3.32 (1.43, 7.73)	0.0053
aCL-G (+) vs (-)	0.64 (0.22, 1.83)	0.4045	0.48 (0.11, 2.14)	0.3351	1.09 (0.31, 3.77)	0.8962
Model 2: LAC + aCL-M						
LAC (+) vs (-)	3.82 (2.13, 6.87)	<0.0001	4.57 (2.07, 10.08)	0.0002	3.69 (1.61, 8.46)	0.0021
aCL-M (+) vs (-)	0.51 (0.16, 1.65)	0.2576	0.68 (0.16, 2.93)	0.6019	0.61 (0.14, 2.64)	0.5075
Model 3: LAC+ aCL-A						
LAC (+) vs (-)	3.34 (1.88, 5.96)	0.0001	4.14 (1.9, 9)	0.0003	3.29 (1.47, 7.38)	0.0038
aCL-A (+) vs (-)	2.33 (0.56, 9.70)	0.2459	2.44 (0.32, 18.4)	0.3858	2.2 (0.29, 16.49)	0.4415
Model 4: LAC+ aB2GPI-G						
LAC (+) vs (-)	3.52 (1.94, 6.39)	0.0001	4.21 (1.85, 9.57)	0.0006	3.4 (1.48, 7.79)	0.0038
aB2GPI-G (+) vs (-)	0.91 (0.32, 2.61)	0.8655	1.1 (0.31, 3.88)	0.8849	0.96 (0.22, 4.18)	0.957
Model 5: LAC+ aB2GPI-M						
LAC (+) vs (-)	3.53 (1.97, 6.31)	0.0021	4.17 (1.9, 9.14)	0.0004	3.58 (1.58, 8.1)	0.0023
aB2GPI-M (+) vs (-)	0.91 (0.49, 1.73)	0.7782	1.17 (0.51, 2.68)	0.7101	0.74 (0.29, 1.9)	0.5285
Model 6: LAC+ aB2GPI-A						
LAC (+) vs (-)	3.16 (1.77, 5.65)	0.0001	3.68 (1.68, 8.08)	0.0012	3.19 (1.41, 7.2)	0.0052
aB2GPI-A (+) vs (-)	1.68 (1.01, 2.79)	0.0441	2.01 (1.02, 3.97)	0.0434	1.4 (0.67, 2.91)	0.3738

Conclusion: Our study shows that LAC is still the best predictor of risk of any, arterial and venous thrombosis in SLE. Moreover, aB2GPI IgA positivity appeared to add also a significant risk to any and venous thrombosis. Therefore, the clinical significance of IgA anti-β2GPI deserves further investigation in SLE patients.
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FRI0164 BANFF INFLAMMATORY INDICES MAY BE SUPERIOR TO THE NIH SCORING IN PREDICTING CKD PROGRESSION IN LUPUS NEPHRITIS

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Background: Chronic kidney disease/end stage renal disease (CKD/ESRD) from lupus nephritis (LN) is a major cause of morbidity and mortality.

Advanced tubulointerstitial disease (TID) in LN is a better predicor of renal outcome than glomerular lesions. The current NIH classification is heavily weighted towards glomerular lesions and only provides a semiqualitative assessment of TID. In contrast, Banff classification of renal allograft pathology provides 6 reproducible scores for TID (inflammation, fibrosis, atrophy). Banff scoring may better predict CKD/ESRD in LN than NIH scores

Objectives: We compared Banff grading vs. NIH scoring as predictors of CKD progression at 5 years, defined as a decline in estimated glomerular filtration rate (eGFR) ≥30%, a strong risk factor for ESRD and mortality

Methods: We included patients with LN class III, IV, V on the index biopsy Jan 2005 and Dec 2018. H&E/PAS stained slides were reviewed and scored by an experienced pathologist. Six TID Banff scores (0/1 vs. 2/3), NIH activity/chronicity (AI/CI) and NIH interstitial fibrosis/tubular atrophy (IF/TA), tubulointerstitial inflammation (TII) scores (none/mild vs. moderate/severe) were evaluated as predictors of CKD progression using survival analyses

Results: Of the 125 patients, 46 had CKD progression and 20 subsequently developed ESRD. There were no differences between progressors and non-progressors in terms of baseline demographic, clinical data, LN class (Tab 1). Banff ti score (total inflammation) was associated with CKD progression in bivariate and time-dependent analyses. However, NIH TII score and corresponding Banff i score were not predictive (Tab 2, Fig 1). Overall NIH AI and CI were not predictive of CKD progression. Moderate/severe NIH IF/TA was associated with CKD progression as was Banff ci (interstitial fibrosis) score (Tab 2, Fig 2). Banff score for atrophy was not predictive. In a subset of 92 patients with baseline eGFR≥60ml/min/1.73m^2 only Banff ti score (but not i score or NIH TII, IF/TA) was predictive of CKD progression (Fig 1)

Table 1. Baseline data in patients with/without CKD progression

	Progressors[1] n=46	Non-progressors n=79	p
n (%) or median (IQR)			
Female	36 (78)	69 (87)	0.18
Age (years)	26 (20-41)	29 (21-43)	0.53
<18 years	7 (15)	13 (16)	0.86
Race			0.82
White	4 (9)	4 (5)	
Black	18 (39)	35 (44)	
Asian	1 (2)	1 (1)	
Unknown	23 (50)	39 (50)	
Diabetes	5 (11)	3 (4)	0.12
Hypertension	33 (72)	55 (70)	0.8
eGFR ml/min/1.73m^2	96.1 (56.6-117.8)	88.9 (47-117)	0.51
C3 mg/dL	71 (52-88)	67.5 (43-94)	0.58
C4 mg/dL	12.65 (9-23)	12 (7-20)	0.48
Anti-ds DNA titer IU	108.7 (36.6-194.9)	151.3 (39.2-200)	0.57
Total SLEDAI	11 (8-16)	12 (8-16)	0.47
Renal SLEDAI	8 (4-12)	8 (4-12)	0.9
LN			
Proliferative GN[2]: III, IV	18 (39)	30 (38)	0.15
Nonproliferative GN: V	9 (20)	27 (34)	
Mixed GN: V and III/IV	19 (41)	22 (28)	

[1] Progressors: LN patients with eGFR decline ≥30% within 5 years. [2] GN: glomerulonephritis

Table 2. NIH and Banff scores with/without progressors

	Progressors n=46	Non-progressors n=79	p
n (%) or median (IQR)			
NIH			
Overall AI	1 (0-4)	1 (0-3)	0.61
AI ≥ 11	1 (2)	3 (3.8)	0.62
Overall CI	3 (0-5)	2 (0-3)	0.33
CI ≥ 3	24 (52)	28 (35.4)	0.07
Moderate/severe TII	7 (15.2)	4 (5)	0.05
Moderate/severe IF/TA	16 (35)	15 (19)	0.049
Banff			
Tubulitis: t	0	0	
Interstitial inflammation: i 2/3	3 (6.5)	5 (6.3)	0.9
Total inflammation: ti 2/3	16 (34.8)	12 (15.2)	0.01
Tubular atrophy: ct 2/3	16 (34.8)	16 (20.3)	0.07
Interstitial fibrosis: ci 2/3	17 (37)	15 (19)	0.03
Inflammation in area of interstitial fibrosis and/or tubular atrophy: i-IFTA 2/3	n=26* 18 (69)	n=51* 25 (49)	0.09

* Biopsy number is smaller due to inability to apply score to biopsies without areas of fibrosis/tubular atrophy

Figure 1: Association of NIH and Banff inflammation scores with ESRD progression

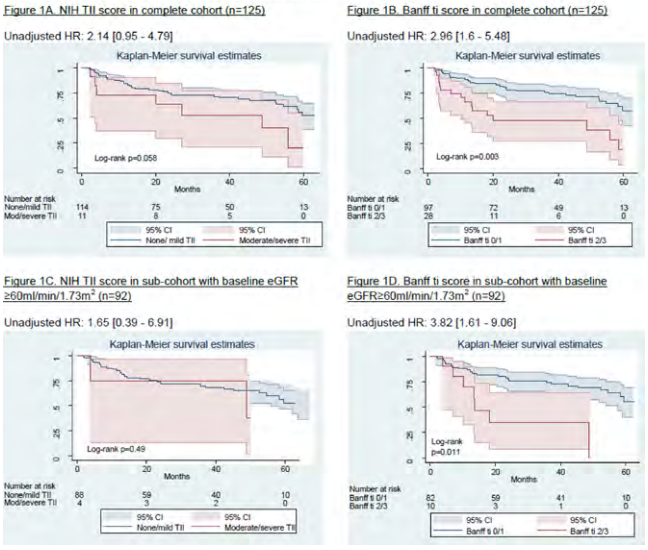
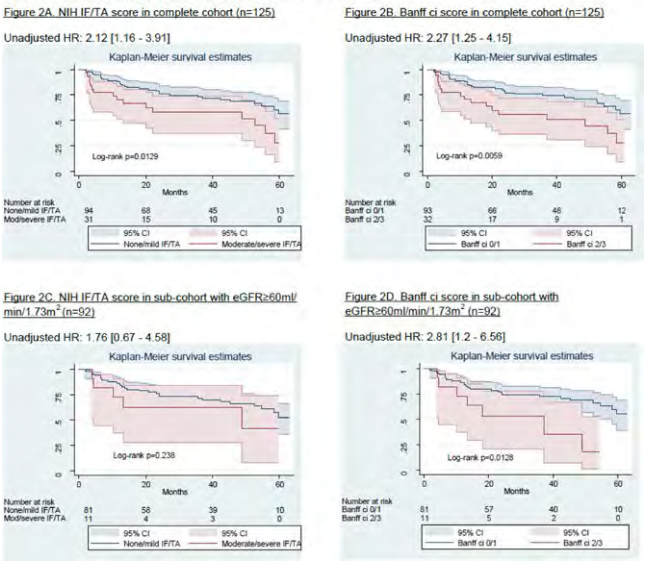


Figure 2: Association of NIH and Banff fibrosis scores with ESRD progression



Conclusion: Banff inflammation scores may be superior predictors of CKD/ESRD progression at 5 years, compared to the currently used NIH classification. Detection of inflammation by Banff scores may allow earlier interventions to prevent ESRD

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FRI0165 RISK OF CKD IN MEMBRANOUS AND PROLIFERATIVE LUPUS NEPHRITIS - ANALYSIS OF A NATIONWIDE MULTICENTRE COHORT

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Background: Lupus nephritis (LN) is one of the most severe manifestations of Systemic Lupus Erythematosus.

Objectives: 1) To compare proliferative (PLN), membranous (MLN) and mixed LN regarding clinical and laboratory presentation. 2) To investigate predictors of progression to chronic kidney disease (CKD).

Methods: Multicentre observational study, with retrospective analysis of a prospective cohort, using data from the Portuguese registry of rheumatic diseases – Reuma.pt. Patients with biopsy-proven PLN, MLN and mixed LN were included. Groups were compared using Pearson's Chi-Square for categorical variables and One-Way ANOVA or Kruskal-Wallis for numerical variables. COX regression analysis was used to investigate predictors of CKD (defined as estimated glomerular filtration rate [eGFR] lower than 60 mL/min/1.73m^2 for at least 3 months) and Kaplan-Meier curves were drawn.

Results: 236 patients were included. Median follow-up was 8 years (IQR 11; maximum 35 years). As seen in table 1, the level of proteinuria did not differ between groups; however, MLN patients presented with significantly lower serum creatinine. Levels of complement C3 and C4 were reduced in PLN but normal in MLN patients, and there were fewer patients with positive anti-dsDNA antibodies in the MLN group (p<0.001). On univariable COX regression, mixed histology was associated with progression to CKD (HR 26 [95% CI 3 - 255], p 0.005) (figure 1), however, it lost significance after adjusting for eGFR. In fact, eGFR≤75 at one year after the renal biopsy (HR 21 [95% CI 7 - 65], p<0.001) was the strongest predictor of CKD, even after adjusting for hypertension or histology.

Table 1. Comparative description of the Reuma.pt cohort of patients with proliferative, membranous and mixed LN

	PLN	MLN	Mixed	P
Total, N	186	42	8	
Females, N (%)	157 (85)	39 (95)	4 (50)	0.004
Ethnicity White European, N (%)	163 (90)	31 (78)	7 (88)	0.115
Other, N (%)	19 (10)	9 (23)	1 (13)	
Age LN diagnosis(y), median (IQR)	30 (20)	34 (16)	42 (25)	0.409
SLEDAI at LN diagnosis, median (IQR)	16 (9)	10 (10)	21 (17)	0.006*
uPCR at LN diagnosis, median (IQR)	1675 (2598)	1698 (2153)	2160 (3320)	0.629
Creatinine at LN diagnosis, median (IQR)	0.80 (0.32)	0.70 (0.20)	1.00 (0.95)	0.006*
eGFR at LN diagnosis, mean ± SD	98 ± 33	112 ± 17	82 ± 45	0.019*
Albumin at LN diagnosis, mean ± SD	34 ± 7	34 ± 7	30 ± 6	0.390
C3 at LN diagnosis, mean ± SD	0.65 ± 0.26	0.90 ± 0.35	0.53 ± 0.30	<0.001*
Positive anti-dsDNA LN diagnosis, N (%)	115 (91)	11 (48)	6 (86)	<0.001*
Use of antimalarials, N (%)	166 (94)	36 (92)	8 (100)	0.688
Use of immunosuppressants, N (%)	163 (94)	33 (87)	8 (100)	0.245
Use of corticosteroids, N (%)	145 (84)	33 (85)	7 (100)	0.511
CKD after LN diagnosis, N (%)	27 (15)	1 (3)	3 (38)	0.018*
ESRD, N (%)	7 (4)	1 (3)	2 (25)	0.016
Deaths, N (%)	14 (8)	2 (5)	0	0.610

uPCR: urinary protein-creatinine ratio, mg/g; y: years; Creatinine presented in mg/dL, eGFR in mL/min/1.73m^2; albumin in g/L and C3 in g/L
Note: Baseline data (LN diagnosis) in grey; other data refer to the course of disease
*Significant difference between the proliferative and membranous groups

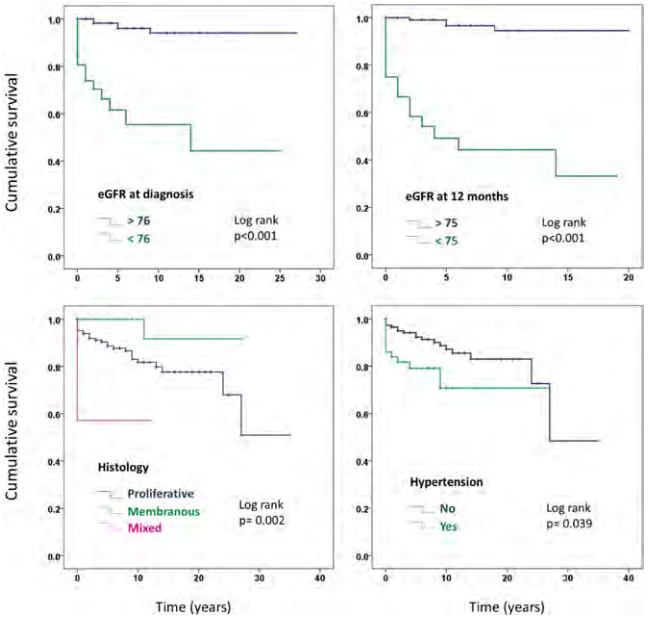


Figure 1. Kaplan-Meir curves showing cumulative survival free of CKD in patients with PLN, MLN and mixed LN

Conclusion: Our results support previous findings from single-centre studies suggesting that MLN has a different serological profile than PLN, possibly reflecting different pathogenesis. Renal function at one year predicts long-term outcome in LN.

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FRI0166 HIGH FREQUENCY OF KIDNEY STONES AND/OR NEPHROCALCINOSIS IN PRIMARY SJOGREN'S SYNDROME MIGHT ACCELERATE CHRONIC RENAL DYSFUNCTION DUE TO TUBULOINTERSTITIAL DISEASE

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Background: The renal involvement of primary Sjögren's syndrome (pSS) is characterized by distal renal tubular acidosis (RTA), tubulointerstitial nephritis (TIN), and/or glomerulonephritis [1,2]. Kidney stones and nephrocalcinosis are presumably caused by subclinical distal tubular acidosis, but its clinical significance has not been clarified.

Objectives: This study aimed to clarify the frequency and clinical features of patients with pSS with kidney stones and/or nephrocalcinosis.

Methods: We examined 59 patients with anti SS-A/Ro positive pSS who underwent abdominal computed tomography and/or ultrasound between 1998 and 2019 at Kanazawa University Hospital. We identified 2 groups of patients with primary Sjögren's syndrome: 1) patients with kidney stones and/or nephrocalcinosis (group A: n=19) and 2) those without kidney stones and/or nephrocalcinosis (group B: n=40), and retrospectively analyzed their clinical features.

Results: Kidney stones and/or nephrocalcinosis were confirmed in 19 of 59 (32%) patients with pSS. The patients comprised 4 males and 55 females with an average age of 60 years (range, 30 to 83 years) and mean observation period of 96 months (range 1 to 336 months). Estimated glomerular filtration rate (eGFR) at the time of diagnostic imaging (group A vs group B: 71.5 ml/min/1.73 m^2 vs 82.8 ml/min/1.73 m^2; p=0.37) and eGFR at last follow up (group A vs group B: 59.3 ml/min/1.73 m^2 vs 74.7 ml/min/1.73 m^2;p=0.03) of group A were lower than those of group B and urinary β2-microgloblin (group A vs group B: 7222 μg/mL vs 437 μg/mL; p=0.01) and urinary N-acetyl-β-D-glucosaminidase (group A vs group B: 5.8 U/L vs 3.9 U/L; p=0.22) of group A were higher than those of group B, while serum electrolytes (sodium, potassium, chloride, calcium, phosphorus), fractional excretion of calcium (group A vs group B: 1.2% vs1.5%; p=0.916), ESSDAI (group A vs group B: 7.6 vs 4.3; p=0.069), and eGFR decrease rate were not significantly different.

Conclusion: 32% patients with anti SS-A/Ro positive pSS had kidney stones and/or nephrocalcinosis in our cohort and their presence might accelerate chronic renal dysfunction due to tubulointerstitial disease (subclinical RTA or TIN).

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FRI0167 LONG TERM CLINICAL OUTCOME IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS FOLLOWED FOR MORE THAN 20 YEARS IN THREE ITALIAN TERTIARY REFERRAL CENTERS: THE MILAN SYSTEMIC LUPUS ERYTHEMATOSUS CONSORTIUM (SMILE) COHORT

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Background: the prognosis of Systemic lupus Erythematosus (SLE) patients has significantly improved over time, raising the need for more data about disease activity and damage accrual in the long term.

Objectives: to investigate the risk of long term disease activity and to identify viable prognostic markers for disease flares in SLE patients with long standing disease

Methods: data on SLE patients regularly followed at ASST PINI-CTO, Fondazione Ca' Granda Policlinico and Ospedale San Raffaele, Milan (Milan Systemic Lupus Erythematosus Consortium, SMiLE, cohort) with disease duration ≥ 20 years, were retrospectively analyzed. Organ involvement as per the British Isles Lupus Assessment Group (BILAG) definitions was recorded along with achievement of clinical and complete remission (CR and CCR: clinical SLEDAI =0, PGA <0.5 and no prednisone or immunosuppression ± negative serology) and lupus low disease activity state (LLDAS) at 15 (T15) and 20 (T20) years of follow up. Damage accrual was estimated according to the SLE International Collaborating Clinics/American College of Rheumatology damage index (SDI).

Results: data from 168 patients (table 1) were available for analysis. Remission (CR+CCR) and LLDAS were achieved in 22% and 61% at T15 and 25% and 71% at T20. LLDAS was not associated with a history of involvement in any BILAG domain, but it was inversely associated with treatment with mycophenolate at any time (50 vs 23% treated vs not treated; p=0.02). SDI>0 was found in 49% patients at T15 and in 71% at T20. LLDAS at T15 was associated with lower flare rates in the following five years (HR= 0.395, 95%, CI=0.239-0.653; Figure, left panel; p<0.001). The risk of flaring for LLDAS was largely comparable to CCR and CR (Figure, middle panel). In the T15-T20 timeframe, 37% of patients had a flare. Patients with both low complement and anti-dsDNA positivity at T15 had an increased risk of flaring compared to serologically inactive patients (HR=2.86, 95%, CI=1.572-5.19; Figure right panel). Flaring patients were more likely to show an increase in SDI from T15 to T20 (37% vs 9% in patients with stable SDI; p<0.001)

Table 1. Demographic, laboratory and clinical characteristics of patients with SLE

Characteristics	(n=168)
Demographic characteristics	
Female, n (%)	150 (89.3)
Age at diagnosis years, median (IQR)	24 (18-32)
Clinical and serological features during 15 years follow up, n (%)	
Musculoskeletal	140 (83)
Mucocutaneous	135 (80)
Constitutional	114 (68)
Haematological	103 (61)
Nephritis	81 (48)
Cardiopulmonary	49 (29)
NPSLE	31 (18)
Positive anti-dsDNA	136 (81)
Hypocomplementemia	136 (81)
Positive antiphospholipid	73 (44)
CR / CCR at T15	13 (8) / 23 (14)
CR / CCR at T20	17 (10) / 25 (15)

Conclusion: LLDAS is common in SLE patients with long disease duration although up to 37% of patients with 15-year disease duration may experience a flare during the following 5 years. The flare risk increases with failure to attain LLDAS at T15 and with active serology. Late flares associate with damage accrual.

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Table 2. therapy during the 20 year follow up

Therapy (ever)	%
Prednisone	83
Hydroxychloroquine	91
Mycophenolate mofetil	33
Azathioprine	50
Methotrexate	23
Cyclophosphamide	36

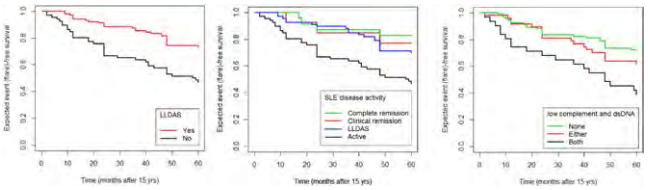


Fig 1: risk of flare according to disease activity

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FRI0168

ASSOCIATION OF OVERWEIGHT/OBESITY WITH IMPAIRED HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Patients with systemic lupus erythematosus (SLE) experience a considerably impaired health-related quality of life (HRQoL) compared with the general population. Previous literature has implied an association between high body mass index (BMI) and HRQoL diminutions. However, data are scarce and further exploration in large study populations and, importantly, with regard to the clinical significance of this association is needed.

Objectives: The aim of this study was to determine whether overweight and/or obesity were associated with impaired physical and/or mental HRQoL aspects in the SLE population of two large clinical trials.

Methods: We utilised pooled baseline data from the BLISS-52 (NCT00424476) and BLISS-76 (NCT00410384) clinical trials of belimumab (N=1684). Access to data was granted by GlaxoSmithKline. The patients were stratified into four groups based on their body mass index (BMI), according to WHO guidelines. We conducted comparisons between non-overweight versus overweight, and non-obese versus obese SLE patients. HRQoL was self-reported using the Medical Outcomes Study (MOS) short form 36 (SF-36) health survey, the functional assessment of chronic illness therapy (FACIT)-Fatigue scale and the three-level EuroQol- 5 Dimension (EQ-5D) questionnaire. We explored whether the differences in scores were clinically meaningful using previously determined thresholds for minimal clinically important differences (MCIDs). The non-parametric Mann-Whitney U test was used for comparisons between different BMI groups. Linear regression analysis was next applied to test independence in multivariable models, adjusting for age, sex, ethnicity, disease duration, disease activity, organ damage and standard of care treatment.

Results: Forty-four per cent (44%) of the patients had a BMI score over the normal range, and 18% were obese. The overweight group performed worse than the non-overweight with regard to FACIT-Fatigue scores (mean ± standard deviation: 27.7 ± 12.1 vs 32.0 ± 11.3; P<0.001), EQ-5D score (0.70 ± 0.19 vs 0.76 ± 0.18; P<0.001) and all SF-36 subscales and component summaries. The differences were greater than the MCIDs for physical component summary (PCS) scores (36.9 ± 9.3 vs 40.8 ± 9.6; P<0.001), physical functioning (53.3 ± 25.1 vs 63.6 ± 25-1; P<0.001), role physical (48.0 ± 27.1 vs 55.6 ± 26.9; P<0.001), bodily pain (43.8 ± 22.4 vs 52.5 ± 25.1; P<0.001), vitality (39.6 ± 21.7 vs 46.6 ± 21.3; P<0.001), and social functioning scores (55.8 ± 25.2 vs 62.6 ± 25.2; P<0.001). Likewise, obese patients reported worse FACIT-Fatigue scores (25.7 ± 11.9 vs 31.1 ± 11.6; P<0.001), EQ-5D scores (0.68 ± 0.20 vs 0.75 ± 0.18; P<0.001) and clinically important diminutions of HRQoL in all SF-36 items, except for the mental component summary (MCS), role emotional and mental health.

In multivariable linear regression analysis, the overweight and obese group showed worse PCS scores (standardised coefficient: β=-0.09; P<0.001 and β=-0.13; P<0.001, respectively) and FACIT-Fatigue scores (β=-0.11; P<0.001 and β=-0.10; P<0.001, respectively), and overweight patients had significantly impaired MCS scores (β=-0.05; P=0.039), irrespective of other factors. High

disease activity and organ damage were associated with impaired HRQoL in all aspects, while Asian patients reported better PCS scores (and β=0.29; P=0.007) and FACIT-Fatigue scores (β=0.33; P=0.002).

Conclusion: BMI above normal was highly associated with HRQoL impairment, especially in physical aspects. Further survey to examine causality is warranted to support structured weight control strategies as an intervention towards a more favourable HRQoL.

Disclosure of Interests: None declared

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FRI0169 ANTINUCLEAR ANTIBODY SEROCONVERSION DURING FOLLOW-UP IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by the presence of autoantibodies and a variable spectrum of clinical manifestations and disease severity. The 2019 criteria for SLE classification by the American College of Rheumatology and European League against Rheumatism define ANA positivity by immunofluorescence or by an equivalent solid-phase assay as the entry criterion (1). However, the prevalence of ANA positivity and the reliability of solid-phase assays in SLE are still a matter of controversy (2). Furthermore, the significance of ANA negativisation during follow-up is uncertain (3).

Objectives: Our aim was to retrospectively analyse data on the frequency of ANA seroconversion during the follow-up in a cohort of SLE patients with renal involvement.

Methods: Adult patients independent of age at SLE onset with a follow-up duration of at least 36 months starting from January 2009 (for standardization of ANA measurement) and with at least one ANA measurement per year were included in this retrospective longitudinal study. Data on demographic, clinical and laboratory characteristics of the study population are reported in table 1. ANA have been measured with Hep2 cell immunofluorescence assay.

Table 1. Demographic, clinical and laboratory baseline characteristics of the 121 patients suffering from systemic lupus erythematosus (SLE).

Demographics	
Gender, *%F (n)*	93 (112)
Age in years, *mean±SD*	41.6±12.6
Clinical features	
Age at SLE onset in years, *mean±SD*	28.0±11.9
SLE duration in years, *mean±SD*	13.8±9.5
SLEDAI, *median (min-max)*	4 (0 – 27)
Laboratory profile	
Serum creatinine mg/dL, *median (min-max)*	0.8 (0.4 – 2)
24h urine protein g/24h, *median (min-max)*	0.5 (0 – 13.8)
ANA, *%pos (n)*	93 (112)
Anti-ENA, *%pos (n)*	49 (59)
Anti-dsDNA, *%pos (n)*	43 (51)

Results: A total of 121 SLE subjects with renal involvement were enrolled. Mean follow-up ± standard deviation (SD) was 8 ± 2 years. Ten subjects (8.3%) with positive ANA at the beginning resulted ANA negative at the end of the follow-up. These subjects had different initial ANA titres: 1:1280 (n=1), 1:640 (n=2), 1:320 (n=2), 1:160 (n=3) and 1:80 (n=2); 48 subjects (39.7%) showed a decrease in ANA titre. Of the 9 patients (7.4%) that were negative at the beginning of follow-up, 6 remained negative, whereas 3 showed ANA positivity at the end of the follow-up with ANA titres 1:160 (n=2) and 1:320 (n=1). No differences between subjects with and without ANA titre variations in terms of age (p=0.551), disease duration (p=0.786), SLEDAI at the beginning (p=0.453) and at the end of follow-up (p=0.169) were observed. ANA negativisation and titre variations at the end of follow-up did not correlate with any of the treatments taken during follow-up, including a history of cyclophosphamide (p=0.788).

Conclusion: In our cohort of patients with SLE and renal involvement, 10% of patients experienced negativisation and around 40% of patients showed a decrease in ANA titre during follow-up, independent of disease characteristics and previous treatment. Further studies are warranted to clarify the underlying mechanisms and clinical significance of ANA seroconversion and titre variation in SLE patients. However, based on our results, ANA positivity seems to be a relatively stable parameter further supporting its use as an entry classification criterion for SLE.

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FRI0170 THERAPEUTIC TARGETS AND QUALITY INDICATORS IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE), DEFINED ACCORDING TO THE 2019 UPDATE OF THE EULAR RECOMMENDATIONS: DATA FROM THE "ATTIKON" LUPUS COHORT

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Background: Targets of therapy and quality of care are receiving increased attention in the management of SLE, as outlined in the 2019 update of the EULAR recommendations for SLE treatment.

Objectives: To assess compliance with quality indicators and attainment of treatment targets, according to recent EULAR recommendations, in the SLE cohort of "Attikon" Rheumatology Unit.

Methods: 100 consecutive SLE patients followed for at least one year were. A 30 item Quality Indicator Set (QIS) was developed, according to the 2019 EULAR recommendations for SLE, to include laboratory tests for diagnosis and monitoring, evaluation of disease activity and damage using validated indices, use of patient-reported outcomes, counselling for women's health and reproduction issues, attainment of targets of therapy [remission or low disease activity state (LLDAS) with low-dose glucocorticoids (GC, ≤7.5mg/day prednizone) and hydroxychloroquine (HCQ dose≤5mg/kg/day)], prevention of disease flares and prevention and management of co-morbidities. Chart review and patient interview was performed to assess the degree of compliance with each item of the QIS and achievement of treatment targets.

Results: Disease activity was monitored by means of validated indices in 31% and antiphospholipid antibody testing during the first 6 months from diagnosis was performed in 58.8% of patients. Sustained remission (defined as remission of a sustained period of 12 months) or LLDAS was achieved by only 3% and 22% respectively; in contrast, other targets of therapy, such as ≤1 minor flares during last year, were achieved by 85% (43% had complete absence of flares), with 90.2% of patients receiving low-dose GC and 81.8% corrected HCQ dose. Fertility and pregnancy counselling were offered in 40% (12/30 eligible women) and 63.3% (19/30) of patients, respectively, while 65.4% had a Pap Test and only 3 of 32 eligible patients had received the HPV vaccine. Annual lipid status was assessed in 43% and counselling for smoking cessation in 44.6%. Flu vaccination was performed in 77%, while pneumococcal (including both of the pneumococcal vaccines) and herpes-zoster vaccination, were given in 32.7% and 2% (1/44 eligible patients) respectively.

Conclusion: Our real-life data suggest low vaccination rates (excluding flu) and suboptimal management of cardiovascular risk factors in lupus patients. While the majority of patients received the suggested doses of GC and HCQ, only one quarter of patients achieved remission or LLDAS. There is an unmet need for new therapies in SLE to improve therapy targets.

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FRI0171 THE CHANGES OF IMMUNE FUNCTION AND CLINICAL INDEXES WITH SYSTEMIC LUPUS ERYTHEMATOSUS AFTER IMMUNOREGULATORY COMBINATION THERAPIES

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Background: Recent studies have reported that some drugs such as low-dose interleukin-2, rapamycin, metformin, retinoic acid and coenzyme Q10 could promote the proliferation and functional recovery of regulatory T cells (Treg) in patients with autoimmune diseases. However, the effects on the balance of Treg cells and pro-inflammatory lymphocytes and long-term efficacy have rarely been reported.

Objectives: To evaluate the changes of peripheral lymphocyte subsets, conventional drugs and remission rate in patients with systemic lupus erythematosus (SLE) after immunomodulatory combination therapies.

Methods: A total of 189 patients with SLE from the Second Affiliated Hospital of Shanxi Medical University from January 2016 to October 2019 were enrolled, who were divided into well-controlled group and untargeted control group taking a full consideration of the patient's symptoms, signs and related laboratory findings. We measured the absolute counts of B, NK, CD8+T and helper T 1 (Th1), helper T 2 (Th2), helper T 17 (Th17) and Treg cells in peripheral blood of patients before immunomodulatory combination therapies and during the 3 months and 6 months of follow-up and 190 sex- and age- matched control individuals using flow cytometry. Moreover, the ratios of various cells to Treg cells were calculated.

Results: Compared with healthy controls, Treg cells in SLE patients were significantly lower before the treatment with immunomodulator, while the ratios of various pro-inflammatory lymphocytes to Treg cells (such as Th2/Treg, Th17/Treg, CD8+T/Treg, etc.) were higher. After 3 months and 6 months with immunomodulatory therapy, the absolute number of Treg cells in peripheral blood of SLE patients increased obviously reaching to normal level. Accordingly, the ratios of various pro-inflammatory lymphocytes to Treg cells recovered. At the same time, the dose of glucocorticoid and disease-modifying antirheumatic drugs (DMARDs) decreased distinctly. Additionally, the well-controlled group was able to maintain a high remission rate, and the untargeted control group could achieve a higher response rate after immunomodulatory treatment.

Conclusion: The imbalance between pro-inflammatory lymphocytes and Treg cells caused by the significant decrease of Treg cells may be the main cause of SLE. And immunomodulatory combination therapies we came up with may reverse the imbalance of proinflammatory lymphocytes and Treg cells, which is an potential and effective treatment for SLE.

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Table1. The changes of remission rate in the no-remission group during follow-up.

Follow-up period	Total patients	Remission	No-remission	Remission rate(%)
Baseline	92	0	92	0
3 Months	72	33	39	45.8[a]
6 Months	74	42	32	56.8[a]

a: Compared with baseline; b: Compared with 3 months.

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FRI0172 THE INFLUENCE OF CALCINEURIN INHIBITORS ON DEVELOPMENT OF CANCER IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A RETROSPECTIVE OBSERVATIONAL STUDY IN THE LUNA REGISTRY

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Background: It has been reported that the incidence of cancer in patients with systemic lupus erythematosus (SLE) is higher than that in healthy individuals, but the findings are inconsistent[1]. In the transplantation field, a few studies indicated an association between the use of immunosuppressants and an increased risk of cancer[2]. Calcineurin inhibitors (CNIs), which include cyclosporine and tacrolimus, have been used for >30 years to treat renal and extrarenal manifestations of SLE, but the effects of exposure to CNIs among SLE patients have not been established.

Objectives: We investigated the incidence of various cancers (including cervical dysplasia) among SLE patients registered in the LUpus registry of NAtionwide institution (LUNA). We also investigate whether the registrants' exposure to CNIs increased the risk of cancer.

Methods: We calculated the standardized incidence ratio (SIR) of cancer among SLE patients based on the age-standardized incidence rate of cancer reported by Japan's Ministry of Health, Labour and Welfare. A multivariate analysis of the risk of cancer was performed using the covariates of age, smoking history, CNI treatment history, maximum steroid dose in the past, and Systemic Lupus International Collaboration Clinics/American College of Rheumatology Damage Index [SDI]) value (excluding the occurrence of cancer) at the time of the patient's registration.

Results: We studied 714 patients (663 females; 88.9%).The median age at registry was 44 [interquartile range (IQR): 35–56] years. The median past max. steroid dose was 40 mg/day (IQR: 30–60 mg/day), and the SDI at registration was 1 (IQR 0–2). Smoking history was present in 248 patients (34.9%), and 53 patients (7.4%) experienced cancer complications. Gynecologic malignancies accounted for 71% of all cancers, including 12 cervical dysplasia cases. The standardized incidence rate of cancer in these SLE patients was 1.46 (95%CI: 1.07–1.85, p<0.01). The multivariate analysis showed that a CNI treatment history was not a risk factor for the development of cancer (OR 1.76, 95%CI: 0.63–4.88, p=0.30). After the covariance was adjusted for the propensity score, the risk of cancer in the CNIs group was not increased compared to the non-CNIs group (adjusted OR 2.46, 95%CI: 0.68–8.91, p=0.20).

Conclusion: The incidence of cancer in SLE was higher in the LUNA cohort than in the general population. Our results suggest that CNI treatment for individuals with SLE is not a risk factor for the development of cancer.

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FRI0173 IDENTIFICATION OF RISK FACTORS FOR DEVELOPMENT OF OSTEONECROSIS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Patient with Systemic Lupus Erythematosus (SLE), particularly those who received corticosteroids are at a high risk of osteonecrosis (ON).

Objectives: In this analysis, we aimed at determining the predictors of ON in a longitudinal lupus cohort in which Caucasian and African-American ethnicities are well represented.
Methods: The data were reviewed from the initiation of the cohort in 1987 until October 2019. 2428 patients were included in the analysis based on 224295 person-months of follow-up. ON was recorded using the Systemic Lupus Erythematosus International Collaborating Clinics/ American College of Rheumatology (SLICC/ACR) Damage Index. To calculate the rate of ON in each demographic and clinical subgroup, we calculated the number of ON events divided by the number of person-months at risk and converted this rate to rates per person-year. To assess the relationship between risk factors and rates of ON events, we used the pooled logistic regression. Rate ratios were adjusted for age. After identifying a set of variables related to ON incidence, we fit a final multivariable model to identify the most important risk factors for incident ON.
Results: 287 ON cases were identified, giving a point prevalence of 11%. ON cases that occurred before cohort entry were excluded. 122 incident events of ON occurred after cohort entry and were included in the final analysis. In the multivariable analysis, African-Americans were at twice the risk for ON compared to Caucasians. Male gender and smokers had about 80% and 50% increased risk of ON compared to females and non-smokers respectively. For every 10 year increase in the age there was a 20% reduced risk for ON. Patients diagnosed after the 1990's had a 50% reduced risk of ON compared to those diagnosed before 1990's. A highest daily dose of prednisone of 40 mg or higher, even when administered for a month or less, increased significantly the risk of ON. Use of pulse steroid was not associated with an increased risk of ON.
Conclusion: Ethnicity remains an important determinant in the risk of ON. African-American SLE patients are at double the risk of ON compared to Caucasians. APOL1 risk variants confer an increased risk of ON in this high-risk ethnic group. Oral prednisone more than 40 mg daily administered for a month or less, at any point in the disease course, remains the most important predictor of ON. Prednisone-free or prednisone-limited regimens should be reinforced in SLE trials.

Table 1. Associations between ON rates and corticosteroids dose and duration based on a multivariable model

Predictor		RR (95% CI)	p-value
Max prednisone and duration	0- 40 mg/day for <=1 month	1.00 (Ref)	
	0- 40 mg/day for >1 month	1.49 (0.68, 3.26)	0.3162
	40-60 mg/day for <=1 month	2.76 (1.18, 6.39)	0.0182
	40-60 mg/day for >1 month	3.87 (1.73, 8.62)	0.0009
	>=60 mg/day for <=1 month	6.6 (3.37, 12.93)	<0.0001
	>=60 mg/day for >1 month	5.15 (2.55, 10.4)	<0.0001
Sex	Male (vs. Female)	1.79 (1.04, 3.10)	0.0373
Ethnicity	African American (vs. Caucasian)	1.94 (1.32, 2.83)	0.0007
Year of SLE diagnosis	1990 and after (vs. before 1990)	0.53 (0.36, 0.77)	0.0008
Age	Per 10 year increase	0.77 (0.66, 0.89)	0.0006
Smoking	Ever (vs. never)	1.51 (1.04, 2.19)	0.0293

Table 2. Associations between ON rates and pulse steroid stratified by max prednisone

Subgroup		No. of ONs	Person years	Rate per 1000 person years	Age-adjusted RR (95% CI)	Age-adjusted p-value
Pulse among those with maximum prednisone dose of <40 mg	No	21	6752.1	3.11	1.00 (Ref)	
	Yes	2	387.8	5.16	1.69 (0.40, 7.20)	0.4801
Pulse among those with maximum prednisone dose of >=40 mg	No	88	7202.3	12.2	1.00 (Ref)	
	Yes	8	959.2	8.3	0.71 (0.35, 1.48)	0.3618
Pulse among those with maximum prednisone dose of >=60 mg	No	64	4329.9	3.11	1.00 (Ref)	
	Yes	7	622.4	5.16	0.79 (0.36, 1.72)	0.5477

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Disclosure of Interests: None declared
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FRI0174 THE LONGER THE DELAY IN DIAGNOSIS, THE WORSE THE OUTCOME IN SLE – CROSS SECTIONAL ANALYSIS OF A GERMAN LONG-TERM STUDY (LULA COHORT)

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Background: Patients with systemic lupus erythematosus (SLE), even compared to those with other rheumatic diseases, are thought to often experience a long delay from the onset of symptoms to diagnosis.
Objectives: Our aim was to study the association of this delay to the long-term outcome of the disease.
Methods: Information on demographics, onset of first symptoms, first physicians visit, time of diagnosis and organ involvement was assessed by self-reported questionnaires among SLE patients in Germany in 2011 (LuLa cohort, n=585). Disease related damage (Brief Index of Lupus Damage; BILD), disease activity (Systemic Lupus Activity Questionnaire; SLAQ) and health related quality of life (SF-12) were chosen as proxies for outcome. The association to the outcome of the disease was analyzed by linear regression analysis, adjusted for age, disease duration, organ involvement and sex.
Results: In our cohort, the mean reported duration between the onset of symptoms and the diagnosis of SLE was 46 months (SD 73), which includes 13 months (SD 41) between the onset of symptoms and the first physicians visit. The participating patients were diagnosed between 1960 and 2004.
Linear regression analysis revealed that longer time to diagnosis was associated with (i) higher disease activity (SLAQ, p<0.0001, β=0.199), (ii) higher disease-related damage (BILD, p=0.002, β=0.137) and (iii) lower health-related quality of life (SF-12 physical p=0.004, β=-0.136, SF-12 mental p=0.004, β=-0.143) in the year 2011. The organ involvement at the time of diagnosis did not alter these results.
Conclusion: A delay in diagnosis was associated with a worse outcome in SLE (disease activity, disease-related damage and health-related quality of life). Therefore, an early diagnosis seems to be important to improve the long-term outcome of the disease. It will be interesting to see whether adopting the new EULAR/ACR 2019 classification criteria can contribute to a faster diagnosis and a better outcome in consequence.
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FRI0175 SEMI-DYNAMIC MRI OF THE EXTENSOR DIGITORUM TENDONS IN JACCOUD ARTHROPATHY

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Background: Jaccoud arthropathy (JA) is a rare joint deformity mostly associated with systemic lupus erythematosus (SLE) (1). JA may be defined as a reversible deformity of the hands during flexion with ulnar deviation and swan neck deformities of the fingers. The physiopathology and the mechanisms leading to JA still remain to be elucidated.
Objectives: To test the hypothesis that Jaccoud arthropathy (JA) in systemic lupus erythematosus (SLE) patients is associated with abnormal extensor digitorum (ED) tendons displacement during flexion of the metacarpophalangeal (MCP) joints.
Methods: 16 SLE patients with JA (JA+), 12 SLE patients without JA (JA-) and 24 control subjects were included in the study. Transverse spin echo T1-weighted MR sequences of the MCP joints in flexion and in extension were obtained in each hand of SLE patients and in one randomly-selected hand of control subjects. Two radiologists separately measured the amplitude and the direction of the displacement of the ED tendons with respect to the midline at the level of the MCP joints. Statistical analysis included two-way ANOVA with random effects to assess differences in amplitude (p<0.0083), Fisher-Freeman-Halton exact test to

assess differences in direction (p<0.0063) and Gwet's AC1 score to determine interobserver agreement.
Results: Amplitude of the displacement of the ED tendons was statistically significantly higher in JA+ patients than in JA- patients and controls in flexion for both readers (p<0.0001) and in extension for one reader (p<0.0048). Ulnar deviation of the ED tendons was statistically significantly more frequent in JA+ patients than in JA- patients and controls in flexion and in extension for both readers (p<0.0001). Interobserver agreement for the assessment of displacement was moderate to very good (0.51≤kappa≤0.93).
Conclusion: JA is associated with abnormal displacement of the ED tendons in flexion and extension. Abnormal displacement of the ED tendons is absent in patients without JA.
References:
[1] Santiago MB. Miscellaneous non-inflammatory musculoskeletal conditions. Jaccoud's arthropathy. Best Pract Res Clin Rheumatol. 2011;25(5):715-25.

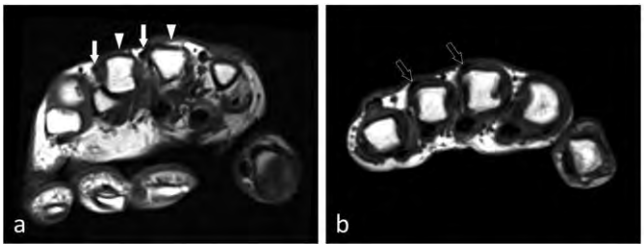


Figure 1. Axial spin echo T1-weighted images of a 49-year-old woman with SLE and JA (a) in flexion and (b) extension. In flexion, the extensor digitorum (ED) tendons of the 3rd and 4th fingers are completely displaced on the ulnar aspect of the metacarpal heads (white arrows) with no tendon visible on the dorsal aspect (arrowheads). In extension, the ED tendons of the 3rd and 4th fingers are slightly displaced on the ulnar side of the dorsal aspect of the metacarpal heads (black arrows).

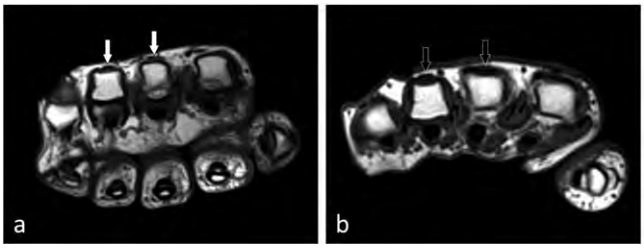


Figure 2. Axial spin echo T1-weighted images of the sex- and age-matched control subject of the patient from Figure 1 (a) in flexion and (b) extension. The extensor digitorum tendons of the 3rd and 4th fingers are normally positioned on the dorsal aspect of the metacarpal heads in flexion (white arrows) and extension (black arrows).

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FRI0176 NON-HISTOLOGIC FACTORS DISCRIMINATING PROLIFERATIVE LUPUS NEPHRITIS FROM MEMBRANOUS LUPUS NEPHRITIS

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Background: The treatment strategy and renal prognosis between proliferative lupus nephritis (LN) and membranous LN are different. Therefore, it is important to distinguish one from the other. To date, data regarding non-histologic factors that can discriminate proliferative LN from membranous LN are limited.
Objectives: To investigate non-histologic factors that can discriminate proliferative LN from membranous LN in patients with systemic lupus erythematosus with renal manifestations.
Methods: Patients with biopsy-proven proliferative LN and membranous LN were included. Non-histologic factors were compared between the two groups. A logistic regression analysis was performed to identify the factors associated with proliferative LN. To assess the accuracy of these factors in discriminating between proliferative LN and membranous LN, we performed a receiver-operating characteristic analysis.
Results: Of the total 168 patients with biopsy-proven LN, 150 patients (89.3%) had proliferative LN, and 18 patients (10.7%) had membranous LN. In the multivariable logistic regression analysis, positive anti-double-stranded DNA (anti-dsDNA) antibody (adjusted OR = 11.200, 95% CI = 2.202–56.957, p = 0.004) was associated with proliferative LN, while positive anti-U1RNP antibody (adjusted OR = 0.176, 95% CI = 0.040–0.769, p = 0.021) and higher glomerular filtration rate (GFR) (adjusted OR = 0.973, 95% CI = 0.951–0.994, p = 0.013) were inversely associated with proliferative LN. Among these covariates, the anti-dsDNA antibody (area under the curve = 0.806, 95% CI = 0.695–0.916) had the highest accuracy in discriminating between proliferative LN and membranous LN.
Conclusion: The positivity of anti-dsDNA antibody was associated with proliferative LN, while the positivity of anti-U1RNP antibody and GFR were inversely associated with proliferative LN. The anti-dsDNA antibody had a good accuracy in discriminating proliferative LN from membranous LN.
References: Not applicable

Table. Factors associated with proliferative LN

	Univariable analysis		Multivariable analysis	
	OR (95% CI)	p	OR (95% CI)	p
Age	0.982 (0.951–1.014)	0.269		
Female sex	1.437 (0.295–7.006)	0.653		
Positive anti-Sm Ab	0.648 (0.243–1.728)	0.386		
Positive anti-Ro Ab	0.928 (0.341–2.529)	0.885		
Positive anti-La Ab	2.075 (0.572–7.528)	0.267		
Positive anti-U1RNP Ab[a]	0.271 (0.085–0.861)	0.027	0.176 (0.040–0.769)	0.021
Positive anti-dsDNA Ab[a]	7.333 (2.574–20.893)	<0.001	11.200 (2.202–56.957)	0.004
Low C3[a]	9.970 (3.117–31.891)	<0.001	1.886 (0.255–13.932)	0.534
Low C4[a]	3.839 (1.405–10.486)	0.009	1.224 (0.229–6.552)	0.813
GFR	0.980 (0.964–0.997)	0.021	0.973 (0.951–0.994)	0.013
Urine PCR	1.000 (0.987–1.013)	0.986		
Urine RBC of ≥ 5/HPF	4.178 (1.516–11.509)	0.006	2.053 (0.426–9.893)	0.370
Urine WBC of ≥ 5/HPF	2.687 (0.958–7.543)	0.060		
Urine cast	4.429 (0.567–34.578)	0.156		
SLEDAI-2K	1.173 (1.063–1.294)	0.001	1.046 (0.900–1.216)	0.557

Variables with P value less than 0.05 in the univariable analysis were selected for inclusion in the multivariable analysis.
[a]Analyzed as binary variables (Anti-U1RNP Ab, positive/negative; Anti-dsDNA Ab, positive/negative; C3, low/not low; C4, low/not low)
Ab, antibody; anti-dsDNA, anti-double-stranded DNA; GFR, glomerular filtration rate; PCR, protein/creatinine ratio; RBC, red blood cell; HPF, high power field; WBC, white blood cell; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; OR, odds ratio; CI, confidence interval

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FRI0177 MULTI-MODALITY IMAGING TO EVALUATE LUPUS NEPHRITIS

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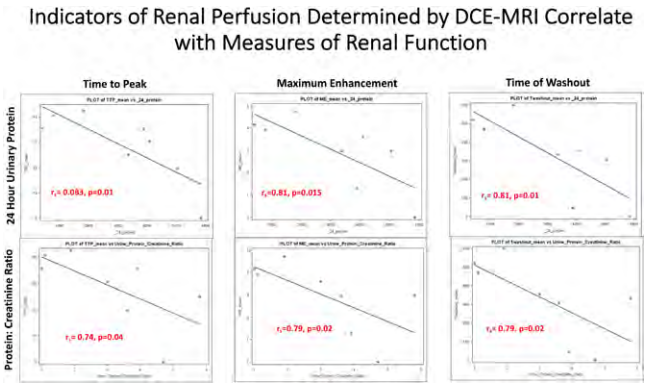
Background: Lupus nephritis (LN) remains a significant cause of morbidity and mortality in subjects with Systemic Lupus Erythematosus (SLE). The gold standard for evaluation of LN remains the kidney biopsy, whereas renal function is usually evaluated by eGFR and urinary protein:creatinine ratio. More effective and sensitive methodology is needed to assess LN and also the response to treatment. Functional imaging of the kidney using quantitative techniques has great potential, as it can assess kidney function and pathologic changes non-invasively by evaluating perfusion, oxygenation, cellular density and fibrosis.
Objectives: The objective of this study was to develop a multi-modality imaging approach for the evaluation of the spectrum of pathologic changes in LN and to determine when imaging data correlated with renal function
Methods: In this multi-center study (NCT03180021), subjects who were having a standard of care renal biopsy for LN were asked to participate in the imaging evaluation. Local Institutional Review Board approval was obtained, and subjects signed an Informed Consent Form. Dynamic contrast enhanced MRI (DCE-MRI) was employed to detect changes in vascularization and perfusion, Diffusion Weighted Imaging (DWI) to assess interstitial diffusion, T2*Map/BOLD to evaluate tissue oxygenation and T1rho to evaluate fibrosis (Figure 1). Regions of interest were identified in the imaged kidneys and imaging parameters were correlated with measures of renal function, including eGFR and urinary

protein: creatinine ratio. In DCE-MRI, we specifically focused on mean Maximum Enhancement (ME), mean Time to Peak Enhancement (TTP) and mean Time of Washout (Twashout) as indicators of renal perfusion.

Results: Nine subjects have been evaluated to date and their imaging data assessed for quality. Evaluation of mean data from DCE-MRI has shown a significant correlation between renal perfusion and renal function. For example, as shown in the figure, the 24 hour protein concentration negatively correlated with ME (r_s=-0.81, p=0.015), TTP (r_s=-0.83, p=0.01) and Twashout (r_s=-0.81.p=0.01, Spearman rank correlation). In addition, the protein:creatinine ratio also negatively correlated with ME (r_s=-0.79, p=0.02), TTP (r_s=-0.74, p=0.04) and Twashout (r_s=-0.79, p=0.02, Spearman rank correlation).

Conclusion: These initial results have established the feasibility of multi-modality imaging as a tool to evaluate LN in a multi-center study. Moreover, changes in perfusion detected by DCE-MRI significantly correlate with proteinuria and urinary protein:creatinine ratio. These results suggest that multiparameter imaging may contribute useful data in the evaluation of subjects with LN.

Figure:



Disclosure of Interests: Claire Dykas: None declared, Brad H Rovin Grant/research support from: GSK, Consultant of: GSK, Mikael Boesen Consultant of: AbbVie, AstraZeneca, Eli Lilly, Esaote, Glenmark, Novartis, Pfizer, UCB, Paid instructor for: IAG, Image Analysis Group, AbbVie, Eli Lilly, AstraZeneca, esaote, Glenmark, Novartis, Pfizer, UCB (scientific advisor)., Speakers bureau: Eli Lilly, Esaote, Novartis, Pfizer, UCB, Olga Kubassova Shareholder of: IAG, Image Analysis Group, Consultant of: Novartis, Takeda, Lilly, Employee of: IAG, Image Analysis Group, Peter Lipsky Consultant of: Horizon Therapeutics

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FRI0178 PREDICTIVE FACTORS FOR POOR SLEEP QUALITY IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Poor sleep quality is common in systemic lupus erythematosus (SLE) and could contribute to fatigue, which is regarded as one of the most disabling symptoms in SLE. The Pittsburgh sleep quality index (PSQI) is a validated self-administered questionnaire that measures sleep quality over the previous month.[1]

Objectives: The aim of this study was to analyse the relationship of sleep quality with several variables including depression, anxiety, pain, disease activity, fatigue and functional disability in patients with SLE. A further aim was to establish the prevalence of poor sleep quality in SLE.

Methods: A cohort cross-sectional study was carried out including 92 SLE patients who fulfilled the SLICC classification criteria for SLE and who provided informed consent for participation. The patients were interviewed and they were asked to fill in questionnaires including PSQI, Fatigue Severity Scale (FSS), Hospital Anxiety and Depression Scale (HADS), visual analogue scale (VAS) for pain and modified Health Assessment Questionnaire (mHAQ). Blood and urine tests enabled the calculation of SLE disease activity index-2K (SLEDAI-2K). The study was approved by the University Research Ethics Committee.

Results: 92.4% of the cohort studied were females, and the mean age was 46.9 years (range 19-79 years). 55.4% were noted to have poor quality sleep (PSQI >5), and the median PSQI was 6 (range 0-18). Sleep quality measured by PSQI, had a significant correlation with SLEDAI-2K (R=0.254, p=0.014), VAS pain (R=0.515, p<0.001), HADS-D (R=0.605, p<0.001), HADS-A (R=0.375, p<0.001), estimated glomerular filtration rate (eGFR) (R=-0.211, p=0.044), FSS (R=0.551, p<0.001) and mHAQ (R=0.559, p<0.001). ANCOVA analysis showed that PSQI was significantly dependant on VAS pain (p<0.001), HADS-D (p<0.001) and eGFR (p=0.003).

Conclusion: Poor sleep quality is highly prevalent in SLE patients. This study has shown that the strongest predictive factors for poor sleep quality are pain, depression and impaired renal function. Since poor sleep quality is significantly related to fatigue and functional disability, its identification and management is important for patients' wellbeing.

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Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.931

FRI0179 A STUDY ON THE ACHIEVEMENT OF LUPUS LOW DISEASE ACTIVITY STATE AND QUALITY OF LIFE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: FROM THE JUNTENDO UNIVERSITY SLE PROSPECTIVE REGISTRY STUDY

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Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease of unknown etiology that affects mostly young women. Multiorgan complications and prolonged treatment significantly cause physical and mental stress in patients. Improving patients' quality of life (QOL) in SLE treatment is essential. We examined the treatment effects on disease activity and QOL of SLE patients.

Objectives: In recent years, lupus low disease activity state (LLDAS) has been proposed as a treatment target for SLE. Patients who achieve LLDAS have a low recurrence rate for lupus and a low risk of serious complications (1). The aim of this study is to investigate whether achieving LLDAS reduces not only recurrence rate and complications of SLE but also improves patients' QOL.

Methods: A total of 104 SLE patients were enrolled in our prospective SLE registry study (Juntendo, Multi-center, Prospective cohort for investigation of clinical course and outcome in SLE: JUMP) conducted at our institution. SLE was diagnosed using the American College of Rheumatology (ACR) 1982 criteria (revised in 1997). QOL was evaluated using the standard version of the 36-item short form health survey version 2 (SF36v2). Participants were divided into the LLDAS achievement and non-achievement groups, and the characteristics of each group including results of SF36v2 were examined.

Results: This study included 104 SLE patients, 94 female and 10 male, and the average age and disease duration were 46.4±13.8 and 14.5±11.3 years, respectively. The average corticosteroid dose was 8.0±17.4 mg/day in terms of prednisolone, and anti-dsDNA antibody titer was 16.8±38.5 IU/ml. Of the 104 patients, 57 achieved LLDAS. The subscale's standard scoring using SF36v2 for role physical (RP) was 78.9±24.0 and 64.6±27.6 (P<0.01), general health (GH) was 50.0±17.0 and 42.0±19.3 (P<0.05), vitality (VT) was 55.8±15.8 and 38.0±24.1 (P<0.01), social functioning (SF) was 82.0±20.7 and 66.5±26.3 (P<0.01), role emotional (RE) was 89.0±16.1 and 73.4±28.1 (P<0.01), and mental health (MH) was 72.4±15.9 and 58.3±21.8 (P<0.01) in the LLDAS achievement and non-achievement groups, respectively. Furthermore, scoring based on the national standard value in the LLDAS achievement group showed that two categories were >50. However, in the LLDAS non-achievement group, all categories were <50. In particular, RP, GH, VT, SF, RE, and MH of the LLDAS achievement group had significantly higher scores than the LLDAS non-achievement group (RP and GH: p<0.05 and VT, SF, RE and MH: p<0.01).

Conclusion: Results of examining the association between LLDAS and QOL using SF36v2 in SLE patients showed that patients who achieved LLDAS had significantly better standard statistical scores in many subscale categories. Thus, LLDAS achievement as a treatment target for SLE patients greatly contributes to improving patients' QOL.

References:

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Disclosure of Interests: None declared
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FRI0180 SURVEY ON HELP-SEEKING AND DISEASE TRAJECTORY IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Few studies in Latin America have analysed the time lag since patients experience the first joint symptoms until they consult a physician, and a diagnosis is made, and most of them have dealt with patients sustaining Rheumatoid Arthritis (RA)[1-2].
Objectives: To study both patient and disease factors that have some bearing on the time lag until a physician is first consulted and a diagnosis is made.
Methods: Multiple-choice survey to patients of 18 years of age or older who met **Systemic Lupus Erythematosus (SLE)** Classification Criteria (2012). The following aspects were measured: **time lag from symptom onset to first medical consultation (Time 1), time lag since first medical consultation until a diagnosis is made (Time 2), and time lag until the first consultation with a rheumatologist**.
Patients were interviewed at the time or within 6 months of diagnosis, and asked about the physician they first consulted and the one who made the diagnosis. They were also requested to describe one disease onset out of 4 trajectories: acute, acute with temporary remissions, chronic with partial improvements, or sustained chronic. Patients were required to recount their response to the first symptoms, the limitations brought about by the disease (employing the Steinbrocker scale), and whether help-seeking was first aimed at consulting a physician or they decided to wait. A group of patients with Rheumatoid Arthritis (RA) answered the same survey. Every patient signed an informed consent form, and the study was approved by the Hospital Bioethics Committee.
Results: Twenty-eight patients with SLE and 29 patients with RA filled in the survey. SLE patients were younger as expected (32 years vs 49 years; p <0.001). Acute was the most common disease trajectory in SLE patients (36% vs 34%; p 0.8) and chronic in RA (38% vs 32%; p 0.8). The first professional consulted was an on-duty physician in SLE (36% vs 24% in RA; p 0.5). Except for the matter of computer at home and/or a mobile phone with an Internet connection at home, both groups were similar, although SLE patients showed a trend to better level education and lesser impact of the disease on daily life at the beginning (see Table 1).

Table 1.

	SLE	RA	P
n	28	29	
Education (median)	Secondary	Secondary	0.07
Had a job	11 (39%)	15 (52%)	0.5
Had health insurance	8 (29%)	15 (52%)	0.1
Had computer/mobile phone with an Internet connection	25(89%)	18(62)%	0.04
Steinbrocker (median with range 25-75%)	3 (2-3)	3 (3-4)	0.06
Immediately sought medical help	15 (54%)	16 (56%)	0.9
Did not know what to do when the first symptoms appeared	7 (25%)	13(45%)	0.2
Diagnosis made by a rheumatologist	20 (71%)	23 (80%)	0.7

Time 1 in patients with SLE was significantly lower with a median of 7 days, range **(25-75%)** 1-30 days vs 30 days in RA, range 14-180 (p 0.01), and the former also showed a trend to lower median Time 2: 81 days, range 25-209 vs 185 days in RA, range 60-275 (p 0.1). Besides, they showed a significantly shorter time lag until the first visit to a rheumatologist with a median of 120 days, range 35-225 vs 330 days, range 120-450 in patients with RA (p 0.005).
Conclusion: SLE patients consult a physician and visit a rheumatologist sooner than RA patients do, and they also show a trend to obtain a faster diagnosis. Education, health insurance, employment, the disease impact on their daily life and initial response to the symptoms do not appear to account for their swiftness in seeking medical help.
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FRI0181 ORGAN DAMAGE FREE SURVIVAL IN SOUTHERN CHINESE PATIENTS WITH ACTIVE LUPUS NEPHRITIS

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Background: The goals of treatment of lupus nephritis (LN) are to induce remission, retard the progression of chronic kidney disease, prevent organ complications and ultimately reduce mortality. Previous cohort studies of LN have mainly focused on the risk of mortality and development of end stage renal failure (ESRF) (renal survival). The cumulative frequency of LN patients who survive without organ damage, which correlates better with the balance between treatment efficacy and toxicity, as well as quality of life, has not been well studied.
Objectives: To study the organ damage free survival and its predictive factors in patients with active LN.
Methods: Consecutive patients who fulfilled ≥4 ACR/SLICC criteria for SLE and with biopsy proven active LN between 2003 and 2018 were retrospectivey analyzed. Those with organ damage before LN onset were excluded. Data on renal parameters and treatment regimens were collected. Complete renal response (CR) was defined as normalization of serum creatinine (SCr), urine P/Cr (uPCR) <0.5 and inactive urinary sediments. Partial renal response (PR) was defined as ≥50% reduction in uPCR and <25% increase in SCr. Organ damage of SLE was assessed by the ACR/SLICC damage index (SDI). The cumulative risk of having any organ damage or mortality since LN was studied by Kaplan-Meier's analysis. Factors associated with a poor outcome were studied by a forward stepwise Cox regression model, with entry of covariates with p<0.05 and removal with p>0.10.
Results: 273 LN patients were identified but 64 were excluded (organ damage before LN onset). 211 LN patients were studied (92% women; age at SLE 30.4±13.5 years; SLE duration at LN 1.9±3.1years). 47 (22%) patients had nephrotic syndrome and 60 (29%) were hypertensive. Histological LN classes was: III/IV±V (75.1%), I/II (7.8%) and pure V (17.1%) (histologic activity and chronicity score 7.0±4.2 and 1.8±1.5, respectively). Induction regimens were: prednisolone (33.1±17.5mg/day) in combination with intravenous cyclophosphamide (CYC) (21.4%; 1.0±0.2g per pulse), oral CYC (8.6%; 96.4±37.8mg/day), azathioprine (AZA) (14.3%; 78.6±25.2mg/day), mycophenolate mofetil (MMF) (22.8%; 1.9±0.43g/day) and tacrolimus (TAC) (17.1%; 4.3±1.1mg/day). After a follow-up of 8.6±5.4 years, 94(45%) patient developed organ damage (SDI≥1) and 21(10%) patients died. The commonest organ damage was renal (36.3%) and musculoskeletal (17.9%), and the causes of death were: infection (38.1%), malignancy (19.0%), cardiovascular events (9.5%) and ESRF complications (9.5%). At last visit, 114 (55%) patients survived without any organ damage. The cumulative organ damage free survival at 5, 10 and 15 years after renal biopsy was 73.5%, 59.6% and 48.3%, respectively. The 5, 10 and 15-year renal survival rate were 95.2%, 92.0% and 84.1% respectively. In a Cox regression model, nephritic relapse (HR 3.72[1.78-7.77]), proteinuric relapse (HR 2.30[1.07-4.95]) and older age (HR 1.89[1.05-3.37]) were associated with either organ damage or mortality, whereas CR (HR 0.25[0.12-0.50]) at month 12 were associated with organ damage free survival. Baseline SCr, uPCR and histological LN classes were not significantly associated with a poor outcome. Among patients with class III/IV LN, the long-term organ damage free survival were not significantly different in users of MMF (reference) from CYC (IV/oral) (HR 1.45[0.76- 2.75]) or TAC (HR 1.03[0.26-1.62]) as induction therapy.
Conclusion: Organ damage free survival is achieved in 55% of patients with active LN upon 9 years of follow-up. CYC/MMF/TAC based induction regimens did not differ for the long-term outcome of LN. Targeting complete renal response and preventing renal relapses remain important goals of LN treatment.
Acknowledgments: NIL
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FRI0182 RISK FACTORS ASSOCIATED WITH RENAL INVOLVEMENT IN PRIMARY SJÖGREN'S SYNDROME: DATA FROM THE SPANISH SJÖGRENSER COHORT

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Objectives: To investigate the prevalence, risk factors, and effects of primary renal disease on morbidity and mortality in patients with primary Sjögren's syndrome (pSS).
Methods: All patients in the SJÖGRENSER (registry of adult SSp patients of the Spanish Society of Rheumatology, cross-sectional phase) cohort were retrospectively investigated for the presence of clinically significant renal involvement directly related to pSS activity.
Results: Of the 437 patients investigated, 39 (9%) presented overt renal involvement during follow-up. Severe renal disease necessitating kidney biopsy was relatively rare (23%).
Renal involvement may complicate pSS at any time during the disease course and is associated with severe disease (indicated by higher scores of involvement, activity, and damage), systemic multiorgan involvement, and a higher frequency of lymphoma. Multivariate analysis showed that older age (odds ratio [OR] 1.03, 95% confidence interval [CI] 1.00–1.07), higher European League Against Rheumatism Sjogren's Syndrome Disease Activity Index scores (OR 1.1, CI 1.03–1.18), serum anti-La/SSB positivity (OR 6.44, CI 1.36–30.37), and non-vasculitic cutaneous involvement (OR 8.64, 1.33–55.90) were independently associated with this complication.
Chronic renal failure developed in 23 of 39 patients (59%); only 1 of them progressed to end-stage renal disease necessitating renal replacement therapy. Patients with renal disease showed higher Sjögren's syndrome disease damage index scores (SSDDI), higher rates of hospitalization due to disease activity and higher rates of clinically relevant comorbidities.
Conclusion: Renal involvement is an uncommon complication in pSS that was observed in 9% of patients. Although categorized as a non-negligible comorbidity, this condition shows a favorable prognosis.
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FRI0183 DISTINCTIVE TRAITS OF MYOCARDIAL INFLAMMATION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A MULTICENTRE STUDY

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Background: Myocarditis is an infrequent but potentially life-threatening inflammatory disorder and might be part of the spectrum of systemic lupus erythematosus (SLE). Little is known about the clinical and histologic features of myocarditis in SLE, especially compared to other forms of myocarditis.
Objectives: to test for potential distinctive traits among myocarditis in SLE (MyoSLE), SLE without myocarditis (OnlySLE) and myocarditis without SLE (OnlyMyo)
Methods: Patients with MyoSLE were identified from three centres and compared with 231 cross-sectionally enrolled patients with OnlySLE and 87 patients with OnlyMyo. MyoSLE patients were split into two groups based on myocarditis onset within (early onset) vs after (late onset) the first year from SLE diagnosis. OnlySLE patients were dichotomised in the same way based on disease duration at time of enrolment. Demographics and general clinical features were collected retrospectively. SLE disease activity index 2000 (SLEDAI-2K), SLE International Collaborating Clinics/American College of Rheumatology damage index (SDI), clinical and laboratory features were collected at time of myocarditis onset in MyoSLE and at enrolment in OnlySLE. Quantitative data are expressed as median [interquartile range].
Results: Fourteen MyoSLE patients were identified, 50% with early onset. Women were equally frequent among MyoSLE (71%) and OnlySLE patients (87%) and less frequent in the OnlyMyo group (43%; p<0.001). Age was comparable among groups. Clinical features at presentation, including left ventricular ejection fraction, were similar between MyoSLE and OnlyMyo, although the former had higher levels of pro-brain natriuretic peptide (1.1 [0.4-1.8] vs 0.1 [0.1-0.5] ng/ml; p=0.004). Patients with MyoSLE also had a lower frequency of left ventricle lateral wall involvement (36 vs 68%; p=0.035) and of oedema (20 vs 71%; p=0.036) and necrosis (0 vs 64%; p=0.009) at biopsy. Antiphospholipid antibodies (aPL) were more frequent in MyoSLE (57%) compared to both OnlyMyo (16%; p=0.003) and OnlySLE (28%; p=0.031). Compared to OnlySLE, patients with MyoSLE also had a higher prevalence of aPL-syndrome (APS: 36 vs 7%; p=0.003), neuropsychiatric (NPSLE: 43 vs 19%; p=0.039) and gastrointestinal manifestations (21 vs 5%; p=0.045). Early and late onset patients had similar demographics and clinical features and did not differ from patients with OnlySLE with similar disease duration in terms of SLEDAI-2K and SDI. Late onset MyoSLE patients had a higher prevalence of NPSLE (57 vs 18%; p=0.026) and APS (57 vs 7%; p=0.001) and higher C-reactive protein levels (6 [2-12] vs 1[0-4] mg/l; p=0.024) compared to OnlySLE patients with the same disease duration.
Conclusion: Demographics of patients with MyoSLE are more similar to patients with OnlySLE than to OnlyMyo patients. MyoSLE might have distinct histological and pathogenic features compared to OnlyMyo. Patients with MyoSLE show similar patterns of disease activity and accrued damage at time of myocarditis onset compared to patients with OnlySLE with the same disease duration but might diverge later on in SLE course. aPL are frequent in MyoSLE and might both contribute to the pathogenesis of myocardial inflammation and account for the high prevalence of NPSLE and APS, especially in late onset cases.
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FRI0184 ATTRIBUTION OF NEUROPSYCHIATRIC MANIFESTATIONS TO SYSTEMIC LUPUS ERYTHEMATOSUS IN POLISH COHORT OF PATIENTS WITH THE USE OF THE ITALIAN MODEL

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Background: Distinguishing primary NPSLE (neuropsychiatric systemic lupus erythematosus) from secondary causes remains challenging (1). Attribution models were developed in order to aim clinicians in correct classification of NPSLE cases (2).
Objectives: To investigate the prevalence of primary NPSLE manifestations assigned with Italian model of attribution (2).
Methods: We retrospectively assessed clinical details of 164 patients with SLE classified with 2012 SLICC (Systemic Lupus International Collaborating Clinics) classification criteria, 21 were excluded due to incomplete information. Data was gathered with a questionnaire comprising demographics, medical history, laboratory results (concentrations of antibodies against double stranded DNA – anti-dsDNA, complement components C3 and C4), disease activity measured with Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) and Physician Global Assessment (PGA) and damage determined with SLICC/ACR (American College of Rheumatology) Damage Index (SDI). Neuropsychiatric manifestations were categorized in accordance with 1999 ACR glossary and attribution of manifestations was performed with the use of Italian model with the score ≥7 out of 10 points enabling assignment to primary NPSLE group (2). Statistical analysis was conducted with Statistica v.13.3 using Mann-Whitney U, chi-square and Fisher exact test.
Results: We encountered 155 NP manifestations in our cohort and 52 (34%) were attributed to SLE. Characteristics of the study groups are presented in Table 1. Exact manifestations and their attribution rates are presented on

Graph 1. Patients with attributable NPSLE were younger, had earlier disease onset, presented higher disease activity, lower damage accrual without taking NP damage into account and more often had increased anti-dsDNA serum concentration.

Table 1. Demographic and laboratory characteristics with disease activity and damage of the study groups, N(%) or mean(±SD).

Characteristic	Patients with attributed NPSLE manifestations	Patients without attributed NPSLE manifestations
Patients	34 (23.8%)	109 (76.2%)
Sex, female	30 (88.2%)	102 (93.6%)
Age (years)	37.6 (±11.7)	44.3 (±13.9)*
Age of disease onset (years)	32.5 (±11.4)	37.6 (±12.6)*
Disease duration (years)	5.1 (±4.1)	6.8 (±5.6)
SLEDAI-2K	29.2 (±10.7)	12.2 (±8.1)*
patients with clinically active disease (defined as SLEDAI-2K≥6 in clinical manifestations)	34 (100%)	93 (85.3%)*
SLEDAI-2K without NP manifestations	14.8 (±8.4)	11.0 (±6.7)*
PGA	2.1 (±1.0)	1.2 (±1.0)*
SDI	0.5 (±0.8)	0.7 (±1.1)
SDI without NP damage	0.3 (±0.6)	0.7 (±1.1)*
low C3/C4 complement component concentration in serum	21 (61.8%)	55 (50.4%)
elevated anti-dsDNA autoantibody concentration in serum	27 (79.4%)	55 (50.4%)*

NPSLE – neuropsychiatric systemic lupus erythematosus, SLEDAI-2K – Systemic Lupus Erythematosus Disease Activity Index version 2000, PGA – physician global assessment, SDI – SLICC/ACR (Systemic Lupus International Collaborating Clinics/American College of Rheumatology) Damage Index

*p<0,05, Mann-Whitney U, χ^2 or Fisher's exact test, as appropriate

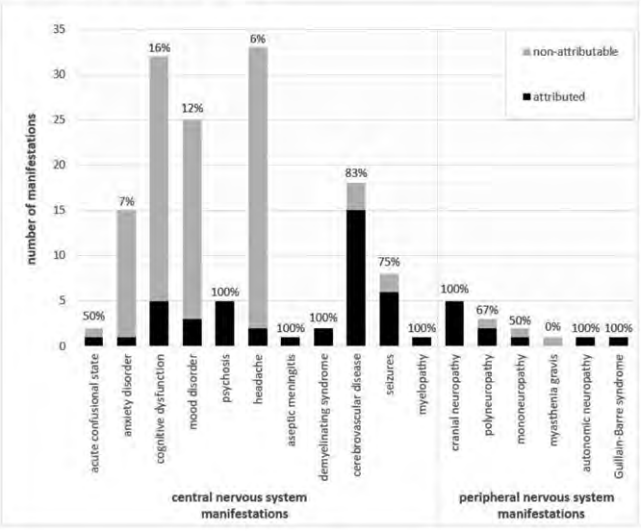
Conclusion: Primary NP manifestations in patients with SLE occur mainly in young patients with high disease activity. Cerebrovascular disease, seizures, psychosis and cranial neuropathy are most frequent primary NPSLE manifestations.

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Graph 1. Attribution of neuropsychiatric manifestations to systemic lupus erythematosus (% of attributed manifestations are presented above the bars).



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FRI0185 DIAGNOSTIC SIGNIFICANCES OF BOTH MICRORNA-146A AND KALLIKREIN-1 IN PATIENTS WITH LUPUS NEPHRITIS

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Background: Lupus nephritis (LN) is one of the most critical complications of systemic lupus erythematosus (SLE). Approximately 30–50% of SLE patients develop LN with 5-year survival rate of about 70-80%. Thus, finding reliable non-invasive biomarkers at the early stages of SLE is of great interest (1). Many studies focused on the association between microRNAs and the risk of LN. miRNA-146a (miR-146a) was one of the most promising circulating markers which was suggested recently for early diagnosis of SLE but its diagnostic relevancies regarding LN have not been extensively investigated.

Objectives: This study aims to test the expression of miR-146a in patients with LN in relation to Kallikrein-1 as another widely investigated diagnostic marker for LN along with other conventional measures.

Methods: One hundred and thirty subjects were enrolled in this study. They were divided into forty six patients with LN, forty four patients with SLE but without nephritis and forty healthy controls. The expression levels of miR-146a in peripheral blood mononuclear cells (PBMCs) were detected via RT-qPCR analysis. Besides, serum Kallikrein-1 levels were determined by ELISA. The diagnostic role of miR-146a and Kallikrein-1 in LN was evaluated by Receiver operating curve (ROC). The impact of miR-146a and Kallikrein-1 on renal disease was compared to albumin creatinine ratio, renal biopsy findings as well as renal SLEDAI.

Results: Levels of miR-146a were significantly lower in the plasma of LN patients than both patients of SLE without LN and normal controls ($p < 0.05$). However, serum levels of Kallikrein-1 were significantly higher in LN patients when compared to SLE patients and normal population ($p < 0.05$). ROCs were conducted to assess the diagnostic values of both miR-146a and kallikrein-1. They revealed good diagnostic values with AUC of 0.888 and 0.913 respectively. Also, plasma miR-146a was observed to be negatively associated with serum creatinine, proteinuria as well as SLEDAI score ($p < 0.01$) while serum Kallikrein-1 was positively correlated with them ($p < 0.05$) and inversely correlated with miR-146a ($p < 0.01$).

Conclusion: The expression levels of miR-146a are reduced in SLE patients with more reduction with LN. Therefore, miR-146a could be considered as potential biomarker for detecting LN either alone or in combination with Kallikrein-1. However, more studies are required.

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Disclosure of Interests: None declared

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FRI0186 JOINT INVOLVEMENT AND DISEASE ACTIVITY IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: CALCULATION OF SWOLLEN TO TENDER JOINT COUNT RATIO IN A REAL WORLD COHORT IN THE US

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Background: Joint swelling and tenderness are common in patients with systemic lupus erythematosus (SLE). Swollen to tender joint count ratio (STR) is an index originally used in rheumatoid arthritis (RA) which assesses severity of disease activity based on 28 joint counts [1]. In RA, STR is a predictor of treatment response with a higher score indicating greater likelihood of responding.

Objectives: To characterize SLE patients in a real-world cohort based on disease activity as defined by STR.

Methods: The OM1 SLE Registry (OM1, Boston, MA) follows more than 37,000 SLE patients longitudinally with deep clinical data, including laboratory, patient-reported and disease activity information, and linked administrative claims, starting from 2013. Patients ≥16 years of age with swollen and tender joint counts based on 28 joints on the same encounter were included. STRs were calculated by inserting 1 if the denominator was 0 [2]. Patients were categorized by first available STR as having low (STR <0.5), moderate ($0.5 \leq STR \leq 1.0$), and high (STR >1.0) disease activity. Clinical characteristics were summarized by disease activity group. Definitions of SLE treatments were based on 2019 EULAR recommendations [3].

Results: As of December 2019, there were 9,919 patients with at least one STR available in the OM1 SLE Registry. STR was low in 80.4%, moderate in 12.2%, and high in 7.4% of patients. Mean age overall was 52.1 years (standard deviation: 14.8), 92.1% were female, and 71.8% of 7,730 patients with known race were white. Clinical characteristics by STR group are described in Table 1. Antimalarial use decreased and immunosuppressant use increased with increasing STR. Use of select disease-modifying antirheumatic drugs

(DMARDs) was higher among patients with moderate or high STR. Lupus nephritis was more common in patients with low STR. A higher proportion of patients with moderate STR had osteoarthritis. The proportion of patients with anxiety and depression decreased with increasing STR. On average, patient and physician global assessments from MDHAQ were higher for patients with moderate STR.

Table 1. Clinical characteristics of patients with SLE by swollen:tender joint count ratio group

	Low STR <0.5 (N=7,970)	Moderate 0.5 ≤ STR ≤ 1.0 (N=1,211)	High STR >1.0 (N=738)
Treatment prior to STR, n (%)			
Antimalarial	5,106 (64.1%)	702 (58.0%)	427 (57.9%)
Biologics (belimumab or rituximab)	662 (8.3%)	113 (9.3%)	70 (9.5%)
Immunosuppressants	2,310 (29.0%)	398 (32.9%)	252 (34.1%)
Select DMARDs	635 (8.0%)	165 (13.6%)	94 (12.7%)
Steroids	4,437 (55.7%)	785 (64.8%)	434 (58.8%)
Disease conditions prior to STR, n (%)			
Anxiety	266 (3.3%)	25 (2.1%)	12 (1.6%)
Depression	1,127 (14.1%)	149 (12.3%)	80 (10.8%)
Lupus nephritis	984 (12.3%)	117 (9.7%)	72 (9.8%)
Osteoarthritis	2,336 (29.3%)	393 (32.5%)	193 (26.2%)
Osteoporosis	631 (7.9%)	95 (7.8%)	47 (6.4%)
MDHAQ, N	1,991	388	230
MDHAQ, mean (SD)			
Patient global assessment (0-10)	4.5 (2.9)	5.3 (2.7)	4.4 (2.8)
Physician global assessment (0-10)	2.8 (2.7)	3.8 (2.6)	2.8 (2.3)

Conclusion: Differences in treatments received were apparent between patients of varying disease activity groups with trends towards increased use among patients with higher disease activity. Additional research is needed to determine the utility of this measure for assessing SLE-related outcomes.

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Disclosure of Interests: None declared
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FRI0187 IMMUNOGENICITY OF 23-VALENT POLYSACCHARIDE PNEUMOCOCCAL VACCINE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: EFFECT OF BIOLOGIC THERAPY ON THE VACCINAL RESPONSE

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Background: Vaccination with 23-valent polysaccharide pneumococcal vaccine (PPV-23) in systemic lupus erythematosus (SLE) provides the prevention of severe respiratory infections in patients receiving immunosuppressive therapy. The importance of this vaccination significantly increases before and during treatment with biologics.

Objectives: The aim of the study was to evaluate the immunogenicity of PPV-23 in SLE patients.

Methods: The study included 52 patients with SLE, including 44 women and 8 men, aged 19 to 68 years. The duration of the disease varied from 9 months to 39 years. At the time of vaccination 7 patients had high, 10 – moderate, 30 – low activity of the disease according to SLEDAI 2K, and 5 had remission. 50 patients received glucocorticoids (GC) 5-30 mg/day equivalent to prednisone, 39 – hydroxychloroquine (GCH), 29 – cytostatics (CS), 20 – biologics: 10 – rituximab (RTM), 10 – belimumab (BLM). 1 dose (0.5 ml) of PPV23 was administered subcutaneously. During the visits, standard clinical and laboratory tests were performed, and the level of antibodies (Ab) to S.pneumoniae in blood serum was determined (VaccZymeTMPCPIg 2 kits – The Binding Site Ltd, Birmingham, UK).

Results: In 1-2 months after the vaccination 78.7% of patients had a significant (more than 2 times compared to baseline) increase in the concentration of Ab to the pneumococcal cell wall polysaccharides. A year after vaccination, 61.5% of patients ("responders") had a significant increase in the concentration of anti-pneumococcal Ab. 20 (38.5%) of 52 patients were considered "non-responders". Median concentration of anti-pneumococcal Ab was 67[42.6; 105.8] mg/l at visit 1 (initially), 405[143.5; 468.4] mg/l at visit 2 (in 1-2 months), 166.9[77.5; 377.4] mg/l at visit 3 (in 12 months).

There were clear differences in the degree of the vaccinal response depending on the therapy: in 20 patients receiving biologics full vaccinal response was achieved significantly less frequently than in patients who did not receive these drugs (40% and 75%, respectively), p=0.02. There were no obvious differences in the vaccinal response during treatment with RTM and BLM (40% of responders in both groups). The vaccinal response significantly decreased during treatment with biologics in combination with GC+/ - GCH (50% of responders). The lowest vaccinal response was observed in patients receiving biologics in combination with GC and CS + / - GCH (33.3% of responders).

The analysis of the degree of the vaccinal response depending on the timing of vaccination and the time of biologics infusion was carried out. In the first group (n=6), vaccination was carried out at the optimal time in accordance with the recommendations of EULAR (2020). In the second group (n=14) vaccination was carried out in suboptimal time: during regular treatment with BLM (n=6), 1 week before the next introduction of RTM (n=2), 3-5 months after the last introduction of RTM (5), 1 week before the next introduction of RTM (n=1), 20 days after the BLM termination (n=1). In the first group with optimal vaccination terms, the number of responders was 66.7%, in the second group with suboptimal terms – 28.6%, p=0.27.

Conclusion: Sufficient immunogenicity of PPV-23 was shown in SLE patients receiving immunosuppressive therapy. The negative impact of biologics on the vaccinal response was confirmed, especially if the vaccination was not performed at the optimal time in relation to the infusion of the drug or during monthly administration of BLM. If optimal vaccination terms are maintained during the treatment with or initiation of biologics (6 months after the last administration of RTM and 1 month before the next (or first) administration of RTM, 4 months after the last and 1 month before the next (or first) administration of BLM), the number of responders increases significantly. The lowest vaccinal response was obtained in patients receiving combined immunosuppressive therapy with biologics + GC+CS.

Disclosure of Interests: None declared
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FRI0188 THE CLINICOPATHOLOGICAL SIGNIFICANCE OF MODIFIED NATIONAL INSTITUTES OF HEALTH ACTIVITY AND CHRONICITY SCORING SYSTEM IN LUPUS NEPHRITIS; A MULTICENTER RETROSPECTIVE STUDY

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Background: The revised International Society of Nephrology/Renal Pathology Society (ISN/RPS) Classification of lupus nephritis (LN) 2018 defined a modified National Institutes of Health activity and chronicity scoring system for all LN classes [1]. As this was not arrived at by an evidence-based approach, its clinicopathological significance including prognostic value should be validated [1]. Furthermore, though the activity index included wire-loop lesion and hyaline deposits (WL), we previously demonstrated that WL was associated with serological immune abnormality, but not renal prognosis [2].

Objectives: We conducted this study to clarify the relationships of modified activity score (AS) and chronicity score (CS) to clinical parameters at the time of renal biopsy and renal and life prognoses, and also to investigate the impact of AS without WL.

Methods: We enrolled 138 Japanese LN patients subjected to renal biopsy in 11 hospitals from 2000 to 2019. We measured clinical findings at the time of renal biopsy, and determined the presence of comorbidities. We also measured serum creatinine and estimated glomerular filtration rate (eGFR) at the last patient visit, and recorded medications prescribed for LN. Renal biopsy findings were classified by the modified ISN/RPS classification 2018 including AS and CS for all LN classes. On stepwise multivariate analysis, we applied the variables with significant differences in univariate comparisons. The primary endpoint was chronic kidney disease (CKD; eGFR <60 ml/min/1.73m^2) and/or death.

Results: Of 138 patients (116 females; median 39 years old), class I, II, III, IV, and V included 2 (1.4%), 13 (9.4%), 43 (31.2%), 69 (50.0%), and 11 (8.0%), respectively. Median AS, AS without WL (AS-WL), and CS were 4, 3, and 2, respectively. AS ≥5 group (61 patients, 44.2%) had higher proteinuria, hematuria and serum anti-ds DNA antibodies levels and lower serum total protein (TP) and C3 levels than AS <5 group. CS ≥3 group (58 patients, 42%) had higher age, proteinuria, serum C3 levels, and frequency of hypertension (HT) and lower eGFR and serum anti-ds DNA antibodies and IgG levels than CS<3 group. Multiple regression analysis revealed significant associations between AS and hematuria, TP and C3 (β=0.312, -0.281, -0.213; p<0.001, 0.001, 0.009), and between CS and age (β=0.300; p=0.010). Next, patients who achieved the primary endpoint had higher age, frequencies of HT and hyperlipidemia and lower eGFR, serum TP and IgG levels than patients who did not. Observation period (median 36 vs 47 months, p=0.696) and medications for LN did not differ between these groups. Cox regression analysis revealed significant associations of prognosis

with eGFR and TP clinically (β=0.955, 3.349; *p*=0.025, 0.008), and with CS pathologically (β=1.231, *p*=0.028). Neither AS nor AS-WL was included in the prognostic factors. Kaplan-Meier method with log-rank tests showed a significant difference in cumulative rate of CKD and/or death between CS ≥3 and CS <3 groups (*p*=0.049).

Conclusion: AS and CS were related to different clinical parameters at the time of renal biopsy. CS was associated with renal and life prognoses, while neither AS nor AS-WL was. These results revealed that these scores have different clinicopathological significance in LN.

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FRIDAY, 05 JUNE 2020

Vasculitis

FRI0189 ENDOTHELIAL PROTEIN C RECEPTOR AND SCAVENGER RECEPTOR CLASS B TYPE 1 NEGATIVELY REGULATE ENDOTHELIAL ACTIVATION AND REPRESENT NOVEL AUTOANTIGENS IN TAKAYASU ARTERITIS

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Background: Takayasu arteritis (TAK) is a chronic granulomatous vasculitis and affects large vessels in young female. It has been recognized that high numbers of patients with TAK possessed autoantibodies against vascular endothelium, which are called anti-endothelial cell antibodies (AECAs). Although their target antigens had not been identified for a long time, we utilized an expression cloning system for specific identification of cell-surface antigens and successufully identified endothelial protein C receptor (EPCR) and scavenger receptor class B type 1 (SR-BI) as major novel autoantigens in TAK. It was possible that identified novel autoantibodies were utilized for clinical application and elucidating pathomechanisms of TAK.

Objectives: To reveal the clinical impact and pathogenic potential of novel autoantibodies in TAK

Methods: Three hundred twenty-five patients with autoimmune diseases were enrolled: 80, TAK; 10, giant cell arteritis (GCA); and 235, other autoimmune diseases. The expressions of EPCR and SR-BI were examined in the aortic tissue from several diseases by immunohistochemistry. The presence of novel autoantibodies was measured in TAK and other autoimmune diseases. Clinical characteristics of patients with these autoantibodies were evaluated in TAK. To investigate the pathogenetic potential of these novel autoantibodies, vascular endothelial cells from umbilical vein, aortic artery, and pulmonary artery were examined for the endothelial cell activation. The effects of the novel autoantibodies upon the differentiation of immune cells were also evaluated.

Results: In non-inflammatory aortic tissue, the expressions of EPCR and SR-BI were observed in the endothelium of vasa vasorum. Their expressions in the endothelium were augumented in TAK tissue. Novel autoantibodies against EPCR or SR-BI were detected in 34.6 % or 36.5 % of cases, respectively in TAK, and overlap was obsereved only in two cases, indicating their exclusive nature. These autoantibodies were specific for TAK among autoimmune rheumatic diseases, and they were not detected in patients with GCA with cranial involvement, suggesting different pathomechanisms among these diseases. The clinical characteristics of patients with anti-EPCR autoantibodies included high prevalence of stroke and ulcerative colitis. Surprisingly, anti-EPCR autoantibodies were also detected in patients with primary ulcerative colitis, suggesting their common pathomechanisms with TAK. Serial measurement of these novel autoantibodies revealed their correlation with disease activity of TAK. In machanistic studies, EPCR and SR-BI functioned as negative regulators of endothelial activation and chemokine production. EPCR further functioned in human T cells and ameliorated Th17 differentiation. Autoantibodies against EPCR and SR-BI blocked the functions of their targets, thereby promoting pro-inflammatory phenotype.

Conclusion: EPCR and SR-BI are preferentially expressed in the endothelium of vaso vasorum and upregulated in TAK tissue. Autoantibodies against EPCR or SR-BI are specific for TAK among autoimmune rheumatic conditions and detected in about 70 % of TAK, suggesting their usefulness for the diagnosis, subclassification, and monitoring of TAK. Autoantibodies inhibit the resolution of activated immune responses and thus would lead to the chronic vascular inflammation.

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FRI0190 COMPARATIVE EFFICACY AND SAFETY OF MYCOPHENOLATE MOFETIL VERSUS CYCLOPHOSPHAMIDE IN PATIENTS WITH ACTIVE ANTINEUTROPHIL CYTOPLASMIC ANTIBODY-ASSOCIATED VASCULITIS: A META-ANALYSIS OF RANDOMIZED TRIALS

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Background: Cyclophosphamide (CYC) is effective for induction of remission of AAV, resulting in complete remission rates of around 70%. Thus, CYC has been the standard remission induction therapy for antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV); however, it is toxic and causes infections, malignancies, and infertility. Therefore, other agents that are less toxic but that have similar efficacy were explored. Since the disease course of AAV usually requires long-term immunosuppression, mycophenolate mofetil (MMF), a less toxic agent compared to CYC, has been explored as an alternative to CYC.

Objectives: The aim of this study is to assess the efficacy and safety of MMF versus cyclophosphamide CYC in patients with active AAV.

Methods: We performed a meta-analysis of four randomized clinical trials (RCTs) (300 patients) to examine the relative efficacy and safety of MMF compared to CYC in patients with active AAV.

Results: There was no significant difference in remission at 6 months between MMF and CYC (OR 1.311, 95% confidence interval [CI] 0.570 – 3.017, *P* = 0.524). Additionally, the relapse rate did not differ between the MMF group and CYC group (OR 1.331, 95% CI 0.497 – 3.568, *P* = 0.570). There was no significant difference in serious adverse event (SAE) (OR 1.232, 95% CI 0.754 – 2.014, *P* = 0.404) and infection rate (OR 0.958, 95% CI 0.561 – 1.634, *P* = 0.873) between the MMF and CYC groups. Some heterogeneity was found in the meta-analysis of remission and relapse rate (*I2* = 57.4%, 63.4%), but no between-study heterogeneity was found during the meta-analysis of the SAE and infection rate. Egger's regression test showed no evidence of publication bias (Egger's regression test *P*-values > 0.1).

Conclusion: MMF was an equally effective alternative treatment to CYC, and MMF was comparable to CYC in patients with active AAV in terms of safety, suggesting that MMF can be used as an alternative to CYC for remission induction in AAV.

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FRI0191 CRANIAL-LIMITED AND LARGE-VESSEL GIANT CELL ARTERITIS: PRESENTING FEATURES AND OUTCOME

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Background: Giant cell arteritis (GCA) comprises two main phenotypes: cranial (C) and large-vessel (LV) disease[1]. A full baseline steroid-free vascular imaging evaluation is required to properly diagnose LV involvement[2]

Objectives: To compare presenting and prognostic features of LV-GCA and C-GCA patients after an adequate vascular imaging evaluation at baseline
Methods: Data from GCA patients followed-up at our Institution were retrospectively collected. Only patients who underwent large-vessel imaging (PET, CTA, MRA) at disease onset or within 1 week after steroid introduction were included. Patients with evidence of LV involvement were classified as LV-GCA. Differences between LV-GCA and C-GCA patients regarding presenting features, treatment, prognosis were evaluated. Non-parametric tests were used
Results: In our cohort, we identified 161/280 patients who underwent LV-imaging study at baseline. Of these, 100 (62.1%) had signs of LV inflammation. Table 1 compares demographic features, diagnostic delay, pre-existing comorbidities and complementary treatment between the 2 groups. Table 2 compares disease features at diagnosis. Mean follow-up was similar between LV- and C-GCA patients (31.8±31.8 vs 27.8±29.1 months; 70% vs 73.8% followed-up ≥12 months). Corrected cumulative prednisone dose (CCPD, grams/months) was equivalent (LV, 0.67±0.57; C, 0.87±1.37; p=0.871). A DMARD was added in 73% of LV- and in 55.7% of C-GCA patients (p=0.027), but, notably, it was introduced at baseline in 52% of LV- vs 23.5% of C-GCA patients (p=0.006). CCPD was equivalent even considering only patients who did not receive DMARDs (LV, 0.92±0.81; C, 0.94±1.18; p=0.522). Frequency of relapses was not significantly different (LV, 51%; C, 57.3%, p=0.515), even when considering only DMARD-receiving patients (LV, 36.1%; C, 38.2%, p=0.833). Aortic aneurysms incidence at 5 years was similar (LV, 17.3%; C, 15.7%; p=0.826). Rate of metabolic and infective complications was similar, in terms of arterial hypertension (LV, 3%; C, 0%, p=0.286), diabetes (2% vs 0%, p=0.524), osteoporotic fractures (7% vs 5%, p=0.742), severe infections (3% vs 3.3%, p=1)

Table 1. Demographic features, diagnostic delay, pre-existing comorbidities, and complementary treatment at baseline in LV and C-GCA patients

	LV imaging + n=100 (%)	LV imaging - n=61 (%)	p-value
Age (years)	73.2 ± 8.9	76 ± 8.8	0.018
Sex (female)	65 (65)	40 (65)	1
Diagnostic delay (months)	3.5 ± 4.6	2.3 ± 4.9	0.001
Pre-existing comorbidities			
- CAD	3 (3)	7 (11.5)	0.043
- Diabetes	4 (4)	6 (9.8)	0.181
- Dyslipidemia	17 (17)	17 (27.9)	0.114
- Hypertension	42 (42)	34 (55.7)	0.105
- Stroke	3 (3)	3 (5)	0.674
- Cancer	20 (20)	6 (9.8)	0.122
Ongoing complementary treatment			
- Antiplatelet	18 (18)	15 (25)	0.322
- Anticoagulant	1 (1)	6 (9.8)	0.012
- Statin	14 (14)	14 (23)	0.198

Table 2. Diseases features at onset in LV and C-GCA patients

	LV imaging + n=100 (%)	LV imaging - n=61 (%)	p-value
Temporal biopsy positive	17/31 (55)	9(43)	0.573
Symptoms			
- Headache	65 (65)	52 (85)	0.006
- Jaw claudication	22 (22)	20 (32.8)	0.142
- Scalp tenderness	31 (31)	26 (42.6)	0.174
- Ocular symptoms	14 (14)	20 (32.8)	0.006
- Ischemic optic neuropathy	7 (7)	17 (27.9)	<0.001
- Stroke	3 (3)	0 (0)	0.290
- Polymyalgia rheumatica	42 (42)	31 (50.8)	0.328
- Fever	44 (44)	12 (19.7)	0.002
- Fatigue	72 (72)	21 (34.4)	<0.001
- Weight loss	37 (37)	7 (11.5)	<0.001
- Cough	10 (10)	1 (1.6)	0.053
Laboratory findings, mean			
- C-reactive protein, mg/L	80.8 ± 60.8	65.7 ± 58.2	0.057
- Erythrocyte sedimentation rate	76.8 ± 30	71.5 ± 27	0.360
- Hemoglobin, g/dL	11.4 ± 1.5	12 ± 1.6	0.007
- Platelet count	389.4 ± 116.6	366.8 ± 125.2	0.758

Conclusion: LV-GCA patients are younger and suffer of a greater diagnostic delay. Although a greater systemic inflammation seems to be a feature of LV-GCA patients, the vascular prognosis is similar to C-GCA patients, who, conversely, have a greater incidence of ocular complications
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FRI0192 **MORTALITY IN IGA VASCULITIS: A LONGITUDINAL POPULATION-BASED STUDY**

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Background: There is sparse population-level data on outcome in patients with Immunoglobulin-A vasculitis (IgAV) and none from Australia
Objectives: We compared long-term mortality for paediatric and adult IgAV patients with age- and gender-matched controls.
Methods: Linked health data for pediatric (<20 years=473) and adult (20+ years, n=267) IgAV patients were obtained from state-wide hospital and deaths registries in Western Australia for the period 1980-2015. All-cause mortality rates (MR) (deaths/1000 person-years) were compared with controls using mortality rate ratios (MRR) and with the general population of Western Australia by standardised mortality rate ratios (SMRR) with Poisson derived 95% confidence intervals (CI). We used Kaplan-Meier survival estimates and multivariate Cox regression derived hazard ratios (HR) for time dependent analyses.
Results: In pediatric patients (mean age 7.2 years, 60 % male) MRR was 1.27 (CI: 0.34-4.08, p=0.68) and SMRR was 2.31 (CI: 0.72-5.7, p=0.47) (Table 1) with a 20-year survival rate (>99%) similar to controls. Despite higher rates of renal failure (1.5% vs 0.2%, p=0.002) deaths in pediatric IgAV patients were mainly from unrelated causes. In adult IgAV patients (mean age 55.8 years, 48% males) MMR was 2.06 (CI 1.70-2.50, p<0.01) and SMRR 6.16 (3.04 -14.3, p<0.01) (Table) during a mean of 19.5 years follow-up with significantly reduced survival at five (72.7 vs. 89.7 %) and twenty years (45.2% vs. 65.6 %) (p<0.05). Renal disease (HR: 1.47, CI 1.04 - 2.06), the presence of any comorbidity (HR:1.30, CI 1.23 - 1.37) and male gender (HR:1.23; CI 1.04 - 1.47) were independent predictors of death. While cardiovascular events (34.2%) and malignancy (19.4%) were the most frequent causes of death, only death from infections (5.8 vs 1.8%, p=0.02) and renal disease (3.6 vs 1.8%, p=0.03) were more frequent in adult IgAV patients than controls.
Mortality data for childhood and adult-onset IgAV patients and controls. Figures indicate mean (±SD), numbers (%) or rate/1000 patient months (95% CI)

	Pediatric			Adult		
	IgAV	Controls	P value	IgAV	Controls	P
Mean follow-up (yrs)	22.71 (±5.2)	23.75 (±3.17)	0.001	11.9 (±9.04)	15.94 (±8.30)	0.001
Non-survivors (%)	<5 (0.8)	9 (0.9)	0.5	137 (51.3)	394 (33.4)	<0.001
Person-years	10275	29520		3178	18815	
MR	0.39 (0.1, 0.9)	0.30 (0.1, 0.5)		43.11 (36,1,50.9)	20.94 (18.9, 23.1)	
MRR	1.27 (0.34, 4.08)		0.67	2.06 (1.70, 2.50)		<0.001
SMRR	2.31 (0.71, 5.71)		0.71	6.16 (3.04, 14.3)		<0.001

Conclusion: Compared to controls and general population, mortality risk was not increased in paediatric IgAV patients for at least 20 years following diagnosis despite a higher rate of end stage renal failure. However, in adult IgAV patients, all-cause mortality risk was six times higher than in the general population leading to significantly reduced five-year survival, especially for male patients with comorbidity including renal disease.
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FRI0193 **ULTRASONOGRAPHY IN THE DIAGNOSIS OF GIANT CELL ARTERITIS**

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Background:
Objectives: To evaluate the frequency of cranial and aortic arch artery involvement in GCA using color Doppler ultrasonography (CDS).
Methods: We performed CDS of cranial and aortic arch arteries in 248 incipient, clinically diagnosed, GCA patients (64.9% females, median (IQR) age 75 (67-80) years) between October 2013 and September 2019, using a Philips IU22 with 5–17.5 MHz linear probe or Philips Epiq 7 with 5–18.5 MHz linear probe. Temporal, facial, occipital, carotid, vertebral, subclavian, and axillary arteries were examined bilaterally. A halo with positive compression sign was considered a positive finding. Additionally, the thickness of intima-media complex (IMT) of individual vessel was measured, and compared to the IMT of 97 consecutive suspected GCA cases (60.8% females median (IQR) age 74 (65-81) years), in whom GCA was excluded, that served as a control group.
Results: The CDS was positive in 244 (98.4%) patients in at least one of the examined arteries. Temporal arteries were most commonly affected, and were involved in 192 (77.4%) patients, followed by facial and occipital arteries, involved in 122 (49.2) and 72 (29.0%) patients, respectively. Extracranial large vessel involvement (LVV) was found in 87 (35.1%) patients (32 patients had isolated LVV, and 55 concomitant cranial and LVV artery involvement). Among the 161 patients without LVV, 12 (4.8% of the studied cohort) had involvement of cranial arteries other than temporal arteries (we found facial and occipital artery involvement in 11 and 3 patients, respectively). Table 1 shows the frequency of individual vessel involvement in GCA, and the IMT of CDS inflamed and non-inflamed arteries in GCA, and in controls.

Table 1. The involvement of cranial and aortic arch arteries in GCA assessed by CDS and intima-media thickness of inflamed and non-inflamed arteries in GCA, and controls

Artery	GCA No (%)	IMT (mm) in GCA		IMT (mm) in Controls
	Positive CDS	Positive CDS*; minimal	Negative CDS	Negative CDS; maximal
Temporal	192 (77.4)	0.71±0.19; 0.33	0.25±0.07	0.23±0.05; 0.46
Facial	122 (49.2)	0.75±0.27; 0.41	0.29±0.07	0.26±0.07; 0.47
Occipital	72 (29.0)	0.73±0.33; 0.45	0.26±0.06	0.23±0.05; 0.46
Carotid	34 (13.7)	1.53±0.44; 0.88	0.78±0.18	0.72±0.15; 1.09
Vertebral	25 (10.1)	1.33±0.47; 0.74	0.45±0.10	0.42±0.08; 0.63
Subclavian	67 (27.0)	1.65±0.45; 0.91	0.70±0.14	0.70±0.13; 0.99
Axillary	59 (23.8)	1.74±0.65; 1.00	0.61±0.17	0.57±0.13; 0.97
Any artery	244 (98.4)	-	-	-

Legend: GCA giant cell arteritis; IMT thickness of intima-media complex; * mean±SD;

Conclusion: CDS of seven preselected cranial and aortic arch arteries provides a high diagnostic yield in GCA.
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FRI0194 **IDENTIFYING PHENOTYPES OF PATIENTS WITH BEHÇET'S SYNDROME BY A CLUSTER ANALYSIS IN A LARGE COHORT**

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Background: Behçet's syndrome (BS) is a clinical entity with heterogeneous clinical manifestations (1). The symptoms and major organ involvement of BS tend to vary among gender and age (2).
Objectives: To investigate the gender associated clinical features and aggregate of patients with BS based on phenotypes and organ involvement in a well-defined large cohort of patients with BS.
Methods: This was a single-center study of 1,596 consecutive BS patients in Shanghai, China from 2012 September to 2019 December. We compared clinical variables and conducted a hierarchical cluster analysis applied according to twenty-five clinical variables to determine subgroups of patients.
Results: A total of 850 BS patients were included. Male gender was associated with ocular involvement (RR 2.33), vascular involvement (RR 2.05) and cardiac lesions (RR 5.52). Female gender associated with genital ulcers (RR 0.85). Four clusters (C1–C4) were yielded. Cluster C1 (n=165, 19.9%), merely oral and genital ulcer type: consisted predominantly of older females. Disease severity was relatively low, Krause score = 2.32. In C2 (n=365, 43.9%), mix type: was an equal gender distribution with older onset age. Most patients had erythematous nodosum (64.1%) and genital ulcers (82.2%). Cardiac and vascular involvement were observed in 9.3% and 12.1%, which were the highest frequencies among the four clusters. C3 (n=160, 19.3%), intestinal type: was an equal sex ratio with older onset age. All patients presented with intestinal ulcer, while fewer patients had erythematous nodosum and pseudofolliculitis, 20.0% and 25.0% respectively. In C4 (n=141, 17.0%), uveitis type: was predominantly male with younger onset age. Intestinal involvement was negatively associated with uveitis [0.24, (0.13, 0.46), P < 0.0001]. No patients had cardiac involvement in C3 or C4. Regarding the sensitivity of classification criteria, Cheng and Zhang (China) remain the highest in all clusters compared with Japan revised criteria, ICBD, ISG.
Conclusion: From our large cohort, the gender-phenotypes analyses suggest that male is a risk factor for ocular and cardiovascular in BS patients. We identify four unique subphenotypes representing different clinical features, intestinal and ocular phenotype clusters represent the two most common manifestations of major organ involvement in BS.
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TABLE 1. Characteristics of patients with Behçet's syndrome after clustering on clinical manifestations

Characteristics	C1 (n=165)	C2 (n=356)	C3 (n=160)	C4 (n=141)
Age at onset (IQR), years	29 (20-40)	28 (20-35)	27 (20-38)	**25 (19-32)**
Disease duration (IQR), years	5 (3-10)	8 (3-10)	6 (3-10)	7 (4-10)
Male gender (%)	**38.9**	52.3	51.2	**75.2**
Classification criteria				
JPN (%)	0	69.6	25.0	83.7
CHN (%)	98.8	96.7	97.5	99.3
ICBD (%)	98.8	89.9	65.6	99.3
ISG (%)	0.6	72.1	25.0	81.6
Oral ulceration (%)	100	100	98.1	99.3
Genital ulceration (%)	98.2	82.2	63.1	58.9
Erythema nodosum (%)	0	64.1	20.0	48.9
Pseudofolliculitis (%)	0	34.5	25.0	27.0
Arthritis/Arthralgia (%)	0	36.2	11.6	14.2
Uveitis (%)	0.6	0.8	1.9	**100**
Gastrointestinal involvement (%)	0	1.1	**100**	**2.7**
Vascular involvement (%)	2.4	**12.1**	1.2	4.3
Cardiac lesion	3.6	9.3	**0**	**0**
Central nerve system involvement (%)	4.2	3.8	2.5	3.5

JPN: Japan revised criteria; CHN: Cheng and Zhang (China) criteria; ICBD: International Criteria for Behçet's disease; ISG: International Study Group for Behçet's disease.

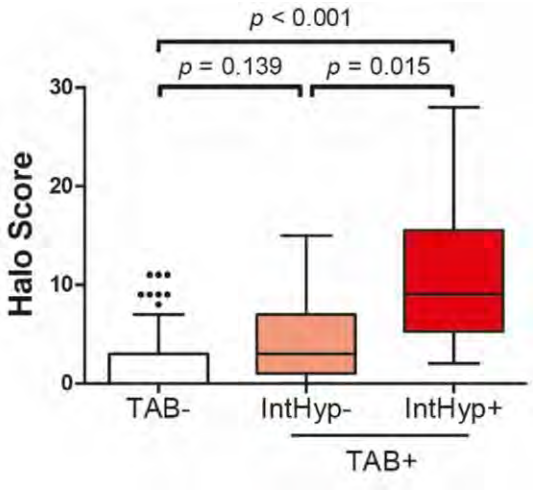
Disclosure of Interests: None declared
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FRI0195 **ULTRASONOGRAPHIC HALO SCORE ASSOCIATES WITH INTIMAL HYPERPLASIA IN GIANT CELL ARTERITIS**

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Background: We have recently developed a novel ultrasonographic Halo Score to quantify the extent of vascular inflammation in GCA [1]. High Halo Scores were associated with a high rate of ocular ischaemia among patients with GCA. Earlier studies have shown that GCA patients with intimal hyperplasia in their temporal artery biopsy (TAB) are at the highest risk of neuro-ophthalmic, ischaemic complications [2,3]. We therefore questioned whether the ultrasonographic Halo Score might be linked to the presence of intimal hyperplasia in patients with GCA.
Objectives: To investigate the relationship between the ultrasonographic Halo Score and intimal hyperplasia.
Methods: This is a prospective study including 92 patients suspected of having GCA, who underwent both ultrasound of temporal/axillary arteries and TAB at diagnosis. Ultrasonographic halo counts and Halo Scores were determined [1]. An experienced pathologist determined whether or not the TAB findings were consistent with GCA. TABs were systematically evaluated for the presence of a transmural infiltrate and intimal hyperplasia. Multiple linear regression analysis was performed with either halo counts or Halo Scores as the dependent variable.

Predictive variables included the presence of a transmural TAB infiltrate, intimal hyperplasia and male sex.
Results: The TAB was consistent with GCA in 27 patients. The TAB revealed transmural inflammation in 18 patients and giant cells in 24 patients. Intimal hyperplasia was found in 20 patients with a positive TAB. Patients with a positive TAB showed higher halo counts and Halo Scores than patients with a negative TAB. Overall, patients with a positive TAB and intimal hyperplasia presented with the highest halo counts and Halo Scores (Figure). Among patients with a positive TAB, only intimal hyperplasia and male sex were predictive of higher halo counts and Halo Scores in the multiple linear regression analysis. Ocular ischaemia was present in 14% of patients with a positive TAB without intimal hyperplasia. However, 40% of patients with a positive TAB and intimal hyperplasia suffered from ocular ischaemia.
Conclusion: The ultrasonographic Halo Score is strongly influenced by the presence of intimal hyperplasia, a TAB feature that associates with cranial ischemic complications in patients with GCA [2,3].
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Figure

Disclosure of Interests: Kornelis van der Geest Speakers bureau: Roche (2019), Frances Borg: None declared, Konrad Wolfe: None declared, Wolfgang A. Schmidt Grant/research support from: GSK, Novartis, Roche, Sanofi, Consultant of: GSK, Novartis, Roche, Sanofi, Chugai, Raashid Luqmani Grant/research support from: Arthritis UK, the Medical Research Council, the University of California San Francisco/Oxford Invention Fund, the Canadian Institutes of Health Research, The Vasculitis Foundation, GSK, Consultant of: GSK, Medpace, MedImmune, Roche, Bhaskar Dasgupta Grant/research support from: Roche, Consultant of: Roche, Sanofi, GSK, BMS, AbbVie, Speakers bureau: Roche
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FRI0196 **INVOLVEMENT OF THE PULMONARY ARTERIES IN PATIENTS WITH TAKAYASU ARTERITIS**

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Background: Takayasu arteritis (TA) is a chronic, granulomatous large-vessel vasculitis. It involves the aorta and its main branches predominantly, and leads to vascular thickness, stenosis and occlusion [1]. Besides the aorta and its branches, pulmonary arteries (PAs) are involved in TA. PAs have been reported to be involved in 6.9% to 80% of TA patients from different populations [2-3].
Objectives: We investigated the clinical characteristics, pulmonary parenchymal features and cardiac functions in TA patients with PA involvement by combining multiple imaging modalities (MRA, CTA, PET-CT, lung VQ scan, echocardiography and high-resolution computed tomography (HRCT)). Our aim was to elicit better understanding of TA patients with PA involvement to aid rational treatment for these patients and improve their prognosis.
Methods: We enrolled 216 patients with TA from a large prospective cohort. PAI was assessed in each patient based on data from magnetic resonance angiography/computed tomography angiography. Pulmonary hypertension, cardiac function, and pulmonary parenchymal abnormalities were evaluated further in patients with PAI based on echocardiography, New York Heart Association Functional Classification and pulmonary computed tomography, respectively. These abnormalities related to PAI were followed up to evaluate treatment effects.
Results: PAI was detected in 56/216 (25.93%) patients, which involved the pulmonary trunk, main PAs and small vessels in the lungs. Among patients with PAI, 28 (50%) patients were accompanied by pulmonary hypertension, which was graded as 'severe' in 9 (16.07%), 'moderate' in 10 (17.86%) and mild in 9 (16.07%). Forty (71.43%) patients had cardiac insufficiency (IV: 6, 10.71%; III: 20, 35.71%; II: 14, 25.00%). Furthermore, 21 (37.50%) patients presented with abnormal parenchymal features in the area corresponding to PAI (e.g., the mosaic sign, infarction, bronchiectasis). During follow-up, two patients died due to abrupt pulmonary thrombosis. In the remaining patients, the abnormalities mentioned above improved partially after routine treatment.
Conclusion: PA involvement is very common in TA patients. Physicians should be alerted to PA involvement even if obvious pulmonary symptoms are absent because they can cause PH, cardiac insufficiency as well as pulmonary parenchymal lesions, which will worsen the prognosis.
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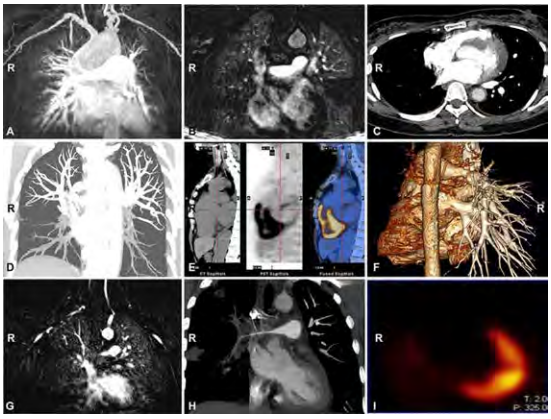


Figure 1. Imaging of PA lesions in TA patientsA: **Dilation** of the pulmonary trunk; B: thickness of the pulmonary trunk; C: stenosis of the right main PA; D: embolism of lower PAs on both sides; E: inflammation of the pulmonary-trunk root upon PET–CT; F: absence of left PAs and stenosis of the right main PA; G–I: pulmonary MRA (G), CTA (H) and VQ scan (I) of a patient with TA. MRA shows a fine right main PA and low perfusion in the right lung (G); CTA demonstrates a fine right main PA and fewer PA branches in the right lung (H); lung VQ scan shows multiple arterial emboli in the right lung and obvious less blood supply to the right lung.

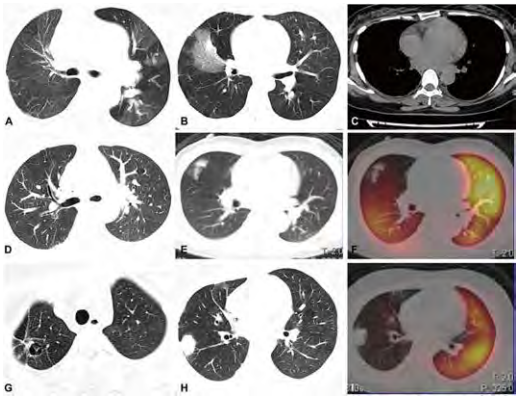


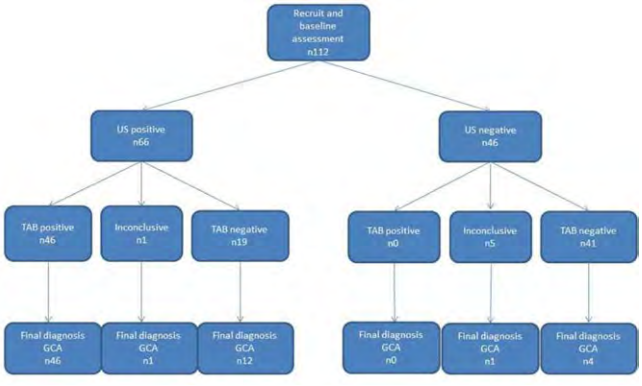
Figure 2. Pulmonary lesions on HRCT. A: The **mosaic** sign in the left lung; B: Pulmonary infarction of the right middle lobe; C: Mild pleural effusion on the left side; D: Bronchiectasis in the right lung; E–F: Ground-glass opacity (E) in the right upper lobe of a TA patient with an embolism of the right upper pulmonary branches (F); G–I: Cavitation (G) and mass-like consolidation (H) in the patient with severe stenosis of right main pulmonary artery (I).

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FRI0197 **THE DIAGNOSTIC ACCURACY OF VASCULAR ULTRASOUND IN PATIENTS SUSPECTED OF GCA: A DANISH MULTICENTRE PROSPECTIVE COHORT STUDY**

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Background: Giant Cell Arteritis (GCA) is one of the most common systemic vasculitis. Temporal artery biopsy (TAB) has been the standard test to confirm the diagnosis of GCA. However, TAB has a lower sensitivity than clinical diagnosis and up to 44% of biopsy-negative patients are clinically diagnosed as having GCA. In a recent meta-analysis of the diagnostic performance of ultrasound (US) in GCA the sensitivity was 77 % (1). The included studies were performed by expert groups in single centres. In the to date only multicentre study (TABUL) investigating the diagnostic accuracy of US compared to clinical diagnosis after 6 months the sensitivity was lower (54%) (2)
Objectives: To evaluate the diagnostic accuracy of vascular US compared to TAB in a multicentre study.
Methods: In three Danish centres patients suspected for GCA were included during a period of two years. At baseline, clinical and laboratory data were collected and vascular US of temporal, facial, common carotid and axillary artery were performed. The US examinations were performed with high frequency transducers (15-18 MHZ) and followed by a TAB. All ultrasonographers had participated in the same standardized US educational program and were blinded to clinical and laboratory data. An external expert blinded to clinical and laboratory data evaluated all images and made the final US diagnosis.
A positive sign for vasculitis in cranial arteries was defined as a hypoechoic intima media complex (IMC) thickening (halo sign) and a positive compression sign. A homogeneous IMC increased thickness in axillary artery of ≥1mm and in common carotid artery ≥1.5mm was defined as vasculitis.
The consultant rheumatologist's diagnosis at 6 months after initial presentation was considered as the reference standard for the diagnosis of GCA.
Results: During the recruitment period, 112 patients were included, 59% females, mean (SD) age 72.4(7.9) years, among which 91(81.3%) fulfilled the ACR 1990 classification criteria for GCA. 92% of the patients reported a newly emerged localized headache, while 49 (43.8%) experienced polymyalgia rheumatic symptoms.
TAB was positive in 46(41.1%) and inconclusive in 6 patients, who were excluded from the analysis. Mean (SD) duration of glucocorticoid therapy prior to US and TAB was 0.91(1.55) and 4.02(2.61) days, respectively. In 62 patients, the final diagnosis was GCA.
In all patients with a positive TAB, the US of the temporal artery was also positive for GCA. Of 19 cases with positive US and negative TAB, 12 were clinically diagnosed with GCA of whom 6 had isolated large vessel involvement on US. Among 41 patients with both negative US and TAB, 4 were clinically diagnosed with GCA (Box 1)
US had a sensitivity of 93% and specificity of 84% for the diagnosis of GCA, while the sensitivity for TAB was lower (74%) with a specificity of 100%. For the diagnosis of GCA, US had a PPV of 89.2 % and a NPV of 90.2%, while for TAB the PPV was 100% and the NPV 73.3%.
Conclusion: US evaluation of the temporal, facial and selected supraaortic arteries performed by trained ultrasonographers can replace biopsy in the diagnosis of GCA.



Box.1

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Disclosure of Interests: stavros chrysidis: None declared, Uffe Møller Døhn: None declared, Lene Terslev Speakers bureau: LT declares speakers fees from Roche, MSD, BMS, Pfizer, AbbVie, Novartis, and Janssen., Ulrich Fredberg: None declared, Tove Lorenzen: None declared, Robin Christensen: None declared, Per Søndergaard: None declared, Jakob Matthisson: None declared, Knud Larsen: None declared, Andreas Diamandopoulos: None declared
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FRI0198 **OCULAR MORBIDITY IN PATIENTS WITH PMR AND GCA IN THE UK - A CPRD STUDY**

M. Yates[1,2], A. Clark[1], R. Watts[2], A. Macgregor[1], S. Mackie[3]on behalf of Dr Max Yates is part of the TARGET (Treatment According to Response in Giant ceLL arTeritis) consortium, the UK BioBank Eye and Vision Consortium and an active member of two OMERACT (Outcome Measures in Rheumatology) Working Groups: PMR and Patient Outcomes in Longitudinal Observational Studies.. [1]*University of East Anglia, Norwich Medical School, Norwich, United Kingdom*; [2]*Ipswich Hospital, Rheumatology, Ipswich, United Kingdom*; [3]*Chapel Allerton Hospital, Rheumatology, Leeds, United Kingdom*

Background: Visual loss is the most serious consequences of a diagnosis of polymyalgia rheumatic (PMR) and giant cell arteritis (GCA). To date, information on the occurrence of eye disease in GCA has been based almost exclusively on small hospital-based patient series. Furthermore the lack of control group for these studies results in a lack of relative risk estimates for visual loss.
There are no accurate data on the prevalence and nature of eye complications among patients in the community. Patients with GCA may be exclusively managed in the primary care setting without referral for either temporal artery biopsy or ophthalmic department examination. Currently the incidence and prevalence of eye complications within this group are unknown.
Objectives: Examine the absolute rate and relative risk of ocular morbidity, in a longitudinal community setting, in patients with PMR and or GCA including visual loss, AOIN including optic atrophy, cataract and glaucoma identified from Read codes in the (Clinical Practice Research Datalink) CPRD dataset.
Methods: Construction of a disease cohort of incident diagnoses of PMR and GCA from patients in the CPRD matched to controls on age, sex (+/- 2 years) and practice location. Diagnosis were identified by CPRD researchers of those individuals between January 1997 to December 2015, with a minimum age at diagnosis of 50 years. Those with both a diagnosis of PMR and GCA were analysed in the GCA group. The outcomes of ocular morbidity included Read codes for severe visual impairment (multiple codes covered: blindness, severe visual impairment, registered partially sighted, issue of certificate of visual impairment, examination findings of 4/60 or worse), anterior ischaemic optic neuropathy (including codes of optic neuropathy and atrophy but not codes of glaucomatous atrophy), cataract, cataract extraction and glaucoma. Statistically modelling with Cox proportional hazards was used to generate hazard ratios for ocular morbidity taking account of censorship through death and moving out of area.
Results: We identified 30,714 individuals with PMR (20,270 women; 66%) with a mean age at diagnosis of 72.9 year (sd 9.1) and 6,104 with GCA (4,309 women; 70.6%) with a mean age of 72.1 years (sd 9.4). Of those diagnosed with GCA 1,669 were also diagnosed with PMR. Using Read codes for severe visual impairment and blindness 5.9% of patients with GCA and 2.7% with PMR had this complication compared with 1.6% of the matched controls. The hazard ratio for the various ocular morbidities and by cases of PMR or GCA are shown in the table below:

Ocular morbidity	PMR HR (95% CI) p value	GCA HR (95% CI) p value
Severe visual impairment	1.76 (1.60, 1.94) p=<0.001	3.55 (3.10, 4.08) p=<0.001
Anterior ischaemic optic atrophy	3.37 (2.15, 5.31) p=<0.001	36.33 (25.19, 52.39) p=<0.001
Cataract	2.18 (2.04, 2.32) p=<0.001	2.48 (2.22, 2.78) p=<0.001
Cataract operation	2.11 (1.97, 2.25) p=<0.001	2.41 (2.13, 2.72) p=<0.001
Glaucoma	2.10 (1.91, 2.32) p=<0.001	2.50 (2.10, 2.97) p=<0.001

Conclusion: These community-based national data on risk of ocular morbidity in PMR and GCA show for the first time the risk of various ocular morbidities are increased for both groups. In addition this are the first estimates of relative risk compared to an age and sex matched population. These data are crucial

for providing information to patients about their relative risk of ocular morbidity following a diagnosis of PMR or GCA.

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FRI0199 PRESENCE AND DISTRIBUTION OF VASCULITIS IN TEMPORAL, AXILLARY AND SUBCLAVIAN ARTERIES IN GIANT CELL ARTERITIS ASSESSED BY ULTRASONOGRAPHY AT ONSET OF DIAGNOSIS

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Background: In the last two decades ultrasound (US) has become a significant and valuable mode of diagnosing giant cell arteritis (GCA) in clinical practice (1). This is also reflected in the suggested expansion of the ACR 1990 criteria where imaging including US is equated with biopsy (2). Favorable sensitivity compared to biopsy has been shown and explained with the widespread uneven distribution of inflammation in cranial and extracranial arteries (3).

Objectives: To explore the prevalence and distribution of inflammatory involvement in temporal, axillary and subclavian arteries in patients diagnosed with GCA at an ordinary rheumatology clinic.

Methods: In this retrospective study we identified all patients diagnosed with GCA between 2006 and 2019. Since 2006 US has been used at the clinic to diagnose GCA. The vascular US examination was performed by two experienced ultrasonographers (HB, APD). The medical records were reviewed and data were collected using a predefined protocol including data collection for US at the time of diagnosis. Standard US procedure contained an assessment of both temporal arteries (superficial artery, frontal artery and parietal artery) in longitudinal and transversal planes with and without colordoppler mode. A positive US test was defined in presence of hypoechoic vessel wall thickening (halo sign). The axillary and subclavian arteries where assessed in B-mode and intima media thickness (IMT) was measured. A positive test was defined if IMT > 1 mm.

Results: A total of 69 GCA patients (20 men and 49 women) with US performed at the time of diagnosis were identified. Among them, 67 (97.1%) patients met the suggested expansion ACR 1990 criteria. The mean age was 69.9 years. Detailed results for vasculitis distribution for the temporal artery with its branches and the axillary and subclavian arteries are shown in the table below. Positive US findings were recorded in 61 patients (88.4%). A total of 45 patients (65.2%) had a positive US test in the temporal artery and 41 patients (59.4%) in the extracranial arteries. Solely extracranial arteritis was observed in 18 patients (29.5%), 22 (36.0%) had exclusively temporal involvement. Involvement of both cranial and extracranial arteries was observed in 21 patients (34.4%). Only nine patients had positive findings at just one site. Five patients had isolated unilateral subclavian affection, and two patients had isolated unilateral frontal artery and superficial artery involvement each.

Table. Positive US finding in 69 GCA patients

	Extracranial arteries		Temporal arteries		
	Subclavian	Axillary	Superficial	Parietal	Frontal
Right side	13	36	19	20	32
Left side	13	27	18	18	32
total	15	38	22	20	40
total	41			45	

Conclusion: Our data highlights the importance and value of a complete US of cranial and extracranial arteries diagnosing GCA in daily clinical care. The data demonstrate the widespread nature of arterial affection in GCA and the fact that it is often more than one site that is affected. The spreading pattern was comparable to older studies in the respect of large vessel and multisite involvement.

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FRI0200 TIME TO FLARE IN GIANT CELL ARTERITIS AND POLYMYALGIA RHEUMATICA AND REVIEW OF THE LITERATURE

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Background: Giant cell arteritis (GCA) and polymyalgia rheumatica (PMR) are two closely related inflammatory rheumatic diseases of the elderly. While glucocorticoid treatment leads to a dramatic initial improvement, the course of the diseases remains unpredictable and multifarious. Flare and relapses are common, however, data on this is limited [1][2].

Objectives: We set out to evaluate the flare rate, time to first flare and steroid dose during flare of patients diagnosed with GCA and PMR in our practice. The aim was to identify optimal timing for clinical review and contribute towards best practice.

Methods: A total of 218 patients diagnosed with GCA (38) and PMR (180) seen between 2015 and 2020 were audited. Demographic data was collected. Relapse rate, time to initial flare and steroid dose during flares were the primary endpoints for our analysis. Steroid sparing agent use was also documented.

Results: Our cohort comprised of 38 GCA patients (M=15; F=23) and 180 PMR patients (M=71; F=99) who were diagnosed between January 2015 and January 2020.The mean age of diagnosis for patients with GCA and PMR was 73 years and 71 years respectively. 10 patients (4.6%) with PMR later progressed to develop Rheumatoid Arthritis and hence, were excluded from subsequent analyses. Most patients received an initial treatment of corticosteroid therapy for both diseases with a mean dose of 39.74mg for GCA and 18.23mg for PMR. During a mean follow up time of 13.8 months, 75 patients (36%) (GCA= 6; PMR =69) experienced at least one flare which was determined by clinical diagnosis either by unremitting reversion of initial symptoms and/or elevated inflammatory markers. While 13 patients (6%) (GCA = 2; PMR =11) had a flare following completion of initial steroid therapy, 62 patients (30%) (GCA = 4; PMR = 58) experienced flares during steroid tapering, the mean steroid dose observed during disease flare for the latter was 5.25 mg for GCA and 4.67 for PMR. Majority of relapses/flares for PMR patients occurred within the first year of diagnosis (mean = 8.38 months) and after the first year of diagnosis in GCA patients (mean = 15 months). Methotrexate was the most common traditional DMARD trialed as a steroid sparing alternative (GCA = 4; PMR =23) mostly introduced post flare/relapse. The mean appointment intervals for flares/relapses in our cohort was noticed to be during the 5th and 6th scheduled clinical review for GCA and between the 3rd and 4th clinical review for PMR patients.

Conclusion: A flaring and relapsing course is common to both GCA and PMR especially during steroid dose tapering. Increased clinical surveillance and more gradual steroid tapering, particularly at the time when most flares/relapses are observed may help improve clinical outcomes and reduce glucocorticoid requirements in patients.

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FRI0201

OPHTHALMOLOGICAL FEATURES AT DIAGNOSIS AND IN RECURRENCES IN PATIENTS WITH GIANT CELL ARTERITIS CONFIRMED BY BIOPSY IN A TERTIARY HOSPITAL

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Background: Giant cell arteritis (GCA) presents with visual symptoms in approximately 37%[1] of patients at diagnosis. Patients with visual symptoms present, according to some series, lower levels of C-reactive protein (CRP) at diagnosis and associate less headache, fever, cranial nodules or polymyalgia (PM).
Relapses despite glucocorticoid treatment (GC) are frequent (40-60%). Visual symptoms are very rare in relapses (0% in several series). Since most series focus on northern European populations, it is interesting to study the characteristics in our population.
Objectives: To describe visual manifestations in both diagnosis and recurrence of stroke, only in patients diagnosed with temporal artery biopsy. To analyze demographic, clinical and analytical features in patients with and without visual symptoms.
Methods: We retrospectively reviewed the medical records of patients with positive biopsy for GCA at our center from January 2000 through December 2018. Relapse was defined as the appearance of clinical symptoms in a previously asymptomatic patient requiring a dose increase or restart of GCS. Patients with no response to GCS were not included. Qualitative variables are shown with absolute value and percentage and quantitative variables with mean and standard deviation (SD). Kruskal Wallis, Fisher test and Mann-Whitney U test were used for bivariate analysis.
Results: 52 patients were found: 39 women (73.6%), with an average age at diagnosis of 77.6 years (SD 6.3). At diagnosis, 28 presented visual symptoms (53.84%): oculomotor paralysis 5 (9.61%), amaurosis fugax 8 (15.38%), blindness 6 (11.54%), decreased visual acuity 8 (28.57%) and other visual symptoms 1 (1.92%). Eleven had monocular symptoms (38%) and 9 binocular (32%), in 10 patients this data was not collected. The symptoms were permanent in 11 (39.2%) despite GC. Type of visual impairment was: Anterior Ischemic Optic Neuropathy (AION) (12, 42.86%), impairment of cranial pairs (5, 17.86%), central retinal artery occlusion (1, 3.57%), cilioretinal artery occlusion (1, 3.57%) and Posterior Ischemic Optic Neuropathy (1, 3.57%).
Of the 52 patients, 17 (32.69%) presented a minimum of one recurrence and 3 (5.77%) presented 2 or more. No patient relapsed with visual clinic.
There were no differences among patients with and without visual symptoms in the variables studied (table 1). However, patients with visual symptoms at diagnosis had numerically less PM and cranial nodules.

Table 1. Demographic, clinical and analytical differences between patients with/without visual symptoms

Variables	With visual symptoms (28)	Without visual symptoms (24)
ESR >50	17 (60.7%)	15 (62.5%)
ESR <50	4 (14.3%)	2 (8.33%)
CRP>10	17 (60.7%)	13 (54.16%)
CRP <10	3 (10.7%)	2 (8.33%)
Cephalea	24 (85,7%)	23 (95,8%)
Polymyalgia	9 (32,1%)	12 (50%)
Constitutional syndrome	9 (32,1%)	7 (29,1%)
Jaw claudication	17 (60.7%)	12 (50%)
Cranial nodules	4 (14,3%)	8 (33,3%)
Sex: Man/Woman	9/19	5/19
Previous PM diagnosis	4 (14,3%)	3 (12,5%)

Conclusion: In our series, 53% of the patients presented visual symptoms at diagnosis, a number higher than that described in the literature. It is important to remember that only patients with biopsy-confirmed ACG were included. The most frequent manifestations were AION followed by oculomotor paralysis. A numerically lower percentage of PM and cranial nodules was observed at diagnosis in patients with visual symptoms compared to patients without them, as seen in some series. The absence of visual clinic in recurrences coincides with that reported in the available literature.

References:

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FRI0202

WHAT IS NOT NERVOUS SYSTEM INVOLVEMENT IN BEHÇET SYNDROME: A SURVEY OF PATIENTS WITH BEHÇET SYNDROME REFERRED TO NEUROLOGY

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Background: Nervous system involvement of Behçet syndrome (neuroBS) is a serious, but infrequent manifestation of Behçet syndrome (BS). Although many BS patients present with signs and symptoms related to the nervous system, several of these are diagnosed with conditions other than neuroBS. The differential diagnosis may be difficult in such patients.
Objectives: To identify conditions mimicking neuroBS among patients with BS and to determine clinical, laboratory and imaging findings that may help the differential diagnosis.
Methods: We retrospectively screened the charts of 500 BS patients who were registered to our clinic between February 2012 and April 2015, to identify those who were referred to neurology at any time during their follow-up. We follow our BS patients in a multidisciplinary clinic and all patients with a sign or symptom related to the nervous system are seen by one of the neurologist members of the clinic. The final diagnoses, as well as presenting signs and symptoms, laboratory and imaging results and results of any other diagnostic modalities were retrieved from patient charts. Patients who did not have a follow-up visit during the last 3 months were invited to the clinic for their final condition. Those who were not able to come, or one of their family members if they were not able to talk, were interviewed on the phone.
Results: Among the 500 BS patients who were screened, 116 (23%) were referred to neurology (53 men, 63 women, mean age 32.8 (±9.8), 98 (84%) fulfilled ISG criteria). Among these, 29 (5.8%) were diagnosed with neuroBS, 30 (6%) had other conditions related to the nervous system, 46 (9.2%) were not diagnosed with a nervous system disorder and their symptoms disappeared and 11 (2.2%) were inconclusive and lost to follow-up. Of the 29 patients with neuroBS, 20 had parenchymal involvement, 7 had cerebral venous sinus thrombosis, 1 had concurrent parenchymal involvement and cerebral venous sinus thrombosis and 1 had atypical neuroBS. Of the 30 BS patients who were diagnosed with another nervous system condition, 14 (2.8%) had primary headache syndromes including tension type headache (n=5) and migraine (n=9), 6 (1.2%) had psychiatric disorders including psychotic disorder (n=1), depression (n=4) and somatization disorder (n=1), the remaining patients had other diagnoses which were entrapment neuropathy (n=2), epilepsy, glial tumor, multiple sclerosis, Meniere's disease, optic neuritis, neuroretinitis, steroid myopathy and polyneuropathy in one patient each. Presentation features such as cerebellar symptoms, motor symptoms, visual problems, altered consciousness, seizure, fever and facial palsy were more common among patients with neuroBS, whereas sensory symptoms and isolated headache were more common among BS patients with other nervous system conditions (Table).

Table. Clinical characteristics of patients with neuroBS versus other diagnoses

Clinical findings at presentation	BS patients with nervous system involvement (neuroBS) (n=29)	BS patients with other nervous system conditions (n=30)
Only headache	2 (7%)	17 (56%)
Cerebellar symptoms*	8 (27%)	4 (13%)
Motor symptoms*	4 (14%)	2 (7%)
Sensory symptoms*	3 (10%)	5 (17%)
Visual problems*(diplopia, blurred vision)	9 (31%)	1 (3%)
Cognitive symptoms*	2 (7%)	2 (7%)
Other* (Alteration of consciousness, seizure, fever, facial palsy)	9 (31%)	1 (3%)

* Accompanying more than 1 symptom/sign

Conclusion: Nervous system conditions other than neuroBS are common in patients with BS who present with nervous system findings. Caution is required to avoid misdiagnosis of these patients as neuroBS.

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FRI0203

A SINGLE-CENTER INVESTIGATION ON THE PREVALENCE OF MALIGNANCIES IN PATIENTS WITH POLYMYALGIA RHEUMATICA AND GIANT CELL ARTERITIS BY WAY OF 18F-FDG PET/CT: A PROSPECTIVE COHORT STUDY

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Background: Several chronic inflammatory diseases are associated with a higher risk of cancer.[1] Whether, this is the case in Polymyalgia Rheumatica (PMR) and Giant Cell Arteritis (GCA) is still a matter of debate.
Objectives: To identify the prevalence of newly diagnosed cancers in patients with PMR and GCA by means of 18F-FDG PET/CT. Moreover, to compare the characteristics of the patients with and without cancer.
Methods: Eighty consecutive patients with newly diagnosed PMR/GCA were studied. Diagnosis of PMR/GCA was confirmed by a 40-weeks follow up. A unilateral temporal artery biopsy (TAB) was also performed at the time of diagnosis. All included patients underwent an 18F-FDG PET/CT before, or in case of GCA, within 3 days of initiation of high dose oral glucocorticoid (40-75mg). All cancer-suspicious 18F-FDG-PET/CT findings were assessed thoroughly and malignant diseases were confirmed by histology. Total PMR and GCA scores were defined as the sum of a 4-point visual grading scale in each articular/periarticular site as well as arterial segment.
Results: Of the 80 patients, 64 (83.1%) were diagnosed with pure PMR, 10 (13.0%) with concomitant GCA with PMR and 3 (3.9%) with pure GCA. Three patients were diagnosed with rheumatoid arthritis during follow up and excluded from the study. Five types of cancer in 4 (5.2%;95% CI:1.4-12.8%) patients were found. Two patients had breast cancer, one patient had adenocarcinoma of colon and one patient had adenocarcinoma of colon together with skin cancer. Besides, 4 (5.2%;95% CI:1.4-12.8%) patients had Monoclonal Gammopathy of Unknown Significance (MGUS). Age and C-reactive protein were significantly higher among those with solid cancers (p:0.049) and MGUS (p:0.017), respectively (Table1).

Table 1. Characteristics of the patients with and without solid cancer ae well as MGUS

Variables	Cancer –,n=73	Cancer +, n=4	P-value	MGUS -, n =73	MGUS +, n =4	P-value
Age, mean±SD	71.4±7.8	79.7±7.5	***0.049***	71.9±8.0	70.2±9.2	0.79
Gender, n(%) Female	46(59.7%)	3(3.9%)	0.99	47(61.0%)	2(2.6%)	0.62
Constitutional symptoms, n(%)	70(90.9%)	4(5.2%)	0.99	70(90.9%)	4(5.2%)	0.99
Shoulder girdle symptoms, n(%)	68(88.3%)	4(5.2%)	0.99	68(88.3%)	4(5.2%)	0.99
Hip girdle symptoms, n(%)	65(84.4%)	3(3.9%)	0.40	64(83.1%)	4(5.2%)	0.99
Cranial symptoms, n(%)	19(24.7%)	0(0%)	0.57	17(22.1%)	2(2.6%)	0.25
Patients pain VAS	75(50-85)	62.5(50-75)	0.53	72.5(50 -80)	87.5(77.5-95)	0.07
Patients global VAS	80(60-90)	62.5(50-75)	0.37	80(60-90)	89.5(79.5-95)	0.23
Physician global VAS	30(25-40)	24.5(20-29)	0.15	30(22.5-40)	37.5(32.5-45)	0.17
Erythrocyte sedimentation rate, mm[2-20]	54(38-79)	62.5(37.5-76)	0.93	54(38-77.5)	57.5(39 -73.5)	0.94
C-reactive protein, mg/L[<6.0]	37(17-64)	34(17.0-76)	0.80	33(17-60)	98(68 -115)	0.017
TAB positive	7(9.1%)	0(0%)	0.99	7(9.1%)	0(0%)	0.99
Total PMR score	14(10-17)	12(5-15)	0.39	14(10-17)	13(6-15.5)	0.64
Total GCA score	0(0-0)	0(0-0.5)	0.89	0(0-0)	0(0-0)	0.34
Clinical diagnosis, n(%)			0.99			0.53
Pure PMR	60(77.9%)	4(5.2%)		61(79.2%)	3(3.9%)	
Pure GCA	3(3.9%)	0(0%)		3(3.9%)	0(0%)	
Concomitant PMR and GCA	10(13.0%)	0(0%)		9(11.7%)	1(1.3%)	

VAS: Visual analogue scale

Conclusion: The prevalence of cancers in this cohort was higher, compared to the 1-year prevalence of all cancer sites of 1.2% among age-, gender- and region-matched background population in 2016. Occult malignancies are important and relatively prevalent findings in newly diagnosed PMR/GCA patients.
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FRI0204

COMPARISON BETWEEN TRANSMURAL AND ISOLATED (PERI)ADVENTITIAL INFLAMMATION AT TEMPORAL ARTERY BIOPSY: A SINGLE CENTER COHORT OF BIOPSY-POSITIVE GCA WITH LONG TERM FOLLOW-UP

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Background: Temporal artery biopsy (TAB) showing transmural inflammation is considered the gold standard for the diagnosis of giant cell arteritis (GCA). In some cases, inflammation is confined to periadventitial small vessels and/or the adventitia. However, the clinical significance of this more limited inflammation remains unclear. Up to date, no studies have compared treatment, prognosis and long-term outcomes of patients with transmural inflammation with those of patients with isolated (peri)adventitial inflammation.
Objectives: To compare treatment and long-term outcomes of patients with transmural inflammation with those of patients with (peri)adventitial inflammation in a single center cohort of patients with biopsy-positive GCA with long-term follow-up.
Methods: All TABs performed for suspected GCA between 1986 and 2013 were reviewed by a single pathologist. Based on the localization of the inflammation, inflamed TABs were classified into 2 categories: transmural inflammation (TMI), with external elastic lamina disruption and extension of the inflammation to the media; (peri)adventitial inflammation (PAI), with inflammation limited to small periadventitial vessels and/or to the adventitia without extension to the media. All medical records of these patients were retrospectively reviewed from the date of TAB to 31 December 2018 or death. Only patients with a follow-up of at least 18 months after GCA diagnosis were included. Cohort characteristics were compared using Wilcoxon rank sum tests for continuous variables and chi-square tests for categorical variables. Kaplan-Meier methods and log-rank tests were used to estimate the rate of development of outcomes.
Results: In the study period 254 TMI and 80 PAI were identified. Baseline clinical manifestations and laboratory findings of the 2 cohorts were previously reported (1). Similar frequencies of systemic symptoms, visual manifestations and polymyalgia rheumatica were found in the 2 cohorts. Compared with patients with TMI, those with PAI had a significantly lower frequency of cranial symptoms, abnormalities of TA at physical examination, halo at TA color duplex sonography, lower levels of ESR and CRP and higher frequency of male gender and peripheral arthritis. Large vessel involvement was found in 6/22 (27%) patients with PAI and 32/81 (40%) patients with TMI, p=0.292.
118 patients with TMI and 35 with PAI had a follow-up longer than 18 months and were included for outcome analysis. Median (IQR) follow-up was 79.8 months (52, 115) for patients with TMI and 67.9 (34, 125) for those with PAI, p=0.125. Compared to patients with TMI, those with PAI received a significantly lower initial prednisone dose (35.8±22.0 vs 46.8±15.0 mg, p<0.0001), reached sooner a prednisone dose <10 mg/day (median 4.7 months vs 6.3, p=0.001) and <5 mg/day (median 7.5 months vs 10.3, p=0.005), had a lower cumulative prednisone dose at 1 year (5.7±3.8 vs 7.2±2.3 g, p=0.005) and at the end of the follow-up period (10.0±9.0 vs 12.9±9.6 g, p=0.015). There were no differences in the frequencies of relapses, long-term remission, time to first GC discontinuation and treatment duration between patients with TMI and PAI (p>0.05).
Conclusion: Patients with PAI seem to have a disease course similar to those with the transmural pattern, but may require lower GC dosage. Our data confirm that inflammation confined to periadventitial small vessels and/or the adventitia could be considered part of the histopathologic spectrum of GCA.
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FRI0205 **CLINICAL FEATURES OF MONONEURITIS MULTIPLEX ASSOCIATED WITH ANCA-ASSOCIATED VASCULITIS**

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Background: ANCA-associated vasculitis sometimes presents mononeuritis multiplex which worsens the prognosis and activity of daily living in patients.
Objectives: This study aimed to determine the clinical feature of mononeuritis multiplex associated with AAV.
Methods: Consecutive patients with AAV who visited Tokyo Medical Center between April 2006 and December 2019 were included in this study. We examined the following clinical features: prevalence of neuropathy, age of onset, sex, the worst blood test values before the initial therapy (white blood cell count (WBC), eosinophil count (Eo), MPO-ANCA, PR3-ANCA, and C-reactive protein(CRP) levels), manual muscle testing (MMT)score of 20 muscles (Max 100 points), and time (days) from the initial symptoms to the initial induction therapies.
Results: A total of 89 patients with AAV were identified. Among them, 19 patients had eosinophilic granulomatosis with polyangiitis (EGPA) (8 males and 11 females, mean age 63.3 ± 2.7), 9 patients had granulomatosis with polyangiitis (GPA) (0 males, 9 females, mean age 75.6 ± 3.9), and 61 patients had microscopic polyangiitis (MPA) (17 males, 44 females, mean age 78.2 ± 1.5). Of the 89 AAV patients, 26 had sensory neuropathy (15/19 EGPA (78.9%), 11/61 MPA (18.0%), and 0/9 GPA (0%)). Motor neuropathy was observed in 19 patients (EGPA 14/19 (73.7%), MPA 5/61 (8.2%), GPA 0/9 (0%)). 15 patients had both sensory and motor neuropathies (EGPA 12/19 (63.2%), MPA 3/61 (4.9%), GPA 0 (0%)). In patients with both sensory and motor neuropathy, sensory impairment preceded in all cases. Among patients with neuropathy, the time from initial symptoms to initial induction therapy in patients with and without motor neuropathy was 34 ± 10.1 days and 30 ± 10.8 days (p = 0.776), respectively. Also, when comparing those who were treated within 7 days from the onset of movement disorders with those who were treated later, MMT score two weeks after the start of treatment were 92.15 ± 1.47 vs. 91.25 ± 2.65 (p = 0.77).
Between the patients with EGPA with and without sensory neuropathy, there were no significant differences in the following: highest WBC(19620.0 ± 2082.6 vs. 19350.0 ± 4033.5 cells/uL (p = 0.953)), highest Eo(10790.6 ± 1774.8 vs 12440.8 ± 3436.9 cells/uL (p = 0.6750)), and highest CRP levels (4.467 ± 0.96 vs 2.70 ± 1.85 mg/dL (p = 0.41)) before the initial therapy. On the other hand, comparing the EGPA patients with and without motor neuron disorder, CRP levels were significantly higher in those with motor impairment than those without(WBC 20978.6 ± 2049.8 vs. 15600.0 ± 3429.9 cells/uL (p = 0.20); Eo 12213.4 ± 1775.5 vs. 8127.0 ± 2971.0 cells/uL (p = 0.25); CRP 5.13 ± 0.89 vs. 1.20 ± 1.48 mg/dL (p = 0.04)). And in patients with motor neuropathy, the decrease in MMT score was significantly correlated with the worst levels of CRP(p = 0.001)while the decrease was not correlated with the other blood tests. ANCA levels were not associated with sensory or motor neuropathy. In similar analyses of patients with MPA and GPA, there were no significant findings.
Conclusion: Worst CRP levels before the initial therapy can be a poor prognosis factor for motor neuropathy in patients with EGPA. Therefore, EGPA patients with high CRP levels need to be paid more attention to because of possible development of motor neuropathy.
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FRI0206 **THE RELEVANCE OF SERUM IGA LEVEL MEASUREMENT IN ADULT IGA VASCULITIS**

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Background:
Objectives: To evaluate the role of serum IgA level as a biomarker in adult IgA vasculitis (IgAV).
Methods: This prospective study included large cohort of histologically proven adult IgAV cases diagnosed between January 2013 and December 2019 at our secondary/tertiary rheumatology centre. All patients underwent a detailed clinical evaluation and laboratory workup. Patients were then stratified based on baseline serum IgA level into two groups (elevated serum IgA vs. normal serum IgA), and clinical features were compared between the two groups. Next we used multivariable logistic regression analysis to determine factors predicting gastrointestinal (GI) or renal involvement in adult IgAV.
Results: During the 84-month observation period, we identified 227 incipient adult IgAV cases (60.6% males, median (interquartile range) age 64 (47–76) years, 44 (19.4%) current smokers). One hundred and eleven (48.9%) patients had elevated serum IgA level at baseline, the rest had normal IgA level. None of the patients had subnormal serum IgA level. Skin involvement, constitutional symptoms, arthritis, GI tract and renal involvement developed in 227 (100%), 32 (14.1%), 30 (13.2%), 62 (27.3%), and 93 (41.0%) patients, respectively. Patients with elevated serum IgA less frequently developed constitutional symptoms (p=0.036) and GI tract involvement (p=0.017), but had more commonly renal involvement (p <0.001), compared to those with normal serum IgA. Results of univariate analysis are shown in Table 1. In the multivariable logistic regression model, elevated serum IgA level persisted as a factor associated with lower risk of GI tract involvement (OR 0.47 (95%CI 0.23–0.95), and a higher risk of renal involvement (OR 2.71 (95%CI 1.48–4.96). The other factors associated with risk of GI and renal involvement are presented in Table 2.

Table 1. Clinical characteristic of IgAV patients with and without elevated serum IgA

Characteristic	All IgAV	Elevated s++++IgA	Normal sIgA	p value
Number of patients (%)	227	111 (48.9)	116 (51.1)	–
Males (%)	60.8	67.6	54.3	0.043
Age (years)#	64 (47-76)	58 (37-74)	66 (55-77)	0.289
Prior infection (%)	32.2	26.1	37.9	0.065
Constitutional symptoms (%)	14.1	9.0	19.0	0.036
Generalized purpura* (%)	52.0	55.0	49.1	0.426
Necrotic purpura (%)	46.3	53.2	39.7	0.046
Arthritis (%)	13.2	9.0	17.2	0.079
GI involvement (%)	27.3	19.8	34.5	0.017
Renal involvement (%)	41.0	53.2	29.3	<0.001

Legend: # median (IQR); GI gastrointestinal; * above the waistline;

Table 2. Risk factors of GI and renal involvement, multiple logistic regression

Characteristic	GI involvement	Renal involvement
	OR (95%CI)	OR (95%CI)
Age	0.98 (0.96-1.0)	1.02 (1.00–1.04)
Current smoking	–	3.32 (1.56–7.07)
Generalized purpura*	5.86 (2.82–12.16)	2.03 (1.13–3.66)
↑ serum IgA	0.47 (0.23–0.95)	2.71 (1.48–4.96)
NLR >3.5	3.37 (1.59–7.12)	2.24 (1.19–4.23)

Legend: * purpura above the waistline; NLR neutrophil to lymphocyte ratio

Conclusion: Serum IgA level might be a useful biomarker in IgA vasculitis, identifying patients at risk for visceral (GI and renal) involvement.
Disclosure of Interests: ALOJZIJA HOCEVAR: None declared, Matija Tomsic: None declared, Vesna Jurcic: None declared, Katja Perdan-Pirkmajer: None declared, Ziga Rotar Consultant of: Speaker and consulting fees from Abbvie, Amgen, Biogen, Eli Lilly, Medis, MSD, Novartis, Pfizer, Roche, Sanofi., Speakers bureau: Speaker and consulting fees from Abbvie, Amgen, Biogen, Eli Lilly, Medis, MSD, Novartis, Pfizer, Roche, Sanofi.
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FRI0207 **CANCER INCIDENCE AND FEATURES IN ADULT VASCULITIS PATIENTS**

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Background: Vasculitis, like other diseases with chronic inflammation, may be associated with increased cancer risk; possibly due to the inflammation triggering and advancing the neoplastic process. (1-3).

Objectives: The primary objective of this study was to determine the incidence of cancer cases among systemic vasculitis cases followed in a university hospital clinic. Secondary objective was to analyze the relationship between the vasculitis and cancer subtypes and their demographical and clinical features.
Methods: In this study, adult vasculitis patients followed at Hacettepe University Cancer Research, Diagnosis and Treatment Center (HUVAM) between October 2014 and May 2019 were reviewed for neoplastic development and cancer features. Standardized cancer incidence rate was calculated using the online International Agency for Research on Cancer GLOBOCAN database and the population data for Turkey published by Turkish Statistical Institute.
Results: Among 684 patients with a mean age of 46.4±16.9 years and a median follow up duration of 29 months, 38 patients (5.6%) developed cancer. Colon (5 cases, 13%) and lung (4 cases, 11%) were the most commonly seen types of cancer. Among the patients with cancer, giant cell arteritis was the most common type of vasculitis (8 cases, 11%; Table 1). There was no statistically significant association between different cancer and vasculitis subtypes; however, there was increased trend for association between lung cancer and giant cell arteritis (data not shown).

Table 1. Distribution of patients and number of cancer in each vasculitis subgroup

Type of vasculitis	Total	With cancer	
	N	N	%**
Takayasu arteritis	123	4	3%
Granulomatous polyangiitis	100	4	4%
Giant cell arteritis	71	8	11%
Vasculitis limited to skin	62	4	6%
IgG4-related disease	41	1	2%
Polyarteritis nodosa	34	1	3%
Vasculitis secondary to CTD	32	2	6%
Eosinophilic granulomatous polyangiitis	32	2	6%
IgA vasculitis	30	2	7%
Renal limited AAV	17	4	24%
Buerger disease	17	1	6%
Isolated aortitis	13	1	8%
Microscopic polyangiitis	10	1	10%
Cryoglobulinemic vasculitis	8	2	25%
Drug-induced Vasculitis	1	1	100

Compared to the general population in Turkey, cancer incidence was four times higher (SIR: 4.1, 95% CI: 2.9–5.5, *P*<0.001). Patients whom both the vasculitis and cancer diagnosis was within the same year, had a higher ratio of male patients (87%, *P*=0.01), had a higher rate of smoking (77%, *P*<0.001) and had a worse rate of survival (median survival: 54 months, 95% CI: <1 month–125.9 months, *P*=0.005). There was no association between cyclophosphamide (CYC) use and cancer development, with a low cumulative CYC dose among cancer patients (median: 2 g).
Conclusion: The increase in the cancer incidence may indeed be due to chronic inflammation; however, VDI and BVAS scores during the last visit (median: <0.1) indicate that non-inflammatory factor may play a role as the inflammatory damage caused by vasculitis in these patients seem to be low. Similar to other recent cohorts in the literature, there was no association between CYC usage and cancer development.
In conclusion, compared to the general population, cancer incidence is significantly higher in patients with vasculitis and the timing of diagnosis between vasculitis and cancer may be associated with different clinical features.
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FRI0208 **CORRELATIONS BETWEEN NEUTROPHIL-TO-LYMPHOCYTE RATIO AND TH17/TREG IMMUNE BALANCE IN PATIENTS WITH BEHCET'S DISEASE**

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Background: Behcet's disease(BD) is a systemic perivasculitis where mucocutaneous manifestations are well known to show neutrophilic dermatosis denoted by significant neutrophil infiltration[1]. The neutrophil-to-lymphocyte ratio has been proved as an inflammatory biomarkers in BD[2].At present, the Th17/Treg immune imbalance may be the involved factors in the pathway of BD[3].However, the correlations between the number of neutrophil, the number of lymphocyte, the neutrophil-to-lymphocyte ratio(NLR) and Th17/Treg immune imbalance remain unclear.
Objectives: The aim of this study was to examine correlations between the number of neutrophil, the number of lymphocyte, the neutrophil-to-lymphocyte ratio and Th17/Treg immune balance in patients with BD.
Methods: The study included 59 BD patients and 66 healthy controls. The absolute counts of lymphocyte subsets and CD4+T cell subsets were detected by flow cytometry for all participants. The neutrophil and lymphocyte were measured by routine blood test for all BD patients. To calculate the NLR, the ratio of absolute neutrophil count to absolute lymphocyte count was obtained. The Mann–Whitney U test was used to compare continuous measures. Correlations between the number of neutrophil, the number of lymphocyte, the NLR and Th17/Treg immune balance were assessed by Spearman's rank correlation tests.
Results: (1)Compared to healthy controls, the absolute counts of NK cells were decreased (*P*=0.047), the absolute counts of B cells were increased(*P*=0.021), the absolute counts of $CD4^+$T cells were also increased(*P*=0.035), the absolute counts of Th1 and Th17 cells were significantly increased(*P*< 0.005), the absolute counts of Th2 and Treg cells were decreased (*P*< 0.05), the ratio of Th1/Th2 and Th17/Treg were increased(*P*< 0.001) in BD group. (2)The numbers of neutrophil were positively correlated with Th17/Treg(*r*=0.344,*P*=0.008); The NLR was positively correlated with Th17/Treg(*r*=0.291,*P*=0.026).
Conclusion: Our research shows that T cell homeostasis perturbation, especially Th17 expansion, Treg insufficiency and Th17/Treg immune imbalance, is the cornerstone of BD pathogenesis. Except neutrophil, these findings suggest that imbalance Th17/Treg may be dominant in the pathogenesis of BD. The NLR was positively correlated with Th17/Treg.Further studies are required to evaluate these preliminary findings in different patient populations and also examine the possible molecular mechanisms behind our observations.
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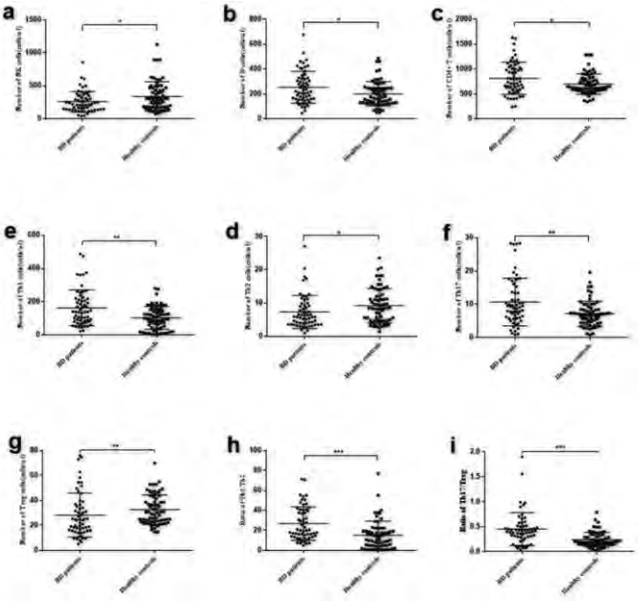


Figure 1. The absolute counts of lymphocyte subsets in BD patients and healthy controls. Data are expressed as means ±SD.

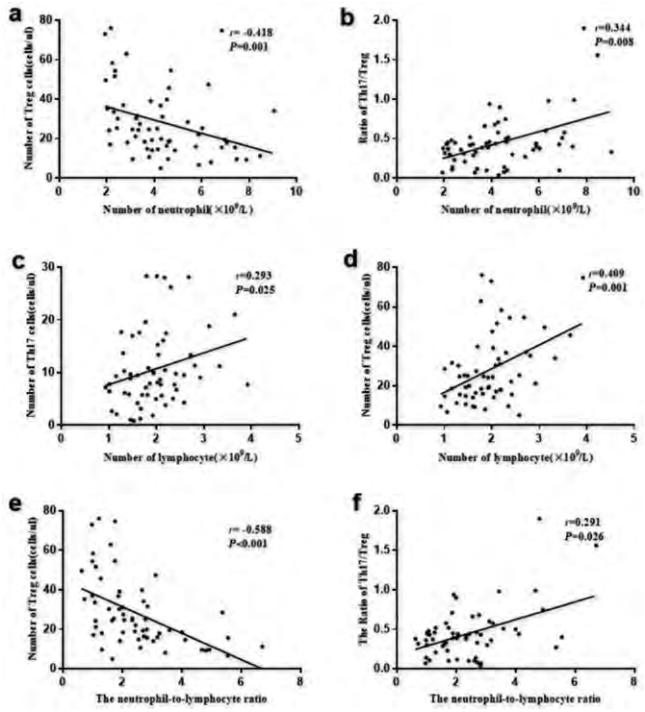


Figure 2. Correlation coefficient and regression line of the number of Th17 cells, the number of Treg cells, Th17/Treg with the the number of neutrophil, the number of lymphocyte, the NLR were represented as scatter plots.

Disclosure of Interests: None declared
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FRI0209 **EFFECTS OF ADD-ON METHOTREXATE IN POLYMYALGIA RHEUMATICA PATIENTS: A RETROSPECTIVE STUDY**

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Background: Guidelines on polymyalgia rheumatica (PMR) recommend early introduction of methotrexate (MTX), especially in patients with worse prognosis such as flare or glucocorticoid (GC)-related adverse events (AE).[1] GC-AE are reported in up to 65% of PMR patients,[2] and 50% of secondary care patients are unable to discontinue GCs, emphasizing the need for GC-sparing agents.[3] However, evidence regarding MTX efficacy in PMR remains limited.[2]
Objectives: To assess the efficacy of add-on MTX in preventing subsequent flares and GC- sparing in PMR patients.
Methods: In a retrospective cohort of newly diagnosed PMR patients visiting our hospital from April 2008 - January 2018, patients starting methotrexate (index event) were compared to first-time flaring PMR patients in whom MTX was not started (control group). Concomitant inflammatory rheumatic diseases were excluded. Data on patient, disease and treatment characteristics were compared. Main outcomes were difference in number of subsequent flares per year between groups (multivariable Poisson regression) and mean GC-use (total GC-dose/total follow-up; multivariable linear regression). In the MTX group only, also incidence rate ratio of flare before vs. after starting MTX was assessed.
Results: Of 454 PMR patients, 262 were selected; 42 receiving MTX and 220 in the control group. Reasons for prescribing MTX were GC ineffectiveness and/or GC-related AE and MTX starting dose was 10, 15 and 25 mg/week in 11 %, 82% and 2% respectively. Adjusted for covariates, mean GC-use was 1.21 higher in the MTX group compared to the control group (p = 0.155). The yearly incidence rate of flares in the MTX group did not differ from the control group: incidence rate ratio (IRR) 0.93, (95% CI 0.53-1.63). The yearly flare rate was 1.19 before and 0.42 after MTX initiation, resulting in an IRR of 0.36 (95% CI 0.24-0.53).
Conclusion: MTX is infrequently prescribed in daily clinical practice, despite guideline recommendations. No difference in GC use or flare incidence was seen between MTX treated patients and controls, although within MTX treated patients, flare rates were lower after MTX start. Confounding by indication may explain the lack of difference in the outcomes between groups. The optimal timing and dosage of MTX in PMR remains unclear, justifying a clinical trial.

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Table 1. Patients characteristics methotrexate versus controls

	MTX N = 42	Controls N = 220	P-value	Difference (95% CI)
Time of PMR diagnosis				
Female(%)	22(52)	127(58)	0.611	-5.3 (-11.0; 21.7)
Age,years*(SD)	**62(7)**	**67(10)**	**0.002**	**-5.0 (-8.2;- 1.8)**
Previous history PMR*(%)	**7(17)**	**13(6)**	**0.025**	**10.8 (2.0; 19.5)**
PMR symptoms,weeks(IQR)	9(6-16)	5(5-16)	0.639	
Bilateral shoulderpain(%)	42(100)	209(95)	0.221	5.0 (-1.6; 11.6)
Morning stiffness>45 minutes(%;n=33 versus 159)	32(76)	177(80)	0.533	-4.3 (-17.5; 9.0)
Elevated ESR/CRP*, (%;n=41 versus 218)	**40(96)**	**185(84)**	**0.023**	**12.7 (1.4; 24.0)**
At index event				
PMR duration, weeks*:**(IQR)	**87(41-116)**	**53(33-80)**	**0.001**	
GC-dose index event	39(93)			
Oral	**10(5-15)**	210(95)		
Mg(IQR)*	3(7)	**5(0-8)**	**0.000**	
Intramuscular(%)	120(100-	10(5)		
Mg(IQR)	120)	100(80-120)	0.355	
Mean GC-dose until index event, mg, (IQR; n=33 versus 170) *	**7.1 (5.9-9.0)**	**5.7 (3.8-7.4)**	**0.000**	
During follow-up				
Flares, n(%)	21 (50)	100 (45)	0.616	4.5 (-21.0; 11.9)
Weeks to first flare (IQR)	36 (24-51)	39 (22-66)	0.517	
Mean GC-dose, mg (IQR)	**6.2 (4.6-9.7)**	**4.7 (2.9-6.9)**	**0.004**	
Daily GC-dose year1,mg (IQR; n=32 versus 153)*	**5 (2.5-7.9)**	**2.5 (0-5)**	**0.03**	

* Significant alpha level < 0.05
**Before diagnosis until index event

Disclosure of Interests: None declared
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FRI0210 **ORBITAL PSEUDOTUMOR AMONG PATIENTS WITH GRANULOMATOSIS WITH POLYANGIITIS – DATA FROM THE POLISH REGISTRY POLVAS**

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Background: Orbital inflammatory masses have been described as the common manifestation of granulomatosis with polyangiitis (GPA) occuring in 7- 45% of patients.
Objectives: Identification and characterization of patients with orbital pseudotumor among Polish patients based on the national vasculitis registry, POLVAS.
Methods: Clinical presentation and management of all GPA patients fulfilling ACR criteria or Chapel Hill Consensus Conference definition included to the Polish registry POLVAS who developed orbital masses in the course of GPA were evaluated.

Results: Ocular involvement was found in 114 (27%) of 417 GPA patients registered in POLVAS, 34 (8%) developed orbital masses. Mean patients' age was 47.8 (range from 19-75) yrs., 23 (67%) were women. Forty four per cent of the patients developed tumor at the beginning of the disease, 56% during relapse. Patients' characteristics on diagnosis of orbital mass: 24 cANCA, 2 pANCA, and 8 ANCA negative, 9% active smokers and 31% past smokers, 29% had localized disease, 21% early systemic and 50% systemic with organ involvement, 29% had other type of ophthalmological involvement before pseudotumor occurred, 88% had active paranasal sinus involvement, 41% lungs, 15% CNS, 15% skin and 6% heart manifestations. Thirty seven per cent of patients had positive nasal swabs cultures, 50% of which were positive for Staphylococcus aureus. In 65%, tumor occurred during steroid therapy (46% had prednisone more than 5mg/d) and 45% on immunosuppressive treatment (19% when treated with AZA, 16% MTX, 6,5% MMF and 3,5% CYC). Due to orbital mass 86.5% were treated with CYC and 13.5% with RTX. Twenty one per cent had complete remission of the pseudotumor, 76% partial remission and in 3% patients there was no response to the treatment; 43% developed visual impairment, 20% suffered from blindness.
Conclusion: Orbital inflammatory mass was not common manifestation of GPA among our patients. The mass developed at the beginning or in the course of the disease, even during immunosuppressive treatment. Orbital masses have been resistant to therapeutic interventions and were accompanied by high risk of visual impairment.
Disclosure of Interests: Anna Masiak: None declared, Marcin Ziętkiewicz: None declared, Krzysztof Wójcik: None declared, Katarzyna Wawrzycka-Adamczyk: None declared, Radoslaw Jeleniewicz: None declared, Marta Madej: None declared, Joanna Kur-Zalewska: None declared, Katarzyna Jakuszko: None declared, Małgorzata Wisłowska: None declared, Hanna Storoniak: None declared, Michał Komorniczak: None declared, Barbara Bułło-Piontecka: None declared, Iwona Brzosko: None declared, Małgorzata Stasiek: None declared, Eugeniusz Kucharz: None declared, Alicja Dębska-Ślizień: None declared, Maria Majdan Consultant of: Roche, Amgen, Speakers bureau: Roche, Amgen, Jacek Musiał: None declared, Zbigniew Zdrojewski: None declared
DOI: 10.1136/annrheumdis-2020-eular.2881

FRI0211 VASCULITIS ASSOCIATED WITH MYELODYSPLASTIC SYNDROME AND CHRONIC MYELOMONOCYTIC LEUKEMIA: FRENCH MULTICENTER CASE CONTROL STUDY

A. Roupie[1], B. Terrier[2], P. Fenaux[1], O. Fain[1], A. Mekinian[1]on behalf of Minhemon. [1]*Sorbonne University, Internal Medicine Department, Saint Antoine Hospital, Paris, France;* [2]*Paris Descartes V University, Internal Medicine Department, Saint Antoine Hospital, Paris, France*

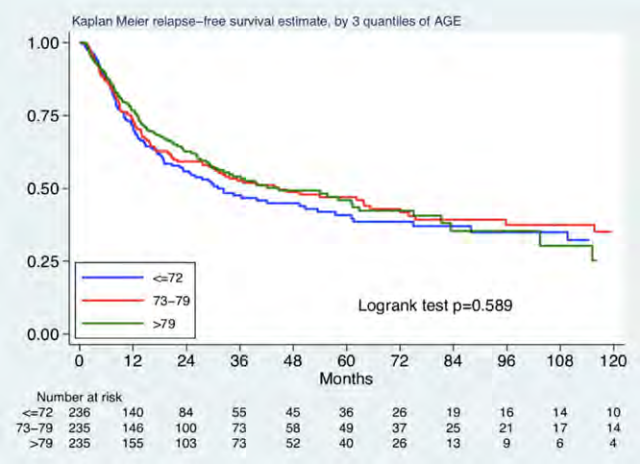
Background: Myelodysplastic syndromes (MDS) and MDS/myeloproliferative neoplasms (MDS/MPN) can be associated with vasculitis.
Objectives: In this nationwide study by the "French Network of dysimmune disorders associated with hemopathies" (MINHEMON) the objective was to evaluate characteristics, treatment and outcome of vasculitis MDS-MDS/MPN.
Methods: Retrospective analysis of patients that presented a MDS/MPN associated with vasculitis and compared the overall survival and acute leukemia with MDS without vasculitis.
Results: Seventy patients with vasculitis and MDS/MPN were included, with a median age of 71.5 [21-90] years and male/female ratio of 2.3. Vasculitis was diagnosed prior to MDS/MPN in 31 patients (44.3%), with a median time of 27 months [1-120] between two diagnosis, and after in 20 patients (6 months [1-59]). In comparison to 183 MDS/MPN without dysimmune features showed no difference in MDS/MPN subtypes distribution nor median IPSS/CPSS scores in patients with and without vasculitis. The vasculitis subtypes was giant-cell arteritis (GCA) in 24 patients (34%). Eleven patients (20%) had Behçet's-like syndrome and 6 patients (9%) presented with polyarteritis nodosa. Steroids (60 mg/day [0-500] of prednisone equivalent) were used as first-line therapy for MDS/MPN vasculitis in 64/70 patients (91%) and 41 (59%) received combined immunosuppressive therapies during the follow-up. After the follow-up of 33.2 months [1-162], 31 patients (44%) finally experienced sustained remission. At least one relapse during the 33.2 months [1-162] follow-up occurred in 43 patients (61%). Relapse rates were higher in patients treated by DMARDs (odds ratio at 4.86 [95% CI 1.38 - 17.10]), but did not differ from biologics (odds ratio 0.59 [95% CI 0.11-3.20]) and azacytidine (odds ratio 1.44 [95% CI 0.21-9.76]) (steroids considered as reference). Overall survival and progression to acute myeloid leukemia in MDS/MPN vasculitis were not significantly different from MDS/MPN patients without any dysimmune features (p=0.5).
Conclusion: This first largest study of MDS/MPN vasculitis show no correlation of vasculitis subtypes with various subtypes and severity of MDS/MPN, and no significant impact of vasculitis on overall survival and progression to acute myeloid leukemia. The high relapse rats and steroid dependence raise the question of combined therapies to steroids. Whereas DMARDs use seem to be avoid specific azacytidine therapy could be considered for even low-risk MDS/MPN vasculitis.

Acknowledgments: minhemon gfm gfev
Disclosure of Interests: None declared
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FRI0212 THE ROLE OF AGE ON THE CLINICAL PRESENTATION AND RELAPSE RATES IN A LARGE COHORT OF 720 PATIENTS WITH GIANT CELL ARTERITIS

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Background: Giant cell arteritis (GCA) is the most frequent systemic vasculitis after the age of 50 years old. Recent interest in the processes of immune and vascular aging have been proposed as a disease risk factor. Data on the impact of age at diagnosis of GCA on the clinical course of the disease are scarce
Objectives: To assess the role of age at diagnosis of GCA on the risk and time to relapse
Methods: Centres participating in the Italian Society of Rheumatology Vasculitis Study Group retrospectively enrolled patients with a diagnosis of GCA until December 2019. The cohort was divided in tertiles according to age at diagnosis (≤ 72; 73-79; > 79 years old). Negative binomial regression was used to assess the relapse rate according to age groups, and Cox regression for time to first relapse.
Results: Of 720 patients enrolled in 14 Italian reference centres, 711 had complete follow-up data (female 50%; mean age 75±7). Median follow-up duration was 34 months (IQR 16;70). Patients in the older group at diagnosis (> 79 years) had more frequent visual loss compared to the 73-79 and ≤ 72 age groups (31% vs 20% vs 7%; p<0.001), but lower rates of general symptoms (56% vs 70% vs 77%; p<0.001). Large-vessel (LV)-GCA was less frequent in the older group (18% vs 22% vs 43%; p<0.001). At least one relapse occurred in 47% of patients. Median time to relapse was 12 months (IQR 6;23). Age did not influence the rate of relapses [18 per 100 persons/years (95%CI 15;21) vs 19 (95% CI 17;22) vs 19 (95%CI 17;22)], nor the time to first relapse (Figure 1). LV-GCA, presentation with significantly elevated c-reactive protein (> 50 mg/L) and general symptoms were independent predictors of relapse.



Conclusion: Age at diagnosis of GCA influenced the clinical presentation and risk of ischaemic complications, but did not affect the relapse rate during follow-up. LV-GCA occurred more frequently in younger patients and was an

independent predictor of relapse risk, highlighting the need for a correct characterization of the clinical subtype at the early stages of disease.

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FRI0213 ASSOCIATION BETWEEN SPECIMEN LENGTH AND NUMBER OF SECTIONS AND DIAGNOSTIC YIELD OF TEMPORAL ARTERY BIOPSY: A RETROSPECTIVE, SINGLE CENTER EXPERIENCE OVER A 21 YEARS' PERIOD

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Background: Temporal artery biopsy (TAB) showing inflammation is considered the gold standard for the diagnosis of giant cell arteritis (GCA). However, sampling error may lead to a negative TAB, and a negative TAB does not rule out GCA. The diagnostic sensitivity of TAB can be affected by the discontinuous character of the histopathologic changes (skip lesions) and by the length of specimens. The optimal TAB length and the optimal number of sections that need to be evaluated in order to avoid missing skip lesions are controversial.

Objectives: To investigate the association between specimen length and number of section and the diagnostic yield of TAB for GCA.

Methods: A pathologist with expertise in vasculitis and blinded to clinical data and final diagnosis reviewed all TABs performed for suspected GCA at our hospital between January 1991 and December 2012. The biopsies were routinely fixed in formalin and completely embedded in paraffin. Sections of 4 microns thickness were cut from paraffin blocks and stained with hematoxylin-eosin. TABs were classified into three categories: inadequate, when the biopsy did not sample the muscular artery; negative when the temporal artery was devoid of inflammation and positive when the temporal artery showed inflammation, arbitrarily defined as at least 1 aggregate of at least 15 inflammatory cells. The blocks of all the inadequate and negative biopsies were recut, and at least three further slides at deeper levels were stained with hematoxylin-eosin.

Results: 694 TABs were performed in the study period and were reviewed. 32 (4.6%) were classified as inadequate and were excluded from the analysis. Of the remaining 662 TABs [71% female; mean (SD) age, 73.2 (8.8) years], mean (SD) post fixation length was 6.63 (4.42) mm, and median number of sections evaluated was 3 (range 1-33). 382 (58%) TABs were classified as negative and 280 (42%) as positive. Compared with negative TAB, patients with positive TAB were older [mean age (SD) 74 (7.5) years vs 72 (9.6), p=0.009] and there was a trend for female predominance (75% vs 68%, p=0.077). Post fixation length of the specimens was significantly lower in negative compared with positive TAB [mean (SD) 6.37 (4.26) mm vs 6.99 (4.61) respectively, p=0.026]. Piecewise logistic regression identified 5 mm as the TAB length change point for diagnostic sensitivity. Compared with TAB length of <5 mm, age- and sex-adjusted odds ratio for positive TAB in samples ≥5 mm long were 1.536 (95% confidence interval, 1.108 to 2.130).

The median (IQR) number of sections evaluated were 2 (1-3) for positive TAB and 4 (2-5) for negative TAB, p<0.0001. In 26/280 (9.3%) positive TABs, the first section was negative, and the inflammation was detected only in deeper sections (the positive section was the second in 14 TABs, the third in 9 and the fourth in 3). In all 26 cases, inflammation detected in deeper section was not transmural, but limited to adventitial or periadventitial small vessels.

Conclusion: Our data confirm that a post fixation TAB length of at least 5 mm should be sufficient to make a histological diagnosis of inflamed temporal artery. According to our data, in order to avoid missing skip inflammatory lesions, at least 3 further sections at deeper levels should be cut and evaluated in all negative TABs.

Disclosure of Interests: None declared

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FRI0214 PERSISTENT LOW-GRADE FDG-PET VASCULAR INFLAMMATION IN REMITTED LVV-GCA PATIENTS IS ASSOCIATED TO A SIGNIFICANT HIGH RISK OF RELAPSE

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Background: Persistent low-grade vascular inflammation in giant cell arteritis (GCA) with large vessel involvement (LVV) treated patients could represent the expression of persistent subclinical disease activity or post-inflammatory vascular remodelling. Whether these findings have any impact on future vascular outcomes is still an unmet need.

Objectives: To evaluate the frequency and evolution of FDG-PET low-grade vascular inflammation in remitted LVV-GCA patients.

Methods: We included all consecutive patients classified as GCA with LVV involvement, with a minimum disease duration of 12 months and clinically remitted, who underwent to at least one PET/MR scan between January 2015 and January 2020. For each scan vessel's metabolic activity was assessed using the Meller's grading[1]. Low-grade inflammation was defined as Meller 1 and 2 (inferior or equal to liver), as reported in previous studies. Demographic and clinical data, as well as disease remission or flares, were recorded and compared to vascular metabolic activity.

Results: In total 88 PET scans were performed in 54 LVV-GCA patients, predominantly female (77.8%), aged 68[7,8] years, with a regular BMI (23.9[2.8]) and with a long-standing disease (27[32.6] months). A subsequent PET/MR scan was available in 34 patients (median time between the two scans 9[6.3] months).

At first PET examination, low-grade metabolic activity was reported in 68,5% of the cases, while complete remission in 15% and high metabolic activity in 25%. Comparing patients with low-grade vascular inflammation to those with complete remission (Meller 0), they had lower disease duration (28[25.9] vs 73[68] months, but without significance) and they were treated with higher daily prednisone dosage (5[3.8] vs 0[2.2], p=0.042). No significant differences were noted in age, acute phase reactants and type of treatment. Moreover, when compared to those with high metabolic activity (Meller 3), the latter had only significantly higher CRP levels (8.3[13.8] vs 4.1[3.9], p=0.03) and lower disease duration (19[20.6] vs 28[25.9] months, but without significance). While no significant differences were noted in age and type of treatment (both glucocorticoids and immunosuppressants).

Among all patients with low-grade vascular inflammation, 81% of them underwent to steroids or immunosuppressants tapering due to clinical remission. At the subsequent PET examination, a worsening of metabolic activity (Meller 3) was found in 4/20 patients, with 1 clinical flare. While in 14/20 patients the subsequent PET revealed a persistent metabolic activity. Only in 2/20 there was a complete metabolic remission. Change or increase of the treatment regimen led to an improvement (Meller 0 or 1) in all the cases. Low-grade metabolic activity was associated with a significant increased risk of worsening/flare at the subsequent PET examination (RR 5.29[1.87-16.11], p=0.002).

Conclusion: Low-grade vascular inflammation at PET examination is a common feature in remitted patients. It is associated with older age, lower disease duration and clinical remission. Treatment tapering is associated with an increased risk of worsening/flare. Further research is urgently needed to address this issue.

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Speakers bureau: Novartis, Pfizer, Roche, GSK, SOBI, Elena Baldissera Speakers bureau: Novartis, Pfizer, Roche, Alpha Sigma, Sanofi, Filippo Crimì: None declared, Pietro Zucchetta: None declared, Diego Cecchin: None declared, Maria Picchio: None declared, Lorenzo Dagna Grant/research support from: Abbvie, BMS, Celgene, Janssen, MSD, Mundipharma Pharmaceuticals, Novartis, Pfizer, Roche, SG, SOBI, Consultant of: Abbvie, Amgen, Biogen, BMS, Celltrion, Novartis, Pfizer, Roche, SG, and SOBI, Andrea Doria Consultant of: GSK, Pfizer, Abbvie, Novartis, Ely Lilly, Speakers bureau: UCB pharma, GSK, Pfizer, Janssen, Abbvie, Novartis, Ely Lilly, BMS, Franco Schiavon: None declared

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FRI0215 RESPONSE TO TOCILIZUMAB IN LARGE VESSEL VASCULITIS ACCORDING TO THE EXTENT OF BASELINE 18F-FDG VASCULAR UPTAKE

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Background: ^{18}F-FDG PET/CT is useful to establish the presence and extent of large vessel vasculitis (LVV)**(1-2).** Early therapy is needed to prevent severe complications.Tocilizumab (TCZ) has shown efficacy in LVV **(3-5).** However, it is unknown if the extent of FDG vascular uptake may influence on clinical response to TCZ

Objectives: To assess the correlation of the extent of baseline FDG vascular uptake in PET/CT scan with clinical response to TCZ in patients with LVV.

Methods: Single center study of patients with LVV treated with TCZ who were divided into 2 groups depending on the extent of vascular uptake in baseline PET/CT scan: **a)** 1-2 affected areas **b)** ≥affected 3 areas. Vascular uptake was qualitatively assessed by two experienced nuclear medicine physicians in five areas (supraaortic trunks, thoracic aorta, abdominal aorta, iliac and femorotibial arteries). We assessed clinical improvement (no improvement/partial/complete), normalization of CRP (≤0.5mg/dL) and/or ESR (≤ 20 mm/1st h) and reduction of prednisone dose (mg/day).

Results: 30 patients (24 w/6 m); mean age 65.3±10.6 yrs. In baseline PET/CT, vascular uptake was observed in 1 or 2 areas (n=13) and in ≥3 areas (n=17). There was a trend to higher ESR/CRP and shorter evolution of clinical symptoms before TCZ onset in patients with ≥3 affected areas (TABLE 1). Clinical/serological evolution and reduction of prednisone dose is shown in TABLE 2. No statistical differences were found. However, patients with ≥ 3 affected areas tended to experience a slower clinical response.

TABLE 1.

	1-2 vascular affected areas (n=13)	≥3 vascular affected areas (n=17)	P
Demographic data			
Age, *mean ± SD*	66.0 ± 10.8	64.8 ± 10.7	0.77
Sex (women), *n (%)*	11 (84.6)	13 (76.5)	0.67
Evolution time before TCZ (months), *median [IQR]*	26.0 [3.5-34.0]	5.0 [1.5-10.0]	0.02
Laboratory markers			
ESR (mm/1st h), *mean ± SD*	30.0 ± 27.3	34.8 ± 27.6	0.64
CRP (mg/dL), *mean ± SD*	1.3 ± 1.2	1.8 ± 1.7	0.28
Previous treatment			
Prednisone dose (mg/day), *mean ± SD*	9.4 ± 6.2	7.9 ± 6.9	0.53
TCZ therapy			
Intravenous, n *(%)*	10 (76.9)	11 (64.7)	0.47
Combined with MTX, n *(%)*	6 (46.2)	8 (47.1)	0.96

TABLE 2.

	1-2 vascular affected areas (n=13)	≥ 3 vascular affected areas (n=17)	P
Complete clinical improvement, *n/N (%)*			
6 m	11/13 (84.6)	12/17 (70.6)	0.43
12 m	12/13 (92.3)	13/17 (76.5)	0.36
18 m	10/11 (90.9)	11/12 (91.7)	0.99
24 m	8/8 (100)	9/10 (90.0)	0.99
Normalization of ESR and/or CRP, *n/N (%)*			
6 m	13/13 (100)	16/17 (94.1)	0.99
12 m	13/13 (100)	16/17 (94.1)	0.99
18 m	11/11 (100)	11/12 (91.7)	0.99
24 m	8/8 (100)	10/10 (100)	0.99
Dose of Prednisone (mg/day), *median [IQR]*			
6 m	5.0 [1.3-5.0]	5.0 [0.0-5.0]	0.98
12 m	2.5 [0.0-3.8]	0.0 [0.0-5.0]	0.97
18 m	0.0 [0.0-2.5]	0.0 [0.0-1.9]	0.72
24 m	0.0 [0.0- 2.2]	0.0 [0.0-2.5]	0.77

Conclusion: TCZ therapy was effective in patients with LVV regardless the extent of FDG vascular uptake in baseline PET/CT scan. However, a trend to a slower clinical response was observed in patients with ≥3 affected areas.

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FRI0216 STEROID SPARING EFFECT, LOWER INCIDENCE OF DISEASE RELAPSE AND DIABETES IN GIANT CELL ARTERITIS TREATED WITH IMMUNOSUPPRESSORS AB INITIO OR VERY EARLY: A MULTICENTER RETROSPECTIVE CASE-CONTROL STUDY

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Background: Glucocorticoids (GC) are associated with serious side effects in giant cell arteritis (GCA). Immunosuppressive therapies (IT) gave conflicting results in GCA, regarding GC sparing effect. Recently, tocilizumab by blocking IL-6, has been licensed as first biologic treatment for GCA, being clinically effective and saving GC (1).

Objectives: To evaluate the usefulness of IT for GCA in: 1) minimizing the rate of GC-induced adverse events (AEs) and 2) reducing the risk of relapse.

Methods: A multicenter retrospective case-control study included 165 GCA was performed. The first group of patients (GCA-IT) included 114 patients who were treated with at least one IT given ab initio or within 3 months from the start of GC. The control group included 51 GCA who received only GC or an IT later than 3 months (GCA-steroid). The primary endpoints were the rate of GC-related side effects: infections, hospitalized infections, new onset systemic arterial hypertension, GC-induced diabetes and osteoporotic fractures.

Results: Methotrexate up to 20 mg/week (138 patients), followed by cyclophosphamide (48 patients) and tocilizumab (27 patients) were the most frequently used IT. No difference was observed as concerns the follow-up time between the two groups [48.5 (IQR 26-72) vs 40 (IQR 24-69), p=0,3, rank-sum test)]. The two groups were similar as concerns sex (p=0,13), while the first group (69±8 yrs) was slightly younger than the second one (72±7 yrs) (p=0,005). Comorbidity was similar between groups. Patients in the GCA-IT group showed a significant lower incidence of GC-induced diabetes (8/114, 7% vs 12/51, 23,5%; p=0,003, chi-square test), while no differences were documented for rate of infections (p=0,64), including hospitalized infections (p=0,44), new onset systemic arterial hypertension (p=0,68), or osteoporotic fractures (p=0,32). Forty-four patients in the GCA-IT group (38,6%), while 34 patients in the GCA-steroid group (66,7%) experienced at least one relapse (p=0,001, chi square test). There was no difference in terms of time to first relapse between the two groups (p=0,53, log-rank test). GCA-IT group was exposed to lower dose of GC at first (p<0,0001,

rank-sum test) and third (p<0,0001, rank-sum test) month, while no differences were recorded at the other time points. Clinical outcomes were similar between the two groups.

Conclusion: Very early introduction of IT in GCA provided a greater steroid sparing in the first 3 months of treatment, leading to a lower incidence of diabetes. Relapse rate was even lower. IT was usually well tolerated without an increase incidence of infections. A randomized prospective trial is required to support this strategy in the management of GCA.

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Disclosure of Interests: Luca Quartuccio Consultant of: Abbvie, Bristol, Speakers bureau: Abbvie, Pfizer, Miriam Isola: None declared, Dario Bruno: None declared, Elena Treppo: None declared, Laura Gigante: None declared, Francesca Angelotti: None declared, Riccardo Capecchi: None declared, Gianfranco Vitiello: None declared, Elena Cavallaro: None declared, Antonio Tavoni: None declared, Silvia Laura Bosello: None declared, Daniele Cammelli: None declared, Salvatore De Vita Consultant of: Roche, GSK, Speakers bureau: Roche, GSK, Novartis, Elisa Gremese Speakers bureau: Abbvie, BMS, Celgene, Jannsen, Lilly, MSD, Novartis, Pfizer, Sandoz, UCB

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FRI0217 SENSITIVITY AND SPECIFICITY OF 2019 DCVAS DRAFT CLASSIFICATION CRITERIA FOR GIANT CELLS ARTERITIS AND TAKAYASU ARTERITIS IN A MONOCENTRIC COHORT OF PATIENTS WITH CLINICAL DIAGNOSIS OF LARGE VESSEL VASCULITIS

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Background: Recently, a new set of classification criteria for Giant Cells Arteritis (GCA) and Takayasu Arteritis (TA) has been developed by the DCVAS project and presented as draft criteria at the 19th International Vasculitis and ANCA Workshop held in Philadelphia in 2019.

Objectives: The purpose of the present study is to analyze the performance of the 2019 DCVAS Draft Classification Criteria in differentiating GCA and TA in a cohort of patients with Large Vessel Vasculitis (LVV), comparing their sensitivity and specificity to 1990 ACR Classification Criteria.

Methods: 2019 DCVAS Draft Criteria and 1990 ACR Criteria were retrospectively applied to a cohort of 130 consecutive patients with Large Vessel Vasculitis. In all patients the diagnosis of vasculitis was histologically and/or radiologically confirmed.

Results: One-hundred patients had a clinical diagnosis of GCA, 25 patients of TA and 5 patients of other form of LVV, different from GCA and TA (idiopathic isolated aortitis n:2, aortitis with retroperitoneal fibrosis n:2, isolated pulmonary arteritis n:1).

Among the 100 patients clinically diagnosed as GCA (F/M: 68/32, age: 74 (60-83)) only 82 fulfilled the 1990 ACR Criteria for GCA, while all of them fulfilled the 2019 DCVAS Draft Criteria for GCA.

Instead, among the 25 patients with a clinical diagnosis of TA (F/M: 21/4, age: 34 (16-48)), 22 (88%) could be classified as TA according to the 1990 ACR Criteria, 25 (100%) according to 2019 DCVAS Draft Criteria.

In the group of patients diagnosed with other form of LVV (F/M: 2/3, age: 56 (38-71)) 4 patients (80%) fulfilled the 2019 DCVAS Draft Criteria for GCA, while none of them fulfilled the 2019 DCVAS Draft Criteria for TA or the 1990 ACR Criteria for GCA or TA. One of these patients did not fulfilled any classification criteria.

On the contrary, one GCA patient could be classified both as GCA or TA according to the 2019 DCVAS Draft Criteria but didn't fulfilled the 1990 ACR Criteria for GCA or TA.

For GCA, 2019 DCVAS Draft Criteria shown a sensitivity of 100% and a specificity of 80%, compared to 82% and 100% of 1990 ACR Criteria. For TA, 2019 DCVAS Draft Criteria shown a sensitivity of 100% and a specificity of 99%, compared to 88% and 100% of 1990 ACR Criteria.

For GCA the agreement between the two different sets of criteria was 85.5% (Cohen's k coefficient: 0.64), for TA the agreement was 85.1% (k: 0.58).

Conclusion: The new draft classification criteria shown a lower specificity if compared to the older ones, but also a higher sensitivity: in particular 2019 DCVAS Draft Criteria can better identify GCA patients with extracranial involvement, historically excluded from the 1990 ACR criteria.

both GCA and TA 2019 DCVAS Draft Criteria, demonstrating that this classification well performs in differentiating GCA and TA.

Table:

	GCA (n:100)	TA (n:25)	Other LVV (n:5)
Morning stiffness in shoulders or neck	43 (43%)	3 (12%)	0 (0%)
Sudden visual loss	33 (33%)	2 (8%)	0 (0%)
Jaw or tongue claudication	35 (35%)	0 (0%)	0 (0%)
New headache/	77 (77%)/	5 (20%)/	1 (20%)/
Scalp tenderness	30 (30%)	0 (0%)	0 (0%)
Temporal Artery Exam: pathological findings	34 (34%)	0 (0%)	0 (0%)
Elevated ESR or CRP	100 (100%)	16 (64%)	5 (100%)
Temporal Artery Biopsy: vasculitis	53 (53%)	0 (0%)	0 (0%)
Temporal Artery halo sign (US)/	11 (11%)/	0 (0%)/	0 (0%)/
Bilateral axillary involvement	11 (11%)	4 (16%)	0 (0%)
FDG-PET activity throughout aorta	32 (32%)	13 (52%)	4 (80%)
Angina or ischemic cardiac pain	5 (5%)	4 (16%)	1 (20%)
Arm or leg claudication	5 (5%)	12 (48%)	0 (0%)
Arterial bruit	2 (2%)	19 (76%)	1 (20%)
Reduced pulse in upper extremity	1 (1%)	15 (60%)	0 (0%)
Carotid: reduced pulse or tenderness	0 (0%)	8 (32%)	0 (0%)
SBP difference in arms: >10/ >20 mmHg	0 (0%)/ 1 (1%)	14 (56%)/ 6 (24%)	0 (0%)/ 0 (0%)
Pathological Angiography or AngioCT: number of affected arteries: 1/2/>3	19 (19%): 7/3/9	22 (88%): 0/1/19	5 (100%): 3/0/2
Paired branch arteries involvement	7 (7%)	20 (80%)	2 (40%)
Abdominal aorta with renal or mesenteric involvement	0 (0%)	17 (68%)	0 (0%)

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FRI0218 PREVALENCE, BURDEN OF DISEASE AND HEALTHCARE UTILIZATION AMONG PATIENTS WITH EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS (EGPA) IN JAPAN 2005-2017

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Background: EGPA is a rare vasculitis condition with very limited data available from real-world settings on burden and health care utilization (HCU), particularly in Japan.

Objectives: To estimate the prevalence (overall and age, gender stratified) and describe HCU and treatment patterns among Japanese EGPA patients.

Methods: This was a retrospective descriptive cohort study using a large administrative claims database covering up to more than 5 million corporate employees and their dependents (JMDC claim database) in Japan. Annual prevalence from 2005-2017 was estimated using two EGPA case definitions: a) patients with ≥1 ICD-10 code (2003 version) for EGPA (M30.1), b) patients with ≥2 ICD-10 codes for EGPA (M30.1) during the year in which prevalence was calculated. Among newly identified EGPA patients with no EGPA code in at least 12 months before, clinical burden, comorbidities, after hour visiting (AHV), all cause hospitalization, and treatment with drugs, including oral corticosteroid (OCS) was described. OCS dose was expressed as prednisone equivalent.

Results: The total number of newly identified patients in 2006-2016 was 45 persons and the mean (SD) age was 42.3 years (SD 14.7 years). The prevalence (per 1,000,000 patients) of EGPA with case definition a) in Japan in 2017 was estimated to be 38.0. The stratified prevalence (per 1,000,000) by age was: 2.3 in the group aged <18 years, 34.0 in those aged 18-50 years, and 91.1 in those aged ≥50 years, respectively. The prevalence in females (50.0) was approximately 1.7-fold higher than that in male (28.7). The prevalence, including stratified results, with definition b) was similar to that with definition a). In the newly identified patients, 60% of patients had at least one hospitalization and 55.6% had AHV, in the year after the first observed EGPA code during the study period. Following index date, new patients were treated: 77.8% with OCS, 11.1% with Azathioprine, 8.9% with intravenous immunoglobulin, 6.7% with Cyclophosphamide, 4.4% with Methotrexate, and 2.2% with Rituximab (non mutually exclusive). The mean (SD) maximum recorded daily dose of OCS in the 12 months follow up period was 53.5 (39.9) mg in new patients. The average dose (SD) of OCS in first month and last month in new patients was 39.1 (29.0) and 9.8 mg (4.8), respectively. Among those with at least a 14-day supply of OCS, 73.1% could be classified as adherent (≥80%) based on their 1-year proportion of days covered. 6.7% of EGPA patients experienced a potentially worsening with an increase of ≥10 mg daily OCS dose prescription following a previous prescription of <10mg.

Conclusion: Analysis of the burden of disease and the use of medical resources in newly identified EGPA patients revealed that EGPA patients require hospitalizations and AHV, in addition to exposure to high doses of OCS. The appropriate medication for the treatment of EGPA to reduce burden on patients may need consider the pathophysiological state of EGPA patients.

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FRI0219 MEPOLIZUMAB FOR EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS IN REAL WORLD DATA

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Objectives: To investigate the treatments of eosinophilic granulomatosis with polyangiitis (EGPA) and evaluate the usage of mepolizumab in clinical settings.

Methods: The subjects were consecutive EGPA patients who were hospitalized and treated at our department and the Rheumatology, Department of Internal Medicine IV, Osaka Medical College between 2002 and 2018. Their clinical data, treatments, and courses were examined, and the usage of mepolizumab was evaluated.

Results: Of 49 EGPA patients, 41 could be analyzed (14 males and 27 females, mean age of onset: 56.4 years). The percentage of positive ANCA was 31.7%, and affected sites were peripheral nerve (92%), central nervous system (17%), skin (51%), ENT (39%), lungs (29%), heart (22%), digestive organs (12%), and kidneys (15%). Remission induction therapy was performed with PSL (41 cases, 100%), PSL pulse (16 cases, 39%), IVCY (17 cases, 41%), RTX (4 cases, 10%), IVIG (22 cases, 54%), AZA (22 cases, 54%), MTX (4 cases, 10%), MMF (2 cases, 5%), MIZ (1 case, 2%), and MEPO (1 case, 2%). Maintenance therapy was performed with PSL (41 cases, 100%), AZA (21 cases, 51%), MTX (6 cases, 15%), MMF (2 cases, 5%), MIZ (3 cases, 7%), and MEPO (10 cases, 24%). In 10 patients who received mepolizumab, the percentage of positive ANCA was 40%, and the median dose of PSL was reduced from 9.5 mg to 5.5 mg after administration. Neither relapses nor adverse events occurred in patients who had received mepolizumab.

Conclusion: Mepolizumab reduced the dose of steroids and improved tolerability in EGPA patients with or without ANCA.

Disclosure of Interests: None declared

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FRI0220 EFFICACY OF ADJUNCTIVE METHOTREXATE IN PATIENTS WITH GIANT CELL ARTERITIS TREATED WITH TOCILIZUMAB PLUS PREDNISONE TAPERING: SUBANALYSIS OF THE GIACTA TRIAL

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Background: There is conflicting evidence regarding the efficacy of methotrexate (MTX) in giant cell arteritis (GCA).[1,2] The benefit of adjunctive treatment with MTX remains to be determined in these patients. Data are presented from a subanalysis of the 52-week, double-blind, randomized controlled GiACTA trial in a subgroup of patients with GCA who received MTX in addition to tocilizumab (TCZ) or placebo (PBO) in combination with prednisone tapering.

Objectives: Assess the efficacy of adjunctive MTX in patients with GCA.

Methods: In part 1 of GiACTA, patients were randomly assigned to TCZ administered subcutaneously every week (QW) or every other week (Q2W) plus 26-week prednisone tapering or PBO plus 26-week (PBO+26) or 52-week (PBO+52) prednisone tapering.[3] MTX could be initiated at a stable dose during screening, continued during the double-blind period, and reduced or discontinued at the investigator's discretion according to disease status. Efficacy was determined as the achievement of sustained remission (absence of GCA flare and C-reactive protein <1 mg/dL from weeks 12 to 52 and adherence to the prednisone taper).[3]

Results: During part 1 of GiACTA, 28 of 250 (11%) treated patients received adjunctive MTX for a median duration of 52.1 weeks: 14 of 149 (9%) TCZ-treated patients received MTX for a median of 52.1 weeks, and 14 of 101 (14%) PBO-treated patients received MTX for a median of 51.9 weeks. Baseline characteristics (Table 1) were balanced between patients who received and did not receive MTX, except for longer disease duration and a higher proportion of patients with relapsing GCA among those who received MTX. The MTX-treated patients tended to have lower prednisone doses at baseline. The median cumulative glucocorticoid dose received over 52 weeks was similar between PBO-treated patients who received MTX and those who did not (3033 mg and 3672 mg, respectively) and between TCZ-treated patients who received MTX and those who did not (1339 mg and 1862 mg, respectively). Sustained remission was achieved by 6 of 14 (43%) patients treated with TCZ + MTX and by 76 of 135 (56%) patients treated with TCZ without MTX (Figure 1). None of the 14 PBO + MTX-treated patients achieved sustained remission, whereas 16 of 87 (18%) patients who received PBO without MTX achieved sustained remission (among all patients in the primary analysis,[3] 82 of 149 [55%] in the TCZ groups and 16 of 101 [16%] in the PBO groups achieved sustained remission). The mean annualized relapse rate at 52 weeks was not different between the MTX-treated and MTX-untreated groups for the TCZ (0.76 with MTX vs 0.47 without MTX; $p = 0.2549$) or PBO (1.89 vs 1.46; $p = 0.4611$) groups (p values based on t tests). Rates of adverse events per 100 patient-years were numerically higher in MTX-treated than MTX-untreated patients: 1267 and 858, respectively, in the TCZ groups and 1331 and 952, respectively, in the PBO groups.

Conclusion: Preliminary data from a small subgroup of patients suggest that adjunctive MTX does not increase the likelihood of sustained remission, reduce disease relapse rate, or improve steroid sparing in patients with GCA. Response rates in TCZ-treated patients appear to be independent of treatment with MTX. The results from this post hoc analysis in a small sample of GCA patients treated with MTX should be confirmed in larger studies.

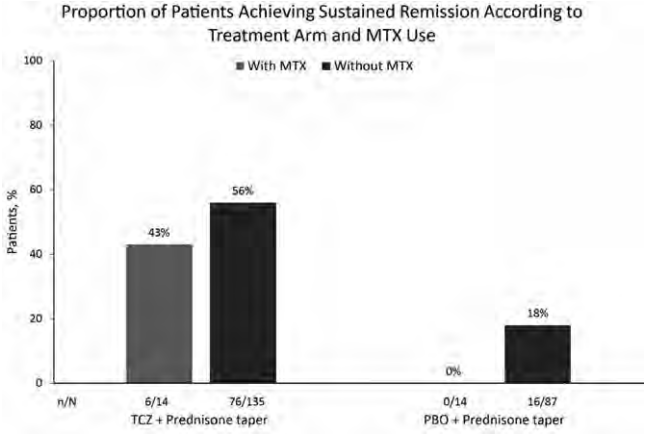
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Baseline Demographics and Disease Characteristics

	PBO+Pred		TCZ+Pred	
	MTX n=14	No MTX n=87	MTX n=14	No MTX n=135
Age, y, median	71.5	68.0	63.0	71.0
Female, %	93	71	71	76
White, %	100	98	100	96
Body mass index, kg/m^2, median	27.5	24.8	25.6	25.5
GCA duration, days, median	303.0	42.0	306.5	42.0
Relapsing GCA, %	93	48	79	48
Pred dose ≤30 mg/day, %	71	49	86	47
CRP, mg/L, median	5.8	3.4	3.7	4.1
ESR, mm/h, median	16.0	20.0	15.5	17.5

Pred, prednisone.



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FRI0221

GIANT CELL ARTERITIS PRESENTING AS FEVER OF UNKNOWN ORIGIN AND DELAY IN DIAGNOSIS: ANALYSIS OF TWO DIFFERENT DECADES

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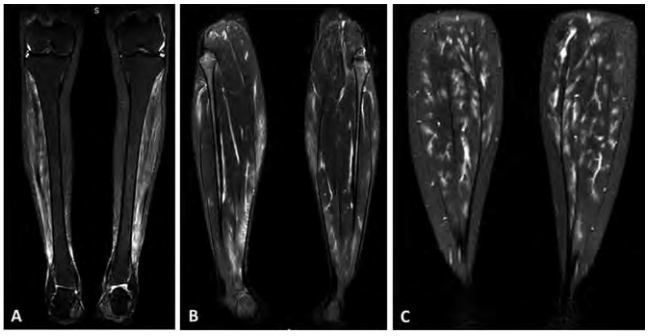
Background: Giant cell arteritis (GCA) represents the most common primary vasculitis of the elderly, that usually involves large and medium sized arteries. The wide spectrum of clinical manifestations can extensively vary, from cranial symptoms, such as headache, jaw claudication or visual alterations, to constitutional symptoms, like fever, weight loss or asthenia. Fever of unknown origin (FUO) may sometimes represents the initial symptom of GCA and when it is not associated with other typical GCA features, the diagnosis can be unluckily delayed.
Objectives: The primary aim of the study was to identify the prevalence of GCA patients presenting as FUO. The secondary aims were to identify the delays in the diagnosis and to compare them between the last two decades.
Methods: Epidemiological and clinical data of 274 GCA patients followed in the last 20 years in our Unit were analysed. We quantified the latency period between the onset of signs and symptoms and the final diagnosis of GCA in terms of months.
Results: One hundred and eighty-five patients (49 males and 136 females, mean ± SD age at the onset 71±7 years) had shown at the onset signs and symptoms suggestive of GCA (new onset headache and/or scalp pain 86%, jaw claudication 39%, vision loss 35%, abnormal temporal artery on examination 49%, dizziness 31%) while 89 patients (33 males and 56 females, mean age at the onset 69±4 years) were sent to our attention just for the onset of FUO and for an increase of erythrocyte sedimentation rate and C-reactive protein not otherwise justified. After an extensive work-up aimed at excluding any kind of infection, malignancy or hematological disorder, the patients with FUO performed a temporal artery biopsy (TAB) and/or a (18)F-fluorodeoxyglucose positron emission tomography (18F-FDG PET). The results from histology and/or imaging allowed us to perform the diagnosis of GCA in all cases; moreover the main PET alterations reported were characterized by a (18)FDG uptake of the aortic arch and its major braches, including the carotid, subclavian, thoracic aorta and, less frequently, the abdominal aorta. Considering the different decades, the mean latency period between the onset of FUO and the diagnosis of GCA was 6±3 months in the decade from 2000 to 2010 and 3±2 months in the last decade, that was significantly higher compared with the mean latency period between the onset of signs and symptoms suggestive of GCA and the definitive diagnosis (3±1 months) in the other patients of the cohort in the first decade. Notably the latency period between the onset of signs and symptoms suggestive of GCA and the definitive diagnosis was more close (2±1 months) to the latency period of diagnosis in FUO presenting GCA in the last decade.
Conclusion: Our data underline that there is a major focus on the diagnosis of GCA, even when the presentation is not typical; this is probably due to the major knowledge reached in the last decade, to an improved sensibilization regarding the different profiles of presentation and surely on the bigger use of 18F-FDG PET in the work-up of GCA patients.
Acknowledgments: none
Disclosure of Interests: None declared
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FRI0222

MAGNETIC RESONANCE IMAGING OF MUSCLE INVOLVEMENT IN POLYARTERITIS NODOSA

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Background: muscle involvement is frequently reported in polyarteritis nodosa (PAN), mostly as myalgia, muscle swelling, and gait difficulty due to intramuscular arteries involvement, peripheral neuropathy, or myositis with slightly or no elevation of muscle enzymes. Magnetic resonance imaging (MRI) findings of compromised muscles have been reported in isolated cases, mainly as a limited form of PAN, however, muscular involvement patterns in MRI of patients with PAN have been recently described
Objectives: to describe MRI of legs findings in patients with PAN in a tertiary center from Medellin-Colombia.
Methods: it was performed a retrospective cross-sectional descriptive study of 15 adult patients who were clinically assessed as having PAN and who had undergone MRI of legs between January 2011 and December 2019. Characteristics already informed in previous studies, affected structures (muscle, subcutaneous tissue, and bone) and pattern of hyperintensities were described as diffuse pattern (signal alterations affecting the entire area of the involved muscle), patched pattern (areas of hyperintensities alternating areas of normal muscle signal intensity), and fluffy nodular pattern or cotton-wool appearance (round hyperintense lesions with fluffy margins centered on blood vessels).
Results: ***clinical characteristics:*** myalgia, especially calf pain, was the most frequent muscular complaint; other clinical manifestations were: constitutional symptoms (80%), arthralgias or arthritis (50%), mono/polyneuropathy (33%), subcutaneous nodules (33%), livedo reticularis (20%), lower limbs ulcers (13%), abdominal symptoms (13%), and purpura (7%). ***MRI findings:*** bilateral muscular edema was found in all patients (100%), fatty infiltration (20%), edema of the subcutaneous cellular tissue (20%), and muscular atrophy (13%) were also described. A diffuse pattern occurred in 46% (n=7) of patients (figure panel A), a patched pattern (figure panel B) in 46% (n=7), and a fluffy nodular pattern or cotton-wool appearance (figure panel C) in 6% (n=1). The most frequently affected muscular group was gastrocnemius and soleus (67%), followed by anterior tibialis (27%), plantar, long peroneus, first finger flexors, and long flexors only affected in 7%. Bone involvement was found in 53%, being the tibia the most affected, followed by the fibula and the calcaneus. MRI led to guide the site of muscle biopsy to prove histological medium-size vasculitis in half of the patients.
Conclusion: in patients with PAN suspicion who have muscular complaints, especially calf pain, MRI arises as an important diagnostic tool, and also as a guide to muscular biopsy to prove vasculitis. The patterns associated with PAN are diffuse, patched or fluffy nodular hyperintensities in gastrocnemius and soleus with or without bone compromise.
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Figure

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FRI0223

SUBPHENOTYPES OF ANCA ASSOCIATED VASCULITIS IDENTIFIED BY LATENT CLASS ANALYSIS

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Background: ANCA associated vasculitides (AAV) are a heterogeneous group of rare diseases with unknown etiology and the clinical spectrum ranging from life-threatening systemic disease, through single organ involvement to minor isolated skin changes. Thus there is an unmet need for phenotype identification especially among patients with granulomatosis with polyangiitis GPA, patients with microscopic polyangiitis MPA group seems to be more

uniform. Recently, based on previous clustering analysis and clinical, histopathological, serological and prognostic aspects three subcategories of AAV have been proposed and named as: non-severe AAV, severe PR3-AAV and severe MPO-AAV [1].

Objectives: In line with these attempts to subcategorize AAV we decided to use latent class analysis (LCA) on a large multicenter cohort of polish AAV patients from POLVAS [2] registry to identify potential new subphenotypes or confirm already proposed ones.

Methods: Latent Class Analysis (LCA) approach was used as a model based clustering method of objects described by dichotomous (e.g., gender; ANCA status – cANCA, pANCA; organ involvement - skin, eye, ENT, respiratory, heart, GI, renal, urinary, CNS, peripheral nerves) and polytomous (number of relapses) variables supported by quantitative covariates (e.g., age at diagnosis, CRP at diagnosis, maximal serum creatinine concentration ever).

Results: Results of LCA on our AAV group returned four class model of AAV subphenotypes, confirming existence of the previously proposed by Mahr at al. [1] and revealed fourth – previously not described clinically relevant subphenotype. To this fourth class - belong patients only with GPA, diagnosed at young age, with multiorgan involvement, high relapse rate and relatively high risk of death.

Table 1. AAV subcategorization – summary of clinical characteristics and ANCA specificity

	LCA Class 1	LCA Class 2	LCA Class 3	LCA Class 4
No of patients	130	194	102	97
AAV type	Mainly GPA	Mainly GPA	mainly MPA	Only GPA
Age at diagnosis	Middle age	Middle age	Old	Young
Male/female ratio	1:2	2:1	1:1	1:1
Main organ involvement	ENT, respiratory, eye	Renal, respiratory, ENT	Renal, respiratory, skin	Multiorgan involvement
Relapse rate	intermediate	intermediate	low	high
Modified class description (based on ref. [1])	Non severe AAV	Severe PR3 AAV	Severe MPO AAV	**Severe non-renal PR3 AAV**

Conclusion: Based on multiple clinical and serological variables LCA methodology identified 4-class subphenotypes model of AAV. Fourth-class is a new clinically important subphenotype including exclusively PR3-positive young AAV patients with multiorgan involvement, high risk of relapse and distinct mortality.

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FRI0224 IDENTIFICATION OF RISK AND PROGNOSTIC FACTORS FOR POLYARTERITIS NODOSA PATIENTS WITH DIGITAL GANGRENE

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Background: Polyarteritis nodosa (PAN) is a segmental, necrotizing vascular disease that primarily impacts medium-sized muscle arteries. The estimated annual incidence of PAN is still lacking in China. Digital gangrene is an ischemic manifestation of the limb. However, the causes and the treatment methods vary from case to case, and the outcome is unpredictable. These features emphasize the need to identify measurable variables that accelerate digital gangrene development in PAN patients. However, little effort has been made to identify the clinical and laboratory factors that affect PAN patients with digital gangrene to anticipate their natural history and response to therapy.

Objectives: Many patients with polyarteritis nodosa (PAN) complicated with digital gangrene have poor outcomes and related research information is limited. This study was carried out to identify the associated risk and prognostic factors.

Methods: We conducted a retrospective study of 148 PAN patients admitted to Peking Union Medical College Hospital (PUMCH) from September 1986 to December 2018. The characteristics, therapeutic regimens, and outcome data for patients with and without gangrene were compared. The Kaplan–Meier method and Cox hazard regression model were used to evaluate the prognostic factors.

Results: Forty-seven (31.8%) PAN patients had digital gangrene complications. The average age was 40.4±17.9 years and the average disease duration was 11 (4-27) months. The presence of digital gangrene was correlated with smoking history [odds ratio (OR), 4.27; 95% confidence interval (95% CI), 1.56-11.66] and eosinophil elevation (28.12; 10.30-76.8). Thirty-two (68.1%) gangrene patients received methylprednisolone pulse therapy and all of these patients were treated with cyclophosphamide. Nine patients suffered irreversible organ injury and two died. Disease duration ≥ 24 months and elevated serum C-reactive protein (CRP) were identified as hazardous factors for poor prognosis in patients with gangrene (P=0.003, HR=8.668, 95% CI 2.11, 35.55 and P=0.042, HR=27.062, 95% CI 1.13, 648.57, respectively).

Conclusion: Smoking history and eosinophil elevation in PAN patients were more prone to digital gangrene and high serum CRP level predicted poor outcomes. PAN patients with smoking history and elevated eosinophils need to be seriously evaluated by clinicians. Furthermore, the CRP level should be efficiently controlled for good prognosis.

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FRI0225 THE CLINICAL FEATURES AND OUTCOME OF VENA CAVA INVOLVEMENT IN BEHCET'S DISEASE

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Background: Behcet's disease (BD) is a systemic disease that can affect vessels of any size and type. However, only limited cases of BD patients with vena cava involvement have been reported.

Objectives: To investigate the clinical features and outcome of vena cava involvement in BD patients.

Methods: We retrospectively reviewed the clinical data of BD patients with vena cava involvement in our institute from August 2001 to October 2019. The treatment and outcome of these patients were also analyzed.

Results: Fifty BD patients with vena cava involvement were included. The median interval between BD onset and diagnosis of vena cava involvement was 2.8 (range 0-19.4) years. Superior vena cava (SVC) involvement was detected in 22 (44.0%) patients, and 21 patients had typical manifestations of SVC syndrome. Inferior vena cava (IVC) was detected in 35 (70.0%) patients, including 7 patients diagnosed with Budd-Chiari syndrome. Seven patients had both superior and inferior vena cava involvement. Forty-five (90.0%) patients had venous involvement other than vena cava, including 19 patients with common iliac thrombosis, 12 patients with common femoral vein thrombosis, 11 patients with external iliac vein thrombosis, etc. For the other BD manifestations, oral ulceration was presented in all patients, followed by genital ulceration (35, 70.0%), Erythema nodosum (27, 54.0%) and pathergy reaction (25, 50.0%). Thirteen (26%) patients had eye involvement. Ten (20%) patients had pleural and/or pericardial effusions. Eleven (22.0%) patients had pulmonary thromboembolism, and 4 (8.0%) patients had arterial involvement.

Inflammatory markers were significantly elevated in 41 (82.0%) patients when the vena cava involvement developed, the mean ESR was 34.0±29.2mm/hr, and the median CRP level was 19.9(0.2-177.0) mg/L. The mean BDCAF2006 score of all patients was 4.6±1.6. Glucocorticoid was used in 47 (94.0%) patients after vena cava involvement was diagnosed, and cyclophosphamide was the first-choice immunosuppressant. Forty-one (82.0%) patients received anticoagulation treatment. Five patients had received placement of IVC filter, and 3 patients had taken balloon dilation of IVC. With a mean follow up of 4.1±3.8 years, 45 patients (90.0%) achieved clinical improvements, 6 patients (12.0%) had relapse of vascular involvement, 5 patients (10.0%) died. The respective estimated cumulative 1- and 5- years relapse-free rates were 90.9% and 83.1%, and the respective estimated 1- and 5- years survival rates were 95.9% and 90.1%.

Conclusion: Vena cava involvement is a rare complication in BD patients. The prognosis of these patients is relatively optimistic after proper treatment. To the best of our knowledge, our study is the largest cohort of BD patients with vena cava involvement.

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FRIDAY, 05 JUNE 2020

Scleroderma, myositis and related syndromes

FRI0226 OPTICAL COHERENCE TOMOGRAPHY OF THE SKIN DETECTS SCLERODERMA CHANGES IN CLINICALLY UNAFFECTED SKIN: AN OPPORTUNITY FOR EARLY DETECTION OF SYSTEMIC SCLEROSIS

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Background: The Very Early Diagnosis Of Systemic Sclerosis (VEDOSS) study has shown that 82% of patients with Raynaud's Phenomenon, specific ANA positivity and scleroderma pattern at nail fold videocapillaroscopy will fulfil classification criteria within 5 years. This is suggesting that there is a subclinical window of opportunity to diagnose systemic sclerosis (SSc) before clinical manifestations occur. In this scenario, a non-invasive tool to diagnose SSc in clinically unaffected skin might improve the early detection of disease in at risk-patients. Optical coherence tomography (OCT) of the skin has been shown to be a sensitive and accurate biomarker of skin fibrosis in SSc.

Objectives: Here we aimed to assess the ability of skin OCT to "detect" SSc in clinically unaffected skin from a multicentre cohort.

Methods: Dorsal forearm skin of SSc patients and matched-healthy controls (HC) was evaluated using VivoSight scanner (Michelson Diagnostics). Mean A-scans (mean OCT signal plotted against depth-in-tissue) were derived as previously described. Minimum Optical Density (MinOD), Maximum OD (MaxOD) and OD at 300 micron-depth (OD300) were calculated. Clinical involvement was assessed by an operator blinded to OCT findings using the mRSS. Receiver-operating characteristic (ROC) curve analysis was carried out for MinOD, MaxOD, and OD300 to evaluate their ability to discriminate between SSc and HC. Statistical analysis was performed using GraphPad Prism software V.7.0.

Results: One hundred seventy four OCT images were collected from 87 subjects [43 SSc (39 Female, mean age 49.7±9.1 years) and 44 gender/age-matched healthy controls (HC) (36 Female, mean age 50.2±8.3 years)] in two different SSc centres. All patients fulfilled classification criteria for SSc. OCT measures demonstrated discriminative ability in SSc skin detection with any clinical skin involvement (0-3 at site of analysis) with an AUC of 0.73 (MinOD, 95%CI 0.64-0.81), 0.77 (MaxOD, 95%CI 0.7-0.85) and 0.82 (OD300, 95%CI 0.76-0.89); p<0.0001 for all as previously indicated. Most importantly, all three measures showed comparable performance in detecting scleroderma also in clinically unaffected skin (mRss=0 at site of analysis), with an AUC of 0.7 (95%CI 0.6-0.81, p=0.001), 0.72 (95%CI 0.61-0.83, p=0.0003) and 0.72 (95%CI 0.61-0.83, p=0.0003) for MinOD, MaxOD and OD300 respectively.

Conclusion: Virtual biopsy by OCT recognises clinically unaffected skin of SSc patients from the HC skin. This is consistent with gene array data showing that scleroderma specific signatures are consistent in affected and clinically unaffected skin. These results inform future studies on at risk patients with clinically unaffected skin which may define a role for OCT in detecting subclinical SSc.

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FRI0227 A USABILITY SURVEY OF WRIST MOUNTED DISPOSABLE HEAT PAD ON RAYNAUD'S PHENOMENON IN PATIENTS WITH CONNECTIVE TISSUE DISEASES

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Background: For patients with connective tissue diseases (CTD), vasodilators are used to treat Raynaud's phenomenon (RP), they are difficult to control only by medication. Although physicians recommend the use of a portable handwarmer or gloves to patients with CTD presenting with RP, sustained heat-retention effects cannot be obtained from them because the patients' daily life-related activities prevent their continued use. Since the wrist mounted disposable heat pad maintains the degrees of freedom of the hands and fingers and can remain usable during the daily activities, we considered this heat pad as a useful and highly practical heating method for CTD patients presenting with RP.

Objectives: To investigate the usability and changes in symptoms resulting from the use of the wrist mounted disposable heat pad in CTD patients presenting with RP.

Methods: Subjects were 23 outpatients with CTD presenting with RP (23 females; mean age 62.6 years; mean duration following the onset of RP 10.3 years; 12 systemic sclerosis, 5 mixed connective tissue disease, 5 Sjögren's syndrome, and 1 systemic lupus erythematosus) who had used the wrist mounted disposable heat pad (put the pad in a specifically designed holder and wrap it around wrist joint (max. temperature 42 degrees Celsius, heat-retention time 6 hours)). We investigated through interviews with them the use situations, usability, and changes in RP. During their using the heat pad, medication and daily life-related precautions against RP continued to be implemented as before.

Results: Many patients had no knowledge of the heat pad (n=17, 73.9%). The most common wearing time of the heat pad was 5–6 hours (n=8, 34.8%). As for scenes of wearing the heat pad, patients who wore the pad when being out of the home accounted for the highest proportion (n=16, 69.6%), and as follows: at home (n=6, 26.1%), during kitchen work (n=3, 13.0%), and during housework (n=2, 8.7%). 17 patients (73.9%) replied that usability was "good", and 18 (78.3%) replied that usability was "better" compared with conventional measures. Moreover, many patients (n=16, 69.6%) replied that RP and associated symptoms had become reduced or alleviated. No patients replied that RP and associated symptoms had become exacerbated or severer. In terms of advantages of using the heat pad, patients who replied that the site on which the pad was mounted was felt to be warm accounted for the highest proportion (n=8, 34.8%), and those who replied that sites other than where the pad was mounted (such as fingertips, hands, and arms) were also warmed accounted for virtually the same proportion (n=7, 30.4%). Over 60% of the patients (n=14, 60.9%) replied that symptoms associated with RP (skin color, cold sensation, and pain) had become reduced or disappeared. In terms of disadvantages of using the heat pad, patients who replied that it was bothersome to use the pad accounted for the highest proportion while other patients made replies referring to cost and bad appearance. No significant accident occurred and as many as 17 patients (73.9%) replied that they would like to continue to use the heat pad in the future.



Conclusion: There have been few reports evaluating the usefulness of a heat pad for RP. The wrist mounted disposable heat pad was thought to be a heating method having the potential to achieve high levels of usability and practicality on CTD patients presenting with RP. Given that the heat pad alleviated RP or caused sites other than where the pad was mounted to be felt warm even though it did not directly heat the hands and fingers, the pad seemed to have usefulness attributed to the heating of the wrist. Although the heat pad seems to be an excellent method for addressing RP in patients' daily lives, we hope that this heat pad will be evaluated on a larger number of patients with the addition of objective indices.

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FRI0228

TOFACITINIB IN THE TREATMENT OF SKIN AND MUSCULOSKELETAL INVOLVEMENT IN ADULT PATIENTS WITH EARLY SYSTEMIC SCLEROSIS, EVALUATED BY ULTRASOUND

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Background: The whole management of systemic sclerosis (SSc) remains to be defined while trials mainly focus on the treatment of different organ involvement and disease-modifying treatments are still not available.

Objectives: To assess the safety and efficacy of tofacitinib (TOF) treatment on skin and musculoskeletal involvement as compared to methotrexate (MTX) treatment in patients with early SSc.

Methods: In this 52-week, prospective, investigator-initiated, open-label, single-centre study, 66 patients with SSc were enrolled. Thirty-three patients received 5mg of oral TOF twice a day; and thirty-three received 7.5-10 mg of MTX weekly. The primary outcome measures were: skin fibrosis improvement at week 26, assessed by the reduction in skin thickness - evaluated by the modified Rodnan skin score (mRSS) and the ultrasound (US) measured skin thickness; improvement in the musculoskeletal involvement, assessed by the reduction in the joint and tendon score (US10SSc score); and adverse events from baseline to week 26. The dynamics in the outcome measures within each group were examined through Wilcoxon tests and between-group comparisons were performed through Mann-Whitney U and Chi-square tests.

Results: At baseline, both groups of patients had similar median scores with no significant differences on all measures: mRSS (p = 0.589), US measured skin thickness (p = 0.822), and US10SSc score (p = 0.918). At week 26, significant differences were observed between the two treatment groups as the TOF treated patients showed a greater reduction in mRSS and musculoskeletal manifestations. In the TOF group, the median mRSS score decreased by 50% from 24 to 12 (IQR = 7.50) versus a smaller decrease of 8.70% in the MTX group, from 23 to 21 (IQR = 8.00), p < 0.001. The median US measured skin thickness in the TOF treated patients decreased by 12.87% from 1.71 to 1.49 (IQR =0.31) versus a decrease of 4.73%, from 1.69 to 1.61 (IQR =0.52) in the MTX group, p = 0.040. The US10SSc median score in the TOF group decreased by 56.25% from 16 to 7 (IQR = 6.50) versus a decrease of 12.5% in MTX group from 16 to 14 (IQR =10.50), p < 0.001. There was no significant difference between the groups in the number of adverse events from baseline to week 26. No cases of herpes zoster and deep vein thrombosis were observed in the TOF group.

Conclusion: The data show that in early SSc TOF may lead to a significant improvement of skin thickness, measured with the mRSS and US, and of the musculoskeletal involvement, measured by the US10SSc score. TOF has also shown a satisfactory safety profile.

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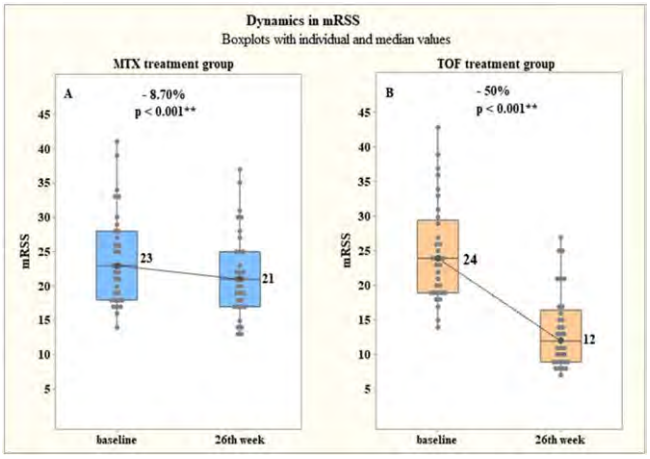


Figure 1. Panel A - Dynamics in mRSS between baseline and week 26 in the MTX group; **Panel B** - Dynamics in mRSS between baseline and week 26 in the TOF group.

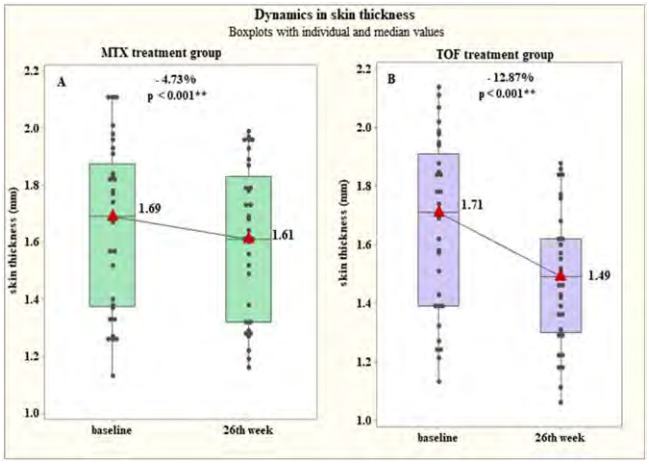


Figure 2. Panel A - Dynamics in skin thickness between baseline and week 26 in the MTX group; **Panel B** - Dynamics in skin thickness between baseline and week 26 in the TOF group.

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FRI0229 **THE IMPACT OF SYSTEMIC SCLEROSIS ON BODY IMAGE PATIENTS**

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Background: Satisfaction with body image has a major impact in quality of life. Systemic sclerosis (SSc) is a can result in disfiguring physical changes.
Objectives: Our aim was to determine the impact of systemic sclerosis on body image using the Satisfaction with Appearance Scale (SWAP). (1)
Methods: Cross-sectional study including patients satisfying the 2013 American College of Rheumatology criteria for SSc diagnosis, aged ≥ 18 years, treated in a tertiary Rheumatology Department. Demographic and clinical data were collected from Reuma.pt and clinical records. All patients provided informed consent and fulfilled SWAP questionnaire, which consists of 14 questions in 4 subscales: satisfaction with facial appearance, satisfaction with non-facial appearance, social discomfort due to appearance and perceived social impact of appearance. Patients rate each item on a numerical rating scale from 1 (strongly disagree) to 7 (strongly agree). Scores for the facial and non-facial appearance range from 0-24 and scores for the social discomfort and perceived social impact subscales range from 0-18. Total SWAP score can range from 0-84 and higher values indicate greater dissatisfaction with appearance and poorer body image. A descriptive analysis was used to summarize demographic and clinical data; categorical variables were described using frequencies; and continuous data using mean and standard deviation. Correlation between variables [Rodnan, age, disease duration, Hospital Anxiety and Depression Scale (HADS) and Short Form Health Survey (SF36)] and SWAP score was tested with Pearson or Spearman coefficient, as appropriated. Scores of SWAP and its subscales in preclinical, limited and diffuse forms of SSc were compared using ANOVA test. Analyses were performed with SPSS Statistics, V.21 and $p<0.05$ was considered statistically significant.
Results: We enrolled 38 patients, 84.2% (n=32) female, with mean age 60.3±14.5 years and mean disease duration 13.3±6.5 years. All but one were caucasian. Fifty percent (n=19) had a limited form, 26.3% (n=10) had preclinical scleroderma and 23.7% (n=9) had a diffuse form of SSc. Regarding the autoantibody profile: 63.2% (n=24) had anti-centromere antibodies, 28.9% (n=11) had anti-Scl-70 antibodies, 5.3% (n=2) had anti-PM antibodies and 2.6% (n=1) had no positive antibodies. The median of Rodnan scores was 4 (IQR 0-9). The total mean SWAP score was 44.8±12.5 with worse results at "Satisfaction with facial appearance" subscale (mean score 14.4±6.1). There is no statistically significant difference in the SWAP score (or its subscales) between the three diagnosis subtypes. No statistically significant correlation was found between the total and subscale SWAP scores and any of the continuous variables considered and no statistically significant difference was found between the different forms of SSc.
Conclusion: We found no significant differences between preclinical, limited or diffused SS. SWAP scores were not significantly correlated with the total Rodnan score, age or disease duration. Contrary to our expectations SWAP did not show any relationship with depression, anxiety (HADS) or quality of Life (SF-36) However, our sample is too small to support definite conclusions. Further studies assessing body image in SSc and its impact in quality of life are warranted to support the holistic care of these patients.
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[2] 10.1037/0278-6133.22.2.130;
[3] 10.3899/jrheum.141482.
Disclosure of Interests: Luisa Brites: None declared, Flavio Costa: None declared, LILIANA SARAIVA: None declared, Ana Rita Cunha: None declared, José Antonio P. da Silva Grant/research support from: Pfizer, Abbvie, Consultant of: Pfizer, AbbVie, Roche, Lilly, Novartis, Tânia Santiago: None declared, Maria Joao Salvador: None declared
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FRI0230 **THE 2009-2019 SURVIVAL AND MORTALITY PREDICTORS IN A LARGE MULTICENTRE SYSTEMIC SCLEROSIS COHORT**

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Background: Systemic sclerosis (SSc) is one of the connective tissue diseases with the poorer prognosis and disease-related causes, particularly pulmonary fibrosis, PAH and cardiac involvement, accounting the most deaths.
Objectives: This multicentre study aimed to evaluate the global survival and any predictor of mortality in a large multicentric cohort of SSc patients.
Methods: We performed a retrospective analysis examining the medical records of our longitudinal SSc cohorts with a median (IQR) follow-up of 11 (6-18) years from 3 Scleroderma Units since January 2009. All clinical, laboratory and instrumental findings have been recorded and analyzed using Chi-squared tests, Kaplan-Meier curves, log-rank tests, and Cox proportional hazards models.
Results: Data from 750 SSc patients (91.9% female; mean (SD) age at first Non-Raynaud symptom 48.4 (15.3) years, median (IQR) disease duration 3 (0-8) years; diffuse cutaneous involvement 162 (21.6%) patients) fulfilling the 1980 ARA and/or 2013 ACR/EULAR classification criteria, were collected. All patients were positive for ANA, anti-Topo-I Abs were found in 235 (31.3%) and Cenp-B Abs in 300 (40%) patients. 98 (13.1%) patients were positive to other Abs (Anti-RNA polymerase III, anti-Pm/Scl) and anti-ENA were negative/unknown for 117 (15.6%) patients. Interstitial lung disease (ILD) was present in 202 (26.9%), pulmonary arterial hypertension (PAH) was found in 29 (3.9%), and 50/750 (6.7%) patients presented pulmonary hypertension combined with ILD (PH-ILD). The overall 10-years survival was 93.1% and, it was significantly impaired by the presence of ILD, PAH or PH-ILD [Figure]. The univariate analysis showed that female gender, higher age at first Non-Raynaud symptom, earlier referral to a tertiary Scleroderma center, absence of any ENA antibodies, and PH-ILD presence were survival predictors. After multivariate analysis the significance of PH-ILD was lost [Table]. Disease duration, basal Rodnan skin score, smoking, renal or gastrointestinal comorbidities, NYHA functional class, steroid or immune-suppressive treatments did not reach the statistically significance.
Conclusion: Our study demonstrated a global 10-years survival rate over 93%. Male patients and rapid evolution of Non-Raynaud symptoms represent the main death predictors in our SSc cohort. A rapid referral to a tertiary rheumatological centre and early treatment with effective agents are associated to a better prognosis.

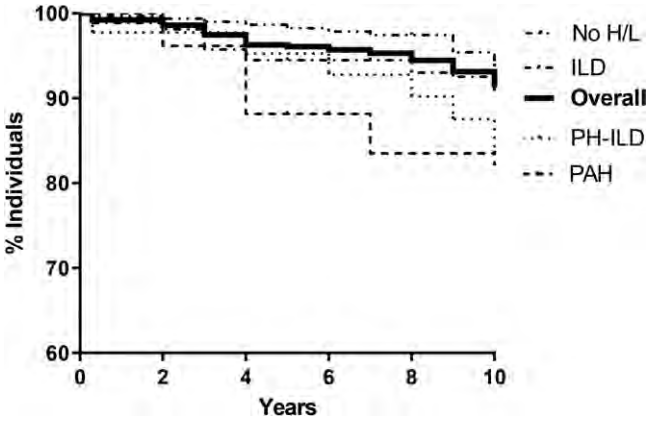


Figure. Kaplan-Meier curves for 5-years survival in SSc patients (Log-rank 8.96, p=0.03).

Table. Prognostic factors for 10-years survival at univariate and multivariate analysis.

	UNIVARIATE ANALYSIS			MULTIVARIATE ANALYSIS		
	HR	**95%IC**	*P*	**HR**	**95%IC**	*P*
Female gender	0.35	0.15-0.81	0.01	0.31	0.15-0.66	0.002
Age at first Non-Raynaud symptom	1.07	1.04-1.1	0.001	1.08	1.05-1.11	0.001
Time referral to a tertiary SSc centre	0.83	0.76-0.92	0.001	0.84	0.77-0.93	0.001
Absence of any ENA antibodies	0.08	0.01-0.62	0.01	0.09	0.01-0.71	0.02
PH-ILD presence	2.6	1.01-6.82	0.04	2.4	0.93-6.1	0.069

Disclosure of Interests: Fabio Cacciapaglia Speakers bureau: BMS; Roche; Pfizer; Abbvie, Enrico De Lorenzis: None declared, Addolorata Corrado: None declared, Silvia Laura Bosello Speakers bureau: Abbvie, Pfizer, Boehringer, Marco Fornaro: None declared, Fabio Montini: None declared, Livio Urso: None declared, Lucrezia Verardi: None declared, Alberto Altomare: None declared, Francesco Paolo Cantatore: None declared, Elisa Gremese Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Merck Sharp & Dohme, Novartis, Sanofi, UCB, Roche, Pfizer, Speakers bureau: AbbVie, Bristol-Myers

Squibb, Celgene, Eli Lilly, Janssen, Merck Sharp & Dohme, Novartis, Sanofi, UCB, Roche, Pfizer, Florenzo Iannone Consultant of: Speaker and consulting fees from AbbVie, Eli Lilly, Novartis, Pfizer, Roche, Sanofi, UCB, MSD, Speakers bureau: Speaker and consulting fees from AbbVie, Eli Lilly, Novartis, Pfizer, Roche, Sanofi, UCB, MSD

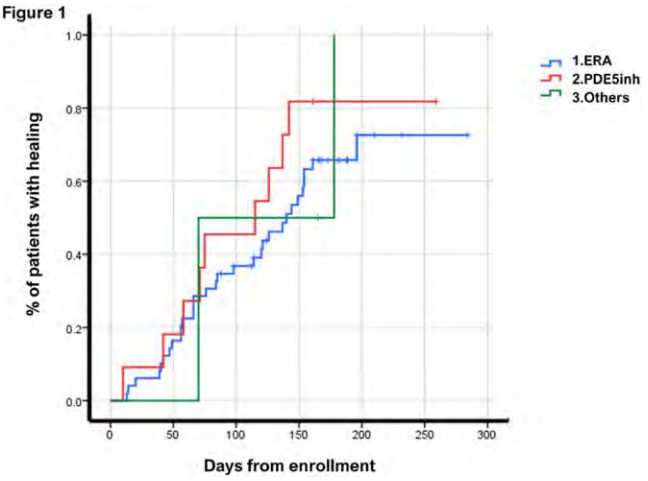
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FRI0231 TREATMENT OF DIGITAL ULCERS IN PATIENTS WITH SYSTEMIC SCLEROSIS: PROSPECTIVE COHORT STUDY

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Background: Digital ulcer (DU) is a common clinical manifestation in patients with systemic sclerosis (SSc). About 70% of patients with SSc experience DUs during the first 10 years, which limit daily activities and may result in digital gangrene or amputation. Several vasoactive/vasodilating agents have been suggested for treatment, but few studies have compared the efficacy of those drugs.
Objectives: The objective of our study was to compare the efficacy of medical treatment for SSc related-DUs, focusing on on endothelin receptor antagonist (ERA) and phosphodiesterase-5 inhibitors (PDE5inh).
Methods: In this prospective observational cohort study, we recruited patients who had one or more active SSc-related DUs and newly started or changed a medical treatment for SSc-related DUs from 13 medical centers in South Korea. The primary outcome was to compare the time to resolution of cardinal DU (CU) according to the treatments. The secondary outcomes included changes in the size or number of CU and changes in the number of DUs. CU was defined as the most clinically significant DU chosen by the investigators. Patients were followed up at every 4 weeks after enrollment until 12 weeks and finally at 24 weeks.
Results: Seventy-one patients were enrolled. Seven patients were excluded due to follow-up loss or withdrawal of consent. A total of 64 patients were analyzed. Seventy-eight percent (n=50) were female. The mean age at enrollment was 49.6 ± 11.6 year-old, and the mean disease duration was 7.1 ± 5.9 years. Twenty-eights pateitns (43.8%) were limited SSc. Forty-nine patients (n=76.6%) started ERA treatment (bosentan=49). Eleven patients (17.2%) started PDE5inh treatment (n=9 for sildenafil, n=1 for udenafil, and n=1 for tadalafil). Four patients who started medication other than ERA or PDE5inh classified as other treatment groups. Seventeen patients (26.6%) were on background calcium channel blockers (CCBs). CU healed in 25 patients (39.1%) at 12 weeks and 43 patients (67.2%) at 24 weeks. The mean time to heal CUs were 54.4 ± 22.7 days at 12 weeks and 91.6 ± 49.2 days at 24 weeks. Time to heal CU was comparable among patients on ERA, PDE5inh, and others (p=0.53, figure 1). The CU area was comparable among the three groups at baseline, 12, and 24 weeks. The mean area of CU in patients on ERA at baseline at 12, and 24 weeks was 21.3±19.4 mm^2, 8.2±14.6 mm^2, and 4.6±7.7 mm^2, respectively. The mean area of CU in patients with PDE5inh at baseline at 12, and 24 weeks was 26.2±28.1 mm^2, 3.5±3.6 mm^2, and 1.3±4.3 mm^2. New DUs developed in 4 patients (8.3%) in ERA, whereas 4 patients (40.0%) in PDE5inh at 4 weeks. The use of ERA was significantly associated with less new DUs development than the use of PDE5inh at 4 weeks follow-up (RR for developing new DU patients on ERA, 0.21; 95% CI 0.06-0.70; p=0.02) At 24 weeks follow-up, none of the patients on CCB developed new DUs.
Conclusion: The time to heal CU for ERA and PDEinh users was comparable in the current study. ERA treatment was associated with reduced new DU occurrence compared with PDE5inh treatment. None of the patients with CCB treatment developed new DU development at 24 weeks.
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Disclosure of Interests: Sung Hae Chang: None declared, Jae-Bum Jun Grant/research support from: Clinical trials; Corbus, JW Pharmaceutical, Speakers bureau: SK Chemical, Yun Jong Lee: None declared, Tae Young Kang: None declared, Yongbeom Park: None declared, Seung-Geun Lee: None declared, Shin-Seok Lee: None declared, Eun Bong Lee: None declared
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Figure 1



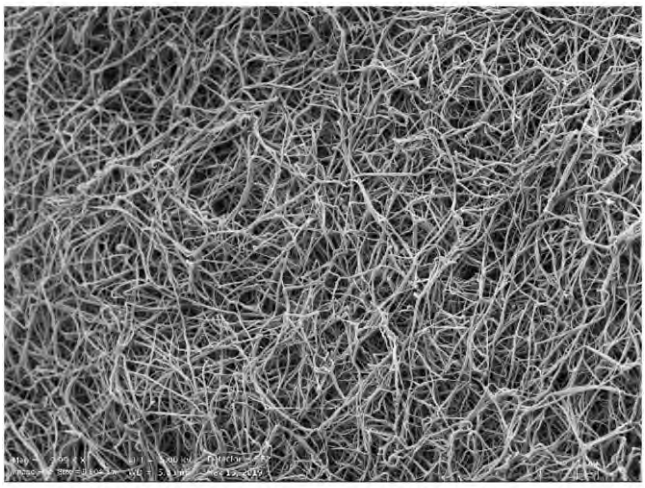
FRI0232 ALTERED FIBRIN CLOT PROPERTIES IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Vasculopathy in Systemic sclerosis (SSc) is connected with the activation of coagulation. However, the fibrinolytic activity still remains unclear since the most preliminary evidences are discordant (1, 2).
Objectives: To assess the haemostatic function, fibrin clot density and clot lysis time in SSc patients and healthy controls (HC) to determine their relation to disease findings.
Methods: Patients who fulfilled the 2013 ACR/EULAR SSc criteria and have never been treated with endothelin receptor antagonist, phosphodiesterase 5 inhibitors or prostanoids were eligibile. Our study included 58 SSc patients [36 limited (lcSSc) and 22 diffuse cutaneous SSc (dcSSc)] and 46 sex/age-matched HC. Clinical evaluation of patients was performed, including high-resolution CT (HRCT), pulmonary function tests and the revised EUSTAR activity index. The interstitial lung disease (ILD) group (n = 15) was defined as moderate or severe changes on HRCT, with a forced vital capacity (FVC) < 85% predicted, without evidence of significant pulmonary arterial hypertension. The serum concentration of ICAM1 and von Willebrand factor antigen (VWF) were measured by ELISA. Haemostatic potential parameters; including overall haemostasis (OHP), overall coagulation (OCP) and overall fibrinolysis (OFP) potential, were assessed and endogenous thrombin potential (ETP) was determined. Maximum absorbance (Cmax), reflects the fibrin clot density and clot lysis time (Lys50t0), reflects fibrinolytic susceptibility, were calculated from OHP and OCP curves (3). Fibrin structure was visualised using scanning electron microscopy (SEM).
Results: The OFP value was significantly decreased, Lys50t0 prolonged ($p<0.05$), while OHP and ETP were increased ($p<0.05$) in patients. In dSSc group ETP, OHP, Cmax and Lys50t0 were higher compared to HC ($p<0.05$). In SSc group, a positive association was found between coagulation parameters (OCP, OHP, Cmax) and the erythrocyte sedimentation rate (ESR), fibrinogen and ICAM1 (respectively $p<0.05$). Lys50t0 was positively correlated with ICAM1, ESR and VWF (respectively $p<0.001$, $p<0.05$, $p<0.05$). An inverse correlation was found between Cmax and both the diffusing capacity of the lungs for carbon monoxide ($r=-0.408$, $p<0.01$) and FVC ($r=-0.318$, $p<0.01$). Increased Cmax was found in ILD respect to HC ($p<0.01$). Denser plasma clot was associated with active disease ($p<0.01$). Longer Lys50t0 was observed in pitting scars group ($p<0.01$). Prolonged Lys50t0 was independently predicted by ICAM1 (OR 1.12, 95% CI 1.03–1.2, $p<0.01$).
Conclusion: Our results provide evidences of denser plasma fibrin clot among patients with lung involvement and impaired fibrinolysis, selectively presented among SSc patients with piting scars. Thus, these patients might be at risk for thrombotic complications. Raised ICAM-1 levels could reflect impaired fibrinolysis, giving insight the important role of this molecule in endothelial homeostasis.
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A



B

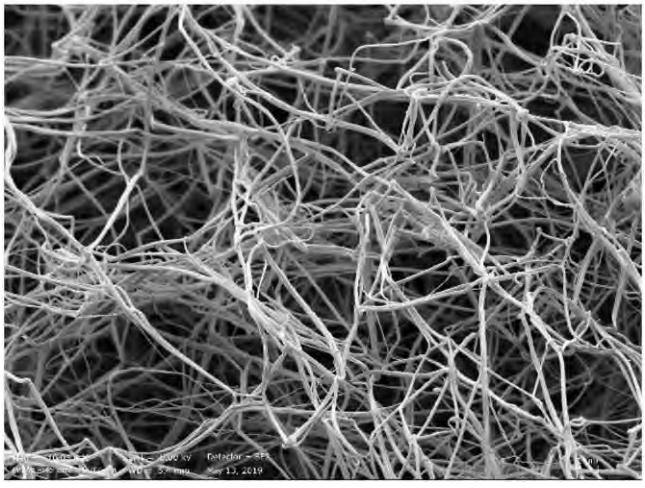


Figure 1. SEM images of fibrin network in 1 representative sample from a SSc (A) and 1from HC sample (B).

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FRI0233

IMPACT AND ADHERENCE TO THE MEDITERRANEAN DIET IN SYSTEMIC SCLEROSIS ITALIAN PATIENTS: CORRELATION WITH GASTROINTESTINAL SYMPTOMS, MOOD DISTURBANCES AND QUALITY OF LIFE

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Background: Gastrointestinal involvement(GI) is a common feature of systemic sclerosis(SSc) and can be highly disabling, representing a major cause of morbidity and reduced quality of life(QoL). The impact of dietary habits on GI symptoms, mood and QoL has not been extensively evaluated.
Objectives: To evaluate the adherence to the Mediterranean Diet(MD) in an Italian multicenter cohort of SSc patients, and its impact on GI symptoms and other disease features, depression, anxiety and overall QoL.
Methods: Consecutive SSc(ACR/EULAR2013) patients from 4 Italian cohorts were enrolled. Dietary habits and adherence to the MD were assessed using the 14-item MEDAS and QueMD questionnaires. Presence and severity of depressive/anxious symptoms and QoL were evaluated with the Hospital Anxiety and Depression Scale(HADS) and the SSc-HAQ(S-HAQ). GI symptoms were assessed with the Reflux Disease Questionnaire(RDQ) and the UCLA SCTC GI Tract 2.0 questionnaire(USG). Associations with patients' lifestyle, disease characteristics, and nutritional status were explored.
Results: 265 patients (94.7% females; age 55.8±13.6years; disease duration 9.1±7.0years; diffuse SSc 31.8%; Scl70+35.8%;ulcers 23.4%;ILD 29.4%;BMI 23.7±4.4 Kg/m^2; obese 11.3%,overweight 23.4%,underweight 4.9%) were enrolled.
Overall MD adherence was moderate(7.5±1.9) according to MEDAS and it correlated with QueMD score(4.53±1.96)(R=.371,p<0.001). MD adherence was optimal in 39 patients(14.7%), more frequently from Central-Southern Italy(p=0.036); 189 patients(71.3%) had a good and 37(14.0%) a poor MD adherence.
GI symptoms were moderate/severe according to USG in 37(14.0%) patients(USG:0.41±0.40), and heartburn was the most common GI symptom(35.2%). The prevalence of significant anxiety and depression was 24.1% and 17.0%.
An inverse correlation was found between MD adherence and mood disturbances at HADS(MEDAS; R=-0.181,p=0.04), work impairment(QueMD;R=-0.247,p=0.005) and reduced QoL, both for GI (constipation at USG: R=-0.133,p=0.032) and general S-HAQ items(bowel:R=-0.181,p=0.04;severity R=-0.202,p=0.01;Raynaud:R=-0.217,p<0.001;ulcers: R=-0.207,p=0.01). MD adherence directly correlated with lung function(MEDAS;R=0.181,p=0.023 for FVC and R=0.170,p=0.03 for DLCO). Patients with MD optimal adherence had lower HADS depression(p=0.04) and S-HAQ scores(HAQ,p=0.04; Raynaud,p=0.005; ulcers,p=0.02) and lower work impairment and lost work time(p=0.03). No significant correlation emerged between MD adherence and BMI, or specific symptoms. Depression and anxiety directly correlated with the severity of reported upper GI symptoms according to both scales (RDQ-GERD:R=0.261,p=0.001; USG:R=0.263,p<0.001) and general S-HAQ items (HAQ: R=0.136,p=0.032;severity R=0.233,p<0.001;bowel: R=0.135,p=0.04;breath: R=0.133,p=0.03; ulcers: R=0.132,p=0.037). Results were confirmed after exclusion of psychiatric(11.7%) and fibromyalgic(15.5%) patients.
Conclusion: Unsatisfactory MD adherence is associated with a low mood, impaired QoL, work impairment, GI and vascular symptoms in Italian SSc patients. The promotion of a healthy lifestyle could positively impact on QoL and disease status of SSc patients.
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Acknowledgments: GILS
Disclosure of Interests: Giacomo De Luca Grant/research support from: SOBI, Speakers bureau: SOBI, Novartis, Pfizer, MSD, Celgene, Gerlando Natalello: None declared, Giuseppina Abignano: None declared, Corrado Campochiaro Speakers bureau: Novartis, Pfizer, Roche, GSK, SOBI, Duygu Temiz Karadağ: None declared, Maria De Santis: None declared, Elisa Gremese Speakers bureau: Abbvie, BMS, Celgene, Jannsen, Lilly, MSD, Novartis, Pfizer, Sandoz, UCB, Silvia Laura Bosello Speakers bureau: Abbvie, Pfizer, Boehringer, Lorenzo Dagna Grant/research support from: Abbvie, BMS, Celgene, Janssen, MSD, Mundipharma Pharmaceuticals, Novartis, Pfizer, Roche, SG, SOBI, Consultant of: Abbvie, Amgen, Biogen, BMS, Celltrion, Novartis, Pfizer, Roche, SG, and SOBI
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FRI0234

A HIGH NEMO SCORE IN VIDEOCAPILLAROSCOPY IS PREDICTIVE OF FUTURE DEVELOPMENT OF DIGITAL ULCERS IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Nailfold videocapillaroscopy (NVC) is a feasible method that allows the observation and follow-up of the microvascular changes that mark the course of Systemic Sclerosis (SSc). In previous studies, we demonstrated that the NEMO score, namely the cumulative Number of microhaEMOrrhages and microthromboses, is a good indicator of the steady state level and over time changes of disease activity (DA) in SSc (1-3).
Objectives: To verify whether a high NEMO score, and then a high level of active microvascular derangement in the fingers may be predictive of the subsequent development of ischemic digital ulcers (IDUs).
Methods: The NEMO score was assessed at baseline (T0) in 98 patients affected by SSc, according to the ACR-EULAR criteria. Out of them, 90 were females, 48 had the limited form and 50 the diffuse cutaneous variant of SSc. ACA and anti-Scl-70 antibodies were positive in 42 and 50 patients, respectively. The NVC pattern was early, active and late in 16, 42 and 40 patients, respectively.
Afterwards, patients were closely followed up for 3 years, and the appearance of new IDUs was recorded in any time of the follow up.
The T0-NEMO score values of patients who developed IDUs were compared to those of patients who did not. A receiver operating curve (ROC) was constructed, and the area under the curve (AUC) calculated, by plotting the sensitivity and 1-specificity of the different NEMO score values in predicting the development of IDUs.
Results: During the follow up, 38 out of 98 patients developed one or more DUs. The NEMO score at T0 was significantly higher in those who developed IDUs with respect to those who did not [median 14.5 (CI 11.0-21.5), and 4.5 (CI 4.0-6.0), respectively, p<.0001]. The AUC was 0.79 (CI 0.69-0.86, p<0.0001). A NEMO score of 12 or more had a sensitivity of 83.3 (CI 71.5-91.7), and a specificity of 63.2 (CI 46.0-78.2), with positive (P) and negative (N) predictive values (PV) of 59.1 (CI 44.9-72.3), and 85.6 (CI 71.7-94.3), respectively. A NEMO score of 16 or more had a sensitivity of 95.0 (CI 86.1-99.0), and a NPV of 93.3 (CI 77.4-99.2).
Conclusion: NEMO score is not only a valid tool to assess the level of DA in the course of SSc, but this NVC parameter could also be used as a good predictor of the future development of IDUs in patients with this disease.
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Disclosure of Interests: Nicoletta Del Papa: None declared, Francesca Pignataro: None declared, Wanda Maglione: None declared, Antonina Minniti: None declared, Domenico Sambataro: None declared, Gianluca Sambataro: None declared, Gabriele Valentini Grant/research support from: BMS, MSD, NOVARTIS, LILLY, PFIZER, ABBVIE, CELGENE, Claudio Vitali: None declared, Roberto Caporali Consultant of: AbbVie; Gilead Sciences, Inc.; Lilly; Merck Sharp & Dohme; Celgene; Bristol-Myers Squibb; Pfizer; UCB, Speakers bureau: Abbvie; Bristol-Myers Squibb; Celgene; Lilly; Gilead Sciences, Inc; MSD; Pfizer; Roche; UCB
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FRI0235

PHASE 1 CLINICAL STUDY OF MGTA-145 IN COMBINATION WITH PLERIXAFOR SHOWS RAPID SINGLE-DAY MOBILISATION AND COLLECTION OF CD34+ HAEMATOPOIETIC STEM CELLS WITHOUT G-CSF

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Background: Autologous haematopoietic stem cell (HSC) transplantation is a recommended therapeutic option for selected patients with autoimmune diseases. G-CSF mobilisation of HSCs requires 4-7 days of injections that are associated with significant side effects and potential for severe complications including disease flares (e.g., scleroderma and multiple sclerosis). MGTA-145 is a biologic that activates CXCR2 on neutrophils, and with plerixafor rapidly mobilises HSCs in mice and non-human primates. The combination promises to be a same-day, G-CSF-free mobilisation regimen.
Objectives: To evaluate the safety, tolerability, and mobilisation efficacy of MGTA-145 monotherapy and combination therapy with plerixafor in healthy volunteers.
Methods: This healthy volunteer phase 1 study consisted of 4 parts- Part A: single-agent MGTA-145 or placebo; Part B: MGTA-145 or placebo given immediately or 2 hours after plerixafor; Part C: MGTA-145 or placebo given 2 hours after plerixafor on 2 consecutive days; Part D: MGTA-145 given 2 hours after plerixafor, just prior to apheresis cell collection.
Results: Monotherapy of MGTA-145 mobilised CD34+ cells within minutes and peaked within 1 hour post MGTA-145 (median 11 CD34+ cells/μL, a 7-fold increase vs baseline). White blood cells and neutrophils followed a similar pattern. Importantly, markers of neutrophil activation were relatively unchanged (≤2-fold vs baseline).
MGTA-145 combined with plerixafor increased CD34+ cell mobilisation, whether given simultaneously or 2h after plerixafor (Fig. 1A). Mobilisation was highly enriched for CD34+CD90+CD45RA- HSCs, which tracked closely with the total CD34 count. At the 0.03 mg/kg dose with 2h stagger, median peak CD34+ peripheral blood mobilisation was ≥40 cells/μL in Part B. On a second consecutive day of dosing, MGTA-145 + plerixafor mobilises HSCs to levels comparable to day 1. Initial data from the ongoing Part D show that sufficient numbers of cells (median 4.3 x 10^6 CD34+ cells/kg) for transplant were collected in a single day.. Preliminary data from NSG mouse transplant studies of those mobilised HSCs in part D show higher engraftment rates of MGTA-145 + plerixafor mobilised HSCs, compared to G-CSF-mobilised HSCs.

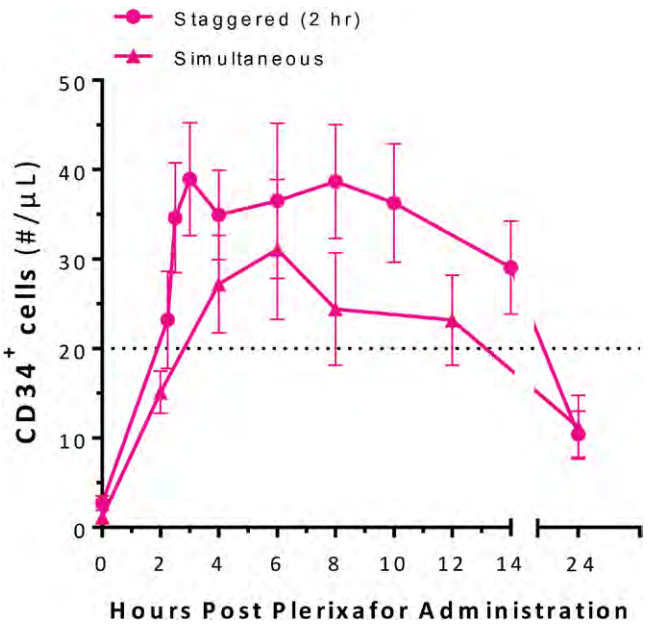


Figure. Peripheral blood mobilisation after plerixafor + 0.03 mg/kg MGTA-145 in healthy subjects with simultaneous and 2h stagger dosing after plerixafor. Dotted line: previously reported CD34+ counts with plerixafor alone mobilisation (Chen *et al*, *Blood Advances*. 2018).

MGTA-145 monotherapy was well tolerated with no significant adverse events (AEs). Grade 1, transient lower back pain that dissipated within minutes was reported. The combination of MGTA-145 with plerixafor was well tolerated, with some subjects experiencing grade 1/2 gastrointestinal AEs commonly observed with plerixafor and one grade 2 back pain with MGTA-145 at 0.075 mg/kg that resolved within minutes.
Conclusion: MGTA-145 monotherapy was well-tolerated and induced rapid mobilisation of significant numbers of HSCs. CD34+ cell mobilisation with MGTA-145 + plerixafor was immediate and superior to plerixafor alone. These data suggest that the combination can enable the collection of sufficient HSCs for transplant in one day without the need for G-CSF. Further development as a first line mobilisation product is warranted in autoimmune diseases, gene therapy and haematologic malignancies.

Table. Single-day Mobilisation and Apheresis Cell Yields in Part D

Subject	Total CD34+ Yield (x106 cells)	CD34+/kg (x106 cells)	CD90+ (%)
801	319	4.1	39%
807	322	4.4	41%
817	500	5.3	26%
821 (*completed only 13L of planned 20L collection)	239	2.7	19%
Median	**321**	**4.3**	**33%**

Disclosure of Interests: John Dipersio Shareholder of: Magenta, Consultant of: Cellworks, Tioma, Rivervest, Bioline, Asterias, Amphivena and Bluebird, Celgene, Incyte, NeoImuneTech, Macrogenics, Steven Devine: None declared,

Jonathan Hoggatt Shareholder of: Magenta, Grant/research support from: Magenta, Consultant of: Magenta, David Scadden Shareholder of: Magenta, Consultant of: Magenta, Haley Howell Shareholder of: Magenta, Employee of: Magenta, Veit Schmelmer Shareholder of: Magenta, Employee of: Magenta, Jason Neale Shareholder of: Magenta, Employee of: Magenta, Tony Boitano Shareholder of: Magenta, Employee of: Magenta, Michael Cooke Shareholder of: Magenta, Employee of: Magenta, Dwight Morrow Shareholder of: Magenta, Employee of: Magenta, Glen Raffel Shareholder of: Magenta, Employee of: Magenta, Will Savage Shareholder of: Magenta, Employee of: Magenta, Kevin Goncalves Shareholder of: Magenta, Employee of: Magenta, Pat Falahee Shareholder of: Magenta, Employee of: Magenta, John Davis Shareholder of: Magenta, Employee of: Magenta

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FRI0236

FIRST PILOT STUDY OF T1 MAPPING MRI WITH ECV MEASUREMENT OF PERIPHERAL MUSCLE IN SYSTEMIC SCLEROSIS PATIENTS SHOWS DIFFUSE FIBROSIS

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Background: Peripheral myositis in systemic sclerosis (SSc) is associated with poor prognosis and myocarditis[1] but non-inflammatory myopathy, which also represents a significant cause of disability in SSc remains poorly understood. Cardiovascular magnetic resonance (CMR) T1 mapping studies in asymptomatic SSc patients show increased extracellular volume (ECV), suggestive of diffuse fibrosis in both the myocardium and thoracic muscle[2].

Objectives: To evaluate the feasibility of T1 mapping MRI and determine ECV in peripheral muscle of SSc patients with and without myopathy and explore the association between cardiac and peripheral muscle T1 mapping in SSc.

Methods: This was a hypothesis-generating pilot and feasibility study. SSc patients, fulfilling the 2013 ACR/EULAR criteria, with no cardiovascular disease or myositis but either minimal muscle symptoms (non-inflammatory myopathy) or no muscle involvement and healthy volunteers (HV) underwent peripheral muscle T1 mapping-MRI for native T1 and extracellular volume (ECV) quantification of the dominant thigh. Patients also had T1 mapping CMR, and creatine-kinase (CK) measured. Non-inflammatory myopathy was defined as current/history of minimally raised CK (<600 IU/l) +/- presence of clinical signs-symptoms (including proximal myasthenia and/or myalgia) +/- a Manual Muscle Testing (MMT) score <5 in the thighs.

Results: 12 SSc patients and 10 HV were recruited. SSc patients had a median (IQR) age of 52 (41,65) years, 9/12 had limited cutaneous SSc, 4/12 interstitial lung disease, 7/12 non-inflammatory myopathy. Higher skeletal muscle ECV was recorded in SSc patients compared to HV [mean (SD) 23(11)%, vs 11(4)% p=0.04]. Skeletal muscle native T1 values were comparable between the 2 groups although modestly higher in SSc patients [mean (SD) 1396ms (56) vs 1387ms (42)] (Figure 1A).

Peripheral muscle ECV associated with CK (R^2 =0.307, rho=0.554, p=0.061) and was higher in SSc patients with evidence of myopathy compared to those with no myopathy [28 (10)% vs 15 (5)%, p=0.023] (Figure 1B). An ECV of 22% was determined to best identify myopathy with a sensitivity of 71% and a specificity of 80%.

SSc patients had raised myocardial ECV and native T1 with means (SD) of 31 (3) % and 1287 (54) ms respectively (normal reference range ECV ≤29%, native T1 ≤1240ms). No clear association between myocardial and peripheral muscle ECV (rho=-0.485) or between myocardial ECV and peripheral muscle native T1 (rho=0.470) of SSc patients was observed.

Conclusion: This pilot study to determine ECV-MRI of the peripheral muscle showed higher ECV in SSc patients compared to HV, suggesting the presence of diffuse fibrosis in the peripheral muscle of SSc patients. These data support further investigation to understand the pathophysiological involvement and relationship of peripheral and cardiac muscle in SSc.

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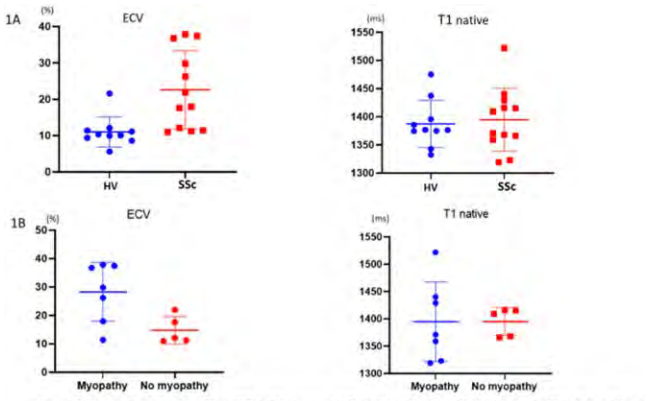


Figure 1A. Peripheral muscle native T1 and ECV in HV compared to SSc patients. 1B. Mean (SD) ECV and native T1 in those with and without myopathy

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FRI0237

COMPARISON OF DIFFERENT PULMONARY HYPERTENSION SCREENING ALGORITHMS IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Pulmonary hypertension (PH) is an important cause of morbidity and mortality in patients with systemic sclerosis (SSc). Different screening algorithms have been proposed for identifying patients who have a high probability of PH and require right heart catheterization (RHC), which is the gold standard for diagnosing PH.

Objectives: To compare the performance of PH screening algorithms in our patients with SSc.

Methods: Sixty-nine consecutive pts fulfilling ACR/EULAR 2013 SSc criteria have been screened for PH until now, using the 2015 ESC/ERS, DETECT and ASIG algorithms. Pulmonary function tests (PFT), diffusing capacity of the lung for carbon monoxide (DLCO), trans-thoracic echocardiography, serum NT-proBNP and uric acid assay and high-resolution computed tomography (HRCT) were performed as needed. Patients with known PH, severe interstitial lung disease and severe left ventricular dysfunction (LVD) were not included. RHC was performed in all patients with positive screening according to any one of the screening algorithms. Pts with PH were classified according to the updated PH classification criteria. Sensitivity and specificity of the 3 screening algorithms were evaluated according to the established cut-off value of 25 mmHg for mean systolic pulmonary artery pressure and for the recently proposed cut-off value of 20 mmHg.

Results: Among the 69 SSc pts, 27 were excluded due to ILD(n=6), LVD(n=6), already diagnosed PH(n=4) no measurable TRV(n=5), lung cancer (n=2), pulmonary embolism (n=1) and nephrotic syndrome (n=1). Among the remaining 42 patients, 17 required RHC according to at least one of the screening algorithms (Table 1). Number of patients who had suspected pulmonary hypertension and required RHC according to ESC/ERS 2015, DETECT and ASIG were 7 (%17), 13 (%31), and 12 (%29) respectively (Figure 1). Among the 17 pts. who had RHC, PH was present in 3 pts according to the 25-mmHg cut-off (Group 2 in 2, Group 3 in 1) and in 9 pts according to the 20-mmHg cut-off (Group 1 in 5, Group 2 in 3, Group 3 in 1). The sensitivity and specificities were presented in Table 2. ASIG and DETECT had better sensitivity for 25-mmHg cut-off and was better with ASIG for 20 mmHg cut-off. The specificity was better with ESC/ERS for both cut-off values.

Conclusion: The ASIG algorithm has a better sensitivity and ESC/ERS algorithm has a better specificity for detecting PH in patients with SSc. A limitation of this study was that RHC was not performed in patients who did not fulfill criteria according to any of the screening algorithms. The sensitivities may be lower than what we propose if there are patients with PH who are asymptomatic and not captured with any of the algorithms.

Table 1. Clinical Features of Patiens

	All Patients n=42	ESC/ESR screen positive, n=7 (17%)	ESC/ESR screen negative, n=35 (83%)	DETECT screen positive, n=13 (31%)	DETECT screen negative, n= 29 (69%)	ASIG screen positive, n=12 (29%)	ASIG screen negative, n=19 (59%)
Age, median [IQR]	51 [46.75-59.75]	66.5 [59-69.75]	48 [38.75-52]	66.5 [58.25-69.75]	48 [38.5-51.5]	61 [52.75-68.5]	48 [38-51]
Male/Female, n (%)	3/39	-	3/32	2/11	1/28	0/12	3/27
Duration of SSc symptoms, year [IQR]	13.5 [5-20.75]	52 [39-57]	65 [51-79.5]	24 [5-38]	12 [5.25-16.75]	14 [5-37]	13 [5-19]
Diffuse	12 (28)	2 (29)	10 (29)	2 (15)	10 (34)	4 (67)	8 (27)
Limited	30 (72)	5 (71)	25 (71)	11 (85)	19/ (66)	8 (67)	22 (73)
Anti-Scl70 (+)	20/33 (61)	3/6 (50)	17/27 (63)	5/11 (44)	15/22 (68)	5/9 (56)	15/24 (62.5)
Anticentromere (+)	8/39 (21)	3/7 (43)	5/32 (16)	6/12 (50)	2/27 (7)	4 (33)	4/27 (15)
Presence of ILD, n (%)	25 (60)	4 (57)	21 (60)	9 (69)	16 (55)	7 (58)	18 (60)
Presence of digital ulcer(ever), n (%)	26 (62)	3 (43)	23 (66)	8 (62)	18 (64)	8 (67)	18 (62)
Presence of GIS involvement, n (%)	20 (48)	5 (71)	15 (43)	6 (52)	14 (50)	6 /11 (55)	14 (50)
Presence of telangiectasia, n (%)	23 (55)	5 (71)	18 (58)	9 (75)	14 (54)	8/10 (80)	15/28 (54)
sPAP on TTE, median (mmHg) [IQR]	30 [26 -34]	41 [34-46]	28 [26-32]	32 [30-43]	28 [26-34]	38 [30-42]	28 [26-32]
FVC, median (% predicted) [IQR]	87.5 [71.5-100.25]	94 [62-117]	86 [72-99]	82 [71-96]	79 [69.25-100]	94 [69.25-115.25]	84.5 [71.5-97.5]
DLCO, median (% predicted) [IQR]	60.50 [50.75 – 72.5]	52 [39-57]	64 [51-78]	57 [43.5-73.5]	61 [51-76]	53 [43-59.25]	65 [51.75-78.5]
FVC / DLCO ratio, median [IQR]	1.39 [1.18-1.72]	2.11 [1.58-2.18]	1.35 [1.16-1.55]	1.64 [1.29-2.15]	1.36 [1.13-1.57]	1.84 [1.41-2.12]	1.35 [1.0-1.47]
NT-proBNP, median (pg/mL) [IQR]	141 [62.75-196]	310 [210-887]	120 [52-168]	4210 [133.5-546]	120 [45-163.5]	260 [149-593.5]	114.5 [48.5-165.75]
Presence of dyspnea, n (%)	16 (38)	7 (100)	9 (26)	6 (46)	10 (35)	7 (58)	9 (30)
Class 1	-	-	-	-	-	-	-
Class 2	14 (93)	6 (86)	8 (100)	5 (83)	9 /9 (100)	6 (86)	8 (100)
Class 3	1 (7)	1 (14)	-	1 (17)	-	1 (14)	-
Class 4	-	-	-	-	-	-	-

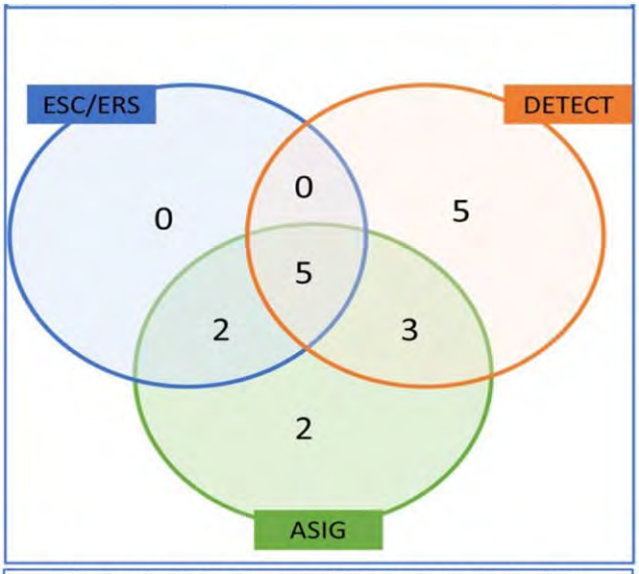


Figure. Number of patients who required RHC according to the algorithms

Table 2. Performance of the algorithms for screening PHT in patients

	25 mmHg cut-off			20 mmHg cut-off		
	ESC/ESR	ASIG	DETECT	ESC/ESR	ASIG	DETECT
Sensitivity, %	67	100	100	56	89	56
Specifity, %	64	36	29	75	50	0
PPV, %	29	25	23	71	67	39
NPV,%	90	100	100	60	80	0

PPV:Positive predictive value NPV: Negative predictive value

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FRI0238 AUTOLOGOUS FAT GRAFTING IN THE TREATMENT OF FACIAL SCLERODERMA: A SINGLE - CENTRE EXPERIENCE

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Background: Systemic sclerosis (SSc) is a systemic autoimmune disease characterized by progressive cutaneous and internal organ fibrosis. Orofacial manifestations are disabling and treatment options are limited. Fat Tissue Grafting (FTG) can be used for treating facial manifestations of the fibrosis.

Objectives: In this study, we aimed to assess the safety and efficacy of FGT of our cohort of patients with SSc.

Methods: We enrolled 20 SSc (18W, 2M) patients, from 2016 to 2019, suffering from facial sclerosis and restricted mouth opening capacity. FTG was carried out in accord with modified Colemans' procedure (1): fat tissue was taken from periumbilical or trochanteric areas and was injected in 8 different points around the mouth. No side effects or adverse reactions have been documented. Evaluations included mouth opening capacity by measuring interincisal distance, oral functionality (MHISS scale) and patient global satisfaction (by Global Health scale).

Results: A 11 mm (8 - 18mm range) median increase of interincisal distance was reported at month 6 and in 80% of patients at month 12, too ($p<0.03$). A significant improvement in MHISS scale was also observed ($p<003$). The patient satisfaction questionnaire showed 95% positive results and 80% of the patient replied affirmatively to the question about the repetition of FTG but only 2 patients required new FTG after 12 months.

Conclusion: Our results showed that FTG improved mouth opening capacity and that aesthetic and functional results were satisfying to about 90% of the patients; long-term effects of this type of treatment are currently unknown. However, our and litterature data at 12 months follow-up seems to confirm the benefits in long term, despite the filling effect is over.

This study – that's one of the largest case series described right now (2) - supports the possible therapeutic role of autologous FTG in improving facial scleroderma both in aesthetic and in functional aspects.

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FRI0239 ANTI-NXP2 ANTIBODIES: CLINICAL AND SEROLOGICAL ASSOCIATIONS IN A MULTICENTRIC ITALIAN STUDY

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Background: anti-NXP2 antibodies is considered a serological marker of dermatomyositis (DM), with calcinosis, severe myositis and, in some series, cancer. Historically, these associations have been detected with immunoprecipitation (IP), but in the last few years commercial lineblot (LB) assay have been released.

Objectives: to analyze the clinical features associated to anti-NXP2 antibodies, including the onset of concomitant cancers, both with LB and homemade IP

Methods: clinical and serological data from medical charts of 213 patients with a diagnosis of inflammatory miosidites without anti-NXP2 (NXP2-), followed-up by two third-level Centers, and 61 anti-NXP2+ patients from 10 Rheumatological centers were analyzed. Anti-myositis specific (MSA) and anti-myositis associated antibodies (MAA) were detected in single centers by LB (Euroimmun Autoimmune Inflammatory Myopathies 16 antigens). Anti-NXP2 was confirmed by protein and RNA IP, as previously described (1)

Results: clinical diagnosis of anti-NXP2+ positive with LB were 42 DM, 11 PM, inclusion body myositis (IBM) 4, necrotizing myositis and overlap (OM) 1 each. Anti-NXP2+ showed a lower age at onset ($p<0.0001$) more frequent diagnosis of DM (68.8%vs30%,OR5.2) and IBM (6.5%vs0.49%,OR14.8), typical skin manifestations, myositis (93%vs79% OR3.3), concomitant presence of another MSA (12.7%vs2%, OR6.41) and lower rate of features associated with OM or anti-synthetase syndrome. Serum from 49 NXP2+ was available and IP analysis

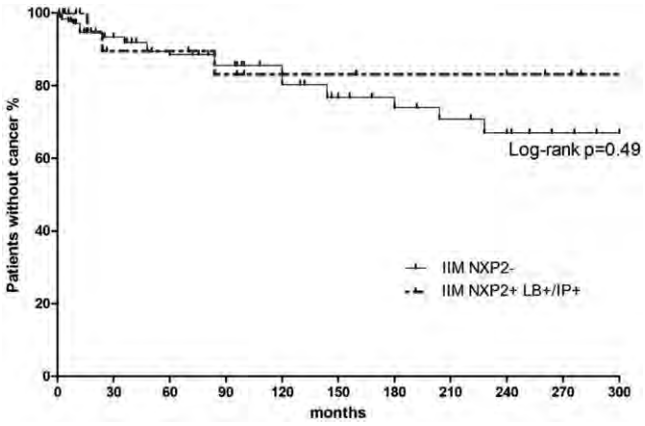
was made with the confirmation of NXP2 in 31 sera (63.2%) with the following diagnosis: DM 27 cases, PM 3, IBM 1. Whilst the majority of the associations were confirmed comparing NXP2LB+/IP+ with the IIM NXP2-, some peculiar associations were found significant only for the double positive patients: dysphagia (53%vs 30%,OR 2.56) and calcinosis (22%vs6.5% OR4) whereas IBM diagnosis and the presence of concomitant MSA antibodies were lost. Survival time from cancer onset is shown in figure.

IP did not confirmed anti-NXP2 antibodies in 18 sera: in 4 cases at least one MSA/MAA was identified by IP; these 18 patients did not show differences when compared with 213 anti-NXP2-.

Conclusion: Protein IP confirmed anti-NXP2 antibodies in 63% of LB+ sera. Double positive cases showed more typical DM features and rarely occurred in IIM not DM. Anti-NXP2 positivity by LB should be confirmed by other methods in order to correctly diagnose and characterize IIM patients.

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[1] Arthritis Res Ther 2012,30;14:R97



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FRI0240 HOSPITAL ANXIETY AND DEPRESSION SCALE AND SENSE OF COHERENCE 13-ITEM SCALE IN A SWISS COHORT OF SYSTEMIC SCLEROSIS PATIENTS: VALIDITY, RELIABILITY AND SENSITIVITY TO CHANGE

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Background: Depression, anxiety and distress affect the quality of life of patients with systemic sclerosis (SSc) [1]. The Hospital Anxiety and Depression Scale (HADS) and Sense of Coherence 13-item scale (SOC-13, measuring comprehensibility, manageability and meaningfulness) are screening tools used in patients with different medical conditions. However, their validity, reliability and sensitivity to change in SSc patients has not been evaluated yet.

Objectives: To examine the psychometric properties of HADS and its subscales HADS-A and HADS-D (measuring anxiety and depression symptoms, respectively), and unidimensional SOC-13 in a large cohort of Swiss SSc patients.

Methods: Consecutive patients fulfilling the ACR/EULAR 2013 classification criteria for SSc who completed the HADS, SOC-13, Short Form-36 Health Survey (SF-36) and Scleroderma Health Assessment Questionnaire (SHAQ) were included in a cross-sectional and longitudinal analysis. Cronbach's α, split-half reliability and construct validity were measured. Sensitivity to change (Cohen's d coefficient) was assessed in patients who worsened within 12±3 months, defined as occurrence of any of the following events: decline in forced vital capacity (FVC)≥10%, new diagnosis of interstitial lung disease (ILD) on high-resolution computed tomography (HRCT), progression of known ILD to >20% lung involvement on HRCT (ILD20), new-onset pulmonary hypertension (PH), increase in European Scleroderma Study Group activity index (EScSG-AI) >3 points, new active digital ulcers, increase in modified Rodnan skin score (mRSS) > 7 points.

Results: Of 345 patients (aged 59.34±14.17, 82.9% female, 18.8% with diffuse cutaneous SSc, 47.6% anti-centromere Ab-positive, 23.5% anti-Scl-70 Ab-positive, 13% anti-U1RNP Ab-positive and 11.3% anti-RNA polymerase III Ab-positive) 85 participated with a second visit to the sensitivity to change analysis.

Internal consistency was excellent for the HADS (Cronbach's α=0.91; split-half reliability r=0.92), and very good for HADS-A, HADS-D and SOC-13 (Cronbach's α=0.85-0.89; split-half reliability r=0.86-0.89).

Regarding construct validity, all four scales showed a strong to very strong correlation to each other, as well as with the mental components of SF-36 (Spearman's r=0.63-0.85). There was a moderate to strong correlation with the SHAQ (Spearman's r=0.45-0.64).

Regarding sensitivity to change: HADS-A showed a large to very large effect size (ES) for progression of ILD as assessed on HRCT and increase in EScSG-AI (Cohen's d=1-1.63), and a very small to small ES for changes in FVC, DU and mRSS (Cohen's d=0.02-0.45). HADS-D showed a large ES for changes in the ILD20, mRSS and EScSG-AI (Cohen's d=0.82-1), and moderate ES for changes of FVC, ILD, PH, DU (Cohen's d=0.1-0.49). SOC-13 showed generally a very small to small EF, except for change in mRSS (Cohen's d=0.56).

Conclusion: The HADS(A/D) and SOC-13 are valid and easy-to-use tools to detect depression, anxiety and distress in SSc. However, their sensitivity to change might be limited by the respective type of organ involvement and its impact on the patients' psychological wellbeing.

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Disclosure of Interests: Alexandru Garaiman: None declared, Carina Mihai: None declared, Rucsandra Dobrota: None declared, Suzana Jordan: None declared, Britta Maurer Grant/research support from: AbbVie, Protagen, Novartis, congress support from Pfizer, Roche, Actelion, and MSD, Speakers bureau: Novartis, Oliver Distler Grant/research support from: Grants/Research support from Actelion, Bayer, Boehringer Ingelheim, Competitive Drug Development International Ltd. and Mitsubishi Tanabe; he also holds the issued Patent on mir-29 for the treatment of systemic sclerosis (US8247389, EP2331143)., Consultant of: Consultancy fees from Actelion, Acceleron Pharma, AnaMar, Bayer, Baecon Discovery, Blade Therapeutics, Boehringer, CSL Behring, Catenion, ChemomAb, Curzion Pharmaceuticals, Ergonex, Galapagos NV, GSK, Glenmark Pharmaceuticals, Inventiva, Italfarmaco, iQvia, medac, Medscape, Mitsubishi Tanabe Pharma, MSD, Roche, Sanofi and UCB, Speakers bureau: Speaker fees from Actelion, Bayer, Boehringer Ingelheim, Medscape, Pfizer and Roche, Mike-Oliver Becker: None declared

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FRI0241 INFLUENCE OF PATIENT REPORTED ''ARTHRITIS ACTIVITY'' IN DETERMINING SHAQ, HAQ-DI AND COCHIN SCORES IN SYSTEMIC SCLEROSIS

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Background: Arthritic involvement in systemic sclerosis (SSc) is a common manifestation impacting on the quality of life. A wide range of articular involvement is recognised including from arthralgia to inflammatory joint and tendon disease.

Objectives: To assess the weight of patient reported ''arthritis activity'' in determining Patient Reported Outcome Measures (PROMs) in an observational cohort of SSc patients.

Methods: We conducted a retrospective study of 330 clinic episodes from 121 unselected patients diagnosed with SSc according to EULAR/ACR 2013

classification criteria, in annual follow-up (for a total of 165 patients/year) with Pulmonary Function Tests (PFTs), Health Assessment Questionnaire - Disability Index (HAQ-DI), Scleroderma Health Assessment Questionnaire (sHAQ) and Cochin Hand Function Score (CHFS). Hand disability index was assessed by CHFS and global disability index was assessed by HAQ and sHAQ. Patient reported arthritis activity was assessed by Visual Analogical Scale for Arthritis Activity (VAS3). Based on the median of VAS3, patients were classified in two groups and the evaluation of global and hand disability index was performed for each group. Furthermore, we assessed the correlation between the change of VAS3 and the modification of disability scores (ΔHAQ, ΔSHAQ, ΔCHFS) over 12 months of follow-up. Following analysis of distribution, Spearman or Pearson Test were used to determine correlation coefficients, as appropriate (Prism 7).

Results: The median disease duration was 5 years (IQR 3-10). The median of VAS3 was 35 (IQR 2 - 66). In patients with VAS3 <35 and VAS ≥35 the HAQ-DI medians were 0.625 (IQR 0.25 - 1.5) and 1.75 (IQR 1.125-2.25) respectively, (p<0.0001); the sHAQ medians were 0.628 (IQR 0.255 - 1.114) and 1.701 (IQR 1.234-2.059), respectively, (p<0.0001); and the CHFS medians were 4 (IQR 0 – 19) and 28 (IQR 10 – 46) respectively, (p<0.0001). A significant correlation was observed between VAS3 and HAQ (r= 0.463, p<0.0001), SHAQ (r=0.651, p<0.0001), CHFS (r=0.497, p<0.0001); between ΔVAS3 and ΔSHAQ (r=0.493, p<0.0001).

Conclusion: This analysis of a monocentric non-selected population supports the key role of joint involvement in determining global patient reported functional and hand disability in SSc. Severity of musculoskeletal involvement should be carefully considered when interpreting PROs in patients with SSc.

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Disclosure of Interests: None declared

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FRI0242 IMPACT OF PULMONARY ARTERIAL HYPERTENSION WITH OR WITHOUT INTERSTITIAL LUNG DISEASE ON SCLERODERMA: A RETROSPECTIVE COHORT STUDY FROM THE NATIONWIDE SPANISH SCLERODERMA (RESCLE) AND PULMONARY ARTERIAL HYPERTENSION (REHAP) REGISTRIES

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Background: Pulmonary arterial hypertension (PAH) and interstitial lung disease (ILD) are the major life-threatening complications in systemic sclerosis (SSc). Data on the impact of PAH and/or ILD in SSc patients (pts) are limited by their low prevalence.

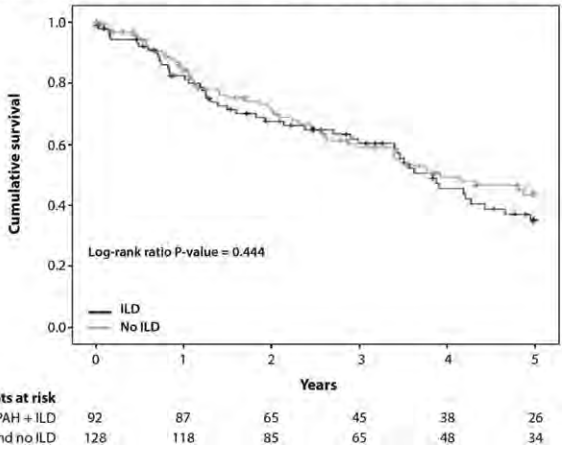
Objectives: To assess differences in demographic/clinical characteristics of SSc pts according to presence of PAH and how these are affected by ILD. The impact on characteristics and survival of PAH + ILD was also assessed.

Methods: We compared data on SSc pts without PAH from the Spanish registry of patients with SSc (RESCLE) (SSc pts) and SSc pts with PAH from the Spanish registry of pts with PAH (REHAP) (SSc-PAH pts). Only data common in both registries were analyzed. Sub analyses were performed according to the presence/absence of ILD. Transplant-free survival from diagnosis of PAH was estimated using the Kaplan-Meier method.

Results: 1,579 pts with SSc (RESCLE) and 364 pts with SSc-PAH (REHAP) were analyzed. Compared to SSc pts, SSc-PAH pts had worse functional status (NYHA FC III/IV: 70.6% vs. 8.2% in SSc pts) and pulmonary function (lower mean forced vital capacity [FVC, 81.2±20.6% vs. 93.6±20] and diffusing capacity for carbon monoxide [DLCO, 45.3±17.7% vs. 79.0±36.6%]). More patients had FVC/DLCO ≥1.4 (77.8% vs. 34.8%), tricuspid regurgitation (91.4% vs. 46.1%) or pericardial effusion (30.0% vs. 5.1%). Mean systolic pulmonary artery pressure (sPAP) was higher (70.0±21.3 vs. 27.5±9.1 mmHg) (all respectively; P<0.001 for all). Prevalence of ILD on high-resolution computerized tomography was similar (44.9% [n=92] vs. 41.8% [n=422] in SSc pts; P=0.408). These differences were also found when splitting both cohorts according to the presence / absence of ILD. Compared to SSc-PAH pts without ILD (n=128), pts with PAH + ILD (n=92) had worse functional status (NYHA FC III: 69.6% vs. 55.5% in SSc-PAH pts without ILD; P=0.036), lower mean FVC (70.9±21.9 vs. 86.2±18.6) and lower DLCO (39.4 ±17.0 vs. 49.1±17.9) both P<0.001. Five-year survival rate was 35% in SSc-PAH pts with ILD vs. 45% in SSc-PAH without ILD (P=0.444 [figure 1]).

Conclusion: PAH has a profound impact on functional status, pulmonary function and right ventricle function of SSc patients, independently of presence of ILD. Despite the deleterious effect of functional status and pulmonary function, in pts with SSc and PAH, presence of concomitant ILD has no impact on 5-year survival.

Figure 1. Survival rate estimates in SSc-PAH pts with and without ILD



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FRI0243 SARCOPENIA IS ASSOCIATED WITH MALNUTRITION IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Sarcopenia is one of the major health problems in older patients and is defined as a progressive decrease in muscle mass and function[1]. Sarcopenia has only rarely been studied in systemic sclerosis (SSc) and its impact in clinical characteristics of SSc is poorly investigated.

Objectives: To evaluate the associations between sarcopenia and clinical features in SSc patients.

Methods: Cross-sectional study, including 82 patients who met the ACR/EULAR 2013 classification criteria for SSc. Dual-energy X-ray absorptiometry, handgrip strength, and short physical performance battery were used to assess sarcopenia according the European Working Group on Sarcopenia in Older People's (EWGSOP) diagnostic criteria updated in 2019[1]. Malnutrition was evaluated according to the European Society of Clinical Nutrition and Metabolism (ESPEN)[2], using the Malnutrition Universal Screening Tool (MUST) to screen risk for malnutrition.

Results: The mean age was 60.4 years and 91.5% were women (table 1). Sarcopenia was identified in 15 (18.3%) SSc patients. Malnutrition was diagnosed in 12 (14.6%) and was more common in patients with sarcopenia (*P*=0.038). Also, there were significant differences between patients with and without sarcopenia regarding Body Mass Index (*P*=0.001), Fat Free Mass Index (*P*<0.001), knee extension strength (*P*=0.049), and Timed Up and Go test (*P*=0.041). There were no differences regarding age, disease duration, Rodnan skin score (mRSS), FVC and DLCO.

Table 1. Clinical characteristics of SSc patients with and without sarcopenia. Data presented as number (%) of patients, except when indicated otherwise.

Patients features	Whole (n=82)	SSc patients without sarcopenia (n=67)	SSc patients with sarcopenia (n=15)	*P* value
Females	75 (91.5)	62 (92.5)	13 (86.6)	0.606
Caucasian	68 (82.9)	53 (79.1)	15 (100)	0.258
Age (years)[b]	60.4 (10.6)	60.2 (10.3)	61.5 (12.3)	0.678
Diffuse skin involvement	16 (19.5)	16 (23.8)	0 (0)	0.082
Disease duration (years)[a]	12.8 (7.5, 19.2)	12.7 (7.1,19.2)	13.4 (8.9, 19.8)	0.324
Rodnan skin score[a]	4.0 (2.0, 10.0)	5.0 (2.0, 10.0)	2.0 (2.0,10.0)	0.076
Interstitial lung disease on HRCT	32 (39.5)	25 (37.3)	7 (10.4)	0.737
FVC (% predicted)[b]	88.4 (16.6)	88.4 (16.9)	88.3 (15.3)	0.991
DLCO (% predicted)[b]	63.7 (11.9)	63.6 (12.2)	64.2 (11.2)	0.855
BMI (kg/m^2)[b]	25.6 (4.6)	26.5 (4.4)	21.8 (4.1)	**0.001**
FFMI (kg/m^2)[b]	15.6 (1.7)	16.1 (1.6)	13.8 (1.2)	**<0.001**
FMI (kg/m^2)[b]	9.5 (3.7)	9.9 (3.6)	7.5 (3.5)	**0.023**
Malnutrition	12 (14.6)	7 (10.4)	5 (33.3)	**0.038**
MUST - Low risk	58 (70.7)	51 (76.1)	7 (46.7)	**0.046**
Moderate and high risk	24 (29.3)	16 (23.9)	8 (53.3)	
HAQ[b]	0.778 (0.591)	0.797 (0.575)	0.833 (0.576)	0.825
Timed Up and Go test (s)[a]	8.41 (7.41, 10.59)	8.39 (7.5, 9.4)	10.23 (7, 14)	**0.041**
Knee extension strength (kgf)[a]	21.40 (15.65, 27.52)	21.70 (18.05, 28.35)	14.82 (9.5, 24)	**0.049**

[a] Median (25, 75th percentiles)
[b] Mean (standard deviation)
Abbreviations: BMI: body mass Index; DLCO: diffusion capacity of carbon monoxide; FFMI: fat free mass index; FMI: fat mass index; FVC: forced vital capacity; HAQ: Health Assessment Questionnaire; HRCT: high-resolution computed tomography; MUST: Malnutrition Universal Screening Tool; SSc: systemic sclerosis.

Conclusion: Sarcopenia is relatively common and is associated with malnutrition in patients with SSc. In our population, sarcopenia was not associated with other features related to a more severe disease. The role of sarcopenia in the prognosis of SSc needs to be better understood in longitudinal studies.

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FRI0244 EOSINOPHILIC FASCIITIS-LIKE SECONDARY TO CHRONIC GRAFT-VERSUS-HOST DISEASE: CLINICAL DESCRIPTION OF 28 PATIENTS

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Background: Eosinophilic fasciitis (EF) is an uncommon chronic inflammatory disease characterized by myalgia, soft tissue hardening, peripheral eosinophilia and increased acute phase reactants, often triggered after strenuous physical exercise. Its appearance has been described as a rare complication after allogeneic transplantation of hematopoietic progenitors in the context of chronic graft-versus-host disease (cGVHD). Its etiopathogenesis is not well known and usually the treatment with systemic corticosteroids is effective
Objectives: Describe the clinical and transplant-related characteristics of a cohort of patients with eosinophilic fasciitis-like in the context of cGVHD
Methods: Observational, retrospective and descriptive study of the clinical characteristics of 28 patients affected by EF-like followed in a multidisciplinary consultation of cGVHD, started in March, 2014. Regular demographic variables, clinical characteristics related to the transplant and with the cGVHD, laboratory parameters, rescue therapies and their response were collected. The statistical analysis was done with Microsoft Excel 2007.
Results: Seventeen (60.7%) patients were male and 11 (39.35%) were women with a mean age of 48.75 years (range from 10 to 74). Acute myeloid leukemia was the most frequent cause of the transplant in 11 patients (39.3%). Transplant related characteristics are reflected in Table 1 and the clinical manifestations, therapies received and their response in Table 2. Four (14.2%) patients died during their follow-up, being the cause of death in 2 cases due to sepsis, and in 1 case attributable to GVHD.

Table 1. Baseline and transplant related characteristics (N = 28).

Variables	N (%)
Donor Type (related / not related)	13(46.4%)/15(53.6%)
Type of conditioning (reduced intensity / myeloablative)	18(64.25%)/10(35.7%)
Source of cells (Peripheral blood / bone marrow)	27(96.4%/1(3.6%)
cGVHD type quiescent / de novo / progressive	11(39.3%)/13(46.4%)/4(14.3%)
Other affected organs (cGVHD score)	
-Mouth	6(21.4%)
-Eyes	10(35.7%)
-Lung	2(7.1%)
-Liver	3(10.7%)
-Gastrointestinal tract	0(0%)
-Genital	2(7.1%)
-Cutaneous	16(57.14%)
Global Score	4(14.2%)/14(50%)/10(35.7%)
NIH[1] (mild / moderate / severe)	

[1] NIH: National Institute of Health.

Table 2. Clinical manifestations and therapies (N = 28).

Variables	N (%)/Median (range)
Prodromic symptoms: yes / no	20(71%)/8(29%)
- Stiffness	2(7.1%)
- Artromyalgia	17(60.7%)
- Edema	3(10.7%)
Time until first visit	31.3 months (range 9-73)
Contracture Yes / No	18(64.3%)/10(35.7%)
Mobility limitation (mild / moderate)	13(46.4%)/9(32.1%)
ECOG[1] affected	11(39.2%)
Eosinophilia	17(60.7%)
Positive autoantibodies	8(28.5%)
First line therapies (corticosteroids)	28(100%)
Extracorporeal photoapheresis	19(67.9%)
Therapies of 2nd line/ 3rd or more	6(21.4%)/12 (42.8%)
Physiotherapy	14 (50%)
Response: complete / sequels	10(35.7%)/18(64.2%)

[1]ECOG: Eastern Cooperative Oncology Group scale to assess the quality of life

Conclusion: Nonspecific joint symptoms such as stiffness, edema or arthromyalgia in patients undergoing allogeneic transplantation of hematopoietic progenitors may be factors that predict the development of sclerotic GVHD type eosinophilic fasciitis-like and should be closely monitored in order to be able to perform early stage diagnoses of the disease. It is necessary to deepen the pathogenesis of this entity and the multidisciplinary approach to improve the prognosis of patients with GVHD

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FRI0245 PULMONARY ARTERIAL HYPERTENSION IN SYSTEMIC SCLEROSIS IS NEARLY ALWAYS ACCOMPANIED BY A LOW DIFFUSING CAPACITY

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Background: Scleroderma (systemic sclerosis; SSc) has high morbidity and mortality. Pulmonary hypertension (PH) and pulmonary arterial hypertension

(PAH) is common with a high mortality (1). SSc patients are screened with pulmonary function tests (diffusing capacity of the lung for carbon monoxide; DLCO) (2).

Objectives: The DLCO%predicted was analyzed comparing patients with and without PAH to determine if it is always low at time of PAH diagnosis.

Methods: The Canadian Scleroderma Research Group (CSRG) database was used containing more than 1300 SSc patients with a mean disease duration of 8 years. All patients with at least one follow up visit and DLCO recorded at least twice were eligible for enrolment into this nested case control study. Diagnosis of PH was verified using several algorithms within the database including R heart catheterization, use of PH medications and physician response of 'yes' to question has this patient been diagnosed with pulmonary hypertension. Sensitivity, specificity and positive (PPV) and negative predictive values (NPV) were calculated for DLC0%predicted <50% and presence of PH/PAH.

Results: At time of PH diagnosis, the mean DLCO% predicted was 47% (N=30) vs no PH 73% (N=960) P<0.0001, and proven documented PAH also showed the differences (PAH, N=22 DLCO% predicted 51% vs. PAH negative (N=968) DLCO% pred 72%, P<0.0001) (Table 1). The OR of a DLCO%predicted less than 60 was 4.7 for PAH and 7.6 for PH (both P<0.001) and even higher if DLCO<50% (OR 11.5 for PH and 7.6 for PAH). Table 2 shows the PPV of DLCO at varying levels.

Table 1. DLCO comparison between PH+ and PH- SSc patients and between PAH+ and PAH- SSc patients, at the time of diagnosis.

	PH+ (n=30)	PH- (n=960)	P-value	PAH+ (n=22)	PAH- (n=968)	P-value
mean±SD	47.17±17.53	72.74±20.79	<0.0001	51.23±17.55	72.44±20.99	<0.0001
Range	18-81	13-147		25-81	13-147	

Table 2. Sensitivity, specificity and predictive values in SSc-PH and -PAH for DLCO at various cut points.

		OR	PPV	Specificity	NPV	Sensitivity
PH	DLCO<50%	11.5 (CI 95% 5.4-24.8),p<0.0001	13.2%	87.0%	98.7%	63.3%
	DLCO<60%	7.6 (CI 95% 3.3-17.2), p<0.0001	7.9%	73.3%	98.9%	73.3%
	DLCO>80%	0.06 (CI 95% 0.008-0.46), p=0.007	0.3%	64.5%	95.5%	3.3%
PAH	DLCO<50%	7.6 (CI 95% 3.2-17.9), p<0.0001	8.3%	86.4%	98.8%	54.5%
	DLCO<60%	4.7 (1.9-11.3), p<0.001	5.0%	72.7%	98.9%	63.6%
	DLCO>80%	0.1 (0.01-0.7), p=0.018	0.3%	64.8%	96.8%	4.5%

Conclusion: A low DLCO is associated with a high odds of PH/PAH in SSc and the NPV is very high at both DLCO<50% predicted and <60% predicted. This may aid in determining who should recieve a right heart catheterization in SSc patients.

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FRI0246

GENOTYPING OF CYP3A5 IS USEFUL FOR TREATMENT WITH TACROLIMUS IN INTERSTITIAL LUNG DISEASE IN DERMATOMYOSITIS

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Background: Tacrolimus (TAC), an immunosuppressant, can be used in second-line maintenance therapy of interstitial lung disease (ILD) in patients with dermatomyositis (DM) [1]. In Japan, TAC is approved for DM-ILD and often used as induction therapy for severe cases, especially in patients with anti-MDA5-Ab (melanoma differentiation-associated gene 5 antibody) positive, in combination with glucocorticoids (GC) and intravenous cyclophosphamide (IVCY). Some studies reported the clinical efficacy of initial high-trough level TAC for DM-ILD in combination with GC and IVCY [2]. Adjustment to target concentration of TAC in early stage of treatment is important for controlling disease activity. The concentration of TAC depends on genetic polymorphisms in cytochrome P450 (CYP) 3A5 enzyme expression and several reports showed that the bioavailability and concentration of TAC in patients with a CYP3A5 *1 allele (*1) was lower than those with a CYP3A5 *3/*3 (*3/*3) [3].

Objectives: To examine the usefulness of CYP3A5 polymorphisms in decision of initial dose to achieve the target concentration of TAC and to evaluate the clinical efficacy in patients of DM-ILD who achieved the enough concentration of TAC in early stage of treatment.

Methods: We investigated CYP3A5 polymorphisms and TAC concentration in 9 patients of DM-ILD without renal dysfunction (eGFR>60). TAC was taken after both morning and evening meals and blood samples were taken 12h after TAC administration. The blood concentration of TAC normalized to the corresponding dose per body weight (C/D, ng/ml per mg/kg) was analyzed according to genetic variation in CYP3A5. Based on the retrospective analyzation, we chose proper dose of TAC in initial treatment for an anti-MDA5-Ab positive DM-ILD patient, whose genotype was *3/*3.

Results: The C/D value in the *3/*3 group (n=6) was 154.6±25.6, which was significantly higher than that in the *1 group (n=3;79.0±2.8; P =0.028). When the target concentration was set at 5-10 ng/ml, the required dose was (0.0316 to 0.0633) mg/kg in the *1 group and (0.0162 to 0.0324) mg/kg in the *3/*3 group. The *1 group needs more dose than that of the *3/*3 group to achieve the same target trough of TAC, suggesting that the examination of CYP3A5 genotype is useful for deciding initial dose of TAC (Fig.1). We started TAC 6mg/day with setting target concentration at 15-20 ng/ml to a *3/*3 patient of DM-ILD with anti-MDA5-Ab positive, resulting in good clinical course with making rapid attainment of target concentration in early stage of treatment (Fig.2).

Conclusion: To examine the CYP3A5 genotype is valuable for deciding the initial dose of TAC, especially in patients who need achievement to target concentration rapidly.

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Fig.1 <CYP3A5 *1/*3 needs higher dose of TAC than that of CYP3A5 *3/*3>

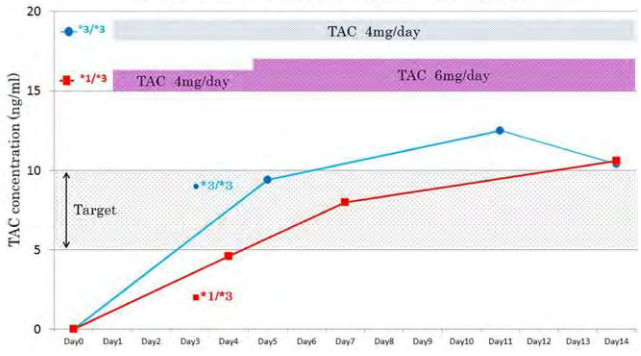
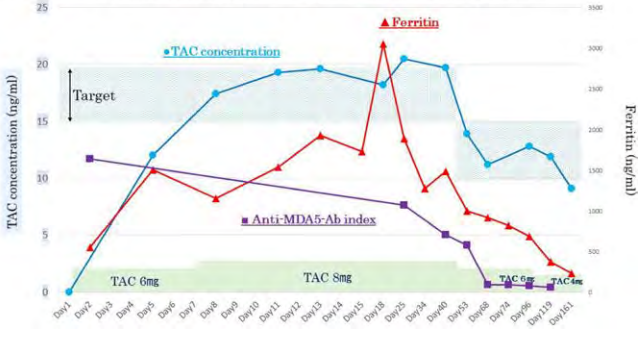


Fig.2 < Clinical course of a CYP3A5 *3/*3 patient with anti-MDA5-Ab positive >



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FRI0247

COMPARISON OF THE RITUXIMAB(RTM) IN MONOTHERAPY REGIMEN AND MYCOPHENOLATE MOFETIL (MMF) EFFICACY AND SAFETY IN SYSTEMIC SCLEROSIS (SSC) WITH INTERSTITIAL LUNG DISEASE (ILD)

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Background: Although ILD occurs in the majority of patients with SSc, treatment options for this manifestation is empirical and at present consists of cyclophosphamide or MMF. However, the immunosuppressants(IS) use leads to rather limited improvement of ILD and is associated with many adverse reactions. The search for novel, more efficacious agents has been continued, such as attracting much attention RTM.

Objectives: To compare the impact of MMF and RTM a single-agent therapy on SSc clinical manifestation and activity, and the safety of these agents in the open-label prospective non-randomized study.

Methods: 80 patients with the confirmed SSc diagnosis and ILD evidence based on MSCT findings were enrolled into the study. All patients received low and moderate-dose glucocorticoids regimens. Group A(n=35) received RTM as a single therapy agent for 13.3±2.3 months at total dose 1.35±0,5g(the patient's average age was 45.0±15 years, with female proportion 80%; SSc duration 6.3±2.3 years; diffused/localized forms 1.3/1). Group B(n=36) received MMF for 12±6 months at total dose 10.6±5 g(the average age 49±13 years, females 91%, SSc duration 7.1±5 years, diffused/localized forms 1/1.3). The time courses of FVC, DLCO, modified skin count(mRss, points), activity index (EScSG, points), and cardiac rhythm and conductivity disorders(ECG) were assessed into the study.

Results: In Groups A and B the therapy was associated with significant decrease in mRss(p=0.02 and 0.009, respectively) and EScSG(p=0.00017 and 0.000165, respectively). Reducing the number of patients with cardiac conductivity disorders was observed only in MMF-treated patients(p=0.03).

Evaluation of FVC time course revealed significant FVC increase only in Group A(p= 0.002), with median increment about 5%.

In Group A 10% FVC increase was found in the third of the patients thus exceeding respective parameter in Group B(p=0.2). The patient percentage with FVC decrease by ≥10% did not differ significantly between groups.

During the follow-up period no change of the other studied parameters was observed.

The therapy was better tolerated in RTM-treated group: during RTM therapy adverse reactions emerged in lower proportion of the patients(4/11%) compared with MMF-treated group(12/27%), p=0,5.

Parameters	Group A	Group B
Activity Index1 *M ± SD*	2.8±1.4*	1.9±1.5*
Activity Index2 *M ± SD*	1.4±1.2*	1.2±0.9*
Skin count1 *M ± SD*	11.5±9.5 *	7.5±6.9 *
Skin count2 *M ± SD*	8.2±6.2 *	4.8±3.9 *
FVC1 *M ± SD*	78.7±20.0 *	90.3±20.8
FVC2 *M ± SD*	84.2±20.0*	92.2±21.0
ΔFVC %	5.3 [0.8; 11.1]	1.9 [-3.5; 6.0]
FVC increment by≥10%, n/%	9/26	6/13.3
FVC decrement by≥10% n/%	2/5.7	4/8.9
DLCO1 *M ± SD*	51.8±19.9	52.2±17.4
DLCO2 *M ± SD*	49.5±16.0	51.9±17.0
ΔDLCO %	0.5 [-4.5; 8.8]	-1.15 [-6.6; 3,65]
DLCO increment by≥10%, n/%	3/8.6	4 /8.9
DLCO decrement by≥10% n/%	3/8,6	6/13.3
number of patients with cardiac conductivity disorders1, n/%	13/37	13/29*
number of patients with cardiac conductivity disorders2, n/%	14/40	5/11*

Notes: in Parameters column 1 = before treatment, 2 = after treatment; M ± SD = mean value and standard deviation; * = significant difference between the vales measured before and after the treatment

Conclusion: Both agents effectively alleviated skin induration and EScSG, and significantly improved FVC. However, only RTM use revealed significant FVC increase including clinically significant FVC increase. RTM was slightly better tolerated compared to MMF. The study findings substantiate potential use of RTM both as a first-line agent for ILD treatment in the patients with SSc, and in the event of IS inefficacy of poor tolerability. The MMF use is more preferable in patients with less pronounced ILD and cardiopathy.

Disclosure of Interests: None declared

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FRI0248

PROGNOSTIC FACTORS FOR STEROID-FREE REMISSION IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES: IMPORTANCE OF ANTHROPOMETRIC MEASUREMENTS

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Background: Several studies have been conducted on factors associated with mortality in idiopathic inflammatory myopathies (IIM), but few studies have assessed prognostic factors for steroid-free remission in IIM.

Objectives: We investigated the various clinical factors, including body measurements, that affect IIM treatment outcomes.

Methods: Patients who were newly diagnosed with IIM between 2000 and 2018 were included. Steroid-free remission was defined as at least three months of normalisation of muscle enzymes and no detectable clinical disease activity. The factors associated with steroid-free remission were evaluated by a Cox regression analysis.

Results: Of the 106 IIM patients, 35 displayed steroid-free remission during follow-up periods. In the multivariable Cox regression analyses, immunosuppressants' early use within one month after diagnosis [hazard ratio (HR) 6.21, 95% confidence interval (CI) 2.61–14.74, p < 0.001] and sex-specific height quartiles (second and third quartiles versus first quartile, HR 3.65, 95% CI 1.40–9.51, p = 0.008 and HR 2.88, 95% CI 1.13–7.32, p = 0.027, respectively) were positively associated with steroid-free remission. Polymyositis versus dermatomyositis (HR 0.21, 95% CI 0.09–0.53, p = 0.001), presence of dysphagia (HR 0.15, CI 0.05–0.50, p = 0.002) and highest versus lowest quartile of waist circumference (WC) (HR 0.24, 95% CI 0.07–0.85, p = 0.027) were negatively associated with steroid-free remission.

Conclusion: The early initiation of immunosuppressant therapy, type of myositis and presence of dysphagia are strong predictors of steroid-free remission in IIM; moreover, height and WC measurements at baseline may provide additional important prognostic value.

Disclosure of Interests: None declared

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FRI0249

IN MYOSITIS PATIENTS, SJÖGREN'S SYNDROME IS ASSOCIATED WITH INCLUSION BODY MYOSITIS AND WITH ANTI-CN1A ANTIBODIES INDEPENDENTLY OF THE MYOSITIS SUBTYPE

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Background: Myositis are characterized by weakness and muscle inflammation. They encompass heterogeneous conditions, which include dermatomyositis (DM), inclusion body myositis (IBM) and polymyositis (PM) according to the EULAR/ACR 2017 criteria. We recently recorded a high prevalence of IBM in a cohort of primary Sjögren's syndrome (SS) (1). The signification of SS in the setting of myositis is unanswered.

Objectives: To refine the signification of SS in the setting of myositis.

Methods: Among a monocentric myositis cohort (according to the EULAR/ACR 2017 criteria), SS patients (according to the ACR/EULAR 2016 criteria) were identified (myositis/SS+ group) and compared to myositis patients without SS (myositis/SS- group).

Results: Among 414 myositis patients, SS criteria were available for 96 patients. Thirty two (33%) presented SS. Patients with SS tended to be more frequently women (F/M ratio 9.7 vs 3.0, p = 0.07). Age at diagnosis of myositis was similar in both groups (53 years [range 21-74] vs 53 years [range 16-77], p = 0.51).

Myositis subtypes repartition (as defined by EULAR/ACR 2017 criteria) was different in myositis/SS+ and myositis/SS- groups (p = 0.021), IBM being four-fold more prevalent in myositis/SS+ group (25% vs 6%, p = 0.018). Accordingly, the delay between the first muscle symptoms and myositis diagnosis was longer in myositis/SS+ group (7 months [0-336] vs 4 months [0-122], p = 0.041). Moreover, aside anti-cN1A antibodies, myositis-specific antibodies were less frequently found in myositis/SS+ patients than in myositis/SS- ones (16/32 [50%] vs 46/64 [72%], p = 0.035).

Anti-cN1A antibodies were more prevalent in myositis/SS+ patients (33% vs 5.8%, p = 0.0032). However, in myositis/SS+ group, anti-cN1A were frequent in each of the EULAR/ACR 2017 myositis subtypes and the association between SS and anti-cN1A positivity was maintained in a multivariate analysis adjusted with the diagnosis of IBM (p = 0.023).

Seven of the myositis/SS+ patients (22%) had systemic involvement typical of SS (vs 6 [9%] of the myositis/SS- patients, p = 0.12) including polyneuropathy (6 [20%] vs 6 [10%]) and type 2 cryoglobulinaemic vasculitis (1 [3%] vs 1 [1.6%]). In addition, 2 (6%) myositis/SS+ patients developed a lymphoma (one B diffuse large cell lymphoma of the parotid and one non-Hodgkin lymphoma), vs none of the myositis/SS- patients (p = 0.11). Only one (3%) of the myositis/SS+ patients developed myositis-associated cancer (diagnosed within 3 years of myositis diagnosis) versus 6 (9%) of the myositis/SS- patients (p = 0.66).

Aside hydroxychloroquine, more frequently used in myositis/SS+ group (38% vs 16%, p = 0.018), no significant difference was found in the management of the patients (taking into account the myositis subtype).

Conclusion: Myositis patients with SS have more frequently IBM than myositis patients without SS. They also have more frequently anti-cN1A antibodies, independently of the myositis subtype. They might develop systemic complications of SS.

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FRI0250 "ARE MYOSITIS ANTIBODIES SPECIFIC FOR IDIOPATHIC INFLAMMATORY MYOPATHY DIAGNOSIS?" CLINICAL CORRELATION OF A COHORT OF PATIENTS POSITIVE FOR MYOSITIS ANTIBODIES

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Background: Idiopathic inflammatory myopathies (IIM) are a group of immune-mediated diseases characterized my muscle weakness, skin rash and systemic involvement. Myositis-specific antibodies (MSA) and myositis-associated antibodies (MAA) play a major role in IIM diagnosis, classification and prognosis. Nevertheless, MSA/MAA testing is not standardized and there very few studies addressing their relationship with other diseases.

Objectives: To describe a cohort of patients tested positive for MSA/MAA, and to explore it´s relationship with IIM and other autoimmune diseases.

Methods: We retrospectively review all the serum samples obtained from patients tested for MSA/MAA during 2019 in the Immunology department of Ramón y Cajal University Hospital (Madrid, Spain). These antibodies were tested by specific immunoblot (EUROLINE: Autoimmune Inflammatory Myopathies 16 Ag) with highly purified MSA/MAA. Positivity was stablished according to absorbance titer and adjusted by positive control of each test (arbitrary units, AU). Patients were diagnosed with IIM according to their clinician diagnosis. Diagnosis and classification were confirmed by an independent rheumatologist (JL) according to current understanding of IIM classification.

Results: Three-hundred-seventy-five samples were tested for MSA during the study period. Two-hundred-seventy-nine were negative for all antibodies tested. Ninety-six samples were positive for one or more MSA/MAA, corresponding to 74 patients (11 patients had 2 different samples). Forty-nine (66.2%) of the patients who tested positive were female and 25 (33.8%) were male. Mean age was 58.65 years. Only 22 patients (29.7%) had a confirmed diagnosis of IIM, 24 (32.4%) had a diagnosis of other autoimmune disease, and 11 (14.9%) were diagnosed with interstitial lung disease (ILD) (Figure 1). Six ILD patients had anti-PM-Scl or anti-Ku antibodies, which are associated with scleroderma or overlap-CTD myositis, nevertheless, they remained classified as ILD as no other features were described in this group.

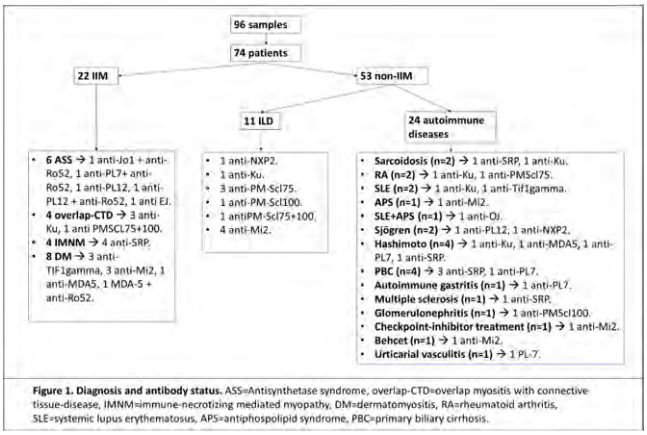


Figure 1. Diagnosis and antibody status. ASS=Antisynthetase syndrome, overlap-CTD=overlap myositis with connective tissue-disease, IMNM=immune-necrotizing mediated myopathy, DM=dermatomyositis, RA=rheumatoid arthritis, SLE=systemic lupus erythematosus, APS=antiphospolipid syndrome, PBC=primary biliary cirrhosis.

Seventeen patients were positive for more than 1 MAA or MSA, including 14 patients positive for anti Ro-52. Antibody titer was higher in the IIM group compared to non-myositis group (59.59 vs 44.16, p=0.015). Anti Mi-2 was positive in 4 ILD without any other myositis features, and high titer anti-SRP (n=4, mean 59.75 AU) was found in primary biliary cirrhosis (PBC) patients. Additionally, 5 patients positive for antiJo-1 using ELIA (Thermo Fisher) were diagnosed with antisynthetase syndrome. IIM diagnosis and its relationship with antibody titer is represented in table 1.

Table 1. Autoantibody titer according to diagnosis.

Antibody (Number of patients)	Number of samples	IIM	IIM antibody titer (AU)	Non-IIM	Non-IIM antibody titer (AU)	Other AI diseases	Anti Ro-52
Anti Jo-1 (n=1)	1	1 (100%)	92.7	0	-	0	1 (100%)
Anti PL-7 (n=8)	11	3 (37.5%)	29.59	5 (62.5%)	25.59	5 (62.5%)	2 (25%)
Anti PL-12 (n=3)	2	1 (33.3%)	53.95	2 (66.6%)	69.97	1 (33.3%)	2 (50%)
Anti EJ (n=1)	1	1 (100%)	99.46	0	-	0	1 (100%)
Anti OJ (n=2)	4	0	-	2 (100%)	23.04	1 (50%)	0
Anti Ku (n=14)	19	3 (21.4%)	107.25	11 (78.6%)	31.85	5 (35.7%)	0
Anti Tif1gamma (n=5)	6	3 (60%)	40.12	2 (40%)	23.84	1 (20%)	0
Anti NXP2 (n=2)	3	0	-	2 (100%)	13.99	1 (50%)	1 (50%)
Anti Mi2 (n=12)	17	3 (25%)	48.65	9 (75%)	26.67	4 (33.3%)	0
Anti SAE (n=1)	1	0	-	1 (100%)	18	0	0
Anti MDA5 (n=2)	3	2 (100%)	30.54	0		1 (50%)	1 (50%)
Anti SRP (n=9)	12	4 (44.4%)	42.69	5 (55.6%)	68.16	5 (55.5%)	2 (22.2%)
Anti PM-Scl75 and PM-Scl100 (n=2)	2	1 (50%)	68.6	1 (50%)	36.67	0	0
Anti PM-Scl75 (n=8)	10	0	16.26	8 (100%)	22.72	3 (37.5%)	1 (12.5%)
Anti PM-Scl100 (n=4)	5	0	-	4 (100%)	23.62	2 (50%)	0

Conclusion: Only 28.7% of the patients that were MAA/MSA positive had a diagnosis of IIM. Other autoimmune diseases and ILD were commonly found in this group of MSA/MAA positive patients.

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FRI0251 COMBINATION OF COMPUTED TOMOGRAPHY SCAN AND SERUM MYOSITIS SPECIFIC/ASSOCIATED AUTOANTIBODIES HELPS EARLY IDENTIFY AND TREAT PATIENTS WITH IPAF AND CTD-ILD

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Background: Interstitial lung diseases (ILD) could originate from idiopathic cause or secondary to connective tissue diseases (CTD). The most common causes of CTD associated ILD (CTD-ILD) include mixed connective tissue disease, systemic sclerosis (SSc), inflammatory myositis such as polymyositis (PM) and dermatomyositis (DM). Our preliminary data had demonstrated that ILD is not uncommon in patients with rheumatoid arthritis (RA) and Sjogren's syndrome

(SS) in Asia. Myositis-specific autoantibodies (MSAs) and myositis associate autoantibodies (MAAs) have been used for the early diagnosis of PM/DM and could be noticed in patients with idiopathic ILD. Our previous data also had identified that MSA/MAA were detected quite often in patients with CTD-ILD in addition to inflammatory myositis. Nonetheless, a specific group of ILD patients like interstitial pneumonia with autoimmune features (IPAF) are still challenging for pomologists, rheumatologist and radiologists, either in accurate diagnosis or treatment.

Objectives: We aimed to identify the prevalence of serum MSA/MAAs and clinical diagnosis on imaging in patients with IPAF and CTD-ILD and define the correlation between MSA/MAA and clinical imaging features.

Methods: Patients who had been suspected with autoimmune rheumatic diseases in the presence of interstitial lung diseases were included in this prospective study at a single medical center in Taiwan between February 2018 and November 2019. All enrolled patients had experienced clinical symptoms of ILD and been identified abnormalities on the chest plain films. All patients were inspected by both pulmonologists and rheumatologist. Computed tomography scans of chest had been reviewed by at least two pulmonary radiologists. Serological immunotherapy strips were performed to detect MSA/MAAs. Correlation analysis was performed among the different collected variables.

Results: 870 patients were reviewed by both pulmonologists and rheumatologists and received blood sampling including autoantibody profiling and MSA/MAA tests. The clinical diagnosis of CTD-ILD or IPAF were confirmed in 603 patients, who received 1078 chest CT scan due to clinically suspected CTD-ILD or IPAF. 33 patients received lung biopsies since other CTD-ILD or IPAF patients hesitate to receive invasive procedures. 78 patients had been admitted to intensive care units and received mechanical ventilation and were not suitable for lung biopsies. 22 of 33 patients received more than twice lung biopsies due to challenging diagnosis. 6 patients with CTD-ILD or IPAF had received extracorporeal membrane oxygenation (ECMO) due to ILD with secondary pulmonary infection and acute respiratory distress syndrome. The most commom detected MSA/MAA were anti-Ro-52 (27%), followed by anti-Ku (3.9%), and anti-Mi-2 (3.6%).

SS is the most common rheumatic disease in patients with CTD-ILD. MSA/MAAs were identified in patients with IPAF (36.4 %) in the absence of specific rheumatic diseases. Anti-nuclear antibody (27.4%), rheumatoid factor immunoglobulin M (21.6%) and anti-Ro (13.7%) were the most common autoantibodies identified in patients with IPAF. Anti-Ro-52 was positively corelated with nonspecific interstitial pneumonia in patients with CTD-ILD or IPAF, Phi= 0.371 and 0.326, both $p < 0.001$, respectively.

Conclusion: Early diagnosis of CTD-ILD and IPAF is still challenging for both pulmonologists, rheumatologists and radiologists. Identifying how serum MSA/MAAs contribute clinical manifestations on chest CT imaging is warranted and help clinical physicians and patients recognize the necessity of lung biopsy to reduce comorbidity.

References:

[1] Jee AS, et al. J Clin Med 2017
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Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.5594

FRI0252

HIGH EARLY MORTALITY IN IDIOPATHIC INFLAMMATORY MYOPATHIES: RESULTS FROM INCEPTION COHORT AT A TERTIARY CARE CENTER IN NORTHERN INDIA

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Background: The idiopathic inflammatory myopathies (IIM) lead to significant morbidity and mortality. Understanding short term outcomes is the 1st step towards addressing risk factors for poor prognosis.

Objectives: To assess the response to therapy, disease and treatment related morbidity and mortality in an inception cohort of IIM and determine the predictors of early mortality.

Methods: Sixty-nine patients with a physician diagnosis of IIM as per 2017 ACR/EULAR classification criteria were recruited into an inception cohort from Dec 2017 to Nov 2019. Their follow-up data was recorded from June 2019 to December 2019.

Clinical, laboratory and outcome variables were recorded as delineated in Figure 1A. Baseline characteristics were compared between deaths versus survivors, responders versus non-responders and those with and without major infections.

Results are expressed as median (IQR). SPSS, v23, IBM 2010 was used for statistical analysis.

Results: Of the 69 (54 female and 15 male) patients of median age 40 (23-51) and disease duration 3 (IQR 1-6) months, Dermatomyositis (DM) was the most common subset 26 (37.6%) (Fig, 1B). Myositis Specific and Myositis Associated Antibody (MSA and MAA) were positive in 30 (43.4%) and 11 (17%) respectively (Fig. 1 C).

Forty-eight patients followed-up over 10 (IQR 4.5-13) months accounting for 473 patient years, of which 8 (16.6%) suffered mortality and three PM were reclassified (Fig, 1B). Four (10%) had minimal, 3 (7.5%) had moderate and 33 (82.5%) had a major clinical response (Fig. 2A) with treatment. Eight (20%) of the 40 who survived had a relapse and 13 (32.5%) had steroid related complications. Eleven (27.5%) had at least 1 infection and it correlated with duration of steroid use (p-0.009, RR 0.78, 0.6-0.9) but not the cumulative dose of steroid (p-0.147) Duration of symptoms prior to treatment, subtype of myositis, MSA or presence of ILD did not predict the short-term response.

6-month survival was 83.3% (Figure 2B). Rapidly progressive ILD was the most common cause of death followed closely by malignancy and infection (n=3, 37.5%)(Table 1). Diagnosis of Cancer associated myositis (OR 6.1), positive anti-MDA5 (OR 5.8) and a negative ANA (OR 5.8) were predictors of early mortality.

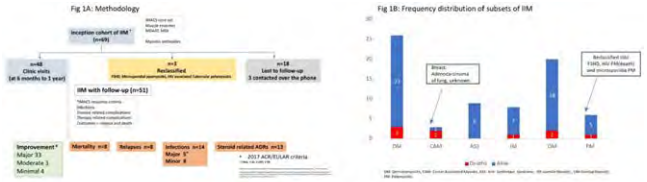
Table 1. Clinical details of the 8 patients who died on follow up.

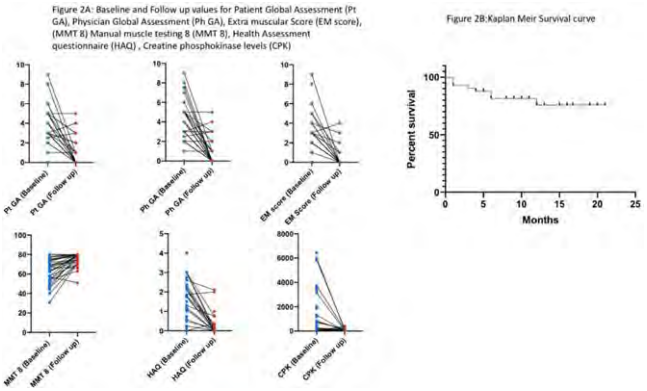
Case No.	Diagnosis	Gender	Age at disease onset (y)	Duration of disease in months	MSA	MAA	Cause of death	Place of death
1	DM	M	57	4	Anti-MDA 5	Anti- Ro 52	RP ILD	Hospital
2	DM	M	53	12	Negative	Negative	Disseminated Tuberculosis	Hospital
3	DM	F	68	6	Anti-TIF 1 γ	Negative	Malignancy	Home
4	JDM	F	14	1	Negative	Negative	RP ILD	Hospital
5	OM	F	43	1	Negative	Anti-PM/ Scl	Unclear	Home
6	OM	F	45	6	Anti-Jo 1	Anti- Ro 52	LRTI	Home
7	DM	M	80	1	Negative	Anti- Ro 52	Malignancy	Home
8	DM	F	31	3	Anti-MDA 5	Negative	RP ILD	Hospital

DM- Dermatomyositis, JM- Juvenile Dermatomyositis, OM- Overlap Myositis, M- Male, F- Female, MSA- Myositis Specific Autoantibodies, MAA- Myositis Associated Autoantibodies, RP ILD- Rapidly Progressive Interstitial Lung Disease, LRTI- Lower Respiratory Tract Infection

Conclusion: Indian patients with IIM suffer high early mortality attributable to RP ILD, cancer and infections.

Positive anti-MDA 5 and a negative ANA predict poor survival.





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FRI0253 OCULAR MANIFESTATIONS IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a connective tissue disease with heterogeneous manifestations. It affects different organs and therefore requires interdisciplinary diagnostic and therapeutic management.
Objectives: The aim of this study is to evaluate the frequency and characteristics of ocular manifestation in patients with systemic sclerosis.
Methods: The study involved 31 patients with SSc. All the study subjects underwent complete ophthalmological examination involving visual acuity assessment, examination of anterior and posterior eye segments, Schirmer I test, diameter and mobility of pupils, as well as eyeball mobility assessment of intraocular pressure and ultrasound assessment of vitreous body. Data regarding age, gender, SSc subtype, disease duration, age at diagnosis, nailfold capillaroscopic pattern, systemic corticosteroid or chloroquine use, blood pressure, ocular symptoms and detailed ophthalmic history were recorded.
Results: 31 patients (3 male, 28 female, mean age 42,7 ± 14,3 years; mean disease duration 10,3±8,1 years) were enrolled in this study. 7 (22,58 %) of them had no ocular symptoms. Among the patients with ocular symptoms, 20 (64.52%) complained of decreased vision, 13 (41,93 %) - of itching, 14 (45,16%) - of burning, 8 (25,81%) - of eye fatigue,4 (12,90 %) - of ocular pain, 4 (12,90%) - of foreign body sensation, 16 (51,61 %) - of dry eye, 5 (52,03 %) -photophobia, 2 (6,45 %) - of floaters, 10 (32,26 %) - of redness. Hardening and thickening of palpebral skin was noted in 27 (87,10 %) patients. Ophthalmological examination revealed higher incidence of the following abnormalities in the study group: myopic astigmatism - in 20 (32,26 %) eyes, vascular abnormalities within fundus - in 24 (38,71%) eyes, increased intraocular pressure (> 21 mm Hg) - in 13 (20,97%) eyes. Mean IOP values were 18,21 ±4,2 mm Hg.Eyelid telangiectasias was noted in 9 (29,03 %) patients, chronic blepharitis - in 13(41,94 %). Lens opacity was found in 16 (51,61 %) patients (27 eyes), mostly in the form of posterior subcapsular cataract (in 20 eyes), nuclear cataract (in 6 eyes) and cortical cataract appearing as focal cystic opacities (in 1 eye). The mean age of patients with cataracts was 49,2 ± 12,3 years (11,4 years older than patients without cataracts). Additionally, 14 of the patients with cataracts were either currently taking or had previously taken systemic corticosteroids. Superficial conjunctival hyperaemia was noted in 20 (64,52 %), and varicose dilatation of subconjunctival and episcleral blood vessels in 9 (29,03 %) and 7 (22,58 %) patients, respectively. In 9 eyes (14,52 %) foci of pigment epithelium were found peripherally on the optic disc, In 6 (9,68 %) eyes - thinning of choroidal capillaries and retinal pigment epithelium, in 8 (12,90 %) - ischemic areas surrounded by microaneurysms and intraretinal extravasation, dilatation of the vessel-free fovea. conjunctival fibrosis - in 8 (25,81 %) patients. In 25 eyes Schirmer I test results were below 10 mm, and in 7 eyes - below 5 mm. Eyelid stiffness was associated with difficulty in lid eversion and a woody texture upon palpation. Comparing patients with and without eyelid stiffness, we found that the mean age and the age at diagnosis were significantly lower in the former group ($p < 0.01$ and $p < 0.05$, respectively). The diffuse subtype was more prevalent among pts with eyelid skin changes ($p < 0,05$).
Conclusion: In patients with SSc numerous abnormalities within the vision of organ may be found. Ocular symptoms are relatively common complications of SSc, and may result in serious, irreversible changes in the organ of vision. Regular ophthalmological examinations are essential among the patients with SSc.
Disclosure of Interests: None declared
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FRI0254 SERUM IL-17 AND IL-21 AFFECT THE HEMODYNAMICS IN CONNECTIVE TISSUE DISEASE ASSOCIATED-PULMONARY HYPERTENSION

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Background: Pulmonary hypertension associated with connective tissue disease (CTD-PH) has complicated pathology including immune abnormalities, cardiac and pulmonary lesions. Therefore, it is difficult for rheumatologist to manage CTD-PH. We hesitate to use immunosuppressants in addition to pulmonary vasodilators to treat CTD-PH. Although there is a report that the cytokine such as Interleukin (IL)-6, IL-17 and IL-21 are involved in the development of PH[1)], changes in the hemodynamics of theses cytokines with treatment are not clear.
Objectives: We investigate serum cytokine profile and clinical appearance in CTD-PH, and clarify the relationship between change in cytokines and hemodynamics before and after treatment.
Methods: 14 cases of CTD-PH (8 cases in Scleroderma; SSc-PH group, 4 cases in Mixed connective tissue disease; MCTD-PH group, 2 cases in Systemic lupus erythematosus; SLE-PH group), 6 cases in Other-PH group, and 2 cases of SSc without PH as controls were included. The following clinical data were collected: age, gender, underlying disease, complication of interstitial lung disease, treatment (immunosuppressant and pulmonary vasodilator). Serum samples in pre- and post-capillary before and after treatment were collected during cardiac catheterization examination. Serum cytokines (MCP-1, IL-6, IL-17 and IL-21) of these samples were measured by ELISA (ABCAM, UK).
Results: Serum MCP-1, IL-6, and IL-21 levels were higher in SSc-PH group than in the other groups. Conversely, serum IL-17 levels tended to be higher in non-SSc group compared to SSc-PH group. Additionally, serum MCP-1 levels in SSc-PH group decreased in post-capillary as compared to pre-capillary. Furthermore, patients with decreased serum IL-17 and IL-21 levels before and after treatment showed improved pulmonary hemodynamics.
Conclusion: SSc-PH had a different cytokine profile compared with non-SSc-PH. We suggested that the serum IL-17 and IL-21 levels effect the hemodynamics in CTD-PH.
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FRI0255 BODY COMPOSITION IN SCLERODERMA PATIENTS IS ASSOCIATED WITH DISEASE ACTIVITY, SERUM LEVELS OF INFLAMMATORY CYTOKINES AND PARAMETERS OF NUTRITION AND LIPID METABOLISM

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Background: Fibrosis of the skin and visceral organs, especially digestive tract, and musculoskeletal involvement in systemic sclerosis (SSc) can have a negative impact on body composition, physical activity and nutritional status.
Objectives: The aim was to assess body composition and physical activity of SSc patients and healthy controls (HC) and the association with selected inflammatory cytokines/chemokines and laboratory markers of nutritional status and lipid metabolism in SSc.
Methods: 59 patients with SSc (50 females; mean age 52.5; disease duration 6.7 years; lcSSc: 34/dcSSc: 25) and 59 age-/sex-matched HC (50 females, mean age 52.5) without rheumatic or tumour diseases were included. SSc patients fulfilled ACR/EULAR 2013 criteria. We assessed body composition (densitometry: iDXA Lunar, bioelectric impedance: BIA-2000-M), physical activity (Human Activity Profile, HAP questionnaire), disease activity (ESSG activity index), serum levels of 27 cytokines/chemokines (commercial multiplex ELISA kit, Bio-Rad Laboratories) and serum levels of chosen parameters of nutrition and lipidogram. Data are presented as mean±SD.
Results: Compared to HC, patients with SSc had significantly lower body mass index (BMI, 27.4±8.3 vs. 22.4±4.3 kg/m^2, p<0,001), body fat % (BF%, iDXA: 38.0±7.6 vs. 32.6±8.2 kg, p<0,001; BIA: 31.3±7.6 vs. 24.3±7.9 kg, p<0,001) and visceral fat weight (VF, 1.0±0.8 vs. 0.5±0.5 kg, p=0,001), and also significantly decreased lean body mass (LBM, iDXA: 51.9±8.4 vs. 47.8±7.0 kg, p=0,005; BIA: 45.4±7.3 vs. 40.9±6.8 kg, p=0,005), and bone mineral density (BMD, 1.2±0.1 vs. 1.0±0.1 g/cm^2, p<0,001). Compared to HC, patients with SSc had increased extracellular mass/body cell mass (ECM/BCM, 1.03±0.1 vs. 1.28±0.4, p<0,001) ratio, reflecting deteriorated nutritional status and worse muscle predispositions for physical activity. Increased ECM/BCM in SSc was associated with higher disease activity (ESSG), increased skin score (mRSS) and inflammation (CRP, ESR), and with worse quality of life (HAQ, SHAQ), fatigue (FSS), and decreased physical activity (HAP). ESSG negatively correlated with BF%. HAP positively correlated with BMD. Serum levels of several inflammatory cytokines/chemokines (specifically

IL-1b, IL-5, IL-6, IL-8, IL-17, TNF, Eotaxin) and markers of nutrition (specifically total protein, albumin, insulin and C-peptide) and lipid metabolism (specifically triglycerides, high-density lipoprotein, apolipoprotein A, atherogenic index of plasma) were significantly associated with alterations of body composition in patients with SSc ($p<0.05$ for all correlations).

Conclusion: Compared to healthy age-/sex-matched individuals we found significant negative changes in body composition of our SSc patients, which are associated with the disease activity and physical activity, and could reflect their nutritional status, and gastrointestinal and musculoskeletal involvement. Detected alterations of body composition in SSc patients were significantly associated with serum levels of several inflammatory cytokines/chemokines and markers of nutrition and lipid metabolism, which might further support the role of systemic inflammation and nutritional status on the negative changes in body composition of SSc patients

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FRI0256 ADVANCED MICROCIRCULATORY DAMAGE IS ASSOCIATED WITH INCREASED PULSE WAVE REFLECTIONS IN PATIENTS WITH SSC

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Background: In systemic sclerosis (SSc), inflammation and microvascular damage are fundamental in the progressive fibrotic process. Although the presence of accelerated atherosclerosis in SSc is not as well-described as in other systemic disorders namely rheumatoid arthritis, it appears that individuals suffering from the disease are at higher risk for cardiovascular events. Nailfold Video Capillaroscopy (NVC) is a non-invasive and reproducible imaging technique of the capillary vascular bed, used in the evaluation of microvascular involvement in SSc. Previous data on the association between micro- and macrovascular damage are scarce.

Objectives: The aim of this study was to examine the association between micro- and macrovascular involvement in patients with SSc.

Methods: This is a cross-sectional study including consecutive SSc patients attending to a Scleroderma Outpatient Clinic between March and September 2018. All the study participants underwent NVC and the findings were classified in one of the following qualitative patterns: early, active, and late NVC pattern. Capillary's density was evaluated in the distal row of each finger, based on the number of capillaries per 1 mm and the mean capillaroscopic skin ulcer risk index (CSURI) was automatically calculated with software image analysis. Carotid intima-media thickness (cIMT) was measured in the common carotid artery bilaterally, according to the relevant guidelines. Aortic blood pressure (BP), heart rate adjusted augmentation index [AIx(75)] and carotid-femoral pulse wave velocity (PWV) were evaluated with applanation tonometry (Sphygmocor).

Results: Sixty-four (95,3% women) SSc individuals with mean age 57.54±12.99 years were included in this analysis. AIx(75) was significantly associated with CSURI (r=0.261; p=0.038) and inversely associated with the number of capillaries (r=-0.271; p=0.030) suggesting a link between the degree of microvascular disease and arterial stiffening. Regarding SSc-specific NVC patterns, AIx(75) were marginally lower in patients with early compared to active or late patterns (25.95±11.27 vs 32.50±11.17 vs 31.62±10.32%; p=0.081 and p=0.083) confirming a trend between progressive microvasculopathy and arterial stiffness. Mean cIMT was negatively correlated with enlarged capillary loops. Brachial or aortic systolic BP (SBP) and pulse pressure (PP) levels were not correlated with any of the studied NVC parameters.

Conclusion: Microvascular vasculopathy is associated with higher wave reflections, indicating an association between atherosclerotic disease and microvascular injury in SSc patients. Such observations may provide possible explanations for the excessive cardiovascular and mortality risk in this population.

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FRI0257 CAPILLAROSCOPIC VERY EARLY MORPHOLOGICAL AND QUANTITATIVE SPECIFIC ABNORMALITIES ANTICIPATE THE DEVELOPMENT OF THE "SCLERODERMA PATTERN" IN PATIENTS WITH RAYNAUD'S PHENOMENON

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Background: Nailfold videocapillaroscopy (NVC) abnormalities in subjects with isolated Raynaud's phenomenon (RP) may be present before transition to secondary RP(SRP) and development of a NVC "scleroderma pattern" and are known to predict for evolution to a connective tissue disease (CTD) within few years [1]. In a previous study, we have demonstrated that the very early increase of capillary diameter over 30 µm is an independent predictor for development of Systemic Sclerosis (SSc) associated SRP [2].

Objectives: Present pilot retrospective study aimed to investigate in a cohort of patients affected by CTD–related RP the presence of very early capillaroscopic morphological and quantitative abnormalities in the acquired pictures of NVC performed before the development of the NVC scleroderma-pattern. In particular, the study was addressed to identify a *"very early"* scleroderma pattern, in order to intercept patients with RP at high risk of evolution in a CTD, specifically SSc.

Methods: We selected the NVCs of 273 SSc patients presenting one of the validated NVC "scleroderma patterns". We enrolled 26 SSc patients having a NVC analysis performed before the development of *the "very early"* NVC pattern. As controls, we evaluated 26 patients affected by other CTDs with stable non-scleroderma pattern over time. The 16 images per patient obtained by NVC examination were analyzed for total number of capillaries, number and the limbs diameters of capillaries with a diameter >30 µm, and microhemorrhages. Statistical analysis was performed using non-parametric tests.

Results: All 26 SSc patients showed dilated capillaries with a diameter >30 µm in their previous NVC. Patients later developing scleroderma pattern had statically higher number and percentage of capillaries with a diameter >30 µm (p=0.0004 and p=0.0005), as well as a larger apical dilatation >40 µm (p=0.002). A progressive and significant increase in all capillary diameters were only detected in patients later diagnosed for SSc (apical p=0.006, venous p=0.02, arterial p=0.03). A significant homogeneous and progressive dilation was observed from the apical region and then involving both venous and arterial branches, only in SSc patients (p=0.002).

Conclusion: Present pilot study demonstrates, for the first time that, before to develop a validated NVC scleroderma-pattern, all potential SSc patients present significant very early morphological and quantitative NVC changes. In particular, the progressive and homogeneous capillary loop dilation over 40 µm in over 40%

of total number capillaries significantly could contribute to identify RP patients who will develop a SSc pattern after 4-5 years.

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FRI0258

CUMULATIVE INCIDENCE, SURVIVAL AND PREDICTORS OF PULMONARY HYPERTENSION IN SYSTEMIC SCLEROSIS SUBSETS: PAH IS NOT INCREASED IN LIMITED VS DIFFUSE PATIENTS BY ADJUSTED COMPETING RISK ANALYSIS

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Background: Pulmonary hypertension (PH) is a life-threatening complication of systemic sclerosis (SSc), thought to be more commonly found in limited cutaneous (lcSSc) compared to diffuse (dcSSc) subset. Since lcSSc has a better prognosis, it is unclear whether a higher occurrence of PH in lcSSc reflects survival bias.

Objectives: To compare the cumulative PH incidence in disease subsets, after accounting for death as a competing event, in a large multi-center SSc cohort.

Methods: Cumulative incidence of PH was studied in 1431 Canadian Scleroderma Research Group (CSRG) database patients (57% lcSSc; follow-up 3.5±2.9 years, range 1-14) by Fine-Gray analysis, unadjusted and adjusted for sex, age and SSc-related autoantibodies (SAS 9.4). Survival curves, predictors of PH development and survival were analyzed by Kaplan-Meier and Cox proportional hazards analyses (SPSS 25.0). Subgroup analysis was performed for PAH.

Results: 157 SSc patients had PH (including 117 PAH), either confirmed by RHC or postmortem. Compared to those without PH, lcSSc-PH patients had longer disease and older age at SSc diagnosis, while dcSSc-PH patients - more severe peripheral vascular and gastrointestinal involvement. The cumulative incidences of PH/PAH were similar in dcSSc and lcSSc after accounting for death in the adjusted competitive risk model (Table 1; Fig.1). 47% of PH- and 42% of PAH-patients died over a FU period. Male gender (p<0.0001) and anti-Scl-70 (p<0.001) were associated with earlier PH development, while older age (p=0.006) - with PAH (Table 2). ACA-negativity and older age predicted worse PH prognosis.

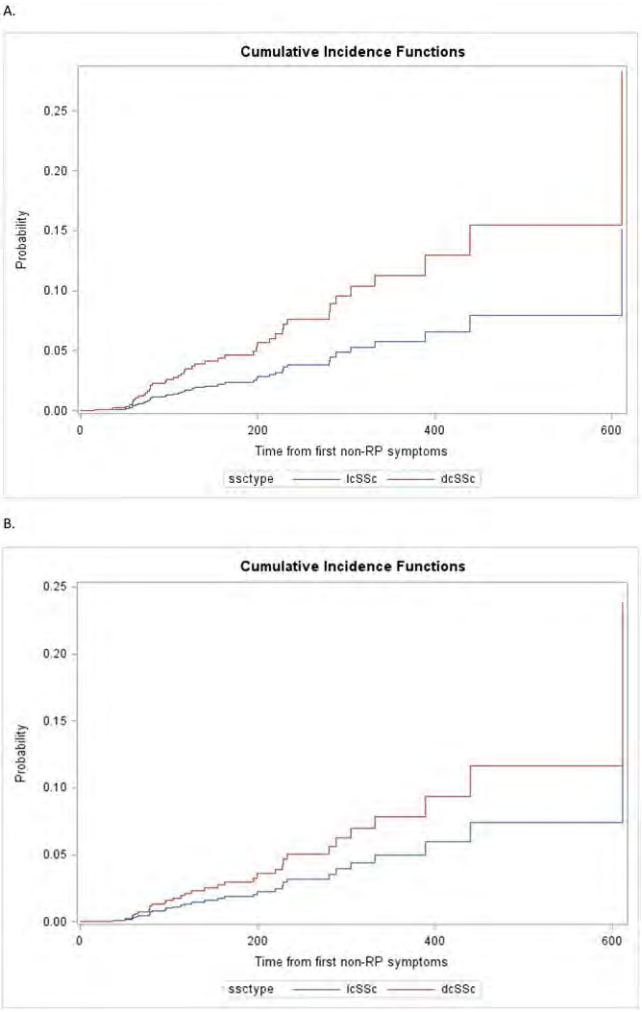


Figure 1. Cumulative incidence curves for PH (A) and PAH (B).

Conclusion: Cumulative incidence of PH, after accounting for death as competing event, was comparable in SSc subsets. Vigilance should be considered in males, Scl-70 positive and late age-onset SSc.

Table 1. Sub-distribution Hazard ratio of incident PH and PAH.

		PH		PAH	
		Hazard ratio (95% CIs)	P values	Hazard ratio (95% CIs)	P values
Crude Model	DcSSc vs lcSSc	2.03 (1.13, 3.66)	0.0186	1.60 (0.82, 3.16)	0.1710
Adjusted model	DcSSc vs lcSSc	1.82 (0.93, 3.57)	0.0818	1.57 (0.69, 3.59)	0.2812
	Female vs male	0.98 (0.42, 2.32)	0.9660	2.10 (0.51, 8.65)	0.3040
	Age	1.00 (0.99, 1.02)	0.7041	1.01 (0.98, 1.03)	0.5498
	Antibodies				
	ACA vs negative	0.95 (0.46, 1.96)	0.8991	1.08 (0.50, 2.35)	0.8391
	ATA vs negative	1.93 (0.84, 4.42)	0.1198	0.59 (0.13, 2.73)	0.4970
	Anti-RNAP vs negative	1.24 (0.45, 3.43)	0.6841	1.77 (0.58, 5.44)	0.3181

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FRI0259

THE CLINICAL VALUE OF GDF-15 IN ASSESSING MYOCARDIAL INVOLVEMENT OF IDIOPATHIC INFLAMMATORY MYOPATHY

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Background: Cardiac involvement is a serious complication of idiopathic inflammatory myopathy (IIM). Early diagnosis and intervention can improve prognosis. At present, myocardial biopsy is the gold standard for its diagnosis, but it is not commonly used because of its invasiveness. Biomarkers can be invoked as a non-invasive and convenient choice. The traditional markers of myocardial injury, as troponin and creatine kinase are lack specificity in inflammatory myopathy, so the novel biomarkers are getting attention.GDF-15 can predict the risk of cardiovascular disease and the prognosis of coronary atherosclerosis, heart failure and other diseases.
Objectives: This article was intended to investigate the diagnostic value of GDF-15 for myocardial involvement in inflammatory myopathy.
Methods: This retrospective study included 54 patients with inflammatory myopathy from May 2018 to October 2019.Of these,30 patients underwent cardiac magnetic resonance examination due to increased myocardial markers, excluding 1 case of severe lung infection. 33 patients with systemic lupus erythematosus (SLE),16 normal patients were used as the control group.The concentration of GDF-15 in the serum of all groups of patients was measured by ELISA.
Results: 1. There were significantly differences in GDF-15 levels in patients with inflammatory myopathy, systemic lupus erythematosus and normal subjects (H =39.870, P <0.001).2. 29 patients with cardiac magnetic resonance on the basis of the delayed enhancement (LGE) and ECV results were divided into two groups in which 19 patients with myocardial injury group and 10 patients without myocardial injury. The best cut-off value was calculated by ROC curve,and comparing GDF-15 and CKMB with the optimum cut-off values in predicting cardiac involvement in IIM.GDF-15 levels were statistically significant between the myocardial injury group (1765.868±1068.549 pg/ml) and the group without myocardial injury(689.967±458.12 pg/ml)(p =0.0011).At the same time, the creatine kinase isoenzyme (CKMB)(158.583±119.389 U/L vs 57.96±52.673 U/L, p =0.005) was statistically different between the two groups.3.GDF-15≥1005.3650pg/ml (AUC =0.853,95% CI 0.694-1.000) predicted myocardial involvement in inflammatory diseases with a sensitivity of 0.765 and specificity of 0.900.The AUC of the ROC curve for the joint detection of GDF-15 and CKMB was 0.888,95% CI0.757-1.000,with the predicted probability cut-off value in 0.3895, the sensitivity 0.941 and the specificity 0.800.The combined detection of the two increased the sensitivity of myocardial damage detection in IIM patients. 5. After adjusted for age, renal function, the risk of myocardial injury in IIM patients increased by an average of 0.3% per unit of GDF-15(OR =1.003,95% CI 1.000–1.005).
Conclusion: GDF-15 can predict myocardial injury in patients with inflammatory myopathy which have high specificity.The prediction sensitivity can be improved by combining with the traditional myocardial enzyme CKMB.More further studies are needed to confirm the specific mechanism of GDF-15 for myocardial involvement to assess the prognosis of such patients and guide further treatment.

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FRI0260

NAILFOLD VIDEOCAPILLAROSCOPY IS A USEFUL TOOL TO RECOGNIZE SYSTEMIC SCLEROSIS AND IDIOPATHIC INFLAMMATORY MYOPATHIES IN INTERSTITIAL LUNG DISEASE PATIENTS

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Background: Nailfold Videocapillaroscopy (NVC) is an essential tool for the assessment of Raynaud's Phenomenon (RP) among the Scleroderma Spectrum Disorders (SSDs). Recently, NVC abnormalities have been associated with a diagnosis of Idiopathic Inflammatory Myopathies (IIMs), independently of the presence of RP (1). Moreover, both SSDs and IIMs are commonly associated with Interstitial Lung Disease (ILD), which is the main cause of mortality in these conditions.
Objectives: To verify whether NVC may allow a better diagnostic classification in a cohort of patients with ILD followed by pulmonologists.
Methods: 361 patients affected by ILD were prospectively enrolled in a 30-months observational study. All these patients were clinically evaluated by rheumatologists and pulmonologists together and performed general blood tests, autoantibody research, chest High-Resolution Computed Tomography and NVC. The latter was considered positive in the presence of avascular areas or giant capillaries, and also the presence of Bushy Capillaries (BCs) was recorded.
Results: NVC was positive in 17.7% of ILD patients, and a third of these patients did not present RP. Patients with NVC abnormalities had a diagnosis of definite Connective Tissue Disease in 78.1% of cases. NVC resulted decisive in 25% of patients with a final diagnosis of Systemic Sclerosis according to the ACR/EULAR 2013 criteria. The presence of BCs and/or NVC+ in ILD patients with normal serum levels of muscular enzymes was associated with amyopathic IIM (BCs= OR 3.9, 95CI 1.05-14.38, p=0.04; NVC+= OR 5, 95CI 1.29-19.3 p=0.02; BCs and/or NVC+= OR 5.41 95CI 1.24-23.48 p=0.02), regardless the presence of RP.
Conclusion: NVC proved to be a valid tool in the correct assessment of ILD patients secondary to SSDs and amyopathic IIMs. Therefore, it could be considered in the diagnostic evaluation of patients affected by ILD, regardless of the presence of RP.

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Table 1. Comparison between ILD patients with and without NVC positivity.

Items	NVC+ patients	NVC- patients	p
Number	64	297	
Mean Age (±SD)	61.4±13.3	67.8±9.8	0.001
Female%	65.6	49.1	0.01
RP%	68.7	17.1	<0.0001
HRCT patterns%			
NSIP	51.5	36.8	0.02
OP	3.1	8	n.s.
UIP-like	31.15	44.8	n.s.
DIP	1.5	3.4	n.s.
LIP	1.5	0.4	n.s.
Indeterminate	10.9	6.7	n.s.
Final Diagnosis%			
SSDs	45.3	1	<0.0001
IIMs	25	6.4	<0.0001
Other CTDs	6.2	13.5	n.s.
IPAF	10.9	19.5	n.s.
IPF	7.8	27.9	0.0007

Legend: DIP: Desquamative Interstitial Pneumonia; HRCT: High Resolution Computed Tomography; IIMs: Idiopathic Inflammatory Myopathies, Poly/dermatomyositis, antisynthetase syndrome; IPAF: Interstitial Pneumonia with Autoimmune Features; IPF: Idiopathic Pulmonary Fibrosis; LIP: Lymphocytic Interstitial Pneumonia; NSIP: Nonspecific Interstitial Pneumonia; OP: Organising Pneumonia; RP: Raynaud's Phenomenon; SSDs: Scleroderma Spectrum Disorders, Systemic Sclerosis + Mixed Connective Tissue Disease; UIP: Usual Interstitial Pneumonia.

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FRI0261

DIFFERENTIAL EXPRESSION OF PERIPHERAL CD4+ T CELLS IN PATIENTS WITH SYSTEMIC SCLEROSIS AND MIXED CONNECTIVE TISSUE DISEASE

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Background: The CD4$^+$ T cell subsets plays an important role in its pathogenesis, and its new research are constantly being published, but its specific changes between SSc and MCTD are still unclear.

Objectives: The aim of the present study was to explore the absolute numbers of CD4$^+$ T subsets in peripheral blood(PB) of patients with SSc and MCTD using our modified flow cryometric method and investigate the role in the pathogenesis of both.

Methods: The PB samples from 54 patients with SSc, 51 patients with MCTD as well as 30 healthy control subjects were analyzed for lymphocyte subsets using flow cytometry. Of these patients, 19 had pulmonary involvement, including 9 patients with SSc and 10 patients with MCTD. Using directly the percentages from flow cytometry combined with internal standard beads calculated absolute number of peripheral lymphocyte subsets from the subjects in each group.

Results: Although there were some changes among CD4$^+$ T cell subsets in PB from these SSc patients and MCTD patients, the major alteration was the reductions of Treg cells. Compared with the normal controls, the absolute number of CD4$^+$CD25$^+$FOXP3$^+$Treg cells were significantly decreased in SSc patients and MCTD patients, and the absolute number of Th1 cells in MCTD patients is also significantly reduced. Notably, the absolute numbers of Th17 and Th2 cells were not different from those of normal controls, but the ratios of Th17/Treg in SSc patients and MCTD patients were significantly higher, causing by insufficient number of Treg cells (Fig 1). In addition, in patients with pulmonary involvement, we found that the absolute number of Treg cells was significantly reduced in patients with MCTD, while the absolute number of Th2 cells and Th17 cells was significantly reduced in patients with SSc(Fig 2).

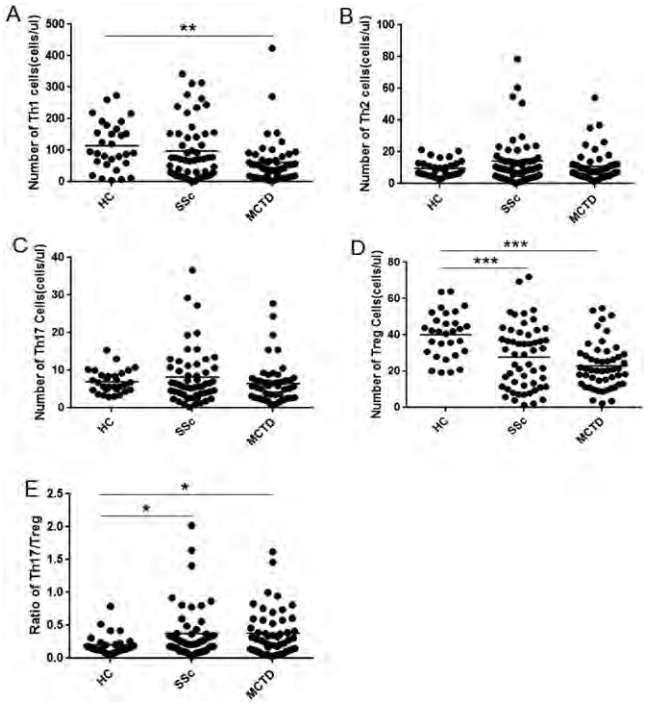


Fig 1. Comparison of the levels of CD4$^+$ T lymphocyte subsets in SSc patients, MCTD patients and healthy controls: (A) The absolute number of peripheral Th1 cells in patients with MCTD was significantly reduced; (B and C) There was no significant difference in the absolute number of Th2 cells in peripheral blood of different subjects; (D and E) The ratio of Th17/Treg cells in PB of patients with SSc and MCTD were significantly higher.*P < 0.05; **P < 0.01; ***P < 0.001.

Conclusion: The number of peripheral Treg cells in patients with SSc and MCTD was significantly reduced, suggesting that that SSc and MCTD progression is associated with the imbalances between pro-inflammation cells to anti-inflammation Treg cells. In addition, we also found that the decrease in peripheral numbers of Treg cells may contribute to the development of MCTD-associated lung disease, whereas in SSc patients who had lung involvement, the reduce in peripheral number of Th17 cells may result in a severe imbalance of Th17/Treg cells, thereby promoting disease progression.

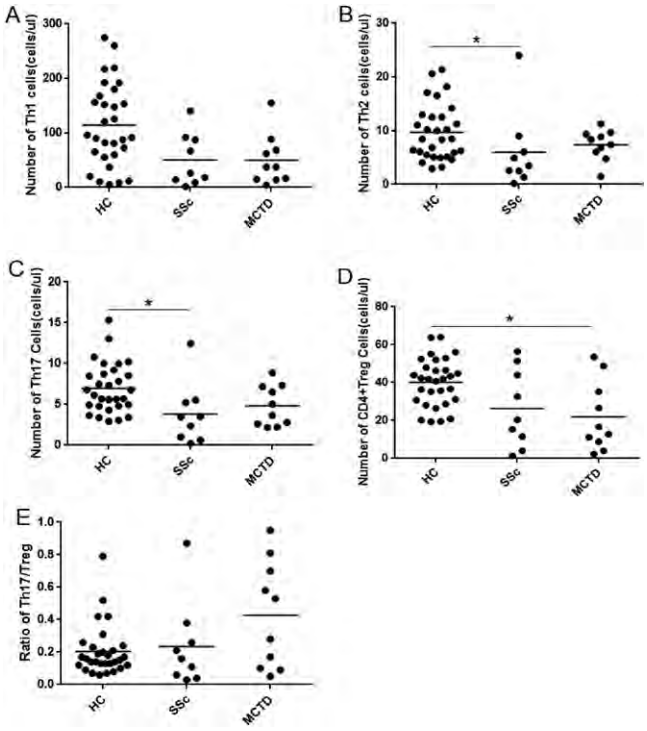


Fig 2. Comparison of the levels of CD4$^+$ T lymphocyte subsets in patients who had pulmonary involvement and healthy controls: (A) There was no significant difference in the absolute number of Th1 cells in peripheral blood of different subjects; (B and C) The absolute number of peripheral Th2 cells and Th17 cells in patients with SSc were significantly reduced; (D and E) The ratio of Th17/Treg cells in PB of patients with MCTD were higher.*P < 0.05; **P < 0.01; ***P < 0.001.

References:

[1] Liu M, Wu W, Sun X, et al. New insights into CD4(+) T cell abnormalities in systemic sclerosis. Cytokine Growth Factor Rev. 2016 Apr; 28:31-6. doi: 10.1016/j.cytogfr.2015.12.002.

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FRI0262

INCREASED PLASMA LEVELS OF HSP90 ARE ASSOCIATED WITH MORE SEVERE LUNG AND SKIN INVOLVEMENT IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Our previous study demonstrated that Hsp90 is overexpressed in the skin of patients with systemic sclerosis (SSc), in cultured SSc fibroblasts and preclinical models of SSc in a TGF-β dependent manner. We showed that Hsp90 is a new regulator of canonical TGF-β signaling and its inhibition prevents the stimulatory effects of TGF-β on collagen synthesis and dermal fibrosis[1].

Objectives: The aim of this study was to evaluate plasma Hsp90 of SSc patients and characterize its potential association with skin changes and SSc-related features.

Methods: A total of 92 patients (79 females; mean age 52.7; disease duration 6.0 years; diffuse cutaneous (dc)SSc / limited cutaneous (lc)SSc = 38/54) and 92 age- and sex- matched healthy individuals were included. Plasma Hsp90 levels were measured by ELISA (eBioscience, Vienna, Austria). Data are presented as median (IQR).

Results: Plasma Hsp90 levels were increased in SSc patients compared to healthy controls [12.5 (9.6–17.9) vs. 9.8 (7.7–12.4) ng/mL, p=0.0001]. Hsp90

levels in all patients positively correlated with CRP (r=0.271, p=0.015). Furthermore, Hsp90 concentrations were negatively associated with functional parameters of ILD: FVC (r=-0.291, p=0.013), FEV1 (r=-0.248, p=0.036), DLCO (r=-0.290, p=0.012) and SpO_2 (r=-0.317, p=0.038). When adjusted for CRP, these correlations still remained significant in multivariate analysis. Higher Hsp90 concentrations were associated with presence of synovitis [17.6 (15.4 – 24.0) vs. 12.2 (9.3 – 17.3), p=0.039]. In addition, only in patients with dcSSc, Hsp90 levels positively correlated with the mRSS (r=0.437, p=0.006). In a prospective analysis of patients with progressive SSc-ILD treated with 6 (n=21 patients) or 12 (n=14 patients) monthly i.v. pulses of cyclophosphamide (CPA, 10 mg/kg) we did not observe any significant differences between the baseline sample (month 0) and blood drawn after 1, 6 and 12 months. However, baseline Hsp90 was able to predict long-term response after one year of CPA treatment ($DLCO_{m12-m0}$; r=-0.494, p=0.037). Moreover, change in Hsp90 after one month of CPA treatment ($Hsp90_{m1-m0}$) was able to predict the short-term inflammatory response (CRP_{m3-m0}, r=-0.495, p=0.019; ESR_{m3-m0}, r=-0.496, p=0.031). Concentrations of extracellular Hsp90 were not significantly affected by other main clinical parameters of SSc.

Conclusion: We demonstrated higher plasma levels of Hsp90 in SSc patients compared to healthy controls. Concentrations of extracellular Hsp90 increase with higher inflammatory activity, with deteriorated lung functions in ILD and also with the extent and severity of the skin involvement in patients with diffuse cutaneous SSc. These data further highlight the role of Hsp90 as a significant regulator of fibroblast activation and tissue fibrosis in SSc. In addition, Hsp90 could become a predictor of treatment response.

References:

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Disclosure of Interests: Hana Štorkánová: None declared, Sabina Oreska: None declared, Maja Špiritović: None declared, Barbora Heřmánková: None declared, Kristyna Bubova: None declared, Martin Komarc: None declared, Karel Pavelka Consultant of: Abbvie, MSD, BMS, Egis, Roche, UCB, Medac, Pfizer, Biogen, Speakers bureau: Abbvie, MSD, BMS, Egis, Roche, UCB, Medac, Pfizer, Biogen, Jiří Vencovský: None declared, Jörg Distler Grant/research support from: Boehringer Ingelheim, Consultant of: Boehringer Ingelheim, Paid instructor for: Boehringer Ingelheim, Speakers bureau: Boehringer Ingelheim, Ladislav Šenolt: None declared, Radim Bečvář Consultant of: Actelion, Roche, Michal Tomcik: None declared

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FRI0263 QUANTITATIVE MUSCLE ULTRASOUND IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES-A PRELIMINARY STUDY

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Background: Muscle involvement is the most frequent clinical feature in patients with idiopathic inflammatory myopathies (IIM). In addition to muscular enzymes, muscular magnetic resonance has been investigated for the assessment of disease activity, but it is limited by high costs and it is not readily available. Muscle ultrasound (MUS) has been recently proposed as a valuable tool for the diagnosis and activity assessment of muscle involvement in IIM patients.

Objectives: To define the role of MUS in the diagnosis and assessment of disease activity in IIM through quantitative analysis of MUS

Methods: This was a prospective study conducted from February 2019 to November 2019. 41 patients with IIM: 17 men and 24 women, median age 61.4 years, of which 20 were polymyositis (PM), 16 dermatomyositis (DM) and 5 inclusion body myositis (IBM) were included. 30 healthy subjects (HS), comparable in age and gender to patients, were recruited as controls. In every patient and control MUS of upper and lower extremities was performed (in total 10 muscles per side) and digital images were saved. Quantitative muscle echo intensity (QME) was calculated using an image processing program (ImageJ) to obtain the mean value of greyscale (mGS) for each muscle. For patients with IIM creatine phosphokinase (CPK) levels were recorded, duration of disease (in months) was calculated and clinical evaluation tools for the assessment of disease activity were performed, such as manual muscle testing (MMT8), patient and physician visual analogue scales (pVAS, phVAS), health assessment questionnaire (HAQ) and myositis disease activity assessment tool (MDAAT).

Results: Patients had higher values of mGS across all muscles examined than controls (p<0.001). Among patients QME showed a negative correlation with MMT8 (p<0.001, -0.641<r<-0.412), but no correlation with CPK levels or duration of disease. A positive correlation was found between QME and HAQ (p<0.05; 0.320<r<0.599), pVAS (0.003<p<0.046; 0.314<r<0.455) and phVAS (0.029<p<0.002; 0.341<r<0.471). No significant correlation was found between QME and MDAAT and no statistically significant differences of muscle echo intensity were observed between patients with IBM, DM and PM.

Conclusion: Quantitative analysis of MUS showed to be useful to differentiate IIM patients from healthy subjects, therefore it could be a helpful technique to screen patients with muscular symptoms in which perform additional investigations. In our study, the data collected did not allow to assess the disease activity of IIM patients and did not allow to distinguish between the 3 different subgroups of IIM patients, but further studies may help in the identification of different muscular patterns to guide the clinical suspect and the possible role of MUS in the follow-up of the patients.

Disclosure of Interests: Alessandra Tripoli: None declared, Simone Barsotti: None declared, Andrea Delle Sedie Speakers bureau: MSD, Lilly, Novartis, Abbvie, Celgene, Giacomo Aringhieri: None declared, Saverio Vitali: None declared, Rossella Neri: None declared, Davide Caramella: None declared, Marta Mosca: None declared

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FRI0264 EFFECTIVENESS, SAFETY AND PATTERNS OF USE OF RITUXIMAB IN SCLERODERMA, IN CLINICAL PRACTICE: 9 YEARS' EXPERIENCE IN A TERTIARY HOSPITAL

E. Vicente[1], J. Fernández[2], I. Llorente[1], L. Vega[3], S. Castañeda[1,4], A. García-Vadillo[1], I. González-Álvaro[1], A. Humbría[1], A. Ortiz[1], E. Patiño[1], E. Tomero Muriel[1], R. Garcia de Vicuna[1]. *[1]H.U. de La Princesa, IIS-Princesa, Rheumatology, Madrid, Spain*; *[2]Undergraduate Student of Medicine, UAM, H.U. de La Princesa, IIS-Princesa, Rheumatology, Madrid, Spain*; *[3]H.U. de la Princesa, IIS-Princesa, Unidad Apoyo Metodológico, Madrid, Spain*; *[4]Cátedra UAM-Roche, EPID-Future, UAM, Madrid, Spain*

Background: Systemic sclerosis (SSc) is a clinically complex and heterogeneous disease. Interstitial lung involvement (ILD) is the main cause of mortality, but progression of skin fibrosis has also been associated with pulmonary dysfunction and mortality. Recently, Rituximab (RTX) has been postulated as a promising therapeutic alternative to cyclophosphamide (CF) or mycophenolate (MFM), but long-term experience is scarce.

Objectives: Describe the effectiveness, safety and long-term use of RTX, in a series of cases with SSc.

Methods: Retrospective observational study of patients with SSc (EULAR/ACR 2013 criteria) treated with RTX in a university hospital from 2010 to 2019. Sociodemographic data related to SSc and treatments were collected. The effectiveness of RTX was evaluated at 6-12 months and at the end of follow-up, by means of these main outcomes: Rodnan's modified cutaneous index (mRSS) for skin fibrosis; CK leves for myopathy, variation >10% in forced vital capacity (FVC) and >15% in lung diffusion capacity of carbon monoxide (DLCO) for ILD. Adverse events (AE) were recorded. Statistical analysis performed with Stata v.14 and statistical significance set for p≤0.05.

Results: 14 women with SSc (mean age 47±13 years, mean evolution 6.2±4.5 years) were treated with RTX for ILD (n=9), skin involvement (n=11) and/or inflammatory myopathy (n=3). The mean±SD of follow-up was 3.36±2.17 years. SSc type: diffuse cutaneous 35.71%, limited cutaneous 21.44%, overlap 35.71% and sine scleroderma 7.14%. Type of antibodies: 50% anti-Scl-70, 14.3% anti-centromere, 21.4% anti-RNA polymerase III and 7.14% anti-Ku. ILD was classified as NINE in 8 patients and NIU in 1. The first cycle of RTX included 2 infusions of 1g and was initiated a mean of 3.36±2.17 years after diagnosis. The retreatments were initially fixed every 6 months and later on demand in 4 patients, and in the rest on demand from the beginning, according to duration of clinical response. A mean of 3.9±2.5 cycles/patient (range: 1-11) were administered. 30% of patients had previously received CF and 21.5% MFM. RTX was administered in association with other DMARDs (MTX 64.29%, hydroxychloroquine [HCQ] 35.71%, MFM 57.14%, others 14.28%), CF (14.29%), intravenous immunoglobulins (7,14%) and prednisone (78.57%). In the final visit, the percentage use of DMARDs (50% MTX, 50% MFM and 28.57% HCQ) and prednisone (62.5% patients, 30% doses) was reduced. mRSS improved significantly. Muscle weakness disappeared in 3/3 with normal CK levels in 2/3

patients with myopathy. The FVC improved or stabilized in 22% and 56% of ILD, respectively, and the DLCO stabilized in 66.70% (not significant). TACAR stabilized in 55.56% of ILD, with some degree of worsening in the rest. Outcomes evolution in the Table:

Functional Parameters	Basal (mean±SD)	6-12 m (mean±SD)	CI 95%	P	Final (mean±SD)	CI 95%	P
FVC (n=9)	63.2±16.8	70.3±18.6	[-13.3–6.1]	0,40	71.9±21.1	[-14.4–5.9]	0.36
DLCO (n=9)	46.3±18.5	46.1±20.3		0,34	45.2±22.03	[-3.9–12.8]	0.24
Clinical Parameters	**Basal (mean±SD)**				**Final (mean±SD)**	**CI 95%**	***P***
mRSS (n=11)	13.1±7.2				8.8±7.1	[0.9–9.4]	0.02
CK (n=3)	1786.7 ±1483.8				134.7±119	[-2181.9 –5485.9]	0.2

CK: Creatine kinase; SD: Standard deviation; CI: Confidence interval; m: months.
The AE were mostly mild: 13 infusional reactions (6 patients), 1 uncomplicated herpes zoster and 2 serious infections that required admission. There were no exitus.

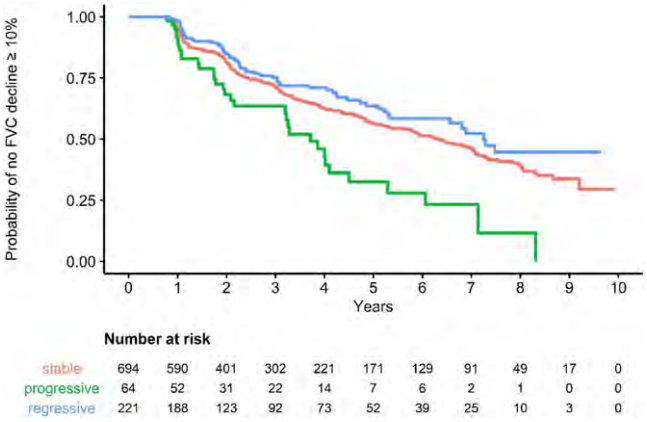
Conclusion: Our results, with a limited sample, suggest that the long-term use of RTX in real world clinical practice may be beneficial for the cutaneous, pulmonary and myopathic manifestations of SSc, with an acceptable security profile.

Disclosure of Interests: Esther Vicente Speakers bureau: BMS, Roche., Javier Fernández: None declared, Irene Llorente Speakers bureau: Gebro, Janssen, Sanofi, Lilly., Lorena Vega: None declared, Santos Castañeda: None declared, Alberto García-Vadillo: None declared, Isidoro González-Álvaro Grant/research support from: Roche Laboratories, Consultant of: Lilly, Sanofi, Paid instructor for: Lilly, Speakers bureau: Abbvie, MSD, Roche, Lilly, Alicia Humbría: None declared, Ana Ortiz: None declared, Esther Patiño: None declared, Eva Tomero Muriel: None declared, Rosario Garcia de Vicuna Grant/research support from: BMS, Lilly, MSD, Novartis, Roche, Consultant of: Abbvie, Biogen, BMS, Celltrion, Gebro, Lilly, Mylan, Pfizer, Sandoz, Sanofi, Paid instructor for: Lilly, Speakers bureau: BMS, Lilly, Pfizer, Sandoz, Sanofi
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FRI0265 IS AN IMPROVEMENT IN SKIN FIBROSIS ASSOCIATED WITH BETTER OUTCOME IN PATIENTS WITH SYSTEMIC SCLEROSIS? A EUSTAR ANALYSIS

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Background: In previous studies, we showed that in patients with diffuse cutaneous systemic sclerosis (dcSSc), worsening of skin fibrosis predicts later decline in lung function and worse survival. However, in many patients, an improvement of skin fibrosis is the natural course of dcSSc, and many current clinical trials are designed to show improvement of skin fibrosis rather than prevention of skin fibrosis progression.
Objectives: To investigate whether an improvement in skin fibrosis is associated with less progression of visceral organ involvement and better overall-survival during follow-up.
Methods: We evaluated patients from the European Scleroderma Trials and Research Group (EUSTAR) database with diffuse cutaneous systemic (dcSSc), baseline modified Rodnan skin score (mRSS) ≥7, valid mRSS at 12±3 months after baseline and ≥1 follow-up visit. Regression of skin fibrosis was defined as a decrease in mRSS >5 and ≥25% and progression as increase by the respective numbers from baseline to 12±3 months. Outcomes were pulmonary progression, cardiac progression, intestinal progression, new onset of scleroderma renal crisis and all-cause death using recently specified definitions (1). Associations between skin changes and outcomes were evaluated by Kaplan-Meier analysis and multivariable Cox regression.
Results: Of 1257 included patients, 282 (22.4%) showed a regression of skin fibrosis, 883 (70.2%) were categorized as stable patients and 92 (7.3%) showed progression of skin fibrosis at 12±3 months. Median long-term follow-up for organ involvement/death was 4.2 years. Cox regression analyses indicated that skin fibrosis regression had a significantly lower probability of later FVC decline ≥10% than non-regressive (stable and progressive) patients when controlled for baseline mRSS (p=0.013). No significant association of skin fibrosis regression was found with other organ manifestations or all-cause death. Conversely, associations of skin fibrosis progression were found for later FVC decline ≥10% with a more significant p-value (p<0.001, Figure 1), and there was also an association with all cause death (p=0.026).



Conclusion: Progression of skin fibrosis is stronger associated with organ changes and all-cause death at follow up than improvement of skin fibrosis. These data suggest a prevention of progression paradigm for clinical practice. They also suggest that clinical trials designed for prevention of skin fibrosis progression are more meaningful for long-term outcome of SSc patients than trials designed to show improvement of skin fibrosis

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FRI0266 THE REAL-WORLD EFFICACY OF THE 2015 EULAR/ACR RECOMMENDATIONS FOR THE MANAGEMENT OF POLYMYALGIA RHEUMATICA WITH ADDITIONAL TOCILIZUMAB THERAPY

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Background: A Part of patients with polymyalgia rheumatica (PMR) are refractory to the 2015 EULAR/ACR algorism for the management of PMR. Recent

reports have demonstrated that tocilizumab (TCZ) may be efficacious for refractory and relapsing PMR.

Objectives: To determine the real-world efficacy of the 2015 EULAR/ACR algorism for the management of PMR plus introduction of TCZ for refractory and relapsing PMR.

Methods: Patients who had been diagnosed with PMR according to the 2012 EULAR/ACR provisional classification criteria for PMR were recruited in the study. Registered variables included demographic data, disease characteristics, prednisolone (PSL) dosage and duration, addition of methotrexate (MTX) and TCZ, adverse effects, and clinical outcomes.

Results: There were 101 patients who had originally diagnosed as PMR (50 males and 65 females) and followed up for at least one year; the mean ± SD age at onset was 73 ±11 years at onset, with the mean observational period being 44 ± 26 months. Their treatments were initiated with PSL of 15.5 ± 4.3 mg/day. 41 patients experienced disease recurrence after 9.6 ± 6.7 months (median 9 month) of GC therapy, while receiving PSL at 5 ± 4.5 mg/day (3.7 mg/day). Baseline factors that were associated with relapse in our cohort were higher-grade thrombocytosis and higher-dose of initial GC by multivariate analysis. In 30 of the 41 patients who failed GC monotherapy, MTX was added. Five patients reached GC-free remission, but 25 patients failed GC tapering. In such refractory patients to a combination of GC plus MTX, 8 patients agreed to add TCZ therapy, and 5 of them reached drug-free remission. At present, 67 of the total 101 patients maintained drug-free remission, but most others were still receiving low-dose GC and/or MTX (n=17). No significant adverse effects did not occur during therapy, except for GC-related adverse effects such as diabetes, dyslipidemia and osteoprotic fractures.

Conclusion: Our experience indicated that there is notable heterogeneity across PMR patients in terms of drug response, and the patients with severe inflammation, e.g. thrombocytosis, may need higher-dose of initial GC and addition of biologics such as TCZ on the 2015 EULAR/ACR algorism.

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FRI0267

CLINICAL CORRELATES AND RELEVANCE OF UCLA GIT 2.0 FOR ESOPHAGITIS AND INDICATION FOR ESOPHAGOGASTRODUODENOSCOPY IN REAL-LIFE PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: The gastrointestinal (GI) tract is frequently involved in systemic sclerosis (SSc). The University of California Los Angeles Scleroderma Clinical Trial Consortium Gastrointestinal Tract Instrument 2.0 (UCLA GIT 2.0) is validated to capture GI morbidity in patients with SSc (1). The routine clinical investigation of GI involvement in these patients is not standardized and there is no consensus about when and how frequently an esophagogastroduodenoscopy (EGD) should be performed.

Objectives: The main aim of this study was to analyze the capacity of UCLA GIT 2.0 to identify patients with erosive esophagitis in an unselected, real-life SSc patients' cohort. Secondary aim was to determine whether the UCLA GIT 2.0 could discriminate SSc patients for whom an expert rheumatologist would recommend an EGD.

Methods: We selected patients fulfilling the ACR/EULAR 2013 criteria for SSc from the Zurich cohort, having completed at least once the UCLA GIT 2.0 questionnaire. We reviewed the medical charts of SSc patients from 2013 to 2019 and recorded data on EGD. We analyzed by univariable logistic regression several parameters, including UCLA GIT 2.0, considered as potentially associated with 1) the referral to EGD and 2) macroscopic esophagitis according to the Los Angeles criteria.

Results: We identified 346 patients (82.7% female, median age 63 years, median disease duration 10 years, 23% with diffuse cutaneous SSc) satisfying the inclusion criteria, who filled in 940 UCLA GIT 2.0 questionnaires.

From 940 visits, 31 were excluded because EGD was done within 3 months before completing the UCLA GIT 2.0. In the 909 remaining visits, EGD was recommended by the expert rheumatologists in 128 cases. In logistic regression, UCLA GIT 2.0 total score and some of its subscales, but also the modified Rodnan skin score (mRSS) and esophageal and stomach symptoms by past medical history, associated with the referral to EGD (Table 1).

Table 1. Logistic regression of factors associated with referral to EGD

	OR (95% CI)	p-value
mRSS	1.04 (1.01 - 1.06)	0.009
Hemoglobin (Hb)	1.00 (0.96 - 1.04)	0.978
Proton pump inhibitor (PPI)	0.37 (0.12 - 1.15)	0.086
Esophageal symptoms	3.37 (2.28 - 4.96)	<0.001
Stomach symptoms	2.93 (2.02 - 4.26)	<0.001
Reflux subscale	2.04 (1.52 - 2.73)	<0.001
Distention/bloating subscale	1.53 (1.24 - 1.89)	<0.001
Social functioning	2.20 (1.57 - 3.07)	<0.001
Emotional wellbeing	1.42 (1.03 - 1.97)	0.034
Total score of UCLA GIT 2.0	**2.27 (1.55 - 3.32)**	**<0.001**

We found data on 177 EGD performed in 150 patients, meaning that 49 EGD were performed on indication by another physician. In logistic regression, mRSS and esophageal symptoms correlated with esophagitis, while neither the total ULCA GIT 2.0 score nor the reflux subscale or any of the other subscales showed an association with esophagitis (Table 2).

Table 2. Logistic regression of factors associated with esophagitis

	OR (95% CI)	p-value
mRSS	1.09 (1.03 - 1.15)	0.001
Hb	1.03 (0.99 - 1.06)	0.126
PPI	0.52 (0.27 - 1.03)	0.059
Esophageal symptoms	2.92 (1.29 - 6.61)	0.010
Stomach symptoms	1.60 (0.80 - 3.21)	0.183
Reflux subscale	1.07 (0.60 - 1.93)	0.816
Distention/Bloating subscale	0.63 (0.39 - 1.01)	0.054
Social functioning	0.65 (0.31 - 1.35)	0.245
Emotional wellbeing	0.77 (0.36 - 1.61)	0.483
Total score of UCLA GIT 2.0	**0.67 (0.28 - 1.60)**	**0.367**

Conclusion: In a real-life setting, UCLA GIT 2.0 subscales (reflux, distention/bloating, social functioning, emotional wellbeing) and total score strongly associated with expert interpretation of gastroesophageal symptoms and consecutive referral to EGD. However, they showed no correlation with esophagitis on EGD. The main clinical association of esophagitis was the presence of esophageal symptoms.

References:

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FRIDAY, 05 JUNE 2020

Spondyloarthritis - treatment

FRI0268

REMISSION IN AXIAL SPONDYLOARTHRITIS: IS THERE A DIFFERENCE BETWEEN NSAIDS AND BIOLOGICS IN THE REAL LIFE?

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Background: Randomized-controlled trials (RCTs) done in axial spondyloarthritis (AxSpA) patients have shown that remission in AxSpA and nonradiographic

axial SpA patients treated without biologics (BIOL) occurs infrequently (Ref 1, 2). Few are known about remission rate (RR) in daily clinical practice.

Objectives: Our aim was to assess the remission rate (RR) in AxSpA patients in Real life, and to compare the RR in AxSpA patients on NSAIDs to RR for those on Biologics (TNFα blockers or IL-17A blockers).

Methods: This cross-sectional study reviewed clinical data from a single center (St-Luc university hospitals, UCLouvain, Brussels) from 01/2013 to 03/2019. Last visit available for clinical assessment was evaluated. Disease activity was measured using the Bath Ankylosing Spondylitis disease activity index (BASDAI), and the Ankylosing Spondylitis disease activity score (ASDAS) using the C-reactive protein. Remission was defined as BASDAI < 4 and ASDAS < 1.3.

Results: Data from 551 AxSpA patients were reviewed. 353 were men (64.3%). In the entire cohort, 478 BASDAI and 317 ASDAS were recorded. The RR according to the BASDAI was 46.7% (n = 223), and 17.3% for the ASDAS (n = 55). To look for the treatment-related RR, we stratified by the treatment (NSAIDs vs Biologics). We had 285 patients on NSAIDs (177 men, 62.5%) and 266 on BIOL (176 men, 66%). 245 BASDAI were available for NSAIDs and 233 for BIOL. 110 patients on NSAIDs (44.9%) and 113 on BIOL (48.5%) were in remission for BASDAI. Regarding ASDAS (table below), data from 172 patients on NSAIDs and 144 on BIOL were available. Out of them, 27 (15.7%) and 28 (19.4%) were in remission for NSAIDs and BIOL respectively. Chi-square test: p = 0.853.

Table. Distribution of ASDAS values in both groups.

	ASDAS <1.3	ASDAS ≥ 1.3 < 2.1	ASDAS ≥ 2.1 < 3.5	ASDAS > 3.5
NSAIDs (n = 172)	N = 27 (15.7%)	N = 41 (23.8%)	N = 70 (40.7%)	N = 34 (19.8%)
BIOL (n = 144)	N = 28 (19.4%)	N = 30 (20.8%)	N = 57 (39.6%)	N = 29 (20.1%)

Conclusion: The real life RR in AxSpA seems to be higher on BIOL, even if compared to NSAIDs, the difference is not significant. However, many patients on NSAIDs achieve the remission.

References:

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Disclosure of Interests: Charlotte Baert: None declared, Charlene MOUAFO TOUKAM: None declared, Tatiana Sokolova: None declared, Adrien Nzeusseu Toukap Grant/research support from: AbbVie, Celgene Corporation, Janssen, Pfizer, UCB – grant/research support, Consultant of: AbbVie, Eli Lilly, Janssen, Novartis, UCB – consultant, Speakers bureau: AbbVie, Eli Lilly, Janssen, Novartis, UCB – advisory board member

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FRI0269

CHARACTERIZATION OF PATIENTS WITH ANKYLOSING SPONDYLITIS WHO INITIATED SECUKINUMAB: ELECTRONIC HEALTH RECORDS DATA FROM THE COLUMBUS REPOSITORY

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Background: Secukinumab was the first anti-interleukin 17A monoclonal antibody treatment approved by the FDA for ankylosing spondylitis (AS). There is scarce information on the characteristics of secukinumab vs other biologic initiators with AS.

Objectives: To describe real-world physician and patient characteristics, and treatment patterns of secukinumab and tumor necrosis factor inhibitor (TNFi) initiators.

Methods: Electronic health records (EHR) data from adult patients with AS who initiated a biologic therapy between January 2018 and March 2019 (index date) were included from the Columbus Repository, a network capturing EHR data from 120 US rheumatology providers. Physician and patient characteristics, and treatment patterns were reported for patients who were prescribed secukinumab and TNFis (adalimumab, etanercept, certolizumab pegol, infliximab, infliximab-abda, and golimumab). Categorical variables were summarized using frequency counts and percentages and continuous variables were presented using means and standard deviations. Standardized mean differences and *P* values were used to compare treatment groups.

Results: As of March 2019, AS treatment data were available for 82 secukinumab initiators and 160 TNFi initiators. Regarding overall practice size, 33% of practices had a single physician, and 65% of physicians were located in the South US region. Secukinumab initiators were younger than TNFi initiators (47.4 vs 49.8 years) and had a similar prevalence of HLA-B27 positivity (≈ 55%; Table 1). Comorbid psoriatic arthritis (PsA) was more commonly reported among secukinumab initiators vs TNFi initiators (17% vs 9%), while hypertension (5% vs 11%), obesity (2% vs 11%), and uveitis (2% vs 9%) were less common (Figure 1). Secukinumab initiators were more likely to have prior opioid use vs TNFi initiators but were less likely to have prior methotrexate use (Figure 2**A**); 67% of secukinumab initiators and 49% of TNFi initiators were biologic experienced, of whom 73% and 76%, respectively, used 1 prior biologic, 25% and 20% used 2 prior biologics, and 2% and 4% used ≥ 3 prior biologics (Figure 2**B**). The most common reasons for discontinuation of prior biologics among secukinumab and TNFi initiators were because the biologic was no longer required (47% vs 41%) and lack of efficacy (20% vs 24%) (Figure 2**C**).

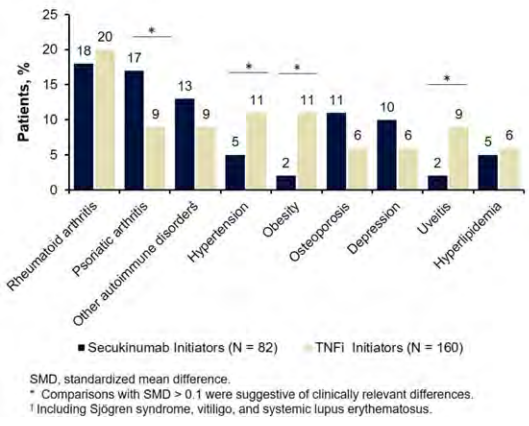
Table 1. Baseline Demographics and Disease Characteristics Among Patients With AS at the Index Date.

Characteristic	Secukinumab (N = 82)	TNFi (N = 160)	SMD*	*P* Value
Age, mean (SD), years	47.4 (12.8)	49.8 (14.6)	0.17	0.21
Female, n (%)	43 (52)	90 (56)	0.08	0.57
Race/ethnicity, n (%)	N = 65	N = 129	0.20	0.66
White	52 (80)	106 (82)		
Hispanic	8 (12)	13 (10)		
Black	3 (5)	8 (6)		
Asian	1 (2)	2 (2)		
Other	1 (2)	0		
Geographic distribution, n (%)			0.37	0.05
South	49 (60)	113 (71)		
Midwest	27 (33)	28 (18)		
West	5 (6)	16 (10)		
Northeast	1 (1)	3 (2)		
Health insurance, n (%)	N = 79	N = 156	0.41	0.39
Commercial	57 (72)	94 (60)		
Medicare	8 (10)	33 (21)		
Medicaid	2 (3)	4 (3)		
Other	12 (15)	25 (16)		
HLA-B27 positivity, n (%) [N]	14 (54) [N = 26]	31 (56) [N = 55]	0.05	1.00
Body mass index, mean (SD), kg/m^2	30.6 (6.1)	30.9 (7.7)	0.03	0.82

SMD, standardized mean difference.

* Comparisons with SMD > 0.1 were suggestive of clinically relevant differences.

Figure 1. Comorbidity Profile (≥ 5% of Patients) of Secukinumab vs TNFi Initiators With AS*



SMD, standardized mean difference.
* Comparisons with SMD > 0.1 were suggestive of clinically relevant differences.
† Including Sjögren syndrome, vitiligo, and systemic lupus erythematosus.

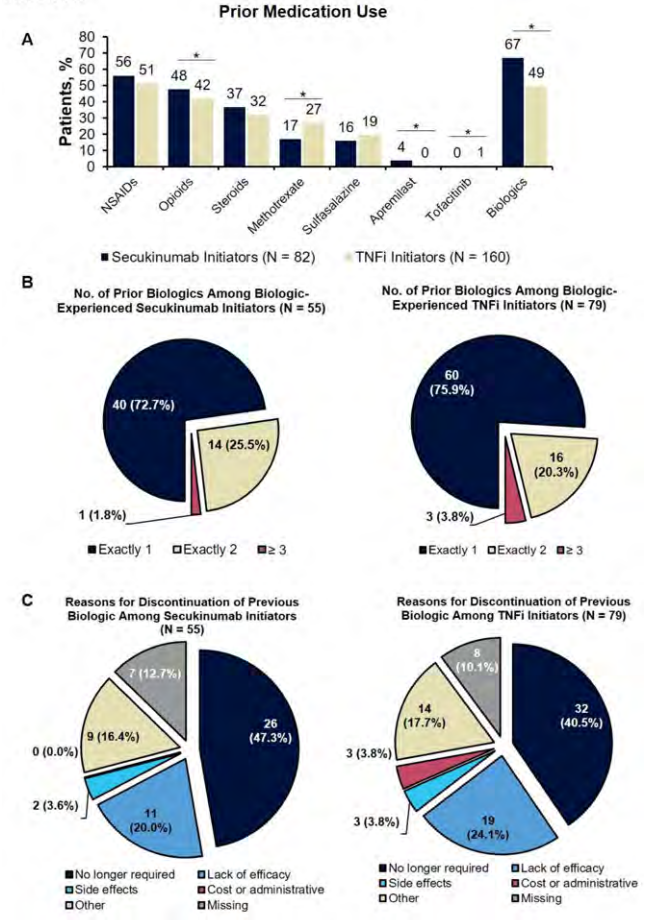
Conclusion: Secukinumab initiators with AS were younger and more opioid and biologic experienced, were more likely to have a PsA diagnosis, and were more likely to discontinue their previous biologic because the biologic was no longer required compared to patients who initiated TNFis.

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Pharmaceuticals Corporation, Esther Yi Employee of: Novartis Pharmaceuticals Corporation
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Figure 2. (A) Prior Medication Use, **(B)** Number of Prior Biologics Used, and **(C)** Reasons for Discontinuation of Previous Biologic* Among Patients With AS at the Index Date



SMD, standardized mean difference.
* Comparisons with SMD > 0.1 were suggestive of clinically relevant differences.

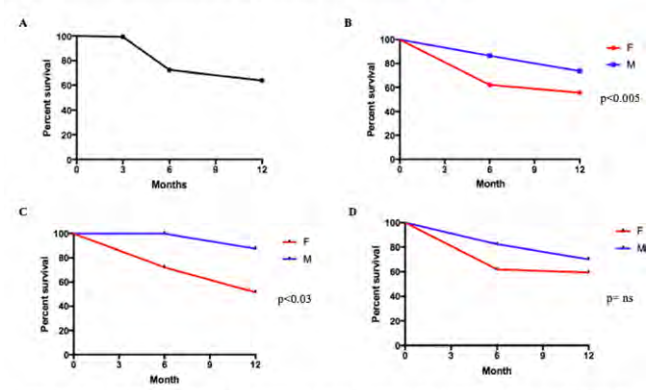
FRI0270

ONE-YEAR EFFECTIVENESS, RETENTION RATE AND SAFETY OF SECUKINUMAB IN ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS: A REAL-LIFE MULTICENTRE STUDY

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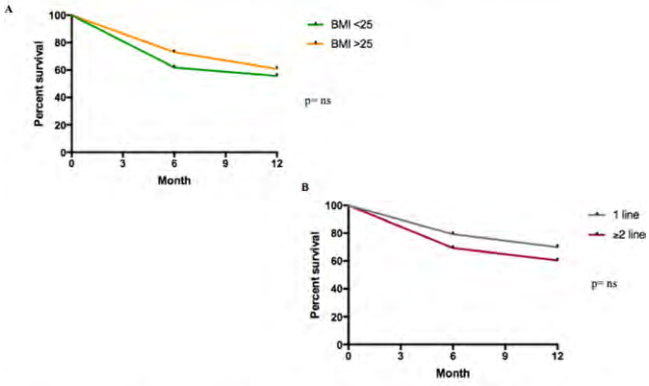
Background: Secukinumab (SEC) is the first interleukin-17A inhibitor showing efficacy in both ankylosing spondylitis (AS) and psoriatic arthritis (PsA) in randomised trials, but real-life data are lacking.
Objectives: In this prospective observational study, we evaluated the effectiveness and safety of SEC in patients with AS and PsA in a real-life setting.
Methods: From September 2018 to September 2019, data were collected from 168 consecutive outpatients at baseline (T0) and at 6 (T6) and 12 months (T12) after starting SEC (39 AS, 23%; 129 PsA, 77%).
Results: Significant improvement was seen at T6 and T12 for all clinical variables, including TJC, SJC, ESR, CRP, DAPSA, ASDAS-CRP, and BASDAI, as well as in patient-reported outcomes such as VAS-pain. By multivariable regression analysis, in AS patients high BASDAI at T0 correlated with diagnostic delay (R^2=0.4; p=0.009) and peripheral joint involvement (R^2=0.4; p=0.04). During follow-up, reduction of BASDAI positively correlated with high ESR (R^2=0.65; p=0.04). ASDAS-CRP at T0 positively correlated with high ESR (R^2=0.34; p=0.004). Reduction of ASDAS-CRP from T0 to T6 correlated with current smoking status (R^2=0.42; p=0.0005). In PsA patients, reduction of DAPSA score from T0 to T12 negatively correlated with the presence of metabolic syndrome (R^2 =0.41; p= 0.0025). Retention rate showed good drug survival and an influence of female sex (Figure 1) in the survival curve in only AS patients, but no differences based on BMI, gender and lines of treatment were observed (Figure 2). SEC was well tolerated: Eleven patients discontinued treatment for non-severe adverse events.
Conclusion: We demonstrated the effectiveness and safety of SEC in patients with AS and PsA in a real-life setting for the first time. No gender differences were observed; however, less clinical improvement was seen in smokers and in patients with metabolic syndrome
References: No references.

Figure 1. Twelve months retention rate of secukinumab in AS e PsA patients according to gender



A. Global retention rate; B. Global retention rate according to gender; C. Retention Rate according to gender in AS patients; D. Retention Rate according to gender in PsA patients

Figure 2. Twelve months retention rate of secukinumab in AS e PsA patients according to BMI and to lines of biologics



A. Retention Rate according to BMI; B. Retention Rate according to lines of biologics

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FRI0271

IMPACT OF HLA-B27 STATUS ON CLINICAL OUTCOMES AMONG PATIENTS WITH ANKYLOSING SPONDYLITIS TREATED WITH SECUKINUMAB

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Background: Ankylosing spondylitis (AS) is strongly associated with the genetic marker HLA-B27. Approximately 80%-90% of white patients with AS express HLA-B27 compared with < 8% of the general population. In patients with AS, negative HLA-B27 status is a predictor of worse response to TNFis.[1] The impact of HLA-B27 status on clinical efficacy of secukinumab, a fully human monoclonal antibody that selectively inhibits IL-17A, has not been studied.

Objectives: To analyze the impact of HLA-B27 status on clinical outcomes at Week 16 in patients with AS treated with secukinumab vs placebo.

Methods: Patients with AS were pooled from the MEASURE 1-4 studies (NCT01358175, NCT01649375, NCT02008916, and NCT02159053) and stratified by HLA-B27 status. All trials included patients who received secukinumab 150 mg every 4 weeks with or without an initial loading dose (10 mg/kg IV at Weeks 0, 2, 4 or 150 mg SC at Weeks 0, 1, 2, and 3) or placebo control. MEASURE 3 included patients receiving secukinumab 300 mg every 4 weeks following the initial IV loading dose. Efficacy at Week 16 was determined by the proportion of patients achieving ASAS20/40, ASAS5/6, ASAS partial remission, BASDAI50, ASDAS-CRP < 2.1, ASDAS-CRP < 1.3, and improvement in Patient Global Assessment (VAS) and total spinal/back pain (VAS) scores. In MEASURE 1, 2, and 4, quality of life (QOL) was assessed at Week 16 by the SF-36 PCS, SF-36 MCS, and ASQOL. ASAS, BASDAI, and ASDAS-CRP responses were analyzed by nonresponder imputation, and all other outcomes by mixed models for repeated measures. For hypothesis generation, outcomes at Week 16 with secukinumab vs placebo within HLA-B27 strata were compared by logistic regression analysis without adjustment for multiple comparisons.

Results: Baseline characteristics were balanced across treatment groups, although more HLA-B27+ patients than HLA-B27– patients were male (71%-73% vs 43%-50%). HLA-B27+ patients receiving any dose of secukinumab were significantly more likely to achieve ASAS, BASDAI50, and ASDAS-CRP responses vs those receiving placebo ($P < .05$; Figure 1). HLA-B27– patients receiving secukinumab 300 mg were significantly more likely to achieve ASAS40, ASAS partial remission (Figure 1**A**), and BASDAI50 (Figure 1**B**) responses than those receiving placebo ($P < .05$). Patients receiving any dose of secukinumab were more likely to achieve ASAS5/6 and ASDAS-CRP < 2.1 than those receiving placebo, regardless of HLA-B27 status ($P < .05$; Figure 1**B**). All secukinumab-treated patients experienced significant improvement in Patient Global Assessment at Week 16 vs placebo, regardless of HLA-B27 status, while only HLA-B27+ patients experienced significant reduction in total spinal/back pain vs placebo ($P < .05$; Figure 2**A**). Numerical improvements in QOL were observed in all patients receiving secukinumab 150 mg vs placebo; these reached significance for HLA-B27+ patients (Figure 2**B**).

Conclusion: Secukinumab is effective in patients with AS regardless of HLA-B27 status; HLA-B27+ patients may derive increased therapeutic benefit compared with HLA-B27– patients.

Reference:

[1] Alazmi M, et al. *Arthritis Care Res (Hoboken)*. 2018;70:1393-9.

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Figure 1. Percentage of Patients With AS Achieving **(A)** ASAS Responses and **(B)** BASDAI50 and ASDAS-CRP Responses at Week 16 (nonresponder imputation)

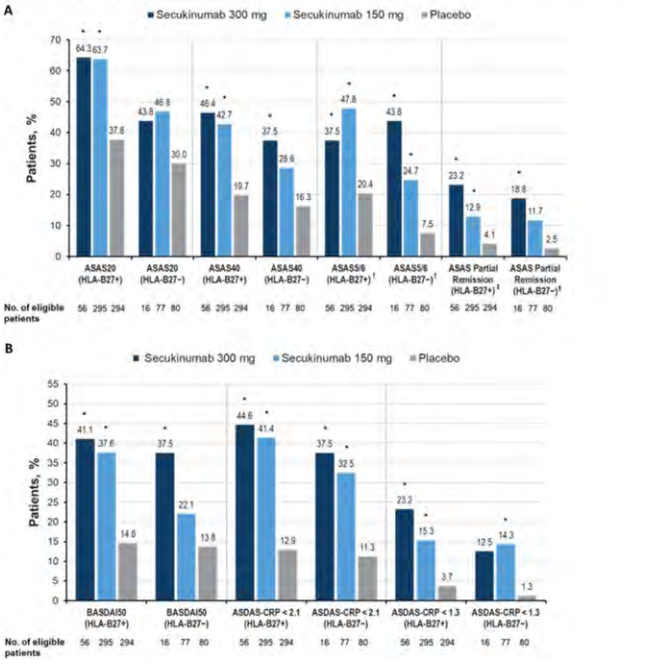
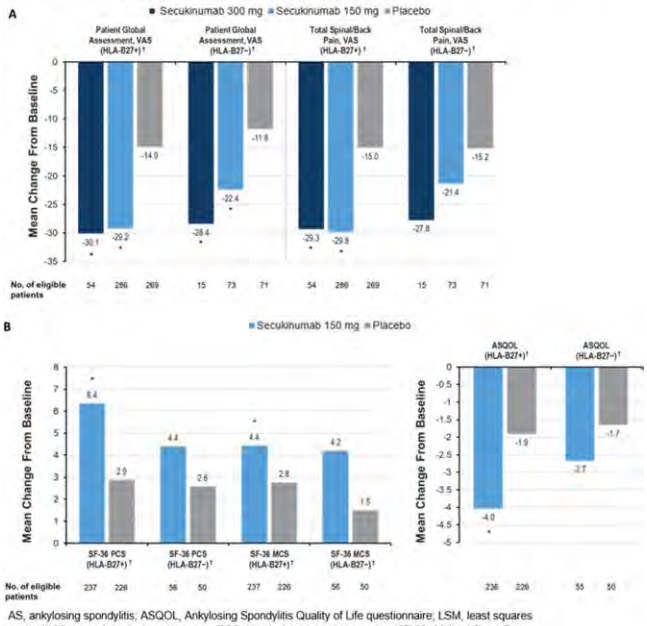


Figure 2. Improvements in **(A)** Disease Activity and Pain and **(B)** Quality of Life at Week 16 in Patients With AS (mixed models for repeated measures)



AS, ankylosing spondylitis; ASQOL, Ankylosing Spondylitis Quality of Life questionnaire; LSM, least squares mean; MCS, mental component summary; PCS, physical component summary; SF-36, 36-Item Short Form Survey; VAS, visual analog scale.
* $P < .05$ compared with placebo.
† LSM change from baseline.

FRI0272

SECUKINUMAB DEMONSTRATES A CONSISTENT SAFETY PROFILE IN PATIENTS WITH PSORIASIS, PSORIATIC ARTHRITIS AND ANKYLOSING SPONDYLITIS OVER LONG TERM: UPDATED POOLED SAFETY ANALYSES

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Background: Pooled safety data has been reported with secukinumab (SEC) in patients (pts) with Psoriatic arthritis (PsA), Ankylosing Spondylitis (AS) and Psoriasis (PsO).[1]

Objectives: To report longer-term safety data of SEC treatment in PsA, AS, PsO pts up to 5 years.

Methods: The integrated clinical trial safety dataset included data pooled from 28 randomised controlled clinical trials of SEC 300 or 150 or 75 mg in PsO (11 Phase 3 and 8 Phase 4 trials), PsA (5 Phase 3 trials), and AS (4 Phase 3 trials), along with post-marketing safety surveillance data with a cut-off date of 25 December 2018. Adverse events (AEs) were reported as exposure-adjusted incident rates (EAIRs) per 100 pt-years. Analyses included all pts who received ≥1 dose of SEC.

Results: A total of 12637 pts (8819, 2678 and 1140 pts with PsO, PsA and AS, with an exposure of 15063.1, 5984.6 and 3527.2 pt-years, respectively) were included. The most frequent AE was upper respiratory tract infection and EAIR per 100 pt-years for IBD, malignancies and MACE remained low. The EAIR per 100 pt-years for adverse events (AEs) of special interest are reported in Table 1. The cumulative post-marketing exposure to SEC was estimated to be ~285,811 pt-years across the approved indications. Safety data from post-marketing surveillance are reported in Table 2.

Table 1. Selected AEs of interest with SEC across pooled clinical trials

Variable	PsO	PsA	AS
	SEC N=8819	SEC N=2678	SEC N=1140
Exposure (Days), Mean (SD)	623.9 (567.7)	816.2 (580.7)	1130.1 (583.0)
Death, n (%)	15 (0.2)	13 (0.5)	10 (0.9)
Selected AE's of interest, EAIR (95% CI)			
Serious infections[1]	1.4 (1.2, 1.6)	1.8 (1.5, 2.2)	1.2 (0.9, 1.6)
Candida infections[2]	2.9 (2.7, 3.2)	1.5 (1.2, 1.9)	0.7 (0.5, 1.1)
IBD[3]	0.01 (0.0, 0.05)	0.03 (0.0, 0.1)	0.03 (0.0, 0.2)
Crohn's disease[3]	0.1 (0.05, 0.2)	0.1 (0.04, 0.2)	0.4 (0.24, 0.7)
Ulcerative colitis[3]	0.1 (0.08, 0.2)	0.1 (0.04, 0.2)	0.2 (0.1, 0.5)
MACE[4]	0.4 (0.31, 0.5)	0.4 (0.3, 0.6)	0.7 (0.4, 1.0)
Uveitis[3]	0.01 (0.0, 0.05)	0.1 (0.04, 0.2)	1.2 (0.9, 1.7)
Malignancy[5]	0.9 (0.7, 1.0)	1.0 (0.77, 1.3)	0.5 (0.3, 0.8)

[1]Rates for system organ class; [2]Rates for high level term; [3]Rates for preferred term (PT; IBD for unspecified IBD); [4]Rates for Novartis MedDRA Query term; [5]Rates for standardized MedDRA query term – 'malignancies and unspecified tumour'; EAIR, exposure adjusted incidence rate per 100 pt-years; N, number of pts in the analysis

Table 2. Summary of SEC post-marketing safety

Exposure (PTY)	PSUR1 26Dec14 -25Jun15	PSUR2 26 Jun -25Dec15	PSUR3 26Dec15 -25Jun16	PSUR4 26Jun -25Dec16	PSUR5 26Dec16 -25Dec17	PSUR6 26Dec17 -25Dec18	Cumulative
	1838	7450	16871	28549	93744	137325	285811
	n (Reporting rate PTY)						
Serious infections	89 (4.8)	149 (2.0)	232 (1.4)	475 (1.7)	649 (0.7)	1841 (1.3)	3980 (1.4)
Malignancy	2 (0.1)	15 (0.2)	21 (0.1)	50 (0.2)	225 (0.2)	422 (0.3)	788 (0.3)
Total IBD	4 (0.2)	12 (0.2)	37(0.2)	46 (0.2)	185 (0.2)	340 (0.3)	693 (0.2)
MACE	6 (0.3)	15 (0.2)	16 (0.1)	39 (0.1)	151 (0.2)	238 (0.2)	504 (0.2)

PSUR, periodic safety update report; PTY, pt-treatment years

Conclusion: In this long-term analysis across clinical trials and post-marketing surveillance, of pts with PsO, PsA and AS, SEC was well tolerated, with a safety profile consistent with previous reports.[1]

Reference:

[1] Deodhar et al. Arthritis Research & Therapy (2019) 21:111.

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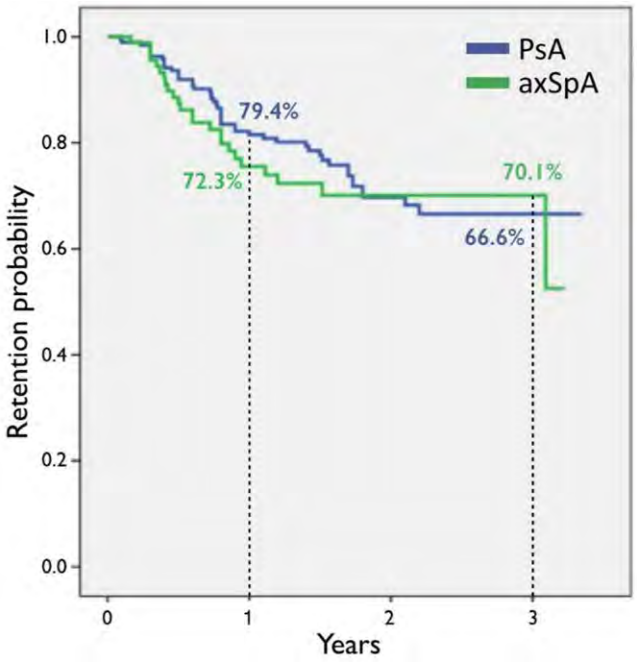
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FRI0273

EFFECTIVENESS AND RETENTION RATE OF SECUKINUMAB FOR PSORIATIC ARTHRITIS AND AXIAL SPONDYLOARTHRITIS: REAL-LIFE DATA FROM THE ITALIAN LORHEN REGISTRY

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Background: Observational data on the use of secukinumab for the treatment of spondyloarthritides are still lacking. Large population-based registries that allow long-term follow-up have been increasingly used to investigate the performance of biologic drugs in a real life setting.
Objectives: The aim of this study is to evaluate the effectiveness and the retention rate of secukinumab in psoriatic arthritis (PsA) and axial spondyloarthritis (axSpA) patients in a real-life setting over a 3-year follow-up period.
Methods: Data of all PsA and axSpA patients (diagnosed according to CASPAR and ASAS criteria, respectively) treated with secukinumab were prospectively collected in the Italian multicentric LORHEN registry. Effectiveness was measured as the mean change from baseline of Disease Activity in PSoriatic Arthritis score (DAPSA) in PsA and Ankylosing Spondylitis Disease Activity Score (ASDAS) in axSpA patients. Rates of DAPSA remission and ASDAS inactive disease were also computed. The 3-year retention rate was calculated by the Kaplan-Meier method and compared between PsA and axSpA by a log-rank test. A descriptive analysis of reasons for discontinuation was performed.
Results: The study population included 195 PsA (55.4% females, mean age 50.7 [±11.8] years, mean disease duration 10 [±7.8] years, mean baseline DAPSA 23.12 [±12.3]) and 94 axSpA (61.7% males, mean age 49.1 [±12.7] years, mean disease duration 10.4 [±9.4] years, mean baseline ASDAS 3.41 [±1.1]) patients who received secukinumab as first (26.5 and 33%, respectively) or subsequent biologic agent. Compared with baseline, the 3-, 6- and 12-month mean values of both DAPSA (12.6 [±9], 11.2 [±10.5] and 9.3 [±7.5], respectively) and ASDAS (2.23 [±0.9], 2.15 [±0.9], and 1.84 [±0.9], respectively) were significantly decreased (p<0.001 for all the timepoints). The 3-, 6-, and 12-month rates of remission/inactive disease were 15.5, 25.4, and 30.5% in PsA and 18, 23.7, and 28.6% in axSpA group, respectively. One- and 3-year retention rate (figure 1) were respectively 79.4% and 66.6% in PsA and 72.3% and 70.1% in axSpA patients, with no significant difference between the two groups (p=0.517). The most frequent reason for withdrawal was inefficacy in both PsA (n=41) and axSpA (n=20), whereas only 8 PsA and 6 axSpA patients discontinued secukinumab because of adverse events.



Conclusion: Our data confirmed in a real-life setting the 1-year clinical efficacy and the 3-year survival of secukinumab in both PsA and axSpA. The safety profile of secukinumab was very favorable for both the indications. No significant differences were observed in the performance of secukinumab between ax-SpA and PsA.
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[1] Deodhar A, et al. Arthritis Research & Therapy; 2019.
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Disclosure of Interests: Ennio Giulio Favalli Consultant of: Consultant and/or speaker for BMS, Eli-Lilly, MSD, UCB, Pfizer, Sanofi-Genzyme, Novartis, and Abbvie, Speakers bureau: Consultant and/or speaker for BMS, Eli-Lilly, MSD, UCB, Pfizer, Sanofi-Genzyme, Novartis, and Abbvie, Antonio Marchesoni Speakers bureau: Abbvie, Pfizer, UCB, Novartis, Celgene, Eli Lilly, Silvia Balduzzi: None declared, Carlomaurizio Montecucco: None declared, Claudia Lomater Consultant of: Advisory board for Sanofi, Novartis, Abbvie, Gloria Crepaldi Consultant of: Advisory board for Sanofi and Celgene, Speakers bureau: BMS, MSD, Silvia Talamini: None declared, Chiara Bazzani: None declared, Enrico Fusaro: None declared, Marta Priora: None declared, Aurora Iannello: None declared, Giuseppe Paolazzi: None declared, Roberto Caporali Consultant of: AbbVie; Gilead Sciences, Inc.; Lilly; Merck Sharp & Dohme; Celgene; Bristol-Myers Squibb; Pfizer; UCB, Speakers bureau: Abbvie; Bristol-Myers Squibb; Celgene; Lilly; Gilead Sciences, Inc; MSD; Pfizer; Roche; UCB
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FRI0274

HISTORY OF BIOLOGICS AND FEMALE GENDER ARE LINKED TO GOLIMUMAB DISCONTINUATION IN AXIAL SPONDYLOARTHRITIS: A SUB-ANALYSIS OF THE GO-PRACTICE STUDY

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Background: Golimumab (**GLM**) is the latest anti-TNFα to be indicated for treating rheumatoid arthritis (**RA**), psoriatic arthritis (**PsA**) and axial spondyloarthritis (**axSpA**). The GO-PRACTICE study was performed in France at the request of the French Health Authorities, for the reevaluation of GLM in real-life.
Objectives: The primary objective was to estimate GLM persistence at 2 years from initial prescription. This abstract focuses on a post-hoc analysis of the factors linked to GLM discontinuation in axSpA patients.
Methods: Observational, prospective, multicenter study, that consecutively recruited adult patients with RA, PsA and axSpA who were newly prescribed GLM. Patients were followed-up for 2 years and outcomes data were collected at baseline (**BL**), 1 and 2 years. Patients' sociodemographic characteristics, disease history, comorbidities and treatment history were also collected at BL. Persistence was estimated with the Kaplan-Meier method. Cox proportional hazard models were used to assess factors associated with persistence. Selected BL characteristics were studied in univariate models, where those associated with *p*-value <0.20 were included in multivariate analysis. Significance level was set at $p<0.05$.
Results: 478 patients with axSpA were included from Jan 2015 to Mar 2016. Mean age was 43 years and 55% were female; 61% of patients were biologic-naïve (BN, n=291) and 39% (n=187) were biologic-pretreated (BP). Median time-elapsed in years since axSpA diagnosis was 1.7 (range 0–45.1) and 6.9 (range 0.2–51.8) in BN and BP patients, respectively (P <0.001); 97% patients were prescribed 50 mg GLM monthly and co-treatments included DMARD (34%), corticosteroids (17%) and NSAIDs/analgesics (90%).
Cumulative persistence probability of GLM at 2-years was 52.6% (Fig 1). Table 1 details the binary variables associated with GLM discontinuation at $p<0.20$. Among continuous variables, BL CRP level was associated with $p<0.20$. A multivariate analysis of these factors revealed that being female (HR 1.92, 95%CI 1.43–2.56, $P<0.001$) and being BP (HR 1.45, 95%CI (1.11–1.90), $P=0.007$) were risk factors for GLM discontinuation (Table 1).

Table 1. Logistic model results for variables of interest and their link to GLM discontinuation in axSpA

Factor	Modalities	χ^2 (p)	Hazard ratio (HR)	95% CI
HR following univariate analysis (p>0.20)				
Age	Continuous variable	0.520	1.00	0.99–1.02
Disease duration		0.401	1.01	0.99–1.03
Inflammatory bowel disease	Yes vs. No	0.277	0.74	0.43–1.28
Gastrointestinal disease		0.344	1.27	0.78–2.06
Uveitis		0.237	0.80	0.55–1.16
Psoriasis		0.238	0.92	0.64–1.31
HR following multivariate analysis (variables with p<0.20 at univariate analysis)				
Gender	Female vs. Male	< 0.001	1.92	1.43–2.56
Biologics history	Pretreated vs. naïve	0.007	1.45	1.11–1.90
Serum CRP	Continuous variable	0.177	0.99	0.98–1.00
DMARD history	Yes vs. No	0.062	1.37	0.99–1.90
Ongoing corticosteroids		0.693	1.08	0.73–1.61
Anemia		0.170	1.82	0.78–4.24
Kidney Disease		0.508	1.50	0.45–4.97
Other physical illness		0.435	1.28	0.69–2.34

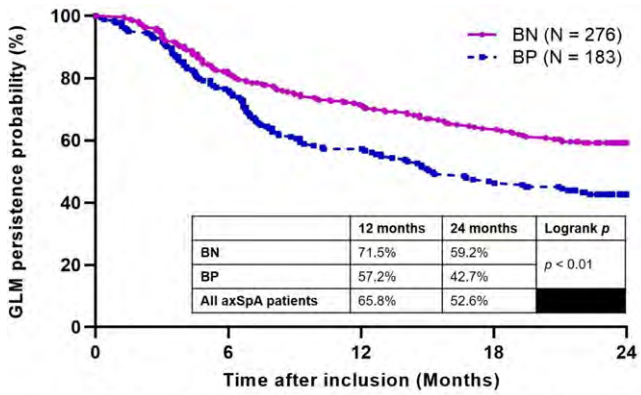


Figure 1: Kaplan-Meier curve of golimumab persistence in biologic-naïve (BN) and biologic-pretreated (BP) patients with axSpA

Conclusion: 2-year GLM persistence in axSpA patients was 52.6%. Females and those who were biologics-pretreated were at greater risk for discontinuing GLM before 2 years.

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FRI0275

ONE-YEAR TREATMENT RETENTION OF SECUKINUMAB VERSUS TUMOR NECROSIS FACTOR INHIBITORS IN SPONDYLOARTHRITIS. RESULTS FROM FIVE NORDIC BIOLOGIC REGISTRIES

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Background: Tumor necrosis factor inhibitors (TNFi) have been available for more than a decade for treatment of spondyloarthrtitis (SpA). Secukinumab (SEC) represents a new mode of action, but few studies have compared outcomes in patients(pts) treated with SEC vs TNFi – and the optimal treatment strategy in routine care remains to be established. Comparative studies between SEC and adalimumab (ADA) are ongoing.

Objectives: To describe baseline characteristics and compare 1-yr treatment retention of SEC vs TNFi (ADA/certolizumab pegol(CLZ)/etanercept(ETN)/golimumab(GOL)/infliximab(IFX)) in SpA-pts from 5 Nordic countries.

Methods: Observational, prospective cohort study. Pts with SpA (ankylosing spondylitis/non-radiographic axial SpA/undifferentiated SpA) starting SEC or any TNFi during 2015-2018 were identified in clinical rheumatology registries of the Nordic countries. Baseline characteristics were retrieved. Country-specific data were pooled. 1-yr treatment retention of SEC vs TNFi was assessed through crude survival probability curves, retention rates and adjusted Cox regression analyses (ADA reference). Analyses were stratified by line of bDMARD and TNFi type.

Results: In total, 10692 treatment courses (834 SEC, 9858 TNFi) in 7952 patients were included. SEC was rarely used as 1st bDMARD (Table 1), whereas it was the drug most frequently used as 3rd+ line (Table 2). Baseline characteristics were numerically similar for SEC vs TNFi (Table 1).

Table 1. Patient characteristics at treatment start

	1st line		2nd line		3rd+ line	
	SEC	TNFi	SEC	TNFi	SEC	TNFi
N	70	5186	156	2605	608	2067
Male, %	53	55	44	53	45	46
Age, yrs	45 (14)	41 (14)	45 (12)	44 (13)	47 (12)	46 (13)
BASDAI, mm	45 (28)	53 (22)	52 (22)	52 (24)	63 (22)	58 (24)
Concomitant csDMARD, %	18	27	23	23	27	26

Means (SD) unless otherwise stated

Table 2. 1-yr treatment retention (Kaplan Meier, Cox Regression)

	Drug	Retentions rates, 1 yr % (95% CI)	Adjusted* HR (95% CI) for discontinuation
1st line	ADA	76 (73-79)	1
	CLZ	68 (63-72)	1.4 (1.1-1.8)
	ETN	74 (71-76)	1.1 (0.9-1.3)
	GOL	80 (77-84)	0.8 (0.6-1.0)
	IFX	65 (62-67)	1.5 (1.3-1.8)
	SEC	76 (62-85)	0.9 (0.5-1.6)
2nd line	ADA	72 (68-75)	1
	CLZ	58 (51-64)	1.5 (1.2-1.9)
	ETN	65 (61-68)	1.2 (1.0-1.5)
	GOL	73 (67-77)	0.9 (0.7-1.2)
	IFX	67 (63-71)	1.2 (0.9-1.5)
	SEC	67 (58-74)	1.1 (0.8-1.5)
3rd+ line	ADA	73 (68-77)	1
	CLZ	52 (46-57)	2.0 (1.6-2.6)
	ETN	65 (61-70)	1.3 (1.0-1.6)
	GOL	65 (60-70)	1.3 (1.0-1.7)
	IFX	61 (56-66)	1.5 (1.2-1.9)
	SEC	61 (57-65)	1.4 (1.1-1.8)

* by sex, baseline age, BASDAI, concomitant csDMARD (y/n/missing). Pts with missing baseline BASDAI (41-60%) excluded

1-yr treatment retention varied between the TNFi (**Figure,** Table 2), with SEC showing retention rates comparable to ADA when used as 1st or 2nd line therapy. However, SEC retention was poorer than ADA when used as 3rd+ therapy, but comparable to retention of other TNFi.

In adjusted Cox regression analyses, confidence intervals were wide and included 1 for SEC vs ADA (1st, 2nd line), whereas there was slightly poorer retention of SEC versus ADA when used as 3rd+ bDMARD (Table 2).

Conclusion: These observational data in >10.000 biological treatment courses in SpA, showed that SEC was mainly used in bDMARD experienced pts. Baseline characteristics were similar in pts treated with SEC vs TNFi. The 1-yr retention for SEC was similar to that of the TNFi when used as 1st or 2nd line, but poorer than ADA regarding 3rd+ courses. Further analyses are planned to explore confounding by indication and channeling towards treatment.

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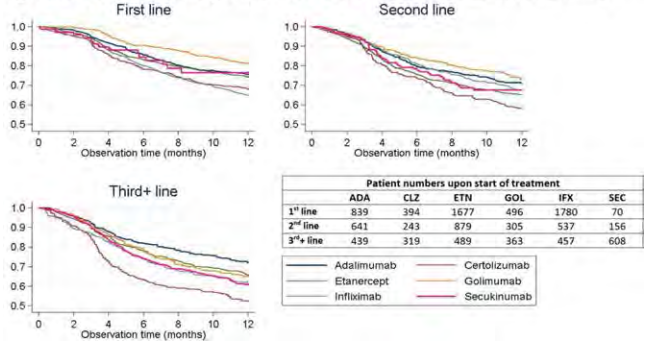
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Figure. Survival probability curves for SEC and the 5 TNFi. Stratified by line of treatment



FRI0276

EARLY TREATMENT WITH ANTI-TNF IS ASSOCIATED WITH HIGHER RESPONSE RATES IN PATIENTS WITH ACTIVE AXSPA

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Background: Treatment options for axial spondyloarthritis (axSpA) is currently limited, and up to 40% of the patients require biologic therapies to control symptoms. Early commencement of biologics suggested to have higher response rates but data regarding this subject is limited.

Objectives: The primary aim was to investigate tumor necrosis factor inhibitor (TNFi) response and retention rates in axSpA patients who were treated in the early disease period (symptom duration (≤5 years). Our secondary aim was to identify factors predicting response to TNFi.

Methods: Adult axial SpA patients who started TNFi treatments within the five years of their symptoms were identified and defined as "Group 1". Patients whose TNFi treatments started five years after their initial symptoms served as a control group (Group 2: 5-10 years and Group3: ≥10 years). Response and survival rates at 6, 12, and 24 months were calculated. Predictors of response on TNFi survival at 24 months were also analyzed.

Results: There was a total of 364 axiSpA (Group 1: 95, Group 2: 82 and Group 3: 187) patients in the study (69.8% male, 46.8±12.6 years). Group 1 patients tended to be younger, with a lower baseline CRP titers and lower HLA–B27 rate compared to the other groups. Drug survival rates were similar between the groups. This finding also remained similar when AS and nraxSpA patients analyzed separately. However, regardless of symptom duration, the drug retention rates were significantly higher in the AS group than in nraxSpA (Table 2). ASAS40 responses were higher in Group 1 than in Group 3 both at 12 and 24 months. Predictors of response based on ASAS40 at 24 months were treatment within the five years of the symptoms (OR:2.2) and age at baseline (OR:0.97) in univariate analysis. However, baseline ASDAS (OR:1.4) was the only factor in multiple regression.

Conclusion: In this study we showed the following: 1) TNFi started in the early disease course resulted in a better ASAS40 response at both 12 and 24 months, 2) TNFi timing (started in the early or late disease period) seems not affecting drug retention rates, and 3) baseline disease activity is the most important predictor in achieving ASAS40 response at 24 months.

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FRI0277

EFFECTIVENESS OF BDMARDS IN AS AND NR-AXSPA PATIENT POPULATIONS: EXPERIENCE FROM THE CORRONA REGISTRY

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Background: Axial spondyloarthritis (axSpA) consists of ankylosing spondylitis (AS), also referred to as radiographic axSpA (r-axSpA) and non-radiographic axSpA (nr-axSpA). AxSpA can lead to reduced mobility, pain, fatigue, and impact quality of life. While bDMARDs are available for treatment, the literature lacks studies exploring their real-world effectiveness in clinical registry patients with axSpA.

Objectives: To describe patient characteristics of bDMARD initiators among the AS and nr-axSpA populations and the effectiveness of bDMARDs at the 6-month (± 3) post-initiation follow-up (FU) visit in the Corrona PsA/SpA Registry.

Methods: This study included patients aged ≥ 18 years with AS per modified NY criteria and nr-axSpA per ASAS criteria enrolled between 3/2013 and 9/2019. Concurrently diagnosed patients with PsA were excluded. Baseline characteristics, such as demographic, clinical, disease activity, treatment, and patient-reported outcomes (PRO), were collected for those initiating a bDMARD at enrollment or during FU; response rates and mean change in disease activity and PRO between initiation and 6-month FU were calculated.

Results: The AS (n=179) and nr-axSpA (n=32) bDMARD initiators groups were similar at initiation for mean age (AS: 49.1 yrs, nr-axSpA: 48.9 yrs), ASDAS scores (AS: 2.9, nr-axSpA: 2.8) and patient global assessment (AS: 59.6, nr-axSpA: 60.0). The two groups were different for time from disease duration (AS 8.5 yrs, nr-axSpA, 6.6 yrs), current NSAID use (AS: 64.2%, nr-axSpA: 46.9%) and naivete to cDMARDS (AS: 70.4%, nr-axSpA: 40.6%), TNFs (AS: 47.5%, nr-axSpA: 21.9%), non-TNFs (AS: 96.1%, nr-axSpA: 93.8%) and bDMARDs (AS: 46.9%, nr-axSpA: 21.9%). Patients were similarly impacted by their condition for BASDAI (AS: 5.0, nr-axSpA, 5.6), pain (AS: 55.8, nr-axSpA, 60.8) and fatigue (AS: 51.6, nr-axSpA, 59.9), but there was an imbalance in tender joint count (AS: 2.6, nr-axSpA, 13.4).

At 6-month FU, both populations experienced minimal or no change in ASDAS scores (AS: -0.3, nr-axSpA: 0.0) remaining in a high state of disease activity (ASDAS, ≥2.2). A small percent of both groups achieved ASAS20 (AS: 20.1%; nr-axSpA: 21.9%) and ASAS40 (AS: 14 %, nr-axSpA: 15.6%). Further, bDMARD initiators had minimal decreases in BASDAI (AS: -0.6, nr-axSpA: -0.8), pain (AS: -8.5, nr-axSpA: -12.2), and fatigue (AS: -5.0, nr-axSpA: -7.9) scores.

Table 1. Demographic characteristics and clinical response rates of AxSpA patients

	≤5 years (A) (Group 1)	5-10 year (B) (Group 2)	≥10 years (C) (Group 3)	P
	(n=95) Mean±SD.	(n=82) Mean±SD.	(n=187) Mean±SD.	
Age (year)	39,9±12,9 [BC]	44,9±11,0 [C]	51,0±11,4	**<0,001**
BASDAI (baseline)	51,1±19.9	56,2±18,2	54,4±20,0	0,133
	n (%)	n (%)	n (%)	
Gender, Male	70 (73,7)	52 (63,4)	132 (70,6)	0,346
Diagnosis, AS	60 (63,8)[C]	63 (76,8)[C]	170 (90,4)	**<0,001**
	Median (Min./Max.)	Median (Min./Max.)	Median (Min./Max.)	
CRP (baseline)	10 (0 / 140) [C]	9,75 (0,4 / 95)	13 (0 / 177)	**0,049**
	n (%)	n (%)	n (%)	
HLAB27 (+)	52 (54,7)	46 (56,1)	127 (67,9) [A]	**0,007**
ASAS 40				
6th Month	42 (45,7)	36 (46,8)	76 (42,7)	0,611
12th Month	59 (68,6) [C]	45 (62,5)	94 (55,0)	**0,032**
24th Month	34 (63,0) [C]	24 (50,0)	49 (45,4)	**0,042**
ASDAS-CRP MI				
6th Month	42 (46,2)	36 (48,0)	66 (37,3)	0,568
12th Month	40 (47,6)	38 (53,5)	83 (48,5)	0,788
24th Month	29 (53,7)	19 (38,8)	44 (40,7)	0,738

OneWay ANOVA (Robuts Statistic:Brown-Forsythe)

Table 2. TNFi drug survival rate results of early and late disease course

	TNFi retention rates (24 months)	Follow-up period (month)	Proportion of Drug Retention Rate (month)	P
	n(%)	Median ± Se.	6 / 12 / 24	
Symptom duration, Disease				0.203
≤5 years, AS	34 (75,6)	80,0±14,4	93,2 / 86 / 75,6	
≤5 years, nrAxSpA	18 (58,3)	36,0±11,9	91,2 / 64,6 / 58,3	
5-10 years, AS	38 (61,7)	57,0±25,0	92,1 / 81 / 61,7	
5-10 years, NrAxSpA	8 (44,9)	23,0±4,2	89,5 / 73 / 44,9	
≥10 years, AS	119 (72,1)	52,0±4,0	92,4 / 85,9 / 72,1	
≥10 years, NrAxSpA	11 (61,1)	37,0±7,6	88,9 / 66,7 / 61,1	
Diagnosis				
nrAxSpA	37 (55,7)	37,0±7,6	84,6 / 67,3 / 55,7	<0,001
AS	193 (70,6)	59,0±6,5	90,1 / 84,2 / 70,6	

Kaplan Meier Test; Log Rank (Mantel-Cox)

Conclusion: AS and nr-axSpA bDMARD initiators had a modest improvement in outcomes at six months. Twenty percent or fewer patients achieved ASAS20 or ASAS40, with many having residual impairment based on ASDAS, BASDAI, pain, and fatigue outcomes at six months. While patients are initiating biologic agents, room for improvement exists as many are not achieving optimal treatment response of inactive (ASDAS, <1.3) or low disease activity (ASDAS, <2.1).

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FRI0278

IXEKIZUMAB IMPROVES SELF-REPORTED OVERALL FUNCTIONING AND HEALTH AS MEASURED BY THE ASAS HEALTH INDEX IN PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: 52-WEEK RESULTS OF A PHASE 3 RANDOMIZED, ACTIVE AND PLACEBO-CONTROLLED TRIAL (COAST-X)

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Background: Ixekizumab has demonstrated efficacy in treating signs and symptoms of patients with non-radiographic axial spondyloarthritis (nr-axSpA).[1] The Assessment of SpondyloArthritis International Society Health Index (ASAS HI) is a composite measure consisting of 17 dichotomous items to assess overall functioning and health in patients with spondyloarthritis.[2]

Objectives: To assess health outcomes using ASAS HI in patients with nr-axSpA treated with ixekizumab (IXE) for 52 weeks.

Methods: COAST-X (NCT02757352) was a 52-week, randomized, double-blind, placebo (PBO)-controlled study enrolling adults with an established diagnosis of axSpA (ASAS classification criteria, but not modified New York criteria for sacroiliitis), had Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score ≥4, back pain score ≥4, inflammation (sacroiliitis on magnetic resonance imaging [MRI] per ASAS criteria) or an elevated C-reactive protein [CRP] level >5 mg/L), and inadequate response or intolerance to nonsteroidal anti-inflammatory drugs. Patients were randomized 1:1:1 to receive PBO or 80 mg IXE every 4 weeks (Q4W) or every 2 weeks (Q2W). Changing background medications or switching to open-label IXE Q2W, or both, was allowed after week 16 at investigator discretion. Change from baseline in ASAS HI (score 0-17 with higher score indicating worse health) was analyzed using logistic regression analysis at Weeks 0, 4, 8, 16, 36, and 52. For the ASAS HI, the smallest detectable change was calculated as 3.0. Patients having an ASAS HI score ≤5 were defined as being in a good health state.[3] Comparisons between IXE treatments and PBO were made using logistic regression analysis. Non-responder imputation was used for missing data. Patients who switched to open label IXEQ2W were considered non-responders after they switched.

Results: At baseline, ASAS HI scores were similar between the three groups (PBO 9.0 ± 3.7; IXE Q4W 8.6 ± 3.4; IXE Q2W 9.6 ± 3.4). Significantly more patients receiving IXE Q4W versus PBO achieved ASAS HI score ≤5 at Week 16 (p<0.05; Fig. A). From Week 36 to 52, significantly more patients receiving IXE Q4W and Q2W achieved ASAS HI score ≤5 (p<0.05; Fig. A). Significantly more patients receiving IXE Q2W versus PBO achieved a clinically meaningful improvement in ASAS HI score ≥3 at Week 16 (p<0.05; Fig. B). From Week 36 to 52 significantly more patients receiving IXE Q4W and Q2W achieved a clinically meaningful improvement in ASAS HI score ≥3 compared with PBO (p<0.05; Fig. B).

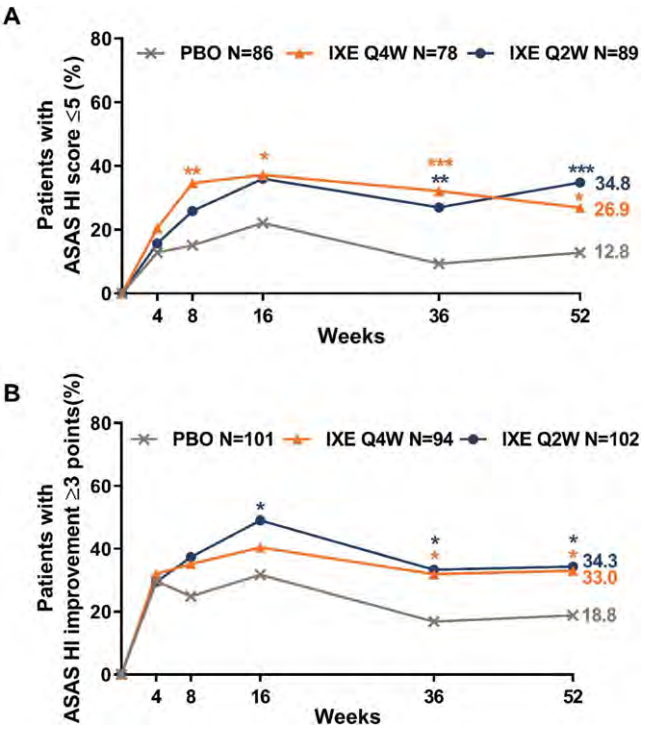


Figure. Improvement in ASAS HI scores through Week 52. A: Proportion of patients who achieved an ASAS HI score ≤5 in patients with baseline ASAS HI score >5. B: Proportion of patients who achieved ≥3-point improvement in ASAS HI in patients with baseline ASAS HI score ≥3. ***p<0.001, **p<0.01, *p<0.05 versus PBO. Asterisk color indicates which IXE treatment group was compared with PBO. ASAS HI= Assessment of SpondyloArthritis International Society Health Index; IXE=ixekizumab; PBO=placebo; Q2W=every 2 weeks; Q4W=every 4 weeks

Conclusion: Ixekizumab improves overall functioning and health in patients with nr-axSpA as assessed by ASAS HI, with significantly more patients achieving good health status.

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FRI0279

USE OF TNF-INHIBITORS BEFORE, DURING AND THE FIRST YEAR AFTER PREGNANCY IN WOMEN WITH SPONDYLOARTHRITIS

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Background: Treat to target is a goal in pregnant women with spondyloarthristis. There is increasing evidence on safe use with TNF inhibitors during pregnancy (1). Adjusted use of TNF inhibitors preconception and throughout pregnancy may stabilize disease activity and prevent flares (2). Low disease activity is also beneficial for the fetus.
Objectives: To study the use of TNF-inhibitors among women with spondyloarthritis in Norway before, during and after pregnancy.
Methods: RevNatus is a Norwegian, nationwide quality register that monitors treatment of inflammatory rheumatic diseases before, during and after pregnancy. Data from RevNatus in the period October 2017 to October 2019 were used to map the use of all types of TNF inhibitors among 208 women with spondyloarthritis, fulfilling the ASAS criteria.
The use of medication was reported at the time of visit in outpatient clinic. The frequency of use of TNF inhibitors is registered at seven timepoints from pre-pregnancy to twelve months after delivery.
Results: The use of TNF-inhibitors was reported at each visit for all the women with spondyloarthritis. Most women are not using TNF inhibitors before and beyond conception. Most of the women continuing TNF inhibitors beyond conception, used certolizumab, etanercept, or adalimumab. Infliximab or golimumab were not used in pregnancy (tabell 2).

Table 2:

SPA	Certoli-zumab	Etaner-cept	Adali-mumab	Golim-umab	Inflik-simab	No TNF -inhibitor
Before Pregnancy n=139	10% (14)	8% (11)	6% (9)		6% (9)	69% (96)
1.trimester n=102	7% (7)	7% (7)	2 % (2)			84% (86)
2.trimester n=104	7% (7)	6% (6)	1% (1)			87% (90)
3. trimester n=95	3% (3)	2% (2)	1% (1)			94% (89)
6 weeks post partum n=100	15% (15)	10% (10)	8% (8)	3% (3)		64% (64)
6 months post partum n=82	19% (16)	12% (10)	7% (6)	2% (2)	2% (2)	55% (46)
12 months post partum n=74	22% (16)	15% (11)	7% (5)	4% (3)	5% (4)	47% (35)

Conclusion: A majority of the women with spondyloarthritis were not treated with TNF inhibitors before or during pregnancy. Only a few of the women with spondylosthritis continued treatment with TNF inhibitors during pregnancy.
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FRI0280

COMPARATIVE DRUG SURVIVAL OF TNF INHIBITORS AND SECUKINUMAB IN BIOLOGIC NAÏVE PATIENTS WITH ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS

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Background: Secukinumab (SEC) was approved for treating ankylosing spondylitis (AS) and psoriatic arthritis (PsA) in the UK in 2016/17 respectively, providing an alternative mechanism of action to TNF inhibitors (TNFi), which were, until that time, the most frequently prescribed biologic therapies for these rheumatic conditions. SEC's efficacy and safety has been shown in clinical trials[1, 2], but real world data on its survival remains scarce.
Objectives: This study aimed to compare SEC and TNFi drug survival in AS and PsA biologic naïve patients.
Methods: Observational retrospective study of consecutive biologic naïve patients attending the Dudley Group NHS Foundation Trust (DGFT) with a clinical diagnosis of AS (fulfilling ASAS criteria) or PsA (fulfilling CASPAR criteria) who received at least one dose of biologic therapy between 01/07/2017 and 30/09/2019, with a follow-up period until December 31st, 2019. The biologics database, patient medical records and investigations were reviewed and data on demographics, disease characteristics, previous cDMARD therapy and reasons for discontinuation of biologic were collected. Analysis was performed using descriptive statistics, Kaplan-Meier plots and Cox regression on SPSS version 23.
Results: We identified 153 AS or PsA patients starting biologic therapy in this time interval. 103 (68.7%) were biologic naïve, commencing either TNFi (38, 36.9%), SEC (63, 61.1%) or Ixekizumab (2, 1.9% -excluded from analysis) for AS (45.5%) and PsA (54.5%). The patients were evenly distributed in terms of sex (female 50.5%), had a mean (±SD) age of 45 (±13.8) years and a median (IQR) disease duration of 5 (7.7) years. The median (IQR) follow up time was 13 (13) months.
The overall 1 and 2-year drug survival was 86.8% and 79.3% respectively for TNFi and 81.5% and 77.4% for SEC treated patients. There was no statistically significant difference between the estimated means for drug survival time for the two treatment modalities (TNFi: 24.4 vs SEC:22.9 months, *log rank:0.991*) (Figure 1). The analysis of SEC's drug survival in AS in comparison to PsA did not show statistically significant difference (21.8 vs 22.0 months respectively, *log rank: 0.419*). We observed a trend for worse TNFi survival in AS compared to PsA, but this did not reach statistical significance (18.9 vs 26.1 months respectively, *log rank: 0.09*).

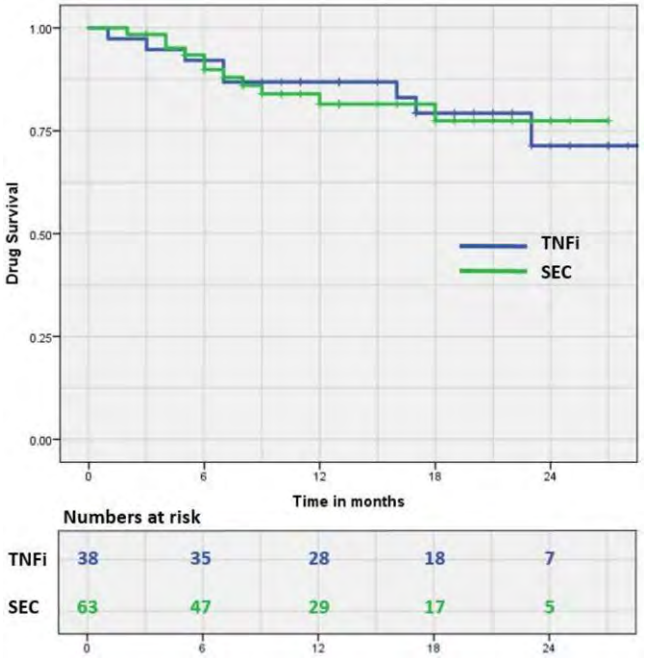


Figure 1. Comparative cumulative drug survival (months) in biologic naïve AS and PsA patients

No significant difference in reasons for discontinuation between treatments was observed. Age, sex, disease duration, previous DMARD use and extra-articular manifestations were variables that were not associated with drug survival on Cox regression analysis.
Conclusion: The estimated 1 year drug survival for TNFi and SEC was 86.8% and 81.5% respectively. Data from our cohort of real-life previously biologic naïve patients with AS and PsA showed no difference in drug survival and reasons for discontinuation between TNFi and SEC. Age, sex, previous DMARD use and extra-articular manifestations were not predictors for drug survival.
References:
[1] Kavanaugh et al. Secukinumab for Long-Term Treatment of Psoriatic Arthritis: A Two-Year Followup From a Phase III, Randomized, Double-Blind Placebo-Controlled Study. Arthritis Care Res (Hoboken). 2017 Mar;69(3):347-355.

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FRI0281 NON-STEROIDAL ANTI-INFLAMMATORY DRUGS IN PATIENTS WITH STABLE ANKYLOSING SPONDYLITIS RECEIVING TUMOR NECROSIS FACTOR INHIBITOR: CONTINUED VS WITHDRAWN

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Background: A recent recommendation from the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network (ACR/SAA/SPARTAN) suggests withdrawing non-steroidal anti-inflammatory drugs (NSAIDs) in patients with stable ankylosing spondylitis (AS) receiving tumor necrosis factor inhibitor (TNFi) and NSAIDs.[1] However, the level of evidence for this statement is very low with lack of evidence supporting this recommendation. No studies have directly compared stable AS patients receiving TNFi with NSAIDs, and those receiving TNFi without NSAIDs.
Objectives: To compare the disease activity in stable AS patients receiving TNFi, according to the use of NSAIDs.
Methods: In total, 189 patients with stable AS receiving TNFi were included. Patients were classified into NSAID withdrawn group (n=48) and NSAID continued group (n=141), according to the use of NSAIDs. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were measured every 3 months, and Bath ankylosing spondylitis disease activity index (BASDAI) was measured every 6 months as parameters to evaluate disease activity. ESR, CRP, and BASDAI at each time point, and time-averaged values of each parameter during the observation period of one-year were compared between the two groups. Repeated-measure ANOVA was performed to compare changes in disease activity parameters during the observation period between the two groups.

Table. Disease activity measures during observation period

	NSAID withdrawn (N = 48)	NSAID continued (N = 141)	P value
At 3 months			
ESR (mm/hr), median (IQR)	5.0 (2.0–14.0)	7.0 (2.0–15.0)	0.712
CRP (mg/L), median (IQR)	0.5 (0.2–1.5)	0.8 (0.3–1.8)	0.613
At 6 months			
ESR (mm/hr), median (IQR)	5.0 (2.0–15.0)	7.0 (2.0–15.0)	0.278
CRP (mg/L), median (IQR)	0.6 (0.3–1.8)	0.8 (0.3–2.1)	0.335
BASDAI, mean ± SD	2.019 ± 0.569	2.226 ± 1.028	0.187
At 9 months			
ESR (mm/hr), median (IQR)	4.5 (2.0–13.8)	7.0 (2.8–17.0)	0.261
CRP (mg/L), median (IQR)	0.5 (0.3–1.6)	0.8 (0.3–2.2)	0.129
At 12 months			
ESR (mm/hr), median (IQR)	6.0 (2.0–13.0)	9.0 (3.0–19.0)	0.050
CRP (mg/L), median (IQR)	0.6 (0.3–2.1)	1.0 (0.4–3.1)	0.151
BASDAI, mean ± SD	2.168 ± 1.066	2.197 ± 1.002	0.867
Time-averaged values			
ESR (mm/hr), median (IQR)	5.3 (2.6–15.2)	8.4 (3.8–14.7)	0.096
CRP (mg/L), median (IQR)	0.8 (0.4–1.8)	1.1 (0.5–2.9)	0.136
BASDAI, mean ± SD	2.137 ± 0.557	2.227 ± 0.706	0.421

Abbreviations: NSAIDs, non-steroidal anti-inflammatory drugs; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; BASDAI, Bath ankylosing spondylitis disease activity index.

Results: The level of ESR, CRP, and BASDAI at baseline and during the observation period did not differ between the two groups. The time-averaged values of ESR (p=0.096), CRP (p=0.136), and BASDAI (p=0.421), and changes of ESR (p=0.101), CRP (p=0.714), and BASDAI (p=0.613) during the observation period were not significantly different between the two groups.
Conclusion: The continued use of NSAIDs in patients with stable AS receiving TNFi had no additional benefit in controlling the disease activity, as compared to patients who withdrew NSAIDs. Considering the risk of toxicity of long-term NSAID use, withdrawal of NSAIDs in stable AS patients receiving TNFi may be preferable.
References:

[1] Ward MM, Deodhar A, Gensler LS, *et al.* 2019 Update of the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis. *Arthritis Rheumatol* 2019;71:1599-613 doi: 10.1002/art.41042.

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FRI0282 CONVENTIONAL DISEASE-MODIFYING ANTIRHEUMATIC DRUGS THERAPY HAS NO EFFICACY IN SLOWING SPINAL RADIOGRAPHIC PROGRESSION IN ANKYLOSING SPONDYLITIS: RESULTS FROM 18-YEAR LONGITUDINAL DATA

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Background: In the treatment of ankylosing spondylitis (AS), conventional disease-modifying antirheumatic drugs (cDMARDs) are generally recommended only in patients with peripheral arthritis. However in daily clinical practice, sulfasalazine (SSZ) and methotrexate (MTX) have still been considered on the basis of their anti-inflammatory effect when non-steroidal anti-inflammatory drugs (NSAIDs) are not available and when it is difficult to start tumor necrosis factor (TNF) inhibitors. Nonetheless there is few data about the impact of the cDMARDs on the prognosis of spinal progression.
Objectives: The aim of this study was to investigate the effectiveness of SSZ and MTX on the spinal radiographic progression in patients with AS.

Table 1. Association of clinical covariates and DMARD intervals with the rate of mSASSS change

Variable	Multivariate analysis			
	Model 1		Model 2	
	β (95% CI)	p	β (95% CI)	p
On-DMARD intervals	-0.081 (-0.276 to 0.115)	0.418		
On-SSZ intervals			-0.001 (-0.211 to 0.189)	0.913
On-MTX intervals			-0.180 (-0.439 to 0.078)	0.172
Sex (female)	-0.449 (-0.782 to -0.117)	0.008	-0.440 (-0.775 to -0.105)	0.010
Age	0.012 (-0.001 to 0.026)	0.061	0.012 (-0.001 to 0.025)	0.076
Eye involvement	0.572 (0.264 to 0.880)	< 0.001	0.577 (0.268 to 0.886)	< 0.001
Peripheral joint involvement	-0.508 (-0.810 to -0.206)	0.001	-0.513 (-0.817 to -0.210)	0.001
HLA-B27 positivity	†		†	
NSAIDs	†		†	
Glucocorticoids	†		†	
ESR (log)	0.176 (0.087 to 0.265)	< 0.001	0.178 (0.088 to 0.268)	< 0.001
BASDAI (square root)	†		†	

†Not included in the model because the value did not show potentially significant association in univariate analysis (p > 0.1).

Methods: A total of 301 patients who have been treated with cDMARDs were enrolled from 1,280 patients in a single center cohort during 18 years of follow up. For each patient, time intervals of periods were created according to the prescription records. 'On-DMARD' intervals were time intervals of periods with SSZ or MTX treatment and 'off-DMARD' intervals were time intervals of periods without both SSZ and MTX treatment. The intervals were the periods excluding the treatment periods of TNF inhibitors. Radiographic progression was evaluated by the rate of Modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) change, an increase or decrease of mSASSS change per year. A generalized estimating equation models with adjustment for confounding covariates were used to evaluate the efficacy of cDMARDs on the radiographic progression.
Results: The number of 732 on-DMARD intervals and 1,027 off-DMARD intervals were obtained. Among the on-DMARD intervals, the proportion of intervals treated with SSZ (on-SSZ intervals), MTX (on-MTX intervals) and both of them (on-SSZ/MTX intervals) were 96.2%, 19.9% and 16.1%, respectively. In the multivariable regression analysis, there was no significant decrease in the rate of mSASSS change during cDMARDs therapy (β = -0.081, p = 0.418) (Table 1). And the mean rate of mSASSS change were 0.61 during on-DMARD intervals and 0.69 during off-DMARD intervals after adjustment of other covariates.
Conclusion: Treatment with cDMARDs in AS did not show significant impact in retarding spinal progression. In patients with AS, treatment with biologics rather than cDMARDs may be more effective in slowing radiographic progression.

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FRI0283

CO-MEDICATION WITH CSDMARD HAS LITTLE EFFECT ON THE RETENTION OF TNF INHIBITORS IN PSORIATIC ARTHRITIS, RESULTS FROM THE EUROSPA COLLABORATION

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Background: Previous studies have suggested similar effectiveness, but longer treatment retention, for tumor necrosis factor inhibitors (TNFi), when used in combination with a conventional synthetic disease modifying anti-rheumatic drug (csDMARD) in psoriatic arthritis (PsA).
Objectives: To describe patients with PsA initiating a first TNFi as monotherapy compared to combination therapy, and to explore 1-year treatment retention of TNFi in the two groups.
Methods: Patients with PsA starting a first TNFi (2006-2017) were identified in biologics registers of 13 European countries, and data were pooled for analysis. Co-medication with csDMARD was determined at TNFi start.
Because of large inter-country variation in TNFi retention, countries were split into two strata, depending on each country's 1-year retention rate for TNFi being above (stratum A) or below (stratum B) the average 1-year retention rate.
TNFi treatment retention was compared through Kaplan-Meier curves; the proportion remaining on the TNFi at one year; and hazard ratios (HR) during the first year: (i) crude; adjusted for (ii) country-strata, and (iii) country-strata, sex, age, calendar year, DAS28 and disease duration. In model (iii) only registers contributing >1000 patients or <33% missing data for DAS28 were included.
Results: A total of 14778 patients with PsA starting a first TNFi were included. Baseline disease activity was similar within stratum B, but higher for the combination treatment group in stratum A (table 1).

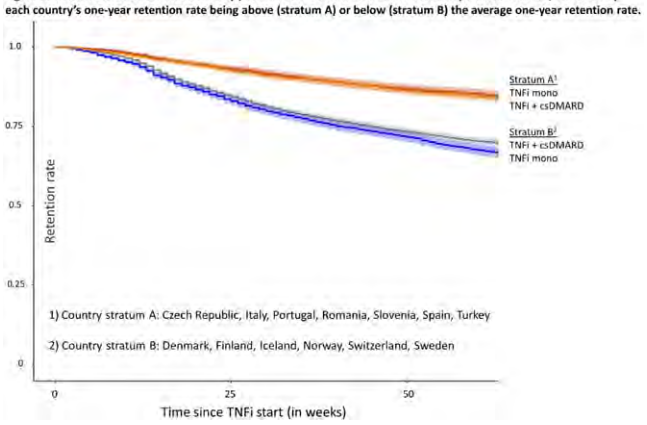
Table 1. Baseline characteristics

Country strata	Stratum A		Stratum B	
	TNFi monotherapy N=2120	TNFi/ csDMARD combination N=2128	TNFi monotherapy N=3369	TNFi/ csDMARD combination N=7161
Females	52%	51%	53%	51%
Age, years	49.7 (12.2)	48.7 (11.8)	48.8 (13.0)	48.9 (12.2)
Disease duration, yrs	6.4 (7.0)	6.8 (6.8)	5.9 (7.5)	5.9 (7.1)
Tender joints 28	5.5 (6.3)	8.0 (6.3)	5.6 (6.0)	5.6 (5.7)
Swollen joints 28	2.8 (4.3)	5.6 (5.0)	3.0 (3.8)	3.3 (3.8)
VAS pain	54 (29)	62 (24)	59 (23)	56 (24)
DAPSA-28	24.6 (18.6)	36.2 (17.6)	27.3 (15.6)	27.2 (15.2)
DAS28 (CRP)	3.5 (1.4)	4.7 (1.3)	4.0 (1.2)	4.0 (1.1)
Concomitant csDMARD				
Methotrexate	-	76%	-	79%
Sulfasalazine	-	15%	-	15%
Other csDMARD	-	49%	-	25%

Numbers are means (sd) unless otherwise stated.

The Kaplan-Meier curves for the treatment groups were similar within each stratum (fig 1), as were the proportions remaining on TNFi after one year, stratum A: monotherapy 86% (95%CI: 85-88) vs. combination 86% (84-87), stratum B: 71% (69-72) vs. 73% (72-74). The HRs for TNFi discontinuation (ref=TNFi monotherapy) were: (i) 1.06 (0.98-1.13), (ii) 0.94 (0.87-1.01), (iii) 0.89 (0.83-0.96), including 13078 patients (9 countries) for model (iii).
Conclusion: In this exploratory study no benefit in TNFi retention was observed for csDMARD combination therapy in crude analyses, while in adjusted analyses an 11% lower risk of TNFi discontinuation was found. These preliminary results offer limited support for use of combination therapy in PsA. Further analyses will explore to what extent the results are affected by inter-country heterogeneity and differences between TNFi.

Figure 1. Retention rate of TNFi monotherapy vs. TNFi and csDMARD co-medication in psoriatic arthritis, stratified by each country's one-year retention rate being above (stratum A) or below (stratum B) the average one-year retention rate.



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FRI0284

EFFECTIVENESS AND SAFETY OF SECUKINUMAB IN NAÏVE OR TNF-INHIBITORS FAILURE PSORIATIC ARTHRITIS PATIENTS IN REAL LIFE: A 24-MONTHS PROSPECTIVE MULTICENTER STUDY

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Background: Secukinumab (SEC) is a novel treatment for psoriatic arthritis (PsA),but data from real life are still missing.

Objectives: 1)to evaluate the effectiveness and safety of a wide cohort of PsA patients on SEC followed in 7 Italian rheumatologic centers for 24 months;2)to compare the features and disease activity indices of SEC-treated PsA patients subdivided in naïve biological drugs (**group A**) and in TNF-inhibitors (TNFi) failure patients (**group B**).

Methods: Consecutive patients with moderate-severe PsA,who begun SEC treatment were evaluated prospectively.Data on disease characteristics,previous and ongoing treatments,comorbidities and duration of follow-up were collected. Disease activity,functional and clinimetric scores and biochemical values were recorded at baseline (t0),at 6 (t6),12 (t12),and 24 (t24) months.Anova (Kruskal Wallis) and generalized linear models were used to compare variables over time. Infections and adverse events were also collected.

Results: PsA **345** patients [38.84% men;mean age 52.9 (11.27) years] were enrolled;mean treatment duration was 18.53 (9.97) years.SEC was prescribed as first line biologic treatment in 133 (38.55%) patients and as second or more line biological treatment in 212 (61.45%) patients. Enthesitis was present as a prominent manifestation in 61.44% of patients (Figure 1). In all population significant decrease in tender/swollen joints;Visual Analogue Scale of pain (VASp) and general health (VASgh);Psoriasis Area Severity Index (PASI);Leeds Enthesitis Index (LEI);number of dactylitis;Health Assessment Questionnaire modified for spondyloarthritis (HAQ-S);Bath Ankylosing Spondylitis Disease Activity Index (BASDAI);Bath Ankylosing Spondylitis Functional Index (BASFI);C-reactive protein (CRP) was achieved. Effectiveness of all PsA patients was associated to an improvement in Ankylosing Spondylitis disease activity score (ASDAS) [t0=3.45 (0.69) vs t24=1.48 (0.23);p<0.01] and in Disease Activity in PsA (DAPSA) [t0=29.52 (12.56) vs t24=11.41 (7.63);p<0.001].At t0 **group B** had a more erosive (p=0.04) and polyarticular pattern (p=0.04),a longer disease duration (p=0.001),a greater prevalence (p=0.04) of psoriasis and dactylitis (p=0.01),a higher PASI score (p=0.01),while no significant difference was observed for uveitis,inflammatory bowel diseases,enthesitis.At t24 **group A** showed better physical functioning and lower disease activity compared to **group B** [HAQs A vs B=0.03 (0.16) vs 0.69 (0.73);BASDAI A vs B=2.37 (0.66) vs 4.27 (2.33);ASDAS A vs B=1.4 (0.62) vs 1.99 (0.86);CRP A vs B=2.03 (1.94) vs 3.11 (1.55) mg/L;DAPSA A vs B=7.03 (3.57) vs 12.41 (8.05)].After t24 of treatment 74.6% of **Group A** and 72.8% of **Group B** articular had an inactive\low disease activity (MDA),accordingly to ASDAS and DAPSA respectively.Forty-three patients (12.46%) stopped the treatment during the follow-up mainly because of primary or secondary loss of efficacy (29 and 24, respectively).Only 14 patients suspended SEC because of adverse events (of which 9 for reactions at site of injection).A low number of episodes of mild infections (16) occurred;SEC was instead permanently discontinued in 7 cases for:oral refractory mucositis (3);recurrent aphthosis (2);diverticulitis (2).The retention rate at t24 was good in the whole population.Interestingly no differences were found between **Group A** and **B**(p=0.815).

Conclusion: In a real life clinical setting,SEC was safe and effective in PsA. as shown by a significant decrease of DAPSA and ASDAS over a 24-months follow up.

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Baseline characteristics of 345 PsA patients of AOP treated with secukinumab in the period September 2016- November 2019.

PsA Features	Total patients	GROUP A	GROUP B	p
Male sex (N,%)	134 (38.84%)	52 (39.09%)	82 (38.68%)	ns
Age (years), mean (SD)	52.90 (11.27)	48.59 (13.79)	53.30 (7.99)	0.05
Age of diagnosis (years), mean (SD)	38.86 (12.98)	39.20 (13.82)	37.69 (9.98)	ns
Disease duration (years), mean (SD)	10.68 (7.64)	9.18 (6.82)	15.76 (8.32)	0.001
PsA (n)	345	133	212	NA
Poliarticular	209 (60.58%)	74 (55.63%)	135 (63.68%)	0.04
Mono/Oligoarticular	106 (30.72%)	45 (33.83%)	61 (28.77%)	ns
Axial	84 (24.35%)	28 (21.05%)	56 (26.42%)	ns
Enthesitis	212 (61.44%)	81 (60.91%)	131 (61.79%)	ns
Dactylitis	50 (14.49%)	13 (9.77%)	37 (17.45%)	0.01
Psoriasis, N (%)	247 (71.59%)	91 (68.42%)	156 (73.58%)	0.04
Onicopathy, N (%)	138 (40%)	47 (35.34%)	91 (42.93%)	0.05
IBD, N (%)	4 (1.15%)	0 (0%)	4 (1.89%)	ns
Uveitis, N (%)	14 (4.06%)	9 (6.77%)	5 (2.36%)	ns
Erosions, N (%)	174 (50.43%)	59 (44.36%)	115 (54.25%)	0.04
Weight (kg), mean (SD)	75.32 (12.73)	75.64 (13.09)	74.23 (11.84)	ns
Height (m), mean (SD)	1.71 (0.08)	1.74 (0.35)	1.69 (0.19)	ns
BMI, mean (SD)	25.86 (3.73)	25.84 (3.58)	25.93 (4.37)	ns
TJ [0-68], mean (SD)	6.94 (5.07)	6.65 (3.63)	7.56 (5.74)	ns
SJ [0-66],mean (SD)	3.77 (2.67)	2.28 (2.87)	4.21 (2.16)	0.04
LEI [0-6]mean (SD)	1.92 (1.5)	1.81(1.56)	2.14 (1.48)	ns
Dactylitis [0-20] number digit, mean (SD)	0.68 (0.87)	0.66 (0.95)	0.85 (0.77)	ns
PASI [0-72] mean (SD)	3.21 (5.59)	1.05 (2.25)	4.5 (6.64)	0.01
ESR [0-25](mm/h), mean (SD)	18.57 (12.56)	16.45 (11.61)	19.73 (12.19)	ns
CRP [0-6](mg/L), mean (SD)	8.81 (8.29)	8.69 (8.72)	9.57 (8.17)	0.05
DAPSA [0-164], mean (SD)	29.52 (12.56)	28.59 (13.34)	31.25 (11.10)	0.05
ASDAS [0-6], mean (SD)	3.45 (0.69)	3.35 (0.78)	3.51 (0.65)	0.04
HAQ-S [0-8], mean (SD)	1.08 (0.55)	0.96 (0.45)	1.14 (0.59)	0.05
VAS-pain [0-10], mean (SD)	6.96 (1.37)	6.92 (1.44)	7.13 (1.35)	ns
VAS-gh [0-10], mean (SD)	6.47 (1.84)	6.15 (1.93)	6.68 (1.79)	ns
BASDAI [0-10], mean (SD)	7.02 (1.54)	6.62 (1.44)	7.23 (1.51)	ns
BASFI [0-10], mean (SD)	6.43 (1.94)	5.77 (2.08)	6.82 (1.78)	ns
Mean treatment duration (months), mean (SD)	17.24 (11.25)	16.13 (10.17)	18.53 (9.97)	ns
1st line (N,%)	134 (38.84%)	134 (100%)	0 (0%)	NA
2nd line (N,%)	66 (19.13%)	0 (0%)	66 (31.13%)	NA
3rd line (N,%)	67 (19.42%)	0 (0%)	67 (31.60%)	NA
4th line (N,%)	45 (13.04%)	0 (0%)	45 (21.23%)	NA
5th line (N,%)	15 (4.34%)	0 (0%)	15 (7.08%)	NA
6th line (N,%) or more	19 (5.50%)	0 (0%)	19 (8.96%)	NA
Concomitant NSAIDs, N (%)	211 (61.16%)	95 (71.43%)	116 (54.72%)	0.04
Concomitant steroid, N (%)	95 (27.54%)	28 (21.05%)	67 (31.60%)	0.05
Concomitant csDMARDs, N (%)	159 (46.08%)	67 (50.37%)	92 (43.39%)	ns
Methotrexate	118 (34.20%)	51 (38.35%)	67 (31.60%)	ns
Sulphasalazine	41 (11.88%)	18 (13.53%)	23 (10.85%)	ns
Leflunomide	17 (4.93%)	6 (4.51%)	11 (5.19%)	ns
Hydroxychloroquine	3 (0.86%)	2 (1.50%)	1 (0.47%)	ns
cyclosporine	6 (1.73%)	1 (0.75%)	5 (2.36%)	ns

Legend: Data are expressed as mean (standard deviation=SD) unless otherwise specified; range of possible values are indicated in square brackets. p§ Anova (Kruskal Wallis) a t0: p<0.05; GROUP A= naive to anti-TNFalpha inhibitors; GROUP B= TNFalpha failure inhibitors; PsA, psoriatic arthritis; IBD, inflammatory bowel disease; PASI, Psoriasis Area Severity Index; TJ,Tender Joint; SJ, Swollen Joint; LEI, Leeds Enthesitis Index; DAPSA, Disease Activity Index for Psoriatic Arthritis; BMI, body mass index; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; ASDAS, Ankylosing Spondylitis disease activity score; HAQ-S, Health Assessment Questionnaire modified for spondyloarthritis; NSAIDS, non -steroidal inflammatory drugs; csDMARDs, conventional synthetic diseasemodifying antirheumatic drugs. ns=not statistical significant. NA= not applicable

FRI0285

FILGOTINIB TREATMENT RESULTS IN REDUCTION OF BIOMARKERS ASSOCIATED WITH DISEASE IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Ankylosing spondylitis (AS) is a chronic, immune-mediated disease characterized by inflammation of the sacroiliac joints and spine, and a young age of onset of 20–40 years. In the recent TORTUGA study, filgotinib (FIL), an oral, selective Janus kinase 1 (JAK1) inhibitor, significantly reduced AS disease activity compared with placebo (PBO).[1] Selective JAK1 inhibition by FIL has the potential to simultaneously block multiple inflammatory pathways, thus we analyzed biomarker concentrations in serum samples from TORTUGA.

Objectives: To evaluate the impact of selective JAK1 inhibition with FIL on circulating disease associated biomarkers in adult patients with active AS enrolled in the TORTUGA study.

Methods: TORTUGA (Clinicaltrials.gov identifier NCT03117270) was a 12-week, randomized, double-blind, placebo-controlled, phase 2 study. Patients were randomized 1:1 to FIL 200 mg (n=58) or PBO (n=58) once-daily. Serum samples (FIL n=56, PBO n=53) were collected at baseline (BL) and weeks 1, 4 and 12, and analyzed using the Meso Scale Discovery immunoassay platform (Meso Scale Diagnostics, Rockville, MD, USA) to evaluate 135 biomarkers. Biomarker concentration changes from BL were analyzed on paired patient data and reported for weeks 1, 4 and 12, and clustering analysis was performed. Correlation between the 135 biomarkers and selected clinical scores at BL was assessed by Spearman rank correlation analysis.

Results: FIL treatment produced significant reductions in serum concentrations of multiple biomarkers associated with AS disease activity. Five clusters of biomarker response were identified based on the kinetics and magnitude of percent changes from BL. These clusters also represented discrete biological functions:

cluster 1 (rapid, strong >50% decrease in all three time points) included systemic inflammation biomarkers eg, CRP, SAA; cluster 2 (>20% decrease in at least one time point) included immune cell biomarkers eg, MIP3B, IL12p40; cluster 3 (<20% decrease in all three time points) included cellular adhesion biomarkers eg, ICAM-1, VCAM-1; cluster 4 (delayed decrease) included matrix remodelling biomarkers eg, MMP1, TIMP1; and cluster 5 included biomarkers that exhibited a gradual increase in serum concentration with FIL treatment.

Spearman rank correlation analyses showed that at BL, the systemic inflammation biomarkers CRP and SAA, as well as a number of biomarkers including ICAM-1 and MMP3, were positively correlated with BL AS disease activity score (ASDAS); conversely, only a few biomarkers showed a negative correlation with BL ASDAS, the cytokine receptor FLT3 and the chemotactic cytokine fractalkine (FRACTAL).

Conclusion: In patients with active AS, FIL treatment significantly decreased levels of circulating biomarkers associated with active AS disease, including proinflammatory cytokines and chemokines, cell adhesion molecules, and markers of matrix remodelling. Clustering analysis revealed early and late biomarker changes associated with disease. These data are consistent with reduced AS disease activity in TORTUGA and suggest that FIL treatment leads to a rapid and sustained reduction of inflammation in AS.

References:

[1] van der Heijde D *et al. Lancet* 2018;392:2378–87

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FRI0286

IXEKIZUMAB TREATMENT IMPROVES FATIGUE, SPINAL PAIN, STIFFNESS, AND SLEEP IN PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS

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Background: Common symptoms of axial spondyloarthritis (axSpA) include fatigue, spinal pain, stiffness, and sleep problems, which can impair health-related quality of life. Ixekizumab (IXE) treatment shows efficacy in active non-radiographic axSpA (nr-axSpA).[1]

Objectives: To assess fatigue, spinal pain, stiffness, and sleep with IXE treatment versus (vs) placebo (PBO) in patients (pts) with active nr-axSpA up to 16 and 52 weeks (wks).

Methods: In COAST-X, pts with active nr-axSpA were randomized to 52 wks of double-blind IXE 80 mg once every 4 wks (Q4W) or 2 wks (Q2W), or PBO. Data were collected from baseline to Wk 52.

Results: At Wk 16, IXE Q4W significantly improved fatigue, spinal pain, and stiffness, and IXE Q2W improved spinal pain, spinal pain at night, and stiffness vs PBO (Table). At Wk 52, IXE Q4W significantly improved stiffness, and IXE Q2W improved spinal pain, spinal pain at night, and stiffness vs PBO. Numeric improvements in sleep were not significant vs PBO. Wk 1, and up to Wk 16, IXE Q4W and Q2W significantly reduced spinal pain and stiffness vs PBO; stiffness was significantly reduced vs PBO up to Wk 52 (Figure).

Least squares mean (standard error) change from BL-ITT population (mixed-effect model of repeated measures)

Measure	Timepoint	PBO N=105	IXE Q4W N=96	IXE Q2W N=102
Spinal pain[a]	Wk 16	-1.45 (0.244)	-2.35 (0.248)*	-2.59 (0.244)†
	Wk 52	-2.29 (0.350)	-2.92 (0.305)	-3.32 (0.304)*
Spinal pain at night[a]	Wk 16	-1.71 (0.262)	-2.43 (0.267)	-2.79 (0.263)*
	Wk 52	-2.25 (0.358)	-3.04 (0.312)	-3.58 (0.311)*
BASDAI-stiffness[b,c]	Wk 16	-1.44 (0.242)	-2.44 (0.246)*	-2.89 (0.242)†
	Wk 52	-1.94 (0.332)	-3.15 (0.290)*	-3.48 (0.289)†
Fatigue severity NRS[d]	Wk 16	-1.4 (0.24)	-2.1 (0.24)*	-1.9 (0.24)
	Wk 52	-2.1 (0.38)	-2.6 (0.32)	-2.7 (0.32)
Sleep disturbance[e]	Wk 16	-2.3 (0.45)	-2.0 (0.45)	-2.5 (0.45)
	Wk 52	-2.9 (0.63)	-3.6 (0.52)	-3.6 (0.53)
Pt Global Assessment of Disease Activity[f]	Wk 16	-1.30 (0.246)	-2.32 (0.251)*	-2.64 (0.247)†
	Wk 52	-1.81 (0.378)	-2.77 (0.320)	-3.30 (0.321)*

*P<.05 vs PBO; †P≤.001 vs PBO. ITT population: all randomized pts. Pts needing rescue treatment after Wk 16 per investigator could switch to open-label IXE Q2W; observations at visits thereafter not included in analyses. BL values similar across treatments. Numerical improvements in BASDAI-fatigue not significant vs PBO.

[a]Scored 0 (no pain) to 10 (most severe pain) on NRS

[b]Mean score BASDAI questions 5 (intensity) and 6 (duration)

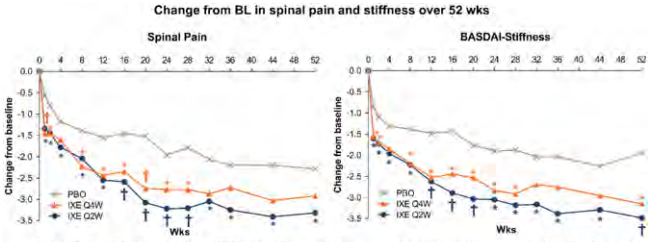
[c]Scored 1–10 on NRS

[d]Scored 0 (no fatigue) to 10 (as bad as you can imagine)

[e]Jenkins Sleep Evaluation Questionnaire scored 0 to 20: each of 4 items scored 0 (0 days) to 5 (22–30 days)

[f]Scored 0 (not active) to 10 (very active) on NRS

BASDAI=Bath Ankylosing Spondylitis Disease Activity Index *BL*=baseline *ITT*=intent-to-treat *IXE*=ixekizumab *N*=number of pts in ITT population *NRS*= numeric rating scale *PBO*=placebo *pt*=patient *Q2W*=every 2 wks *Q4W*=every 4 wks *vs*=versus *wk*=week



*P<.05 vs PBO; †P≤.001 vs PBO. Significant differences between placebo and IXE Q4W and IXE Q2W are shown by orange and blue symbols, respectively. Changes from BL (least squares mean) up to Wk 52 were analyzed using MMRM analysis in the ITT population, which includes all randomized pts. *BASDAI*=Bath Ankylosing Spondylitis Disease Activity Index *BL*=baseline *ITT*=intent-to-treat *IXE*=ixekizumab *MMRM*=mixed-effects model of repeated measures *PBO*=placebo *pt*=patient *Q2W*=every 2 weeks *Q4W*=every 4 weeks *vs*=versus *wk*=week

Conclusion: IXE Q4W and/or Q2W significantly improved spinal pain, spinal pain at night, and stiffness vs PBO at 16 and 52 wks in pts with nr-axSpA. IXE Q4W also improved fatigue at 16 wks in these pts. Numerical improvements in sleep were not significant vs PBO.

References:

[1] Deodhar A, et al. Lancet. 2019

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FRI0287 BIOLOGIC DRUG RESPONSE DOES NOT APPEAR RELATED TO RADIOGRAPHIC STATUS IN AXIAL SPONDYLOARTHRITIS: DATA FROM THE BSRBR-AS REGISTRY

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Background: The concept of axial spondyloarthritis (axSpA) incorporates the full range of inflammatory spinal disease. In the absence of specific immuno-genetic biomarkers, classification criteria differentiate two groups (non-radiographic [nr-axSpA] and radiographic axSpA [r-axSpA]) based on the presence of structural damage of the sacroiliac joints. Controversy remains as to whether nr-axSpA represents a milder form with biologic DMARD (bDMARD) treatment restrictions still in place in many countries.

Table 1. Baseline characteristics of nr-axSpA and r-axSpA patients starting biologics.

Variables	Level	nr-axSpA n=418	r-axSpA n=727	p-value
Age, mean (SD), years		39.7 (12.4)	46.1 (13.4)	<0.001
Sex, n (%)	Male	239 (57%)	529 (73%)	<0.001
Symptom duration, mean (SD), years		11.2 (10.9)	16.7 (12.9)	<0.001
Diagnostic delay, median (IQR), years		3.0 (1.0, 10.0)	3.0 (0.0, 11.0)	0.83
HLA-B27 (missing=325)		227 (73%)	387 (76%)	0.40
Inflammatory back pain, n (%)		384 (92%)	619 (92%)	0.95
Uveitis, n (%)		92 (22%)	205 (30%)	0.003
Crohn's / Colitis, n (%)		55 (13%)	113 (17%)	0.11
Psoriasis, n (%)		79 (19%)	115 (17%)	0.43
Smoking status, n (%)	Never smoked	148 (43%)	218 (38%)	0.040
	Ex-smoker	95 (28%)	207 (36%)	
	Current smoker	100 (29%)	154 (27%)	
NSAID use, n (%)		311 (75%)	560 (77%)	0.43
CRP, median (IQR), mg/dL		0.5 (0.1, 1.3)	0.9 (0.3, 2.5)	<0.001
BMI, mean (SD)		27.5 (5.6)	28.2 (5.8)	0.10
BASDAI, median (IQR)		6.7 (5.4, 7.8)	6.5 (5.0, 7.7)	0.12
BASFI, median (IQR)		5.9 (4.2, 7.8)	6.5 (4.4, 8.3)	0.043
VAS-G, mean (SD)		7.0 (2.0)	6.8 (2.0)	0.056
ASDAS-CRP, mean (SD)		2.8 (0.8)	2.8 (0.9)	0.32
ASQOL, median (IQR)		13.0 (9.0, 16.0)	13.0 (9.0, 15.5)	0.29
Biologic (to start), n (%)	Adalimumab	238 (57%)	436 (60%)	0.20
	Etanercept	131 (31%)	220 (30%)	
	Certolizumab	35 (8%)	47 (6%)	
	Golimumab	5 (1%)	12 (2%)	
	Secukinumab	7 (2%)	10 (1%)	
	Infliximab	2 (<1%)	2 (<1%)	

Objectives: To describe the baseline characteristics and bDMARD response at one year in axSpA patients in the British Society for Rheumatology Biologics Register in Ankylosing Spondylitis (BSRBR-AS) according to radiographic status.

Methods: BSRBR-AS is a national prospective cohort including participants who fulfil the ASAS classification criteria for axSpA. In this analysis, cross-sectional baseline data of patients starting bDMARDs including clinical, demographic and patient-reported outcomes (PROs) were compared. Follow-up data at one year was identified if 12±4 months from baseline and PROs completed within 2 months of visit date. Ankylosing Spondylitis Disease Activity Scores (ASDAS) for low disease status, clinically important improvement (CII) and major improvement (MI) were used to assess treatment response.

Results: Baseline characteristics were available for 1,145 patients. Those with r-axSpA were more likely to be male, were older, and had longer disease duration (Table 1). Follow-up ASDAS was available in 290 patients. Two thirds of the patients achieved ASDAS low disease state at one year regardless of radiographic status (nr-axSpA: 64.2% vs r-axSpA: 66.1, Diff: -1.9%, 95% CI -13.7 to 9.8). Further, no significant differences were seen between the groups in attaining ASDAS CII (nr-axSpA: 50.7% vs r-axSpA: 44.7%, Diff: 6.0%, 95% CI -7.8 to 19.8%) or MI (nr-axSpA: 20% vs r-axSpA: 18.7%, Diff: 1.3%, 95% CI -9.7 to 12.3%).

Conclusion: Although there appeared to be some differences in the baseline characteristics when exploring this cohort, according to radiographic status, which are likely related to the natural history of the disease; the level of biologic response was comparable between the groups supporting the concept of axSpA as a single disease entity.

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FRI0288 TREATMENT PATTERNS AND PHARMACOUTILIZATION AMONG PATIENTS AFFECTED BY ANKYLOSING SPONDYLITIS: AN ITALIAN REAL-WORLD STUDY

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Background: Ankylosing spondylitis (AS) is a chronic rheumatologic condition requiring lifelong treatments. To date, few real-world studies on AS patients in Italy are reported.

Objectives: Aims of the study were to evaluate treatment patterns and to analyse pharmacoutilization on patients affected by AS in a real-world setting of Italian clinical practice.

Methods: This observational study was based on administrative databases of a pool of Italian settings. A retrospective cross-sectional analysis was performed for years 2015-2017 to evaluate AS-diagnosed patients and, among them, to estimate percentage of treated and untreated ones. Patients were included if having a hospitalization discharge diagnosis at any level of AS (ICD-9-CM: 720.0) or exemption code for AS (054.720.0). Index date (ID) was date in which patients met one of the inclusion criteria. Patients with a prescription for drugs indicated for AS [non-steroidal anti-inflammatory drugs, disease-modifying antirheumatic drugs (DMARDs) - targeted synthetic (tsDMARDs) and biological (bDMARDs)] at ID were defined "treated". Patients without such drug prescriptions at ID were considered "untreated". To analyse treatment patterns of b/tsDMARDs-treated patients a longitudinal cohort study was conducted considering as inclusion periods the year 2014 and a period from 01/07/2016 to 30/06/2017. ID was date of first b/tsDMARDs prescription during inclusion period. Follow-up (F-up) lasted one year after ID. The interruption of treatment was defined as the absence of prescriptions in the last 3 months of F-up.

Results: For cross-sectional-cohort: AS-diagnosed patients were 4,824 in 2015, 5,357 in 2016, 5,894 in 2017. In all years analysed, about 50% of patients were male. Mean age±SD ranged from 51.5±13.7 (2015) to 52.4±14.0 (2017). Untreated patients were 33.6% (2015), 35.1% (2016) and 37.9% (2017), while patients in therapy with b/tsDMARDs were 22.7% (2015), 22.3% (2016) and22.2% (2017). The remaining percentage of patients were treated with csDMARDs/NSAIDS: 43.7% (2015), 42.6% (2016), 39.9% (2017)). In 2015 and 2016 all b/tsDMARDs-treated patients were in therapy with anti-TFN agents, while the advent of IL-inhibitors was observed starting from 2017 (8.2% b/tsDMARDs-treated patients with IL-inhibitors). For longitudinal-cohort: in 2014, 310 patients had a b/tsDMARDs prescription and during 1-year F-up 11.9% of them interrupted the treatment after a mean time ±SD of 83.3±66.9 days. Of the 183 patients who had a prescription of b/tsDMARDs at ID during 2016-2017, 22.4% had a treatment interruption after a mean time±SD of 134.4±86.1 days during F-up.

Conclusion: This real-world study provided insights on AS treatment patterns. Preliminary results showed that approximately one third of AS patients are untreated and about one in five are treated with b/tsDMARDs. Despite the improvement in treatment duration observed from 2014 to 2016/17, still 22.4% of b/tsDMARDs-treated patients interrupted therapy in the most recent cohort. A larger sample size is needed to confirm results.

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FRI0289 DOES SMOKING AFFECT SECUKINUMAB TREATMENT OUTCOMES AND SAFETY IN PATIENTS WITH ANKYLOSING SPONDYLITIS? – REAL WORLD DATA FROM THE GERMAN AQUILA STUDY

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Background: There is growing body of evidence that smoking is associated with more active and severe disease in patients (pts) with ankylosing spondylitis (AS).[1,2] The German non-interventional study AQUILA provides real-world data on the influence of smoking on therapeutic effectiveness and safety under secukinumab (SEC), a fully human monoclonal antibody that selectively inhibits interleukin-17A.

Objectives: The aim of this interim analysis is to describe selected baseline (BL) demographics, to evaluate SEC effectiveness on disease activity and global functioning and health, and to report safety profile depending on smoking status of AS pts.

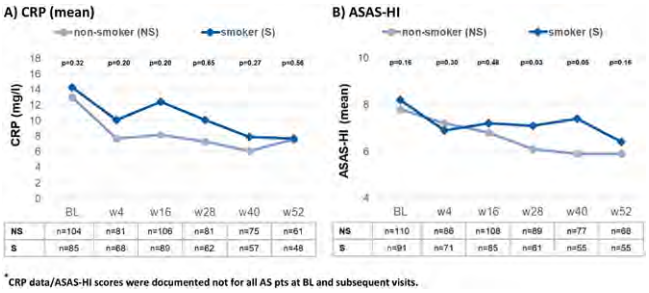
Methods: AQUILA is an ongoing, multi-center, non-interventional study including up to 2700 pts with active AS or psoriatic arthritis. Pts were observed from BL up to week (w) 52. Real-world data was assessed prospectively and analyzed as observed. Assessment of CRP and validated questionnaires were used to collect data on disease activity (Bath Ankylosing Spondylitis Disease Activity Index, BASDAI), global functioning and health (Assessment of SpondyloArthritis-Health Index, ASAS-HI) and depressive mood (Beck´s Depression Inventory version II, BDI-II). For calculation of proportion of pts who experienced (serious) adverse events ((S)AEs), all AS pts were included who received at least one dose of SEC irrespective of further documentation of any study visit. This analysis focuses on the subgroups non-smoker (NS) and smoker (S).

Results: At BL, 311 AS pts were included: 42.1% (n=131) NS and 32.8% (n=102) S. Remaining subgroups were 15.1% (n=47) ex-smoker and 10.0% (n=31) of unknown smoking status. About half of AS pts in NS were male, while in S (69.6%) portion of men was more than twice as high as of women. S were slightly younger than NS (mean age: 43.9/49.0 years). During the study, CRP value decreased irrespective of smoking status with numerically higher fluctuations in S (Fig. 1A). BASDAI (NS: 5.2 at BL to 3.7 at w52, S: 5.6 at BL to 4.1 at w52) and ASAS-HI (Fig. 1B) scores numerically improved best in NS, whereas more variations were seen in S; the same was observed for BDI-II score values (NS: 11.8 at BL to 9.2 at w52, S: 13.0 at BL to 12.1 at w52). Although no major significant differences in mean values existed between NS and S, S displayed – except in w4 – overall higher mean values in the parameters mentioned above. Regarding the occurrence of AEs/SAEs with or without suspected relationship to SEC, there was no significant difference between NS and S (Table 1).

Table 1. Overview of AEs (and SAEs) under SEC treatment depending on smoking status in AS pts

Number of pts with	NS (N=140), n (%)	S (N=110), n (%)	P value
AE	95 (67.9)	78 (70.9)	0.80
AE with suspected relationship to SEC	66 (47.1)	41 (37.3)	0.29
SAE	39 (27.9)	30 (27.3)	0.95
SAE with suspected relationship to SEC	15 (10.7)	10 (9.1)	0.87

Conclusion: In a real-world setting, SEC improved disease activity and global functioning and health in AS pts with slight (mostly non-significant) differences between NS and S. Overall, this interim analysis shows that SEC is an effective treatment with a favorable safety profile up to 52 weeks, irrespective of the pts' smoking status. Further progress of the AQUILA study will reveal whether this trend will continue.



*CRP data/ASAS-HI scores were documented not for all AS pts at BL and subsequent visits.

Figure 1. CRP and global functioning and health in AS pts treated with SEC depending on smoking status* *CRP data/ASAS-HI scores were documented not for all AS pts at BL and subsequent visits.

References:

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FRI0290 FACTORS ASSOCIATED WITH PERSISTENCE OF GOLIMUMAB TREATMENT IN THE BIOBADASER REGISTRY, UP TO 7 YEARS OF FOLLOW-UP

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Background: Persistence in treatment with a biological drug can be considered an indirect measure of efficacy,safety and tolerability

Objectives: We assessed the probability of persistence of golimumab treatment in patients with rheumatic diseases and the factors associated with persistence up to 7 years of follow-up

Methods: BIOBADASER is the Spanish registry of biological drugs of the Spanish Society of Rheumatology and the Spanish Medicines Agency.A data-base analysis was done in Dec 2019 on all the patients aged 18 years or older who had initiated golimumab for rheumatoid arthritis (RA),psoriatic arthritis (PsA) and axial spondyloarthritis (SpA).The probability of persistence was calculated with a Kaplan-Meier test.Factors related to persistence were analyzed with a Cox-regression model

Results: There were 685 patients included (195 [28.5%] RA, 294 [42.9%] axial SpA and 196 [28.6%] PsA) in the analysis (Mean age 51.3 [12.6] years, 53.7% women). Median duration of disease at the onset of golimumab therapy was 7.6 (3.0-14.5) years. Golimumab was prescribed as first biological drug in 36.4%, as second in 31.7% and as third or further in 31.9% of the patients. Concomitant medication at golimumab initiation included methotrexate (40.0%), corticosteroids (34.2%), leflunomide (17.8%) and sulphasalazine (8.1%). The probability of persistence with golimumab treatment was 71.7% (95% CI 68.1–74.9) at year 1,60.5% (56.5–64.2) at year 2, 55.6% (51.5–59.5) at year 3, 50.6% (46.2–54.8) at year 4, 45.1% (40.1–50.0) at year 5, 44.2% (39.0–49.3) at year 6 and 39.5% (32.8–46.2) at year 7. As the first biological agent the probability of persistence was 83.2% at year 1 and 60.0% at year 5. As a second biological drug persistence was 70.4% and 39.9% (year 1 and 7). Cox-regression analysis (table) showed that the probability of persistence with golimumab treatment was higher in first vs second or third biological line (Hazard Ratio[HR] for discontinuation: 1.45 for second and 3.04 for third or further vs first line), in SpA and PsA patients (HR discontinuation vs RA:0.56 and 0.49 respectively) and in patients with methotrexate (HR:0.61) and lower in those needing corticosteroids(HR:1.71) or DMARDs different to methotrexate (HR:1.88) and in patients with higher disease activity at golimumab onset (HR:1.45)

Conclusion: The probability of persistence on golimumab therapy was high and remained relatively stable up to 7 years of follow-up. A lower risk of treatment

discontinuation was observed in patients who received golimumab as first biological agent and in PsA and SpA patients. Persistence was lower in patients needing corticosteroids, DMARDs different to methotrexate and in those with higher disease activity at golimumab onset

Cox-regression analysis.HR for discontinuation of golimumab

	HR	95% CI	p
Age at golimumab initiation	1.01	(0.99-1.02)	0.480
Gender (women vs men)	1.15	(0.69-1.90)	0.595
Smoking habit (smoker vs non-smoker)	1.46	(0.90-2.37)	0.128
Smoking habit (past smoker vs non-smoker)	0.94	(0.48-1.84)	0.859
Overweight (vs normal)	1.10	(0.63-1.93)	0.728
Obesity (vs normal)	0.90	(0.51-1.59)	0.708
SpA vs RA	0.56	(0.31-1.00)	0.050
PsA vs RA	0.49	(0.28-0.87)	0.015
Second vs first biological drug	1.45	(0.85-2.46)	0.171
Third or further vs first biological drug	3.04	(1.86-4.98)	0.001
MTX	0.61	(0.38-0.97)	0.037
Other DMARD	1.88	(0.90-3.93)	0.091
Corticosteroids	1.71	(1.04-2.83)	0.036
Activity higher than median	1.45	(0.96-2.19)	0.078

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FRI0291 SAFETY AND SURVIVAL OF SECUKINUMAB IN SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS: REAL-LIFE DATA. A MULTICENTER STUDY

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Background: Secukinumab is a human monoclonal antibody directed against IL-17A, approved for the treatment of psoriatic arthritis (PsA) and ankylosing spondylitis (AS). The safety profile of secukinumab was favourable in clinical studies, but there is still scarce evidence in clinical practice. Similarly, we currently have less data regarding the real survival of secukinumab compared to other biological therapies such as anti-TNF.

Objectives: To analyze the retention rate and safety of secukinumab as well as the causes and factors associated with its survival in patients with ankylosing spondylitis and psoriatic arthritis in real clinical practice.

Methods: we conducted a retrospective longitudinal observational multicenter study of all patients with PsA and Spondyloarthritis (SpA) who had received at least one dose of secukinumab. Adverse events and drug retention were considered the main variables. In addition, we collected variables predicting drug retention. We estimated the total adverse event rate, by severity and type of event, and drug retention (mean duration and retention at 6 months, 1 year and 2 years), all with 95% confidence intervals (95% CI). Survival was analyzed using Kaplan-Meier curves and predictive factors using Cox regression, with the Hazard Ratio (HR) as a measure of the association.

Results: 154 patients were included, 59 with PsA (38%) and 95 with SpA (62%), with a mean age of disease onset of 49 years (SD ± 11), being 55% men. The mean disease duration was 6.5 years (ICR 2-8). The median number of previous biologics was 2 (SD ± 1). Secukinumab was the first line of treatment in 13 patients (8%), the second line in 46 (30%), the third line in 54 (35%) and subsequent lines in 41 (27%). The median survival of secukinumab was 23 months (ICR 5-32), with a 1-year retention rate of 66% and a 2-year retention rate of 43%. The most frequent cause of discontinuation was inefficacy (59%) and the second one was adverse events (AE) (36%). Most patients who discontinued due to AEs (71%) did so during the first 6 months of treatment. Only 2 major cardiovascular events were collected, and 2 cases of Crohn's disease occurred during the exposure. The factors identified as predictors of survival for secukinumab were: duration of disease (HR 0.96, 95% CI 0.93-0.99 p=0.012), number of previous biologics (HR 1.18, 95% CI 1.04-1.34 p=0.011), male gender (HR 0.63, 95% CI 0.43-0.90 p=0.013), obesity (HR 0.31, 95% CI 0.18-0.54 p=0.000) and depression (HR 2.54, 95% CI 1.64-3.94 p=0.000).

Conclusion: In this study of real clinical practice, secukinumab showed a 66% retention rate at one year in a population mostly refractory to biological therapy. The main cause of discontinuation was lack of efficacy. The AAs that led to drug discontinuation occurred mainly in the first 6 months of treatment

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FRI0292 TREATMENT RESPONSE TO BIOLOGICAL DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS IS ASSOCIATED WITH FAVORABLE CHANGES OF THE BODY COMPOSITION IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: There is few data available regarding differences in body composition and its possible changes in patients with ankylosing spondylitis (AS) treated with biological disease-modifying anti-rheumatic drugs (bDMARDs). An increase of body weight and lean mass in patients receiving TNF inhibitors, as well as a possible muscle wasting by high disease activity have been previously described. Bioelectrical impedance analysis (BIA) is a valid method to assess body composition and allows to distinguish between fat, fat-free mass and skeletal muscle mass.

Objectives: To evaluate changes in body composition in patients with AS after 6 months of treatment with bDMARDs.

Methods: Patients with a diagnosis of AS, fulfilling the modified New York criteria and starting a bDMARD therapy were included in the extension of the prospective German Spondyloarthritis Inception Cohort (GESPIC). All patients had high disease activity (BASDAI >=4 and/or ASDAS >=2.1) despite previous treatment with nonsteroidal anti-inflammatory drugs. Disease activity and body composition were assessed at baseline and after 6 months of bDMARD treatment. Body composition was assessed by the BIA with the seca© mBCA 515 device (SECA Deutschland GmbH, Hamburg/Germany) and included the following parameters: weight, body mass index (BMI), fat mass index (FMI), fat free mass index (FFMI), skeletal muscle mass value (SMM), and visceral adipose tissue value (VAT). Response to a bDMARD therapy was defined as achievement of clinically important improvement of ASDAS (>=1.1).

Results: A total of 129 patients (66.7% male) with AS were recruited in this cohort extension between 2015 and 2019. The mean (mean ± SD) age was 36.2 ± 10.3 years, and symptom duration was 10.7 ± 9.1 years. HLA-B27 test was positive in 89.1% patients. BIA was assessed in 77 patients; the baseline characteristics of these patients were similar to those of the whole cohort. Of these, 75 patients were treated with TNF inhibitors and 2 patients were treated with an IL-17A inhibitor.

After 6 months of a bDMARD treatment, body composition changed significantly with an increase of weight and BMI due to the gain of FMI but also of FFMI and SMM, while there was no increase of the visceral fat – table. In responders (improvement of ASDAS>=1.1 after 6 months) the results were similar to the whole group with a significantly gain (mean±SD) on BMI, FMI, FFMI and SMM ($0.3 \pm 1.4\,kg/m^2$, $0.3 \pm 1.0\,kg/m^2$, $0.2 \pm 0.5\,kg/m^2$, $0.5 \pm 1.2\,kg$, $p<0.05$, respectively). In non-responders, there were no significant changes on the body composition after 6 months of treatment.

Conclusion: Treatment with bDMARDs is associated with favorable changes of the body composition with increase of the muscle mass but not of the visceral fat. These changes were evident in treatment responders only.

TABLE 1. Body composition parameter at baseline and after 6 months of treatment with a bDMARDs in patients with AS (n=77)

	Mean±SD	Difference, mean±SD	95% CI		P*	
			Lower	Upper		
Weight at baseline, kg	77.19±15.71	0.75±3.80	0.04	1.47	0.04	Weight at 6 months, kg
77.94±16.25	BMI at baseline, kg/m^2					25.03±4.32
0.30±1.29	0.06	0.55	0.02	BMI at 6 months, kg/m^2	25.33±4.43	FMI at baseline, kg/m^2
				6.74±3.39	0.31±0.97	0.07
0.54	0.01	FMI at 6 months, kg/m^2	7.05±3.42	FFMI at baseline, kg/m^2		
		18.27±2.18	0.15±0.48	0.04	0.27	0.01
FFMI at 6 months, kg/m^2	18.42±2.27	SMM at baseline, kg				
27.40±5.85	0.32±1.11	0.05	0.59	0.02	SMM at 6 months, kg	27.73±5.90
					1.94±1.62	-0.12±0.63
VAT at baseline, liters						
-0.27	0.04	0.14	VAT at 6 months, liters	1.82±1.56		

BMI: Body Mass Index; FMI: Fat Mass Index; FFMI: Free Fat Mass Index; SMM: Skeletal Muscle mass; VAT: Visceral Adipose Tissue.
*Wilcoxon test

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FRI0293 EFFECTIVENESS OF SWITCHING BETWEEN TNF INHIBITORS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: IS THE REASON TO SWITCH RELEVANT?

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Background: It has been common practice to start a second TNF inhibitor (TNFi) in patients with axial spondyloarthritis (axSpA) who discontinue their first TNFi. It remains unclear if the reason for discontinuation of the first TNFi influences the response to the second.

Objectives: To assess if the reason of discontinuation of the first TNFi influences the response to the second TNFi.

Methods: Patients with axSpA from the ReumaPt registry, who discontinued their first TNFi and started a second TNFi and who had complete data on Ankylosing Spondylitis Disease Activity Score (ASDAS) and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) at baseline, 3 and 6 months for their first TNFi were included. Then, they were followed every 6 months up to 12 years. The main outcome was the ASDAS clinically important improvement (ASDAS CII). Secondary outcomes were ASDAS major important improvement (ASDAS MI); ASDAS low disease activity (ASDAS LDA); ASDAS inactive disease (ASDAS ID) and BASDAI 50. The reason for discontinuation of the first TNFi was defined as: i) Primary failure, ASDAS CII was not achieved at 3 or 6 months; ii) Secondary failure, ASDAS CII achieved at 3 or 6 months but lost in ≥1 follow-up visit; iii) Adverse events; iv) Other (e.g. pregnancy, surgery). The response to the first TNFi at 3 and 6 months was compared to the response to the second TNFi at the same visits, adjusting for age, gender and C-reactive protein (CRP). The association between the reason of discontinuation of the first TNFi and response the second TNFi over time was tested in generalized estimating equations (GEE) models, adjusted for age, gender and CRP.

Results: In total, 193 patients (53% male, mean age 45 (SD:11) years) were included, with a median follow-up time on the second TNFi of 1.5 years. Patients had a lower response to the second TNFi compared to the first TNFi according to the main outcome (ASDAS CII) at 3 months (41% vs 51%) and 6 months (35% vs 56%). There was an association between the reason to discontinue the first TNFi and response to the second TNFi as defined by the most stringent outcomes (ASDAS MI and ASDAS ID), but not for ASDAS CII (Table). Compared to patients who discontinued their first TNFi due to primary failure, patients were more likely to achieve ASDAS ID with the second TNFi when they discontinued their first TNFi due to secondary failure (OR: 7.3 [(95%CI: 1.9; 27.7]), adverse events (OR: 9.1 [2.5; 33.3]), or other reasons (OR: 7.7 [1.6; 37.9]).

Conclusion: In axSpA, response to the second TNFi is worse compared to the first TNFi. Patients with a secondary failure to the first TNFi have a better response to the second TNFi compared to those discontinuing the first TNFi due to primary failure, particularly for most stringent outcomes.

Table. Association between the reason for discontinuation of the first TNFi and response to the second TNFi

Reason to discontinue first TNFi*	Outcome for the second TNFi OR (95% CI)				
	ASDAS-CII (N=135)	ASDAS-MII (N=135)	ASDAS-LDA (N=166)	ASDAS-ID (N=166)	BASDAI50 (N=147)
(ref Primary failure)					
-Secondary failure	1.9 (0.7;4.8)	**4.8 (1.3;18.2)**	1.2 (0.6;2.4)	**7.3 (1.9;27.7)**	1.4 (0.6;3.0)
-Adverse events	1.5 (0.6;3.5)	2.4 (0.6;9.6)	0.9 (0.5;1.7)	**9.1 (2.5;33.3)**	1.1 (0.5;2.3)
-Other	1.0 (0.3;3.8)	1.7 (0.1;19.4)	1.0 (0.4;2.4)	**7.7 (1.6;37.9)**	0.5 (0.1;1.7)

*GEE models with the reason of discontinuation of the first TNFi as predictor (reference category: primary failure); all models adjusted for age, gender and C-reactive protein. OR in bold are statistically significant (p<0.05).

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FRI0294 MUSCULOSKELETAL MANIFESTATIONS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE TREATED WITH VEDOLIZUMAB

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Background: Musculoskeletal manifestations (MEM) are frequent extraintestinal symptoms in patients suffering from inflammatory bowel disease (IBD), affecting up to 40% of them. Tumor necrosis factor inhibitors (TNFi) are effective in both IBD and IBD-related spondylarthritis (SpA). Additionally, vedolizumab (VDZ), an α4β7 integrin inhibitor with selective action on intestinal tissue, has been recently proposed as 1st line treatment on TNFi refractory IBD. The effectiveness of VDZ in MEM has not been properly evaluated but even exacerbation of previously diagnosed SpA has been described.

Objectives: The main objective is to analyse the occurrence of articular exacerbations in patients with IBD-related SpA treated with VDZ. The secondary objective is to analyse the new-onset MEM in IBD patients treated with VDZ.

Methods: Descriptive study of a retrospective cohort of every adult with IBD (Crohn's disease -CD- and ulcerative colitis -UC-) patients starting treatment with VDZ in a tertiary hospital. All data were collected as a collaboration between the Rheumatology and Gastroenterology Departments, through revision of the clinical history and databases from both departments. In patients previously diagnosed of SpA exacerbation was assessed, defined as a clinical worsening causing a treatment modification. The patients with new-onset MEM were classified as: i) nonspecific arthralgia (NsA), not suggestive of SpA; and ii) SpA according to ASAS criteria. A statistical analysis was performed using frequency charts

Results: A total of 61 patients were included, 55.7% women and with an mean (SD) age of 50 (17) years. The proportion of UC and CD was similar (49% and 51%, respectively). Among the patients studied, 12 (19.7%) had a diagnosis of IBD-related SpA and 3 (25%) of them suffered articular exacerbation of SpA within 3,5 and 6 months of treatment. On the other hand, 9 (14.7%) patients showed new-onset MEM, 3 (33%) of them showed symptoms and clinical and/or radiological findings compatible with axial SpA. In 2 of the cases a treatment with a cDMARD was used and the other one required a combination therapy between iTNF and VDZ. The remaining 6 (67%) patients were classified as NsA and inflammatory arthritis was discarded. Table 1 shows the demographic and clinical characteristics of patients included in the analysis.

Table 1. Demographic, clinical characteristics and symptoms onset in patients included in the study.

	Total (n=61)	Diagnosed SpA (n=12		New-Onset MEM (n=9)	
		Stable (n=9)	Exacerbation (n=3	New-onset SpA (n=3)	NsA (n=6)
Age (years), mean ± SD	50 ± 17	55 ± 19	50 ± 7.5	38 ± 13	50 ± 14
Gener (female), n (%)	34 (55.7%)	6 (66.7%)	3 (100%)	1 (33.3%)	3 (50%)
BMI (Kg/m2), mean ± SD	24.7 ± 4.3	27.5 ± 5.5	28.3 ± 3.9	30.2 ± 0.5	24.3 ± 4.6
Smoking habit (smokers), n (%)	11 (18%)	1 (11.1%)	0 (0%)	2 (66.7%)	0 (0%)
CD diagnosis, n (%)	31 (50.8%)	2 (22.2%)	1 (33.3%)	3 (100%)	2 (33.3%)
UC diagnosis, n (%)	30 (49.2%)	7 (77.8%)	2 (66.7%)	0 (0%)	4 (66.7%)
IBD follow-up, (years) mean ± SD	11 ± 9.6	10.6 ± 10	2 (1-29) *	12 ± 6.8	9.8 ± 4.6
bDMARD naïve, n (%)	7 (11.5%)	2 (22.2%)	0 (0%)	0 (0%)	0 (0%)

*shown as median (range).

Conclusion: Switching TNFi treatment to VDZ in patients with IBD-related SpA was found to be associated with articular exacerbation of SpA in 1 out of 4 patients within the first 5 months. New-onset MEM is also observed in up to 15% of patients with IBD treated with VDZ. A multidisciplinary assessment of these patients is necessary in order to achieve a proper management of their diseases.

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FRI0295

ADALIMUMAB LEVELS ARE ASSOCIATED WITH DRUG RETENTION RATES IN AXIAL SPONDYLOARTHRITIS PATIENTS

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Background: Production of anti-drug antibodies (ADA) could cause low serum anti-TNF levels and low drug retention rates.

Objectives: To assess the relationship between serum adalimumab (ADL) levels and drug retention rates in patients with axial SpA.

Methods: Single-center prospective study in patients with axial SpA, according to ASAS criteria, being treated with ADL. In the first part of the study, from December 2010 to June 2016, data was collected and serum samples were taken. In a second part of the study, clinical records were reviewed to find out the dates and reasons of treatment discontinuation. Information was collected on age gender, body mass index (BMI), date of diagnosis of SpA, laboratory data, including HLAB27, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), prior biological treatment for SpA, concomitant conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs). SpA disease activity was assessed by BASDAI, ASDAS and PGA scores. A serum sample was taken from all patients just before the next adalimumab dose. ADL and ADA levels were analysed with ELISA Promonitor®, (Proteomika, Progénica, Griffols) and correlated with SpA activity using BASDAI and ASDAS scores. Cox proportional hazards model was performed in order to assess the relation of variables with drug interruption.

Results: Up to January 2016, 51 consecutive patients were included. The mean (range) age was 46,9 (18–68) and 47.1% were women. HLAB27 was positive in 82,4% of patients. Mean disease duration was 122,9 months (2-408) and mean duration of treatment with adalimumab was 17,8 months (1-69). ADL was the first biological agent received in 36 patients (70.6%). Eleven patients (21.6%) were on concomitant treatment with receiving concomitant csDMARDs, mainly methotrexate (MTX) (15.7%) and sulfasalazine (5.9%). The mean (SD) activity scores were BASDAI 4,0 ± 2,3; ASDAS-PCR 2,1 ± 1,1 and ASDAS-VSG 2,1 ± 1,0.

ADA prevalence was 27.5%, with none detected in the 21.6% taking csDMARDs (p = 0.021). ADL level was normal (> 3 mg/l) in 36 patients (70.6%), all without ADA. Fifteen patients (29.4%) had subtherapeutic ADL levels (< 3 mg/l), with ADA in 14 (93%).

Total ADL treatment time was 241,16 patient/years, and mean ADL treatment time was 4,73 years. Cox model results were resumed in table 1. Multivariate study show that ADL level > 3 mg/L was a protective factor for ADL interruption (HR 0.01 (0.00-0.59, p=0.026), while previous etanercept treatment was a risk factor for ADL interruption 9.54 (1.23-74.08, p=0.031).

Table 1. Cox model.

		Continue	Discon= tinue	Univariate HR	Multivariate HR
ADL level	<3 mg/L	13 (86,7%)	2 (13,3%)	0.05 (0.00-0.65,	0.01 (0.00-0.59,
	≥3 mg/L	28 (77,8%)	8 (22,2%)	p=0.022)	p=0.026)
Concomitant DMARD	Yes	8 (72,7%)	3 (27,3%)	0.56 (0.14-2.26,	0.28 (0.05-1.65,
	No	33 (82,5%)	7 (17,5%)	p=0.419)	p=0.159)
BMI	Normal	13 (86,7%)	2 (13,3%)	2.56 (0.54-12.23,	0.48 (0.02-9.75,
	Overweight/ obese	27 (77,1%)	8 (22,9%)	p=0.239)	p=0.634)
Age	Mean (SD)	46,4 (12,2)	48,7 (11,6)	0.93 (0.24-3.60, p=0.912)	0.60 (0.10-3.84, p=0.594)
Gender	Men	19 (70,4%)	8 (29,6%)	0.43 (0.09-2.03,	0.58 (0.03-
	Women	22 (91,7%)	2 (8,3%)	p=0.283)	10.06, p=0.705)
Infliximab previous	Yes	4 (40,0%)	6 (60,0%)	3.31 (0.92-11.87,	1.37 (0.23-8.24,
	No	37(90,2%)	4 (9,8%)	p=0.066)	p=0.731)
Etanercept previous	Yes	2 (22,2%)	7 (77,7%)	8.17 (2.09-31.90,	9.54 (1.23-74.08,
	No	39 (92,9%)	3 (7,1%)	p=0.003)	p=0.031)

ADL: adalimumab; BMI: body mass index; DMARD: disease modifying antirheumatic drug; SD: standard deviation.

Conclusion: Adalimumab drug levels > 3 mg/L is a protective factor against treatment interruption.
Etanercept previous treatment was a risk factor for treatment interruption.

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FRI0296 AN ALTERNATIVE APPROACH TO SPONDYLOARTHRITIS TREATMENT: PAMIDRONATE CASE SERIES

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Background: Spondyloarthritis (SpA) is a common group of chronic inflammatory diseases with substantial morbidity seen in rheumatology clinics. Its standardized treatment includes non-steroidal anti-inflammatory drugs (NSAIDs), TNF-alpha inhibitors and IL-17 inhibitors. However, some patients remain refractory to conventional treatments and these treatments are contraindicated in malignancies and infections, which indicates the need for new therapeutic approaches. Pamidronate, a bisphosphonate with antiosteoclastic action, has been found useful in a few studies (1-2).
Objectives: The aim is to evaluate the effectiveness and safety of pamidronate treatment in SpA in a single tertiary center.
Methods: SpA patients who were treated with pamidronate due to lack of response to standard treatment or in patients where standard treatment is contraindicated in 2014-2019 are evaluated retrospectively. Patients' files were evaluated for the indications, efficacy and the side effects of pamidronate as well as for the clinical and demographic features. Pamidronate intravenous dose was 90 mg/month.

Patient ID#	Age	Sex	Comorbidities	Previous treatments	Duration of pamidronate treatment(mo)	PGAS before treatment	PGAS after treatment
1	48	M	OP, FMF	NSAID, IFX, ETN	6	9	1
2	66	F	OP, Rectum cancer	NSAID, SSZ	28	10	4
3	36	M	Gastric cancer	NSAID, SSZ, IFX	10	10	10
4	57	M	CAD, IBD	NSAID,SSZ,MTX, ADA, CZP	2	5	4
5	50	M	none	NSAID, IFX	6	9	2
6	69	M	DM,HT,CMD, PsO	NSAID, SSZ	37	9	1
7	62	M	Bladder cancer	NSAID	4	9	4
8	40	M	none	NSAID,GOL,ETN	2	6	6
9	46	M	none	NSAID,SSZ, MTX, ADA, CZP, IFX, ETN, ADA, GOL	8	5	2
10	40	M	none	NSAID,SSZ, ADA, GOL, CZP, ETN, IFX	3	8	6
11	58	F	SLE	NSAID, HCQ, MTX	3	8	7

Table. F: female M: male OP: osteopenia, FMF: familial Mediterranean fever, CAD: coronary artery disease, IBD: inflammatory bowel disease, DM: diabetes mellitus, HT: hypertension, CMD: chronic myeloproliferative disorder, PsO: psoriasis, SLE: systemic lupus erythematosus IFX: infliximab, ETN: etanercept, SSZ: sulfasalazine, NSAID: non-steroidal anti-inflammatory drug, MTX: methotrexate, ADA: adalimumab, CZP: sertolizumab, GOL: golimumab, HCQ: hydroxychloroquine, PGAS: Patient Global Assessment Score

Results: There were 11 patients (9 male and 2 female). 4 patients were diagnosed as non-radiographic SpA. The mean disease duration was 29±12 years (range 12-49). The comorbidities of the patients included diabetes mellitus and hypertension in 1 patient, coronary artery disease in 1 patient, psoriasis in 1 patient, inflammatory bowel disease in 1 patient, Familial Mediterranean fever in 1 patient, systemic lupus erythematosus in 1 patient, and osteopenia in 2 patients. 3 of the patients had malignancies (bladder, rectum and stomach carcinomas) and 1 patient had chronic myeloproliferative disorder. 4 patients could never use the TNF-alpha inhibitors (1 rectum cancer, 1 bladder cancer, 1 systemic lupus erythematosus, 1 essential thrombocytemia). The median duration of pamidronate use was 6 (interquartile range 3-10). Mean Patient Global Assessment Score (PGAS) was 8±2 before the pamidronate treatment and 4±3 after the treatment ($p<0.001$). The treatment of 6 patients was terminated due to inadequate response which is shown in Table. One patient died from bladder carcinoma during follow-up.
Conclusion: In SpA patients, with biological agents (anti-TNF, IL-17) being contraindicated due to malignancies and tuberculosis in some patients, alternative treatment methods such as pamidronate should be considered bearing in mind the results of our study showing the effectiveness and safety of it.
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FRI0297 COMPARISON OF EFFICACY OF SECUKINUMAB VS ANTI-TNF AS SECOND LINE BIOLOGIC THERAPY IN AXIAL SPONDYLOARTHROPATHY BASED ON BASDAI RESPONSE IN AN OBSERVATIONAL STUDY

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Background: Modern biologic therapies have demonstrated encouraging results in the treatment of axial spondylarthropathy (AxSpA). The benefits of interleukin-17 inhibitors (IL-17i), as first and second line therapies, are well established [1, 2]. A systematic literature review by Navarro-Compán has shown some benefit of second line therapies using both anti-tumour necrosis factor (anti-TNF) and IL-17i [3]. To our knowledge, there are currently no studies that have directly compared which pathway has a better overall outcome. This is therefore the first observational study directly comparing both treatment arms after anti-TNF had been administered as first line therapy.
Objectives: To investigate which second line therapy is superior, anti TNF or IL-17i (secukinumab), in patients with AxSpA, that have failed first line anti-TNF therapy.
Methods: Patient data was extracted from the Whipps Cross Hospital Rheumatology biologics registry database. All patients selected were required to have a diagnosis of AxSpA on magnetic resonance imaging (MRI). The patient cohort that was selected had previously been treated with anti-TNF as a first line therapy and were being considered for second line therapy with either anti-TNF or IL-17i. Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) scores were recorded at 3, 6 and 12 months to assess treatment response. The unpaired t-test was used to assess the significance between the treatment groups and were analysed using the R statistical package.
Results: Seventy patients were identified for this study of which, 57% (46/70) were male and 37% (26/70) were female. The age ranged from 30-97 years, with an average age of 72. The HLA-B27 gene association in this cohort was 71% (50/70). Three patients out of the cohort had psoriatic spondylarthropathy and the remaining had isolated AxSpA. There were an equal number of secukinumab and anti-TNF patients. The anti-TNF patients were subdivided into their respective anti-TNF drug (listed in Table 1).

Table 1. Frequency of individual anti-TNF drugs used in this cohort.

Anti-TNF drug	Frequency used
Adalimumab	9/35
Certolizumab	8/35
Etanercept	17/35
Golimumab	1/35

This study revealed that the patients experienced an average of a 52% reduction in the BASDAI score after 6 months of anti-TNF treatment compared to only a 6% reduction in patients on secukinumab (P 0.009). However, the disease activity improvement at 12 months was not sustained in the anti-TNF group and at this stage there was no difference between the groups. Overall both treatment groups

showed an average reduction in the BASDAI score by more than 30% at each 3 monthly interval.

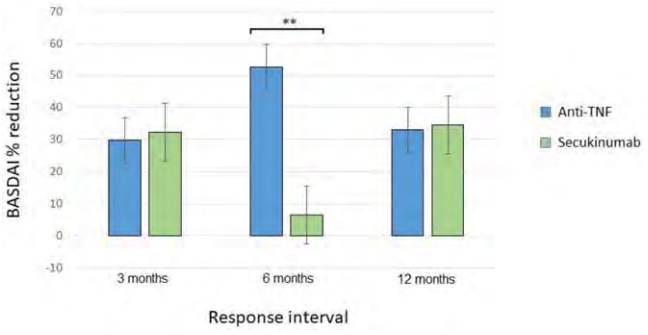


Figure 1. BASDAI percentage reduction at 3 monthly intervals between the two second line treatment groups using anti-TNF and Secukinumab.

Conclusion: A significant difference could not be demonstrated between the anti-TNF and secukinumab groups in this observational cohort. Interestingly, at 6 months, anti-TNF demonstrated better outcomes according to BASDAI scores than Secukinumab but this efficacy was lost at 12 months. It was difficult to interpret these isolated results without further testing, as this is a small non-randomised study. We observed similar outcomes to the Navarro-Compán review where there was a low percentage change in the BASDAI improvement in patients on second line therapy when compared to first line treatment BASDAI scores. Therefore, exploring the mechanism for the reduction in the BASDAI response would be an interesting future study. Moreover, to fully understand these results, randomised controlled studies would need to be conducted.

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FRIDAY, 05 JUNE 2020

Spondyloarthritis - clinical aspects (other than treatment)

FRI0298 ASAS MODIFICATION OF THE BERLIN ALGORITHM AND THE DUET ALGORITHM FOR DIAGNOSING AXIAL SPONDYLOARTHRITIS: RESULTS FROM THE SCREENING IN AXIAL SPONDYLOARTHRITIS FOR PSORIASIS, IRITIS, AND COLITIS COHORT

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Background: Patients presenting with back pain and psoriasis, iritis, or colitis, represent a high-risk population for the presence of axial spondyloarthritis (axSpA). The Dublin Evaluation Tool (DUET)[1], the Berlin algorithm[2], and the ASAS modification of this algorithm[3] are recommended referral strategies aimed at early diagnosis of axSpA. DUET was developed for patients presenting with AAU. Validation of these algorithms in inception cohorts is limited.

Objectives: 1. To assess the performance of referral algorithms for diagnosis of axSpA when tested against the final local rheumatologist diagnosis in an inception cohort of patients presenting with undiagnosed back pain and extra-articular manifestations. 2. To determine whether different criteria for inflammatory back pain (IBP) impact the performance of the algorithms.

Methods: The multicenter Screening for Axial Spondyloarthritis in Psoriasis, Iritis, and Colitis (SASPIC) Study at 11 sites is aimed at early detection of axial SpA in patients presenting with undiagnosed back pain to the rheumatologist. Consecutive patients ≤45 years of age with ≥3 months undiagnosed back pain with any one of psoriasis, acute anterior uveitis (AAU), or colitis diagnosed by the relevant specialist undergo routine clinical evaluation by a rheumatologist for axial SpA. The rheumatologist determines the presence or absence of axial SpA at 3 consecutive stages: 1. After the clinical evaluation; 2. After the results of labs (B27, CRP) and radiography; 3. After the results of MRI evaluation. Final diagnosis by the rheumatologist was used as external standard to test the performance of the algorithms. We tested the following criteria for IBP in the algorithm: ASAS, Berlin, rheumatologist global for likelihood of IBP >5 (0-10 scale), and DUET algorithm in AAU patients.

Results: A total of 246 patients were recruited, 73 presented with iritis, 46 with psoriasis, and 127 with colitis, 47.6% were diagnosed with axSpA. The diagnosis of axSpA was established in 45.7%, 61.6%, and 40.2% of patients with psoriasis, AAU, and IBD, respectively. The performance of the ASAS-modification of the Berlin algorithm was superior to the original algorithm as reported previously[3], primarily for enhanced sensitivity, and this was observed irrespective of the criteria used to define IBP (Table 1). Conversely, the performance of the Duet algorithm in the subset of patients with AAU was substantially worse than previously reported[1].

Conclusion: The ASAS modification of the Berlin algorithm is the preferred referral strategy for patients presenting with undiagnosed back pain to the rheumatologist.

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Algorithm	Sensitivity (%)	Specificity (%)	Correct diagnosis (%)	False negative (%)	False positive (%)
Original Berlin (ASAS criteria for IBP)	65.3	76.6	71.1	16.7	12.2
Original Berlin (Berlin criteria for IBP)	64.4	76.6	70.7	17.1	12.2
Original Berlin (IBP global >5)	67.8	78.1	73.2	15.4	11.4
ASAS Modification of Berlin algorithm (ASAS criteria for IBP)	73.7	75.8	74.8	12.6	12.6
ASAS Modification of Berlin algorithm (Berlin criteria for IBP)	73.7	75.0	74.4	12.6	13.0
ASAS Modification of Berlin algorithm (IBP global >5)	76.3	77.3	76.8	11.4	11.8
DUET	84.4	50.0	71.2	9.6	19.2

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FRI0299 EVALUATION OF ENTHESITIS INDICES AND RESPONSE TO BDMARD THERAPY IN PORTUGUESE PATIENTS WITH SPONDYLOARTHRITIS

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Background: Enthesitis is a hallmark clinical feature of spondyloarthritis (SpA), but to date, few studies have investigated how the overall response to biological treatment relates to the evolution of enthesitis counts.
Objectives: Assess whether the variation in enthesitis indices reflects the overall response to bDMARD therapy in SpA.
Methods: This longitudinal, retrospective study included patients who met Assessment of Spondyloarthritis international Society (ASAS) criteria for SpA followed at the Rheumatology Department of a tertiary hospital, under bDMARD therapy. Demographic, laboratorial and clinical data were collected, including Bath Ankylosing Spondylitis Metrology Index (BASMI), Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Activity Index (BASDAI), Ankylosing Spondylitis Disease Activity Score-C-reactive protein (ASDAS-CRP), Maastrich Ankylosing Spondylitis Enthesitis Score (MASES), Leeds Enthesitis Index (LEI) and Spondyloarthritis Research Consortium of Canada (SPARCC) scores. All were evaluated at baseline and at 6, 12, 18 and 24 months after starting the first biological therapy. The variation in each parameter compared with the baseline values was calculated at 6, 12, 18 and 24 months and represented in the form of delta. Correlations between variables were assessed using Spearman test and comparison between groups using Wilcoxon, Mann-Whitney U and Kruskal-Wallis tests.
Results: We included 273 patients, 123 (45,1%) females, aged 42,0±12,3 years and with diagnosis of SpA for 15,4±11,2 years at the start of bDMARD therapy. Eighteen (6,6%) had depression. At baseline, mean BASDAI was 6,43 ±1,62, ASDAS-CRP was 4,01 ± 0,86, median MASES was 1 (0-4), LEI 0 (0-1,75) and SPARCC 1 (0-4). Seventy-two patients (26,4%) started golimumab, 71 (26,0%) adalimumab, 66 (24,2%) infliximab, 54 (19,8%) etanercept, 9 (3,3%) certolizumab and 1 (0,4%) secukinumab. Enthesitis indices were significantly higher at baseline in females [median MASES-females 2 (0-5) vs 0 (0-2), p<0,001; LEI-females 0 (0-2) vs 0 (0-1), p=0,03; and SPARCC-females 2 (0-5) vs 0 (0-2), p<0,001], and remained so at 24 months [median MASES-females 1 (0-3,5) vs 0 (0-0), p<0,001; LEI-females 0 (0-0,5) vs 0 (0-0), p<0,001; and SPARCC-females 1 (0-3) vs 0 (0-0), p<0,001]. MASES and SPARCC, but not LEI, at baseline were significantly higher in patients with depression [median MASES-depression 3,5 (2-6) vs 1 (0-4), p=0,01; SPARCC-depression 4 (0-8) vs 1 (0-3), p=0,03], but at 24 months no differences were observed. There was a significant difference between each of the 3 scores of enthesitis when assessed at 6, 12, 18 and 24 months, compared to baseline (p <0.004). No differences were observed regarding the choice of bDMARD. At baseline, MASES had a significant correlation with patient visual analogic scale (VAS) (r=0,18; p=0,01), BASDAI (r=0,36; p<0,001) and BASFI (r=0,21; p=0,003); LEI had a significant correlation with BASDAI (r=0,31; p<0,001) and BASFI (r=0,21; p=0,003); SPARCC had a significant correlation with patient VAS (r=0,19; p=0,01), BASDAI (r=0,37; p<0,001) and BASFI (r=0,26; p<0,001). ΔLEI at 6 months had a significant correlation with ΔBASDAI (r=0,25; p=0,005), ΔASDAS (r=0,190; p=0,03), Δpatient VAS (r=0,23; p=0,01) and Δphysician VAS (r=0,25; p=0,01), but not with ΔESR, ΔCRP and ΔBASMI; no correlation was found at 6 months for ΔMASES or ΔSPARCC. At 12 months, ΔMASES had a significant correlation with ΔBASDAI (r=0,18; p=0,03); ΔLEI with ΔBASDAI (r=0,23; p=0,01) and Δpatient VAS (r=0,19; p=0,03); for ΔSPARCC no significant correlations were found. At 18 months and 24 months, no correlations were found.
Conclusion: The initiation of bDMARD led to improved enthesitis indices over a 24-month period. ΔLEI correlates better with SpA activity scores and measurements than the other indices, especially at the first 12 months of initiation of bDMARD therapy.
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FRI0300

ARE COPING STRATEGIES, ANXIETY AND DEPRESSION ASSOCIATED WITH DAILY PHYSICAL ACTIVITY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS?

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Background: Patients with axial spondyloarthritis (axSpA) who are more physically active experience less pain and better physical functioning.[1] Psychological factors such as anxiety and depression are associated with physical functioning and reduction of Quality of Life (QoL).[2] Furthermore, evasive coping strategies are commonly used in health-related coping.[3] However, as far as we know, no data is available regarding the influence of coping strategies, anxiety and depression on daily physical activity in axSpA.
Objectives: To determine if coping strategies, anxiety and depression are associated with daily physical activity in patients with axSpA.
Methods: Consecutive outpatients from the Groningen Leeuwarden AxSpA cohort (GLAS) participated in this study. Additionally to the standardized follow-up assessments, patients filled out the axSpA-Short Questionnaire to assess health-enhancing physical activity (axSpA-SQUASH), the Coping with Rheumatic Stressors (CORS) and the Hospital Anxiety and Depression Scale (HADS). Univariable and multivariable linear regression analyses were performed to explore associations of copings strategies, anxiety and depression, and patient- and disease related factors with daily physical activity. Additionally, patients were stratified into three tertiles of physical activity: low, intermediate and high. To identify group differences, Kruskal-Wallis test or Chi-Square test were used with post-hoc testing.
Results: In total 85 patients were included; 59% were male, mean age was 49±14, median symptom duration 19.5 years (IQR 12.0-31.0), 71% were HLA-B27 positive and mean ASDAS was 2.1±1.0. Median axSpA-SQUASH total physical activity score was 9406.3 (IQR 5538.8–12081.3). Median scores of HADS-Anxiety (scale 7-28) and HADS-Depression (scale 7-28) were scores of 12 (IQR 10.0-14.0) and 10(IQR 9.0-12.5). The mostly frequently used coping strategie was comforting cognitions (for pain, range 9-36); median of 25.5 (IQR 22.0-28.0).
Univariable analysis showed that lower daily physical activity was significantly associated with gender (female), higher disease activity (BASDAI), worse physical function (BASFI), worse quality of life (ASQoL), coping strategies 'decreasing activities' and 'pacing', higher depression score (HADS) and higher perceived influence of axSpA on general well-being. In multivariable analysis, only the coping strategy "decreasing activity" was independently associated with physical activity (β: -419.3, R^2: 0.155, P<0.001). Additionally, patients in the highest physical activity tertile were significantly more often male, had higher working status, lower BASDAI and ASDAS, better BASFI and ASQoL and scored lower on the coping strategy "decreasing activities".
Conclusion: In this cross-sectional study in axSpA patients with established disease, multiple patient and disease related factors were associated with daily physical activity. The evasive coping strategy 'decreasing activities' was the only independently associated factor. These findings suggest that to improve daily physical activity in axSpA patients attention should be paid not only on targeting disease activity, but also to other patient and disease related aspects, especially coping strategies used.
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FRI0301

DO PATIENTS AND PHYSICIANS AGREE ON THE DEFINITION OF REMISSION AND LOW DISEASE ACTIVITY IN AXIAL SPONDYLOARTHRITIS?

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Background: Current recommendations for axial Spondyloarthritis (axSpA) include the treat-to-target concept and suggest that the ideal target should be remission or low disease activity (LDA). Also, the importance of a shared decision is highlighted. Unfortunately, the definition of remission is not consensual, and most of the definitions are difficult to evaluate in clinical practice

Objectives: To propose an evaluation of remission by a single question to the patient, by comparing it to the different available definitions. To analyze the metric properties of the current definitions against patient's perception

Methods: One-center cross-sectional study in a tertiary care hospital including consecutive patients with a diagnosis of axSpA (and fulfilling the ASAS criteria) were included between February to November 2019. Patient's perception of remission and LDA was evaluated by a single question. Physician's perception of remission and LDA was assessed identically. The level of agreement between patients' perception and the other available definitions was tested by the Prevalence and Bias adjusted Kappa (PABAK). The metric properties Sensitivity (S) and Specificity (Sp) of the available definitions (BASDAI cut-offs, ASDAS disease states, ASAS criteria for partial remission and patient acceptable symptom state), were tested against the patients perspective, as the gold standard.

Results: A total of 105 axSpA patients were included. 63,8% were males and 67,6% had radiographic sacroiliitis (Table 1). 21% and 72% of them considered themselves in remission and LDA, respectively. Physician's perception was 45.7% and 81% for remission and LDA, respectively. The prevalence of the different definitions are shown in Figure 1. The best agreement for patients's perception of remission was found with a BASDAI <2 + normal CRP (Table 2). This definition was also the most sensitive (S=72,7%) and specific (Sp=83,1%) when taking the patient's perception as a reference.

Table 1. Characteristics of 105 patients with axSpA

	All (N:105)	Patients in self-defined REM (N:22)	Patients in self-defined LDA (N:54)	Patients No REM no LDA (N:29)
Male, n (%)	67 (63,8)	18 (81,8)	34 (63)	15 (51,7)
r-axSpA, n (%)	71 (67,6)	17 (77,3)	33 (61,1)	21 (72,4)
Mean age, years (SD)	49 (13)	51(15)	47 (13)	50 (11)
Mean AxSpA duration, years (SD)	12,2 (13)	17,1 (16,2)	11,2 (11,7)	10,3 (12,3)
HLA- B27+, n (%) Data from 104	72 (69,2)	17/22 (77,3)	33/54 (61,1)	22/28 (78,6)
Periferic arthritis, n (%)	34 (32,4)	7 (31,8)	17 (31,5)	10 (45,4)
Uveitis, n (%)	22 (21)	6 (27,3)	10 (18,5)	6 (20,7)
Biological treatment, n (%)	43 (41)	14 (63,6)	19 (35,1)	10 (34,5)
CRP, mean (SD)	3,61 (5,36)	2,31 (2,17)	2,84 (3,87)	6,04 (8,14)
ASDAS, mean (SD)	1,78 (1,08)	0,98 (0,71)	1,63 (0,89)	2,68 (1,03)
BASDAI, mean (SD)	3,35 (2,32)	1,39 (1,30)	3,13 (1,84)	5,26 (2,33)
BASFI, mean (SD)	2,81 (2,45)	1,24 (1,37)	2,57 (2,00)	4,43 (2,92)

Table 1.REM: Remission; LDA: Low Disease Activity; SD: Standard Desviation; CRP: C-Reactive Protein IBD: Inflammatory Bowel Disease.

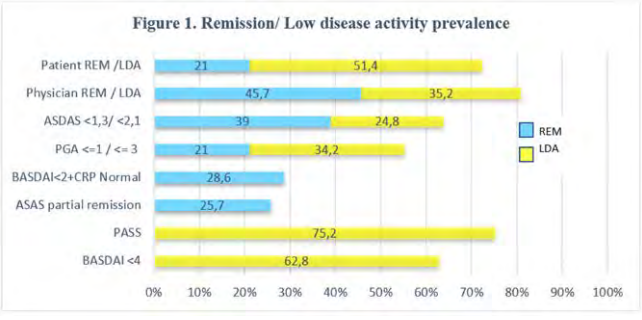


Fig. 1. REM/LDA: remission/ low disease activity self-defined patient or physician through a simple question. ASDAS <1,3: inactive disease; ASDAS <2,1: low activity; PGA: Patient global assessment; PASS: Patient acceptable symptom state.

Table 2. Agreement between different definitions of remission

	ASDAS <1,3	BASDAI<2+ Normal CRP	PGA ≤1	Physician REM	Patient REM
ASAS PR	0.53 (0.58)	0.59 (0.68)	0.76 (0.83)	0.22 (0.26)	0.39 (0.56)
ASDAS <1,3		0.64 (0.68)	0.50 (0.56)	0.44 (0.45)	0.28 (0.37)
BASDAI <2+ Normal CRP			0.60 (0.69)	0.25 (0.28)	0.50 (0.62)
PGA ≤1				0.20 (0.24)	0.42 (0.62)
Physician REM					0.20 (0.24)

Agreement is presented as Cohen's Kappa (PABAK: prevalence and bias adjusted kappa). Patient and Physician remission (REM) are based on the single question; ASAS PR: ASAS partial remission; PGA: Patient global assessment.

Conclusion: In this real-life population, the evaluation of remission by the patient through a single question was shown to be feasible and to present an acceptable agreement with other definitions.

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FRI0302

WHAT IS THE IMPACT OF DISCREPANCY BETWEEN CENTRAL AND LOCAL READERS IN EVALUATION OF MRI SCANS ON THE CLASSIFICATION OF AXIAL SPONDYLOARTHRITIS? DATA FROM THE ASAS CLASSIFICATION COHORT STUDY

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Background: Active MRI lesions typical of axial spondyloarthritis (axSpA) were reported in 61.6% and 2.2% of axSpA and not-axSpA patients, respectively, from the ASAS classification cohort (ASAS-CC)[1]. Discrepancy between local and central reader evaluation of MRI scans could result in differences in numbers of patients fulfilling the imaging arm of the ASAS classification criteria. But final classification may not be impacted if discrepant patients still fulfill the clinical arm.

Objectives: We aimed to assess the impact of reader discrepancy in detection of active MRI lesions on the number of patients classified as having axSpA in patients recruited to the ASAS-CC.

Methods: MRI images of the sacroiliac joints (SIJs) were available from 252 cases in the ASAS-CC, and these also had clinical and radiographic data. Seven central readers from the ASAS-MRI group recorded MRI lesions in an eCRF that included active lesions typical of axSpA in the SIJ (MRI-active) that was worded exactly the same as in the original ASAS-CC eCRF permitting comparisons between central and local site readers. Active lesions were deemed to be present according to majority agreement (≥4/7) of central readers and also any 2 central readers. We calculated the number of patients that were classified differently after central evaluation for overall fulfilment of the ASAS criteria and for the imaging arm.

Results: Discordance between central and local readers for detection of MRI-active was recorded in 45(17.8%) and 47(18.2%) of cases according to 2-reader and majority (≥4/7) central reader data, respectively (kappa (95%CI) of 0.64 (0.54-0.73) and 0.62 (0.53-0.72). With central reading as external standard the false-positive rate for active lesions was 26.9%% and 32.2% ('local overcall') for 2-reader and majority reader data, respectively. There were 159(63.1%) patients who fulfilled the ASAS axSpA criteria based on local-reading, and 148(58.7%) and 143(56.7%) patients based on 2-reader and majority central-reading, respectively (Table). When fulfillment of the imaging arm was the primary consideration

(irrespective of the clinical arm), 126 (50%) patients fulfilled the criteria based on local-reading, and 111 (44%) and 102 (40.5%) patients based on 2-reader and majority central-reading, respectively.

Conclusion: Despite substantial overcall for positive MRI SIJ inflammation by local readers, the number of patients classified as having axSpA did not change substantially. This is due to the alternate mechanism for classification through the clinical arm.

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Impact of Central Vs. Local Reader SIJ MRI Inflammation Assessment on SpA Classification in cases with all clinical, radiographic, and central and local MRI inflammation data available (n=252)

MRI assessment used	SpA Classification = Yes N(%)	SpA Classification = No N(%)	Imaging Arm SpA Classification = Yes N(%)	Imaging Arm SpA Classification = No N(%)
Local Reader MRI positive	159 (63.1%)	93 (36.9%)	126 (50%)	126 (50%)
>2 Central Reader MRI positive	148 (58.7%)	104 (41.3%)	111 (44.0%)	141 (56.0%)
Majority Central Reader (≥4/7) MRI positive	143 (56.7%)	109 (43.2%)	102 (40.5%)	150 (59.5%)

Disclosure of Interests: Walter P. Maksymowych Grant/research support from: AbbVie, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Boehringer Ingelheim, Celgene, Eli Lilly, Galapagos, Janssen, Novartis, Pfizer, and UCB, Employee of: Chief Medical Officer of CARE Arthritis Limited, Speakers bureau: AbbVie, Janssen, Novartis, Pfizer, and UCB, Susanne Juhl Pedersen Grant/research support from: Novartis, Ulrich Weber: None declared, Pedro M Machado Consultant of: PMM: Abbvie, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Roche and UCB, Speakers bureau: PMM: Abbvie, BMS, Lilly, MSD, Novartis, Pfizer, Roche and UCB, Xenofon Baraliakos Grant/research support from: Grant/research support from: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB and Werfen, Consultant of: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB and Werfen, Speakers bureau: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB and Werfen, Joachim Sieper Consultant of: AbbVie, Boehringer Ingelheim, Eli Lilly and Company, Janssen, Merck, Novartis, Pfizer, Roche, and UCB Pharma, Speakers bureau: AbbVie, Boehringer Ingelheim, Eli Lilly and Company, Janssen, Merck, Novartis, Pfizer, Roche, and UCB Pharma, Stephanie Wichuk: None declared, Denis Poddubnyy Grant/research support from: AbbVie, MSD, Novartis, and Pfizer, Consultant of: AbbVie, Bristol-Myers Squibb, Eli Lilly, MSD, Novartis, Pfizer, Roche, UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, MSD, Novartis, Pfizer, Roche, UCB, Martin Rudwaleit Consultant of: AbbVie, BMS, Celgene, Janssen, Eli Lilly, MSD, Novartis, Pfizer, Roche, UCB Pharma, Désirée van der Heijde Consultant of: AbbVie, Amgen, Astellas, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Cyxone, Daiichi, Eisai, Eli-Lilly, Galapagos, Gilead Sciences, Inc., Glaxo-Smith-Kline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB Pharma; Director of Imaging Rheumatology BV, Robert B.M. Landewé Consultant of: AbbVie; AstraZeneca; Bristol-Myers Squibb; Eli Lilly & Co.; Galapagos NV; Novartis; Pfizer; UCB Pharma, Joel Paschke: None declared, Mikkel Østergaard Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Merck, and Novartis, Consultant of: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo Nordisk, Orion, Pfizer, Regeneron, Roche, Sandoz, Sanofi, and UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo Nordisk, Orion, Pfizer, Regeneron, Roche, Sandoz, Sanofi, and UCB, Robert G Lambert: None declared

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FRI0303

PERIPHERAL SYMPTOMS ARE ASSOCIATED WITH LESS SPINAL RADIOGRAPHIC PROGRESSION IN PATIENTS WITH EARLY AXIAL SPONDYLOARTHRITIS: RESULTS FROM THE GERMAN SPONDYLOARTHRITIS INCEPTION COHORT

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Background: Peripheral symptoms (PS), such as arthritis, enthesitis, and dactylitis, are common in axial spondyloarthritis (axSpA); data showing the association of PS and spinal radiographic progression in axSpA are controversial.

Objectives: To analyze the association of PS and spinal radiographic progression in patients with axSpA.

Methods: A total of 210 patients with axSpA (115 with radiographic and 95 with non-radiographic axSpA) were selected for analysis. Spinal radiographs were scored by two readers in a random order according to the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS). Pelvic radiographs were scored according to the grading system of the modified New York criteria; a sacroiliitis sum score was calculated as a sum of the grades for both sacroiliac joints. Mann-Whitney and Fisher exact tests were performed for group comparisons. A multivariable regression analysis was performed to analyze the influence of PS on radiographic progression.

Results: Of the 101 (48.1%) patients with PS, 78 had peripheral arthritis, 48 - enthesitis, 12 - dactylitis. 32 patients had ≤1 PS. Patients with PS were older, less frequently HLA-B27 positive, compared with patients with no PS (73 (73.0%) vs. 93 (85.3%), p=0.028), had higher disease activity (time-averaged ASDAS over 2 years 2.6 ± 0.9 vs. 2.3 ± 0.9; p=0.032), worse physical function (BASFI 3.5 ± 2.3 vs. 2.3 ± 2.2, p<0.001), higher exposure to disease modifying anti-rheumatic drugs (39 (38.6%) vs. 22 (20.2%), p=0.003) and lower baseline radiographic sacroiliitis sum score (3.8 ± 1.9 vs. 4.4 ± 2.1, p=0.026); other baseline characteristics were similar. Patients with PS had lower absolute progression in mSASSS after 2 years of follow-up than those without (0.28 ± 1.39 vs 1.15 ± 2.9, p=0.045); 7.9% of patients with PS had a progression of mSASSS by ≥2 points compared to 20.2% in patients without PS (p=0.011). Radiographic progression of sacroiliitis was similar in both groups. In a multivariable regression analysis, presence of PS was associated with a lower mSASSS progression and lower odds for the mSASSS progression by ≥2 points after 2 years of follow-up: β=-0.98 (95% -1.68 to -0.28) OR=0.33 (95% CI 0.12 to 0.91), respectively – Table 1.

Table 1. Association of peripheral symptoms with radiographic progression in axial spondyloarthritis after 2 years of follow-up.

Multivariable linear regression analysis	
Outcome	β (95 %CI)
mSASSS change score	–0.98 (-1.68 to -0.28)*
Change of the sacroiliitis sum score	–0.06 (-0.32 to 0.20)**
Multivariable logistic regression analysis	
Outcome	Odds ratio (95 %CI)
Progression of mSASSS by ≥2 points	0.33 (0.12 to 0.91)*
Progression of sacroiliitis by at least 1 grade in opinion of both readers	0.84 (0.33 to 2.09)**

mSASSS - modified Stoke Ankylosing Spondylitis Spine Score.

*Adjusted for the smoking status, HLA-B27 status, NSAIDs intake, baseline syndesmophytes, and time-averaged ASDAS.

**Adjusted for the smoking status, HLA-B27 status, NSAIDs intake, sacroiliitis sum score at baseline, and time-averaged ASDAS.

Conclusion: Presence of PS is associated with distinct characteristics of SpA including slower radiographic spinal progression which might be explained partly by the numerically lower mSASSS score at baseline.

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FRI0304

SERUM IGG-UNDERGALACTOSYLATION PROFILES REFLECT CUMULATIVE EXPOSURE TO SYSTEMIC INFLAMMATION IN SPONDYLOARTHRITIS PATIENTS

A. S. De Craemer[1,2], Z. Lukasik[3], L. Meuris[4], L. Deroo[1,2], T. Renson[1,2], M. De Hooge[1,2], P. Carron[1,2], A. Van Hecke[4,5], N. Callewaert[4,5], F. Van den Bosch[1,2], D. Elewaut[1,2]on behalf of the Be-Giant Consortium. *[1]Ghent University Hospital, Rheumatology, Gent, Belgium*; *[2]VIB, Inflammation Research Center, Gent, Belgium*; *[3]Medical University of Lodz, Łódź, Poland*; *[4]VIB, Center for Medical Biotechnology, Gent, Belgium*; *[5]Ghent University, Department of Biochemistry and Microbiology, Gent, Belgium*

Background: Inflammation in spondyloarthritis (SpA) is often not reflected by elevated acute phase reactants such as C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR). It has been shown that IgG glycosylation patterns are subject to specific alterations (i.e. undergalactosylation) in chronic inflammatory diseases. Since these changes only occur in persistent inflammatory processes, lasting at least one to two $t_{1/2}$ of IgG (24 days), it was hypothesized that IgG-glycan profiles could serve as a surrogate marker for chronic inflammation in SpA patients.

Objectives: To assess the value of serum IgG-undergalactosylation in SpA patients in relation to outcome measures for disease activity, determined by patient reported outcomes, serum inflammatory markers and imaging outcomes.

Methods: Serum samples were obtained from SpA patients at the baseline visit of Be-Giant: a Belgian observational cohort including SpA patients who fulfill the ASAS classification criteria for axial or peripheral SpA. IgG Fc N-glycans were released directly in whole serum by endo-β-N-acetyl-glucosaminidase from *Streptococcus pyogenes* (EndoS), fluorescently labeled with ATPS and analyzed by capillary electrophoresis, rendering glycan profiles with six peaks (Figure 1). Relative peak heights were combined in the undergalactosylation score (UGS), capturing the relative upregulation of non-galactosylated glycans normalized to the total peak height (1). Baseline radiographs (X-SIJ) and magnetic resonance images (MRI) of the sacroiliac joints (SIJ) were assessed by three calibrated readers for sacroiliitis (fulfillment of the modified New York criteria; grading 0 to 4 per SIJ) and for inflammatory lesions according to the Spondyloarthritis Research Consortium of Canada (SPARCC) method (score from 0 – 72) respectively. Grades and inflammatory lesions that were seen by at least 2 readers were used for further analysis.

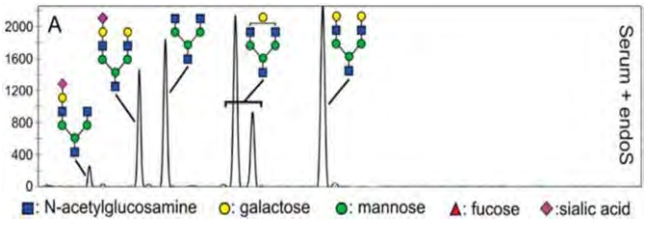


Figure 1. Example of a serum IgG-specific glycan profile. Adapted from (1), with permission.

Results: Glycan profiles were obtained from 376 SpA patients; UGS was scaled (mean = 0, SD = 1) for further analysis. UGS was independently associated with ASDAS-CRP (β_1 = 0.15, 95% CI 0.04 – 0.26, p = 0.006) and BASFI (β_1= 0.44, 95% CI 0.16 – 0.72, p = 0.002) but not with BASDAI (β_1 = 0.12, 95% CI -0.13 – 0.38, p = 0.34). UGS showed a weak to moderate correlation with CRP (R_s = 0.30, p < 0.001) and ESR (R_s = 0.27, p <0.001). In axial SpA, UGS was significantly higher in patients with ankylosing spondylitis compared to non-radiographic axial SpA (OR = 2.41, 95% CI 1.60 – 3.73, p < 0.001) and showed an independent association with the total grading of the SIJ (β_1= 0.44, 95% CI 0.09 – 0.80, p = 0.01, Figure 2) and SPARCC score (β_1= 2.64, 95% CI 0.98 – 4.31, p = 0.002). All models were adjusted for age, gender, BMI, CRP, anti-TNF treatment and symptom duration.

Conclusion: This study shows and independent association of serum IgG undergalactosylation with disease activity and functional impairment in SpA patients. Moreover, UGS was significantly higher in advanced compared to early-stage axial disease and therefore may reflect the cumulative exposure to systemic inflammation.

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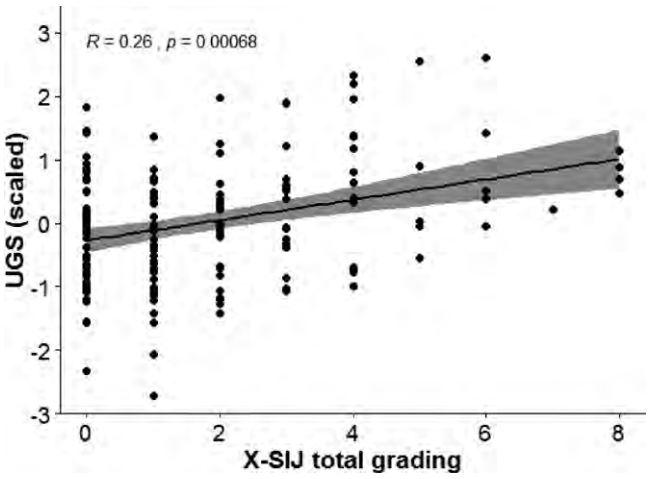


Figure 2. Correlation between UGS and X-SIJ total grading of sacroiliitis. R = Spearman's correlation coefficient.

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FRI0305

FERTILITY AND PREGNANCY OUTCOMES IN WOMEN WITH SPONDYLOARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Women with spondyloarthritis (SpA) are often affected by the disease during their reproductive years[1]. However, little is known about the impact of the disease and its treatments on fertility and pregnancy outcomes, as well as the effect of pregnancy itself on disease activity[2].

Objectives: The aim of the study was to determine the effects of spondyloarthritis on fertility and pregnancy outcomes in women with SpA.

Methods: We searched Pubmed, Embase, and Web of Science until 1 November 2019, without any language restriction. All studies assessing fertility, pregnancy outcomes and disease activity during pregnancy in women with spondyloarthritis (axial SpA (axSpA) but also peripheral SpA, including psoriatic arthritis (PsA)) were eligible. The heterogeneity between studies was quantified (I^2), and multiple meta-regressions were carried out to identify potential sources of heterogeneity. In case I^2 was < 50%, a random-effects model was used to pool the available data. Prevalence of events was described as percentages. The odds ratio (OR) and corresponding 95% confidence interval (CI) were used to assess the associations between the disease and the pregnancy outcomes.

Results: Within 4397 eligible studies, 21 articles fulfilling the selection criteria were included in the review, assessing overall 3306 patients (2578 with axSpA and 728 with PsA) and 4104 pregnancies compared to 42248 healthy controls (in 11 studies with a control group). Among the included studies, the risk of bias was evaluated as high, moderate and low in respectively 12, 1 and 8 studies. Regarding pregnancy outcomes, several studies report an increased risk of preterm birth, small for gestational age (pooled OR 2,05, [1,09-3,89], *I2*=5,8% in axSpA) and caesarean section (pooled OR 1,77 [1,45-2,17], *I2*=27,5% in axSpA and pooled OR 1,47 [1,22-1,76], *I2*=0,0% in PsA), without any other unfavourable pregnancy outcome (miscarriage, stillbirth, gestational diabetes or preeclampsia). Further analysis found a significant higher risk for elective caesarean (pooled OR 2,64, [1,92-3,62], *I2*=0,0% in axSpA and pooled OR 1,47, [1,15-1,88], *I2*=0,0% in PsA), without increased risk for emergency caesarean. There was no substantial heterogeneity in the majority of meta-analyses.

Conclusion: Although based on observational data, this work is to our knowledge, the first systematic review and meta-analysis concerned with this subject. SpA and PsA seem to be associated with an increased risk of preterm birth, small for gestational age and elective caesarean section. The analysis of the impact of pregnancy on disease activity in this setting is currently ongoing.

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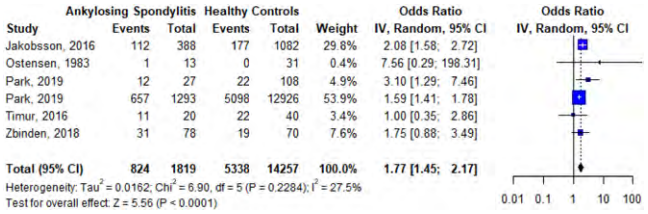


Fig. 1. Association between caesarean section and axSpA

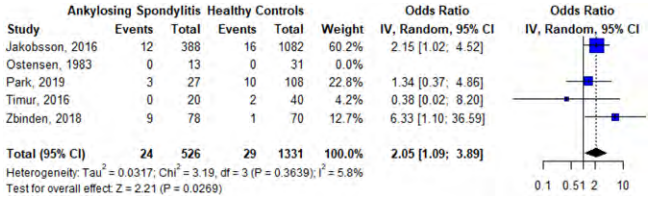


Fig. 2. Association between small for gestational age and axSpA

Disclosure of Interests: SABRINA HAMROUN: None declared, Aghilès Hamroun: None declared, Jean Joël Bigna: None declared, Edem Allado: None declared, Frauke Förger Grant/research support from: Unrestricted grant from UCB, Consultant of: UCB, GSK, Roche, Speakers bureau: UCB, GSK, Anna Moltó Grant/research support from: Pfizer, UCB, Consultant of: Abbvie, BMS, MSD, Novartis, Pfizer, UCB

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FRI0306 WOMEN WITH AXIAL SPONDYLOARTHRITIS HAVE COMPARABLE RATES OF COMPLICATIONS IN PREGNANCY TO WOMEN IN THE GENERAL POPULATION BUT MORE CAESAREAN DELIVERIES: RESULTS FROM NATIONWIDE CLAIMS DATA

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Background: In contrast to other rheumatic inflammatory diseases, studies on pregnancy outcomes in axial spondyloarthritis (axSpA) are scarce, despite its onset in early adulthood affecting women in their reproductive years.

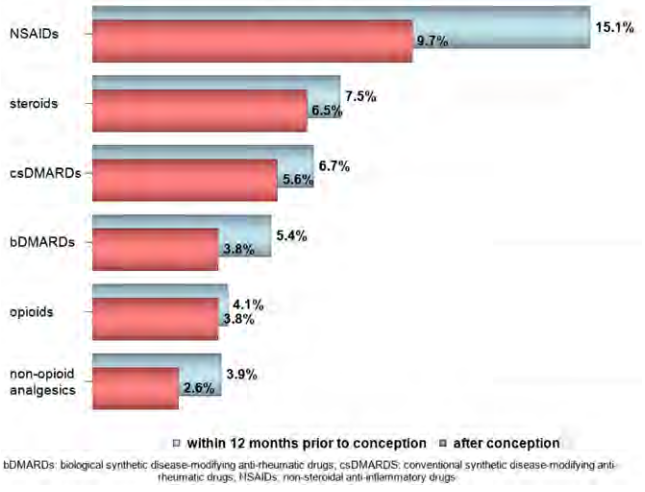
Objectives: To investigate maternal and infant pregnancy outcomes among women with axSpA compared with population-based controls.

Methods: Taking advantage of a large health insurance dataset, comprising the period 2006 – 2018, maternal and infant pregnancy outcomes and delivery outcomes of women with axSpA were assessed and compared with population-based controls (matched by maternal age and calendar year of birth). Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated using generalised estimating equation analyses.

Results: A total of 611 singleton births among 535 women with axSpA were included in the analysis. The mean age at delivery was 32.5 years. The pharmacological treatment within 12 months prior to and after conception is illustrated in the Figure. Infants of women with axSpA were only slightly more often preterm (5.2% vs 4.7%) and small-for-gestational-age (1.6% vs 1.1%) than infants of matched population-based controls, respectively. Caesarean section was performed in 36% of deliveries among women with axSpA compared with 29.5% in population-based controls, resulting in a significantly increased risk for receiving caesarean section (OR 1.35; 95% CI 1.06-1.73) (Table). The occurrence of pre-eclampsia, preterm birth, and small-for-gestational-age was moderately higher, but not significantly increased, among women with axSpA as compared to population-based controls.

Conclusion: Women with axSpA had no significantly increased risks for adverse maternal or infant pregnancy outcomes compared to non-axSpA women. However, a significantly increased risk for receiving caesarean section and a tendency for a higher number of preterm deliveries and of small-for-gestational-age infants was observed in women with axSpA.

Figure Pharmacological treatment within 12 months prior to conception and after conception in women with axial spondyloarthritis



bDMARDs: biological synthetic disease-modifying anti-rheumatic drugs; csDMARDS: conventional synthetic disease-modifying anti-rheumatic drugs; NSAIDs: non-steroidal anti-inflammatory drugs

Table. Prevalences and odds ratios with 95% confidence intervals for adverse pregnancy outcomes

	Pregnancies in women with axSpA N=611	Pregnancies in population-based controls N=611	Odds Ratio (95% CI)
Preterm birth (< week 37)	5.2% (32)	4.7% (29)	1.11 (0.66, 1.85)
Gestational week 28-36	4.9% (30)	4.7% (29)	1.03 (0.61, 1.75)
Gestational week <28	0.3% (2)	0.2% (1)	2.01 (0.18, 22.18)
Small for gestational age	1.6% (10)	1.1% (7)	1.43 (0.54, 3.79)
Low birth weight (<2500 g)	2.8% (17)	2.6% (16)	1.06 (0.53, 2.13)
Exceptionally large baby (birth weight ≥4500 g)	1.1% (7)	0.2% (1)	7.07 (0.87, 57.63)
Pre-eclampsia	7.5% (46)	6.4% (39)	1.21 (0.78, 1.90)
Assisted vaginal delivery	4.3% (26)	3.1% (19)	1.39 (0.76, 2.56)
Caesarean section	36.0% (220)	29.5% (180)	1.35 (1.06, 1.73)

axSpA, axial Spondyloarthritis; CI, confidence interval.

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FRI0307 DETERMINANTS OF PATIENT-PHYSICIAN DISCORDANCE IN GLOBAL ASSESSMENT IN SPONDYLOARTHRITIS

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Background: Patient's Global Assessment of Disease Activity (PtGA) and Physician's Global Assessment of Disease Activity (PhGA) are important measures in the evaluation of patients with Spondyloarthritis (SpA), but often provide discordant results.[1] Both PtGA and PhGA are assessed as part of ankylosing spondylitis disease activity score (ASDAS), that is a measure of axial SpA disease activity endorsed by the Assessment of SpA International Society (ASAS) and Outcome Measures in Rheumatology.[2,3] In peripheral SpA, although there are no formally validated indexes, the American College of Rheumatology (ACR) and Disease Activity Score 28 (DAS 28) response criteria have shown reliable discriminant characteristics and both include PtGA and PhGA.[3] The lack

of concordance between PtGA and PhGA may mislead treatment decisions, namely switches.

Objectives: To assess the determinants of patient-physician discordance in SpA patients under biologic treatment.

Methods: Cross-sectional study, including 72 with SpA according ASAS criteria. Physicians' evaluation included comorbidities, parameters of inflammatory activity (erythrocyte sedimentation rate [ESR] and C-reactive protein [CRP], PhGA, ASDAS PCR and, DAS 28, and Participants completed patient-reported outcomes (PROs) and sociodemographic characteristics. For statistical analysis, SPSS was used and significance level was 2-sided p<0.05.

Results: Clinical and laboratory characteristics of patients are shown in table 1. PtGA and PhGA were significantly different (34.8±21.2 *vs* 7.8±12.5 mm, respectively, p< .001) and patient-physician discordance (ΔPtGA - PhGA) was 27.5±14.3 mm.

In peripheral SpA, patient-physician discordance had a correlation with patient age, Health Assessment Questionnaire (HAQ), Functional Assessment of Chronic Illness Therapy (FACIT), EuroQol-5 dimension (EQ5D), Short Form (36) Health Survey (SF-36), Hospital Anxiety and Depression scales (HADS), CRP, ESR, number of comorbidities and daily medication, and an association with employment status (employees had lesser discordance), anxiety/depression, fibromyalgia and osteoarthritis (OA). In multivariable analysis including employment status, SF-36, OA, number of comorbidities, and ESR (R^2 adjusted= .505), the main predictors of patient-physician discordance were lower SF36, higher number of comorbidities and employment status.

In axial SpA, patient-physician discordance had a correlation with nocturnal back pain and total back pain VAS, FACIT, EQ5D, SF-36, HADS, Bath Ankylosing Spondylitis Functional Index (BASFI) and Bath Ankylosing Spondylitis Activity Index (BASDAI) scales, age, number of comorbidities and daily medication and an association with employment status (employees had lesser discordance), anxiety/depression and fibromyalgia. In multivariable analysis including employment status, SF-36, fibromyalgia, and number of comorbidities (R^2 adjusted= .738), the main predictors of patient-physician discordance were lower SF36, higher number of comorbidities and concomitant diagnosis of fibromyalgia.

Neither for peripheral SpA nor for axial SpA an association with SpA subtype, HLA-B27 positivity, patient or physician gender, or patient education level was found.

Conclusion: This study shows the variability implied in patient-physician discordance. We have demonstrated that comorbidities, employment status, and other factors not directly related to the disease are determinants for the patient-physician discordance.

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FRI0308 ANKYLOSING SPONDYLITIS PATIENTS AT RISK OF DEVELOPING AORTIC VALVE REGURGITATION, NEED FOR MANDATORY ECHOCARDIOGRAPHY?

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Background: The overall mortality rate in ankylosing spondylitis (AS) patients is increased by 60–90% compared with the general population. This higher mortality rate is predominately caused by cardiovascular disease (CVD) comprising an increased prevalence of cardiac diseases such as valvular heart disease, conduction disturbances and cardiomyopathies as well as atherosclerotic diseases such as myocardial infarctions. However, there is a lack of contemporary studies. Therefore, we investigated current prevalences of cardiac disorders in a well characterized cohort of Dutch patients with AS compared to osteoarthritis (OA) controls.

Objectives: To assess the prevalence of CVD in AS patients in comparison to OA controls in a Dutch population.

Methods: We performed a cross-sectional study in AS and OA patients between 50-75 years. Subjects were recruited from a large rheumatology outpatient clinic (Reade) in Amsterdam, the Netherlands. Patients underwent echocardiography with 2D, spectral and Color Doppler imaging. The echocardiogram was evaluated by an experienced and certified cardiologist. Diastolic dysfunction was assessed according to the ASE/EACVI 2016 guideline. Furthermore, blood sample, surveys and physical examination were done. Disease activity and function were measured with the BASFI, BASDAI and the ASDAS-CRP.

Results: A total of 193 consecutive AS patients were included with a median age of 60 (±7) years of which 72% men (138). The control group consisted of 70 OA patients (table 1). In the AS cohort the disease activity measures, BASDAI, ASDAS-CRP and BASFI, indicated moderate disease activity and were, respectively 3.1 (1.6-5.0), 2.1 (±1.0) and 3.5 (1.7-5.7). Anti-TNF was used by 43% of the AS patients. History of cardiovascular disease (CVD), i.e. angina pectoris, myocardial infarction, stroke and/or peripheral ischemia was comparable between the AS and OA cohort, respectively 9% (17) and 10% (7), p=0.81. Antihypertensives were significantly more often used in AS patients, 85 (44%) vs 19 (27%), p=0.02. Prevalences of systolic dysfunction and diastolic dysfunction did not differ significantly in AS and OA patients, respectively 6 (5%) vs 2 (5%), p=0.96 in systolic dysfunction and 7 (3%) vs 2 (3%), p=0.86 in diastolic dysfunction. Prevalence of aortic valve (AV) regurgitation was significantly higher in AS patients compared to OA patients, respectively 41 (22%) and 7 (10%), mostly with mild severity. The prevalence of mitral valve (MV) regurgitation did not differ between the AS and OA patients, respectively 68 (36%) vs 21 (33%), p=0.59. When corrected for age, gender and cardiovascular risk factors in a regression analysis, AS patients still had a substantially increased risk for AV regurgitation, odds ratio (OR) 2.8 95%CI 1.1-7.2, p=0.038.

Table 1. Patient characteristics

	AS	OA	p
N	193	70	
Men (n, %)	138 (72)	40 (57)	0.028*
Age (years)	60 ±7	63 ±7	0.004*
Disease activity			
BASDAI	3.1 (1.6-5.0)	-	
ASDAS-CRP	2.1 ±1.0	-	
BASFI	3.5 (1.7-5.7)	-	
CVD			
History of CVD* (n, %)	17 (9)	7 (10)	0.81
Antihypertensives (n, %)	85 (44)	19 (27)	0.02
Aortic valve regurgitation (n, %)	41 (22)	7 (10)	0.04*
Trace (n, %)	16 (9)	6 (9)	
Mild (n, %)	23 (12)	6 (9)	
Moderate (n, %)	1 (1)	0	
Severe (n, %)	1 (1)	0	
Prosthesis (n, %)	1(1)	0	
Mitral valve regurgitation (n, %)	68 (36)	21 (33)	0.59
Diastolic dysfunction (n, %)	7 (3)	2 (3)	0.86

*Angina pectoris, myocardial infarction, stroke and/or peripheral ischemia

Conclusion: This study demonstrates an almost tripled risk for developing AV regurgitation in Dutch AS patients. Although mostly mild in this age, due to the progressive nature of AV regurgitation in AS, echocardiographic screening should be considered in elderly AS patients.

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FRI0309 DAILY SELF-REPORTED FLARE PROFILES IN AXIAL SPONDYLOARTHRITIS: ASSOCIATIONS BETWEEN FLARE, SYMPTOMS AND BEHAVIOUR

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Background: Axial spondyloarthritis (axSpA) is a chronic inflammatory disease, characterised by fluctuating periods of flare and remission. Flare is a multidimensional change of disease state; whereby flare definitions have previously been formulated using validated composite indices, or through qualitative retrospective investigation of flare states. Smartphone technologies for tracking disease symptoms provide unique, daily insights into self-reported individual flare experience, and may present an opportunity to gain a more complete understanding of flare burden and symptom patterns.

Objectives: To assess frequency and characteristics of axSpA flares, utilising data collected in the uMotif symptom tracking app.
Methods: Patients with axSpA attending the Royal National Hospital for Rheumatic Diseases in Bath were invited to participate. Through the uMotif app, patients were sent daily reminders to log flare, pain, fatigue, sleep, recommended exercise, mood and stress using 5-point Likert scales, in addition to optional variables such as smoking and menstrual cycle. Self-reported periods of flare were identified. For each patient reporting flare within the study period, a mean 'flare' and 'non-flare' score was calculated for each variable. Paired t-tests were conducted for each variable, to investigate which variables correlate with flare status.
Results: Between 5th April 2018 and 8th March 2019, 174 patients consented for research and logged a mean of 99.73 (SD 99.97, range 1 - 323 days) days of data. 136/174 (78%) patients recorded at least 1 flare, with 1330 flares recorded in total. For patients reporting at least 1 flare, each flare lasted a mean of 2.20 days (SD 2.53 days, range 1 – 33 days), with a mean frequency of once every 45.19 days (SD 53.06, range 3.2 -314 days). Significant relationships were identified between flare status and uMotif scores (Table 1).

Table 1. Paired t-tests: flare vs. non-flare scores for each variable

Estimated difference^	p-value	N	95% CI (lower limit)	95% CI (upper limit)	Variable
-0.87	0.26	6	-2.63	0.88	Red Painful Eyes
-0.67	0.000*	130	-0.78	-0.56	Pain
-0.57	0.004*	25	-0.94	-0.20	Chest Pain
-0.51	0.005*	15	-0.83	-0.18	Hot Flushes
-0.50	0.000*	129	-0.61	-0.40	Fatigue
-0.44	0.196	2	-2.23	1.35	Blood in Stool
-0.38	0.000*	128	-0.47	-0.29	Mood
-0.36	0.000*	127	-0.52	-0.20	Anti-Inflammatory Use
-0.36	0.000*	128	-0.48	-0.23	Recommended Exercise
-0.34	0.000*	33	-0.51	-0.17	Confidence in Self-Management
-0.26	0.000*	128	-0.37	-0.15	Stress
-0.25	0.170	15	-0.62	0.12	Screen Time
-0.19	0.000*	130	-0.26	-0.12	Sleep Quality
-0.15	0.458	12	-0.59	0.28	Menstrual Cycle
-0.11	0.103	22	-0.25	0.02	Eyesight
0.09	0.195	3	-0.12	0.30	Flare of Psoriasis
0.05	0.656	26	-0.17	0.26	Medication Adherence
0.04	0.797	3	-0.53	0.61	Smoking Today
-0.03	0.484	50	-0.11	0.05	Caffeine Intake

N= number of patients with both a flare and non-flare entry for each variable; CI=confidence interval
Higher variable scores indicate more positive outcomes (e.g. a higher pain score indicates less pain)
^Estimated difference between flare and non-flare entries (e.g. on average, the mean pain score of a flare entry is 0.67 [0.56– 0.78 CI] less than a non-flare entry)
*p<0.01

Conclusion: These findings demonstrate significant relationships between a variety of patient-reported symptoms and flare, including variables that to our knowledge, have not yet been explored in axSpA. Small estimated differences were found between scores for 'flare' versus 'no-flare'. Further work is needed to characterise fluctuating flare/no-flare patterns of individuals tracking daily symptoms in the uMotif app. In future research, it will be important to determine whether there is a chronological pattern of variables during the pre-flare period that can predict a flare. Greater understanding of such patterns may allow identification of the optimal timing of intervention to prevent a period of flare and improve quality of life for patients with axSpA.
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FRI0310 **HIGHER RISK OF INCIDENT FRACTURE IN PATIENTS WITH ANKYLOSING SPONDYLITIS COMPARED TO THE GENERAL POPULATION**

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Background: Ankylosing spondylitis (AS) is characterized by pathologic new bone formation and bone loss. Vertebral fracture (VF) is a known complication of AS, whereas the risk of other major osteoporotic fractures (MOFs) is less studied.
Objectives: To estimate incidence rates (IRs) of incident fractures (any, VF and other MOF (humerus, forearm and hip)) in patients with AS compared to controls from general population.
Methods: This is a nationwide, register-based and observational cohort study including patients diagnosed with AS (n=11611, 65% men, mean age 48 years) identified in the National patient register (NPR) 2001 through 2015, and age- and sex-matched controls (n=58050) from the Swedish Population Register. The study period started 1 January 2007 or 3 months after the first AS diagnosis, whichever came later, and ended at the first occurrence of each fracture outcome (identified in the NPR), death, emigration or 31 December 2016. Patients and controls with any prior fracture in NPR within a 6-year period before start of the study period were not included. Any fracture (except skull and phalangeal fractures), VF and other MOF were identified in NPR according to pre-specified ICD codes. Each fracture outcome was analysed separately. Poisson regression was used to calculate IRs and incidence rate ratios (IRRs), overall and stratified by sex. Kaplan-Meier curves were plotted.
Results: In total 807 (7.0%) of patients with AS and 3201 (5.5%) of matched controls had a history of prior fracture within a 6-year period, and were excluded from further analyses. We noted higher IRs for any fracture, VF and other MOF in AS vs controls, see Figure for Kaplan-Meier curves and Table for IRs and IRRs. In sex-stratified analyses, men with AS (vs. male controls) had a higher relative risk for all fracture outcomes, whereas among women with AS (vs. female controls), a higher relative risk was demonstrated for any fracture and VF. 5-year cumulative incidence for any fracture, VF and other MOF was 6.2%, 1.6% and 1.7%, respectively in AS and 4.3%, 0.3% and 1.2%, respectively in controls.

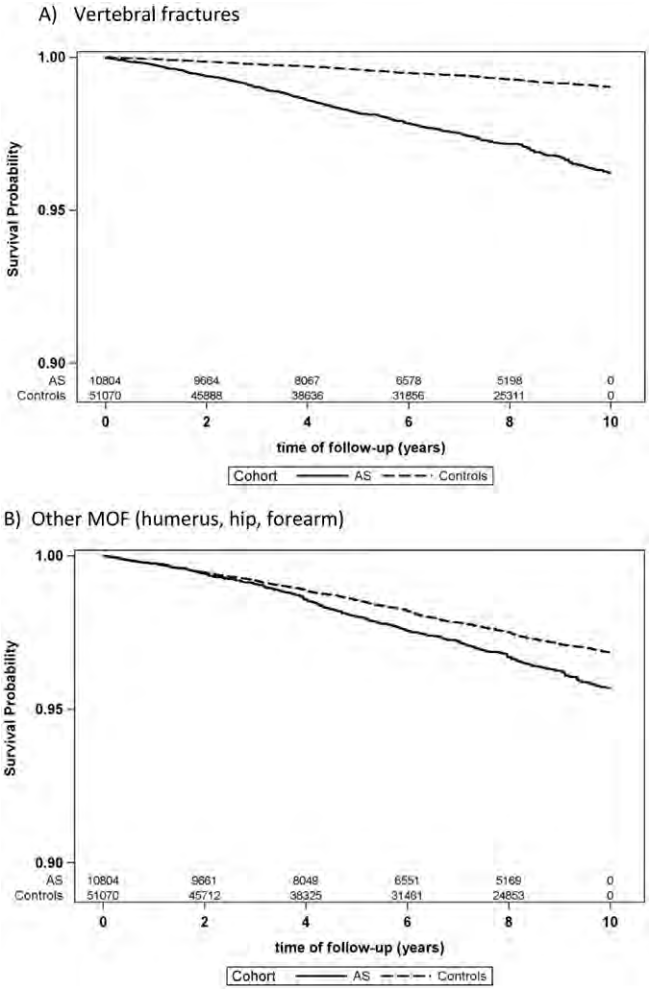


Figure. Kaplan-Meier curves. A) Vertebral fractures B) Other MOF (humerus, hip, forearm)

Conclusion: Patients with AS have a higher risk of any fracture, VF and other MOF compared to general population. This was especially pronounced for VF in both sexes and for hip fracture in men with AS.

Table. IRs, presented as number of events per 1000 person-years at risk, and IRRs for each fracture outcome.

	AS		Controls		AS vs Controls
	Event	IR (95% CI)	Event	IR (95% CI)	IRR (95% CI)
Any fracture	1060	14.9 (14.1 to 15.9)	3605	10.5 (10.2 to10.9)	1.4 (1.3 to 1.5)
-Men	685	14.6 (13.5 to 15.7)	2282	10.1 (9.7 to 10.5)	1.4 (1.3 to 1.6)
-Women	375	15.6 (14.1 to 17.3)	1323	11.3 (10.7 to 12.0)	1.4 (1.2 to 1.5)
Vertebral fractures	277	3.7 (3.3 to 4.2)	328	0.9 (0.8 to 1.0)	4.1 (3.5 to 4.8)
-Men	206	4.2 (3.7 to 4.8)	230	1.0 (0.9 to 1.1)	4.3 (3.6 to 5.2)
-Women	71	2.8 (2.2 to 3.5)	98	0.8 (0.7 to 1.0)	3.5 (2.6 to 4.7)
MOF (humerus, hip, forearm)	311	4.2 (3.8 to 4.7)	1105	3.1 (2.9 to 3.3)	1.3 (1.2 to 1.5)
-Men	176	3.6 (3.1 to 4.2)	540	2.3 (2.1 to 2.5)	1.5 (1.3 to 1.8)
-Women	135	5.4 (4.6 to 6.4)	565	4.7 (4.3 to 5.2)	1.1 (0.9 to 1.4)
MOF humerus	78	1.0 (0.8 to 1.3)	283	0.8 (0.7 to 0.9)	1.3 (1.0 to 1.7)
-Men	42	0.8 (0.6 to 1.1)	137	0.6 (0.5 to 0.7)	1.5 (1.0 to 2.1)
-Women	36	1.4 (1.0 to 2.0)	146	1.2 (1.0 to 1.4)	1.2 (0.8 to 1.7)
MOF hip	93	1.2 (1.0 to 1.5)	260	0.7 (0.6 to 0.8)	1.7 (1.4 to 2.1)
-Men	70	1.4 (1.1 to 1.8)	173	0.7 (0.6 to 0.9)	1.9 (1.5 to 2.5)
-Women	23	0.9 (0.6 to 1.4)	87	0.7 (0.6 to 0.9)	1.3 (0.8 to 2.0)
MOF forearm	156	2.1 (1.8 to 2.4)	631	1.8 (1.6 to 1.9)	1.2 (0.99 to 1.4)
-Men	73	1.5 (1.2 to 1.9)	262	1.1 (1.0 to 1.3)	1.3 (1.0 to 1.7)
-Women	83	3.3 (2.7 to 4.1)	369	3.1 (2.8 to 3.4)	1.1 (0.8 to 1.4)

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FRI0311 TRANSVERSAL STUDY OF CARDIAC RHYTHM DISORDERS IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Ankylosing spondylitis (AS) has been associated with different comorbidities, particularly some of cardiac origin. Recently, some studies have been published that suggest that certain arrhythmias may be more frequent in AS than in the general population.

Objectives: To estimate the prevalence of arrhythmias in patients diagnosed of AS in our environment and to compare it with that of the general population.

Methods: Descriptive cross-sectional study in patients diagnosed with AS by New York criteria, seen in our Department from 1st January 2018 to 30th March 2019, with age ≥ 18 years. A baseline 12-lead ECG was performed unless patients already had an ECG or a 24-hour Holter in the previous year. Likewise, demographic and disease-related variables were collected, such as: sex, age, body mass index (BMI), HLA-B27, year of diagnosis, pattern of involvement, comorbidities, ESR and CRP, BASFI and BASDAI (scales of 0 to 100), questionnaire about physical exercise, tobacco habits and treatments received. Descriptive statistical analysis was performed by calculating means with their standard deviation (SD) and percentages with their confidence intervals (CI). Prevalence of arrhythmias obtained in AS was compared with studies that determined the prevalence in the general population (statistical tool: SPSS).

Results: 117 patients with AS (62.4% men), mean age 54.8 years (± SD: 15.7), disease progression of 14.7 ± 9.6 years were included. HLA B27 was positive in 75.4%. Mean values of ESR and CRP were 14.4 mm/h and 0.6 mg/dl, respectively, and the average of the BASFI and BASDAI scores were 26/100 and 30/100, respectively. The prevalence of heart rhythm disorders was 19.7% (95% CI 12.3-27.0), which was significantly associated with advanced age, arterial hypertension and body mass index (BMI). No association was found with other activity or functional disease parameters (CRP, BASDAI, BASFI). The rhythm disorders found were: 9.4% (95% CI: 4.0-14.8) of the patients presented supraventricular tachyarrhythmias; 7.7% (95% CI: 2.7-12.6) had atrioventricular blocks and 6.8% (95% CI: 2.2-11.5) intraventricular conduction disorders. Although no differences were found regarding the prevalence described in the general population, an associative trend was observed, although it did not reach statistical significance probably due to the small sample size recruited.

Conclusion: There seems to be an increased tendency of heart rhythm disorders in patients with AS compared to the general population, which may have clinical and therapeutic implications. However, studies with larger sample size are needed to corroborate these results. In addition, there was a relationship between the presence of arrhythmias and certain pro-inflammatory situations (older age and BMI, although not CRP), which supports the hypothesis that some underlying inflammation status in these patients could partly justify an increased arrhythmogenesis.

Disclosure of Interests: Carlos Rodríguez-López: None declared, Esther Vicente Speakers bureau: BMS, Roche., Eva Tomero Muriel: None declared, Juan Pedro López-Bote: None declared, Lorena Vega: None declared, Isidoro González-Álvaro Grant/research support from: Roche Laboratories, Consultant of: Lilly, Sanofi, Paid instructor for: Lilly, Speakers bureau: Abbvie, MSD, Roche, Lilly, Alicia Humbría: None declared, Jesús Jiménez Borreguero: None declared, Rosario Garcia de Vicuna Grant/research support from: BMS, Lilly, MSD, Novartis, Roche, Consultant of: Abbvie, Biogen, BMS, Celltrion, Gebro, Lilly, Mylan, Pfizer, Sandoz, Sanofi, Paid instructor for: Lilly, Speakers bureau: BMS, Lilly, Pfizer, Sandoz, Sanofi, Fernando Alfonso Manterola: None declared, Santos Castañeda: None declared

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FRI0312 ANTI-CD74 IGA ANTIBODIES ARE MOST SENSITIVE AND SPECIFIC TO IDENTIFY YOUNG MALE AXIAL SPONDYLOARTHRITIS PATIENTS

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Background: CD74 is involved in the assembly of and the prevention of premature peptide-binding to major histocompatibility complex (MHC) class II. IgG autoantibodies directed against CD74 have been shown to be highly prevalent in patients with ankylosing spondylitis (AS). In contrast, conflicting results have been reported on the sensitivity and specificity of anti-CD74 IgA both in patients with non-radiographic axial spondyloarthritis (nr-axSpA) as well as AS.

Objectives: To assess the performance of anti-CD74 IgA for identification of patients classified as nr-axSpA or AS compared to non-SpA controls.

Methods: Serum samples of patients who were classified as having axial SpA according to the ASAS classification criteria, were collected at inclusion in the Be-Giant (a Belgian observational cohort enrolling patients in 7 peripheral and an academic hospital). Patients with chronic back pain of non-inflammatory origin and rheumatoid arthritis patients without back pain served as a control group. Serum aliquots were stored immediately after sampling at -80°C until further analysis. Anti-CD74 IgA antibodies were measured using the AESKULISA SpA Detect Kit (AESKU Diagnostics, Wendelsheim, Germany) as described in (1); values are expressed in U/mL. Analyses were restricted to patients ≤ 45 years of age who were anti-TNF naïve prior to inclusion.

Results: Table 1 shows the patients' demographic and clinical characteristics. Mean±SD anti-CD74 IgA concentration was significantly higher in AS (18.3±11.20) and nr-axSpA (19.3±12.6) compared to controls (9.8±6.35) (Figure 1). However, anti-CD74 IgA levels were higher in males than in females ($p = 0.01$) and in old (≥32 y/o) vs. younger patients ($p = 0.13$). Anti-CD74 IgA yielded an adjusted OR (95% CI) of 1.10 (1.03 – 1.19) for discrimination of nr-axSpA from controls. Table 2, which shows the performance of anti-CD74 IgA in 4 subgroups of patients divided by age and sex, shows that the highest AUC was seen in young male nr-axSpA patients. Similar results were found

on the discrimination between AS patients and controls (AUC 0.827 in young males).

Table 1. Demographic and clinical characteristics

	nr-axSpA	AS	control
	n = 150	n = 58	n = 14
Age, y (mean, SD)	31 (6.9)	32 (7.4)	30 (7.0)
Male, n (%)	68 (45.3)	26 (44.8)	4 (28.5)
Symptom duration, m (median, IQR)	35 (13 - 98)	111 (27 - 176)	-
HLA B27 positive, n (%)	103 (68.7)	48 (82.8)	-
Peripheral manifestations, n (%)	41 (27.3)	18 (31.0)	-
Extra-articular manifestations, n (%)	32 (21.3)	19 (32.8)	-
BASDAI (mean, SD)	4.4 (1.97)	4.1 (2.03)	-
CRP > ULN, n (%)	45 (30.0)	33 (56.9)	-

Table 2. Performance of anti-CD74 IgA in discriminating nr-axSpA from controls, according to sex and age (young: <32 y/o). AUC= area under the curve, PPV/NPV = positive/negative predictive value, LR+ = positive likelihood ratio.

	Cut-off (U/mL)	AUC	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	LR+
Male & young	16.9	0.806	65.8	92.3	96.2	48.0	8.6
Male & old	17.4	0.795	55.6	92.3	93.8	50.0	7.2
Female & young	16.7	0.647	50.0	92.3	94.4	41.4	6.5
Female & old	16.9	0.741	46.8	92.3	95.7	42.2	6.0

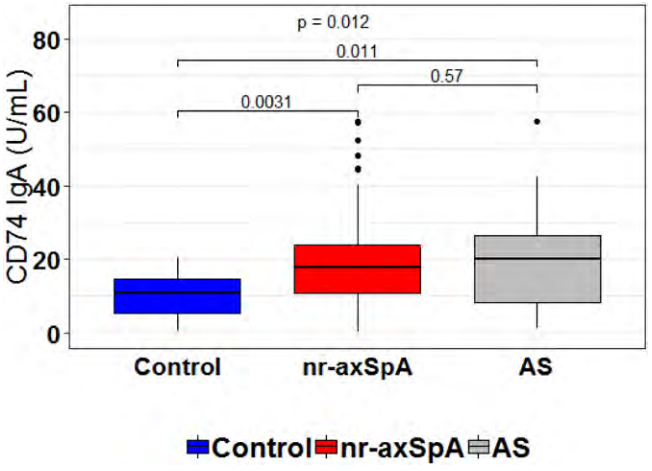


Figure 1. Univariate comparison of anti-CD74 IgA concentrations between nr-axSpA, AS and control patients (<45 y/o).

Conclusion: In this study, mean anti-CD74 IgA concentrations were higher in axial SpA patients compared to non-SpA controls. Application of this biomarker in young (<32 y/o) male nr-axSpA or AS patients yielded the highest sensitivity and specificity.

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FRI0313 DOES INTERSTITIAL LUNG DISEASE REPRESENT A REAL COMORBIDITY IN SPONDYLOARTHRITIS PATIENTS? RESULTS FROM AN ULTRASOUND MONOCENTRIC PILOT STUDY

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Background: Interstitial lung disease (ILD) is a frequent complication in rheumatoid arthritis (RA) where it represents the most common extra-articular involvement (with a prevalence of about 10-60%) and the second cause of mortality (after cardiovascular diseases). Spondyloarthritides (SpA) are chronic arthritides that share with RA both a similar disease burden and similar therapeutical approaches. ILD evaluation is challenging, given the low sensitivity of X-ray and pulmonary function tests, and radiation linked to repetitive HRCT. Lung Ultrasound (LUS) has shown potential in the evaluation of ILD in autoimmune diseases.

Objectives: To assess the prevalence of ILD in a cohort of SpA patients (pts) using LUS with respect to healthy controls (HC).

Methods: Consecutive SpA out-pts were examined by LUS, applying the definition for pleural line irregularity (PLI) recently provided by the OMERACT taskforce for LUS in systemic sclerosis (1). Seventy-one intercostal spaces were studied (14 in the anterior chest, 27 lateral and 30 posterior) in all the pts/HC using an Esaote MyLab25 Gold US machine with a linear 7.5-10 MHz probe. The scoring system by Pinal-Fernandez et al (2) was applied and a total pleural score was calculated. Each patient answered to Italian-validated PROs on respiratory function (Leicester and Saint-George), global health (SF-36) and dyspnea (mMRC scale). Clinical data on disease-duration, disease-onset, disease-activity (at the moment of the examination) and MTX/biologics treatment were collected from the medical records.

Results: Fifty-six SpA pts (35 psoriatic arthritis -PsA- and 21 ankylosing spondylitis -AS-) and 56 HC were studied. No significant differences were demonstrated between groups (SpA vs HC and PsA vs AS) for age, sex, BMI and smoking habits. The total pleural score was significantly higher in SpA pts than in HC (20.9±11.8 vs 10.3±7.7; p<0.001). A positive correlation was found between total PLI score and PLI score from anterior, posterior and lateral chest. The posterior part of the chest showed a higher PLI score than the anterior and lateral one (with the latter resulting to be significantly lower than the posterior PLI score). Higher differences in the PLI average value between SpA pts and HC were registered for posterior and anterior part of the chest. No differences were found between PsA and AS (with a not statistically significant difference in the posterior PLI score, which was slightly higher in AS pts) (Tab.I).

Table 1. average PLI score (N±SD)

	Total	Anterior	Posterior	Lateral
HC	10.3 ± 7.7	4 ± 3.2	5 ± 3.7	1.4 ± 2.2
PsA	20.1 ± 12.5	6.8 ± 3.9	10.2 ± 6.9	2.9 ± 4.1
AS	22.1 ± 10.7	7 ± 2.8	12 ± 9.5	3 ± 3.1

Conclusion: LUS examination shows a higher amount of PLI in SpA with respect to HC.

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Disclosure of Interests: Andrea Delle Sedie Speakers bureau: MSD, Lilly, Novartis, Abbvie, Celgene, Emanuele Calabresi: None declared, Ilaria Romagnoli: None declared, Linda Carli: None declared, Marta Mosca: None declared

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FRI0314 ANNUAL DIAGNOSTIC PREVALENCE OF ANKYLOSING SPONDYLITIS (AS) IN THE UNITED STATES USING MEDICARE AND MARKETSCAN DATA

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Background: Axial spondyloarthritis (axSpA) is a chronic inflammatory disease that affects the axial skeleton and sacroiliac joints, and can be classified as ankylosing spondylitis (AS) or non-radiographic (nr)-axSpA.[1] A 2016 analysis estimated the US diagnostic prevalence of axSpA to be 0.2% and AS to be 0.1%.[2] Previous studies use disparate populations and diagnostic definitions;[3,4] it is therefore unclear how AS prevalence has changed over time.

Objectives: To investigate the annual diagnostic prevalence of AS in US healthcare insurance claims databases.
Methods: A retrospective, observational cohort study was conducted using 2006–2014 data from US Medicare Fee-for-Service Claims (5% random sample of all enrolled patients [pts]) and Truven MarketScan®. Eligible pts were ≥20 years (yrs) and had ≥6 months of continuous medical and pharmacy enrolment prior to diagnosis. Diagnoses used relevant International Classification of Disease, 9th version (ICD-9) diagnosis codes: ICD-9 720.x [x=any number] for "AS and other inflammatory spondylopathies [SpA]" or 720.0 for "AS". Two diagnosis definitions were used: Definition 1, ≥1 relevant ICD-9 code from hospital discharge or ≥2 from rheumatologist visit; Definition 2, ≥1 relevant ICD-9 code from hospital discharge or rheumatologist visit. Annual diagnostic prevalence of SpA/AS was calculated as "number of enrolled pts who met the definition of SpA/AS within each calendar yr and had full insurance coverage (medical and pharmacy)", divided by "total number of pts with full insurance coverage in the same yr". A primary analysis of SpA prevalence rates used Definitions 1 and 2, followed by a sensitivity analysis for AS prevalence rates using only Definition 2. All prevalence rates are shown per 10,000 pts enrolled.
Results: The annual diagnostic prevalence of SpA appeared to increase from 2006–2014 (**Table**). Similarly, the sensitivity analysis showed the annual diagnostic prevalence of AS appeared to increase during the period from 2006 (Medicare: 2.87/10,000 pts [n=501,031]; MarketScan: 1.37/10,000 pts [n=17,562,637]) to 2014 (Medicare: 4.77/10,000 pts [n=1,046,107]; MarketScan: 2.14/10,000 pts [n=34,553,135]; **Figure**).
Conclusion: The apparent increase in diagnostic prevalence of SpA and AS during the period from 2006–2014 may be a consequence of increased awareness and availability of effective treatments. Furthermore, the 2009 Assessment of SpondyloArthritis international Society development of the axSpA classification criteria to include pts with both established AS and nr-axSpA may have accelerated this increase.[5]
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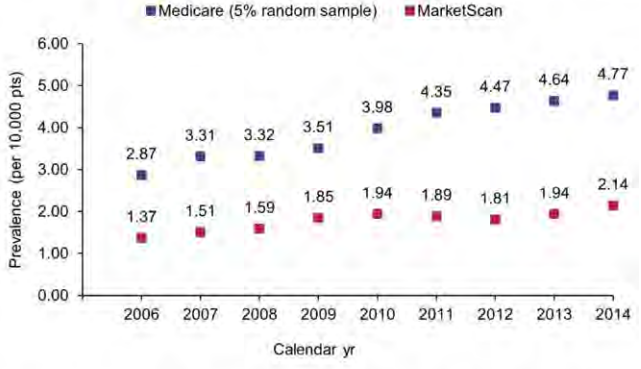
Table. Prevalence of SpA by calendar year and data source

Calendar yr	Medicare (5% random sample)			MarketScan		
	Total number of eligible pts	Prevalence/ 10,000 pts		Total number of eligible pts	Prevalence/10,000 pts	
		Definition 1	Definition 2		Definition 1	Definition 2
2006	501,031	4.39	7.62	17,562,637	1.33	2.17
2007	816,970	5.25	8.72	19,518,066	1.47	2.37
2008	825,445	4.89	8.78	28,603,525	1.58	2.53
2009	830,967	5.22	9.21	31,757,069	1.90	3.09
2010	844,528	5.49	9.90	31,126,172	1.96	3.17
2011	879,996	6.30	10.71	38,295,121	1.94	3.11
2012	921,994	6.17	10.88	40,320,437	1.91	3.04
2013	1,032,827	6.74	10.82	33,826,041	2.00	3.19
2014	1,046,107	6.52	10.85	34,553,135	2.21	3.51

Medicare data included a 5% random sample of all enrolled pts age ≥20 yrs. pts: patients; SpA: ankylosing spondylitis and other inflammatory spondylopathies; yr: year.

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Figure. Prevalence of AS (Definition 2) by calendar year and data source



Medicare data included a 5% random sample of all enrolled pts age ≥20 yrs. AS was defined according to Definition 2. AS: ankylosing spondylitis; pts: patients; yr: year.

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FRI0315

GENDER DIFFERENCES IN PATIENT JOURNEY TO DIAGNOSIS AND PATIENT-REPORTED OUTCOMES: RESULTS FROM THE EUROPEAN MAP OF AXIAL SPONDYLOARTHRITIS (EMAS)

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Background: Growing evidence of similarities in male-female prevalence of axial spondyloarthritis (axSpA) has stimulated the need to evaluate gender differences in patient experiences.
Objectives: To evaluate gender differences in diagnostic journey, disease-characteristics and patient-reported outcomes (PROs) in axSpA patients.
Methods: Data from 2846 unselected patients of the European Map of Axial Spondyloarthritis (EMAS) through an online survey (2017-2018) across 13 countries were analysed. Socio-demographic characteristics, diagnosis, disease-characteristics, and PROs [BASDAI (0-10), spinal stiffness (3-12), functional limitation (0-54) and psychological distress (0-12, GHQ-12)] were compared between genders. X^2 (for categorical variables) and student-t (for continuous variables) were employed.
Results: 1,746 (61.3%) females participated in the EMAS, with homogeneous gender distribution across most countries (Fig 1). Compared to males, females reported longer diagnostic delay (6.1±7.4 vs 8.2±8.9; p<0.001), more visits to physiotherapists (34.5% vs 49.5%; p<0.001) and osteopaths (13.3% vs 24.4%; p<0.001) before being diagnosed (Table 1), higher disease activity in all BASDAI items and greater functional limitation, psychological distress and self-reported anxiety and depression (Table 2).

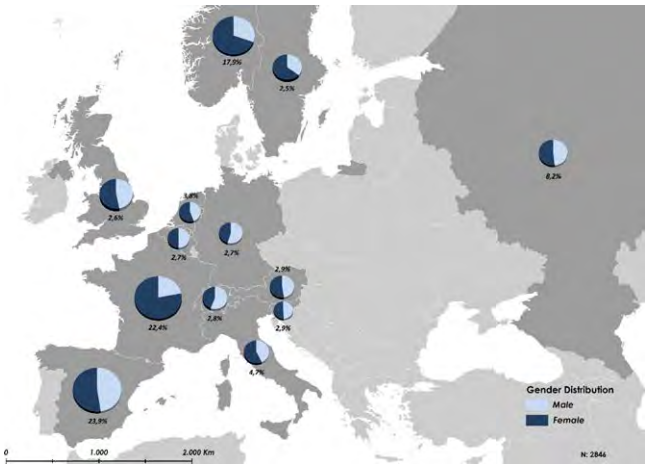


Figure 1. Countries' sample distribution stratified by gender (N: 2846)

Table 1. Disease characteristics by gender (N: 2846, unless specified)

	Men (n: 1100) (mean ± SD or %)	Women (n: 1746) (mean ± SD or %)	p value
Age at onset of first symptoms, n: 2721	27.0 ± 11.8	26.4 ± 10.7	0.342
Age at diagnosis, n: 2722	32.6 ± 12.2	34.4 ± 10.9	<0.001
Diagnostic delay, n: 2652	6.1 ± 7.4	8.2 ± 8.9	<0.001
Disease Duration, n: 2716	18.9 ± 13.3	16.1 ± 11.7	<0.001
HCP seen before diagnosis			
- General practitioner	822 (74.7)	1434 (82.1)	<0.001
- Orthopaedic specialist	377 (34.3)	557 (31.9)	0.190
- Physiotherapist	380 (34.5)	865 (49.5)	<0.001
- Osteopath, n: 2166	103 (13.3)	339 (24.4)	<0.001
- Other, n: 2220	135 (14.0)	233 (18.5)	0.005
Family history of axSpA (yes), n: 2244	291 (33.5)	584 (42.5)	<0.001
HLA-B27 (positive), n: 1799	497 (80.2)	786 (66.7)	<0.001
Uveitis (yes), n: 2096	199 (25.2)	270 (20.7)	0.023
IBD (yes), n: 2096	113 (14.3)	181 (13.9)	0.688

Table 2. PROs by gender (N: 2846, unless specified)

	Men (n: 1100) (mean ± SD or %)	Women (n: 1746) (mean ± SD or %)	p value
BASDAI, (0-10) n: 2584	5.1 ± 2.0	5.7 ± 1.9	**<0.001**
- Fatigue, n: 2636	5.7 ± 2.4	6.6 ± 2.2	<0.001
- Neck, back or hip pain, n: 2636	5.6 ± 2.4	6.2 ± 2.2	<0.001
- Pain other than neck, back or hip, n: 2636	4.3 ± 2.7	4.9 ± 2.6	<0.001
- Discomfort to touch or pressure, n: 2636	4.5 ± 2.7	5.6 ± 2.6	<0.001
- Morning stiffness level, n: 2636	5.3 ± 2.6	5.9 ± 2.6	<0.001
- Morning stiffness duration, n: 2584	4.5 ± 2.8	4.7 ± 2.8	0.070
Stiffness, (3-12) n: 2707	7.7 ± 2.6	7.8 ± 2.4	0.107
Functional Limitation, (0-54) n: 2771	19.1 ± 16.7	21.2 ± 16.0	<0.001
GHQ-12 ≥3, n: 2640	564 (55.4)	1060 (65.4)	<0.001
Anxiety	243 (30.6)	566 (43.3)	<0.001
Depression	238 (30.1)	472 (36.1)	<0.001

Conclusion: Important gender differences are observed in axSpA such as a longer patient journey to diagnosis, poorer PROs, and greater psychological burden in females. These results point to unmet needs in females with axSpA, requiring particular attention.

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FRI0316

CAN THE MOMENT OF OCCURRENCE OF THE FIRST EPISODE OF UVEITIS PREDICT DIFFERENCES IN THE PROGNOSIS OF SPONDYLOARTHRITIS? DATA FROM THE SPANISH REGISTRY REGISPONSER

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Background: Uveitis is one of the most usual extraaxial manifestations of spondyloarthrities (SpA) but the impact of the date of the onset is no well-known.

Objectives: a) To assess the prevalence of acute anterior uveitis (AAU) in the Spanish population with SpA; b) To describe the time of appearance of the AAU regarding to the onset of rheumatic symptoms and SpA diagnosis; c) To evaluate the impact of the moment of appearance of the AAU on the treatment and disease activity.

Methods: A cross-sectional study with data extracted from REGISPONSER registry. First, the prevalence of AAU was determined. Patients were classified as AAU before/ concomitant/ after the onset of rheumatic symptoms and as AAU before/ concomitant/ after the SpA diagnosis regarding the date of appearance of each symptom and SpA diagnosis. Treatment and disease activity were compared between 'AAU before or concomitant with rheumatic symptoms' vs. 'AAU after rheumatic symptoms' groups, as well as 'AAU before or concomitant with SpA diagnosis' vs. 'AAU after the SpA diagnosis' groups using Chi-square and T-Student tests.

Results: Among the 2346 patients included in REGISPONSER, 379 (16.2%) had at least one episode of AAU. Information concerning the date of occurrence of rheumatic symptoms and SpA diagnosis was available in 280 and 284 patients, respectively. A total of 28 (9.7%), 31 (10.8%) and 229 (79.5%) patients suffered the first episode of AAU before, concomitantly and after the rheumatic symptoms, respectively; while 108 (38.0%), 38 (13.4%) and 138 (48.6%) suffered the episode of AAU before, concomitantly and after the SpA diagnosis, respectively. The comparison of patients with 'AAU before or concomitant with rheumatic symptoms' vs 'AAU after rheumatic symptoms' (Table 1), showed in the second group a younger age of symptoms onset, a greater diagnosis delay, higher disease activity (CRP and BASDAI), greater structural damage (BASRI). No significant differences were found in the use of biological (27.9% vs. 23.2%) or synthetic DMARDs (14.8% vs. 20.3%). The comparison of 'AAU before or concomitant with the SpA diagnosis' vs. 'AAU after the SpA diagnosis' groups (Table 1) showed similar results to the previous ones with no significant differences were obtained in the use of biological (28.8% vs 20.4%) or synthetic (17.2% vs 20.4%) DMARDs.

Conclusion: These results suggest that patients who presented the first episode of AAU prior to the onset of rheumatic symptoms showed a later start of the disease with a shorter diagnosis delay, lower disease activity and less structural damage.

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FRI0317

CONSENSUS DEFINITIONS FOR MRI LESIONS IN THE SPINE OF PATIENTS WITH AXIAL SPONDYLOARTHRITIS: FIRST ANALYSIS FROM THE ASSESSMENTS IN SPONDYLOARTHRITIS INTERNATIONAL SOCIETY CLASSIFICATION COHORT

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	AAU regarding the rheumatic symptoms onset (n=280)			AAU regarding the SpA diagnosis (n=284)		
	Before or concomitant N = 61 (%)	After N = 229 (%)	p	Before or concomitant N = 146 (%)	AfterN = 138 (%)	p
Gender (male)	32/61 (52,5%)	160/229 (69,9%)	NS	88/146 (60,3%)	100/138 (72,5%)	NS
Age of symptoms onset (years), mean (SD)	31,02 (9,12)	24,49 (9,89)	<0,001	27,01 (9,77)	24,66 (9,65)	0,042
Diagnosis delay (years), mean (SD)	3,00 (4,98)	9,68 (10,73)	<0,001	10,90 (11,76)	5,59 (7,32)	<0,001
Clinical classification						
Axial	40/61 (65,%)	144/228 (62,9%)	NS	96 (66,2%)	85 (61,6%)	NS
Peripheral	4/61 (6,6%)	9/228 (4,0%)	NS	7 (4,8%)	4 (2,9%)	NS
Mixed	17/61 (27,9%)	75/228 (32,9%)	NS	42 (29%)	47 (34,1%)	NS
HLAB27+	50/57 (87,7%)	195/213 (91,5%)	NS	119/135 (88,1%)	121/130 (93,1%)	NS
ESR (mm/h), mean (SD)	16,47 (12,88)	18,04 (16,34)	NS	17,44 (15,57)	18,41 (16,27)	NS
CRP (mg/l), mean (SD)	5,57 (9,63)	8,96 (11.62)	0,044	6,82 (9,88)	9,86 (12,65)	0,031
BASDAI, mean (SD)	3,57 (2,25)	4,31 (2,33)	0,027	3,92 (2,30)	4,42 (2,37)	0,073
Spinal BASRI, mean (SD)	3,00 (2,63)	6,06 (3,58)	<0,001	4,99 (3,31)	5,60 (5,45)	NS

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Background: A recent consensus from the ASAS MRI group has culminated in updated spine lesion definitions for axial spondyloarthritis (ASAS_MRI_def^n)[1]. There has been no central reader evaluation of MRI scans from the ASAS Classification Cohort (ASAS-CC)[2] to determine the spectrum of MRI lesions in the spine in this cohort.

Objectives: To determine the spectrum of active and structural lesions on MRI images of the spine from the ASAS-CC according to the consensus ASAS_MRI_def^n update.

Methods: ASAS_MRI_def^n were recorded by 9 central readers in an eCRF for global assessment and detailed scoring of each discovertebral unit and postero-lateral structures. Vertebral corner bone marrow edema (VCBME) and corner fat (VCFAT) lesions were recorded if present on 2 slices; facet joint, lateral, and posterior inflammatory lesions were recorded if present on a single slice. Vertebral corner erosion, bone spurs, and ankylosis were each scored on a single slice. Comparison of active and structural lesion frequencies by local rheumatologist diagnosis of axSpA was assessed descriptively according to ≥2 and majority reader (≥5/9) concordant data.

Results: MRI scans of the spine were available from 69 cases with axSpA diagnosed in 44/64 (68.8%). VCBME was most frequent with ≥1 lesion in 32(46.4%) and 19 (27.5%) by ≥2 and ≥5/9 readers, respectively. VCFAT was the most frequent structural lesion with ≥1 lesion in 24 (34.8%) and 14 (20.3%) by ≥2 and ≥5/9 readers, respectively. There were significantly more VCBME lesions in axSpA patients than non-axSpA (mean(SD):1.8(2.7) vs 0.3 (0.5)) (p<0.001) while differences in VCFAT were not significant (Table). The presence of ≥2 VCBME had 90-95% specificity for axSpA. Significantly more VCBME and VCFAT were observed in the setting of radiographic sacroiliitis (modified New York criteria (mNY)).

Conclusion: Spine lesions on MRI are relatively frequent in patients with undiagnosed back pain presenting to the rheumatologist. The presence of ≥2 VCBME, but not VCFAT, may have some diagnostic utility.

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Vertebral Corner MRI lesions	majority of readers (>=5)			≥2 readers		
	axSpA=Yes (n=44)	axSpA=No (n=20)	p-value	axSpA=Yes (n=44)	axSpA=No (n=20)	p-value
Corner Fat ≥1	12 (27.3%)	2 (10%)	0.19	17 (38.6%)	7 (35%)	0.78
Corner Fat ≥2	10 (22.7%)	2 (10%)	0.31	13 (29.5%)	4 (20%)	0.64
Corner Fat ≥3	8 (18.2%)	1 (5%)	0.25	10 (22.7%)	3 (15%)	0.74
Corner Fat ≥4	7 (15.9%)	1 (5%)	0.42	9 (20.5%)	2 (10%)	0.48
Corner BME ≥1	17 (38.6%)	1 (5%)	0.006	25 (54.5%)	6 (30%)	0.047
Corner BME ≥2	15 (34.1%)	1 (5%)	0.013	19 (43.2%)	2 (10%)	0.009
Corner BME ≥3	11 (25%)	0 (0%)	0.013	16 (36.4%)	1 (5%)	0.008
Corner BME ≥4	8 (18.2%)	0 (0%)	0.094	12 (27.3%)	1 (5%)	0.048
	mNY=Yes (n=10)	mNY=No (n=49)	p-value	mNY=Yes (n=10)	mNY=No (n=49)	p-value
Corner Fat ≥1	5 (50%)	9 (18.4%)	0.047	5 (50%)	17 (34.7%)	0.48
Corner Fat ≥2	5 (50%)	7 (14.3%)	0.022	5 (50%)	11 (22.4%)	0.12
Corner Fat ≥3	4 (40%)	5 (10.2%)	0.036	4 (40%)	9 (18.4%)	0.20
Corner Fat ≥4	4 (40%)	4 (8.2%)	0.022	4 (40%)	7 (14.3%)	0.079
Corner BME ≥1	5 (50%)	11 (22.4%)	0.116	7 (70%)	22 (44.9%)	0.18
Corner BME ≥2	5 (50%)	9 (18.4%)	0.047	5 (50%)	14 (28.6%)	0.27
Corner BME ≥3	5 (50%)	6 (12.2%)	0.014	5 (50%)	11 (22.4%)	0.12
Corner BME ≥4	5 (50%)	3 (6.1%)	0.002	5 (50%)	7 (14.3%)	0.022

Disclosure of Interests: Walter P. Maksymowych Grant/research support from: AbbVie, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Boehringer Ingelheim, Celgene, Eli Lilly, Galapagos, Janssen, Novartis, Pfizer, and UCB, Employee of: Chief Medical Officer of CARE Arthritis Limited, Speakers bureau: AbbVie, Janssen, Novartis, Pfizer, and UCB, Iris Eshed: None declared, Pedro M Machado Consultant of: PMM: Abbvie, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Roche and UCB, Speakers bureau: PMM: Abbvie, BMS, Lilly, MSD, Novartis, Pfizer, Roche and UCB, Susanne Juhl Pedersen Grant/research support from: Novartis, Ulrich Weber: None declared, Manouk de Hooge: None declared, Joachim Sieper Consultant of: AbbVie, Boehringer Ingelheim, Eli Lilly and Company, Janssen, Merck, Novartis, Pfizer, Roche, and UCB Pharma, Speakers bureau: AbbVie, Boehringer Ingelheim, Eli Lilly and Company, Janssen, Merck, Novartis, Pfizer, Roche, and UCB Pharma, Stephanie Wichuk: None declared, Denis Poddubnyy Grant/research support from: AbbVie, MSD, Novartis, and Pfizer, Consultant of: AbbVie, Bristol-Myers Squibb, Eli Lilly, MSD, Novartis, Pfizer, Roche, UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, MSD, Novartis, Pfizer, Roche, UCB, Martin Rudwaleit Consultant of: AbbVie, BMS, Celgene, Janssen, Eli Lilly, MSD, Novartis, Pfizer, Roche, UCB Pharma, Désirée van der Heijde Consultant of: AbbVie, Amgen, Astellas, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Cyxone, Daiichi, Eisai, Eli-Lilly, Galapagos, Gilead Sciences, Inc., Glaxo-Smith-Kline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB Pharma; Director of Imaging Rheumatology BV, Robert B.M. Landewé Consultant of: AbbVie; AstraZeneca; Bristol-Myers Squibb; Eli Lilly & Co.; Galapagos NV; Novartis; Pfizer; UCB Pharma, Robert G Lambert: None declared, Mikkel Østergaard Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Merck, and Novartis, Consultant of: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo Nordisk, Orion, Pfizer, Regeneron, Roche, Sandoz, Sanofi, and UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo Nordisk, Orion, Pfizer, Regeneron, Roche, Sandoz, Sanofi, and UCB, Xenofon Baraliakos Grant/research support from: Grant/research support from: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB and Werfen, Consultant of: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB and Werfen, Speakers bureau: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB and Werfen

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FRI0318 REAL-LIFE EVALUATION OF HEALTH STATUS USING ASAS HEALTH INDEX ON PATIENTS WITH AXIAL AND PERIPHERAL SPONDYLOARTHRITIS IN ARGENTINA

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Background: The questionnaire "Assessment of Spondyloarthritis international Society Health Index" (ASAS HI) was developed to measure functionality and health status in patients with spondyloarthritis (SpA)[1].

Objectives: To describe the state of health measured by ASAS HI in Argentinian patients with SpA and to evaluate factors associated with poor health.

Methods: Analytical, cross sectional, multicenter study. Patients with SpA according to ASAS criteria were consecutively included from 15 Argentinian centers. Statistical analysis: frequencies and percentages (%), mean and standard deviation (SD) or median and interquartile range (IQR). Bivariate analysis and logistic regression were performed to evaluate the factors associated with poor health status (ASAS HI > or equal to 12). Correlation with other parameters was evaluated by Spearman correlation.

Results: We included 274 patients with a mean age 49 (SD 14) years, median disease duration 60 month (IQR 24-135), 155 (56.6%) of patients are male, 47% (n:129) axial SpA and 52.9 (n:145) peripheral SpA. One hundred and nine patients (43.4%) presented good health status, 117 (42.7%) had moderate state of health and 38 (13.9%) had poor health. In the bivariate analyses patients with ASAS health index greater than or equal to 12 (poor status), were older [54 (11) vs 48 (14), p: 0.01], had higher disease duration [11(IQR 57-192) vs 60 (IQR 24-120), p: 0.02], more hypertension [20 (52.6%) vs 67 (28.4%), p:0.004], more diabetes mellitus [10 (26.3%) vs 22(9.3%), p: 0.006], depression [6 (15.8%) vs 10 (4.2%), p:0.013], anxiety [8 (21%) vs (22 (9.3%),p:0.046], less years of education [9.8 (SD 3.5) vs 13 (SD 10), p:0.001], higher ASQol [12.6 (SD 4.6) vs 5.7 (SD4), p < 0.001], BASFI [7(SD2) vs 4(SD6), p: 0.001], DAS28 [4.71 (SD3.2) vs 2.8 (SD1),p: <0.001]. In the multivariate analyses the following variables were independently associated with poor health status: duration of disease, ASQol and DAS28. ASAS HI showed positive correlation with the following parameters: BASDAI (r:0.67, p< 0.001), HAQ (r:0.54, p< 0.001), ASDAS (r:0.67, p< 0.001), ASQol (r:0.80, p< 0.001), BASFI (r:0.72, p< 0.001) and DAS28 (0.56, p< 0.001).

Table. Charactheristics of studies included in the meta-analysis and of the studied patients

Author and year	Design	Country	N° of patients	Age (years)	Male sex	HLAB27+	Disease duration (years)
Al-Osami 2018	cohort	Iran	170	36.1 (9.0)	158 (93)	68(40)	8.3 (5.9)
Durcan 2012	cross-sectional	Ireland	46	45.1(11.2)	35 (76)	N/D	12.9 (10.9)
Hernandez-Breijo 2019	cohort	Spain/Netherlands	180	47.0 (12.7)	107 (59)	131 (73)	8.0 (5.9)
Lee 2017	cross-sectional	China	194	38.7 (13.7)	150 (77)	159 (82)	7.1 (8.6)
Maas 2016	cross-sectional	Netherlands	461	45.3 (12.8)	303 (66)	361 (80)	17 (15.2)
Micheroli 2017	cohort	Switzerland	624	39.4 (11.6)	388 (62)	487 (78)	13 (10.9)
O'Shea 2015	cross-sectional	Ireland	267	47.8 (N/D)	212 (79)	N/D	21.7 (N/D)
Ottaviani 2012	cohort	France	155	43.1 (12.4)	98 (63)	96 (65)	8.0 (4.8)
Rosas 2017	cross-sectional	Spain/Mexico	57	47.1 (10.4)	37 (65)	44 (77)	9.8 (9.3)
Rubio-Vargas 2016	cross-sectional	Netherlands	168	30.2 (8.2)	81 (48.2)	156 (93)	N/D

Legend. Results are expressed as mean (SD) or number of patients (%). HLA= Human Leukocyte Antigen; N/D= not determined

Conclusion: Poor health status is associated with disease activity, poor quality of life and functional activity. ASAS HI has a good correlation with other parameters to evaluate SpA, reinforcing the construct validity of this new tool.

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FRI0319 DO OBESITY AND OVERWEIGHT INFLUENCE DISEASE ACTIVITY MEASURES IN AXIAL SPONDYLOARTHRITIS? A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: obesity is apparently related with worse treatment response in axial spondyloarthritis (axSpA). However, it is unclear whether obesity or overweight per se are associated to higher disease activity scores compared to non-obese individuals, and what is the effect size of this difference.

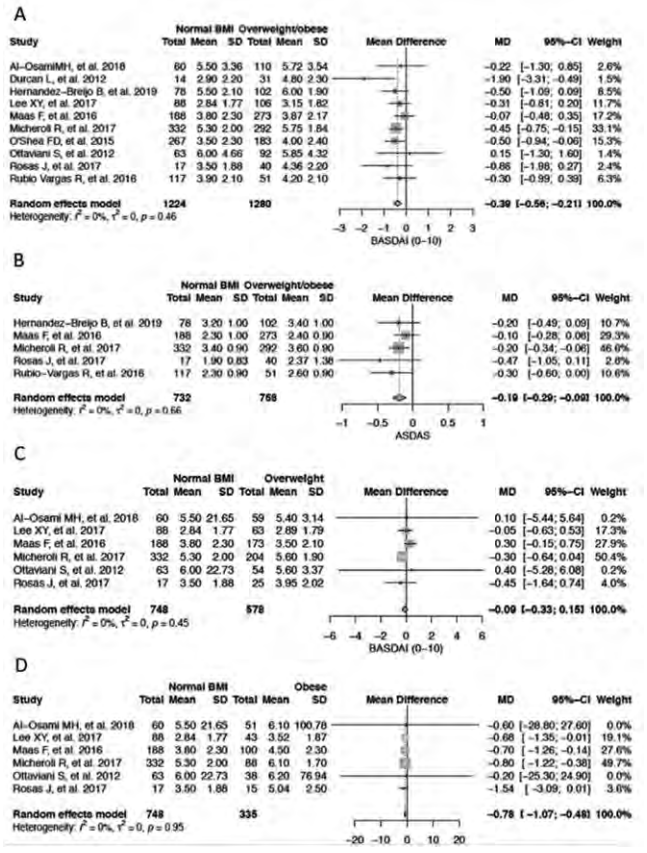
Objectives: to investigate whether overweight/obesity are associated to higher disease activity as measured by Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) or Ankylosing spondylitis disease activity score (ASDAS) in axSpA patients.

Methods: MEDLINE, PubMed and Web of Science were searched using key terms corresponding to population (axSpA), exposure (overweight/obesity) and outcome (BASDAI, ASDAS). Predefined inclusion criteria were: 1) adult axSpA patients, both radiographic and non-radiographic 2) exposure classified according to Body Mass Index-BMI-; 3) BASDAI/ASDAS reported for each BMI group; 4) observational studies. Patients classified according to CASPAR or Moll&Wright criteria for psoriatic arthritis were excluded. Newcastle-Ottawa Scale for cohort, cross-sectional and case-control studies was used for quality check. BASDAI and ASDAS estimates were reported as mean difference (MD) and standard deviation (SD) between the normal BMI axSpA patients and the overweight or obese patients. The statistical heterogeneity of meta-analysis was assessed using the I^2 statistic. Random-effects meta-analysis was used to pool results.

Results: A total of 330 references were generated by the database search. After removing duplicates, 250 references remained and were assessed for eligibility. A further 206 articles were excluded by titles and abstracts' reading, 44 articles were examined full text. Only 11 articles fulfilled inclusion/exclusion criteria. Following quality check, 10 articles were finally included in the meta-analysis (Table). Among these, 4 studies reported two BMI groups (normal vs overwight+obese), while 6 studies reported three (normal, overweight, obese). In the studies reporting 3 BMI group, weighted means and standard deviation were calculated to create a merged overweight+obese group. The mean difference (MD) between pooled BASDAI and ASDAS of normal BMI patients and those of overweight+obese patients were respectively -0.38 (95%CI: -0.56, -0.21) and -0.19 (95%CI: -0.29, -0.09). In the articles reporting 3 BMI groups, the MD between BASDAI of normal BMI and overweight only patients was -0.09 (95% CI: -0.33; 0.15); between normal BMI and obese only patients MD was -0.77 (95%CI -1.07; -0.48, p<0.0001) (Figure). Heterogeneity statistics revealed low estimates, though with wide CI across all the groups (Figure).

Conclusion: disease activity scores of normal BMI axSpA patients tend to be lower than overweight or obese patients. However, this difference seems to be relevant in practice especially when normal BMI patients are compared to truly obese patients (BMI ≥ 30).

Figure. Results of the meta-analysis of Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) in normal BMI vs overweight or obese individuals (A); in normal BMI vs overweight individuals (C); in normal BMI vs obese individuals (D); meta-analysis of Ankylosing spondylitis disease activity score (ASDAS) in normal BMI vs overweight or obese individuals (B)



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FRI0320 MULTICENTER VALIDATION OF THE DETECTION OF ARTHRITIS IN INFLAMMATORY BOWEL DISEASES (DETAIL) QUESTIONNAIRE FOR THE SCREENING OF SPONDYLOARTHRITIS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES

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Background: Spondyloarthritis (SpA) is the most frequent extra-intestinal manifestation in inflammatory bowel diseases (IBD), since it may occur in up to 25% of patients. The early referral to a Rheumatology Unit may lead to proper treatment and better outcomes for patients with suspect SpA. Recently, we have developed

and preliminarily validated a self-administered screening questionnaire, called DETection of Arthritis in Inflammatory boweL diseases (DETAIL)[1].
Objectives: To validate the DETAIL questionnaire in a multicenter cohort of IBD patients enrolled at ten Gastroenterology and Rheumatology Units in Italy.
Methods: The DETAIL instrument is a 6-item questionnaire developed through a Delphi method[1]. From October 2018 to March 2019, consecutive adult patients with IBD, Crohn's disease (CD) or ulcerative colitis (UC), filled out independently the DETAIL in the outpatient waiting room. Thereafter, within 2 weeks a blinded rheumatologist assessed all the patients, irrespectively of the DETAIL results, and classified them to be affected or not by SpA according to ASAS criteria. The performance of the DETAIL was evaluated trough Bayesian analysis, defining for each item of the questionnaire the sensitivity, specificity, positive (LR+) and negative (LR-) likelihood ratios.
Results: Overall, 418 IBD patients filled out the DETAIL questionnaire. Upon rheumatological evaluation, 102 (24.4%) patients received a diagnosis of SpA. Of the six questions, the best performances were found in item 6 (LR+ 3.77), reporting inflammatory back pain at night, and in item 3 (LR+ 3.31), exploring Achilles enthesitis. The presence of back pain lasting more than three months (LR+ 2.91), of back pain with inflammatory features (LR+ 2.55) and a history of dactylitis (LR+ 2.55), showed also a fairly good performance, whereas a history of peripheral synovitis was slightly worse (LR+ 2.16). The combination of at least three items answered affirmatively yielded a post-test probability of SpA of 75% or more. The presence of alternative diagnoses, such as osteoarthritis and fibromyalgia, represented a minor confounder.
Conclusion: The DETAIL questionnaire is the first screening tool for the early detection of SpA/IBD that has been validated by a multicenter study group.
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FRI0321 UTILITY OF THE ASAS HEALTH INDEX QUESTIONNAIRE AS A TOOL FOR HEALTH ASSESSMENT IN PATIENTS WITH SPONDYLOARTHRITIS AND ITS ASSOCIATION WITH DISEASE ACTIVITY, FUNCTIONALITY, MOBILITY, AND STRUCTURAL DAMAGE

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Background: The ASAS Health Index (ASAS-HI) questionnaire, a tool that measures the impact of the disease on the health in patients with Spondyloarthritis (SpA), has been recently validated. However, there are still no studies evaluating the utility of this questionnaire in daily clinical practice.
Objectives: The objective of this study is to evaluate the association of ASAS-HI with disease activity, functionality, mobility, and structural damage in patients with SpA.
Methods: This is an observational, cross-sectional and single-center study in which 126 consecutive patients with SpA were included. Sociodemographic data, scores related to disease activity (BASDAI and ASDAS), functionality (BASFI), structural damage (cervical, lumbar and total mSASSS), mobility (BASMI and UCOASMI), quality of life (ASAS-HI) and the presence of concomitant fibromyalgia (evaluated with the FIRST questionnaire) were obtained from all patients. The ASAS-HI questionnaire was considered as the main outcome (scale from 0 to 17). Pearson's correlation coefficient was used to evaluate the association of the different continuous variables with each other. Student's t-test was used to compare the ASAS-HI between different subgroups of patients (men vs. women, ASDAS>2,1 vs. ASDAS≤2,1 and fibromyalgia + vs. fibromyalgia-). Finally, a multivariate linear regression was performed to determine which factors explain the variability of ASAS-HI in these patients
Results: Among the 126 patients included, 83 (65.9%) were men, with a mean age of 45.1±12.3 years and a mean disease duration of 18.7±14.5 years. The mean ASAS-HI score in all patients was 4.7±4.0, showing a "strong" positive linear correlation (r>0.60) with BASDAI and BASFI, and "moderate" positive (r=0.40 to 0.60) with Global VAS and ASDAS (Figure 1). Patients with fibromyalgia showed a significantly higher ASAS-HI score compared with patients without fibromyalgia (9.5±3.2 vs 3.7±3.4, respectively). In addition, patients with high disease activity (ASDAS>2,1) showed a higher mean score in ASAS-HI compared with those with low activity (ASDAS≤2,1) (5.8 ± 3.8 vs 2.0 ± 2.4, p<0,001).

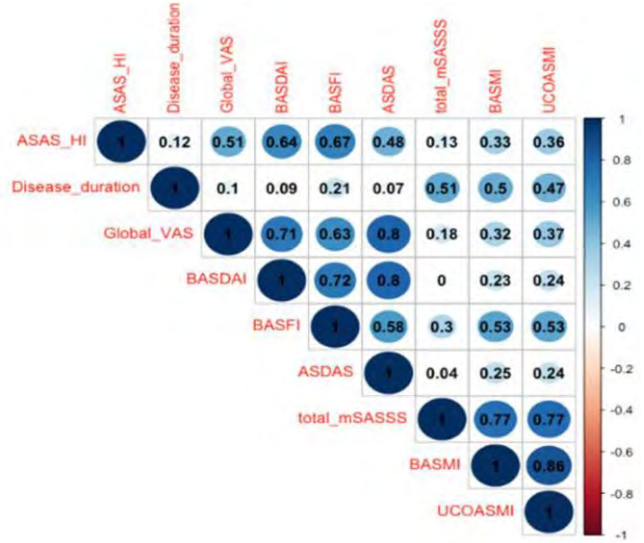


Figure 1. Simple linear correlation (Pearson's r) between the different variables studied.

Finally, multiple linear regression showed that 57,4% (R2=0,574) of the ASAS-HI variability is explained by the presence of concomitant fibromyalgia (β = 2.23, 95%IC 0.73 to 3.80, p=0.004), BASDAI (β = 0.62, 95%IC 0.25 to 0.97, p=0.001) and BASFI (β = 0.57, 95%IC 0.26 to 0.88, p=0.001).
Conclusion: In our study, the impairment of the quality of life in patients with SpA was mainly associated with a high disease activity (BASDAI), worsening functionality (BASFI) and with the presence of concomitant fibromyalgia. Neither mSASSS nor UCOASMI was associated with a change in ASAS-HI; thus, in our patients neither structural damage nor mobility seem to influence the quality of life. In a patient with a high ASAS-HI we must evaluate the presence of concomitant fibromyalgia.
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Disclosure of Interests: María Ángeles Puche Larrubia: None declared, Clementina López-Medina: None declared, María del Carmen Castro Villegas: None declared, Rafaela Ortega Castro: None declared, MLourdes Ladehesa Pineda: None declared, Pérez Sánchez Laura: None declared, Gómez García Ignacio: None declared, José Miguel Sequí-Sabater: None declared, Maria del Carmen Abalos-Aguilera: None declared, Inmaculada Concepcion Aranda-Valera: None declared, Garrido Castro Juan Luis: None declared, Alejandro Escudero Contreras Grant/research support from: ROCHE and Pfizer, Speakers bureau: ROCHE, Lilly, Bristol and Celgene., Eduardo Collantes-Estevez: None declared
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FRI0322 INSULIN RESISTANCE IN NON-DIABETES PATIENTS WITH SPONDYLOARTHRITIS

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Background: Insulin resistance (IR) is a state in which a given concentration of insulin is associated with a subnormal glucose response. IR constitutes a major underlying abnormality driving cardiovascular disease in the general population

and has been linked to inflammatory diseases. In this sense, several reports have confirmed that inflammation worsens IR and impairs pancreatic β-cell function in inflammatory diseases such as rheumatoid arthritis and systemic lupus erythematosus.

Objectives: In this study we aimed to determine the prevalence of IR in patients with spondyloarthritis (SpA) compared to controls, and whether IR can be explained by disease-related features in SpA patients.

Methods: Study of 577 subjects, 306 patients diagnosed with SpA according to ASAS criteria and 271 controls. Insulin and C-peptide serum levels, IR and β-cell function (%B) indexes by homeostatic model assessment (HOMA2), and lipid profiles were assessed in patients and controls. A multivariate regression analysis was performed to evaluate the differences in IR indexes between patients and controls and to determine how IR is associated with disease-related characteristics.

Results: SpA patients showed higher serum levels of insulin (8.7 [4.8-15.9] vs. 8.0 [5.7-11.2] uU/ml, p=0.001) and C peptide (1.4 [0.7-2.5] vs. 1.2 [0.7-1.7] ng/ml, p=0.000) than controls in the univariate analysis. Similarly, HOMA2-B% and IR were all significantly higher in SpA patients. These differences were still evident when the comparisons were made after the multivariate analysis had been adjusted for traditional IR-related factors (sex, age, BMI, hypertension, dyslipidemia, smoking and, cholesterol), glucocorticoids intake, insulin and C-peptide. Moreover, HOMA2-B% and HOMA2-IR scores, both calculated with insulin or C-peptide, yielded statistically higher significant values in SpA patients than controls.

Classic IR-related factors (age, BMI, waist circumference, hypertension, obesity, dyslipidemia, atherogenic index, and triglycerides), as well as CRP serum levels, were all related, to a greater or lesser degree, with IR and β-cell function. Regarding disease-related data, ASDAS-CRP, BASFI and BASMI scores were positively associated with IR; and BASMI and BASDAI scores were positively related to HOMA2-%B-C peptide. Moreover, the use of NSAID and prednisone were, respectively, positive and negatively related to β-cell function. However, only some of the associations of the univariate analysis were maintained after adjusting for confounders. In this sense, disease duration (beta coefficient 2 [95% CI 1-3], p=0.001) and positivity for HLA-B27 (beta coefficient 30 [95% CI 12-49], p=0.002) were associated with higher β-cell functionality after the multivariate analysis.

Conclusion: Patients with SpA have an increased IR compared to controls. SpA disease-related data like disease duration and HLA-B27 are independently associated with β-cell dysfunction.

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FRI0323

THE PRESENCE OF SPONDYLOARTHRITIS IS ASSOCIATED WITH HIGHER CLINICAL DISEASE ACTIVITY IN PATIENTS WITH EARLY CROHN'S DISEASE: RESULTS OF A PROSPECTIVE COHORT STUDY

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Background: Inflammatory bowel disease (IBD) and specifically Crohn's disease (CD) is known to be associated with spondyloarthritis (SpA). However, only little is known about factors associated with the development of spondyloarthritis in CD.

Objectives: To identify factors associated with the presence of SpA in a cohort of patients with CD.

Methods: Patients with a definite diagnosis of CD naïve to or not being treated with biological agents for at least 3 months were included in a CD-arm of the German Spondyloarthritis Inception Cohort (GESPIC-Crohn). Gastroenterologists were encouraged to include consecutively recently diagnosed CD patients. Patients were classified according to the Montreal classification including location and behavior of CD. Patients received a structured assessment of SpA manifestations (including magnetic resonance imaging of sacroiliac joints and spine) by a rheumatologist who was responsible for the final diagnosis of SpA / no SpA. Clinical activity of CD was assessed by the Harvey-Bradshaw Index (HBI). In addition, colonoscopy was performed, Simple endoscopic Score for Crohn's Disease (SES-CD) was determined and fecal calprotectin was measured.

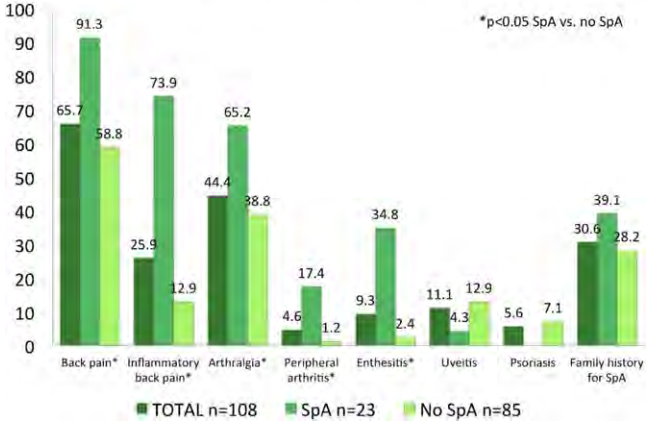
Results: A total of 108 patients with CD were enrolled. The mean (mean ± SD) age was 36.6 ± 12.7 years, and CD symptom duration was 5.3 ± 7.4 years. At baseline, 44 (40.7%) patients were treated with non-biologic immunomodulating drugs: 16 (14.8%) patients received mesalazine, 27 (25.0%) azathioprine, and 1 (0.9%) methotrexate. Oral steroids were given to 38 (35.2%) patients. A total of 103 (96.3%) patients were biologics naïve. SpA was diagnosed in 23 (21.3%) patients: 12 had axial SpA and 11 peripheral SpA. Patients with SpA had higher prevalence of HLA-B27, of clinical SpA features (back pain, inflammatory back pain, peripheral arthritis, enthesitis), higher level of CRP and higher activity of CD as measured by the HBI. There were not substantial differences between SpA vs. non-SpA patients in terms of CD duration, endoscopic activity, disease location or behavior, or treatment, except for mesalazine, which was more frequently administered in patients with SpA than non-SpA (39.1% vs. 8.2%, p=0.001, respectively).

Conclusion: SpA was present in 21% of patients with CD in this early cohort with almost equal proportions of axial and peripheral forms. Presence of HLA-B27 and higher clinical activity of CD were associated with the presence of SpA.

TABLE. Baseline demographic and clinical characteristics of the included patients with Crohn's disease with or without spondyloarthritis.

VARIABLE	TOTAL n=108	SpA n=23	No SpA n=85	P
Age, years, mean ± SD	36.6 ± 12.7	37.5 ± 11.3	36.3 ± 13.1	0.44
Male sex, n (%)	50 (46.3)	10 (43.5)	40 (47.1)	0.82
CD symptom duration, years, mean ± SD	5.3 ± 7.4	5.4 ± 7.2	5.1 ± 7.5	0.63
HLA-B27 positive, n (%)	13 (12.0)	6 (26.1)	7 (8.2)	0.03
Montreal classification				
Location: L1 - ileal	68 (63.0)	13 (56.5)	55 (64.7)	0.48
L2 - colonic	0	0	0	
L3 - ileocolonic	39 (36.1)	7 (30.4)	32 (37.6)	0.63
L4 – isolated upper disease	10 (9.3)	3 (13.0)	7 (8.2)	0.44
Behavior:	69 (63.9)	15 (65.2)	54 (63.5)	1.00
B1 – non-stricturing, non-penetrating				
B2 - stricturing	19 (17.6)	4 (17.4)	15 (17.6)	1.00
B3 - penetrating	6 (5.6)	0	6 (7.1)	0.34
Peri-anal disease	7 (6.5)	2 (8.7)	5 (5.9)	0.64
C-reactive protein, mg/l, mean ± SD	10.7 ± 24.8	13.6 ± 23.2	10.0 ± 25.3	0.02
Harvey-Bradshaw Index, mean ± SD	3.6 ± 4.0	5.5 ± 4.7	3.1 ± 3.6	0.01
Fecal calprotectin, mcg/d, mean ± SD	185.9 ± 213.7	211.7 ± 243.8	179.5 ± 207.9	0.43
Treatment of CD				
Mesalazine, n (%)	16 (14.8)	9 (39.1)	7 (8.2)	0.001
Methotrexate, n (%)	27 (25.0)	3 (13.0)	24 (28.2)	0.18
Azathioprine, n (%)	1 (0.9)	0	1 (1.2)	1.00
Biologics naive, n (%)	103 (96.3)	22 (95.7)	81 (96.4)	1.00

Figure. Spondyloarthritis manifestations in patients with Crohn's disease.



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UCB, Speakers bureau: Consultancy / speaker fees from: Abbvie, BMS, Celgene, Lilly, MSD, Novartis, Pfizer, Roche, UCB, Susanne Lüders: None declared, Judith Rademacher: None declared, Hildrun Haibel Consultant of: Abbvie, Jansen, MSD, and Novartis, Speakers bureau: Abbvie, Jansen, MSD, and Novartis, Maryna Verba: None declared, Joachim Sieper Consultant of: AbbVie, Boehringer Ingelheim, Eli Lilly and Company, Janssen, Merck, Novartis, Pfizer, Roche, and UCB Pharma, Speakers bureau: AbbVie, Boehringer Ingelheim, Eli Lilly and Company, Janssen, Merck, Novartis, Pfizer, Roche, and UCB Pharma, Elena Sonnenberg: None declared, Michael Schumann: None declared, Lea Isabell Kredel: None declared, Britta Siegmund Consultant of: Abbvie, Boehringer, Celgene, Falk, Janssen, Lilly, Pfizer, Prometheus, Takeda, Speakers bureau: Abbvie, CED Service GmbH, Falk, Ferring, Janssen, Novartis, Takeda (BS served as representative of the Charité), Denis Poddubnyy Grant/research support from: AbbVie, MSD, Novartis, and Pfizer, Consultant of: AbbVie, Bristol-Myers Squibb, Eli Lilly, MSD, Novartis, Pfizer, Roche, UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, MSD, Novartis, Pfizer, Roche, UCB

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FRI0324 NO RADIOGRAPHIC SACROILIITIS PROGRESSION OVER 6 YEARS IN PATIENTS WITH EARLY SPONDYLOARTHRITIS FROM THE ESPERANZA COHORT

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Background: Longitudinal studies about the change from non-radiographic axial Spondyloarthritis (nr-axSpA) to r-axSpA (radiographic axial Spondyloarthritis) are scarce but show a 9-10% progression rate over 2 years (1-2) and a 24% progression rate over 10 years in another study (3). However, in early cohorts such as DESIR, this only represents a 5% over 5 years (4).

Objectives: The aim of this study was to know the rate of progression from nr-axSpA to r-axSpA over 6 years in the early Esperanza cohort.

Methods: This study included 94 patients of the Spanish early spondyloarthritis (SpA) Esperanza cohort, 60 fulfilled the ASAS classification criteria for SpA. Every patient had a baseline and a six years sacroiliac X-ray. Nine readers, blinded for the diagnosis, participated in the reliability exercise, all of them experienced rheumatologists and members of the Spanish spondyloarthritis working group (GRESSER). Patients with SpA were classified as having r-axSpA, at baseline or after 6 years of follow-up, if they fulfilled the radiographic item of the modified New York criteria (mNY) (presence of radiographic changes in the sacroiliac joints -SIJ- of at least grade II bilaterally or grade III or IV unilaterally). The gold standard of SIJ X-Ray was the categorical opinion of at least five of the expert readers. For the statistical analysis, the Chi-square and Kappa tests were performed.

Results: Demographic data of the SpA patients were: mean age 33.4±7.5 years; 37 (61.7%) male; mean CRP 6.4±6.5 mg/dl and ESR 10.3±10.6. Present smokers 30.6%; and past smokers 16.3%. HLA-B27 (+) 56.7%. Regarding the presence of X-Ray sacroilitis: 20 patients had baseline sacroilitis and 18 at the final visit; 11 had sacroiliitis at both baseline and final visits; 9 patients changed from baseline sacroiliitis to no-sacroiliitis and 7 changed from baseline no-sacroiliitis to sacroiliitis at the 6 year visit. The reliability of the readers was fair with a mean inter-reader kappa test of 0.375 (range 0.146 - 0.652) and a mean agreement of 73.7% (range 58.7% - 90%).

Conclusion: In this group of patients with early SpA no progression from nr-axSpA to r-axSpA over 6 years was observed. It appears that early diagnosis and standard treatment seem to reduce SIJ radiographic progression.

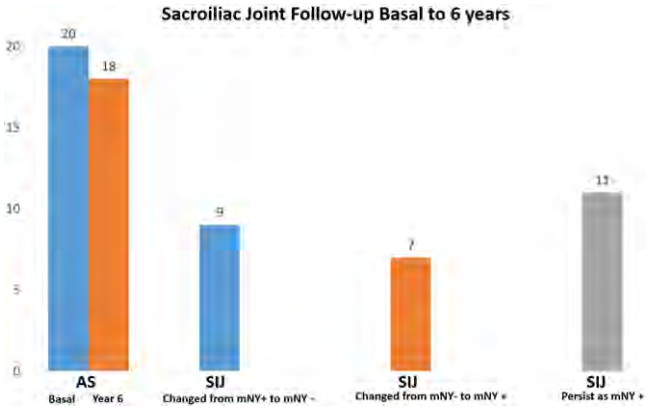
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Disclosure of Interests: Carolina Tornero: None declared, María del Carmen Castro Villegas: None declared, Xavier Juanola-Roura: None declared, Maria Luz García-Vivar: None declared, Cristina Fernández-Carballido Consultant of: Yes, I have received fees for scientific advice (Abbvie, Celgene, Janssen, Lilly and Novartis), Speakers bureau: Yes, I have received fees as a speaker (Abbvie, Celgene, Janssen, Lilly, MSD, Novartis), Jose Francisco Garcia LLorente: None declared, Beatriz Joven-Ibáñez Speakers bureau: Abbvie, Celgene, Janssen, Merck Sharp & Dohme, Novartis, Pfizer, E. Galindez: None declared, Claudia Urrego-Laurín: None declared, Eugenio de Miguel Grant/research support from: Yes (Abbvie, Novartis, Pfizer), Consultant of: Yes (Abbvie, Novartis, Pfizer), Paid instructor for: yes (AbbVie, Novartis, Pfizer, MSD, BMS, UCB, Roche, Grunental, Janssen, Sanofi), Speakers bureau: yes (AbbVie, Novartis, Pfizer, MSD, BMS, UCB, Roche, Grunental, Janssen, Sanofi)

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FRI0325 UVEITIS OCCURRENCE IN EARLY INFLAMMATORY BACK PAIN. FIVE YEARS DATA FROM A PROSPECTIVE FRENCH NATIONWIDE COHORT

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Background: Uveitis is the most frequent extra rheumatological manifestation in axial Spondyloarthritis (SpA). DESIR is a prospective multicenter cohort of patients with early inflammatory back pain suggestive of SpA. We reported previously a 8.5% baseline prevalence of uveitis for the patients included in the cohort; this history of uveitis at the first visit of the cohort was associated with inflammatory bowel disease (IBD) and preceding infection (1).

Objectives: The aim of the study was to evaluate the prevalence and incidence of uveitis over the first five years of prospective follow-up of the cohort, and to evaluate its associated factors.

Methods: DESIR is a prospective observational cohort of patients with recent onset inflammatory back pain (more than 3 months, less than 3 years), suggestive of axial SpA, All available factors in the database were compared between patients with and without uveitis at 5 years, by uni and then multivariate analysis. Baseline factors associated with new cases of uveitis occurrence over the 5 years were also analyzed. Significance: p less than 0.05.

Results: After 5 years, 91 patients (out of 480 with complete follow-up) had at least one uveitis episode, giving an estimated prevalence of 18.9% [95%CI: 15.4-22.4]. In multivariate analysis, uveitis was associated with dactylitis (OR 2.92 [2.06 – 4.14]; p=0.002**), ESR > 7mm (median value) (OR 2.19 [1.57 – 3.06]; p=0.018*).

New incident uveitis occurred in 31 cases over 5 years, giving an estimated incidence rate of 1.29 [0.84 – 1.74] / 100 patient-years. New incidence of uveitis was

associated in multivariate analysis with the following baseline factors: diagnosis of SpA (OR 9.65 [3.21 – 28.96]; p=0.039*), total sacro iliac MRI inflammatory SPARCC score (central reading) over median (OR 3.98 [2.26 – 7]; p=0.015*), dactylitis (OR 4.7 [2.65 – 8.36]; p=0.007**), syndesmophyte score over median (central reading) (OR 0.22 [0.1 – 0.45]; p=0.039*).

No significant association was found with HLA-B27, cs or b DMARDs, BASDAI, ASDAS, BASFI.

Conclusion: Five-years data of the DESIR cohort allowed an estimation of incidence rate of uveitis of 1.3/100p-y; over five years, uveitis was associated with dactylitis, biologic and sacro iliac MRI inflammation.

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[1] Wendling D, et al.Arthritis Care Res(Hoboken). 2012 Jul;64(7):1089-93.

Disclosure of Interests: Daniel Wendling: None declared, Clément Prati: None declared, Thierry Lequerre: None declared, Corinne Miceli Richard: None declared, Maxime Dougados Grant/research support from: AbbVie, Eli Lilly, Merck, Novartis, Pfizer and UCB Pharma, Consultant of: AbbVie, Eli Lilly, Merck, Novartis, Pfizer and UCB Pharma, Speakers bureau: AbbVie, Eli Lilly, Merck, Novartis, Pfizer and UCB Pharma, Anna Moltó Grant/research support from: Pfizer, UCB, Consultant of: Abbvie, BMS, MSD, Novartis, Pfizer, UCB, xavier guillot: None declared

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FRI0326 PREVALENCE AND IMPACT OF COMORBIDITIES IN AXIAL SPONDYLOARTHRITIS: SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Comorbidities are common among patients with axial spondyloarthritis (axSpA). The majority of axSpA patients have at least one comorbid medical condition in addition to any extra-articular manifestations [1]. Comorbidity 'burden' is associate with poorer function, quality of life and work-related outcomes [2]. They also influence treatment decisions and are key drivers of mortality.

Objectives: We performed a systematic review and meta-analysis to 1) describe the prevalence of commonly reported comorbidities, 2) compare the prevalence of comorbidities between axSpA and control populations.

Methods: A systematic review was performed in September 2019 using Medline, PubMed, Scopus and Web of Science, in accordance with PRISMA guidelines. Studies were included if they reported the prevalence of comorbidities on disease outcomes, and excluded if they focused on a single comorbidity or closely related diseases in one organ system. Two independent reviewers screened titles and abstracts, assessed full-texts for eligibility and extracted data from qualifying studies. Where possible, we performed meta-analyses for comorbidities reported by at least 3 studies using random-effects models. Pooled prevalence estimates were reported as percentages (95% confidence interval, I^2 statistic for heterogeneity).

Results: 36 studies reported prevalence of of individual comorbidities, amounting to a combined sample size of 119,427 patients. The most prevalent individual comorbidities were hypertension (pooled prevalence 22%), hyperlipidaemia (17%) and obesity (14%) (Figure 1). Eleven studies consistently showed higher prevalence of comorbidities in axSpA than controls (Table 1); odds ratios (OR) were particularly large for depression (pooled OR 1.80) and congestive cardiac failure (OR 1.84). There was significant heterogeneity for the majority of meta-analysis estimates.

Table 1. Meta-analysis estimates for odds ratios (OR) of comorbidities compared between axSpA and control groups.

	Number of studies	Pooled OR	95% confidence interval	I^2, %
Hypertension	9	1.58	1.29 to 1.92	98
Any cardiovascular disease	3	1.42	0.999 to 2.03	99
Any ischaemic heart disease	7	1.51	1.21 to 1.87	87
Congestive cardiac failure	4	1.84	1.25 to 2.73	89
Stroke	6	1.30	1.04 to 1.62	81
Peripheral vascular disease	5	1.47	1.10 to 1.96	83
Diabetes	8	1.14	1.001 to 1.30	83
Hyperlipidaemia	5	1.18	1.01 to 1.39	94
Cancer	5	1.22	1.01 to 1.47	93
Depression	4	1.80	1.45 to 2.23	92

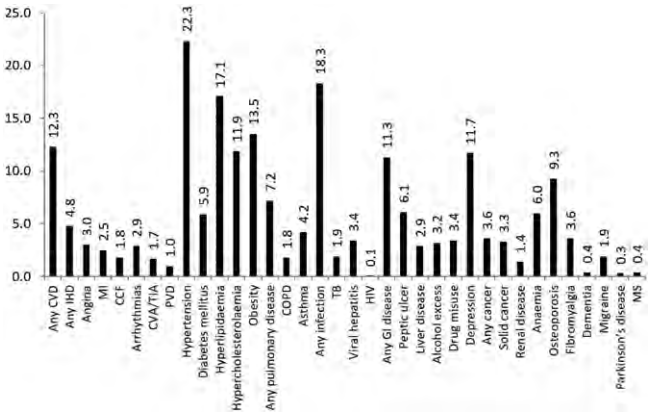


Figure 1. Pooled prevalence of individual comorbidities.

Conclusion: Comorbidities are common in axSpA. Almost all comorbidities examined were more prevalent in axSpA patients than age and sex matched controls, with ≥80% higher odds for congestive cardiac failure and depression. Systematic and repeated assessments should therefore be integrated into routine clinical practice to ensure holistic patient-centred management. Additional studies are needed to validate comorbidities indices for axSpA research.

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Disclosure of Interests: None declared

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FRI0327 QUALITY OF LIFE, QUALITY OF SLEEP AND PRESENCE OF RESTLESS LEG SYNDROME IN ANKYLOSING SPONDYLITIS

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Background: For chronic diseases like ankylosing spondylitis (AS), improving patients quality of life (QOL) is one of the main aims of the therapy. Sleep quality is an important determinant of QOL. Restless leg syndrome (RLS) is a frequent disorder that disturbs patients QOL.

Objectives: The aim of this study is to evaluate the sleep quality of patients with AS and to determine the possible reasons of sleep disorder like pain, disease activity, functional status, depression, anxiety, presence of RLS and their impact on patients QOL.

Methods: One hundred twenty two patients with ankylosing spondylitis were enrolled in the study. Quality of life was evaluated by using short form-36 (SF-36). Beck depression and Beck anxiety indices were used to evaluate the mood of the patients. Sleep quality was determined with Pittsburg Sleep Quality Index. International Restless Leg Study Group (IRLSSG) criteria was used to determine the co-existing restless leg syndrome. Demographic data including age, sex, height, weight, marital status, educational status, disease duration and medical treatments were noted. BASDAI (Bath ankylosing spondylitis disease activity index),BASMI (Bath ankylosing spondylitis metrology index) and BASFI (Bath ankylosing spondylitis functional index) are determined and perceived pain level was evaluated by visual analog scale for pain (VASpain) for all patients.

Results: According to Pittsburg Sleep Quality Index 48 patients (39.3%) had bad sleep quality. When patients with bad sleep quality were compared with the patients with good sleep quality according to SF-36, BASDAI, BASMI,BASFI, VAS pain, Beck depression and Beck anxiety indices worse scores were obtained in patients with bad sleep quality. The difference between two groups were statistically significant for almost all of the listed parametres (Table-1). Restless leg syndrome (RLS) was determined in 36.06% (44/122) of AS patients. RLS was more common in patients with bad sleep quality but the difference did not reach statistical significance.

Conclusion: Sleep disorders are common in patients with AS and these disorders are found to be closely associated with pain, disease activity, anxiety, depression and poor quality of life. Restless leg syndrome (RLS) is also common in patients with AS and it is not always associated with bad sleep quality. RLS was determined in 32.4% (24/74) of patients whose sleep quality is good according to the Pittsburg Sleep Quality Index. So to improve the quality of life in AS, presence of RLS must be evaluated along with the sleep quality.

References:

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Table 1.

Parametres median (min-max)	Good sleep Quality	Bad sleep quality	P
SF36 physical functioning	85(20-100)	65(25-100)	**0,0001**
SF36 Social functioning	87,5(25-100)	62,5(12,5-100)	**0,0001**
SF36 Role physical	100(0-100)	0(0-100)	**0,0001**
SF36 Role emotional	100(0-100)	33,3(0-100)	**0,003**
SF36 Mental health	74(20-100)	52(12-88)	**0,0001**
SF36 Vitality	55(10-90)	30(0-80)	**0,0001**
SF36 Bodily pain	88,8(11,1-100)	44,4(0-100)	**0,0001**
SF36 General health	50(15-100)	35(0-95)	**0,0001**
Beck depression	5 (0-28)	14.5 (1-44)	**0.0001**
Beck anxiety	5.5 (0-45)	14.5 (1-49)	**0.0001**
BASDAI	1.6 (0- 5.91)	3.8 (0.8-8.3)	**0.0001**
BASFI	1.2 (0- 8.1)	2.85 (0.3-7.6)	**0.0001**
BASMI	1 (0-9)	1.5 (0-8)	0,087
VAS pain	1 (0-8)	5 (0-10)	**0.0001**
Restless Leg Syndrome (%)	32.4%(24/74)	41.7% (20/48)	0.299

Disclosure of Interests: None declared

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FRIDAY, 05 JUNE 2020

Psoriatic arthritis

FRI0328 PROFILING OF THE IMMUNE COMPARTMENT IN THE TISSUE ENVIRONMENT OF PSORIATIC ARTHRITIS USING RNASEQ

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Background: Psoriasis is a chronic inflammatory disease of the skin with a reported prevalence of 0.09-11.4% of the population (1). 1 in 4 psoriasis patients also have psoriatic arthritis (PsA) (2), with additional joint involvement that can be associated with significant morbidity. Despite its relative commonness, the aetiology of psoriasis is not well understood, and there is no cure for this disease. Additionally, up to 30% of PsA patients with active disease are recalcitrant to treatment. Thus it remains a prerogative to understand the immune mechanisms contributing to the development of the disease in order to inform strategies for novel therapies.

Objectives: Our aim was to identify perturbations in local tissue immune networks that could contribute to the pathology of psoriasis and psoriatic arthritis. We hypothesise that psoriasis is driven by a disrupted tissue microenvironment, which then provides cues to a susceptible peripheral immune system to drive pathology. Thus as the first part of our study, we investigated the transcriptional profiles of normal and lesional skin.

Methods: Skin punch biopsies were obtained from both lesional and morphologically normal skin of 4 PsA patients with active disease. CD45+ cells were isolated using magnetic enrichment for RNA purification and subsequent RNAseq. Differently expressed genes (DEG) were identified and pathway analysis performed using the integrated Differential Expression and Pathway (iDEP) analysis tool. Gene set enrichment analysis was performed using GSEA.

Results: Transcriptomic analyses of skin revealed that lesional skin, compared to non-lesional sites, was enhanced for expression of genes associated with immune processes (including genes such as such as *IL17A*, *FCN1*, and *CTLA4*) anti-microbial responses (such as *DEF4BA* and *S100A8*) and immune cell chemotaxis (notably *CXCL13* and *SELPLG*), suggesting a possible inflammatory response to skin microbiota. Interestingly, lesional skin showed a deficiency in expression of genes associated with tRNA metabolic processes (including *AARS*, *YARS*, and other aminoacyl tRNA synthetases), suggesting a possible defect in protein translation. Similarly, pathway analysis revealed an enrichment in humoral immune response pathways in PsA lesional skin, and a comparative deficiency in RNA metabolic pathways.

Conclusion: Our transcriptional approach provides a comprehensive overview of localised immunity in psoriasis and predicts intimate interactions with the peripheral immune system. Further studies are ongoing to uncover cell types involved, as well as parallels at other disease sites (joints). These findings will facilitate the identification of novel targets for treatment of PsA.

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FRI0329 ASSOCIATION BETWEEN PERITENON EXTENSOR TENDON INFLAMMATION AND ENTHESITIS IN TUNISIAN PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Ultrasonography (US) is a useful tool in assessing psoriatic arthritis (PsA) by detecting synovitis and Power Doppler (PD) activity. Enthesitis is well known as a cornerstone of PsA physiopathology. Recently, more specific US features of PsA have emerged, such as peritenon extensor tendon inflammation (PTI) and edema of soft tissues, with value in the positive diagnosis of the disease.

Objectives: The aim of our study was to determine the association between PTI, edema and enthesitis in PsA patients.

Methods: Patients with peripheral PsA responding to the Classification Criteria for Psoriatic Arthritis (CASPAR) were included. US examination was performed by an experimented rheumatologist blinded to clinical data using a machine type Esaote MyLAb 60 with a linear probe of 6-18 MHz. Wrists, metacarpo-phalangeal (MCP), proximal inter-phalangeal (PIP) and distal inter-phalangeal (DIP) joints were assessed in mode B and PD. PTI was defined as a hypoechoic image surrounding the digitorum tendon with or without PD signal in the dorsal aspect of MCP joints. Soft tissue edema was defined as a diffuse enlargement of soft tissue around the flexor tendon, with an increased PD signal, from finger pad to MCP joint and was evaluated by volar scan. Enthesitis of the digitorum extensor tendon at the dorsal aspect of DIP joint and synovitis were defined according to the OMERACT definitions.

A $p<0.05$ was considered statistically significant.

Results: A total of 600 joints were assessed in 20 PsA patients, 8 men and 12 women, with a mean age of 55 ± 11 [33-77] years old. The mean disease duration was of 10±8 [1-34] years. Clinically, 25% of joints were tender and 6% were swollen. The mean DAPSA (Disease Activity in PSoriatic Arthritis) score was of 32±27 [4-112].

On US examination, synovitis was detected in 54 joints (9%), with PD signal in 53% of them. The sites of synovitis by decreasing order of frequency were: MCP in 38%, wrists in 26%, PIP in 19% and PID in 13% of cases.

PTI was noted in 24 MCP joints (12%) with PD signal in one case, and soft tissue edema in 6 MCP joints (3%).

Enthesitis was noted in 59 DIP joints (37%). The elementary lesions recorded were: enthesophytes in 64 %, erosions in 20 %, calcifications in 13 % and thickened and/or hypoechoic tendon in 12 % of cases. However, no PD signal at the enthesis was found.

PTI and soft tissue edema had no association with enthesitis (p=0.399 and p=0.374 respectively). PD synovitis showed a significant association with enthesitis (p=0.034), but not with PTI and soft tissue edema. GS synovitis had no association with any of these lesions.

Conclusion: Our study found PTI and soft tissue edema not to be associated with enthesitis as opposed to PD synovitis. A larger sample size is necessary to support the role of PTI as an enthesis related lesion in PsA patients.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.3931

FRI0330

BODY MASS INDEX AND DISEASE ACTIVITY IN CHRONIC INFLAMMATORY RHEUMATIC DISEASES: RESULTS OF THE CARDIOVASCULAR IN RHEUMATOLOGY (CARMA) PROJECT

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Objectives: Since obesity has been associated with higher inflammatory burden and worse response to therapy in patients with chronic inflammatory joint diseases (CIJDs), we aimed to confirm the potential association between body mass index (BMI) and disease activity in a large series of patients with CIJDs included in the Spanish CARdiovascular in rheuMAtology (CARMA) registry.

Methods: Baseline data assessment of patients included from the CARMA project, a 10-year prospective study of patients with rheumatoid arthritis (RA), ankylosing spondylitis (AS) and psoriatic arthritis (PsA) attending outpatient rheumatology clinics from 67 Spanish hospitals. Obesity was defined when BMI (kg/m^2) was>30 according to the WHO criteria. Scores used to evaluate disease activity were DAS28 in RA, BASDAI in AS, and modified DAS for PsA.

Results: Data from 2,234 patients (775 RA, 738 AS and 721 PsA) were assessed. The mean±SD BMI at the baseline visit were: 26.9±4.8 in RA, 27.4±4.4 in AS and 28.2±4.7 in PsA. Multivariate analyses shown a positive association between BMI and disease activity in patients with RA (β-coefficient: 0.029; 95% CI: 0.01-0.05; p=0.007) and in those with PsA (β-coefficient: 0.036; 95% CI: 0.015-0.058; p=0.001). By contrast, there was no significant association between BMI and disease activity in patients with AS (β-coefficient: 0.001; 95% CI: -0.026-0.03; p=0.926).

In patients with RA, female gender (β-coefficient: 0.546; 95% CI: 0.316-0.775; p<0.001) and rheumatoid factor status (seropositivity for RF) (β-coefficient: 0.328; 95% CI: 0.106-0.549; p=0.004) also showed a positive association with disease activity, while physical activity revealed a negative association with disease activity (β-coefficient: -0.280; 95% CI: -0.479-(- 0.081); p=0.006).

Besides BMI, female gender (β-coefficient: 0.720; 95% CI: 0.524-0.916; p<0.001), Psoriasis Area Severity Index (β-coefficient: 0.038; 95% CI: 0.012-0.066; p=0.005) and enthesitis (β-coefficient: 0.256; 95% CI: 0.199-0.313; p<0.001) were also positively associated with disease activity in PsA.

As observed in RA and PsA, female gender was also associated with disease activity patients with AS (β-coefficient: 0.565; 95% CI: 0.299-0.832; p<0.001).

Conclusion: BMI is associated with disease activity in RA and PsA but not in AS. Since obesity is a potentially modifiable factor, disease activity was associated with female gender and RF status in RA and with Psoriasis Area Severity Index and enthesitis in PsA. Adequate control over body weight may improve the outcome of patients with CIJDs and, therefore, weight control should be included in the strategy of management of these patients.

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FRI0331

COMPARISON OF THE THERAPEUTIC TRAJECTORIES OF PATIENTS WITH OLIGO AND POLYARTICULAR PSORIATIC ARTHRITIS. A REPORT FROM THE RHUMADATA® CLINICAL DATABASE AND REGISTRY

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Background: Psoriatic Arthritis (PsA) most frequently presents as a polyarthritis or (less often) as an oligoarthritis [1]. Most of the patients in the original description of Moll and Wight had an oligoarticular presentation [2]. However, other studies have not found the same distribution in all patient populations [3]. Treatment response over time across presentation types has not been explored thoroughly in recent medical literature.

Objectives: Using our proposed definition of oligo and polyarticular PsA status, based on the (rounded) mean of the first four available joint counts, we examine treatment sequences in each group.

Methods: Data from patients participating in the RHUMADATA® clinical database and registry diagnosed with PsA were extracted on January 5th, 2020. Joint count classification (oligo vs. poly) was assessed from the average of the first four available 66/68 joint counts. Patients were classified as having a polyarticular form of PsA if the (rounded) average, five or more of their joints were assessed as being swollen and/or tender. Subjects with four or less swollen or tender joints were classified as patients having oligoarticular PsA. Time spent treated with non-DMARDs, csDMARDs and bDMARDs, time to treatment (to csDMARDs and bDMARDs) and treatment selection were assessed from the entire PsA cohort. Continuous variables were tested using t-tests and binary variables using Fisher's exact test.

Results: The data from all patients diagnosed with PsA (n=1029) was extracted from the RHUMADATA® clinical database and registry. All but 151 (15%) were classifiable, 470 (46%) were classified as oligoarticular PsA patients and 408 (39%) as polyarticular. Time from the first symptoms to the first clinic visit was 4.6 ± 6.5 years and 3.7 ± 6.6 (p-value=0.1311) years for the patients classified as oligo and poly respectively. A total oh 951 patients were treated with a csDMARD (144 of those could not be classified as oligo or poly). For those, time from diagnosis to first csDMARD (prior to any bDMARD) treatment was 1.7 ± 5.3 (oligo) years and 2.0 ± 7.0 (poly) years (p-value=0.4114). Methotrexate (MTX), hydroxychloroquine (HCQ) and leflunomide (LEF) were more frequently prescribed to polyarticular than oligoarticular PsA patients (MTX: 70% (poly) vs. 48% (oligo), p-value<.0001, HCQ: 41% vs. 25%, p-value <.0001, LEF: 17% vs. 8%, p-value<.0001, Sulfasalazine (SSZ): 17% vs. 19%, p-value=0.5232, Other csDMARDs: 5% vs. 4.5%, p-value=0.8688). A total of 648 patients were treated with a bDMARD (151 of those could not be classified as oligo or poly). For those, time from first csDMARD Rx to first bDMARD treatment was 6.3 ± 4.6 (oligo) years and 7.0 ± 4.7 years (p-value=0.0865). On average, over the entire treatment history, oligoarticular patients received 1.7 ± 1.2 biologic agents and polyarticular 2.0 ± 1.4, p-value=0.0110. bDMARDs were administered over 3.6 ± 3.6 years for oligo and 4.5 ± 3.9 years for poly, p-value=0.2122.

Conclusion: Polyarticular PsA patients appear to be more aggressively treated than oligoarticular patients during the csDMARDs period. Although durations on bDMARDs are statistically similar, polyarticular patients change biotreatment more frequently.

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Disclosure of Interests: Denis Choquette Grant/research support from: Rhumadata is supported by grants from Pfizer, Amgen, Abbvie, Gylead, BMS, Novartis, Sandoz, eli Lilly,, Consultant of: Pfizer, Amgen, Abbvie, Gylead, BMS, Novartis, Sandoz, eli Lilly,, Speakers bureau: Pfizer, Amgen, Abbvie, Gylead, BMS, Novartis, Sandoz, eli Lilly,, Loïc Choquette Sauvageau: None declared, Louis Bessette Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer, Roche, Sanofi, UCB Pharma, Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer, Roche, Sanofi, UCB Pharma, Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer, Sanofi, Isabelle Ferdinand Consultant of: Pfizer, Abbvie, Amgen, Novartis, Speakers bureau: Pfizer, Amgen, Paul Haraoui Grant/research support from: AbbVie, Amgen, BMS, Janssen, Pfizer, Roche, and UCB, Consultant of: AbbVie, Amgen, BMS, Celgene, Eli Lilly, Janssen, Merck, Pfizer, Roche, and UCB, Speakers bureau: Pfizer, Speakers bureau: Amgen, BMS, Janssen, Pfizer, and UCB, Frédéric Massicotte Consultant of: Abbvie, Janssen, Lilly, Pfizer, Speakers bureau: Janssen, Jean-Pierre Pelletier Shareholder of: ArthroLab Inc., Grant/research support from: TRB Chemedica, Speakers bureau: TRB Chemedica and Mylan, Jean-Pierre Raynauld Consultant of: ArthroLab Inc., Marie-Anaïs Rémillard Consultant of: Abbvie, Amgen, Eli Lilly, Novartis, Pfizer, Sandoz, Paid instructor for: Abbvie, Amgen, Eli Lilly, Novartis, Pfizer, Sandoz, Speakers bureau: Abbvie, Amgen, Eli Lilly, Novartis, Pfizer, Sandoz, Diane Sauvageau: None declared, Édith Villeneuve Consultant of: Abbvie, Amgen, BMS, Celgene, Pfizer, Roche, Sanofi-Genzyme,

UCB, Paid instructor for: Abbvie, Speakers bureau: AbbVie, BMS, Pfizer, Roche, Louis Coupal: None declared
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FRI0332

EVALUATION OF THE INDIVIDUAL COMPONENTS OF ACR50+PASI100 AND MDA AT WEEK 24 FROM THE SPIRIT-H2H TRIAL COMPARING THE EFFICACY AND SAFETY OF IXE VERSUS ADA IN PATIENTS WITH PSA NAÏVE TO BDMARDS

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Background: Psoriatic arthritis (PsA) is a chronic systemic disease with manifestations affecting musculoskeletal and extra-articular domains. Treatment and assessment of response are therefore major challenges in routine clinical practice. Minimal disease activity (MDA) is a multidimensional endpoint that can define a treatment target[1]. In SPIRIT-H2H[2], a head-to-head clinical trial comparing the efficacy and safety of ixekizumab (IXE) versus) to adalimumab (ADA), the percentage of patients simultaneously achieving American College of Rheumatology 50 (ACR50) and Psoriasis Area and Severity Index 100 (PASI100), was the primary endpoint in order to reflect improvement in two domains of PsA.

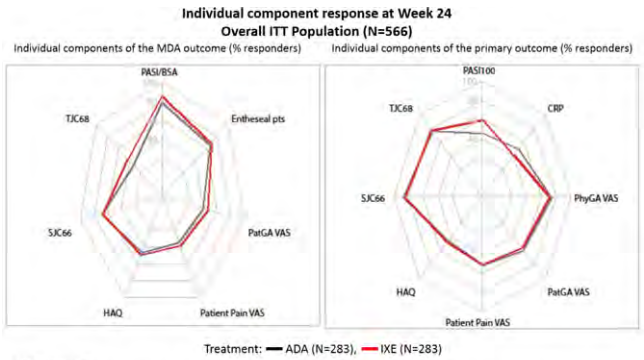
Objectives: To evaluate how individual components of the simultaneous achievement of ACR50 and PASI100 compare with those of MDA at week 24.

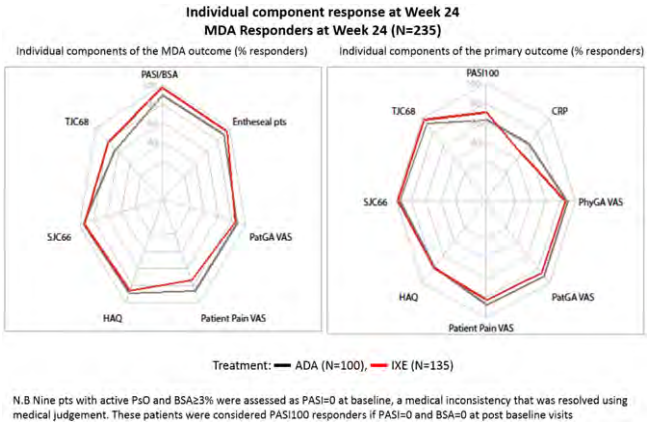
Methods: Patients with active PsA (defined as those with a tender joint count [TJC] ≥ 3/68, a swollen joint count [SJC] ≥ 3/66 and a body surface area [BSA] of active plaque psoriasis ≥ 3%) were randomised 1:1 to approved dosing (according to baseline psoriasis involvement) of IXE or ADA in SPIRIT-H2H, an open label, assessor-blinded study.

The proportion of patients meeting each criterion of the composite endpoints was calculated for the intent-to-treat ([ITT], N=566) population and the population of MDA responders at Week 24 (N=235). Missing individual responses were imputed with non-responder status. Spidergrams were generated using SAS 9.4.

Results:

For both the overall ITT population and the MDA responders population, the use of PASI≤1 or BSA≤3% in the skin-related component of the MDA contributed to the higher response rate relative to the PASI100 response. Thus, the PASI100 response is a more stringent endpoint. Proportions of responders are similar across MDA and ACR50+PASI100 individual components for HAQ and SJC. The high baseline TJC levels (mean TJC: IXE=19.1, ADA=21.3) as opposed to lower levels observed for baseline SJC (mean SJC: IXE=10.1, ADA=10.7) made MDA-TJC criterion (≤1) more difficult to achieve than the equivalent criterion of the ACR50+PASI100 endpoint.





Conclusion: Despite the differences in criteria definitions, there are consistent response patterns in the individual components of the simultaneous ACR50+PASI100 and MDA endpoints in particular for the peripheral arthritis domain.

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FRI0333

ACHIEVEMENT OF VERY LOW DISEASE ACTIVITY AND REMISSION TREATMENT TARGETS IS ASSOCIATED WITH REDUCED RADIOGRAPHIC PROGRESSION IN PATIENTS WITH PSORIATIC ARTHRITIS TREATED WITH CERTOLIZUMAB PEGOL

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Background: Several disease activity measures and thresholds have been recommended as psoriatic arthritis (PsA) treatment targets, although consensus on the most appropriate assessment tool is lacking.[1] Reports suggest low disease activity (LDA) and remission may be associated with minimal structural progression in PsA.[2]

Objectives: To report the relationship between PsA disease activity and structural progression over 216 weeks' (wks) treatment with certolizumab pegol (CZP), an Fc-free, PEGylated, tumour necrosis factor inhibitor (TNFi) that has shown long-term efficacy and safety in PsA.[3]

Methods: Patients (pts) enrolled in RAPID-PsA (NCT01087788) with active PsA (≥3 tender joints; ≥3 swollen joints; ESR ≥28 mm/hour and/or CRP >upper limit of normal) who had failed treatment with ≥1 csDMARD were randomised 1:1:1 to CZP 200 mg every 2 wks (Q2W), CZP 400 mg every 4 wks (Q4W), or placebo (PBO). All CZP pts received CZP 400 mg at Wks 0/2/4. PBO pts were re-randomised to CZP 200 mg Q2W or 400 mg Q4W at Wk 16 or 24.[3]

Pts were heterogenous for structural damage and disease duration at baseline. Disease activity was assessed using minimal disease activity (MDA) criteria (MDA: 5–6/7 criteria; very LDA [VLDA]: 7/7 criteria), Psoriatic Arthritis Disease Activity Score (PASDAS) (LDA: >1.9–≤3.2; remission: ≤1.9), or Disease Activity Index for Psoriatic Arthritis (DAPSA) (LDA: >4–≤14; remission: ≤4). Radiographs were read in four reading campaigns using the van der Heijde modified Total Sharp Score (mTSS) for PsA. A risk of structural progression (RSP) subgroup (baseline mTSS >median for all pts) was also assessed. Mean change from baseline (CFB) in mTSS and associations with disease activity states were estimated using a hierarchical linear mixed effects model (fixed effects: reading campaign/interactions of concurrent disease activity levels with time; random effects: pt/reading campaign nested within pt) which allowed mean mTSS trajectory, and impact of disease activity levels on this, to differ over time.

Results: 407/409 randomised pts were assessed for mTSS at least once. At Wk 0, mean (standard deviation) DAPSA=44.5 (22.7), PASDAS=6.0 (1.1). 3/409 (0.7%) pts reported MDA. The proportion of pts achieving remission/VLDA states increased to Wk 216, as did estimated mean mTSS. Estimated mean mTSS CFB remained low overall (0.46 at Wk 216; standard error 0.16; **Figure**). Across disease activity measures, remission/VLDA states were associated with mTSS estimated mean CFB ≤0 in both the overall group and RSP subgroup (**Table**).

Conclusion: These data indicate that achievement of remission in PsA is important to prevent further structural damage, particularly in pts with pre-existing structural changes. This supports the rationale for strict disease activity targets.

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Table. Estimated mTSS (mixed effects model)

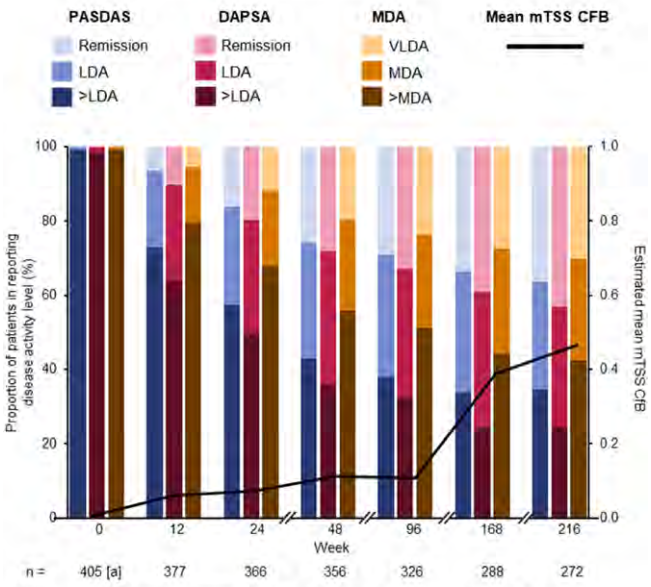
		mTSS estimated mean CFB (standard error)	
		All patients (N=407)	RSP (n=202)
PASDAS	Remission	-0.20 (0.25)	-0.55 (0.49)
	LDA	0.01 (0.23)	-0.07 (0.47)
	>LDA	1.31 (0.22)	2.54 (0.43)
DAPSA	Remission	-0.34 (0.23)	-0.67 (0.46)
	LDA	0.40 (0.22)	0.81 (0.44)
	>LDA	1.37 (0.24)	2.46 (0.48)
MDA	VLDA	-0.40 (0.28)	-0.84 (0.55)
	MDA	0.39 (0.24)	0.55 (0.48)
	>MDA	0.89 (0.20)	1.73 (0.39)

mTSS estimated mean CFB: ≤0; ≤0.5; >0.5. Data to Wk 216 pooled for all pts randomised.

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Figure: Observed disease activity levels and estimated mean CfB in mTSS (mixed effects model) through Wks 0–216 pooled for all randomised patients



[a] Baseline PASDAS data were only available for 398 patients. Data were pooled for all patients randomised to CZP and PBO. Radiographs were taken at Wks 0, 12, 24, 48, 96, 168 and 216. Mean CfB in mTSS was estimated using a hierarchical mixed effects model for repeated measures. The proportion of patients achieving each disease activity level is observed case. CfB: change from baseline; CZP: certolizumab pegol; DAPSA: Disease Activity Index of Psoriatic Arthritis; LDA: low disease activity; MDA: minimal disease activity; mTSS: modified Total Sharp Score; PASDAS: Psoriatic Arthritis Disease Activity Score; PBO: placebo; VLDA: very low disease activity.

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FRI0334 COMPARATIVE ASSESSMENT OF COMORBIDITY IN ANKYLOSING SPONDYLITIS, PSORIATIC ARTHRITIS WITH AND WITHOUT SPINAL INVOLVEMENT

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Background: Axial spondyloarthritis (axSpA) is a chronic inflammatory disease is associated with a lot of comorbidities, especially the diseases of cardiovascular system. [1] These diseases not only lead to a decrease in the quality of life and disability of patients, but also to a decrease in life expectancy in comparison with the general population. [2]

Objectives: The goal of study is to identify the most significant and common comorbid conditions in patients with axial spondylitis and compare their prevalence in three groups: in patients with ankylosing spondylitis, patients with psoriatic arthritis with and without spinal involvement.

Methods: The study included 140 patients with a reliable diagnosis of axSpA (ASAS criteria, 2009), which were subsequently divided into three groups: patients with ankylosing spondylitis, patients with psoriatic arthritis with and without spinal involvement. In all patients comorbid conditions was evaluated.

Results: The most common comorbid conditions among patients with axSpA were overweight (65%), included obesity (44%), hypertension (45%), diabetes and prediabetes (31,4%), dyslipidemia (23,6%), coronary heart disease (9,3%), diseases of the gastrointestinal tract (38,6%). Then we analyzed the prevalence of these comorbid pathologies in three groups.

The characteristics of the groups are presented in Table 1.

Table 1. Characteristic of the patients with axial spondyloarthritis (n=140).

Indicator	Results		
	ankylosing spondylitis	psoriatic arthritis without spinal involvement	psoriatic arthritis with spinal involvement
Quantity	48	47	45
Male, n (%)	30 (62,5)	19 (40,4)	25 (55,6)
Age, years (mean±SD)	41,6 ± 11,0	53,32 ± 11,0	46,9 ± 10,4
Disease duration, years (mean±SD)	14,8 ± 9,4	17,1 ± 8,6	13,6 ± 5,9
BMI, kg/m2 (mean±SD)	25,0 ± 4,2	29,2 ± 5,0	29,3 ± 4,0
Overweight, n (%)	18 (37,5)	35 (74,5)	38 (84,4)
Included obesity, n (%)	7 (14,6)	19 (40,4)	18 (40)
Hypertension, n (%)	11 (22,9)	32 (68,1)	21 (46,7)
Diabetes and prediabetes, n (%)	4 (8,3)	13 (27,7)	8 (17,8)
Dyslipidemia, n (%)	4 (8,3)	13 (27,7)	16 (35,6)
Coronary heart disease, n (%)	2 (4,2)	8 (17,0)	3 (6,7)
Diseases of the gastrointestinal tract, n (%)	19 (39,6)	20 (42,6)	16 (35,6)

Conclusion: The prevalence of diseases of the gastrointestinal tract is approximately equal in all three groups, which is probably due to the use of non-steroidal anti-inflammatory drugs and glucocorticoids. The prevalence of the other pathology presented is significantly higher in the groups of psoriatic arthritis and does not significantly differ depending on the involvement of the spine in the pathological process. Due to the high prevalence of cardiovascular disease among patients with psoriatic arthritis, careful monitoring and timely administration of therapy is necessary.

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FRI0335

THE EFFECT OF TOFACITINIB ON RESIDUAL PAIN IN PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Current treatments for PsA have proven effective in reducing patient (pt)-reported pain;[1,2] however, residual pain often remains. Tofacitinib is an oral Janus kinase inhibitor for the treatment of PsA.

Objectives: This descriptive analysis evaluated the effect of tofacitinib, adalimumab and placebo on residual pain in pts with PsA whose inflammation was attenuated after 3 months of therapy.

Methods: Data were included from OPAL Broaden (NCT01877668), a randomised, double-blind, placebo-controlled Phase 3 trial of 12 months' duration in pts with PsA.[3] Pts were randomised to receive tofacitinib 5 mg twice daily (BID), tofacitinib 10 mg BID, adalimumab 40 mg subcutaneous injection once every 2 weeks or placebo. This analysis assessed pts with 'residual pain' at Month (M)3. Residual pain was considered as pain in pts with complete attenuation of inflammation at M3, defined by a swollen joint count (SJC) of 0 and CRP levels <6 mg/L. Pain was measured by a visual analogue scale (VAS; 0 ["no pain"] – 100 mm ["most severe pain"]). Changes in pain from baseline to M3 and residual pain (VAS pain reported at M3) were assessed.

Results: Demographics and baseline disease characteristics have previously been reported in the primary study, and were generally similar between treatment groups.[3] At M3, 100/422 (23.7%) pts with PsA had achieved SJC of 0 and CRP <6 mg/L. At M3, more tofacitinib-treated (tofacitinib 5 mg BID, n=23/107 [21.5%]; tofacitinib 10 mg BID, n=33/104 [31.7%]) and adalimumab-treated pts (n=31/106 [29.2%]) achieved SJC of 0 and CRP <6 mg/L vs placebo (PsA: n=13/105 [12.4%]). Baseline pain appeared numerically higher in tofacitinib-treated pts (tofacitinib 5 mg BID, 54.7 mm; tofacitinib 10 mg BID, 58.4 mm) vs adalimumab-treated pts (47.7 mm) and placebo (50.4 mm). In pts who achieved SJC of 0 and CRP <6 mg/L at M3, improvements in pain from baseline to M3 appeared numerically greater in pts receiving tofacitinib vs those receiving placebo (Figure 1a). When considering absolute (residual) pain at M3, mean residual pain was similar across treatment groups (ranging from 22.7–29.2 mm; Figure 1b), despite a higher baseline pain in tofacitinib treatment groups.

Conclusion: Changes from baseline in pain and absolute pain at M3 suggest that in pts with PsA whose inflammation has been completely attenuated, tofacitinib might have an effect on residual pain not obviously attributable to inflammation. However, the sample population was small, and there were large standard deviations. To confirm these results and to understand the mechanisms by which tofacitinib may improve residual pain, a meta-analysis will be performed using individual participant data from pts with rheumatic disease who have participated in tofacitinib randomised controlled trials.

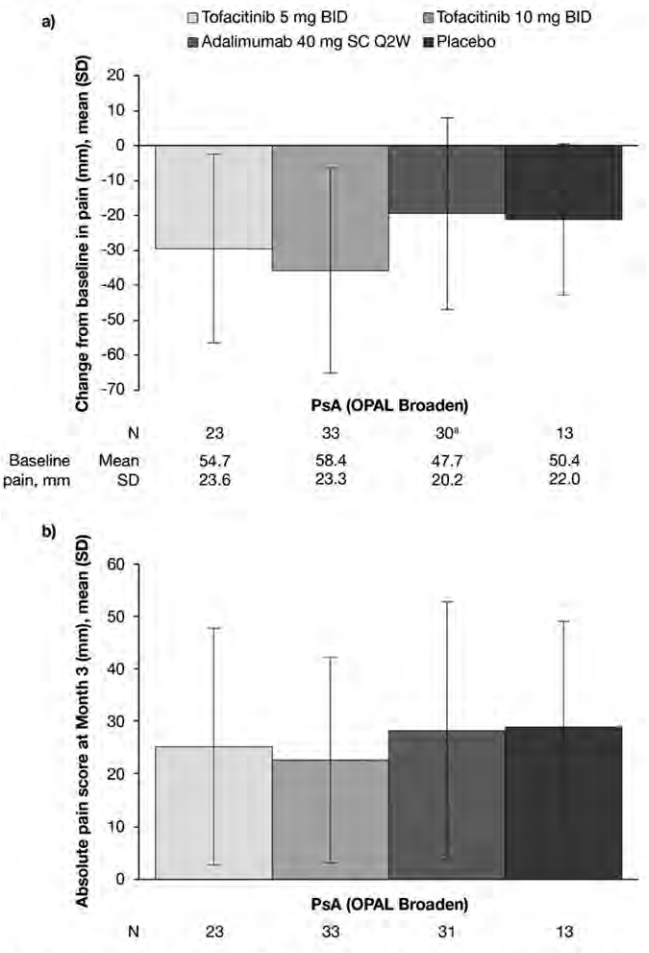
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Figure 1. Change from baseline in a) pain to Month 3 and b) absolute pain at Month 3 in patients with PsA and SJC=0 and CRP <6 mg/L by treatment group



Only patients who reported SJC of 0 and CRP <6 mg/L at Month 3 were included in this analysis. Mean pain is measured by a visual analogue scale from 0-100 mm where 0 = "no pain" and 100 = "most severe pain"
[a]One patient did not have baseline pain data
BID, twice daily; CRP, C-reactive protein; PsA, psoriatic arthritis; Q2W, once every 2 weeks; SC, subcutaneous injection; SD standard deviation; SJC, swollen joint count

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FRI0336 CONCOMITANT USE OF BIOLOGIC DMARDS WITH CSDMARDS INCREASES DRUG RETENTION RATE AND IMPROVES TREATMENT RESPONSE IN THE PSORIATIC ARTHRITIS. HUR-BIO REAL LIFE RESULTS

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Background: For inflammatory arthritis, drug retention is accepted as an important indicator of the effectiveness and safety of biological drugs.

Objectives: The objective of this study was to determine of the effects first and overall bDMARD drug retention rate during concomitant csDMARD in psoriatic arthritis (PsA).

Methods: HUR-BIO (Hacettepe University Rheumatology Biologic Registry) is a prospective, single center database of biological treatments since 2005. All PsA patients (469) who enrolled in HUR-BIO registry and prescribed at least once biologic DMARD (bDMARD) were included in the study. The subjects were divided into two groups depending on whether or not to use csDMARDs (methotrexate, sulphasalazine or leflunomide) at the last control visit. Demographic, clinical and therapeutic data were collected from this database. Baseline disease activity before the first bDMARD initiation was assessed with DAPSA and PsAID-12.

Table. Demographics, baseline and follow-up clinical characteristics of PsA patients

	With concomitant csDMARD n=288	Without concomitant csDMARD n=167	p
Age (mean, SD)	48.9 (12.1)	45.1 (12.4)	0.002
Female n (%)	204 (70.8)	113 (67.7)	0.48
PsA disease duration (med, IQR)	7 (13)	7 (14.5)	0.53
Age at PsA diagnosis (mean, SD)	39 (11.7)	40.8 (12.9)	0.81
BMI (mean, SD)	29.6 (6.0)	29.2 (5.9)	0.53
Axial involvement n (%)	68 (34.0)	37 (44.6)	0.09
HLA-B 27 (+) n (%)	21/76 (27.6)	17/69 (24.6)	0.68
Duration of use first bDMARD (months) (med, IQR)	22.4 (51.3)	14.1 (31.4)	0.003
Duration of use overall bDMARD (months) (med, IQR)	56.8 (69.4)	24.4 (57.7)	<0.001
Switching bDMARD (+) n (%)	148 (52.5)	71 (42.8)	0.04
Initial DAPSA[1] (med, IQR)	19.4 (11.7)	17.3 (10.2)	0.04
Initial PSAID[2] (med, IQR)	5.7 (3)	5.6 (2.8)	0.55
Final visit PSAID[3] (med, IQR)	2.8 (3.8)	2 (5.7)	0.41
Final visit DAPSA[4] (med, IQR)	10.2 (12.4)	12.5 (12.5)	0.01
Remission (n,%)	61 (23.9)	27 (17.6)	0.13
Low disease activity	111 (43.5)	59 (38.6)	
Moderate disease activity	72 (28.2)	58 (37.9)	
High disease activity	11 (4.3)	9 (5.9)	

[1]: n=249, [2]: n=214, [3]: n=109, [4]: n=408
p<0.001
p=0.003

Results: HUR-BIO PsA registry included 469 PsA patients. Baseline, clinical characteristics and follow-up parameters were given in Table. The using overall bDMARD were adalimumab 294 (62.0%), etanercept 135 (28.8%), infliximab 119 (25.4%), certolizumab pegol 107 (22.8%), secukinumab 67 (14.3%), golimumab 58 (12.4%), ustekinumab 25 (5.3%) and tofacitinib 11 (2.3%). Two hundred eighty eight (61.4%) patients used concomitant cDMARDs [methotrexate 176 (37.5%), leflunomide 94 (20.0%), sulphasalazine 35 (7.5%) and two csDMARD combination 17 (3.6%)]. The first-year retention rate of first bDMARD with or without concomitant csDMARDs were 88% and 80%, respectively. The median duration of first bDMARD retention with or without concomitant csDMARDs were 131.7 and 91.4 months, respectively (Figure). The first-year retention rate of overall bDMARDs with or without concomitant csDMARDs were 92% and 85%, respectively. The median drug retention rate of overall bDMARD in using csDMARD and not using csDMARD were 141.5 and 131.5 months, respectively. Retention rates (both for first bDMARD and overall bDMARDs) were significantly higher in concomitant csDMARDs using group (p=0.003 for first bDMARD retention, p<0.001 for overall bDMARDs retention, log-rank; Figure). In concomitant csDMARD using group, no differences were identified methotrexate or other csDMARDs.

Conclusion: In this study, csDMARDs, either methotrexate or leflunomide/sulphasalazine have additional effect for both retention rate and treatment response of bDMARDs. On the other hand, using bDMARD monotherapy is relatively higher than rheumatoid artritis (1).

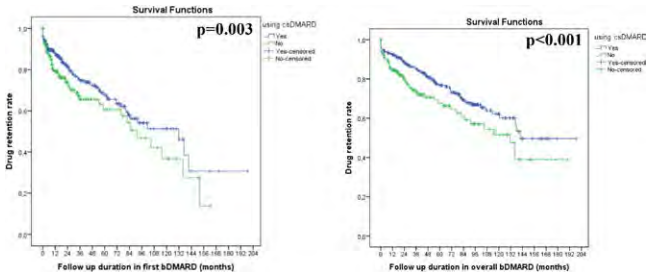


Figure. Drug retention rate of the first bDMARD and overall bDMARDs according to concomitant csDMARD use (*csDMARD:conventional synthetic Disease Modifiying Antirheumatic Drug*)

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FRI0337 REAL WORLD SECUKINUMAB DRUG-SURVIVAL IN PSORIATIC ARTHRITIS

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Background: Secukinumab (Cosentyx) is a human IgG1 monoclonal antibody that selectively binds to and neutralizes IL-17A. Several prospective randomized control trials have demonstrated the efficacy and safety of secukinumab in PsA, but there is a paucity of real life data in the PsA population.

Objectives: To prospectively study secukinumab's safety, efficacy, and tolerability in the cohort of PsA patients from the Israeli registry of inflammatory diseases.

Methods: PsA patients fulfilling the CASPAR criteria from the Israeli registry of inflammatory diseases were included in the analysis, from 2010 to November 2019. The primary end point was secukinumab drug survival compared to other available TNFi drug. Bivariate and multivariate analysis of the factors that affect the drug event free survival was done by cox regression analysis. Drug survival according to treatment line (all treatment lines, or 2nd and above treatment lines) was examined using Kaplan-Meier curves.

Results: Four hundred and four PsA patients were included, which had 709 treatment episodes (initiations) during the study period. Ninety patients had been treated with secukinumab (22%). Secukinumab treated patients were significantly older at time of initiation of treatment, and disease duration was longer. Secukinumab was more likely to be a second, third or forth line of treatment than the TNFi. . Time to an inefficacy event was longer for secukinumab than any other anti-TNF treatment. As a first line treatment secukinumab had drug survival similar to other TNFi. As a second or third line treatment, secukinumab had a better drug survival than other TNFi. Methotrexate did not have a significant effect on inefficacy event rate in combination treatment with secukinumab. Secukinumab, as infliximab and golimumab, was as effective in the higher BMI group as it was in the normal weight to obese groups. Smokers (current or past) did better on secukinumab than on TNFi. Secukinumab had a similar rate of adverse events compared to TNFi.

Conclusion: In this multicenter real world study, secukinumab had a comparable drug survival to TNFi. As a second and beyond line of treatment secukinumab had a better drug survival and lower HR for an inefficacy event. IL-17 inhibition is an effective mechanism of action to treat PsA in real life, and should be used more frequently as a first and second line treatment.

Tables and a graph:

Table 1. Inefficacy events according to treatment and drug survival in 1, 2, and 3 years.

Drug	Total episodes	Inefficacy events (%)	HR	95% CI	P value	1st year survival %	2nd year survival %	3rd year survival %
SEC	90	30 (33.3)	1		0.095	86	58	41
ETA	202	86 (42.6)	1.16	0.77-1.76	0.479	75	58	50
IFX	87	34 (39.1)	1.01	0.62-1.65	0.966	82	64	52
ADA	227	103 (45.4)	1.36	0.9-2.04	0.143	71	53	46
GOL	103	103 (50)	1.64	1.05-2.59	0.031	63	50	42

Table 2. inefficacy events and drug survival according to line of treatment.

Drug	Total episodes	Inefficacy events (%)	HR	95% CI	P value	1st year survival %	2nd year survival %	3rd year survival %
1st line								
SEC	13	2 (15.4)	1		0.216	92	92	76
ETA	130	55 (42.3)	3.25	0.79-13.34	0.101	76	59	51
IFX	28	11 (39.3)	2.88	0.64-13.01	0.168	81	63	52
ADA	103	37 (35.9)	2.63	0.63-10.91	0.183	79	63	59
GOL	25	14 (56)	4.55	1.03-20	0.045	60	50	40
2nd and 3rd lines								
SEC	34	7 (20.6)	1		0.039	90	66	66
ETA	68	29 (42.6)	1.68	0.74-3.85	0.218	73	57	51
IFX	51	20 (39.2)	1.42	0.6-3.36	0.431	85	64	54
ADA	119	62 (52.1)	2.5	1.15-5.48	0.022	65	46	35
GOL	52	23 (44.2)	2.26	0.97-5.27	0.06	65	50	46
4th line								
SEC	43	21 (48.8)	1		0.082	82	44	24
ETA	4	2 (50)	1.1	0.25-4.73	0.902	67	33	–
IFX	8	3 (37.5)	0.83	0.25-2.79	0.762	69	69	–
ADA	5	4 (80)	4.87	1.6-14.81	0.005	30	–	–
GOL	26	13 (50)	1.29	0.64-2.58	0.473	62	52	31

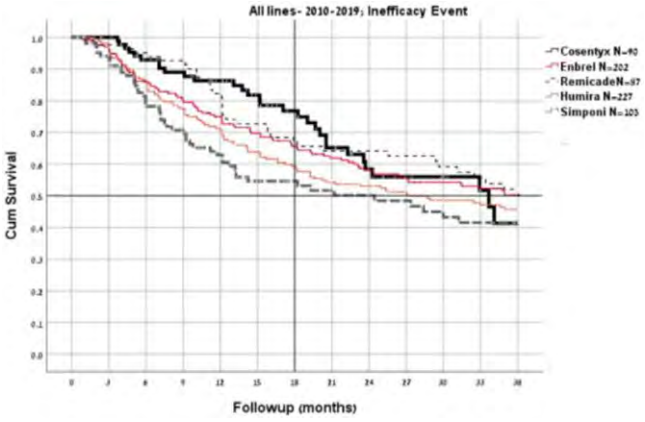


Figure 1. Cumulative survival without an inefficacy event of secukinumab compared to TNFα inhibitors regardless of treatment line.

Disclosure of Interests: Tali Eviatar: None declared, Devy Zisman Consultant of: Novartis, Merav Lidar Consultant of: Novartis, Tatyana Reitblat Consultant of: Novartis, Alexandra Balbir-Gurman Consultant of: Novartis, Ori Elkayam Speakers bureau: AbbVie, BMS, Pfizer, Roche, Sanofi-Aventis, Novartis, Jansen

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FRI0338

SIMILAR CARDIOVASCULAR COMORBIDITY AND HIGHER DEPRESSION RATES IN PSORIATIC ARTHRITIS COMPARED TO AGE- AND SEX-MATCHED RHEUMATOID ARTHRITIS AND DIABETES MELLITUS PATIENTS

G. E. Fragoulis[1], G. Evangelatos[2], N. Tentolouris[3], K. Fragkiadaki[1], S. Panopoulos[1], G. Konstantonis[1], A. Iliopoulos[2], K. Chatzidionysiou[1], P. Sfikakis[1], M. Tektonidou[1]. [1]*National and Kapodistrian University of Athens, "Laiko" General Hospital, First Department of Propaedeutic Internal Medicine, Joint Rheumatology Program, Athens, Greece*; [2]*417 Army Shared Fund Hospital "NIMTS", Rheumatology Department, Athens, Greece*; [3]*National and Kapodistrian University of Athens, "Laiko" General Hospital, First Department of Propaedeutic Internal Medicine, Diabetes Centre, Athens, Greece*

Background: Comorbidities are frequent in psoriatic arthritis (PsA) but it is not known how they differ from other high comorbidity burden diseases like rheumatoid arthritis (RA) and diabetes mellitus (DM).

Objectives: To compare the prevalence of comorbidities in PsA vs. RA and DM patients.

Methods: 215 PsA patients were age/gender-matched with 215 RA and 215 DM patients from two tertiary hospitals. Prevalence of comorbidities (hypertension, current smoking, hyperlipidemia, obesity (BMI≥30), coronary disease [CD], stroke, MACE [combined CD and stroke], depression, osteoporosis, history of malignancies) were compared across the three groups. Within PsA group, associations between comorbidities and demographic and clinical features (e.g entheitis), including PsA phenotypes (RA-like vs oligoarthritis pattern and Axial-involvment vs Non-Axial-involvement) were assessed.

Results: Hyperlipidaemia, obesity and depression were more frequent in PsA vs. RA. Depression and osteoporosis were more common in PsA vs DM. In contrast, hypertension was more frequent in DM. All other comorbidities, including frequency of stroke, CD and major adverse cardiovascular events did not differ between groups. Results remain unchanged after adjustments (Table 1).

Within PsA group, depression was associated with female gender (p=0.02), older age (p=0.03), higher disease duration (p=0.04) and current smoking (p=0.04). MACEs in PsA, were associated with male gender (p=0.03), older age (p=0.0002), dyslipidaemia (p=0.003) and hypertension (p<0.0001). No differences were found between different phenotypes of PsA.

Conclusion: PsA patients had higher BMI and hyperlipidaemia compared to RA but not to DM. MACE is comparable between PsA and RA or DM, while depression is more common in PsA. Taking into account certain risk factors, screening for and management of comorbidities in PsA is important in the clinical setting.

Disclosure of Interests: George E. Fragoulis: None declared, Gerasimos Evangelatos: None declared, Nikolaos Tentolouris: None declared, Kalliopi Fragkiadaki: None declared, Stylianos Panopoulos: None declared, George Konstantonis: None declared, Alexios Iliopoulos: None declared, Katerina Chatzidionysiou Consultant of: AbbVie, Pfizer, Lilly., Petros Sfikakis Grant/research support from: Grant/research support from Abvie, Novartis, MSD, Actelion, Amgen, Pfizer, Janssen Pharmaceutical, UCB, Maria Tektonidou Grant/research support from:

Table 1. Comparison of comorbidities between psoriatic arthritis (PsA), rheumatoid (RA) arthritis and Diabetes mellitus (DM) patients. OR: odds ratio, MACE: major adverse cardiovascular events. CI: Confidence Intervals

				PsA vs RA		PsA vs DM	
Comorbidity	PsA n=215 n (%)	RA n=215 n (%)	DM N=215 n (%)	Crude OR (95% CI)	Adjusted OR (95% CI)	Crude OR (95% CI)	Adjusted OR (95% CI)
Smoking	76 (35.4)	62 (28.8)	85 (39.5)	1.35 (0.90-2.03)		0.84 (0.57-1.24)	
Obesity	50 (29.4)	24 (12.8)	79 (36.7)	2.83 (1.65-4.86)		0.72 (0.47-1.10)	
Hyperlipidemia	101 (47.0)	67 (31.2)	101 (47.0)	1.96 (1.32-2.90)	-	1	-
Hypertension	62 (28.8)	51 (23.8)	97 (45.1)	1.30 (0.84-1.99)	-	0.49 (0.33-0.74)	-
Coronary disease	10 (4.7)	10 (4.7)	16 (7.4)	1 (0.41-2.45)	0.97 (0.34-2.79)*	0.61 (0.27-1.37)	0.66 (0.23-1.91)*
Stroke	8 (3.7)	2 (0.9)	7 (3.3)	4.12 (0.86-19.6)	3.74 (0.73-19.3)*	1.15 (0.41-3.22)	1.20 (0.35-4.12)*
MACE	12 (5.6)	12 (5.6)	22 (10.2)	1 (0.44-2.28)	0.94 (0.36-2.46)*	0.52 (0.25-1.08)	0.42 (0.16-1.10)*
Osteoporosis	9 (5.5)	24 (11.2)	2 (0.9)	0.46 (0.21-1.03)	0.67 (0.28-1.64)**	6.22 (1.33-29.2)	-
Depression	42 (19.5)	15 (7.0)	12 (5.6)	3.24 (1.74-6.04)	3.02 (1.57-5.81)***	4.11 (2.10-8.05)	4.85 (2.37-9.93)***
Malignancy	12 (5.6)	7 (3.3)	-	1.76 (0.68-4.55)	1.60 (0.60-4.26)****	-	-

* adjusted for age, gender, smoking, hypertension, dyslipidemia, body mass index, ** adjusted for steroids, *** adjusted for age, gender, disease duration, smoking, **** adjusted for age, disease duration

AbbVie, MSD, Novartis and Pfizer, Consultant of: AbbVie, MSD, Novartis and Pfizer

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FRI0339

LONG-TERM EFFICACY OF THE ORAL SELECTIVE JANUS KINASE 1 INHIBITOR FILGOTINIB IN PSORIATIC ARTHRITIS: WEEK 52 RESPONSE PATTERNS IN INDIVIDUAL PATIENTS FROM AN OPEN-LABEL EXTENSION (OLE) STUDY (EQUATOR2)

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Background: EQUATOR (NCT03101670) was a 16-week, Phase 2, multicenter, double-blind, placebo-controlled, randomized controlled trial (RCT) of filgotinib in patients with active psoriatic arthritis.[1] Filgotinib demonstrated rapid efficacy compared with placebo across multiple domains, including the primary endpoint of Week 16 American College of Rheumatology (ACR) 20 response.[1] Patients completing the RCT could join an ongoing 148-week OLE (EQUATOR2; NCT03320876).

Objectives: In this prespecified interim analysis at Week 52 of the OLE, individual patient responses with respect to disease activity were evaluated.

Methods: Placebo-treated RCT patients switched to filgotinib (200 mg once daily) at Week 16 and entered the OLE; patients previously assigned to filgotinib continued. Individual response patterns at Week 52 of the OLE were evaluated for ACR20/50/70, Psoriatic Arthritis Disease Activity Score (PASDAS) low disease activity (LDA), minimal disease activity (MDA), and MDA/very low disease activity (VLDA).

Results: 124 patients (95%) completed EQUATOR; 122 (93%) enrolled in the OLE. At Week 52, 11 patients (9%) had discontinued treatment in the OLE. Median (range) exposure to filgotinib was 66.0 (0.4–104.1) weeks. In patients originally assigned to filgotinib, sustained efficacy was seen through to OLE Week 52 for ACR20, 50, and 70; PASDAS LDA; MDA (**Table;** Figure 1**a**); and MDA/VLDA. In total, 77% and 93% of those achieving MDA and ACR50 response in the RCT period maintained this at Week 52 (**Table**). A substantial proportion of RCT non-responders also achieved a treatment response in the OLE, meeting MDA and ACR50 criteria (22% and 37%, respectively; **Table**). Response patterns in the OLE were similar regardless of prior RCT treatment. In total, at Week 52 of the OLE, 33.6% of patients achieved MDA response (Figure 1**a**); 55.0% achieved ACR50 response. Figure 1**b** shows individual patient response over time for MDA.

Conclusion: Data from this 52-week OLE interim analysis suggest that further improvement in disease activity can be expected with filgotinib beyond 16 weeks in patients with active psoriatic arthritis. Sustained efficacy was demonstrated across several measures of disease activity, including MDA and ACR50.

References:

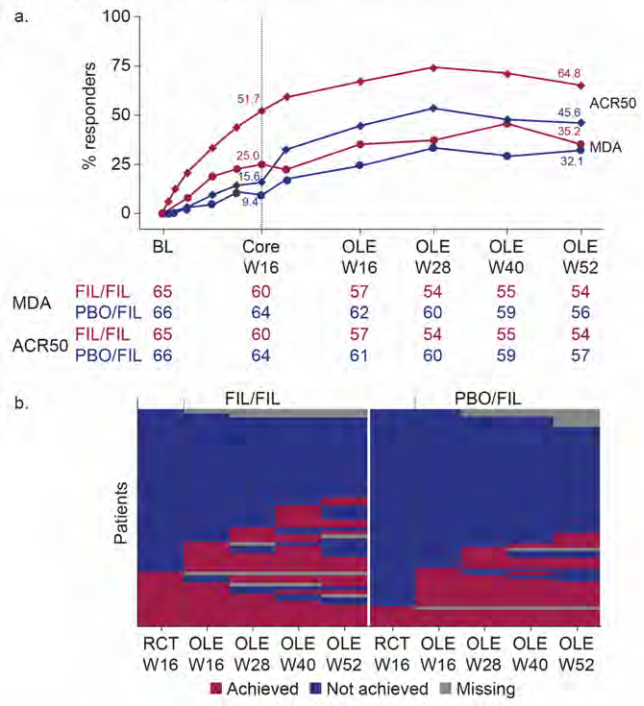
[1] Mease P, et al. Lancet 2018;392:2367–77.

Table. Responders at Week 52 of the OLE, by treatment and previous RCT responder status (observed cases).

Treatment	Filgotinib (N=59) → Filgotinib (N=54)[a]		Placebo (N=63) → Filgotinib (N=57)[a]	
n/N, %	OLE responders/ RCT responders	OLE responders/RCT non-responders	OLE responders/ RCT responders	OLE responders/RCT non-responders
ACR20	40/47 (85.1)	5/7 (71.4)	17/18 (94.4)	27/38 (71.1)
ACR50	25/27 (92.6)	10/27 (37.0)	5/8 (62.5)	21/49 (42.9)
ACR70	10/13 (76.9)	12/41 (29.3)	3/4 (75.0)	12/53 (22.6)
PASDAS LDA[b]	19/21 (90.5)	12/32 (37.5)	5/6 (83.3)	21/48 (43.8)
MDA	10/13 (76.9)	9/41 (22.0)	4/5 (80.0)	14/51 (27.5)

[a]Indicates number remaining at OLE Week 52 interim analysis, after dropouts
[b]PASDAS information was not available for one patient at Week 16 of the RCT

Figure 1. Patients achieving ACR50 and MDA over time (a) and MDA per patient over time (b).



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Disclosure of Interests: Dafna D Gladman Grant/research support from: AbbVie, Amgen Inc., BMS, Celgene Corporation, Janssen, Novartis, Pfizer, UCB – grant/research support, Consultant of: AbbVie, Amgen Inc., BMS, Celgene Corporation, Janssen, Novartis, Pfizer, UCB – consultant, Laura C Coates: None declared, Filip van den Bosch Consultant of: AbbVie, Celgene Corporation, Eli Lilly, Galapagos, Janssen, Novartis, Pfizer, and UCB, Speakers bureau: AbbVie, Celgene Corporation, Eli Lilly, Galapagos, Janssen, Novartis, Pfizer, and UCB, Philip Helliwell: None declared, Chantal Tasset Shareholder of: Galapagos (share/warrant holder), Employee of: Galapagos, Luc Meuleners Employee of: Galapagos, Leen Gilles Consultant of: Galapagos, Lien Gheyle Employee of: Galapagos, Mona Trivedi Shareholder of: Amgen and Gilead Sciences, Employee of: Gilead Sciences, Muhsen Alani Employee of: Gilead Sciences, Robin Besuyen Shareholder of: Galapagos, Employee of: Galapagos, Philip J Mease Grant/research support from: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Eli Lilly, Novartis, Pfizer, Sun Pharmaceutical, UCB – grant/research support, Consultant of: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Eli Lilly, Novartis, Pfizer, Sun Pharmaceutical, UCB – consultant, Speakers bureau: Abbott, Amgen, Biogen Idec, BMS, Eli Lilly, Genentech, Janssen, Pfizer, UCB – speakers bureau

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FRI0340

COMPARISON OF SECUKINUMAB VERSUS ADALIMUMAB EFFICACY ON SKIN OUTCOMES IN PSORIATIC ARTHRITIS: 52-WEEK RESULTS FROM THE EXCEED STUDY

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Background: Psoriatic arthritis (PsA) is a heterogeneous disease comprising musculoskeletal and dermatological manifestations, especially plaque psoriasis.[1] Secukinumab (SEC), an IL-17A inhibitor, provided significantly greater PASI 75/100 responses in a head-to-head trial *versus (vs.)* etanercept, a TNF inhibitor, in patients (pts) with moderate-to-severe plaque psoriasis.[2] The objective of the EXCEED study (NCT02745080) was to investigate whether SEC is superior to

adalimumab (ADA), a TNF inhibitor, as monotherapy in biologic-naive active PsA pts with active plaque psoriasis (defined as having at least one psoriatic plaque of ≥2 cm diameter or nail changes consistent with psoriasis or documented history of plaque psoriasis).

Objectives: To report the pre-specified skin outcomes from the EXCEED study in the subset of pts with at least 3% body surface area (BSA) affected with psoriasis at baseline.

Methods: Head-to-head, phase-3b, randomised, double-blind, active-controlled, multicentre, parallel-group trial: pts were randomised to receive SEC 300 mg subcutaneous at baseline, Week 1-4, followed by dosing every 4 weeks (q4w) until Week 48 or ADA 40 mg subcutaneous at baseline followed by same dosing q2w until Week 50. The primary endpoint was superiority of SEC *vs.* ADA on ACR20 response at Week 52. Pre-specified outcomes included the proportion of pts achieving a combined ACR50 and PASI 100 response, PASI 100 response, and absolute PASI score ≤3. Missing data was handled using multiple imputation.

Results: 853 pts were randomised to receive SEC (n=426) or ADA (n=427). At baseline, there were 215 and 202 pts having at least 3% BSA affected with psoriasis in the SEC and ADA groups, respectively. A higher proportion of patients achieved simultaneous improvement in ACR50 and PASI 100 response with SEC *vs.* ADA (30·7% *vs.* 19·2%; P=0·0087 [Figure]). Higher efficacy was demonstrated for SEC *vs.* ADA for PASI 100 responses and for the proportion of pts achieving absolute PASI score ≤3 (Table).

Conclusion: In this pre-specified analysis, SEC provided higher responses compared to ADA in achievement of simultaneous improvement of joint and skin disease (combined ACR50 and PASI 100 response) and in skin specific endpoints (PASI 100 and PASI score ≤3) at Week 52.

References:

[1] Coates LC and Helliwell PS. *Clinical Med*.2017;17:65–70.
[2] Langley RG et al. *N Engl J Med.* 2014;371:326–38.

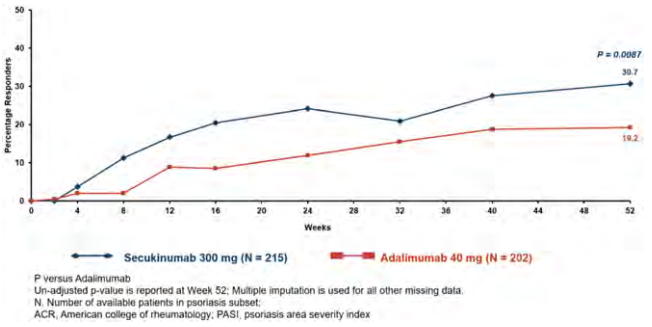


Figure. Combined ACR50 and PASI 100 Response through Week 52

Table. Skin Specific Outcomes at Week 52

Endpoints, data is presented as % response	SEC 300 mg (N = 215)	ADA 40 mg (N = 202)	P-value (unadjusted)
PASI 100	46·0	29·7	0·0007
Absolute PASI score ≤3	79·2	65·0	0·0015

P value vs. adalimumab; Unadjusted P values are presented
N, number of patients in psoriasis subset
Multiple imputation was used for handling missing data
ADA, adalimumab; BSA, body surface area; PASI, psoriasis area severity index; SEC, secukinumab

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Disclosure of Interests: Alice B Gottlieb Grant/research support from:: Research grants, consultation fees, or speaker honoraria for lectures from: Pfizer, AbbVie, BMS, Lilly, MSD, Novartis, Roche, Sanofi, Sandoz, Nordic, Celltrion and UCB., Consultant of:: Research grants, consultation fees, or speaker honoraria for lectures from: Pfizer, AbbVie, BMS, Lilly, MSD, Novartis, Roche, Sanofi, Sandoz, Nordic, Celltrion and UCB., Speakers bureau:: Research grants, consultation fees, or speaker honoraria for lectures from: Pfizer, AbbVie, BMS, Lilly, MSD, Novartis, Roche, Sanofi, Sandoz, Nordic, Celltrion and UCB., Frank Behrens Grant/research support from: Pfizer, Janssen, Chugai, Celgene, Lilly and Roche, Consultant of: Pfizer, AbbVie, Sanofi, Lilly, Novartis, Genzyme, Boehringer, Janssen, MSD, Celgene, Roche and Chugai, Peter Nash Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Gilead, Janssen, MSD, Novartis, Pfizer Inc, Roche, Sanofi, UCB, Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, MSD, Novartis, Pfizer Inc, Roche, Sanofi, UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, MSD, Novartis, Pfizer Inc, Roche, Sanofi, UCB, Joseph F. Merola Consultant of: Merck, AbbVie, Dermavant, Eli Lilly, Novartis, Janssen, UCB Pharma, Celgene, Sanofi, Regeneron, Arena, Sun Pharma, Biogen, Pfizer, EMD Sorono, Avotres and LEO Pharma, Kevin Ding Employee of: Novartis, Pascale Pellet Shareholder of: Novartis, Employee of: Novartis, Lumanita Pricop Shareholder of: Novartis, Employee of: Novartis, Iain McInnes Grant/research support from: Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Janssen, and UCB, Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Gilead, Janssen, Novartis, Pfizer, and UCB

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FRI0341

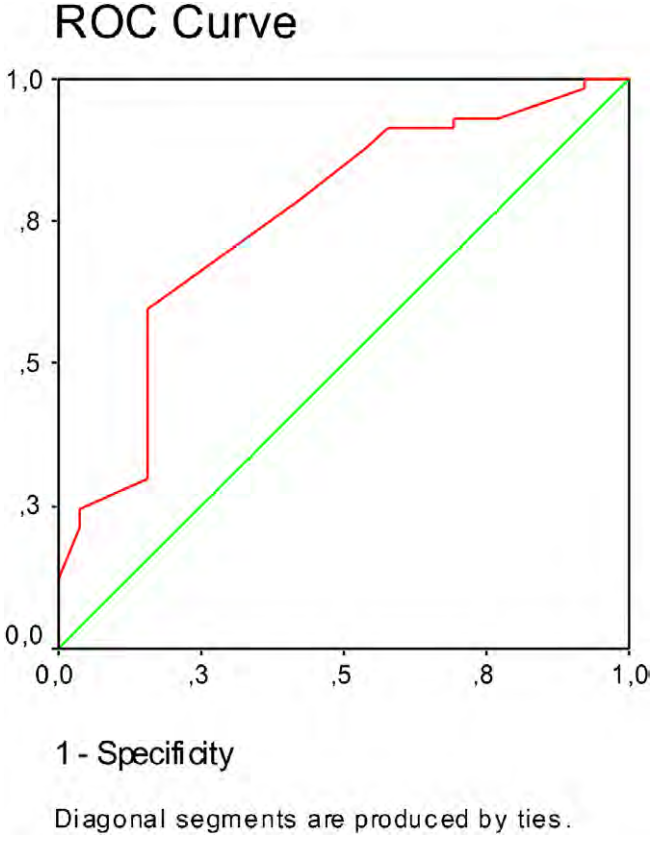
RISK FACTORS FOR AXIAL INVOLVEMENT IN EARLY PSORIATIC ARTHRITIS

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Background: Axial Involvement in psoriatic arthritis (PsA) is quite common [1]. Predictors of axial involvement at early-stage of disease haven't been sufficiently studied.

Objectives: To identify predictors of axial involvement in PsA patients (pts) at early-stage of disease.

Methods: 95 patients (pts) (M/F–47/48) with early PsA fulfilling the CASPAR criteria were included. All pts had peripheral arthritis for≤2 years; no inflammatory back pain (IBP) pts were specifically selected. Mean (Me) age 36.5±10.7 yrs, disease duration 12.2±10.3 mo. Pts underwent standard clinical examination of PsA activity. Me disease activity indexes DAS=4.0±1.4, DAS28=4.2±1.1, BASDAI=4.5±1.6; Me pts global disease activity VAS 56.9±17.1. All patients were evaluated for the presence of IBP by ASAS criteria, underwent sacroiliac joints (SIJs) X-ray (pelvic radiographs) and HLA B27 antigen status study. MRI of SIJs was performed in 79 pts, regardless of IBP presence, on Signa Ovation 0.35T. Radiographic sacroiliitis (R-SI) was identified according to New York criteria (unilateral grade≥3 or bilateral grade≥2). Bone marrow edema/ osteitis on MRI (STIR) was considered active MRI sacroiliitis (MRI-SI). X-ray and MRI results were evaluated by an independent reader. IBP was observed in 63 (66.3%) cases, MRI-SI in 28 of 79 (35.4%) examined cases, R-SI in 29 (30.5%) cases. Skin lesion severity was evaluated as body surface area (BSA) affected: minor at <3%, mild at 3-10%, severe at >10%. Pts were split into 2 groups (gr.): those with axial involvement (axPsA), that is with IBP and/or R-SI and/or MRI-SI; and those without axial involvement (having only peripheral PsA [pPsA]).The axPsA gr. included 65 (68.4%) cases, the pPsA gr. 30 (31.6%) cases. Multi-dimensional step-by-step discriminant analysis was used to identify a group of features that are more typical for the axPsA patients.



Results: The following features proved to be the most informative: male sex (p = 0.300), presence of HLA B27 (p = 0.107), mild or high DAS (p = 0.098), skin lesion severity BSA>3% (p = 0.118), and CRP > 5 mg/L (0.038).
Sensitivity of model 79.0%, specificity of model 57.7%. Area under ROC curve 0.756; 95% CI (0.642-0.869).
Conclusion: It is a combination of features – male sex, HLA-B27 positivity, mild or high activity of peripheral arthritis according to DAS, CRP > 5 mg/L, and BSA> 3% – that constitutes a clinical predictor for the development of axial involvement in early psoriatic arthritis.
References:
[1] V. Chandran et al. Curr Opin Rheumatol. 2019;31:329-34
Disclosure of Interests: ELENA GUBAR: None declared, Elena Loginova Speakers bureau: Janssen, Svetlana Glukhova: None declared, Tatiana Korotaeva Grant/research support from: Pfizer, Consultant of: Abbvie, BIOCAD, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Merck Sharp & Dohme, Novartis, Novartis-Sandoz, Pfizer, UCB, Speakers bureau: Abbvie, BIOCAD, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Merck Sharp & Dohme, Novartis, Novartis-Sandoz, Pfizer, UCB
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FRI0342 POST-EFFORT SYNOVIAL AND ENTHESIC RESPONSE IN PATIENTS WITH PSORIATIC ARTHRITIS IN REMISSION OF LOW DISEASE ACTIVITY

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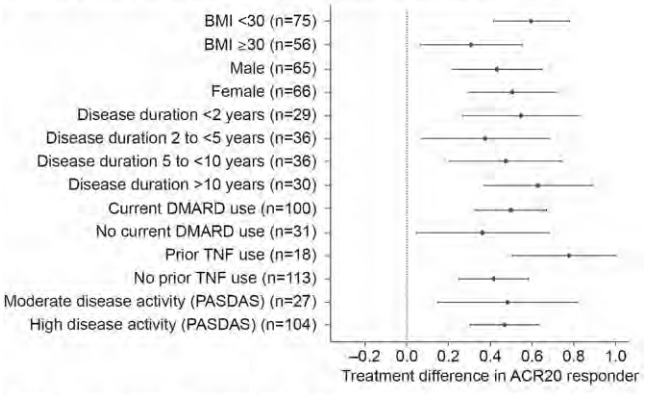
Background: Synovial inflammation is part of the pathophysiological process of PsoA although it is considered secondary to enthesitis. It is of interest to assess the synovial joint, peritendinous and enthesic response of patients with PsoA in remission under controlled mechanical stress.
Objectives: Our aim is to present our observational experience in patients with APso in remission or low activity of the disease exposed to controlled manual physical efforts adapted to the own grasping capacity of each subject.
Methods: Before-after study of a consecutive cohort of patients with PsoA (CASPAR criteria), of at least two years d evolution and DAPSA≤14 at present. Patients with positive rheumatoid factor, patients with exclusively axial forms and patients on biological therapy at the beginning of the study were excluded. All patients underwent controlled basal ultrasound and post-dynamometric exercise (CAMRY EH101-17) of the dominant hand which included the carpus, MCFs, IFPs and IFDs of the 2nd to 5th fingers. The ultrasound findings were scored according to EULAR recommendations in grey scale (GS) and power Doppler (PD) for synovitis, enthesitis and tenosynovitis (maximum scores 71 and 87, respectively). For statistical analysis, comparisons were made with the results of their baseline and post-exercise ultrasound scores between subjects diagnosed with PsoA and controls. The Student's T test was used for related and unrelated data according to correspondence.
Results: Nineteen patients and controls were included, of which 73.7% were male. Mean age: 42.2 SD 6.6 and 42.21 SD 8.28, respectively. Basal DAPSA among patients: 7.26 SD 4.53. Mean traction strength of patients and controls: 23.8 SD 7.3 and 26.1 SD 6.9 kg, respectively (P=0.336). In the group of patients, the post exercise DAPSA had a mean of 7.52 SD 4.62 (P=0.021, with respect to the basal DAPSA). The mean total GS score in the patient group was 3.94 SD 2.36 and 7.31 SD 3.3, pre- and post-exercise, respectively (P<0.001). The mean total score in the PD study was 0.73 SD 0.73 and 2.57 SD 1.16, respectively (P<0.001). In patients with PsoA there were no detectable enthesic changes. In the control group, no ultrasound changes were statistically significant, although the score for tenosynovitis ranged from 0.1 SD 0.31 to 0.42 SD 0.6 (P=0.055).
Conclusion: Patients with APso in clinical remission or low disease activity develop ultrasound changes after controlled exercise. These changes are appreciable in the joint synovium and tendon but not at an enthesic level. Although these changes are also detectable in a healthy population, their prevalence is much lower. Our interpretation is that control of the disease correlates with an absence of enthesic inflammatory activity although synovial susceptibility remains less evident. This reinforces the idea that PsoA is an inflammatory enthesitis with associated arthritis and not its opposite.
Disclosure of Interests: None declared
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FRI0343 EFFICACY AND SAFETY OF FILGOTINIB, A SELECTIVE JANUS KINASE 1 INHIBITOR, IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: SUBGROUP ANALYSES FROM A RANDOMIZED, PLACEBO-CONTROLLED, PHASE 2 TRIAL (EQUATOR)

P. Helliwell[1], F. Van den Bosch[2], L. C. Coates[3], D. D. Gladman[4], C. Tasset[5], L. Meuleners[5], L. Gilles[6], L. Gheyle[5], M. Trivedi[7], M. Alani[7,8], R. Besuyen[9], P. J. Mease[8,10]. [1]*University of Leeds, Leeds, United Kingdom*; [2]*Ghent University Hospital, Ghent, Belgium*; [3]*Botnar Research Centre, University of Oxford, Oxford, United Kingdom*; [4]*University of Toronto, Toronto, Canada*; [5]*Galapagos NV, Mechelen, Belgium*; [6]*LACO, contracted by Galapagos NV, Mechelen, Belgium*; [7]*Gilead Sciences, Inc, Foster City, CA, United States of America*; [8]*University of Washington, Seattle, United States of America*; [9]*Galapagos BV, Leiden, Netherlands*; [10]*Swedish Medical Centre, Seattle, United States of America*

Background: Treatment with the oral selective Janus kinase 1 inhibitor filgotinib was associated with rapid and significant improvements in multiple domains of active psoriatic arthritis versus placebo in the 16-week Phase 2, multicenter, double-blind, randomized EQUATOR trial (NCT03101670).[1] A significantly greater proportion of patients receiving filgotinib, versus placebo, achieved the primary endpoint of 20% improvement in American College of Rheumatology (ACR) 20 response at Week 16 (80% vs 33%, respectively).[1]
Objectives: The aim of this predefined analysis was to evaluate the consistency of the response to filgotinib across predefined relevant subpopulations participating in the EQUATOR trial.
Methods: In EQUATOR, patients with active psoriatic arthritis were treated with filgotinib 200 mg (n=65) or placebo (n=66) once daily for 16 weeks. Key clinical endpoints, including ACR20 and ACR50 (50% improvement) response rates, Psoriatic Arthritis Disease Activity Score (PASDAS), and Disease Activity Index for Psoriatic Arthritis (DAPSA) were evaluated according to the following baseline characteristics: sex, body mass index, disease duration, baseline disease severity, concurrent use of disease-modifying antirheumatic drug(s), and prior exposure to tumor necrosis factor inhibitor(s). For PASDAS and DAPSA scores, statistical analysis of changes from baseline was performed using analysis of covariance with factors for treatment, randomization stratification, subgroup, and an interaction between treatment and subgroup. Least-squares (LS) mean difference between treatment arms and the corresponding 95% confidence intervals (CI) were calculated. For ACR20 and ACR50 response rates, statistical analysis used the point estimate and corresponding 95% CI, based on the Newcombe method.
Results: Sixty patients (92%) in the filgotinib group and 64 (97%) in the placebo group completed the study. The total number of patients in each subpopulation ranged from 18 to 104 (Figure 1). Differences in the proportions of patients achieving ACR20 consistently favored filgotinib, compared with placebo, across all subgroups (Figure 1); all differences reached statistical significance. Similarly, differences in the proportions of ACR50 responders and LS mean treatment differences for PASDAS and DAPSA consistently favored filgotinib, reaching statistical significance in most subgroups. No clinically relevant differences in the effect of filgotinib were observed across subgroups. Filgotinib was generally well tolerated and no new safety signals were identified.

Figure 1. Effect of filgotinib on ACR20 response across subgroups.



ACR20, 20% improvement in American College of Rheumatology response criteria; BMI, body mass index; DMARD, disease-modifying antirheumatic drug; PASDAS, Psoriatic Arthritis Disease Activity Score; TNF, tumor necrosis factor

Conclusion: In the 16-week EQUATOR trial, the effects of filgotinib on key efficacy endpoints were generally consistent across a range of subgroups based on patient, disease, and treatment characteristics.

References:
[1] Mease P, et al. Lancet 2018;392:2367–77.

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FRI0344

THE LONG-TERM EFFECT OF TREATING PSORIATIC ARTHRITIS WITH THE JANUS KINASE 1-SELECTIVE INHIBITOR FILGOTINIB ON LIPID PROFILES: AN ANALYSIS OF THE EQUATOR AND EQUATOR2 TRIALS

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Background: Cardiovascular (CV) comorbidities are common in psoriatic arthritis (PsA); patients are at high risk for major adverse cardiovascular events (MACE).[1] In the Phase 2, double-blind, randomized EQUATOR trial, significant improvements across multiple PsA domains were observed with the oral selective Janus kinase (JAK) 1 inhibitor filgotinib compared with placebo.[2] Inhibition of JAK signal transducer and activator of transcription signaling is associated with raised serum lipids.[3]

Objectives: To evaluate the effects of filgotinib on the lipid profile of PsA patients and determine if those with higher MACE risk show similar changes in lipid profile compared with the overall population.

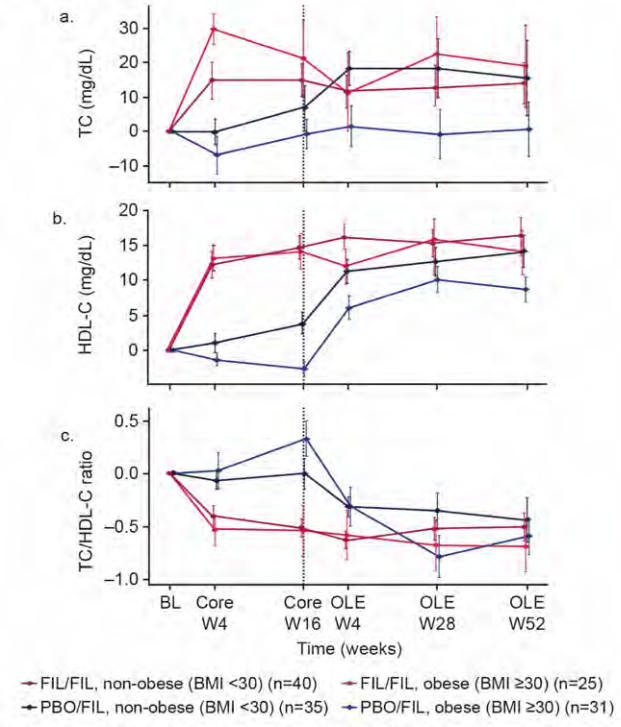
Methods: In EQUATOR, 131 patients with active PsA received filgotinib 200 mg (n=65) or placebo (n=66) once daily for 16 weeks. Patients completing EQUATOR could enter the ongoing EQUATOR2 open-label extension (OLE; NCT03320876), in which patients receive filgotinib 200 mg for up to 148 weeks. Effects of filgotinib on total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and TC/HDL-C ratio at OLE Week 52 (68 weeks after EQUATOR initiation) were analyzed. In a post hoc analysis, patients were classified into subgroups according to presence/absence of obesity (baseline body mass index [BMI]; ≥30 vs <30 kg/m^2, respectively), diabetes mellitus, arterial hypertension (≥130/80 mmHg), hyperlipidemia, and metabolic syndrome. Changes in lipid levels were explored graphically.

Results: 124 patients (95%) completed EQUATOR; 122 (93%) enrolled in the OLE. Of these, 11 patients (9%) discontinued treatment by OLE Week 52. Median (range) exposure to filgotinib was 66.0 (0.4–104.1) weeks. In the OLE, TC, LDL-C, and HDL-C levels increased versus baseline with filgotinib, resulting in a decreased TC/HDL-C ratio. Changes in lipid levels were consistent irrespective of presence of obesity (n=56; **Fig**), diabetes (n=53), arterial hypertension (n=80), hyperlipidemia (n=108), or metabolic syndrome (n=36); baseline lipid values were greater in the higher risk groups. In patients who were assigned placebo in the randomized controlled trial (RCT), HDL-C increased on switching to filgotinib in the OLE (in a manner similar to that seen in filgotinib-treated patients during the RCT), and remained elevated compared with baseline (**Fig**). Triglyceride levels remained stable throughout, across all subgroups. Seventeen patients (13%) were taking lipid-lowering drugs (LLDs) prior to the start of the trial (and continued to do so); the effect of filgotinib on the lipid profile in these patients was similar to that in the overall population. During the RCT phase, another six patients in the filgotinib group and one in the placebo group began taking LLDs.

Conclusion: In patients exposed to filgotinib for ≥52 weeks, the effects on lipid profile were consistent regardless of baseline CV risk. Lipid changes included an elevation in TC and HDL-C, with a decrease in TC/HDL-C ratio.

References:
[1] Haddad A & Zisman D. Rambam Maimonides Med J 2017;8:e0004
[2] Mease P, et al. Lancet 2018;392:2367–77
[3] Sands B, et al. Clin Gastroenterol Hepatol 2020;18:123–32

Figure 1. Change from baseline in lipid profile in non-obese and obese patients



BL, baseline; BMI, body mass index; FIL, filgotinib; HDL-C, high-density lipoprotein cholesterol; OLE, open-label extension; PBO, placebo; TC, total cholesterol; W, Week

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FRI0345

HEAD-TO-HEAD STUDY EVALUATING THE COMBINED ACR50/PASI100 TREATMENT RESPONSE OF IXEKIZUMAB VERSUS ADALIMUMAB: INDIVIDUAL PATIENT DATA FROM A RANDOMIZED, OPEN-LABEL STUDY IN BIOLOGIC-NAÏVE PATIENTS WITH PSORIATIC ARTHRITIS THROUGH WEEK 52

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Background: Multiple biologic DMARDs (bDMARDs) are available for the treatment of psoriatic arthritis (PsA), but there are few direct comparisons of their efficacy and safety. In SPIRIT-H2H study, ixekizumab (IXE), a high-affinity monoclonal antibody selectively targeting IL-17A, was superior to adalimumab (ADA) at Week 24 for simultaneous achievement of ACR50 and 100% improvement from baseline in the Psoriasis Area and Severity Index (PASI 100) in patients (pts) with active PsA. Efficacy on other PsA domains was shown.[1]
Objectives: To provide individual patient data demonstrating the simultaneous improvement in musculoskeletal and skin symptoms as assessed by American College of Rheumatology (ACR) response criteria and Psoriasis Area and Severity Index (PASI) percent improvement, respectively.
Methods: Pts with active PsA fulfilling Classification for Psoriatic Arthritis (CASPAR) criteria, ≥3/66 tender and ≥3/68 swollen joints, ≥3% psoriasis body surface area (BSA) involvement, no prior treatment with bDMARDs, and prior inadequate response to ≥1 conventional synthetic DMARD (csDMARD), were randomized 1:1 to open-label IXE or ADA (label dosing according to presence/absence of moderate-to-severe psoriasis [baseline BSA≥10%, PASI≥12, and static Physician's Global Assessment≥3]) in Study I1F-MC-RHCF (NCT03151551). In this analysis, max ACRx was defined as the maximum ACRx response a patient can achieve where ACRx derivation follows the typical ACR response criteria: ≥x% improvement in both tender joint count (TJC) and swollen joint count (SJC) and ≥x% improvement in ≥3 of the 5 remaining components, Health Assessment Questionnaire-Disability Index total score (HAQ-DI), C-reactive protein (CRP), Patient Global Assessment (PatGA), Physician Global Assessment (PhyGA), and patient assessment of joint pain (patJP). Missing data were imputed using the last observation carried forward (LOCF) method.
Results: At baseline, demographic and disease characteristics were similar across treatment groups. Mean baseline values for the ACR core data set were 20.2 (TJC), 10.4 (SJC), 63.8 (PatGA), 10.2 (CRP), 59.2 (PhyGA), 1.2 (HAQ-DI), and 61.0 (patJP). Mean PASI total score was 7.8. Figures 1 and 2 show the maximum ACR response by PASI percent improvement at Weeks 24 and 52, respectively. Independent of joint improvement, more ixekizumab-treated patients compared to adalimumab-treated patients achieved ≥PASI 90 (76.6% vs. 57.5% at week 24 and 83.0% vs. 59.6% at Week 52). Evaluation of patient-level data shows that while very few patients had joint improvement but little skin improvement (max ACRx≥50 and PASI<50; Figures 1 and 2) in both treatment arms (IXE: 1.8%; ADA: 1.4%), fewer patients treated with IXE had no to little improvement in both joint and skin symptoms (PASI<50 and max ACRx<50) than those treated with ADA at Week 24 (IXE: 3.6%; ADA: 13.3%). A similar pattern was observed at Week 52 (Figure 2).
Conclusion: Ixekizumab treatment was superior to adalimumab when evaluating the combination of musculoskeletal and skin symptoms of PsA as measured by ACR response and PASI response.

References:

[1] Mease PJ, Smolen JS, Behrens F et al., Ann Rheum Dis 2019; 79(1):123-131.

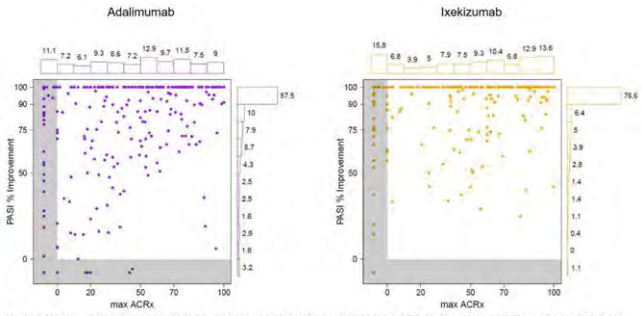


Figure 1. Maximum ACR response–by–PASI Percent Improvement at Week 24. Abbreviations: ACR, American College of Rheumatology; BSA, body surface area; PASI, Psoriasis Area and Severity Index; PsA, psoriatic arthritis. Please note: Nine patients with active PsA and BSA ≥3% were assessed as PASI=0 at baseline, a medical inconsistency that was resolved using medical judgement. These patients were considered PASI100 responders if PASI=0 and BSA=0 at post baseline visits.

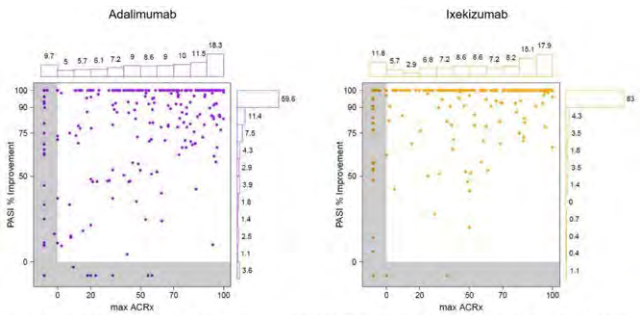


Figure 2. Maximum ACR response–by–PASI Percent Improvement at Week 52. Abbreviations: ACR, American College of Rheumatology; BSA, body surface area; PASI, Psoriasis Area and Severity Index; PsA, psoriatic arthritis. Please note: Nine patients with active PsA and BSA ≥3% were assessed as PASI=0 at baseline, a medical inconsistency that was resolved using medical judgement. These patients were considered PASI100 responders if PASI=0 and BSA=0 at post baseline visits.

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FRI0346

EFFICACY OF NETAKIMAB IN THE TREATMENT OF AXIAL DISEASE IN PATIENTS WITH PSORIATIC ARTHRITIS: RESULTS OF SUBANALYSIS FROM A DOUBLE-BLIND RANDOMIZED PHASE 3 TRIAL (PATERA)

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Background: The presence of axial involvement significantly impacts on psoriatic arthritis (PsA) activity, outcomes and patients (pts) quality of life. IL-17A inhibitors were previously shown to improve axial disease in PsA. Netakimab (NTK) is a humanized anti-interleukin 17A antibody approved for the treatment of moderate-to-severe plaque psoriasis.
Objectives: To evaluate the effects of NTK on axial symptoms in patients with PsA, based on data of 24-week (wk) observation from an ongoing phase 3 PATERA study (NCT03598751).
Methods: PATERA is a phase 3 international double-blind, placebo-controlled clinical study. After completion of screening 194 eligible adult patients with PsA fulfilling the CASPAR criteria, with inadequate response to csDMARD or one TNFi, were randomly assigned (1:1) to receive NTK 120 mg or placebo (PBO) at Wks 0, 1, 2, 4, 6, 8, 10, 14, 18 and 22. 84 patients from PBO arm, failed to achieve ACR20 (20% improvement the American College of Rheumatology criteria) by Wk 16, were switched to NTK. A subset of pts with axial involvement (defined by presence of inflammatory back pain (IBP) according to ASAS IBP criteria, 2009) was evaluated with spondylitis-specific assessments: spinal pain (10-item numerical rating scale), nocturnal back pain (10-item numerical rating scale), BASDAI (Bath Ankylosing Spondylitis Disease Activity Index), ASDAS-CRP (Ankylosing Spondylitis Disease Activity Score with C-reactive protein.
Results: 104 PsA patients (NTK N=54, PBO N=50) with IBP at baseline (BL) were included in the analysis. Demographic and BL disease characteristics were comparable across the groups (Table 1). During the analyzed period, BASDAI and ASDAS-CRP scores significantly decreased in NTK-treated patients (Figure 1). Maximum decrease in axial disease activity developed by Wk 4-8

depending on index of assessment. The achieved values maintained throughout the entire analyzed period (Table 2). At Wk 24, mean changes in ASDAS-CRP and BASDAI were -1.57 and -2.83 in NTK arm vs -0.11 and -0.19 in PBO arm respectively (p<0.0001).

Table 1. Baseline demographics and mean composite endpoint scores

Arm	NTK (N=54)	PBO (N=50)
Age (years) *	43.5 (12.16)	42.7 (10.76)
Male, n (%)	27 (50)	26 (52)
PsA duration, mo*	70.0 (78.78)	79.0 (81.62)
BASDAI score*	5.58 (1.80)	5.79 (1.94)
ASDAS-CRP score*	3.38 (1.16)	3.38 (1.28)
nocturnal pain*	4.2 (2.42)	5.1 (2.29)
spinal pain*	4.4 (2.41)	5.3 (2.40)

* mean (standard deviation) BASDAI=Bath Ankylosing Spondylitis Disease Activity Index, ASDAS-CRP=Ankylosing Spondylitis Disease Activity Score with C-reactive protein

Table 2. Changes in BASDAI and ASDAS-CRP vs baseline

	BASDAI		ASDAS-CRP	
	NTK (N=54)	PBO (N=50)	NTK (N=54)	PBO (N=50)
Wk 4	-2.45 (1.94)	-0.51 (1.26)	-1.44 (1.06)	-0.19 (0.60)
Wk 8	-2.77 (2.22)	-0.38 (1.55)	-1.53 (1.07)	-0.21 (0.74)
Wk 16	-2.77 (1.83)	-0.17 (1.67)	-1.52 (0.98)	-0.10 (0.97)
Wk 24	-2.83 (2.15)	-0.19 (1.70)	-1.57 (1.06)	-0.11 (0.95)

mean (standard deviation)

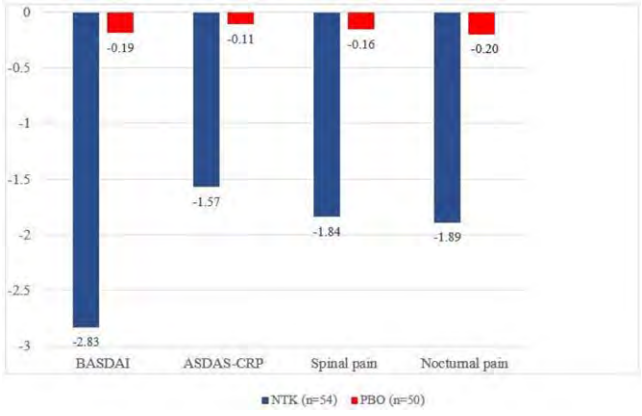


Figure 1. Mean change in BASDAI, ASDAS-CRP, spinal pain, and nocturnal pain at Wk 24

Conclusion: About 50% of subjects, randomized to PATERA study, had IBP at baseline. NTK leads to rapid and sustained improvement in axial disease in patients with active PsA.

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Disclosure of Interests: Tatiana Korotaeva Grant/research support from: Pfizer, Consultant of: Abbvie, BIOCAD, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Merck Sharp & Dohme, Novartis, Novartis-Sandoz, Pfizer, UCB, Speakers bureau: Abbvie, BIOCAD, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Merck Sharp & Dohme, Novartis, Novartis-Sandoz, Pfizer, UCB, Inna Gaydukova Grant/research support from: JSC BIOCAD, Speakers bureau: Pfizer, Novartis, AbbVie, JSC BIOCAD, Celgene, MSD, Sanofi, V Mazurov: None declared, Aleksey Samtsov Grant/research support from: JSC BIOCAD, Novartis, Eli Lilly, Johnson&Johnson, Celgene, Glenmark, Galderma, Sanofi, Vladislav Khayrutdinov Grant/research support from: Akrikhin, Alkoy, Belupo, JSC BIOCAD, Bosnalijek, Verteks, Glenmark, Elfa, Leo Pharma, MSD, Novartis, Pfizer, Sun Pharma, Sanofi, Celgene, Pharmtec, AbbVie, Eli Lilly, Jadran, Janssen, Andrey Bakulev Grant/research support from: AbbVie, Eli Lilly, Pfizer, UCB, MSD, Novartis, Galderma, Celgene, Leo Pharma and Johnson&Johnson, JSC BIOCAD, Consultant of: Novartis, Celgene and Johnson&Johnson, Speakers bureau: AbbVie, Eli Lilly, Galderma, UCB, Novartis, Celgene and Johnson&Johnson, Muza Kokhan Grant/research support from: AbbVie, Eli Lilly, Pfizer, UCB, MSD, Novartis, Galderma, Celgene, Leo Pharma and Johnson&Johnson, JSC BIOCAD, Consultant of: Novartis, Celgene and Johnson&Johnson, Speakers bureau: AbbVie, Eli Lilly, Galderma, UCB, Novartis, Celgene and Johnson&Johnson, Alena Kundzer: None declared, Nikolaj Soroka Grant/research support from: JSC BIOCAD, Ekaterina Dokukina Employee of: JSC BIOCAD, Anna Eremeeva Employee of: JSC BIOCAD

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FRI0347

PREVALENCE OF OBESITY AND ITS LINK TO PSORIATIC ARTHRITIS (PSA) ACTIVITY AND RESPONSE TO THERAPY: DATA FROM THE RUSSIAN PSA REGISTRY (RU-PSART)

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Background: Obesity is a common comorbidity of psoriasis and PsA. It is connected to low-grade inflammation and it has a negative impact on the response to therapies. Although a high prevalence of obesity has been shown in a whole number of epidemiology and observational studies, its relationship to PsA activity has been less investigated. In the RU-PsART registry data was collected from 43 rheumatology centers of the Russian Federation

Objectives: to evaluate the prevalence of obesity and its association to PsA activity as well as its impact on therapy response in real clinical practice

Methods: 614 (M/F=331(54%)/283(46%) PsA pts fulfilling the CASPAR criteria were included from the RU-PsART cohort. Mean age 45.2±0.52 yrs, PsA duration 5.7±0.27 yrs, PsO duration 15.71±0.56 yrs, DAPSA 28.79±0.75. At baseline (BL) and 6 mo/12 mo of observation PsA activity was evaluated by Tender Joint Count (TJC68), Swollen Joint Count (SJC66); PGA, physician global assessment by Visual Analog Scale (VAS); PtGA VAS; PtPain VAS; DAPSA and body mass index (BMI, kg/m^2) were calculated. Pts were treated with conventional/target synthetic disease-modifying antirheumatic drugs csDMARDs (55%)/tsDMARDs (5%), biological DMARDs (23%), NSAID (17%) according to physician's decision. At BL/6/12 mo all pts were categorized according to DAPSA as high activity (DAPSA>28) and Moderate (Mo≤28)/Low Activity (LA≤14)/Remission DAPSA (REM≤4). All pts were divided into three groups according to BMI (kg/m^2): normal<25, overweight >25-30, obese>30. M±m,%, multivariate analysis of variance (MANOVA), ANOVA, OR 95% (CI) were performed. All p<0.05, were considered to indicate statistical significance

Results: The baseline BMI was 27.7±0.23 kg/m^2 with the following BMI categories: normal - 212 pts (34.6%), overweight - 214 pts (34.8%) and obese - 187 (30.45%). In all pts DAPSA significantly improved to 16.11±0.82/14.71±1.17 at 6/12 mo accordingly. At BL and 6/12 mo of therapy DAPSA was significantly higher in the obese pts compared to the normal and the overweight pts despite of improvements seen in all groups (table 1). By the last visit significant differences were found in DAPSA depending on BMI at BL (ANOVA, p<0.031). BMI>30 at BL was associated with lower probability of DAPSA improvement from high activity to Mo/LA/REM state compared to normal BMI pts and the overweight pts: OR 2.484 (95% CI 1.135-5.439) and OR 2.346 (95% CI 1.07-5.143) accordingly (Fig 1)

Table 1. Dynamics of DAPSA from BL to 6/12 mo depending on BMI categories.

BMI (kg/m^2)	DAPSA BL	DAPSA 6 mo	DAPSA 12 mo
<25	27.20 ± 1.15	13.84 ± 1.01	13.33 ± 1.53
25-30	26.93 ± 1.17	14.48 ± 1.43	13.83 ± 2.36
>30	32.86 ± 1.57	21.19 ± 1.84	18.92 ± 2.54

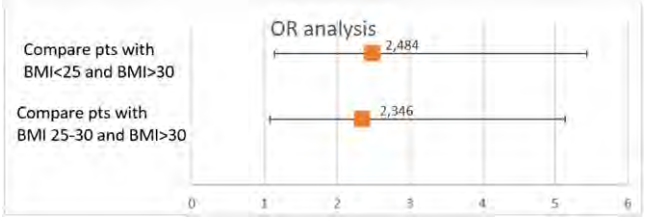


Fig. 1. OR analysis of relationship between BMI at BL and treatment response.

Conclusion: The high prevalence of overweight/obesity PsA pts was associated with higher PsA activity and lower response to therapy in our cohort

Disclosure of Interests: Yulia Korsakova: None declared, Elena Loginova Speakers bureau: Janssen, ELENA GUBAR: None declared, Elizaveta Vasilenko: None declared, Aleksey Vasilenko: None declared, Natalia Kuznetsova: None declared, Irina Patrikeeva: None declared, Tatiana Korotaeva Grant/research support from: Pfizer, Consultant of: Abbvie, BIOCAD, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Merck Sharp & Dohme, Novartis, Novartis-Sandoz, Pfizer, UCB, Speakers bureau: Abbvie, BIOCAD, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Merck Sharp & Dohme, Novartis, Novartis-Sandoz, Pfizer, UCB, Evgeny Nasonov: None declared

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FRI0348 PERSISTENCE OF SECUKINUMAB AND USTEKINUMAB IN PSORIATIC ARTHRITIS: A REAL-WORLD MULTICENTRIC COHORT OF 409 PATIENTS

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Background: Real-world data are missing for Ustekinumab (UST) and secukinumab (SEK) in psoriatic arthritis (PsA).

Objectives: To evaluate the characteristics of the patients (pts) with PsA treated by UST or SEK and to assess real world persistence of UST and SEK in PsA.

Methods: This is a retrospective, multicenter study of pts with PsA (CASPAR criteria or diagnosis confirmed by a rheumatologist) initiating UST or SEK with a follow-up ≥ 6 months from January 2011 to April 2019. The comparison of persistence between UST and SEK was analysed using a Cox model with an inverse probability of treatment weighting propensity score including 11 confounding factors. Subgroup analyses (age>65 years, gender, Body Mass Index (BMI), Charlson score>2, psoriasis, CRP>5mg/L, number (nb) of prior biotherapies, proportion of pts on maximum dose of UST or SEK, combination with methotrexate (MTX), enthesitic and axial forms of PsA) were also performed to test the heterogeneity of UST and SEK persistence. Finally, 2 sensitivity analyses were performed, first excluding the pts treated before the marketing authorization of SEK, and then excluding the pts that underwent a molecule switch. Causes of discontinuation were also collected.

Results: 406 pts were included: 245 with UST and 161 with SEK. At baseline before propensity score-matching, the UST group has a higher BMI (28.9 ± 6.4 kg/m^2 vs. 27.4 ± 6.0 kg/m^2), more peripheral forms (98% vs. 90.8%), a higher nb of active smokers (27.1% vs. 19.9%), a higher frequency of psoriasis (96.3% vs. 83.2%), less MTX users (38.9% vs. 44.2%), a higher nb of pts with CRP >5mg/L (54.3% vs. 47%), a higher nb of pts naïve to biotherapies (22% vs. 13%) and a higher nb of pts with recommended dosing (97.3% vs 50.9%). The median persistence was 9.4 months and 14.7 months for UST and SEK, respectively. The persistence rate was lower in the UST group compared to the SEK group (40.9% vs. 59.1% % at 1 year; 26.4% vs. 38.0% at 2 years; weighted HR=1.42; 95% CI 1.07 to 1.92; p=0.015) (Fig 1). In subgroup analysis, combination with MTX was associated with a higher persistence rate in the patients with SEK compared to those receiving UST: 43.6% vs. 23.2% (HR=2.20; 95% CI 1.30 to 3.51; p=0.001), whereas no difference was observed in SEK and UST monotherapy: 33.8% vs 28.4%, respectively (HR=1.06; 95% CI 0.74 to 1.53; p=0.75) (Fig 2). A similar difference was found in the sensitivity analyses, with however a difference at the limit of significance for the analysis excluding pts with a molecule switch (adjusted HR=1.35; IC95% 0.96 to 1.92; p=0.085). The causes of discontinuation were due to inefficacy in 85% of cases and an adverse event in 12% of cases (19% in the SEK group and 9% in the UST group).

Conclusion: In this first real-world study comparing UST and SEK persistence in PsA, the persistence of SEK was longer than that of UST. Subgroup analysis revealed this difference of persistence was restricted to patients treated in combination with MTX.

Figure 1. Persistence with Ustekinumab (UST) and Secukinumab (SEK) in IPTW cohort

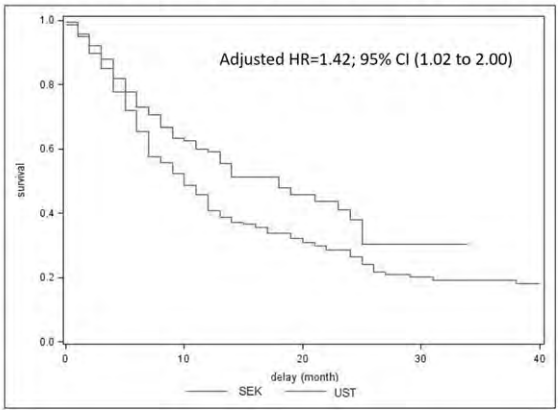
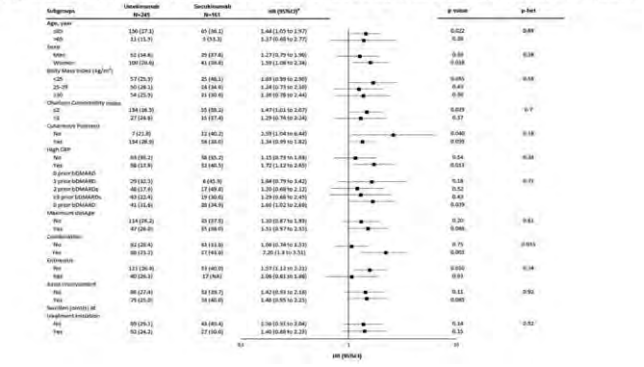


Figure 2. Follow-up 2-year persistence of molecules according to different subgroups In IPTW Cohorts



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FRI0349 PSORIATIC ARTHRITIS AND CENTRAL OBESITY: STRONG ASSOCIATION WITH FUNCTIONAL DISABILITY AND A WORSE QUALITY OF LIFE

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory arthritis associated with comorbidities like obesity, metabolic syndrome, and cardiovascular disease. Adipose tissue leads to a pro-inflammatory status in obese subjects. For this reason, central obesity may determine a worsening in both disability index or quality of life in PsA patients treated with biologic agents.
Objectives: Our study aimed to evaluate the relationship between central obesity and disability index or the impact of the disease on quality of life in a real-world sample of PsA patients.
Methods: A cross-sectional study was conducted. Patients with PsA were enrolled at the PsA clinic at the ARNAS Civico in Palermo (Italy) from March 2018 to December 2019. Clinical, pharmacological, anthropometric, laboratoristic variables, and patient-reported outcomes, including the Health Assessment Questionnaire (HAQ) and Psoriatic Arthritis Impact of Disease (PsAID) were evaluated. STATA 14.1 was used to perform statistical analysis.
Results: A total of 143 outpatients aged 55.6 (47.7-63.7) affected by PsA, according to CASPAR criteria, were consecutively evaluated. The average years of illness were 10.8 (9.5-12.1). Patients were treated with biological therapy (81.3%), DMARDS (41.6%), small molecules (9.9%), or their combinations. Both sexes were equally represented. 71.9% of enrolled patients had central obesity (64.9% men and 78.1% women) with an average waist circumference of 104.2 (101.8 - 106.6) for women and 103.6 (100.0 -107.2) for men. Average HAQ was 1.05 (0.92 - 1.19), and data analysis showed 50.3% of patients with normal-mild functional disability, 30.1% moderate to severe disability, and 19.6% severe to very severe disability [Fig 1]. 51,7% of the sample had a high impact of the disease on life, according to the PsAID questionnaire [Fig 2]. A strong association was observed between functional disability measured by HAQ >2 and central obesity [OR (95% CI) 16.94 (2.22 - 129.48); p < 0.006]. Moreover, data analysis showed an association between high impact of disease on life (PsAID >4) and central obesity [OR (95% CI) 3.33 (1.56 - 7.13); p<0,002].

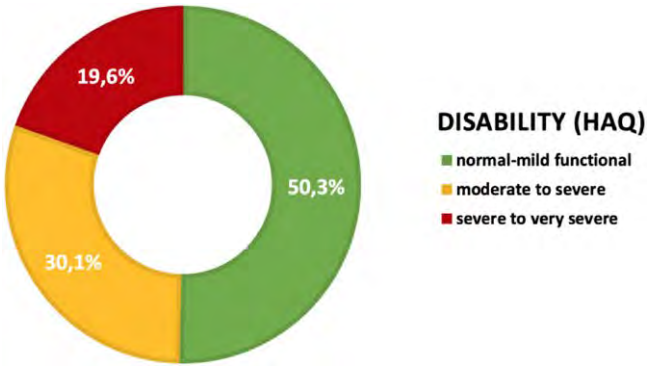


Fig 1. Functional disability on PsA patients

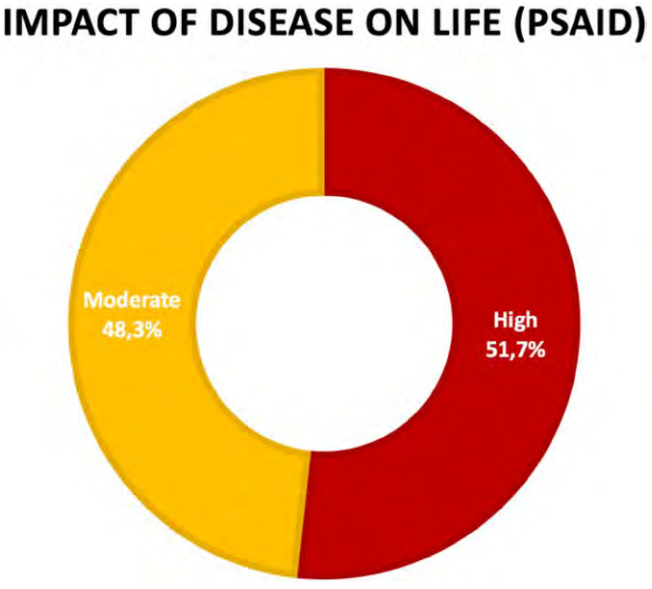


Fig 2. Impact of disease on PsA patients quality of life

Conclusion: Our study demonstrated a high association between functional disability studied subjectively using the HAQ, the impact of the disease on patients' quality of life using PsAID, and central obesity in Sicilian outpatients affected by PsA. Data suggest that therapeutic goals should not be focused on treatment but also on waist circumference reduction in order to reduce inflammation and improve patients' functional ability and quality of life.
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FRI0350

FACTORS ASSOCIATED WITH PERIPHERAL EROSIVE RADIOGRAPHIC DISEASE IN A CONSECUTIVE SERIES OF 794 PSA PATIENTS

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Background: Few studies have examined the correlation between clinical demographic and laboratory parameters with peripherical radiological erosive disease in PsA pts.
Objectives: To examine the association between clinical, demographical and laboratory data and the presence of radiographic erosions (RE) in the peripheral joints of psoriatic arthritis (PsA) pts.
Methods: A cross-sectional study was conducted in consecutive patients with PsA afferring 7 rheumatological italian tertiary care centers. Demographical, clinical, laboratory and imaging data were collected according to a standardized protocol. A patient was considered as affected by erosive disease (ED) if at least one joint presented radiographic erosions at hand and/or feet rx examination. Patients with ED at early rx examination (before 5 y from disease diagnosis) were considered as early ED (EED) pts and pts without ED at 6 y or more rx examination from disease diagnosis were considered as not EED (NEED).The association between the presence of joint erosions and demographical, clinical and laboratory data was assessed using logistic regression analysis. The results were expressed in terms odds ratios (OR), and 95% confidence intervals (CI).
Results: Rx hand and feet examination were available for analysis in 492/794 (39.9 % females, mean age 53.3 ± 13.2 y, mean PsA duration 16.9 ± 16.8 y, ED 171 pts). 48 pts had EED and 133 pts had NEED. At univariate analyses factors significantly associated with EED (p < 0.20) were PsA duration (OR=0.979,95%CI 0.953-1.006, p = 0.119), diagnostic delay (OR=1.077, 95%CI 1.018-1.138, p = 0.009), history of peripheral enthesitis (OR=2.308,95%CI 0.904-5.888, p= 0.080), hypertrigliceridemia (OR=2.756,95%CI 0.997-7.618, p = 0.0.051), hypercholesterolemia (OR=1.687, 95%CI 0.777-3.661, p = 0.186), hyperuricemia (OR=0.450, 95%CI 0.174-1.166, p = 0.10), use of biological agents (OR=1.712, 95%CI 0.873-3.355, p=0.118). Factors significantly associated with EED at multivariate regression analyses were diagnostic delay (OR = 1.11, 95% CI: 1.01, 1.22), history of enthesitis (OR = 3.15, 95% CI: 1.23, 8.22), use of therapy with biological agents (OR = 3.60, 95% CI: 1.31, 9.85) with protective effect of hyperuricemia (OR = 0.25, 95% CI: 0.07, 0.90).
Conclusion: The presence of EED in a group of consecutive PsA patients is correlated to diagnostic delay and history of enthesitis. Longitudinal study may confirm these associations.
Disclosure of Interests: Maria Grazia Catanoso: None declared, Pierluigi Macchioni: None declared, Antonio Marchesoni Speakers bureau: Abbvie, Pfizer, UCB, Novartis, Celgene, Eli Lilly, Salvatore D'Angelo Speakers bureau: AbbVie, Biogen, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Sanofi, and UCB, Roberta Ramonda Speakers bureau: Novartis, Celgene, Janssen, Pfizer, Abbvie, Lilly, Alberto Cauli: None declared, fabio perrotta: None declared, Roberto Bortolotti: None declared, mariana lofrano: None declared,

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FRI0351

DOES SEX OR BODY MASS INDEX IMPACT RESPONSE TO THERAPY IN PSORIATIC ARTHRITIS?: RESULTS FROM A PHASE 3, DOUBLE-BLIND, RANDOMIZED TRIAL EXAMINING METHOTREXATE AND ETANERCEPT AS MONOTHERAPY OR IN COMBINATION FOR TREATING PSORIATIC ARTHRITIS

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Background: In psoriatic arthritis (PsA), contextual factors such as sex and body mass index (BMI) may affect response to therapy.

Objectives: To examine if sex and BMI influenced 24-week (wk) outcomes in a 48-wk PsA trial of methotrexate (MTX) and etanercept (ETN) as monotherapy (mono) or combined.[1]

Methods: MTX- and biologic-naïve adult patients with active PsA were randomized to weekly: MTX 20mg (n=284), ETN 50mg (n=284), or MTX 20mg+ETN 50mg (n=283). Wk-24 outcomes included ACR 20, MDA, VLDA, PASDAS, DAPSA, LDI, SPARCC, BSA, sPGA, and mNAPSI. Descriptive statistics examined outcomes in each treatment arm by sex (male vs female) or BMI (≤30kg/m^2 vs >30kg/m^2). Modeling analyses also examined sex or BMI effect on outcomes when comparing MTX mono to the ETN-containing arms (analyses were adjusted for any prior use of a nonbiologic disease-modifying antirheumatic drug; the model for the influence of sex also adjusted for baseline BMI status). Nominal P-values are provided.

Results: Baseline disease activity was slightly higher in women, especially with MTX+ETN. Descriptive statistics showed men and women had similar results at wk 24 in the MTX mono and ETN mono arms; with MTX+ETN, men had better outcomes for ACR20, MDA, VLDA, and PASDAS. In treatment-interaction analyses, men had more favorable responses at wk 24 with MTX+ETN vs MTX mono for PASDAS, MDA, and LDI (Table).

Baseline disease activity was similar in both BMI categories. Descriptive statistics in each treatment arm showed no consistent differences in results at wk 24 between BMI categories. In treatment-interaction analyses, BMI ≤30kg/m^2 had a more favorable response at wk 24 with MTX+ETN vs MTX mono for sPGA (Table).

Conclusion: Results suggest contextual factors may affect response to therapy in PsA. The treatment-interaction analyses suggest disparate responses to MTX+ETN by sex; BMI only affected skin response.

References:

[1] Mease et al. *Arthritis Rheumatol*. 2019;71:1112-24

Disclosure of Interests: Philip J Mease Grant/research support from: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Eli Lilly, Novartis, Pfizer, Sun Pharmaceutical, UCB – grant/research support, Consultant of: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Eli Lilly, Novartis, Pfizer, Sun Pharmaceutical, UCB – consultant, Speakers bureau: Abbott, Amgen, Biogen Idec, BMS, Eli Lilly, Genentech, Janssen, Pfizer, UCB – speakers bureau, Dafna D Gladman Grant/research support from: AbbVie, Amgen Inc., BMS, Celgene Corporation, Janssen, Novartis, Pfizer, UCB – grant/research support, Consultant of: AbbVie, Amgen Inc., BMS, Celgene Corporation, Janssen, Novartis, Pfizer, UCB – consultant, Joseph F. Merola Consultant of: Merck, AbbVie, Dermavant, Eli Lilly, Novartis, Janssen, UCB Pharma, Celgene, Sanofi, Regeneron, Arena, Sun Pharma, Biogen, Pfizer, EMD Sorono, Avotres and LEO Pharma, Atul Deodhar Grant/research support from: AbbVie, Eli Lilly, GSK, Novartis, Pfizer, UCB, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myer Squibb (BMS), Eli Lilly, GSK, Janssen, Novartis, Pfizer, UCB, Speakers bureau: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myer Squibb (BMS), Eli Lilly, GSK, Janssen, Novartis, Pfizer, UCB, Alexis Ogdie Grant/research support from: Novartis, Pfizer – grant/research support, Consultant of: AbbVie, BMS, Eli Lilly, Novartis, Pfizer, Takeda – consultant, David Collier Shareholder of: Amgen Inc., Employee of: Amgen Inc., Elaine Karis Shareholder of: Amgen Inc., Employee of: Amgen Inc., Lyrica Liu Shareholder of: Amgen Inc., Employee of: Amgen Inc., Arthur Kavanaugh Grant/research support from: AbbVie, Amgen, Eli Lilly, Novartis, Janssen, Pfizer, Gilead, UCB, Consultant of: AbbVie, Amgen, Eli Lilly, Novartis, Janssen, Pfizer, Gilead, UCB

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FRI0352

PROBABILITY OF ACHIEVING LOW DISEASE ACTIVITY OR REMISSION WITH APREMILAST TREATMENT AMONG DMARD-NAIVE SUBJECTS WITH ACTIVE PSORIATIC ARTHRITIS

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Table. Week 24 Treatment-Interaction Outcomes Adjusted by Sex and BMI

	MTX Mono			ETN Mono			MTX+ETN		
Adjusted by Sex[a]	Male	Female	Male vs Female	Male	Female	Male vs Female	Male	Female	Male vs Female
PASDAS[b] (Full Analysis Set)	-1.80 (0.17)	-1.95 (0.15)	0.15 (0.21)	-2.45 (0.15)	-2.59 (0.16)	0.13 (0.20) P=0.96[c]	-2.87 (0.15)	-2.14 (0.16)	-0.74 (0.20) P=0.002[c]
MDA[d] (Full Analysis Set)	0.23 (0.04)	0.19 (0.03)	0.04 (0.05)	0.34 (0.04)	0.31 (0.04)	0.03 (0.06) P=0.86[c]	0.42 (0.04)	0.22 (0.04)	0.21 (0.05) P=0.02[c]
LDI[b] (LDI Analysis Set)	-186.67 (37.69)	-70.17 (34.51)	-116.51 (46.64)	-120.15 (34.23)	-109.17 (37.07)	-10.98 (46.75) P=0.11[c]	-85.80 (36.10)	-127.90 (34.82)	42.10 (47.05) P=0.017[c]
Adjusted by BMI[e]	**≤30kg/m^2**	**>30kg/m^2**	**≤30 vs >30kg/m^2**	**≤30kg/m^2**	**>30kg/m^2**	**≤30 vs >30kg/m^2**	**≤30kg/m^2**	**>30kg/m^2**	**≤30 vs >30kg/m^2**
sPGA of 0 or 1[d] (Full Analysis Set of Patients With Baseline BSA ≥ 10%)	0.49 (0.08)	0.58 (0.07)	-0.10 (0.10)	0.69 (0.07)	0.74 (0.07)	-0.05 (0.08) P=0.75[c]	0.81 (0.05)	0.64 (0.08)	0.17 (0.09) P=0.05[c]

[a]Adjusted for sex by treatment arm, prior nonbiologic DMARD use, and baseline BMI

[b]Least square estimate (SE) change from baseline at week 24

[c]P-value is nominal and for comparison with MTX mono

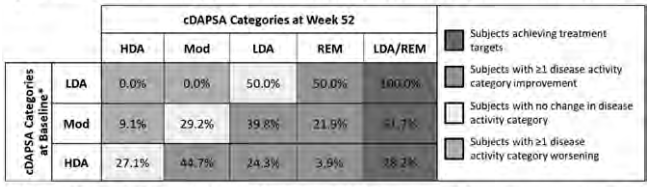
[d]Adjusted risk ratio (SE)

[e]Adjusted for BMI by treatment arm and prior nonbiologic DMARD use

BMI, body mass index; BSA, body surface area; DMARD, disease-modifying antirheumatic drug; ETN, etanercept; LDI, Leeds Dactylitis Index; MDA, Minimal Disease Activity; Mono, monotherapy; MTX, methotrexate; PASDAS, Psoriatic Arthritis Disease Activity Score; SE, standard error; sPGA, static Physicians' Global Assessment

Background: Apremilast (APR) is associated with comparable ACR response rates in DMARD-naive vs DMARD-experienced patients (pts) with psoriatic arthritis (PsA).[1,2] A question that remains is if DMARD-naive pts treated with APR have greater chances of achieving treatment targets than DMARD-experienced pts. cDAPSA is a commonly used treatment target.
Objectives: To assess the predictive value of baseline (BL) clinical disease status on achieving long-term cDAPSA treatment targets at Wk 52 among DMARD-naive subjects in PALACE 4; to compare these findings vs those recently reported from the PALACE 1-3 studies in subjects with prior exposure to DMARDs; and to provide further evidence that at a group level, achievement of cDAPSA disease targets with APR is associated with no or mild articular and extra-articular disease activity by Wk 52.
Methods: This post hoc analysis included subjects assigned to APR 30 mg twice daily at BL who had available cDAPSA data at BL. We calculated the probabilities of shifting across different cDAPSA categories (remission [REM]: ≤4; low disease activity [LDA]: >4 to ≤13; moderate disease activity [Mod]: >13 to ≤27; high disease activity [HDA]: >27[3]) from BL to Wk 52. Mean values of articular and non-articular variables (e.g., PASI, SJC/TJC, MASES, dactylitis) from BL to Wk 52 were assessed by cDAPSA category achieved at Wk 52 to determine the association between achievement of targets and control of articular and non-articular manifestations. Results from the current analyses were compared with the previously reported results from PALACE 1-3.
Results: A total of 175 subjects receiving APR were included; at BL, 66.3% were in HDA, 31.4% in Mod, and 2.3% were in LDA. Overall, subjects who achieved treatment targets (LDA or REM) by Wk 52 had lower levels of disease activity at BL, as shown by a lower number of swollen and tender joints and lower presence of enthesitis and dactylitis. Higher prevalence of psoriasis-involved body surface area ≥3% at BL was observed. Subjects in Mod at BL were estimated to be more than twice as likely to achieve REM or LDA at Wk 52 vs subjects in HDA at BL; for subjects in LDA at BL, the estimated probability of achieving cDAPSA treatment targets was 100% (Figure). PALACE 4 subjects with LDA and Mod at BL exhibited higher estimated probabilities of achieving treatment targets (100.0% and 61.7%, respectively) than those observed in the DMARD-experienced population of PALACE 1-3 (71.1% and 46.9%). Subjects in PALACE 4 who achieved REM or LDA by Wk 52 showed no or mild articular and extra-articular disease activity by Wk 52, similar to what was observed in the PALACE 1-3 population.[4]
Conclusion: DMARD-naive subjects in PALACE 4 who had LDA or Mod at BL had the highest likelihood of achieving treatment targets (cDAPSA REM or LDA) by Wk 52 with continued APR treatment. Results from the current probability analyses revealed higher probability rates than those observed in the DMARD-experienced PALACE 1-3 population; control of articular and extra-articular manifestations was observed in the DMARD-naive and DMARD-experienced populations.
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Figure. Probability of Achieving cDAPSA Treatment Targets at Week 52 by Baseline cDAPSA Category



*Subjects randomized to APR 30 mg twice daily with cDAPSA scores available at baseline (n=175). Percentage represents the proportion of subjects in each cDAPSA category at baseline (from left to right, HDA, Mod, LDA, and REM at Week 52=100%). Multiple imputation. REM, cDAPSA ≤4; LDA, cDAPSA >4 to ≤13; Mod, cDAPSA >13 to ≤27; HDA, cDAPSA >27. Mod=moderate disease activity.

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FRI0353 FACTORS ASSOCIATED WITH DISCORDANCE BETWEEN PATIENT AND RHEUMATOLOGIST ASSESSMENT OF DISEASE ACTIVITY IN PSORIATIC ARTHRITIS CONSIDERED IN REMISSION

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Background: Assessment of disease activity in psoriatic arthritis (PsA) requires evaluation of multiple aspects. Perception of disease activity by patient and physician is frequently discordant.
Objectives: The aim of our study was to evaluate factors associated with persistence of disease activity evaluated by patients yet considered in remission by their rheumatologist.
Methods: We performed a transversal monocentric study. PsA patients were included if they met the CASPAR criteria and if they were considered in remission. Disease activity was evaluated by scores: Disease Activity Score (DAS28-CRP), Simple Disease Activity Index (SDAI), Clinical Disease Activity Index (CDAI), Disease Activity in Psoriatic Arthritis (DAPSA), Minimal Disease Activity (MDA), modified Boolean remission criteria for PsA. We collected multiple Patient's Reported Outcomes (PROs): Psoriatic Arthritis Impact of Disease (PsAID), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), Health Assessment Questionnaire (HAQ), Dermatology Life Quality Index (DLQI), Beck Depression Inventory (BDI), Fibromyalgia Rapid Screening Tool (FiRST), Pain Catastrophizing Scale (PCS). Discordance was defined by a difference between patient's and rheumatologist's global assessment ≥30/100 on a Visual Analogue Scale (VAS). Univariate and multivariate analyses were performed to evaluate factors associated with the presence of discordance.
Results: 62 PsA patients were included. 40.3 % were women and the mean (SD) age was 55 (14) years. 61% patients were in remission (rheumatologist definition) for more than 12 months and 19% for less than 3 months. 50% met MDA, 63% DAS28-CRP < 2,6, 39% SDAI and CDAI remission, 27% DAPSA remission. 39% had a discordant disease activity assessment from their rheumatologist. In univariate analysis, factors associated with discordance were a history of depression, an associated fibromyalgia, a history of clinical enthesitis and a history of corticosteroid use (Table 1). All disease activity scores and PROs were higher in discordant group and were associated with discordance in univariate analysis. In multivariate analysis, discordance was associated with no previous corticosteroid use (OR 24.5 (95%CI 2.9-203.7), p=0.003), a higher BDI scale (OR 1.4 (95%CI 1.1-1.8) by supplementary point, p=0.017) and a higher DAPSA score (OR 1.5 (95%CI 1.2-2), p<0.001) by supplementary point.
Conclusion: In this PsA cohort, discordance between patient and rheumatologist is very common. Discordance in assessment of disease activity was associated with no previous corticosteroid use, probably reflecting a less severe disease, presence of depressive symptoms and an increase of DAPSA, reflecting a more active disease.
Disclosure of Interests: Marie Moly: None declared, Cédric Lukas: None declared, Jacques Morel: None declared, Bernard Combe Grant/research support from: Novartis, Pfizer, Roche-Chugai, Consultant of: AbbVie; Gilead Sciences, Inc.; Janssen; Eli Lilly and Company; Pfizer; Roche-Chugai; Sanofi, Speakers bureau: Bristol-Myers Squibb; Gilead Sciences, Inc.; Eli Lilly and Company; Merck Sharp & Dohme; Pfizer; Roche-Chugai; UCB, Gael Mouterde: None declared
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Table 1. Factors associated with discordance: Univariate analysis

	Discordant group n=24	Concordant group n=38	OR (95%CI)	P
History of depression, n (%)	9 (37.5)	1 (2,6)	22 (2.58-190.84)	<0.001
Fibromyalgia (ACR criteria), n (%)	5 (20.8)	1 (2.6)	9.74 (1.06-89.4)	0.028
At least one enthesitis on the Leeds Enthesitis Index, n (%)	14 (58.3)	34 (89.5)	0.17 (0.04-0.61)	0.006
Treatments				
Previous corticosteroid use, n (%)	8 (33.3%)	26 (68.4%)	0.23 (0.08-0.69)	0.007
Disease activity scores et Patients Reported Outcomes PROs				
DAS28-CRP > median (2.3), n (%)	19 (79.2)	12 (31.6)	8.23 (2.48-27.32)	<0.001
SDAI > median (5.09), n (%)	21 (87.5)	10 (26.3)	19.6 (4.79-80.18)	<0.001
DAPSA > median (7.97), n (%)	22 (91.7)	9 (23.7)	35.4 (6.9-180.8)	<0.001
BDI > median (3), n (%)	14 (58.3)	10 (26.3)	3.92 (1.32-11.62)	0.012
FiRST > median (2), n (%)	17 (70.8)	11 (28.9)	5.95 (1.94-18.37)	0.001
BASDAI > median (2.45), n (%)	19 (79.2)	12 (31.6)	8.23 (2.48-27.32)	<0.001
HAQ> median (0.1), n (%)	16 (66.7)	11 (28.9)	4.91 (1.63-14.76)	0.004
PCS > median (9), n (%)	18 (75)	11 (28.9)	7.36 (2.3-23.5)	<0.001
PsAID > median (2.1), n (%)	18 (75)	13 (34.2)	5.77 (1.84-18.06)	0.002

FRI0354

FACTORS AFFECTING SELF-REPORTED PHYSICAL CTIVITY IN PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Despite the known benefits of exercise[1], patients with osteoarthritis (OA) and rheumatoid arthritis (RA) are reported to have low levels of physical activity[2]. Exercise participation is not well studied in psoriatic arthritis (PsA) cohorts. This study aims to explore which factors predict exercise participation across cohorts and specifically in the PsA cohort.

Objectives: The primary aim of this study was to determine which clinical factors were predictive of self- reported physical activity levels in patients with PsA. A secondary aim was to explore differences in self-reported physical activity levels amongst patients with PsA, OA and RA.

Methods: Patients with the diagnosis of PsA, RA or OA are recruited prospectively at two tertiary hospital rheumatology clinics over 12 months. Demographic data is captured by the multi-dimensional health assessment questionnaire, the international physical activity questionnaire short form captures self-reported physical activity and self-efficacy for exercise (SEE) is assessed using the SEE scale. Clinical data including joint count, body mass index and co-morbidities including fibromyalgia are collected for all patients, in addition to PsA specific data including skin and enthesitis indices.

Results: 205 patients (PsA n=62, RA n=83, OA n=60) were recruited across two sites. There was no significant difference in self-reported physical activity between OA, RA and PsA cohorts. Fibromyalgia was present in 30% of each cohort. In patients with PsA, univariate analysis showed that co-existent fibromyalgia, age and self-efficacy for exercise were predictors of physical activity levels. Skin disease and enthesitis were not predictors of physical activity in the PsA cohort.

Table 1. Univariate Analyses of effect of Clinical Features on Physical Activity levels in PsA

	Non-exercisers versus Exercisers	
	OR (95% CI)	**P-value**
LEI	1.35 (0.92-1.97)	0.127
PASI	0.8 (0.6-1.07)	0.133
DLQI	1.03 (0.92-1.16)	0.589
BMI	0.97 (0.91-1.04)	0.415
DAS28	0.79 (0.55-1.14)	0.205
Concurrent Fibromyalgia	4.46 (1.37-14.49)	0.012
Age	1.05 (1.00-1.10)	0.013
Self-efficacy for exercise	0.97 (0.95-0.99)	0.019
Pain	1.17 (0.99-1.37)	0.061
Function	1.3 (1.02-1.65)	0.031
Patient global	1.14 (0.96-1.34)	0.128
Depression	0.97 (0.51-1.84)	0.930

Table 2. Multivariable Analysis on Physical Activity in PsA

	Non-exercisers vs Exercisers	
	OR (95% CI)	**P-value**
Concurrent fibromyalgia	5.1 (1.44-18.08)	0.0117
Age	1.05 (1.00-1.11)	0.0342

Conclusion: In the PsA cohort, fibromyalgia and age were associated with lower levels of physical activity. DLQI, PASI, LEI did not predict physical activity in PsA. Multivariate analysis showed higher pain levels and lower self-efficacy scores were associated with lower physical activity across arthritis groups.

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FRI0355

IMPACT OF BIOLOGIC THERAPY ON THE INCIDENCE OF PSA AMONG PATIENTS WITH PSORIASIS

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Background: One of the strongest known risk factors for the development of psoriatic arthritis (PsA) is psoriasis. A key question is whether treatment of psoriasis may prevent or delay onset of PsA.

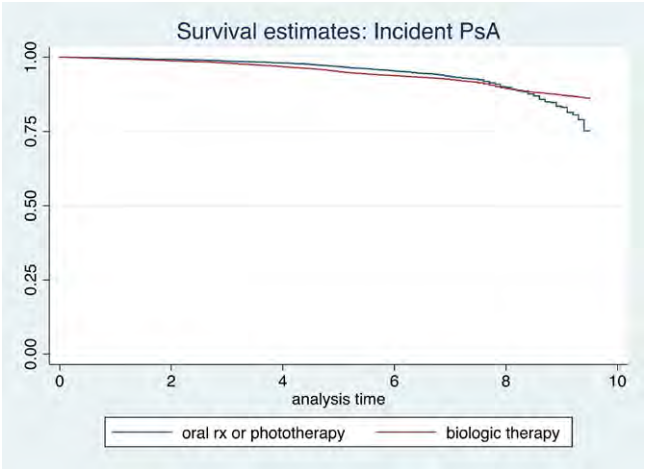
Objectives: To compare the incidence of PsA among patients with psoriasis treated with a biologic compared to those treated with a non-biologic therapy for psoriasis

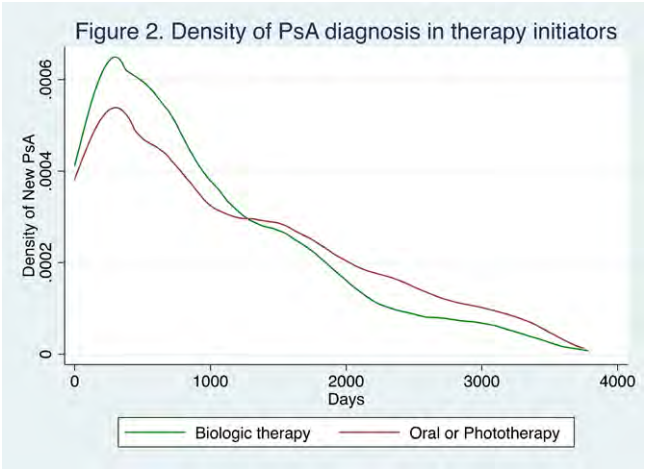
Methods: We performed a retrospective cohort study in the Optum de-identified Electronic Health Record dataset between 2006-2017. Patients with two or more ICD codes for psoriasis between the ages of 16 and 90, who were initiating an oral medication, a biologic therapy, or phototherapy (defined as no preceding codes for the therapy in the prior 12 months) were identified. Covariates at baseline were determined in the 12 months prior to therapy initiation. The outcome of interest was PsA as defined by one ICD code. The incidence of PsA was described overall and within each therapy group. We analyzed the data in two ways: a) a multivariable Cox model using a time varying exposure (once the patient was exposed to a biologic, they were considered always exposed) derived from automated stepwise regression and b) propensity score matching (greedy matching, caliper 0.1) between biologic-exposed patients and oral/phototherapy exposed patients.

Results: Among 215,386 patients with psoriasis without PsA at baseline, 9,848 were excluded for prior biologic exposure, and among the remaining, 60,258 initiated phototherapy, oral or biologic therapy during follow up. Among 22,461 new biologic initiations, 29,121 oral therapy and 8,676 phototherapy initiations, the mean age was lower in the biologics group compared to the non-biologic groups (46.9 vs 50.8), with a similar proportion of females and Caucasians. Observational time was also similar. A total of 1,643, 1,813, and 122 new PsA cases occurred over 60,739, 85,670, and 28,528 person/years (PY) of follow up, respectively (incidence 27.1, 21.2 and 4.2 per 1,000 person years respectively). Using a traditional multivariable adjustment approach with time varying exposure, the age and sex adjusted and fully adjusted HR (95% CI) for biologic users were 1.01 (0.99-1.04) and 0.93 (0.91-0.95), respectively. However, after propensity score matching, the HR (95% CI) was 1.64 (1.51-1.77). Survival curves cross, however, at approximately 8 years (Figure 1) and most of the new diagnoses of PsA occurred shortly after therapy initiation (Figure 2).

Conclusion: Confounding by indication or protopathic bias may explain the observed association of biologic therapy with the development of PsA among patients with psoriasis. Some patients may be receiving therapy because they have both psoriasis and early symptoms of PsA or their PsA diagnosis is not recorded appropriately. Given the directional discrepancy in the results between traditional modeling and propensity score analysis, further work is needed to understand the nature of this relationship.

Figure: 1





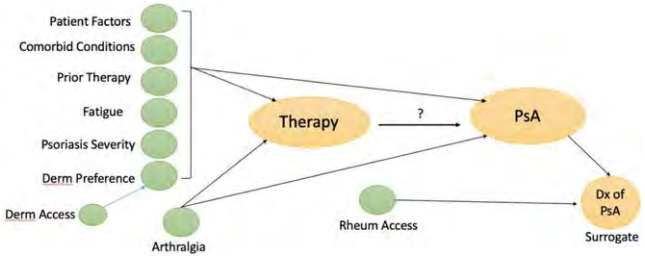


Figure 3. Directed Acyclic Graph describing potential confounders in relationship between therapy prescription and diagnosis of PsA

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FRI0356

BURDEN OF DISEASE IN PATIENTS INITIATING APREMILAST TREATMENT: 2014-2019 FINDINGS FROM THE CORRONA PSORIATIC ARTHRITIS/ SPONDYLOARTHRITIS REGISTRY

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Background: The prospective, US-based, observational Corrona PsA/SpA Registry collects real-world data on patients (pts) with PsA provided by pts and their providers.
Objectives: To examine trends in characteristics of pts initiating apremilast (APR) from 2014-2019 and compare characteristics of treatment-naive pts initiating APR or methotrexate (MTX).
Methods: PsA pts aged ≥18 yrs enrolled in the registry who initiated APR, MTX, and/or biologics for PsA from January 2014-August 2019 were included and stratified by year of initiation (2014-2015, 2016-2017, or 2018-2019). Demographics, clinical characteristics, treatment history, disease activity, and pt-reported outcomes (PROs) were analyzed at treatment initiation. Comparisons between treatment-naive APR vs MTX initiators during the entire 2014-2019 study period were summarized descriptively.
Results: 1460 PsA pts initiated APR (n=238), MTX (n=178), and/or a biologic (n=1044), including treatment-naive APR (n=20) and MTX (n=99) initiators from 2014-2019. For APR initiators in the 3 successive time periods, respectively, mean disease duration was 10.5, 12.2, and 11.4 yrs, and 87.5%, 82.5%, and 68.6% of pts had prior use of csDMARDs (similar to biologic initiators: 77.9%, 77.2%, and 68.8%). Over time, lower joint, enthesitis, and dactylitis counts, composite disease activity, and PRO measures of disease burden were observed (Table). Compared with treatment-naive MTX initiators, treatment-naive APR initiators had longer duration of PsA (8.5 vs 5.5 yrs) and time since PsA diagnosis (3.3 vs 1.8 yrs). Rates of comorbidities such as hypertension (50.0% vs 37.8%), diabetes mellitus (38.9% vs 13.3%), and metabolic syndrome (33.3% vs 8.9%) were higher in treatment-naive APR vs MTX initiators. Greater proportions of treatment-naive APR initiators had high/very high disease activity according to CDAI, DAPSA, cDAPSA, PASDAS, and DAS-28 vs MTX initiators.
Conclusion: In this Corrona Registry analysis, PsA pts initiating APR had lower disease burden in recent vs prior yrs, indicating use of APR earlier in the course of PsA is increasing in real-world practice. Treatment-naive APR initiators had greater disease activity and severity vs MTX initiators. Comorbidities were common at APR initiation.

Table:

Disease Severity and Activity, and PROs for APR Initiators in the Corrona PsA/SpA Registry

Characteristic	2014-2015 n=72	2016-2017 n=80	2018-2019 n=86
SJC (0-66), median (IQR)	2.0 (4.0)	1.0 (3.0)	0.0 (3.0)
TJC (0-68), median (IQR)	5.0 (14.0)	2.0 (4.0)	2.0 (10.0)
SPARCC enthesitis*, mean (SD)	4.7 (3.0)	3.8 (2.2)	3.7 (3.1)
Dactylitis count†, mean (SD)	2.5 (2.5)	2.3 (1.0)	2.2 (2.3)
cDAPSA category, n (%)			
Remission	4 (7.4)	8 (14.8)	13 (15.9)
Low disease activity	12 (22.2)	18 (33.3)	30 (36.6)
Minimal disease activity, n (%)	8 (15.1)	14 (26.9)	21 (25.6)
DAS-28 remission, n (%)	5 (19.2)	8 (32.0)	24 (43.6)
Pain VAS (0-100 mm) >15, n (%)	47 (85.5)	47 (83.9)	60 (73.2)
Pt's Global Assessment of Arthritis VAS (0-100 mm) >20, n (%)	47 (82.5)	45 (77.6)	54 (65.9)
HAQ >0.5, n (%)	39 (69.6)	35 (59.3)	44 (53.7)
Fatigue VAS (0-100 mm), mean (SD)	56.7 (25.4)	49.8 (25.9	45.6 (31.5)
Spine pain VAS (0-100 mm), mean (SD)	38.8 (27.6)	36.5 (29.6)	28.8 (34.1)
BASDAI‡, mean (SD)	5.4 (2.4)	4.9 (2.5)	4.4 (2.6)
Morning stiffness VAS (0-100 mm), mean (SD)	52.8 (27.3)	51.4 (28.3)	48.0 (31.2)

The n represents the total sample. Number of pts with data available may vary. *Among pts with enthesitis at baseline. †Among pts with dactylitis at baseline. ‡Among pts thought to have spondylitis by the investigator. IQR=interquartile range.

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FRI0357 IMPROVED PAIN AND FATIGUE WITH IXEKIZUMAB TREATMENT IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS AND PREVIOUS INADEQUATE RESPONSE TO TNF INHIBITORS: THREE YEAR FOLLOW-UP FROM A PHASE 3 STUDY (SPIRIT-P2)

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Background: Psoriatic arthritis (PsA) is a chronic and complex inflammatory disease with both articular and extra-articular symptoms. Pain and fatigue are two of the most common patient-reported symptoms. Improvements in pain and fatigue have been demonstrated with up to 2 years of treatment with ixekizumab (IXE) in patients who had an inadequate response or intolerance to tumor necrosis factor inhibitors (TNFi).[1,2]

Objectives: To report improvements in pain and fatigue in TNFi-experienced patients with PsA who were treated with IXE for 3 years (156 weeks).

Methods: SPIRIT-P2 (NCT02349295) was a 156-week, Phase 3 study that included patients who met the Classification Criteria for Psoriatic Arthritis (CASPAR) and had an inadequate response or intolerance to 1 or 2 TNFi. Although there was a placebo group through Week 24, these data were derived only from patients in the intent-to-treat population randomized to IXE at baseline. After a 160-mg starting dose, patients received 80 mg subcutaneous IXE every 2 or 4 weeks (Q2W or Q4W). Patients self-rated their symptoms using the Joint Pain Visual Analog Scale (Joint Pain VAS; 0 [none] to 100 [worst imaginable]), the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36; with the domains ranging from 0 [worst] to 100 [best]), and the Fatigue Severity Numeric Rating Scale (Fatigue NRS; 0 [none] to 10 [worst imaginable]). Minimum clinically important difference (MCID) cutoffs were ≥10 for Joint Pain VAS, ≥5 for SF-36 domains, and ≥3 for Fatigue NRS. Missing values were imputed by modified baseline observation carried forward for continuous variables and modified non-responder imputation for categorical variables.

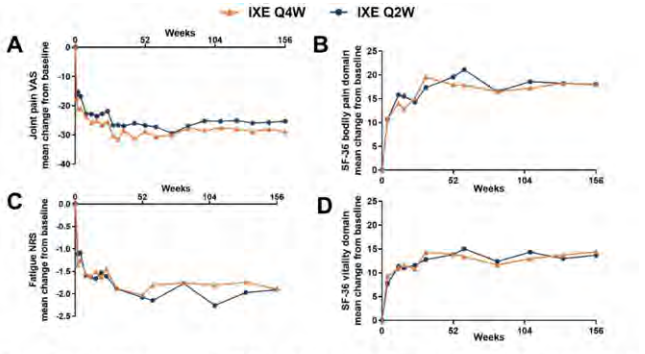


Figure. Pain and fatigue outcomes after 156 weeks of treatment with ixekizumab. Mean change from baseline is shown for (A) Joint pain VAS, (B) SF-36 bodily pain domain, (C) Fatigue NRS, and (D) SF-36 vitality domain. IXE=ixekizumab; NRS=numeric rating scale; Q2W=every 2 weeks; Q4W=every 4 weeks; SF-36= Medical Outcomes Study 36-Item Short Form Health Survey; VAS=visual analog scale.

Results: The proportions of patients who completed Week 156 were 70/122 (57.4%) in the IXE Q4W group and 55/123 (44.7%) in the IXE Q2W group. At Week 156, mean change from baseline for the Joint Pain VAS was -28.9 (IXE Q4W) and -25.3 (IXE Q2W) (Fig. A). In addition, 51.8% of patients on IXE reported clinically meaningful improvement of joint pain (56.1% IXE Q4W, 47.5% IXE Q2W) at Week 156. Patients reported an 18-point mean improvement in the SF-36 bodily pain domain at Week 156 (Fig. B). Patients also reported improvements in fatigue up to Week 156 (Fig. C), with 35.0% of patients achieving the MCID on the Fatigue NRS (39.4% IXE Q4W, 30.6% IXE Q2W). Improvement in fatigue was supported by a14-point mean improvement in the vitality domain of the SF-36 at Week 156 (Fig. D).

Conclusion: In patients with PsA who had an inadequate response or intolerance to TNFi, improvements in pain and fatigue were sustained through 3 years of IXE treatment in both the Q2W and Q4W treatment groups.

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FRI0358 USAGE OF C-REACTIVE PROTEIN TESTING IN THE DIAGNOSIS AND MONITORING OF PSORIATIC ARTHRITIS (PSA): RESULTS FROM A REAL-WORLD SURVEY IN THE US AND EUROPE

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Background: C-reactive protein (CRP) is an important non-specific marker of both acute and chronic inflammation and can be elevated in patients with PsA. The role of CRP in the management of PsA is unclear.

Objectives: To describe how CRP testing is implemented in real-world clinical practice for disease management of PsA.

Methods: A cross-sectional study among patients with PsA recruited by rheumatologists and dermatologists was conducted in France, Germany, Italy, Spain, UK and US. Data were collected from Jun-Aug 2018 via physician-completed patient record forms. Use of CRP testing was obtained by asking the physician to state (yes/no) whether CRP was used to aid PsA diagnosis, confirm the patient's PsA and to monitor the patient's PsA. Where physicians stated use of CRP testing, they were then asked to provide the number of CRP tests conducted in the last 12 months.

Results: Data were collected for 2270 patients with PsA (595 US, 1675 EU5). In EU5, 78.7% of patients had CRP conducted to aid diagnosis (vs 43.4% in US) and 72.0% had CRP conducted to monitor their condition (vs 34.6% in US). Patients seen by rheumatologists (vs dermatologists) were at least 50% more likely to have CRP used for monitoring purposes, this difference being most pronounced in the US. In EU5, CRP was conducted a mean [SD] of 2.7 [1.7] times in the last 12 months, versus 2.0 [1.4] in the US. Country level usage of CRP testing is shown in Table 2.

Table 1. Patient demographic and clinical characteristics

	Overall (n=2270)	EU5 (n=1675)	US (n=595)
Patient seen by rheumatologist, n (%)	1130 (49.8)	834 (49.8)	296 (49.7)
Age, mean [SD]	46.6 [13.3]	48.1 [13.1]	50.0 [13.5]
Female, n (%)	1047 (46.1)	774 (46.2)	273 (45.9)
BMI, mean [SD]	26.8 [4.7]	26.3 [4.3]	28.1 [5.5]
Caucasian, n (%)	2051 (90.4)	1551 (92.6)	500 (84.0)
Current smoker, n (%)	403 (20.3)	352 (24.3)	51 (9.5)
Employment, n (%) -Working full-time	1271 (58.2)	894 (55.6)	377 (65.3)
Current disease severity, n (%)			
-Mild	1702 (75.0)	1253 (74.8)	449 (75.5)
-Moderate/Severe	568 (25.0)	422 (25.2)	146 (24.5)
Current treatment, n (%)			
-Receiving bDMARD*	1231 (54.2)	910 (54.3)	321 (53.9)
-Receiving tsDMARD*	251 (11.1)	121 (7.2)	130 (21.8)
-Receiving csDMARD*	835 (36.8)	698 (41.7)	137 (23.0)
-Receiving opioid	55 (2.4)	29 (1.7)	26 (4.4)
Total number of HCP visits in last 12months, mean [SD]	6.5 [5.8]	7.0 [6.3]	5.0 [3.6]

*bDMARD: biologic DMARD, tsDMARD: targeted synthetic DMARD, csDMARD: conventional synthetic DMARD

Table 2. Purpose and frequency of CRP testing

CRP conducted…	EU5 (n=1675)	France (n=277)	Germany (n=360)	Italy (n=360)	Spain (n=369)	UK (n=309)	US (n=595)
To aid diagnosis, n (%)	1319 (78.7)	233 (84.1)	282 (78.3)	283 (78.6)	315 (85.4)	206 (66.7)	258 (43.4)
To confirm PsA, n (%)	692 (41.3)	83 (30.0)	156 (43.3)	151 (41.9)	179 (48.5)	123 (39.8)	110 (18.5)
To monitor PsA, n (%) [n]	1190 (72.0) [1652]	209 (75.7) [276]	261 (74.1) [352]	256 (72.9) [351]	283 (77.1) [367]	181 (59.2) [306]	203 (34.6) [586]
Patients with ≥1 CRP in last 12 months, n (%)	1355 (80.9)	238 (85.9)	291 (80.8)	304 (84.4)	319 (86.4)	203 (65.7)	255 (42.9)
Number conducted in last 12months, mean [SD]	2.7 [1.7]	3.1 [2.5]	2.4 [1.7]	2.5 [1.3]	2.6 [1.2]	2.9 [2.0]	2.0 [1.4]

Conclusion: The majority (80.9%) of patients with PsA in EU5 had at least one CRP test in the last 12 months, versus 42.9% in the US. CRP is more commonly used for diagnosis and monitoring of PsA in Europe compared to the US and is more commonly ordered by rheumatologists than dermatologists.

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FRI0359

INTEGRATED SAFETY RESULTS OF TWO PHASE-3 TRIALS OF GUSELKUMAB IN PATIENTS WITH PSORIATIC ARTHRITIS THROUGH THE PLACEBO-CONTROLLED PERIODS

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Background: DISCOVER 1 & 2 are phase 3 psoriatic arthritis (PsA) trials investigating guselkumab (GUS), an IL-23 inhibitor that specifically binds the IL-23p19 subunit. In both studies, GUS showed significant improvement vs placebo (PBO) through week (W) 24 in the PBO-controlled period.[1,2]

Objectives: To present integrated safety results of DISC 1 & 2 through the PBO-controlled periods.

Methods: Adult patients (pts) with active PsA despite standard therapy were enrolled. All pts were biologic-naïve, except ~30% in DISC 1 with previous exposure to 1-2 TNF inhibitors. Pts were randomized to SC GUS 100 mg Q4W; GUS 100 mg at W0, W4, then Q8W; or PBO. Adverse events (AEs) and lab results were analyzed from pooled data.

Results: The rates of pts experiencing ≥1 AE, serious AE, infection, serious infection, and discontinuation due to an AE were similar between GUS and PBO (Table 1). There were 2 deaths, 3 malignancies, 2 Major Adverse Cardiac Events (MACE), and no opportunistic infections (treatment group not shown to prevent unblinding). Among the AEs reported by ≥5% pts in any group (Table 1), nasopharyngitis and elevated serum hepatic aminotransferases were more common with GUS vs PBO. Laboratory ALT and AST elevations were mostly mild, transient, and not associated with significant bilirubin elevation. There was a trend to decreased neutrophil count (mostly Grade 1, transient, and not associated with infection) with GUS vs PBO (Table 2). Low rates of injection-site reactions were seen with GUS vs PBO. Anti-drug antibody development was also low (Table 1).

Table 1. Patient Reported AEs, n (%)

	GUS 100 mg Q8W	GUS 100 mg Q4W	PBO
N	375	373	372
≥1 AE	182 (48.5)	182 (48.8)	176 (47.3)
≥1 Serious AE	7 (1.9)	8 (2.1)	12 (3.2)
Discontinuation due to AE	5 (1.3)	8 (2.1)	7 (1.9)
≥1 Infection	73 (19.5)	80 (21.4)	77 (20.7)
≥1 Serious infection	1 (0.3)	3 (0.8)	3 (0.8)
≥1 Opportunistic Infection (including Candida)	0	0	0
Active Tuberculosis	0	0	0
≥1 Injection-site reaction	5 (1.3)	4 (1.1)	1 (0.3)
Anti-GUS antibody +, n/N (%)	6/373 (1.6)	9/371 (2.4)	--
AEs* reported by ≥5% of patients in any treatment group			
Nasopharyngitis	26 (6.9)	19 (5.1)	17 (4.6)
Upper respiratory tract infection	13 (3.5)	23 (6.2)	17 (4.6)
Increased ALT	23 (6.1)	28 (7.5)	14 (3.8)
Increased AST	23 (6.1)	14 (3.8)	9 (2.4)

* Medical Dictionary for Regulatory Activities (MedDRA) preferred term

Table 2. Lab Results*

	GUS 100 mg Q8W	GUS 100 mg Q4W	PBO
N	373	*371*	*370*
ALT Increased (%)			
Grade 1	28.2	35.0	30.1
2	1.1	2.7	1.4
3-4	0.8	1.1	0.8
Neutrophil Count Decreased (%)			
Grade 1	5.6	5.9	3.2
2	1.6	1.6	0.8
3-4	0	0.3	0.3

* NCI toxicity grade
ALT=Alanine aminotransferase

Conclusion: GUS was safe and well tolerated through the PBO-controlled period in 2 randomized, phase 3 trials of patients with active PsA. There were no meaningful safety differences between the Q8W and Q4W groups, no significant safety issues identified when comparing GUS to PBO, and no safety signals with regards to infections, malignancy, and MACE. The safety profile of GUS Q4W and Q8W in PsA pts was generally consistent with that in the Phase 3 trials of GUS Q8W for psoriasis.[3,4]

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FRI0360

IMPACT OF METHOTREXATE ON DISEASE PATTERN IN ACTIVE PSORIATIC ARTHRITIS PATIENTS ELIGIBLE FOR A RANDOMIZED CLINICAL TRIAL WITH USTEKINUMAB: COMPARATIVE BASELINE DATA FROM MULTICENTRE INVESTIGATOR-INITIATED MUST TRIAL

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Background: Methotrexate (MTX) is a csDMARD treatment that is initiated as first-line therapy (after NSAID) in active psoriatic arthritis (PsA). Randomized clinical trials mostly require treatment failure or intolerance of csDMARD/MTX therapy before initiation of a biological treatment. We designed an investigator-initiated (IIT) randomised blinded study comparing PsA patients starting open label Ustekinumab (UST) combined with blinded MTX or placebo (PLC). Patients are stratified regarding their previous MTX therapy (continuation or discontinuation of MTX (MTX-pre-treated patients –group A) or newly initiate MTX or continue without MTX (MTX-naïve patients – group B).

Objectives: To determine disease characteristics of patients with active psoriatic arthritis regarding their skin and musculoskeletal manifestations in dependence of their MTX treatment status.

Methods: A total of 186 patients with active PsA (defined as TJC ≥4, SJC ≥4 (68/66 joint count) and DAS28 ≥ 3,2) were screened for eligibility. At baseline (BL) 173 patients starting open label UST were randomised to receive either MTX or PLC. At Screening (SCR) and BL, demographic data, PsA and PsO disease activity (joint count (TJC/SJC), enthesitis (LEI), dactylitis (number of digits), PASI, BSA, mtNAPSI), previous medication as well as quality of life (QoL) and function (documented as PRO using DLQI, HAQ and subjects assessment of pain as visual analogue scale (VAS) was documented.

Results: Our preliminary blinded data export comprised all documented and released data for SCR and BL until Mid-January 2020 - in total 154 randomized patients. Thereof, 78 patients were randomized in group A and 76 in group B. BL characteristics were well balanced between groups (mean age A: 50,7 years vs. 46,4 in B, BMI 29 vs. 29,6 in B). More male were included in B (72% vs. 50 %). In median, patients in A had a disease duration of 2,9 y whereas duration in B was in median 0,3 y. More patients in A had failed previous biological therapy (17 to 6 in B), discontinued due to intolerability or ineffectiveness as allowed for study inclusion. Mean DAS28 was 4,5 (moderate disease activity) for both groups and mean values for SGA, PGA were comparable (SGA: 59,1 vs 54,9 PGA: 61,4 vs. 55.6) reflecting comparable disease activity in peripheral arthritis. Mean LEI was comparable in both groups (A: 1,3 vs B: 1,1). Mean number of digits with dactylitis were slightly higher in B (0,8) than in A (0,2). Overall HAQ showed no differences (1.0 in B vs. 0.8 in A – missing data 45 and 29 resp.) and pain VAS did not differ between groups (A: 54,9 mm vs. 56,6 mm in B). PASI and NAPSI were higher in B at BL than in group A (PASI: 7,2 vs. 3,3, mtNAPSI 5,0 vs. 3,0) and PRO showed a higher skin disease burden experienced by MTX-naïve patients prior randomization: in DLQI more patients on MTX experience "no effect" of their skin disease on QoL (22% vs. 7%) whereas more MTX naïve patients see a "moderate" "large" to "extreme large effect" of their disease on QoL (16%, 11%, 5% in B vs. 10%, 8%, 3% in A).

Conclusion: Our results give important information about comparability of patient population on MTX or without MTX therapy eligible for biological trials. Despite a comparable disease activity in peripheral arthritis scores, skin disease activity was increased in patients without MTX compared to MTX treated patients. Number of affected digits in dactylitis was lower with MTX, whereas its impact on enthesitis seems to be neglectable.

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FRI0361

CARTILAGE DEGRADATION IN PSORIATIC ARTHRITIS IS ASSOCIATED WITH INCREASED SYNOVIAL PERFUSION AS DETECTED BY MAGNETIC RESONANCE IMAGING

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Background: Even though cartilage loss is a known feature of psoriatic arthritis (PsA), research is sparse on its role in the pathogenesis of PsA and its potential use for disease detection and monitoring. Using delayed gadolinium-enhanced magnetic resonance imaging of cartilage (dGEMRIC) and dynamic contrast-enhanced MRI (DCE MRI), research has shown that early cartilage loss is strongly associated with synovial inflammation in rheumatoid arthritis (RA). The aim of this study was to determine if acute inflammation is associated with early cartilage loss in small finger joints of patients with PsA.

Objectives: Is local perfusion in PsA patients measured by dynamic MRI associated to local cartilage loss?

Methods: Metacarpophalangeal (MCP), proximal interphalangeal (PIP), and distal interphalangeal (DIP) joints of 17 patients with active PsA were evaluated by high-resolution 3 Tesla dGEMRIC and DCE MRI using a dedicated 16-channel hand coil. Semi-quantitative and quantitative perfusion parameters were calculated. Images were analyzed by two independent raters for dGEMRIC indices, PsA MRI scores (PsAMRIS), total cartilage thickness (TCT), and joint space width (JSW).

Results: We found significant negative correlations between perfusion parameters (except K_{ep}) and dGEMRIC indices, with the highest value at the MCP joints (K_{Trans}: $\tau = -0.54$, $p = 0.01$; K_{ep}: $\tau = -0.02$, $p = 0.90$; IAUC: $\tau = -0.51$, $p = 0.015$; Initial Slope: $\tau = -0.54$, $p = 0.01$; Peak: $\tau = -0.67$, $p = 0.002$). Heterogeneous correlations were detected between perfusion parameters and both, total PsAMRIS and PsAMRIS synovitis sub-scores. No significant correlation was seen between any perfusion parameter and JSW and/or TCT.

Conclusion: As examined by DCE MRI and dGEMRIC, there is a significant association between early cartilage loss and acute synovial inflammation in small finger joints of PsA patients.

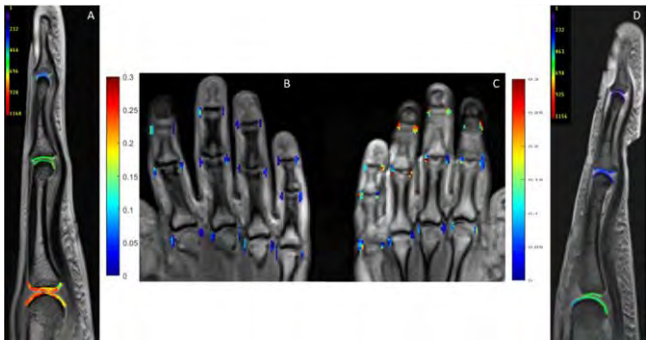


Figure 1. dGEMRIC maps (third digit) and perfusion maps (peak parameter) of MCP, PIP, and DIP joints in 26-year-old male (A and B) and a 59-year-old female (C and D) with PsA. Lower dGEMRIC values are illustrated in D, indicating more proteoglycan loss than in A. Higher peak values are depicted in C, indicating a higher severity of synovitis than in B. Peak parameter is illustrated in mM/l per second, dGEMRIC indices in ms.

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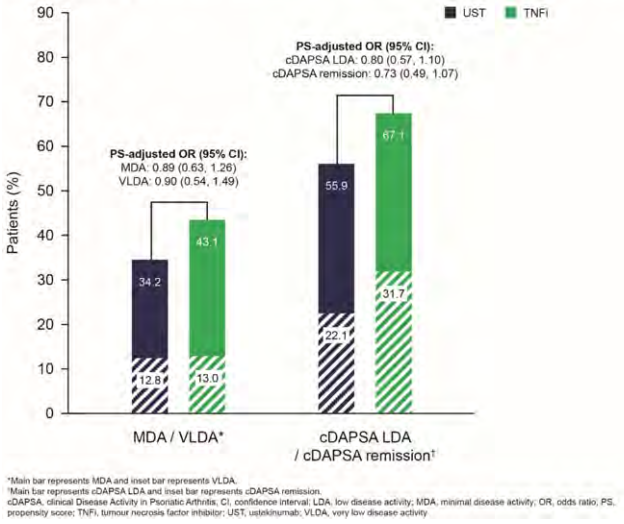
FRI0362

COMPARATIVE EFFECTIVENESS OF USTEKINUMAB (UST) AND TNF INHIBITORS (TNFI) IN PATIENTS WITH PSORIATIC ARTHRITIS (PSA) IN THE REAL-WORLD, MULTINATIONAL PSABIO STUDY: 12-MONTH FOLLOW-UP

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Background: Among treatment options for PsA, IL-12/23 inhibition with UST was the first new biologic mode of action after TNFi. Few real-world data comparing UST with TNFi are available.
Objectives: Comparison of UST and TNFi treatment effectiveness within the prospectively followed PsABio cohort at 12-month (mo) follow-up.
Methods: The PsABio study (NCT02627768) evaluates effectiveness, tolerability and persistence of 1st, 2nd or 3rd-line UST or TNFi in PsA. Proportions of patients (pts) reaching MDA/very low disease activity (VLDA) and clinical Disease Activity index for PSoriatic Arthritis (cDAPSA) LDA/remission are described. Comparison across UST and TNFi cohorts was done on last observation carried forward up to 12 (±3) mo, with non-response imputation for pts who had stopped/switched initial treatment. Logistic regression analysis was used, including propensity score (PS) analysis to adjust for imbalanced prognostic baseline (BL) covariates: country, age, sex, BMI, smoking (yes/no), comorbidities (cardiovascular/metabolic syndrome), PsA type (axial, polyarticular, oligoarticular), psoriasis body surface area (BSA), disease duration, cDAPSA, 12-item PsA Impact of Disease (PsAID-12), dactylitis, enthesitis, Fibromyalgia Rapid Screening Tool (FiRST) score, line of biologic (b)DMARD, synthetic DMARD use, and steroid or NSAID use.
Results: Of 929 eligible pts, 893 had evaluable data at BL and at follow-up; 438 (95.6%) were treated with UST and 455 (96.6%) with TNFi (including stoppers/switchers). UST and TNFi groups had BL differences in mean age (51.0 vs 48.5 years, respectively), concurrent comorbidities (68.7% vs 60.9%), time since diagnosis (7.5 vs 6.2 years), line of treatment (1st-line 45.0% vs 55.2%; 3rd-line 20.5% vs 12.1%), NSAID use (54.8% vs 68.8%), concomitant MTX use (29.9% vs 42.0%) and psoriasis skin involvement (BSA >10% in 26.6% vs 14.8%).
In 714 pts with available data, mean (standard deviation) BL cDAPSA was 30.6 (20.2; n=358) for UST and 29.3 (18.6; n=356) for TNFi. Observed data showed differences in proportion of pts achieving MDA/VLDA and cDAPSA LDA/remission in favour of TNFi, but after PS adjustment for BL differences (such as line of therapy, skin psoriasis, concomitant conventional DMARD, etc.), odds ratios for reaching targets at 12 mo did not significantly differ between UST and TNFi groups (Fig. 1).

Figure 1. Observed proportion of pts (and PS-adjusted ORs [95% CI]) achieving MDA/VLDA and cDAPSA LDA/remission with UST vs TNFi up to 12 mo



*Main bar represents MDA and inset bar represents VLDA.
†Main bar represents cDAPSA LDA and inset bar represents cDAPSA remission.
cDAPSA, clinical Disease Activity in Psoriatic Arthritis; CI, confidence interval; LDA, low disease activity; MDA, minimal disease activity; OR, odds ratio; PS, propensity score; TNFi, tumour necrosis factor inhibitor; UST, ustekinumab; VLDA, very low disease activity

Comparison of 6- and 12-mo unadjusted data showed sustained MDA/VLDA responses with both UST (21.8%) and TNFi (29.5%), with comparable proportions of additional pts achieving these targets between 6 and 12 mo (17.0% and 20.3%, respectively). Sustained efficacy became lower with successive lines of treatment (data not shown).
Conclusion: Various factors, including patient characteristics such as comorbidities, influence the physician's selection of treatment modality for patients needing a bDMARD. Our real-world results demonstrate differences in observed clinical effectiveness between UST and TNFi. However, after PS adjustment for a number of BL differences, clinical results at 12 mo were comparable between UST and TNFi groups. Data at 12 mo also show sustained response with both UST and TNFi treatment, as well as a similar rate of pts achieving targets after 6 to 12 mo of treatment.
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Squibb, Celgene, Eli Lilly, Janssen, Merck Sharp & Dohme, Novartis, Sanofi, UCB, Roche, Pfizer, Beatriz Joven-Ibáñez Speakers bureau: Abbvie, Celgene, Janssen, Merck Sharp & Dohme, Novartis, Pfizer, Wim Noel Employee of: Janssen Pharmaceuticals NV, Michael T Nurmohamed Grant/research support from: Abbvie, Bristol-Myers Squibb, Celltrion, GlaxoSmithKline, Jansen, Eli Lilly, Menarini, Merck Sharp & Dohme, Mundipharma, Pfizer, Roche, Sanofi, USB, Consultant of: Abbvie, Bristol-Myers Squibb, Celltrion, GlaxoSmithKline, Jansen, Eli Lilly, Menarini, Merck Sharp & Dohme, Mundipharma, Pfizer, Roche, Sanofi, USB, Speakers bureau: Abbvie, Bristol-Myers Squibb, Celltrion, GlaxoSmithKline, Jansen, Eli Lilly, Menarini, Merck Sharp & Dohme, Mundipharma, Pfizer, Roche, Sanofi, USB, Petros Sfikakis Grant/research support from: Grant/research support from Abvie, Novartis, MSD, Actelion, Amgen, Pfizer, Janssen Pharmaceutical, UCB, Elke Theander Employee of: Janssen-Cilag Sweden AB, Laure Gossec Grant/research support from: Lilly, Mylan, Pfizer, Sandoz, Consultant of: AbbVie, Amgen, Biogen, Celgene, Janssen, Lilly, Novartis, Pfizer, Sandoz, Sanofi-Aventis, UCB

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FRI0363 CLINICAL PREDICTORS OF SECUKINUMAB RETENTION IN A REAL WORLD COHORT OF PATIENTS WITH PSORIATIC ARTHRITIS AND AXIAL SPONDYLOARTHRITIS

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Background: There are increasing treatment options for patients with psoriatic arthritis (PsA) and axial spondyloarthritis (AxSpA). Whilst there are several studies identifying predictors of response to TNF inhibitors[1] there is little data so far predicting response to the IL-17A inhibitor secukinumab which given its different mechanism of action may have different predictors of response.

Objectives: To identify demographic or clinical factors at initiation of secukinumab associated with stopping treatment due to inefficacy in PsA and in AxSpA in a real world cohort.

Methods: Retrospective analysis of all rheumatology patients' notes in Glasgow who had received secukinumab. Demographics, disease activity at baseline and retention of secukinumab were collected from medical records in patients with a diagnosis of PsA or AxSpA. Patients who discontinued due to adverse events or other events (e.g. pregnancy) were excluded. Patients who remain on secukinumab but have not yet had their six-month review to assess response or who started secukinumab via a clinical trial were also excluded. Unpaired T-test of unequal variance used to assess differences between groups with p-value ≤0.05 considered significant.

Results: 352 rheumatology patients in Glasgow had ever received secukinumab. 266 had PsA, 76 had AxSpA (others: SAPHO, JIA, reactive arthritis).

77 PsA patients discontinued secukinumab, 48 due to inefficacy. 157 PsA patients remain on secukinumab and have had at least an initial six-month review.

Table 1 shows results for PsA. Inefficacy was associated with higher levels of current smoking and higher levels of ESR and CRP but not tender or swollen joints.

Table 1. Demographics and clinical characteristics of PsA patients starting secukinumab

	Stopped due to Inefficacy (n=48)	Remain on Secukinumab (n=157)	Significance (p value)
Gender (M:F)	1:1.86	1:2.3	0.24
Age (years)	47.8	50.8	0.078
Current Smoking	37%	21%	0.040
Socioeconomic Decile	4.9	5.0	0.39
Weight (kg)	81.6	85.9	0.11
Number of Comorbidities	1.72	1.85	0.31
Disease Duration (years)	10.4	11.2	0.24
Number Previous bDMARDs	1.69	1.40	0.095
Tender Joint Count	16.6	16.6	0.50
Swollen Joint Count	6.4	7.3	0.29
Patient Global Score (VAS)	62.4	67.7	0.19
ESR (mm/hr)	24.1	14.8	0.017
CRP (mg/L)	12.8	6.2	0.049

Values are mean unless stated

21 AxSpA patients discontinued secukinumab, 13 due to inefficacy. 49 AxSpA patients remain on secukinumab and have had at least an initial six-month review. AxSpA patients who stopped due to inefficacy had higher mean BASDAI (8.47 vs 7.02, p=0.007) but there was no difference in mean ESR (31 vs 27.1, p=0.31) or CRP (23.6 vs 23.0, p=0.48). Surprisingly, disease duration was lower in inefficacy group (7.8 years vs 13.5, p= 0.003); this could reflect a higher proportion in the inefficacy group with non-radiographic AxSpA which is known to be associated with earlier disease and to have a lower response to biologic treatments than ankylosing spondylitis. Smoking did not show significant difference in AxSpA but numbers are small and there is numerically higher level of smoking in the inefficacy group (58% vs 32%, p=0.063). No other significant differences in demographics or clinical characteristics were noted.

Conclusion: Smoking predicted inefficacy in secukinumab in PsA patients, with a similar trend in AxSpA patients, reinforcing the importance of promoting smoking cessation. Higher levels of ESR and CRP negatively predicted secukinumab response in PsA. High BASDAI and low disease duration in AxSpA predicted inefficacy. These clinical factors may be helpful in informing treatment decisions in PsA and AxSpA in the absence of therapeutic biomarkers.

References:

[1] Maneiro JR et al. Predictors of response to TNF antagonists in patients with ankylosing spondylitis and psoriatic arthritis: systematic review and meta-analysis. *RMD Open*. 2015;1(1):e000017.

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FRI0364 PREVALENCE OF THE METABOLIC SYNDROME IN PSORIATIC ARTHRITIS: SYSTEMATIC LITERATURE REVIEW AND RESULTS OF THE CARMA COHORT

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Background: The cardiovascular burden in psroriatic arthritis (PsA) is well recognized[1].

Objectives: To analyze the prevalence of metabolic syndrome (MetS) in patients with PsA.

Methods: We conducted a systematic literature review (SLR) and a sub-analysis of the CARMA cohort. In the SLR, we searched in Pubmed, Embase, the Cochrane Central Library, and the ClinicalTrial until March 2019 using Mesh terms and free text words. We included SLR, clinical trials and observational studies analyzing the prevalence or frequency of MetS in PsA. Two reviewers selected articles, assessed the quality of the studies and collected data independently. The CARMA cohort was designed to establish the cardiovascular (CV) morbidity and associated risk factors for CV disease. It includes data from patients with chronic inflammatory rheumatic diseases (including PsA) of 67 Spanish hospitals. A sub-analysis of the prevalence of metS in PsA was performed using the National Cholesterol Education Program Adult Treatment Panel III criteria updated in 2005, which requires the presence of ≥3 of the following: high waist circumference, low HDL cholesterol level, high triglyceride level, high blood pressure and high fasting glucose values.

Results: A total of 18 articles of moderate to high quality, were selected in the SLR. The included patients presented a balanced distribution by sex, with an average age ranging from 42 to 59 years. The frequency of MetS varied from 23.5% to 62.9% depending on the definition of MetS. The most widely used classification method was the National Cholesterol Education Program, followed by the method recommended by the International Diabetes Federation in 2009. A total of 724 patients with PsA were included in the CARMA study, of whom 327 (45.4%) were women and 157 (21.8%) smokers. The mean age at baseline was 51 ± 12 years and the mean duration of PsA disease 9 (4-16) years. Hypertension was the most frequently altered parameter (66.8%), followed by fasting glucose (42.6%) and hypertriglyceridemia (30.6%). Table 1 shows the frequency of patients according to the number of MetS components. A total of 222 (30.6%) PsA patients presented metabolic syndrome.

Table 1. Prevalence of metabolic syndrome.

Number of components N 0-5	Patients (n) CARMA study	Percentage of patients, SLR (%)
0	101	13,95
1	208	28,73
2	193	26,66
3	151	20,86
4	59	8,15
5	12	1,66
Total	724	100

Conclusion: The frequency of the individual components of the MetS is variable according to the method of classification, which makes it difficult to compare between studies. In the CARMA study, the prevalence of MetS was around 30%, which supports the control of individual factors to prevent CV disease.

References:
[1] Liew JW, et al. Best Pract Res Clin Rheumatol. 2018;32(3):369-389.
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FRI0365 REAL-WORLD EFFECTIVENESS AND SAFETY OF APREMILAST IN A LARGE COHORT OF GERMAN PATIENTS WITH PSORIATIC ARTHRITIS: 1-YEAR ANALYSIS OF AN ONGOING MULTICENTER, PROSPECTIVE, NON-INTERVENTIONAL STUDY

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Background: Apremilast (APR) has been studied extensively in phase III randomized, controlled trials. However, real-world information is limited on the effectiveness and safety of APR in patients with psoriatic arthritis (PsA).
Objectives: To assess the effectiveness and safety of APR in a large cohort of patients with active PsA from routine clinical practice settings in Germany.
Methods: In this multicenter, prospective, non-interventional study, the primary endpoint was the proportion of patients reaching ≥1 point (≥20%) improvement from baseline (BL) in the Physician's Global Assessment of Disease Activity (PhGA) score. Other endpoints included effects on swollen and tender joint counts (SJC/TJC), psoriasis-involved body surface area (BSA), enthesitis, dactylitis, Patient's Global Assessment of Disease Activity score (PtGA), Psoriatic Arthritis Impact of Disease (PsAID) tool, pain, and pruritus. The current analysis is based on observed data through 1 year of study duration.
Results: A total of 545 German patients were enrolled and followed up to 12 months of APR treatment; 488 patients were included in the safety analysis and 418 in the full analysis set. The mean age was 55 years, mean body mass index was 29.5 kg/m^2, and 60% were female. The mean duration of psoriasis and PsA was 26 years and 18 years, respectively. At BL, 46.7% of patients had enthesitis based on the Leeds Enthesitis Index (LEI; mean [SD]: 2.9 [1.72]) and 23% had dactylitis (mean [SD]: 2.2±2.03); 74% of patients were biologic-naive. Effectiveness is shown after ~1 month (Visit 1 [V1]) and ~4 months (Visit 2 [V2]) and for up to 225 patients after 12 months (Visit 5 [V5]) of treatment (Table).
Improvements were also seen in PtGA, overall pain, and pruritus. A subanalysis suggests APR was associated with greater benefits in biologic-naive patients compared with patients who previously received biologic therapy. Observed safety and tolerability through V5 were consistent with the known overall safety profile of APR. Common adverse events in clinical trials were similar, with a lower incidence of diarrhea (11.1%), nausea (7.0%), headache (3.9%), and respiratory tract infection (0.8%).
Conclusion: Data from this large, real-world cohort of patients with PsA show the effectiveness of APR. In patients with up to 12 months of follow-up, APR was associated with rapid and maintained improvements in physician-assessed and patient-reported outcomes. Safety and tolerability were consistent with the known profile of APR.

Table. Effectiveness of APR Treatment

	BL n=418*	V1 n=326*	V2 n=360*	V5 n=214*
≥1-point PhGA improvement, %	NA	56.2	77.2	86.4
PhGA score, mean (95% CI)	2.5 (2.4, 2.5)	1.8 (1.7, 1.9)	1.4 (1.3, 1.5)	1.1 (1.0, 1.2)
PhGA score=0-1, %	NA	34.3	60.8	77.0
SJC mean improvement, % (95% CI)	NA	42.1 (34.7, 49.5)	54.7 (45.4, 64.1)	75.7 (65.5, 86.0)
TJC mean improvement, % (95% CI)	NA	38.3 (27.2, 40.4)	36.0 (23.8, 48.3)	57.1 (41.1, 73.1)
Psoriasis-involved BSA (%), mean (95% CI)	10.0 (8.6, 11.4)	7.7 (6.3, 9.1)	4.7 (3.8, 5.7)	2.4 (1.8, 2.9)
Achievement of LEI=0†, %	NA	38	50	58
Achievement of dactylitis count=0†, %	NA	48	71	88
PsAID score, mean (95% CI)	5.33 (5.12, 5.53)	4.65 (4.41, 4.89)	3.97 (3.73, 4.20)	3.22 (2.94, 3.50)

*Based on the number of patients with data available at the given visit; the n may vary for individual parameters at a given visit. †In patients affected at BL. CI=confidence interval; NA=not applicable.

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FRI0366 CARDIOVASCULAR RISK RECLASSIFICATION USING CAROTID ULTRASOUND IN PSORIATIC ARTHRITIS: A CASE-CONTROL STUDY

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Background: Patients with psoriatic arthritis (PsA) have an increased risk of cardiovascular disease (CVD). Risk stratification algorithms for general population, such as cardiovascular risk calculators, have been developed to improve primary prevention and early detection of CVD; however, it underestimates cardiovascular risk in PsA patients[1]. Carotid ultrasound, which measures both carotid intima-media thickness (cIMT) and carotid plaque (CP), is useful in the detection of subclinical carotid atherosclerosis improving risk stratification.
Objectives: This study aimed to evaluate the use of carotid ultrasound in the reclassification of cardiovascular risk in PsA patients and compare it with controls.
Methods: This cross-sectional study included 70 PsA patients that fulfilled the CASPAR criteria and 70 controls subjects matched by age and comorbidities. Patients with a history of previous atherosclerotic CVD and pregnancy were excluded. Clinical examination, blood tests and Framingham Risk Score Lipids and BMI based (FRS-Lipids/FRS-BMI) and ACC/AHA 2013 calculators were performed. Carotid B-mode ultrasonography was used for measurements of cIMT and CP presence. *Increased cIMT was defined as ≥0.9 mm. CP was defined* as a *focal narrowing ≥0.5 mm of the surrounding* lumen or a *cIMT ≥1.2 mm.* Descriptive analysis was done with measures of central tendency and dispersion and comparisons with Chi-square, Student´s t and Mann-Whitney U tests.
Results: A total of 138 subjects were included. Clinical and demographic characteristics are shown in Table 1. Differences were found in the cardiovascular risk classification between the calculators and the carotid ultrasound. However, these were not significant when compared to controls, with the exception of the FRS-Lipids which had a significant difference when recategorized as high risk by the increase in the cIMT (p = 0.016). A 70.8% and a 56% of patients with PsA who had CP were not classified as high risk according to FRS-Lipids (p = 0.010) and ACC / AHA 2013 (p <0.001) respectively.

Table 1. Clinical and demographic characteristics.

	PsA (n=69)	Controls (n=69)	P
Age, (mean±SD)	53.58±10.946	53.86±7.313	NS
Women, n (%)	38(55.1)	59(85.5)	**<0.001**
Type 2 Diabetes Mellitus, n (%)	14(20.3)	9(13)	NS
Hypertension, n (%)	27(39.1)	19(27.5)	NS
Dyslipidemia, n (%)	29(42)	24(34.8)	NS
Obese, n (%)	26(37.7)	28(40.6)	NS
Active smoker, n (%)	15(21.7)	12(17.4)	NS
Disease duration, median (q25-q75)	5(2.5-8)	-	-
DAS28-ESR, (mean±SD)	3.74±1.477	-	-
DAPSA, median (q25-q75)	35(27.5-58.5)	-	-

Conclusion: None of the traditional calculators used in the general population correctly estimates cardiovascular risk in patients with PsA. Among the calculators we performed, FRS-Lipids was the worst, underestimating PsA individuals with CP up to 70.8%. Therefore, it is advisable to perform a carotid ultrasound without relying on the results obtained by any of these calculators in order to achieve an adequate classification and accomplish a correct management of the disease.
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Table 2. Ultrasound Characteristics in PsA patients

	CP	Without CP	P
FRS-Lipids, n (%)			**0.010**
Low and Moderate risk	17(70.8)	39(95.1)	
High risk	7(29.2)	2(4.9)	
FRS-BMI, n (%)			NS
Low and Moderate risk	15(62.5)	32(80)	
High risk	9(37.5)	8(20)	
ACC/AHA 2013, n (%)			**<0.001**
Low, Borderline and Moderate risk	14(56)	35(97.2)	
High risk	11(44)	1(2.8)	

Disclosure of Interests: None declared
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FRIDAY, 05 JUNE 2020

Bone diseases, including osteoporosis and osteoimmunology: aetiology, pathology and animal models

FRI0367 ADALIMUMAB IS MORE EFFECTIVE THAN ETANERCEPT AT PREVENTING TNF-ENHANCED OSTEOCLAST DEVELOPMENT THROUGH DOWNREGULATION OF PRO-OSTEOCLASTOGENIC FACTORS ICAM-1 AND IGFBP2 AND UPREGULATION OF ANTI-OSTEOCLASTOGENIC FACTOR FABP4

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Background: TNF has been shown to contribute to osteoclastogenesis independently and in conjunction with M-CSF and RANKL. We have previously demonstrated that TNF enhances the kinetics of RANKL-induced human osteoclastogenesis and that its effects are mitigated more effectively by the anti-TNF biologic adalimumab (ADA) as compared to etanercept (ETN).
Objectives: To determine the mechanism responsible for the difference in effectiveness between the two biologics, a label-free quantitative proteomics study was conducted on TNF-activated human osteoclasts (OC) upon biologic treatment.
Methods: Human bone marrow-derived OC precursors (OCP, 3 donors) were exposed for 5 days to M-CSF, M-CSF+RANKL (RANKL) alone or in combination with 100 ng/mL TNF +/- 5 ug/mL ADA, ETN or human IgG1 (IGG) as pre-formed complexes. OC differentiation was confirmed by measuring TRAP5b activity. Shotgun proteomics was performed on peptides generated from detergent based cell extracts subjected to methanol/chloroform precipitation and trypsin/Lys-C digestion. Data acquisition was performed with Orbitrap Q Exactive™ HF-X mass spectrometer. MaxQuant was utilized to quantify proteins based on MS1 peak intensities. Data matrix was normalized, imputed and subjected to differential expression analysis by limma. DAVID pathway analysis (DPA) was used to identify pathways impacted by various treatment conditions based on proteins exhibiting significant ($p<0.05$) 1.2-fold change in expression as compared to RANKL. Protein levels within culture supernatant or cell lysate were verified by ELISA or MSD.
Results: Principle component analysis (PCA) of the proteomic profiling data for the 3 donors indicated that exposure of OCP to TNF induced a distinct profile from that of M-CSF and RANKL. The addition of ADA:TNF complexes restored the profile to that of RANKL, whereas those exposed to ETN:TNF complexes exhibited an intermediate profile matching differences observed in TRAP 5b activity levels. DPA identified 3 pathways most associated with osteoclastogenesis: receptor-mediated endocytosis (e.g. CD163, IGFBP2), oxidation-reduction process (e.g. FABP4), and cell adhesion (e.g. ICAM-1, TGFBI) that were significantly impacted by TNF with ADA:TNF being more effective than ETN:TNF in restoring most pathway-associated proteins to RANKL levels. Based on ELISA, two pro-osteoclastogenic factors IGFBP2 and ICAM-1 were increased 2-fold in OCP culture supernatants in response to TNF with only ADA:TNF complexes reducing these levels of both to RANKL. TNF-induced reduction of intracellular levels of CD163, an M2 macrophage polarization marker, and TGFBI were not only restored to RANKL levels by ADA:TNF but brought to a level closer to M-CSF alone, unlike ETN:TNF. One anti-osteoclastogenic factor FABP4 was found to be increased intracellularly above that of RANKL only following exposure to ADA:TNF complexes.
Conclusion: Shotgun proteomic profiling of human OCP differentiated *in vitro* with TNF revealed at least 3 novel pathways by which TNF exerts its pro-osteoclastogenic effects. Only with the addition of ADA:TNF, not with ETN:TNF, were most pathway-associated proteins significantly restored to RANKL levels including pro-osteoclastogenic factors ICAM-1 and IGFBP2. Moreover, ADA:TNF complexes enhanced the intracellular levels of CD163 and the anti-osteoclastogenic factor FABP4, suggesting these complexes are exerting an effect on OCP beyond simple TNF neutralization. Additional *in vitro* and *in vivo* studies need to be performed to verify our findings.
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FRI0368 GLUCOCORTICOID THERAPY MIGHT SUPPRESS WNT SIGNALING BY REDUCING THE RATIO OF SERUM WNT3A TO WNT INHIBITORS, SFRP-1 AND WIF-1, AND IMPAIR BONE FORMATION

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Background: Glucocorticoids decrease bone density by multiple mechanisms, including suppression of bone formation *via* Wnt/β-catenin signaling. Binding of Wnt ligands to a specific receptor and its co-receptors is required for activation of the Wnt pathway, whereas this pathway is inactivated by some negative regulators of Wnt signaling. Sclerostin (Scl) and Dickkopf-1 (Dkk-1) bind to Wnt co-receptors, and secreted Frizzled-related protein 1 (sFRP-1) and Wnt inhibitory factor 1 (Wif-1) bind to Wnt ligand, thereby inactivating the Wnt pathway [1-4]. However, the detailed changes of Wnt signaling in patients with glucocorticoid-induced osteoporosis have not been clarified.
Objectives: We measured serum levels of Scl, Dkk-1 and Wnt3a before and after starting glucocorticoid therapy in our previous study, and the results suggested that suppression of Wnt/β-catenin signaling by increasing serum Scl and Dkk-1 might impaired bone formation at least in the first week of the initiation of glucocorticoid therapy [5]. However, the involvement of Wnt signaling in subsequent suppression of bone formation was unclear. The objective of this study was to investigate the involvement of the Wnt/β-catenin signaling pathway and its clinical significance after the early phase of glucocorticoid therapy in glucocorticoid-induced osteoporosis.
Methods: A total of 53 patients with systemic autoimmune diseases who received initial glucocorticoid therapy with prednisolone (30-60 mg daily) were prospectively enrolled. We measured serum levels of sFRP-1, Wif-1 and Wnt3a before starting glucocorticoid therapy and every week for four weeks after its initiation. Patients underwent measurement of bone mineral density (BMD) of the lumbar spine (L2-4) by dual-energy X-ray absorptiometry before starting therapy and after 16.3 ± 1.4 months (the mean ± SEM).
Results: Serum sFRP-1 and Wif-1 level tended to decrease compared to before therapy from the first week. Serum level of Wnt3a also decreased from the first week. Both the ratio of Wnt3a to sFRP-1 and the ratio of Wnt3a to Wif-1 decreased from the first week onward. Moreover, we stratified the subjects into two groups according to the baseline serum sFRP-1 level at median and found that the decrease of BMD after initiation of glucocorticoid therapy in the High sFRP-1 group was larger than that in the Low sFRP-1 group. There was no difference in BMD changes between High Wif-1 and Low Wif-1 group, when stratified into two groups according to the median baseline serum Wif-1 level.
Conclusion: Our previous study indicated that increase of Scl and Dkk-1 could inhibit Wnt signaling pathway in the early phase of glucocorticoid therapy. Current study suggested that the reduction in the ratio of Wnt3a to Wnt inhibitors, sFRP-1 and Wif-1, would suppress Wnt signaling, which might result in impairment of bone formation subsequent. Taken together, bone formation was impaired via suppressing Wnt signaling in patients treated with glucocorticoid. Furthermore, higher serum sFRP-1 level before glucocorticoid administration might be a predictor of future severity of glucocorticoid-induced osteoporosis.
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Co., Pfizer Japan Inc., Daiichi Sankyo Co., Ltd., Shionogi & Co., Ltd., Sanofi K.K., Nippon Kayaku Co., Ltd., Yutoku Pharmaceutical Ind. Co., Ltd., UCB Japan Co. Ltd., Nihon Pharmaceutical Co., Ltd., and Bayer Yakuhin, Ltd., Consultant of: UCB Japan Co., Ltd., Eisai Co., Ltd., and Chugai Pharmaceutical Co., Speakers bureau: Mitsubishi-Tanabe Pharma Co., Chugai Pharmaceutical Co., Eisai Co., Ltd., Astellas Pharma Inc., Janssen Pharmaceutical K.K., Ayumi Pharmaceutical Co., Pfizer Japan Inc., Asahikasei Pharma Corp., Sanofi K.K., Novartis Pharma K.K., Eli Lilly Japan K.K., Nippon Kayaku Co., Ltd., Teijin Pharma Ltd., Takeda Pharmaceutical Co., Nippon Boehringer Ingelheim Co., Ltd., and AbbVie GK.
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FRI0369 MIMICKING GLUCOCORTICOID-INDUCED OSTEOPOROSIS USING AN IN VITRO TRABECULAR HUMAN BONE MODEL

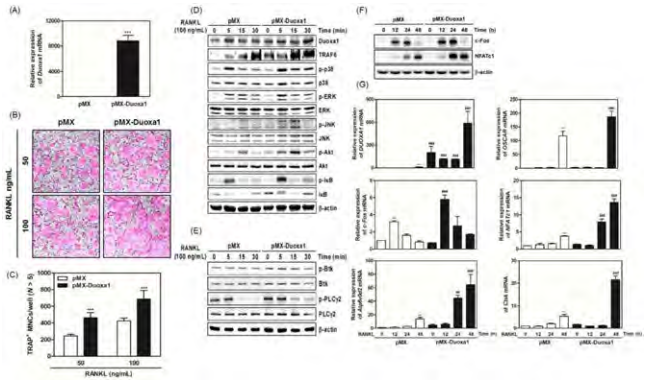
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Background: The bone matrix consists of inorganic and organic components and a variety of specialized cells such as osteoblasts, osteocytes and osteoclasts. The bone-forming osteoblasts are responsible for the production of organic matrix components; they differentiate later into osteocytes which is accompanied by matrix mineralization. Osteoclasts are multinuclear giant cells, which resorb bone. Healthy bone homeostasis is characterized by a balanced, dynamic and continuous remodeling process. Glucocorticoids (GCs) are commonly used to successfully treat patients with inflammatory rheumatic and other autoimmune diseases. However, long-term treatment with GC can potentially lead to several adverse effects such as the inhibition of osteoblast proliferation and the increase of osteoclastic activity resulting in osteoporosis.
Objectives: Hence, the aim of our project is to i) develop an *in vitro* trabecular human bone model, ii) integrate this bone model into a perfusion system to accelerate mineralization and provide biomechanical stimuli and iii) applying prednisolone to induce osteoporosis. Here we present our initial results describing the successful differentiation of osteoblasts and osteoclasts in a 3D environment, and the accomplished integration of the bone model into a perfusion system.
Methods: In a first step, different cultivation conditions were tested to allow optimal osteogenic or osteoclastic differentiation. To this end, a) human bone marrow derived mesenchymal stromal cells (hMSCs) were treated with osteogenic medium, and b) monocytes (isolated from buffy coats) were differentiated into osteoclasts using following protocol: incubation for 3 days with 25 ng/ml M-CSF followed by an 18-day incubation with M-CSF and 50 ng/ml RANKL. Calcification of hMSCs was evaluated via Alizarin Red S staining. Osteoclasts were identified using immunofluorescence staining observing multinucleated (DAPI) giant (ß-Actin) cells with TRAP and Cathepsin K activity. Additional gene expression analyses are currently conducted using qRT-PCR and looking for osteoclast-specific genes. In parallel to the monolayer cultures, cells were transferred on β-tricalcium phosphate (βTCP) – a suitable bony-like scaffold. Furthermore, first experiments in a dynamic bioreactor platform (OSPIN GmH) were conducted to evaluate the influence of shear stress on the cells and model systems.
Results: We have been able to populate the βTCP scaffold with monocytes, which were differentiated into osteoclasts (morphological changes) without any effect on cellular viability as measured by Live/Dead staining. The morphological changes of those osteoclasts such as formation of filopodia could be demonstrated by scanning electron microscopy. In addition, the cultivation of βTCP populated with hMSCs in a perfusion system showed the upregulation of osteogenic markers (RUNX2, OSX) on mRNA-level.
Conclusion: These first results of our approach to develop an *in vitro* 3D model for glucocorticoid-induced osteoporosis are promising. Our next step will be the co-cultivation of osteoblasts and osteoclasts under dynamic and optimized cultivation conditions. By combining several cell types, a suitable scaffold and biomechanical stimuli (perfusion), we aim to provide a valid testing platform to study underlying disease mechanisms and for drug development.
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FRI0370 DUAL OXIDASE MATURATION FACTOR 1 POSITIVELY REGULATES RANKL-INDUCED OSTEOCLASTOGENESIS VIA ACTIVATING REACTIVE OXYGEN SPECIES PRODUCTION AND TRAF6-MEDIATED SIGNALING

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Background: Reactive oxygen species (ROS) are one of the significant factors of chemical or physical cell signaling in a wide variety of cell types including skeletal cells. Receptor activator of NF-βB ligand (RANKL) induces generation of intracellular ROS, which act as second messengers in RANKL-mediated osteoclastogenesis. Dual oxidase maturation factor 1 (Duoxa1) was first identified as a *Drosophila* Numb-interacting protein (NIP), and has been associated with the maturation of ROS generating enzymes including dual oxidases (Duox1 and Duox2). In the progression of osteoclast differentiation using mouse bone marrow-derived macrophages (BMMs), we identified that only Duoxa1 level showed an effective change upon RANKL stimulation, but not Duox1, Duox2, and Duoxa2.
Objectives: we hypothesized that Duoxa1 could independently act as a second messenger for RANKL stimulation and regulate ROS production during osteoclast differentiation.
Methods: Using siRNA or retrovirus transduction and knockdown of Duoxa1 via siRNA



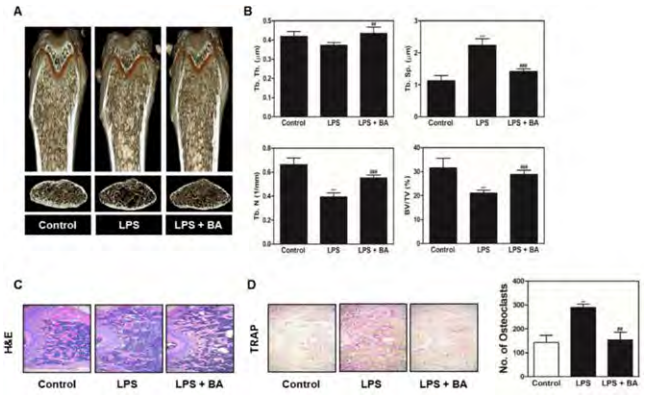
Results: Duoxa1 level gradually increased during RANKL-induced osteoclast differentiation. We found that Duoxa1 regulated RANKL-stimulated osteoclast formation and bone resorption positively. knockdown of Duoxa1 via siRNA decreased the RANKL-induced ROS production. During Duoxa1-related control of osteoclastogenesis, activation of tumor necrosis factor receptor (TNFR)-associated factor 6 (TRAF6)-mediated early signaling molecules including MAPKs, Akt, IβB, Btk, and PLC 2 was affected, which sequentially modified the mRNA or protein expression levels of key transcription factors in osteoclastogenesis, such as c-Fos and NFATc1, as well as mRNA expression of osteoclast-specific markers including OSCAR, ATP6v0d2, and CtsK.
Conclusion: Overall, our data indicate that Duoxa1 plays a crucial role in osteoclastogenesis via regulating RANKL-induced intracellular ROS production and activating TRAF6-mediated signaling.
Disclosure of Interests: None declared
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FRI0371 BETULINIC ACID INHIBITS RANKL-INDUCED OSTEOCLASTOGENESIS VIA ATTENUATING AKT, NF-KB, AND PLCG2-CA2+ SIGNALING AND PREVENTS INFLAMMATORY BONE LOSS

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Background: Betulinic acid (BA), a natural plant-derived pentacyclic triterpenoid compound, is known to possess numerous pharmacological and biochemical properties including anti-inflammatory, anti-cancer, and anti-adipogenic activity.

Objectives: we investigated that BA could suppress RANKL-induced osteoclastogenesis and bone resorption.
Results: BA significantly suppressed osteoclastogenesis by decreasing the phosphorylation of Akt and IkB, as well as PLCγ2-Ca^{2+} signaling, in pathways involved in early osteoclastogenesis as well as through the subsequent suppression of c-Fos and NFATc1. The inhibition of these pathways by BA was once more confirmed by retrovirus infection of constitutively active (CA)-Akt and CA-Ikkβ retrovirus and measurement of Ca^{2+} influx. BA also significantly inhibited the expression of osteoclastogenesis-specific marker genes. Moreover, we found that BA administration restored the bone loss induced through acute lipopolysaccharide injection in mice by a micro-CT and histological analysis.



Conclusion: Our findings suggest that BA is a potential therapeutic candidate for bone diseases involving osteoclasts.
Disclosure of Interests: None declared
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FRI0372 **INCREASED EXPRESSION OF NOTCH RECEPTORS ON OSTEOCLAST PROGENITORS INDUCED BY RHEUMATOID ARTHRITIS**

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Background: Systemic and periarticular bone loss in rheumatoid arthritis (RA) is mediated by osteoclasts, multinucleated cells originating from the myeloid lineage. Recently, Notch signaling pathway has emerged as a potential regulator of osteoclast progenitor (OCP) differentiation and activation.
Objectives: The exact role of Notch signaling in the context of arthritis is still unknown; however, its inhibition has beneficial effects in animal arthritis models. We aimed to determine the expression of Notch receptors and ligands on specific OCP subpopulations and define changes that occur in murine collagen-induced arthritis (CIA) and RA patients.
Methods: Peripheral blood, synovial tissue and subchondral bone marrow were collected from RA patients, and periarticular bone marrow (PBM) and spleen (SPL) were harvested from male C57/Bl6 mice immunized with chicken type II collagen. Notch 1 to 4 receptor expression on OCPs was analyzed by flow cytometry. Gene expression of Notch receptors/ligands was determined by qPCR from tissues and sorted OCPs. Sorted OCPs were cultured, with addition of MCSF and RANKL, in control, IgG, Jagged (Jag) 1 or Delta (DLL) 1 coated wells. Immunohistochemistry (IHC) for Notch 1 and 2 was performed on sections of murine hind paws. Research was approved by Ethics committee.
Results: We previously identified peripheral and periarticular subpopulations of murine and human OCPs, as $CD45^+CD3^-B220^-NK1.1^-CD11b^{lo/+}CD115^+CCR2^+$ and $CD45^+CD3^-CD19^-CD56^-CD11b^+CD14^+CCR2^+$ respectively, specifically associated with arthritis. Flow cytometry revealed that majority of murine splenic and periarticular OCPs express Notch 2, whereas Notch 1 and 4 were expressed on approximately 10% of cells. In CIA, this highly osteoclastogenic population is expanded as is the expression of Notch 4 in PBM and Notch 3 in SPL. Majority of human peripheral-blood OCPs express Notch 2 and 4, with a specific increase in the expression of Notch 1 and 3 in RA. In contrast, RA synovial-derived OCPs mostly express Notch 1 to 3, whereas subchondral OCPs mostly express Notch 1 and 4. Notch ligands were analyzed at mRNA level and revealed expression of Jag1, Jag2 and DLL4 in murine sorted OCPs and Jag1 and DLL1 in human sorted OCPs. Expression of Notch 1 and 2 was confirmed by IHC on arthritic murine hind paws, with Notch 2 expressed by bone marrow, synovial tissue and chondrocytes and Notch 1 expressed by chondrocytes and synovial tissue. Increased expression of Notch 1, Notch 2 and Jag1 was also confirmed in murine arthritic periarticular tissue by qPCR. During osteoclastogenic culture, murine and human OCPs exhibit a similar gene expression pattern with higher initial expression of Notch 1 and 2, and increase in the expression of Notch 3 and 4 with differentiation. Osteoclasts were also differentiated under Notch-ligand stimulation. Coating with DLL1 results in a greater number of cells expressing osteoclast-specific TRAP, whereas Jag1 seemed to inhibit osteoclastogenesis.
Conclusion: Our results indicate that murine and human OCPs express a distinct tissue-specific pattern of Notch receptors. Notch signaling in OCPs is increased in arthritis and may contribute to the osteoclastogenic potential and increased bone resorption. Our next aim would be to determine the effect of Notch inhibition on OCP activity and arthritis severity.
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FRI0373 **ASSOCIATIONS OF VASCULAR PATHOPHYSIOLOGY AND BONE METABOLISM IN ANTI-TNF- TREATED RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDYLITIS PATIENTS**

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Background: Cardiovascular (CV) disease and osteoporosis (OP) have become increasing challenges in the ageing population, even more in patients with inflammatory rheumatic diseases, such as rheumatoid arthritis (RA) and spondyloarthropathies. Both RA and ankylosing spondylitis (AS) have been associated with generalized and localized bone loss, accelerated atherosclerosis, increased CV morbidity and mortality.
Objectives: Bone and vascular biomarkers and parameters along with the effect of one-year anti-TNF therapy on these markers were assessed in order to determine correlations between vascular pathophysiology and bone metabolism in RA and AS.
Methods: Fifty-three patients including 36 RA patients treated with etanercept (ETN) or certolizumab pegol (CZP) and 17 AS patients treated with ETN were included in a 12-month follow-up study. Bone and vascular markers were assessed by ELISA. Bone density was assessed by DXA and quantitative CT (QCT). Flow-mediated vasodilation (FMD), common carotid intima-media thickness (ccIMT) and pulse-wave velocity (PWV) were assessed by ultrasound. The effects of vascular markers on bone and bone effects on vasculature undergone statistical analysis.
Results: Serum levels of vascular endothelial growth factor (VEGF), PDGF-BB, angiopoietin 2 (Ang2) and cathepsin K (CathK) decreased, procollagen type 1 N-propeptide (P1NP) and sclerostin (SOST) levels increased, soluble receptor activator nuclear kappa B ligand (sRANKL) and osteoprotegerin (OPG) levels showed no differences. When bone and vascular markers were correlated with each other, at baseline, OPG correlated with Ang2 and adiponectin. SOST correlated positively with ccIMT. DXA L2-4 BMD, DXA L1 BMD and DXA femoral neck (FN) BMD correlated with FMD and CRP. QCT trabecular BMD correlated with ccIMT and PON1. According to the univariate analysis, FMD correlated with OPG, ccIMT correlated with SOST and QCT trabecular BMD. Ang1, Ang2 and PDGF-BB showed correlation with Dickkopf-1 (DKK1). Ang2 also correlated with OPG. As suggested by the multivariate analysis, OPG determined FMD; DKK1 was an independent predictor of Ang1, Ang2 and PDGF-BB. OPG was a predictor of Ang2.
Conclusion: In our study of anti-TNF treated RA and AS patients, vascular and bone parameters showed numerous correlations. The therapy was clinically effective, it halted further bone loss over 1 year and reduced the production of angiogenic markers.
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FRI0374 PLASMA LEVELS OF 14-3-3 PROTEIN, S100A8/S100A9-PROTEIN, INTERLEUKIN-6, INTERLEUKIN-18, INTERLEUKIN-4, INTERLEUKIN-17, INTERLEUKIN-1B AND TUMOR NECROSIS FACTOR-A IN CHRONIC NON-BACTERIAL OSTEOMYEILITIS AND NON-SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

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Background: Chronic non-bacterial osteomyelitis (CNO) is an immune-mediated disease associated with cytokine dysbalance.
Objectives: The aim of our study was to evaluate the cytokines levels in CNO and compare to juvenile idiopathic arthritis (JIA) – disease with immune-mediated mechanism.
Methods: The diagnosis of CNO made with criteria, proposed by Jansson (2007, 2009), after the exclusion of other causes of bone disease [1]. We included 42 patients with NBO, 28 patients with non-systemic juvenile idiopathic arthritis (JIA). We evaluated plasma levels of 14-3-3 protein, S100A8/S100A9-protein, interleukine-6 (IL-6), interleukine-18 (IL-18), interleukine-4 (IL-4), interleukine-17 (IL-17), interleukine-1β (IL-1 β) and tumor necrosis factor-α (TNFα) in 2 groups by the ELISA. Statistical analysis was carried out with Statistica 10.0 software. We utilized descriptive statistics (Me; IQR), Mann-Whitney tests.
Results: We have found differences in the proinflammatory biomarkers between CNO, JIA. Patients with NBO had lower levels of studied cytokines, exclude14-3-3-protein, S100A8/S100A9 and interleukin-6 compare to JIA patients (table 1).

Table 1. Comparison the cytokine levels between CNO, JIA N

Parameter	NBO (n=42)	JIA (n=28)	p
Hemoglobin, g/l	112 (104; 124)	120 (114.5; 126.0)	0.02
WBC x 10^9/l	7.9 (7.0; 10.5)	8.0 (6.7; 10.0)	0.86
PLT x 10^9/l	347 (259; 408)	336.5 (274.0; 390.5)	0.98
ESR. mm/h	25.0 (9.0; 46.0)	8.5 (2.5; 13.0)	0.013
CRP, mg/l	6.1 (0.6; 2.4)	1.8 (0.4; 11.9)	0.027
14-3-3, ng/ml	21.4 (18.5; 27.1)	19.9 (18.0; 27.8)	0.77
S100A8/S100A9, ng/ml	5.9 (5.2; 6.5)	5.9 (5.0; 6.2)	0.76
IL-6, ng/ml	126,2 (112.8; 137.5)	132.4 (117.4; 142.9)	0.16
IL-18, ng/ml	270.1 (200.1; 316.1)	388.3 (373.9; 405.1)	0.0000001
IL-4, ng/ml	15.3 (11.5; 18.2)	18.7 (16.2; 20.2)	0.003
IL-17, ng/ml	83.1 (71.1; 97.3)	99.2 (87.3; 115.8)	0.003
IL-1b, ng/ml	47.4 (42.0; 51.3)	70.8 (65.3; 73.6)	0.0000001
TNFa, ng/ml	19.4 (17.8; 21.3)	23.1 (20.2; 25.9)	0.0006

Conclusion: Patients with CNO had less proinflammatory activity then JIA patients, besides IL-6 and S100A8/S100A9. Further investigations required for finding new more precise biomarkers and finding possible molecular targets for treatment.
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References:
[1] Jansson AF, et al. Clinical score for nonbacterial osteitis in children and adults. Arthritis Rheum. 2009;60(4):1152-9.
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FRI0375 VISFATIN EFFECTS ON MSCS DURING OD VIA DIFFERENTIAL REGULATION OF LNCRNA H19 AND MICRO RNA 675-3P

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Background: Long non-coding (lnc-)RNA are regulatory molecules transcribed from DNA similar to mRNA and interact directly with DNA, RNA and proteins. Some lncRNAs have been shown to contain micro (mi-)RNAs in their sequence that can be released by splicing and lead to active miRNA molecules, e.g. lncRNA H19 includes two miRNAs 675-3p and -5p in its sequence.
Adipose tissue derived factors (adipokines) are involved in inflammation processes and osteoarthritis (OA) development. The proinflammatory adipokine visfatin has been shown to alter osteogenic differentiation (OD) of pluripotent mesenchymal stem cells (MSCs) and reduces elastic fiber expression, increases matrix mineralization and proinflammatory cytokine and chemokine production [(1)].
Objectives: We evaluated a novel effect of visfatin on lncRNA H19 in MSCs during OD. The goal was to explore the kinetics of the visfatin effect during OD with regard to H19 regulation and to investigate H19 downstream mechanisms leading to the observed altered MSC differentiation and osteoblast activity.
Methods: MSCs isolated from OA hip or knee bone (phMSC) and commercially obtained healthy human (h-)MSCs were differentiated towards osteoblasts with/without visfatin, resistin, leptin, TNF and Wnt/TGFβ1 pathway inhibitors. Supernatants were collected at days 2, 7, 9, 14 and 21 of OD, cell lysates at day 2, 7, 9, 14 and matrix mineralization assays conducted at day 21. H19 and miRNA expression was evaluated by real-time PCR after mi-/RNA isolation. IL-6 was analyzed by ELISA.
Results: H19 was continuously upregulated in unstimulated controls as expected during OD but also when stimulated with other adipokines. In contrast, stimulation with visfatin significantly decreased H19 (day 2 to 14 of OD, hip-phMSCs: p = 0.0097, knee-phMSCs: p=0.0075, h-MSC: p = 0.044). Visfatin increased matrix mineralization and IL-6 production as expected (hMSC: p = 0.03, phMSC: p = 0.013) [(1)]. TNF stimulation during OD did not lead to a downregulation of H19 nor increased matrix mineralization, thus showing that the effects were visfatin-dependent. H19s endogenous miRNA 675-5p was changed in parallel with H19, increased during control OD and significantly down-regulated by visfatin (e.g. day 14 p = 0.015). However, H19s endogenous miRNA 675-3p was inversely regulated, downregulated during control OD while visfatin stimulation attenuated this effect (e.g. day 14 p = 0.025). Altered Wnt-signaling and involvement of the TGFβ1 pathway could not be observed.
Conclusion: H19 is upregulated during OD and may therefore play a regulatory role in the process of osteogenesis. Visfatin stimulation of MSCs during OD showed pro-inflammatory effects, increased matrix mineralization while reducing elastic fiber production [(1)]. These effects were associated with a downregulation of H19, a specific visfatin effect not triggered by other adipokines or TNF. The H19 sequence includes two endogenous micro-RNAs 675-3p and 5p. We demonstrated miRNA 675-5p to be regulated in parallel to H19, whereas miRNA 675-3p was inversely regulated and increased continuously upon visfatin stimulation. Based on these results, we hypothesize that visfatin provides a specific stimulus for the splicing of miRNA 675-3p from H19, in turn leading to H19 reduction. miRNA 675-3p thus represents an effector mechanism of visfatin that contributes to the observed functional effects in differentiating MSCs.
References:
[1] Tsiklauri, L. *et al.* Visfatin alters the cytokine and matrix-degrading enzyme profile during osteogenic and adipogenic MSC differentiation. *Osteoarthr. Cartil.* **26**, 1225–1235 (2018).
Disclosure of Interests: Dennis Küppers: None declared, Lali Tsiklauri: None declared, Marie Hülser: None declared, Klaus Frommer: None declared, Stefan Rehart: None declared, Caroline Ospelt Consultant of: Consultancy fees from Gilead Sciences., Ulf Müller-Ladner Speakers bureau: Biogen, Elena Neumann: None declared
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FRI0376 EFFECT OF CARBAMYLATED LOW-DENSITY LIPOPROTEINS ON BONE CELLS HOMEOSTASIS

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Background: Carbamylation is a post-translational modification occurring under several conditions such as uremia, smoking and chronic inflammation as in rheumatoid arthritis (RA). Low-density lipoproteins (LDL) represent a target of carbamylation. Carbamylated-LDL (cLDL) have an increased inflammatory and atherogenic potential. Growing evidence supports an influence of modified lipids on bone cells homeostasis. However, the role of cLDL on bone cells physiology is still unknown.
Objectives: Considering the rate of carbamylation and the role of anti-carbamylated proteins antibodies as markers of erosive disease in RA, the purpose of this study is to investigate the effect of cLDL on bone homeostasis.
Methods: *In-vitro* carbamylation of LDL was performed as previously described by Ok et al. (Kidney Int. 2005). Briefly, native LDL (nLDL) were treated with potassium cyanate (KOCN) for 4 hours, followed by excessive dialysis for 36 hours to remove KOCN. Both osteoclasts (OCs) and osteoblasts (OBLs) were treated at baseline with 20 µg/ml, 100 µg/ml and 200 µg/ml of cLDL or nLDL. To induce osteoclast differentiation, CD14+ monocytes were isolated from peripheral blood of healthy donors by magnetic microbeads separation and then cultured on a 96-wells plate in DMEM media supplemented with RANKL and M-CSF. After 10 days cells were fixed, stained for tartrate-resistant acid phosphatase (TRAP), a marker of OC differentiation, and counted. OBLs were isolated from bone specimens of 3 patients who had undergone to knee or hip arthroplasty for osteoarthritis and treated for 5 days with different concentrations of cLDL and nLDL. OBLs were fixed and stained for alkaline phosphatase positive activity (ALP), a marker of osteogenic differentiation. Total RNA was extracted from cell lysates. Copies of single-stranded complementary DNA (cDNA) were synthesized and analyzed by real-time PCR to evaluate RANKL and Osteoprotegerin (OPG) mRNA expression levels.
Results: In OCLs culture, cLDL significantly decreased the number of OC compared to untreated cells (200 µg/ml p=0,0015) and nLDL treated cells (200 µg/ml p= 0,011; 20 µg/ml p= 0,0014) (Fig 1). Moreover, treatment with cLDL induced an increase of not terminally differentiated OCs, reduced dimensions of OCs, less intense TRAP staining and vacuolization (Fig 2). In OBLs culture, cLDL (20, 100 µg/ml) significantly reduced the ALP activity of OBLs compared with untreated cells (p<0.05) (Fig 3). nLDL did not affect the ALP expression. Treatment with cLDL stimulated RANKL mRNA expression in osteoblasts increasing the RANKL/OPG ratio (Fig 4).

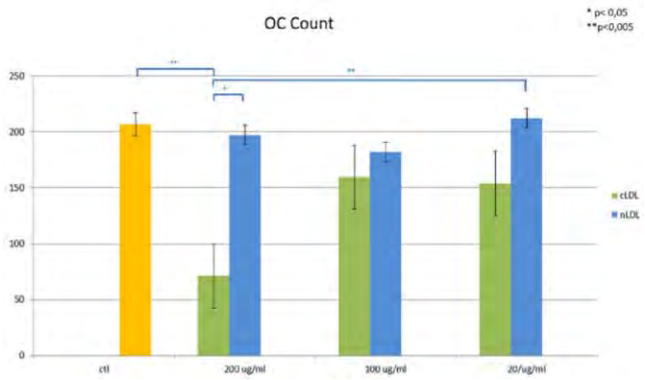


Fig 1.

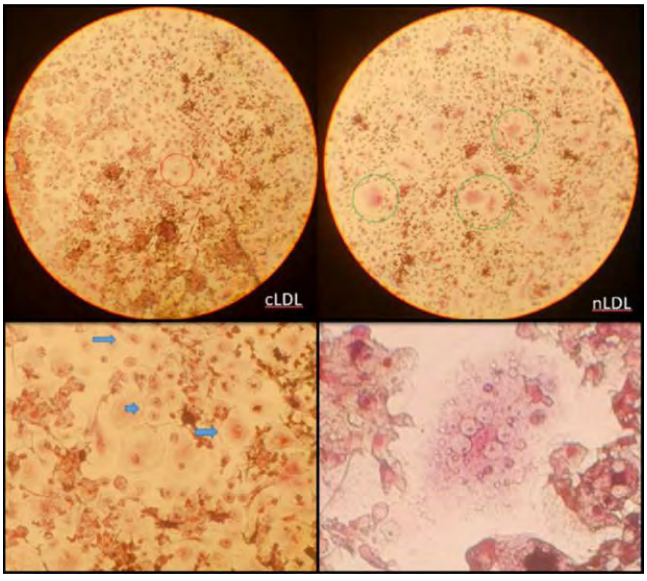


Fig 2.

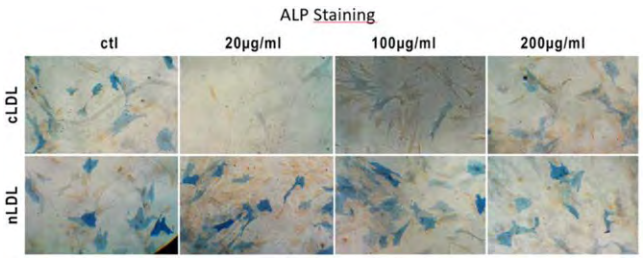


Fig 3.

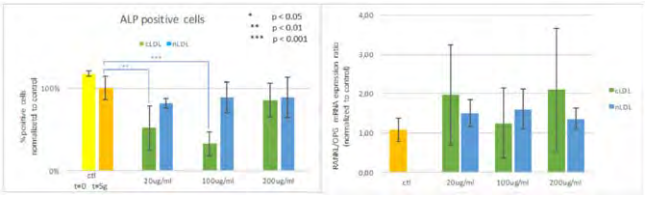


Fig 4.

Conclusion: cLDL induce a significant depression of OC and OBL differentiation. Moreover, cLDL increase RANKL expression in OBL, unbalancing bone tissue turnover towards bone resorption. Accordingly, cLDL could be implicated in the bone loss characterizing several conditions associated to an increased carbamylation, such as RA
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FRI0377 **BARIATRIC SURGERY: EFFECTS ON BONE METABOLISM**

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Background: There are few data about variations in bone metabolism associated with weight loss in obese patients undergoing bariatric surgery.
Objectives: To assess the influence on the bone metabolism of bariatric surgery in morbidly obese patients.
Methods: Longitudinal pre-post study with analytical components. All morbidly obese patients undergoing bariatric surgery were, prior to this, referred to Rheumatology Department. In all cases, the baseline characteristics of the patients were collected and a complete bone metabolic analytical study and bone densitometry (BMD) were requested. This same study was repeated one year later, with a window period of ± 3 months. Statistical analysis was performed with the SPSS 20.0 software.
Results: Of the 91 patients included in the study and who underwent baseline BMD and analytical tests prior to surgery, only follow-up data of 27 patients could be collected at the time of the present data analysis. Within this sample, the median age was 54 years (AIQ 11), with 6 men and 21 women (11 premenopausal, 10 postmenopausal). Prior to surgery, median body mass index (BMI) was 39.2 (AIQ4.43) and median vitamin D (25OHD) level was 22 (AIQ 16). High values of PTH were detected in two patients. Regarding baseline BMD, 78% had normal values and 22% had values in the range of osteopenia.
After surgery, all patients presented a significant weight loss, being the median loss in BMI per year 9.8 Kg/m^2 (AIQ 3.8) as absolute value, and 25% (AIQ 8.12) as a percentage value. This weight loss was accompanied by a significant BMD worsening that was evident in all locations: lumbar spine (median -6.97%, AIQ 6.3), total hip (median -6.4%, AIQ 7.7) and femoral neck (median -3.57 %, AIQ 8); so that an additional 22% of patients changed to osteopenia values. All this despite a significant increase in 25OHD levels in all cases (35.7%; AIQ 52.3). No clinical or morphometric fractures were collected. Despite the parallel

evolutionary course, the loss of BMI only showed a tendency to correlate with the decrease in bone mass in the femoral neck (p-value 0.089), but not in the other locations.

Conclusion: In our sample of morbidly obese patients undergoing bariatric surgery, there is a significant and widespread loss of bone mineral density one year after the procedure, all this despite the supplementation and the increase in 25OHD levels. This loss only seems to be directly related to the decrease in weight at the femoral neck, just probably by a mechanism to reduce mechanical load.

Disclosure of Interests: I Vázquez-Gómez: None declared, Ramón Trullenque Juan: None declared, Carlos Morillas Ariño: None declared, L Montolio-Chiva: None declared, Ana V Orenes Vera: None declared, Eduardo Flores: None declared, Elia Valls-Pascual Grant/research support from: Roche, Novartis, and AbbVie, Speakers bureau: AbbVie, Lilly, Pfizer, MSD, Novartis, Janssen, Bristol Myers Squibb, UCB Pharma, Desamparados Ybañez: None declared, À Martínez-Ferrer: None declared, Inmaculada Torner Hernández: None declared, V Núñez-Monje: None declared, A Sendra-García: None declared, Juanjo J Alegre-Sancho Consultant of: UCB, Roche, Sanofi, Boehringer, Celltrion, Paid instructor for: GSK, Speakers bureau: MSD, GSK, Lilly, Sanofi, Roche, UCB, Actelion, Pfizer, Abbvie, Novartis

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FRIDAY, 05 JUNE 2020

Osteoarthritis

FRI0378 GENERAL SAFETY AND TOLERABILITY OF SUBCUTANEOUS TANEZUMAB FOR THE TREATMENT OF OSTEOARTHRITIS: A POOLED ANALYSIS OF RANDOMIZED, PLACEBO-CONTROLLED TRIALS

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Background: Tanezumab, a monoclonal antibody against nerve growth factor, is in development for the treatment of signs and symptoms of osteoarthritis (OA).

Objectives: To assess the safety and tolerability of subcutaneous (SC) tanezumab in patients with OA.

Methods: Data were derived from 3 randomized placebo-controlled OA trials. SC treatment (every 8 weeks for 16–24 weeks with 8–24 week follow-up) included placebo, tanezumab 2.5 mg, tanezumab 2.5/5 mg (2.5 mg at day 1 and 5 mg at week 8), and tanezumab 5 mg. Overall treatment-emergent adverse events (TEAEs) and TEAEs of abnormal peripheral sensation were pooled from all 3 trials (placebo N = 586; tanezumab: 2.5 mg N = 602, 2.5/5 mg N = 219, 5 mg N = 347). Pre-specified TEAEs potentially associated with sympathetic neuropathy (anhidrosis, bradycardia, hypohidrosis, orthostatic hypotension, or syncope) and pre-specified joint events (primary osteonecrosis, rapidly progressive OA [RPOA] type 1 or type 2, subchondral insufficiency fracture, or pathological fracture; adjudicated by an independent committee of experts) were pooled from the 2 trials that included prospective evaluation of sympathetic and joint safety (placebo N = 514; tanezumab: 2.5 mg N = 528, 2.5/5 mg N = 219, 5 mg N = 284). TEAEs are presented for the treatment period; joint safety is presented for the full study (treatment plus follow up) period.

Results: Patient demographics (80.7% white, 66.8% female, mean age ≈ 63 years) and clinical characteristics were similar across groups. TEAE rates were: placebo = 51.7%, tanezumab 2.5 mg = 52.3%, tanezumab 2.5/5 mg = 47.0%, and tanezumab 5 mg = 54.8%. Of TEAEs occurring in ≥2% of patients in any group, only oedema peripheral, joint stiffness, and paraesthesia had a higher incidence (95% confidence interval excluded 0) in any tanezumab group relative to placebo. Serious TEAE rates were: placebo = 1.5%, tanezumab 2.5 mg = 2.2%, tanezumab 2.5/5 mg = 1.4%, and tanezumab 5 mg = 2.6%. Rates of treatment and/or study discontinuation due to TEAEs were: placebo = 2.2%, tanezumab 2.5 mg = 1.8%, tanezumab 2.5/5 mg = 0.5%, and tanezumab 5 mg = 1.4%. Only arthralgia and OA led to discontinuation in >1 patient in any group. TEAEs of abnormal peripheral sensation rates were: placebo = 2.2%, tanezumab 2.5 mg = 5.1%, tanezumab 2.5/5 mg = 3.2%, and tanezumab 5 mg = 6.1%. Paraesthesia and hypoaesthesia were the most common events. Potential sympathetic neuropathy TEAE rates were: placebo = 0.8%, tanezumab 2.5 mg = 1.5%, tanezumab 2.5/5 mg = 0.5%, and tanezumab 5 mg = 2.8%; exposure-adjusted rates were not statistically different between any tanezumab group and placebo. Bradycardia and orthostatic hypotension were the most common events. No patient was considered to have a sympathetic neuropathy. TEAEs of abnormal peripheral sensation and potential sympathetic neuropathy were mostly mild and resolved. Joint safety event rates were statistically different for tanezumab 5mg (3.2%), but not 2.5mg (1.9%) or 2.5/5mg (0.5%), compared to placebo (0%). RPOA type-1 was the most common event. Total joint replacement rates were: placebo = 4.5%, tanezumab 2.5 mg = 5.9%, tanezumab 2.5/5 mg = 6.8%, and tanezumab 5 mg = 7.0%; rates were not statistically different between any tanezumab group and placebo.

Conclusion: Tanezumab was generally safe and well tolerated in most patients, with rates of overall TEAEs and treatment/study discontinuations similar to placebo and no evidence of a sympathetic safety signal. TEAEs of abnormal peripheral sensation and joint safety events were infrequent but more common with tanezumab than placebo.

Disclosure of Interests: Francis Berenbaum Grant/research support from: TRB Chemedica (through institution), MSD (through institution), Pfizer (through institution), Consultant of: Novartis, MSD, Pfizer, Lilly, UCB, Abbvie, Roche, Servier, Sanofi-Aventis, Flexion Therapeutics, Expanscience, GSK, Biogen, Nordic, Sandoz, Regeneron, Gilead, Bone Therapeutics, Regulaxis, Peptinov, 4P Pharma, Paid instructor for: Sandoz, Speakers bureau: Novartis, MSD, Pfizer, Lilly, UCB, Abbvie, Roche, Servier, Sanofi-Aventis, Flexion Therapeutics, Expanscience, GSK, Biogen, Nordic, Sandoz, Regeneron, Gilead, Sandoz, Thomas Schnitzer Consultant of: Pfizer, Lilly, AstraZeneca, GSK, Alan Kivitz Shareholder of: AbbVie, Amgen, Gilead, GSK, Pfizer Inc, Sanofi, Consultant of: AbbVie, Boehringer Ingelheim,,Flexion, Genzyme, Gilead, Janssen, Novartis, Pfizer Inc, Regeneron, Sanofi, SUN Pharma Advanced Research, UCB, Paid instructor for: Celgene, Genzyme, Horizon, Merck, Novartis, Pfizer, Regeneron, Sanofi, Speakers bureau: AbbVie, Celgene, Flexion, Genzyme, Horizon, Merck, Novartis, Pfizer Inc, Regeneron, Sanofi, Lars Viktrup Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Anne Hickman Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Glenn Pixton Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Mark Brown Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Isabelle Davignon Shareholder of: Pfizer, Employee of: Pfizer, Christine West Shareholder of: Pfizer Inc, Employee of: Pfizer Inc

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FRI0379 VARIATIONS IN THE UTILIZATION OF BILATERAL TOTAL KNEE ARTHROPLASTY IN THE MANAGEMENT OF OSTEOARTHRITIS

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Background: A third of knee osteoarthritis presents with bilateral symptomatic arthritis. In these patients, treatment options include either a staged Unilateral Total knee arthroplasty (UTKA) procedure, or a simultaneous Bilateral TKA (BTKA) procedure. Even though literature regarding outcomes in BTKA procedure has not consistently been favorable, it remains popular in select patients due to use of a single anesthetic, shorter overall surgical time, lower cost and lower overall use of narcotics. African Americans (AAs) have lower utilization and worse outcomes in UTKA literature. It is unclear whether these racial variations extend to BTKA.

Objectives: We sought to examine BTKA vs UTKA utilization rates and outcomes comparing AA and White patients.

Methods: National Inpatient Sample (NIS) - Healthcare Cost and Utilization Project (HCUP) database (2007-2016) was used. We identified all patients ≥ 50 years who underwent elective primary TKA using ICD-9-CM code 81.54 for UTKA and BTKA from January 1, 2012 to September 30, 2015, and ICD-10-CM codes 0SRC0x and 0SRD0x thereafter. Patients with inflammatory arthritis, pathologic fractures, metastatic disease and avascular necrosis were excluded. Major in-hospital complications included post-operative myocardial infarction, prosthetic device complication, surgical wound infection, and venous thromboembolism. Differences in temporal trends in utilization and major in-hospital complications of BTKA vs UTKA were compared between AAs and Whites. Multivariable logistic regression models were used to assess differences in both these trends between AAs and Whites after adjusting for individual (age, sex, Elixhauser comorbidity index, and morbid obesity), hospital level (hospital volume, bed size, region and teaching status) and community level (median household income) variables. Discharge weights were used to enable nationwide estimates. Multiple imputation was performed for missing race variable (11.9%).

Results: From 2007 to 2016, an estimated 276,194 BTKA (unweighted observations 56,675) and 5,528,429 UTKA (unweighted observations 1,131,329) were identified (Table 1). Females had a higher proportion of TKAs performed (62.1% UTKA vs 55.9% BTKA). Patients had fewer comorbidities (measured by the Elixhauser Index) when undergoing BTKA compared to UTKA. The proportion of BTKA amongst all TKAs declined from 5.53% in 2007-08 to 4.03% in 2015-16. AAs continued to have significantly lower proportion of BTKA utilization compared to Whites (4.68% in AAs vs 6.08% in Whites in 2007-08, whereas 3.28% in AAs vs 4.19% in Whites in 2015-16, adjusted $p < 0.001$) (Figure 1a). In-hospital complication rates for UTKA and BTKA were significantly higher in Whites compared to AAs throughout the study period (0.77% in AAs vs 0.9% in Whites in 2007-08, whereas 0.69% in AAs vs 0.83% in Whites in 2015-16,

adjusted p < 0.001) (Figure 1b). The results were similar after imputation of missing race values.

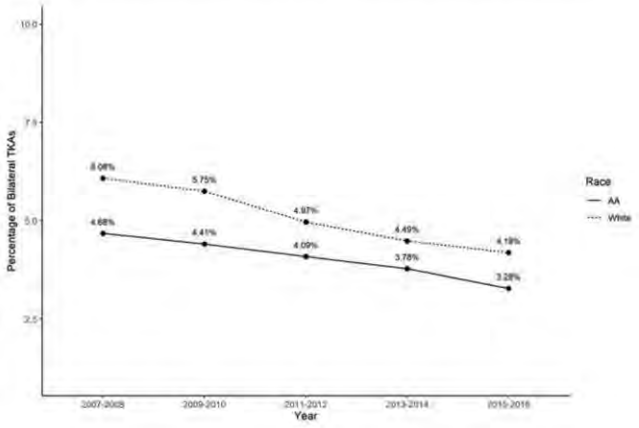
Conclusion: In this nationwide sample of patients from 2007 to 2016, we found that AAs have lower utilization rate of BKTA compared to Whites, however the in-hospital complication rates were significantly higher in Whites.

References: N/A

Table 1. Weighted frequencies and percentages of demographic characteristics among unilateral TKA vs. bilateral TKA (N = 6, 236, 426).

Variable	Unilateral TKA	Bilateral TKA	P[a]
	N = 5,528,429 (Unweighted N = 1,131,329)	N = 276,194 (Unweighted N = 56,675)	
Patient Characteristics			
Age, mean (SD)	67.4 (0.02)	65.0 (0.06)	<.0001
Sex: Female, n(%)	3,429,484 (62.1)	154,442 (55.9)	<.0001
Race, n(%):			
White	4,051,648 (50.9)	212,468 (76.9)	<.0001
African American	352,933 (6.4)	14,441 (5.2)	
Other	464,407 (8.4)	16,443 (6.0)	
Missing	659,439 (11.9)	32,842 (11.9)	
Morbid Obesity, n(%)	401,892 (7.3)	20,411 (7.4)	0.47
Elixhauser Index[d], n(%):			<.0001
0	716,559 (13.0)	41,550 (15.0)	
1-4	4,484,941 (81.1)	220,638 (80.0)	
≥ 5	326,928 (5.9)	14,007 (5.1)	

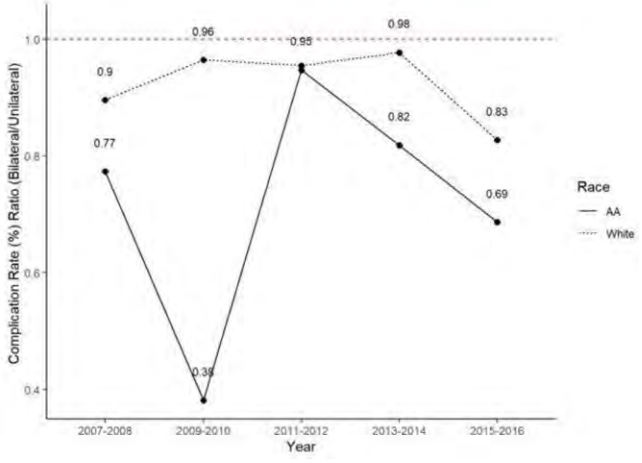
Figure 1a: Difference in trends in Utilization of BTKA vs UTKA between Whites and African Americans (AAs).



Note: Percentage of bilateral TKAs is defined as the number of bilateral TKAs among total TKAs in each period

Disclosure of Interests: Bella Mehta: None declared, Kaylee Ho: None declared, Jennifer Bido: None declared, Michael Parks Consultant of: Zimmer Biomet, Linda Russell: None declared, Susan Goodman Shareholder of: Reginosine- Investment, Grant/research support from: Novartis, Horizon, Consultant of: Novartis, Celgene, UCB, Said Ibrahim: None declared

Figure 1b: Trends in in-hospital complications of BTKA vs UTKA between Whites and African American (AAs).



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FRI0380

ITEMS DRIVING WOMAC PAIN SUBSCORE CHANGES DUE TO LORECIVIVINT, A POTENTIAL DISEASE-MODIFYING TREATMENT FOR KNEE OSTEOARTHRITIS: A POST HOC ANALYSIS OF PHASE 2B TRIAL DATA

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Background: Knee osteoarthritis (OA) is a disease characterized by pain, loss of function, and structural deformities, leading to a heterogeneous disease state that can confound patient-reported outcomes (PROs). The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain subscore addresses this reporting variability by capturing multiple pain items related to 'active' and 'static' subject states. We hypothesize that measurement of these 'active' versus 'static' pain items may demonstrate differential effect sizes when assessing treatment benefit. Lorecivivint (LOR; SM04690), a small-molecule, intra-articular CLK/DYRK1A inhibitor that modulates the Wnt pathway, is currently in development as a potential disease-modifying treatment for knee OA.[1,2]

Objectives: To test the hypothesis, a post hoc analysis of Pain NRS, the WOMAC Pain subscore, and individual WOMAC PROs (items A1–A5) from a Phase 2b LOR trial was performed to examine effect size (ES) changes.

Methods: The original 24-week Phase 2b trial has been previously reported. In this study, pain was assessed using the weekly average of daily Pain NRS and WOMAC Pain subscore. In the post hoc analysis, items A1–A5 (pain walking on a flat surface? [A1], going up/downstairs? [A2], at night in bed? [A3], sitting or lying down? [A4], and while standing? [A5]) were individually analyzed for subjects treated with 0.07 mg LOR and compared with the primary study outcomes of mean Pain NRS and summed mean WOMAC Pain subscore at Week 12. Baseline-adjusted analysis of covariance for WOMAC A1–A5 scores was conducted on LOR-treated subjects compared with placebo (PBO) in 1) the Full Analysis Set (FAS) of all dosed subjects and 2) a target population of subjects with fixed baseline joint space width (JSW) [2–4] mm without widespread pain (Widespread Pain Index [WPI] ≤4, Symptom Severity Score Question 2≤2).

Results: In this analysis, 231 subjects (KL grade 3 63.2%) were included. The primary study analysis demonstrated efficacy of LOR compared with PBO for Pain NRS and WOMAC Pain, with respective effect sizes of 0.450 and 0.293 (Figure). In the target population, Pain NRS and WOMAC A effect sizes increased (0.637 and 0.410, respectively). Each WOMAC A item showed less of an effect size than Pain NRS at Week 12. Treatment with 0.07 mg LOR compared with PBO showed significant improvements in effect sizes of WOMAC A1 (FAS: ES=0.315, *P*=0.028; target population: ES=0.421, *P*=0.035) and A2 (FAS: ES=0.392, *P*=0.006; target population: ES=0.510, *P*=0.011). A3–A5 did not show statistical improvement for LOR compared with PBO.

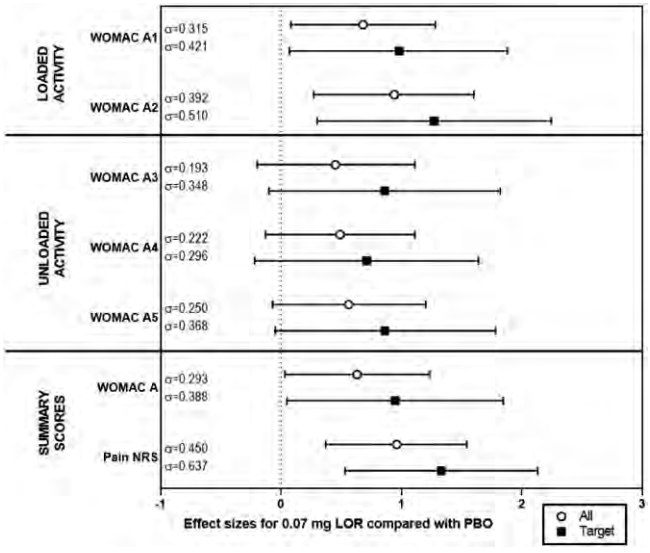


Figure. Effect sizes for 0.07 mg LOR compared with PBO for the FAS and target population at Week 12.

Conclusion: In the post hoc analysis, Pain NRS exhibited the greatest effect size of tested PROs after treatment with 0.07 mg LOR compared with PBO. These effect sizes were enhanced in the target population with fixed baseline JSW and without widespread pain for all scores relative to the FAS. WOMAC 'active' questions demonstrated greater effect sizes with LOR treatment than 'static' questions and the full WOMAC Pain domain, providing support for the hypothesized dimensional constructs in knee OA pain assessment.

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Disclosure of Interests: Sarah Kennedy Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Christopher Swearingen Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Ismail Simsek Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Jeyanesh Tambiah Shareholder of: Samumed, LLC, Employee of: Samumed, LLC
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FRI0381 ASSOCIATIONS BETWEEN MEASURES OF OVERWEIGHT/OBESITY AND JOINT PAIN IN PERSONS WITH HAND OSTEOARTHRITIS: RESULTS FROM THE NOR-HAND STUDY

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Background: Overweight and obesity are well-known risk factors for osteoarthritis (OA) in weight-bearing joints. However, the role of increased body mass index (BMI) and waist circumference in OA of the non-weight-bearing joints is more controversial. Few hand OA studies have explored the associations between increased BMI/waist circumference and pain.
Objectives: The aim of this study was to explore whether BMI and waist circumference were associated with self-reported pain in the hands, feet, knees and hips as well as pain sensitization in persons with hand OA. Further, we examined whether synovitis could partly explain the association between BMI/waist circumference and pain, due to a low-grade inflammatory state in overweight persons.
Methods: The Nor-Hand study is an observational study of 300 participants with hand OA. We measured their height and weight in addition to their waist circumference. Participants completed Numeric Rating Scales (NRS) (0-10) about pain during the last 24 hours in their hands and feet, in addition to the Western Ontario and McMaster Universities OA Index (WOMAC) knee/hip pain subscale (0-20). Pressure pain thresholds (PPTs) (kg/cm^2) were measured at both a painful and a non-painful interphalangeal joint of the hand, the left distal radioulnar joint and at the tibialis anterior and trapezius muscles. Temporal summation (TS) was measured with a weighted probe that was tapped 10 times at the left distal radioulnar joint. We considered TS to be present if the pain rating increased by ≥2 (i.e., >smallest detectable change) points on the NRS during the test. Ultrasound was used to score grey-scale synovitis on 0-3 scales in a total of 30 joints in the hands, 26 joints in the feet and the bilateral knees. We evaluated the relation of BMI and waist circumference to the pain scales and synovitis sum scores using linear regression, and to presence of pain sensitization assessed by PPT values and TS using linear and logistic regression, respectively. All analyses were adjusted for age, sex and education.
Results: The majority of participants were female (n=266, 89%), and the median (IQR) age was 61 (57-66) years. Persons with higher BMI and waist circumference reported higher pain intensity in their hands, feet, knees and hips (Table). Higher BMI and waist circumference were associated with lower PPTs at the tibialis anterior muscle (Table). No associations were found between BMI/waist circumference and PPTs at the other test sites (data not shown). Persons with higher BMI and waist circumference were more likely to have TS (Table). Increased BMI and waist circumference were not associated with more synovitis in the hands, feet or knees (data not shown).

Table. Data presented as B (95% CI) for the pain measures/PPT value and OR (95% CI) for presence of TS. All analyses were adjusted for age, sex and education.

	NRS hand pain (0-10)	NRS feet pain (0-10)	WOMAC knee/hip pain (0-20)	PPT tibialis anterior (kg/cm^2)	Presence of TS
BMI per SD increase*	0.5 (0.2, 0.7)	0.7 (0.4, 1.0)	1.3 (0.8, 1.8)	-0.4 (-0.7, -0.1)	1.4 (1.1, 1.8)
Waist circumference per SD increase**	0.5 (0.3, 0.8)	0.6 (0.3, 0.9)	1.3 (0.8, 1.8)	-0.4 (-0.7, -0.1)	1.4 (1.1, 1.8)

*Standard deviation (SD)=5.0 kg/m^2, **SD=12.9 cm

Conclusion: In the Nor-Hand cohort, persons with higher BMI and waist circumference reported higher pain intensity in their hands, feet, knees and hips. This relation was not explained by higher levels of synovitis in the joints. However, the association may at least partly be driven by a higher prevalence of central pain sensitization in persons with higher BMI. Due to the cross-sectional study design we cannot conclude about causality.
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FRI0382 EFFECTS OF GENICULAR NERVE BLOCK IN PATIENTS WITH KNEE OSTEOARTHRITIS WHO HAVE NEUROPATHIC OR NOCICEPTIVE PAIN

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Background: Genicular nerve block (GNB) is a safe and effective therapeutic procedure for intractable pain associated with chronic knee osteoarthritis (OA) (1). There is increasing support for the neuropathic component to the knee OA pain. Investigators proposed that targeting treatment to the underlying pain mechanism can improve pain management in knee OA (2). There is a debate on injectable solutions used in nerve blocks (3).
Objectives: To investigate the analgesic and functional effects of USG-guided GNB in patients with chronic knee OA (with/without neuropathic pain) and to evaluate the efficacy of the anesthetic and non-anesthetic solutions used.
Methods: Ninety patients with chronic knee OA between the ages of 50-80 were divided into two groups with and without neuropathic pain according to painDETECT questionnaire (4). The groups were randomized into three subgroups to either the lidocaine group (n=30) or dextrose group (n=29) or saline solutions (n=31). After the ultrasound-guided GNB, quadriceps isometric strengthening exercises and cryotherapy were recommended to the patients. Visual analog scale (VAS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and Lequesne-algofunctional Index were assessed at baseline and at 1 week, 1 and 3 months later after the procedure.
Results: Statistically significant improvement was observed in all groups with or without neuropathic pain according to VAS values at the 1st week, 1st month and 3rd month compared to baseline ($p<0.05$). Statistically significant improvement was observed in all groups with neuropathic pain according to painDETECT values at the 1st week, 1 st month and 3rd month compared to baseline ($p<0.05$). There was a statistically significant improvement in the groups without neuropathic pain which received dextrose and saline solutions, according to painDETECT values, but not in the group which received lidocain at the 1st week, 1st month and 3rd month compared to baseline ($p>0.05$). There was a statistically significant improvement in all groups with or without neuropathic pain according to WOMAC and Lequesne total scores at the 1st week, 1st month and 3rd month compared to baseline ($p<0.05$).
Conclusion: We conclude that in patients with chronic knee OA (with/without neuropathic pain), the use of GNB with USG is an analgesic method which provides short to medium term analgesia and functional recovery and has no serious side effects. The lack of significant difference between the anesthetic and non-anesthetic solutions used in the GNB suggests that this may be a central effect rather than a symptom of peripheral nerve dysfunction. It suggests that injection may have an indirect effect through nociceptive processing and changes in neuroplastic mechanisms in the brain. In addition, we can say that regular exercise program contributes to improved physical function with the decrease in pain.
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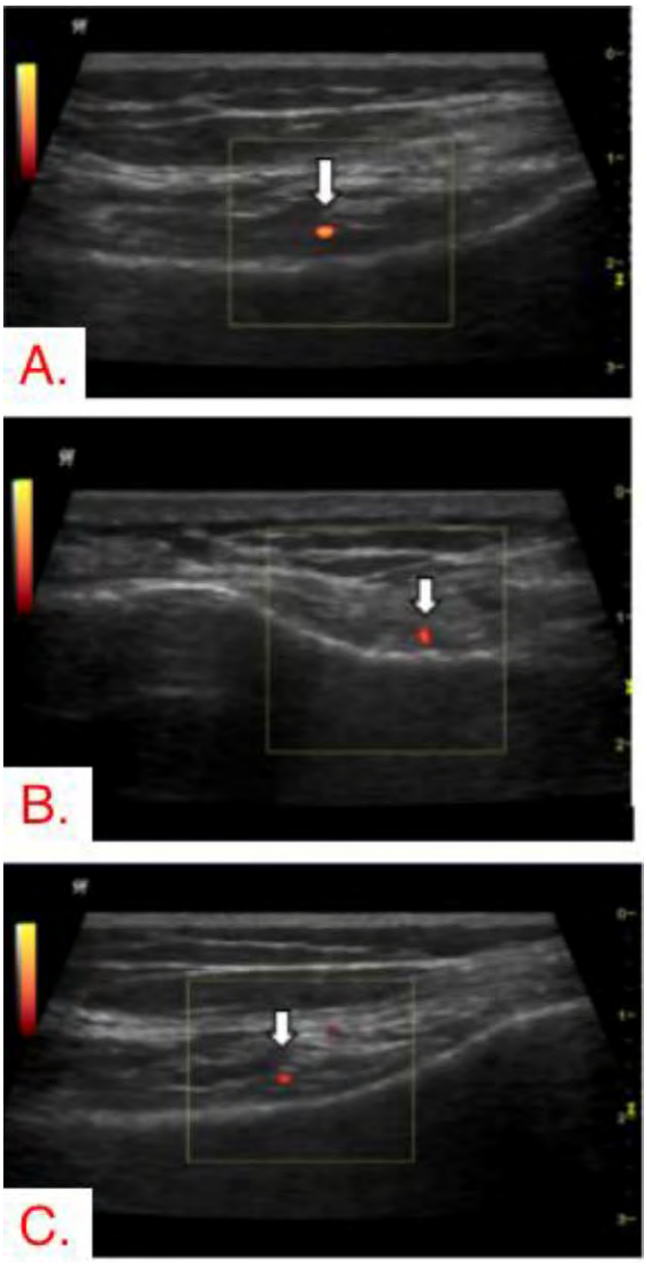


Fig. 1: Ultrasound- guided identification of GNB target sites. Doppler mode. White arrows indicate genicular arteries. **A.** Superior medial genicular artery. **B.** Inferior medial genicular artery. **C.** Superior lateral genicular artery.

Disclosure of Interests: None declared
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FRI0383

A RANDOMISED PLACEBO-CONTROLLED CLINICAL TRIAL OF CURCUMA LONGA EXTRACT FOR TREATING SYMPTOMS AND EFFUSION-SYNOVITIS OF KNEE OSTEOARTHRITIS (CURKOA TRIAL)

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Background: Pharmacological therapies are limited, associated with off-target effects, are frequently contraindicated, and only modestly effective for pain in osteoarthritis (OA). Effusion and synovitis are common in OA and are associated with symptomatic and structural progression of OA. *Curcuma longa* (Turmeric) extract has anti-inflammatory effects and is gaining popularity in the treatment of OA despite the lack of high-quality evidence.
Objectives: The CurKOA trial aimed to determine the efficacy of *Curcuma longa* extract for reducing knee symptoms and effusion-synovitis in patients with symptomatic knee OA and knee effusion-synovitis.
Methods: In this randomised, double-blind, placebo-controlled trial, participants with significant knee pain (≥ 40 mm on a 100-mm visual analog scale [VAS]), symptomatic knee OA (by ACR criteria) and ultrasound defined effusion-synovitis were randomised to receive *Curcuma longa* extract (80% aqueous based extract standardized to turmerosaccharides + 20% curcuminoids, 2 × 500 mg capsules/day) or identical placebo for 12 weeks. Knee MRI scans were obtained at baseline and 12 weeks. Coprimary outcomes were changes in knee pain assessed by VAS and change in knee effusion-synovitis volume assessed by MRI over 12 weeks.
Results: Among 70 participants (36 received *Curcuma longa*, 34 received placebo, age 61.8±8.6 years, 56% female), *Curcuma longa* significantly improved VAS knee pain compared to placebo (-9.11mm, 95% confidence interval [CI] [- 17.79 to -0.44]) over 12 weeks, equivalent to a standardised effect size of 0.50. There was no significant between group difference in change in effusion-synovitis volume (3.24 mL [-0.33, 6.82]). There were significantly greater reductions in WOMAC knee pain (-47.22mm [-81.22, -13.22]), WOMAC function (-112.26mm [-222.79 to -1.74]) and significantly more OARSI-OMERACT treatment responders (63% treatment vs. 38% placebo [Risk Ratio=1.64 (1.00 to 2.70)]) in the *Curcuma longa* group compared to the placebo group. There was no significant between-group difference in lateral femoral cartilage T2 relaxation time (-0.38 ms [- 1.10 to 0.34]) assessed from compositional MRI. The incidence of adverse events was similar in the *Curcuma longa* (n=14 (39%)) and placebo (n=18 (53%)) groups over 12 weeks (P=0.24).
Conclusion: An extract of *Curcuma longa* significantly improved knee pain in an inflammatory phenotype of knee OA patients over 12 weeks compared to placebo but had no effect on knee effusion-synovitis and cartilage composition assessed using MRI. The moderate effect size of the treatment supports the use of *Curcuma longa* extract for the symptomatic management of knee OA.

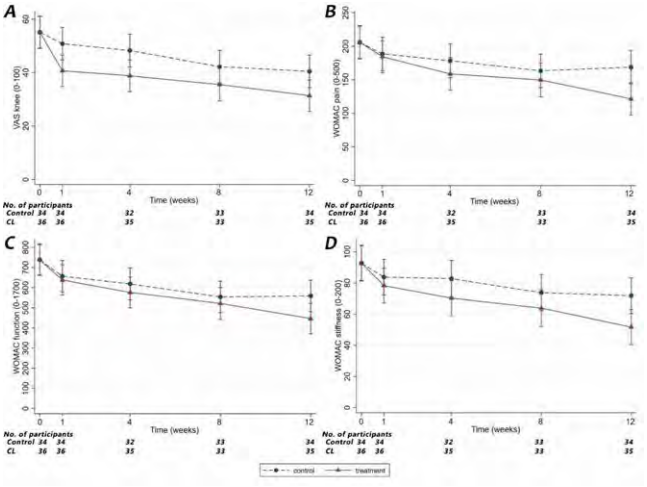


Figure 1. Change in VAS and WOMAC subscale scores in treatment and control groups over the course of the study. (VAS = Visual analog scale, WOMAC = Western Ontario and McMaster University Index, CL = Curcuma longa extract)

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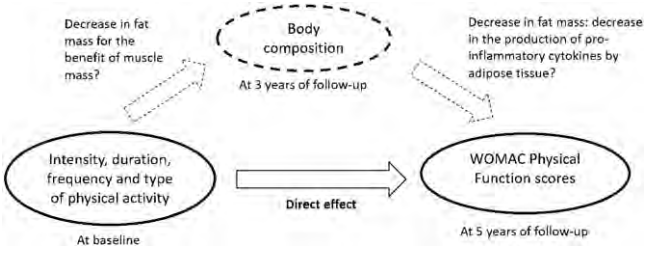
FRI0384

BODY COMPOSITION AS A MEDIATOR IN THE RELATIONSHIP BETWEEN PHYSICAL ACTIVITY AND PHYSICAL FUNCTION IN LOWER-LIMB OSTEOARTHRITIS: RESULTS FROM THE KHOALA COHORT

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Background: Many trials investigated the beneficial effect of physical activity (PA) on physical function (PF) in people with osteoarthritis (OA), but factors involved in this relationship are poorly understood. Considering the link between OA and obesity and obesity-related disorders, body composition (BC) could be one of these factors.
Objectives: To examine the relationships between baseline components of PA and 5-year PF scores, considering BC variables measured at 3 years as potential mediators in theses associations (Figure).
Methods: We used data from the KHOALA cohort, a French population-based multicenter cohort of 878 patients with symptomatic knee and/or hip OA, aged between 40 and 75 years old. Baseline PA intensity (Metabolic Equivalent of Task, MET), frequency (times/week), duration (hours/week) and type (weight-bearing or not) were assessed by the Modifiable Activity Questionnaire. PF was measured with the WOMAC questionnaire at 5 years (higher scores = greater functional limitations).
Skeletal muscle mass (grams) and fat mass (grams) were measured by dual X-ray absorptiometry (DXA) in 358 patients at 3 years. Fat mass index (kg/m^2), appendicular fat mass (kg), % of fat mass, lean mass index (kg/m^2), appendicular muscle mass (kg), skeletal muscle mass index (kg/m^2 or %) were calculated based on DXA data. Sarcopenia was defined according to the FNIH Sarcopenia Project recommendations.
A causal mediation analysis was used to highlight the mediating role of BC variables. Bivariate analyses (multiple linear and logistic regressions) were performed to select the variables of interest. Separate generalized linear models were used to describe the relationships between PA components, PF and selected BC variables. Unadjusted and adjusted for baseline confounders (age, gender, number of comorbidities, disease duration, mental health and vitality scores) models were ran.
Results: A 1-MET increase in baseline PA intensity was significantly associated with an improvement in PF at 5 years (-3 points). Weight-bearing PA was also significantly associated with better PF scores (-5 points).
A 1-MET-increase in PA intensity at baseline was associated with a subsequent decrease at 3 years in fat mass index (-0.86 k/m^2), an increase in skeletal muscle mass index (≥ 6%), and a decrease in % of fat mass (-2%). Non-weight-bearing PA was significantly associated with a decrease in fat mass index (-2.5 kg/m^2).
A 1-point increase in PF score was associated with a reduction in skeletal muscle mass index (calculated from body mass index, -0.3%) and an increase in skeletal muscle mass index (calculated from height, +3 kg/m^2). The presence of sarcopenia was significantly associated with a degradation of PF (+7 points).
Crude analyses indicated that 20.4% of the effect of baseline PA intensity on PF scores at 5 years was mediated by skeletal muscle mass index (calculated from height), 23.2% by fat mass index and 26.6% by % of fat mass. Similarly, 19.3% of the effect of baseline PA type on PF scores at 5 years was mediated by fat mass index and 15.1% by % of fat mass. After adjustment, we found no longer evidence of a mediating role of BC variables in these associations.
Conclusion: We found significant associations between a 1-MET increase in PA intensity, weight-bearing PA at baseline and improvement in PF at 5 years, without any mediating role of BC variables. Further studies are needed to better understand the factors involved in these associations, especially psychosocial variables.



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FRI0385 MUSCLE FUNCTION AND QUALITY BUT NOT MASS PROTECT AGAINST MORE SEVERE KNEE PAIN TRAJECTORIES

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Background: Evidence suggests that periarticular muscles have a role in the pathogenesis of pain, but results have not been consistent. We recently reported that pain population is heterogenous and consists of different subgroups of which the causes and mechanisms differ.
Objectives: To examine the association of muscle mass, leg strength, knee extensor strength, low-limb muscle quality with knee pain trajectories.
Methods: Data on 975 participants from a population-based older adult cohort study were utilised. Dual-energy X-ray absorptiometry was used to assess muscle/fat mass. Leg strength in both legs and dominant knee extensor strength were measured. Low-limb muscle quality was calculated (i.e. leg strength divided by lower-limb muscle mass). The Western Ontario and McMaster Universities Osteoarthritis Index pain questionnaire was used to measure knee pain at each time-point. Radiographic knee osteoarthritis (ROA) was assessed by X-ray. Group-based trajectory modelling was applied to identify pain trajectories. Multi-nominal logistic regression was used for the analyses.
Results: A total of 975 participants [Mean±SD: age 62.2±7.4 years, body mass index (BMI) 27.8±4.6 kg/m^2 and 51% of females] were included in the analysis. Three distinct pain trajectories were identified: 'Minimal pain' (53%), 'Mild pain' (34%) and 'Moderate pain' (13%). In multivariable analysis, both greater total and low-limb muscle mass were associated with an increased risk of 'Mild pain' [total muscle mass: relative risk (RR): 1.51 per SD increase, 95%CI: 1.14–1.98; low-limb muscle mass RR: 1.33 per SD increase, 95%CI: 1.07–1.66] and 'Moderate pain' [total muscle mass: RR: 2.57 per SD increase, 95%CI: 1.70–3.89); low-limb muscle mass RR: 2.03 per SD increase, 95%CI: 1.47–3.80)] compared to the 'Minimal pain' trajectory group. After further adjustment for fat mass, these associations disappeared. Total muscle mass percentage was associated with a reduced risk of being worse pain trajectories. In relative to the 'Minimal pain' trajectory group, leg strength, knee extensor strength and quality were associated with a reduced risk of being in more severe pain trajectories after adjustment for covariates (RR=0.56 to 0.71 per SD increase, all P<0.05). Similar results were observed in those with ROA.
Conclusion: Muscle percentage, strength and quality, but not muscle mass itself are associated with a reduced risk of being more severe pain trajectories, suggesting that improving muscle composition, muscle function and power are of more clinically relevance to preventing the development and maintenance of worse pain trajectories.
Disclosure of Interests: None declared
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FRI0386 EARLY OSTEOARTHRITIS: IS ASYMPTOMATIC CLINICAL COURSE REAL?

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Background: Osteoarthritis (OA) is the leading cause of disability among all RMDs. Early diagnosis of OA is complicated. So, there is an absence of clear markers of the diagnosis of OA, and this issue is now being discussed.
Objectives: The aim of this study is to examine relatively healthy individuals without symptoms in order to evaluate MR-markers of early OA of the knee.
Methods: We included 29 relatively healthy individuals. 55,17% (n=16) were women. Median age was 35 (32-41) years. They didn't have any complaints, according to the preliminary criteria of early OA, symptoms of OA (1), didn't have any significant concomitant diseases and elevated ESR, CRP. The exclusion criteria were previous trauma, orthopedic surgery, X-Ray signs of OA. MRI was performed on 1,5 Tl Siemens Magnetom Essenza. WORMS-scale was used to evaluate the knee joint structures.
Results: In all examined joints we observed small changes characteristic of symptomatic OA (osteophytes, cartilage damage etc.). In 4 knees we found undamaged cartilage (0 points). In 5 knees we observed cartilage damage >=4 points with marrow abnormality. In the Table 1 we present the frequency of any abnomaly (>=1 points) in each parameter present in examined joints. The most commonly asymptomatic changes were observed in the patellofemoral joint. Small osteophytes were the most common changes.

Table 1. Number of examined knee joints with different anomalies according to WORMS (>=1 point).

Parameter	MFTJ (percent, total)	LFTJ, (percent, total)	PFJ (percent, total)	S-region, (percent, total)	Total, (percent, total)
Cartilage	19,44% (n=7)	19,44% (n=7)	75,00% (n=27)	-	83,33% (n=30)
Marrow abnormality	0,00%	2,78% (n=1)	0,00%	13,89% (n=5)	16,67%(n=6)
Bone cysts	0,00%	0,00%	0,00%	0,00%	0,00%
Bone attrition	66,67% (n=24)	0,00%	-	-	66,67% (n=24)
Osteophytes	88,89% (n=32)	86,11% (n=31)	97,22% (n=35)	-	100,00% (n=36)
Menisci	0,00%	2,78% (n=1)	-	-	2,78% (n=1)
Ligaments	-	-	-	-	0,00%
Synovitis	-	-	-	-	33,33% (n=12)
Total	–	–	–	–	100,00% (n=36)

Besides, we calculated mean points in each parameter in the scale and compared it with the maximum score in this parameter (in percent). Table 2 shows the results. The most severe change was bone attrition.

Table 2. Mean points of different WORMS parameters in examined knee joints.

Parameter	MFTJ (percent, total)	LFTJ, (percent, total)	PFJ (percent, total)	S-region, (percent, total)	Total, (percent, total)
Cartilage	1,30%	1,02%	7,64%	-	2,91%
Marrow abnormality	0,00%	0,37%	0,00%	4,63%	0,31%
Bone cysts	0,00%	0,00%	0,00%	0,00%	0,00%
Bone attrition	15,37%	0,00%	0,00%	-	1,75%
Osteophytes	6,59%	5,48%	8,33%	-	6,69%
Menisci	0,00%	0,93%	-	-	0,46%
Ligaments	-	-	-	-	0,00%
Synovitis	-	-	-	-	12,04%
Total	-	-	-	-	3,61%

We didn't observe asymptomatic lesions in the medial meniscus, marrow abnormality in MFTJ and LFTJ, subchondral cysts in any location, ligament lesions. Despite minimal osteophytes almost in all individuals, they didn't have any clinical features of knee OA.

Conclusion: MRI of the knee joints in the cohort of young relatively healthy individuals without clinical features of OA revealed irreversible structural changes characteristic of symptomatic OA. There is no association between symptoms and structural damage. Based on these, we can make an assumption about asymptomatic stage of OA. In order to distinguish between definitions of early asymptomatic OA as a disease onset and asymptomatic structural changes as reflection of metabolic disorders it is necessary to follow up and to perform an in-depth examination of these individuals.

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Disclosure of Interests: Natalia Martusevich Shareholder of: k, Svetlana Duben: None declared, Alexander Aleshkevich: None declared, Alena Dmitrieva: None declared, Tatsiana Bondar: None declared, Katsiarina Gudkevich: None declared
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FRI0387 A PROGNOSTIC MODEL OF PRE-RADIOGRAPHIC KNEE OSTEOARTHRITIS: DATA FROM THE OSTEOARTHRITIS INITIATIVE

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Background: The improvement of the existing diagnostic methods to detect pre-radiographic knee OA (KOA) may facilitate the development of preventive strategies. It has been postulated that combining biochemical with clinical markers, may increase the prognostic power to detect who is at high risk for developing KOA.

Objectives: To validate and qualify the ability of 6 proteins with biomarker potential to generate a prognostic model of knee OA prediction through the combination of validated OA biomarkers and clinical markers.

Methods: In the *validation phase* (Figure 1), 749 sera at the baseline visit belonging to participants from the Osteoarthritis Initiative (OAI) Cohort were randomly selected to blindly quantify 6 biomarkers using in-house custom sandwich microarrays built using the xMAP technology. Among these, only 540 participants have a Kellgren and Lawrence (KL) grade = 0-1 at the beginning of the OAI study in at least one knee. After a follow-up period of 96 months, 209 participants developed KOA in at least one knee (KL ≥ 2) and were classified as incident group, whereas 331 did not developed the disease (KL = 0-1) and were classified as not-incident group. Statistical differences between the outcome groups were assessed by non-parametric Mann-Whitney U tests. In the *qualification phase* (n=540), univariate regression analyses were carried out to investigate whether the individual biomarkers were associated with the risk of KOA development. A clinical prognostic model was defined by stepwise regression analysis using clinical non-radiographic variables significantly associated with the OA incidence. The utility of the potential biomarkers, alone or in combination, was evaluated by comparing the Area Under the Curve (AUC) of the clinical prognostic model with the biomarkers plus clinical prognostic models. In addition, sen

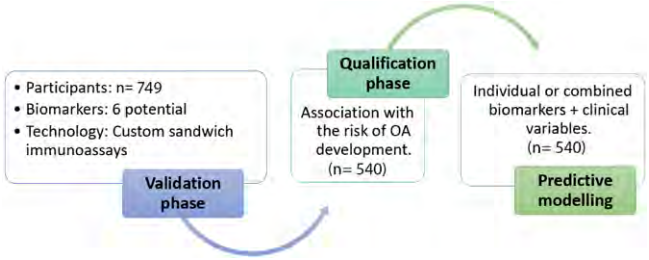


Figure 1. Study desing

Results: The incident group showed significant higher serum concentrations at the baseline visit ($p < 0.05$) for all the potential biomarkers analyzed in this study. Moreover, 5 of them were also significantly associated with the future appearance of radiographic KOA, yielding Odds Ratios (OR) ≥ 10 per 10 µg/ml increase. Among all the possible combinations, the inclusion of 2 biomarkers to the clinical prognostic model showed a significant improvement of the predictive capacity (AUCs = 0.78 vs 0.82, p= 0,044) with 65% (95% Confidence Interval (95%CI): 60-70%) specificity and 88% (95%CI: 81-91%) sensitivity. Variables included in the regression model and all metrics comparing the biomarkers plus clinical prognostic model with the clinical prognostic model are shown in Figure 2A. The ROC curves of the biomarkers-only model, clinical prognostic model and biomarkers plus clinical prognostic model are represented in Figure 2B.

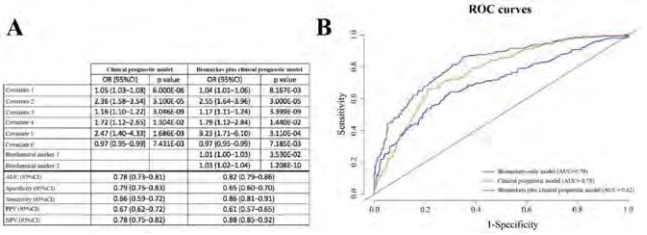


Figure 2. (A) Multivariate regression analysis (B) ROC curves of the models

Conclusion: We have generated a prognostic model for the prediction of KOA by combining biomarkers and clinical variables, which showed a putative utility in the clinical setting by improving the predictive capacity of a clinical prognostic model to identify patients at a higher risk to develop radiographic KOA.

Disclosure of Interests: Maria Camacho Encina: None declared, Vanesa Balboa-Barreiro: None declared, Ignacio Rego-Perez: None declared, Rocío Paz González: None declared, Valentina Calamia: None declared, Lucía Lourido: None declared, Cristina Ruiz-Romero: None declared, Francisco J. Blanco Grant/research support from: Sanofi-Aventis, Lilly, Bristol MS, Amgen, Pfizer, Abbvie, TRB Chemedica International, Glaxo SmithKline, Archigen Biotech Limited, Novartis, Nichi-iko pharmaceutical Co, Genentech, Jannsen Research & Development, UCB Biopharma, Centrexion Theurapeutics, Celgene, Roche, Regeneron Pharmaceuticals Inc, Biohope, Corbus Pharmaceutical, Tedec Meiji Pharma, Kiniksa Pharmaceuticals, Ltd, Gilead Sciences Inc, Consultant of: Lilly, Bristol MS, Pfizer
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FRI0388 ARE WE OVERLOOKING OSTEOARTHRITIS? – A COMPARATIVE STUDY OF PAIN, FUNCTION AND QUALIFY OF LIFE IN PATIENTS WITH HAND OSTEOARTHRITIS AND RHEUMATOID ARTHRITIS

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Background: Osteoarthritis (OA) is frequently regarded by patients and health care providers as a normal consequence of ageing (1). On the other hand, it is well established that rheumatoid arthritis (RA) is a pathological condition requiring prompt and efficacious treatment and in which remarkable progresses have been achieved in the last decades. Pain and physical limitations are hallmarks of both conditions. Some previous studies suggest that OA and RA may have a similar burden (2,3).
Objectives: To compare levels of pain, physical disability and health-related quality of life in patients with primary hand osteoarthritis (hOA) and with RA: active disease (aRA) or in remission (rRA).
Methods: Observational cross-sectional study including patients of two clinical centres with hOA and RA, either in remission or with active disease (at least two swollen and/or tender hand joints). Matching for sex and age was performed. Patients were asked to complete a survey consisting of visual analogic scale (VAS) for pain, Health Assessment Questionnaire (HAQ) and Short Form 36 (SF36). Mean values for each domain were compared between the three groups using one-way ANOVA test with significance accepted for p<.05.
Results: Thirty patients with hOA and 93 with RA (33 with aRA and 60 with rRA) were included. All patients were caucasian females with no significant differences in age between groups. Patients with hOA reported higher levels of pain in comparison with aRA patients (mean VAS 57.3 *vs* 49.3mm, respectively, p=.265) and with rRA patients (57.3 *vs* 28.6mm, respectively, p<.001) [F(2.120)=25.907, p<.001]. Regarding physical function, patients with hOA reported levels of disability similar to rRA patients, but significantly lower disability than patients with aRA [F(2.120)=6.962, p=.001]. Patients with hOA evaluated their quality of life significantly better than patients with aRA and in similar levels to patients with rRA, as measured by mental health and general health status domains of SF36.
Conclusion: Our results show that hOA may have similar or even higher burden of pain than RA; this is in line with previous studies, although most of them did not consider the level of inflammatory activity of RA. On the other hand, patients with hOA seem to preserve function and have better health-related quality of life despite the higher levels of pain. These results highlight OA as a cause of severe pain, which should lead us to try an optimal symptom control for these patients. These findings should also encourage rheumatologists to endeavor efforts to perform more studies in the field of OA, to better understand its pathogenesis and to eventually find disease modifying drugs.
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FRI0389

TOWARDS ONE-STAGE ARTICULAR CARTILAGE REPAIR USING DEVICE BASED ARTHROSCOPIC MECHANICAL RELEASE OF SYNOVIAL MESENCHYMAL STEM CELLS WITH CHONDROGENESIS AUGMENTATION WITH AUTOLOGOUS PLATELET CONCENTRATE WITHOUT CELL CULTURE EXPANSION

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Background: Synovial fluid contains resident mesenchymal stem cells (SF-MSCs) that are derived from the synovial membrane and may interact with superficial cartilage injury sites. We previously reported on a novel methodology for increasing the number of MSCs in the knee joints using synovial brushing combined with platelet lysate (PL) as a chondrogenic inducer [1, 2].
Objectives: The purpose of this study was to evaluate autologous and allogenic PL as a chondrogenic inducer and the chondrogenic potential of the mobilised MSCs without further ex vivo expansion. The desired goal of the study was to provide in vitro proof of concept of direct chondrogensis without resort to MSC expansion protocols, since adequate MSCs towards repair could be mechanically procured in a minimally invasive fashion.
Methods: SF-MSCs were derived from the joint cavity of patients undergoing arthroscopy procedures. For the mechanical release of MSCs 'before' and 'after' brushing the synovium with the novel device (Figure 1A), samples of irrigation fluid were collected and MSC numbers were evaluated by CFU-F assay and flow cytometry for stromal and immune populations. Standard chondrogenic assay was performed on uncultured and cultured expanded synovial MSCs. Pellet cultures were maintained in complete chondrogenic media (CCM), DMEM+50% autologous filtered platelet concentrate (fPC), 50% Stemulate (allogeneic human PL; Cook Regentec, Indianapolis, IN), or expansion media (control). Chondrogenesis was assessed by Glycosaminoglycan (GAG) and *Toluidine blue* staining. Autologous blood was processed through a gravity-based filtration system, HemaTrate® (HT; Cook Regentec, Indianapolis, IN), to produce a PC.

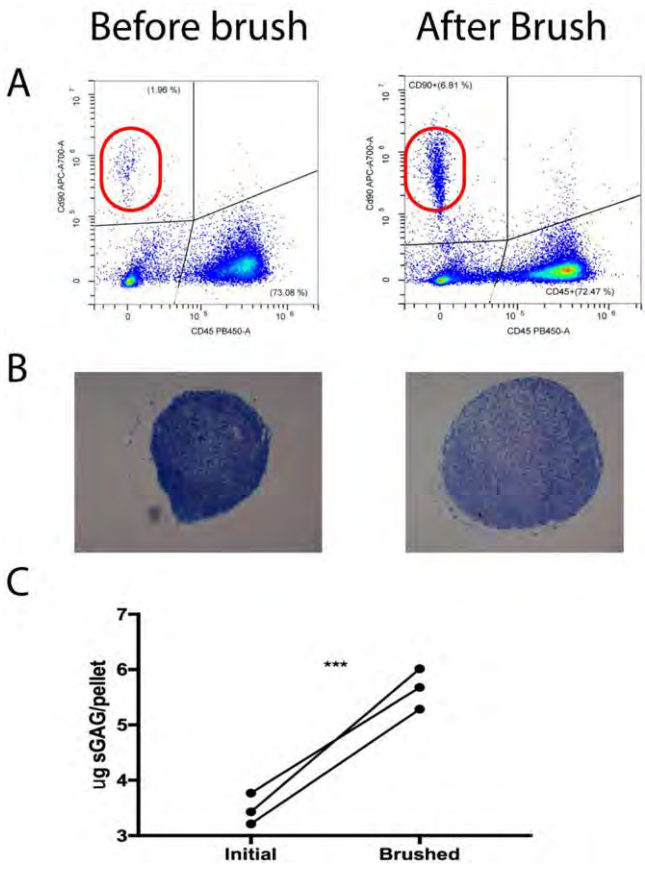


Figure 1. Flow cytometry analysis of stromal and immune populations before' and 'after' mechanically release of synovial with the novel device ($CD90^{high}$ $CD45^{Low}$ in red circle) (A). Uncultured synovial cells after 21 days exposure to complete chondrogenic media Toulid Blue staining (B) Gags level (C) n=3.

Results: Mechanically mobilized SF-MSC numbers increased as measured by CFU-F assay and flow cytometry for $CD90^{High}CD45^{Low}$ cells (p<0.001), and $CD14^{+}HLA\text{-}DR^{+}CD206^{+}CD86^{+}$ M2 macrophages also increased (p<0.05). The HT system significantly concentrated platelets and WBCs by 6- (p<0.0001) and 1.8-folds (p<0.001), respectively. Device-mobilized SF-MSC proliferation significantly increased after 6 days in DMEM + 10% PC (p<0.001) and correlated with PC platelet number (p<0.005). Autologous PC increased GAG levels compared to control (p<0.0001), and there was no significant difference compared to allogenic PL (p>0.5). Uncultured synovial cells produced significantly more GAG when cultured in CCM or DMEM + 50% autologous PC compared to control (p<0.0001). The GAG levels of uncultured synovial cells positively correlated with CFU-F (p<0.005). Chondrogenic potential of uncultured synovial cells that were mechanically mobilized with initial irrigation exhibited an increase (1.5-fold) in GAG levels (p<0.001) figure 1-B and also positively correlated with CFU-F (p<0.005).
Conclusion: Synovial MSCs can be mechanically released in sufficient number to undergo in vitro chondrogenic induction with significant chondrogenic activity without the need for ex vivo culture expansion. In vitro, autologous PC can be used as chondrogenic inducer for uncultured SF-MSCs. The data presented here supports one stage arthroscopy procedures for cartilage repair
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FRI0390 IMPACT OF ULTRASONOGRAPHY-DETECTED QUADRICEPS CALCIFIC TENDONITIS ON PAIN AND FUNCTION IN PATIENTS WITH PRIMARY KNEE OSTEOARTHRITIS

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Background: Calcific tendonitis is most commonly seen around shoulder joint. Few cases of quadriceps calcific tendonitis (QCT) of were reported. Routine use of ultrasonography in diagnosis of knee osteoarthritis has resulted in detection of many cases of QCT.

Up to the best of our knowledge, this is the first study to detect impact of QCT in knee osteoarthritis by ultrasonography.

Objectives: To compare pain, function, and clinical and radiological findings among primary KOA patients with or without ultrasonography-detected QCT.

Methods: A prospective, observational study study was conducted on 214 patients with knee OA in the period between february 2019 to july 2019. Ultrasonography of knee joints was done according to EULAR guidelines. Quadriceps calcific tendonitis is defined as hyperechoic mass within the quadriceps tendon with posterior shadowing. The patients were categorized into two groups according to the presence or absence of QCT.

Radiological grades of Kellgren–Lawrence were recorded. Pain and functional status was assessed by visual analog scale (VAS), Health Assessment Questionnaire-II (HAQ-II), and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)

Results: QCT were detected in 25 (11.6%) patients. Most cases of QCT were detected in vastus lateralis 18 (72%), then in vastus intermedius 5 (20%) and only 2 cases were detected in vastus medialis.

QCT were detected mainly in advanced stages of knee OA; 22 cases of QCT were found in patients with grade 4 KOA.

The presence of QCT was statistically significant related ($P < 0.05$*) with age, VAS, HAQ-II, WOMAC subscales, synovitis and effusion.

Conclusion: Quadriceps calcific tendonitis is not rare. Ultrasonography can detect QCT in many cases with advanced knee OA. QCT is associated with increased pain and dysfunction in knee OA

References: None

Disclosure of Interests: None declared

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FRI0391 METABOLIC FACTORS ASSOCIATED TO RADIOGRAPHIC KNEE OSTEOARTHRITIS IN INDIVIDUALS WITH KNEE PAIN

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Background: Metabolic factors have been shown to be associated to radiographic knee osteoarthritis (OA) [1]. More knowledge about associations between metabolic factors and early clinical knee OA is needed.

Objectives: The aim was to study associations between metabolic factors and radiographic knee OA in individuals with knee pain

Methods: In total 272 individuals with radiographs at baseline, from an ongoing longitudinal study of knee pain (without cruciate ligament injury), were included in the present cross-sectional study. At baseline BMI, waist circumference (WC) and visceral fat area (VFA) were assessed. Fasting plasma glucose, triglycerides, cholesterol, HDL-and LDL-cholesterol were analysed. Metabolic syndrome (MetS) was present if central obesity (WC ≥94 cm in men and ≥80cm in women) plus any two of the following factors: raised blood pressure (systolic blood pressure ≥ 130 or diastolic blood pressure ≥ 85 mm Hg or treatment of hypertension), raised triglycerides (≥ 1.7 mmol/L or specific treatment), reduced HDL-cholesterol (men < 1.03 mmol/L and women < 1.29 mmol/L or specific treatment), raised glucose (glucose ≥ 5.6 mmol/L, or type 2 diabetes).

The individuals were divided in two groups according to Ahlbäck [2], one group, who had grade I or more in at least one knee (radiographic knee OA, ROA) n=62 and the other group, not fulfilling Ahlbäck criteria (no radiograhic knee OA, No OA) n=211. The associations between metabolic factors and knee OA were calculated by crude logistic regression analyses, adjusting for age and sex.

Results: The group with radiographic knee OA were older, had higher BMI, higher amount of visceral fat and more had central obesity, table 1. Ninety- four percent of the group with ROA had central obesity compared to 76%, p=0.002 in the no OA group. There was no difference between the groups regarding MetS, 44% in the ROA group vs. 39%, p=0.5. The group with ROA had increased cholesterol, triglycerides and LDL-cholesterol. There were no differences in fasting glucose between the groups, though both groups had a mean glucose value in the upper range of normal value, table 1. Factors associated to having radiographic knee OA were age (OR 1.11, 95% CI 1.06-1.17), BMI (1.07, 1.003-1.13), central obesity (3.91, 1.32-11.61) and raised triglycerides (2.35, 1.03-5.38).

Table 1. Baseline descriptives

	No OA Mean (sd)	ROA Mean(sd)	p-value
N	**211**	**62**	
Age	**50 (9)**	**56 (4)**	**<0.001**
Sex, women, %	66	71	0.454
BMI	**25.9 (4.7)**	**27.7 (4.7)**	**0.007**
VFA (cm^2)	**109 (53)**	**126 (52)**	**0.026**
WC, cm	**94 (13)**	**99 (13)**	**0.006**
Raised Blood pressure, %	66	53	0.063
Cholesterol (mmol/L)	**5.2 (1.0)**	**5.5 (1.1)**	**0.033**
Triglycerides (mmol/L)	**1.0 (0.6)**	**1.2 (0.7)**	**0.035**
Raised triglycerides, %	**9**	**21**	**0.008**
LDL-cholesterol (mmol/L)	**3.4 (1.0)**	**3.7 (1.1)**	**0.027**
HDL-cholesterol (mmol/L)	1.7 (0.4)	1.7 (0.5)	0.547
Reduced HDL	11	15	0.460
Glucose (mmol/L)	5.5 (0.9)	5.5 (0.5)	0.858

Conclusion: There were associations between some metabolic factors and radiographic knee OA in individuals with knee pain. Fasting glucose was increased in both groups. The associations between metabolic risk factors and the development of knee OA needs to be assessed in longitudinal studies.

References:

[1] Sellam J, Bone Spine 2013;80:568-73.
[2] Ahlback S,. Acta Radiol Diagn (Stockh) 1968Suppl 277:7-72.

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FRI0392 ADVERSE EVENTS IN PATIENTS WITH OSTEOARTHRITIS TREATED WITH SUBCUTANEOUS TANEZUMAB: A POOLED ANALYSIS OF THE OVERALL POPULATION AND SELECTED SUBGROUPS FROM 3 RANDOMISED PLACEBO-CONTROLLED TRIALS

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Background: Tanezumab, a monoclonal antibody against nerve growth factor (NGF), is in development for the treatment of osteoarthritis (OA).

Objectives: To assess the effects of gender, age and body mass index (BMI) on the incidence of adverse events (AEs) in patients (pts) treated with subcutaneous (SC) tanezumab in pooled data from three phase 3 OA studies. Anti-NGF therapy has been associated with joint safety events[1]. Here we focus on treatment emergent AEs, including abnormalities of peripheral sensation (APS).

Methods: All three randomised, double-blind, placebo-controlled studies enrolled pts with radiographically-confirmed OA of the hip or knee, who had inadequate response or could not tolerate standard of care analgesics. In the 16-week (wk) Study 1 (NCT01089725), pts received placebo, tanezumab 2.5 mg, 5 mg or 10 mg at baseline and wk 8[2]. Due to a clinical hold on NGF antibodies, <10% of pts received the 2nd dose at wk 8. Pts in the 16-wk Study 2 (NCT02697773), received placebo or tanezumab 2.5 mg at baseline and wk 8 or tanezumab 2.5mg at baseline and 5mg at wk 8[1]. Pts in the 24-wk Study 3 (NCT02709486), received

placebo, tanezumab 2.5 mg or 5 mg at baseline, wks 8 and 16. All treatments were given SC. AE data from the treatment period of each study were pooled for placebo, tanezumab 2.5 mg and 5 mg groups and examined by subgroups of gender, age and BMI. Data from the 10 mg group of Study 1 were not included due to the low sample size.

Results: The incidence of any AE was numerically higher in females across treatment groups and in pts with a BMI ≥30 kg/m^2 in the tanezumab 5mg, but not 2.5 mg group, vs the overall population (Table 1). SAEs were infrequent but numerically higher across all tanezumab 5 mg subgroups vs placebo (Table 2). Paraesthesia and hypoaesthesia were the most common AEs of APS and were increased in all tanezumab groups in the overall population vs placebo. In any of the subgroups, the incidence of paraesthesia or hypoaesthesia was ≤7.8% and ≤3.9%, respectively. The difference within a patient subgroup for paraesthesia or hypoaesthesia was typically comparable with that of the overall population across treatments.

Table 1. Incidence of AEs during the treatment period

% of pts with an AE in each subgroup	Placebo n=586	Tanezumab 2.5 mg n=602	Tanezumab 2.5 mg/5 mg n=219	Tanezumab 5 mg n=347
Overall population	51.7	52.3	47.0	54.8
Gender				
Male	51.1	49.7	41.3	46.6
Female	52.0	53.6	50.4	59.0
Age (years)				
<65	55.0	54.0	44.0	54.5
≥65	47.2	50.0	52.6	54.9
BMI (kg/m^2)				
<25	58.1	46.6	51.9	45.5
25–<30	51.4	55.9	43.7	50.0
30–<35	49.2	51.5	43.2	58.9
≥35	52.7	52.3	55.3	60.9

BMI, body mass index; kg/m2, kilogram per square metre

Table 2. Incidence of SAEs during the treatment period

% of pts with a SAE in each subgroup	Placebo n=586	Tanezumab 2.5 mg n=602	Tanezumab 2.5 mg/5 mg n=219	Tanezumab 5 mg n=347
Overall population	1.5	2.2	1.4	2.6
Gender				
Male	1.6	3.0	1.3	2.5
Female	1.5	1.7	1.4	2.6
Age (years)				
<65	1.2	2.6	1.4	1.9
≥65	2.0	1.6	1.3	3.1
BMI (kg/m^2)				
<25	1.6	1.1	0	2.3
25–<30	1.6	2.7	0	2.7
30–<35	1.6	2.0	1.4	3.1
≥35	1.3	2.3	4.3	1.6

BMI, body mass index; kg/m2, kilogram per square metre

Conclusion: This pooled analysis showed that the safety profile of tanezumab in the subgroups studied is broadly similar to that of the overall study population.

References:

[1] Schnitzer, T. J. *et al. JAMA* (2019)

[2] Birbara, C. *et al. J Pain Res* (2018)

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FRI0393

BASELINE CHARACTERISTICS OF THE STUDY POPULATION IN ROCCELLA, A PHASE 2 CLINICAL TRIAL EVALUATING THE EFFICACY AND THE SAFETY OF S201086/GLPG1972 IN PATIENTS WITH KNEE OSTEOARTHRITIS

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Background: Osteoarthritis (OA) is a degenerative joint disease involving structural pathology of all joint tissues, and most commonly affecting the knee, hip and hand. Degradation of the cartilage extracellular matrix represents a central feature of OA and is widely thought to be mediated by proteinases that degrade primarily aggrecan and collagen. ADAMTS-5, a Disintegrin And Metalloproteinase with ThromboSpondin-motif-5, is a key aggrecan-cleaving enzyme involved in cartilage degradation. S201086/GLPG1972, a potent and highly selective inhibitor of ADAMTS-5, is an oral Disease-Modifying OsteoArthritis Drug (DMOAD) candidate.

Objectives: The primary objective of the ROCCELLA phase 2 clinical trial (NCT03595618) is to evaluate the effect of S201086/GLPG1972 over 52 weeks of treatment (3 dose groups compared to placebo) in reducing cartilage loss. Cartilage thickness of the knee is being measured quantitatively by Magnetic Resonance Imaging. Here, we describe the baseline characteristics of patients included in the ROCCELLA clinical trial.

Methods: The main inclusion criteria were: male or female, aged 40 to 75, with a diagnosis of knee OA according to the clinical and radiological criteria of the American College of Rheumatology. The target knee had to meet a pain score between 40 and 90 mm on a 100 mm Visual Analog Scale (VAS), and the following radiographic feature upon central radiographic readings: Kellgren/Lawrence (KL) 2 or 3 and OARSI medial joint space narrowing (JSN) 1 or 2 (for more details see Deckx *et al*. OARSI 2020). The rationale for these specific radiographic inclusion criteria was to ensure sufficient cartilage loss over 12 months to assess the efficacy of S201086/GLPG1972.

Results: Across 12 countries, 3319 patients were screened and 932 were finally included in the study. The screen failure of 72% is mainly due to the radiological criteria. The age of the patients was 62.9 ± 7.3 years (mean ± SD) with a majority of women (69.3%). The BMI was 30.5 ± 4.7 kg/m^2. The duration of knee OA was 7.2 ± 6.9 years. Five hundred and one (53.8%) patients reported a medical history of musculoskeletal and connective tissue disorders, mainly osteoarthritis in other sites (20.2%), back pain (13.6%), and arthralgia (9.8%). At inclusion, 97.2% of the patients were taking different types of drug treatments, mainly anti-inflammatory and anti-rheumatic products (69.4%) and analgesics (42%). At baseline, 11% of the target knees were KL2 and 89% were KL3; 32% were OARSI medial JSN grade 1 and 68% grade 2. Target knees at inclusion had a pain score on the VAS of 63.5 ± 11.4 mm (range 0-100, with 0 for no and 100 for extreme pain) and a total WOMAC (Likert 3.1) score of 48.0 ± 15.0 (range 0-96). The WOMAC subscores for pain, stiffness and physical function were 10.0 ± 3.2 (range 0-20), 4.2 ± 1.6 (range 0-8) and 33.8 ± 11.2 (range 0-68, indicating functional limitation), respectively.

Conclusion: For this clinical trial, patients were selected to present radiological criteria (*i.e.* OARSI JSN 1 and 2) to ensure sufficient structural progression (cartilage loss) over 12 months, as well as clinical symptoms. These stringent selection criteria were the main cause for the high screen failure rate. These baseline characteristics should warrant the ability to evaluate the efficacy of S201086/GLPG1972 as a DMOAD candidate. The search for an effective pharmacological treatment that can prevent or cure OA remains a major challenge and unmet medical need.

Disclosure of Interests: Katy Bernard Employee of: Institut de Recherches Internationales Servier, Sergey GRANKOV Employee of: Institut de Recherches Internationales Servier, Marjolijne van der Stoep Employee of: Galapagos, Agnès Lalande Employee of: Institut de Recherches Internationales Servier, Olivier Imbert Employee of: Institut de Recherches Internationales Servier, De Phung Employee of: Galapagos, Damien Chimits Employee of: Institut de Recherches Internationales Servier, Karine Muller Employee of: Galapagos, Ellen van der Aar Employee of: Galapagos, Henri Deckx Employee of: Galapagos, Maria Pueyo Employee of: Institut de Recherches Internationales Servier, Felix Eckstein

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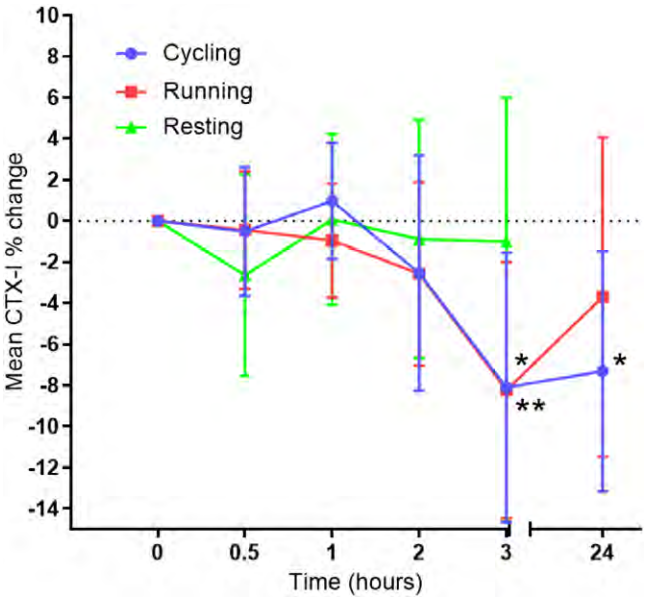
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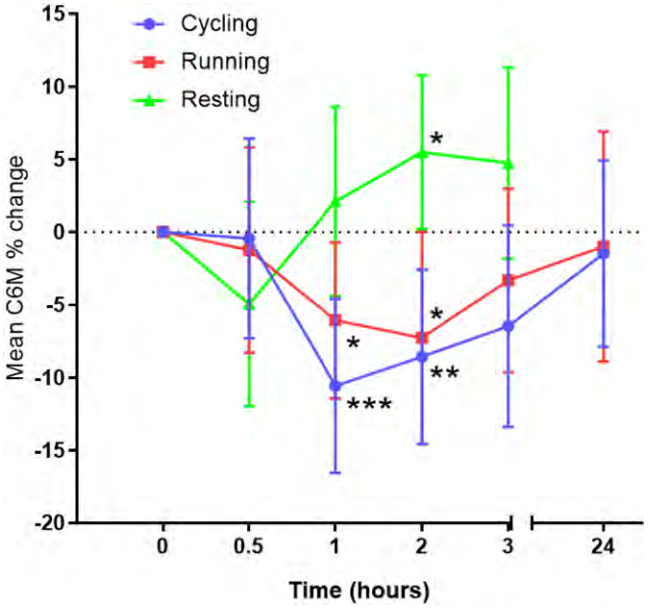
MODERATE WEIGHT BEARING AND MINIMAL WEIGHT BEARING EXERCISE INDUCE ACUTE IMPACT ON COLLAGEN BIOCHEMICAL MARKERS RELATED TO OSTEOARTHRITIS IN HUMANS

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Background: Exercise is recommended in osteoarthritis (OA) to limit pain and preserve joint function. Cycling is considered healthy, while the safety of running in OA has been controversial. The acute impact on cartilage in response to exercise (weight bearing vs non-weight bearing) remains to be explored.
Biomarkers originating from type I-III and VI collagen can be measured in serum and urine and may reflect cartilage turnover.
We report the first ever data on acute effects of exercise on a panel of collagen biomarkers in OA.
Objectives: To investigate the effect of running vs cycling on biomarkers of collagen type I-III and VI reflecting cartilage turnover.
Methods: We conducted a randomized, crossover clinical study (approval number: H-18038807) of subjects with primary knee OA. Screening included a maximal heart rate test to standardize exercise intensity. Participants underwent 30 minutes of running and cycling on separate days with blood samples taken at baseline and 0.5, 1, 2 and 3 hours after exercise initiation and again 24 hours after the exercise in order to evaluate the dynamic levels of biomarkers. Urine samples were collected before exercise and approximately 1 hour and 24 hours after. Potential diurnal variation was taken into account by measurements at comparable times from participants on a separate day with no exercise (resting). Levels of serum CTX-I, C2M, C3M, C6M and urine CTX-II were measured by enzyme-linked immunosorbent assays.
Biomarker dynamics were plotted. Error bars represent 95% CI. CTX-I and C6M are displayed.
Results: 20 subjects were included of which 20 completed cycling and resting and 15 completed running. Subject characteristics displayed in table.
CTX-I decreased significantly from baseline at three hours after both running ($p<0.01$) and cycling ($p<0.05$) and was still decreased the day after running ($p<0.05$). No change in CTX-I levels was seen during rest. This suggests that exercise acutely reduces bone-turnover.
C2M was decreased at 1 hour after running (Change: -9.4%, 95%CI: -18.4--1.0, $p<0.05$), but was found to be increased from baseline at 2 hours after cycling (Change: 19.0%, 95%CI: 6.0-32.0, $p<0.01$). C2M decreased below baseline 24 hours after running (Change: -9.4%, 95%CI: -16.1--2.7, $p<0.01$). This suggests that the load from cycling and running, respectively, affects tissues containing type II collagen differently.
C3M was decreased at 2 hours after cycling (Change: -6.3%, 95%CI: -12.1--0.5, $p<0.05$) and 3 hours after running (Change: -7.6%, 95%CI: -16.4—0.8, $p<0.05$), and C3M levels had returned towards baseline after 24 hours.
C6M was increased at 1 hour after initiating rest and decreased 1 and 2 hours after running ($p<0.05$) and cycling ($p<0.01$), and C6M levels had returned to baseline after 24 hours. These results indicate reduced enzymatic degradation of collagens type III and VI following exercise.
The variation in CTX-II was higher, compared with the serum-based markers. A trend of decreasing CTX-II in response to rest was observed, but no significant changes were seen in response to exercise.

Group	Cycling/Resting (N = 20)	Running (N = 15)
Mean age, years (SD)	61.8 (9.1)	61.9 (7.5)
Male sex, n (%)	5 (25)	4 (26.6)
Mean BMI (kg/m^2) (SD)	26.3 (3.4)	26.5 (3.6)
Baseline KL-grade, n (%)	1: 3 (15.0)	1: 2 (13.3)
	2: 8 (40.0)	2: 8 (53.3)
	3: 9 (45.0)	3: 5 (33.3)





Conclusion: Cycling and running acutely influenced markers of type I-III and VI collagen. The results suggest no harmful effects on bone and cartilage in OA. The sensitivity of biomarkers to physical activity and inactivity is important to take into account, when using them in clinical research.

Disclosure of Interests: Jonathan Bjerre-Bastos: None declared, Henning Bay Nielsen: None declared, Abigail Mackey: None declared, Morten Karsdal Shareholder of: Nordic Bioscience A/S., Employee of: Full time employee at Nordic Bioscience A/S., Anne-Christine Bay-Jensen Shareholder of: Nordic Bioscience A/S, Employee of: Full time employee at Nordic Bioscience A/S., Jeppe Ragnar Andersen Shareholder of: Nordic Bioscience A/S., Employee of: Full time employee of Nordic Bioscience., Mikael Boesen Consultant of: AbbVie, AstraZeneca, Eli Lilly, Esaote, Glenmark, Novartis, Pfizer, UCB, Paid instructor for: IAG, Image Analysis Group, AbbVie, Eli Lilly, AstraZeneca, esaote, Glenmark, Novartis, Pfizer, UCB (scientific advisor)., Speakers bureau: Eli Lilly, Esaote, Novartis, Pfizer, UCB, Yi He Employee of: YH is a full time employee of Nordic Bioscience A/S, Asger Reinstrup Bihlet Shareholder of: Nordic Bioscience A/S.
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FRI0395 **PROGNOSIS OF TREATMENT OUTCOMES IN PATIENTS WITH ANKLE JOINT OSTEOCHONDRAL LESIONS AND DEFECTS**

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Background: in most cases osteochondral lesions and defects (OHLD) in the ankle joint are the consequences of trauma, and the results of their treatment depend on a number of factors. Some factors are directly related to the area of damage (depth, localization, size), others are connected to the patients age, presence of degenerative changes in the affected joint, comorbidities, body mass index (BMI), etc.
Objectives: to develop an effective system for predicting long-term outcomes in patients with ankle joint OHLD.
Methods: 24 prognostic factors (age, gender, severity of injury, Charlson comorbidity index, BMI, OA stage, size of defect, localization of injury, degree of osteoporosis, contracture, instability, etc.) influence on the long-term (36 ± 4.5 months) treatment outcomes was analyzed by Bayesian probability analysis in 223 patients after ankle joint OHLD. The prognostic coefficient (PC) was calculated by Wald sequential analysis for each prognostic factor and prognostic system was developed for prediction of high, medium or low probability of positive treatment result, which was determined as a functional joint outcome in AOFAS 75 - 100 points.
Results: the greatest predictive value for the positive result of OHLD treatment had the following factors: age< 40 years (PC = 8.5); BMI < 25 kg/m^2 (PC=7.0), time from trauma < 1 year (PC = 4,1); OA stage < II (PC = 7.2); size of OHLD <1.0 cm^2; volume <1.5 cm^3 (PC = 8.0). The prognostic system is based on the calculating of total factors values for individual patients case in points (Σ PC). If Σ PC is less (-20) the probability of achieving a positive joint-saving result is absent; at Σ PC from (-20) to (+40) the probability is medium; and at Σ PC above (+40) probability is high. The accuracy of the prognostic assessment was retrospectively tested with a 95% confidence interval, the accuaracy of predicitive method – 84,17% (76,59-89,62)%.
Conclusion: the size and volume of osteochondral damage, BMI, age and time from trauma has the greatest predictive value for the determination of the long-term results of treatment in patients with ankle joint OHLD; use of the developed prognostic method can be used as a basis for the clinical decision making in choosing different approaches in treatment.
Disclosure of Interests: None declared
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FRI0396 **HOW DOES OSTEOARTHRITIS PAIN IMPACT FUNCTION, MOBILITY AND REQUIREMENT FOR HELP IN DAILY ACTIVITIES IN EUROPEAN PATIENTS?**

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Background: Symptomatic osteoarthritis (OA) leads to functional limitations and loss of independence. OA management focuses on pain relief and preserving physical function using non-pharmacologic and pharmacologic therapy. Additionally, patients commonly manage OA pain by avoiding activities that exacerbate their pain. Informal care, i.e. assistance from an unpaid caregiver, plays a major role in the total care provided to patients with chronic diseases like OA.
Objectives: To evaluate how OA pain severity affects physical functioning and the subsequent need for assistance with mobility and daily activities in 5 EU countries: France, Germany, Italy, Spain and UK.
Methods: Data were drawn from the Adelphi OA Disease Specific Programme (2017-18), a point-in-time study of physicians and their OA patients. Patients rated their average pain intensity over the last week on a 0-10 scale (0 = no pain; 10 = worst possible pain) and were then categorised into mild (0-3), moderate (4-6) and severe (7-10) pain groups. Patients also provided an assessment of their physical function (0-10 WOMAC scale where higher scores indicated greater functional impairment), impact on mobility, whether caregiver assistance was required, daily activities requiring caregiver assistance and home modifications made due to their OA. Physicians also rated patients' functioning on a 0 to 10 scale (0 = fully functional; 10 = completely impaired). Comparisons among pain severity groups were made using chi-squared tests and analysis of variance.
Results: The analysis included 1750 OA patients: 24% mild pain (n=413); 47% moderate pain (n=822); 29% severe pain (n=515). The patients were predominantly women (58%) and had a mean (SD) age of 65.6 (11.5).
Increased pain severity was associated with greater functional impairment scores as reported by patients (WOMAC scores: mild pain=2.1; moderate pain=4.1; severe pain=5.9) and physician-rated functional impairment (mild pain=3.5; moderate pain=4.3; severe pain=5.6). Mobility was impacted for 78% of patients with severe pain (vs. 41% mild; 63% moderate) and the need for a walking aid such as a walking stick or walking frame increased with worsening severity; wheelchair assistance was needed for 7% of severe patients (compared with <1% of mild or moderate patients). Furthermore, 31% of patients with severe pain reported having to modify their home due to their OA (vs. 11% mild; 18% moderate [p<0.001]), typically adapting their bathroom (23%) or fitting a stairlift (6%).
The need for assistance from a caregiver to help with daily activities was associated with an increase in patients' pain (9% mild; 20% moderate; 42% severe [p<0.001]). For most patients this was an immediate family member, however, the proportion of patients paying for professional care also increased with severity (1% mild; 2% moderate; 7% severe). Taking the patient to work or doctor's appointments; help with shopping; preparing/cooking meals and help with travelling out of the home were most frequently reported activities needing caregiver assistance.
Conclusion: In this study of European patients, increased pain severity was associated with greater functional impairment and impact on mobility as expected; however, this study highlights the substantial need for assistance with daily activities as well as modifications to the home. The unseen costs to the patient with moderate to severe OA pain are significant.
Disclosure of Interests: Philip G Conaghan Consultant of: AbbVie, BMS, Eli Lilly, EMD Serono, Flexion Therapeutics, Galapagos, GSK, Novartis, Pfizer, Speakers bureau: AbbVie, Eli Lilly, Novartis, Pfizer, Lucy Abraham Shareholder of: Pfizer, Employee of: Pfizer, Peita Graham-Clarke Shareholder of: Eli Lilly and Co, Employee of: Eli Lilly and Co, Lars Viktrup Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Joseph C Cappelleri Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Craig Beck Shareholder of: Pfizer, Employee of: Pfizer, Andrew G Bushmakin Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Niall Hatchell: None declared, Emily Clayton: None declared, James Jackson: None declared
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FRI0397 **THE IMPACT OF OSTEOARTHRITIS DISEASE SEVERITY ON HEALTHCARE RESOURCE USE: ANALYSIS OF REAL-WORLD EUROPEAN DATA**

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Background: Osteoarthritis (OA) is a chronic joint disease associated with pain and impaired activity. With increasing obesity trends and an ageing population, the prevalence of OA is expected to rise in the future. This represents an increasing societal problem which will lead to an increased burden on healthcare services.
Objectives: To understand the pattern of healthcare resource utilisation (HCRU) across France, Germany, Italy, Spain and the UK, as OA disease severity increases.
Methods: Data were drawn from the Adelphi OA Disease Specific Programme (2017-18), a point-in-time study of physicians and their OA patients. OA disease severity was reported by physicians, who categorised patients' OA severity as mild, moderate or severe. Patients were excluded from the analyses if they suffered from back and neck OA only, and shoulder OA that had not been diagnosed by X-ray. Physicians provided information, on a patient record form, about OA-related visits to healthcare professionals (HCPs), tests/scans conducted, emergency room (ER) visits and surgeries. Statistical comparisons among disease severity groups were made by analysis of variance and chi-squared tests.
Results: The study included 489 physicians (primary care physicians, rheumatologists, orthopaedists) reporting on 3596 of their patients with OA: 24% mild (n=874), 53% moderate (n=1904) and 23% severe (n=818). Over the last 12

months, the mean number of consultations with HCPs increased with disease severity (3.7 mild, 4.2 moderate and 5.7 severe [<0.001]). This pattern was also observed in relation to the mean number of tests/scans conducted in the last 12 months (6.9 mild, 7.9 moderate and 9.3 severe [<0.001]). More than a quarter of severe patients visited the ER in the last 12 months (26% vs. 4% mild; 9% moderate [<0.001]) and visits to hospital increased with disease severity (Table 1). The proportion of patients that have had a surgery due to their OA rose with worsening disease severity (11%, 13% and 27% for mild, moderate and severe, respectively [<0.001]).

Table 1. Physician-reported healthcare burden by OA disease severity

	Mild (n=874)	Moderate (n=1904)	Severe (n=818)
Number of patient visits to ER in the last 12 months, mean (SD)	0.1 (0.4)	0.1 (0.6)	0.5 (1.0)
Patients with ≥1 emergency visit in the last 12 months, n (%)	13 (1.5)	43 (2.3)	79 (9.7)
Patients with ≥1 hospitalisation in the last 12 months, n (%)	11 (0.1)	9 (0.5)	26 (3.2)
Number of patient outpatient hospital visits in the last 12 months, mean (SD)	0.5 (1.4)	0.6 (1.1)	1.2 (1.4)

Conclusion: This real-world data demonstrated an increase in visits to HCPs, monitoring tests and scans, hospitalisations, ER visits and surgery as OA disease severity worsened.

Disclosure of Interests: Philip G Conaghan Consultant of: AbbVie, BMS, Eli Lilly, EMD Serono, Flexion Therapeutics, Galapagos, GSK, Novartis, Pfizer, Speakers bureau: AbbVie, Eli Lilly, Novartis, Pfizer, Lucy Abraham Shareholder of: Pfizer, Employee of: Pfizer, Peita Graham-Clarke Shareholder of: Eli Lilly and Co, Employee of: Eli Lilly and Co, Lars Viktrup Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Joseph C Cappelleri Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Craig Beck Shareholder of: Pfizer, Employee of: Pfizer, Andrew G Bushmakin Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Niall Hatchell: None declared, Emily Clayton: None declared, James Jackson: None declared

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FRI0398 COMPARISON OF THE EFFICACY AND SAFETY OF TWO HYALURONIC ACIDS IN THE TREATMENT OF KNEE OSTEOARTHRITIS

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Background: Several viscosupplement treatments are available to patients suffering from osteoarthritis (OA) but few comparative clinical trials have been conducted.

Objectives: The primary objective of the study was to demonstrate at 24 weeks the non-inferiority of on hyaluronic acid over a second one in terms of efficacy (pain relief) in knee OA patients (Kellgren and Lawrence radiologic stage II or III) with whom oral treatment had failed.

Methods: This was a prospective, multicenter, comparative, randomized, double-blinded study (one independent physician evaluator–one physician injector), comparing two viscosupplements: one containing a solution of hyaluronic acid (SYNOLIS VA® 80mg hyaluronic acid and 160 mg sorbitol – Group HA1) and the other containing one of Hylan (SYNVISC ONE ® 48 mg Hylane GF-20 – Group HA2) over a period of 24 weeks. At inclusion, the average VAS Pain (1-100) was 62.5. The patients were randomized in 2 parallel groups at D0 and followed until D168. They received an injection of either HA1 or HA2. Efficacy was primarily assessed using the WOMAC Pain index (daily assessed by the patient during seven days following the injection, and then at D14). During the follow up visits (D28-D84-D168) WOMAC pain, stiffness and function scores were assessed as secondary objectives. At D168, efficacy and satisfaction were also evaluated by the evaluator and by the patient using Likert scale (7 points). Moreover, the number of responders strict each group was evaluated according to the OMERACT-OARSI criteria. According to methodology guidelines, the per protocol (PP) population has been used as primary analysis. The PP population included all patients from the intention to treat (ITT) population who completed the study without any major protocol violation.

Results: 202 patients were randomized (ITT population, 96 in the HA1 group and 106 in the HA2 group). Baseline demographic data for the PP population at the time of randomization by treatment group. Patients were predominantly female (66%). The median age of the whole population was 65 years and the median body mass index of 27.4 kg/m^2. No statistically significant differences between the two treatment groups were observed for any demographic criteria. At D168, 197 presented no protocol violations (94 in the HA1 group and 103 in the HA2 group). This population had a decrease on the overall score of the WOMAC Pain at -29.2+/- 24.1 (SD) in the HA1 group and -31.6 +/-25.5 (SD) in the HA2 group confirming the non-inferiority (P = 0.57 for the difference between groups). Regarding the secondary endpoints, no significant difference has been observed at D14, D28, D84, D168, in the PP population for all the outcome except stiffness at D28. There was also no difference between the responders rate in two groups (79 % for HA1 and 77% for HA2). In terms of safety, both products were well tolerated. No case of allergy or infection in the course of the injection was reported. Serious adverse events have been reported by 4 patients in HA1 group and 3 in HA2 group.

Conclusion: In this study, we confirmed the non-inferiority of HA1 compared with HA2 in terms of both efficacy and safety.

Disclosure of Interests: Bernard Cortet Consultant of: Aptissen, Sandrine Lombion Consultant of: Aptissen, Olivier Bruyere Consultant of: Aptissen

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FRI0399 COLCHICINE IS NOT EFFECTIVE FOR REDUCING OSTEOARTHRITIC HAND PAIN COMPARED TO PLACEBO: A RANDOMISED, PLACEBO-CONTROLLED TRIAL (COLAH)

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Background: Current pharmacotherapies to treat or prevent hand osteoarthritis are limited. Colchicine, an anti-inflammatory agent effective at reducing joint pain and swelling in gouty arthritis, may offer relief in hand osteoarthritis, though this has not been investigated before.[1]

Objectives: To investigate the efficacy of colchicine compared to placebo on VAS pain scores over 12 weeks in adults with hand osteoarthritis in a randomised, double-blind controlled trial.

Methods: 64 community-dwelling adults with hand osteoarthritis (American College of Rheumatology criteria)[2] (54 females, 48-79 years) were randomised 1:1 to colchicine (0.5mg twice daily) or placebo for 12 weeks. VAS pain scores (worst affected hand) were obtained at baseline and weeks 6, 12, and after treatment withdrawal at week 16. Secondary outcome measures included grip strength, C-reactive protein (CRP) and tender and swollen joint count (TSJC). Grip strength, TSJC and CRP were obtained at baseline and week 12. Intention-to-treat analyses, adjusted for age and gender, were performed using constrained longitudinal data analysis models in Stata v16.[3] This study is registered with the Australia New Zealand Clinical Trials Registry, ACTRN12617001524381.

Results: 58 participants completed the study (N=27 colchicine, N=31 placebo, withdrawal rate 9%). Mean (S.D) VAS score of the affected hand at baseline was 71.4 (14.5) mm in the placebo and 65.4 (15.0) mm in the colchicine group (p = 0.11). VAS scores improved during treatment, but were comparable between groups at week 6, 12 and 16 (Table 1). There were no differences between groups at week 12 for CRP, TSJC or grip strength (Table 1). Adverse events related to study medications included nausea (n=4), diarrhoea (n=9), vomiting (n=3), bloating (n=1) and reflux (n=1).

Table 1. COLAH study primary and secondary outcomes, from constrained longitudinal data analysis model

Outcome	Timepoint	Colchicine (SE)	Placebo (SE)	Colchicine-Placebo (95% CI)	p-value
VAS Pain (mm)	6 weeks	53.5 (4.5)	53.9 (4.6)	-0.4 (-12.3, 13.1)	0.95
	12 weeks	57.1 (4.4)	48.4 (4.6)	8.7 (-21.2, 3.9)	0.18
	16 weeks	62.0 (4.3)	61.6 (3.7)	-0.4 (-11.4, 10.5)	0.94
TSJC (0-20)	12 weeks	5.6 (0.7)	3.8 (0.7)	1.8 (-4.1, 0.5)	0.13
Grip strength (kg)	12 weeks	14.4 (0.8)	15.3 (0.8)	-0.9 (-0.2, 2.0)	0.10
CRP (mg/L)	12 weeks	4.5 (1.4)	4.0 (1.3)	0.5 (-3.8, 2.9)	0.77

Conclusion: Colchicine 1mg daily for 12 weeks was not effective in improving pain, tender and swollen joint count or grip strength in symptomatic hand osteoarthritis patients. This study does not support colchicine for treatment of symptoms of hand osteoarthritis.

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FRI0400

EFFICACY AND SAFETY OF AN INTRA-ARTICULAR INJECTION OF JTA-004, A NOVEL ENHANCED PROTEIN SOLUTION, IN KNEE OSTEOARTHRITIS PAIN: A RANDOMISED, DOUBLE-BLIND CONTROLLED PHASE II/III STUDY

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Background: Osteoarthritis (OA) is a degenerative, chronic, and progressive joint disease. It is associated with chronic pain, joint function impairments and disabilities, causing a poorer quality of life with physical and/or mental co-morbidity. Along with population ageing and increasing obesity, the incidence of OA is rising and there is an urgent need for new treatment options.

Objectives: JTA-004 is a novel protein solution in development for the treatment of knee OA pain. Supplemented with hyaluronic acid and clonidine, it is designed to provide a fast-acting and long-lasting pain relief. To evaluate efficacy and safety and to select the most effective formulation, single intra-articular administration of 3 JTA-004 formulations were tested and compared to Hylan G-F 20 during a 6-month period.

Methods: In this prospective, multicentre, double-blind phase II/III trial (NCT02740231), eligible participants were 50-79-year-old men and women with primary knee OA classified with Kellgren-Lawrence grade II or III and a body mass index (BMI) under 35. 164 patients were randomly assigned to one of the three JTA-004 formulations or the reference treatment (Hylan G-F 20) in a 1:1:1:1 ratio. The three JTA-004 formulations differed in their clonidine concentration (50 or 100 µg/ml) and/or their volume of injection (2 or 4 ml) (Table 1). Patients were evaluated using Western Ontario McMaster Universities (WOMAC®) scores and Short-Form health survey (SF-12). The primary efficacy endpoint was the change from baseline at 6 months in WOMAC® VA3.1 Pain Subscale. Safety was assessed by monitoring and reporting vital signs, physical examination, adverse events and concomitant medications throughout the study.

Table 1. Description of the three JTA-004 formulations administered

JTA-004 formulation	Plasma protein solution		Clonidine		HA		Volume of
	Concentration	Amount	Concentration	Amount	Concentration	Amount	injection
JTA-100/2	1.02 g/ml	2.04 g	50 µg/ml	100 µg	10 mg/ml	20 mg	2 ml
JTA-200/2	1.02 g/ml	2.04 g	100 µg/ml	200 µg	10 mg/ml	20 mg	2 ml
JTA-200/4	1.02 g/ml	4.08 g	50 µg/ml	200 µg	10 mg/ml	40 mg	4 ml

Results: At 6 months, patients in the three JTA-004 groups showed a better improvement in pain compared to patients in the reference group. The between-group difference (between each JTA-004 test group and reference group) in adjusted (adapted to difference in baseline values) mean change in WOMAC® Pain Subscale Score from baseline ranged between -9.49 mm and -11.63 mm at 6 months post-injection. Statistical superiority of each JTA-004 formulation over Hylan G-F 20 was however not demonstrated (p-value between 0.052 and 0.141) (Figure 1, *JTA 200/2, 100/2 and 200/4*). As the three JTA-004 formulations had a similar efficacy in terms of pain reduction, a *post hoc* analysis was subsequently performed between the pooled JTA-004-treated patients and the reference group. This analysis showed a 26.1 ± 2.4 (adjusted mean ± SE) mm improvement in pain in the pooled JTA-004 group vs. 15.6 ± 4.1 mm in the reference group at 6 months, demonstrating a statistically significant superiority of JTA-004 over the reference (between-group difference = -10.57; p = 0.030) (Figure 1, *pooled JTA*).

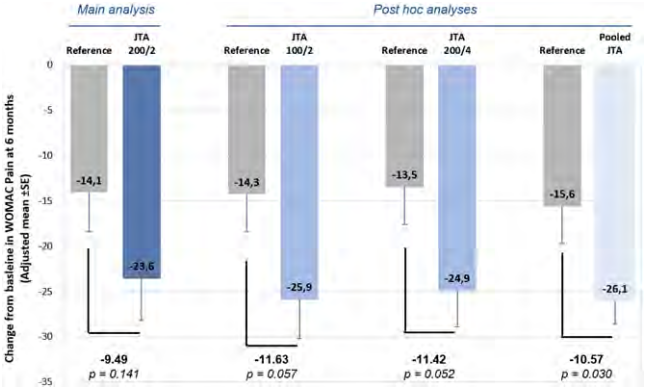


Figure 1. *Main and post hoc analyses.*

All JTA-004 formulations were shown to be well tolerated and had a clinically acceptable safety profile. There was a trend for fewer treatment-related events in the JTA-100/2 group, notably no cases of post-injection mild and transient hypotension.

Conclusion: This study provides a first evidence of efficacy and safety of JTA-004 in the treatment of knee OA pain.

Disclosure of Interests: Marie Bettonville Employee of: Bone Therapeutics, Marc Leon: None declared, Joëlle Margaux: None declared, Didier Urbin-Choffray: None declared, Emilie Theunissen: None declared, Tatiana Besse-Hammer: None declared, Yves Fortems: None declared, Séverine Verlinden: None declared, Olivier Godeaux Consultant of: Bone Therapeutics, Anne-Sophie Delmarcelle Employee of: Bone Therapeutics, Jean-François Kaux Consultant of: Bone Therapeutics

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FRI0401 **IMPLEMENTATION OF NICE GUIDELINES FOR OSTEOARTHRITIS IN PRIMARY CARE. FEASIBILITY STUDY OF JIGSAW-E IN SCOTLAND**

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Background: In the UK osteoarthritis (OA) is a common musculoskeletal problem with 8.75 million people seeking treatment in 2015[1]. Evidence-based guidelines are available for the management of OA but implementation into routine daily practice remains complex. The Joint Implementation of Guidelines for Osteoarthritis in Western Europe (JIGSAW-E) model of care was developed and evaluated in England and implemented in Europe with an aim to optimise quality primary care for OA, support self-management and promote use of NICE guidelines[2]. The intervention includes:

1. An OA guidebook for patients
2. A model OA consultation for primary care
3. Training for practitioners to deliver the model consultation
4. Measures of quality care using an e-template

Objectives: To explore the feasibility of implementing the JIGSAW-E model to support people with OA in Scottish primary care.

Research questions were informed by the Theoretical Domains Framework with an aim of:

1) Exploring knowledge and beliefs about OA and its management in primary care.
2) Identifying determinants for change; barriers and facilitators to implementing the JIGSAW-E model in Scotland.

Methods: This qualitative study was comprised of 2 phases:

Phase 1 included semi-structured interviews with health professionals (GPs and Extended Scope Practitioners) working in primary care. A purposeful sampling approach aimed to provide geographical and professional representation across Scotland. Interviews were recorded, transcribed and analysed using a theoretically-informed thematic framework approach.

Phase 2 involved an engagement workshop that allowed for refinement and direct validation of emergent findings.

Results: 90 invitations were sent to practice managers in primary care. 14 participants from 10 practices across 6 Health Boards in Scotland were recruited for interviews, including 6 GPs and 8 Physiotherapy Extended Scope Practitioners (ESPs). 23 participants attended the engagement workshop (ESPs = 22, GPs =1). Thematic analysis indicated four main themes related to the research questions:

1) Most participants were aware of NICE guidelines and believed they provided evidence-based OA care, and yet, for example, prescribing of co-codamol remained high. Physiotherapy ESPs were more likely to follow OA guidelines than GPs.
2) Adaptations of the JIGSAW-E model are needed to support OA management in the Scottish context. For example, in addition to adapting the guidebook for local relevance, the e-template was met with resistance due to technological barriers.
3) System-based barriers to implementation of the JIGSAW-E model included; lack of overall time for external training for practitioners; limited time in GP/patient appointments to consult and explain medication use and importance of physical activity. In part because patients usually present with multi-morbidities.
4) The roll out of ESPs across Scotland in primary care provides a potential key for the delivery of sustainable evidence-based care in the Scottish health system.

Conclusion: Overall, participants were in favour of the JIGSAW-E model in Scotland. Contextual adaptation of written materials would increase acceptance, ownership and usability by both practitioners and patients. The evolving role of GPs and ESPs is key to implementation, where ESPs provide leadership in the delivery of evidence-based care for patients with osteoarthritis.

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FRI0402 **MAGNETIC RESONANCE IMAGING EVALUATION OF CARTILAGE EROSION AND LIGAMENT INTEGRITY IN EARLY STAGE THUMB CARPOMETACARPAL JOINT OSTEOARTHRITIS**

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Background: Most of the studies on pathogenesis of thumb carpometacaral joint (CMCJ-1) osteoarthritis were from cadavers or patients with advanced osteoarthritis, therefore the findings may not reflect any early changes of cartilage wear and ligament condition.

Objectives: We evaluated MRI to address where articular degeneration begins and which ligaments are most often involved in the early clinical stage CMCJ-1 osteoarthritis.

Methods: We retrospectively analyzed MRI examinations of 26 patients with early clinical stage CMCJ-1 osteoarthritis without radiologic abnormality and 19 control patients without CMCJ-1 pain or osteoarthritis who underwent MRI for dorsal or ulnar wrist pain. Two independent and blind observers assessed chondral defect of the CMCJ-1 divided into four quadrants: volar-ulnar (VU), volar-radial (VR), dorso-ulnar (DU), and dorso-radial (DR). They assessed the integrity of the four major ligaments of CMCJ-1: the anterior oblique ligament (AOL), the intermetacarpal ligament (IML), the posterior oblique ligament (POL), and the dorsal radial ligament (DRL). The prevalence of cartilage lesion and ligament abnormality between the osteoarthritic and control patients was compared using Fisher's exact test.

Results: Cartilage lesion was significantly more common in the VU quadrant of the trapezium in the osteoarthritic patients than in the control patients (17/26 vs. 2/19; P = 0.002). AOL abnormality was more common in the osteoarthritic patients than in the control patients (14/26 vs. 3/19; P = 0.009). In the osteoarthritic patients, 10 of 17 patients with VU quadrant cartilage erosion had AOL rupture, while four of nine patients without VU cartilage erosion had AOL rupture, thus there was no association between VU quadrant erosion and AOL rupture (10/17 vs 4/9, P = 0.484).

Conclusion: MRI evaluation of early clinical CMCJ-1 osteoarthritis commonly demonstrate cartilage lesion in the VU quadrant of the trapezium and ligament abnormality in the AOL. However, no association of cartilage erosion in the VU region and AOL rupture suggests that AOL rupture is not a mechanical factor leading to TMCJ osteoarthritis in specific area, but a common finding secondary to arthritic changes.

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FRI0403 **CLINICAL FEATURES OF PROSTHETIC JOINT INFECTIONS DIFFER IN PATIENTS WITH INFLAMMATORY ARTHRITIS AND OSTEOARTHRITIS**

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Background: Inflammatory arthritis (IA) patients are at increased risk for prosthetic joint infections (PJI). However, because active IA patients without infections can have elevated inflammatory markers that mimic joint infection, PJI diagnosis is challenging in this population.

Objectives: We used an institutional PJI registry to identify and compare the clinical, microbiologic, and histopathologic features of culture positive (CP) and culture negative (CN) total hip and knee PJI in IA and OA patients. We

also evaluated the relationship between culture positivity, IA, and clinical outcomes.

Methods: A retrospective cohort of THA/TKA PJIs, from 2009 to 2016, were identified by ICD codes, and confirmed by chart review. IA diagnosis was also confirmed by use of IA-specific medications. CN cases were defined as PJIs with no evidence of microbial growth in intraoperative cultures and CP PJI cases were defined by positive microbial growth in intraoperative cultures. Treatment failure was defined as subsequent surgical treatment for infection after the initial infection surgery. H&E slides of OA and IA PJI cases matched by age (+/-5) sex, and culture status were reviewed by a pathologist for evidence of the histopathologic features listed in Table 2. Fisher's exact test, chi-square test, and Kaplan-Meier estimates were used.

Results: 807 PJI cases were identified including 36 IA (33 RA and 3 SLE) and 771 OA. A higher proportion of IA PJI were CN (N=10, 27%) vs. OA PJI (N=109, 14%, p=0.02). IA-PJI were younger, female, on glucocorticoids, and with more comorbidities. Type of surgical treatment did not differ significantly between IA and OA groups. Comparing CN-IA vs. CP-IA, no difference was observed in age, smoking, diabetes, surgical treatment, IA-specific meds or Charlson comorbidities. One-year survivorship of CN-IA and CN-OA were 66% and 87% (p>0.05). Across all CP cases, 57% were staphylococcal, with no differences between groups. Treatment failure was more frequent for CP-IA (42%) compared to CP-OA (30%), (p=0.2).

Histopathology of 88 PJIs (31 IA and 57 OA) was reviewed. The IA cohort presented with more chronic inflammation (p=0.001) than the OA cohort. Within the IA cohort, a higher proportion of CP-IA had >10PMN per HPF (p= 0.003) and met MSIS criteria (p=0.009). Comparing CP-OA and CN-OA, there were no significant differences in histopathology findings or number of patients meeting MSIS criteria.

Conclusion: IA PJIs are more likely to be culture negative than OA PJIs. Although our analysis was limited by our cohort size, our findings including differences in histopathology, and better clinical outcomes suggest the presence of biologic differences between CN and CP PJI that require further study.

TABLE 1. Patient characteristics in IA and OA PJIs

	IA		OA		
	N	%/SD	N	%/SD	p-value
Total	36		771		
Age	58.5	11.4	66.8	12	<.001
BMI	30.2	6.7	30	6.7	0.861
Female	28	77.8	332	43.1	<.001
CCI	2.8	1.7	1.7	2.1	0.002
Smoking	4	11.1	86	11.2	0.792
Glucorticoids	10	27.8	39	5.1	<.001
Culture Negative	10	27.8	109	14.1	0.024
Treatment Success at 2 years	19	52.8	509	66	0.146

IA- inflammatory arthritis; OA – osteoarthritis; PJI -prosthetic joint infection; CCI – Charlson Comorbidity Index

TABLE 2. Histopathology and clinical presentation in IA and OA PJIs

	OA (N=57)	IA (N= 31)		CP-IA (N=23)	CN-IA (N=8)	
	N (%)		p-value	N (%)		p-value
Pathology Review						
>10 PMN per HPF	42 (74)	22 (71)	0.806	20 (87)	2 (25)	0.003
Chronic Inflammation	13 (23)	23 (74)	0.001	18 (78)	5 (63)	0.393
Necrosis	17 (30)	9 (29)	1	8 (35)	1 (13)	0.38
Clinical Presentation						
MSIS	50 (88)	26 (84)	0.747	22 (96)	4 (50)	0.009
Sinus Tract	7 (12)	7 (23)	0.233	5 (22)	2 (25)	1
Elevated ESR or CRP	41 (72)	24 (77)	0.622	17 (74)	7 (88)	1
Elevated Synovial WBC	33 (58)	19 (61)	0.823	13 (57)	6 (75)	1
Elevated Synovial %PMN	31 (54)	20 (65)	0.377	14 (61)	6 (75)	0.333

OA – osteoarthritis; IA – inflammatory arthritis; CP – culture positive; CN – culture negative; MSIS – meets Musculoskeletal Infection Society diagnostic criteria

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FRI0404

SEPERATION OF HIGH AND LOW RESPONSE GROUPS IN OSTEOARTHRITIS USING SERUM CARTILAGE DEGRADATION AND FORMATION MARKERS – A 3 YEAR FOLLOW-UP ON THE FORWARD STUDY TESTING THE EFFICACY OF SPRIFERMIN

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Background: In osteoarthritis (OA), response to different interventions could be more pronounced in different endotypes of cartilage turnover. Data from UK biobank suggest that an endotype of low cartilage repair is associated with structural progression in osteoarthritis (OA)[1]. Sprifermin a truncated and recombinant FGF18 have been shown to induce chondrocyte proliferation and cartilage formation in in vitro settings[2–4]. Efficacy on cartilage thickness in OA was recently demonstrated in the FORWARD study[5].

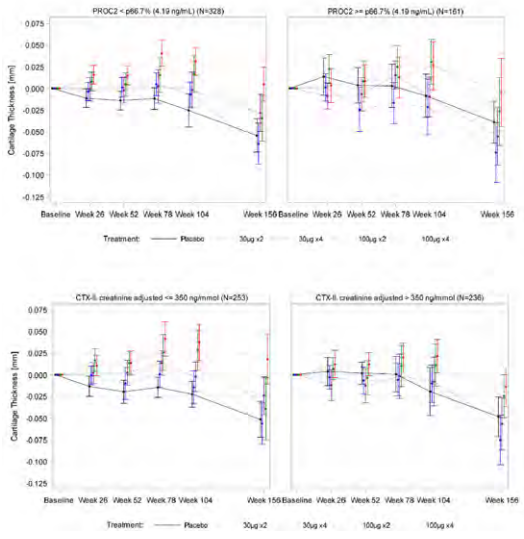
Objectives: We investigated markers of cartilage formation (serum PRO-C2) and degradation (urine CTX-II), to assess profiles indicative of chondrocyte metabolic activity would be associated with both structural and symptomatic responses to sprifermin.

Methods: Serum and urine from participants of the FORWARD study, a phase II clinical trial testing the efficacy of intra-articular (IA) sprifermin, were collected throughout the study. Clinical data recorded at baseline, year 2 and year 3 follow-up were used, including cartilage thickness and WOMAC. All available baseline samples of the placebo and treatment arms were assessed for serum PRO-C2 and urinary CTX-II. Patients were separated into dichotomized groups based on 33, 50 or 66 percentiles cut-points and two-year treatment responses were compared in a prospective-retrospective statistical design manner.

Results: Patients with low baseline PRO-C2 (<66%), in the 100ug/4x treatment arm, had greater difference to placebo in cartilage thickness as compared to the high PRO-C2 and all-comers groups (0.06 vs 0.03 and 0.05 mm, respectively) at two and three years (Fig.). Similar effect was seen for low CTX-II (<50%) (0.07 vs -0.03 and 0.05 mm, respectively). In addition, the WOMAC placebo effect was reduced in the low PRO-C2 and the low CTX-II groups, resulting in a difference compared to placebo of -0.81vs. 1.35 (low vs high proC2 and -2.35 vs 1.47 (low vs high CTX-II).

Conclusion: We noticed that low baseline PRO-C2 and CTX-II indicative for low metabolic activity of chondrocytes were associated with improved symptomatic outcome and slightly increased cartilage thickness compared to high metabolic activity. The parallelism between PRO-C2 and CTX-II point towards the existence of a low cartilage repair endotype and might reflect a subgroup of patients with higher sensitivity towards interventions - an effect that was maintained over three years.

Fig. 1: Longitudinal change in cartilage thickness (mm) in the total femorotibial joint in patients with low and high levels of PRO-C2 (top panel) and CTX-II (lower panel). Data are shown as mean with 95% CI of absolute change from baseline up to 3 Years.



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Disclosure of Interests: Hans Gühring Employee of: Merck KGaA, Anne-Christine Bay-Jensen Shareholder of: Nordic Bioscience A/S, Employee of: Full time employee at Nordic Bioscience A/S., Flavie Moreau Employee of: Merck KGaA, Jeppe Ragnar Andersen Shareholder of: Nordic Bioscience A/S., Employee of: Full time employee of Nordic Bioscience., Asger Reinstrup Bihlet Shareholder of: Nordic Bioscience A/S., Morten Karsdal Shareholder of: Nordic Bioscience A/S., Employee of: Full time employee at Nordic Bioscience A/S.
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FRI0405 CARTILAGE BIOMARKERS S-COLL2-1 AND S-COLL2-1NO2 ARE HELPFUL IN IDENTIFYING KNEE OSTEOARTHRITIS PATIENTS AT RISK OF DISEASE WORSENING

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Background: Coll2-1 is a peptide of 9 amino acid located in the triple helix of type II collagen molecule reflecting cartilage degradation (1). Coll2-1NO2 is the nitrated form of Coll2-1 and considered as a biomarker of the inflammatory-related cartilage degradation (2). This peptide is involved in osteoarthritis physiopathology since it was demonstrated that Coll2-1 induced synovitis in rat.
Objectives: To identify if biochemical markers s-Coll2-1 and s-Coll2-1NO2 are associated to knee osteoarthritis (OA), focusing on pain, function as well as structural features assessed by MRI in various knee compartments and to assess their ability at predicting knee OA worsening.
Methods: 116 subjects with knee OA were followed during one year with pain, function and MRI evaluation (PRODIGE study, NCT02070224). Type II collagen-specific biomarker Coll2-1 and its nitrated form Coll2-1NO2 were directly measured in serum using immunoassays at baseline and after three, six and twelve months follow-up.
Results: sColl2-1 and sColl2-1NO2 were associated to several baseline knee features quantified with Whole-Organ Magnetic Resonance Imaging Score (WORMS). S-Coll2-1 was significantly correlated with bursitis (r=0.29, P<0.01), bone attrition (r=0.25, P=0.01), cysts (r=0.24, P=0.02) and cartilage (r=0.23, P=0.03) WORMS sub-scores for the whole joint as well as with the medial femorotibial joint sum score (r=0.26, P=0.01) and medial femorotibial joint cartilage (r=0.23, P=0.02). s-Coll2-1NO2 was correlated with WORMS total score (r=0.23, P=0.02), WORMS scores in the patellofemoral (r=0.23, P=0.02) and medial femorotibial compartments (r=0.21, P=0.03) and with osteophytes scores (r=0.27, P<0.01). Baseline s-Coll2-1NO2 was higher in subjects with a pain worsening (426.4 pg/mL [278.04-566.95]) as compared to non-progressors (306.84 [200.37-427.84]) over one year (AUC=0.655, P=0.015).
Conclusion: Cartilage biomarkers s-Coll2-1 and s-Coll2-1NO2 are associated to several knee OA features quantified with WORMS scoring system on MRI. Serum values of Coll2-1NO2 are also associated to a worsening of target knee pain over one year. Coll2-1 and Coll2-1NO2, in association with other structural features, pain and function, could help at identifying OA phenotypes and patients at risk of OA worsening.
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Acknowledgments: PRODIGE study (NCT02070224) was performed in the framework of a convention between the Walloon region and ARTIALIS SA. (convention n°6905).
Disclosure of Interests: Yves Henrotin Grant/research support from: HEEL, TILMAN, Berenice Costes Employee of: Artialis SA, Michel Malaise: None declared, Damien Loeuille: None declared, Thierry Conrozier Consultant of: LABRHA, SANOFI, MEDAC, Yves Maugars: None declared, Franz Pelousse Shareholder of: Sodiray, Jean-Marc Lemaire Shareholder of: Sodiray, Thibault Helleputte Shareholder of: DNAlytics, Cedric Tits Employee of: DNAlytics, Elisabeth Cobraiville Employee of: Artialis SA, Sebastien Pirson Employee of: Artialis, Laetitia Garcia Employee of: Artialis, Alain Labasse Employee of: Artialis SA, Anne-Christine Hick Employee of: Artialis SA
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FRI0406 CARTILAGE REPAIR ACTIVITY DURING JOINT-PRESERVING TREATMENT MAY BE ACCOMPANIED BY OSTEOPHYTE FORMATION

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Background: Knee joint distraction (KJD) is a joint-preserving treatment to postpone total knee arthroplasty (TKA) and has shown cartilage repair and clinical improvement in patients with severe knee osteoarthritis (OA), as has high tibial osteotomy (HTO). The observed cartilage repair activity could be related to an increase in transforming growth factor-β1 (TGFβ-1), which increases in the synovial fluid (SF) during KJD treatment.[1] However, animal and ex vivo human studies have shown that TGFβ-1 also induce formation of osteophytes, generally seen as an OA severity hallmark. Similarly, interleukin-6 (IL-6) was observed to increase in SF during KJD treatment and may also be associated with osteophytosis.
As such, we hypothesized that joint-preserving regenerative treatments demonstrating cartilage repair activity lead to general tissue (re)generation, including osteophytosis.
Objectives: To analyze osteophytosis after KJD and compare this to HTO and natural progression in knee OA.
Methods: 63 KJD patients were included in several clinical trials, one of which was a randomized controlled trial comparing patients indicated for HTO, but treated with KJD (KJD_{HTO}; n=23) vs. patients treated with HTO (n=46). All patients received standardized radiographs before and one and two years after treatment, used to measure osteophyte size. Only patients with measurements at baseline and two-year follow-up were included. As a control group for natural progression, untreated knee OA patients from Cohort Hip & Cohort Knee (CHECK; n=1002) were studied. Only patients who received a TKA during follow-up were included, using their last two measurements before treatment to reflect natural two-year progression (n=44).
A separate group of 20 patients treated with KJD in regular care underwent SF aspirations before and after treatment, and TGFβ-1 and IL-6 levels were measured by immunoassay (Mesoscale Discovery). Unstandardized radiographs were acquired before and one year after treatment, used to score osteophytes with the revised Altman score, resulting in a 0 (normal) to 12 (severe) whole-joint score. Only patients with radiographs and SF aspirations at both baseline and one-year follow-up were included.
Results: After two years, both KJD (n=58) and HTO (n=38) patients showed a significant increase in osteophyte size (+6.2mm2 and +7.0mm2 resp.; both p<0.003; figure 1), with no significant differences between the treatments (p>0.38). Untreated CHECK patients who underwent TKA did not show significant two-year osteophyte changes before treatment (+2.1mm2; p=0.207; figure 1) and showed significant differences compared with KJD and HTO groups (both p<0.044). In the KJD SF aspiration group (n=17), the Altman osteophyte score was not different at one year compared to baseline (+0.2 points; p=0.653) and there was no association between baseline biomarker values and the baseline Altman osteophyte score, or between changes in these parameters (all p≥0.28). Trichotomization of patients in groups with a decrease, no change or increase in total Altman osteophyte score indicated that there was a statistically significant difference between the three groups in changes in TGFβ-1 (p=0.044; figure 2A), but not IL-6 (p=0.898; figure 2B).
Conclusion: After KJD treatment, joint space widening and clinical improvement are accompanied by osteophytosis. Similar results were observed after treatment with HTO, suggesting effects occur in regenerative joint-preserving

treatments in general. The increased osteophytosis may be a bystander effect of cartilage repair activity related to intra-articular factors like TGFβ-1 and questions whether osteophytosis should necessarily be considered a hallmark of OA worsening.

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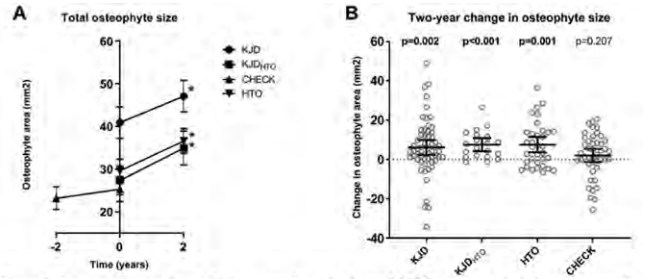


Figure 1: Two year changes in total joint osteophyte size in mm². (A) Osteophyte size after treatment for all patients treated with knee joint distraction (KJD), high tibial osteotomy (HTO), HTO-indicated KJD patients (KJD_{HTO}), and for untreated knee osteoarthritis patients before receiving a total knee arthroplasty (CHECK). Mean and standard error of the mean (SEM) are shown, * indicates significant changes ($p<0.05$) compared to baseline. (B) Two-year osteophyte size changes for individual KJD, HTO, KJD_{HTO} and CHECK patients. Mean and 95% confidence interval are shown, p-values above groups indicate significance of two-year changes.

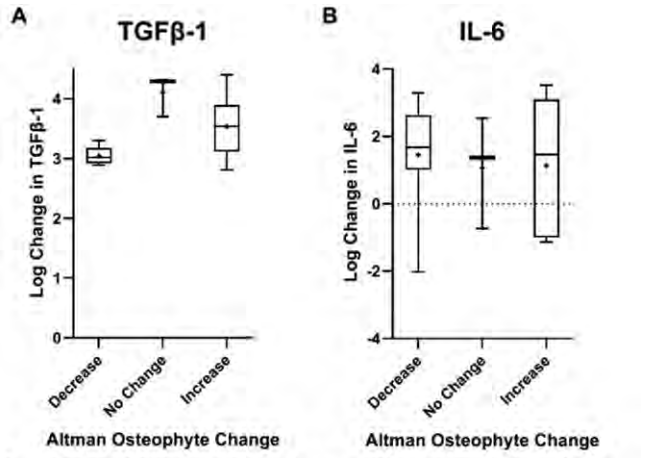


Figure 2: Box plots for the changes in synovial fluid concentrations during treatment with knee joint distraction, of (A) transforming growth factor-β1 (TGF-β1) and (B) interleukin-6 (IL-6), categorized into groups of patients with a decrease, no change or increase in total Altman osteophyte score. The bar represents the median, whiskers represent the minimum and maximum value, the + represents the mean.

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FRI0407

USER-FRIENDLINESS OF A NOVEL DEDICATED KNEE JOINT DISTRACTION DEVICE: EXPERIENCES FROM CLINICAL PRACTICE

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Background: Knee joint distraction (KJD) is a validated surgical technique that aims to postpone arthroplasty for a prolonged time in younger knee osteoarthritis (OA) patients (<65 years). In absence of dedicated devices intended for KJD, this procedure has thus far been performed with general purpose external fixation devices.[1] The demonstrated clinical benefits of KJD raised a clinical demand for a dedicated device (DD), including a desire for increased user-friendliness and decreased treatment burden. As such, in a multi-disciplinary setting with clinicians, patients, and medical device experts, several desired device characteristics were determined. These included perpendicular positioning of bone pins relative to the longitudinal tibia axis, surgery time < 45 minutes, no protruding parts above the most proximal and below the most distal bone pins, and pin tracts that are accessible for pin tract care. Based on the desired characteristics, a dedicated distraction device was developed and made available for clinical application.

Objectives: To compare user-friendliness between the developed DD and previously used concept device (CD) used in regular care.

Methods: Patients were treated with either the CD (n=22) or DD (n=22) in clinical practice. For both devices, the surgical technique was identical: fixation to the tibia and femur with 8 bone pins (figure 1) and 5 mm distraction for 6 weeks. The intervention duration when placing the device (defined as time between first incision and the surgeon being finished) was registered for all patients. After treatment, patients were asked to fill out a custom questionnaire about user-friendliness of the device during treatment, consisting of 25 questions on difficulties performing activities regarding clothing, sleeping, device care, daily activities, movement and complications. Intervention duration was compared between groups using an independent t-test while for questionnaire answers Mann Whitney U tests were used. Chi-square tests were used when comparing (complication) occurrences between groups.

Results: Intervention duration was on average shorter for the DD (44 vs 56 minutes; p<0.001). 34 Patients (16 CD, 18 DD) completed the questionnaire. Patient user-friendliness of the DD was higher rated for 6 questions (all p<0.05), and similar to the CD for the remaining questions (all p>0.01). Besides advantages in daily living activities with the use of the DD, also less pin tract infections were registered with this device (88% of patients with CD vs 56% with DD). Results of all questions are provided in figure 1. Three patients who were treated with both devices (left and right knee, separately and subsequently) generally rated the DD similar to be or slightly better than the CD.

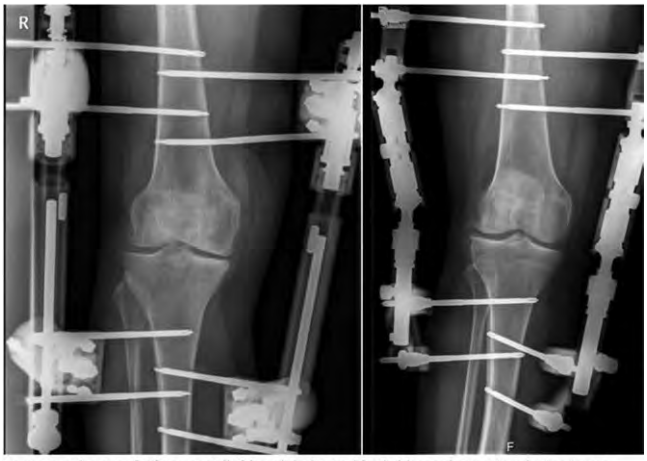


Figure 1: The proof-of-concept (left) and dedicated (right) knee distraction device in use

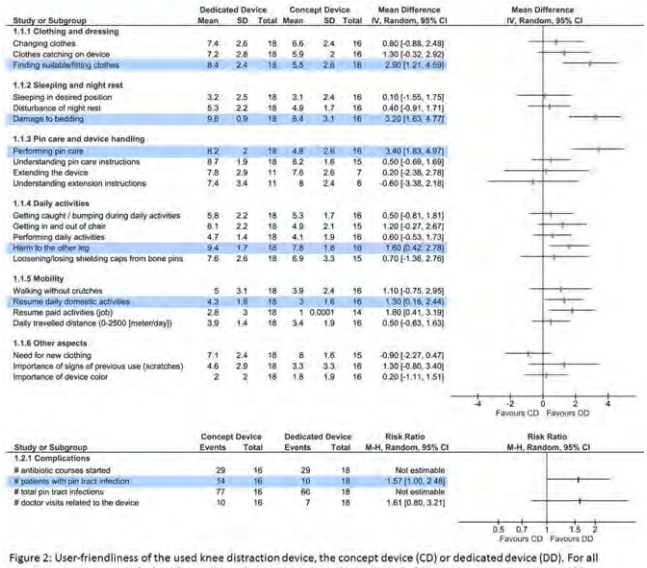


Figure 2: User-friendliness of the used knee distraction device, the concept device (CD) or dedicated device (DD). For all questions, 10 represents the best (most desired) answer. Statistically significantly different parameters are marked blue. SD: standard deviation; CI: confidence interval.

Conclusion: The dedicated KJD device provides user-friendly equipment for clinicians and patients, as indicated by the shorter intervention duration and patient questionnaire outcomes, and contributes to further implementation of KJD as treatment for end-stage knee OA.

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FRI0408

KNEE JOINT DISTRACTION AS TREATMENT FOR OSTEOARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Knee osteoarthritis (OA) is a common cause of invalidity and is often treated with a total knee arthroplasty (TKA). While TKA is cost-effective, reduces pain and improves function, it brings a greater risk of a future revision surgery when performed in younger patients. Knee joint distraction (KJD) is a joint-preserving OA treatment that may postpone TKA and possibly prevent a revision. In the past years, multiple studies have investigated this surgical treatment.

Objectives: To evaluate short- and long-term clinical benefit and tissue structure changes after KJD treatment for knee OA.

Methods: MEDLINE, EMBASE and Web of Science were searched for eligible clinical studies evaluating a change in at least one of: Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Visual Analogue Score of pain (VAS-pain), Knee injury and Osteoarthritis Outcome Score (KOOS), EuroQol-5D (EQ5D), radiographic joint space width (JSW) or MRI cartilage thickness after KJD. The primary clinical and structural outcome parameters were the WOMAC and minimum JSW, respectively. Random effects models were applied on all outcome parameters and outcomes were compared with control groups found in the included studies. For continuous data the mean difference (MD) and 95% confidence interval (95%CI) were calculated and for dichotomous data the risk difference and 95%CI, following the Cochrane handbook.

Results: In total 11 articles reporting on 7 different KJD cohorts with in total 127 patients and 5 control groups at multiple follow-up moments were included, with 2 of the studies being randomized controlled trials (RCTs). The WOMAC (figure 1) was compared to pre-treatment in 3 cohorts after 1 year (patients n=62) and 2 years (n=59) and in 1 cohort after 5 years (n=20) and 9 years (n=8), showing a significant increase at all time points (all p<0.001). The VAS-pain showed similar results at the same 4 time points, as did the KOOS and EQ5D, which were evaluated only after 1 (n=42) and 2 (n=39) years.

The minimum (figure 2) and mean JSW are reported in 3 cohorts after 1 (n=59) and 2 (n=59) years and in 1 cohort after 5 (n=20) and 7 (n=8) years. Both JSW measures were statistically significantly increased after 1 and 2 years, but after 5 and 7 years the JSW increase was no longer statistically significant. Similarly, the MRI cartilage thickness showed an increase at 1 and 2 years, but not at 5 years (all n=20).

Complications were reported in 5 studies with 87 patients, with 57 patients developing one or more pin tract skin infections, giving a risk of pin tract infections of 63% (95%CI 45-81), the majority of which could be treated with oral antibiotics. Only a small amount of other complications occurred and were all treated successfully.

Overall, clinical and structural outcomes were comparable with control groups, including high tibial osteotomy and TKA as compared after 1 and 2 years in the two RCTs. Apart from pin tract infections, complications were not different in severity and number between control groups and KJD.

Conclusion: KJD causes clear benefit in clinical and structural parameters over time, short- and long-term. Although the total number of patients is limited, effect sizes are large. Longer follow-up with more patients is necessary and could improve patient selection for this intensive treatment, while preventing pin tract infections could lighten the patients' treatment burden. Irrespectively, KJD provides an additional option in joint-preserving treatments for OA and a viable alternative to joint replacement, especially in younger patients.

Figure:

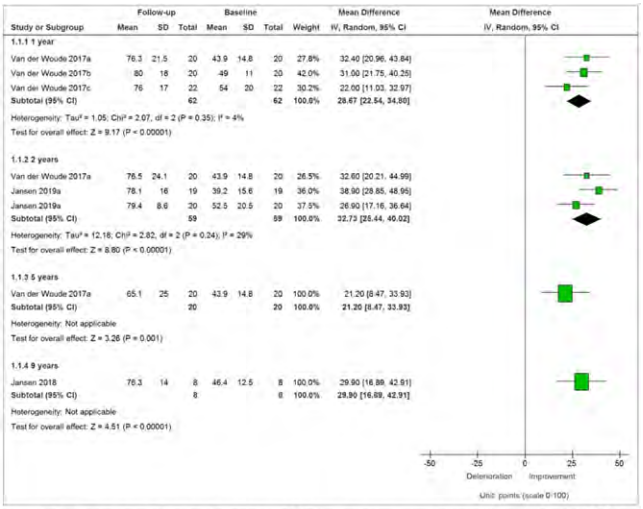


Figure 1: Change in total Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score 1, 2, 5 and 9 years after treatment with knee joint distraction.
References can be used multiple times because of division in patient cohort and years of follow-up. SD: standard deviation; CI: confidence interval.

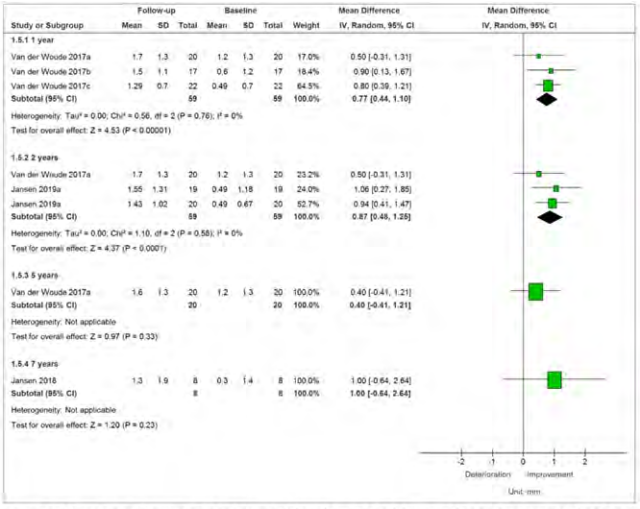


Figure 2: Change in minimum joint space width (JSW) 1, 2, 5 and 7 years after treatment with knee joint distraction.
References can be used multiple times because of division in patient cohort and years of follow-up. SD: standard deviation; CI: confidence interval.

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FRI0410

PREVALENCE AND FACTORS ASSOCIATED WITH CHRONIC PAIN WITH NEUROPATHIC CHARACTERISTICS IN PATIENTS WITH KNEE OSTEOARTHRITIS IN CAMEROON, SUB-SAHARAN AFRICA

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Background: Recent studies suggest that pain in osteoarthritis (OA) is not only nociceptive, but also has neuropathic characteristics (1). To our knowledge, no study has been carried out in sub-Saharan Africa to assess the neuropathic pain associated with knee OA.

Objectives: To determine the prevalence of chronic pain with neuropathic characteristics and associated factors in patients with knee OA in Cameroon.
Methods: We performed a cross-sectional study at the Douala General Hospital from December 2018 to April 2019. Patients over the age of 21 with a diagnosis of knee OA (ARA, 1986; Kellgren–Lawrence radiographic grading ≥ 2) were included. The intensity of the pain was measured using the visual analog scale. Neuropathic pain was detected using the DN4 questionnaire with a cut-off at DN4 ≥ 4 (2) and functional impairment assessed using the Lequesne algofunctional index. Logistic regression analysis was used to assess the association between patients' characteristics and DN4. The p <0.05 was considered significant.
Results: We included 151 patients (120 women) with knee OA, mean age at 59.8 ± 12.8 years (31 to 86) years, with a mean duration of knee OA at 38 ± 44.9 months and a mean BMI at 30.4 ± 6.2 kg/m2.
The mean DN4 score was 2.5±2. It was higher in women compared to men (2.7 ± 2 vs. 1.9 ± 1.7; p = 0.04). Tingling (58.9%) was the most frequently encountered item in the DN4 questionnaire (Table 1). A DN4 ≥ 4 was found in 41 patients (27.1%). Patients with neuropathic pain (DN4 ≥ 4) were older (63.7 ± 10.6 years vs. 58.4 ± 13.2; p = 0.02) and had higher VAS pain (6.17 ± 1.6 vs. 5.02 ± 1.5; p < 0.01) than patients without neuropathic pain (DN4 < 4). In multivariate analysis, only the intensity of pain ≥ 70mm (OR = 2.1, 95%CI: 1.1–5.5; p = 0.02) and a Lequesne index ≥ 11 (OR = 2.4, 95% CI: 1.1–6.7; p = 0.04) were associated with neuropathic pain. Patient's age at diagnosis, sex, occupation, monthly income, radiological characteristics, BMI, joint effusion, duration of illness, and the existence of comorbidities such as low back pain, diabetes, or hypertension were not associated with the diagnosis of neuropathic pain (p<0.05).

Table 1. Frequency of items in the DN4 questionnaire

DN4 items			Frequency, n (%)
Interview of the patient	Question 1	Burning	58 (38.4)
		Painful cold	8 (5.3)
		Electric shocks	50 (33.1)
	Question 2	Tingling	62 (41)
		Pins and needles	89 (58.9)
		Numbness	68 (45)
		Itching	14 (9.2)
Examination of the patient	Question 3	Hypoesthesia to touch	16 (10.6)
		Hypoesthesia to pinprick	8 (5.3)
	Question 4	Brushing	22 (14.5)

Table 2. Univariate and multivariate logistic regression analysis of factors associated with neuropathic pain

Variables	CateLgory	Unadjusted OR	95% CI	*p*	Adjusted OR	95% CI	*P*
Age, year	<40	0.2	0-2.2	0.37			
	40-65	1.4	0.1-2.9	0.43			
	>65	0.5	0.2-1.1	0.14			
Sex	Female	2.2	0.7-6.2	0.18			
	Male	1					
Occupation	Student	1.3	0.1-15.3	1			
	Employed	3.1	1.3-6.9	0.008	1.4	0.3-4.4	0.54
	Unemployed	2.6	1.2-5.4	0.01	0.9	0-2.8	0.87
	Retired	1.1	0.4-2.9	1			
Education	Primary	0.59	0.2-1.3	0.27			
	Secondary	1.5	0.7-3.1	0.34			
	University	0.1	0-0.5	0.02	0.2	0-9	0.05
	Illiterate	0.53	0.1-2	0.56			
BMI	Normal	1.6	0.6-4.1	0.39			
	Overweight	1.8	0.8-4.2	0.2			
	Obesity	0.7	0.3-1.4	0.49			
Comorbidities	Hypertension	0.6	0.3-1.4	0.38			
	Diabetes	0.4	0.1-1.2	0.2			
	Low back pain	0.5	0.3-1	0.1			
	Joint effusion	1.1	0.5-2.9	0.96			
Pain, VAS	Mild pain	3.1	0.8-11	0.1			
	Moderate pain	1.6	0.7-3.3	0.25			
	Severe pain	0.2	0.1-0.6	<0.01	0.4	0.2-0.9	0.03
Disability	Moderate handicap	0.5	0.2-1.4	0.32			
	Severe handicap	1.3	0.7-2.9	0.48			
	Very severe handicap	0.3	0.1-0.6	<0.01	0.3	0.1-0.7	0.04
Kellgren – Lawrence radiographic grading	Grade 2	1.7	0.8-3.5	0.19			
	Grade 3	0.64	0.3-1.3	0.32			
	Grade 4	0.6	0.2-1.9	0.35			

Conclusion: Neuropathic pain exists during knee OA. We found it in 27.1% of patients followed in a hospital in Cameroon. It is associated with the severity of pain and functional disability.
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FRI0411

SAFETY, TOLERABILITY, PHARMACOKINETICS AND PHARMACODYNAMICS IN HEALTHY MALE JAPANESE SUBJECTS OF THE ADAMTS-5 INHIBITOR S201086/GLPG1972, A POTENTIAL NEW TREATMENT IN OA

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Background: The disintegrin and metalloproteinase with thrombospondin motifs-5 (ADAMTS-5) is a key enzyme in OA (Verma P, *et al.* J Cell Biochem 2011;112:3507-14). In preclinical models of OA, S201086, a potent and selective ADAMTS-5 inhibitor, protects from cartilage degradation (Clement-Lacroix, *et al.* Osteoarthritis Cartilage 2017;25:S58). Therefore, S201086 is co-developed by Servier and Galapagos (GLPG1972) as a potential new treatment in OA.
Objectives: This phase I study was to assess and compare the safety, tolerability, pharmacokinetics and pharmacodynamics of S201086 in healthy male Japanese and Caucasian subjects.
Methods: Six ascending single doses of S201086 (50 to 1500 mg) were administered orally as tablets in fasting conditions in 6 groups of 8 Japanese subjects (aged 20-45 years) and 3 ascending multiple doses (300, 600 or 1050 mg/day for 14 days) were administered orally as tablets in fed conditions in 3 groups of 8 Japanese subjects. Additionally, 2 cohorts of 8 Caucasian subjects received either a single oral dose of 300 mg or repeated oral dose of 300 mg once daily for 14 days. In each group, 6 subjects received S201086 and 2 placebo. Plasma was collected at several time points for the quantification of S201086 by LC-MS/MS. Plasma pharmacokinetic parameters were calculated via non-compartmental analysis using Phoenix® WinNonlin® software. Pharmacodynamics was assessed by measurement of the aggrecan ARGS neoepitope levels in serum by ELISA.
Results: No serious adverse drug reactions were observed after administration of single and multiple ascending doses of S201086 in either Japanese or Caucasian subjects. Most adverse events were of mild to moderate intensity and were resolved by the end of the study. Following single administration to Japanese subjects, Cmax and AUC increased proportionally with doses from 50 to 600 mg and slightly less than dose-proportionally from 600 to 1500 mg, consistent with what was previously observed in the first in-human study in healthy Caucasian subjects (van der Aar E, *et al.* Osteoarthritis Cartilage 2018;26:S310). In Japanese subjects, after 14-days administration, a limited 1.2- to 1.4-fold accumulation was observed on both Cmax and AUC at Day14 as compared to Day1, and the steady-state exposure increased dose-proportionally within the 300-1050 mg dose range. Taking the inter-subject variability into account, no difference was observed in Cmax and AUC between Caucasian and Japanese subjects after single administrations of 300 mg and repeated administrations of 300 mg once daily for 14 days. The serum ARGS neoepitope levels decreased between baseline and last day of treatment for S201086-treated subjects but not for subjects receiving placebo. This decrease was similar for the 3 tested doses in Japanese subjects and was significant as compared to the placebo-treated subjects.

Table. Comparison of ARGS concentration relative change from baseline to last day of treatment according to dose in Japanese participants

		S 201086 300 mg (N = 6)	S 201086 600 mg (N = 6)	S 201086 1050 mg (N = 6)	Placebo (N = 6)
Descriptive Statistics (D14 pre-dose – Baseline) / Baseline	n	6	6	4	6
	Mean ± SD	-42.67 ± 8.81	-53.70 ± 6.50	-54.11 ± 5.20	13.35 ± 16.53
Statistical analysis					
	E (SE)	56.01 (6.156)	67.04 (6.156)	67.45 (6.883)	
	95% CI	43.08; 68.95	54.11; 79.97	52.99; 81.91	
	p-value	< 0.0001	< 0.0001	< 0.0001	

Conclusion: S201086 was shown to be safe and well-tolerated in Japanese and Caucasian healthy male subjects with a suitable PK profile and a significant decrease of the ARGS neoepitope, indicating target engagement. A global Phase 2 study to evaluate the efficacy of S201086 in patients with knee OA is ongoing (NCT03595618).

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FRI0412 DOES SEVERE ACUTE POSTOPERATIVE PAIN RESULT IN MORE LONG-TERM PAIN AFTER TOTAL HIP OR KNEE ARTHROPLASTY (THA OR TKA) FOR OSTEOARTHRITIS?

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Background: Chronic pain is a frequently reported unfavourable outcome of total hip and knee arthroplasties (THA/TKA) (7-23% and 10-34%, respectively) in osteoarthritis (OA) patients (1), which is difficult to treat as underlying mechanisms are not fully understood. Acute postoperative pain has been identified as risk factor for development of long-term pain in other surgical procedures, such as mastectomy and thoracotomy (2). However, the effect of acute postoperative pain on development of long-term pain in THA and TKA patients is unknown.

Objectives: To investigate if acute pain following THA/TKA in OA patients is associated with long-term pain and if acute pain affects the course of pain up to 1-year postoperatively.

Methods: From a longitudinal multicenter study, OA patients scheduled for primary THA or TKA were included. Acute pain scores, using Numeric Rating Scale (NRS), were routinely collected as part of standard care (≤72 hours after surgery). In case of ≥2 NRS scores the two highest scores were averaged (n=160), else the single score was taken. Pain was dichotomized into severe (NRS≥5) and mild (NRS<5). Pain was assessed preoperatively, at 3 (only THA), 6 and 12 months postoperatively using HOOS/KOOS subscale pain. Separate mixed-effect models for THA and TKA patients were used, with dichotomized acute pain as fixed-effect and long-term pain as outcome, while adjusting for confounders (age, sex, BMI, preoperative pain, mental component scale of the SF12 (MCS-12), and duration of the surgery and hospitalization). We included an interaction between time of measurement and acute postoperative pain to analyse whether effect modification was present. Missing values in preoperative pain and MCS-12 were imputed using multiple imputation methods.

Results: 81 THA and 87 TKA patients were included, of whom 32.1% and 56.3% reported severe acute pain. The results did not show an associated between severe acute pain and long term pain (THA: β=2.0, 95%-CI:-10.9-7.0; TKA: β=3.8, 95%-CI:-10.6-2.9). Furthermore, It seems that there is no effect present of difference in severity of acute pain and the course of pain over time (THA 6-months: β=6.4, 95%-CI:1.9-10.9 and 12-months: β=0.2, 95%-CI:-4.4-4.8; TKA 12-months: β=3.2, 95%-CI:-0.5-6.8).

Conclusion: We did not find an association between acute pain and the development of long-term pain nor that severity of acute pain affects the course of postoperative pain in THA and TKA patients. The fact that THA and TKA patients often experience chronic preoperative pain might be a possible explanation for this finding. Nonetheless, future studies including additional measures of acute pain and pain sensitization in patients with chronic preoperative pain are necessary to draw stronger conclusions.

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FRI0413 THE ASSOCIATION OF OBESITY WITH OSTEOARTHRITIS IS LIMITEDLY MEDIATED BY HYPERTENSION AND SUBCLINICAL ATHEROSCLEROSIS

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Background: Obesity-related metabolic dysregulation may lead to atherosclerotic vascular changes. It has been hypothesized that a compromised blood flow may cause detrimental changes to the subchondral bone and decrease nutrient supply to the cartilage. To which extent atherosclerosis may explain the association between obesity and OA has not been investigated.

Objectives: To investigate the role of hypertension and subclinical atherosclerosis (carotid intima-media thickness (IMT), popliteal vessel wall thickness (VWT), aortic pulse wave velocity (PWV)) as mediators of the association of obesity with hand and knee OA.

Methods: We used cross-sectional data from the population-based NEO study, excluding participants with concomitant rheumatic diseases (n = 323), resulting in 6,334 participants. Clinical hand and knee OA were defined by the ACR classification criteria. Popliteal VWT was assessed on MR images in a subpopulation (n = 1,095), using VesselMASS for semi-automated detection of the vessel wall boundaries. Aortic PWV was estimated on abdominal velocity-encoded MR images in a subpopulation (n = 2,580). Carotid IMT was assessed by ultrasonography. Hypertension was defined as a systolic blood pressure ≥ 130 mmHg or a diastolic blood pressure ≥ 85 mmHg, or using antihypertensive medication. Continuous variables were standardized (mean 0, standard deviation 1). Associations between BMI and OA were assessed with logistic regression analyses, adjusted for age, sex and education. Subsequently, possible mediators were added to the model and the percentage mediation was calculated.

Results: The population consisted of 55% women, with a mean (SD) age of 56 (6) years and BMI of 26 (4) kg/m^2. Hand OA was present in 8% and knee OA in 10% of participants. Hypertension was present in 61.6% of participants. Mean (SD) carotid IMT was 0.62 (0.09) mm, popliteal VWT was 0.53 (0.05) mm, and aortic PWV was 6.56 (1.30) m/s. BMI was associated with the presence of hand OA and knee OA (table 1). BMI was positively associated with hypertension and carotid IMT, but not with popliteal VWT and aortic PWV. The association between BMI and hand OA was partially mediated by hypertension (5.9%) and carotid IMT (10.6%). Hypertension (4.9%) showed a weak mediating effect for the association between BMI and knee OA.

Table 1. Mediation of the association of BMI with OA by hypertension and atherosclerosis

	Hand OA OR (95% CI)	Mediator OR/β (95% CI)	Hand OA OR (95% CI)	Mediation % (95% CI)
BMI	1.21 (1.08; 1.36)	1.72 (1.56; 1.90)	1.20 (1.06; 1.36)	5.9 (3.4; 17.4)
Hypertension			1.15 (0.82; 1.60)	
BMI	1.21 (1.08; 1.36)	0.23 (0.19; 0.27)	1.19 (1.05; 1.34)	10.6 (6.2; 30.5)
Carotid IMT			1.09 (0.94; 1.25)	
BMI	1.56 (1.17; 2.08)	0.01 (-0.06; 0.09)	1.55 (1.16; 2.07)	0.5 (0.3; 1.7)
Popliteal VWT			1.14 (0.84; 1.55)	
BMI	1.41 (1.15; 1.73)	0.05 (-0.01; 0.11)	1.41 (1.15; 1.73)	0.7 (0.4; 2.0)
Aorta PWV			1.04 (0.81; 1.33)	
	Knee OA OR (95% CI)	**Mediator** OR/β (95% CI)	**Knee OA** OR (95% CI)	
BMI	1.46 (1.32; 1.62)	1.70 (1.55; 1.87)	1.43 (1.29; 1.59)	4.9 (3.7; 7.0)
Hypertension			1.25 (0.93; 1.67)	
BMI	1.46 (1.32; 1.62)	0.24 (0.20; 0.27)	1.47 (1.33; 1.62)	-1.6 (-2.4; -1.2)
Carotid IMT			0.97 (0.86; 1.09)	
BMI	1.20 (0.88; 1.64)	0.03 (-0.04; 0.11)	1.21 (0.89; 1.64)	-0.5 (-7.4; 13.3)
Popliteal VWT			0.95 (0.74; 1.24)	
BMI	1.37 (1.12; 1.67)	0.05 (-0.00; 0.11)	1.37 (1.12; 1.67)	-0.5 (-1.8; -0.3)
Aorta PWV			0.96 (0.76; 1.21)	

Results are based on analyses weighted towards the BMI distribution of the general population (n = 6,334). Analysis regarding popliteal VWT (n = 1,095) and aorta PWV (n = 2,580) were assessed in a subpopulation Continuous variables were standardized (mean 0, SD 1), SD BMI = 4.41, SD carotid IMT = 0.09, SD popliteal VWT = 0.05, SD aorta PWV = 1.30.

Conclusion: We assessed whether the association between BMI and OA was mediated by hypertension and atherosclerosis. Our results imply that either such mediation is absent or trivial, or that the atherosclerosis measures were too weak.
Disclosure of Interests: None declared
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FRI0414 FACTORS ASSOCIATED WITH THE IMPACT OF GONARTHROSIS ON MUSLIM PRAYER

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Background: Gonarthrosis is a frequent and chronic pathology, which can cause painful functional impotence and limit the performance of activities of daily living[1].
Objectives: This study aimed to assess the patient's perception of the physical and psychological repercussions of his illness on the practice of prayer and to determine the factors associated with this repercussion.
Methods: It was a cross-sectional prospective study conducted in the rheumatology department in 56 patients with gonarthrosis who regularly practiced prayer before the onset of the disease. The socio-demographic data, the clinical characteristics of gonarthrosis were studied and a pre-established questionnaire was offered to patients to assess the physical and psychological impact of gonarthrosis on their prayer practice.
Results: Fifty-six patients were included, 83.3% of whom were female. The average age was 56.1 years [38-78 years]. The disease has progressed for an average of 6.14 years [1-13 years]. Gonarthrosis was bilateral in 80.4% of cases. The average body mass index (BMI) was 30.29 kg / m^2 ± 3.061 with extremes ranging from 24 to 36 kg / m^2. Quadriceps (Q) retraction was noted in 64.28% of cases. Gonarthrisis was classified as stages I, II and III according to the classification of Kellegren and Lawrence in 14.3%, 57.1% and 28.6% of patients respectively.
In 71.4% of cases (40 patients), the practice of prayer after the onset of gonarthrosis was considered more difficult with a degree of difficulty of 4.23/10 ± 2. Initial standing was considered possible by all patients. Inclination was possible in 89.2% of patients, whereas it was replaced by sitting on a chair by the rest. Prostration and final sitting station were considered impossible by 64.3% of patients and were therefore performed on chairs (36 patients). The limiting factor cited by patients was pain in 100% of cases. A psychological impact was reported in 53.6% of cases. It was explained by the feeling of guilt in 22 cases, the relatives' comments in 8 cases and the suffering related to disability in 7 cases.
Prayer position was associated with Q retraction (p = 0.001) and knee pain seniority (6.81 ± 3.608vs4.95 ± 3.017, p = 0.05). The degree of difficulty was associated with the BMI (p = 0.013), knee pain seniority (p <0.001) and Q retraction (5.74 ± 1.851 vs 3.46 ± 1.789, p <0.001).
Conclusion: Prayer is an activity that is part of the daily lives of many Muslim patients, its evaluation should be considered as one of the elements of the quality of life and functional impact of gonarthrosis.
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Disclosure of Interests: None declared
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FRI0415 BODY MASS INDEX AND STATIC FOOT DISORDERS IN GONARTHROSIC PATIENTS

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Background: Several studies have shown that there is a link between body mass index (BMI) and painful foot imputed to a biomechanical change in foot structure [1].
Objectives: Our objective was to study the association between BMI and static foot disorders in gonarthrosic subjects.
Methods: It was a prospective descriptive study conducted in the rheumatology department of the Mohamed Kassab Institute of Orthopedics with 60 patients with Gonarthrosis. The socio-demographic data of the patients were studied. BMI was calculated for all patients. Static foot disorders have been studied.
Results: Sixty patients were included, 83.3% of whom were female. The average age was 55.2 years [38-78 years]. The disease has been evolving for an average of 6 years [1-13 years]. The lesion was bilateral in 80% of cases, the average body mass index was 30.4 kg / m2 [24-36]. Knee arthritis was classified as stage I, II and III according to the Kellgren and Lawrence classification in 18.5%, 55.6% and 25.9% of patients respectively. The foot examination involved 108 gonarthrosic limbs. Examination of the integuments showed hyperkeratosis in 94.4% of the cases (79.6% calluses and 83.3% callosities). Forefoot deformities were Hallux valgus (HV) in 52.8% of cases and overlapping toes in 18.5% of cases. Pronation deformity using the Foot Posture Index (FPI) was found in 51.9% of cases. Abnormal lowering of navicular bone was noted in 51.9%. The podoscopic impression revealed flat feet in 73.2% of the cases.
A statistically significant association was found between BMI and the presence of calluses (31.21 ± 2.897 vs26.83 ± 1.425, p <0.001), with HV (31.37 ± 3.086 vs29.49 ± 2.969, p = 0.002), at the overlap of the toes (33.2 ± 1.361vs29.86 ± 1.130, p <0.001), with the lowering of the navicular bone (31.17 ± 2.885vs29.68 ± 3.304, p = 0.015), FPI (p = 0.003) and flat podoscopic impression (p <0.001).
Conclusion: BMI is strongly associated with static feet disorders in gonarthrosic patients by aggravating the postural changes in the foot caused by knee osteoarthritis [2]. Obesity is associated mainly with the existence of flat feet, pronation of the foot, toes deformities and hyperkeratosis.
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FRI0416 COMBINATION OF SERUM ADIPOKINES/RELATED INFLAMMATORY FACTORS AND RATIOS AS PREDICTORS OF INFRAPATELLAR FAT PAD VOLUME IN KNEE OSTEOARTHRITIS PATIENTS: USAGE OF A COMPREHENSIVE MACHINE LEARNING APPROACH

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Background: One of the hurdles in osteoarthritis (OA) drug discovery and the improvement of therapeutic approaches is the early identification of patients who will progress. It is therefore crucial to find efficient and reliable means of screening OA progressors. Although the main risk factors, age, gender and body mass index (BMI), are important, they alone are poor predictors. However, serum factors could be potential biomarkers for early prediction of knee OA progression.
Objectives: In a first step toward finding early reliable predictors of OA progressors, this study aimed to determine, in OA individuals, the optimum combination of serum levels of adipokines/related inflammatory factors, their ratios, and the three main OA risk factors for predicting knee OA infrapatellar fat pad (IPFP) volume, as this tissue has been associated with knee OA onset and progression.
Methods: Serum and magnetic resonance images (MRI) were from the Osteoarthritis Initiative at baseline. Variables (48) comprised the 3 main OA risk factors (age, gender, BMI), 6 adipokines, 3 inflammatory factors, and their 36 ratios. IPFP volume was assessed on MRI with a neural network methodology. The best variables and models were identified in Total cohort (n=678), High-BMI (n=341) and Low-BMI (n=337), using an artificial intelligence selection approach: the adaptive neuro-fuzzy inference system embedded with fuzzy c-means clustering (ANFIS-FCM). Performance was validated using uncertainty analyses and statistical indices. Reproducibility was done using 80 OA patients from a clinical trial (female, n=57; male, n=23).
Results: For the three groups, 8.44E+14 sub-variables were investigated and 48 models were selected. The best model for each group included five variables: the three risk factors and adipsin/C-reactive protein combined for Total cohort, adipsin/chemerin; High-BMI, chemerin/adiponectin high molecular weight; and Low-BMI, interleukin-8. Data also revealed that the main form of the ratio used for the model was justified, as the use of the inverse form slightly decreased the performance of the model in both training and testing stages. Further investigation indicated that gender improved (13-16%) the prediction results compared to the BMI-based models. For each gender, we then generated a pseudocode (an evolutionary computation equation) with the 5 variables for predicting IPFP volume. Reproducibility experiments were excellent (correlation coefficient: female 0.83, male 0.95).

Conclusion: This study demonstrates, for the first time, that the combination of the serum levels of adipokines/inflammatory factors and the three main risk factors of OA could predict IPFP volume with high reproducibility, and superior performance with gender separation. By using the models for each gender and the pseudocodes for OA patients provided in this study, the next step will be to develop a predictive model for OA progressors.

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FRI0417 IDENTIFICATION OF THE MOST IMPORTANT FEATURES OF KNEE OSTEOARTHRITIS PROGRESSORS USING MACHINE LEARNING METHODS

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Background: Knee osteoarthritis (OA), a leading cause of disability worldwide, can be difficult to define as its development is often insidious and involves different subgroups. We still lack robust prediction models that are able to guide clinical decisions and stratify OA patients according to risk of disease progression.

Objectives: This study aimed at identifying the most important features of knee OA progressors. To this end, we used machine learning (ML) algorithms on a large set of subjects and features to develop advanced prediction models that provide high classification and prediction performance.

Methods: Participants, features and outcomes were from the Osteoarthritis Initiative. Features were from baseline (1107), including articular knee tissues (135) assessed by quantitative MRI. OA progressors were ascertained by four outcomes: cartilage volume loss in medial plateau at 48 and 96 months (Prop_CV_48M, 96M); Kellgren-Lawrence (KL) grade ≥2; and medial joint space narrowing (JSN) ≥1 at 48 months. Subjects' numbers were as follows: 1598 for the outcome Prop_CV_96M, 1044 for the Prop_CV_48M, and 1468 for each KL grade ≥2 at 48 months and JSN ≥1 at 48 months. Six feature selection models were used to identify the common features in each outcome. Six classification methods were applied to measure the accuracy of the selected features in classifying the subjects into progressors and non-progressors. Classification of the best features was done using auto-ML interface and the area under the curve (AUC). To prioritize the top features, Sparse Partial Least Square (sPLS) method was used.

Results: For the classification of the best common features in each outcome, Multi-Layer Perceptron (MLP) achieved the highest AUC in Prop_CV_96M, KL, and JSN (0.80, 0.88, 0.95), and Gradient Boosting Machine (GBM) for Prop_CV_48M (0.70). sPLS revealed that the baseline top five features to predict knee OA progressors are the joint space width (JSW), mean cartilage thickness of peripheral, medial, and central tibial plateau, and JSN.

Conclusion: This is the first time that such a comprehensive study was performed for identifying the best features and classification methods for knee OA progressors. Data revealed that early prediction of knee OA progression can be done with high accuracy and based on only a few features. This study identifies the baseline X-ray and MRI-based features as the most important for predicting knee OA progressors. These results could be used for the development of a tool enabling prediction of knee OA progressors.

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FRI0418 SELECTIVE PATELLAR RESURFACING IN TOTAL KNEE ARTHROPLASTY FOR THE OSTEOARTHRITIC KNEE: A PROSPECTIVE STUDY

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Background: No widely accepted view or criteria currently exist concerning whether or not patellar replacement (resurfacing) should accompany total knee arthroplasty for osteoarthritis of the knee.1)2)3)

Objectives: We recently devised our own criteria for application of patellar replacement and performed selective patellar replacement in accordance with this set of criteria. The clinical outcome was analyzed.

Methods: The study involved 1150 knees on which total knee arthroplasty was performed between 2005 and 2019 because of osteoarthritis of the knee. The mean age at operation was 73, and the mean postoperative follow-up period was 91 months. Our criteria for application of patellar replacement are given below. Criterion A pertains to evaluation of preoperative clinical symptoms related to the patellofemoral joint: (a) interview regarding presence/absence of pain around the patella, (b) cracking or pain heard or felt when standing up from a low chair, (c) pain when going upstairs/downstairs. Because it is difficult for individual patients to identify the origin of pain (patellofemoral joint or femorotibial joint), the examiner advised each patient about the location of the patellofemoral joint when checking for these symptoms. Criterion B pertains to intense narrowing or disappearance of the patellofemoral joint space on preoperative X-ray of the knee. Criterion C pertains to the intraoperatively assessed extent of patellar cartilage degeneration corresponding to class 4 of the Outerbridge classification. Patellar replacement was applied to cases satisfying at least one of these sets of criteria (A-a,-b,-c, B and C). Postoperatively, pain of the patellofemoral joint was evaluated again at the time of the last observation, using Criterion A-a,-b,-c.

Results: Patellar replacement was applied to 110 knees in accordance with the criteria mentioned above. There were 82 knees satisfying at least one of the Criterion sets A-a,-b,-c, 39 knees satisfying Criterion B and 70 knees satisfying Criterion C. (Some knees satisfied 2 or 3 of Criteria A, B and C).When the pain originating from patellofemoral joint (Criterion A) was clinically assessed at the time of last observation, pain was not seen in any knee of the replacement group and the non-replacement group.

Conclusion: Whether or not patellar replacement is needed should be determined on the basis of the symptoms or findings related to the patellofemoral joint, and we see no necessity of patellar replacement in cases free of such symptoms/findings. When surgery was performed in accordance with the criteria on patellar replacement as devised by us, the clinical outcome of the operated patellofemoral joint was favorable, although the follow-up period was not long. Although further follow-up is needed, the results obtained indicate that selective patellar replacement yields favorable outcome if applied to cases judged indicated with appropriate criteria.

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FRI0419 LOW DOSE OF GLUCOCORTICOIDS FOR PAIN CONTROL IN THE ESTROGEN-DEPENDENT PRIMARY POLYARTICULAR OSTEOARTHRITIS

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Background: Low doses of glucocorticoids (GCs) can be useful in the management of osteoarthritis when it is related to hypoestrogenic states (estrogen-dependent primary polyarticular osteoarthritis [EDPOA]), that usually can appear after the menopause. Deflazacort is a GC that has similar anti-inflammatory effects than other steroids, but with fewer side effects.

Objectives: To describe the average dose of GCs that best controlled articular pain, based on tender joint count in patients with EDPOA.

Methods: The diagnosis of EDPOA was made in postmenopausal patients with polyarticular compromised (six or more joints affected), morning stiffness less

than 30 minutes, erythrocyte sedimentation rate less than 45mm/hour and imaging studies with changes related to osteoarthritis (radiography, magnetic resonance imaging or bone scintigraphy). Patients with autoimmune diseases such as rheumatoid arthritis, lupus or Sjögren syndrome were excluded.
The clinical records of patients diagnosed with EDPOA and treated between January 2015 and June 2019 at the Valle del Lili foundation Hospital were reviewed. The patients treated with deflazacort GC were included. Pain was assessed by the treating rheumatologist using the visual analog scale (VAS, possible score 0-10). Tender joints were those with VAS> 5. The count of compromised joints was compared with inflammatory findings on bone scintigraphy (Figure 1).

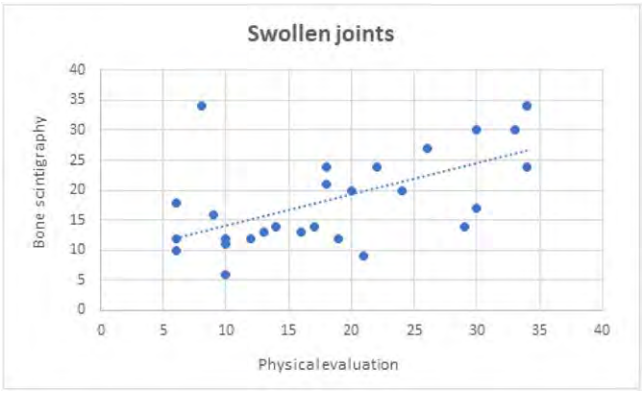


Figure 1. Comparison between number of joints with inflammatory findings on bone scintigraphy and number of swollen joints in physical evaluation

The number of tender joints was recorded at the start of treatment, which was a dose of 6mg/day of deflazacort for two months. Subsequently, the dose was reduced depending on the improvement of pain (items: intensity of pain and number of tender joints) until achieving a stabilization along the time with an improvement of 75% of the items evaluated. The number of painful joints was recorded again two months after the stabilization on pain control was achieved.
Quantitative variables were described with medians and interquartile ranges because the absence of normal distribution of the sample size. To assess the presence of a significant decrease on the number of tender joints the Wilcoxon range test was used, a value of p<0.001 was considered statistically significant. The data were analyzed with Stata v.15.
Results: Twenty-eight patients with EDPOA were included, with a median of age of 50 years (IQR 44-51), 56 years (IQR 52-66) and 61 years (IQR 54-69) at the time of menopause, onset of symptoms and the diagnosis of EDPOA respectively. A median of 18 tender joints (IQR 10-27) was obtained from the physical examination of the records reviewed. The dose of deflazacort that achieved stabilization on the improvement of the pain along the time was 21mg/week (IQR 12-21); after 8 weeks of treatment the number of tender joints was 2 (IQR 1-4), which implies a reduction of 14 (IQR 8-20; p<0.0001) on the tender joint count (Figure 2).

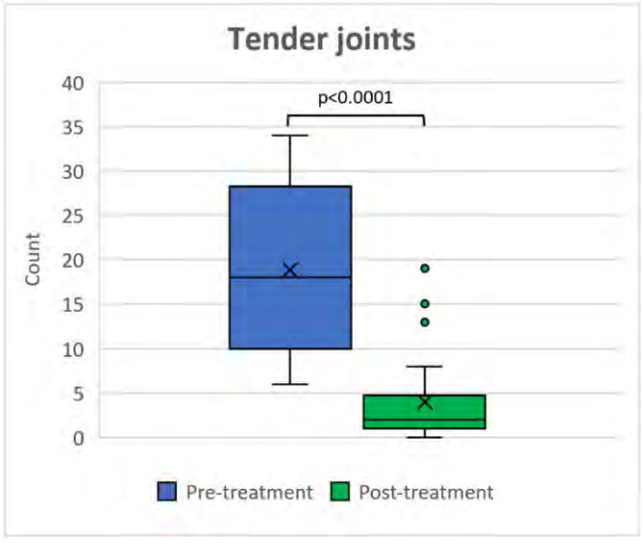


Figure 2. Number of tender joints before and after eight weeks of treatment achieving with a stable pain control in patients with EDPOA treated with deflazacort with a media dose of 3mgr/day.

Conclusion: In this case series a media dose of deflazacort of 21mg per week (3mg/day) was useful to significantly reduce the number of tender joints in patients with EDPOA.
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FRI0420 ASSOCIATION BETWEEN RED BLOOD CELLS DISTRIBUTION WIDTH AND CARDIOVASCULAR RISK IN OSTEOARTHRITIS

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Background: Osteoarthritis (OA) is the most common joint disease that results in patient's morbidity and disabilities. There is strong evidence that OA is a significant risk factor for cardiovascular disease (CVD). Red cell distribution width (RDW) blood test is a measure of the variation in red blood cell volume and size. Elevated RDW has recently been found to correlate with CVD risk in patients with and without heart disease and autoimmune diseases. RDW may be a marker for factors driving CVS risk.
Objectives: : To investigate whether RDW can serve as a potential parameter for indicating cardiovascular risk in OA patients.
Methods: A subsample of 819 OA patients was extracted from 2003-2006 National Health & Nutrition Examination Survey in a cross-sectional study. 63.7% of them were females. Their mean age was 66.4 ± 14.1 yrs. Demographic, medical data, inflammatory markers & lipid panel were obtained. Only patients with Haemoglobin>12mg/dl were included. Functional limitations were assessed using a physical function questionnaire.
Results: Elevated levels of RDW were associated with CVD risk factors in OA patients. 532 (65.8%) OA patients had functional limitations, while 78 (9.5%) and 63 (7.6%) known to have heart attacks or stroke ever. Mean RDW was 12.9±1.1fL. There was a positive significant correlation between RDW & CVD risk factors including body mass index (r=0.17, p<0.001), C-reactive protein (r=0.29, p<0.001), serum uric acid (r=0.12, p<0.001), and functional limitation (0.16, p<0.001). No significant association between RDW & lipid panel was found. In multiple regression analysis controlling for age, sex as covariates, body mass index (β =0.02, 95%CI: 0.01, 0.03, p=0.002), C-reactive protein (β =0.35, 95%CI: 0.26, 0.45, p<0.001), and functional limitation (β =0.18, 95%CI: 0.13, 0.35, p=0.03).
Conclusion: In addition to known CVD risk in OA patients, elevated RDW levels should prompt physicians to aggressively screen and treat their patients for modifiable CVS risk factors, in addition to OA.
Disclosure of Interests: None declared
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FRI0421 RATES OF PROGRESSION DIFFER BETWEEN STRUCTURAL PHENOTYPES OF KNEE OSTEOARTHRITIS: A SECONDARY ANALYSIS FROM THE FNIH COHORT

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Background: Imaging plays an important role in determining structural disease severity and potential suitability of patients recruited to disease-modifying osteoarthritis drug (DMOAD) trials. It has been suggested that there may be three main structural phenotypes in OA, i.e., inflammation, meniscus/cartilage and subchondral bone. These may progress differently and may represent distinct tissue targets for DMOAD approaches.
Objectives: To stratify the Foundation for National Institutes of Health Osteoarthritis Biomarkers Consortium (FNIH) cohort, a well-defined subsample of the larger Osteoarthritis Initiative (OAI) study, into distinct structural phenotypes

based on semiquantitative MRI assessment and to determine their risk for progression over 48 months.

Methods: The FNIH was designed as a case-control study with knees showing either 1) radiographic and pain progression (i.e., "composite" cases), 2) radiographic progression only ("JSL"), 3) pain progression only, and 4) neither radiographic nor pain progression. MRI of both knees was performed on 3 T systems at the four OAI clinical sites. Two musculoskeletal radiologists read the baseline MRIs according to the MOAKS scoring system. Knees were stratified into subchondral bone, meniscus/cartilage and inflammatory phenotypes[1]. A secondary, less stringent definition for inflammatory and meniscus/cartilage phenotype was used for sensitivity analyses. The relation of each phenotype to risk of being in the JSL or composite case group compared to those not having that phenotype was determined using conditional logistic regression. Only KL2 and 3 and those without root tears were included.

Results: 485 knees were included. 362 (75%) did not have any phenotype, while 95 (20%) had the bone phenotype, 22 (5%) the cartilage/meniscus phenotype and 19 (4%) the inflammatory phenotype. The bone phenotype was associated with a higher risk of the JSL and composite outcome (OR 1.81;[95%CI 1.14,2.85] and 1.65; 95%CI [1.04,2.61]) while the inflammatory (OR 0.96 [95%CI 0.38,2.42] and 1.25; 95%CI [0.48,3.25]) and the meniscus/cartilage phenotypes were not (OR 1.30 95%CI [0.55,3.07] and 0.99; 95%CI [0.40,2,49]).

In sensitivity analyses, the bone phenotype and having two phenotypes (vs. none) were both associated with increased risk of experiencing the composite outcome (bone: OR 1.65; 95% CI 1.04, 2.61; 2 phenotypes: OR 1.87; 95% CI 1.11, 3.16.

Conclusion: The bone phenotype was associated with increased risk of having both radiographic and pain progression together, or radiographic progression alone, whereas the inflammatory phenotype or meniscus/cartilage phenotype each individually were not associated with either outcome. Phenotypic stratification appears to provide insights into risk for structural or composite structure plus pain progression, and therefore may be useful to consider when selecting patients for inclusion in clinical trials.

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Disclosure of Interests: Frank Roemer: None declared, Jamie Collins Consultant of: Boston Imaging Core Lab (BICL), LLC., Tuhina Neogi Grant/research support from: Pfizer/Lilly, Consultant of: Pfizer/Lilly, EMD-Merck Serono, Novartis, Michel Crema: None declared, Ali Guermazi Consultant of: AventisGalapagos, Pfizer, Roche, AstraZeneca, Merck Serono, and TissuGene

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FRI0422 HOW MANY OA PATIENTS WILL BE OVERTREATED IF TREATED WITH DMOADS? ANALYSIS OF OSTEOARTHRITIS INITIATIVE DATA

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Background: Significant research effort is currently put on discovering drugs able to slow structural progression of osteoarthritis (OA). In many patients OA shows little or no increase in pain or function deterioration over time. Thus, giving disease-modifying OA drugs (DMOAD) for long periods to this subset of patients can be considered as overtreatment. There is a lack of studies directly evaluating how many patients with diagnosed OA experience no impact of the disease during long-term follow up and thus probably do not need any disease modification.

Objectives: To assess proportions of patients with diagnosed symptomatic knee OA or frequent knee pain that does not result in sustained pain and limitation of function during long-term follow up.

Methods: For the current study we used 8-year longitudinal data obtained from the Osteoarthritis Initiative (OAI) progression (n= 1390) and incidence (n = 3284) subcohorts, which are publically available at https://oai.nih.gov . For the analyses we included knees having frequent knee symptoms in the past 12 months before the baseline for at least one month. Thus the analyzed group comprised patients fulfilling the definition of symptomatic knee OA (frequent symptoms + Kellgren-Lawerence (KL) grade ≥ II) and people who might have early OA (frequent symptoms + KL grade < II) in accordance with the proposed draft classification criteria [1].

The proportion of knees experiencing no impact of OA at the 8 years follow-up was assessed.

No impact of OA was defined if a knee fulfilled all the following criteria: 1. WOMAC pain score within normative values 2. WOMAC disability score within normative values 3. Absence of joint replacement.

We used previously reported reference population age and gender adjusted values for WOMAC knee pain and WOMAC knee function [2]. It is unlikely that any OA treatment is capable to improve WOMAC pain and function measures above these reference ranges in a given person [2].

Results: We included 3092 knees from 2147 participants in the analysis. The mean age of participants was 61.16 years, the mean BMI was 28.59. Almost half of symptomatic knees with baseline KL grades 0-I were not impacted by the disease at 8 year follow up. Every fifth knee with symptomatic knee OA (KL grades ≥ II) had no impact of the disease at the end of follow up. Every third knee with symptomatic KL grade II OA did not develop pain or disability outside the reference range. The percentage of symptom-free knees at year 8 declined progressively with higher KL grades (Table).

Table. Percentage of knees with no impact of OA on 8 year follow up depending on baseline KL grade.

Baseline KL grade	Total n of knees	Percentage of knees with no impact of OA	
0	894	47 %	45.78%
I	469	43.1%	
II	923	31.31%	19%
III	609	17.7%	
IV	197	7.1%	

Conclusion: If given DMOADs, a substantial proportion of OA patients would be overtreated, especially those with early OA.

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Disclosure of Interests: None declared

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FRI0423 CLINICAL BURDEN OF TREATING COMMERCIALLY-INSURED OSTEOARTHRITIS PATIENTS WITH PRESCRIPTION NSAIDS

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Background: Prescription NSAIDs/Cox-2s ("NSAIDs") are commonly prescribed by physicians to treat patients with chronic pain, and much is known about the potential negative outcomes associated with their use[1]. Such negative outcomes include gastrointestinal ("GI") issues and hepatorenal toxicity.[1] In addition, CV risk of Cox-2s has not been completely clarified.[1,2] However, less is known about the extent to which these outcomes are pervasive and problematic in specific patient populations such as those diagnosed with osteoarthritis ("OA").

Objectives: The goal of this research is to assess the clinical burden of commercially-insured patients diagnosed with OA of the hip and/or knee before and after treatment with prescription NSAIDs, in a large, national database in recent years.

Methods: The Optum Healthcare Solutions, Inc. data (1/2012-3/2017) were used to identify patients ≥18 years old with ≥2 diagnoses of hip and/or knee OA, and ≥90 days supply of NSAIDs during the three-year period from first prescription (*index date*) after their first OA diagnosis. Patients were required to be continuously-enrolled during the six months before (baseline period) and 36 months after (follow-up period) the index date. Selected clinical outcomes such as GI issues, CV events, and renal toxicity were compared between the baseline and follow-up periods. Costs and resource use were normalized to account for differential duration in analytic time periods.

Results: Data for 22,435 patients (60.8% as female, with an average age of 62) with hip and/or knee OA were analyzed. On average, patients were prescribed NSAIDs for 489 days during the follow-up period. From the baseline period to follow-up period, negative clinical outcomes associated with GI issues increased by 393% (1.5% v 7.5%), driven by a 667% (0.3% v 2.3%) increase in acute GI hemorrhages. Additionally, negative clinical outcomes

associated with CV events increased by 73% (40.7% v 70.6%), largely due to a 600% (0.3% v 2.1%) increase in acute myocardial infarction. Lastly, negative clinical outcomes associated with renal toxicity increased by 433% (1.5% v 8.0%), with a 740% (0.5% v 4.2%) increase in acute renal failure being the most substantial.

Conclusion: These findings suggest that prescribing of NSAIDs among OA patients is associated with an increase in negative clinical outcomes. This suggests that new treatment options other than NSAIDs should be evaluated.

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Disclosure of Interests: Stuart Silverman Consultant of: Pfizer and Eli Lilly for this project., Speakers bureau: Amgen, Radius, James Rice Consultant of: Pfizer and Eli Lilly have funded this project., Alan White Consultant of: Pfizer and Eli Lilly have funded this project., Nguyen Le Consultant of: Pfizer and Eli Lilly have funded this project., Michael Somma Consultant of: Eli Lilly and Pfizer have funded this project., Craig Beck Shareholder of: Pfizer, Employee of: Pfizer, Rebecca Robinson Shareholder of: Eli Lilly, Employee of: Eli Lilly, Patricia Schepman Shareholder of: Pfizer, Employee of: Pfizer

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FRI0424

PROGRESSION OF PAIN, STIFFNESS, FUNCTION CHANGES AND ULTRASOUND DETECTED CHANGES IN THE GROUP OF 151 PATIENTS WITH HAND OSTEOARTHRITIS OVER THREE YEARS

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Background: Hand osteoarthritis (HOA) is a common and frequent cause of pain. HOA is a heterogeneous group of disorders with two main subsets including non-erosive and erosive disease. Few studies demonstrated inflammatory ultrasound changes and more severe clinical symptoms in patients with erosive compared with non-erosive disease, however the results are inconsistent.

Objectives: The aim of this study was to evaluate progression of pain, stiffness, physical impairment and ultrasound features in patients with erosive and non-erosive HOA in a three years longitudinal study.

Methods: Consecutive patients with symptomatic HOA fulfilling the American College of Rheumatology (ACR) criteria were included in this study. Joint pain and swelling were assessed. Patients reported joint pain on 100 mm visual analogue scale (VAS). Pain, joint stiffness and disability were assessed by the Australian/Canadian OA hand index (AUSCAN). Erosive disease was defined by at least one erosive interphalangeal joint. Synovial hypertrophy and power Doppler signal (PDS) were scored with ultrasound. Synovitis was graded on a scale of 0–3 and osteophytes were defined as cortical protrusions seen in two planes. Patients were examined at baseline and at the first, second and third year of follow-up.

Results: Altogether, 151 patients (16 male) with symptomatic nodal HOA were included in this study and followed between April 2012 and January 2020. Out of these patients, 84 (4 male) had erosive disease. The disease duration ($p<0.05$) was higher in patients with erosive compared with non-erosive disease.

Pain reported on VAS was significantly higher ($p<0.01$) in patients with erosive compared with non-erosive disease at baseline. Progression of pain after the third year of follow up was significantly higher in patients with erosive disease ($p<0.01$). The number of painful and clinically swollen joints ($p<0.05$) was significantly higher in patients with erosive compared with non-erosive disease at baseline. It fluctuated over the second and third year of follow up, but it still remained statistically higher ($p<0.01$) at the third year of follow up in patients with erosive disease.

According to the AUSCAN, patients with erosive compared with non-erosive disease had more pain ($p<0.01$) and stiffness ($p<0.01$) at baseline. Pain ($p<0.05$), stiffness and also function ($p<0.05$) worsened in patients with erosive compared with non-erosive disease at the third year of follow up.

US-detected pathologies such as gray-scale synovitis ($p<0.001$), intensity of PDS ($p<0.01$) and number of osteophytes ($p<0.01$) were significantly higher in patients with erosive compared with non-erosive disease at baseline. There were improvements in gray-scale synovitis total score and intensity of PDS in patients with non-erosive disease while patients with erosive disease worsened after the second and third year of follow up. US-detected gray-scale synovitis ($p<0.001$), intensity of PDS ($p<0.01$) remained significantly higher in patients with erosive compared with non-erosive disease after the third year of follow up. On the other hand, the progression of US-determined osteophyte formation was observed in both groups but was significantly higher ($p<0.05$) in patients with erosive compared with non-erosive disease after the third year of follow up. .

Conclusion: The findings of this study show that pain and number of painful and clinically swollen joints associated with US-detected synovial changes and osteophyte formation is more severe in patients with erosive HOA than in patients with non-erosive disease. In addition, osteophyte formation is more likely to progress independent of synovial inflammation.

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FRI0425

EVALUATION OF THE DOYLE INDEX AS A MEASURE OF PAIN SENSITIZATION IN PERSONS WITH HAND OSTEOARTHRITIS: EXPLORATORY ANALYSES FROM THE NOR-HAND STUDY

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Background: Pressure pain threshold (PPT) is a measure of pain sensitization; altered pain mechanisms in the peripheral and/or central nervous system causing increased pain sensitivity. PPT testing may be a useful tool to classify pain phenotypes but requires special equipment not available in the clinic. The Doyle index (DI) is a clinical measure of joint tenderness upon palpation. It is considered as an outcome measure of pain and disease activity in hand OA and is a potential alternative to PPT. It is unclear if joint tenderness is related to pain sensitization, as joint tenderness could reflect pure nociceptive pain without sensitization.

Objectives: Using data from the Nor-Hand study we will explore how DI performs as a measure of pain sensitization in hand OA by examining associations and agreements between DI and PPT at joint level, and correlations between PPT values and DI sum score at person level.

Methods: PPT was tested with a hand-held algometer (FPIX25, 1cm^2 flat rubber tip) at the dorsal side of the most painful DIP/PIP and a non-painful DIP/PIP joint (local PPTs) and left radioulnar joint and mid-portions of the trapezius and tibialis anterior muscle (remote PPTs). Low local PPTs indicate peripheral and/or central sensitization, while low remote PPTs indicate central sensitization. According to DI, tenderness in the bilateral thumb base and finger joints were graded by a rheumatologist by pressing on the lateral joint margins: 0=no pain, 1=patient complains of pain, 2=patient complains of pain and winces, 3=patient complains of pain, winces and withdraws joint. We examined whether increasing DI was associated with local PPT using mixed models. To assess agreement between DI and PPT, we categorized PPT of the painful finger joints into a semi-quantitative scale with the same number of categories (n=4) as DI. We identified the cut-offs for the PPT categories that maximized the agreement (weighted kappa) with DI. Finally, we examined Spearman's correlations between DI sum score [range 0-90] and PPTs of local and remote sites.

Results: The majority of the 285 eligible participants were women (88%) and mean (SD) age was 61 (6) years. Joints with high DI had lower PPT values (Figure 1). We found a linear association of lower PPT with increasing DI for all joints combined (beta -0.7, 95% CI -0.8, -0.6). Similar results were found for the painful joints (beta -0.8, 95% CI -1.0, -0.6), but weaker for non-painful joints (beta -0.5, 95% CI -1.0, 0.0) where few joints had DI grade 2-3 (Figure 1). The analyses on maximized agreement between DI and the PPT categories gave a weighted kappa equal to 0.32 (Table).

Median (IQR) DI sum score was 9 (5, 15). We found weak inverse correlations between DI sum score and PPT at local (painful finger: ρ -0.24 (95% CI -0.32, -0.16), non-painful finger: ρ -0.22 (95% CI -0.29, -0.11) and remote sites (radioulnar joint: ρ -0.17 (95% CI -0.29, -0.06), trapezius: ρ -0.25 (95% CI -0.36, -0.14), tibialis anterior: ρ -0.20 (95% CI-0.31, -0.09)).

Conclusion: The DI was associated with lower PPT at painful finger joints. Large variance of PPT within each DI grade resulted in fair agreement. DI of non-painful

finger joints was weakly associated with PPT, demonstrating that the DI does not differentiate pain sensitization in joints without ongoing nociceptive pain. Correlations between DI sum score and PPT of remote sites were also weak. The two measures seem to assess different constructs and are therefore not interchangeable.

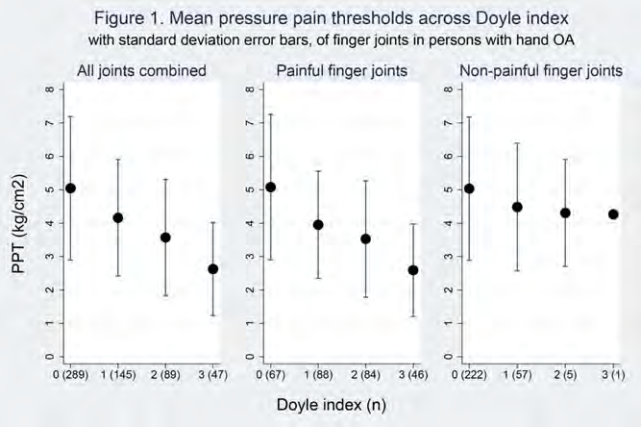


Table. Cross tabulation of DI with the best PPT categorization of painful finger joints. Cells = joint count

PPT categories (range, kg/cm^2)	0 (4.7-12)	1 (3.4-4.6)	2 (2.1-3.3)	3 (0-2.0)
DI				
0	32	21	11	3
1	21	29	31	7
2	15	22	31	16
3	2	7	15	22

PPT categories 0-3 (i.e. decreasing PPT) represent the categorization that gave maximized agreement with DI (weighted kappa = 0.32)

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FRI0426

EMOTIONAL COMPONENTS AND INFLAMMATION ARE HIGHLY RELEVANT IN PAIN REPORTED BY KNEE OSTEOARTHRITIC PATIENTS

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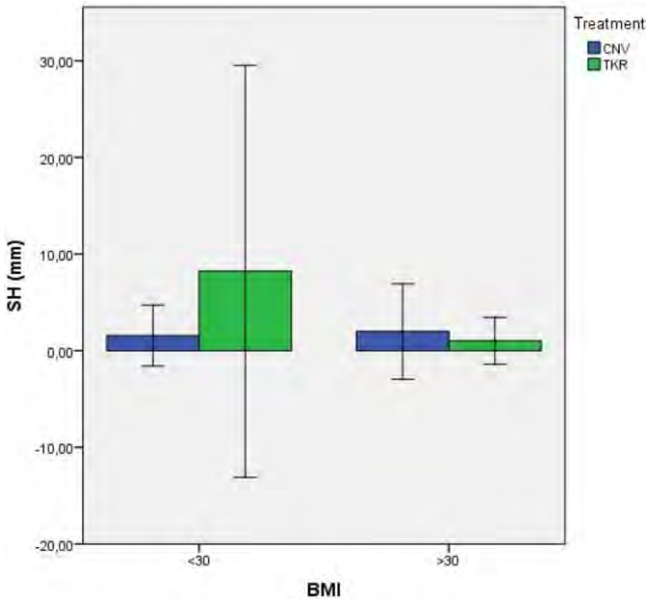
Background: Osteoarthritis (OA) is a leading cause of disability in elderly and the most frequent form is knee OA (KOA) (1). Pain is the principal symptom that leads patients to visit clinicians, and it is the main reason, together with functionality, for patients to undergo a total knee replacement (TKR) after apparently unsuccessful conservative (CNV) treatments (2). It is well-known that there is a poor correlation between the radiographic severity (based on Kellgren & Lawrence (KL) score) and the reported pain (3), so other variables may be responsible for the intensity of pain.

Objectives: Identifying the leading causes of pain in each patient would improve the management of the disease. In this study we aim to investigate the role of emotional components, nociception process and inflammation in treatment decision, as a global measure of pain suffered by KOA patients, taking into account sex, age and BMI.

Methods: KOA patients, carefully selected to be idiopathic, graded 2-3 in KL, were recruited at Hospital del Mar. The following variables were recorded: WOMAC, Hospital Anxiety and Depression Scale (HAD), Pain Catastrophizing Scale (PCS), tender points (TP) (measure with a pressure algometer at points defined in the Arendt-Nielsen extended peripatellar map), synovial hypertrophy (SH) and effusion (SE) (measure by ultrasounds), and PCR and ESR serum levels. Patients were classified according to 4 factors: treatment (CNV/TKR), sex, age (60-67/68-75) and BMI (<30/>30). All groups were balanced. Multivariate and correlations analysis were performed.

Results: Eighty-seven patients have been recruited. Patients from the TKR group present significant higher WOMAC (p=0.000), PCS (p=0.002) and SE (p= 0.038) values than CNV ones, without interaction with the other factors, except for SE, that presents interaction with BMI (Fig. 1). Women reported significant upper WOMAC (p=0.001) and HAD rates (p=0.020), but also higher number of TP and ESR levels (p= 0.000 and 0.002, respectively). The level of sensitization was significantly higher in women than in men (p=0.000). Several significant correlations were found, mainly between WOMAC and emotional components, as well as between TP and WOMAC, PCS, and inflammation markers (Table 1).

Conclusion: PCS is an emotional component that could explain in part the lack of correlation between joint status and patient's symptomatology. Working



		HAD	PCS	TP	SH	SE	PCR	ESR
WOMAC	r	,382**	,703**	,316**				
	p-value	.000	.000	.003				
	N	87	87	86				
HAD	r		,486**					
	p-value		.000					
	N		87					
PCS	r			,218*				
	p-value			.044				
	N			86				
TP	r						,332**	,533**
	p-value						.002	.000
	N						85	80
SH	r							
	p-value							
	N							
SE	r							
	p-value							
	N							
PCR	r							,427**
	p-value							.000
	N							81

out strategies for pain management could improve this PCS values and therefore reduce the need for TKR. Furthermore, this study also highlights the two mainly types of OA etiology: mechanical and inflammatory. It suggests that inflammation is mostly responsible for OA progression in patients with low BMI, and plays a strong role in women pathology. Finally, specific treatments targeting central pain sensitization could also improve the management of the pathology in women.

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FRI0427 EULAR RECOMMENDATIONS FOR INTRA-ARTICULAR TREATMENTS FOR ARTHROPATHIES

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Background: Intra-articular therapies (IAT) are widely used in clinical practice to treat patients with rheumatic and musculoskeletal diseases (RMDs). Many factors influence their efficacy and safety. There is a wide variation in the way IATs are delivered by health professionals. In an attempt to standardise these procedures, evidence-based recommendations are the right way forward.

Objectives: To establish evidence-based recommendations to guide health professionals using IAT in adult patients with peripheral arthropathies.

Methods: At a first face-to-face meeting, the results of an overview of systematic reviews were presented to the multidisciplinary task force of members from 8 countries. The aim, scope and outline of the taskforce were also established at this meeting. Thirty-two clinical questions ranked for priority (relevance for practice plus feasibility) drove the systematic reviews performed by two fellows. In addition, two surveys addressed to physicians, health professionals and patients throughout Europe were agreed to acquire more background information. At the second face-to-face meeting, the evidence for each research question was discussed, and each recommendation shaped and voted in a first Delphi round. Level of agreement was numerically scored 0 to 10 (0 completely disagree, 10 completely agree). All panellists voted anonymously using a sli.do app. Agreement needed to be greater than 80% to be included in a second Delphi round, which also allowed reformulation of statements. Finally, a third Delphi round was sent to the taskforce. The level of evidence was assigned to each recommendation according to the EULAR SOP for establishing recommendations.

Results: Recommendations focus on practical aspects for daily practice to guide health professionals before, during and after IAT in adult patients with peripheral arthropathies. Five overarching principles were established, together with 11 recommendations that address the following issues: (1) patient information; (2) procedure and setting; (3) accuracy issues; (3) routine and special antiseptic care; (4) safety issues and precautions to be addressed in special populations; (5) efficacy and safety of repeated joint injections; (6) the usage of local anaesthetics; and (7) aftercare. The document includes the supporting evidence and results from the surveys, level of evidence and agreement.

Conclusion: We have developed the first evidence and expert opinion based recommendations to guide health professionals using IAT.

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FRI0428 RESULTS FROM A CROSS-SECTIONAL, OBSERVATIONAL STUDY TO ASSESS INADEQUATE PAIN RELIEF IN PATIENTS WITH KNEE AND/OR HIP OSTEOARTHRITIS IN CHINA

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Background: Osteoarthritis (OA) of the knee and hip is a leading cause of disability worldwide, particularly due to the primary symptom of pain in the weight-bearing joints. There is limited data that characterizes patients who experience moderate to severe pain despite analgesic treatment in China.

Objectives: This study estimates the real-world prevalence of inadequate pain relief (IPR) among patients with knee and/or hip OA who have been prescribed analgesic therapy and characterizes this patient population. The study was conducted in China, the Philippines, Thailand, Russia, and Mexico. This abstract presents results from China.

Methods: This is a multinational, multi-site, cross-sectional, observational study. Physicians managing patients with OA were recruited and asked to enroll patients over 50 years of age with knee and/or hip OA who had been prescribed topical and/or oral pain medication for at least 30 days prior to study visit. Patients completed a one-time assessment of pain, function, and health-related quality of life (HRQOL) using patient reported outcome (PRO) instruments. Physicians abstracted data from patient charts. IPR was defined as an average pain score of >4/10 on Brief Pain Inventory Question #5 (average pain). Statistical tests including chi-square for categorical variables and Mann-Whitney Wilcoxon test for continuous variables were conducted to assess differences in demographic and clinical characteristics as well as PROs between patients with and without IPR. A multivariate regression analysis was conducted to assess the relationship between IPR and PROs.

Results: 571 patients treated at 10 hospital centers in China were enrolled. 73% were female, the mean (SD) age was 62 (8.32) years. The number of years with OA ranged from less than one year to over 37 years, suggesting a broad sample of patients. Most patients were impacted by knee OA only (90%). Almost half (43%) of the study population met the definition of IPR. Patients with IPR tended to be older, have greater prevalence of obesity, have more comorbidities, and had longer disease duration. The majority (98%) of patients were receiving nonsteroidal anti-inflammatory drugs (NSAIDS), followed by chondroprotective

medications (23%). However, more patients with IPR mentioned being dissatisfied with treatment (38% vs. 21%). After adjusting for covariates, patients with IPR reported worse HRQOL, more functional limitations, and reduced work productivity compared to patients without IPR.

Conclusion: IPR is highly prevalent among individuals with knee and/or hip OA in China and is associated with decreased HRQOL and work productivity, impaired function, and treatment dissatisfaction. Developing awareness among healthcare professionals about the presence and potential impact of IPR is important for the ultimate improvement of OA patient management.

PRO mean (SE)	No IPR (N=328)	IPR (N=243)
EQ-5D Index	0.72 (0.01)	0.49 (0.02)
EQ-5D VAS	72.3 (0.85)	65.5 (1.00)
WOMAC Pain Subscale	13.1 (0.78)	22.7 (1.52)
WOMAC Stiffness Subscale	4.2 (0.27)	7.4(0.51)
WOMAC Physical Function Subscale	44.8 (2.61)	76.9 (5.07)
Work Productivity Loss	30.0 (4.07)	47.5 (10.46)

Multivariate analysis adjusted for age, year since OA diagnosis/follow-up, gender, BMI, number of medication classes, insurance, physician specialty/academic responsibilities, number of affected joints, diabetes, CVD, hyperlipidemia/hypertension, and depression. All differences were statistically significant ($p < 0.05$) except work productivity loss ($p=0.11$)

Disclosure of Interests: Xiaofeng Zeng Consultant of: MSD Pharmaceuticals, Xiaomei Leng Consultant of: MSD Pharmaceuticals, Knightley Wei Employee of: Employed by MSD Pharmaceuticals (China), Wen Min Tang Employee of: Employed by MSD Pharmaceuticals (China), Cai Hua Tang Employee of: Employed by MSD Pharmaceuticals (China), Kaan Tunceli Shareholder of: Holds company stock at Merck Sharp & Dohme Corp., Employee of: Employed by Merck Sharp & Dohme Corp., Jyoti Aggarwal Consultant of: Merck & Co., Inc., Dena Ramey Shareholder of: Holds company stock at Merck Sharp & Dohme Corp., Employee of: Employed by Merck Sharp & Dohme Corp., Fidel Lozano Employee of: Merck & Co. salaried employee, Ishita Doshi Shareholder of: Holds company stock at Merck Sharp & Dohme Corp., Employee of: Employed by Merck Sharp & Dohme Corp., Cynthia Macahilig Consultant of: Consultant to Merck Sharp & Dohme Corp., Shardul Odak Consultant of: Consultant to Merck Sharp & Dohme Corp., Kelly Johnson Employee of: Employed by Merck & Co., Inc.

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FRI0429 UROLITHIN B ATTENUATES THE INFLAMMATORY AND NITROSATIVE STRESS ON INTERLEUKIN-1 INDUCED CHONDROCYTES

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Background: Osteoarthritis (OA) is one of the most common degenerative disorders with cartilage degradation especially to the elderly resulting in disability. Many inflammatory cytokines involve the pathogenesis of the OA and causes destruction and decomposition of articular cartilage, including interleukin 1 beta (IL-1β). Urolithin B is a small polyphenolic compound, produced by gut flora from ellagitannins-rich foods, such as pomegranate, strawberries, raspberries, etc. Urolithin B has been documented in anti-inflammatory and antioxidant properties. However, the mechanism underlying the effects of Urolithin B on IL-1 stimulated human osteoarthritis (OA) chondrocytes remains unrevealed

Objectives: The aim of this study was to investigate the biologic effects of Urolithin B on OA models and associated mechanism.

Methods: Primary culture of human chondrocyte, knee joint obtained from total knee replacement of patients with osteoarthritis, were used IL-1β induced and treated with/without 100μM Urolithin B for 24 hours respectively. Total cell lysates were collected for western blotting to analyze the catabolic molecules. Culture medium were collected for gelatin zymography to analyze the secretion of MMP 2 and 9.

Results: Urolithin B inhibits the overexpression of not only inflammatory marker COX2 and nitrosative marker NOS2, but also matrix metalloproteinases (MMPs)-1, -3, 13 in IL-1β induced chondrocytes by western blotting. It also restored the IL-1β induced glycosaminoglycan degeneration in ex vivo articular cartilage evaluated by Safranin O stain. Meanwhile, Urolithin B can activate autophagy, increasing LC3 II/I ratio, in IL-1β induced chondrocytes.

Conclusion: Collectively, the study demonstrates that Urolithin B may be of value in the treatment of osteoarthritis through its anti-inflammatory, anti-oxidant and anti-proteinase activities.

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Title:

Urolithin B attenuates the inflammatory and nitrosative stress on interleukin-1 induced chondrocytes

Key words: Urolithin B, Osteoarthritis, chondrocytes, Cyclooxygenase 2, Nitric Oxide Synthase 2, matrix metalloproteinase

Disclosure of Interests: None declared

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FRI0430 THE NOVEL, INTRA-ARTICULAR CLK/DYRK1A INHIBITOR LORECIVIVINT (LOR; SM04690), WHICH MODULATES THE WNT PATHWAY, IMPROVED RESPONDER OUTCOMES IN SUBJECTS WITH KNEE OSTEOARTHRITIS: A POST HOC ANALYSIS FROM A PHASE 2B TRIAL

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Background: Lorecivivint (LOR; SM04690) is a small-molecule, intra-articular (IA) CLK/DYRK1A inhibitor that modulates the Wnt pathway[1] and has demonstrated some beneficial effects on patient-reported outcomes (PROs) relative to placebo (PBO) in two Phase 2 knee OA trials. With subjective measures such as PROs, meaningful benefits may be better characterized by representation as discrete threshold responses rather than by changes in mean point estimates.

Objectives: To conduct a post hoc analysis of subjects in a 24-week Phase 2b study by measuring the proportions of subjects treated with LOR and placebo (PBO) who achieved 30%, 50%, or 70% threshold responses of improvement over baseline in Pain Numeric Rating Scale (NRS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain, WOMAC Function, and Patient Global Assessment (PtGA) at Week 12. Results from the Phase 3-selected dose of 0.07 mg LOR are presented here.

Methods: Subjects had ACR-defined knee OA, Kellgren-Lawrence (KL) grades 2–3, and Pain NRS scores ≥4 and ≤8 in the target knee and <4 in the contralateral knee. A single 2mL IA injection of 0.03 mg, 0.07 mg, 0.15 mg, or 0.23 mg LOR, or vehicle PBO was given in the target knee at baseline. The proportion of subjects meeting 30%, 50%, or 70% threshold responses over baseline in the weekly average of daily Pain NRS [0–10], WOMAC Pain [0–100], WOMAC Function [0–100], and PtGA [0–100] at Week 12 was determined. The odds ratios (OR [95% CI]) of achieving each threshold response level were calculated and compared between LOR and PBO.

Results: In total, 635 subjects (91.4%) completed the study (mean age 59.0±8.5 years, BMI 29.0±4.0 kg/m^2, female 58.4%, KL grade 3 57.3%). At Week 12, treatment with 0.07 mg LOR significantly ($P<0.05$) increased the odds of a 30% threshold response in Pain NRS (OR 2.47 [1.45, 4.19]) and WOMAC Function (OR 1.86 [1.10, 3.12]) and a 50% threshold response in WOMAC Pain (OR 1.79 [1.06, 3.03]) and PtGA (OR 2.28 [1.25, 4.16]). Numerically, more (not statistically significant) subjects achieved a 70% threshold response in all PROs. All improvements were maintained through Week 24.

Conclusion: In this post hoc analysis, LOR-treated subjects reported greater improvements in PRO threshold responses versus PBO from Week 12 through Week 24. LOR demonstrated significantly higher odds of achieving and maintaining improvements in PROs at 30% and 50% thresholds. Phase 3 studies of 0.07 mg LOR are ongoing.

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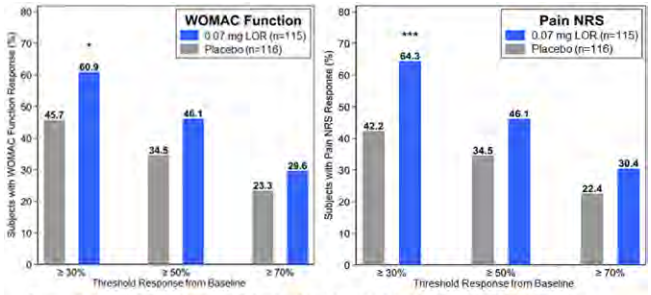


Figure 1. Percentage of Phase 2b trial subjects in the LOR and placebo (PBO) groups responding to treatment with 30%, 50%, or 70% threshold responses over baseline at Week 12. The Pain NRS and WOMAC Function outcomes are shown. *P<0.05, **P<0.01, ***P<0.001 vs. PBO by logistic regression using the Full Analysis Set and non-responder imputation.

Disclosure of Interests: Yusuf Yazici Shareholder of: Samumed, LLC, Grant/research support from: Bristol-Myers Squibb, Celgene, and Genentech, Consultant of: Celgene and Sanofi, Employee of: Samumed, LLC, Sarah Kennedy Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Christopher Swearingen Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Jeyanesh Tambiah Shareholder of: Samumed, LLC, Employee of: Samumed, LLC

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FRIDAY, 05 JUNE 2020

Infection-related rheumatic diseases

FRI0431 PROFILE OF INFECTIOUS SPONDYLODISCITIS ACCORDING TO THE SITE: UNIFOCAL VERSUS MULTIFOCAL

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Background: Infectious spondylodiscitis is a therapeutic emergency and is a current problem. It can affect the different levels of the spine. Multifocal forms, touching several floors, however remain rare.

Objectives: To compare the clinical, biological, radiological and therapeutic aspects of unifocal versus multifocal spondylodiscitis.

Methods: This is a retrospective study of 113 patients admitted to our service over a period of 20 years [1998-2018]. The diagnosis of spondylodiscitis was made on the basis of clinical, biological, radiological and bacteriological data. We have divided our population into two groups: unifocal and multifocal spondylodiscitis.

Results: Spondylodiscitis was more frequently unifocal (75.2%) than multifocal (24.8%). The average age of the patients was 55.8 years. There were 62 men and 51 women. There was no difference in age and sex between the two groups (p=0.5 and p=0.8, respectively).

Diabetes was more frequent in the group of multifocal spondylodiscitis but with no statistically significant difference (p=0.4). No statistically significant difference between the two groups regarding the start mode (p=0.7), the schedule (p=0.3), the presence of neurological signs (p=0.7), fever (p = 0.2), impaired general condition (p=0.6) and biological inflammatory syndrome (p=0.6).

Cervical and dorsal spine involvement was more common in multifocal spondylodiscitis (p = 0.02 and p = 0.01; respectively). There were 11 spondylodiscitis involving 2 floors (cervical and dorsal: 2 cases, cervical and lumbar: 3 cases, dorsal and lumbar: 6 cases) and 3 spondylodiscitis involving 3 floors.

Radiologically, the presence of vertebral fracture and involvement of the posterior arch was more frequent during the multifocal form (p=0.03 and p=0.001; respectively). The frequency of para-vertebral abscesses, epiduritis and the presence of spinal cord compression were similar in the two groups (p=0.6; p=0.7 and p=0.2, respectively).

Tuberculosis was more frequent during the multifocal form (p = 0.05) and brucellosis during the unifocal form (p = 0.03). Disco-vertebral biopsy was performed in 79 cases. It was more often contributory during multifocal spondylodiscitis (p = 0.03).

The occurrence of immediate complications was more frequent in multifocal spondylodiscitis but with no statistically significant difference (p=0.2).

Conclusion: Multifocal sppondylodiscitis is seen mainly in immunocompromised subjects. Our study found that diabetes is the most common factor in immunosuppression. Note also the predominance of involvement of the posterior elements, tuberculous origin and immediate complications.

Disclosure of Interests: None declared

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FRI0432 INTEREST OF IMAGING IN THE DIAGNOSIS OF INFECTIOUS SPONDYLODISCITIS (ABOUT 113 CASES)

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Background: Infectious spondylodiscitis is a diagnosis and therapeutic emergency. Its clinical presentation can be insidious and standard radiographs can be falsely reassuring. This explains the interest of cross-sectional imaging and more particularly magnetic resonance imaging (MRI).

Objectives: To analyse the contribution of imaging in the diagnosis of infectious spondylodiscitis.

Methods: These are 113 cases of spondylodiscitis collected in a rheumatology department over a period of 20 years [1998-2018]. The diagnosis is made on the basis of clinical, biological, radiological and bacteriological data.

Results: Our population was divided into 62 men (54.9%) and 51 women (45.1%) (p = 0.8) with an average age of 55 years [16–86]. Predisposing factors were found in 52.2% of cases: diabetes (23%), neoplasia (2.7%), hepathopathy (5.3%), long-term corticosteroid therapy (1.8), recent surgery (3.5%), history of tuberculosis (2.7%) and consumption of unpasteurized dairy products (28.3%).

The approximate time between onset of symptoms and diagnosis ranged from 0.23 to 24 months (median 3 months). Impaired general condition was observed in 81% of the cases and fever in 34.5% of the cases. Radiculalgia was found in 46% of the cases and a neurological deficit was noted in 16% of the cases. Biological inflammatory syndrome was found in 91.2% of the cases.

Standard radiographs of the spine were abnormal in 85% of cases, showing disc space narrowing (72%), irregularity of the vertebral plates (35.5%), erosions (13.1%) and para-vertebral spindle (4.7%). CT and spinal MRI were performed respectively in 57.5% and 70.8% of cases and revealed: erosions (46.2%), mirrored geodes (16.9%), para-vertebral abscess (57.5%), epiduritis (71.3%) and spinal compression (26.3%). The lumbar spine was the most affected (55.8%), followed by the dorsal spine (30.1%) and the cervical spine (8.8%). The Infectious spondylodiscitis was multifocal in 24.8% and multi-stage in 12.4% of cases.

A disco-vertebral biopsy was performed in 70% of cases and was contributory in 44.3% of cases. The causative organism was tuberculosis in 55.8% of cases, brucellosis in 21.2% of cases and pyogenic germs in 23% of cases.

Conclusion: Imaging plays an important role in the diagnosis of spondylodiscitis. MRI is considered the key examination, capable of mapping injuries and detecting potentially serious neurological complications. The importance of imaging the entire spine to detect multifocal forms should also be emphasized.

Disclosure of Interests: None declared

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FRI0433 HAS THE PROFILE OF INFECTIOUS SPONDYLODISCITIS CHANGED IN 20 YEARS?

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Background: Infectious spondylodiscitis represents 2 to 4% of osteoarticular infections. Their incidence is constantly increasing. Early microbiological diagnosis and targeted multidisciplinary management are the main prognostic factors for infectious spondylodiscitis.

Objectives: To compare the epidemiological, clinical, biological, radiological, bacteriological profile as well as the management and prognosis of spondylodiscitis over the last 20 years.

Methods: Retrospective study including 113 patients hospitalized in our department between 1999 and 2018. The diagnosis was based on clinical, biological, radiological and bacteriological data. Spondylodiscitis were divided into two groups: spondylodiscitis occurring between 1998 and 2008 (1st decade) and those between 2009 and 2018 (2nd decade).

Results: Of the 113 identified patients, 54 (47.8%) occurred between 1998 and 2008, with male predominance in both groups (50.2 and 59.3% respectively; p=0.3). The average age was 55 years (p=0.7). Diabetes was more frequent in the 1st decade but without a statistically significant difference (p=0.1). On the other hand, consumption of unpasteurized dairy products was more frequent during the 2nd decade (p<0.001) as well as the presence of intercurrent infection (p=0.01).

The estimated delay between symptom onset and diagnosis was longer between 1998 and 2008 (5.6 months and 3.2 months respectively, p=0.005). The presence of neurological signs was more frequent between 2009 and 2018 (p=0.001), especially radiculalgia (p=0.02). The sedimentation rate was higher in the 1st decade (93mm and 72mm respectively, p=0.002).

We found no statistically significant difference in the location of spondylodiscitis (p=0.4) and the multifocal involvement (p=0.5).

Radiographic signs were significantly more prevalent in the 1st decade (p=0.002), in particular disc space narrowing (p=0.03) and irregularity of the intervertebral plates (p=0.01). Computed tomography was more often performed during the 1st decade (p = 0.008), unlike magnetic resonance imaging, performed in 88.1% of cases during the 2nd decade (p <0.001). In contrast, the frequency of para-vertebral abscesses, epiduritis and spinal cord compressions were similar in the two groups (p = 0.6; p = 0.9 and p = 0.3, respectively).

Tuberculosis was more frequent in the 1st decade (p=0.009). Disco-vertebral biopsy was more often performed in the 1st decade (p=0.04), but its efficiency was similar between the two groups (p=0.1). For pyogenic spondylodiscitis, blood cultures were more often positive in the 2nd decade but without a statistically significant difference (p=0.6). On the other hand, the anatomopathological aspect was more frequently suggestive of a pyogenic germ in the 2nd decade (p=0.04).

A surgical procedure was more frequently performed between 2009 and 2018 but with no statistically significant difference (p = 0.2). All patients received antibiotic therapy. A change in treatment was made in 23.7% of cases between 2009 and 2018 (p = 0.01). The prognosis was better during the 1st decade (p = 0.01). On the other hand, the occurrence of immediate complication during tuberculous spondylodiscitis was more frequent during the 2nd decade (p = 0.03), in particular the toxicity of anti-tuberculosis treatment (p = 0.04).

Conclusion: In the last decade, the diagnosis of spondylodiscitis has been made earlier. However, these are more severe forms with an increased frequency of neurological complications, probably due to an increase in the proportion of virulent germs. Moreover, the effectiveness of the bacteriological investigation does not differ between the two periods studied.

Disclosure of Interests: None declared

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FRI0434 PREDICTIVE FACTORS OF SERIOUS INFECTIONS IN PATIENTS WITH CHRONIC INFLAMMATORY ARTHRITIS ON TREATMENT WITH TNF INHIBITORS: REAL LIFE DATA

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Background: Serious infections are one of the most feared adverse events in patients treated with biologics. To this regard data coming from randomized and long-term extension studies may not totally applied to the usual clinical practice due to the different profile of the treated patients. To study the associated factors for serious infections in patients with inflammatory arthritis treated with TNF inhibitors

Objectives: To study the associated factors for serious infections in patients with inflammatory arthritis treated with TNF inhibitors

Methods: All the medical records of the patients with inflammatory arthritis being treated with TNF inhibitors at the beginning of 2016 were retrospectively reviewed. All serious infections suffered for these patients until the end of 2018 were recorded. Serious infections were defined as those which required to admitted at the hospital for intravenous treatment. Potential variables associated with the development of these infections including: demographic and clinical characteristics, concomitant treatments or comorbidity (by Charlson index) were studied. Standard statistical tests for descriptive and univariate analyses were used and a multivariable logistic regression model was built to check independent associations.

Results: Overall 334 patients (50.3% women) with a mean age of 56.67 (±12.853) were studied: 140 (41.92%) Rheumatoid arthritis (RA), 55 (16.46%) psoriatic arthritis (PsA) and 138 (41.62%) spondyloarthritis (Sp). Forty-five serious infections were observed in 30 patients, being respiratory (40%) and urinary (8.8%) the most frequent localizations. Only one patient died. By univariate analysis, disease duration, age, concomitan use of glucocorticoids (GC) (but not of synthetic DMARDs), Charlson index and specifically Diabetes Mellitus were associated with infection (p< 0.05). The type of arthritis was not associated and the results in the subset of RA patients were overall similar. In the multivariate analysis the use of GC [OR: 5.31 (1.98.14.26)] and the Charlson index [OR:2.48 (1.70;3.60)] were found to be independently associated to infection.

Conclusion: In patients with inflammatory arthritis and treated with TNF inhibitors around a 10% developed any serious infection along three years of follow up. Use of GC and comorbidity emerged as the main risk factors for this complication.

Disclosure of Interests: None declared

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FRI0435 THE CLINICAL SIGNIFICANCE OF SERUM AUTOANTIBODIES AND HLA-B27 MOLECULE TESTING IN UYGUR PATIENTS WITH HUMAN IMMUNODEFICIENCY VIRUS INFECTION

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Background: AIDS is a deadly infectious disease caused by the HIV. When HIV infects a host, it may induce production of autoantibodies due to the structural antigen similarity between viral proteins and selfantigens.The molecular mimicry between HIV protein and self-antigens could cause antibody cross-reactions and lead to development of autoimmune disease.

Objectives: To explore the clinical value of serum autoantibodies and human leukocyte antigen (HLA-B27) molecular testing in Uygur patients with human immunodeficiency virus (HIV) infection.

Methods: A total of 727 HIV-infected Uygur patients who visited Kuche Infectious Diseases Hospital during May 2016 to March 2017 were include in this study. The other 390 healthy people were enrolled as controls. Serum antinuclear antibodies (ANA) and ANA Profile, anti-cyclic citrullinated peptide (CCP) antibody, and HLA-B27 molecule were tested.

Results: Among 727 HIV-infected Uygur patients, 317 were males and 410 were females with mean age (35.52±13.44) years old. The mean duration of disease was (6.34±3.05)years. There were 697(95.87%) patients receiving Highly active antiretroviral therapy (HAART) with mean duration of treatment (6.34±3.05)years. Rheumatic manifestations were recorded in 238 (32.74%) HIV-infected Uygur patients, mainly with dry mouth and dry eye (15.41%), alopecia (9.90%), arthralgia (8.94%), ect. Compared with the health controls, positive ANA was more common in HIV infected Uygur patients (33.42% *vs.* 17.43%, $P < 0.001$) with low titers (ANA titer:1:100). HIV-infected Uygur patients had higher positive anti-u1-RNP antibodies positive rate (1.10%), but lower anti-SSA antibodies positive rate (0.14%) and anti-CCP antibodies positive rate (0.28%). Patients with positive ANA in HAART group were significantly less than that in non-treatment group (38.72% *vs.* 50.00%, P=0.049).Only one female patient was HLA-B27 positive (0.14%), which was significantly lower than that in healthy controls (3.08%) (P<0.001). Also, only one patient was diagnosed with rheumatoid arthritis (RA).

Conclusion: Rheumatic manifestations are common in HIV-infected Uygur patients. Several autoantibodies are positive, but the coincidence of rheumatic diseases is rare. It's noted that patients with Rheumatic manifestations and low titre positive ANA should be considered as a differential diagnosis of HIV infection.

Disclosure of Interests: None declared

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FRI0436 ARTICULAR AND PERIARTICULAR INFECTIOUS DISEASES: REVIEW AND ANALYSIS OF A COHORT IN A 3RD LEVEL HOSPITAL

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Background: Infectious diseases in Rheumatology are still a prevalent healthcare issue nowadays. Microbiological tests and early beginning of antibiotic

treatment are basic supportive therapy for those patients. In some cases, surgery is needed and it can involve prognostic features.

Objectives: To analyze prognostic factors related to articular and periarticular infectious diseases.

Methods: Patients hospitalized between January and December 2019 in Rheumatology Service (CHUS) and diagnosed of articular or periarticular infectious disease were enrolled. Demographic, clinical and therapeutic data were collected.

Stata 15.1 was used to perform statistical analysis.

Results: 21 patients diagnosed of articular or periarticular infectious disease were included (138 patients hospitalized in 2019). Mean age was 57,3 years old (SD 18,2) and 76,2% were males. One cardiovascular risk factor was achieved, at least, by 71,4% (arterial hypertension the most frequent, followed by hypercholesterolemia and hyperuricemia). Gram positive cocci were identified in 76,2% of patients (*Staphylococcus aureus* in 47,6%, only one case oxacillin-resistant). A concomitant rheumatic disease was present in 4 patients (2 suffer from gout). No statistical association was found between this topic and acute-phase reactants (APR), complication rates or days of hospitalization. At hospitalization time, mean values of erythrocyte sedimentation rate (ESR) were 65,6 mm (SD 30,8) and C-reactive protein (CRP) 11,7 mg/dl (SD 7,7). Both have a positive association with days of hospitalization (r_{ESR}=0,282 r_{CRP}=0,424) and further, ESR demonstrates a positive correlation with this topic (CI95% -0,009 to 0,723 p=0,05569). Only 3 patients needed adjuvant surgery (articular infectious diseases with higher APR values). Surgery demonstrates a relationship statistically significant with articular involvement (t=-3,72 p=0,00), higher hospitalization rates (t=-2,51 p=0,02) and complication rates (Chi2=4,67 p=0,03 as decease, recurrence, bacteriemia, aftermath or soft tissue abscess).

Conclusion: Gout is the main rheumatic disease associated, in this study, to infectious diseases of musculoskeletal system. As opposed, to suffer a rheumatic disease isn't associate to a bad prognostic (hospitalization or complication rates). Furthermore, this cohort shows us the high prevalence of cardiovascular risk factors related with these diseases (hyperuricemia as predecessor of gout). Surgery intensifies as the main bad prognostic factor regarding days of hospitalization, complication rates and higher APR.

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Disclosure of Interests: None declared

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FRI0437 CT GUIDED NEEDLE BIOPSY IN VERTEBRAL OSTEOMYELITIS: RELIABILITY ANALYSIS AND STUDY OF WHICH FACTORS COULD INFLUENCE ON THE RESULT

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Background: Vertebral Osteomyelitis is an infectious disease of the vertebral body, also termed spondylodiscitis if the intervertebral disc is involved (which its avascular). Since the bacteriological characterization is in many times difficult and blood cultures are often negative, a bone biopsy is in most of the cases encouraged.

Objectives: The aim of this study is to analyze which factors could influence on the result of a CT guided biopsy (CTGB) in vertebral spondylodiscitis patients.

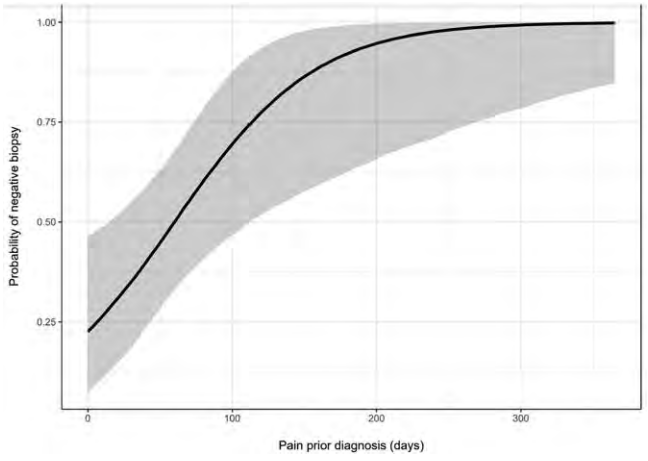
Methods: A retrospective observational study was performed including patients diagnosed of spondylodiscitis in a single center who underwent a CTGB. Demographic features and comorbidities, acute phase markers, microbiological results, radiological data, antibiotic exposure, medical complications and the clinical outcomes were also collected for analysis. Standard procedure in our center is performed by Musculoskeletal Specialized Radiologist under local anesthesia and CT control. Abscess sample is collected with a 18G needle with coaxial technique, trying to obtain at least 3 samples. For discal space, a thicker needle (13.5G-15G) is used. A logistic regression including cofounding factors was performed using R software.

Results: A total of 86 were included with a mean age of 62.75 (14.98) years old and predominationg male sex (68.60%). 15 patients (17.44%) presented any kind of immunosuppression. Clinical data are summarized in Table 1. Blood cultures were positive in 39.71% and sample culture showed a reliability of 49%. Organism which grew were gram + (66.67%), gram – (12.70%), mycobacteria (12.7%) and fungi (7.94%). In only 16 cases (18.6%) there was isolated the same organism in blood and on biopsy culture. From admission to procedure, a mean of 6 days was observed. Antibiotic treatment had a median value of 2 days (0, 6) and its exposure did not modified the culture positivity (IC 95% [0.274-5.211] p=0.816). Detailed analysis was performed looking for the influence of the days of exposure, which also failed (IC 95% [0.939-1.101] p=0.747). The longer duration of the pain was related to a higher probability of obtaining a negative result on the biopsy (IC 95% [1.004-1.035] p=0.026) (graphic 1). Neither fever (p=0.303) or higher CRP (IC 95% [0.992-1.006] p=0.761) value modified the culture result.

Table 1. Demographic and clinical characteristics.

	N=86	%
Clinical history		
High blood pressure	42	48.84
Diabetes Mellitus	19	22.09
Liver cirrhosis	16	18.60
Chronic kidney failure	13	15.12
Active Systemic Malignancy*	2	2.33
Rheumatoid arthritis*	3	3.49
Spondyloarthritis*	1	1.16
HIV infection*	4	4.65
Solid organ transplant receptor*	3	3.49%
Systemic Amyloidosis*	1	1.16
Splenectomy*	2	2.33
Previous spine pathology	50	58.14
Underlying/associated endocarditis	2	2.33%

*Considered as immunosuppressed patients



Conclusion: Even in cases under antibiotic treatment, CTGB displays an acceptable reliability. The longer the length of painful period before diagnosis was related to a higher chance of obtaining a negative result on culture. This result could be explained by a greater aggressiveness of pyogenic organisms that perhaps congregate in the lesser time span instead of non-pyogenic agents, that could deliver in more silent infection.

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Disclosure of Interests: None declared

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FRI0438 POST-CHIKUNGUNYA CHRONIC ARTHRITIS - SHARING OF BANGLADESH EXPERIENCE OVER ONE YEAR FOLLOW UP OF 60 PATIENTS

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Background: Chikungunya virus (CHIKV) infection is an emerging disease which is responsible for several epidemics around the world[1]. Systematic review and meta-analysis had shown that approximately 25% of cases of Chikungunya(-CHIK) would develop CHIK-Chronic Inflammatory Rheumatism and 14% would develop persistent arthritis (or spondylitis)[2].
Objectives: To describe the frequency of the clinical patterns of chronic arthritis & to characterize the clinical symptoms in a Bangladeshi cohort of CHIK patients 12months post-infection.
Methods: In 2017, a Chikungunya outbreak occurred in Dhaka, Bangladesh, during which a prospective cohort of CHIK patients with confirmed diagnosis was constituted. A longitudinal follow up of 60 patients from an initial cohort of 142 patients, attending the out-patient department of Rheumatology, BSMMU, was done. Patients having arthritis/ arthralgia or both lasting more than 3 months were considered as chronic cases. Their baseline and follow-up symptoms at 3m, 6m and 12months were evaluated. Functional status was assessed with the Bengali Version Health Assessment Questionnaire (HAQ).
Results: Of the initial 142 patients enrolled in the study, 135(95.1%) had CHIKV-IgM and 29(20.4%) had IgG positive. Patients that followed up in-person were predominantly adult (age 43.73 ± 11.09 years) and female 34 (56.7%). The majority of the patients 35 (58.3%) had undifferentiated arthritis. After three months, 8 (16.3%) had oligoarthralgia, 26 (53.1%) had polyarthralgia and 8 (16.3%) had polyarthralgia with oligoarthritis. At the end of one year, 13 (21.7%) patients underwent complete remission. Among the 47 patients, 21 had joint involvement where 11(52.4%) had polyarthralgia, 5(23.8%) had polyarthralgia with oligoarthritis, 5 (23%) had oligoarthralgia and 4 (19%) had monoarthralgia. Among the 47 patients, mild, moderate and severe functional disability was present in 89.4%, 6.4% and 4.3% patients respectively.
Conclusion: After one year of follow up, one-third of the patients remained symptomatic. Polyarthralgia was the predominant clinical feature. Mild functional disability was also observed in a significant number of patients.
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Table 1. Socio-demographic and clinical pattern of patients with Chronic CHK arthritis (n=60)

Variables	n(%)
Age (in years)	
Mean ±SD	43.73 ±11.1
Sex	
Female	34 (56.7)
Male	26 (43.3)
First joint involvement	
Generalized	34 (56.7)
Ankle	12 (20.0)
Knee	6 (10.0)
Wrist	5 (8.3)
Others (MTP, shoulder, neck and axial plane)	3 (5.0)
Clinical pattern	
Undifferentiated	35(58.3)
Spondyloarthritis	10 (16.7)
Rheumatoid Arthritis	7 (11.7)
Pre-existing Spondyloarthritis	6(10.2)
Pre-existing Rheumatoid Arthritis	1(1.7)
Pre-existing Osteo-arthritis Arthritis	1(1.7)

Table 2. Joint involvement of patients with Chronic CHIK arthritis

Joint characteristics	3 m (n=49)	6 m (n=36)	1yr (n=21)
	f(%)	f(%)	f(%)
Type of involvement in persistent pain			
Joint only	33 (55.0)	28 (46.7)	20 (33.3)
Both joint & soft-tissue	16 (26.7)	8 (13.3)	1 (1.7)
Joint involvement			
Monoarthralgia	1 (2.0)	5 (13.9)	4 (19.0)
Oligoarthralgia	8 (16.3)	6 (16.7)	5 (23.0)
Polyarthralgia	26 (53.1)	18 (50.0)	11 (52.4)
Monoarthritis	1 (2.0)	0(0.0)	0(0.0)
Oligoarthritis	6 (12.2)	3 (8.3)	0(0.0)
Polyarthritis	7 (14.3)	9 (11.1)	1 (4.8)
Oligoarthralgia & monoarthritis	1 (2.0)	0 (0.0)	0 (0.0)
Polyarthralgia & monoarthritis	0 (0.0)	1 (2.8)	0 (0.0)
Polyarthralgia & oligoarthritis	8 (16.3)	4 (11.1)	5 (23.8)
Polyarthralgia & Polyarthritis	1 (2.0)	0 (0.0)	0 (0)

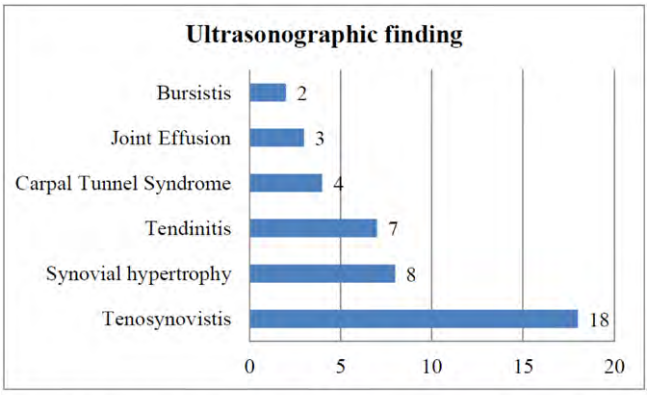


Figure 1: Distribution of patients by ultrasonographic findings (n=60)

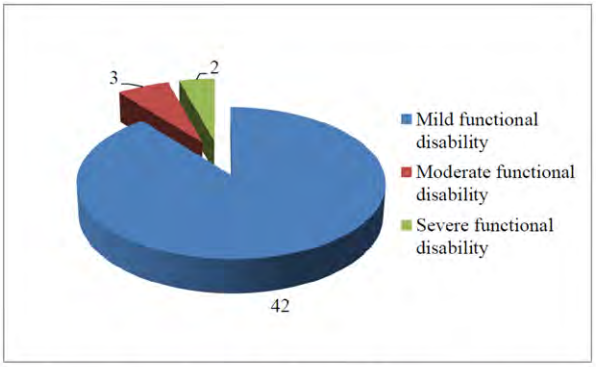


Figure 2: Distribution of patients by functional disability after 1 year (n=47)

Disclosure of Interests: None declared
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FRI0439

PET-CT IN THE ASSESSMENT OF OSTEOARTICULAR INFECTIONS ASSOCIATED WITH INFECTIVE ENDOCARDITIS

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Background: Five to eleven percent of infective endocarditis (IE) are associated with a musculoskeletal infection. Thanks to its good sensitivity, the use of PET-CT in this pathology makes it possible to confirm the diagnosis by seeking valvular hypermetabolism but also by mapping distant septic foci.
Objectives: The main objective of our study was to assess the prevalence of osteoarticular fixation (OAF) with PET-CT, symptomatic or not, in patients with IE. The secondary objectives were to determine predictive factors for osteoarticular infections such as the type of valve damage (native or prosthetic) and germ.
Methods: This study was carried out on the basis of a prospective cohort of patients admitted in the department of cardiology in Henri Mondor Hospital for IE suspicion between August 2015 and July 2019. Demographic, clinical, bacteriological, imaging and therapeutic data have been collected. Patients matching Duke's modified criteria according to ESC 2015 (Duke + IE) and / or a cardiac fixation according to standard whole-body PET-CT were included in the analysis. All of the PET-CT scans were reviewed by a nuclear medicine specialist to confirm whether or not there was a heart condition and to look for septic-looking OAF.
Results: From this cohort, we included 90 IE Duke + patients and 42 patients with cardiac PET-CT fixation (including 31 IE Duke +). In the IE Duke + group, we found OAF in 18 patients (20%), 39% of whom were asymptomatic. There were 9 spondylodiscitis (4 on the cervical level, 7 on the thoracic level, and 2 on the lumbar level), 5 glenohumeral arthritis, 2 coxofemoral arthritis, 1 sternoclavicular arthritis and 1 sacroiliac arthritis. The IE affected the aortic valve in 50% of the cases and the mitral valve in 22%. In other cases, the infection involved the internal automatic defibrillator (ICD) or the pacemaker. The valves were prosthetic in 73% of the cases. The bacterial ecology was mainly represented by

Enterococcus faecalis (39%) then staphylococcus aureus (17%) against 14% and 13% respectively in the entire IE Duke + group. In the group with cardiac PET-CT fixation, OAF was found in 10 patients (40%), 70% of whom were asymptomatic. Among them, there were 5 spondylodiscitis (2 cervico- thoracic and 3 exclusively thoracic), 2 glenohumeral arthritis (20%), 2 coxofemoral arthritis and 1 sternoclavicular arthritis. The IE affected the aortic valve in 60% of the cases, mitral in 30% of the cases and it was an infection on ICD in 10% of the cases. The main germs found were Enterococcus faecalis (30% of cases) and Staphylococcus epidermidis (20% of cases).

Conclusion: In patients with IE, PET-CT seems to be interesting in detection of osteoarticular infections, and consequently, could impact the diagnosis and the treatment modalities. In our cohort, 1 patient in 5 had an OAF and nearly 40% of them were asymptomatic. The overrepresentation of enterococcus is consistent with recent data in the literature

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Disclosure of Interests: Benjamin HUGUES: None declared, Bérivan EMSEN: None declared, Julien TERNACLE: None declared, Raphaëlle HUGUET: None declared, Antonio FIORE: None declared, Raphaëlle LEPEULE: None declared, Xavier Chevalier: None declared, Mukedaisi ABULIZI: None declared, Florent Eymard Consultant of: Regenlab

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FRI0440 RISK FACTORS FOR CYTOMEGALOVIRUS INFECTION IN PATIENTS WITH AUTOIMMUNE DISEASES

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Background: The risk for opportunistic infections in patients with autoimmune diseases requiring intensive immunosuppressive therapy is high and cytomegalovirus (CMV) infection is one of the most common opportunistic infections. Since 2011, we have performed weekly CMV pp65 antigen testing for patients at risk of opportunistic infections owing to autoimmune diseases to ensure appropriate patient management.

Objectives: To evaluate the risk factors that predict CMV infection in patients that received remission-induction therapy for autoimmune diseases.

Methods: We enrolled 254 patients (93 male, 161 female) from our hospital with autoimmune disease and who received remission-induction therapy with prednisolone at a dose greater than 0.5 mg/kg/day between January 2011 and December 2018. We retrospectively analysed their clinical characteristics and laboratory data, including treatment regimens and CMV pp65 antigen test results. The presence of more than five CMV pp65 antigen-positive cells over two slides was considered a positive result. We conducted univariate and multivariate analyses to extract CMV risk factors.

Results: Of the patients we evaluated, 60 suffered from systemic lupus erythematosus (SLE), 55 from anti-nucleolar cytoplasmic antibody-associated vasculitis (AAV), 31 from dermatomyositis (DM), 14 from interstitial pneumonia with anti-aminoacyl tRNA synthetase antibody, 14 from adult-onset Still's disease (AOSD), 14 from rheumatoid arthritis (RA), 11 from mixed connective tissue disease (MCTD), 10 from Takayasu's aortitis, and 45 suffered from other autoimmune diseases. Pulse therapy with methylprednisolone (mPSL) and immunosuppressive reagents were administered to 103 (40.6 %) and 97 (38.2 %), respectively. The median follow-up period was 61.0 days, and 66 patients became CMV pp65 antigen-positive during this period (SLE, 15; DM, 14; AAV, 9; AOSD, 8; and other, 20). Univariate analysis revealed that when compared to patients testing negative for the CMV pp65 antigen patients testing positive had lower total lymphocyte count (TLC) (825 /uL vs. 1220 /uL; $p < 0.01$), a lower serum albumin level (2.70 g/dL vs. 3.30 g/dL; $p < 0.01$), a higher HbA1c level (6.3 % vs. 5.9 %; $p<0.01$), and were older (66.0 vs. 59.5 year old; $p < 0.01$). Forty-nine of the 66 patients in the positive group received mPSL pulse therapy ($p < 0.01$), and 38 received immunosuppressive reagents ($p < 0.01$). Logistic regression analyses indicated that a higher age by decade (OR; 1.46 [95%CI 1.06 - 2.00]), a lower TLC per 100/uL (OR; 0.83 [95%CI 0.73 -0.94]), a higher HbA1c level per 1% (OR; 2.37 [95%CI 1.25-4.53]), and mPSL pulse therapy (OR; 3.92 [95%CI 1.33-11.5]) were risk factors for CMV pp65 antigen positivity.

Conclusion: Higher age, lower TLC, higher HbA1c, and treatment with mPSL pulse therapy were risk factors for acquiring CMV infection, as measured by the presence of the CMV pp65 antigen, in patients receiving remission-induction therapy for autoimmune diseases. Careful monitoring of these, at risk, patients is necessary.

Disclosure of Interests: None declared

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FRI0441 INFECTIOUS DISEASES RISK ASSESSMENT PRIOR TO IMMUNOMODULATION THERAPY - EXPERIENCE FROM AN INFECTIOUS DISEASES UNIT

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Background: The increasing use of immunomodulatory therapies has motivated the development of strategies to assess and prevent infectious diseases in these immunosuppressed patients, in whom the risk of serious infections is higher.

Objectives: The aim of this study was to recognize the need to standardize prophylactic and therapeutic strategies in this population.

Methods: Retrospective review of clinical files of patients evaluated in the infectious risk assessment in an outpatient clinic at the Infectious Diseases Unit at Hospital de Curry Cabral in Lisbon, between June 2016 and November 2019. We reviewed information regarding sex, age, origin, occupation, past travels as well as plans of future ones, contact with live animals, intake of unpasteurized products or unsafe drinking water, along with relevant data regarding past medical history and previous and/or ongoing treatments, including immunomodulatory ones.

Results: During the established timeline,1305 appointments were carried out, corresponding to a total of 415 patients. The majority of patients were female (263; 63.7%), the average age was 50 years and 82% were of Portuguese nationality. The most frequent groups of diseases were autoimmune/inflammatory (84.1%) and demyelinating (10.1%). At the date of the first consultation, 70% were already under immunosuppression. Screening for latent tuberculosis infection (LTBI) was done in 99% of the patients (n = 410) and treatment was proposed to 160 patients (38.5%). At the time of screening, 56,8% of the patients were under immunossuppressive therapies, which included high doses of systemic corticosteroids (37%), anti-TNF alpha (7,7%) and combine therapy with non-biologic agents. Active disease was diagnosed and treated in two patients. Interferon gamma release assay test (IGRA) was positive in 56.8% of patients (n = 91), negative in 32.5% (n = 52) and indeterminate in 7.5% (n=12). Of the 69 patients (43%) with indeterminate/negative or not performed IGRA, Mantoux test (TST) was positive in 48 patients. In the remainder, the treatment proposal for LTBI was based on clinical, epidemiological or radiological signs suggestive of past infection.

In order to prevent hyperinfection/disseminated strongyloidiasis, 354 individuals were screened with *Strongyloides stercoralis* serology, of which 51 patients (14.4%) had a positive result and were treated with ivermectin. Regarding vaccination, the recommendation for annual influenza vaccination was reinforced, together with the prevention of invasive pneumococcal disease. In view of future travelling plans, vaccination against yellow fever (n = 10), meningococcal disease (n = 7), typhoid fever (n = 6), and polio (n = 2) was recommended. In cases without a previous history of measles and according to the year of birth, VASPR was prescribed to 6 patients. Vaccination to prevent herpes zoster was recommended to 20 patients. After serological evaluation, the vaccine against hepatitis A and hepatitis B was prescribed to 89 and 132 patients, respectively, the latter when serological evidence of previous vaccination or contact was absent. We identified 10 cases of positive anti-HCV antibodies, with undetectable viral load. Primary prophylaxis for *Pneumocystis jirovecii* pneumonia was recommended to 104 patients. Prophylaxis against reactivation of Herpes simplex infection was initiated in 4 patients.

Conclusion: The decision to start immunosuppressive therapy comes with benefits and risks. Appropriate screening prior to starting therapy is an essential tool for its safe use. Referral to a specialised Infectious Risk Assessment consultation should be done promptly in order to review and address accordingly the risk of specific infections taking in to account the patients clinical and epidemiologic history.

Disclosure of Interests: None declared

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FRI0442 **APPROPRIATE USE OF SEROLOGY TESTS FOR THE DIAGNOSIS OF LYME DISEASE. EXPERIENCE IN AN URBAN AREA**

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Background: Lyme disease (LD) is a multisystemic animal-borne disease caused by spirochetes of the *Borrelia burgdorferi s.l* complex and transmitted by ticks of the species *Ixodes ricinus*. In Spain, most cases occur in rural areas of the north-east region with a peak of maximum incidence between spring and early autumn. The diagnosis is based on a history of potential exposure to ticks, the recognition of characteristic clinical manifestations and serological testing.
Objectives: To assess the suitability of serological study for the diagnosis of LD in an urban area.
Methods: Retrospective observational study that included all LD serology tests made between April 2017 and September 2019 at a tertiary hospital in Barcelona covering a population of 450,000 people. Demographic data and the medical department that requested the serology test were collected along with serology test results. The medical records of patients with positive serology were consulted to identify which patients were finally diagnosed with LD along with their clinical manifestations, treatment and outcome.
Results: A total of 574 serological tests were included and 78 (13.59%) of them were positive. Only 1.04% (6) of all serological tests belonged to patients finally diagnosed with LD. The department that made most requests was Neurology (37.3%) followed by Infectious Diseases (21%), Internal Medicine (14.5%), Emergency Medicine (4.7%), Dermatology (4.5%), Critical Care Medicine (2.3%) and Rheumatology (2.1%). 50% of the diagnosed patients were women with a mean age of 57.7±7.7DE years. In 50% of diagnosed cases, patients remembered a tick bite during activities in the mountain or rural areas. The most common clinical manifestations were erythema migrans (67%), non-inflammatory arthralgias (50%), fatigue and malaise (67%), together with one case of meningoencephalitis and one of knee monoarthritis. All diagnosed patients received antibiotic treatment with ceftriaxone (33%) or doxycycline (66%). Only one patient presented post-Lyme syndrome.
The serological test for LD in our center had a total individual cost of 15.75 eur, so the cost of the 574 requests was 9,040.5 eur. 7,812 eur corresponded to negative results and 1,134 eur to false positive results.
Conclusion: Our study indicates the overuse of diagnostic testing for LD with implications for patient care and cost-effective health management. In the absence of a history of potential exposure to infected vector ticks or characteristic clinical manifestations, unnecessary microbiological tests should not be performed.
Disclosure of Interests: David Lobo Prat: None declared, Luís Sainz Comas: None declared, Virginia Pomar: None declared, Ana Milena Millán Arciniegas: None declared, HyeSang Park: None declared, Andrea García-Guillén: None declared, Sicylle Jeria: None declared, Ana Laiz: None declared, Berta Magallares: None declared, Ivan Castellví Consultant of: Boehringer Ingelheim, Actelion, Kern Pharma, Speakers bureau: Boehringer Ingelheim, Actelion, Bristol-Myers Squibb, Roche, Patricia Moya: None declared, Cesar Díaz-Torné: None declared, Susana P. Fernandez-Sanchez: None declared, Hector Corominas: None declared
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FRI0443 **CLINICAL CHARACTERISTICS AND RELATED FACTORS OF COMMON RHEUMATIC DISEASES COMPLICATED WITH TUBERCULOSIS INFECTION**

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Background: Rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and syndrome(SS) are common rheumatic diseases with high incidence. Patients with those rheumatic diseases are at high risk of tuberculosis (TB) infection. However, manifestations can be atypical and easily confused with those of rheumatic disease itself. For those patients, diagnosis is usually much more difficult and further make treatment delayed. Sometimes it may lead to mistreatment. Therefore, it is important to recognize the clinical characteristics of those patients.
Objectives: To explore the clinical characteristics and high risk factors of common systemic rheumatism complicated with tuberculosis infection.
Methods: A total of 3,906 cases of RA, SLE, and SS common systemic rheumatism diagnosed in the People's Hospital of Sichuan Province from January 2007 to January 2017 were collected with carefully exclusion with other infectious diseases and neoplastic disease. One hundred and five patients with TB were included as infection group, including 42 cases of RA, 41 cases of SLE, and 22 cases of SS. In the control group, 84 patients with RA, 82 patients with SLE, and 44 patients with SS were randomly selected from the corresponding rheumatoid non-infected patients hospitalized during the same period.
Results: Fever was the most common symptom among 42 cases of RA, 41 cases of SLE, and 22 cases of SS with TB, accounting for 83.3%, 92.7%, and 68.2%, respectively. Cough, weight loss or fatigue was less common. For 41 cases of SLE and 22 cases of SS with TB, the proportion of pulmonary was 46.3%, 59.01%, respectively.In TB infection group, 27 cases of RA, 21 cases of SLE, and 13 cases of SS with TB had two or more chest CT findings, accounting for 59%, 57%, 62%, respectively. Lesions located in the posterior or posterior segment which TB usually affected were 9 cases(33.3%),9cases(42.9%),6cases(27.2%),respectively.The daily average dose of hormones within 1 year in TB infection group was higher than that in the control group ($P<0.05$). For SLE patients, lower counts of CD4+TL were found in TB infection group ($P<0.05$), while no such differences were found in RA and SS group.
Conclusion: Patients with RA who have TB infection are mainly pulmonary TB. For SLE and SS patients, the chance of pulmonary tuberculosis and extra-pulmonary tuberculosis is similar.Symptoms of RA, SLE, SS with TB, such as fever, cough, weight loss, fatigue, are similar with the primary disease or other infection. Chest imaging is diversity. It is difficult to diagnose.Daily average dose of hormone within one year may be a common risk factor for RA, SLE and SS patients with TB. Decreased CD4+TL may also be a risk factor for SLE patients with TB.
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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.3717

FRI0444 **HPVB19 INFECTION IN ADULT 53 CASES**

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Background: Human parvovirus B19(HPVB19) is a member of the large *Parvoviridae* family and, as a human pathogen, is responsible for various diseases. [1)] In children, HPVB19 infections usually presents as red rash, which is often described as a"slapped cheek." However, the presentation varies in adults.[2)] HPVB19 outbreaks mostly occur in the winter and spring.[1)] The serum IgM test is the preferred means for diagnosing acute HPVB19 infections.[2)]
Objectives: We investigated the epidemiology, clinical symptoms, and time course of HPVB19 infections in real-world practice by examining patients treated at a community hospital in Japan.
Methods: We studied adult patients with HPVB19 infections at Suwa Central Hosptial from April 2010 to November2019. Patients who were age 18 years or older, anti HPV B19 IgM antibody-positive, and symptomatic were included. We retrospectively examined the patients' medical records to determine onset days, clinical symptoms and antinuclear antibody(ANA)-postitive rates. We defiend day 1 as the day when clinical symptoms first appeared.
Results: 53 patients were included in the study. Patient characteritistics were mean age 43 years, female 79.2%, mean period from onset to diagnosis 13days. Epidemic season were 4year cycle. (Figure 1) Clinical symptoms and time course from onset day were upper respiratory symptoms(17.0%, 1.7days), fever(54.7%, 1.9days), abdominal symptoms(15.1%, 4.4days), edema(47.2%, 5.6days), arthralgia(71.7%, 6.6days), itching(15.1%, 6.9days), rash(62.3%, 8.9days) and lymphoadenopathy(30.2%, 10.2days). (Figure 2) ANA positive rate was 50%(13/26) and average was 92.3.

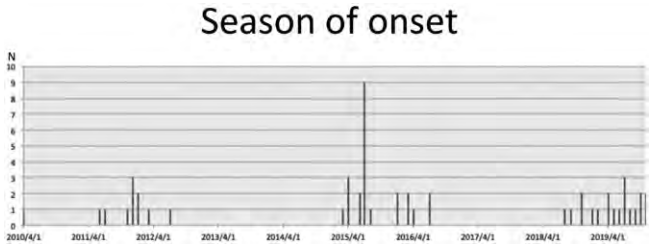
Conclusion: 53 adult patients infected HPVB19 in 10 years at community hospital in Japan. Epidemic season were 4year cycle and skin eruption and joint symptoms appeared 4-5 days after upper respiratory symptoms. Previous study show that a second-phase illness with rash and arthralgia appear 10-11 days after the appearance of upper respiratory sympotms.[3)] In our study, a second-phase symptoms appeared about one week earlier than in previous study. Half of the patients were weakly ANA positive.

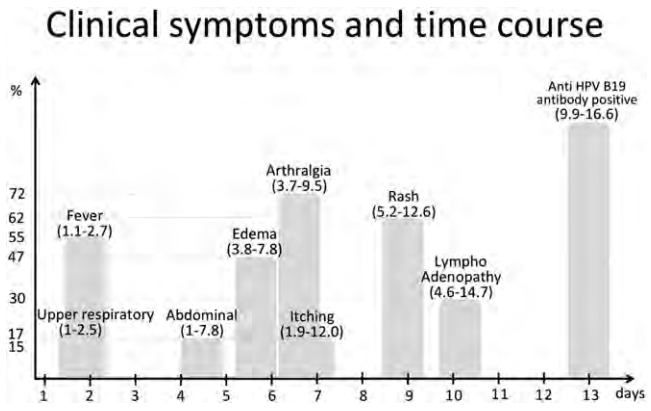
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FRI0445 HLA-B27 IN POSTSTREPTOCOCCAL REACTIVE ARTHRITIS WITH ENTHESITIS

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Background: Poststreptococcal reactive arthritis (PSRA) is a very common diagnosis in rheumatology practice, which develops after recent pharyngeal streptococcal infection and characterized by aseptic inflammation in one or more joints and periarticular involvement. Now no diagnostic criteria have been agreed [2,4]; association of the expression of HLA-B27 and PSRA is not clear [1,3].

Objectives: In our study we analyzed the features of PSRA in presence of HLA-B27.

Methods: 88 patients (48 female and 40 male) aged between 18-55 years with complains of pain, tender and swollen joints developed after recent pharyngeal streptococcal infection underwent standard physical and laboratory rheumatological examinations. Acute rheumatic fever and other inflammatory arthritis were excluded.

Results: 60 patients (68,2%) had oligo-polyarthralgia, 10 patients (11,4%) - monoarthritis, 24 patients (27,3%) had asymmetrical olygoarthritis, 4 patients (4,5%) had polyarthritis, enthesitis was found in 4 (4,5%) patients, tenosynovitis of the palmar flexor tendons in 10 cases (11,4%) and the peroneal tendons of the ankles in 5 patients (5,7%), one-sided sacroiliitis (confirmed by MRI) in 5 patients (5,7%).The mean level of ASL-O was 542 U/ml, CRP -15 mg/L, ESR - 34 mm/H; HLA-B27 was present in 24 (30,7%) patients. HLA-B27 positivity was connected to enthesitis, sacroiliitis, more joint involvement with higher levels of ESR and CRP.

Conclusion: 30% of patients with poststreptococcal reactive arthritis are HLA-B27 positive, the presence of HLA-B27 leads to more frequent development of enthesitis, polyarthritis and sacroiliitis with higher level of inflammatory activity which dictate the need for longer supervision of such patients for possible triggering of ankylosing spondylitis development.

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FRI0446 VIRAL ARTHRITIS: DESCRIPTIVE ANALYSIS OF A SERIES OF 131 PATIENTS

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Background: Arthritis of viral aetiology is considered the most frequent cause of acute arthritis. The most common etiologic agent is parvovirus B19 (B19). Besides, other viruses can lead to inflammatory joint disease, such as Epstein-Barr virus (EBV), Cytomegalovirus (CMV), Human immunodeficiency virus (HIV), Rubella, Mumps, Hepatitis B and C virus (HBV and HCV) and Chikungunya (in transcontinental travellers or immigrants).

Objectives: To describe the epidemiological characteristics, clinical and analytical course, evolution and treatment of a series of patients with a confirmed diagnosis of viral arthritis.

Methods: A descriptive study was performed, considering a series of cases of viral arthritis collected between 2000 and 2019. Epidemiological (sex, age, the season of the year, year of diagnosis, children of pediatric age), clinics (joint pattern, prodromes, accompanying clinic) and analytical (CRP, ESR, ANA, RF) variables were collected. Statistical analysis was performed with the SPSS 22.0 program.

Results: The data of 131 patients (109 women, 22 men), with a mean age of 39.7 years (SD 11.9) were collected. 93.9% of the cases were produced by B19, 3.8% by EBV, and only 3 by other viruses (1 by CMV, 1 by HBV, 1 by Mumps). The highest incidence years were 2005(55 cases), 2000(10 cases) and 2016(8 cases). Almost half of the cases (46.6%) occurred in spring, while 32.8% in summer, 15.3% in winter and 5.3% in autumn. Contrary to the expectations, only 20% of the patients had children in pediatric age.

The most frequent clinical picture was acute polyarthritis (53.4%), followed by inflammatory polyarthralgias (19.1%). Moreover, acute oligoarthritis was present in 10.7% of cases, and acute monoarthritis in 3.1% of cases. More than half of the patients (54.2%) had prodromes, most frequently respiratory symptoms, and the joint clinic was accompanied by a skin rash in 35.1% and fever in 29% of cases. Analytically, 33.6% presented high CRP, 39.7% high ESR, 19.8% transient anemia, 9.9% positive ANA (4.6% transiently), 9.1% anti dc-DNA (7.6% transiently), and 10.7% positive RF (3.1% transiently). In 79.4% of cases, the clinic picture was limited, with a mean duration of 36 days (SD 47.7), but 12.3% had recurrences. The 69.5% of the patients needed treatment with acetaminophen and/or NSAIDs (6.7% did not need treatment), but corticotherapy was needed in 21.4% of cases. 4.6% of the cases evolved to chronicity, which made DMARD necessary in 3 patients (two of them with a final diagnosis of rheumatoid arthritis, being treated with Methotrexate and Leflunomide, and the third one had a diagnosis of undifferentiated connective disease, treated with Hydroxychloroquine).

Conclusion: B19 remains the most common cause of viral arthritis in our population. It appears with a sporadic, occasionally epidemic, pattern of presentation, predominantly in warm seasons. A clinical presentation as an oligoarthritis or an acute monoarthritis or even the positivity of autoimmunity markers, should not make us rule out this possible aetiology. One out of 20 cases can evolve to chronicity and even make necessary the addition of DMARD.

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FRI0447 FIRST COMPREHENSIVE LONG-TERM ASSESSMENT OF MUSCULOSKELETAL CONSEQUENCES AMONG EBOLA SURVIVORS

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Background: The tremendous size of the 2013-2016 West African outbreak of Ebola virus disease (EVD) resulted in a sizeable population of survivors, many reporting short-term sequelae such as arthralgia and myalgia.
Objectives: We aimed to report a detailed and long-term description of patients' musculoskeletal (MS) symptoms.
Methods: We performed a cross-sectional study following systematic rheumatological screening of patients included in the Postebogui cohort (Conakry district). We used regression models to establish the magnitude of EVD as a risk factor for developing chronic MS pain by comparison with a control cohort and to establish risk factors for developing MS pain among survivors.
Results: The study included 313 patients (55.6% female), with a median age of 28.2 years (IQR 21-37), and a median time from ETC discharge to rheumatological visit of 26.2 months (IQR 23-30). Chronic MS pain was reported in 216 (69%) patients, and was predominantly mechanical (48%). Enthesis and painful peripheral joints were largely involved (91%) with symmetrical distribution. Previous Ebola infection was a major risk factor for chronic MS pain (aOR, 6.662 [95% CI, 4.522–9.921]). Among survivors, increasing age (OR 1.14, 95% CI 1.08-1.22) and female gender (OR 3.58, 95% CI 1.22-11.80) were both associated with persistent MS pain, while myalgia experienced during the acute phase of EVD appeared protective (OR 0.14, 95% CI 0.04-0.42).
Conclusion: Our study provides the most accurate long-term description of MS disorders among Ebola survivors. Joint and muscle pain sequelae are frequent and require specialized care.
Disclosure of Interests: None declared
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FRI0448 FOUR CASES OF SYPHILIS MIMICKING RHEUMATOLOGICAL CONDITIONS PRESENTING TO THE GENERAL RHEUMATOLOGY SERVICE AT ST GEORGES HOSPITAL, LONDON, UK IN 2018-2019

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Background: Sir William Osler once wrote: "He, who knows syphilis, knows medicine".
Whilst the Tuskegee Syphilis trials live in infamy, the advent of succesful penicillin treatment and sexual health education resulted in the lowest recorded incidence ever in 2001[1].
Unfortunately, cases of syphilis have nearly tripled in the past decade (from 2,847 in 2009 to 7,541 in 2018 in the UK)[1]. WHO now estimates the global median prevalence of Syphilis, among men who have sex with men, is 6%[2]
The current cohort of clinicians will therefore have limited clinical experience of Syphilis, which can often mimic rheumatic conditions. We present the clinical experience of a tertiary teaching centre hospital.
Objectives: To identify the scope of clinical cases, with a diagnosis of Syphilis, during 2018-2019 at St Georges University Hospital, London, UK.
Methods: Clinical cases were identified by health professionals and a retrospective review of medical records was undertaken.
Results: There were 4 cases identified during 2018-19.
Case 1: The patient was diagnosed with bilateral uveitis secondary to primary syphilis, and immunosuppression may have contributed to this.
Case 2: The rash developed after the initial presentation and an extended infection screen was performed.
Case 3: The patient had a 6 month duration of symptoms and had had a negative sexual health screen 1 year prior to presentation.
Case 4: The patient had no features of extra pulmonary sarcoidosis and an infectious screen was undertaken.
All 4 cases were referred to the Infectious Disease Unit for treatment. 3 patients received standard treatment with Penicillin, and 1 patient received an oral course of Doxycycline, due to a penicillin allergy.
2 of the 4 cases had complete resolution of symptoms, and 2 of the cases had only partial resolution of symptoms at the time of publication.
Conclusion: Syphilis can present with an inflammatory arthritis, PMR and GCA –type symptoms, ocular inflammation, neurological disturbance and rashes that can mimic autoimmune conditions.
Our cases highlight the increasing incidence, as well as the risk of reactivation following immunosuppression. Current practice does not advise routine testing for syphilis prior to initiation of immunosuppressive therapy. However the rising incidence should prompt careful evaluation, and detailed sexual history, particularly in high risk groups. The diagnostic test interpretation and treatment requires close collaboration with Infectious Diseases Specialists.
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FRI0449 MANAGEMENT AND OUTCOME OF SEPTIC ARTHRITIS OF NATIVE JOINT: A NATIONWIDE SURVEY

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Patient	Age	Sex	Past Medical History	Symptomatology	Risk Factors	Presumed Diagnosis	Serology
1	69	Male	Hypertension GCA	Bilateral visual loss, rash	MSM Prednisolone Tocilizumab	GCA-related visual loss	RPR 1:64 TPPA 1: 10248
2	46	Female	Nil	Joint pain and swelling, rash	Hepatitis B Core Antibody positive	Undifferentiated Inflammatory Arthritis	RPR 1: 16
3	40	Male	Nil	Joint pain, alopecia, uveitis and rash, weight loss	MSM	Primary Syphilis	RPR 1: 16 TPPA 1: 10248
4	86	Female	Pulmonary Sarcoidosis, Squamous cell carcinoma of left maxillary sinus	Lower motor neuron facial nerve palsy	Prednisolone	Sarcoidosis	RPR 1:4 TPPA 1:80

GCA: Giant cell arteritis, MSM: Men who have sex with men, RPR: rapid plasma regain, TPPA: Treponema pallidum particle agglutination assay

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Background:
Objectives: To describe current management and outcome of septic arthritis on native joint in French rheumatology departments.
Methods: Retrospective, nation-wide multicentric study. 127 French rheumatology departments were contacted to report 10 successive cases of septic arthritis on native joint that occurred between the 01/01/16 to 31/12/17 (excluding mycobacteria). Characteristics, diagnosis procedure, therapeutic management and outcome were recorded.
Results: 52 centers included 363 patients (mean age 64± 18.7 years, mean Charlson comorbidity index 4±3). 28.3% patients had a preexisting arthropathy on affected joint. Monoarthritis was observed in 89.6% patients, knee was the most frequent site (38.9%). The most frequent pathogens were *Staphylococcus sp* (50.7%) and *Streptococcus sp.* (23.3%). Bacteremia was found in 156 (45.1%) patients and endocarditis in only 12 (3.0%). Management was heterogeneous. All patients received antibiotics for a mean duration of 46.7±22 days (including intravenous route: 17.3±15.4 d). An initial monotherapy was administered in 42.3% of patients. Surgical procedure (mostly lavage 70.6%) was performed in 171 (48.3%), joint immobilization in 128 (35.3%) (median duration of 21.7±14.1 days). 94 (29.2%) patients have had serious complications including 29 (9.5%) death. Factors associated with death are reported in the table.
Conclusion: This study shows that management of septic arthritis is very heterogenous with a still high rate of morbidity and mortality. We identified age, comorbidities, bacteremia and recent antibiotherapy were associated with mortality. Of note, duration of antibiotics was not. Thus, new guidelines are needed in order to facilitate septic arthritis management.
Table:

Factors	Survivor (N=276)	Dead (N=29)	Univariate analysis p	Adjusted Odds ratio (95%IC)	Multivariate analysis p
Age	65 (16-97)	82 (32-98)	<0,001	1,07 (1,03-1,12)	< 0.001
Charlson's index	1 (0-12)	2 (0-9)	0,0001	1,3 (1,05-1,63)	0,018
Delay before antibiotic initiation	8,5 (0-310)	5 (0-75)	0,0484	0,99 (0,96-1,02)	0,562
Corticosteroid in the previous 3 months	13,9%	33,3%	0,0184	2,56 (0,75-8,74)	0,133
Bacteriemia	42,4%	71,4%	0,0061	5,07 (1,4-18,37	0,013
Antibiotics in the previous 3 months	26,6%	56,6%	0,0056	6,7 (2,04-22,01)	0,002

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FRI0450

MEASURES OF DISEASE SEVERITY PREDICT DISABILITY AND QUALITY OF LIFE DIFFERENTLY IN RHEUMATOID ARTHRITIS AND CHRONIC CHIKUNGUNYA DISEASE

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Background: Chronic rheumatological manifestations similar to those of rheumatoid arthritis (RA) have been described after chikungunya virus infection. However, the clinical significance of the symptoms and disease severity in the two conditions has not been directly compared.
Objectives: To compare, using identical measures of disease severity and patient outcomes, the impact of disease severity measures and symptoms on outcomes in RA and chronic chikungunya disease.
Methods: Forty patients with chronic chikungunya arthralgia two years post-infection and 40 matched patients with RA were enrolled in Roraima, Brazil. Twenty-eight joints were assessed for tenderness and swelling, a pain intensity visual analogue scale, musculoskeletal stiffness questionnaire, modified Health Assessment Questionnaire and the EuroQol EQ5D-5L quality of life assessment were completed. The importance of the various measures of disease severity were analysed using Spearman's rank correlation and regression analysis.
Results: Tender and swollen joint counts, pain and stiffness were all predictive of the HAQ disability index in RA, but only stiffness was significantly associated with disability in chikungunya patients (Table 1). Tender and swollen joint counts, pain and stiffness were predictive for all EQ5D quality of life domains (except anxiety/depression) in RA patients. In contrast, in chikungunya disease, tender joint counts were predictive only of usual daily activities; pain was predictive of impaired mobility, self-care and discomfort, while stiffness was predictive for the mobility and anxiety/depression domains (Figure 1). Swollen joint counts were not associated with any of the patient outcomes in chikungunya disease. Linear regression analysis confirmed (p=0.003) that the effect of swollen joint count on the HAQ disability index depends on the underlying disease.

Table 1. Association of disease severity with HAQ disability index in rheumatoid and CHIKV+ arthritis

Severity measure	Rheumatoid arthritis	CHIKV+ arthritis
	r (p)	r (p)
Tender joint count	0.56 (0.0002)	0.24 (0.14)
Swollen joint count	0.60 (<0.0001)	0.002 (0.99)
Joint pain (VAS)	0.55 (0.0002)	0.29 (0.07)
Stiffness severity	0.57 (0.0001)	0.38 (0.02)

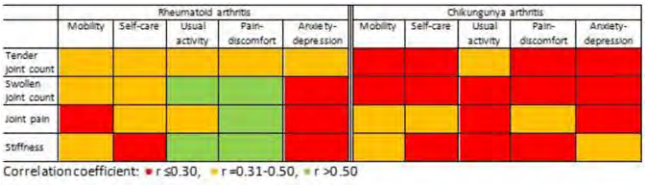


Figure 1. Association of disease severity with quality of life domains in rheumatoid and CHIKV+ arthritis

Conclusion: The value of all the disease severity measures tested in RA were confirmed, but tender joint counts may have more limited value in the assessment of chronic chikungunya disease. Joint swelling appears to have little impact for chikungunya patients, while stiffness appears to be an important metric to quantify chikungunya arthritis disease severity.
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Basic and translational science in paediatric rheumatology

FRI0451

RELATIONSHIP BETWEEN MEMBRANE-BOUND AND SOLUBLE RECEPTOR FOR ADVANCED GLYCATION END PRODUCTS AND DISEASE ACTIVITY IN JUVENILE IDIOPATHIC ARTHRITIS PATIENTS

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Background: Membrane-bound receptor for advanced glycation endproducts (mRAGE) expression increases in the presence of its ligands (e.g., High Mobility Group Box 1, HMGB1) and triggers an inflammatory immune response. In contrast, soluble RAGE (sRAGE) acts as a decoy receptor and downmodulates inflammation. Some studies have demonstrated that decreased sRAGE levels are negatively correlated with disease activity in juvenile idiopathic arthritis (JIA) but expression of mRAGE has not been studied.

Objectives: The aim of this study is to evaluate mRAGE and sRAGE on peripheral blood (PB) and synovial fluid (SF) mononuclear cells (MC) of patients with JIA and healthy controls and to assess whether there is an association with established inflammatory markers and clinical measures.

Methods: Matching samples of blood and synovial fluid were collected from patients with JIA (n=33) with active arthritis. RAGE expression on mononuclear cells was analyzed using flow cytometry. The intensity of RAGE expression was measured as mean fluorescence intensity (MFI). Levels of sRAGE and HMGB1 were determined with a specific ELISA kit in the serum and synovial fluid (SF) of patients with JIA. Relation between cellular RAGE and sRAGE with disease activity parameters [JADAS71, CHAQ, C reactive protein (CRP) and erythrocyte sedimentation rate (ESR)] and HMGB1 were described. We compare mRAGE expression in PBMC and serum sRAGE levels between JIA patients and age-matched healthy controls (n=43).

Results: 24 patients with oligoarticular JIA and 9 patients with poliarticular JIA were studied, 8/23 females with a mean age of 7,7 ± 3,6. MFI of mRAGE in PBMC and SFMC of JIA patients were significantly decreased in comparison with MFI of mRAGE in PBMC of healthy controls. Although serum levels of sRAGE were not different between patients and controls, sRAGE levels were lower in SF (570.2 [458.5- 773.0]) compared to PB (759.7 [628.6-890.3]) in JIA patients, especially in the poliarticular group. By contrast, HMGB1 levels in SF were significantly higher than in PB of JIA patients. MFI of mRAGE in PBMC was correlated with JADAS71 (p 0.01) and CHAQ (p 0.07). There were no significant correlations between serum sRAGE and HMGB1 with JADAS71, CHAQ, CRP and ESR.

Conclusion: The sRAGE/RAGE system may be a modulator of inflammation in JIA patients. Differences between levels of sRAGE and HMGB1 in synovial fluid versus peripheral blood in patients with JIA may suggest a local role in the pathogenesis of JIA.

	JIA patients (n=33)	Healthy controls (n=43)
Age (years)	7,7 ± 3,6	7,9 ± 4,7 SD
Sex (boys/girls)	9/24	30/13
JIA category		
Oligoarticular	24	
Poliarticular	9	
Treatment		
NSAIDs	20	
MTX	12	
ANTI-TNFα	1	
ESR (mm/h)	26.3 (4-78)	
CRP (mg/dL)	1.4 (0,5-6,5)	
CHAQ	0.375 (0-2.375)	
JADAS-71	8.1 (2.8-16.3)	

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FRI0452 THE IMPACT OF SINGLE NUCLEOTIDE POLYMORPHISMS IN ADORA2A AND ADORA3 ON THE EARLY RESPONSE TO METHOTREXATE AND PRESENCE OF THERAPY SIDE EFFECTS IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Juvenile idiopathic arthritis (JIA) is the most frequent rheumatic disease in children, with an estimated prevalence between 16 and 150 per 100 000 [1]. Methotrexate (MTX) administered at the dose 10-15mg/m^2 is currently recommended as the first-line treatment in most of JIA subtypes [2]. Despite its widespread use in rheumatology, the mechanism of MTX immunomodulatory action remains incompletely understood [3]. Free adenosine is one of the particles possibly associated with the action of MTX, acting via three types of adenosine receptor: ADORA2A, ADORA2B, and ADORA3 [4].

Objectives: The aim of our study was to determine the association between single nucleotide polymorphisms in *ADORA2A* (rs2236624, rs2298383) and *ADORA3* (rs3393) receptors genes on the disease activity and presence of MTX therapy side effects in patients with JIA.

Methods: One hundred children with JIA of all subtypes treated with MTX were recruited to the study. Demographic and clinical parameters were collected at the baseline of MTX therapy and on a control visit 4-6 months (median 5.09 months) after starting MTX. The clinical parameters included inflammatory markers values, number of joints with active arthritis, number of joints with restricted range of movement, physician's global assessment of disease activity, parent/patient global assessment of overall well-being, functional ability (measured by the Childhood Health Assessment Questionnaire – CHAQ) and the value of Juvenile Idiopathic Arthritis Disease Activity Score 71 (JADAS 71). Presence of MTX side effects was evaluated on the control visit. SNP genotyping was performed using genomic DNA isolated from peripheral blood samples.

Results: Both polymorphic variants of *ADORA2A* (rs2236624, rs2298383 - CC/CT) were significantly associated with 3.5 times higher odds of gastrointestinal side effects occurrence (OR: 3.52, 95%CI: 1.12-11.03, p=0.03 and OR: 3.49, 95%CI: 0.89-13.66 p=0.07) after adjustment to age, sex, dose and route of MTX administration. In addition, children with the *ADORA3* rs3393 polymorphic variant (CT/CC) after six months of MTX treatment had significantly lower number of joints with active arthritis (0.0 vs 1.0, p=0.04), lower JADAS 71 score (3.0 vs 5.1, p=0.16) and lower value of CRP (0.6 vs 2.4, p=0.02).

Conclusion: Although future studies are needed to verify our findings, polymorphisms in *ADORA2A* and *ADORA3* genes may become the determinants of MTX treatment efficacy and gastrointestinal toxicity in children with JIA.

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FRI0453 COMPARATIVE GENE PROFILE IN MONOCYTES FROM CHILDHOOD- AND ADULT-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS: CLUES TO DIFFERENT SYSTEMIC INVOLVEMENT

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Background:

Objectives: 1. This study, developed within the Innovative Medicines Initiative Joint Undertaking project PRECISESADS framework, aimed at identify specific inflammatory and oxidative stress determinants involved in the enhanced CV-risk present in SLE patients and to analyze the relevance of the sustained positivity for anti-dsDNA on the establishment of their atherothrombotic status.

Methods: One hundred and twenty-four SLE consecutive patients (not including patients with associated antiphospholipid syndrome), belonging to the PRECISESADS project, were evaluated for the presence of CVD and its association

with positivity for anti-dsDNA antibodies. A second cohort of 62 SLE patients was included, of which endothelial dysfunction, lipid profile, the presence of atheroma plaques (identified by a pathologic increase in the carotid intimae media thickness -CIMT-), and the frequencies of anti-dsDNA positivity for 7 years, were evaluated. Serum inflammatory and oxidative stress biomolecules, and NETosis-derived bioproducts were further evaluated by multiplex assay and specific commercial kits, respectively. Besides, miRNnomes were identified using next-generation sequencing. Clinical significance of the biomolecules analyzed was explored by correlation/association studies with immunological and CV-risk features.

Results: A significant relationship among the incidence of CVD (i.e. thrombosis or cardiac involvement) and the positivity for anti-dsDNA antibodies was recognized in the first SLE cohort. Accordingly, in the second SLE cohort, significantly impaired micro-vascular endothelial function (identified by reduction of hyperemia post-occlusion area), increased atherogenic index and pathologic increase in the CIMT were assessed in patients positive for anti-dsDNA in relation to anti-dsDNA negative patients. Around a 65% of SLE patients displayed a sustained positivity for anti-dsDNA antibodies for more than 7 years. These patients showed a distinctive and specific molecular profile compared with patients that had remained negative for anti-dsDNA, including increased inflammatory profile (IL1B, IL2, IL6, IL17, EOTAXIN, FGF, GMCSF, IFNγ, IP10, RANTES, TNF), enhanced oxidative status (lipoperoxides), and higher NETosis (nucleosomes, elastase). Levels of those biomolecules were closely interconnected and associated to their regulatory miRNAs, which accordingly exhibited differential expression in SLE anti-dsDNA(+) *vs* anti-dsDNA(-) patients. Finally, the frequency for positivity of anti-dsDNA significantly correlated both with markers of endothelial dysfunction and with the presence of atheroma plaques in SLE patients, pointing at the direct involvement of anti-dsDNA-Abs in the development of these processes.

Conclusion: 1. Positivity for anti-dsDNA antibodies confers a specific inflammatory/oxidative profile linked to an enhanced CV-risk in SLE patients. 2. Moreover, the sustained positivity for anti-dsDNA antibodies fosters the establishment of an atherothrombotic status in these autoimmune patients.

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Paediatric rheumatology

FRI0454 UNDER DETECTION OF INTERSTITIAL LUNG DISEASE IN JUVENILE SYSTEMIC SCLEROSIS (JSSC) UTILIZING PULMONARY FUNCTION TESTS. RESULTS FROM THE JUVENILE SCLERODERMA INCEPTION COHORT

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Background: Juvenile systemic sclerosis (jSSc) is an orphan disease with a prevalence in around 3 in a million children. Pulmonary involvement in jSSc occurs in approximately 40 % in the inception cohort. Traditionally in jSSc, pulmonary function testing (PFT) with FVC and DLCO are used for screening and computed tomography (HRCT) was more reserved for those with abnormal PFTs. More recently, it has become apparent that PFTs might not be sensitive enough for detecting ILD in children.

Objectives: Utilizing a prospective international juvenile systemic scleroderma cohort (JSScC) [2], to determine if pulmonary screening with FVC and DLCO is sufficient enough to assess the presence of interstitial lung disease in comparison to CT evaluation.

Methods: The international juvenile systemic scleroderma cohort database was queried for available patients with recorded PFT parameters and HRCT performed to determine sensitivity of PFTs detecting disease process.

Results: Of 129 patients in the jSScC, 67 patients had both CT imaging and an FVC reading from PFTs for direct comparison. DLCO readings were also captured but not in as many patients with tandem HRCT (n =55 DCLO and HRCT scan). Therefore, initial analyses focused on the sensitivity, specificity and accuracy of the FVC value from the PFTs to capture the diagnosis of interstitial lung disease as determined by HRCT.

Overall, 49% of the patients had ILD determined by HRCT, with 60% of patients having normal FVC (>80%) with positive HRCT findings, and 24% of patients having normal DLCO (> 80%) with positive HRCT findings. Fourteen percent (n = 3/21) of patients with both FVC and DLCO values within the normal range had a positive HRCT finding.

Conclusion: The sensitivity of the FVC in the JSScC cohort in detecting ILD was only 39%. Relying on PFTs alone for screening for ILD in juvenile systemic sclerosis would have missed the detection of ILD in almost 2/3 of the sample cohort, supporting the use of HRCT for detection of ILD in children with SSc. In addition, the cut off utilized, of less than 80% of predicted FVC or DLCO could be too low for pediatric patients to exclude beginning ILD. This pilot data needs confirmation in a larger patient population.

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FRI0455 IS THERE AN INCREASE IN THE FREQUENCY OF INFLAMMATORY DISEASES IN THE FAMILIES OF PATIENTS WITH FMF?

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Background: Familial Mediterranean Fever (FMF) is the most common periodic fever syndrome in childhood with an autosomal recessive inheritance pattern and is characterized by unprovoked fever attacks, serositis episodes. The causative gene of the disease is MEFV that encodes pyrin protein. The pyrin protein takes a role in pathways related to inflammation, and mutations of it lead to increased inflammation. It is already shown that frequencies of some certain diseases like PAN, HSP increase in patients with FMF. Nevertheless,

frequencies of inflammatory diseases in families of patient with FMF haven't been investigated.

Objectives: In this study, we have aimed to evaluate the comorbid disorders in a large cohort of families of patients with FMF.

Methods: Four hundred and ninety-eight children with FMF, one hundred and forty patients with JIA and ninety-two healthy children were interviewed between December 2019 and January 2020. In JIA group and healthy control group, patients who have family history for FMF were excluded from the study. Patients were asked about characteristics of their disease attacks and if there is a relative with any inflammatory diseases who does not have FMF in patient's 1st and 2th degree relatives.

Results: Demographic features of study group have shown in Table 1. The most common MEFV mutations in patients with FMF were: M694V homozygotes (13.2 %), M694V heterozygotes (12 %), M694V homozygotes and R202Q homozygotes (6,8 %). Type II diabetes, asthma and hypothyroidism were the most commonly detected diseases in all cohorts. Frequency of Behçet's disease, allergic rhinitis and type II diabetes were significantly higher in families of patients with FMF than other groups ($p<0.05$) (Table 2).

Table 1. Demographic features of study population.

	FMF†	JIA††	Healthy Control
	n: 498 (%) mean +/- SD	n: 140 (%) mean +/- SD	n: 92 (%) mean +/- SD
Female	284 (57)	91 (65)	55 (59.8)
Age (years)	12.9 ± 8.2	11.7 ± 5.1	7.4 ± 4.6
Age at Onset (years)	4.3 ± 3.3	5.4 ± 4.1	-
Age at Diagnosis (years)	6.3 ± 3.6	6.3 ± 4.5	-
Delay in Diagnosis (months)	23.8 ± 29.2	11.3 ± 28.2	-
Follow-up Duration (years)	6.9 ± 8.3	5.3 ± 4.0	-
Consanguinity	100 (20)	25 (17.8)	8 (8.6)
Family History of FMF	282 (56.6)	0 (0)	0 (0)
JIA subgroup	-		-
Oligoarticular		72 (51.4)	
Polyarticular (RF negative)		16 (11.4)	
Polyarticular (RF positive)		3 (2.1)	
Enthesitis Related Arthritis		14 (10)	
Psoriatic Arthritis		7 (5)	
Systemic		23 (16.4)	
Other		5 (3.5)	
Clinical Findings		-	-
Fever	392 (78.1)		
Abdominal Pain	429 (86.1)		
Chest Pain	102 (20.5)		
Arthralgia	334 (67.1)		
Arthritis	157 (31.5)		
Extremity Pain	64 (12.8)		
Heel Pain	44 (8.8)		
Myalgia	43 (8.6)		
**ELE*	13(2.6)		
Serositis	10 (2)		

†Familial Mediterranean Fever ††Juvenile Idiopathic Arthritis **Erysipelas like erythema*

Table 2. Comparison of frequencies of diseases detected among families of patient groups (shortened).

Diseases	FMF	JIA	Healthy Control	p[1]
Type II Diabetes	284 (57)	64(45.7)	44 (47.8)	**0.02**
Asthma	139 (27.9)	30 (21.4)	20 (21.7)	0.19
Hypothyroidism	122 (24.4)	27 (19.2)	14 (15.2)	0.09
Eczema	68 (13.6)	14 (10)	5 (5.4)	0.06
Psoriasis	49 (9.8)	6 (4.2)	7 (7.6)	0.10
Allergic Rhinitis	49 (9.8)	3 (2.1)	1 (1)	**0.001**
Hyperthyroidism	40 (8)	9 (6.4)	3 (3.2)	0.24
Behçet's Disease	31 (6.2)	1 (1)	2 (2.1)	**0.01**
Rheumatic Fever	30 (6)	10 (7.1)	2 (2.1)	0.25

Conclusion: In this study, we have reported increased frequencies of Behçet's disease, allergic rhinitis and type II diabetes in families of patients with FMF. Our results suggest that possible increased mutation load among families of patients with FMF may cause increased inflammatory diseases.

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FRI0456 EARLY IMPLEMENTATION OF TREATMENT WITH ETANERCEPT INCREASES THE LIKELIHOOD TO ACHIEVE REMISSION

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Background: Juvenile idiopathic arthritis (JIA) is the most common chronic inflammatory rheumatic disease in children and adolescents. A consistent therapy is required to avoid consequential damage and permanent loss of function. Biologic disease modifying anti-rheumatic drugs (bDMARDs) provide a well-accepted option for treatment of patients with a severe course of JIA. Etanercept (ETA) is still the most commonly prescribed bDMARD for JIA in Germany.

Objectives: To analyze adherence to treatment with ETA with special attention on discontinuation after achieving an inactive disease and recurrence of active disease after ETA withdrawal.

Methods: Data from two ongoing prospective, multicenter, non-interventional registries BiKeR and JuMBO were used for the analysis. JuMBO is the follow-up study to BiKeR and follows patients who have reached the age of 18. Both registers provide treatment data, individual trajectories of clinical data and outcomes from childhood into adulthood in JIA patients treated with bDMARDs and csDMARDs. Clinical disease characteristics, such as disease activity, were reported by the rheumatologists in addition to patient-reported outcomes at each six-months follow-up. Remission was defined as inactive disease defined by the Wallace Criteria (1).

Results: Data from 2,500 patients who were included in BiKeR and had an age ≥18 at the time of analysis were considered. A subset of 1,535 were enrolled in JuMBO. The mean follow-up was 8.6 (SD 4.2) years for the JuMBO patients. The majority of them had polyarthritis (35%), followed by enthesitis-related arthritis (20%). A total of 1,779 (68.8% of 2,584) patients were ever treated with ETA, providing 2,178 ETA treatment courses. There were 1,724 (67%) patients with first, 338 patients with a second and 54 with a third course of ETA treatment course. 710 (41.2%) discontinued ETA by ineffectiveness in the first course with similar rates of discontinuation due to ineffectiveness in the first and second course. A total of 332 (+/-MTX, 19.3%) discontinued ETA after achieving remission in the first ETA course. Among those, 129 (38.9%) patients did not require treatment with any other bDMARD subsequently until last follow-up (3.9 years, SD 3.5), while 169 (50.9%) re-started treatment with ETA, 14 (4.2%) with adalimumab and 4 with other bDMARDs. The likelihood of discontinuing ETA due to an inactive disease was positively associated with a younger age (hazard ratio (HR) 1.08, $p<0.001$), persistent oligoarthritis (HR 1.89, $p=0.004$), a shorter duration between JIA onset and ETA start (HR 1.10, $p<0.001$) as well as a good response to therapy within the first six months of treatment (HR 1.11, $p<0.001$). 209 (of 332) had ETA monotherapy at withdrawal. Of those, 77% (n=161) experienced recurrence of disease with a mean time to flare of 12.1 (SD 13.7) months. 129 patients restarted bDMARD therapy (n=117 ETA). We could not identify any correlates for the risk of flare. 70% re-achieved remission and 20% again discontinued therapy thereafter.

Conclusion: The study confirms the good effectiveness of ETA, even in the re-treatment of patients with JIA. Our data highlight the association of an early bDMARD treatment with a higher likelihood to achieve an inactive disease indicating a window of opportunity.

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FRI0457 LONG-TERM OUTCOMES AND TREATMENT EFFICACY IN PATIENTS WITH TNF RECEPTOR-ASSOCIATED AUTOINFLAMMATORY SYNDROME (TRAPS) FROM THE EUROFEVER INTERNATIONAL REGISTRY

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Background: Tumour necrosis factor (TNF) receptor-associated periodic syndrome (TRAPS) is one of the best-known monogenic auto-inflammatory disorders resulting from an autosomal dominant variation in the TNF super family receptor 1A (*TNFRSF1A*) gene (1).
Objectives: To define best treatment approach in patients with TRAPS and effect on long-term outcomes.
Methods: We reviewed all data on patients with TRAPS enrolled in the Eurofever international registry according the INSAID gene variant classification and the new Eurofever/PRINTO classification criteria (EPCC).
Results: Data on 226 patients were available. Patients not fulfilling the EPCC carrying likely benign/benign variants (21 patients, 9%) or VOUS/not classified variants (40 patients, 18%) displayed a milder disease than the patients fulfilling the EPCC with VOUS/not classified variants (38 patients, 17%) or pathogenic/likely pathogenic variants (127 patients, 56%). In particular, in patients not fulfilling the EPCC, less frequent abdominal pain and skin rashes, higher efficacy rate of colchicine and no development of AA amyloidosis have been reported. Almost 90% of patients fulfilling the EPCC required maintenance therapy and anti-interleukin (IL)-1 drugs were the most frequently used, with the highest efficacy rate (>85% complete response), while Etanercept was less effectively used and discontinued in 65% of patients.
Conclusion: Anti-IL-1 drugs are the best maintenance treatment in TRAPS with potential to reverse the most serious disease complications of AA amyloidosis and infertility. The diagnosis of TRAPS should be considered very carefully in patients carrying VOUS/not classified variants not fulfilling the EPCC.
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FRI0458 EFFICACY AND SAFETY OF PCV13 VACCINATION IN JIA PATIENTS WITH SYSTEMIC MANIFESTATIONS ON TOCILIZUMAB AND CANAKINUMAB TREATMENT

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Background: The need for continuous use of immunosuppressive drugs leads to increased risk of developing infectious diseases in children with juvenile idiopathic arthritis with systemic manifestation (sJIA). Questions about choosing the optimal vaccination time and the effect of different classes of therapy on vaccination effectiveness are still open.
Objectives: To study clinical and laboratory effectiveness of PCV13-vaccination in children with sJIA on tocilizumab (TOC) and canakinumab (CAN) treatment depending on disease activity stage.
Methods: Prospective cohort study included 2 groups of sJIA patients: in stable remission (Remission group, n=53) receiving CAN (n=10) or TOC (n=43) treatment, and in acute stage of disease (Acute group, n=25) which started to received CAN (n=7) or TOC (n=18) either before vaccination (Acute Treated Before subgroup, n=17) or after vaccination (Acute Treated After subgroup, n=8). 0.5 ml of the 13-valent PCV was administered once subcutaneously. Efficacy was evaluated by achieving of protection level of anti-pneumococcal antibodies after 4 weeks and by clinical indicators after 6 month follow-up: frequency of acute respiratory infections, frequency of antibiotics treatment courses, frequency of temporary withdrawal of biologics treatment due to severe infections. Frequency of events were counted per patients-years.
Results: Four weeks after vaccination, protection level of anti-pneumococcal antibodies was achieved by for 36 (67.9%) patients in Remission group, 16 (64%) patients in Acute group (intergroup p=0.932), and in 8 (47.06%) patients in Acute Treated Before subgroup and in 8 (100%) patients in Acute Treated After subgroup (intersubgroup p=0.022). PCV13 have shown high clinical effectiveness in both Remission group and Acute group. Reducing of acute respiratory infections frequency was as follows: from 4.57 to 2.15 episodes per patient-year in Remission group (p<0.001) and from 4.32 to 1.28 per patient-year in Acute group (p<0.001). Duration of antibiotics treatment reduced from 2.31 to 0.81 weeks per 1 patient-year in Remission group (p<0.001) from 1.97 to 0.74 in Acute group (p<0.001). Among patients who were previously treated with biologics, frequency of therapy withdrawal reduced from 4.34 to 2.42 per patient-year in Remission group (p<0.001) and from 3.53 to 1.18 in Acute Treated Before subgroup (p=0.002). The incidence of reactions to vaccination of PCV13 (local hyperemia, pain, subfebrile temperature) was similar in groups (22 (41.5%) for Remission group and 7 (28%) for Acute group, p= 0.319).
Conclusion: Vaccination with the 13-valent PCV has demonstrated high clinical efficacy and safety in children with sJIA both in the acute stage of the disease and during remission. Vaccination of patients in acute stage of sJIA before treatment has advantages over vaccination during remission or after prolonged immunosuppressive therapy in terms of achieving an adequate vaccine response.
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FRI0459 TOFACITINIB TREATMENT IN RECALCITRANT JDM PATIENTS

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Background: Juvenile dermatomyositis (JDM) is a systemic, autoimmune inflammatory muscle disorder and vasculopathy that affects children younger than 18 years. Although the cause of JDM remains unknown it is clear that genetic and environmental influences play a role in the aetiology. New treatments are becoming available and being tested through international multicentre trials. Increasing evidence suggests a role for types I and II IFN in juvenile and adult dermatomyositis, including elevated IFN-response gene signatures in the muscle, skin and blood. It has recently been reported that patients with refractory JDM responded well to treatment with tofacitinib, a JAK inhibitor, with corresponding downregulation in selected IFN-response genes.
Objectives: In this study, we evaluated our cases with resistant JDM who received tofacitinib treatment.
Methods: Six patients who received tofacitinib because of severe skin involvement of JDM were included in the study. The data were obtained retrospectively from the hospital records.
Results: The age ranges of the cases were between 7-17 years and the ratio of girls and boys was 1 (3/3). The age of diagnosis was between 2-13 years, and the follow-up period was between 3-9 years. Calcinosis cutis in 5 cases, decreased muscle strength in 3 cases, joint involvement in 4 cases were detected.. Systemic steroids, methotrexate, and non-steroid anti-inflammatory drugs were given in all cases before tofacitinib treatment. Pamidronate was used in 4 cases because of severe skin calcinosis, high dose intravenous immunoglobulin in 4 cases, mycophenolate mofetil in 3 cases, rituximab in 3 cases and cyclophosphamide in 1 case previously. Tofacitinib treatment (10mg/gün) was started in six cases with treatment-resistant JDM. Five cases had been treated with tofacitinib for 6-24 month intervals. The treatment was discontinued in one case because of severe allergic reaction. Variable level of improvement were detected in the skin findings of all cases during the therapy period. The treatment was interrupted for 1 month in only one case due to neutropenia.
Conclusion: Tofacitinib seems to be an effective and safe treatment option in patients with JDM who are resistant to conventional treatments. More studies are needed on this subject.
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FRI0460 SAFETY OF BIOLOGICAL AGENTS IN JUVENILE IDIOPATHIC ARTHRITIS: A META-ANALYSIS OF OBSERVATIONAL STUDIES

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Background: Follow-up cohorts (observational studies) were initiated consecutively or simultaneously to the development of randomised controlled trials (RCTs) in JIA patients [(1,2)]. They help to identify many complications observed only in clinical practice related to off label use, coadministration of treatments, drug misuse, and occurrence of rare or unexpected event. In addition, observational studies include a higher number of patients with a longer duration of follow-up compared to randomised trials. Hence, they have a higher power to capture the occurrence of serious adverse events (SAE) in daily clinical practice [3].
Objectives: To estimate the incidence of serious adverse events (SAEs) including serious infections, malignancies, and death in patients with juvenile idiopathic arthritis (JIA) treated with biological agents (BAs) in daily clinical practice, using meta-analysis techniques.
Methods: We systematically searched, up to May 2019, Medline and Embase databases for observational studies performed in JIA disease under BAs treatment. Outcomes were SAEs, serious infections, malignancies and all-cause mortality. Complementary, the incidence of SAEs in randomised controlled trials (RCTs) with withdrawal and parallel designs was performed by meta-analysis.
Results: A total of 31 observational studies were included (6811 patients totalizing 17530 patients-years [PY] of follow-up). The incidence rate of SAEs was similar in observational cohorts and withdrawal RCTs (4.46 events per 100 PY, 95% CI 2.85- 6.38, I^2= 95%) and 3.71 events per 100 PY (95%CI 0.0-13.34), I^2= 56%, respectively). The incidence of SAE was lower in parallel RCT. The incidence rate of serious infections, malignancies and death in observational cohorts was estimated at 0.74 events per 100 PY (95%CI 0.32-1.30, I^2=83%), 0.10 events per 100 PY (95% CI 0.06-0.16, I^2=0%) and 0.09 events per 100 PY (95% CI 0.05-0.14, I^2=0%), respectively. Infections were the known cause of death in 8 of the 14 deaths. In meta-regression and subgroup analysis, variation of serious infections rates were partially explained by follow-up time (R^2= 30.3%, p= 0.0008), JIA categories (all JIA versus polyarticular versus systemic JIA categories, p= 0.001) and cohort quality (Newcastle-Ottawa score ≥ to 6 versus ≤ to 5 stars, p= 0.0025).
Conclusion: Our results suggest that the incidence rate of SAEs related to BAs in JIA disease is similar to those observed in randomised withdrawal trials. The overall incidence remained low. However, unsatisfactory description of SAEs prevents analysis of hospitalisation causes. Infection and, to a lesser extent, cancer and death, explain only part of burden of BAs.
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FRI0461 THE ANTI-VACCINE ANTIBODY AGAINST MEASLES, PAROTITIS, RUBELLA, DIPHTHERIA AND HEPATITIS B IN 170 JUVENILE IDIOPATHIC ARTHRITIS PATIENTS

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Background: Patients with juvenile idiopathic arthritis (JIA) may have lower protective levels of anti-vaccine antibodies due to high inflammatory activity, interrupted or incomplete vaccination schedule, and due to using of immune-modulating drugs, e.g. systemic corticosteroids (CS), methotrexate (MTX) and biologics.
Objectives: The aim of our study was to find the predictors of low levels of anti-vaccine antibodies in patients with JIA.
Methods: In the present study were included data 170 JIA (55 boys and 115 girls) aged from 2 to 17 years, who received scheduled vaccination before the age of 2 years and before JIA onset against measles, parotitis, hepatitis B, diphtheria and rubella. In all patients the Ig G anti-vaccine antibodies levels were detected with ELISA. In each patient we evaluate the type of the disease (oligoarthritis - 73, polyarthritis - 61, systemic-16 and enthesitis-related arthritis - 20), onset age, presence of uveitis, duration of JIA, treatment with corticosteroids (CS), methotrexate (MTX) and biologics. Data presented with median and 25%-75%.
Results: The main demographic characteristics: age of inclusion in the study 11.4 (7.6-14.8) years, disease onset – 6.0 (3.7-9.0) years, disease duration – 3.8 (1.9-6.5) years. Treatment with CS was in 43 (25.3%), MTX in 154 (90,6%) and biologics 82 (48.2%) patients, among them 53 had TNFa-inhibitors. More than 1 biologic consequently received 16/82 (19.5%) patients. Protective levels of anti-measles antibodies was in 98 (57,6%) of all JIA population, anti-parotitis – 136 (80.0%), anti-hepatitis B – 85 (50.0%), anti-diphtheria – 88 (51,7%), anti-rubella – 167 (98.8%). Data of vaccination status and anti-vaccine antibodies levels in the table. In univariate and multivariate regression analysis the main risk factors for anti-measles antibodies levels were MTX using (p=0.045), more than 1 biologics (p=0.0004); for anti-hepatitis B – MTX (p=0.03), for anti-diphtheria antibodies: onset age (p=0.0002), JIA duration (p=0.00007), number vaccine doses (p=0.02), more than 1 biologics (p=0.01); combined treatment with biologics and other drugs (MTX or CS).

Parameter	No treatment (n=14)	MTT, only (n=74)	Biologics±MTT ±CS (n=82)	P
# anti-measels vaccine doses	2.0 (2.0; 2.0)	2.0 (1.0; 2.0)	2.0 (1.0; 2.0)	0.19
Anti-measels IgG, Me/ml	0.28 (0.1; 0.6)	0.4 (0.1-0.7)	0.17 (0.0; 0.29)	0.0002
Protective anti-measels IgG level, n (%)	8 (57)	50 (68)	40 (49)	0.06
# anti-parotitis vaccine doses	2.0 (2.0; 2.0)	2.0 (1.0; 2.0)	2.0 (1.0; 2.0)	0.19
Anti-parotitis IgG, Me/ml	2.0 (1.2; 4.3)	2.8 (1.3; 5.6)	2.5 (1.0; 5.1)	0.47
Protective anti-parotitis IgG level, n (%)	12 (86)	62 (84)	62 (76)	0.38
# anti-diphtheria vaccine doses	5.0 (4.0; 5.0)	4.0 (4.0; 5.0)	5.0 (4.0; 5.0)	0.39
Anti-diphtheria IgG, Me/ml	0.17 (0.0; 1.2)	0.18 (0.0; 0.4)	0.1 (0.0; 0.2)	0.18
Protective anti-diphtheria IgG level, n (%)	9 (64)	42 (57)	37 (45)	0.22
# anti-hepatitis B vaccine doses	3.0 (3.0; 3.0)	3.0 (3.0; 3.0)	3.0 (3.0; 3.0)	0.91
Anti-hepatitis B IgG, Me/ml	0.56 (0.0; 7.5)	11.4 (0.3; 44.8)	10.0 (0.0; 44.1)	0.08
Protective anti-hepatitis B IgG level, n (%)	3 (21)	40 (54)	42 (51)	0.08
# anti-rubella vaccine doses	2.0 (2.0; 2.0)	2.0 (1.0; 2.0)	2.0 (1.0; 2.0)	0.19
Anti-rubella IgG, Me/ml	121.8 (70.0; 200.0)	95.6 (53.3; 198.2)	56.4 (37.0; 100.1)	0.008
Protective anti-rubella IgG level, n (%)	14 (100)	73 (100)	80 (98)	0.34

Conclusion: MTX, biologics and JIA durations are factors influenced on anti-vaccine antibody level. It is necessary to regularly check the levels of anti-vaccine antibodies, especially anti-measels and anti-diphtheria for creation of the individual vaccination plan for JIA patients, treated with MTX and biologics.

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FRI0462

PREDICTIVE FACTORS OF RELAPSE AFTER METHOTREXATE DISCONTINUATION IN JIA PATIENTS WITH INACTIVE DISEASE

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Background: Methotrexate (MTX) is the most widely used conventional synthetic disease-modifying antirheumatic drug (csDMARD) in the treatment of juvenile idiopathic arthritis (JIA).[1,2] When remission is achieved, questions remain about discontinuing MTX. There is some evidence that a longer period of inactive disease before MTX withdrawal is associated with lower likelihood of relapse, while both rheumatoid factor (RF) positive polyarthritis and extended oligoarthritis categories are associated with higher probability of disease relapse.[2,3]

Objectives: To identify predictive factors of relapse after discontinuation of MTX in JIA patients with inactive disease.

Methods: Prospective multicentre cohort study in patients diagnosed with JIA, according to the ILAR classification, using real world data from the Portuguese national register database, Reuma.pt (Fig 1).[4] We evaluated patients who have reached JADAS27 inactive disease (≤1 and no active extra-articular manifestations) and discontinued MTX before the age of 18 years-old.[5] Relapse was defined as recurrence (>1 or extra-articular manifestations) or restarting a DMARD.[5] To identify differences of relapse risk, univariate analyses were performed. Persistence in remission was estimated using the Kaplan-Meier method. Subsequently, Cox regression analyses were performed to identify predictors of relapse.

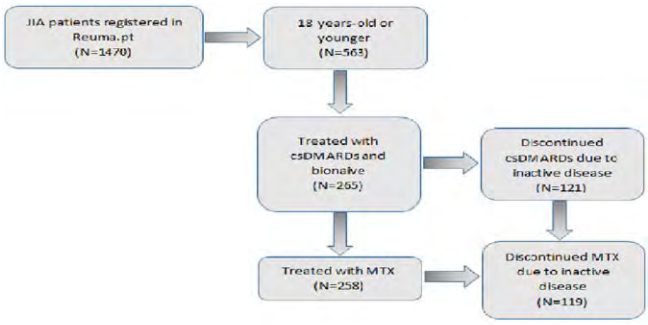
Results: 119 JIA patients discontinued MTX due to inactive disease (Fig 1). 69.7% were females and 60.6% had oligoarticular JIA. Sociodemographic and clinical characteristics are shown in Table 1. Relapse has occurred in 32.8%. Table 2 shows the disease characteristics at MTX initiation and discontinuation and at relapse or last visit.

In univariate analysis, relapse was associated with the use of NSAIDs at the time of MTX discontinuation (p=.027) and with a period of less than two years in inactive disease before MTX suspension (p=.040). We found no association with gender, race, immunology (RF, antinuclear and cyclic citrullinated peptide antibodies), MTX dose, discontinuation modality (tapering and spacing the doses or just tapering the dose), extra-articular manifestations, previous corticotherapy, family history, body mass index, JADAS, CHAQ index, inflammatory parameters, tender and swollen joint counts at MTX initiation or discontinuation nor with age at remission or at MTX suspension. Median persistence in inactive disease was significantly higher in patients with more than two years in remission before MTX discontinuation (p=.034) and in those who did not use NSAIDs at time of MTX discontinuation (p=.026) (Fig 2). After adjustment for age at diagnosis, MTX tapering and JIA category, use of NSAIDs at the time of discontinuation (HR, 1.98 95%CI 1.03-3.82) and less than two years in remission (HR, 3.12 95%CI 1.35-7.13) remained associated with relapse.

Conclusion: In this large cohort we found that the use of NSAIDs at the time of MTX discontinuation was associated with two times the likelihood of relapse. Like in other studies we also showed that the time in remission before MTX discontinuation is the main predictor of relapse. We found no association between the JIA category and the risk of relapse.

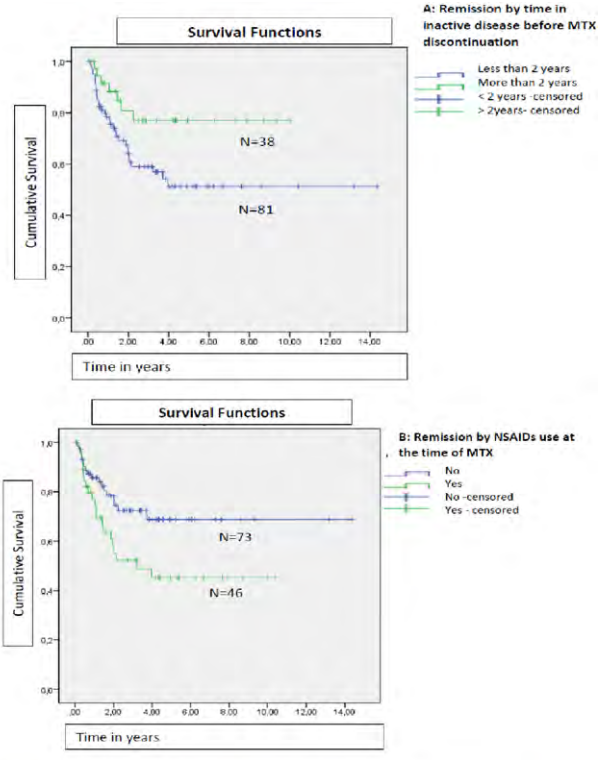
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csDMARDs: conventional synthetic disease-modifying antirheumatic drugs; MTX: Methotrexate;

Figure 1: Patient flowchart.



MTX: Methotrexate; NSAIDs: Non-Steroidal Anti-inflammatory Drugs

Figure 2: Kaplan-Meier survival curves showing persistence in remission by A: time in remission before MTX discontinuation and B: use of NSAIDs at the time of MTX discontinuation.

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FRI0463 IDENTIFICATION OF EARLY CLINICAL AND LABORATORY CHARACTERISTICS OF MACROPHAGE ACTIVATION SYNDROME ASSOCIATED WITH SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

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Background: Macrophage activation syndrome (MAS) is a severe, potentially life-threatening complication of systemic juvenile idiopathic arthritis (SJIA). However, early recognition of MAS remains challenging. Because it is clinically heterogeneous, hemophagocytosis is often not detected, and histopathological features lack the specificity associated with hemophagocytic syndromes. In addition, it is often difficult to distinguish early MAS from SJIA or sepsis-like syndromes.
Objectives: To identify early clinical and laboratory characteristics of MAS associated with SJIA.
Methods: This is a retrospective cohort study of 149 SJIA patients treated at the Children's Hospital of Zhejiang University School of Medicine between January 2010 to December 2017. All patients fulfilled 2001 ILAR criteria for SJIA, and 27 fulfilled 2016 Classification Criteria for MAS. We evaluated the clinical and laboratory features of SJIA patients with MAS and compared them to those without MAS. We focused our analysis on early MAS, which was defined as the time when the initial clinical and/or laboratory abnormalities suggestive of MAS were first detected.
Results: The clinical features associated with early MAS were hypotension, absence of arthritis and lymphadenopathy, bone marrow hemophagocytosis, central nervous system dysfunction, and gastrointestinal involvement. The best laboratory parameters for early MAS detection were platelet counts ≤275.0 × 10^9/L, lactate dehydrogenase >596.0 U/L, aspartate aminotransferase >47.0 U/L, erythrocyte sedimentation rates ≤41.0 mm/h, ferritin >1400.0 ng/mL, D-dimer >1.40 mg/L, triglyceride >1.30 mmol/L, alanine aminotransferase >33.0 U/L, C-reactive protein ≤68.0 mg/L, fibrinogen ≤4.1 g/L, absolute neutrophil counts ≤5.2 × 10^9/L, serum total protein ≤66.0 g/L, and white blood cell ≤9.8 × 10^9/L. The combination of cytokines of IFN-γ >17.1 pg/mL and IL-10 >7.8 pg/mL were found to be a specific and good prognostic cytokine pattern for early recognition of MAS, the sensitivity and specificity as 71.4% and 98.2%. (Table 1, Fig 1, 2)

Table 1. Identification of clinical and Cytokine characteristics differentiating patients with MAS onset from SJIA patients without MAS

Characteristics	Sensitivity (%)	Specificity (%)	OR (95% CI)	p value
Clinical characteristics				
Hypotension	35.5	98.4	33.0 (6.8–160.1)	0.000
Absence of Arthritis	77.4	85.2	19.8 (7.4–52.7)	0.000
Hemophagocytosis in the bone marrow	28.6	97.3	14.5 (2.0–107.5)	0.009
Central nervous system involvement	25.8	91.0	3.5 (1.3–9.7)	0.015
Gastrointestinal involvement	22.6	91.8	3.3 (1.1–9.4)	0.029
Absence of lymphadenopathy	77.4	51.6	2.6 (1.1–6.1)	0.027
Cytokine levels				
IFN-γ >17.1 pg/mL	82.1	83.6	49.5 (15.6–156.9)	0.000
IL-10 >7.8 pg/mL	78.6	93.1	23.5 (7.9–69.5)	0.000
IFN-γ >17.1 pg/mL and IL-10 >7.8 pg/mL	71.4	98.2	142.5 (28.2–720.6)	0.000

OR, odds ratio. CI, confidence interval. PLT, platelet. LDH, lactate dehydrogenase. AST, aspartate aminotransferase. ESR, erythrocyte sedimentation rate. FER, ferritin. D-D, D-dimer. TG, triglycerides. ALT, alanine aminotransferase. CRP, C-reactive protein. FIB, fibrinogen. ANC, absolute neutrophil count; TP, total protein. WBC, white blood cells. ALB, albumin. IL, interleukin. IFN, interferon.

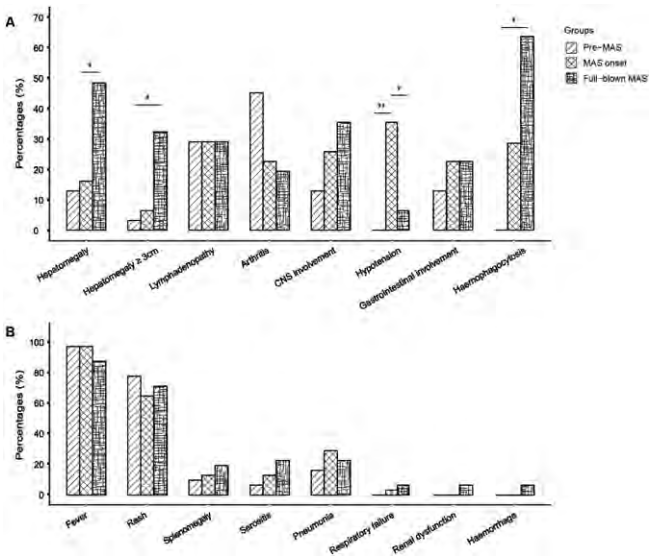


Fig 1. Comparison of clinical characteristics in the MAS process. * P < 0.05. ** P < 0.01.CNS involvement: Central nervous system involvement.

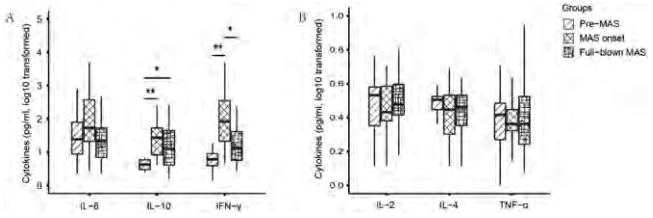


Fig 2. Comparison of serum cytokine levels in the MAS process. * P < 0.05. ** P < 0.01.

Conclusion: Sudden hypotension, absence of arthritis, and significantly increased IFN-γ and IL-10 levels are important clinical and laboratory markers for early MAS identification in addition to the traditional features of SJIA-associated MAS.
References: (not show references here)
Disclosure of Interests: None declared
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FRI0464 GENOTYPING AND PHENOTYPING PATTERNS IN PATIENTS WITH CAPS IN RUSSIAN FEDERATION

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Background: Cryopyrine-associated periodic syndromes (CAPS) are a group of rare congenital auto-inflammatory diseases (AID) that include diseases such as familial cold auto-inflammatory syndrome (FCAS), Muckle-Wells syndrome (MWS), and CINCA/NOMID syndrome. At present, there are limited data on demographic and clinical features of children with CAPS in Russia.
Objectives: To reveal demographic, genotype and phenotype characteristics in CAPS patients at the National Medical Research Center of Children`s health, Moscow, Russia.
Methods: Retrospective study included 12 patients (7 females, 58.3%) with CAPS confirmed by next generation sequencing (NGS). Median age of disease onset was 5.7 (interquartile range (IQR) 0.5:12.8) years. Characteristics of disease onset as well as dynamics of disease activity during long-term treatment were evaluated.
Results: At the onset, systemic features were as follows: fever in 11 (91.6%) patients, rash in 8 (66.7%), hepatosplenomegaly in 7 (58.3%) patients, and lymphadenopathy in 6 (50%). Active arthritis in the onset of the disease was in 9/12

patients (75%), presented by polyarthritis in 7/9 (77.8%), and oligoarthritis in 2/9 (22.2%). Two patients (16.7%) had cataract, one (8.3%) had bilateral uveitis, and one (8.3%) had optic atrophy. Sensorineural hearing loss was observed only in 3/12 (25%). Hydrocephalus was detected in 3/12 (25%). Delayed mental and psycho-speech development was observed in 6/12 (50%) patients. In 3/12 (25%), the development of MAS was recorded.

All patients had nucleotide variants in *NLRP3* gene. According to NGS results and clinical characteristics, 8/12 (66.7%) patients were diagnosed with MWS and 4/12 (33.3%) had CINCA/NOMID syndrome. In children with MWS, heterozygous variant *c.2113C>A* in *NLRP3* gene was the most common (5/8 (62.5%) patients). One of 8 (12.5%) patients with novel heterozygous variant *c.2861C>T* was detected; also one child (12.5%) have heterozygous variant *c.598G>A* and one (12.5%) – heterozygous variant *c.943A>G*. Four patients with CINCA/NOMID syndrome also had heterozygous variants in *NLRP3* gene: *c.598G>A*, *c.2173C>A*, *c.1991T>C* and *c.796C>T*.

Prior to genetic testing, 12/12 (100%) patients received NSAIDs; 6/12 (50%) were treated with oral glucocorticoids (GC), 3/12 (25%) – with intravenous GC, 2/12 (22.2%) – with methotrexate. Biologics treatment included: 5/12 (41.7%) CAN, 4/12 (33.3%) tocilizumab, and 1/12 (8.3%) etanercept. After genetic testing, 7/12 (58.3%) patients were successfully switched to CAN. Only 1/12 (8.3%) child with MWS developed secondary inefficiency on CAN treatment.

Conclusion: Systemic manifestations were detected in 91.6% of children, while active arthritis was observed in 75% of patients, which can cause difficulties in the diagnosis and treatment of CAPS. The effectiveness of canakinumab therapy was estimated in 91.6% of patients. The most frequent variant of the *NLRP3* gene in MWS was *c.2113C>A*. In patients with CINCA/NOMID syndrome all nucleotide variants were individual.

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FRI0465 TOFACITINIB POPULATION PHARMACOKINETICS IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS: A POOLED ANALYSIS OF DATA FROM THREE CLINICAL STUDIES

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Background: Tofacitinib is an oral JAK inhibitor that is being investigated for juvenile idiopathic arthritis (JIA).

Objectives: To describe tofacitinib pharmacokinetics (PK) in patients with JIA, identify potential covariates accounting for variability in exposure, assess the formulation effect of oral solution vs tablet and propose a simplified dosing regimen.

Methods: This was a pooled analysis of data from 3 tofacitinib clinical studies in patients with JIA aged 2–<18 years: a Phase 1, open-label (OL), non-randomised study (NCT01513902); a Phase 3, randomised, double-blind, placebo-controlled, withdrawal study (NCT02592434); and an OL long-term extension study (NCT01500551). Tofacitinib was dosed at 5 mg twice daily (BID) in patients ≥40 kg or at body weight (BW)-based lower doses BID in patients <40 kg, to achieve average concentrations (C_{avg}) comparable with those in patients receiving 5 mg BID. A sparse PK sampling scheme was applied, and the plasma samples were assayed using a validated, sensitive and specific high-performance liquid chromatography tandem mass spectrometric method (lower limit of quantification = 0.100 ng/mL). A nonlinear mixed-effects modelling approach was used for the population PK model, and population parameter variability was assumed to be log-normally distributed. Covariates relating to patient demographics, disease characteristics, concomitant medications and formulation (oral solution vs tablet) were selected using a stepwise covariate modelling approach, and parameter-covariate relationships were evaluated using stepwise forward-inclusion ($p<0.05$) backward-deletion ($p<0.001$) procedures. The effect of time-varying BW on oral clearance (CL/F) and apparent volume of distribution (V/F) was characterised using an allometric model. Final model quality was assessed by Visual Predictive Checks (VPCs).

Results: Of 246 patients in the analysis, 74.0% were female; 87.8% were white, 2% were black, 10.2% were 'other' races and no patients were Asian. Median (range) BW was 46.3 (11.1–121.8) kg. Initially, 100 patients received oral solution and 146 patients received tablets; 11 patients switched formulations during the studies. A one compartment disposition model with first-order absorption and a lag time sufficiently described the data. Final estimates for CL/F, V/F and the first-order absorption rate constant (k_a) for tablets were 26.1 L/hr, 89.2 L and 2.78 hr^{-1}, respectively. The only statistically significant covariate was a formulation effect on k_a. All parameters were estimated adequately. Estimated allometric exponents were 0.310 for CL/F and 0.537 for V/F. Absorption was described with an estimated lag time of 0.186 hr, and the oral solution had a 1.64-fold faster absorption rate vs the tablet. VPCs sufficiently described the observed data over time, across BWs and ages. Given the PK characterisation and variability in patients with JIA, a simplified dosing scheme was proposed, targeting C_{avg} values equivalent to those in patients receiving 5 mg BID: 3.2 mg BID solution in patients 10–<20 kg; 4 mg BID solution in patients 20–<40 kg; and 5 mg BID tablet or solution in patients ≥40 kg.

Conclusion: Tofacitinib population PK in patients with JIA were adequately described by a one compartment model parameterised in terms of CL/F, V/F and first-order absorption with a lag time. Drug absorption from the oral solution was faster than from the tablet. Tofacitinib does not require dose modification or restrictions for any covariates, except BW, to account for differences in C_{avg}. Based on the results of this analysis, a simplified BW-based dosing regimen was proposed.

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FRI0466 NO DISEASE PROGRESSION AFTER 36 MONTHS FOLLOW UP IN THE JUVENILE SYSTEMIC SCLERODERMA INCEPTION COHORT

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Background: Juvenile systemic scleroderma (jSSc) is an orphan disease with a prevalence of 3 in 1 000 000 children. There is rare longitudinal prospective follow up data of patients with jSSc. In the international juvenile systemic scleroderma cohort (JSScC) patients are followed with a standardized assessment prospectively.

Objectives: To assess the changes regarding organ involvement pattern and patients related outcomes after 36 months follow up in the JSScC.

Methods: Patients diagnosed according the ACR 2013 criteria for systemic sclerosis were included, if they developed the first non-Raynaud symptom before the age of 16 and were under the age of 18 at the time of inclusion. Patients were followed prospectively every 6 months with a standardized assessment.

Results: 39 patients in the JSScC had 36 months follow up. 80% had a diffuse subtype. 95% of the patients were Caucasian origin. 31 of the patients were female (80%). Mean disease duration at time of inclusion was 3.5 years. Mean age onset of Raynaud's was 8.8 years and mean age of onset at the first non-Raynaud´s was 9.5 years. Around 30% of the patients were anti-Scl70 positive and none of them anti-centromere positive. The MRSS dropped from the time point of the inclusion into the cohort from 13.9 to 11.8 after 36 months. Pattern of organ involvement did not show any significant change, beside the increase of the nailfold capillary changes from 49% to 73% ($p=0.037$). No renal crisis occurred. No mortality was observed.

They were positive significant changes in the patient related outcomes. The physician global disease activity decreased from 40.0 to 22.1 assessed on a VAS scale of 0 to 100 ($p<0.001$).

Patients global disease activity decreased from 43.3 to 20.4 and patients global disease damage from 45.0 to 21.7 both assessed on a VAS scale of 0 to 100 ($p<0.001$).

Conclusion: After 36 months follow up, we could observe a significant improvement of patient related outcomes and only one significant change in organ pattern involvement. In a mostly diffuse subset patient population this is a very promising result regarding outcome.

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FRI0467 DRUG SURVIVAL AND SAFETY OF BIOLOGICAL THERAPIES IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Biological treatment (BT) has changed perspectives of JIA patients. Increasing data from real life experience have been reported.
Objectives: To compare drug survival, safety and efficacy of BT in patients with Juvenile Idiopathic Arthritis (JIA).
Methods: A retrospective observational study was conducted on JIA patients followed in a referal hospital and who had received at least one BT between 1999 and 2019.
Results: 218 BT in 130 JIA patients were analyzed. 67.7% were women with a median age at diagnosis of 8 years old IQR (3-13) and a median age at the beginning of the BT of 15 years old IQR(7.8-21). 21.5% of the patients had uveitis during follow-up. BT were indicated due to: arthritis(73.9%), uveitis(10.1%), arthritis and uveitis(2.7%), systemic activity(8.3%) and macrophage activation syndrome (1,8%).There were 130 BT started in 1st line, 55 in 2nd line, 20 in 3rd line, 10 in 4th line and 3 in 5th line.
The 1st line BT most frequently indicated was Etarnecept(ETN) up to 40%, followed by 30% Adalimumab(ADA) and 16,2% Infliximab(INF). The median duration of the 1st line was 51 months IQR (14-109,3). However, 53.8% of the 1st line BT were swiched: 28.3% due to adverse events, 25.7% due to 1º failure and 25.7% due to 2º failure. The BT that were discontinued were: INF (76.2%) and Anakinra (ANAK) (75%) due to adverse events and ETN (59.6%) due to 1º and 2º failure. 55 patients started a 2nd BT: 43.6% received ADA and 20% Tocilizumab (TCZ) with a median duration of 43 months IQR (12-90). 22 of 55 BT required a change: 75% of ETN and 59% of INF prescribed in 2nd line were discotinued. The causes were: 40% 1º failure, 28% 2º failure and 12% remission. In 1st line 87,6% of patients received TNF inhibitors, 74% mantained the target in 2nd line. In 3rd line TCZ was the most frequent BT. 71.5% of patients continue on BT. BT was withdrawn in 20 of 130 patients due to remission (40%), adverse events (30%), and pregnancy (10%).
In the analysis by decades, 80 BT (36.7%) were started from 1999 to 2008 and 138 BT (63.3%) from 2009 to 2019. In the 1st decade ETN and INF were the most frequently prescribed and in the 2nd decade, ADA and TCZ ($p < 0.0001$). The 1st BT in the 2nd decade were indicated sooner compared to the 1st decade (1st decade: mean 119.5months SD(109.2); 2nd decade: mean 53.9 months SD(99.7); $p < 0.0001$). In 1st line BT, the BT prescribed in the 2nd decade had a shorter duration than those in the 1st decade (1st decade: mean 84.1 months SD(71.8); 2nd decade: mean 51.7 months SD(5); $p < 0.0001$).
In the survival analysis, TCZ and ADA were the BT with the highest survival ($p=0.001$). Of the 31 patients that started TCZ, 61.3% continue on TCZ, with a median duration of 46 months IQR(25-99) and 36/68(52,9%) still on ADA with a median duration of 61,5 months IQR(30.5-98).
Conclusion: 42.3% of patients required more than one BT. Since the onset of the BT there has been a change in prescription, probably related to the emerge of new targets and the evidence provided by clinical trials and guidelines. TCZ and ADA were the BT with the highest survival rate. On the other hand, INF and ANAK were the ones with the lowest survival rate. The most common causes of BT change in 1st line were adverse events in relation to INF and ANAK. In 2nd line there was a high rate of change in those patients who maintained TNFi, related to 1º failure.
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FRI0468 SYSTEMIC AND CUTANEOUS POLYARTERITIS NODOSA IN COLOMBIAN PEDIATRIC PATIENTS: CUTANEOUS POLYARTERITIS IS NOT SO BENIGN

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Background: Polyarteritis nodosa (PAN) is the third most frequent vasculitis in pediatrics, Cutaneous PAN (CPAN) being more common that Systemic PAN (SPAN). CPAN is frequently described as a benign disease. In children, PAN onset is frequent between 9 and 11 years of age, with no sex differences, and its clinical features may be nonspecific.
Objectives: To characterize pediatric patients who were diagnosed with CPAN and SPAN and to compare their clinical features, treatments, and outcome.
Methods: A descriptive study was conducted in two centers from Medellin- Colombia, using retrospective data from January 2010 to December 2019. Patients under 18 years of age classified as PAN according to EULAR/PRINTO/PRES(1) criteria were included. CPAN patients were defined according to EULAR/PRES definition (2). Data from medical records were registered, and were expressed in median and ranges and mean and standard deviation (SD) according to their distribution. A univariate analysis was carried out by comparing signs, symptoms, and treatment between CPAN and SPAN, and a *p-value < 0,05* was considered as significant.
Results: Twenty patients were included. The median age at diagnosis was ten years. 60% were boys. The median follow-up period was 27 months. CPAN was diagnosed in 11 (55%) and SPAN in 9 patients (45%). The most frequent symptoms were cutaneous manifestations (95%), fever (60%) and Calf Pain (55%). Mucosal ulcers were described in four patients; 3 of them were defined as CPAN. Lingual necrosis was present in two CPAN, and peripheral nervous system involvement was found in one SPAN and two CPAN patients in skin affected with lesions; even though, no significant statistical differences between CPAN and SPAN were found in constitutional, cutaneous, muscle-skeletal symptoms, and acute phase reactants. Arteriographic anomalies as hepatic and renal microaneurysms, carotidal aneurysms without aortic involvement, and renal infarction were found in one patient each. Skin Biopsy was performed in 18 patients, being compatible with PAN in 16. All PAN patients (CPAN and SPAN) required treatment with glucocorticoids. None of the patients died during the follow-up period.
Conclusion: In this Colombian pediatric cohort of PAN patients, the disease was more common in boys than girls, and CPAN was more frequent than SPAN, as already been described. As is evident in this cohort, although CPAN has been considered a benign disease, these patients may be severely ill, requiring glucocorticoid treatment. Pediatric CPAN patients should be strictly followed with particular attention to identify systemic involvement, considering that constitutional, cutaneous, and muscle-skeletal features may be very similar between CPAN and SPAN.
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FRI0469 TO DISTINGUISH BETWEEN DISEASE FLARE AND ACTIVE INFECTION IN PEDIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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Background: SLE is the autoimmune disease involving multiple systems. Infections might mimic SLE flare, leading to confusion over the diagnosis and appropriate treatment. To distinguishing acute infection from active flare always remains a clinical challenge.
Objectives: We aim to explore the potential parameters in identifying active infection and disease activity in pediatric SLE.

Methods: We reviewed the medical charts of the pediatric SLE patient in National Taiwan University Hospital from August 2015 to September 2019, and 50 SLE patients presented 185 episodes of suspicious activity or infection and received CRP, ESR, and Procalcitonin measurement were included. Time matched other laboratory parameters and clinical assessments were also collected. Episodes were divided into 4 groups: infected-active, infected-inactive, noninfected-active, and noninfected-inactive. Association of parameters with outcomes were predicted by generalized estimating equation. The receiver operating curve and the area under the curve were used to evaluate the diagnostic performance. We also used multinomial logistic regression model for nominal outcome, by setting noninfected-inactive group as the reference category.

Results: There were 7 males (14%) and 43 females (86%), with the mean ages 13.9 ± 4.4 years old. Most of the patients had renal (72%) or mucocutaneous (72%) involvement. The most common infection site was respiratory system (56%). Multivariate GEE analysis showed Damage index(DI), SLEDAI-2k, neutrophil-to-lymphocyte ratio (NLR), hemoglobin, platelet, RDW-to-platelet ratio (RPR), and C3 are independent parameters for predicting SLE activity flare. Combination of these seven parameters resulted in a model with calculated AUC of 0.8964 and with sensitivity of 82.2 % and specificity of 90.9%. Multivariate GEE analysis showed DI, fever, CRP, Procalcitonin, lymphocyte percentage, NLR, hemoglobin, and renal score in SLEDAI-2k are independent parameters for predicting acute infection. These eight parameters resulted in a model with calculated AUC of 0.7886 and with sensitivity of 63.5% and specificity of 89.2%. We select a total of 10 variables (DI, SLEDAI-2k, Fever, Procalcitonin, lymphocyte percentage, NLR, hemoglobin, platelet, RPR, C3) to establish multinomial logistic regression, then predict four groups with accuracy of 70.13% for infected-active, 10% for infected-inactive, 59.57% for noninfected-active, and 84.62% for noninfected-inactive.

Conclusion: The proposed predictive calculator could be a useful tool for differentiation between activity flares and acute infections in pediatric SLE. Obtaining and combination of several parameters is effective and helpful to make appropriate judgement and treatment decisions for SLE patients.

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FRI0470 CARDIORESPIRATORY FITNESS IN JUVENILE IDIOPATHIC ARTHRITIS IN 6 – 17-YEAR-OLD CHILDREN- CROSS-SECTIONAL STUDY

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Background: Children with juvenile idiopathic arthritis (JIA) have been found to have reduced cardiorespiratory fitness and lower physical activity. Poor cardiorespiratory fitness is associated with a risk of cardiometabolic diseases.

Objectives: The aim of this study was to study the levels of cardiorespiratory fitness, respiratory function and hemodynamic responses during and after maximal cycle ergometer exercise test in children with JIA aged 6-17 years and compare the results with healthy controls.

Methods: Study group in this analysis consisted of 43 patients with JIA who were treated in Department of Pediatrics in Kuopio University Hospital, Finland and 40 healthy age- and sex matched controls. Maximal exercise tests were carried out with an electromagnetic cycle ergometer using a pediatric saddle module. Maximal workload per kilogram (W_{max}/kg) was used as a measure of cardiorespiratory fitness and was presented relative to bodyweight. In addition the peak values of VO_2 per kilogram ($VO2_{max}$/kg) were used as a measure of highest amount of oxygen that an individual can consume during exercise. Values of $VO2_{max}$ were collected from respiratory gases measured directly from breath by breath method and was presented relative to body weight.

Physical activity and sedentary behavior (minutes per day) was assessed by the PANIC (Physical activity and nutrition in children -study) Physical Activity Questionnaire which the participants filled.

Results: Statistical analyses were performed for 43 children with JIA and 40 controls. Mean age in JIA group was 12.09 years (95%CI 11.04-13.14), and 11.72 years (95%CI 10.52-12.93) in controls (p=0.572). Mean body mass index for age (BMI) was 22.58 kg/m^2 (95%CI 21.54-23.62) in JIA and 18.95 kg/m^2 (95%CI 17.73-20.16) in controls (p<0.05). In JIA group BMI was 19.18 % higher compared to controls. Mean physical activity in JIA group was 94.11 minutes per day (95% CI 81.09-107.13), and 122.54 minutes per day (95% CI 102.84-142.24) in controls, thus JIA group was 23.20 % less physically active than controls (p=0.015).

Mean W_{max}/kg was 2.65 W/kg (95% CI 2.49-2.82) in JIA and 3.01 W/kg (95%CI 2.86-3.15) in controls thus W_{max}/kg in JIA was 0.36 W/kg (11.8 %) lower than in controls, (p = 0.002). $VO2_{max}$/kg was 37.00 (95%CI 33.96-40.84) ml/kg/min in JIA and 43.30 (95%CI 40.79-45.82) ml/kg/min in controls thus in JIA group mean $VO2_{max}$/kg was 6.3 ml/kg/min (14.4 %) lower than in controls (p=0.001).

Conclusion: Children with JIA were found to have significantly lower cardiorespiratory fitness. In addition, BMI in JIA patients was higher compared to healthy age- and sex-matched controls. Impaired cardiorespiratory fitness and higher BMI may predispose children with JIA to cardiometabolic comorbidities later in life. In addition to disease-control, more attention should be paid to maintaining good cardiorespiratory fitness and normal BMI in these patients already before adulthood.

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FRI0471 ADVERSE FACTORS OF COMORBID DISEASES DEVELOPMENT AT DIFFERENT VARIANTS OF JUVENILE IDIOPATHIC ARTHRITIS (JIA)

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Background: It is known that rheumatic diseases are the pathogenetic basis for the formation of many comorbid conditions, the most important of that are cardiovascular pathology, atherosclerosis, osteoporosis, chronic kidney disease and amyloidosis, chronic obstructive pulmonary disease. The start of the disease at an early age, the long-term duration of JIA, the use of basic immunosuppressive therapy lead to the possibility of the onset of the first signs of comorbid conditions in childhood.

Objectives: To study risk factors for the formation of damage of internal organs and systems in children with non-systemic JIA.

Methods: The case histories of 121 patients aged 7-18 years (mean age 11.0 ± 0.3 years) with polyarticular (67.7%), oligoarticular (14.88%) and uveitis-associated (17.35%) JIA were studied, mainly of females (73.5%). The age of the start of the disease was 5.9 ± 0.4 years, the duration of JIA at the time of analysis reached 67.1 ± 4.3 months. All children received basic methotrexate therapy (plus folic acid), short courses of NSAIDs. There are studied changes in the cardiovascular system (ECG, ultrasound, 6-minute walk test),

lungs (spirography), kidneys (concentration function, glomerular filtration rate, daily microalbuminuria), lipid spectrum and blood coagulation. Deviations from standard age-gender normal values were taken into account. It was used statistical methods for identifying relationships (stepwise multiple regression). As the dependent value the number of detected changes in the state of internal organs and systems is taken. The independent variables included standard clinical and laboratory parameters, the age of the onset of JIA, the total duration of the disease, the characteristic of the articular syndrome, activity indicators (C-reactive protein, RF and ANA titers, JADAS27), as well as the term for the appointment of basic therapy relative to the debut of the disease, the nature of the dosage methotrexate (mg / m2 / week), the duration of its use at the time of examination.

Results: Based on the analysis and the obtained regression models for the formation of extra-articular lesions in children with various JIA options, it was found that the leading factors in the formation of comorbidity are the duration of the disease (p = 0.01), VAS results (including the child, parents and the physician) (p = 0.01), the dose of methotrexate (p = 0.01).

In the polyarticular variant, the body mass index (p = 0.02), erythrocyte content (p = 0.007) were significant for the formation of comorbid states and should be distinguished.

The overall duration of the disease (p = 0.02), the low age of initiation of therapy (p = 0.05), VAS of child (p = 0.003), CRP (p = 0.007), dose of methotrexate (p = 0.001) had the greatest significance level among the clinical and laboratory indicators included in the regression model of the formation of comorbidity with the oligoarticular variant.

A features of the prognostic model for the formation of organ lesions and metabolic disorders in uveitis-associated arthritis were GCS therapy presence (p <0.001), patient age (p <0.001), JADAS27 (p <0.001) and methotrexate dose (p <0.001).

Conclusion: Thus, in children with JIA, the formation of comorbid pathology is associated with a lower age of JIA debut in oligoarthritis and uveitis-associated arthritis, low body weight in poly- and oligoarticular JIA variants, an increase in the duration of the disease in the polyarticular variant, and the level of activity of the process, respectively, JADAS 27(p <0.01) and VAS. Prognostically unfavorable for the formation of pathological changes in the internal organs and homeostasis are anemia, high white blood cell count and ESR level.

Disclosure of Interests: None declared

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FRI0472 DIAGNOSIS AND MANAGEMENT OF ADENOSINE DEAMINASE 2 DEFICIENCY CHILDREN: THE EXPERIENCE FROM CHINA

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Background: Adenosine deaminase 2 deficiency (DADA2) is a rare antoinflammatory disease caused by mutations in ADA2 gene, few Chinese cases have been reported.

Objectives: To describe and compare the clinical features, genotypes, and treatments of Chinese DADA2 patients and foreign cases.

Methods: Primary immunodeficiency disease Panel or Whole Exome Sequencing was performed to suspected subjects, and assays for adenosine deaminase 2(ADA2) enzyme activity were also carried out to them and their parents. Case reports of Chinese and foreign patients with DADA2 were searched from PubMed and Chinese domestic databases.

Results: Seven unrelated DADA2 children from China were included in our study, 5 were identified at Peking union medical college hospital and 2 had been reported previously (1 on PubMed and 1 in Chinese literatures). 14 mutations in ADA2 were identified, and 9 of which have not been found in other countries. Four children receiving enzymatic analysis had lower ADA2 enzyme activity compared to their parents. Phenotypic manifestations included fever, skin symptoms, vasculitis, neurologic involvement, et al. The treatments varying from steroids, immunosuppressants, and tocilizumab, anti-TNF therapy and hematopoietic stem cell transplantation (HSCT) were effective depending on different phenotype and severity.

Conclusion: This study includes the biggest number of Chinese DADA2 patients at present. We recommend combination of enzymatic analysis with gene screening to confirm the diagnosis. Genotypes of patients from China were some different, the clinical manifestations were similar. We suggest anti-TNF therapy may not be necessary for mild case and HSCT should be considered even without hematological phenotype.

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Disclosure of Interests: None declared

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FRIDAY, 05 JUNE 2020

Other orphan diseases

FRI0473 ASSESSMENT OF FEMORAL VEIN WALL THICKNESS WITH DOPPLER US AS A DIAGNOSTIC TOOL FOR BEHCET'S DISEASE

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Background: Diagnosing Behcet's disease(BD) is a challenge, especially in countries with a low prevalence. International Study Group Criteria, accepted to as diagnostic, has low sensitivity, especially in early cases when major organ involvement such as uveitis or deep vein thrombosis(DVT) presents alone. We recently published a controlled study of assessing venous wall thickness(VWT) as a surrogate marker of venous disease in BD with ultrasound(US) and observed a very sensitive and specific VWT in male BD patients. The common femoral vein(CFV) thickness measurement, as the primary site of US with the cut-off values > 0.48-0.49 mm, had a high area under the receiver operating characteristic curve(>0.8) with sensitivity and specificity of around 80%(1).

Objectives: In this study, we aimed to investigate the diagnostic performance of CVF thickness measurement in BD including females comparing with multiple control disease groups.

Methods: One hundred-ten patients with BD, 47 healthy controls(HC), 21 patients with systemic vasculitides, 28 patients with venous insufficiency,29 patients with antiphospholipid syndrome (APS) having DVT history, were included the study. Bilateral CFV thickness was measured with US by an experienced radiologist blinded to cases(Figure 1).

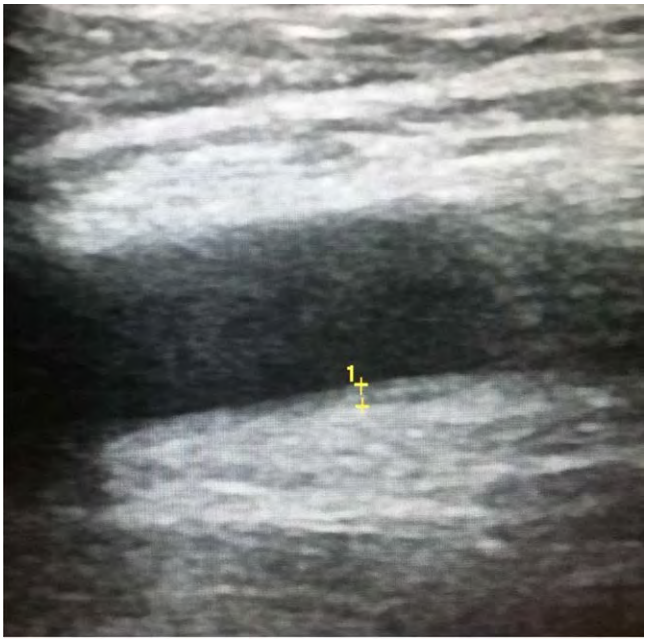


Figure 1. Measurement of common femoral vein thickness

Results: Bilateral CFV thickness was significantly higher in BD compared to all comparative groups (p<0.001 for all)(Table 1,Figure 2). No correlations were present between CFV thickness and both BSAS and CRP levels (p>0.05 for all). In only 2 (8%) patients with venous insufficiency and 2 (10%) patients with systemic vasculitis, bilateral CVF thickness was higher than the cut- off values. Interestingly, APS was the only control group with positivity, in 12 (41%) patients with APS, bilateral CFV thickness was higher than the cut-offs. There was no difference between male vs female BD patients regarding CFV thickness (right CFV:0.78 mm vs 0.79 mm,p=0.96, left CFV:0.78 vs 0.8, p=0.80). Although a higher CVF thickness tendency was observed in VBD, no statistically significant difference was present between BD patients with (n=40) and without (n=58) vascular involvement (right CFV:0.82±0.3 mm vs 0.75±0.3 mm, p=0.122, left CFV:0.84 ± 0.3 vs 0.76±0.3, p=0.165).

Table 1. Venous Wall Measurements of Lower Extremity in Study Groups

	Behcet's Disease (n=110)	Healthy Controls (n=47)	Systemic Vasculitis (n=21)	Venous Insufficiency (n=28)	Anti-phospholipid Syndrome with DVT (n=29)
Age (years)	33.5 ± 6	30.1 ± 5	33.3 ± 7	36.7 ± 6	38.3± 9
Gender, male n (%)	89 (81)	40 (85)	12 (57)	13 (46)	9 (31)
Body Mass Index, kg/m2	25.5 ± 4	24 ± 2	23.8 ± 3.5	27.7 ± 4	27.2 ± 7
Right CFV Thickness (mm)	0.79 ± 0.3	0.34 ± 0.1	0.34 ± 0.15	0.38± 0.1	0.48 ± 0.15
Left CFV Thickness (mm)	0.78 ± 0.3	0.3 ± 0.1	0.36 ± 0.14	0.38 ± 0.2	0.48 ± 0.15

CFV: Common Femoral vein, DVT:Deep Venous Thrombosis

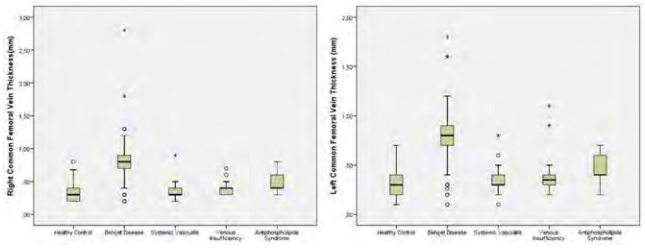


Figure 2. Distribution of common femoral vein thickness in study groups

Conclusion: Increased CFV thickness is present in BD patients,independent of vascular involvement.We also found that CFV thickness is a distinctive feature of BD, rarely present in other inflammatory/vascular diseases such as ankylosing spondylitis (previously shown),systemic vasculitides and venous insufficiency(except APS with DVT).CFV thicknesses are easily and reliably measured by Doppler US. We, therefore, suggest that assessment of CFV can be a diagnostic tool for BD with a good sensitivity and specificity to differentiate BD from similar disorders.

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Disclosure of Interests: None declared

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FRI0474 IMMUNE CHECKPOINT INHIBITOR-INDUCED MUSCULOSKELETAL MANIFESTATIONS. A SYSTEMATIC REVIEW

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Background: Immune checkpoint inhibitors (ICI) are potent anti-cancer drugs that associate with a wide range of immune related adverse events (Ir-AE), including musculoskeletal manifestations.

Objectives: We performed a systematic literature review of ICI-induced musculoskeletal manifestations aiming at exploring the following: 1) the prevalence of these manifestations and the time from first ICI administration to symptom onset, 2) the main clinical phenotypes and the type of treatment required to control symptoms (steroids/DMARDs), 3) the type of ICI (CTLA-4 vs PD-1/PD-L1 inhibitors) mostly associated with Ir-AE, 4) the percentage of patients with positive auto-antibodies and family history of autoimmune disease, 5) the percentage of patients requiring permanent ICI discontinuation due to musculoskeletal Ir-AE, 6) the association between musculoskeletal Ir-AE and oncologic response and 7) the risk of flare in patients with pre-existing autoimmune disease (PAD).

Methods: An electronic (PubMed) search was performed aiming at identifying all studies reporting musculoskeletal Ir-AE.

Results: We identified 3 prospective studies, 17 retrospective studies and 4 case series reporting 363 patients in total. Combined data from all 3 prospective studies provide a prevalence rate of 6.13%. Most patients were males (59.68%) and the vast majority (73%) were on programmed death-1 (PD-1)/programmed death ligand-1 (PD-L1) inhibitors. Most studies report a median time of ≤ 12 weeks from first ICI administration to symptom onset. The main clinical phenotypes reported were: a) inflammatory arthritis (57.57%), b) myositis (14.04%) and c) polymyalgia rheumatica (PMR) (12.12%). A total of 256 patients required steroids (70.52%) and 67 patients (18.45%) were treated with DMARDs. From the 363 patients reported in total, 265 (73%) were treated with PD-1/PD-L1 inhibitors in sharp contrast to only 11 (3.03%) with CTLA4 inhibitors with the rest patients receiving combination immunotherapy Positive auto-antibodies and family history of any autoimmune disease were present in 18.48% and 19.04% of cases, respectively. Only a few patients (19%) had to discontinue treatment due to musculoskeletal Ir-AE. Two prospective studies show that significantly more patients with musculoskeletal Ir-AE exhibit a favorable oncologic response compared to patients not exhibiting such manifestations whereas retrospective studies show that 77.22% of patients with musculoskeletal Ir-AE have a good tumor response.

Conclusion: One out of 15 patients treated with ICI will develop musculoskeletal Ir-AE; in most cases the severity of these manifestations is mild/moderate and usually ICI is continued. Rheumatologists should familiarize themselves with this new clinical entity and develop relevant therapeutic algorithms.

Disclosure of Interests: None declared

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FRI0475 STEROID SPARING AGENTS IN POLYMYALGIA RHEUMATICA: A SYSTEMATIC REVIEW

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Background: Polymyalgia rheumatica (PMR) is the commonest chronic inflammatory musculoskeletal disease of the elderly. The mainstay of treatment for PMR is long term systemic glucocorticoid (GC), which is associated with significant systemic toxicity. There is a need for steroid sparing drugs in PMR to reduce GC cumulative dose and GC induced adverse effects.(1)

Objectives: To evaluate the role of steroid sparing agents in PMR.

Primary outcomes:

1. Steroid sparing effect of the intervention, measured by difference in cumulative glucocorticoid dose
2. Percentage of patients in remission.

Secondary outcomes:

1. Mean reduction of CRP/ESR
2. Adverse event/toxicity the drugs being compared—measured as number of patients with adverse events in the compared groups
3. Percentage of patients with relapse during study period
4. Mortality

Methods: Electronic databases including Medline, Embase and Cochrane databases (CENTRAL) were searched since inception for prospective randomized control trials comparing disease modifying anti rheumatic drugs (DMARDs) and biologics with systemic GC in PMR, published in English with more than 20 patients and a minimum study duration of 24 weeks. As different classification criteria for PMR exist, studies were included if they used any accepted classification criteria for PMR. Case series, case reports, retrospective, non-randomized trials, abstracts, systematic reviews and non English language trials were not included. Patients with Giant cell arteritis (GCA) were excluded. Risk of bias and quality was assessed using the Cochrane tool.

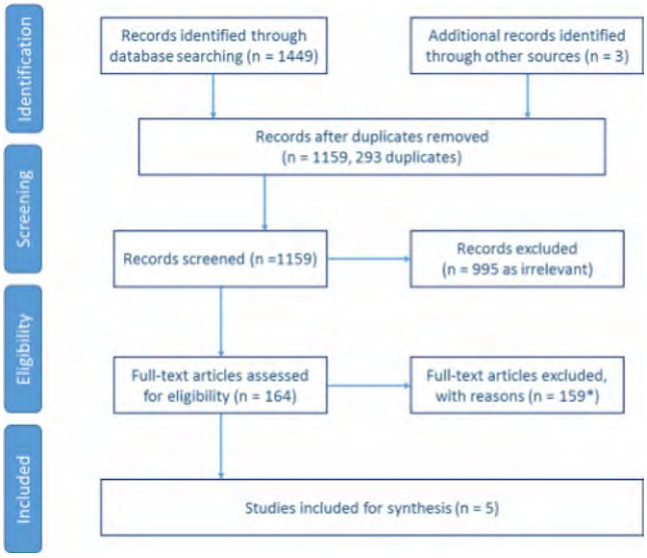
The studies were assessed for cumulative GC dose, proportion of patients in remission, proportion of patients with relapse, reduction in inflammatory markers, adverse events and mortality.

Results: 5 studies were selected for final review-- 3 studies involving Methotrexate, one study on azathioprine, one on Infliximab. The study on Azathioprine

had high risk of bias, small sample size and low quality (Level 2 evidence) with high attrition rate but it revealed reduction of daily prednisolone with Azathioprine. A high quality RCT (Level 1) did not confirm a steroid sparing effect with Infliximab vs placebo, and there was no significant difference between relapse or remission rate. Methotrexate studies showed conflicting results: one high quality RCT (Level 1) and one low quality RCT (Level 2) on Methotrexate revealed statistically significant steroid sparing effect, however the remaining study did not demonstrate between Methotrexate and placebo. Two methotrexate studies assessed the risk of relapse, with conflicting results (relapses 73% placebo vs 47% methotrexate; or no difference).

Methotrexate was not associated with increased adverse effects in any of the studies. Azathioprine was associated with significant adverse events resulting in high attrition.

A meta analysis was not performed for methotrexate as the studies were heterogenous.



Conclusion: There is a lack of evidence regarding DMARDs and biologics in PMR. Methotrexate is an effective steroid sparing agent, and is not associated with increased adverse events. Azathioprine may be effective but is associated with significant adverse events. Infliximab is not an effective steroid sparing agent in PMR. More high quality RCTs are needed to study the efficacy of steroid sparing agents.

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Disclosure of Interests: None declared

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FRI0476 RHEUMATIC MANIFESTATIONS DURING INFLAMMATORY BOWEL DISEASE

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Background: Rheumatologic manifestations are frequent extraintestinal manifestations (MEI) of chronic inflammatory bowel disease (IBD). Some of these manifestations develop in parallel with the underlying disease, others evolve on their own account. They sometimes lead to reconsider the initial therapy for intestinal purposes.

Objectives: The aim of our study is to specify the epidemioclinical characteristics of osteoarticular manifestations of chronic inflammatory bowel disease and their possible impact on intestinal disease

Methods: This is a retrospective study conducted between January 2000 and December 2015 including patients hospitalized in our department for chronic inflammatory bowel disease (IBD).

Results: During the study period, 206 patients with IBD were hospitalized in our department, 78 of whom had rheumatic MEI (frequency equal to 37.8%). These 78 patients were divided into 48 men and 30 women with a sex ratio of 1.6 and an average age of 40.7 ± 13.6 years (18–79). They had Crohn's disease in 60% of the cases. The average length of service for IBDs was 83 ± 73 months (4–360). Osteoarticular MEIs were peripheral in 56.4% of cases, axial in 29.5% of cases, mixed in 6.41% of cases with the presence of osteopenia in 6.41% of cases and osteoporosis in 1 28%. The activity of IBD associated with these MEI was moderate with an average number of outbreaks / year of 1.6 ± 0.8. These patients were treated with salicylates in 30.7% of the cases using corticosteroid therapy at least once in 23% of the cases. Maintenance treatment based on immunosuppressants was found in 38.46% of cases and anti-TNF alfa in 10.25% of cases. During follow-up, 3 patients died (3.84%). There was no significant difference between patients with IBD with rheumatic MEI and without rheumatic MEI regarding epidemiological data and disease activity.

Conclusion: Rheumatic MEIs are found in almost 40% of IBDs. They affect men more frequently than women and Crohn's disease than UC. They are rather peripheral and do not associate with a more important activity of the disease.

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Disclosure of Interests: None declared

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FRI0477 SYSTEMIC TREATMENT IN SARCOIDOSIS. STUDY OF 377 PATIENTS FROM A SINGLE UNIVERSITY HOSPITAL

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Background: Sarcoidosis is a multisystemic disease characterized by the formation of non-necrotizing granulomas. The most frequently affected organs are lungs, skin and eyes. Systemic corticosteroids are the most used drugs in the treatment of this disease. Conventional and biological immunosuppressants (IS) may also be used **(1-3).**

TABLE. Systemic treatment of sarcoidosis according to clinical domains.

		CONVENTIONAL IS								BIOLOGICAL IS							
ORGAN INVOLVEMENT	**Cases**	**NT**	**OCS**	**MD of OCS (mg/d)***	**IVMP**	**MTX**	**AZA**	**CFM**	**MMF**	**BT**	**IFX**	**ADA**	**ETN**	**GLM**	**TCZ**	**RTX**	**CR**
Pulmonary, n(%)	319(84.6)	128(40.1)	185(58)	43.6±18.8	13(4.1)	46(14.4)	13(4.1)	2(0.6)	3(0.9)	21(6.6)	12(3.8)	16(5.0)	0	1(0.3)	2(0.6)	3(0.9)	64(33.5)
Cutaneous, n(%)	124(32.9)	50(40.3)	66(53.2)	38.0±20.2	4(3.2)	18(14.5)	4(3.2)	1(0.8)	0	9(7.3)	5(4)	9(7.3)	1(0.8)	2(4.2)	0	1(0.8)	29(39.2)
Ocular, n(%)	48(12.7)	5(10.4)	38(79.2)	41.5±17.6	10(20.8)	23(47.9)	8(16.7)	1(2.1)	1(2.1)	13(27.1)	5(10.4)	11(22.9)	1(2.1)	2(4.2)	2(4.2)	0	10(23.3)
Musculo-eskeletal, n(%)	108(28.6)	41(38)	65(60.2)	39.2±18.7	5(4.6)	26(24.1)	6(5.6)	0	0	12(11.1)	8(7.4)	8(7.4)	1(0.7)	2(1.9)	0	1(0.9)	24(35.8)
Hepatic, n(%)	41(10,9)	12(29.3)	27(65,9)	43.8±15.2	3(7.3)	6(14.6)	1(2.4)	1(2.4)	0	1(2.4)	1(2.4)	1(2.4)	0	0	0	0	6(20.7)
Neurologic, n(%)	27(7.2)	4(14.8)	23(85,2)	50.9±20.2	5(18.5)	14(51.9)	5(18.5)	0	0	9(33.3)	7(25.9)	5(18.5)	1(3.7)	2(7.4)	1(3.7)	1(3.7)	6(26.1)
Cardiac, n(%)	8(2.1)	4(50)	4(50)	40.0±28.3	1(12.5)	2(25)	1(12.5)	1(12.5)	0	2(25)	2(25)	2(25)	0	0	0	0	1(25)
Renal, n(%)	22(5.8)	2(9.1)	20(90,9)	47.1±13.8	1(4.5)	6(27.3)	2(9.1)	0	0	2(9.1)	1(4.5)	2(9.1)	0	0	0	0	3(15)
Löfgren's síndrome, n(%)	44(11.7)	18(40.9)	24(54,5)	29.8±15.3	0	3(6.8)	1(2.3)	0	0	2(4.5)	1(2.3)	2(4.5)	0	0	0	1(2.3)	19(69.2)
Heerfordt's síndrome, n(%)	2(0.5)	0	2(100)	57.5±17.7	2(100)	2(100)	1(50)	0	0	2(100)	2(100)	2(100)	0	0	0	0	0
TOTAL,n(%)	377(100)	161(42.7)	206(54.6)	48.2±19.0	15(4.0)	53(14.1)	16(4.2)	2(0.5)	3(0.8)	28(7.4)	15(4.0)	20(5.3)	1(0.3)	2(0.5)	3(0.8)	3(0.8)	72(33.3)

NT: no treatment; **MD:** maxim dose; **OCS:** oral corticosteroids; **IVMP:** intravenous methylprednisolone; **BT:** biological therapy, **CR**: complete response

* Mean (±SD)

Table 1. Characteristics and treatment of Rh-irAEs patients.

	Age, Sex	Cancer	ICI	Onset (monts)	Rhem-irAE	Treatment	Response	ICI stop	AutoAb
1	69, M	Lung, adeno	Nivo	3	Myo	CS, MMF, ANK, TCZ	LDA	Y, D	pANCA
2	70, M	Bladder	Atezo	1	A,	CS, MTX	Rem	Y, T	Neg
3	79, M	Lung SCC	Pembro	1	A	CS	Rem	No	Ro52
4	52, M	Lung, LCC	Nivo	6	A, CV	CS, MTX, ANK, TCZ	LDA	No	ANA 1:160 s
5	82, M	Lung, LCC	Pembro	3	PMR	CS	Rem	No	Neg
6	56, M	Melanoma	Pembro	26	PMR, PM	CS, MTX	Death	Y, D	ANA 1:160 s, pANCA
7	72, M	Lung, adeno	Pembro	5	A, CV	CS, MTX, TCZ	HDA (TCZ)	Y, T	ANA 1:160 s
8	74, M	Lung, adeno	Pembro	1	PMR	CS, MTX	LDA	No	ANA 1:160 s
9	75, M	Lung, adeno	Pembro	1	PM, Myo	CS	Rem	Y, D	Neg
10	75, M	Lung, adeno	Nivo	9	A	CS	Rem	No	Neg
11	68, F	Lung, adeno	Atezo	18	A	CS, MTX	LDA	Y, T	Neg
12	35, M	Melanoma	Nivo	2	A	CS, MTX	LDA	No	ANA 1:640 s
13	79, M	Lung, SCC	Nivo	15	A, PMR	CS, MTX, ANK	Death (NR)	Y, D	Ro52
14	77, M	Lung, adeno	Pembro	8	DM	CS, HCQ, IVIG	LDA	Y, D	ANA 1:320 PCNA
15	67, M	Lung, adeno	Nivo	13	A	CS, MTX	LDA	No	ASMA
16	74, M	Lung, SCC	Atezo	1	A, CV	CS, HCQ, Colch	LDA	Y, D	Neg
17	70, M	Lung, adeno	Nivo	5	A, CV	CS	Rem	Y, D	Neg
18	70, M	Lung, adeno	Pembro	15	A	CS	LDA	No	ASMA
19	69, M	Lung, adeno	Nivo	5	DM	CS, HCQ, MMF, IVIG, Tacro	MDA	Y, T	ANA 1:!60 s
20	84, M	H&N, SCC	Nivo	3	Ph	CS	Rem	Y, D	Neg
21	67, M	Lung, adeno	Durva	5	A, PM, Myo	CS	LDA	Y, D	ANA 1:160 h
22	50, F	Lung, LCC	Nivo	1	A, CV	CS, HCQ	Rem	Y, D	Neg

Objectives: To evaluate the systemic treatment of sarcoidosis according to clinical domains.

Methods: Study of all consecutive patients diagnosed with sarcoidosis between 1/1/1999 and 1/1/2019 in a tertiary university hospital. The diagnosis was established following the ATS/ERS/WASOG criteria *(Eur Respir J. 1999;14(4):735-737):* compatible clinical and radiological presentation, evidence of non-caseifying granulomas and exclusion of other granulomatous diseases.

Results: We studied 377 patients (188 men/189 women), mean age at diagnosis of 46.0±14.8 years. After a mean follow-up of 13.0±9.3 years, 161 (42.7%) patients did not require treatment. The remaining 216 (57.3%) received oral glucocorticoids (206, 54.6%) with a maximum mean dose of 43.2±19.0 mg/day, conventional IS (60, 16.2%), biological therapy (28, 7.4%) and/or endovenous methylprednisolone (15, 4.0%). Biological therapy was indicated by pulmonary (9, 32.1%), ocular (9, 32.1%), neurological (3, 10.7%), muskuloeskeletal (3, 10.7%), cutaneous (2, 7.1%), nephrological involvement (1, 3.6%); and Heerfordt's syndrome (1, 3.6%). Adalimumab and Infliximab were the biologics used more frequently (**Table**).

Conclusion: Compared to other studies, the high percentage of patients who required systemic treatment is remarkable. It also highlights the frequency of the use of biological drugs in more severe organ involvement (ocular and neurological), which is consistent with the trend in recent years.

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FRI0478 SEROLOGICAL AUTOIMMUNITY IN PATIENTS WITH RHEUMATIC IMMUNE-RELATED ADVERSE EVENTS: CORRELATION WITH SEVERITY AND TREATMENT

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Background: Immune checkpoint inhibitors (ICIs) can induce a variety of rheumatic immune-related adverse events (Rh-irAEs). Few data are available on which features can predict the occurrence of long-lasting and severe Rh-irAE

Objectives: To describe the serological features associated with long-lasting and severe Rh-irAE.

Methods: ICI-treated patients were identified. Patients' demographics, histotype of cancer, ICI, time interval from ICI start to Rh-irAE onset, characteristics of Rh-irAEs were recorded. Patients were tested for autoimmunity panel (a-IP): RF, ACPA, ANA, anti-SSA, anti-SSB, anti-Sm, anti-RNP, anti-Jo1, ANCA, ASMA, AMA, anti-dsDNA, anti-tireoglobulin, anti-tireoperoxidas, IgM and IgG anti-cardiolipin and anti-β2 glicoprotein I, crioglobulins. All patients were treated with steroids (CS). In case of flare of the Rh-irAE, csDMARDs or bDMARDs were started. Associations between a-IP status and need for DMARD start was evaluated. Non parametric tests were used.

Results: 22 Rh-irAE were included (see Table 1). Median age at Rh-irAE onset was 70 (50 – 84) years. 2 patients (9%) had a personal history of psoriasis. Median time from ICI start to Rh-irAE onset was 5 (1 – 26) months. 11 patients (50%) developed 1 Rh-irAE, 10 (45.4%) 2 and 1 (4.5%) 3. The most frequent were arthritis (A, 14, 63.6%), cutaneous vasculitis (CV, 5, 22.7%), PMR-like (4, 18.2%), polymyositis (PM, 4, 18.2%), myocarditis (Myo, 3, 13.6%) and dermatomyositis (DM, 2, 9.1%). Median initial prednisone dose was 25 (10 – 75) mg daily. In 14 patients (63.6%) a csDMARD was started upon steroids tapering. 9 patients (41%) were treated with methotrexate (MTX, 4, 18.2%) with hydroxychloroquine (HCQ, 2, 9.1%) with mycophenolate (MMF, 2, 9.1%) with colchicine (colch). 6 patients were treated with bDMARDs. 3 patients (50%) were treated with anakinra (ANK), 2 (33.3%) with IVIG and 3 (50%) with tocilizumab (TCZ). 13 patients (59.1%) were a-IP+. A significantly higher percentage of a-IP+ patients received DMARDs (11, 84.6%) compared to a-IP- patients (2, 22.2%,p = 0.0007). A significantly higher percentage of a-IP+ patients were treated with bDMARDs (5, 38.5%) compared to a-IP- patients (0, 0%, p = 0.05). We analysed whether in csDMARD-treated patients the need for bDMARDs was higher in a-IP+ but we found no statistical significance (45.4% vs 0%, p = 0.487).

Conclusion: The presence of serological autoimmunity might be helpful in detecting patients with Rh-irAEs refractory to steroid therapy.

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FRI0479 REWIRED CELL ENERGY METABOLISM IN A NOVEL KRAS-MUTATED HISTIOCYTOSIS CHARACTERIZED BY SEVERE SYNOVITIS

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Background: Histiocytoses are disorders characterized by tissue infiltration by macrophages, dendritic cells, or monocyte-derived cells. These diseases are classified in five groups based on histologic, clinical, and molecular features: Langerhans-related, cutaneous/mucocutaneous and malignant histiocytoses, Rosai-Dorfman disease, and hemophagocytic lymphohistiocytosis (1). Langerhans-related histiocytoses comprise Langerhans cell histiocytosis and Erdheim-Chester disease, both inflammatory myeloid-driven diseases characterized by clonal activating mutations along the MAPK or related pathways, most commonly *BRAFV600E*, and by severe tissue and systemic inflammation (2). Here, we describe and characterize a novel, related histiocytosis chiefly manifested with severe synovial involvement.
Objectives: Here, we describe a novel histiocytosis whose histologic and clinical picture (severe synovial involvement, systemic inflammation, skin lesions, and diabetes insipidus) differed from known histiocytic disorder. In addition, we performed molecular studies aimed at identifying causative activating mutations. Finally, by means of a dynamic 3D tissue culture system we characterized immune-metabolic mechanisms underlying disease pathogenesis and clinical response to treatment.
Methods: The mutational status of oncogenes was determined with a mass spectrometry multiplexed genotyping approach (PentaPanel). Biospy samples were cultured in RCCSTM bioreactor (Synthecon) in the presence/absence of a MEK inhibitor (GSK1120212, 1nM), and then either processed for immunohistochemical analyses, or lysed for western blot analysis. Culture supernatants were collected for cytokine, chemokine and metabolome determination. The Bio-Plex Multiple-Cytokine Assay (Bio-Rad) and the Ella assay (ProteinSimple) were used to determine cytokine concentrations in supernatants and serum, respectively. Metabolomic studies were performed as described (3).
Results: We identified a causative mutation in the proto-oncogene *KRAS* (*KRASG12D*, not previously reported in related histiocytoses). In addition, 3D culture studies of patient's biopsies revealed KRAS-driven signaling, phenotypic, and immunometabolic features. These included constitutive ERK and AKT phosphorylation, up-regulated glucose metabolism with glycolysis and TCA cycle activation, and deregulated release of pro-inflammatory cytokines IL-1β, IL-6 and TNFα. All these features reverted upon pharmacologic inhibition of the MAPK pathway. Characterization of this novel condition instructed effective treatment of the patient with the MEK inhibitor cobimetinib.
Conclusion: Genetic, clinical, and histopathology features differentiate this condition from known histiocytic disorders. Mechanistically, *KRASG12D* causes constitutive activation of the MAPK pathway in macrophages, which results in maladaptive changes in cell energy metabolism sustaining rampant production of pro-inflammatory cytokines. Besides instructing effective treatment of this patient, these studies revealed metabolic rewiring as key to pathologic inflammatory activation of macrophages in human disease.
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FRI0480 SCHNITZLER'S SYNDROME: DESCRIPTION OF AN ITALIAN MULTICENTER COHORT

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Background: Schnitzler's syndrome is an autoinflammatory disease characterized by monoclonal gammopathy and recurrent episodes of urticaria accompanied by clinical and laboratory signs of acute inflammation. Although the exact pathogenic mechanisms have not been fully clarified, the role of Interleukin-1 seems to be central.
Objectives: To describe clinical features and therapeutic approach in patients with Schnitzler's Syndrome.
Methods: Retrospective analysis of an Italian multicenter cohort. Data are expressed as the median (IQR).
Results: The clinical data of 24 patients from 9 centers (median follow-up 6 years [2-10]; median age at diagnosis 56.5 years [51.25-64.25]) were collected. The median diagnostic delay was 2 years (0-10); the diagnosis was made consensually at the onset of symptoms in 4 cases. The main clinical and laboratory features are shown in Table 1. Therapeutic response was evaluable in 20 patients: all received corticosteroids (CS; 25mg/day [25-50]); in one case, a good clinical response was observed. Eight patients were initially treated with colchicine: in 3 cases it was effective in controlling symptoms and reducing the dose of CS; other 8 patients were treated with csDMARDs (n:1 [1-2]): only 1 patient had a good response to cyclosporin.

Table 1. Clinical and laboratory features

Chronic Urticarial Rash, n (%)	24/24 (100)
Pruritus, n (%)	17/24 (71)
Intermittent fever, n (%)	23/24 (96)
Arthralgia/Arthritis, n (%)	20/24 (83)
Bone pain, n (%)	8/24 (33)
Weight loss, n (%)	9/24 (38)
Angioedema, n (%)	4/24 (17)
Lymphoadenopathy, n (%)	7/24 (29)
Hepatomegaly, n (%)	3/24 (12)
Splenomegaly, n (%)	3/24 (12)
Neuropathy, n (%)	4/24 (17)
Raised ESR or CRP, n (%)	24/24 (100)
Leukocytosis, n (%)	17/24 (71)
Anemia, n (%)	9/24 (38)
Monoclonal Gammopathy	
IgG λ, n (%)	5/22 (23)
IgG κ, n (%)	6/22 (27)
IgM λ, n (%)	1/22 (5)
IgM κ, n (%)	12/22 (55)
Bence Jones Protein, n (%)	6/23 (26)

A bDMARD was initiated in 15 patients. In 7 of the 14 patients initially treated with anakinra this therapy was continued with benefit whereas in the other 7 patients the treatment was discontinued for primary inefficacy (1 patient), secondary inefficacy (3 patients) and adverse events (3 patients; 2 injection site reaction, 1 severe allergic reaction). After anakinra discontinuation, 5 patients were treated with canakinumab with a good response in 3 cases and a partial response in 1 case (persistent arthritis); 1 patient died during the treatment. No response was observed in 3 patients treated with TNF inhibitors as a 2nd or 3rd line bDMARDs, as well as in 1 case initially treated with tocilizumab (in which a good response was afterwards obtained with canakinumab). bDMARDs were associated with a csDMARD in 2 patients (methotrexate and methotrexate + cyclosporine).
In one case monoclonal gammopathy evolved into Multiple Myeloma and the patient died 15 years after the onset of symptoms. Idiopathic myelofibrosis and myelodysplasia were found in one and in two patients, respectively.
Conclusion: In most cases csDMARDs and bDMARDs like anti-IL6 and anti-TNFα were not able to control the disease. In contrast, in some cases, a good response to colchicine was observed; refractory patients may be successfully treated with anti-IL1 agents. Patients should be supervised for possible evolution towards lymphoproliferative disease.
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FRI0481 HEMOPHAGOCYTIC SECONDARY SYNDROME. DIFFERENCES BETWEEN AUTOIMMUNE AND HEMATO-ONCOLOGICAL ETIOLOGIES

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Background: The Hemophagocytic Syndrome (HPS) is has been classified into 2 groups: primary and secondary. The secondary form is mainly associated with hemato-oncological diseases (HOD) and autoimmune diseases (AID). The

present work aims to obtain clinical and analytical data that can guide us to an etiological diagnosis.

Objectives: To describe and identify the differences between HPS secondary to AID and HOD during their admission to a tertiary hospital between 2005 and 2019.

Methods: This is a retrospective observational study. We include patient meeting the diagnostic criteria for HLH proposed by Henter JI. (1), or who presented haemophagocytic cells (HC) in the bone marrow biopsy (BMB), or who had HPS in the hospital discharge report. Demographic, clinical, analytical, etiological, underlying disorders and prognosis variables were collected. Continuous variables are described with the mean or median according to the degree of normality. Kruskal Wallis, Fisher test and Mann-Whitney U test were used for the bivariate analysis, and also a multivariate logistic regression analysis was performed.

Results: We found 30 patients with secondary HPS, 22 of which corresponded to the AID [Systemic Lupus Erythematosus (n=5), Adult Still's Disease (n=3), Rheumatoid arthritis (n=1) and IgG4 Sclerosing Disease (n=1)] and HOD [Non-Hodgkin's Lymphoma (n=3), Myelodysplastic syndrome (n=3), Acute leukemia (n=3), Extranodal NK cell lymphoma (n=1), Multiple Myeloma (n=1) and probable lymphoproliferative process (n=1)]. The coincidence of an infectious disease with HPS was observed in 8 of the 22 cases [AID: 5 cases (2 *Cytomegalovirus*, 2 viral respiratory infections and 1 bacterial infection) and HOD: 3 cases (2 *Epstein Barr virus* and 1 bacterial infection)]. In two patients with HPS secondary to HOD (acute leukemia), allogeneic transplantation was associated as a possible trigger. In a patient with myelodysplastic syndrome, HPS was associated with the development of graft versus host disease. The age at diagnosis was lower in the AID [40 (26.5 - 56.3); p 0.001]. The HOD had more severe cytopenias [platelets 4500 (650 - 15,750; p 0.009), leukocytes 2050 (20 - 728; p 0.0001) and neutrophils 0 (0 - 280; p 0.002)]. Overall mortality (n=30 patients) was 43.3% (HOD: 66.7%; p 0.029) (table 1). In the final multivariate model according to AID and HOD, the following independent associations were observed: age (p 0.002), platelets (p 0.031), GOT (p 0.012), GPT (p 0.015), total proteins (p 0.007) and mortality (p 0.007).

Conclusion: The HOD presented higher mortality and severe cytopenias. The AID presented a higher elevation of transaminases and better prognosis.

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FRI0482

A SYSTEMATIC REVIEW FOR THE MANAGEMENT OF THE GENETICALLY DEFINED IL-1-MEDIATED AUTOINFLAMMATORY DISEASES, CAPS, TRAPS, MKD AND DIRA

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Background: Ultra-rare genetically defined IL-1 mediated autoinflammatory diseases (AIDs) include mevalonate kinase deficiency (MKD), tumor necrosis factor receptor associated periodic syndrome (TRAPS), cryopyrinopathies (CAPS) and deficiency of the IL-1 receptor antagonist (DIRA). These disorders start perinatally, the clinical disease manifestations include systemic inflammation; and late diagnosis and inappropriate treatment cause irreversible organ damage. The varying skills of treating rheumatologists and paediatricians illustrate the need for management guidance, however criteria for validated methodology is geared towards common diseases with more heterogeneous pathogenesis.

Objectives: The focus of this systematic review includes the evaluation of the existing literature and the evaluation of existing EULAR methodology for use in the ultra-rare diseases with defined pathomechanisms, CAPS, TRAPS, MKD and DIRA

Methods: EULAR standardized operating procedures were followed during the review, including a meeting of experts to discuss key words, inclusion/exclusion criteria and PICO questions. Three fellows established the protocol of the review under the supervision of the EULAR methodologist and PubMed, Embase, and Cochrane databases were searched up to September 30, 2019.

Results: We found 1582 articles for CAPS, 1109 articles for TRAPS,1741 articles for MKD and 557 articles for DIRA. Duplications, animal models and basic science studies, conference papers, systematic reviews/meta-analysis and articles not in English language is excluded. If we excluded case reports (n<4), then 72 articles for CAPS, 40 articles for TRAPS,44 articles for MKD and 1 article for DIRA should be included for full text evaluation and data extraction (Figure 1). However among the case reports, patients excluded achieved complete remission, assessed by clinical criteria and biomarkers. Of the studies included only few randomized studies for CAPS, TRAPS, MKD, and DIRA and would achieve higher level of evidence (Figure 1).

Conclusion: CAPS, TRAPS, MKD and DIRA are monogenic diseases with defined pathways and outcomes that include inflammatory remission based on clinical and biomarker data. Current methodological evaluations for genetically complex diseases undervalue the published evidence in case reports that report on remission and IL-1 biomarkers. We suggest that case studies that include hard outcomes including **inflammatory remission, and open label withdrawal studies that are both backed by biomarkers could be allowed to be included and be considered for a stronger evidence level.**

Table 1. Characteristics and comparative analysis of HPS secondary to AID and HOD

	Total		AID		HOD		
n	30		10		12		*p<0,05
Age (*x* ± s)	55,5	±18,3	40	26,5-56,3	68	57,5-73,8	0,001
Gender, male	14	46,7%	3	30%	9	75%	0,084
Spenomegaly	16	53,3%	5	50%	8	66,7%	0,666
Hepatomegaly	10	33,3%	4	40%	4	33,3%	1,000
Hb (g/dL)	7,1	6,4-7,9	7,2	6,6-8,4	6,5	5,9-7,3	0,05
Pt (x10^9/L)	13 500	5 000-52 500	31 650	11 000-100 250	4 500	650-15 750	0,004
Leu (x10^9/L)	1 250	238-3 153	1 985	1 350-3 382	185	20 – 728	0,000
Neu (x10^9/L)	615	0-1 550	948	633-1 808	0	0-280	0,001
Fb (mg/dL) (n=24)	171	111-358	212	90-450	167	114-354	1,00
Fer (ng/mL) (n=28)	15 330	5 434-38 284	14 263	4 254-14 263	16 796	8 287 - 56 969	0,314
Tg (mmol/L)	341	226-438	411,5	234-572	321	233,8-403,8	0,314
GOT (U/L)	139	78-406	457	289-1 140	106	71-193	0,003
GPT (U/L)	162	46-388	432	174-599	109	54-263	0,017
T.P. (n=29)	4,8	±,1,04	5,0	4,5-5,8	4,3	3,9-4,5	0,003
Hospital stay	35,5	20,0-60,8	30,5	9,5-53,3	61,5	29,3-93,3	0,036
Hospital stay pre-dx	16,5	8,5-29,8	10	5,0-16,5	26	10-39	0,038
Mortality	13	43,3%	1	10%	8	66,7%	0,011

Hb: hemoglobin, Pt: platelets, Leu; leukocytes, Neu, neutrophils, Fb: fibrinogen, Fer: ferritin, Tg: triglycerides, GOT: aspartate aminotransferase, GPT: alanine aminotransferase, T.P.: total proteins, pre-dx: prior to the diagnosis of HPS according to BMO. *Analysis between AID and HOD.

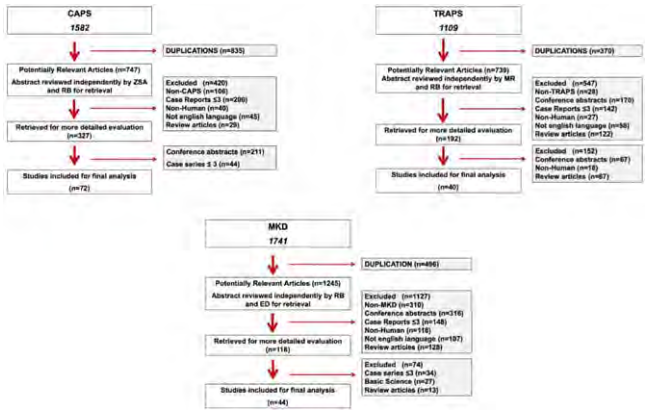


Figure 1. Flow-charts of systematic review for CAPS, TRAPS and MKD.

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FRI0483 SUBCLINICAL INFLAMMATION AND RELATED PARAMETERS IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER

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Background: Familial Mediterranean Fever (FMF), which is more common in groups in the Mediterranean basin, is a monogenic autoinflammatory disease characterized by recurrent attacks of febrile peritonitis, pleuritis and arthritis.

Objectives: In this study, we aimed to investigate the clinical, demographic and genotypic features that may be associated with subclinical inflammation in FMF and to determine the related parameters with subclinical inflammation.

Methods: FMF patients according to the Tel-Hashomer criteria were included into the study. The demographic characteristics of the patients, duration of the disease, concomitant diseases, MEFV genotype mutation, colchicine use and resistance were collected. Acute-phase reactants such as white blood cell count, erythrocyte sedimentation rate, and C-reactive protein levels during the attacks and attack-free periods were noted. Subclinical inflammation was defined as the continuation of the acute phase response (CRP) between episodes. We divided study population into two groups as; patients with or without subclinical inflammation (Group 1 and Group 2, respectively) and these group were compared with the parameters described above. Patients with infectious disease (viral or bacterial) in the past two months were excluded from the study

Results: Eigthy patients (72.5% female) with mean age 37.1 SD 11.2 years were recruited into the study. Twenty-three (28.7%) patients were determined with subclinical inflammation. Group 1 had significantly higher rate of concomitant rheumatic disease(i.e spondyloarthropathy), erythrocyte sedimentation rate and MEFV homozygous mutation compared with Group 2 ($p<0.05$, for each). Disease duration, months PRASS score, FMF quality of life, age at onset of symptoms, family history of FMF, response to colchicine, attack time, attack in the last 6, delay in diagnosis parameters were not significantly different between groups ($p> 0.05$).

Conclusion: FMF patients whose elevated erythrocyte sedimentation rate and MEFV homozygous mutation should be closely monitored for subclinical inflammation even during attack-free periods. Concomitant disease should be detected in FMF patients with subclinical inflammation.

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[2] Bayram MT, Çankaya T, Bora E, Kavukçu S, Ülgenalp A, Soylu A, Türkmen M. Risk factors for subclinical inflammation in children with Familial Mediterranean fever. Rheumatol Int. 2015 Aug;35(8):1393-8.

Table 1: Demographic and clinical features of the patients with familial Mediterranean fever

	Without Subclinical inflamation n= (57)	With Subclinical inflamation n= (23)	P value
Age (years; mean SD)	37,78 SD 13,22	36,82 SD 10,49	0.987
Female, gender, n (%)	45(%78)	13(%56)	0.055
Disease duration (month; mean SD)	255,3 SD 195,1	180,2 SD 121,1	0.191
PRASS score (mean SD)	6,08 SD 2,15	5,36 SD 1,59	0.147
BMI, kg/m^2	26,12 SD 4,8	32,13 SD 28,48	0.629
Current smoking status (%)	17(%29)	3(%13)	0.067
Age at onset of symptoms (month; mean SD)	15,69 SD 9,41	17,28 SD 10,34	0.54
Family history of FMF(%)	37(%64)	18(%78)	0.295
Response to colchicine(%)	6(%10)	4(%17)	0.462
Attack time (day; mean SD)	1,9 SD 1,1	2,26 SD 1,4	0,523
Attack in the last 6 months (mean SD)	2,79 SD 3,1	4,56 SD 5,5	0,184
FMF quality of life (mean SD)	31,5 SD 13,6	25.7 SD 16,4	0,130
Delay in diagnosis(month; mean SD)	12,29 SD 10,9	14,3 SD 14,9	0,840

Disclosure of Interests: None declared

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FRI0484 SAFETY PROFILE, CLINICAL AND RADIOLOGICAL EFFICACY OF ANAKINRA, TARGETED AND COMBINED TREATMENT IN ERDHEIM-CHESTER DISEASE

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Background: Erdheim-Chester disease (ECD) is a rare non-Langerhans histiocytosis. Combined treatment with anakinra (ANK) and targeted MAPK-inhibiting therapies (vemurafenib – VMF - or cobimetinib - CBM) has been recently used to treat severe cases of ECD.

Objectives: To evaluate the safety and the clinical and radiological efficacy of ANK, targeted and combined treatments in ECD patients in a real-world setting.

Table 1. Disease characteristics and therapy-related adverse reactions of Erdheim-Chester patients treated with vemurafenib, cobimetinib and/or anakinra.

	Vemurafenib (n=19)	Cobimetinib (n=10)	Anakinra (n=12)
Clinical Manifestations			
Cardiovascular	79%	70%	75%
Retroperitoneal	84%	60%	42%
Pleuropulmonary	63%	80%	42%
Neurological and/or orbital	90%	90%	92%
Adverse reactions	74%	60%	25%
Renal	26%	10%	0%
Cutaneous	26%	30%	17%
Systemic Inflammation	11%	10%	0%
Cardiovascular	11%	10%	0%
Gastrointestinal	0%	30%	0%
Haematological	0%	10%	0%
Herpes Zoster	0%	0%	8%

Table 2. Efficacy and discontinuation rates of monotherapy and combined treatment in Erdheim-Chester disease. * Referred to imaging re-staging.

	Therapy courses	Clinical efficacy	Improving disease *	Stable disease *	Progressive disease *	Discontinuation due to toxicity	Discontinuation due to inefficacy
Vemurafenib	19	93%	73%	27%	0%	37%	0%
Cobimetinib	6	80%	100%	0%	0%	50%	0%
Anakinra	10	86%	0%	25%	75%	20%	40%
Vemurafenib + Anakinra	3	100%	100%	0%	0%	0%	0%
Cobimetinib + Anakinra	4	100%	100%	0%	0%	25%	0%

Methods: ECD patients followed at our Center who received at least one targeted therapy and/or ANK were selected. Data about disease characteristics, adverse reactions, clinical and radiological efficacy (by means of CT, CT/PET, MRI when appropriate and repeated 6 months apart) were collected.
Results: Among the 48 ECD patients followed up at our Center, 27 were treated with at least one drug between VMF and CBM, accounting for a total of 22 and 10 therapy courses respectively. 12 patients were treated with ANK as monotherapy or combination treatment (a total of 17 therapy courses). Disease characteristics and adverse reactions to the treatments are shown in Table 1. All 3 drug proved to have a high clinical efficacy (Table 2). No patient treated with VMF or CBM showed radiological progression neither discontinued treatment due to inefficacy. Conversely, 75% of patients receiving ANK monotherapy showed progression at imaging re-staging and inefficacy was the main discontinuation cause. ANK showed the lowest incidence of adverse reactions. Drug toxicity was instead the only reason for discontinuation of targeted monotherapies. The combined approach had a clinical efficacy in all cases and it was always associated with imaging improvement. One patient treated with ANK and CBM discontinued the therapy due to drug-related toxicity. No patient receiving both VMF and ANK experienced drug-related toxicities; in these patients ANK led to a reduction in mean acute phase reactants levels and concomitant prednisone dose (Figure 1).

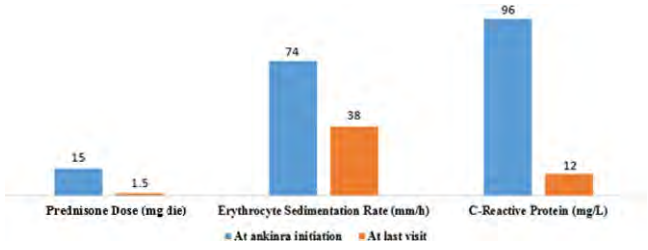


Figure 1. Mean acute phase reactant levels and concomitant prednisone dose in Erdheim-Chester disease patients treated with vemurafenib before and after the initiation of anakinra.

Conclusion: Combined treatment had a higher clinical and radiological efficacy than ANK monotherapy and led to a reduction in targeted therapies-related toxicities, acute phase reactant levels and concomitant prednisone dose.
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[1] Efficacy and improved tolerability of combination therapy with interleukin-1 blockade and MAPK pathway inhibitors for the treatment of Erdheim-Chester disease; Campochiaro et al; Ann Rheum Dis. 2019; 10.1136/annrheumdis-2019-216610
Disclosure of Interests: Nicola Farina: None declared, Corrado Campochiaro Speakers bureau: Novartis, Pfizer, Roche, GSK, SOBI, Alessandro Tomelleri: None declared, Giacomo De Luca Speakers bureau: SOBI, Novartis, Celgene, Pfizer, MSD, Giulio Cavalli Speakers bureau: SOBI, Novartis, Pfizer, Lorenzo Dagna Grant/research support from: Abbvie, BMS, Celgene, Janssen, MSD, Mundipharma Pharmaceuticals, Novartis, Pfizer, Roche, SG, SOBI, Consultant of: Abbvie, Amgen, Biogen, BMS, Celltrion, Novartis, Pfizer, Roche, SG, and SOBI
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FRI0485

RISK OF PROGRESSION OF IDIOPATHIC PULMONARY FIBROSIS TO CONNECTIVE TISSUE DISEASE

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Background: Connective tissue disease (CTD) may be observed during the course of idiopathic pulmonary fibrosis (IPF). However, clinical factors associated with the development of CTD in patients with IPF have not yet been identified. These factors might be valuable clues for determining the pathogenesis of pulmonary fibrosis in patients with CTD. We hypothesize that some IPF patients have a clinically significant association with autoimmunity, and that autoantibodies are important biomarkers for identifying these patients.
Objectives: Based on this hypothesis, we investigated whether the serology criteria (anti-neutrophil cytoplasmic antibody (ANCA) or autoantibodies that met the serology criteria for interstitial pneumonitis with autoimmune features (IPAF)) were associated with the development of CTD during the clinical course of IPF in the patients from our previous study(1), with a particular focus on which antibodies have a significant association with the development of CTD.
Methods: We retrospectively reviewed the records of 527 patients with a first diagnosis of IPF between January 2007 and March 2014, and investigated the length of time from first visit to the clinic for IPF diagnosis (baseline) to CTD diagnosis by an expert rheumatologist in patients with IPF. Multivariable Cox proportional-hazards models with backward elimination were used to investigate the risk factors for the development of CTD.
Results: CTD developed in 15 patients at a median of 2.1 years (range 1.2 to 4.8) after IPF diagnosis. All these patients had ANCA or autoantibodies that met the serology criteria for IPAF. A significant number of IPF patients with high titers of RF, ACPA or MPO-ANCA tested at first visit to the clinic progressed to CTD(Figure 1). Survival duration for IPF patients with progression to CTD was 5.3 [3.8; 6.7] years, which was significantly longer than for the IPF patients without progression to CTD (2.9 [1.7; 4.8], p = 0.001). Independent risk factors for development of CTD in IPF patients included female gender (adjusted hazard ratio (HR) 5.319, p = 0.0082), titer of rheumatoid factor (RF) (adjusted HR 1.006, p = 0.022), titer of anti-citrullinated protein antibody (ACPA) (adjusted HR 1.009, p = 0.0011), and titer of myeloperoxidase (MPO) ANCA (adjusted HR 1.02, p < 0.0001).

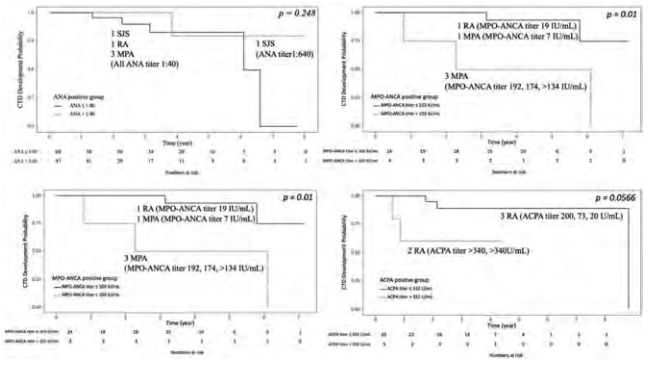


Figure 1. Connective tissue disease development in each autoantibody positive IPF patient. ACPA = anti–citrullinated protein antibody; ANA = antinuclear antibody; CTD = connective tissue disease; MPA = microscopic polyangiitis; PAN = polyarteritis nodosa; RA = rheumatoid arthritis; RF = rheumatoid factor; UCTD = Undifferentiated connective tissue disease; SjS = Sjögren's syndrome.

Conclusion: We observed development of CTD in IPF patients with ANCA or autoantibodies that met the IPAF serology criteria. Among these autoantibodies, RF, ACPA, and MPO-ANCA were significantly associated with the development of CTD in IPF patients. Progression to CTD is uncommon in IPF patients, but a significant number of IPF patients with high titers of RF, ACPA or MPO-ANCA progressed to connective tissue disease. IPF with high titers of RF, ACPA or MPO-ANCA might be the initial clinical manifestation of connective tissue disease. Further studies are needed to investigate the role of RF, ACPA, and MPO-ANCA in development of pulmonary fibrosis.

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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.1376

FRI0486 LONG-TERM EFFICACY AND SAFETY OF CANAKINUMAB IN PATIENTS WITH AUTOINFLAMMATORY PERIODIC FEVER SYNDROMES – FIRST INTERIM ANALYSIS OF THE FMF/TRAPS/HIDS SUBGROUPS FROM THE RELIANCE REGISTRY

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Background: Autoinflammatory periodic fever syndromes characterized by excessive interleukin(IL)-1b release and severe systemic and organ inflammation have been successfully treated with the anti-IL-1 inhibitor canakinumab (CAN). In clinical trial situations and real life, rapid remission of symptoms and normalization of laboratory parameters were observed in most patients.[1-3]
Objectives: The present study explores long-term effectiveness and safety of CAN under routine clinical practice conditions in pediatric and adult patients with CAPS (cryopyrin-associated periodic syndromes), FMF (familial Mediterranean fever), TRAPS (tumor necrosis factor receptor-associated periodic syndrome) and HIDS/MKD (hyperimmunoglobulinemia D syndrome/mevalonate kinase deficiency).
Methods: RELIANCE is a prospective, non-interventional, multi-center, observational study based in Germany with a 3-year follow-up period. Pediatric (age ≥2 years) and adult patients with clinically confirmed diagnoses of CAPS, FMF, TRAPS and HIDS/MKD that routinely receive CAN are enrolled in order to evaluate effectiveness and safety of CAN in clinical routine.
Results: This first interim analysis of patient subgroups diagnosed with FMF, HIDS and TRAPS includes baseline data of 41 patients (10 TRAPS, 2 HIDS, 29 FMF), including preliminary 6-month data of a FMF-subset (N=16).
Evaluation of disease activity and fatigue by patients' assessment, days absent from school/work, inflammatory markers and physician global assessment (PGA) was performed at baseline and will be further assessed at 6-monthly intervals within the 3-year observation period. Preliminary results of a first subset of 16 patients diagnosed with FMF are available and indicate stable remission and disease control upon long-term CAN treatment: within the first study interval, no major changes were observed regarding the analyzed parameters (table 1).
Conclusion: Baseline characteristics of all subgroups and first interim data of FMF patients are available from the RELIANCE study, the longest running real-life CAN registry. Further interval data will be analyzed to assess efficacy and safety of long-term CAN-treatment in patients with autoinflammatory periodic fever syndromes.
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FRI0487 APREMILAST IN MONOTHERAPY OR COMBINED IN NON-ULCER MANIFESTATIONS OF BEHÇET'S DISEASE. NATIONAL MULTICENTER STUDY OF 34 REFRACTORY CASES OF CLINICAL PRACTICE

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Background: Apremilast (APR) has demonstrated efficacy in orogenital ulcers of Behçet´s disease (BD). Response of other clinical manifestations remains unknown.
Objectives: To assess the efficacy and safety of APR in monotherapy or combined with disease-modifying anti-rheumatic drugs (DMARDs) in non-aphthous ulcers of BD.
Methods: National multicenter open-label study on 34 BD patients treated with APR at maintained standard dose of 30 mg twice daily.
Results: From a cohort of 51 patients with APR by refractory orogenital ulcers of BD, we selected 34 (24 women/10 men, mean age 43.8±14.3 years), cases with another clinical manifestation/s.
Excluding CTs, colchicine or NSAIDs, APR was given in monotherapy (n=21) or combined with conventional and/or biologic DMARDs in 13 cases (5 methotrexate, 3 azathioprine, 3 hydroxychloroquine, 1 sulfasalazine, 1 dapsone, 2 tocilizumab, 1 IFX). Other active manifestations present at APR onset were: arthralgia/arthritis (16, true arthritis in 5), folliculitis/pseudofolliculitis (14), erythema nodosum (3), furunculosis (2), paradoxical psoriasis by TNFi (2), intestinal ileitis (2), deep venous thrombosis (2), leg ulcers (1),

Table 1. Baseline characteristics of the TRAPS/HIDS/FMF-subgroups and preliminary 6-month data of FMF subset.

	TRAPS	HIDS	FMF		
	Baseline	Baseline	Baseline all FMF patients	Baseline FMF subset	6 months FMF subset
Number of patients, N	10	2	29	16	16
Mean age, years (SD)	22 (4; 43)	11 (5; 18)	26 (5; 56)	16 (5; 47)	16 (5; 47)
Female (%), N=9 (1 missing)	5 (56)	1 (50)	15 (52)	7 (44)	7 (44)
Mean duration of prior canakinumab treatment, years (min; max)	1 (0; 2)	3 (2; 4)	n. a.	2.2 (0; 6)	2.2 (0; 6)
Patient's assessment of disease activity 0-10, mean (min; max)	2.1 (0; 5)	0 (0; 0)	3 (0; 10)	2.8 (0; 8)	2.2 (0; 7)
Patient's assessment of fatigue 0-10	3.4 (0; 8)	0 (0; 0)	4.4 (0; 9)	4.6 (0; 9)	3.9 (0; 8)
Number (%) of patients with days absent from school/work due to study indication during last 6 months	4 (44)	2 (100)	5 (17)	2 (13)	5 (31)
Inflammatory markers, CRP/SAA, mean (mg/dL)	2.0 7.9	0.1 0.6	0.9 5.3	0.5 2.4	0.6 2.4
PGA of disease activity: no/mild to moderate/severe; N (%)*	1 (11) 6 (67) 0 (0)	2 (100) 0 (0) 0 (0)	10 (35) 8 (28) 2 (7)	5 (31) 7 (44) 1 (6)	6 (38) 7 (44) 0 (0)
SAE, N (%)	0 (0)	0 (0)	2 (6.9)	n. a.	2 (12.5)

TABLE.

Non-aphthous manifestations at APR onset (n)	1-2 Weeks		6 Months		12 Months		24 Months	
	C	M	C	M	C	M	C	M
Folliculitis/ pseudofolliculitis (14)	**n=5** CR (2) PR (1) NC (2)	**n=9** CR (4) PR (2) NC (3)	**n=4** CR (4)	**n=4** CR (2) NC (1) ND (1)	**n=1** CR (1)	**n=2** ND (2)	**n=0**	**n=0**
Arthralgias (11)	**n=5** NC (5)	**n=6** CR (1) NC (5)	**n=4** CR (3) NC (1)	**n=3** PR (2) ND (1)	**n=4** CR (2) PR (1) ND (1)	**n=3** CR (1) PR (1) ND (1)	**n=0**	**n=0**
Arthritis (5)	**n=3** PR (1) NC (2)	**n=2** NC (2)	**n=3** CR (3)	**n=1** PR (1)	**n=0**	**n=1** PR (1)	**n=0**	**n=0**
Erythema nodosum (3)	**n=0**	**n=3** CR (2) PR (1)	**n=0**	**n=1** CR (1)	**n=0**	**n=0**	**n=0**	**n=0**
Psoriasis/ erythematosus-scaly skin lesions (3)	**n=0**	**n=3** NC (2) ND (1)	**n=0**	**n=2** PR (2)	**n=0**	**n=2** PR (2)	**n=0**	**n=1** PR (1)
Ileitis (2)	**n=0**	**n=2** CR (1) PR (1)	**n=0**	**n=2** CR (2)	**n=0**	**n=1** CR (1)	**n=0**	**n=0**
Deep venous thrombosis (2)	**n=1** CR (1)	**n=1** PR (1)	**n=1** CR (1)	**n=1** PR (1)	**n=1** CR (1)	**n=0**	**n=0**	**n=0**
Furunculosis (2)	**n=1** CR (1)	**n=1** CR (1)	**n=1** CR (1)	**n=0**	**n=0**	**n=0**	**n=0**	**n=0**
Leg ulcers (1)	**n=1** PR (1)	**n=0**	**n=1** CR (1)	**n=0**	**n=0**	**n=0**	**n=0**	**n=0**
Unilateral anterior uveitis (1)	**n=1** CR (1)	**n=0**	**n=0**	**n=0**	**n=0**	**n=0**	**n=0**	**n=0**
Neurobehçet (1)	**n=0**	**n=1** NC (1)	**n=0**	**n=1** NC (1)	**n=0**	**n=0**	**n=0**	**n=0**
Fever (1)	**n=0**	**n=1** NC (1)	**n=0**	**n=0**	**n=0**	**n=0**	**n=0**	**n=0**

CR= complete remission; ND= non-data; NC= no changes; PR= partial remission

erythematosus and scaly skin lesions (1), fever (1), unilateral anterior uveitis (1) and neurobehçet (1).

After a median follow-up of 6 [3-12] months, folliculitis and ileitis improved, neurobehçet remained stable and musculoskeletal manifestations evolved in a variable way. **(TABLE)**

Conclusion: In addition of orogenital ulcers, APR in monotherapy or combined, seems to be useful in skin manifestations of BD

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FRI0488

CLINICAL AND LABORATORY FEATURES OF PATIENTS WITH REMITTING SERONEGATIVE SYMMETRICAL SYNOVITIS WITH PITTING EDEMA COMPARED TO PATIENTS WITH SERONEGATIVE RHEUMATOID ARTHRITIS

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Background: In the case of seronegative arthritis, it was difficult to make a differential diagnosis between remitting seronegative symmetrical synovitis with pitting edema syndrome (RS3PE) and seronegative rheumatoid arthritis (seronegative RA) because the distribution of affected joints was similar and the patients with RS3PE or seronegative RA may have edema.

Objectives: To compare the clinical characteristics of RS3PE and seronegative RA

Methods: We retrospectively examine consecutive patients diagnosed with RS3PE or seronegative RA in our hospital from 2007 to 2019. Patients in whom both ACPA and RF were negative were included. The patients with RS3PE met the criteria of McCarty et al.: (1) pitting edema of the dorsum of both hands and both feet, (2) sudden onset of polyarthritis, (3) seronegative for ACPA and RF. (4)no radiologically evident erosions developed. The patients with seronegative RA met the EULAR/ACR 2010 criteria. The patients who were diagnosed with RS3PE at first and then diagnosed with seronegative RA afterward were included in seronegative RA group. The first analysis was performed on the affected joints, CRP, ESR, Hb, LDH, edema, the history of malignancy 2 years before and after the diagnosis, treatment, and the history of infection requiring hospitalization after the start of treatment. The affected joints were shoulders, elbows, wrists, finger joints (the MCP, and PIP joints), hips, knees, ankles, and toe joints (the MTP and PIP joints). The secondary analysis was performed on the above evaluations with a propensity score (PS) matching for age.

Results: In the first analysis, 20 patients with RS3PE and 122 patients with seronegative RA were enrolled. The mean ages (RS3PE, seronegative RA) were 81.1, 67.4 years old. Females were 60.0%, 63.1%. The mean observation period was 25.4, 63.6 months. The proportion of affected joints were shoulders

(25.0%, 42.6%), elbows (10.0%, 29.5%: p=0.06), wrists (85.0%, 73.8%), finger joints (80.0%, 95.1%: p=0.01), hips (0%, 9.8%), knees (40.0%, 37.7%), ankles (65.0%, 39.3%: p=0.03) and toe joints (40.0%, 32.8%). Edema at diganosis was observed in 100%, 17.21% (p <0.0001). The mean levels of the following blood tests at diagnosis were noted: CRP, 9.0 and 4.8 mg/dL (p=0.02); ESR, 87.6 and 60.7 mm/1h (p=0.003); Hb, 10.4 and 11.8 mg/dl (p=0.001); LDH, 198.3 and 177.9 U/L (p = 0.12); MMP-3, 742.5 and 633.8 ng/mL (p = 0.14). The proportion of patients with high LDH levels (>222 U/L) was 13.6% and 9.0% (p=0.0269). The proportion of patients having the history of malignancy was 20.0%, 8.2% (p=0.10). The patient treated with prednisolone as the initial treatment was 100% and 41.0%; the mean dose was 14.3 and 9.9 mg/d. After the start of treatment, the proportion of infection requiring hospitalization was 20.0 and 3.28% (p=0.002).

In the secondary analysis with PS, 17 patients with RS3PE and 17 patients with seronegative RA were enrolled. The mean ages were 80.4, 78.9 years old. Females were 52.9, 76.4%. The affected joints with difference were elbows (11.8, 35.3%: p=0.10), wrists (82.4, 100%: p=0.06), and finger joints (82.4, 100%: p=0.06). The mean levels of Hb at diagnosis was 10.4, 11.4 mg/dL (p=0.01). The proportion of patients having the history of malignancy was 23.5% and 0% (p=0.03). After the start of treatment, the proportion of infection requiring hospitalization was 23.5% and 0% (p=0.03).

Conclusion: When the ankles are affected and edema is observed, RS3PE is more likely than seronegative RA. RS3PE had higher levels of CRP, ESR, and LDH. The proportion of anemia was higher in RS3PE. The proportions of infection requiring hospitalization and the history of malignancy were higher in RS3PE.

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FRI0489 ARE WE MISSING CASES OF HAEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS (HLH)? A FIVE YEAR RETROSPECTIVE SERVICE EVALUATION OF RECOGNITION AND RESPONSE TO FERRITIN >10,000MG/L IN THE ADULT POPULATION OF A LARGE UK HOSPITAL TRUST

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Background: Haemophagocytic lymphohistiocytosis (HLH) is a hyperinflammatory syndrome presenting with fever, cytopaenias and multi organ failure, and carries a high mortality rate[1]. Primary HLH is genetic and presents in infancy. Secondary HLH (sHLH) presents in children or adults, and macrophage activation syndrome (MAS)[1] is sHLH in the context of rheumatological disease. Risk factors include immunosuppression, infection, malignancy and autoimmunity. The HScore can be used to calculate probability of HLH[2]. Gold standard diagnosis is bone marrow aspirate (BMA)[1]. In paediatrics, ferritin >10,000µg/L is highly specific for HLH[3], but less so in adults[4]. There is no validated treatment pathway for sHLH. Current recommendations are methylprednisolone and IVIG first line, and anakinra or etoposide if these are ineffective[1].

Objectives: This service evaluation assessed patients with a ferritin >10,000µg/L in Portsmouth Hospitals NHS Trust (PHT) against diagnostic criteria and recommended treatment for sHLH, with the aim of sharing results to improve recognition and management.

Methods: Serum ferritin results >10,000µg/L from 1st March 2014 to 31st March 2019 were requested from PHT central laboratories. Paediatric and duplicate results were excluded. Electronic patient records were used to collect the parameters of the HScore[2]. HScore and probability of sHLH was calculated using a validated calculator[2,5]. Patient notes were requested for patients with missing data or probability of HLH >1%.

Results: Fifty four results were obtained from central laboratories, of which thirty eight were eligible for analysis. Mean age was 63.6 (range 19 to 96), 34.2% male. 47.4% died within one year of ferritin >10,000µg/L. One patient was diagnosed with Adult Onset Still's Disease. Of the remainder, 73% had risk factors for sHLH.

Accurate assessment of sHLH incidence was not possible due to incomplete data, particularly triglycerides, fibrinogen, and BMA. AST is not routinely collected in PHT, therefore ALT was used for audit. Within these limits, fifteen patients had a probability >1% of sHLH, and five had a probability >50%. Only one patient had confirmed haemophagocytosis on BMA, and was treated for sHLH with oral steroids in addition to usual care.

Conclusion: Although only one patient had confirmed sHLH on BMA, five patients had a >50% probability of sHLH despite missing parameters for the HScore. It can be seen that potential cases of sHLH might easily be missed. Using a lower level ferritin cut-off for inclusion may have led to an even higher number of potential sHLH cases in our adult patient population. We suggest that sHLH should be considered as a plausible diagnosis in patients with raised ferritin, cytopaenias or organ failure. Local education work is planned to raise awareness of these learning points.

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FRI0490 INVESTIGATING THE ROLE OF IL-1THETA IN PATHOGENESIS OF BEHÇET'S DISEASE

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Background: Behçet's disease (BD) is a chronic inflammatory disease that may involve many systems including mucocutaneous, vascular, articular, gastrointestinal, neurological and cardiopulmonary systems. Although the pathogenic mechanisms of BD remain unclear, increased release of proinflammatory cytokines and chemokines may play a role in inflammatory stages of the disease.

Objectives: IL-1 theta is a member of IL-1 family. A variety of tissue cells, such as endothelial cells, keratinocytes, dendritic cells macrophages, B cells can produce IL-1 theta under the stimulation of pro-inflammatory factors. Several studies have shown that IL-1 theta can promote the production of proinflammatory cytokines. In this study, we investigated the relationship between serum IL- 1 theta levels and disease activity and clinical findings of BD.

Methods: 59 patients with BD (48 female, 11 male) and 20 healthy controls (17 female, 3 male; mean age 41.0 ± 9.3 years) were enrolled in this study. Thirty five patients were in active stage (mean age; 40.3 ± 11.0 years, median disease duration 7 years) and 24 patients were in inactive stage (mean age; 42.9 ± 13.2 years, median disease duration; 8 years). Serum IL-1 theta levels were evaluated by ELISA.

Results: The mean serum IL-1 theta levels were 8.65 ± 4.41 pg/ml in patients with BD and 3.9 ± 2.54 pg/ml in healthy controls. The mean serum IL-1 theta levels were 10.34 ± 5.52 pg/ml in active patients with BD and 6.92 ± 2.43 pg/ml in inactive patients with BD. Serum IL-1 theta levels were significantly high in active Behçet's patients compared with in inactive Behçet's patients (p<0.01) and the controls (P<0.001).

Serum IL-1 theta levels were significantly higher in the presence of neurological, vascular and mucocutaneous involvement in subgroup analysis according to the clinical findings of Behçet's patients. IL-1 theta levels were negatively correlation with Platelet count and ESR (r=0.332 p=0.050, r=0.382 p=0.024 respectively). There was no statistically significant difference between IL-1 theta levels disease duration, and CRP.

Conclusion: In this study, we demonstrated that serum IL-1 theta levels were significantly elevated in patients with BD. The high levels of serum IL-1 theta, in active and inactive patients with BD suggest that IL-1 theta may play a significant role of in the pathogenesis of BD.

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FRI0491 IS THERE A RELATIONSHIP BETWEEN VOGT-KOYANAGI-HARADA AND INFLAMMATORY RHEUMATOLOGICAL DISEASES

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Background: Vogt-Koyanagi-Harada Disease (VKHD) is a systemic autoimmune disease characterized by bilateral granulomatous panuveitis associated with systemic symptoms, including neurological, dermatological and audiovestibular systems. Due to its systemic nature, it may accompany with other autoimmune conditions. However, there is a considerably limited number of reports on the association of VKHD and rheumatologic diseases.

Objectives: To investigate the relationship between VKHD and inflammatory rheumatological diseases.

Methods: Patients who had bilateral granulomatous uveitis and fulfilled the 2001 revised diagnostic criteria for VKHD were included in our study. All patients were systematically reviewed in terms of the presence of any rheumatological manifestations including connective tissue diseases, spondyloarthritis (SpA), vasculitis, Behcet's disease and sarcoidosis.

Results: Demographic findings: There were fifteen patients in the study (86,7%,female), the mean age at diagnosis was 31,2 ± 11,1 years.

Comorbidities: Six patients (4 hashimoto thyroiditis, 2 diabetes mellitus) had comorbid diseases.

Rheumatological findings: Mechanical back pain in 4 patients, 1 patient had morning stiffness without any other SpA related features; 2 patients had inflammatory arthralgias in small joints, 4 patients had sicca symptoms, 1 patient had arthritis in knee joint, 3 patients had oral aphthae and 1 patient had photosensitivity.

Laboratory tests and autoantibodies: The acute phase reactants were within normal ranges. The mean CRP value at the time of diagnosis was 2,7 ± 3,2 mg/L and ESR was 14,4 ± 9,2 mm/h. Two (15,3%) out of 13 patients had high serum ACE levels. RF, anti-CCP and anti-dsDNA were negative in all patients. ANA was positive (>1/160 titers) in 4 patients (28,6%) and 3 patients had a titer above 1/320. Anti-ENA profile was positive in 2 patients with anti-SS-B and anti-histone components. MPO-ANCA was positive in one patient.

HLA test: HLA-B27 was negative in all patients. HLA-B51 and B18 were positive in 2 patients.

Radiographic findings: One patient had heel enthesitis on X-ray, 4 patients had bilateral grade 1 and one patient had unilateral grade 2 sacroiliitis. None of them fulfilled the Modified New York criteria for radiographic sacroiliitis. Hand X-rays of all patients were normal. One patient had reticular density on chest X-ray.

Pathergy: The pathergy test was negative in all patients.

Capilleroscopy: Four patients had pathological capilleroscopy findings (3 patient tortuous loops, 1 patient tortuous loops and microhemorrhages).

Conclusion: This study suggests that; 1) inflammatory arthralgias and sicca symptoms were the most common rheumatological findings, 2) the frequency of SpA related features were not increased in VKHD, 3) increased autoantibody frequency, particularly in high titers of ANA could be seen in VKHD possibly reflecting the autoimmune nature of the disease, 4) even though there were signs of rheumatic diseases, none of the patients were grouped into any rheumatologic diagnostic classification.

Demographic findings and rheumatological manifestations in VKHD patients

	VKHD patients (n=15)
Females,n (%)	13 (86,7)
Age,yrs (mean ± std)	34,6 ± 12,6
Age of diagnosis, yrs (mean±std)	31,2 ± 11,1
CRP baseline (mean±std)	2,7 ± 3,2 mg/L
ESR baseline (mean±std)	14,4 ± 9,2 mm/H
High ACE levels,n(%)	2/13 (15,3)
RF positivity,n(%)	0/14 (0)
Anti-CCP positivity,n (%)	0/6 (0)
ANA positivity,n(%)	4/14 (28,6)
ANA pattern,(n)	Homogeneous (2) Nuclear (1) Homogeneous speckled (1)
Anti-dsDNA positivity,n(%)	0/11 (0)
Anti-ENA profile positivity,n(%)	2/14 (14,2)
ANCA positivity,n(%)	1/12 (8,3)
Pelvis X-Ray abnormality,n(%)	5/12 (41,7)
Sacroiliitis (n)	Bilateral grade 1 (4) Unilateral grade 2 (1)
Capilleroscopy abnormality,n(%)	4/9 (44,5)
Pathergy,n (%)	0/12 (0)

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FRI0492 CLINICAL AND LABORATORY DATA AND ALGORITHM OF MANAGEMENT OF ADULT PATIENTS WITH OLIGO-ARTICULAR VARIANTS OF JIA

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Background: The oligo-articular JIA is a disease that begins in childhood and can lead to joint damage and disability in adulthood with significant social losses.

Objectives: The aim of this study was to evaluate the clinical and laboratory status and to develop an algorithm of managment adult patients with oligo articular variant of JIA, depending on the detection of RF or/and A-CCP, ANA, HLA-B27.

Methods: The study included 168 adult patients from different regions of Ukraine who were diagnosed with JIA in childhood between 1984 and 2014 without severe comorbidities. Inclusion criteria were: age 16 to 60 years; duration of the disease > 3 years. Among patients with JIA were identified 64 patients with oligo-articular variant: 44 (26,2%) - with persistant oligo-arthritis, and 20 (11,9%) with extended oligo-arthritis. The disease activity was evaluated by DAS28 and JADAS-10. The questionaries SF-36, HAQ, TAS-20, PHQ-9 were analyzed and remote articular JADI-A and extra-articular JADI-E damages were evaluated. Statistical studies were performed using IBM SPPS Statistics version 25.0.0.0 software, the results were considered to be reliable at 5% critical level (P <0.05). The distribution of quantitative variables was tested by the Shapiro-Wilk test. Quantitative variables with a normal distribution were expressed as mean ± SD, quantitative variables that showed a non-normal distribution were expressed with a median (P25-P75), also performed correlative analysis of the variables

Results: It was found that patients with active JIA in 26.5% have depression according to the PHQ-9, while patients in remission have no signs of depression. Most adult patients with JIA (86.4%) have elevated and high levels of alexithymia. The predictors of JIA remission in adulthood are male sex (OR = 0.453; 95% CI 0.253-3.556); arthritis of more than 3 joints (OR = 0.459; 95% CI 0.347-0.770); wrist arthritis in childhood (OR = 0.082; 95% CI 0.009-0.739) and JADAS-10 in the disease onset (OR = 0.758; 95% CI 0.589-0.896) <6 points, treatment with IB in the history (OR = 0,767; 95% CI 0.054-0.811) and the duration of DMARDS treatment (OR = 0.741; 95% CI 0.636-0.863) > 1.5 years. The negative correlation of JADI-A and the patient's physical well-being PCS (r = -0.27, p <0.05) and physical functioning (r = -0.24, p < 0.05), pain intensity (r = -0.24, p <0.05), general health (r = -0.24, p <0.05), vital activity (r = -0,19, p <0,05), social functioning (r = -0,27, p <0,05), mental health (r = -0,22, p <0,05) according to SF-36. The severity of extra-articular damages JADI-E correlated with PCS (r = -0.22, p <0.05) and physical functioning (r = -0.28, p<0.05), pain intensity (r = -0.20, p <0.05), general health (r = -0.23, p <0.05), and mental health (r = -0.23, p <0.05), but also had a positive correlation with HAM-A (r = 0.25, p <0.05), depression scale (r = 0.28, p <0.05) and PHQ-9 (r = 0.28, p <0.05). Significantly lower level of physical health was established in patients who requires prosthetics (p <0.001) compared to those who did not need prosthetics.

Conclusion: Based on the obtained results, algorithms of management of adult patients with JIA oligoarthritis were developed, depending on the detected

articular and extra-articular damages and the need for prosthetics and the psychological status.

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FRI0493 THE INTERLEUKIN-1B INHIBITOR CANAKINUMAB FOR REFRACTORY STILL'S DISEASE: LONG-TERM EXPERIENCE IN 50 CONSECUTIVE PATIENTS

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Background: Interleukin-1 (IL-1) is a major mediator of the inflammatory cascade in Still's disease and an established therapeutic target.

Objectives: To assess the efficacy and safety of the IL-1b inhibitor canakinumab in adolescent and adult patients with refractory Still's disease.

Methods: We conducted a retrospective longitudinal outcome study of 50 consecutive patients aged 39 years (median, range 14-72), fulfilling the Yamaguchi disease classification criteria, with active disease despite treatment with corticosteroids (CS) (n=11) and/or methotrexate (n=9) and/or biologics (n=30) [tumor necrosis factor inhibitors (n=13), IL-6 blockade (n=7), abatacept (n=2), anakinra (n=24); ≥1 biologics (n=13)]. Canakinumab 150-300 mg was administered sc, starting every 4 (n=48) or 8 weeks (n=2), for a median of 24 months (range 3-84). Concomitant treatment included CS (n=41), methotrexate (n=12) and leflunomide (n=3).

Results: Complete remission was initially achieved in 78% of patients within a median time of 3 months, irrespective of age at disease onset. Partial clinical and laboratory response was evident in 20%. Canakinumab was discontinued in one patient with resistant disease (primary failure) and in 6 out of 10 initial responders, who relapsed during treatment (secondary failure). Of 39 patients in complete remission, increase in drug administration interval and/or drug dose reduction was attempted in 7, of which only 1 relapsed, whereas drug discontinuation was attempted in 19 patients for a median time of 8 months (range 3-68), of which 8 relapsed. Overall, in half of all disease flares, canakinumab re-introduction or intensification was successful. Canakinumab had a significant CS sparing effect permitting weaning in 21 of 41 cases. Infections (20%, severe 4%) and leucopenia (6%) led to treatment cessation in one patient.

Conclusion: In this largest so far real-life patient cohort with refractory Still's disease, high rates of sustained remission were induced by canakinumab both in adolescent and adult patients.

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FRI0494 RHEUMATIC IMMUNE RELATED ADVERSE EVENTS OF CHECKPOINT INHIBITORS: A RETROSPECTIVE REVIEW OF 70 PATIENTS

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Background: Immune Checkpoint inhibitors (ICI) have revolutionized cancer therapy by achieving remarkable survival benefits however, at the cost of a myriad of immune-related adverse events (irAEs)[1]. Rheumatic irAE can develop in 5-10% of patients although the true incidence is unknown given the lack of prospective studies [2]. Symptoms are heterogenous and probably underreported with few data available about their management and outcome [3].

Objectives: To describe the clinical, biological, and radiological features of the largest cohort of rheumatic irAEs from ICI along with their therapeutic management, outcome and follow-up in real-world practice.

Methods: A referral process for emergent rheumatic irAEs was initiated in February 2016 between the oncology and rheumatology departments at the Cleveland Clinic Foundation. All patients were evaluated by authors CC and/or LHC. Patients' characteristics were retrospectively collected from medical charts after IRB approval.

Results: 70 patients referred for one or more rheumatic irAEs between February 2016 and January 2020 were included. 66% were male, median age was 60.8 years. Among them, 24 (34%) had pre-existing rheumatic complaints. Melanoma was the most frequent malignancy (56%). ICI therapy included anti-CTLA4 (40%), anti-PD1/L1 (79%), and dual therapy ipilimumab/nivolumab (41%). Rheumatic irAE occurred in a median 4 months after ICI initiation, with phenotypes including inflammatory arthritis (32 patients), sicca-like symptoms (12), polymyalgia rheumatica-like (7), and myositis (2). Oral, intravenous or intraarticular glucocorticoids (GC) were administered to 54 patients (77%). Of these 54 patients, 22 (41%) required long term GC, 19 had bone density scan and 15 received pneumocystis (PJP) prophylaxis. One PJP case, 1 osteoporotic fracture and 2 avascular necrosis cases were reported. 16 patients received conventional DMARDS (23%) and 9 received biologics (13%). ICI therapy was held for rheumatic irAE in 31% of cases and for another systemic irAE in 29%. Median follow-up was 13.6 months, at end of follow-up 51 patients were still on treatment for rheumatic irAE and 41% of them were still symptomatic despite ongoing treatment.

Conclusion: Rheumatic irAEs are heterogeneous and often chronic requiring prolonged immunomodulatory therapy. Prospective studies are required to define optimal management of rheumatic irAEs that maintain long-term oncologic outcomes.

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Crescendo, Novartis, Genentech, Janssen, and AbbVie, cassandra calabrese Consultant of: Abbvie
GSK, Speakers bureau: Sanofi-Genzyme
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FRI0495 FOLLOW UP OF INTERSTITIAL PNEUMONIA WITH AUTOIMMUNE FEATURES – THE EXPERIENCE OF ONE CENTRE

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Background: Interstitial Lung Diseases (ILD) may present features suggesting an underlying autoimmune process, which seem to differentiate them from idiopathic interstitial pneumonias, although without fully meeting the classification criteria (CC) for a specific connective tissue disease. Different terms had been used to describe these conditions and, to reach a consensus, the European Respiratory Society/American Thoracic Society proposed the CC for an entity named Interstitial Pneumonia with Autoimmune Features (IPAF). Clinical evolution and prognosis of this entity are still poorly understood.
Objectives: To evaluate clinical evolution and prognosis of a population of patients with IPAF.
Methods: Retrospective analysis of clinical files of patients followed by the Pulmonology Department since 02/2012 until 06/2019, who met the CC for IPAF, regarding clinical, functional and radiological evolution. Patients were considered to have a progressive phenotype in 24±3 months from their 1st evaluation if they fulfil 1 of the 4 criteria: relative decline in FVC ≥10% predicted; relative decline in FVC ≥5–<10% predicted and worsened respiratory symptoms; relative decline in FVC ≥5–<10% predicted and increased extent of fibrosis on High-resolution Computed Tomography (HRCT); worsened respiratory symptoms and increased extent of fibrosis on HRCT.
Results: 22 (7.4%) of 296 ILD patients met IPAF CC. 59.0% were female with an age at the 1st evaluation of 66.7±12.4 years. They were all non-smokers (63.6%) or ex-smokers (36.4%). Serologic and morphologic criteria were both present in 21 (95.4%) and clinical criteria in 5 patients (22.7%). Antinuclear antibodies (ANA) were identified in 19, rheumatoid factor in 4, SSA in 3 and anti-Jo-1 in 1 patient. HRCT patterns were identified in 21 patients: 15 nonspecific interstitial pneumonia (NSIP), 5 organizing pneumonia (OP) and 2 lymphocytic interstitial pneumonia (LIP). One NSIP and 1 LIP identified on HRCT were confirmed by histopathology. Three patients had inflammatory arthritis and 2 had Raynaud's phenomenon. Immunosuppressive therapy was introduced in most cases (18 patients, including systemic corticotherapy in 17, azathioprine in 4, mycophenolate mofetil in 1), azithromycin was prescribed in 2 patients and 3 remained without therapy. Regarding the follow up at 24±3 months from the 1st evaluation (3 patients were excluded due to too recent follow-up), 4 patients (18.2%) had progressive phenotype, 7 (31.8%) had a favourable evolution and 3 (13.6%) patients had died. During a follow-up of 31.1±19.8 months, this number rose to 6 patients (27.3%), all of them died by respiratory cause and had NSIP pattern. No differences were found in age, last FVC, therapy and time of disease evolution between those who died and the others.
Conclusion: Our study showed that a small proportion of IPAF patients had a progressive phenotype and the NSIP pattern seemed to be a poor prognosis factor for survival.
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FRI0496 FRECUENCY OF POLYAUTOIMMUNITY IN RHEUMATOID ARTHRITIS AND SYSTEMIC LUPUS ERITHEMATOSUS

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Background:
Objectives: To study the frequency of polyautoinmunity and multiple autoinmune syndrome (MAS) in patients with rheumatoid arthritis (RA) and systemic lupus erithematosus (SLE).
Methods: Study design: We performed a cross-sectional study in patients with RA and SLE, and compared them with healthy subjects. Cases: RA patients classified by ACR/EULAR 2010 criteria and SLE patients classified by ACR/EULAR 2019 criteria. SLE and RA patients were compiled consecutively from a rheumatology clinic of the Regional University hospital of Malaga. Controls: subjects without rheumatologic autoimmune disease (AD) from the same population area. Protocol: All subjects filled out a predesigned questionnaire for the collection of polyautoimmunity data on the cut-off date. Main variables: polyautoimmunity was defined as co-occurrence of SLE or RA and other AD. Secondary variables: Rheumatologic, cutaneous, endocrine, digestive and neurological AD. MAS was defined as presence of three or more AD. Family history of SLE, RA and other autoimmune diseases were also collected. Statistic analysis: descriptive analysis, bivariate analysis and multivariable analysis were done. (Dependent variable: Polyautoimmunity).
Results: We recruited 109 patients with RA, 105 with SLE and 88 controls. Fifteen patients with RA (13.8%), 43 with SLE (41%) and 2 controls (2.2%) reported polyautoimmunity. Table 1 describes the epidemiological characteristics, comorbidities and polyautoimmunity in study population. The most frequent AD associated with RA was Sjögren's syndrome (SS) (53.3%) and SS (55.8%) followed by the antiphospholipid syndrome (30.2%) were associated with SLE. Hashimoto's thyroiditis and psoriasis were the next most frequent AD. According to family history, 5 patients with RA (33.3%) and 12 with SLE (27.9%) had a family history of first degree of other AD. Obesity was associated with polyautoimmunity in RA (OR = 3,362, p = 0.034). In SLE, joint damage (OR = 2.282, p = 0.038) and anti-RNP antibodies (OR = 5.095, p = 0.028) were factors associated with polyautoimmunity and taking hydroxychloroquine was a protective factor (OR = 0.190, p = 0.004).
Conclusion: Polyautoimmunity in RA and especially in SLE is frequent. It was associated with obesity in RA and in SLE with joint damage and anti-RNP antibodies. The hydroxychloroquine appeared as a protective factor.

Variables	RA (N=109)	SLE (N=105)	Controls (N=88)	P value
Epidemiological characteristics				
Sex: female, n (%)	85 (78.0)	99 (94.3)	68 (77.3)	0.001
Age, mean (SD), years	56.5 (10.8)	50.8 (13.2)	57.1 (10.6)	0.133
Caucasic race, n (%)	107 (98.2)	105 (100)	88 (100)	0.168
Comorbidities				
Smoking				0.001
No smoking, n (%)	55 (50.5)	78 (74.3)	56 (63.6)	
Smoking history, n (%)	54 (49.5)	27 (25.7)	32 (36.4)	
Obesity, n (%)	38 (34.9)	21 (20.0)	22 (25.0)	0.044
Dyslipidemia, n (%)	24 (22.0)	22 (21.2)	17 (19.3)	0.896
Hypertension, n (%)	27 (24.8)	28 (26.7)	23 (26.1)	0.746
Diabetes mellitus, n (%)	7 (6.4)	1 (1.0)	1 (1.1)	0.031
Polyautoimmunity, n (%)	15 (13.8)	43 (41)	2 (2.2)	<0.001
MAS, n (%)	1 (0.9)	9 (8,6)	0 (0.0)	<0.001
FH polyautoimmunity, n (%)	19 (17.6)	26 (24.8)	15 (17.0)	0.060

RA: rheumatoid arthritis; SLE: systemic lupus erithematosus; SD: standard desviation; MAS: multiple autoinmune syndrome; FH:Family history

Disclosure of Interests: None declared
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FRI0497 THERAPEUTIC STRATEGIES AND LONG-TERM OUTCOME IN PATIENTS WITH INTERSTITIAL PNEUMONIA WITH AUTOIMMUNE FEATURES: A SINGLE CENTER LARGE-SCALE OBSERVATIONAL COHORT STUDY

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Background: Patients with idiopathic interstitial pneumonia (IIP) may have features of connective tissue diseases (CTDs). The term interstitial pneumonia with autoimmune features (IPAF) has been recently proposed for such patients [1]. To date, only few studies have comprehensively described outcomes over a long-term period and choices of treatment [2-4].
Objectives: The aim of this study was to investigate the therapeutic strategies and long-term outcome among patients with IPAF, IIP, and CTD-ILD.
Methods: Six hundreds- and seventy-two patients who had visited our department between April 2009 and March 2019 and were evaluated by chest HRCT scan. They were clinically and radiologically diagnosed as having interstitial lung disease (ILD), including IIP, CTD-ILD, undifferentiated connective tissue diseases associated ILD or other ILD. Then, we applied IPAF criteria to these patients, 68 patients were diagnosed as IPAF. We extracted the

treated patients from IPAF patients. Then, the treated patients were divided into two groups, which were treated with monotherapy (glucocorticoid: GC) and with combination therapy (GC and immunosuppressant: IS). Clinical, laboratory and imaging data were collected from medical records and statistically analyzed.

Results: Proportion of treatment received patients with IPAF, IIP, or CTD-ILD was 44.1%, 28.1%, and 88.0%, respectively. Then we compared long-term outcomes among patients with IPAF, IIP, and CTD-ILD, 5-year non-exacerbation rate in IPAF patients, IIP patients, and CTD-ILD patients was 53.7%, 28.3%, and 59.5%, respectively (Figure 1.). No significant difference between IPAF and CTD-ILD group was found (P=0.71). Next, we focused on IPAF and compared characteristics at diagnosis between the treatment group (n=30) and non-treatment group (n=38) in patients with IPAF. Interestingly, treatment group was significantly associated with signs of mechanic's hands, arthritis, anti-SS-A antibody positivity, and anti-ARS antibody positivity (P=0.009, 0.05, 0.05, and 0.007). Among the treatment group, GC monotherapy was received in 46.7% (n=14), whereas GC+IS combination therapy group was 50% (n=15). When we compared long-term outcomes between two groups, 3-year non-exacerbation rate was 70.1%, 43.5%, and 83.3% (Figure 2.). No significant difference was not seen between two different treatment groups (P=0.24).

Conclusion: Our large-scale cross-sectional cohort study identified that the prognosis of IPAF patients was poor as same as that of CTD patients, and even though GC mono or GC+IS combination treatment was applied for IPAF patients, prognosis was still poor and thus new intervention for IPAF should be needed to improve their prognosis.

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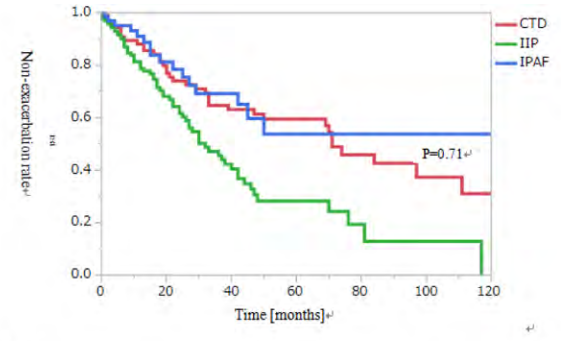


Figure 1. Kaplan-Meier survival curves of interstitial pneumonia with autoimmune features (IPAF) (n=68), idiopathic pulmonary fibrosis (IIP) (n=170) and connective tissue disease (CTD)-interstitial lung disease (ILD) (n=92).

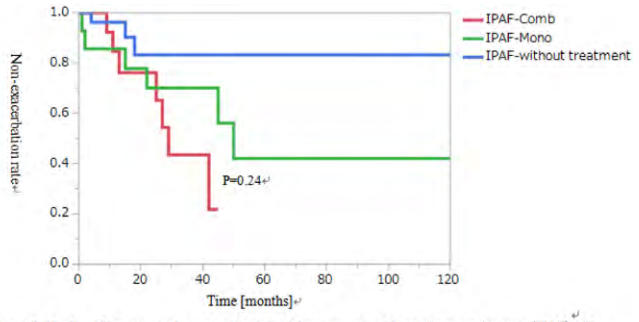


Figure 2. Kaplan-Meier survival curves of interstitial pneumonia with autoimmune features (IPAF) with monotherapy (n=14), with combination therapy (n=15) and without treatment (n=38).

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FRI0498 DOES TESTING FOR SAA IS MORE BENEFICIAL THAN CRP FOR THE FOLLOW-UP OF FMF PATIENTS WITH M694V HETEROZYGOUS OR M694V HOMOZYGOUS MUTATIONS?

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Background: In order to follow subclinical inflammation and adjust the therapy for an optimal Familial Mediterranean Fever (FMF) disease control, clinicians seek for readily accessible, affordable and reproducible markers. C-reactive protein (CRP) is widely used for this purpose. Some suggest that CRP measures are not conclusive in all cases, especially at initial stages of inflammation. It is suggested that Serum Amyloid A (SAA) may be more reliable and sensitive in predicting an ongoing inflammation.

Objectives: In order to evaluate and to compare the sensitivity of SAA and CRP in FMF patients with M694V homozygous and M694V heterozygous mutations respectively.

Methods: Blood samples from 28 patients with M694V homozygous mutation and from 15 patients with M694V heterozygous mutation were obtained during a mean follow-up of 1 year. Multiple samples were drawn in both attacks and attack-free periods of FMF (153 from M694V Homozygous and 31 from M694V Heterozygous). For the analysis of the correlation, the folds of normal CRP and SAA levels were used. Serum levels of the given markers were measured with nephelometric kits (normal CRP levels <5 mg/L and SAA levels <6,8 mg/L). More than one-and-a-half-fold increase of CRP and SAA was defined as an active inflammation.

Results: Except in one patient, all patients in the whole cohort were on prophylactic colchicine. Among 28 patients with M694V homozygous mutation, one patient was treated with adalimumab, and 12 patients with anti-IL-1 regimens. Among 15 patients with M694V heterozygous mutation, 4 were under anti-IL-1 treatment. There were a total of 183 measurements of CRP and SAA from 43 patients. Twenty-three measurements were obtained during the attack period in M694V homozygous group and the remaining 160 measurements were obtaine in attack-free period. The figure demonstrates the correlation between CRP and SAA results (r=0.745, p<0.001). Both acute phase reactants were increased in 69 measurements, while in 13, CRP was high but SAA was normal and in 31, SAA was high however CRP was within normal limits. The mean increase in CRP of the whole cohort was 2,37 ± 3,22-fold of the normal, whereas mean increase in SAA was 6,77 ± 13,23-fold of the normal.

Conclusion: According to these results, serial testing of SAA does not provide any additional advantages over CRP. As it is readily accessible and affordable, CRP seems to be sufficient for the follow-up of FMF patients.

Figure:

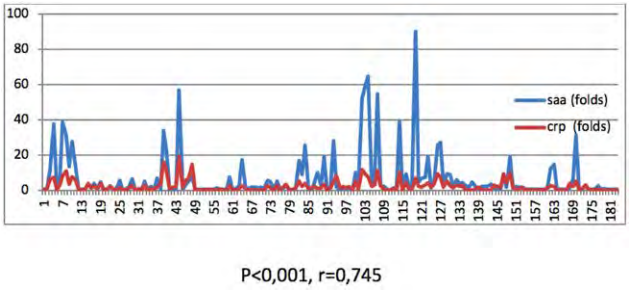


Figure. The folds CRP and SAA in whole M694V homozygous and heterozygous mutant population

Disclosure of Interests: None declared

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FRI0499

ACROMEGALY ARTROPATHY: IS THERE SOMETHING MORE BEHIND THE PAIN? A CROSS-SECTIONAL STUDY TO EVALUATE RHEUMATIC DISEASE IN GROWTH HORMONE SECRETING TUMOR PATIENTS

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Background: Acromegaly is a rare disease with a remarkable impact on patients, both in terms of life expectancy and quality of life. Osteo-articular complications are one of the most frequently reported bothers. The "acromegaly artropathy" characterizes more than 70% of patients at diagnosis. Artropathy affects both spine and peripheral joints. A recent prospective study documented progression of acromegalic arthropathy identified as a worsening of osteophytes and joint space narrowing in 72–74% of patients despite long-term biochemical control. In addiction the Literature has occasionally reported cases of simultaneous presence of rheumatic diseases (rheumatoid arthritis, polymyalgia rheumatica, undifferentiated connective tissue diseases) and acromegaly and in all these cases the treatment has been delayed, because of wrong symptoms attribution to acromegaly artropathy.

Objectives: The primary goal of the study is to better characterize joint pain in acromegaly patients and to evaluate the prevalence of rheumatic disease in growth hormone (GH) secreting pituitary tumor patients.

Methods: We enrolled 20 acromegaly subjects (AS) and 20 control subjects (CS). In each subject immunological pattern (rheumatoid factor – RF; antinuclear antibodies - ANA, ENA; anti-citrullinated protein antibodies - ACPA; erythrocyte sedimentation rate – ESR) has been evaluated; they, also, underwent bilateral joint ultrasound of hands and wrists and nail capillaroscopy. The Chi square test and the Fisher's exact test were used to evaluate the association between binary variables, while the Spearman's test to evaluate the correlation of continuous ones. A multiple or logistic regression model was calculated in order to define the association between the capillaroscopic alterations and other detected variables.

Results: Articular pain emerged as significantly more frequent in AS (p = 0.0269). No statistically significant differences are detected regarding immunological pattern. ANA and ENA screening resulted positive in 10% in AS and in 5% in CS. No IgA ACPA were detected in AS or CS, while IgG ACPA were positive only in one AS subject. No significant differences were detected between IgM and IgG RFin the two groups (AS 5% and CS 0%). Three fold higher IgG FR in AS compared to CS were detected. ESR levels were significantly higher than CS (p = 0.0405), as well as increased power doppler (PWD) articular uptake (AS 30% vs CS 5% p 0.081). The capillaroscopic evaluation showed a significant difference in almost each parameter that has been evaluated (logistic regression: number of enlargement p 0.004, hemorragies p 0.01 and capillaries p 0.001), showing a moderate-severe microangiopathy in AS. Interestingly, analyzing only the acromegaly cohort, we noticed higher GH levels at the enrollment in patients which developed capillary enlargements (GH: 0.95 ng/ml IQ 0,6-1,6) compared to other ones (GH: 0.55 ng/ml IQ 0.4-0.7; p = 0.08) and a significant lower number of hemorrhages (p = 0.02) in patients treated with GH antagonist pegvisomant.

Conclusion: Our results demonstrated that joint damage in acromegaly does not seem to have an autoimmune etiology. Therefore, articular damage is mechanical and increased ESR and PWD alterations seems to confirm the presence of an inflammatory component. In addition, acromegaly is characterized by a microvascular pattern of moderate-severe microangiopathy, without correlation to IGF-I, but GH levels. Although requiring further confirmatory studies, our preliminary results seem to indicate how the capillaroscopic examination could be useful to detect earlier microangiopathy and to identify patients with a greater risk of macroangiopathy development..

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FRI0500

BEHÇET SYNDROME AND CENTRAL NERVOUS SYSTEM INVOLVEMENT: A DESCRIPTIVE STUDY IN A COHORT OF PATIENTS IN OUR RHEUMATOLOGY DEPARTMENT

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Background: Behçet's disease (BD) is a variable vessel vasculitis characterized by mucocutaneous lesions (oral and genital ulcers). In addition, it can affect other systems such as vascular, ophthalmological, gastrointestinal tract or central nervous system (CNS). The latter being one of the most serious manifestations of Behçet's disease. We present a descriptive observational study of a cohort of patients diagnosed with Behçet's disease with CNS involvement.

Objectives: Our objective is to describe the prevalence and characteristics of various clinical manifestations in patients with Behçet.

Methods: Observational, descriptive, cross-sectional, retrospective design performed in patients with Behçet's disease in follow-up by the Rheumatology department of the Hospital de Valme, until October 2019. The following information is collected from medical records; sex, mean age at diagnosis, clinical characteristics, HLA B51 positivity and treatment.

Results: Thirty-three patients were diagnosed with Behçet's disease, with a mean age at diagnosis of 36.22 +/- 10.94 years, female predominance 19 (57.57%). Regarding the determination of HLA B 51; 5 (15.15%) positive, 6 (18.18%) negative and 22 (66.66%) not determined. The following information about clinical manifestations is collected:

Clinical manifestations n (%)	
Oral aphtosis	33 (100)
Genital ulceration	23 (69.69)
Skin (Pseudofolliculitis/Erythema Nodosum)	12 (36.36)
Ocular	22 (66.66)
Anterior Uveitis	*8/22 (36.36)*
Posterior uveitis	*3/22 (13.63)*
Panuveitis	*5/22 (22.72)*
Vitritis	*1/22 (4.54)*
Retinal vasculitis	*6/22 (27.27)*
Vascular	7 (21.21)
Arthralgias/arthritis	20 (60.60)
Gastrointestinal	2 (6.06)
Central Nervous System	**9 (27.27)**
Demyelinating lesions	*5/9 (55.55)*
Stroke	*2/9 (22.22)*
Epilepsy	*1/9 (11.11)*
Vasculitis	*1/9 (11.11)*

We identified 9 patients with CNS involvement; 5 demyelinating lesions (55%), 2 strokes (22%), 1 epilepsy/seizure (11%) and 1 case of CNS vasculitis (11%). Fifty-five percent of the patients were female (55%). Two patients were positive for HLA B51 (22%) and the rest had not been determined. Regarding treatment, all patients received both, oral and intravenous, corticosteroids (prednisone, methylprednisolone) and seven of them received DMARDs; 2 methotrexate (28%), 2 cyclosporine (28%), 1 sulfasalazine (14%), 1 azathioprine (14%) and 1 mercaptopurine (14%, due to intestinal involvement). Two of them needed biologic DMARD with TNF inhibitor agents (Infliximab and Adalimumab).

Conclusion: Although neurological involvement is not common in BD, we describe higher prevalence (22%) than other series in the literature[1,2]. Given the heterogeneity of the clinical presentation there is a wide differential clinical diagnosis to rule out; demyelinating diseases (multiple sclerosis), such as demyelinating lesions presented in 5 of our patients (55%), infectious diseases (tuberculosis), other autoimmune diseases (Vogt–Koyanagi–Harada Syndrome, Eales Sd) or ischemic stroke due to atherosclerosis[3].

References:

[1] 10.1016/B978-0-7020-4088-7.00110-3

[2] 10.1046/j.1365-4362.2003.01741

[3] 10.1007/s00415-013-7209-3

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FRI0501

CARDIOVASCULAR DISEASE RISK ASSESSMENT IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER RELATED AMYLOIDOSIS

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Background: FMF is an autosomal recessive disorder. Systemic inflammation in autoinflammatory disorders cause secondary systemic AA amyloidosis, which has been suggested as an important contributing factor to the excess cardiovascular disease (CVD) risk in patients with FMF.

Objectives: Our aim was to investigate the CVD-related clinical outcomes in patients with FMF-related amyloidosis and to define risk factors for CVD events (CVDEs).

Methods: A cross-sectional evaluation with prospective follow-up of consecutive patients with FMF-related amyloidosis or other non-diabetic primary glomerulonephropathy (PGN) was performed. Patients were followed for CVDEs. Flow-mediated dilatation (FMD), FGF-23 levels, serum lipid levels, hsCRP, BMI and homeostasis model assessment (HOMA) were assessed. A Cox regression analysis was performed to evaluate the probability of CVDEs associated with each risk factor.

Results: There were 107 patients in FMF-related amyloidosis group and 126 patients with PGN group. Forty-seven CVDEs were registered during the 4.2-years follow up; all 28 patients in the FMF-related amyloidosis versus 14/19 patients with PGN group who developed CVDEs before 40 years of age (P=0.002) (Figure 1). CVD mortality was 2.8 times higher (95% CI 1.02-7.76, p=0.03) in patients with FMF-related amyloidosis (n=12) than PGN (n=5). Mortality due to CVD was higher in patients less than 40 years old with amyloidosis than PGN (12/107 and 3/126 respectively, RR=4.71, 95% CI 1.36-16.25, p=0.006). Patients with CVDEs had higher levels of proteinuria, hsCRP and FGF23, and lower FMD compared to patients without CVDEs. Across both groups, FGF23 and FMD levels were independently associated with the risk of CVDEs (Table 1).

Conclusion: Patients with FMF-related amyloidosis are at increased risk of CVDEs with early mortality age. These patients should be closely monitored and if inflammation is poorly controlled with colchicine, biological agents must be added to treatment even if they develop amyloidosis. We also found that hsCRP, FGF 23 and FMD levels were the strongest predictors of CVD risk in patients with FMF. These biomarkers can stratify risk of early CVD in patients with FMF-related amyloidosis.

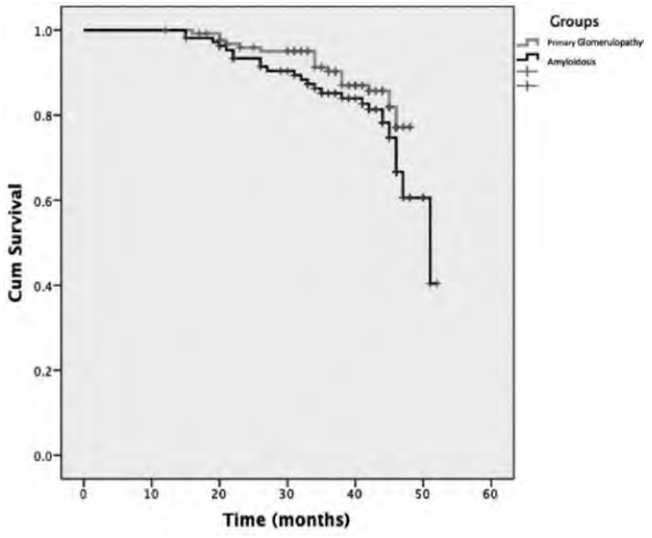


Figure 1. Comparison of cardiovascular disease survival between patients with FMF-related amyloidosis or primary glomerulopathy.

Table 1. Multivariate analysis of factors associated with the risk of suffering a cardiovascular event

		B	HR	95.0% CI for Exp(B)		p
	Variables			Lower	Upper	
All Groups	FGF23	.033	1.034	1.017	1.051	<.001
	FMD	-.946	.388	.262	.575	<.001
Primary glomerulopathy	FGF23	.050	1.051	1.019	1.084	.002
	FMD	-.651	.522	.300	.908	.021
Amyloidosis	FGF23	.034	1.035	1.012	1.058	.003
	FMD	-1.531	.216	.109	.430	<.001
	hsCRP	-.040	.961	.915	1.009	.108

FMD, Flow-mediated dilatation; hsCRP, high sensitivity C reactive protein; CI, Confidence interval

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FRI0502

SEASONAL CLUSTERING OF ACUTE SARCOIDOSIS IN GERMANY AND ASSOCIATIONS WITH AIR POLLUTION

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Background: Sarcoidosis is a multisystemic granulomatous disorder of unknown origin. The central role of macrophages and granuloma formation, the predominant involvement of lung and skin, and certain risk populations (e.g. firefighters[1, 2]) might be explained by causative airborne antigen(s)[3]. Whether air pollution is involved in pathogenesis and seasonal clustering of sarcoidosis is uncertain.

Objectives: This study has been set to analyze seasonal clustering of acute sarcoidosis and associations to air pollution.

Methods: Patients with acute sarcoidosis, defined by bihilar lymphadenopathy, ankle swelling, and/or erythema nodosum plus physician's diagnosis,were included in this retrospective study. Disease onset (seasonal clustering) and associations to air pollution (particulate matter (PM_{10}) and nitrogen dixoide (NO_2)) were analyzed. Google Trends queries were conducted to address seasonal clustering on a global scale.

Results: A total of 185 patients with acute sarcoidosis were included; 48.7 % of the enrolled patients were female and Löfgren triad was complete in 73.5 % of patients. Acute sarcoidosis clustered from December to June in West Germany ($p<0.005$, Kendall τ=-0.68), peaking in January (17.8 % of cases) and in the first third of the year (54.5 %). Mean PM_{10} values clustered from December to April with values between 15 and 40 µg/m^3. NO_2 levels were measured highest from November to March (45 µg/m^3) and lowest between April and August (25 µg/m^3). Elevated air pollution markers (PM_{10} and NO_2) were associated with higher monthly incidence rates of acute sarcoidosis (Cross correlation coefficient ranging between 0.7 -0.8). Google Trends analysis yielded seasonal clustering ($p<0.005$, Kendall τ = -0.64) in winter and spring months on the northern hemisphere.

Conclusion: In Central Europe acute sarcoidosis peaks in winter and spring months (December until March) shortly after PM_{10} and NO_2 maxima are reached. Whether components of particulate matter might be involved in the pathogenesis of sarcoidosis has to be elucidated by further studies.

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FRI0503

VALIDATION OF THE 2019 ACR/EULAR CLASSIFICATION CRITERIA FOR IGG4-RELATED DISEASE IN A JAPANESE KIDNEY DISEASE COHORT: A MULTI-CENTER RETROSPECTIVE STUDY BY THE IGG4-RELATED KIDNEY DISEASE (IGG4-RKD) WORKING GROUP OF THE JAPANESE SOCIETY OF NEPHROLOGY

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Background: The 2019 ACR/EULAR classification criteria for IgG4-RD have recently been published[1]. In the criteria, patients with an inclusion criteria score of >20 without exclusion criteria are classified as having IgG4-RD.
Objectives: To validate the 2019 ACR/EULAR classification criteria for IgG4-RD in a Japanese kidney disease cohort.
Methods: The study involved Japanese patients diagnosed as having kidney disease between April 2012 and May 2019, for whom sufficient clinical information and data on serum IgG4 values and/or immunohistological staining for IgG4 in renal biopsy samples were known. These patients were classified as having IgG4-RKD or non-IgG4-RKD (mimickers) based on the 2019 ACR/EULAR classification criteria for IgG4-RD, and the results were evaluated by expert opinion.
Results: Among 105 included patients, the expert panel diagnosed 55 as having true IgG4-RKD and 50 as mimickers. The final diagnoses among the mimickers were vasculitis (n=11), idiopathic tubulointerstitial nephritis (TIN) (n=5), drug-induced TIN (n=5), Sjögren's syndrome (n=4) and others. Among the 55 true IgG4-RKD patients, 4 had exclusion criteria, and 50 of the remaining 51 had an inclusion criteria score of ≥20 points (sensitivity 90.9%). On the other hand, 49 of the 50 mimickers were classified as having non-IgG4-RKD (specificity 98.0%) (Table 1).

Table 1. General characteristics and prevalence of individual items of true IgG4-RKD and non-IgG4-RKD (mimicker)

	IgG4-RKD (true IgG4-RKD) (n=55)	Non-IgG4-RKD (mimicker) (n=50)	*P*
Age at diagnosis, mean ±SD (years)	69.9 ± 9.4	56.7 ± 17.4	<0.001
Male (%)	76.4	44	0.001
Elevated serum IgG4	54/55 (98.2%)	18/50 (36.0%)	<0.001
Serum IgG4 (mg/dl), mean±SD	1028 ± 796	226 ± 261	<0.001
Dense IgG4+Plasma cells (>10/hpf) in the kidney biopsy	48/51 (94.1%)	13/40 (32.5%)	<0.001
Storiform fibrosis in the kidney biopsy	28/51 (54.9%)	3/50 (6%)	<0.001
Hypocomplementemia	39/55 (70.1%)	7/42 (16.7%)	<0.001
Renal pelvis thickening/ soft tissue	5/55 (9%)	1/50 (2%)	0.20
Bilateral renal cortex low-density areas	29/55 (52.7%)	7/50 (14.0%)	<0.001
Exclusion criteria present	4/55 (7.3%)	22/50 (44%)	<0.001
Total inclusion criteria points >20 without exclusion criteria	50/55 (90.9%)	1/50 (2%)	<0.001

Conclusion: The 2019 ACR/EULAR classification criteria for IgG4-RD showed good agreement with expert classification in this Japanese kidney disease cohort.
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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.1097

FRI0504

TOCILIZUMAB IN GRAVES' ORBITOPATHY. MULTICENTER STUDY OF 48 PATIENTS.

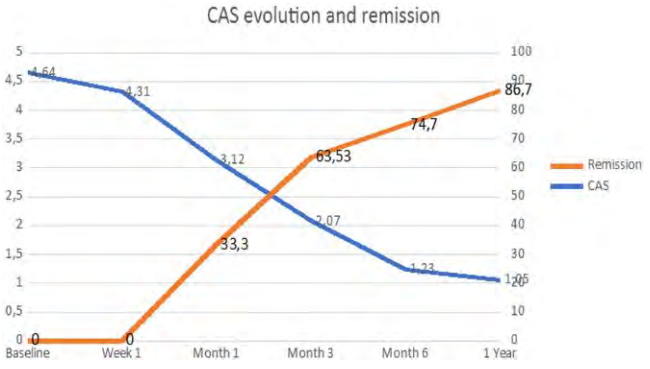
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Background: Tocilizumab (TCZ) has shown promising results in the treatment of inflammatory ocular disease, especially in uveitis (1-3). Graves orbitopathy (GO) is the most common complication of Graves' disease (GD). Conventional immunosuppressive drugs are not always effective or well tolerated. TCZ may be useful in the treatment of GO.
Objectives: To assess the efficacy of TCZ in corticoid-resistant GO.
Methods: Multicenter open study of corticoid-resistant GO. We measured clinical activity using the clinical activity score (CAS). CAS evaluates 10 different ocular items, ranging from 0 (no symptoms) to 10. We defined remission as the presence of CAS ≤ 3.
Results: We studied 48 (95 eyes) patients (**TABLE)**. Besides oral corticosteroids, they had received iv Methylprednisolone (n=43), methimazole (n=20), selenium (n=11) or radioactive iodine (n=5). According to the classification of severity (EUGOGO group), before of TCZ onset our patients had severe (n=19) or moderate (n=29) disease. TCZ was used in monotherapy (n=45) or combined with methotrexate (n=2) or azathioprine (n=1) at a dose of 8 mg/kg/iv/4 weeks (n=43) or 162 mg/sc/week (n=5). TCZ yielded rapid and maintained improvement and most patients achieved remission (**FIGURE).**
After a mean follow-up of 16.1±2.1 months, most patients experienced ocular improvement, with TCZ withdrawal in 29 cases due to remission (n=25) or inefficacy (n=4). Only 5 relevant adverse events were observed (neutropenia, external otitis, otitis media, costal osteitis and gingival hyperplasia). None of these events resulted in discontinuation of the treatment.
Conclusion: TCZ appears to be an effective and safe treatment in corticoid-resistant GO.

TABLE:

Number of patients/eyes affected, n/n	48/96
Age, mean (SD), years	50.96 (11.78)
Sex, men/women, n/n (%)	10/38 (20.8 / 79.2)
Regimen of TCZ therapy	
Monotherapy/combined treatment, n (%)	45/3 (93.8/6.2)
• AZA	1 (2.1)
• MTX	2 (4.2)
TCZ dosage, n (%)	
• 8 mg/kg/iv/4 weeks	43 (89.6)
• 162 mg/sc/week	5 (10.4)
Follow-up on TCZ therapy, mean (SD), months	16.05±2.06
• Remission, n (%)	72 (75.8)
• Discontinuation treatment, n (%)	29 (60.4)
• Remission	25 (86.2)
• Inefficacy	4 (13.8)
• Side effects	0

FIGURE.



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FRI0505 TOCILIZUMAB DISCONTINUATION AFTER REMISSION ACHIEVEMENT IN PATIENTS WITH ADULT STILL'S DISEASE

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Background: The efficacy of tocilizumab, an interleukin (IL)-6 receptor inhibitor, has been proved in patients with adult Still's disease on suppressing systemic inflammation and decreasing glucocorticoid dose. However, whether tocilizumab can be discontinued after remission achievement is unclear.

Objectives: To clarify the possibility of tocilizumab discontinuation in patients with adult Still's disease who achieved remission with tocilizumab.

Methods: Consecutive patients with adult Still's disease diagnosed according to the Yamaguchi's criteria in our hospital from April 2012 until September 2019 were retrospectively reviewed. Patients who were in good control with tocilizumab were included in the analysis, and their clinical courses were collected from their medical charts. Patients were divided according to the presence of recurrence after tocilizumab discontinuation and compared.

Results: Among 42 patients with adult Still's disease who had a history of intravenous tocilizumab of 8mg/kg use, 13 patients discontinued tocilizumab following a good disease control. During the mean observation period of 26.4 months, six patients (46%) remained in remission while seven patients (54%) developed recurrence after tocilizumab discontinuation. The sex and the mean observation period were not different between the patients with recurrence and those without (71% vs 50%, p=0.43; 27.3 months vs 25.4 months, p=0.93, respectively), but the age at tocilizumab discontinuation tended to be higher in the recurrence group than the non-recurrence group (64.0 years vs 46.5 years, p=0.08). The disease activity including swollen joint counts and laboratory data at tocilizumab discontinuation were comparable between the two groups (serum ferritin levels, 88 ng/mL vs 122 ng/mL, p=0.67). While the duration of tocilizumab use was not different between the two groups (29.4 months vs 39.5 months, p=0.40), the mean interval of tocilizumab infusion at tocilizumab discontinuation in the recurrence group was 3.6 weeks, shorter than the 6.7 weeks in the non-recurrence group (p=0.03). The median dose of prednisolone at tocilizumab discontinuation was 5.0 mg/day in the recurrence group and 0.0 mg/day in the non-recurrence group (p=0.06). In the recurrence group, the duration from the last tocilizumab administration to recurrence was 7.8 months, and the median dose of prednisolone at recurrence was 5.0 mg/day.

Conclusion: Patients with adult Still's disease remaining in remission with a longer interval of tocilizumab administration and a lower dose of prednisolone was likely to succeed in withdrawal of tocilizumab.

Disclosure of Interests: Hiroya Tamai: None declared, Yuko Kaneko Speakers bureau: Dr. Kaneko reports personal fees from AbbVie, personal fees from Astellas, personal fees from Ayumi, personal fees from Bristol-Myers Squibb, personal fees from Chugai, personal fees from Eisai, personal fees from Eli Lilly, personal fees from Hisamitsu, personal fees from Jansen, personal fees from Kissei, personal fees from Pfizer, personal fees from Sanofi, personal fees from Takeda, personal fees from Tanabe-Mitsubishi, personal fees from UCB, Tsutomu Takeuchi Grant/research support from: Eisai Co., Ltd, Astellas Pharma Inc., AbbVie GK, Asahi Kasei Pharma Corporation, Nippon Kayaku Co., Ltd, Takeda Pharmaceutical Company Ltd, UCB Pharma, Shionogi & Co., Ltd., Mitsubishi-Tanabe Pharma Corp., Daiichi Sankyo Co., Ltd., Chugai Pharmaceutical Co. Ltd., Consultant of: Chugai Pharmaceutical Co Ltd, Astellas Pharma Inc., Eli Lilly Japan KK, Speakers bureau: AbbVie GK, Eisai Co., Ltd, Mitsubishi-Tanabe Pharma Corporation, Chugai Pharmaceutical Co Ltd, Bristol-Myers Squibb Company, AYUMI Pharmaceutical Corp., Eisai Co., Ltd, Daiichi Sankyo Co., Ltd., Gilead Sciences, Inc., Novartis Pharma K.K., Pfizer Japan Inc., Sanofi K.K., Dainippon Sumitomo Co., Ltd.

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FRI0506 EFFICACY AND SAFETY OF CANAKINUMAB IN ADULT-ONSET STILL'S DISEASE: A SINGLE-CENTER REAL-LIFE EXPERIENCE

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Background: The pro-inflammatory cytokine interleukin (IL)-1 has a central role in the pathogenesis of adult-onset Still's disease (AOSD), a rare auto-inflammatory condition. Anakinra, has been for years the cornerstone of IL-1-blocking therapy in AOSD. More recently, the monoclonal antibody canakinumab, a new agent blocking IL-1, has become available

Objectives: To describe our real-life experience with CNK in a cohort of AOSD patients from a single Italian Center

Methods: AOSD patients diagnosed according to Yamaguchi's criteria followed-up at our Autoinflammatory Unit and treated with CNK for at least 3 months were included. Demographic features, disease characteristics, reasons for CNK introduction, concomitant therapies, variation in systemic steroids dose, adverse events, and response to treatment were retrospectively evaluated. Non-parametric tests were used for statistical comparison

Results: 13 patients (5 women; median age 49 years, range 21-74), treated with subcutaneous CNK 4 mg/kg 4-weekly, were identified. Median disease duration before CNK introduction was 12 (6-240) months. After CNK introduction, 2 patients were followed-up for 18 months, 3 for 12 months, 6 for 6 months, 2 for 3 months. CNK was introduced as first-line biologic DMARD in 6 patients. The other 7 patients had been already treated with at least one other bDMARD, for a total of 15 treatment courses (7, anakinra, ANK; 4, tocilizumab; 4, TNF-inhibitors), with a median bDMARD therapy duration of 8 (4-178) months. Previous bDMARDs had been interrupted because of inefficacy (8 cases) or adverse events (AE, 7 cases); of the 7 ANK-treated patients, therapy interruption was due to inefficacy in 3 cases. At CNK introduction, 11 patients were on systemic steroid therapy, prednisone (PDN) equivalent dose 15 (5-80) mg, and 10 were concomitantly receiving a conventional DMARD (7, methotrexate; 2, colchicine; 1, cyclosporine-A). **Graphic 1** summarizes main clinical features at CNK introduction. After CNK start, a striking and rapid clinical response was observed, as demonstrated by a substantial decrease of modified Pouchot score and a normalization of acute phase reactants after only 3 months (see Table 1 for details). CNK showed also a significant steroid-sparing effect: median PDN dose was reduced to 7.5 (2.5-12.5)

Table 1. Disease activity and blood tests at canakinumab introduction and during follow-up

Daily prednisone dose mg	Baseline (n=13)	3 months (n=13)	6 months (n=11)	12 months (n=5)	18 months (n=2)
Pouchot score	15 (5-80)	7.5 (2.5-12.5)	5 (0-7.5)	5 (0-7.5)	2.5
VAS pain	3 (2-5)	1 (0-2)	0 (0-1)	0	0
Erythrocyte sedimentation rate mm/h	7 (2-10)	3 (1-8)	2 (1-4)	1 (1-2)	1
C-reactive protein mg/L	42 (8-120)	21 (2-69)	13 (2-55)	14 (2-41)	11
Ferritin ng/mL	20.8 (3-180)	3.1 (0.5-22.5)	1.6 (0.5-8.4)	1 (0.3-6.3)	0.5
Hemoglobin g/dL	379.5 (161-914)	282 (82-552)	215 (34-464)	177 (77-401)	199
	13.1 (9.4-15.7)	13.2 (10.7-15.3)	13.8 (11.5-15.5)	13.9 (11.3-14.3)	13.5

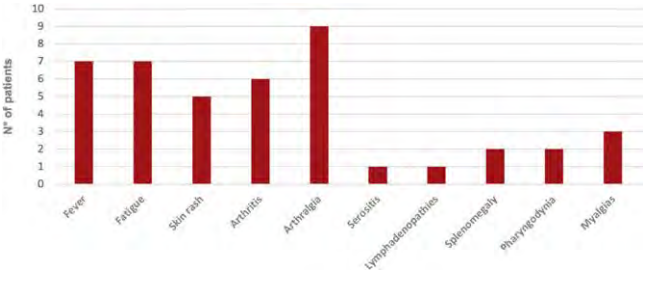


Figure 1. Graphic 1 Main clinical features at canakinumab introduction

mg at month 3 and 5 (0-7.5) mg at month 6; PDN was stopped in 3 patients (1 at month 3, 1 at month 6, 1 at month 12) due to optimal disease control. CNK was temporarily held-off in 3 patients (zoster reactivation, 1; prostatitis, 1; mild leukopenia, 1). We observed no case of primary inefficacy

Conclusion: Our real-life data confirm that CNK is highly effective and safe in AOSD treatment and has significant steroid-sparing effects. CNK showed its efficacy both as first-line therapy and after other bDMARDs failure, also in patients who have previously failed IL-1 inhibition through ANK

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Disclosure of Interests: Alessandro Tomelleri: None declared, Corrado Campochiaro Speakers bureau: Novartis, Pfizer, Roche, GSK, SOBI, Giacomo De Luca Speakers bureau: SOBI, Novartis, Celgene, Pfizer, MSD, Nicola Farina: None declared, Elena Baldissera Speakers bureau: Novartis, Pfizer, Roche, Alpha Sigma, Sanofi, Giulio Cavalli Speakers bureau: SOBI, Novartis, Pfizer, Lorenzo Dagna Grant/research support from: Abbvie, BMS, Celgene, Janssen, MSD, Mundipharma Pharmaceuticals, Novartis, Pfizer, Roche, SG, SOBI, Consultant of: Abbvie, Amgen, Biogen, BMS, Celltrion, Novartis, Pfizer, Roche, SG, and SOBI

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FRI0507 COLCHICINE INTOLERANCE IN FMF PATIENTS AND PRIMARY OBSTACLES FOR OPTIMAL DOSING

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Background: Colchicine is the mainstay of treatment in FMF. However, in daily practice it is not easy to maintain effective colchicine doses in substantial number of patients, due to its side effects.

Objectives: It was aimed to investigate prevalence and risk factors for colchicine side effects that limit optimal drug dosing and permanent discontinuation.

Methods: All patients were recruited from "FMF in Central Anatolia" (FiCA) cohort, 915 adult subjects with minimum follow up time of 6 months and had compliance of treatment were included. Demographic and anthropometric data, FMF disease characteristics, disease severity, complications and treatment features were recorded on a web based registry. Prevalence of colchicine intolerance and characteristics of intolerant patients were analyzed.

Results: Effective colchicine doses cannot be maintained in 172 (18.7%) subjects. Main side effects that limit optimal dosing were as follows; diarrhea in 99 (10.8%), elevation in transaminases in 54 (5.9%), leukopenia in 10 (%1.1), renal impairment in 14 (1.3%), myopathy in 5 (0.5%) and allergic skin reaction in two. Colchicine had to be permanently ceased in 18 (2%) patients because of serious toxicity. Male gender and obesity were found to be associated with liver toxicity and having normal body weight was associated with diarrhea. Chronic inflammation and proteinuria were more common in colchicine intolerant patients and they had reported more frequent attacks compared to those tolerating optimal doses.

Table 1. Prevalence of all side effects of colchicine and reasons for drug discontinuation

Side effect	All side effects N=172*	Permanent cessation N=18*
Diarrhea	99	11
Liver toxicity	54	4
Leukopenia	10	1
Muscle toxicity	5	2
Skin reaction	2	-
Nausea	4	-
Infertility	2	-

* some patients had more than one clinically significant side effect

Table 2. Disease course in colchicine tolerant and intolerant patients

	Colchicine Tolerant N=743	Colchicine Intolerant N=172	p value
Chronic inflammation	115 (15.4%)	45 (26.1%)	**<0.001**
Number of attacks in the last year	4.05±6.08	7.60±9.6	**<0.001**
Proteinuria	44 (5.9 %)	20 (11.6%)	**0.025**
Amyloidosis	33 (% 4.4)	23 (13.3%)	**<0.001**
ADDI (median)	1 (1)	1 (1)	**<0.001**

ADDI: auto-inflammatory disease damage index, FMF: familial Mediterranean fever

Conclusion: Colchicine intolerance is an important problem in daily clinical practice, mainly due to diarrhea and liver toxicity. Suboptimal colchicine dosing associated with complications.

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Disclosure of Interests: Hasan Satış: None declared, Berkan Armagan: None declared, Erdal Bodakci: None declared, Nuh Atas: None declared, Alper Sarı: None declared, Dilek Yapar: None declared, Nazife Sule Yasar Bilge: None declared, reyhan bilici salman: None declared, Gözde Kübra Yardımcı: None declared, Hakan Babaoglu: None declared, Levent Kılıç: None declared, mehmet akif ozturk: None declared, Berna Goker: None declared, seminur haznedaroglu: None declared, Umut Kalyoncu Consultant of: Abbvie, Amgen, Janssen, Lilly, Novartis, UCB, Timuçin Kaşifoğlu: None declared, abdurrahman tufan: None declared

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FRI0508 MALIGNANCY AND IGG4-RELATED DISEASE: THE INCIDENCE, RELATED FACTORS AND PROGNOSIS FROM A PROSPECTIVE COHORT STUDY IN CHINA.

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Background: The association between IgG4-related disease (IgG4-RD) and malignancies is unclear. No epidemiological data for malignancies in Chinese IgG4-RD patients is available. It is also important to know the risk factors and prognosis for IgG4-RD patients harboring malignancies.

Objectives: To investigate the incidence, related factors and prognosis of IgG4-related disease (IgG4-RD) with malignancies in the Chinese cohort.

Table 1. Baseline characteristic of IgG4-RD patients with malignancy

Patient	Sex	Age	Age at diagnosis of IgG4-RD	Age at diagnosis of malignancy	Serum IgG4 (g/L)	Organs involvements of IgG4-RD (*Organ with biopsy)	Sites of malignancy
P1	F	59	58	54	1499	Parotid gland*, salivary gland	Breast cancer
P2	M	74	66	68	10402	Pancreas, bile duct, retroperitoneal fibrosis, kidney, prostate, lymph nodes	Rectal cancer
P3	M	46	42	40	2630	Lacrimal gland, parotid gland	Lipoblastoma
P4	M	70	68	64	5780	Pancreas, bile duct, lung, prostate, lymph nodes	Thyroid carcinoma
P5	F	62	61	61	11600	Pancreas, bile duct, salivary gland*, periaortitis, lymph nodes, pituitary	Thyroid carcinoma
P6	M	72	68	68	3490	Pancreas, bile duct, lymph nodes	Rectal cancer
P7	M	60	58	58	2410	Pancreas, bile duct, lymph nodes	Renal cancer
P8	M	68	63	68	3520	Pancreas, bile duct, retroperitoneal fibrosis, lung, kidney, artery, lymph nodes	Rectal cancer
P9	M	36	30	35	12400	Pancreas, bile duct	Skin cancer
P10	M	52	49	52	10000	Pancreas, parotid gland*, lacrimal gland, lung, prostate, lymph nodes	Thyroid carcinoma
P11	F	70	68	69	17300	Parotid gland, lacrimal gland, salivary gland, sinus	Lung cancer
P12	M	82	79	79	58000	Pancreas, lacrimal gland*	Colon cancer
P13	F	50	49	45	14300	Uterus*, ovary	Ovarian carcinoma
P14	F	52	46	50	10000	Parotid gland*, lacrimal gland	Breast cancer
P15	F	60	55	57	12500	Pancreas, parotid gland, lacrimal gland, lymph nodes, sinus	Lymphoma
P16	M	42	37	40	7490	Lung*, lymph nodes	Renal cancer
P17	M	71	68	69	415	Pancreas*, bile duct	Prostate cancer

Table 2. Related factors for malignancies in patients with IgG4-RD

Variables	Univariate analysis		Multivariate analysis	
	Univariate OR (95%CI)	P-value	Multivariate OR (95%CI)	P-value
Head and Neck involvement	0.304 (0.097- 0.952)	0.041	0.604 (0.152-2.401)	0.474
Autoimmune pancreatitis	5.359 (1.651-17.393)	0.005	6.230 (1.559-24.907)	0.010
Eosinophilia	0.117 (0.014-0.966)	0.046	0.094 (0.010-0.883)	0.039

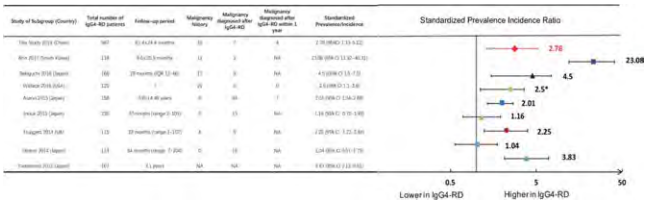


Figure 1. Standardized incidence ratios of malignancies in patients with IgG4-RD from different studies.

Methods: We prospectively analyzed the IgG4-RD patients recruited in Peking Union Medical College Hospital from January 2011 to August 2018 and identified patients diagnosed with IgG4-RD complicating malignancies. Data regarding demographics, clinical features, treatment and prognosis of IgG4-RD patients complicating malignancies were collected and compared to those of age- and sex-matched controls.

Results: Among the 587 Chinese patients with IgG4-RD, 17 malignancies were identified. Ten of them developed malignancy after the diagnosis of IgG4-RD, given a standard incidence ratio (SIR) of 2.78 (95%CI 1.33-5.12). Multivariate logistic analysis indicated that autoimmune pancreatitis (OR= 6.230, 95%CI 1.559-24.907, p=0.010) was positively associated with malignancy, whereas eosinophilia (OR= 0.094, 95%CI 0.010-0.883, p=0.039) was negatively related with malignancies. During a median follow-up period of 61.4±26.4 months, all patients with IgG4-RD and malignancies survived.

Conclusion: An increased incidence of malignancy was found in Chinese IgG4-RD cohort. Autoimmune pancreatitis is a potential risk factor, whereas eosinophilia is a possible protective factor for complicating malignancies.

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FRI0509

COMPARISON OF MS SCORE AND HSCORE FOR THE DIAGNOSIS OF ADULT-ONSET STILL'S DISEASE ASSOCIATED MACROPHAGE ACTIVATION SYNDROME

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Background: Adult-onset Still's disease (AOSD) is a rare multisystemic auto-inflammatory disease.Macrophage activation syndrome (MAS) is a life-threatening complication of rheumatic disorders, including sJIA, adult-onset Still's disease (AOSD) and lupus. Many tools have been developed for the diagnosis of MAS, including HScore and MS score. Although some authors have tried to apply these tools for the diagnosis of ASOD-associated MAS, there are no studies comparing the diagnostic ability of HScore and MS score.

Objectives: We aimed to compare the capacity of HS score and MS score for the diagnosis of AOSD-associated MAS.

Methods: Patients diagnosed as AOSD during January,2012 and October,2019 in our hospital were retrospectively analyzed. Clinical and laboratory data were compared between patients with pure AOSD and those with AOSD associated MAS. HScore and MS score were calculated respectively and the diagnostic capacity of MAS was compared by means of receiver operating characteristic (ROC) curve analysis.

Results: We included 174 patients with pure AOSD and 35 patients with AOSD-associated MAS. Patients with AOSD-associated MAS were younger than those with pure AOSD (32+/-11.4 yrs vs 36.9+/-13.5 yrs, P=0.028). More death were observed among patients with AOSD-associated MAS (17.1% vs 3.4%, P=0.001). Patients with AOSD-associated MAS had higher HScore (median[range] 196[98-333] vs 68[33-156], P<0.001) and higher MS score (median[range] 1.05[-1.26-26.55] vs -1.17[-1.26-2.52],P<0.001) than those with pure AOSD.The difference of different parameters of these two groups of patients

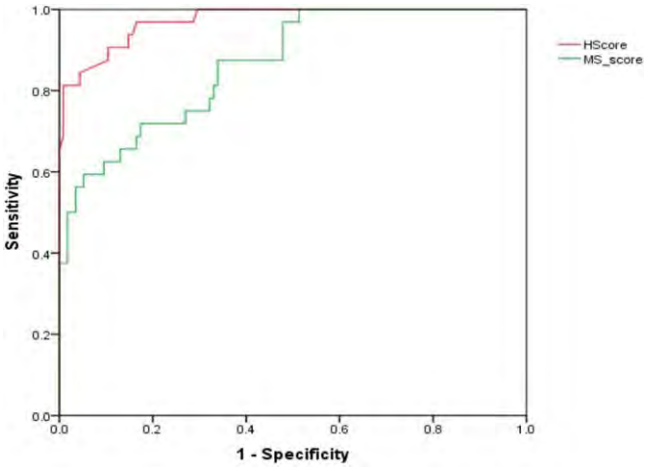


Figure 1. ROC curve of HScore and MS score. HScore=120, sensitivity=90.6%, specificity= 89.6%. MS score=-0.45,sensitivity=75%, specificity=73%. AUC-HScore=0.973, AUC-MS score=0.865, P<0.001

were detailed in Table 1 and Table 2. ROC curve analysis (Figure 1) revealed that HScore has stronger ability to diagnose AOSD-associated MAS compared with MScore (AUC=0.973 and 0.865 for HScore and MS score repectively, P<0.001). HScore≥120 perform best (sensitivity 90.6% and specificity 89.6%). MS score≥-0.25 yielded a sensitivity of 75% and a specificity of 73%.

Conclusion: HScore seems to perform much better than MS score for the diagnosis of AOSD-associated MAS in our cohort.

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Disclosure of Interests: None declared

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FRIDAY, 05 JUNE 2020

Public health, health services research, and health economics

FRI0510

THE FREQUENCY OF CONTRACEPTION DOCUMENTATION IN WOMEN ON AND OFF TERATOGENIC ANTI-RHEUMATIC MEDICATIONS IN THE RISE REGISTRY

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Background: Several of the most commonly prescribed medications for women with rheumatic disease are teratogens, posing a risk for pregnancy loss and birth defects if taken in pregnancy. To prevent these life-altering complications, it is important that all women taking teratogenic medications avoid pregnancy through abstinence or contraception.

Objectives: We sought to understand the accessibility to contraceptive data within the RISE Registry and to test whether, compared to other women,

those prescribed a teratogen would be more likely to have documentation of contraceptive.

Methods: Data were derived from Rheumatology Informatics System for Effectiveness (RISE), a national EHR-enabled rheumatology registry that passively collects data on all patients seen by participating practices. As of 2018, RISE held validated data from 1,113 clinicians in 226 practices, representing an estimated 32% of the U.S. clinical rheumatology workforce. Female patients between the ages 18-45 with an anti-rheumatic medication prescribed within the RISE system in 2018 were stratified into one of 3 groups: 1) Any teratogen (methotrexate, mycophenolate, mycophenolic acid, cyclophosphamide, leflunomide, thalidomide, lenalidomide); 2) Only pregnancy-compatible medications (hydroxychloroquine, azathioprine, or a TNF-α inhibitors [TNFi]); and 3) Any medication with unknown teratogenicity (non-TNF biologics and new small molecule medications). We identified the most recent contraceptive medication or device reported in 2018 using structured fields in the EHR. Contraceptive effectiveness was classified as 'highly effective' (IUD, Nexplanon, and surgical) and 'effective' (oral contraceptives, depo-provera, patch, ring), and unknown (type not reported). Statistical significance was assessed using Stata SE 15.1.

Results: In 2018, 110,359 women between the ages of 18-45 were prescribed an anti-rheumatic medication within the RISE Registry. Of these, 11,569 (10.5%) had a contraceptive documented at the last visit. The frequency of contraception documentation varied between practices, ranging from 0% to 28.7% (median 9.2%). Contraception was documented slightly less often in women receiving teratogens (9.8%) compared to women receiving only pregnancy-compatible medications (10.4%, p=0.04) and medications with unknown pregnancy risks (10.0%, p=0.67). The frequency of contraceptive documentation in women prescribed a teratogen varied significantly by race with white women having the highest rate (11.0%) compared to African-American women (7.4%, p<0.001), Hispanic women (5.5%, p<0.001), and Asian women (8.4%, p=0.08).

The type of contraceptive documented did not vary significantly between medication group. Highly effective contraception was rarely documented (1.4-1.6%) and moderately-effective hormonal contraceptives were more frequently documented (6.3-8.2%).

Conclusion: This study is limited to the analysis of structured fields within the RISE Registry, thereby missing contraceptive documentation within the clinician notes. Increased uniformity in documentation and/or analysis of visit notes will be essential to use the RISE Registry to study the implementation of published contraceptive guidelines. While the documentation of contraception identified in this analysis of the RISE Registry likely under-estimates actual contraceptive use, it reveals important gaps in care. Contrary to what was expected, women prescribed a teratogen were not more likely than other women to have a documented contraceptive. Additionally, important racial disparities in contraception documentation suggest that rheumatologists may not addressing reproductive health needs equally across patient populations.

Acknowledgments Disclaimer: This data was supported by the ACR's RISE Registry. However, the views expressed represent those of the authors, not necessarily those of the ACR

Disclosure of Interests: Megan Clowse Grant/research support from: GSK, Pfizer, Consultant of: UCB, Astra-Zeneca, Speakers bureau: UCB, Jing Li: None declared, Mehret Birru Talabi: None declared, Amanda Eudy: None declared, Gabriela Schmajuk Grant/research support from: Pfizer

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FRI0511

THE DESCRIPTIVE EPIDEMIOLOGY AND SECULAR TRENDS OF LOWER BACK PAIN PROCEDURES IN ROUTINE UK NHS CARE FROM 2000 TO 2016

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Background: The lifetime prevalence of lower back pain is between 60% and 70%, with surgical treatments spared for those not responding to other options.

Objectives: To investigate the age, gender and socio-economic status differences in back pain procedures in the UK between 2000, 2008 and 2016.

Methods: Data was obtained from primary care electronic medical records (CPRD GOLD) linked to English hospital admissions data. Lower back procedures in patients aged 35+ were identified using OPCS-4 codes for Decompression (Dc), Fusion (F), Therapeutic injections (TI) and Denervation (Dn). Standardised incidence rates (IR) of each type of lower back procedures were calculated per 10,000 CPRD registered person years for each age group, gender, region and SES strata in 2000, 2008 and 2016. IR were also calculated for combinations of age and gender. Negative binomial regression calculated incidence rate ratios (IRR) and 95% confidence intervals.

Results: The IR of lower back procedures was 21.5 [20.7, 22.3] per 10,000 person years in 2000. This doubled by 2008 (45.5 [44.5, 46.5]) and trebled by 2016 (62.5 [60.8, 64.2]). Number of events and incidence rates of each procedure type are shown in table 1 below. The incidence of Dn has increased 6-fold whilst Dc and F have doubled. Female (IR in 2016 of 73.99 [71.43, 76.61] vs 50.08 [47.90, 52.33] in men, IRR 1.50 [1.41, 1.59]) and age are associated with back procedure rates (figure 1). Large socio-economic differences were observed, with higher procedure rates seen in the most deprived areas. These differences did however narrow over time during the study period (figure 2).

Table 1. Event numbers and incidence rates of different types of lower back procedure.

	Fusion		Decompression		Therapeutic Injection		Denervation	
	Events	IR (95% CI)	Events	IR (95% CI)	Events	IR (95% CI)	Events	IR (95% CI)
2000	109	0.86 (0.71, 1.04)	466	3.69 (3.36, 4.04)	2035	16.11 (15.42, 16.82)	91	0.72 (0.58, 0.88)
2008	333	1.77 (1.58, 1.97)	1197	6.35 (6.00, 6.72)	6283	33.35 (32.53, 34.18)	596	3.16 (2.91, 3.43)
2016	159	1.93 (1.65, 2.26)	525	6.39 (5.85, 6.96)	3865	47.03 (45.56, 48.54)	487	5.93 (5.41, 6.48)

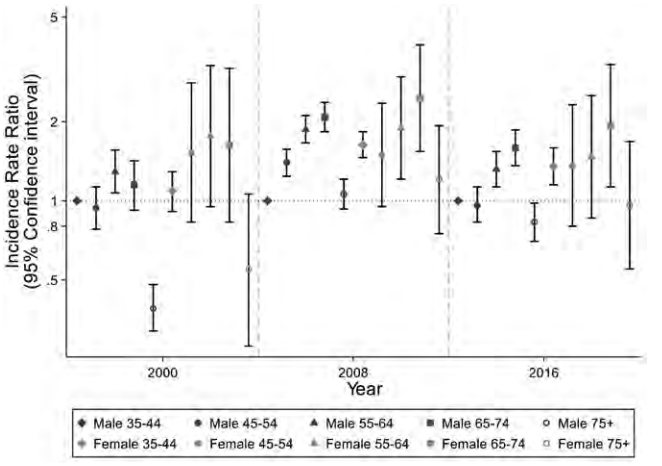


Figure 1. Age and Gender stratified incidence rate ratios of all back procedures in 2000, 2008 and 2016

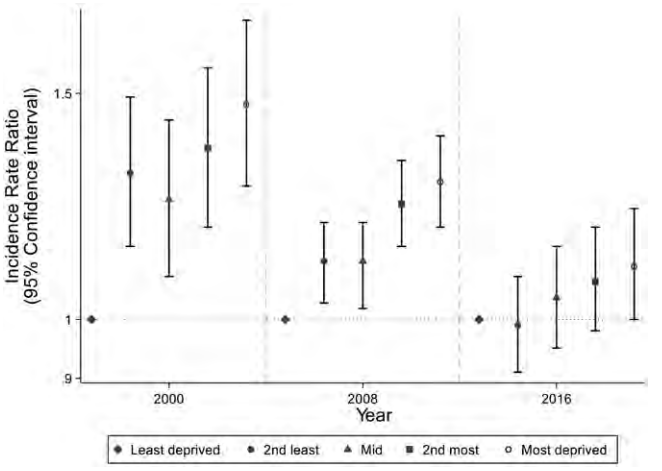


Figure 2. Deprivation status incidence rate ratios by year

Conclusion: The incidence of lower back procedures has more than trebled since 2000. Women are more likely to have lower back procedures than men, with patients aged 65-74 the most likely to have a procedure. Procedures in those aged 75+ have become more common over time, potentially increasing the risk of post-operative complications. Socio-economic differences in the incidence of low back procedures are probably related to the known higher prevalence of back pain in deprived areas. Whether the observed narrowing in socio-economic variation over time is explained by a reduced need or by lowered provision needs further research.

Disclosure of Interests: Danielle E Robinson: None declared, Jennifer Lane: None declared, Richard Craig: None declared, Andrew Judge: None declared, James Bailey: None declared, Dahai Yu: None declared, Kelvin Jordan: None declared, George Peat: None declared, Ross Wilkie: None declared, Alan Silman: None declared, Victoria Y Strauss: None declared, Daniel Prieto-Alhambra Grant/research support from: Professor Prieto-Alhambra has received research Grants from AMGEN, UCB Biopharma and Les Laboratoires Servier, Consultant of: DPA's department has received fees for consultancy services from UCB Biopharma, Speakers bureau: DPA's department has received fees for speaker and advisory board membership services from Amgen

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FRI0512 INTEGRATED CARE NETWORK AS A BUILDING STONE FOR SUSTAINABLE AND COMPREHENSIVE CARE FOR PATIENTS WITH ARTHRALGIA

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Background: Western countries experience an increasing demand for care, particularly for inflammatory arthritis (IA), while the healthcare budget decreases[1]. The innovative value-based primary care strategy[2] includes integrated care networks, where primary and secondary care bundle their expertise to improve patient value by providing the right care at the right place.

General practitioners (GPs) have difficulties recognising IA, leading up to only 20% IA diagnoses of all newly referred arthralgia patients. However, since IA needs to be treated as early as possible to overcome progression, it is worthwhile to analyse whether integrated care networks have an impact on patient outcomes and cost-effectiveness. Triage by a rheumatologist in a primary care setting is one of the most promising integrated care networks for efficient referrals[3].

Objectives: To assess the effect of triage by a rheumatologist in a primary care setting in patients suspect for inflammatory arthritis.

Methods: The present study follows a cluster randomized controlled trial design. The intervention, triage by a rheumatologist in a local primary care centre, will be compared to usual care. Usual care means that patients are referred to a rheumatology outpatient clinic based on the opinion of the general practitioner.

The primary outcome is the frequency of IA diagnoses assessed by a rheumatologist. Patient reported outcome measures (PROMs (EQ-5D)) and costs (work productivity (iPCQ) and healthcare utilization (iMCQ)) were determined at baseline, after three, six and twelve months. The target was to include 267 patients for each study group (power level 0.8). Since this study is still ongoing we can only show first results on the efficiency of referrals.

Results: In the period between February 2017 and December 2019 a total of 543 participants were included; 275 in the usual care group and 268 in the triage group. Mean age (51.3 ± 14.6 years) and percentage of men (23.6%) were comparable between groups (p_{age}=0.139; p_{sex}=0.330).

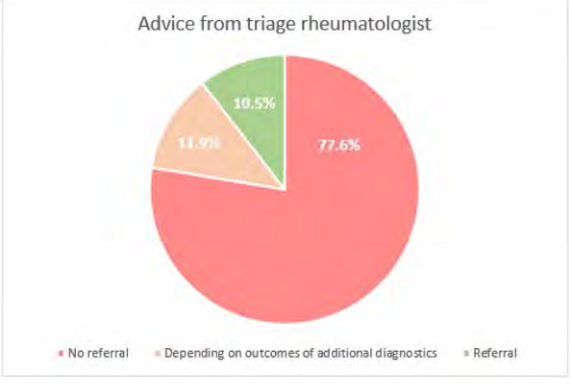


Figure 1: Advice on referral towards an outpatient rheumatology department according to the triage rheumatologist

The preliminary data show that the number of referred patients in the triage group is n=28 (10.5%) (Fig. 1). 32 patients (11.9%) were not referred directly but advice was given for additional diagnostics. Since all patients in the usual care group were referred there is a decrease of at least 77.6% in referrals when rheumatologists are participating in the integrated practice units.

Preliminary data on diagnosis are available for all referred patients in the triage group and for n=137 (49.8%) in the usual care group at this point. In the triage group n=18 (64.2%) of referred patients were diagnosed with IA (6.7% of the total study population). In the usual care group this was n=52 (38.0%) of the patients yet diagnosed.

Conclusion: These preliminary results of an integrated care network are promising. Approximately three-quarters of all patients can be withheld from expensive outpatient care. PROMs data and cost-effectiveness analysis will give clear answers in order to provide evidence whether this integrated care network can be implemented as a standard of care.

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Disclosure of Interests: None declared

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FRI0513 TREATMENT PERSISTENCE IN PATIENTS CYCLING ON SUBCUTANEOUS TUMOR NECROSIS FACTOR-ALPHA INHIBITORS IN INFLAMMATORY ARTHRITIS – A RETROSPECTIVE STUDY

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Background: Patient persistence with biologic treatment of rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS) (collectively inflammatory arthritis, IA) may be considered a proxy for efficacy, safety and treatment satisfaction. Patients who discontinue their first line of subcutaneous tumor necrosis factor alpha inhibitors (SC-TNFis) and switch to at least one subsequent line of SC-TNFi can be defined as cyclers.

Objectives: To assess persistence by line of therapy in Swedish IA patients cycling on SC-TNFis.

Methods: Using data from the Swedish Health Data Registers, adult IA patients initiating treatment with any available SC-TNFi (adalimumab, etanercept, certolizumab, or golimumab) between May 1st 2010 and October 31st 2016 were eligible for inclusion. Treatment persistence was derived using information from filled prescriptions (e.g. dispensing date, pack information, and defined daily dose) with a 60-day grace period. Analyses were restricted the first two lines of treatments (i.e. 1st and 2nd) in patients defined as SC-TNFi cyclers. Persistence estimates across treatment lines were assessed graphically using Kaplan-Meier curves. Unadjusted and adjusted marginal Cox proportional hazards models were fitted to estimate the relative risk of discontinuation across treatment lines, using robust sandwich covariance matrix estimates to account for intrapatient dependence (i.e. multiple treatment lines per patient). Covariates in the adjusted analysis included age, gender, diagnosis, year of treatment initiation, comorbidities, co-medication, and the number of specialized outpatient care visits and inpatient stays.

Results: Of 11,668 patients initiating SC-TNFi treatment, 3,181 patients were identified as cyclers. Among these, a majority were female (68%) with a mean age of 50 years; 46%, 28%, and 26% were diagnosed with RA, AS and PsA, respectively. Figure 1 indicated that, among cyclers, persistence with second line treatment was higher compared to first line treatment persistence. This finding was confirmed by the analyses accounting for intrapatient dependence. Both the unadjusted and the adjusted analyses showed that the relative

Table 1. Relative risk of discontinuing subcutaneous Tumor Necrosis Factor-α inhibitor treatment for IA in 2nd line treatment compared to 1st line treatment, by analysis population

Analysis population	N	Unadjusted analysis, HR [95%CI]	Adjusted analysis, HR [95%CI]
Cyclers overall	3,181	0.60 [0.57, 0.63]	0.59 [0.56, 0.62]
RA	1,479	0.62 [0.57, 0.67]	0.61 [0.56, 0.66]
PsA	891	0.60 [0.54, 0.67]	0.59 [0.53, 0.65]
AS	811	0.58 [0.52, 0.64]	0.55 [0.50, 0.61]

HR: Hazard Ratio, 95%CI: 95% confidence interval

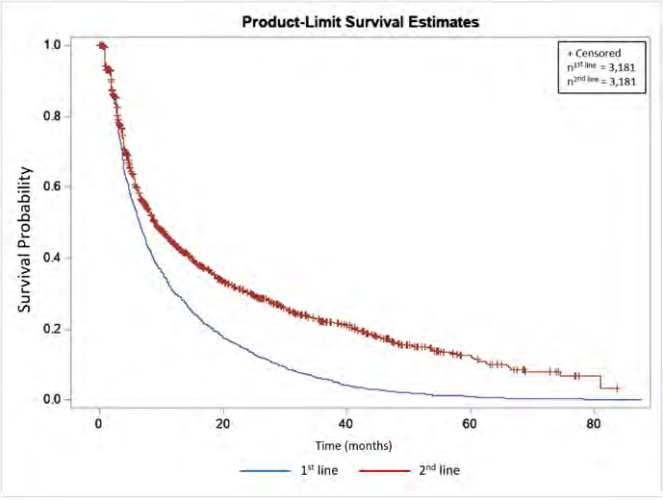


Figure 1. Persistence, among cyclers, with subcutaneous Tumor Necrosis Factor-α inhibitors treatment for IA by line of treatment

risk of discontinuing SC-TNFi treatment were significantly lower in 2nd line compared to 1st line (Hazard Ratio [HR]; 0.60 [0.57, 0.63] and 0.59 [0.56, 0.62], respectively). This finding was also consistent across IA indications (Table 1).

Conclusion: In this preliminary analysis of IA patients cycling on SC-TNFis, persistence was greater in 2nd line compared to 1st line treatment. The finding was consistent across all IA indications. Hence, IA patients who fail to respond, lose response, or for other reasons discontinue their 1st line treatment may still benefit from switching to an alternative SC-TNFi as a 2nd line therapy.

Disclosure of Interests: Johan Dalén Consultant of: Merck & Co., Inc. in conjunction with the development of this abstract. JD is an employee of ICON plc. ICON plc have received funding from several pharmaceutical companies involved in the marketing products for treatment of inflammatory arthritis., Amy Puenpatom Shareholder of: shareholder at Merck & Co, Inc, Employee of: Employed at Merck & Co, Inc., Karin Luttropp Consultant of: Merck & Co., Inc. in conjunction with the development of this abstract. KL is an employee of ICON plc. ICON plc have received funding from several pharmaceutical companies involved in the marketing products for treatment of inflammatory arthritis., Christopher Black Shareholder of: I own shares of MSD, Employee of: I am an employee of MSD

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FRI0514 USE OF OPIATE FOR HIP AND KNEE OSTEOARTHRITIS BEFORE AND AFTER JOINT REPLACEMENT SURGERY

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Background: Osteoarthritis of the hip and knee is one of the most common causes of reduced mobility. It also causes stiffness and pain. Opioids can offer pain relief but is usually used for severe acute pain caused by major trauma or surgery. The use of opioids for relief of chronic pain caused by arthritis has increased over the last few decades.[1]

Objectives: This study aims to investigate the use of strong opiates for patients with hip and knee osteoarthritis before and after joint replacement surgery, over a 13 years period in New Zealand.

Methods: This study included patients with osteoarthritis who underwent publicly funded primary hip and knee replacement surgeries in 2005-2017 in New Zealand. These records were identified from the National Minimum Dataset (NMD). They were cross referenced with the NZJR data to exclude the admissions not for primary hip or knee replacement surgeries. Patients without a diagnosis of osteoarthritis were excluded.

The PHARMS dataset was linked to the NMD to identify the use of strong opiates before and after surgeries. The strong opiates available for community dispensing in New Zealand and included in this study are: dihydrocodeine, fentanyl, methadone, morphine, oxycodone and pethidine. Use of opiate within three months prior to surgery and within 12 months post-surgery were examined by gender, age group, ethnicity, Charlson Comorbidity Index score and year of surgery. Differences by subgroup was examined with Chi- square test. Logistic regression model was used to calculate the adjusted odds ratios of strong opiate use before and after surgery compared with no opiate use.

Results: We identified 53,439 primary hip replacements and 50,072 primary knee replacements with a diagnosis of osteoarthritis. Of patients with hip osteoarthritis, 6,251 (11.7%) had strong opiate before hip replacement surgeries and 11,939 (22.3%) had opiate after surgeries. Of patients with knee osteoarthritis, 2,922 (5.8%) had strong opiate before knee replacement surgeries and 15,252 (30.5%) had opiate after surgeries.

The probability of patients with hip and knee osteoarthritis having opiate decreased with age, increased with Charlson comorbidity index score, and increased over time both before and after surgeries. Male patients with hip and knee osteoarthritis were less likely to have opiate than female patients both before and after surgeries. New Zealand Europeans with hip and knee osteoarthritis were more likely to receive opiate than other ethnic groups prior to surgeries, but were less likely to have opiate than Asians post-surgeries.

Patients who had opiate before surgeries were more likely to have opiate after surgeries than those who did not have opiate before surgeries. The odds ratio was 8.34 (95% confidence interval (CI): 7.87-8.84) for hip osteoarthritis and 11.94 (95% CI: 10.84-13.16) for knee osteoarthritis after adjustment for age, gender, ethnicity, year of surgery and Charlson comorbidity index score. Having opiate prior to surgeries also increased the probability of having opiate for 6 weeks or more after surgeries substantially. The adjusted odds ratio was 21.46 (95% CI: 19.74-23.31) for hip osteoarthritis and 27.22 (95% CI: 24.95-29.68) for knee osteoarthritis.

Conclusion: Preoperative opiate holidays should be encouraged. Multiple strategies need to be used to develop analgesic plans that allow adequate rehabilitation, without precipitating a chronic opiate dependence. Clinicians would also benefit from clear guidelines for prescribing strong opiates.

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FRI0515 MATERNAL AND PERINATAL OUTCOMES IN WOMEN WITH RHEUMATIC DISEASES – A 10-YEAR EXPERIENCE FROM A PORTUGUESE TERTIARY CENTRE

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Background: Pregnant women with rheumatic diseases (RD) represent a population at a higher risk for adverse pregnancy outcomes (APO). At our unit, these patients (pts) are surveilled at a high-risk pregnancy clinic, by both rheumatologists and obstetricians.

Objectives: To assess pregnancy outcomes in pts with RD surveilled at our unit over the last decade.

Methods: Single-centre observational retrospective study of pregnant women with RD followed at a portuguese tertiary centre between 2009 to 2019.

Results: Overall, 353 pregnancies (preg) in 295 pts with RD were managed at our unit. Table 1 summarizes clinical data and the main APO recorded. Systemic lupus erythematous (SLE) was the leading diagnosis followed by spondyloarthritis (SpA) and rheumatoid arthritis (RA). Antiphospholipid syndrome (APS) was diagnosed in 49 (13.9%) preg. We documented 284 (78%) live births (9 twin preg), 32 (10%) miscarriages, 7 (2%) elective abortions, 2 stillbirths (0.6%) and 2 ectopic preg; 35 (10%) of the overall preg were lost to follow up before delivery. Miscarriages occurred predominantly in pts with APS (34%). Fetal growth restriction (FGR) was recorded in 6% of preg, more than 1/3 of those in pts with APS. Preeclampsia (PE) complicated a total of 10 (4%) preg, 3 of those with superimposed HELLP syndrome, with SLE and APS accounting for 60% of the cases. Preterm births (15.5%) occurred mainly in APS, SLE and juvenile idiopathic arthritis (JIA) pts. Neonatal lupus ensued in 3 (3.8%) preg positive for anti-Ro/La antibodies. No neonatal deaths were recorded. SpA and RA represented the diseases which flared the most considering both pregnancy and the postpartum period.

Table 1. Pregnancy outcomes by disease

Main diagnosis	N, %	Gest age at delivery (weeks)	Miscarr	FGR	PE	Preterm births	Flares in preg	Flares in PP
SLE	116, 32.9	38±2.3	13/110, 11.8	6/82, 7.3	5/78, 6.4	15/76, 21.1	16/92, 17.4	5/79, 6.3
SpA	60, 17	39±2.6	2/55, 3.6	5/44, 11.4	1/45, 2.2	5/40, 12.5	18/40, 45	5/23, 21.7
RA	51, 14.4	39±1.2	6/49, 12.2	1/35, 2.9	1/33, 3	1/29, 3.4	10/37, 27	7/30, 23.3
Vasculitis	25, 7.1	38±1.8	1/24, 4.2	1/21, 4.8	0/19, 0	4/21, 19	7/23, 30.4	2/17, 11.8
Primary APS	22, 6.2	38±1.6	3/22, 13.6	1/17, 5.9	1/16, 6.3	2/16, 12.5	NA	NA
JIA	17, 4.8	38±2.5	1/17, 5.9	0/12, 0	0/11, 0	4/12, 33.3	2/13, 15.4	1/8, 12.5
UCTD	15, 4.2	39±1.5	2/15, 13.3	0/11, 0	1/10, 10	1/11, 9.1	0/15, 0	0/15, 0
Primary Sjögren Syndrome	12, 3.4	39±1.4	0/11, 0	0/9, 0	0/10, 0	1/9, 11.1	1/8, 12.5	0/6, 0
Others	35, 9.9	38±2.3	4/31, 12.9	2/20, 10	1/18, 5.6	3/18, 16.7	4/27, 14.8	1/22, 4.5
Total	353, 100	38±2.2	32/334, 9.6	16/251, 6.4	10/240, 4.2	36/232, 15.5	58/255, 22.7	21/200, 10.5
Secondary diagnosis								
APS	27	37±2.7	8/26, 30.8	5/16, 31.3	2/12, 16.7	5/15, 33.3	NA	NA
Sjögren Syndrome	9	37±2.5	1/9, 11.1	1/7, 14.3	0/7, 0	3/6, 50	NA	NA

Legend - gest: gestational; miscarr: miscarriages; NA – not applicable; PP: postpartum; preg: pregnancy; UCTD - Undifferentiated connective tissue disease. Continuous variables are presented as mean±SD. Categorical variables as n/mN, % - modified(m)N stands for total N – (not applicable+missing data); "Others" accounts for diagnosis with N≤6, such as APS non criteria, mixed connective tissue disease, myositis, overlap syndromes, Still's disease and systemic sclerosis.

Conclusion: In pregnant women with RD, it is of vital importance to be aware of the increased risk for APO. In our cohort, APS and SLE were the conditions most associated with APO, while SpA and RA were responsible for most maternal flares. Nevertheless, the majority of these pts, surveilled by a multidisciplinary team, had successful gestations.

Disclosure of Interests: None declared

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FRI0516 FACTORS ASSOCIATED WITH DECREASED CERVICAL CANCER SCREENING IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that carries an increased risk for both viral illnesses and malignancies, including a greater risk for both human papilloma virus (HPV) infection and cervical cancer. Due to this increased risk, the American Society of Colposcopy and Cervical Pathology guidelines for SLE patients recommend more frequent cervical cancer screening. Few studies have examined patient characteristics associated with decreased cervical cancer screening in patients with autoimmune disease, specifically SLE.

Objectives: To estimate cervical cancer screening rates in women with recently diagnosed SLE, and to identify characteristics associated with decreased screening.

Methods: We identified women with an initial diagnosis of SLE in the United States MarketScan Commercial Claims and Encounter (CCAE, age 18-64) administrative claims database. We included patients with at least three claims with a lupus diagnosis (first and last at least >90 days apart), no lupus claims within the year before initial claim, and who had been on antimalarial drugs for at least 90 days. We excluded all patients with a previous claim for hysterectomy.

Cervical cancer screening was ascertained using diagnosis and procedure codes within 1 year before and 2 years after the first SLE claim. Our covariates included the year of first SLE claim (2001-2014), age at first SLE claim, comorbidity score, insurance type, geographical region, and prescriptions for multiple types of corticosteroids. Control patients included age-matched females without autoimmune disease. Univariate comparison and multivariate logistic regression models were built to evaluate determinants of screening.

Results: We included 4,316 SLE patients (median age 45) and 86,544 control patients. The screening rate in SLE patients was 73.4% vs 58.5% in the controls (P < 0.001). The screening rate was 71% in 2001, increased to 75% in 2004, then decreased to 70% in 2014 (trend P =0.005). In the multivariate model the following factors were associated with decreased cervical cancer screening: year of first SLE claim 2012-2014 versus 2001-2005 (odds ratio (OR) 0.67, 95% confidence interval (CI) 0.53 – 0.84, P < 0.001); older age 61-64 versus 21-30 (OR 0.27, 95% CI 0.19 – 0.39, P < 0.001); comorbidity score of ≥2 versus <2 (OR 0.71, 95% CI 0.6 – 0.83, P < 0.001); and use of corticosteroids for ≥ 90 days versus <90 days (OR 0.73, 95% CI 0.59 – 0.9, P = 0.003). Insurance type and geographical region were not associated with cervical cancer screening.

Conclusion: About three quarters of women with SLE underwent cervical cancer screening within 3 years of their first lupus claim, at higher rates than controls. However, there was a concerning downward trend in screening rates in recent years. In addition, higher risk populations for cervical cancer (older age, increased comorbidities, and longer duration of corticosteroids) had lower screening rates. These findings highlight the need to enhance education for healthcare providers to improve utilization of screening in women with SLE at high risk of cervical cancer.

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FRI0517 POSSIBLE EARLY DETECTION OF ADVERSE EVENTS USING A STRUCTURED, STANDARD, 60-SYMPTOM CHECKLIST ON A MULTIDIMENSIONAL HEALTH ASSESSMENT QUESTIONNAIRE (MDHAQ)

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Background: Adverse events of medications are reported to account for 5% of hospital admissions in the USA, including 10% in the elderly, despite extensive warnings to patients by health professionals and pharmacies concerning the problem. Some adverse events are relatively obvious, such as a severe rash or severely abnormal laboratory test. However, many adverse events are common symptoms, such as headache or fatigue, which may not necessarily be recognized as adverse events, particularly in elderly patients with many comorbidities. In clinical trials and other clinical research, a structured, standard, protocol-driven symptom checklist is recorded according to the "scientific method." In routine care, by contrast, recognition and recording of adverse events is elicited by health professionals at patient encounters or contact initiated by patients between visits, as "subjective" medical history information, which may be highly variable. Use of a standard symptom checklist on an electronic patient questionnaire has been reported in oncology, pulmonology and other specialties, but not in rheumatology. A multidimensional health assessment questionnaire (MDHAQ) includes a standard 60-symptom checklist, to recognize comorbidities, provide a review of systems, and serve on a fibromyalgia assessment screening tool (FAST3) as a clue to identify patients with fibromyalgia. The MDHAQ 60–symptom checklist can identify new symptoms after initiation of a medication which may be adverse events.

Objectives: To analyze an MDHAQ 60-symptom checklist as a cost-effective approach to recognize medication-associated adverse events.

Methods: All patients at one site complete an MDHAQ at each visit, which includes a standard, structured 60-symptom checklist, in addition to RAPID3 (routine assessment of patient index data) and FAST3. Paper MDHAQs from routine care are scanned into an Epic electronic medical record (EMR) and copied into a data repository for retrospective analyses. A list of common adverse events of many specific DMARDs (disease-modifying antirheumatic drugs) and biological agents used to treat rheumatoid arthritis (RA) was compiled from websites of the FDA, pharmaceutical companies, and Up-to-date.® Most listed symptoms are found on the structured MDHAQ 60-symptom checklist. A retrospective review of scanned MDHAQs at the first visit was conducted to recognize the presence or absence of self-reported symptoms which were listed as common adverse events for specific DMARDs on the MDHAQ 60-symptom checklist, using simple descriptive statistics. Only methotrexate (Mtx) is presented here due to space limitations.

Results: All symptoms listed as adverse events of specific DMARDs were reported at higher frequencies in 379 DMARD-treated RA patients or 153 Mtx-treated patients, compared to 149 DMARD-naïve patients (Table). More than 30% of DMARD-treated patients reported headache and/or unusual fatigue, 27% anxiety; 10-20% cough, dizziness, hair loss, nausea, skin rash or hives,

Symptom listed on MDHAQ/MEDI60	DMARD naïve N=149 (28%)	DMARD treated N=379 (72%)	Methotrexate N=153 (29%)
Headache	28%	36%	36%
Unusual fatigue	31%	33%	34%
Anxiety	23%	27%	
Cough	16%	18%	
Dizziness	14%	18%	20%
Hair loss	10%	17%	19%
Nausea	11%	13%	18%
Skin rash or hives	11%	14%	13%
Stomach pain/cramps	9%	16%	15%
Eye problems	9%	13%	14%
Anorexia/weight loss	10%	16%	17%
Diarrhea	5%	9%	8%
Fever	5%	8%	7%
Mouth sores	3%	7%	8%

stomach pain or cramps, eye problems, and/or weight loss; and 5-10% diarrhea, fever, and/or mouth sores (Table). Similar proportions were seen for Mtx-treated patients, although anxiety and cough were not listed as specific adverse events.

Conclusion: The MDHAQ symptom checklist may prove valuable to detect adverse events of high-risk medications, including on an electronic MDHAQ, which could be completed at home for 12 weeks after initiation of a new medication as a cost-effective approach for early detection of adverse events.

Disclosure of Interests: Kyle Schroeder: None declared, Sara Abu Mehsen: None declared, Isabel Castrejon: None declared, Theodore Pincus Shareholder of:

Dr. Pincus holds a copyright and trademark on MDHAQ and RAPID3 for which he receives royalties and license fees from profit-making organizations, all of which are used to support further development of quantitative clinical measures for patients and health professionals.

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FRI0518

BIOSIMILAR INFLIXIMAB THERAPY IN RHEUMATOID ARTHRITIS, SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS: A LONG-TERM FOLLOW-UP STUDY

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Background:

Objectives: REFLECT study has been carried out to assess in real life the use of CT-P13, the first monoclonal antibody biosimilar to infliximab (IFX) approved in France. Long-term real-life data on CT-P13 use are limited in patients (pts) suffering from rheumatic diseases and inflammatory bowel diseases.

Methods: REFLECT is a multicenter, prospective, observational study conducted in France which aims to describe characteristics of pts' receiving CT-P13 and to assess its safety and effectiveness in real-life conditions. Eligible pts for inclusion were pts (≥ 6 years old) with RA, axSpA, PsA, and inflammatory bowel disease treated with CT-P13. IFX naive pts (IFX-N) or those having switched from IFX originator to CT-P13 were enrolled (IFX-S). An intermediate result in pts with rheumatic diseases using descriptive statistical analyses from inclusion after 18-month-follow-up period are described below.

Results: From 19 October 2016 to 31 January 2019, 1321 pts were included by 70 centres, and 616 pts with rheumatic diseases were analysed: 132 RA (25.0% males; mean age: 61.5 ± 10.5; median time since diagnosis: 12.9 years), 398 axSpA (59.0%; 48.0 ± 13.1 years; 10.7 years, respectively), and 86 PsA (41.9%; 53.0 ± 14.1 years; 10.3 years). Previous bDMARDs other than IFX were reported in 40.1%, 42.1% and 47.4% of RA, axSpA and PsA pts, respectively. More than ⅓ of pts switched from the IFX originator to CT-P13 (40.2% of RA, 42.7% of axSpA and 35.5% of PsA). At the first administration of CT-P13, the majority of IFX-N pts had active disease (92.0% of RA, 76.4% of axSPA and 55.0% of PsA) compared to IFX-S pts (39.5% of RA, 23.1% of axSPA and 26.3% of PsA). At the first infusion of CT-P13, the median DAS28 scores were 4.8 and 2.4 for RA pts in IFX-N and INF-S pts, and 4 and 2.2 for PsA pts, respectively. In axSpA pts, the median BASDAI at baseline were 5.6 and 2.4 and the median BASFI was 5.3 and 2.8 in IFX-N and IFX-S pts, respectively. From the first administration of CT-P13 to 18 months follow-up the median DAS 28 decreased (-1 point) in both IFX-N pts and IFX-S for RA pts; for axSPA pts the BASFI and BASDAI scores decreased by -2 and -1, respectively in IFX-N and remained stable in IFX-S.

The analysis of pts suffering from PsA has not been reported due to the small number of patients with a follow-up at 18 months (4 IFX-N pts and 1 IFX-S pts).

Table 1. Reasons for treatment withdrawing

	RA		Ax Spa		PsA	
IFX pts (N)	IFXn (N=16)	IFXs (N=9)	IFXn (N=28)	IFXs (N=30)	IFXn (N=5)	IFXs (N=6)
Missing	0	0	1	0	0	0
Remission	0 (0.0%)	2 (22.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Therapeutic failure	9 (56.3%)	3 (33.3%)	18 (56.3%)	19 (63.3%)	3 (60.0%)	4 (66.7%)
Intolerance	2 (12.5%)	1 (11.1%)	3 (11.1%)	2 (6.7%)	0 (0.0%)	0 (0.0%)
Other	5 (31.3%)	3 (33.3%)	6 (22.2%)	9 (30.0%)	2 (40.0%)	2 (33.3%)

Table 2. Safety data

	RA (N=132)	ax Spa (N=398)	PsA (N=86)
Patients with at least one adverse event (AE)	49 (37.1%)	141 (35.4%)	25 (29.1%)
Patients with at least one serious AE	11 (8.3%)	19 (4.8%)	1 (1.2%)
Patients with at least one allergic infusion reaction†	3 (2.3%)	9 (2.3%)	-
Patients with at least one infection‡	3 (2.3%)	4 (1.0%)	1 (1.2%)

† Including acute and delayed hypersensitivity reactions

‡ Including severe infections, tuberculosis, opportunistic infections, hepatitis.

78,8%, 82,9% and 87,2% remain on treatment with CT-P13 in RA, AxSpa and PsA pts respectively. The reasons for treatment withdrawing are reported in table 1. The safety data are presented in Table 2.

Conclusion: The results from this long-term follow-up period show that CT-P13 was effective in inducing and maintaining remission in both naive and switched patients. This real-life study did not highlight any new safety concerns.

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FRI0519

IMPROVING RHEUMATOID ARTHRITIS COMPARATIVE EFFECTIVENESS RESEARCH USING THE TARGET TRIAL EMULATION FRAMEWORK: A SYSTEMATIC REVIEW

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Background: Methods used in observational comparative effectiveness research (CER) are highly variable. Target trial emulation is an intuitive design approach that encourages researchers to formulate their question as a hypothetical randomised controlled trial (RCT), or the "target trial." Using observational data to emulate the target trial helps avoid common biases and has been shown to better align results with actual RCTs.

Objectives: We systematically reviewed observational CER studies in rheumatoid arthritis to provide examples of design issues that might have been avoided by using target trial emulation.

Methods: We searched for head-to-head effectiveness comparisons of biologic DMARDs in RA. Study designs were reviewed for components of target trial emulation: 1) eligibility criteria, 2) treatment strategies, 3) assignment procedures, 4) follow-up period, 5) outcome, 6) causal contrasts of interest (i.e., intention-to-treat or per-protocol effect), and 7) analysis plan. Reported methods were taken as the "emulation" of a corresponding target trial, to assess design issues that might introduce bias.

Results: We found 31 CER studies, the majority of which had one design issue belonging to one of the 7 protocol components (Table 1). The most common issues were: 1) 17 out of 31 studies used post-baseline information to define baseline eligibility (e.g. requiring ≥1 follow-up), which can bias results; 2) 26 out of 31 studies did not declare their causal contrast of interest, which is often made difficult by issue 1 and impacts data analysis and interpretation; and 3) 9 out of 31 studies used statistical selection of confounders rather than pre-defining them, which can also introduce bias (e.g. through adjustment of collider or intermediate variables).

Table 1. Design issues identified in 31 studies and reasons why they do not correspond to well-defined "target trials"

	Design issues identified in study methods	How these issues can be conceptualized in a RCT protocol
1. Eligibility criteria	Post-baseline data requirement (17 out of 31 studies).	Impossible to use future data at enrolment.
	Differential eligibility for each arm (5 studies).	Breaks the notion of one group of people randomized to 2+ arms.
2. Treatment strategies	Mixing prevalent users and new users (1 study)	Impossible to assign/randomize to "*having* used drug A for X months"
	Not defining treatment strategies beyond "initiate drug A at baseline" (31 studies)	Implied protocol leaves everything up to the treating physician and patient
3. Assignment procedures	Weak substantive justification for confounder selection (31 studies)	Broken randomization (due to insufficient emulation of randomization)
4. Follow-up	Unspecified follow-up duration in longitudinal analyses (5 studies)	Infeasible to conceive an RCT with unspecified duration. Analysis results may lack interpretability.
5. Outcome	Joint outcome of remaining on treatment *and* having a good response, to avoid missingness (3 studies)	Unusual outcome for RCT although technically possible.
6. Causal contrasts (i.e., ITT or per-protocol effect)	Failure to clarify the estimand (26 studies)	Problem also common in RCTs
7. Analysis plan	ITT-type analysis among those with follow-up	Deviates from the ITT principle (all randomized should be analysed)
	Per-protocol analyses did not account for post-baseline selection bias	Problem also common in RCTs

Conclusion: The majority of observational CER studies in RA have one or more design issues that may introduce bias. Target trial emulation is a structured approach for designing observational CER studies that helps to avoid common biases.

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FRI0520

HOSPITALIZATIONS FOR HEMATOLOGICAL MALIGNANCIES WITH RHEUMATIC DISEASES: A NATIONAL INPATIENT SAMPLE ANALYSIS OF TEN YEARS (2005-2014)

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Background: Several rheumatic conditions have been associated with increased risk of malignancies, especially hematopoietic and lymphoproliferative malignancies. Rheumatoid arthritis has been associated with a relative risk of 1.5-4 for the development of hematological malignancies (HM)1. A variety of immunosuppressive and immunomodulatory medications have also been linked to increased risk of HM2. Moreover, with advances in the field of biologic agents being used in the treatment of rheumatic diseases (RD), the landscape keeps changing. To our knowledge, data on general trends of HM as well as in RD is limited.

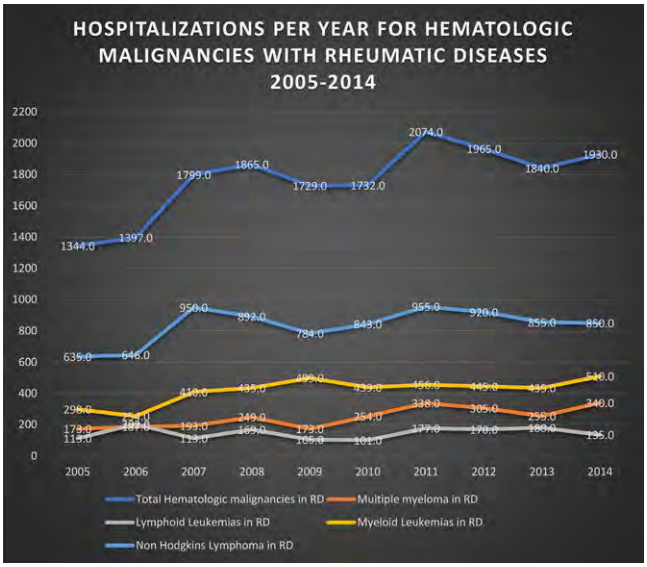
Objectives: Our study aimed to determine the trends of hospitalizations for HM in patients with RD.

Methods: We identified admissions with HM with underlying RD (including rheumatoid arthritis systemic lupus erythematosus, inflammatory myositis, scleroderma, polymyalgia rheumatica, and connective tissue disease) from the NIS database using International Classification of Diseases, Ninth Revision (ICD-9) diagnosis codes from years 2005 to 2014. The primary outcome was the trends in hospitalizations for HM. We studied the yearly trends and the types of HM among hospitalizations with or without RD.

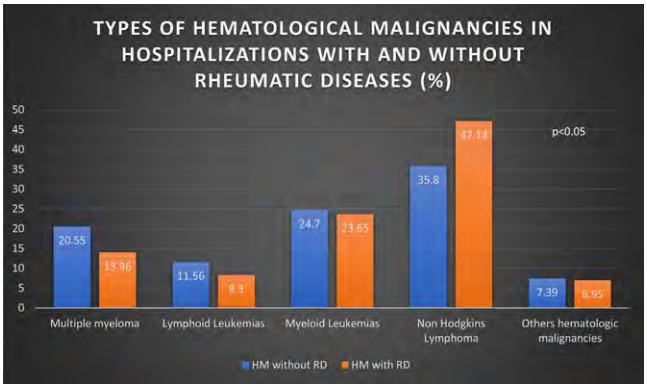
Results: 906,556 weighted hospitalizations were estimated for HM, and amongst those, 17,675 had underlying RD. The demographic analysis suggested that the average age of hospitalizations with HM and RD was higher, were more often females, and a higher number of comorbidities (Table 1). The average number of admissions remained stable for HM with and without HM, as described in Graph 1. There was a significant difference in the frequency of various subtypes in patients with and without RD (Graph 2). Non-Hodgkin's Lymphoma was the most common subtype in HM without and with RD (35.8% and 47.14%).

Table 1. Baseline Demographics of Hospitalizations for HM with and without RD

Characteristics	HM without RD	HM with RD	p value
Age (in years ± SD)	62.05 ± 0.23	67.41 ± 0.29	<0.05
Gender (%)			<0.05
Males	55.99	33.35	
Female	44.01	66.65	
Race (%)			<0.05
White	71.24	75.88	
Black	12.27	11.31	
Hispanic	10.21	7.62	
Asian or Pacific Islander	2.66	2.01	
Native American	0.43	0.62	
Other	3.18	2.55	
Charlson Category (%)			<0.05
2	55.07	3.76	
3	21.83	46.93	
4	11.55	23.71	
5	5.54	12.88	
>=6	6.01	12.73	
Type of Insurance (%)			<0.05
Medicare	49.49	66.35	
Medicaid	10.93	6.04	
Private	35.8	26.19	
Self-Pay	3.78	1.42	



Graph 1. Hospitalizations per year for Hematologic Malignancies With Rheumatic Diseases 2005-2014



Graph 2. Types Of Hematological Malignancies In Hospitalizations With And Without Rheumatic Diseases (%)

Conclusion: To our knowledge, this is the first study to analyze trends in HM with RD. There has not been any significant change in the number of hospitalizations for HM from 2005-2014 with or without RD. The most common HM in admissions with RD were Non-Hodgkin's Lymphomas (NHL) and myeloid leukemias, followed by multiple myeloma. The trends suggest no significant change in subtypes of HM over the study period.

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FRI0521 EARLY RECOGNITION OF PATIENTS WITH AXIAL SPONDYLOARTHRITIS BY USING A PRACTICAL REFERRAL SYSTEM – EVALUATION OF THE RECENTLY PROPOSED 2-STEP STRATEGY

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Background: Chronic back pain (CBP) of the inflammatory type (IBP) is frequently reported in axSpA but also in the general population.
Objectives: We evaluated a recently proposed two-step referral system for early recognition of axSpA (concentrating on patients ≤45 years with chronic back pain who present with buttock pain, improvement by movement, psoriasis, positive testing for HLA-B27) in primary care and compare it to other combinations of symptoms and SpA-related items.
Methods: Consecutive patients ≤45 years who presented in PC to general practitioners or orthopedic surgeons working in PC with back pain lasting ≥2 months who had not been diagnosed before received questionnaires (Q1) relevant for the referral process. Thereafter, the PC physician asked the same questions in a separate questionnaire (Q2), including the decision on HLA-B27 testing. All patients were then referred to two experienced rheumatologists in a tertiary center who performed a complete workup including clinical, laboratory and imaging with radiographs and magnetic resonance imaging (MRI) examinations before their final diagnosis of axSpA or non-SpA (Q3).
Results: A total of 320 patients (mean age 35.9±10.3 years) was recruited. The proposed referral strategy (prS) was fulfilled by 127 patients in Q1 (39.7%), 160 in Q2 (50%), 102 by both, Q1 and Q2 (31.9%), and 83 with either Q1 or Q2 (25.9%). Overall, 47 patients were diagnosed with axSpA by the rheumatologist at Q3 (14.7%), 66% of which were male, mean age 34.7±10.1 years, 70.2% HLA-B27 positive, mean CRP 0.8±1.4mg/dl, mean ASDAS 3.2±0.8, mean BASDAI 5.1±2.0. Of these, 37 patients had fulfilled the prS in Q1 or Q2 (78.7%), and 31 in both Q1 and Q2 (66%), respectively. In the latter, the HLA-B27 prevalence was significantly higher (27/31, 87.1%) as compared to patients diagnosed with axSpA at Q3 but who did not fulfill the prS in Q1 and Q2 (5/16, 31.3%) (p<0.001).
The sensitivity and specificity of the prS was 78.7% and 69.2% in Q1, 78.7% and 62.2% in Q2, and in both, Q1 and Q2, 66% and 74%, respectively.
AxSpA patients correctly identified by the prS in Q1 and Q2, were significantly more frequently positive for HLA-B27 and CRP and fulfilled more frequently the ASAS definition of inflammatory back pain in Q3.
Conclusion: A simple two-step referral strategy using a combination of clinical features for identifying axSpA patients in PC without laboratory and imaging examinations was confirmed in a large population from daily practice. This strategy performed well as selection for referral at the patient and PC physician level.
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Disclosure of Interests: Xenofon Baraliakos Grant/research support from: Grant/research support from: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB and Werfen, Consultant of: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB and Werfen, Speakers bureau: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB and Werfen, Styliani Tsiami: None declared, Doris Morzeck: None declared, Kirill Fedorov: None declared, Uta Kiltz Grant/research support from: AbbVie, Amgen, Biogen, Novartis, Pfizer, Consultant of: AbbVie, Biocad, Eli Lilly and Company, Grünenthal, Janssen, Novartis, Pfizer, UCB, Speakers bureau: AbbVie, MSD, Novartis, Pfizer, Roche, UCB, Juergen Braun Grant/research support from: Abbvie (Abbott), Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, Eli Lilly and Company, Medac, MSD (Schering Plough), Mundipharma, Novartis, Pfizer (Wyeth), Roche, Sanofi- Aventis, and UCB Pharma, Consultant of: Abbvie (Abbott), Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, EBEWE Pharma, Eli Lilly and Company, Medac, MSD (Schering-Plough), Mundipharma, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis, and UCB Pharma, Speakers bureau: Abbvie (Abbott), Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, EBEWE Pharma, Eli Lilly and Company, Medac, MSD (Schering-Plough), Mundipharma, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis, and UCB Pharma
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FRI0522 OPIOIDS PRESCRIPTION AT DISCHARGE IN HOSPITALIZED PATIENTS: AN ANALYSIS FROM A RHEUMATOLOGY WARD OF A SWISS TERTIARY HOSPITAL

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Background: Opioids prescription for non-cancer pain has come under intense scrutiny as opioids abuse has become a major public health issue. Chronic opioid use is common among patients with rheumatic diseases. There are data showing that opioids are associated with a higher mortality in osteoarthritis patients receiving joint replacement. However, more data are needed on opioids use and prescription in rheumatology inpatients [1].
Objectives: To evaluate inpatient characteristics on opioid prescription at discharge from our rheumatology ward in 2017 and 2019.
Methods: We prospectively recorded analgesics prescription patterns of paracetamol, nonsteroidal anti-inflammatory drugs (NSAIDs), weak opioids (tramadol/codeine) and strong opioids at discharge for all patients hospitalized in the Rheumatology Department from May to October 2017 and from October to December 2019. Statistical analyses consisted of descriptive statistics and univariate/multivariate logistic regression. P≤0.05 was considered statistically significant.
Results: We analysed 240 hospital inpatient stays of 223 patients (mean age 64 years). At discharge, 25% of patients were respectively on weak opioids (tramadol/codeine) and 23% were on strong opioids, at a fixed dosage.
Overall, a minority of patients were on opioids monotherapy (20% for weak opioids and 22% for strong opioids), the majority receiving combined treatments with WHO class I analgesics.
The highest rate of opioids prescription at discharge was observed in patients hospitalized for severe low back pain (40%) and osteoporotic fracture (30%). At discharge, all patients transferred to a nursing home and 35% of patients transferred to a transitional care unit were on opioids compared to only 16% of the patients discharged home. The majority of patients being on opioids when transferred to a transitional care unit were prescribed opioids when discharged home (86%).
Opioids prescription at discharge was negatively associated with home discharge in multivariate analysis (0.23, 0.09 to 0.55, adjusted OR, 95%CI), Table 1. There was no significant association between inpatient stay length and opioids prescription at discharge. Between 2017 and 2019, we observed a non-significant decrease in opioids prescription at discharge (absolute difference -4.7%).

Table 1.

	OR (95% CI)	Overall P value
Inpatient stay duration	0.87 (0.82, 0.93)	<0.001
Opioids prescribed at discharge	0.23 (0.09, 0.55)	0.001
Patient's location before admission:		0.02
Home	1.0 (réf.)	
A&E Department	0.25 (0.10, 0.65)	
Other Department	0.35 (0.05, 2.53)	
Charlson comorbidity index	0.76 (0.82, 0.93)	
Main diagnosis (only significant conditions displayed):		0.03
Low back pain, sciatica	1.0 (réf.)	
Abarticular conditions	0.03 (0.002, 0.47)	
Osteoporotic fracture	0.17 (0.05, 0.52)	

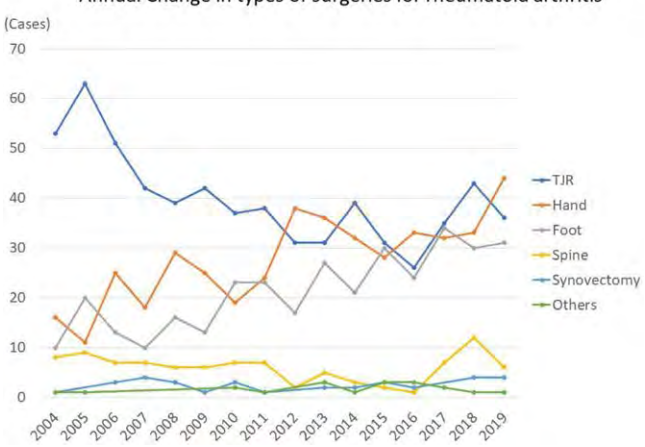
Predictors of home discharge. Multivariate logistic regression analysis. N=223.

Conclusion: Analysis of opioids prescription from a Swiss rheumatology service of a tertiary hospital show frequent opioids prescription at inpatients discharge, mainly for non-inflammatory disorders. Opioids prescription negatively predict home discharge.
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Disclosure of Interests: Alexandre Dumusc: None declared, Flore Valerio: None declared, Thomas Hügle Grant/research support from: Abbvie, Novartis, Consultant of: Abbvie, Pfizer, Novartis, Roche, Lilly, BMS
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FRI0523 THE RECENT TREND OF ORTHOPAEDIC SURGERIES FOR RHEUMATOID ARTHRITIS. AN ANALYSIS OF 1569 CASES FROM 2004 TO 2019.

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Fig1



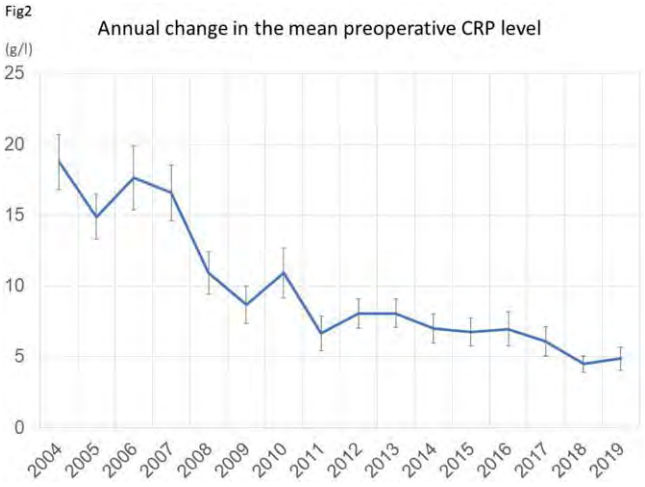
Background: In Japan, Methotrexate (MTX) has been approved in 1999, the first biologic DMARD (bDAMRD) in 2003, and the Janus kinase (JAK) inhibitors have been used since 2013. Although it is expected that the recent advancement of drug therapy would contribute the decrease in the incidence of orthopaedic surgeries by preventing structural damages[1, 2], we are still facing a considerable number of patients who require surgical interventions[3].

Objectives: To investigate the recent trends of patient's background who underwent the orthopaedic surgery for rheumatoid arthritis, number of orthopaedic intervention, and the type of the surgery.

Methods: We reviewed the records of 1569 patients with RA who underwent orthopedic surgeries between 2004 and 2019 in our institution. The mean age of patients was 62.8 (22-88) years-old with disease duration of 20.9 (0.5-64) years. Data of these patients such as age, disease duration, medication (Glucocorticoid; GC, MTX, b/tsDMARD), type of surgeries (total joint replacement; TJR, hand surgery, foot surgery, spine surgery, and others), and preoperative serum CRP level were collected. We analyzed the annual change of these demographic and clinical data. Then, we compared them between CRP negative (<1.5g/l) and CRP positive group. Cochran-Armitage trend test,χ square test, or unpaired T-test was performed for statistical analysis. P <0.05 was considered significant.

Results: Among all cases, 426 cases (27.2%) were treated with b/tsDMARDs at the time of operation. MTX and GC were used in 937 cases (59.7%) and 1015 cases (64.7%), respectively. The mean age and disease duration of RA showed an increasing trend, although the CRP level was dramatically decreased during the study period. While the rate of MTX use has not changed significantly (p=0.102), the number of cases treated by b/ts DMARD increased significantly to 46.7% (p<0.001). In contrast, the rate of GC use dicreased significantly (p<0.001). Although the annual number of surgeries have not changed, the proportion of cases who performed TJR decreased dramatically (59.6% in 2011, 29.5% in 2019), and the surgeries for hand and foot increased significantly (p<0.001) (Fig 1). The annual mean preoperative CRP level also decreased from 18.8±1.95 to 4.89±0.81 (Fig 2). Compared to CRP positive group (n=1,113), the patients in CRP negative group (n=446) showed significantly younger age(p<0.001), shorter disease duration (p=0.031), lower late of GC use, and a higher rate of b/tsDAMRD use. The proportion of patients who underwent TJR was significantly higher in CRP positive group (p<0.001).

Fig2



Conclusion: Along with the increasing use of b/tsDMARD, the preoperative disease control of RA, as well as the type of demanded surgeries have dramatically changed.

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FRI0524

THE ACR'S RHEUMATOLOGY INFORMATICS SYSTEM FOR EFFECTIVENESS (RISE) REGISTRY SUPPORTS SMALL RHEUMATOLOGY PRACTICES FOR FEDERAL QUALITY REPORTING PROGRAM

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Background: The Rheumatology Informatics System for Effectiveness (RISE) Registry was developed by the ACR to help rheumatologists improve quality of care and meet federal reporting requirements. In the current quality program administered by the U.S. Centers for Medicare and Medicaid services, rheumatologists are scored on quality measures, and performance is tied to financial incentives or penalties. Rheumatoid arthritis (RA)-specific quality measures can only be submitted through RISE to federal programs.

Objectives: This study used data from the RISE registry to investigate rheumatologists' federal reporting patterns on five RA-specific quality measures in 2018 and investigated the effect of practice characteristics on federal reporting of these measures.

Methods: We analyzed data on all rheumatologists who continuously participated in RISE between Jan 2017 to Dec 2018 and who had patients eligible for at least one RA-specific measure. Five measures were examined: tuberculosis screening before biologic use, disease activity assessment, functional status assessment, assessment and classification of disease prognosis, and glucocorticoid management. We assessed whether or not rheumatologists reported specific quality measures via RISE. We investigated the effect of practice characteristics (practice structure; number of providers; geographic region) on the likelihood of reporting using adjusted analyses that controlled for measure performance (performance in 2018; change in performance from 2017; and performance relative to national average performance). Analyses accounted for clustering by practice.

Results: Data from 799 providers from 207 practices managing 213,757 RA patients was examined. The most common practice structure was a single-specialty group practice (53%), followed by solo (28%) and multi-specialty group practice (12%). Most providers (73%) had patients eligible for all five RA quality measures. Federal reporting of quality measures through RISE varied significantly by provider, ranging from no reporting (60%) to reporting all eligible RA measures (12.2%). Reporting through RISE also varied significantly by quality measure and was highest for functional status assessment (36%) and lowest for assessment and classification of disease prognosis (20%). Small practices (1-4 providers) were more likely to report all eligible RA quality measures compared to larger practices (21%, 6%; p<0.001). In adjusted analyses, solo practices were more likely than single-specialty group practices to report RA measures (42%, 31%; p<0.027) while multispecialty group practices were less likely (18%, 31%; p<0.001). Additionally, higher performance in 2018 and performance ≥ the national average performance was associated with federal reporting of the measures through RISE (p≤0.004).

Conclusion: Forty percent of U.S. rheumatologists participating in RISE used the registry for federal quality reporting. Physicians using RISE for reporting were disproportionately in small and solo practices, suggesting that the registry is fulfilling an important role in helping these practices participate in national quality reporting programs. Supporting small practices is especially important given the workforce shortages in rheumatology. We observed that practices reporting through RISE had higher measure performance than other participating practices, which suggests that the registry is facilitating quality improvement. Studies are ongoing to further investigate the impact of federal quality reporting programs and RISE participation on the quality of rheumatologic care in the United States.

Disclaimer: This data was supported by the ACR's RISE Registry. However, the views expressed represent those of the authors, not necessarily those of the ACR.

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FRI0525 INFLUENZA VACCINATION COMPLIANCE AND RESPONSE IN AUTOIMMUNE INFLAMMATORY RHEUMATIC DISEASE PATIENTS: A COHORT STUDY

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Background: Patients diagnosed with autoimmune inflammatory rheumatic diseases (AIIRD) have higher risk of developing infections due to immunological dysfunction and immunosuppressive treatments. Current guidelines recommend annual influenza vaccination to reduce infection risk in this group of patients. However, vaccination response in these patients is uncertain.

Objectives: To study influenza vaccination compliance and response in a Danish AIIRD patient population.

Methods: AIIRD patients on biological treatment ± synthetic disease-modifying antirheumatic drugs (sDMARDs) in our department of rheumatology and registered in the Danish Rheumatology database (DANBIO) were included in the current study. The patients were encouraged to be vaccinated against influenza in the 2018/19 winter season. Status of influenza vaccination for the period of 1.9.2018 to 31.12.2018 was reviewed in each patient using the Danish Vaccination Register (DDV) and Danish Electronic Medicine Module (FMK). Patient data were collected by review of the medical files. Serum samples from each patient were collected on two occasions: 1) from 1.6.2017 to 15.5.2018 (before vaccination) and 2) from 1.11.2018 to 1.3.2019 (after vaccination), respectively. Antibody titers against the three antigens included in the trivalent 2018/2019 seasonal influenza vaccine were measured by hemagglutination inhibition assay followed by determination of geometric mean titers (GMT).

Results: Among a total of 226 study eligible AIIRD patients, 111 (49%) had been influenza vaccinated. In the remaining group of 115 (51%) non-vaccinated patients, 50 were randomly contacted by telephone to ensure the accuracy of DDV registration. All 50 confirmed non-vaccinated status. Median age of vaccinated group was 65 years while of non-vaccinated group was 57 years ($p \leq 0.00001$). Median GMT increased from 10 to 22 in the group of vaccinated patients versus from 6 to 10 in the group of non-vaccinated patients ($p<0.0001$). GMT increased ≥2-fold in 79 (71%) of 111 influenza vaccinated in comparison to 60 (52%) of 115 non-vaccinated patients ($p \leq 0.003$). Among influenza vaccinated patients, median age of responders (≥2-fold increase in GMT) was 66 years versus non-responders 63 years (p=0.3). In the influenza vaccinated group, ≥2-fold increase in GMT was seen in 51 (73%) of 70 patients receiving methotrexate compared to 28 (68%) of 41 in patients not receiving methotrexate (p=0,6).

Conclusion: Only half of the patients were compliant to the vaccination recommendations in the 2018/2019 influenza season despite the information campaign. Response rate of influenza vaccination (≥2-fold GMT increase) was 71% in AIIRD patients receiving immunosuppressive treatments. In contrast to other studies, concurrent methotrexate treatment did not attenuate serological response of influenza vaccination. We are still exploring the causes of increased influenza antibody titers in non-vaccinated group.

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Disclosure of Interests: None declared

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FRI0526 THE INCIDENCE, PREVALENCE AND MEDICATION USE OF RHEUMATOID ARTHRITIS AMONG KOREAN WOMEN IN CHILDBEARING YEARS: A NATIONWIDE POPULATION-BASED STUDY

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Background: Rheumatoid arthritis (RA) predominantly affects women and has a significant impact on childbearing. Several population-based studies identifying incidence, prevalence, and medication use of RA have been reported, yet epidemiological studies focusing on women with RA in childbearing years are missing.

Objectives: We aimed to identify the incidence, prevalence and medication use of RA among Korean women in childbearing years.

Methods: From National Health Insurance Service (NHIS) data (2009-2016), containing inpatient and outpatient claim information for approximately 97% of the Korean population, we identified 9,217,139 women aged between 20-44 years. Incidence and prevalence of RA in the specific sociodemographic group of women in childbearing age were analyzed, and the prevalence of medication prescription were compared between women with RA and controls without rheumatic diseases such as RA, systemic lupus erythematosus, and ankylosing spondylitis. Individuals with RA were defined by the presence of International Classification of Disease, 10th revision code, M05. The medication use was defined as receiving > 90days prescriptions of NSAIDs, corticosteroids (CSs), and conventional synthetic (cs) disease modifying antirheumatic drugs (DMARDs) or > 1day prescription of biologic (b) DMARDs.

Results: Total 24,590 women with RA were identified. The average incidence of RA during 2011-2016 among women in childbearing years was 24.1/100,000 person-years (PYs) (95% CI 20.91-27.31) with a yearly increase from 20.99/100,000 PYs in 2011 to 28.38/100,000 PYs in 2016. The average prevalence of RA during 2009-2016 among women in childbearing years was 105.2/100,000 PYs (95% CI 99.0-111.5) with a minimum of 95.7/100,000 PYs in 2009 and a maximum of 110.5/100,000 PYs in 2016. There were increasing trends in both incidence and prevalence of RA according to age among women in childbearing years peaking in the age group of 40-44 years. The prescriptions of NSAIDs, CSs, csDMARDs and bDMARDs were more frequent in women with RA than controls (NSAIDs; 94.21% vs 21.79%, CSs; 83.65% vs 4.28%, csDMARDs; 91.23% vs 0.41%, bDMARDs; 0.11% vs 0%, $p<0.001$).

Conclusion: The incidence and prevalence of RA are high among Korean women in childbearing years, and medication use was significantly more frequent in this specific population than controls. High disease burden is imposed upon women in childbearing years.

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Table 1. Medication use among women with RA and controls in childbearing age between 20-44 years during 2009-2016

	Control (n=155,486)		RA (n=23,756)		
	n	(%)	n	(%)	P
NSAIDs	33,887	(21.79)	22,380	(94.21)	<.0001
Steroids	6,653	(4.28)	19,871	(83.65)	<.0001
csDMARDs	634	(0.41)	21,673	(91.23)	<.0001
bDMARDs	0	(0.00)	27	(0.11)	<.0001

RA, rheumatoid arthritis; NSAID, non-steroidal anti-inflammatory drug; cs, conventional synthetic; b, biologic; DMARDs, disease modifying antirheumatic drugs

Disclosure of Interests: None declared
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FRI0527 THE EFFECT OF A NURSE-LED PREDNISOLONE TAPERING REGIME IN POLYMYALGIA RHEUMATICA: A RETROSPECTIVE COHORT STUDY

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Background: The cornerstone treatment of polymyalgia rheumatic (PMR) is prednisolone, which has several side effects such as osteoporosis and type 2 diabetes [1]. Therefore, the duration of prednisolone treatment should be as short as possible. Previous studies indicate that only 10-30% has discontinued prednisolone after 1 year and approximately 50% after 2 years [2].
Objectives: To investigate the efficacy of a nurse-led prednisolone tapering regime in patients with PMR compared to usual care.
Methods: The study is a single center retrospective cohort study with a 2-year follow-up. Prednisolone dose was evaluated after 1 and 2 years.
A nurse-led PMR clinic was introduced June 1st, 2015 and patients diagnosed until June 7th, 2017 were included. Patients were diagnosed by a physician, and subsequently managed by nurses according to a specific protocol, with prednisolone tapering from 15 mg to discontinuation after 52 weeks. Regularly blood tests and telephone interviews were performed and a rheumatologist was involved if deemed necessary.
Patients diagnosed with PMR between June 1st, 2012 and June 1st, 2015 served as controls. They received standard care by a rheumatologist.
The Danish guidelines for managing PMR remained unchanged throughout the study period.
The study population was identified by searching the electronic patient journal for the PMR diagnosis. Data collection was performed by four experienced reumatologists. Data were obtained from the Electronic Patient Journal of Central Denmark Region and recorded in the RedCap database.
Results: Five hundred and seventy patients were screened. Patients not diagnosed with PMR, with simultaneously giant cell arteritis, with relapse of known PMR, or prednisolone treatment for more than 4 weeks prior to the diagnosis were excluded. Sixty eight patients received standard care and 107 nurse-led care. There was no statistical difference between groups regarding reason for exclusion.
At baseline there was no difference between patients receiving standard care and nurse-led care regarding gender, mean age (70.7 years vs. 72.2 years), clinical findings, symptoms, level of C-reactive protein (43.4 mg/L vs. 39.7 mg/L), anti-citrullinated protein antibody and reumatoid factor status. Median (IQR) prednisolone starting dose in the standard care group was 15 mg (15-25) vs. 15 mg (15-15) in the nurse-led care group (p=0.008).
After 1 year 29.4% of patients receiving standard care had discontinued prednisolone vs. 35.5% receiving nurse-led care (p=0.403). Median (IQR) prednisolone dose after 1 year was 3.75 mg (0-5) in the standard care group and 1.25 mg (0-3.75) in nurse-led care group (p=0.004). After 2 years 60.3% of patients receiving standard had discontinued prednisolone vs. 82.2% receiving nurse-led care (p=0.001). Median (IQR) prednisolone dose after 2 years was 0 mg (0-2.5) in the standard care group and 0 mg (0-0) in the nurse-led care group (p=0.004). There was no difference between groups regarding relapse of PMR and initiation of MTX treatment in either year 1 or 2.
Conclusion: A tight and systematic approach to prednisolone tapering in PMR is more effective than usual care. The results should be confirmed in a prospective setting.
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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.6179

FRI0528 INDICATORS OF EFFECTIVENESS AFTER 6 YEARS OF FOLLOW-UP OF PATIENTS IN THE FLS DR. NEGRIN

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Background: Data on the effectiveness of FLS in the medium and long term in Spain are needed
Objectives: To analyze the indicators of long-term persistence to treatment, refracture and mortality in our Fracture Liaison Service (FLS)
Methods: Throughout 2019, the medical records of patients with an indication of treatment to prevent new fractures whose baseline visit took place between 2012 and 2014 were reviewed. The data included those of the baseline visit (age, sex, type of index fracture, FRAX scale and DXA results) and for the follow-up (death and date, refracture including revision of spine x-rays - it was considered only the first refracture and, in the case of several fractures the most serious was chosen-, prescribed treatment, persistence of treatment trough electronic prescription on the date of review or death, and MPR or proportion of days covered by treatment).
Results: 399 patients were included, 335 of them women (84%), mean age 73.8 years (range 51-93) and average follow-up of 6 years (range 5.5-7 years).
Baseline visit.- The average FRAX was 15 and 7 for major fracture and femoral fracture respectively. DXA was normal in 22 patients (5.5%), osteopenia in 143 (35.8%) and osteoporosis in 234 (58.6%). 78 patients (19.5%) had a previous fragility fracture.
Type of fracture index: femur 126 (31.5%), forearm 119 (29.8%), humerus 76 (19%), vertebra 24 (6%), others 54 (13.5%). 80 patients (20%) had received prior treatment for osteoporosis.
Follow-up.- The persistence of treatment was assessed in 394 patients; 245 patients (62%) were prescribed a treatment on the most recent date, 200 (51%) with MPR≥80%. When analyzing patients with prescribed treatment, in 176 cases (72%) it was a bisphosphonate in a sustained manner, in 23 cases (9%) a bisphosphonate was prescribed and subsequently changed to denosumab, while in 45 cases (18%) it was initiated and maintained denosumab.
71 of 397 patients presented a new fracture (17.8%). The type of incident fracture was as follows: femur in 24 patients (34%), vertebra in 20 patients (28%), forearm in 9 patients (12%) and other fractures in 18 patients (25%). Refracture occurred in 9 patients in the first year, 16 in 2nd, 12 in the 3rd, 9 in 4th, 14 in 5th, 6 in 6th and 3 in 7th year. The persistence of treatment with MPR≥80% was similar in patients with and without refracture (52 vs 51%). The average baseline age and FRAX for major fracture in the fractured and non-fractured were 75 vs. 73 years (p = 0.10) and 17 vs. 14 respectively (p <0.01).
92 patients (23%) died, 25% of them in the two years that followed the baseline visit and 61% in the following 4 years. The persistence of treatment was 37% in those who died and 69% in those who remained alive (p <0.01).
Conclusion: After an average of 6 years after the assessment in an FLS, the persistence of treatment was 62% (MPR≥80% in 51%), the mortality was 23% and the percentage of refractured patients was 17%.
Disclosure of Interests: Antonio Naranjo Grant/research support from: amgen, Consultant of: UCB, Speakers bureau: AMGEN, Amparo Molina Speakers bureau: AMGEN, STADA, Cristina Sepúlveda: None declared, Francisco Rubiño: None declared, Soledad Ojeda Speakers bureau: AMGEN, LILLY, GEBRO
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FRI0529 IS COTRIMOXAZOLE PROPHYLAXIS AGAINST PNEUMOCISTIS JIROVENCII PNEUMONIA RECOMMENDED IN PATIENTS WITH SYSTEMIC AUTOIMMUNE DISEASES REQUIRING IMMUNOSUPPRESSIVE THERAPIES? A SYSTEMATIC LITERATURE REVIEW.

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Background: The incidence of Pneumocistis jirovencii pneumonia (PCP) has increased substantially during the past years in patients with systemic autoimmune diseases (SAD). Mortality associated to PCP was reported to be up to 20 to 58%, particularly in those receiving immunosuppressive therapy, such as tumoral necrosis antagonist factors or glucocorticoid therapy. Though, there is clear evidence of the effectiveness of Cotrimoxazole against PCP, the risk of adverse effects is important, increasing morbidity and mortality. Up to date, there is no consensus about the need of PCP prophylaxis in SAD patients with immunosuppressed therapies.
Objectives: To analyse the efficacy and safety of Cotrimoxazole prophylaxis against PCP in SAD adult patients receiving immunosuppressive therapies.
Methods: We performed a comprehensive literature search, screening different databases, MEDLINE, EMBASE and Cochrane Library up to April 2019. Outcomes covered prevention of PCP or other infections, morbidity, mortality and safety. All categories of studies were included. Two reviewers selected and

extracted data from studies. The information obtained was summarized through a narrative review and results tabulated.

Results: From the initial 340 identified references, 12 were finally included. Two were randomized controlled trials, six observational studies, and four case reports. The quality in the majority of studies resulted moderate or low, with limited level of evidence. Besides, all Cotrimoxazole prophylaxis regimens described in each study were distinct. Results were consistent to exhibit the efficacy of Cotrimoxazole prophylaxis, compared to non-prophylaxis in the prevention of PCP in patients receiving immunosupresor therapy, particularly, those taking high glucocorticoid dose above 20mg/day. In terms of efficacy, Cotrimoxazole 400mg/80mg/day, given three times per week, or 200mg/40mg/day or in dose escale exhibited a similar performance. In contrast, Cotrimoxazole 400mg/80mg/day displayed a higher incidence of adverse effects.

Conclusion: Cotrimoxazole prophylaxis against PCP exhibited efficacy compared to non-prophylaxis, mainly in patients treated with high dose of glucocorticoids (≥20mg/day), causing a significant reduction in mortality. Positive efficacy results did not differ despite the diverse Cotrimoxazol regimens exposed. However, Cotrimoxazole adverse effects were observed after two months from initiation; particularly with daily dose of 400mg/80mg. In contrast, escalate dose or 200mg/40mg/day dose regimens appeared better tolerated.

**This review is part of the Spanish Rheumatology Society –SER- recommendations on Systemic Autoimmune Diseases.

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Disclosure of Interests: None declared

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FRI0530

THE PREVALENCE AND DETERMINANTS OF SLEEP PROBLEMS IN PATIENTS ACROSS RHEUMATIC DISEASES AND THEIR CORRELATION WITH DISEASE INDICES USING THE ROUTINE ASSESSMENT OF PATIENT INDEX DATA 3 (RAPID3) QUESTIONNAIRE.

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Background: Sleep problems are common in rheumatology patients. RAPID3 is a patient reported outcome measure (PROM) that efficiently screens for problems with sleep, anxiety or depression in routine care.

Objectives: To study prevalence and determinants of self-reported sleep problems across rheumatic diseases in Rheumatology clinics in Singapore, and its correlation with disease indices.

Methods: RAPID3 questionnaire was filled electronically over 6 months. Demographic data and SNOWMED diagnoses codes were matched through hospital electronic medical records. RAPID3 comprised of 3 questions measuring the extent of difficulty getting a good night's sleep and dealing with anxiety or depression. Significant problems were considered if they had "much difficulty" or were "unable to do" the component. The relationship of sleep with anxiety, depression, physical function (measured by modified health assessment questionnaire, mdHAQ), pain and patient global assessment (using visual analogue scale, VAS), was evaluated using Pearson's correlation. Factors associated with significant sleep problems were evaluated by logistic regression.

Results: 4078 patients [mean (SD) age 55.8 (16.3) years, 67.9% female, 70.6% Chinese] were invited to participate, of which 2625 (64.4%) responded. SNOMED diagnosis codes were available for 1570 (59.8%) patients- majority had inflammatory arthritides (n= 843, 53.7%) (Figure 1).

Mean mdHAQ was 0.3 (0.5), pain VAS was 2.4 (2.3) and global VAS was 2.6 (2.2). Data on disease duration, clinical features and medications were not available. 39.3%, 27.5% and 23.8% had problems with sleep, anxiety and depression respectively; and 7.3%, 4.5% and 4.3% had significant problems respectively. Sleep moderately correlated with anxiety (r=0.463, p<0.001) and depression (r=0.436, p<0.001) and weakly correlated with mdHAQ (r= 0.289, p<0.001), global (r=0.339, p<0.001) and pain VAS (r= 0.314, p<0.001).

In multivariable logistic regression, significant sleep problems were associated with anxiety (OR 4.733, CI 2.172-10.310, p<0.001), mdHAQ score ≥ 1 (OR 2.920, CI 1.691-5.043, p< 0.001) and pain VAS >3 (OR 1.884, CI 1.093-3.247, p=0.023). Patients with osteoarthritis and fibromyalgia were more likely than those with inflammatory arthritides to have significant sleep problems, though we were unable to adjust for body mass index as data were unavailable (Table 1).

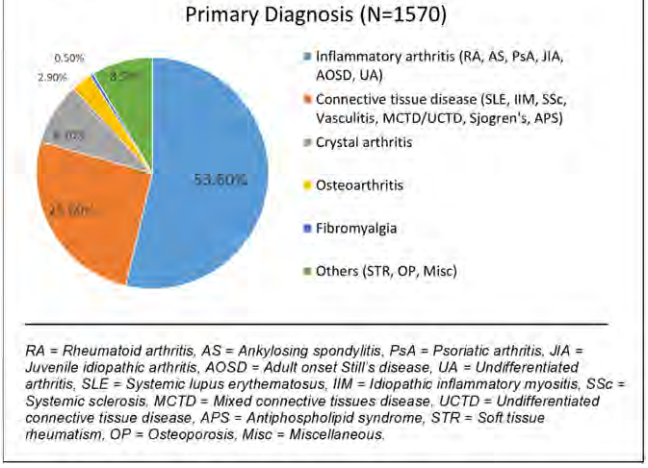
Table 1. Determinants of significant disturbances in sleep in patients with rheumatic diseases

Variables		Univariable		Multivariable	
		Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value
Gender	Female	1.79 (1.245-2.57)	0.002	1.49 (0.86-2.59)	0.16
Ethnicity	Chinese	Ref		Ref	
	Malay	1.04 (0.62-1.73)	0.89	0.73 (0.33-1.61)	0.43
	Indian	1.59 (1.03-2.44)	0.04	0.97 (0.49-1.90)	0.92
	Others	1.05 (0.62-1.77)	0.87	0.92 (0.43-2.00)	0.84
Age (years)		1.00 (1.00-1.01)	0.36	-	-
mdHAQ ≥1		6.25 (4.46-8.75)	<0.001	2.92 (1.69-5.04)	0.001
Pain VAS >3		4.15 (3.07-5.61)	<0.001	1.88 (1.09-3.25)	0.02
Global VAS > 3		4.25 (3.13-5.76)	<0.001	1.63 (0.95-2.80)	0.07
Significant anxiety		15.99 (10.71- 23.89)	<0.001	4.73 (2.17-10.31)	<0.001
Significant depression		15.58 (10.35-23.45)	<0.001	3.02 (1.29-7.10)	0.11
Primary rheumatological diagnosis	Inflammatory arthritides	Ref		Ref	
	Connective tissue diseases	1.18 (0.73-1.90)	0.51	0.9 (0.51-1.59)	0.71
	Crystal arthritides	1.06 (0.48-2.33)	0.88	0.83 (0.34-2.03)	0.68
	Osteoarthritis	3.09 (1.31-7.32)	0.01	2.96 (1.19-7.36)	0.02
	Fibromyalgia	9.05 (2.04-40.05)	0.004	9.62 (2.11-43.84)	0.003
	Others	1.63 (0.82-3.29)	0.17	1.20 (0.58-2.47)	0.63

Conclusion: Sleep problems are common in rheumatology patients and correlate significantly with disease indices and psychological distress. Rheumatologists should routinely screen for sleep difficulties, especially in patients with osteoarthritis and fibromyalgia.

References: -

Figure 1



Acknowledgments: Nil.

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FRIDAY, 05 JUNE 2020

Epidemiology, risk factors for disease or disease progression

FRI0531

AIR POLLUTANTS AND DEVELOPMENT OF INTERSTITIAL LUNG DISEASE IN PATIENTS WITH AUTOIMMUNE DISEASES

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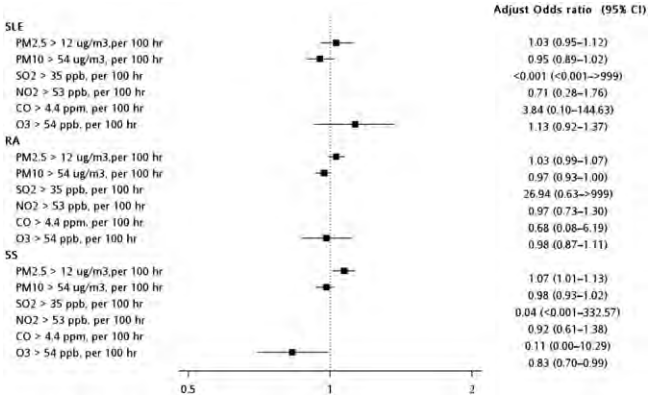
Background: Interstitial lung disease (ILD) is characterized by progressive inflammation and fibrosis, and accumulating evidence have shown that exposure to air pollutants was associated with the development of ILD. Autoimmune diseases are highly correlated with ILD, including connective tissue disease-associated ILD (CTD-ILD) as well as interstitial pneumonia with autoimmune features (IPAF), and the development of ILD is a crucial cause of morbidity and mortality in patients with autoimmune diseases. One recent Taiwanese study reported that exposure to air pollutants was associated with incident systemic lupus erythematosus (SLE). However, the impact of air pollutants on the development of ILD among patients with autoimmune diseases remains unknown.

Objectives: The study aimed to address the impact of accumulating exposure to air pollutant above moderate level, defined by Air Quality Index (AQI) value higher than 50, on the development of ILD in patients with autoimmune diseases including SLE, rheumatoid arthritis (RA) and primary Sjögren's syndrome (SS).

Methods: We used a National Health Insurance Research Database in Taiwan to enroll patients with SLE (International Classification of Diseases (ICD)-9 code 710.0, n=13,211), RA (ICD-9 code 714.0 and 714.30–714.33, n=32,373), and primary SS (ICD-9 code, 710.0, n=15,246) between 2001 and 2013. We identified newly diagnosed ILD cases (ICD-code 515) between 2012 and 2013 and selected age, sex, disease duration and index-year matched (1:4) patients as non-ILD controls. The hourly levels of air pollutants one year prior to the index-date were obtained from 60 air quality monitoring stations across Taiwan, and the air pollutants in the present study consisted of particulate matter <2.5 μm in size (PM2.5), particulate matter <10 μm in size (PM10), nitrogen dioxide (NO2), carbon monoxide (CO), sulfur dioxide (SO2) and ozone (O3). We used a spatio-temporal model built by a deep-learning mechanism to estimate levels of air pollutants at 374 residential locations based on data of 3 air quality monitoring stations near the location (8). Notably, we used cumulative exposed hours to air pollutants higher than modest level, defined by AQI criteria, given that daily mean level of air pollutants might possibly underestimate the triggered inflammatory effect by a temporary exposure of high-level air pollutant. A conditional logistic regression was used to determine the association between exposure to air pollutant and the development of ILD, adjusting age, gender, Charlson Comorbidity Index (CCI), urbanization, family income, and medications for autoimmune diseases.

Results: A total of 272 patients with newly diagnosed ILD were identified among patients with autoimmune diseases, including 39 with SLE, 135 with RA, and 98 with primary SS. We found that the duration of exposure to PM 2.5 higher than modest level was associated with the risk of ILD development in patients with SS (adjOR 1.07, 95% CI 1.01–1.13), and similar trends were also found in patients with SLE (adjOR 1.03, 95% CI 0.95–1.12) and RA (adjOR 1.03, 95% CI 0.99–1.07). Intriguingly, we observed an inverse correlation between the duration of exposure to O3 and the development of ILD in patients with SS (adjOR 0.83, 95% CI 0.70–0.99); however, the finding was not found in patients with SLE (adjOR 1.13, 95% CI 0.92–1.37) and RA (adjOR 0.98, 95% CI 0.87–1.11).

Conclusion: In conclusion, we identified that longer exposure to PM2.5 higher than modest level tended to be associated with the development of ILD in patients with autoimmune diseases, mainly SS.



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FRI0532

THE IMPACT OF GENETICALLY DETERMINED SERUM URATE LEVELS ON THE DEVELOPMENT OF CARDIOVASCULAR DISEASES: A SYSTEMATIC REVIEW AND META-ANALYSIS OF MENDELIAN RANDOMIZATION STUDIES

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Background: Conventional observational studies have identified serum urate (SU) as an independent risk factor for cardiovascular diseases (CVDs),[1,2] but the causal relationships remain unsettled, with potential confounding and reverse causality. When applied correctly, Mendelian randomization (MR) employing genetic variants as instrumental variables can eliminate these biases and allow for causal inference.

Objectives: To conduct a systematic review and meta-analysis of English-language, peer-reviewed MR studies on the causal effects of SU on CVDs and assess validation of key MR assumptions.

Methods: A research librarian conducted a search (inception to January 2020) of four databases (Medline, Embase, Cochrane Library, and Web of Science),

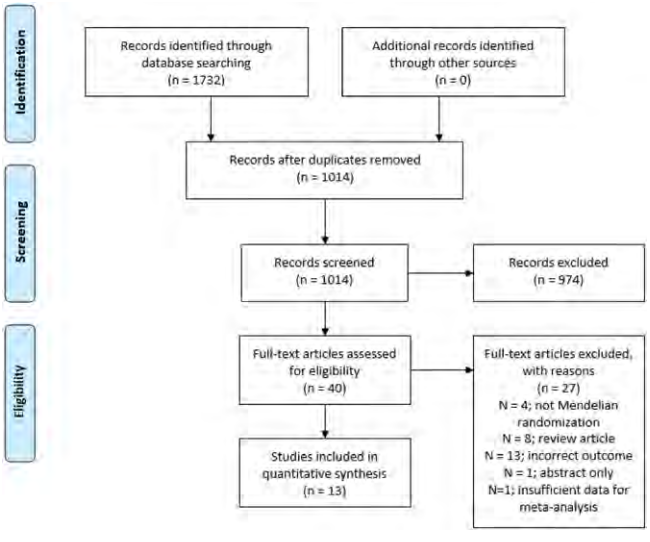


Fig. 1 : PRISMA flow diagram.

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[2] Tang KT, Tsuang BJ, Ku KC, Chen YH, Lin CH, Chen DY. Relationship between exposure to air pollutants and development of systemic autoimmune rheumatic diseases: a nationwide population-based case-control study. Ann Rheum Dis 2019;78:1288-1291.

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which was supplemented by hand-search. Titles and abstracts were screened by two independent reviewers, who subsequently evaluated and extracted data from full-text of selected articles. Pooled meta-analysis was performed using random-effects weighting.

Results: Of 1014 articles identified, 40 were selected for full-text review and 13 studies reporting on CVDs were included in the systematic review (Figure 1). The first was published in 2009 and five were published in 2018 or 2019 alone. The included studies were of varying quality in regards to satisfying the assumptions for MR design.

Overall, there was little evidence for a causal association between SU and risk of CVDs (Table 1). Random-effects meta-analysis revealed that SU was not significantly associated with risk of CVDs (OR=1.04; 95% CI=0.99-1.09) (Figure 2). 11 of the 13 studies reported null estimates for the effects of genetically-determined SU levels on CVDs. Two studies with small numbers of cases (N=125 and 222) reported significant associations, but these pertained to highly-specific subgroups.

Table 1. Summary of included studies. CAD: Coronary Artery Disease; CHD: Coronary Heart Disease; IHD: Ischaemic heart disease; MI: Myocardial Infarction; MR: Mendelian Randomization; PVD: Peripheral Vascular Disease; SNP: Single Nucleotide Polymorphism

First author; year	Number of SNPs analyzed	Outcome (n cases)	Power	MR criteria validated: 1. relevance 2. pleiotropy 3. confounding	Conclusion
Stark; 2009	10 separately	CAD (1,473)	30%-66%	1, 3	Null
Yang; 2010	8 combined	CHD (3,050)	<80%	1, 2, 3	Null
Palmer; 2013	1 (rs7442295)	IHD (3,742)	N/A	1, 2*, 3	Null
Kleber; 2015	8 combined	CAD (2,418) PVD (295)	N/A	1, 2, 3	Null
Han; 2015	2 separately	CHD (1,146)	80%	1, 2*, 3	Null
Testa; 2015	1 (rs734553)	CVD events (CVD death, stroke, MI) (222)	N/A	1, 2*	Significant for CV events
White; 2016	31 combined	CAD (65,877)	83%	1, 2, 3	Null
Keenan; 2016	14 combined	CHD (54,501) Stroke (14,779)	>80%	1, 2, 3	Null
Li; 2018	31 combined	IHD (9,467) MI (3,625)	70%	1, 2, 3	Null
Li; 2019	31 combined	CHD (60,801) MI (43,676) Stroke (10,307)	N/A	1, 2, 3	Null
Macias-Kauffer; 2019	2 separately	CAD (704)	N/A	1, 2*, 3	Null
Efstathiadou; 2019	28 separately	CHD (184,305) MI (54,162) Stroke (514,791)	>80%	1, 2, 3	Null
Chiang; 2019	8 combined	CHD (125) Stroke (57)	N/A	1, 2, 3	Significant for CHD

* Risk of pleiotropy (assumption 2) is low when utilizing few well-established SNPs

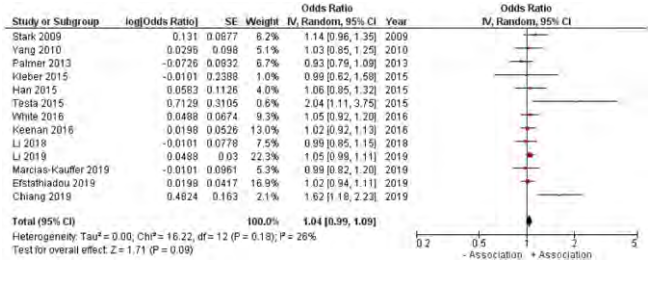


Fig. 2 : Pooled meta-analysis results.

Conclusion: Evidence from this systematic review does not support a causal role for SU levels and CVDs. As such, interventions targeting SU levels alone are unlikely to lower the risk of CVDs.

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FRI0533

SMOKING AS A PREDICTIVE FACTOR FOR SPONDYLOARTHRITIS RELATED UVEITIS: RESULTS FROM A SINGLE CENTRE CROSS-SECTIONAL STUDY.

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Background: Although spondyloarthritis (SpA) is primarily a musculoskeletal condition, ocular involvement is an important clinical feature and contributes to the burden of disease. Acute anterior uveitis (AAU) is classically described as the most frequent extra-articular manifestation of SpA and in some cases the first clinical presentation. The prevalence of AAU varies according to the subtype of SpA. In a systematic literature review, the mean prevalence of AAU was 32.7% and a positive association between HLA-B27 positivity, axial SpA, male sex and uveitis has been reported (1). More recently, some cross-sectional studies have described lower odds of spondyloarthritis-related uveitis (SpA-U) in smokers than in patients who are ex smokers or never smokers (2). Predictors of SpA-U are poorly defined in literature and the influence of smoking status remains controversial.

Objectives: To analyse the factors associated with uveitis in SpA patients in a Tertiary Rheumatology Center.

Methods: An observational cross-sectional study was performed including patients fulfilling the ASAS criteria for axial SpA with a follow-up visit between January and June 2019. Clinical patients' charts were reviewed and the following variables were considered: age, gender, history of uveitis (confirmed by ophthalmologist observation), number of AAU episodes, smoking status (never smoker or ever smoker), HLA-B27, disease duration, disease involvement (exclusively axial or axial and peripheral), history of enthesitis and syndesmophytes. History of AAU and associated variables were determined in this subset of patients.

Statistical analysis was performed with logistic regression model. P value <.05 was defined as statistically significant.

Results: The study included 164 patients (62.3% men) with median age of 44.0 years (IQR 37 to 54) and a median disease duration of 14.6 years (IQR 9.28 to 20.32). SpA diagnosis was ankylosing spondylitis in 70.7% cases and the remaining were non-radiographic axial SpA. HLA-B27 was positive in 84.8%, 31.1% of patients were ever smokers and 21% had both axial and peripheral joint involvement. Twenty four percent of patients had at least one AAU episode. Recurrence of uveitis occurred in 70% of patients. Ever smoking (OR=2.256; 95%CI [1.077-4.276]; p<.05) and syndesmophytes (OR=2.125; 95%CI [1.009-4.475]; p<.05) showed a statistically significant association with uveitis in univariated logistic regression. Althougth not statistically significant, a trend to association was found between smoking and recurrence of AAU (OR=2.235; 95%ICI [.973-5.135], p=.058). In multivariated logistic regression only ever smoking was independently associated with uveitis (OR=2.542; 95%CI [1.007-6.420]; p<.05). We did not find association between presence of uveitis and gender, age, disease duration, disease involvement, HLA-B27 positivity and enthesitis.

Conclusion: Contrary to few cross-sectional studies showing a possible protective effect of smoking in SpA-U, and in line with new data from Zhao *et al* (3), we report a statistically significant independent association between history of smoking and uveitis. Nevertheless, we emphasize the need of more studies to confirm these findings.

References:

[1] Zeboulon N, et al. Prevalence and characteristics of uveitis in the spondyloarthropathies: a systematic literature review. Annals of Rheumatic Diseases 2008;67:955.

[2] Zhao S, et al. Associations between smoking and extra-axial manifestations and disease severity in axial spondyloarthritis: results from the BSR Biologics Register for Ankylosing Spondylitis (BSRBR-AS). Rheumatology 2018;69.

[3] Zhao S, et al. Smoking does not protect patients with axial spondyloarthritis from attacks of uveitis. Annals of Rheumatic Diseases 2019;78(9).

Disclosure of Interests: None declared

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FRI0534

PATIENT-REPORTED MEASURES OF DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS VARY ACROSS THE NORDIC COUNTRIES, RESULTS FROM A NORDIC COLLABORATION

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Background: Disease activity in rheumatoid arthritis (RA) patients is measured through composite scores which are considered treatment targets and thus facilitate clinical decision making. Scores often combine a mix of objective and

subjective measures, and, although the latter (e.g. pain, patient's global, 28 tender joint count (TJC)) may be impacted by contextual and cultural factors, these clinical metrics are often assumed to be comparable across different settings and reflecting the RA disease.

Objectives: To explore whether there are systematic differences in patient-reported measures of RA disease activity (i.e. TJC and a measure of pain on a Visual Analog Scale (VAS)) across countries, at similar time-points in the course of the RA disease, taking objective measures of concomitant disease activity and other factors into account.

Methods: RA patients starting a first ever tumor necrosis factor inhibitor (TNFi) 2008 through 2017 were identified in rheumatologic registers in five Nordic countries. Data were pooled for analysis. Clinical metrics were retrieved at three time-points: at TNFi start, and after three and twelve months, irrespective of treatment. Baseline clinical variables distributions were compared between countries. The correlation between pain and patient's global VAS was calculated with the Pearson correlation coefficient (r). At each time-point the subjective measures (TJC and pain) were compared between countries and analyzed with linear models: (i) crude; (ii) adjusted for age, sex, birth decade, disease duration (DD), year of TNFi treatment start (year), C-reactive protein (CRP) and 28 swollen joint count (SJC)) from the time-point in question.

Results: A total of 23 796 RA patients were included (Table 1). At baseline, the significant differences between Nordic countries for TJC and pain (crude model) were slightly modified after adjustment but remained statistically significant (Table 2). Compared to baseline, the inter-countries differences were reduced at 3 and 12 months, but also were statistically significant (Figure 1).

Figure 1: Country-specific cross-tabulation of median values of subjective measures (y axis: TJC, Pain VAS) versus objective measures (x axis: CRP, SJC). Baseline TNFi start (upper panel) and at 3 months (lower panel).

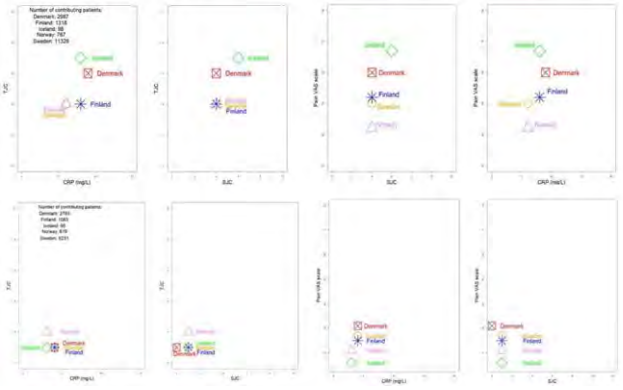


Table 1. RA patients starting a first TNFi baseline characteristics, median [Interquartile range].

	Sweden	Denmark	Finland	Norway	Iceland
N (% female)†	13621 (75)	6701 (75)	1946 (73)	1113 (71)	415 (73)
CRP (mg/L)‡	6 [3-17]	9 [3-20]	8 [3-20]	6 [3-14]	8 [3-19]
Physician's global VAS‡	30 [14-50]	31 [19-47]	35 [20-50]	32 [23-45]	60 [43-70]
Patient's global VAS#‡	50 [28-70]	67 [46-82]	50 [28-70]	48 [26-69]	71 [53-86]
Pain VAS‡	50 [26-70]	60 [37-76]	52 [30-71]	42 [23-65]	67 [49-79]
SJC‡	4 [1-8]	4 [1-7]	4 [1-9]	4 [1-7]	6 [3-11]
TJC‡	4 [1-9]	6 [3-11]	4 [1-10]	4 [1-9]	7 [4-12]
DAS28‡	5 [3-5]	5 [4-5]	4 [3-5]	4 [3-5]	5 [4-6]

Patient's global and pain correlation: r=0.85
† χ^2 test; p-value=0.04
‡ One-way ANOVA; all p-values < 0.001

Table 2. Mean crude and adjusted differences in baseline TJC and pain between countries, using the largest (Sweden) as reference.

	SE	DK	FI	NO	IS
Crude model					
TJC	ref	1.8	0.8	0.5*	3.7
Pain	ref	7.2	1.4†	-4.0	11.1
Adjusted model#					
TJC	ref	2.3	0.7	0.6**	2.4
Pain	ref	7.9	0.7NS	-3.3	7.2**

All p-values <0.001 except: NS > 0.10; † < 0.10; * < 0.05; ** < 0.01
adjusted for age, sex, birth decade, year, DD, CRP, SJC

Conclusion: In this observational study of 23 796 RA patients from 5 Nordic countries starting 1st TNFi, patient-reported variables related to RA disease activity (pain VAS, TJC) varied across countries. These differences were not explained by differences in demographic (age, sex, birth decade, year) or objective RA measures (DD, CRP, SJC). This implies a limit to the direct comparability of results obtained from subjective measures from different countries.

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Disclosure of Interests: Bénédicte Delcoigne: None declared, Sella Aarrestad Provan: None declared, Hilde Berner Hammer Consultant of: Has received fees as consultant from Roche, AbbVie and Novartis., Speakers bureau: Has received fees for speaking from AbbVie, BMS, Pfizer, UCB, Roche, MSD and Novartis, Daniela Di Giuseppe: None declared, Thomas Frisell: None declared, Bente Glintborg Grant/research support from: Grants from Pfizer, Biogen and Abbvie, Gerdur Gröndal: None declared, Björn Gudbjornsson Speakers bureau: Novartis and Amgen, Merete L. Hetland Grant/research support from: BMS, MSD, AbbVie, Roche, Novartis, Biogen and Pfizer, Consultant of: Eli Lilly, Speakers bureau: Orion Pharma, Biogen, Pfizer, CellTrion, Merck and Samsung Bioepis, Brigitte Michelsen: None declared, Dan Nordström Consultant of: Abbvie, Celgene, Lilly, Novartis, Pfizer, Roche and UCB., Speakers bureau: Abbvie, Celgene, Lilly, Novartis, Pfizer, Roche and UCB., Heikki Relas Grant/research support from: Abbvie., Consultant of: Abbvie, Celgene, and Pfizer., Speakers bureau: Abbvie, Celgene, and Pfizer., Niels Steen Krogh: None declared, Johan Askling Grant/research support from: JA acts or has acted as PI for agreements between Karolinska Institutet and the following entities, mainly in the context of the ARTIS national safety monitoring programme of immunomodulators in rheumatology: Abbvie, BMS, Eli Lilly, Merck, MSD, Pfizer, Roche, Samsung Bioepis, Sanofi, and UCB Pharma

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FRI0535

NEWLY DETECTED HYPERTHYROIDISM WITH THERAPEUTIC INDICATIONS IN RHEUMATIC DISEASE PATIENTS AND HEALTHY CONTROLS IN JAPAN: A RETROSPECTIVE COHORT STUDY

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Background: Thyroid disorders are known as common comorbidities of rheumatic diseases(RD) [1]. However, data regarding prevalence of hyperthyroidism with treatment indication in RD patients are limited.

Objectives: This study aims to reveal and compare the frequency of newly developed hyperthyroidism with treatment indication between RD patients and healthy controls (HC), and identify risk factors to identify patients whose thyroid function should be followed up carefully.

Methods: We retrospectively reviewed charts of RD patients and HC who had thyroid stimulating hormone (TSH) measured at least once between 2004 and 2018 from immuno-rheumatology center and preventive medicine center in St. Luke's International Hospital, Japan. We compared frequency of hyperthyroidism requiring treatment (TSH ≦ 0.1μU/mL or for which physicians started treatment) with Kaplan-Meier curve and log rank test. Cox regression multivariate analysis was performed to reveal risk factors for the new onset of hyperthyroidism with treatment indication in participants without treatment-indicated hyperthyroidism at initial assessments.

Table1. Patients characteristics and results of hyperthyroidism

	Rheumatic Disease (n = 2307)	Control (n = 78251)	p. value
Age(yr)	53.7 (16.2)	46.1 (11.9)	<0.001
Female (%)	1826 (79.2)	38632 (49.4)	<0.001
Rheumatoid arthritis (%)	1091 (47.3)	-	NA
Spondyloarthritis	161 (7.0)	-	NA
ANA associated disease (%)	944 (40.9)	-	NA
SLE(%)	363 (15.7)	-	NA
SS (%)	396 (17.2)	-	NA
PMDM(%)	104 (4.5)	-	NA
SSc (%)	222 (9.6)	-	NA
MCTD (%)	43 (1.9)	-	NA
Vasculitis (%)	202 (8.8)	-	NA
Others (%)	244 (10.6)	-	NA
Times of TSH measurement	2.0 [1.0, 5.0]	5.0 [3.0, 9.0]	<0.001
Follow up of TSH (days)	258.00 [0, 1315]	1992 [958, 3632]	<0.001
Baseline TSH (μU/mL)	2.28 (3.21)	2.15 (4.07)	0.137
≦0.45 μU/mL (%)	86 (3.7)	1371 (1.8)	<0.001
≦0.1 μU/mL (%)	29 (1.3)	389 (0.5)	<0.001
Baseline FreeT4 (μU/mL)	1.16 (0.24)	1.30 (0.20)	<0.001
≧1.65 μU/mL (%)	17 (0.8)	2355 (3.0)	<0.001
TSH level in follow up			
≦0.45 μU/mL (%)	231 (0.0)	3926 (5.0)	<0.001
≦0.1 μU/mL (%)	84 (3.6)	1388 (1.8)	<0.001
Newly detected hyperthyroidism with treatment indication (%)	68 (2.9)	1350 (1.7)	<0.001
At initial assessment (%)	29 (1.3)	389 (0.5)	<0.001
In follow up (%)	39 (1.6)	961 (1.2)	<0.001
Treatment for hyperthyroidism (%)	21 (0.9)	325 (0.4)	0.002

Results: Overall, 2307 RD patients and 78251 HC were included. Newly detected hyperthyroidism with treatment indication were significantly more frequent in RD patients at initial assessment (1.3% vs 0.5 %, p < 0.001) and in total (2.9% vs 1.7%, p<0.001) (Table 1, Figure 1). Cox regression multivariate analysis revealed systemic lupus erythematosis (SLE), polymyositis dermatomyositis (PMDM), mixed connective tissue disease (MCTD) as significant risk factors of new developments of hyperthyroidism during follow up after adjusting confounders. (Table2)

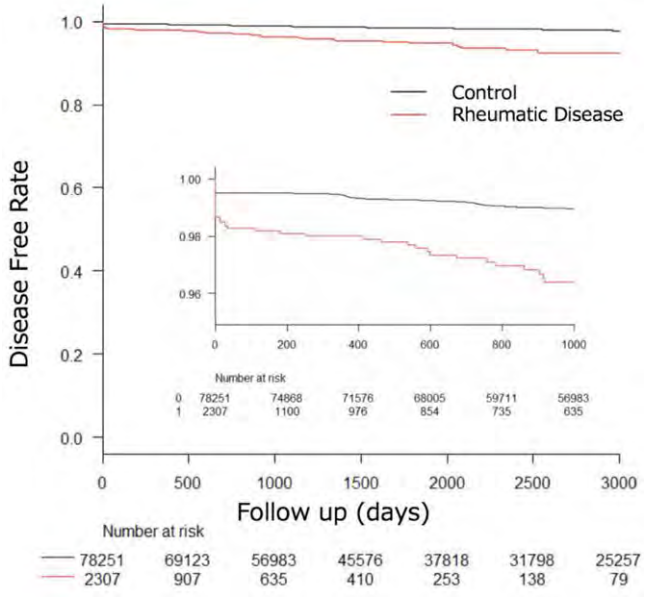


Figure 1. Hyperthyroidism with treatment indication in rheumatic patients and control

Table 2. Risk factors for newly detected hyperthyroidism with treatment indication

	Adjusted HR	p value
Age	0.99 (0.98-0.99)	< 0.001
Female	2.68 (2.31-3.12)	< 0.001
BMI	1.04 (1.02-1.06)	< 0.001
Baseline TSH ≦ 0.45	5.71 (4.47-7.30)	< 0.001
Baseline Free T4 ≧ 1.65	1.16 (0.79-1.69)	0.45
Rheumatoid arthritis	1.05 (0.50-2.21)	0.90
ANA associated diseases	-	-
SLE	2.29 (1.11-4.71)	0.025
SS	1.91 (0.91-4.01)	0.089
PMDM	12.90 (5.50-30.22)	< 0.001
SSc	0.67 (0.18-2.43)	0.541
MCTD	8.02 (2.62-24.51)	< 0.001
Vasculitis	1.44 (0.35-5.92)	0.610
Spondyloarthritis	3.04 (0.74-12.52)	0.120
Others	1.98 (0.67-5.81)	0.214

Conclusion: Hyperthyroidism with therapeutic indications are considerably more frequent in RD patients (particularly with SLE, PMDM and MCTD) both at initial assessment and during follow up. We recommend routine screening at initial assessment and careful follow up of thyroid function test in those patients.

References:
[1] Rev Bras Rheumatol 2012;52(3):417-430

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FRI0536

SERUM GOLIMUMAB CONCENTRATIONS AND ANTI-DRUG ANTIBODIES ARE ASSOCIATED WITH TREATMENT RESPONSE AND DRUG SURVIVAL IN PATIENTS WITH INFLAMMATORY JOINT DISEASES: DATA FROM THE NOR-DMARD STUDY

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Background: Lack or loss of response to TNFα-inhibitors can be caused by subtherapeutic drug levels and anti-drug antibodies (ADAb). Knowledge about associations between clinical efficacy and drug levels as well as occurrence of ADAb is limited in patients with inflammatory joint diseases (IJD) treated with golimumab.

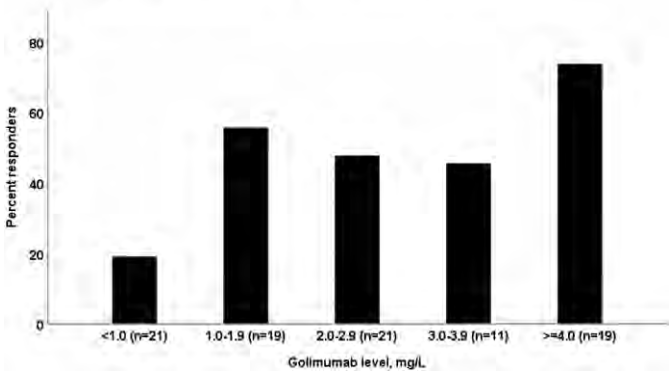
Objectives: To identify the therapeutic target concentration and assess the frequency of ADAb in golimumab-treated patients with IJD.

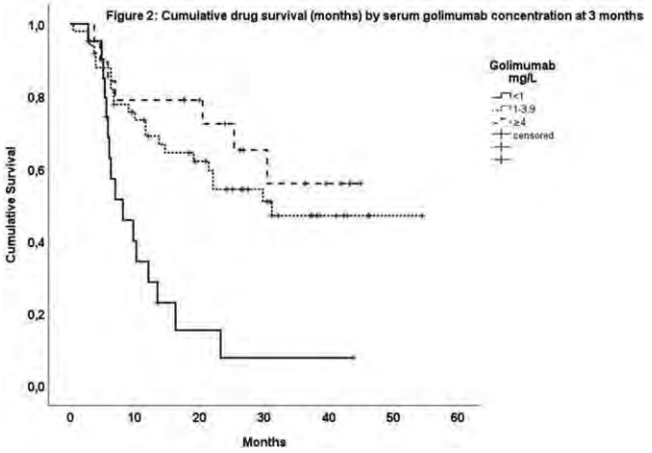
Methods: 91 patients from the NOR-DMARD study with a clinical diagnosis of axial spondyloarthritis (n=41), rheumatoid arthritis (n=20) or psoriatic arthritis (n=30) starting treatment with golimumab, with an available biobank sample at 3 months follow-up, were included. Treatment response was defined by ASDAS Clinically important improvement in axial spondyloarthritis, EWULAR good/moderate response in rheumatoid arthritis and improvement of ≥50% in modified DAPSA (using 28 swollen/tender joint counts) in psoriatic arthritis. Serum drug concentrations were analysed in non-trough samples collected 3 months after treatment initiation, using an automated in-house target-based immunofluorometric assay. ADAb was measured with an inhibition assay that measures neutralising antibodies. The association between drug levels and treatment response was assessed by multivariable logistic regression (adjusted for age, sex and prior bDMARD (Y/N)). Drug-survival was assessed by Kaplan-Meier curves and Cox proportional hazard regression analysis.

Results: Golimumab serum concentrations varied considerably between patients on standard dose (range 0.0-8.2 mg/L) with a median of 2.2 (IQR 1.0-3.5) mg/L. The proportions of responders after 3 months among patients with golimumab concentration <1.0, 1.0-3.9 and ≥4.0 mg/L, were 19%, 49% and 74%, respectively (Fig.1). The likelihood of response after 3 months of treatment was significantly higher among patients with serum golimumab concentration ≥1.0 mg/L compared to those with golimumab <1.0 mg/L (OR 5.8 (95% CI 1.7-19.7), P =0.005). The proportion of responders was highest among patients with golimumab concentrations ≥4.0 mg/L, but the difference in response between patients with concentrations ≥4.0 mg/L compared to 1.0-4.0 mg/L was not statistically significant (OR 2.1 (95% CI 0.6-7.1), P=0.24). We also found a higher rate of treatment discontinuation in patients with serum golimumab concentration <1.0 mg/L compared to ≥1.0 mg/L (HR 3.6 (95% CI 1.9-6.9), P <0.001) (Fig.2). ADAb were detected in 5 of 91 samples and were associated with lower drug concentrations. Only 1 out of 5 ADAb-positive patients was a responder at 3 months, and all 5 ADAb positive patients discontinued treatment within the first 14 months.

Conclusion: Golimumab concentrations ≥1.0 mg/L were associated with improved treatment response and better drug survival, but our results also indicate that some patients might benefit from higher concentrations. ADAb were associated with lower drug concentrations and both reduced treatment response and drug survival. These findings suggest a rationale for personalised dosing guided by measurements of drug concentration and ADAb in golimumab-treated patients with IJD, which should be addressed in future randomised strategy trials.

Figure 1: Percent responders at 3 months by serum golimumab concentration





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Table 1. Change in FVC(ml) and DLCO% in the 6–12 months before and after different treatment

Treatment group			Pre-Tx	Post-Tx	p
R	9.8% (11)	FVC	2015±746	2024±803	0.78
		DLCO	72.4±17.2	60.7±27.9	0.43
CYC	25.0% (28)	FVC	1853±585	1796±578	0.74
		DLCO	61.2±23.8	61.4±23.9	0.79
R+CYC	17.9% (20)	FVC	1901±667	1922±672	0.90
		DLCO	58.2±14.5	46.7±18.8	0.90
Non-R, CYC	47.3% (53)	FVC	2177±657	2286±704	0.47
		DLCO	46.7±18.8	45.8±19.6	0.69
Subgroup					
UIP	31.3% (35)	FVC	2053±721	1949±727	0.57
		DLCO	58.9±22.7	49.3±25.1	0.15
Non-UIP	68.8% (77)	FVC	1908±608	1961±654	0.53
		DLCO(%)	59.0±18.7	60.5±185	0.46

Table 2. Secondary outcome and multivariable Cox model for overall survival

Secondary outcome	Overall	R	CYC	R+CYC	Non-R, CYC	p
Hospitalization for AE (patient/total)	78.6%(88)	72.7%(8)	96.4%(27)	90%(18)	66%(35)	0.06
AE/year	1.4±2.1	0.41±0.45	1.28±1.81	0.86±1.14	1.49±3.23	0.43
Hospitalization for infection(patient/total)	59.8%(67)	54.5%(6)	57.1%(16)	80%(16)	82.9%(29)	0.23
Infection/yr	1.3±1.6	0.40±0.48	0.85±1.57	0.79±1.13	2.07±7.42	0.62
Respiratory failure(n)	30.4%(34)	18.2%(2)	32.1%(9)	30%(6)	30.2%(16)	0.89
1-year survival	88.6%	100%	92%	89.5%	84.1%	0.67
5-year survival	67.1%	75%	71.4%	75%	60%	0.79

Cox proportional hazard model for mortality

Variable	Hazard ratio(95% CI)	p-value
Multivariate	29.7(4.61-191)	*<0.001
Respiratory failure	2.17(1.36-3.5)	*<0.005
Acute exacerbation per year	1.2(1.0-1.4)	*0.011
Infection		

FRI0537

INTERSTITIAL LUNG DISEASE IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME—AN OVERVIEW OF CLINICAL CHARACTERISTICS AND TREATMENT IN A TERTIARY CENTER IN TAIWAN

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Background: Interstitial lung disease(ILD) is one of the major contributor to morbidity and mortality in primary Sjögren's syndrome(pSS)[1]. However, the clinical features and prognosis were various in literatures[1-3]; and the optimal management were still under investigation

Objectives: To characterize the clinical feature, treatment and prognosis predictor of ILD of pSS in a tertiary medical center in Taiwan.

Methods: Patients who had pSS and ILD confirmed with HRCT of lung between 1999-2019 were retrospectively identified. Demographic data, autoimmune feature, complementary examinations and treatments were recorded. Change in pulmonary function tests compared with pre-rituximab or pre-cyclophosphamide levels was assessed at 6–12 months post-treatment. Secondary analyses included acute exacerbation(AE), infection, and survival between different treatment groups.

Results: 112 patients (mean age 68(56-80); 67% female) were analyzed with the median pSS duration 3.1 (0.8-8.0) years. Most patients presented dyspnea and cough. NSIP was the most common radiological pattern (42.9%), followed by UIP (31.3%). Rituximab was used in 11(9.8%) patients, cyclophosphamide(-CYC) was used in 28(25%) patients, and combination was used in 20(17.9%) patients. The FVC level and DLCO% were stable after 6-12month post-treatment in these groups. During the median 3.4(1.3-7.7) years ILD follow up, 88 patients (78.6%) had been hospitalized because of AE or infection; with 34(30.4%) of them experiencing respiratory failure. 1-year and 5-year survival was 88.6% and 67.1%. No significant overall survival was distinguished between different treatment groups(p=0.36). Frequent AE (HR=2.17, 95% CI: 1.36-3.5) and respiratory failure (HR=29, 95% CI: 4.61-191) contributed to mortality, while UIP pattern did not (HR=1.6, 95% CI: 0.77-3.3).

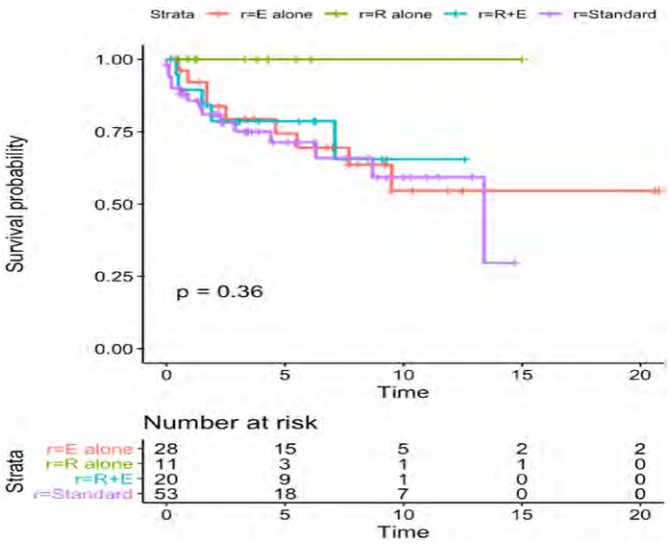


Figure 1. Kaplan-Meier survival plot of different treatment group: R, E+R, E

Conclusion: Rituximab or CYC may stabilize pulmonary function but may not benefit on overall survival. Frequent ILD AE and respiratory failure are risk factors of mortality in pSS-ILD.

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Disclosure of Interests: None declared

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FRI0538

PREGNANCY IN WOMEN WITH RHEUMATIC DISEASES: MATERNAL AND FETAL COMPLICATIONS

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Background: Most of the rheumatic diseases are more common in women than in men. Because many of these conditions may interact with pregnancy, reproductive issues related to disease management should be discussed with all women with rheumatic diseases who are in reproductive age group. Some rheumatic diseases (i.e. systemic lupus erythematosus (SLE) are associated with flares in pregnancy, while others (i.e. rheumatoid arthritis (RA) have been known to improve or not deteriorate during pregnancy. However, pregnancies in women with rheumatic diseases are still at risk of maternal/fetal complications. Nevertheless, no detailed analysis of pregnancy outcomes in women with various types of systemic connective tissue diseases has been carried out in the recent studies.

Objectives: This study aimed to compare pregnancy outcomes in women with various types of systemic rheumatic disease and analyze influence of clinical features/laboratory parameters on risk of maternal and fetal complications.

Methods: A retrospective single-center cohort study 11/2014-12/2019: 191 pregnancies in 181 patients with proved rheumatic diseases > 20 weeks of gestation, mean age was 31.6 years. Proved SLE was observed in 67 patients, 8 of them had antiphospholipid syndrome (APS) secondary to SLE. 40 patients had proved RA, 24 – vasculitis, 18 – primary Sjögren syndrome (pSS), 30 – seronegative spondyloarthropathies (SpA). Clinical and laboratory parameters, renal function at conception and after delivery and pregnancy outcomes were collected. Preeclampsia (PE) was diagnosed by the 2008 WHO criteria.

Results: Rate of PE was significantly higher in women with SLE and SLE+APS compared to women with RA ($p < 0.05$). We found a threefold increase of PE risk in patients with high activity of the rheumatic disease ($p = 0.001$, OR = 3.4, 95% CI 1.7-6.7) and fivefold increase of PE risk in patients with chronic hypertension ($p = 0.002$, OR = 5.3, 95% CI 1.9-15).

Week of delivery was significantly lower in women with SLE+APS compared to women with RA, vasculitis, systemic sclerosis (SSc), in women with SLE compared to women with SSc and SpA and in women with SSc compared to women with SpA ($p < 0.05$).

Rate of preterm birth was higher in patients with SLE+APS compared to women with SLE, RA and vasculitis, in patients with SLE compared to patients with RA and SpA, in patients with RA compared to patients with vasculitis, SSc and SpA ($p < 0.05$).

Birth weight was significantly higher in babies born to women with SSc compared to newborns to women with SLE, RA, pSS, SpA and SLE+APS and lower in newborns to women with SLE+APS compared to other groups ($p < 0.05$).

Newborns to women with SLE and SLE+APS had lower Apgar scores than newborns to women with SpA. Low GFR ($p = 0.004$, OR = 1.03), high urea ($p < 0.001$, OR = 1.5, 95% CI 1.2-1.8), creatinine ($p = 0.005$, OR = 1.02, 95% CI 1-1.04) and LDH concentrations ($p = 0.009$, OR = 1.01, 95% CI 1-1.02) in 3rd trimester increased the risk of low Apgar scores of a newborn ($p < 0.05$).

Conclusion: Patients with SLE with/without secondary APS have significantly increased rates of preeclampsia, preterm birth and lower Apgar scores. Risk of adverse pregnancy outcomes can be significantly reduced by good disease control.

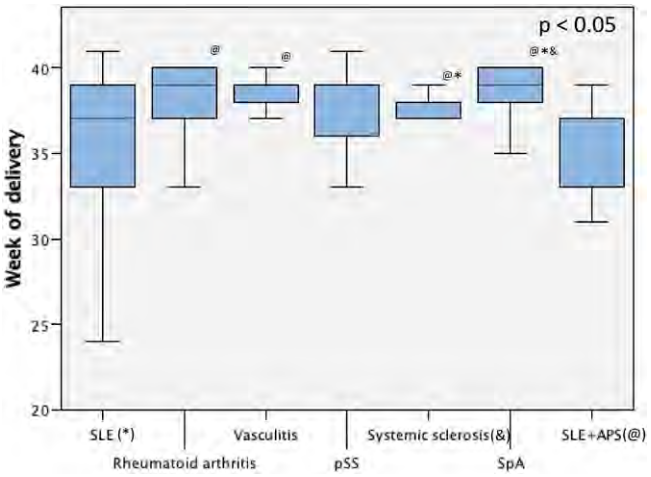
Table 1. Comparison of the pregnancy outcomes in women with various rheumatic diseases

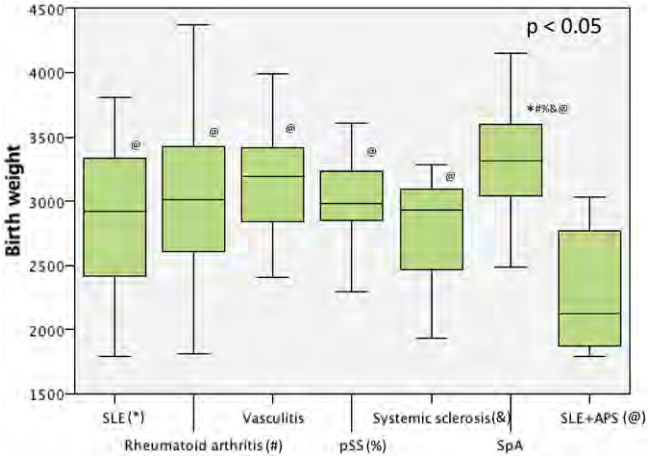
	SLE (*) n = 67	RA (#) n = 40	Vasculitis ($) n = 24	pSS (%) n = 18	SSc (&) n = 12	SpA (^) n = 30	SLE + APS n = 8
Age, *M ± SD*	31 ± 4	32 ± 5	30 ± 7	32 ± 5	32 ± 5	33 ± 6	32 ± 4
Preterm birth, *n (%)*	25 (37.3%)$^{\&}$^	9 (22.5%)$^{\$\&}$^	2 (8.3%)	6 (33.3%)	1 (8.3%)	2 (6.7%)	5 (62.5%)$^{*\$\#}$
Preeclampsia *n (%)*	13$^{\#}$ (19.4%)	0	1 (4.2%)	0	3 (25%)	2 (6.7%)	3$^{\#}$ (37.5%)
Low Apgar score *n (%)*	14^ (21%)	4 (10%)	2 (8.3%)	4 (22.2%)	1 (8.3%)	2 (6.7%)	3^ (37.5%)

$^{*,\#,\$,\%,\&,\^}$ $p < 0.05$

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FRI0539

SURVIVAL IN PATIENTS WITH CONNECTIVE TISSUE DISEASE-ASSOCIATED PULMONARY ARTERIAL HYPERTENSION (CTD-PAH): A META-ANALYSIS OF OBSERVATIONAL REGISTRIES

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Background: Although patients with CTD-PAH comprise approximately one third of the overall PAH population, the literature on survival outcomes in CTD-PAH patients overall and by CTD subtype is limited by small sample sizes. We conducted a meta-analysis of more than 4,000 patients with CTD-PAH enrolled in observational registries.

Objectives: To determine survival rates in patients with CTD-PAH overall and by CTD subtypes.

Methods: The PubMed and EMBASE databases were searched for English-only articles published between January 1, 2000 and November 25, 2019. Inclusion criteria were multicenter registries of adults with WHO group 1 pulmonary hypertension (PAH); conducted in 2000 or later; and survival data for ≥30 patients with CTD-PAH. Meta-analysis of survival was performed using a random-effects model. Survival was estimated for CTD-PAH overall; for CTD-PAH stratified by registries primarily conducted before and after 2010 to assess the impact of new therapies, as well as combination therapy approaches targeting multiple pathways; and for CTD subtypes (systemic sclerosis [SSc] and systemic lupus erythematosus [SLE]).

Results: Nineteen registries met inclusion criteria and reported data on 4,008 patients with CTD-PAH. Of these patients, 1,485 had SSc, 456 had SLE, and

CTD subtype was not specified in 2,067. CTD-PAH patients had a mean age of 55 years and 87% were female. Most patients (70%) had functional class III or IV disease and the mean 6-minute walk distance at enrollment was 327 m. Among registries that enrolled patients of all PAH etiologies (N=7,829), survival rates in the CTD-PAH subpopulation (n=2113), were 83%, 73%, and 62% at 1-, 2-, and 3- years, respectively. These survival rates were lower than those reported for the overall PAH population: 88%, 79%, and 72% at 1-, 2-, and 3- years, respectively. Numerically higher survival rates at 1-, 2-, and 3- years were observed in CTD-PAH patients treated in 2010 and later: 85% vs 90%, 74% vs 82%, and 65% vs 73%. Among all CTD-PAH patients, survival rates were lower for patients with SSc compared to those with SLE: 88% vs 92%, 75% vs 90%, 67% vs 87% at 1-, 2-, and 3- years, respectively (Figure).

Conclusion: Patients with CTD-PAH have a substantial risk of death, however, CTD-PAH patients treated within the last ten years have numerically higher survival rates than those treated earlier. This may be related to increased screening for PAH, especially in SSc (leading to earlier diagnosis) and/or the availability of new treatment approaches. Consistent with clinical observations, patients with SSc have worse survival rates than those with SLE. Given the high risk of mortality in these patients, early detection and upfront aggressive treatment are warranted.

References:



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Disclosure of Interests: Dinesh Khanna Shareholder of: Eicos, Grant/research support from: NIH NIAID, NIH NIAMS, Consultant of: Acceleron, Actelion, Bayer, BMS, Boehringer-Ingelheim, Corbus, Galapagos, Genentech/Roche, GSK, Mitsubishi Tanabi, Sanofi-Aventis/Genzyme, UCB Pharma, Carol Zhao Shareholder of: Actelion Pharmaceuticals US, Inc., Employee of: Actelion Pharmaceuticals US, Inc., Lorinda Chung Grant/research support from: United Therapeutics, Boehringer Ingelheim, Consultant of: Bristol-Myers Squibb, Boehringer Ingelheim, Mitsubishi Tanabe, Eicos Sciences, Gerry Coghlan Grant/research support from: Johnson & Johnson, Consultant of: Bayer, Johnson & Johnson, GlaxoSmithKline, Speakers bureau: Bayer, Johnson & Johnson, GlaxoSmithKline, Rajan Saggar Grant/research support from: Actelion, Gilead Science, United Therapeutics, Consultant of: Actelion, Gilead Science, United Therapeutics, Speakers bureau: Actelion, Gilead Science, United Therapeutics, Stephen Mathai Consultant of: Actelion, Liquidia, Arena, United Therapeutics, Mehul Shah Shareholder of: Actelion Pharmaceuticals US, Inc, Employee of: Actelion Pharmaceuticals US, Inc, John Hartney Shareholder of: Actelion Pharmaceuticals US, Inc, Employee of: Actelion Pharmaceuticals US, Inc, Vallerie McLaughlin Grant/research support from: Reata Pharmaceutics, SoniVie, United Therapeutics, Bayer, Acceleron, Actelion Pharmaceuticals US, Inc., Consultant of: Actelion Pharmaceuticals US, Inc., Acceleron, Arena Pharmaceuticals, Bayer, Caremark, CiVi Biopharma, United Therapeutics

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FRI0540 DIFFERENT ASSOCIATION BETWEEN BONE MINERAL DENSITY AND OSTEOARTHRITIS ACCORDING TO THE SITE OF OSTEOARTHRITIS

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Background: Osteoarthritis (OA) and osteoporosis (OP) are both high prevalence at old age, and there are various reports on the association between the two diseases. Some studies have shown that high bone mineral density (BMD) is a risk factor for OA incidence, while others have mentioned the possibility of OP contributing to onset of hip OA. Recent study described that higher BMD reduce the risk of hip OA and raise the risk of knee OA. So, the relationship between BMD and OA or the effects of BMD on different OA site are not clear yet.

Objectives: In this study, we investigated the association between BMD and radiographic OA using representative sample data of Korean adults.

Methods: The study included 6345 subjects aged 50 years or older who underwent BMD measurements using dual-energy X-ray absorptiometry and X-rays of at least one site of the spine, hip, and knee in the Korean National Health and Nutrition Examination Survey conducted in 2010-2011. OA was defined according to radiographic finding (KL grade ≥ 2). Weighted multivariable logistic regression was used to analyze the association between BMD and OA. Since gender differences are evident, men and women were analyzed separately.

Results: Spine OA was about 60% in both men and women, and hip OA was about 35% in men but only 1% in women. Knee OA was 76% in women and 58% in men. In men, the risk of OA increased 1.24 times as BMD increased by 1 g/cm^2. By site, knee and spine OA were statistically significant in relation to BMD, but hip OA was not statistically significant. In women, the association between BMD and knee and hip OA was insignificant. In spine OA, the risk of OA increased 1.2 times when BMD increased by 1 g/cm^2.

Conclusion: In conclusion, high BMD increased the risk of knee and spine OA in men, but did not affect hip OA. In women, high BMD increased the risk of spine OA. Differences in the mechanism of OA development by site are thought to be possible explanations for the differences in the association between BMD and OA.

Disclosure of Interests: None declared

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FRI0541 TEN-YEAR OUTCOME OF DIFFERENT SUBTYPES OF UNDIFFERENTIATED INFLAMMATORY ARTHRITIS

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Background: A group of patients with recent onset of arthritis always presents a certain difficulty for the practitioner due to its marked heterogeneity. This especially concerns the patients with undifferentiated inflammatory arthritis (UIA).

Objectives: To characterize the long-term nosological outcome of clinical and immunological subtypes of early UIA.

Methods: A cohort study of patients with recent onset of arthritis with a duration of not more than 12 months (n = 761, 82.8% females, 55.2% RF +) was initiated in 2003. All patients were referred to rheumatologist from GP with suspicion on inflammatory arthritis. Inclusion criteria: age 18 years or more, at least 1 swollen joint at 1st visit and/or positive squeeze test or morning stiffness for at least 30 minutes. 243 patients were initially classified as having UIA: 46 (18,9%) males, 197 (81,1%) females, age (median, quartiles)- 44 [29;53] years, duration of symptoms- 3 [2;5] months, swollen joints count (66/68)- 2 [1;4], tender joints count 3 [2;6], 85 (35%) rheumatoid factor (RF)+, 63 (25,9%) anti-CCP+. Patients with UIA were followed up for at least 10 years.

Results: 28 (11,5%) of patients were lost to follow up. Long-term observation was conducted in 215 patients. 22 (10,2%) of them developed persistent spontaneous (without use of DMARDs) remission. Other patients were finally classified as having: rheumatoid arthritis (RA) 138 (64,2%) and non-RA (25,6%). The spectrum of diagnoses in non-RA group included: ankylosing spondylitis, osteoarthritis, gout, psoriatic arthritis, polymyalgia rheumatica, systemic lupus, mixed connective tissue disease, sarcoidosis, paraneoplastic syndromes. The following characteristics at baseline positively correlated with the development of RA: arthritis of 3 or more joints (p=0,011), arthritis of hand (p=0,005), high ESR (p<0,001), high CRP (p=0,003), PF-positivity (p<0,001), anti-CCP-positivity

Table. Outcome of different subtypes of patients with UA after 10 years of follow up (n=215).

Subtypes of UA	Outcome			P (Pearson chi-squared test)
	Non-RA (n=55)	RA (n=138)	Spontaneous remission (n=22)	
Mono- and oligo arthritis (n=140)	40 (28,6%)	81 (57,9%)	19 (13,6%)	0,016
Polyarthritis (n=75)	15 (20%)	57 (76%)	3 (4%)	
RF-negative AND anti-CCP-negative (n=90)	34 (37,8%)	41 (45,6%)	15 (16,7%)	
RF+ OR anti-CCP+ OR low levels (<3 ULN) (n=92)	20 (21,7%)	65 (70,7%)	7 (7,6%)	<0,001
High RF+ AND High anti-CCP+ (n=33)	1 (3%)	32 (97%)	0	

(p<0,001), older age of onset (p=0,019), higher levels of RF IgM (p=0,027) and anti-CCP (p<0,001). Development of persistent spontaneous remission negatively correlated with polyarthritis (p=0,033), PF-positivity (p=0,034), anti-CCP-positivity (p=0,001). Positive seroconversion was observed: of RF in 10 (4,7%) patients, 8 developed RA, of anti-CCP – in 3 (1,4%) patients, all developed RA.

Conclusion: Seronegative oligoarticular disease and highly seropositive disease are different subtypes of UIA. Combination of seronegativity and oligoarticular disease (n=52) associated with relatively rare development of RA (36,2%) and high proportion of spontaneous remission (22,4%). Patients who were highly positive (>3 ULN) for both RF and anti-CCP developed RA in 97% of cases and never remitted spontaneously.

Disclosure of Interests: Elena Luchikhina Consultant of: Abbvie, Biocad, Sanofi, Celgene, Speakers bureau: Abbvie, Roche, Pfizer, Biocad, MSD, Sanofi, Johnson & Johnson, Glaxo, UCB, Celgene, Novartis, Dmitry Karateev Consultant of: Abbvie, Pfizer, Biocad, Sanofi, Novartis, Lilly, Speakers bureau: Abbvie, Roche, Pfizer, Biocad, MSD, Sanofi, Johnson & Johnson, Glaxo, UCB, Celgene, Novartis, Lilly, Bayer, Alexander Novikov: None declared, Galina Lukina Speakers bureau: Novartis, Pfizer, UCB, Abbvie, Biocad, MSD, Roche, Elena Aleksandrova: None declared, Natalia Demidova: None declared

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FRI0542 OBTAINING HIGH POSITIVE PREDICTIVE VALUES FOR THE DEVELOPMENT OF CLINICALLY APPARENT ARTHRITIS IN PATIENTS PRESENTING WITH CLINICALLY SUSPECT ARTHRALGIA; IS IT FEASIBLE?

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Background: The hypothesis that initiation of DMARD-treatment before arthritis becomes apparent could permanently modulate the disease process, such that persistent RA is prevented, is being studied in several ongoing trials. Essential for such studies is the ability to accurately predict clinically apparent inflammatory arthritis (IA). However there are two hurdles: first, it is insufficiently known whether it is possible to obtain high positive predictive values (PPV) in patients presenting with clinically suspect arthralgia (CSA). Second, none of current predictive models is validated in independent cohorts. We here aimed to evaluate the first question, incorporating improved markers of MRI-detected subclinical inflammation that were recently identified but have not yet been combined with other known predictors.[1]

Objectives: To assess the feasibility of achieving high PPVs in prediction of IA-development in patients with CSA by combining clinical, laboratory and imaging parameters.

Methods: 580 patients with CSA were consecutively included in the Clinically Suspect Arthralgia (CSA)-cohort and followed on the development of IA, determined by physical examination of joints. Unilateral contrast-enhanced 1.5 Tesla MRIs were made of MCP(2-5), wrist and MTP(1-5)-joints at baseline and scored in line with the RAMRIS. The number of locations with subclinical inflammation (0/1-2/≥3) and the presence of MCP peritendinitis were defined as described previously.[1] Other studied clinical and laboratory variables were based on the literature: initial localisation of complaints (small/large joints), functional disability (health assessment questionnaire (HAQ) ≥1), ACPA-positivity (Anti-CCP2), RF-positivity (IgM-RF) and elevated CRP. [2,3] LASSO Cox regression with a 10-fold cross-validated shrinkage parameter was used for predictor selection. Regression coefficients were rounded to the nearest number ending in .5 or .0 and multiplied by two, resulting in a weighted score. Kaplan Meijer curves were used to obtain PPVs of this weighted score and the area under the curve (AUC) was determined at 2-year follow-up.

Results: Mean age was 44, 78% was female, and 18% progressed to IA within 2 years. The following parameters were selected with LASSO: RF-positivity, ACPA-positivity, HAQ≥1, >2 locations of subclinical inflammation and presence of MCP-extensor peritendinitis. Based on the beta of LASSO-regression, patients were assigned 2 points for the risk-factors ACPA-positivity and >2 locations of subclinical inflammation, 1 point for RF-positivity and presence of MCP-extensor peritendinitis and 0 points for HAQ≥1. Kaplan Meijer curves show PPVs of 8%, 9%, 30%, 54%, 73%, 79% and 86% at two years (Figure 1). This model yielded an AUC of 0.79.

Conclusion: High PPVs for IA-development can be achieved in patients with CSA by weighting a combination of known predictors. Although encouraging, these data are based on one observational cohort study and have not been validated in independent cohorts, limiting the relevance. To support future research in the field of arthralgia, it is needed that different research groups work together to come to risk estimations that are validated and accepted.

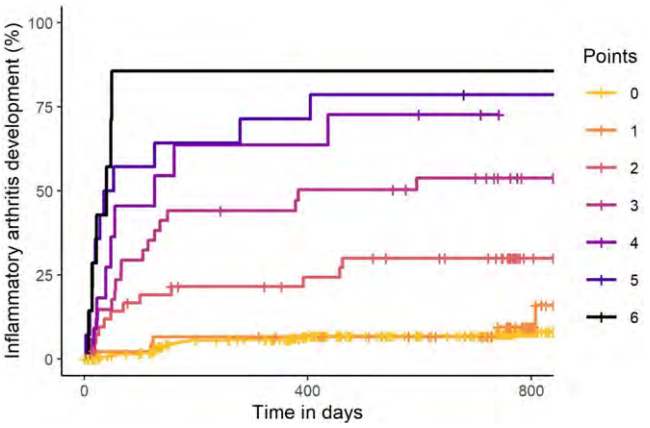


Figure 1. Kaplan Meijer curves on inflammatory arthritis development stratified for number of points based on LASSO regression. Legend: Points were based on the regression coefficients yielded by Cox LASSO-regression. 2 points were assigned for the risk factors ACPA-positivity and >2 locations of subclinical inflammation and 1 point was assigned for RF-positivity and presence of MCP-extensor peritendinitis.

References:
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[2] van Steenbergen HW et al. ART 2014;16(2):R92.
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FRI0543 BIRTH REGISTRY OF WOMEN WITH SYSTEMATIC LUPUS ERYTHEMATOSUSAND COURSE OF THE DISEASE DURING FIRST YEARS POST-PARTUM-THE GREEK EXPERIENCE

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Background: Pregnancy in women with SLE Systematic Lupus Erythematosus (SLE) has been related with adverse events both in the mother and the foetus.1 Many studies have reported relapse of the disease during the pregnancy and post-labour, while others have not confirmed this finding.2To this end, most of these results originate from retrospective studies with patients of diverge ethnicities.

Objectives: To record the Greek experience with pregnancies in mothers with SLE and their outcomes, as well as the course of the disease during first year post labor.

Methods: This is a prospective, multicentre, observation study lasting three years. Women diagnosed with SLE who became pregnant consented to be monitored by their treating Rheumatologist. A structured questionnaire is used for monitoring at the beginning of pregnancy (positive pregnancy test) and at least every 3 months thereafter, depending on the course of the disease and pregnancy, until one year after childbirth.

Results: A total 64 women and 81 pregnancies were recorded (1.27 pregnancies per patient). Patient's age at conception was 32.8 ± 5.9 years (mean ± standard deviation). Thirteen patients (20.3%) had past history of nephritis. Regarding pregnancy outcomes, 62 (76.5%) pregnancies ended in live births, miscarriages during 1st, 2nd and 3rd trimester occurred in 13 (16%). Six pregnancies were lost to followup. Prematurity occurred in 28 live births (45.1% in total), 26-32w (3.2%), 32-36w (22.5%), <37w (19.3%). No cases of preeclampsia occurred. Mean age of birth **36.9 weeks** and mean birth weight **2750gr.** The majority (72.5%) of deliveries were performed by caesarean section. In terms of disease activity, most of the women had mild disease at conception, (SLEDAI-2K: 2.67±2.69) that

declined during 1st/2nd pregnancy trimester (SLEDAI-2K:1.91±2.09, 1.70±2.22)) but increased during the 1st and 2nd trimester post labor (SLEDAI-2K: 2.47±4.29 and 2.52±3.2).

Conclusion: This is the first Greek inception cohort with prospective monitoring of pregnant SLE patients. Adverse outcomes occur with prematurity being the most frequent. In our cohort disease activity tends to increase during 1st and 2nd trimester post-labor without serious relapses. Vigilant monitoring during pregnancy and post-labour is advised.

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FRI0544

THE EFFECT OF PATERNAL EXPOSURE TO IMMUNOSUPPRESSIVE DRUGS ON SEXUAL FUNCTION, REPRODUCTIVE HORMONES, FERTILITY, PREGNANCY AND OFFSPRING OUTCOMES: A SYSTEMATIC REVIEW

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Background: Information regarding the possible influence of immunosuppressive drugs on male sexual function and reproductive outcomes is scarce. Men diagnosed with immune-mediated diseases and a wish to become a father represent an important neglected population since they lack vital information to make balanced decisions about their treatment.

Objectives: To systematically review the literature for the influence of paternal immunosuppressive drug use on many aspects of male sexual health, such as sexual function, fertility, pregnancy outcomes and on their offspring health outcome.

Methods: A systematic literature search was performed in the bibliographic databases: Embase (via Elsevier embase.com), MEDLINE ALL via Ovid, Cochrane Central Register of Trials (via Wiley) and Web of Science Core Collection. Additionally, Google Scholar and the Clinical trial registries of Europe and the USA were searched. The databases were searched from inception until August 31th 2019. The searches combined keywords regarding male sexual function and fertility, pregnancy outcomes and offspring's health with a list of immunosuppressive drugs. Studies were included if they were published in English and if they included original data on male human exposure to immunosuppressive drugs.

Results: A total of 5867 references were identified among which we identified 163 articles fulfilling the eligibility criteria. Forty nine articles included pregnancy and offspring outcomes and 116 articles included sexual health outcomes. With the exception of large Scandinavian cohorts, most of the identified articles included a small number of participants. While a clear negative effect on sperm quality was evident for sulfasalazine and cyclophosphamide a dubious effect was identified for colchicine, methotrexate and sirolimus. In 3 articles exposure to TNF-a inhibitors in patients diagnosed with ankylosing spondylitis resulted in improved sperm quality. The information regarding pregnancy and offspring outcomes was scant but no large negative effect associated with paternal immunosuppressive drug exposure was reported.

Conclusion: Evidence regarding the safety of immunosuppressive drugs in men with a wish to become a father is inconclusive. The lack of standardization on how to evaluate and report male sexual function, fertility and reproduction as study outcomes in men exposed to immunosuppressive drugs is an important contributor to this result. Future research on this topic is needed and should be preferably done using standardized methods.

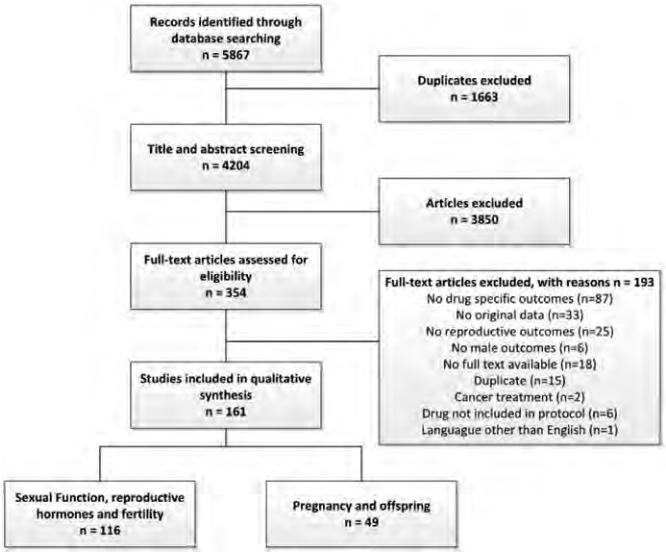


Figure 1. Flow diagram for study selection.

Disclosure of Interests: Luis Fernando Perez: None declared, Radboud Dolhain Grant/research support from: unrestricted grant from UCB Pharma, Saskia Vorstenbosch: None declared, Wichor Bramer: None declared, Eugène van Puijenbroek: None declared, Johanna Hazes: None declared, Bernke te Winkel: None declared

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FRI0545

A META-ANALYSIS OF GIANT CELL ARTERITIS TEMPORALLY AND ACROSS REGIONS

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Background: Giant cell arteritis (GCA) is an immune-mediated disease of the large vessels, and occurs in adults over 50 years old[1]. It is the most commonly seen form of chronic vasculitis and is associated with significant rates of morbidity[2]. This meta-analysis examines the geographical and temporal epidemiology of GCA, including incidence, prevalence and mortality.

Objectives:

1.To identify changes in incidence rate, prevalence, and mortality rate over time

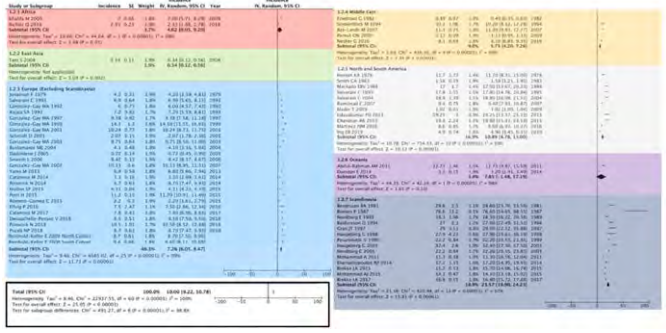
2.To compare these rates between geographic regions around the world

Methods: A systematic review of the English literature was conducted using the EMBase, Scopus and PubMed databases. Articles were included if they were cohort or cross-sectional studies with 50 or more patients with GCA and reported on population, location and time-frame parameters. Articles on mortality were included if they compared mortality to age and gender matched population. Review articles, case-control studies and case series were excluded. Two reviewers extracted data and a third verified inclusion of studies. Study quality was assessed by using the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist. Mortality rate was standardized across cohorts to deaths per 1000 people per year.

Results: Of the 3569 citations identified by the literature search, 107 were included in analysis. The pooled incidence of GCA internationally was 10.00 [9.22, 10.78] cases per 100 000 people over 50 years old (Figure). This incidence was highest in Scandinavia 21.57 [18.90, 24.23], followed by North and South America 10.89 [8.78, 13.00], Europe 7.26 [6.05, 8.47], and Oceania 7.85 [1.48,17.19]. Nine studies reported prevalence. Pooled prevalence from these 9 was 51.74 [42.04,61.43] cases per 100 000 people over 50 years old. Overall, pooled mortality was 20.44 [17.84,23.03] deaths/1000 per year. Mortality had a generally decreasing trend over the years of publication.

Conclusion: The incidence of GCA varies regionally almost 3-fold. Likely genetic and environmental factors may explain this trend. Incidence and prevalence are important for tracking the efficacy and side effects of current therapies, as well as planning for the costs of biologic treatment.





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FRI0546 GENDER DIFFERENCES OF RHEUMATIC DISEASES IN MEXICAN POPULATION: DATA FROM THE MEXICAN BIOLOGICS REGISTRY

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Background: Most autoimmune diseases are more prevalent in women. Symptom severity, disease progression, response to therapy and overall survival differ between males and females with rheumatic diseases.

Objectives: To identify the characteristics of autoimmune diseases presentation and treatment between male and female population using information from the Mexican Adverse Events Registry (BIOBADAMEX).

Methods: BIOBADAMEX is a Mexican ongoing cohort that collects the information of patients using biologic and biosimilar drugs since 2016. For this study we included all patients enrolled in the registry and compared baseline clinical and disease characteristics, treatment and presence of adverse events between genders. We used logistic regression to analyze univariable associations.

Table 1. Baseline characteristics in the cohort by sex

	Women n=532 (82%)	Men n=123 (18%)	Univariable[a] OR(95%CI)
Age, median (IQR)	53 (44-60)	47 (34-55)	1.02 (1.0-1.1)*
Body Mass Index, median (IQR)	27 (23-31)	26 (23-30)	1.0 (0.9-1.1)
Smoking, n(%)	28 (5)	18 (16)	0.3 (0.2- 0.6)*
Disease duration, median (IQR)	9 (4-16)	7 (2-13)	1.0 (1.0-1.1)*
Diagnosis, n(%):			
RA	414 (78)	37 (30)	2.4 (1.0-5.7)*
AIJ	12 (2)	5 (4)	0.5 (0.1-1.9)
AS	37 (7)	56 (46)	0.1 (0.1-0.4)*
PsA	19 (4)	15 (12)	0.3 (0.1-0.8)*
SLE	17 (3)	3 (2)	1.2 (0.3-5.2)
Others	33 (6)	7 (6)	1
Disease Activity indexes, median (IQR)			
DAS28[a]	4.9 (3.6-5.9)	4.9 (3.0-5.9)	1.1 (0.9-1.3)
BASDAI[b]	4.8 (2.9-8)	5.3 (2.8-7.5)	0.9 (0.8- 1.1)
ASDAS[c]	3.2 (1.9-4.5)	3.9 (2.5-4.7)	0.8 (0.6-1.2)
SLEDAI[d]	14.5 (5.0-19.5)	25 (25.0-31.0)	0.6 (0.4-1.1)
High blood pressure, n(%)	77 (15)	14 (12)	1.3 (0.7-2.4)
Diabetes mellitus, n(%)	46 (9)	7 (6)	1.5 (0.7-3.5)
High cholesterol, n(%)	41 (8)	8 (7)	1.2 (0.4-2.6)
Other comorbidities, n(%):	173 (33)	26 (21)	1.8 (1.1 -2.8)*
Use of previous biologic, n(%):	216 (40)	44 (36)	1.2 (0.8- 1.8)
Use of steroids, n(%):	215 (42)	34 (29)	1.7 (1.1 -2.7)*
Use of DMARD, n(%):	418 (79)	89 (72)	1.4 (0.9-2.2)
Adverse events[b], n(%):	69 (13)	14 (11)	1.2 (0.7-2.1)
Severe[b], n(%):	12 (17)	3 (21)	0.8 (0.2-3.1)

Univariable logistic regression analysis. *p<0.05. [a]n=469, [b]n=99, [c]n=71, [d]n=19,

Results: A total of 655 participants were analysed, of which 82% were female (Table 1). We found women were older with a median of 53 years compared to 46 years in men (OR 1.02, CI 1.0-1.1). Smoking was higher in men (16%) compared to women (5%), (OR 0.3, CI 0.2-0.6). Women had longer disease duration, 9 years compared to 7 years in men (OR 1, CI 1.0-1.1). Rheumatoid arthritis (RA) was more prevalent in women (OR 2.7, CI 1-6.9), while ankylosing spondylitis (AS) and psoriatic arthritis (PsA) were more prevalent in men (OR 0.2, CI 0.1-0.4, and OR 0.3, CI 0.1-0.9 respectively). Women had more comorbidities than men (OR 1.8, CI 1.1-2.8) and used steroids more frequently (OR 1.7, CI 1.1-2.7). Differences in disease activity were not found, however we noticed high activity scores among participants.

Conclusion: In our study we found sex differences regarding age and disease duration, being higher in women. As expected, the prevalence of RA was higher in women and AS and PsA in men. Overall, women used more steroids than men. An interesting finding was that patients had high disease activity. Future longitudinal analyses will allow us to analyse sex differences in disease progression and treatment response.

References:

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Disclosure of Interests: Vijaya Rivera Teran: None declared, Deshire Alpizar-Rodriguez: None declared, Sandra Sicsik: None declared, Fedra Irazoque-Palazuelos Consultant of: Bristol-Myers Squibb, Janssen, Pfizer Inc, Roche and UCB, Dafhne Miranda: None declared, David Vega-Morales: None declared, Julio Cesar Casasola: None declared, Sandra Carrilo: None declared, angel castillo: None declared, Sergio Duran Barragan: None declared, Omar Muñoz: None declared, Aleni Paz: None declared, Angélica Peña: None declared, Alfonso Torres: None declared, Daniel Xavier Xibille Friedmann Consultant of: Lilly, Abbvie, Speakers bureau: Lilly, Abbvie, Azucena Ramos: None declared, José Francisco Moctezuma: None declared, Francisco Aceves: None declared, Estefania Torres: None declared, Natalia Santana: None declared, Miguel Vazquez: None declared, Erick Zamora: None declared, Francisco Guerrero: None declared, Claudia Zepeda: None declared, Melanea Rivera: None declared, Kitzia Alvarado: None declared, Cesar Francisco Pacheco Tena: None declared

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FRI0547 THE EFFECT OF CORRECTED INFLAMMATION, OXIDATIVE STRESS AND ENDOTHELIAL DYSFUNCTION ON FMD LEVELS IN PATIENTS WITH SELECTED CHRONIC DISEASES: A QUASI-EXPERIMENTAL STUDY

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Background: While the pathophysiology of chronic disorders varies there are three basic mechanisms - inflammation, oxidative stress and endothelial dysfunction – that are common in many chronic diseases. These mechanisms,

which have a dynamic structure, are key to homeostasis. However, the failure of these mechanisms to work synchronously can lead to morbidity complicating the course of many chronic diseases.

Objectives: To evaluate the effect of anti-atherosclerotic liquid (AAL), anti-inflammatory capsules (AIC) and anti-oxidant liquid (AOL) supplementation on the flow-mediated dilatation (FMD), inflammatory, oxidative stress and endothelial dysfunction markers in patients with selected chronic diseases

Methods: We analyzed data of 178 patients from cohorts with selected chronic diseases (Rheumatoid arthritis, familial Mediterranean fever, DM type-2, Hypertension, Multiple sclerosis, Chronic obstructive pulmonary disease, Alzheimer disease and Cancer) in this quasi-experimental study. Endothelial dysfunction was determined by FMD and serum asymmetric dimethylarginine (ADMA) levels. Serum ADMA, high sensitive C-reactive protein (hs-CRP), serum PTX3, malondialdehyde (MDA), Cu/Zn-superoxide dismutase (Cu/Zn-SOD), glutathione peroxidase (GSH-Px) levels and FMD were studied in baseline and after 12 weeks of Morinda citrifolia (AAL, 3ml once per day), omega-3 (AIC, 3 capsules once per day) and extract with Alaskan blueberry and 21 different red purple fruit vegetables (AOL, 30ml once per day). Stepwise multivariate regression analysis evaluated the association of FMD with clinical and serologic parameters.

Results: Serum ADMA, MDA, PTX3, hsCRP and albumin levels, and proteinuria were significantly decreased and CuZn-SOD, GSH-Px and FMD levels were significantly increased following AAL, AIC and AOL therapies. FMD was negatively correlated with serum ADMA, MDA, PTX3, hsCRP levels, SBP and DBP and positively correlated to CuZn-SOD and eGFR levels both at baseline and after the 12-weeks treatment period. Multivariate regression analysis revealed that ADMA and PTX3 levels were independently related to FMD both before and after AAL, AIC and AOL therapies (Table 1, Figure 1).

Conclusion: Our study shows that serum ADMA, MDA, PTX3 levels are associated with endothelial dysfunction in patients with selected chronic diseases. Short-term AAL, AIC and AOL therapies significantly improves FMD and normalizes ADMA, PTX3, hsCRP and MDA. This may have implications for adjunctive therapy in a number of chronic disorders.

References:

[1] Yilmaz MI, Saglam M, Caglar K, Cakir E, Sonmez A, Ozgurtas T et al. The determinants of endothelial dysfunction in CKD: oxidative stress and asymmetric dimethylarginine. Am J Kidney Dis. 2006;47(1):42-50. doi:10.1053/j.ajkd.2005.09.029.

Table 1. Analysis of association between change (Δ) in FMD and relevant parameters by univariate and multivariate linear regression analysis.

	Univariate Rho (p)	Multivariate Beta (p)
Δ FMD (%) *(r^2=0.30)*		
Change		
ADMA (µmol/l)	-0.63 (<0.001)	-0.25 (0.01)
MDA (nmol/ml)	-0.58 (<0.001)	-0.18 (0.02)
SOD (U/ml)	0.48 (<0.001)	NS
GSH (U/ml)	0.02 (0.75)	NS
HOMA	-0.21 (0.001)	NS
eGFR (ml/min/ 1.73 m^2)	-0.03 (0.62)	NS
hsCRP (mg/l)	-0.45 (<0.001)	NS
PTX3 (ng/ml)	-0.49 (<0.001)	-0.21 (0.01)
SBP (mmHg)	-0.26 (<0.001)	NS
DBP (mmHg)	-0.11 (0.12)	NS
Hemoglobin (g/dl)	0.07 (0.32)	NS
Total Cholesterol (mg/dl)	-0.05 (0.49)	NS
Triglyceride (mg/dl)	-0.11 (0.12)	NS
LDL (mg/dl)	-0.12 (0.07)	NS
HDL (mg/dl)	0.02 (0.82)	NS
HbA1c (%)	-0.26 (<0.001)	NS

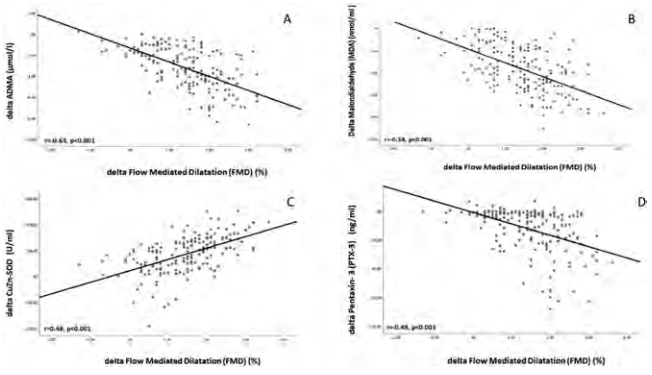


Figure 1. Scatter-plot graphs between FMD and ADMA, MDA, CuZn-SOD, PTX-3.

Disclosure of Interests: None declared

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FRI0548 PREVALENCE AND THERAPY OF RHEUMATOLOGICAL ADVERSE EVENTS DUE TO IMMUNE CHECKPOINT INHIBITOR THERAPY

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Background: Immune checkpoint inhibitors (ICIs) have improved cancer therapy and especially clinical outcomes for patients with many malignancies [1]. ICIs lead to a higher immune system activity and subsequent attack of tumor cells. However, this effect can cause rheumatological immune related adverse events (rh-irAE), which have not yet been extensively studied.

Objectives: To determine the prevalence and type of rh-irAE in patients treated with ICIs. Additionally, our study focused on duration, severity and therapy of rh-irAE as well as the correlation between tumor response rate and patients with or without rh-irAE.

Methods: We analysed 437 patients between January 2014 and October 2019, treated with ipilimumab (anti-CTLA-4) and/ or nivolumab (anti-PD-1) or pembrolizumab (anti-PD-1) at the Department of Oncology, Hematology and Rheumatology at the University Hospital in Bonn, Germany.

Results: Of the 437 patients, 260 (60%) were males, 177 (40%) were females with a mean age of 64 years (SD ± 14) at the beginning of the ICI-therapy. 152 patients (34.8%) displayed at least one irAE.

We identified 20 patients (4.6%) with a minimum of one rh-irAE due to ICI-therapy, seven of those had a pre-existing rheumatological disease. Those 20 patients were initially treated for melanoma, lung cancer, head and neck tumor and gastrointestinal carcinoma. Rh-irAE occurred in one patient (2.6%) with ipilimumab, in nine patients (4.8%) with nivolumab, in nine patients (5.7%) with pembrolizumab and in one patient (1.9%) with a combination of ipilimumab and nivolumab.

Arthralgia developed most frequently in nine of the 20 patients (45%). Arthritis and myositis occurred with equal frequencies, in three cases each (3 patients, 15%). Furthermore, three of the 20 patients (15%) developed a psoriatic arthritis and one patient (5%) osteoarthritis. The time to the first rh-irAE after exposure to ICIs was in median 100 days (IQR 45 – 406 days). Most rh-irAE were classified as moderate severe (CTCAE [Common Terminology Criteria of Adverse Events] grade 2: 55%).

15 patients (75%) were treated with systemic corticosteroids. In three cases (15%) additional therapy with methotrexate and in one patient (5%) with tocilizumab was required. Other therapies including non-steroidal anti-inflammatory drugs and opioids were also used in eight patients. Even though patients benefited from ICI treatment, therapy had to be discontinued in nine of them (45%).

Interestingly, patients with rh-irAE had a significantly higher tumor response rate compared to patients without any irAE (95% vs. 33%; p<0,0001).

Conclusion: Our results show, that rh-irAE occur under ICI-therapy and in patients with higher tumor response. However, they are not the most frequent irAE after ICI exposure: 10.2% of all irAE were rheumatological (22 rh-irAE cases in 20 patients of a total of 216 irAE cases in 152 patients). As the use of ICIs is increasing for different malignancies the incidence of rh-irAE can be expected to increase.

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Acknowledgments

Disclosure of Interests: None declared

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FRI0549 RISK OF INVASIVE FUNGAL INFECTION IN SYSTEMIC LUPUS ERYTHEMATOSUS: A NATIONWIDE POPULATION-BASED STUDY IN TAIWAN

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Background: Infectious disease is one of the leading causes of mortality in systemic lupus erythematosus (SLE). Among these infections, invasive fungal infection (IFI) carries high mortality rate (25-70%), but the literature of IFI in SLE is limited.

Table 1. Independent risk factors of IFI in patients with SLE[a]

	Candidiasis		Cryptococcosis		Aspergillosis	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Age>50	1.77 (1.27-2.47)	<0.001				
Diabetes mellitus	1.65 (1.16-2.35)	0.006				
End-stage renal disease	1.76 (1.29-2.41)	<0.001				
Stroke	1.77 (1.26-2.47)	<0.001	1.96 (1.09-3.53)	0.024		
Mycophenolate mofetil	2.72 (1.60-4.61)	<0.001			4.02 (1.32-12.26)	0.015
Cyclosporin					4.94 (1.61-15.10)	0.005
Cyclophosphamide	1.50 (1.07-2.10)	0.019				
Intravenous steroid	28.19 (21.17-37.52)	<0.001	63.51 (36.10-111.71)	<0.001	34.80 (15.09-80.24)	<0.001

[a] All factors with *P*<0.05 in univariate analysis were selected for Cox multivariate analysis. CI, confidence interval; HR, hazard ratio.

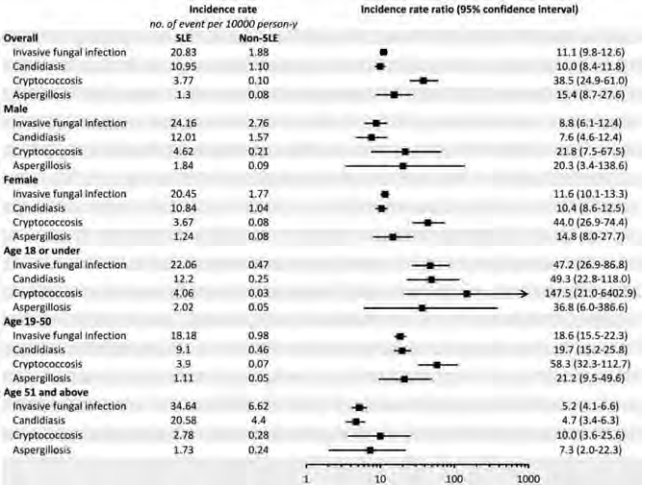


Figure 1. Incidence rate and incidence rata ratio of invasive fungal infection

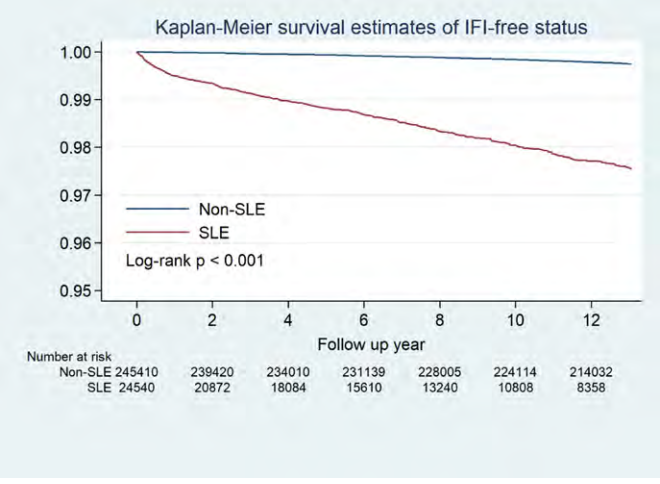


Figure 2. Kaplan-Meier curve of invasive fungal infection-free status in SLE versus non-SLE group.

Objectives: To investigate the epidemiology and risk factors of invasive fungal infection and its subtypes, including candidiasis, aspergillosis, and cryptococcosis, in SLE patients.

Methods: All patients with newly diagnosed SLE between 1997-2012 were enrolled from Taiwan National Health Insurance Research Database, with an age- and sex-matched non-SLE control group in a ratio of 1:10. IFI was identified by ICD9 codes[1] from discharge record and validated by use of systemic anti-fungal agents. The incidence rate (IR), incidence rate ratio (IRR), cause mortality rate of IFI and its subtypes were compared. A Cox multivariate model with time-dependent covariates was applied to analyse the independent risk factors of IFI.

Results: A total of 269 951 subjects (24 541 SLE and 245 410 control) were included. There were 445 episodes of IFI in SLE group. Candida was the most common pathogen (52.8%), followed by cryptococcus and aspergillus. The IR of IFI in SLE was 20.83 per 10,000 person-years with an IRR of 11.1 (95% CI 9.8-12.6) compared to the control (figure 1). Kaplan-Meier curve also disclosed a lower IFI-free survival in SLE (figure 2). The all-cause mortality rate was similar between SLE and the control (26.7 vs 25.7%). In SLE, treatment with mycophenolate mofetil (HR=2.24, 95% CI 1.48-3.37), cyclosporin (HR=1.65, 95% CI 1.10-1.75), cyclophosphamide (HR=1.37, 95% CI 1.07-1.75), oral daily dose of steroid>5 mg prednisolone (HR=1.26, 95% CI 1.01-1.58), and intravenous steroid therapy (HR=29.11, 95% CI 23.30-36.37) were identified as independent risk factors of IFI. Similar analyses were performed for subtypes of IFI. Distinctive risk factors were found between different subtypes of IFI (table 1).

Conclusion: SLE patients have a higher risk of IFI. Intravenous steroid therapy is the most important risk factor of IFI. This study provides crucial information for risk stratification of IFI in SLE.

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[1] Winthrop KL, Novosad SA, Baddley JW, et al. Opportunistic infections and biologic therapies in immune-mediated inflammatory diseases: consensus recommendations for infection reporting during clinical trials and postmarketing surveillance. Ann Rheum Dis. 2015 Dec; 74(12):2107-2116.

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FRI0550

CAN CYTOKINE GENE POLYMORPHISMS BE USEFUL FOR THE THERAPEUTIC CHOICE IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS?

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Background: Rheumatoid arthritis (RA) is a common autoimmune disease. It is characterized by systemic synovitis with bone erosion and joint cartilage degradation(1). Production of autoantibody is important for autoimmune disease. Cytokines play crucial roles in its pathogenesis(2). SNP distribution varies between races. Few studies have examined SNP targeted at Japanese patients. The analysis of cytokine gene polymorphisms is important factor of pathophysiology and treatment.

Objectives: This analysis was aimed to investigate the association between cytokine gene polymorphisms and autoantibody and therapeutic response in Japanese RA patients.

Methods: This study subjects consisted of 100 RA patients and 50 healthy controls. We extracted data on patient sex, age, disease duration, rheumatoid factor (RF), anti cyclic citrullinated peptide (anti-CCP) antibody and therapeutic response including methotrexate (MTX) and biological DMARDs. Genomic DNA was isolated from peripheral blood, these were genotyped for TNFα, $TGF\beta_1$, IL-6, IL-10 and IFNγ polymorphisms. We analyzed these data using a chi-square test.

Results: IL-10 (-819 C/T and -592 C/A) revealed that there were significant decrease in the frequency of IL-10 (-819) CC genotype and (-592) CC genotype as compared to controls in RA patients. Genotyping of IL-10 showed that there was significant decrease ACC/ACC genotype (Table 1).

IFNγ (+874 A/T) revealed that there was significant decrease in the frequency of TT genotype as compared to controls (Table 1).

No significant differences in TNFα, $TGF\beta_1$ and IL-6 genotypes and alleles frequency were observed between RA patients and control.

$TGF\beta_1$ (+869 A/T) in patients with anti-CCP antibody positive revealed that there was significant decrease in the frequency of TT genotype as compared to patients with anti-CCP antibody negative (Table 2).

No significant association between RF and any cytokine gene polymorphism.

Analyzing cytokine gene polymorphisms could be useful for treatment with MTX and biological DMARDs.

Conclusion: IL-10 (-819 C/T, -592 C/A) and IFNγ (+874 A/T) polymorphism might be related to RA in Japanese population. In addition, TGFβ$_1$ (+869 A/T) polymorphism might be associated with the production of anti-CCP antibody. These results suggest that the analyzing cytokine gene polymorphisms may offer promise as useful factors in the choice of treatment for Japanese RA patients.

Table 1.

Cytokine GT & alleles*	RA (n=100)	Controls (n=50)
IFN γ +874		
A/T	21.0% (21/100) χ^2=5.7736	16.0% (8/50)
T/T	0% (0/100) (p=0.0163)	6.0% (3/50)
A/A	79.0% (79/100)	78.0% (39/50)
A allele	89.5% (179/200)	86.0% (86/100)
T allele	10.5% (21/200)	14.0% (14/100)
IL-10		
Genotypes	χ^2=7.8022 (p=0.0052)	
ACC/ACC (Lo)	5.0% (5/100)	22.0% (11/50)
ACC/ATA (Lo)	43.0% (43/100)	32.0% (16/50)
ATA/ATA (Lo)	46.0% (46/100)	40.0% (20/50)
GCC/ACC (Int)	3.0% (3/100)	1.0% (1/50)
GCC/ATA (Int)	2.0% (2/100)	2.0% (2/50)
GCC/GCC (Hi)	0% (0/100)	0% (0/50)
***IL-10* −819 (C/T)**	χ^2=5.4162 (p=0.0200)	
C/C	8.9% (8/100)	24.0% (12/50)
C/T	45.6% (46/100)	36.0% (18/50)
T/T	45.6% (46/100)	40.0% (20/50)
C allele	31.0% (62/200)	42.0% (42/100)
T allele	69.0% (138/200)	58.0% (58/100)

* : genotype

References:

[1] Scott DL, Wolfe F, Huizinga TW. Rheumatoid arthritis. Lancet. 2010; 376: 1094–108.
[2] McInnes IB, Schett G. Cytokines in the pathogenesis of rheumatoid arthritis. Nat Rev Immunol. 2007 Jun;7(6):429-42.

Disclosure of Interests: None declared

Table 2.

*Cytokine GT** and alleles	RA (n=100)	ACPA−positive (n= 70)	ACPA−negative (n= 30)	Controls (n= 50)
TGF β$_1$ +869				
T/C	52.0% (52/100)	60.0% (42/70) χ^2=3.8788	33.3% (10/30)	52.0% (26/50)
C/C	28.0% (28/100)	20.0% (14/70) (p=0.0489)	46.7% (14/30)	22.0% (11/50)
T/T	20.0% (20/100)	20.0% (14/70)	20.0% (6/30)	26.0% (13/50)
T allele	46.0% (92/200)	50.0% (70/140)	36.7% (22/60)	52.0% (52/100)
C allele	54.0% (108/200)	50.5% (70/140)	63.3% (38/60)	48.0% (48/100)

* : genotype

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FRI0551 PERFORMANCE OF THE 2019 AMERICAN COLLEGE OF RHEUMATOLOGY/EUROPEAN LEAGUE AGAINST RHEUMATISM SYSTEMIC LUPUS ERYTHEMATOSUS CLASSIFICATION CRITERIA

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Background: Systemic lupus erythematosus (SLE) is a heterogenous autoimmune disease, with increased morbidity and mortality, often diagnosed in advanced stages. The recently published 2019 American College Of Rheumatology/European League Against Rheumatism (ACR/EULAR) classification criteria for SLE are weighted, hierarchically clustered criteria developed to increase reliability and the identification of early SLE.
Objectives: To compare the sensitivity and specificity of the 2019 ACR/EULAR criteria with the 2012 SLICC criteria in a large single-centre cohort of patients with SLE, diagnosed according to expert oppinion.
Methods: Data of SLE patients evaluated in our centre between 1996-2019 have been retrospectively analyzed. The control cohort included patients with positive antinuclear antibodies of other ethiology than SLE, evaluated between 2001-2019. The sensitivity and specificity of the 2019 ACR/EULAR and 2012 SLICC criteria were tested using the McNemar test for correlated proportions.
Results: Four hundred and forty-six patients with SLE (413 women, mean±SD age 40.5±12.7 years, disease duration 10.1±9.2 years) and 67 controls (63 women, mean±SD age 50.4±12.6 years, disease duration 7.6±6.9 years; 29 systemic sclerosis (SSc), 18 mixed connective tissue dissease (MCTD), 15 undifferentiated CTD, 2 rheumatoid arthritis (RA), 2 SSc – RA overlaps and 1 dermatomyositis) were included. The sensitivity of the 2019 ACR/EULAR and 2012 SLICC criteria were similar 85.4% and 83.6 %, respectively (p=0.3). The specificity of the 2019 ACR/EULAR and 2012 SLICC criteria were 70.2 % and 86.6%, respectively (p=0.007). In the SLE group, patients missclassified according to the new 2019 ACR/EULAR criteria were 65, whereas according to the 2012 SLICC criteria were 73; of them, 44 patients did not fulfill any criteria. In the control group, patients misclassified had mainly MCTD (13/20 patients according to the new 2019 ACR/EULAR, and 8/9 according to the 2012 SLICC criteria).
Conclusion: In this real-life cohort, the 2019 ACR/EULAR criteria have a similar sensitivity and lower specificity than the 2012 SLICC criteria, misclassifying especially MCTD patients. These results might be due to the long disease duration in our cohort.

References:

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Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.3786

FRI0552 GLOBAL, REGIONAL, AND NATIONAL BURDEN OF LOW BACK PAIN, 1990-2019: A SYSTEMATIC ANALYSIS FOR THE GLOBAL BURDEN OF DISEASE STUDY 2019

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Background: Low back pain (LBP) has become a major public health problem worldwide although the burden and underlying causes differ across locations and demographic groups.
Objectives: To report the distribution, trend and risk factor in the burden of LBP from the Global Burden of Disease Study 2019 (GBD 2019).
Methods: Based on GBD 2019, decomposition analyses were performed according to gender, age, geography and sociodemographic index (SDI). The number and age standardized rate of incidence, prevalence and disability adjusted life years (DALYs) with 95% uncertainty intervals (UI) were calculated.
Results: In 2019, female patients have a slightly higher number of prevalence (17%), incidence (15%) and DALYs (16%) than male patients. Out of twenty 5-year age group, the number of incidences, prevalence, DALYs peak at 50-54 age group, while the rate of incidence, prevalence, DALYs peaked at 80-84 age group. From 5 SDI regions, the highest number and age-standardized rate of incidence, prevalence, DALYs were observed in middle and high SDI region, respectively. Considering 21 GBD regions, the highest number of incidence, prevalence, and DALYs were observed in East Asia, while the highest age standardized rate of incidence, prevalence and DALYs all found in Central Europe, High-income North America, High-income North America, respectively. In 204 countries and territories, the top 3 highest number of incidence, prevalence and DALYs were from China, India, United States of America. The top 3 highest age-standardized rate of prevalence, and DALYs were Georgia, United States of America, Denmark, while top 3 highest age-standardized rate of incidence were Poland, Vanuatu, Romania.
From 1990 to 2019, globally, the number of incidence, prevalence, DALYs increased by 50%, 47%, 47% to 223,738,363 (95%UI 197,935,799-253,300,243), 569,089,727 (95% UI 505,632,980-641,256,710), 63,533,528 (95%UI 44,883,714-84,975,210), while age standardized rate of incidence, prevalence and DALYs decreased by 13%, 16%, 16% to 2,750 (95%UI 2,427-3,108), 6,974 (95%UI 6,192-7,862), 778 (95%UI 548-1,043). In 5 SDI regions, low SDI region has the highest percentage increases in number of incidence, prevalence and DALYs, the highest percentage decrease in age standardized rate of incidence, prevalence and DALYs were observed in High-middle SDI. In 21 GBD regions, the highest percentage increase in number of incidence, prevalence and DALYs

were found in Central Sub-Saharan Africa, while East Asia has the highest percentage decrease in age standardized rate of incidence, prevalence and DALYs. In 204 countries and territories, the greatest percentage increase in number rate of incidence, prevalence, and DALYs were observed in Qatar, while the greatest percentage decrease in age-standardized rate of incidence, prevalence, and DALYs were found in China.

In 2019, three risk factors account for 40% (95%UI:36%, 40%) DALYs due to LBP, including smoking (16%, 95%UI:12%, 20%), high body-mass index (7%,95%UI: 4%, 10%), occupational ergonomic factors (24%, 95%UI:22%, 26%).

Conclusion: There is significant varied and increased disease burden of LBP by gender, age and geography, partly due to population growth and ageing. The age-standardized rate of prevalence, incidence and DALYs are decreasing, especially in countries such as China and India. Cost effective interventions targeted risk factors are required to minimize the ongoing burden of this condition.

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[2] Maher C, et al. Lancet. 2017;389(10070):736–747.
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[4] GBD 2017 Risk Factor Collaborators. Lancet. 2018;392(10159):1923–1994.

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FRIDAY, 05 JUNE 2020

Validation of outcome measures and biomarkers

FRI0553

DEVELOPMENT AND VALIDATION OF A BIOMARKER-BASED CARDIOVASCULAR RISK PREDICTION SCORE IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) patients are at elevated risk for cardiovascular (CV) events, but risk stratification based on CV prediction models is not part of routine rheumatology practice.

Objectives: To develop and validate a biomarker-based CV risk prediction model and compare it to alternative risk prediction models.

Methods: We constructed a cohort of RA patients - age ≥40 with ≥1 RA diagnosis from a rheumatologist, excluding patients with malignancy, past myocardial infarction (MI) or stroke - by linking Medicare administrative data from 2006-2016 to multi-biomarker disease activity (MBDA) test results obtained as part of routine care. The cohort was split 2:1 to create training and internal validation datasets. The composite CV outcome was MI, stroke or CV death occurring within 3 years. Clinical predictors examined were: age, sex, race, traditional CV risk factors (e.g. diabetes, hypertension, hyperlipidemia, high-risk CV conditions [e.g. angina]), RA-related factors (e.g. glucocorticoid use, MTX, number of prior biologics), adjusted MBDA score[1] and its 12 biomarkers, log-transformed. Backward elimination was used to remove predictors with p ≥0.05. The resulting CV risk score was compared to four prediction models (age+sex; age+sex-+CRP; age+sex+diabetes+hypertension+ smoking+high risk CV [±CRP]) in the validation dataset. We evaluated: 1) incremental improvement in the likelihood ratio test (LRT) statistic, 2) discrimination (AUROC), and 3) goodness-of-fit (predicted vs. observed, based on Kaplan-Meier estimates). Validation analyses were prespecified.

Results: 30,751 RA patients with 904 CV events were linked to MBDA test results and eligible for analysis. Patient characteristics were mean (SD) age 68.7 (9.5) years; 23.4% age <65; 82% women. Comorbidities included diabetes (39%), hypertension (78%), smoking (24%) and history of high-risk CV condition (37%). RA-related features included use of glucocorticoids (58%), MTX (60%), TNFi (33%) and other biologics (16%). Mean (SD) MBDA score was 41 (14). The final covariates included in the MBDA-based CV risk score were age, diabetes, hypertension, smoking, history of high-risk CV conditions, adjusted MBDA score, leptin, TNFRI and MMP-3. Median (IQR) of the predicted 3-year CV risk was 3.4% (2.1%, 5.6%). Based on extrapolation to 10-year risk, 9.4% of patients would be considered low, 10.2% borderline, 52.2% intermediate, and 28.2% high risk per 2019 ACC/AHA guidelines.

Compared to four simpler CV prediction models, significant improvement in the LRT statistic was observed with the addition of the biomarker-based CV risk score (Figure 1). Model fit was good across deciles (Figure 2). The AUROC was 0.70. The MBDA-based model reclassified 28.5% of patients vs. the model based on age+sex+diabetes+hypertension +smoking+high risk CV+CRP.

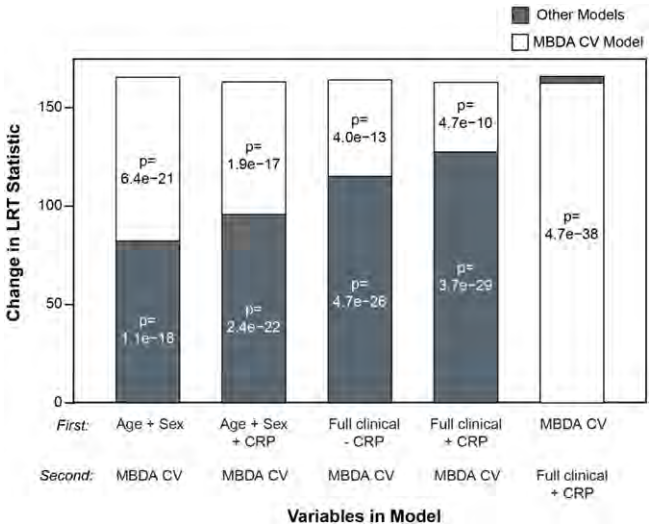


Figure 1. Incremental Improvement of MBDA-based CV Risk Score Compared to Other CV Risk Prediction Models

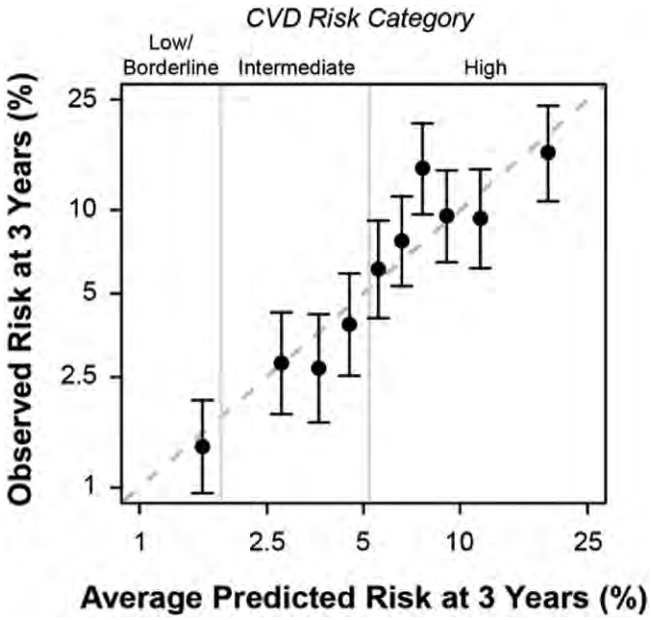


Figure 2. MBDA-Based CV Risk Score Calibration for Composite CV Outcome at 3 Years

Conclusion: A biomarker-based prediction score incorporating a few clinical risk factors appears to have good accuracy to predict CV risk in RA. Additional validation in independent cohorts will help verify its performance characteristics.

References:

[1] Curtis et al., *Rheumatology* 2018;58:874.

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Genetics, Inc., Employee of: Myriad Genetics, Inc., Eric Sasso Shareholder of: Myriad Genetics, Inc., Employee of: Myriad Genetics, Inc., Elena Hitraya Shareholder of: Myriad Genetics, Inc., Employee of: Myriad Genetics, Inc., Rotem Ben-Shachar Shareholder of: Myriad Genetics, Inc., Employee of: Myriad Genetics, Inc., Alexander Gutin Shareholder of: Myriad Genetics, Inc., Employee of: Myriad Genetics, Inc., Jerry Lanchbury Shareholder of: Myriad Genetics, Inc., Employee of: Myriad Genetics, Inc.

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FRI0554 **DEVELOPMENT OF A DISEASE ACTIVITY INDEX FOR RA PATIENTS USING HANDSCAN.**

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Background: Disease activity in RA patients is usually measured by DAS28,[1] a composite measure consisting of 28 swollen and/or tender joint counts (SJC28/TJC28), an acute phase reactant (APR, e.g. ESR/CRP) and patient's general health typically using a visual analogue scale (VAS). Particularly assessment of joint counts is time consuming, requires a trained health professional and its inter-observer variety is high. The HandScan is developed to measure inflammation in hand joints using optical spectral transmission (OST, score 0 to 66) without taking time of a health professional.[2] The correlation between DAS28 and a single measurement of OST is moderate.[3] We hypothesised that a composite measure including OST (representing joint inflammation), VAS and APR would lead to an appropriate disease activity index.

Objectives: To establish a method for assessing disease activity in RA patients using HandScan +/- other disease activity parameters, with cut-offs for remission and low disease activity (LDA).

Methods: RA patients, visiting the outpatient clinic of Máxima Medical Center Eindhoven, were eligible for inclusion. Inclusion criteria were; (1) RA according to classification criteria, (2) at least one HandScan and DAS28 measurement performed at the same visit, and (3) aged ≥18. Data was extracted from medical records. A random sample of 2/3 of included patients was used as development cohort, the remaining 1/3 was used as validation cohort. In the development cohort, linear regression analyses were performed to create a formula for an OST index (DASost). In these, DAS28 was the outcome variable and, OST, ESR and VAS were predictors. Also other parameters were tested in the model to see if they increased the fit of the model or modified the association between OST and DAS28. A final model was derived, based on statistical significance of predictors and improvement of model fit (adjusted R-square). Agreement of DAS28 with DASost was tested with the random one-way intraclass correlation coefficient (ICC). DAS28 based remission and LDA were calculated for DASost using the established DAS28 cut-offs (i.e. DASost<2.6 and DASost<3.2). A cut-off for DASost for Boolean remission was defined using receiver operating characteristic (ROC) curves and Youden's index. In the validation cohort, diagnostic values were calculated for DASost using the cut-offs as defined above.

Results: Data of 3358 observations within 1505 unique RA patients were extracted. Patients' demographic and clinical data are shown in Table 1. The formula for DASost derived in the development cohort was: -0.44 + (OST*0.03) + (male*-0.11) + (LN(ESR)*0.77) + (VAS*0.03). The optimal cut-off on DASost found for Boolean remission was 2.2. The ICC was 0.88 (95%CI 0.87 - 0.89). The explained variance of DASost in the validation cohort was 78%. Diagnostic accuracy of DASost in the validation cohort for DAS28 based remission, LDA and Boolean remission are shown in Table 2.

Table 1. Patients' demographics and clinical data

Patient demographics	
Number of patients	1505 (100%)
Females	976 (65%)
Age (year)	65.5 (12.1)
duration of RA (year)	11.5 (8.3)
Seropositivity	1068 (71%)
Clinical data	
Number of observations	3358
DAS28	2.5 (1.3)
ESR (mm/hr)	9.0 (5.0 – 21.0)
SJC	0 (0 – 2)
TJC	0 (0 – 2)
VAS	30.0 (10.0 – 50.0)
OST	12.6 (5.0)

Data are n (%), mean (SD), or median (IQR).

Table 2. Diagnostic values of DASost

Disease activity state	AU ROC	Sensitivity	Specificity	PPV	NPV	accuracy
Remission	0.93	89%	83%	88%	84%	86%
LDA	0.92	91%	67%	89%	73%	85%
Boolean remission	0.87	91%	95%	39%	98%	94%

AU ROC= area under the receiver operating characteristic curve, PPV= positive predictive value, NPV= negative predictive value.

Conclusion: The HandScan could be used as a tool to quickly assess disease activity in RA patients, if OST is combined with other disease activity parameters into an index.

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Epidemiology, risk factors for disease or disease progression

FRI0555 **DO TNF INHIBITORS DECREASE RISK OF INCIDENT PSORIATIC ARTHRITIS IN PSORIASIS PATIENTS COMPARED TO THOSE TREATED WITH METHOTREXATE ALONE?**

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory arthritis characterized by joint and entheseal inflammation seen in 30% patients with psoriasis (Pso). In 90% of patients, Pso precedes PsA. Inhibitors of tumor necrosis factor (TNFi) are efficacious treatment options for both, though whether they prevent development of incident PsA in Pso patients is unknown.

Objectives: To determine if the use of TNFi reduces the risk of developing psoriatic arthritis in Pso patients compared to those treated with methotrexate alone.

Methods: Records on all Pso patients seen at dermatology clinic at our University from January 2006 - June 2019 were reviewed. Patients with any musculoskeletal symptoms were referred to rheumatology and were considered to have PsA if they were diagnosed by a rheumatologist. We used Student's t-test to compare continuous covariates and Pearson's chi-squared test or Fisher's exact test to compare categorical covariates. Variables that were found to be significantly associated with PsA diagnosis were included as potential confounders in the multivariate model. We used Cox proportional hazards models to compare the risk of incident PsA diagnosis for those who initiated TNFi compared to those who initiated methotrexate. A propensity score of TNFi therapy compared to methotrexate therapy was calculated using variables associated with treatment choice and adjusted for in the model. Variables that were associated with both treatment choice and PsA risk were not included in the propensity score. We used backwards stepwise variable selection to build the final model.

Results: Out of 154 Pso patients who did not have PsA at baseline, and were started exclusively on a TNFi or methotrexate during the study period,, 85 (55.2%) initiated methotrexate and 69 (44.8%) initiated a TNFi. Mean duration of therapy for those on TNFi was 3.95 (standard error: 0.50) years while mean duration of therapy for those on methotrexate was 1.93 years (standard error: 0.28). Mean follow-up time for those on TNFi was 5.18 years (standard error: 0.49) and for those on methotrexate was 2.71 years (standard error: 0.37) Seventy nine (51.3%) of the cohort were women. Thirty five (22.7%) of subjects developed PsA over the course of the study. After adjusting for propensity score, nail pitting, body surface area (BSA) involved in psoriasis, and depression, TNFi did not significantly reduce the risk of PsA as compared to methotrexate (HR: 0.68 [95% CI: 0.32, 1.41]).

Conclusion: Use of TNFi was not associated with a statistically significant decreased risk of incident PsA compared to methotrexate in this study, but a larger cohort with longer follow up will have better power to estimate the true association.

Table 1. Characteristics of the psoriasis cohort starting exclusively TNFi or methotrexate

	Incident PsA n = 35	PsA negative n = 119	p-value
Treatment [n (%)]			0.37
TNFi	18 (51.4)	51 (42.9)	
Methotrexate	17 (48.6)	68 (57.1)	
Sex [n (%)]			0.24
Female	21 (60.0)	58 (48.7)	
Male	14 (40.0)	61 (51.3)	
Age [median (IQR)]	47.0 (39.4, 59.7)	48.9 (35.3, 61.7)	0.71
Pso manifestations [n (%)]			
Nail pitting	27 (77.1)	51 (42.9)	<0.01
Scalp psoriasis	31 (88.6)	105 (89.0)	0.95
Inverse psoriasis	14 (40.0)	37 (31.09)	0.33
BSA [median (IQR)]	6 (3, 15)	12 (5, 22)	0.06
BMI [median (IQR)]	31.7 (25.9, 40.4)	29.1 (26.3, 34.7)	0.30
Therapy duration (years)			
TNFi [median (IQR)]	4.38 (1.34, 8.13)	2.26 (0.76, 5.82)	0.29
Methotrexate [median (IQR)]	2.44 (0.06, 3.44)	0.94 (0.27, 2.39)	0.43

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FRI0556

INCREASED RISK OF MORTALITY AND CANCER IN SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS FROM A LUPUS COHORT STUDY FROM 1998 TO 2015

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Background: Systemic lupus erythematosus (SLE) is a chronic systemic autoimmune inflammatory disease with increased risk for mortality and cancers possibly because of the effects of systemic inflammation and immunodeficiency due to disease itself and/or cytotoxic agents for SLE management. Although there has been improvement in the prognosis of SLE over decades with the treatment advance including standardized treatment strategy for lupus nephritis and less cytotoxic agents, the improvement also is fixed nowadays.
Objectives: In this study, we we are to investigate the mortality and cancer of SLE patients in a longitudinal SLE cohort and compare the morality ratio and incidence of cancer with general population over time.
Methods: This study was conducted in Hanyang BAE lupus cohort during the period of 1998 to 2015. Mortality data and malignancy data were derived in connection with data from the Korean National Statistics Office and the Korea Central Incidence Database, respectively. The Standardized Mortality Ratio (SMR) and Standardized Incidence Ratio (SIR) was estimated yearly by dividing the observed number deaths/cancers by the expected number of deaths/cancers of age- and sex- matched general population from matched year.
Results: Mortality data were available in 1284 patients and total 71 deaths were observed. The most common cause of death was SLE itself (52.1%) followed by infection (18.3%), cerebrovascular disease (8.5%) and suicide (7.0%). The total age and sex adjusted SMR was 3.4 [95% CI (Confidential Interval) 2.6-4.1]. When we conduct subgroup analysis by age, the sex-adjusted SMR was significantly increased in young and middle aged adult patients: the SMR in patients younger than 20 was 12.2, but it was not significant due to the small number of young patients (observed death 3, expected death 0.3, 95% CI 0-26.0). The adjusted SMR in patients aged 20-39, aged 40-59 and aged over 60 were 9.8 (observed death 35, expected death 4.8, 95% CI 6.5-13.0), 3.7 (observed death 24, expected death 11.5, 95% CI 2.2-5.2), and 1.0 (observed death 9, expected death 10.3, 95% CI 0.3-1.6), respectively. Compared with alive patients, died patients had more serositis and more neurologic disorder according to American College of Rheumatology classification criteria for SLE despite the shorter observational period (5.6 years vs. 9.4 years).
Malignancy data were available in 1,020 patients and 56 primary cancers were diagnosed. Solid tumor was developed in 51 patient and hematologic malignancy was developed in 5 patients (3 non-Hodgkin's lymphoma, 1 solitary plasmacytoma and 1 acute lymphoblastic leukemia). Thyroid cancer was the most common solid cancer (24 patients) followed by colorectal (5 patients), breast (4 patients), cervical cancer (4 patients) and hepatocellular carcinoma (3 patients). The total age and sex adjusted SIR was 1.1 (95% CI 0.8-1.4).
Conclusion: Patients with SLE had higher risk of mortality than general population and the younger patients had the higher risk of mortality. The leading cause of death was SLE itself followed by infection and cerebrovascular disease. The risk for cancer in patient with SLE was similar with that of general population.
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FRI0557

IN INDIVIDUALS AT-RISK OF RHEUMATOID ARTHRITIS, ULTRASOUND BONE EROSIONS AT THE V METATARSOPHALANGEAL JOINTS ARE THE MOST PREDICTIVE FOR THE DEVELOPMENT OF CLINICAL ARTHRITIS.

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Background: While the central role of bone erosions in the pathogenesis and diagnosis of patients with rheumatoid arthritis (RA) is widely recognized, their prevalence, pattern, and relationship with subclinical synovitis in individuals at-risk of RA (positive autoantibodies without clinical arthritis) is not well understood.
Objectives: To investigate, in individuals at-risk of RA, the prevalence and distribution of ultrasound (US) bone erosions, their correlation with subclinical synovitis at joint level, and their association with the development of inflammatory arthritis (IA).
Methods: Baseline US scans of 2nd generation anti-cyclic citrullinated peptide (CCP) positive at-risk subjects with musculoskeletal symptoms (without clinical arthritis) taking part in the Leeds CCP study were analyzed. The presence of bone erosions was evaluated in the classic sites for RA damage: the II and V metacarpophalangeal (MCP) joints, and the V metatarsophalangeal (MTP) joints[1]. US synovitis was defined as synovial hypertrophy (SH) ≥2 or SH ≥1 + power Doppler signal ≥1[2]. Only subjects with ≥1 follow-up visit were included in the progression analysis (n=400). Progression to IA was defined as the development of clinical synovitis in ≥1 one joint.
Results: US bone erosions: prevalence, distribution, and association with subclinical synovitis
A total of 2514 joints, in 419 subjects were evaluated.
Bone erosions were found in ≥1 joint in 41/419 subjects (9.8%), in 55/2514 joints (2.2%). The prevalence of bone erosions was significantly higher in the V MTP than

Table 1.

	Ever		At 1 year		At 3 years	
	HR (95%CI)	**P value**	**HR (95%CI)**	**P value**	**HR (95%CI)**	**P value**
Presence of bone erosion in ≥1 joint (any joint)	**3.98 (1.82-8.7)**	<0.01	**3.57 (1.7-7.5)**	<0.01	**3.48 (1.63-7.4)**	<0.01
- *in the II MCP joints*	2.4 (0.52-11.08)	0.26	1.07 (0.2-5.76)	0.94	1.67 (0.38-7.04)	0.5
- *in the V MCP joints*	1.37 (0.06-31)	0.85	0 (N/A)	1	0 (N/A)	1
- *in the V MTP joints*	**4.79 (1.97-11.63)**	<0.01	**5.23 (2.32-11.8)**	<0.01	**5.43 (2.28-12.92)**	<0.01
Presence of bone erosion and synovitis in the same joint (any joint)	**3.9 (1.19-12.77)**	0.02	**6.03 (2.07-17.55)**	<0.01	**3.91 (1.29-11.85)**	0.02
Presence of bone erosion and synovitis in the same V MTP joint	**5.08 (1.37-18.9)**	0.02	**7.03 (2.28-21.71)**	<0.01	**4.89 (1.48-16.19)**	<0.01
Presence of bone erosion in >1 joint (any joint)	**10.63 (1.87-60.42)**	<0.01	**5.68 (1.66-19.5)**	<0.01	**7.26 (1.67-31.66)**	<0.01

IA free survival rates are showed in Figures 1 and 2.

in the MCP joints (p<0.01). They were detected in 42V MTP (31 subjects; 7.4%), in 10 II MCP (10 subjects; 2.4%), and in 3V MCP (3 subjects; 0.7%) joints. US synovitis was detected in 22/55 joints (40%) with bone erosions, in 17/41 subjects (42%). It was found in 48.6% of the V MTP, in 20% of the II MCP and in none of the V MCP joints with bone erosions. A significant correlation between bone erosions and synovitis in the same joint was detected (Cramer's V=0.22, p<0.01).

Seven out of the 55 joints (12.7%) with bone erosions were tender on physical examination: 14.3% of the V MTP, 10% of the II MCP, and none of the V MCP joints.

US bone erosions: predicting development of IA

A total of 122 subjects (30.5%) developed IA (median follow-up: 301 days, IQR 112-721). The hazard ratios of the US findings for the development of IA (adjusted for age, sex, smoking, anti-CCP and rheumatoid factor titer) are reported in Table 1.

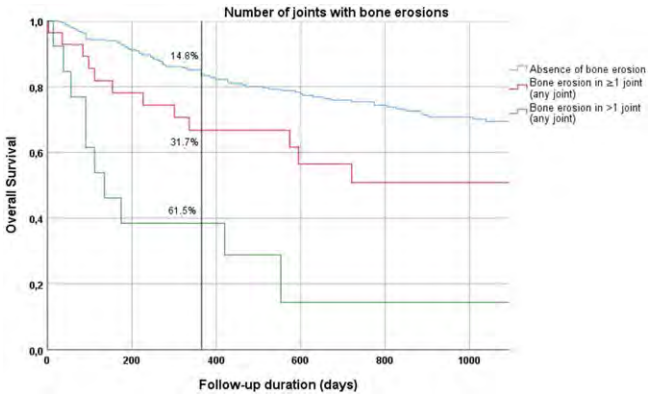


Figure 1.

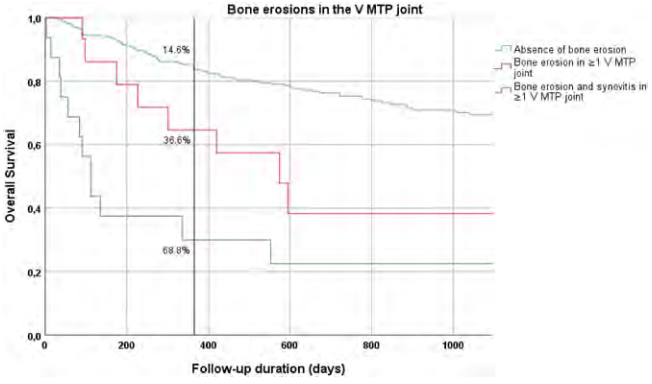


Figure 2.

Conclusion: The feet appear to be an early site for damage in individuals at-risk of RA. US bone erosions were mainly detected in asymptomatic joints, but frequently in association with subclinical synovitis. In individuals at-risk of RA, bone erosions in the V MTP joints are more predictive than in the hands (II and V MCP joints) for the development of IA.

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[2] D'Agostino, et al. RMD Open. 2017;

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FRI0558

PREGNANCY OUTCOMES IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS – A FIRST JOINT ANALYSIS OF A EUROPEAN COLLABORATION OF PREGNANCY REGISTERS

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Background: Axial spondyloarthritis (axSpA) can affect women in their childbearing age. But data on pregnancy in axSpA patients are mainly retrospective and highly heterogeneous [1].

Objectives: The aim of this analysis was to investigate pregnancy outcomes and health of live born children in women with axSpA in four prospective cohort studies.

Methods: Data of European pregnancy registries that collaborate in the European Network of Pregnancy Registries in Rheumatology (EuNeP) were analysed: EGR2 (France), RePreg (Switzerland), RevNatus (Norway) and Rhekiss (Germany). Eligible women had a diagnosis of axSpA and a pregnancy outcome reported until June-September 2019. Data were analysed descriptively by every registry and provided to the coordinating centre.

Results: A total of 328 pregnancies in 288 women were investigated. Mean age of patients ranged from 31 to 33 years. Disease duration (3-8 years) and proportion of patients with a positive HLA-B27 (64-74%) varied (Table 1). The axSpA diagnosis was either classified by ASAS criteria (fulfilment in EGR2: 93%, RePreg: 65%, RevNatus: 86%) or by ASAS criteria for axial/ peripheral SpA (Rhekiss: 81/ 34%). Rates for preterm birth were ≤5%, and congenital malformations were reported in 4 out of 287 neonates (Table 2).

Table 1. Maternal and disease characteristics

	EGR2 (FR)	RePreg (CH)	RevNatus (NO)	Rhekiss (DE)
# Pregnancies	45	31	160	92
# Patients	44	31	125	88
Age in years	32.0 ± 4.2	31.4 ± 4.0	30.5 ± 4.5	33.2 ± 4.4
Disease duration in years	6.0 ± 5.6	7.7 ± 4.6	3.2 ± 3.3	6.2 ± 5.3
HLA-B27 positive	26 (66.7)	23 (74.2)	79 (71.2)	54 (73.0)
Pre-gestational diabetes	0	0	1 (0.6)	1 (1.4)
IBD	0	0	4 (2.6)	5 (7.2)
Uveitis	0	0	3 (1.9)	3 (4.3)
BMI	26.5 ± 4.8	22.6 ± 2.5	24.4 ± 4.3	23.4 ± 4.3

Results as mean ± SD or number (percentage)

Table 2. Pregnancy characteristics, obstetric and neonatal outcomes

	EGR2 (FR)	RePreg (CH)	RevNatus (NO)	Rhekiss (DE)
WGA at 1st visit in pregnancy	11.9 ± 8.2	19.7 ± 9.4	12.9 ± 5.7	13.4 ± 5.4
Patients with 1 pregnancy	43 (95.5)	31 (100.0)	101 (80.8)	84 (95.5)
Primigravidae	18 (40.0)	15 (48.4)	47 (29.4)	37 (45.1)
Adverse events of interest				
Preeclampsia	1 (4.4)	0	4 (2.6)	0
Gestational diabetes	4 (8.9)	2 (6.5)	n.a.	5 (6.2)
Pregnancy outcomes			*(5 Outcomes missing)*	*(1 Outcome missing)*
Elective termination	1 (2.2)	0	2 (1.3)	0
Miscarriage (< WGA 20)	2 (4.4)	0	13 (8.4)	4 (4.4)
Pregnancy loss >WGA 20	2 (4.4)	0	0	0
Live birth	40 (88.9)	31 (100.0)	140 (90.3)	87 (95.6)
Outcomes of live births				
# Neonates, singleton pregn.	40	30	139	78$
# Neonates, multiple pregn.	0	2	2	4
Neonatal outcomes, only singleton pregnancies				
WGA at delivery	39.1 ± 1.2	39.5 ± 1.5	38.9 ± 2.3	39.4 ± 2.0
Preterm birth	0	0	6 (4.3)	4 (5.4)
Birth weight in g	3253 ± 395	3314 ± 519	3446 ± 526	3377 ± 522
Congenital malformation	0	0	n.a.#	4 (5.1)

Results as mean ± SD or number (percentage). WGA: gestational age in weeks
#Malformations can be retrieved by national birth registry with a lag time of 2 years.
$Missing information for 7 infants.

Conclusion: Differences in study design and classification criteria result in slightly different patient populations in each registry. The outcome of pregnancies was favourable. Preterm birth rates are within rates reported by the WHO for the EU general population. However, a selection bias of rather planned and well-controlled pregnancies cannot be ruled out. This is the first collaborative analysis of the EuNeP registries. Descriptive data were combined, and will be – as a next step – pooled together.

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FRI0559 ASSOCIATION BETWEEN DIET QUALITY IN CHILDHOOD AND ADULTHOOD AND KNEE SYMPTOMS IN YOUNG ADULTS

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Background: Knee osteoarthritis (OA) is the most prevalent joint disease worldwide, but no disease-modifying treatments are available. Existing treatments largely focus on relieving symptoms, but they may have substantial adverse effects. Identifying risk factors affecting knee symptoms is important for developing safer prevention strategies of knee OA symptoms.

Objectives: To describe the associations between diet quality in childhood and adulthood and knee symptoms in young adults.

Methods: Participants were from the Australian Schools Health and Fitness Survey (ASHFS) in 1985, which was conducted to provide benchmark data on the health and fitness of Australian schoolchildren. During 2004-2006, participants were followed up in the Childhood Determinants of Adult Health (CDAH) Study. Dietary measures were collected in ASHFS (aged 10-15 years) and CDAH Study (aged 26-36 years) using food questionnaires. Diet quality was assessed by Dietary Guidelines Index (DGI), reflecting the adherence to Australian Dietary Guidelines. The DGI comprises 9 components and its maximum possible score is 100. A higher score indicated higher diet quality. During 2008-2010, participants (aged 31-41years) were followed up in the CDAH Knee Study. Knee symptoms were collected using Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). Zero-inflated negative binomial regression analyses were used to assess the associations between diet quality and knee symptoms. Age, sex, body mass index, physical activity, total energy intake, and knee injury history were included as potential confounders based on biological plausibility.

Results: A total of 399 participants (48.4% were female) were included in analysis. The average childhood and adult DGI was 46.5 and 55.4, respectively. The prevalence of knee pain, stiffness and dysfunction was 35.1%. 31.6% and 39.9%, respectively. The overall childhood DGI was not associated with adult knee symptoms. However, the limited intake of discretionary foods in childhood was associated with lower pain (Mean ratio (MR): 0.96, 95% confidence interval (CI): 0.92-1.00) and dysfunction (MR: 0.94, 95% CI: 0.90-0.99). The overall adult DGI was not associated with knee symptoms. However, replacing saturated fats with unsaturated fats in adulthood was associated with lower WOMAC (Pain: MR 0.93, 95% CI 0.87-0.99; stiffness: MR 0.93, 95% CI 0.87-0.99; dysfunction: MR 0.91, 95% CI 0.83-0.99), drinking water in adulthood was associated with lower stiffness (MR: 0.90, 95% CI: 0.83-0.99), and fruit intake in adulthood was associated with lower dysfunction (MR: 0.90, 95% CI: 0.81-0.99). Moreover, higher DGI score for dairy in adulthood was associated with higher WOMAC (Pain: MR 1.07, 95% CI 1.00-1.13; stiffness: MR 1.13, 95% CI 1.05-1.21; dysfunction: MR 1.11, 95% CI 1.02-1.21). The overall score change of DGI from childhood to adulthood was not associated with adult knee symptoms. However, the score change of replacing saturated fats with unsaturated fats from childhood to adulthood was associated with lower stiffness (MR 0.89, 95% CI 0.80-0.98), and the score change of fruit intake was associated with lower dysfunction (MR 0.92, 95% CI 0.86-0.99).

Conclusion: Several DGI component scores in childhood and adulthood and some changes of DGI component score from childhood to adulthood were associated with knee symptoms in young adults. The results suggested that early-life diet quality may affect knee symptoms in young adults.

Disclosure of Interests: None declared

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FRI0560 INCREASED RISK OF RHEUMATOID ARTHRITIS DIAGNOSIS IN STATIN USERS IN A LARGE NATIONWIDE US STUDY

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Background: Studies evaluating the effect of statin use on the risk of rheumatoid arthritis (RA) onset have shown conflicting results. Most of these studies evaluated European populations while data from the US are scarce.

Objectives: We aimed to assess the association between statin use (and intensity) and RA occurrence using claims data from the US population.

Methods: For this case-control study, we used the OptumLabs Data Warehouse, a large administrative database of commercially insured and Medicare Advantage beneficiaries, to identify cases of RA and matched controls. Cases were defined as patients with 2 or more diagnoses of RA in January 1, 2010 - June 30, 2019 who were ≥18 years old, filled ≥1 prescription for a conventional or biologic disease modifying anti-rheumatic drug, and had no diagnoses of RA during the prior year. Controls were persons without RA matched 1:1 to RA cases on age, sex, census region, calendar year of index date (corresponding to the date of second diagnosis code for RA), and length of prior medical/pharmacy coverage. Statin use was defined as any filled prescription for a statin medication during prior coverage (excluding any new statin prescriptions filled up to 90 days before first RA diagnosis or index date). Logistic regression models were used to estimate odds ratios (OR) **with 95% confidence intervals (CI) adjusted for age, sex, race, census region, calendar year and Charlson comorbidity index (excluding RA component).**

Results: The study included 32,465 cases with RA (mean age 57.0, 72.2% female) and 32,465 matched controls (mean age 57.0, 72.2% female). There were 10,759 (33.1%) statin users among RA patients and 4,016 (12.4%) statin users among the matched controls. Statin use was associated with increased risk of RA (adjusted OR 3.34, 95%CI 3.19-3.49). All levels of statin intensity were associated with increased risk of RA (high OR: 3.60, 95% CI 3.28-3.94; medium OR: 3.20, 95% CI 3.04-3.37; low OR: 3.72, 95% CI 3.34-4.15) compared to non-users. Both former and current statin users showed an increased risk of RA (current OR: 3.04, 95% CI 2.80-3.30 and former OR: 3.37, 95% CI 3.20-3.54) compared to non-users.

Conclusion: This large nationwide study showed increased risk of RA in statin-users vs non-users. The lack of dose dependence may suggest confounding by indication or a common genetic predisposition for cardiovascular disease and RA. The underlying mechanisms for these associations require further investigation.

Disclosure of Interests: Madeline Peterson: None declared, Hayley J. Dykhoff: None declared, Cynthia S. Crowson Grant/research support from: Pfizer research grant, John M Davis III Grant/research support from: Research grants from Pfizer, Consultant of: Served on advisory boards for Abbvie and Sanofi-Genzyme, Lindsey Sangaralingham: None declared, Elena Myasoedova: None declared

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FRI0561 PRO-INFLAMMATORY DIETS ARE ASSOCIATED WITH INCREASED C-REACTIVE PROTEIN AND RHEUMATOID ARTHRITIS IN THE UK BIOBANK COHORT

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United Kingdom; [4]*Norfolk & Norwich University Hospital, Norwich, United Kingdom*

Background: Several individual dietary components have been associated with the risk of rheumatoid arthritis (RA) and recent studies have suggested that dietary indices, which account for the consumption of multiple foods, can be used as more complete measures of risk.
Objectives: In this study we aimed to use the Dietary Inflammatory Index (DII), an independent index of dietary variable associated with inflammatory biomarkers, to evaluate potential associations between pro-inflammatory exposures in the diet, an inflammation biomarker (C-reactive protein) and RA onset using the UK Biobank cohort.
Methods: The DII was calculated from data obtained in 24-hour dietary recall questionnaires collected on healthy participants on four separate occasions over an approximate annual period between Feb 2011 and April 2012. Cases of RA in the UK Biobank cohort were identified from the participants with appropriate ICD10 codes and compared against a randomly selected subsample of controls matched (20:1) for age, sex, smoking status and BMI.
Results: Among the 502,519 subjects enrolled in Biobank, 141,769 had completed 24-hour dietary recall questionnaires and had full data for the 18 dietary variables that were required to create the DII (mean=0.03, range: -3.88, 4.22). Higher (positive) DII values indicate more pro-inflammatory diets. This index was positively correlated ($p<0.001$) with C-reactive protein (CRP), attesting to the validity of this index for assessing dietary inflammatory potential. A total of 1,423 participants were classified as having RA (1% prevalence in 'dietary' cohort of 141,769) according to their ICD10 codes that were last updated in 2018. Their mean age at enrolment (2006-10) was 59 years. There was a significant association between DII and RA: OR 1.05 [1.01-1.09]; $p=0.028$) that suggested RA cases were more likely to be consuming a pro-inflammatory diet.
Conclusion: These data show a significant association between diet, inflammation (CRP) and RA in the UK Biobank population. The findings are consistent with a recent analysis of the US Nurse's Health Study which was based on data only from females, indicating that these findings are likely to be robust and generalisable. Diet is one of the few modifiable factors that has the potential to reduce the risk of future RA onset. These results open the way to providing evidence-based health advice and for designing clinical interventions.
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Acknowledgments: This research has been conducted using the UK Biobank Resource under Application Number '33557'
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.5961

FRIDAY, 05 JUNE 2020

Validation of outcome measures and biomarkers

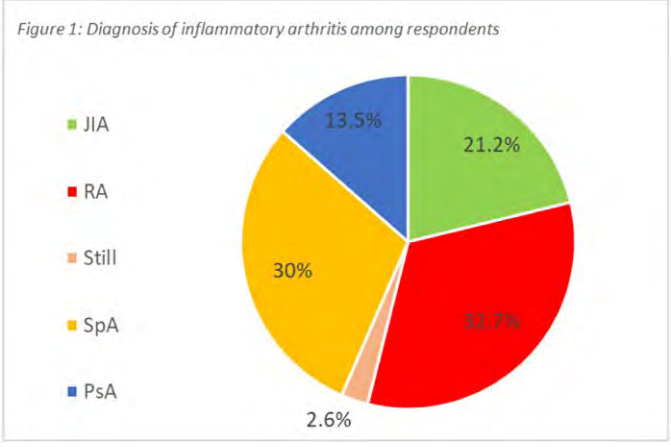
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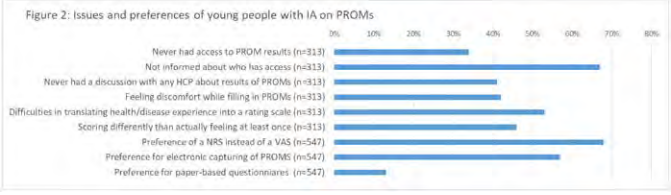
THE PERSPECTIVE OF YOUNG PEOPLE WITH INFLAMMATORY ARTHRITIS ON PATIENT REPORTED OUTCOME MEASURES: RESULTS OF A EUROPE-WIDE SURVEY

A. Alunno[1], E. Mosor[2], T. Stamm[2], P. Studenic[2]on behalf of the EULAR Task Force to develop points to consider (PtC) for including the perspective of young patients with inflammatory arthritis into PROMs.
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Background: Although patient-reported outcome measures (PROMs) are widely used in clinical practice and research, it is unclear if these instruments adequately cover the perspective of young people (18-35 years) with inflammatory arthritis (IA). We recently performed focus groups on PROMs with 53 young IA patients from 4 European countries, but the perspective of these patients has never been explored on a large scale.
Objectives: To explore personal experience, opinions and beliefs of young people with IA across Europe concerning PROMs content, characteristics and ways of administration in order to inform EULAR points to consider (PtC) for including the perspective of young patients with IA into PROMs.
Methods: Based on the results of our previous qualitative study, a task force including patients, rheumatologists and health professionals developed an online survey. The survey covered personal experience, preferences and opinions concerning PROMs. After being pilot tested and revised accordingly, the survey was distributed through the EULAR people with arthritis and rheumatism in Europe (PARE), Young PARE networks and the Emerging EULAR Network (EMEUNET).
Results: 547 people (88% females) from 29 countries aged 18-35 years with a diagnosis of juvenile idiopathic arthritis, rheumatoid arthritis, Still's disease, psoriatic arthritis or spondyloarthritis completed the survey (Figure 1). Thirty-seven percent of respondents reported they never filled a PROM. A North-South and West-East Europe gradient was observed (30.4% vs 56.3% and 25.5% vs 58.8% respectively). Figure 2 outlines key findings of our survey. Among respondents having filled PROMs (n=313), two thirds perceived their access to PROM results useful for self-management of their health. Discomfort while filling PROMs was an issue for nearly half of the respondents, as questions were perceived as scaring or not relevant. This discomfort, the fear of judgement, or inadequate assessed time frames were major reasons for difficulties in translating the health experience into a rating scale. Still 75% use their own experience in the past as reference. Among several reasons, people scored differently from what they felt to emphasize how much better or worse they felt from previous assessment. Concerning preferences of numerical rating scales (NRS) or visual analogue scales (VAS) explored in all respondents regardless having ever filled in PROMs, those in favour of VAS mainly reasoned this by having more possibilities to select and those favouring NRS by better readability and interpretation. Maintaining a sitting position, preparing food, doing physical activity, intimacy and sleep problems were the items selected most frequently in the survey as in the qualitative study to be included in PROMs. The implementation of discussion on self-management, education/work and support possibilities at regular clinic visits was considered important by over 60% of responders. Overall, electronic capturing of PROMs was preferred over paper-based questionnaires (57% vs 13%).
Conclusion: Our survey explored for the first time the personal experience and opinions of young people with IA concerning PROMs on a large scale and confirmed the results obtained in the qualitative study. This survey informed the EULAR PtC for including the perspective of young patients with IA into PROMs.
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Disclosure of Interests: Alessia Alunno: None declared, Erika Mosor: None declared, Tanja Stamm Grant/research support from: AbbVie, Roche, Consultant of: AbbVie, Sanofi Genzyme, Speakers bureau: AbbVie, Roche, Sanofi, Paul Studenic Grant/research support from: Abbvie
DOI: 10.1136/annrheumdis-2020-eular.4618

FRIDAY, 05 JUNE 2020

Epidemiology, risk factors for disease or disease progression

FRI0563 **COMPARISON OF TWO DIFFERENT APPROACHES TO INVOLVE PARTICIPANTS IN CONSECUTIVE ROUNDS OF A DELPHI CONSENSUS TECHNIQUE.**

A. Boel[1], V. Navarro-Compán[2], R. B. M. Landewé[3,4], D. Van der Heijde[1]. [1]*Leiden University Medical Center, Leiden, Netherlands*; [2]*University Hospital La Paz, Madrid, Spain*; [3]*Zuyderland Medical Centre Heerlen, Heerlen, Netherlands*; [4]*Amsterdam University Medical Centre, Amsterdam, Netherlands*

Background: There is no guidance on which participants to invite to consecutive rounds of a Delphi exercise. There are two options: 1) Invite only participants that have completed the previous round for the consecutive round; 2) Invite every participant for all consecutive rounds irrespective of whether they have responded. It is unknown whether different invitation-procedures provide similar results.
Objectives: To investigate the effect of two different approaches to involve participants in consecutive rounds of a Delphi exercise on response rate and final outcome.
Methods: Patients with and experts in spondyloarthritis were invited to partake in a 3-round Delphi exercise to update a core outcome set. A randomised controlled study with 1:1 allocation to two experimental groups was built in, to compare two approaches of invitation. The 'all-rounds group' includes patients invited for each round independent of response to the previous round; the 'respondents group' includes patients invited for the next round only if they responded to the previous round. A 9-point Likert scale (1=not important; 9=critical) was used to score the importance of domains. Additionally, participants provided their six most important domains.
Results: The overall response rate after 3 rounds was lower in the 'respondents' compared to the 'all-rounds group' (46% vs. 61%) (table 1).

Table 1. Response rates per group per round of the Delphi exercise

	'Respondents group' (N=187)	'All-rounds group' (N=189)
Round 1	Invited: 187	Invited: 189
	Completed: 122	Completed: 110
	Response rate: 65%	**Response rate: 58%**
Round 2	Invited: 122	Invited: 189
	Completed: 95 [response rate (78%)]	Completed: 105
	Overall response rate: 51%	**Response rate: 56%**
Round 3	Invited: 95	Invited: 189
	Completed: 86 [response rate (91%)]	Completed: 116
	Overall response rate: 46%	**Response rate: 61%**

There was no difference in mean (standard deviation) scores between the 'respondents' and 'all-rounds' groups for any domain (figure 1).

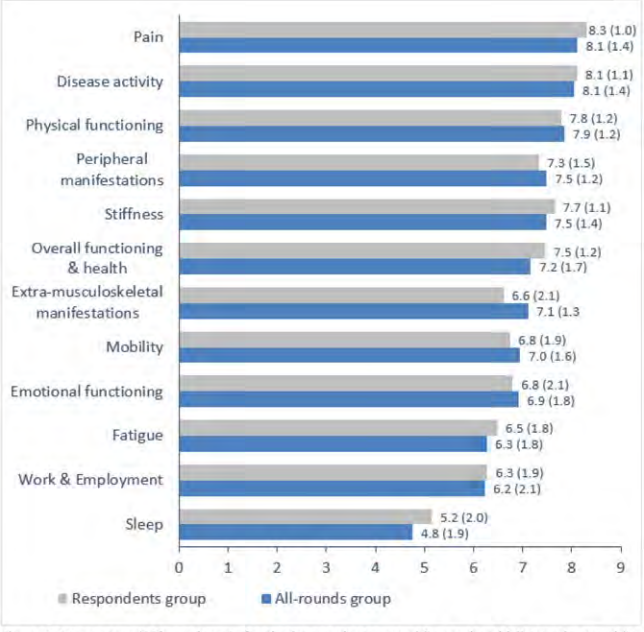


Figure 1 Mean score (SD) per domain for the 'respondents group' (in grey) and 'all-rounds group' (in blue) from the round when the domain was selected (i.e. the last available scores).

After the final round, the 4 outcomes with the highest percentage of votes were identical between experimental groups, with only small differences in percentages between groups (table 2). The only difference in the 6 most important domains was selection of disease activity by the 'respondents group', whereas the 'all-rounds group' selected overall functioning & health, while these domains were ranked as the 7th domain in the other group.

Table 2. Most important domains after round 3 for the 'respondents' and 'all-rounds' groups ranked in descending order, based on selection by the 'respondents' and matched in the 'all-rounds group'; and the difference in percentage of votes between groups. Domains in *italic* and bold represent the top 6 in each experimental group.

'Respondents group' N=86		'All-rounds group' N=116		Difference between groups	
Pain	95%	Pain	91%	Pain	4%
Stiffness	62%	Stiffness	62%	Stiffness	0%
Physical functioning	62%	Physical functioning	61%	Physical functioning	1%
Mobility	59%	Mobility	54%	Mobility	5%
Disease activity	55%	Disease activity	49%	Disease activity	6%
Fatigue	50%	Fatigue	55%	Fatigue	-5%
Overall functioning & health	47%	Overall functioning & health	57%	Overall functioning & health	-10%
Extra-musculoskeletal manifestations	44%	Extra-musculoskeletal manifestations	45%	Extra-musculoskeletal manifestations	-1%
Peripheral manifestations	34%	Peripheral manifestations	44%	Peripheral manifestations	-10%
Sleep	30%	Sleep	26%	Sleep	4%
Work & Employment	21%	Work & Employment	23%	Work & Employment	-2%
Emotional functioning	16%	Emotional functioning	18%	Emotional functioning	-2%

Conclusion: Inviting persons for all rounds irrespective of a response to the previous round increases the generalisability, while the content of the outcome of a Delphi procedure is similar to using data of those persons who participate in all rounds only.
Disclosure of Interests: Anne Boel: None declared, Victoria Navarro-Compán Consultant of: Abbvie, Lilly, Novartis, Pfizer, UCB, Speakers bureau: AbbVie, MSD, Lilly, Novartis, Pfizer, UCB, Robert B.M. Landewé Consultant of: AbbVie; AstraZeneca; Bristol-Myers Squibb; Eli Lilly & Co.; Galapagos NV; Novartis; Pfizer; UCB Pharma, Désirée van der Heijde Consultant of: AbbVie, Amgen, Astellas, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Cyxone, Daiichi, Eisai, Eli-Lilly, Galapagos, Gilead Sciences, Inc., Glaxo-Smith-Kline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB Pharma; Director of Imaging Rheumatology BV
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FRIDAY, 05 JUNE 2020

Validation of outcome measures and biomarkers

FRI0564 **SERUM LEVELS OF IL-6 AND IL-8 IN ANKYLOSING SPONDYLITIS PATIENTS: ASSOCIATIONS WITH DISEASE ACTIVITY**

E. Aleksandrova[1], A. Novikov[1], P. Kulakova[1], A. Dorofeev[1], N. Savenkova[1], E. Volnukhin[1], A. Kovshik[1], G. Lukina[1]. [1]*A.S. Loginov Moscow Clinical Research and Practical Center, Moscow Healthcare Department, Moscow, Russian Federation*

Background: Ankylosing spondylitis (AS) is a chronic inflammatory disease of the spine and sacroiliac joints characterized by new bone formation (syndesmophytes) and ankyloses. In AS cases, along with the damage to the musculoskeletal system, impairment of other organs and systems is often observed (uveitis, inflammatory bowel and heart diseases). Pro-inflammatory cytokines (TNF-α, IL-6,-17,-23,-21,-22,-31) and chemokines (IL-8) are key pathogenic markers in AS.
Objectives: The aims of the study were to determine the serum levels of IL-6 and IL-8 in AS and investigate their relationship with disease activity.
Methods: We studied 140 patients (pts) with AS fulfilled modified New York criteria (1984); (102M/38F); median and interquartile range (25th—75th percentile) of age 43.0; 35.0-51.0 years; disease duration 6.0; 4.0-12.0 years; BASDAI - 5.4; 4.1-6.6; ASDAS ESR - 3.6; 2.6-4.4; ASDAS CRP - 3.8; 2.7-4.5; 86% HLA-27 positive. In 50% of pts with AS, inflammatory bowel diseases (IBD) (Crohn's disease and ulcerative colitis) were diagnosed. The control group included 17 healthy donors (HC). The serum concentrations of IL-6 and IL-8 were detected by chemiluminescence immunoassay using IMMULATE 1000 analyzer (Siemens Healthcare Diagnostics, USA).
Results: AS pts had significantly higher serum level of IL-6 than HC (4.3; 0.1-8.0 pg/ml vs 2.3; 0.1-2.7 pg/ml, p <0.006). The median concentration of IL-8 didn't differ

between AS pts and HC (10.5; 8.3-18.0 pg/ml vs 11.9; 8.2-18.3 pg/ml, p>0.05). The same levels of IL-6 and IL-8 were detected in AS with IBD and AS without signs of IBD (p>0.05). In AS pts, serum IL-6 concentration was positively correlated with ASDAS ESR (r = 0.3), ASDAS CRP (r = 0.3), ESR (r = 0.3) and CRP (r = 0.5) (p <0.05); IL-8 was negatively associated with presence of fecal calprotectin (r = -0.3) (p <0.05).

Conclusion: Elevated serum concentration of IL-6 in AS is associated with clinical and laboratory markers of high inflammatory activity of the disease. The levels of IL-8 in the sera of AS patients were negatively correlated with the concentration of fecal calprotectin. Data on the relationship of IL-8 with the activity of the pathological process in AS require further study.

Disclosure of Interests: Elena Aleksandrova: None declared, Alexander Novikov: None declared, Polina Kulakova: None declared, Aleksey Dorofeev: None declared, Nadezhda Savenkova: None declared, Evgeniy Volnukhin: None declared, Anton Kovshik: None declared, Galina Lukina Speakers bureau: Novartis, Pfizer, UCB, Abbvie, Biocad, MSD, Roche

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FRI0565 **PREVALENCE AND SIGNIFICANCE OF ANTIBODIES AGAINST CITRULLINATED ALPHA-ENOLASE (ANTI-CEP1) IN CONNECTIVE TISSUE DISEASES.**

A. Alunno[1], F. Carubbi[2], O. Bistoni[1], M. Antonucci[1], E. Bartoloni Bocci[1], R. Giacomelli[2], R. Gerli[1]. *[1]Rheumatology Unit, University of Perugia, Perugia, Italy*; *[2]Rheumatology Unit, University of L'Aquila, L'Aquila, Italy*

Background: Anti-cyclic citrullinated peptide (anti-CCP) auto-antibodies represent the current gold standard for the diagnosis of rheumatoid arthritis (RA). However, growing evidence suggests that a variety of other citrullinated self-proteins may act as autoantigens and lead to the production of autoantibodies (1). Furthermore, autoantibodies believed to be RA-specific have been detected also in patients with connective tissue diseases (CTDs). We recently demonstrated that antibodies against citrullinated alpha-enolase (anti-CEP1) are a biomarker of erosive disease and RA-associated interstitial lung disease (2).

Objectives: The purpose of this study was to investigate the prevalence and possible prognostic value of anti-CEP-1 in patients with CTDs.

Methods: Two hundred and twelve consecutive patients with CTDs (51 systemic lupus erythematosus (SLE), 85 primary Sjogren's syndrome (pSS) and 76 systemic sclerosis (SSc)) were studied and compared to 97 sex and age matched normal controls (NC) and 267 patients with RA. Anti-CEP1 IgG were detected in serum samples with a commercial ELISA kit (Euroimmun).

Results: The overall prevalence of anti-CEP1 in CTDs was 7% (15/212 patients). In detail, these antibodies were detectable in 4 out of 85 pSS (5%), 5 out of 51 SLE (10%) and 6/76 SSc (8%). The prevalence and the titer of anti-CEP1 in CTDs was significantly higher compared to NC and significantly lower compared to RA. Anti-CEP1 positive patients did not display a specific clinical and serological picture. Unlike in RA, anti-CEP1 did not correlate with CTD-associated ILD.

Conclusion: This is the first study assessing anti-CEP1 in a large cohort of patients with CTDs. We demonstrated that the association of these autoantibodies with ILD is specific for RA since it is not observed in SLE, pSS and SSc. Furthermore, although being significantly more prevalent and at higher titer compared to NC, anti-CEP1 do not allow to discriminate different patient subsets displaying peculiar clinical or serological phenotypes. Based on our results, the application of anti-CEP1 in CTDs is not advisable, however larger studies may possibly identify correlations not evident in our cohort.

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Disclosure of Interests: Alessia Alunno: None declared, Francesco Carubbi Speakers bureau: Francesco Carubbi received speaker honoraria from Abbvie and Celgene outside this work., Onelia Bistoni: None declared, Matteo Antonucci: None declared, Elena Bartoloni Bocci: None declared, Roberto Giacomelli Grant/research support from: Actelion, Pfizer, Speakers bureau: Abbvie, Roche, Actelion, BMS, MSD, Ely Lilly, SOBI, Pfizer, Roberto Gerli: None declared

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FRI0566 **THE FLARE-RA QUESTIONNAIRE CAN IDENTIFY OMERACT FLARES IN PATIENTS WITH RHEUMATOID ARTHRITIS INCLUDED IN THE TAPERA TRIAL**

D. Bertrand[1], V. Stouten[1], S. Pazmino[1], D. De Cock[1], A. Moeyersoons[2], R. Westhovens[1,2], J. Joly[2], P. Verschueren[1,2]. *[1]KU Leuven, Skeletal Biology and Engineering Research Center, Leuven, Belgium*; *[2]UZ Leuven, Rheumatology, Leuven, Belgium*

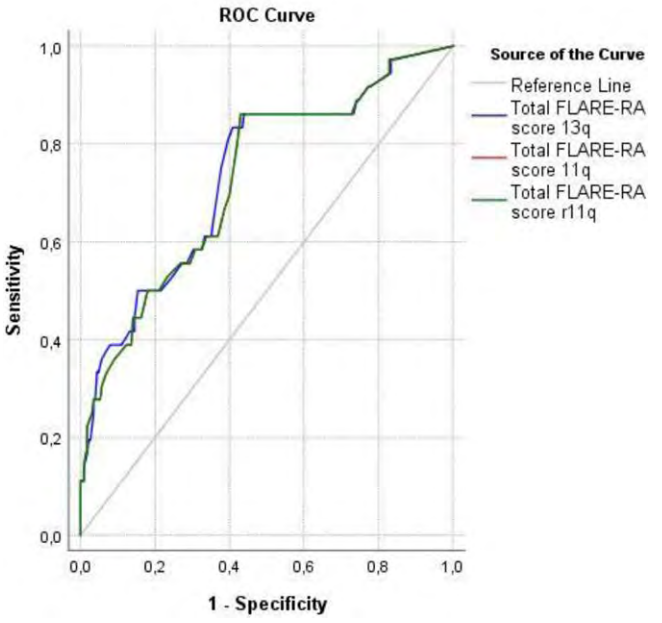


Figure 1. ROC curves of the total FLARE-RA scores (13q, 11q and r11q version) for identifying a flare according to the OMERACT definition.FLARE Q is expressed in mean ± SD. M month, FLARE Q FLARE-RA questionnaire 13q, n number, LDA low disease activity, MDA moderate disease activity, HDA high disease activity

Background: The Flare assessment in rheumatoid arthritis (FLARE-RA) questionnaire has been developed to identify flares in patients with rheumatoid arthritis (RA). The first version was published by Berthelot et al. (2012) and consisted of 13 questions on a Likert-scale of 1-6 ranging from 'completely untrue' to 'completely true'. When the FLARE-RA questionnaire was validated by Fautrel et al., 2 questions were removed, and it was rescaled to 0–10. The questionnaires' usefulness has been tested in few studies. Further external validation in a well-defined cohort of patients with RA is needed.

Objectives: To externally validate the FLARE-RA questionnaire and determine cut-offs for identifying a flare in an established RA population in which biologicals are tapered.

Methods: Patients who were in remission according to the DAS28CRP or ESR (≥6 months) and treated with etanercept 50 mg weekly (≥1 year), were enrolled between 2012 – 2014 in the pragmatic 1-year open-label randomised controlled TapERA (Tapering Etanercept in RA) trial. Patients were randomised to continue etanercept 50 mg weekly or taper to 50 mg every other week. The FLARE-RA questionnaire (version of 2012) was completed every 3 months. Outcomes were based on 3 versions of the questionnaire (13 questions (13q), 11 questions (11q) and 11 questions rescaled (r11q)). Per time point, the average of the answers was calculated to obtain a total score of the FLARE-RA questionnaire. The total scores were compared between patients in remission (DAS28CRP <2.6), low (DAS28CRP ≥2.6 - ≤3.2), moderate (DAS28CRP >3.2 - ≤5.1) and high disease activity (DAS-28CRP >5.1) using the Kruskal-Wallis test and between patients with and without a flare according to the OMERACT definition (increase in DAS28 >1.2 compared to baseline or increase in DAS28 >0.6 and current DAS28 ≥3.2) using the Mann-Whitney U test. The total FLARE-RA scores of the different time points were combined to determine the receiver operating characteristics (ROC) curves, the corresponding cut-off values and the area under the curve (AUC) for identifying an OMERACT flare. An AUC of <0.5, between 0.5 and 0.7 and >0.7 stands for having no, moderate and a good predictive value, respectively.

Results: FLARE-RA questionnaires of 66 patients (68% female, mean ± standard deviation (SD) age of 55 ± 11 years) were collected. The FLARE-RA score (13q) did increase when disease activity increased at month (M) 3 and M12 (p<0.01) (table 1). Patients presenting with an OMERACT flare had a statistically significantly higher total FLARE-RA score (13q) compared to patients without a flare, except at M12 (M3 and M6: p<0.05, M9: p<0.01). The AUC - ROC curve of the FLARE-RA questionnaire (13q) for identifying an OMERACT flare was 0.736 and the cut-off value was 2.3 (1-6 scale). The AUC - ROC curve was the same for the 11q and r11q version, namely 0.727. The cut-off values were 2.4 (1-6 scale) and 2.7 (0-10 scale), respectively (figure 1).

Table 1. Comparison of the total FLARE-RA scores (13q) between the disease activity groups (DAS28CRP)

		Remission	LDA	MDA	HDA	P-value
BL	Patients (n)	62	3	1	0	
	FLARE Q	1.8 ± 0.8	1.5 ± 0.3	1.3		0.800
M3	Patients (n)	50	11	5	0	
	FLARE Q	2.1 ± 1.0	3.0 ± 0.9	3.5 ± 1.4		0.004
M6	Patients (n)	52	5	9	0	
	FLARE Q	2.1 ± 0.8	3.1 ± 1.3	3.1 ± 1.9		0.057
M9	Patients (n)	48	10	7	1	
	FLARE Q	2.1 ± 0.9	2.8 ± 1.1	3.3 ± 1.6	2.4	0.079
M12	Patients (n)	52	8	6	0	
	FLARE Q	2.1 ± 1.0	3.1 ± 0.8	3.2 ± 1.0		0.002

Conclusion: The FLARE-RA scores seem to reliably discern between patients with and without an OMERACT flare. A cut-off of 2.7 on the current questionnaire (r11q) had the optimal sensitivity and specificity to identify an OMERACT flare.

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FRI0567

CONSTRUCT VALIDATION OF PROMIS SHORT FORM AND PROFILE-29 T-SCORES WITH SF-36 IN RHEUMATOID ARTHRITIS PATIENTS TREATED FOR 1 YEAR: RESULTS FROM A REAL-WORLD EVIDENCE-BASED STUDY IN THE UNITED STATES

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Background: Use of patient-reported outcomes (PROs) to assess health-related quality of life in clinical practice, research studies, and clinical trials in rheumatoid arthritis (RA) remains an ongoing area of research. SF-36 is commonly used in RA trials but is not feasible for routine use in clinical practice settings. The **P**atient **R**eported **O**utcomes **M**easurement **I**nformation **S**ystem (PROMIS) may address this gap but has not been widely assessed in RA patients starting therapy in a real-world comparative effectiveness study, nor examined in that setting in relation to the SF36 and Clinical Disease Activity Index (CDAI).

Objectives: To assess validity of PROMIS based on Comparative and Pragmatic Study of Golimumab Intravenous (IV) Versus Infliximab in Rheumatoid Arthritis (AWARE), an ongoing Phase 4 study providing real-world assessment of IV tumor necrosis factor inhibitor (TNFi) medications in RA patients.

Methods: AWARE is a prospective, non-interventional, 3-year study conducted at 88 US sites. RA patients were enrolled when initiating TNFi treatment. Treatment decisions were made by treating rheumatologists. We report baseline PROMIS-29 (7 domains and pain intensity), PROMIS Pain Interference (PI) Short Form (SF) 6b (PI6b) and PROMIS Fatigue (F) Short Form 7a (F7a), domain T-Scores, and SF-36 subdomain and Component Scores (CS) in AWARE patients. Here we report baseline data obtained from the final 1-year AWARE dataset. Correlations between PROMIS measures and comparable SF-36 component scores were calculated using Pearson correlations. Data is shown as mean ± standard deviation (SD).

Results: At baseline, mean CDAI of all patients (n=1262) was 32.3±15.6, with 70.4% in high disease activity (HDA, CDAI>22), 22.8% in moderate disease activity (MDA, CDAI: >10 and ≤22), 6.1% in low disease activity (LDA, CDAI: >2.8 and ≤10), and 0.7% in remission (CDAI ≤2.8). Mean PROMIS scores were >0.5 SD worse than population means for Physical Function (PF, 38.1±6.84), PI (63.4±7.68), F (58.8±9.95), Sleep Disturbance (55.1±8.68); and Ability to Participate in Social Roles/Activities (PSRA, 43.4±8.58). Baseline Depression and Anxiety were within 0.5 SD of population T-scores. PI6b, F7a, and P29 domain T-scores correlated with the comparable SF-36 subdomain and component scores (r's >0.58), except sleep for which no comparable SF-36 element was applicable. Examples include: P6b (r=-0.80) and P29-PI (0.81) with SF-36 Bodily Pain; F7a (-0.77) and P29-F (-0.77) with SF-36 Vitality; P29-PF with SF-36 PF (0.77), Role-Physical (0.69), and Physical CS (0.73); P29 Anxiety with SF-36 Mental Health (-0.72), Role-Emotional (-0.56), Mental CS (-0.70); and P29-PRSA with SF-36-Social Functioning (0.71). Mean PROMIS-29 T-scores (except Anxiety and Sleep Disturbance) among patients with HDA were significantly different from patients with MDA, LDA or remission ($p < 0.001$ for all). Further, mean PROMIS T-scores of PF, F, PSRA, PI, Pain Intensity, PI6b and P7a among patients with MDA were significantly different from patients with more or less active RA (by CDAI category).

Conclusion: Analysis of baseline results from a large cohort of RA patients indicates high correlations between individual P29 domain T-scores and SF-36 component scores, as well as categorical CDAI, providing strong evidence of PROMIS construct validity in a real-world population of RA patients.

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FRI0568

MEASURING DAILY PHYSICAL ACTIVITY IN AXSPA PATIENTS: CONTENT VALIDITY AND MEASUREMENT PROPERTIES OF THE NEW AXSPA-SQUASH

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Background: The ASAS-EULAR recommendations for management of axial Spondyloarthritis (axSpA) includes that patients should be encouraged to exercise.[1] So far, there is no validated instrument for measuring daily physical activity in axSpA. Our previous study recommends to adapt the Short QUestionnaire to Assess Health-enhancing physical activity (SQUASH) to improve the validity in axSpA patients.[2]

Objectives: AxSpA-disease specific adaptation of the physical activity questionnaire SQUASH to improve content validity and measurement properties.

Methods: This study was conducted according to the OMERACT-filter within the Groningen Leeuwarden AxSpA (GLAS) cohort and was performed in two parts. Part 1: adaptation and evaluation of content validity using a qualitative stepwise approach with in-depth interviews with different healthcare professionals (n=9) and patients (n=8), field testing in patients (n=10), and consensus meeting for final adaptations. Thereafter, content validity (n=45) was tested by filling out axSpA-SQUASH and SQUASH in random order two weeks apart. Part 2: measurement properties were tested using the International Physical Activity Questionnaire (IPAQ) as comparator. Criterion validity (n=40): Spearman's correlation with accelerometer as golden standard and classification accuracy of intensity. Construct validity (n=106): Spearman's correlation with disease activity, physical functioning and quality of life as clinical outcome with expected fair to moderated associations. Test-retest reliability (n=45): intraclass correlation coefficients (ICC) after 2 weeks. Responsiveness (n=47): standardized response mean (SRM) after 3 months stratified by Ancor method.

Results: In total 156 patients were included: mean age 48±13 years, 56% males, 72% HLA-B27 positive, symptom duration 21±13.3 years and ASDAS 2.0±1.0. Part 1: main adaptations were better explanation of intensities, adding answer option "not applicable", examples were modernized, physiotherapy and activity "shopping" were added. Compared to the original SQUASH, the adapted axSpA-SQUASH measured a systematically higher activity count and had less missing values (8% vs. 32%). Part 2: criterion validity: axSpA-SQUASH correlated better with accelerometer compared to IPAQ (ρ=0.51 vs. ρ=0.35). Classification accuracy: accelerometer defined most activity as light (97%), whereas axSpA-SQUASH and IPAQ defined most activity as moderate intensity (55% and 62% resp.). Construct validity: correlations were low to moderate and strongest for axSpA-SQUASH compared to IPAQ. Construct validity: correlations were low to moderate and stronger for axSpA-SQUASH compared to IPAQ (BASDAI -0.27 vs -0.15, BASDAI –0.27 vs. -0.15, ASDAS -0.24 vs -0.09, BASFI -0.39vs. -0.21, ASQoL -0.39 vs. -0.35). Test-retest reliability: ICC axSpA-SQUASH: 0.80. Responsiveness: axSpA-SQUASH changed over time in the corresponding direction (Table 1). Feasibility: considered comprehensible and average completion time was 7 minutes.

Table 1. Responsiveness of the axSpA-SQUASH versus change in BASDAI

	SRM	95% CI	BASDAI T1	BASDAI T2
Improved (n=12)	-0.36	-0.99 to 0.28	5.01 (2.10)	3.93 (1.60)
Stable (n=21)	0.28	-0.18 to 0.73	3.76 (2.05)	3.76 (2.05)
Decreased (n=14)	0.75	0.18 to 1.33	4.71 (1.96)	5.79 (2.42)

Conclusion: The new axSpA-SQUASH resulted in improved content validity and measurement properties. It seems the most appropriate questionnaire and can be used to assess daily physical activity in patients with axSpA.

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FRI0569 SERUM AMYLOID A: ASSESSMENT OF REFERENCE VALUE AND COMPARISON OF SERUM CONCENTRATION IN HEALTHY SUBJECTS AND PATIENTS WITH BEHÇET SYNDROME

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Background: Serum amyloid A (SAA) is a family of acute-phase reactants. The rise of SAA concentration in blood circulation is a clinical marker of active inflammation in several auto-inflammatory diseases, including Behçet syndrome (BS). Despite its practical and analytical advantages, SAA measurement by ELISA has been mainly used as a research tool rather than for the routine laboratory testing due to the lack of a robust reference data in the literature.

Objectives: Using the recommended procedures of the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC), we aimed to develop the SAA reference interval for a well-defined Italian healthy population (HC). Secondly, we compared the SAA serum concentration between HC and patients with BS.

Methods: Sera specimens were collected from adult healthy blood donors after rule out the exclusion criteria (inflammatory disorders, ongoing infections, pregnancy and breastfeeding, obesity, using oral contraceptives, use of any medication, or consumed of alcohol), and from unselected BS patients fulfilling the International Study Group (ISG) classification criteria. Serum SAA concentrations were detected and quantified with a commercial solid phase sandwich enzyme-linked immunosorbent assay (Human SAA ELISA kit, IBL International GmbH, Hamburg, Germany) used on automated analyzer (Immunomat, SERION Diagnostic, Alifax, Polverara (PD), Italy) according to the manufacturer's protocol. Statistical analysis and data normalization of HC SAA values were carried out to determine the reference cut off. In the second step of the study, HC and BS patients were stratified in two groups according to the cut-off value.

Results: We recruited 141 HC (84 M and 57 F; mean age, 44.5±13.2 years) and 63 BS patients (39 M and 24 F mean age, 45.3±13.2 years) assayed for SAA. The reference cut-off was calculated as 225 ng/ml. No statistically significant differences were found between males and females when SAA means were compared, suggesting that not gender-partitioned reference range is recommended for this analyte. After the stratification according to the cut-off value (group 1: < 225 ng/ml and group 2: > 225 ng/ml), we found 53/63 (84.1%) BS patients and 133/141 (94.3%) HC with concentration less than cut-off value, respectively. We identified 10/63 (15.9%) BS patients and 8/141 (5.7%) HC within the second group. The difference was statistically significant (p=0.0177; OR: 3.14, 95% CI: 1.17-3.38).

Conclusion: This study allowed to define a widely accepted reference cut-off for the SAA detected by ELISA, responding to an unmet need of laboratory medicine. We found a statistically significant higher frequency of BS patients compared with HC when SAA values is higher than cut-off (225 ng/ml). This preliminary data could add significant information for better clarify the role of SAA as biomarker of inflammation and in guidance of clinical practice. Further studies will be required to stratify SAA values in relation to disease activity of BS.

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FRI0570 IDENTIFICATION OF OSTEOPONTIN/SECRETED PHOSPHOPROTEIN 1 AS A BIOMARKER FOR PSORIATIC ARTHRITIS

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Background: Early diagnosis of psoriatic arthritis (PsA) can be facilitated by appropriate referral of psoriasis patients to rheumatologists. Soluble biomarkers for PsA may help screen psoriasis patients for PsA.

Objectives: To identify novel biomarkers for PsA by investigating serum levels of candidate biomarkers identified through proteomic analysis of synovial fluid (SF) and skin biopsies and literature review.

Methods: We first (discovery phase) identified markers using: i) proteomic analysis of SF[1], ii) proteomic analysis of skin biopsies[2], and iii) literature review. In verification phase 1, we measured serum levels of the selected potential protein markers, using commercially available ELISA kits, to identify differentially expressed markers in healthy controls and patients with PsA (≥3 swollen joints, not treated with biologics) and psoriasis without PsA (PsC; matched with PsA patients on age, sex and psoriasis duration) (100 subjects each group). In verification phase 2, using less strict criteria (no restriction on pharmacotherapy or disease activity) and larger sample size, we confirmed the association with PsA of markers identified in phase 1 using samples from 200 patients each with PsA and PsC. Statistical methods used included descriptive statistics, t-tests and logistic regression.

Results: The discovery phase identified the following 31 markers for testing in verification phase 1- hsCRP, MMP3, CD5L, M2BP, MPO, ITGB5, DKK1, FGF23, IL-6, IL-1β, leptin, osteocalcin, OPG, OPN, SOST, TNFα, adiponectin, periostin, RANKL, YKL40, KLK6, KLK8, CS846, C2C, CPII, TNFSF14, COMP, ALP, CXCL10, S100A8/A9 and DEFA. The following 21 markers remained differentially upregulated in PsA after testing in verification phase 1- hsCRP, MMP-3, M2BP, ITGB5, leptin, OPG, OPN, SOST,TNFα, periostin, RANKL, YKL40, KLK8, C2C, CPII, TNFSF14, COMP, ALP, CXCL10, S100A8/A9 and DEFA. Univariate logistic regression analyses adjusted for age, sex, and disease duration confirmed the association between hsCRP, OPN, S100A8/A9, OPG and the ratio CPII/C2C in verification phase 2. Multivariate logistic regression demonstrated that hsCRP and OPN (both p<0.001) are independently associated with PsA.

Conclusion: OPN, a cytokine involved in enhancing production of IFNγ and IL-12, reducing production of IL-10 and promoting attachment of osteoclasts to mineralized bone matrix, is a potential biomarker of PsA.

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FRI0571 THE DIAGNOSTIC VALUE OF KL-6 IN RHEUMATOID ARTHRITIS ASSOCIATED WITH INTERSTITIAL LUNG DISEASE IN XINJIANG OF CHINA

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Background: Rheumatoid arthritis (RA) is a systemic inflammatory disease.Many researchers have observed that extra articular organs were highly involved in RA patients.The most common extra-articular manifestations were pulmonary involvement.Serum levels of KL-6 have been reported to be elevated in various ILD such as idiopathic pulmonary fibrosis, collagen vascular disease associated interstitial pneumonias, and other interstitial lung disorders.However, little is known regarding

the usefulness of this biomarker in connective tissue diseases related interstitial lung diseases(CTD-ILD). Especially,the diagnostic value of KL-6 in interstitial lung disease associated with rheumatoid arthritis(RA-ILD) still has a dispute.

Objectives: To assess the diagnosis of the serum Krebs von den Lungen-6(KL-6) for RA-ILD patients in Xinjiang of China.

Methods: This retrospective study included 184 patients with RA in who visited the department of rheumatology and immunology of People's Hospital of Xinjiang Uygur Autonomous Region between January, 2015 and December, 2019.The patients were divided into RA-ILD group(n=95) and RA group(n=89) according to the presence of ILD. Serum KL-6 concentration (U/mL) was measured using the chemiluminescent enzyme immunoassay kit.

Results: The mean age($p < 0.001$) and median value of CCP ($p = 0.006$) were significantly higher in the RA-ILD group.RA-ILD group had elevated serum KL-6 levels compared to RA group [447(281, 687)U/ml vs 195(151.5,265.5)U/ml]($p < 0.001$)(figure 1).According to the Receiver Operating Characteristic Curve (ROC) analysis, the area under the curve was of 0.879 and the optimal cut-off value of serum KL-6 to discriminate the presence of ILD was 277 U/ml, with sensitivity of 77.9%, specificity of 79.8%(figure 2).

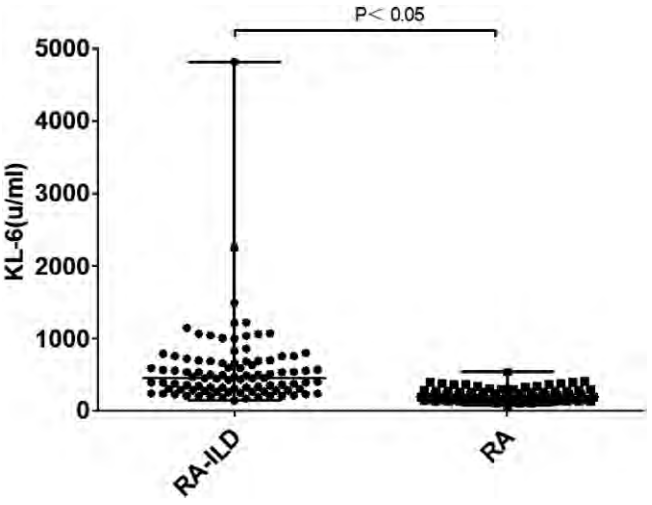


Figure 1. Comparison of serum KL-6 concentrations in RA-ILD group and RA group.

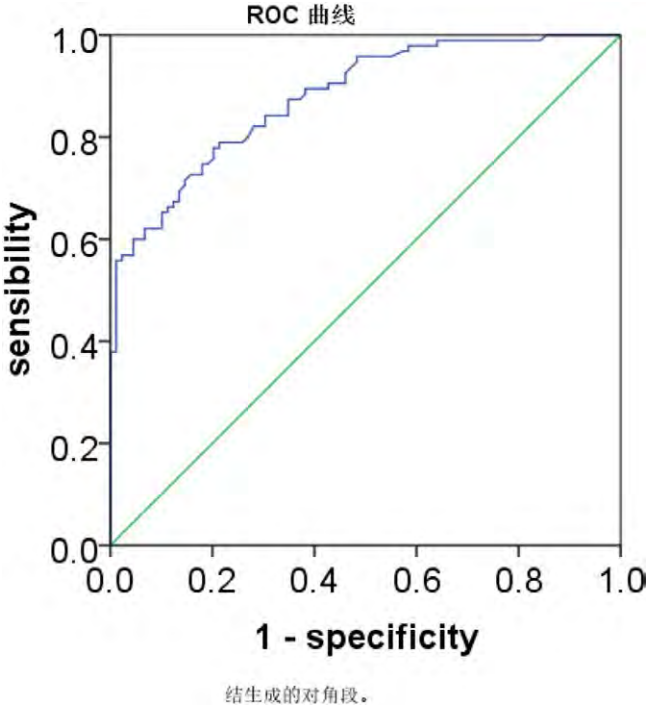


Figure. 2. Receiver-operating characteristic curve(ROC) of KL-6 for the diagnosis of RA-ILD

Conclusion: The present study confirms that KL-6 is a biological marker which is associated with RA-ILD. Furthermore, Patients with RA who are older and have a higher value of CCP are more likely to develop ILD.

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FRI0572

LEPTIN-ADJUSTMENT OF THE MULTI-BIOMARKER DISEASE ACTIVITY (MBDA) SCORE REDUCES THE INFLUENCE OF ADIPOSITY

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Background: Obesity and excess adiposity influence inflammatory markers and bias disease activity assessment, especially among women. A multi-biomarker disease activity (aMBDA) score has been developed to account for the effects of age, sex and adiposity (leptin) and improves prediction of radiographic damage progression.[1]

Objectives:

1) Determine if the adjusted measure demonstrates a reduced association with adiposity.
2) Assess the impact of the leptin-adjustment on the score over the range of adiposity.
3) Assess relationships between MBDA scores and clinical disease activity.

Methods: Patients with rheumatoid arthritis (RA), ages 18-75 years, completed whole-body dual-energy x-ray absorptiometry to quantify fat mass indices (FMI, kg/m^2). Age-, sex-, and race-specific Z-Scores were calculated based on the distributions in a healthy reference population. Disease activity was assessed with the CDAI and swollen joint count (SJC). Baseline van der Heijde-Sharpe (vdHS) scores were determined by a radiologist. MBDA assays were performed on stored serum samples. Descriptive statistics described relationships between the FMI Z-Score and the MBDA and the aMBDA. Clinical disease activity, SJC, and radiographic damage were also compared across MBDA score categories.

Results: Of 104 participants (50% female), the mean (SD) age was 56.1 (12.5) and mean BMI was 28.8 (6.9) (Table 1). The unadjusted MBDA score was strongly associated with BMI among women (Women: Rho=0.46 [p< 0.001]; Men: Rho=-0.12), while the aMBDA was not associated with BMI in women and was inversely correlated in men (Women: Rho=0.17; Men: Rho=-0.32 [p=0.02]). The unadjusted MBDA score was also strongly associated with FMI Z-Score among women (Figure; Women: Rho=0.42 [p=0.002]; Men: Rho=-0.10; p=0.01). The aMBDA was not significantly associated with FMI Z-Score (Female: Rho= 0.17; Male: Rho=-0.26). Leptin-adjustment reduced the MBDA score in the highest quartile of FMI in women but not men, and increased the MBDA score in the lowest FMI quartiles in both women and men; these patients in the lowest FMI quartile had the highest median SJC (p=0.05 for men, p=0.78 for women; Figure). The aMBDA reclassified 4 women (8%) and 9 men (17%) into higher disease activity categories and 2 women (4%) and 2 men (4%) into lower categories. CDAI, SJC, and radiographic scores were similar across activity categories for the unadjusted MBDA score and aMBDA (Table 2).

Table 1. Baseline Characteristics.

	Men	Women
N	52	52
Age (yrs)	59.1 (11.5)	53.0 (12.8)
Black, N (%)	13 (25%)	19 (36%)
BMI	27.3 (5.4)	30.3 (8.0)
FMI Z-Score	-0.28 (1.3)	0.05 (1.1)
DAS28(CRP)	3.09 (1.13)	3.21 (1.24)
Disease Duration	11.4 (10.9)	11.6 (11.9)
CRP, mg/dL	0.8 (0.5, 1.2)	0.8 (0.5, 1.4)
CCP Positive, N (%)	45 (87%)	40 (78%)
vdHS (N=93)	13 (4, 73)	10.5 (2, 47)
HAQ	0.71 (0.59)	0.83, (0.67)
MBDA	40.0 (13.8)	42.1 (16.6)
aMBDA	43.6 (13.4)	42.1 (15.3)
Leptin, ng/mL	15.1 (21.5)	48.9 (41.5)

Table 2. Clinical assessments across MBDA score categories.

	CDAI		SJC		vdHS	
	MBDA	aMBDA	MBDA	aMBDA	MBDA	aMBDA
MBDA Category						
Low	14.6 (10.9)	13.9 (9.9)	2 (1, 5)	2 (1, 5)	9 (1, 33.5)	9 (3, 32)
Moderate	13.2 (10.0)	14.4 (11.4)	2 (0, 5)	3 (0, 6)	10 (4, 49)	10 (2, 53)
High	18.4 (12.3)	17.7 (11.8)	4 (1, 8)	5 (2, 7)	20.5 (5, 70.5)	18 (4, 73)

Conclusion: Leptin-adjustment of the MBDA score reduced bias related to excess adiposity in women with RA. Adjustment results in lower MBDA scores in women with greater adiposity, and higher MBDA scores in women and men with lesser adiposity. The aMBDA may reduce misclassification due to excess adiposity and improve identification of active disease among patients with lower adiposity. High aMBDA scores among men with low adiposity may reflect severe disease or excess comorbidity in this group.

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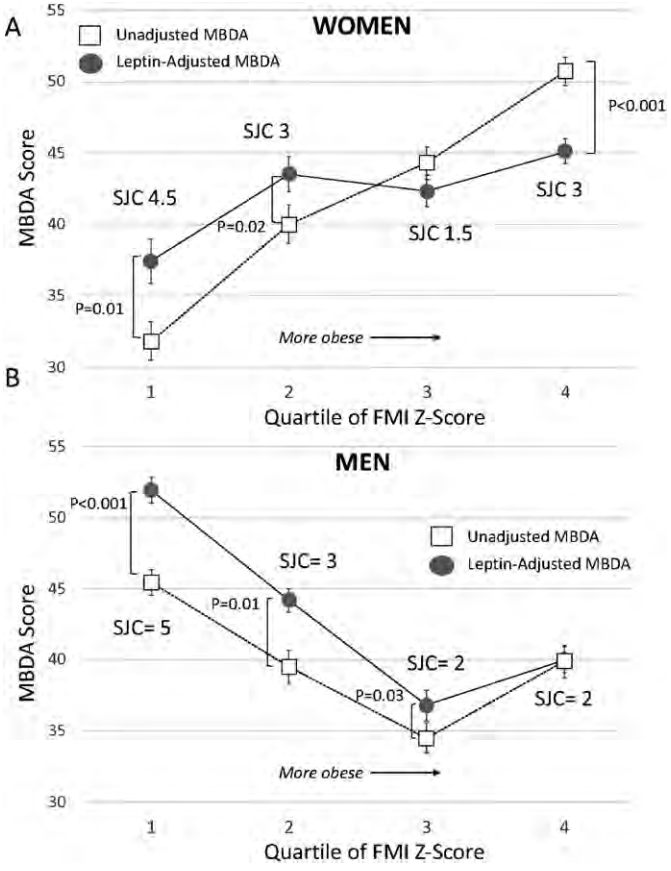


Figure. Impact of Adjustment on MBDA Score by FMI Z-Score Quartile.

Disclosure of Interests: Joshua Baker Grant/research support from: Myriad RBM, Consultant of: Bristol-Myers Squib, Burns-White LLC, Jeffrey Curtis Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Janssen, Lilly, Myriad, Pfizer, Regeneron, Roche, UCB, Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Janssen, Lilly, Myriad, Pfizer, Regeneron, Roche, UCB, David Chernoff Employee of: Myriad, Michael George Grant/research support from: Bristol Myers Squibb, Consultant of: AbbVie

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FRI0573

VALIDATION OF FOUR SCREENING TOOLS FOR PSORIATIC ARTHRITIS IN CHINESE PATIENTS WITH PSORIASIS: A MULTICENTER STUDY

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory arthropathy affecting 6~30% of patients with skin or nail psoriasis. If PsA is not identified early and managed appropriately, progressive joint damage with deformities and disability may occur. Preliminary efforts to develop screening tools for the identification of PsA have met with variable success. Whether the tools function well or not in Chinese patients remains unknown.

Objectives: We aimed to validate and compare the performance of 4 PsA screening tools in Chinese psoriasis patients.

Methods: Consecutive psoriasis patients (dermatology cohort) attending dermatology clinics without previous diagnosis of inflammatory arthritis and consecutive newly diagnosed PsA patients (rheumatology cohort) attending rheumatology clinics were invited to complete the questionnaires: early arthritis for psoriatic patients (EARP), psoriatic arthritis screening and evaluation(PASE), psoriasis and arthritis screening questionnaire(PASQ), and psoriasis epidemiology screening tool (PEST). Receiver operating characteristic (ROC) curves were utilized to calculate diagnostic accuracy, least absolute shrinkage and selection operator(lasso) and binary logistic regressions to identify the most discriminative questions.

Results: In this multicenter study, 379 patients in the dermatology cohort and 72 in the rheumatology cohort were recruited. In the dermatology cohort, 7.9% (30/379) were newly diagnosed with PsA. The EARP and PASQ tools demonstrated better discriminating ability for identifying PsA from psoriasis patients (yielded sensitivities/specificities were: 93.3%/92.3% and 90.0%/90.5%, while optimal cut-off values were: 3 and 5, respectively), and the good performance of EARP and PASQ was further confirmed in the rheumatology cohort. However, all these tools demonstrated low sensitivities (about 30%) with regard to screening the axial PsA. Based on the questions, a risk prediction model of PsA was established.

Conclusion: The prevalence rate of undiagnosed PsA in the patients with psoriasis is 7.9%. Both EARP and PASQ tools show better favorable trade-off between sensitivity and specificity than PASE and PEST, while all the 4 tools are not sensitive to identify axial PsA.

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FRI0574

RENAL TISSUE EPIGENETIC BIOMARKERS' CHARACTERIZATION IN PATIENTS WITH LUPUS NEPHRITIS AS PARAMETERS OF DISEASE ACTIVITY, REMISSION AND FLARE

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Background: Epigenetic factors such as non-coding RNA (miRNA) have been shown to be deregulated in Systemic Lupus Erythematosus (SLE). In particular, in mouse model (1), different miRNAs have been associated with lupus nephritis (LN), one of the most severe manifestations of the disease.
Objectives: The aim of the study was to evaluate the expression of miR-155 and miR-34a in renal tissue as biomarkers of organ involvement and inflammatory tissue activity in patients with LN.
Methods: Thirty-two LN patients with active renal involvement were enrolled (age: 32.2 ± 9.2 years). The nephritic onset of the disease (early-SLE) was present in 13 patients (41%), while 19 patients (59%) showed a renal involvement during the follow-up (long-SLE). Clinical, laboratory and demographic data were collected for each patient. Disease activity was recorded using SLEDAI-2K and renal activity, using the total SLEDAI-2K fraction including the items related to the renal involvement. Ultrasound-guided renal biopsy has been performed for each patients for the definition of the nephritic class according to the ISN / RPS classification of 2003 revised in 2018(2). The expression of miR-155 and miR-34a in renal tissue was carried out by extraction of total RNA from paraffin-preserved biopsies and after a retrotrascription protocol was evaluated using SYBR® Green-based real-time PCR by relative quantification considering the ΔCt (Ct miRNA- Ct housekeeping gene)(3).
Results: Mir-155 and miR-34a expression in renal tissue were comparable in the different histological classes. Dividing patients on the base of nephritic onset, patients with early SLE showed lower expression of miR-155 (ΔCt 12.8 ± 10.8) and miR-34a (ΔCt 14.6 ± 9.9) than patients with long-SLE (miR-155: ΔCt 6.1 ± 8.7 p = 0.02; miR-34a: ΔCt 7.1 ± 9.0 p = 0.03). Furthermore, a direct correlation was observed between the expression of miR-155 and miR-34a (r = 0.91, p <0.001). Considering patients with early-SLE, the expression of miR-34a was slightly significant in patients who had relapsed (ΔCt 8.2 ± 11.4 vs ΔCt 18.4 ± 7.9 p = 0.08), although no correlation emerged between the expression of miR-155 and miR-34a both at the time of the biopsy and with the disease activity indices. At the histological evaluation, miR-155 and miR-34a were more expressed in Early-SLE patients who had wire loop lesions (miR-155: ΔCt 19.5 ± 7.7 vs ΔCt 7.3 ± 9.6 p = 0.05; miR-34a: ΔCt 21,7 ± 1.1 vs ΔCt 8,8 ± 9.7 p= 0.05) possibly associated with a greater activation of the inflammatory component.
Conclusion: MiR-155 and miR-34a may represent tissue biomarkers of inflammatory activation in patients with LN in particular the higher expression of these miRNA in Long-SLE patients could indicate a possible role of these biomarkers in renal involvement in patients with SLE with later renal onset. The increased expression of miR-34a could give indications of a disease recurrence suggesting a closer monitoring of the patient.
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Disclosure of Interests: None declared
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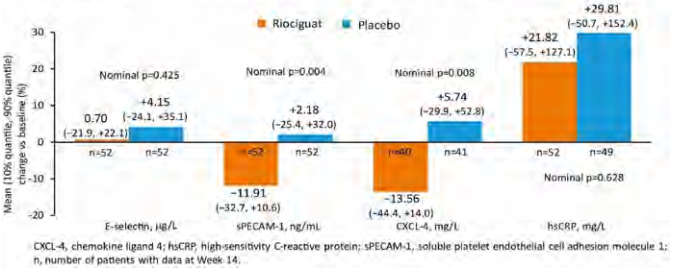
FRI0575

BIOMARKER ANALYSIS FROM THE RISE-SSC STUDY OF RIOCIGUAT IN EARLY DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS (DCSSC)

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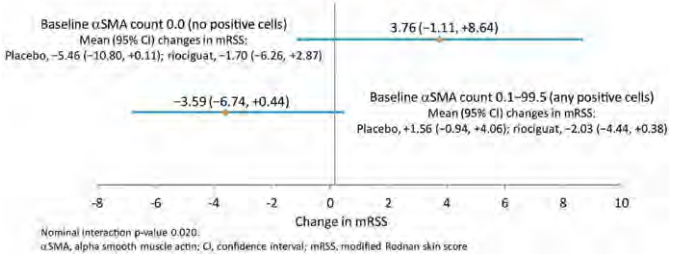
Background: RISE-SSc (NCT02283762) was a multicenter, double-blind, Phase IIb study of riociguat in early dcSSc. Primary endpoint was change in mRSS from baseline to Wk 52.
Objectives: Exploratory, descriptive analyses of riociguat target engagement and effects on disease biomarkers in RISE-SSc and their relationship with effects on the primary endpoint. All biomarker p-values are for information only.
Methods: Pts with dcSSc (duration ≤18 mo; modified Rodnan skin score [mRSS] 10–22 units) were randomized to riociguat 0.5–2.5 mg tid (n=60) or placebo (n=61). Biomarkers of target engagement (cGMP), inflammation and/or vascular/endothelial function (e.g. high-sensitivity C-reactive protein [hsCRP], soluble platelet endothelial cell adhesion molecule 1 [sPECAM-1], soluble E-selectin, chemokine ligand 4 [CXCL-4]), and fibrosis (e.g. alpha-smooth muscle cell actin [alphaSMA], pro-collagen mRNA expression) were measured in plasma, serum, and skin biopsies at baseline and Wk 14.
Results: Mean±SD change from baseline in mRSS was –2.09±5.66 (n=57) with riociguat and –0.77±8.24 (n=52) with placebo (p=0.08). From baseline to Wk 14, plasma cGMP rose by mean (SD) 94% (78%) (n=52) with riociguat and 10% (39%) (n=52) with placebo (nominal p<0.001). Serum sPECAM-1 and CXCL-4 fell with riociguat vs placebo; changes in hsCRP or E-selectin differed little between groups (Fig 1). Pts with higher baseline sPECAM-1 showed larger mRSS reductions with riociguat vs placebo than pts with lower levels (nominal interaction p=0.004). In baseline skin biopsies, 34% and 31% of pts in the riociguat and placebo groups, respectively, had no alphaSMA-positive cells; other pts had +ve cells (alphaSMA counts 0.1–99.5, median 2.5), a potential indicator of higher disease activity. Pts with +ve baseline alphaSMA counts showed a reduction of mRSS with riociguat vs placebo (Fig 2). Skin collagen mRNA expression biomarkers in skin biopsies showed no differences between groups.
Conclusion: Primary study endpoint (change in mRSS) was not met. Plasma cGMP rose with riociguat, confirming engagement with the NO-sGC-cGMP pathway. Serum sPECAM-1 (marker of endothelial activation) and CXCL-4 (marker of progressive SSc) fell with riociguat; hsCRP and E-selectin did not. Some serum and skin biomarkers of higher disease activity at baseline were associated with a greater effect of riociguat on skin fibrosis.

Figure 1. Changes in selected serum biomarkers in riociguat and placebo groups from baseline to Week 14



CXCL-4, chemokine ligand 4; hsCRP, high-sensitivity C-reactive protein; sPECAM-1, soluble platelet endothelial cell adhesion molecule 1; n, number of patients with data at Week 14.

Figure 2. Treatment difference (riociguat–placebo) for primary endpoint (change in mRSS from baseline to Week 52) according to baseline aSMA count



Nominal interaction p-value 0.020.
αSMA, alpha smooth muscle actin; CI, confidence interval; mRSS, modified Rodnan skin score

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Disclosure of Interests: Oliver Distler Grant/research support from: Grants/Research support from Actelion, Bayer, Boehringer Ingelheim, Competitive Drug Development International Ltd. and Mitsubishi Tanabe; he also holds the issued Patent on mir-29 for the treatment of systemic sclerosis (US8247389, EP2331143)., Consultant of: Consultancy fees from Actelion, Acceleron Pharma, AnaMar, Bayer, Baecon Discovery, Blade Therapeutics, Boehringer, CSL Behring, Catenion, ChemomAb, Curzion Pharmaceuticals, Ergonex, Galapagos NV, GSK, Glenmark Pharmaceuticals, Inventiva, Italfarmaco, iQvia, medac, Medscape, Mitsubishi Tanabe Pharma, MSD, Roche, Sanofi and UCB, Speakers bureau:

Speaker fees from Actelion, Bayer, Boehringer Ingelheim, Medscape, Pfizer and Roche, Frank Kramer Employee of: Bayer AG, Josef Höfler Employee of: Josef Höfler is an employee of Staburo GmbH, Munich, Germany, contracted by Bayer AG to perform the biomarker analyses, Mercedeh Ghadessi Employee of: Bayer AG, Peter Sandner Employee of: Bayer AG, Yannick Allanore Grant/research support from: BMS, Inventiva, Roche, Sanofi, Consultant of: Actelion, Bayer AG, BMS, BI, Christopher Denton Grant/research support from: GlaxoSmith-Kline, CSL Behring, and Inventiva, Consultant of: Medscape, Roche-Genentech, Actelion, GlaxoSmithKline, Sanofi Aventis, Inventiva, CSL Behring, Boehringer Ingelheim, Corbus Pharmaceuticals, Acceleron, Curzion and Bayer, Masataka Kuwana Grant/research support from: Acetelion, Consultant of: Acetelion, Bayer, Chugai, Corbus Pharmaceuticals, CSL Behring and Reata Pharmaceuticals. He was a member of the SENSCIS trial Steering Committee (Boehringer Ingelheim), Marco Matucci-Cerinic Grant/research support from: Actelion, MSD, Bristol-Myers Squibb, Speakers bureau: Acetelion, Lilly, Boehringer Ingelheim, Janet Pope Grant/research support from: AbbVie, Bristol-Myers Squibb, Eli Lilly & Company, Merck, Roche, Seattle Genetics, UCB, Consultant of: AbbVie, Actelion, Amgen, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Eicos Sciences, Eli Lilly & Company, Emerald, Gilead Sciences, Inc., Janssen, Merck, Novartis, Pfizer, Roche, Sandoz, Sanofi, UCB, Speakers bureau: UCB, Tatsuya Atsumi Grant/research support from: Eli Lily Japan K.K., Alexion Pharmaceuticals, Inc., Bristol-Myers Squibb Co., AbbVie Inc., Daiichi Sankyo Co., Ltd., Pfizer Inc., Chugai Pharmaceutical Co., Ltd., Mitsubishi Tanabe Pharma Co., Astellas Pharma Inc., Consultant of: Gilead Sciences, Inc., Eli Lilly Japan K.K., UCB Japan Co. Ltd., AbbVie Inc., Daiichi Sankyo Co., Ltd., Pfizer Inc., Chugai Pharmaceutical Co., Ltd., Speakers bureau: Eli Lilly Japan K.K., UCB Japan Co. Ltd., Bristol-Myers Squibb Co., AbbVie Inc., Eisai Co. Ltd., Otsuka Pharmaceutical Co., Ltd., Daiichi Sankyo Co., Ltd., Pfizer Inc., Chugai Pharmaceutical Co., Ltd., Mitsubishi Tanabe Pharma Co., Takeda Pharmaceutical Co., Ltd., Astellas Pharma Inc., Radim Bečvář Consultant of: Actelion, Roche, László Czirják Consultant of: Actelion, BI, Roche-Genentech, Lilly, Medac, Novartis, Pfizer, Bayer AG, Ellen De Langhe Consultant of: member of advisory board for Boehringer, Eric Hachlla: None declared, Tomonori Ishii: None declared, Osamu Ishikawa: None declared, Sindhu Johnson Grant/research support from: Boehringer Ingelheim, Corbus Pharmaceuticals, GlaxoSmithKline, Roche, Merck, Bayer, Consultant of: Boehringer Ingelheim, Ikaria, Kaisa Laapas Employee of: Partly in-sourced to Bayer, Valeria Riccieri: None declared, Elena Schiopu: None declared, Richard Silver: None declared, Vanessa Smith Grant/research support from: The affiliated company received grants from Research Foundation - Flanders (FWO), Belgian Fund for Scientific Research in Rheumatic diseases (FWRO), Boehringer Ingelheim Pharma GmbH & Co and Janssen-Cilag NV, Consultant of: Boehringer-Ingelheim Pharma GmbH & Co, Speakers bureau: Actelion Pharmaceuticals Ltd, Boehringer-Ingelheim Pharma GmbH & Co and UCB Biopharma Sprl, Chiara Stagnaro: None declared, Viginia Steen Grant/research support from: The associated affiliation has received grants/research from Boehringer Ingelheim, Corbus Pharmaceuticals, CSL Behring, Eicos, Galapagos, Immune Tolerance Network, Reata, Consultant of: Virginia Steen has acted as a consultant for Boehringer Ingelheim, Corbus, CSL Behring, Eicos, Forbius, Wendy Stevens: None declared, Gabriella Szücs: None declared, Marie-Elise Truchetet: None declared, Melanie Wosnitza Employee of: Bayer AG, Dinesh Khanna Shareholder of: Eicos Sciences, Inc./Civi Biopharma, Inc., Grant/research support from: Dr Khanna was supported by NIH/NIAMS K24AR063120, Consultant of: Acceleron, Actelion, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Corbus Pharmaceuticals, Horizon Therapeutic, Galapagos, Roche/Genentech, GlaxoSmithKline, Mitsubishi Tanabe, Sanofi-Aventis/Genzyme, UCB

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FRI0576

IDENTIFICATION OF SERUM PROTEIN BIOMARKERS ASSOCIATED WITH RA DISEASE SEVERITY

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Background: RA is a systemic autoimmune disease with heterogeneous manifestation. Recent advances in serum proteomics, such as the SomaScan® platform (SomaLogic, Inc., Boulder, USA), allow for a deeper exploration of the protein biomarkers associated with RA and a better understanding of the molecular aetiology of the disease.

Objectives: To characterise the differences in baseline serum proteome of patients with RA (enrolled in the Phase IIIb Abatacept vs adaliMumab comParison in bioLogic-naïvE RA subjects with background MTX [AMPLE] study)[1] compared with a healthy population, and to identify serum protein biomarkers associated with disease severity and radiographic progression.

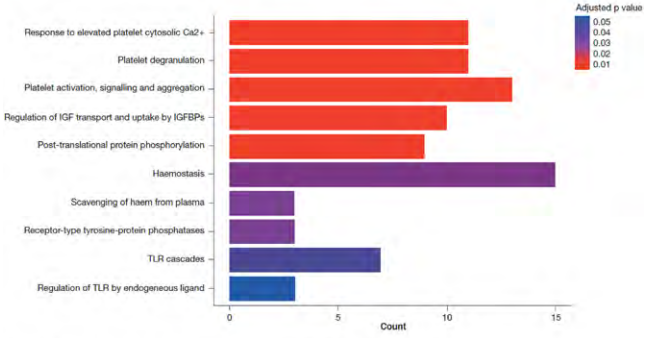
Methods: Patients in the AMPLE study had an inadequate response to MTX and were naïve to biologic DMARDs. Protein abundance was assessed in baseline serum samples from 440 AMPLE study patients and 123 healthy individuals with matching demographics using the SomaScan® platform, with 5000+ slow off-rate modified aptamers and up to 8 log of dynamic range.[2] Differential abundance testing was performed using linear models to identify differences in protein abundance in patients with RA vs healthy individuals. A separate analysis using a linear model was conducted in only the patients with RA to identify the proteins associated with DAS28 (CRP) and TSS. Pathway analyses were performed for proteins significantly (false discovery rate-adjusted p value <0.05) associated with RA and the disease severity measurements to identify over-representation of the molecular pathways.

Results: Compared with healthy individuals, >2000 serum proteins were significantly differentially expressed in patients with RA, including many proteins that have been associated with RA (e.g. serum amyloid A [SAA], CRP) and complement. Most of the protein expression differences were of small magnitude (fold change <2). Proteins that were differentially expressed between patients with RA and healthy individuals were enriched in interleukin signalling, neutrophil degranulation, platelet activation/degranulation and extracellular matrix organisation pathways. DAS28 (CRP) was significantly associated with several biomarkers, including SAA, fibrinogen and CRP; in general, proteins associated with DAS28 (CRP) were most strongly enriched in the platelet activation/degranulation pathways (Figure 1), also seen in patients with RA vs healthy individuals. Additionally, many proteins were significantly associated with TSS, including SAA, matrix metalloproteinase-3 and cartilage acidic protein 1. Here, the proteins were most strongly enriched in the extracellular matrix remodelling pathways (Figure 2).

Conclusion: Our study revealed that thousands of serum proteins are differentially expressed and several pathways are dysregulated between patients with RA and healthy individuals. Additional pathways were identified that reflect disease severity, including joint damage, distinct from those pathways associated with the disease. The SomaScan® platform provides a unique proteomic tool with a wide dynamic range for the identification of serum protein biomarkers associated with RA and disease severity. Proteomic signatures should be considered in clinical trials to better understand disease pathogenesis and predict risk in response to treatment.

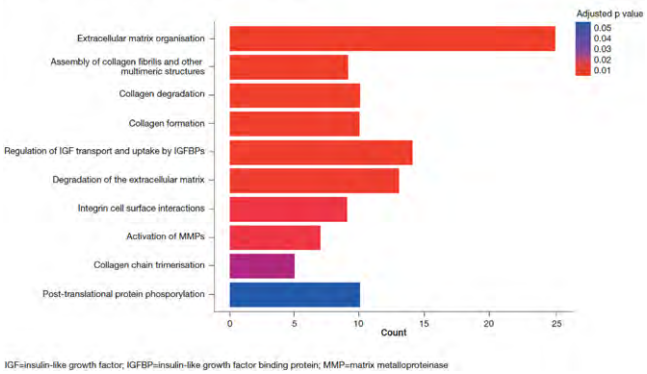
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[**2**]Gold L, et al. *PLoS One* 2010;**5**:e15004.

Figure 1. Pathways Associated With Disease Severity Metrics in RA: DAS28 (CRP)



IGF=insulin-like growth factor; IGFBP=insulin-like growth factor binding protein; TLR=toll-like receptor

Figure 2. Pathways Associated With Disease Severity Metrics in RA: TSS



IGF=insulin-like growth factor; IGFBP=insulin-like growth factor binding protein; MMP=matrix metalloproteinase

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Disclosure of Interests: David Galbraith Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Minal Caliskan Employee of: Bristol-Myers

Squibb, Omar Jabado Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Sarah Hu Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Roy Fleischmann Grant/research support from: AbbVie, Akros, Amgen, AstraZeneca, Bristol-Myers Squibb, Boehringer, IngelhCentrexion, Eli Lilly, EMD Serono, Genentech, Gilead, Janssen, Merck, Nektar, Novartis, Pfizer, Regeneron Pharmaceuticals, Inc., Roche, Samsung, Sandoz, Sanofi Genzyme, Selecta, Taiho, UCB, Consultant of: AbbVie, ACEA, Amgen, Bristol-Myers Squibb, Eli Lilly, Gilead, GlaxoSmithKline, Novartis, Pfizer, Sanofi Genzyme, UCB, Michael Weinblatt Grant/research support from: Amgen, Bristol-Myers Squibb, Crescendo, Lily, Sanofi/Regeneron, Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Crescendo, Gilead, Horizon, Lily, Pfizer, Roche, Sean Connolly Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Michael A Maldonado Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Sheng Gao Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb

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FRI0577 VITAMIN D LEVEL IN HEALTHY CANARIAN ADULT POPULATION

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Background: Vitamin D (VitD) was first used to treat rickets in children in depressed urban areas of England, due to malnutrition and lower sun exposure. During the last decade its use has become widespread in western societies because it has been associated with lower risk of suffering from multiple diseases and there is also a lack of consensus in establishing adequate levels for the general population. Regarding the beneficial effects of VitD, well-designed current observational studies are calling them into question and many authors believe that levels of 30 ng/mL, adopted as optimal, are overestimated[1-2]. All this has led many individuals who come to our consultations to use supplements without scientific evidence of their benefits.

Objectives: The main objective was to determine the distribution of VitD levels in the healthy canarian population, an area with high solar radiation and stratified according to demographic factors (age, sex and place of residence). As a secondary objective, the study was established to determine prevalence of hyperparathyroidism hypercalcemic in the canarian population.

Methods: Cross-sectional population study to determine VitD levels in healthy subjects. The EPIRCAN study screen was used, a population study carried out between 2004 and 2005 to determine the prevalence of rheumatic diseases in the Canary Islands. In 949 serums, the levels of VitD, phosphorus and calcium were determined, as well as Parathyroid hormone (PTH), only in which calcium levels were >10,4 mg/dl. Data were analysed according to demographic characteristics, comorbidities and medication. For the statistical analysis the SPSS was used.

Results: The sociodemographic characteristics (age, sex and rural/urban population) of the 949 samples were representative of the Canarian population in the period studied according to data of the ISTAC (Canary Institute of Statistics) with a level of accuracy of 0.7 ng/ml for the vitD and a confidence level of 95%. Healthy (n=876, 92.3%) and sick subjects (n= 73, 7.7%) (renal failure, dialysis, Crohn's, ulcerative colitis, osteoporosis, calcium supplements, vitD, bisphosphonates or calcitonin). The median and Interquartile range of vitD levels in the entire population studied was 26.3 (20.9-32.9) ng/ml. The VitD levels distribution of healthy population was: 66% were below 30 ng/ml,23% were below 20 mg/ml and 4% were below 12,5 ng/ml. According to the age groups, sex and location: women versus men have 2.8 ng/ml less VitD (CI95%: 1.487;4.177). As the age increases the VitD values decrease; those aged 20-45 with respect to ≥65 years have 5.5 ng/ml more (CI95%: 3.574;7.592), those 45-65 years old have 2.397 ng/ml more (CI95% 0.255;4.539) with respect to ≥65 years, being statistically significant. There were no significant differences between the rural and urban population. The prevalence of hyperparathyroidism hypercalcemic was 0.2%.

Conclusion: In the healthy population, baseline levels of VitD are higher in men than in women and tend to decrease with age. Due to the distribution of VitD levels in a healthy population, in an area of high sun exposure, seems to be more reasonable to establish the optimal VitD levels in the general population at 20 ng/ml instead of the established 30 mg/ml.

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FRI0578 DEVELOPMENT OF A MOBILE APP AND WIRELESS SENSORS SYSTEM TO ASSESS SPINAL MOBILITY IN AXIAL SPONDYLOARTHRITIS: PRELIMINARY RESULTS.

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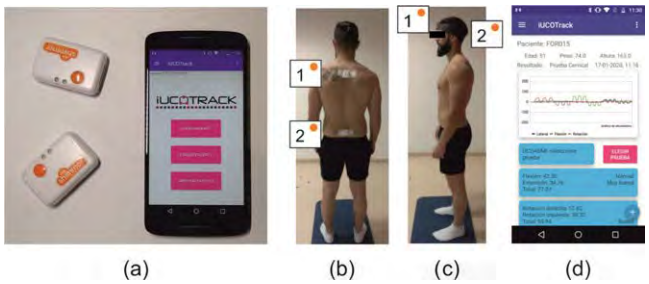
Background: Spinal mobility is an important assessment outcome in axial spondyloarthritis (axSpA). Until now, conventional metrology (Schober test, lateral flexion, BASMI, …) has been used to assess spinal mobility, however, new technologies have been developed that provide better accuracy, reliability and responsiveness. Motion capture has been validated and Inertial Measurement Unit (IMU) sensors, appears to be a promising alternative. To use this IMU sensors in axSpA patients, wireless systems must be developed and validated allowing to doctors and patients to use them in hospitals and at home.

Objectives: To develop an easy to use mobile app and IMU sensors system for analyse mobility for axSpA patients.

Methods: A mobile app has been developed (iUCOTrack) that communicates with two IMU sensors (Shimmer 3©, Fig-a). These sensors are attached in different locations: at forehead and T12 for cervical mobility (Fig-c) and T12 and Sacrum for thoracolumbar mobility (Fig-b). The app provides mobility results for the different tests (Fig-d) and store results in the cloud. Validation tests of these sensors, using Matlab©, were done previously [1]. Our study test the validity of this app against a motion capture system, the UCOTrack®, and its metrology index, the UCOASMI [2], and conventional metrology as reference standards. Patiens with axSpA were recruited consecutively from the COSPAR cohort. Conventional metrology, PRO questionnaires and mobility (Cervical and thoracolumbar - flexion, lateral bending, rotation) using the iUCOTrack app and the UCOTrack were registered. Intraclasss Correlation Coefficients (ICC 3,1) between systems and correlations (spearman) with other axSpA outcome measures were performed for testing validity.

Results: 15 axSpA patients (47% female, age 52±12 years, disease duration 21±16 years) were included. Table shows ROM (SD) in degrees obtained for cervical and thoracolumbar spine measured by motion capture (UCOTrack) and the app (iUCOTrack). In the last column appears the UCOASMI (SD) calculated using angles obtained by each system. All ICC were good (ICC>0.8), and correlations were significant (p<0.05, r>0.8) specially the UCOASMI. Cervical rotation using a goniometer was 106.2±36°, with a significant correlation with both systems (p<0.05; r>0.8). Schober correlation with lumbar flexion was poor (NS;r>0.5) but a good correlation appeared with lateral flexion (p<0.01;r>0.9). Mean BASMI was 4.0± 1.8 with an excellent correlation with UCOASMI measured by Mocap (p<0.01;r=0.93) and by IMU (p<0.001;r=0.98).

	Cervical			Thoracolumbar			
	Flex	Rot	Lat	Flex	Rot	Lat	UCOASMI
UCOTrack	79.5(24.7)	109.8(29.6)	62.5(25.1)	100.7(21.6)	61.8(25.3)	54.7(22.9)	6.07(1.66)
iUCOTrack	83.0(33.6)	112.6(44.3)	73.9(29.7)	114.4(28.1)	51.4(16.1)	59.4(15.4)	6.15(1.65)
ICC	0.864	0.903	0.812	0.936	0.798	0.901	0.970
Corr	0.89*	0.96**	0.82*	0.97**	0.88*	0.97***	0.97**



(a) (b) (c) (d)

Conclusion: New metrology tools are needed to improve features of convencional metrology. Motion Capture has proved to be valid but has feasibility problems. IMU sensor based systems provide similar results to motion capture but it can be faster and cheaper. A system based on mobile app connected to wireless IMU sensors could be a solution to improve metrology in axSpA. Further studies and developments are needed to introduce these technologies in research and clinical daily practice.

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Disclosure of Interests: Juan L. Garrido-Castro: None declared, Francisco Torres Vidal: None declared, MLourdes Ladehesa Pineda: None declared, María del Carmen Castro Villegas: None declared, Inmaculada Concepcion Aranda-Valera: None declared, Rafaela Ortega Castro: None declared, Cristina Gonzalez-Navas: None declared, Eduardo Collantes Estevez Grant/research support from: ROCHE and Pfizer, Speakers bureau: ROCHE, Lilly, Bristol and Celgene
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FRI0579

RHEUMATOID FACTOR IS ASSOCIATED WITH FALSELY ELEVATED RESULTS IN COMMERCIAL IMMUNOASSAYS: DATA FROM AN EARLY ARTHRITIS COHORT

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Background: Immunoassays are used to measure a range of analytes in clinical laboratories. Rheumatoid factor (RF) and other patient antibodies, such as heterophilic antibodies, can bind animal antibodies used in immunoassays and cause erroneous results, which may lead to misdiagnosis and incorrect treatment of patients.[1]
Objectives: To assess RF reactivity to animal antibodies and to test if selected commercial immunoassays are vulnerable to interference from RF-positive sera.
Methods: Samples from 124 patients with RF-positive rheumatoid arthritis (RA) included in the Norwegian Very Early Arthritis Clinic (NOR-VEAC)-cohort[2] were included in the study. Samples from patients with seronegative RA (n=51) and psoriatic arthritis (n=15) from the same cohort were included as controls. Reactivity to mouse IgG1, mouse IgG2a, rabbit IgG, bovine IgG, sheep/goat IgG and human IgG was analysed using in-house interference assays detecting antibodies able to cross-link the animal or human antibodies. RF-positive sera with strong reactivity to mouse IgG1 were selected for testing in three commercial immunoassays previously shown to be susceptible to interference from heterophilic antibodies; Abbott Architect Total β-hCG assay, Bio-Rad 27-plex cytokine assays and Roche Elecsys Soluble Transferrin Receptor (sTfR).[3] Samples were tested before and after addition of blocking aggregated murine IgG1 (interference protection). Interference was defined as a discrepancy between the unblocked and blocked samples likely to influence clinical interpretation of the results and exceeding the reported assay imprecision with a considerable margin.
Results: We found considerably stronger reactivity toward animal antibodies, particularly mouse IgG1 and rabbit IgG, in sera from RF-positive RA-patients compared to the control group (Fig. 1a-b). In the Abbott β-hCG assay, interference was shown in 6 out of the 30 tested sera (Fig. 2a). In the 27-plex cytokine assays, interference was demonstrated in 7 out of 10 tested sera (for 3-14 analytes). Furthermore, 17 out of the 27 cytokine assays were found to be susceptible to interference (Fig. 2b). Interference was shown in 2 out of 33 samples in the sTfR assay. In unblocked samples, sTfR values were 8.1 and 8.2 mg/L, vs. 4.2 mg/L and 6.0 mg/L in blocked samples, respectively. Additionally, 3 sera had >25% relative difference, but the results were within the reference range.

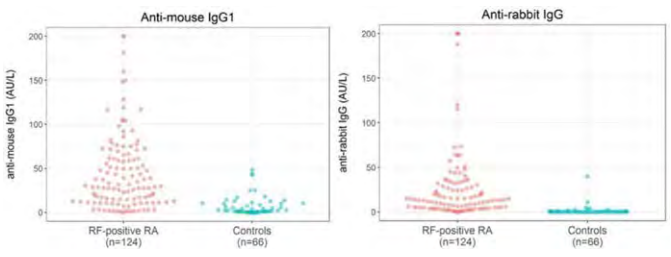


Figure. 1 (a-b)

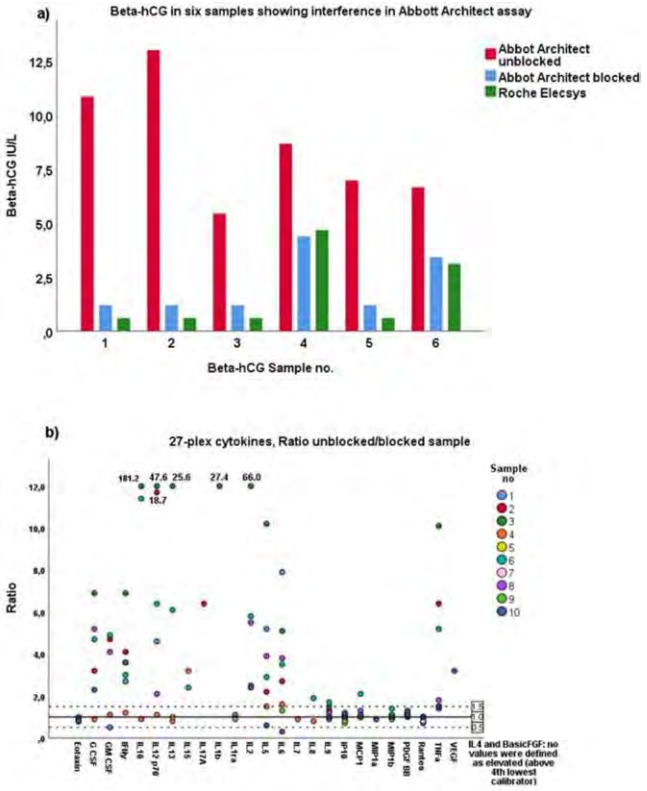


Figure. 2 (a-b)

Conclusion: Reactivity to animal antibodies used in immunoassays is common in sera from RF-positive RA patients and are associated with falsely elevated results in commercial immunoassays. In our cohort, interference was demonstrated in a considerable proportion of samples in the Abbott hCG and 27-plex cytokine assays. Physicians as well as researchers, laboratories and assay manufacturers must be alert to the risk of falsely elevated test results in RF positive RA patients, particularly when results are unexpected or discordant with clinical findings. False test results may interfere with research results, and also lead to potentially harmful diagnostic and therapeutic interventions if unrecognised.
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FRI0580

DISCORDANCE BETWEEN OBJECTIVE ELBOW ASSESSMENT AND PATIENTS REPORTED OUTCOMES (PROS) AFTER TOTAL ELBOW ARTHROPLASTY IN PATIENTS WITH RHEUMATOID ARTHRITIS.

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Background: Patient-reported outcomes (PROs) have become widespread in daily clinical evaluation in patients with rheumatoid arthritis (RA). However, there are few reports for the relationship or discordance between the subjective assessment by the physician and the objective assessment by the patient with RA in surgical treatment.

Objectives: We examined the relationship or discordance about the PROs in patients with RA who underwent total elbow arthroplasty (TEA).

Methods: We retrospectively identified 53 elbows of 48 patients with RA who underwent TEA at Okayama University Hospital, collected from January 2012 to December 2016.

We collected clinical data for the grip strength, range of motion, the Mayo Elbow Performance Scale (MEPS) as objective assessments, and the Patient-Related Elbow Evaluation (PREE), Disability of the Arm, Shoulder, and Hand (DASH) Japanese version and Hand20 as subjective assessments.

For statistical analysis, we performed t-tests for pre- and post-operative physical findings and subjective evaluations, and Spearman rank correlation to examine the relationship between objective and subjective assessments.

Results: The mean age of the patients at the time of arthroplasty was 63 years, the average disease duration was 23 years, and the average postoperative observation period was 32 months. The average DAS28-CRP was 3.01, and biological uses were 18 cases.

The range of motion of the elbow joint and the grip strength was significantly improved postoperatively. All outcome assessments improved significantly except for HAQ (see table1).

There was significantly correlated PREE with DASH, Hand20, and MEPS preoperatively. Postoperative PREE showed a significant and robust correlation in postoperative DASH, Hand20, whereas not associated with postoperative MEPS (see table2).

To investigate the discordance between PREE and MEPS after TEA, we focused on changes in each item of PREE. Pain- and reach-related items improved postoperatively. But, it was difficult to improve in items affected by hand and finger functions, such as "tie shoelaces."

To explore the effects of finger and hand functions on postoperative assessments, we performed multiple regression analyses. Both preoperative grip strength (unstandardized coefficient [B] =-0.07; 95%CI -0.148 to -0.006, t value=-2.18, P=0.03) and preoperative Hand20 (B = 0.27, 95%CI 0.029 - 0.518, t=2.25, p=0.02) were significant predictors of postoperative PREE.

Conclusion: Surprisingly, the PROs of patients and the surgeon's evaluations correlated well before surgery but resulted in discordance after TEA. We improved elbow functions by TEA, but since rheumatoid arthritis was a polyarticular disorder, improvement of a single joint function did not improve utterly subjective assessment in patients with RA. We found that the upper limb functions after TEA were significantly affected by preoperative finger and hand function. A rheumatologist should consider the dysfunctions of finger and hand when planning for elbow surgery in patients with RA.

Table 1. Pre- and postoperative range of motion of elbow and forearm, grip strength, and measurement

Characteristic	Preoperative	Postoperative	P value
Elbow flexion, degree	116 ± 19	134 ± 9	< 0.001
- extension	-34 ± 21	-25 ± 16	0.005
- total arc	82 ± 32	109 ± 19	< 0.001
Grip power, mmHg	106 ± 66	130 ± 74	0.007
DASH	50.5 ± 20.5	35.8 ± 25.4	< 0.001
Hand20	60.4 ± 19.1	38.9 ± 29.6	< 0.001
PREE	55.6 ± 18.8	18.5 ± 17.1	< 0.001
- pain	29.7 ± 11.3	6.5 ± 7.9	< 0.001
- function	25.9 ± 11.5	12.0 ± 11.9	< 0.001
- specific function	56.9 ± 25.5	25.4 ± 25.3	< 0.001
- usual function	20.8 ± 11.3	10.5 ± 11.3	< 0.001
HAQ-DI	1.06 ± 0.70	1.07 ± 0.80	0.607
MEPS	51.3 ± 16.6	97.9 ± 3.6	< 0.001

Table 2. Spearman's correlation coefficients for pre- and postoperative PREE score*

Questionnaire	Preoperative Correlation estimate	P value	Postoperative Correlation estimate	P value
DASH	0.56	< 0.0001	0.84	< 0.0001
Hand20	0.58	< 0.0001	0.84	< 0.0001
MEPS	- 0.39	< 0.01	-0.27	N.S.

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FRI0581

IN ELDERLY PATIENTS, CAPS THAT RECORD MEDICATION BOTTLE OPENINGS ARE UNRELIABLE AND THUS NOT THE GOLD STANDARD FOR ADHERENCE

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Background: Adherence is a serious problem in treatment of inflammatory diseases. To measure adherence, caps that record medication bottle openings may be superior to capsule counts (1). In the ongoing two-year GLORIA trial on the addition of low-dose (5 mg) prednisolone or placebo to standard of care in elderly patients (65+ years) with rheumatoid arthritis, adherence was measured in both ways during the whole trial.

Objectives: To describe adherence patterns, and to compare adherence as assessed with adherence caps and with capsule counts in the GLORIA trial.

Methods: The recorded adherence patterns of patients (blinded for treatment group) were classified according to descriptive categories. Overall adherence according to number of bottle openings was compared with adherence according to the capsule count. Good adherence was defined as 80%: i.e. for caps 80% of days one opening recorded, and for counts less than 20% of prescribed tablets returned at the subsequent visit. Each patient has a maximum of 8 periods of 90 days.

Results: Trial inclusion has closed in 2018 at 452 patients; the current dataset contains adherence data of 385 patients. Mean number of recorded 90-day periods per patient was 4 (range 1-8). Based on capsule counts over all periods, 90% of the patients met the 80% threshold of adherence; based on cap data only 31% met this criterion.

The four adherence patterns are shown in a calendar matrix, with yellow for zero, green for one and blue for ≥two openings on a day (Figure 1). Bottles were supposed to be opened once a day.



Figure 1. Examples of adherence patterns.
Yellow = no opening, green=1 opening, blue=≥2 openings

Patients were categorized according to the opening pattern seen in at least 50% of assessed periods:

32% non-use	(<20% of the days an opening);
26% stable use	(≥80% of the days 1 opening);
40% irregular use	(different adherence patterns, in or between periods);
2% weekly use	(1 opening per week).

Conclusion: In our trial of elderly rheumatoid arthritis patients, patients appeared to be mostly adherent according to conventional capsule counts. Results from adherence caps were highly discrepant with the capsule counts, with patterns suggesting patients did not use the bottle for daily dispensing, despite specific advice to do so.

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FRI0582 GM-CSF PRODUCED BY CD4+ T CELLS AS A MARKER OF CLINICAL REMISSION IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH TNF INHIBITORS

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Background: According to the EULAR recommendations, the therapeutic target in patients with RA should be remission (REM). However, no more than 50% of the patients treated with TNF inhibitors (TNFi) attains this outcome. Previous investigations suggested the peripheral blood mononuclear cells (PBMC) as markers associated with the TNFi treatment success[1,2]. Granulocyte-monocyte colony-stimulating factor (GM-CSF) plays a relevant role in the pathogenesis of rheumatoid arthritis (RA) because it promotes the macrophage differentiation, survival and activation[3].

Objectives: To analyse the intracellular cytokine production by PBMC and its association with REM attainment after 6 months (m) of TNFi treatment in patients with RA.

Methods: This was a prospective bi-center pilot study including 36 patients with RA. PBMC were isolated from patients at baseline and after 6m of treatment with TNFi and cryopreserved until studied. Intracellular cytokine production by PBMC was stimulated in the presence of 2µg/mL brefeldin as follow: monocytes were stimulated with 20ng/mL LPS during 4h; and simultaneously lymphocytes were stimulated with 50ng/mL phorbol 12-myristate 13-acetate (PMA) and 750ng/mL ionomycin during 4h at 37ºC. To identify IL-10-producing B cells, PBMC were pre-incubated with 3µg/mL of CpG oligonucleotide during 20h at 37°C prior to stimulation in presence of 2µmol/L monensin. Intracellular cytokine production (TNFα, IL6, GM-CSF, IL10) by the different cell subsets (monocytes, $CD4^+$ and $CD8^+$ T cells, naïve and memory B cells) was analysed by flow-cytometry. Clinical activity at baseline and after 6m was assessed by DAS28. REM was defined as DAS28≤2.6 at 6m. The association between REM and the change in cytokine production (Δ, 6m-0m) by each PBMC subset was analysed through univariable and multivariable logistic regression models.

Results: Seventy-eight percent of the patients were female. After 6m of TNFi treatment, 47% patients attained REM. Univariable analyses was performed to investigate the association between REM and the baseline variables. Male sex (OR: 12.6; 95% CI: 1.35-117.57; p=0.03) and having lower baseline DAS28 (OR: 0.4; 95% CI: 0.19-0.85; p=0.02) were independently associated with attaining REM after 6m of TNFi. In the multivariable analysis, only being male (OR: 19.7; 95% CI: 1.4-273.9; p=0.03) remained independently associated with REM after 6m of treatment. Therefore, further analyses were adjusted by sex. Decreased production of GM-CSF by $CD4^+$ T cells percentage was found after 6m of TNFi treatment in REM patients (0m: 6.07%; 6m: 3.87%; p=0.007) while no-REM patients did not show differences with the baseline (0m: 3.70%; 6m: 3.75%; p=0.9). The decrease was significantly associated with attaining REM (OR: 0.56; 95% CI: 0.33-0.95; p: 0.03). No significant association was found between any other analysed intracellular cytokine produced by the different PBMC subsets and REM.

Conclusion: GM-CSF intracellular production by $CD4^+$ T cells was significantly decreased by TNFi treatment only in patients who attained REM. Therefore, our results suggest that GM-CSF production by $CD4^+$ T cells may be a useful marker of REM to TNFi in RA.

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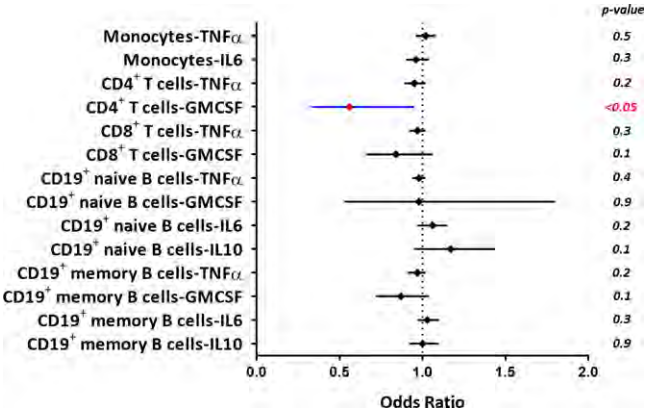


Figure. 1: Association between the change in intracellular cytokine production (Δ, 6m-0m) by each PBMC subset and REM. Adjusted logistic regression analyses were performed for each cytokine.

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FRI0583 VALIDATION OF THE MODIFIED FATIGUE IMPACT SCALE IN DANISH PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Patients with systemic lupus erythematosus (SLE) experience significant fatigue, a debilitating symptom associated with reduced quality of life. A simple, reliable multidimensional method for assessing fatigue has not yet been validated for Danish patients with SLE.

Objectives: The primary objective was to study the internal consistency, test-retest reliability, and construct validity (convergent and discriminant validity) of the multidimensional Modified Fatigue Impact Scale (MFIS) in patients with SLE. The secondary objective was to investigate the contribution of disease activity and organ damage to fatigue.

Methods: Data from the "Bio and Genome Bank Study in Centre for SLE and Vasculitis" obtained through routine visits were used. Fatigue was assessed using the MFIS and Short Form 36 (SF36). Internal consistency of the MFIS was assessed with Cronbach's alpha (α). Test-retest reliability was evaluated using the intraclass correlation coefficient (ICC). Construct validity was studied using Spearman's rank correlation coefficient (r_s) and Principal Component Analysis (PCA) between MFIS and SF36 vitality (VT-SF36) and mental health (MH-SF36) subscales. Association between MFIS and disease activity and organ damage was estimated with Spearman's rank correlation coefficient.

Results: The study included 30 patients with SLE. Internal consistency of the MFIS was excellent with Cronbach's α = 0.97 for the complete scale. Excellent test-retest reliability was found with ICC = 0.95 (95% confidence interval: 0.88-0.98, p < 0.05). Construct validity was confirmed by Spearman's correlation (VT-SF36: r_s = −0.73, p < 0.001 (Fig. 1). MH-SF36: r_s = −0.74, p < 0.001 (Fig. 2)) and PCA with explained variance from the first two principal components (PC) (VT-SF36: PC1 = 60.2%, PC2 = 8.5%. MH-SF36: PC1 = 58.5%, PC2 = 7.4%). No significant correlation was found between the MFIS and SLEDAI (r_s = 0.04, p = 0.84) or SLICC Damage Index (r_s = 0.32, p = 0.08).

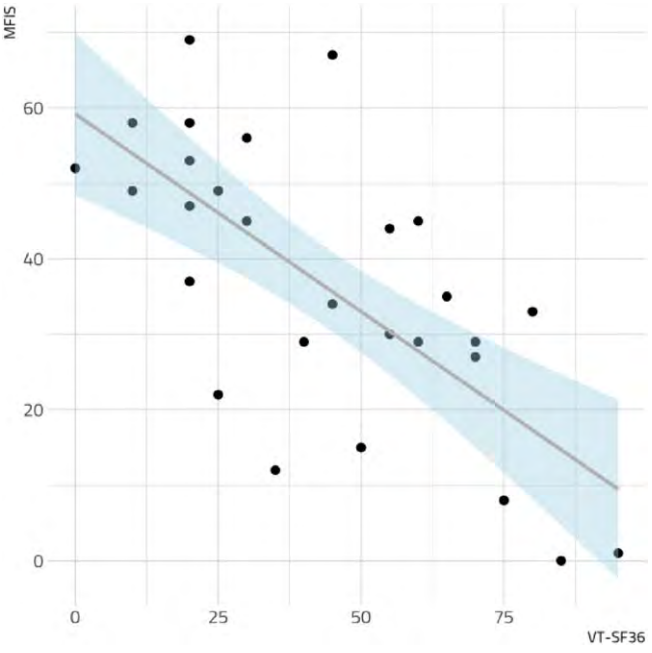


Figure 1. Scatter plot of the Modified Fatigue Impact Scale (MFIS) and the Short Form 36 vitality (VT-SF36) subscale.

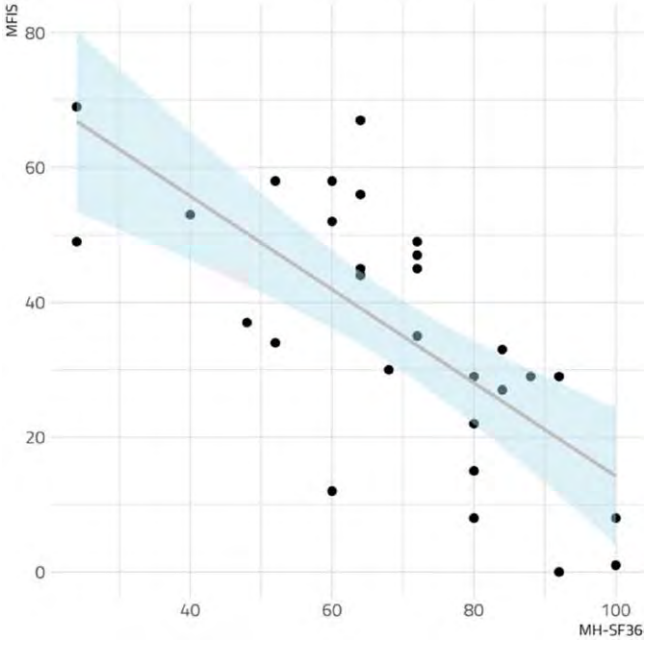


Figure 2. Scatter plot of the Modified Fatigue Impact Scale (MFIS) and the Short Form 36 mental health (MH-SF36) subscale.

Conclusion: The present study found the multidimensional assessment of fatigue with MFIS to be a reliable and valid instrument in SLE. The MFIS might provide more detailed information about fatigue in future studies. In agreement with some previous studies we found no association between fatigue and SLEDAI or SLICC which raises questions about the cause of this symptom. Further and larger studies are needed to investigate if any association between fatigue and disease components exist.

Disclosure of Interests: None declared
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FRI0584 SCREENING AND IDENTIFICATION OF BIOMARKERS IN MYOSITIS

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Background: Myositis, including dermatomyositis and polymyositis, is autoimmune disorders that is characterized by muscle degeneration in the proximal extremities, with the complications of weakness of muscles, interstitial lung disease and vascular lesions, even leading to death in an acute progressive process[1,2]. However, the molecular mechanisms of myositis are rarely understood.
Objectives: Identify the candidate genes in myositis.
Methods: Microarray datasets GSE128470, GSE48280 and GSE39454 were extracted from the Gene Expression Omnibus (GEO) database. The differentially expressed genes (DEGs) and function enrichment analyses were conducted. The protein-protein interaction network and the analyses of hub genes were performed with STRING and Cytoscape.
Results: There were 98 DEGs, of which the function and pathways enrichment analyses showed defense response, immune response, response to virus, inflammatory response, response to wounding, cell adhesion, cell proliferation, cell death and macromolecule metabolic process. 20 hub genes were identified, of which 7 including IRF9 TRIM22 MX2 IFITM1 IFI6 IFI44 IFI44L had not been reported in the literature, related to the response to virus, immune response, transcription from RNA polymerase II promoter, cell apoptosis, cell death. The verification analysis about the 7 genes in GSE128314 showed significant differences in myositis.
Conclusion: In conclusion, DEGs and hub genes identified in our study showed the potential molecular mechanisms in myositis, providing the helpful targets for diagnosis and clinical strategy of myositis.

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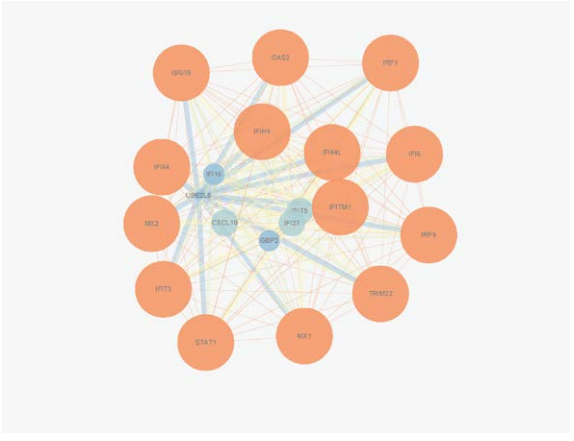


Figure 1. The protein-protein interaction network of 20 hub genes

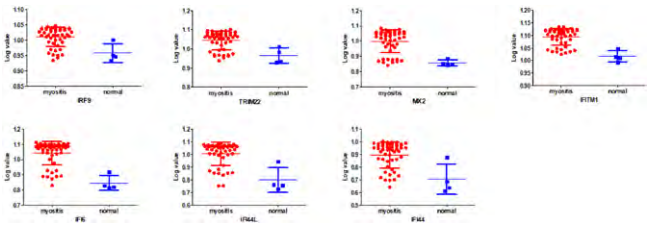


Figure 2. 7 genes in GSE128314 showed significant differences in myositis

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Disclosure of Interests: None declared
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FRI0585

HIGH-THROUGHPUT METHODOLOGY FOR EMR-BASED IDENTIFICATION OF CLINICAL SUB-PHENOTYPES IN COMPLEX PATIENT POPULATIONS

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Background: Heterogeneity in disease populations complicates discovery of risk factors. To identify risk factors for subpopulations of diseases, we need analytical methods that can deal with unidentified disease subgroups.
Objectives: Inspired by successful approaches from the Big Data field, we developed a high-throughput approach to identify subpopulations within patients with heterogeneous, complex diseases using the wealth of information available in Electronic Medical Records (EMRs).
Methods: We extracted longitudinal healthcare-interaction records coded by 1,853 PheCodes[1] of the 64,819 patients from the Boston's Partners-Biobank. Through dimensionality reduction using t-SNE[2] we created a 2D embedding of 32,424 of these patients (set A). We then identified distinct clusters post-t-SNE using DBscan[3] and visualized the relative importance of individual PheCodes within them using specialized spectrographs. We replicated this procedure in the remaining 32,395 records (set B).
Results: Summary statistics of both sets were comparable (Table 1).
We found 284 clusters in set A and 295 in set B, of which 63.4% from set A could be mapped to a cluster in set B with a median (range) correlation of 0.24 (0.03 – 0.58).

Table 1. Summary statistics of the total Partners Biobank dataset and the 2 partitions.

	Set-A	set-B	Total
Entries	12,200,311	12,177,131	24,377,442
Patients	32,424	32,395	64,819
Patientyears	369,546.33	368,597.92	738,144.2
unique ICD codes	25,056	24,953	26,305
unique Phecodes	1,851	1,853	1,853

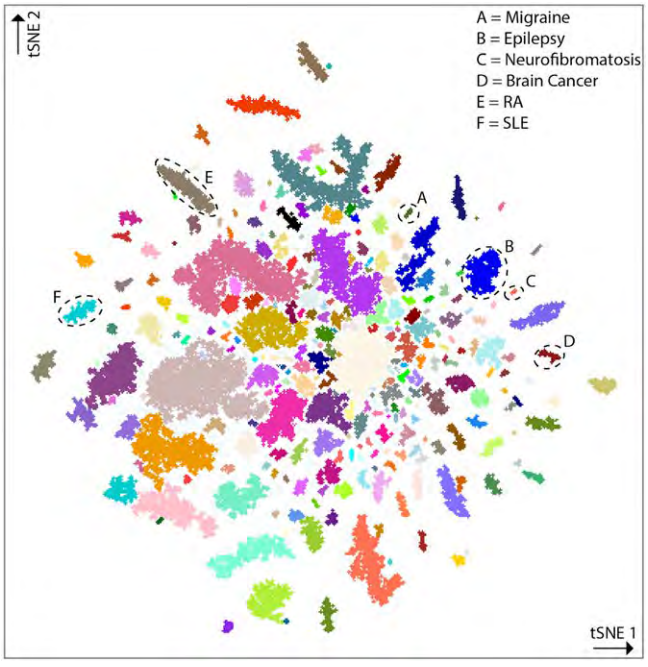


Figure 1. Two dimensional representation of Set A generated using dimensionality reduction (tSNE) and clustering (DBScan).

Clusters represented similar yet distinct clinical phenotypes; e.g. patients diagnosed with "other headache syndrome" were separated into four distinct clusters characterized by migraines, neurofibromatosis, epilepsy or brain cancer, all resulting in patients presenting with headaches (Fig. 1 & 2). Though EMR databases tend to be noisy, our method was also able to differentiate misclassification from true cases; SLE patients with RA codes clustered separately from true RA cases.

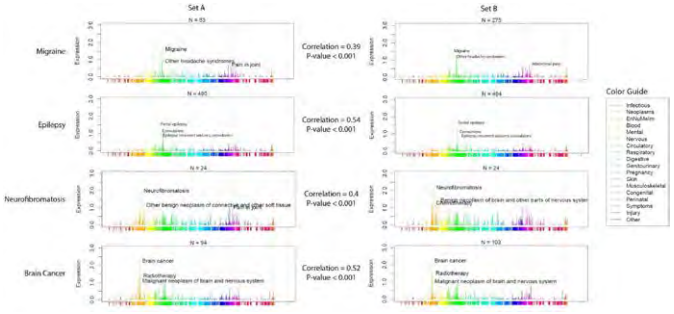


Figure 2. Phenotype Spectrographs (PheSpecs) of four clusters characterized by "Other headache syndromes", driven by codes relating to migraine, epilepsy, neurofibromatosis or brain cancer.

Conclusion: We have shown that EMR data can be used to identify and visualize latent structure in patient categorizations, using an approach based on dimension reduction and clustering machine learning techniques. Our method can identify misclassified patients as well as separate patients with similar problems into subsets with different associated medical problems. Our approach adds a new and powerful tool to aid in the discovery of novel risk factors in complex, heterogeneous diseases.

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Disclosure of Interests: Marc Maurits: None declared, Thomas Huizinga Grant/research support from: Ablynx, Bristol-Myers Squibb, Roche, Sanofi, Consultant of: Ablynx, Bristol-Myers Squibb, Roche, Sanofi, Marcel Reinders: None declared, Soumya Raychaudhuri: None declared, Elizabeth Karlson: None declared, Erik van den Akker: None declared, Rachel Knevel: None declared
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FRI0586

HOW TO GET FROM THE MULTIDIMENSIONAL HEALTH ASSESSMENT QUESTIONNAIRE TO STANFORD HEALTH ASSESSMENT QUESTIONNAIRE DISABILITY INDEX SCORES IN PATIENTS WITH RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS AND AXIAL SPONDYLOARTHRITIS: DEVELOPMENT AND VALIDATION OF A CONVERSION ALGORITHM

E. Svensson[1], K. Løngaard[1], L. Midtbøll Ørnbjerg[2], R. Meincke[2], J. K. Pedersen[3], L. Dreyer[4], N. Steen Krogh[5], D. V. Jensen[2], M. L. Hetland[2]. *[1]RKKP - the Danish Clinical Quality Program, Aarhus, Denmark*; *[2]DANBIO, Copenhagen Center for Arthritis Research, Rigshospitalet, Copenhagen, Denmark*; *[3]Svendborg Hospital, Svendborg, Denmark*; *[4]Aalborg University Hospital, Aalborg, Denmark*; *[5]Zitelab Aps, Frederiksberg, Denmark*

Background: In the DANBIO quality registry in Denmark, patients with rheumatoid arthritis (RA) psoriatic arthritis (PsA) and axial spondyloarthritis (axSpA) have reported Patient Reported Outcomes (PROs) including the Stanford Health Assessment Questionnaire Disability Index (HAQ-DI) for nearly twenty years as part of routine care. Patients' feedback have stressed a need for a shorter registration of disability (1). While the shorter Multidimensional Health Assessment Questionnaire (MDHAQ) is preferred by patients, the original HAQ-DI is the preferred tool in observational studies. Thus, a conversion algorithm between the MDHAQ and HAQ-DI scores is warranted.
Objectives: To develop and validate a simple conversion algorithm between MDHAQ and HAQ-DI scores in RA, PsA and axSpA patients.
Methods: Patients registered in DANBIO with a diagnosis of RA, PsA or axSpA who had completed both HAQ-DI and MDHAQ simultaneously at a visit +/- 30 days from start of conventional synthetic (cs)DMARD or biological (b)DMARD were eligible for the analysis, and randomly divided into development and validation cohorts stratified by diagnosis. The conversion algorithm was developed in the RA development cohort using linear regression with HAQ-DI as the dependent variable and MDHAQ as the independent variable. The predicted HAQ (pHAQ) scores were then

calculated by applying the conversion algorithm to the MDHAQ scores in the RA, PsA and axSpA validation cohorts. The pHAQ was validated against the HAQ-DI in the validation cohorts regarding criterion, correlational and construct validity.

Results: We included 8983/4410/1760 patients with RA/PsA/axSpA, respectively. The conversion algorithm pHAQ=0.15+MDHAQ*1.08 had the best fit (R^2=0.83) in the RA development cohort.

Criterion validity: The correlation coefficients between HAQ-DI/pHAQ and patient global score at baseline were 0.66/0.65. In groups of patients with high and low disability (defined as patient global score ≥50), standardized mean difference was -1.4 for HAQ-DI, and -1.4 for pHAQ.

Correlational validity: Correlation coefficients between HAQ-DI/pHAQ and ΔHAQ-DI/ΔpHAQ between baseline and first follow-up visit were r=0.91 and r=0.87, respectively. Correlation coefficients between HAQ-DI/pHAQ and pain score, DAS28CRP and physician global score were 0.63/0.64, 0.55/0.55 and 0.34/0.34, respectively. A Bland-Altman plot showed good agreement of HAQ-DI and pHAQ across all functional states.

Construct validity: HAQ-DI/pHAQ at the first follow-up visit after baseline was comparable between Patient Acceptable Symptom State groups (PASS=No: mean 1.17 vs 1.18/PASS=Yes: 0.55 vs 0.60). Similar results were seen for the external anchor (Figure 1).

In PsA and axSpA validation cohorts, similar results were found.

Conclusion: A conversion algorithm from MDHAQ to HAQ-DI was developed in ≈ 4500 RA patients. In separate large validation cohorts of RA, PsA and axSpA patients, the predicted HAQ calculated from the MDHAQ scores showed good criterion, correlational and construct validity comparable to the original HAQ-DI. The results suggest that for research purposes the MDHAQ can be converted to HAQ-DI if a full HAQ-DI has not been performed.

References:

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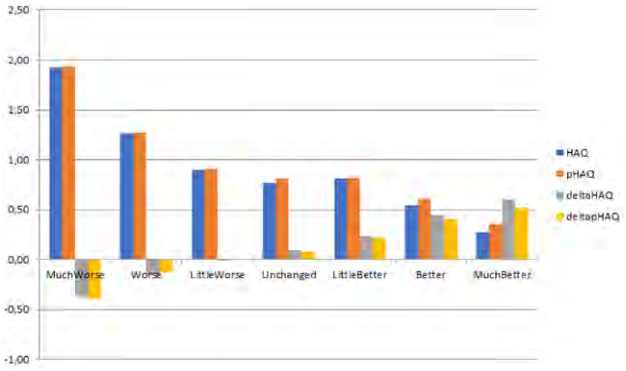


Figure 1

Construct validity: Mean of HAQ-DI/pHAQ and ΔHAQ-DI/ΔpHAQ across external anchor responses

Acknowledgments: The authors thank all Danish patients and Departments of Rheumatology, who conscientiously report to the DANBIO registry.

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FRI0587

A NEW APPROACH TO EARLY DETECTION OF ADVERSE EVENTS OF HIGH-RISK MEDICATIONS USING A STRUCTURED, STANDARD, PROTOCOL DRIVEN WEEKLY REMOTE ELECTRONIC MDHAQ 60-SYMPTOM CHECKLIST

T. Pincus[1], N. Steen Krogh[2]. [1]*Rush University, Rheumatology, Chicago, United States of America*; [2]*ZiteLab, Copenhagen, Denmark*

Background: A multidimensional health assessment questionnaire (MDHAQ) includes RAPID3, which distinguishes active from control treatments in rheumatoid arthritis clinical trials, and documents change comparably to disease-specific indices in all diseases studied. The MDHAQ also includes a standard, structured 60-symptom checklist, to recognize comorbidities, provide a review of systems, and serve on a fibromyalgia assessment screening tool (FAST3) as a clue to identify patients with fibromyalgia. A new MDHAQ application is to recognize adverse events to high-risk medications on a standard, structured, protocol-driven MDHAQ 60-symptom checklist. A structured list, rather than a "subjective" narrative medical history, is needed as many adverse events are common symptoms, e.g., headache, fatigue; prior negative data facilitates recognition of a new symptom as a possible adverse event. Similar strategies have been reported in oncology, pulmonology and other specialties, but not in rheumatology.

Objectives: To use a remote electronic MDHAQ, completed weekly at home, to recognize RAPID3 clinical status changes and adverse events on the 60-symptom checklist, for early detection of medication adverse events.

Methods: All patients with all diagnoses complete an MDHAQ at all visits in routine care at one rheumatology site. An electronic flowsheet (Table) is used to monitor 0-30 RAPID3, its components, and report of specific symptoms on the 60-symptom checklist, which appears required to document earlier absence of a common symptom and signal that a common symptom may be an adverse event. Results are depicted for an individual patient with pulmonary fibrosis, seen because of a positive rheumatoid factor.

Results: A flowsheet of a pulmonary fibrosis patient over 2018 indicates initial RAPID3 of 14/30 and 10 symptoms at first visit of 19 Jan (Flowsheet). Treatment with low-dose methotrexate (MTX) and prednisone (PRED) led to substantial improvement over 6 months - RAPID3 3.5 and 6 symptoms on 2 Aug. On 15 Aug, MTX and PRED were discontinued by another physician, who prescribed pirfenidone. The patient telephoned on 24 Sep indicating distress. A home-completed remote MDHAQ indicated RAPID3 of 19.5 and 15 symptoms - 7 not reported on 2 Aug were among 16 listed pirfenidone adverse events. Discontinuation of pirfenidone and resumption of PRED and MTX with weekly remote electronic MDHAQ monitoring documented improvement of RAPID3 to 4.2 and 6 symptoms, including resolution of pirfenidone-specific symptoms, on 24 Dec (Flowsheet).

Conclusion: Weekly remote electronic MHDAQ monitoring after initiation of a high-risk medication to monitor treatment responses and adverse events may provide a cost-effective approach to reduce morbidity and mortality of adverse events, involving about 10 minutes weekly (2 hours over 12 weeks) of patient time. 78-year-old man monitored over 2018–all data from self-report on MDHAQ – pirfenidone highlighted (many entries deleted for space considerations)

Date	19 Jan 2018	25 Jan 2018	2 Aug 2018	15-29 Aug 2018	24 Sep 2018	26 Sep 2018	4 Oct 2018	9 Oct 2018	9 Nov 2018	25 Nov 2018	28 Dec 2018
Site of MDHAQ	Clinic	Clinic	Clinic	None	Home	Home	Home	Home	Home	Home	Home
RAPID3 (0-30)*	14.0	10.2	3.5	?	19.5	10.2	6.7	6.5	4.8	6.0	4.2
Prednisone mg/day	B 40	↓20	↓6	D/C 0	R 10	5	5	5	5	5	5
Methotrexate mg/w			20	D/C 0	0	0	0	0	R 10	10	10
pirfenidone				B3-9/d	9/d	D/C	0	0	3/D	D/C	0
#Symptoms (0-60)*	10	5	6		15	15	13	13	6	8	6
Weight loss	+	+			+	+	+	+			
Feeling sickly	+										
Unusual fatigue	+				+	+	+	+	+	+	
Loss of appetite					+	+	+	+	+	+	
Stuffy nose	+		+		+	+	+	+	+	+	+
Dry mouth	+	+			+	+	+	+	+	+	+
Problems with smell/taste			+		+	+	+	+			
Cough	+	+	+		+	+	+	+	+	+	+
Dyspnea	+	+	+		+	+	+	+	+	+	+
Heartburn/gas	+				+	+	+	+			
Joint pain					+	+	+	+			+
Back pain					+	+					
Sleep problems					+	+					

*Actual total - a few less relevant symptoms deleted for abstract requirements

Disclosure of Interests: Theodore Pincus Shareholder of:

Dr. Pincus holds a copyright and trademark on MDHAQ and RAPID3 for which he receives royalties and license fees from profit-making organizations, all of which are used to support further development of quantitative clinical measures for patients and health professionals., Niels Steen Krogh: None declared

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Table 1. RF diagnostic performance in rheumatic diseases

Group	n	Isotype**	Cut-off UR/ml	Significance	AUC (95% CI)	Sensitivity %	Specificity %	Youden Index	Sensitivity % Manufacturer cut-off +	Specificity % Manufacturer cut-off +
RA	22	IgM	135.3	0.06	0.722(0.604 to 0.839)	60%	85.2	0.45	68.2	55.5
Psa	44	IgA	47.2	0.074	0.698(0.553 to 0.842)	54.5	81.8	0.35	54.5	77.3
ASP	44	IgA	39.5	0.080	0.668(0.511 to 0.826)	54.5	88.6	0.43	54.9	79.5
SS	44	IgM	180.6	0.088	0.535(0.088 to 0.708)	54.5	74.4	0.28	68.2	9.3
Healthy	44	IgM	16.3	0.046	0.896(0.806 to 0.986)	77.3	88.9	0.66	68.2	97.8
SLE	41	IgA	42.6	0.073	0.701(0.557 to 0.845)	54.5	85.3	0.39	54.5	73.5
FBM	35	IgM	68.6	0.071	0.752(0.612 to 0.892)	63.6	82.8	0.46	68.2	51.7
OA	38	IgM	48.0	0.053	0.873(0.770 to 0.976)	63.6	96	0.59	68.2	88
PG	20	IgM	117.0	0.076	0.758(0.609 to 0.908)	59.1	89.5	0.49	68.2	63.2
Total	**332**									

** The isotype with the best AUC for each clinical scenario. + Manufacturer cut-off value: 20UR/ml

FRI0588

DIAGNOSTIC PERFORMANCE OF THE RHEUMATOID FACTOR ISOTYPES IN RHEUMATIC DISEASES

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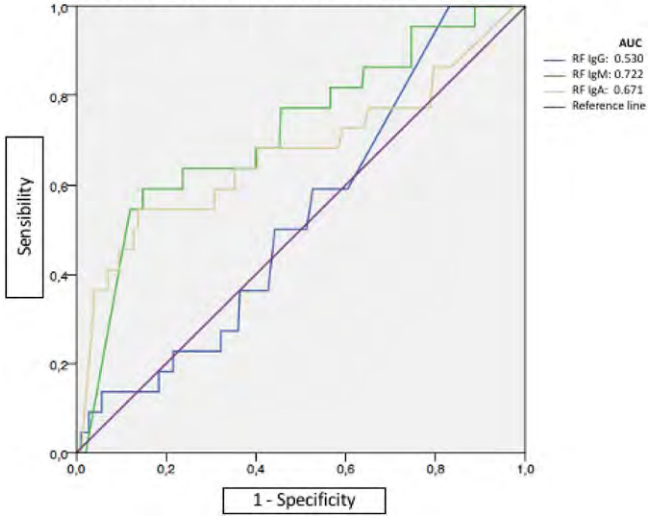
Background: Rheumatoid Factor (RF) is used for the classification of Rheumatoid arthritis (RA) in patients whose main complaint is hand arthritis but is well known that other conditions have positive RF. Differences in analytical performance between assays were found in previous studies, there was a poor numerical agreement, and using the cut-off proposed by the manufacturer, variation in sensitivity and specificity can be seen.[2]

Objectives: To determine the cut-off value for RF with the best diagnostic performance for RA in patients with hand arthritis compared with their main differential diagnoses.

Methods: Descriptive, cross-sectional, diagnostic test study. Sampling size was calculated 2:1, with the area under the ROC curve (AUC): 0.708, power 80% and significance 0.05. Patients with RA, Systemic Lupus Erythematosus (SLE), Osteoarthritis (OA), fibromyalgia (FBM), Polyarticular Gout (PG), Psoriatic Arthritis(Psa), Sjögren Syndrome (SS), Arthralgia suspicious for progression to RA (ASP) and healthy subjects, previously classified with the current criteria by certified rheumatologist were included. EUROINMMUN ® assays for RF isotypes IgA, IgM, IgG were used. ROC curves and Youden index for determining the cut-off with the best sensitivity and specificity for each RF isotype comparing RA with other diseases were used. Statistical analyses were performed with SPSS V.24.

Results: Three hundred and thirty-two serum samples from patients were included, in the other rheumatic diseases different from RA, we found positive RF IgM in 141 (45.5%), 82 (26.5%) IgA and 25 (8.1%) IgG. For each clinical scenario the cut-off with the best sensitivity and specificity was different from the manufacturer proposed, and isotypes with the best diagnostic performance was not the same for each disease, Table 1. We present the ROC curve for RF isotypes in Figure 1.

Figure 1
ROC Curve – Diagnostic performance of the RF in RA



Conclusion: In order to improve the diagnosis of Rheumatoid Arthritis, different cut-off points of RF and isotypes should be used.

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FRI0589

CLINICAL ACCURACY OF ANTI-PHOSPHATIDYLSERINE/PROTHROMBIN AND ANTI-BETA2GLYCOPROTEIN I DOMAIN I FOR PREDICTING CLINICAL MANIFESTATIONS OF ANTIPHOSPHOLIPID SYNDROME

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Background: Antiphospholipid antibody (aPL) specificities are increasing, however the best accuracy for predicting the clinical manifestations of the diseases is still under debate.

Objectives: To evaluate the clinical accuracy of aPL specificities both individually and/or in combination, to identify a panel of tests that may provide the best accuracy for predicting clinical manifestations of antiphospholipid syndrome (APS).

Methods: We chart-reviewed patients that presented at San Giovanni Bosco Hospital in the last 5 years who tested persistently positive for at least one aPL[1]. Inclusion criteria comprehended: a)Primary APS(PAPS); b) Secondary APS(SAPS), c)aPL positive asymptomatic and d)Patients with clinical manifestations of APS and either inconsistent previous LA positivity and/or low-medium titers aPL(suspect APS).

Results: A total of 122 patients were included in the study 38 PAPS, 31 SAPS, 23 aPL positive asymptomatic and 30 low titers APS patients). Table1 resumes the main clinical and laboratory characteristics of the patients included in the study. All patients were tested for five aPL: criteria aPL, anti-phosphatidylserine/prothrombin(aPS/PT) and anti-Beta2Glycoprotein I Domain I(β2GPI-D1).

Among the single aPL positivity, β2GPI-D1 showed the best accuracy in predicting the clinical manifestations of APS (AUC 0.639,CI95% 0.539–0.74,p=0.011). Similarly, when investigating the possible combinations of aPL panels, the positivity for aPS/PT IgG/IgM and/or β2GPI-D1 showed the best accuracy in predicting the clinical manifestations of APS (AUC 0.698, CI95%0.604 –0.793, p<0.001) while triple criteria aPL IgG positivity had the best accuracy for predicting recurrences (AUC 0.720, CI95% 0.569–0.871, p=0.012). Results of the ROC curves are illustrated in Figure 1.

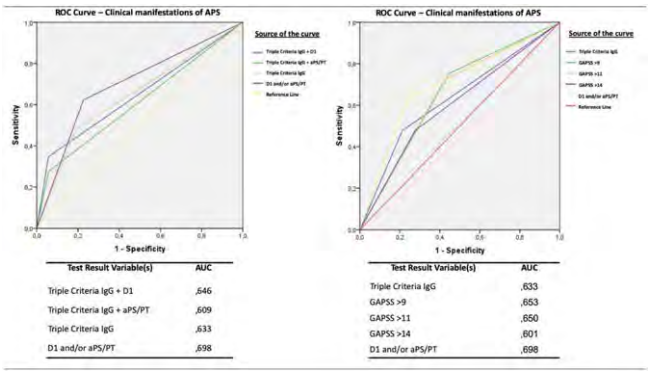


Figure 1.

When considering aPL asymptomatic patients and APS patients (both PAPS and SAPS), the only two aPL combinations that showed a statistically significant association with the APS group were aPS/PT IgG/IgM and/or β2GPI-D1 (OR 4.86,CI95%1.76-13.3,p<0.05) and Global APS Score >11 (OR 2.87, CI95% 1.08-7.6, p<0.05). Interestingly, also adding the patients with suspect APS to the equation, the combination of aPS/PT IgG/IgM and/or β2GPI-D1 remained statistically significant (OR 2.5,CI95%1.02-7.05 p<0.05).

Conclusion: Combining anti-β2GPI D1 and aPS/PT improves the diagnostic power of aPL testing and might improve in risk stratification in patients with aPL positivity.

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Table 1.

	PAPS (n=38)	SAPS (n=31)	aPL+ (n=23)	Low titers (n=30)
Demographics				
Age at study inclusion; years (±SD)	50,2 (±13,7)	49,3 (±12,3)	48,78 (±12,8)	50,6 (±11,3)
Clinical Characteristics				
Thrombosis; n, (%)	31 (82)	30 (97)	0	26 (87)
Arterial; n, (%)	21 (55)	16 (52)	0	14 (47)
Venous; n, (%)	15 (39)	16 (52)	0	13 (43)
Pregnancy Morbidity*; n, (%)	8 (21)	3 (10)	0	5 (17)
Recurrences of APS clinical manifestations; n, (%)	7 (18)	5 (16)	0	2 (7)
Laboratory Profile				
LA; n, (%)	32 (84)	26 (84)	21 (91)	16 (53)
aCL (IgG/M); n, (%)	25 (66)	22 (71)	15 (65)	14** (47)
ß2GPI (IgG/M); n, (%)	26 (68)	23 (74)	15 (65)	14** (47)
Triple aPL (IgG/M); n, (%)	23 (61)	19 (61)	13 (57)	4** (13)
Triple aPL (IgG); n, (%)	17 (45)	16 (52)	10 (44)	0**
aPS/PT (IgG/M); n, (%)	24 (63)	20 (65)	15 (65)	6 (20)
ß2GPI-D1; n, (%)	13 (34)	15 (48)	3 (13)	4 (13)
Triple aPL and aPS/PT (IgG/M); n, (%)	16 (42)	14 (45)	10 (44)	0**
Triple aPL and ß2GPI-D1; n, (%)	12 (32)	12 (39)	3 (13)	0**
aPS/PT (IgG) and/or ß2GPI-D1; n, (%)	22 (58)	24 (77)	7 (30)	6 (20)
Cardiovascular Risk Factors				
Hypertension; n, (%)	15 (39)	14 (45)	5 (22)	9 (30)
Hyperlipidemia; n, (%)	14 (37)	11 (35)	2 (9)	7 (23)
Smoking; n, (%)	4 (11)	7 (23)	2 (9)	4 (13)
Diabetes; n, (%)	4 (11)	2 (6)	1 (4)	1 (3)
GAPSS; value (±SD)	13,8 (±6)	14 (±5,5)	12,6 (±5,3)	7,3 (±4,8)
GAPSS >9; n, (%)	30 (79)	22 (71)	14 (61)	7 (23)
GAPSS >14; n, (%)	17 (44)	16 (52)	11 (48)	2 (7)

Disclosure of Interests: None declared

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FRI0590

BIOMARKERS OF HEMODYNAMIC SEVERITY OF SYSTEMIC-SCLEROSIS ASSOCIATED PULMONARY ARTERIAL HYPERTENSION BY SERUM PROTEOME ANALYSIS

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Objectives: To investigate alterations in the serum proteome of patients with systemic sclerosis (SSc)-associated pulmonary hypertension (PAH), to identify proteins that correlated with hemodynamic severity and to determine their possible pathogenic role.

Methods: Patients were included if they fulfilled the following criteria: diagnosis of limited cutaneous SSc, no extensive interstitial lung disease (ILD), and no treatment with PAH-specific therapy. Patients were classified as cases if they had a definitive diagnosis of PAH confirmed by right heart catheterization (RHC) and a serum sample collected on the same day as RHC. They were classified as controls if they had no sign suggestive of PAH on echocardiography.

Results: In a first exploratory step, serum expression of 1129 proteins was assessed in 15 cases and 16 controls by a high-throughput proteomic assay (SOMAscan). We identified 53 proteins differentially expressed between the 2 groups. Among these 53 candidates, only 2 correlated significantly with pulmonary vascular resistance (PVR): chemerin (p=0.01, ρ=0.62) and SET nuclear proto-oncogen (SET) (p=0.01, ρ=0.62).

To validate these results, serum levels of chemerin and SET were measured by ELISA assay in 25 additional cases and 19 additional controls. Chemerin levels were confirmed to be significantly higher in cases (p=0.01) and correlated with PVR (p=0.01, ρ=0.46).

In a second step, to study the potential pathophysiological role of chemerin, we performed confocal immunofluorescence analyses on explanted lungs of healthy controls, SSc-ILD without PAH and SSc-PAH patients. Chemerin receptor, CMKLR1, was significantly increased on SSc-ILD and SSc-PAH pulmonary artery smooth muscle cells (PA-SMC).

We then tested the effect of chemerin on PA-SMC proliferation by stimulating PA-SMCs from idiopathic pulmonary arterial hypertension (iPAH) patients with serum from SSc patients with and without PH, in the presence or absence of a CMKLR1 inhibitor. PA-SMCs from iPAH were confirmed to have higher mRNA expression of CMKLR1 than controls (p=0.03). Serum from SSc-PH patients induced a significantly higher PA-SMC proliferation (p=0.005) than serum from controls. This difference was no longer significant (p=0.69) when adding the CMKLR1 inhibitor α–NETA.

Conclusion: Chemerin is a surrogate biomarker for PVR in SSc-PAH. Increased chemerin and its receptor, CMKLR1, contribute to the SSc-PAH pathogenesis by inducing PA-SMC proliferation.

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FRI0591

VALIDITY OF THE GERMAN VERSION OF BOTH THE PARENT ADHERENCE REPORT QUESTIONNAIRE (PARC) AND THE CHILD ADHERENCE REPORT QUESTIONNAIRE (CARQ) - DATA OF THE INCEPTION COHORT OF NEWLY DIAGNOSED PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS (ICON)

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Background: Juvenile idiopathic arthritis (JIA) is the most common chronic inflammatory rheumatic disease in childhood. A multimodal treatment is needed to reduce pain, control inflammation and maintain joint functioning. Adherence to prescribed therapies is necessary for an optimal outcome. Measuring adherence in children with JIA and their caregivers by a validated questionnaire provides important information about benefits and problems with treatment.

Objectives: To evaluate adherence in JIA patients and to validate the German version of both the parent adherence report questionnaire (PARQ) and the child adherence report questionnaire (CARQ).

Methods: The PARQ and CARQ were translated from its original English version into German and cross-culturally adapted. Parents and children completed the PARQ and CARQ 4 years after enrolment in the Inception cohort ICON. These questionnaires measure child ability (by VAS 0-100, 100 = best) related to i) general level of difficulty in following treatment, ii) frequency of following treatment, iii) negative reactions in response to treatment [i)-iii) summarized to child ability total score], iv) perceived helpfulness of treatment, and 4 categorical questions on errors in medication behavior. Reliability was tested by re-administering the questionnaire after a mean of 13 days. Reproducibility was analysed using intraclass correlation coefficients (ICC). VAS scores were correlated with the Pediatric Quality of Life Inventory (PedsQL) treatment scale items for convergent validity, and with sociodemographic parameters for discriminant validity.

Results: 481 parents and 465 children completed the PARQ and the CARQ, respectively, 56 parents and 37 children took part in the re-test. The mean age at assessment was 10.1±3.7 years, mean disease duration was 4.7±0.8 years. The majority of patients suffered from oligoarthritis (49%), followed by rheumatoid-factor negative polyarthritis (30%). Treatment with a DMARD received 60% (MTX 46%), 28% received a biological drug, 16% both. Disease activity measured by the clinical juvenile arthritis disease activity score-10 (cJADAS-10) was 2.6 ± 3.4 (range 0 – 30, best = 0), functional status was good (mean CHAQ 0.2 ± 0.4). Exercise and splints were prescribed to 57% and 21% of patients, respectively.

PARQ/CARQ mean child ability total scores for medication were 73.1 ± 23.3/76.5 ± 24.2, for exercise: 85.6 ± 16.5/90.3 ± 15.0, for splints: 72.9 ± 24.2/82.9 ± 16.5. About a third of parents and children reported any error in medication behavior. Perceived helpfulness was highest for medication (PARQ/CARQ 87.4 ± 20.6/83.6 ± 26.1) and lowest for splints. (PARQ/CARQ 80.8 ± 28.4/73.5 ± 33.6).

ICCs related to medication indicated good to excellent concordance (PARQ ICC = 0.69 - 0.96; CARQ ICC = 0.53 - 0.75), to exercise moderate (PARQ ICC = 0.28 - 0.45; CARQ ICC = 0.67 - 0.93) and to splints disparate concordance (PARQ ICC = 0.01 - 0.90, CARQ ICC = 0.86 - 0.93).

Scores for medications (PARQ: r 0.06 - 0.38, CARQ: 0.06 - 0.49), exercise (PARQ: r 0.03 - 0.30, CARQ: 0.01 - 0.34) and splints (PARQ: r 0.09 - 0.52, CARQ: 0.11 - 0.62) showed a fair to good correlation with the PedsQL scales. Gender and socioeconomic status were not associated with the level of adherence.

Conclusion: The German version of the PARQ and CARQ appears to be a valuable tool to measure adherence in patients with JIA and to evaluate helpfulness of treatments.

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FRI0592

IMPACT OF INDIVIDUAL SYMPTOMS OF PSORIATIC ARTHRITIS ON PHYSICAL COMPONENT SCORE AND MENTAL COMPONENT SCORE OF SF-36 AS A MEASURE OF HEALTH RELATED QUALITY OF LIFE (QOL): AN OBSERVATIONAL COHORT STUDY

M. Skougaard[1], T. Schjødt Jørgensen[1], M. J. Jensen[1], C. Ballegaard[1], J. Guldberg-Møller[1], A. Egeberg[2], R. Christensen[1], J. F. Merola[3], L. C. Coates[4], V. Strand[5], P. J. Mease[6], L. E. Kristensen[1]. [1]*The Parker Institute, Bispebjerg and Frederiksberg Hospital, Copenhagen, Denmark*; [2]*Department of Dermatology and Allergy, Herlev and Gentofte Hospital, Copenhagen, Denmark*; [3] *Department of Dermatology and Department of Medicine, Division of Rheumatology, Brigham and Women's Hospital, Harvard Medical School, Boston, United States of America*; [4]*Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, United Kingdom*; [5]*Division Immunology/Rheumatology, Stanford University, Palo Alto, United States of America*; [6]*Swedish Medical Centre, and University of Washington, Seattle, United States of America*

Background: Patients with Psoriatic Arthritis (PsA) experience diverse symptoms including skin and nail psoriasis, swollen and tender joints, enthesitis, and fatigue that have shown to impair health related quality of life (QoL). We hypothesized that different elements of disease influence SF-36 physical (PCS) and mental (MCS) component summary scores differently.

Objectives: The objective of the study was to assess the interaction between change in disease activity (DAS28CRP), PsA symptoms (psoriasis [PsO], nail PsO, enthesitis, fatigue, pain, and physical function) with changes in PCS and MCS scores in a PsA patient cohort exploring effect of treatment on clinical manifestations and patient-reported outcome (PRO).

Methods: Data were obtained from the PIPA cohort (1) at baseline and after 4 months of treatment. Patients' characteristics were described as medians with interquartile ranges (IQRs) and numbers with percentages. Data were presented as

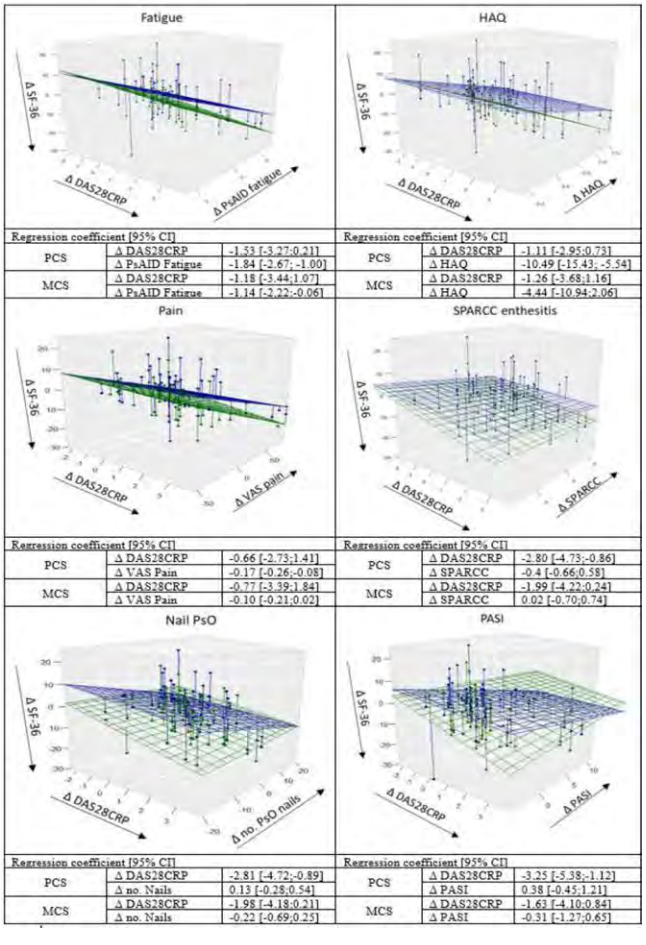


Figure 1. Association between disease activity, individual symptoms and PCS/MCSPCS; physical component summary (green regression plane), MCS; mental component summary (blue regression plane). Arrows indicate the positive improvement vector. SF-36: short form-36, CI: Confidence Interval, DAS28CRP: disease activity score with 28 joints and c-reactive protein, PASI: Psoriasis Area Severity Index, SPARCC: Spondyloarthritis Research Consortium of Canada enthesitis index, VAS: visual analogue scale, PsAID: Psoriatic Arthritis Impact of Disease, HAQ: Health Assessment Questionnaire

changes between baseline and follow-up with delta (Δ) values on xyz-plots. Associations between PCS and MCS scores, DAS28CRP, and PsA symptoms were described with fitted linear regression plane models. PCS and MCS were derived from 8 domains of SF-36 and ranged from 0-100 with lower values reflecting more impaired QoL.

Results: 71 PsA patients were included in the study. 40 (56%) patients were female with a mean age of 50 (IQR 41-60) years and disease duration of 2.15 (IQR 0.2-9) years. Figure 1 shows associations between PsA symptoms, DAS-28CRP, and PCS (green regression plane) and MCS (blue regression plane). For all PROs; pain, fatigue and physical function, improvements in both ΔPCS and Δ MCS scores were associated with improvements in either Δpain, ΔPsAID fatigue, and/or ΔHAQ, and to a larger extent than improvements in ΔDAS28CRP. Improvements in Δnail PsO (regression coefficient (RC): -0.22) and ΔPASI (RC: -0.31) positively impacts ΔMCS, without a clear association in PCS scores (RC: 0.13 and 0.38 for Δnail PsO and ΔPASI, respectively). Improvement in inflammatory features SPARCC enthesitis and DAS28CRP showed improvement in both ΔPCS and ΔMCS.

Conclusion: Pain and fatigue are well-known factors to impair QoL in PsA patient. Here we show that diminishing these factors, pain and fatigue, improved both PCS and MCS scores more than changes in DAS28CRP. Improvements in skin and nail manifestations impacted MCS scores and are as important as changes in joint manifestations which affect PCS and MCS scores equally.

References:

[1] Hojgaard P et al. Pain mechanisms and ultrasonic inflammatory activity as prognostic factors in patients with psoriatic arthritis (…) BMJ Open. 20

Disclosure of Interests: Marie Skougaard: None declared, Tanja Schjødt Jørgensen Speakers bureau: Abbvie, Pfizer, Roche, Novartis, UCB, Biogen, and Eli Lilly, Mia Joranger Jensen: None declared, Christine Ballegaard: None declared, Jørgen Guldberg-Møller Speakers bureau: Novartis, Ely Lilly, AbbVie, BK Ultrasound, Alexander Egeberg Grant/research support from: Pfizer, Eli Lilly, Novartis, AbbVie, Janssen Pharmaceuticals, the Danish National Psoriasis Foundation and the Kgl Hofbundtmager Aage Bang Foundation, Consultant of: UCB Pharma (Advisory Board), Speakers bureau: AbbVie, Almirall, Leo Pharma, Samsung Bioepis Co. Ltd., Pfizer, Eli Lilly, Novartis, Galderma, Dermavant, UCB Pharma, Mylan, Bristol-Myers Squibb and Janssen Pharmaceuticals, Robin Christensen: None declared, Joseph F. Merola Consultant of: Merck, AbbVie, Dermavant, Eli Lilly, Novartis, Janssen, UCB Pharma, Celgene, Sanofi, Regeneron, Arena, Sun Pharma, Biogen, Pfizer, EMD Sorono, Avotres and LEO Pharma, Laura C Coates: None declared, Vibeke Strand Consultant of: AbbVie, Amgen, Biogen, Celltrion, Consortium of Rheumatology Researchers of North America, Crescendo Bioscience, Eli Lilly, Genentech/Roche, GlaxoSmithKline, Hospira, Janssen, Merck, Novartis, Pfizer, Regeneron Pharmaceuticals, Inc., Sanofi, UCB, Philip J Mease Grant/research support from: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Eli Lilly, Novartis, Pfizer, Sun Pharmaceutical, UCB – grant/research support, Consultant of: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Eli Lilly, Novartis, Pfizer, Sun Pharmaceutical, UCB – consultant, Speakers bureau: Abbott, Amgen, Biogen Idec, BMS, Eli Lilly, Genentech, Janssen, Pfizer, UCB – speakers bureau, Lars Erik Kristensen Consultant of: UCB Pharma (Advisory Board), Sannofi (Advisory Board), Abbvie (Advisory Board), Biogen (Advisory Board), Speakers bureau: AbbVie, Amgen, Biogen, Bristol-Myers Squibb,Celgene, Eli Lilly, Gilead, Forward Pharma, Janssen Pharmaceuticals, MSD, Novartis, Pfizer, and UCB Pharma

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FRI0593 CORRELATION BETWEEN DISEASE ACTIVITY AND MENTAL HEALTH OF AS PATIENTS: A CROSS-SECTION STUDY WITH SELF-ASSESSMENTS BASED ON SMART SYSTEM OF DISEASE MANAGEMENT (SSDM) MOBILE TOOLS

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Background: WHO survey showed that the prevalence of anxiety and depression in Chinese population and Chinese patients with chronic diseases were between 3.1% - 4.2% and 3.1% - 7.3%, respectively. Ankylosing Spondylitis Disease Activity Score (ASDAS) and Hospital Anxiety and Depression Scale (HADS) are commonly used to evaluate AS patients' disease activity and mental health. All those assessments were mainly performed by health professionals (HCPs) with paper questionnaire previously. SSDM is a novel smart disease management tool that allows patients to do self-assessments on ASDAS and HADS by mobile terminals.

Objectives: To estimate the prevalence of anxiety and depression in Chinese patients with AS and to analyze the potential association between disease activity and mental health.

Methods: Under the guidance and training by HCPs, AS patients downloaded SSDM and performed self-assessments bundle of ASDAS and HADS with SSDM. ASDAS<=1.3, 1.3-2.1, 2.1-3.5 and >3.5 are defined as inactive (IDA), moderate (MDA), high (HDA) and very high (VHDA) disease activity, respectively. ASDAS score <=1.3 represents inactive disease status and achievement of T2T. HADS score >=8 can be diagnosed with anxiety or depression.

Results: From June 2016 to Jan 2020, 1,931 AS patients (1,118 male, 813 female) with a mean age of 34.09 ± 11.86 (12-82) years and the median disease duration of 2.61 years from 207 hospitals performed bundle self-assessments for 2,477 times in total. According to the HADS and ASDAS assessment results, the prevalence of anxiety and depression in all patients was 36.7% and 39.3% respectively, which was significantly higher than that in the WHO survey in Chinese population and chronic disease patients. The proportion of patients achieved and failed on T2T was 29% and 71%, respectively. The prevalence of anxiety (A) and depression (D) was 25% and 23% among T2T achievers; and 37% and 32% among T2T failures, respectively (pA<0.05, pD<0.05).

According to ASDAS, in IDA, MDA, HDA and VHDA subgroups, the prevalence of anxiety and depression was 27%, 36%, 41%, 52% and 29%, 38%, 45%, 56%, respectively. The correlation coefficients of anxiety (A) and depression (D) with ASDAS were rA=0.9908 and rD=0.9964. It suggested that with the increase of disease activity, the proportion of AS patients with anxiety and depression increased significantly. (Figure 1)

Conclusion: The prevalence of anxiety and depression in AS patients was significantly higher than that in the WHO survey in Chinese population and chronic disease patients. Higher prevalence of anxiety and depression were associated with higher levels of disease activity. SSDM is an effective mobile interface to monitor and study entanglement of disease activity and mental health in AS patients, which build a foundation for proactive interventions in future.

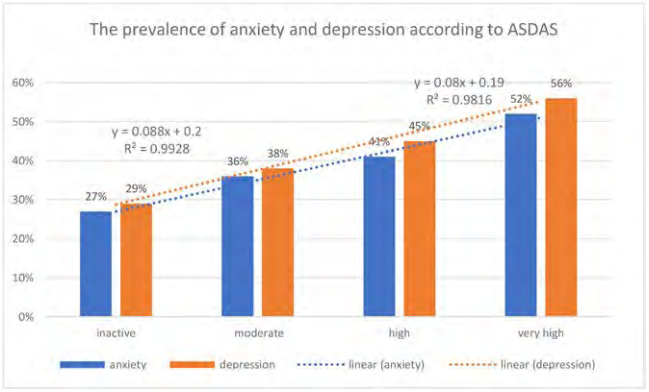


Figure 1. The prevalence of anxiety and depression according to ASDAS.

Acknowledgments: Smart system of disease management (SSDM) was developed by Shanghai Gothic Internet Technology Co., Ltd.

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FRI0594 USE OF ANTI-DFS70 ANTIBODIES IN RHEUMATOLOGICAL PATIENTS WITH SUSPICION OF SYSTEMIC AUTOIMMUNE DISEASE

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Background: Positivity of dense fine speckles antibodies (anti-DFS70) has been associated with antinuclear antibodies positivity in people with no evidence of

Table 1.

		RHEUMATOLOGY (n=75)			OTHER SPECIALTIES (n=27)	
		antiDFS70(+) n=25(100%)	antiDFS70(-) n=50(100%)		antiDFS70(+) n=13(100%)	antiDFS70(-) n=14(100%)
Women		20(80)	43(86)		8(62)	9(64)
Age years (ED)		47,1 (±20,1)	50,4 (±15,5)		45,1(±26,7)	54,7(±15,6)
ANA Pattern IIF	Homogeneous	8(32)	23(46)		2(15)	4(29)
	Speckled	22(88)*	30(60)		12(92)	9(64)
	Other	0	10(20)		1(8)	4(29)
Final diagnosis	Arthralgia	12(48)	15(30)	**Speciality**		
	Fibromyalgia	3(12)	6(12)	Dermatology	4(31)	7(49)
	Drug-induced SLE	2(8)	2(4)	Gastroenterology	3(23)	3(21)
	SLE	3(12)	17(34)*	Hematology	1(8)	2(14)
	Cutaneous lupus	0	8(16)*	Other	5(38)	2(14)
	PsA	0	6(12)*			
	Other	6(25)	16(32)			
SLE	Arthritis	3(12)	13(26)			
	Arthralgia	13(52)	18(36)			
	Cutaneous	3(12)	12(24)			
	Oral ulcers	0(0)	6(12)*			
	Leukopenia	0(0)	4(8)			
	Thrombocytopenia	0(0)	1(2)			
	Fever	1(4)	1(2)			
	Pleuritis	0(0)	1(2)			
	Pericarditis	0(0)	1(2)			
	Nephritis	0(0)	4(8)			
	Myositis	1(4)	0(0)			

ANA (antinuclear antibody), IIF (indirect immunofluorescence), SLE (systemic lupus erythematosus), PsA (psoriatic arthritis), *p<0, 05.

systemic autoimmune disease. They could be useful to distinguish patients with these characteristics that do not meet diagnostic and/or classifying criteria for any systemic autoimmune disease (SAD).

Objectives: To evaluate the use of anti- DFS70 in patients with suspicion of SAD.

Methods: A cross-sectional observational study was conducted at 2 tertiary-level hospitals. We included a cohort of patients visited in the last year by either rheumatology or other specialties, under suspicion of SAD, in which the IgG isotype anti-DFS70 was obtained by recombination with the Euroline Immunoblot of Euroimmun. Demographic, clinical and immunological variables were collected.

Results: 102 patients (78% women) were included, median age of 49 years old. The descriptive statistics are summarized in Table 1. All patients had ANA titters > 1/80. 37% were positive for anti-DFS70, with homogeneous, speckled and other patterns in 36%, 72% and 15% respectively.74% were visited by rheumatologists under the suspicion of systemic lupus erythematosus (SLE) in 27%, other SAD 25%, arthralgia 36% and fibromyalgia 12%. 13% presented high DNA titters, low C3/C4 levels in 14% and 9%. SLE's symptoms were: arthritis 21%, arthralgia 41%, cutaneous 20% and oral ulcers 8%. Anti-DFS70(+) was related to the speckled pattern in 46% compared to other patterns (p=0,009), which had a negative association with anti-DFS70(p=0,003). Regarding the diagnoses, there was a negative association with SLE, other SAD and other rheumatologic diagnoses in 88%, 75% and 55% respectively(p=0,006). Anti-DFS70(-) was associated with oral ulcers (p=0,024), decreased C3/C4 levels (p=0,007/p=0,018), psoriatic arthritis (p=0,024) and cutaneous lupus (p=0,008), but not with drug-induced SLE (p=0,48) or lupus nephritis (p=0,067). There was no statistical significance between anti-DFS70(+) and arthralgia or fibromyalgia, but these patients don't have a SAD diagnosis.

Conclusion: Our results suggest that patients with suspicion of SAD, especially SLE, presented a greater proportion of negative anti-DFS70 compared to other diagnoses, including SAD, along with a decrease in complement levels and the presence of oral ulcers, being useful at the initial study of these patients. More studies are needed to characterize this association.

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FRI0595

CAN A SINGLE QUESTION ON FUNCTIONAL IMPAIRMENTS FACILITATE THE IDENTIFICATION OF EARLY INFLAMMATORY ARTHRITIS? A LARGE CROSS-SECTIONAL DERIVATION AND VALIDATION STUDY

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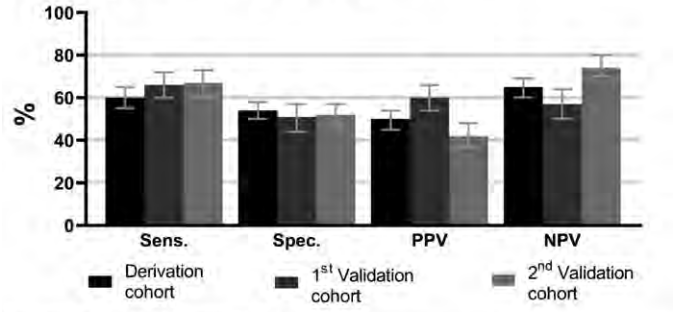
Background: Early treatment initiation in inflammatory arthritis (IA), and specifically in RA, is associated with improved outcomes but requires early identification of synovitis. However, healthcare professionals other than rheumatologists, e.g. general practitioners (GPs), experience difficulties in detecting early IA by joint examination. In this light, two Early Arthritis *Recognition* Clinics (EA*R*Cs) were initiated in the Netherlands in 2010. EA*R*Cs are easy-access outpatient rheumatology clinics, intermediary between primary and secondary care, to which GPs can refer patients when in doubt about the presence of IA (instead of 'watchful waiting'). Although this approach markedly reduced referral delay,[1] it may not be easily implemented in other places due to shortage of rheumatologists. Therefore, other new tools to support early identification of IA are needed.

Objectives: Aiming for simple and time-efficient use in daily practice, we evaluated if just a single question on functional impairments could aid the identification of early IA.

Methods: Data from two EA*R*Cs in the Netherlands were studied. Between 2010 and 2014, 997 patients with suspected IA visited the Leiden EA*R*C (derivation cohort). Patients visiting the Groningen EA*R*C (2010–2014, n = 506) and Leiden EA*R*C (2015–2018, n = 557) served as validation cohorts. Physical functioning was assessed with the Health Assessment Questionnaire Disability Index (HAQ); IA by joint examination by rheumatologists. Discriminative abilities for IA of the 20 HAQ-questions were compared based on the area under the curve (AUC). For the best discriminating question, test characteristics and odds ratios (ORs) were calculated. ORs were adjusted for clinical characteristics that were previously reported to be predictive of the presence of IA (gender, age ≥60 years, symptom duration, acuteness of symptom onset, morning stiffness >60 minutes, number of painful joints, presence of patient-reported swollen joint(s) and difficulty with making a fist)[2] using multivariable logistic regression.

Results: IA was identified in 43% (derivation cohort), 53% and 35% (validation cohorts). In the derivation cohort, presence of IA associated with higher mean HAQ-scores (0.84 versus 0.73, p=0.003). The HAQ-question on difficulties with dressing yielded the highest AUC (0.58), which equalled discriminative ability of the total HAQ-score (AUC 0.55). Responses to this question were dichotomised into a simple binary score since loss of discriminative ability was minimal (AUC 0.57). Presence of any difficulties with dressing yielded ORs for IA of 1.80 (95%CI 1.39–2.33) in the derivation cohort; 2.00 (1.39–2.87) and 2.14 (1.48–3.10) in the validation cohorts. After adjustments for clinical characteristics the presence of any difficulties with dressing remained associated with the presence of IA; OR 1.71 (1.27–2.32) in derivation cohort and 1.64 (1.08–2.50) and 1.87 (1.20–2.92) in the validation cohorts. The prevalence of IA in case of presence of difficulties with dressing (positive predictive value) ranged 42–60% (see Figure).

Figure. Test characteristics of the presence of difficulties with dressing, with IA at physical examination as outcome



Error bars indicate the 95% confidence interval.
Sens.: sensitivity; Spec.: specificity; PPV: positive predictive value; NPV: negative predictive value.

Conclusion: A yes/no answer on a simple question ("Are you able to dress yourself, including shoelaces and buttons?") was helpful in discriminating patients with and without IA. Findings were validated in independent 1.5-line settings and need to be validated further in primary care. This is a step forward to arrive at practical tools that are helpful for GPs in identifying early IA.

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FRI0596 NOVEL AUTOANTIBODY BIOMARKERS FOR THE PREDICTION OF THERAPY RESPONSE IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is an autoimmune disorder that is characterized by chronic inflammation of the joint synovium and presence of autoantibodies in most patients. For RA, many treatments are currently available but each treatment will only induce disease remission in a subset of patients. Moreover, finding out which patients respond well to first-line therapy with classical synthetic disease modifying anti-rheumatic drugs (csDMARDs), still largely depends on trial and error.

Objectives: In this study, we aim to find novel RA autoantibody biomarkers that predict therapy response to csDMARDs before the initiation of treatment.

Methods: In the CareRA trial, a Flemish multicenter study of different treatment regimes, serum samples were collected from RA patients that did or did not show disease remission (DAS28(CRP)<2.6) in response to csDMARDs, combined with a step down glucocorticoid treatment. In our study, baseline samples, collected before the start of treatment, were used to determine predictive antibody reactivity. A cDNA phage display library, representing the antigens from RA synovial tissue, was constructed and screened for antibody reactivity in baseline serum samples of RA patients that failed to reach remission at week 16. Using enzyme-linked immunosorbent assays (ELISA), antibody reactivity against the identified antigens was initially determined in pooled baseline serum samples of RA patients that did (n=50) or did not (n=40) reach disease remission at week 16. Antigenic targets that showed increased antibody reactivity in pools from patients that did not reach disease remission, were further validated in individual serum samples of 69 RA patients that did not reach DAS28(CRP) remission at week 16, and 122 RA patients that did.

Results: Screening and validation of antibody reactivity resulted in 41 novel antigens. The retrieved antigenic sequences correspond to (parts of) known proteins and to randomly formed peptides. A panel of 3 of these peptide antigens could be composed, whose baseline antibody reactivity correlated with lack of therapy response at week 16. Presence of antibodies against at least one of these 3 antigens was significantly higher in individual samples of RA patients that did not reach DAS28(CRP) remission (43 vs. 29%, p=0.041), or that failed to reach ACR 70 (42 vs. 26%, p=0.029) response criteria at week 16, compared to RA patients that did reach these respective criteria. In addition, RA patients which were positive for this antibody panel at baseline, also showed less DAS(CRP) remission at week 4 and week 8.

Conclusion: We have identified a set of 3 antibody biomarkers that can predict failure of early disease remission after first-line RA therapy, which might contribute to personalized medicine decisions.

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FRI0597 IMMUNOGLOBULIN A FOR CD74 AS AN ALTERNATIVE LABORATORY MARKER FOR DETERMINING THE ACTIVITY OF AXIAL SPONDYLOARTHRITIS

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Background: The level of acute phase indicators does not always correspond to the activity of axial spondyloarthritis (axSpA). The level of C-reactive protein (CRP) is remain normal in a third of cases of axSpA with present of active clinical symptoms [1]. Search for new biomarker that should have increased sensitivity and specificity compared to the CRP is needed. An alternative biomarker of axSpA activity could be an immunoglobulin (Ig) A antibody to an invariant chain peptide associated with class II human leukocyte antigen (HLA) (anti-CD74) [2].

Objectives: is to determine the level of IgA anti-CD74 in patients with axSpA and its relationship with traditional indicators of disease activity.

Methods: Totally, 137 patients with a reliable diagnosis of axial spondylitis (ASAS criteria, 2009) and 47 healthy volunteers were involved in the study. AxSpA activity indices (ASDAS, BASDAI) were calculated for all patients and IgA levels of anti-CD74, ESR and CRP were determined. The normal level according to the instructions for the laboratory kit for determining the level of IgA anti-CD74 is 12.0 U/L.

Results: Patients and volunteers characteristics are present in Table 1.

Table 1. Characteristic of the patients with axial spondyloarthritis (n=137) and healthy volunteers (n=47)

Indicator	Results	
	AxSpA patients	Healthy volunteers
Male, n (%)	101 (73.7)	19 (40.4)
Age, years (mean±SD)	43.4±13.3	49.0±11.0
Disease duration, years (mean±SD)	12.6±8.3	
Activity indices		
ASDAS, points (mean±SD)	2.29±1.17	
BASDAI, points (mean±SD)	3.02±2.0	
Laboratory markers		
CRP, mg/L (mean±SD)	9.61±18.3	2.3±1.9
Abnormal level of CRP, n (%)	114 (83.2)	4 (8.5)
IgA anti-CD74, U/L (mean±SD) (fig.1)	16.9±11.0	9.3±5.5
Abnormal level of IgA anti-CD74, n (%)	96 (70.1)	15 (31.9)
ESR, mm/h (mean±SD)	24±7.8	8.5±7.9

A direct relationship was found with a high power between an increase in the level of anti-CD74 (R=0.667) and an increase in the ASDAS (R=0.857) and BASDAI (R=0.842). The factor analysis showed that an increase in activity level according to ASDAS, BASDAI indices was associated with an increase in concentration of IgA anti-CD74. While CRP indicators (R=0.530) were associated only with the ASDAS index (R=0.760) (Table 2).

Table 2. Factor loads of the relationships identified between the concentration of IgA anti-CD74 and the activity indices of axial spondyloarthritis

Indicator	Factor loading (R)		
Factor	Factor 1	Factor 2	Factor 3
IgA anti-CD74	-	-	0.667
BASDAI	-	0.844	0.842
ASDAS	0.530	0.959	0.857
BASFI	-	0.614	0.820
CRP	0.760	-	-

«-» no significant association present.

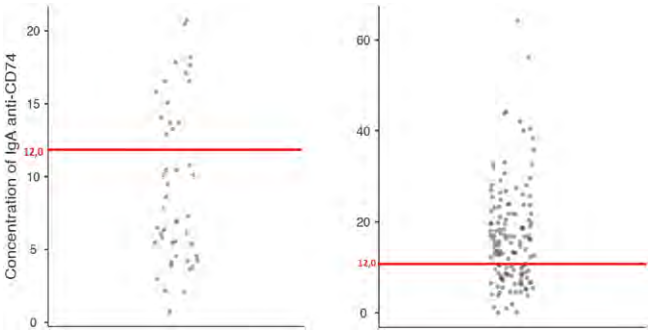


Figure. 1. Concentration of IgA anti-CD74 for healthy volunteers (left) and patients with axial spondylitis (right)

As compared to controls sensitivity of IgA to anti-CD74 was 64,7%, specificity of this method was 68,1%.

Conclusion: The concentration of IgA to anti-CD74 is increased in 70.1% of pts with axSpA and associated with an increase in disease activity detected with ASDAS and BASDAI, independently from CRP. More data are needed in detection of sensitivity and specificity of IgA to CD74 in axSpA.

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FRI0598 DMARD-FREE REMISSION IN RHEUMATOID ARTHRITIS: AN ACHIEVABLE AND SUSTAINABLE OUTCOME? A SYSTEMATIC LITERATURE REVIEW

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Background: Current treatment guidelines for rheumatoid arthritis (RA) suggest tapering DMARDs.[1] Discontinuation of DMARD-treatment is of increasing interest, and DMARD-free remission (DFR) is regarded an important future outcome.[2 3] However, lack of knowledge on DFR prevalence, its sustainability, and the characteristics of patients achieving DFR currently hampers the use of DFR as primary outcome.

Objectives: To increase the understanding of DFR in RA, and to support studies aiming to include this as primary outcome, we systematically reviewed the literature to determine prevalence and sustainability of DFR. Potential predictors of DFR were evaluated to increase insight in patient characteristics favourable for achieving this outcome.

Methods: A systematic literature search was performed in March 2019 in multiple databases. All clinical trials and observational studies reporting on discontinuation of DMARDs in RA-patients in remission were included. Our quality assessment included a general assessment and assessment of the description of DFR. Prevalence of DFR and its sustainability, flares during tapering and after DMARD-stop were summarized. Also, potential predictors of achieving DFR were reviewed.

Results: From 631 articles, 51 were included, comprising 14 clinical trials and 5 observational studies. DFR-definition differed, especially for the duration of DMARD-free state. Considering only high and moderate-quality studies, DFR was achieved in 5.0%-24.3%, and sustained DFR (duration>12 months) in 11.6%-19.4%. Flares occurred frequently during DMARD-tapering (41.8%-75.0%) and in the first year after achieving DFR (10.4%-11.8%), whilst late flares, >1 year after DMARD-stop, were infrequent (0.3%-3.5%). Many patient characteristics lacked association with DFR. Absence of auto-antibodies and shared epitope alleles increased the risk of achieving DFR.

Conclusion: DFR is achievable in RA, and is sustainable in ~10%-20% of patients. [1]DFR can become an important outcome measure for clinical trials, and requires consistency in the definition. Considering the high rate of flares in the first year after DMARD-stop, a DMARD-free follow-up of >12 months is advisable to evaluate sustainability.

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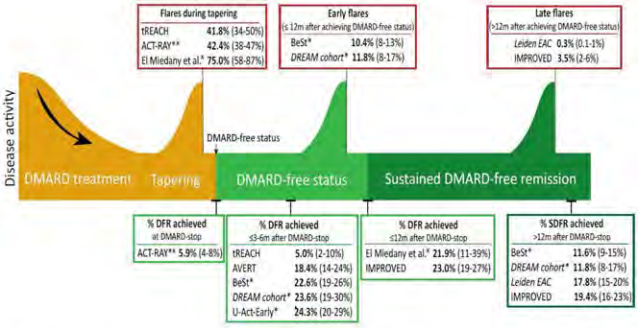


Figure 1. Summary of flare rates and DFR-prevalence depicted on a timeline, prevalence are grouped based on the reported duration of DFR.
DFR percentages of all high and moderate-quality studies with confidence intervals, indicated parenthetical. Prevalence and confidence intervals were calculated using number of DFR patients divided by the number of patients eligible for tapering. Flares were calculated using number of flares, divided by the number of patients eligible for tapering. Patients were considered eligible for tapering when they had achieved remission and subsequently were allowed to start tapering. Results from observational studies are indicated in italic, others are clinical trials.
* indicates that studies that allowed the use of i.a. or systemic corticosteroids in patients that were considered to be in DFR (absolute number of patients that used corticosteroids after DMARD-stop was not reported). ** indicates moderate-quality studies.
DMARD: Disease-modifying antirheumatic drugs, DFR: DMARD-free remission, SDFR: sustained DMARD-free remission.

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FRI0599 USEFUL II: DERIVATION OF THE LUPUS ARTHRITIS AND MUSCULOSKELETAL DISEASE ACTIVITY SCORE (LAMDA) USING DATA FROM A MULTICENTRE LONGITUDINAL STUDY

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Background: Musculoskeletal (MSK) disease is the commonest manifestation of SLE. We showed that the MSK components of the BILAG index and SLEDAI have limited sensitivity, specificity and responsiveness compared to ultrasound

(US) synovitis. The USEFUL study evaluated response to glucocorticoids in SLE patients with inflammatory pain.

Objectives: To develop a disease activity tool for lupus MSK manifestations that is continuous, responsive, sensitive, and correlates with US-synovitis

Methods: 133 patients who received depomedrone 120mg IM were assessed at 0, 2 and 6 weeks for 66/68 swollen and tender joint counts, BILAG2004 index, SLEDAI-2K, physician global and MSK-VAS, inflammatory markers, patient pain and disease activity-VAS. Total US score (OMERACT-EULAR) in the hands and wrists was calculated blinded to patient and clinical assessor. Patients reported overall response using a Likert scale.

The LAMDA was developed by modelling a core set of clinical variables against total US score using penalized (Lasso) regression. Responsiveness was compared between LAMDA and other variables at week 6 using effect sizes. Minimum clinically important difference (MCID) was explored using the SEM and minimal disease activity threshold using ROC.

Results: The variables selected for the LAMDA score were swollen joint count, patient MSK pain VAS, physician MSK disease activity VAS and ESR. A continuous score was derived. This had a theoretical range from 0 to 26.5 based on maximum ESR of 100. The highest value observed in USEFUL was 15. LAMDA was significantly higher in patients with active US (mean (SD) 5.71 (2.67), n=78) compared to patients with normal US (3.27 (1.77), n=55; difference (95% CI) -2.45 (-3.26, -1.63), t=-5.93, p<0.001). This difference remained significant in patients with no swollen joints (difference (95% CI) -0.71 (-1.40, -0.02), t=-2.06, p=0.044). Effect size was greater for the LAMDA (0.37) than the BILAG-MSK (0.31), SLEDAI-MSK (0.27) and total US score (0.33). In patients with active US at baseline, LAMDA's effect size was 0.42.

The MCID was 0.71 and correlated with patient-reported change in pain. A threshold for minimal disease activity of 3.23 optimized sensitivity (0.77 (0.65, 0.89)) and specificity (0.80 (0.68, 0.92)) against US score >0.

Conclusion: The LAMDA score is a novel continuous disease activity instrument for MSK manifestations of SLE derived from variables familiar to rheumatologists. The LAMDA score is sensitive to imaging detected synovitis without swelling and more responsive than other instruments. . LAMDA may improve the ability of clinicians to accurately determine therapeutic efficacy in clinical trials and practice. Future work will validate the LAMDA score in independent cohorts and randomized trials.

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FRI0600 DIAGNOSTIC VALUE OF SERUM CONNECTIVE TISSUE GROWTH FACTOR IN RHEUMATOID ARTHRITIS

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Background: Many autoantibodies are found in the serum of rheumatoid arthritis (RA) patients, including RF, ACPA and so on, which are essential for the disease diagnosis and prognosis judgment. However, 20-30% of patients are still seronegative, so more investigations are needed to find new biomarkers in RA.

Objectives: To investigate the prevalence of serum connective tissue growth factor (CTGF) and the association with the clinical features in RA patients.

Methods: Serum samples were obtained from 180 patients with RA, 168 patients with other rheumatic diseases, including 43 systemic lupus erythematosus (SLE), 34 osteoarthritis (OA), 17 primary Sjögren's syndrome (pSS), 20 ankylosing spondylitis (AS), 23 psoriatic arthritis (PsA), 6 reactive arthritis (ReA), 20 systemic sclerosis (SSc), and 5 systemic vasculitis (SV), and 64 healthy individuals in Peking University Third Hospital. The clinical and laboratory data of patients with RA were collected. Levels of CTGF in serum were measured by ELISA. The cut-off value of CTGF was determined by 95 percent of the concentration of the healthy controls. Statistical analyses were performed using the SPSS 24.0 software. Associations between CTGF and the clinical features of RA were evaluated.

Results: The prevalence of serum CTGF among RA patients (33.89%) was significantly higher than those of SLE (9.3%), OA (0%), AS (0%), pSS (0%), PsA (0%), ReA (0%), SSc(5%), SV(0%) and healthy controls (4.69%) (p<0.0001). The mean titer of serum CTGF in RA was also significantly higher than those in other rheumatic diseases and healthy controls (p<0.001). At the cutoff value of 264.30 pg/ml, the sensitivity, specificity, positive predictive value and negative predictive value of serum CTGF for RA were 33.89%, 96.55%, 88.41% and 55.45% respectively. Anti-cyclic citrullinated peptide (CCP) antibody (p<0.001), rheumatoid factor (p<0.001), IgG (p=0.025) and IgM (p=0.004) in CTGF-positive patients were higher than those in CTGF-negative patients. Besides, more patients with interstitial lung disease (ILD) were found in CTGF-positive RA.

Conclusion: Serum CTGF, as a novel biomarker, has certain diagnostic value for RA. Further studies are necessary to get more knowledge for the diagnostic performance of CTGF in RA.

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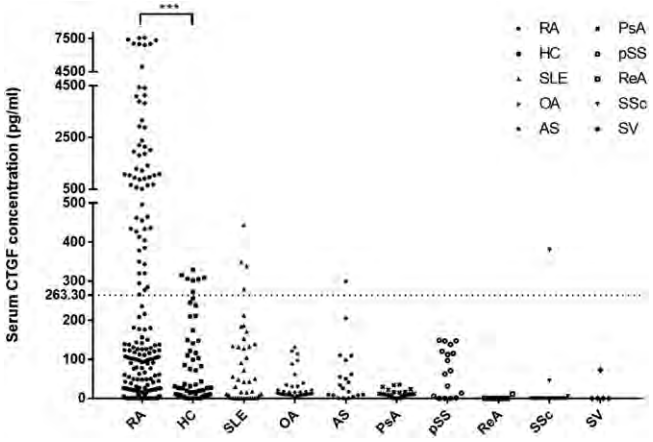


Fig 1. Distribution of serum CTGF in RA, other rheumatic diseases and healthy control. Serum sample were from 180 patients with rheumatoid arthritis (RA), 168 patients with other rheumatic diseases and 64 healthy individuals (HC). Levels of serum CTGF were measured by CTGF ELISA kit. The cut-off value was 263.30 pg/mL (black horizontal dotted line); ***p <0.001

Table 1. Demographic, clinical and laboratory features of total RA patients and grouped with serum CTGF.

	Total (n=180)	Positive (n=61, 33.89%)	Negative (n=119, 66.11%)	P value
Age, mean±SD, years	59.90±13.457	62.67±10.730	58.48±14.497	p=0.030
Women, n (%)	134/180 (74.4)	43/61 (70.5)	91/119 (76.5)	p=0.384
Disease duration, month (range)	54 (10.3-154.5)	72 (12.0-168.0)	36 (9.0-140.0)	p=0.206
<12month	55/180 (30.6)	16/61 (26.2)	39/119 (32.8)	p=0.367
Smoking, n (%)	28/180 (15.6)	14/61 (23.0)	14/119 (11.8)	p=0.061
Morning stiffness, min (range)	30 (0.0-90.0)	35 (10.0-90.0)	30 (0.0-90.0)	p=0.279
SJC28, n (range)	4 (1.0-12.0)	4 (1.0-13.0)	5 (1.0-11.0)	p=0.642
TJC28, n (range)	8 (2.0-16.0)	8 (2-15.0)	8 (2.0-18.0)	p=0.829
ESR, mm/h (range)	33 (14.0-66.0)	36 (16.0-66.0)	32(11.5-66.0)	p=0.478
CRP, mg/dl (range)	2.88 (0.795-8.065)	2.52 (0.780-7.420)	3.12 (0.795-8.200)	p=0.565
DAS28-ESR	6.83±1.969	6.91±1.885	6.79±2.018	p=0.704
DAS28-CRP	4.33±2.450	4.21±2.252	4.39±2.557	p=0.656
Positivity of anti-CCP antibody, n (%)	99/159 (62.3)	48/57 (84.2)	51/102 (50.0)	p<0.001
Positivity of RF, n (%)	90/170 (52.9)	46/59 (78.0)	44/111 (39.6)	p<0.001
IgG, IU/ml (range)	14.50 (11.100-17.425)	15.15 (11.700-19.950)	14.15 (10.575-17.000)	p=0.025
IgM, IU/ml (range)	1.04 (0.718-1.400)	1.17 (0.890-1.720)	1.01 (0.700-1.180)	p=0.004
IgA, IU/ml (range)	2.78 (1.920-3.940)	3.12 (2.685-4.118)	2.77 (1.820-3.865)	p=0.078
Radiographic changes				
Erosion	38/143 (26.6)	15/54 (27.8)	23/89 (25.8)	p=0.800
Joint-space narrowing	97/144 (67.4)	38/54 (70.4)	31/90 (34.4)	p=0.551
ILD, n(%)	49/180(27.2)	25/61(41.0)	24/119(20.2)	p=0.003

Abbreviations: RA=rheumatoid arthritis; SJC=swollen joint count; TJC=tender joint count; ESR=erythrocyte sedimentation rate; CRP=C-reactive protein; DAS=disease activity score; CCP=cyclic citrullinated peptid; RF=rheumatoid factor. CTGF=connective tissue growth factor; ILD= interstitial lung disease

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FRIDAY, 05 JUNE 2020

HPR Epidemiology and public health (including prevention)

FRI0601-HPR IMPACT OF LIFE STYLE MODIFICATION TECHNIQUE IN SYSTEMIC SCLEROSIS (SSC) PATIENTS: A STUDY BY RHEUMATOLOGY NURSES COUNSELOR

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Background: Systemic sclerosis (SSc) is an autoimmune the disease of the connective tissue that is clinically characterized by the involvement of skin (fibrosis, contractures of the finger joints), microvascular abnormalities (Raynaud's phenomenon and complications), gastrointestinal involvement (gastroesophageal reflux disease - GERD, the lower GI tract involvement), musculoskeletal involvement (polyarthralgia, muscle disease), and involvement of internal organs (especially lungs, heart, and kidneys). Lifestyle modification techniques could have significant impact on various aspects of the disease including early disease control, increased drug adherence, positive attitude towards life, decreased financial burden of treatment, maintaining mobility and joints range of motion, minimizing or delaying joint contractures and decreased dependency with regular physical therapy. Counselling explaining the benefits of lifestyle modification related to these aspects of daily living may make a major difference in the quality of life of the patients with SSc.
Objectives: To assess the benefits of lifestyle modification technique in improving the quality of life in patients with SSc.
Methods: Patients with SSc attending the Rheumatology clinic of this institution, willing to participate in the survey, were enrolled in this study. All the information including the follow-up details were recorded in a pre-designed form. Their demographic information (age, gender) and disease characteristics (diagnosis, duration, treatment) were recorded, All the patients were explained the lifestyle modifications and their benefits, reinforced at each follow-up visit using posters (visual), written lifestyle modification techniques (using printed material) to raise their awareness of how to improve several of the above manifestations of SSc.
Results: One hundred fifty (n=150) consecutive SSc patients were included in the study. It was observed that with repeated counselling 125 (83.3 %) patients adopted the lifestyle modification technique according to the advice imparted and felt a positive benefit in their daily life. However, 25 (16.6%) could not or did not follow the imparted lifestyle change advice on a regular basis. Those who were able to modify the life-style as counselled showed the following results:

- 80 % were able to avoid exposure to cold by adopting the following measures: Wearing gloves and extra woolen socks, using mittens most of the time, wearing woollen undergarments to keep the central regions of the body region warm. These patients noted 55% decrease in the episodes of Raynaud's phenomenon.
- Early evening meals and raising the head-end of the bed: 60% decrease in gastrointestinal symptoms.
- Regular physiotherapy: 65 % decrease dependency on others; 55% could maintain flexibility with physical exercises.
- Regular application and rubbing of the skin with lanoline-containing skin moisturizers 60 % improve your skin's health
- 80% were able to avoid active and passive tobacco use.

Conclusion: The lifestyle modification techniques are important to control disease and its complications. Thus, after intense and regular counselling by the specialist rheumatology nurses on the lifestyle modification technique (83.3%) adapted the advised lifestyle modifications. The study showed the important role specialist rheumatology nurses can play in educating patients and helping them improving their quality of life.

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FRI0602-HPR PERSISTENT HYPOCOMPLEMENTEMIA IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is a systemic, chronic, autoimmune disease of unknown cause characterized by a wide variety of clinical manifestations and autoantibody production. The complement is useful in the initial diagnosis, as an activity marker and for the follow-up of patients with SLE. Individual components may fluctuate only slightly with disease activity and C4 may even remain low during remission. Hypocomplementemia is associated with renal involvement, cutaneous vasculitis, diffuse alveolar hemorrhage, however, patients with persistent hypocomplementemia are not characterized yet.
Objectives: 1) Determine the prevalence of persistent hypocomplementemia in patients with SLE.
2) Identify clinical characteristics, disease activity and accumulated damage in these patients.
Methods: A longitudinal study was conducted with a review of the medical records of patients diagnosed with SLE (ACR criteria 82/97) who attended the Rheumatology Service between January 2000 and December 2015. Patients with a minimum evolution time of 6 months from the diagnosis of SLE with quarterly controls and monitoring for 2 years. Persistent Hypocomplementemia (PHC) was defined at C3 and / or C4 values below the normal range of the reference laboratory in a sustained form for at least 24 months. Demographic variables, clinical manifestations, disease activity by SLEDAI 2k, flare by SELENA SLEDAI and accumulated damage by SLICC / SDI were analyzed.
Results: Clinical records of 254 patients with SLE were reviewed and 144 were included; 96% were women, with a mean age at diagnosis of SLE of 30.5 ± 11.2 years and a time of evolution of the disease at the last control 11.85 ± 7.8 years. Forty-one patients had PHC (28.5%; 95% CI 21.1, 35.8). The median of evolution time disease at the moment of PHC was 1 year (0-24) and the mean time of persistence of hypocomplementemia was 56 ± 46 months. In the univariate analysis, PHC was associated with hematological involvement during the course of the disease (p=0.01). Patients with PHC had a higher frequency of severe flare during follow-up (p=0.02). PHC was not associated with age of onset of SLE, disease activity (maximum SLEDAI reached), accumulated damage or death. Applying Logistic Regression Model with dependent variables with a level of significance <0.25, PHC was associated independently with hematological compromise (OR 3.2).
Conclusion: In this cohort of patients, the prevalence of PHC was 28.5%. PHC was associated with severe flare and hematological compromise.
Disclosure of Interests: None declared
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FRI0603-HPR COMORBIDITIES IN RHEUMATOID ARTHRITIS: UTILITY OF RACI SCORE (RHEUMATOID ARTHRITIS COMORBIDITY INDEX)

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Background: One third of patients with rheumatoid arthritis have some comorbidity at the time of diagnosis and 80% during the evolution. The presence of each additional comorbidity reduces the chances of remission by 28%.
Objectives: To determine the prevalence of comorbidities in Rheumatoid Arthritis (RA) and to evaluate associated variables.
Methods: A descriptive cross-sectional study was conducted. It were included patients over 18 years of age, who attended the Rheumatology office between May and August 2018 with a diagnosis of RA according to the ACR 1987 and ACR/EULAR 2010 criteria. Demographic variables were studied along with disease-related variables (time of evolution, disease activity by DAS-28 and CDAI, treatment and functional capacity (HAQ-A)). The presence of comorbidities was evaluated using two indexes: Rheumatoid Arthritis Comorbidity Index (RACI) and

Disease Comorbidity Index (RDCI). RACI consists of 31 comorbidities grouped into 11 categories: DAS 28 >3.6, local inflammation, smoking, tumors, systemic involvement, infection, vascular disease, bone health, mood, metabolic and cardiovascular disorders (score range 0-36). RDCI consists of 11 comorbidities (categories according to ICD-10) and a formula to calculate it (range 0-9). For both indexes; higher score, greater comorbidity.

Results: In this cross-sectional study, 345 patients were evaluated, of which 176 were included, 85.8% of the patients were female and the mean age was 52.7 ± 10.9 years; 31.2% of the cases finished primary school, the median of disease duration was 9 years (1-40), the mean DAS28 3.8 ± 1.4, and the mean CDAI 12.4 ± 11.3. 52.3% of the patients received treatment with glucocorticoids, 60.8% with NSAID, 60.2% with methotrexate, 39.2% with leflunomide, 17.6% with biologic DMARds and 5.6% with tofacitinib. 90.3% of the patients (95% CI 84.8, 94.3) presented some comorbidity measured by RACI. The average score was 4.7 ± 3.4 and the most frequent comorbidity were: elevated DAS28 (40.9%), dyslipidemia (38.1%), AHT (36.4%), prednisone >5 mg/d in 31.8%, endocrinopathies 19.3%. 73.3% of the patients had more than one comorbidity. Regarding RDCI, 47.2% of the cases presented some comorbidity with an average score of 0.95 ± 1.3; the most frequent were: AHT 36.4%, lung disease 12.5% and diabetes 8%. The oldest patients had more than one comorbidity (RACI), and also presented a higher HAQ score than those with only one (p<0.0001). Higher RACI score was associated with higher CDAI (p<0.001) and the use of glucocorticoids (p=0.008).

Conclusion: The prevalence of comorbidities in RA by RACI was elevated (90.3%) and 73.3% of the patients presented more than one comorbidity. The patients with the highest RACI score had higher disease activity and used glucocorticoids more frequently.

Disclosure of Interests: None declared

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FRI0604-HPR IS STRESS A TRIGGER FOR THE DEVELOPMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS?

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Background: Systemic Lupus Erythematosus (SLE) implies multifactorial psychological stress. Although stress has been spreaded as a "trigger" for the onset or flare of connective tissue diseases, there is controversial evidence of the association between stress and the diagnosis of SLE.

Objectives: To assess the frequency of stressors and vital events in patients with SLE and their relationship with the diagnosis.

Methods: A descriptive cross-sectional study was conducted. It were included patients over 18 years old with SLE diagnosis (ACR/SLICC criteria), attended in the Rheumatology Unit between May and August 2019; and 101 patients without any autoimmune disease. Demographic and disease-related variables were studied. The Holmes and Rahe Vital Events scale (43 questions) was used to evaluate vital events and measure the magnitude of stress that a person has experienced for a while and predict the onset of SLE. The sum of the scores indicates the magnitude of vital stress experienced by a person and the predisposition to acquire a disease. It was classified as: <150: small risk of illness due to stress; 150-299: moderate risk; and ≥ 300: high risk.

Results: 94 patients with SLE were included, of which 94% were women. The mean age was 36.3 ± 10.3 years. 41.9% of the cases had a family history of rheumatic disease and 31.2% of them were unemployed. During the year before the diagnosis of SLE, 48.4% of the patients suffered a stressful situation, the most frequent cause was the death of a close family member (44.1%). Patients with SLE presented significantly higher stress scores than the healthy group (140 ± 27 vs. 45.1 ± 43, p=0.0001); 54.8% of patients with SLE had a score <150; 23.65% between 150-299; and 10.75% ≥ 300. The number of patients with SLE was higher in the moderate and high risk categories (>150) than the healthy group (34% vs. 2%, p=0.0001). When studying the Holmes and Rahe scale factors individually, patients with SLE had a higher frequency of situations related to: death of the couple (p=0.029), death of a close relative (p=0.0001), injury or personal illness (p=0.006), change in living conditions (p=0.0001) and poor relationship with the couple (p=0.017).

Conclusion: Patients with SLE presented high frequency of stressful situations before diagnosis (48.4%), and higher scores compared to the healthy group. The death of a close family member was the most frequent stressful event.

Disclosure of Interests: None declared

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FRI0605-HPR MORTALITY AND SURVIVAL IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN ARGENTINA. A MULTICENTER STUDY ON BEHALF GESAR-LES

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Background: The mortality rate in patients with systemic lupus erythematosus (SLE) is 2–3 times higher than in the general population. However, survival in these patients has improved significantly and is currently 95% at 5 years according to different studies. Since the last 20 years, there are no new reports on this issue in Argentina.

Objectives: To analyze the factors associated with mortality, survival and causes of death in patients with SLE.

Methods: Longitudinal - multicenter study, in which 10 rheumatology centers of Argentina participated. Patients with SLE (ACR 1997 and / or SLICC 2012 criteria) with a minimum follow-up of 6 months monitored between January 2008 and December 2018 were included. Demographic, clinical, laboratory, therapeutic variables (treatments received during the evolution of the disease and within 60 days prior to death or last control); mortality, causes of death and survival at 5, 10 and 20 years were evaluated. Statistical analysis: descriptive statistics, Kaplan-Meier survival curves and Cox regression model.

Results: Three hundred and eighty two patients were included; 90% women and 82% mestizos. The mean of evolution time of SLE was 4.1 ± 6.7 years. The mean age at the last control or death was 37.2 ± 12.7 years, SLEDAI 3.2 ± 4.2 and SLICC 1.2 ± 1.9.

Mortality was 12% (95% CI [8-15]) and the causes of death were: Infections (27), cardiovascular disease (6), SLE activity (3), catastrophic antiphospholipid syndrome (2) and other causes (8). Using the variables associated with mortality in different Cox regression models, the variables that increased the risk of death significantly were: renal involvement (RR 3.3), cardiac involvement (RR 2.7), central nervous system involvement (RR 2.1), arterial thrombosis (RR 2.3), hyperlipemia (RR 2.4), number of infections (RR 1.2) and last SLEDAI (1.1).

The time of HCQ use greater than 36 months decreased the risk of death in this cohort by 40% (p 0.03). Prednisone (maximum dose and time) was not associated with mortality (p NS). When analyzing the last treatment and adjusting it for final SLEDAI, HCQ was a mortality protection factor (RR 0.4) while the use of cyclophosphamide alone or associated with prednisone was a risk factor for death (RR 5.2).

Significant differences were found when analyzing the causes of death according to the SLE evolution time (p 0.017): patients who died from infection had less evolution time (Me 2.25 years), than those who died due to cardiovascular causes (Me 10 years) or SLE activity (Me 15 years). In this cohort of patients, survival was 93% at 5 years, 88% at 10 years and 72% at 20 years.

Conclusion: Mortality in this series of patients was 12% and infection was the leading cause of death. The use of HCQ for a period greater than 36 months, decreased the risk of death 40%.

Disclosure of Interests: None declared

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FRI0606-HPR REMISSION IN SYSTEMIC LUPUS ERYTHEMATOSUS, WHAT IS THE IMPACT ON ACCUMULATED DAMAGE?

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Background: The objective of the treatment in rheumatic diseases is to achieved the remission or minimal disease activity of these patients. Previous studies in Systemic Lupus Erythematosus (SLE) showed that reaching remission had a positive impact on the prognosis of the disease.

Objectives: To determine the frequency of remission in a cohort of patients with SLE.

To evaluate the effect of disease activity on accrual damage.
Methods: A retrospective study was carried out from January 2010 to December 2018. Clinical records of patients with SLE (ACR criteria 1982/97) were reviewed considering baseline visit as the first clinical or control visit of 2010. For subsequent visits, data were collected annually until 2018. SLE activity was defined for each visit according to GLADEL´s definition: 1- Remission Without Treatment (RwT): SLEDAI 0, without prednisone or immunosuppressive drugs (IS); 2- Remission on Treatment (RoT): SLEDAI 0, prednisone up to 5mg/day or immunosuppressive drugs in maintenance doses; 3- LDAS (Low Disease Activity Status): SLEDAI ≤ 4, prednisone up to 7.5mg/ ay and/or IS in maintenance doses; 4- Non-Optimal Activity Control (NOC): SLEDAI> 4, prednisone> 7.5 mg/ day and/or IS in induction dose. The use of hydroxychloroquine was allowed for all groups. For the analysis, patients who remained in remission (with and without treatment) or LDAS for at least 75% of the follow-up time were grouped and compared with patients who remained active during that same period. Demographic, laboratory, treatment related variables and death were studied. Accrual damage was assessed with SLICC / SDI. Patients with less than two annual visits were excluded.
Statistical analysis: descriptive measures, Test T, Mann Whitney, Chi2 Test, Fisher's exact test, bivariate correlation, logistic regression model with mixed effects.
Results: Two hundred eighty-five medical records were reviewed and 100 patients with SLE were included, 89% women, mean age at baseline visit 38.5 ± 12 years old and mean time of disease 9.3 ± 7.3 years. The average SLEDAI and SLICC/ SDI baseline scores were 3.7 and 0.8 respectively. The SLICC/ SDI score at last visit was 2.2 and the average SLICC/SDI change (ΔSLICC) compared to baseline visit score was 1.4 ± 1.6.
The prevalence of patients who were in remission for at least 75% of the follow-up time was 38% [95% CI 26.6, 45.4]. NOC patients categorized at baseline visit had the highest ΔSLICC (p 0.0001). The ΔSLICC was significantly lower in patients who were at least 75% of the follow-up time in remission (p 0.01) or LDAS (p 0.01) compared to those with NOC. In the Logistic Regression Model, the chance of changing the SLICC/SDI score was 2.9 times higher for the NOC group than for RwT.
Conclusion: The frequency of remission in this cohort of patients with SLE was 38%.
Worse control of disease activity, was associated with higher accumulated damage.
Disclosure of Interests: None declared
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FRI0607-HPR FREQUENCY AND PATIENTS BELIEFS ON VACCINATION IN RHEUMATIC DISEASES

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Background: Infectious diseases are increased in patients with rheumatic disorders; vaccination improves morbidity and mortality
Objectives: The aim of this study was to describe the frequency of vaccination in patients with rheumatic disorders and to compare the results with those obtained in 2009 and 2013 in a similar population. We also identified factors leading to lack of vaccination and patients beliefs on vaccines.
Methods: Multicentric cross sectional study in patients with autoinmune diseases from external rheumatology offices. Evaluation of vaccination status and patients´ knowledge about vaccines were studied. A comparative analysis was carried out with the series registered in 2009 and 2013 in a similar population.
Results: 179 patients (158 female, 88.3% and 21 male, 11.7%) were evaluated. Median age was 52 years. Main pathologies were: Rheumatoid Arthritis 65.9% (n:118), Systemic Lupus Erythematosus 11.7% (n:21), Systemic Sclerosis 3.9% (7), Sjogren Syndrome n = 3.4% (n:6), other diseases 15% (n: 27). Median disease duration: 8.87 years. Ninety three percent of patients (n:167) were taking inmunomodulators and 36.8% (n: 66) were using oral corticosteroids (20mg/ day or less); 26,8% patients (n: 48) were receiving biological therapies. Vaccination frequency in the population was: Influenza 82% (147); 13-valent conjugate pneumococcal 69.3% (124), 23-valent pneumococcal 64.2% (115) and hepatitis B 62% (111). Comparative with 2009 and 2013 series there was an increase in the rate of vaccinated patients: influenza (82% vs. 39,1% and 74,2% respectively), antineumococcal (64% vs. 17% and 29%) and hepatitis B (62% vs. 6,7% and 26,7%).
Reasons for non-vaccination were absence of medical indication (41% of patients for hepatitis B; 32% for 23-valent pneumococcal; 38% for 13-valent pneumococcal and 34% for influenza).
139 patients (77, 7%) knew the benefits of vaccines, 164 (91, 6%) thought vaccines are useful; 134 (74,9%) reported that vaccines may decrease dying probability, 155 (86,5%) thought that vaccines are effective to prevent diseases and 149 patients (83,2%) believed that they prevent serious infections. 71 patients (39%) believed that vaccines can lead to serious consequences and 99 (55,3%) that they are more likely to acquire infections than the rest of the population.
Conclusion: Frequency of vaccination has increased since 2009 but there is still misinformation regarding vaccines risks and benefits. Promotion and information is essential to improve adherence.
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FRI0608-HPR SEVERITY AND PREDICTORS OF PAIN INTENSITY AND HAND DISABILITY IN PATIENTS WITH TRAPEZIOMETACARPAL OSTEOARTHRITIS

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Background: Trapeziometacarpal osteoarthritis (TMO) is one of the most prevalent and painful forms of hand osteoarthritis.[1] It limits thumb mobility,[2] reduces hand functions, and manual activities.[1] Yet, no study has exhaustively documented the characteristics of this pathology using a biopsychosocial approach (e.g., pain, disability, psychological well-being, pain-related catastrophic thinking, quality of life). Furthermore, radiographic TMO severity and symptomatology are only weakly to moderately correlated.[3, 4] The extent to which biopsychosocial factors (e.g., pain duration, depression, education) contribute to interindividual variability in TMO pain and hand disability merits further investigation.
Objectives: This study aimed at 1) describing the pain experience of patients with trapeziometacarpal osteoarthritis (TMO) from a biopsychosocial perspective, and 2) identifying predictors of their pain intensity and hand disability.
Methods: A total of 227 TMO patients recruited from 16 healthcare institutions completed validated questionnaires assessing their biopsychosocial characteristics. The associations of pain severity and hand disability with various biopsychosocial characteristics were analyzed by linear regression.
Results: The participants' mean age was 62.6 ± 8.5 years and 78% were women. Their mean pain intensity on the average in the last seven days was 5.8 ± 2.1 while their hand disability scores averaged 45.4 ± 18.8 on the QuickDASH. In terms of health-related quality of life, the participants' scores on the physical and mental summary scales of the SF-12v2 were 41.0 ± 9.4 and 48.7 ± 9.7 respectively. Results of the multivariable linear regression analyses revealed that age, living condition, pain frequency, pain-related catastrophic thinking, and depression levels accounted for 43.3% of the variance in pain intensity while age, sex, pain intensity, pain-related catastrophic thinking, depression, level of education, employment status and living condition accounted for 60.6% of the variance in hand function.
Conclusion: This comprehensive study showed that patients with TMO experience pain of moderate to severe intensity which can affect various aspects

of their daily living and their physical health-related quality of life. Greater tendency to catastrophize in the face of pain and higher depression levels were associated with more severe pain suggesting that psychological interventions aiming at reducing these factors could be beneficial for some patients with TMO.

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FRI0609-HPR NUTRIENTS INTAKE CONDITION RELATES TO MAINTENANCE LOW DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS DURING 6 YEARS: TOMORROW STUDY

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Background: We have previously reported that nutritional intake status might relate to disease activity (1). Nutritional survey on prospective cohort study in rheumatoid arthritis (RA) patients and information about relationship between nutritional intake status and disease activity was very limited.

Objectives: This study aimed to obtain data from a cohort study for new nutritional therapy in RA patients.

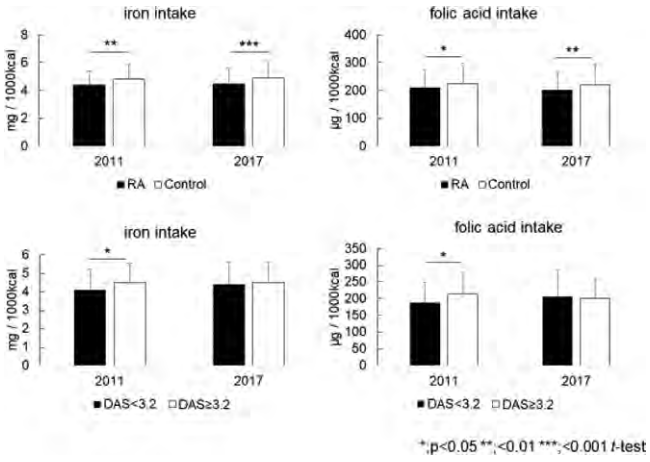
Methods: We used TOMORROW cohort study data which conducted from years of 2010 to 2020. Two hundred and eight RA patients, and 205 non-RA sex and age matched controls were investigated, and we analyzed data from 2011 to 2017. Nutritional intake status was compared between who maintain lower disease activity during 2011 to 2017 (LDA group) and being higher disease activity even once in 2011 to 2017 (non-LDA group). Disease activity was evaluated by DAS28-ESR in every year and nutritional intake status was surveyed by brief self-administered diet history questionnaire (BDHQ) in 2011 and 2017.

Results: In RA patients, the change value from 2011 to 2017 of iron (odds ratio; 2.37), thiamin (OR; 2.96) and folic acid (OR; 3.16) intake which adjusted by energy intake, age, rheumatoid factor and medication status were extracted as independent factors for maintain LDA by multivariate logistic regression. These nutrients intake in RA patients was significantly lower than control both in 2011 and 2017. In RA patients, iron and folic acid intake in LDA group was significantly lower than non-LDA group in 2011. Folic acid intake was increased in LDA group and decreased in non-LDA group over time, and these nutrients showed significant differences in change value between LDA group and non-LDA group ($p<0.05$).

Conclusion: The overtime change value in iron, thiamin and folic acid related to maintain six years low disease activity in RA patients.

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FRI0610-HPR β-ADRENORECEPTOR BLOCKING DRUGS ASSOCIATE WITH LOWER RISK OF KNEE OSTEOARTHRITIS AND KNEE PAIN CONSULTATIONS IN PRIMARY CARE: A PROPENSITY SCORE MATCHED COHORT STUDY USING THE CLINICAL PRACTICE RESEARCH DATALINK.

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Background: The pharmacologic management of OA is centred around optimising pain control but first-line analgesics only have modest efficacy[1]. Findings from several studies suggest that *β*-adrenoreceptor blocking drugs (*β*-blockers) have anti-nociceptive effects[2 3]. However, evidence for the benefits of β-blockers in the context of OA pain is scarce. We recently demonstrated, for the first time, an association between beta-blockers and lower pain severity, and less opioid analgesic use in a secondary analysis of data for community dwelling adults with large-joint lower OA[4]. This association, however, was not confirmed in a hospital-based study[5].

Objectives: We examined [1] the association between *β*-blocker prescription and first primary care consultation for knee OA, hip OA, knee pain, and hip pain and [2] the classes of *β*-blocker drugs that reduce the risk of these outcomes.

Methods: This was a cohort study using data from the UK Clinical Practice Research Datalink. Participants aged ≥40 years, in receipt of ≥2 β-blocker prescriptions within 60 days were matched by age, sex, and propensity score (PS) for β-blocker prescription to one control using greedy nearest neighbour matching. Participants with chronic painful conditions, contra-indications to β-blockers,

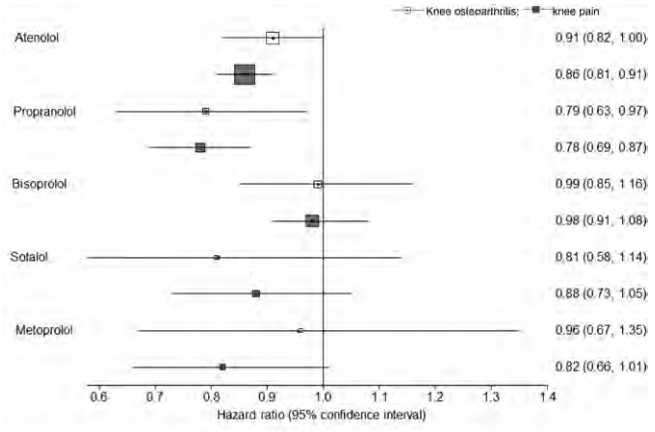
maintenance analgesic prescriptions, and with <2-years registration before index or matched follow-up start date were excluded. Cox proportional hazard ratios (aHRs) and 95% confidence intervals (CI) were calculated to examine the associations adjusted for other covariates. Analyses were stratified according to β-blocker classes.

Results: Data for 223,436 PS-matched exposed and un-exposed participants were included. β-blocker prescription associated with a significantly reduced risk of knee OA, knee pain, and hip pain consultations with aHR(95%CI) 0.90(0.83–0.98), 0.88(0.83–0.92), 0.85(0.79–0.90) respectively. The reduction in hip OA lacked statistical significance (aHR 95%CI 0.94; 0.83-1.07) (Table 1). On stratified analysis, propranolol and atenolol had a statistically significant protective effect on knee OA and knee pain consultations with aHRs between 0.78 and 0.91 (Figure 1).

Table 1. The association between β-blocker prescription and incident osteoarthritis and joint pain

Outcomes	Exposed	Events (n)	Person-time	Event rate (95% CI)*	HR (95% CI)[1]
Knee OA	No	986	262,003	3.76 (3.54 – 4.01)	1.00
	Yes	1,101	307,231	3.58(3.38 – 3.80)	0.90(0.83 – 0.98)
Hip OA	No	451	263,753	1.71(1.56– 1.87)	1.00
	Yes	530	310,045	1.71(1.57 – 1.86)	0.94(0.83 – 1.07)
Knee pain	No	3,074	255,003	12.06(11.64 – 12.49)	1.00
	Yes	3,560	297,027	11.99(11.60 – 12.37)	0.88(0.83 – 0.92)
Hip pain	No	1,767	259,515	6.81 (6.50 – 7.13)	1.00
	Yes	1,981	304,454	6.51 (6.23 - 6.80)	0.85(0.79 – 0.90)

OA; osteoarthritis, *1,000 person-years,[1]PS matched and, additionally adjusted for age, number of GP consultations, hospital out-patient referrals, hospital admissions in the 12 month period preceding cohort entry, total number of GP consultations for knee or hip injury prior to cohort entry and non-osteoporotic fractures.



[1]Comparison group is unexposed to β-blockers; size of the square is proportional to number of events.

Figure 1. The association between individual β-adrenoreceptor blocking drugs and incident knee osteoarthritis and knee pain[11]Comparison group is unexposed to β-blockers; size of the square is proportional to number of events.

Conclusion: β-blockers appear to reduce consultations for knee OA, and knee or hip pain. Our results imply that, atenolol might be used preferentially for the treatment of people with cardiovascular comorbidities, while, propranolol with its' anti-anxiety effect may be a suitable analgesic in people with OA and comorbid anxiety.

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FRI0611-HPR

EUROPEAN PRESCRIBERS' PERSPECTIVES ON BIOSIMILARS

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Background: Biosimilars are highly similar, but not identical to originator biologics. In an increasingly resource-constrained environment, switching patients from originator biologics to biosimilars is a growing practice in many jurisdictions. Though automatic substitution of originator biologics with biosimilars is rare in Europe, this practice excludes physicians from decisions regarding the treatment of their patients.

Objectives: As countries seek to control health costs and expand access to biologic therapies, building physician confidence in biosimilars is critical to promoting their use and reaping the cost benefits. This survey will empirically document their perspectives on biologic substitution. These findings may serve as a resource for countries in developing biosimilar policies which build physician confidence in biosimilars.

Methods: The Alliance for Safe Biologic Medicines (ASBM) commissioned 15-minute web-based surveys among biologic prescribers in 6 Western European countries. Respondents must prescribe biologic medicines, must practice in France, Germany, Italy, Spain, Switzerland, or United Kingdom, must specialize in one of 10 practice areas: Dermatology, Endocrinology, Gastroenterology, Hematology Oncology, Immunology, Nephrology, Neurology, Oncology, Ophthalmology, Rheumatology. This survey is a refresh of one conducted in 2013 (n=470) available at www.safebiologics.org/surveys.

Results: 579 responses were received, 14% from Rheumatologists (n=80). Biosimilar familiarity was high, increasing from 76% to 90% from the 2013 survey; with Rheumatologists the most familiar (99%). Similarly, the % of physicians who felt sole treatment decision authority was very important or critical had increased from 72% to 82%; among Rheumatologists again this figure was higher (85%). This pattern was found across many questions, for example the importance of retaining authority to prevent a substitution (a jump from 74% in 2013 to 84% in 2019 saying "very important or critical", with Rheumatologists higher than average at 90%). Rheumatologists had a higher than average comfort level prescribing biosimilars to new patients, but were the least comfortable with a third party switching their patient for non-medical reasons (e.g. cost): 49% were "very uncomfortable" compared to an average of 29% across specialties.

Conclusion: European physicians have increased their familiarity with biosimilars since 2013, with Rheumatologists the practice area with greatest familiarity. After 13 years of experience with biosimilars, Europe's prescribers consider maintaining physician control of treatment decisions to be highly and increasingly important; Remain uncomfortable with switching a patient to a biosimilar for non-medical reasons; Are highly (and increasingly) uncomfortable with a non-medical substitution performed by a third party. When looking specifically at Rheumatologists, these trends are even more pronounced.

Disclosure of Interests: Michael Reilly Grant/research support from: The organization of which I am executive director (ASBM) has received general grants from pharmaceutical companies., Madelaine Feldman: None declared

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FRIDAY, 05 JUNE 2020

HPR Interventions (educational, physical, social and psychological)

FRI0612-HPR

EFFECT OF THERMOFORMABLE ORTHOSES ON FOOT FUNCTION IN RHEUMATOID ARTHRITIS PATIENTS: PRELIMINARY RESULTS FROM AN OPEN CLINICAL TRIAL.

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Background: Orthoses and footwear can play an important role in managing foot pathology in patients whose systemic disease is controlled. Foot orthoses are frequently prescribed in clinical practice as an intervention for people with rheumatoid arthritis (RA).

Objectives: The aim of our study is to evaluate the impact of thermoformable orthoses on the functional index of the foot (FFI) in patients with rheumatoid arthritis.

Methods: We conducted an open clinical trial, having consecutively included 14 patients (85.7% female, average age 54.8 ± 10 years) suffering from rheumatoid arthritis (median progression time of 9 years [5 - 12]). The average DAS28 was 2.7 ± 1.2 and the functional impact objectified by the Health Assessment Questionnaire (HAQ) was on average 0.9 ± 0.7.

The median deadline from the start of RA and the onset of the foot problem was 3 years [0 – 7,75]. The foot problem was bilateral in 100% of the cases and inaugural in 85.7% of the cases.

We evaluated the functional impact of foot injury for all our patients at baseline and 8 weeks after the use of thermoformable orthoses, based on the FFI (Foot function Index) measuring the impact of foot pathology on function in terms of pain, disability and activity limitation.

The comparison of the FFI domains before and after the use of orthoses was carried out using parametric or nonparametric paired tests using The SPSS statistical software.

Results: With the use of foot orthoses, FFI values decreased in all subscales (p=0,024) (pain, disability and activity limitation). This reduction was significant for disability (0,011) but not for pain and activity limitation.

There were no significant correlations between the global FFI and the progression of RA, the duration of foot damage and the functional impact measured by the HAQ.

Table 1. The comparison of the FFI domains before and after the use of orthoses.

		Before orthoses	After orthoses	*p*-value
Pain scale	When the pain was the worst	9 [5,7 – 10]	7 [4,7 – 8]	0,09
	Pain in the morning	4,5 [2,2 – 6]	2 [0 – 3,5]	0,046
	Pain when walking barefoot	6 [4 – 8]	6,5 [3,7 – 8]	0,719
	Pain when standing barefoot	6 [3,7 – 7,2]	6 [3 – 7,2]	0,723
	Pain when walking with shoes	5 [2,7 – 5,2]	3,5 [2 – 5,2]	0,378
	Pain when standing with shoes	5 [2,7 – 6]	3,5 [2 – 5,2]	0,342
	Pain when walking with orthoses	0 [0 – 0]	0 [0 – 2]	0,157
	Pain when standing with orthoses	0 [0 – 0]	0 [0 – 2]	0,317
	Pain at the end of the day	6 [4 – 8]	3 [2 – 5,2]	0,027
Disability scale	Difficulty walking at home	4 [3 – 5,2]	2 [0 – 2]	0,002
	Difficulty walking outside	6 [4,7 – 7]	2 [1,5 – 2,5]	0,019
	Difficulty walking 800m	6 [3,7 – 7]	2 [1,5 – 2,5]	0,003
	Difficulty climbing stairs	5,5 [3 – 7,2]	3 [1 – 5,2]	0,032
	Difficulty descending stairs	5,5 [3 – 7,2]	3 [1 – 5,2]	0,022
	Difficulty standing on tiptoe	6,5 [5 – 10]	7 [2,5 – 9,2]	0,687
	Difficulty getting up from a chair	5 [4 – 6,2]	3 [3 – 5]	0,032
	Difficulty climbing a sidewalk	4 [2 – 5,5]	3 [0 – 5]	0,137
	Difficulty walking fast	5[2,2 – 6]	3,5[0 – 8]	0,648
Activity limitation	Stay all day at home	2[1,5 – 5,2]	0 [0 – 2]	0,077
	Stay all day lying down	2[0 – 4]	0 [0 – 2]	0,122
	Limitation of activities	2 [2 – 5]	1 [1 – 2,2]	0,1
	Use of indoor walking aids	0 [0 – 0]	0 [0 – 0]	1
	Use of walking aid outside	0 [0 – 0]	0 [0 – 0]	0,18
Pain scale		37[32,5 – 47,5]	36[24,5 – 40,5]	0,198
Disability scale		49[34 – 59]	27[13,2 – 46,2]	**0,011**
Activity limitation		7[5,5 – 7]	2,5[0 – 5,2]	0,126
Total FFI score		95[82 – 106]	65,5[37,5 – 87]	**0,024**

p significatif if< 0,05; Test used: Non-parametric test for two linked samples.

Conclusion: Foot orthoses were effective as an adjuvant in the management of rheumatoid foot. They significantly reduced disability as measured by the FFI. The absence of factors associated with pain and limitation of activity could possibly be related to the small sample size.

Disclosure of Interests: None declared

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FRI0613-HPR THE EFFECTS OF PILATES TRAINING ON RESPIRATORY MUSCLE STRENGHT IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Ankylosing Spondylitis (AS) is a chronic, inflammatory rheumatic disease that effects primarily axial spine. Reduction in flexibility and mobility is important factors that can cause muscle weakness, impairment quality of life, reduction of exercise tolerance and pulmonary capacity with the progression of AS.

Objectives: The purpose of this study was to investigate the effects of pilates exercises on mobility, quality of life and respiratory muscle strength in patients with AS.

Methods: Forty patients with AS were randomly divided into two groups as pilates group and control group. Pilates group was performed pilates exercises and control group performed conventional exercises at home for 8 weeks, 3 days a week. Main outcome measures were maximal inspiratory pressure (MIP), maximal expiratory pressure (MEP). Secondary outcome measures were Forced Vital Capacity (FVC), Forced expiratory volume in one second/Forced Vital Capacity (FEV1/FVC), chest expansion, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Metrology Index (BASMI) and Ankylosing Spondylitis Quality of Life Questionnaire (ASQoL), 6 minutes walk test (6MWT). All participants were assessed by a blind assessor before and after the study.

Results: Thirty-six AS patients (n=19 in the pilates group, n= 17 in the control group) completed the study. In the pilates group, respiratory muscle strength, FEV1/FVC, chest expansion, BASDAI, BASMI, ASQoL and 6MWT showed significant improvements at 8th week ($p<0.05$), while inspiratory muscle strength, FEV1/FVC, chest expansion and 6MWT showed significant improvements in the control group at 8th week compared to baseline ($p<0.05$). Although the pilates group had better outcomes for all parameters compared to the control group, significant differences were only observed in MIP and MEP.

Conclusion: Pilates method is an effective method for improving respiratory parameters, spinal mobility, disease activity and quality of life. Additionally, pilates training is found to be superior compared to conventional exercise training in improving respiratory muscle strength.

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Disclosure of Interests: None declared

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FRI0614-HPR RECOMMENDATIONS FOR PATIENTS WITH RHEUMATIC DISEASES IN TREATMENT WITH METHOTREXATE

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Background: Methotrexate (MTX) is the first choice disease-modifying anti-rheumatic drug (FAME) in the treatment of rheumatoid arthritis among other rheumatic diseases. It is therefore very important that patients are aware of this treatment and have an adequate management of it.

Objectives: The development of a recommendation leaflet for patients with rheumatic diseases in treatment with MTX.

Methods: A systematic review of the literature was conducted, defining the criteria for inclusion and exclusion of content. The coordinators of the work generated preliminary recommendations that were evaluated and discussed in GESVR meetings and 10 recommendations on the use of MTX were accepted, which were later ratified by the Valencian Society of Rheumatology.

Results: The final document with a brief introduction indicates that MTX can be administered orally or subcutaneously, depending on the prescribed dose and its tolerance. In the case of subcutaneous administration, pre-filled syringes or pens are used which do not require any preparation, so there is no risk of handling and/or inhalation toxicity. The proposed recommendations are described below:

[1] MTX should be taken or administered ONLY once a week, and always on the same day of the week. It is important to follow these recommendations to ensure adequate effectiveness and avoid side effects.

[2] It is common to add a folic acid supplement the day after MTX is taken to avoid certain side effects of the drug. In some cases it may be necessary to increase the dose to other days of the week.

[3] Alcohol consumption should be avoided, as it increases the likelihood of adverse effects from the treatment.
[4] Common side effects include nausea or gastrointestinal distress, loss of appetite, headache and fatigue after taking each weekly dose of the drug.

If this happens, you can take the daily dose in two doses, avoid taking large amounts and drink plenty of water on the day of administration. If in spite of everything, they do not disappear, you should consult the Rheumatology Unit.

[5] It is recommended to use sun protection.
[6] Pregnancy and breastfeeding should be avoided while taking MTX. In case of pregnancy desire, you should consult the Rheumatology service in order to schedule a withdrawal of the treatment. In case of unplanned pregnancy, stop treatment and contact the Rheumatology Unit immediately.
[7] The annual flu vaccine is recommended. Consultation with the Rheumatology Unit is recommended for additional vaccines.
[8] The benefits of MTX take several weeks to appear, so you should not modify or interrupt the treatment on your own.
[9] Throughout the treatment, regular tests will be performed to monitor the safety and effectiveness of the drug.
[10] In case of doubts, and in case of infection, surgical intervention, oncological pathology or pregnancy, contact the Rheumatology Unit.

Conclusion: This leaflet is intended to resolve common doubts of patients receiving treatment with MTX, and thus contribute to improve the therapeutic adherence and avoid errors in the drug taking.

Disclosure of Interests: None declared

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FRI0615-HPR CAN DEDICATED COMMUNITY HEALTH HUBS IMPROVE PHYSICAL ACTIVITY IN A MULTI-ETHNIC RHEUMATOLOGY PRACTICE?

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Background: Self care is an important management strategy for people with inflammatory arthritis (IA). Focused education should enable people to manage their life with IA and optimise their health and well-being. Several studies have shown positive effects of dedicated health programs on a range of patient reported outcomes such as self-efficacy, pain, fatigue, quality of life and overall well-being. However these benefits are only achievable and long lasting if people are provided with professional support to stay motivated and make appropriate adjustments to obtain better health.

Objectives: The objective of our intervention was to assess the outcomes of a dedicated health education program delivered in a diverse community setting represented by minorities with poor educational and socio-economic background.

Methods: We partnered with our local authority to establish a dedicated rheumatology community health hub for our patients with long term rheumatic conditions. Both clinical and paramedical staff in rheumatology clinics advertised the service and those who consented were referred. They were offered a 1:1 assessment with a health and well-being practitioner who would refer onwards based on the needs of the patient. In this pilot study we analysed the outcomes achieved at one year.

Results: 187 patients were referred to the service. 158 had IA and 29 had osteoporosis. 57 (30%) were White, 86 (46%) Asian, 26 (14%) Afro-Caribbean and 18 (10%) of other ethnicity. Mean age was 64 years (range 36-95). Interventions included weight management (10%), general health check (4%), dedicated exercise program (30%), physical activities (46%) and talking therapies (8%) and smoking cessation (2%). 100% responded to the contact and signed up for the intervention. 80% completed a minimum of 12 week intervention. 89% continued to attend physical activity at least once a week long term. Only five service users dropped out for varying reasons.

Conclusion: Physical activity programs can be successful in a diverse community setting with patients from low socio-economic and educational classes. There is a need to engage these patients and offer professional support which can produce carry-over effects on physical outcomes and enhance patients' long-term adherence to such programmes. Our study demonstrates that patient activation for self management and improved physical activity can be attained irrespective of patients' backgrounds.

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FRI0616-HPR SOCIAL SUPPORT WORKS BETTER IN RHEUMATOID ARTHRITIS THAN FIBROMYALGIA

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Background: Social support is defined as a helpful resource that can meet an individual's urgent needs and is provided by a network of others, such as family members, friends, colleagues and other communities. Perceived social support (PSS) is the subjective support that individuals may experience, emphasizing the individual's self-understanding, experience and feelings of social support from different sources. Social support directly exerts beneficial effects on the health-related quality of life in rheumatoid arthritis and fibromyalgia patients.

Objectives: The aim of this study is to compare the effect of perceived social support on quality of life of rheumatoid arthritis and fibromyalgia patients. The effect of social support from family, friends and significant others are examined separately.

Methods: Fifty-eight patients with rheumatoid arthritis, fifty patients with fibromyalgia and fifty healhy controls were enrolled in the study. Short form 36 (SF-36) was used to determine the quality of life and Multidimensional Perceived Social Support Scale (MSPSS) was used to determine the percieved social support. The effect of three factors in MSPSS (family, friends, significant others) on quality of life of rheumatoid arthritis and fibromyalgia patients were examined seperately.

Results: Fibromyalgia patients had lower scores than the rheumatoid arthritis patients and healthy controls regarding the physical function, pain, social functioning and mental health subscales of SF-36 ($p<0.05$). Regarding the all MSPSS scores, there was no significant difference between the three groups ($p>0.05$). In rheumatoid arthritis patients, MSPSS-friend and MSPSS-significant others scores were positively correlated with all subscales of SF-36. MSPSS-family score was only correlated with pain, social functioning and mental health subscales of SF-36. But in fibromyalgia patients none of the three MSPSS scores had significant correlation with SF-36 subscales (Table-1).

Conclusion: Perceived social support especially from friends and significant others, has an important positive effect on the quality of life of rheumatoid arthritis patients. For fibromyalgia patients the effect of perceived social support on quality of life is lower than that is seen in rheumatoid arthritis.

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Table 1. The effect of perceived social support on quality of life in fibromyalgia and rheumatoid arthritis patients (FMS: Fibromyalgia, RA: Rheumatoid arthritis, *p<0.05 **p<0.01)

		SF-36 Physical functioning	SF-36 Pain	SF-36 General health	SF-36 Social functioning	SF-36 Mental health
FMS-MSPSS	r	-0.034	0.015	-0.187	-0.121	-0.115
Family	p	0.816	0.915	0.194	0.401	0.428
FMS-MSPSS	r	0.154	0.192	0.221	0.182	0.089
Friend	p	0.285	0.181	0.123	0.206	0.539
FMS-MSPSS	r	0.163	0.248	0.119	0.175	-0.004
Significant others	p	0.258	0.082	0.412	0.225	0.976
RA-MSPSS	r	0,181	0,290	0,225	0,448	0,340
Family	p	0,173	0,027 *	0,089	0,001**	0,009**
RA-MSPSS	r	0,357	0,352	0,333	0,376	0,389
Friend	p	0,006*	0,007**	0,011*	0,004**	0,003**
RA-MSPSS	r	0,310	0,310	0,329	0,315	0,463
Significant others	p	0,018*	0,018**	0,012*	0,016*	0,001*
RA-MSPSS	r	0,334	0,366	0,350	0,432	0,487
Total	p	0,010*	0,005**	0,007**	0,001**	0,001**
FMS-MSPSS	r	0.144	0.251	0.093	0.153	0.024
Total	p	0.320	0.279	0.519	0.290	0.867

Disclosure of Interests: None declared

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FRI0617-HPR GRADED MOTOR IMAGERY IN POSTTRAUMATIC STIFFNESS OF THE ELBOW: A PILOT STUDY

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Background: Elbow fracture is treated either conservatively or surgically followed by a period of immobilization with casting or splinting. A splint used to immobilize

upper limbs for many weeks results in changes in both the peripheral musculature and the central nervous system. It is well known that common complaints after upper limb fractures include weakness, pain, and stiffness; therefore, pain management is important in the early stages of the rehabilitation of upper limb fractures.

Objectives: This pilot study aimed to investigate the efficacy of graded motor imaginary (GMI) on pain, range of motion (ROM), and function in patients with posttraumatic stiff elbow.

Methods: Fourteen patients with posttraumatic stiff elbow (6 women, mean age: 45.42 ± 11.26 years, mean body mass index: 24.29 ± 3.38 kg\m^2 and mean duration of immobilization: 4.75 ± 1.03 weeks) were randomly allocated to either GMI or control groups. The GMI group received GMI treatment in addition to a structured exercise program, and the control group received a structured exercise program (two days per week for six weeks) (Figure 1). The assessments included pain at rest and during activity using the visual analog scale (VAS), elbow active ROM with a digital goniometer (Baseline Evaluation Instrument, Fabrication Enterprises, Inc., White Plains, NY), and upper extremity functional status using the Disability of the Arm, Shoulder and Hand Questionnaire (DASH). The assessments were performed at baseline and after the 6-week intervention.

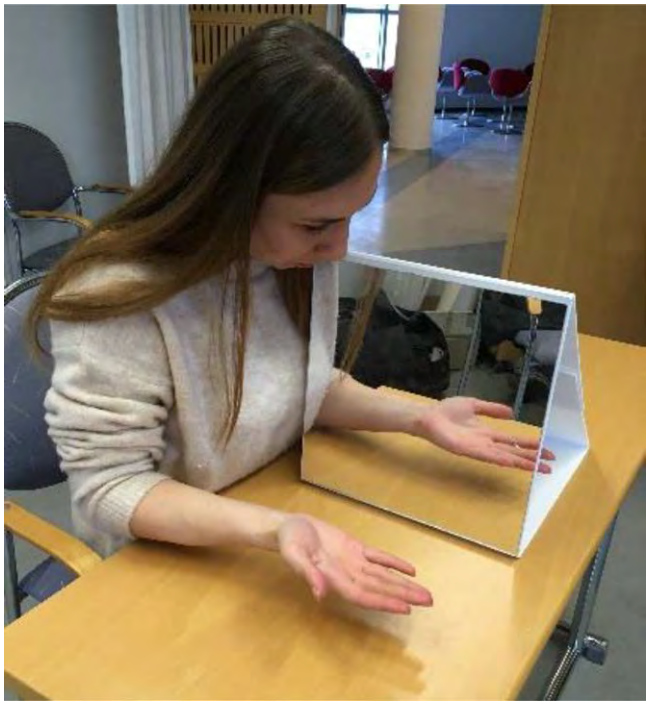


Figure 1. Graded motor imagery performed with mirror box

Results: After the 6-week intervention, there was a significant increase in elbow flexion-extension ROM and supination-pronation ROM, and improvement in DASH score in both groups ($p<0.05$). However, improvement in VAS-rest and VAS-activity was significantly higher in the GMI group than the control group ($p=0.03$ and $p=0.01$, respectively).

Conclusion: A conservative treatment program consisting of GMI treatment in addition to a structured exercise program applied twice a week for 6 weeks, has been found more effective in decreasing pain in the posttraumatic stiff elbow. It could be concluded that GMI is an effective treatment method for elbow fracture in patients with predominant elbow pain.

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FRI0618-HPR

EFFECTS OF MUSIC THERAPY ON PAIN, ANXIETY, AND VITAL SIGNS IN CHRONIC INFLAMMATORY RHEUMATIC DISEASES PATIENTS DURING BIOLOGICAL DRUGS INFUSION

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Background: Music therapy is based on ancient cross-cultural beliefs that music can have a "healing" effect on mind and body. Research determined that listening to music can increase comfort and relaxation, relieve pain, lower distress, reduce anxiety, improve positive emotions and mood, and decrease psychological symptoms. Music therapy has been used greatly in various medical procedures to reduce associated anxiety and pain. Patients have a high level of anxiety when they are in the hospital, this is the case of patients with rheumatic diseases who consult regularly to have intravenous infusion of biological therapies.

Objectives: The purpose of this study was to examine the effectiveness of music therapy on pain, anxiety, and vital signs among patients with chronic inflammatory rheumatic diseases during intravenous infusion of biological drugs.

Methods: Fifty patients were divided into two groups: The experimental group G1 (n=25) received drug infusion while lestening to soft music (30 minutes); and the control group G2 (n=25) received only drug infusion. Measures include pain, anxiety, vital signs (blood pressure, heart rate and respiratory rate). The pain was measured using visual analogic scale (VAS). The state-trait anxiety inventory (STAI) was used for measuring anxiety, low anxiety ranges from 20 to 39, the moderate anxiety ranges from 40 to 59, and high anxiety ranges from 60 to 80. Vital signs (systolic blood pressure [SBP], diastolic blood pressure [DBP], heart rate [HR], and respiratory rate [RR]) were measured before, during and immediately after the infusion. Statistical package for social sciences (SPSS) was used for analysis.

Results: The mean age in G1 was 44.45 years (26-72) with a sex ratio (M/F) of 0.8. Including the 25 patients, 12 had rheumatoid arthritis, 10 had ankylosing spondylitis and 3 had psoriatic arthritis. The mean disease duration was 8 years. In G2, the mean age was 46 years (25-70) with a sex ratio (M/F) of 0.75, 12 had rheumatoid arthritis, 11 had ankylosing spondylitis and 2 had psoriatic arthritis. The mean disease duration was 7.5 years. The biological drugs used were: Infliximab in 30 cases, Tocilizumab in 12 cases and Rituximab in 8 cases.

Before the infusion, the patients of experimental group had a mean VAS of 5/10±3, a mean STAI of 50.62±6.01, a mean SBP of 13.6 cmHg±1.4, a mean DBP of 8.6 cmHg±1, a mean HR of 85±10 and a mean RR of 18±3. While in control group the mean VAS was 5.5±2, the mean STAI was 50.89±5.5, the mean SBP was 13.4±1.2, the mean DBP was 8.8±1.1, the mean HR was 82±8 and the mean RR was 19±2.

During the infusion and after music intervention in G1, the mean STAI became 38.35±5 in G1 versus 46.7±5.2 in G2 (p value=0.022), the mean SBP became 12.1±0.5 in G1 versus 13±1 in G2 (p=0.035), the mean DBP became 8.1±0.8 in G1 versus 8.4±0.9 in G2 (p=0.4), the mean HR became 76±9 in G1 versus 78±7 in G2 (p=0.04) and the mean RR became 17.3±2.1 in G1 versus 18.2±1.7 in G2 (p=0.39). This study found a statistically significant decrease in anxiety, systolic blood pressure and heart rate in patients receiving music interventions during biological therapies infusion, but no significant difference were identified in diastolic blood pressure and respiratory rate.

Conclusion: The findings provide further evidence to support the use of music therapy to reduce anxiety, and lower systolic blood pressure and heart rate in patients with rheumatic disease during biological therapies infusion.

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Disclosure of Interests: None declared

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FRI0619-HPR

INVESTIGATION OF THE RELATIONSHIP BETWEEN BIOPSYCHOSOCIAL STATUS AND QUALITY OF LIFE, EMOTION - STATUS AND FUNCTIONALITY IN INDIVIDUALS WITH PSORIATIC ARTHRITIS.

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Background: Due to the chronic processes of rheumatological diseases, patients' biopsychosocial effects are revealed.

Objectives: The aim of this study is to evaluate the biopsychosocial status of individuals diagnosed with psoriatic arthritis; to examine the relationship between quality of life, emotion - status and functionality.

Methods: 105 individuals were included in the study. To evaluate the biopsychosocial situation, BETY-BQ (Bilişsel Egzersiz Terapi Yaklaşımı – Biopsychosocial Questionnaire)(1); Psoriatic Arthritis Quality of Life (PsAQoL) Scale to assess quality of life; For the emotion-status assessment; Hospital Anxiety and Depression Scale (HADS-A, HADS-D); Health Assessment Questionnaire (HAQ) was used for functionality. Pearson Correlation Analysis was used in statistical analysis.

Results: Descriptive data of the individuals participating in the study were recorded (Table 1).While BETY-BQ was highly correlated with PSAQoL Scale(r = 0.826,

p <0.001), moderate correlations were found with HADS-A and HADS-D (HADS-A (r = 0.618, p <0.001), HADS-D (r = 0.507, p <0.001)). Low correlation was found between BETY-BQ and HAQ (r = 286, p = 0.003) (Table 2).

Table1. Descriptive Statistics

	Minimum	Maximum	Mean	Standart Deviation
Age (years)	20	60	44.98	11.04
Height (cm)	145.00	190.00	165.61	8.88
Weight (kg)	44	138	75.54	17.36
VKI (kg/m^2)	17.85	49.00	27.54	6.02

Table 2.

	PsAQoL	HADS-A	HADS-D	HAQ
BETY-BQ	r 0.826** p<0.001	r=0.618** p<0.001	r=0.507** p<0.001	r=286** p=0.003

** Correlation is significant at the 0.01 level (2-tailed)

Conclusion: In this study, it was found that BETY-BQ is a scale that can be used in total to evaluate the quality of life, emotion-status level and functionality of individuals diagnosed with PsA. It was thought that BETY-BQ could be considered and preferred by clinicians when individuals with PsA should be evaluated from a biopsychosocial point of view.

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FRI0620-HPR THE EFFECT OF THERMOFORMABLE FOOT ORTHOSES ON WALKING IN RHEUMATOID ARTHRITIS PATIENTS: PRELIMINARY RESULTS FROM AN OPEN CLINICAL TRIAL

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Background: Foot pain is common in rheumatoid arthritis and appears to persist despite modern day medical management.

Objectives: To evaluate the impact of thermoformable foot orthoses on walking in rheumatoid arthritis (RA) patients.

Methods: This is a open clinical trial, that included 14 consecutive patients (85,7% female, mean age 54,8 ± 10 years) with RA (median duration of progression of 9 [5-12] years), the average DAS28 was 2,7+/-1,2 and the functional impact objectified by the Health Assessment Questionnaire (HAQ) was on average 0.9 ± 0.7. The foot problem was bilateral in 100% and inaugural in 85.7% of the cases.

The 14 rheumatoid subjects were examined and appropriate foot orthoses were prescribed according to each patient's needs. All the patients were evaluated at baseline and 8 weeks after use of orthoses. Gait pain, difficulty walking and the 10 Meter Walk test were noted at each appointment.

We used dynamic baropodometric analysis to assess postural evaluation. We calculated the lateral-medial index of each foot before and after the use of orthoses.

Table 1. Assessment of walking before and after the use of orthoses

	Before orthoses	After orthoses	p
Pain when walking*(EVA 0-10)	5 [3-5,2]	0 [0-2]	**0,002**
Difficulty walking* (0-10)			
- In house	4 [3-5,2]	2 [0-2]	**0,002**
- Outside	6 [4,7-7]	2 [1,5-2,5]	**0,02**
10 Meter Walk test**(Normal comfortable speed)			
- Nomber of steps	18,64 ± 3,7	16,9 ± 5	0,2
- Duration (sec)	11,9 ± 4,6	11,8 ± 5,2	0,9
- Walking speed (m/min)	56,4 ±17,7	58,6 ± 20,3	0,6
latero-medial (L/M) index**			
- L/M index of the right foot	1,18 ± 0,17	1,23 ± 0,23	0,1
- L/M index of the left foot	1,25 ± 0,17	1,26 ± 0,19	0,9

*median and quartile

**average and standard deviation

p significant if< 0,05

Results: A significant decrease in walking pain (p = 0.002) and difficulty walking (p = 0.02) was found with the use of orthoses. The variations in 10 meter walk test and dynamic baropodometric parameters were not significant (p>0,05).

There were no significant correlations between pain and difficulty walking, the progression of RA, the duration of foot damage and the functional impact measured by the HAQ.

Conclusion: Thermoformable foot orthoses significantly reduced pain and difficulty walking. The absence of factors associated with pain and difficulty walking could possibly be related to the small sample size.

Disclosure of Interests: None declared

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FRI0621-HPR CHANGES IN LOCUS OF CONTROL LEVEL IN PATIENTS WITH RHEUMATOID ARTHRITIS AFTER THE COURSE OF BIOFEEDBACK TRAINING

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Background:

Objectives: Our aim was to study the effect of biofeedback (BFB) training on the locus of control in patients suffering from rheumatoid arthritis (RA), and to justify the use of this method in the complex treatment of the disease.

Methods: 40 RA patients hospitalized in the rheumatology department were examined. The average age of patients was 48. 6 years ± 7.73 years (from 30 to 70 years), women accounted for the majority = 26 (86%), the average duration of the disease was 12 years ± 3.44 years. We use J. Rotter's Locus of Control Scale in E.F.Bazhin adaptation. RA patients were divided into two groups: the main (20 patients) and control (20 patients). Patients of the main group received complex therapy with 12 sessions of BFB training, mainly based on the parameters of the brain's electrical activity — EEG relaxation using the Reakor™ psychophysiological rehabilitation complex manufactured by Medicom MTD (Taganrog).

Results: We revealed externality in RA patients in the general field (3.03 ± 0.3), as well as in the field of relation to the disease (3.86 ± 0.23) and in the field of production relations (3.43 ± 0, 25). After BFB trainings, an increase in internality was observed on the scales of the general sphere (p <0.05) and attitude to the disease (p <0.01) in patients of the main group. In the group of patients receiving conventional treatment, the dynamics of the results was unreliable.

Conclusion: It should be noted that the locus of control (or subjective control) is a quality that characterizes a person's tendency to attribute responsibility for the results of his activity to external forces, or to his own abilities and efforts. Externality is manifested when people prefer to shift responsibility for important events of their life to external circumstances, and external forces (bosses, colleagues, etc.). In the field of attitude to the disease, externality is manifested when patient behaves passively, and believes that he cannot influence the course of the disease in any way, shifting all responsibility for the treatment results to medical staff, which can lead to non-compliance with the treatment regimen and an increase in the level of anxiety and depression, decreased self-esteem. The onset of the disease and its associated social consequences (disability, loss of social roles, etc.) can cause a negative mental state of learned helplessness. Learned helplessness is defined as a condition that occurs as a result of uncontrolled, mainly negative events, which manifests itself in violations of emotional, motivational and cognitive processes. In other words, RA patient suffering from this condition expects treatment failures and reduces control over compliance with the treatment regimen. BFB therapy can be used in order to correct and prevent the state of learned helplessness by increasing the level of internality.

It is assumed that increasing internality in the BFB process is associated with teaching the patient the skills of self-regulation of physiological processes. The mechanisms of BFB therapeutic effect are not only changes in physiological parameters (improvement of cerebral and peripheral blood flow, muscle relaxation, and improvement of sleep) but also in a shift in the locus of control from external to internal, which can increase compliance, reduce neurotic complaints, mobilize volitional potential and improve patient self-esteem.

As a result of BFB course, an increase in the internality was noted in patients on the scales of the general sphere and the sphere of attitude to the disease. It is advisable to use the BFB to increase the compliance and effectiveness of complex treatment of RA patients.

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FRI0622-HPR IMPACT OF A PHARMACIST'S INTERVENTION ON THE KNOWLEDGE OF BIOLOGICS AND ADHERENCE IN PATIENTS WITH SPONDYLOARTHRITIS: A RANDOMIZED, OPEN-LABEL, CONTROLLED TRIAL

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Background: In chronic rheumatic diseases, non-adherence to treatment is associated with a progression of disease and an increased morbidity (1). In spondyloarthritis (SpA), improving patients' knowledge on their subcutaneous biologic disease-modifying antirheumatic drugs (bDMARDs) is a key factor to enhance medication adherence (2). The patient information has to ensure the acquisition of safety skills regarding their treatment management.

Objectives: To evaluate the impact of a pharmacist's educational interview on knowledge and therapeutic adherence of subcutaneous bDMARDs in patients with SpA.

Methods: *Population and study design:* consecutive adult patients with well-controlled axial SpA, stable on subcutaneous bDMARDs were enrolled in a randomized, controlled, single-center, open-label, 6-months trial. *Intervention:* A pharmacist's educational interview provided information on bDMARDs management at baseline in the intervention group (IG) and at month 6 (M6) in the control group (CG). A booklet containing essential information was given to the patient. *Intervention allocation:* After written consent, the study treatment was randomly allocated via a computer program by simple randomization, with an allocation ratio of 1:1. *Outcome measures:* The change of a weighted knowledge score (0 – 100) concerning the bDMARDs management and the change in the Medication Possession Ratio (MPR) at M6 were primary outcomes. The changes in disease activity (BASDAI) and patients' satisfaction regarding the pharmacists' interview were secondary outcomes. *Statistics:* Changes in knowledge score, MPR and BASDAI were compared between the two groups using the T-Student test. Statistical analysis was performed in intention-to-treat. Missing data was handled with multiple imputations.

Results: Patients' characteristics at baseline were comparable among the 89 included patients (46 in IG, 43 in CG). The means ± SD of the knowledge score were 75.3 ±14.2 versus 73.0 ±13.2 and 86.3 ±12.6 versus 76.0 ±14.1 in the IG versus CG at baseline and at M6, respectively. The patient's knowledge score improved at a greater magnitude in the IG (+11.0 ±11.5 versus +3.0 ±10.6 in the IG versus the CG respectively, p<0.0001). The MPR at baseline were very high in both groups (92.9 ±14.6% versus 96.6 ± 15.6% in the IG versus the CG, respectively). There was a trend in a better adherence (+2.2 ±13.9 versus -0.6 ±18.9 in the IG versus the CG in the MPR score respectively, p = 0,691). The disease activity (changes in BASDAI) remained stable during the study in both groups. All the patients were mostly or totally satisfied by the pharmacists' interview.

Conclusion: Pharmacists' educational interview on subcutaneous bDMARDs is effective in improving the knowledge of patients with SpA on their treatment. Regarding therapeutic adherence, a trend in favor of an improvement was observed in the intervention group but did not reach the statistically significance. Nevertheless, the results observed in this study are an argument to propose to include the pharmacists in the multidisciplinary team in charge of the management of patients with SpA.

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FRI0623-HPR HEALTHCARE RESOURCE USE IN PATIENTS WITH TRAPEZIOMETACARPAL OSTEOARTHRITIS

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Background: Trapeziometacarpal osteoarthritis (TMO) is one of the most debilitating forms of hand osteoarthritis (OA). According to the recent EULAR guidelines[1, 2] and a systematic review,[3] the efficacy of topical/oral non-steroid anti-inflammatory drugs (NSAIDs), orthoses, hand exercises, and psychosocial interventions for hand OA or TMO are supported by scientific evidence. Cortisone injections and acetaminophen are generally not recommended.[1, 3] Besides, TMO management is suboptimal: only 21% of patients receive rehabilitative interventions prior to referral to hand surgeons.[4]

Objectives: We aimed at documenting the types of treatment TMO patients employ and their healthcare resource use.

Methods: A total of 227 TMO patients recruited from 16 healthcare institutions completed a questionnaire about 1) received interventions, 2) analgesic strategies, and 3) healthcare professional consultations.

Results: Acetaminophen (64.3% of the participants), oral NSAIDs (31.7%), topical NSAIDs (11.9%), and nutraceuticals (7.9%) were the most commonly used medications. More than 70% of the participants reported having received cortisone injection(s) (72.5%) and orthosis (75.7%). More than half employed hand exercises, massage and heat/cold application. Relaxation/respiration, meditation, distraction, assistive devices, and joint protection principles were used by smaller percentages of participants (13.0-30.9%). Patients with TMO reported having consulted various types of healthcare professionals: family physicians, plastic/orthopaedic surgeons, radiologists-interventionists, rheumatologists, physiatrists, occupational/physical therapists, osteopaths, chiropractors, pharmacists, and acupuncturists. Only 4.8% of the participants reported having received psychosocial interventions.

Conclusion: TMO patients use numerous types of modalities to relieve their pain. Provision of evidence-based interventions tailored to their needs is clearly needed.

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FRI0624-HPR A SYSTEMATIC REVIEW OF JOB LOSS PREVENTION INTERVENTIONS FOR PERSONS WITH INFLAMMATORY ARTHRITIS.

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Background: Persons with inflammatory arthritis (IA) have a higher level of absenteeism from work than those without IA and up to 20-30% become permanently work-disabled during the first years after being diagnosed with IA. Despite developments of new pharmacological and surgical treatments, people with IA still report reduced work ability. It is therefore relevant to offer effective interventions designed to prevent job loss and improve work function (i.e. job loss prevention interventions) to support people with IA to stay connected to the labour market. Initial effects of job loss prevention interventions have been established in a Cochrane review by Hoving et al. 2014 (1), but as only three randomized controlled trials (RCT) were identified, it seems relevant to investigate if new evidence has emerged.

Objectives: The aim of this study was to present an overview of the evidence of the effect of job loss prevention interventions, which can improve work participation and decrease absenteeism and job loss in persons with IA.
Methods: A systematic literature search was performed in the databases PubMed, EMBASE, CINAHL, PsycINFO and the Cochrane Library in two steps: 1) an update of the Cochrane review, restricted to studies published from January 2014 to February 2019 and 2) an additional search with updated keywords with no time restriction. Quality assessment and data extraction were performed independently by two authors. The results were summarized narratively.
Results: The first search identified 1276 titles and the second search identified 2384 titles. Six studies (including the three RCT´s included in the Cochrane review (1)) were included. The results indicated that job loss prevention interventions may have effect on work ability, absenteeism and in particular job loss, but the results across study outcomes, were not consistent. This may be due to heterogeneity in the interventions delivered (i.e. dose, duration and setting) and outcome measures used. Most of the studies were of low quality. Therefore, the results should be interpreted with caution.
Conclusion: Job loss prevention interventions may have an effect on work ability, absenteeism and in particular job loss among persons with IA. Further studies of high quality regarding job loss prevention interventions for people with IA are recommended.
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Disclosure of Interests: Christina Merete Tvede Madsen: None declared, Sara Kjaer: None declared, Jette Primdahl Speakers bureau: BMS and Pfizer, Jeanette Reffstrup Christensen: None declared, Cecilie von Bülow: None declared
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FRI0625-HPR APPS TARGETING SYMPTOMS ASSOCIATED WITH SJÖGREN'S SYNDROME AND POTENTIAL USERS' PERCEPTIONS OF THEIR FEATURES: CONTENT ANALYSIS AND THINK ALOUD STUDY

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Background: Sjögren's syndrome (SS) is a rheumatic disease requiring self-management which may be delivered through smartphones. When developing digital interventions it is important to review what is already available (market segmentation)[1] to identify unique selling points and aid uptake and adoption. While there are no dedicated SS apps, many are publicly available for other rheumatic conditions[2]. Understanding user preferences for existing apps may help to design an engaging app for SS self-management.
Objectives: To explore apps targeting SS symptoms of dryness, sleep disturbances, fatigue and pain. To explore views of people with SS on these app features.
Methods: Apple Store apps were retrieved on 04 March 2019 using the following search terms: *dry, dry eye, sleep, insomnia, fatigue, tiredness* and *pain*. Included apps were English and in Medical or Health & Fitness genres. Exclusion criteria were; duplicates, additional external devices required and apps targeting alcohol reduction or children.
Included apps were grouped by symptom. App descriptions were open-coded to generate a thematic coding framework (i.e. full list of features) for each symptom which was then applied to all app descriptions. To obtain views of people with SS, several of the reviewed apps for each symptom covering the full list of features were given to 13 focus group participants to use in 'think aloud' sessions (n=4). Audio data was recorded, transcribed and deductively analysed using the framework to gather opinions relating to each feature.
Results: Of 914 apps retrieved, 542 were included. Features within apps targeting dryness (n=15) provided dry eye information, self-assessment and reminders to blink or look away from screens. Apps targeting sleep (n=310) included features to support sleep restriction, sleep hygiene, sleep tracking (sleep onset and wake up times, time in bed, overall sleep quality), relaxing sounds, guided meditation, sleep stories, snore recording and alarms. Fatigue apps (n=79) included features to detect current physical and mental fatigue levels, support pacing (i.e. track fatigue, label tasks as 'high energy', prioritise tasks), and self-massage instructions. Apps targeting pain (n=138) featured pain tracking (of severity, affected body areas), guided exercises, and mindfulness.
Dryness apps prompted participants to reflect on its impact on daily activities, but further dryness features were desired relating to: using a humidifier; eye drop reminders; and dryness tips for other body areas e.g. vaginal dryness. Sleep restriction features were believed to be irrelevant but viewing and selecting sleep hygiene tips to "try" were considered useful. Beyond entering sleep onset and wake up times, participants wished to track "when and why I woke up", to understand night awakenings in relation to other symptoms. Fatigue detection features were felt to be more useful for those recently diagnosed, as experienced participants could easy identify when they were fatigued ("I don't need an app to tell me!"). Participants valued pacing features but found them difficult to use. Daily pain tracking was considered demotivating, but useful for remembering and explaining issues to healthcare professionals. Participants believed that a dedicated app for SS would support self-management and raise SS awareness.
Conclusion: Existing apps targeting SS symptoms do not meet the needs of those with SS. App features should be tailored to SS by supporting dryness management in body areas beyond eyes, and night-awakenings. Pacing features must be easy to use. The ability to track pain should be optional and tracking prompts should be limited. Design considerations should be implemented alongside evidence-based behaviour change techniques to support self-management.
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FRI0626-HPR DEVELOPMENT OF A TOOL TO SUPPORT PATIENT AND NURSE IN COMMUNICATING ON SELF-MANAGEMENT SUPPORT NEEDS PROJECT OF V&VN RHEUMATOLOGY RESEARCH GROUP

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Background: Self-management, ability of patients to optimally integrate their illness or disorder into their daily lives, is explicitly part of the new definition of health.
Self-management is considered essential in rheumatology care but is also a challenge for patients and rheumatology nurses. Often patients need support, but clarifying their support needs is difficult. Also, nurses experience difficulties in providing self-management support. A communication tool might help patients and nurses.
Objectives: In preparation for development of an online self-management program, a framework comprising 55 needs from 11 different domains has been developed (1).
The objective of this study is to develop a tool, based on this existing framework that can support patients and nurses in making targeted choices for adequate support.
Methods: The tool was developed in two steps. First, it was explored if existing framework as such was useful as a basis for the tool. It was discussed in a brainstorming session with rheumatology patients and rheumatology nurses. Second, two additional workshops, one with patients and one with nurses were organised. In these sessions, yellow cards with 55 needs from the framework (1) were compared with a more generic framework for self-management support in chronic diseases: the self-management web (2), figure 1. Goal of the workshop was to gain insight into usability of models and to gauge the ideas for a tool. The choice for these two models was based on the scientific background as well as the use with patients with a chronic or rheumatic disease.



Picture 1 : Workshop

Results: In the first brainstorming session 5 patients and 5 rheumatology nurses participated.

In the workshops, 11 patients and 130 nurses participated. Eligible adult patients, diagnosed with a rheumatic disease, were recruited by newsletter from the Dutch Arthritis Foundation. Nurses were recruited by newsletter from the Dutch Nurses Organisation (V&VN).

According to participants, the framework alone is only useable when additional explanation and illustration of concepts will be provided and following missing topics are added; communication between specialisms, knowledge of the healthcare system, responsibility allocation, faith, religion, culture, nutrition, lifestyle, prevention.

The self-management web appeared to be helpful. Not all cards with needs could be placed in this web. It was suggested to add following topics to the web: Peer support or experience experts' contact, handling treatment recommendations, patient empowerment, defining limitations and supporting services like physiotherapy and municipality.

There is overlap between topics of the web: Lifestyle, leisure and self-care. It was suggested to place associated topics together or give the same colour.

Practical ideas for application of the web and about involving an experienced expert were discussed as well as the role of health professionals. Integration in e-health, linked to the medical file with visual support is preferred. Patients have to prepare themselves for consulting the nurse or doctor.

Communication plays a very important role for all elements. The tool should be usable for people with limited health literacy skills and nurses need skills like motivational interviewing for using the tool.

Conclusion: Existing frameworks seem useful as a scientific basis for the development of a communication tool for self-management support. Usability of a draft tool will be explored in a pilot study.

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FRI0627-HPR COGNITIVE DISORDERS IN SYSTEMIC LUPUS ERYTHEMATOSUS WITH JUVENILE-ONSET: ONE SINGLE CENTER EXPERIENCE

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Background: Juvenile-onset SLE (jSLE) is a more aggressive disease than in adults due to several reasons including cognitive dysfunction, significantly affected the compliance and social rehabilitation of patients (pts).

Objectives: To analyze the cognitive, emotional and communicative status of pts with jSLE.

Methods: The study included 31 pts (90.3% girls) with jSLE, verified in accordance to SLICC criteria 2012. All pts underwent standard examination in accordance with the diagnosis; in case of suspected neuropsychiatric disorders pts were examined by a neurologist, psychiatrist. Classifying of neuropsychiatric disorders was performed in accordance with the recommendations of the ACR,1999. SLEDAI 2K was used for disease activity assessment. All pts were examined by a clinical psychologist using the standard pathodiagnostic testing.

Results: The median age at the onset was 12.0 y.o. [10.6;14.5]. The median disease duration at the time of diagnosis - 0.75 ys [0.5;2.1]. 35.5% pts had neuropsychic disorders at the onset: psychoses – 12.9%, headaches – 12.9%, cognitive disorders – 19.4%, mood disorders – 16.1%, distal polyneuropathy – 12.9%. MRI of the brain was performed in 15 pts: CNS vasculitis was diagnosed in 3 pts (2 – with psychosis, 1 – with cognitive impairment). Median disease activity by SLEDAI at the time of diagnosis was 15 scores [10;23].

At the time of examination by the clinical psychologist, the median age of pts was 15.2 ys [12.9;16.5]. The median disease duration was 1.1 ys [0.6;3.8]. Cognitive disorders were detected in 96.8% of the pts. The auditory-speech short-term memory was distributed between the medium and high levels (54.8% and 45.2%, respectively), and the high level of memorization prevailed in the long-term memory (67.7% high, 32.3% medium). A high level of indirect memory was revealed in 67.8% of pts, medium - in 25.8%, and low - in 6.4%. Distribution of the difficulties of attention were identified (64.5% - uneven distribution, 35.5% - sufficient distribution), as well as increased attrition of attention (74.2% - attrition is detected, 25.8% - no attrition). 58.1% of pts demonstrated a high level of inclusion into work, 41.9% - a low one. Concentration of attention was recognized as sufficient in 87.1% of pts, insufficient in 12.9%. The effectiveness of attention was rated as good in 87.1%, decreased – in 12.9%; stability is sufficient - in 64.5%, low - in 35.5%. In the operational side of thinking, a decrease in the level of generalization was revealed (48.4%); there were no disturbances in the motivational component, lability of thinking in the dynamic (12.9%). Various neurotic fears are characteristic for 54.8% of pts; the level of personal anxiety was increased in 41.9%, moderate - in 48.4%, low - in 9.7%. Signs of aggression were revealed in 19.4% of pts, a decrease in the level of social adaptation - in 51.6%. Communication difficulties experienced 83.9% of pts. According to the results of the clinical conversation, attention was focused on availability of conflict situations with peers in the disease onset in 38.7% of pts.

Conclusion: Cognitive disorders were detected in the majority of pts with jSLE, regardless of the presence of neuropsychiatric disorders at the onset. The revealed features of the clinical and psychological status of pts with jSLE must be considered when working out an individual rehabilitation model and develop psycho-correctional programs.

Disclosure of Interests: None declared

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FRI0628-HPR EVALUATING A COMPLEX PACKAGE OF CARE IN THE EAST-MIDLANDS KNEE PAIN FEASIBILITY COHORT RANDOMISED CONTROLLED TRIAL

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Background: The role of nurses in managing painful knee OA has been advocated but whether nurses can deliver such interventions as a package of care is unknown.The overall aim of this research is to develop and test a nurse-led complex intervention for knee pain comprising non-pharmacological and pharmacological components. In the first study phase, we report on fidelity and acceptability of a non-pharmacological intervention, to resolve possible challenges to delivery.

Objectives: To evaluate fidelity of delivery and acceptability of non-pharmacological components of a complex intervention.

Methods: This was a mixed-methods study. Participants with chronic knee pain were recruited from the community to receive the intervention, delivered in 4-sessions over a 5-week period by a trained research nurse. The intervention consisted of holistic assessment, patient education and advice, aerobic and strengthening exercise and weight-loss advice if required. All sessions were video-recorded. Fidelity checklists were completed by the nurse (nurse-rated) and two researchers from the video-recordings (video-rated). Median fidelity scores (%) and interquartile ranges (IQR) were calculated for each component and each session. Semi-structured interviews were conducted with participants. These were audio recorded, transcribed and analysed following the framework approach.

Results: 18 participants (34% women), with a mean (SD) age and BMI of 68.7 (9.0) years and 31.2 (8.4) kg/m^2, took part in the study. Of these, 14 completed all visits. In total, 62 intervention sessions were assessed for fidelity. Overall fidelity was rated high by both nurse-rated scores (97.7%) and video-rated scores (84.2%). The level of agreement between nurse-rated and video-recorded methods was 73.3% (CI 71.3, 75.3) and the inter-rater agreement was 65.5% (CI 60.3, 70.5). Fidelity of delivery was lower for advice on footwear modification and walking aids in all sessions and moderate for education in session 1 and for exercise in session 4 (Table 1).

Table 1. Fidelity scores of the components of the intervention for each session,

Intervention components	Session 1*	Session 2*	Session 3*	Session 4*
Education	78.1 (74.1, 93.7)	87.5 (50, 100)	87.5 (50, 100)	100 (93.7, 100)
Exercise	94.4 (88.9, 100)	88.9 (75, 94)	86.1 (72, 100)	75 (67.6, 82.8)
Adjunctive treatments	50 (45.83, 100)	0 (0, 50)	50 (0, 100)	-

*median (IQR)

17 participants were interviewed. Most found advice supplied straightforward. They were satisfied with the package, which changed their perception of

managing knee pain, understanding it can be improved though self-management. However, too much information was provided in a short time-span and it was difficult to fit exercises into their daily routine.

Conclusion: Delivery of a non-pharmacological intevention by a nurse is feasible within a research setting. Most components of the intervention were delivered as intended, except for advice about the use of adjunctive treatment.

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2019: Consultancy to AbbVie Ltd; 13.06.19; presentation on RA pain at EULAR, Madrid, and webinar (payments to University).
2019: Consultancy to Eli Lilly and Company Ltd. 06.06.19 Centre for Collaborative Neuroscience, Windlesham, Surrey, UK (payment to University).
2019: Consultancy to Pfizer (payment to University).
2018: Consultancy to Pfizer. 07.12.18. USA. 1 day. Tanezumab (payment to University).
2018: Consultancy to Pfizer. 23.11.18. Manchester UK. 1 day. Tanezumab (payment to University).
2018: Consultancy to Pfizer. 1.11.18. Skype. 4h. Tanezumab (payment to University).
2018: Consultancy to GlaxoSmithKline Plc. 1 day. Pain in RA and anti-GM-CSF (payment to University).
2018: Consultancy to Pfizer Ltd; Presentation at OARSI; non-personal financial disclosure (payment to University)
2018: Consultancy to Pfizer Ltd; Patient preference study; non-personal financial disclosure (payment to University)
2017: Consultancy to Pfizer Ltd; personal financial disclosure
2017: Consultancy to Pfizer Ltd through Nottingham University; non-personal financial disclosure (payment to University).
2015: Consultancy to GSK Consumer Healthcare; personal financial disclosure., Speakers bureau: 2019: Irish Society of Rheumatology: speaker fees (personal pecuniary), Ana Valdes Grant/research support from: Awarded a grant from Pfizer, Abhishek Abhishek: None declared

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FRI0629-HPR USE AND USABILITY OF THE DR. BART APP AND ITS RELATION WITH CLINICAL OUTCOMES IN PEOPLE WITH KNEE AND/OR HIP OSTEOARTHRITIS

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Background: Self-management is of paramount importance in non-surgical treatment of knee and/or hip osteoarthritis(OA). Modern technologies offer the possibility to support self-management 24/7. We developed an e-self-management application (dr. Bart app) for people with knee and/or hip OA.

Objectives: To document the use of the dr. Bart app and its relation with health care utilization and clinical outcomes in people with knee and/or hip OA.

Methods: For this study we used back end data of the first 26 weeks from the intervention group (N=214) of a RCT (total included 427) examining the effectiveness of the dr. Bart app. Participants were included based on self-reported knee and/or hip OA. In figure 1 the theoretical framework of the dr. Bart app is presented. A central element of the dr. Bart app is that the app proposes a selection of 72 preformulated goals for health behaviours based on the 'tiny habits method'[1] (e.g. today I rise 12 times from my chair to train my leg muscles). The proposals are tailored to user characteristics and related to four themes that are core elements in the non-surgical management of OA. After a user completes one or more of the selected goals, a new selection is proposed by dr. Bart. A user can work on 3 goals simultaneously. Goals can be completed more than once by the same user. To assess the association between intensity of use of the app and health care utilization and clinical outcomes, we calculated Spearman rank correlation coefficients.

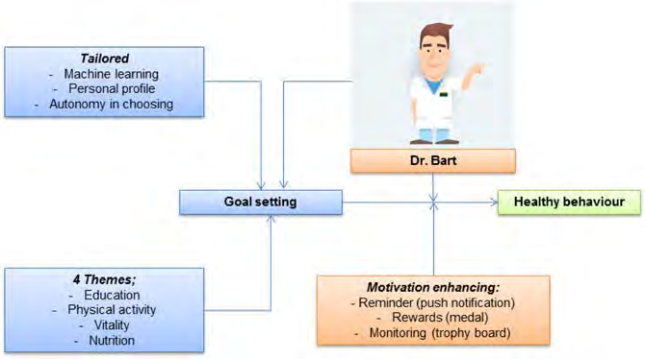


Figure 1. Theoretical framework of the dr. Bart app.

Results: 171 / 214 participants (80 %) logged in at least once whilst 151 (71%) chose at least one goal and 114 (53 %) completed at least one goal during the 26 weeks. Of those who chose at least one goal, 56 participants (37 %) continued to log in up to 26 weeks, 12 (8 %) continued to select new goals from the offered goals and 37 (25 %) continued to complete goals (Figure 2). Preformulated goals regarding the themes activity (e.g. performing an exercise from the exercises library of the app) and nutrition (e.g. eat 2 pieces of fruit today) were found to be most popular by users. We found no correlations between intensity of use and health care utilization and clinical outcomes.

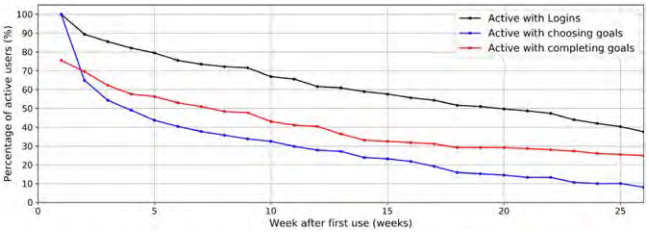


Figure 2. Percentage of active users (N=151) over time.

Conclusion: A considerable proportion of persons with knee and/or hip OA persistently used the app up to 26 weeks. Patients appear to have preferences for goals related to activity and nutrition, rather than for goals related to vitality and education. We found no relation between intensity of use of the dr. Bart app and health care utilization and clinical outcomes.

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FRI0630-HPR ONE-YEAR FOLLOW-UP OF A NURSE-LED TEAM INTERVENTION EFFECTIVE IN REDUCING THE NOCEBO EFFECT WHEN SWITCHING FROM ORIGINATOR INFLIXIMAB TO A BIOSIMILAR.

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Background: Nonspecific subjective adverse effects and symptoms (NSAE/NSS), usually considered as related to a nocebo effect (NE), have been identified as a barrier to the acceptability of switches from biologic originators (BO) to biosimilars (BS) in rheumatology. A multidisciplinary team intervention with a prominent role of nurses has provided a reduction of the NE assessed in the short-term during a systematic switch from originator Infliximab (OI) to the biosimilar infliximab SB2 (ref.1).

Objectives: To assess the intervention outcomes after one-year follow up in comparison with a historical cohort.

Methods: The intervention was developed after a literature search and semi-directive interviews of patients, and included consensual communication towards patients, with a prominent role of nurses (Ref.1). All patients with chronic inflammatory rheumatic diseases (CIRD) treated by OI were included and followed-up

in routine care. The outcomes were I) SB2 retention rate (RR) II) SB2 discontinuation rate due to a presumed NE, defined as lack of efficacy with no objective criteria for increased inflammation or non-objective and non-specific adverse event, either occurring after the switch and disappearing after back-switch or change of biologic. Criteria for NSAE/NSS in the historical cohort were the same lack of efficacy or subjective adverse events and disappearance after change of biologic BD. Medium-term (12 months) SB2 outcomes were assessed and compared with I) the data obtained in the short-term (34 weeks) II) the data from an historical cohort of CIRD patients treated by OI in the same rheumatology department, using Kaplan-Meier survival curve.

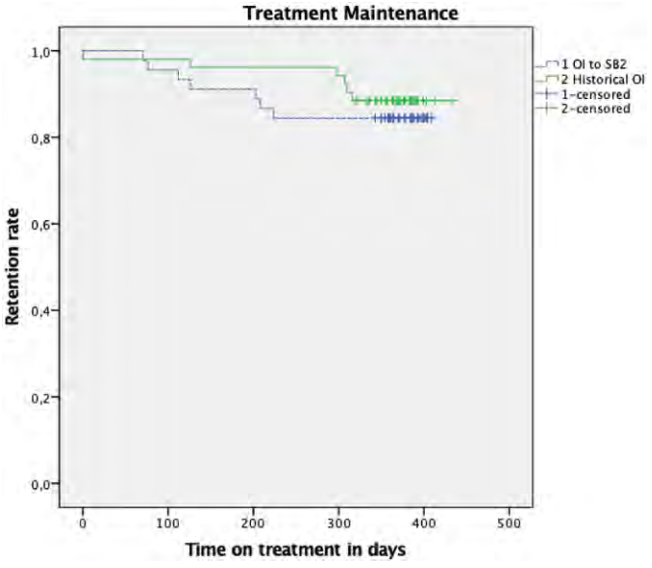
Results: Forty-five patients were prospectively included for the switch from March 2018 to August 2018: 17 with rheumatoid arthritis (RA), 28 with spondylarthritis (SpA); 55% were women, mean age was 53.2 (SD: 2,1), and mean time under OI was 113.5 (SD9.3). For the historical cohort, the 52 patients treated with OI between December 2016 and January 2017 were included and their data collected at baseline and one year. Fifty-nine percent were women, mean age at inclusion was 50.25 (1.2), and mean time under OI was 94.8 (9.4).

SB2 RR did not differ from the OI RR in the historical cohort: 91.2% and 96.2% respectively at 34 weeks (p = 0.41); 84.4% and 88.5% respectively at 12 months (p = 0.52) (figure 1). The SB2 RR was significantly higher than in three other European cohorts at 34 weeks (mean RR 73.6%, p<0.05, ref.1) but not at 12 months (mean RR 80.9%, ref.2,3,4).

SB2 and OI discontinuations due to NSAE/NSS at 34 weeks were 2,2 % and 1.9% respectively; at 12 months 6,6% and 1.9% respectively (p= 0.6).

Conclusion: An intervention based on a tailored communication with a prominent role of nurses was effective in reducing the NE when switching from OI to SB2 in the short term, compared with an historical cohort and other European cohorts. The one-year follow-up showed no statistical difference in RR or NE compared with our historical cohort. The present study shows that appropriate interventions may be developed to improve the outcome of switches to biosimilars.

Figure 1: Treatment withdrawal free survival curves (SB2 in switched cohort and OI in historical cohort).



Kaplan Meir survival curves. Comparison with Log-Rank test between OI to SB2 cohort and historical OI cohort, p = 0.520. OI : original infliximab.

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FRI0631-HPR SUPPLEMENTATION WITH CREATININE, GLUTAMINE AND Β-HYDROXY-Β-METHYLBUTYRATE IMPROVES MUSCLE MASS AND STRENGTH AND QUALITY OF LIFE IN PATIENTS WITH SARCOPENIA AND KNEE OSTEOARTHRITIS: THE DIMMUS RANDOMIZED STUDY

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Background: Sarcopenia is characterized by progressive loss of muscle mass, strength, and physical function, and often accompanies other diseases such as osteoarthritis (OA)[1]. Both conditions are also significantly associated with poor quality of life (QoL).

Objectives: A randomized controlled study was conducted to evaluate the effectiveness of creatinine, glutamine and β-hydroxy-β-methylbutyrate (HMB) supplementation in enhancing muscle mass and strength, physical function and QoL in adults with sarcopenia and knee OA.

Methods: Sixty-two patients aged 40 years and above with sarcopenia diagnosed according to the European Working Group on Sarcopenia and with knee OA according to the criteria of American College of Rheumatology were included in the study DIMMUS. The participants were randomly assigned into two groups of intervention (n=31) and control (n=31). The intervention group received oral nutritional supplementation daily plus standardized exercise programme for 12 weeks and the control group received only rescue analgesic medication and exercise training. Muscle mass (appendicular skeletal muscle mass index [ASMMI] estimated by the Baumgartner et al.'s equation), muscle strength (handgrip strength), physical function (4-m gait speed) and QoL (SARQoL) were measured before and after the 12-week intervention. Safety was also recorded by assessments of adverse events.

Results: There was no significant difference in baseline characteristics between the two groups (85.5% women, 63.5 ± 9.6 years, body mass index of 26.8 ± 4.5 kg/m^2, 83.9% Kellgren-Lawerence grade II OA and 91.9% mild sarcopenia). A statistically significant improvement in the mean change of ASMMI (3.7 ± 1.0 kg/m^2 to 3.96 ± 1.1 kg/m^2; *P*=0.0074), handgrip strength (18.8 ± 8.7 kg to 20.5 ± 8.5 kg, *P*=0.0089), and SARQoL score (59.3 ± 8.8 vs 70.7 ± 16.6; *P*=0,0003) from baseline to 12 weeks was observed for the intervention group but not for the control group. Both groups showed significant improvements on 4-m gait speed (5.0 ± 0.9 s to 4.4 ± 0.9 s in the intervention group; 5.2 ± 2.9 to 5.0 ± 2.3 m in the control group; *P*<0.001). One patient reported a treatment-related bad taste in the intervention group.

Conclusion: The findings of the present study demonstrated that the combined supplementation of creatinine, glutamine and HMB together with exercise training for 12 weeks may have a positive effect on the muscle mass and strength and QoL in adults with mild sarcopenia and OA. The results provide preliminary experiences and guidance for further clinical trials in both OA and sarcopenic patients.

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Disclosure of Interests: None declared

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FRI0632-HPR PSYCHOLOGICAL PARTICULIARITIES OF PATIENTS SUFFERING FROM MONOGENIC AUTO-INFLAMMATORY DISEASES.

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Background: Monogenic auto-inflammatory diseases (mAID) are a group of severe chronic multisystemic diseases with recurring episodes of fever and other manifestations that significantly affect the patients' life quality. Moreover, the hyper expression of pro-inflammatory cytokines (IL1β, etc.) observed in these patients may have a negative effect on the central nervous system.

Objectives: to study the state of the cognitive and emotional spheres in children suffering from monogenic auto-inflammatory diseases.

Methods: there were examined 22 children at the age of 7 to 17 years old diagnosed with CAPS-9, TRAPS-8, FMF-5. Among them there were 12 boys and 10 girls. The diagnosis in all the patients was confirmed through detection of pathogenic mutations in the NLRP3, TNFRSF1A and MEFV genes. The following methods were used: a clinical conversation; memory diagnostics (learning by heart of 10 words, a pictogram using cues taking into account the patients' age); attention diagnostics (Schulte tables); thinking diagnostics (establishing a sequence of events, "four is a crwod", simple analogies, interpretation of proverbs); emotional and communicative fields (the Eight-Color Luscher Test; CMAS (adaptation by A. Prikhozhan); STAI test, a drawing called "an animal that does not exist" and "a house-a tree-a man").
Results: The memory study revealed in all patients with TRAPS and FMF high and medium values of short-term and long-term memory, in patients with CAPS - a low level of short-term auditory-speech memory, information storage and indirect memorization in 1/3 of patients. In 100% of the examined patients with TRAPS, a significant decrease in all processes of attention and distribution of attention. In 1/3 of patients with CAPS, an increased exhaustion of attention was registered and in 11% - a decrease in its stability. In patients with FMF, attention disorders were not detected. In 44% of patients with CAPS, a decrease in the level of generalization and difficulties in establishing causal relationships were registered. In 25% of patients with TRAPS a decrease in the level of generalization, in 12.5%- difficulties in establishing cause-effect relationships, inertia of thinking in 37.5%. In 60% of patients with FMF: a decrease in the level of generalization, in 80%: difficulties in establishing cause-effect relationships, inertia of thinking in 20%. In the emotional sphere, patients with CAPS, TRAPS, and FMF demonstrated signs of aggression (11.1%, 20% and 20% of patients, respectively), communicative disorders (77.8% -80% - 80%), and reduced social adaptation (55.5% - 80% - 80%), a tendency to form neurotic fears (22% - 40% - 40%). A high level of personal anxiety was noted in 1/3 of patients with CAPS and 40% of patients with FMF.
Conclusion: various psychological disorders in the cognitive and emotional fields were noted in the majority of the examined patients with monogenic auto-inflammatory diseases. In patients with TRAPS, attention processes are most significantly affected; in patients with CAPS, memory is more often affected. In patients with FMF, disorders in thinking processes are revealed more often. In the emotional sphere, most patients with all the three forms of AID note communicative disorders and social adaptation.
Disclosure of Interests: None declared
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FRI0633-HPR PHYSICAL AND SOCIAL ACTIVITY OF PATIENTS SUFFERING FROM JUVENILE IDIOPATHIC ARTHRITIS

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Background: Juvenile Idiopathic Artritis (JIA) is a chronic, disabling disease of a childhood age that significantly limits the patient's capabilities and affects the life quality. Modern drug therapies can prevent most of the negative consequences of the disease and maintain satisfactory functional abilities of patients.
Objectives: to examine the nature of the daily physical and social activities of patients suffering from JIA.
Methods: the study included 236 patients aged from 4 to 17 years old undergoing in-patient treatment. Among them, 146 (62%) - polyarthritis and spreading oligoarthritis, including 13 (5.5%) - with damage to the eyes, persistent oligoarthritis - 60 (25%), including 26 (11%) with damage to the eyes, systemic JIA 22 (16%), enthesitis-associated 8 (3%). The patients were divided into the following age groups: pre-school age (4-6 years old) – 26 patients (11%), primary school age (7-10 years old) - 54 patients (23%); an average school age (11-12 years old) – 49 patients (21%), senior school age (13-15 years old) -52 patients (22%), youth (16-17 years old) -55 patients (23%). The assessment methods: collection of their pharmacological history, questioning (with an author's questionnaire) the parents of children aged from 4 to 10 years and older patients themselves, VAS pain evaluation, a CHAQ questionnaire.
Results: 10 (4%) patients received NSAID, 88 (38%) patients - synthetic basic anti-inflammatory drugs, biological therapy - 133 (56%), 5 patients (2%) did not receive any drug therapy. An average value of the VAS pain evaluation: 2.5 cm, the CHAQ functional insufficiency is low: 137 patients (58%), medium insufficiency in 88 patients (37%), a severe one in 11 patients (5%). Children's educational institutions were regularly visited by 199 (85%) patients, leisure activities were enjoyed by 90 (38%) patients; at that, the highest rate of leisure activities was recorded for the age group 112-12 years (67% of the entire group), daily walks were recorded in 172 (73%) patients, doing homework on a regular basis by 155 (66%) patients, regular doing exercises of therapeutic gymnastics recorded in 55 (24%) patients.
Conclusion: The social activity of patients suffering from JIA can be estimated as satisfactory, while their physical activity as inadequate. An adequate social and physical activation of patients with JIA being in the remission status is required. This can be facilitated by educational programs for patients and their parents, a joint discussion of issues on the social and physical activity of patients and their parents with rheumatologists and rehabilitation therapy specialists.
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Disclosure of Interests: None declared
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FRI0634-HPR LEVEL OF PHYSICAL ACTIVITY IN ANTIPHOSPHOLIPID SYNDROME AND ITS RELATIONSHIP TO ATHEROSCLEROSIS PROGRESSION – ANALYSIS OF THE SERBIAN COHORT

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Background: Systemic lupus erythematosus (SLE) and antiphospholipid syndrome (APS) are associated with an increased risk of developing cardiovascular diseases as a result of complex interaction between traditional risk factors, chronic inflammation and specific impact of antibodies on endothelium. There are very limited data regarding level of physical activity (PA) in APS patients.
Objectives: To analyze different domains of PA in Serbian APS patients and their possible relationship to clinical and laboratory criteria of the main disease.
Methods: From a large Serbian APS database comprehending 527 APS patients (371 Primary – PAPS, and 156 APS associated with other autoimmune diseases, predominantly systemic lupus erythematosus (SLE)) we interviewed 51 APS patients, age range of 15-69 years: 29 patients with primary APS (PAPS), 25 women, 4 men, age 44±11.50, and 22 APS/SLE, 18 women, 4 men, age 48.41±11.75, using a long form of The International Physical Activity Questionnaire (IPAQ), translated onto Serbian language. Data on last seven days of PA divided onto leisure time PA, domestic and gardening (yard) activities, work-related PA and transport-related PA were acquired, and proposed scoring method was used. Based on the level of PA, patients were categorized to low, moderate or high level of PA. For the purpose of insight into atherosclerotic progression, we performed color Doppler scan of carotid arteries in all patients and presence of atherosclerotic plaques has been notified.
Results: Average total PA score was 7706.18±11771.97 MET-minutes/week. The greatest average values for different PA domains were for work (2733.21±6158.66 MET-minutes/week) and domestic/garden/yard (2522.31±3847.24 MET-minutes/week) and the lowest scores achieved in leisure time (500.87±695.45 MET-minutes/week). Majority of Serbian APS patients had low or moderate level of PA (37.3%, 43.1%, respectively) whereas lowest percentage was in high category of PA (19.6%). All domains of PA were significantly negatively correlated to age and BMI. There were no significant difference regarding PA scores between PAPS and APS/SLE patients. Although higher percentage of PAPS patients had high level of PA (27.65 compared to 9.1% of SLE/APS), the overall difference was not significant. There was no significant difference regarding antiphospholipid antibody (aPL) type or thrombotic/obstetric events presence. Significant difference occurred regarding presence of carotid arteries plaques. APS patients with lower PA scores had significantly higher prevalence of carotid arteries plaque especially for PA in transportation (p=0.004), and total PA (p=0.025)
Conclusion: Serbian APS patients at younger age, tend to have low or moderate level of PA, with the lowest level of activity in leisure time. Low level of PA was undoubtedly related to progression of atherosclerosis in these patients, emphasizing a need for PA promotion in APS.
Disclosure of Interests: Aleksandra Djokovic Speakers bureau: KRKA, Astra Zeneca, Actavis, Ljudmila Stojanovich: None declared, Natasa Stanisavljevic: None declared, Gordana Bogdanovic: None declared, Sandra Djokic: None declared
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FRI0635-HPR PATIENTS' MOTIVATION AND GOALS FOR THUMB CARPOMETACARPAL OSTEOARTHRITIS SURGERY

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Background: Osteoarthritis (OA) in the thumb carpometacarpal joint (CMCJ) is a prevalent disease which may lead to structural damage, severe pain and

functional limitations, but for which there is yet no cure. Evidence-based treatment recommendations state that all patients with hand OA should be offered patient education, hand exercises, and provision of assistive devices and orthoses. Pharmacological therapy is recommended as a symptom relieving supplement. The main indication for CMCJ surgery is pain and poor function, and such surgery should be considered only when other treatment has proven insufficient in relieving pain (1). Previous research has shown that high motivation is a significant predictor for deciding to undergo CMCJ surgery (2), but there is little knowledge regarding which factors that motivates patients for undergoing such surgery.

Objectives: The objective of this study was to explore patient goals and motivation for surgery, and factors characterizing patients highly motivated for surgery.

Methods: This cross-sectional study included 180 patients referred from their general practitioner for CMCJ surgical consultation. Goals for surgery were collected with an open-ended question and analysed by linking the content of each goal to domains in the International Classification of Functioning, Disability and Health coding system. Motivation for surgery was rated with a Numeric Rating Scale (NRS, 0-10, 0=no motivation). Activity limitations was self-reported using the Measure of Activity Performance of the Hand (MAP-Hand, score 1 to 4, 1=no activity problems) and the Disabilities of the Arm, Shoulder and Hand questionnaire (QuickDASH; score 0-100, 0=no disability). Factors that characterized patients highly motivated for surgery (NRS≥8) were explored with multivariate regression analyses.

Results: Mean age of participants was 63 years (SD 7.6) and 142 (79%) were women. The most common goals for surgery were to reduce pain and improve arm and hand use. Fifty-six (31%) of the patients were characterized as highly motivated for surgery. High motivation for surgery was strongly associated with more activity limitations (MAP-Hand; (OR 4.00, p=0.008)), living alone (OR 3.18, p=0.007) and a young age (OR 0.94, p=0.002).

Conclusion: Decisions on CMCJ OA surgery should be based on assessment and discussion of patients' life situation, hand pain, activity limitations and motivation and goals for surgery. According to the EULAR recommendations, previously received conservative and pharmacological treatment should also be evaluated.

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FRI0636-HPR COMPARING THE EFFECTS OF YOGA AND HOME EXERCISE PROGRAMS ON FUNCTIONAL STATUS IN CHILDREN WITH ENTHESITIS RELATED ARTHRITIS

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Background: Enthesitis-Related Arthritis (ERA), also referred as the juvenile ankylosing spondylitis, is a subtype of Juvenile Idiopathic Arthritis (JIA). However, ERA patients were reported as having higher pain levels, lower functional status and lower quality of life level compared to other JIA subtypes. Yoga is used as an exercise method in adult patients with rheumatic diseases and positive effects on physical and psychosocial symptoms were reported. However, no study was conducted related to yoga in pediatric population with rheumatic diseases.

Objectives: The aim of this study was to investigate effects of performing yoga or home exercises on functional status in children with ERA.

Methods: Twenty-one children with ERA were allocated into two groups as yoga group (n=11) and home exercise group (n=10). Yoga group performed yoga exercises supervised by a physiotherapist for twice a week, for eight weeks, while the home exercise group performed video-based home exercises for the same period. Pain in rest and activity (Numeric Rating Pain Scale), functional status (Six-Minute Walk Distance, Stair Climb Test), and quality of life (PedsQL Children and Parent Form) were evaluated at baseline and following eight weeks.

Results: The groups were similar regarding to physical characteristics, pain, functional status, and quality of life at baseline (p>0.05, Table 1). While, all the parameters (except PEDSQL Parent Form) in yoga group significantly improved at the end of the study (p<0.05, Table 2), only stair climb test results significantly improved in home exercise group (p<0.05, Table 2).

Table 1. Comparison of the groups at baseline

	Yoga Group (n:11) Median (IQR 25/75)	Home Exercise Group (n:10) Median (IQR 25/75)	p*
Physical parameters			
Age (year)	15.0 (13.0/15.5)	16.0 (14.0/17.0)	0.099
BMI (kg/m^2)	20.7 (18.3/23.1)	21.2 (19.9/22.0)	0.756
Pain			
Rest pain (score)	0 (0/5.0)	1.0 (0/3.0)	0.705
Activity pain (score)	4.0 (1.0/6.5)	2.0 (0/7.0)	0.387
Functional Status			
Six-minute walk distance (m)	600.0 (552.5/664.5)	626.0 (556.0/650.0)	1.000
Stair climb test (sec)	7.6 (6.8/8.3)	7.4 (7.0/8.0)	1.000
Quality of Life			
PedsQL Children (score)	13.0 (10.0/23.5)	12.5 (6.0/20.0)	0.654
PedsQL Parent (score)	21.0 (8.5/31.5)	26,0 (15.0/39.0)	0.387

*: Mann-Whitney U test; IQR 25/75: Interquartile Range 25/75, PedsQL: Pediatric Quality of Life Inventory, p<0.05

Table 2. Changes in the Groups

	Before Median (IQR 25/75)	After Median (IQR 25/75)	p*
Yoga Group			
Pain			
Rest pain (score)	0 (0/5.0)	0 (0/2.5)	**0.039**
Activity pain (score)	4.0 (1.0/6.5)	0 (0/1.5)	**0.012**
Functional Status			
Six-minute walk distance (m)	600.0 (552.5/664.5)	692.0 (595.0/705.5)	**0.011**
Stair climb test (sec)	7.6 (6.8/8.3)	6.2 (6.0/7.0)	**0.008**
Quality of Life			
PedsQL Children (score)	13.0 (10.0/23.5)	9.0 (4.0/17.0)	**0.021**
PedsQL Parent (score)	21.0 (8.5/31.5)	18.0 (8.0/22.0)	0.169
Home Exercise Group			
Pain			
Rest pain (score)	1.0 (0/3.0)	0 (0/3.0)	0.715
Activity pain (score)	2.0 (0/7.0)	2.0 (0/7.0)	0.892
Functional Status			
Six-minute walk distance (m)	626.0 (556.0/650.0)	601.5 (585.0/707.0)	0.093
Stair climb test (sec)	7.4 (7.0/8.0)	7.0 (6.5/7.8)	**0.028**
Quality of Life			
PedsQL Children (score)	12.5 (6.0/20.0)	8.5 (7.0/18.0)	0.475
PedsQL Parent (score)	26.0 (15.0/39.0)	22.5 (14.0/30.0)	0.192

*: Wilcoxon Signed Rank Test, IQR 25/75: Interquartile Range 25/75, PedsQL: Pediatric Quality of Life Inventory, p<0.05

Conclusion: Yoga seems promising for improving functional status in children with ERA compared to a home-based exercise program. Therefore, yoga can be implemented as an exercise intervention in rehabilitation programs in children with ERA.

Disclosure of Interests: None declared

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FRI0637-HPR INDIVIDUALISED EXERCISE INTERVENTION FOR HIP AND KNEE OSTEOARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMISED CONTROLLED TRIALS

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Background: Osteoarthritis (OA) is a leading cause of disability worldwide. Currently, exercise is recognised to be one of the core treatments for OA (NICE, 2014). Convincing evidence shows that exercise can have positive effects on pain and function in people with OA (Fransen et al., 2015). However, a standardised exercise regimen may not suit all patients and adherence to exercise is always an issue. Therefore, several international guidelines recommended individualisation of the exercise regimen according to individual patient characteristics (e.g. pain severity, personal goals and co-morbidities), as this may enhance take up and adherence, hence treatment effect of the intervention (Fernandes et al., 2013).

Objectives: The aims of this systematic review were: (1) to evaluate the current evidence for efficacy in randomised controlled trials (RCTs) of individualised exercise (IE) interventions for people with hip or knee OA; and (2) compare this to the efficacy of non-individualised exercise (NIE).
Methods: A systematic search was carried out, up until March 6th 2018, on the following databases: MEDLINE, CINAHL, AMED, PsycINFO and EMBASE. RCTs of IE interventions, or with subgroup analysis based on specific patient characteristics, were searched. Standardised mean difference and 95% confidence interval (CI) were calculated using random effects model. Risk of bias was evaluated using the modified Cochrane tool. Pain was the primary outcome of interest. Results of IE interventions were then compared to the NIE interventions identified from a previous systematic review (Goh et al., 2019).
Results: We reviewed titles of 1,766 records in the systematic search. The screening process (Figure) identified 15 studies (1,826 participants) that met the inclusion criteria, of which 7 were included in a meta-analysis. Most included studies had high risk of bias. Blinding was a consistent problem due to the nature of the intervention. Within the trials exercise was individualised according to factors including severity of symptoms, exercise performance, lower limb muscle strength and presence of co-morbidities (e.g. heart failure, chronic obstructive pulmonary disease (COPD) and diabetes mellitus (DM) type 2).
The analysis showed that IE significantly improved pain, physical function, performance and quality of life outcomes (Table). When compared to NIE interventions, IE showed greater effect size for all outcomes but their 95% CIs were overlapping.

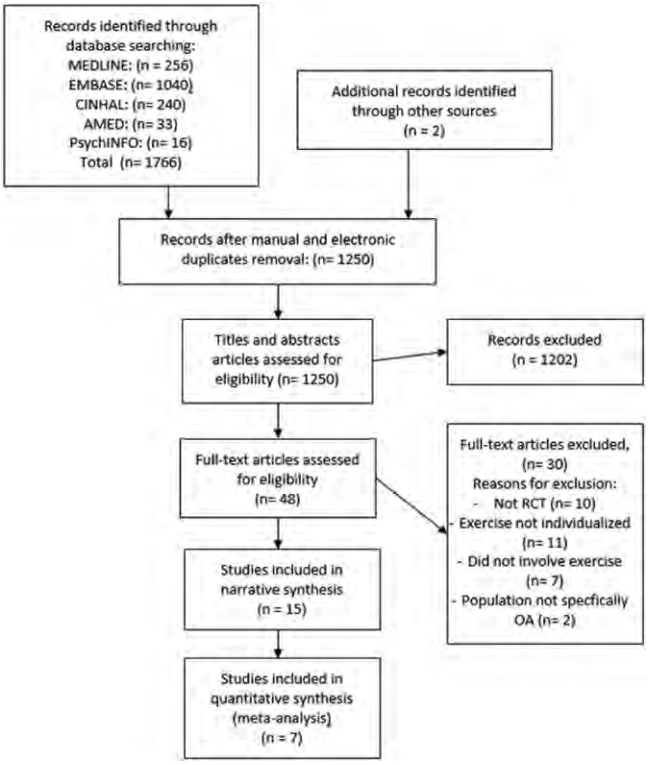


Figure showing Summary of screening process

Table 1. Summary of results

Outcome	Type of exercise program	ES	95% CI	Number of studies (Number of patients)
Pain	IE	1.04	0.32 - 1.77	7 (991)
	NIE	0.57	0.44 - 0.69	65 (4,723)
Function	IE	1.37	0.50 - 2.24	7 (991)
	NIE	0.51	0.38 - 0.64	63 (4,829)
Performance	IE	2.00	0.07 - 3.93	2 (291)
	NIE	0.51	038 - 0.63	66 (4,889)
QoL	IE	1.30	-0.52 - 3.12	2 (226)
	NIE	0.32	0.15 - 0.49	34 (2,545)

ES= Effect size. CI= Confidence Interval. IE= Individualised Exercise. NIE= Non-Individualised Exercise. QoL= Quality of Life

Conclusion: The results of this review show that IE may have better outcomes on people with hip or knee OA compared to NIE. However, the small study effect may inflate the estimates of the individualised exercise group, and further head to head comparisons are required.

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FRIDAY, 05 JUNE 2020

HPR Interdisciplinary research

FRI0638-HPR

IMPACT OF PARENTAL MIGRATION IN THE CONTEXT OF THE MULTIFACTORIAL ETIOLOGY OF CHRONIC ARTHRITIS IN CHILDHOOD

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Background: Migration of Romanians to work abroad began after 1990 with the aim to provide a better income and life for their family. Current studies show that the migration of one parent or both, even when it is temporary, produces negative long-term effects on the health and psychosocial evolution of the children affected. Children and adolescents exposed to chronic stress due to migration, misunderstandings between the parents, alcoholism, violence, divorce of the parents etc., present an increased risk of illness. More and more data from the literature suggest that prolonged stress and depression induces inadequate cortisol along with norepinephrine secretion, increased synthesis of proinflammatory cytokines, which are the basis for autoimmune pathologies, such as chronic arthritis.
Objectives: Given the extended phenomenon of migration from Romania and the increase in the cases with autoimmune pathology in children and adolescents, we aimed to evaluate the association between the disorders related to the permanent stress induced by the parental migration abroad and the risk of developing arthritis during childhood.
Methods: The study included 201 children and adolescents aged 13.4 ± 3.7 years, who were in evidence of an outpatient health unit, from 2016-2019. These cases were included in a chronic disease registry with the diagnosis of Juvenile Idiopathic Arthritis (JIA), established by a pediatric rheumatologist.
For the initial evaluation, we used a questionnaire that included the socio-demographic data. In comparison, we studied 40 healthy children (control group). The family drawing test was used for patients between 5 and 16 years of age to identify possible conflicts with certain family members, to assess the emotional and psychological maturity of the child or adolescent, and to find out if are there any problems at home.
Results: At the end of the study, only 181 (90%) of the eligible patients completed the questionnaire and the family drawing test. Demographic data showed that patients from rural areas predominated (71.8%), compared to 28.2% from urban areas.
In terms of sex, 52.5% were male, compared to 47.5% female. Family history (mother, father, sister, brother, grandfather, aunt, uncle) of autoimmune disease was encountered in 28.1% of patients, as follows: spondylarthritis in 9.4% cases, rheumatoid arthritis in 8.8% cases, JIA in 3.9% cases and other autoimmune diseases (Systemic Lupus Erythematosus, Scleroderma, Diabetes, Asthma) in 6% cases. Patients from low-income families were in 82.3% of cases. 72.5% of the cases had a prolonged state of stress by migrant parents for working abroad [38.7% only one parent (30% mother) and both parents in 17.7% of cases], divorce in the family in 11.6% of cases, unmarried mother in 2.8% of cases, and a close relative recently deceased in 1.7% of patients.

Subcategories of JIA included: polyarticular JIA negative Rheumatoid Factor (RF) in 39.77% of cases, enthesitis-related arthritis in 27.07% of cases, polyarticular JIA positive RF in 14.36% of cases, oligoarticular JIA in 14.9% of cases, systemic JIA in 3.31% of cases and psoriatic JIA in 0.59% of patients.

Conclusion: Both the data from the questionnaires, but especially the family drawing tests, suggest that the prolonged state of stress with anxiety, sadness, pain and depression, in combination with starvation, lack of parental love and the genetic predisposition, have contributed to the emergence of chronic arthritis, pathology that is growing more and more in recent years in Romania.

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FRI0639-HPR EFFECTS OF VIBROACOUSTIC THERAPY IN CHRONIC MUSCULOSKELETAL PAIN IN CHILDREN AND ADOLESCENTS

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Background: Musculoskeletal chronic pain in children and adolescents is a major cause of locomotor and mental disabilities, with a significant impact on school activities and social costs. Vibroacoustic therapy is used to reduce stress, pain, anxiety and to increase the well-being of children and adults, in order to relax the body, brain and to relieve the symptoms of the disease. It was proved that sound waves imprint movement in water molecules, accelerate lymph and blood circulation, eliminate toxic metabolic waste, vitalize the "good bacteria" by suppressing the activities of "bad bacteria" and balancing the gut microbiota.

Objectives: Aim of study was to evaluate the effect of vibroacoustic therapy on pain and well-being of patients with chronic musculoskeletal pain.

Methods: Between 2017 and December 2019, 84 patients with a mean age of 11.9 years with chronic pain from different musculoskeletal disorders were studied. Patients were randomly divided into: group I (46 patients) received vibroacoustic therapy and group II (38 patients), control, received *placebo* vibroacoustic therapy.

All patients and parents/legal guardians were informed about the treatment and signed an informed consent. Inclusion criteria were: diagnosis of the disease by the rheumatologist specialist and the initial pain measured on the Visual Analog Scale (VAS)> 5. Exclusion criteria were: patients with acute inflammatory conditions, mental retardation, psychosis, high blood pressure, internal or external bleeding, pregnancy, hearing loss. Group I (46 patients) received vibroacoustic therapy with a special system, in which the patient listens in the headphones a healing music and at the same time, a therapist posts a special pillow that imprints music vibrations on the painful areas. Patients had a session three times a week, for 20 minutes, with a vibrational frequency of 115 Hz, for 4 weeks, then repeated the protocol after a break of 8 weeks.

Group II (38 patients), control, was treated with conventional drugs and placebo vibroacoustic.

Effects of vibroacoustic therapy were evaluated by the pediatric rheumatologist who completed a questionnaire for the evolution of the functional ability in daily living activities (Child Health Assessment Questionnaire) (scores 0–3; 0 = without disabilities; 3 = disabled) and the intensity of the child's pain by VAS score 0–10, (0 = no pain, 10 = severe pain), at the beginning of treatment, after 4 weeks and in the end.

Results: In group I, after 12 sessions of the vibroacoustic therapy, VAS pain scores decreased from 8.6 to 4.2, comparatively to only a decrease from 8.2 to 6.7 in the control group ($p = 0.05$); the functional activity score was improved with 47%, comparatively with only 23% in the control group ($p = 0.02$).

At the end of the study, the VAS pain score improvement in group I was 68%, compared to only 29% in the control group ($p = 0.01$). All patients who were treated with vibroacustic music had a better functional activity score in the end of the study, significantly better compared to the placebo control group ($p < 0.05$).

Conclusion: Vibroacoustic therapy had positive effects in significantly reducing pain, and especially for the areas of the body where the vibrational cushion was applied, comparatively with control group ($p < 0.05$).

Vibroacoustic therapy is a non-pharmacological, non-invasive, no-side-effect treatment modality which has induced patient relaxation, has reduced muscle tension and improved the range of motion, helping a lot in the process of patient's rehabilitation. Sonic vibrations transmitted by the bone conduction adjust the balance of the autonomic nerves, deeply relax the mind and remove excess body tension.

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Disclosure of Interests: None declared

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FRI0640-HPR USEFULNESS OF ISOTOPIC RADIOSYNOVIORTESIS IN RHEUMATIC DISEASES WITH CHRONIC REFRACTORY SYNOVITIS.

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Background: Radioactive synoviortesis consists of the intra-articular injection of particles from a radioisotopic colloidal suspension, to achieve the selective destruction of the synovial membrane, respecting the cartilage and bone

Objectives: To describe the experience of performing isotopic radiosynoviortesis (RSO) as an alternative technique to the traditional procedures in the treatment of chronic synovitis refractory in patients of our health area and to define the pathologies, clinical improvement and safety in patients treated with the above described method.

Methods: Observational, descriptive and cross-sectional study by reviewing radiosynoviortesis performed in patients with chronic arthritis refractory between 2005 and 2019 at the General University Hospital of Ciudad Real and comparing to common treatments, which normally consist of corticosteroids, disease-modifying drugs, biological therapy, nonsteroidal anti-inflammatory drugs and opioids. The study group involved 65 patients aged 37 to 75 years that had been diagnosed of rheumatic diseases such as rheumatoid arthritis, spondyloarthropathy, gout, osteoarthritis, villonodular synovitis, lupus and undifferentiated arthritis.

Once medical records were reviewed, and prior to the procedure, the following information was registered into a database: age, sex, pathology, treatment received, infiltrations, affected joint, mobility, radiographic stage, laboratory parameters (VSG and PCR), Health Assessment Questionnaire (HAQ) and visual analog pain scale (VAS). After 6 months of treatment, clinical improvement provided by radiosynoviortesis was evaluated and a second database was created by collecting the following data: physical examination, HAQ, laboratory parameters (VSG and PCR), VAS, mobility and subjective perception of the patient. In addition, short-term complications were also recorded.

After 6 months of radiosynoviortesis treatment, clinical improvement was established as a consequence of the following parameters: absence of inflammation on physical examination, improvement of inflammation reactants in comparison to the beginning of the procedure –assuming a decrease of ≥2 mm in ESR and ≥O, 2 mg / dl in CPR as such–, enhancement of HAQ –decrease of ≥ 0.25 compared to the beginning of the treatment–, EVA improvement determined by a reduction of > 25% in relation to the initial value and increase of mobility. Additionally, the subjective perception of the patient was also considered as evidence of the. clinical improvement.

Results: on the sixth month of treatment, 58.4 % of the individuals perceived a good clinical improvement, which was qualified as excellent by 6.2% of them. 56.9% of patients also presented pain reduction in the VAS scale, together with a decrease in joint swelling in 66% of the cases and an enhanced joint mobility in 69.2% of them. No side effects appeared due to treatment. An improvement in HAQ was observed in 67.7% of the observations and inflammation parameters (both ESR and CRP) were reduced in 64.6% of the subjects. The pathologies in which the technique has been most frequently prescribed are villonodular synovitis (27.7%) and rheumatoid arthritis (20%).

Conclusion: Isotopic radiosynoviortesis is a useful and safe therapeutic alternative, that leads to a clinical improvement demonstrated by a reduction of pain and inflammation and increased mobility in those patients with chronic synovitis refractory. Compared to usual treatments, currently available data supports the effectiveness and safety of radiosynoviortesis as an alternative therapy for these patients

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FRI0641-HPR

INTERSTITIAL LUNG DISEASE AS INITIAL MANIFESTATION OF SYSTEMIC AUTOIMMUNE RHEUMATIC DISEASES IN A MONOCENTRIC COHORT: THE IMPORTANCE OF A MULTIDISCIPLINARY APPROACH

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Background: Interstitial lung disease (ILD) can be the first manifestation of connective tissue disease (CTD) and rheumatoid arthritis (RA). Pulmonologists are usually the first referral in these patients.
Objectives: To determine: 1) the prevalence of ILD as initial manifestation of CTD or RA 2) clinical characteristics of such patients.
Methods: From a database of consecutive patients with CTD or RA referred to our academic hospital from 2009 and 2017, we selected all the patients with ILD as initial manifestation of the disease. Periodic multidisciplinary evaluations were performed during a median follow-up of 48 (35-50) months.
Results: 1) Fifty-four of the 427 patients with CTD or RA (12.6%) had ILD as initial manifestation (mean age: 63.9±12.9 yrs, F/M ratio: 20/34). Autoimmune myositis was diagnosed in 16/54 patients (29.6%), systemic sclerosis in 11 patients (20.4%), RA in 9 patients (16.7%), Sjogren syndrome in 9 patients (16.7%) and SLE in 3 patients (5.5%). Six patients remained classified as IPAF (11.1%). Among the Rheumatology patients we followed-up in the same period, autoimmune myositis had the highest prevalence of ILD as initial manifestation (63.6%), followed by Sjogren syndrome (20.5%), systemic sclerosis (20.0%), RA (3.4%), and SLE (3.3%). 2) Patients with initial ILD were all firstly evaluated by the Pulmonologist and the main reasons for Rheumatology referral were positivity for one or more autoantibodies (57.4%), mainly ANA≥1:320, and joint pain (29.6%). Thirty-six patients (66.7%) received steroid and/or immunosuppressive therapy in the six months before the first Rheumatology visit to relieve respiratory symptoms. Twenty of these patients (58.8%) had rheumatic manifestations during steroid tapering. ILD CT patterns were NSIP (25 patients, 52.1%), UIP (18 patients, 33.4%), and organizing pneumonia (5 patients, 9.3%). In four patients (4.5%), autoantibodies became positive during the follow-up. The final diagnosis of CTD- or RA-ILD was made after a median period of 16.5 (6-39) months from the clinical onset. At the time of diagnosis, average FVC was 90.4±18.7% of predicted, DLCO 55.4±20.2% and the median GAP index was 3 (2-3). During the median follow-up of 48 months, eight patients (14.8%) had a decline in DLCO of ≥ 15% predicted and/or a decline in FVC of ≥ 10% despite immunosuppressive drugs. Nine patients (17%) died and six of these patients (11.1%) for causes related to ILD.
Conclusion: In our study population, the prevalence of ILD as initial manifestation of CTD or RA was 12.6%. Autoimmune myositis, systemic sclerosis and Sjogren syndrome were the most frequent diagnosis. As our data confirmed, ILD is a major cause of death in patients with systemic autoimmune diseases and can progress despite immunosuppression [1]. Furthermore, clinical features may become evident even months after the disease onset. A multidisciplinary evaluation is therefore essential, not only at the time of diagnosis but also during the follow-up [2].

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BARRIERS AND FACILITATORS FOR PHYSICAL ACTIVITY ARE MAINLY RELATED TO PSYCHOLOGICAL ISSUES IN INFLAMMATORY ARTHRITIS – A MIXED-METHODS STUDY OF 66 PATIENTS IN FRANCE.

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Background: Patients with inflammatory arthritis (IA) like (ankylosing spondylitis (AS), rheumatoid arthritis (RA), and psoriatic arthritis (PsA) are more prone to physical inactivity but derive specific benefits from regular physical activity (PA) (1). Barriers and facilitators to PA are key elements that have not yet been well described.
Objectives: To assess if barriers and facilitators for PA in patients with IA are mostly related to disease, psychological, social or environmental factors.
Methods: A list of the most important barriers and facilitators was derived from a systematic review of barriers and facilitators to PA in rheumatoid arthritis (2). This list was assessed for face validity by 11 experts from Rheumatology or physiotherapy then tested by 10 patients through structured interview.
The list of barriers and facilitators was completed in a binary way: "barriers or facilitators are relevant to me" yes or no, for 66 patients in a monocentric, cross-sectional study. Then, patients assessed the level of each barrier or facilitator on a 0-10 scale. Statistics were descriptive. There was no imputation of missing data.
Results: The study included 66 patients (27 axial spondyloarthritis, 26 rheumatoid arthritis, 13 psoriatic arthritis), mean age 52.0 (standard deviation (SD) 16.6) years, mean disease duration 14.3 (SD 11.7) years, 53% women. Disease activity was moderate (mean DAS28 2.1 (SD 1.1), mean BASDAI 2.8 (SD 1.4)), and 75.4% received a biologic. The main factors described by patients were related to the knowledge of the benefits of PA and symptoms (table 1). Psychological factors were more reported and social factors less reported as influential for PA.

Table 1. Barriers and facilitators for physical activity reported by patients with inflammatory arthritis.

Barriers or facilitators	Categories	Modifiable	N (%) reporting this barrier or facilitator	Level of patients reporting this item (0-10) (mean (SD))
Knowledge of benefits of physical activity for health	Psych	Yes	49 (78)	6.6
Knowledge of benefits of physical activity for mood	Psych	Yes	47 (75)	6.8 (3.4)
Level of symptoms (pain, fatigue, lack of mobility)	Phy	Yes	44 (69)	5.7 (2.8)
External reminders (eg: from health professionals, calendars…)	Soc	Yes	36 (57)	6.2 (3.1)
Presence or absence of activity facilities (ex: green area for walking, gym …)	Evmt	No	34 (56)	6.3 (3.7)
Lack of motivation	Psych	Yes	34 (55)	5.7 (3.2)
Weather conditions	Evmt	No	33 (52)	5.7 (3.2)
Confidence on how to exercise safely	Psych	Yes	31 (49)	6.0 (2.6)
Contact and proximity with others during physical activity	Soc	No	29 (47)	6.1 (3.7)
Presence or absence of support from others (friends, family)	Soc	No	26(42)	6.5 (3.9)
Lack of time	Evmt	No	35 (40)	5.4 (3.4)
Presence or absence of support and/or advice from healthcare professionals	Soc	Yes	25 (40)	6.0 (3.7)
A belief that physical activity will make symptoms worse	Psych	Yes	17 (27)	4.8 (3.3)
Lack of knowledge on which exercises to do and how much	Psych	Yes	17 (27)	4.7 (3.0)

Psych = psychological, Evmt = environmental, Phy = physical, Soc = social

Conclusion: The main factors that influence PA in patients with IA were mostly related to psychological aspects, and could be modifiable. The role of health professionals supporting patient PA is key. Interventions should be further explored to meet these important barriers and facilitators.

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CARDIOVASCULAR DISEASE AMONG PATIENTS WITH RHEUMATOID ARTHRITIS COMPARED WITH THOSE WITH OSTEOARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic immune mediated systemic disease known to affect multiple organs. It is known that cardiovascular disease accounts for nearly half the mortality among RA patients[1,2,3]. Osteoarthritis (OA), on the other hand, is not an inflammatory arthritis. No prior study has compared the prevalence of cardiovascular disease (CVD) among these two groups of patients.
Objectives: The purpose of this study was to compare the prevalence of CVD among U.S. veterans with RA versus those with OA.
Methods: The study was conducted in a metropolitan Veterans Affairs Medical Center in the U.S. Information was collected from 125 consecutive patients with RA and 125 consecutive patients with OA as they presented to the clinic. Patient characteristics were noted as well as the presence of CVD and certain subgroups: Cardiac arrhythmias[4], coronary artery disease (CAD), congestive heart failure (CHF), cerebrovascular accident (CVA), abdominal aortic aneurysm (AAA), peripheral vascular disease (PVD), deep vein thrombosis (DVT), pulmonary embolism (PE), or any other form of embolism. The chi square test and the mann-whitney test were used for statistical analyses.
Results: Patient characteristics did not differ between the two groups for age, race, smoking status, or for the presence of hypertension or diabetes. There were more women in the RA group. The OA group had a higher BMI and a higher prevalence of hyperlipidemia. RA patients compared to OA patients had a higher incidence of CVD as a whole (60% vs. 42%, $p < 0.004$) and of cardiac arrhythmias (33.6% vs. 13.6%, $p = 0.001$). There was no difference between the 2 groups for the incidence of CAD, CHF, CVA, AAA, PVD or DVT/PE. RA seropositive and seronegative patients did not differ in the prevalence of CVD. RA duration was not related to the increased prevalence of CVD. Among the cardiac arrhythmias, patients with RA had a higher prevalence of atrial fibrillation (19.2% vs. 8.8%, $p < 0.03$), and arrhythmias requiring pacemaker or defibrillator implant (12.8% vs. 4.0%, $p < 0.02$).
Conclusion: The findings of this study demonstrate that our patients with RA have a statistically higher prevalence of CVD compared to OA patients. Among the subgroups, RA patients had a higher prevalence of cardiac arrhythmias, specifically atrial fibrillation and arrhythmias requiring pacemaker or defibrillator implant.
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FRIDAY, 05 JUNE 2020

HPR Interventions (educational, physical, social and psychological)

FRI0644-HPR **PATIENT EDUCATION AND BASIC BODY AWARENESS THERAPY VERSUS PATIENT EDUCATION ONLY IN PATIENTS WITH HIP OSTEOARTHRITIS: A RANDOMIZED CONTROLLED TRIAL.**

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Background: Patients with hip osteoarthritis tend to develop stereotype and energy demanding movement strategies with potential negative effects on disease progression and daily life functioning. A multi-perspective view on movement quality is applied in the physiotherapy modality Basic Body Awareness Therapy (BBAT), with its movement awareness learning pedagogy. BBAT has been found beneficial for functional movement quality, symptoms, and psychological aspects of health in patients with various long-lasting conditions.
Objectives: To investigate the short-term (6 months) effects of BBAT, added to Patient Education (PE) compared with PE only in patients with hip osteoarthritis.
Methods: A block-randomized controlled trial with 6 months follow-up was conducted. Patients were allocated to 3.5 hours of PE plus 12 weekly sessions of BBAT, each lasting 90 minutes (intervention group), or to PE only (comparison group). Primary outcomes: Numeric Rating Scale (NRS) for pain during walking and Hip Osteoarthritis Outcome Score, subscale Activities of Daily Life (HOOS A). Secondary outcomes included physical capacity tests: Chair test, Stairs test, six-minutes walking test (6MWT), movement quality evaluation: Body Awareness Rating Scale – Movement Quality and Experience (BARS-MQE), and self-reported measures: Activity level (UCLA), function (HOOS subscales P, S, SP, QL and Harris Hip Score (HHS), self-efficacy (Arthritis Self-efficacy Scale, ASES), and health (EuroQol, EQ-5D-5L).
Patient Global Impression of Change (PGIC) on pain and function was registered at 6 months.
ANCOVA of change was used in intention-to-treat and per protocol analysis.
Results: 101 patients were included, average age 63 years, 80% female. There was no difference in change between the groups on the primary outcomes at 6 months. However, movement quality (BARS-MQE) improved more ($p<0.001$) in the intervention group, and the patients reported more improvement in pain (PGIC) than the comparison patients ($p=0.031$). In per protocol analysis, including 30 patients who attended at least 10 BBAT sessions, intervention patients had statistically significant better scores on self-efficacy (ASES pain, $p=0.049$), health (EQ5D5L VAS, $p=0.037$) and function (HHS, $p=0.029$) than the comparison patients.
Conclusion: Patients with hip osteoarthritis were not found by the primary outcome measures to improve more by BBAT added to PE than by PE alone. Movement quality improved, however, significantly more in the intervention group. With sufficient compliance to BBAT, significant more improvement in additional health indicators was demonstrated.
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FRIDAY, 05 JUNE 2020

HPR Patients' perspectives, functioning and health (descriptive: qualitative or quantitative)

FRI0645-HPR **QUALITY OF DUTCH KNEE OSTEOARTHRITIS CARE: THE PATIENT'S PERSPECTIVE**

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Background: In the Netherlands over 1.2 million people have OA of which almost half have knee OA. Recently, several international and national guidelines and quality standards have been developed and adopted to improve the quality of knee OA care. Mapping the patient perspective is a valuable and important step to get insight into the current status of the quality of knee OA care and the uptake of the quality of care standards endorsed by current guidelines.
Objectives: To investigate the quality of knee osteoarthritis care from the patients' perspective in the Netherlands.
Methods: Members of a large observational prospective cohort (n=622), consisting of people clinically diagnosed or suspected with knee OA, were invited to compete an online survey. Besides demographic characteristics participants were inquired whether they contacted a health care professional(s) in the last year for their knee OA and, to fill in a slightly adapted version of the "OsteoArthritis Quality Indicator (OA-QI) questionnaire. In addition, participants rated the quality of knee osteoarthritis care in the Netherlands on a 10-point scale (1: very poor - 10: excellent), and were invited to make recommendations for knee OA healthcare improvement via open-ended questions.

Results: Between September and October 2019, 434 participants completed the survey. Preliminary results show that most participants (78%) contacted one or more health care professional(s) for their knee OA complaints in the last year; most often an exercise and/or physical therapist (53.2%), the general practitioner (43.8%) and/or an orthopedist/orthopedic surgeon (41.5%). Furthermore, there were large variations in self-reported quality indictor achievements (checked "Yes") with the lowest rate for referral for weight reduction and, the highest rate for advice on managing/living with osteoarthritis (table 1). On average, a score of 6.5 was given by the participants for the quality of knee OA healthcare in the Netherlands. Participants' suggestions for OA care improvement comprised of, among others, more attention to pain and fatigue symptoms, expanding and researching treatment options, more information on OA, more attention to the personal situation and, improvement of multidisciplinary care.

Table 1. Self-reported Quality Indicator achievement

Self-reported Indicators	Eligible n*	Checked "Yes" n(%)
Received information about OA	417	310 (74.3)
Received Information about treatment	424	252 (59.4)
Advised on managing/living with OA	421	313 (74.4)
Was offered support on managing/living with OA	421	253 (60.1)
Received information about exercise	426	306 (71.8)
Was offered a referral for (muscle-strengthening) exercises and exercise activities	423	211 (49.9)
Advised to lose weight	303	111 (36.6)
Was offered a referral to services for losing weight	247	37 (15.0)
Assessment of problems in daily activities	301	89 (29.6)
Assessed for walking aid	273	65 (23.8)
Assessed for daily living appliances/aids	284	52 (18.3)
Assessment of pain	426	240 (56.3)
Advised paracetamol	424	312 (73.6)
Offered stronger painkillers	421	132 (31.4)
Offered anti-inflammatory medicine	422	229 (54.3)
Offered joint injection	429	239 (55.7)
Conversation about knee replacement surgery	362	223 (61.6)
Discussed follow-up appointment to monitor OA and evaluate treatment	427	144 (33.7)

* Excluding "not applicable" and "do not remember"

Conclusion: There is room for improvement from the patients' perspective to increase the quality of knee OA care in the Netherlands.

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FRI0646-HPR

MAPPING THE PATIENT JOURNEY OF NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: PERSPECTIVE OF PROFESSIONALS AND PATIENTS

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Background: Non-radiographic axial spondyloarthritis (nr-ax-SpA) is a relatively new disease classification that has generated controversy among payers.

Objectives: To explore the perspective of patients and health care professionals (HCPs) on the journey from first symptoms to a diagnosis of non-radiographic axial spondyloarthritis (nr-ax-SpA), in order to identify gaps and unmet needs.

Methods: Qualitative study in two phases: (1) focus groups with HCPs and personal interviews with patients; (2) nominal group in which results were discussed with all stakeholders and possible solutions were proposed. Content analysis, patient journey mapping, and ideas generation techniques were used.

Results: Five focus groups were organised with rheumatologists, GP, orthopaedic surgeons, physiotherapists, and radiologists, and six patient interviews were held. HCPs recognised poor communication among specialists and contradictory or redundant approaches. Non-rheumatologists recognise poor training on spondyloarthritis, difficulty in identifying red-flags, and biases in differential diagnosis. Rheumatologists recognise that SpA nomenclature can be confusing, nevertheless nr-ax-SpA term is defining an early stage of ankylosing spondylitis, and it could lead to over-diagnosis.

Most of the patients agreed in the narrative of a very long journey with a multitude of diagnoses, mostly wrong, ineffective treatments and much frustration; acknowledging the need for psychological support during the process and the importance of receiving a diagnosis in order to cope with the disease.

The participants in the nominal group meeting recognised and discussed the problems derived from the diagnostic delay and care gaps that clearly affect people with nr-ax-SpA (Table 1).

Table 1. Problems recognised by the different actors involved in the journey.

Problem	Recognised by					
	Pt	**PT**	**Or**	**GP**	**Rh**	**Ra**
Non-recognition of symptoms	X	X				
Delay first visit to doctor	X					
Cancel appointments	X					
Self-medication	X					
Disease denial	X					
Invisibility	X					
Lack of adherence	X					
Ignorance of medication	X					
Unclear symptoms	X	X	X	X		
No clinical filter by back problems		X				
Treatments variability		X				
Ineffective protocols		X	X			
Lack of time		X	X	X	X	
Lack of resources (human and material)		X	X	X		
Lack of commitment		X	X	X	X	X
Not outcome measurement		X	X	X	X	
Inadequate knowledge/training		X	X	X		
Few explanations / patient education		X	X	X	X	
Focused on "our" diagnostic codes		X	X	X	X	X
No relation between specialties		X	X	X	X	X
Prioritization of tests over solutions		X		X		X
Labelling patients (prejudice)		X	X	X	X	
Inadequate referral circuits		X	X	X	X	X
Demotivating delays			X			
Limited medical history / little research			X			
Temporality of work contracts				X		
Limited access to tests		X		X		
Non-sustainability threat				X		
Lack of specialised support				X		
Diagnostic dispersion				X		
Too much weight of local issues				X		
Absence of protocols or outdated		X		X		
Poor information transmission in all directions	X	X	X	X	X	X
Focus on pharmacological treatments					X	
Ignorance of others' roles					X	
Gender bias					X	
Incomplete order forms						X

Abbreviations: Pt, patient; PT, physical therapist; Or, orthopaedic surgeon; GP, general practitioner; Rh, rheumatologist; Ra, radiologist.

The following were indicated as possible solutions: (1) Improving relations between specialities, (2) High resolution consultations, (3) Rethinking disability scales, (4) Better information, (5) Visibility, (6) Resource maps and (7) Citizen training.

Conclusion: The patient's journey with an nr-ax-SpA is long, complicated and frustrating for both the person who experiences it and the HCPs who care for them. It is necessary to improve the knowledge about nr-ax-SpA among non-rheumatology health HCPs along with low back pain in general, among doctors and the general population, as well as other feasible measures that affect multiple levels.

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Rehabilitation

FRI0647

COMPARATIVE EFFECTIVENESS OF LAND AND WATER-BASED EXERCISE PROGRAMS ON FATIGUE IN WOMEN WITH FIBROMYALGIA: PRELIMINARY FINDINGS FROM THE AL-ÁNDALUS RANDOMISED CONTROLLED TRIAL.

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Background: Land and water-based exercise intervention programs have demonstrated positive effects on fibromyalgia symptoms[1]. However, research comparing the efficacy of both protocols is limited.
Objectives: The aim of this study was to assess the effect of two exercise interventions (land-based and water-based training) and a subsequent detraining period on fatigue in women with fibromyalgia.
Methods: Among the 272 participants initially randomised, a total of 161 women (age: 50.7±7.7) completed all the assessments with an attendance of at least of 70% (land-based *n*=50, water-based *n*=44, control *n*=67). The intervention groups trained 3 non-consecutive days/week (60 min/ses) during 24 weeks. Each session involved exercises to improve cardiorespiratory fitness, muscle strength, and flexibility. Four dimensions of fatigue were assessed using the Multidimensional Fatigue Inventory. Participants were evaluated at baseline (pre-test), at the end of the intervention (post-test) and following a detraining period of 12 weeks (re-test). Land-based, water-based, and control groups were comparable in sociodemographic characteristics, disease duration, drugs intake, and body mass index. Age, tenderness, and baseline outcomes values were used as covariates in the comparisons (analysis of covariance) of the changes from baseline (post-test vs. pre-test and re-test vs. pre-test) between groups.
Results: The land-based exercise group reduced general fatigue (mean difference: -1.17; 95% confidence interval: -2.30 to -0.03; *P*=0.04) and physical fatigue (-2.48; -3.80 to -1.16; *P*<0.001) compared to the control group. The water-based exercise group reduced physical fatigue compared to the control group (-1.61; -3.04 to -0.19; *P*=0.02). No significant reductions were observed in other dimensions of fatigue in either group compared to the control group and no differences between intervention groups were observed (all comparisons, *P*>0.05). The reductions in fatigue were not sustained after the detraining period in any of the intervention groups (all comparisons, *P*>0.05).
Conclusion: Twenty-four weeks of land or water-based exercise were both effective in reducing physical fatigue of women with fibromyalgia. Furthermore, land-based exercise led to additional reductions in general fatigue. Reductions in fatigue were not sustained after a 12-week detraining period. Participation in regular exercise, specially land-based, might be an easily accessible treatment option to manage fatigue in this population.
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HPR Service developments, innovation and economics in healthcare

FRI0648-HPR OUTPATIENT FOLLOW-UP ON DEMAND IN RHEUMATOID ARTHRITIS HAS SAME CLINICAL AND RADIOGRAPHIC OUTCOMES BUT FEWER VISITS THAN SCHEDULED ROUTINE CARE

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Background: Medical treatment and care are often life-long in patients with rheumatoid arthritis (RA). During periods of stable disease, patients typically attend routine visits every 3–8 months at the rheumatology outpatient clinic. Between scheduled medical visits, it may be difficult to get acute appointments with the rheumatologist. Scheduled routine visits may be in a stable period without any symptoms and with no need for control and adjustment of treatment. Consequently, there is a demand for developing outpatient control procedures that cater to the needs of the individual patient and which support the patient's experience of active participation in the control and treatment of their own disease.
Objectives: To compare a patient self-controlled outpatient follow up system (Open Outpatient Clinic System (OOCS)) with traditional scheduled routine visits at a rheumatology outpatient clinic.
Methods: A two-year randomised controlled trial with RA patients aged 18 to 80 years with a disease duration of at least one year. Patients were recruited consecutively from the rheumatology outpatient clinic of a major university hospital in the Copenhagen region of Denmark from February 2015 to January 2017. Patients were randomised electronically. Joints were examined by a blinded rheumatologist. Patients in the OOCS group had no scheduled appointments but were allowed to book acute appointments with their contact rheumatologist within 5 days and had access to nurse-led consultations without pre-booking, and a nurse-led telephone helpline. Appointments for the control group were scheduled according to routine procedures. Outcome measures were collected at baseline, year 1 and year 2. Clinical parameters: DAS28, CRP, VAS pain, 28-tender and swollen joint count (28-TJC and 28-SJC), HAQ score and radiographs of hands and feet. Psychological parameters: VAS patient satisfaction (Pt satisfact) and quality of life (EQ-5D).
Results: Of 282 patients, 266 completed the first year, 239 the second year. Patient characteristics (OOCS/controls): age 61.4±10.5/60.9±12.2 years, females 77/74%, ACPA positive 66/65%, treatment with synthetic DMARDs 67/65% and/or biologics 33/35%. Clinical and psychological parameters are shown in Table 1. OOCS at year one and two was comparable to traditional scheduled routine procedures regarding clinical and psychological outcome measures. Radiographic progression was detected in 2.9% (4/138) and 2.1% (3/140) of the OOCS and control group, respectively (p=0.69; Chi-squared test).

Table 1. Outcome measures in patients with RA randomised to on demand Open Outpatient Clinic System (OOCS) or traditional follow-up (control group) in a rheumatology out-patient clinic. Results are shown as mean±SD.

	OOCS	Controls	OOCS	Controls	OOCS	Controls
Time	Baseline	Baseline	Year 1	Year 1	Year 2	Year 2
Visits			3.2±1.9	3.8±1.6*	2.6±1.6	3.5±2.2**
Phone calls			1.8±3.3	0.4±0.8**	0.7±1.4	0.1±0.3**
DAS28	3.0±1.2	2.9±1.0	2.6±1.1	2.6±1.0	2.7±1.2	2.5±1.0
CRP	10.2±7.2	10.1±8.0	8.2±9.9	5.7±5.1*	9.6±8.8	5.5±8.9*
28-SJC	0.6±1.5	0.6±1.2	0.2±0.5	0.3±1.0	0.3±0.9	0.4±1.2
28-TJC	3.3±5.7	2.4±4.2	2.4±4.7	2.1±3.7	2.4±4.9	2.3±4.7
VAS pain	27±25	26±21	28±26	28±24	32±27	29±25
HAQ-score	0.6±0.6	0.6±0.6	0.7±0.6	0.6±0.6	0.8±0.7	0.6±0.7
EQ-5D	0.8±0.2	0.8±0.1	0.8±0.2	0.8±0.2	0.8±0.2	0.8±0.1
Pt satisfact	88±21	87±19	84±25	82±23	82±24	83±23

*p<0.05; **p<0.0005, OOCS vs. control group (Student's t-test).

Conclusion: The patient self-controlled outpatient follow up system OOCS was associated with fewer visits, but more phone calls to the nurse, and was comparable with traditional scheduled routine procedures regarding clinical, psychological and radiographic outcomes after two years. Thus, organisation of outpatient care according to OOCS may be applied to strengthen patient-centred care in patients with RA.
Disclosure of Interests: René Panduro Poggenborg Speakers bureau: Novartis, Ole Rintek Madsen: None declared, Lene Dreyer: None declared, Annette Hansen Consultant of: AbbVie, Speakers bureau: Eli Lily
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FRI0649-HPR HYDROXYCHLOROQUINE PRESCRIBING AND OPHTHALMOLOGY SCREENING WITHIN RHEUMATOLOGY DEPARTMENTS IN THE NORTH-WEST OF THE UNITED KINGDOM: A PROSPECTIVE REGIONAL AUDIT

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Background: Hydroxychloroquine (HCQ) is widely used in the management of rheumatoid arthritis and connective tissue disease. The prevalence of retinopathy in patients taking long-term HCQ is approximately 7.5%, increasing to 20-50% after 20 years of therapy. Hydroxychloroquine prescribed at ≤5 mg/kg poses a toxicity risk of <1% up to five years and <2% up to ten years, but increases sharply to almost 20% after 20 years. Risk factors for retinopathy include doses >5mg/kg/day, concomitant tamoxifen or chloroquine use and renal impairment. The UK Royal College of Ophthalmologists (RCOphth) 2018 guidelines for HCQ screening recommend optimal treatment dosage and timing for both baseline and follow-up ophthalmology review for patients on HCQ, with the aim of preventing iatrogenic visual loss. This is similar to recommendations made by the American Academy of Ophthalmology (2016).

Objectives: To determine adherence to the RCOphth guidelines for HCQ screening within the Rheumatology departments in the North-West of the UK.
Methods: Data for patients established on HCQ and those initiated on HCQ therapy were collected over a 7 week period from 9 Rheumatology departments.
Results: 473 patients were included of which 56 (12%) were new starters and 417 (88%) were already established on HCQ. 79% of the patients were female, with median ages of 60.5 and 57 years for new and established patients respectively. The median (IQR) weight for new starters was 71 (27.9) kg and for established patients, 74 (24.7) kg.
20% of new starters exceeded 5mg/kg daily HCQ dose. 16% were identified as high risk (9% had previously taken chloroquine, 5% had an eGFR <60ml/min/m^2 and 2% had retinal co-pathology). Of the high-risk group, 44% were taking <5mg/kg. In total, 36% of new starters were referred for a formal baseline Ophthalmology review. In the established patients, 74% were taking ≤5mg/kg/day HCQ dose and 16% were categorized as high risk (10% had an eGFR less than 60ml/min/m^2, 3% had previous chloroquine or tamoxifen use and 2% had retinal co-pathology). In the high-risk group, 75% were not referred for spectral domain optical coherence tomography (SD-OCT). 41% of patients established on HCQ for <5 years, and 33% of patients on HCQ for >5 years were not referred for SD-OCT. Reasons for not referring included; awaiting 5 year review, previous screening already performed and optician review advised.
Since the introduction of the RCOphth guidelines, 29% patients already established on HCQ had an alteration in the dosage of HCQ in accordance with the guidelines. In the high-risk group, 16% were not on the recommended HCQ dose.
Conclusion: This audit demonstrates inconsistencies in adherence to the RCOphth guidelines for HCQ prescribing and ophthalmology screening within Rheumatology departments in the North-West of the UK for both new starters and established patients. Plans to improve this include wider dissemination of the guidelines to Rheumatology departments and strict service level agreements with ophthalmology teams to help optimize HCQ prescribing and screening for retinopathy.
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HPR Epidemiology and public health (including prevention)

FRI0650-HPR SEXUAL DYSFUNCTION IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Sexual dysfunction is the alteration in one or several phases of sexual activity (desire, excitement, plateau, orgasm and resolution), which can culminate in frustration, pain and a decrease in the frequency of sexual intercourse. There are few studies that associate sexual dysfunction with Systemic Lupus Erythematosus (SLE) due to the difficulty in assessing it and its multifactorial cause.
Objectives: Determine the frequency of sexual dysfunction and analyze associated factors in patients with SLE.
Methods: A descriptive cross-sectional study was conducted. We included patients who attended the Rheumatology unit between May and July 2019; over 18 years of age, with a diagnosis of SLE according to the ACR 1997 and / or SLICC 2012 criteria, and healthy patients matched by age as control. Demographic and disease-related variables were studied. The DASS-21 (Depression Anxiety Stress Scale) scale that evaluates depression, anxiety and stress, and the Female Sexual Function Index (FSFI) that assesses 6 domains (desire, excitement, lubrication, orgasms, satisfaction and pain) were applied with a cut-off point ≤ 26.5 to define sexual dysfunction. Women over 50 years old, with secondary Sjogren's syndrome, menopause, severe depression and illiterate patients were excluded.
Results: One hundred and twenty three women were included (60 with SLE and 63 controls), with a mean age of 34.3 ± 8.3 and 31.7 ± 4.4 years respectively. The prevalence of sexual dysfunction in the SLE group was 71.7%; 95% CI = [58.5 – 82.5], and 23.8%, 95% CI = [13.9 – 36.2] in healthy patients. There were significant differences in all domains of sexual function between women with SLE and healthy group. In the desire, excitement and pain domains the differences were notable. The total FSFI score in patients with SLE was 18.2 ± 11.2 and in healthy women 28.3 ± 6.9 (p=0.001). Stress, anxiety and depression were observed in 58.4%, 58.3% and 50% of women with SLE and 19%, 20.6% and 28.5% of healthy women respectively (p=0.001). No association was found between sexual dysfunction and age, age at diagnosis, disease activity or treatment (pNS). No association was found in patients with SLE when analyzing the effect of sexual dysfunction in stress, depression and anxiety variables, in opposition to the healthy group (p<0.05).
Conclusion: The prevalence of sexual dysfunction in patients with SLE was high (71.7%). Depression, Anxiety, and Stress were not decisive variables in Sexual Dysfunction.
Disclosure of Interests: None declared
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FRIDAY, 05 JUNE 2020

HPR Service developments, innovation and economics in healthcare

FRI0651-HPR A RANDOMIZED PROSPECTIVE OPEN-LABEL CONTROLLED TRIAL COMPARING THE PERFORMANCE OF A CONNECTED MONITORING INTERFACE IN PATIENTS WITH RHEUMATOID ARTHRITIS VERSUS PHYSICAL ROUTINE MONITORING

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Background: Telemedicine has found wider application in chronic diseases for encouraging tight home-monitoring in order to improve patients' outcome (Smolen et al. 2017).
In previous studies, a high feasibility and high patient-satisfaction rate was found as well as the evidence for a superior or equal effectiveness of telemedicine compared to the standard face-to-face approach, however the results were weakened by some methodological biases and wide heterogeneity of interventions, thus preventing to draw definitive conclusions (Piga et al. 2017; Najm, Gossec, et al. 2019).
Objectives: In rheumatoid arthritis (RA), telemedicine may allow a tight control of disease activity while reducing hospital visits. We developed a smartphone application connected with a physician's interface to monitor RA patients. We aimed to assess the performance of this e-Health solution in comparison with routine practice in the management of patients with RA.
Methods: A 6-month pragmatic, randomized, controlled, prospective, clinical trial was conducted in RA patients with high to moderate disease activity starting a new Disease Modifying Anti-Rheumatic Drug (DMARD) therapy. Two groups were established: "connected monitoring" and "conventional monitoring". The primary outcome was the number of physical visits between baseline and 6 months. Secondary outcomes included adherence, satisfaction, changes in clinical, functional, and health status scores (SF-12).
Results: Of the 94 randomized patients, 89 completed study: 44 in the "conventional monitoring" arm and 45 in the "connected monitoring" arm. The total number of physical visits between baseline and 6 month was significantly lower in the "connected monitoring" group (0.42 ± 0.58 versus 1.93 ± 0.55; p<0.05). No differences between groups were observed in the clinical and functional scores. A better quality of life for SF-12 subscores (Role-Physical, Social-Functioning and Role-Emotional) were found in the "connected monitoring" group.
Conclusion: According to our results, a connected monitoring reduces the number of physical visits while maintaining a tight control of disease activity and improving quality of life in patients with RA starting a new treatment.
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FRI0652-HPR **DEVELOPMENT OF THE ADVANCED PRACTICE NURSING CONSULT IN RHEUMATOLOGY IN THE MULTIDISCIPLINARY APPROACH OF INFLAMMATORY DISEASES MEDIATED BY IMMUNITY**

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Background: Patients with immunity mediated inflammatory diseases (IMID) often have clinical manifestations and comorbidity in the field of various medical specialties. A center has been created in our hospital for the comprehensive care of patients with IMID. It is an innovative healthcare model, that incorporate patients into its governance. Physicians, pharmacists and advanced practice nurses (APN), collaborates in consultation or in the day hospital (DH).
Objectives: To analyze the activity of the rheumatology APN consult integrated in the multidisciplinary team, and the impact on health care and quality of life on IMID patients.
Methods: Descriptive study of the rheumatology APN activity since the opening of the center for a year. The APN consultations were face-to-face (scheduled or demanded) or by telephone. Variables measured: demography, diagnosis, treatments, clinic activity and patient reported outcomes (PRO). In the face-to-face consultation, was included: integral valuation (clinic, functional and psychosocial), education for Health (information about disease and treatments, adverse effects, healthy living habits), drug administration, emotional support. In the telephone consultation, the rheumatology APN is the reference professional for monitoring, question solving and advice in case of flare or adverse event.
Results: 721 patients were evaluated, mean age 54.6 years, (range, SD) (20-90, 13.9), 61.3% women, with a total of 1737 consults. Diagnosis: 324 (44.9%) RA, 221 (30.6%) SpA, 100 (13.9%) PsA and 76 (10.5%) other diseases. Treatment modality: IV 293 (40.4) SC 399 (55.3%) and oral 29 (4.0%). Rheumatology APN activities are described in Table 1. 1415 face-to-face consultation were made, 82.7% scheduled and 17.2% demanded either by the patient, the rheumatologist or another member of the multidisciplinary work-team. Among the face-to-face consultations, 62 (4.4%) patients were attended the same day in the medic consult due to disease flare or other disease problems, 38 (2.7%) patients were sent to another specialist of the work-team due to co-morbidity. The activity executed in the rheumatology APN consultation is shown in Table 2

Table 1. Educative interventions by the APN.

•Information about the disease
•Information about the treatment
•Medicine administration
•Adverse effects of the medicine
•Healthy life style habits
•Vaccines
•Evaluation of cardiovascular risk
•Signs and symptoms of alerts due to the pathology
•Ongoing following of the evolution of the disease.
•Support for the achievement of the treatment and possible difficulties.

Table 2. Activity done in the consult. Nº 1.737

Face-to-face activity	Nº consults 1.415	**Non face-to-face activity**	Nº consults 322
Complete valuation due to necessities	721 (51%)	Valuation	58 (18.0%)
Educative Interventions	1.305 (92.2%)	Questions	96 (29.8%)
Valuation and following	1.372 (97.0%)	Test result	26 (8.1%)
PRO execution	1.156 (81.7%)		
Articular counting's	733 (51.8%)		
Valuation of the diseases activity	737 (52.1%)	Process of appointment	105 (32.61
•DAS28 PCR	419 (26.6%)	•Requested by the doctor	50 (47.0%)
•ASDAS-PCR		•Requested by the patient.	55(53.0%)
Cardiovascular risk valuation.	721 (51.0%)	Derivative to different medical consults	37 (11.5%)
Blood extraction	724 (51.2%)	Solved by APN	285(88.5%)
Analytics monetarization	1.171 (82.8%)		
Medicine monetarization	1.372 (97.0%)		

Day Hospital Management

Conclusion: The rheumatology APN takes a vital part in the multidisciplinary team, offering a holistic approach, as well as efficient and high-quality care, offering quick response, reducing waiting time and becoming an important part of this patient-centered model.
Disclosure of Interests: None declared
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FRIDAY, 05 JUNE 2020

HPR Interventions (educational, physical, social and psychological)

FRI0653-HPR **AN OLEUROPEIN-BASED DIETARY SUPPLEMENT IMPROVES JOINT FUNCTIONALITY IN OLDER PEOPLE WITH HIGH KNEE JOINT PAIN**

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Background: OLE provides oleuropein the most prevalent phenolic component in olive leaves and has been shown to have potent anti-inflammatory and anti-oxidant effects potentially interesting for joint health (1).
Objectives: The aim of this study was to investigate the effects of a 6-month intervention with an Olive Leaf Extract (OLE) standardized for oleuropein content on knee functionality and biomarkers of bone/cartilage metabolism and inflammation.
Methods: The study was a randomized, double-blind, placebo-controlled, multi-centric trial of 124 subjects with mild knee pain or mobility issues. Subjects were randomized equally to receive twice a day one capsule of either maltodextrin (control treatment, CT) or 125-mg OLE (BonoliveTM, an Olive Leaf Extract containing 50 mg of Oleuropein) for 6 months. The co-primary endpoints were Knee injury and Osteoarthritis Outcome Score (KOOS) using a self-administered questionnaire and serum Coll2-1NO2 specific biomarker of cartilage degradation. The secondary endpoints were each of the five sub-scales of the KOOS questionnaire, Knee pain VAS score at rest and at walking, OARSI core set of performance-based tests and serum biomarkers (Coll2-1, MPO, CTX1, osteocalcin, PGE2 and Vplex cytokines assay in serum) and concentration of Oleuropein's metabolites in urine.
Results: Primary (global KOOS score, biomarker Coll2-1 NO2) and secondary endpoints (the five subscales of the KOOS score) improved time dependently in both groups. OLE treatment showed significantly elevated urinary oleuropein metabolites (oleuropein aglycone, hydroxytyrosol, homovanillyl alcohol and isomer of homovanillyl alcohol), and was well tolerated without significant differences in number of subjects with adverse events. At 6 months, OLE group showed a higher global KOOS score compared to placebo (treatment difference = 3.73; 95% CI = [-4.08;11.54]; p = 0.34), without significant changes of inflammatory and cartilage remodeling biomarkers. Subgroup analyses demonstrated a large and significant treatment effect of OLE in subjects with high walking pain at baseline (14.4; 95% CI = [1.19;27.63], p=0.03). This was observed at 6 months for the global KOOS score and each different subscale and for pain at walking (-23.07;95% CI = [-41.8;-4.2];p=0.02). These treatment effects at 6 months were significant for KOOS score as well as for the subscales Pain and QoL and the pain at walking.
Conclusion: OLE was not effective on joint discomfort in people with low to moderate pain at baseline but significantly benefited subjects with high pain at treatment initiation. As oleuropein is well-tolerated, OLE can be used to relieve knee joint pain and enhance mobility in subjects with articular pain the most painful subjects.
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Disclosure of Interests: Marie-Noelle Horcajada Employee of: nestlé, Maurice Beaumont Employee of: nestle, Nicolas Sauvageot Employee of: Nestlé, Laure Poquet Employee of: Nestlé, Madleen Saboudjian Employee of: Nestlé, Anne-Christine Hick Employee of: Artialis SA, Berenice Costes Employee of: Artialis SA, Laetitia Garcia Employee of: Artialis, Yves Henrotin Grant/research support from: HEEL, TILMAN
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Poster Presentations

SATURDAY, 06 JUNE 2020

Rheumatoid arthritis - aetiology, pathogenesis and animal models

SAT0001 **L-ARGININE SUPPLEMENTATION AMELIORATES BONE EROSION IN RHEUMATOID ARTHRITIS THROUGH INHIBITION OF RANKL/RANK/TRAF6 PATHWAY AND REPROGRAMMING OSTEOCLAST METABOLISM**

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Background: L-arginine is of great importance in numerous biological procedures in human body, e.g. it participates in the urea cycle for detoxification of ammonia, and functions as a modulator in immune responses (1). Our previous investigation demonstrated that treatment with L-arginine reduced clinical symptoms, bone erosion and osteoclast numbers in serum-induced arthritis (K/BxN) (2). In addition, a decreased concentration of L-arginine has been observed in the serum of rheumatoid arthritis (RA) patients. Altogether, it is suggesting that L-arginine supplementation might be a potential treatment against RA.

Objectives: This study aims to investigate the treatment role of L-arginine supplementation in murine arthritis models. The project also plans to delineate the metabolic action of L-arginine supplementation during osteoclast differentiation in the presence of an inflammatory milieu.

Methods: Three murine arthritis models (serum-induced arthritis (K/BxN) model, collagen-induced arthritis model and hTNFtg mice model) were applied in the presence or not of oral L-arginine supplementation. MicroCT and histomorphometry analyses were performed to quantify bone erosion and numbers of osteoclasts. In addition, in vitro osteoclastogenesis were performed in the presence of various amounts of L-arginine with or without treatment with 40ng/ml TNFa. OC differentiation was characterized by TRAP staining. Resorption activity was assessed by pit formation assay. Osteoclast markers and metabolic genes were determined with quantitative real-time PCR analysis and western blot. Dihydrorhodamine 123 staining was used to determine the level of intracellular ROS. Seahorse analyses and mass spectrometry metabolites analyses were conducted to address the metabolic condition.

Results: Arthritis severities were reduced after L-arginine supplementation in arthritis models. Moreover, an amelioration of bone erosion and reduced osteoclast numbers were observed in arthritic mice treated with L-arginine. *In vitro* treatment of L-arginine inhibited osteoclastogenesis, especially in the late phase of the differentiation, even with exposure to TNFa stimulation. The L-arginine induced osteoclast differentiation inhibition is likely due to an alteration in the RANKL/RANK/Traf6 pathway. L-arginine also boosted the intracellular production of ATP and ROS, promoting mitochondria-driven oxidative phosphorylations (OXPHOS), leading to the failure of activation and even death of the osteoclasts.

Conclusion: These data strongly suggested that L-Arginine ameliorates bone erosion in RA through the inhibition of RANKL/RANK/Traf6 pathway as well as reprogramming of the cellular metabolism during osteoclastogenesis. The immunometabolism action of L-Arginine might therefore help to reduce joint inflammation and destruction in RA.

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SAT0002 **ANTI-PEPTIDE ANTIBODIES SPECIFIC FOR THE HUMAN FIBRINOGEN B CHAIN COULD PLAY AN ESSENTIAL ROLE IN THE PROGNOSIS IN EARLY RHEUMATOID ARTHRITIS AND FAMILY RISK GROUPS**

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Background: Rheumatoid Arthritis (RA) is a chronic systemic and autoimmune disease. The identification of antibodies has contributed to understanding RA. Recently, anti-carbamylated protein antibodies are the new autoantibodies present in RA and have been associated with severity and detected before the onset of RA. However, it is not clear the precise target antigen of anti-CarP antibodies

Objectives: To determine associations between the anti-carbamylated protein and peptides antibodies with genetic and rheumatic indexes in patients with early RA (eRA) and individuals with family history of RA (FDR)

Methods: A cross-sectional study involving 51 eRA patients, according to ACR/EULAR 2010 and 124 FDR matched by sex and age with healthy controls (HC). Two peptides of fibrinogen beta chain (Anti-Ca-Fib2 and Anti-Ca-Fib3) and a peptide without modification were synthesized. Antibodies against carbamylated peptides were measured using in-house indirect ELISA. RF and anti-CCP by turbidimetry and ELISA, hs-CRP by chemiluminescence. ESR by capillary photometry, disease activity was measured by SDAI, DAS28, RAPID3, and disability was assessed using MDHAQ. HLA-DRB1 (shared epitope SE) typing was made using the Luminex 200 TM. The comparisons were performed by McNemar and Wilcoxon tests. The chi-squared and Fisher's tests were used in categorical variables. The associations were evaluated by the Mann–Whitney U test or t-test and conditional logistic regressions

Results: In FDR anti-Ca-Fib2 and anti-Ca-Fib3 were more frequent than HC (25.0% vs 14.5%, 34.7% vs 15.3% and 33.1% vs 11.3%, respectively). The anti-Ca-Fib2 antibodies were associated with the HLA DRB1 SE* 1501 allele (p=0.03), with non-SE *0901 allele (p=0.01) (Fig. 1), the anti-Ca-Fib3 was associated with positive RF (p=0.0012). The FDR condition was associated with the presence of anti-Ca-Fib3 (OR=4.7; 95%CI=1.8–11.7; p=0.001) and painful joints (OR=2.2; 95%CI=1.01–4.68; p=0.045). In eRA anti-Ca-Fib2 were more frequent 47.1% vs. 13.7% in HC (OR 6.6 95% CI: 1.97-35.0 p = 0.0005) showing a risk of present anti-Ca-Fib2 antibodies six times higher in patients, without no differences in the frequency of anti-Ca-Fib3 between patients and controls. The anti-Ca-Fib2 antibodies were associated with positive RF (p = 0.022) and with high positive anti-CCP (p = 0.032) additionally we observed association with HLA-DRB1 SE * 0405 (p = 0.050) and non SE alleles * 1501 (p = 0.026) and * 0407 (p = 0.010)(Fig.2). Anti-Ca-Fib3 were associated with DAS28 ESR (p = 0.046) and with the HLA-DRB1 SE * 1402 allele (p = 0.050) and non-SE *0301 allele (p = 0.025). We found an association between eRA diagnosis with the presence of anti-Ca-Fib2 (OR 6.72 95% CI: 1.09-41.38 p = 0.040) and positive anti-CCP (OR 7.94 95% CI: 1.44-43.77 p = 0.017)

Conclusion: Anti-Ca-Fib3 and anti-Ca-Fib2 antibodies might have significant prognostic value because the relationship with joint inflammatory manifestations in FDR. These results suggest a role for these antibodies as early biomarkers of RA, probably including additional mechanisms related to other non-SE alleles, especially in high-risk individuals. Finally, the anti-peptide antibodies in the present study may represent a straightforward way to identify antibodies directed to a specific carbamylated target

Figure 1 association of carbamylated anti-peptide antibodies with the presence of HLA DRB1 SE and non-SE in eRA

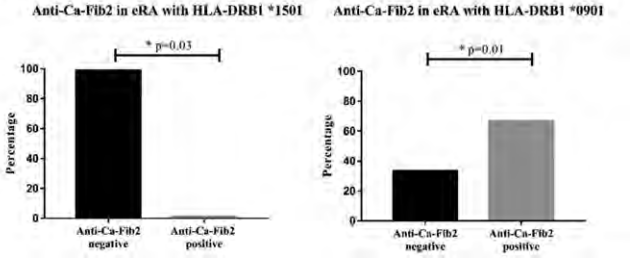
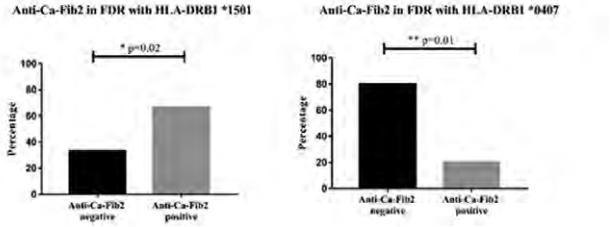


Figure 2 association of carbamylated anti-peptide antibodies with the presence of HLA DRB1 SE and non-SE in FDR



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SAT0003 ELEVATED BASELINE AND INCREASING AUTOANTIBODY LEVELS ARE ASSOCIATED WITH INCREASED RISK FOR IMMINENT ONSET OF INFLAMMATORY ARTHRITIS IN A PROSPECTIVELY STUDIED ANTI-CITRULLINATED PROTEIN ANTIBODY POSITIVE COHORT: THE TIP-RA COLLECTIVE

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Background: The Targeting Immune Responses for Prevention of RA (TIP-RA) Collaborative prospectively studies individuals at high risk for developing RA because of serum ACPA positivity in absence of baseline inflammatory arthritis (IA).

Objectives: The objective of the analyses presented herein is to evaluate the role of baseline and changing levels of ACPA and rheumatoid factor (RF) in relationship to incident IA/RA.

Methods: ACPA+ subjects and ACPA- controls were identified who did not have baseline historical or examination evidence of IA. ACPA+ was defined by serum elevation of anti-CCP3 ≥20 units (Inova). Subjects were evaluated annually or sooner if they had changes in joint symptoms. Factors including RFIgM and RFIgA (Inova) were also assessed, and relationships between autoantibody levels at baseline and over time and incident IA/RA were evaluated using t-tests, with paired testing where applicable.

Results: Baseline characteristics of ACPA+ and ACPA- subjects are in Table 1. Sixteen of the 94 (17%) ACPA+ subjects developed IA/RA a mean of 518 days from the baseline visit; 14 of these met 2010 ACR/EULAR criteria for RA at the time of detection of IA. There was a trend for ACPA+ subjects who later developed IA/RA to have higher baseline levels of anti-CCP3 compared to those who did not develop IA/RA (Table 2). In addition, those who developed IA/RA had significantly higher mean levels of RFIgM and RFIgA compared to those who did not. While not statistically significant, in longitudinal analyses in the ACPA+ subjects with incident IA/RA, anti-CCP3 levels increased from baseline to identification of IA (mean [SD] of 119 [102] to 126 [100], p=0.42). Furthermore, RFIgM levels increased from 36 [49] at baseline to 43 [51] at the time of IA (p=0.31), and RFIgA levels increased from 16 [29] to 21 [31] (p=0.10). In contrast, in ACPA+ subjects who did not develop IA/RA, anti-CCP3 levels increased only slightly over follow-up of a mean of 712 days: 75 [75] to 80 [76], p=0.70 while the levels of RFIgM and RFIgA decreased slightly during the same follow-up: for RFIgM mean [SD] levels went from 9 [22] to 8 [19], p=0.74; for RFIgA, 5 [16] to 3 [12], p=0.67.

Table 1. Baseline characteristics of ACPA+/- subjects

	ACPA- (n=162)	ACPA+ (n=94)	**p-value**
Age, mean	58	58	0.90
% Female	69	68	0.67
% Ever smoker	33	34	0.87
RF-IgM, mean (SD)	3.2 (10.0)	13.5 (30.2)	<0.01
RF-IgA, mean (SD)	0.3 (0.6)	6.5 (19.1)	<0.01

Table 2. Baseline characteristics of 16 ACPA+ subjects who developed incident IA/RA vs. 78 ACPA+ who did not

	Did not develop IA/RA (n=78)	Developed IA/RA (n=16)	p-value
Days from baseline to IA/RA or follow-up, mean (SD)	712 (124)	518 (295)	–
% Meeting 2010 criteria at time of IA	-	88	–
CCP3, mean (SD)	74.5 (75.3)	119.1 (102.1)	0.05
RFIgM, mean (SD)	**9 (22)**	**36 (49)**	**<0.01**
RFIgA, mean (SD)	**4 (16)**	**16 (29)**	**0.03**

Conclusion: In this prospectively followed cohort of ACPA+ subjects, higher levels of RFIgM and RFIgA at baseline were significantly associated with development of IA/RA within the follow-up period. Furthermore, there was a trend for rising levels of anti-CCP3 and RFIgM and A to be associated with development of IA/RA. These finding support the use of higher and/or rising levels of autoantibodies as additional features to predict imminent onset of IA/RA in ACPA+ individuals as well as potentially to use as outcomes of success of preventive interventions. Furthermore, the trend of increasing levels of RFIgM and RFIgA over time in individuals who developed IA/RA suggests that targeting pathways of RF development may lead to preventive interventions in a subset of RA.

References: None

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SAT0004 INCREASED M1 INFLAMMATORY PHENOTYPE OF CIRCULATING MONOCYTES IS ASSOCIATED WITH HISTORY OF CARDIOVASCULAR EVENTS IN RA PATIENTS

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Background: Cardiovascular (CV) Disease is the main cause of death in Rheumatoid Arthritis (RA). Current tools like Framingham or European SCORE underestimate CV risk in RA patients. Efforts to improve the assessment including RA biomarkers (disease activity) have been only partially successful. There is a need for better biomarkers to identify AR patients at high risk for CV disease. Monocytes have an important role in plaque development. Monocytes differentiates into 2 main phenotypes M1 and M2 (1). In RA and in post-MI patients M1 monocytes are expanded (2). mTORC influences monocyte phenotype *in vitro* and has been associated with development of atheromatous plaque (3).

Objectives: To evaluate the phenotype of circulating monocyte in RA patient with or without previous CV events (RA-CV(-)RA-CV(+)), and its possible association with mTORC activity.

Methods: 9 RA-CV(+)patients aged between 18 and 65 yo with RA (EULAR/ACR 2010 criteria), were paired with RA-CV(-)patients. 6 healthy individuals (HI) were also studied. Pairing criteria were classic CV risk factors (AHA 2018), sex, age, years since RA diagnosis, comorbidities, number of DMARDs previously used and use of bDMARDS. M1 and M2 circulating Monocytes were evaluated in PBMC obtained from patients and controls by flow cytometry analysis. Intracellular inflammatory cytokines (IL1, Il6) and phosphorylated S6R (P-S6R) as a measure of mTORC activation was also evaluated. M1 was defined as CD14+HLA-DR+CCR2+ and M2 CD14+CD163+CCR2-. DAS28-RCP, DAS28-ESR and Lipid profile was also measured. The differences among groups was analysed using Mann–Whitney U nonparametric. The relationship between variables with Spearman rank correlation test.

Results: There were no differences in demographic, RA characteristic and CV risk factors between RA-CV (+) and RA-CV (-) patients. Male/Female 4/5, age 62±3 and 63±2 respectively. HI were younger than RA patients (32.5±7). CV events were 8 patients with MI and one Stroke. DAS28-RCP was 2.96±0.23 and 2.88±0.43 respectively. One patient in each group had failed to more than 2 sDMARDs

and one in each group was receiving bDMARD. M1 circulating monocytes were expanded in RA as compared to HI. This difference was at RA-CV (+) expense. RA monocytes had higher Intracellular levels of IL-1b and IL-6 as compared to HI. M1 from RA-CV (+) had higher intracellular levels of IL-1b and IL-6 than RA-CV (-). M1 monocytes have higher levels of inflammatory cytokines than M2. P-S6R protein, (mTORC activation), was higher in RA patients than HI. The highest levels of P-S6R was observed in M1 monocytes from RA-CV(+) population.

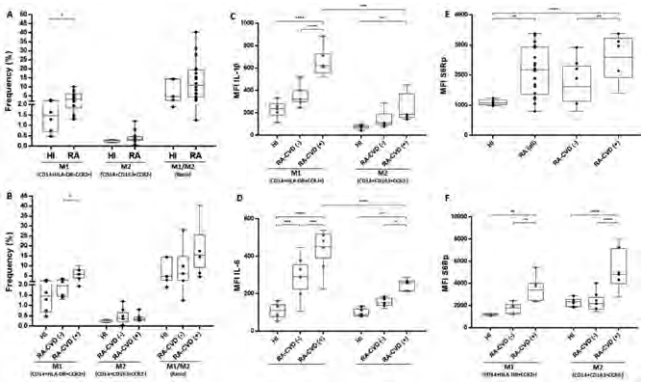


FIGURE 1. Circulating monocytes phenotype, intracellular cytokines and phosphorylated S6R in HI and RA-CV (+), RA-CV (-) and the combined RA patients.

A) *=0,02; B) *=0,016; C) ****=0,0001, **=0,002; D) ****=0,0001, ***=0,0008, **=0,001, *=0,01; E) ****0,0001, **=0,002; F) ****=0,0001, **=0,001, **=0,003.

Conclusion: RA-CV+ patients, have a significantly higher number of pro-inflammatory circulating monocytes, using a multiparametric classification method. These monocytes also express higher levels of inflammatory cytokines and higher activation of mTORC, which also participate in the development of atheromatous plaque, suggesting that these monocytes could be a key element in the non-clarified-yet, excess of CV risk of RA patients.

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SAT0005 INHIBITION OF HEPATOCYTE GROWTH FACTOR/C-MET SIGNALING ABROGATES JOINT DESTRUCTION BY SUPPRESSING MIGRATION OF MONOCYTES TO SYNOVIUM IN RHEUMATOID ARTHRITIS

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Background: Hepatocyte growth factor (HGF), originally discovered as a mitogen of hepatocytes, binds to receptor-tyrosine kinase c-Met and has been shown to be a multi-functional cytokine that promotes processes such as cell proliferation, survival, differentiation, migration, and angiogenesis[1]. Since HGF/c-Met signaling also leads to tumorigenesis and cancer invasion, that has recently attracted attention as a target for anticancer agents[2]. However, in reports of rheumatoid arthritis (RA), though anti-inflammatory and antiangiogenic mechanisms related to HGF/c-Met signal inhibition have been reported, the role of HGF in RA bone destruction through monocyte migration remains unclear[3].

Objectives: To determine the expression of HGF in RA biological fluids, the role it plays in monocyte migration and the therapeutic effect of a savolitinib, a specific c-Met inhibitor, in arthritis model mice.

Methods: HGF/c-Met expression in serum, synovial fluid (SF), and synovial tissues (STs) obtained from RA patients and control subjects, as well as RA fibroblast-like synoviocytes (FLSs) was evaluated by ELISA and immunostaining. To determine the function of HGF in RA SFs, we preincubated RA SFs with a neutralizing anti-HGF antibody and measured the ability of these SFs to induce the human acute monocytic leukemia cell line (THP-1) chemotaxis. Additionally, examinations of SKG mice treated with savolitinib (2.5 mg/kg/day) for 4 weeks were conducted.

Results: HGF level in serum from RA patients was significantly higher as compared to the controls (930 ± 97 vs. 476 ± 97 pg/mL, p <0.01) and decreased by drug treatment for 24 weeks (1147 ± 284 vs. 539 ± 160 pg/mL, p <0.05). Additionally, HGF level in SF from RA patients was higher as compared to SF from osteoarthritis patients (1632 ± 366 vs. 566 ± 140 pg/mL, p <0.05). HGF and c-Met expressions were also noted in RA STs. Stimulation of RA-FLS with TNF-α increased HGF/c-Met expression in a concentration-dependent manner, and c-Met signal inhibition by SU11274 suppressed production of fractalkine/CX3CL1, CXCL16, and MIP-1α/CCL3 (mean 50%, 56%, 90%, respectively). When HGF was removed by immunoprecipitation, migration of THP-1 in RA-SF was suppressed (mean 23%). In SKG mice, savolitinib significantly suppressed ankle bone damage on μCT, with an associated reduction in number of tartrate-resistant acid phosphatase-positive osteoclasts.

Conclusion: HGF is produced by inflammation in synovium associated with RA, and then activates monocyte migration to synovium tissue and promotes bone destruction through its own chemotactic effect as well as enhanced chemokine production. These results indicate that a strategy that targets c-Met signaling may be important for resolving bone destruction in RA.

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SAT0006 SIMULTANEOUS ANALYSIS OF ANTI-CCP, RHEUMATOID FACTOR, ANTI-PAD4 AND ANTI-CARBAMYLATED PROTEIN ANTIBODIES REVEALS INTERACTION EFFECTS WITH RESPONSE TO ANTI-TNF THERAPY IN RHEUMATOID ARTHRITIS

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Background: Blocking of the Tumor Necrosis Factor (TNF) activity is a successful therapeutic approach for 2 out of 3 Rheumatoid Arthritis patients. Identifying the patients that will not respond to this therapeutic approach is a major translational goal in RA. Association of seropositivity to rheumatoid factor (RF) or anti-cyclic-citrullinated antibodies (anti-CCP) with anti-TNF response has proven inconclusive, suggesting that other yet unexplored biomarkers could be more informative for this goal.

Objectives: We tested the association of two recently introduced biomarkers in RA: anti-carbamylated protein antibodies (anti-CarP) and anti-peptidylarginine deiminase type 4 (anti-PAD4).

Methods: A prospective cohort of n=80 RA patients starting anti-TNF therapy was recruited and levels for all four autoantibodies -RF, anti-CCP, anti-CarP and anti-PAD4- were measured at baseline. The change in DAS28 score between baseline and week 12 of therapy was used as the clinical endpoint.

Results: Single marker-analysis showed no significant association with drug response. However, when testing for interactions between autoantibodies, we found highly significant associations with drug response. Anti-CCP and RF showed a positive interaction with the response to anti-TNF therapy (P=0.00068), and anti-PAD4 and antiCarP titers showed a negative interaction with the clinical response at week 12 (P=0.0062). Using an independent retrospective sample

(n=199 patients), we validated the interaction between anti-CCP and RF with the clinical response to anti-TNF agents. (P=0.044).
Conclusion: The results of this study show that interactions between antibodies are important in the response to anti-TNF therapy and suggest potential pathogenic relationships.
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SAT0007 BLOCKING HISTAMINE-RELEASING FACTOR/ TRANSLATIONALLY CONTROLLED TUMOR PROTEIN (HRF/TCTP) ATTENUATES AGGRESSIVENESS OF FIBROBLAST-LIKE SYNOVIOCYTES AND AMELIORATES COLLAGEN-INDUCED ARTHRITIS IN RHEUMATOID ARTHRITIS

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Background: Histamine-releasing factor/translationally controlled tumor protein (HRF/TCTP) stimulates cancer progression and allergic responses. Increased expression of HRF/TCTP occurs in joints of rheumatoid arthritis (RA) patients, but the role of HRF/TCTP in RA remains undefined
Objectives: In this study, we explored the pathogenic significance of HRF/TCTP and evaluated therapeutic effects of HRF/TCTP blockade in RA.
Methods: HRF/TCTP transgenic (TG) and knockdown (KD) mice with collagen-induced arthritis (CIA) were used to determine experimental phenotypes of RA. HRF/TCTP levels were measured in sera and joint fluids in patients with RA and compared to those with osteoarthritis, ankylosing spondylitis, Behcet disease, and healthy controls. HRF/TCTP expression was also assessed in synovium and fibroblast-like synoviocytes (FLS) obtained from RA or OA patients. Finally, we assessed effects of HRF/TCTP and dimerized HRF/TCTP binding peptide-2 (dTBP2), an inhibitor of HRF/TCTP, in RA-FLS and CIA mice.
Results: Our clinical, radiological, histological, and biochemical analyses indicate that inflammatory responses and joint destruction were increased in HRF/TCTP TG mice, and decreased in KD mice compared to wild-type littermates. HRF/TCTP levels were higher in sera, synovial fluid, synovium, and FLS of patients with RA than in control groups. Serum levels of HRF/TCTP correlated well with disease activity in RA. Tumor-like aggressiveness of RA-FLS was exacerbated by HRF/TCTP stimulation and ameliorated by dTBP2 treatment. dTBP2 exerted protective and therapeutic effects in CIA mice, and had no detrimental effect in a murine tuberculosis model.
Conclusion: Our results indicate that HRF/TCTP represents a novel biomarker and therapeutic target for diagnosis and treatment of RA.
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SAT0008 INDIVIDUAL FUNCTIONS OF THE HISTONE-ACETYLTRANSFERASES CBP AND P300 IN REGULATING THE INFLAMMATORY RESPONSE BY AFFECTING HISTONE ACETYLATION AND MRNA STABILITY

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Background: Prolonged TNF-induced H3K27 acetylation (H3K27ac) and increased mRNA stability in rheumatoid arthritis (RA) synovial fibroblasts (SF) are leading to a sustained inflammatory response. Underlying enzymes coordinately regulating these pathways have not been identified so far. The histone acetyltransferases cAMP-response element binding protein binding protein (CBP) and p300 are writers of activating H3K27ac marks and close homologues with widely accepted redundant functions.
Objectives: To analyze individual functions of CBP and p300 in regulating the inflammatory response of RA SF.
Methods: SF were isolated from patients with RA undergoing joint replacement surgery. The expression of CBP and p300 was silenced by transfection of antisense LNA gapmeRs (12.5 nM). SF were stimulated with TNF (10 ng/ml) for 24h. Actinomycin D (10 µg/ml) was added 4h after TNF-treatment for 2h and 4h (n=3) to test mRNA stability. Transcriptomes were determined by RNA-seq (Illumina NovaSeq 6000, n=6). We mapped raw reads from RNA-seq reference genome using STAR. Counts for genes were obtained using Feature counts. We searched for differential expression genes (DEG) across experimental conditions using general linear models (glm) implemented in 'edgeR' package of R. Significantly affected genes (± fold change > 1.5, FDR < 0.05, top 3000 genes included) entered pathway enrichment analysis for Gene Ontology (GO) biological process, and KEGG pathways in DAVID. Changes in the mRNA (n=12-14) and protein expression (n=6-12) were confirmed by quantitative Real-time PCR and ELISA. The levels of activating histone marks H3K27ac and nuclear localization of p50 and p65 were analyzed by Western blotting.
Results: DEG revealed that silencing of p300 affected the expression of 6026 and 5138 genes in unstimulated and stimulated SF, respectively. In contrast, only 285 and 1911 genes were affected by CBP silencing in unstimulated and stimulated SF, respectively. In TNF-stimulated SF, pathway enrichment analysis of DEG revealed a key role of CBP in regulating the "type I interferon signaling pathway" ($p=2.12x10^{-6}$). Both, silencing of CBP and p300 regulated genes enriched in the "TNF signaling pathway" (CBP: p=0.005; p300: p=0.031). In contrast to CBP silencing that had anti-inflammatory effects, silencing of p300 had pro-and anti-inflammatory effects. ELISA experiments suggested that silencing of CBP reduced the secretion of IL6 (p<0.01), CCL2, CXC3L1 (p<0.05), and CXCL12 (p<0.001). Silencing of p300 reduced the secretion of CCL2 (p<0.001) and CXC3L1 (p<0.05) but increased the expression of IL8 (p<0.001) and CXCL2 (p<0.05). Western blotting revealed that neither CBP, nor p300 silencing affected the nuclear expression of the NF-κB subunits p65 and p50. Silencing of p300 reduced the levels of H3K27ac by 30% in unstimulated SF, and by 61.4% (p<0.05) in presence of TNF. In addition to regulating H3K27ac, silencing of p300 regulated the expression of TNF-induced cytokines by increasing the mRNA stability of IL8, IL6 and CCL2 mRNA but not of CXCL2. Silencing of CBP reduced H3K27ac by 43.5% only in presence of TNF and did not affect TNF-induced mRNA stability of cytokines. This is in line with the enrichment of the GO biological process "regulation of mRNA stability" ($p=2.61x10^{-8}$) being enriched only after silencing of p300.
Conclusion: Our results suggested that p300 is the major writer for H3K27ac marks in SF. Additionally, p300 regulated cytokine expression by affecting mRNA stability in a target-specific manner. We identified overlapping and distinct functions for CBP and p300 in regulating the inflammatory response of SF.
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SAT0009 ROLE OF EC-18 IN AUTOIMMUNE ARTHRITIS AND INTERSTITIAL LUNG DISEASE IN CURDLAN-ADMINISTERED SKG MICE

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Background: Although the mortality of patients with rheumatoid arthritis (RA), for which interstitial lung disease (ILD) is one of the major contributors, has still not decreased, new target therapies for RA have shown good response in peripheral arthritis. EC-18 (acetylated diacylglycerol 1-palmitoyl-2-linoleoyl-3-acetyl-rac-glycerol) is a mono-acetyl-diglyceride that has been isolated from the

antlers of sika deer and can be chemically synthesized from glycerol, palmitic acid, and linoleic acid. Research using LPS-induced acute lung injury murine model has reported that EC-18 stimulates a more rapid resolution of LPS-induced lung Inflammation. In addition, it has been reported that in a murine model of collagen-induced arthritis, EC-18 treatment ameliorated arthritis, with down-regulation of IL-6 level by regulating the activity of STAT3 in the synovium. Curdlan-administered SKG mice develop ILD spontaneously followed by peripheral arthritis, which resembles RA-ILD.

Objectives: We evaluated the modulatory effect of the EC-18 on arthritis and ILD in autoimmune arthritis animal model.

Methods: Male SKG mice were obtained from Dr. S. Sakaguchi. We injected curdlan (3 mg/mice) in 8-week-old SKG mice and identified the presence of ILD by histological analysis at 20 weeks post-injection. Arthritis score was measured every week for up to 20 weeks. EC-18 (250 mg/kg body weight/day, Enzychem Lifesciences Co., Daejeon, Korea) was administered every day orally. At 20 weeks post-injection, lung sections were stained with H&E and Masson's trichrome. Using the Opal method, multiplexed immunofluorescent staining of lung tissue was performed. According to the scale by Ashcroft et al., fibrosis severity of lung sections was assessed by a system of eight grades. Analysis of serum cytokines by the luminex multiplex cytokine assay was performed at 20 weeks post-injection.

Results: Oral administration of EC-18 decreased arthritis score significantly until 8 weeks post-injection and remained unchanged thereafter. At 20 weeks post-injection, histological analysis showed severe pulmonary destruction, including bronchial alveolar tissue damage and massive leukocyte infiltration, and fibrosis in the curdlan-administered mice, which was attenuated in EC-18 treated mice. In particular, 67% of curdlan-administered mice showed ILD-like phenotype, whereas the incidence rate in EC-18-treated mice was 17%. Furthermore, immunofluorescent-staining showed both IL-17A and neutrophil accumulation in lung in curdlan-administered mice; these were decreased in EC-18-treated mice. Interestingly, at 20weeks post-injection, EC-18 treatment down-regulated serum levels of IL-6 and TNF-α and up-regulated sIL-7Rα (anti-fibrotic molecule).

Conclusion: Taken together, EC-18 exerts an anti-arthritic effect in early phase, but a long-term effect was not indicated. We emphasize the effect on ILD prevention of EC-18 via up-regulation of sIL-7Rα and inhibition of neutrophil accumulation, suggesting a therapeutic agent potentially for RA-ILD.

Disclosure of Interests: None declared

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SAT0010 ANTI-CD30 IMMUNOTHERAPY AMELIORATES BONE AND CARTILAGE DESTRUCTION IN EXPERIMENTAL MODEL OF RHEUMATOID ARTHRITIS IN MICE

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Background: CD30 is a member of the TNF-receptor family and commonly expressed on lymphocytes of Hodgkin lymphoma and anaplastic large cell lymphoma. It has been reported that levels of soluble CD30 in serum and joint fluid is significantly elevated in rheumatoid arthritis (RA). Although RA patients may develop lymphoproliferative disorders (LPD) as a result of immunosuppression by MTX or bDMARDs, safety medications after the regression of LPD for RA have not yet been established.

Objectives: To explore the potential of CD30 targeting therapy for RA.

Methods: (1) Immuno-histological staining of CD30 was performed for fresh synovial tissues of RA and osteoarthritis (OA). In addition, double immunofluorescence staining of CD30 with CD3, CD20, CD68, CD138 were performed on RA synovial tissue. (2) Brentuximab vedotin (BV) is an anti-CD30 antibody conjugated with monomethyl auristatin E, designed to induce apoptosis of CD30 expressing cells. A multiple myeloma cell line (RPMI8226) was used as a non-lymphoma cell line and plasma cell-like cell line. Immuno-cytological staining for CD30 was performed on RPMI8226. Cells were cultured and harvested on days 0, 1, and 3 to evaluate the effects of BV (50 μl / ml per well). Cytospin specimens were stained by May-Grunwald-Giemsa (MGG) staining for cell counting and by FIFC-terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) staining for detection of apoptosis. (3) Collagen antibody induced arthritis (CAIA) was induced in DBA/1 mice by arthritogenic cocktail of monoclonal antibodies against type II collagen. BV was administered to the treatment groups (30mg/kg and 70mg/kg n=4 each) and evaluated clinical score, histological findings and levels of SAA, IL-6, and TNFα in serum by ELISA. Student's *t*-test (two-tailed) was used to determine statistical significance for analysis of synovial tissues and cell line assay. Two way ANOVA with Dunnett's post hoc analysis was used for multiple comparisons of mice model.

Results: (1) The number of CD30-positive cells was significantly higher in RA synovial tissue than in OA synovial tissue ($p<0.01$) (Fig. 1). CD30-positive cells were detected around the lymphoid follicles. Double immunofluorescence showed CD30 and CD138 double-positive cells in the synovial tissue of RA, suggesting CD30 is predominantly expressed by plasma cells. (2) RPMI8226 cells expressed CD30. BV caused apoptosis of RPMI8226 cells, and the number of cells treated with BV decreased to 95% compared to controls. (3) All control mice (n=4) developed severe arthritis, and their scores reached a peak (score: 13.3) on day 10. In the mice of treatment group of 30 mg/kg, paw swelling was slightly decreased, their clinical score reached a peak (score: 9.3) on day 10. In contrast, paw swelling was significantly reduced in the 70 mg/kg treatment group. The peak of the clinical score was 4.3 on day 10 (Fig.2). Histological score evaluated synovitis with infiltration of inflammatory cells, pannus formation, and erosion of bone and cartilage. Histological score of hind paws were 3.0 ± 0.8 for the control group, 2.7 ± 1.0 for 30 mg/kg group, and 0.7 ± 1.1 for 70 mg/kg group ($p<0.01$), respectively. The serum levels of SAA and IL-6 of treatment group were lower than those of no treatment group ($p<0.01$).

Conclusion: We showed the expression of CD30 on synovial tissue of RA and the expression of CD30 on plasma cells. In addition, the current study provides the first evidence that BV depletion of CD30-positive cells suppressed arthritis and osteochondral destruction in CAIA mice. Our results may provide an important clue for the development of an effective treatment for RA with iatrogenic immunodeficiency-related LPD.

Fig. 1: Immuno-histological staining of CD 30 for fresh synovial tissues

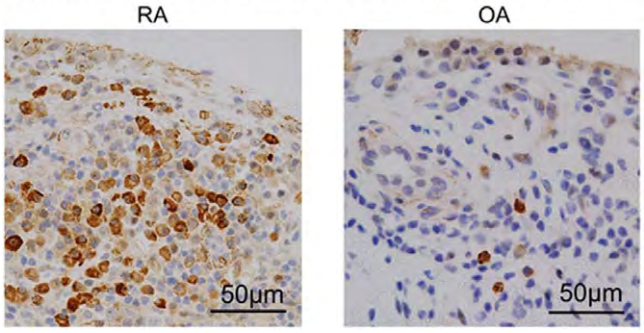
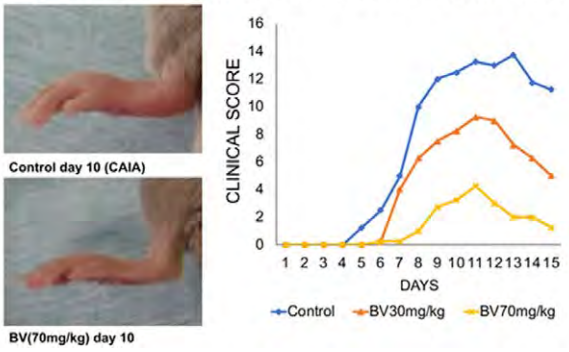


Fig. 2: BV dose-dependently suppress paw swelling and the clinical score of CAIA



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SAT0011 COMBINED INHIBITION OF AUTOPHAGY AND GLUTAMINE METABOLISM SUPPRESSES CELL GROWTH OF RA SYNOVIOCYTES AND AMELIORATES ARTHRITIS IN SKG MICE

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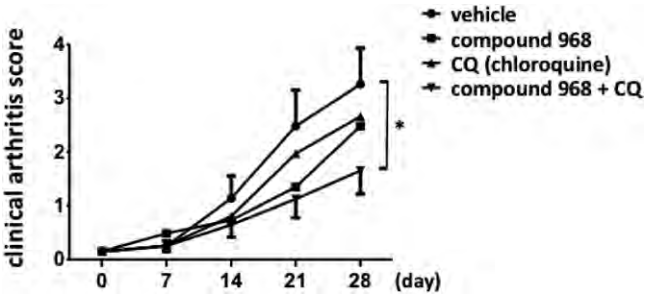
Background: Immunometabolism is now recognaized to be crucial in the pathogenesis of rheumatoid arthritis (RA). We have recently shown that the expression of glutaminase 1 (GLS1), a key enzyme in glutaminolysis, is upregulated in fibroblast-like synoviocytes from RA patients (RA-FLS) and that GLS1 inhibition

suppresses RA-FLS proliferation (1). However, glutaminolysis has been known to suppress autophagy by activating mTORC1 or counteracting ROS production (2). Given the possibility of autophagy upregulation following glutamiolysis inhibition, therapies targeting both autophagy and glutaminolysis may be more effective in suppressing cell growth of RA-FLS, yet the relation between glutaminolysis and autophagy in RA-FLS has not been investigated.

Objectives: To examine the effects of inhibiting both glutaminolysis and autophagy on RA-FLS and autoimmune arthritis in SKG mice.

Methods: GLS1 inhibitor, compound 968 (C968), was used to suppress glutaminolysis, and Chloroquine (CQ) was used to inhibit autophagy. To detect autophagy, the expression of ATG5 and LC3B was measured by real-time PCR and the production of LC3-II was analyzed by Western blotting. The formation of autophagic vacuoles was identified by immunfluorescense. Cell growth was evaluated by BrdU assay. Apoptosis was analyzed by flow cytometry staining with Annexin V-FITC and PI. C968 and CQ were administered subcutaneously to Zymosan A-injected SKG mice.

Results: C968 upregulated the expression of ATG5 and LC3B, and increased the protein level of LC3-II in RA-FLS. C968 also facilitated autophagosome formation. These results suggested that inhibition of glutaminolysis promoted autophagy in RA-FLS. The combined treatment with C968 and CQ significantly suppressed cell proliferation of RA-FLS more strongly than did C968 or CQ alone. In addition, C968 combined with CQ increased the apoptosis rate, whereas either C968 or CQ alone did not. Furthermore, combination of C968 and CQ significantly attenuated the degree of arthritis in SKG mice, while C968 or CQ monotherapy did not (Figure).



Conclusion: The GLS1 inhibitor C968 promotes autophagy in RA-FLS. C968 in combination with CQ reduces proliferation and enhances apoptosis in RA-FLS, and ameliorates the arthritis in SKG mice. Suppressing C968-induced autophagy may be a promising therapy for arthritis.

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SAT0012 ANTIBODY REACTIVITY AGAINST NATIVE PROTEINS IN RHEUMATOID ARTHRITIS

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Background: The majority of patients with rheumatoid arthritis (RA) produce autoantibodies against proteins that have undergone post-translational modfication, e.g. citrullination or carbamylation. There is growing evidence of their relevance and their potential utility to improve diagnosis, patient stratification, and prognosis for precision medicine. Investigating new autoantibody patterns may allow further stratification of patients and identifying subsets of patients that benefit from different treatment modalities. Following the discovery of high autoantibody reactivity against multiple modified proteins the interest in native targets decreased. Even though antibodies reacting with native proteins may also have a role in RA pathogenesis, their reactivity patterns are much less studied.

Objectives: To identify novel native autoantigens in RA patients and elucidate patterns within autoantibody reactivity against native autoantigens.

Methods: We investigated the reactivity of autoantibodies in plasma pools from 15 anti-CCP positive and 10 anti-CCP negative RA patients and 10 healthy donors against more than 1600 human proteins in native configuration using the Immunome high-density protein microarray.

Results: We identified 86 native proteins that were recognized by IgG antibodies from anti-CCP positive RA patients and 76 native proteins recognized by IgG antibodies from anti-CCP negative RA patients, but not by antibodies from healthy donors. Examples of proteins recognized by both patient subgroups are calcium/calmodulin-dependent protein kinase type II subunits, histone deacetylases, keratin, and vimentin. Reactivity against the ribonucleic protein SSB was observed in anti-CCP negative RA patients only.

Conclusion: Several human proteins in their native conformation are recognized by autoantibodies from anti-CCP positive as well as anti-CCP negative RA patients. In general, anti-CCP positive patients had higher autoantibody activity than anti-CCP negative patients and healthy donors.

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SAT0013 PIM-1 KINASE IS A MEASURABLE MEDIATOR OF CD4+ T CELL DYSREGULATION AND THERAPEUTIC TARGET IN EARLY RHEUMATOID ARTHRITIS

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Background: As well as being an established oncoprotein and a therapeutic target in cancer, *Proviral Integration site for murine Moloney leukemia virus-1* (pim-1) has been implicated in human autoimmunity. We previously confirmed this serine-threonine protein kinase to be strikingly upregulated in circulating CD4+ T cells of untreated rheumatoid arthritis (RA) patients as a consequence of IL-6 signalling[1-2]. Evidence for the relevance of pim-1 signalling in the disruption of RA synovial fibroblast (RASF) homeostasis[3] further supports its candidacy as a therapeutic target.

Objectives: To investigate PIM1 and its family members (PIM2 and PIM3) as potential candidates for drug repurposing in RA.

Methods: A flow cytometric assay for PIM1 transcript measurement in circulating CD4+ T cells of early arthritis patients was validated against real-time PCR in paired cells isolated by bead selection. Synovial protein expression in tissue from the same cohort of untreated RA patients and disease controls was determined by quantitative multiplex immunofluorescence. The functional consequences of manipulating pim kinase family expression in freshly purified T cell receptor (TCR)-stimulated CD4+ T cells from early RA patients was explored. The impact of pim-1 specific and pim-1-3 (pan-pim) kinase inhibition on progression of the IL-6 dependent collagen-induced arthritis (CIA) model was assessed.

Results: The percentage of circulating CD4+ T cells positive for *PIM1* transcript by flow cytometry proved a faithful surrogate for gene expression in early arthritis (Figure 1*A*), distinguishing RA from other pathologies (Figure 1*B*). Pim-1 protein expression was increased in the synovium of untreated RA compared with disease controls, including amongst infiltrating CD4+ T cells

(Figure 1*C-D*). *In vitro*, exposure of TCR-stimulated early RA CD4+ T cells to pim kinase inhibitors restrained their activation and proliferative capacity; diminished pro-inflammatory cytokine production (IFN-g and IL-17) and an expanded CD25^{hi}FoxP3+ regulatory T cell (Treg) fraction were also observed in treated *versus* un-treated cells. Finally, administration of pim inhibitors robustly attenuated clinical scores of arthritis in the CIA model, with reduced cartilage loss observed in animals treated with a pan-PIM inhibitor compared with vehicle control (Figure 2).

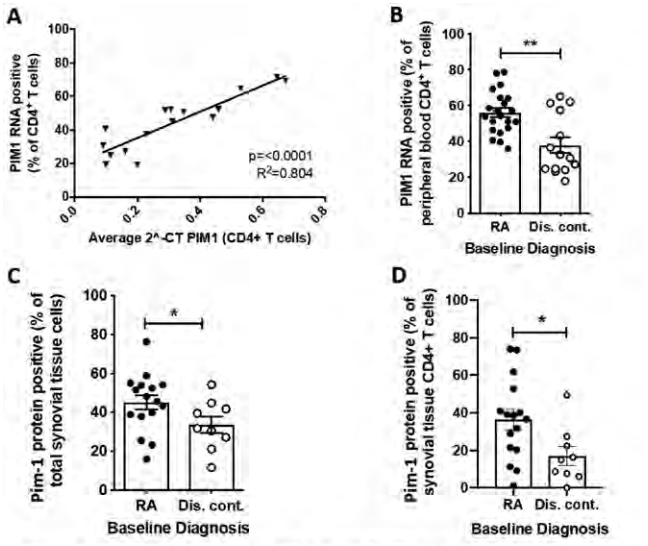


***Figure 1**. **A**. Correlation between CD4+ T cell PIM1 readouts of flow cytometric assay and real-time PCR. **B**. PIM1 transcript in circulating RA and disease control CD4+ T cells. Quantitative immunofluorescence staining for pim-1 in (**C**) nucleated (DAPI+) synovial cells and (**D**) CD3+CD4+ T cells in particular.*

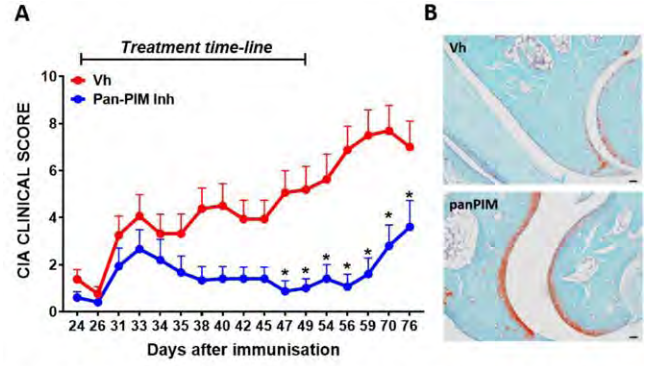


***Figure 2**. **A**. Significantly reduced arthritis severity amongst CIA mice treated with pan-pim inhibitor (n=15) compared with vehicle control (Vh; n=16). **B**. Representative images depicting preserved ankle joint cartilage layer (safranin O) following pan-pim kinase inhibition (day 50; separate experiment).*

Conclusion: Our data highlight pim kinases as plausible therapeutic targets for a subgroup of early RA patients that may be identifiable using tractable in vitro assays. Pim kinase inhibitors could simultaneously target immune inflammation and RASF dysregulation; consideration should now be given to their repurposing for this condition.

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Disclosure of Interests: Nicola Maney Consultant of: Current employee of Eli Lilly, Henrique De Paula-Lemos: None declared, Ben Barron-Millar: None declared, Andrew Mellor Shareholder of: NewLink Genetics PLC, and has received patent licensing income from this source., John D Isaacs Consultant of: AbbVie, Bristol-Myers Squibb, Eli Lilly, Gilead, Janssen, Merck, Pfizer, Roche, Amy Anderson: None declared, Arthur Pratt Grant/research support from: Pfizer, GlaxoSmithKlein

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SAT0014 ENDOTHELIAL PROGENITOR CELLS: ROLE IN ENDOTHELIAL DAMAGE OF INTERSTITIAL LUNG DISEASE ASSOCIATED TO RHEUMATOID ARTHRITIS

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Background: Interstitial lung disease (ILD) is one of the most significant comorbidities of rheumatoid arthritis (RA), increasing the mortality in these patients [1,2]. Although the pathogenesis of ILD associated to RA (RA-ILD$^+$) remains poorly defined [1], it is known that vascular tissue plays a crucial role in lung physiology [3]. In this context, a population of cells termed endothelial progenitor cells (EPC) are involved in vasculogenesis and endothelial tissue repair [4]. Previous reports suggest the implication of EPC in different conditions such as RA and idiopathic pulmonary fibrosis (IPF), the most common and destructive ILD [5,6]. Nevertheless, little is known about their specific role in RA-ILD$^+$.

Objectives: The purpose of this study was to shed light on the potential role of EPC in endothelial damage in RA-ILD$^{+\cdot}$

Methods: Peripheral venous blood was collected from a total of 68 individuals (18 with RA-ILD$^+$, 17 with RA-ILD$^-$, 19 with IPF and 14 healthy controls). All subjects were recruited from the Rheumatology and Pneumology departments of Hospital Universitario Marqués de Valdecilla, Santander, Spain. Quantification of EPC was analyzed by the expression of surface antigens by flow cytometry. The combination of antibodies against the stem cell marker CD34, the immature progenitor marker CD133, the endothelial marker VEGF receptor 2 (CD309) and the common leukocyte antigen CD45 was used. EPC were considered as CD34$^+$, CD45^{Low}, CD309$^+$ and CD133$^+$. All statistical analyses were performed using Prism software 5 (GraphPad).

Results: EPC frequency was significantly increased in patients with RA-ILD$^+$, RA-ILD$^-$ and IPF compared to controls (p=0.001, p=0.002, p< 0.0001, respectively). Nevertheless, patients with RA, both RA-ILD$^+$ and RA-ILD$^-$, showed a lower frequency of EPC than those with IPF (p= 0.048, p= 0.006, respectively).

Conclusion: Our results provide evidence for a potential role of EPC as a reparative compensatory mechanism related to endothelial damage in RA-ILD$^+$, RA-ILD$^-$ and IPF patients. Interestingly, EPC frequency may help to establish a differential diagnostic between patients with IPF and those who have an underlying autoimmune disease (RA-ILD$^+$).

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SAT0015 ROCK INHIBITION REDUCES THE SEVERITY OF K/BXN SERUM-TRANSFER INDUCED ARTHRITIS

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Background: Fibroblast-like synoviocytes (FLS) are pivotal in inflammation and joint damage of rheumatoid arthritis (RA). These cells acquire an aggressive and invasive phenotype and secrete inflammatory mediators, metalloproteases and cathepsins that perpetuate inflammation and lead to cartilage and bone damage. We have previously shown that non-canonical Wnt5a pathway is involved in the aggressive phenotype of FLS by increasing their migration and invasion ability, and by stimulating the inflammatory response. The non-canonical Wnt signaling pathway included the planar cell polarity (PCP), with the activation of Rho and Rac GTPases, and the Wnt/Ca2+ pathways. We have also shown that Wnt5a contributes to the aggressive phenotype of RA FLS by binding to RYK receptor, through Rho-ROCK pathway and the activation of MAPKs, ERK and P38, as well as the activation of AKT and GSK3β.
Objectives: To elucidate the therapeutic potential of the ROCK inhibitor (Y-27632) in the K/BxN serum transfer arthritis model.
Methods: Two groups of C57BL/6J mice were used, in the control group, mice were treated with physiological serum and in the experimental group with a ROCK inhibitor (Y-27632). Arthritis was induced by intraperitoneal injection of 100 µl of K/BxN serum on days 0 and 2. In the experimental group, mice were treated with intraperitoneal injections of 10 mg/kg from day 0 until sacrifice, on day 10. Control mice were treated with the same volume of physiological serum. Arthritis was assessed by two observers using a semiquantitative clinical score. For histological analysis, it was decided to obtain the right ankle joints and foot. Joints were fixed in formalin for 6h and were decalcified and embedded in paraffin. Sections were stained with hematoxylin and eosin (H&E) and toluidine. Finally, total RNA was obtained from wrist and ankle joints of mice and the expression of inflammatory mediators and metalloproteases was analyzed by real-time PCR.
Results: Arthritis was induced in C57BL/6J mice, which were treated with Y-27632 (ROCK inhibitor) or with physiological serum. The incidence of arthritis was 100% in both groups of mice and there were no differences in the course of the disease. Clinical score was significantly lower in the Y-27632-treated mice, all along the follow-up, compared with controls. Similar results were observed in the histological analysis. We also analyzed the effect of ROCK inhibitor on the inflammatory response of K/BxN serum-transfer induced arthritis. This analysis revealed that expression of IL6, IL1β, CXCL1, MMP3, MMP9 and MMP13 were significantly decreased in Y-27632-treated mice compared with control mice. In addition, TNF and NOS2 expression was reduced in Y-27632-treated mice to reach the same levels that observed in C57BL/6J mice without arthritis.
Conclusion: These results indicate that the inhibition of the Rho-ROCK pathway decreases the severity of arthritis in the K/BxN serum transfer model, and point to ROCK as potential therapeutic target for RA. Supported: ISCIII / PI17 / 01660 / RETICS Program, RD16 / 0012/0014 / Cofinanced FEDER.
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SAT0016 DEVELOPMENT OF FIBROBLAST-LIKE SYNOVIOCYTE ASSAYS FOR TARGET DISCOVERY IN RHEUMATOID ARTHRITIS

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Background: The rheumatoid arthritis (RA) synovium is characterized by an overabundance of fibroblast-like synoviocytes (FLS), which play a central role in the initiation and perpetuation of disease via multiple mechanisms.[1] FLS promote disease progression by producing high levels of proinflammatory factors, migrating to and invading cartilage and bone, and promoting self-proliferation and resistance to apoptosis. Our current understanding of the molecular mechanisms that govern FLS-mediated pathology in the synovial joint remains incomplete. Importantly, almost 30% of treatment-naïve early RA patients exhibit a strong fibroid phenotype that correlates with relatively poor response to disease-modifying anti-rheumatic drugs.[2] Yet, current therapies in RA are not directly aimed at FLS pathology, creating an opportunity for novel therapeutic target discovery.
Objectives: Our aim is to develop a broad suite of screening-amenable assays in RA patient-derived FLS for the discovery of target pathways that control multiple pathological properties, including cytokine secretion, migration, and invasion.
Methods: A sensitive high-throughput RA-FLS secretion assay was developed to examine the ability of small-molecule inhibitors to block the production of interleukin (IL)-6 and matrix metalloproteinase (MMP)-3 in response to stimuli. To create a physiologically relevant stimulus, a surrogate synovial fluid cocktail (composed of 12 factors) was defined and titrated for optimal concentration selection. Small-molecule inhibitors (N=170) of diverse biological pathways were screened using the full cocktail or individual stimulation (TNFα, IL-1α, or IL-17) to characterize assay performance. In addition, an FLS platelet-derived growth factor (PDGF)-mediated migration screening assay was developed using a live cell imaging system (IncuCyte) to quantify real-time FLS migration.
Results: Due to the variability and limited volume of synovial fluid, we developed a surrogate synovial fluid cocktail to mimic the relevant stimulation of RA-FLS in the inflamed joint. The surrogate cocktail was composed of 12 factors: TNFα, IL-1α, IL-17, IFNγ, OSM, LIF, GM-CSF, IP-10, VEGF, PDGF, AREG, and FGF2. Individual titration of these factors demonstrated that only 3 stimulatory factors (TNFα, IL-1α, and IL-17) resulted in a robust increase of IL-6 production. Importantly, when all 12 factors were combined, a synergistic increase in IL-6 and MMP-3 production by FLS was observed. Screening results identified several reference compounds, including an inhibitor of transforming growth factor-b–activated kinase 1 (TAK1), that was previously reported to block cytokine secretion in FLS.[3] Treatment with this compound showed complete inhibition of IL-6 and MMP-3 secretion. In addition to the cytokine secretion assay, treatment of FLS with this TAK1 inhibitor resulted in almost complete inhibition of migration (Fig. 1).
Conclusion: Novel FLS assays were developed to discover new targets and interrogate pathways involved in multiple disease-driving mechanisms of FLS in RA. In order to mimic the inflammatory environment present in the RA synovium, we developed a 12-factor surrogate synovial fluid cocktail. A synergistic release of both IL-6 and MMP-3 was demonstrated following cocktail stimulation compared to individual cytokines. This points to the important contribution that multiple factors play in the FLS pathogenic processes and will allow us to uncover pathway interactions that may not be captured with single stimuli. In addition, the development of a real-time, 96-well, imaging-based assay to interrogate FLS migration will allow us to identify targets that control this critical pathological function of FLS.
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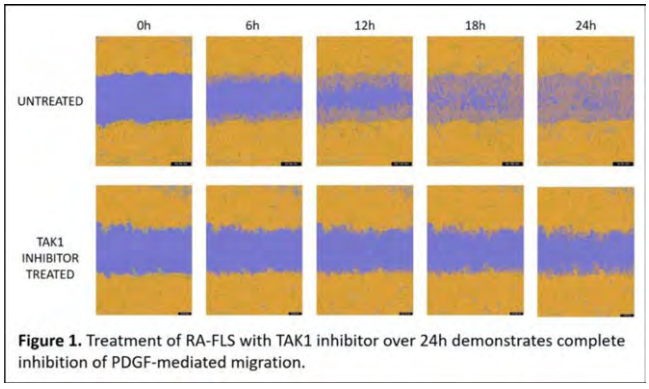


Figure 1. Treatment of RA-FLS with TAK1 inhibitor over 24h demonstrates complete inhibition of PDGF-mediated migration.

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SAT0017 METABOLIC CHANGES INDUCED BY ANTI-MALONDIALDEHYDE/MALINDIALDEHYDE-ACETALDEHYDE ANTIBODIES PROMOTE OSTEOCLAST DEVELOPMENT

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Background: Malondialdehyde (MDA) is a highly reactive compound produced by lipid-peroxidation in situations associated with oxidative stress. MDA can irreversibly modify proteins residues such as lysine, arginine and histidine. In addition, MDA adducts can further react with acetaldehyde to generate malondialdehyde-acetaldehyde (MAA) modifications. Such modifications can give rise to immunogenic neo-epitopes that are recognized by autoantibodies. In fact, anti-MDA/MAA IgG antibodies are significantly increased in the serum of patients with autoimmune diseases, such as rheumatoid arthritis (RA) (1) and systemic lupus erythematosus (2). Recently, we have shown that anti-MDA/MAA IgG antibodies are able to promote osteoclast (OC) differentiation *in vitro* (1).

Objectives: To investigate the molecular mechanisms triggered by anti-MDA/MAA autoantibodies during osteoclastogenesis.
Methods: OCs were generated from monocyte-derived macrophages in the presence of the cytokines RANK-L and M-CSF. The development of OCs was monitored by light microscopy following tartrate-resistant acid phosphatase (TRAP) staining and erosion area on synthetic calcium phosphate-coated plates. Three different recombinant human monoclonal anti-MDA/MAA antibodies, cloned from single synovial B cells of RA patients, control antibodies and Fab fragments of the antibodies were added to OC cultures. Glycolysis was inhibited by 2-deoxyglucose, and Fc-gamma receptor I or II by anti-CD64 or anti-CD16 neutralizing antibodies. IL-8 levels were measured by enzyme linked immunosorbent assay. Cellular metabolism was monitored using Seahorse XF Analyzer (extracellular acidification rate and oxygen consumption) and a colorimetric L-Lactate assay.
Results: Lactic acid production correlated with the osteoclastogenetic effect of some but not all anti-MDA/MAA antibodies on OCs (R=0.4758, p=0.0252) suggesting an antibody-mediated regulation of glycolysis. Further, extracellular acidification (ECAR) and oxygen consumption (OCR) rate of the developing OCs were increased by the osteoclastogenic anti-MDA/MAA clones (maximum increase of 54% for the ECAR and 78% for the OCR by clone 146+:01G07, and maximum increase of 28% for the ECAR and 39% for the OCR by clone 1103:01H05), but not by the non-osteoclastogenetic anti-MDA/MAA clones or control antibodies. The glycolysis inhibitor 2-deoxyglucose completely abolished the osteoclastogenetic effect of the anti-MDA/MAA clones at drug concentrations that did not influenced baseline OC development. Fab2 fragments of the osteocalstogenetic anti-MDA/MAA clones had no effect on OC development and metabolism. In accordance with this, Fc-gamma receptor I neutralizing antibodies completely abolished the osteocalstogenetic effect of the anti-MDA/MAA clones. The osteoclastogenetic effect of the anti-MDA/MAA antibodies was independent of IL-8 production. In contrast to anti MDA/MAA antibodies, ACPA-mediated osteoclastogenesis was independent of glycolysis and Fc-gamma receptors but dependent on IL-8.
Conclusion: Our results describe a novel glycolysis-dependent mechanism by which anti-MDA/MAA antibodies promote osteoclast development that is different from the one previously described for ACPA.
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SAT0018 THE THERAPEUTIC EFFECT OF STIMULATION OF THE SPLENIC NEUROVASCULAR BUNDLE IN MICE WITH COLLAGEN-INDUCED ARTHRITIS IS ENHANCED BY CONCOMITANT ANTI-TNF TREATMENT

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Background: Vagus nerve (VN) stimulation has shown the potential to improve the disease development in animal models of arthritis and in patients with RA. However, the VN can affect respiratory, cardiovascular, endocrine and gastro-intestinal physiology. The splenic nerve (SpN) has been confirmed to be the principal effector nerve for the VN-mediated immune control. Previous studies have shown that stimulating the splenic nerve resulted in an increase of norephiniphrine in the spleen, as well as a significant reduction in LPS-induced TNF (1).
Objectives: To test the therapeutic efficiency of splenic nerve stimulation (SNS) in collagen-induced arthritis (CIA) in mice alone or in combination with anti-TNF treatment.
Methods: CIA was induced in DBA1/J mice by immunization with bovine type II collagen at days 0 and 21. At day 11, mice were implanted with micro-cuff electrode (CorTec) onto the SpN or VN. From day 16 to day 45, SNS were applied as rectangular charged-balanced biphasic pulses with 650 µA pulse amplitude, 200 µs pulse width at 10 Hz frequency for 2 min 1 or 6 times a day using a Plexon stimulator. In order to investigatedthe mechanism of action in more detail, propranolol, a beta-adrenergic receptor (β-AR) antagonist, was added to the drinking water of mice receiving SNS. In addition, a control group was treated with anti-TNF (etanercept, 3 times/week; 10mg/kg i.p.). In curative settings, SNS and/or anti-TNF treatment was applied starting when mice scored positive for 3 consecutive days. Clinical arthritis was determined by visual examination of swelling and redness of the paws and measurement of paw thickness. Sham mice were undergoing the same procedure but did not receive stimulation.
Results: In CIA in mice all sham animals developed arthritis, compared to only 14% following six times per day SNS ($p < 0.001$) in a prophylactic setting. In contrast, 85% of the animals developed arthritis ($p = 0.35$) when SNS was applied only once a day. In both stimulated groups a significant decrease in clinical scores and paw thickness was observed compared to unstimulated group ($p < 0.01$ and $p < 0.05$, respectively). While etanercept treatment reduced clinical scores ($p < 0.001$) an immediate rebound in clinical score was seen following treatment arrest, while mice with SNS were still partially protected 35 days after treatment discontinuation ($p = 0.013$, compared to sham). Propranolol inverted the effect of SNS in CIA mice. Finally, when SNS was applied as a curative treatment, clinical scores were significantly reduced ($p < 0.001$). Importantly, these clinical scores even further decreased when anti-TNF treatment was given to mice receiving SNS.
Conclusion: These studies demonstrate that SNS suppresses pro-inflammatory cytokine production, and reduces clinical symptoms in mice with CIA which is at least partially mediated by the β-AR. The additive effect of anti-TNF in reducing the clinical scores demonstrates that that mechanism of action of SNS is not primarilys mediated by reducing TNF levels. Moreover, anti-TNF potentiating the inhibitory effect of SNS is supporting a combined use of these treatments, or even a combination of SNS with other biologicals, to treat RA, potentially getting more patients closer to remission. In conclusion, the data is providing compelling scientific rationale and pre-clinical evidence that splenic neuromodulation might be a new treatment modality for RA.
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SAT0019 HISTOPATHOLOGICAL CHANGES OF SYNOVIAL TISSUE IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH TNF INHIBITORS

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by hyperplasia of synovial tissues [1]. Tumor necrosis factor (TNF)-α is one of the pro-inflammatory cytokines that play a crucial role in the pathogenesis of RA synovitis, and TNF inhibitors (TNFi) were reported to force the RA to go into remission or low disease activity and have brought revolutionary impacts on RA treatment [2]. TNFi have been shown to act on inflammatory cells and form the discoid fibrosis in the sublining layers [3,4]. However, the changes of synovial tissue and the cause of discoid fibrosis in RA patients treated with TNFi has not been determined in detail.
Objectives: The purpose of this study is to demonstrate the histological changes and the types of cells around discoid fibrosis in RA synovium treated with TNFi.
Methods: Synovial tissues were obtained from 30 patients with RA during joint surgeries. 6 patients were treated with TNFi (1 patient with golimumab, 3 patients with etanercept, 2 patients with infliximab). As a control, synovial tissues were obtained from 6 patients who were treated only with csDMARDs (6 patients with MTX). The frozen sections were stained by hematoxylin and eosin (HE). To detect the apoptosis, TdT-mediated dUTP nick end labeling (TUNEL) was performed. The immunohistochemical characterization of the synovial cells was performed by using following antibodies: CD20 and CD3 for detecting B and T lymphocytes respectively, CD163 and CD86 for detecting M1 and M2 macrophage respectively.
Results: In the sections stained with HE, the formation of discoid fibrosis and the other characteristic changes including hydropic degeneration, vacuolation, sclerosis of small vasculature, and the number of multilayered synovial cells was decreased in synovium from RA patients treated with TNFi. In the sections with TUNEL stain, apoptosis of lining cells around the discoid fibrosis was detected in RA synovium treated with TNFi (Figure 1a, 1b). In the sections with immunohistochemistry stain, CD86 expression increased in lining layer of RA synovium treated with TNFi. CD163 positive cells showed diffuse expression in RA synovium treated with TNFi. In contrast, CD20 and CD3 positive cells decreased around discoid fibrosis compared to control sections. These results showed indicated that the types of cells in lining and sublining layers were mainly macrophages and that the apoptosis of macrophages might form the discoid fibrosis in lining layers.

Conclusion: This study showed the apoptosis of lining cells derived from macrophages resulted in the formation of the discoid fibrosis. These findings indicated TNFi might induce apoptosis of macrophage leading to the suppression of RA synovitis.

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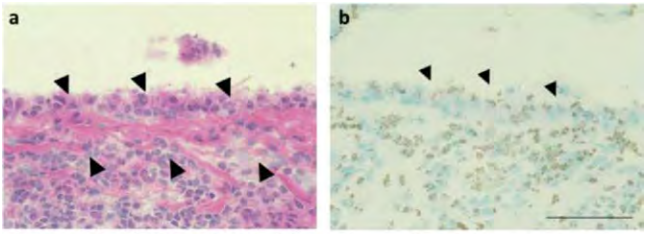


Fig.1 a Discoid fibrosis in sublining layers. **b** TUNEL stain positive cells are around Discoid fibrosis

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SAT0020 MOMELOTINIB, A JANUS KINASE 1/2 AND ACTIVIN RECEPTOR 1 INHIBITOR, AMELIORATES JOINT INFLAMMATION, SYSTEMIC TH17 DIFFERENTIATION AND ARTHRITIS-LINKED ANEMIA IN PRE-CLINICAL AUTOIMMUNE RA

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Background: Janus kinases (JAKs) serve as signaling hubs orchestrating inflammation, innate and adaptive immunity and erythropoiesis. Unfortunately, some of these agents cause suppression of JAK-dependent erythropoiesis, thereby exacerbating inflammation-associated anemia, leading to potential under-dosing and reduced therapeutic benefit. We previously showed that the JAKi momelotinib (MMB) can correct anemia in a rat model of RA, an effect that has been clinically reproduced in myelofibrosis patients treated with MMB. Subsequently, the molecular basis for MMB's anemia benefit was determined to be a consequence of its potent inhibition of Activin Receptor Type 1 (ACVR1), resulting in decreased hepcidin and, as a consequence, increased systemic iron availability and improved erythropoiesis.
Objectives: The goal of the current study was to investigate the effects of MMB on arthritis in pre-clinical RA models.
Methods: The anti-arthritic activity of daily administration of MMB was assessed in Streptococcus cell wall-induced arthritis in Lewis rats (PG-PS model) and in collagen antibody-induced arthritis (CAIA) in DBA/1 mice. Consecutive assessment of arthritis was performed by joint thickness measurements and paw scoring. Following 3 weeks of treatment, synovial immune cell infiltration and T cell subset differentiation was quantified. Cytokine gene expression was profiled by quantitative rt-PCR. Anemia was assessed by determination of blood hemoglobin and serum, spleen and liver iron levels.
Results: MMB reduced inflammatory granulocyte and macrophage infiltration in synovial tissue by more than 60% at all tested doses as compared to vehicle treatment in PG-PS animals. Importantly, MMB treatment effectively decreased arthritogenic Th17 cell differentiation and overall CD4+ T cells in the synovia beginning at the lowest tested dose and coincided with complete remission of joint swelling at 25 mg/kg. Anti-arthritic activity of MMB was confirmed with significant reductions in arthritis scoring, which demonstrated non-inferiority versus the TNF-α inhibitor, etanercept, in the CAIA model. Consistent with its inhibitory activity on the ACVR1-hepcidin axis, MMB reduced circulating hepcidin levels and mobilized systemic iron, resulting in substantial improvement of the RA-associated anemia in rats.
Conclusion: MMB is a highly efficacious anti-arthritic agent that ameliorates local joint inflammation and reduces the systemic differentiation of major arthritogenic effector cell population, Th17 lymphocytes. In accord with our previous report, MMB is distinct from other JAKi due to its ability to inhibit ACVR1 signaling leading to decreased plasma hepcidin, improved iron homeostasis and increased erythropoiesis. The dual anti-inflammatory and anemia-improving pharmacologic activities of MMB position it as a promising and differentiated therapeutic agent for the treatment of RA and other inflammatory diseases with an anemia component.
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SAT0021 STRUCTURAL EFFECTS OF LOCAL CRYOTHERAPY IN RHEUMATOID ARTHRITIS: A STUDY IN ADJUVANT-INDUCED ARTHRITIS

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Background: The control of joint destruction caused by rheumatoid arthritis (RA) is a key issue in the treatment of this disease. Recent evidence showed that radiographic progression of joint damage occur despite a sharp decrease in disease activity and the use of aggressive Disease Modifying Anti-Rheumatic Drug (DMARD) therapies [1]. Whether alternative treatments such as cryotherapy may have beneficial effects on joint destruction at the early stages of the disease remains to be demonstrated, but such strategy would be of interest as it would not interfere with DMARDs treatment.
Objectives: The aim of this study was to evaluate the effect of a 14-days-treatment of local cryotherapy on radiological outcomes in rat adjuvant induced arthritis.
Methods: Adjuvant-induced arthritis (AIA) was induced in 6-weeks old male Lewis rats by injection of *Mycobacterium butyricum* in Freund's incomplete adjuvant at the basis of the tail. A control group received saline. At the onset of arthritis, AIA rats were treated or not by application of cryotherapy on paws using either a cold spray or ice, twice a day for 14 days. Arthritis score and paws skin temperature was daily monitored. At the end of treatment, radiological exam of hind paws was performed and a score taking into account (swelling, osteoporosis, cartilage destruction, bone erosion, bone destruction and new bone formation) was assigned, according to Ackerman *et al* [2]. Circulating levels of cytokines (IL-6, IL-1β, TNF-α) was measured by Magpix Luminex kit.
Results: Compared to untreated AIA, local cryotherapy significantly reduced the progression of arthritis score, whatever the modality ($p<0.05$), and to the same extent (reduction of arthritis score at day 24 post-immunization: -38% with cold spray, $p<0.01$, -37% with ice, $p<0.01$). Radiological score was significantly reduced by both treatments with no difference between the two treatments (-33% with cold spray, $p<0.01$, -44% with ice, $p<0.01$). All the items of the radiological score were equally reduced by ice and cold spray except swelling that was significantly reduced only by ice. Interestingly, the use of the cold spray induced a greater decrease in the skin temperature than the ice treatment (18.32 ± 0.07 °C vs 20.46 ± 0.08 °C, $p<0.001$). Conversely, cryotherapy did not significantly change the level of cytokines. No correlation was found between radiological score and arthritis score or cytokine levels.
Conclusion: These data demonstrated that local cryotherapy had positive effects on structural damage in adjuvant-induced arthritis. The mechanisms involved remain now to be determined. These results suggest that local cryotherapy would be an interesting complement to conventional DMARDs in early RA.
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SAT0022 CXCL7 PROMOTES OSTEOCLASTOGENESIS IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease characterized by bone destruction[1]. Chemokine signaling by skeletal cells or by other cells of the bone marrow niche regulates bone formation and resorption[2]. Recent studies have found that CXCL7 enhanced the osteoclast formation in mouse bone marrow cells[3, 4]. Whether CXCL7 plays a role in human osteoclastogenesis especially in RA patients remains unclear.
Objectives: To examine the functional role of CXCL7 in the induction of osteoclastogenesis in RA.
Methods: The level of CXCL7 in $CD14^+$ monocyte supernatant was assessed via enzyme-linked immunosorbent assay. Osteoclastogenesis of $CD14^+$ monocyte from RA patients and healthy donors were evaluated by TRAP staining and F-actin ring immunofluorescence. Bone resorption pit was observed by scanning electron microscopy. We performed quantitative reverse transcription polymerase chain reaction (RT-PCR) to detect changes in osteoclast markers. RAW264.7 macrophages were also used to investigate specific signaling pathway by which CXCL7 stimulated during osteoclast formation.
Results: CXCL7 level in $CD14^+$ monocyte supernatant from RA patients (5690 ±627.05 pg/ml) was significantly higher than that in healthy controls (2301 ±535.52 pg/ml) (n=5, P<0.001). In the presence of M-CSF and RANKL, CXCL7 promoted osteoclast formation(Figure 1A and B) and increased bone resorption area(Figure 1C) of $CD14^+$ monocyte from healthy donors in the low concentration (10ng/ml) group (n=3, $p < 0.05$). While in high concentration of CXCL7 (50ng/ml) group, there were no significant changes in the number of osteoclasts. Transcription level of the osteoclast markers RANK, cathepsin K, and MMP-9 was significantly increased in the CXCL7 (10 ng/mL) group after 3 days in the presence of M-CSF and sRANKL (n=3, $p < 0.05$). When using CD14+ monocyte from RA patients, the optimal concentration of CXCL7 was 50ng/ml, which significantly increased the number of osteoclasts (Figure 2A and B)and bone resorption area (Figure 2C) (n=3, $p < 0.01$). Flow cytometry analysis revealed that a higher proportion of $CD14^+$ monocytes expressed CXCR2 from healthy donors than those from RA patients (n=6, $p < 0.01$). Consistent with the results obtained in $CD14^+$ monocytes, the effects of exogenous CXCL7 on osteoclast formation were also observed in RAW264.7 cells ($p < 0.01$). The addition of CXCL7 dramatically promoted phosphorylation ERK1/2 in RAW264.7 cells, but it did not affect the phosphorylation of P65.
Conclusion: CXCL7 level in $CD14^+$ monocyte supernatant was higher in RA patients than that of healthy donors. CXCL7 promoted osteoclastogenesis in $CD14^+$ monocyte both from RA patients and healthy donors. CXCL7 could be a potential therapeutic target for bone destruction in RA.
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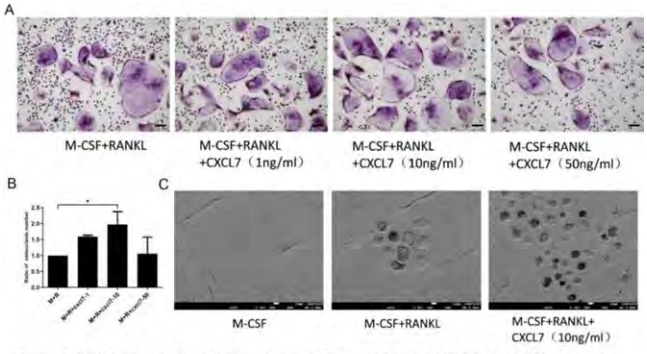


Figure1. CXCL7 induced osteoclast differentiation and bone resorption in healthy donors. CD14+ monocytes isolated from healthy donors were cultured in the presence of M-CSF(50 ng/ml) and RANKL (100 ng/ml) with CXCL7(1, 10, 50ng/ml) during the whole period of osteoclastogenesis.

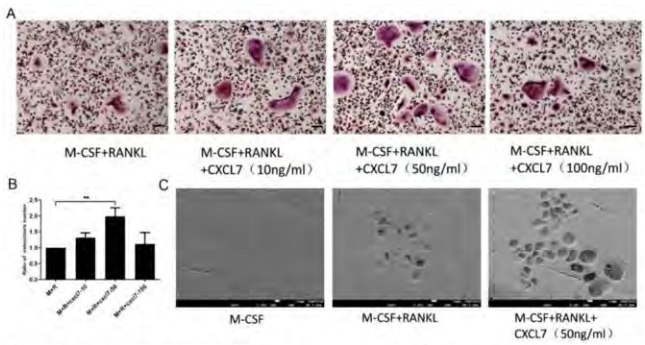


Figure2. CXCL7 induced osteoclast differentiation and bone resorption in RA patients. CD14+ monocytes isolated from RA patients were cultured in the presence of M-CSF(50 ng/ml) and RANKL (100 ng/ml) with CXCL7(10, 50, 100ng/ml) during the whole period of osteoclastogenesis.

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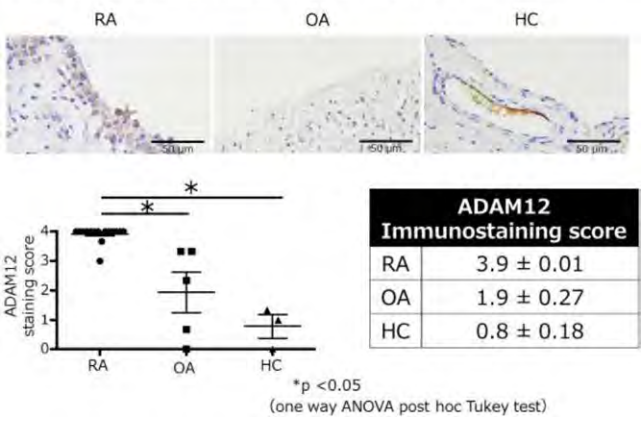
SAT0023 THE ROLE OF ADAM12 UPREGULATED PROLIFERATION OF SYNOVIAL MEMBRANE IN RHEUMATOID ARTHRITIS

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Background: ADAM12 is a member of a disintegrin and metalloproteinase family and has been reported to participate in the development of a variety of tumors by degrading ECM and shed precursors, thus promoting cell proliferation, invasion, and metastasis[1]. Additionally, ADAM12 is involved in chondrocyte differentiation from osteoarthritis (OA) patients by regulation of TGFβ1-induced IGF-1 and RUNX-2 expressions[2]. However, there is no report on the role of ADAM12 for rheumatoid arthritis (RA).
Objectives: To investigate the expression and role of ADAM12 in the synovial tissue of RA.
Methods: (1) The expression of ADAM12 in synovial tissues from RA (18 cases), OA (5 cases) and healthy control (HC) (3 cases) was examined by immunohistochemistry. The synovial tissues of HC were obtained during surgery of hemiarthroplasty for bone tumors. Three researchers evaluated the positive cell ratio. The samples were scored according to the percentage of positive staining: 0 points (weak positive, positive expression was less than 5%), 1 point (moderate positive, positive expression was between 5% and 50%) and 2 points (strong positive, positive expression was greater than 50%). In addition, the samples were scored according to the staining intensity: 0 points (weak intensity), 1 point (moderate intensity) and 2 points (high intensity). (2) The cultured synovial fibroblasts obtained from RA patients at the surgery (RASF) were stimulated by TNFα (1, 5, 10 ng/mL), TGFβ1 (1, 5, 10 ng/mL), PDGF-BB (1, 5, 10 ng/mL) and TNFα+TGFβ1+PDGF-BB (all 10 ng/mL), and the expression levels of ADAM12 relative mRNA was examined by real-time PCR. (3) siADAM12 was transfected in RASF, and the proliferation was examined by WST-1 assay, and the expression of ADAM12 protein was examined by western blotting.
Results: (1) ADAM12 positive cells were found in synovial lining cells, plasma cells, and vascular endothelial cells. ADAM12 was highly expressed in RA synovial tissues. The immunostaining scores of RA, OA, and HC were 3.9±0.01, 1.9±0.27, and 0.8±0.18, respectively. (2) Stimulation by TNFα, TGFβ1, and PDGF-BB resulted in the upregulation of the expression of ADAM12 relative mRNA in RASF, and TGFβ1 stimulation notably tended to increase the expression by about 5 to 6 times. (3) siADAM12 successfully suppressed the expression of ADAM12 protein and simultaneously suppressed the proliferation of RASF.
Conclusion: ADAM12 might be involved in the pathogenesis of RA, promoting the cell proliferation of RASF.

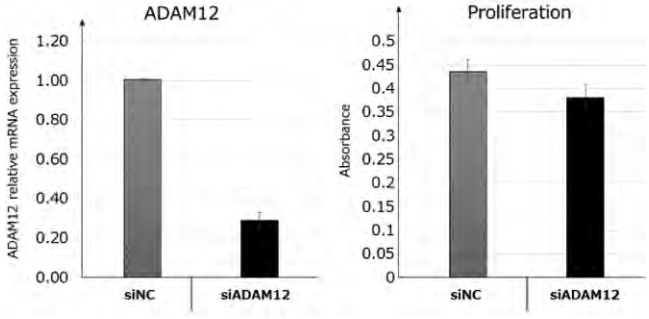
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Fig. 1: Immunohistological staining of ADAM12 for synovial tissues



ADAM12 Immunostaining score	
RA	3.9 ± 0.01
OA	1.9 ± 0.27
HC	0.8 ± 0.18

Fig. 2: ADAM12 relative mRNA expression and the proliferation of RASF after siADAM12 transfection



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SAT0024 JAK-INHIBITION WITH BARICTINIB INHIBITS ACTIVATION OF NLRP1/CASPASE1/GDMSD PYROPTOSIS PATHWAY IN RHEUMATOID ARTHRITIS SYNOVIAL FIBROBLASTS

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Background: Synovial fibroblasts (SFs) play a major role in the pathogenesis of rheumatoid arthritis (RA) and develop an aggressive phenotype destroying cartilage and bone, thus termed RASFs.
Objectives: We aim to examine the presence of GSDMD-mediated pyroptosis and its role in activated RASFs.
Methods: Fibroblasts were isolated from RA synovium obtained from knee replacement surgeries. NLRP1, Caspase-1, GSDMD expression in synovial tissue and TNF-treated RASFs were assessed by qPCR and Western blot. Interleukin (IL)-1 was measured by ELISA in supernatant after pretreated with TNF and baricitinib. LDH release was measured using the CytoTox 96 Non-Radioactive Cytotoxicity Assay Kit. Endogenous NLRP1, Caspase-1, and GSDMD was knocked down using small interfering RNA.
Results: The expressions of NLRP1, pro-Caspase-1, Caspase-1 p10, GSDMD and its pyroptosis-inducing fragment GSDMD-N were greater in RA synovium than OA synovium. TNF-induced NLRP1, pro-Caspase-1, Caspase-1 p10, GSDMD, and GSDMD-N expression at the transcript and protein level in a time-dependent manner ($P < 0.05$). Meanwhile, the release of LDH and IL-1 were significantly increased in RASFs after treated with TNF. We also confirmed the presence of pyroptosis in electron microscopy. Furthermore, blocking the JAK pathway with baricitinib significantly reduced TNF-induced pyroptosis at the transcriptional, protein and activity levels ($P < 0.05$). Finally, blocking the JAK pathway, we observed a reduction of IL-1 bioactivity in RASFs ($P < 0.05$).
Conclusion: Our results demonstrate an important role of GSDMD-mediated pyroptosis and shed lights on a potential pyroptosis-targeted treatment. Meanwhile, JAK inhibition alleviates inflammasome-induced pyroptosis by blocking pyroptosis pathway in RASFs.
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SAT0025 NEUROMEDIN U SUPPRESSES COLLAGEN-INDUCED ARTHRITIS THROUGH ACTIVATION OF ILC2

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Background: Reduction and dysregulation of ILC2 was linked to delayed resolution of arthritis. The neuropeptide Neuromedin U (NMU) has been reported to rapidly activate ILC2 and initiate a Th2 type immune response through NMUR1 expressed on the surface of ILC2. However, one previous study reported that NMU promoted autoantibody-mediated arthritis.
Objectives: The aim of this work was to investigate the effect of NMU on collagen-induced arthritis (CIA) mice and the potential mechanisms.
Methods: CIA was induced in C57BL/6 WT and C57BL/6^{Nmu} deficient mice on day 1. WT mice were treated i.p. daily by NMU-23 (20ug/mice) or by PBS for 10 days from day 1 to 5 and day 21 to 25. The clinical scores of CIA mice were assessed every two days from day 22 and determined on a scale of 0–4 for each paw. The proportion of ILC2 as well as Th1, Th2, Th17 and Treg in spleen, mesenteric lymph node (mLN) and joints of arthritic mice were analyzed by flow cytometry on day 42.
Results: NMU-23 dramatically inhibited clinical onset and severity of arthritis in treated WT mice compared with control mice. Interestingly, NMU-deficient mice also developed significantly less severe arthritis compared with WT control (Fig 1). Flow cytometry analyses showed that the proportion of ILC2, which defined as Lin-CD45+CD127+KLRG1+ICOS+ST2+, was elevated in the joint but not in the spleen and mLN of arthritic mice treated with NMU-23. In contrast, the proportion of ILC2 was significantly lower in the spleen of NMU-deficient mice than WT control. The percentage of Th2 cells in the spleen and mLN tend to be higher in NMU-23 treated mice, but there is no statistical significance. Surprisingly, Th1 cells were increased in the mLN of NMU-23 treated and NMU-deficient mice compared with control whereas Th17 was comparable among groups. In addition, the proportion of Treg was decreased in the joint of NMU-23 treated and NMU-deficient mice compared with control mice.
Conclusion: Our preliminary results show that repeated injection of NMU-23 during induction (early) and development (late) stage of CIA strongly suppressed clinical onset and severity of arthritis, which might be ascribed to activation of ILC2 in the joint. Further study is needed to explore other cellular and molecular mechanisms in the effect.
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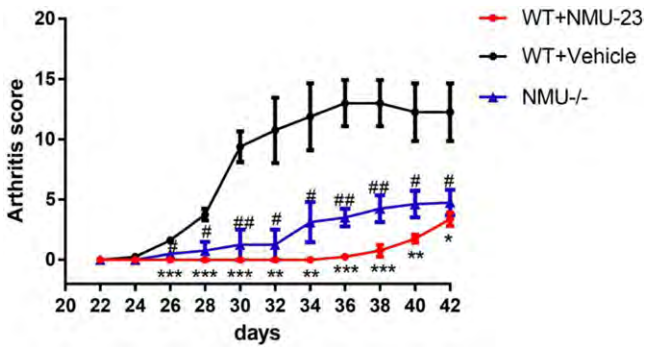


Figure 1. Arthritis score among 3 group of mice.

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SATURDAY, 06 JUNE 2020

Rheumatoid arthritis - prognosis, predictors and outcome

SAT0026

HIGHER LEVELS OF NATURAL ANTI-PHOSPHORYLCHOLINE ANTIBODIES ARE ASSOCIATED WITH LOWER RISK OF INCIDENT CARDIOVASCULAR EVENTS IN YOUNGER PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The increased cardiovascular (CV) risk in rheumatoid arthritis (RA), especially in seropositive RA, is not fully explained by traditional risk factors. Immuno-inflammatory mechanisms and autoantibodies could be involved in the pathogenesis of atherosclerotic disease. Recent studies have suggested that anti-phosporylcholine antibodies (anti-PC) of IgM subclass counteract the generation of senescent and IL-17+ T-cells, have atheroprotective effects and may play a role in formation and stabilization of atherosclerotic plaque.
Objectives: To investigate the association between IgM anti-PC antibodies with cardiovascular (CV) morbidity in patients with RA in age and sex groups and by serostatus.
Methods: The study population was derived from the BARFOT early RA cohort, recruited in 1994-1999. The outcome was CV events i.e. AMI, angina pectoris, coronary intervention, ischemic stroke and TIA tracked through the Swedish Hospital Discharge and the National Cause of Death Registries. The RA-disease measures and traditional risk factors were assessed according to the protocol. Sera collected at inclusion and the 2-year visit were analyzed with ELISA to determine levels of anti-PC IgM (Athera CVDefine kit, Athera Biotechnologies AB). The Kaplan-Meier estimates and Cox proportional-hazards regression models were applied. Analysis were stratified by median level of IgM anti-PC and performed within strata of age, sex and RA-autoantibodies.
Results: In all, 654 patients with early RA, 68% women, mean (SD) age 55(14.7) years, DAS28 5.2(1.3), 60% RF-positive and 60% ACPA-positive without prevalent CVD were included in this analysis. The level of IgM anti-PC at baseline was median (IQR) of 60.9(36.4-94.9) and at 2 years 56.0(32.3-84.2) U/ml. During follow-up of > 10 years, 141 incident CV events (21.6%) were registered. The levels of anti-PC both at inclusion and after 2 years of observation were lower in participants who experienced CV event than in those who did not, p=0.020 and p=0.012. The CV event-free survival differed between patients with levels of anti-PC above median compared with those with levels below, p=0.003 by log-rank test. The risk for incident CV event showed a 0.6-fold hazard (95% CI, 0.4-0.8) among patients with higher anti-PC levels as compared with those with lower levels, p=0.003. In the age groups, the risk for incident CV event was lower in patients aged <55 years at inclusion than in those who were older, hazard ratio (HR) 0.40 (0.17-0.94), p=0.036. This result persisted when adjusted for sex and all traditional risk factors, HR 0.36 (0.14-0.92), p=0.032. Also, the risk for incident CV events was lower in patients with higher anti-PC levels in females, HR 0.61 (0-39-0.45), and double RF- and ACPA- negative patients, 0.44 (0.21-0.90), in crude analyses.
The favourable effect of anti-PC at baseline and the CV outcome was not observed in ages >55 years, males, ACPA+ and RF+ patients. There were no significant association between anti-PC level at 2 years and outcome.
Conclusion: These results suggest that higher levels of IgM anti-PC are associated with a lower risk of incident CV events over 10 years in younger patients. The favourable atheroprotective effect of IgM anti-PC may be a part of explanation of lower risk of atherosclerotic disease in younger persons, females and in those with seronegative RA.
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SAT0027

DEVELOPMENT AND VALIDATION OF A NOMOGRAM COMBINING CLINICAL AND HISTOPATHOLOGICAL SYNOVIAL FEATURES FOR PREDICTING EARLY TREATMENT RESPONSE IN NAIVE TO TREATMENT RHEUMATOID ARTHRITIS

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Background: Rheumatoid Arthritis (RA) is characterized by synovial tissue (ST) heterogeneity at disease onset in terms of inflammatory degree and microanatomical organization being related to treatment response.
Objectives: To develop a multiparametric tool for baseline treatment response prediction including disease characteristics and histopathologic features of ST biopsies, using a large single center (SYNGem Unit) naive to treatment RA cohort.
Methods: 240 naive to treatment RA who underwent US-guided ST biopsy, at the first clinical evaluation, were enrolled. Clinical and immunological characteristics were recorded for each patient. All ST FFPE specimens were stained with H&E and classified by a pathologist, blinded to clinical characteristics, using the Krenn score [1] to assess the degree of ST inflammation. All naive to treatment RA were treated according to the T2T scheme and DAS remission rate at 6-12 months was recorded. On the basis of the regression analysis, a nomogram was constructed that incorporated the significant factors predicting the "achievement of DAS-Remission at 6 months follow-up" in naive RA. The performance of the nomogram was assessed by discrimination and calibration.
Results: Univariate analysis showed that RA who achieved early (6 months) DAS-remission had, at baseline, significantly lower total Krenn score (p<0.001), shorter symptoms duration (p=0.005) and lower disease activity (p<0.001) than RA not achieving this clinical outcome. ROC curve analysis revealed that RA having, at baseline, a total Krenn score <4.5 [(AUC)95%C.I.: 0.67(0.60-0.74),p<0.001] achieved more likely DAS-remission at 6 months (53.1%) than RA with total Krenn score ≥4.5(28.9%,p<0.001). Interestingly, RA whose ST was biopsied within 3 months from joint symptoms beginning showed significantly lower ST inflammation as total Krenn score than RA whose ST was analyzed among 3-12 months (p=0.04) or after 12 months (p=0.002) since symptoms beginning. However, in terms of follicular structure presence, the microanatomical organization of the synovial inflammatory infiltrate did not differ comparing RA whose ST was biopsied within 3 months from joint symptoms beginning (44.4%) and RA whose ST was biopsied among 3-12 months (47.6%, p=0.74) or after 12 months (52.7%,p=0.33) since symptoms beginning.
Logistic regression analysis revealed that, at baseline, being VERA, not having HDA and having a total Krenn score <4.5 were synergistic factors of DAS-remission achievement at 6 months [OR:10.5(95%IC:2.28-48.01);p<0.05]. Based on the regression analysis, a nomogram integrating baseline clinical (disease activity and duration) and histological (total Krenn score) characteristics was developed in which the value of each of the variables was given a point score. A total score was calculated by adding each single point score and, by projecting the value of the "total points" score to the "probability" line up to 87.5%.
Conclusion: Krenn score is a reliable tool for the semi-quantitative assessment of ST inflammation on US-guided ST biopsies being contingent to baseline disease characteristics and can be integrated within a nomogram to better predict the therapeutic response in naive to treatment RA.
References:
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Disclosure of Interests: Stefano Alivernini: None declared, Barbara Tolusso: None declared, Marco Gessi: None declared, Maria Rita Gigante: None declared, Alice Mannocci: None declared, Luca Petricca: None declared, Simone Perniola: None declared, Clara Di Mario: None declared, Anna Laura Fedele: None declared, Laura Bui: None declared, Annunziata Capacci: None declared, Dario Bruno: None declared, Giuseppe La Torre: None declared, Francesco Federico: None declared, Gianfranco Ferraccioli: None declared, Elisa Gremese Speakers bureau: Abbvie, BMS, Celgene, Jannsen, Lilly, MSD, Novartis, Pfizer, Sandoz, UCB
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SAT0028

THE FLARE-RA QUESTIONNAIRE CAN PREDICT FLARES IN PATIENTS WITH ESTABLISHED RHEUMATOID ARTHRITIS PARTICIPATING IN THE TAPERA TRIAL

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Background: The Flare assessment in Rheumatoid Arthritis (FLARE-RA) questionnaire was developed to identify Rheumatoid Arthritis (RA) flares, but it is unknown if this questionnaire can also predict flares.
Objectives: To identify if the FLARE-RA questionnaire has a predictive capacity for OMERACT flares in patients with established RA participating in a tapering trial.
Methods: Patients, participating in the 1-year open-label pragmatic randomised controlled TapERA (Tapering Etanercept in RA) trial, were included in the analysis. Patients had to be in DAS28CRP or ESR remission (≥6 months) and treated with etanercept 50 mg weekly (≥1 year). Participants were randomised to continue etanercept 50 mg weekly or to taper to 50 mg every other week.
The FLARE-RA questionnaire was completed every 3 months in the trial. This questionnaire consists of 13 questions on a Likert-scale from 1 to 6 reflecting 'completely untrue' to 'completely true'. Validation by Fautrel et al. leaded to elimination of 2 questions ('steroid intake' and 'overall worsening of RA') and rescaling to 0-10. Our outcomes were based on these 3 versions of the questionnaire, namely 13 questions (13q), 11 questions (11q) and rescaled 11 questions (r11q). The FLARE-RA questionnaire can be divided in 2 subscales: the FLARE-RA arthritis subscale (questions regarding morning stiffness, night disturbances, joint swelling, joint pain, analgesics) and FLARE-RA general symptoms subscale (questions regarding fatigue, functional limitation, irritability, mood disturbances, withdrawal, need for help).
The total FLARE-RA score was calculated by taking the average of all the questions per time point. A flare was defined according to the OMERACT definition, namely an increase in DAS28CRP > 1.2 compared to baseline or increase in DAS-28CRP > 0.6 and current DAS28CRP ≥ 3.2. All the total FLARE-RA scores of the baseline, month 3, 6 and 9 visit were grouped and the mean ± standard deviation (SD) FLARE-RA score was compared between patients with or without an OMERACT flare on the next study visit using the Mann-Whitney U test. Logistic regressions using the total FLARE-RA score to predict an OMERACT flare 3 months later were carried out for the 13q, 11q and r11q versions and the FLARE-RA subscales. Missing data were imputed using expectation maximisation.
Results: Sixty-six patients (68% female, mean ± SD age of 55 ± 11 years) completed the FLARE-RA questionnaire. This yielded 264 FLARE-RA scores, of which the total mean ± SD FLARE-RA score was 2.1 ± 1.0 and 2.7 ± 1.1 for patients without and with an OMERACT flare on the next study visit, respectively (p<0.01). This was comparable for the 11q and r11q versions (Table 1). For the total FLARE-RA score (13q), the odds ratio of having an OMERACT flare 3 months later is 1.6 (95% confidence interval (CI) 1.2 – 2.2, p=0.004). This was 1.5 (95% CI 1.1 – 2.1, p=0.006) for the 11q and 1.2 (95% CI 1.1 – 1.4, p=0.006) for the r11q version. The odds ratio of having an OMERACT flare on the next visit was 1.5 (95% CI 1.2 – 2.0, p=0.002) and 1.4 (95% CI 1.0 – 2.0, p=0.025) for the arthritis and general symptoms subscale, respectively.

Table 1. Comparison of overall total FLARE-RA scores between patients with or without an OMERACT flare on the next visit

	Questionnaire version	No OMERACT flare on next visit	OMERACT flare on next visit	P-value
Overall total FLARE-RA score (mean ± SD)	13q	2.1 ± 1.0	2.7 ± 1.1	0.002
	11q	2.2 ± 1.1	2.7 ± 1.1	0.004
	r11q	2.3 ± 2.1	3.4 ± 2.2	0.004

Overall total FLARE-RA score was derived by grouping the total FLARE-RA scores of the baseline, month 3, 6 and 9 visit.

Conclusion: Higher total FLARE-RA questionnaire scores seem to indicate a higher risk of an OMERACT flare 3 months later, regardless of which versions or subscales of the FLARE-RA questionnaire were used. Hence, our findings suggest that the FLARE-RA questionnaire could be used as a predictive tool for flares.
Disclosure of Interests: Delphine Bertrand: None declared, Diederik De Cock: None declared, Veerle Stouten: None declared, Sofia Pazmino: None declared, Anneleen Moeyersoons: None declared, Johan Joly: None declared, Rene Westhovens Grant/research support from: Celltrion Inc, Galapagos, Gilead, Consultant of: Celltrion Inc, Galapagos, Gilead, Speakers bureau: Celltrion Inc, Galapagos, Gilead, Patrick Verschueren Grant/research support from: Pfizer unrestricted chair of early RA research, Speakers bureau: various companies
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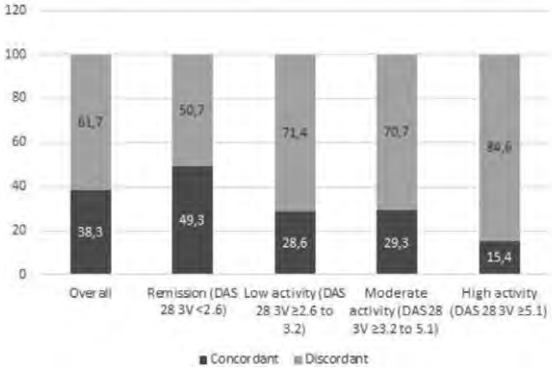
SAT0029

PATIENT-PHYSICIAN DISCORDANCE IN ASSESSMENT OF DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS

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Background: In rheumatoid arthritis (RA), global disease activity is commonly assessed, from the patient's and the physician's perspective, through a 100mm VAS. Previous studies have commonly shown a considerable discrepancy between the patient's and physician's assessment.
Objectives: This study aimed evaluating patient-physician discordance in the assessment of disease activity and to explore its determinants.
Methods: Cross sectional study including RA patients (ACR/EULAR 2010 classification criteria), aged ≥ 18 years, followed in a single tertiary centre. Data were collected from the most recent evaluation including sociodemographic features, disease duration (years), disease activity (DAS 28 3V-PCR), tender and swollen joint count 0-28 (TJC and SJC), VAS-pain-patient, patient and physician global assessment (PGA and PhGA respectively), erythrocyte sedimentation rate (ESR), C-reactive protein (CPR), Health assessment questionnaire (HAQ) and EuroQol five-dimension scale (EQ5D). The discrepancy between patients and physicians (ΔPPhGA) was defined as PGA minus PhGA, and a difference > |20mm| was considered as "discordant". A descriptive analysis was performed and variables described as proportions or means (+/- SD), as adequate. Correlation between ΔPPhGA and other variables was assessed through Pearson's correlation and comparison between groups through t-test. Variables with p<0.05 or otherwise considered clinically relevant were included in multiple linear regression analysis to identify predictors for ΔPPhGA. A p≤0.05 was considered statistically significant.
Results: In total, 467 patients with RA were included (81.2% female; mean age 63.9% ± 12.2 years). PGA and PhGA were discordant in 61.7% of the cases, the patient scoring higher than the physician in 95% of these cases. The proportion of concordance increased ($p < 0.01$) when considering only patients in remission (DAS 28 3V <2.6), (Graph 1). ΔPPhGA was moderately correlated with VAS-pain-patient (r = 0.59) and weakly correlated with SJC (r = -0.12), HAQ (r= 0.27), EQ5D (r = -0.28) and age (r = 0.21); all p<0.01. In multivariate analysis, VAS-pain-patient (β 0.74, 95% CI 0.62-0.88, p=0.00) and TJC (β 0.16, 95% CI 0.45-0.48, p=0.02) remained associated with a higher ΔPPhGA.
Conclusion: Our study confirmed that a significant discrepancy between patients and physicians in the assessment of global disease activity is frequent in clinical practice, probably due to valorization of different parameters. This was much less pronounced among patients in remission. Higher VAS-pain-patient and TJC were independent predictors of greater discrepancy between patients and physician's assessment.

Graph 1. Concordance level (%) between PGA and PhGA according to the disease activity



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SAT0030

A NOVEL ASSOCIATION BETWEEN ANTI-CARBAMYLATED ANTIBODIES AND INTERSTITIAL LUNG DISEASE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Interstitial lung disease (ILD) is associated with a significant increase in morbidity and mortality in patients with rheumatoid arthritis (RA). Therefore, an early diagnosis is fundamental. Anti-carbamylated proteins (Anti-CarP) have been described in different chronic respiratory diseases without a previous history of RA.
Objectives: The aim of this study was to analyse the association between Anti-CarP and ILD in RA patients.
Methods: We performed a cross-sectional study, including RA patients fulfilling the 2010 ACR/EULAR criteria. The main population comprised 2 groups: 1) RA patients diagnosed with ILD (RA-ILD group) and 2) RA patients without ILD (non-ILD RA group). ILD was diagnosed by high-resolution tomography and confirmed by a multidisciplinary committee. Three IgG Anti-CarP autoantibodies against fetal calf serum (Anti-FCS), fibrinogen (Anti-Fib), and fibrine/filagrine homocitrullinated peptide (Anti-CFFHP) and one IgA against FCS (Anti-FCS-IgA) were determined by home-made ELISA. Associations between Anti-CarPs and ILD were explored using multivariable logistic regression adjusted by a set of variables known to be related to the development of ILD: smoking, sex, age, RA disease duration, RF and ACPA. An independent replication sample was obtained to validate our findings from another hospital.
Results: The main population included 179 patients: 37 were included in the RA-ILD group, and 142 in the non-ILD RA group. Most patients were female (79%), with a mean age of 59.7±13 years with a mean disease duration of 6.6±5 years. Baseline features are shown in table 1. The replication sample was composed of 25 patients in the RA-ILD group and 50 patients in the non-ILD RA group. We found that Anti-CarPs specificities were more frequent in RA-ILD patients (Anti-FCS 70% vs. 43%; Anti-Fib 73% vs. 51%; Anti-CFFHP 38% vs. 19%; Anti-CarP-IgA 51% vs. 20%, p<0.05 for all comparisons). Serum mean titers of Anti-CarPs were higher in RA-ILD patients with significant statistical differences for all of them, except Anti-Fib. The multivariate analysis showed that Anti-CarPs specificities were independently associated with ILD (Anti-FCS (OR: 3.42; CI95%: 1.13-10.40), Anti-Fib (OR: 2.85; CI95%: 0.83-9.70), Anti-CFFHP (OR: 3.11; CI95%: 1.06-9.14) and Anti-FCS-IgA (OR: 4.30; CI95%: 1.41-13.04). In the replication sample our findings were validated only for Anti-FCS (OR: 10.42; CI95%: 1.68-64.46).

TABLE 1. Main population demographic, clinical, therapeutic, and autoantibody status features.

	RA-ILD *n:37*	Non-ILD RA *n:142*	p value
Female (%)	25 (68)	116 (82)	NS
Age mean (±SD)	67.3 (10.1)	57.7 (12.9)	<0.005
Mean disease duration (±SD)	11.6 (7.1)	5.3 (13.3)	<0.005
Ever smokers (%)	21 (57)	62 (44)	NS
Smoking cumulative dose (±SD)	30.7 (11.1)	21.8 (12)	<0.005
Caucasian (%)	31 (84)	120 (85)	NS
Treatment			
Glucocorticoids (%)	25 (68)	81 (57)	NS
csDMARDs (%)	33 (89)	132 (86)	NS
MTX (%)	20 (54)	95 (67)	NS
bDMARDs (%)	11 (30)	36 (25)	NS
Mean DAS28 (±SD)	3.71 (1.35)	2.74 (1.05)	<0.005
Erosive disease (%)	26 (70)	63 (44)	<0.005
Mean HAQ-DI (CI-95%)	0.69 (0.53-0.85)	0.31 (0.24-0.38)	<0.005
ACPA positive (%)	29 (78)	99 (70)	NS
Median titer ACPA (IQR) CU	674 (2,215)	143 (1,132)	NS
RF positive (%)	28 (76)	83 (59)	NS
Median titer RF (IQR) IU	105 (298)	34 (110)	NS

Conclusion: A strong association between RA-ILD and Anti-CarP was found independently of cofounders, including RF and ACPA. Our findings suggest a possible link between Anti-CarP and the development of ILD.
Disclosure of Interests: Raul Castellanos-Moreira Speakers bureau: Lilly, MSD, Sanofi, UCB, Sebastian Rodriguez-Garcia: None declared, Katherine Cajiao: None declared, Gabriela Jimenez: None declared, Maria Jose Gomara: None declared, Virginia Ruiz Speakers bureau: Lilly, Pfizer, Ivette Casafont-Solé: None declared, Julio Ramirez: None declared, José Gomez Puerta Speakers bureau: Abbvie, Eli Lilly, BMS, Roche and Pfizer, Susana Holgado Pérez: None declared, Juan de Dios Cañete: None declared, Isabel Haro: None declared, Raimón Sanmartí Speakers bureau: Abbvie, Eli Lilly, BMS, Roche and Pfizer
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SAT0031

CORRELATION BETWEEN IRREVERSIBLE PHYSICAL DISABILITY AND JOINT DAMAGE IN RHEUMATOID ARTHRITIS

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Background: In rheumatoid arthritis (RA), irreversible physical disability appears to be more clearly associated with cartilage damage rather than with bone erosions (BE) using conventional radiography (CR) imaging.
Objectives: To investigate the correlation between the ultrasound (US) and CR findings indicative of joint damage and irreversible physical disability in patients with RA in sustained clinical remission.
Methods: Patients in sustained clinical remission according to the Simplified Disease Activity Index (SDAI)≤3.3 for at least 6 months were enrolled. The following data were regireted: age, disease duration, anti-cyclic citrullinated peptide (ACPA) antibody and rheumatoid factor (RF) status, Health Assessment Questionnaire (HAQ), CR of hands and feet [evaluated using the Simple Erosion Narrowing Score (SENS) method]. A standardized US examination was carried out to investigate the presence of BE (lateral side of II metacarpophalangeal, V metacarpophalangeal and V metatarsophalangeal joints and ulnar styloid) and of cartilage damage (II to V metacarpal heads), bilaterally. BE and cartilage damage were assessed according to OMERACT definitions. A semiquantitative scoring system for both BE (1) and cartilage damage (2) was adopted.
Results: Ninety patients were consecutively enrolled. Average time for US evaluation was 10±2 minutes. Both SENS-JSN and US score of cartilage damage (US-CD) were significantly associated with irreversible disability (R=0.39, p<0.01 and R=0.46, p<0.01). US and CR showed a moderate agreement in the evaluation of cartilage damage (kappa=0.52, 95% confidence interval: 0.44-0.61).

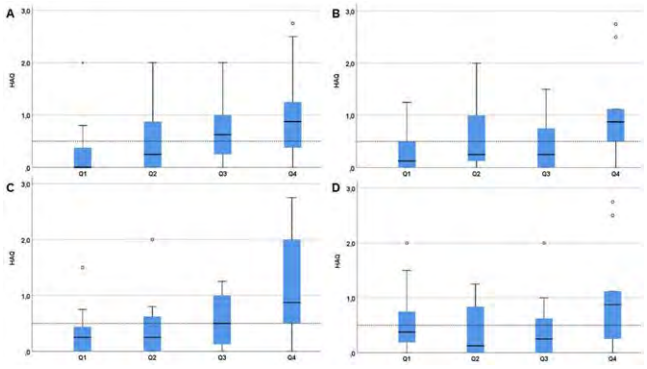


Figure 1. shows the association between disability and structural damage (A: US-CD, B: US-BE, C: SENS-JSN and D: SENS-BE).After adjusting for confounding factors (age, disease duration, ACPA and RF status, SENS-BE and US-BE) cartilage damage was the only significant predictor of irreversible disability both using CR (R^2=0.31, adjusted R^2=0.26, standardized β=0.36, p<0.01) and US (R^2=0.31, adjusted R^2=0.26, standardized β=0.34, p<0.01).

Conclusion: This study supports the hypothesis that cartilage damage is more relevant than BE in determining irreversible disability in RA. Our data provide further evidence in favor of the external validity of US in the assessment of cartilage damage.
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Disclosure of Interests: Edoardo Cipolletta: None declared, Antonella Incorvaia: None declared, Riccardo Mashadi Mirza: None declared, Andrea Di Matteo Grant/research support from: the publication was conducted while Dr. Di Matteo was an ARTICULUM fellow, Marika Tardella: None declared, Walter Grassi

Speakers bureau: Prof. Grassi reports personal fees from AbbVie, personal fees from Celgene, personal fees from Grünenthal, personal fees from Pfizer, personal fees from Union Chimique Belge Pharma, outside the submitted work., Emilio Filippucci Speakers bureau: Dr. Filippucci reports personal fees from AbbVie, personal fees from Bristol-Myers Squibb, personal fees from Celgene, personal fees from Roche, personal fees from Union Chimique Belge Pharma, personal fees from Pfizer, outside the submitted work.

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SAT0032 INCIDENCE OF RHEUMATOID ARTHRITIS IN PATIENTS WITH NEW ONSET OF MUSCULOSKELETAL SYMPTOMS AND ANTI-CPP POSITIVITY COMPARED TO ANTI-CPP NEGATIVE PATIENTS

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Background: Rheumatoid Arthritis (RA) is a chronic inflammatory joint disease. Strategies for its early detection and diagnosis are of high importance as prompt treatment improves clinical and structural outcome. Autoantibodies against cyclic citrullinated proteins (anti-CCP) have been associated with RA-development. Non-specific musculoskeletal (nsMSK) symptoms are often described prior to RA development. Majority of patients with nsMSK symptoms present to their general practice (GP) first. Studies of early arthritis cohorts have shown that many early arthritis patients cannot be accurately diagnosed at their first visit and are often referred as undifferentiated arthritis patients.

Objectives: To evaluate the incidence of anti-CCP positivity in patients with new onset of nsMSK symptoms and the incidence of RA in these patients over a 3-year follow-up period compared to anti-CPP negative patients.

Methods: In this prospective study (PANORA), 978 patients with new onset of nsMSK symptoms were included in 77 GP sites in Germany. Patients with a positive anti-CCP rapid-test (CCPoint®) were referred to Rheumatology Department (RD) for rheumatological assessment, RA-evaluation and an anti-CCP validation test (ELISA). ELISA anti-CCP positive patients without RA were monitored every 6 months for a total follow-up of 36 months or until RA-diagnosis. Patients with a negative anti-CPP result (CCPoint® or ELISA) are followed up with a questionnaire after 1 and 3 y.

Results: From 978 included patients, 105 (10.7%) were CCPoint® positive. 96 were tested with ELISA and 27 (28.1%) were confirmed anti-CCP positive. 9 (33.3%) were diagnosed with RA at the first RD visit (study visit 2); 4 further patients were diagnosed with RA during the follow-up (FU) period so far. Overall, 48.1% of ELISA-positive (ELISA+) patients were diagnosed with RA up to now; 11 ELISA+ patients are still in the FU period of the study. Of the 868 CCPoint® negative patients, currently, 282 have filled out a 1-year FU questionnaire; 3.5% of those reported a RA diagnosis (Table 1). As expected, clinical parameters at V2 (e.g. CRP, swollen and tender joint count) were worse in the ELISA+/RA+ group compared to the ELISA-/RA- group, but no obvious differences were detected between ELISA+ patients who were diagnosed with RA during the FU period (after V2) and ELISA-/RA- patients

Table 1. Number and percentage of patients with a RA diagnosis

Anti-CCP status	Visit 2	Follow-up*	Total
Point-of-Care Test -	-	3.5% (10 of 282)[#]	3.5% (10 of 282)[#]
Point-of-Care Test + / ELISA -	2.9% (2 of 69)	0% (0 of 34)[#]	2.9% (2 of 69)
Point-of-Care Test + / ELISA +	33.3% (9 of 27)	14.8% (4 of 27)	48.1% (13 of 27)[$]

* 1 year-questionnaire for Point-of-Care Test and ELISA negative patients or every 6 months follow-up for ELISA positive patients; [#]Patient-reported; [$]11 patients are still in the follow-up phase of the study

Conclusion: Currently, 48.1% of anti-CCP+ (ELISA) patients have received a RA diagnosis, whereas 3.5% of the anti-CCP- (CCPoint®) received a RA diagnosis (patient reported), which underlines, that anti-CCP can be used as a marker to identify high-risk patients in GP setting. While clinical parameters are correlated with the diagnosis of RA, they are not suited for predicting future RA development alone. Anti-CCP, possibly in combination with additional parameters imaging, might increase the likelihood to early diagnose or predict RA development.

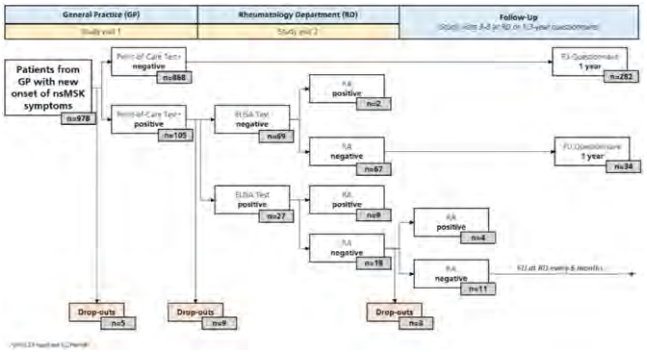


Figure 1. Study overview: Patient distribution depending on anti-CCP results and RA diagnosis.

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SAT0033 USING CHROMOSOME CONFORMATION FOR INSIGHT INTO PATHOGENESIS OF EARLY RHEUMATOID ARTHRITIS ENDOTYPES

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Background: Rheumatoid arthritis (RA) is a chronic autoimmune disease with substantial immunopathogenic heterogeneity. It is well established that early diagnosis and initiation of effective therapy is crucial to prevent loss of function. Previously, various RA treatment trajectories have been identified, however there are currently no clinically validated biomarkers that can identify these trajectories at the start of treatment. Evaluation of the structural epigenome has revealed that chromosome conformation signatures (CCS) offer great potential as binary, informative biomarkers, and have been previously shown to predict early RA patient response to Methotrexate with 90% sensitivity (1). These signatures can also reveal highly regulated areas of the genome, which may be underpinning disease endotypes.

Objectives: The objective of this study was to evaluate the structural epigenome in early RA over longitudinal samples to determine whether it is associated with treatment trajectories.

Methods: Patient data and samples were from the Scottish Early Rheumatoid Arthritis (SERA) cohort; a pan-Scotland inception cohort. CDAI, DAS28 ESR and DAS28 CRP measurements were calculated at baseline, 6 months and 12 months to determine longitudinal treatment response. From 3 principal longitudinal response trajectories, 18 patients (who had equivalent disease activity at baseline) were chosen to investigate the structural epigenome. These 18 comprised of responders (R), non-responders (NR) and initial responders (IR; low disease activity/remission at 6 months but moderate/high disease activity at 12 months) with 6 patients per group at each time point. 20 pooled healthy samples were used as a comparator population. EpiSwitch libraries were probed on 180K Agilent SureSelect custom arrays that were designed using EpiSwitch propriety information and publicly available data from Walsh *et al* (2). Microarray data was analysed using the Limma package within R studio.

Results: EpiSwitch array analysis showed that there were >10,000 statistically significant differential chromosomal loops between R, NR and IR. Evaluation of the 3 trajectory groups (R, NR and IR), taking into account the healthy chromosomal conformation, revealed an RA-associated structural epigenome that comprised of 10,445 chromosomal loops that were stable, over the three time points. Subsequent analysis of the distinct treatment

trajectories demonstrated that 3683 of the stable, disease-associated chromosomal loops were shared by all 3. However, 4496 were associated with distinct response trajectories, with 1221, 2574 and 701 loops unique to R, NR and IR respectively.

Conclusion: The stable chromosomal architecture unique to each treatment trajectory suggests that various underlying molecular endotypes may exist. Moreover, the stable loops common to all groups allude to a baseline level of dysregulation in RA and offers the potential to discover novel drivers of disease. This work provides the foundation to further our understanding of RA pathogenesis and the potential of finding a biomarker that would be of significant value in a clinical setting.

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SAT0034 CLINICAL SIGNIFICANCE OF ANTI-CARBAMYLATED PROTEIN ANTIBODIES IN PREMENOPAUSAL RHEUMATOID ARTHRITIS WOMEN: RELATION TO DISEASE ACTIVITY AND BONE LOSS

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Background: Anti carbamylated protein anti carP are present in patients with Rheumatoid Arthritis RA and are associated with erosions. However their association with systemic or local bone loss in RA patients is still not confirmed.

Objectives: The purpose of this study was to measure the serum level of anti carP in premenopausal women with RA and determine its relation to disease activity and bone loss.

Methods: This case control study was conducted on forty eight RA premenopausal female patients diagnosed according to 2010 ACR/EULAR criteria and forty eight ages and body mass index matched healthy premenopausal females. RA patients with other autoimmune diseases, viral hepatitis malignancy or erosive joint disease and systemic diseases that affect bone quality were excluded from the study. All RA women were subjected to history taking, clinical examination, assessment of disease activity using disease activity score-28 DAS28 and clinical disease activity index CDAI functional assessment using health assessment questionnaire HAQ physical activity assessment using international physical activity questionnaire short form IPAQ fatigue assessment using modified fatigue impact scale MFIS, routine laboratory investigations, serological tests as well as Anti carP using ELISA kit. Moreover the bone mineral density was measured by a lunar Prodigy Advanced DEXA scanner system and plain x-ray of both hands and wrists in the anteroposterior view was done to assess the juxta articular osteopenia and erosions.

Results: Anti carP level was significantly higher in RA patients than in healthy controls table 1. The serum level of anti carP had a significant positive correlation with RA DAS, CDAI, HAQ, IPAQ, MFIS and erosion and joint space narrowing in original sharp score. Also the anti carP had a significant negative correlation with the bone mineral density BMD of spine. The AUC of anti carP level showed a high level of accuracy AUC 0.857 figure 1 and the calculated cutoff value >65 can precisely discriminate subjects with RA from those without RA with 85.42% sensitivity and 85.11% specificity.

Table 1. Comparison between the patient and healthy groups according to anti carp level

Anti-carp	RA patients	Healthy control	U	p
Min – Max	15.0 – 90.0	1.0 – 78.50	322.0*	<0.001*
Mean ± SD	71.24 ± 14.70	45.99 ± 21.99		
Median (IQR)	72.75 (70.5–78.3)	55.0 (32.5–61.5)		

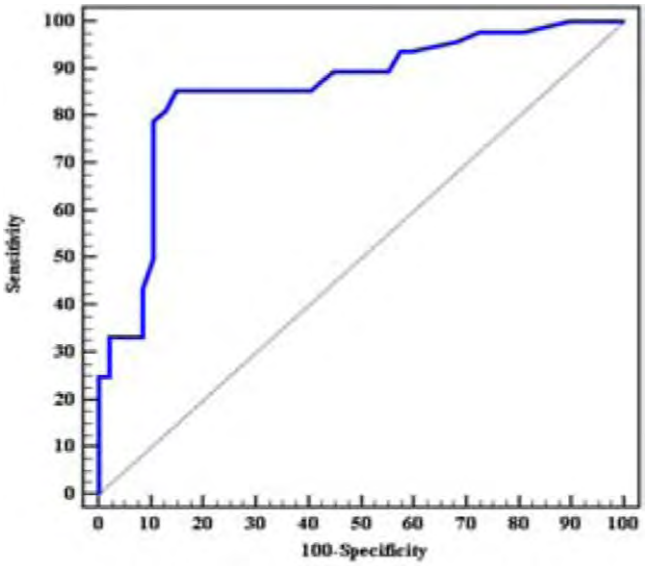


Figure 1. ROC curve for anti carP to diagnose RA patients from healthy subjects

Conclusion: Anti carbamylated antibodies were higher in premenopausal RA women compared to ages and body mass index matched healthy women. Anti carP are associated with higher RA disease activity, increased disability and decreased physical activity. Moreover anti carP are associated with systemic trabecular bone loss manifested by decreased bone mineral density of the spine as well as local bone loss as manifested by increased number of joint erosions in premenopausal RA women.

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Disclosure of Interests: None declared

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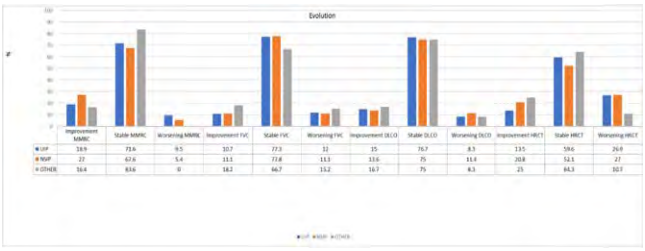
SAT0035 RESPONSE TO ABATACEPT OF DIFFERENT PATTERNS OF INTERSTITIAL LUNG DISEASE IN RHEUMATOID ARTHRITIS: NATIONAL MULTICENTER STUDY OF 263 PATIENTS

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Background: Interstitial Lung Disease (ILD) is a severe extraarticular manifestation of rheumatoid arthritis (RA). In this line, several radiological patterns of RA-ILD have been described: i) usual interstitial pneumonia (UIP), ii) nonspecific interstitial pneumonia (NSIP), iii) obliterating bronchiolitis, iv) organized pneumonia and mixed patterns. Abatacept (ABA) could be an effective and safe option for patients with RA-ILD, although the response in the different radiological patterns is not well defined.
Objectives: Our aim was to assess the response to ABA in different radiological patterns of ILD.
Methods: Observational retrospective multicenter study of RA-ILD treated with ABA. ILD was diagnosed by HRCT and classified by radiological patterns in 3 different subgroups of RA-ILD: a) UIP, b) NSIP and c) "other". ABA was used sc. or iv. at standard dose. We assessed: a) Dyspnoea (MMRC scale; significant variation ≥1); b) Respiratory function tests (significant changes ≥10% in FVC and DLCO); c) HRCT imaging; d) DAS28 e)prednisone dose.
Variables were collected at months 0, 3, 6, 12 months and subsequently every 12 months until a maximum of 60 months.
Results: We included 263 patients: 106 UIP, 84 NSIP and 73 others (150 women / 113 men), mean age 64.64±10 years. Total patients positive for RF or CCPA were 235 (89.4%) and 233 (88.6%), respectively. In 26 out of 263 patients, the development of ILD was closely related to the administration of sDMARDs (MTX n = 11 and LFN n = 1) or bDMARDs (ETN n = 5, ADA n = 4, CZP n = 2 and IFX n = 3). Patient characteristics are shown in table 1. Figure 1 shows the evolution of the cases with available data after a mean follow-up of 22.7±19.7 months. Mean DLCO and FVC remained stable in the 3 groups without statistically significant changes, and all the groups showed a statistically significant reduction in DAS28 and prednisone dose.
Conclusion: ABA could be a good choice of treatment in patients with RA-ILD independently of the radiological pattern of ILD.
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, CLARA AGUILERA CROS: None declared, Ignacio Villa-Blanco Consultant of: UCB, Speakers bureau: Novartis, MSD, Lilly, Sergi Ordoñez: None declared, Susana Romero-Yuste: None declared, C. Ojeda-Garcia: None declared, Manuel Moreno: None declared, Gemma Bonilla: None declared, I. Hernández-Rodriguez: None declared, Mireia Lopez Corbeto: None declared, José Luis Andréu Sánchez: None declared, Trinidad Pérez Sandoval: None declared, Alejandra López Robles: None declared, Patricia Carreira Grant/research support from: Actelion, Roche, MSD, Consultant of: GlaxoSmithKline, VivaCell Biotechnology, Emerald Health Pharmaceuticals, Boehringer Ingelheim, Roche, Speakers bureau: Actelion, GlaxoSmithKline, Roche, Natalia Mena-Vázquez: None declared, C. Peralta-Ginés: None declared, ANA URRUTICOECHEA-ARANA: None declared, Luis Marcelino Arboleya Rodríguez: None declared, J. Narváez: None declared, DESEADA PALMA SANCHEZ: None declared, Olga Maiz-Alonso: None declared, J. Fernández-Leroy: None declared, I. Cabezas-Rodriguez: None declared, Ivan Castellví Consultant of: Boehringer Ingelheim, Actelion, Kern Pharma, Speakers bureau: Boehringer Ingelheim, Actelion, Bristol-Myers Squibb, Roche, A. Ruibal-Escribano: None declared, JR De Dios-Jiménez Aberásturi: None declared, Paloma Vela-Casasempere: None declared, C. González-Montagut Gómez: None declared, J M Blanco: None declared, Noelia Alvarez-Rivas: None declared, N. Del-Val: None declared, M. Rodíguez-Gómez: None declared, Eva Salgado-Pérez: None declared, Carlos Fernández-López: None declared, E.C. Cervantes Pérez: None declared, A. Devicente-DelMas: None declared, Blanca Garcia-Magallon Consultant of: MSD, Speakers bureau: Pfizer, Amgen, Celgene, MSD, Cristina Hidalgo: None declared, Sabela Fernández: None declared, R. López-Sánchez: None declared, Edilia García-Fernández: None declared, S. Castro: None declared, P. Morales-Garrido: None declared, Andrea García-Valle: None declared, Rosa Expósito: None declared, L. Exposito-Perez: None declared, Lorena Pérez Albaladejo: None declared, Ángel García-Aparicio: None declared, Miguel A González-Gay Grant/research support from: Pfizer, Abbvie, MSD, Speakers bureau: Pfizer, Abbvie, MSD, Ricardo Blanco Grant/research support from: AbbVie, MSD, and Roche, Speakers bureau: AbbVie, Pfizer, Roche, Bristol-Myers, Janssen, and MSD

	UIP (n=106)	NSIP (n=84)	OTHERS (73)
Sex (F/M)	59/47	49/35	42/31
Age (years)	66.8±10.0	63.2±9.8	65.0±9.9
RF/CCPA + (%)	94.4/92.3	84.5/91.5	87.7/86.1
Smoking or past smoking (%)	48.1%	53.6%	61.6%
Follow-up (months)	20.37±17.85	21.57±18.2	27.25±22.4
DAS28 at baseline	4.48±1.50	4.42±1.47	4.65±1.47
DAS28 at last visit	2.99±1,27	3.14±1.29	3.21±1.47
Prednisone at baseline, median (IQR) (mg)	7.5 (5-10)	10 (5-10)	7.5 (5-10)
Prednisone at the end of study, median (IQR) (mg)	5 (2.5-5)	5 (2.5-10)	5 (2.5-7.5)
DLCO at baseline (%)	62.78±18.80	65.01±21.14	71.76±21.14
DLCO at the end of study (%)	62.04±18.86	66.06±18.70	70.07±22.19
FVC at baseline (%)	82.60±21.39	89.47±19.39	89.89±21.14
FVC at the end of study (%)	81.40±20.73	87.86±22.65	89.44±17.5



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SAT0036 ULTRASOUND IN THE ASSESSMENT OF JOINT DAMAGE IN RHEUMATOID ARTHRITIS: A SYSTEMATIC LITERATURE REVIEW BY THE OMERACT ULTRASOUND WORKING GROUP

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Background: The detection of damage in patients with rheumatoid arthritis (RA) is crucial for monitoring of therapy targets as well as for early diagnosis. Conventional radiography (CR) is commonly used to detect structural damage, in the form of bone erosions or loss of hyaline cartilage. Over the last years, musculoskeletal ultrasound (MSUS) was shown to be a sensitive and reliable method to detect erosion and cartilage loss as well as damage to soft tissue structures.
Objectives: To identify and synthesize the evidence for the use and measurement properties of MSUS in assessing structural damage in patients with RA.
Methods: A systematic literature search (SLR) of the PubMed, Embase and Cochrane Library was performed. Original articles were included that were published in English until 01/01/2019, reporting MSUS of bone erosion, cartilage loss or damage and tendon damage, and the measurement properties of MSUS according to the OMERACT Filter 2.1.
Results: Of the 1.266 identified articles 79 were finally included, most of which reported on cross-sectional studies. The majority of the studies used the OMERACT definitions for ultrasonographic pathology. Among these, erosions were assessed in 72 (91.1%), cartilage damage in 12 (15.2%), tendons in 4 (5.1%) studies and enthesophytes in a single (1.3%) study. Erosions were rated by binary grading in 56 (77.8%) studies and by semiquantitative scoring in 27 (37.5%) studies. Global or sum scores were calculated in only 9 (12.5%) studies. Among 23 studies assessing erosions both by US and CR, only 1/23 (4.3%) study found a higher sensitivity of CR as compared to MSUS. Among studies assessing tendons, 3 (75%) used a semiquantitative score and one scored tendon rupture as being present or absent. Cartilage damage was graded in binary fashion, quantitatively by measuring cartilage thickness or semi-quantitatively. Hand joints were the most frequently evaluated joints (58, 73.4%). The overwhelming majority of studies assessed structural damage bilaterally (68, 86.1%), with 5 (6.3%) studies assessing only the dominant hand, 5 (6.3%) studies evaluating the clinically more affected side and 1 (1.3%) study assessing only the right hand. Validity, reliability and responsiveness were assessed in only 8 (10.1%), 10 (12.7%) and 4 (5.1%) studies respectively. Feasibility was not considered in any of the studies.
Conclusion: While the results of this SLR suggest that US is a sensitive and feasible tool to detect damage in RA, they also highlight the need for further research and validation. Findings of this SLR will inform the next steps of the Working Group in developing an ultrasound score for assessing structural damage in patients with RA.
Disclosure of Interests: None declared
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SAT0037

HIGH AGREEMENT BETWEEN ANTIBODIES AGAINST MALONDIALDEHYDE PROTEIN ADDUCTS AND ANTIBODIES AGAINST MALONDIALDEHYDE-ACETALDEHYDE ADDUCTS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) presents high levels of oxidative stress and reactive species such as malondialdehyde, which modifies proteins forming malondialdehyde adducts (MaP) and, in the presence of acetaldehyde generates adducts called malondialdehyde-acetaldehyde (MaaP). Recently, the presence of malondialdehyde modified proteins in the synovium and antibodies against these adducts (AMaPA) in the serum of patients with RA has been described (1). Previously, a high frequency of antibodies against MaaP (AMaaPA) had been reported in patients with RA (2).
Objectives: We aimed to confirm the presence of AMaPA in patients with RA and define its relationship with AMaaPA.
Methods: The sera of 204 healthy controls and 205 patients with established RA that met the 1987 ACR classification criteria and selected to represent the different AMaaPA status were studied. All had information on their status for FR, anti-CCP and AMaaPA antibodies (IgG, IgM and IgA). The AMaPA were determined by indirect ELISA using malondialdehyde-modified serum bovine albumin as antigen and specific secondary antibodies against the IgG and IgM isotypes following the same protocol of the previous study (1). The results were analyzed with the gamma coefficient (γ) for concordance in status and with the Spearman coefficient (ρ) for correlation of titres. The study was approved by the CEIC of Galicia.
Results: The AMaPA showed higher titres in the patients with RA than in the controls, the positive frequencies being: 17.1% for IgG AMaPA and 25.4% for IgM AMaPA. An important fraction of the patients with RA showed the same status with the two AMaPA isotypes, as reflected in the significant concordance between them (γ = 0.74, Table 1). When comparing the AMaPA and AMaaPA status in patients with RA, a remarkable concordance was observed among the antibodies of the same isotype, especially between the IgM AMaPA and IgM AMaaPA: γ = 0.83 (Table 1). There were fewer patients with the same status when different antibody isotypes were compared, although some of these comparisons reached statistically significant concordance. However, the titres were not significantly correlated in any of the comparisons, even in those that showed the greatest agreement in status (Table 1).

Table 1. Relationship of antibodies against malondialdehyde adducts (AMaPA) with other autoantibodies in patients with RA.

AMaPA	2nd antibody	ϒ	*P*	ρ	*P*
IgG	IgM AMaPA	0.74	1.5E-14	0.23	0.3
IgM	IgM AMaaPA	0.83	3.4E-25	0.26	0.1
IgG	IgG AMaaPA	0.65	2.4E-08	0.11	0.7
IgM	IgA AMaaPA	0.42	0.0017	0.26	0.4
IgG	IgM AMaaPA	0.39	0.00096	0.08	0.8
IgG	IgA AMaaPA	0.21	0.2	-0.09	0.9
IgM	IgG AMaaPA	0.16	0.3	0.13	0.7
IgM	RF	0.48	0.000011	na	na
IgM	Anti-CCP	0.39	0.00076	-0.34	0.031
IgG	Anti-CCP	0.05	0.7	-0.18	0.4
IgG	RF	0.02	0.9	na	na

In relation to the typical RA autoantibodies, significant concordances were observed between the IgM AMaPA and RF or anti-CCP, although they were lower than those observed with the AMaaPA. In contrast, the IgG AMaPA showed no significant agreement with RF or anti-CCP antibodies. These low levels of concordance were reflected in the lack of significant difference in the prevalence of AMaPA between seronegative and seropositive patients (24.1% vs. 35.4%, *P* = 0.1).
Conclusion: The presence of AMaPA in patients with RA has been confirmed, and a high concordance between the AMaPA and AMaaPA status has been observed, especially between those with an IgM isotype. However, the lack of correlation in the titres indicates that these two types of autoantibodies are independent. The potential utility as biomarkers of the AMaPA should be similar to that of the AMaaPA.
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SAT0038

CHANGES IN ILLNESS PERCEPTIONS IN PEOPLE WITH RHEUMATOID ARTHRITIS OVER THE FIRST YEAR OF TREATMENT WITH METHOTREXATE

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Background: Illness perceptions at treatment onset are known to be important predictors of treatment response in rheumatoid arthritis (RA). Yet it is unknown how these perceptions change over time after the initiation of treatment, or which factors are associated with changing perceptions.
Objectives: To identify groups of patients with early RA who have similar changes in illness perceptions over the first year following treatment, and assess predictors of these changes.
Methods: Patients starting methotrexate (MTX) for the first time were recruited to the Rheumatoid Arthritis Medication Study (RAMS), a one-year prospective cohort. The DAS28 was calculated and patients completed a questionnaire at baseline and 12 months, reporting demographics and completing the HAQ, the Hospital Anxiety and Depression Scale (HADS), pain and fatigue visual analogue scales (VAS) and the Brief Illness Perception Questionnaire (B-IPQ). The B-IPQ consists of eight Likert scales: five represent cognitive illness perceptions (B-IPQ1-5), two represent emotional representations (B-IPQ6 & 8) and one represents illness comprehensibility (B-IPQ7). Change in illness perceptions and EULAR response were calculated over 12 months in those with data at both timepoints. Latent profile analysis was used to identify profiles of patients with similar changes in illness perceptions. Candidate predictors of profile membership were assessed using logistic regression. The association between profile and EULAR response was assessed using ordered logistic regression.
Results: In total 1188 patients were included (mean [SD] age: 59.8 [12.7], 781 [65.7%] women). On average, illness perceptions for the whole cohort improved over 12 months, other than patients' perception of longevity of arthritis (B-IPQ2) and of treatment helpfulness (B-IPQ4). Three profiles were identified: Small Improvers (N=900), Small Deteriorators (N=78) and Large Improvers (N=210) (Figure). Small Improvers improved on all B-IPQ items other than their perception of longevity of arthritis (B-IPQ2) and of treatment helpfulness (B-IPQ4). All B-IPQ items improved in the Large Improvers group to a greater extent than the Small Improvers, other than arthritis longevity (B-IPQ2). The perceptions of Small Deteriorators all worsened, other than arthritis comprehensibility (B-IPQ7). Higher baseline pain was associated with greater odds of being in both the Small Deteriorators and Large Improvers compared to Small Improvers (Small Deteriorators: OR 1.56 per standard deviation (SD) increase in pain [95% CI 1.11, 2.18]; Large Improvers: OR 1.46 per SD increase in pain [95% CI 1.15, 1.85]). Odds of better EULAR response were greater in the Large Improvers (OR 4.37 [95% CI 3.01, 6.33]) and worse in the Small Deteriorators (OR 0.50 [95% CI 0.29, 0.87]) compared to Small Improvers.
Conclusion: In general, illness perceptions improved over the first year of MTX treatment and improvements were associated with better treatment response. Worsening illness perceptions may be driven by poor treatment response. These poor illness perceptions at follow-up may compound poor treatment response in the future. Greater understanding of patients' initial and subsequent illness perceptions is crucial, given the association with treatment response.

Figure:

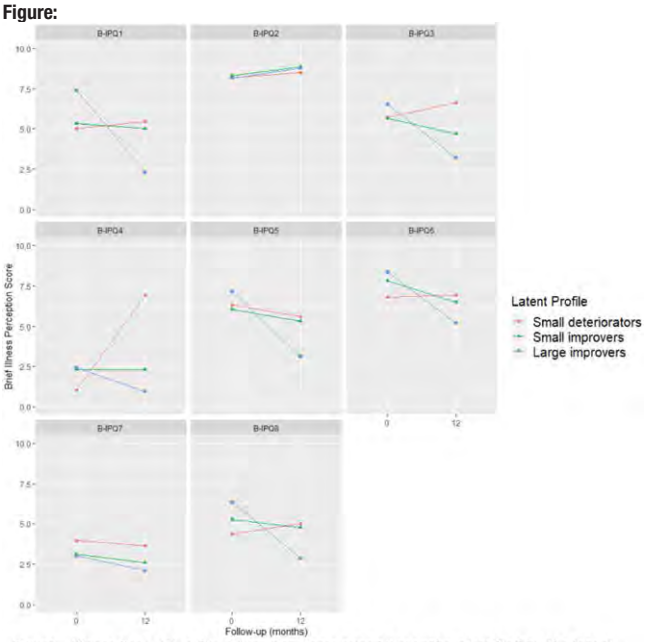


Figure – Illness Perception Questionnaire items over 12 months, stratified by the latent profiles [10 represents worst illness perception]

B-IPQ1: How much does arthritis affect your life?
B-IPQ2: How long do you think your arthritis will continue?
B-IPQ3: How much control do you feel you have over your arthritis? (reverse coded)
B-IPQ4: How much do you think your treatment can help your arthritis? (reverse coded)
B-IPQ5: How much do you experience symptoms from your illness?
B-IPQ6: How concerned are you about your arthritis?
B-IPQ7: How well do you feel you understand your arthritis? (reverse coded)
B-IPQ8: How much does your arthritis affect you emotionally?

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SAT0039 ADAPTIVE DEEP LEARNING FOR THE PREDICTION OF INDIVIDUAL DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) lacks reliable biomarkers that predict disease evolution on an individual basis, potentially leading to over- and under-treatment. Deep neural networks learn from former experiences on a large scale and can be used to predict future events as a potential tool for personalized clinical assistance.

Objectives: To investigate deep learning for the prediction of individual disease activity in RA.

Methods: Demographic and disease characteristics from over 9500 patients with 65.000 visits from the Swiss Quality Management (SCQM) database were used to train and evaluate an adaptive recurrent neural network (AdaptiveNet). Patient and disease characteristics along with clinical and patient reported outcomes, laboratory values and medication were used as input features. DAS28-BSR was used to predict active disease and future numeric individual disease activity by classification and regression, respectively.

Results: AdaptiveNet predicted active disease defined as DAS28-BSR>2.6 at the next visit, with an overall accuracy of 75.6% and a sensitivity and specificity of 84.2% and 61.5%, respectively. Apart from DAS28-BSR, the most influential characteristics to predict disease activity were joint pain, disease duration, age and medication. Longer disease duration, age >50 or antibody positivity marginally improved prediction performance. Regression allowed forecasting individual DAS28-BSR values with a mean squared error of 0.9.

Conclusion: Deep neural networks have the capacity to predict individual disease outcome in RA. Low specificity remains challenging and might benefit from alternative input data or outcome targets.

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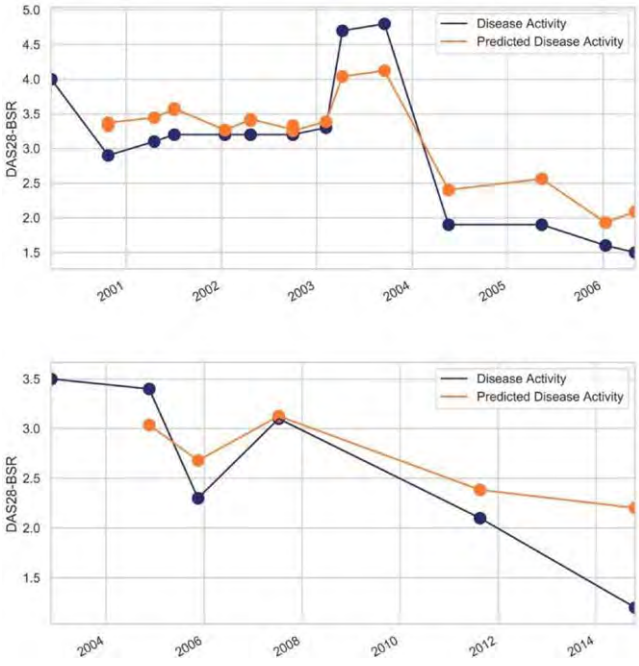


Figure 1. Examples of true disease activity and corresponding predictions of AdaptiveNet by regression analysis. Predictions are made step to step from the current to next visit.

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SAT0040 RISK FACTORS FOR DEVELOPING AND MORTALITY FOR ACUTE EXACERBATION OF RHEUMATOID ARTHRITIS-ASSOCIATED INTERSTITIAL LUNG DISEASE

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Background: Among collagen vascular diseases, rheumatoid arthritis-associated interstitial lung disease (RA-ILD) is the most commonly associated with ILD with acute exacerbation (AE) [1]. One study reported that ILD diagnosis at an older age, the usual interstitial pneumonia (UIP) pattern on high-resolution computed tomography, and methotrexate (MTX) use were associated with AE in patients with RA-ILD [2]. However, because these studies included few patients, the risk factors and prognosis of AE in patients with RA-ILD remain unclear.

Therefore, this study examined the characteristics of RA-ILD patients with AE, and the variables associated with mortality due to AE of RA-ILD.
Objectives: To investigate the risk factors for AE and mortality of RA-ILD.
Methods: We retrospectively collected the clinical data of 165 RA-ILD patients admitted to our hospital between July 2010 and October 2019. We compared clinical characteristics between patients who developed AE (AE group) and those who did not (non-AE group), and identified the variables significantly associated with AE occurrence. We also compared the admission characteristics of those who survived (survivor group) and those who died (non-survivor group) after admission for AE. AE was defined using previously proposed criteria [3], which were modified slightly for application to RA-ILD.
Results: The mean patient age was 73.6 ± 9.7 years and 97 (71.9%) patients were female. Thirty (22.2%) patients developed AE, of whom thirteen (43.3%) died (mean follow-up, 64.9 months). In univariate analyses UIP pattern and MTX were not associated with AE. However, in multivariate analyses, UIP pattern was associated with AE (OR 2.68, 95% CI 1.10–6.52, p=0.03). Median age (70 *vs*. 80 years, p=0.003), non-use of MTX (70.6% *vs*. 23.1%, p =0.025), and C reactive protein level (median 9.38 *vs*. 18.12 mg/dL, p=0.02) on admission were significantly higher in patients who died of AE. In the Cox proportional hazard model, UIP pattern (HR 4.67, 95% CI 1.02–21.5, p=0.048) and non-use of MTX (HR 0.16, 95% CI 0.04–0.72, p=0.016) were associated with death.
Conclusion: Our data suggest that the UIP pattern is related to AE, and non-use of MTX and UIP pattern are related to death due to AE of RA-ILD.
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SAT0041 EFFECT OF INTRA-ARTICULAR GLUCOCORTICOID INJECTION ON RADIOGRAPHIC DAMAGE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Intra-articular glucocorticoid injection (IAGI) has been used as part of a treat-to-target strategy in patients with rheumatoid arthritis (RA). However, recent studies revealed that repeated intra-articular triamcinolone injection into knees with osteoarthritis resulted in significant greater cartilage volume loss after two years. Limited knowledge exists about the long-term efficacy of IAGI in RA, assessed by radiographic changes.
Objectives: To investigate whether IAGI have an additional benefit on achieving remission or low disease activity (REM/LDA) after 3 month, and radiographic progression over the next two years. Additionally, we identified the factors associated with early achievement of REM/LDA and radiographic progression.
Methods: We performed a retrospective study of RA patients who had active arthritis in the hand or wrist joints and received IAGI adjunct to disease modifying anti-rheumatic drugs, compared with those never had received IAGI. Short-term efficacy was assessed by changes of disease activity score in 28 joints (DAS28) after 3 months and long-term efficacy by changes of Sharp score of hand radiographs (HSS) taken before and two years after the onset of active arthritis. The radiographic progression was defined as ΔHSS/year ≥ 1.5. Conditional logistic regression analysis was used to identify predictors for radiographic progression.
Results: We identified 116 RA patients who received IAGI on the hand or wrist joints and 102 IAGI-naïve patients. After 3 months after active arthritis, 61% patients treated with IAGI and 39% of IAGI naïve patients achieved low disease activity or remission (P = 0.009). In the next two year, 45% of patients with IAGI and 34% of IAGI-naive patients were radiographically progressed (P = 0.114). The ΔHSS/year of patients received IAGI was 1.0 (Interquartile ranges [IQR], 0–3.8), while that of IAGI-naïve patients was 0 (IQR, 0–2.5) (P = 0.005). After adjusting disease duration, baseline HSS and 3-month DAS28, IAGI and wrist joint involvement were associated with radiographic progression.
Conclusion: IAGI given in the hand and wrist joints of patients with RA were associated with short-term control of disease activity, however, long-term structural damage in the subsequent two years. Wrist joint arthritis had higher potential for radiographic progression, which should be carefully monitored.
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SAT0042 PREDICTIVE VALUE OF IMMUNOLOGICAL AND IMAGING BIOMARKERS ON ACHIEVING REMISSION AT 6 MONTHS IN RHEUMATOID ARTHRITIS PATIENTS TREATED BY INTRAVENOUS BDMARDS

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Background: RA is the most prevalent chronic inflammatory rheumatism, responsible of functional impairment.
Objectives: To investigate the value of biological and imaging biomarkers on predicting DAS 28 remission at 6 months, in RA patients initiating IV bDMARD.
Methods: From 2008 to 2017, 317 RA patients fulfilling ACR 1987 and/or ACR-EULAR 2010 criteria for RA, initiated IV bDMARDs in our department of Rheumatology. Patients were excluded in cases of lack of information on disease activity assessment before and at 6 months of treatment and on immunological status and titers (ACPA, RF, ANA) at baseline. For patients receiving successive IV bDMARDs during this time period (n=30), a randomization permitted to select 1 treatment sequence. On 173 patients eligible to the study, 4 were lost to follow-up and 14 stopped treatment due to adverse events before 6 months. Clinical, biological and imaging (US and RX) data, were collected when available at treatment initiation. US examination was performed on 12 targeted joints (wrist, MCP2-3-5 and MTP2-3-5) with qualitative and quantitative evaluation on B mode and Power Doppler (PD) for synovitis, tenosynovitis and erosion. The modified Sharp/van der Heijde erosion score was performed by 2 independent readers blindly from clinical and US informations. Remission was defined by a DAS 28 < 2.6 at 6 months. Only variables with a p<0.2 in univariate analysis were included in the multivariate model.
Results: On 155 RA patients, 11 had a disease duration < 2 year, 44 (28.3%) were on first line of IV bDMARDs and 111 patients received at least one IV bDMARD (mean 2.5 (1.3)).

Table 1. Characteristics of the patients (n=155) at baseline

Variables	N (%)	Mean (SD)
Clinical characteristics Age (years)		54.8 (12.2)
Female	113 (72.9)	
Disease duration (months)		166.9 (118.8)
DAS 28		5.2 (1)
Treatments Corticosteroids / dose (mg/day)	99 (85.3)	10.9 (6)
Monotherapy	56 (36.1)	
IV bDMARD Abatacept	27 (17.4)	
Infliximab	11 (7.1)	
Rituximab	84 (54.2)	
Tocilizumab	33 (21.3)	
Immunology ACPA + /titer (IU)	132 (85.2)	618.5 (791.0)
RF + /titer (IU/ml)	114 (74.5)	184.7 (351.3)
ANA + / levels	87 (56.1)	1453 (3836)
Radiography Sharp's erosion score (n=110)		49.4 (46.2)
US Nb Erosion (n=95)		3.0 (2.3)
Nb B mode Synovitis (n=128)		6.0 (4.1)
Nb PD+ Synovitis (n=130)		4.8 (3.8)
Nb B mode Tenosynovitis (n=129)		1.6 (2)
Nb PD+ Tenosynovitis (n=129)		1.3 (2.1)

At 6 months, 33 patients (21.3%) were in remission. Predictive values of biomarkers are presented in table 2.

Table 2. Variables predictive of a DAS 28 remission at 6 months for IV bDMARDs

Biomarkers	Univariate Analysis			Bivariate Logistic regression Analysis
	DAS 28 remission (n= 33)	No Remission (n=122)	p value	OR (CI95%)
Clinical data				
Nb of sequence >1 Radiography (n=110)	19 (57.6%)	92 (75.4%)	0.052	0.4 (0.2-1.0)
Erosive RA US (n=127)	22 (88.0%)	61 (71.8%)	0.118	0.3 (0.1-1.3)
Erosive RA	28 (96.6%)	82 (83.7%)	0.117	0.2 (0.0-1.4)
Nb B mode synovitis	7.7 (4.5)	5.5 (3.9)	0.013	0.9 (0.8-1.0)
Nb PD+ synovitis	6.5 (5.0)	4.3 (3.3)	0.031	0.9 (0.8-1.0)

All qualitative variables with a p value <0.2 on bivariate analysis were incorporated in the multivariate model (RF +, ACPA +, US erosive RA, Nb B mode synovitis, Nb PD+ synovitis, RX erosive RA). Only patients with all data available were incorporated in the multivariate logistic regression analysis (n=103/155). In multivariate analysis only the number of B mode synovitis was still significant with OR =1.1 (CI 95%: 1.0-1.3) (p<0,019).

Conclusion: In RA patients treated by IV bDMARDs, number of PD+ synovitis on ultrasonography was the only predictive biomarker of DAS 28 remission.
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SAT0043 SERUM BIOMOLECULES AS POTENTIAL BIOMARKERS OF CLINICAL EFFICACY AND PREDICTORS OF RESPONSE TO BIOLOGIC DISEASE MODIFYING ANTI-RHEUMATIC DRUGS IN RHEUMATOID ARTHRITIS PATIENTS

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Objectives: To evaluate the changes promoted in levels of circulating inflammatory mediators in RA patients in response to TNF-α inhibitors (TNFi) and anti-CD20 therapies, in order to identify biomarkers of clinical efficacy and potential predictors of therapeutic response to these drugs.
Methods: In a prospective RA cohort multicenter study, we collected serum from RA patients with moderate or high disease activity prior and after 6 months of treatment with TNFi or rituximab (RTX), and analyzed levels of 27 proteins that constitute a multi-biomarker test of the inflammatory profile of these samples, using a multiplex immunoassay. Patients' response was determined according to the EULAR response criteria (good/moderate/no). We compared basal levels of inflammatory molecules between the differential response patient groups and analyzed their discriminative ability. Logistic prediction models were created to assess the added value of potential inflammatory predictors.
Results: Among 111 total RA patients, 50 of 85 (59%) patients in the TNFi group and 18 of 26 patients in the RTX group (69%) responded to the biologic treatment. High DAS28 or SDAI scores, or titers of auto-antibodies (RF or ACPA) at baseline were not predictive of response to any treatment. Instead, smoking habit and hyperlipidemia at baseline were predictors of a worse response to any of these bDMARDs.
Of the molecules analyzed by the multiplex assay, 14 inflammatory mediators showed a significant downregulation on patients' responders to TNFi therapy. Moreover, the decline on 7 biomolecules was related to reduced DAS28. After RTX treatment, 15 inflammatory mediators were reduced in patients with good clinical response; downregulation in 4 of those biomolecules correlated with reduced DAS28.
In the search for predictors of response to each bDMARD, by using the MetaboAnalyst software, we could classify patients with distinctive therapeutic response based on the baseline levels of the inflammatory molecules analyzed. Receiver operating characteristic (ROC) analyses for those multiple biomarkers allowed us to further identify specific signatures of inflammatory biomolecules that may serve as predictors of response to each bDMARD therapy with high sensitivity and specificity. Thus, a signature of five molecules was identified as potential predictor of TNFi response [Vascular endothelial growth factor (VEGF), Eotaxin, RANTES, IL7 and IL-17]. Indeed, a signature including three highly expressed cytokines/chemokines in RA serum were identified as predictors of RTX response [interferon-inducible protein 10 (IP10), Eotaxin and monocyte chemotactic protein 1 (MCP-1)].
Conclusion: The extensive analysis of serum inflammatory profile allowed to identify specific and distinctive signatures of biomolecules that, in coordination with known clinical and serological profiles, might predict the response of RA patients to TNFi or RTX treatments.
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SAT0044 ADIPOCYTOKINE FLUCTUATES WITH INFLAMMATORY MARKERS OR DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS FROM FIVE-YEAR DATA OF TOMORROW STUDY

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Background: Leptin and adiponectin have been thought to be adipocytokines that promote or suppress inflammation, respectively.
Objectives: The aim of this study was to investigate the relationship between adipocytokine and inflammatory markers or disease activity in patients with rheumatoid arthritis (RA) by using 5-year data of TOMORROW study which is a cohort study and started from 2010.
Methods: We evaluated inflammatory markers, disease activity score (DAS)-CRP, medication and levels of adipocytokines in 202 patients with RA (mean age, 58.6 y; medication with biological agents, 54.9%) and 202 age- and sex-matched healthy volunteers (controls; mean age, 57.4 y). We eventually compared leptin or adiponectin concentrations in 183 RA patients and 190 controls from 2010 (BL) to 2015 (5Y) and investigated the relationship between adipocytokines and CRP or DAS in patients by using Spearman correlation analysis.
Results: The levels of leptin and adiponectin in patients were significantly higher than controls at all time points. Adiponectin level of patients significantly increased from BL to 5Y compared to controls (Table 1). In patients, adiponectin showed significant negative correlation with CRP at both of BL and 5Y (BL:R=-0.174, 5Y:R=-0.240; p<0.05), however, not with DAS at BL and 5Y. Leptin positively correlated with CRP at 5Y(R=0.207; p<0.05), but not with CRP at BL or DAS at any time. Adiponectin levels at BL and 5Y were significantly higher in biologics users at BL and significantly increased from BL to 5Y compared to patients without biologics. No association between leptin levels and the use of biologics (Table 2).
Conclusion: The level of adiponectin in RA patients with continuous treatments for 5 years increased, and the trend was more pronounced in biologics users. These results might indicate that adiponectin is a cytokine involved in anti-inflammatory effects.
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Table 1. The levels of Leptin and Adiponectin in RA patients and controls at BL and 5Y, and the changes of them from BL to 5Y

		RA	Controls	p
BL	Leptin (ng/ml)	7.43	5.63	0.006
	Adiponectin (μg/ml)	16.67	14.41	0.007
5Y	Leptin (ng/ml)	10.89	8.18	0.004
	Adiponectin (μg/ml)	19.79	13.76	<0.001
Δ5Y-BL	Leptin (ng/ml)	3.46	2.55	0.232
	Adiponectin (μg/ml)	3.12	-0.64	<0.001

Table 2. The levels of Leptin and Adiponectin at BL and 5Y in RA patients with and without biologic treatment at BL.

		Biologics (+)	Biologics (-)	p
BL	Leptin (ng/ml)	6.85	8.09	0.126
	Adiponectin (μg/ml)	17.97	15.20	0.020
5Y	Leptin (ng/ml)	10.18	11.69	0.157
	Adiponectin (μg/ml)	22.17	17.16	0.005
Δ5Y-BL	Leptin (ng/ml)	3.34	3.59	0.419
	Adiponectin (μg/ml)	4.15	1.96	0.032

Speakers bureau: Daiichi Sankyo Co. Ltd., Mitsubishi Tanabe Pharma, Janssen Pharmaceutical K.K., Astellas Pharma Inc., Takeda Pharmaceutical Co. Ltd., Ono Pharmaceutical Co. Ltd., Abbvie GK, Pfizer Inc., Eisai Co.,Ltd., Chugai Pharmaceutical Co., Ltd., Tadashi Okano Grant/research support from: AbbVie, Eisai, Mitsubishi Tanabe Pharma Corporation and Nipponkayaku, Speakers bureau: AbbVie, Asahikasei, Astellas Pharma Inc, Ayumi Pharmaceutical, Bristol-Myers Squibb, Chugai Pharmaceutical, Daiich Sankyo, Eisai, Janssen, Lilly, Mitsubishi Tanabe Pharma Corporation, Novartis Pharma, Ono Pharmaceutical, Pfizer, Sanofi, Takeda Pharmaceutical, Teijin Pharma and UCB, Yuko Sugioka: None declared, Masahiro Tada: None declared, Tatsuya Koike Grant/research support from: AbbVie, Astellas Pharma Inc, Bristol-Myers Squibb, Chugai Pharmaceutical, Eisai, Janssen, Lilly, Mitsubishi Tanabe Pharma Corporation, MSD, Ono Pharmaceutical, Pfizer, Roche, Takeda Pharmaceutical, Teijin Pharma, and UCB, Speakers bureau: AbbVie, Astellas Pharma Inc, Bristol-Myers Squibb, Chugai Pharmaceutical, Eisai, Janssen, Lilly, Mitsubishi Tanabe Pharma Corporation, MSD, Ono Pharmaceutical, Pfizer, Roche, Takeda Pharmaceutical, Teijin Pharma, and UCB, Hiroaki Nakamura Grant/research support from: Astellas Pharma Inc. and Asahi Kasei Pharma Co.

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SAT0045

DISTRIBUTION AND SEVERITY OF PERIODONTITIS PREDICTS PROGRESSION TO INFLAMMATORY ARTHRITIS IN ANTI-CCP POSITIVE AT-RISK INDIVIDUALS WITHOUT CLINICAL SYNOVITIS

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Background: The prevalence of periodontal disease and the citrullinating bacterium *Porphyromonas gingivalis* are increased in anti-CCP positive individuals at-risk of rheumatoid arthritis (RA) (1). This suggests periodontal inflammation may have an important role in the initiation and development of RA. Despite significant interest in the role of the periodontium and other mucosal sites in the initiation of RA-related autoimmunity, the influence of mucosal inflammation on progression to inflammatory arthritis (IA) in at-risk individuals remains unclear.

Objectives: To investigate the association between periodontitis and progression to inflammatory arthritis in anti-CCP+ at-risk individuals without synovitis.

Methods: Anti-CCP positive individuals with musculoskeletal symptoms but no clinical synovitis (CCP+ at-risk) were recruited as part of a national prospective cohort study. Comprehensive periodontal examination was performed at baseline by a dentist; six sites per tooth were assessed for clinical attachment level (CAL), pocket depth (PD) and bleeding on probing (BOP). Periodontal disease sites (PDD) were defined as CAL ≥2mm and PD ≥4mm. The distribution of PDD was classified in line with recent guidelines (2). The severity i.e. total burden of periodontal inflammation, was quantified at patient level using the periodontal inflamed surface area (PISA) index(3). CCP+ at-risk were monitored for progression to IA. Multivariable Cox regression was used to assess the effect of PDD distribution and PISA on progression to IA.

Results: 126 CCP+ at-risk underwent full periodontal examination and were followed up for median 23.4 months (range 0.6 – 56.8 months). Mean age was 49 years, 86 (68%) were females. At baseline, 42(33%) subjects had no PDD, 51(40%) had localised PDD (<30% teeth with one or more PDD site) and 33 (26%) had generalised PDD (≥ 30% of teeth with one or more PDD site). Mean (SD) PISA for all subjects was 267(319)mm^2. 31 subjects (25%) progressed to IA after median of 12.6 months (range 0.6 – 49.5 months). Progression to IA was significantly higher in subjects with localised PDD compared with those without PDD (33% vs 16%, HR (95% CI) 2.45 (1.02, 5.94) p=0.02), figure 1. Interestingly, this association was not seen in subjects with generalised PDD (19% progression, HR 0.68 (0.20, 2.32). In addition, severity (i.e. total burden) of periodontal inflammation (PISA) was not significantly predictive of progression to IA alone (HR 1.001 (0.999-1.002), p=0.08). However, when adjusting for distribution of PDD, PISA was significantly associated with progression to IA (HR 1.0016 (1.0003- 1.003), p=0.00163).

Conclusion: Periodontal inflammation predicts progression to IA in CCP+ at-risk individuals without clinical synovitis. The severity (i.e. total burden) of periodontitis appears to be particularly predictive of progression to IA in patients with localised periodontitis. These data suggest periodontitis may be an important factor in the development of RA and provide rationale for periodontal intervention with the aim of arthritis prevention in at-risk individuals.

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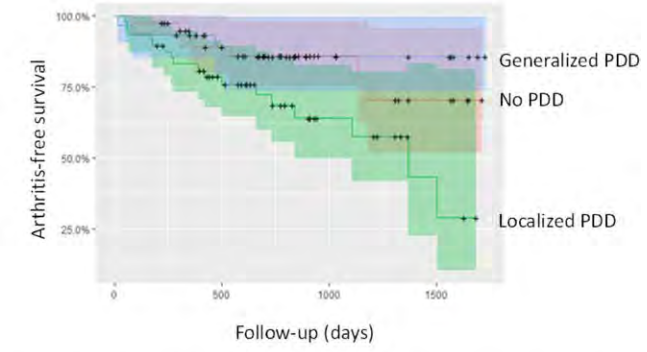


Figure 1: Survival plot of anti-CCP positive at-risk individuals showing cumulative inflammatory arthritis-free survival according to the *distribution* of periodontal disease sites at baseline. Localized PDD; periodontal disease sites in <30% of teeth. Generalized PDD; periodontal disease sites in ≥30% of teeth.

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SAT0046

MODIFIED DISEASE ACTIVITY SCORE AT 3 MONTHS IS A SIGNIFICANT PREDICTOR FOR RAPID RADIOGRAPHIC PROGRESSION AT 12 MONTHS COMPARED WITH OTHER MEASURES

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Background: Progressive rheumatoid arthritis (RA) is responsible for joint damage causing disabilities with no agreement on which disease measures best predict radiographic progression

Objectives: We aimed to determine which disease activity measures including disease activity score (DAS), modified (M) DAS28 (CRP), clinical disease activity index (CDAI), and health assessment questionnaire disability index (HAQ-DI) best predict rapid radiographic progression (RRP) in early RA patients at baseline (BL) and 3 months.

Methods: PREMIER data, a 2-year, multicenter, double-blind active comparator–controlled study with methotrexate (MTX) naïve RA patients and active disease <3 years, were used. Only patients in the MTX arm were analyzed. RRP was defined as change in modified total Sharp (mTSS) > 3.5 at month 12. Logistic regression analysis assessed impact of measures at BL and 3 months on RRP at 12 months. Best cut-off points of M-DAS28(CRP) was also estimated using area under the receiver operating characteristic curve.

Results: 149 patients were included: female (n=113; 75.8%), positive RF (n=127; 85.2%), mean (SD) age 52.9 (13.3) years, disease duration 0.8 (0.9) year, DAS28(CRP) 6.3 (0.9). After adjusting for potential confounders, only M-DAS28(CRP) at BL ($_{adj}$OR=3.29; 95% CI: 1.70-6.36) and 3 months ($_{adj}$OR=2.56; 95% CI: 1.43-4.56) strongly predicted RRP at 12 months. M-DAS28(CRP) 4.5 and 2.6 at BL and 3 months maximized sensitivity and specificity for prediction of RRP.

Conclusion: M-DAS28(CRP) was a stronger predictor at BL and 3 months for RRP compared with other disease activity measures. Removing tender joint count and patient global assessment from DAS28(CRP) improves prediction of RRP.

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SAT0047

RISK FACTORS FOR THE POSTOPERATIVE DELAYED WOUND HEALING IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH A BIOLOGICAL AGENT

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Background: It has been suggested that perioperative use of biological disease-modifying anti-rheumatic drugs (bDMARDs) in rheumatoid arthritis (RA) patients carries risks for the surgical-site infection and the delayed wound healing (DWH); however, the risk of DWH with perioperative use of bDMARDs has not reached a general consensus.

Objectives: This retrospective study aimed to investigate the risk factors associated with DWH after orthopedic surgery in RA patients treated with bDMARDs.

Methods: We reviewed medical records of 277 orthopedic procedures for 188 RA patients treated with bDMARDs between from 2014 to 2017 in Niigata Rheumatic Center. As preoperative nutritional status assessment, we evaluated body mass index (BMI), prognostic nutritional index (PNI), and CONtrolling NUTritional status (CONUT). In addition, we evaluated DAS28-CRP, DAS28-ESR, face scale for pain, global health (GH), and Health Assessment Questionnaire-Disability Index (HAQ-DI) to assess the disease activity. Univariate and multivariate logistic regression analyses were performed to evaluate the risk factor for DWH.

Results: The major characteristics of the patients in 277 procedures were mean age of 63.2 years old and mean disease duration of 18.2 years. Surgical site were hand and wrist (145 procedures), foot and ankle (76), hip and knee (31), elbow and shoulder (24), and spine (1). Seventy-four patients were treated with tocilizumab, 62 with etanercept, 55 with golimumab, 49 with abatacept, 16 with infliximab, 15 with adalimumab, and 6 with certolizumab. According to nutritional assessment in PNI and CONUT, 63% (n=175) and 47% (n=130) were normal nourished patients, respectively.

In 277 procedures, DWH were identified in 24 patients (8.6%). The following variables were significant in the univariate analyses: disease duration (OR 1.053; 95% CI 1.010–1.099; p=0.016), foot and ankle surgery (OR 7.091; 95% CI 2.130–23.603; p=0.001), tocilizumab (OR 0.286; 95% CI 0.093–0.881; p=0.029) (Table 1). These variables were entered into a multivariate model, and it was revealed that pre-operative use of tocilizumab (OR 0.265; 95% CI 0.074–0.953; p=0.042) and procedures in the foot and ankle (OR 6.915; 95% CI 1.914–24.976; p=0.003) were associated with an increased risk of DWH (Table 1).

Conclusion: As previous study on tocilizumab described, the current retrospective study suggested that pre-operative use of tocilizumab and procedures in the foot and ankle were risk factors for DWH. Pre-operative disease activity and nutritional status were not independent risk factors for an increase in the prevalence of DWH.

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Table 1. Risk factors for DWH after orthopedic surgery in RA patients treated with bDMARDs

	Univariable		Multivariable	
	OR (95% CI)	p value	OR (95% CI)	p value
Age	1.012 (0.967-1.059)	0.610		
Disease duration	1.053 (1.010-1.099)	**0.016**	1.035 (0.980-1.093)	0.220
Surgical site				
hand and wrist	Ref		ref	
elbow and shoulder	n.c.		n.c.	
hip and knee	n.c.		n.c.	
foot and ankle	7.091 (2.130-23.603)	**0.001**	6.915 (1.914-24.976)	**0.003**
Smoking	0.708 (0.085-5.905)	0.749		
Diabetes Mellitus	0.698 (0.150-3.252)	0.647		
DAS28-CRP	0.558 (0.302-1.029)	0.062		
HAQ-DI	0.986 (0.923-1.054)	0.686		
use of PSL	1.039 (0.343-3.147)	0.946		
bDMARDs				
TNF inhibitors	ref		ref	
tocilizumab	0.286 (0.093-0.881)	**0.029**	0.265 (0.074-0.953)	**0.042**
abatacept	0.370 (0.072-1.889)	0.232	0.515 (0.085-3.107)	0.469
PNI	0.986 (0.896-1.084)	0.767		
CONUT	0.892 (0.594-1.338)	0.580		

Disclosure of Interests: Shunji Okita: None declared, Hajime Ishikawa: None declared, Asami Abe: None declared, Satoshi Ito Speakers bureau: Abbvie,Eisai, Akira Murasawa: None declared, Keiichiro Nishida Grant/research support from: K. Nishida has received scholarship donation from CHUGAI PHARMACEUTICAL Co., Eisai Co., Mitsubishi Tanabe Pharma and AbbVie GK., Speakers bureau: K. Nishida has received speaking fees from CHUGAI PHARMACEUTICAL Co., Eli Lilly, Janssen Pharmaceutical K.K., Eisai Co. and AYUMI Pharmaceutical Corporation., Toshifumi Ozaki: None declared

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SAT0048

THE CLINICAL USE OF F-18 NAF BONE PET/CT FOR EVALUATING DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Bone positron emission tomography/computed tomography (PET/CT) using F-18 sodium-fluoride (NaF) has been widely used in various bone and joint diseases. However, only a few studies had evaluated the clinical implication of F-18 NaF bone PET/CT in patients with rheumatoid arthritis[1].

Objectives: The aim of our study is to investigate the clinical usefulness of F-18 NaF bone PET/CT for evaluating disease activity in patients with rheumatoid arthritis.

Methods: Seventeen patients with rheumatoid arthritis prospectively enrolled. All patients underwent whole-body F-18 NaF bone PET/CT and ultrasonography simulataneously. The baseline disease activity score with 28 joints using erythrocyte sedimentation rate (DAS28-ESR) and the results of blood tests were collected. From F-18 NaF bone PET/CT images, uptake of the 28 joints used in DAS28-ESR, expressed as standardized uptake value (SUV), and joint-to-normal bone uptake ratios of those joints were measured for each patient. Using SUV and joint-to-normal bone uptake ratios of the 28 joints, the relationship of bone PET/CT findings with clinical factors and ultrasonography findings were assessed.

Results: SUVs and joint-to-normal bone uptake ratios in the joints with active synovitis were significantly higher than those in the joints without definite synovitis ($p < 0.05$). The sum of SUVs and joint-to-normal bone uptake ratios of 28 joints showed significant positive correlations with DAS28-ESR as shown in Figure 1 and Figure 2 ($p < 0.001$ and correlation coefficient 0.775 for SUV; $p < 0.001$ and correlation coefficient = 0.828 for joint-to-normal bone uptake ratio) and patient global assessment score ($p = 0.002$ and correlation coefficient 0.697 for SUV; $p = 0.002$ and correlation coefficient = 0.705 for join-to-normal bone uptake ratio). On correlation analysis with blood test results, only serum ESR level showed a positive correlation with the sum of joint-to-normal bone uptake ratios of the 28 joints ($p = 0.047$; correlation coefficient = 0.470) and other serum markers showed no significant association with bone PET/CT results ($p > 0.05$). On correlation analysis with ultrasonography findings, both power Doppler and gray-scale joint inflammation scores showed significant positive correlations with both the sum of SUVs and joint-to-normal bone uptake ratios of ultrasonography-examined joints ($p < 0.05$).

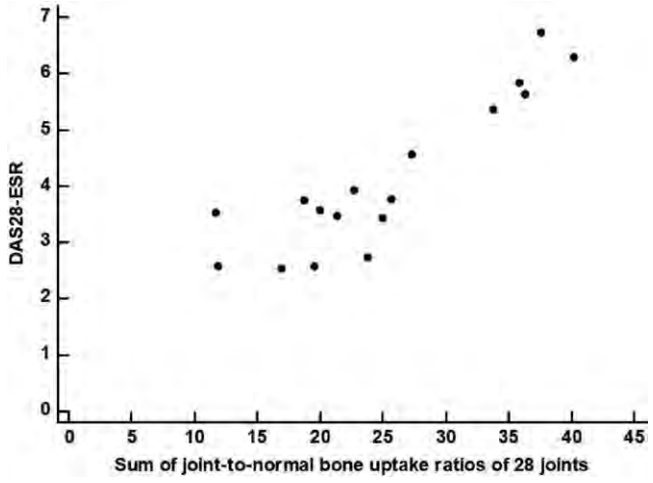


Figure1. Correlation between the sum of SUVs of 28 joints in F-18 NaF bone PET/CT and DAS28-ESR ($p < 0.001$ and correlation coefficient 0.775)

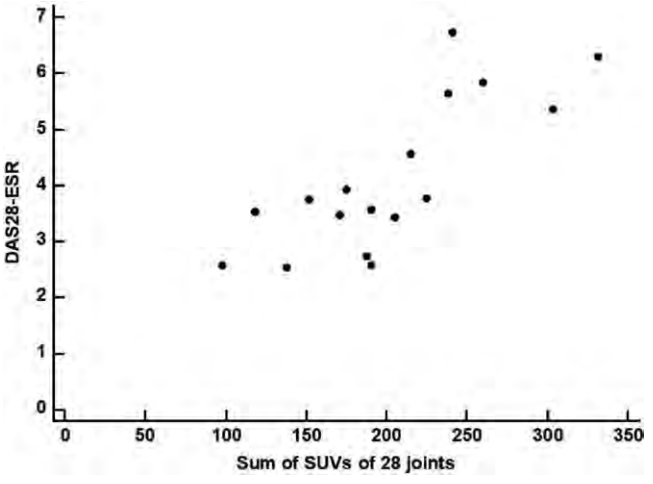


Figure 2. Correlation between the joint-to-normal bone uptake ratio of 28 joints in F-18 NaF bone PET/CT and DAS28-ESR ($p < 0.001$ and correlation coefficient = 0.828)

Conclusion: The sum of joint uptake on F-18 NaF bone PET/CT has significant positive correlations with DAS28-ESR, serum ESR level, and ultrasonography findings in patients with rheumatoid arthritis. The findings on F-18 NaF bone PET/CT might be used as an imaging biomarker for disease activity of rheumatoid arthritis.

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SAT0049 DIFFERENCES BETWEEN EARLY AND ESTABLISHED RHEUMATOID ARTHRITIS IN TIME TO ACHIEVING CDAI BUT NOT FATIGUE LOW DISEASE ACTIVITY AND REMISSION: DATA FROM THE OBRI REGISTRY

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Background: Previous studies have shown that early diagnosis and treatment of rheumatoid arthritis (RA) is important for achieving comprehensive disease control and have identified established disease as an independent predictor of worse clinical outcomes. However, it is not clear whether these differences are driven by patient-reported or objective outcome measures.

Objectives: The aim of this analysis was to compare the time to achieving low disease activity (LDA) and remission based on both objective and patient-reported outcomes in people with early vs. established RA followed in routine clinical care.

Methods: RA patients enrolled in the Ontario Best Practices Research Initiative (OBRI) registry that were not in a low disease state at baseline based on the CDAI, SJC28, PtGA, pain and fatigue criteria below, and had at least six months of follow-up, were included in the analysis. LDA was defined as CDAI≤10, SJC28≤2, TJC28≤2, PtGA≤2cm, pain≤2cm, fatigue≤2cm, and MDGA≤2cm; remission was defined as CDAI≤2.8, SJC28≤1, TJC28≤1, PtGA≤1cm, pain≤1cm, fatigue≤1cm, and MDGA≤1cm. Between group (early vs. established) differences in time to first LDA/remission were assessed with Kaplan-Meier survival analysis and the log-rank test.

Results: A total of 986 patients were included, 347 (35%) with early RA and 639 (65%) with established RA. At baseline, patients with early RA were significantly younger (55.8 vs. 58.3 years) and were less likely to have a comorbidity (94.5% vs. 97.5%) or an erosion (26.7% vs. 62.6%), be RF-positive (65.6% vs. 74.2%), use bDMARDs (7.5% vs. 26.6%), and be non-smokers (38.9% vs. 47.3%).

Time to achieving LDA based on CDAI (HR [95%CI]: (1.23 [1.07,1.43]), SJC28 (1.32 [1.15,1.51]), TJC28 (1.18 [1.02,1.36]), MDGA (1.28 [1.10,1.49]), PtGA (1.23 [1.05,1.44]), and pain (1.29 [1.09,1.52]) were significantly shorter in early RA compared to established RA. Similarly, time to achieving remission based on CDAI (HR [95%CI]: (1.50 [1.22,1.84]), SJC28 (1.35 [1.17,1.55]), MDGA (1.25 [1.06,1.47]), PtGA (1.22 [1.02,1.47]), and pain (1.37 [1.14,1.65]) were significantly shorter in early RA. However, no differences were observed in time to remission based on TJC28 (1.12 [0.96,1.31]) and either LDA or remission based on fatigue (LDA (1.10 [0.94,1.30]); remission (1.09 [0.92,1.31]).

Adjustment for age, gender, presence of comorbidities, and baseline scores did not alter the results.

Conclusion: Time to achieving low disease state or remission based on various objective and patient-reported measures is significantly shorter in early compared to established RA with the exception of fatigue.

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Emmanouil Rampakakis: None declared, Angela Cesta: None declared, John Sampalis: None declared, Claire Bombardier Grant/research support from: Dr Bombardier reports sources of funding for Ontario Best Practice Research Initiative Research grants from Abbvie, Janssen, Amgen, Medexus, Merck, Pfizer, and Novartis outside of the submitted work. Consulting Agreements: Abbvie, Covance, Janssen, Merck, Pfizer, Sanofi and Novartis outside of the submitted work. Advisory Board Membership: Hospira, Sandoz, Merck, Pfizer and Novartis outside of the submitted work.

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SAT0050

PREDICTION OF RESPONSE TO CERTOLIZUMAB PEGOL TREATMENT BY FUNCTIONAL MRI OF THE BRAIN: AN INTERNATIONAL, MULTI-CENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL (PRECEPRA)

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Background: Personalization of RA treatment is not optimal due to lack of predictors. We previously demonstrated in RA patients that central nervous system (CNS) pain response to tender joint compression, measured by using functional MRI (fMRI) of the brain rapidly wanes after 24 hours of anti-TNF administration and that a higher pre-treatment BOLD signal volume seems to predict clinical response to treatment with certolizumab-pegol (CZP)[1,2]. We therefore hypothesized that the CNS pain response upon compression of a painful joint could predict subsequent anti-TNF treatment response.

Objectives: To compare disease activity after 12-weeks of CZP treatment to that of placebo in DMARD-refractory RA patients based on pre-treatment baseline CNS pain response measured using BOLD fMRI.

Methods: Adult RA patients fulfilling the 2010 ACR/EULAR classification criteria with a DAS28>3.2 under stable DMARD treatment for at least 3 months were eligible. Patients underwent fMRI scanning of the brain at screening for stratification by CNS pain response. Whole brain BOLD-signal-voxel-count of 700 units classifying between low and high, and were randomized to CZP or placebo (2:1) The primary outcome was low disease activity (LDA, DAS28 ≤3.2) after 12 weeks of treatment.

Results: 156 RA patients, inadequate responders to csDMARD, signed the informed consent. 139 patients (46/47, 46/49 and 42/43) (99 females, 71%) with moderate-high disease activity (mean (SD) DAS-28: 4.83 (1.03)) could be included respectively and completed the 12-week study treatment. Geometric mean (SD) numbers of baseline BOLD signal positive voxels were 559 (10), 81 (12) and 2498 (3) in the 3 arms respectively. The mean DAS28 (SD) scores after 12 weeks of study treatment were Placebo: 3.89 (1.29), CZP-L: 3.42 (1.06) and CZP-H: 3.06 (1.04). LDA was achieved in 12/47 patients (25.5 %) in placebo, 22/49 (44.9%) in the CZP-L, and 25/43, (58.1%) in the CZP-H arm. The linear effect term for the ordinal study group variable supported a linear trend of increasing CZP treatment effect with increasing baseline CNS pain response. RR (95% CI) for achieving LDA with each unit increase in treatment category over placebo was 1.79 (1.24 to 2.74, p=0.003).

Conclusion: A higher pre-treatment brain activity in response to pain measured with fMRI predicts the chance of achieving low disease activity with CZP treatment.

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[2] Rech, J. *et al. Arthritis & Rheumatism* (2013).

-1 Baseline characteristics of the study population overall and by study groups.

		Overall	Study group		
			Certolizumab-Hig	Certolizumab-Lc	Placebo
		139	43	49	47
, mean (SD)		54.3 (11.8	54.3 (10.8)	56.5 (12.2)	52.1 (12.0)
	Female	99 (71.2)	34 (79.1)	35 (71.4)	30 (63.8)
	Male	40 (28.8)	9 (20.9)	14 (28.6)	17 (36.2)
n, years	Mean(SD)	6.2 (8.1)	6.0 (8.3)	6.4 (8.6)	6.2 (7.6)
	Median(IQR)	2.0 (1.0-8.(	2.0 (1.0-9.0)	3.0 (1.0-8.0)	3.0 (1.0-8.0)
s)	Negative	34 (24.5)	15 (34.9)	9 (18.4)	10 (21.3)
	Positive	105 (75.5	28 (65.1)	40 (81.6)	37 (78.7)
	Negative	39 (28.1)	12 (27.9)	13 (26.5)	14 (29.8)
	Positive	100 (71.9	31 (72.1)	36 (73.5)	33 (70.2)
nts (28), mean (SD)		10.2 (6.5	9.3 (6.4)	11.3 (6.7)	9.9 (6.2)
ints (28), mean (SD)		7.9 (5.3)	7.0 (4.4)	8.7 (6.3)	8.0 (4.8)
bal VAS, mm, mean (SD)		58.0 (20.0	57.2 (19.9)	59.1 (17.0)	57.6 (22.5)
global VAS, mm, mean (SD)		49.6 (18.7	46.0 (20.2)	49.5 (19.2)	53.1 (16.2)
mm, mean (SD)		55.2 (19.3	53.5 (18.0)	57.1 (17.0)	54.9 (22.7)
n, mean (SD)		25.8 (19.9	23.7 (19.0)	25.2 (17.1)	28.2 (23.2)
, mean (SD)		8.7 (13.0	6.8 (12.7)	7.9 (8.7)	11.2 (16.5)
s/h, mean (SD)		4.8 (1.0)	4.7 (1.0)	5.0 (1.1)	4.9 (1.0)

rd deviation; IQR, interquartile range; ACPA, anti-citrullinated peptide antibodies; RF, Rheumatoid factor; VAS, visual analogue s. rocyte sedimentation rate; CRP, C reactive protein; DAS-28, disease activity score 28 joints.

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SAT0051

REMISSION IN RHEUMATOID ARTHRITIS PATIENTS: A CLUSTER ANALYSIS TO IDENTIFY AND CHARACTERIZE SUBPOPULATIONS OF PATIENTS

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Background: Disease Activity Score (DAS) is a continuous measure of Rheumatoid Arthritis (RA) activity, used in clinical practice for monitoring disease progression and for documenting treatment response. According to EULAR, the clinical desired target is to achieve a remission state (or failing that, low disease activity). However, the population of RA patients in this state could be heterogenous.

Objectives: To characterize the level of heterogeneity of RA patients in remission by identifying clusters based on the DAS28 components; and to describe inter and intra-class cluster demographic and clinical characteristics

Methods: Patients from Hospital Clínico San Carlos cohort, stored in a departmental electronic health record from January 1st, 2000 to December 30th, 2018, diagnose with RA according ACR 1986/ 2010 criteria were eligible for this study. Only observations with a DAS28 Erythrocyte Sedimentation Rate (ESR) value < 2.6 value were considered. ESR, patient's Global Health (GH), and tender and swollen joints were used for calculating the clusters. Different aggregation levels for joints were studied as well as the input variable types. Isolated joints, joints grouped by the type of affectation (swollen or tender) or anatomic location or laterality aggregation levels were considered. Variables expressed as present or absent (i.e. dichotomous), continuous (count of joins) and categorical (type of joints) were also studied. Gower's distance, used for dealing with variables of different type, was employed to calculate the distance matrix. The number of suitable clusters was chosen from two to seven clusters based on the width value of a Silhouette analyses. Finally, Partitioning Around Medoids (PAM) was used as the clustering algorithm. Differences among clusters regarding demographic and clinical characteristics were analyzed using t-student chi2 test.

Results: 812 patients with 1,431 observations were analyzed in this study. The joint aggregation level which showed a highest Silhouette width value (0.708) was the anatomic one. In this aggregation level, five dichotomous variables (presence of tenderness and/or swelling in right and/or left shoulder, elbow, wrist, knee and hand (including both metacarpophalangeal and proximal interphalangeal joints) and two continuous variables (ESR and GH) were used. Two clusters were found: the cluster A) with 1,305 observations and 742 patients and the B) with 126 observations and 115 patients. Cluster b) had a statistically significant higher DAS28-ESR value (higher number of tender and swollen joints, and higher GH, but lower ESR), longer follow-up time (6.5 vs. 4.7 years), higher VAS-pain score (10 vs. 2), and higher HAQ score (0.25 vs. 0.12). In addition, the proportion of patients treated with oral corticosteroids (63% s. 50%) and biological therapy (29% vs. 12%) was higher.

Conclusion: We have identified two clinically distinct populations of RA patients in remission according to DAS28-ESR <2.6. Each subgroup could be associated with different outcomes during follow-up, such as radiographic progression or risk of relapse.

Disclosure of Interests: Alfredo Madrid García: None declared, Dalifer Freites Nuñez: None declared, Judit Font: None declared, Isabel Hernandez: None declared, Leticia León: None declared, Jose Ignacio Colomer: None declared, Isidoro González-Álvaro Grant/research support from: Roche Laboratories, Consultant of: Lilly, Sanofi, Paid instructor for: Lilly, Speakers bureau: Abbvie, MSD, Roche, Lilly, Benjamin Fernandez: None declared, J Angel Jover: None declared, Lydia Abasolo: None declared, Luis Rodriguez Rodriguez: None declared

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SAT0052

THERAPEUTIC STRATEGIES IN DIFFICULT-TO-TREAT RHEUMATOID ARTHRITIS: PRELIMINARY RESULTS OF A SYSTEMATIC LITERATURE REVIEW INFORMING THE 2020 EULAR RECOMMENDATIONS FOR THE MANAGEMENT OF DIFFICULT-TO-TREAT RHEUMATOID ARTHRITIS

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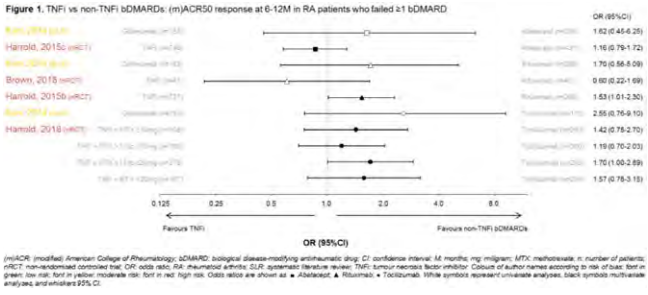
Background: Rheumatoid arthritis (RA) patients treated according to European League Against Rheumatism (EULAR) recommendations failing ≥2 biological or targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs) with a different mode of action who still have complaints which may be suggestive of active disease may be defined as suffering from 'difficult-to-treat RA' Management recommendations for RA focus predominantly on the earlier phases of the disease and specific recommendations for difficult-to-treat RA patients are currently lacking.[1]

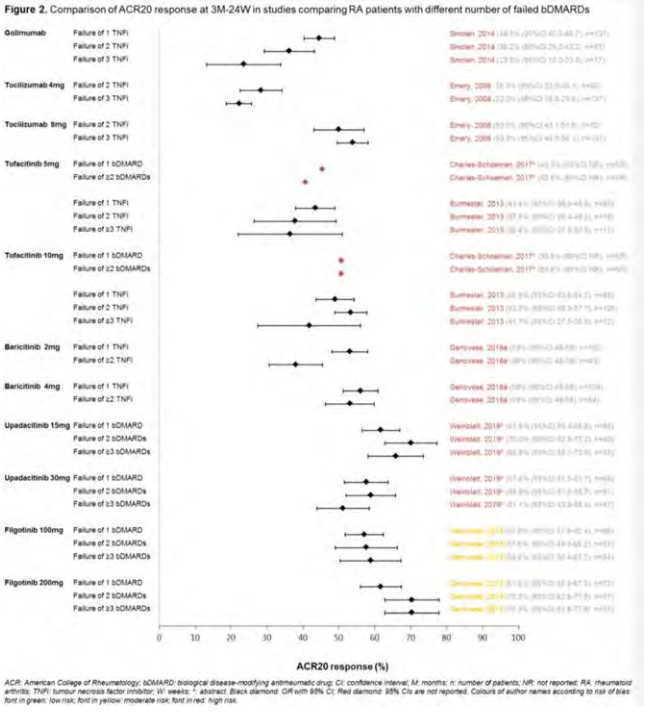
Objectives: To systematically summarise evidence in the literature on pharmacological and non-pharmacological therapeutic strategies for difficult-to-treat RA patients, informing the 2020 EULAR recommendations for the management of difficult-to-treat RA.

Methods: A systematic literature review (SLR) was performed: PubMed, Embase and Cochrane databases were searched up to December 2019. Relevant papers were selected and appraised.

Results: Thirty articles were selected for therapeutic strategies in patients with limited DMARD options due to contraindications, 73 for patients in whom previous b/tsDMARDs were not effective ('true refractory RA'), and 51 for patients with predominantly non-inflammatory complaints. For patients with limited DMARD options, limited evidence was found on effective DMARD options for patients with concomitant obesity, and on safe DMARD options for patients with concomitant hepatitis B and C. In patients who failed ≥2 bDMARDs, tocilizumab, tofacitinib, baricitinib, upadacitinib and filgotinib were found to be more effective than placebo, but evidence was insufficient to prioritise. In patients who failed ≥1 bDMARD, there was a tendency of non-tumour necrosis factor inhibitor (TNFi) bDMARDs to be more effective than TNFi (Figure 1). Generally, b/tsDMARDs become less effective when patients failed more bDMARDs, this tendency was not clear for upadacitinib and filgotinib (Figure 2). In patients with predominantly non-inflammatory complaints (mainly function, pain and fatigue), exercise, education, psychological and self-management interventions were found to be of additional benefit.

Conclusion: This SLR underscores the scarcity of evidence on the optimal treatment of difficult-to-treat RA patients. As difficult-to-treat RA is a newly defined disease state, all evidence is to an extent indirect. Several b/tsDMARDs were found to be effective in patients who failed ≥2 bDMARDs and generally effectiveness decreased with a higher number of failed bDMARDs. Additionally, a beneficial effect of non-pharmacological interventions was found on non-inflammatory complaints.





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SAT0053

ESTIMATING REAL-WORLD UNMET NEEDS FOR REACHING REMISSION IN THE FIRST YEAR FOLLOWING EARLY RA DIAGNOSIS: RESULTS FROM THE CANADIAN EARLY ARTHRITIS COHORT (CATCH)

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Background: Several composite RA disease activity indices are commonly used in clinical practice and research. Different disease activity indices however can be inconsistent in classifying remission (REM).
Objectives: 1) Compare remission prevalence across 4 common RA indices; 2) compare changes in remission across indices; and, 3) Identify predictors of persistent active disease across all indices, in real-world early RA patients over 1 year follow up.
Methods: Data were from patients with early RA (symptoms < 1 year) enrolled in the Canadian Early Arthritis Cohort (CATCH) between 2007 and 2018. Participants had active disease at enrolment, were treated with csDMARDs and completed standardized clinical assessments every 3-months. Remission status was assessed using 4 indices: 1) DAS28< 2.6 OR DAS28CRP < 2.5, 2) CDAI ≤ 2.8, 3) SDAI≤ 3.3, and 4) ACR/EULAR Boolean remission – SJC28, TJC28, CRP, PGA all ≦1. T-tests/ chi-squared tests were used to compare differences in remission prevalence by 1 year, and changes in remission before and after a QI program. Logistic regression was used to identify predictors of persistent active disease on all 4 indices.
Results: 1202 adults were eligible for this analysis. At enrolment, 877 (73%) were women, mean (sd) age was 55 (14), average disease activity was high (DAS28 5.1 (1.4); CDAI 27 (14); SDAI 29 (15)). Prevalence of remission by 12-months follow up was 14-21% higher when estimated with the DAS28 compared with CDAI, SDAI and Boolean criteria, and 378 (31%) did not achieve remission according to any of the 4 indices (Fig 1). Improvement in remission after a QI program however was similar across all 4 indices(~+15-17%). In adjusted logistic regression, Persistent active disease across all measures was most strongly associated with positive serostatus and smoking in men, and with obesity and more tender joints in women. Pain and lower education were predictors in BOTH men and women (Table 2)

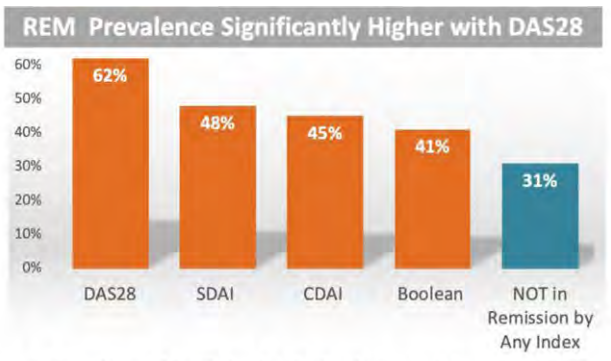


Figure 1. Prevalence of Remission by 12-Months across 4 Common RA Indices

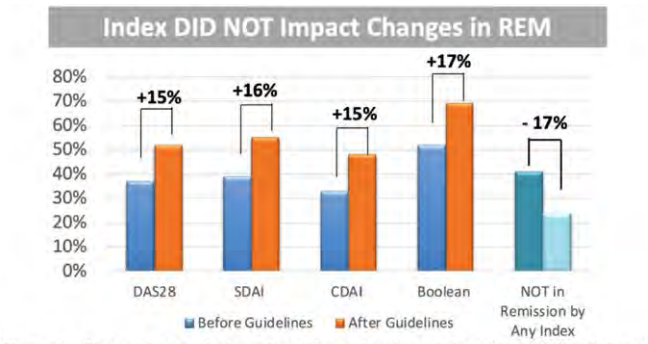


Figure 2. Change in Remission after Dissemination of Canadian RA Guidelines

Table 1. Multivariable Logistic Regression Predicting Persistent Active Disease by 12-months across ALL RA indices

	Women OR (95% CI)	Men OR (95% CI)
Age	**1.01 (1.00, 1.02)**	**1.03 (1.00, 1.05)**
Female sex	**NA**	**NA**
Postsecondary education	**0.57 (0.40, 0.80)**	**0.59 (0.31, 1.11)**
Symptom duration, mos	**1.07 (1.01, 1.13)**	**1.06 (0.95, 1.18)**
RF+ or ACPA +	**1.15 (0.75, 1.77)**	**2.32 (1.02, 5.29)**
Current Smoking	**0.86 (0.56, 1.34)**	**2.03 (0.96, 4.30)**
Obese BMI > 30	**2.19 (1.43, 3.34)**	**0.95 (0.43, 2.10)**
Comorbidity (RDCI 0-9)	**1.04 (0.91, 1.19)**	**1.21 (0.94, 1.55)**
TJC28	**1.07 (1.03, 1.11)**	**0.99 (0.93, 1.05)**
SJC28	**0.98 (0.94, 1.02)**	**1.04 (0.97, 1.10)**
Pain	**1.12 (1.05, 1.19)**	**1.15 (1.02, 1.30)**

Conclusion: In the absence of a single "best measure" that also takes in to account the patient's perspective, we estimate unmet needs for achieving remission in the first year of follow up in 1 in 3 ERA patients who did not achieve remission by ANY of the 4 indices.
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Disclosure of Interests: Orit Schieir: None declared, Susan J. Bartlett Consultant of: Pfizer, UCB, Lilly, Novartis, Merck, Janssen, Abbvie, Speakers bureau: Pfizer, UCB, Lilly, Novartis, Merck, Janssen, Abbvie, Marie-France Valois: None declared, Louis Bessette Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer, Roche, Sanofi, UCB Pharma, Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer, Roche, Sanofi, UCB Pharma, Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer, Sanofi, Gilles Boire Grant/research support from: Merck Canada (Registry of biologices, Improvement of comorbidity surveillance)
Amgen Canada (CATCH, clinical nurse)
Abbvie (CATCH, clinical nurse)
Pfizer (CATCH, Registry of biologics, Clinical nurse)
Hoffman-LaRoche (CATCH)
UCB Canada (CATCH, Clinical nurse)
BMS (CATCH, Clinical nurse, Observational Study Protocol IM101664. SERO-POSITIVITY IN A LARGE CANADIAN OBSERVATIONAL COHORT)
Janssen (CATCH)
Celgene (Clinical nurse)
Eli Lilly (Registry of biologics, Clinical nurse), Consultant of: Eli Lilly, Janssen, Novartis, Pfizer, Speakers bureau: Merck, BMS, Pfizer, Glen Hazlewood: None declared, Carol Hitchon Grant/research support from: UCB Canada; Pfizer Canada, Edward Keystone Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, F. Hoffmann-La Roche Inc, Gilead, Janssen Inc, Lilly Pharmaceuticals, Pfizer Pharmaceuticals, Sanofi-Aventis, Consultant of: AbbVie, Amgen, AstraZeneca Pharma, Biotest, Bristol-Myers Squibb Company, Celltrion, Crescendo Bioscience, F. Hoffmann-La Roche Inc, Genentech Inc, Gilead, Janssen Inc, Lilly
Pharmaceuticals, Merck, Pfizer Pharmaceuticals, Sandoz, UCB., Speakers bureau: Amgen, AbbVie, Bristol-Myers Squibb Canada, F. Hoffmann-La Roche Inc., Janssen Inc., Merck, Pfizer Pharmaceuticals, Sanofi Genzyme, UCB, Janet Pope Grant/research support from: AbbVie, Bristol-Myers Squibb, Eli

Lilly & Company, Merck, Roche, Seattle Genetics, UCB, Consultant of: AbbVie, Actelion, Amgen, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Eicos Sciences, Eli Lilly & Company, Emerald, Gilead Sciences, Inc., Janssen, Merck, Novartis, Pfizer, Roche, Sandoz, Sanofi, UCB, Speakers bureau: UCB, Carter Thorne Consultant of: Abbvie, Centocor, Janssen, Lilly, Medexus/Medac, Pfizer , Speakers bureau: Medexus/Medac, Diane Tin: None declared, Vivian Bykerk: None declared

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SAT0054 PREVALENCE AND PREDICTORS OF METHOTREXATE-ASSOCIATED ADVERSE EVENTS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Methotrexate (MTX) is the first-choice treatment for rheumatoid arthritis (RA), but the exact prevalence rates and predictors of important adverse events (AEs) associated with MTX treatment are less well investigated.

Objectives: To determine the prevalence of MTX AEs (gastrointestinal (GI), mucocutaneous, neurological, haematological, pulmonary, and liver enzymes elevation), and to identify baseline demographic, clinical and drug related predictors of liver and GI AEs.

Methods: The Rheumatoid Arthritis Medication Study (RAMS) is a UK multi-centre prospective cohort study of patients with RA commencing MTX for the first time. Relevant demographic, medication, clinical and disease related data, and blood samples were collected from patients at baseline. Data on MTX therapy and occurrence of AEs were reported at six and twelve month follow-ups, and include recorded laboratory values of alanine transaminase (ALT) enzyme.

The prevalence rates of AEs were calculated based on the number of patients who reported the AE at either 6 or 12 month follow-up visits. The association between candidate baseline predictors and occurrence of GI or liver AEs was assessed using multivariable logistic regression.

Results: In total, 2089 participants were included (mean age=58.4±13.5 years; 1390 [66.5%] women). Of those, 1816 and 1584 completed their visits at 6 and 12 months, respectively.

The frequency of abnormal ALT values (>1xULN) was 10.8% (183/1685) and 11.6% (170/1461) at 6 and 12 month follow-up visits, and 15.5% (286/1845) for either visits. The number of patients who reported GI AEs was 777 (40.6%) within 1 year of follow-up. The prevalence of mucocutaneous, neurological, haematological and pulmonary AEs were 441 (23.1%), 487 (25.5%), 116 (6.1%), and 406 (21.3%), respectively.

Male sex, having high ALT at baseline and a history of diabetes were all associated with increased risk of ALT elevation during the study period (Table 1). Contrarily men were 47% less likely to report GI AEs compared to women. Furthermore, younger age and higher baseline disease activity score (DAS28-CRP) were associated with increased risk of GI AEs occurrence.

Table 1. Baseline predictors of elevated alanine transaminase (ALT) and gastrointestinal (GI) adverse events

Variable	Elevated ALT	GI adverse events
	Adjusted Odds Ratio (95% CI)	
Age (years)	1.00 (0.99, 1.01)	**0.99 (0.98, 1.00)**
Male sex	**1.39 (1.02, 1.90)**	**0.53 (0.42, 0.67)**
Drink alcohol	1.23 (0.88, 1.73)	1.09 (0.86, 1.37)
Current or past smoking	1.10 (0.80, 1.49)	1.10 (0.88, 1.37)
BMI (kg/m^2)	1.01 (0.98, 1.03)	1.02 (1.00, 1.03)
Symptoms duration (months)	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)
RF positivity	0.81 (0.60, 1.10)	0.93 (0.75, 1.16)
DAS28-CRP	0.97 (0.87, 1.08)	**1.13 (1.04, 1.23)**
ALT at baseline (IU)	**1.03 (1.02, 1.04)**	–
History of diabetes	**1.94 (1.22, 3.08)**	0.91 (0.62, 1.34)
History of liver disease	1.73 (0.43, 6.95)	–
History of renal disease	1.29 (0.42, 3.96)	1.13 (0.50, 2.52)
MTX starting dose (mg/week)	1.03 (0.98, 1.08)	1.03 (0.99, 1.06)

Conclusion: GI events were the most commonly reported AEs among patients with RA in the first year of MTX treatment, followed by neurological, mucocutaneous and pulmonary AEs. Identifying predictors of AEs may help to optimise drug therapy in RA by tailoring the dosing strategy or frequency of monitoring. This may lead to increased adherence and consequently improved effectiveness.

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SAT0055 PREDICTION OF FLARES FOR RHEUMATOID ARTHRITIS PATIENTS ON BIOLOGIC DMARDS USING MACHINE LEARNING AND SUBSETS OF VARIABLES AVAILABLE TO PHYSICIANS, PATIENTS AND PAYERS

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Background: Today approximately 50 percent of patients with RA reach sustained remission. In a specific subset of RA patients in stable remission, biological Disease Modifying Anti-Rheumatic Drugs (bDMARDs) may be successfully tapered. However, it remains challenging to predict the patients' individual flare risk. As we have recently shown, machine learning based on extensive clinical and laboratory data could be used to estimate individual flare risk [1].

Objectives: In this study we aimed to investigate the performance of machine learning models trained with variables that are typically (1) immediately available to a physician during patient visits (clinical and demographic variables without laboratory values and composite disease activity scores), (2) theoretically available to patients at home and (3) available to payers in large health-system databases.

Methods: Longitudinal clinical data of RA patients on bDMARDs from the first interim analysis of the phase-3, multicentre, randomised, open, prospective, controlled, parallel-group RETRO study (EudraCT number 2009-015740-42) was used [2] to build a predictive model for estimating the flare probability within 3 months from the current patient visit. A flare was defined as a DAS-28 ESR score over 2.6. Four different models (log. regression, random forest, k-NN and naïve Bayes) were trained which output the flare probability at each patient visit. These probabilities were used as an input for a stacking logistic regression meta-classifier [3]. The final model performance expressed as the AUROC was assessed using nested cross-validation [4]. We applied this method to three variable subsets (physician, patient, payer, Table 1).

Table 1. List of variables used in three subsets:

Variable / Role	Physician	Patient	Payer
Gender (m/f)	x	x	x
Disease duration (years)	x	x	x
Methotrexate co-use (yes/no)	x	x	x
Other DMARDs co-use (yes/no)	x	x	x
Drug ATC code	x	x	x
IV-administration (yes/no)	x	x	x
Dose percentage	x	x	x
Age	x	x	x
Body mass index	x	x	x
Dose percentage change	x	x	x
Swollen joint count	x		
Tender joint count	x		
VAS_GH (pat. global disease activity)	x	x	
HAQ (health assessment questionnaire)	x	x	
Smoking status (yes/no/ex)	x	x	
Alcohol consumption (yes/no)	x	x	
Previous flares (yes/no)	x		

Results: Data from 135 follow-ups of 41 patients were used. The measured AUROC of the best performing model using all RETRO variables was 0.802 (95%CI 0.717 – 0.887) [1]. When a subset based on demographic and clinical variables is used that is available to a physician immediately during a patient visit the AUROC drops about 5 percent points. When only variables theoretically available to patients at home are used, the performance drops about 10 percent points comparing to the original model. Similar observation holds for the variable subset typically available to payers (Figure 1).

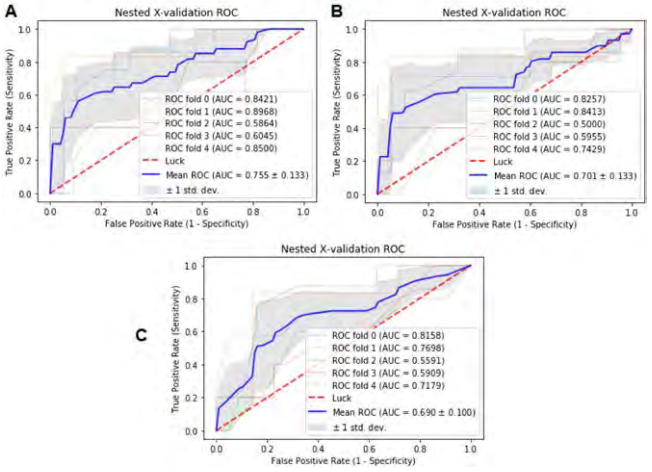
Conclusion: This study shows that predictive models for flares have the potential to support physicians in making decisions immediately during the patient visit, even though laboratory values and respective activity scores are not yet

available. In the future, machine learning applications may allow fast and reliable decisions on flare prediction in RA patients. These data can guide decisions about DMARD tapering at in real time during the physician-patient contact and allow to reduce costs not only by selective treatment tapering but also by sparing additional laboratory examinations.

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Figure 1: AUROC curves for three variable subsets. A: Variables available to a clinician immediately at patient visits, B: Variables available to a patient at home, C: Variables available to a payer.



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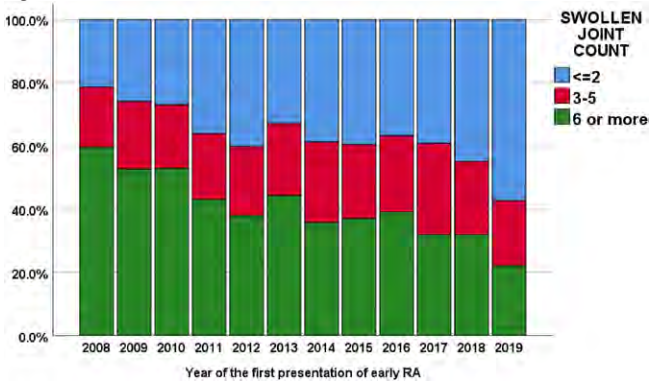
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SAT0056 INITIAL PRESENTATION OF RHEUMATOID ARTHRITIS (RA) – IS IT STILL "SYMMETRIC POLYARTHRITIS"?

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Background: RA is traditionally described as a symmetric polyarthritis. The ACR/EULAR 2010 criteria are met if patient has high positive ACPA, symptoms >=6 wks and one small joint swollen. The public and all steps of health care have been informed for many years that RA should be found early.
Objectives: To study variations in pattern on first presentation of RA.
Methods: All patients with the new diagnosis of RA were extracted from the GoTreatIT clinical database between 2008 to 2019 at a single RA clinic that covers a population of 250.000. Demographic data, clinical variables, labs, x-rays, joint status and PROs at baseline were included in the analysis. Appropriate parametric/non-parametric tests were used to study differences between groups.
Results: A total of 1044 (73.5% CCP+) patients with no prior diagnosis of RA were included; 683 (65%) female, mean age 56; 361 (35%) male, mean age 61. At initial presentation in 2008, 60% had >=6 swollen joints (Figure) and a mean DAS28 of 4.4 compared to 22% and 3.8 respectively, in 2019 (p<0.007). Duration of symptoms prior to diagnosis decreased from 6 to 4 months (p=0.033), and the proportion of patients with erosions from 20% in 2008 to 14% in 2019 (ns). Symptoms (PROs) such as pain, fatigue and global health were similar/slightly worse in 2019 compared to 2008.
Conclusion: RA cannot be marketed as "symmetric polyarthritis", as more than half of the patients have a maximum of 2 swollen joints at the time of the diagnosis at the most recent years. Patients with RA can be identified earlier, with less disease activity and damage, compared to previous years.

Figure:



Disclosure of Interests: None declared

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SAT0057 PREDICTING INADEQUATE RESPONSE TO JAK INHIBITORS BY CLUSTER ANALYSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Oral Janus kinase inhibitors (JAKi) have dramatically altered outcomes in patients with rheumatoid arthritis (RA). However, there remains some proportion of patients who respond to inadequately JAKi treatment (JAKi-IR) [1,2]. The characteristics in RA patients associated with JAKi-IR have not been fully demonstrated.
Objectives: To clarify the characteristics of JAKi-IR in patients with RA by cluster analysis.
Methods: This retrospective study comprised 120 RA patients who were treated with JAKi (Tofacitinib or Baricitinib) between July 2013 and September 2019 in five facilities. The disease status at the baseline, at 12 weeks after JAKi treatment and at the time point of withdrawing JAKi was assessed using the Disease Activity Score (DAS28) and the American College of Rheumatology (ACR) response criteria. JAKi-IR was defined as follows, primary non-response at 12 weeks after JAKi treatment: withdrawal of JAKi with ACR20 non-response or non-improvement in DAS28-CRP (ΔDAS28-CRP<1.2 from baseline), secondary non-response: withdrawal of JAKi without clinical remission after 12 weeks. Hierarchical cluster analysis was performed with the following variables: gender, age, disease duration, bone erosion, ACR functional classification (Class ≥3), comcomitant rheumatoid arthritis related interstitial lung disease (RA-ILD) or other autoimmune disease (AID), anti-citrullinated protein antibody (ACPA) positivity, rheumatoid factor (RF) at baseline, use/dose of methotrexate (MTX) and prednisolone (PSL), serum ESR/CRP, tender/swollen joint counts (TJC/SJC), visual analog scale by patients (VAS-Pt), and prior of biologic DMARDs.
Results: The 120 enrolled patients were classified into 4 groups by cluster analysis(Figure1), The characteristics of each group are as follows, Group A(n=21): female + bone erosion + RF/ACPA positive + AID + MTX non-user, Group B(n=36): male + older age + RA-ILD + RF/ACPA positive + MTX non-user, Group C(n=35): RF/ACPA positive + absence of RA-ILD + MTX user, Group D (n=28): seronegative + MTX user + absence of RA-ILD + history of biologic DMARDs failure. The rate of JAKi-IR was A:9%, B:8%, C:20%, D:32%, and the significant difference between Group B and D was identified (p=0.02). In multiple comparison of 4 groups, no significant difference was identified (p=0.06) (Figure2).
Conclusion: JAKi-IR would be more likely to be seronegative, MTX use, absence of RA-ILD and history of biologic DMARDs failure. Cluster analysis is an exploratory tool that aids in the analysis of huge amount of data.

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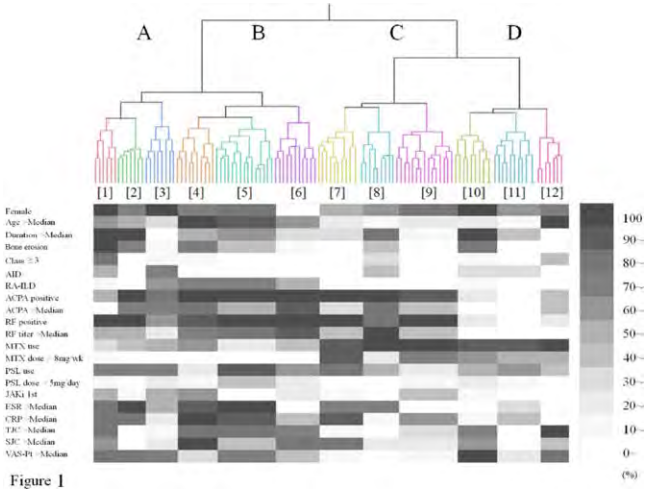


Figure 1

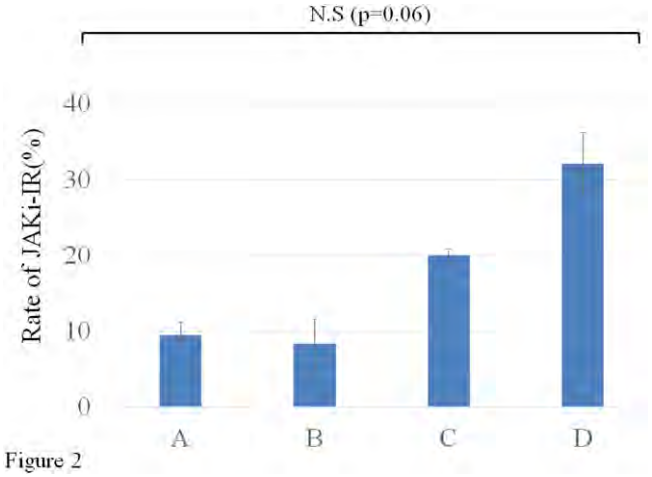


Figure 2

Disclosure of Interests: Masanari Sugawara: None declared, Yuichiro Fujieda: None declared, Atsushi Noguchi: None declared, Shun Tanimura: None declared, Yuka Shimizu: None declared, Ikuma Nakagawa: None declared, Michihito Kono: None declared, Masaru Kato: None declared, Kenji Oku: None declared, Tatsuya Atsumi Grant/research support from: Eli Lily Japan K.K., Alexion Pharmaceuticals, Inc., Bristol-Myers Squibb Co., AbbVie Inc., Daiichi Sankyo Co., Ltd., Pfizer Inc., Chugai Pharmaceutical Co., Ltd., Mitsubishi Tanabe Pharma Co., Astellas Pharma Inc., Consultant of: Gilead Sciences, Inc., Eli Lilly Japan K.K., UCB Japan Co. Ltd., AbbVie Inc., Daiichi Sankyo Co., Ltd., Pfizer Inc., Chugai Pharmaceutical Co., Ltd., Speakers bureau: Eli Lilly Japan K.K., UCB Japan Co. Ltd., Bristol-Myers Squibb Co., AbbVie Inc., Eisai Co. Ltd., Otsuka Pharmaceutical Co., Ltd., Daiichi Sankyo Co., Ltd., Pfizer Inc., Chugai Pharmaceutical Co., Ltd., Mitsubishi Tanabe Pharma Co., Takeda Pharmaceutical Co., Ltd., Astellas Pharma Inc.

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SAT0058

AGE DEPENDENT EFFECTS OF BODY MASS INDEX AND SMOKING ON THE RISK OF RHEUMATOID ARTHRITIS IN MEN – RESULTS FROM A NESTED CASE CONTROL STUDY

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Background: As rheumatoid arthritis (RA) is more common in women compared to men, most studies of disease predictors have mainly included women, and data on risk factors in men are limited. Smoking is an established predictor of RA. A negative association between body mass index (BMI) and the risk of RA in men has been reported from several studies of Scandinavian populations.

Objectives: To investigate whether the impact of smoking and BMI on the risk of subsequent development of RA in men differs by age.

Methods: A total of 22 444 men from a defined catchment area were included in a Preventive Medicine Program (PMP). Height and weight were measured as part of the health survey, and BMI was calculated as weight (in kg)/height (in m^2). Information on smoking was obtained using a structured self-administered questionnaire. Normal BMI, overweight and obesity was defined according to the WHO criteria. From this population, we identified individuals who developed RA after inclusion by linking the PMP register to the local community based RA register and to local and national patient administrative databases. In a structured review of the medical records, patients were classified according to the 1987 ACR criteria for RA. Four controls for each validated case, matched for sex, year of birth and year of screening, who were alive and free of RA when the index person was diagnosed with RA, were selected from the PMP register. The impact of BMI category and smoking on the risk of RA was examined in multivariable conditional logistic regression models, stratified by age at inclusion in the health survey (above vs below the median).

Results: A total of 151 men were diagnosed with RA and fulfilled the ACR criteria after inclusion in the PMP (median time to diagnosis 13 years, interquartile range 9-19; 76 % rheumatoid factor positive at diagnosis). These pre-RA cases were compared to 604 matched controls. Among men aged >46 years, overweight/obesity was associated with a significantly reduced risk of subsequent RA (odds ratio (OR) 0.40; 95 % confidence interval (CI) 0.21-0.76, adjusted for smoking), whereas there was no such association in younger men (adjusted OR 0.75 (95% CI 0.42-1.36). Smoking was a significant predictor of RA in men aged >46 years (Table 1). There was a similar trend in those aged ≤46 years, but it did not reach statistical significance (Table 1).

Conclusion: Overweight/obesity was associated with a reduced risk of subsequent RA in men aged >46 years. The relative importance of life style factors for the risk of RA may be greater in older men compared to younger.

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Table 1. Smoking, body mass index (BMI) and the risk of subsequent rheumatoid arthritis in men, stratified by age at inclusion in the health survey. Conditional logistic regression analysis. Odds ratios (95 % intervals)

Age >46 years at inclusion (N=342)	**Crude**	**Multivariable***
No current smoking (n=172)	1.00 (reference)	1.00 (reference)
Current smoking (n=170)	2.39 (1.24-4.16)	2.33 (1.18-4.61)
Normal BMI** (n=176)	1.00 (reference)	1.00 (reference)
Overweight/Obese** (n=165)	0.39 (0.20-0.73)	0.40 (0.21-0.76)
Overweight** (n=154)	0.44 (0.23-0.83)	0.47 (0.24-0.90)
Obese** (n=11)	0.20 (0.02-1.84)	0.16 (0.02-1.55)
Age ≤46 years at inclusion (N=413)		
No current smoking (n=210)	1.00 (reference)	1.00 (reference)
Current smoking (n=203)	1.75 (0.99-3..13)	1.66 (0.94-3.05)
Normal BMI** (n=227)	1.00 (reference)	1.00 (reference)
Overweight/Obese** (n=184)	0.74 (0.41-1.33)	0.75 (0.42-1.36)
Overweight** (n=158)	0.77 (0.42-1.38)	0.79 (0.43-1.44)
Obese** (n=26)	0.88 (0.27-2.87)	0.93 (0.28-3.06)

*Models include smoking status and overweight/obese vs normal BMI, or smoking status and category of obese or overweight vs normal BMI
**Normal BMI: 18.5-24.99 kg/m^2, overweight 25-30 kg/m^2, obese > 30 kg/m^2

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SAT0059

PLASMA ADIPONECTIN ASSOCIATES WITH CLINICAL MARKERS OF DISEASE ACTIVITY AND CIRCULATING CHEMOKINES IN SUBJECTS WITH UNTREATED EARLY RHEUMATOID ARTHRITIS

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Background: Adiponectin is an adipokine that circulates in blood in three main forms, low molecular weight trimers, middle molecular weight hexamers, and high molecular weight (HMW) multimers [1]. It is still unclear which form of adiponectin is the predominant one to mediate the protein functions. Total adiponectin levels are elevated in both serum and synovial fluid of patients with rheumatoid arthritis (RA) [2], and total circulating adiponectin levels associate with inflammatory markers in a population at high risk for future RA [3]. However, the association of circulating adiponectin with markers of disease activity in subjects with RA is still matter of debate.

Objectives: The aim of the study was to determine whether total and/or HMW adiponectin levels associate with markers of disease activity and/or plasma chemokine levels in a cohort of subjects with untreated early RA.

Methods: The cohort consisted of 70 untreated subjects with newly diagnosed RA. Clinical disease activity markers, including DAS28, CDAI, CRP and ESR, were assessed and data on patient history were recovered from clinical files. The plasma levels of 15 chemokines were measured with LEGENDplex™ Human Proinflammatory Chemokine Panel or ELISA, and total and HMW adiponectin plasma levels were determined with ELISA. Multivariate factor analysis was used to examine the association between total and HMW adiponectin plasma levels with clinical disease activity markers and plasma chemokine levels. The multivariate models were used to select potentially associated markers and chemokines, which were then tested with linear regression.

Results: Both total and HMW adiponectin levels were associated with several clinical markers of disease activity (CRP, ESR, DAS28-ESR). Total adiponectin levels were also associated with DAS28-CRP. Furthermore, a positive association was found between total adiponectin levels and the pro-inflammatory chemokines CXCL10, CXCL9, and CCL2, whereas HMW adiponectin levels only associated with CXCL9.

Conclusion: This study shows for the first time that both total and HMW adiponectin levels are associated with several markers of disease activity as well as pro-inflammatory chemokines in a well-characterized cohort of subjects with untreated early RA. Those findings indicate adiponectin as a potential disease marker in subjects with RA.

Table 1. Clinical parameters

Characteristic	no=70
Women, no (%)	47 (69)
Age, yr	55 (42-64)
BMI	25 (23-28)
CRP, mg/L	9 (4-31)
ESR, mm/hour	24 (12-38)
SJC28	9 (5-12)
TJC28	9 (4-13)
DAS28-CRP	5 (4-6)
DAS28-ESR	5 (5-6)
ACPA+, no (%)	57 (81%)
RF+, no (%)	48 (69%)
CDAI	28 (22-38)
Symptom Duration, months	5 (3-8)
Smoking, no (%)	8 (11%)

Data shown as median (interquartile range), unless otherwise noted.

Abbreviations: BMI, Body-mass index; *CRP,* C-reactive protein; *ESR,* erythrocyte sedimentation rate; *SJC28,* swollen joint counts of 28; *TJC28* tender joint counts of 28; *DAS28,* disease activity score in 28 joints; *ACPA*, Anti–citrullinated protein antibody; *RF*, Rheumatoid factor; *CDAI*, Clinical Disease Activity Index.

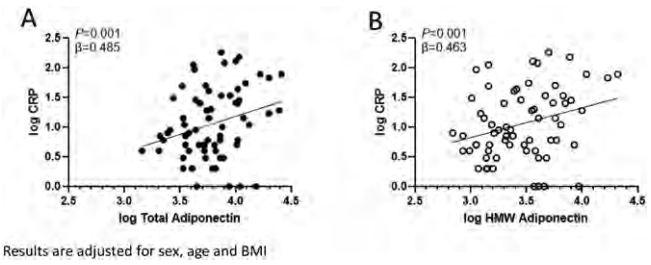


Figure 1. Linear regression analysis of total and HMW adiponectin with CRPResults are adjusted for sex, age and BMI

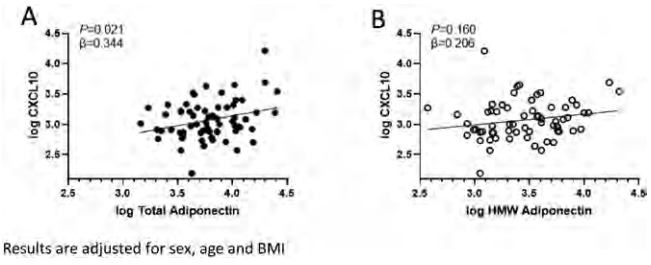


Figure 2. Linear regression analysis of total and HMW adiponectin with CXCL10Results are adjusted for sex, age and BMI

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SAT0060

OVERLAPPING SJOGREN'S SYNDROME REDUCES THE PROBABILITY OF REACHING TARGET IN RHEUMATOID ARTHRITIS PATIENTS: A PROPENSITY SCORE MATCHED REAL-WORLD COHORT FROM 2009 TO 2019

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Background: Overlapping Sjogren's syndrome (SS) is not uncommon in rheumatoid arthritis (RA), and considered as a probable detrimental factor of RA. But data on the impact of overlapping SS on RA therapeutic response is limited.

Objectives: Our current study aimed to identify the effect in a real-world cohort from 2009 to 2019.

Methods: The medical records of RA patients who attended the outpatient department of our medical center from 2009 to 2019 were reviewed, and the disease activity based on DAS28-ESR, DAS28-CRP, SDAI and CDAI at each follow-up point were collected. To correct confounders which may affect the therapeutic response between those RA patients with SS (RA-SS) and without (RA-noSS), we compared both the propensity score-matched and unmatched cohorts using the Cox proportional hazards model.

Results: Among the 1099 RA patients, 129 (11.7%) overlapped with SS validated by positive anti-SSA or pathological minor salivary gland biopsy (MSGB). After propensity score matching based on their baseline characteristics, 126 of 129 RA-SS and 126 of 970 RA-noSS patients were statistically extracted. Overlapping SS was associated with a 29%, 26%, 18%, 22% lower probability of reaching remission in RA patients based on DAS28-ESR, DAS28-CRP, SDAI, CDAI, respectively, which trend kept true for reaching low disease activity (LDA) either. Although overlapping SS had the most significant impact on ESR (HR 0.69, 95%CI 0.61-0.79), other components assessing RA disease activity were also in jeopardy. When stratified by age, RA duration, RF and ACPA status, baseline DAS28-CRP, the trend remained.

Conclusion: Overlapping SS is associated with a lower probability of reaching target in RA patients, and should be regarded as one of the poor prognostic factors in the management of RA.

Table Hazard Ratios for Reaching Remission/Low disease activity and Individual Components in RA patients Associated with Overlapping SS

	Unmatched cohort (n=1099)	Matched cohort (n=252)	Trimmed cohort (n=242)
Remission Based on Composite Disease Activity Score			
DAS28-ESR	0.68 (0.62, 0.75)	0.71 (0.62, 0.82)	0.74 (0.64, 0.85)
DAS28-CRP	0.80 (0.74, 0.87)	0.74 (0.66, 0.83)	0.74 (0.66, 0.83)
SDAI	0.82 (0.74, 0.91)	0.82 (0.70, 0.94)	0.83 (0.72, 0.97)
CDAI	0.77 (0.70, 0.86)	0.78 (0.67, 0.91)	0.78 (0.67, 0.91)
Boolean	0.83 (0.75, 0.92)	0.80 (0.69, 0.93)	0.82 (0.70, 0.95)
Remission/LDA Based on Composite Disease Activity Score			
DAS28-ESR	0.76 (0.70, 0.82)	0.73 (0.65, 0.82)	0.74 (0.66, 0.83)
DAS28-CRP	0.80 (0.74, 0.86)	0.76 (0.68, 0.84)	0.75 (0.68, 0.84)
SDAI	0.79 (0.73, 0.85)	0.74 (0.66, 0.82)	0.74 (0.66, 0.82)
CDAI	0.78 (0.73, 0.84)	0.74 (0.66, 0.82)	0.74 (0.66, 0.82)
Individual Components of Disease Activity Score			
28SJC≤1	0.83 (0.77, 0.89)	0.77 (0.69, 0.85)	0.76 (0.68, 0.84)
28TJC≤1	0.81 (0.75, 0.87)	0.79 (0.70, 0.88)	0.78 (0.70, 0.88)
PtGA≤1	0.81 (0.74, 0.89)	0.82 (0.71, 0.94)	0.82 (0.72, 0.95)
PrGA≤1	0.81 (0.74, 0.88)	0.78 (0.69, 0.88)	0.79 (0.70, 0.89)
ESR≤ULN	0.66 (0.61, 0.73)	0.69 (0.61, 0.79)	0.74 (0.65, 0.84)
CRP≤1mg/dL	0.84 (0.78, 0.90)	0.76 (0.68, 0.84)	0.77 (0.69, 0.85)

Disclosure of Interests: None declared
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SAT0061

ROLE OF SHARED EPITOPE IN THE PROGNOSIS OF RHEUMATOID ARTHRITIS IN RELATION TO ACPA POSITIVITY

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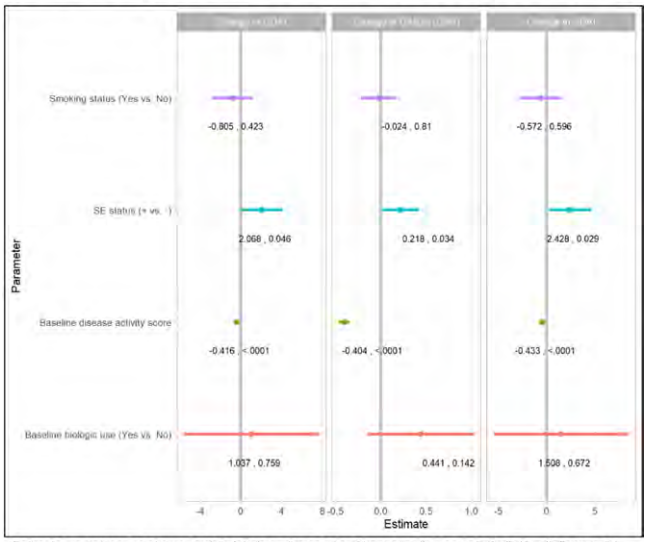
Background: The mechanistic association of *HLA-DRB1* alleles that code a "shared epitope" (SE) with rheumatoid arthritis (RA) is not yet clear. Previous data has suggested the carriage of SE is associated with the production of cyclic citrullinated peptide antibodies (anti-CCP)[1] and severe RA[2-4]. The interrelationship among SE, anti-citrullinated protein antibody (ACPA) positivity and disease outcomes is not fully understood.

Objectives: To assess the RA prognosis associated with the carriage of SE, in relation to ACPA positivity.

Methods: Pts enrolled in a large RA registry, Brigham and Women's Hospital RA Sequential Study between March 2003 to June 2018, with known SE and ACPA status were included in the analysis. HLA-DRB1 SE status was determined by allele-specific polymerase chain reaction and DNA sequencing for most of the subjects and by GWAS-based imputation for the rest. Disease activity (DA) was measured at baseline (BL) and 1-year follow-up by DAS28(CRP), CDAI and SDAI. Pts were stratified by SE+ (1 or 2 SE alleles) and SE- (0 alleles) and ACPA status. We analyzed the relationship of SE with ACPA positivity and change in DA by a linear regression model separately. A mediation analysis was used to examine the mediating effect of ACPA on association between SE and change in DA.

Results: Out of 926 pts included in the analysis, 65.1% were SE+, of whom 75.6% were ACPA+. In comparison, 51.7% were ACPA+ in SE- pts. SE+ pts were similar with SE- pts in age, gender, BMI and smoking status, but had longer disease duration, were more likely to be rheumatoid factor positive, have erosive disease and higher comorbidity burden irrespective of ACPA status. The differences were more pronounced if the pts were also ACPA+. Adjusting for BL differences, pts with SE 1 and 2 alleles (vs 0) had an odd ratio of 1.97 (95% CI:1.36-2.84; p=0.0003) and 3.82 (95% CI: 2.44-5.98; p<.0001) to be ACPA +, respectively. The regression analysis suggests that SE+ (vs SE-) pts had an average increase in DAS28 (CRP) of 0.22 (p=0.033), CDAI of 2.07 (p=0.045) and SDAI of 2.43 (p=0.029) over a year (Fig 1). Using a mediation analysis, the direct effect of SE+ account for 78.8% to 81.0% of total effect in the increase in DAS28 (CRP), CDAI and SDAI, and the indirect effect mediated by ACPA account for 19.0% to 21.2% (Table 1).

Figure 1. Linear Regression Model for SE Association with Change in Disease Activity



**Estimates, p-values are shown as data labels on the graphs; Change in disease activity (DA) = (follow-up DA-baseline DA); The above model is adjusted for age, gender, CCI, baseline DA, baseline biologic use, SE status and smoking status*

Table 1. Mediation Analysis for SE and ACPA Association with Change in DA

Parameter	Change in DAS28 CRP (N=666)		Change in CDAI (N=653)		Change in SDAI (N=629)	
	Estimate	P-value	Estimate	P-value	Estimate	P-value
Total Effect of SE on DA change	0.22	0.034	2.05	0.047	2.40	0.030
Direct effect of SE on DA change excluding mediation of ACPA	0.17	0.101	1.57	0.140	1.89	0.098
Indirect effect of SE on DA change due to ACPA mediation and interaction	0.04	0.183	0.48	0.133	0.51	0.143

*The model is adjusted with other covariates: Age, Gender, Charlson comorbidity score; baseline biologic use, Smoking status, baseline DA, Interaction term (ACPA*SE)*

Conclusion: SE is strongly related to ACPA and a greater burden of disease in RA pts. In pts receiving standard treatments including biologics, SE is predictive of a greater increase in DA, which is partially mediated by the presence of ACPA.

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SATURDAY, 06 JUNE 2020

Rheumatoid arthritis - comorbidity and clinical aspects

SAT0062

INCIDENCE OF STAPHYLOCOCCUS AUREUS BACTEREMIA IN PATIENTS WITH RHEUMATOID ARTHRITIS: A NATIONWIDE COHORT STUDY

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Background: *Staphylococcus aureus* is a frequent cause of bacteremia (SAB) associated with high mortality and morbidity. Patients with rheumatoid arthritis (RA) are at increased risk of septic arthritis and prosthetic joint infection with *S. aureus*.

Objectives: To assess the incidence rate (IR) of first-time SAB in patients with RA and to estimate the incidence rate ratio (IRR) of SAB with a general population cohort without RA serving as the reference.

Methods: Individuals with no prior history of SAB or RA were included consecutively from 31 December 1996, their 18th birthday or date of immigration, whichever came latest, and followed until first-time SAB, death, emigration or 31 December 2017, whichever came first. Information on RA diagnosis, vital status, age, sex, place of residence, comorbidities, medication and first-time SAB were achieved on an individual level through cross-linkage between five virtually complete Danish nationwide registries (Civil Registration System, National Patient Registry, Register of Medicinal Product Statistics, DANBIO rheumatology registry and the SAB database). We used Poisson regression to estimate adjusted IRRs overall and stratified by age and sex.

Results: In total, 6,127,150 individuals were included of whom 34,627 individuals developed RA. In the RA cohort, 228 first-time SAB events occurred during 283,186 person years (PY) of follow-up (IR 80.5/100,000 PY) compared with 25,268 events during 87,521,120 PY of follow-up in the general population cohort (IR 28.9/100,000 PY). Median follow-up was 7.2 years (IQR 3.5-12.3) after RA diagnosis and 18.7 years (IQR 6.8-21) in the general population cohort. Individuals with RA who developed SAB were more often women, had an orthopaedic implant and had recent use of glucocorticoids compared with individuals with SAB without RA. (Table 1) IRs of SAB were higher among patients with RA compared with the general population in all age categories. The IRs increased with age and were higher in men, both in patients with RA and in the general population cohort. After adjustment, the IRR remained higher for individuals younger than 70 years with RA compared with the general population but was similar for older individuals. (Figure 1)

Conclusion: In this nationwide cohort with more than 25,000 observed first-time SAB events, patients with RA younger than 70 years old had a 1.5-2 times higher incidence rate compared with the general population. The significance of anti-rheumatic treatments on risk and the prognosis of SAB in patients with RA remain to be explored.

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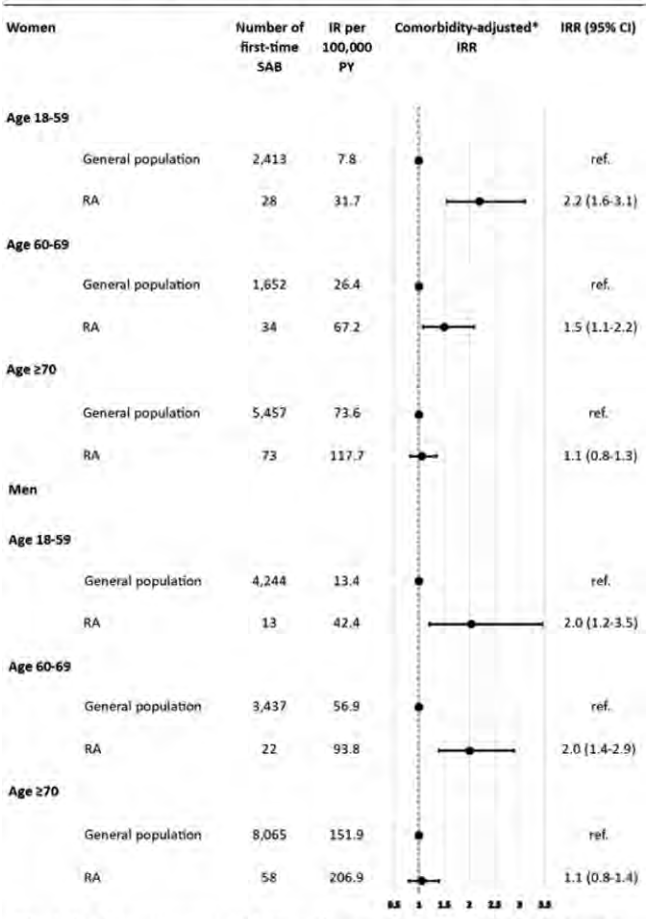
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Table 1 Characteristics of patients with RA at time of RA diagnosis and patients with SAB with/without RA at time of SAB diagnosis

Characteristic, n (%)	*At RA diagnosis*	*At first-time SAB*	
	RA (n=34,627)	RA (n=228)	Non-RA (n=25,268)
Age, years (IQR)	59.8 (48.8-70.3)	71.8 (62.3-79.2)	69.7 (57.7-79.7)
Female, %	69%	59%	38%
Diabetes mellitus	2,467 (7.1%)	51 (22.4%)	5,678 (22.5%)
Heart failure	1,018 (2.9%)	42 (18.4%)	4,718 (18.7%)
Liver disease	454 (1.3%)	12 (5.3%)	2,189 (8.7%)
Chronic obstructive pulmonary disease	1,677 (4.8%)	36 (15.8%)	3,412 (13.5%)
Cancer	2,124 (6.1%)	60 (26.3%)	6,742 (26.7%)
HIV	11 (0.0%)	0 (0%)	127 (0.5%)
Solid organ transplant	8 (0.0%)	0 (0%)	357 (1.4%)
Alcohol abuse	642 (1.9%)	12 (5.3%)	3,356 (13.3%)
Chronic dialysis	29 (0.1%)	11 (4.8%)	2,256 (8.9%)
Orthopedic implant	3,807 (11.0%)	89 (39.0%)	5,422 (21.5%)
Cardiac or vascular implant	731 (2.1%)	18 (7.9%)	1,940 (7.7%)
Glucocorticoid (0-90 days prior)	7,062 (20.4%)	99 (43.4 %)	2,911 (11.5%)
Invasive surgery (0-30 days prior)	1,962 (5.7%)	62 (27.2%)	8,451 (33.5%)

Figure 1

Age and sex stratified first-time *S. aureus* bacteremia (SAB) cases, incidence rates (IR) and comorbidity-adjusted incidence rate ratios (IRR) of SAB in patients with rheumatoid arthritis (RA) compared with the general population



* Results from Poisson regression model. Adjusted for age (as a continuous variable), calendar year (3-year intervals), diabetes mellitus, alcohol abuse, chronic dialysis, cancer, orthopedic implants, cardiac or vascular implants, chronic obstructive pulmonary disease and chronic heart failure. Follow-up time was split according to exposure status of these time-dependent covariates

SAT0062

THE COMBINED VACCINATION SCHEME AGAINST STREPTOCOCCUS PNEUMONIAE IS EFFECTIVE IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH DMARD: DATA FROM BIOBADASER 3.0

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Background: Respiratory tract infections are among the leading causes of hospitalization in rheumatoid arthritis (RA) and Streptococcus Pneumoniae (Sp) is one of the most frequent pathogens involved. For these patients, the CDC recommends a combined vaccination scheme (CVS) using two types of Sp vaccines but evidence on its effectiveness remains insufficient.1
Objectives: To assess the impact of the combined vaccination scheme on the incidence of Sp infections in patients with RA treated with DMARD.
Methods: A cohort was nested in a register including patients with RA who were prescribed a bDMARD or tsDMARD -either naïve or switch- from 2000 to March 2019. The target outcomes were invasive pneumococcal disease (IPD) and all-cause community-acquired pneumonia (CAP), as defined by relevant MedDRA codes. Demographic and clinical features were also retrieved. Each participant centre informed about the date when they implemented a systematic Sp vaccination protocol and whether they were using the CVS. Those not adopting this practice were excluded from the analysis.
Crude incidence rates (IRs) were calculated for each outcome as well as for its combination (combined variable defined as "Sp infections"). Exposure was split into two periods, considering the date when the CVS was officially recommended in Spain (May 2015). The incidence rate ratio (IRR) comparing pre and post implementation periods was estimated with a Poisson regression model adjusted for sex, age and comorbidities (Charlson Index).
Results: 1704 patients were included, their characteristics are shown in table 1. One centre was excluded for not using any Sp vaccination protocol while the remaining ones reported using the CVS. Crude IRs by periods (pre and post CVS implementation) and age groups are shown in table 2. The IRR of the post-vaccination period after adjusting for age, sex and comorbidities (Charlson index) was 0.40 (95% CI: 0.29 - 0.56), p<0.001.

Table 1. Baseline features of the cohort.

Demographics	
Age, years *	60.6 (12.5)
Female	1356 (79.6%)
Current smoking	287 (16.8%)
RA clinical characteristics	
Disease duration, years*	9.1 (7.9)
RF positive	875 (74%)
ACPA positive	831 (71%)
DAS28*	4.6 (1.4)
Other clinical characteristics	
Body Mass Index*	27.5 (5.2)
Charlson index*	2.3 (1.5)
Chronic pulmonary Disease	125 (9.3%)
Diabetes mellitus	147 (9%)

*Data presented as mean (standard deviation).

Table 2. Crude IRs (95% CI) of the outcomes of interest split by age.

Overall		**<65**		**≥65**	
Pre	**Post**	**Pre**	**Post**	**Pre**	**Post**
SP-Infections					
33 (27.4-39.9)	12.7 (9.8-16.4)	28 (22.4-35)	11.8 (8.9-15.6)	60.3 (42.4-85.8)	19.5 (10.8-35.2)
IPD					
–	0.4 (0.1-1.6)	–	0.4 (0.1-1.8)	–	–
All cause CAP					
23.6 (19.0-29.3)	11.5 (8.8-15)	18.7 (14.4-24.4)	10.4 (7.7-14)	50.8 (34.8-74)	19.5 (10.8-35.2)

Conclusion: The incidence of Sp infections experienced a decrease in RA patients taking bDMARD or tsDMARD after the introduction of the stepwise combined vaccination scheme that is not related to age, sex or comorbidities.
References:
[1] Furer V, *et al*. *Ann Rheum Dis* 2019;0:1–14
Disclosure of Interests: Sebastian C Rodriguez-García Speakers bureau: Novartis Farmaceutica, S.A., Merck Sharp & Dohme España, S.A., Sanofi Aventis, UCB Pharma, Carlos Sánchez-Piedra: None declared, Raul Castellanos-Moreira Speakers bureau: Lilly, MSD, Sanofi, UCB, Dolores Ruiz-Montesinos: None declared, Victoria Hernandez: None declared, Manuel Pombo: None declared, Fernando Sánchez-Alonso: None declared, Loreto Carmona Grant/research support from: Novartis Farmaceutica, SA, Pfizer, S.L.U., Merck Sharp & Dohme España, S.A., Roche Farma, S.A, Sanofi Aventis, AbbVie Spain, S.L.U., and Laboratorios Gebro Pharma, SA (All trhough institution), Juan Jesús Gómez-Reino: None declared
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SAT0064 VACCINATION RATE AND RISK FACTORS FOR NON-VACCINATION IN RHEUMATOID ARTHRITIS: A CROSS-SECTIONAL PROSPECTIVE MULTICENTRIC OBSERVATIONAL STUDY

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Background: Rheumatoid arthritis (RA) patients are at increased risk of infections, some of which could be prevented in part by vaccination (1). Influenza and pneumococcal vaccines are recommended in RA (2). However, vaccination coverage of these patients remains very low. Five years ago, we found in a previous study that vaccination rates in France were 55% for pneumococcal and 60% for influenza vaccines (3).
Objectives: The aim of our study was to evaluate the vaccination rate among RA patients, compare it with our previous results, and identify factors associated with non-vaccination.
Methods: We conducted a cross sectional multicentric observational study in the rheumatology departments of 5 university hospitals in France. Data were collected from December 2018 to July 2019. Outpatients and hospitalized adult patients with RA according to the ACR/EULAR 2010 criteria were included. Data were collected during a single visit through an anonymous questionnaire completed by the patients. Pearson Chi-squared analysis and multivariable logistic regression were used to compare characteristics of vaccinated versus non vaccinated patients.
Results: 584 patients (77.9% of women, mean age 61.8±12.6 years old) were included. 81.7% were RF and/or ACPA positive, with a mean RA duration of 15.7±10.5 years, 58.2% were treated with methotrexate (MTX), and 68.6% with a biologic. Vaccination rate against pneumococcal was 78.9% (versus 55% in 2013, p<0.0001) and 60.4% for influenza (versus 60% in 2013). The main reason for non-vaccination was absence of vaccine proposal (59.2%) for pneumococcal, and fear of vaccines (56.7%) for influenza. In the multivariate analysis, a higher level of education (OR [CI95] 4.4 [2.3-8.4], p<0.0001), a very good opinion on vaccination (2.1 [1.1-4.1], p=0.003), vaccination against influenza done (2.3 {1.3-4.2], p=0.006), and exposure to biologics (4.0 [2.2-7.4], p<0.0001) were associated with vaccination against pneumococcal. Age over 65 years old (2.0 [1.2-3.2], p=0.006), participation in a patients' association (3.6 [1.4-8.9], p=0.006), vaccination against pneumococcal done (2.4 [1.3-4.5], p=0.004), exposure to biologics (2.1 [1.2-3.7], p=0.006), a good (3.3 [1.4-8.9], p=0.03) and a very good opinion on vaccination (6.6 [2.8-15.6], p<0.0001) were associated with vaccination against influenza.
Conclusion: Vaccination rate against pneumococcal increased over the last 5 years but remained stable for influenza vaccine in French RA patients. This could be improved with patient's information and education, especially in patients age under 65, biologic naïve and with a bad opinion about vaccination.
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Disclosure of Interests: Claire Rempenault: None declared, Thomas Barnetche: None declared, Marion Magnol: None declared, Benjamin Castagne: None declared, marine pugibet: None declared, Eleonore Berard: None declared, Marie-Elise Truchetet: None declared, Pascale Vergne-Salle: None declared, Anne Tournadre: None declared, Adeline Ruyssen-Witrand Grant/research support from: Abbvie, Pfizer, Consultant of: Abbvie, BMS, Lilly, Mylan, Novartis, Pfizer, Sandoz, Sanofi-Genzyme, Cédric Lukas: None declared
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SAT0065 TIMING OF PNEUMOCOCCAL VACCINATIONS IN RELATION TO STARTING DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS IN RHEUMATOID ARTHRITIS

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Background: Pneumococcal vaccinations are recommended for patients with rheumatoid arthritis (RA). There is evidence that pneumococcal vaccinations are less effective when administered after starting conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs). Vaccination guidelines have changed over time, since 1992 UK guidelines recommend pneumococcal vaccination for the immunocompromised, and in 2003 was expanded to all individual's age ≥65 years. Guidelines from British Society of Rheumatology (2011) and EULAR (2019) advise to vaccinate prior to starting csDMARDs where possible. There is little evidence about whether these guidelines are being followed.

Objectives: The aims of this study were to explore the timing of pneumococcal vaccination in patients with RA in relation to starting csDMARDs and examine whether this has changed over time.

Methods: This was a cross-sectional study using UK electronic health records from primary care between 1st January 2000 and 31st December 2018. To be included in the study patients needed to 1) have a diagnosis of RA, 2) be prescribed csDMARDs up to 3 months prior to, or after RA diagnosis date and 3) have received a pneumococcal vaccination. Index date was considered the start of csDMARDs and vaccinations were required to be up to 5 years prior to the index date or after index date until leaving the practice, death or the end of the study period. For each patient it was determined if the first vaccination was prior to starting csDMARDs. For those vaccinated up to 3 years prior to, or up to 3 years after starting csDMARDs, the time between vaccination and starting csDMARDs in months was determined and this distribution was plotted in a bar chart. To explore how timing of vaccination has changed over time the proportion (with 95% confidence intervals (CI)) of people vaccinated prior to starting csDMARDs was plotted by year.

Results: Of 21461 people with RA identified who were prescribed their first csDMARD on or after 1st January 2000, there were 8205 (38.2%) patients vaccinated and eligible to be included in the study. The cohort had a mean age 62 years, 66.4% were female. There were 2997 (36.5%) patients vaccinated prior to starting csDMARDs. Those vaccinated prior to starting csDMARDs were older, with 72% (n=2168) being aged 65 years or over vs 28% (n=1465) in those vaccinated after starting csDMARDs. 5358 (65.3%) were vaccinated up to 3 years prior to, or up to 3 years after starting csDMARDs. The distribution showed that the most frequent time of vaccination was in the 3 months after starting csDMARDs and the frequency was higher in the months after starting csDMARDs than in the months preceding (Figure 1). Of those vaccinated outside these times, 1000 (12.2%) were vaccinated >3 years prior and 1844 (22.5%) were vaccinated >3 years after starting csDMARDs. The proportion vaccinated prior to starting csDMARDs has increased over time from a minimum of 17.2% in 2001 to a maximum of 55.6% in 2016. The greatest increases were seen between 2003 and 2007 (Figure 2).

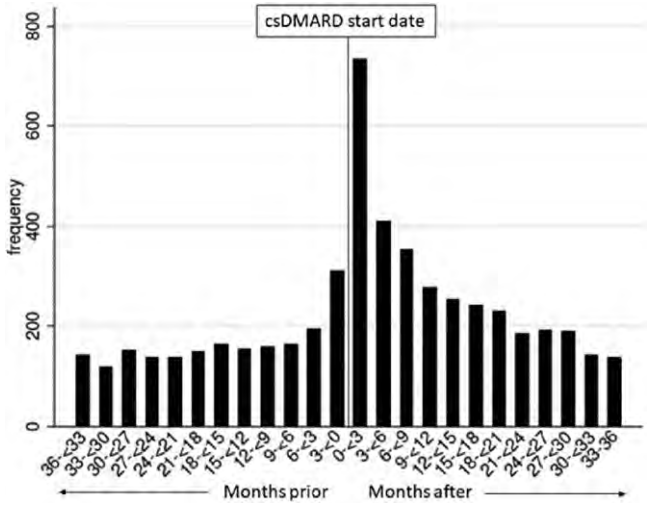


Figure 1. Time between starting csDMARDs and pneumococcal vaccination

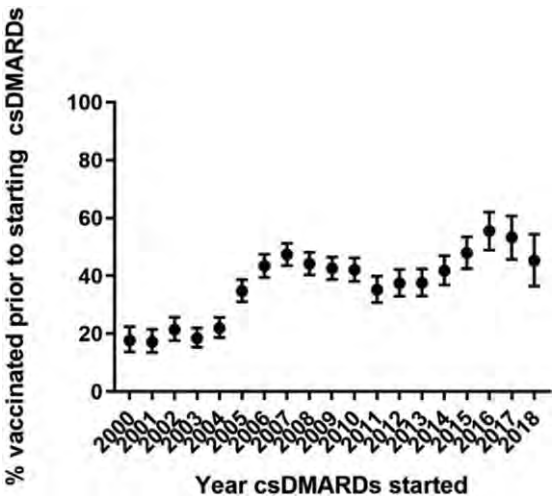


Figure 2. Proportion and 95% confidence interval of those vaccinated prior to starting csDMARDs by year.

Conclusion: This study shows that timing of pneumococcal vaccination is improving with a trend towards increasing vaccination prior to starting csDMARDs and a high proportion of patients were vaccinated around the time of csDMARD initiation. However, just over a fifth (22.5%) were vaccinated more than 3 years after starting csDMARDs. Rheumatologists need to continue to work to raise awareness of the importance of vaccinations through better communications to patients and primary care physicians, to ensure best practice is being followed.

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SAT0066

BURDEN OF MALIGNANCY, VENOUS THROMBOEMBOLISM, ANEMIA, AND INFECTIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO SWITCHED FROM A FIRST CONVENTIONAL SYNTHETIC DISEASE-MODIFYING ANTIRHEUMATIC DRUG TO ANOTHER DISEASE-MODIFYING ANTIRHEUMATIC DRUG REGIMEN

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Background: EULAR and ACR guidelines recommend a variety of treatment options for rheumatoid arthritis (RA) patients who failed a first conventional synthetic disease-modifying antirheumatic drug (csDMARD). The recent launches of Janus kinase inhibitors (JAKi) have stimulated interest in comorbidities such as malignancy, venous thromboembolism (VTE: deep vein thrombosis [DVT] or pulmonary embolism [PE]), anemia, and infections in patients with RA. Understanding the epidemiology of these conditions can help optimize treatment decisions within the treat-to-target approach following the first csDMARD.

Objectives: Estimate the real-world prevalence, incidence, and costs of these comorbidities among patients switching from a first csDMARD to another DMARD.

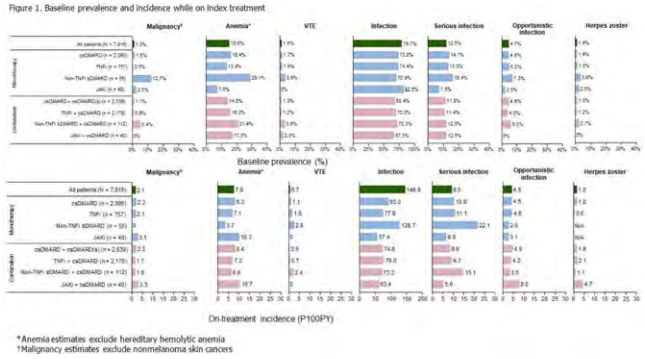
Methods: From a large US health claims database, the study selected adults with RA (≥2 RA claims ≥30 days apart) who started a csDMARD regimen as first DMARD, then switched (index date [ID], 1/1/2012–3/31/2017) to another DMARD regimen (monotherapy or combination with csDMARD). All patients had continuous enrollment 1 year before and ≥1 year after the ID. The study estimated baseline prevalence (%) and on-treatment incidence (per 100 patient-years [P100PY]) of malignancy, VTE, anemia, and infections (any, serious, opportunistic, and herpes zoster). Generalized linear models with gamma distribution and log link function estimated the impact of baseline characteristics on mean annualized healthcare costs per-patient-per-year (PPPY) associated with incident conditions. The recycled prediction method calculated adjusted total costs differences of these conditions.

Results: Among study patients (N = 7,816, median age 54 yrs, 74% female), the 38% on monotherapy index treatments had mean (standard deviation) treatment

duration 9.2 (10.1) mo and the 52% on combination therapies had treatment duration 16.9 (13.0) mo.

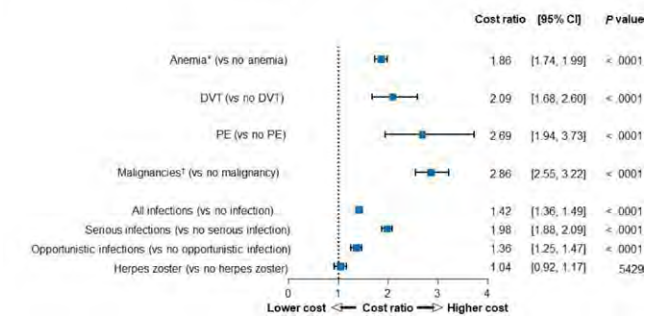
Baseline prevalence was 1.5% for VTE, 1.3% for malignancy, 15.6% for anemia, and 71.0% for infection (Figure 1). During next treatment, the incidence rates (P100PY) were: 0.7 for VTE, 2.1 for malignancy, 7.8 for anemia and 79.4 for infection (Figure 1). Modeling showed that total healthcare cost more than doubled for RA patients with vs without incident occurrence of malignancy (2.9), followed by PE (2.7) and DVT (2.1) ($P < .0001$) (Figure 2). Total PPPY adjusted healthcare costs were higher in patients with vs without incident conditions: DVT $60,430 vs $28,927, PE $77,942 vs $29,000, malignancy $81,779 vs $28,565, anemia $50,097 vs $26,959, and infection $32,431 vs $22,774, including serious infections $52,935 vs $26,723, opportunistic infections $39,239 vs $28,947, and herpes zoster $30,638 vs $29,515.

Figure 1. Baseline prevalence and incidence while on index treatment



*Anemia estimates exclude hereditary hemolytic anemia
†Malignancy estimates exclude nonmelanoma skin cancers

Figure 2. Cost ratios for incident comorbidity from adjusted healthcare cost models



Conclusion: In the real world, RA patients were affected by VTE, malignancy, anemia and infections prior to switching from first csDMARD to the next treatment. While on the next treatment, patients developed new cases of these comorbidities, most of which were associated with increased adjusted total healthcare costs. Clinicians should account for the burden of these comorbidities in selecting treatments for RA patients who failed their first csDMARD.

Disclosure of Interests: Robin K Dore Grant/research support from: AbbVie, Amgen, Biogen, Bristol-Myers Squibb, Eli Lilly and Co., Gilead Sciences, Inc., GlaxoSmith-Kline, Myriad, Novartis, Pfizer, Radius, Regeneron, Sanofi, and UCB., Consultant of: AbbVie, Amgen, Biogen, Bristol-Myers Squibb, Eli Lilly and Co., Gilead Sciences, Inc., GlaxoSmithKline, Myriad, Novartis, Pfizer, Radius, Regeneron, Sanofi, and UCB., Jenya Antonova Employee of: Gilead Sciences. Inc., Lawrence Chang Consultant of: Gilead Sciences, Inc., Huan Huang Consultant of: Gilead Sciences, Inc., Hyunchung Kim Consultant of: Gilead Sciences, Inc., Mark C. Genovese Grant/research support from: Abbvie, Eli Lilly and Company, EMD Merck Serono, Galapagos, Genentech/Roche, Gilead Sciences, Inc., GSK, Novartis, Pfizer Inc., RPharm, Sanofi Genzyme, Consultant of: Abbvie, Eli Lilly and Company, EMD Merck Serono, Genentech/Roche, Gilead Sciences, Inc., GSK, Novartis, RPharm, Sanofi Genzyme
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SAT0067

SEVERE INFECTIONS REMAIN COMMON IN A REAL-WORLD RHEUMATOID ARTHRITIS COHORT: A SIMPLE CLINICAL MODEL TO PREDICT INFECTION RISK

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Background: Patients with rheumatoid arthritis (RA) have a higher risk of infection due to immunological dysfunction, immunosuppressive use, and coexisting comorbidities[1]. An understanding of these risk factors has helped develop infection risk calculators[2]. However, there are currently no screening tools available to *rapidly* identify patients with high infection risk.

Objectives: To investigate the incidence of severe infection in a real-world RA cohort, identify associated risk factors, and propose a simple infection risk screening tool.

Methods: Between January and July 2019, patients were recruited consecutively from an Australian tertiary hospital's RA clinic. We included all adult patients with RA. The primary outcome was a severe infection (any infection requiring hospital admission) between January 2018 and July 2019. We collected data using hospital notes, medical records and pathology results. We used validated scores such as the disease activity score of 28 joints (DAS28) and the Charlson comorbidity index to assess disease activity and comorbidity burden. Multivariable regression was used for statistical analysis.

Results: We recruited 263 eligible patients. 45 severe infections occurred in 34 patients (13%), corresponding to 10.8 infections per 100 patient years. Respiratory (53%) and urinary tract infections (13%) were the most common. On multivariable analysis, the most significant risk factors for severe infection included low lymphocyte counts (odds ratio (OR) 4.08), a previous infection within the last three years (OR 3.58), a Charlson comorbidity index of two or more (OR 2.69) and higher disease activity (OR 1.35 per 0.5-increase in DAS-28). The multivariable model incorporating these factors had a large area under receiver operating characteristic (ROC) curve of 0.82. Glucocorticoid and biologic use were not significantly associated with infection.

Conclusion: To our knowledge, this was one of the first Australian studies to evaluate severe infection rates in a real-world RA cohort. Rates remained high and comparable with older studies[3]. Lymphopenia, high disease activity, comorbidity burden and a previous infection were independent risk factors for infection. Our multivariable model is a composite of easily assessible clinical and biological parameters, with excellent predictive potential for infection. Once validated, it may be developed into a screening tool to help clinicians rapidly identify high risk patients and inform tailored clinical decision making.

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Table 1. Cohort Demographics

Characteristic	Median (Interquartile Range) or Number (%)
Age (years)	62 (50-70)
Sex (female)	191 (73)
Length of diagnosis (years)	9 (5-18)
Biologic use over study period	106 (40)
Steroid use over study period	77 (29)
Charlson comorbidity index (excluding age)	0 (0-1)

Table 2. multivariable logistic regression model for severe infection

Variables	Odds Ratio	*p* value
Age ≥50*	0.60	0.368
Charlson comorbidity index (≥2)	2.69	**0.043**
Previous severe infection in last 3 years	3.58	**0.015**
Disease activity score of 28 joints (per 0.5 increase)	1.35	**0.005**
Low lymphocyte counts (<1)	4.08	**0.028**

*Age was included despite insignificance due to an *a priori* decision about its clinical relevance

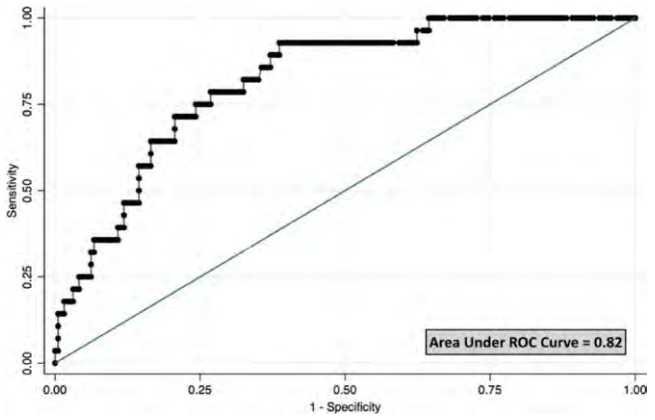


Figure 1. Receiver operating characteristic curve (ROC) of the multivariable model for infection

Disclosure of Interests: None declared
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SAT0068

THE RECENT INCIDENCE OF SURGICAL SITE INFECTION AND DELAYED WOUND HEALING AFTER ELECTIVE ORTHOPAEDIC SURGERIES FOR PATIENTS WITH RHEUMATOID ARTHRITIS WHO TREATED WITH B/TSDMARDS

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Background: In Japan, Methotrexate (MTX) has been approved in 1999, the first biologic DMARD (bDAMRD) in 2003, and the Janus kinase (JAK) inhibitors have been used since 2013. Although it is expected that the recent advancement of drug therapy would contribute the decrease in the incidence of orthopaedic surgeries by preventing structural damages[1, 2], we are still facing a considerable number of patients who require surgical interventions[3].

Objectives: To investigate the recent trends of patient's background who underwent the orthopaedic surgery for rheumatoid arthritis, number of orthopaedic intervention, and the type of the surgery.

Methods: We reviewed the records of 1569 patients with RA who underwent orthopedic surgeries between 2004 and 2019 in our institution. The mean age of patients was 62.8 (22-88) years-old with disease duration of 20.9 (0.5-64) years. Data of these patients such as age, disease duration, medication (Glucocorticoid; GC, MTX, b/tsDMARD), type of surgeries (total joint replacement; TJR, hand surgery, foot surgery, spine surgery, and others), and preoperative serum CRP level were collected. We analyzed the annual change of these demographic and clinical data. Then, we compared them between CRP negative (<1.5g/l) and CRP positive group. Cochran-Armitage trend test,χ square test, or unpaired T-test was performed for statistical analysis. P <0.05 was considered significant.

Results: Among all cases, 426 cases (27.2%) were treated with b/tsDMARDs at the time of operation. MTX and GC were used in 937 cases (59.7%) and 1015 cases (64.7%), respectively. The mean age and disease duration of RA showed an increasing trend, although the CRP level was dramatically decreased during the study period. While the rate of MTX use has not changed significantly (p=0.102), the number of cases treated by b/ts DMARD increased significantly to 46.7% (p<0.001). In contrast, the rate of GC use dicreased significantly (p<0.001). Although the annual number of surgeries have not changed, the proportion of cases who performed TJR decreased dramatically (59.6% in 2011, 29.5% in 2019), and the surgeries for hand and foot increased significantly (p<0.001) (Fig 1). The annual mean preoperative CRP level also decreased from 18.8±1.95 to 4.89±0.81 (Fig2). Compared to CRP positive group (n=1,113), the patients in CRP negative group (n=446) showed significantly younger age(p<0.001), shorter disease duration (p=0.031), lower late of GC use, and a higher rate of b/tsDAMRD use. The proportion of patients who underwent TJR was significantly higher in CRP positive group (p<0.001).

Fig1

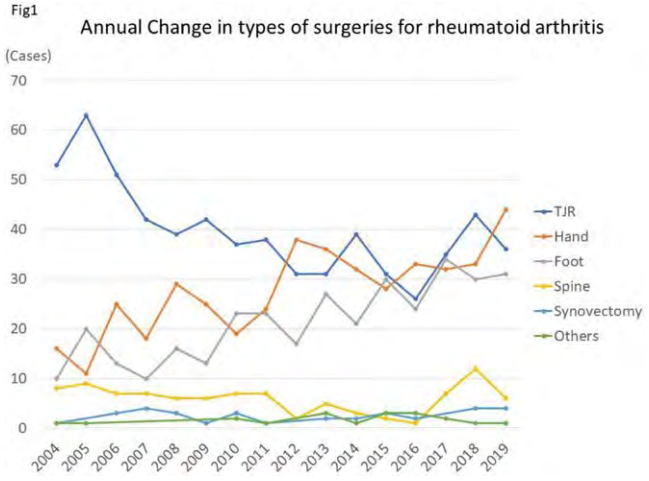
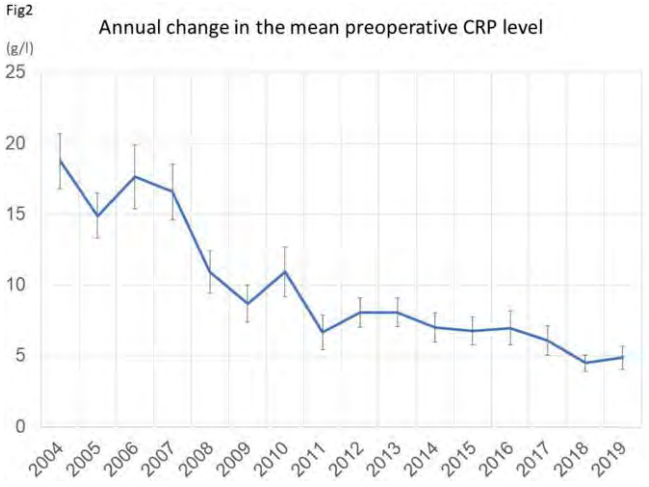


Fig2



Conclusion: Along with the increasing use of b/tsDMARD, the preoperative disease control of RA, as well as the type of demanded surgeries have dramatically changed.

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SAT0069

TUBERCULOSIS IN BIOLOGIC-NAÏVE PATIENTS WITH RHEUMATOID ARTHRITIS - RISK FACTORS AND TUBERCULOSIS CHARACTERISTICS

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Background: The risk of tuberculosis (TB) has decreased in biologic disease modifying anti-rheumatic drugs (bDMARDs) treated rheumatoid arthritis (RA) patients, but remains unaltered 4-fold increased in bio-naïve RA patients compared to the general population in Sweden (1). In absolute numbers, most TB cases in contemporary RA patients occur in the group of bio-naïve patients. Knowledge about risk factors for TB and TB characteristics in bio-naïve RA patients is still limited.

Objectives: To investigate risk factors for TB and TB characteristics in bio-naïve RA patients.

Methods: Population-based case-control study. A national bio-naïve RA cohort was identified from the National Patient Register and the Swedish Rheumatology Quality Register. RA cases with TB were identified by linkage to the Swedish Tuberculosis Register (with mandatory TB registration) 2001-2014 (n=42). For each case, four matched RA controls without TB were identified. Clinical data were obtained from medical records. Univariate and multivariable logistic regression analyses were used to estimate risk for TB expressed as adjusted (adj) odds ratio (OR) with 95% confidence intervals (CI).

Results: After review of the medical records and validation of diagnoses, 31 cases with RA and TB and 122 controls remained in the study. The TB cases had a median of 3 (1-6) reported TB risk factors, and almost 90% were born before 1950. Only one case was screened for TB (with negative result of tuberculin skin test). Active TB occurred at a mean of 15 years after RA diagnosis, and all except three cases were considered as reactivation of latent TB. Exposure to leflunomide (5 cases, 4 controls) (adj OR 6.02; 95% CI 1.47-24.65) and azathioprine (5 cases, 6 controls) (adj OR 3.85; 95% CI 1.06-13.79) were associated with increased risk for TB. Methotrexate, used in 67.7% of cases and 73.9% of controls, was not associated with increased risk of TB (adj OR 0.83; 95% CI 0.34-1.98). Exposure to corticosteroids was more common among cases than controls (74.2% vs 53.8%, p= 0.04), and was associated with an adj OR for TB of 2.44 (95% CI 1.00-5.92). No significant differences were identified between prednisolone-treated cases and controls in terms of maximum dose ever of prednisolone, treatment duration before TB, or cumulative dose of prednisolone during the last year before diagnosis of TB. Obstructive pulmonary disease was the only comorbidity linked to an increased TB risk (adj OR 3.94; 95% CI 1.45-10.69). Pulmonary TB dominated (84%) followed by TB lymphadenitis (19%). Treatment success was 94%, comparable to TB patients in general.

Conclusion: Several RA-associated risk factors may contribute to increased TB risk in bio-naïve RA patients (treatment with leflunomide, azathioprine, or prednisolone and concomitant obstructive lung disease). We could not confirm previous findings of an association with the use of moderate to high doses of prednisolone (≥15 mg). TB risk seems difficult to predict with precision in the individual bio-naïve patient based on RA-associated risk factors. To further decrease the TB risk in RA patients TB screening should also be considered in the group of bio-naïve patients.

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Disclosure of Interests: Johanna Sundbaum: None declared, Elizabeth Arkema: None declared, Judith Bruchfeld: None declared, Jerker Jonsson: None declared, Johan Askling Grant/research support from: JA acts or has acted as PI for agreements between Karolinska Institutet and the following entities, mainly in the context of the ARTIS national safety monitoring programme of immunomodulators in rheumatology: Abbvie, BMS, Eli Lilly, Merck, MSD, Pfizer, Roche, Samsung Bioepis, Sanofi, and UCB Pharma, Eva Baecklund: None declared

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SAT0070

LUNG ULTRASOUND IN PATIENTS WITH RHEUMATOID ARTHRITIS AND THE DEFINITION OF SIGNIFICANT INTERSTITIAL LUNG DISEASE

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Background: In recent years, a growing interest has grown around interstitial lung disease (ILD) in patients with rheumatoid arthritis (RA). While high resolution computed tomography (HRCT) of the chest remains the diagnostic method of choice, increasing attention has been directed towards lung ultrasound (LUS) in the diagnosis of ILD in connective tissue diseases. LUS allows the detection of artifacts (B-lines) characteristic of ILD, without the need to use ionizing radiation. However, it is not yet well defined how to interpret the LUS findings under suspicion of RA-ILD.

Objectives: To determine the cut-off number of LUS B-lines that identifies a significant RA-ILD.

Methods: A cross sectional study was conducted on consecutive RA patients with suspected RA-ILD. The inclusion criteria were clinical (dyspnea, velcro sounds), instrumental (suggestive anomalies on conventional radiography, DLco reduction), or in presence of at least two of the following risk factors for RA-ILD: smoking habit, male sex, advanced age, and ACPA presence.

Patients underwent LUS, chest HRCT, pulmonary function tests, and clinical evaluation. The diagnosis of RA-ILD was based on a semi-quantitative evaluation of HRCT using a computer-aided method (CaM). The 10% of fibrosis, measured with this method, was considered as a cut-off for the presence of significant RA-ILD. The LUS was carried out in 14 defined intercostal spaces using a linear multifrequency probe 6-18 MHz (MyLab Class C, Esaote S.p.A., Genoa, Italy) and the number of B-lines present in each intercostal space was counted and summed up (Figure 1). The discriminating validity of the LUS versus HRCT has been studied by using the receiver operating characteristic (ROC) curve analysis.

Results: 72 consecutive RA patients (21 male, 51 female) were evaluated, with a mean age of 63.0 (SD 11.5 years), a mean ACPA titre of 327.6 (SD 633.3) U/ml and a rheumatoid factor of 324.6 (SD 748.7) U/ml. The mean estimate of pulmonary fibrosis using the CaM was 11.2% (SD 7.5) at HRCT, while at LUS the mean number of B-lines was 10.6 (SD 15.1). Pulmonary fibrosis of 10% as measured by the CaM at HRCT was detected in 25 patients (34.72%). Applying this HRCT cut-off point as an estimate of significant fibrosis, the presence of 9 B-lines was found to be the optimal cut-off at ROC curve analysis. This LUS cut-off defines the presence of significant fibrosis with a sensitivity of 70.0%, a specificity of 97.62%, and a positive likelihood ratio of 29.4 (Figure 2).

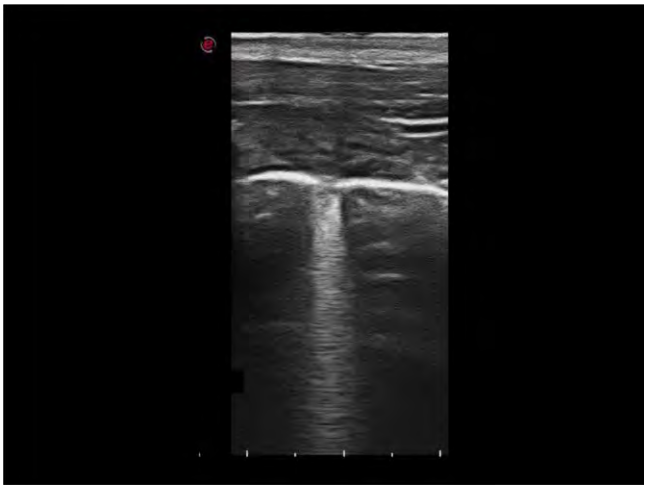


Figure 1. LUS B-line illustrative.

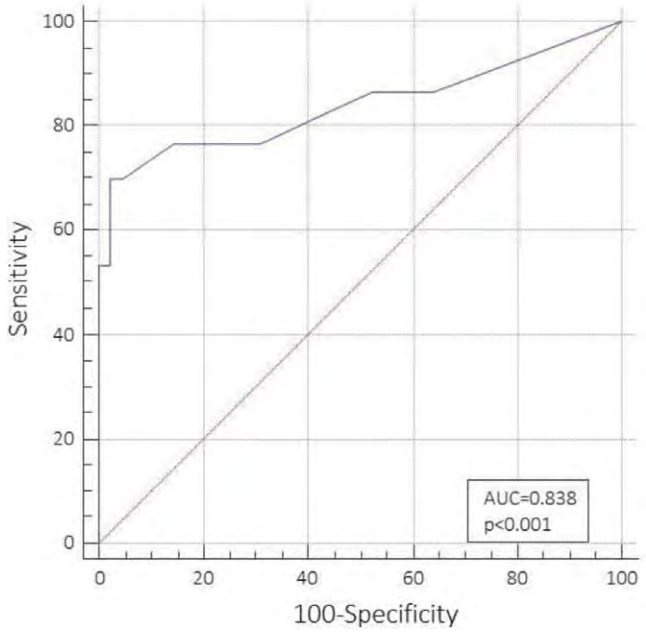


Figure 2. Area under the ROC curve to determine the number of B-lines at LUS to define a significant RA-ILD, applying the 10% of fibrosis at chest HRCT measured by OsiriX as external criterion.

Conclusion: The present study provided data to determine the number of B-lines to identify a significant RA-ILD. LUS may represent a useful technique to select RA patients to be assessed by chest HRCT.

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Disclosure of Interests: Marco Di Carlo: None declared, Marika Tardella: None declared, Emilio Filippucci Speakers bureau: Dr. Filippucci reports personal fees from AbbVie, personal fees from Bristol-Myers Squibb, personal fees from Celgene, personal fees from Roche, personal fees from Union Chimique Belge Pharma, personal fees from Pfizer, outside the submitted work., Fausto Salaffi: None declared

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SAT0071 SUBCLINICAL SYNOVITIS IN ARTHRALGIA: HOW OFTEN DOES IT RESULT IN CLINICAL ARTHRITIS? A LONGITUDINAL STUDY TO REFLECT ON STARTING POINTS FOR DMARD TREATMENT

C. Rogier[1], F. Wouters[2], L. Van Boheemen[3], D. Van Schaardenburg[3], P. De Jong[1], A. Van der Helm-van Mil[1,2]. *[1]Erasmus MC, Rheumatology, Rotterdam, Netherlands*; *[2]Leiden University Medical Centre (LUMC), Rheumatology, Leiden, Netherlands*; *[3]Reade, Rheumatology, Amsterdam, Netherlands*

Background: Clinically apparent arthritis is mandatory for diagnosing and classifying RA. It is often used as endpoint in arthralgia cohorts and as a starting point for DMARD therapy in clinical practice. In recent literature subclinical synovitis, visualized with MRI or ultrasound, is increasingly used as a starting point for DMARD therapy in absence of clinically apparent arthritis. However, not all patients with a subclinical synovitis will develop clinically apparent arthritis, and thus may be overtreated. It has even been suggested to replace the entry-criterion of clinical arthritis by subclinical synovitis within the 2010 classification criteria for RA to diminish overtreatment. However this might lead to an overclassification of the disease. Because of aforementioned reasoning we aimed to evaluate the risk of overtreatment of these approaches and therefore performed a longitudinal study in three observational arthralgia cohorts.

Objectives: To determine the frequency of non-progression to clinical arthritis in patients with subclinical synovitis, also after considering the 2010-criteria.

Methods: Three individual cohorts of arthralgia patients without clinically apparent arthritis (n=166, 473 and 168) were followed for 1-year on the development of inflammatory arthritis (IA). At baseline subclinical synovitis in hands or feet was visualized with ultrasound (US) (defined as greyscale≥2 and/or power-doppler≥1) in cohort 1 and 3 and MRI (synovitis score ≥1 by two readers) in cohort 2. For all patients with subclinical synovitis the proportion of progressors ('true positives') and non-progressors ('false positives') were determined. The same analysis was done in the subgroup of patients that fulfilled the 2010 criteria for RA, if subclinical synovitis was used as entry criterion. Analyses were stratified for ACPA.

Results: At baseline 36%, 41% and 31% of patients had subclinical synovitis. Of the ACPA-positive arthralgia patients with subclinical synovitis 46%, 56% and 29% respectively developed IA, whereas 54%, 44% and 71% did not progress. Within ACPA-negative arthralgia patients with subclinical synovitis 34%, 15% and 10% developed IA; whereas 66%, 85% and 90% did not progress (Figure 1A). Similar results were seen in the subgroup of patients that fulfilled the 2010 criteria with subclinical synovitis as entry criterion (Figure 1B).

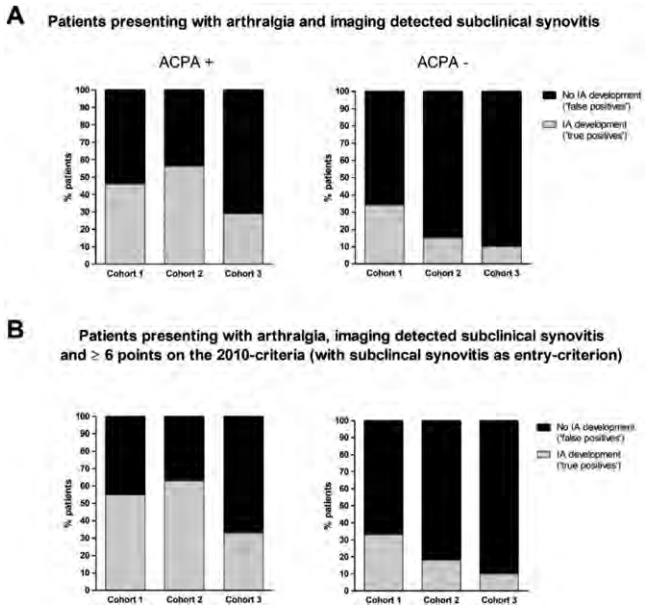


Figure 1. Percentage of arthralgia patients with subclinical synovitis that did and did not develop IA, in three independent cohorts: (A) Percentage of patients with subclinical synovitis that did and did not progress to IA after one-year follow-up, stratified for ACPA status. (B) Percentage of patients with subclinical synovitis and ≥6 points at baseline that did and did not progress to IA after one-year follow-up stratified for ACPA status.

Conclusion: Replacing clinical arthritis by subclinical synovitis in arthralgia introduces a high false-positive rate: 44-71% (ACPA-pos) and 66-90% (ACPA-neg) of patients with subclinical synovitis did not develop clinically apparent arthritis within one year. Applying the 2010-criteria in this setting did not diminish the false positive rate. Starting DMARDs in patients without clinical synovitis may therefore introduce considerable overtreatment.

Acknowledgments *: C Rogier and F Wouters contributed equal to this study

Disclosure of Interests: None declared

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SAT0072 THE IMPACT OF COMORBIDITIES ON ABSENTEEISM, PRESENTEEISM AND EMPLOYMENT STATUS IN PEOPLE LIVING WITH RHEUMATOID ARTHRITIS

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Background: Many people with rheumatoid arthritis (RA) have comorbidities. However, there is limited research on the impact of multimorbidity on absenteeism (e.g. sick leave) and presenteeism (i.e. reduced productivity while at work due to ill health) in people with RA.

Objectives: i) to explore the impact of comorbidities on absenteeism and presenteeism in patients with RA and ii) to evaluate the association between multimorbidity and employment status.

Methods: A cross-sectional survey was conducted by the National Rheumatoid Arthritis Society (NRAS), UK, collecting information on: demographics, education, employment status (i.e. employed (Empl), stopped/retired early because of RA (Stop_RA), stopped/retired early because of other health issues (Stop_Health)), and disease related variables (e.g. symptom duration, rheumatoid arthritis impact of disease (RAID) questionnaire). Participants were asked to report whether they

had or were treated for any of 15 predefined comorbidities (categorised into 0, 1, 2, 3, or ≥4 (Table)). Percentage of number of hours missed due RA (i.e. absenteeism) and presenteeism (10-point Likert scale) were assessed using the Work Productivity and Activity Impairment Questionnaire (WPAI-RA). For the purpose of this study both absenteeism and presenteeism outcomes were dichotomized (no presenteeism/absenteeism versus any) and only patients aged <65yrs were included. Logistic regression analysis were applied to assess the association between number of comorbidities and absenteeism/presenteeism, adjusting for the categorical variables age, gender and education. Chi2-square test was applied to assess frequencies of individual comorbidities between the three employment status groups.
Results: 868 participants were included; 91.7% women with a median symptom duration of 8.3 years [IQR 4.4-13.7]. The average RAID score was 5.2 (SD 2.2). 80.4% were in paid employment, including those currently on sick leave, 16.9% stopped early because of their RA and 2.7% reported stopping early because of other health reasons. In those employed most commonly occurring comorbidities were: back pain (28.8%%), osteoarthritis (21.5%), depression (26.3%) and anxiety (22.6%). Compared to people with RA with no comorbidities, the odds associated with time off work due to RA increased from 1.7 up to 3.4 with increasing number of comorbidities (Table). Although a similar trend was observed for presenteeism, the effect sizes were smaller. Significant differences (p<0.05) in frequencies of the following comorbidities were observed between the three employment status groups (Empl, Stop_RA, Stop_Health, respectively): heart disease (3.9%, 7.9%, 20.0%), blood pressure (18.0%, 29.5%, 36.7%), lung disease (5.7%, 16.3%, 26.7%), diabetes (4.4%, 4.2%, 26.7%), ulcer (6.1%, 11.1%, 13.3%), cancer (3.3%, 2.6%, 13.3%), depression (26.3%, 33.6%, 50.0%), OA (21.5%, 44.7%, 63.33%), and back pain (28.8%, 48.4%, 60.0%).

		Absenteeism (yes/no)		Presenteeism (yes/no)	
Number of comorbidities	**N**	**OR**	**95%CI**	**OR**	**95%CI**
0	206	*Ref.*		*Ref.*	
1	174	**1.70**	**1.06-2.71**	**1.66**	**1.00-2.73**
2	136	**1.77**	**1.08-2.92**	**1.99**	**1.13-2.86**
3	85	1.75	1.00-3.08	1.53	0.82-2.86
4-15max	86	**3.38**	**1.98-5.78**	**2.64**	**1.28-5.44**

OR=odds ratio; 95%CI=95% confidence interval; Comorbidities included: heart disease, blood pressure, lung disease, diabetes, ulcer or stomach disease, kidney disease, liver disease, anaemia or other blood disease, cancer, depression, anxiety, OA, back pain, osteoporosis and Sjögren. Bold figures *P*<0.05.

Conclusion: Although the study is cross-sectional and no temporal association can be determined, this study shows that not only personal and work related contextual factors should be considered when preventing worker productivity loss, but also other comorbidities.
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SAT0073 MYOPENIA AGGRAVATES RHEUMATOID ARTHRITIS IN ELDERLY PATIENTS AS A MEDIATOR

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Background: Ageing affects different systems resulting in a special clinical phenotype of rheumatoid arthritis (RA) in elderly patients who are characterized by higher level of systemic inflammatory and poor function. It also leads to loss of muscle mass causing functional limitation and reduced quality of life. However, little is known about muscle loss in growing elderly RA patients.
Objectives: To explore the characteristics of muscle mass and clinical significance in elderly RA patients.
Methods: Consecutive RA patients were recruited and clinical data including disease activity (DAS28-CRP), function (HAQ-DI) and radiographic indicators (modified Sharp score) were collected. The mass and distribution of muscle were assessed by bioelectric impedance analysis. Myopenia was defined as appendicular skeletal muscle mass index (ASMI) ≤7.0kg/m^2 in men and ≤5.7kg/m^2 in women.
Results: (1) There were 643 RA patients recruited with 82.3% female, mean age 49.7±12.9 years and median disease duration 48 (IQR 21,108) months. There were 414 (64.4%) RA patients with active disease (DAS28-CRP≥3.2) and 229 (35.6%) with remission. (2) There were 165 (25.7%) elderly RA patients (age≥60 years) with mean age 65.1±4.5 years. Compared with young patients (age<60 years), elderly RA patients had significantly higher disease activity indicators including PtGA, PrGA, ESR, CRP, DAS28-CRP, DAS28-ESR, SDAI and CDAI, higher HAQ-DI (0.38 vs. 0.13) and higher modified total Sharp score (mTSS, 16 vs. 9, all *P*<0.001). There were 288 (44.8%) RA patients with myopenia and elderly RA patients had higher proportion of myopenia than young patients (54.5% vs. 41.4%, *P*=0.003). (3) Among 4 subgroups according to age and ASMI, elderly RA patients with myopenia (*n*=90, 14.0%) had significant higher DAS28-CRP (3.6 vs. 3.0), higher HAQ-DI (0.50 vs. 0.12) and higher mTSS (21 vs. 7) than those in young patients without myopenia (*n*=280, 43.5%), and had higher mTSS (21 vs. 10) than those in elderly patients without myopenia (*n*=75, 11.7%, all *P*<0.0083). (4) Adjusted for confounding factors including gender, disease duration, BMI, smoking habit, RF, ACPA and treatment naïve, multiple linear regression analysis showed that age was positively correlated with DAS28-CRP (*β*=0.010), HAQ-DI (*β*=0.003) and mTSS (*β*=0.005, all *P*<0.05), while ASMI was negatively correlated with DAS28-CRP (*β*= -0.445), HAQ-DI (*β*= -0.124) and mTSS (*β*= -0.247, all *P*<0.001). (5) Mediation analysis showed that old age (≥60 years) had total effect on DAS28-CRP (*β*=0.353), HAQ-DI (*β*=0.132) or mTSS (*β*=7.909, all *P*<0.05), but no direct effect on them (all *P*>0.05). ASMI fully mediated the associations between old age and DAS28-CRP, HAQ-DI or mTSS.
Conclusion: Half of elderly RA patients manifest myopenia which aggravates the whole disease of disease activity, joint function and destruction as a mediator. Myopenia, a neglected comorbidity in elderly RA should be emphasized.
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SAT0074 RHEUMATOID ARTHRITIS AT TREATMENT WITH BDMARD OR TSDMARD: VACCINATION RATES AND INCIDENCE OF RESPIRATORY INFECTIOUS DISEASES, RESULTS FROM A COHORT

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Background: Vaccination regimes have been evaluated for long time in rheumatic diseases, being a strong recommendation to vaccinate against Influenza and Pneumococcus (13 and 23-valent). Rheumatoid arthritis (RA) patients have higher rates of infectious diseases, caused by many reasons, being patient's comorbidities, rheumatic disease and treatments used the most important[1-2].
Objectives: To analyze the incidence of respiratory infectious diseases in these patients regarding for vaccination status. Also prove the degree of accomplishment of vaccination calendar.
Methods: Patients diagnosed of RA at treatment with bDMARD or tsDMARD, in Rheumatology Department of aforementioned hospital, during Influenza vaccination campaign in 2018 (October 2018 – February 2019) were included. Clinical, demographic and therapeutic data were reviewed. Stata 15.1 was used to perform statistical analysis.
Results: 237 patients finally fulfilled inclusion criteria, excluding deceases or finished treatment (460 patients were diagnosed of RA and 954 patients conform all bDMARD and tsDMARD of Rheumatology Department). Mean age at beginning of vaccination campaign was 61,5 years old (SD 13,6). 79% were female. Mean time of diagnosis was 15,4 years (SD 9,4). 79,7% patients receive Influenza vaccine, although higher rates were found in Pneumococcal vaccine (86,9% 13-valent and 81,8% 23- valent). Most patients were at treatment with anti-TNF (57,2%, the most prevalent was etanercept 27,5% followed by adalimumab 11,0% and infliximab 10,2%). csDMARD concomitant was achieved by 67,4% patients (methotrexate 73%) and 61% receive corticosteroids. Only 3 patients got hospitalized by pneumonia. As opposed, 39 patients suffer from a respiratory infectious disease without hospitalization (mean of 1,33 infections/patient). After multivariate analysis, only 13-valent Pneumococcal vaccine is related statistically significant with higher rates of respiratory infectious diseases (Chi2=6,25 p=0,012; OR 2,86 CI95% 1,22 to 6,68). Other variables analyzed were kind of bDMARD/tsDMARD, Influenza vaccine, 23-valent Pneumococcal vaccine, concomitant csDMARD/corticosteroids, but no relationship was found.
Conclusion: Vaccination status is still incomplete in majority of rheumatic patients. Its benefits have been explained in a variety of studies. That is the

reason why, supporting this study, vaccination status must be checked in the daily practice.

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SAT0075 ABATACEPT IN COMBINATION WITH METOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS ASSOCIATED TO INTERSTITIAL LUNG DISEASE: NATIONAL MULTICENTER STUDY OF 263 PATIENTS

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Background: Interstitial Lung Disease (ILD) is an extra-articular complication of rheumatoid arthritis (RA) that is associated with increased morbidity and mortality. Conventional disease-modifying drugs (DMARDs) such as methotrexate (MTX) have been implicated in the development and exacerbation of a pre-existing ILD.

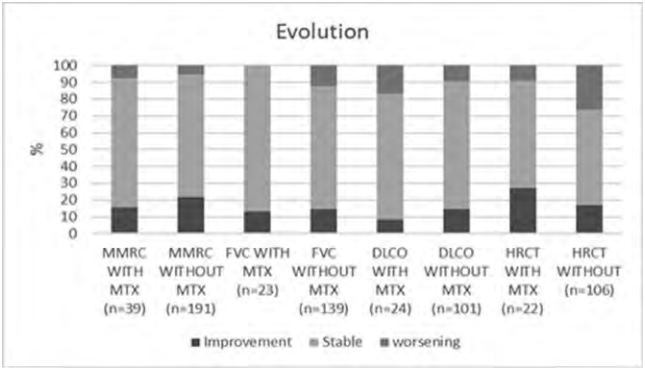
Objectives: The aim of our study was to check the influence of combined MTX treatment in patients with RA-ILD treated with abatacept (ABA).

Methods: National multicentre retrospective registry of 263 patients with RA-ILD treated with ABA. RA was diagnosed according to the ACR classification criteria of 1987 or by the EULAR/ACR criteria of 2010. ILD was diagnosed by high resolution computed tomography (HRCT). In this study we have done a subanalysis of the 46 patients treated with ABA in combination with MTX (ABA+MTX) vs. 217 patients treated with ABA in monotherapy or in combination with other synthetic DMARDs. Efficacy was evaluated according to the following parameters: a) Dyspnoea (MMRC) considering variations ≥ 1; b) Lung function test (LFT) considering variations ≥ 10% in FVC and a variation of DLCO ≥ 10%; c) Imaging test (HRCT) d) DAS28 score e) prednisone dose. Variables were collected at the beginning of the study and at months 3, 6, 12 and then every 12 months until a maximum of 60 months.

Results: 263 patients with ILD associated with RA were included in the study with mean age 64.64±10 years. RF or CCPA were positive in 235 (89.4%) and 233 (88.6%) cases, respectively, with a mean follow-up of 22.7±19.7 months. Baseline characteristics of both groups are shown in table 1, while data obtained during evolution of this complication are presented in Figure 1.

Conclusion: Despite the baseline differences of both groups, the good evolution in the ABA+MTX subgroup suggests that this therapeutic strategy can be a safe combination for patients with RA-ILD.

	ABA with MTX (n=46)	ABA w/t MTX (n=217)	*P*
Sex (F/M)	28/18	122/95	0.625
Age (years)	65.11±10.21	6.2±9.8	0.202
RF/CCPA + (%)	91.3/91.3	89.8/90.1	0.810
Smoking or past smoking (%)	47.8	55.1	0.417
Follow-up (months)	22.73±18.00	22.3±20.85	0.916
DAS28 at baseline	4.08±1.51	4.61±1.47	0.056
DAS28 at last visit	3.00±1.46	3.13±1.31	0.642
Prednisone at baseline, median (IQR) (mg)	5 (5-7.5)	7.75 (5-15)	0.008*
Prednisone at the end of study, median (IQR) (mg)	5 (1-5)	5 (5-7.5)	0.032*
DLCO at baseline (%)	66.85±19.04	65.43±18.21	0.823
DLCO at the end of study (%)	66.05±20.95	65.17±19.72	0.831
FVC at baseline (%)	90.06±17.77	85.40±21.56	0.164
FVC at the end of study (%)	90.58±15,45	84.21±21.49	0.038*



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SAT0076 VERY ELDERLY ONSET RHEUMATOID ARTHRITIS (VEORA): CLINICAL CHARACTERISTICS AND THERAPEUTIC IMPLICATIONS

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Background: There are differences in the characteristics of patients with Rheumatoid Arthritis (RA) depending on their age at onset with two traditional groups: YORA (young onset RA) and EORA (elderly onset RA). These aspects have not been studied in cases of very late onset (≥ 80 years)

Objectives: To describe the clinical characteristics, treatments and evolution at one year in "very elderly onset RA" (VEORA). Compare these characteristics with YORA (40-50 years) and EORA (60-70 years).

Methods: Retrospective and longitudinal study of RA patients from 2 spanish hospitals. From their databases, VEORA patients were identified and their clinical characteristics were analyzed at onset, treatments at diagnosis and in the first 12 months, as well as DAS28-ESR activity after 1 year. These variables

were compared between cases belonging to one of the hospitals and 2 control groups of YORA and EORA patients of the same center, matched by sex, diagnosis date ± 2 years, RF and / or ACPA status and presence of erosions in baseline Rx.

Results: A total of 2790 records of RA patients were analyzed, identifying 59 cases of onset in "very elderly" (2% of the total). Table 1 shows its clinical, analytical characteristics and treatments at diagnosis.

Table 1. Demographic and clinical data of the 59 VEORA patients

		n=59
	Female, n(%)	43 (73)
	Age at onset, years	83 ± 3
Comorbidity		
	Hypertension, n(%)	54 (92)
	Diabetes, n(%)	19 (32)
	CV disease	20 (34)
Clinical and analytical data at diagnosis		
	Acute onset, n(%)	26 (44)
	Polyarticular onset, n(%)	37 (63)
	Specific forms, n(%)	21 (36)
	Polymyalgia Rheumatica, n	16
	RS3PE, n	5
	Rheumatoid factor, n(%)	40 (68)
	ACPA, n(%)	24 (41)
	DAS28-ESR	5 (4,4-5,7)
	high activity, n(%)	32 (54)
First visit treatment		
	NSAIDs, n(%)	5 (9)
	Steroids, n(%)	55 (93)
	starting dose, mg/day*	10 (7,5-15)
	DMARD, n(%)	52 (88)
	Hidroxychloroquine	14 (24)
	Methotrexate	36 (61)
	starting dose, mg/week	10 (7,5-10)
	Combined therapy	5 (8)

DAS28-ESR and the number of patients in remission or low activity at one year showed no differences between EORA and VEORA, or between these groups and that of younger patients.

Elderly patients (EORA and VEORA), compared with YORA, presented with higher frequency hypertension and CV disease, higher elevation in acute phase reactants at the onset and disease activity at diagnosis. VEORA patients, compared to EORA, showed a higher frequency of dyslipidemia (p = 0.04). There were also no significant differences between VEORA and EORA in the distribution and type of joints affected, time to diagnosis, acute phase reactants or disease activity at the onset. A higher frequency of special forms (such as PMR or RS3PE) was close to statistical significance in the VEORA group (p = 0.054).

Regarding initial treatment, both EORA and VEORA received steroidal treatment more frequently and a lower dose of Methotrexate during the first year. Biological treatments was also significantly higher in YORA (p=0,000). When comparing VEORA and EORA, differences related to the use of NSAIDs were found, lower in VEORA (p = 0.000), as well as in the maximum dose of Methotrexate reached in the next 12 months, higher in the EORA group (p = 0.01). No differences in adverse events with DMARDs were observed.

Conclusion: There have been few differences in the comorbidity profile and clinical characteristics at the onset between VEORA and EORA patients. Despite the differences observed in its management (more conservative in EORA and VEORA vs YORA, and in VEORA vs EORA), we have not observed differences in DAS28-ESR activity after one year.

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SAT0077

CARDIOVASCULAR RISK ASSESSMENT WITH CAROTID ULTRASONOGRAPHY IN ADDITION TO THE TRADITIONAL CARDIOVASCULAR RISK FACTORS IN RHEUMATOID ARTHRITIS PATIENTS: A CASE CONTROL STUDY

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Background: Cardiovascular disease (CV) is the most frequent cause of death in rheumatoid arthritis (RA) patients. It is well known that RA acts as an independent cardiovascular risk factor.

Objectives: To assess the CV risk in RA patients using carotid ultrasonography (US) additionally to the traditional CV risk factors.

Methods: A prospective transversal case control study was performed, including adult RA patients who fulfilled ACR/EULAR 2010 criteria and healthy controls matched according to CV risk factors. Population over 75 years old, patients with established CV disease and/or chronic kidney failure (from III stage) were excluded. The US evaluator was blinded to the case/control condition and evaluated the presence of plaques and the intima-media thickness. Statistical analysis was performed with R (3.6.1 version) and included a multivariate variance analysis (MANOVA) and a negative binomial regression adjusted by confounding factors (age, sex and CV risk factors).

Results: A total of 200 cases and 111 healthy controls were included in the study. Demographical, clinical and US data are exposed in table 1. Not any difference was detected in terms of CV risk factors between the cases and controls. In both groups a relationship between age, BMI and high blood pressure was detected (p<0.001).

Table 1.

	RA cases n=200	Controls n=111
Age	60,56 (10,71)	56,79 (12,15)
Sex	Female 163 (81,5%)	Female 73 (65,77%)
	Male 37 (18,5%)	Male 38 (34,23%)
Smoking status	Active smoker 42 (21%)	Active smoker 20 (18,02%)
	No 107 (53,5%)	No 71 (63,96%)
	Ex-smoker 51 (25,5%)	Ex-smoker 20 (18,02%)
High blood pressure	83 (41,5%)	34 (30,63%)
Diabetes Mellitus	16 (8%)	9 (8,11%)
Dyslipidemia	93 (46,5%)	39 (35,14%)
Daily physical activity	138 (69%)	64 (57,66%)
Family history of CVD	26 (13%)	9 (8,11%)
BMI	26,38 (5,03)	26,2 (5,19)
Blood pressure	127,2 (18,36)/ 78,67 (10,21)	127,77 (19,42)/ 78,28 (10,59)
Total cholesterol	197,88 (37,17)	194,77 (35,79)
cLDL	108,79 (34,38)	114,44 (30,93)
CT/cHDL	3,28 (0,97)	3,77 (1,05)
Tryglicerides	119,56 (63,83)	121,58 (75,08)
CRP (mg/L)	5,46 (8,5)	2,31 (2,32)
ERS	20,75 (16,58)	11,25 (7,42)
Right/Left carotid cIMT	0,78 (0,15)/0,77 (0,14)	0,62 (0,11)/0,64 (0,12)
Plaques	101 (50,5%)	32 (28,83%)
Bilateral	64 (32%)	11 (9,91%)
Right carotid	17 (8,5%)	7 (6,31%)
Left carotid	20 (10%)	14 (12,61%)
Number of plaques	1,61 (2,16)	0,55 (1,14)

Table 2. RA basal characteristics

Disease duration (years)	16,98 (11,38)
Erosions (X-Ray of hands/feet)	163 (81,5%)
Seropositive (RF/anti-CCP)	146 (73%)
Extra-articular symptoms	44 (22%)
Intersticial difusse lung disease	10 (5%)
Rheumatoid nodules	14 (7%)
Prednisone use	103 (51,5%)
Median dose of Prednisone last year (mg)	2,34 (2,84)
sDMARDs	
Methotrexate	104 (52%)
Leflunomide	29 (14,5%)
Hydroxycloroquine	9 (4,5%)
bDMARDs	89 (44,5%)
TNFi	41 (20,5%)
Abatacept	15 (7,5%)
IL6i	22 (11%)
RTX	11 (5,5%)
JAKi	26 (13%)
Baricitinib	11 (5,5%)
Tofacitinib	15 (7,5%)
DAS 28-ESR	3,1 (2,3, 3,9)
SDAI	7,85 (4,04, 13,41)
HAQ	0,88 (0,22, 1,5)
RF (U/mL)	51 (15, 164,25)
Anti-CCP (U/mL)	173 (22, 340)

Patients showed higher intima-media (both right and left) thickness compared to controls (p<0.006). Moreover it was also related to the disease duration and DAS28 score (p<0.001). A higher plaque account was noted in cases(p<0.004) and it was also related to the disease duration (p<0.001).

Conclusion: RA implies a higher CV risk. Traditional CV risk factors explains only partially the global risk. These findings support that RA acts as an independent cardiovascular risk factor.
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SAT0078 SAFETY OF LOW DOSE METHOTREXATE (MTX) IN HUMAN IMMUNODEFICIENCY VIRUS (HIV) INFECTION

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Background: Increased awareness of the efficacy of MTX in rheumatic disease is leading to more MTX use in patients from HIV endemic areas. While HIV related immunosuppression may contribute to improvement of some rheumatic diseases, immune reconstitution from highly active antiretroviral therapy (HAART) may lead to exacerbation or presentation of autoimmune disorders for which MTX therapy may be warranted. Most management guidelines for rheumatic disease do not address MTX use in the context of HIV.
Objectives: To systematically review the published literature on the safety of using MTX ≤30 mg per week in HIV.
Methods: We searched CINAHL, Embase, Global, MEDLINE and World of Science databases (Jan 1990 to May 2018) for terms including 'methotrexate' and 'human immunodeficiency virus'. We also searched citations from review articles. Titles, abstracts or full manuscripts were screened independently by 2 reviewers to identify studies reporting HIV in patients taking MTX. Study quality was assessed using the McGill Mixed Methods Appraisal Tool (MMAT). Data was extracted on MTX and HIV adverse events (MTX toxicity, HIV viral load, CD4 count). Descriptive summaries are presented for studies providing outcomes in patients taking MTX ≤30 mg per week.
Results: After removing duplicates and studies not meeting criteria or not providing sufficient information, 42 of the 2714 identified reports were included (1 clinical trial, 2 cohort, 1 cross-sectional study, 38 case reports/case series). Most reports (81%) originated from USA or Europe. Study quality was generally good with most studies fulfilling 50-100% of MMAT criteria. The randomized controlled trial (USA) assessing MTX on atherosclerotic disease in HIV showed that adverse events were more common in MTX versus placebo (12.8% vs 5.6%, p non-inferiority <0.05) and included infection, transient CD4 and CD8 drop, pulmonary toxicity, and death (1 attributed to MTX/HIV, 1 unrelated). One cohort study (South Africa) reported 43 RA patients on MTX who acquired HIV. In this cohort, RA generally improved despite only 5 individuals continuing MTX. No data on MTX adverse event rates was reported. One cohort study (USA) reported 13 HIV patients with myositis. One received MTX (with other immunosuppression) without MTX adverse effects but died due to AIDS. A cross-sectional study (France) of 43 HIV pts with autoimmune disease reported one patient on MTX (and other immunosuppression) developed an adverse event (cytopenia) compared to 5/33 patients not on MTX (cytopenia). The 38 case reports/series described 54 individuals with HIV receiving MTX. Of these studies, 27 (describing 42 subjects) reported on MTX adverse events and 35 (describing 46 subjects) reported on HIV adverse events. MTX adverse events developed in 29 subjects (hematologic 13, renal/hepatic 1, opportunistic infections 10, other events 2). HIV adverse events were noted in 23 subjects (Kaposi's sarcoma 4, CD4 decrease 16, HIV viral titer increase 4). Five deaths were reported (2 infection, 1 infection and wasting, 2 HIV related deaths). Most subjects also received corticosteroids or other immunosuppressants including biologics.
Conclusion: There remains limited data on the safety of low dose MTX in HIV. Surveillance for HIV is warranted for individuals on MTX who are at risk for acquiring HIV. Caution and careful monitoring for MTX toxicity, opportunistic infections and HIV state is suggested if MTX is used in the setting of HIV particularly if combined with other immunosuppression.
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SAT0079 FEATURES OF CLINICAL MANIFESTATIONS IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS IN THE PRESENCE OF SIGNS OF CENTRAL SENSITIZATION

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Background: The presence of central sensitization (CS) is observed in 25-30% of patients with rheumatoid arthritis (RA). CS is associated with more severe pain, depression, and anxiety.
Objectives: To evaluate the effect of CS on activity indicators and clinical manifestations in patients with active RA.
Methods: The study group consisted of 60 patients with medium or high RA activity (DAS28 ≥3.2), 75% female, age 54.5±17.8 years, 82.1% RF "+", 75% ACPA "+". DN4 and PainDETECT questionnaires were used to identify CS signs. Signs of CS were detected in 43% of patients. Clinical parameters and indicators of disease activity in patients with RA CS "+" and CS "- "were compared.
Results: Groups of patients with RA CS "+" and CS "-" did not differ in age - 55.5 [48.0; 67.5] and 54.0 [40.0; 62.0], p=0.26, body mass index - 24.54 [22.6; 26.78] and 25.04 [21.34; 29.665] kg/m2, p=0.64, duration of illness: 6.5 [2.5; 13.0] and 10.0 [5.0; 16.5] years, p=0.13, level of C-reactive protein: 7.2 [1.0; 23.4] and 8.1 [3.6; 24.3], p=0.53.
SC "+" patients had a higher level of pain on a visual analog scale, VAS (patient score) - 70.0 [60.0; 80.0] and 60.0 [40.0; 70.0], P=0.01; DAS28 - 5.33 [3.38; 6.42] and 4.5 [3.645; 5.4], p=0.04; EQ-5D - 0.52 [0.02; 0.52] and 0.59 [0.52; 0.71], p=0.01; anxiety level (Hads-T) - 8.0 [7.0; 10.0] and 4.5 [2.5; 6.0], p=0.001 and depression (Hads-D) - 7.5 [6.0; 10.5] and 5.0 [2.5; 7.5], p=0.02. The groups did not differ significantly in the values of SDAI, CDAI, and HAQ, as well as in the assessment of health by the doctor (VAS) - 60.0 [50.0; 70.0] and 60.0 [50.0; 60.0], p=0.42.
Conclusion: The presence of SC is associated with more intense pain, anxiety, depression, and DAS28 activity. This should be taken into account when planning therapy, including deciding whether to "switch" DMARDs and prescribing antidepressants and anticonvulsants.
Disclosure of Interests: None declared
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SAT0080 COMPARATIVE ANALYSIS OF FRAGILITY FRACTURE IN PATIENTS WITH ELDERLY ONSET RHEUMATOID ARTHRITIS AND YOUNG ONSET RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic autoimmune disease, characterized by erosive arthritis and systemic organ involvement. Chronic inflammation, long RA disease duration, decreased physical activity, immobilization, glucocorticoids use lead to local (periarticular osteoporosis) and generalized loss of bone tissue, decrease in bone mineral density, contravention of microarchitectonics and increased risk of fragility (low-energy) fractures. The structure and density of bone tissue at elderly onset RA, in addition to the above factors, are affected by comorbid diseases, sex steroids level decrease and molecular changes in bone tissue, specifically attributed to aging, followed by increased bone resorption. Fractures reduce the quality of life, have a negative impact on the course of the underlying and concomitant diseases.
Objectives: Compare frequency of fragility fracture in patients with elderly onset rheumatoid arthritis and young onset rheumatoid arthritis.
Methods: We included 474 patients with RA diagnosed at 25– 78 years old and fulfilled the American College of Rheumatology (formerly American Rheumatism Association) classification criteria for RA revised in 1987. The patients were divided into two groups depending on age at the RA-onset: The first group (group I) included 217 patients with young onset RA (at 25 to 44 years), second group (group II) included 66 patients with elderly onset RA (aged ≥60 years). The distribution of patients into groups was consistent with the age classification of the World Health Organization. In total, it was selected 283 RA patients. The mean age in group I was 50.4 years, in group II - 71.2 years. The mean age at the onset

of RA in group I was 35.0 years, in group II - 66.2 years.; RA duration was 14.4 years and 4.6 years, respectively. Long-term history of glucocorticoids use (for more than 3 months) was observed in 50% of patients in group I, and in 42% of patients in group II.

Results: 40 (18%) patients in group I and 17 (26%) patients in group II had fragility fractures. Among patients with fragility fracture, 23 (57,5%) patients in group I and 6 (35%) patients in group II received glucocorticoid therapy for more than 3 months. Two or more fractures in history had 16 (40%) in group I, and 3 (18%) in group II.

Conclusion: The frequency of fragility fracture in the study groups was comparable (p> 0.05), despite the age of patients. But, the frequency of refractures was higher in patients with RA-onset at young age, which, apparently, is a consequence of long RA disease duration and use of glucocorticoids.

Disclosure of Interests: None declared

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SAT0081 FOOTPRINT OF THE BRAIN-DERIVED NEUROTROPHIC FACTOR ON PAIN AND MOOD PERCEPTION OF PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Depression and cognitive impairment have been frequently reported in rheumatoid arthritis (RA) (1). Studies of the molecular mechanisms behind these phenomena attract increasing attention. We previously reported that signaling through the insulin-like receptor is impaired in RA and has consequences for pain processing (2).

Objectives: We investigated the central and peripheral footprint of the major neurotrophin in the central nervous system, brain-derived neurotrophic factor (BDNF), on pain and mood perception of RA patients.

Methods: Pain symptomatology was assessed in 216 female RA patients (mean age 52y, mean disease duration 10 years) by a visual analogue scale (VAS), 18 tender points count (TPC), and by pressure-induced pain threshold measurement. The mood was patient-reported based on the Hospital Anxiety and Depression Scale (HADS). Clinical RA activity was assessed by DAS28. Serum levels of BDNF, IL6, IL1b, IL10 and IFN-gamma were measured by ELISA. Transcription of FOXO1 and FOXO3 was measured by RT-PCR in whole-blood RNA. Effect of BDNF signaling in leukocytes was assessed by differentially expressed gene (DEG) analysis in RNAseq of 24 female RA patients (R-studio, Bioconductor). High-resolution brain MRI was performed in a representative selection of 16 patients. Brain volumes were analyzed with MAPER software for accurate measurement of 83 anatomical regions (3) and compared between two groups of patients with high and low serum BDNF, respectively.

Results: In RA patients, high serum levels of BDNF were associated with low TPC (4.1 vs 5.3, p=0.04) and higher pain threshold (kPa, 416 vs 382, p=0.09). No connection between BDNF and mood measures was evident. High BDNF was associated with high serum VEGF (p<0,001), IFNg (p=0.0004), IL1b (p=0.036) and serum insulin (p<0,001), but low resistin (p=0.059). No correlation was found between BDNF with either serum IGF1 or inflammation parameters DAS28 and IL6. Serum BDNF was functional, since the RA patients with high BDNF had significantly larger brain volumes in specific regions and significantly lower FOXO1 mRNA in blood leukocytes (p=0.03). Specifically, structures of the limbic system, parahippocampus, lingual gyrus, nucleus accumbens and thalamus, key regions for the transmission of nociceptive information and central modulation of pain, were enlarged. BDNF production was measured in CD4-CD8- PBMC and was inversely related to expression of its high-affinity receptor TrkB in CD4+ PBMC. DEG analysis in CD4 T cells showed that low TrkB was associated with CD28+ transitional memory phenotype.

Conclusion: We conclude that high serum BDNF was associated with larger volumes of nociception-related brain regions and lower pain perception, acting independently of IGF1 and systemic inflammation.

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SAT0082 FRAX AND DAS IN MOROCCAN RHEUMATOID ARTHRITIS PATIENTS

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Background: Rheumatoid Arthritis (RA) is one of the risk factors for the calculation of the 10 years fracture probability assessed by the FRAX tool.

Objectives: The aim was to study the association of disease activity and the 10 year fracture risk probability by the FRAX tool in our RA patients and their impact on fracture prevalence.

Methods: Cross-sectional study of the association FRAX and disease activity score (DAS 28 CRP) was designed. Patients with RA were included. Mean DAS was calculated for each patient adjusted on his follow-up duration. Data about patients (demographic, disease characteristics and fracture assessment) were collected. The 10 year fracture risk probability for major osteoporotic fracture was calculated with and without BMD (bone mineral density) using the FRAX tool for Morocco. Descriptive analysis and regressions were performed with SPSS.20. p<0.05 was considered significant.

Results: One hundred and ninety nine RA patients were included with mean age of 55.5±12 years. Women represented 91% and 40.1% had osteoporosis. Remission was observed in 86.4% with 95.5% taking methotrexate. 17.1% had vertebral fractures. FRAX and DAS were associated (p=0.03), and both explained vertebral fracture (VF) prevalence. When adjusted on disease parameters, FRAX with and without BMD explained the vertebral prevalence (p=0.02, OR=1.09[1.01-1.19]). However, age remains the only predictor of VF when adjusted on osteoporosis factors (DAS28CRP, menopause, BMI, smoking, diabetes, gender, steroid use, HAQ) and FRAX BMD.

Conclusion: Persistent disease activity was associated to high 10 year fracture risk probability calculated by the FRAX tool in RA.

Disclosure of Interests: None declared

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SAT0083 PREVALENCE OF DYSPHAGIA AND ASSOCIATED RISK FACTORS IN ELDERLY PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Dysphagia (swallowing disorder) is an important health concern among the elderly that is associated with a poor prognosis [1]. Rheumatic diseases such as dermatomyositis are thought to represent an important risk factor for dysphagia, but few studies have described the association between dysphagia and rheumatoid arthritis (RA), and details on the prevalence of dysphagia in RA patients is not known [2] [3].

Objectives: The present study aimed to determine the prevalence of dysphagia and associated risk factors among elderly patients with rheumatoid arthritis.

Methods: We conducted a cross-sectional study including 93 patients with RA and osteoarthritis (OA) over 65 years of age. OA patients were included in the study as healthy controls. Patients with a history of stroke, neuromuscular disease, or head and neck tumors were excluded from the study. From July to November 2019, the water swallowing test (WST) and repetitive saliva swallowing test (RSST) were performed to evaluate the presence or absence of dysphagia in the patients. We also checked oral conditions, hoarseness, temporomandibular joint symptoms, cervical range of motion limitations, and grip strength. In addition, interviews were conducted to investigate swallowing ability and aspiration history. We compared the prevalence of dysphagia between RA and OA patients and explored potential risk factors for dysphagia in RA patients using logistic regression models.

Results: Our study subjects comprised 63 RA patients (mean age, 73.8 years; 86.5% female) and 30 OA patients (mean age, 75.8 years; 82.3% female). The WST and RSST revealed that RA patients had a significantly higher prevalence of dysphagia than OA patients (23.8% vs 6.7%, p<0.05). While RA patients with dysphagia (n=15) were significantly older and had a longer disease duration than the OA patients, we observed no difference in disease activity or administrated drugs. Of the RA patients with dysphagia, 60% reported no previous episodes of aspiration. Increasing age (odds ratio (OR) 3.21, 95% confidence interval (CI) 1.06-4.56), cervical range of motion limitations (OR 3.14, 95% CI 1.02-7.24), opening disorder of the jaw (OR 2.26, 95% CI 1.12-4.86), and decreased grip strength (OR 1.96, 95% CI 1.01-4.15) were identified as factors related to the presence of dysphagia. Coexistence of Sjogren's syndrome did not significantly affect the prevalence of dysphagia.

Conclusion: Dysphagia was more prevalent among RA patients than in OA patients, suggesting an association with temporomandibular involvement, cervical disorder, and muscle weakness. Subclinical dysphagia should be assessed and monitored carefully in the clinical course of elderly patients with RA.

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SAT0084 SERUM ADIPOKINES PROFILE IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH TNF-INHIBITORS

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Background: In recent years, the relationship between obesity and autoimmune diseases has taken interest, since adipose tissue has been identified as an endocrine organ that secretes cytokines (adipokines), among which leptin stands out as a soluble pro-inflammatory mediator associated with the body mass index (BMI).
Objectives: The main objectives of this study are: i) to analyse the influence of BMI on clinical response in Rheumatoid Arthritis (RA) patients who initiate TNF-inhibitor (TNFi) therapy; ii) to analyse the differences in the serum profile of adipokines (leptin and adiponectin) according to BMI and their association with response to treatment.
Methods: Observational study of a prospective cohort of 73 RA patients who initiated biological treatment with TNFi from the Complex Therapy Unit (CTU) of our Hospital. Patients were classified according to their BMI in normal-weight (BMI<25) and overweight/obesity (O/O) (IMC≥25). Demographic, clinical and laboratory variables were collected at baseline and at 6 months. Our outcome measures were DAS28-VSG remission (DAS28<2.6) at 6 months after TNFi initiation. Serum leptin and adiponectin levels were measured by Enzyme-Linked Immuno Sorbent Assay (ELISA) at baseline and 6 months. A descriptive sample analysis comparing the characteristics of both patient subgroups was performed using Chi-square, T-test for independent samples and U-Mann Whitney. Likewise, a bivariate analysis was carried out by means of binary logistic regression to assess the probable association of the parameters studied with remission.
Results: Of the 73 patients studied, 51% were classified in O/O group. The O/O patients presented higher levels of baseline CRP (16.69±6.16 vs 8.74±3.81, p=0.01). No statistically significant differences were observed in the remaining variables (sex, age at the beginning of the TNFi, disease duration, baseline DAS-28), as well as therapeutic variables (use of previous DMARDs and doses of methotrexate and/or steroids). Patients with overweight/obesity presented higher DAS28-ESR values at 6 months of treatment (3.59±1.14 vs 2.93±1.27, p=0.02) and achieved remission less frequently (18.9% vs 48.6%, p=0.007). Serum leptin levels were significantly higher in O/O patients, both baseline (29.39±21.50 vs 13.49±8.78, p<0.001) and 6 months (33.06±22.03 vs 14.77±9.50, p<0.001) after TNFi initiation. In addition, O/O patients were less likely to reach remission at 6 months than normal-weight patients. [OR= 4.04 IC95% (1.40-11.64); p=0.009]. Lower frequency of remission was associated to greater leptin levels at 6 months [OR=0.94 CI95% (0.90-098); p=0.012]. No differences in serum adiponectin were found between both subgroups of patients.
Conclusion: In this RA patient cohort, overweight/obesity is associated with i) a reduced response to TNFi therapy and ii) a lower short-term remission rate. Within the adipokine profile, leptin seems to play a relevant role in the maintenance of pro-inflammatory activity with a negative influence on the response to TNFi therapy in O/O patients.
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Disclosure of Interests: Marta Novella-Navarro: None declared, Borja Hernández-Breijo: None declared, Fernanda Genre: None declared, Leticia Lera-Gómez: None declared, Verónica Pulito-Cueto: None declared, Laura Nuño: None declared, Alejandro Villalba: None declared, Alejandro Balsa Grant/ research support from: BMS, Roche, Consultant of: AbbVie, Gilead, Lilly, Pfizer, UCB, Sanofi, Sandoz, Speakers bureau: AbbVie, Lilly, Sanofi, Novartis, Pfizer, UCB, Roche, Nordic, Sandoz, Chamaida Plasencia: None declared
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SAT0085 METABOLIC SYNDROME AND ITS ASSOCIATION WITH RHEUMATIC DISEASES IN PARAGUAYAN PATIENTS

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Background: Metabolic syndrome (MS) is associated with increased abdominal adipose tissue and production of inflammatory cytokines. Patients with MS are at increased risk for developing cardiovascular disease and diabetes mellitus, which are among the leading causes of death in chronic rheumatic diseases.
Objectives: To characterize patients with rheumatic disease and MS and its association with inflammatory markers.
Methods: Descriptive, cross sectional, prospective study, in 3 Paraguayan cohorts of patients with rheumatoid arthritis (RA), systemic sclerosis (SSc) and systemic lupus erythematosus (SLE). This study had two phases: the first one, included a standardized questionnaire according to the variables included in the Cardiovascular Risk project (PINV15-0346), from the Consejo Nacional de Ciencias y Tecnología (CONACYT), and physical examination; the second one included laboratory sample collection performed by a specialized laboratory for serum biomarkers measurement for cardiovascular risk prediction (i.e endothelin, alpha-TNF, E-selectin, t-PA, VCAM, PAI-1 and high sensitivity-CRP levels). MS patients were categorized according to 2007 ALAD criteria. All patients signed informed consent. SPSS Statistics v23 was used for data analysis. Quantitative variables were presented as means and qualitative variables as frequencies. Chi square test was performed for comparisons between dichotomous variables. A p value ≤ 0.05 was used for statistical significance.
Results: We included a total of 253 patients, 100 with RA, 100 with SLE and 52 with SSc. Metabolic syndrome was found in 23,58% (50/212). There was no significant difference in MS prevalence between diseases, but there was a higher frequency of increased abdominal circumference in RA and low HDL in SLE. Frequencies for different features of MS in RA, SLE and SSc are detailed in table 1.

Table 1. Frequencies of MS component in SLE, SSc and RA.

	SLE	SSc	RA	p
Abdominal circumference criteria	43,4% (43/99)	46,66% (21/46)	64% (64/100)	0,009
Hypertension criteria	67% (67/100)	67,3% (35/52)	55% (55/100)	0,152
HDL criteria	55,22% (37/67)	52,63% (20/38)	16,12% (15/93)	0,000
TAG criteria	22,38% (15/67)	28,94% (11/38)	22,58% (21/93)	0,703
Glycemia criteria	7,69% (4/52)	13,15% (5/38)	25,67% (19/74)	0,114
Metabolic Syndrome	24,35% (19/78)	25% (9/36)	22,44% (22/98)	0,934

Regarding inflammatory biomarkers, there was a significant difference between biomarkers elevated in each disease: hsCRP was found more frequently in RA, E-Selectin in SSc and VCAM and PAI-1 were more prevalent in SLE.

Table 2. Frequency of high serum inflammatory biomarkers in SLE, RA and SSc.

	SLE	SSc	RA	p
hsCRP	23,52% (16/68)	26,31% (10/38)	42,85% (36/84)	0,027
E-Selectin	5,88% (4/68)	21,05% (8/38)	5,95% (5/84)	0,014
t-PA	0% (0/68)	2,63% (1/38)	5,95% (5/84)	0,111
VCAM	20,58% (14/68)	8,1% (3/37)	0% (0/83)	0,000
TNF-α	7,35% (5/68)	18,42% (7/38)	13,09% (11/84)	0,229
Endotelin	20,58% (14/68)	31,57% (12/38)	19,75% (16/81)	0,192
PAI-1	11,36% (5/44)	0% (0/38)	0% (0/83)	0,002

Conclusion: We found a similar frequency of metabolic syndrome in our cohorts of RA, SSc and SLE Paraguayan patients but they had a different clinical and serological profile, suggesting that the pathways leading to metabolic syndrome are dissimilar in each disease. We need more studies to confirm this hypothesis.
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SAT0086 THE PRESENCE OF COMORBIDITIES IN PATIENTS WITH RHEUMATOID ARTHRITIS IS ASSOCIATED WITH BAD PATIENT-REPORTED OUTCOMES (PROS)

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Background: Patients with rheumatoid arthritis have more cardiovascular comorbidities which contributes to hospitalization and mortality.
Objectives: .This study aims to investigate whether there is an association between cardiovascular comorbidities in RA with subgroup of patients and clinical findings of the disease
Methods: This study is a cross-sectional part of Rheumatoid Arthritis in Real Life (REAL), which is a multicenter prospective study conducted in Brazil, involving 13 centers specialized in the care of patients with RA. All subjects met the ARA (1987) or ACR/EULAR (2010) RA classification criteria. Subjects were submitted to clinical interview with physical exam and review of medical records. A sample of 1116 patients was selected for convenience. The association between cardiovascular comorbidities (systemic arterial hypertension (HA), diabetes mellitus (DM) type2, dyslipidemia, stroke and heart failure), the clinical characteristics and laboratory parameters of RA was evaluated through chi-square hypothesis tests, Student`s t-test, Fischer exact test, correlations test and ANOVA. Also, correction Bonferoni test was used for multiple comparisons. Differences were considered statistically significant only when $p \leq 0.05$.
Results: 89% of the patients were female, with a mean age of 58 years. 62% of patients with RA had comorbidities, with HA the most prevalent. There were statistically significant association between cardiovascular comorbidities with age (61.71±9.69years old vs 53.03±12.10) (p <0.001), lower educational level (n=282±66.5vs 143±33,5) (p <0.001), lower physical activity (n=132±73.3 vs 48±26.7) (p <0.001), disease duration (18.5±9.75 years vs 14.4±8.61) (p <0.001), positive anti-CCP test (60.5% vs 39.5%) (p = 0.027), high clinical disease activity index CDAI) (65.9%vs 34.1%) (p <0.001), DAS28VHS (3.72±1.46 vs 3.45±1.58) (p = 0.008) and HAQ score (1.00±0.76) vs 0.83±0.77 (p <0.001).
Conclusion: The frequency of cardiovascular comorbidities is high in RA patients and is associated with age, disease duration and positive anti-CCP test. It is also important to see that these comorbidities are more common in patients with lower frequency of physical activity and lower functional capacity, higher disease activity score and lower level of education. Better control of disease activity and extensive information to patients about the importance of exercise should be parallel objectives in RA.
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SAT0087 ESTIMATED SLEEP DURATION AND CARDIOVASCULAR RISK IN RHEUMATOID ARTHRITIS: A CASE CONTROL STUDY

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Background: Sleep is essential to human health and it is increasingly regarded as an important lifestyle behavior. The reduction in sleep duration have been linked to an increased risk of cardiovascular disease (CVD) and death in general population (1). Patients with rheumatoid arthritis (RA) have a higher risk of CVD and as in other pain conditions, commonly report poor sleep quality as well as feeling unrested and fatigued after sleep (2). This can be attributed to a lack of awareness of sleep hygiene.
Objectives: To determine the prevalence of self-reported estimated duration of total daily sleep, daytime naps and quality of sleep of patients with RA and without rheumatic diseases and its association with cardiovascular risk factors.
Methods: Observational, cross-sectional study. RA patients aged 40 to 75 years that fulfilled 2010 ACR/EULAR criteria and controls (without RA) were included. Sleep duration and quality, daytime naps and awareness of sleep hygiene were assessed with self-administered questionnaire. Descriptive analysis was done with frequencies (%), mean (SD), median (q25-q75). Comparisons with Chi-square, Mann-Whitney U test and Wilcoxon. Binary regression analysis was used to test association between estimated sleep duration (<6h), cardiovascular risk factors and RA diagnosis.
Results: A total of 217 subjects were included. RA patients 93 (91.2%) vs 55 (47.8%) controls were female. Mean (SD) age was RA 56.68 (± 10.73) vs 57.27 (± 10.06) controls. Estimated sleep duration (<6h) was higher in RA with 20.6% vs 8.7% in controls (p=0.012). There was no significative difference of the awareness of sleep hygiene 7.8% and 12.2% in the case and control group, respectively (p= 0.291). Obstructive sleep apnea was higher in controls 9.6% (p=0.047). The rest of the characteristics are displayed in table 1. Binary regression showed that having RA makes you 60% more likely to sleep less than six hours OR 0.40, 95% CI (0.17-0.92) (p=0.031). Patients with estimated sleep duration (<6h) had higher prevalence of Hypertension 51.6% vs 48.4% (p=0.022)

Table 1. Cardiovascular risk factors and sleep characteristics

	RA (n=102)	Controls (n=115)	*p*
Obesity, n (%)	23 (25.3)	31 (31.3)	NS
Current smoker, n (%)	12 (11.8)	21 (18.3)	NS
Diabetes Mellitus, n (%)	15 (14.7)	13 (11.3)	NS
Dyslipidemia, n (%)	32 (31.5)	30 (26)	NS
Hypertension, n (%)	40 (39.2)	33 (28.7)	NS
Cardiovascular event, n (%)	5 (4.9)	3 (2.5)	NS
Obstructive Apnea Sleep, n (%)	3 (2.9)	11 (9.6)	**0.047**
Estimated sleep time (<6h), n (%)	21 (20.6)	10 (8.7)	**0.012**
Participants taking naps, n (%)	47 (46.1)	50 (43.5)	NS
Number of daytime naps at week, median (q25-q75)	0 (0-7)	1 (0-7)	**0.007**
Duration of daytime naps (min), median (q25-q75)	0 (0-30)	15 (0-40)	NS
Good Sleep quality, n (%)	67 (65.7)	69 (60)	NS

Conclusion: Patients with RA had a higher frequency of less estimated sleep time, this is associated with hypertension, risk of deaths and major cardiovascular events. Additionally, to inflammation and coexistence of CVD risk in RA. There was an absence of awareness of most of the individuals of sleep hygiene. Therefore, in clinical practice, assessment and education of sleep patterns may be of value

in identifying higher risk individuals. An integrated care approach may contribute to the awareness of healthcare professionals to develop appropriate interventions.

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SAT0088 NO INCREASED RISK OF FALLS IN PATIENTS TREATED WITH BIOLOGICS COMPARED TO THOSE UNDER CSDMARDS

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Background: Adults with rheumatoid arthritis (RA) have an increased risk of falling. Previous studies on causes of falls have neither sufficiently nor adequately considered the effects of bDMARDs. In addition, a risk analysis of the individual substances has been lacking until now.
Objectives: To analyze the fall risk under exposure to TNFi's, abatacept (ABA), rituximab (RTX) and tocilizumab (TOC) in comparison to csDMARDs taking co-medication and other risk factors such as disease activity, comorbidities and other biological risks into account.
Methods: Data of RA patients observed in RABBIT from 01/2009 - 02/2018 with a follow-up of up to 5 years was used for the analysis. In accordance with consensus guidelines, a fall was defined as "an unexpected event in which participants come to rest on the ground, floor or other lower level" [1].
Effects of bDMARDs were examined using "inverse probability weighting" (IPW) with time-varying treatment on a monthly basis. Directed acyclic graphs were applied to support causal considerations.
Results: The percentage of patients with falls (2.7%) was significantly lower than the previously reported 10% and 50% [2]. This underreporting is explained by the fact that falls in RABBIT are reported by the physicians and are not recorded in patient diaries. In line with other studies, falls occurred with older age, longer disease duration, poorer physical function and higher DAS28. Patients with a higher number of comorbidities had a significantly higher risk of falling. The number of patients treated with analgesics was higher in the fall group and fallers had higher glucocorticoid doses. However, the values for pain and fatigue were comparable between the two groups (Table 1). The descriptive analysis showed that patients starting second / third line biologics therapy had a shorter duration from the initiation of treatment to the fall event than patients starting with csDMARDs. None of the regression models showed an increased risk for biologics compared to csDMARDs.
Conclusion: None of the inferential analyses could demonstrate an increased risk of falling for any of the bDMARDs compared to csDMARDs. Although descriptive analyses pointed to an earlier fall event in patients treated with second-/third line biologics, these results could be explained by their particular characteristics. These patients tended to be older and were more affected by RA. This suggests that these risks override the effects of bDMARDs.

Table 1. Characteristics at baseline in fallers and non-fallers

	Faller	*Non- Faller*
N	263	9405
Age, years	62.9 (11.9)	57.3 (12.6)
BMI, kg/m^2	27.4 (5.8)	27.3 (5.5)
Female, %	79.5	74.2
Disease duration, years	10.8 (9.8)	8.7 (8.5)
ACPA+, %	46.4	55.1
RF+, %	59.7	65.3
DAS28	5 (1.3)	4.8 (1.3)
% of full physical function	61.2 (24.2)	67.3 (22.7)
Joint replacement, yes %	16.3	9.8
Pain, 0 – 10 scale	5.8 (2.3)	5.8 (2.3)
Fatigue, 0 – 10 scale	5.1 (2.7)	5.2 (2.7)
No. of comorbidities	3.4 (3)	2.2 (2.2)
Osteoporosis, %	33.5	14.4
Analgesics, yes %	24	15.8
Glucocorticoid dose, mg/d	6 (5.1)	5.4 (6.3)

Values are means (SDs) unless otherwise specified

Table 2. Results of weighted* Cox regression, Reference are csDMARDs

Variables	*Univariate HR*	*95% CI*	*Weighted HR*	*95% CI*
TNFi's	1.12	(0.85; 1.48)	1.05	(0.80; 1.39)
ABA	1.00	(0.57; 1.74)	0.98	(0.57; 1.70)
RTX	1.39	(0.88; 2.22)	1.09	(0.65; 1.81)
TOC	0.88	(0.59; 1.33)	0.77	(0.50; 1.18)

*Include: age, disease duration, gender, education, joint replacement, fatigue, functional status, pain, stiffness, analgesics, no. of comorbidities, selected comorbidities

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SAT0089 FEATURES OF THE SECRETION OF INTERLEUKIN-6, INTERLEUKIN-10, TUMOR NECROSIS FACTOR ALPHA IN PATIENTS WITH RHEUMATOID ARTHRITIS ASSOCIATED WITH ANEMIA

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Background: Anemia is widespread in rheumatic patients and is an important extra-articular manifestation that correlates with physical disability and increased mortality. The pathogenesis of such anemia is complex and multifactorial, including due to the influence of pro-inflammatory cytokines.
Objectives: Our aim was to study the characteristics of the secretion of interleukin-6 (IL-6), interleukin-10 (IL-10), tumor necrosis factor-alpha (TNF-α) in patients with rheumatoid arthritis (RA) with anemia of chronic diseases (ACD), iron deficiency anemia (IDA) and a combination of ACD / IDA, as well as to study the effect of these cytokines on the development of anemia.
Methods: There were examined 69 (54 (7 men /47 women, 50.6 ± 4.1 years) with anemia, 15 (6 men/9 women, 53.5 ± 2.74 years) without anemia) of RA patients. According to the criteria of Van Santen and Worwood, by determining the transferrin saturation index (TSI), ferritin, C-reactive protein (CRP), patients were divided into 4 groups: group 1 - ACD, 22 (5/17) patients (hemoglobin 79 [IQR, 95.6-111], red blood cells 3.5 [IQR, 3.6-4], TSI 25 [IQR, 14.7-26.2], ferritin 326.2 [IQR, 197.8-451.7], CRP 63.7 [IQR, 10.2-104.8]), group 2 - ACD / IDA, 18 (0/18) patients (hemoglobin 101 [IQR, 94-114], red blood cells 3.9 [IQR, 4-4.4], TSI 12.5 [IQR, 7.7-15], ferritin 50.1 [IQR, 11.9-74.9], CRP 45.8 [IQR, 17.6-54.9]), group 3 - IDA, 14 (2/12) patients (hemoglobin 108 [IQR, 100-115], red blood cells 4.5 [IQR, 4.1-4.9], TSI 9.7 [IQR 3-14], ferritin 21.8 [IQR, 7.2-28.9], CRP 8.6 [IQR, 2.7-8.6]), group 4 (control) - 15 patients without anemia (hemoglobin 141.4 [IQR, 133-147], red blood cells 4.6 [IQR, 4.3-4.9], TSI 23.1 [IQR, 16.6-27.8], ferritin 78.5 [IQR, 36-90.7], CRP 4.6 [IQR, 1.2-5.8]). The diagnosis of rheumatoid arthritis was made based on the 2010 ACR/EULAR classification criteria. The number of red blood cells and hemoglobin levels were determined on a Sysmex XS-500i analyzer (Japan). Concentrations of ferritin, CRP, TSI were determined on an Olympus Au 480 analyzer (Beckman Coulter, USA). Concentrations of IL-6, IL-10, and TNF-α were determined using a Stat Fax 2100 analyzer (Awareness Technology Inc., USA). The significance of differences between several unrelated groups was determined using the Kruskal-Wallis test at a significance level (p) of less than 0.05. To assess the relationship between the variables, the Spearman correlation coefficient (r) was calculated
Results: In the ACD group, there were the highest concentrations of CRP, ferritin in comparison with the other groups (p <0.05). TSI in the ACD group was higher compared with the IDA and ACD / IDA groups (p <0.05) and did not differ from the control group (p> 0.05). The maximum concentration of IL-6 was found in the ACD group (36.2 [IQR, 6.7-41]) compared with the ACD / IDA group (21.7 [IQR, 7.2-20.4]) (p <0, 05) and the IDA group (5.9 [IQR, 1.5-3.7]) (p <0.05) and without anemia (2.7 [IQR, 1.5-3) (p <0.05). Regarding IL-10 and TNF-α, no intergroup

differences were found. A moderate correlation was found between the number of red blood cells and the concentration of IL-6 (r = -0.3), IL-10 (r = -0.4), TNF-α (r = -0.3). The relationship between the concentration of hemoglobin and IL-6 (r = -0.6), IL-10 (r = -0.4), TNF-α (r = -0.3) was revealed.

Conclusion: In RA patients, IDA, ACD, as well as their combination, may occur. It is very important to clarify the genesis of anemia. ACD should be isolated separately because it has a complex pathogenesis, one of the important components of which are cytokines and their effect on erythropoiesis. The increased concentration of IL-6 in the group of patients with ACD, as well as the presence of a correlation between IL-6, red blood cells and hemoglobin, indicate the importance of this cytokine in the development of anemia. An increase in the concentration of ferritin and CRP also reflects the inflammatory genesis of anemia in patients with this anemia. The presence of a correlation between IL-10, TNF-α and hemogram indices suggests their influence on the development of anemia.

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SAT0090 EFFECTS OF ADHERENCE TO MEDITERRANEAN DIET ON RHEUMATOID ARTHRITIS IMPACT OF DISEASE (RAID) SCORE

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Background: Mediterranean diet (MD) is a well-balanced, nutritionally adequate and potentially anti-inflammatory diet that encompasses all food groups. Presently, there are conflicting data about the benefits of MD in rheumatoid arthritis (RA). Not enough evidence support a role of MD in the prevention and treatment of RA, and a modest impact of MD on laboratory parameters has been described. Greater effect on subjective aspects of the disease such as joint pain, morning stiffness, and fatigue was reported.

Objectives: To investigate whether the adherence to MD affects RA perception as measured by Rheumatoid Arthritis Impact of Disease (RAID) score.

Methods: Consecutive patients <65 years with RA attending our outpatient clinic were enrolled in this cross-sectional study. For each patient we collected: 1) RAID that consists of 7 single-item domains (pain, functional disability, fatigue, sleep, physical well-being, emotional well-being and coping), each rated by patients on an 11-point numerical rating scale from 0 (best) to 10 (worst) [1], and 2) MD score, a self-reported questionnaire that evaluates the adherence to MD through the consumption of 11 food groups, ranging from 0 (no adherence) to 55 (high adherence) [2]. Univariate analysis was performed using MD score as independent variable. Moreover, to evaluate the adjusted relationship between the single item of RAID and MD score, a multiple regression model was used.

Results: 205 RA patients were enrolled: median age at visit 53 (q1-q3: 44-59) years, female 80.5 %. The median MD and RAID score were 35 (q1-q3: 32-39) and 2.42 (q1-q3: 0.63-4.51) respectively.

RAID total score had a statistically significant negative relationship with MD score (regression coefficient -0.08; p-value=0.016). Concerning the single RAID items, a statistically significant negative association was found for pain (regression coefficient -0.08; p-value=0.025), functional disability (regression coefficient -0.13; p-value<0.001), sleep (regression coefficient -0.08; p-value=0.041), physical well-being (regression coefficient -0.08; p-value=0.027) and coping (regression coefficient -0.11; p-value=0.008).

Multiple regression analysis to evaluate the relationship between significant RAID items and MD score did not show any statistical significance as all items are strongly related to each other.

Conclusion: To our knowledge, this is the first study addressing the relationship between the adherence to MD and the perception of RA impact. A better MD adherence was associated with lower self-reported composite total RAID score as well as lower pain, functional disability, sleep, physical well-being and coping. The effect of MD adherence on overall RAID is relevant but, at the same time, a prominent effect of one single item on the others could not be documented. This study confirmed the importance of non-pharmacological interventions, such as diet, in RA management.

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SAT0091 SURVEY OF CARDIOVASCULAR DISEASE AND RISK FACTOR MANAGEMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS ACROSS 5 WORLD REGIONS: RESULTS FROM THE SURF-RA

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Background: Patients with rheumatoid arthritis (RA) are at high risk for cardiovascular disease (CVD).

Observational data suggest a need for improved risk factor recording and management in such subjects.

Objectives: The aim of this survey was to evaluate updated information on CVD risk factors, comorbidities, RA and CVD preventive medication in patient with RA.

Methods: The audit is termed **SU**rvey of cardiovascular disease **R**isk **F**actors in patients with **R**heumatoid **A**rthritis (SURF-RA) and was performed in 53 centres in 19 countries across 5 world regions during 2014 and 2019. SURF-RA is part of the SURF family of audits which have been performed in patients with CHD, in primary care[2], and now in patients with stroke and SLE. Data including demographics, RA disease characteristics, CVD, risk factors and medications was collected. The survey was approved by the Data Protection Officer (2017/7243) and a General Data Protection evaluation has been performed (10/10-2018).

Results: Among 14 503 patients with RA in West (n= 8 493) and East (n=923) Europe, Latin (n=407) and North (n=4030) America and Asia (n=650) the mean (SD) age was 59.9 (13.6) years, and 2/3 or more were female (table). RA disease duration was comparable across the world regions, ranging from 9.9 to 12.6 years. The average disease activity was low [disease activity score including 28 joints and C-reactive protein; DAS28CRP: mean (SD): 2.6 (1.2)]. The prevalence of atherosclerotic CVD (ASCVD) was lowest in Latin America (2.5%) and highest in East Europe (21.4%), and this pattern was similar regarding familial premature CVD. The mean prevalence (% of each entity) of blood pressure above 140/90 mmHg was 5.3%, of low density lipoprotein cholesterol > 2.5 mmol/L: 63.3%. Overall, 29% used anti-hypertensive medication, lowest in West Europe (17.4%) and highest in East Europe (57.0%), and 26.4% used lipid lowering agent(s), lowest in Asia (7.2%) and highest in North America (31.1%). Body mass index > 30 kg/m2 was present in 26.6%, with the smallest waist circumference in Asia [mean (SD): 84.1 (13.6) cm] and highest in East Europe [92.5 (15.5) cm]. The proportion of current smokers was on average: 16.2 %, lowest in Asia (7.8%) and highest in East Europe (28.5%).

Conclusion: The high prevalence of CVD risk factors and ASCVD in patients with RA across five world regions shows that there is still an unmet need for vigilance and improved implementation of preventive measures in this high CVD risk patient population.

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	All	West Europe	East Europe	Latin America	North America	Asia	p-value
Number of patients	14503	8493	923	407	4030	650	
Age mean(SD)	59.8 (13.6)	60.7 (13.2)	58.8 (11.8)	52.8 (11.6)	59.4 (14.8)	55.7 (13.1)	<0.001
Sex female (%)	74.5	74.1	78.5	92.4	72.2	77.3	
Disease duration (yrs) mean(SD)	10.8 (9.5)	10.5 (9.5)	12.1 (9.3)	9.9 (7.5)	12.6 (9.8)	10.5 (9.8)	<0.001
DAS28-CRP mean(SD)	2.6 (1.2)	2.5 (1.1)	2.9 (1.2)	2.8 (1.3)	2.8 (1.2)	2.8 (1.4)	<0.001
Atherosclerotic CVD (%)	13.3	11.4	21.4	2.5	16.2	10.3	<0.001
Lipid lowering medication (%)	26.4	25.1	28.5	22.4	31.1	7.2	<0.001
Any anti-hypertensive (%)	29.0	17.4	57.0	24.8	46.8	31.8	<0.001

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SAT0092

CARDIOVASCULAR RISK ASSESSMENT IN PATIENTS WITH AUTOIMMUNE RHEUMATIC DISEASES: AN ITALIAN RHEUMATOLOGISTS' SURVEY

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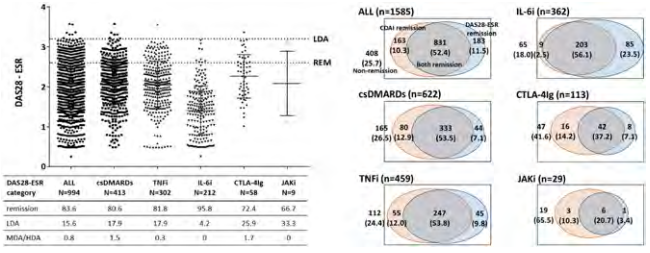
Background: Cardiovascular (CV) disease is the leading cause of morbidity and mortality in patients with inflammatory arthritis. The growing attention to the CV risk characterizing patients with autoimmune inflammatory disease led EULAR to provide recommendations on CV risk management (1). To date, there are no data on the adherence to EULAR recommendation among Italian rheumatologists.
Objectives: Our objective was to measure the level of awareness and the attitude to manage CV risk.
Methods: Italian rheumatologists were invited to anonymously answer a web-based questionnaire designed by the steering committee of the Cardiovascualr and Obesity in Rheumatic Diseases (CORDIS) study group of the Italian Society of Rheumatology. The first part of the questionnaire concerned demographic information; the subsequent questions concerned the attitude to assess CV risk and the limitations for not assessing, the specific CV risks considered in the clinical practice and their management. Data are presented using standard summary statistics and were expressed as mean+/-standard deviation or median (interquartile range) according to variables' distribution.
Results: One thousand-three hundred rheumatologists (of whom 500 are under 40 and 100 over 70 years of age) have been invited by email to complete the survey. The questionnaire has been filled by 102 rheumatologists (7.85%) (53 females and 49 males) with a median age of 38 years (32-48) and a median of 4 (0-15) years of specialization. Most of the physician who answered the questionnaire works in University Hospitals (67/102; 65.7%), 22 out of 102 (21.6%) in non-academic Hospitals, and the remaining 12,7% in territorial outpatient clinics.
When asked if they usually evaluate CV risk in patients with autoimmune rheumatic diseases, 67/102 (67.2%) answered positively, 18 no (17.6%) and 7 did not answer the question; 82% of those who routinely assess the CV do it by themselves. The barriers limiting the assessment of CV risk included: i) lack of time (79%); ii) complex management (12%); inadequate training (9%).
As for the CV risk factors, lipid profile, hypertension and diabetes are assessed by most of the rheumatologists (90%, 89% and 88%, respectively), family history by 78% and body mass index by 75.3% and waist circumference only by 25% of those who completed the survey.
Finally, only 18.6% stated that they manage by themselves CV risk in patients with autoimmune rheumatic diseases while 50% refer patients to other specialists and 23.4% to general practitioner.
Conclusion: Despite the growing awareness on the CV risk characterizing patients with autoimmune rheumatic disease, about one third of young Italian rheumatologists does not strictly adhere to the EULAR recommendations on CV management, mostly due to insufficient time during the routine care visits.
References:
[1] Agca R et al. Ann Rheum Dis 2017; 76: 17-28.
Disclosure of Interests: Francesca Romana Spinelli Grant/research support from: Pfizer, Speakers bureau: Lilly, BMS, Celgene, Fabio Cacciapaglia Speakers bureau: BMS; Roche; Pfizer; Abbvie, Fabiola Atzeni: None declared, Gianluca Erre: None declared, Andreina Manfredi: None declared, Elena Bartoloni Bocci: None declared, Matteo Piga: None declared, Garifallia Sakellariou Speakers bureau: Abbvie, Novartis, MSD, Ombretta Viapiana: None declared, Elisa Gremese Speakers bureau: Abbvie, BMS, Celgene, Jannsen, Lilly, MSD, Novartis, Pfizer, Sandoz, UCB
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SAT0093

CDAI AND DAS28 IN THE MANAGEMENT OF RHEUMATOID ARTHRITIS IN CLINICAL PRACTICE

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Background: The primary therapeutic target for rheumatoid arthritis (RA) is remission, assessed using validated composited measures. Currently, index-based remission frequently used in clinical practice are disease activity (CDAI) and disease activity score for 28 joints (DAS28). Generally, CDAI is believed more stringent than DAS28 in assessing clinical remission, however, this confirmation was mainly derived from trial results.
Objectives: To investigate the real-world performance of CDAI and DAS28 -erythrocyte sedimentation rate (ESR) in RA.
Methods: We reviewed consecutive RA patients who are receiving any disease modifying anti-rheumatic drug (DMARDs) in Keio University Hospital between 2016 and 2017 and collected medical information. We focused on the patients in CDAI remission and/or DAS28-ESR remission at the time of last visit, and analyzed their clinical characteristics.
Results: A total of 1585 patients with RA were reviewed. Their characteristics were mean age of 64 years old, female of 84% and mean disease duration of 12.0 years. Current treatments were conventional synthetic (cs) DMARDs alone, TNF inhibitors (TNFi), IL-6 receptor inhibitors (IL-6i), CTLA-4Ig, and JAK inhibitors (JAKi) in 39.2%, 29.0%, 22.8%, 7.1%, and 1.8% patients, respectively. Of them, 62.7% were in CDAI remission and 64% were in DAS28-ESR remission. Among patients in CDAI remission, the proportion of DAS28-ESR non-remission was 19.4% in those treated with csDMARDs, 18.2% treated with TNFi, 4.2% treated with IL-6i, 27.6% treated with CTLA-4Ig, and 33.3% treated with JAKi (Figure). In contrast, among patients in DAS28 remission, the proportion of CDAI non-remission was 11.7% in those treated with csDMARDs, 15.4% treated with TNFi, 29.5% treated with IL-6i, 16.0% treated with CTLA-4Ig, and 14.3% treated with JAKi. Venn diagrams of CDAI remission and DAS28-ESR remission demonstrated that more patients satisfied the CDAI remission criteria without satisfying the DAS28-ESR remission criteria than vice versa, except for those treated with IL-6i (Figure). Patients in CDAI remission and DAS28-ESR non-remission had higher C-reactive protein, ESR and comorbidity rates (0.37 vs 0.07 mg/dL, p<0.001; 45.7 vs 8.0 mm/h, p<0.001; 26.4 vs 18.0%, p=0.07, respectively), and those in CDAI non-remission and DAS28-ESR remission had worse patient-reported outcomes including patient global assessment and health assessment questionnaire-disability index (31.1 vs 9.5 mm, p<0.001; 0.82 vs 0.41, p<0.001, respectively). Patients in both CDAI and DAS28-ESR remission were apparently in better disease activity than those who met either criteria.
Conclusion: Assessing patients with two composite measures simultaneously is important to evaluate patients' condition from view points of RA itself and comorbidities and adjust treatment appropriately.
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DAS28-ESR category	ALL N=994	csDMARDs N=413	TNFi N=302	IL-6i N=212	CTLA-4Ig N=58	JAKi N=9
remission	83.6	80.6	81.8	95.8	72.4	66.7
LDA	15.6	17.9	17.9	4.2	25.9	33.3
MDA/HDA	0.8	1.5	0.3	0	1.7	0

Disclosure of Interests: Satoshi Takanashi: None declared, Yuko Kaneko Speakers bureau: Dr. Kaneko reports personal fees from AbbVie, personal fees from Astellas, personal fees from Ayumi, personal fees from Bristol-Myers Squibb, personal fees from Chugai, personal fees from Eisai, personal fees from Eli Lilly, personal fees from Hisamitsu, personal fees from Jansen, personal fees from Kissei, personal fees from Pfizer, personal fees from Sanofi, personal fees from Takeda, personal fees from Tanabe-Mitsubishi, personal fees from UCB, Tsutomu Takeuchi Grant/research support from: Eisai Co., Ltd, Astellas Pharma Inc., AbbVie GK, Asahi Kasei Pharma Corporation, Nippon Kayaku Co., Ltd, Takeda Pharmaceutical Company Ltd, UCB Pharma, Shionogi & Co., Ltd., Mitsubishi-Tanabe Pharma Corp., Daiichi Sankyo Co., Ltd., Chugai Pharmaceutical Co. Ltd., Consultant of: Chugai Pharmaceutical Co Ltd, Astellas Pharma Inc., Eli Lilly Japan KK, Speakers bureau: AbbVie GK, Eisai Co., Ltd, Mitsubishi-Tanabe Pharma Corporation, Chugai Pharmaceutical Co Ltd, Bristol-Myers Squibb Company, AYUMI Pharmaceutical Corp., Eisai Co., Ltd, Daiichi Sankyo Co., Ltd., Gilead Sciences, Inc., Novartis Pharma K.K., Pfizer Japan Inc., Sanofi K.K., Dainippon Sumitomo Co., Ltd.
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SAT0094

ASSESMENT OF BONE MINERAL DENSITY AND FRACTURE RISK IN PATIENTS WITH RHEUMATOID ARTHRITIS AND SARCOPENIA

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Background: The problem of sarcopenia (SP) in rheumatoid arthritis (RA) is particularly significant in terms of assessing the risk of fractures, since SP leads to falls, which are an independent risk factor for fractures along with RA and osteoporosis.
Objectives: To evaluate the bone mineral density (BMD) and fracture risk in women with RA and SP.
Methods: 79 women with RA based on the 2010 ACR/EULAR classification criteria were included: 20 (25%) women with confirmed SP (age median 59 [53; 64]) according to EWGSOP2 criteria and 59 (75%) women without SP (age median 60 [55; 67]) (p>0.05). We assessed clinical data: age, body mass index (BMI), disease duration, anthropometric measurements, C-reactive protein level, disease activity score in 28 joints-erythrocyte sedimentation rate (DAS28-ESR), previous medication use including glucocorticoids and methotrexate, muscle strength and function. Dual-energy X-ray absorptiometry (DXA) to measure BMD of lumbar spine (LS), femoral neck (FN) and total hip (TH) was performed. The 10-year probability of major osteoporotic fracture (clinical spine, forearm, hip or shoulder fracture) and the 10-year probability hip fracture was calculated using the Russian version of the FRAX® tool. Statistical analysis was performed using non-parametric methods. All patients signed an informed consent to participate.
Results: Median BMD in LS was 0.892 [0.772; 1.024] g/cm^2 in patients with SP and 0.910 [0.785; 1.028] g/cm^2 - without SP (p>0.05). There was significant difference between groups in the proximal femur BMD: 0.760 [0.731; 0.826] g/cm^2 in TH and 0.681 [0.607; 0.703] g/cm^2 in FN in patients with SP and 0.838 [0.735; 0.921] g/cm^2 in TH and 0.719 [0.622; 0.804] g/cm^2 in FN in patients without SP (p=0.009 and p=0.048, respectively). The frequency of osteoporosis was 35% and 22% in patients with and without SP (p>0,05). The 10-year probability of major osteoporotic fracture with / without femoral neck BMD data was 22,0% [17,0; 32,0] / 19,5% [18,5; 22,5 and 13,3% [9,8; 18,5] / 12,8% [9,3; 17,0] in patients with SP and without SP (p<0.05) and the 10-year probability of hip fracture with / without femoral neck BMD data - 3,1% [3,0; 7,5] / 3,1% [2,3; 3,3] and 1,4% [0,9; 2,78] / 0,65 [0,4; 1,7], respectively (p<0.05).
Conclusion: There were no differences in the frequency of osteoporosis between patients with SP and without SP, however women with SP had proximal femur BMD less than women without SP. The probability of major osteoporotic fracture and hip fracture was significantly higher in patients with RA and SP compared with patients without SP.
Disclosure of Interests: None declared
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SAT0095 REAL LIFE SEVERE INFECTIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS ON TREATMENT WITH BIOLOGICAL THERAPY AND JAKI

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Background: Infections are one of the main complications among patients with rheumatoid arthritis (RA) with immunosuppressive treatment. The differences between treatments and the influence of other factors is unclear.
Objectives: To evaluate the frequency and factors associated with serious infections in patients with RA treated with biological therapy (BT) and JAKi and the differences between treatments.
Methods: Descriptive and retrospective study (January 2015-December 2019) of patients with RA treated with BT (TNFi, non-TNFi) and JAKi (tofacitinib, bariticinib) in a single center. Severe infection was considered a life-threatening infection or one that required hospitalization and intravenous treatment. Epidemiological variables, clinical characteristics, Charlson comorbidity index, type of BT or JAKi and concomitant treatment were collected.
For the analysis frequencies and percentages are used in qualitative variables, and mean ± SD in the quantitative ones. Statistical analysis was performed with IBM SPSS v 23.
Results: We registered 246 patients (85% women) mean aged 55.8±13.5 years. RF was positive in 87%, anti-CCP in 75.6% and 15.4 % presented extra-articular manifestations (nodulosis 8.9%, intersticial lung disease 5.3%, other 1.2%). At the start of the study 149 patients (60.6%) were with TNFi, 79 (32.1%) non-TNFi and 18 (7.3%) with JAKi and non-biologic DMARD (nbDMARDs) were used in 84.1% of cases (methotrexate 71.2%, leflunomide 21.4%, other 7.4%).
During the study 176 patients (71.5%) continued with the same treatment and in 70 (28.5%) it was changed at least once. 5 patients discontinued the treatment. At the end of the study, 124 patients (50.4%) were with TNFi, 83 (33.7%) non-TNFi and 34 (13.8%) with JAKi.
Severe infection was developed in 17 (6.9%) patients (respiratory 7, se sis 4, urinary 3, cellulitis 2, osteomyelitis 1) among them 2 patients had severe infection and herpes zoster and 3 developed a second infection. 9 patients were with TNFi (52.9%), 6 non- TNFi BT (35.3%) and 2 JAKi (11.8%). Table 1

TABLE 1. CHARACTERISTICS OF PATIENTS WITH INFECTION VS. WITHOUT INFECTION

	INFECTION		
	YES n:17	**NO** n:229	**p**
FEMALE, n (%)	13 (76.5)	196 (85.6)	0.297
AGE years, (mean±SD)	60.8 ± 13	55.4 ± 13.5	0.112
AGE ≥ 65 n (%)	9 (52.9)	63 (27.5)	0.070
RF +, n (%)	17 (100)	197 (86)	0.139
ANTI-CCP +, n (%)	14 (82.4)	172 (75.1)	0.770
ILD, n (%)	1 (25)	12 (35.3)	0.708
ALCOHOL, n (%)	1 (5.9)	19 (8.3)	1.00
SMOKER, n (%)	5 (29.4)	60 (26.2)	0.772
COPD, n (%)	5 (29.4)	24 (10.5)	**0.036***
DM, n (%)	7 (41.2)	19 (8.3)	**0.001***
SEVERE LIVER DISEASE, n (%)	2 (11.8)	1 (0.4)	**0.013***
RENAL INSUFFICIENCY, n (%)	2 (11.8)	3 (1.3)	**0.040***
PERIPHERAL VASCULAR DISEASE, n (%)	7 (41.2)	25 (10.9)	**0.003***
CHARLSON INDEX (mean±SD)	2.35 ± 2.1	0.66 ± 1.2	**0.014***
TNFi, n (%)	9 (52.9)	115 (50.2)	
NON-TNFi n (%)	6 (35.3)	77 (33.6)	
JAKi, n (%)	2 (11.8)	32 (14)	
nbDMARDs, n (%)	12 (70.6)	156 (68.1)	0.833
GCC, n (%)	13 (76.5)	115 (50.2)	**0.037***

The inflammatory activity of RA was mild at the time of infection (DAS28: 2.7±1.2). The median time until infection was: TNFi 28.05 months, non- TNFi BT 25.03 and Jakinibs 16.97.
The Charlson index, concomitant treatment with glucocorticoids (GCC) (not treatment with nbDMARDs), chronic obstructive pulmonary disease (COPD), diabetes (DM), severe liver disease and moderate-severe renal insufficiency were statistically significantly associated with infection. Table 1
Conclusion: In our study, 6.9% of patients with RA treated with BT or JAKi developed severe infection during 4 years of follow-up. Concomitant GCC therapy and comorbidity increased the risk of presenting this complication.
Disclosure of Interests: None declared
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SAT0096 DISCORDANCE BETWEEN SUBJECTIVE AND OBJECTIVE INDEX OF THE DISEASE ACTIVITY SCORE MAY REDUCE THE CORRELATION BETWEEN CLINICAL AND ULTRASOUND ASSESSMENT IN RHEUMATOID ARTHRITIS

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Background: There was discordance between subjective and objective index of the disease activity score, or between clinical parameters and ultrasound findings in some RA patients. Therefore, we set out to determine whether the discordance between subjective and objective index of the composite score could reduce the correlation between clinical and ultrasound parameters in RA.
Objectives: To investigate whether the discordance between tender and swollen joint count (TJC and SJC) as well as patient's and evaluator's global assessment (PGA and EGA) influences the correlation between clinical and US parameters in RA.
Methods: RA patients with available ultrasonography of 28 joints from Jan 2014 to Jan 2018 were enrolled in the study. Gray-scale (GS) synovial hypertrophy and Power Doppler (PD) synovitis were measured and semi-quantitatively graded. The total GS/PD score was the sum score of 28 joints. SJC and TJC based on 28 joints, PGA and EGA of all the patients were evaluated by one rheumatologist. The numeric difference between TJC and SJC (ΔTSJ) and that between PGA and EGA (ΔPEG) were calculated. The correlation between clinical and ultrasound parameters in different ΔTSJ and ΔPEG subgroups was explored.
Results: Totally 163 patients were enrolled in the study. Clinical composite disease activity scores and all the components were significantly correlated with the total GS and PD scores (p<0.01 for all). But the relevance between the clinical disease parameters and total PD score became weak, with the increase of ΔTSJ. For the patients with ΔTSJ > 5, the total PD score was only correlated with CRP, EGA and PGA, while the total GS score was only correlated with CRP. Similarly, no correlation between total PD score and clinical parameters, except for SJC, was observed in patients with ΔPEG < 0 (p < 0.05).
Conclusion: Total PD/GS score was correlated well with the clinical parameters of disease activity, including both the subjective and objective indexes. But for patients with ΔTSJ > 5,there was no correlation between total GS/PD scores and clinical composite disease activity scores, except that only the objective index (CRP, SJC and EGA) were more likely to correlate with total GS/PD scores.

Disclosure of Interests: None declared
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SAT0097

DO COMORBIDITIES IMPACT PERSISTENCE OF FIRST TUMOR NECROSIS FACTOR INHIBITOR TREATMENT IN RHEUMATOID ARTHRITIS? DATA FROM TURKBIO

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Background: Studies indicate that patients with rheumatoid arthritis (RA) are at increased risk of developing several comorbid disorders. Comorbidities affect treatment decisions, the effectiveness of the treatment, quality of life, RA prognosis, and survival rate [1].
Objectives: The aim of this *study* to investigate the impact of comorbidity on the first TNF inhibitor treatment persistence in RA.
Methods: In the TURKBIO database, patients with an ICD 10-diagnosis of RA (M05 or M06) who started TNF inhibitor therapy between January 2011 and June 2019 were enrolled. Demographic and clinical characteristics, acute phase reactants, disease activity scores (DAS 28 CRP, HAQ, CDAI, VAS global), initial comorbidities and numbers, drug persistence, were evaluated. Kaplan-Meier plots and Cox proportional hazard regression analyses were performed.
Results: A total of 1172 patients >18 years of age treated with TNF-α inhibitors were included in the study. The most prevalent comorbidities were: hypertension in 262 patients (32.6%), obesity in 254 (32.6%), osteoporosis in 178 (22.3%), chronic lung disease in 143 (17.9%) and depression in 126 (15.8%). The baseline characteristics are summarised in Table 1. The presence of comorbidity did not affect the survival rate of the first TNF inhibitor therapy in the RA patients (p: 0.65). Comorbidities had no effect on DAS28 CRP (> 1.2 reduction) responses at 6 and 12 months of treatment (p: 0.18, p: 0.83, respectively). As the mean disease duration increases, the persistence of the first TNF inhibitor decreases by 5%.
Conclusion: This study demonstrated the increasing burden of comorbidities in RA. However, it suggested that the presence and number of comorbidities did not influence the rate of persistence in the first TNF inhibitor drug and the response to treatment.

Table 1 Characteristics of RA patients

Female, n (%)	935 (79.8)
Age, years*	51.0 ±13.7
Current smokers, n (%)	256 (23.2)
RF Positivity, n (%)	404 (55.6)
Anti-CCP Positivity, n (%)	430 (58.2)
X-ray Erosion, n (%)	317 (61.9)
ESR, mm/h*	31.2±21.9
CRP, mg/L*	17.2±3.9
DAS 28-CRP*	3.8±1.6
VAS global*	46.6±28.6
HAQ*	0.9±0.7
First TNFi	
Etanercept, n (%)	525 (38.7)
Adalimumab, n (%)	379 (27.9)
Infliximab, n (%)	118 (8.7)
Certolizumab, n (%)	188 (13.8)
Golimumab, n (%)	147 (10.9)

* mean ±S.D
RF, Rheumatoid factor; Anti-CCP, Anti- cyclic citrullinated peptid; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; DAS28–CRP, Disease Activity Score using 28 joints–CRP; VAS, Visual analog scale; HAQ, Health Assessment Questionnaire

References:

[1] Gabriel, S.E. and K. Michaud, *Epidemiological studies in incidence, prevalence, mortality, and comorbidity of the rheumatic diseases.* Arthritis research & therapy, 2009. **11**(3): p. 229.

Disclosure of Interests: None declared
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SATURDAY, 06 JUNE 2020

Rheumatoid arthritis - biological DMARDs

SAT0098

TREATMENT OF A COHORT OF PATIENTS WITH INTERSTITIAL LUNG DISEASE AND RHEUMATOID ARTHRITIS

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Background: There is no specific treatment for interstitial lung disease (ILD) secondary to Rheumatoid Arthritis (RA) other than the treatment of RA without extra-articular involvement. Current regimens usually include corticosteroid therapy with or without immunosuppressants (IS), there is no consensus for the treatment.
Objectives: To analyze the different treatment regimens in a cohort of patients with ILD and RA in our clinical practice.
Methods: Descriptive study of 57 patients treated in our Hospital (1/1/2018 until 12/31/2019) with a diagnosis of RA (ACR 2010 criteria) and secondary ILD.
The most recent American Thoracic Society (ATS)/European Respiratory Society (ERS)/Japanese Respiratory Society (JRS)/Latin American Thoracic Society (ALAT) guidelines define three HRCT (High Resolution Computed Tomography) patterns of fibrosing lung disease in the setting of idiopathic pulmonary fibrosis (IPF): definite Usual Interstitial pneumonia (UIP) (traction bronchiectasis and honeycombing), possible UIP and inconsistent with UIP. The distinction between definite UIP and possible UIP in these to the presence or absence of honeycombing. Approved by the Ethics Committee. Quantitative variables are expressed as mean (SD) and dichotomous variables as percentages (%). Statistical analysis with SPSS version 21.
Results: 21 men and 36 women were included, with a mean age of 69 ± 10 years (mean ± SD), history of smoking (smokers 14%, non-smokers 43%, former smokers 42%). Clinical ILD at diagnosis (dyspnea 61%, dry cough 56%, crackling 70%, acropachy 7%). 84% were positive rheumatoid factor and 70% positive anticitrullinated protein antibody.
Diagnosis of ILD by HRCT in 100% of patients with different patterns: defined UIP 26 (45%), probable UIP 2 (3%) and not UIP 29 (50%). The diagnosis of ILD was confirmed by biopsy in 12 patients.
79% underwent (T) treatment prior to the diagnosis of ILD with glucocorticoids and disease-modifying drugs (DMARD). Among the traditional DMARDs used were: Methotrexate 68% (there were no cases of MTX pneumonitis), Leflunomide 47%, Hydroxychloroquine 26% and Sulfasalazine 21%. Biological therapy in 15 patients: Etanercept 19%, Adalimumab 5%, Infliximab 3% and Certolizumab 2%. Two patients presented an exacerbation and rapid progression of the ILD during the T with Etanercept with the final result of death.
T with IS after the diagnosis of ILD in 80% of patients (Azathioprine 15, Rituximab 14, Abatacept 10, Tocilizumab 4, Sarilumab 1, Mofetil mycophenolate 1 and Cyclophosphamide 1).
Two patients with defined UIP perform T with antifibrotic: 1st Nintedanib (INBUILD Trial, This article was published on September 29, 2019, at NEJM.org) 2nd Pirfenidone (initial diagnosis of IPF Idiopathic Pulmonary Fibrosis and subsequent of seropositive RA with UIP). Both improved greater than 10% in forced vital capacity (FVC) and diffusion capacity of the lung for carbon monoxide (DLCO) in the 6 months after onset of T.
Conclusion: Our results, in general, agree with what is published in the literature. Prospective, multicentre and larger sample studies are necessary to better define which patients would benefit more from IS T or antifibrotic T (or if the antifibrotic should be added to the previous IS).
Disclosure of Interests: None declared
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SAT0099

BMI AND TREATMENT SURVIVAL IN RA PATIENTS STARTING TREATMENT WITH TNFA-INHIBITORS: LONG TERM FOLLOW-UP IN THE REAL LIFE METEOR REGISTRY

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Background: BMI appears to be associated with treatment response on TNFi(nhibitors) in rheumatoid arthritis (RA), but large heterogeneity between studies exists. More extreme BMI categories are rarely studied and it is unclear if differences exist between various TNFi.[1]

Objectives: To study whether there is an association between BMI category and drug survival in RA patients starting treatment with various TNFi in a real life longitudinal international registry.

Methods: Data from 5230 RA patients starting a TNFi were included from the METEOR registry. Timing of follow-up visits was daily practice based. Follow-up was censored at 5000 days (±13.5 years). Patients were divided into 6 BMI categories (WHO definition): underweight BMI <18.5, normal weight BMI 18.5-25, pre-obesity BMI 25-30, obesity class I BMI 30-35, class II BMI 35-40, and class III BMI >40. Missing data were imputed using chained equations. The association between BMI category and time on treatment was investigated using Kaplan-Meier (KM) curves and Cox regression analyses, for time on first TNFi and for the first prescribed course of adalimumab (ADA), etanercept (ETA) and infliximab (IFX) separately. All analyses were adjusted for the potential confounders age, gender, smoking, baseline DAS28, concomitant glucocorticoid use and country. Potential effect modification by reported pain was tested by adding an interaction term between BMI category and baseline pain category (VAS pain 0-25, 25-50, 50-75 and 75-100).

Results: Most patients had a normal weight (46%) or pre-obesity (32%). 4% of patients were underweight, 10% had obesity class I, 3% obesity class II and 1% obesity class III. N=2936 patients ever started ETA, n=2069 ADA, n=1390 IFX, n=263 certolizumab and n=84 golimumab. The KM curve in fig 1A shows TNFi survival in patient starting their first TNFi per BMI category. Patients with normal weight and pre-obesity had longest drug survival and patients with obesity class II and especially patients with obesity class III had shortest drug survival. The adjusted Cox regression support these findings, with statistically significantly shorter drug survival for patients with obesity class III [HR (95% CI) 1.67 (1.29; 2.18)] and class II [1.28 (1.06; 1.54)], but also for underweight patients [1.3 (1.07; 1.58)], compared to normal weight patients. KM curves for individual TNFi showed shorter drug survival on ADA for patients with obesity class II and III (fig 1B), on ETA for patients with obesity, especially in class III (fig 1C) and on IFX, for patients with obesity class II and III and underweight patients (fig 1D). After adjustment in Cox regression, statistical significant BMI-drug survival associations remained for patients with pre-obesity starting ADA [HR (95% CI) 0.86 (0.75; 0.99)], for patients starting ETA with obesity class II [HR (95% CI) 1.27 (0.98; 1.65) or class III [1.79 (1.25; 2.55)] and for patients on IFX who were underweight [HR (95% CI) 1.82 (1.20; 2.76)] or in obesity class II [1.49 (0.98; 2.26)]. No effect modification was found for reported pain.

Conclusion: Both underweight (as identified in IFX treated patients) and overweight patients (in ADA, ETA and IFX treated patients) discontinued a first TNFi treatment earlier than normal weight patients. Reported pain was not the main determinant. It remains uncertain what determines TNFi survival in individual patients.

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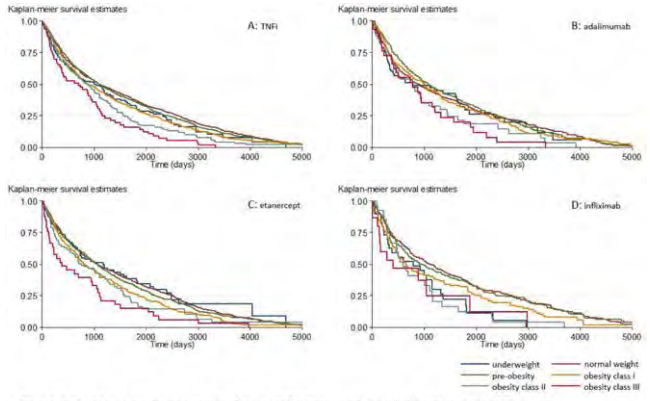


Figure 1. Kaplan-Meier curves for the association between BMI category and drug survival in patients starting TNFi.
Fig 1-A shows data of all patients starting their first TNFi. Data for patients starting adalimumab (1-B), etanercept (1-C) and infliximab (1-D) are shown separately. Kaplan-Meier curves are based on non-imputed and non-adjusted data.

Disclosure of Interests: Sytske Anne Bergstra: None declared, David Vega-Morales: None declared, Elizabeth Murphy: None declared, Marieke de Buck: None declared, Karen Solomon-Escoto: None declared, Thomas Huizinga Grant/research support from: Ablynx, Bristol-Myers Squibb, Roche, Sanofi, Consultant of: Ablynx, Bristol-Myers Squibb, Roche, Sanofi, Cornelia Allaart: None declared

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SAT0100

ASSOCIATION BETWEEN LOW HEMOGLOBIN AND RADIOGRAPHIC PROGRESSION OVER 52 WEEKS IN PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS FROM A PHASE 3 TRIAL OF SARILUMAB

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Background: Anemia is a common comorbidity in patients with rheumatoid arthritis (RA).

Objectives: Assess whether low hemoglobin (Hb) identifies a subgroup of patients at increased risk of joint damage progression, and investigate whether sarilumab modulates this risk.

Methods: The 52-week, double-blind, Phase 3 MOBILITY trial (NCT01061736) in patients with active RA and inadequate response to methotrexate (n = 1197) demonstrated the tolerability and efficacy (clinical and radiographic) of subcutaneous sarilumab 150 and 200 mg every 2 weeks versus placebo, both in combination with methotrexate (MTX). In this *post hoc* analysis, baseline characteristics and radiographic outcomes in MOBILITY were analyzed by baseline Hb category (low or normal) according to World Health Organization criteria, with low Hb defined as <120 g/L for women and <130 g/L for men. Nominal *P* values are presented.

Results: A total of 414 patients (35%) had low Hb at baseline. Patients with low Hb were more likely than patients with normal Hb to be female (86% vs 79%, respectively), Asian (14% vs 5%), younger (mean age 49 vs 51 years), and to have lower body weight (mean 69 vs 77 kg); all nominal *P* <0.01. Duration of RA, prior biologic use, rheumatoid factor positivity, and baseline tender and swollen joint counts were similar between patients with low and normal baseline Hb, but there was a nominally significant difference in C-reactive protein (mean 30.2 [SD 28.5] vs 17.3 [18.5] mg/L; *P* <0.0001). Patients with low Hb generally exhibited more joint damage progression over 52 weeks than patients with normal Hb (Table). In the sarilumab + MTX groups, joint damage progression was mitigated compared with placebo + MTX in patients with low Hb and in patients with normal Hb. Mean change from baseline in Hb at 52 weeks in the placebo + MTX, sarilumab 150 mg + MTX, and sarilumab 200 mg + MTX groups was +3.7 (SD 10.8), +14.7 (12.1), and +14.0 (10.5) g/L, respectively, in patients with low Hb at baseline, and –2.5 (9.9), +6.2 (9.3), and +8.0 (9.9) g/L in patients with normal Hb at baseline.

Table. Mean change from baseline (SD) in radiographic measures of joint damage

	Placebo + MTX		Sarilumab 150 mg + MTX		Sarilumab 200 mg + MTX	
	Low Hb (n = 140)	Normal Hb (n = 258)	Low Hb (n = 145)	Normal Hb (n = 255)	Low Hb (n = 129)	Normal Hb (n = 270)
mTSS	3.75 (9.00)	2.29 (6.98)	1.20*** (5.58)	0.73** (4.07)	0.60*** (4.13)	0.08*** (4.83)
Joint space narrowing	1.52 (3.71)	1.22 (3.92)	0.79* (3.17)	0.30** (2.70)	0.50** (2.93)	0.06*** (3.33)
Erosion score	2.24 (6.24)	1.07 (3.91)	0.41*** (3.18)	0.44* (2.05)	0.10*** (2.13)	0.02*** (2.19)

Nominal *P* *<0.05, **<0.01, ***<0.001 versus placebo by rank ANCOVA model stratified by prior biologic use and region; mTSS, modified total Sharp score

Conclusion: Overall, sarilumab slowed joint damage progression in patients with RA. Additionally, in those patients with low Hb, who may suffer greater damage than those with normal Hb, sarilumab also increased Hb.

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Disclosure of Interests: Gerd Rüdiger Burmester Consultant of: AbbVie Inc, Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB Pharma, Speakers bureau: AbbVie Inc, Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB Pharma, Jean-Pierre Morello Shareholder of: Regeneron Pharmaceuticals, Inc., Employee of: Regeneron Pharmaceuticals, Inc., Owen Hagino Shareholder of: Sanofi, Employee of: Sanofi, Amy Praestgaard Employee of: Sanofi Genzyme, Stefano Fiore Shareholder of: Sanofi, Employee of: Sanofi, Mark C. Genovese Grant/research support from: Abbvie, Eli Lilly and Company, EMD Merck Serono, Galapagos, Genentech/Roche, Gilead Sciences, Inc., GSK, Novartis, Pfizer Inc., RPharm, Sanofi Genzyme, Consultant of: Abbvie, Eli Lilly and Company, EMD Merck Serono, Genentech/Roche, Gilead Sciences, Inc., GSK, Novartis, RPharm, Sanofi Genzyme

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SAT0101 ABATACEPT IN RHEUMATOID ARTHRITIS ASSOCIATED-INTERSTITIAL LUNG DISEASE: SHORT TERM OUTCOME AND PROGNOSTIC FACTORS

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Background: The prevalence of interstitial lung disease (ILD) in rheumatoid arthritis (RA) varies in the medical literature from 1% to 67% and is a major cause of mortality. Previous works have identified increased age, smoking and anticytrullinated protein antibodies (ACPA) titre as risk factors for RA-ILD (RA-ILD). Conventional treatments for RA may lead to a new onset or worsening of RA-ILD, so treatment should be identified to prevent the onset or exacerbation of RA-ILD. Studies have shown that abatacept (ABA) may improve the outcome of RA-ILD.
Objectives: The aim of our study is to evaluate ABA effectiveness and safety in patients with RA-ILD.
Methods: We enrolled RA-ILD patients who started treatment with ABA. All patients underwent thoracic high-resolution computed tomography (HRCT) at the beginning of ABA treatment and after 18 months of therapy. HRCT abnormalities were evaluated using a a computer-aided method (CaM). At each visit clinical, laboratory and respiratory function characteristics were collected and the Clinical Disease Activity Index (CDAI) and the Health Assessment Questionnaire Disability Index (HAQ-DI) for disease activity and functional disability were measured. The cohort was divided into three groups based on the CaM-HRCT results: patients with a lung fibrosis progression of 15% or more were defined as "worsened", those with a reduction of 15% or more were defined as "improved", all other patients were defined as "stable". The 15% threshold of change, derived from the CaM assessment, results from the determination of the standard deviation of the mean value change after 18 months of follow-up of the cohort. The multivariate regression model was used to assess the strength of the association between RA characteristics and HRCT response to ABA.
Results: Forty-four patients (81% women) with a mean age of 59.1±8.0 years and a mean duration of the disease of 7.5±3.1 years were recruited. Twenty-three (52.3%) patients were positive for ACPA and 28 (63.6%) for rheumatoid factor. Five patients (11.4%) showed deterioration of ILD, 31 (70.6%) were in the "stable" group, and 7 patients (16.0%) experienced improvement over a mean follow-up period of 18 months. The factors related to ILD deterioration were use of methotrexate (MTX) (p=0.0078), and current smoking habit (p=0.0054), according to multivariate regression analysis (Table).
Conclusion: Treatment with ABA is associated with an RA-ILD stability or improvement rate of 86.6% of patients, while the worsening rate is 11.4%. Concomitant treatment with MTX and current smoking habit are factors associated with RA-ILD worsening. MTX discontinuation and smoking cessation should be strongly promoted in patients with RA-ILD.
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Table. Multivariate regression analysis of the variables related to the worsening of RA-ILD

Independent variables	Coefficient	Std. Error	t	P	$r_{partial}$
(Constant)	*1.6370*				
Age	-0.0012	0.0050	-0.2	0.8131	-0.042
Sex	0.025	0.1	0.23	0.8161	0.042
Disease duration	0.015	0.017	0.89	0.3799	0.15
ACPA positivity	-0.012	0.071	-0.18	0.8566	-0.032
RF positivity	0.0030	0.079	0.038	0.9694	0.0069
Current smokers	-0.34	0.11	-2.99	0.0054	-0.47
MTX use	-0.39	0.13	-2.84	0.0078	-0.45
DLco	0.0052	0.0061	0.84	0.4030	0.15
FVC	-0.0088	0.0088	-1.006	0.3224	-0.17
CAM-HRCT (% fibrosis)	0.00082	0.0091	0.09	0.9285	0.016
CDAI	-0.0074	0.0038	-1.96	0.0588	-0.33
HAQ-DI	-0.017	0.14	-0.11	0.9059	-0.021

Disclosure of Interests: None declared
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SAT0102 NONINFLAMMATORY PAIN IS A FREQUENT PHENOMENON IN RHEUMATOID ARTHRITIS AND RESPONDS WELL TO TREATMENT WITH SARILUMAB

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Background: Inflammation is clearly a key driver of pain in rheumatoid arthritis (RA). However, in some patients the level of pain exceeds what would be expected based on the amount of synovitis observed, which may indicate the presence of noninflammatory pain (NIP). Interleukin-6 (IL-6) has been shown in animal models to increase sensitization to pain and may play a role in NIP.
Objectives: To assess the effect of sarilumab, a human IL-6 receptor inhibitor approved for the treatment of adults with moderate to severely active RA, on NIP and disease activity, stratified by baseline (BL) NIP status.
Methods: The analysis included data from three Phase 3 studies of sarilumab: MOBILITY (NCT01061736), MONARCH (NCT02332590), and TARGET (NCT01709578). Patients received double-blind placebo or sarilumab 150 mg or 200 mg subcutaneously (SC) every 2 weeks (q2w), plus weekly csDMARD (MOBILITY and TARGET), or adalimumab 40 mg or sarilumab 200 mg SC q2w as monotherapy (MONARCH).
NIP was defined using an established formula: tender 28-joint count (TJC) – swollen 28-joint count (SJC) ≥7.[1,2] Patients were assessed for NIP at study BL and for change in NIP status at Weeks 12 and 24. The proportion of patients achieving ACR20/50/70, Clinical Disease Activity Index (CDAI) ≤10, and DAS28-CRP <3.2 at Week 24 was assessed in patients with and without BL NIP. No inferential statistics were performed.
Results: Of 2112 patients in the analysis, 490 (23%) met the criteria for NIP at study BL: MOBILITY, n = 294/1197 (25%); MONARCH, n = 90/369 (24%); TARGET, n = 106/546 (19%). BL demographics were similar for patients with or without BL NIP: mean age (SD) was 52.6 (10.7) versus 51.2 (12.3) years, and 85% versus 81% were female. Patients with BL NIP had higher CDAI, DAS28-CRP, pain Visual Analog Scale (VAS), and TJC at BL versus patients without NIP (Table). Of patients with NIP at BL, those who received sarilumab were more likely to have no NIP at Weeks 12 and 24 versus patients who received placebo or adalimumab (Figure 1). The percentage of patients achieving improvements in disease activity at Week 24 was greater for sarilumab versus adalimumab among both patients with and without BL NIP, and these differences were larger among patients with BL NIP for all assessments except ACR50 (Figure 2).

Table. Baseline characteristics

	Patients with TJC – SCJ ≥7	
Mean (SD)	**Yes (n = 490)**	**No (n = 1622)**
Duration of RA, years	9.1 (8.6)	9.7 (8.4)
TJC, 0–28	21.7 (4.7)	14.3 (6.2)
SJC, 0–28	10.7 (4.3)	13.1 (6.0)
CRP, mg/L	22.7 (27.0)	22.9 (24.0)
HAQ-DI, 0–3	1.8 (0.6)	1.7 (0.6)
DAS28-CRP	6.4 (0.7)	5.9 (0.9)
CDAI	46.0 (9.4)	40.4 (13.0)
Pain VAS	72.3 (18.2)	67.0 (20.7)

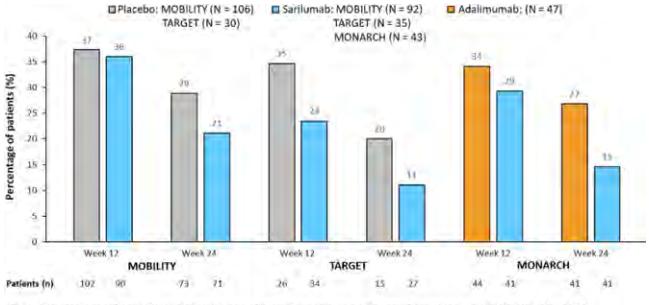


Figure 1 Percentages of patients with baseline noninflammatory pain who had noninflammatory pain at Weeks 12 and 24*
*For MOBILITY and TARGET, data are shown only for patients who received sarilumab 200 mg

Conclusion: NIP was prevalent at BL in the patient populations assessed. Among patients with BL NIP, a lower proportion continued to have NIP at Weeks 12 and

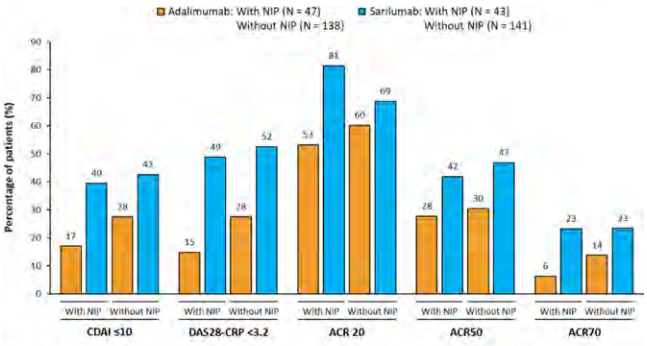


Figure 2 Percentages of sarilumab and adalimumab responders at Week 24 by baseline noninflammatory pain status

24 when treated with sarilumab versus placebo or adalimumab. Patients with and without BL NIP had greater improvements in pain when treated with sarilumab versus adalimumab. The difference in clinical improvement was greater among patients with BL NIP versus without BL NIP for most measures. These trends support the emerging concept that mechanisms other than direct inflammation may contribute to pain in RA, potentially mediated via IL-6 signaling.

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Acknowledgments: Study funding and medical writing support (Joseph Hodgson, PhD, Adelphi Communications Ltd, Macclesfield, UK) provided by Sanofi Genzyme (Cambridge, MA, USA) and Regeneron Pharmaceuticals, Inc. (Tarrytown, NJ, USA) in accordance with GPP3 guidelines.

Disclosure of Interests: Ernest Choy Grant/research support from: Amgen, Bio-Cancer, Chugai Pharma, Ferring Pharmaceuticals, Novimmune, Pfizer, Roche, UCB, Consultant of: AbbVie, Amgen, AstraZeneca, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Chelsea Therapeutics, Chugai Pharma, Daiichi Sankyo, Eli Lilly, Ferring Pharmaceuticals, GlaxoSmithKline, Hospita, Ionis, Janssen, Jazz Pharmaceuticals, MedImmune, Merck Sharp & Dohme, Merrimack Pharmaceutical, Napp, Novartis, Novimmune, ObsEva, Pfizer, R-Pharm, Regeneron Pharmaceuticals, Inc., Roche, SynAct Pharma, Sanofi Genzyme, Tonix, UCB, Speakers bureau: Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Chugai Pharma, Eli Lilly, Hospira, Merck Sharp & Dohme, Novartis, Pfizer, Regeneron Pharmaceuticals, Inc., Roche, Sanofi-Aventis, UCB, Vivian Bykerk: None declared, Yvonne Lee Shareholder of: Cigna-Express Scripts, Grant/research support from: Pfizer, Consultant of: Highland Instruments, Inc., Gregory St John Shareholder of: Regeneron Pharmaceuticals, Inc., Employee of: Regeneron Pharmaceuticals, Inc., Hubert van Hoogstraten Shareholder of: Sanofi, Employee of: Sanofi, Kerri Ford Shareholder of: Sanofi Genzyme, Employee of: Sanofi Genzyme, Amy Praestgaard Employee of: Sanofi Genzyme, Anthony Sebba Consultant of: Genentech, Gilead, Lilly, Regeneron Pharmaceuticals Inc., Sanofi, Speakers bureau: Lilly, Roche, Sanofi

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SAT0103 THE EFFECT OF BODYWEIGHT ON RESPONSE TO INTRAVENOUS OR SUBCUTANEOUS TOCILIZUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Tocilizumab is an IL-6 receptor humanised monoclonal antibody treatment option in rheumatoid arthritis (RA) who have not responded or are intolerant of disease modifying anti-rheumatic drugs (DMARDs) or other biologics. Tocilizumab was available initially as an intravenous (IV) preparation, dosed according to weight, and more recently as a subcutaneous (SC) preparation given at 162mg/weekly irrespective of bodyweight.

Obesity is highly prevalent in RA and there has been concern that starting or switching patients to SC tocilizumab could reduce its effectiveness in those patients with a higher body weight when compared to IV tocilizumab.

Objectives: To investigate the relationship between bodyweight and DAS28 response at 6 months in tocilizumab naïve RA patients starting IV or SC tocilizumab.

Methods: The study population comprised RA subjects recruited to the BSRBR-RA up to 30/11/2018 commencing IV or SC tocilizumab for the first time. Patients had to be tocilizumab naïve and have at least one six monthly study follow-up recorded after starting tocilizumab. Baseline characteristics at point of starting tocilizumab are described. Linear regression, fully adjusted for relevant confounders, was used to investigate the relationship between change in DAS28 score from baseline to six months and body weight per ten kilograms (kg), and in a separate analysis, as BMI category. Multiple imputation was used to handle missing data.

Results: 1241 patients starting tocilizumab (902 IV, 339 SC) were eligible for analysis. The median age was 59 years, majority were female, and had median disease duration of 11 years at baseline. Over seventy percent had prior biologic exposure. Median weight was 77kg for IV and 76kg for SC starters, and the majority of patients were categorised as normal weight (30% IV, 37% SC) or pre-obesity (31% IV & SC) according to BMI. Median DAS28 score was 5.8 (IV) and 5.5 (SC) at start of treatment with median improvement after 6-months of 1.50 and 2.02 units respectively. The fully adjusted linear regression model showed no association between body weight or BMI and change in DAS28 score at six months for patients starting IV or SC tocilizumab. (Table).

Table

Baseline Variable	Intravenous TCZ patients (n=902)	Subcutaneous TCZ patients (n=339)
Age, median (IQR)	58 (50-67)	60 (51-70)
Gender, n (%) female	708 (78)	233 (74)
Disease duration, median (IQR) years	11 (4-21)	11 (4-21)
DAS28 score, median (IQR)	5.8 (5.1-6.6)	5.5 (4.7-6.5)
Change in DAS28 score, median (IQR)	-1.50 (-3.10 - -0.23)	-2.02 (-3.72- -0.37)
Weight in KGs, median (IQR)	77 (64-91)	76 (64-88)
		Change in DAS28, coefficient (95% CI)
Body weight per 10kgs*	0.04 (-0.01-0.09)	-0.005 (-0.11-0.10)
BMI category*		
Normal weight	ref	ref
Underweight	-0.41 (-1.27-0.46)	0.08 (-1.62-1.77)
Pre-obesity	-0.26 (-0.57-0.05)	0.02 (-0.44-0.48)
Obesity class I, II & III	-0.03 (-0.35-0.29)	0.08 (-0.40-0.55)

*Fully adjusted for age, gender, disease duration, baseline DAS28 score, baseline HAQ score, co-morbidities, and number of previous biologics

Conclusion: Data from this study show that body weight does not appear to affect initial response to IV or SC tocilizumab. This is reassuring given that patients are likely to be given SC tocilizumab due to ease of administration and reduced hospital costs.

Disclosure of Interests: Rebecca Davies: None declared, Arani Vivekanantham: None declared, Mark Lunt: None declared, Kath Watson: None declared, Kimme Hyrich Grant/research support from: Pfizer, UCB, BMS, Speakers bureau: Abbvie, James Bluett: None declared

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SAT0104 MAINTENANCE OF SDAI REMISSION AND PATIENT-REPORTED OUTCOMES (PROS) FOLLOWING DOSE DE-ESCALATION OF ABATACEPT IN MTX-NAÏVE, ANTI-CITRULLINATED PROTEIN ANTIBODY (ACPA)+ PATIENTS WITH EARLY RA: RESULTS FROM AVERT-2, A RANDOMISED PHASE IIIB STUDY

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Background: The Phase IIIb Assessing Very Early RA Treatment (AVERT)-2 trial (NCT02504268) evaluated SC abatacept (ABA) + MTX vs ABA placebo (PBO) + MTX in ACPA+ patients (pts) with early, active RA.[1] Results from the 56-wk induction period (IP) showed a significantly greater proportion of pts treated with ABA + MTX (vs MTX alone) reported clinically meaningful improvements in HAQ-DI, global disease activity and pain, which were sustained at 52 wks.[2]

Objectives: To report maintenance of SDAI remission and PROs from the AVERT-2 de-escalation (D-E) period.

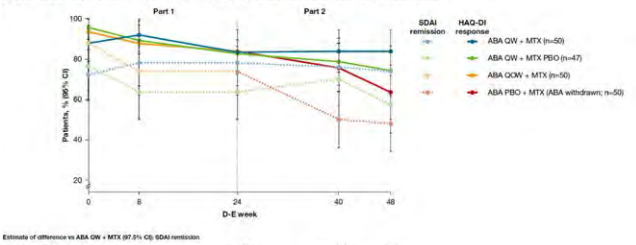
Methods: Pts received blinded SC ABA (125 mg once wkly [QW]) + MTX or ABA PBO + MTX induction treatment for 56 wks. In this analysis, pts who completed induction with ABA + MTX and had sustained SDAI remission (≤3.3 at Wks 40 and 52) were re-randomised 1:1:1 to ABA QW + MTX, stepwise D-E (ABA every other wk + MTX for 24 wks then ABA PBO + MTX for 24 wks), or ABA QW + MTX PBO for 48 wks in the D-E period. PROs included physical function (HAQ-DI [0–3; decrease=improvement] and Short-Form 36 [SF-36] v2.0 Physical Functioning Scale [PFS]; 0–100; increase=improvement), and fatigue (Functional Assessment of Chronic Illness Therapy-Fatigue [FACIT-F] score; 0–52; decrease=-improvement). Endpoints included: proportion of pts in SDAI remission and pts with HAQ-DI response (decrease from IP Day [D]1 in HAQ-DI ≥0.30); adjusted mean change (adMC) from D-E D1 in HAQ-DI, SF-36 PFS or FACIT-F to D-E Wk 48. adMCs were estimated using a mixed effect model with repeated measures.

Results: 147 ABA + MTX-treated pts were re-randomised in the D-E period. Across re-randomised arms, the range of mean scores was 1.87–2.52 for SDAI and 0.18–0.30 for HAQ-DI at entry into D-E period (D-E D1). 74% of pts receiving ABA QW + MTX maintained SDAI remission at D-E Wk 48 (Fig 1); this proportion was higher than in the ABA withdrawal and ABA QW + MTX PBO arms. Pts continuing ABA QW + MTX maintained HAQ-DI response during D-E (Fig 1), but by D-E Wk 48 the proportion of pts with HAQ-DI response in the ABA withdrawal arm declined by 30%. At D-E Wk 48, a small numerical decrease (adMC –0.04) in HAQ-DI was observed in the ABA QW + MTX arm; increases were seen in the withdrawal (adMC 0.26) and ABA QW + MTX PBO arms (adMC 0.16). By D-E Wk 48, SF-36 PFS increased (adMC 1.68) in the ABA QW + MTX arm but decreased in the withdrawal (adMC –3.34) and ABA QW + MTX PBO (adMC –1.45) arms. FACIT-F score increased during D-E in all arms, but the increase at D-E Wk 48 was lower in the ABA QW + MTX arm (adMC 0.79) vs the withdrawal (adMC 4.12) and ABA QW + MTX PBO (adMC 2.41) arms. Similar trends were seen for other PROs including Work Productivity and Activity Impairment-RA; while activity impairment remained stable in the ABA QW + MTX arm, there was a trend for worsening in the withdrawal arm.

Conclusion: In the AVERT-2 D-E period, continued combination therapy (abatacept + MTX) resulted in maintenance of benefits on PROs, particularly physical functioning, in seropositive pts with early RA. D-E of abatacept followed by complete withdrawal was associated with the greatest loss of remission as well as worsening of PROs. The PRO results corresponded well to the maintenance of clinical (SDAI) remission.

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SAT0105 INFLUENCE OF RITUXIMAB ON DIASTOLIC FUNCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: One of the drugs used in the treatment of rheumatoid arthritis (RA) is rituximab. Given the fact that the RA affects not only the joints, but, in addition to other organs, and the heart, our interest has caused the likelihood of the impact of rituximab on non-articular manifestations of rheumatoid arthritis, in particular, related to the cardiovascular system.

Objectives: to study the effect of rituximab on the development of diastolic dysfunction of the heart in patients with RA.

Methods: 98 patients with RA were examined, of which 28 patients took rituximab 1000 mg according to the scheme for 6-12 months and methotrexate up to 25 mg per week per os (1st group), and 70 patients – only methotrexate up to 25 mg per week at least 12 months (2nd group). They were held echocardiography with calculation of the E/a of mitral valve, E/a of tricuspid valve, end-diastolic size of left ventricle, electrocardiography with calculation of the dispersion of QT interval and vectorcardiography with determination of the areas of the P loop, QRS loop, T loop, and the maximum vector (MV), MV-azimuth and MV-lift.

Results: the E/a of mitral and tricuspid valves in 1st group were higher than in 2nd group ($p<0.05$). In 1st group, a correlation was found between the E/a of both valves and the MV-lift; and also between the dispersion of QT interval and the maximum vector ($p<0.05$).

Conclusion: in patients taking rituximab, there is a relationship between diastolic dysfunction, electrical instability of the ventricles and signs of electrophysiological remodeling. In addition, the use of rituximab is associated with a lower severity of diastolic dysfunction of both ventricles and a lower risk of life-threatening arrhythmias compared to the group that did not take this drug.

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SAT0106

LONG-TERM SAFETY AND EFFICACY OF SARILUMAB OVER 5 YEARS IN PATIENTS WITH RHEUMATOID ARTHRITIS WITH 1 OR >1 PRIOR TUMOR NECROSIS FACTOR INHIBITOR FAILURES

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Background: A proportion of adult patients with rheumatoid arthritis (RA) are refractory to tumor necrosis factor inhibitors (TNFi), and treatment with subsequent biologics is commonly associated with reduced response. Sarilumab is a human IL-6 receptor inhibitor approved for the treatment of adults with moderate to severely active RA. In the Phase 3 TARGET study (NCT01709578), significant improvements in the signs and symptoms of RA and physical function were shown with sarilumab plus conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) versus placebo in patients refractory to TNFi.

Objectives: To investigate long-term safety and efficacy of subcutaneous sarilumab over 5 years in patients with 1 or >1 TNFi treatment failure prior to their enrollment in TARGET, who continued onto the open-label extension (OLE) study, EXTEND (NCT01146652).

Methods: In the 24-week randomized controlled trial (RCT), patients received placebo, sarilumab 150 mg, or sarilumab 200 mg every 2 weeks (q2w), and were eligible to receive open-label sarilumab 200 mg q2w in the OLE. Dose reduction to 150 mg q2w was permitted per investigator's discretion, or to manage laboratory abnormalities. Safety outcomes are presented for the entire follow-up period from RCT baseline through the OLE. Efficacy was assessed using Clinical Disease Activity Index (CDAI) score.

Results: Of the 546 patients randomized in the RCT, 454 (83%) entered the OLE, of whom 339 had 1 TNFi failure and 115 had >1 TNFi failure. Patients with >1 TNFi failure were older and had a longer duration of RA than patients with 1 TNFi failure (mean age [SD] 55.3 [12.6] and 52.5 [11.9] years, mean RA duration [SD] 13.9 [9.1] and 11.1 [8.8] years, respectively). Kaplan–Meier estimates of the probability of continuation at 5 years were similar between groups: 48% and 54% for patients with >1 and 1 TNFi failure, respectively. At the time of data cut-off (January 15, 2019) 199/546 patients (36%) had discontinued through the RCT and OLE. The rates per 100 patient-years of treatment-emergent adverse events (AEs) and AEs leading to discontinuation for patients with >1 and 1 TNFi failure were 290.6 and 197.9, and 6.5 and 8.1, respectively. Clinical efficacy of sarilumab was sustained in the OLE through 5 years in both groups, regardless of initial treatment in the RCT (Table).

Table Mean CDAI and proportion of CDAI responders

Treatment allocation in 24-week RCT	Placebo +DMARD		Sarilumab 150 mg +DMARD		Sarilumab 200 mg +DMARD	
	(n=156)		(n=145)		(n=153)	
TNFi failures	**1**	**>1**	**1**	**>1**	**1**	**>1**
CDAI, mean (SD)						
RCT baseline	43.7 (12.7)	42.5 (10.3)	42.0 (13.0)	44.3 (13.5)	42.1 (13.5)	48.5 (13.0)
Change after 216 weeks' follow-up	–30.9 (17.5)	–32.6 (15.2)	–33.3 (15.8)	–33.1 (12.7)	–30.3 (13.6)	–36.0 (18.1)
CDAI ≤10, n (%)*						
OLE baseline	48 (42)	14 (33)	59 (53)	16 (47)	56 (49)	20 (51)
After 216 weeks' follow-up	24 (21)	10 (24)	29 (26)	7 (21)	29 (25)	8 (21)

*Nonresponder imputation

Conclusion: The long-term safety and efficacy of sarilumab were similar in patients with 1 or >1 prior TNFi failure over 5 years' follow-up. Clinical efficacy could be sustained through 5 years of treatment.

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SAT0107

BIOLOGIC THERAPY WITH RITUXIMAB DECREASES PREVALENCE OF ANXIETY AND DEPRESSION IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Evidence suggests rheumatoid arthritis (RA) confers an increased risk of psychological morbidity, particularly anxiety and depression, which may affect the subsequent management and treatment adherence.[1,2] Few studies have studied psychological factors over time in RA patients.[3]

Objectives: To evaluate the prevalence of anxiety and depression in RA patients following rituximab treatment.

Methods: 92 biologics-naïve RA patients [mean (SD) age 49.5 (9.9) years, 78 women; median (IQR) DAS28 5.67 (3.94–8.45); median (IQR) HAQ 1.87 (1.2–3.5)] were followed up for 27 months after commencing and continuing rituximab therapy (1, 2, 3 standard courses). Anxiety and depression, and health-related quality of life (HRQoL) were assessed at baseline, 3, 15 and 27 months using the Hospital Anxiety and Depression Scale (HADS) and the Short Form (SF-36 v.1) Health Survey questionnaire, respectively.

Results: Median anxiety and depression scores decreased significantly between baseline and 3 months and continued depress over the 27-month period – Table. The prevalence of depression cases decreased twice from baseline to 27 months ($p<0.01$), as did the prevalence of anxiety ($p<0.01$). Patients reported poor baseline HRQoL. SF-36 domain scores substantially rose after 15 and 27 months.

Anxiety, depression, and quality of life

	Baseline	3 months	15 months	27 months
	(n=92)	(n=92)	(n=53)	(n=14)
Anxiety cases (HADS-A score ≥8), n (%)	72 (78.3)	48 (52.2)	24 (45.3)*	5 (35.7)**
Median (IQR) Anxiety score	12.6 (10–15)	8.2 (5–12)*	6.4 (3–10)**	5.5 (3–8)***
Depression cases (HADS-D score ≥8), n (%)	62 (67.4)	50 (54.3)	19 (35.8)*	4 (28.6)**
Median (IQR) Depression score	9.2 (7.8–9.6)	5.6 (3–8)**	4.5 (2–7)**	3.6 (2–6)***
Mean (SD) Mental Health score	42.8 (15.2)	51.2 (18.3)	68.7 (11.2)*	72.9 (10.5)**
Mean (SD) Physical Function score	24.4 (8.3)	32.5 (9.8)	53.8 (10.5)*	54.5 (9.3)*
Mean (SD) Social Function score	48.2 (15.4)	56.8 (25.5)	59.8 (18.7)	65.9 (9.2)*
Mean (SD) General Health score	35.8 (11.2)	48.7 (10.8)	67.8 (8.6)**	75.9 (12.6)**

* p<0.05, ** p<0.01, *** p<0.001 differences between baseline and follow-up

Conclusion: Anxiety and depression levels decrease significantly in RA patients following commencement and continuity of rituximab. B cell-directed therapy for patients with RA helps achieve remission of both anxiety and depression, and improves HRQoL.

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SAT0108

RESPONSE TO ABATACEPT IS ASSOCIATED WITH THE INHIBITION OF PROTEASOME B1I EXPRESSION IN T CELLS OF PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Abatacept (CTLA4-Ig) is a biological DMARD (bDMARD) for treatment of rheumatoid arthritis (RA) and selectively modulates the co-stimulatory signal by CD28: CD80/CD86 interaction required for T cell activation. CD28 mediated signaling regulates many T cell functions including cytokine production. The role of proteasome was approved in many autoimmune diseases, and the effect of Abatacept on modifying cytokines including interferon-γ that alters proteasome proteolytic activities was shown in RA.
Objectives: To characterize the effect of Abatacept on the expression and proteolytic activity of the immunoproteasome.
Methods: Effects of Abatacept on the proteasome system were investigated in 39 patients with rheumatoid arthritis over a period of 24 weeks. Using real time PCR, transcript expression levels of constitutive and corresponding immunoproteasome catalytic subunits were investigated at baseline (T0), week 16 (T16) and week 24 (T24) in sorted blood cells. Proteasomal activity and induction of apoptosis after proteasome inhibition were also evaluated in cellular subsets.
Results: Upon treatment with Abatacept, remission or low disease activity according to DAS28 was achieved in 55 % of patients at T16 and in 70 % at T24. By Two- (time and type of response) way ANOVA, a significant reduction of proteasome immunosubunit β1i expression was shown only in CD4+ and CD8+ T cells of prolonged responders at both T16 and T24 (P = 0.0390 and P = 0.0198, respectively). One-way ANOVA analysis for each response group separately confirmed the results and showed significant reduction at T24; P = 0.0396 difference between T0 and T24, P = 0.0260 between T16 and T24 in CD4+ T cells of the same group. Abatacept did not influence chymotrypsin like activity of proteasome, which is carried out by the subunit β5i and had no effect on induction of apoptosis under exposure to a proteasome inhibitor in-vitro.
Conclusion: Treatment with Abatacept showed a clear effect on the expression of the proteasome immunosubunit β1i. This phenomenon was only seen in CD4+ and CD8+ T cells of prolonged responding patients with RA suggesting an association between persistent induction of β1i and failure to the T cell directed therapy with Abatacept.
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SAT0109

DISTINCT EFFECTS OF METHOTREXATE IN COMBINATION WITH ADALIMUMAB OR ETANERCEPT ACCORDING TO CCP ANTIBODY STATUS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Considerable evidence suggesting enhanced efficacy of anti-TNF therapy for rheumatoid arthritis (RA) when co-administered with methotrexate (MTX) led us to explore the applicability of the published data to our patient cohort.
Objectives: This retrospective study aimed to investigate the efficacy of MTX in combination with adalimumab (ADA) and etanercept (ETN) for RA, examining changes in disease activity score (DAS28-CRP) on first starting treatment, and rates of withdrawal due to inefficacy over up to 10 years of treatment in routine clinical practice.
Methods: 309 patients with RA who had started ADA or ETN as a first-line biologic at UCLH from 2003 onwards were identified. Demographic and treatment details, DAS28-CRP (DAS) at the biologic-naïve baseline and at a first appointment for review on anti-TNF were extracted from clinical records. ANOVA was used to investigate the level of association between change in DAS and anti-TNF type, concomitant therapy, anti-CCP (CCP), rheumatoid factor (RF), age, disease duration and number of DMARD trials by anti-TNF initiation, year of initiation and gender. Kaplan-Meier with log rank tests were used to explore associations between anti-TNF type, MTX, CCP and RF and rates of withdrawal due to inefficacy, and Cox Proportional Hazards to check whether these remained significant after controlling for any other significant factors.
Results: 179 patients were on ADA and 130 ETN; 44% were on concomitant MTX (Table 1).

Table 1. Numbers of patients co-prescribed MTX with ADA or ETN according to CCP status

	CCP positive n	Total n
ETN without MTX	37	54
with MTX	57	76
ADA without MTX	54	82
with MTX	65	97

Median follow up since anti-TNF initiation was 7 years. Median age at initiation was 51 years, and disease duration 4 years. 82% were female. 241 were seropositive, including 24 positive for CCP only and 28 RF only.
Mean biologic-naïve (baseline) DAS was 5.75, and 3.52 on first review (mean 20 weeks of treatment, n= 274) with mean change -2.23. MTX, even accounting for dose, failed to explain a significant amount of the variance in DAS response at first review either as a main effect or in interaction with anti-TNF type, CCP or RF. The only significant factor was 4+ DMARD trials prior to initiation (lower mean DAS response, p=0.010).
Next, we analysed withdrawal of anti-TNF for inefficacy over up to 10 years. Kaplan-Meier analyses revealed that CCP positive patients had higher inefficacy withdrawal rates (p =0.004). Of note, CCP positive patients treated with MTX had lower withdrawal rates for inefficacy (Figure 1, p=0.006). Intriguingly, there was a trend towards higher rates in patients treated with MTX if CCP negative (p=0.14). Co-administration of MTX appeared to reduce rates of inefficacy withdrawal for patients on ETN (p=0.006) but not ADA (p =0.784). For CCP positive patients on ETN, MTX was strongly associated with lower rates of inefficacy withdrawal (Figure 1, p=.002). CCP status and the CCP*MTX interaction remained significant in the multivariate Cox model (Table 2). The MTX*ETN interaction was also included by the backward stepwise variable selection procedure although with p 0.069.

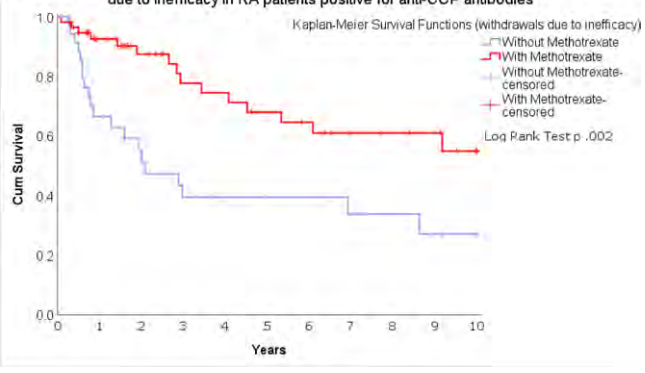
Table 2. Variables in the Cox Model

	Hazard Ratio for discontinuation related to inefficacy	95% CI for HR
MTX	2.18	0.93, 5.13
CCP	3.71	1.74, 7.92
CCP*MTX	0.35	0.14, 0.91
ETN*MTX	0.61	0.36, 1.04
Disease duration > 5 years	0.61	0.41, 0.90
Gender (male)	0.62	0.36, 1.05
4+ DMARD trials	1.65	1.02, 2.67
Biologic-naive Global VAS/cm	1.26	1.11, 1.42

Overall model p < .0005
RF with a univariate Cox significance of 0.172 was less closely associated with rate of withdrawal for inefficacy compared to anti-CCP positivity (p 0.005).

Conclusion: There was no apparent benefit of MTX with anti-TNF with respect to initial DAS response, but MTX was associated with a reduction in withdrawals for inefficacy though only in CCP positive patients treated with ETN.

Figure 1. Association between concomitant methotrexate and rate of withdrawal of etanercept due to inefficacy in RA patients positive for anti-CCP antibodies



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SAT0110

SARCOPENIA IN PATIENTS WITH RHEUMATOID ARTHRITIS ON THE TREATMENT WITH BIOLOGIC DISEASE MODIFYING ANTI-RHEUMATIC DRUGS

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Background: Sarcopenia is characterized by loss of muscle mass and strength, which lead to lower physical ability, less quality of life (QoL), frailty and mortality. Rheumatoid arthritis (RA) is considered to be one of the causes of sarcopenia.
Objectives: To clarify the effectiveness of biologic disease modifying anti-rheumatic drugs (bDMARDs) on sarcopenia, including physical ability, body composition and nutritional status.
Methods: This is a prospective cohort study including consecutive 48 patients (male 11, female 37, age 64.2±15.1) with RA who started bDMARDs in Niigata Rheumatic Center. Diagnosis of sarcopenia was according to the diagnostic algorithm of European Working Group on Sarcopenia in Older People (EWGSOP). We monitored disease activity of RA, physical ability, body composition, nutritional status and QoL at baseline, 6 months and at 12 months. Disease activity was measured by disease activity score-28 joint count based on erythrocyte sedimentation rate (DAS28-ESR), clinical disease activity index (CDAI). Physical activity was measured by Health Assessment Questionnaire (HAQ), 10m walking test (10MWT). Nutritional status was measured by controlling nutrition status (CONUT) score, and prognostic nutritional index (PNI). Overall QoL was measured by EuroQol 5 dimentions (EQ5D).
Results: Among 48 patients who started bDMARDs, 21 patients were classified as having sarcopenia. The bDMARDs used were adalimumab in 10 cases, certolizumab pegol in 9 cases, abatacept in 9 cases, golimumab in 7 cases, tocilizumab in 5 cases, infliximab in 5 cases and etanercept in 3 cases. DAS28-ESR (4.7±1.4 vs. 2.7±1.0, $p < 0.001$) and CDAI (18.4±9.4 vs. 7.4±5.5, $p<0.001$) were significantly decreased by 12 months of bDMARDs therapy. Physical activity was significantly ameliorated after 12 months of bDMARDs; HAQ(1.1±0.9 vs. 0.6±0.8, $p<0.001$), 10MWT(1.5±0.7 m/s vs. 1.7±0.6, $p=0.002$). EQ-5D was also ameliorated(0.63±0.15 vs. 0.74±0.19, $p=0.0002$). As for body composition analysis, there were significant increase in body weight(54.6±12.4kg vs. 55.8±13.6, $p=0.006$), but there was no significant increase in skeletal muscle mass index(5.9±1.1kg/m2 vs. 5.9±1.1, $p=0.229$). Among 21 patients who were classified as sarcopenia when starting bDMARDs, the number of patients having sarcopenia significantly decreased after 12 months of bDMARDs (100% vs. 52.3%, $p=0.0005$) and skeletal muscle index of these patients were significantly increased (5.1±0.5kg/m2 vs. 5.3±0.7, $p=0.046$).
Conclusion: Twelve months of bDMARDs therapy significantly ameliorated disease activity, nutritional status and physical activity. In RA patients with sarcopenia, bDMARDs significantly increased skeletal muscle and may be effective for treatment of sacrcopenia.
Disclosure of Interests: : Eriko Hasegawa: None declared, Satoshi Ito Speakers bureau: Abbvie,Eisai, Yoichi Kurosawa: None declared, Shinji Taniguchi: None declared, Daisuke Kobayashi: None declared, Asami Abe: None declared, Hiroshi Otani: None declared, Kiyoshi Nakazono: None declared, Akira Murasawa: None declared, Ichiei Narita: None declared, Hajime Ishikawa: None declared
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SAT0111

THE RELATIONSHIP BETWEEN THE ADMINISTRATION OF IL-6 INHIBITORS AND INSULIN RESISTANCE IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is associated with an increased cardiovascular (CV) risk, due not only to the traditional risk factors (hypertension, insulin resistance/diabetes, obesity, smoking), but to the inflammatory status as well. The blockade of interleukin-6 (IL-6) can regulate the glucose metabolism, reducing the glucose level and insulin resistance (IR). This beneficial effect is seen more in patients with normal values of body mass index (BMI), compared to the obese population.
Objectives: Given the mentioned existing data, we aim to demonstrate the positive effect of IL-6 inhibitors in active RA patients with normal or increased BMI.
Methods: We recruited 56 consecutive patients with definite and active RA, non-responders/partial responders to conventional synthetic Drug Modifying Anti-Rheumatic Drugs (csDMARDs)/biological therapy. For a period of 52 weeks, patients received subcutaneous Tocilizumab (TCZ) in a dose of 162mg once a week, according to European League Anti Rheumatism (EULAR) recommendation and National Protocol. We assessed demographics, RA-related parameters (clinical, inflammatory and immune) and metabolic markers, as well as the peripheral response to insulin, quantified by Homeostasis Model Assessment for insulin resistance (HOMA-IR) and the Quantitative Insulin Sensitivity Check Index (QUICKI). We did not include in the study the patients known with diabetes mellitus (DM) and those undergoing glucocorticoids.
Results: After 52 weeks of treatment, most of the patients showed a statistically significant reduction of HOMA-IR (3.61 ± 1.21 at the onset vs. 2.45 ± 1.46 at the end of the study, $p<0.001$), while QUICKI registered a slight increase (0.32 ± 0.01 at the onset vs. 0.33 ± 0.01 at the end of the study, $p<0.001$). Also, the decrease in insulin and glucose levels were more obvious in patients with normal BMI, strictly related to disease activity.
Conclusion: Long-term administration of TCZ in active RA is associated with a significant reduction of disease activity and IR, especially in normal weight patients. This confirms that obesity, as a CV risk factor, represents one of the main causes of IR.
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Disclosure of Interests: Alexandra Jitaru: None declared, Cristina Pomirleanu: None declared, Maria-Magdalena Leon-Constantin: None declared, Florin Mitu: None declared, CODRINA ANCUTA Consultant of: AbbVie, Pfizer, Roche, Novartis, UCB, Ewopharma, Merck Sharpe and Dohme, and Eli Lilly, Speakers bureau: AbbVie, Pfizer, Roche, Novartis, UCB, Ewopharma, Merck Sharpe and Dohme, and Eli Lilly
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SAT0112

EFFECT OF RITUXIMAB ON IMMUNOGLOBULIN LEVELS AND RISK OF ASSOCIATED INFECTION

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Background: Rituximab (RTX) is an anti-CD20 monoclonal antibody that suppresses B-lymphocytes and may induce hypogammaglobulinemia. Studies have shown that sustained low levels of immunoglobulins (Ig) are associated with significantly increased risks of infections.
Objectives: To determine the relationship between the serum Ig levels and risk of infection during (RTX) therapy for rheumatic diseases. We also aimed to identify the most common type of infections and pathogens associated with them.
Methods: A multi-centre retrospective observational study of patients with autoimmune diseases treated with RTX between 2009-2019. Serum Ig levels (IgM, IgG and IgA) were measured at baseline and 6-12 months after each cycle and note was made of any hypogammaglobulianemia. Infections, evidenced by a positive microbiology sample, radiograph or requirement of antibiotics and/or hospitalization, were recorded.
Results: 146 patients were included with a mean age of 61.5 years (standard deviation 13.8). 105 patients (71.9%)) had Rheumatoid Arthritis. 51/146 had had 1or more episodes of infections whilst on Rituximab which required treatment. Of these, 26 (50.9%) had recurrent infections. 33/51 had low immunoglobulins of at least 1 type. After receiving RTX treatment, 14 had low IgG, 29 had low IgM and only 4 had low IgA. 6 patients with low IgG, but 13 patients with low IgM suffered with recurrent infections.
There was a statistically significant higher proportion of patients with infection who had low Ig levels compared to those with normal levels, with a $p < 0.01$ on chi square testing.
Lower respiratory tract infections were the commonest infection seen with 28 cases, with most cases (15/28) caused by Haemophilus Influenza. 18 cases of urinary tract infections were seen, with 12/18 being caused by E. Coli. 3 cases of shingles were also seen.
Conclusion: Our study shows that an increased risk of infection was associated with hypogammaglobulinemia after rituximab therapy and highlights the importance of monitoring these patients. In our data set, more patients with recurrent infections had low IgM, supporting a need for better understanding of low IgM and its relation to infection. Respiratory tract infections were the most common infection with Haemophilus Influenza being the commonest pathogen. Recent studies have shown an increase in haemophilus influenza infections. Reasons for the increase may include a waning immunity to Haemophilus, changes in the organism and greater numbers of high-risk people- such as in our study. This supports a rationale

for extended indication for immunisation against Haemophilus in vulnerable groups of adults and has implications for targeted adult Haemophilus influenzae vaccine development.

	Infection	Uninfected	*Marginal Row Totals*
Normal IG	18 (26.2) [2.57]	57 (48.8) [1.38]	75
Low IG	33 (24.8) [2.71]	38 (46.2) [1.45]	71
Marginal Column Totals	51	95	146 (Grand Total)

The chi-square statistic is 8.1083. The *p*-value is .004406. Significant at $p < .05$.

The chi-square statistic with Yates correction is 7.1494. The *p*-value is .007499. Significant at $p < .05$.

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SAT0113 DISCORDANCE OF CLINICAL REMISSION AND IMAGING REMISSION BY ULTRASONOGRAPHY IN PATIENTS WITH RHEUMATOID ARTHRITIS WITH BIOLOGIC AGENTS

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Background: Residual synovitis can be detected by sensitive modalities such as ultrasonography in patients with rheumatoid arthritis in clinical remission. On the other hand, a previous study has shown that ultrasound-guided treatment provides modest benefit compared to a conventional strategy aiming clinical remission in early patients. It is still unclear how discordant clinical remission is from imaging remission by ultrasonography in patients treated with biologic agents

Objectives: To clarify the discordance between clinical remission and imaging remission in patients with rheumatoid arthritis treated with biologic agents.

Methods: Patients with rheumatoid arthritis who were treated with biologic agents and in clinical remission defined as disease activity score for 28 joints (DAS28)<2.6 were enrolled. All patients were performed comprehensive ultrasound examination of 44 joints as well as physical examinations. Ultrasound images of gray scale (GS) and power doppler (PD) were evaluated with a semi-quantitative score of 0-3. Imaging remission with ultrasound was defined as no PD signal detected in any joints. Clinical information was collected from their medical charts.

Results: A total of 41 patients were enrolled with 22 patients treated with tumor necrosis factor (TNF)-α inhibitors and 19 with interleukin (IL)-6 inhibitors. The mean age, female ratio, the mean disease duration, and the mean duration of clinical remission were 60 years old, 87%, 5.1 years and 11.5 years. The imaging remission by ultrasonography was observed only in 51.2 %. When patients were divided according to biologic agents, baseline characteristics including median age, disease duration and clinically remission duration were comparable between both groups, while the rates of seropositivity and the stage of radiological progression was higher in IL-6 group (seropositivity, p=0.04; radiological progression, p=0.02). The mean DAS28 was 1.93 in the TNFα group and 1.02 in the IL-6 group. The discordance of clinical remission and imaging remission was observed in 28.6% of the TNFα group and 71.4% of the IL-6 group (p=0.03). The residual synovitis scores of GS and PD in 44 joints were significantly lower in the TNFα than the IL-6 group (GS, 1.1±1.8 vs 4.7 ± 4.6, p<0.01; PD, 0.6 ± 1.3 vs 3.3 ± 3.5, p<0.01, respectively). A receiver operating characteristic curve demonstrated an optimal score of DAS28 that discriminated imaging remission as 1.89 in the TNFα group and 1.25 in the IL-6 group.

Conclusion: Our results showed that there was substantial discordance between clinical remission and imaging remission, especially in the patients treated with IL-6 inhibitors. In patients treated with biologic agents, clinical remission should be assessed more stringently than the usual 2.6, and ulltrasound-guided management may be useful.

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Disclosure of Interests: Yasushi Kondo: None declared, Yuko Kaneko Speakers bureau: Dr. Kaneko reports personal fees from AbbVie, personal fees from Astellas, personal fees from Ayumi, personal fees from Bristol-Myers Squibb, personal fees from Chugai, personal fees from Eisai, personal fees from Eli Lilly, personal fees from Hisamitsu, personal fees from Jansen, personal fees from Kissei, personal fees from Pfizer, personal fees from Sanofi, personal fees from Takeda, personal fees from Tanabe-Mitsubishi, personal fees from UCB, Shuntaro Saito: None declared, Yuichiro Ohta: None declared, Komei Sakata: None declared, Yumiko Inoue: None declared, Chihiro Takahashi: None declared, Kazuoto Hiramoto: None declared, Jun Inamo: None declared, Tsutomu Takeuchi Grant/research support from: Eisai Co., Ltd, Astellas Pharma Inc., AbbVie GK, Asahi Kasei Pharma Corporation, Nippon Kayaku Co., Ltd, Takeda Pharmaceutical Company Ltd, UCB Pharma, Shionogi & Co., Ltd., Mitsubishi-Tanabe Pharma Corp., Daiichi Sankyo Co., Ltd., Chugai Pharmaceutical Co. Ltd., Consultant of: Chugai Pharmaceutical Co Ltd, Astellas Pharma Inc., Eli Lilly Japan KK, Speakers bureau: AbbVie GK, Eisai Co., Ltd, Mitsubishi-Tanabe Pharma Corporation, Chugai Pharmaceutical Co Ltd, Bristol-Myers Squibb Company, AYUMI Pharmaceutical Corp., Eisai Co., Ltd, Daiichi Sankyo Co., Ltd., Gilead Sciences, Inc., Novartis Pharma K.K., Pfizer Japan Inc., Sanofi K.K., Dainippon Sumitomo Co., Ltd.
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SAT0114 IMPACT OF DOSE TAPERING REIMBURSEMENT POLICY ON PRESCRIPTION PATTERN OF ADVANCED THERAPY FOR RHEUMATOID ARTHRITIS IN TAIWAN

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Background: Rheumatoid arthritis (RA) patients treated with advanced therapy (biologic disease-modifying antirheumatic drugs and targeted synthetic disease-modifying antirheumatic drugs) may be considered dose tapering after reaching treatment goal.[1] In EULAR 2016 recommendations, dose reduction can be considered if patients reach sustained remission.[2] A dose tapering policy of advanced therapy was introduced in the treatment guideline of RA since 2014 under the National Health Insurance (NHI) in Taiwan. The new reimbursement policy requests the dosage to be tapered in patients who received advanced therapy for 2 years and reached low disease activity defined by DAS28 (ESR).

Objectives: This retrospective study aims to investigate the impact of dose tapering policy on prescription pattern of advanced therapy for RA patients in Taiwan.

Methods: This study was an observational retrospective analysis on the population-based National Health Insurance Research Database (NHIRD) in Taiwan. Patients with RA aged ≥18, initiated an index advanced therapy - abatacept, adalimumab, etanercept, golimumab, tocilizumab, or tofacitinib, during 2011-2017 were included (Figure 1). Patients were followed-up until the index advanced therapy was switched/discontinued or the end of data, whichever came first. The 4-week moving average of proportion of days covered (PDC) of the index therapy within each 12-week period were assessed. The outcome variable was whether dose tapering occurred which was defined as PDC being less than 0.5. The odds ratios (ORs) and the 95% confidence intervals (CIs) were estimated using Generalized Estimating Equation (GEE) with logistic specification to examine the independent effect of tapering policy and treatment

duration on the probability of dose tapering, after controlling for age, sex, and index advanced therapy.

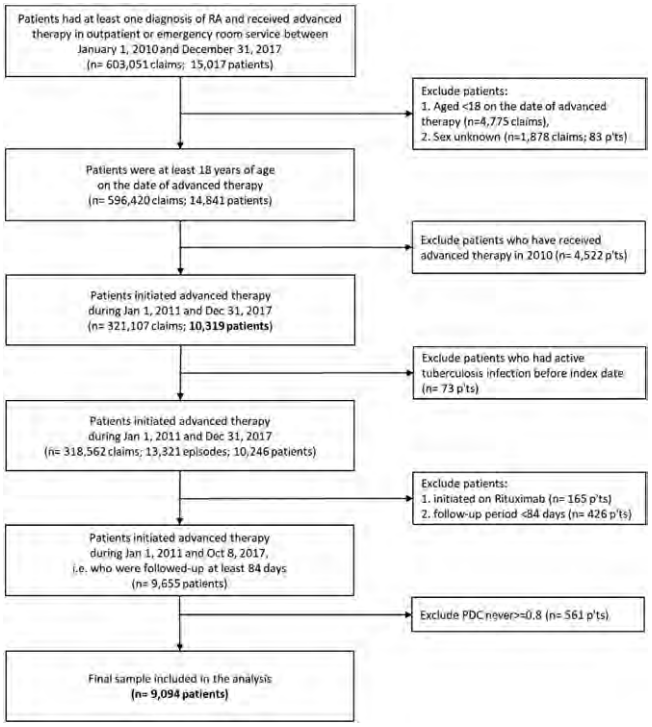


Figure 1. Flow chart of patient selection:

Results: The study comprised 9,094 patients initiated advance treatment for RA, with mean age of 57.3 (SD 13.3) years and 78.8% were female. The median PDC dropped remarkably after 28 months since treatment initiation (Figure 2). Probability of dose tapering increased significantly when treatment duration ≥24-month (OR=2.73, p<0.001). When treatment duration < 24-month, Dose Tapering policy was not significantly associated with tapering prescription. However, implementation of the policy further increased the probability of dose tapering for patients with treatment duration ≥ 24-month, OR for interaction of policy by duration was 1.17, and test for interaction p=0.014. There were about 3 times increase in the odds of dose tapering probability for patient treated longer than 24 months after the policy implemented in April 2014.

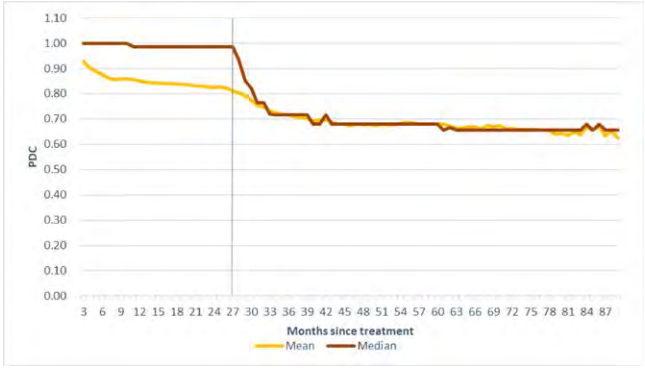


Figure 2. The change of PDC of advanced therapy over the treatment period

Conclusion: For RA patients, PDC of advanced therapy dropped notably after patients received advanced therapy for more than 24 months. The tapering policy implementation significantly increased the probability of dose tapering of advanced therapy in patients with treatment duration ≥ 24 months.

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Table 1. effect of treatment duration and dose tapering policy on the probability of dose tapering

	Odds ratio	95%	CI	p value
Effect of Treatment Duration (in pre-policy period) ≥24-month vs <24-month	2.73	(2.45,	3.05)	<.001
Effect of Dose Tapering policy (in treatment duration <24 months) Post-policy* vs Pre-policy	0.94	(0.87,	1.01)	0.110
Interaction of Treatment Duration by Dose Tapering policy ≥24-month x Post-policy	1.17	(1.03,	1.32)	0.014

* Dose Tapering policy was implemented on April 1st, 2014

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SAT0115

COGNITIVE IMPAIRMENT WAS FREQUENT IN PATIENTS WITH RHEUMATOID ARTHRITIS STARTING A BIOLOGIC, WITH SIMILAR RATES OF INHIBITION OR OVERSTIMULATION: AN ANALYSIS OF 84 PATIENTS FROM THE SARIPRO STUDY

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Background: While cognitive impairment is an issue for patients with rheumatoid arthritis (RA), there are few data available on its frequency and possible link with other outcomes in RA.
Objectives: To assess cognitive impairment in RA and its association with RA and patients' characteristics.
Methods: The SariPRO study (NCT 03449758) was a French multicenter study assessing the effects of sarilumab 200 mg on patient-reported outcomes in patients with moderately to severely active RA with an inadequate response or intolerance to conventional synthetic or biologic DMARDs. This report focuses on baseline data.
The main outcome of this analysis was cognitive impairment evaluated by the cognitive sub-score of the patient-reported multidimensional assessment of mood disorders (MAThyS) scale. This sub-score is scored between 0 (i.e. feeling that thoughts occur slower) and 40 (i.e. racing thoughts) where 20 is the best state. This sub-score was analyzed by tertiles where the lowest tertile indicates general inhibition, the second tertile includes normal states, and the highest tertile indicates general excitation. In addition to the MAThyS total score and sub-scores (Cognition, Emotion, Psychomotricity, Motivation and Sense perception), age, gender, duration of RA, methotrexate use, antibody status (rheumatoid factor/ACPA positivity), fatigue (FACIT-F), anxiety /depression (HADS), as well as patient global assessment (PGA) were collected. Cognitive impairment was defined as inhibition (first tertile) and excitation (third tertile). The association between cognitive inhibition and patients' characteristics (demographic, psychological and disease activity) was estimated by univariate and multivariate logistic regression in an exploratory analysis. There was no imputation of missing data.
Results: In all 84 patients were included, characteristics at baseline were as expected for an RA population initiating a biologic: mean (SD) age: 59.1 (12.3) years, 75.0% female, disease duration 10.0 (10.3) years, rheumatoid factor positivity 76.1%, ACPA positivity 81.3%, and DAS28 5.0 (1.1). The mean (SD) MAThyS cognition score was 18.2 (4.9). In the exploratory multivariate analysis, factors associated to cognitive inhibition were depression (HADS depression score ≥ 8, odds ratio, OR=3.15 [95% confidence interval, 1.16; 8.59], p=0. 025), emotion inhibition (lower tertile of the MATHYS emotion regulation: OR=4.76 [1.54; 14.28]; p=0.007) and low motivation (lower tertile of motivation: OR=4.17 [1.54; 11.11]; p=0.005).
Conclusion: Cognitive impairment was frequent in this population of patients with active RA, with similar rates of cognitive inhibition and cognitive excitation. The results suggest that there may be an association between cognitive inhibition, depression, emotion dysregulation and absence of motivation. Unexpectedly, this

exploratory analysis did not show an association between cognition impairment and demographic characteristics or disease activity.

References:

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SAT0116 COMPARISON OF THE EFFICACY OF ABATACEPT ON ELDERLY AND YOUNG PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The widespread use of biologic agents has greatly improved the prognosis of rheumatoid arthritis (RA). On the other hand, elderly patients with RA are relatively increasing. Although achieving low disease activity is a goal for those elderly patients as well as young patients, the efficacy of tumor necrosis factor inhibitors were reported to be equally or slightly less effective in elderly patients than in young patients. There is a lack of evidence for the efficacy of abatacept (ABT) in elderly patients.

Objectives: In this study, we aimed to clarify the efficacy of ABT in elderly and young patients with RA compared to csDMARDs.

Methods: This is a multicenter, open-label, prospective, observational study. All patients with RA enrolled this study are refractory to csDMARDs and have not received any biologics. Either ABT or csDMARDs was administered at the discretion of physicians to elderly (65 years and older) and young (20-64 years) patients (ABT-elderly, ABT-young, control (CTL)-elderly, and CTL-young groups). Comparison was made between 4 groups of patients. The primary study endpoint was a good response by EULAR response criteria at week 24 after administration. The research procedure has been approved by the ethics committee of Toho University School of Medicine (Approval number: A17112).

Results: A total of 219 patients, 127 in the ABT group and 92 in the CTL group, were enrolled in this study. The majority of patients were women (82.7%) with a mean age (±SD) of 64.9±13.6 years (74.5±5.9 years in the elderly group and 52.4±10.1 years in the young group). The ABT group had higher disease activity, higher HAQ, and higher steroid use rates and dosage than the CTL group. These were also observed in the elderly group. In the young group, although the ABT group had higher disease activity and higher HAQ than the CTL group, no difference was observed in steroid use rates and dosage. The ABT group more frequently achieved a good response by EULAR response criteria compared to the CTL group at week 24 (58.8% and 27.2%, respectively, p<0.0001). The ABT group also showed higher efficacy than the CTL group in the elderly and young groups with a good response. Regarding the improvement in DAS28-ESR and DAS28-CRP, the ABT group was also superior to the CTL group. There was no difference on efficacy between elderly and young patients from the ABT groups.

Based on propensity score matching for disease activity at baseline, 61 matched pairs of patients treated with ABT or csDMARDs were statistically extracted. Although there was no significant difference in the rate of patients with a good response by EULAR response criteria between the ABT and the CTL groups, the ABT group showed significantly better response than the CTL group in the elderly. Furthermore, the ABT group was superior to the CTL group in improvement in both DAS28-ESR and DAS28-CRP, and similar results were obtained in the elderly. However, there was no significant difference between the ABT group and the CTL group in the young. In addition, elderly patients had significant improvement in DAS28-ESR compared with young patients in the ABT group.

Conclusion: Treatment with ABT showed higher efficacy compared with CTL, particularly in elderly patients with RA.

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SAT0117 TRIMESTER EXPOSURE AND PREGNANCY OUTCOMES IN WOMEN EXPOSED TO GOLIMUMAB – RESULTS FROM THE COMPANY PHARMACOVIGILANCE DATABASE

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Background: Rheumatologic disorders and inflammatory bowel disease can affect women of childbearing potential. Golimumab (GLM) is approved for several rheumatologic indications and ulcerative colitis (UC).

Objectives: To characterize pregnancy outcomes in patients treated with GLM, data obtained from maternal exposure to GLM are presented.

Methods: This dataset includes individual patient cases reported to the manufacturer through 06 April 2019. Cases included in the analysis were medically confirmed cases of maternal exposures to GLM during pregnancy or within 3 months prior to conception, and a reported pregnancy outcome. Both prospectively reported (ie, pregnancy outcome not known when first reported) and retrospectively reported cases (ie, pregnancy outcome known when first reported) were included. Cases originated from various sources, including spontaneous reporting, clinical studies, and registries.

Results: Two hundred eight pregnancy cases (131 rheumatologic indications; 43 UC; and 34 other) with 211 reported birth outcomes were identified. Of these 208 pregnancy cases, 119 were prospective and 89 were retrospective. Average maternal age was 31.9 years. Of the 119 prospectively reported pregnancy cases, 89 (74.8%) resulted in live births, 19 (16.0%) resulted in spontaneous abortion (of these, 42.1% (8/19) received GLM in combination with methotrexate [MTX]), 10 (8.4%) resulted in induced/elective abortion, and 1 (0.8%) resulted in ectopic pregnancy. Overall, 9 congenital anomalies were reported (2 prospective and 7 retrospective cases).

For 183 of the 208 pregnancy cases with reported outcomes, the trimester of exposure to GLM was known. Among the 110 prospectively reported cases, 82 (74.5%) were exposed during trimester 0 or 1. Of these, 19 had concomitant exposure to MTX, with the following birth outcomes: 8 live births, 8 spontaneous abortions, 3 elective/induced abortions. Eighteen of the prospectively reported cases (16.4%) were exposed to GLM through trimesters 1-3 and all resulted in live births (none with congenital anomalies; 1 infant with exposure to GLM and MTX was born preterm).

Conclusion: The rates of congenital malformations and spontaneous abortions were consistent with published background rates for the general population. Persistent exposure throughout pregnancy was rare. Limitations of this analysis include the lack of a direct comparison group, the variable amount of data available in the reports, and the possible bias towards reporting more negative outcomes in retrospective cases.

Disclosure of Interests: Marijo Otero-Lobato Shareholder of: Johnson & Johnson, Employee of: Johnson & Johnson, Suzan Esslinger Shareholder of: Johnson & Johnson, Consultant of: Johnson & Johnson, Novartis, Eli Lilly and Sandoz, Employee of: Johnson & Johnson, Susan Gabriel Shareholder of: Johnson & Johnson, Employee of: Johnson & Johnson, Merck, GSK, Michael Clark Shareholder of: Johnson & Johnson, Employee of: Johnson & Johnson, Pamela Sheridan Shareholder of: Johnson & Johnson, Roche Pharmaceuticals, Employee of: Johnson & Johnson, Roche, Novartis, Bayer, Anja Geldhof Shareholder of: Johnson & Johnson, Employee of: Johnson & Johnson

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SAT0118

COMPARATIVE EFFECTIVENESS OF TOCILIZUMAB IN COMBINATION WITH METHOTREXATE VERSUS TUMOR NECROSIS FACTOR INHIBITORS (TNFIS) IN COMBINATION WITH METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS WITH PRIOR EXPOSURE TO TNFIS

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Background: Clinical studies have demonstrated the efficacy of tocilizumab (TCZ) administered with methotrexate (MTX) in improving rheumatoid arthritis (RA) disease activity in patients who have had an inadequate response to tumor necrosis factor inhibitors (TNFis).
Objectives: To compare the effectiveness of TCZ + MTX with that of TNFis + MTX in patients with RA who had prior exposure to TNFis in routine clinical practice.
Methods: Eligible participants were TCZ-naïve patients from the Corrona RA registry who initiated TCZ + MTX or a TNFi + MTX after January 1, 2010 and had a 6-month follow-up visit. Patients in both groups must have used ≥ 1 TNFi, had a Clinical Disease Activity Index (CDAI) score available at initiation (baseline) and 6 months and had a CDAI score > 10 at baseline. The primary outcome was mean change in CDAI from baseline to 6 months. Secondary outcomes included achievement of low disease activity (LDA; CDAI ≤ 10) and mean change in modified Health Assessment Questionnaire (mHAQ) at 6 months. Patients were grouped by baseline MTX dose (≤ 10 mg; > 10 to ≤ 15 mg; > 15 to ≤ 20 mg; > 20 mg); outcomes were compared between patients initiating TCZ and those initiating a TNFi overall and within each MTX dose group using propensity score (PS)-trimmed populations. As a sensitivity analysis, TCZ and TNFi initiators in each group were PS-matched 1:1 and outcomes were assessed in the matched populations. Linear and logistic regression models were estimated in the trimmed and matched populations, adjusting for covariates not balanced after PS trimming or matching, respectively.
Results: A total of 415 TCZ + MTX initiators and 725 TNFi + MTX initiators met the inclusion criteria prior to PS trimming or matching. The overall trimmed population included 402 TCZ + MTX initiators and 703 TNFi + MTX initiators. In the trimmed population, patient demographics were generally comparable between TCZ + MTX and TNFi + MTX initiators; the mean age was 57.1 years in the TCZ + MTX group and 57.7 years in the TNFi + MTX group, the majority of patients in both groups were female (≥ 80%) and white (≥ 82%) and the mean duration of RA was 11.8 and 10.5 years in the TCZ + MTX and TNFi + MTX groups, respectively. Higher proportions of patients initiating TCZ had received ≥ 2 prior biologics (66.0% to 76.3%) compared with those initiating a TNFi (33.2% to 42.2%) across all MTX dose groups. Patients initiating TCZ had higher mean baseline CDAI scores (26.5 to 29.3) than those initiating a TNFi (24.7 to 27.5). Patients in both cohorts had improvements in CDAI and mHAQ scores and achieved LDA in similar proportions at 6 months regardless of baseline MTX dose (Fig 1). Results were comparable between TCZ and TNFi initiators across all MTX groups in the trimmed population after adjustment for potential confounding variables. Similar results were observed in the PS-matched cohorts.
Conclusion: In this real-world population of US patients with RA who had prior TNFi exposure, there was no statistically significant or clinically meaningful difference in the effectiveness of therapy in patients who initiated TCZ + MTX compared with TNFi + MTX.
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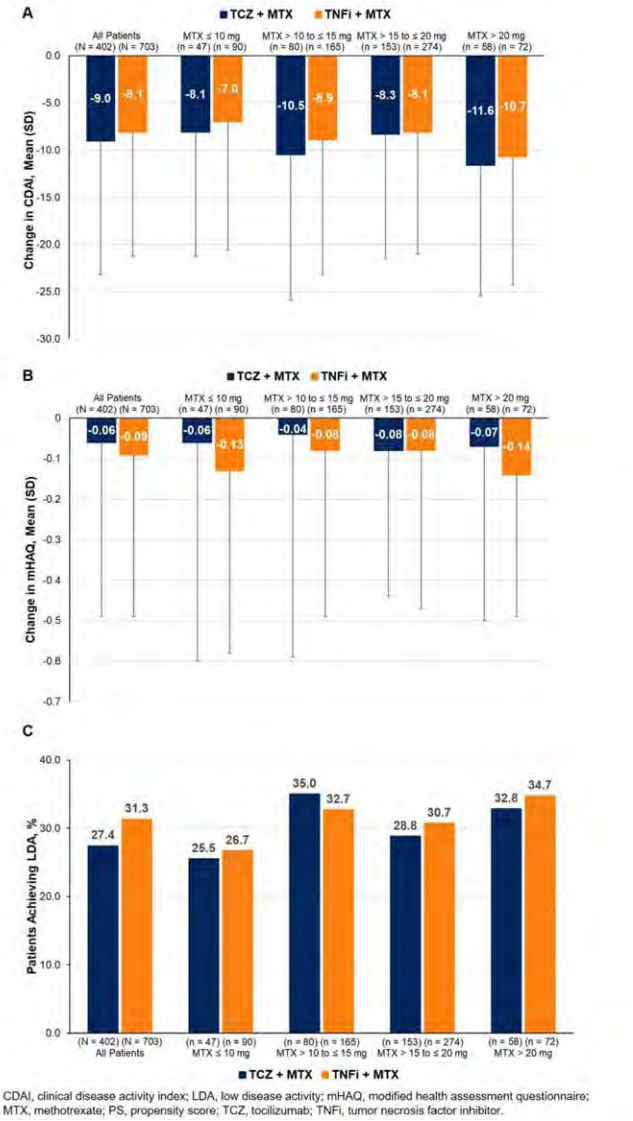
SAT0119

PARADOXICAL NEUTROPHIL ACTIVATION BY ANTI-IL6 THERAPY: TRANSCRIPTOME ANALYSIS SHOWS A RATIONALE FOR DERMATOLOGICAL ADVERSE REACTIONS AND DECREASED NEUTROPHIL COUNTS AFTER TOCILIZUMAB TREATMENT

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Background: Skin rashes as a side effect of Tocilizumab therapy (TCZ- Tx) has not been paid much attention, because the incidence was only 1~2% in the drug information sheets. However, we experienced several RA cases with development of various skin rashes associated with neutrophil activation after TCZ-Tx. On the other hand, it is well known that the neutrophil counts in peripheral blood decreases after TCZ-Tx, whereas it does not affect the rate of serious infections. The detailed mechanism is still unclear.
Objectives: To detect the characteristics of the changes in gene expressions of peripheral blood associated with TCZ-Tx and the development of skin rashes as its side effect.

Figure 1. PS Trimmed Unadjusted Outcomes at 6 Months Stratified by Baseline MTX Dose. (A) Mean Change in CDAI. (B) Mean Change in mHAQ. (C) Proportion of Patients Who Achieved LDA.



CDAI, clinical disease activity index; LDA, low disease activity; mHAQ, modified health assessment questionnaire; MTX, methotrexate; PS, propensity score; TCZ, tocilizumab; TNFi, tumor necrosis factor inhibitor.

Methods: Total of 14 RA patients with TCZ-Tx were included. Among them, 4 patients developed TCZ-related rashes (group S) and 10 patients did not show any side effects (group C). Peripheral whole blood at just before (pre) and 3 months after (post) TCZ-Tx from each patient were subjected to the analysis. Total RNAs were extracted with PAXgene miRNA kit and analyzed with next-generation sequencing. First, group C was investigated for the normal response to TCZ-Tx. Differentially expressed genes (DEGs) were selected by paired comparison (post vs. pre). And then, enrichment analysis using gene ontology (GO) terms were performed. Second, to explore the characteristics of group S, all expressed genes in 14 cases at just before TCZ-Tx

were subjected to a hierarchical clustering analysis. The DEGs (group S vs. C and post vs. pre) were also investigated with weighted gene co-expression network analysis (WGCNA) and GO analysis. Meanwhile, the total eigengene expressions of the important modules identified by WGCNA in each cases were also calculated.

Results: Surprisingly, 8 out of the top 10 enriched GO terms in the up-regulated genes were relevant to leukocyte activation such as 'neutrophil migration" by the analysis of DEGs (post vs. pre) in group C. The cluster analysis of 'pre' genes confirmed that the patterns of gene expression between group S and C was different. WGCNA analysis of DEGs (group S vs. C) revealed that genes related to acute inflammation such as 'leukocyte mediated immunity' were activated in group S. Interestingly, it was not correlated with disease activity score (DAS) of RA. By the analysis of DEGs (post vs. pre) of upregulated genes, we found that the total eigengene expressions of the module enriched with genes related to 'cell adhesion' or 'leukocyte migration' were significantly increased in all cases of group S.

Conclusion: This is the first evidence that the genes associated with neutrophil migration is significantly activated after TCZ-Tx. It is noteworthy that the gene activation was observed in cases without any side effects. The decreased neutrophil counts in peripheral blood have been known after initiation of TCZ-Tx, which did not affect the rate of serious infections. Recently, It was reported that TCZ affects neutrophil trafficking to the bone marrow[1)]. Our findings will provide a rationale for its cause. On the other hand, we experienced several RA cases with development of various skin rashes associated with neutrophil activation after TCZ-Tx. However, majority of patients do not develop the side effect, even though genes related to 'neutrophil migration' are activated. In group S, our findings indicate that the genes related to 'leukocyte mediated immunity' was already activated at the initiation of treatment without correlating to DAS of RA, furthermore, the gene upregulation related to 'leukocyte migration' was more prominent after TCZ-Tx. Although it is difficult to predict the patients developing skin rashes before TCZ-Tx, we do not recommend to use TCZ for the patients with neutrophilic dermatosis which is often associated with RA.

References: :

[1] Lok LSC *et al.*, *Eur J Clin Invest*. 47(10):736-745 (2017).

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SAT0120

UNITED STATES RHEUMATOLOGY PRACTICE-BASED REAL-WORLD EVIDENCE OF INFUSION REACTIONS IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH INTRAVENOUS GOLIMUMAB OR INFLIXIMAB: IMPACT OF PRIOR BIOLOGIC EXPOSURE AND METHOTREXATE UTILIZATION

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Background: AWARE (Comparative and Pragmatic Study of Golimumab IV Versus Infliximab in Rheumatoid Arthritis) is an ongoing Phase 4 comparator study designed to provide a real-world assessment of intravenous golimumab (GLM) and intravenous infliximab (IFX) in patients (pts) with rheumatoid arthritis (RA). The study recently reached its primary endpoint (comparison of overall incidence of infusion reactions in GLM- vs IFX-treated pts after 52 weeks) with the last patient reaching 52 weeks of treatment or discontinuation from the study. AWARE also records prior use of biologic medications and concomitant use of methotrexate (MTX).

Objectives: To assess the incidence of infusion reactions among GLM and IFX pts reported at baseline by examining the influence of prior biologic exposure or concurrent use of MTX.

Methods: AWARE is a prospective, noninterventional, observational, multicenter, 3-year study conducted in the US. RA patients (1,270 adults) were enrolled at the time of initiating treatment with GLM or IFX. All treatment decisions were made at the discretion of the treating rheumatologist. An infusion reaction was any adverse event that occurred during an infusion or within 1 hour after the infusion of either GLM or IFX. Imputations were not performed on these AWARE data. Data shown are mean ± standard deviation.

Results: Demographics are shown in Table 1 and the incidence of infusion reactions in different AWARE cohorts is shown in Table 2. GLM and IFX pts were comparable in sex and utilization of MTX at baseline. Both age and disease duration of GLM pts was greater than IFX pts by ~2 years. There was a higher proportion of bionaïve pts in IFX-treated group compared to GLM-treated group. Overall, infusion reactions occurred more frequently among IFX-treated pts compared to GLM-treated pts. The difference in infusion reaction rates between IFX- and GLM-treated pts was also evident among subgroups of bionaïve vs non-bionaïve pts, and among MTX non-users vs MTX users (characteristics reported at baseline). GLM pts did not report any serious or severe infusion reactions. These were reported rarely (3/585 pts) in IFX-treated pts. Among GLM and IFX pts with an infusion reaction, 55.6% of GLM and 77.1% of IFX pts had at least one medication for infusion reaction. Infusion reactions accounted for 9.7% and 35.1% of discontinuations due to adverse events in GLM and IFX pts, respectively.

Table 1. Baseline Characteristics in the AWARE Study

	GLM (n=685)	IFX (n=585)
Age (years)	60.9 ± 13.43	58.0 ± 12.85
Sex (% female)	85.0 %	79.5 %
Disease Duration (years)	9.16 ± 9.975	7.20 ± 9.716
Bionaïve (%)	33.0%	48.6%
MTX plus (%)	75.4%	75.1%

MTX=methotrexate

Table 2. Infusion Reactions in AWARE in Subsets of Patients ± Prior Biologic Use or ± Concurrent MTX

	GLM (n=685)		IFX (n=585)		GLM (n=685)		IFX (n=585)	
	Bionaïve	Non-Bionaïve	Bionaïve	Non-Bionaïve	No MTX Use	MTX Use	No MTX Use	MTX Use
Infusion Reactions	6/242 (2.5%)	21/443 (4.7%)	36/251 (14.3%)	47/334 (14.1%)	15/265 (5.7%)	12/420 (2.9%)	44/229 (19.2%)	39/356 (11.0%)
Medication for Infusion Reactions	33.3%	59.1%	78.9%	73.6%	50.%	58.3%	73.6%	77.6%

MTX=methotrexate

Conclusion: Whether bionaïve, non-bionaïve, MTX non-user or MTX user at baseline, the incidence of infusion reactions was notably lower among GLM- vs IFX-treated pts. Serious and/or severe infusion reactions did not occur among GLM pts and were rare among IFX pts. IFX was more commonly administered mediation for an infusion reaction compared to GLM. Infusion reactions accounted for almost four times the number of discontinuations related to adverse events in IFX pts compared to GLM pts.

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SAT0121

PAIN AND OTHER PATIENT-REPORTED OUTCOMES IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO DID OR DID NOT ACHIEVE TREATMENT RESPONSE BASED ON IMPROVEMENT IN SWOLLEN JOINTS IN TOCILIZUMAB CLINICAL TRIALS

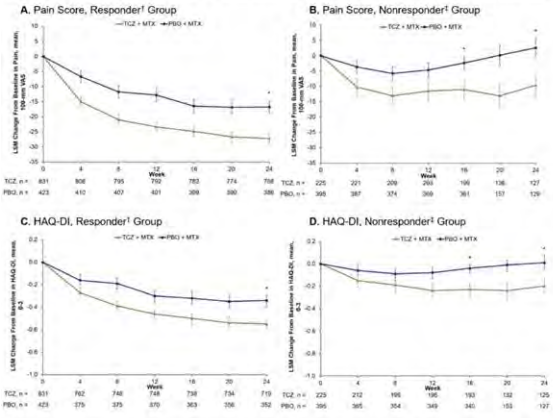
A. Sebba[1,2], J. Han[3], S. Mohan[3]. [1]*Arthritis Associates, Palm Harbor, United States of America*; [2]*University of South Florida, Tampa, United States of America*; [3]*Genentech, Inc., South San Francisco, United States of America*

Background: Significant improvements in pain and other patient-reported outcomes (PROs) have been shown in large clinical trials in patients with rheumatoid arthritis (RA) who receive tocilizumab (TCZ) compared with placebo (PBO). Recent data suggest that pain in RA may be noninflammatory as well as inflammatory, and

improvement in pain scores and other PROs may be seen in patients who do not respond to treatment based on disease activity measures that evaluate inflammation.
Objectives: To assess changes in pain scores and other PROs in patients with RA who did or did not achieve ≥ 20% improvement in SJC in TCZ clinical trials.
Methods: Data from patients with active RA who received intravenous TCZ 8 mg/kg + MTX or PBO + MTX in 3 Phase III studies (OPTION [NCT00106548], TOWARD [NCT00106574] and LITHE [NCT00109408]) were included. All patients had moderate to severe RA with an inadequate response or intolerance of MTX (OPTION, LITHE) or conventional synthetic disease-modifying antirheumatic drugs (csDMARDs; TOWARD). Changes in pain (visual analog scale [VAS], 0-100 mm), Health Assessment Questionnaire Disability Index (HAQ-DI, 0-3), 36-Item Short Form Survey (SF-36) physical component score (PCS) and mental component score (MCS; 0-50) and Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue score (0-52) from baseline to Week 24 were evaluated. Results were compared between patients receiving TCZ + MTX and those receiving PBO + MTX in both patients who achieved ≥ 20% improvement in SJC (responders) and those who did not (nonresponders). The changes from baseline were analyzed using a mixed model with repeated measures, including the following covariates and interactions: treatment, visit, baseline of endpoint, region, baseline DAS28 and interactions of visit with treatment and baseline of endpoint.

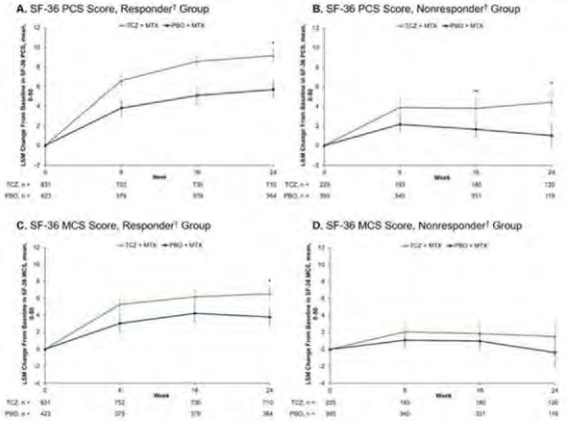
Figure:

Figure 1. LSM Change in Pain Score and HAQ-DI From Baseline to Week 24 in Responder and Nonresponder Groups



HAQ-DI, Health Assessment Questionnaire Disability Index; LSM, least squares mean; MTX, methotrexate; PBO, placebo; TCZ, tocilizumab; VAS, visual analog scale.
*P < 0.0001 for comparison between TCZ + MTX and PBO + MTX.
†Patients who achieved ≥ 20% improvement in swollen joint counts.
‡Patients who did not achieve ≥ 20% improvement in swollen joint counts; at Week, 16 patients were permitted to receive rescue therapy.

Figure 2. LSM Change in SF-36 PCS and MCS From Baseline to Week 24 in Responder and Nonresponder Groups



LSM, least squares mean; MTX, methotrexate; MCS, mental component score; PCS, physical component score; PBO, placebo; SF-36, 36-Item Short Form Survey; TCZ, tocilizumab.
*P < 0.0001 for comparison between TCZ + MTX and PBO + MTX.
**P < 0.005 for comparison between TCZ + MTX and PBO + MTX.
†Patients who achieved ≥ 20% improvement in swollen joint counts.
‡Patients who did not achieve ≥ 20% improvement in swollen joint counts; at Week 16, patients were permitted to receive rescue therapy.

Results: Data from 1254 responders (TCZ + MTX, n = 831; PBO + MTX, n = 423) and 620 nonresponders (TCZ + MTX, n = 225; PBO + MTX, n = 395) were included. Patients receiving TCZ + MTX had significantly greater improvement in pain scores and HAQ-DI compared with PBO + MTX in the responder group (–27.19 vs –16.77 and –0.55 vs –0.34, respectively; P < 0.0001 for both) and nonresponder group (–9.59 vs 2.53 and –0.20 vs 0.01; P < 0.0001 for both) at Week 24 (Figure 1). Similar results were seen at Week 16 in the nonresponder group (–11.06 vs –2.38 and –0.23 vs –0.04; P < 0.0001 for both) prior to initiation of rescue treatment. At Week 24 in the responder group, patients receiving TCZ + MTX had significantly greater improvements compared with PBO + MTX in SF-36 PCS and MCS (9.16 vs 5.71 and 6.55 vs 3.79, respectively; P < 0.0001 for both) (Figure 2) and FACIT-Fatigue (8.39 vs 5.11; P < 0.0001). In the nonresponder group, patients receiving TCZ + MTX had significantly greater improvements compared with PBO + MTX in SF-36 PCS at Week 16 (3.81 vs 1.65; P = 0.0006) and Week 24 (4.42 vs 1.01; P < 0.0001) (Figure 2) and FACIT-Fatigue at Week 16 (3.82 vs 1.32; P = 0.0039) and Week 24 (3.90 vs 1.40; P = 0.0111).
Conclusion: Patients with RA who received TCZ + MTX had significantly greater improvements in pain score and other PROs than those who received PBO + MTX regardless of whether they achieved ≥ 20% improvement in SJC. Clinical outcome at Week 24 correlated well with PROs, with a relatively larger improvement in pain score and other PROs in the responder group than in the nonresponder group; relative to PBO + MTX, these improvements appear numerically similar in the responder and nonresponder groups with consistently smaller difference between the groups in TCZ-treated arms. The consistent effect of TCZ on PROs in both responder and nonresponder groups warrants further study on the impact of TCZ on sources of pain independent of that caused by joint inflammation.

Acknowledgments: This study was sponsored by Genentech, Inc. Support for third-party writing assistance, furnished by Health Interactions, Inc, was provided by Genentech, Inc.

Disclosure of Interests: Anthony Sebba Consultant of: Genentech, Gilead, Lilly, Regeneron Pharmaceuticals Inc., Sanofi, Speakers bureau: Lilly, Roche, Sanofi, Jian Han Shareholder of: Genentech, Inc., Employee of: Genentech, Inc., Shalini Mohan Shareholder of: Genentech, Inc., Employee of: Genentech, Inc.
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SAT0122

HIGHER DOSES OF METHOTREXATE ASSOCIATED WITH DISCONTINUATION OF ORAL GLUCOCORTICOIDS AFTER INITIATION OF BIOLOGICAL DMARDS: A RETROSPECTIVE OBSERVATIONAL STUDY BASED ON DATA FROM A JAPANESE MULTICENTER REGISTRY STUDY

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Background: Glucocorticoids exert anti-inflammatory effects and are important drugs used to treat rheumatoid arthritis(1). We recommend glucocorticoid discontinuation as soon as possible because glucocorticoid caused several side effects, but many patients continue to take oral glucocorticoids long-term in daily clinical practice. The frequency of use of glucocorticoid has gradually declined, and there are several reports on discontinuation of glucocorticoid due to the initiation of biological disease-modifying antirheumatic drugs (bDMARDs)(2). However, there is no report showing the relation between discontinuation of glucocorticoid and MTX dose.
Objectives: The present study aimed to explore factors associated with glucocorticoid discontinuation at 52 weeks after initiating bDMARDs.
Methods: We established the large observational cohort, the Nagoya University orthopedic facility multicenter study (TBCR), and a total of 3119 patients used bDMARD and examined the status of oral glucocorticoid use at 52 weeks after initiating the 1st bDMARD. In predictive analyses, the outcome variable was glucocorticoid discontinuation at 52 weeks after bDMARD initiation. Factors associated with baseline characteristics at bDMARD initiation were assessed with univariate and stepwise forward multivariate logistic regression analyses. This cohort study was not randomized. Propensity score (PS) matching was used to align patient backgrounds to avoid selection bias.
Results: Subjects were 564 patients administered glucocorticoids and methotrexate (MTX) following initiation of the 1st bDMARD (Figure 1). Mean DAS28-CRP at bDMARD initiation was 4.70 ± 1.16. Percentages of patients with low, moderate, and high disease activity as evaluated by DAS28-CRP at bDMARD initiation were 4.7%, 23.5%, and 71.8%, respectively. By 52 weeks after bDMARD initiation, 164 patients (29.1%) discontinued glucocorticoids. Multivariate analysis identified age (odds ratio (OR), 0.98), MTX dose (OR, 1.11), and glucocorticoid dose (OR, 0.87) as factors independently associated with glucocorticoid discontinuation at the time of bDMARD initiation (Table 1). After adjusting for baseline characteristics using propensity score matching among patient groups administered MTX ≤ 8 mg/week and MTX > 8 mg/week, 105 pairs remained. Among patients administered MTX > 8 mg/week, 41.0% discontinued glucocorticoids. Among those administered MTX ≤ 8 mg/week, 22.9% discontinued glucocorticoids, with a significant difference between the two groups (Figure 2, P=0.007).

Table 1. Factors associated with baseline characteristics at bDMARD initiation

	Continuation (n=400)	Discontinuation (n=164)	Univariate Odds ratio (95% CI)	Multivariate Odds ratio (95% CI)
Age, years	58.4 ± 12.9	54.3 ± 14.3	0.98 (0.97-0.99) *	0.98 (0.97-0.99) *
Disease duration, years	9.4 ± 9.4	7.5 ± 8.5	0.98 (0.95-0.99) *	–
Female, %	80.3	81.1	1.06 (0.67-1.68)	–
DAS28-CRP	4.78 ± 1.15	4.50 ± 1.16	0.81 (0.69-0.96) *	–
Seropositivity, %	90.0	86.1	0.69 (0.38-1.25)	–
MTX dose, mg/week	7.7 ± 2.5	8.8 ± 3.0	1.16 (1.09-1.24) *	1.11 (1.03-1.21) *
Glucocorticoid dose, mg/day	4.9 ± 2.1	4.3 ± 2.1	0.86 (0.78-0.95) *	0.87 (0.78-0.97) *
TNF inhibitor use, %	88.8	85.4	0.74 (0.43-1.26)	-

Data are presented as mean ± standard deviation.

Conclusion: Data from the TBCR revealed that, from a clinical perspective, glucocorticoid use decreased among RA patients treated with bDMARDs. Higher doses of MTX (> 8 mg/week) at the time of bDMARD initiation were found to be associated with glucocorticoid discontinuation in patients treated with bDMARDs. In addition, we found that aggressive use of MTX was sufficient to fulfill the Treat-to-Target approach, demonstrating that glucocorticoid discontinuation is a viable option.

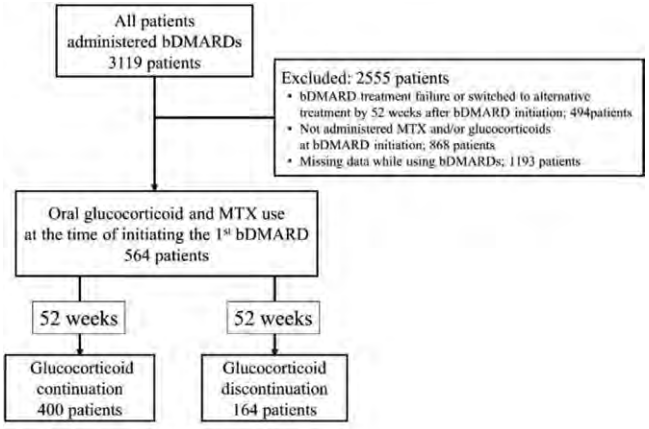


Figure 1: Flowchart depicting the study design.

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[1] Smolen JS. Ann Rheum Dis. 2014;73(3):492-509.
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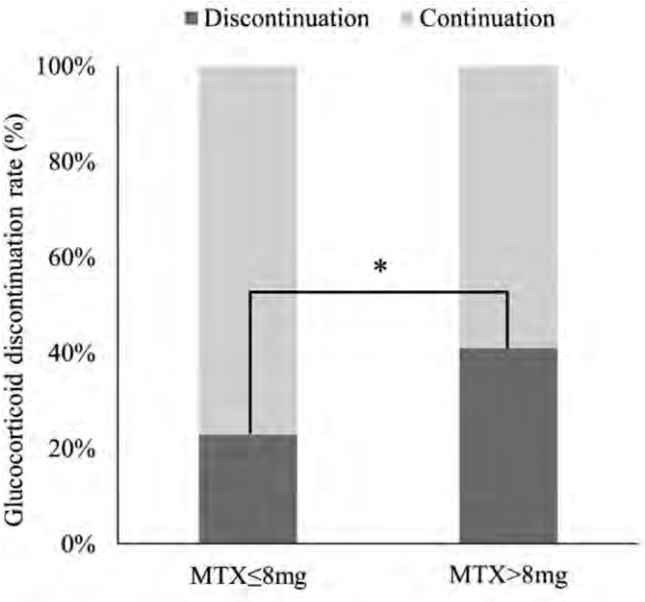


Figure 2: Glucocorticoid discontinuation rates in groups administered MTX ≤ 8 mg/week and MTX > 8 mg/week after propensity score matching. * P < 0.05.

Disclosure of Interests: Mochihito Suzuki Speakers bureau: Bristol-Myers Squibb, Eisai, and Asahi Kasei, Toshihisa Kojima Grant/research support from: Chugai, Eli Lilly, Astellas, Abbvie, and Novartis, Consultant of: AbbVie, Speakers bureau: AbbVie, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eli Lilly, Janssen, Mitsubishi Tanabe, Pfizer, and Takeda, Nobunori Takahashi Speakers bureau: AbbVie, Asahi Kasei, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eisai, Eli Lilly, Janssen, Mitsubishi Tanabe, Ono, Pfizer, Takeda, and UCB Japan, Shuji Asai Speakers bureau: AbbVie, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eisai, Janssen, Takeda, and UCB Japan, Kenya Terabe: None declared, Naoki Ishiguro Grant/research support from: AbbVie, Asahi Kasei, Astellas, Chugai, Daiichi-Sankyo, Eisai, Kaken, Mitsubishi Tanabe, Otsuka, Pfizer, Takeda, and Zimmer Biomet, Consultant of: Ono, Speakers bureau: Astellas, Bristol-Myers Squibb, Daiichi-Sankyo, Eli Lilly, Pfizer, and Taisho Toyama

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SAT0123

TREATMENT SATISFACTION, EXPECTATIONS, PATIENT PREFERENCES AND CHARACTERISTICS, INCLUDING DIGITAL HEALTH LITERACY (DHL), AND THE IMPACT OF SUBOPTIMAL DISEASE CONTROL IN A LARGE INTERNATIONAL COHORT OF PATIENTS WITH RHEUMATOID ARTHRITIS (RA): THE SENSE STUDY

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Background: Patient characteristics, their treatment preferences and goals are important determinants of treatment success in rheumatoid arthritis (RA).
Objectives: SENSE study aimed at assessing the impact of inadequate response to disease-modifying anti-rheumatic drugs on disease outcomes, and analyze their attitude, their treatment and disease.
Methods: Non-interventional, cross-sectional study conducted in 18 countries in Europe, Asia, and America. Adult RA patients with moderate/high disease activity were eligible. Patient satisfaction was assessed by Treatment Satisfaction Questionnaire for Medication, Version 1.4 (TSQM v1.4). Treatment adherence, patient preferences, and expectations were evaluated by visual analog scale. eHealth Literacy Scale was employed for evaluating DHL. Work Productivity and Activity Impairment Questionnaire-Rheumatoid Arthritis, v2.0 (WPAI-RA) was used to assess workability and patient documentation for healthcare resource utilization (HRU).
Results: 1624 patients were included in this analysis; most were female (84.2%), middle-aged, and had a mean (standard deviation [SD]) disease duration of 10.5 (9.3) years. 11.9% of the patients had retired early and 6.0% were unemployed due to RA. Mean (SD) total WPAI-RA score was 55.1% (26.7). In the previous 3 months, the mean (SD) number of healthcare professional and emergency room visits were 2.2 (2.5) and 1.6 (1.3), respectively. Mean (SD) TSQM v1.4 global satisfaction subscore was 60.9 (20.9), with only 13.5% reporting good treatment satisfaction (TSQM global ≥80). The leading treatment expectations were 'general improvement of arthritis,' 'less joint pain,' and 'lasting relief of RA symptoms,' with mean (SD) scores of 5.7 (1.6–1.7) for each. 60.7% of patients preferred oral administration and 31.3% preferred not to use drug combinations for RA. Preferred time to effect was predominantly 'up to one week' (71.1%). Least frequently side effects rated 'acceptable' were 'increased risk for malignancies' (3.5%) and 'increased risk for cardiovascular diseases' (3.3%). Most patients (67.4%) had poor DHL. Good adherence (in 87.4% of patients) was significantly associated with lower levels of joint pain.
Conclusion: Suboptimal disease control has a significant impact on satisfaction, workability, and HRU. Our results can support shared decision-making when setting RA treatment strategy.

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SAT0124

RISK OF SERIOUS INFECTION, MALIGNANCY, OR DEATH IN JAPANESE RHEUMATOID ARTHRITIS PATIENTS TREATED WITH A COMBINATION OF ABATACEPT AND TACROLIMUS: A RETROSPECTIVE COHORT STUDY

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Background: Both Abatacept (ABT) and Tacrolimus (Tac) suppress T cell immunity, but it is unknown whether combinations of these will increase the risk of adverse events.

Objectives: To evaluate whether combining ABT and Tac increases the risk of infection and malignancy compared to their individual use in Japanese rheumatoid arthritis (RA) patients.

Methods: We conducted a retrospective cohort study of RA patients using the multicenter database in Japan (NinJa). The dataset was clinical information at a certain point within each year, and the point was any point selected by a registered physician. RA was clinically diagnosed in the dataset. (1)

We analyzed the data from RA patients registered in NinJa during the period from April 2010 to March 2019. In this study, we compared three groups who received Tac, ABT or a combination of both. We included patients who had just begun initiating treatment with ABT or Tac, and we excluded patients who used TNF inhibitors, IL-6 inhibitors, and Jak inhibitors in the first year. The primary outcome was defined the composite events including infections that require hospitalization, newly diagnosed malignancy, and death from any cause after initiation of ABT or Tac. We assessed whether the combination contributed to increase the risk of outcome by performing a Cox regression analysis.

Results: Among the 27032 RA patients in the registry, 2009 patients were included. The Tac, ABT and combination groups consisted of 1328, 563 and 118 patients, respectively. (Figure 1) (Table 1) Primary outcomes occurred in 149 (13.4%), 62 (13.5%), 14 (13.9%) patients, of the Tac, ABT and combination groups, respectively. The incidence between groups was not significantly different (p= 0.638). (Figure 2) A Cox regression analysis was adjusted for the following parameters: age, sex, disease duration, modified health assessment questionnaire, disease activity score 28-CRP, CRP, use of prednisolone, and use of methotrexate. The analysis revealed no significant differences between groups. The hazard ratio (95% confidence interval) was as follows: Tac 1.00 (Ref), ABT 1.02 (0.74-1.40), and combination 1.15 (0.65-2.05).

Table1. baseline characteristics

		Tacrolimus	Abatacept	Combination	p value
N (person-year)		1328 (2505)	563 (944)	118 (193)	
age (median [IQR])		69.00 [60.00, 76.00]	70.00 [61.00, 76.00]	67.00 [59.00, 74.00]	0.169*
sex female (%)		1038 (78.2)	468 (83.1)	97 (82.2)	0.039†
disease duration (yr) (median [IQR])		9.00 [4.00, 18.00]	11.00 [5.00, 21.00]	11.00 [7.00, 20.00]	0.002*
Steinbrocker stage (%)	I	285 (23.5)	82 (15.6)	12 (12.1)	<0.001†
	II	361 (29.8)	125 (23.8)	25 (25.3)	
	III	232 (19.1)	150 (28.5)	31 (31.3)	
	IV	334 (27.6)	169 (32.1)	31 (31.3)	
mHAQ (median [IQR])		0.25 [0.00, 0.75]	0.38 [0.00, 1.00]	0.50 [0.00, 1.13]	<0.001*
DAS28CRP (median [IQR])		2.58 [1.88, 3.40]	2.77 [2.09, 3.62]	3.01 [2.27, 3.98]	<0.001*
CRP (mg/dL) (median [IQR])		0.30 [0.10, 1.02]	0.35 [0.13, 1.10]	0.30 [0.14, 0.82]	0.590*
RF positivity (%)		708/895 (79.1)	331/400 (82.8)	57/71 (80.3)	0.314†
Tacrolimus (mg/d) (median [IQR])		1.50 [1.00, 2.00]	0.00 [0.00, 0.00]	2.00 [1.00, 2.50]	<0.001*
MTX use (%)		619 (46.6)	264 (46.9)	32 (27.1)	<0.001†
PSL use (%)		749 (56.4)	299 (53.1)	71 (60.2)	0.253†

Abbreviations: anti-CCP, anti-cyclic citrullinated peptide; mHAQ, modified Health Assessment Questionnaire; MTX, methotrexate; PSL, prednisolone; RF, rheumatoid factor * Kruskal-Wallis test; † chi square test; ‡ analysis of variance (ANOVA)

Conclusion: The combination of ABT and Tac does not increase the risk of adverse events in patients with rheumatoid arthritis in Japan when compared to the use ABT or Tac alone. Further evaluation is needed.

References:

[1] Matsui T, et al. Ann Rheum Dis 2007;66:1221–6.

Figure 1. Flow chart of the patients

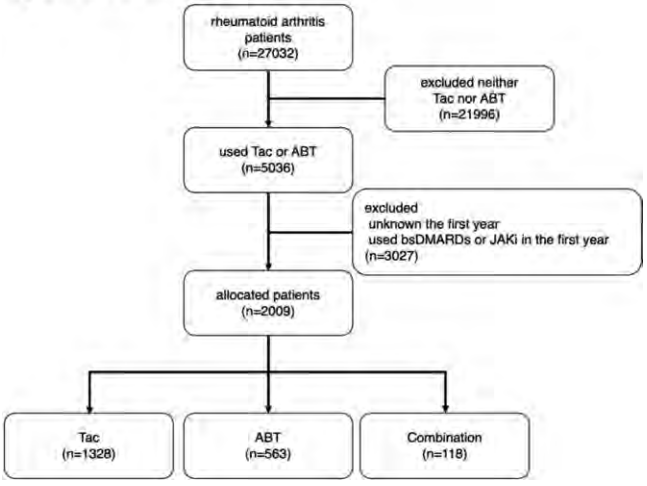
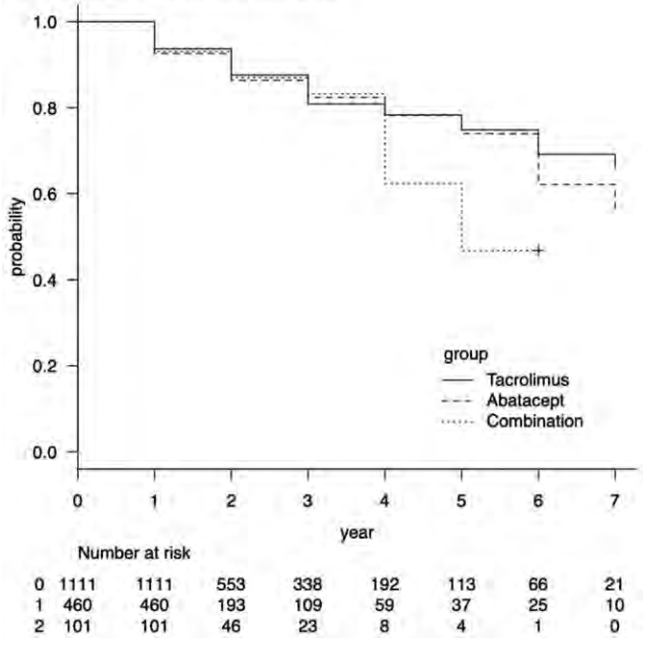


Figure 2. Kaplan-Meier curve of each group



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SAT0125

ASSOCIATION BETWEEN CHANGE IN HEALTH ASSESSMENT QUESTIONNAIRE DISABILITY INDEX AND TREATMENT RESPONSE IN PATIENTS WITH RHEUMATOID ARTHRITIS IN TOCILIZUMAB CLINICAL TRIALS

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Background: The efficacy and safety of intravenous (IV) and subcutaneous (SC) tocilizumab (TCZ) in combination with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) and as monotherapy in patients with rheumatoid arthritis (RA) has been demonstrated in large clinical trials and real-world data studies. The Health Assessment Questionnaire Disability Index (HAQ-DI) is commonly used to assess physical function in patients with RA. While HAQ-DI outcomes at Week 24 in TCZ clinical trials have been reported, outcomes at Week 12 and results stratified by treatment response categories at Weeks 12 and 24 have not been previously described.

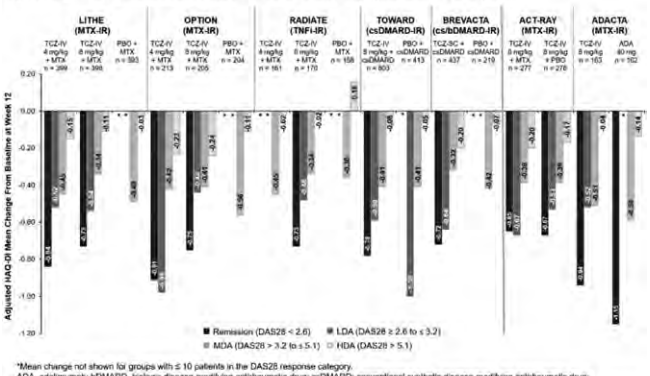
Objectives: To report the association between change in HAQ-DI from baseline to Weeks 12 and 24 and Disease Activity Score in 28 joints (DAS28) response categories in patients who received TCZ or comparators in TCZ clinical trials.

Methods: Data from patients with active RA who received TCZ or a comparator from 6 Phase III or IV TCZ-IV studies (OPTION [NCT00106548], RADIATE [NCT00106522], TOWARD [NCT00106574] LITHE [NCT00109408], ACT-RAY [NCT00810199] and ADACTA [NCT01119859]) and 1 Phase III TCZ-SC study (BREVACTA [NCT01232569]) were analyzed. Mean change in HAQ-DI score at Weeks 12 and 24 was assessed in patients stratified by DAS28 disease activity level (DAS28 < 2.6 [remission], DAS28 ≥ 2.6 to ≤ 3.2 [low disease activity; LDA], DAS28 > 3.2 to ≤ 5.1 [moderate disease activity; MDA], DAS28 > 5.1 [high disease activity; HDA] at Weeks 12 and 24. The adjusted least squares mean (LSM) change from baseline was estimated using a mixed model with repeated measures, including region (North America vs non-North America), RA duration (> 2 years vs ≤ 2 years), baseline HAQ-DI and DAS28, treatment, visit, visit by treatment and visit by baseline HAQ-DI.

Results: Data from 5051 patients were included. Across all studies, the mean duration of RA ranged from 6.3 to 12.6 years. At baseline, patients had severe RA with a mean DAS28 ≥ 6.3; baseline HAQ-DI was ≥ 1.5. At Week 12, patients who achieved remission or LDA had greater improvements in HAQ-DI than those in MDA or HDA (Figure 1). Results were similar at Week 24 (Figure 2). Among patients who received TCZ and achieved remission or LDA, mean improvement in HAQ-DI was ≥ 0.65 and ≥ 0.44, respectively, at Week 12 (Figure 1) and ≥ 0.48 and ≥ 0.43 at Week 24 (Figure 2). Mean changes in HAQ-DI were similar between patients who received TCZ-IV in combination with MTX or as monotherapy (ACT-RAY) and in those who received TCZ-IV or ADA as monotherapy (ADACTA).

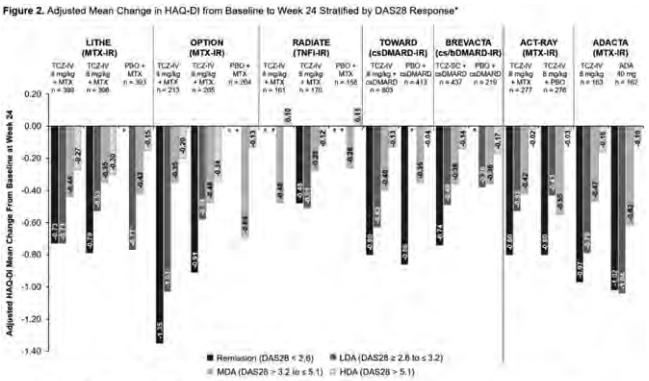
Conclusion: Patients with long-standing, severe RA who received IV or SC TCZ as monotherapy or in combination with csDMARDs had improvement in physical function and disease activity at Week 12 that was maintained at Week 24. Overall, across all the trials, response to treatment was associated with improvement in physical function.

Figure 1. Adjusted Mean Change in HAQ-DI from Baseline to Week 12 Stratified by DAS28 Disease Activity Level*



*Mean change not shown for groups with ≤ 10 patients in the DAS28 response category.
ADA, adalimumab; bDMARD, biologic disease-modifying antirheumatic drug; csDMARD; conventional synthetic disease-modifying antirheumatic drug; DAS28; disease activity score based on 28 joints; HAQ-DI, Health Assessment Questionnaire Disability Index; HDA, high-disease activity; IR, inadequate response; IV, intravenous; LDA, low-disease activity; MDA, moderate-disease activity; MTX, methotrexate; PBO, placebo; SC, subcutaneous; TCZ, tocilizumab; TNFi; tumor necrosis factor inhibitor.

Figure 2. Adjusted Mean Change in HAQ-DI from Baseline to Week 24 Stratified by DAS28 Response*



*Mean change not shown for groups with ≤ 10 patients in the DAS28 response category.
ADA, adalimumab; bDMARD, biologic disease-modifying antirheumatic drug; csDMARD; conventional synthetic disease-modifying antirheumatic drug; DAS28; disease activity score based on 28 joints; HAQ-DI, Health Assessment Questionnaire Disability Index; HDA, high-disease activity; IR, inadequate response; IV, intravenous; LDA, low-disease activity; MDA, moderate-disease activity; MTX, methotrexate; PBO, placebo; SC, subcutaneous; TCZ, tocilizumab; TNFi; tumor necrosis factor inhibitor.

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Disclosure of Interests: : Sebastian Unizony Grant/research support from: Genentech, Inc., Joseph Dang Shareholder of: Genentech, Inc., Employee of: Genentech, Inc., Jian Han Shareholder of: Genentech, Inc., Employee of: Genentech, Inc., Margaret Michalska Shareholder of: Genentech, Inc., Employee of: Genentech, Inc., Jennie H. Best Shareholder of: Genentech, Inc., Employee of: Genentech, Inc.

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SAT0126

BIOLOGICAL MANAGEMENT IN RHEUMATOID ARTHRITIS: RESULTS OF A REAL-WORLD COHORT FROM THE NETHERLANDS

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Background: Management of rheumatoid arthritis (RA) has improved dramatically due to early diagnosis, treat-to-target approaches based on disease activity measures, and the introduction of biological disease modifying anti-rheumatic drugs (bDMARDs). Tumor necrosis factor inhibitors (TNFis) are the most frequently prescribed bDMARDs after failure on conventional synthetic (cs)DMARDs. However, data on drug survival and predictors that influence the survival time are sparse. Moreover, drug survival could decrease with the number of bDMARDs that have been used.

Objectives: To investigate drug survival for first and second line biologicals and factors that influence survival time.

Methods: We used a retrospective observational cohort in which data were retrieved from the local pharmacy database and patient records of the Erasmus Medical Center in the Netherlands. We included patients who started with a TNF-inhibitor between 2000 and 2020 and were diagnosed with RA. Data on age, gender, disease duration, time to first biological, survival time, co-medication and reasons for discontinuation were collected.

Results: Data were already derived from 216 RA patients (table 1). Of the included patients 28 (13%) started their first TNFi within 6 months after diagnosis, while 56 (26%) patients started their first TNFi two years after diagnosis. Median (95%) survival time of the first-line biological was 1.6 years (1-2), and for the second-line biological 0.8 years (0.5-0.9). Biological survival was significantly longer for the first-line biological compared to the second (p=0.0008) (Figure 1A). Discontinuation reasons for the first-line biological were ineffectiveness (38%), adverse events (13%), remission (18%), pregnancy (17%), patient preference (4%) or other reasons (10%). Discontinuation reasons for the second-line biological were ineffectiveness (51%), adverse events (17%), remission (7%), pregnancy (13%), patient preference (2%) or other reasons (10%)(table 1). Drug survival for the first-line biological was significantly longer when it was combined with a csDMARD (p=0.05) (Figure 1B). Furthermore, multivariable cox regression analyses showed a significant relation between first-line biological survival time and gender (p=0.005, hazard ratio 0.28 (95% CI 0.12-0.68)) and erosions (p=0.004, hazard ratio 0.37 (95% CI 0.19-0.73)) when discontinuation due to remission was omitted from the analysis. Within aforementioned analyses we corrected for ACPA, age of diagnosis, age at first biological, and BMI. The chance that patients stopped with their biological due to remission was negatively influenced by having erosions (p=0.02, hazard ratio 0.07 (95% CI 0.007-0.66)) and positively influenced by age at first biological (p=0.03, hazard ratio 1.4 (95% CI 1.03-1.94)) in a multivariable cox model in which we corrected for gender, ACPA, erosions, BMI, and age of diagnosis.

Table 1. Characteristics of patient population

		RA patients, n=216
Age at diagnosis, mean (sd)		37.5 (16)
Age at first biologic, mean (sd)		42.4 (16)
Gender, female, n (%)		194 (90)
ACPA positive, n (%)		157 (73)
RF positive, n (%)		158 (73)
Erosive disease, n (%)		85 (40)
BMI, mean (sd)		26.9 (6.7)
Time to first biological, years, mean (sd)		4.9 (5.7)
Discontinuation reasons 1st biological, n(%)	Ineffective	58 (38)
	Adverse event	20 (13)
	Remission	27 (18)
	Pregnancy	26 (17)
	Patient preference	6 (4)
	Other	16 (10)
Discontinuation reasons 2nd biological, n(%)	Ineffective	42 (51)
	Adverse event	14 (17)
	Remission	6 (7)
	Pregnancy	11 (13)
	Patient preference	2 (2)
	Other	8 (10)

Conclusion: Median drug survival of the first biological is 1.6 years. Drug survival time is prolonged if patients are using co-medication and shortened in the presence of erosions. Furthermore, drug survival diminishes with the number of bDMARDs that are used.

References:

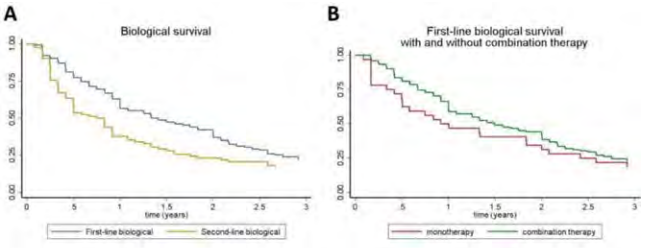


Figure 1 Kaplan Meier curves for biological survival. (**A**) Biological survival of first- and second-line biological in rheumatoid arthritis patients. (**B**) Biological survival with and without combination therapy with a csDMARD.

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SAT0127

REAL-WORLD PREDICTORS OF STARTING DIFFERENT ADVANCED DMARD TREATMENTS IN RHEUMATOID ARTHRITIS: A PROSPECTIVE INVESTIGATION FROM THE CANADIAN EARLY ARTHRITIS COHORT (CATCH) GROUP

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Background: RA patients with inadequate DMARD response may be treated with a TNF inhibitor (TNFi), non-TNFi or janus kinase inhibitor (JAKi) [1].
Objectives: Compare characteristics of real-world early RA (ERA) patients starting TNFi, non-TNFi, and JAKi post DMARD failure.
Methods: Data were analyzed from early RA patients (symptoms < 1 year) enrolled in CATCH who started TNFi, non-TNFi or JAKi as first line advanced therapy from 2014 to 2019. Descriptive statistics, t-tests and chi-square tests summarized and compared secular trends and patient characteristics initiating each class of therapy. Multinomial logistic regression analyses were done.
Results: 246 participants started advanced therapy during the study period; (75%) female, mean(SD) age 50(14) years. First line prescriptions for JAKi increased and TNFi decreased (Fig. 1). Those receiving JAKi had longer disease duration, fewer tender joints, and lower DAS28, CDAI, ESR, MD global (all p <0.05) (Table 1). The strongest predictor of starting JAKi was province (Ontario where access is preferential for JAKi and biosimilar TNFi) (Table 2). Those prescribed TNFi had shorter disease duration, younger age, fewer comorbidities, and treatment location outside Ontario (Table 1,2). Those starting non-TNFi had higher DAS28; predictors included older age, higher education, and more comorbidities (Table 1,2).

Table 1. Characteristics prior to starting advanced therapy

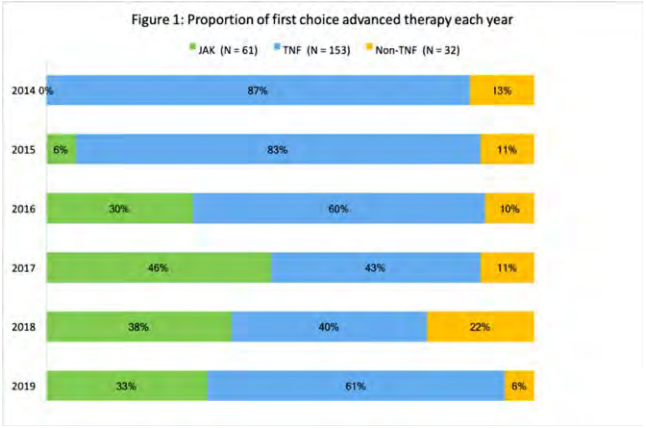
Variable	Total Sample (N = 246)	JAKi (N = 61)	TNFi (N = 153)	Non-TNFi (N = 32)	p-value£
Disease duration (months) mean (SD)	39 (34.1)	50.8 (39.3)	32.5 (29.1)	48 (38.6)	0.0006
DAS28 (ESR - CRP if ESR was missing) mean (SD)	4.2 (1.4)	3.6 (1.4)	4.3 (1.4)	4.8 (1.5)	0.0012
CDAI mean (SD)	21.5 (14.8)	16.5 (13.7)	22.9 (14.8)	24.8 (14.9)	0.0089
Tender joint count (0-28), median (IQR) §	4 (7)	2 (6)	5 (8)	6 (9)	0.0224
ESR median (IQR) §	13 (20)	12 (13)	13 (20)	28.0 (23.5)	0.0448
MD Global (0-10) mean (SD)	4.2 (2.7)	3.2 (2.7)	4.4 (2.6)	4.8 (2.8)	0.0030

§ IQR: 75 – 25 percentile
£ p-value: ANOVA for continuous variable, chi-square for categorical

Table 2. Multinomial regression for initiating advanced DMARD therapy

Disease stage & Clinical Disease Activity	Advanced DMARD			
	Adjusted for Age, sex, education, comorbidity		Fully Adjusted$^{\varphi}$	
	Non-TNF vs TNF	JAK vs TNF	Non-TNF vs TNF	JAK vs TNF
Age	1.01 (0.98, 1.05)	1.01 (0.99, 1.04)	1.01 (0.97, 1.05)	1.02 (0.99, 1.05)
Women vs Men	1.98 (0.71, 5.58)	1.33 (0.63, 2.80)	2.35 (0.76, 7.27)	1.72 (0.73, 4.02)
Education (< HS vs ≥ HS)	**2.92 (1.28, 6.63)**	1.49 (0.78, 2.86)	**2.83 (1.12, 7.15)**	2.08 (0.97, 4.47)
RDCI baseline	**1.35 (1.01, 1.81)**	1.21 (0.95, 1.53)	1.30 (0.95, 1.78)	1.23 (0.94, 1.60)
Private Insurance (No vs Yes)	NI	NI	1.26 (0.47, 3.40)	0.99 (0.44, 2.25)
RF Positive	NI	NI	1.47 (0.56, 3.85)	1.84 (0.82, 4.12)
CDAI	NI	NI	1.01 (0.98, 1.04)	0.97 (0.94, 1.00)
Region				
Quebec vs Ontario (ON)	NI	NI	0.59 (0.20, 1.72)	**0.44 (0.20, 0.94)**
West vs ON	NI	NI	1.32 (0.29, 5.98)	**0.11 (0.01, 0.99)**

$^{\varphi}$ Adjusted for; baseline age, sex, education, RDCI; province; RF positive in first year; private insurance; CDAI at visit prior to initiation



Conclusion: Patient and physician related factors (location of practice) determined which advanced therapeutic was prescribed. JAKi use is increasing in ERA.
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UCB Canada (CATCH, Clinical nurse)
BMS (CATCH, Clinical nurse, Observational Study Protocol IM101664. SEROPOSITIVITY IN A LARGE CANADIAN OBSERVATIONAL COHORT)
Janssen (CATCH)
Celgene (Clinical nurse)
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SAT0128 ARE THERE ANY DIFFERENCES BETWEEN ADULT-ONSET RHEUMATOID ARTHRITIS PATIENTS AND LATE-ONSET RHEUMATOID ARTHRITIS PATIENTS IN TERMS OF USE OF BIOLOGICAL DRUGS AND DRUG RETENTION RATE? RESULTS FROM THE TURKBIO REGISTRY

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Background: Rheumatoid arthritis(RA) is one of the most frequent rheumatic disease, and the age of onset is between 30-50 years old. Late-onset RA(LORA) is usually defined as RA with onset at age 60 or over.
Objectives: To investigate the choice, effectiveness and the retention rate of biological drugs in LORA patients.
Methods: TURKBIO registry is the Turkish version of Danish DANBIO rheumatological database which has been established in 2011. We studied RA patients in TURKBIO registry cohort between the dates of 2011 and 2020. All patients fulfilled the American College of Rheumatology criteria for RA and were classified into two groups based on their age at symptom onset: adult-onset RA(>18-<60 years; AORA) and LORA(≥60 years). In both groups, demographical, clinical and laboratory variables; disease activity, current and previous treatment were compared.
Results: From 10 centers, 2111 RA patients recruited, and 8.8% of them was LORA patients. In LORA, the frequency of female was less than AORA. While, there was no difference between LORA and AORA in terms of erosion presence and RF positivity, antiCCP positivity was more frequent in LORA group. The use of antiTNF was lower, and the use of rituximab was more frequent in LORA. At 12 months after bDMARDs therapy, serum CRP and ESR levels and DAS28-CRP showed higher changes compared to baseline values in LORA. Although the mortality rate was higher in LORA, the adverse reactions were reported to be higher in AORA, and most common advers reaction was infections in both groups(Table). The longest survival was observed in infliximab and rituximab(-median 22 and 20months) in LORA, in rituximab and golimumab(median 16 and 12months) in AORA.

Table. Comparison of demographic, laboratory findings and biological treatment

(median;25-75) n(%)	AORA (<60) (n:1925)	LORA (≥60) (n:186)	*p*
Age (year)	54 (43-61)	71 (68-74)	<0.001
Disease duration (year)	11.4 (7-18)	6 (4-9)	<0.001
Gender (Female)	1562 (81)	124 (67)	<0.001
Anti-CCP positivity	747 (62)	65 (72)	0.044
RF positivity	721 (61)	63 (70)	0.085
Erosion presence	486 (56)	41 (62)	0.955
Drug survival (months)	18 (6-44)	18 (4-31)	0.046
Concomitant csDMARDs			
MTX	629 (34)	39 (22)	0.001
SZP	146 (8)	13 (7)	0.781
LEF	501 (27)	35 (20)	0.032
bDMARDs			
AntiTNF	1068 (56)	73 (39)	<0,001
TCZ	304 (16)	20 (11)	0,069
TOFA	294 (15)	27 (15)	0,784
RTX	439 (23)	57 (31)	0,016
ABA	298 (16)	34 (18)	0,317
Response ΔESH	-6 (-21-4)	-18 (-36--3)	0.016
(12 months) ΔCRP	-2 (-12-0.6)	-9.3 (-28--0.1)	0.014
ΔDAS28-CRP	-1.3 (-3--0.1)	-2.2 (-3--1)	0.023
ΔHAQ	-0.3 (-0.8-0)	-0.4 (-0.8--0.1)	0.114
Adverse effects	440 (23)	32 (17)	0.077
Malignancy	9 (0,5)	3 (1.6)	0.082
Infection	192 (10)	10 (5)	0.042
Allergy	63 (3)	4 (2)	0.404
Dermatitis	62 (3)	1 (0,5)	0.040
Death	18 (0.9)	7 (4)	0.004
Other	136 (7)	11 (6)	0.556

Conclusion: The frequency of LORA who uses bDMARDs was 8.8% in our database. In the elderly patient population, there are some reservations about the use of biological drugs in general due to several co-morbidities and concommitant drug used. Although data on this issue are limited, appropriate biological use can be effective and reliable in required patients.
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SAT0129 ROLE OF SHARED EPITOPE ON THE EFFECTIVENESS OF TNFI TREATMENT FOR PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) has been shown a strong genetic association with particular *HLA–DRB1* alleles containing shared epitope (SE). However, whether SE is clinically useful in treatment choices is insufficiently investigated [1] and previous studies have presented mixed findings in the role of SE in the response of TNFi therapies [2,3].
Objectives: To assess the role of SE in response to TNFi treatment in real-world RA patients (pts).
Methods: Pts enrolled in a large RA registry, Brigham and Women's Hospital RA Sequential Study, with known SE and received TNFi therapies were included for the analysis. TNFi pts were identified by the first-time use of the drugs between March 2003 to June 2018. For this analysis, all pts were followed up to 1 year. Summary statistics are reported for demographics, serostatus and disease activity (DA) at baseline and follow-up, stratified by SE status. Given the strong association of SE and anti-citrullinated protein antibody (ACPA), the analysis was further stratified by ACPA status. The effect of SE on change in DA was assessed using linear regression model with age, gender, RA disease duration, baseline DA, smoking status, SE, ACPA and ACPA-SE interaction as covariates.
Results: Of the 484 TNFi pts included in the study, 68.8% were SE+. SE+ pts (vs SE-) were more likely to be rheumatoid factor positive, have erosive

disease and a higher disease duration, irrespective of ACPA status. No difference in the change of DA was observed by SE. In SE- pts, ACPA+ pts had a greater reduction of DA than ACPA- pts (Table 1). After accounting for baseline differences, there was no significant effect of SE status on the mean change from baseline in any of the 3 DA measures.(Figure 1) The change in DA was not associated with ACPA but was significantly affected by disease duration and baseline DA.

Table 1. Disease Activity in TNFi Patients, Stratified by SE and ACPA Status

Parameter	SE+ (1 & 2 alleles, n=333)			SE- (n=151)		
	ACPA+	ACPA–	Overall	ACPA+	ACPA-	Overall
	(n=264)	(n=69)	(n=333)	(n=90)	(n=61)	(n=151)
Baseline, Mean (SD)						
DAS28 CRP	3.94 (1.69)	3.57 (1.61)	3.86 (1.67)	3.85 (1.49)	3.45 (1.65)	3.69 (1.57)
CDAI	23.06 (18.13)	18.95 (15.96)	22.25 (17.78)	21.91 (15.96)	17.72 (17.06)	20.26 (16.48)
SDAI	24.08 (18.82)	19.96 (16.59)	23.27 (18.45)	22.58 (16.34)	18.55 (17.87)	20.99 (17.01)
Follow-up, Mean (SD)						
DAS28 CRP	3.42 (1.55)	2.69 (1.32)	3.27 (1.53)	3.19 (1.43)	3.11 (1.53)	3.16 (1.47)
CDAI	17.61 (15.53)	12.11 (12.65)	16.51 (15.14)	15.15 (13.35)	14.94 (14.73)	15.07 (13.84)
SDAI	18.35 (15.73)	12.45 (12.78)	17.15 (15.34)	15.31 (13.81)	15.71 (15.45)	15.46 (14.38)
Change, Mean (SD)						
DAS28 CRP	-0.48 (1.31)	-0.65 (1.53)	-0.52 (1.36)	-0.52 (1.50)	-0.24 (0.93)	-0.42 (1.34)
CDAI	-4.29 (13.16)	-4.79 (13.13)	-4.39 (13.12)	-6.45 (13.56)	-2.63 (9.58)	-4.99 (12.28)
SDAI	-4.74 (14.13)	-5.07 (13.90)	-4.80 (14.05)	-6.87 (14.21)	-2.97 (10.32)	-5.41 (12.98)

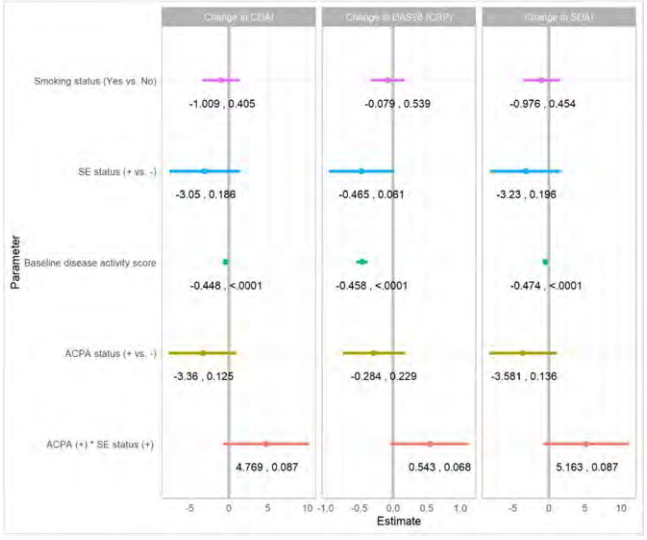


Figure 1. Linear Regression Model for Change in Disease Activity*Estimates, p-values are shown as data labels on the graphs; The above model is adjusted for age, gender, RA duration, smoking status, SE status, baseline DA, ACPA and ACPA*SE status*

Conclusion: This real-world study validates the finding from previous studies conducted in clinical settings that SE does not differentiate treatment response for TNFi therapies.

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SATURDAY, 06 JUNE 2020

Rheumatoid arthritis - non biologic treatment and small molecules

SAT0130

TREAT-TO-TARGET STRATEGY OF >8.000 PATIENTS WITH EARLY RHEUMATOID ARTHRITIS: DOES SMOKING AFFECT ACHIEVEMENT OF REMISSION ON METHOTREXATE AND TIME TO START OF FIRST BIOLOGIC? RESULTS FROM THE NATIONWIDE DANISH DANBIO REGISTRY

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Background: Smoking is a known risk factor for rheumatoid arthritis (RA). It is largely unknown whether smoking has any impact on disease activity and treatment outcomes (e.g. achieving remission on methotrexate and time to first biological disease modifying anti-rheumatic treatments (bDMARD)) in early RA with a modern treat-to-target strategy.

Objectives: To explore if smoking was associated with treatment outcomes in newly diagnosed patients with RA starting first conventional synthetic (cs) DMARDs in routine care.

Methods: Observational cohort study. Adult patients with RA starting first csDMARD during year 2010-2018 were identified in the Danish nationwide quality registry, DANBIO. Smoking status (current/never/previous) upon start of csDMARD (=baseline), disease activity, 1-year treatment outcomes and bDMARD treatment were retrieved from DANBIO. Data were censored Oct 2019.

Impact of smoking status was explored for the following outcomes: 1) median baseline disease activity baseline, 2) remission at 1-year (logistic regression analyses), 3) time to first bDMARD (Cox-regression analyses). Regression analyses were adjusted for gender and age.

Results: Among 9515 patients, 8647 (91%) had available smoking status (Current 23%/never 50%/previous 27%) and were included. Baseline disease activity was independent of smoking status (Table 1). First line csDMARD was methotrexate in 91% of patients. Compared to never smokers, the current smokers were more often men, younger and sero-positive for IgM-RF and anti-CCP.

Table 1. Patient characteristics and disease activity at baseline and 1 year stratified by smoking status. Numbers are medians (IQR) unless otherwise stated.

		Smoking status		
		Current	Never	Previous
Baseline	Patient numbers, N	2007	4308	2332
	Age, yrs	58 (49-66)	61 (48-71)	62 (52-70)
	Female, %	62	71	63
	IgM-RF positive, %	71	54	65
	Anti-CCP positive, %	71	53	65
	DAS28	4.4 (3.4-5.3)	4.4 (3.4-5.3)	4.3 (3.3-5.3)
	CDAI	18.7 (11.7-27.3)	18.4 (10.9-27.4)	18.5 (10.4-27.6)
	VAS patient global, mm	60 (35-81)	55 (30-77)	55 (31-78)
1 year	Patient number, N	1793	3837	2053
	DAS28	2.6 (1.9-3.7)	2.3 (1.7-3.4)	2.5 (1.8-3.4)
	CDAI	6.4 (2.8-12.5)	4.9 (1.8-10.3)	5.4 (2-10.8)
	DAS28-remission, %	49	57	53
	CDAI-remission, %	27	35	33
	VAS patient global, mm	37 (14-67)	29 (10-57)	30 (11-58)

DAS28-response: DAS28(CRP)≤2.6; CDAI-remission: CDAI≤2.8

Never and previous smokers had higher odds of remission at 1 year's follow-up compared to current smokers. In adjusted Cox regression analyses, baseline smoking was associated with shorter time to start of first bDMARD (Table 2).

Table 2. Impact of baseline smoking status on treatment outcomes

	Comparison	Odds Ratio (95% CI)	p
DAS28-remission 1 yr, yes vs. no*	Never vs. current smoker	1.43 (1.27;1.62)	<0.001
	Previous vs. current	1.14 (0.99;1.30)	0.07
CDAI remission 1 yr, yes vs. no*	Never vs. current	1.53 (1.34;1.75)	<0.001
	Previous vs. current	1.29 (1.11;1.50)	<0.001
	Comparison	Hazard Ratio (95% CI)	p
Start of bDMARD during follow-up**	Never vs current smoker	0.85 (0.76;0.96)	0.006
	Previous vs. current	1.05 (0.93;1.19)	0.4

*Logistic regression analyses (adjusted for gender and age)
** Cox regression analyses (adjusted for gender and age)

Conclusion: In this observational study of >8000 patients with RA starting a first csDMARD, current smoking was associated with lower odds of achieving remission on methotrexate and higher chance of having started bMDARD compared to never smokers. Seropositivity may be an intermediate variable. Further analyses are planned to study impact of comorbidities and other confounding factors.

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SAT0131

CARDIO- AND CEREBROVASCULAR RISK WITH CONVENTIONAL SYNTHETIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS (CSDMARDS) IN RHEUMATOID ARTHRITIS (RA): A REAL-WORLD COMPARATIVE ASSESSMENT

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Background: RA is associated with an increased cardiovascular (CV) risk. csDMARDs are first-line treatments for RA and can mitigate this risk, but limited data exist on their CV effects. Previous trials have reported protective effects for methotrexate (MTX) and hydroxychloroquine (HCQ), but no similar data exist on sulfasalazine (SSZ) or leflunomide (LEF).

Objectives: To assess the comparative effect of csDMARDs on the risk of myocardial infarction (MI) and stroke in RA patients

Methods: Data from 6 claims/electronic health records databases across Germany, US, and UK, all mapped to the Observational Medical Outcomes Partnership (OMOP) common data model. A cohort study was conducted including patients ≥18 years old, with first RA diagnosis in 2005-2019, initiating csDMARD monotherapy with MTX, HCQ, SSZ, or LEF. Those with a prior diagnosis of other inflammatory arthritis or <1 year prior follow-up were excluded. Patients were followed until first outcome, death, loss of or 5 years follow-up. Propensity score stratification was used, and hazard ratios (HR) estimated for HCQ, SSZ and LEF compared to MTX in each dataset using Cox regression. HR were calibrated (cHR) for residual confounding using negative control outcomes. Estimates were pooled where I^2 for heterogeneity <0.4. Intention to treat and an on treatment analyses are reported.

Results: 145,248 patients were included (MTX: 73,996, HCQ: 49,752, SSZ: 12,256, LEF: 9,244). Pooled rates of MI and stroke for MTX were 7.64 and 10.26 per 1,000 person years respectively. Detailed estimate cHRs are shown in Figure 1 for the intention to treat analysis. MI risk with SSZ and LEF was comparable to MTX. Risk of stroke was similar between LEF and MTX, but reduced for HCQ and SSZ compared to MTX, with pooled cHR (95% CI) 0.86 (0.78 to 0.95) and 0.71 (0.52 to 0.98) for HCQ and SSZ respectively. Similar results were found for "on treatment" analyses.

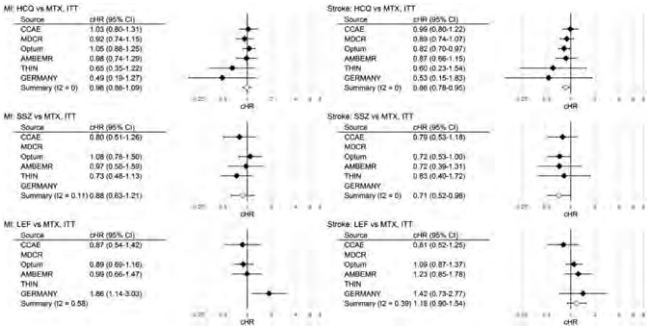


Figure 1. Calibrated hazard ratios (cHRs) for MI and stroke

Conclusion: Overall, all four csDMARDs had similar effects on MI risk. HCQ and SSZ use were associated with a decreased risk of stroke compared to MTX. The observed differences may be attributable to differential effects on the atherosclerotic process, differential disease control, or both.

Database estimates not reported where adequate covariate balance not attained. Meta-analysis results not reported where I2>0.4. MEDICARE did not pass diagnostics for SSZ and LEF analyses. cHR: calibrated Hazard Ratio; CI: Confidence Interval; MTX: Methotrexate; HCQ: Hydroxychloroquine; SSZ: sulphasalazine; LEF: Leflunomide; THIN: The Health Improvement Network (UK); Optum: Optum de-identified Clinformatics Datamart (US); MDCR: Medicare (US); GERMANY: IQVIA Disease Analyzer EMR (Germany); CCAE: IBM MarketScan Commercial Claims and Encounters (US); AMBEMR: IQVIA Ambulatory EMR (US)

Database estimates not reported where adequate covariate balance not attained. Meta-analysis results not reported where I2>0.4. MEDICARE did not pass diagnostics for SSZ and LEF analyses. cHR: calibrated Hazard Ratio; CI: Confidence Interval; MTX: Methotrexate; HCQ: Hydroxychloroquine; SSZ: sulphasalazine; LEF: Leflunomide; THIN: The Health Improvement Network (UK); Optum: Optum de-identified Clinformatics Datamart (US); MDCR: Medicare (US); GERMANY: IQVIA Disease Analyzer EMR (Germany); CCAE: IBM MarketScan Commercial Claims and Encounters (US); AMBEMR: IQVIA Ambulatory EMR (US)

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SAT0132

DOES JANUS KINASE INHIBITION INDUCED HYPERLIPIDAEMIA ASSOCIATE WITH AN INCREASE OF AORTIC STIFFNESS IN PATIENTS WITH ARTHRITIS? PRELIMINARY RESULTS OF A PROSPECTIVE PILOT STUDY ON CARDIOVASCULAR RISK

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Background: Treatment with Janus Kinase inhibitors (JAK-i) (Tofacitinib, Baricitinib) can cause an increase of serum lipids such as total cholesterol, low- (LDL) and high- (HDL) density lipoproteins in patients with arthritis (1). On the other hand, JAK-i can reduce systemic inflammation and have therefore a beneficial effect on the cardiovascular system of treated patients. However, the effects of JAK-i on the CV system have not been adequately examined. In particular, we are not aware of any "real world" data concerning CV risk of patients receiving JAK-i treatment.

Stiffness of the aortic vasculature is a modifiable, valid and independent surrogate predictor of CV risk and can be measured by carotid femoral pulse wave velocity (cfPWV). Its predicted value has been shown in a series of epidemiological studies and cfPWV is characterized as the gold standard marker for the assessment of aortic stiffness (2)

Objectives: Aim of this study was to evaluate for the first time changes of cfPWV, lipid profile and traditional CV risk factors in patients receiving JAK-i therapy.

Methods: Measurements of cfPWV, total cholesterol, LDL, HDL and inflammation markers were performed directly before and 5-12 months (median 6.5 months; 5-7, IQR) after initiation of JAK-i therapy. Additionally, traditional CV risk factors such as nicotine, obesity (Body-Mass-Index), diabetes and arterial hypertension were documented for both time points next to clinical activity markers, such as the Disease Activity Score 28 (DAS28). Differences in lipids, DAS28 and inflammation markers between the two time points were examined by paired t-Test. Given the fact that cfPWV can be confounded by mean arterial pressure (MAP), a mixed linear model, with MAP as a covariate, was used in order to test for differences in adjusted cfPWV values between two measurements.

Results: 29 patients with rheumatoid arthritis (RA) (*72.4%,* female) with a median age of *61.5* (*51-75*, IQR) years and a median DAS28-CRP of *5.27* (*3.62-6.21*, IQR) were recruited before (planed) initiation of JAK-i therapy. *30.7%* of the patients were smokers, *38.5%* had arterial hypertension and *0.4%* diabetes. Median BMI was *24* kg/m^2 (*22-29*, IQR).

Mean total cholesterol and LDL values increased significantly under treatment with JAK-i (*196.76±38.70* vs. *220.28±40.41* mg/dl; *p=0.010* and *119.12±31.88* vs. *138.72±37.43* mg/dl; *p=0.032*, respectively). Moreover, MAP increased significantly during the same time period (*105± 9.82* vs. *109.91±11.22* mmHg*; p=0.005*). On the other hand, C-reactive protein (CRP) had decreased significantly between the two measurements [*15.27* (*3.82-38.9*, IQR) vs. *3.82* (*1.4-15.9*) mg/dl; *p=0.05*]. No statistical significant difference of cfPWV values could be observed under JAK-i treatment *[-0,035 95% CI (-0,615 - 0,545); p=0.903].*

Conclusion: Our results reveal that JAK-i induced hyperlipidaemia did not associate with an increase of a surrogate marker of CV risk, such as aortic stiffness. More data are needed to conclude whether JAK-i could have a (positive or negative) effect on the CV system.

An additional examination of the current patients in 12-18 months from treatment initiation and the recruitment of new RA and psoriatic arthritis patients are currently taking place.

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[2] Laurent S, et al (2006) Expert consensus document on arterial stiffness: methodological issues and clinical applications. EurHear J 27:2588–2605.

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SAT0133

PILOT CLINICAL STUDY OF A NON-INVASIVE AURICULAR VAGUS NERVE STIMULATION DEVICE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Despite the clinical benefit of current pharmacological treatments for rheumatoid arthritis (RA), there remains an unmet need for alternative treatment approaches. Vagus nerve stimulation (VNS) via an implanted device has been shown to attenuate RA disease severity in patients resistant to therapy,[1] as evidenced by a reduction in the DAS28-CRP score following a month of daily stimulation.

Objectives: This pilot study investigated the safety and efficacy of a wearable (non-invasive) device that attaches to the outer ear to treat RA via electrical stimulation of the auricular branch of the vagus nerve.

Methods: Patients with active RA (≥4 tender/swollen joints based on a 28-joint count, Disease Activity Score-28 with C-reactive protein (DAS28-CRP) >3.8, active synovitis detected on ultrasound and MRI) and inadequate response to conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), or csDMARD and biologic DMARDs (bDMARDs), were enrolled in this open-label study. Patients used the device for up to 30 minutes daily over the course of the 12-week study. The primary endpoint was the change in DAS28-CRP score at Week 12. Secondary endpoints included a safety analysis, proportion of patients achieving ACR20/50/70, the mean change in HAQ-DI and the proportion of patients achieving a HAQ-DI MCID of at least 0.22 over 12 weeks. Additionally, sleep scores were assessed using a visual analogue scale (0-100) at baseline and 12 weeks.

Results: Thirty patients with active RA were enrolled, of which 27 patients completed the 12-week protocol. Three patients dropped out of the study: two patients decided to seek other treatment and one patient moved out of the country. Data for three additional patients was not included in this dataset as it was still being collected. Of the 24 patients with complete 12-week datasets, 88% were female, the average age was 54.9 years, mean disease duration was 7.3 years, and four patients had an inadequate response to one or two bDMARDs.

The mean change in DAS28-CRP from baseline to Week 12 was -1.43 ($p<0.05$; Figure 1) and ACR20/50/70 response rates were 58.3%, 37.5%, and 16.7%, respectively (Figure 2). HAQ-DI change from baseline was -0.50 ($p<0.05$) at 12 weeks, and 15 out of 24 patients achieved an overall HAQ-DI reduction of 0.22 (62.5%). VAS sleep scores were significantly improved over the 12-week study. Scores for trouble falling asleep, awakened by pain at night, and awakened by pain in morning decreased by 64%, 70%, and 60%, respectively ($p<0.05$, n = 23). Three study adverse events (AEs) were reported: two device related AEs due skin irritation at the earpiece insertion site and one AE due to mucous accumulation in the throat.

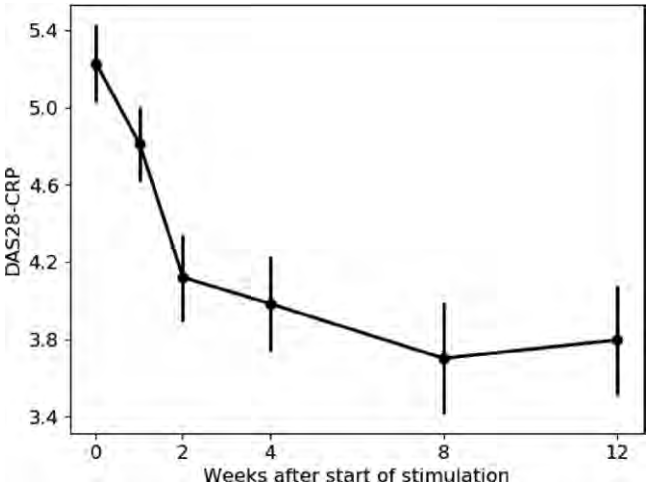


Figure 1

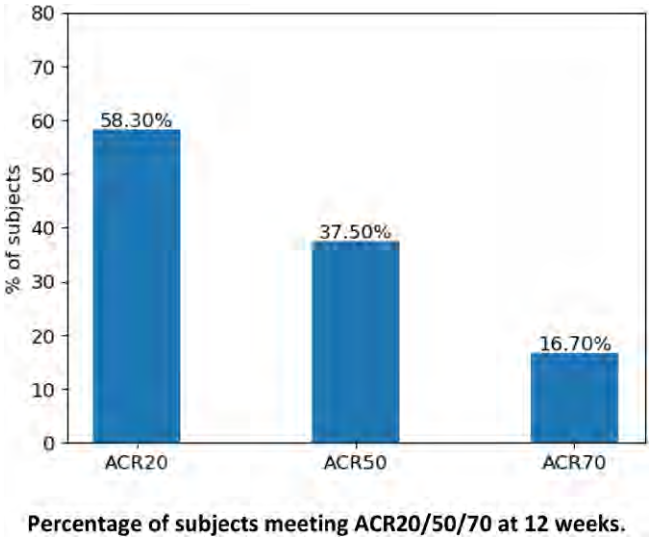


Figure 2 Average DAS28-CRP is shown for each study visit. Error bars indicate standard error of mean.Percentage of subjects meeting ACR20/50/70 at 12 weeks.

Conclusion: In this pilot study, auricular stimulation was well tolerated and daily use over 12 weeks attenuated RA disease severity. Further evaluation in larger controlled studies are needed to confirm whether a non-invasive wearable device might offer an alternative approach for the treatment of RA.

References:

[1] Koopman FA, et al. (2016) Vagus nerve stimulation inhibits cytokine production and attenuates disease severity in rheumatoid arthritis. Proc Nat Acad Sci 2016; 113: 8284–9.

Disclosure of Interests: Sara Marsal: None declared, Héctor Corominas Speakers bureau: Abbvie, Lilly, Pfizer, Roche, Maria Lopez Lasanta: None declared, D Reina-Sanz: None declared, Carolina Perez-Garcia: None declared, Helena Borrell Paños Speakers bureau: Lilly, Novartis, MSD and Janssen, Raimón Sanmartí Speakers bureau: Abbvie, Eli Lilly, BMS, Roche and Pfizer, J. Narváez: None declared, Clara Franco-Jarava: None declared, Jose Antonio Narvaez: None declared, Juan Jose de Agustin: None declared, Vivek Sharma Shareholder of: Vorso Corp., Konstantinos Alataris Shareholder of: Vorso Corp., Mark C. Genovese Grant/research support from: Abbvie, Eli Lilly and Company, EMD Merck Serono, Galapagos, Genentech/Roche, Gilead Sciences, Inc., GSK, Novartis, Pfizer Inc., RPharm, Sanofi Genzyme, Consultant of: Abbvie, Eli Lilly and Company, EMD Merck Serono, Genentech/Roche, Gilead Sciences, Inc., GSK, Novartis, RPharm, Sanofi Genzyme, Matthew Baker Consultant of: Gilead, Vorso, Paid instructor for: Gilead

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SAT0134

COMPARATIVE RISK OF CANCER ASSOCIATED WITH FIRST-LINE DMARDS USE IN RHEUMATOID ARTHRITIS: REAL WORLD EVIDENCE FROM THE OHDSI NETWORK

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Background: Conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) are recommended as first line treatment for rheumatoid arthritis (RA) patients, but limited information exists on the comparative risk of cancer associated with their use.

Objectives: To compare the risk of incident overall (excluding non-melanoma skin) and site-specific cancers (colorectal, lung, lymphoma, leukaemia) associated with first-line use of csDMARDs in patients with RA.

Methods: We conducted a multinational cohort study informed by data from 7 healthcare databases including claims and electronic medical records from 4 countries (SIDIAP-Spain, MDCR-US Optum-US, CCAE-US, IQVIA AMBEMR-US, IQVIA-Germany, THIN-UK) part of the Observational Health Data Sciences and Informatics (OHDSI) network. All patients aged ≥18 years who initiated methotrexate (MTX), hydroxychloroquine (HCQ), sulphasalazine (SSZ), or leflunomide (LEF) as first-line monotherapy after a diagnosis of RA between 2005 to 2018 were eligible. Individuals with a prior diagnosis of another inflammatory arthropathy or cancer, or <1 year of follow-up were excluded. Patients were followed from 1-year after treatment initiation to the earliest of incident cancer, loss to follow-up, or 5-years. Cox proportional-hazard models for MTX against each other csDMARD were performed after propensity score stratification. A large set of negative control outcomes were analysed to calibrate hazard ratios (cHRs). Estimates were pooled where homogeneity across sources was adequate (I^2<0.4).

Results: Across the databases, 127,547 RA patients initiating csDMARD therapy were included in the analyses (MTX: 73,996, HCL: 36,381 SSZ: 9,383 LEF: 7,787). The pooled incidence rate of overall cancer for MTX was 22.8 per 1,000 person years. The pooled summary and source-specific estimated cHRs for overall cancer are shown below in Figure 1. While little difference was seen for HCQ and SSZ compared to MTX, LEF was consistently associated with a reduced cancer risk: pooled cHR (95% CI) 0.67 (0.59 to 0.76) and cHRs ranged from 0.53 (0.36 to 0.80) in CCAE-US to 0.84 (0.58 to 1.22) in SIDIAP-Spain. There were insufficient cases to look site-specific cancers within data sources, although pooled results suggest little risk difference in leukemia, lymphoma, colorectal, or lung cancers.

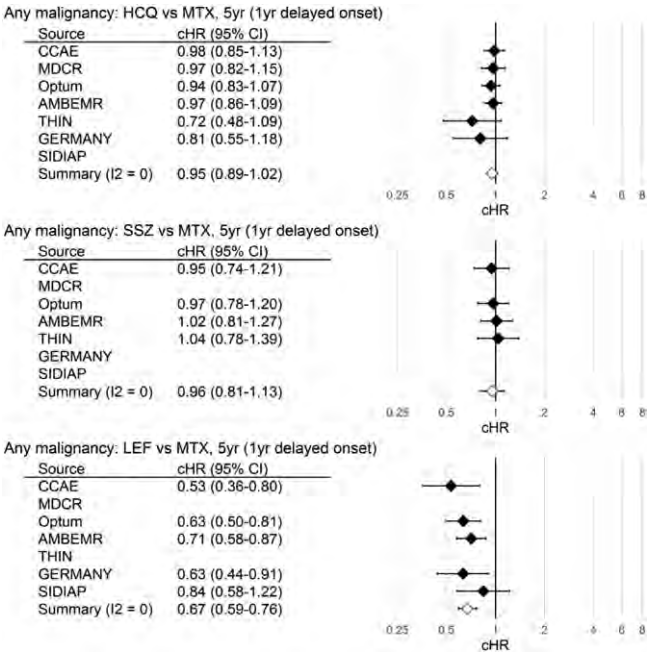


Figure 1. Calibrated hazard ratios (cHRs) of overall cancer risk with their respective confidence intervals (95%CI) by study database.Database estimates not reported where adequate covariate balance not attained. Meta-analysis results not reported where I2>0.4.

Conclusion: Compared to MTX users, patients treated with LEF had a lower risk of overall cancer. Risk of four specific cancers did not differ by first line csDMARD exposure.

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SAT0135

COMPARISON OF THE EFFICACY AND SAFETY OF TWO BRIDGING SCHEDULES OF PREDNISOLONE IN EARLY ACTIVE RHEUMATOID ARTHRITIS (CORRA): A DOUBLE-BLIND, RANDOMISED, PLACEBO-CONTROLLED TRIAL

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory joint disease potentially leading to disability, impaired functioning, and premature death. Most treatment strategies include the early use of disease-modifying antirheumatic drugs (DMARDs) such as methotrexate (MTX) which is considered as an established 'anchor' therapy. Since it takes some weeks until MTX shows clinical efficacy, glucocorticoids (GC) are widely used for bridging.
Objectives: The aim of the study "Comparison of the efficacy and safety of two starting dosages of prednisolone in early active RA" (CORRA) is to compare the efficacy and safety of two standard GC bridging schedules vs. placebo in addition to MTX, following a treat-to-target regimen, in early RA.
Methods: CORRA is an investigator-initiated, randomised, multi-center, double-blind, placebo-controlled trial. Adult RA patients who were eligible for inclusion in the trial if they had a disease duration of less than 3 years and moderate or high disease activity were recruited in one hospital and 18 rheumatology practices in Germany. Patients were randomised (1:1:1) to receive 60 mg or 10 mg prednisolone (Pred) orally once daily (tapered down to 5 mg Pred within 8 weeks) or placebo. The duration of the intervention was 12 weeks, followed by an open observational phase for another 40 weeks. All patients were also treated with MTX (usually starting with 15mg/week followed by a treat-to target scheme). The primary efficacy endpoint was the progression of the radiographic joint damage after one year compared to baseline as determined by the van der Heijde modification of the Sharp score (SHS). Patients, physicians and readers of radiographs were unaware of the treatment assignments. For the comparison of the two GC groups, a non-inferiority margin of 1.3 points of the SHS was set. This trial was registered at ClinicalTrials.gov, number NCT02000336.
Results: Between February 2014 and February 2017, 395 patients were included in the trial, 381 of which had sufficient data also of follow-up visits. A total of 129 patients were assigned to the 60 mg Pred group, 124 to 10 mg Pred and 128 to the placebo group. At baseline, mean age was 58 years, 58% were female, 55% were rheumatoid factor and 52% ACPA positive. The mean number of swollen joints was 12.8 out of 28, mean ESR was 33.6 mm/h, mean CRP 2.2 mg/dL, mean DAS 28 6.0. Radiographic damage was 4.9 as measured by the SHS. In the 60 mg, 10 mg Pred group and in the placebo group, the DAS 28 was 2.6, 3.1, 4.5 at week 4 ($p<0.001$), 3.1, 2.8, 3.6 at week 12 ($p<0.001$), and 2.7, 2.6, 2.8 at week 52 ($p=0.411$), respectively. After 12 months the radiographic progression could be determined in 375 patients. In the 60 mg, 10 mg Pred group, and in the placebo group, the mean progression after 1 year was 1.0, 1.0, 1.1 for the total SHS and 0.5, 0.6, 0.7 for the erosion score of the SHS, respectively. Statistical analysis showed non-inferiority of the 10 mg Pred and of the placebo group in comparison to the 60 mg Pred group. Regarding safety issues, there were 10, 5, 6 serious adverse events and 31, 16, 20 adverse events in the MedDRA system organ class "infections and infestations" for the 60 mg Pred, 10 mg Pred, and the placebo group, respectively.
Conclusion: The bridging schedule starting with 60 mg Pred reduced disease activity better than the 10 mg schedule or placebo only for a short time. The primary outcome structural damage was non-inferior in the 10 mg Pred and the placebo group in comparison to the 60 mg Pred group. Initial advantages of the higher dose may have been compromised by the long follow-up with the possible escalation of therapy due to the treat-to-target regimen.
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SAT0136 RELATIVE EFFICACY AND SAFETY OF TOFACITINIB, BARICITINIB, UPADACITINIB, AND FILGOTINIB, IN COMPARISON WITH ADALIMUMAB IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS: A BAYESIAN NETWORK META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Background: Methotrexate (MTX), an effective disease-modifying antirheumatic drug (DMARD) [2], is the most widely used DMARD for the treatment of rheumatoid arthritis (RA). However, not all patients are responsive to the drug; 30% of the patients discontinue therapy within 1 year of commencing the treatment, usually because of the lack of efficacy or undesirable adverse effects Small-molecule Janus kinase inhibitors are clinically developed for the treatment of RA.
Objectives: The aim of this study is to investigate the relative efficacy and safety of tofacitinib, baricitinib, upadacitinib, and filgotinib in comparison with adalimumab in patients with active RA and having inadequate responses to MTX.
Methods: We performed a Bayesian network meta-analysis to combine direct and indirect evidence from randomized controlled trials (RCTs) to examine the efficacy and safety of tofacitinib, baricitinib, upadacitinib, filgotinib, and adalimumab in RA patients having inadequate responses to MTX.
Results: Four RCTs, comprising 5,451 patients, met the inclusion criteria. The baricitinib 4mg+MTX and upadacitinib 15mg+MTX group showed a significantly higher American College of Rheumatology 20% (ACR20) response rate than the adalimumab 40mg+MTX group. The ranking probability based on the surface under the cumulative ranking curve (SUCRA) indicated that baricitinib 4mg+MTX had the highest probability of being the best treatment for achieving the ACR20 response rate, followed by upadacitinib 15mg+MTX, tofacitinib 5mg+MTX, filgotinib 200mg+MTX, filgotinib 100mg+MTX, adalimumab 40mg+MTX, and placebo+MTX. The upadacitinib 15mg+MTX and baricitinib 4mg+MTX groups showed significantly higher ACR50 and ACR70 response rates than adalimumab 40mg+MTX. In terms of Herpes zoster infection, the ranking probability based on the SUCRA indicated that placebo+MTX were likely to be the safest treatments, followed by filgotinib 200mg+MTX, filgotinib 100mg+MTX, adalimumab 40mg+MTX, tofacitinib 5mg+MTX, upadacitinib 15mg+MTX, and baricitinib 4mg+MTX. Regarding safety analysis, no statistically significant differences were found between the respective intervention groups.
Conclusion: In RA patients with an inadequate response to MTX, baricitinib 4mg+MTX and upadacitinib 15mg+MTX showed the highest ACR response rates, suggesting a difference in efficacy among the different JAK inhibitors.
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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.658

SAT0137 METHOTREXATE ASSOCIATED ADVERSE EVENTS AND THEIR PREDICTORS IN METHOTREXATE-NAÏVE PATIENTS WITH RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW

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Background: The adverse events (AEs) associated with methotrexate (MTX) treatment for rheumatoid arthritis (RA) have been studied extensively, but precise estimates of the incidence and prevalence of AEs are lacking. There is also limited published data on the predictors of AEs.
Objectives: To summarise and pool incidence and prevalence rates of AEs in patients treated with MTX for RA, and to identify treatment, clinical and disease related predictors of AEs.

Methods: A systematic literature search was carried out using Embase, Medline, and CENTRAL databases to identify relevant studies published between 1/1/2005 and 12/2/2019. The eligibility criteria included RCTs, non-randomized trials, and observational studies of first-time users of MTX in adults (≥ 18 years old) with RA and reported incidence, prevalence or predictors of the most common MTX related AEs, including: any AE, serious AEs, discontinuation due to AEs, elevated liver enzymes, gastrointestinal (GI), mucocutaneous (MC), central nervous system (CNS), and pulmonary AEs. Pooled proportions of GI AEs and elevated liver enzymes of patients treated with MTX monotherapy were estimated using random effects meta-analysis.
Results: Of 3142 records screened, we included 46 articles (35 clinical trials and 11 cohort studies) with a total of 9646 patients, and a mean follow-up duration of 70±35 weeks (range: 13 - 104 weeks for RCTs, 40 - 156 weeks for observational cohorts).
Six studies reported incidence rate (IR) of any AE (range: 196 - 595 per 100 person-years), and eight studies reported IR of serious AEs (range: 3.7 - 15.9 per 100 person-years). The percentage of patients with any AE, reported in 32 studies, varied between 37% and 100% in RCTs, and between 13% and 34% in observational studies. Discontinuation of MTX due to AEs ranged between 1% and 29% in RCTs, and between 8% and 38% in observational studies. The reported prevalence of MC events (4% - 54%), CNS events (12% - 59%) and pulmonary events (10% - 67%) varied between studies.
The estimated pooled prevalence from studies with a MTX monotherapy arm was 14% (95% CI: 9%, 19%; N=7 studies) for liver enzymes elevation (Figure 1), and 29% (95% CI: 13%, 44%; N=7 studies) for GI AEs (Figure 2).

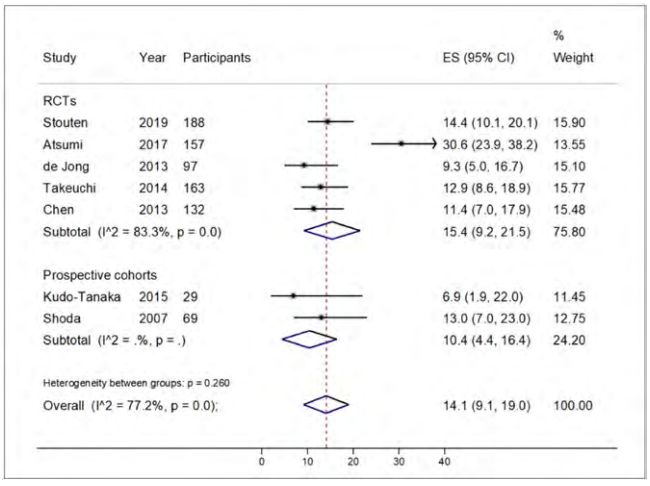


Figure 1. Forest plot of pooled prevalence of elevated liver enzymes

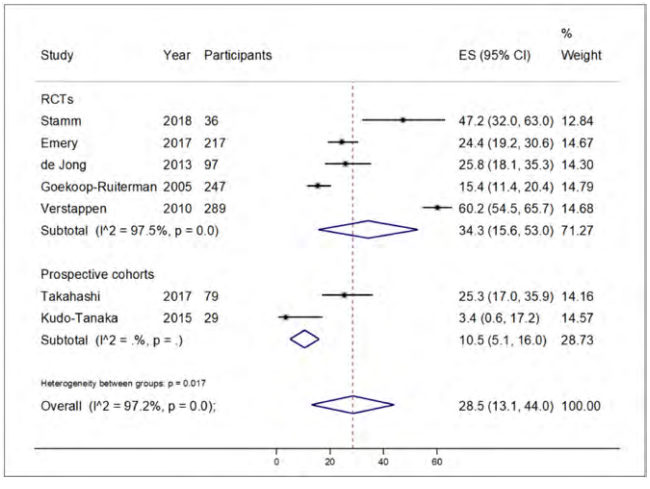


Figure 2. Forest plot of pooled prevalence of gastrointestinal adverse events

No statistically significant predictors of "any AE" were identified. For discontinuation of MTX due to AEs, RF positivity was associated with lower risk of MTX discontinuation due to MTX (HR 0.37, 95%CI: 0.21, 0.64), while other studies found that baseline HAQ score (OR 1.87, 95%CI: 1.11, 3.15) and BMI (OR 1.21, 95%CI: 1.02, 1.44) were associated with increased risk of MTX discontinuation due to AEs. ACPA positivity (OR 1.8, 95%CI: 1.1, 3.1), and high baseline alanine aminotransferase (ALT) (OR 3.1, 95%CI: 1.6, 6.2) were both independent predictors of two-fold elevation of ALT in one paper, and baseline creatinine (OR 1.03, 95%CI: 1.00, 1.07) and high baseline ALT (OR 1.03, 95%CI: 1.00, 1.06) were associated with increased risk of elevated ALT above the upper limit of normal in a different study.
Conclusion: These findings affirm the high prevalence of GI AEs and elevated liver enzymes among patients treated with MTX for RA. The identified predictors of MTX withdrawal and elevated ALTs may be useful for identifying future patients likely to experience these AEs early in the course of treatment. However, the results of the predictors should be interpreted with caution, and further work is needed to replicate the results in studies with larger sample sizes and to assess the prognostic value of established predictors.
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SAT0138

DRUG-RELATED PANCYTOPENIA AND LEUKOPENIA IN RHEUMATOID ARTHRITIS: ARE ALL CSDMARDS EQUAL?

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Background: Cytopenia is a known side-effect of conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs) in rheumatoid arthritis (RA). There is a lack of data on the comparative risk of cytopenia with different csDMARDs.
Objectives: To assess the comparative risk of leukopenia and pancytopenia for the most frequently used first-line csDMARDs: methotrexate (MTX), hydroxychloroquine (HCQ), sulphasalazine (SSZ), and leflunomide (LEF).
Methods: The study used data from 7 databases from 4 countries: CCAE, MDCR, Optum, IQVIA Ambulatory EMR (US); IQVIA THIN IMRD EMR (UK); IQVIA Disease Analyzer EMR (Germany); and SIDIAP (Spain). Cohorts included adult patients with a diagnosis of RA from 2005 to 2019 with at least one-year prior follow-up, no prior inflammatory arthritis, initiaton of first-line csDMARD, and no cytopenia in the preceding 30 days. Participants were followed from one day after treatment initiation to the earliest of event occurrence, treatment discontinuation/switching plus 14 days in the on-treatment analysis, five years in the intent-to-treat (ITT) analysis, or loss to follow-up. MTX was used as reference group. Cox models were fitted with propensity score stratification for observed confounding and negative control outcomes calibration for residual error. Estimates across database were pooled where I^2<40% was seen.
Results: Overall 166,347 patients were included. Pooled rates of leukopenia and pancytopenia for MTX were 10.9 and 3.2 per 1,000 person years, respectively. Figure 1 and 2 show the results for the different databases and pooled estimates where applicable. Database estimates are not reported where adequate covariate balance not attained, and meta-analysis not shown where I2>0.4. MTX showed slightly higher hazards of leukopenia and of pancytopenia compared to LEF but no consistently differential risks compared to HCQ or SSZ.

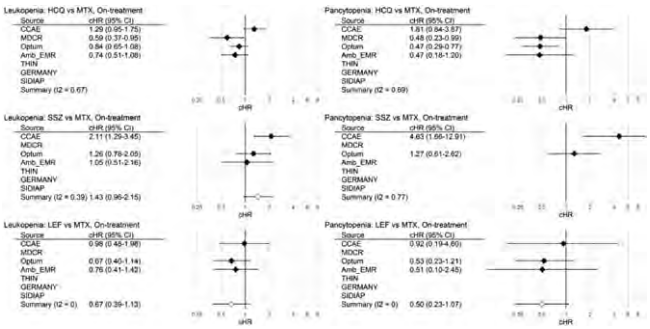


Figure 1. Calibrated hazard ratios (95% CI) vs MTX, on-treatment analysis

Conclusion: Cytopaenia is rare, and apparently more frequent with MTX and less with LEF. Since prior full blood counts were inconsistently obtained in fewer than

50% of csDMARD new users (e.g. more frequent in MTX [42%] than HCQ [32%] in CCAE and Optum; roughly equal in MDCR), these results should inform future monitoring recommendations.

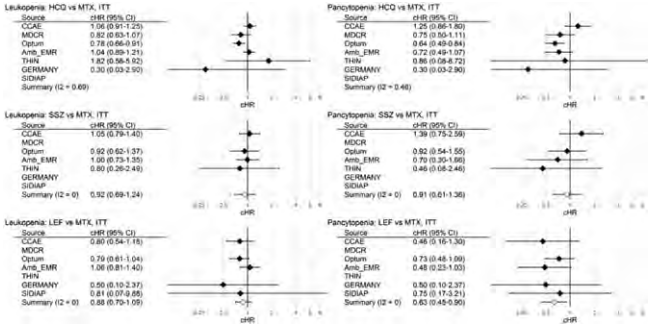


Figure 2. Calibrated hazard ratios (95% CI) vs MTX, ITT analysis

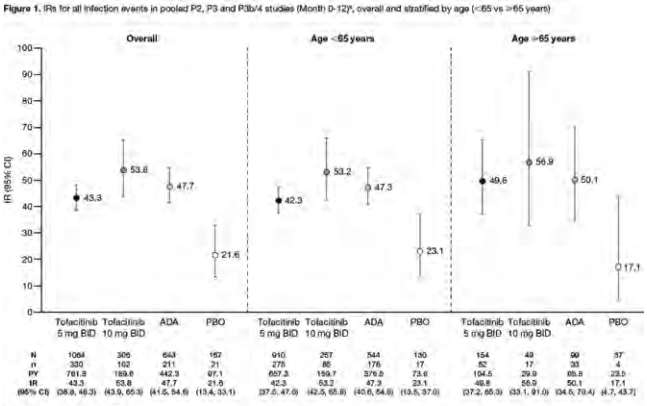
Disclosure of Interests: Loreto Carmona Grant/research support from: Novartis Farmaceutica, SA, Pfizer, S.L.U., Merck Sharp & Dohme España, S.A., Roche Farma, S.A, Sanofi Aventis, AbbVie Spain, S.L.U., and Laboratorios Gebro Pharma, SA (All trhough institution), James Weaver Shareholder of: J&J Shares, Grant/research support from: Full-time employment salary from Janssen, Consultant of: Janssen employee, Employee of: Janssen, Paid instructor for: Janssen employee, have instructed at conferences, Speakers bureau: Janssen employee, have spoken at conferences, Edward Burn: None declared, Ben Illingens: None declared, David Vizcaya Employee of: Bayer, Ruta Sawant Shareholder of: AbbVie, Employee of: AbbVie, Talita Duarte-Salles: None declared, Patrick Ryan: None declared, Daniel Prieto-Alhambra Grant/research support from: Professor Prieto-Alhambra has received research Grants from AMGEN, UCB Biopharma and Les Laboratoires Servier, Consultant of: DPA's department has received fees for consultancy services from UCB Biopharma, Speakers bureau: DPA's department has received fees for speaker and advisory board membership services from Amgen
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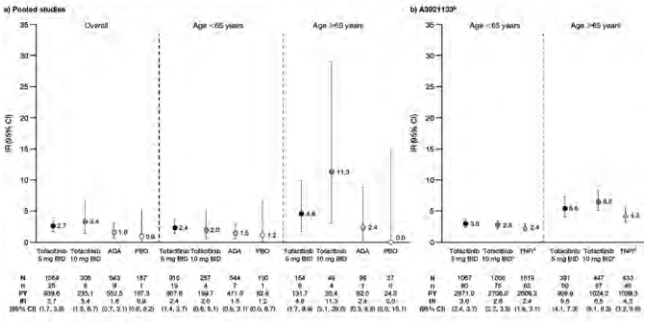
SAT0139

AGE-BASED (<65 VS ≥65 YEARS) INCIDENCE OF INFECTIONS AND SERIOUS INFECTIONS IN TOFACITINIB-, ADALIMUMAB- AND PLACEBO-TREATED PATIENTS WITH RHEUMATOID ARTHRITIS: A POST HOC ANALYSIS OF PHASE 2, PHASE 3 AND PHASE 3B/4 TOFACITINIB STUDIES

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Background: Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA). A recent ad hoc safety analysis (as of August 2019; may be subject to change) from an ongoing, open-label, randomised, post-authorisation safety study, Study A3921133 (NCT02092467), conducted in RA patients (pts) aged ≥50 years with ≥1 cardiovascular risk factor has shown that incidence rates (IRs) of serious infection events (SIEs) were higher with tofacitinib 10 mg BID vs tumour necrosis factor inhibitors (TNFi; adalimumab [ADA] and etanercept) and this difference was more pronounced in pts aged ≥65 years (Pfizer Inc; data on file).
Objectives: To assess the IRs of overall infection events and SIEs in pts from Phase (P)2, P3 and P3b/4 tofacitinib RA trials which had a TNFi (ADA) active control or comparator arm.
Methods: This is a post hoc analysis of Month 0–12 data pooled from P2 (A3921035; NCT00550446 [first 12-week randomised parallel treatment period only]), P3 (ORAL Standard; NCT00853385) and P3b/4 (ORAL Strategy; NCT02187055) studies. Pts randomised to receive tofacitinib 5 mg BID, tofacitinib 10 mg BID, ADA 40 mg subcutaneously every other week and placebo (PBO) were included and assessed overall and by age (<65 or ≥65 years). SIEs were defined as infections requiring hospitalisation or parenteral antimicrobial therapy, or meeting other criteria for a serious adverse event. IRs (pts with events/100 pt-years of exposure [PY]) and 95% confidence intervals (CIs) were calculated for all infection events and SIEs; only the first infection events that occurred up to 28 days after the last dose or to the data cut-off date were considered.
Results: Of 2180 pts included in the pooled studies (tofacitinib 5 mg BID: N=1064 [943.4 PY]; tofacitinib 10 mg BID: N=306 [236.6 PY]; ADA: N=643 [554.3 PY]; PBO: N=167 [108.1 PY]), 1841 (84.4%) were aged <65 years and 339 (15.6%) were aged ≥65 years. In general, the IRs for all infection events and SIEs were higher with tofacitinib 5 mg BID, tofacitinib 10 mg BID and ADA in pts aged ≥65 years compared with pts aged <65 years. Overall and when stratified by age, IRs for all infection events were similar across the active treatment groups (Figure 1); IRs with PBO were lower vs the active treatment groups overall and in pts aged <65 years, and numerically lower vs the active treatment groups in pts aged ≥65 years. IRs for SIEs were comparable across active treatment groups in pts aged <65 years, while among pts aged ≥65 years, IRs were numerically higher for tofacitinib 10 mg BID vs ADA, and appeared to be similar for tofacitinib 5 mg BID and ADA (Figure 2).
Conclusion: In this analysis of data pooled from P2, P3 and P3b/4 tofacitinib RA studies which included a TNFi arm (ADA), the risk of SIEs or infections overall was similar for tofacitinib and ADA with the exception of a numerically higher rate of SIEs with tofacitinib 10 mg BID vs ADA in pts aged ≥65 years. In most countries, tofacitinib 10 mg BID is not an approved dose for the treatment of RA. This post hoc comparison is limited by variation in sample size and PY of exposure between treatment and age groups, and a small number of cases of SIEs in the ≥65-year age group resulting in wide 95% CIs; interpretation of results should be made with caution. The findings in the present analysis are consistent with increasing age being a known risk factor for infections.





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Pfizer Inc, Consultant of: AbbVie, Amgen, Eli Lilly, Gema, Genzyme, Novartis and Pfizer Inc, Hendrik Schulze-Koops Grant/research support from: Pfizer Inc
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SAT0140 SAFETY OF TOFACITINIB THERAPY IN HBSAG CARRIERS WITH RHEUMATOID ARTHRITIS: A PROSPECTIVE STUDY

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Background: Targeted synthetic DMARDs (ts-DMARDs) are becoming more available and affordable in developing countries, where the prevalence of hepatitis B virus (HBV) infection is still an important public health issue. The safety of ts-DMARDs therapy in terms of the reactivation of hepatitis B virus (HBV) infection need more concern. Rare data from a prospective study focus on the use of ts-DMARDs in patients with concurrent rheumatoid arthritis (RA) and HBV infection were available by now.
Objectives: To evaluate the influence of tofacitinib on reactivation of HBV infection in HBsAg carriers with RA.
Methods: In this 52 weeks observation, HBsAg carriers with active RA (DAS28>5.1) despite failed combined treatment with MTX and other non-biological DMARDs were enrolled. Patients must have normal liver function prior to study. All patients received therapy with tofacitinib (5mg twice daily) and concomitant MTX (10-12.5mg/w). Entecavir was prescribed preventively for patients who had a baseline HBV load >2000 copy/ml (group 1), and Lamivudin for patients with HBV load ≤ 2000 copy/ml (group 2). Liver enzymes (AST/ALT) and HBV viral load were monitored every 4 weeks. Increased viral load and abnormal liver function were managed according to expert opinion.
Results: Thirteen patients (10 female) were recruited. Nine patients had a baseline viral load >2000 copy/ml (group 1, with preventive Entecavir), and the other 4 patients had a viral load ≤ 2000 copy/ml (group 2, with preventive Lamivudin). Two patients from group 1 discontinued tofacitinib at week 12 due to ineffectiveness, and both continued taking Entecavir for another 3 months after the discontinuation of tofacitinib.
No reactivation of hepatitis B was observed in patients from group 1. One patients (female, 54 years old) from group 2 underwent a mild increase of both ALT and AST (67 and 56 IU/L, respectively) at week 16. An elevated viral load (4.9e6 copies/ml, baseline 1.4e3) and a HBV YMDD mutant was also found. The tofacitinib treatment continued. After prescription of Adefovir (combined with the pre-existing Lamivudin), both liver enzyme and viral load decreased to normal range in 8 weeks and remained normal throughout the study.
Conclusion: An aggressive Tofacitinib + MTX therapy may be a safe option for HBsAg carriers with cs-DMARDs refractory RA. More active and effective prophylaxis strategy may be recommended to reduce the risk of HBV reactivation during the treatment.
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Disclosure of Interests: : None declared
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SAT0141 LONG-TERM EFFECTIVENESS OF TOFACITINIB IN CONVENTIONAL DMARDS NON-RESPONDERS WITH RHEUMATOID ARTHRITIS: RESULTS OF RUSSIAN NATIONAL REGISTER

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Background: Tofacitinib is an oral Janus Kinase inhibitor for the treatment of rheumatoid arthritis (RA).
Objectives: To evaluate the three-year effectiveness of tofacitinib in RA conventional synthetic (cs) DMARDs non-responders.
Methods: Data from 374 patients from Russian national register OREL of patients with RA treated with tofacitinib not less than 3 years after failure of conventional DMARDs were included in the statistical analysis. Clinical and laboratory data from 4 consecutive visits with an interval of 12 months between the visits (± 28 days) were analyzed. Treatment with any biologics ever was an exclusion criteria. Demographical (age, sex) and disease-related characteristics of RA (symptoms duration, RF- and ACCP positivity, presence of joint erosions, DAS28, CDAI, number of tender and swollen joints (NTJ, NSJ), erythrocytes sedimentation rate (ESR), C-reactive protein (CRP)) collected. Statistical analysis performed with statistical programs SPSS2017 and GraphPadPrizm. p-value < 0.05 considered as significant.
Results: Baseline characteristics of RA patients, involved in the analysis are presented in table 1.

Table 1. Baseline characteristics of the patients with RA (n=374).

Parameter	Characteristics
Male, n (%)	92 (24.5)
Age, years (mean±SD)	53.4±13.38
Symptoms duration, month (mean±SD)	140±137
Positive rheumatoid factor (RF), n (%)	123(32.8)
Positive antibodies to cyclic citrullinated peptide (ACCP), n (%)	329(87.9)
Erosions of hand joints (X-rays), n (%)	372 (99.4)
BMI, kg/m^2(mean ±SD)	26.8 ± 6.14
Smokers (current and in the past), n (%)	54 (14.4)

Changes in the diseases activity parameters in patients with RA, treated with tofacitinib not less than 3 years after cs DMARD failure are presented in table 2, figure 1, and figure 2.

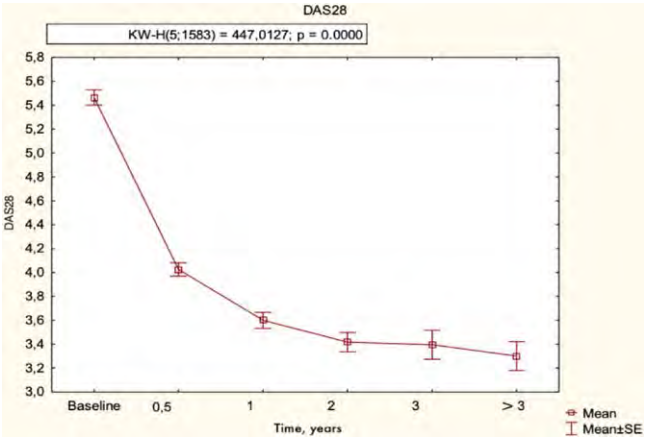


Figure 1. DAS28 of patients with RA, treated with tofacitinib (n=374) – 3-years follow-up (time-points are presented in years ± 28 days).

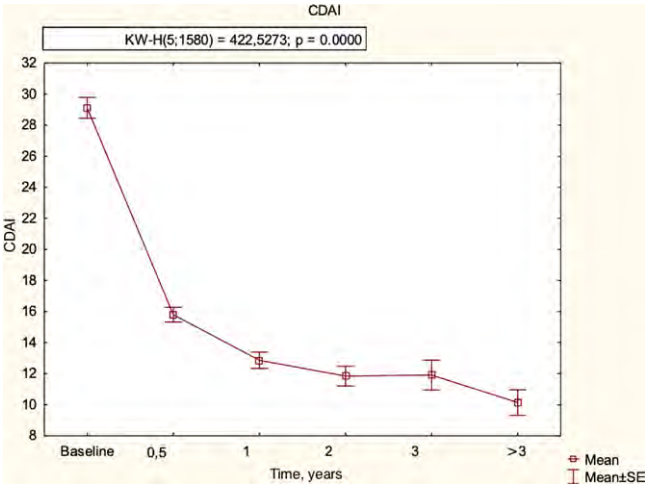


Figure 2. DAS28 of patients with RA, treated with tofacitinib (n=374) – 3-years follow-up (time-points are presented in years ± 28 days).

Table 2. Changes in RA parameters in patients treated with tofacitinib, n=374 (M±SE).

Disease characteristics	Baseline	Year 1#	Year 2#	Year 3#
C-RP, mg/L	30.1±35.0	8.3±12.8	7.6±10.7	9.4±13.5
ESR, mm/h	35.2±21.2	22.7±17.2	21.9±17.7	22.3±17.3
NTJ from 28	11.2±6.5	4.6±4.9	4.8±5.0	3.9±3.8
NTJ from 28	7.6±5.1	2.4±3.2	1.7±3.1	1.4±2.8

*difference with baseline is significant with p<0.000. # - ±28 days

Conclusion: According to the real world data treatment with tofacitinib may provide good response rates in RA patients, refractory to the previous csDMARDs treatment in long-term perspective.

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SAT0142

MATCHING ADJUSTED INDIRECT COMPARISON OF FILGOTINIB VS. TOFACITINIB IN MODERATE-TO-SEVERE ACTIVE RHEUMATOID ARTHRITIS PATIENTS WITH INADEQUATE RESPONSE TO METHOTREXATE

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Background: Filgotinib (FILG) is a JAK1 inhibitor that has been investigated in combination with methotrexate (MTX) for the treatment of moderate-to-severe rheumatoid arthritis (RA). To date, no head-to-head trial has compared the efficacy of FILG versus tofacitinib (TOFA).

Objectives: To compare the efficacy of FILG 200 mg + MTX with TOFA 5 mg + MTX using matching adjusted indirect comparison (MAIC).

Methods: MAIC technique uses individual patient data (IPD) from one trial and aggregate data from the other to enable comparison of outcomes after matching on baseline characteristics [1]. An anchored MAIC was conducted using IPD from the FINCH-1 trial of FILG 200 mg + MTX vs adalimumab (ADA) 40 mg + MTX and published data from ORAL STRATEGY [2] trial of TOFA 5 mg + MTX vs ADA 40 mg + MTX. Patients in the FINCH-1 trial were reweighted based on age, sex, race, tender joint count 28, swollen joint count 28, C-reactive protein and patient's global assessment to match baseline characteristics of the comparator. After matching, Wald tests were used to test for significant differences in ACR 20/50/70 and clinical remission outcomes (SDAI≤3.3, CDAI≤2.8, DAS28(CRP)<2.6, Boolean) between FILG + MTX vs TOFA 5 mg + MTX relative to ADA 40 mg + MTX.

Results: After matching, baseline characteristics were balanced across the trial populations [Table 1]. FILG 200 mg + MTX patients experienced significantly greater improvement in 12 week ACR50 and ACR70 outcomes compared to TOFA 5 mg + MTX with a mean difference in difference (DD) of 13.5% ($p < .05$) and 8.3% ($p < .05$) respectively, as well as numerical improvements on other ACR outcomes at 12, 24 and 52 weeks [Figure 1]. At 24 weeks, FILG 200 mg + MTX patients experienced significantly greater improvement in DAS28(CRP) clinical remission compared to TOFA 5 mg + MTX with DD of 10.1% ($p < .05$) [Figure 2] as well as numerical improvements on other efficacy outcomes. At 52 weeks, FILG 200 mg + MTX patients experienced significantly greater improvement in DAS28(CRP) clinical remission compared to TOFA 5 mg + MTX with DD of 13.2% ($p < .05$) [Figure 2] as well as numerical improvements on other efficacy outcomes.

Table 1. Baseline Characteristics of FINCH-1 vs ORAL STRATEGY

CHARACTERISTIC	BEFORE MATCHING		AFTER MATCHING		ORAL STRATEGY	
	FILG 200 + MTX (N=475)	ADA + MTX (N=325)	FILG 200 + MTX (ESS=340)	ADA + MTX (ESS=233)	TOFA 5mg + MTX BID (N=376)	ADA + MTX BID (N=386)
Sex – Female, %	79.8%	81.8%	83.0%	83.0%	83.0%	83.0%
Age (year), mean (SD)	51.8 (12.8)	53.3 (12.9)	50.0 (13.4)	50.7 (13.4)	50.0 (13.4)	50.7 (13.4)
Race – White, %	65.7%	70.5%	76.0%	76.0%	76.0%	76.0%
Tender Joint Count 28, mean (SD)	15.0 (6.4)	14.6 (6.3)	15.6 (6.5)	15.2 (6.7)	15.6 (6.5)	15.2 (6.7)
Swollen Joint Count 28, mean (SD)	11.2 (5.2)	11.2 (5.0)	11.8 (5.7)	11.0 (5.4)	11.8 (5.7)	11.0 (5.4)
C-Reactive Protein (mg/L), mean (SD)	16.1 (21.0)	14.6 (18.0)	18.7 (21.9)	16.7 (21.3)	18.7 (21.9)	16.7 (21.3)
Patient global assessment baseline, mean (SD)	67.1 (19.2)	67.0 (19.1)	61.7 (22.0)	60.2 (23.5)	61.7 (22.0)	60.2 (23.5)

ESS = effective sample size; SD = standard deviation

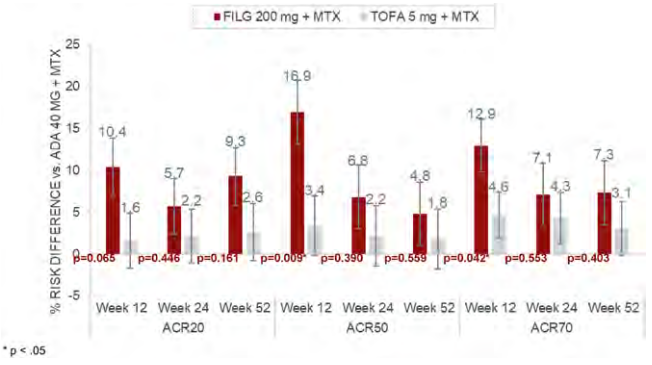


Figure 1. ACR20/50/70 relative to ADA 40 mg+ MTX of FILG 200 mg + MTX vs TOFA 5 mg + MTX* p < .05

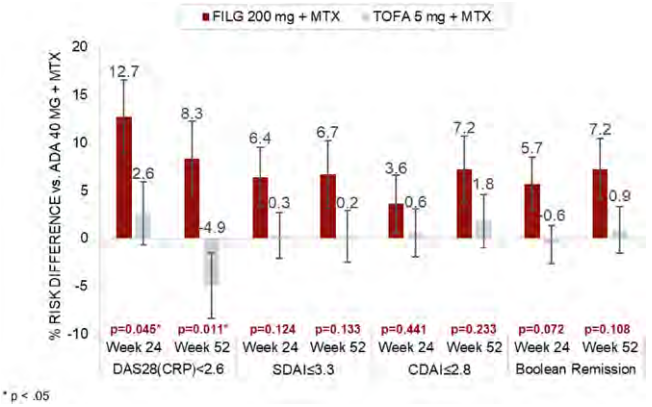


Figure 2. Clinical Remission outcomes relative to ADA 40 mg+ MTX of FILG 200 mg + MTX vs TOFA 5 mg + MTX * p < .05

Conclusion: In this MAIC, compared to TOFA 5 mg + MTX, FILG 200 mg + MTX appears to produce improved efficacy outcomes (ACR20/50/70, DAS28(CRP), SDAI, CDAI and Boolean Remission) at weeks 12, 24 and 52.

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Disclosure of Interests: Mahdi Gharaibeh Shareholder of: Gilead Sciences Inc, Employee of: Gilead Sciences, Amgen, Nate Smith Consultant of: Gilead Sciences Inc, Sushanth Jeyakumar Consultant of: Gilead Sciences, Ejim Mark Shareholder of: Gilead Sciences Inc, Employee of: Gilead Sciences, Novartis, Sanatan Shreay Shareholder of: Gilead Sciences, Employee of: Gilead Sciences
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SAT0143 A PHASE 1 STUDY IN HEALTHY VOLUNTEERS EXPLORING THE SAFETY, PHARMACOKINETICS AND PHARMACODYNAMICS OF ATI-450: A NOVEL ORAL MK2 INHIBITOR

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Background: ATI-450, is an investigational small molecule inhibitor of the MAPK-activated protein kinase 2 (MK2) signaling pathway. This pathway drives the expression of multiple cytokines including TNFα, IL-1α and β, and IL-6.
Objectives: We evaluated the safety and tolerability of ATI-450 in healthy volunteers as well as pharmacokinetics (PK) and pharmacodynamics (PD). Here we present data from single and multiple ascending dose cohorts. The aim was to select a dose for evaluation in phase 2 in patients with rheumatoid arthritis.
Methods: Safety, PK and PD were assessed in a randomized, observer-blind, placebo-controlled, phase 1 study in male and female healthy subjects aged 18-55 (n=77).

- Part A: Single Ascending Dose (SAD) (n=32, 8 subjects per dose cohort - 2 placebo, 6 active). A single dose of 10mg, 30mg, 50mg and 100mg was tested.
- Part B: Multiple Ascending Dose (MAD) (n=30, 10 subjects per dose cohort - 2 placebo, 8 active). 10mg BID, 30mg BID and 50mg BID doses were tested over 7 days of administration.

Safety and tolerability of ATI-450 was evaluated based on adverse events, clinical laboratory, vital signs, 12-lead ECG, Holter monitoring, and physical examination. Blood was drawn for PK analysis at 0.5, 1, 2, 4, 6, 8, 12 hours, 24, 36, and 48 hours post dose in the SAD cohort and on day 7 of the MAD cohort. PD of ATI-450 were explored by investigating the inhibition of a target biomarker, phospho-HSP27 (pHSP27) and proinflammatory cytokines, TNFα, IL1β, IL6 and IL8 in *ex-vivo* LPS-stimulated blood samples collected 4 and 12 hours post dose on day 7 from subjects in the MAD cohorts.
Results: ATI-450 was generally well tolerated. No serious adverse events or severe adverse events were reported, and no adverse events led to discontinuation of the study medication. The most common adverse events (reported by 2 or more subjects who received ATI-450) observed during the trial were dizziness, headache, upper respiratory tract infection, constipation, nausea, and abdominal pain. All adverse events were mild. A trend of a decrease in absolute neutrophil count (ANC) was observed without correlated clinical sequelae.
ATI-450 had dose proportional PK with a terminal half-life (t½) of 9-12 hours in the MAD cohort on day 7. A dose and concentration dependent inhibition of *ex vivo* stimulated cytokines and target biomarker was observed. On day 7, patients in the 50mg BID dose (the dose with the highest degree of inhibition) recorded mean trough drug levels (12 hours post dose) that were 1.4, 2.5, 2.5 and 2.4 times greater than the IC_{80} for TNFα, IL1β, IL8 and pHSP27 respectively. Mean Cmax drug levels (4 hours post dose) were 3.6, 6.4, 6.2 and 6.0 times greater than the IC_{80} for TNFα, IL1β, IL8 and pHSP27 respectively. IL6 levels were inhibited by more than 50% for part of the dosing interval.
Conclusion: Oral ATI-450 was generally well tolerated at all doses with dose proportional PK. The t½ suggests that once or twice daily oral dosing may be possible. At the 50mg BID dose, marked inhibition of TNFα, IL1β and IL8, IL6 and pHSP27 was observed. ATI-450 has the potential to be an oral, small molecule drug which can target multiple cytokines. Exploration of its benefit to risk profile in patients with rheumatoid arthritis is warranted.
Disclosure of Interests: Judy Schnyder Shareholder of: aclaris therapeutics, Employee of: aclaris therapeutics, Joe Monahan Shareholder of: aclaris therapeutics, Employee of: aclaris therapeutics, Walter Smith Shareholder of: aclaris therapeutics, Employee of: aclaris therapeutics, Heidi Hope Shareholder of: aclaris therapeutics, Employee of: aclaris therapeutics, Deborah Kelly Shareholder of: aclaris therapeutics, Employee of: aclaris therapeutics, David Burt Shareholder of: aclaris therapeutics, Employee of: aclaris therapeutics, E Huff Shareholder of: aclaris therapeutics, Employee of: aclaris therapeutics, A Kaul Shareholder of: aclaris therapeutics, Employee of: aclaris therapeutics, A Hildebrand Shareholder of: aclaris therapeutics, Employee of: aclaris therapeutics, B Burnette Shareholder of: aclaris therapeutics, Employee of: aclaris therapeutics, N Klug Shareholder of: aclaris therapeutics, Employee of: aclaris therapeutics, M Bangs Shareholder of: Aclaris Therapeutics, Employee of: Aclaris Therapeutics, David Gordon Shareholder of: aclaris therapeutics, Employee of: aclaris therapeutics
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SAT0144 DOES POLYPHARMACY IN RHEUMATOID ARTHRITIS PATIENTS AFFECT THE TREAT TO TARGET STRATEGY?

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Background: Polypharmacy (PP) is an important risk factor for drug toxicity, delirium, falls, hospitalizations and death. Patients with rheumatoid arthritis (RA) often have comorbid conditions and have PP. Treat to target strategy (T2T) implies a drug escalation and rheumatologists may not apply it in patients with PP.
Objectives: Our objective was to analyze if PP affects T2T in a real-world scenario.
Methods: Observational, retrospective cohort study. Patients with a new RA diagnosis (ACR/EULAR 2010 criteria) after 2010, over 18 years old, belonging to a Health Management Organization (HMO) from a university tertiary hospital, with a minimum follow-up period of 2 years, were included. PP was defined as consumption greater than or equal to 5 medications at the time of RA diagnosis, regardless of the medication used for RA, administered for a minimum period of 6 months. T2T strategy was defined as accomplished if an escalation in treatment was done when the patient had moderate or high disease activity at medical visit (by DAS28 and/or CDAI), without a significant improvement with respect to the previous visit. Prevalence of PP at RA diagnosis was calculated and RA patients were divided in those with PP at RA diagnosis time and those without. The first 2 years of disease were analyzed and compare between both groups: clinical and demographic characteristics, percentage of visits where T2T was applied, treatments received during that period. A multivariate logistic regression analysis was performed in order to identify factors associated with no T2T compliance.
Results: 147 patients with RA were included, 86% women, with an average age at diagnosis of 60 years (SD: 15.8). The prevalence of PP at RA diagnosis was 12% (17 patients). Table 1 shows the comparison between patients with and without PP. Patients with PP showed a greater frequency of erosions at baseline and after 2 years of disease, a greater use of corticosteroids at 2 years, higher percentage of hospitalizations and a higher mortality. In the multivariate logistic regression analysis, no compliance of the T2T strategy was only associated with the consumption of corticosteroids at 2 years (OR: 0.36, CI95%: 0.15-0.85; p=0.019) and no association was found with PP at the beginning of the disease.

Table 1. Demographic and clinical characteristics in patients with and without polypharmacy.

	Patients without Polypharmacy (n= 127)	Patients with Polypharmacy (n= 17)	P
Male sex, n (%)	18 (13.8)	3 (17.6)	0.6
Mean age at diagnosis (SD)	58.5 (15.6)	70.6 (12.2)	0.9
Positive rheumatoid factor, n (%)	87 (66.9)	12 (70.5)	0.7
Positive anti CCP, n (%)	109 (85.8)	13 (81.2)	0.6
Erosions at baseline, n (%)	25 (19.2)	7 (41.1)	0.03
Active smoker, n (%)	28 (21.5)	3 (17.6)	0.2
Past smoker, n (%)	23 (17.6)	7 (35.2)	
Charlson score, median (IQR)	3 (1-4)	4 (4-5)	**<0.0001**
Polypharmacy at 2 years, n (%)	17 (13.0)	46.8 (88.2)	**<0.0001**
Rheumatological consultations in 2 years, mean (DE), (IC 95%)	8.6 (3.3) (8.0-9.2)	8.8 (3.1) (7.2-10.5)	0.6
Corticosteroid therapy at 2 years, n (%)	29 (22.3)	8 (47.0)	0.02
cDMARDs therapy at 2 years, n (%)	114 (87.6)	13 (76.4)	0.2
Biologic therapy at 2 years, n (%)	13 (10)	4 (23.5)	0.1
Erosions at 2 years, n (%)	29 (22.3)	9 (52.9)	0.007
No T2T compliance, n (%)	65 (50)	5 (29.4)	0.1
Hospitalizations, n (%)	12 (9.2)	7 (41.1)	**<0.0001**
Mortality, n (%)	2 (1.5)	2 (11.7)	0.01

Conclusion: The prevalence of PP in our patients with a new RA diagnosis was 12% and was associated with more baseline erosions, a higher consumption of steroids, and a higher frequency of hospitalizations and mortality during the first 2 years of the disease. No relationship between PP and adherence to the T2T strategy was demonstrated. In the multivariate logistic regression analysis, no compliance with the T2T strategy was only associated to the consumption of corticosteroids at 2 years, may be reflecting a poorer disease control.
Disclosure of Interests: JOHN FREDY JARAMILLO GALLEGO: None declared, Javier Rosa: None declared, Marina Scolnik: None declared, Mayra Alejandra Tobar Jaramillo: None declared, LEANDRO FERREYRA: None declared, Enrique Soriano Grant/research support from: AbbVie, Eli Lilly, GlaxoSmithKline, Novartis, Pfizer Inc, Sandoz, Consultant of: AbbVie, Eli Lilly, GlaxoSmithKline, Novartis, Pfizer Inc, Sandoz, Speakers bureau: AbbVie, Amber, Bristol-Myers Squibb, Eli Lilly, Novartis, Pfizer Inc, Roche
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SAT0145

EFFICACY AND SAFETY OF UPADACITINIB MONOTHERAPY IN MTX-NAÏVE PATIENTS WITH EARLY ACTIVE RA RECEIVING TREATMENT WITHIN 3 MONTHS OF DIAGNOSIS: A POST-HOC ANALYSIS OF THE SELECT-EARLY

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Background: Early treatment of RA within the therapeutic window(0-3 months from symptom onset), has been associated with improved clinical outcomes and physical function. However, ≤42% of RA patients(pts) visit a rheumatologist within 90 days of symptom onset[1,2].

Objectives: To assess safety and efficacy of Upadacitinib(UPA), an oral, reversible, potent JAK-1 selective inhibitor[3], in pts with moderate to severely active RA who were MTX-naïve or had an inadequate response to csDMARDs/bDMARDs[4-6].

Methods: In SELECT–EARLY, MTX-naïve pts with active RA and poor prognosis were randomized 1:1:1 to once-daily UPA monotherapy at 15 or 30 mg or weekly MTX (titrated up to 20 mg/week through Week 8). Efficacy (including ACR, DAS28(CRP), CDAI responses and change in mTSS) and safety outcomes from a post-hoc analysis of patients who received treatment within 90 days from diagnosis are reported here. The statistical significance defined as $p<0.05$ was exploratory in nature.

Results: A total of 270 pts commenced treatment within 90 days from RA diagnosis (median: 44 days [11, 89]). Pts in each arm were mostly female (70%), had moderately to severely active RA with mean DAS28(CRP) =5.9±1.02, had structural joint damage (mean mTSS =7.7±21.5) and were seropositive for both ACPA and RF at baseline (72%)[4]. At Week 24, compared to MTX, significantly greater proportions of pts receiving UPA 15 or 30 mg monotherapy achieved efficacy outcomes including ACR20, 50 and 70 responses, DAS28CRP<2.6, CDAI≤2.8 or Boolean remission. Improvements in physical function (HAQ-DI) and decrease in pain were also significantly greater in pts receiving UPA 15 and 30 mg vs MTX at Week 24. Treatment with UPA was also associated with a greater inhibition of structural joint damage compared with MTX (Figure 1). Safety outcomes were consistent with the full study and the integrated safety analysis (all phase 3 studies of UPA). Compared to MTX, higher frequencies of serious infections and herpes zoster were reported in both UPA groups. There were 2 deaths in total (UPA 30 mg: 1 due to cardiovascular death and 1 due to pneumonia and sepsis) (Figure 2).

Conclusion: In RA pts, early initiation of treatment with UPA 15 mg and 30 mg monotherapy within 3 months from diagnosis was associated with clinically meaningful improvements in efficacy, including remission and inhibition of progression of structural joint damage compared to MTX. The safety profile was consistent with the overall study and the integrated phase 3 safety analysis[7]. UPA seems to be a promising treatment option for more patients to reach their treatment targets of remission or low disease activity when treated within 3 months of diagnosis.

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Figure 1.Efficacy at Week 24 in Early RA patients who received treatment within 90 days of diagnosis

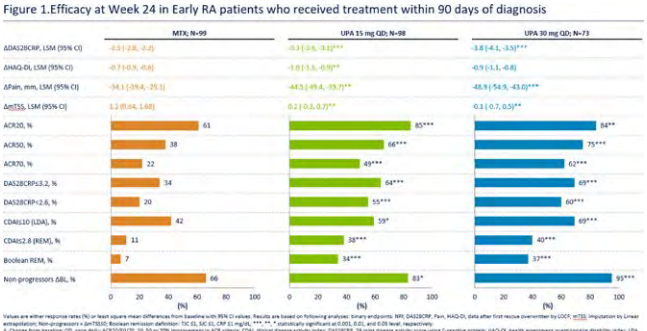
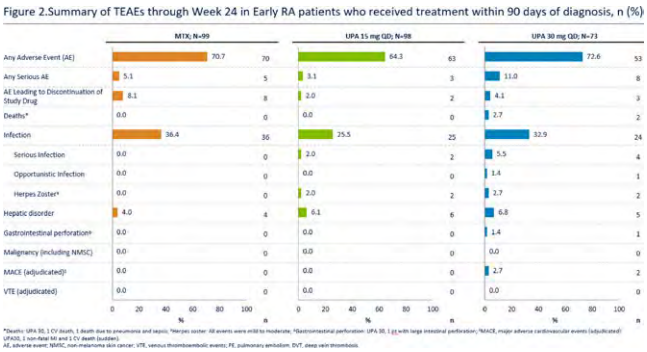


Figure 2.Summary of TEAEs through Week 24 in Early RA patients who received treatment within 90 days of diagnosis, n (%)



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SAT0146

INHIBITION OF RADIOGRAPHIC PROGRESSION BY IGURATINOD IN 116 JAPANESE RHEUMATOID ARTHIRITIS PATIENTS DESPITE CONVENTIONAL SYNTHETIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS THERAPY

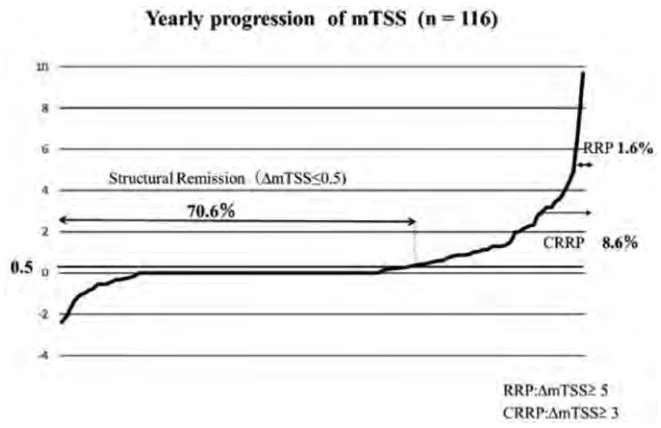
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Background: Japanese double-blind clinical practice studies of Iguratimod (IGU) for active rheumatoid arthritis (RA) patients indicated an early and sustained efficacy as a new conventional synthetic disease-modyfing anti-rheumatic drugs (csDMARDs) [1] as well as the safety of the treatment[2]. IGU also inhibit activation of NFkB and production of RANKL, indicating strong inhibiting activity against bone destruction. However, studies focused on the inhibitory effects of joint destruction by IGU has been poorly documented in clinical practice (3).

Objectives: To evaluate inhibitory effect during 1 year by additional IGU therapy in 116 RA patients despite csDMARDs therapy.

Methods: Inhibitory effects of joint damage were evaluated by modified total Sharp scoring (mTSS) at baseline and 1 year after IGU prescription. RA activity was measured by DAS28-ESR.

Results: The subjects were 116 cases, 30 male, age 63.2 yrs, disease duration 93.7 months. MTX was used weekly (84 cases, 72.4%), and cs DMARDs were used as BUC 43 cases, SASP 13 cases, TAC 5 cases, and LEF 1 cases. bDMARDs were used even in 8 cases, and steroids were used in 3.9 mg (70 cases, 60.3 %). Complications were observed in 70 cases (60.3%). DAS28-ESR were significantly improved from 4.29 (baseline) to 3.65 (6 months), 3.68 (12 months), respectively (P<0.0001). As shown in Figure 1, joint destruction measured by mTSS was significantly suppressed from 7.74 to 0.57 at 1 year (P<0.0001). 70.6% of patients satisfied structural remission (ΔmTSS≤0.5). Clinically relevant radiographic progression (CRRP)(mTSS>3) was observed in 10 cases (8.6%), and rapid radiographic progression(RRP) (mTSS≥5) was observed in 2 cases (1.6%). Adverse events were observed in 26 cases (22.4 %).



To investigate prognostic factor for CRRP, clinical data in baseline, 6, 12 months between ten patients with CRRP and 82 patients with structural remission were compared. As shown in Table 1, longer disease duration, more SJC (P<0.05), High CRP level(P<0.005) were prognostic for CRRP in IGU treated patients.

Conclusion: Iguratimod suppressed not only clinical activities but also joint destruction in RA patients resistant to csDMARDs therapy.

Table 1. Prognostic factor for CRRP

	ΔmTSS>3 (n=10)	ΔmTSS≤ 0.5 (n=82)	P value
Age(yrs)	63.2(12.2)	63.8(11.3)	N.S
Sex(F)	8(80%)	59(72%)	N.S
Disease duration (M)	152.2(28.9)	89.1(88.1)	0.0427*
MTX dose (mg/w)	5.4(1.5)	6.2(4.7)	N.S
PSL dose(mg/d)	2.8(3.2)	2.2(2.2)	N.S
ACPA(U/ml)	210.8(97.5)	212.5(311.3)	N.S
RF(IU/ml)	183.9(137.8)	164.0(285.4)	N.S
MMP3(ng/ml)	183.2(42.5)	165.3(213.1)	N.S
DAS28-ESR	4.6(1.2)	4.3(1.1)	N.S
DAS28-ESR(6M)	3.9(0.4)	3.6(1.2)	N.S
DAS28-ESR(12M)	4.2(1.3)	3.6(1.2)	0.1812
CDAI	17.4(9.5)	16.2(8.5)	N.S
CDAI(6M)	14.3(6.2)	11.5(7.7)	N.S
CDAI(12M)	12.9(7.3)	11.0(9.2)	N.S
mHAQ	0.7(0.6)	0.5(0.6)	N.S
mHAQ(6M)	0.5(0.4)	0.4(0.5)	N.S
mHAQ(12M)	0.4(0.3)	0.4(0.6)	N.S
CRP(mg/dl)	11.6(28.0)	1.5(2.5)	0.0014*
ESR(mm/hr)	44.0(25.6)	30.2(22.5)	0.0743
TJC	2.7(1.7)	4.4(4.7)	N.S
SJC	6.3(4.6)	4.2(2.9)	0.0480*
patient VAS	43.5(8.0)	39.2(25.3)	N.S
mTSS	78.1(87.4)	37.1(67.2)	0.0826
mTSS/y	6.6(5.2)	8.5(13.9)	N.S

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SAT0147

EFFICACY AND SAFETY OF IGURATIMOD AS FIRST-LINE DISEASE-MODIFYING ANTIRHEUMATIC DRUG THERAPY FOR PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Although methotrexate is the anchor drug, it took some days to check contraindications, such as interstitial pneumonia, hepatitis B virus infection, and latent tuberculosis infection. Therefore, we sometimes start rheumatoid arthritis (RA) treatment with other disease-modifying antirheumatic drug (DMARD) in daily clinical setting. Iguratimod (IGU) is a newly developed DMARD approved in Japan in September 2012, and the efficacy of IGU for DMARD naïve patients has not been thoroughly evaluated.

Objectives: The aim of this prospective single-center study was to demonstrate the efficacy and safety of IGU when used as a first-line daily DMARD for patients with RA in a clinical setting.

Methods: Enrolled patients included those diagnosed with RA according to the 2010 American College of Rheumatology/European League against Rheumatism (ACR/EULAR) classification criteria who took IGU as a first-line DMARD at Niigata Rheumatic Center between April 2016 and December 2018 (IGU group). There were no constraints regarding the addition or withdrawal of other DMARDs. Details of the patients' background, clinical parameters, and laboratory findings were obtained, including C-reactive protein (CRP) level, erythrocyte sedimentation rate (ESR), matrix metalloprotease-3 (MMP-3), rheumatoid factor (RF), Disease Activity Score for 28-joint counts based on the erythrocyte sedimentation rate (DAS28-4[ESR]), Clinical Disease Activity Index (CDAI), and Health Assessment Questionnaire Disability Index (HAQ-DI). The efficacy of IGU was evaluated at week 24. The IGU group's data were then compared with 64 patients who took salazosulfapyridine or bucillamine as first-line DMARD in our hospital (other DMARD group). The data were expressed as median values. Comparisons between the parameters were performed using nonparametric method.

Results: Forty-three patients (15 males, 28 females) received IGU as a first-line DMARD for RA. The age was 69.0 years and the duration of disease was 2.0 months. Twenty patients received prednisolone (PSL) concomitantly at a median dose of 5.0 mg/day. At 24 weeks medications were utilized in patients as follows: IGU in 36 (83.7 %), methotrexate in 18 (41.2%), PSL in 17 (39.5%), BUC in 10 (23.2 %), and biological DMARD in 7 (15.2 %) patients. Although 7 patients discontinued taking IGU due to liver enzyme elevation (n=4), nausea (n=1), creatinine elevation (n=1), and skin rash (n=1) during the 24-week period, serious adverse events requiring hospitalization were not observed. Clinical parameters that improved from baseline after 24 weeks of treatment included: ESR from 42.0 mm/h to 16.0 mm/h with $p < 0.001$; CRP from 0.70 mg/dL to 0.10 mg/dL with $p< 0.001$; MMP-3 from 136 ng/mL to 91.5 ng/mL with a p value of 0.11; RF went from 18.0 IU/mL to 8.00 IU/mL with $p < 0.001$; DAS28(4)-ESR dropped from 5.13 to 2.73 with $p< 0.001$; CDAI dropped from 20.0 to 5.00 with $p< 0.001$, and HAQ-DI decreased from 0.55 to 0.00 with $p< 0.001$. Patients who achieved a good or moderate response based on EULAR response at 24 weeks, included 90.7% in the IGU group versus 70.5% in the other DMARD group (Fisher`s exact test, p=0.046). The retention rate of the IGU group was 81.4 %, roughly equivalent to the 81.2% retention rate in the other DMARD group (Log-rank test, p=0.733).

Conclusion: Our study indicates IGU is safe and effective for DMARD naïve RA patients. Starting treatment with IGU might be a new and effective strategy for RA patients without previous use of a DMARD.

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SAT0148

TAPERING OF CONVENTIONAL SYNTHETIC DISEASE MODIFYING ANTI-RHEUMATIC DRUGS IN SUSTAINED RHEUMATOID ARTHRITIS REMISSION: RESULTS FROM A RANDOMIZED CONTROLLED TRIAL

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Background: Sustained remission is the goal of rheumatoid arthritis (RA) care, and more patients reach and maintain this state on conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs) with treat-to-target strategies. The knowledge about whether csDMARDs can be tapered in RA remission is limited.

Objectives: The primary objective of the study was to assess the effect of tapering of csDMARDs on the risk of flares in RA patients in sustained clinical remission.

Methods: In the open, phase 4, non-inferiority ARCTIC REWIND trial, RA patients in clinical remission for ≥ 12 months on stable csDMARD therapy were randomised to continued stable csDMARD or half dose csDMARD. Patients had to be in DAS remission at inclusion with no swollen joints (of 44). The primary endpoint was the proportion of patients with a disease flare during 12 months (defined as a combination of DAS >1.6, change in DAS >0.6 and ≥2 swollen joints, or the physician and patient agreed that a clinically significant flare had occurred). Patients attended visits every 4 months, with extra visits in case of flares. The non-inferiority margin was 20%, with a predefined superiority test if non-inferiority was not shown. Mixed effect logistic regression was used to test the inferiority null-hypothesis in the per-protocol population. Radiographs at 0 and 12 months were scored by van der Heijde Sharp score (average score of two readers, progression: ≥1 unit change/year). Clinicaltrials.gov NCT01881308.

Results: We enrolled 160 patients, 155 received the allocated treatment strategy. Baseline characteristics were overall well balanced (Table). 78% of patients in the stable csDMARD arm and 84% in the half-dose csDMARD arm used methotrexate monotherapy. In the primary analysis, we observed flares in 6% of patients on stable csDMARD, compared to 25% in the half-dose csDMARD arm, giving a risk difference (95% CI) of 18.3% (7.2% to 29.3%, Fig 1). Non-inferiority could not be claimed, with the results showing superiority of the stable arm over the half-dose arm (Fig 1). Similar results were found in methotrexate monotherapy users. In the stable arm, 2/5 (40%) escalated DMARD medication following the flares, compared to 18/19 (95%) in the tapering arm. No progression of radiographic joint damage was observed in 79.5% of patients on stable DMARDs and 62.7% of those tapering, difference (95% CI) -17.7% (-33.0%, -2.3%, Fig 2E). At 12 months, 92% of patients in the stable and 85% of patients in the tapered arm were in DAS remission (Fig 2C). The frequency of adverse events was 75 in the stable arm and 53 in the tapered arm, with serious adverse events in 2 (2.6%) of patients in the stable and 4 (5.1%, including two serious infections) patients in the tapered arm.

Conclusion: In RA patients in sustained remission on csDMARDs, continued csDMARD therapy with stable dosage led to significantly fewer disease activity flares and less frequent radiographic joint damage progression than tapered csDMARD treatment.

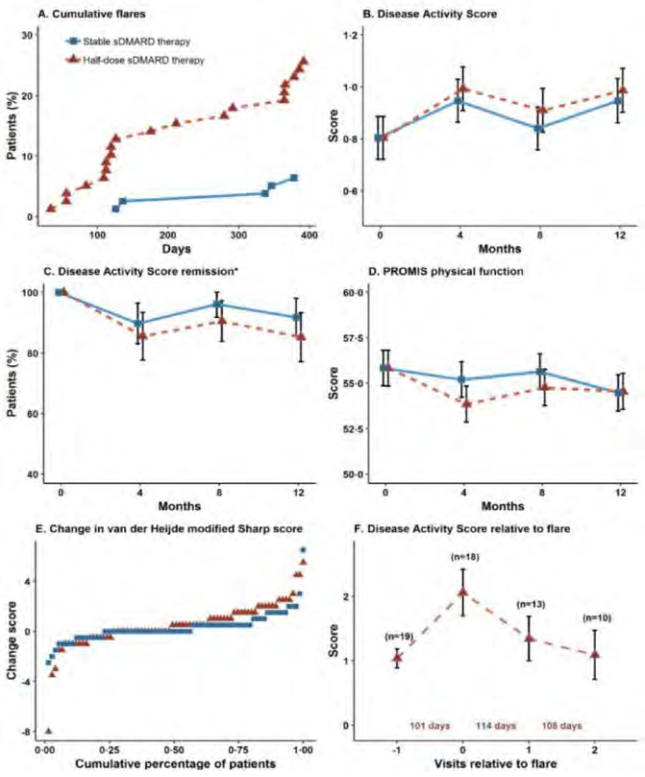
Table. Baseline values; mean (SD), n (%) or median (IQR)

	Stable, n=78	Tapering, n=78
Age, yrs	55 (12)	56 (12)
Female	50 (64%)	54 (69%)
ACPA+	57 (73%)	63 (81%)
Symptom dur., yrs	3.7 (1.8)	3.4 (1.4)
DAS	0.8 (0.4)	0.8 (0.3)
CRP mg/L	2 (1, 3)	2.0 (1,3)
MTX monotherapy	61 (78%)	65 (84%)

Figure 1: Non-inferiority plot of stable vs half-dose csDMARD treatment in per protocol set, full analysis set and in patients treated by methotrexate monotherapy.
The broken vertical line represents the non-inferiority margin.



Figure 2: Secondary endpoints



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SAT0149

EXPOSURE-RESPONSE RELATIONSHIPS FOR EFFICACY AND SAFETY OF FILGOTINIB AND ITS METABOLITE GS-829845 IN SUBJECTS WITH RHEUMATOID ARTHRITIS BASED ON PHASE 2 AND PHASE 3 STUDIES

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Background: Filgotinib is an orally administered small molecule that provides selective inhibition of JAK1, a signaling molecule that helps drive inflammatory pathways underlying rheumatoid arthritis (RA).
Objectives: Exposure-response (ER) analyses were performed for efficacy following completion of Phase 2 studies over a wide range of doses to support evaluation of 200mg and 100 mg once daily in Phase 3 studies. ER analyses were subsequently performed by using Phase 3 efficacy data to support selection of the proposed registrational dose. ER analyses for safety based on pooled Phase 2 and Phase 3 studies were conducted to examine the safety of evaluated doses.
Methods: Population PK analyses were conducted to estimate plasma exposures of filgotinib and GS-829845 (major circulating active metabolite of filgotinib) in both Phase 2 (DARWIN 1 and DARWIN 2) and Phase 3 studies (FINCH 1, FINCH 2, and FINCH 3) encompassing a dose range of 25 to 100 mg twice daily and 50 to 200 mg once daily. As both filgotinib and GS-829845 contribute to efficacy via JAK1 inhibition, their exposures were combined into single parameters, AUCeff and Ctau-eff (effective area under the curve and effective concentration at trough, by accounting for relative inhibition potency and molecular weight) in the ER analyses for various efficacy endpoints (e.g ACR20/50/70 responses) at Week 12 and Week 24. The ER analyses for safety endpoints (the 5 most frequent treatment-emergent adverse events [TEAEs] and Grade 3 or 4 laboratory abnormalities, serious TEAEs, and serious infections) were performed separately for filgotinib and GS-829845 exposures to characterize the individual safety profile of each analyte. The 5 evaluated TEAEs were nausea, nasopharyngitis, upper respiratory tract infection, headache, and hypertension; the 5 Grade 3/4 laboratory abnormalities included lymphocytes decrease, glucose increase, phosphate decrease, triacylglycerol lipase increase, and creatine kinase increase.
Results: In the ER analyses for efficacy based on Phase 2 studies, high response rates were demonstrated in ACR20/50/70 across all octile groups in subjects with RA receiving filgotinib and the ER supported further evaluation of both 200 mg and 100 mg once daily doses in Phase 3 clinical studies. Similarly, ER relationships based on pooled Phase 3 studies across various endpoints (e.g ACR20/50/70) consistently revealed high response rates across the exposure range for both the filgotinib 200 mg and 100 mg doses. A trend of increasing response with increasing exposure was observed over the exposure range for multiple secondary efficacy endpoints including ACR50 and ACR70 with the effective exposures at filgotinib 200 mg primarily residing on the plateau of the ER curves.
Filgotinib was generally well-tolerated with no individual TEAE or Grade 3 or 4 laboratory abnormality > 5% in the filgotinib 200 mg once daily group up to Week 12. No relationships were observed between filgotinib and GS-829845 exposures (AUC0-24 and Cmax) and the most frequent TEAEs, Grade 3/4 laboratory abnormalities, serious TEAEs, or serious infections up to Week 52.
Conclusion: ER analyses demonstrate that both the 200 mg and 100 mg once daily filgotinib doses are efficacious in subjects with moderately to severely active RA without clear dose-dependent effects on safety. The trend towards greater efficacy with higher exposures for some secondary endpoints (ACR50 and ACR70) and a lack of exposure-safety relationship supports a dose of 200 mg once daily over 100 mg once daily since it presents the best benefit/risk ratio among the doses tested.
Disclosure of Interests: : Amy Meng Shareholder of: Gilead Sciences, Employee of: Gilead, Kacey Anderson Shareholder of: Gilead Sciences, Employee of: Sciences, Cara Nelson Shareholder of: Gilead, Employee of: Gilead, Brian Kirby Shareholder of: Gilead, Employee of: Gilead, Liyun Ni Shareholder of: Gilead, Employee of: Gilead, Shu-Min Chuang Shareholder of: Gilead, Employee of: Gilead, Brian Kearney Shareholder of: Gilead, Employee of: Gilead, Anita Mathias Shareholder of: Gilead, Employee of: Gilead
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SAT0150

CHANGES IN PATIENT-REPORTED OUTCOME (PRO) SCORES FOR NAUSEA AND FATIGUE FOLLOWING WEEKLY METHOTREXATE DOSE IN A REAL-WORLD SAMPLE OF RA AND PSA PATIENTS IN THE ARTHRITISPOWER REGISTRY

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Background: Methotrexate (MTX) is frequently used in patients with rheumatoid arthritis (RA) or psoriatic arthritis (PsA) because of its beneficial effects in both populations[1-3]. Despite the well-known benefits of MTX, it is associated with a number of potential side effects[4-6] These include nausea and fatigue, are often temporally related to the timing of weekly MTX administration, and can be severe. The combined patient-reported side effects, along with potential of long-term toxicity, may make use of MTX more burdensome. Currently, there is a gap in patient-centered studies that focus on patients' experience with MTX.
Objectives: Examine patient temporal experience of fatigue and nausea relating to oral MTX therapy for the treatment of RA and PsA.
Methods: Adult US patients in the ArthritisPower registry with self-reported RA or PsA taking MTX for less than 10 years were invited to participate in the study via email invitation. Participants (pts) completed a screener and brief online survey. In an ancillary study to the ArthritisPower registry and using a self-controlled case series study design where pts serve as their own control to avoid between-person confounding, pts were asked to complete a set of up to 8 assessments within 6-36 hours ('risk') and 96-144 hours ('control') after taking their oral dose of MTX each week, for up to 4 weeks. Risk and control windows were selected based on the expected temporal relationship between MTX use and peak onset of these symptoms. Assessments included PROMIS short forms for same-day Fatigue, same-day Nausea/Vomiting, and Patient Global. Descriptive statistics were conducted using paired t-tests two-way comparisons. Within-person change in PROMIS scores between the risk (1-2 days after MTX) and control (4-6 days after MTX) windows were analyzed using mixed models for repeated measures, stratified on whether pts reported fatigue or nausea with MTX at baseline. Recruitment for this study is ongoing.
Results: As of December 2019, 91 pts had participated, of whom 76.9% were living with RA and 28.6% with PsA, with mean baseline PROMIS Patient Global score (SD) of 39.5 (7.1). Mean age (SD) was 50.9 (12.0) years, 84.6% female, 92.3% White, with mean BMI 33.7 (8.8). Mean duration of MTX treatment among current users was 2.1 (2.8) years. Among pts, 41.8% were on a biologic DMARD and 58.2% on non-biologic DMARDs only. Among pts reporting baseline nausea (n=30, 33.0%) where paired within-week measures were observed (n=64 observations among 20 pts), the mean increase in the PROMIS Nausea score was 4.5 units (adjusted p=0.003). Among those reporting MTX-associated fatigue (n=39, 42.9%) as a side effect of MTX on their baseline survey where paired within-week measures were observed (n=96 observations among 28 pts), the mean increase in PROMIS Fatigue was 4.7 (adjusted p=0.004) units. In those pts, the proportion of pts with worsened nausea and fatigue with minimally important difference of >5 units[7-8] was 40.0% (nausea), and 60.7% (fatigue) [Figures 1 and 2].
Conclusion: People taking MTX to manage RA or PsA commonly experience bothersome side effects, notably fatigue and nausea, that are temporally related to weekly MTX dosing. In this sample, one-third or more of pts were bothered by nausea or fatigue shortly after MTX dosing, many of them with clinically meaningful symptoms.
References:
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Disclosure of Interests: W. Benjamin Nowell: None declared, Elaine Karis Shareholder of: Amgen Inc., Employee of: Amgen Inc., Kelly Gavigan: None declared, Laura Stradford: None declared, Scott Stryker Shareholder of: Amgen Inc., Employee of: Amgen Inc., Huifeng Yun Grant/research support from: Bristol-Myers Squibb and Pfizer, Shilpa Venkatachalam: None declared, Greg Kricorian Shareholder of: Amgen Inc., Employee of: Amgen Inc., Lang Chen:

Figure 1. Nausea PROMIS Score Changes Among Patients Reporting Nausea as a Side Effect of MTX [n=64 observations (32 pairs) among 20 unique pts]

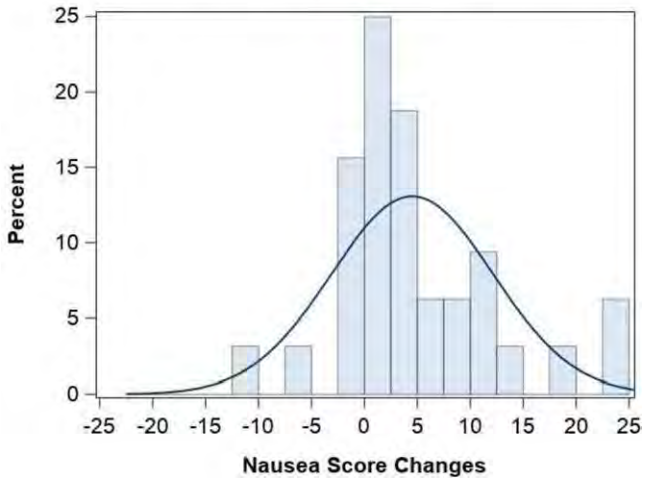
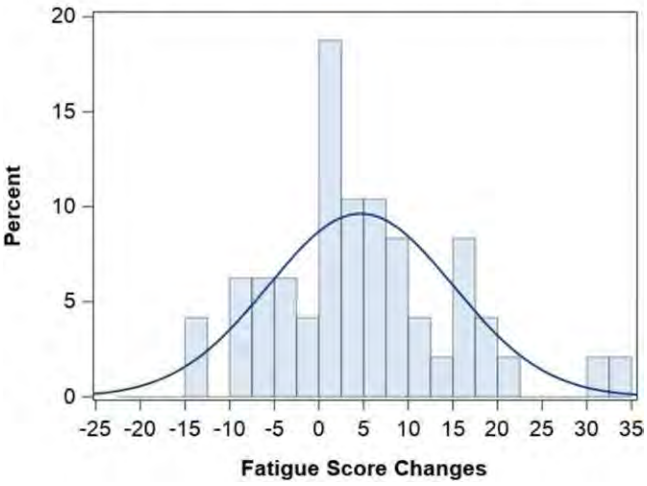


Figure 2. Fatigue PROMIS Score Changes Among Patients Reporting Fatigue as a Side Effect of MTX [n=96 observations (48 pairs) among 28 unique pts]



None declared, Hong Zhao: None declared, Fenglong Xie: None declared, Jeffrey Curtis Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Janssen, Lilly, Myriad, Pfizer, Regeneron, Roche, UCB, Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Janssen, Lilly, Myriad, Pfizer, Regeneron, Roche, UCB

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SAT0151

EFFICACY AND SAFETY OF UPADACITINIB VERSUS ABATACEPT IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS AND PRIOR INADEQUATE RESPONSE OR INTOLERANCE TO BIOLOGIC DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS (SELECT-CHOICE): A DOUBLE-BLIND, RANDOMIZED CONTROLLED PHASE 3 TRIAL

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Background: Upadacitinib (UPA) is an oral, reversible, selective JAK 1 inhibitor approved for the treatment of moderate to severe rheumatoid arthritis (RA). The efficacy/safety of UPA has been demonstrated in phase 3 studies, including superiority to adalimumab in patients (pts) with prior inadequate response (IR) to methotrexate.[1-4]

Objectives: To assess the efficacy/safety of UPA vs abatacept (ABA) in pts with prior IR or intolerance to biologic DMARDs (bDMARDs).

Methods: Pts were randomized to once daily UPA 15 mg or intravenous ABA (at Day 1, Weeks [Wks] 2, 4, 8, 12, 16 and 20 [< 60 kg: 500 mg; 60-100 kg: 750 mg; >100 kg: 1,000 mg]), with all pts continuing background stable csDMARDs. The study was double-blind for 24 wks. Starting at Wk 12, pts who did not achieve ≥20% improvement from baseline (BL) in both tender and swollen joint counts at two consecutive visits, had background medication(s) adjusted or initiated. The primary endpoint was change from BL in DAS28(CRP) at Wk 12 (non-inferiority). The non-inferiority of UPA vs ABA was tested using the 95% CI of treatment difference against a non-inferiority margin of 0.6. The two key secondary endpoints at Wk 12 were change from BL in DAS28(CRP) and the proportion of pts achieving clinical remission (CR) based on DAS28(CRP), defined as DAS28(CRP) <2.6. Both endpoints were to demonstrate the superiority of UPA vs. ABA. Treatment-emergent adverse events (TEAEs) are reported up to Wk 24 for all pts who received at least one dose of study drug.

Results: Of 612 pts treated; 67% of pts had received 1 prior bDMARD, 22% received 2 prior bDMARDs, and 10% received ≥ 3 prior bDMARDs. 549 (90%) completed 24 wks of treatment. Common reasons for study drug discontinuation were AEs (UPA, 3.6%; ABA, 2.6%) and withdrawal of consent (UPA, 1.7%; ABA, 2.6%).

Non-inferiority and superiority were met for UPA vs ABA at Wk 12 for change from BL in DAS28(CRP) (-2.52 vs -2.00; -0.52 [-0.69, -0.35]; p <0.001 for UPA vs ABA). UPA also demonstrated superiority to ABA in achieving DAS28(CRP) <2.6 (30.0% vs 13.3%; p <0.001 for UPA vs ABA; Figure 1). Improvements in disease activity and remission rates were maintained through Wk 24. The proportions of pts achieving low disease activity (defined as DAS28(CRP) ≤3.2), ACR20, ACR50, and ACR70 responses were greater with UPA compared with ABA at Wk 12 (nominal p <0.05). More stringent outcome measures – CR, ACR50, and ACR70 responses - remained higher with UPA than ABA through Wk 24 (nominal p <0.05). Incidence of serious TEAEs, AEs leading to discontinuation, hepatic disorders, and CPK elevations were numerically higher with UPA versus ABA (Figure 2). Eight cases of herpes zoster were reported (4 in each treatment arm). No malignancies were reported. One case of adjudicated MACE, two adjudicated cases of VTE (1 pt with DVT and 1 pt with PE; both pts had at least one risk factor for VTE), and one treatment-emergent death were reported with UPA.

Conclusion: In RA pts with a prior IR or intolerance to bDMARDs, UPA demonstrated superior improvement in signs and symptoms vs ABA based on change in DAS28(CRP) and in achieving CR at Wk 12. The safety profile of UPA was consistent with the phase 3 RA studies with no new risks identified.

References:

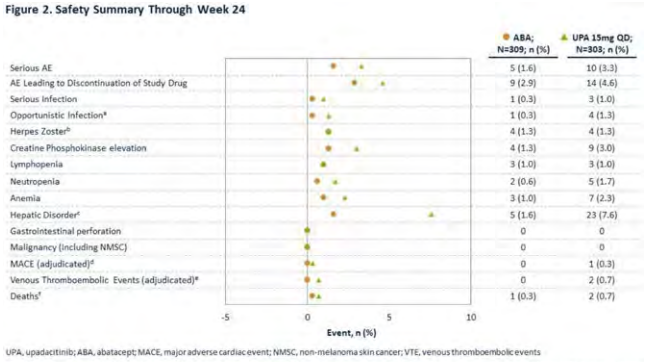
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Figure 1. Efficacy Endpoints



UPA, upadacitinib; ABA, abatacept; DAS28(CRP), 28 joint disease activity score using C-reactive protein; CR, clinical remission; LDA, low disease activity.
CR DAS28(CRP): defined as DAS28(CRP) <2.6; **LDA DAS28(CRP):** defined as DAS28(CRP) ≤3.2.
*, **, *** p ≤ .05, .01, and .001, respectively for UPA versus ABA.
For binary endpoints, treatments were compared using the Cochran–Mantel-Haenszel (CMH) test, adjusting for the number of prior bDMARDs used and geographic region. Non-responder imputation was used for missing data handling. For continuous endpoints, analyses were conducted using the analysis of covariance (ANCOVA) model. Multiplicity adjustments were applied to the primary and key secondary endpoints.

Figure 2. Safety Summary Through Week 24



UPA, upadacitinib; ABA, abatacept; MACE, major adverse cardiac event; NMSC, non-melanoma skin cancer; VTE, venous thromboembolic events
[a]Opportunistic infections: UPA: 3 oral candidiasis, 1 esophageal candidiasis; ABA: oral candidiasis; [b]Herpes zoster: There were no serious cases of Herpes Zoster and majority involved a single dermatome; [c]Hepatic disorders: majority based on asymptomatic ALT/AST elevations; [d]MACE (includes CV death, non-fatal myocardial infarction [MI], non-fatal stroke): UPA: 1 non-fatal stroke; [e]VTE: UPA: 1 pulmonary embolism and 1 deep vein thrombosis; [f]Deaths (includes non-treatment emergent deaths[d]): UPA: 1 atrioventricular block adjudicated as a non-cardiovascular death, 1 undetermined/unknown cause; ABA: 1 undetermined/unknown cause

Disclosure of Interests: Andrea Rubbert-Roth Consultant of: Abbvie, BMS, Chugai, Pfizer, Roche, Janssen, Lilly, Sanofi, Amgen, Novartis, Jeffrey Enejosa Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Aileen Pangan Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Ricardo Xavier Consultant of: AbbVie, Pfizer, Novartis, Janssen, Eli Lilly, Roche, Boulos Haraoui Grant/research support from: Abbvie, Amgen, Pfizer, UCB, Grant/research support from: AbbVie, Amgen, BMS, Janssen, Pfizer, Roche, and UCB, Consultant of: Abbvie, Amgen, Lilly, Pfizer, Sandoz, UCB, Consultant of: AbbVie, Amgen, BMS, Celgene, Eli Lilly, Janssen, Merck, Pfizer, Roche, and UCB, Speakers bureau: Pfizer, Speakers bureau: Amgen, BMS, Janssen, Pfizer, and UCB, Maureen Rischmueller Consultant of: Abbvie, Bristol-Meyer-Squibb, Celgene, Glaxo Smith Kline, Hospira, Janssen Cilag, MSD, Novartis, Pfizer, Roche, Sanofi, UCB, Nasser Khan Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Ying Zhang Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Naomi Martin Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Mark C. Genovese Grant/research support from: Abbvie, Eli Lilly and Company, EMD Merck Serono, Galapagos, Genentech/Roche, Gilead Sciences, Inc., GSK, Novartis, Pfizer Inc., RPharm, Sanofi Genzyme, Consultant of: Abbvie, Eli Lilly

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SAT0152 EFFICACY OF BARICITINIB IN PATIENTS WITH MODERATE-TO-SEVERE RHEUMATOID ARTHRITIS WITH 3 YEARS OF TREATMENT: RESULTS FROM A LONG-TERM STUDY

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Background: Baricitinib (Bari) is an oral, selective and reversible Janus kinase 1 and 2 inhibitor approved for the treatment of adults with active RA. In addition to long-term safety which has been disclosed previously with data up to 7 years [1], an important clinical consideration is whether treatment efficacy can be maintained over the long term.
Objectives: To evaluate the long-term efficacy of once-daily Bari 4 mg in patients with active rheumatoid arthritis (RA) who were either naïve to or who had inadequate response (IR) to methotrexate (MTX)
Methods: Post hoc analyses of data from two phase 3 studies, RA-BEGIN (MTX-naïve) and RA-BEAM (MTX-IR) for 52 weeks, and one long-term extension (LTE) study (RA-BEYOND) for an additional 96 weeks were conducted (148 weeks in total). At week 52, MTX-naïve patients initially treated with MTX monotherapy, Bari 4 mg monotherapy, or Bari 4 mg +MTX in RA-BEGIN were switched to open-label Bari 4 mg monotherapy for treatment in the LTE. Similarly, at week 52, MTX-IR patients initially treated with Bari 4 mg [+ background MTX noted as (+MTX) for RA-BEAM] or adalimumab (ADA) (+MTX) in RA-BEAM were switched to open-label Bari 4 mg (+MTX) for treatment in the LTE. Patients who received placebo (+MTX) were switched to open-label Bari 4 mg (+MTX) at week 24. The analyses of efficacy (SDAI) and physical function (HAQ-DI) were conducted on all patients who were randomized into the RA-BEGIN and RA-BEAM studies and had received ≥1 dose of study drug after randomization (mITT population). The proportion of patients who reached low disease activity (LDA), as measured by SDAI ≤11, was evaluated along with change from baseline in HAQ-DI. The non-responder imputation (NRI) method was used for the categorical analysis.
Results: By week 24 in RA-BEGIN (N=584), 62% of patients treated with Bari 4 mg monotherapy or Bari 4 mg +MTX achieved SDAI LDA in comparison to 40% of pts in the MTX monotherapy group; response rates seen at week 24 in the Bari treatment groups were maintained through week 148 (Fig 1A). Similarly, by week 24 in RA-BEAM (N=1,305), 52% of patients treated with Bari 4 mg (+MTX) and 50% of patients treated with ADA (+MTX) achieved a SDAI LDA in comparison to 26% of patients from the PBO (+MTX) group. The response rate seen at week 24 with Bari 4 mg and ADA were maintained through week 148, even after patients switched from ADA to Bari 4 mg at week 52 (Fig 1B). Similar improvement and maintenance patterns in physical function measured by HAQ-DI were demonstrated. The overall discontinuation rate across treatment groups from RA-BEGIN (19.5%) and RA-BEAM (14.2%) have been published. In the LTE, the discontinuation rate from Bari treatment was 13.7% for patients originating from RA-BEGIN (1.1% due to lack of efficacy, 6.4% due to safety) and 12.6% for patients originating from RA-BEAM (1.8% due to lack of efficacy, 5.9% due to safety).

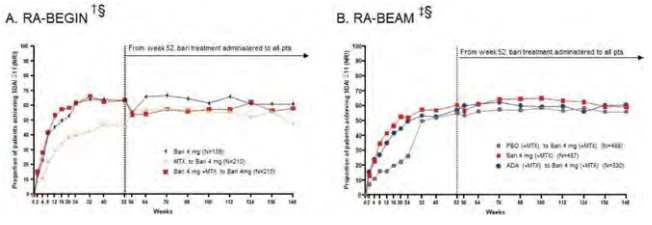


Figure 1. Proportion of patients achieving SDAI ≤11 in the NRI analysis†In RA-BEGIN, rescue to Bari 4 mg + MTX was offered at week 24.‡In RA-BEAM, rescue to Bari 4 mg (+ MTX) was offered at week 16. At week 24, all PBO + MTX patients were switched to Bari 4 mg + MTX.§Upon entering RA-BEYOND at week 52, MTX and ADA patients were switched to Bari 4 mg.

Conclusion: Long-term treatment with Bari 4 mg demonstrated the maintenance of clinically-relevant outcomes for up to 3 years. Low discontinuation rates during the LTE indicated that Bari 4 mg treatment was well-tolerated.

References:
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Disclosure of Interests: : Josef S. Smolen Grant/research support from: AbbVie, AstraZeneca, Celgene, Celltrion, Chugai, Eli Lilly, Gilead, ILTOO, Janssen, Novartis-Sandoz, Pfizer Inc, Samsung, Sanofi, Consultant of: AbbVie, AstraZeneca, Celgene, Celltrion, Chugai, Eli Lilly, Gilead, ILTOO, Janssen, Novartis-Sandoz, Pfizer Inc, Samsung, Sanofi, Li Xie Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Bochao Jia Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Peter C. Taylor Grant/research support from: Celgene, Eli Lilly and Company, Galapagos, and Gilead, Consultant of: AbbVie, Biogen, Eli Lilly and Company, Fresenius, Galapagos, Gilead, GlaxoSmithKline, Janssen, Nordic Pharma, Pfizer Roche, and UCB, Gerd Rüdiger Burmester Consultant of: AbbVie Inc, Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB Pharma, Speakers bureau: AbbVie Inc, Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB Pharma, Yoshiya Tanaka Grant/research support from: Asahi-kasei, Astellas, Mitsubishi-Tanabe, Chugai, Takeda, Sanofi, Bristol-Myers, UCB, Daiichi-Sankyo, Eisai, Pfizer, and Ono, Consultant of: Abbvie, Astellas, Bristol-Myers Squibb, Eli Lilly, Pfizer, Speakers bureau: Daiichi-Sankyo, Astellas, Chugai, Eli Lilly, Pfizer, AbbVie, YL Biologics, Bristol-Myers, Takeda, Mitsubishi-Tanabe, Novartis, Eisai, Janssen, Sanofi, UCB, and Teijin, Ayesha Elias Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Anabela Cardoso Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Robert Ortmann Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Chad Walls Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Maxime Dougados Grant/research support from: AbbVie, Eli Lilly, Merck, Novartis, Pfizer and UCB Pharma, Consultant of: AbbVie, Eli Lilly, Merck, Novartis, Pfizer and UCB Pharma, Speakers bureau: AbbVie, Eli Lilly, Merck, Novartis, Pfizer and UCB Pharma
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SAT0153 GENDER DOES NOT INFLUENCE CLINICAL RESPONSE TO JAK INHIBITORS IN RHEUMATOID ARTHRITIS: AN ITALIAN MULTICENTRE ANALYSIS

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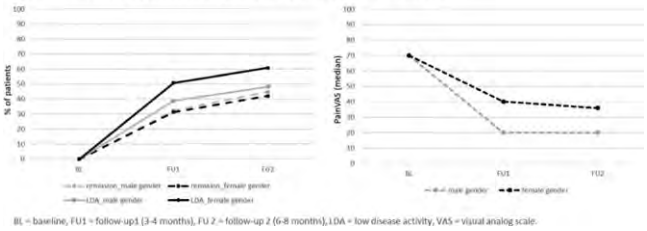
Background: Gender medicine aims at describing how diseases differ between men and women in terms of epidemiology, clinical feature, therapeutic approach, treatment response and prognosis, psychological and social impact. Rheumatoid Arthritis (RA) affects women 2-3 times more than men. Female gender seems to be independently associated to a more refractory disease and a worst response to conventional synthetic Disease Modifying Anti-Rheumatic Drugs (csDMARDs) and biological DMARDs. Male patients achieve remission more often than females probably due to the higher number of tender joints reported by the latter.
Objectives: In the light of the effect of Janus kinases inhibitors (JAKi) on pain, the objective of the study was to investigate whether gender might affect the achievement of remission or low disease activity in RA patients treated with baricitinib and tofacitinib.
Methods: We performed a multicentric, prospective study on consecutive patients starting one of the two available JAKi: baricitinib and tofacitinib. Demographic and clinical data were recorded in a dedicate database and included: gender, age, disease duration, serological status (Rheumatoid Factor – RF; anti-citrullinated peptide antibodies, ACPA) number of previous csDMARDs and bDMARDs, number of tender joints (TJ) and swollen joints (SJ), C reactive protein (CRP); patient global assessment (PGA) and pain were recorded on a 0-100 mm visual-analogue scale (VAS). Disease activity score (DAS) 28 was calculated at baseline and at two follow-up visits (after 3-4 months and after 6-8 months). Data were expressed as mean±standard deviation or median (interquartile range) according to variables' distribution. Continuous variables were compared by Mann Whitney test while dichotomous ones by Chi-squared test; p value < 0.05 were considered statistically significant.
Results: We enrolled 182 RA patients (149 F:33 M) with similar age (F 58±12 vs M 60±10) and disease duration (F 143±101 vs M 147±105 months). Females and males were previously treated with the same number of csDMARDs [2(2)] but female have previously received numerically more bDMARDs [2(3) vs 1(2)]. At the 3 timepoints females and males showed similar number of TJ, SJ, similar values of CRP, PGA and pain. We did not observe any difference in percentage

of males and females achieving remission or low disease activity according to gender (figure 1A) nor in terms of reduction of TJ, SJ and PGA; only pain decreased significantly more in male than in female patients at both timepoints (figure 1B).

Conclusion: In RA patients treated with JAK inhibitors, even if the effect of JAKi on pain seems to be more relevant in male than in female, gender seems not to influence the overall clinical response, allowing men and women the same probability of reaching the therapeutic target

References:

Figure 1. remission and low disease activity (A) and pain (B) in male and female patients



BL = baseline, FU1 = follow-up1 (3-4 months), FU 2 = follow-up 2 (6-8 months), LDA = low disease activity, VAS = visual analog scale.

Disclosure of Interests: Francesca Romana Spinelli Grant/research support from: Pfizer, Speakers bureau: Lilly, BMS, Celgene, Maria Sole Chimenti: None declared, Marta Vadacca: None declared, Cristina Iannuccelli: None declared, Paola Conigliaro: None declared, Silvia Laura Bosello: None declared, Fulvia Ceccarelli: None declared, Cristina Garufi: None declared, Giulia Raffone: None declared, Paola Di Noi: None declared, Dario Bruno: None declared, Antonella Afeltra: None declared, Roberto Perricone: None declared, fabrizio conti Speakers bureau: BMS, Lilly, Abbvie, Pfizer, Sanofi, Elisa Gremese Speakers bureau: Abbvie, BMS, Celgene, Jannsen, Lilly, MSD, Novartis, Pfizer, Sandoz, UCB
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SAT0154 EXAMINATION OF CYP3A5 GENOTYPE IS USEFUL FOR INTRODUCTION OF TACROLIMUS TREATMENT IN OUTPATIENTS WITH RHEUMATIC DISEASES

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Background: Though several studies showed the efficacy of tacrolimus (TAC) in patients with rheumatoid arthritis (RA) in a dose-depending manner [1], the relationship between efficacy and concentration of TAC remained unclear. Genetic polymorphisms of cytochrome P450 (CYP) 3A5 were reported not only to play an important role in pharmacokinetics of TAC but also to have an influence on clinical outcomes in patients of rheumatic diseases. Several reports showed that the blood concentration of TAC in patients with a CYP3A5 *1 allele (EX, expressor) was lower than that of patients with a CYP3A5 *3/*3 (NEX, non-expressor) [2].

Objectives: To assess the relationship between efficacy and concentration of TAC in patients with RA, and to examine the usefulness of CYP3A5 genotype screening to detect outpatients suitable for TAC treatment.

Methods: We examined the relationship between disease activity score (DAS) 28-CRP and concentration of TAC in patients with RA. TAC was taken after the evening meal and blood samples were taken 12±4h after TAC administration. Next we investigated the relationship between genotype frequencies of CYP3A5 and concentration of TAC in patients with rheumatic disease without having renal dysfunction (eGFR<60) and also investigated the influence of concomitant drugs, such as strong inhibitors of CYP3A4/5 or metabolized by CYP3A4/5, to C/D value in each NEX and EX group. The blood concentration of TAC normalized to the corresponding dose per body weight (C/D, ng/ml per mg/kg) was analyzed according to genetic variation in CYP3A5. Furthermore we investigated the relationship between genotype frequencies of CYP3A5 and concentration of TAC in patients with rheumatic disease at first visit and second visit after starting TAC administration to assess the possibility for making rapid attainment of enough concentrations of TAC in early stage of treatment.

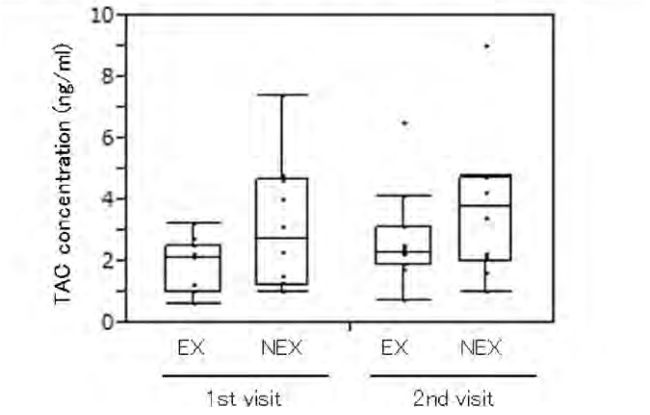
Results: The concentration of TAC tended to be negatively correlated with the disease activity of RA. The C/D value in the NEX group (n=16) was 124.7±62.1, which was significantly higher than that in the EX group (n=23; 67.7±29.8; *P*<0.001). When comparing patients using concomitant drugs which are strong inhibitors of CYP3A4/5 or metabolized by CYP3A4/5 with patients not using those drugs, the each C/D value of NEX group was 122.9±52.3 (n=9) and 126.9±77.3 (n=7), and that of EX group was 71.3±32.2 (n=12) and 63.8±28.0 (n=11). There were no significant differences between these groups. In NEX group, when comparing concentration of TAC at first visit and second visit after starting TAC administration, the each concentration of TAC was 3.14±2.06 ng/ml and 3.80±2.20 ng/ml in NEX group (n=10), and that of TAC was 1.82±0.82 ng/ml and 2.69±1.52 ng/ml (n=11) in EX group (Figure).

Conclusion: TAC showed efficacy in patients with RA in a concentration-dependent manner. EX patients may be impossible to achieve enough concentration of TAC even though using TAC of 3mg/day, approved dose for patients with RA in Japan, and NEX patients could make rapid attainment of enough concentrations of TAC in early stage of treatment, suggesting that we should consider induction of TAC only in NEX outpatients. Furthermore, drugs only slightly affected concentration of TAC in this study, suggesting that we can use TAC without any special attention to concomitant drugs.

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NEX patients rapidly gain higher TAC concentration than EX patients in early stage of treatment



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SAT0155 WHOLE BLOOD TRANSCRIPTIONAL CHANGES FOLLOWING SELECTIVE INHIBITION OF JANUS KINASE 1 (JAK1) BY FILGOTINIB IN MTX-NAÏVE ADULTS WITH MODERATELY-TO-SEVERELY ACTIVE RHEUMATOID ARTHRITIS (RA) (FINCH3)

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Background: Filgotinib (FIL), an oral selective JAK1 inhibitor, has shown efficacy and safety in multiple phase 3 studies in adults with moderately-to-severely active rheumatoid arthritis (RA). We have previously described the molecular response to FIL in large-scale RNA sequencing studies of gene expression in other RA populations[1-3] and conducted a similar study in methotrexate (MTX)-naïve RA patients (pts) (FINCH3).

Objectives: Identify gene transcripts and biological pathways associated with RA and those altered in response to FIL treatment.

Methods: MTX-naïve RA pts who were enrolled in FINCH3 (ClinicalTrials.gov NCT02886728) received a stable dose of MTX with placebo (PBO+MTX), FIL 200mg alone (FIL 200mg monotherapy), or one of two doses of FIL once daily (QD) together with MTX (FIL 100mg+MTX, FIL 200mg+MTX). Whole blood samples were collected from pts using PAXgene tubes at baseline, week 4,

week 12, and week 24. RNA from these samples was extracted and sequenced on the Illumina HiSeq 2500 platform following globin RNA depletion. Correlations between baseline gene expression and disease measurements were performed using Spearman's rank partial correlation to account for covariates. Differentially expressed genes (DEGs) were identified using voom-limma. Biological pathway analyses were performed on v6.1 of the Molecular Signature Database using single sample gene set enrichment analysis (GSEA) with the focus on immune signaling pathways from the Kyoto Encyclopedia of Genes and Genomes (KEGG). A false-discovery rate of 5% was applied for all analyses.

Results: Differential gene expression analyses comparing baseline samples with after-treatment samples revealed rapid onset of transcriptional changes in FIL-treated pts, most notably for the two FIL 200mg arms. Fewer DEGs were observed at all timepoints in PBO+MTX treated patients with a peak number at week 24, an observation consistent with the clinical response kinetics of MTX.[4] Up to 3x as many significant DEGs were observed in the FIL 200mg+MTX arm compared to the FIL 100mg+MTX arm, a finding consistent with the superior clinical efficacy of the FIL 200mg dosage. As with other FIL clinical trial RNA-seq studies and consistent with the selective MoA of FIL, JAK-STAT pathway-induced genes SOCS2 and CISH were significantly downregulated across FIL treatment arms and timepoints, but not for PBO+MTX. RA disease activity-associated genes[2-3] FAM20A and METTL7B were significantly reduced at all timepoints in FIL-treated pts, but only at week 24 in PBO+MTX pts. While no significant changes in KEGG immune signaling pathways were observed in the PBO+MTX arm, a dose-dependent effect on pathway modulation was observed in the FIL arms, including reductions in JAK-STAT, toll-like receptor, chemokine, and RIG-I like receptor signaling.

Conclusion: More rapid and sustained changes of transcriptional activity in the whole blood transcriptional profile of RA pts after FIL treatment were found compared to PBO+MTX. Dose-dependent changes were observed in FIL-treated pts, most notably in the KEGG JAK-STAT signaling pathway. These observations confirm an inhibition of JAK-STAT signaling by FIL and are consistent with the observed clinical efficacy of FIL in these pts.

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SAT0156

EFFECTIVE OF BARICITINIB ON RADIOGRAPHIC PROGRESSION OF STRUCTURAL JOINT DAMAGE AT 48 WEEKS IN PATIENTS WITH RHEUMATOID ARTHRITIS IN REAL-WORLD MULTICENTER CLINICAL DATA

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Background: Baricitinib (bari) is an oral Janus kinase 1 (JAK1)/JAK2 selective inhibitor that has demonstrated good efficacy in patients with rheumatoid arthritis (RA) and adequate response to conventional synthetic (cs) DMARDs in some clinical trials [1,2]. We report the efficacy and safety of bari within 24 weeks in real-world clinical data at EULAR2019.

Objectives: To evaluate the radiographic progression of structural joint damage at 48 weeks in Japanese patients with RA in real-world multicenter clinical data.

Methods: We included 53 Japanese patients with RA who showed an inadequate response to csDMARDs or biologic (b) DMARDs. Patients were scheduled to receive a once-daily dose of 4 or 2 mg/day bari as monotherapy or in combination with other csDMARDs. We divided the patients into two groups: those treated with 2 mg/day of bari (2mg-group; n = 27) and those treated with 4 mg/day of bari (4-mg group; n = 26) throughout the observation period. Patients were allowed to decrease their predonisolone and csDMARDs combined with bari treatment if their disease activity improved. First, we evaluated changes in CDAI and HAQ-DI after 48 weeks. Second, we evaluated the change in the van der Heijdge modified total sharp score (ΔmTSS), erosion score (ΔERN), and joint space narrowing score (ΔJSN). In addition, we assessed predictors for suppression of joint destruction at 48 weeks after bari treatment.

Results: The baseline characteristics of the patients were as summarized in Table 1. There were no significant differences in any items. CDAI scores significantly improved 4 weeks after the treatment. This tendency continued until the final evaluation (Table 2). At 48 weeks, remission and low disease activity rates were 37.0% and 74.1% in the 2-mg group and 38.4% and 76.9% in the 4-mg group, respectively. Structural remission (mTSS ≤ 0.5) was noted in 21 patients (80.8%) and 21 patients (77.8%) in 4-mg group and 2-mg group, respectively (Figure). Mean scores (ΔmTSS, ΔERN, and ΔJSN) of all patients in the 2-mg group and 4-mg groups were (0.26, 0.15, and 0.11), (0.30, 0.17, and 0.13) and (0.23, 0.13, and 0.10), respectively (Figure). There were no significant differences in ΔmTSS scores between the two groups. A matrix metalloproteinase-3 score within the standard value at 12 weeks after the treatment was associated with a predictor for suppression of joint destruction at 48 weeks (logistic regression analysis; odds ratio = 11.6, 95% confidence interval: 1.5–112.4, P = 0.020).

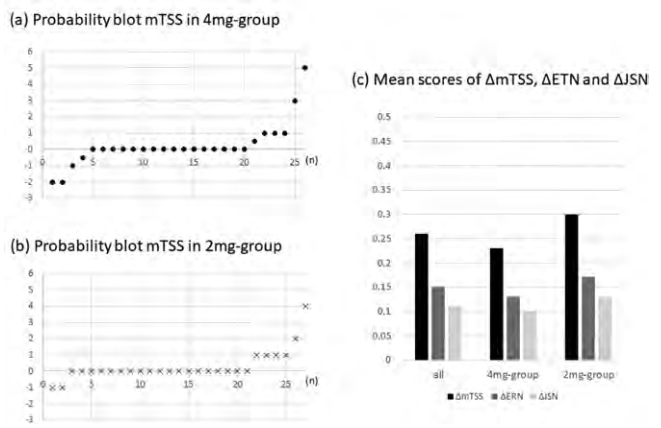
Table 1. Characteristics of patients at baricitinib initiation

	2mg-group (n=27)	4mg-group (n=26)	p-value
Age (years)	69.1 (12.0)	65.6 (10.3)	0.20
Gender, female, n (%)	19 (73.1)	23 (85.2)	0.28
Disease duration (years),	9.7 (10.4)	5.7 (7.4)	0.23
Prior use of biologics, (0/1/2/3)	(18/6/2/1)	(18/2/5/1)	------
MTX (mg/week),	4.5 (3.7)	6.5 (4.29)	0.08
PSL (mg/day)	1.0 (1.9)	1.2 (1.8)	0.49
RF, U/ml	254 (372)	134 (222)	0.21
ACPA, U/m	152 (176)	133 (301)	0.45
MMP-3	196 (220)	215 (221)	0.43

Table 2. Serial change of clinical assessment

2mg-group	Baseline	4 week	12 week	24 week	48 week
CDAI	22.5 (9.2)	7.4 (7.7)	6.7 (6.9)	6.9 (6.8)	6.9 (6.8)
HAQ-DI	0.88 (0.51)	0.45 (0.47)	0.53 (0.58)	0.56 (0.56)	0.56 (0.56)
MMP-3	196 (221)	98.9 (62.2)	115 (164)	106 (78)	106 (78)
4mg-group	Baseline	4 week	12 week	24 week	48 week
CDAI	24.4 (9.7)	9.4 (5.7)	8.6 (6.3)	6.7 (8.6)	6.8 (8.6)
HAQ-DI	1.01 (0.51)	0.58 (0.48)	0.54 (0.60)	0.45 (0.49)	0.44 (0.45)
MMP-3	216 (222)	99 (62)	101 (123)	89 (72)	95 (81)

Figure



Conclusion: The data showed that bari has a favorable effect on the radiographic progression of structural joint damage regardless of its dose in a real-world clinical setting. In consideration of the risk/benefit balance, we suggest that the dose of bari could be reduced in patients with favorable disease activity.

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Disclosure of Interests: Eiji Torikai: None declared, Yuji Hirano Speakers bureau: Tanabe-Mitsubishi, Pfizer, Eisai, Abbie, Chugai, Bristol-Meyers, Jansen, Astellas, UCB, Eli-Lilly, Asahikasei, Daiichi-Sankyo, Amgen, Daisuke Suzuki: None declared, Yasuhide Kanayama: None declared
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SAT0157 NINTEDANIB DOSE ADJUSTMENTS AND ADVERSE EVENTS IN PATIENTS WITH PROGRESSIVE AUTOIMMUNE DISEASE-RELATED INTERSTITIAL LUNG DISEASES IN THE INBUILD TRIAL

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Background: In the INBUILD trial in patients with progressive fibrosing ILDs, the adverse event (AE) profile of nintedanib was characterised predominantly by gastrointestinal AEs. Dose adjustments were used to manage AEs.
Objectives: Assess AEs and dose adjustments in patients with autoimmune disease-related ILDs in the INBUILD trial.
Methods: Patients with progressive fibrosing ILDs other than idiopathic pulmonary fibrosis were randomised to nintedanib 150 mg bid or placebo. Dose reductions to 100 mg bid and treatment interruptions were permitted to manage AEs. AEs over 52 weeks of treatment (or 28 days after last trial drug intake for patients who discontinued drug before week 52) were assessed in patients who received ≥1 dose of trial drug.
Results: Of 663 patients in the INBUILD trial, 170 (82 nintedanib, 88 placebo) had autoimmune disease-related ILDs (89 RA-ILD, 39 SSc-ILD, 19 MCTD-ILD, 23 other autoimmune ILDs). In the nintedanib and placebo groups of patients with autoimmune disease-related ILDs, respectively, over 52 weeks, the proportions of patients with ≥1 dose reduction were 28.0% and 3.4%, with ≥1 treatment interruption were 31.7% and 10.2%, and with ≥1 dose reduction and/or treatment interruption were 40.2% and 12.5% (Table). Dose intensity (amount of drug administered divided by amount that would have been received had 150 mg bid been administered over 52 weeks or until permanent treatment discontinuation) was >90% in 80.5% of patients in the nintedanib group and 95.5% in the placebo group. AEs led to permanent treatment discontinuation in 17.1% and 10.2% of patients treated with nintedanib and placebo, respectively. Diarrhoea was the most common AE, reported in 63.4% and 27.3% of patients in the nintedanib and placebo groups, respectively. Diarrhoea AEs led to dose reduction, treatment interruption and permanent treatment discontinuation in 7.3%, 9.8% and 4.9% of patients in the nintedanib group, compared with 0%, 1.1% and 1.1% of patients in the placebo group, respectively. Of the nintedanib-treated patients who experienced ≥1 diarrhoea AE, 80.8% experienced 1 or 2 events and 76.9% experienced events that were mild at worst (Common Terminology Criteria for Adverse Events [CTCAE] grade 1).
Conclusion: In the INBUILD trial, management of AEs via dose adjustments enabled most patients with autoimmune disease-related ILDs to remain on treatment for 52 weeks. Diarrhoea was the AE that most commonly led to dose adjustment.

Table

	Nintedanib (n=82)	Placebo (n=88)
Patients with ≥1 dose reduction or treatment interruption	33 (40.2)	11 (12.5)
Patients with ≥1 dose reduction	23 (28.0)	3 (3.4)
Total number of dose reductions	25	3
Patients with ≥1 dose re-escalation after dose reduction	5 (6.1)	2 (2.3)
Patients with ≥1 treatment interruption	26 (31.7)	9 (10.2)
Total number of treatment interruptions	32	11
Total duration of treatment interruptions, days, mean (SD)	20.1 (15.1)	19.3 (20.7)

Data are n (%) of patients unless otherwise indicated.

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SAT0158 EFFICACY AND SAFETY OF FILGOTINIB IN METHOTREXATE-NAÏVE PATIENTS WITH RHEUMATOID ARTHRITIS: FINCH 3 52-WEEK RESULTS

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Background: Filgotinib (FIL) is a potent, selective JAK 1 inhibitor. FINCH 3 assessed FIL efficacy and safety in methotrexate (MTX)-naïve patients (pts) with rheumatoid arthritis (RA); week (W)24 primary outcome results were previously presented.[1]
Objectives: To report FINCH 3 (NCT02886728) results through W52.
Methods: This global, phase 3, double-blind, active-controlled study randomised MTX-naïve pts with moderately to severely active RA 2:1:1:2 to oral FIL 200 mg once daily + MTX ≤20 mg weekly, FIL 100 mg + MTX, FIL 200 mg monotherapy (mono) + placebo (PBO), or PBO + MTX up to W52. Comparisons at W52 were not adjusted for multiplicity. Safety was assessed from adverse events and laboratory abnormalities.
Results: Of 1249 treated pts, 975 received study drug through W52. FIL efficacy was sustained up to W52. Treatment with FIL + MTX or FIL mono increased proportions of pts achieving ACR20/50/70 and clinical disease remission by DAS28(CRP) <2.6 (FIL 200 mg + MTX, 53%; FIL mono, 46%), CDAI, SDAI, and Boolean criteria; improved HAQ-DI; and halted radiographic progression vs MTX alone (Table 1 and **Figure**). Safety was consistent with W24 data (Table 2).

Table 1. Efficacy outcomes at week 52

	FIL 200 mg + MTX (n = 416)	FIL 100 mg + MTX (n = 207)	FIL 200 mg (n = 210)	MTX (n = 416)
ACR20, %	75.0***	73.4**	74.8***	61.8
ACR50, %	62.3***	59.4**	61.4**	48.3
ACR70, %	47.8***	40.1*	45.2***	29.8
mTSS[a]	0.21***	0.27*	0.23**	0.74
HAQ-DI[b]	−1.00***	−0.97	−0.95*	−0.88

[a]Least-squares mean change from baseline.
[b]Mean change from baseline.
*, p <0.05; **, p <0.01; ***, p <0.001 vs MTX alone; not adjusted for multiplicity.
FIL, filgotinib; mTSS, van der Heijde modified total Sharp score; MTX, methotrexate.

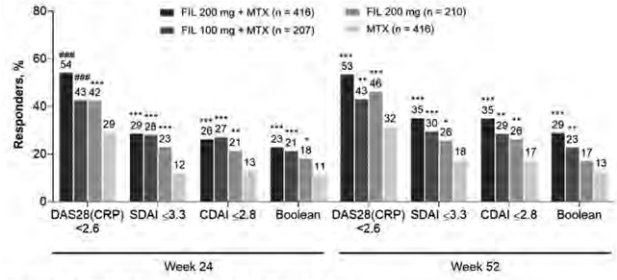
Table 2. Safety outcomes through week 52

Event, n (%)	FIL 200 mg + MTX (n = 416)	FIL 100 mg + MTX (n = 207)	FIL 200 mg (n = 210)	MTX (n = 416)
All AEs	318 (76.4)	164 (79.2)	143 (68.1)	305 (73.3)
Serious AEs	26 (6.3)	13 (6.3)	17 (8.1)	28 (6.7)
Infection	148 (35.6)	76 (36.7)	75 (35.7)	157 (37.7)
Serious infection	5 (1.2)	3 (1.4)	5 (2.4)	8 (1.9)
Herpes zoster	6 (1.4)	3 (1.4)	4 (1.9)	4 (1.0)
VTE	0	0	0	4 (1.0)
MACE (adjudicated)	4 (1.0)	1 (0.5)	2 (1.0)	2 (0.5)
Malignancy[a]	1 (0.2)	0	0	4 (1.0)
NMSC	2 (0.5)	0	0	1 (0.2)
Death	3 (0.7)[b]	1 (0.5)[c]	0	0

[a]Excluding NMSC.
[b]1 lupus cardiomyopathy, 1 atypical interstitial pneumonia, 1 non–treatment-emergent cardiovascular death.
[c]Dissecting cerebral and vertebral aneurysm.
AE, adverse event; FIL, filgotinib; MACE, major adverse cardiovascular event; MTX, methotrexate; NMSC, nonmelanoma skin cancer; VTE, venous thromboembolism.

Conclusion: Efficacy of FIL 200 mg + MTX, FIL 100 mg + MTX, and FIL 200 mg mono was sustained through W52, with faster onset[1] and consistently numerically greater efficacy for FIL 200 vs 100 mg. No new safety signals were observed.

Figure. Patients in clinical remission at week 52



###, p <0.001 vs MTX alone adjusted for multiplicity.
*, p <0.05; **, p <0.01; ***, p <0.001 vs MTX alone; not adjusted for multiplicity.
CDAI, Clinical Disease Activity Index; DAS28(CRP), Disease Activity Score in 28 joints with C-reactive protein; FIL, filgotinib; MTX, methotrexate; SDAI, Simplified Disease Activity Index.

References:
[1] Westhovens, et al. *Ann Rheum Dis.* 2019;78(Suppl2):259–60.
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SAT0159 ASSOCIATION BETWEEN JANUS KINASE INHIBITORS AND ALL-CAUSE MORTALITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: According to preliminary analysis of study A3921133, tofacitinib10 mg twice daily was associated with increased occurrence of all-cause mortality and pulmonary embolism compared with anti-tumor necrosis factor (anti-TNF), whereas 5 mg tofacitinib twice daily exhibited similar safety profile with anti-TNF.
Objectives: We aim to investigate the role of Janus kinase inhibitors (Jakinibs) in all-cause mortality among RA population via a meta-analysis of RCTs.
Methods: PubMed, Embase and Cochrane Library were systemically searched for RCTs reporting adverse events in RA patients receiving Jakinibs, from inception to October 2018. Absolute risk differences (RD) and 95% confidence interval (CI) were used as an effect measure using the Mantel-Haenszel fixed-effect method.
Results: A total of 31 RCTs randomizing 13,065 patients met the inclusion criteria. During the placebo-controlled phase, there were 16 and 6 deaths in Jakinibs and placebo respectively, accompanied by a numerically higher absolute incidence mortality rate in Jakinibs than in placebo (0.651 vs. 0.531 per 100 patient-years). In direct pairwise comparisons, 2,194 and 2,246 patient-years of exposure in lower and higher Jakinibs reported a total of 19 deaths (10 with lower dose [0.456 per 100 patient-years] and 9 with higher dose [0.401 per 100 patient-years]). Compared with placebo, no significant difference was observed in tofacitinib (RD,0.01 events/person-year; 95% CI, -0.01 to 0.02; P =0.52); baricitinib (RD,-0.00 events/person-year; 95% CI, -0.01to 0.01; P =0.59); upadacitinib (RD,0.00 events/person-year; 95% CI, -0.02to 0.03; P =0.71); perficitinib (RD,0.00 events/person-year; 95% CI, -0.05 to 0.06; P =0.86); decernotinib (RD,0.02 events/person-year; 95% CI, -0.03 to 0.06; P =0.44); fligotinib (RD,0.00 events/person-year; 95% CI, -0.05 to 0.06; P=0.85). In pairwise comparisons, no dose-dependent impact of Jakinibs on all-cause mortality was not observed in tofacitinib (5mg vs. 10mg, bid), baricitinib (2mg vs. 4mg, qd) upadacitinib (15mg vs. 30mg, qd).
Conclusion: Compared with placebo, there was no significant difference in the all-cause mortality rate observed in patients receiving Jakinibs treatments, but post-marketing data in real-life setting are sorely needed to ascertain their safety in general population.
Large, prospective, well-designed studies are needed to explore the effects of such drugs on diabetes development in the RA patients with high-risk diabetes.
Disclosure of Interests: None declared
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SAT0160 EFFICACY AND SAFETY OF UPADACITINIB IN PATIENTS FROM CHINA, BRAZIL, AND SOUTH KOREA WITH RHEUMATOID ARTHRITIS WHO HAVE HAD INADEQUATE RESPONSE TO CONVENTIONAL SYNTHETIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS

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Background: Upadacitinib (UPA), an oral, selective JAK-1 inhibitor was effective in global ph 3 trials in rheumatoid arthritis (RA) patients with inadequate response (IR)/intolerance to csDMARDs and bDMARDs.
Objectives: This Phase 3, randomized, double-blind, placebo (PBO)-controlled study assessed the efficacy and safety of UPA in combination with csDMARDs in csDMARD-IR patients with RA from China, Brazil, and South Korea.
Methods: Patients were randomized 1:1 to receive UPA 15 mg once daily (QD) or PBO in combination with csDMARDs. The primary endpoint was ACR20 response at Week 12, using non-responder imputation.
Results: 338 patients were randomized, and 310 (91.7%) completed Week 12. At Week 12, statistically significantly more patients receiving UPA vs PBO achieved

Table 1. Efficacy endpoints at Week 12

Endpoint[a]	UPA 15 mg QD (n=169)	PBO (n=169)
Primary endpoint		
ACR20, %	71.6***	31.4
Secondary endpoints		
Δ DAS28(CRP)	-2.56***	-0.95
Δ HAQ-DI	-0.62***	-0.18
Δ SF-36 PCS	8.93[c]***	3.36[d]
DAS28(CRP) ≤3.2, %	46.2***	13.6
DAS28(CRP) <2.6, %	29.6***	5.3
CDAI ≤10, %	35.5***	11.2
ACR50, %[b]	40.8***	8.3
ACR70, %[b]	21.3***	3.6
ACR20 at Week 1, %[b]	25.4***	5.9

***p<0.001 vs PBO
[a]NRI for binary endpoints; ANCOVA with multiple imputation for DAS28(CRP) and HAQ-DI; mixed model repeated measures for other continuous endpoints
[b]Unranked secondary endpoint. [c]n=143. [d]n=149

the primary endpoint of ACR20 (71.6% vs 31.4%, p<0.001). UPA also demonstrated statistically significant improvements in all ranked secondary endpoints vs PBO at Week 12 (Table 1), including mean change in DAS28(CRP), HAQ-DI, and SF-36 PCS, and patients achieving DAS28(CRP) ≤3.2, DAS28(CRP) <2.6, and CDAI ≤10. Greater responses were also seen with UPA vs PBO for other key secondary endpoints including ACR50 and ACR70. Onset of UPA action was rapid with more patients on UPA achieving ACR20 by Week 1 (25.4% vs 5.9%, p<0.001). The frequency of AEs (61.5% vs 49.1%) and serious AEs (7.1% vs 3.0%) was higher with UPA vs PBO. The frequency of AEs of special interest was generally similar between UPA and PBO, with the exception of herpes zoster (1.8% vs 0.6%), hepatic disorders (9.5% vs 7.1%), neutropenia (3.0% vs 0%), and elevated creatine phosphokinase (1.8% vs 0.6%), which were higher with UPA. One case of breast cancer (on Day 1 of study) and one VTE (pulmonary embolism and deep vein thrombosis in a patient with history of deep vein thrombosis) were reported with UPA treatment.

Conclusion: Efficacy of UPA was demonstrated in this csDMARD-IR population from China, Brazil, and South Korea. The safety of UPA was comparable with the global Phase 3 program.

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SAT0161

THE ANALGESIC EFFECT OF TOFACITINIB MAY HAVE CLINICAL SIGNIFICANCE IN PATIENTS WITH RHEUMATOID ARTHRITIS. DATA FROM THE MOSCOW UNIFIED REGISTER OF ARTHRITIS (MUAR)

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Background: Some theoretical data suggest that the JAK-kinase blocker tofacitinib (TOFA) may have a direct analgesic effect.
Objectives: to evaluate the clinical significance of the analgesic effect in patients with rheumatoid arthritis (RA) in real clinical practice.
Methods: Hypothesis being tested: the analgesic effect of TOFA may be manifested by a decrease in the ratio of subjective to objective indicators of arthritis activity.
Data from RA patients receiving biologics (bDMARD) and/or TOFA and included in the MUAR register were analyzed. The tender joints count (TJC), the HAQ-DI functional ability index, and the RAPID3 disease activity index were considered as subjective estimates. The swollen joints count (SJC) and the level of CRP were treated as objective indicators. The estimation of quotients from the division of subjective indicators into objective ones in all combinations is made.

Table. Ratios of objective and subjective indicators during the treatment with tofacitinib and with tDMARDs therapy in general

Index	Unadjusted values		Identified confounders	Adjusted values (TOFA)	Significance of difference TOFA from average values
	TOFA	Average			
TJC / (SJC +1)	1,93 ± 2,40	2,40 ±2,78	Age, year of inclusion in registry	1,95 ± 0,45	0,014
HAQ/ (SJC +1)	0,78 ± 0,60	0,89 ± 0,64	Age, year of inclusion in registry, duration of RA, duration of treatment	0,583 ± 0,114	0,039
RAPID3 / (SJC +1)	6,69 ± 4,96	8,13 ± 5,36	Age, year of inclusion in registry, duration of treatment	6,75 ± 0,80	0,001
TJC / (CRP +1)*	1,15 ± 1,83	1,17 ± 1,73	Morning stiffness duration at the RA onset	1,15 ± 0,18	0,263
HAQ/ (CRP +1)*	0,38 ± 0,36	0,40 ± 0,41	Gender, RA duration	0,342 ± 0,04	0,123
RAPID3/(CRP +1)*	3,26 ± 2,74	3,78 ± 3,71	BMI, duration of treatment	3,47 ± 0,43	0,527

* - when calculating the indices, episodes of treatment with tocilizumab (n = 113) were excluded, CRP - level of C-reactive protein, mg/l; TJC – tender joints count, SJC – swollen joints count, TOFA – tofacitinib, RA – rheumatoid arthritis, BMI – body mass index.

Taking into account the observational nature of the study, we searched for confounders for each of these ratios. Comparison of the calculated indices during the treatment with various targeted DMARDs (tDMARDs) was made with an adjustment for the detected confounders.
Results: the analysis included 944 treatment episodes in 832 patients, including 93 episodes of TOFA treatment. The average age was 55.3 ± 12.4 years, women - 698 (83.9%), seropositive for RF -672 (80.8%). The analysis of the adjusted values showed that the ratios of the TJC, HAQ-DI and RAPID3 to the SJC during the treatment with TOFA was significantly lower than with tDMARDs on average. There were no significant differences in the ratios of objective indicators to the CRP level (Table).
Conclusion: the severity of subjective feelings and functional disorders in RA patients receiving TOFA may be less with the same level of objective signs of arthritis compared with bDMARDs.
Disclosure of Interests: Evgeniy Zhilyaev Speakers bureau: Novartis, UCB, Pfizer, Biocad, Abbvie, MSD, Roche, Galina Lukina Speakers bureau: Novartis, Pfizer, UCB, Abbvie, Biocad, MSD, Roche, Ekaterina Koltsova: None declared, Evgeniya Shmidt Speakers bureau: MSD, Novartis, Pfizer, Karine Lytkina Speakers bureau: Novartis, Eli Lilly, Pfizer, UCB, Abbvie, Biocad, MSD, Jonson&Jonson
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SATURDAY, 06 JUNE 2020

SLE, Sjögren's and APS - treatment

SAT0162

WITHDRAWAL OF LOW-DOSE STEROIDS IN SYSTEMIC LUPUS ERYTHEMATOSUS IN REMISSION: PREDICTORS OF FLARES AND DIFFERENCE IN OUTCOMES IN SEROLOGICALLY ACTIVE CLINICALLY QUIESCENT PATIENTS

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Background: According to the recent recommendations for Systemic Lupus Erythematosus (SLE), a progressive tapering until withdrawal of glucocorticoids (GC) is considered one of the main goals of SLE management (1). However, which patient may be a candidate for safe GC withdrawal has not been determined yet and a proportion of patients are kept on long-term low-dose prednisone despite clinical remission.
Objectives: to evaluate the rate of low-dose GC withdrawal in SLE patients in remission and to identify predictors of flares.
Methods: Eligible patients were SLE patients according to the ACR criteria (2) who were in prolonged clinical remission defined by a cSLEDAI=0 for at least 2 years and on a stable SLE treatment (immunosuppressive drugs and/

or hydroxychloroquine (HCQ) and daily 5 mg prednisone). A SACQ period was defined as at least 1-year period with persistent serologic activity without clinical manifestations. Flares were defined by SELENA-SLEDAI Flare Index (3). Damage was assessed by SLICC damage index (SDI). Data were compared by the unpaired student's t test or chi-squared test as appropriate. Predictors of flares after GC withdrawal were analyzed by Cox regression.

Results: Out of 246 SLE patients registered in the Naples Lupus Clinic database, 132 eligible patients were identified. Among them, we selected 57 (43%) patients in whom a GC withdrawal was attempted. 75 (57%) patients were in the prednisone maintenance group.

There were no significant differences between the two treatment groups (table 1). The proportion of patients experiencing a flare was not significantly lower in the maintenance group than in the withdrawal group (15/75 vs 16/57; p=0.28). Moreover, the proportion of patients who had an increase in the SDI at the end of follow up was similar between the two groups (14/75 vs 8/57; p=0.48). However, among the withdrawal group, the rate of flares was significantly higher in SACQ patients (10/22 vs 6/35; p=0.02), while the majority of serologically inactive patients (82%) successfully stopped GCs without subsequent flares. At Cox regression analysis (Table 2), duration of HCQ therapy and >4 year remission at withdrawal were protective factors, while a SACQ disease and history of lupus nephritis (LN) increased the risk of disease flare.

Table 1. Baseline characteristics of 132 patients at study entry

Characteristics	Withdrawal group (n=57)	Maintenance group (n=75)	p-value
Female, no. (%)	54 (94)	70 (93)	0.73
Age, years	26.7±10.1	28.5±11.7	0.37
Disease duration, years	8.5±2.9	9.1±12.9	0.73
History of lupus nephritis, no. (%)	13(22)	22(29)	
SDI score	0.40±0.7	0.57±0.8	0.26
Immunosuppressive drugs, no. (%)	31 (54)	33(44)	0.16
HCQ, no. (%)	52 (91)	66 (88)	0.06
Low C3, no. (%)	28 (49)	41(54)	0.52
Increased dsDNA Ab, no. (%)	11 (19)	19 (25)	0.41

Table 2. Factors predicting lupus flares during follow-up at Cox regression analysis

Variables	HR	95% CI	p value
SACQ	2.99	1.08 – 8.25	0.03
Age	0.97	0.93 – 1.02	0.29
Disease duration	0.99	0.94 – 1.04	0.84
History of LN	3.38	1.22-9.33	0.01
SDI score	1.13	0.63 – 2.01	0.66
Immunosuppressive drugs	2.39	0.86 – 6.62	0.09
HCQ, ever	2.92	0.43 – 35.2	0.95
Duration of HCQ	0.84	0.72 – 0.98	0.03
5years remission	0.12	0.04 – 0.39	0.0003

Conclusion: GC withdrawal is an achievable target in SLE and may be attempted in patients in complete remission. In SACQ patients, maintenance of 5mg prednisone is superior to its withdrawal in order to prevent flares. Long-term HCQ therapy and prolonged remission can significantly reduce the risk of disease relapse after GC withdrawal.

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SAT0163

IMMUNOSUPPRESSANT WITHDRAWAL AFTER REMISSION ACHIEVEMENT IN LUPUS NEPHRITIS: EFFECT ON FLARE OCCURRENCE

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Background: Whether and when immunosuppressive therapy may be safely withdrawn in patients with lupus nephritis (LN) is still poorly defined. Indeed, there is no clear agreement about the optimal duration of maintenance treatment.

Objectives: We aimed at assessing the rate and predictors of flare after IS withdrawal in patients with LN in remission.

Methods: Patients with systemic lupus erythematosus (SLE) (ACR criteria) and biopsy-proven LN diagnosed between 1990 and 2019, ever treated with IS and currently in follow-up were considered. IS discontinuation was defined as the complete withdrawal of any immunosuppressive drug in patients in remission. Remission was defined as normal serum creatinine, proteinuria <0.5 g/24h, inactive urine sediment, and no extra-renal SLE activity (clinical SLE Disease Activity Index [c-SLEDAI]-2K=0) on a stable immunosuppressive and/or antimalarial therapy and/or on prednisone ≤5 mg/day. Flares were defined according to SLEDAI Flare Index; renal flare was defined as an increase of proteinuria >0.5 g/24h requiring an increase in corticosteroid therapy or the reintroduction of IS. Predictors of a subsequent flare were analyzed by multivariate logistic regression analysis.

Results: Out of 456 SLE patients regularly followed-up, 206 (45.1%) had LN and were considered in our study. Eighty-three patients (40.3%) discontinued IS after remission achievement (Table 1). After stopping therapy, patients were followed for a mean±SD of 99±77 months (range 12-378). Nineteen patients (22.8%) developed a flare after IS discontinuation, after a mean±SD follow-up of 78±68 months (range 7-312), and were re-treated; among them, 6 patients (7.2%) experienced a renal and 13 (15.6%) an extra-renal flare. Compared to patients who flared, patients in persistent IS-free remission had longer remission before IS withdrawal (51.2±31.5 vs. 29.3±16.5 months, p<0.001), and continued antimalarials after IS discontinuation (p=0.005). No differences in flare occurrence according to the type of IS discontinued were found. At multivariate analysis, therapy with antimalarials was the strongest protective factor against disease flare (OR 0.06, 95% CI 0.11-0.41, p=0.004) (Table 2). At last follow-up, mean±SD SLEDAI-2K was 3.1±2.8 and 1.5±1.6 in patients who experienced or not a flare after IS discontinuation, respectively (p=0.058), Indeed, 10/19 patients (52.5%) who developed a flare re-achieved remission.

Table 1. Characteristics of 83 patients with LN in remission who discontinued immunosuppressive therapy, overall and according to flare occurrence

	Total patients (83)	Patients with flare (19)	Patients without flare (64)	P value
Female, N(%)	72 (88.7)	16 (84.2)	56 (87.5)	ns
Age at 2019, years	43±11	39±11.5	45±10.4	0.049
SLE duration at 2019, years	18±9	16.7±9.0	18.6±8.6	ns
SLE duration at IS discontinuation, years	9.7±7.6	7.1±6.1	10.5±7.8	ns
Time to achieve remission, months	27±37	22.1±35.6	28.5±37.6	ns
Remission duration at IS discontinuation, months	46±30	29 ±16.5	51±31.5	<0.001
IS therapy duration, years	6.7±4.3	5.2±3.8	7.1±4.2	0.061
Anti dsDNA, N(%)	65 (78.3)	18 (95)	47 (73)	0.059
HCQ after IS discontinuation, N(%)	67 (80.7)	12 (63.1)	55 (85.9)	0.005

IS, immunosuppressant; HCQ, hydroxychloroquine

Table 2. Multivariate logistic regression: predictors of flare occurrence

Dependent variable: flare occurrence	OR	95% CI		p value
Number of ISs, ever	3.264	1.030-	10.342	0.044
HCQ therapy after IS discontinuation	0.096	0.014-	0.652	0.017
Remission duration at IS discontinuation	0.954	0.912-	0.997	0.037
Cyclophosphamide, ever	0.065	0.008-	0.548	0.012

IS, immunosuppressant; HCQ, hydroxychloroquine

Conclusion: Based on our experience, withdrawal of IS is feasible in selected patients with LN, i.e. patients who achieved stable remission and received maintenance therapy with antimalarials. Patients who experience new flares can re-achieve remission with an appropriate treatment.

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SAT0164

MC2-03 (CICLOSPORIN EYEDROPS) IMPROVES TEAR PRODUCTION IN SJÖGREN'S PATIENTS WITH MODERATE-TO-SEVERE KERATITIS: RESULTS FROM A PHASE 2B RANDOMIZED, CONTROLLED TRIAL

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Background: Sjögren Syndrome (SS) is a multifaceted disease with variable symptoms, but the SS associated keratoconjunctivitis is one of the most frequent disease manifestations of the syndrome and the manifestation that has the greatest impact on the quality of life for these patients.

Objectives: To report the clinical efficacy of MC2-03 eyedrops in Sjögren's patients with moderate-to-severe keratitis from a 6-month trial looking at the Schirmer score which assess the tear production by the lacrimal gland. A Schirmer score of ≤5mm/5 min is one of the criteria used in the 2016 final classification of ACR/EULAR to diagnose Sjögren`s syndrome.

Methods: The NORTHERN LIGHTS trial is a randomized, double masked, controlled multicentre European trial that assessed MC2-03 eyedrops (ciclosporin 0.03% and 0.06%) for the treatment of moderate-to-severe dry eye disease in 255 patients having corneal fluorescein staining score 3 or 4 at baseline. The Schirmer score (per 5 min) was assessed during this trial. A total of 66 patients (25.9%) with medical history of Sjögren's syndrome were randomized in the trial.

Results: Demographics and baseline disease characteristics were comparable between treatment arms: mean age 60.4 years, 90.9% were females (n=60) and the mean Schirmer score in the worst eye was ~3mm (2.8mm – 3.2mm, except for the vehicle, mean Schirmer score of 5.5mm).

The mean Schirmer score improved rapidly from baseline to month 1 for MC2-03 0.03% eye drops (+2.4mm) reaching statistical significance versus vehicle (-0.5mm, p=0.028) and lubricant therapy (-0.6mm, p=0.020). This improvement was maintained at month 6 where the change was +2.5mm for MC2-03 0.03% eye drops compared to -1.1mm for vehicle (p=0.028). Statistical significance was also achieved at Month 6 comparing the higher strength MC2-03 0.06% eye drops (+2.8mm) to vehicle (-1.1mm, p=0.005) and lubricant alone (-0.5mm, p=0.009).

Three in eleven (27.3%) Sjögren`s patients treated with MC2-03 0.03% eye drops improved from a diagnostically low Schirmer ≤5mm at baseline (10/12, 83.3% ≤5mm) to Schirmer >5mm at month 3 and month 6 (6/11, 54.5% ≤5mm), while on the other hand 1 in 14 (7.1%) patients worsened in the vehicle group. A similar response was seen for MC2-03 eye drops 0.06%.

For Sjögren´s patients with Schirmer ≤5mm at baseline, a greater proportion of patients improved ≥3mm at month 6 when treated with MC2-03 eye drops 0.03% (44.4%, 4/9) and 0.06% (53.8%, 7/13) compared to vehicle (0%, 0/9) and lubricant (7.7%, 1/12). At month 6, a statistically significantly higher proportion of patients achieved clinically meaningful improvements in both corneal staining (≥2 grades improvement) and Schirmer score (≥3mm/5 min) when treated with MC2-03 0.03% eye drops (45.5%, 5/11) compared to both vehicle (0%, 0/14, p=0.009) and lubricant (0%, 0/15, p= 0.007). A higher number of patients treated with MC2-03 0.06% was observed without statistical significance.

Conclusion: MC2-03 eye drops once daily rapidly increased tear production and further improved corneal staining in Sjögren´s patients with moderate to severe keratitis, which both are objectives included as diagnostic criteria for Sjögren's disease. MC2-03 eye drops were well tolerated with no unexpected safety findings.

Disclosure of Interests: : Frederic Gomez Consultant of: MC2 Therapeutics, Morten Præstegaard Employee of: MC2 Therapeutics, Johan Selmer Employee of: MC2 Therapeutics, Jutta Horwath-Winter Consultant of: CromaPharma, Omnivision, MC2 Therapeutics, Speakers bureau: Allergan, Bausch&Lomb, Cromapharma, Ursapharma, Thea, TRB-Chemedica, Santen, Maite Sainz de la Maza: None declared, Steffen Heegaard Consultant of: Sanofi, MC2 Therapeutics, Speakers bureau: Santen, Sanofi, Thea, Leo

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SAT0165

PRECLINICAL AND CLINICAL CHARACTERIZATION OF CENERIMOD, A POTENT, SELECTIVE, AND ORALLY ACTIVE SPHINGOSINE-1-PHOSPHATE RECEPTOR 1 MODULATOR IN SLE

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Background: SLE is an autoimmune disease characterized by aberrant lymphocyte activation and autoantibody production. In SLE, autoreactive lymphocytes migrate from lymphoid organs into the blood, and subsequently into tissue. This leads to systemic and multiorgan inflammation and pathology resulting in significant morbidity and mortality. Lymphocyte migration is a tightly controlled process driven by chemokine gradients. The chemotactic gradient across the vascular barrier established by sphingosine-1-phosphate (S1P) orchestrates egress of lymphocytes out of peripheral lymphoid organs into the blood. Cenerimod is a potent, selective, and orally active S1P receptor 1 ($S1P_1$) receptor modulator that induces receptor internalization and thereby prevents lymphocyte egress from lymphoid organs into the blood [1].

Objectives: In-depth preclinical and clinical characterization of cenerimod in modulating SLE.

Methods: Lymphocytes from patients with SLE and healthy subjects were assessed for cenerimod-induced $S1P_1$ receptor internalization. Efficacy of cenerimod was evaluated in the MRL/lpr lupus mouse model. In a 12-week phase 2 clinical trial in patients with SLE treated with multiple doses of cenerimod (NCT02472795), lymphocyte subsets and inflammatory biomarkers were characterized.

Results: Cenerimod was potent and efficacious at inducing $S1P_1$ receptor internalization in T and B lymphocytes with an EC_{50} of 15 nM in both healthy subjects and patients with SLE. In lupus-like MRL/lpr mice treated with cenerimod, circulating T and B lymphocytes were reduced, which resulted in reduced immune infiltrates into tissue, reduced autoantibody production and inflammation, decreased proteinuria, and increased survival. In patients with SLE treated with cenerimod for 12 weeks, a dose-dependent reduction of circulating T cells (95%), B cells (90%), and antibody-secreting cells (85%) was evident. Furthermore, a reduction in anti-dsDNA antibodies and IFN-α, associated with an inflammatory phenotype, was observed.

Conclusion: Cenerimod was potent and efficacious in reducing $S1P_1$ receptor surface expression on lymphocytes *in vitro*, and in reducing circulating T and B lymphocyte populations, including antibody-secreting cells, and in decreasing inflammatory biomarkers in patients with SLE *in vivo*. Furthermore, cenerimod significantly ameliorated systemic and organ-specific autoimmunity in a mouse model of SLE. These results support the further investigation of the clinical efficacy and safety of cenerimod in the ongoing phase 2b clinical trial (NCT03742037).

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Disclosure of Interests: Daniel Strasser Shareholder of: Idorsia options/shares, Employee of: Idorsia employee, Estelle Gerossier Shareholder of: Idorsia options/shares, Employee of: Idorsia employee, Virginie Sippel Shareholder of: Idorsia options/shares, Employee of: Idorsia employee, Ursula Grieder Shareholder of: Idorsia options/shares, Employee of: Idorsia, Andrea Kieninger: None declared, Gabin Pierlot Shareholder of: Idorsia options/shares, Employee of: Idorsia employee, Hervé Farine Shareholder of: Idorsia options/shares, Employee of: Idorsia employee, Paulina Kulig Shareholder of: Idorsia options/shares, Employee of: Idorsia employee, Marcel Keller Shareholder of: Idorsia options/shares, Employee of: Idorsia employee, Sylvie Froidevaux Shareholder of: Idorsia options/shares, Employee of: Idorsia employee, Marten Trendelenburg Grant/research support from: Idorsia Pharmaceuticals Ltd, Novartis Institute of Biomedical Research, F. Hoffmann-La Roche Ltd, Marianne Martinic Shareholder of: Idorsia options/shares, Employee of: Idorsia employee, Mark Murphy Shareholder of: Idorsia shares and stock options, Employee of: Idorsia employee

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SAT0166

BIOMARKERS OF B-CELL DEPLETION AND RESPONSE IN A RANDOMIZED, CONTROLLED TRIAL OF OBINUTUZUMAB FOR PROLIFERATIVE LUPUS NEPHRITIS

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Background: Incomplete B-cell and plasmablast depletion, as measured using highly sensitive flow cytometry (HSFC), is associated with lower response rates following rituximab in SLE [1]. Enhanced B-cell depletion with the type II anti-CD20 mAb obinutuzumab resulted in increased renal responses in proliferative lupus nephritis (LN) in the NOBILITY trial (NCT02550652) and will be further evaluated in the Phase 3 REGENCY trial (NCT04221477).

Objectives: To measure peripheral B-cells, B-cell subsets (naïve, memory and plasmablast) and B-cell activating factor (BAFF) levels and to assess associations between B-cell depletion and renal response in LN patients in a clinical trial of obinutuzumab.

Methods: 126 patients with active Class III/IV LN were randomized to obinutuzumab or placebo infusions in combination with mycophenolate and glucocorticoids. Peripheral B-cells were measured using a HSFC method with a lower limit of quantitation of 0.441 cells/μL. Serum levels of BAFF were evaluated using ELISA. Sustained depletion was defined by total B-cells below the limit of detection at both weeks 24 and 52. Renal response definitions from Phase 2 NOBILITY and Phase 3 REGENCY trials were used.

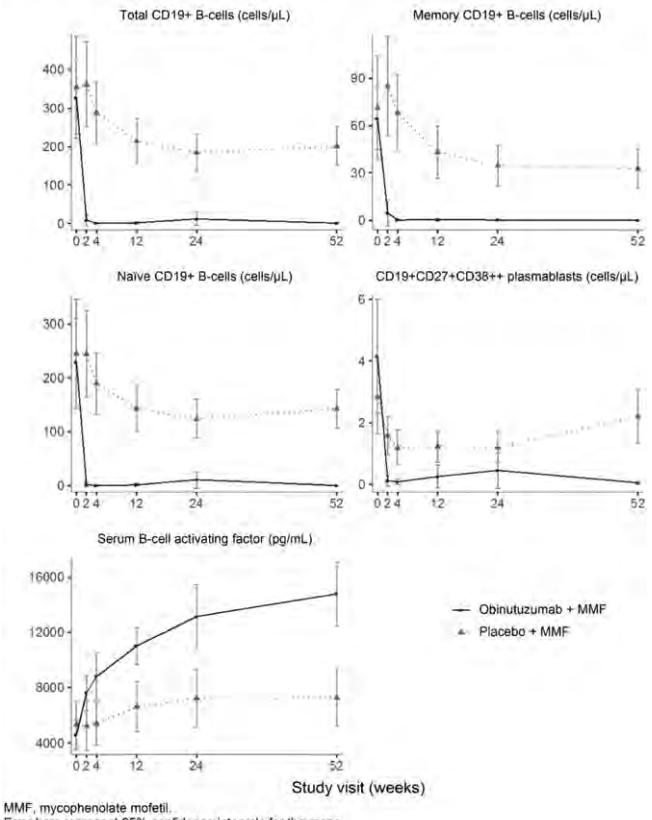
Results: Obinutuzumab resulted in rapid and complete depletion of total B-cells, memory and naïve B-cells, and plasmablasts from peripheral blood, with 88% of obinutuzumab patients depleted to < 0.441 total B-cells/μL at week 2 (Figure). Mean serum BAFF increased from 4,585 pg/mL at baseline to 14,601 pg/mL at week 52 in the obinutuzumab group. Sustained B-cell depletion was achieved in 32/52 (62%) of patients with complete data and was associated with higher renal response rate at week 76 (Table), although patients who achieved sustained depletion also had lower baseline proteinuria and serum creatinine.

Conclusion: Obinutuzumab, a type II anti-CD20 mAb, mediated rapid, complete and sustained depletion of peripheral B-cells and plasmablasts and large increases in serum BAFF. Similar to previous reports, sustained B-cell depletion was associated with increased renal response though there may be confounding factors. REGENCY is being conducted to further evaluate the therapeutic hypothesis with obinutuzumab in LN.

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Figure. Mean levels of selected biomarkers over time by treatment group



MMF, mycophenolate mofetil.
Error bars represent 95% confidence intervals for the mean.

Table. Data from NOBILITY at week 76 by depletion status at weeks 24 and 52

Definition of response	Obinutuzumab sustained depletion (N = 32)[a]	Obinutuzumab detectable B-cells (N = 20)[a]	Placebo group detectable B-cells (N = 62)
NOBILITY complete response UPCR < 0.5, SCr ≤ ULN and not increased > 15% from baseline SCr, and < 10 RBC/hpf without casts	50%**	35%*	18%
NOBILITY overall response CRR or ≥ 50% reduction in UPCRb with SCr not increased > 15% from baseline and urinary RBCs not increased > 50% from baseline	66%***	45%*	29%
REGENCY complete response UPCR < 0.5, SCr ≤ ULN and not increased > 25% from baseline SCr	69%**	45%	31%
REGENCY overall response CRR or ≥ 50% reduction in UPCRb with SCr not increased > 25% from baseline	84%***	55%	50%

* P < 0.2 vs. placebo group.
** P < 0.05 vs. placebo group.
*** P < 0.001 vs. placebo group.
[a] Eleven patients in the obinutuzumab group with insufficient data to determine depletion status were excluded.
[b] ≥ 50% reduction in UPCR to a value < 1 (< 3 if the baseline UPCR was ≥ 3).

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SAT0167

RACIAL DIFFERENCES IN THE IMPACT OF HYDROXYCHLOROQUINE ON IMMUNOLOGIC MARKERS IN SLE PATIENTS

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Background: In patients with Systemic Lupus Erythematosus (SLE), Hydroxychloroquine (HCQ) treatment has been associated with reduced disease activity, lower rates of certain forms of organ damage, and improved survival[1].

Objectives: To gain insight into the mechanisms involved, we examined the impact of HCQ treatment on immunologic biomarkers that have been associated with higher rates of organ damage. These include lupus anticoagulant, anti-dsDNA, low complement, and anticardiolipins (aCL).

Methods: We analyzed retrospective data on more than 56,000 quarterly clinic visits from more than 1000 patients in a large American clinical cohort of SLE patients. Patients visits were classified as "on HCQ" if they reported taking HCQ at that visit and at the previous visit. Patient visits were classified as "off HCQ" if they reported not taking HCQ at that visit and at the previous visit. For each patient, visits on and off HCQ were compared with respect to the rates of biomarker positivity. These comparisons were summarized across patients using using conditional logistic regression controlling for age.

Results: Table 1 shows the results of our analyses. While on HCQ, the odds of being positive was significantly reduced for each biomarker: Lupus Anticoagulant (OR= 0.65), antidsDNA (OR=0.82), Low Complement (OR=.71), aCL IgG (OR=0.26), and aCL IgM (OR=0.45). However, there was a substantial difference between Caucasian Americans (CAs)and African Americans (AAs) with respect to the impact of HCQ. Notably, HCQ was associated with a 62% reduction in the odds of lupus anticoagulant among CAs, but no association was observed among AAs.

In addition, HCQ was associated with a 34% reduction in antidsDNA among AAs, but no significant reduction among CAs.

Table. Impact of treatment with HCQ on the odds of being positive for immunologic markers

Clinical marker	All Patients (n=951)		Caucasian Americans (n=462)		African Americans (n=409)	
	Odds Ratio (95% CI)	P-value	Odds Ratio (95% CI)	P-value	Odds Ratio (95% CI)	P-value
Confirmed Lupus Anticoagulant	0.65 (0.50, 0.85)	0.0019	0.38[1] (0.24, 0.58)	<0.0001	1.05[1] (0.69, 1.60)	0.82
antidsDNA (% positive)	0.82 (0.73, 0.91)	0.0005	0.90[1] (0.76, 1.06)	0.19	0.66[1] (0.56, 0.79)	<0.0001
Low complement	0.71 (0.64, 0.79)	<0.0001	0.71 (0.61, 0.83)	<0.0001	0.73 (0.62 0.86)	<0.0001
aCL IGG (% pos)[3]	0.26 (0.17, 0.39)	<0.0001	0.16[1] (0.09, 0.30)	<0.0001	0.53[1] (0.27, 1.05)	0.069
aCL IGM (% pos)[3]	0.45 (0.29, 0.68)	0.0002	0.17[1] (0.09, 0.32)	<0.0001	2.45[1] (1.09, 5.55)	0.032

[1] P-value for difference between Caucasian and African Americans < 0.0001.

Conclusion: HCQ use was associated with a substantial decline in the rates of positive immunologic biomarkers in SLE patients. The different impact of HCQ in different races suggests the existence of racial differences in SLE subtypes and may indicate the need for different treatment strategies.

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Disclosure of Interests: Laurence Magder: None declared, Daniel Goldman: None declared, Michelle A Petri Grant/research support from: GSK, Eli Lilly and Company, Consultant of: Eli Lilly and Company

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SAT0168 ONLY ONE THIRD OF REAL WORLD LUPUS PATIENTS MEET ELIGIBILITY CRITERIA FOR CLINICAL TRIALS: IMPLICATIONS FOR TRIAL VALIDITY AND GENERALISABILITY

S. Dyball[1], S. Collinson[2], E. Sutton[1], E. Mccarthy[2], B. Parker[1,2], I. N. Bruce[1,2]on behalf of British Isles Lupus Assessment Group Biologics Register (BILAG-BR) consortium. [1]*The University of Manchester, Manchester, United Kingdom*; [2]*The Kellgren Centre of Rheumatology, Manchester, United Kingdom*

Background: Despite unprecedented drug development in SLE, the paucity of approved therapies remains a significant challenge. Recent trials have highlighted the need for minimising heterogeneity within SLE populations; however, there is concern this results in the recruitment of patients that are not representative of the SLE population.

Objectives: Our aim was to apply published trial eligibility criteria to patients with non-renal SLE in a large UK-wide register to quantify how accurately these clinical trials represent a real-world cohort.

Methods: A literature review of all major published double-blinded randomised phase III trials in non-renal SLE was performed (n=12). Inclusion and exclusion criteria common across the majority of clinical trials were applied to all patients recruited to the BILAG-BR (BILAG biologics register) starting either biological therapy or standard of care (SOC). We applied available data to common inclusion criteria including age ≥18 years, ACR 1997 SLE classification criteria, positive anti-dsDNA or ANA antibodies, active disease (defined as a BILAG A in 1 domain or a BILAG B in ≥2 domains, or a SLEDAI ≥6); and common exclusion criteria including restricted medication rules, active renal or neurological SLE (defined as a BILAG A in either domain), a history of hepatitis B or C, a history of malignancy (excluding basal cell carcinoma), CKD stage 4 or 5, a UPCR ≥100mg/mmol, and cytopenias (defined as neutrophils <1.0 x10^9/L, platelets <10 x10^9/L or Hb <70g/L). Baseline variables were compared using chi-squared test.

Results: As of July 2018, 837 patients were recruited to the BILAG-BR starting either SOC (n=125) or a biologic therapy (n=712). The commonest biologic and SOC therapy was rituximab (n=662, 93%) and mycophenolate (n=64, 51%) respectively. Patients taking SOC were more likely to have inactive disease, as well as having higher steroid doses and less exposure to previous cyclophosphamide or B cell therapy. In the biologic and SOC groups, 476 (67%) and 71 (57%) respectively met all inclusion criteria (table 1). One or more exclusion criteria were met by 324 (46%) of the biologics group and 46 (37%) of the SOC group. As such, 562 (67%) patients were not eligible to enrol in a clinical trial. The patients not eligible to participate were similar in age (P=1.0), gender (P=0.7) and ethnicity (p=0.5) to those who were eligible. Median disease duration was longer in patients eligible to participate (2.9 vs. 5.1 years, p<0.01).

Table 1. Patients from the BILAG-BR who meet eligibility criteria for major SLE clinical trials

Inclusion criteria	**Biologic (n=712)**	**SOC (n=125)**	**P value**
Age ≥18 years	706	122	0.1
Meet ACR criteria for SLE	675	116	0.4
Antibody positive	567	99	0.9
Active disease	626	97	**<0.01**
Total meeting all inclusion criteria	**476**	**71**	**0.03**
Exclusion criteria	**Biologic (n=712)**	**SOC (n=125)**	**P value**
Steroids >40mg prednisolone	9	8	**<0.001**
Active CNS SLE	39	7	1.0
Active renal SLE	138	28	0.4
Hepatitis B or C	20	1	0.2
Malignancy	52	5	0.2
Cyclophosphamide <90 days before entry	37	0	**<0.01**
B cell therapy <1 year before entry	50	0	**<0.01**
CKD 4/ 5	22	3	0.7
UPCR ≥100mg/mmol	92	20	1.0
Low blood counts	25	1	0.1
Pregnancy	3	1	0.6
Total number of patients excluded	**324**	**46**	0.1
Total **NOT*** eligible for clinical trial *(n)*	**562/837 (67%)**		1.0

Conclusion: In a large national register of SLE patients, we found that two thirds of patients would not be eligible for recruitment to clinical trials using published inclusion and exclusion criteria. These results suggest that clinical trial recruits are not fully representative of the target disease population. This limits the generalisability of clinical trial results and supports the need for evidence from real world studies to fully understand the effectiveness of new therapies.

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SAT0169 HYDROXYCHLOROQUINE PRESCRIPTION PATTERNS IN EUROPE - THE EUROPEAN SURVEY FOR LUPUS PATIENTS (ESLP)

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Background: Long-term use of hydroxychloroquine (HCQ) is very common in patients with lupus erythematosus. It has been associated with wide-ranging benefits and it is generally well tolerated[1]. However, long-term use (i.e. > 5 years) and high-dose HCQ (i.e. > 5 mg/kg/day) are both considered to be risk factors for developing HCQ retinopathy[2].

Advances in our understanding of HCQ retinopathy has led to changes in the recommendations for HCQ dosing and retinopathy screening[1-3]. The latest EULAR guidelines for the management of systemic lupus erythematosus (SLE)[4] recommend a maximum HCQ dose of 5 mg/kg/day and ophthalmological screening at baseline and annually after 5 years of HCQ treatment.

Objectives: To assess whether recent EULAR guidelines regarding HCQ dosing and retinopathy screening are affecting prescription patterns and screening frequencies in Europe.

Methods: Patients in Europe were given the opportunity to complete the online European Survey for Lupus Patients (ESLP) initiated by LUPUS EUROPE. The survey was promoted on social media from the 26th of June – 11th of July 2019. The survey consisted of 29 questions. Each participant was asked, among other things, to report their body weight (kg), daily HCQ dose and if they have received baseline screening and/or regular eye examinations.

Results: The online survey was completed by 2938 lupus patients from 36 countries. The majority were female (86.5%) and diagnosed with SLE (85.7%). The daily HCQ dose (mg/kg) was available from 1678 patients (57.1%). The median ± IQR HCQ dose was 4.3 ± 2.5 mg/kg/day with a median treatment duration of 7 years (IQR: 3 – 14).

The recommended daily HCQ dose of 5 mg/kg was exceeded by 618 patients (36.8%). Low HCQ dose (≤ 4 mg/kg) was reported by 769 patients (45.8%). In addition, 284 out of 1786 patients (15.9%) reported they skipped HCQ once a week or more often. Nevertheless, only 8.7% of patients reported that they were more likely to skip HCQ than other medication. Patients from Belgium, Israel, France and Portugal reported the highest HCQ dosages. In contrast, patients from Spain reported the lowest HCQ dosages (Figure 1).

Moreover, 935 out of 1137 patients diagnosed in the past 10 years (82.2%) reported that they have received an ophthalmological screening at baseline. Lastly, 1167 patients reported long-term use of HCQ (i.e. ≥ 5 years). Only about 64% of them (n=748) reported that they receive regular eye examinations (i.e. at least once every year).

Conclusion: Studies have suggested that prescription patterns in the USA and UK were already affected by guidelines regarding HCQ dosing[1]. We show large inter- and intra-country variations of HCQ dosing in Europe. Additionally, most centers fail to follow recent recommendations[4] regarding annual screening of retinopathy in case of long-term HCQ use.

More research is needed to assess the clinical efficacy of low-dose HCQ and to confirm whether proper screening modalities are being employed as recommended by recent guidelines[2-4].

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Disclosure of Interests: None declared

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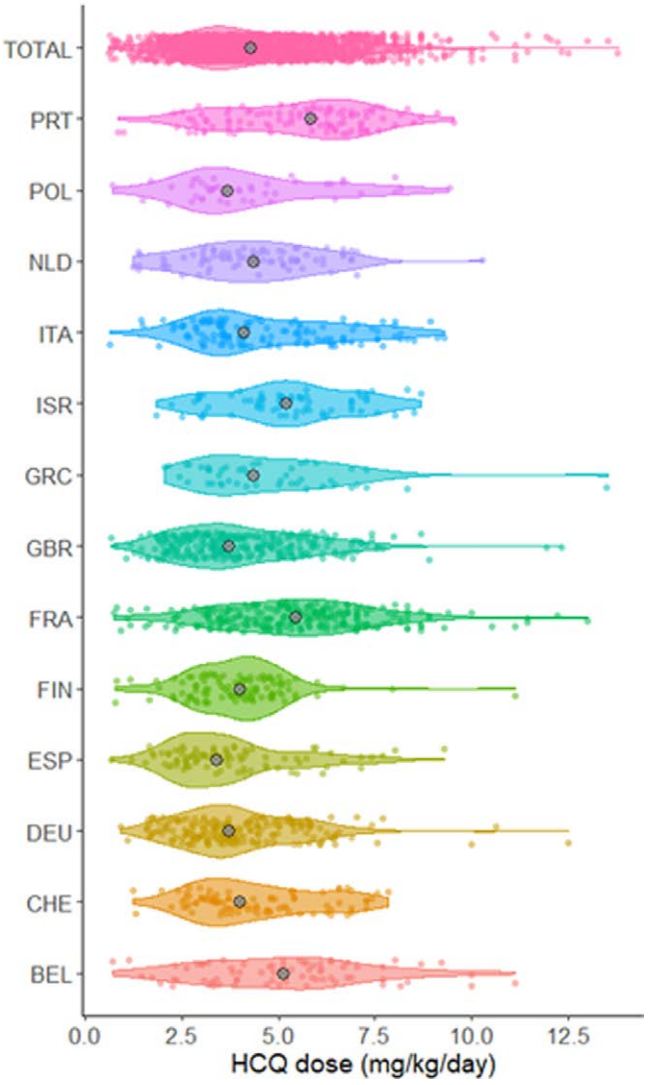


Figure 1. HCQ dose (mg/kg/day) reported by patients (• median HCQ dose). PRT: Portugal, POL: Poland, NLD: Netherlands, ITA: Italy, ISR: Israel, GRC: Greece, FRA: France, FIN: Finland, ESP: Spain, DEU: Germany, CHE: Switzerland, BEL: Belgium.

SAT0170

COMPOSITE OF RELEVANT ENDPOINTS FOR SJÖGREN'S SYNDROME (CRESS)

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Background: Defining a primary study endpoint that is able to discriminate between active treatment and placebo is crucial for clinical trials in primary Sjögren syndrome (pSS). Recent trials used the validated ESSDAI as primary endpoint, but found large 'response rates' in the placebo group too. Since pSS is a very heterogenous disease, a composite endpoint including multiple aspects (i.e., systemic, patient-reported, functional and biological) may be more appropriate to demonstrate clinical efficacy.

Objectives: To develop a composite endpoint for pSS based on expert opinion and analysis of trial data.

Methods: Based on expert opinion, 5 items were found to be most relevant to assess the effect of treatment in pSS patients: ESSDAI, ESSPRI, OSS, SWS and RF/IgG (Figure 1). These items were tested using data at week 24 of the randomized, double blind, placebo-controlled ASAP-III trial.[1] ROC analysis was used to assess the discrimination of effect between the abatacept (n=40) and placebo (n=39) treatment groups. The optimal cut-off point per item was defined by the highest sum of sensitivity and specificity. The percentage of patients responding to the individual items (Figure 1) and the composite endpoint (named CRESS) was calculated.

Results: For ESSDAI, ROC analysis showed that both absolute and relative change in ESSDAI were not able to discriminate between treatment groups (AUC 0.536 and 0.559) and no optimal cut-off point could be identified. According to an in SLE developed endpoint and based on expert opinion, it was decided to aim for the validated definition of low disease activity (ESSDAI<5)[2].

For ESSPRI, ROC analysis (AUC 0.629) showed an optimal cut-off point of -13.8%. Therefore, the validated definition of ESSPRI response (≥-15% or 1 point)[2] was used. For OSS and SWS, ROC analysis (AUC 0.555 for OSS>3 at baseline and AUC 0.556 for SWS>0 at baseline) could not identify an optimal cut-off point, so the definitions based on expert opinion were kept (Figure 1).

For serological items, ROC analysis (AUC 0.861 for RF>0 at baseline and 0.615 for IgG) showed optimal cut-off points of -23% and -2.2%, respectively. It was decided to round these numbers to ≥25% decrease in RF or ≥5% decrease in IgG. Responding to ≥3 of the 5 items discriminated best between the abatacept and placebo groups. The final response rate to our composite endpoint (CRESS responders) was 55% vs. 13% in the abatacept and placebo groups, respectively (P<0.001). Further analysis of how many patients who met the composite endpoint also met the single endpoints and vice versa demonstrated that all individual items contributed to the overall response rate.

Conclusion: This concept of the new 'Composite of Relevant Endpoints for Sjögren's Syndrome' (CRESS) is developed. With this composite endpoint, it is possible to discriminate between abatacept and placebo response in pSS patients. Additional validation analyses in independent, global, multi-center, placebo-controlled trials of biological DMARDs in pSS and NECESSITY will be performed.

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Figure 1. Overview of the Composite of Relevant Endpoints for Sjögren's Syndrome (CRESS): domains, measurements, definition of response and percentage of responders at week 24 of abatacept and placebo groups.

Domain	Measurement	Definition of response	Responders abatacept group	Responders placebo group
Systemic disease activity	ESSDAI	Score<5 (low disease activity)	35%	22%
Patient-reported symptoms	ESSPRI	Decrease of ≥1 point or 15% from baseline	58%	22%
Tear gland function	OSS	Decrease of ≥25% from baseline, or if normal score at baseline (<3) no increase to abnormal as response	60%	51%
Salivary gland function	SWS	Increase of ≥25% from baseline, or if score is 0 at baseline any increase	51%	43%
Serological	RF/IgG	Decrease of ≥25% from baseline in RF or decrease of ≥5% from baseline in IgG	73%	30%
Composite endpoint				
CRESS responder	All above	Response to ≥3 of the 5 items	55%	13%

ESSDAI: EULAR Sjögren's syndrome disease activity index; ESSPRI: EULAR Sjögren's syndrome patient reported index; OSS: ocular staining score; SWS: stimulated whole saliva; RF: rheumatoid factor; IgG: immunoglobulin G.

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SAT0171 RITUXIMAB IN SYSTEMIC AUTOIMMUNE RHEUMATIC DISEASES: ONE CENTER EXPERIENCE OF TREATMENT 515 PATIENTS

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Background: B cells have important functions in the pathogenesis of systemic autoimmune rheumatic diseases (SARDs).
Objectives: The purpose of the research was to study the therapeutic option of Rituximab (RTM), a chimeric anti-CD20 antibody, in SARDs such as ANCA-associated systemic vasculitis (AAV), cryoglobulinemic vasculitis (CV), systemic lupus erythematosus (SLE), systemic sclerosis (SS), primary Sjögren syndrome (pSS) and IgG4-related disease (IgG4-RD).
Methods: We present data on efficacy and safety of RTM in 515 patients (pts) with SARDs. 103 pts had AAV (58- granulomatosis with polyangiitis, GPA; 35- microscopic polyangiitis, MPA and 10- eosinophilic granulomatosis with polyangiitis, EGPA), 21 pts had CV, 167- SLE, 90- SS, 100- pSS, 34- IgG4-RD. Characteristics of pts and results of RTM treatment are present in Table. Mean follow-up duration after initiation of RTM was 25- 58 months.
Results: The average cumulative RTM dose in all groups exceeded 2.4 g, 71% of pts received repeated RTM courses (0.5-1.0 g) every 4 – 12 months. Complete (good) clinical response was achieved in 70-93% pts, except for the SLE (49%- complete response, 32- incomplete and 19%- no response). Usage of repeated RTM courses increased the clinical efficacy and reduced the risk of recurrence. Despite the fact that the study population included a high percentage of pts with severe or refractory SARDs, total mortality rate was about 6% during the follow-up period, highest in CV and AAV (14-11%). In AAV and SLE infections constitute a significant proportion of serious adverse reactions (10-11%). Late-onset neutropenia was only in pts with AAV (12%) and SLE (3%).
Conclusion: Treatment with RTM was highly effective in SARDs. In certain SARDs RTM safety profile of should be considered during treatment planning. Further studies of the targeted anti-B-cell therapy, including RTM efficacy and safety in SARDs, clarification of the indications and optimal RTM regimens are needed.

Table.

Parameters	AAV		CV	SLE	SS	pSS	IgG4-RD
	GPA, MPA	EGPA					
N pts	93	10	21	167	90	100	34
Age, years	41 (16-67)	50 (24-71)	53,6+29	41 (18-52)	47 (17-71)	42+12,2	47,4+15,9
Percentage of females	56%	90%	52%	92%	75%	97%	60%
Duration of disease, months*	14 (1-288)	11 (1-180)	72 (3-96)	18 (2-47)	70 (7-264)	90 (36-168)	24 (6-60)
Cumulative RTM dose, g*	3 (0,5-8)	3 (1,5-5,5)	4,7+3,8	2,4 (1,8±0,8)	2,9 (0,5-6)	5,5+1,5	4+1,5
Follow-up duration after the first RTM course, month*	37 (1–96)	36 (14-94)	52 (6-108)	38 (12-67)	27 (12-42)	58 (24-96)	25 (3-60)
Clinical response, %							
Complete (good)	93%	90%	71%	49%	70%	92,5%	77%
Incomplete response	6%	10%	29%	32%	24%	6,5%	23%
No response	1%	0%	-	19%	6%	1%	-
Relapse	8%	30%	-	-	nd	-	-
Glucocorticoids dose, mg/day*:							
Before RTM	30(5–60)	20(7,5-50)	4,4(0-24)	28(15-40)	12(0-25)	7,5(0-40)	10(2,5-40)
After RTM	5(0-10)	7,5(5-10)	1,5(0-4)	7,5(5-15)	9(0-15)	1,25	0,5
Immunosuppressants							
% pts before RTM	72%	90%	38%	65%	43%	44%	40%
% pts after RTM	43%	70%	5%	46%	50%	8%	10%
Infusion-related reactions, including severe	9% -	20% 10%	24% -	4% 0,6%	2% 1%	10% 1%	3% -

Table.

Parameters	AAV		CV	SLE	SS	pSS	IgG4-RD
	GPA, MPA	EGPA					
N pts	93	10	21	167	90	100	34
Pts with serious adverse reactions,	26%	40%	5%	14%	2%	5%	3%
including: infections,	11%	10%	-	10%	2%	5%	3%
neutropenia	10%	20%	-	3%	-	-	-
Deceased pts during the follow-up	11%	-	14%	5%	6%	2%	-

*Data are provided in the following format: median & min-max range in the brackets

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SAT0172 UTILIZATION OF HYDROXYCHLOROQUINE AND CORTICOSTEROIDS AMONG LUPUS PATIENTS WITH INCIDENT END-STAGE RENAL DISEASE (ESRD) ONSET: A LONGITUDINAL STUDY USING USRDS REGISTRY

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Background: The development of ESRD due to lupus nephritis is one of the most common and serious complications of SLE. Mortality among SLE ESRD patients is 4-fold higher compared to lupus nephritis patients with preserved renal function[1] Mortality in SLE ESRD is also twice as high compared with non-SLE ESRD, even though SLE patients develop ESRD at a significantly younger age. In the absence of ESRD specific guidelines, medication utilization in SLE ESRD is unknown.
Objectives: The objective of this study was to investigate the real-world current US-wide patterns of medication prescribing among lupus nephritis patients with new onset ESRD enrolled in the United States Renal Disease Systems (USRDS) registry. We specifically focused on HCQ and corticosteroids (CS) as the most used medications to treat SLE.
Methods: Inclusion: USRDS patients 18 years and above with SLE as a primary cause of ESRD (International Classification of Diseases, 9th Revision (ICD9) diagnostic code 710.0, previously validated[2]). who developed ESRD between January 1st, 2006 and July 31, 2011 (to ensure at least 6 months of follow-up in the USRDS). Patients had to be enrolled in Medicare Part D (to capture pharmacy claims). The last follow-up date was defined as either the last date of continuous part D coverage or the end of the study period, Dec 31, 2013.
Results: Of the 2579 patients included, 1708 (66%) were HCQ- at baseline, and 871 (34%) were HCQ+ at baseline. HCQ+ patients at baseline had a slightly lower duration of follow-up compared to HCQ- patients at baseline, median (IQR) of 2.32 (1.33, 3.97) years and 2.55 (1.44, 4.25) years, respectively, p= 0.02. During follow-up period, only 778 (30%) continued HCQ either intermittently or continuously to the last follow-up date, 1306 (51%) were never prescribed HCQ after baseline, and 495 (19%) discontinued HCQ before the last follow-up date. Of the 1801 patients who were either never prescribed or discontinued HCQ early after ESRD onset, 713 (40%) were prescribed CS to the end of the follow-up period: 55% were receiving a low dose <10mg/daily, and 43 were receiving moderate dose (10-20mg daily)
Conclusion: HCQ may be underprescribed and CS may be overprescribed in SLE ESRD. Changing the current prescribing practices may improve outcomes in SLE ESRD
References:
[1] Yap DY et al., NDT 2012.
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Acknowledgments : The data reported here have been supplied by the United States Renal Data System (USRDS). The interpretation and reporting of these data are the responsibility of the author(s) and in no way should be seen as an official policy or interpretation of the U.S. government.
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SAT0173

A SYSTEMATIC LITERATURE REVIEW INFORMING THE 2019 UPDATE OF THE JOINT EUROPEAN LEAGUE AGAINST RHEUMATISM AND EUROPEAN RENAL ASSOCIATION–EUROPEAN DIALYSIS AND TRANSPLANT ASSOCIATION (EULAR/ERA-EDTA) RECOMMENDATIONS FOR THE MANAGEMENT OF LUPUS NEPHRITIS

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Background: Lupus nephritis (LN) affects ~ 40% of patients with systemic lupus erythematosus (SLE) and is associated with significant morbidity. New data has emerged since the publication of the EULAR/ERA-EDTA recommendations for the management of LN, involving a multidisciplinary panel of experts.
Objectives: To analyze the current evidence, in order to inform the 2019 update of the EULAR/ERA-EDTA recommendations for the management of LN.
Methods: According to the EULAR standardised operating procedures, a Medline systematic literature review (SLR) was performed, from January 2012 until 31 December 2018. The final level of evidence (LoE) and grading of recommendations considered the total body of evidence, including the LoE of the 2012 recommendations.
Results: We identified 542 relevant articles. High-quality evidence supports the use of immunosuppressive treatment for class III and IV LN (LoE 1a) there is moderate quality evidence for immunosuppression in pure class V LN, with nephrotic-range proteinuria (LoE 2b). Treatment should aim for a 25% reduction in proteinuria at 3 months, 50% at 6 months and complete renal response (< 500-700 mg/day) at 12 months (LoE 2a-2b). Strong evidence supports the use of mycophenolate mofetil/mycophenolic acid (MMF/MPA) or low-dose intravenous cyclophosphamide (CY) for the initial treatment of class III/IV LN (LoE 1a, **Table**); Combination of tacrolimus with MMF/MPA and high-dose CY are alternatives in specific circumstances (LoE 1a, **Table**). There is little evidence to guide optimal duration of immunosuppression in LN (LoE 3). In end-stage kidney disease due to LN, all methods of kidney replacement treatment have been used, but transplantation is accompanied by the most favourable outcomes (LoE 2b).
Conclusion: There is high-quality evidence to guide the initial and subsequent phases of class III/IV LN treatment. There is low quality evidence to guide treatment of class V, monitoring and optimal duration of immunosuppression.

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SAT0174

FLARE ASSESSMENTS IN PATIENTS WITH ACTIVE SYSTEMIC LUPUS ERYTHEMATOSUS TREATED WITH ANIFROLUMAB IN 2 PHASE 3 TRIALS

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Background: Anifrolumab treatment resulted in improved British Isles Lupus Assessment Group (BILAG)–based Composite Lupus Assessment (BICLA) response rates in patients with systemic lupus erythematosus (SLE) in the phase 3 TULIP-2 and TULIP-1 trials.[1,2] In addition, annualized flare rates were lower among the groups treated with anifrolumab compared with placebo.[1,2]
Objectives: TULIP-2 and TULIP-1 data were analyzed to assess the effects of anifrolumab on the number of SLE flares and time to first flare during 52 weeks of treatment.
Methods: The randomized, double-blind, placebo-controlled TULIP-2 and TULIP-1 trials evaluated efficacy and safety of intravenous anifrolumab 300 mg vs placebo every 4 weeks for 48 weeks, with the primary endpoints assessed at Week 52, in patients with moderate to severe SLE despite standard-of-care treatment. Flares were defined as ≥1 new BILAG-2004 A or ≥2 new (worsening) BILAG-2004 B domain scores compared with the prior month's visit. Time to first flare was evaluated using a Cox proportional hazards model. Annualized flare rate was analyzed using a negative binomial regression model.

Table. Randomized trials for induction therapy in LN

Reference	n	Intervention	Control	Prednisone dosing	End-point	Results	Overall risk of bias*
MMF vs CY							
Mendonca et al (2017)	40 (1:1)	MMF + Pz	CY + Pz	0.5 mg/kg/d	24w CR PR	**CR**: CY vs MMF 47.82% vs 52.94% p=0.861 **PR**: CY vs MMF 39.13% vs 35.3% p=ns	High
Sun et al (2015)	82 (1:1)	MMF + CYC + Pz	CY + Pz	1.0 mg/kg/d for 4-8w and tapering	6m RR	**RR:** CY vs CY+MMF 77.5% vs 88.1% p=0.2	High
Rathi et al (2016)	100 (1:1)	MMF + Pz	CY + Pz	1 mg/kg/d for 8w and tapering	24w TRR	**TRR**: CY vs MMF 75.0% vs 76.3% p=0.91	Some concerns
Sedhain et al (2018)	42(1:1)	MMF + Pz	CY + Pz	1 mg/kg/d for 4w and tapered to 5-7.5mg/d	6m TR	**TR:** MMF vs CY 28.6% vs 19% p=0.57	Some concerns
Sahay et al (2018)	144 (1:1:1)	MMF + Pz	NIH regimen vs Eurolupus (ELNT)regimen	1 mg/kg/d and tapered to 10mg/d	6m RR	**RR:** NIH:71.4% ELNT: 65% MMF:72.9% p=0.9	High
Low vs high CY							
Mehra et al (2018)	77 (1:1)	CY 6 x 500mg fortnightly + Pz	CY 6×750 mg/m^2 four-weekly	1 mg/kg/d for 4w and tapered to 5–7.5 mg/d	52w CR PR	**CR:** low vs high 44% vs 65% p=0.08 **CR/PR:** low vs high 50% vs 73% p=0.04	Some concerns
Multitarget vs SoC							
Liu et al (2015)	362 (1:1)	MMF + TAC + Pz	CY + Pz	0.6 mg/kg/d for 4w and tapered to 10 mg/d	24w CR PR	**CR:** Multitarget vs CY 45.9% vs 25.6% p<0.001 **CR+PR**: Multitarget vs CY 83.5% vs 63.0% p< 0.001	Some concerns
Rovin et al (2019)	265	Voclosporin (low or high dose) + MMF + Pz	MMF + Pz	20-25mg/d and tapered to 2.5 mg/d at 16w	48w CRR	**CRR:** low dose multitarget vs MMF OR = 3.21 p<0.001 High dose multitarget vs MMF OR=2.10 p=0.026	Low

Abbreviations: MMF Mycophenolate mofetil, CY cyclophosphamide, Pz Prednizone, CR complete response, PR partial response, RR renal response, TRR treatment response rate, SoC standard of care, OR odds ratio.
*Overall risk of bias was assessed using the Revised Cochrane risk-of-bias tool (ROB2)

Results: In TULIP-2 (anifrolumab, n=180; placebo, n=182) and TULIP-1 (anifrolumab, n=180; placebo, n=184), fewer patients experienced ≥1 BILAG-2004 flare in the anifrolumab groups (TULIP-2: 31.1%, n=56; TULIP-1: 36.1%, n=65) compared with the placebo groups (TULIP-2: 42.3%, n=77; TULIP-1: 43.5%, n=80; Figure 1). Results favoring anifrolumab were observed in time to first flare (TULIP-2: hazard ratio [HR] 0.65, 95% confidence interval [CI] 0.46–0.91 and TULIP-1: HR 0.76, 95% CI 0.55–1.06; Figure 2) and BILAG-based annualized flare rates (TULIP-2: adjusted rate ratio 0.67, 95% CI 0.48–0.94 and TULIP-1: rate ratio 0.83, 95% CI 0.60–1.14) across both trials.

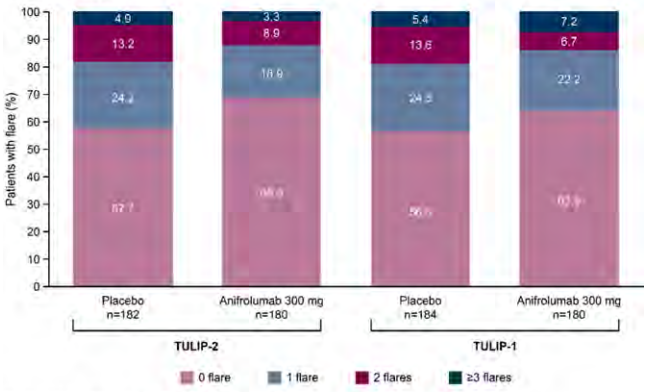
Conclusion: Across 2 phase 3 trials, we observed reductions in the total number of flares and annualized flare rates, as well as prolongation of time to first flare with anifrolumab treatment compared with placebo. These results support the potential of anifrolumab to reduce disease activity and reduce flares, benefiting patients with SLE.

References:

[1] Morand EF, et al. *N Engl J Med*. 2020;382:211–221.

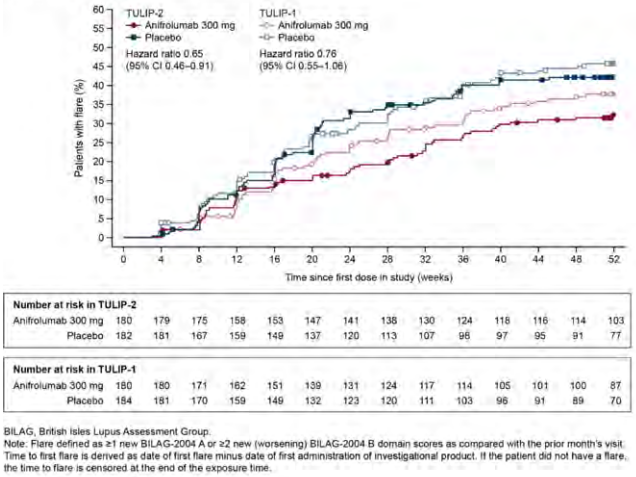
[2] Furie RA, et al. *Lancet Rheumatol.* 2019;1:e208–e219.

Figure 1. Flares Assessed Using BILAG-2004 in Patients Treated With Anifrolumab Compared With Placebo in TULIP-2 and TULIP-1



BILAG, British Isles Lupus Assessment Group.
Note: Flare defined as ≥1 new BILAG-2004 A or ≥2 new (worsening) BILAG-2004 B domain scores as compared with the prior month's visit.

Figure 2. Time to First Flare in TULIP-2 and TULIP-1



Number at risk in TULIP-2														
Anifrolumab 300 mg	180	179	175	158	153	147	141	136	130	124	118	116	114	103
Placebo	182	181	167	159	149	137	120	113	107	98	97	95	91	77

Number at risk in TULIP-1														
Anifrolumab 300 mg	180	180	171	162	151	139	131	124	117	114	105	101	100	87
Placebo	184	181	170	159	149	132	123	120	111	103	96	91	89	70

BILAG, British Isles Lupus Assessment Group.
Note: Flare defined as ≥1 new BILAG-2004 A or ≥2 new (worsening) BILAG-2004 B domain scores as compared with the prior month's visit. Time to first flare is derived as date of first flare minus date of first administration of investigational product. If the patient did not have a flare, the time to flare is censored at the end of the exposure time.

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SAT0175

IMPACT OF ANTIMALARIAL ADHERENCE ON MORTALITY AMONG PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A POPULATION-BASED COHORT STUDY

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Background: Evidence has consistently shown that adherence to AM is poor in systemic lupus erythematosus (SLE) patients. However, data on the impact of adherence to AM on mortality is scarce.

Objectives: To assess the effect of AM adherence on all-cause mortality in SLE patients from the general population.

Methods: This study used administrative databases from British Columbia, Canada. We created an incident SLE cohort between January 01, 1997, and March 31, 2015, using the physician billing data and a 7-year washout period. The inclusion criteria were at least two physician visits, at least two months apart, within two years, with an ICD-9 code (710.0) or ICD-10 code (M32.1, M32.8, M32.9) for SLE. Follow-up started at the first day of having both SLE and AM, i.e., at the SLE index date (second ICD code) for those whose first AM use occurred before the SLE index date, or the date of the first AM use if otherwise. Our outcome was all-cause mortality, obtained from the vital statistics registry. In the analysis, the follow-up time was divided into 30-days windows, for a total of 293,190 person-months. For each window, a measure of adherence, the proportion of days covered (PDC), was calculated and categorized as adherent (PDC≥0.90), non-adherent (0<PDC<0.90), and discontinuer (no drug or PDC = 0). We used both Cox's proportional hazards models and marginal structural models (MSM) to estimate the effect of AM adherence on all-cause mortality. Both analysis controlled for baseline demographics (age, sex, residence, income quintile), as well as the following baseline and time-varying covariates: immunosuppressive and other medications, hospitalizations, impatient, and other visits, and Charlson comorbidity index. To account for the possibility of a few time-varying covariates being mediators in the causal pathway from AM adherence to mortality, which may cause the Cox model to yield biased estimates of the adherence effects, we conducted the MSM analysis that can produce valid estimates as it balances the distributions of time-varying confounders among the three adherence groups via inverse probability weighting.

Results: We identified 3,385 individuals with incident SLE (mean age 47.3 years, 89% were women) who had at least one filled AM prescription. Over the mean follow-up of 6.66 years, 288 (8.5%) incident SLE patients died. The incidence rate (IR) of mortality for AM adherent, non-adherent, and discontinuer patients were 4.31, 11.86, and 19.51 per 1000 person-years, respectively. Using the Cox model, the adjusted hazard ratio (HRs) obtained for AM adherent and non-adherent SLE patients were 0.20 and 0.66, respectively, compared to discontinuer SLE patients (Table 1). Using MSM, those adjusted HRs were found as 0.18 and 0.64. Also, the adjusted HRs for adherers compared to the non-adherers were 0.30 (Cox) and 0.28 (MSM). A statistically significant linear trend in the HRs of mortality risk over the adherence levels was found (Table 1, Linear Trend).

Table 1.

Adherence Levels	No. of Deaths	IR Ratios (95%CI)	Adjusted Cox HRs (95%CI)	Adjusted MSM HRs (95%CI)
Discontinuer (Reference)	198			
Non-adherent	47	0.61(0.44-0.84)	0.66(0.47-0.93)	0.64(0.46-0.89)
Adherent	43	0.22(0.16-0.31)	0.20(0.14-0.28)	0.18(0.12-0.25)
Contrast: Partial vs. Full		0.36(0.24-0.55)	0.30(0.19-0.46)	0.28(0.18-0.42)
Linear Trend			0.32(0.25-0.41)	0.29(0.23-0.37)

Conclusion: SLE patients that adhere to AM therapy have a lower risk of death than patients who do not adhere or who discontinue AM (5 and 3 times, respectively) in both the MSM and Cox analysis. Our findings support the importance of AM adherence to prevent premature deaths in SLE patients.

Disclosure of Interests: None declared

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SAT0176

THERAPEUTIC APHERESIS DURING PREGNANCY IN RHEUMATIC DISEASES

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Background: Therapeutic apheresis (TA) represents a therapeutic option in pre-existing conditions or rheumatic diseases that occur during gestation. Although pregnancy is not a contraindication itself, due to the lack of evidence-based guidelines and the alleged risk of maternal and/or fetal adverse events, there is general resistance to its application during pregnancy.
Objectives: In this observational study we aimed to evaluate the efficacy and safety of TA in high-risk pregnancies in patients with rheumatic diseases, followed over a decade in a tertiary Center.
Methods: Between January 2005 and April 2019, 843 TA procedures were performed during 51 pregnancies in 43 patients: 745 plasma exchange sessions and 98 immunoabsorption sessions. TA was performed in 29 (57%) pregnancies of 21 (48.8%) patients with antiphospholipid antibody syndrome (APS), in 20 (39.2%) pregnancies of 20 (46.5%) patients with congenital heart block (CHB), in 1 (1.9%) pregnancy of 1 (2.3%) patient with systemic sclerosis (SSc) and 1 (1.9%) pregnancy of 1 (2.3%) patient affected by lupic nephritis (SLE).
Results: During the period considered, apheresis sessions applied to pregnant women were 7.1% of the total (n = 13.251). The average age at the first treatment was 33 years (range 24-43). The mean management age at the first apheretic treatment was 21 weeks (range 4-32). Twelve (1.4%) apheresis sessions were complicated by adverse events, none required or prolonged hospitalization. There were 44 (86.3%) live births, 3 (5.9%) spontaneous abortions and 2 (3.9%) voluntary terminations of pregnancy, 2 (3.9%) lost to follow-up. The average gestational age at birth was 35 weeks (range 24-37) and cesarean section was performed in 41 (80.4%) cases. TA was added to conventional therapy in 24/29 (82.7%) patients with APS, to the detection of fetal cardiac activity, while in 5/26 (17.3%) it was introduced when the first signs of pregnancy complications such as mild preclampsia, HELLP and IUGR were detected. TA was started within 24 hours of atrioventricular block (AVB) detection; 10/20 (50%) mothers with CHB were diagnosed with 2nd degree AVB, 9/20 (45%) with 3rd degree AVB and one (5%) with sinus bradycardia and endocardial fibroelastosis. The patient with SSc was treated with TA twice a week from the 32nd SG until delivery, which occurred at the 36th SG, due to severe IUGR and oligohydramnios. The patient with SLE complicated by lupic nephritis was treated with TA twice a week, from the 26th SG until the birth, which took place at the 31st SG.
Conclusion: Our data have shown that TA in pregnancy is well tolerated. Close collaboration between rheumatologist, obstetrician and specialist in TA is essential to ensure a successful outcome of high-risk pregnancies.
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SAT0177 MULTITARGET THERAPY WITH TACROLIMUS AND MYCOPHENOLATE MOFETIL FOR TREATMENT OF LUPUS NEPHRITIS PRESENTED WITH RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS

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Background: Although, most lupus nephritis patients present with chronic glomerulonephritis or nephrotic syndrome, some patients develop rapidly progressive glomerulonephritis (RPGN), which is a clinical syndrome characterized by rapid loss of renal function over a short period of time (days to months). Multitarget therapy using tacrolimus and mycophenolate mofetil (MMF) has been reported to be effective as induction therapy of Class III to Class V lupus nephritis[1]. However, its efficacy on lupus nephritis presented with RPGN has not been well reported.
Objectives: We aimed to examine the efficacy of multitarget therapy on lupus nephritis presented with RPGN.
Methods: We retrospectively analyzed patients with biopsy-proven lupus nephritis, who clinically showed RPGN, and were treated by multitarget therapy with tacrolimus and MMF in our department. Data were expressed as mean±SD.
Results: Five lupus nephritis patients (3 female) with RPGN were treated by multitarget therapy as induction therapy. Mean age was 36.6±13.5 years old. Renal biopsy at treatment revealed Class IV(A) in 2, Class IV(A+C) in 1 and Class IV(A)+V in 2. The percentage of glomerular crescents was 23.1±25.4%. eGFR and proteinuria at the initiation of treatment were 46.8±11.5 mL/min/1.73m^2 and 7.7±3.4 g/gCr, respectively. Patients were initially treated with methylprednisolone pulse therapy followed by 0.8-1.0 mg/kg of prednisolone (PSL), 2-3 mg/day of tacrolimus and 1000 mg/day of MMF. At 6 months, eGFR and proteinuria improved to 72.9±11.3 mL/min/1.73m^2 and 0.19±0.13 g/gCr, respectively. At 12 months, eGFR and proteinuria further improved to 76.8±7.8 mL/min/1.73m^2 and 0.10±0.07 g/gCr, respectively and the dose of PSL was reduced to 6.6±1.5 mg/day. Three patients became positive for cytomegalovirus antigenemia and were successfully treated with antiviral therapy.
Conclusion: Multitarget therapy is effective in lupus nephritis even in patients presented with RPGN.
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Disclosure of Interests: Yoichi Imai: None declared, Hidekazu Ikeuchi Speakers bureau: CHUGAI PHARMACEUTICAL CO., LTD.
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SAT0178 HYDROXYCHLOROQUINE CONTROLS DISEASE ACTIVITY IN SLE AND MULTIMODAL IMAGING TECHNIQUES SHOULD BE USED TO DETECT OCULAR TOXICITY

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Background: Hydroxychloroquine (HCQ) is an immunomodulatory drug that has been shown to improve disease activity in systemic lupus erythematosus (SLE). However, retinal toxicity is an important concern.
Objectives: In this study we sought to evaluate the effect of HCQ on disease activity and damage in patients with SLE in whom HCQ was discontinued due to retinal toxicity and whether it could be restarted by a detailed ophthalmologic examination.
Methods: Patients who met SLE SLICC classification criteria and were on HCQ for at least 3 years after reaching Lupus Low Disease Activity State (LLDAS) following remission induction and were followed up for at least 3 years after termination of HCQ treatment due to retinal toxicity diagnosed with visual field test were analyzed. Disease activity (LLDAS and SLEDAI-2K) and both the number and severity of flares were recorded for each patient whilst on HCQ and after cessation of treatment. All patients were examined by two experienced ophthalmologists and were assessed by computerized visual field, optical coherence tomography (OCT), fundus autofluorescence (FAF) and fundus florescein angiography (FFA) to further analyze toxicity.
Results: Out of 88 patients with recorded HCQ retinal toxicity in a cohort of 1500 patients with SLE, 64 patients (mean age at diagnosis 33.4 ± 10.5 (10-57); 88.5% female) with complete data and opthalmologic re-examination results were included in the analyses. The average duration on HCQ was 122 ±85 (39-336) months, and the mean follow-up time was 74.6 ± 48.3 (36-239) months after the drug was discontinued. Comparison of mean disease activity in the 3-year period when patients were on HCQ to 3 years post-cessation revealed a significantly lower mean SLEDAI-2K score in the former (0.89±1.28 vs.1.3±1.6, p=0.02). The % of visits maintaining LLDAS was higher during HCQ treatment (89.7 ± 17.6 vs. 80.1 ± 23.5, p=0.001). There was significantly a higher frequency of flares with a dominance of mild-moderate types after HCQ was ceased (47.5 vs. 26.2%, p=0.03; 39.3 vs. 22.9%, p=0.024 respectively). There were more patients with serious flares in the post-discontinuation period but without statistical significance (13.1% vs. 4.9% p=0.08). Thirty-seven (60%) of patients restarted the treatment after ophthalmological examination. Although 38 (62,3%) patients had visual field defects in the latest examination, multimodal imaging with OCT, FAF and FFA revealed that only 19 (31%) patient had typical retinal toxicity. Five patients were found to have macular atrophy due to other causes (4 age related macular degeneration and 1 vitromacular adhesion). Since the discrimination of macular pathology would not be possible with imaging in these patients, HCQ was not prescribed. Comparison of patients with and without retinal toxicity showed that duration of HCQ use and HCQ-free time was not significantly different between patients.
Conclusion: HCQ is effective in controlling disease activity in patients with SLE and an opportunity for re-medication with HCQ is valuable. More than half of the

patients being able to restart HCQ after ophthalmologic examination in this study shows that it is important to perform multimodal imaging techniques in patients with retinal toxicity diagnosis. Since macular pathology can have a different etiologic background, an initial opthalmologic examination is also necessary. Lack of difference in the duration of HCQ exposure and drug-free time between patients who restarted treatment and who could not may be a sign of personal sensitivity to HCQ toxicity.

Disclosure of Interests: : None declared

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SAT0179 ADHERENCE TO HYDROXYCHLOROQUINE INFLUENCES THE INCIDENCE OF ORGAN DAMAGE DURING FOLLOW-UP IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background:

Objectives: Hydroxychloroquine (HCQ) is a cornerstone drug in patients with systemic lupus erythematosus (SLE), decreasing the risk of flares and comorbidities and improving survival. This study investigated the effects of HCQ adherence on clinical manifestations, disease activity, and organ damage in Korean patients with SLE.

Methods: Data on 299 SLE patients were obtained from the Korean Lupus Network registry. Demographic variables, clinical manifestations, laboratory findings, PGA, and SLEDAI-2000 and SLICC damage index scores were recorded at the time of enrollment and repeated annually for 4 consecutive years. Patients were divided into two groups according to the level of HCQ adherence. Adherence was defined by the medication possession ratio and dichotomized as ≤ 80% vs. > 80%. Univariate and multivariate analyses were performed to assess the impact of adherence to HCQ on clinical outcomes.

Results: Of the 299 patients, 31 (10.4%) showed poor drug adherence during the follow-up period. Patients with poor HCQ adherence were older (P=0.011), less insured (P=0.024), experienced lower employment (P=0.033), and had a higher rate of comorbidities such as hypertension (P=0.048) and depression (P<0.001). The non-adherent group had higher mean and changed SLICC damage index scores than the adherent group across all 4 years. In the multivariate analysis, HCQ non-adherence was significantly associated with older age (OR, 1.043; 95% CI, 1.006–1.081; P=0.021), depression (OR, 11.98; 95% CI, 1.099–130.6; P=0.042), and an annual increase in the SLICC damage index score (OR, 2.275; 95% CI, 1.369–3.779; P=0.002).

Conclusion: HCQ adherence might be influenced by age and depressive mood. Additionally, the poor adherence to HCQ in SLE patients was correlated with higher cumulative organ damage. Therefore, patients with SLE should be educated to take HCQ appropriately to improve their clinical outcome in clinical practice.

Disclosure of Interests: None declared

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SAT0180 ANTIMALARIAL DRUGS ASSOCIATED RETINOPATHY IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: The antimalarials remain to be the main treatment for Systemic Lupus Erythematosus (SLE). Its most important limitation when you want to increase dose or remain using them is the occurrence of retinal toxicity, which appears in a small number of patients. Since the lesions can progress even with drug withdrawal is important to perform a screening for an early diagnosis.

Objectives: To describe ocular toxicity in patients with SLE treated with antimalarials that attended the rheumatology office and to identify possible associated risk factors.

Methods: We performed a cross-sectional, retrospective study of SLE patients diagnosed of antimalarial drugs associated retinopathy, that were included in the data base of the Rheumatology department in León`s Hospital between 2014-2019. Multiple clinical and therapeutic factors potentially associated with retinal toxicity were analyzed including: age, chronic kidney disease (CKD), liver failure, smoking, hypertension, Diabetes mellitus, presence of previous retinopathy, type of treatment, duration, daily dose and cumulative dose and tamoxifen intake. The diagnosis of retinopathy was performed by the Ophthalmology department. The dose of hydroxychloroquine (HCQ) used was of 400mg/day and chloroquine (CQ) 250mg/day.

Results: 437 medical records were analyzed, 20 patients diagnosed of antimalarial retinopathy were included (4,57%), 90% of them were women. The age of diagnosis was more than 40 years in 18 patients (90%) and more than 60 years in 10 (50%) with a median of 60 years (IQR: 32,25).

The duration of treatment was ≤ 5 years in 10 patients (50%), between 6-10 years in 6 (30%), between 11-15 years in 2(10%) and between 16-20 years in 2 (10%) with a median of exposure of 5,5 years (IQR: 6,5); 15 patients (75%) were in treatment with HCQ, with CQ 2 patients (10%) and with both of them sequentially 3 patients (15%).

Of the group of patients treated with HCQ 35 % were above the global accumulated recommended dose (1000 g) and 71% of them were on treatment more than 10 years. In the group treated with CQ none were above the global recommended dose (460g). Of the 3 patients that took both drugs, two were above the recommended dose for HCQ.

25% of the patients had CKD and 10% liver failure, 20% of the patients were active smokers and 15% ex-smokers.

10% of the sample had previous retinopathy related with other comorbidities (age related retinopathy and diabetes), associating hypertension and diabetes mellitus in the same percentage (15%).

Severe retinopathy was found in 1 patient (5%), mild-moderate in 9 patients (45%), retinopathy stages were not specified in 10 patients (50%).

Conclusion: In our sample we observed a prevalence of antimalarials retinopathy of 4,57%, similar of what is found in the literature. Half of the patients had retinopathy in a period of treatment ≤ 5 years, being a described risk factor the duration of treatment of more than 6 years. This early manifestation could be related to the presence of other comorbidities like hypertension, diabetes and CKD.

Dose readjustment should be considered in patients with a period of treatment of more than 10 years. Age seems to be an associated factor for the development of antimalarials retinopathy and to perform a screening in the first year of treatment is important to rule out basal disease related with more risk to develop ocular toxicity.

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SAT0181 ALTERATIONS OF PERIPHERAL LYMPHOCYTE SUBSETS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND THEIR CHANGES AFTER OUR NEW IMMUNOREGULATORY COMBINATION THERAPIES

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Background: Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease characterized by abnormal activation of circulating lymphocytes and overproduction of autoantibodies[1]. Breakdown of self-tolerance is considered as a critical cause in the development of SLE[2]. However, the quantitative changes of lymphocyte subsets in SLE are unclear. Since low-dose IL-2 and several drugs have been used to promote the proliferation of regulatory T cells (Tregs)[3], we developed immunoregulatory therapies using these drugs to rebalance effector T cells with Tregs and test whether they are benefit to remission disease activity of SLE.

Objectives: To observe the different levels of peripheral lymphocyte subsets at the first laboratory examination of SLE patients with those of healthy controls (HCs) and to evaluate the effect of immunoregulatory combination therapies on levels of lymphocyte subsets in patients with SLE.

Methods: From September 2014 to December 2019, a total of 985 diagnosed patients with SLE (878 females, 107 males, mean age 42.99±13.37 years) and 206 healthy adults were enrolled in this retrospective cross-sectional study. And 795 patients with SLE (711 females and 84 males, mean age 38.26±15.242 years) were received the immunomodulatory drugs (IMiDs) such as low-dose interleukin-2, rapamycin, metformin, retinoic acid, coenzymes Q10 or other immunomodulatory treatments. The absolute numbers of T, B, NK, $CD4^+$T, $CD8^+$T, Th1, Th2, Th17 and $CD4^+CD25^+Foxp3^+$T regulatory cells (Tregs) in peripheral blood (PB) of these individuals were measured by Flow Cytometer (FCM) combined with standard absolute counting beads.

Results: As compared with those of HCs, patients with SLE had lower absolute numbers of total T, NK, and $CD4^+$T but higher proportions of all lymphocyte subpopulations except NK, CD4+T cells($P < 0.001$) (Figure 1 A, C). Notably, the absolute numbers and proportions of Tregs as well as Th1 in $CD4^+$T subsets were decreased ($P<0.05$) (Figure 1 B, D). Further, there was a significant increase in the ratio of Teffs/Tregs such as Th1/Tregs, Th2/Tregs and Th17/Tregs ($P<0.05$) (Figure 1 E). After receiving immunoregulatory combination therapies, the absolute numbers and proportions of T, NK, $CD4^+$T, and $CD8^+$T were increased, while the proportion of B cells was decreased (Figure 2 A, C); the absolute numbers of most $CD4^+$T subsets as well as the proportions of only Th1 and Tregs were significantly increased ($P < 0.001$) (Figure 2 B, D). The ratios of Th1/Th2 and Th1/Tregs increased while that of Th17/Tregs and Th2/Tregs decreased ($P<0.01$) (Figure 2 E).

Conclusion: Quantitative and functional alterations of peripheral lymphocyte subsets, especially reduced Tregs, play crucial roles in the pathogenesis of the patients. Immunoregulatory combination therapies mainly promote the proliferation and functional recovery of Tregs to rebalance pro- and anti-inflammatory T cells in patients with SLE for patients' symptoms remission.

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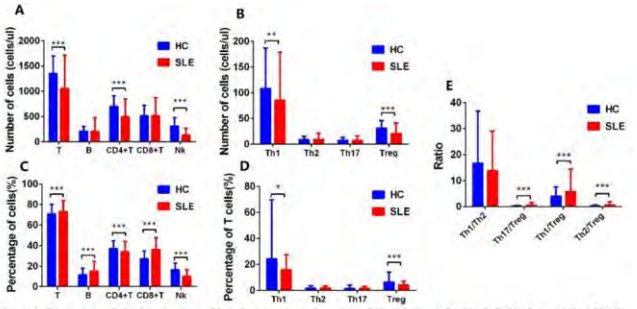


Figure 1: Comparison of absolute numbers of lymphocyte subsets in peripheral blood between healthy individuals (n=206) and SLE patients (n=985). All the lymphocytes subsets were analyzed by detected by flow cytometry combined with standard absolute counting beads. Data were presented as mean±SD and statistical analysis was determined by two-tailed unpaired t-test. *P < 0.05, **P < 0.01, ***P < 0.001.

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SAT0182 THE ASSOCIATION BETWEEN AUTOANTIBODIES AND RITUXIMAB RESPONSE IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic Lupus Erythematosus (SLE) is clinically and immunologically heterogeneous with a variable response to treatment. MASTERPLANS is an MRC-funded consortium that seeks to identify immunophenotypic subgroups of patients that predict response to therapy. Autoantibody profiles can differentiate subgroups of patients and have potential to predict response to treatment.

Objectives: To determine whether known and novel autoantibodies are associated with response to rituximab (RTX), and analyse the association between these antibodies and disease involvement in various organ systems.

Methods: Serum was obtained from 224 SLE patients in the BILAG Biologics Registry who received rituximab according to NHS England criteria (2). Patients were recruited if they were starting a first cycle of rituximab for active SLE (BILAG A or 2xBILAG B) despite previous cyclophosphamide or mycophenolate mofetil. Evidence of any single organ system involvement previous or current was taken as having a BILAG score of A-D but not E. Disease activity was measured using BILAG-2004. Clinical response was defined as improvement by >=1 grade in active BILAG-2004 systems with no worsening in other systems. Autoantibodies were measured by immunoprecipitation of proteins by sera from ^{35}S-labelled K562 cell lines, followed by SDS-PAGE separation and autoradiography. Autoantibodies not able to be detected by this technique (anti-Ro52, anti-dsDNA and aCL) were measured by ELISA. Autoantibody data was analysed in IBM SPSS and GraphPad Prism v8.2. Association between autoantibodies and RTX response was analysed using binary logistic interaction terms and Pearson's Chi-Square test.

Results: Of the 224 patients (201 female, 23 male, median age 40 years) the most common system involvement from the 9 BILAG domains was musculoskeletal (164 patients) and the least ophthalmic (11 patients). Patients with anti-Ro52 and anti-U1RNP/Sm had more frequent involvement of mucocutaneous ($p<0.036$, $p<0.012$) and musculoskeletal domains ($p<0.015$ for U1RNP) respectively.

There were 136 patients with sufficient data to define as either responders (n=67) or non-responders (n=69) to RTX at 6 months. RTX responders had a higher frequency of anti-U1RNP/Sm compared to non-responders (Figure 1). Further Pearson's Chi-Square analysis showed a significant association between presence of anti-U1RNP/Sm and better response to RTX ($p<0.018$).

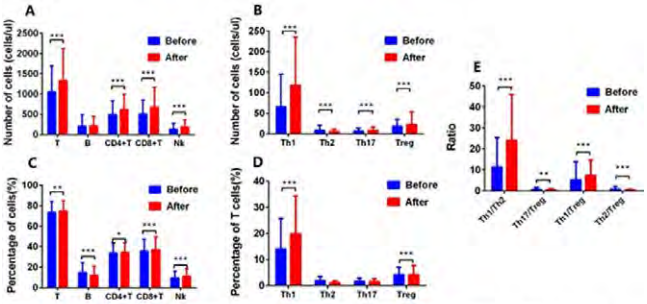


Figure 2: Changes of peripheral lymphocyte subsets after immunomodulatory combination therapy (n=795). Data were presented as mean±SD and statistical analysis was determined by two-tailed paired t-test. *P < 0.05, **P < 0.01, ***P < 0.001.

Conclusion: Our findings suggest that the presence of U1RNP/Sm autoantibodies in a cohort of patients who have received treatment with RTX is associated with more frequent musculoskeletal and mucocutaneous involvement and predicts a more favourable response to treatment.

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SAT0183 STATUS OF LYMPHOCYTE SUBSETS IN PERIPHERAL BLOOD OF PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME AND THEIR CHANGES AFTER RECEIVING OUR NEW IMMUNOREGULATORY COMBINATION THERAPY: A RETROSPECTIVE CROSS-SECTIONAL STUDY

J. Y. Yang[1], S. X. Zhang[2], L. Hao[2], Q. Y. Su[1], J. Bai[1], S. J. Guo[1], J. Luo[2], G. Y. Liu[2], C. Gao[3], X. Li[2]. [1]*Shanxi Medical University, Taiyuan, China*; [2]*The Second Hospital of Shanxi Medical University, Taiyuan, China*; [3]*Brigham and Women's Hospital, Harvard Medical School, Boston, United States of America*

Background: Primary Sjögren's syndrome (pSS) is a chronic inflammatory autoimmune disease mainly involving exocrine glands and involving multiple organs and systems[1]. Recent studies have reported that peripheral lymphocyte subsets such as Th1, Th2, Th17, and regulatory cells (Tregs), have been implicated in the pathogenesis of pSS[2]. However, the detailed statuses of lymphocyte subsets of pSS patients remain to be clearly evaluate and effects of immunomodulatory therapies on the lymphocyte subsets are unknown.

Objectives: To explore the pathogenesis and evaluate the therapeutic effect of immunomodulatory drugs (IMiDs) by comparing the changes of lymphocyte subsets in peripheral blood (PB) before and after treatment.
Methods: This study included 1,221 pSS patients and 206 healthy controls (HCs). Among these patient, 759 patients were received our new immunoregulatory therapies such as low-dose interleukin-2, rapamycin, metformin, retinoic acid etc. The absolute numbers of T, B, NK, $CD4^+$T, $CD8^+$T, Th1, Th2, Th17 and Tregs in PB of these subjects were detected by flow cytometry combined with standard absolute counting beads. Data were expressed as mean ± standard deviation to the distribution. Independent-samples T test and paired-samples T test were applied. *P* value <0.05 were considered statistically significant.
Results: The absolute numbers of circulating Tregs as well as T, NK cells in pSS patients were significantly lower than those of HCs (*P* <0.05). After immunoregulatory combination treatments, the number of Tregs was significantly increased (*P* <0.05). Though the absolute numbers of T, NK, $CD4^+$T, $CD8^+$T, Th1, and Th17 cells were also increased to some degree (*P* <0.05), the increased amount of Tregs was much more than other cells, resulting a new balance between pro- and anti- inflammatory lymphocyte homeostasis.
Conclusion: The decrease of peripheral Tregs played an important role in the pathogenesis of primary Sjögren's syndrome. Immunoregulatory combination therapies promoted the increase of Tregs and might help for the recovery of pSS.

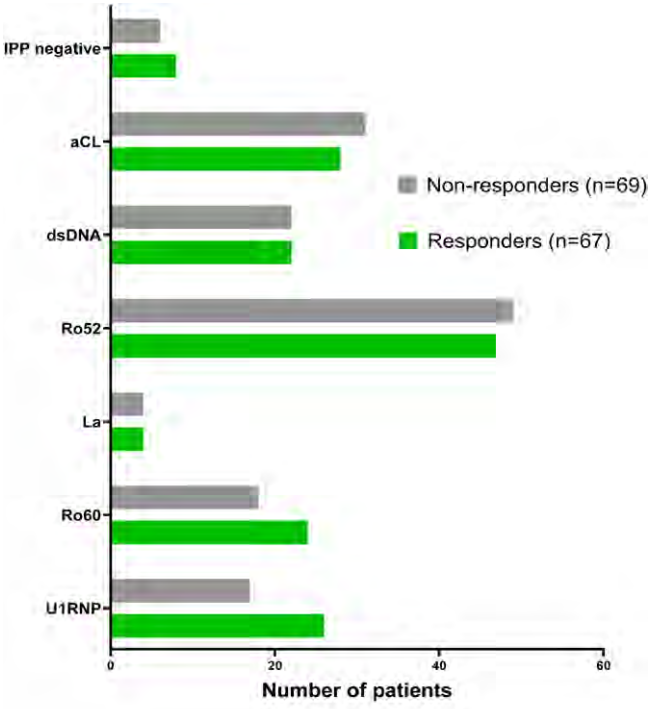


Figure 1

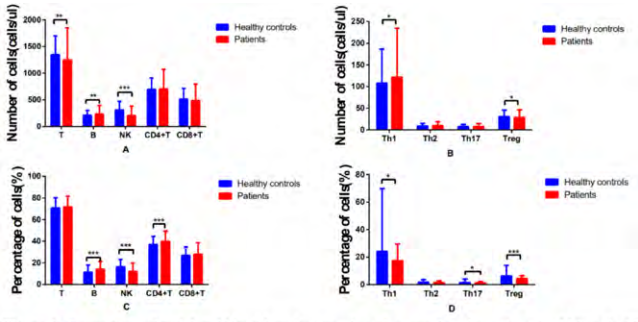


Figure 1: Comparison of peripheral blood lymphocyte subsets between healthy patients (n=206) and pSS patients (n=1221). All the lymphocytes subsets were analyzed by detected by flow cytometry combined with standard absolute counting beads. Data were presented as mean±SD and statistical analysis was determined by two-tailed unpaired t-test.(*P < 0.05, **P < 0.01, ***P < 0.001).

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[2] Miao M, Hao Z, Guo Y, et al. Short-term and low-dose IL-2 therapy restores the Th17/Treg balance in the peripheral blood of patients with primary Sjogren's syndrome. Ann Rheum Dis 2018;77(12):1838-40. doi: 10.1136/annrheumdis-2018-213036 [published Online First: 2018/06/25]
Acknowledgments : None.
Disclosure of Interests: None declared

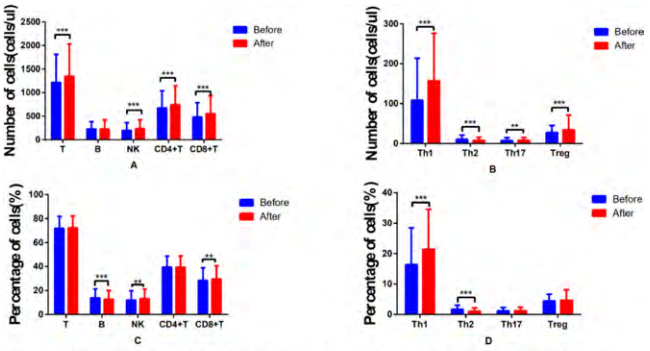


Figure 2: Changes of peripheral lymphocyte subsets after immunoregulatory combination treatment (n=79). Data were expressed as mean ± standard deviation to the distribution. Independent-samples T test and paired-samples T test were applied. P value <0.05 were considered statistically significant. (* *P*<0.05, ***P*<0.01, ****P*<0.001)

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SAT0184

MAINTENANCE THERAPY WITH AZATHIOPRINE ASSOCIATED WITH HIGHER RISK OF FLARE IN PROLIFERATIVE LUPUS NEPHRITIS

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Background: Goals of lupus nephritis (LN) maintenance treatment include prevention of LN flares and long-term preservation of renal function, while minimizing drug iatrogenicity. There is an unmet need for identifying predictors of LN flare in order to guide optimization of maintenance immunosuppression.
Objectives: To identify predictors of LN flare after attainment of complete renal response (CRR) in patients with proliferative LN.
Methods: Retrospective cohort study over 36 months including patients with SLE fulfilling the ACR'97 and/or the SLICC'12 classification criteria, enrolled in the CHUC Lupus Cohort between 1999 and 2018, with a biopsy-proven proliferative LN (class III/IV) and who attained CRR (proteinuria <0.5g/day and normal renal function, according to EULAR/ERA-EDTA definition) following induction treatment. Only proteinuric flares were considered and defined as doubling of proteinuria to >1g/day. Clinical-analytic characteristics at baseline (time of first CRR attainment after induction) were compared using survival analysis for time-to-flare. Variables with p<0.10 on univariate analysis with Log-Rank tests were further evaluated as predictors with multivariate Cox proportional hazards regression models (Backward Stepwise method, Wald-based), with estimation of hazard ratios (HR) with 95% confidence intervals (95%CI).
Results: A total of 50 patients in CRR were included in the analysis (78.4% female, age at baseline 30.0 ± 12.5 years-old). Over the follow-up period, 10 patients (20.0%) experienced a proteinuric flare, within a mean time of 29.1 months (95%CI 26.89-31.37). In univariate analysis, age <30years (p=0.020), arterial hypertension (p=0.020) and presence of anti-RNP antibody (p=0.002) at baseline were associated with higher risk of LN proteinuric flares. In multivariate analysis, age <30 years (HR 26.56; 95%CI 1.93-365.08; p=0.014), arterial hypertension (HR 8.30; 95%CI 1.21-56.92; p=0.031), use of antihypertensive antiproteinuric drugs (angiotensin-converting-enzyme inhibitors or angiotensin receptor blockers) (HR 11.18; 95%CI 1.24-100.66; p=0.031) and maintenance therapy with azathioprine (HR 6.23; 95%CI 1.51-25.66; p=0.011) (Figure 1) were predictors of LN proteinuric flares.

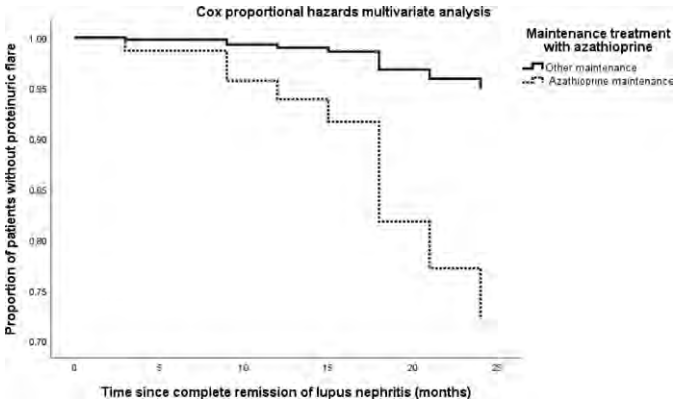


Figure 1.

Conclusion: In patients with proliferative LN, proteinuric flares are a frequent event after induction treatment leads to CRR. Younger age, arterial hypertension, use of antihypertensive drugs and use of azathioprine as maintenance therapy were risk factors for LN proteinuric flare in this cohort.

Disclosure of Interests: Mariana Luis: None declared, Ana Rita Prata: None declared, Helena Assunção: None declared, José Antonio P. da Silva Grant/ research support from: Pfizer, Abbvie, Consultant of: Pfizer, AbbVie, Roche, Lilly, Novartis, Luís Inês: None declared

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SAT0185

PREDICTORS OF POOR RENAL OUTCOME IN PATIENTS WITH PROLIFERATIVE LUPUS NEPHRITIS: A 36-MONTHS COHORT STUDY

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Background: The EULAR/ERA-EDTA recommendations for lupus nephritis (LN) state that renal response should be achieved within 12 months following induction therapy. However, there is an unmet need for early predictors of renal outcome in order to adjust the immunosuppression regimen and optimize the renal outcome.

Objectives: To identify predictors of poor renal outcome at baseline, 3 months and 6 months after starting induction therapy.

Methods: Retrospective cohort study over 36 months including patients with Systemic lupus erythematosus (SLE) fulfilling the ACR'97 and/or the SLICC'12 classification criteria and with biopsy-proven proliferative LN (class III/IV), enrolled in the CHUC Lupus Cohort from 1999 to 2018. Poor renal outcome was defined as longer time to complete renal response (CRR), characterized by proteinuria <0.5g/day and normal renal function, according to EULAR/ERA-EDTA criteria. Clinical-analytical characteristics at baseline, 3 months and 6 months after starting induction treatment were compared using survival analysis for time-to-CRR. Variables with p<0.25 on univariate analysis using Log-Rank tests were further evaluated as predictors applying multivariate Cox proportional hazards regression models (Backward Stepwise method, Wald-based) with estimation of hazard ratios (HR) and 95% confidence intervals (95%CI).

Results: 56 patients were included (76.8% female, age at LN diagnosis 30.0 ± 13.2 years). Over the follow-up, 51 patients (91.1%) achieved CRR, within a median time of 6.0 months. In multivariate analysis, predictors of poor renal outcome were proteinuria >2g/day at baseline (HR 1.98; 95%CI 1.04-3.77; p=0.037) and induction therapy with pulse cyclophosphamide (CYC), as compared to mycophenolate mofetil (MMF) (HR=2.05; 95%CI 1.07-3.94; p=0.030) (Figure 1). Diabetes mellitus (HR=6.0; 95%CI 1.24-29.07; p=0.026) and negative anti-RNP antibody (HR 3.17; 95%CI 1.27-7.93; p=0.013) at baseline predicted poor renal outcome at 3 months. At this timepoint, level of proteinuria and clearance rate were not predictive of renal response. At 6 months, no predictors of LN outcome were found for those patients that did not achieve CRR up to this timepoint. Use of glucocorticoid pulses and/or antihypertensive drugs did not predict LN outcome.

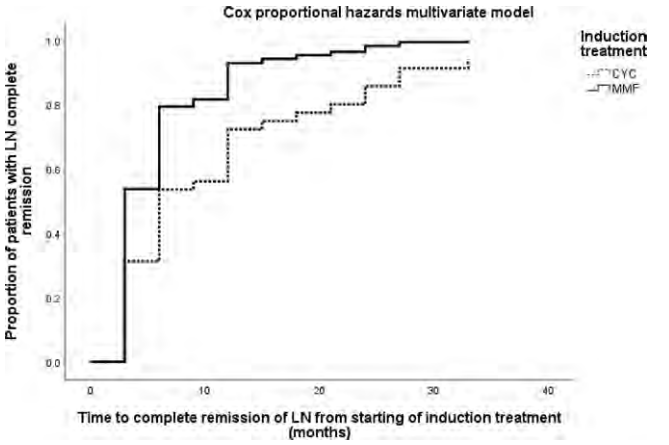


Figure 1.

Conclusion: In this SLE cohort, most patients with proliferative LN achieved CRR. Proteinuria above 2 g/day at baseline and diabetes mellitus were predictors of poor renal outcome, while positive anti-RNP was protective. Induction treatment with CYC was associated with poorer outcome as compared with MMF. Given the retrospective non-randomized nature of this study, caution is needed when drawing conclusions regarding both treatments efficacy.

Disclosure of Interests: Mariana Luis: None declared, Ana Rita Prata: None declared, Helena Assunção: None declared, José Antonio P. da Silva Grant/ research support from: Pfizer, Abbvie, Consultant of: Pfizer, AbbVie, Roche, Lilly, Novartis, Luís Inês: None declared

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SAT0186

DEVELOPING PREDICTORS OF GLOBAL BILAG TREATMENT RESPONSE IN PATIENTS WITH LUPUS NEPHRITIS: MORE LESSONS FROM THE ASPREVA LUPUS MANAGEMENT STUDY GROUP (ALMS) DATA

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Background: Lupus Nephritis (LN) occurs in up to 60% of patients with SLE and is often associated with other organ involvement, morbidity and mortality. Treatment response and clinical improvement rates are limited with conventional therapy. Little is known about clinical predictors of response in SLE overall or in LN.

The ALMS induction trial compared mycophenolate mofetil (MMF) to IV cyclophosphamide (CYC) as induction for LN. MMF was deemed non-superior. The ALMS maintenance trial randomised responders to induction treatment at 6 months to MMF or Azathioprine, with MMF superior during follow-up.

Objectives: To identify predictors of overall clinical response at 6 and 12 months, in a cohort of SLE patients with LN.

Methods: Using the ALMS trial cohort, we analysed predictors of response in all the patients as a single cohort. 'Classic' BILAG scores were used to assess organ responses over time. Endpoints analysed were:

1) Improvement: defined as reduction in BILAG score to ≤ one BILAG B and no new BILAG organ domains involved, no increase in steroids from baseline and no increase in SLEDAI from baseline.

2) Major Clinical Response (MCR): defined as reduction in BILAG score to BILAG C in all domains, a reduction in steroid dose to ≤ 7.5mg daily and a SLEDAI score ≤ 4.

Potential predictors examined included baseline demographics, medication, disease activity (BILAG, SLEDAI), SLICC/ACR damage index (SDI) and serology. Univariate logistic regressions were used to provide odds ratios of predictors. Multivariate logistic regressions with LASSO and cross-validation in randomly split samples were utilised to build prediction models. Predictors were ranked by the percentage of times they were selected by LASSO.

Results: 370 patients enrolled in the ALMS induction trial. 227 patients were randomised at 6 months to maintenance. 313(84.59%) patients were female. 147(39.72%) patients were Caucasian. The mean age was 31.9 years.

236(63.78%) patients had a disease duration of LN of < 1 year. Baseline mean(± SD) SLEDAI score was 15.28 (±6.78) and mean(± SD) numerical BILAG score was 19.61(±7.67).

Improvement at 6 months was attained by 180 (48.65%). Predictors included older age (OR=1.03 [95% CI: 1.01,1.05] per year) and normal haemoglobin (OR=1.90 [95% CI: 1.19, 3.05] vs low hb). Activity (BILAG A or B) in haematological and mucocutaneous domains predicted less improvement (OR [95% CI] = 0.59 [95% CI: 0.38, 0.94] and 0.50 [95% CI: 0.31,0.82] respectively). Baseline damage (SDI >1) negatively predicted improvement (OR 0.54 [95% CI: 0.31,0.92]).

Improvement at 12 months was acheived by 139 (37.57%). Low IgG predicted improvement (OR 4.66 [95% CI: 1.34,16.23]. Black US patients were less likely to improve (OR 0.29 [95% CI: 0.06,0.90] vs Asian patients).

MCR was achieved by 14(3.79%) and 40(10.81%) at 6 and 12 months. We found regional and racial differences in 12-month MCR responses (Figure 1). Baseline normal C4 predicted a decreased likelihood of MCR (OR 0.37 [95% CI: 0.17,0.64] vs normal C4).

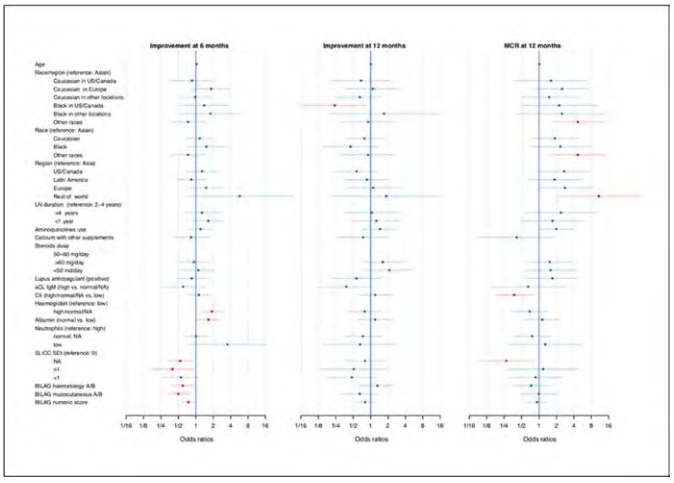


Figure 1. Univariate analysis of Improvement at 6 and 12 months and MCR at 12 months.

Results of multivariate logistic regression with LASSO were consistent with the univariate analyses.

Conclusion: A number of factors were related to improvement and MCR in conventionally treated LN patients. Those with damage and active non-renal disease were less likely to improve at 6 months. Baseline low C4 increased MCR likelihood at 12 months. These factors may help stratify patients based on likelihood of response and help select patients who may need alternative treatment strategies.

Disclosure of Interests: Stephen McDonald: None declared, Sean Yiu: None declared, Li Su: None declared, Caroline Gordon Grant/research support from: UCB, Consultant of: UCB, BMS, EMD Serono, Speakers bureau: UCB, Neil Solomons Shareholder of: Aurinia Pharmaceuticals, Inc. stock, Employee of: Employed currently by Aurinia Pharmaceuticals

Previous employee of Aspreva Pharmaceuticals, Ian N. Bruce Grant/research support from: Genzyme Sanofi, GSK, and UCB, Consultant of: Eli Lilly, AstraZeneca, UCB, Iltoo, and Merck Serono, Speakers bureau: UCB

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SAT0187

DISCRIMINATION OF SYSTEMIC LUPUS (SLE) PATIENTS WITH CLINICAL RESPONSE TO OBEXELIMAB (XMAB®5871) BASED ON A PATTERN OF IMMUNOLOGIC MARKERS

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Background: We recently reported Phase 2 SLE trial results of obexelimab, an FcγRIIb agonist (suppressor of B cell activation). Obexelimab did not meet the primary endpoint (% of patients without flare at Day 225) (p=0.183) but other endpoints such as time to flare (p=0.025) were met.

Objectives: 1. To assign SLE patients to phenotypic subsets based on patterns of gene expression in immune-related pathways.[1] 2. To explore the association of immune patterns and clinical response to obexelimab.

Methods: This analysis included 71 of the 104 participants in the obexelimab study, those who either completed the protocol or terminated for disease flare, if there were adequate blood samples (biomarker subset). At screening, patients were assigned to clusters based on 41 SLE co-expression signature modules from the Human Immune Phenotyping Consortium via unsupervised random forest and K-means clustering.[2] Other markers of SLE disease were also examined. The *BOLD*[3] study design mandated withdrawal of background immunosuppressants, supporting less ambiguous pharmacodynamic analysis as the trial progressed.

Results: Immune pathway expression patterns of 7 patient clusters (Fig 1a) confirmed our prior characterization of 200 non-overlapping SLE patients.[2] The biomarker subset retained a trend of longer time to first flare in patients receiving obexelimab (n=38) vs placebo (n=33) (Fig1b, HR 0.61, p=0.11). A smaller set of only Clusters 3 and 6 demonstrated marked increased time to flare in the obexelimab group (n=13) compared to placebo (n=14) (Fig 1c, HR 0.22, p=0.025). Obexelimab had no effect on other clusters (Fig 1d). The responder clusters shared low expression of inflammation modules ($p < 0.001$) compared to other clusters and high expression of T Cell, immune response, cell cycle, mitochondrial modules (all $p < 0.001$) and B Cell modules (p=0.006). We therefore sorted patients by these specific features regardless of cluster assignment. Figure 2 shows significant impact of obexelimab on time to flare in 64 patients with B Cell pathway activation (HR 0.5, p=0.038), although less robust by itself than found in Clusters 3 and 6. In a group with high B or plasma cell modules but low inflammation (n=46), treatment effect increased (HR 0.35, p=0.019). Between Screening and Baseline, as brief steroids were given and background treatments withdrawn, expression of B Cell and Plasma Cell pathways increased. Both then decreased after treatment with obexelimab but not placebo ($p< 0.0001$ and $p< 0.001$ respectively), an effect not seen with other immune pathway modules.

Conclusion: Precision medicine for SLE has been hampered by heterogenous immune signals with variable expression. Clustering of patients by gene co-expression pathways enabled an efficient, hierarchical array that reduplicated results of a prior SLE cohort, suggesting these are not random phenotypes. Of these 7 reproducible SLE subsets, the combination of clusters 3 and 6 distinguished an obexelimab responder population of 27 out of 71 subjects (38%) with high expression of B and T Cell modules and cell activation pathways. Focus on the defining features shared by these clusters revealed specific factors associated with response, enabling inclusion of some patients from other clusters in an optimized responder population of 46/71 (65% of subjects). B Cell and Plasma Cell pathways demonstrated mechanism-related pharmacodynamic effects of obexelimab. Lack of responders with high expression of inflammation modules could implicate inhibitory factors to obexelimab within inflammatory pathways, potentially targetable by complementary treatments.

References:

[1] Banchereau Cell 165:1548 2016
[2] Lu ACR Abstract #2977 2017
[3] Merrill Arthritis Rheumatol 69: 1257 2017

Fig 1: Effects of Obexelimab Treatment on Time to Flare in SLE Patient Subsets Defined by Patterns of Gene Co-Expression Pathways

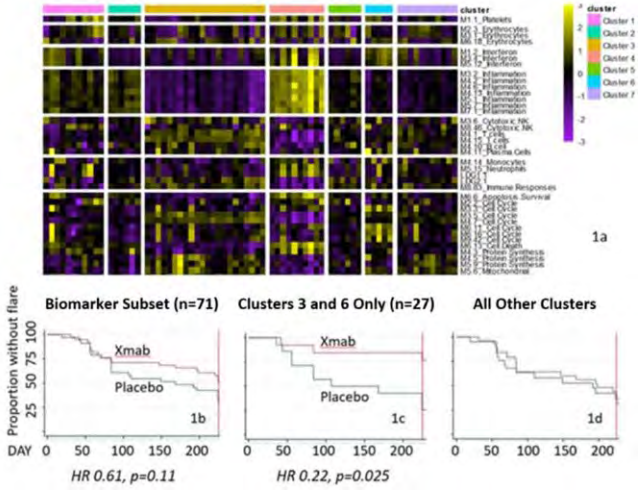
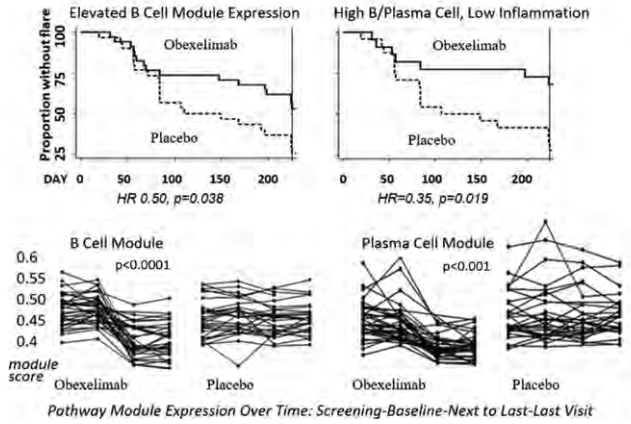


Fig 2: Positive Role of B Cells/Plasma Cells and Negative Role of Inflammation in Response to Obexelimab



Pathway Module Expression Over Time: Screening-Baseline-Next to Last-Last Visit

Disclosure of Interests: : Joan T Merrill Grant/research support from: Xencor, Bristol Myers Squibb, Glaxo Smith Kline, Consultant of: Xencor, Abbvie, UCB, Glaxo Smith Kline, EMD Serono, Astellas, Remegen, Celgene/Bristol Myers Squibb, Exagen, Astra Zeneca, Amgen, Jannsen, Servier, ILTOO, Daitchi Sankyo, Lilly, Paid instructor for: Abbvie, Bristol Myers Squibb, Joel Guthridge Grant/research support from: Xencor, Bristol Myers Squibb, DXterity, Debra Zack Shareholder of: Xencor, Employee of: Xencor, Paul Foster Shareholder of: Xencor Inc, Employee of: Xencor Inc, Bart Burington Shareholder of: Xencor Inc, Employee of: Xencor Inc, Ly Tran: None declared, Miles Smith: None declared, Judith A. James Grant/research support from: Progentec Diagnostics, Inc, Consultant of: Abbvie, Novartis, Jannsen

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SAT0188

HIGH-DOSE STEROIDS ARE IMPORTANT CONTRIBUTORS TO THE INFECTION BURDEN OF PATIENTS WITH LUPUS NEPHRITIS

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Background: Infection remains a major cause of morbidity and mortality in patients with systemic lupus erythematosus (SLE) and lupus nephritis (LN) treated with systemic immunosuppression (IS).

Objectives: We sought to describe the infection profile in patients with LN treated with aggressive immunosuppression (induction and maintenance therapy) and to identify the associated risk factors.

Methods: Patients with LN followed in the Nephrology Department of Fundeni Clinical Institute, were retrospectively reviewed for any infection that occurred from initiation of induction therapy. Infections were graded (1-5) according to the Common Terminology Criteria for Adverse Events. Infection site and type of microorganism were also recorded. Univariate and multivariate Cox proportional hazard regression analysis were performed in order to identify independent risk factors for infection.

Results: The study cohort comprised 101 patients (86.1% females) with a mean age of 34 ± 14 years. Forty-eight patients (47.5%) had at least one infection with a total 92 episodes of infection occurring during a median follow-up of 17 months (IQR:8.5-52.5 months). The majority of patients (31 of 48) had infections during the first 12 months since IS treatment initiation. The most common site was lung infection (in 24.8% of patients), followed by urinary tract (20.8% of patients) and cutaneous/mucosal infections (11% of patients). Thirty-eight percent of patients had bacterial infections. Nineteen percent of patients had severe infections (grade 3 or higher) with 3.3% of infection-related deaths (3 patients). The most common induction regimen was cyclophosphamide in addition to corticosteroids (48.5%), with 44.6% of patients receiving pulse methylprednisolone and 45.5% of patients receiving more than 30 mg/d of prednisone as the maximum oral dose. In univariate Cox regression analysis, female gender (HR 3.34; 95% CI, 1.03-10.8, p=0.04), pulse methylprednisolone (HR 2.9; 95% CI, 1.6-5.24, p=0.001), high-dose (≥30 mg/day) oral corticosteroids (HR 4.22; 95% CI, 2.21-8.02,p=0.001) and SLEDAI score (HR 1.047; 95% CI, 1.012-1.084, p=0.008) were risk factors for infection. In multivariate Cox regression analysis, female gender (HR 6.35; 95%CI, 1.86-21.64,p=0.003), high-dose oral corticosteroids (HR 4.7; 95% CI, 2.25-9.87, p=0.003) and SLEDAI score (HR 1.046; 95% CI, 1.003-1.09, p=0.034) remained independent predictors of infection risk. Of the risk factors associated with severe infections (grade 3 or higher), in univariate analysis we identified younger age (HR 0.96, 95%CI, 0.92-0.99, p=0.035), neurological involvement (HR 2.59; 95%, 0.86-7.83, p=0.09), pulse methylprednisolone (HR 5.42; 95% CI, 1.79-16.35, p=0.003) and high-dose oral corticosteroids (HR 8.32; 95% CI, 2.4-28.77, p=0.001) as risk factors for infection. After multivariate adjustment, neurological involvement (HR 4.33; 95%, 1.29-14.51, p=0.01) and high-dose oral corticosteroids (HR 7.6; 95% CI, 1.6-35.39, p=0.01) were identified as independent predictors of infection risk.

Conclusion: A high-dose oral corticosteroid regimen increased the risk for any infection and for severe infections by 4.7-fold and 7.6-fold, respectively. In addition, female gender and a higher SLEDAI score were identified as risk factors for any infection, while neurological involvement was associated with an increased risk for severe infections.

References:

[1] Jung JY, Yoon D, Choi Y, Kim HA, Suh CH. Associated clinical factors for serious infections in patients with systemic lupus erythematosus. Sci Rep. 2019;9(1):9704.

Disclosure of Interests: : None declared

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SAT0189

SAMPLE SIZES AND RECRUITMENT RATES ARE DECREASING WHILE PLACEBO RESPONSE RATES ARE INCREASING IN CLINICAL TRIALS FOR SYSTEMIC LUPUS ERYTHEMATOSUS - A MANDATE FOR NEW STRATEGIES

E. Olech[1], E. Van Rijen[1], F. Hussain[1], G. Dennis[1], A. Ashrafzadeh[1], J. T. Merrill[2]. [1]*IQVIA, Rheumatology Center of Excellence, San Diego*; [2]*Oklahoma Medical Research Foundation, Oklahoma City, United States of America*

Background: Randomized controlled trials in Systemic Lupus (SLE) have shown disappointing results for decades. Key challenges may include the heterogenous population coupled with high placebo response rates.

Objectives: To evaluate trends in SLE study metrics over time and explore associations between primary endpoint failure and response in placebo/standard of care arms.

Methods: Data from Phase II or III trials which enrolled ≥ 100 patients with SLE and reported SRI-4 and/or BICLA responses after a minimum of 24 weeks were included in the analysis. Sample size, recruitment rates, regional patient distributions, and results in placebo arms (at 24-36 weeks or 48-52 weeks) were examined according to the start date of each study in order to determine trends over time. Placebo group SRI-4 response rates in studies that met their primary endpoint were compared with those that did not.

Results: Twenty-seven (14 phase II and 13 phase III) studies met the search criteria. Eleven of them met their primary endpoints. The study start dates ranged from Dec 2006 to Jan 2017. Mean/median total subject numbers were 461/349. Mean/median placebo subjects' age at baseline were 39.9/39.2 and SLEDAI: 10.6/10.6. Mean/median placebo SRI-4 responses at Week 24-36 were 47.2%/45.8% and 42.8%/43% at Week 48-52. For BICLA, the rates were 40.3%/37.2% at Week 24-36 and 33.2%/33.5% at Week 48-52.

As expected, lower placebo response was found in trials that met primary endpoints vs studies that did not (p=0.005). Total subject numbers and recruitment rates decreased over time while placebo SRI-4 response rates increased overall (Figure). However, there has been a greater range of placebo responses in more recent trials. Similar trends were observed in BICLA responses at Week 24-36 and 48-52, and in a corticosteroid reduction endpoint (percent of patients with reduction in steroid dose by ≥25% and to ≤7.5 mg/day prednisone/equivalent) at Week 48-52. Enrollment of patients from North America decreased while proportions of Eastern Europeans increased over time (Figure).

Conclusion: High placebo response rates pose a continuing challenge in SLE studies and are associated with primary endpoint failures.

Clinical trial metrics have been changing over time, with declining size and recruitment rates, possibly due to competition from increasing numbers of studies.



Figure.

These trends should be considered while designing and conducting future trials. Attention to site training and data quality may be particularly important to control high placebo rates, especially as trial sizes decrease.

Disclosure of Interests: Ewa Olech Grant/research support from: BMS, Consultant of: Abbvie, Amgen, Remegen, Employee of: IQVIA, Speakers bureau: Abbvie, Amgen, Merck, Pfizer, UCB, Eduard van Rijen Employee of: IQVIA, Faizi Hussain Employee of: IQVIA, Gregory Dennis Employee of: IQVIA, Ali Ashrafzadeh Employee of: IQVIA, Joan T Merrill Grant/research support from: Xencor, Bristol Myers Squibb, Glaxo Smith Kline, Consultant of: Xencor, Abbvie, UCB, Glaxo Smith Kline, EMD Serono, Astellas, Remegen, Celgene/Bristol Myers Squibb, Exagen, Astra Zeneca, Amgen, Jannsen, Servier, ILTOO, Daitchi Sankyo, Lilly, Paid instructor for: Abbvie, Bristol Myers Squibb

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SAT0190 CORTICOSTEROID AND OPIOID USE REMAIN HIGH IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) PATIENTS RECEIVING BIOLOGIC THERAPY: A RETROSPECTIVE CLAIMS DATABASE ANALYSIS

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Background: SLE is managed by variable combinations of five drug classes: antimalarials, biologics, corticosteroids, non-steroidal anti-inflammatory agents, and immunosuppressants. Opioids are commonly prescribed to SLE patients despite not being effective for the management of long-term musculoskeletal pain.[1]

Objectives: To describe corticosteroid and opioid use among SLE patients in the United States, and the impact of belimumab initiation on prescribing patterns.

Methods: This retrospective study used MarketScan administrative claims databases to select insured adults, age ≥18, with a diagnosis (ICD-9/10 710.0 & M32) of SLE between 1/1/2012 and 5/31/2018 (earliest SLE diagnosis = index date). Patients were followed from index through the earliest of health plan disenrollment or 5/31/2019 (minimum of 12 months). Corticosteroid use was measured in the 12 months following SLE index date. Average daily dose of oral corticosteroids in prednisone equivalents was measured for 12 months after corticosteroid initiation. Opioid use was measured overall, and by strength and length of treatment (chronic use defined as >90 days of supply). Oral corticosteroid and opioid use were compared in the 6 months before and after initiation of belimumab.

Results: Of 49,413 SLE patients eligible for analysis, mean [SD] age was 50.1 [14.0] years, 90.2% were female, and average follow-up was 3.6 [1.9] years. 89.8% of patients received any SLE treatment and 68.5% received corticosteroids. The average number of corticosteroid prescriptions was 4.6 [4.1] during 12 months of follow-up. 52.6% of patients had ≥1 claim for an opioid prescription in the 12 months after SLE index and 34.6% were identified as having chronic opioid treatment. Among patients with oral corticosteroid treatment and 12 months of study enrollment post-corticosteroid initiation, the average daily dose for oral corticosteroids was 19.4 [14.2] mg and 59.6% had a high average daily dose of >15mg (Figure 1). Among 1,710 patients with belimumab treatment and 6 months of study enrollment after the first prescription, use of oral corticosteroids decreased by 9.1% (p=0.001), average daily dose decreased from 14.5 [18.4] mg to 11.9 [18.0] mg (p<0.001) in the 6 months post initiation as compared to the 6 months prior. However, 48.6% of patients remained on a medium (7.5mg – <15mg) or high dose (≥15mg). Initiation of belimumab resulted in no change in opioid use (Table 1).

Table 1.

	Before Belimumab		After Belimumab		p-value, pre vs.
	(N =	1,710)	(N =	1,710)	post Belimumab
Patients with an oral steroid prescription (N, %)	**1,242**	**72.6%**	**1,086**	**63.5%**	**0.001**
Number of prescriptions (Mean, SD)	2.3	2.3	2.1	2.3	**<0.001**
Average daily dose (Mean, SD)	14.5	18.4	11.9	18.0	**<0.001**
Low average daily dose (>0 to <7.5 mg) (N, %)	210	12.3%	255	14.9%	**0.037**
Medium average daily dose (7.5 - <15 mg) (N, %)	389	22.7%	334	19.5%	**0.041**
High average daily dose (15 mg or more) (N, %)	643	37.6%	497	29.1%	**<0.001**
Patients with an opioid prescription (N, %)	901	52.7%	861	50.4%	0.341
Weak opioids	356	20.8%	312	18.2%	0.089
Strong opioids	699	40.9%	695	40.6%	0.915
Acute Opioid Use	538	59.7%	486	56.4%	0.165
Chronic opioid use	363	40.3%	375	43.6%	0.165

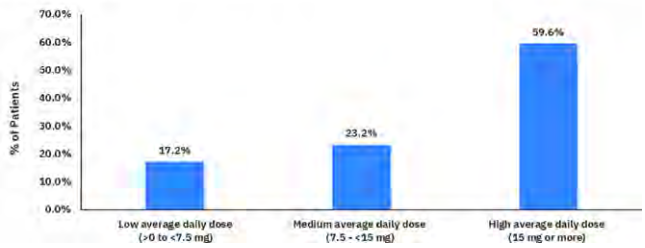
Conclusion: These results suggest that a strikingly high proportion of patients with SLE are treated with corticosteroids to control the disease and opioid therapy to manage chronic pain. While there was no change in opioid use, corticosteroid use decreased following initiation of belimumab.

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Disclosure of Interests: : Julie Birt Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Jianmin Wu Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Kirstin Griffing Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Natalia Bello Vega Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Nicole Princic Employee of: I work for IBM Watson Health who was paid by Eli Lilly who funded this research., Isabelle Winer Employee of: I work for IBM Watson Health who was paid by Eli Lilly who funded this research., Carolyn Lew Employee of: I work for IBM Watson Health who was paid by Eli Lilly who funded this research., Karen Costenbader Grant/research support from: Merck, Consultant of: Astra-Zeneca

Figure 1: Steroid Dosing During the 12 Months Following Initiation of Oral Steroids



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SAT0191 PLASMA PROTEOMICS IDENTIFIES A PROTEIN SIGNATURE ASSOCIATED WITH RESPONSE TO RITUXIMAB IN PATIENTS WITH SLE

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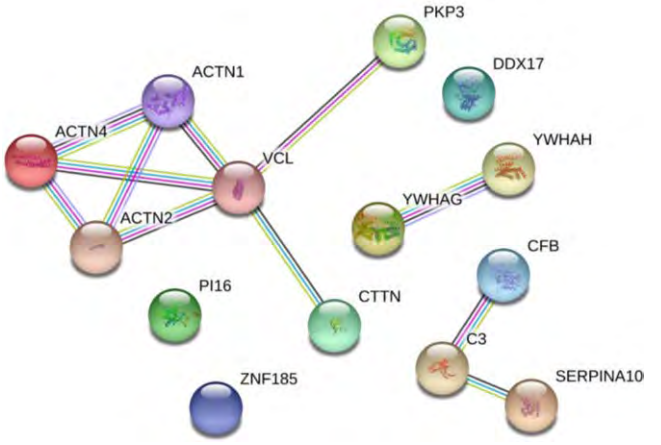
Background: Rituximab (RTX) is B cell-depleting biological therapy used in the treatment of systemic lupus erythematosus (SLE). Response rates are typically around 50% and there are currently no robust biomarkers to identify which patients are more likely to respond.

Objectives: To determine whether proteomic analysis of baseline plasma samples could identify novel biomarkers of response to RTX in patients with active SLE.

Methods: Patients with SLE (≥ 4 ACR criteria) receiving RTX for active disease (BILAG A or 2 BILAG B scores) from the UK-based BILAG-BR register were included. Improvement at 12 months was defined as a reduction to ≤ 1 BILAG B score with no increase in either SLEDAI score or steroid dose. Proteomic analysis was performed on baseline plasma samples using sequential window acquisition of all theoretical fragment ion spectra mass spectrometry (SWATH-MS). Data were aligned and normalised to give relative protein abundance. A Lasso penalised logistic regression, with an outcome of improvement at 12 months, was used to perform the variable selection procedure using the R package 'glmnet'. The penalty metric was set at the value which minimised deviance in a 10-fold cross-validation procedure. Confounding variables of sex, age, ethnicity, oral steroid dose, and SLEDAI score had no penalty applied and were thus forcibly retained in the model. Protein-protein interaction networks were visualised using STRING v11.0.

Results: 70 patients of whom 63/70 (90%) were female with a median (IQR) age of 41 (32, 51) years and disease duration of 11 (6, 20) years at baseline were included. Patients had active disease with a median SLEDAI score of 10 (6, 16). All patients received RTX according to NHS England guidelines. Of 829 proteins, 815 were detected in at least 1 patient. We identified 9 proteins which were associated with clinical improvement at 12 months. A literature search identified that these proteins have relevance to T cell function, complement activation and lupus nephritis. Gender had the greatest weight in the model followed by Serpin Family A Member 10 (SERPINA10) and complement factor B (CFB). Protein interaction networks linked SERPINA10 to CFB by C3 complement (figure).

Conclusion: Plasma proteome analysis has identified a protein signature associated with response to RTX in SLE. These findings will be validated in independent cohorts and may offer the ability to predict response to RTX in lupus patients.



Protein Interaction Network of the 9 proteins from the multivariable model (with one additional level added). Cyan/magenta lines shown known interactions. Other colours show predicted interactions.

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SAT0192

TRAJECTORIES OF LUPUS DISEASE ACTIVITY OVER TIME IN THE CLINICAL TRIAL SETTING REVEALED BY LATENT CLASS MIXED MODELS

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Background: There is considerable debate regarding the most appropriate outcome measures for clinical trials in systemic lupus erythematosus (SLE). We propose that studying changes in disease activity over time may yield important information above and beyond fixed endpoints at 12 months.

Objectives: To compare outcomes and predictors of response using i) traditional response definitions at a fixed time point and ii) trajectories of disease activity over time in a clinical trial dataset.

Methods: Data from the phase 3 clinical trial of Epratuzumab (EMBODY) in patients with active SLE were reanalysed. Response at 12 months was defined as: reduction to ≤1 BILAG B score, no increase in SLEDAI-2K score and no increase in prednisolone dose. Latent class mixed models (LCMM) were constructed using the numerical BILAG-2004 (nBILAG) score (where A=12, B=8, C=1, D/E=0) from the screening visit until trial end. Cumulative prednisolone and Epratuzumab exposure was determined by estimating the area under the dose-time or concentration-time curves (AUC) respectively.

Results: 1202 patients were included with a median disease duration of 5.6 [1.9, 12.7] years and baseline nBILAG score of 20 [16, 24]. At 12 months there were 564/1202 (46.9%) responders. There was no association between receiving Epratuzumab and response. Responders were older, with lower baseline nBILAG score and baseline steroid dose. Using a cubic spline LCMM in the whole cohort, 5 trajectories were identified: Non-responders (NR, 33.9%), rapid responders (RR, 36.7%), slow responders (SR, 20.7%), flare (F, 4.7%) and high disease activity (HDA, 3.9%) (figure). Of the 564 12-month responders, 113 (20.4%) were in the NR latent class whilst 417 (73.9%) were in RR or SR classes. Whilst there were no differences in study drop-out due to adverse events, withdrawal due to inefficacy was 20.6% in NR compared to 8.4% in RR and 7.6% in SR.

In multivariable logistic regression models adjusted for age, gender and study drop-out, being a responder (RR or SR) was significantly associated with activity in constitutional, musculoskeletal and cardiorespiratory BILAG domains, higher baseline and cumulative steroid exposure, and receiving active drug.

There was a trend towards higher baseline CD19+ counts in RR compared to NR or SR (p=0.108) but in a population-averaged multivariable linear model only baseline CD19+ count, Epratuzumab and steroid dose were associated with number of CD19+ cell over time (p<0.001 for each).

Conclusion: Compared to a fixed end-point at 12 months, LCMM identified trajectories of disease activity and an association between clinical improvement and receiving active drug. Predictors of response vary significantly according to the response definition used.

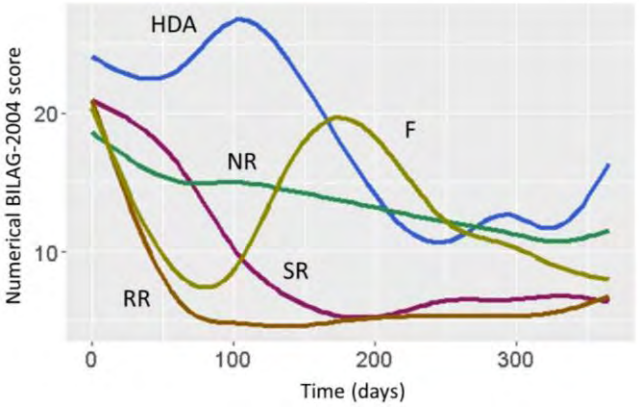


Table. Comparison of predictors of response between the 2 models

	Response at 12 months	Response latent call (RR or SR)
Age	Yes	No
Baseline gBILAG score	Yes (negative)	Yes (positive)
Baseline steroid dose	Yes	Yes
Active disease		
Constitutional	No	Yes
Musculoskeletal	No	Yes
Cardiorespiratory	No	Yes
Gastroenterological	Yes	No
Anti-Smith	Yes	No
Low C3	Yes	No
Epratuzumab	No	Yes

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SAT0193

A PHASE 3, OPEN-LABEL, CONTINUATION STUDY EVALUATING LONG-TERM SAFETY AND EFFICACY OF BELIMUMAB IN PATIENTS FROM JAPAN AND KOREA WITH SYSTEMIC LUPUS ERYTHEMATOSUS, FOR UP TO 7 YEARS

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disorder more prevalent in the Asian population vs Caucasians. Belimumab (BEL), a monoclonal antibody targeting B-lymphocyte stimulator, is approved in patients (pts) ≥5 years with active, autoantibody-positive SLE.

Objectives: Evaluate long-term safety and efficacy of intravenous (IV) BEL + standard SLE therapy (SST) in pts with SLE in Japan/Korea.

Methods: In this Phase 3, multicentre, open-label (OL) study (BEL114333; NCT01597622), eligible (≥18 years of age) completers of the double-blind phase of GSK study BEL113750 in Japan and South Korea or the subcutaneous OL phase of GSK Study BEL112341 in Japan, received monthly BEL 10 mg/kg IV

plus SST. Primary endpoints: safety assessments. Key secondary endpoints: SRI4 response rate at each scheduled visit (observed data), defined as a ≥4-point reduction from baseline in SELENA-SLEDAI score, no worsening in PGA (<0.3-point increase from baseline) and no new BILAG 1A/2B organ domain scores; time to first severe SFI flare over time. Endpoints were analysed relative to first BEL dose (parent or current study). No follow-up data were collected after study withdrawal.

Table.

Endpoint, n (%)	Anytime post baseline N=142	Year 0–1 n=142	Year 1–2 n=136	Year 2–3 n=108	Year 3–4 n=79	Year 4–5 n=32	Year 5–6 n=24	Year 6+ n=13
≥1 AE	139 (97.9)	133	122	81	59	30	24 (100)	9
≥1 severe AE	27 (19.0)	(93.7) 12 (8.5)	(89.7) 10 (7.4)	(75.0) 7 (6.5)	(74.7) 2 (2.5)	(93.8) 1 (3.1)	1 (4.2)	(69.2) 0
≥1 treatment-related AE	81 (57.0)	46 (32.4)	38 (27.9)	20 (18.5)	11 (13.9)	9 (28.1)	3 (12.5)	1 (7.7)
≥1 SAE	48 (33.8)	24 (16.9)	18 (13.2)	9 (8.3)	6 (7.6)	2 (6.3)	3 (12.5)	0
Serious infections and infestations	24 (16.9)	14 (9.9)	5 (3.7)	2 (1.9)	3 (3.8)	0	1 (4.2)	0
Deaths	1 (0.7)*	0	0	0	0	0	0	0
AESI								
Malignancy	1 (0.7)	0	1 (0.7)	0	0	0	0	0
Opportunistic infections	10 (7.0)	3 (2.1)	4 (2.9)	1 (0.9)	1 (1.3)	0	0	0
Post-infusion systemic reactions	20 (14.1)	7 (4.9)	4 (2.9)	4 (3.7)	2 (2.5)	5 (15.6)	1 (4.2)	0
Depression/suicide/ self-injury†	9 (6.3)	4 (2.8)	2 (1.5)	1 (0.9)	1 (1.3)	0	0	0

*Death from an AE of endocarditis that began ~1 month after the exit visit; the investigator considered it to be unrelated to the study drug

†No serious suicide/self-injury AEs were reported during the study

Results: Overall, 142 pts were enrolled (Japan n=72; Korea n=70), 104 (73.2%) completed the study, 1 (0.7%) died and 37 (26.1%) withdrew.

Overall, 139 (97.9%) pts had ≥1 adverse event (AE) (**Table**). Most frequent AEs included: nasopharyngitis (60.6%); headache (28.2%); cough, herpes zoster and viral upper respiratory tract infection (18.3% each). Serious AEs (SAEs) occurred in 48 (33.8%) pts. Most common SAEs were infections and infestations, reported in 24 (16.9%) pts (**Table**). During this study, the annual incidence of AEs, including SAEs and AESI, remained stable or declined, with no trends of clinical concerns regarding the incidence of Grade 3 or 4 values for laboratory parameters. There was 1 transient positive immunogenicity result of no clinical concern.

The proportion of SRI4 responders was 47.8% at Year 1 (Week 24) and tended to increase numerically up to 84.6% at Year 7 (Week 48). The proportion of pts with a ≥4-point decrease from baseline in SELENA-SLEDAI score numerically increased from 51.5% at Year 1 (Week 24) to 84.6% at Year 7 (Week 48). Proportion of pts with no PGA worsening was 91.3-100% and the proportion with no new BILAG 1A/2B organ domain scores was 93.3-100% up to Year 7 (Week 48). A total of 21 (14.8%) pts had 24 severe SFI flares.

Conclusion: BEL was well tolerated as add-on therapy to SST for ≤7 years in pts with SLE from Japan/Korea. Safety results were consistent with the known BEL safety profile.

Study funding: GSK.

Disclosure of Interests: Yoshiya Tanaka Grant/research support from: Received research grants from Asahi-Kasei, Mitsubishi-Tanabe, Chugai, Takeda, Sanofi, Bristol-Myers, UCB, Daiichi-Sankyo, Eisai, Ono, Speakers bureau: Received speaking fees and/or honoraria from Daiichi-Sankyo, Astellas, Chugai, Eli Lilly, Pfizer, AbbVie, YL Biologics, Bristol-Myers, Takeda, Mitsubishi-Tanabe, Novartis, Eisai, Janssen, Teijin, Sang-Cheol Bae: None declared, Damon Bass Shareholder of: GSK, Employee of: GSK, Myron Chu Shareholder of: GSK, Employee of: GSK, Paula Curtis Shareholder of: GSK, Employee of: GSK, Kathleen DeRose Shareholder of: GSK, Employee of: GSK, Beulah Ji Shareholder of: GSK, Employee of: GSK, Regina Kurrasch Shareholder of: GSK, Employee of: GSK, Jenny Lowe Shareholder of: GSK, Employee of: GSK, Paige Meizlik Shareholder of: GSK, Employee of: GSK, David Roth Shareholder of: GSK, Employee of: GSK

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SAT0194 LACK OF EFFICACY OF RIVAROXABAN IN THE TREATMENT OF ANTIPHOSPHOLIPID SYNDROME AND CLINICAL SIGNIFICANCE OF ANTIPHOSPHOLIPID ANTIBODIES

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Background: Chronic anticoagulation with vitamin K antagonists (VKA) is the standard treatment to prevent thrombotic events in antiphospholipid syndrome (APS). But in recent years treatment schemes began to include rivaroxaban. Use of direct oral anticoagulants (DOAC) is an attractive and often preferred alternative to VKAs in other medical settings owing to greater ease of use, fewer food and drug interactions, and lower bleeding risks [1].However, according to last guidelines, rivaroxaban should not be used in patients with triple aPL positivity due to the high risk of recurrent events [2].

Objectives: 1.To determine the risk of recurrent thrombosis in single or double positive APS patients treated with rivaroxaban.

2.Find out possible association between presence of particular antiphospholipid antibodies or high level of lupus anticoagulant (LA) and type of vascular events.

Methods: 33 patients with confirmed APS (25 female (75.8%), 8 male (24.2%), mean age 43.2±11.6 years) were included in the study. 17 (51.5%) of investigated patients had primary APS, in remaining 16 (48.5%) APS was included in the framework of SLE. 18 (54.5%) patients were treated with warfarin 2.5-7.5 mg/daily, 15 (45.5%) patients - with rivaroxaban 20mg/daily for a follow-up period of 12 months. The data is introduced as odds ratios (OR) with 95% confidence interval (CI). The results were considered significant when p <0.05.

Results: At baseline 21 (63.6%) patients had history of arterial thrombosis, 10 (30.3%) - venous thrombosis, 17 (51.5%) - pregnancy loss. According to results of serum immunology check, 29 (87.9%) patients were anticardiolipin antibody (ACA) positive, 9 (27.3%) - LA positive, 19 (57.6%) - anti-ß2-glycoprotein antibodies (anti-ß2-gp) positive; 20 (60.6%) patients were double positive (12 (36.4%) of them had positive ACA and anti-ß2-gp, 6 (18.2%) - ACA and LA, and 2 (6.1%) - anti-ß2-gp and LA), 4 (12.1%) patients were triple positive.

No association between vascular event and/or pregnancy loss in patients with single positive ACA was found. We have found positive association between arterial thrombosis and single positive anti-ß2-gp (OR /CI 95%/ = 5.0 /2.08 – 23.06/, p< 0.05), positive association between positive LA and venous thrombosis (OR /CI 95%/ = 10 /1.7-57.7/, p< 0.05), strong positive association between positive LA and thromboembolism of pulmonary artery (OR /CI 95%/ = 46.0 /4.0-525.1/, p< 0.001), negative association between positive LA and pregnancy loss (OR /CI 95%/ =0.06 /0.03 – 0.1/, p< 0.01).

Risk of thrombosis and/or pregnancy loss was not significantly increased in double positive patients, but triple positive patients had increased risk of venous thrombosis (OR /CI 95%/ =9.4 /3.2 – 105.8/, p<0.04).

Recurrent thrombosis was detected in 16 patients: 2 patients (12.5%) were on warfarin, 14 (87.5%) - on rivaroxaban (10 (71.4%) arterial thrombosis, 4 (28.6%) venous thrombosis).

No association between warfarin 2.5-7.5 mg/daily and occurrence of recurrent thrombosis was detected. An association between use of warfarin and increased risk of bleeding was found, but the risk was not significant (OR /CI 95%/ = 7.0 /0.7 – 66/, p= 0.09). Rivaroxaban 20 mg/daily was associated with recurrent thrombosis not only for triple positive patients (p< 0.02), but also in double positive patients (OR /CI 95%/ = 21.3 /1.8 – 251/, p< 0.04).

Conclusion: Rivaroxaban does not prevent recurrent thrombosis not only in triple positive patients, but also in single and double positive APS patients. Type of antiphospholipid antibodies can be predictive for the type of further vascular event.

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Disclosure of Interests: None declared

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SAT0195 ABNORMITY TFH SUBSETS INDICATE DISEASE ACTIVITY WHILE SIROLIMUS THERAPY RESTORES THE PD-1+ICOS+TFH/ACTIVATED TFR BALANCE IN PRIMARY SJOGREN'S SYNDROME PATIENTS

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Background: Immune imbalance between follicular helper T (Tfh) cells and follicular regulatory T (Tfr) cells is a characteristic of primary Sjogren's syndrome (pSS) [1]. The heterogeneity among Tfh and Tfr can be elucidated by separating them into different subsets based on the expression molecular characteristics.

Objectives: The aim of this study was to investigate the role of Tfh and Tfr subsets, and to evaluate the effects of sirolimus on these cells.

Methods: In this study, we enrolled 51 pSS patient and 26 healthy controls (HCs), and analyzed the frequencies and absolute counts of circulating Tfh and Tfr subsets, and serum levels of cytokines. Within these patients, analyses of above T

cells in twelve patients before and after treatment with sirolimus. Clinical indicators and correlations with follicular T cells were systematically analyzed. The diagnostic value for CD4+CXCR5+T cells was evaluated by the areas under the receiver operating characteristic curves (AUC).

Results: Patients with pSS had higher frequencies and absolute numbers of PD-1+ICOS+Tfh cells, but lower levels of activated Tfr cells cells, thereby resulting in elevated ratios of PD-1+ICOS+Tfh/activated Tfr. In addition, PD-1+Tfh cells levels were lower in pSS patients than in HCs. Interestingly, the ratio of PD-1+ICOS+Tfh/activated Tfr was a strong predictor of pSS diagnosis. However, sirolimus therapy resulted in significant reductions in PD-1+ICOS+Tfh cells and the PD-1+ICOS+Tfh/activated Tfr ratio in pSS patients. We also found increased numbers of PD-1+ICOS+Tfh cells were associated with B cells, while decreased numbers of Tfr and their subsets were strongly associated with aTreg cells in pSS patients. The ESSDAI [2] was positively correlated with PD-1+ICOS+Tfh cell frequency, but was negatively correlated with PD-1+Tfh cell count.

Conclusion: These findings suggest that the PD-1+ICOS+Tfh cell:activated Tfr cell ratio and PD-1+Tfh cells constitute potential novel biomarkers for pSS, and Tfr cells and subsets resemble derived aTreg cells. Furthermore, the PD-1+ICOS+Tfh cells as a biomarker of disease activity and provide new ground to verify the therapeutic implications of sirolimus as an innovative drug in pSS.

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Disclosure of Interests: None declared

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SAT0196

A DOUBLE BLIND, PLACEBO CONTROLLED, SINGLE ASCENDING DOSE (SAD) AND MULTIPLE ASCENDING DOSE (MAD) STUDY OF ALPN-101, A FIRST-IN-CLASS DUAL ICOS/CD28 ANTAGONIST, IN HEALTHY VOLUNTEERS (HV)

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Background: ALPN-101 (ICOSL vIgD-Fc) is an Fc fusion protein of a human inducible T cell costimulatory ligand (ICOSL) variant immunoglobulin domain (vIgD™) designed to inhibit simultaneously the CD28 and ICOS inflammation pathways (1). ALPN-101 is effective in preclinical studies of lupus, arthritis, and Sjögren's, and shows greater activity than single pathway inhibitors (2,3,4). It is in development for the treatment of multiple rheumatic and other inflammatory diseases.

Objectives: To evaluate the safety, pharmacokinetics (PK), and pharmacodynamics (PD) of ALPN-101 in HV

Methods: This was a first-in-human study of ALPN-101 (NCT03748836). 72 HV were allocated 4:2 to single intravenous (IV) or subcutaneous (SC) doses of ALPN-101: placebo at 0.001 – 10 mg/kg; 24 HV were allocated 6:2 to repeated IV doses of up to 1 mg/kg weekly x 4. Subjects were followed for 28 (SAD) or 49 (MAD) days to assess safety, PK, target saturation (TS) on T cells, circulating cytokines and PD, the latter based on suppression of IgG responses to keyhole limpet hemocyanin (KLH).

Results: ALPN-101 was generally well-tolerated, with no treatment related serious adverse events, no cytokine release, no clinical immunogenicity, and no adverse trends in safety laboratories. Overall, adverse events were reported in 74.2% of subjects on ALPN-101 and 66.7% of subjects on placebo. All events were mild or moderate and resolved without sequelae. Dose-dependent increase in ALPN-101 exposure was observed from 0.012 to 10 mg/kg. The estimated $t_{1/2}$ was 2-8.6 days over 0.3 – 10 mg/kg. SC bioavailability was ~60% at 3 mg/kg. Minimal to modest accumulation was observed with repeat IV dosing. The TS at C_{max} increased with dose between 0.001–0.03 mg/kg; thereafter the duration of high level TS (>95%) increased with dose (Figure 1). The duration of suppression of IgG anti-KLH response paralleled the duration of high level TS (Figure 2).

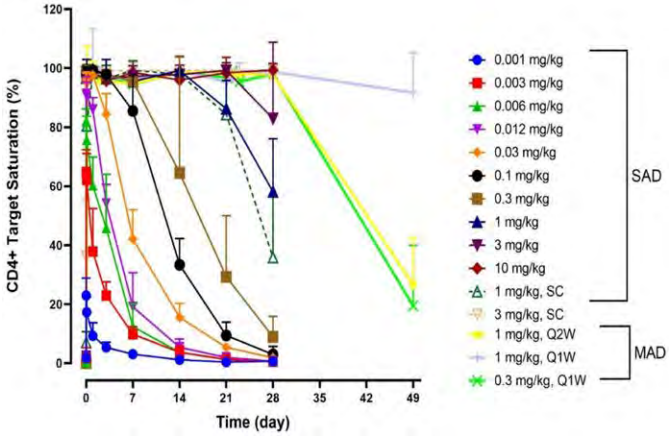


Figure 1. Mean + SD Target Saturation of ALPN-101 on Circulating CD4+T Lymphocytes

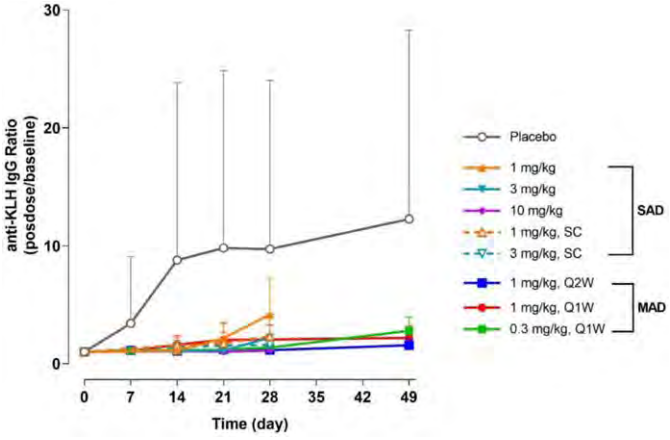


Figure 2. Mean + SD Serum Anti-KLH IgG Change Relative to Baseline

Conclusion: ALPN-101 was well tolerated when administered as single doses up to 10 mg/kg or as repeated doses of up to 1 mg/kg weekly for 4 weeks, exhibiting dose-dependent PK, TS and PD including the inhibition of antibody responses to KLH immunization. These findings support future studies to evaluate the efficacy of ALPN-101 in multiple rheumatic and other inflammatory diseases.

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SATURDAY, 06 JUNE 2020

SLE, Sjögren's and APS - clinical aspects (other than treatment)

SAT0197

NON MYOCARDIAL CARDIAC INVOLVEMENT IN ANTIPHOSPHOLIPID SYNDROME IN A SPANISH REFERENCE CENTER

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Background: Antiphospholipid syndrome (APS) is a systemic autoimmune disease, associated with a hypercoagulable state and fetal loss and with other clinical manifestations including cardiac involvement. APS occurs as a primary disorder (PAPS) or secondary to another autoimmune disease (SAPS). Due to its vascular nature, various organs and tissues may be affected, including the cardiac system. Cardiac manifestations of APS are valve abnormalities (valve thickening and vegetations), occlusive arterial disease (atherosclerosis and myocardial infarction) and pulmonary hypertension (PH).

Objectives: To assess the prevalence of non-myocardial involvement (valvulopathy and pulmonary hypertension) in a cohort of patients with antiphospholipid antibodies (aPLs).

Methods: Retrospective observational study in a Spanish reference center for systemic autoimmune diseases. All patients with aPLs and performed transthoracic echocardiogram (TTE) were included in the study. Patients were divided between PAPS, SAPS and aPLs carriers. A cohort of 50 patients with systemic lupus erythematosus (SLE) without aPLs was used as a control. Anti-cardiolipin, anti-B2GP1 and lupus anticoagulant antibodies were determined by standard techniques.

Results: A total of 220 patients were reviewed. 145 (65.9%) were female. The mean age was 42 years. Among all patients with aPLs, 102 were PAPS, 73 SAPS, and 45 asymptomatic carriers (silent APS). Patients with aPLs, unlike patients with SLE without aPLs, presented more often pathological TTE (114 patients, 52%) (p = 0.02), with more valvular involvement (87, 39%) (p = 0.005) and pulmonary hypertension (21, 9.5%, p = ns). Valve involvement was identified in 99 patients: 45 in PAPS, 27 in SAPS, 14 in aPLs carriers and 13 in the SLE without aPLs, these differences being statistically significant (p = 0.002). Valvulopathy was asymptomatic in the majority of patients but required valve replacement in two patients. Mitral valve was the most affected, especially in the form of insufficiency (57%), followed by aortic valve, combined mitral and aortic valve, and less frequently the pulmonary valve alone (3 cases).

	aPLs global	PAPS	SAPS	aPLs carriers	SLE w/o aPLs
Total	220 (100%)	102 (46.4%)	73 (33.2%)	45 (20.4%)	50 (100%)
Men	75 (34.1%)	41 (40.2%)	23 (31.5%)	11 (24.4%)	6 (12%)
Women	145 (65.9%)	61 (59.8%)	50 (68.5%)	34 (75.6%)	44 (88%)

Conclusion: Subclinical valve involvement was very common in patients with APS. There was no correlation with other clinical manifestations of APS nor were other risk factors identified. PH was less frequent than valvular involvement in patients with APS. However, despite not being statistically significant, close to 10% of patients with APS had PH compared to 6% of patients without APS.

	aPLs global	PAPS	SAPS	aPLs carriers	SLE w/o aPLs	
TTE performed	220 (100%)	102 (46.4%)	73 (33.2%)	45 (20.4%)	50 (100%)	
Pathological TTE	114 (52%)				16 (32%)	p=0.02
Valvular involvement	87 (39%)	45 (20.4%)	27 (12.3%)	14 (6.3%)	13 (26%)	p=0.005
Pulmonary hypertension	21 (9.5%)				3 (6%)	p=ns

Every patient with APS should have an echocardiogram in the initial study protocol in order to rule out both valvulopathy and pulmonary hypertension. This could modify the patient's management both in the short and long term, as well as the prognosis.

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SAT0198

PROBABILITY OF PULMONARY HYPERTENSION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS ACCORDING TO ESC GUIDELINE 2015

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Background: The prevalence of pulmonary hypertension (PH) in systemic lupus erythematosus (SLE) varied according to the definitions and investigations used. Echocardiography should always be performed when PH is suspected, based on symptoms and signs,[1] which may be difficult to be assessed in patients with SLE because early symptoms of PH, including shortness of breath, fatigue, weakness, angina and syncope can be part of disease manifestation.

Objectives: To investigate the probability of PH in patients with SLE based on 2015 ESC Guideline, regardless of symptoms.

Methods: A cross-sectional study was conducted in a rheumatology centre in Malaysia which included patients aged 18 years and above, who fulfilled SLICC2012 criteria. Exclusion criteria were diagnosis of overlap syndrome and pregnancy. Demographic data and immunology profile were obtained from electronic medical records. TTE was performed by one technician who was blinded to other clinical details. Low, intermediate or high probability of PH was determined based on 2015 European Society of Cardiology (ESC) echocardiography criteria of PH.

Results: A total of 60 patients with SLE were recruited. The mean age was 41.6±10.9 years and SLE disease duration was 11.5±9.4 years. The cardiovascular co-morbidities were hypertension (38.3%), dyslipidaemia (25%), diabetes mellitus (5.0%) and ischemic heart disease (1.6%). Based on 2015 ESC echocardiography criteria for PH, 50 (83.3%) patients had low probability of PH, 8 (13.3%) had intermediate probability of PH and 2 (3.3%) with high probability of PH. (Table 1). Further analysis revealed that two patients with high PH probability were asymptomatic at the time of study. They were treated for active SLE after PH was diagnosed from TTE performed within a year of study period and subsequent RHC confirmed pulmonary arteria hypertension (PAH). Among

Table 1. The details of echocardiographic signs of PH in patients with SLE.

Echocardiographic 'signs' of PH		PH probability (no of patients)		
		Low, n=50	Intermediate, n=8	High, n=2
Peak tricuspid regurgitant velocity, m/s	• ≤2.8	50	1	0
	• 2.9-3.4	0	7	0
	• >3.4	0	0	2
Ventricles	• Right/ left ventricle basal diameter ratio >1.0	0	1	2
	• Flattening of interventricular septum	0	0	2
Pulmonary artery	• Right ventricular outflow Doppler acceleration time <105ms and/or mid-diastolic notching	28	5	2
	• Early diastolic pulmonary regurgitation velocity >2.2m/s	0	0	2
	• PA diameter >25mm	4	2	2
Inferior vena cava and right atrium	• Inferior cava diameter >21mm with decreased inspiratory collapse	0	0	0
	• Right atrial area >18cm ^{2}	0	0	2

patients with intermediate probability of PH, one patient had intermittent palpitation and chest pain, while others were asymptomatic including one patient with PAH based on RHC. The most prevalent auto-antibodies among patients with intermediate and high probability of PH were anti-Ro (8 patients), anti-nuclear antibodies (7 patients) and anti-dsDNA (5 patients).

Conclusion: We found 16.6% patients with SLE who had intermediate and high probability of PH, based on 2015 ESC echocardiography criteria for PH. All except one patient had symptoms suggestive of PH at the time of study. RHC performed subsequently on two patients with high PH probability confirmed PAH.

References:

[1] Galie N, Humbert M, Vachiery JL, et al. European Heart Journal, 2016; 37(1):67-119

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SAT0199 PARTICULARITIES OF SJÖGREN SYNDROME IN ELDERLY PATIENTS

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Background: Sjögren syndrome (SS) is a systemic autoimmune disease mainly described in females at a peak incidence age of 50. It was suggested that elderly onset of disease has particular clinical and biological phenotype.

Objectives: The aim of our study is to determine the particularities of SS in elderly patients.

Methods: Data of 332 patient fulfilling the American European Consensus Group criteria for Sjögren's syndrome over a period time of 18 years were studied. Clinical and biological features of elderly patients (G1) were described and compared to those of patients aged below 65 years old (G2) using the X2 and Fisher test.

Results: A total of 35 elderly were retained: 33 females and 2 males. The mean age of disease onset was 68.8 ± 4.4 years. The average delay (from first sign of the disease to diagnosis) was 1.27 years. The mean age at diagnosis was 70.3 ± 4.7 years. Xerostomia was described by 33 patients (94.3%). Focus score in the minor labial salivary glands pathology was ≥ 1 in 32 patients (91.4%). Two patients had abnormalities in parotid scintigraphy. Xeropthalmia was described by 32 elderly patients (91.4%). Schirmer test was abnormal in 20 cases (57.1%) and Break Up Time test was altered in 20 cases (57.1%). Arthralgia was the most frequent extra-glandular manifestation reported in 74.3% of patients. Fatigue was noted in 12 patients. The other systemic manifestations were: interstitial lung disease (n=13), peripheral neuropathy (n=7), central nervous system involvement (n=5), Raynaud's phenomenon (n=4), myositis (n=2) and renal tubulopathy (n=2). Laboratory findings showed hyperglobulinemia (n=19) and lymphopenia (n=15). Antinuclear antibodies were positive in 25 patients (71.4%) with positive anti-SSA antibodies (n=14) and positive anti-SSB antibodies (n=7). SS was primary in 25 patients. Ten patients had one or more associated autoimmune diseases: cryoglobulinemia (n=4), systemic scleroderma (n=3), systemic lupus erythematosus (n=2), rheumatoid arthritis (n=2) and autoimmune hepatopathy (n=2).

Systemic treatments involved corticosteroids for 15 patients, antimalarial agents for 12 patients, nonsteroidal anti-inflammatory drugs for three patients and immunosuppressant agents for nine patients. One patient developed lymphoma.

Comparative analysis showed that SS diagnosis was made earlier in elderly with an average delay of 1.27 years in G1 vs 3 years in G2 (p=0.02). Fatigue was more frequent in elderly (63.2% vs 23.8%) p<0.01. Positivity of anti-SSA was also more frequent in elderly (64.9% vs 46.7%; p=0.04). Anti-malarial agents were less prescribed in elderly (36.4% vs 55.3%; p=0.03). There was no significant differences between the two groups concerning the other clinical features, laboratory findings, treatment and outcomes.

Conclusion: Regardless of the statistical findings in our study and in the literature, treatment and follow-up of elderly patients with SS must obey to closer attention considering their vulnerability and the complexity of their management.

Disclosure of Interests: None declared

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SAT0200 RISK FACTORS FOR ADVERSE PREGNANCY OUTCOMES IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: Pregnancies of patients with systemic lupus erythematosus (SLE) can be risky both for the mother and the fetus because of disease activity and pregnancy complications.[1]

Objectives: In this study, we evaluated the risk factors related to adverse pregnancy outcomes (APO) in our pregnant SLE cohort who were followed up by both Rheumatology and Obstetrics and Gynecology departments at our university.

Methods: 168 pregnancy data were analyzed from 136 patients who fulfilled ACR classification criteria for SLE. The course of pregnancies were monitored and fetal/neonatal outcomes were recorded. Unexplained fetal death after 12 weeks of gestation, neonatal death, preterm birth due to preeclampsia, eclampsia or HELLP and birth of small for gestational age (SGA) infant were defined as APO. Cumulative clinical, laboratory and serological findings, disease activity (SLEDAI-2K) and damage (SLICC/ACR), and conventional risk factors were compared between APO(+) and APO(-) groups.

Results: The comparison of demographics, conventional risk factors and disease characteristics in APO(+) and APO(-) groups are summarized in Table-1. In APO(+) pregnancies, the duration of disease was longer (p <0.05) and the frequency of chronic hypertension was higher (p <0.05) compared to APO(-) pregnancies. Renal and neuropsychiatric (NP) involvement, thrombocytopenia, antiphospholipid syndrome (APS), lupus anticoagulant and anti-cardiolipin IgM positivity were significantly higher in APO(+) group. Mean SLEDAI-2K scores of three trimesters and postpartum 6 months were higher in APO(+) patients compared to APO(-) patients (2.2 ± 3.6 vs 1.2 ± 2.04, p <0.05; 4.9 ± 6.03 vs 2.7 ± 5.01, p = 0.02, respectively). Percentage of patients with damage at the beginning of pregnancy and the mean SLICC damage score were significantly higher in APO(+) group compared to APO(-) group (1.8 ± 2.1 vs 0.8 ± 1.3, p <0.05). In APO(+) group, damage was significantly higher in neuropsychiatric, renal and cardiovascular and locomotor systems (p <0.05).

Conclusion: Although an important proportion of SLE pregnancies result in live birth, active disease, especially renal and NP involvement, and presence of damage at the beginning of pregnancy increase the risk of maternal and fetal complications. Furthermore, the presence of APS or antiphospholipid antibody positivity are important risk factors for obstetric complications. In conclusion, pregnancy should be allowed after controlling the disease activity and patients should be closely monitored in coordination with Obstetrics and Gynecology clinics. In case of presence of damage, both the patient and the physician should be aware of a possible adverse pregnancy outcome.

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Table 1. Demographic data of APO (+) and APO (-) groups, comparison of conventional risk factors, cumulative clinical, serological and laboratory features

	APO (-) (n=111)	APO (+) (n=57)	p
Age	35.1±6.7	34.9±5.9	NS
Age at conception	30.6±5.6	28.9±4.2	NS
Disease duration (months)	141.6±70	166.9±87.9	**<0.05**
Chronic hypertension, n (%)	6 (7)	11 (19.6)	**<0.05**
Photosensitivity, n (%)	86 (77.5)	43 (75.4)	NS
Malar rash, n (%)	66 (59.5)	38 (66.7)	NS
Oral ulcer, n (%)	11 (9,9)	6 (10.5)	NS
Arthritis, n (%)	77 (59.4)	42 (73.7)	NS
Serositis, n (%)	17 (15.3)	13 (22.8)	NS
Renal, n (%)	39 (35.1)	30 (52.6)	**<0.05**
Hematologic, n (%)	78 (70.3)	40 (70.2)	NS
Thrombocytopenia, n (%)	37 (33.3)	30 (52.6)	**<0.05**
AIHA, n (%)	16 (14.4)	14 (24.6)	NS
Neurologic, n (%)	7 (6.3)	9 (15.8)	**<0.05**
Anti-cardiolipin IgG, n(%)	28 (25.2)	18 (32.1)	NS
Anti-cardiolipin IgM, n (%)	18 (16.2)	18 (32.1)	**<0.05**
Lupus anticoagulant, n (%)	26 (23.4)	28 (49.1)	**<0.001**
Antiphospholipid syndrome, n (%)	28 (25.2)	30 (52.6)	**<0.001**

(NS=not significant, APO=adverse pregnancy outcome, AIHA=autoimmune hemolytic anemia)

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SAT0201

ASSOCIATION OF CARDIAC TROPONIN T MEASURED WITH A HIGHLY SENSITIVE ASSAY WITH CARDIOVASCULAR EVENTS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (TROPOPLUS STUDY)

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Background: Mortality is still 2 to 5 times superior in SLE patients as compared to general population and is mainly due to cardiovascular event (CVE). Although cardiovascular traditional risk factors contribute to early-onset atherosclerosis in SLE, the phenomenon is not fully explained by a higher frequency of smoking habits, hypertension, or dyslipidemia and the Framingham risk equation usually underestimates the 10-year cardiovascular risk in this population. Thus, identification of biological markers able to better stratify cardiovascular risks in SLE patients is needed.
Objectives: Our study aimed to determine whether serum cardiac troponin T measured with a highly sensitive assay (HS-cTnT) was associated with CVE in systemic lupus erythematosus (SLE) patients.
Methods: All SLE patients included between 2007 and 2010 in the randomized, double-blind, placebo-controlled, multicenter PLUS trial were retrospectively screened. Patients with no past history of CVE and a follow-up period of > 20 months were analyzed. HS-cTnT concentration was measured using the electrochemiluminescence method on serum collected at PLUS inclusion. The primary outcome was the incident CVE. Factors associated with the primary outcome were identified and multivariate analysis was performed.
Results: Overall, 442 SLE patients (of the 573 included in the PLUS study) were analyzed for the primary outcome with a median follow up of 110 (IQR: 99-120) months. Among them 29 (6.6%) experienced at least one CVE that occurred at a median of 67 (IQR: 31-91) months after inclusion. Six out of 29 patients had more than one CVE. In the multivariate analysis, dyslipidemia, duration of SLE disease and HS-cTnT were associated with the occurrence of CVE. Kaplan-Meier analysis showed that a concentration of HS-cTnT>4.27 ng/L at inclusion increased by 2.7 (HR 2.7 [1.3-5.6], p=0.0083) the risk of CVE in SLE.
Conclusion: HS-cTnT measured in serum is the first identified biomarker independently associated with incident CVE in SLE patients
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SAT0202

C4 LEVELS AS PREDICTOR OF DISEASE FLARES AND ADVERSE PREGNANCY OUTCOMES IN SYSTEMIC LUPUS ERYTHEMATOSUS PREGNANCIES

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Background: SLE pregnancies have an increased risk of Adverse Pregnancy Outcomes (APO). In clinical practice, low C3 and C4 levels are associated with active disease and, during pregnancy, complement activation products are shown to be associated with APO.
Objectives: To analyse potential association between C3 and C4 variations and disease flares and APO during SLE pregnancies.
Methods: Demographic, clinical and laboratory data on SLE pregnancies prospectively-followed by a multidisciplinary team in a pregnancy clinic from 1987 to 2015 were retrospectively analysed at preconception and at each trimester. Hypocomplementemia was defined according to the normality range calculated in healthy pregnancies by Reggia et al[1]. APO were defined as: early miscarriage (<10th week), intrauterine fetal death (>10th week), perinatal death (<30th day of life), pre-eclampsia (PE), severe preterm birth (<34th week).
Results: 134 pregnancies in 98 SLE patients were analysed. APO occurred in 22 (16%) pregnancies: 9 early miscarriages, 4 intrauterine fetal deaths, 3 severe preterm births, 6 PE (hesitated in 1 intrauterine fetal death, 1 perinatal death; 2 preterm birth between 34th and 37th weeks and 2 term births). 13 flares (2 renal, 4 articular, 6 cutaneous and 1 neurological) were recorded in 11 (8%) pregnancies.
The mean C3 and C4 levels at each trimester are shown in table 1.

Table 1. C3 and C4 mean levels (mg/dL) at pre-conceptional visit (T0), 1st trimester (T1), 2nd trimester (T2) and 3rd trimester (T3).

	C3 T0	C3 T1	C3 T2	C3 T3	p T0-T1	p T1-T2	p T2-T3
Pregnancies with flares	73.2	82.2	83.8	97.5	*0.04*	*0.02*	0.06
Pregnancies without flares	85.3	91.8	104.4	114.7	*<0.001*	*<0.001*	*<0.001*
Pregnancies with APO*	84.7	91.5	98.5	106.3	*0.03*	*0.03*	0.89
Pregnancies without APO*	84.5	90.9	102.8	112.8	*<0.001*	*<0.001*	*<0.001*
	C4 T0	**C4 T1**	**C4 T2**	**C4 T3**	***p T0-T1***	***p T1-T2***	***p T2-T3***
Pregnancies with flares	8.6	11.8	10.9	11.4	*0.01*	0.43	0.27
Pregnancies without flares	13.2	14.7	16.3	16.6	*<0.001*	*<0.001*	0.98
Pregnancies with APO**	13.1	16.1	15.9	14.7	*0.01*	0.3	0.13
Pregnancies without APO**	12.9	14.2	15.8	16.1	*<0.001*	*<0.001*	0.42

Comparison of C3 and C4 mean levels between pregnancies with APO vs without APO:
* T0, T1, T2, T3: ns; ** T0, T1, T2, T3: ns

Both in pregnancies with flares and with APO, there was no increase of C3 between the 2nd and the 3rd trimester and of C4 between the 1st and the 2nd trimester.
At preconception, mean levels of C4 were lower in pregnancies with flares compared to those without flares (images 1 and 2); during the 2nd and the 3rd trimesters the mean levels of both C3 and C4 were lower in pregnancies with flares.
In pregnancies with APO, the variation of C4 levels between the 2nd and the 3rd trimester was lower than in pregnancies without APO (-3.18 vs 0.27; p=0.01).
A higher frequency of low C4 was observed at pre-conceptional visit, 1st trimester and 3rd trimester (6/7 vs 25/103 p=0.002; 8/9 *vs* 56/106 p=0.04; 9/11 vs 33/96 p=0.003) in pregnancies with flare as compared with pregnancies without flares.

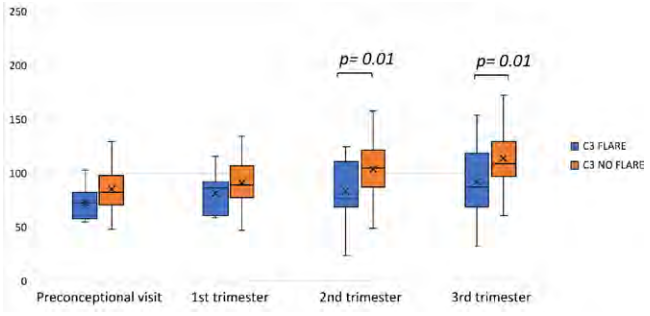


Figure 1. Image 1: comparison of C3 mean levels between pregnancies with fares *vs* without flares

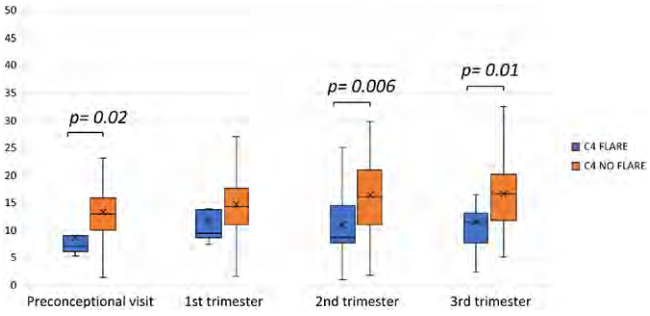


Figure 2. Image 2: comparison of C4 mean levels between pregnancies with fares *vs* without flares

Conclusion: In our cohort of prospectively-followed SLE pregnancies, low C4 levels at preconception seems to predict flares during pregnancy. Low increase of C4 levels between the 2nd and the 3rd trimester could predict an APO.

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SAT0203

SINGLE LAC POSITIVITY VERSUS DOUBLE AND TRIPLE POSITIVITY FOR THROMBOSIS IN SLE

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Background: The antiphospholipid syndrome (APS) is defined by the development of venous and/or arterial thromboses, and pregnancy morbidity, in the presence of antiphospholipid antibodies (aPL); lupus anticoagulant, moderate-to-high titer anticardiolipin (aCL) and anti-β2-glycoprotein (aB2GPI). It has been suggested that the incidence of thromboembolic events were significantly higher in the triple positive subjects, and the rate of pregnancy loss was also significantly much higher in double positive subjects (1). On the other hand several studies showed that LAC is more highly associated with thrombosis risk (2).

Objectives: We aimed to investigate the risk of thrombosis in Systemic Lupus Erythematosus (SLE) patients with single LAC positivity versus double and triple positivity in Hopkins Lupus Cohort.

Methods: The Hopkins Lupus Cohort is a prospective longitudinal cohort of SLE patients ongoing since 1987. This analysis was based on cohort experience from 2003 through October 2019. Anticardiolipin and anti-Beta2 glycoprotein were defined as positive when the antibody titer exceeded 20 units. The lupus anticoagulant was determined by dilute Russell's viper venom time (dRVVT) and confirmatory mixing studies, if prolonged. It is defined as positive if a patient had a dRVVT of 45 or more second and a positive confirm ratio of more than 1.4. For each aPL, we defined the patient as positive at a given month of follow up if they ever had a positivity in previous measures. The relationships between thrombosis and aPL were adjusted for number of prior aPL assessment.

Results: There were 805 patients with a complete profile of 7 antiphospholipid antibodies, with a total of 73417 person months (6118 person years) of follow up. For any thrombosis when compared to patients with LAC positivity only, double positivity with any isotypes [1.15(0.50, 2.66) p=0.7484] and triple positivity with any isotypes [1.68(0.74, 3.80), p=0.2145] showed a higher point estimates but statistically not significant (Table 1).

Table 1. Single, double and triple positive patterns and the risk of any thrombosis.

Pattern	Number of events	Person-years	Rate per 1000 person-years	adjusted RR (95% CI)	p-value
LAC positivity only	10	633	15.8	1.00 (Ref)	
Never any aPL	33	2581	12,8	0.73(0.36, 1.47)	0.3819
any aCL positivity only	6	793	7,6	0.43(0.16, 1.18)	0.1028
any aB2GPI positivity only	7	517	13,5	0.78(0.30,2.05)	0.6195
any aCL and aB2GPI positivity only	5	404	12,4	0.71(0.24,2.04)	0.5211
LAC and ACL positivity	7	406	17,3	1.15(0.50,2.66)	0.7484
LAC and aB2GPI positivity	12	490	24,5		
Triple positivity	0	147	0,0	1.68(0.74,3.80)	0.2145

Conclusion: We found that triple or double positive aPL profiles are not superior to single LAC positivity in their association with any thrombosis in SLE patients.

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SAT0204

COMPARING OCCURRENCE AND CLINICAL SIGNIFICANCE OF ANTI-PHOSPHOLIPID AUTOANTIBODIES AMONG SUDANESE AND SWEDISH SLE PATIENTS USING CONVENTIONAL AND NATION-BASED CUTOFFS

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Table 1.

	FEIA Sudan n=92	FEIA Sweden n=291	P	PMAT/CIA Sudan n=93	PMAT/CIA Sweden n=333	P
IgA CL median/ IQR	6.5/5.2	4.0/4.1	**<0.0001**	194/185	148/112	**<0.0001**
IgG CL	4.1/5.1	3.0/4.5	**0.0002**	205/137	190/215.1	0.09
IgM CL	2.7/6.8	3.7/5.4	**0.02**	214/251.5	193/3502	0.2
IgA β2GPI	6.3/14.2	2.7/3.8	**<0.0001**	212/347	118/152	**<0.0001**
IgG β2GPI	4.2/2.9	1.8/2.3	**<0.0001**	158/110.7	145.2/147.5	**0.04**
IgM β2GPI	2.0/3.0	1.4/2.2	**0.006**	146.2/189.7	132.5/235.4	0.09
IgA B2GP1 D1				1542/1253.5	1683/1518.1	**0.045**
IgA CL common cutoff n(%)	9(9.8)	17(5.8)	0.2	32(35.2)	75(22.7)	**0.02**
IgG CL	4(4.3)	21(6.7)	0.4	14(15)	72(22.1)	0.1
IgM CL	3(3.2)	14(4.5)	0.6	10(11.4)	43(13.1)	0.6
IgA β2GPI	32(34.8)	43(14.9)	**<0.0001**	38(41.8)	76(23)	**0.0004**
IgG β2GPI	10(10.9)	44(14.1)	0.4	5(5.4)	50(15.3)	**0.01**
IgM β2GPI	10(10.9)	27(8.7)	0.5	12(13.6)	42(12.9)	0.8
IgA B2GP1 D1				6(6.4)	38(11.4)	0.2
IgA CL 95th cutoff n(%)	9(9.8)	54(18.6)	**0.047**	36(39.6)	121(26.6)	0.6
IgG CL	8(8.7)	42(13.5)	0.2	24(25.8)	103(31.6)	0.3
IgM CL	8(8.7)	39(12.5)	0.3	16(18.2)	47(14.4)	0.4
IgA β2GPI	18(19.6)	100(34.7)	**0.006**	20(22)	125(37.8)	**0.005**
IgG β2GPI	2(2.1)	67(21.5)	**<0.0001**	19(20.4)	83(25.5)	0.3
IgM β2GPI	14(15.22)	57(18.3)	0.5	20(22.7)	57(17.5)	0.3
IgA B2GP1 D1				25(26.9)	69(20.7)	0.2

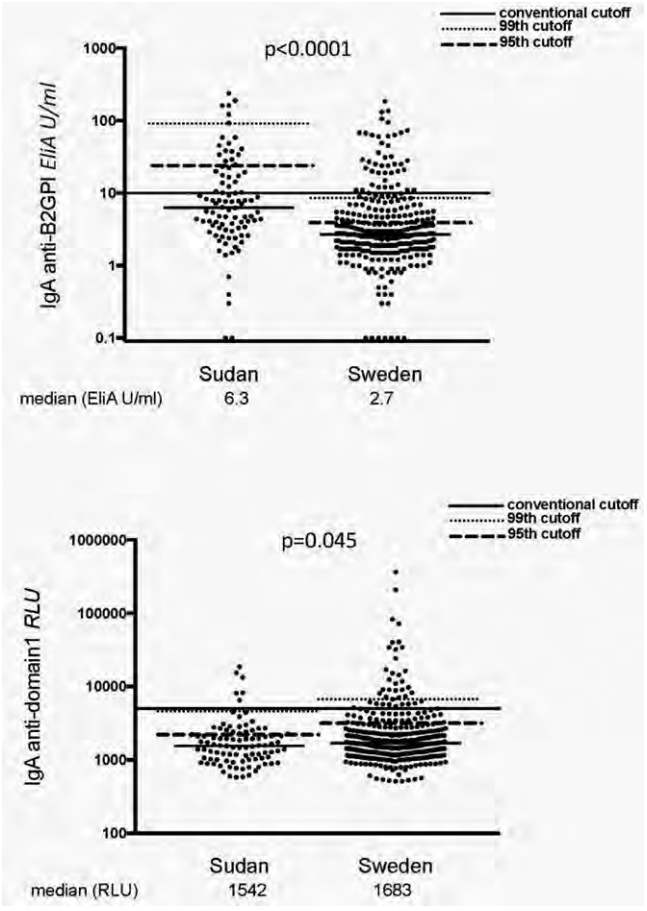


Figure 1.

Background: Antiphospholipid antibodies (aPL) of IgA isotype are prevalent in SLE patients of African-American, Afro-Caribbean and South-African origin, but data from North Africa are lacking

Objectives: To compare and determine clinical significance of aPL isotypes in Sudanese and Swedish SLE patients using nation-based cutoffs

Methods: Consecutive Sudanese (n=115) and Swedish (n=340) SLE patients and 106 and 318 age- and sex-matched national controls were included. All patients fulfilled the 1982 ACR SLE classification criteria. IgA/G/M anti-cardiolipin and anti-β_2GPI were analyzed with two independent assays (Fluorescence Enzyme Immuno Assay (FEIA) from Thermo Fisher Scientific and Particle-based Multi-Analyte Technology (PMAT) from Inova Diagnostics). IgA anti-β_2GPI domain1 (D1) was investigated with chemiluminescence (CIA), Inova Diagnostics. APS-related events were obtained from patients' records. Manufacturers', 95th and 99th percentile cutoffs, based on national controls calculated by non-parametric methods, were used
Results: Sudanese patients had higher levels and prevalence of IgA aPL using manufacturers' cutoffs (Table 1 and Figure 1). IgA/IgG aPL were also higher among Sudanese controls, But, Swedish patients were more often positive for IgA anti-β_2GPI with both assays when national cutoffs were applied (Table 1). Occurrence of IgA anti-D1 did not differ between the countries. Venous thromboses were less common among Sudanese patients and no aPL, including IgA anti-β_2GPI associated with thrombosis in Sudanese patients. Thrombosis in Swedes associated with IgG/IgM aPL. Fetal loss associated with aPL in both cohorts most evident after national adjustments
Conclusion: IgA anti-β_2GPI levels were generally higher among Sudanese compared to Swedish SLE patients and controls, but after national adjustments more Swedish than Sudanese patients were positive. IgA anti-D1 was not increased in Sudanese patients. Previous studies on populations of African-origin, which demonstrate high prevalence of IgA aPL positivity, should be re-evaluated using similar cutoff approach
Acknowledgments: : We thank Maryam Poorafshar at Thermo Fischer Scientific and Silvia Casas and Michael Mahler at Inova Diagnostics for help with analyses
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SAT0205

A MORE SPECIFIC INTEGRATED MODEL FOR IDENTIFYING BACTERIAL INFECTION IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is a multisystemic inflammatory disorder [1]. Given that immunosuppressive therapy is adopted as the predominant treatment option for SLE, up to half of SLE patients develop infections during their disease progress, and bacterial infection serves as the leading cause of morbidity and mortality in SLE patients [2]. Owing to the therapeutic regimen to bacterial infection and SLE flare are absolutely opposite, timely diagnosis and correct treatment are of vital importance, and improper treatment strategy may be fatal. No single biomarker, however, has exhibited sufficient sensitivity and specificity to serve as a standard tool for distinguishing bacterial infection from SLE flare.
Objectives: To find a method by integrating cytokines, lymphocyte cells and routine examination biomarkers to observe its capacity for identifying bacterially infected SLE patients.
Methods: Total 175 SLE patients (65 infected and 110 flare) were recruited into our study. The criteria of bacterial infection was positive isolation of bacteria, typical clinical symptoms and signs, imaging positive results and positive feedback on antibacterial treatment and lupus flare was regarded as three points higher than their previous SLEDAI. The disease activity of SLE patients was evaluated based on Systemic Lupus Erythematosus Disease Activity Index (SLEDAI). Lymphocyte cells ($CD3^+T$, $CD4^+T$, $CD8^+T$, B, NK, Th1, Th2, Th17 and Treg) and cytokines [interleukin-2 (IL-2), IL-4, IL-6, IL-10, tumor necrosis factor-α (TNF-α), interferon-γ (IFN-γ) and IL-17] were measured by flow cytometry. Blood routine examination, erythrocyte sedimentation rate (ESR), C-Reactive Protein (CRP) Complement 3 (C3), C4, procalcitonin (PCT), immunoglobulin M (IgM), IgA and IgG were also evaluated. Partial least square discriminant analysis (PLS-DA) and supervised orthogonal PLS-DA (OPLS-DA) were applied to perform multivariate analysis of the data and further group the patients with bacterial infection. Receiver operating characteristic (ROC) curves were also plotted to investigate the ability of individual indicator and the combination of multiple indicators to identify bacterial infection.
Results: The PLS-DA model showed a clear identification effect by the performance of R2Y=0.991 and Q2=0.970. The OPLS-DA model (R2Y=0.996 and Q2=0.991) exhibited a better separation of patients with bacterial infection. And the Observed vs. predicted plot of the OPLS-DA model demonstrated that all SLE patients were correctly separated into infected or flare groups, indicating that the model had a strong predictive ability for bacterial infection. For single indicator, infected patients had higher WBC, neutrophil (NEUT), ESR, CRP and PCT (P=0.002, 0.019, 0.002, <0.001, <0.001, respectively), and lower Treg cells (P=0.012). The levels of serum IL-6, IL-10, IFN-γ and TNF-α (P<0.001, =0.022, 0.014, 0.011, respectively) were significantly increased in infected group. ROC curves showed that the combination of the ten indicators showed the largest AUC and the highest accuracy, as well as balanced and relatively high sensitivity and specificity. Furthermore, the AUC of the combination was greatly higher than that of WBC, NEUT, ESR, CRP, PCT, Treg, IL-6, IL-10, IFN-γ and TNF-α (P<0.001).
Conclusion: PLS-DA, OPLS-DA models including cytokines, lymphocyte cells and routine biomarkers and combination of WBC, NEUT, ESR, CRP, PCT, Treg,

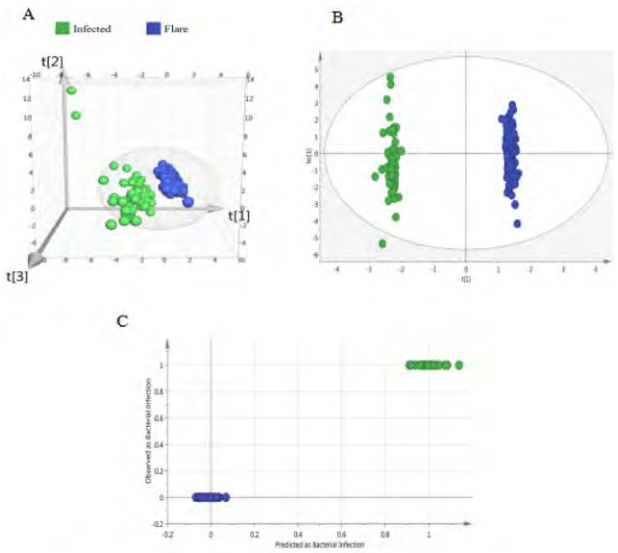


Figure 1. Identification of systemic lupus erythematosus (SLE) patients with bacterial infection and Flare by using partial least square discriminant analysis (PLS-DA) and orthogonal PLS-DA (OPLS-DA) methods. (A) Three-dimensional PLS-DA score scatter plot, (B) the OPLS-DA score scatter plot and (C) the 'Predicted vs. Observed' plot for distinguishing bacterially infected SLE patients (green dots) from non-bacterially infected SLE patients (blue dots) based on 50 indicators. Both groups were greatly separated in the PLS-DA and OPLS-DA models. None of the non-infected SLE patients were predicted as a lupus flare.

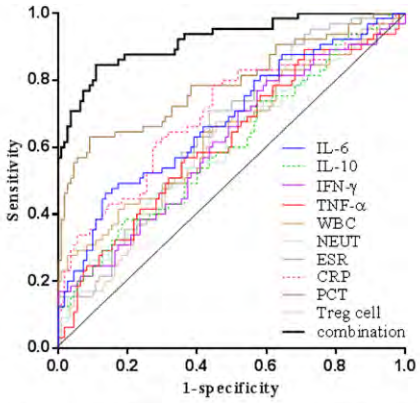


Figure 2. Receiver operating characteristic (ROC) curves of WBC, NEUT, ESR, CRP, PCT, Treg cells, IL-6, IL-10, IFN-γ, TNF-α and their combination were drawn to identify systemic lupus erythematosus (SLE) patiens with or without bacterial infection.

Table 1 Variable of the ROC curve for individual or combined biomarker

biomarker	AUC (%) 95% CI	Accuracy (%)	Sensitivity(%) 95% CI	Specificity(%) 95% CI	PLR/NLR (%)	PPV/NPV (%)
WBC	0.641 (0.565-0.712)	71.43	27.69 (17.31-40.19)	97.27 (92.24-99.43)	10.15/0.74	85.71/69.48
NEUT	0.606 (0.529-0.679)	60.57	53.85 (41.03-66.30)	64.55 (54.85-73.43)	1.52/0.72	47.29/70.30
ESR	0.637 (0.561-0.708)	61.14	63.08 (50.20-74.72)	60.00 (50.22-69.22)	1.58/0.62	48.23/73.34
CRP	0.702 (0.628-0.768)	64.00	78.46 (66.51-87.69)	55.45 (45.67-64.93)	1.76/0.39	51.00/81.34
PCT	0.785 (0.717-0.843)	80.57	56.92 (44.04-69.15)	94.55 (88.51-97.97)	10.44/0.46	86.05/78.79
Treg	0.614 (0.538-0.687)	59.43	67.69 (54.95-78.77)	54.55 (44.77-64.07)	1.49/0.59	46.81/74.08
IL-6	0.682 (0.607-0.750)	70.29	49.23 (36.60-61.93)	82.73 (74.35-89.27)	2.85/0.61	62.74/73.39
IL-10	0.603 (0.527-0.676)	65.14	38.46 (26.65-51.36)	80.91 (72.31-87.78)	2.01/0.76	54.34/68.99
IFN-γ	0.611 (0.535-0.684)	54.86	80.00 (68.23-88.90)	40.00 (30.78-49.78)	1.33/0.50	44.06/77.20
TFN-α	0.616 (0.539-0.688)	68.15	56.92 (44.04-69.15)	63.64 (53.92-72.60)	1.57/0.68	48.05/71.43
Combined	0.921 (0.870-0.956)	87.43	84.62 (73.52-92.37)	89.09 (81.72-94.23)	7.76/0.17	82.09/90.74

AUC: area under the ROC curve; CI, confidence interval; PLR, positive likely ratio; NLR, negative likely ratio; PPV, positive predictive value; NPV, negative predictive value; WBC, white blood cell; NEUT, neutrophile granulocyte; ESR, erythrocyte sedimentation rate; CRP: C-reactive protein; PCT: procalcitonin; IL-6, interleukin-6; IL-10, interleukin-10; IFN-γ, interferon-γ; TNF-α, tumor necrosis factor-α.

IL-6, IL-10, IFN-γ and TNF-α in ROC curve may be more predictive for finding bacterial infection in SLE and may prompt clinicians more promptly and accurately to help them make correct medication.

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Disclosure of Interests: None declared

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SAT0206 MINOR SALIVARY GLAND BIOPSY AND SEROLOGICAL PROFILE IN PRIMARY SJÖGREN'S SYNDROME: A SINGLE TERTIARY REFERRAL CENTER EXPERIENCE

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Background: Minor salivary gland biopsy (MSGB) portrays an important role as part of the diagnostic criteria of primary Sjögren's syndrome (pSS) in the ACR/EULAR 2016 classification. Autoantibodies anti-Ro/SSA and anti-La/SSB embody part of these criteria. Patients with negative serology have been classified as pSS using MSGB outcomes in up to 40% of cases.

Objectives: Compare MSGB and serological characteristics between pSS positive biopsy versus pSS negative biopsy and sicca groups.

Methods: 174 subjects with sicca symptoms and MSGB biopsy were studied. Patients who fulfilled the ACR/EULAR 2016 criteria were classified as pSS. Serological profile: Rheumatoid factor (RF) (IgA, IgG and IgM), Anti La/SSB and Anti-Ro/SSA, available in 148 and 161 patients respectively, as well as histopathological characteristics of MSGB were recollected (Table 2).

Comparison between subgroups according to biopsy status was performed. Differences between serology and MSGB were reported using Chi square, a p<0.05 was considered statistically significant

Results: 95(54.59%) pSS patients with positive biopsy, 47 (27. 02%) pSS with a negative biopsy and 32 (18.39%) sicca patients were included.

A positive serology profile (RF, Anti-Ro/SSA, Anti-La/SSB) was found more frequently in the pSS positive biopsy cohort when compared to the pSS negative biopsy and sicca groups (Table 1).

Table 1. Comparison between serological and histopathological characteristics in pSS and sicca groups.

Groups	Positive biopsy n=95	Negative biopsy n=47	Sicca n=32	p^1	p^2
Age (years) mean, (SD)	54.59 (11.69)	50.17 (12.35)	49.18 (12.74)	0.42 (0.43-0.45)	0.78
Female, n (%)	92 (96.8)	46 (97.87)	32 (100)	0.779	0.58
Serological profile					
Rheumatoid factor					
IgA (%)	26 (27.4)	12 (25.5)	4 (12.5)	0.35 (0.47-0.49)	0.23
IgM (%)	47 (49.5)	25 (53.19)	7 (21.9)	0.34 (0.41-0.43)	0.015
IgG (%)	13 (13.7)	7 (14.8)	1 (3.1)	0.35 (0.45-0.47)	0.25
Positivity Anti-Ro/SSA, n (%)	47 (52.8)	12 (30)	2 (6.3)	0.015 (0.013-0.018)	<0.05
Positivity Anti-La/SSB, n (%)	17 (19.77)	3 (9.09)	0(0)	0.003 (0.002-0.004)	0.019

[1]*p* of the comparison between pSS positive biopsy group vs pSS negative biopsy group
[2]*p* of the comparison of the 3 groups
Anti-Ro/SSA: available in pSS biopsy positive group n=89, pSS negative biopsy group n=40
Anti-La/SSB: available in pSS biopsy positive group n=86, pSS negative biopsy group n=33

Table 2. Histopathologic characteristics and comparison in pSS and sicca groups.

Characteristics	Positive biopsy n=95	Negative biopsy n=47	Sicca n=32	p^1	p^2
Lobules, n (SD)	12.45 (7.24)	15.2 (9.95)	11.84 (9.84)	0.19 (0.13 0.15)	0.43
Foci, n (SD)	3.23 (3.16)	0(0)	0(0)	<0.05	<0.05
Atrophy, n (%)	27 (28.4)	9 (9.5)	7 (21.9)	0.007	0.57
Adipose infiltration, n (%)	22 (23.2)	12 (12.6)	6 (18.8)	0.12	NA
Ductal dilatation, n (%)	22 (23.2)	8 (8.4)	6(18.8)	0.05	0.73

[1]*p* of the comparison between pSS positive biopsy group vs pSS negative biopsy group
[2]*p* of the comparison of the 3 groups

Histopathological characteristics of MSGB are described in Table 2. Sicca group had more alterations when compared to pSS negative biopsy group.

Conclusion: Histopathological alterations in MSGB (atrophy, adipose infiltration and ductal dilatation) can act as confounding data at biopsy interpretation since they were found in close prevalence in the pSS positive biopsy group and sicca group and should be carefully taken into account at diagnosis. A positive serologic profile was associated with more histopathological alterations in the positive biopsy group.

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Disclosure of Interests: None declared

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SAT0207 ANTI-SSA/RO POSITIVITY AND CONGENITAL HEART BLOCK: OBSTETRIC AND FETAL OUTCOME IN A COHORT OF ANTI-SSA/RO POSITIVE PREGNANT WOMEN WITH AND WITHOUT AUTO-IMMUNE DISEASES FROM THREE ITALIAN TERTIARY REFERRAL CENTERS

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Background: neonatal lupus syndrome (NLS) is an acquired disease caused by the trasplacental passage of anti-SSA antibodies. Congenital heart block (CHB) represents the most serious manifestation of NLS. The rate of CHB in Anti-SSA positive pregnant women ranges from 1 to 5% in different studies

Objectives: to retrospectively assess the prevalence of CHB in a cohort of anti-SSA positive pregnant women followed in 3 Italian tertiary centers

Methods: pregnancies of anti-SSA positive women attending the pregnancy clinic of ASST Pini CTO/Policlinico Mangiagalli, Rheumatology Division of Spedali Civili, Brescia and Rheumatology Division of Ospedale S Matteo, Pavia from 2009 to 2019 were included. Patients underwent monthly clinical examination. Fetal heart rate was assessed weekly by Doppler ultrasound from 14th to 26th gestational week. On week 14 and 26, a fetal echocardiography was performed. A EKG was performed at birth

Results: 351 prospectively followed pregnancies in 292 anti-SSA/Ro positive women were included. Table 1 reports diagnosis. None of the prospectively followed pregnancies were complicated by complete CHB. Seven additional patients were referred

Table 1. patients diagnosis

	n	%
Sjogren's Syndrome	58`	20
Systemic lupus erythematosus	76	26
UCTD	74	25
Asymptomatic Ro carriers	56	19
Other	28	10
	292	100

Table 2. maternal and fetal outcome

	healthy controls N=3158	Anti-SSA/Ro pts N=244	P value
Previous CHB n (%)		2 (0.8)	
Anti-SSB pos n (%)		46 (18.8)	
aPL pos n (%)		49 (20)	
Pregnancy			
Live births	3158	241	
Preeclampsia, n (%)	43 (1.1)	2 (0.8)	ns
Delivery			
Delivery <37 wks, n (%) / < 34 wks n (%)	401 (12.6) /201 (6)	35 (15.6) / 14 (6)	ns / ns
Cesarean Section, n (%)	897 (29.3)	115 (47.5)	<0.001

to our clinics after diagnosis of CHB and were subsequently found to be anti-SSA positive, reporting no symptoms of diseases. Considering the 7 additional pregnancies, the incidence of CHB was 1.9%. We observed 3 neonates (0.8%) with cutaneous NLS and 1 case of transient increase of liver enzymes. In another neonate, a 1th degree A-V block was found after birth. A complete analysis of maternal and fetal outcome was possible in 244 cases (Table 2) and compared with 3158 unselected healthy controls. Among these 244 cases, 65% were taking hydroxychloroquine

Conclusion: none of the patients prospectively followed in our centers before and during pregnancy developed complete CHB. If the 7 cases of anti-SSA positivity diagnosed after CHB detection were included in the analysis, the incidence of CHB was comparable to previous reports. Our data suggest that a strict follow up and proper treatment of anti-SSA positive patients with or without an autoimmune disease before and during pregnancy can reduce the risk of NLS. Further studies are warranted to confirm a possible protective role of anti-rheumatic treatments, including HCQ

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SAT0208 INCIDENCES OF ADVERSE EFFECTS AND DISEASE FLARE DUE TO PNEUMOCYSTIS PNEUMONIA PROPHYLAXIS WITH TRIMETHOPRIM/SULFAMETHOXAZOLE IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: Methods of preventing pneumocystis pneumonia (PCP) in systemic lupus erythematosus (SLE) are controversial. Previous studies have verified the efficacy and safety of trimethoprim/sulfamethoxazole (TMP-SMX) in patients with rheumatic diseases[1]. However, as for SLE, some clinicians advise against prescribing TMP-SMX because sulfa allergy is reportedly more common in SLE than in other rheumatic diseases[2, 3]. Anecdotally, sulfonamides may also worsen SLE itself, but few data are available on lupus flares related to sulfonamides[3].

Objectives: This study aimed to assess the incidences of adverse effects and disease flare due to PCP prophylaxis with TMP-SMX in SLE patients.

Methods: SLE patients seen at our hospital between September 2010 and April 2018 who received TMP-SMX as a PCP prophylaxis were enrolled. The clinical manifestations, treatment course, adverse drug reactions, and occurrence of lupus flares were retrospectively assessed from the medical records. The Naranjo adverse drug reaction probability scale4 was used to determine whether the reactions were induced by SMX-TMP. According to the British Isles Lupus Assessment Group (BILAG) 2004 index, a severe flare of lupus was defined as a development of a new grade A manifestation, and a moderate flare as a development of grade B manifestation following grade C, D or E. Two board-certificated rheumatologists reviewed the medical records in a blinded fashion to determine the reason for the flare, with disagreement resolved by consensus.

Results: In total, 188 SLE patients were enrolled; of these, 117 (62.2%) had no adverse events and were able to continue taking SMX-TMP as needed. Seventy-one patients (37.8%) stopped SMX-TMP due to suspected adverse drug reactions, including fever, rash, liver function disorder, and cytopenia. The Naranjo scale indicated “definite” in 4, “probable” in 39, and “possible” in 28. Eighteen-patients restarted the SMX-TMP and 9 patients could continue the prophylaxis without adverse effects. Five patients were hospitalized to treat the adverse events: 3 with drug rash (concomitant use of hydroxychloroquine in 2), 1 with hypersensitivity (concomitant use of azathioprine) and 1 with hyponatremia, respectively.

Lupus flares occurred in 10 patients (5.3%) within one month after the start of the the SMX-TMP prophylaxis. Macrophage activation syndrome (MAS) or neuropsychiatric SLE occurred in 9 of them. Of 188 cases, 2 patients (1.1%) developed a new onset of MAS during the stable clinical course as the flare, which was considered due to SMX-TMP. Confounding factors, including high disease activity and the reduction of glucocorticoids, were identified in other 8 flares.

Conclusion: PCP prophylaxis with SMX-TMP was tolerable in most SLE patients. However, a small number of SLE patients developed severe adverse effects or disease flares due to the SMX-TMP.

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SAT0209 PREVALENCE AND RELATED FACTORS OF SLEEP DISTURBANCE IN PATIENTS WITH PRIMARY SJÖGREN’S SYNDROME

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Background: The incidence of primary Sjögren’s syndrome(pSS) is increasing gradually,and it was ranking second among connective tissue diseases(CTDs)in China.Studies recently have shown that many patients with various CTDs have sleep disturbances,which seriously degraded the patient’s quality of life.As well known, Sleep is an important physiological process to maintain human metabolism, tissue repair,and homeostasis. At present,there are relatively several studies on sleep quality in patients with Rheumatoid arthritis(RA)and Systemic lupus erythematosus(SLE),but less reports on pSS in China have been published. Therefore,it is important to explore the quality of sleep and its influencing factors in such patients.

Objectives: The purpose of this study is to evaluate the quality of sleep and related factors in China Mainland patients with primary Sjögren’s syndrome(pSS),and to provide reference and theoretical basis for constructing targeted sleep interventions and improve their quality of life.

Methods: A all of 103 pSS patients and 40 matched healthy controls were enrolled in a comparative study of sleep quality using the Pittsburgh Sleep Quality Index(PSQI),and demographic,clinical,and laboratory data were collected from them.The patients completed questionnaires on the European League Against Rheumatism (EULAR)SS Patient Reported Index(ESSPRI), EULAR SS Disease Activity Index (ESSDAI),Xerostomia inventory(XI)with the help of researchers,Pain and fatigue were evaluated with a 100-mm visual analogue scale(VAS).Generalized Anxiety Disorder(GAD-7) and Patient Health Questionnaire(PHQ-9) were used to assess anxiety and depression separately,and whether they have autonomic symptoms (such as sweating, palpitations.)will be asked.

Results: The PSQI score and the frequency of poor sleep quality(PSQI>7) were higher in the pSS patients (11.60±5.03,71.8%)than the healthy controls(5.98±3.85,25%).Poor sleepers had a significantly higher GAD-7,PHQ-9,XI,ESSPRI,pain and fatigue VAS,and longer disease duration than good sleepers.Additionally, poor sleepers show more frequent autonomic symptoms.Sleep quality of patients with pSS was positive correlated with GAD-7,PHQ-9,XI,ESSPRI,pain and fatigueVAS scores,but no correlation with disease activity.Meanwhile,depression is a independent factor of sleep quality.

Conclusion: Our study showed that the sleep disturbance seen in patients with pSS may contribute to the depression associated with this disease,Future research should investigate that whether antidepressant treatment improve sleep and directly improve quality of life.

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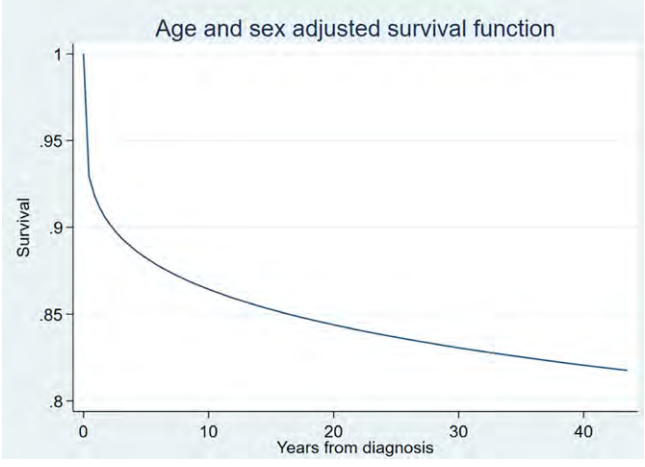
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SAT0210 FACTORS ASSOCIATED WITH TIME TO SEVERE LUPUS NEPHRITIS IN A COHORT OF COLOMBIAN PATIENTS

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Background: Systemic lupus erythematosus (SLE) clinical manifestations, and their severity, vary according to age, ethnicity and socioeconomic status. Both Hispanic and Afro-Americans have a higher incidence and more sever presentation when compared to Caucasian patients with SLE
Objectives: To analyze clinical and immunological characteristics associated with time to severe renal involvement in patients with Systemic Lupus Erythematous in a Colombian cohort followed for one year, between January 2015 and December 2018
Methods: Retrospective follow-up study based in clinical records. Patients with SLE diagnosis that fulfilled either 1987 American College of Rheumatology Classification Criteria for SLE or 2011 Systemic Lupus International Collaborating Clinics (SLICC) classification criteria for SLE. We included patients with diagnosis of lupus nephritis according to Wallace and Dubois criteria. Patients who did not have at least two follow-up measurements or had a cause of nephritis other than lupus were excluded. The main outcome was defined as time from diagnosis to sever renal involvement defined as creatinine clearance ≤50 ml/min, 24-hour proteinuria ≥3.5 grams o end stage renal disease.
We analyzed clinical and immunological characteristics. Descriptive statistical analyses of participant data during the first evaluation are reported as frequencies and percentages for categorical variables, and as medians and interquartile ranges (IQR) for quantitative variables. Age and sex adjusted survival functions and Hazard ratios (HR) with 95% confidence intervals and p-values were estimated using parametric Weibull models por interval-censored data. P values < 0.05 were considered statistically significant
Results: 548 patients were analyzed: 67 were left-censored as they presented renal involvement at entry, 6 were interval censored as outcome occurred between study visits, and 475 were right-censored as involvement was not registered during follow-up. 529 (96.5%) patients were female, median age at entry was 46 (IQR = 23) and median age to diagnosis was 29.5 (IQR = 20.6). 67% were mestizo, 13% Caucasian and 0.3% Afro-Colombian. Age and sex adjusted variables associated with time to severe lupus nephritis were high blood pressure HR = 3.5 (95%CI 2.2-5.6; p-value <0.001) and Anti-RO (per unit increase) HR = 1.002 (95%CI 1.001-1.004; p-value = 0.04). Figure 1 shows age and sex adjusted survival function.



Conclusion: In our cohort the appearance of severe lupus nephritis occurs in less than 15% of patients at 10 years. Both high blood pressure and elevated anti-Ro titers were associated with a higher rate of onset in the presentation of severe lupus nephritis, as seen in some polymorphs of anti Ro.

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Disclosure of Interests: Sebastian Herrera Speakers bureau: academic conference, Juan camilo Diaz-Coronado: None declared, Diego Rojas-Gualdrón: None declared, Laura Betancur-Vasquez: None declared, Daniel Gonzalez-Hurtado: None declared, Juanita Gonzalez-Arango: None declared, laura Uribe-Arango: None declared, Maria Fernanda Saavedra Chacón: None declared, Jorge Lacouture-Fierro: None declared, Santiago Monsalve: None declared, Sebastian Guerra-Zarama: None declared, Juan david Lopez: None declared, Juan david Serna: None declared, Julian Barbosa: None declared, Ana Sierra: None declared, Deicy Hernandez-Parra: None declared, Ricardo Pineda.Tamayo: None declared
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SAT0211 RENAL INJURY IN SYSTEMIC LUPUS ERYTHEMATOSUS CHARACTERIZED BY THROMBOTIC MICROANGIOPATHY

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Background: Classical lupus nephritis (LN) is characterized by glomerular immune complex(IC) deposition with glomerular proliferation, basement membrane destruction and cell infiltration. Non-IC mediated renal injury with thrombotic microangiopathy (TMA) was also reported in patients with systemic lupus erythematosus (SLE-renal TMA), but most studies were reported in patients with both LN and renal TMA.
Objectives: In this study, clinical features and outcomes of SLE-renal TMA in absence of obvious IC in SLE patients were analyzed.
Methods: Patients with glomerular TMA and/or vascular TMA in the absence of obvious subendothelial or epithelial immune deposits were screened out from 2332 biopsied in SLE patients who underwent first renal biopsy from January 2005 to August 2016. Their clinical, histological features and outcomes were retrospectively analyzed.
Results: In 2332 renal biopsies obtained from SLE patients, 257 (11.0%) showed renal TMA, of which 237 showed both renal TMA and LN, and 20 biopsies had only renal TMA (SLE-renal TMA). There were 2 males and 18 females with an average age of (25 ± 10) years. The median course of SLE and LN were 3.0(1.0, 6.0) and 0.8(0.5, 1.9) months. All 20 patients deserved acute kidney injury, of which 11 (55%) needed renal replacement therapy (RRT) and 12 (60%) were nephrotic syndrome. Blood system involvement was found in all cases, including 13 cases (65.0%) with TMA triad (microvascular hemolytic anemia, thrombocytopenia and elevated lactate dehydrogenase).
Pathological examination showed that 17 cases (85.0%) had both glomerular TMA and vascular TMA. Immunofluorescence and electron microscopy showed that 8 cases (40%) had no IC deposition in glomerulus and 12 cases (60%) had only IC deposition in mesangium. Acute tubulointerstitial lesions in patients requiring RRT were more serious than those no needing for RRT((43.6±24.9) % *vs* (21.7±20.1) %, P=0.047). The fusion range of foot process was positively correlated with proteinuria (r^2 = 0.347, P=0.006).
All patients received high-dose methylprednisolone pulse therapy. Four patients received plasma exchange and three patients received gamma globulin, respectively. Eleven patients requiring RRT all stop RRT in a median time of 16.0 (9.0, 30.0) days. During a median follow-up of 58.0 (36.0, 92.3) months, complete remission (CR) was obtained in 15 cases, partial remission in 4 cases and no remission in 1 case. Six cases (30%) relapsed. No case died or progressed to end stage renal disease.
Conclusion: Renal injury characterized by TMA is not uncommon in SLE renal biopsy cases. The clinical manifestation is special and the renal injury is serious. The renal outcome is good by intensive immunosuppressive therapy. It should be considered as a unique type of renal injury in SLE.
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SAT0212

OBSTETRIC AND THROMBOTIC ANTIPHOSPHOLIPID SYNDROME: SIMILAR ANTIBODIES BUT DIFFERENT PHENOTYPES?

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Background: Several studies showed two main clinical phenotypes of antiphospholipid syndrome which could be independent, but only a few data contrast features between these two groups.

Objectives: To investigate whether obstetric and thrombotic manifestations of APS are independent subtypes.

Methods: This was a single center prospective study from the PUMCH database of primary antiphospholipid syndrome followed for over 4years. Comparing demographic data, laboratory tests, pregnancy morbidity and thrombotic events during follow-up between IoAPS (isolated obstetric APS) and ItAPS (isolated thrombotic APS).

Results: A total of 244 patients was registered in PUMCH primary APS cohorts, 157(64.34%) were female patients. In female patients, 44(28.03%) were diagnosed with IoAPS, 42(26.75%) were ItAPS. Demography showed patients in ItAPS group were older than IoAPS group (40 vs 33, p<0.001), presented more cardiovascular risks(33.33% vs 6.8%, p<0.01), neurological disorders (23.8% vs2.3%,p<0.01) and thrombocytopenia (47.6%vs 20.5%,p<0.01). Antibody profiles had no difference in triple positivity, double positivity and partial single positivity (ACL, LA), but presence of single anti-β2GPI positivity showed significant difference between IoAPS and ItAPS (59.09% vs 38.1%, p<0.05). Significant difference was presented in homocysteine(Median) between IoAPS and ItAPS (9.9 vs 11.5, p<0.05), not in inflammatory markers. During 49.5 (Median) months follow-up of ItAPS group, patients got 90 pregnancies, 5 abortions but weren't fulfilled with the diagnosis criteria of pregnancy morbidity. No thrombotic event occurred during 48.5(Median) months follow-up time in IoAPS group.

Conclusion: IoAPS and ItAPS shared similar antibody profile, but presented isolated clinical complications, different demographic features and maintained independent manifestation during follow-up, indicating the underlying pathogeneses are different.

Table1. Demographic characteristics

	IoAPS(n=44)	ItAPS(n=42)	P-value
Age, years, Median (Q1-Q3)	33 (30.00, 36.00)	40(33.75, 55.25)	.00
B.M.I. Median (Q1-Q3)	22.86 (20.70,24.45)	23.52 (21.44, 27.70)	.10
Flow-up time, month, Median (Q1-Q3)	48.50 (36.00,77.00)	49.50 (23.00,103.75)	.44
Smoke (n%)	1(2.27)	0(0)	1.00
Cardiovascular risk factors (n%)	3 (6.82)	14 (33.33)	.00
Coronary heart disease	0(0)	2(4.76)	.24
Hypertension	1(2.27)	5(11.90)	.11
Obesity	2(4.55)	9(21.43)	.03
Diabetes mellitus	0(0)	0(0)	
Complications (n%)	16 (36.36)	30 (71.43)	.00
Kidney diseases	2(4.55)	3(7.14)	.67
Thrombocytopenia	9(20.45)	20(47.62)	.01
Neurological Disorders	1(2.27)	10(23.81)	.00
Stroke	0(0)	8(19.05)	.00
Non stroke CNS manifestations	1(2.27)	2(4.76)	.61
Valvular heart diseases	4(9.09)	2(4.76)	.68
Failed pregnancy during follow-up (%)	116/154(75.32)	5/90(5.56)	.00
Thrombosis during follow-up (n%)	0(0)	4(9.52)	.05

Table 2. Laboratory tests

	IoAPS(n=44)	ItAPS(n=42)	P-value
Antibody categories			
Triple positive (n%)	11(25.00)	15(35.71)	.35
ACL+β2GPI+LA			
Double positive (n%)	7(15.90)	11(26.19)	.29
LA+ACL	0(0)	1(2.38)	.49
LA+anti-β2GPI	2(4.55)	3(7.14)	.67
ACL+anti-β2GPI	5(11.36)	7(16.67)	.55
Single positive (n%)	26(59.10)	16(38.10)	.04
ACL	1(2.27)	1(2.38)	1.00
anti-β2GPI	23(52.27)	10(23.81)	.01
LA	2(4.55)	5(11.90)	.26
Negative after treatment	4(9.09)	1(2.38)	.36
ESR	10(6, 27)	9(4, 16)	.06
CRP	1.03(0.56, 3.85)	1.11(0.43, 3.18)	.63
HCY	9.9(8.10, 12.10)	11.5 (9.30, 14.65)	.04

***** aCL: anticardiolipin antibodies; anti-β2-GPI: anti-β2 glycoprotein I antibodies; LA: lupus anticoagulant; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; HCY: homocysteine.

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SAT0213

IMPACT OF FLARES ON HEALTHCARE RESOURCE USAGE AND PROS IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: The effect of flares on healthcare resource usage and patient-reported outcome scores in SLE patients is not well quantified.

Objectives: To understand how flares impact healthcare resource utilization (HCRU) and patient-reported outcomes amongst an international real-world dataset of SLE patients.

Methods: The Adelphi Real World 2015 Lupus Disease Specific Programme (DSP) is a cross-sectional study of 263 rheumatologists in the US and EU5. Rheumatologists were asked to complete patient record forms (PRFs) for the next 5 prospectively consulting SLE patients; the same patients were asked to complete patient self-completion (PSC) forms describing how SLE affected them. PRFs collected data pertaining to the patient's diagnosis, disease history, current clinical outcomes, treatment and management history. PSCs collected similar data and included patient-reported outcome measures (PROs) to assess humanistic burden. Propensity score matching was used to assess differences in HCRU and health status between SLE patients who had flared (physician defined) in the last 12 months and those who had not. Matching variables were patient ethnicity, time since diagnosis, and severity at diagnosis. Data were extracted from 1278 PRFs, and 591 PSCs. Propensity score matching was carried out on two matched groups of 408 patients.

Results: Demographic data are reported in Table 1. Propensity score matching showed patients who flared in the last 12 months experienced significantly greater hospitalizations, visits to the ER, and total HCP consults in the last 12 months. Significantly greater drug burden lower physician and patient satisfaction, lower EQ-5D score (worse health status), lower FACIT Fatigue score (greater fatigue), and greater overall work impairment (Table 2) were also observed.

Table 1. Demographic data

Variable	Flared in last 12 months	Not flared in the last 12 months
Mean age (years)	41.8	42.4
% Female	86.0	87.0
% White/Caucasian	66.2	76.3
Mean years diagnosed	5.9	5.4

Table 2. Propensity score matching results

Outcome variable	Flared mean	Not flared mean	Coefficient	95% CI	p-value
Hospitalisations in last 12 months	24.26	7.63	0.17	[0.12 – 0.21]	<0.001
Emergency department visits in last 12 months	20.83	4.19	0.17	[0.12 – 0.21]	<0.001
Number of tests in last 12 months	46.49	38.90	7.59	[3.74 – 11.44]	<0.001
Number of current medications	2.76	2.19	0.57	[0.43 – 0.72]	<0.001
Physician satisfied	64.46	86.63	-0.22	[-0.28 – -0.17]	<0.001
Patient satisfied	69.29	85.09	-0.16	[-0.24 – -0.08]	<0.001
EQ-5D-3L	0.72	0.83	-0.11	[-0.15 – -0.07]	<0.001
FACIT Fatigue	30.06	36.48	-6.42	[-8.5 – -4.3]	<0.001
WPAI overall percentage work impairment	42.74	30.23	12.5	[7.51 – 17.50]	<0.001

Conclusion: The analysis of international real-world data confirmed that SLE patients who flared in the last year represent a greater burden on healthcare resource and demonstrate significantly worse health status, greater fatigue, lower

patient and physician satisfaction and greater overall work impairment compared with non-flaring patients. There is a need for more effective treatments in this patient population to reduce patient and healthcare burden.

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SAT0214 ULTRASONOGRAPHIC CHANGES OF SALIVARY GLANDS IN PRIMARY SJOGREN'S SYNDROME: A LONGITUDINAL PROSPECTIVE STUDY

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Background: In the diagnosis of primary Sjogren' syndrome (SS), salivary gland ultrasound is useful tool. Until now, there is no data for ultasonographic changes of major salivary glands over time.

Objectives: This study aimed to evaluate the changes in abnormalities of salivary gland ultrasound (SGUS) over time in patients with pSS.

Methods: Patients with pSS (n=70) and idiopathic sicca syndrome (n=18) underwent SGUS twice at baseline and 2 years later. The semi-quantitative SGUS score (0-48) was used, which comprises five parameters: parenchymal echogenicity, homogeneity, hypoechoic areas, hyperechogenic reflections, and clearness of posterior borders. The intraglandular power Doppler signal (PDS) was also assessed. The changes of these SGUS variables were compared in patients with pSS and idiopathic sicca syndrome.

Results: The median (interquartile range) total SGUS scores at baseline was 27 (14) in patients with and 4 (3) in those with idiopathic sicca syndrome (p<0.001). In the pSS group, the total SGUS scores and the SGUS scores for bilateral parotid glands were significantly increased during median 23.4 month follow-up (p=0.013 and p=0.011, respectively). Homogeneity and hypoechoic areas were the domain to show statistically significant progression of SGUS scores. None of the SGUS scores changed significantly in the patients with idiopathic sicca syndrome. In patients with pSS, baseline and follow-up PDS sum scores of four salivary glands were significant higher in worsening SGUS group (n=13) than no change/improvement SGUS group (n=55/2).

Conclusion: The structural abnormalities in major salivary glands assessed using SGUS scores progressed significantly in patients with pSS. In pSS group, 18.6% patients had worsening SGUS scores during 2 years. Intra-glandular hypervascularity was associated with worsening of salivary gland abnormalities.

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SAT0215 HISTORY OF TONSILLECTOMY IS ASSOCIATED WITH GLANDULAR INFLAMMATION IN SJÖGREN'S SYNDROME

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Background: The palatine tonsils are secondary lymphoid-organs that serve as the first line of defense against pathogens. Whether history of tonsillectomy (TE) is associated with the phenotype of Sjögren`s syndrome (SjS) has not been investigated to date.

Objectives: To test whether TE is linked to SjS phenotype and disease activity scores.

Methods: A total of 183 patients from the Optimising Assessment in Sjögren`s Syndrome (OASIS) cohort with SjS or non-SjS sicca syndrome were analysed. Patients with SjS fulfilled 2016 ACR/EULAR classification for primary SjS; sicca patients had objective and/or subjective dryness, but were anti-Ro/SSA negative and had no physician diagnosis of SjS. One SjS patient who had TE around the time of symptom onset was excluded.

Results: Of the total cohort, 116 were diagnosed with SjS (86.2% SSA/Ro positive) and 67 with non-SjS sicca syndrome. Overall, 29% (53/183) had TE; 24.1% of the SjS patients (28/116) and 37.3% of the sicca patients (25/67). The prevalence of TE was higher in sicca than in SjS (p=0.043). The median age at TE was 8 (range 3-50) years and did not differ between SjS and sicca patients (p=0.629). Neither age at first symptoms (p=0.093) nor disease duration (p=0.623) were associated with TE in patients with SjS. SjS patients with TE showed a higher average histological focus score (2.1 (1.2-2.8) vs. 1.3 (0.0-4.3); p=0.049), and were more likely to have activity in the glandular (53.6 vs. 20.5%; p=0.001) and constitutional (39.3 vs. 14.9%, p=0.014) domains of the ESSDAI, and lower levels of IgG (12.2 (7.8-35.6) vs. 15.6 (5.7-56.4) g/l; p=0.012) and IgA (2.3 (0.9-6.6) vs. 2.9 (0.7-9.4) g/l; p=0.032). Whereas there was no difference in EQ5D utility values (p=0.718), VAS global health was significantly lower in the patients with SjS who had TE (58 (10-78) vs. 70 (10-97); p=0.021). There was no association between the status of TE and autoantibodies (SSA, SSB, RF), lachrymal and salivary glands function (Schirmer`s test, unstimulated saliva flow), complement (C3, C4), serum levels of free light chains, β2-microglobulin, ESSPRI, or total ESSDAI (all p-values >0.1). Of 181 patients, 12.7% (23/283) had appendectomy (AE); 10.5% (12/114) of the SjS patients and 16.4 %(11/67) of the sicca patients (p=0.258). With the exception of lower unstimulated salivary flow (0.086 (0.01-0.43) vs. 0.11 (0.0-1.3) ml/min; p=0.026) in SjS patients with AE, there were no differences in disease phenotype between SjS patients with and without AE (all p-values >0.1).

Conclusion: History of TE in SjS is associated with higher average focus scores and with glandular swelling. It could be speculated that the absence of palatine tonsils is compensated by enhanced lymphocytic infiltrates in the salivary glands. Further research is required to determine if TE is a risk factor for both SjS and non-SjS sicca and to determine the role of the tonsils in the generation of hypergammaglobulinaemia in SjS.

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SAT0216 DISEASE SEVERITY, COMORBID CONDITIONS, TREATMENT PATTERNS, AND FLARES IN ADULTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN THE UNITED KINGDOM: A REAL-WORLD OBSERVATIONAL RETROSPECTIVE COHORT ANALYSIS

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Background: There is limited real-world evidence describing the presentation and treatment patterns of systemic lupus erythematosus (SLE) in the United Kingdom (UK).

Objectives: To characterize disease severity, comorbid conditions, treatment patterns, and flares in a longitudinal cohort of adults with SLE in the UK.

Methods: Patients aged ≥18 years with SLE were identified in the Clinical Practice Research Datalink – Hospital Episode Statistics database from January 1, 2005, to December 31, 2017. Patients were required to have ≥12 months of data before and after index date (date of earliest SLE diagnosis available). SLE disease severity and flares were classified as mild, moderate, or severe using adapted claims-based algorithms[1,2] that use SLE-related conditions (eg, end-stage renal disease), medications (eg, antimalarials, immunosuppressants, and corticosteroids), and health service use (eg, hospitalizations and emergency department visits).

Results: Of 802 patients with SLE, 369 (46.0%) had mild, 345 (43.0%) had moderate, and 88 (11.0%) had severe SLE at baseline. In total, 692 (86.3%) patients were treated with SLE medications in the first year after SLE diagnosis. Among the total population (802), 557 (69.5%) patients received antimalarials, 203 (25.3%) received immunosuppressants, and 416 (51.9%) received corticosteroids (prednisolone); patients may have received ≥1 type of drug. Information on biologic use in hospitals is unavailable in these data. The mean (standard deviation [SD]) time to initiating any medication from index date was 177 (385.3) days (Figure 1**A**). The median time to first flare from index date was 63 days (95% confidence interval 57–71) (Figure 1**B**). A majority of patients (750/802, 93.5%) experienced ≥1 flare during follow-up; the first flare was mild for 73.2% of patients (549/750), moderate for 15.5% (116/750), and severe for 11.3% (85/750). The mean (SD) annual overall flare rate in the first year after index date was 3.5 (2.5) (mild flares: 2.6 [2.5]; moderate flares: 0.7 [1.5]; severe flares: 0.2 [0.6]) (Figure 2). A shorter median time to first flare was significantly associated with moderate or severe disease (P<0.001) and the presence of comorbid conditions (P<0.001).

Conclusion: Our findings suggest some delay in SLE treatment initiation in the UK. Most patients with SLE experience flares within 2 months from diagnosis. Early treatment may delay or reduce the severity of the first SLE flare after diagnosis and may translate to slower disease progression, lower organ damage accrual, and better outcomes.

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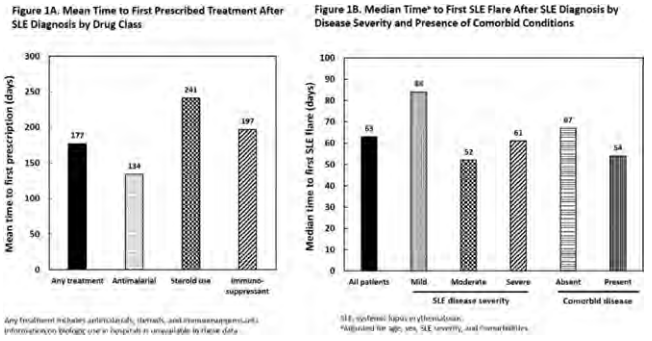
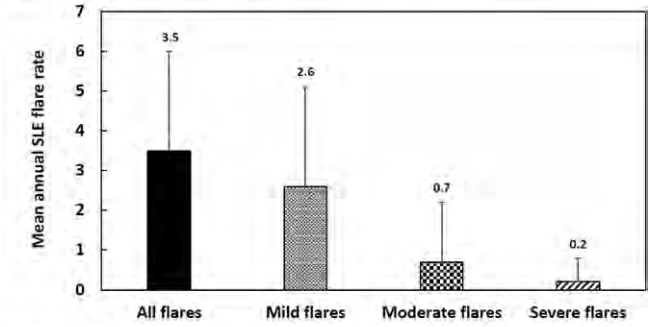


Figure 2. Mean Annual SLE Flare Rates by Severity During First Year After SLE Diagnosis



SLE, systemic lupus erythematosus.
Error bars represent standard deviation.

Disclosure of Interests: Julia Langham Consultant of: AstraZeneca, Volkan Barut Employee of: AstraZeneca, Mihail Samnaliev Consultant of: AstraZeneca, Sue Langham Consultant of: AstraZeneca, Sharada Weir Consultant of: AstraZeneca, Xia Wang Employee of: AstraZeneca, Barnabas Desta Employee of: AstraZeneca, Edward R. Hammond Employee of: AstraZeneca

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SAT0217

PERFORMANCE OF ACR/EULAR 2019, SLICC 2012 AND ACR 1997 CLASSIFICATION CRITERIA IN A COHORT OF SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITH LONGSTANDING DISEASE

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease with variable clinical features and a complex physiopathology. In 2019, EULAR and ACR have jointly developed new classification criteria with both high sensitivity and specificity. These criteria have the particularity of including the presence of ANA as an obligatory entry criterion and the existence of clinical and immunological domains with weighted scores.

Objectives: To evaluate the performance and characteristics of the ACR/EULAR 2019, SLICC 2012 and ACR 1997 classification criteria in a cohort of SLE patients with longstanding disease.

Methods: Descriptive observational study that enrolled a cohort of SLE patients with longstanding disease followed in a tertiary level hospital. Demographic and clinical data were gathered along with the fulfillment of classification criteria. The sensitivity of each classification criteria and the statistically significant associations between criteria fulfillment and clinical and immunological data were calculated. Statistical analyses were performed using the Chi2, T-student and ANOVA tests. Statistical significance was assumed in p values <0.05.

Results: A total of 79 patients (88.6% women) with a mean age of 51.8±14 years, disease duration of 15.2±11.5 years and SLEDAI of 2.65±2.1 were included. The sensitivity of the different classification criteria was 51.9% for ACR 1997, 87.3% for SLICC 2012 and 86.1% for ACR/EULAR 2019 (Table 1).

Table 1. Sensitivity and average scores.

	ACR/EULAR 2019	SLICC 2012	ACR 1997
Sensitivity (%)	86.1	87.3	51.9
Average score of patients classified as SLE (±SD)	18.6±5.8	5.3±1.4	5±0.9
Average score of patients NOT classified as SLE (±SD)	6.1±2.5	2.8±0.4	2.8±0.8

51.9% of patients met all three classification criteria, 29.1% met SLICC 2012 and ACR/EULAR 2019, 5% only met SLICC 2012 and 3.7% exclusively met ACR/EULAR 2019. 11.4% of patients did not meet any classification criteria and were characterized by having a low SLEDAI (0.6±0.9) and fulfilling only skin domains (alopecia or oral ulcers), antiphospholipid antibodies or hypocomplementemia.

Statistically significant associations were found between meeting ACR/EULAR 2019 classification criteria and the presence of low C3 and C4 (p<0.04), DNA (p<0.001), lupus nephritis III-IV (p<0.05) and arthritis (p<0.001), highlighting that all patients with arthritis met these criteria.

In the SLICC 2012 evaluation, significant associations were found between meeting these criteria and the presence of arthritis (p<0.01), renal involvement (p<0.04), leukopenia/lymphopenia (p=0.05), DNA (p<0.03) and hypocomplementemia (p=0.02).

Fullfilment of ACR 1997 was associated to the presence of malar rash (p<0.001), discoid lupus (p<0.05), photosensitivity (p<0.001) and oral ulcers (p<0.04), as well as arthritis (p<0.001), serositis (p=0.02), renal (p<0.05) and hematologic (p=0.05) involvement.

The Kappa concordance coefficient among classification criteria is detailed in Table 2.

Table 2. Kappa concordance coefficient.

	ACR/EULAR 2019 - SLICC 2012	ACR/EULAR 2019 - ACR 1997	SLICC 2012 - ACR 1997
Kappa concordance coefficient	0.61	0.27	0.30

Conclusion: The ACR/EULAR 2019 classification criteria maintain a high sensitivity similar to the SLICC 2012 in SLE patients with longstanding disease, both of which are much higher than ACR 1997. Patients with serological, articular or renal involvement are more likely to meet SLICC 2012 or ACR/EULAR 2019 criteria. It is noteworthy the relevance of dermatological manifestations in ACR1997 classification criteria against the increased weight that a better understanding of

SLE physiopathology has provided to analytic and immunological criteria in the subsequent classification criteria.

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SAT0218 SINGLE NUCLEOTIDE POLYMORPHISMS LOCATED IN REGULATORY REGIONS OF GENES INVOLVED IN SYSTEMIC INFLAMMATION (MAMDC1, ITGAM, AND CRP) CORRELATION WITH THE CLINICAL PICTURE OF DISEASE AND ACTIVITY PARAMETERS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: The exact pathogenesis of systemic lupus erythematosus (SLE) is poorly understood. It is an autoimmune disease that leads to a chronic inflammatory process involving numerous tissues and organs (skin, kidneys, joints, central nervous system, cardiovascular, respiratory, digestive and hematopoietic systems). However, despite the advancement of SLE molecular biology and the wide availability of tests and diagnostic tools, the knowledge about factors predicting the clinical disease activity as well as related changes in the laboratory results is insufficient.

Objectives: The goal of the study was to assess the relationship between selected single nucleotide polymorphisms (SNPs) and the clinical picture of disease **and some activity parameters** in patients with SLE.

Methods: We conducted a study of adult patients with SLE diagnosed and treated in the Rheumatology Department of Medical University of Lublin between 2016-2019. We enrolled 80 patients with SLE (71 women, 9 men), with the median (range) age 36 (19-72) and disease duration 6 (1-37) years. To objectively assess disease activity, standardized SLE activity scale - SLEDAI (Systemic Lupus Erythematosus Disease Activity Index) was used. Using the Real-Time PCR method and specific TaqMan probes SNPs of 3 genes: *MAMDC1* (rs910875; c.-1687G> C), *CRP* (rs3091244; c.-390C> A), and *ITGAM* (rs7193943; c.-323G> A) were analyzed and then their relationship with specific clinical picture of disease, activity and laboratory results were assessed.

Results: Carriers of the CC genotype compared to the remaining polymorphic variants (CG and GG) of the *MAMDC1* gene had an approximately 4-fold higher risk of skin disease compared to other clinical pictures of disease (renal, articular, neuro-psychiatric, hematological) (OR = 4.04; p = 0.0110)). Carriers of this genotype also had a higher risk of hematuria (OR = 4.57; p = 0.0082), sterile leukocyturia (OR = 53.91; p = 0.0071), the presence of anti-Sm / RNP antinuclear antibodies (OR = 4.15, p = 0.0074), reduced values of the C3 complement component (OR = 6.11; p = 0.0071) and the need for oral glucocorticosteroids (OR = 7.01; p = 0.0028). In addition, significantly higher values of SLEDAI disease activity scale were observed in carriers of the CC genotype of the *MAMDC1* gene (medians: 6 vs 4; p = 0.0220). Moreover, we observed a trend towards a higher risk of hepatomegaly in GG genotype carriers of the *ITGAM* gene (OR=18.50; p=0.0525). In addition, the AA genotype of the *CRP* gene was associated with a higher risk of proteinuria (OR = 84; p <0.0001), Anti-SSA / Ro autoantibodies (OR = 3.29; p = 0.0484), and aCL IgM (OR = 3.42; p = 0.0332) occurrence. Carriers of AA genotype of the above gene were also at higher risk of earlier occurrence of first disease symptoms as well as disease diagnosis at a younger age (respectively: 24 vs 31 years; p=0.0225, 23 vs 29 years; 0.0442).

Conclusion: The results suggest the relationship between SNPs in genes involved in systemic inflammation (*MAMDC1, ITGAM, CRP*) and disease activity as well as the occurrence of some specific clinical pictures of disease in patients with SLE.The genetic dispositions described above may serve as attractive markers in SLE, potentially useful in clinical practice.

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SAT0219 PATIENT CHARACTERISTICS, TREATMENT PATTERNS, AND RESOURCE UTILIZATION OF SJOGREN'S SYNDROME PATIENTS IN A LARGE US HEALTH NETWORK

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Background: Sjogren's syndrome (SS) is a chronic progressive autoimmune disorder which occurs as primary (pSS) or secondary SS (sSS). With no approved disease modifying therapy, there is limited information on the treatment patterns and resource utilization among these patients (pts).

Objectives: To describe pts characteristics, treatment patterns and healthcare resource utilization (HCRU) using electronic health records (EHR) of pts with pSS and sSS treated at the Providence St. Josephs Health system (PSJH).

Methods: Pts ≥18 years of age with at least one clinical encounter with ICD-9-CM or ICD-10-CM diagnosis of SS, between Jan 2013 and Mar 2019 were included. Date of first encounter with SS diagnosis (index date) was used to assess pts demographics. Pt baseline comorbidities were evaluated during the 24 months pre-index period. Treatment patterns and HCRU were assessed during the 12 months post-index follow-up. Descriptive statistics were used to

Table 1. Baseline Demographic and Clinical Pts Characteristics

	SS Pts (n=9,108)
Demographics	
Age (years) on index date, mean (SD)	58.3 (15.1)
Female, n (%)	8,338 (91.6)
Caucasian, n (%)	6.936 (76.2)
Western Region, n (%)	8,998 (98.8)
Married, n (%)	5,164 (56.7)
Never Smoked, n (%)	4,847 (53.2)
Primary diagnosis, n (%)	2,137 (23.5)
Comorbidities, n (%)	
Cardiovascular	1,408 (17.2)
Endocrine	3,733 (45.5)
Oncology	800 (9.8)
Blood disorders	1,221 (14.9)
Pulmonary	1,802 (22.0)
Neurological	1,821 (22.2)
Liver/Kidney	1,782 (21.7)
Rheumatologic disorders	2,096 (25.6)
Autoimmune/ Immune related	1,527 (18.6)
Baseline Medications, n (%)	
Symptomatic[1]	1,756 (43.0)
NSAIDs[2]	1,578 (38.6)
cDMARDs[3]	1,435 (35.1)
Corticosteroid[4]	1,393 (34.1)
bDMARDs[5]	266 (6.5)

[1]cevimeline, pilocarpine hydrochloride, ophthalmic insert etc; [2]aspirin, ibuprofen, naproxen; [3]methotrexate, hydroxychloroquine, sulfasalazine, leflunomide, myophenolate mofetil, azathioprine; [4]prednisone; [5]sarilumab, belimumab, ustekinumab, infliximab, adalimumab, certolizumab pegol, golimumab, etanercept, abatacept, tocilizumab, rituximab, tofacitinib, baricitinib

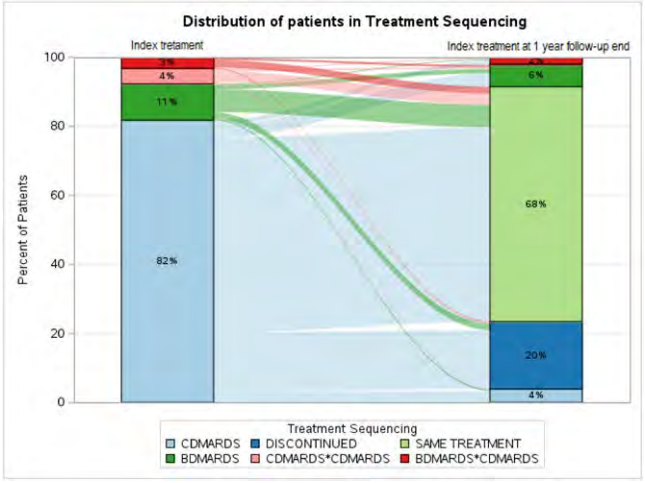


Figure 1. HCRU for pSS and sSS Pts

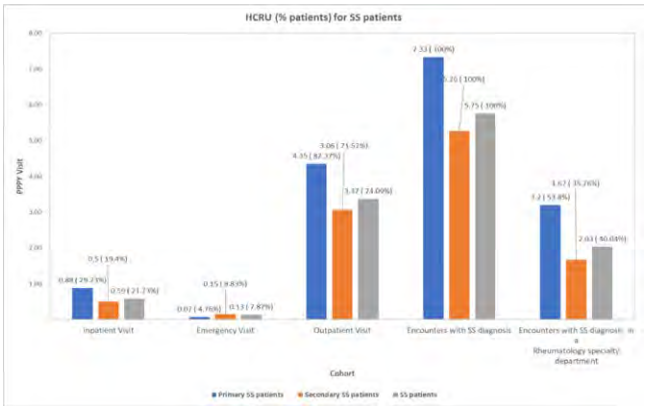


Figure 2. Treatment Sequencing for pSS and sSS PtsNote:Discontinued: pts who discontinued and didn't advance to any therapy; same treatment: pts continued on index treatment till we have information.

describe pts' demographic and clinical characteristics, and medications use in the baseline and follow up.

Results: Study cohort included 9,108 SS pts of which 76.5% had sSS diagnosis on index date. Majority of SS pts were women, Caucasian, with mean age of 58.3 yrs, and from western states in the US (Table 1). Endocrine conditions including hypo- and hyperthyroidism, and diabetes was the most common (45.5%) comorbidity at baseline, followed by rheumatologic disorders (25.6%) and neurological conditions (22.2%). Among patients with treatment information (4088, 44.88%), 42.95% were using symptomatic treatments for dry eye and mouth at baseline (Table 1). In the follow-up, SS pts had average 5.8 healthcare visits per patient per year (PPPY), including 0.6 inpatient and 3.4 outpatient visit respectively. About 40% of the SS pts (53.8% pSS and 35.8% sSS) were diagnosed by rheumatologists. Majority of the SS pts initiated treatment with cDMARDs (82%) and remained on the same treatment during 1 year follow-up (Fig 2).

Conclusion: Observation of higher comorbidities suggests substantial burden of SS pts on healthcare system, with majority of pts being diagnosed outside of rheumatology offices.

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SAT0220 BIOLOGICAL PREDICTORS OF ECHOGRAPHIC SALIVARY GLAND INVOLVEMENT SEVERITY IN PATIENTS WITH SJÖGREN'S SYNDROME

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Background: Echographic evaluation of salivary gland increasingly became a routine imaging modality in patients with Sjogren's syndrome (SS). However, predictive parameters associated with the severity of echographic features are still incomplete evaluated.

Objectives: The aim of this study was to evaluate the predictors for severe echographic involvement in patients with SS followed in a tertiary center.

Methods: We included 63 patients with SS (mean age: 52.3±11.9; 59 female). The complete laboratory workup, clinical manifestations and treatment were reviewed and the EULAR Sjögren's syndrome disease activity index (ESSDAI) was calculated for each patients. We performed the standard echographic evaluation of salivary gland in all patients and used a 4 grade system for severity staging.

Results: The distribution of echographic grade was: no any echographic features – 4 pts (6.3%); grade 1 - 24 pts (38.1%); grade 2 – 20 pts (31.7%); grade 3 – 10 pts (15.9%); grade 4 – 5 pts (7.9%). The ESSDAI and the hydroxichloroquine use were similar in these subgroups. We didn't find differences regarding CRP and fibrinogen and echographic features. The age of the patients, the anti-SSA and anti-SSB, ESR, total protein, IgA, IgG and rheumatoid factor levels were significantly higher and lymphocyte count was lower in patients with echographic severity above grade 2 when compared with patients with no or mild echographic features. However, using ANOVA test and post-hoc analysis, the only parameters associated with the severity of echographic features were high ESR (53 vs 17 in grade 4 vs 1, p=0.02), IgA (363 vs 190 in grade 4 vs 1, p=0.004) and IgG (1985 vs 1191 U/l in grade 4 vs 1, p=0.001) levels.

Conclusion: Parameters linked to polyclonal hypergammaglobulinemia (IgA and IgG levels; and ESR) seem to be linked to the severity of echographic appearance of salivary gland in patients with SS. Further studies are needed in order to better characterize this link.

Disclosure of Interests: Ancuta MIHAI: None declared, DENISE MARDALE: None declared, Daniela Opris-Belinski Speakers bureau: as declared, Ruxandra Ionescu Consultant of: Consulting fees from Abbvie, Eli-Lilly, Novartis, Pfizer, Roche, Sandoz, Speakers bureau: Consulting and speaker fees from Abbvie, Eli-Lilly, Novartis, Pfizer, Roche, Sandoz, Ciprian Jurcut: None declared

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SAT0221 FACTORS AFFECTING MORTALITY OF SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS IN SPAIN IN THE 21ST CENTURY: DATA FROM THE RELESSER REGISTRY

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Background: The mortality in Systemic Lupus Erythematosus (SLE) varies largely across different countries most probably due to social, healthcare and ethnic differences.

Objectives: To analyze the causes and identify predictive factors of mortality of SLE in Spain in the present century.

Methods: We performed a cross-sectional and retrospective study analyzing data from the RELESSER cohort (Spanish Registry of Systemic Lupus Erythematosus of the Spanish Society of Rheumatology). We included all patients diagnosed with SLE since the year 2000 and recorded sociodemographic, clinical and serological variables, comorbidities and treatments, as well as indicators of disease activity, damage and severity. The characteristics of the deceased patients were compared with those of the survivors, and variables with clinical significance or statistical significance were grouped into multivariate models to determine which ones were independently associated with the outcome of the disease.

Results: A total of 2004 patients were included, 88.6% female, the mean age at diagnosis was 38.3 (± 15.3) years, with a mean delay in diagnosis of 28.9 (± 52.6) months. Up to 2.84% of the individuals had died. The leading cause of death was SLE activity (n=16), followed by infections (n=14), vascular events (n=7) and cancer (n=6). The mean age of death was 54.68 (± 20.13) years, and neither age, sex nor delay in diagnosis was independently associated with mortality. The presence of nephritis, depression, severe infections, organ damage (SLICC/ACR DI) or disease activity (SLEDAI), as well as the use of cyclophosphamide, rituximab or high doses of corticosteroids, were predictors of mortality in our cohort. Antimalarial treatment and skin manifestations were linked to improved survival.

Conclusion: In the RELESSER cohort, clinical factors, co-morbidities, as well as therapeutic attitudes were associated with a significant increase in mortality in SLE. Interestingly, depression was independently associated to mortality. The activity of the disease and infections continue to be the main causes of death at the beginning of the 21st century amongst our patients.

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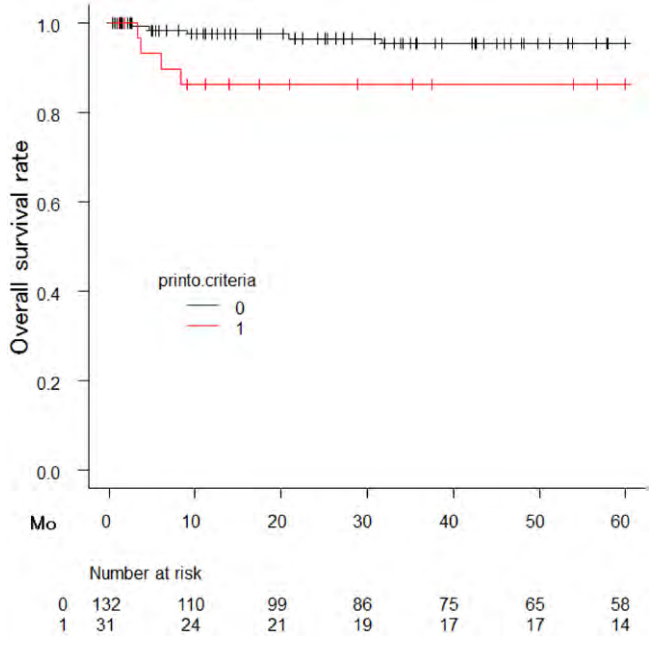
SAT0222 CLINICAL SPECTRUM AND LONG TERM FOLLOWUP OF SYSTEMIC LUPUS ERYTHEMATOSUS-ASSOCIATED MACROPHAGE ACTIVATION SYNDROME

T. Okano[1,2], J. Saegusa[1,2], K. Yoneda[2], I. Shirasugi[2], Y. Ueda[2], K. Akashi[2], A. Onishi[2], A. Morinobu[2]. [1]*Kobe University Hospital, Clinical Laboratory, Kobe, Japan*; [2]*Kobe University Hospital, Rheumatology and Clinical Immunology, Kobe, Japan*

Background: Systemic lupus erythematosus (SLE) patients present with variable clinical features ranging from mild joint and skin involvement to life-threatening organ involvement such as nephritis, neuropsychiatric involvement, diffuse alveolar hemorrhage, and hemophagocytic lymphohistiocytosis (HLH). HLH is rare, but fatal complication of SLE. Recently, European League Against Rheumatism, the American College of Rheumatology, and the Pediatric Rheumatology International Trials Organization was to develop a set of classification criteria for MAS complicating systemic juvenile idiopathic arthritis (PRINTO criteria) [1]. Sung Soo Ahn and his colleagues reported PRINTO criteria predicted mortality of adult SLE patient, but they followed only one year [2].

Objectives: To reveal association PRINTO criteria with long term mortalities in SLE patient in our Hospital.

Methods: We performed a retrospective analysis of SLE patients who received moderate dose glucocorticoid therapy (>0.4mg/kg/d) in our hospital between April 2008 and April 2019. Patients were evaluated for HLH using the 2016 PRINTO classification criteria for MAS. Clinical features and laboratory findings were compared and overall survival rate was analyzed.



Results: Among 164 episode (144 patients) with SLE, 31 episode (31 patients) 5.2% were considered to have MAS on admission.

The overall survival rate was significantly lower in patients with MAS than without MAS (86.2% vs. 95.3%, p = 0.048). Interestingly, SLEDAI had no association with mortality, relapse rate, and MAS complication. SLEDAI more focused on renal and neuropsychiatric symptoms than hematologic features. So SLEDAI might not be associated with MAS secondary to SLE. Furthermore, we observed no death patient with MAS after one year, and only 1 case relapse in MAS patient. So MAS might have fatal but less relapsing property compared with other lupus cases.

Conclusion: PRINTO criteria may be useful to differentiated fatal MAS patients from others. Further investigations are required to confirm our findings.**Limitation :** The main limitations of our study include its retrospective design, single center site, and that the number of admitted patients with SLE was small.

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Disclosure of Interests: None declared

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SAT0223 TUBULO-INTERSTITIAL INFILTRATES IN LUPUS NEPHRITIS

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Background: Lupus nephritis (LN) occurs in up to 60% of patients affected by Systemic Lupus Erythematosus (SLE). The presence of inflammatory infiltrates in glomeruli and/or in tubulo-interstitium (TI) plays an important role in terms of prognosis (1). Ectopic lymphoid structures (ELSs) are clusters of organized lymphoid infiltrates forming at sites of chronic inflammation in non-lymphoid organs (2). Data on ELSs in kidneys of SLE patients are scant (3-5).

Objectives: The aim of the study was to evaluate the tubule-interstitial infiltrates (TI-I) organization and to investigate the presence of ELSs.

Methods: Kidney sections of SLE patients undergoing a renal biopsy for diagnostic purpose were studied; LN was diagnosed according to the 2003 International Society of Nephrology / Renal Pathology Society classification criteria. Clinical, laboratory and histological data were collected in a standardized, computerized and electronically filled form, including past medical history. The presence of lymphoid aggregates and ELS in the kidney sections were firstly evaluated by hematoxylin-eosin (HE). By using immunohistochemistry (IHC), we characterized the infiltrates by identification of T cells (CD3), B cells (CD20) and follicular dendritic cells (CD21).

Results: By HE we evaluated 53 kidney samples from LN patients (F:M = 51:2, mean age at biopsy ± SD years 35±7.7; mean disease duration at date of biopsy ± SD 8±8.3 years). TI-I were found in 33 kidney specimens. By HE we identified a well-defined infiltrate pattern resembling ELS in 13 renal samples. In these samples, we confirmed the presence of organized infiltrates by IHC, with evidence of segregated T and B cells areas in most of them. In one sample, the CD21 staining was positive confirming the presence of ELS (Figure 1). Interestingly, this last patient, who failed ciclophosphamide and mycofenolate, responded to rituximab administration and is now in complete LN remission. Moreover TII was negatively correlated with renal remission after induction therapy (P=0.03) independent of the histological class and the induction treatment.

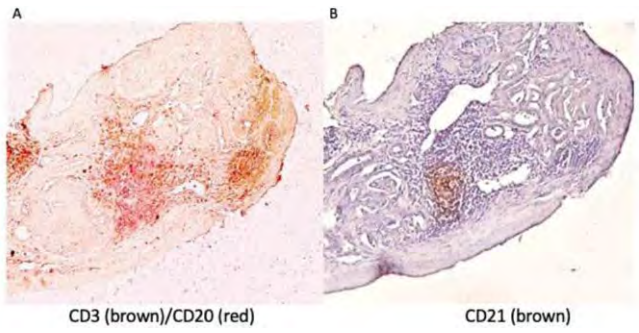


Figure 1. Biopsy specimens showing tubulo-interstitial ELS by IHC (10x).

Conclusion: Assessment and management of LN patients are greatly facilitated by information obtained by renal biopsy. In the present study the evaluation by HE of 53 kidney samples from patients with LN showed TI-I in 62% of the specimens and a well-defined infiltrate pattern with GC-like features in 39% of those specimens with TI-I, confirmed in IHC. The presence of TII was associated with a worse outcome in response to therapy. Our preliminary results obtained by IHC suggest that ELS could be considered as a biomarker of renal response to B-cell depleting therapy supporting the importance of TI disease.

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Disclosure of Interests: viviana antonella pacucci: None declared, Francesca Romana Spinelli Grant/research support from: Pfizer, Speakers bureau: Lilly, BMS, Celgene, Konsantinos Giannakakis: None declared, Serena Colafrancesco: None declared, Simona Truglia: None declared, Fulvia Ceccarelli: None declared, Cristina Garufi: None declared, cristiano alessandri Grant/research support from: Pfizer, Fabrizio Conti Speakers bureau: BMS, Lilly, Abbvie, Pfizer, Sanofi

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SAT0224 ANTIPHOSPHOLIPID ANTIBODIES AND VASCULAR RENAL LESIONS AS PROGNOSTIC FACTORS IN LUPUS NEPHRITIS

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Background: Several studies have showed that antiphospholipid antibodies (aPL) positivity represents a predictor of worse renal outcome in patients with Lupus Nephritis (LN). In addition, an association between aPL positivity and the histological data of vascular lesions on the renal biopsies has been reported.

Objectives: To determine the prognostic role of aPL and vascular renal lesions in the assessment of clinical outcome during the follow up period, in terms of time to achieve remission, number of renal flares and development of chronic renal damage in patients affected by LN.

Methods: Among 120 patients affected by LN from our Rheumatology Unit, 91 patients (age 43.8 ± 12 years, 74 (81.3%) female, disease duration 7.1 ± 7.9 years) have been evaluated and the follow-up data have been collected at the baseline and at 6, 12, 24 months and at the last follow-up visit. Histopathological data of 41 patients were evaluated according to the 2016 revision of ISN/RPS classification.

Results: Among the 91 LN patients, 31 (34.1%) were aPL positive (aPL+), 10 (32.2%) of them were affected by Antiphospholipid Antibodies Syndrome (APS), 53.3% showed a single aPL positivity, 23.1% double aPL positivity and 15.4% triple aPL positivity. At the last follow up visit a significant higher number of aPL+ patients showed a persistent complement consumption than aPL negative (aPL-) patients (p=0.001). Evaluating clinical outcome, we observed that aPL- patients showed a remission achievement time slightly earlier than aPL+ patients (13.6 ± 1.0 months vs 16.5 ± 1.5 months; log-rank test: p=0.06, Breslow test: p=0.08) and as expected, patients with a persistent complement consumption achieve remission later (18.2 ± 1.5 months vs 13.0 ± 1 months; log-rank test: p=0.002, Breslow test: p=0.003). Furthermore at the last follow up, a significant higher percentage of aPL+ patients developed persistent proteinuria (p=0.02) and chronic renal failure (p=0.04). Considering histologic features (activity and chronicity index, glomerulonephritis class, presence of mesangiolysis, glomerular wrinkling, glomerular thrombi, interstitial inflammatory infiltrates, interstitial fibrosis and tubular atrophy,tubulitis and vascular lesions) we didn't observe significant differences between aPL+ and aPL- patients but we found two typical vascular lesions (mesangiolysis and vascular thrombi) only in aPL + patients.

Conclusion: aPL positivity is a predictor of worse renal outcome but in our cohort of LN patients we didn't find an association between aPL positivity and vascular renal lesions at renal biopsy. The worse renal outcome and the late time to achieve remission in aPL+ group can be related to a cumulative vascular damage over time as observed in other organ and systems.

Disclosure of Interests: None declared

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SAT0225 THE POSITIVITY FOR HISTOPATHOLOGIC ASSESSMENT IN SALIVARY GLANDS SHOWED LITTLE IMPACTS ON CLINICAL FEATURES FOR ESTABLISHED PRIMARY SJÖGREN'S SYNDROME IN A CERTAIN ETHNIC POPULATION

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Background: The presence and the severity of focal lymphocytic sialadenitis in minor salivary glands is a pathognomonic feature in primary Sjögren's syndrome (pSS). However, it has not been determined whether performing of minor salivary gland biopsy (MSGB) in a setting of serologically and clinically established pSS give us additional clinical information.

Objectives: To investigate the necessity of MSGB in established pSS patients with the anti-Ro/SSA antibody.

Methods: We extracted 185 patients with anti-Ro/SSA antibody-positive pSS from the Korean Initiative of primary Sjögren's Syndrome, a prospective cohort. We assigned them into two groups, 161 patients with focus score ≥1 and other 24 with focus score < 1. The two groups were compared in various clinical aspects including the severity of glandular dysfunctions, systemic disease activities, extra-glandular manifestations, and other clinical indices and laboratory values. We also evaluated relationship between focus score and clinically important variables in pSS.

Results: Between two groups, there were no significant differences in the severity of secretory dysfunctions, the frequency of extra-glandular manifestations, systemic disease activities represented by various clinical indices, and laboratory findings possibly predicting the risk for lymphoma. Rather, the Sjögren's syndrome disease damage index was higher in the group with focus score < 1. Among all variables, serum immunoglobulin G level solely showed the correlation with focus score.

Conclusion: Given that little influence on clinical phenotypes, unconditional performing of MSGB should be reconsidered for serologically and clinically established pSS, especially in low-risk area for lymphoproliferative diseases.

Disclosure of Interests: None declared

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SAT0226 MINOR SALIVARY GLAND BIOPSY TO DIAGNOSE LYMPHOMA IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

S. Parreau[1], R. Seror[2], B. Terrier[1], B. Burroni[3], C. Jamart[1], A. Régent[1], G. Nocturne[2], L. Mouthon[1], X. Mariette[2], V. Le Guern[1]. *[1]Hôpital Cochin, Internal Medicine, Paris, France*; *[2]Le Kremlin-Bicêtre, Rheumatology, Paris, France*; *[3]Hôpital Cochin, Pathology, Paris, France*

Background: Non-Hodgkin B-cell lymphoma (NHL), especially mucosa-associated lymphoid tissue (MALT) lymphoma, is one of the main complications of primary Sjögren's syndrome (pSS). Frequent extranodal lymphoproliferation makes its diagnosis challenging and obtaining a biopsy difficult. Since pSS-associated lymphomas are very frequently MALT lymphomas with salivary gland involvement, we hypothesized that minor salivary gland biopsy (MSGB) could be useful for NHL diagnosis in this context.
Objectives: To evaluate the potential contribution of MSGB for the diagnosis of pSS-associated MALT lymphoma by comparing patients diagnosed with NHL based on MSGB or another tissue.
Methods: All pSS patients (ACR/EULAR 2016 classification criteria), from the Paris National Referral Centers for Rare Systemic Autoimmune Diseases, diagnosed with NHL between January 2010 and October 2019, were included. Each patient's clinical, biological, radiological and therapeutic information was collected retrospectively at NHL diagnosis and 1-year later. Only patients with MSGB available were analyzed; they were divided into 2 groups according to MSGB results for NHL: $MSGB^+$ and $MSGB^-$.
Results: Among 36 pSS patients diagnosed with NHL during the study period, 25 had an MSGB available at the time of NHL diagnosis. Among them, 13 MSGBs contained NHL ($MSGB^+$). MSGB was the only site enabling NHL diagnosis for 10/13 (77%); pSS and NHL were diagnosed simultaneously in 4/13 (31%). MSBGs were NHL^- for lymphomas diagnosed based on other tissue samples for 12 (48%) patients ($MSGB^-$). The clinical, biological, histological and radiological characteristics of both groups are reported in Table 1. No major differences were found between groups for median ESSDAI at NHL diagnosis and the frequency of salivary gland hypermetabolism on PET-CT. MALT-type NHL was found in 24/25 (96%) patients including 13/13 (100%) of those $MSGB^+$ and 11/12 (92%) of those $MSGB^-$. Six of the 13 (46%) $MSGB^+$ patients received no treatment, while all $MSGB^-$ patients were treated. Between diagnosis and 1 year of follow-up, ESSDAI scores without the NHL item did not differ (6.5 [3.5–9.5]) for the 6 untreated patients, but had significantly decreased for the 19 treated patients (3.5 [2.0–5.8]) (p=0.02).

Table 1. Comparison of the pSS patients' characteristics according to $MSGB^+$ vs. $MSGB^-$ for NHL

Characteristic	$MSGB^+$, n=13	$MSGB^-$, n=12
Female/male (ratio)	12/1 (12)	11/1 (11)
Age at NHL diagnosis, yr	60 (52–72)	58 (49.5–69.8)
pSS duration at NHL diagnosis, yr	2.(0–9)	3.5 (0.8–11)
ESSDAI score without NHL item	9 (6–16)	10.(3.5–19.8)
Cryoglobulinemia$^+$	9 (69)	3/9 (33)
Rheumatoid factor$^+$	9/11 (82)	8/8 (100)
Anti-SSA antibody$^+$	10 (77)	7 (58)
Anemia (Hb<12g/dL)	2 (15)	6/11 (55)
Gammaglobulins, g/L	12.4 (10.8–16.9)	16.1 (12.3–20.0)
Histology		
MALT-type lymphoma	13 (100)	11 (92)
Diffuse-large B-cell lymphoma	0 (0)	1 (8)
[^{18}F]FDG-PET–CT, SUV max >4.7		
Parotid or submandibular gland	6/12 (50)	3/10 (30)
Lymph nodes	1/12 (8)	3/10 (30)

Results are presented as number (%) or median (IQR).

Conclusion: Our results showed that, when MALT lymphoma is suspected, MSGB contributed to diagnosing NHL, either at initial assessment or during pSS evolution, enabling MALT lymphoma diagnosis in at least a third of NHL patients and >50% when MSGB was obtained systematically. Thus, MSGB might avoid the need for a more invasive procedure. Moreover, our findings suggest MSGB should be obtained at pSS diagnosis, and repeatedly during follow-up, when NHL, especially MALT, is suspected.
Disclosure of Interests: Simon Parreau: None declared, Raphaèle Seror Consultant of: BMS UCB Pfizer Roche, Benjamin Terrier: None declared, Barbara Burroni: None declared, Céline Jamart: None declared, Alexis Régent: None declared, Gaetane Nocturne: None declared, Luc Mouthon: None declared, Xavier Mariette Consultant of: BMS, Gilead, Medimmune, Novartis, Pfizer, Servier, UCB, Véronique LE GUERN Grant/research support from: UCB for GR2 study (to our institution)
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SAT0227 CLINICAL AND IMMUNOLOGICAL PROFILE OF NEUROPSYCHIATRIC LUPUS IN SOUTH INDIA

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Background: Neuropsychiatric manifestations are one of the least understood aspects of SLE.
Objectives: To study the prevalence of NPSLE manifestations in our cohort and compare clinical and immunological features of patients with controls.
Methods: This was a retrospective study in a tertiary care centre. Classification of SLE was as per SLICC criteria. All patients of SLE diagnosed in the last 5 years with NP manifestations as per the ACR definitions were included. Consecutive patients of SLE over last 2 years without NP manifestations were taken as controls.
Results: Six hundred and thirty one patients with SLE were seen in our centre from Jan 2013 to Jun-2019. NPSLE manifestations as per the ACR definitions were seen in 100 patients (95 females) .137 (130 females) consecutive SLE patients without NP manifestations were included as controls. The commonest NPSLE manifestation was seizures followed by cerebrovascular accident (Table 1). NPSLE manifestation occurred at the first presentation in 77 patients. Forty patients had more than one NPSLE manifestation. Antiphosholipid (API) antibodies (lupus anticoagulant and anticardiolipin antibody) were tested in 94 patients and positive in 25 (26.3%). Only 10 of the 23 patients with CVA were positive for API. NPSLE syndromes were similar in API positive and negative patients. As compared to controls, NPSLE patients had lower prevalence of mucocutaneous and musculoskeletal manifestations. There were no differences in the autoantibody profile in NPSLE patients versus controls. MRI of the brain was available in 65 NP episodes and 51 were abnormal. Ischaemic changes (22) were the commonest followed by T2/FLAIR hyperintensities (16). Cyclophosphamide was used for induction in 46 and Mycophenolate in 19 patients. Follow up of ≥ 6 months duration was available 93 patients. Over a mean follow up duration of 31.1 ± 22.7 months, 6 patiens had a NPSLE relapse and 10 died.

Table 1. Prevalence of NP SLE manifestations (N=631) and clinical and immunological features

NPSLE manifestations	Prevalence (%)	Clinical Feature	NPSLE (n=100)	Controls (n=137)	P value
All	**100(15.85%)**	Age	29.1±11.6	28.18±9.79	NS
Central Nervous System	65(10.3%)	M:F	5:95	7:130	NS
Aseptic meningitis	2(0.3%)	Mucocutaneous	55(55%)	105(76.6%)	<0.001
Acute Confusional State	12(1.9%)	Musculoskeletal	57(57%)	96(70%)	0.03
Cerebrovascular Disease	23(3.6%)	Hemolytic Anaemia	19(19%)	40(29.2%)	NS
Cognitive Dysfunction	2(0.3%)	Leucopenia	25(25%)	40(29.2%)	NS
Demyelinating Syndrome	3(0.5%)	Thrombocytopenia	22(22%)	36(26.3%)	NS
Headache	12(1.9%)	Serositis	10(10%)	16(11.7%)	NS
Movement Disorder	7(1.1%)	Lupus Nephritis	41(41%)	38(27.7%)	NS
Myelopathy	5(0.8%)	Direct Coomb's Test	44(44%)	55(45.5%)	NS
Seizures	35(5.5%)	Lupus anticoagulant	15(15%)	21(18.6%)	NS
		Anticardiolipin	12(12%)	14(12.5%)	NS
Peripheral Nervous system	28(4.4%)	Low complements	78(78%)	98(78.4%)	NS
AIDP	3(0.5%)	dsDNA	44(44%)	67(52.8%)	NS
Autonomic Disorders	1(0.1%)	Smith	38(38%)	51(40.8%)	NS
Cranial Neuropathy	5(0.8%)	Nucleosome	43 (43%)	52 (41.9%)	NS
Mono neuropathy	9(1.4%)	Histone	27 (27%)	40 (32.3%)	NS
Myasthenia Gravis	0	Ribo P	25(25%)	37(29.6%)	NS
Plexopathy	0	RNP/Sm	43(43%)	52(41.6%)	NS
Polyneuropathy	12(1.9%)	scl70	4(4%)	5(4%)	NS
		SSA	34(34%)	42(33.6%)	NS
Psychiatric	17(2.7%)	SSB	10(10%)	18(14.5%)	NS
Mood Disorders	8(1.3%)	Ro52	32(32%)	39(31.2%)	NS
Psychosis	13(2.1%)	PmScl	0	5(4%)	NS
Anxiety Disorder	4(0.6%)	PCNA	2(2%)	6(4.8%)	NS

Conclusion: Seizures and CVA are the commonest NPSLE syndromes. API positivity was not associated with NPSLE in our cohort.
Disclosure of Interests: None declared
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SAT0228 PREGNANCY OUTCOME IN SYSTEMIC LUPUS ERYTHEMATOSUS: A MONOCENTRIC COHORT ANALYSIS

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Background: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease, affecting prevalently women in childbearing age. Thanks to pre-gestational counseling and multi-disciplinary approach, adopted in daily clinical practice, SLE patients are experiencing even more uncomplicated pregnancies.
Objectives: Here, we evaluated pregnancy outcome in a large SLE cohort, compared to a control group including pregnant women without autoimmune diseases.

Methods: Pregnant SLE patients (diagnosis made according to ACR 1997 criteria) were included in the present study, conducted in the context of a joint rheumatology/gynecology multi-disciplinary team. For each patient we collected demographic information, medical history, treatments, disease activity (SLEDAI-2K) chronic damage (SLICC *damage index)*, clinical and laboratory data, including serum complement level and autoantibodies. Pregnancy outcomes were reported longitudinally as well as disease relapses occurring during pregnancy and puerperium. Flares were defined as new onset or worsening disease-related manifestation in any organ/system.
Results: Since 2008, 70 consecutive pregnancies occurred in 50 SLE patients [(median age at diagnosis 25 years (IQR 12.2), median age at first pregnancy 33 years (IQR 7), median disease duration 72 months (IQR 120)]. As controls, we evaluated 100 consecutive pregnancies in 100 women without autoimmune diseases [(median age 31 years (IQR 9)]. Table 1 reports the obstetric, fetal and neonatal outcomes of SLE patients compared to control group. A positive outcome in terms of live born infants was experienced in 88.6% of SLE pregnancies and in 88% of control group (p=NS). There were no statistically significant differences in any of the pregnancy outcomes evaluated; however, the percentage of small for gestational ages (SGA) was significantly higher in SLE group (22.8% *versus* 11.0% P=0.003). A statistical association was found between SGA and positivity for anti-dsDNA, anti-SSA ed anti-SSB (p=0.0001, p=0.01, p=0.04 respectively). Miscarriage was significantly associated with disease-related serologic abnormalities [anti-dsDNA (p=0.0001), low C3 (p=0.0001) and low C4 (p=0.006)] and past smoking *habitus* (p=0.0001); preterm birth was associated with anti-dsDNA, anti-CL and anti-B2GPI (p=0.001, p=0.0005, p=0.01 respectively). A disease flare was reported in 28 pregnancies (40%) and in 31 puerperium (44.3%). Figure 1 reports SLE relapses divided according to organ involvement. Flare during pregnancy was associated with positivity for anti-SSA (p=0.001), anti-SSB (p=0.01) and a-CL (p=0.006), while *puerperium* relapses were associated with previous renal involvement (p=0.0005), flare during pregnancy (p=0.01) and chronic damage (p=0.0001).

Table 1. Pregnancy outcomes in 50 SLE and 100 controls.

	LES (Pregnancies N=70)	Controls (Pregnancies N=100)	P
OBSTETRIC OUTCOME			
Preterm birth N/%	18/25.7	19/19	NS
Gestational hypertension N/%	5/7.1	3/3	NS
Gestational diabetes N/%	5/7.1	5/5	NS
Pre-eclampsia N/%	2/2.9	1/1	NS
FETAL OUTCOME			
Miscarriages N/%	8/11.4	12/12	NS
PR interval elongation N/%	4/6.4	–	–
IUGR N/%	3/5	1/1	NS
NEONATAL OUTCOME			
SGA< 10° centile N/%	16/22.8	11/11	**0.003**
Weight at birth median-I.Q.R.	2850-688	3250-814	**0.003**
Apgar 1' median-I.Q.R.	8-1	8-1	NS
Apgar 5' median-I.Q.R.	9-1	10-1	NS

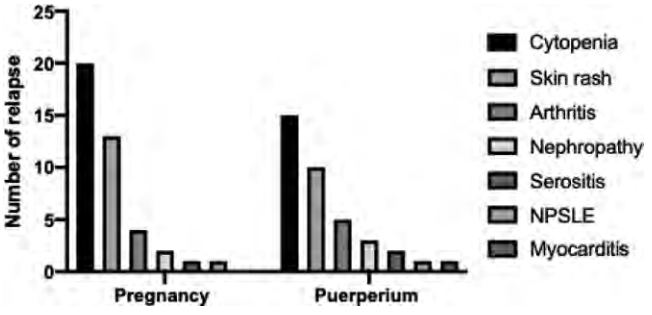


Figure 1. Disease flares during and after 70 SLE pregnancies divided according to organ involvement.

Conclusion: The present study confirms the role of pre-gestational counseling and a multi-disciplinary approach in the outcome of SLE pregnancies. Moreover, the high prevalence of disease relapse even more justifies the need for a combined rheumatology/gynecology multi-disciplinary approach.
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SAT0229

PROTEOMIC ANALYSIS REVEALS ASSOCIATION BETWEEN IMMUNE-METABOLIC BIOMARKERS AND CLINICAL SYMPTOMS IN SICCA PATIENTS

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Background: Sjögren's syndrome (SS) is a systemic autoimmune disease whose main characteristic is involvement of the exocrine glandular system. Thus, its most common clinical manifestation is eye and mouth dryness which, alongside fatigue and pain, contributes to poor health-related quality of life (HRQoL). A growing body of evidence recognises the adipose tissue as an active endocrine organ secreting bioactive mediators involved in metabolic and inflammatory disorders. A relationship between obesity and symptoms in SS has not yet been elucidated.
Objectives: To explore potential associations between obesity-related immune-metabolic biomarkers and clinical symptoms in SS and sicca patients.
Methods: Proteomics analysis of 184 cardio-immuno-metabolic proteins was assessed on sera from 53 SS (50 females (F), 3 males (M); mean age 54 years) and 60 sicca (56 F, 4 M; mean age 57 years) patients. Participants were enrolled in the Birmingham Optimising Assessment in Sjögren`s Syndrome (OASIS) cohort and examinations included the EULAR SS Patient Reported Index (ESSPRI), Schirmer's test, unstimulated whole saliva, minor labial salivary gland biopsy, EuroQoL-5 dimension (EQ-5D) tool, immunological parameters, body max index (BMI) and Hb1Ac. Participants with SS fulfilled 2016 ACR/EULAR criteria. Non-SS sicca patients were anti-Ro antibody negative, displayed objective oral and/or ocular dryness, and did not have a physician diagnosis for SS. Linear regression analysis and univariate models were performed to identify the key predictors of symptoms.
Results: HRQoL as measured as EQ-5D utility values, symptoms as assessed by ESSPRI, and BMI did not differ between the SS and sicca group. However, strong correlations between BMI (or fat or fat-free mass) and EQ-5D and ESSPRI scores were found in the sicca but not in the SS group. Among several proteins investigated, ADM, TNFRSF13B, FGF23, IL10RB, CD5, CD40, IL1RA, TNRSFN9, TNFRSF10A, TNFRSF11A, TRAILR2, GAL9, SPON2, ACE2, LEP, CD4, IL12B, SLAMF1, PD-L1 positively correlated with symptoms in the sicca group ($R \geq 0.3$; Holm's adjusted $P \leq 0.05$). Adrenomedullin (ADM) showed the strongest correlation with ESSPRI ($R = 0.56$; $P < 0.0001$); age ($R = 0.45$; $P = 0.0003$); BMI ($R = 0.43$, $P = 0.0008$); Ocular Surface Disease Index ($R = 0.32$, $P = 0.03$); EQ-5D utility value ($R = -0.45$, $P = 0.001$) and VAS patient ($R = -0.41$, $P = 0.008$). There was no association between ADM and gender, Schirmer`s test, disease and symptom duration ($P > 0.05$). ADM was independently associated with ESSPRI scores in non-SS sicca patients when corrected for BMI, age, HbA1c, depression and anxiety scores. None of the above mentioned proteins correlated with clinical symptoms in the SS group.
Conclusion: The study suggests that obesity-related immune-metabolic factors may play a role in regulating the symptoms in non-SS sicca patients. ADM appears to be a strong independent predictor of symptoms in these patients but not in SS.
Disclosure of Interests: Valentina Pucino: None declared, Jason D. Turner: None declared, Florian Kollert Employee of: Novartis, Saaeha Rauz: None declared, Andrea Richard: None declared, Jon Higham: None declared, Ana Poveda-Gallego: None declared, Simon J. Bowman Consultant of: Astrazeneca, Biogen, BMS, Celgene, Medimmune, MTPharma, Novartis, Ono, UCB, xtlbio, Glapagos, Speakers bureau: Novartis, Francesca Barone: None declared, Benjamin Fisher: None declared
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SAT0230

MACROPHAGE ACTIVATION SYNDROME IN SLE AND SYSTEMIC ONSET JIA: SIMILAR OR DISSIMILAR

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Background: Macrophage activation syndrome (MAS) is a serious complication in rheumatic disease. Fever and hyperferritinemia are common in systemic onset JIA and cytopenias are common in SLE thus recognising MAS in them is a challenge.
Objectives: We compared clinical, laboratory parameters, various classification criteria for MAS, and its outcome in SLE and sJIA.
Methods: Clinical and laboratory data were extracted from clinician diagnosed cases of MAS with SLE/sJIA who were admitted between 2004-2018 at a tertiary care hospital. Percentage of patients satisfying Ravelli, International consensus, HLH 2004 and criteria proposed by Parodi et al[1] were calculated.
Results: Among 33 patients (18 females) with MAS 19 had SLE and 14 had sJIA. MAS was more likely to be the presenting manifestation of disease in SLE as compared to sJIA (p<0.05). There were no differences in the clinical features among these two diseases. EBV and CMV were identified in 2 patients each as the trigger for MAS.
Patients with SLE had lower baseline TLC and platelet whereas patients with sJIA-MAS had significantly higher median CRP (p = 0.002), fall in TLC (p=0.012) and delta ESR/CRP ratio (p=0.02) and lower fibrinogen level (p=0.006). Neutrophil to lymphocyte ratio, Ferritin/CRP ratio and number of patients with Ferritin/ESR >80 were similar. Bone Marrow hemophagocytosis was seen in only in 21% of patients.
Only 6/33 fulfilled HLH criteria but criteria meant for sJIA or SLE performed well for both diseases and majority of patients could be diagnosed using them. Treatment included steroids(100%), cyclosporine(30%), Tacrolimus(21%), cyclophosphamide(21%), etoposide(3%) and thalidomide(12%). Mortality was similar in both groups.

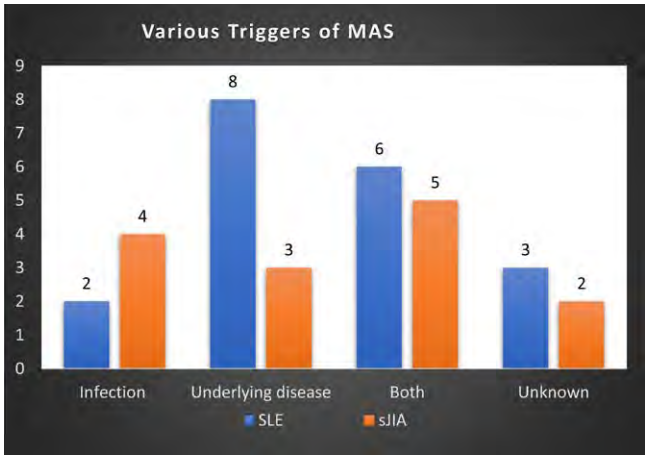


Table 1. Agreement amongst MAS/HLH criteria in SLE and sJIA MAS

SLE-MAS	HLH	Ravelli et al	Consensus	Parodi et al
HLH	4	4	4	4
Ravelli et al	4	19	19	18
Consensus	4	19	19	18
Parodi et al	4	18	18	18
sJIA-MAS	HLH	Ravelli et al	Consensus	Parodi et al
HLH	2	2	2	2
Ravelli et al	2	12	11	12
Consensus	2	11	12	12
Parodi et al	2	12	12	14

Table 2. Comparison with various other cohorts

	Minoia et al sJIA n (%)	Our study sJIA, n (%)	Our Study SLE, n (%)	SLE, n (%) Ai-Chun Liu et al	Juvenile SLE n (%) Parodi et al
Number	362	14	19	32	38
MAS as presenting feature (%)	80 (22)	4 (28)	12 (63)	NA	24 (63)
Most common manifestation (%)	Fever (96)	Fever (100)	Fever (89)	Fever (96)	Fever (89)
Most common trigger	Disease activity	Disease activity	Disease activity	Disease activity	Disease activity
BM done	251 (72.3)	8 (57)	12 (63)	32 (96)	38 (100)
BM hemophagocytosis	150 (60.7)	2 (25)	5 (41)	32 (100)	20 (52)
Mortality	28 (8)	2 (14)	2 (10.5)	4 (12.5)	4 (11.4)
Patients meeting JIA criteria %	NA	-	100	NA	100
Patients meeting HLH criteria %	NA	14	19	NA	66

Conclusion: MAS is more likely to be presenting manifestation in SLE compared to sJIA. Though lab parameters are significantly different in MAS associated with SLE & sJIA, criteria meant for MAS in sJIA or SLE MAS performed equally well in both diseases.
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Disclosure of Interests: None declared
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SAT0231 MULTIDIRECTIONAL DYSFUNCTION OF THE IMMUNE RESPONSE IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is a multi-organ immune-mediated disease characterised by autoimmunity. Dysfunction in immune tolerance towards allergens and protection from infections has less been studied. Human leukocyte antigen (HLA) genotype affects the risk of developing SLE. Little is known on the role of HLA in shaping SLE phenotype.
Objectives: To test for potential associations among active SLE, occurrence of infections and hypersensitivity reactions (HyR) at a clinical level and assess whether these events segregate with patients' HLA-DRB1 typing.
Methods: 224 patients with SLE were prospectively followed up over the course of 1267 consecutive visits with a median interval of five months between each visit. HyR occurring within one month before or after each visit and occurrence of at least one infection leading to antimicrobial treatment and/or absence from work in the interval between each visit were recorded. Disease activity was estimated through the systemic lupus erythematosus disease activity index 2000 (SLEDAI-2K). Remission was surrogated by the Lupus Low Disease Activity State (LLDAS). Demographics and general disease features including a previous history of allergy were retrospectively assessed. HLA-DRB1 genotype was obtained from 188 patients. Data are expressed as median [interquartile range], unless otherwise specified.
Results: Incidence rates for HyR and infections were 80/1000 person-years and 45/100 person-years. Culprit agents for HyR were drugs in 61% of cases, inhalants, food or other allergens in the remainder 42%. Most frequent sites for infections were the airways (55%), skin and mucosae (16%), the genital and/or urinary tracts (14%) and the gastrointestinal tract (7%). LLDAS was inversely associated with HyR (χ^2=20.912; p<0.0001) or infections (χ^2=8.234; p=0.005). patients with a recent HyR had a shorter disease duration (9 [2-15] vs 13 [8-22] years; p=0.006) and higher SLEDAI-2K scores (4 [3.5-11] vs 3 [2-4]; p<0.001) compared to patients without recent HyR. HyR were more frequently observed close to recent infections (χ^2=15.509; p<0.0001). Patients with HLA-DRB1*11:01 (n=28/188) had more frequently a history of allergy than patients with other HLA-DRB1 genotypes (χ^2=4.944; p=0.035). Among patients with at least four prospective visits, HLA-DRB1*11:01 carriers reported a recent infection more frequently (25% [13-40%] vs 14% [0-29%]; p=0.044) and HLA-DRB1*07:01 carriers less frequently (0% [0-17%] vs 18% [11-33%]; p=0.026) compared to patients with other HLA-DRB1 genotypes.
Conclusion: These data suggest that immune dysfunction in SLE not only affects tolerance to self antigens but also antimicrobial and allergic responses and that genetically determined HLA-restricted mechanisms of antigen presentation might influence the shape of this dysfunctional immune response in patients with SLE.
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Disclosure of Interests: Giuseppe Alvise Ramirez: None declared, Andrea Sorce: None declared, Benedetta Allegra Mazzi: None declared, Luca Moroni: None declared, Emanuel Della Torre: None declared, Giselda Colombo: None declared, Mona-Rita Yacoub: None declared, Enrica Bozzolo: None declared, Lorenzo Dagna Grant/research support from: The Unit of Immunology, Rheumatology, Allergy and Rare Diseases (UnIRAR) received unresctricted research/educational grants from Abbvie, Bristol-Myers Squibb, Celgene, Janssen, Merk Sharp & Dohme, Mundipharma Pharmaceuticals, Novartis, Pfizer, Roche, Sanofi-Genzyme, and SOBI., Consultant of: Prof Lorenzo Dagna received consultation honoraria from Abbvie, Amgen, Biogen, Bristol-Myers Squibb, Celltrion, Novartis, Pfizer, Roche, Sanofi-Genzyme, and SOBI., Angelo Manfredi: None declared
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SAT0232 PERCEPTION OF THE DISEASE IN PATIENTS WITH EARLY SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus is an autoimmune disease with a major impact on patient's quality of life.
Objectives: To evaluate patient's attitude toward early disease and factors that influence it.
Methods: Performed case-control study included SLE patients that fulfilled SLICC, 2012 classification criteria. The research included two groups of patients: early SLE – 1st group (disease duration ≤24 months) and non-early SLE – 2nd group control (disease duration >24 months). The pattern of the disease activity was assessed by patient global assessment (PGA), Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) and Systemic Lupus Activity Measure (SLAM), for SLE activity, SLICC/ACR Damage Index (DI) for disease irreversible changes and SF-8 for the Quality of Life (QoL).
Results: A total of 101 SLE patients with 34 in the 1st group (early SLE) and 67 in the 2nd group (non-early SLE) was analyzed. The disease activity showed high disease activity in both groups by SLEDAI (7,02±4,16 and 6,26±4,43 points, p>0,05) and SLAM (7,47±4,40 and 7,31±4,10 points, p>0,05) such as (46,97±19,39 vs 47,98±22,41 points). The QoL was appreciated as low, by both components (mental and physical), in groups. The damage index was higher in the 2nd group (0,23±0,43 and 1,07±1,29, p<0,001), which can be explained by the development of irreversible changes with the increase of disease duration.
The PGA in early SLE was influenced by subjective symptoms contained in SLAM index (r=0,48, p<0,05), such as fatigue and depression, and the level of the quality of life (r=0,65, p<0,001). Meantime, PGA in patients with longer disease duration (>2 years), was influenced by the presence of organ damage by SLICC/ACR DI (0,23, p<0,05) and objective findings of the disease activity contained in SLEDAI (r=0,33, p<0,005) and SLAM (0,44, p<0,001).
Conclusion: The disease recognition in patients with early SLE was determined by subjective and psycho-emotional signs, while in patients with longer disease duration it was influenced by organ damage and complications.
References: no references
Disclosure of Interests: None declared
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SAT0233 CHARACTERISTICS OF PRIMARY SJÖGREN'S SYNDROME INCLUDING ULTRASOUND FINDINGS OF THE SALIVARY GLANDS, ESSDAI AND ESSPRI

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Background: Studies have shown that salivary gland ultrasonography (SGUS) may have a potential value in the diagnosis of Sjogren's Syndrome (SS).
Knowledge of the association between ultrasonography findings, disease activity and damage, serologic markers and patient report outcome is limited.
Objectives: To investigate whether the results of SGUS are associated with disease manifestations and damage measured by doctor-reported activity score index (ESSDAI) and serologic markers. Furthermore to investigate the contribution of patient reported outcome measure (ESSPRI) in disease monitoring.
Methods: Patients registered at Odense University Hospital with the diagnosis primary SS were included in a Danish cohort. The patients were characterized using the ESSDAI, ESSPRI, serologic markers and SGUS-findings in submandibular and parotid glands. Schirmer's test and salivary test were performed for measurement of tear and salivary production.
SGUS was performed using a linear transducer, Siemens (ACUSON Sequoia Ultrasound System) on the two parotid and two submandibular glands. SGUS images was scored according to the OMERACT SS severity scoring system from 0 to 3, where 2 is moderate and 3 severe(1). A reliability study was performed in advance of the present study.
Spearman´s r correlation coefficient was used to assess correlation between scores.
Results: The cohort consisted of 48 Caucasian patients diagnosed with primary SS. Details on patient characteristics are shown in table 1.

Table 1.

Sex, n (%)	
Women	46 (95.8)
Age, mean (95%CI)	60 (57-62)
Smoking, n (%)	
Smoker	1 (2.1)
BMI, n (%)	
< 18.5	5 (10.4)
18.5 – 24.9	20 (41.7)
25.0 – 29.9	12 (25.0)
30.0 – 34.9	10 (20.8)
> 35.0	1 (2.1)
Serologic markers, n (%)	
SSa positive	33 (68.8)
SSb positive	22 (45.8)
ANA positive	38 (79.2)
Cryoglobulin positive	9 (18.8)
ESSPRI 0-10, mean (95%CI)	
Dryness	7.3 (6.7-7.9)
Fatigue	7.1 (6.4-7.7)
Pain	5.9 (5.1-6.7)
SGUS, n (%)	
Score 0	6 (12.5)
Score 1	15 (31.3)
Score 2	13 (27.1)
Score 3	14 (29.2)
ESSDAI, n (%)	
ESSDAI < 5 (low-activity)	22 (45.8)
≤ 5 ESSDAI ≤ 13 (moderate-activity) ESSDAI ≥ 14 (high-activity)	17 (35.4) 9 (18.8)

The correlation between ESSDAI-scores and SGUS-scores was r = 0.153 (p = 0.299). The correlation between ESSDAI-scores and ESSPRI-scores (dryness, fatique, pain) was r = 0.071 (p = 0.632), r = 0.254 (p = 0.082) and r = -0.002 (p = 0.987). The correlation between SGUS-scores and ESSPRI-scores (dryness, fatique, pain) was r = 0.124 (p = 0.400), r = -0.292 (p = 0.044) and r = -0.459 (p = 0.001).

Conclusion: In a Danish cohort of SS most patients had SSa and ANA autoantibodies. SGUS demonstrated high damage (score 2-3) in approximately half of the patients. ESSDAI activity score did not correlate with SGUS damage scores or the ESSPRI. SGUS damage scores correlated with ESSPRI-scores of fatique and pain, but not dryness.
Associations between other factors of importance for damage and SGUS scores are to be analyzed. SGUS and the ESSPRI describe different SS-related dimensions and will probably contribute in disease monitoring in the future.
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SAT0234 SERUM AXL, FERRITIN, IGFBP4 AND STNFR2 AS BIOMARKERS OF PEDIATRIC SLE

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Background: Proteomic screening is an efficient approach for identifying protein biomarkers in various inflammatory diseases. Our preliminary proteomic analysis revealed elevated levels of serum Axl, Ferritin, IGFBP4 and sTNFR2 in adult patients with active lupus nephritis (LN) (1). However, the role of these serum biomarkers in pediatric systemic lupus erythematosus (SLE) patients has not been examined.
Objectives: To evaluate the performance of 4 serum protein markers for detecting disease activity in pediatric patients with SLE.
Methods: 83 pediatric patients who fulfilled ≥4 ACR criteria for SLE and 25 healthy controls were recruited for serological testing of 4 protein markers identified by antibody-coated microarray screen, namely Axl, ferritin, IGFBP4 and sTNFR2. SLE disease activity was assessed using the SLEDAI-2k score, renal disease activity was assessed by the renal SLEDAI (range 0-16; 0= inactive LN, ≥ 8= active renal). 57 patients had clinically active SLE (SLEDAI score ≥ 4 or having a flare) (28 active renal and 29 active non-renal SLE patients). In active renal

patients, concurrent renal biopsy was performed, unless contraindicated. The ISN/RPS criteria were used to assess the histopathologic features of LN. Those Patients were further subcategorized into 2 groups; active proliferative (ISN/RPS classes III/IV) and non-proliferative (classes I/II/V).

Results: The serum concentrations of Axl and ferritin were significantly higher in patients with active SLE than inactive SLE (3765±235 vs. 2513±130 pg/ml, *P* = 0.001) and (111±26 vs. 18±4 ng/ml, *P* = 0.0001) respectively. Serum Axl levels were significantly higher in active renal versus active non-renal SLE patients (3765±235.3 vs. 2825±200.7 pg/ml, *P* = 0.04). In the active renal patients with paired kidney tissue and blood samples, none of the biomarkers tested discriminated classes of LN, although serum Axl, ferritin and IGBPB4 levels were higher in the proliferative subgroup. The levels of Axl, ferritin and IGFBP4 correlated significantly with SLEDAI scores (Axl, r= 0.58, *P* <0.0001; ferritin, r= 0.53, *P* <0.0001; IGFBP4, r= 0.229, *P* = 0.03). However, only serum Axl levels correlated significantly with the renal SLEDAI (r= 0.46, *P* = 0.01). The levels of Axl, IFGBP4 and sTNFR2 correlated with decreased C3 levels (r= - 0.54, *P* <0.0001; r= - 0.29, *P*= 0.007; r= - 0.29, *P*= 0.007) respectively. Only serum Axl and ferritin correlated with urinary PCR (r= 0.42, *P* <0.0001; r= 0.22, *P*= 0.04) respectively. These markers were more specific, but less sensitive, in detecting concurrent SLE activity than elevated anti-dsDNA or decreased C3. The specificity values of serum ferritin and IGFBP4 for concurrent active lupus nephritis were higher than anti-dsDNA or C3. Serum ferritin was the best predictor of global SLE activity (AUC 0.81, *P* <0.0001), followed by C3 (AUC 0.79, *P* <0.0001) then Axl (AUC 0.71, *P*= 0.002), while both Axl and C3 were the best predictors of lupus nephritis activity (AUC 0.72, both).

Conclusion: In pediatric SLE patients, serum ferritin and Axl perform better than traditional yardsticks in identifying disease activity, either global or renal. The performance of these serum markers should be explored further in a longitudinal cohort of pediatric SLE patients.

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SAT0235 THE EFFECT OF ANTIPHOSPHOLIPID ANTIBODIES ON APTT WAVEFORM PATTERNS

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Background: Patients with antiphospholipid antibody (aPL) are said to be at increased risk for thrombosis, however it is difficult to predict whether they will develop thrombosis. In recent years, it has been revealed that the characteristics of the second derivative curve of APTT waveform with aPL positive patient is biphasic changes[1,2]. As first step in predicting the risk of thrombosis, we sought to understand the effect of aPL on APTT waveform patterns.

Objectives: To analyze the characteristics of APTT waveforms according to the background diseases and the presence of aPL

Methods: Patients who underwent coagulation function tests from 2017 to 2019 were analyzed. A coagulation waveform (Clot waveform: CW) was drawn using a fully automatic coagulation time measuring device manufactured by Instrumentation Laboratory From the APTT waveform, the 1st derivative curve (DC) indicating the coagulation speed and the 2nd DC indicating the coagulation acceleration were depicted to measure the 1st DC height, 2nd DC peak 1 time, and 2nd DC peak 1 height (Figure1[2]). Patients were devided into CTD with aPL-negative patients (group A), aPL-positive patients with no prior thrombosis (group B), and antiphospholipid antibody syndrome (APS) (group C). Patients characteristics and aPL (anti-cardiolipin [CL] antibody IgM, anti-CL antibody IgG, anti-CLβ2GP1 complex antibody, LA-APTT, and LA- DRVVT) status were examind. A further analysis was performed according to the numbers of positive aPL. Comparison between the three groups were made by the one-way ANOVA method, with significant differences set as p-values <0.1. Factors with significant differences were analyzed by Steel-Dwass test. APTT waveforms was analyzed according to the numbers of positive aPL by least squares methods. Furthermore, to determine the cut off value of APTT, 1st DC height, 2nd DC peak 1 time, and 2nd DC peak 1 height for each case with 2 or more positive aPLs and 3 positive aPLs, area under the curve (AUC) of the receiver operating characteristic (ROC) curve, sensitivity and specificity were caliculated.

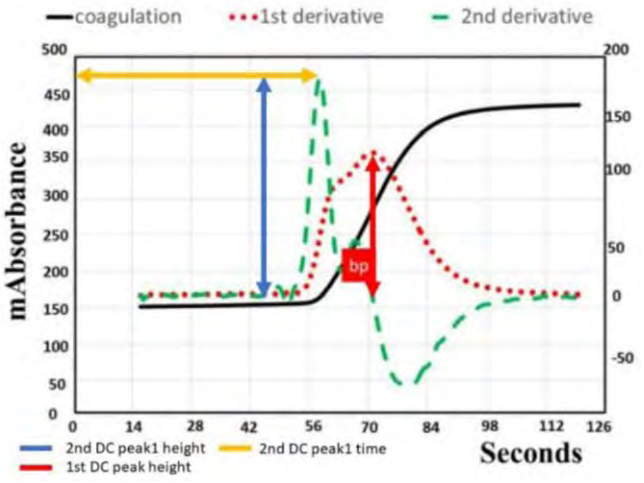


Figure 1.

Results: The APTT waveform was analyzed in 61 patients (51 women, 83.6%) with average age of 54.1 ± 17.1 years. Group A was 26 cases, Group B was 18 cases, and Group C was 17 cases. APTT, 2nd DC peak1 time, 2nd DC peak1 height, 1st DC peak time were significantly different among A, B, and C groups (p <0.01). APTT, 1st DC peak height, 2nd DC peak 1 time, and 2nd DC peak 1 height differed among the number of aPL (p < 0.01, respectively). APTT and 2nd DC peak1 time prolonged by 9.43 (seconds) and 16.3 (seconds) respectively according to the number of aPLs increased, and 1st DC peak height (mabs/s) and 2nd DC peak1 height (mabs/s^2) decreased by 56.4 (mabs/s) and 223.9 (mabs/s^2) respectively according to the number of aPLs decreased (Table 1). APTT> 35.2 (seconds) (sensitivity 80%, specificity 80.4%), 2nd DC peak1 height> 302 (mabs/s^2) (sensitivity 80%, specificity 91.3%) were relevant to the presence of two or more aPLs and APTT> 35.2 (seconds) (sensitivity 100%, specificity 80%), 2nd DC peak1 height> 302 (mabs/s^2) (sensitivity 100%, specificity 90%) were relevant to the presence of three aPLs.

Table 1.

The number of positive aPL	0	1	2	3	p value
The number of cases	27	19	4	11	
APTT	28.9	30.9	31.1	60.7	0.0001
(seconds)	[26.8, 31.4]	[29.1, 38.2]	[27.3, 54.2]	[45.9, 73.7]	
2nd DC peak time (seconds)	29.2	33.7	36.1	75.8	0.0001
	[26.8, 30.7]	[31, 41.7]	[31.5, 99]	[50.5, 102.4]	
2nd DC peak height (mabs/s^2)	839.9	669.6	608.4	119.3	0.0001
	[666.1, 962.2]	[346.4, 946]	[137.8, 956.7]	[30.6, 196]	
1st DC peak height (mabs/s)	309.6	271.5	241.8	135.6	0.0001
	[260.6, 355.1]	[168, 353]	[96.3, 364.0]	[76.8, 163]	

Conclusion: The presence of aPL was more related to the 2nd DC peak1 height of APTT waveform than APTT. A detailed review of the APTT waveform may further predict future thrombosis risk.

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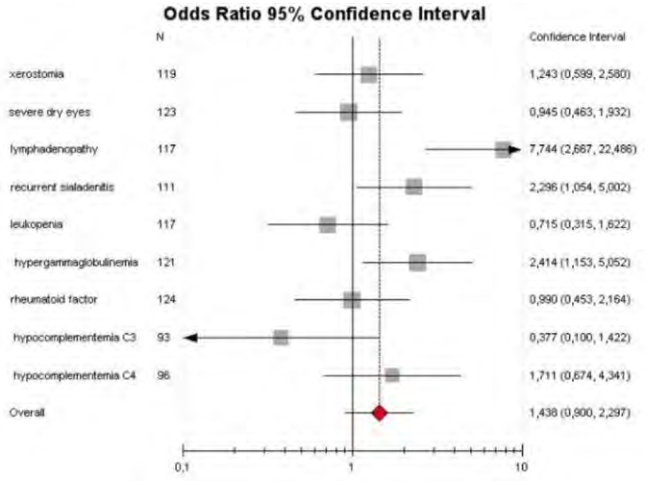
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SAT0236

CLINICAL AND LABORATORY FEATURES OF PATIENTS WITH SJOGREN'S SYNDROME COMPLICATED WITH MALT LYMPHOMA

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Background: The risk of developing lymphomas in *Sjogren's* syndrome (SS) is more than 10-fold higher than in general population. Available publications describe a number of indicators considered as predictors for SS development.
Objectives: To describe clinical and laboratory characteristics of patients with SS and MALT lymphoma and compare them with idem parameters in the control group. To identify factors associated with development of lymphoma.
Methods: The study included 87 SS patients with MALT lymphoma. In all cases lymphoma involved the parotid salivary glands. In all cases MALT lymphoma was diagnosed simultaneously with SS. At the time of inclusion non of the patients was on immunosuppressive therapy. Fifty five SS patients without lymphoproliferative pathology composed the control group. All cases were newly diagnosed and treatment-naïve.
SS was diagnosed based on the ACR-EULAR criteria. The histologic and immunohistochemical diagnosis of lymphoma was performed with B-cell clonality determination in salivary gland tissue.
The following clinical and laboratory parameters were monitored in both groups: rates of stage 3 xerostomia (<0.5 ml/5 min), grade 3 hypolacrimia (<5 mm/5 min), lymphadenopathy, hemorrhagic rashes, decreased C3, C4 complement components, increased RF, high anti-Ro and anti-La antibodies positivity, hematological changes, serum levels of secretory monoclonal antibodies, cryoglobulinemia, etc. Pearson's x2 criterion (analysis of contingency tables) was used for statistical analysis. The differences were considered statistically significant when p values were <0.05. Statistica 10 for Windows (StatSoft Inc., USA) package was used for statistical data processing.
Results: In the study group 84 patients were females, their mean age at the onset of lymphoma was 53±10 years. The disease duration was 7 years (3-12) before the diagnosis was established. All patients in the control group were females, the mean age at diagnosis was 50.2 ±13 years. Patients' age at diagnosis did not differ significantly between the groups. Enlarged salivary or lacrimal glands were found in all SS-MALT patients and in 18% of patients in the control group.
The rates of such systemic manifestations as polyneuropathy, kidney and joint damage was low and did not differ between groups.
Increased levels of anti-Ro antibodies was documented in the majority of patients in both groups (87 % and 81%, p=0.4), while aLa antibodies were significantly more common in MALT lymphoma patients (60% and 40.3%, *p*=0.045).
Similar rates of increased IgG and IgM levels were found in both groups, while increased IgA levels were 6-fold more common in the lymphoma group (*p*<0.00001). Anemia and leukopenia were documented in approximately 25%, and thrombocytopenia - in 2% of patients in both groups. Cryoglobulinemia (36% vs. 24%) and circulation of secretory monoclonal immunoglobulins (32% vs. 18%) were more common in the lymphoma group, but the difference was insignificant (*p*=0.2). The incidence of other clinical and laboratory abnormalities in SS and SS-MALT patients is presented on the graph Forest plot with OR and CI indication.



Graphic 1. Clinical and laboratory features of SS patients with MALT-lymphoma compared with SS patients without lymphoma.

Conclusion: Therefore, universally recognized predictors of lymphoma development, such as cryoglobulinemia and hypocomplementemia did not show reliable association with lymphoma. In analyzed cohort development of MALT lymphoma was statistically significantly associated with recurrent parotitis in past medical history, presence of lymphadenopathy at diagnostic examination, increased levels of anti-La antibodies and IgA, and hypergammaglobulinemia. Probably we should more actively treat patients with these clinical and laboratory features in order to prevent the development of lymphoma in them.
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SAT0237

THE SYSTEMIC LUPUS INTERNATIONAL COLLABORATING CLINICS (SLICC) FRAILTY INDEX (SLICC-FI) PREDICTS DAMAGE ACCRUAL IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) PATIENTS. DATA FROM A LATIN AMERICAN MESTIZO COHORT

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Background: The Systemic Lupus International Collaborating Clinics (SLICC) Frailty Index (SLICC-FI) has been developed as a predictor of outcomes in SLE patients[1-3]. However, it needs to be validated in several populations.
Objectives: To evaluate the SLICC-FI as a predictor of future damage accrual in systemic lupus erythematosus (SLE) patients.
Methods: Patients from a single-center prevalent cohort were included. Damage accrual was defined as the increase in SLICC/American College of Rheumatology (ACR) damage index (SDI) scores between the baseline and last visits. The SLICC-FI was measured at baseline. Univariable and multivariable negative binomial regression were performed to determine the association between the baseline SLICC-FI (per 0.05 increase) and damage accrual during follow-up, adjusted for sex, age at diagnosis, socioeconomic status, disease duration, SLE Disease Activity Index 2000 (SLEDAI-2K), SDI, prednisone daily dose, antimalarial and immunosuppressive drug use at baseline, and duration of follow-up.
Results: Of the 265 patients included, 248 (93.6%) were female with mean (SD) age 35.1 (13.6) years at diagnosis. At baseline, mean (SD) SLE disease duration was 7.3 (6.5) years, SDI was 1.1 (1.3) and SLEDAI-2K was 5.3 (4.6). The mean (SD) baseline SLICC-FI was 0.22 (0.05). After a mean (SD) of 5.2 (2.2) years of follow-up, the SDI increased in 126 (47.5%) patients, and the final mean (SD) SDI score was 1.7 (1.7). Higher SLICC-FI scores at baseline predicted greater damage accrual in the univariable analysis [Incidence Rate Ratio (IRR)=1.283, (CI95% 1.072-1.536); p=0.007]. The SLICC-FI remained associated with damage accrual in the multivariable model, after adjustment for possible confounders [IRR= 1.224 (CI95% 1.007-1.488); p=0.042].
Conclusion: The SLICC-FI predicts damage accrual in prevalent SLE, supporting the relevance of this index in the evaluation of SLE patients. This is the first study validating the SLICC-FI in South American population
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Campos Consultant of: Pfizer, Speakers bureau: Pfizer, Graciela S Alarcon: None declared

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SAT0238 VALIDATION OF THE ADJUSTED GLOBAL ANTIPHOSPHOLIPID SYNDROME SCORE AND CORRELATION WITH EXTRA-CRITERIA MANIFESTATIONS

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Background: Adjusted global antiphosholipid syndrome score (aGAPSS) is the simplified version GAPSS that was recently developed to assess thrombotic risk by the consideration of antiphospholipid antibody (aPL) profile and conventional cardiovascular risk factors.
Objectives: The aim of this study was to evaluate the validity of the aGAPSS in predicting thrombosis and extra-criteria manifestations in our antiphospholipid syndrome (APS) cohort.
Methods: Ninety-eight patients with APS were classified according to clinical manifestations as vascular thrombosis (VT), pregnancy morbidity (PM) or both (VT+PM). The aGAPSS was calculated as defined before. Arterial hypertension and hyperlipidemia definitions were made according to the ESC/ESH ve NCEP/ATP III guidelines, respectively.
Results: Demographic, laboratory and clinical characteristics of patients are summarized in table-1. Mean aGAPSS was calculated as 10.2 ± 3.8. Significantly higher aGAPSS values were seen in VT (n=58) and VT+PM (n=29) compared to PM (n=11) (mean aGAPSS 10.6 ± 3.7 vs 7.3 ± 2.9, P=0.005; 10.5 ± 4 vs 7.3 ± 2.9, P=0.01, respectively). AUC demonstrated that aGAPSS values ≥ 10 had the best diagnostic accuracy for thrombosis (figure-1). Higher aGAPPS values were also associated with recurrent thrombosis (mean aGAPSS 11.5 ± 3.7 vs 9.9 ± 3.6, P=0.04). Regarding extra-criteria manifestations, patients with livedo reticularis (n=11) and APS nephropathy (n=9) had significantly higher aGAPSS values (mean aGAPSS 12.9 ± 3.4 vs 9.9 ± 3.7, P=0.02; 12.4 ± 2.9 vs 10 ± 3.8, P=0.04, respectively).
Conclusion: Our results suggest that patients with higher aGAPSS values are at higher risk for developing vascular thrombosis (either single or recurrent) and extra-criteria manifestations, especially livedo reticularis and APS nephropathy.

Table-1. Demographic, laboratory and clinical characteristics of patients.

	PAPS (*n*=42) *n* (%)	SLE/APS (*n*=56) *n* (%)	*P*
Female	36 (85.7)	47 (83.9)	0.52
Age, years (mean±SD)	44.6 (11.6)	40.8 (10.1)	0.42
Disease duration, years (mean±SD)	10 (8.8)	9.7 (7.1)	0.16
Thrombosis	35 (83.3)	52 (92.9)	0.12
•Arterial	24 (68.6)	34 (65.4)	0.47
•Venous	19 (54.3)	26 (50)	0.43
•Recurrent	15 (42.9)	22 (42.3)	0.56
Pregnancy morbidity	20 (47.6)	20 (35.7)	0.16
•<10 weeks, ≥ 3 abortions	5 (25)	4 (20)	0.5
•≥ 10 weeks, ≥ 1 abortion	14 (70)	15 (75)	0.5
•Pre-eclampsia/eclampsia	3 (15)	5 (25)	0.34
•<34 weeks, ≥ 1 premature birth	1 (5)	5 (25)	0.09
Convensional risk factors			
•Arterial hypertension	17 (40.5)	35 (62.5)	**0.02**
•Hyperlipidemia	21 (50)	26 (46.4)	0.41
•Diabetes mellitus	3 (7.1)	3 (5.4)	0.51
•Obesity	19 (45.2)	16 (28.6)	0.07
•Smoking	12 (28.6)	18 (32.1)	0.43
aPL profile			
•LA	29 (69)	48 (85.7)	**0.04**
•aCL IgG/IgM	31 (73.8)	28 (52.8)	**0.03**
•aβ2GPI IgG/IgM	22 (56.4)	27 (52.9)	0.45
•Triple positive	14 (33.3)	17 (30.4)	0.46

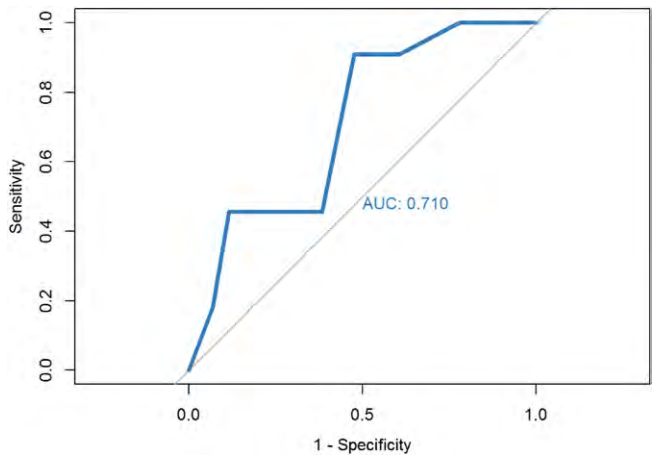


Figure 1. ROC curve according to cut-off aGAPSS value: 10 (AUC: 0.71, sensitivity: 0.52, specificity: 0.91, positive predictive value: 0.98, negative predictive value: 0.19, p-value: 0.01).

Disclosure of Interests: None declared
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SAT0239 LONG TERM OUTCOMES IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME AND RENAL ARTERY STENOSIS

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Background: Antiphospholipid syndrome (APS) is characterized by thrombosis and obstetric morbidity in the context of positive antiphospholipid antibody markers. More than a quarter of hypertensive APS patients (26%) have renal artery stenosis (RAS) (1). Treatment includes anticoagulation, blood pressure control and management of cardiovascular risks. In some cases, the severity of the renal vascular lesion requires surgical intervention
Objectives: To evaluate long term outcomes in APS patients with RAS.
Methods: Retrospective database study. All records of APS patients with RAS were analyzed and demographic variables, comorbidities, treatment received, renal outcome and mortality were recorded.
Uni- and multivariate analyses were performed by logistic regression with death and chronic kidney disease (CKD) as dependent variables. In the multivariate analysis, the covariates considered were age at diagnosis of stenosis, diabetes, smoking, dyslipidemia, unilateral or bilateral stenosis, stenosis greater than 50%, surgery and the use of immunosuppressants, anticoagulation and statins.
Research and development office has approved this study.
Results: 33 RAS patients were analyzed. Diagnosis of RAS was made by MRI renal angiography and in some cases by CT angiogram and intra-arterial digital subtraction angiography. Patient characteristics are detailed in Table 1. The median duration of follow-up was 152 months (IQR 65).

Table 1. Patient Characteristics.

N° Patients 33
Age median 48 (IQR 16)
Smokers% 18.1(6)
Comorbidities %
Diabetes mellitus type 2 6 (2) Hypertension 100(33)
High LDL 36.3(12)
Primary APS % 39.4 (13)
Secondary APS % 60.6 (20)
Unilateral RAS% 75.8 (25)
Bilateral RAS% 24.2 (8)
Degree of stenosis
< 30% 15.1 (5)
30-50% 30.3 (10)
50-80% 33.3 (11)
>80% 21.2 (7)
Treatment%
Medical treatment 75.7 (25)
Surgical treatment 30.3 (10)

Renal biopsy was performed in 3 patients: crescentic glomerulonephritis was found in 2 patients and one had a thrombotic microangiopathy.
Treatment: 25 patients (75.7%) were anticoagulated with vitamin K antagonists, 19 (57.6%) received immunosuppressive therapies, 18 (54.5%) were on statins. Ten patients (30.3%) were managed surgically with balloon angioplasty. Restenosis occurred in 4/10 patients (40%) and percutaneous renal artery stenting was performed successfully in all four. Ten patients died (30.3%). Renal outcomes are shown in Table 2.

Table 2. Outcome in APS with RAS Patients

N %
Died 10 30.3
Transplanted 1 3
Renal Dysfunction 17 51.5
CKD Stage III 10 30.3
CKD Stage IV 4 12.1
CKD Stage V 3 9

In the univariate analysis, surgery was significantly associated with a lower probability of reaching CKD (p=0.042; OR 0.2; 95% CI 0.03-0.94). In the multivariate analysis, the tendency to benefit from surgery was maintained but the statistical significance was lost, probably due to the low number of patients.

In the subgroup analysis, the tendency to benefit from surgery was maintained in patients with or without anticoagulation, immunosuppressants, statins, with primary or secondary APS, with uni- or bilateral stenosis, with or without dyslipidemia, but this benefit was lost in smokers independent of the grade of stenosis.

Conclusion: RAS is a treatable cause of hypertension and a poor prognostic marker in APS patients.

In this study, APS patients with RAS who underwent intervention with angioplasty or stenting had a trend to a lower probability of developing CKD in contrast to studies in atherosclerotic RAS. The beneficial effect of surgery was lost in smoking patients. In this relatively young population mortality was high.

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[1] Sangle SR, D'Cruz DP, Abbs IC, Khamashta MA, Hughes GR. Renal artery stenosis in hypertensive patients with antiphospholipid (Hughes) syndrome: outcome following anticoagulation. Rheumatology (Oxford) (2005) 44:372–7.

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SAT0240 THE PROGNOSIS OF TWO DISTINCT CLINICAL PHENOTYPES OF SLE-PAH

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Background: Based on the characteristics of systemic lupus erythematosus-associated pulmonary arterial hypertension (SLE-PAH), Sun *et al* has put forward a scoring system to distinguish two clinical phenotypes as vasculitic and vasculopathic subtypes[1]. A weighted score ≥2 suggested a vasculitic subtype by combining two factors: The time interval between SLE and PAH diagnosis <2 years and ≥2 years were 1 and 0 point; SLE Disease Activity Index (SLEDAI) >9, 5-9 and <5 were 2, 1, 0 point, respectively. While the vasculitic subtype seemed to have poorer prognosis in Sun's research, other study has shown controversial result[2].

Objectives: To find out the prognosis of two distinct clinical phenotypes of SLE-PAH.

Methods: Between 2008 and 2019, a SLE-PAH cohort confirmed by right heart catheterization (RHC) from Guangdong Provincial People's Hospital was included. Other groups of pulmonary hypertension were excluded. Based on the scoring system, patients were divided into vasculitic (weighted score≥2) and vasculopathic subtypes (weighted score<2). The endpoint was PAH-related mortality. Survival status were confirmed by clinic follow-up data or phone call.

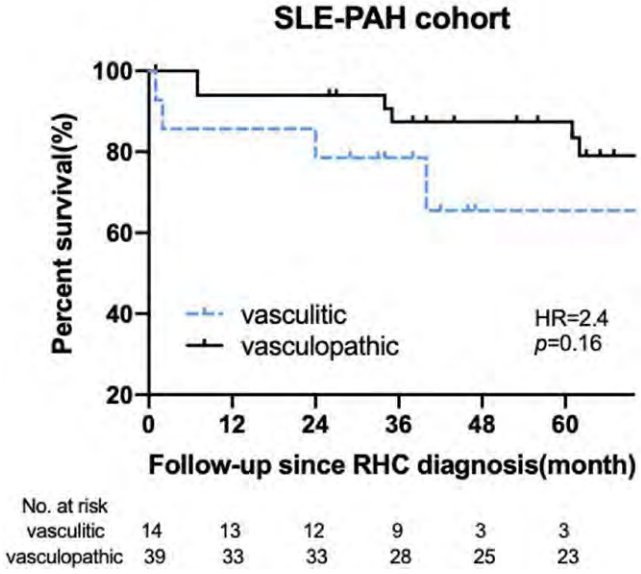


Figure 1. Survival curves for patients with systemic lupus erythematosus-pulmonary arterial hypertension (SLE-PAH) in two distinct subtypes. RHC, Right Heart Catheterization.

Results: A total of 53 SLE-PAH patients were enrolled. The cases of vasculitic and vasculopathic subtype were 14 and 39, respectively. Ten endpoint events occurred. Eight attributed to PAH and the cause could not be traced in two which were still included in study. The pooled 1-, 3-, 5-year survival rates were 85.7%, 78.6%, 65.5% in vasculitic subtype, and 93.9%, 87.5%, 87.5% in vasculopathic subtype, respectively. Kaplan-Meier analysis showed vasculitic subtype tended to have a poorer prognosis than vasculopathic subtype (p=0.16, HR 2.4, 95%CI 0.5-13.8, figure 1).

Conclusion: The prognosis of the two phenotypes of SLE-PAH was statistically indifferent while the vasculitic subtype showed a trend of worse prognosis. Further studies are needed.

References:

[1] F. Sun, Y. Lei, W. Wu, L. Guo, K. Wang, Z. Chen, W. Xu, X. Wang, T. Li, X. Zhang, S. Ye, Two distinct clinical phenotypes of pulmonary arterial hypertension secondary to systemic lupus erythematosus, Ann Rheum Dis 78(1) (2019) 148-150.

[2] J. Qian, M. Li, J. Zhao, Q. Wang, Z. Tian, X. Zeng, Inflammation in SLE-PAH: good news or not?, Ann Rheum Dis (2018). **0**:1–2. doi:10.1136/annrheumdis-2018-214605

Disclosure of Interests: None declared

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SAT0241 PLATELET INDICES COULD BE SIMPLE RELIABLE PREDICTORS OF THROMBOTIC EVENTS IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME

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Background: Platelet activation is considered as a pivot pathogenic process to be responsible for thromboembolism in antiphospholipid syndrome (APS). severalstudies shown that platelet indices including platelet distribution width (PDW), mean platelet volume (MPV), large platelet rate (P-LCR) are associated with platelet activation.

Objectives: This study aims to determine the correlation between platelet indices and thrombotic events in patients with APS.

Methods: Platelet activation is considered as a pivot pathogenic process to be responsible for thromboembolism in antiphospholipid syndrome (APS). severalstudies shown that platelet indices including platelet distribution width (PDW), mean platelet volume (MPV), large platelet rate (P-LCR) are associated with platelet activation.

Results: A total of 207 patients [135(65.2%) female, 72(34.8%) male], medianage 35(IQR 10)] was classified into thrombotic group (n=150,72.5%) and non-thrombotic group(n=57,27.5%). PDW, MPV, P-LCR were significantly higher in thrombotic group than non-thrombotic group (13.0±3.4 vs. 11.2±7.3)p<0.001, 10.7±1.4vs.10.0±3.0,p<0.001, 30.25±11.6vs. 25.1±10.4 p<0.001, respectively]. No differences in age, WBC count, hsCRP and C3 were observed between groups. Also, HGB was found to be notably higher in thrombotic group than non-thrombotic group (143±29 vs. 132±15, p=0.001).Upon univariate logistic analysis, PDW (OR 1.554, 95%CI 1.289-1.873, p<0.001), MPV (OR 1.772, 95%CI 1.268-2.476, p=0.001), P-LCR (OR 1.089, 95%CI 1.040-1.140, p<0.001) were all significantly associated with the occurrenceof thrombosis. In multivariate logistic analysis, only PDW and positive LAwere identified to be risk factors of thrombotic events (Table 1). The ROC curve showed that PDW combinedwith positive LAwas a reliable indicator of thrombotic events with an AUC of 0.796 (95%CI 0.728-0.864). The optimal cut-off value for PDW was 12.4fl with a sensitivity of 72.0% and specificity of 77.2%.

Conclusion: This study confirmed that PDW, P-LCR and MPV (especially PDW) were significantly associated with thrombotic events in APS patients, which could support the theory of platelet activation being a crucial factor of thrombosis inAPS. Caution should be raised when patients with positive LA has relatively high PDW level.

Disclosure of Interests: None declared

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SAT0242 REGIONAL VARIATION IN CARDIOVASCULAR DISEASE AMONG SLE PATIENTS

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Objectives: To evaluate whether the risk of cardiovascular disease (CVD) including myocardial infarction (MI) and cerebrovascular (CVA) differs across geographic regions among SLE patients.

Methods: We identified SLE patients using two ICD codes 60 days apart within two years recorded in Medical Services Plan (MSP) or hospital discharge database (DAD). We defined the second of two diagnosis dates as the index date. We included incident SLE patients (7-year continuous registries in MSP before the first diagnosis date) with an index date between 1997 and 2012 and excluded patients with previous MI or CVA before the index date. We followed each patient from the index date up to 10 years and censored at the date of death date, leaving the province, or March 31, 2015.

We assessed the incident CVD that was defined as the first ever diagnosis of MI or CVA recorded in DAD or as the primary cause of death in Vital Statistics. We also evaluated MI and CVA separately.

The Province's publicly administered and funded health care system is organized into five regional health authorities (HA): Interior (IHA), Fraser (FHA), Vancouver Coastal (VCHA), Vancouver Island (VIHA), and Northern (NHA) [Figure 1(a)].We assigned each patient the HA she/he was registered at the index date. We extracted baseline covariates using the information during a period of 365 days prior to the index date, including socio-demographic characteristics, health care resource use, comorbidities, and prescription medication use. We calculated the incident rate (IR) of MI, CVA, and CVD (first ever MI or CVA) by HA. Using Cox Proportional Hazard model adjusting for potential confounders at baseline, we estimated the adjusted hazard ratios (aHR) of CVD for each HA compared to FHA or VCHA which have the large proportion of provincial population and SLE patients. We evaluated the regional disparities in MI and CVA separately using the same methods.

Results: We included 3,960 incident SLE patients free of CVD at baseline with a mean (SD) age of 48.5 (15.8), including 726 (18.3%) from IHA, 1634 (42.3%) from FHA, 854 (21.6%) from VCHA, 504 (12.7%) from VIHA, and 242 (6.1%) from NHA. During 26378 person-year (PY) follow-up, 133 patients developed incident CVD including 91 MI and 43 CVA. [Table 1]

Table 1. Incident Rates and HR

	HA	Incidence			aHR (95%CI)	
		N	PY	IR (95%CI) 10,000 PY	Reference: FHA	Reference: VCHA
CVD	IHA	35	4579	76(54,105)	**1.93(1.17,3.2)**	**2.05(1.17,3.58)**
	FHA	39	11197	35(25,47)	ref	1.06(0.64,1.76)
	VCHA	27	5844	46(31,66)	0.94(0.57,1.57)	ref
	VIHA	22	3165	70(44,103)	1.65(0.96,2.83)	1.74(0.98,3.11)
	NHA	10	1592	63(31,110)	1.81(0.86,3.8)	1.92(0.88,4.17)
MI	IHA	24	4579	52(34,76)	**2.09(1.14,3.83)**	1.81(0.95,3.47)
	FHA	27	11197	24(16,34)	ref	0.87(0.48,1.56)
	VCHA	21	5844	36(23,54)	1.15(0.64,2.07)	ref
	VIHA	12	3165	38(20,64)	1.29(0.64,2.58)	1.12(0.54,2.31)
	NHA	7	1592	44(19,85)	2.11(0.88,5.11)	1.84(0.74,4.56)
CVA	IHA	11	4579	24(12,41)	1.79(0.71,4.55)	2.35(0.8,6.88)
	FHA	12	11197	11(6,18)	ref	1.31(0.49,3.48)
	VCHA	7	5844	12(5,23)	0.76(0.29,2.03)	ref
	VIHA	10	3165	32(16,55)	**2.79(1.14,6.85)**	**3.66(1.34,10.01)**
	NHA	<5	1592	19(5,49)	1.45(0.36,5.72)	1.89(0.44,8.22)

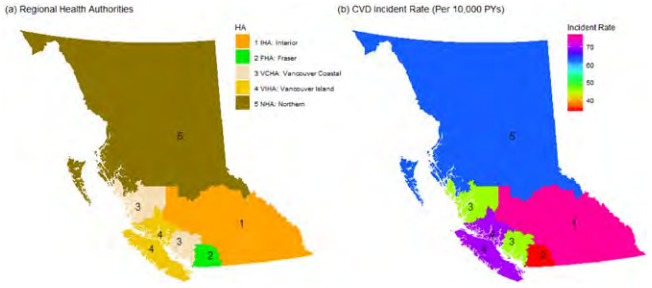


Figure 1. HA and CVD Incident Rate

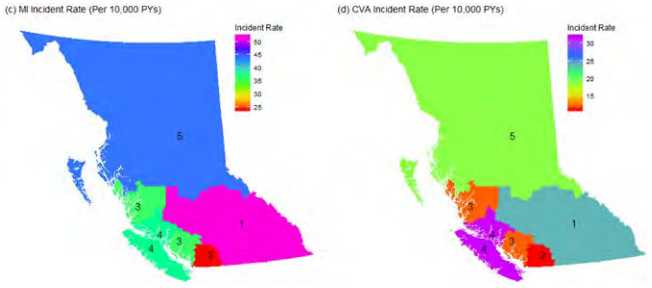


Figure 2. MI and CVA incident Rate by HA

The IR of CVD varied from 35 in FHA to 76 per 10,000 PY in IHA [Figure 1(b)]. IHA had significantly higher risk of CVD than FHA (aHR=1.93, 95%CI=1.17~3.2) and VCHA (aHR=2.05, 95%CI=1.17~3.58).

The IR of MI varied from 24 in FHA to 52 per 10,000 PY in IHA [Figure 2(a)]. IHA had significantly higher risk of MI than FHA (aHR=2.09, 95%CI=1.14~3.83).

The IR of CVA varied from 11 in FHA to 32 per 10,000 PY in VIHA [Figure 2(b)]. VIHA had significantly higher risk of CVA than FHA (aHR=2.79, 95%CI=1.14~6.85) and VCHA (aHR=3.66, 95%CI=1.34~10.01).

Conclusion: Compared with FHA and VCHA, IHA had higher risk of CVD and VIHA had higher risk of CVA. IHA also had higher risk of MI than FHA.

Disclosure of Interests: None declared

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SATURDAY, 06 JUNE 2020

Vasculitis

SAT0243

SUBPHENOTYPES IN POLYARTERITIS NODOSA (PAN): TARGET ORGAN ASSOCIATIONS OF A WORLDWIDE COLLABORATION STUDY

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Background: There is a paucity of information on the current phenotypes, ethnic and geographic differences of PAN. A global PAN study group has been working for clinical subphenotype and GWAS studies.

Objectives: This study is aimed to look for target organ associations in PAN.

Methods: PAN patients fulfilling the EMA vasculitis classification algorithm were recruited. In addition to baseline characteristics, treatment and outcome data, occurrence of any of the clinical manifestations related to PAN during disease course was recorded.

Factor analysis was used to analyse target organ associations of 306 patients. Five factors were identified by factor analysis of variables sex, paediatric-onset, HBV, monogenic disease relationship, cutaneous features, musculoskeletal symptoms, constitutional symptoms and involved areas (abdominal, renal, neurologic, ENT, cardiac, pulmonary).

Results: PAN cohort from 7 countries were used (Italy: n=59, Japan: n=39, Mexico: n=29, Slovenia: n=14, Sweden:11, TUR: n=106, UK: n=48). 306 (M/F: 171/135 and Caucasian 77.1%, Asian 13.4%, and Hispanic 9.5%) patients were included. 8 were HBV-related, and 22 of TUR patients had a monogenic form of disease (FMF n=15, DADA2 n=7). 21.8% of patients were cutaneous-only PAN patients. 48.4% of patients had radiologic, 64% had biopsy-proven PAN. Median age at disease onset was 40 (IQR 27.0-57.5) years. During a median 57 (16-120) months follow-up, 39 (13%) patients died.

Factor analysis revealed 5 factors that explained 54.1% of the original information on the matrix as follows: **Factor 1,** represented the association between gastrointestinal and renal involvement, male gender and negatively associated with cutaneous features; **Factor 2,** the association between monogenic relationship with paediatric onset disease; **Factor 3,** any of musculoskeletal findings with positive constitutional symptoms; **Factor 4** any neurologic involvement was associated with ENT and pulmonary findings; **Factor 5** cardiac involvement in non-HBV patients (Table).

The eigenvalues of the 5 factors were 2.034, 1.470, 1.427, 1.079 and 1.030, in decreasing order, i.e., the highest contribution to the overall variance in the matrix came from the togetherness of the 4 clinical and demographic characteristics that made up Factor 1.

Conclusion: Target organ associations could support distinctive subphenotypes in PAN. Factor 1 seems the most severe form. Patients with FMF or DADA2 have distinct target organ associations. The jury is out to decide whether these patients should be classified as 'vasculitis associated with probable etiology' just as HBV-related-PAN. Factor 4 might define a different subphenotype (ANCA-medium vessel vasculitis?).

Disclosure of Interests: Omer Karadag: None declared, Ertugrul Cagri Bolek: None declared, Shunsuke Furuta: None declared, Giacomo Emmi: None declared, ALOJZIJA HOCEVAR: None declared, Andrea Hinojosa-Azaola: None declared, Aladdin J Mohammad Speakers bureau: lecture fees from Roche and Elli Lilly Sweden, PI (GiACTA study), Serdal Ugurlu: None declared, Fatma Alibaz-Oner: None declared, Ayten Yazici: None declared, Luca Quartuccio: None declared, Enrica Bozzolo: None declared, Lorenzo Dagna Grant/research support from: Abbvie, BMS, Celgene, Janssen, MSD, Mundipharma Pharmaceuticals, Novartis, Pfizer, Roche, SG, SOBI, Consultant of: Abbvie, Amgen, Biogen, BMS, Celltrion, Novartis, Pfizer, Roche, SG, and SOBI, Giuseppe Alvise Ramirez: None declared, Luca Cantarini: None declared, Gina Gregorini: None declared, Jeannin Guido: None declared, Sara Monti: None declared, Eduardo Martin-Nares: None declared, Franco Schiavon: None declared, Roberto Padoan: None declared, Hajime Kono: None declared, Augusto Vaglio: None declared, Saadettin Kılıçkap: None declared, Ali İhsan Ertenli: None declared, Haner Direskeneli: None declared, Seza Özen Consultant of: Novartis, Pfizer, Speakers bureau: SOBI, Novartis, David Jayne Grant/research support from: ChemoCentryx, GSK, Roche/Genentech, Sanofi-Genzyme, Consultant of: Astra-Zeneca, ChemoCentryx, GSK, InflaRx, Takeda, Insmed, Chugai, Boehringer-Ingelheim

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SAT0244 PROGNOSIS OF LARGE VESSEL INVOLVEMENT IN LARGE VESSEL VASCULITIS

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Background: Giant cell arteritis (GCA) and Takayasu arteritis (TAK) are the two main forms of large vessels vasculitis (LVV). Vessel inflammation leads to aneurysms, wall thickening, stenosis, and, in some cases, complete occlusion of the artery. Due to the wide variation in the course of LVV, predicting outcome is challenging. To our knowledge, data regarding prognosis factors of LVI in LVV patients and comparison of outcome of LVI in GCA and TAK are lacking. An early identification of patients with higher mortality could help to prevent deaths and vascular complications.

Objectives: To assess prognosis factors and outcome of large vessel involvement (LVI) in large vessels vasculitis (LVV) patients.

Methods: Retrospective multicenter study of characteristics and outcomes of 417 patients with LVI including 299 Takayasu arteritis (TAK) and 118 Giant cell arteritis (GCA-LVI) were analyzed. Logistic regression analysis assessed prognosis factors in LVV patients. Outcome of LVI among TAK and GCA-LVI patients (ischemic complications, aneurysms complications, relapses and revascularization) were assessed.

Results: In multivariable analysis, stroke/transient ischemic attack [HR: 3.63 (1.46 - 9.04), p=0.006] was independently associated with vascular complications in LVV. The 10-years aneurysm free survival was significantly lower [67% (48 – 93) vs 89% (84 – 95), p=0.02] in GCA-LVI compare to TAK patients. The 5-years relapse free survival was significantly lower [47% (37 – 60) vs 69% (63 – 75), p<0.001,] in GCA-LVI compare to TAK patients. The 10-years revascularization free survival was significantly lower [55% (48 – 64) vs 76% (59 – 99), p<0.001] in TAK compare to GCA-LVI patients. After a median follow-up of 5 years, 16 (5.4%) TAK and 7 (5.9%) GCA-LVI patients died, mainly of aneurysm (26%) and ischemic complications (26%).

Conclusion: This large nationwide cohort of LVI provided prognosis factors of vascular complications in LVV patients. TAK and GCA-LVI have different long-term outcome in term of aneurysm development, relapse and revascularization.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.5252

SAT0245 RENAL INVOLVEMENT AT ONSET IN ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY (ANCA)-ASSOCIATED VASCULITIS: A MAJOR INDEPENDENT RISK FACTOR FOR RENAL RELAPSE

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Background: In ANCA-associated vasculitis (AAV), renal relapses are cause for concern as they are unpredictable and predictors of end-stage renal disease (ESRD).

Objectives: We aimed to assess the frequency of major renal (MR) relapses in AAV in our cohort and identify independent predictors of the first MR relapse at diagnosis.

Methods: We performed a retrospective monocentric observational study in our Vasculitis clinic from January 2000 to August 2019. Inclusion criteria were: 1) granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and limited kidney disease (LKD) diagnosis fulfilling EMA algorithm criteria; 2) achievement of a stable remission, defined as absence of vasculitis symptoms or signs and adherence to the prednisone taper during remission-induction treatment. We excluded patients who developed ESRD before remission and those with incomplete data during the follow-up. Major renal (MR) relapses were defined as occurrence of at least one major item of renal Birmingham Vasculitis Activity Score version 3 (BVASv3).

All remitted patients were allocated in two subgroups: patients without MR relapse and patients with MR relapse. Univariate and multivariable analysis of first MR relapse predictors was performed with Fine and Gray (F&G) sub distribution hazards model to assess all competitive risks (progression to ESRD without MR relapse and death before MR relapse). Due to the relatively low frequency of events and the risk of overfitting, we performed several multivariable models with three variables, as recommended by Peduzzi e al[1]. The best multivariable model was selected accordingly to the Akaike information criterion (AIC).

Results: 96 (53% females) patients met the inclusion criteria: 74 GPA, 21 MPA and 1 LKD. Median age at diagnosis was 54 (44-64) years. ANCA testing was present in 94 patients, 85 were ANCA positive: 56 c-ANCA/PR3, 28 p-ANCA/MPO and 1 double positivity.

During a median follow-up (FU) of 54.5 months (29.3-96.5), we observed 19 MR relapses in 17 patients while 2 patients progressed to ESRD, 3 died without events and 76 reported no MR relapse. Density-incidence of MR relapses since remission was 3.6/100 person-year (CI 95% 2.2-5.6). Median time to first MR relapse after remission was 33 months (14-67.5).

At first MR relapse, 8 (53.3%) patients were on steroids while 10 (66.7%) were on immunosuppressant (5 azathioprine, 5 mycophenolate). In 2 cases, data about remission-maintenance treatment was not available.

MR relapses were observed only in ANCA positive patients with a significantly higher frequency of skin, kidney and nerve involvement at diagnosis (41.2% vs 17.7%, p=0.034, 94.1% vs 57.0% p=0.004, and 52.9% vs 25.3% p=0.024, respectively); while Ear, Nose and Throat (ENT) involvement was significantly lower (35.3% vs 62.0% p=0.043). Mean BVASv3 at diagnosis scored significantly higher in MR relapse group (24.1±6.2 vs 18.1±8.1. p=0.007).

At multivariable analysis with F&G model, renal involvement and induction treatment without cyclophosphamide and/or Rituximab at diagnosis were independent predictors of MR relapse (sHR 20.4 (2.6-158.2), p=0.004 and sHR 4.2 (1.5-12.0), p=0.007, respectively). Moreover, there was a trend of higher risk of MR relapse in PR3-ANCA (sHR 2.5 (0.9-7.1), p=0.091).

Conclusion: Renal involvement at diagnosis and milder remission-induction treatment regimens resulted in a significantly higher risk of MR relapse during the FU in our cohort. PR3-ANCA specificity was not an independent predictor of MR relapse, even if we observed a trend of higher MR relapse risk with this covariate.

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SAT0246

TARGETING JAK/STAT PATHWAY IN TAKAYASU'S ARTERITIS

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Background: Takayasu's arteritis (TAK) is a large vessel vasculitis (LVV) in which the aorta and its main branches are greatly inflamed, leading to wall thickening, fibrosis, stenosis and to artery occlusion(1). The disease is more common in women mostly between 20 and 30 years old. TAK has a high morbidity rate: 50% of patients will relapse within 10 years after diagnosis(2, 3). This inflammation is essentially mediated by infiltration with macrophages and pro-inflammatory Th1/Th17 effector subsets(4–8). But the mechanisms behind these phenomena are essentially unknown. TAK is mainly treated with non-specific steroids(1) which are associated with potential side effects when used for a long-time course.
Objectives: Our work aims to explore the involvement of JAK/STAT signaling pathway and its downstream biological cascades in pro-inflammatory T cells differentiation and disease activity of TAK. Plus, our work allows to consider targeting the JAK/STAT pathway in TAK using JAK inhibitors (JAKinibs).
Methods: We analyzed transcriptome of FACS-sorted CD4+ and CD8+ T cells from healthy donors (HD) and TAK, using differential gene, pathway and network analysis. Then, we assessed in vitro and in vivo effects of JAKinibs in TAK by flow cytometry (FC).
Results: Transcriptome analysis showed hundreds of significantly dysregulated genes/pathways for CD4+ and CD8+ samples between HD and TAK. Among these, we noticed in TAK a great enrichment for pathways linked to type I and II interferons (IFN), JAK/STAT and cytokines/chemokines-related signaling. We confirmed by RT-qPCR the upregulation of a type I IFN-specific gene signature in TAK T cells as compared to HD. Using genes coming from the previous pathways, we constructed networks connecting them according to their respective protein interactions. This representation showed for both CD4+ and CD8+ T cells that JAK and STAT genes were densely connected, thus representing core genes/proteins in the TAK physiopathology. We then performed in vitro cell cultures of PBMCs from HD or TAK supplemented with Ruxolitinib (JAK1/2 inhibitor) or PBS. We observed by FC that JAKinibs significantly induced in TAK CD4+ and CD8+ T cells reduction of CD25 expression, decrease of Th1/Th17 pro-inflammatory cells and increase of Tregs.
Next, we followed by FC 3 TAK (refractory to conventional treatments) treated with JAKinibs. We also observed in their PBMCs a reduction of CD25 expression by CD4+ T cells, a decrease of Th1 and Th17 cells and an increase of Tregs, accompanied by an increase of the Tregs/Teffs ratio. JAKinibs also decreased C-Reactive Protein level, NIH score and co-administered steroids doses (present before JAKinibs introduction) in these 3 in vivo-treated TAK.
Conclusion: JAK/STAT signaling pathway is critical in the pathogenesis of TAK and JAKinibs may be promising in its treatment.
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Disclosure of Interests: Paul Régnier: None declared, Alexandre Le Joncour: None declared, Anna Maciejewski-Duval: None declared, Anne-Claire DESBOIS: None declared, Cloé Comarmond: None declared, Michelle Rosenzwajg: None declared, David Klatzmann Consultant of: ILTOO Pharma, Patrice cacoub: None declared, David Saadoun: None declared
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SAT0247

PREDICTORS OF ADVERSE OUTCOMES IN DIFFUSE ALVEOLAR HEMORRHAGE OF IMMUNE AND NON-IMMUNE CAUSES: 12-YEAR EXPERIENCE FROM A UNIVERSITY HOSPITAL

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Background: Diffuse alveolar hemorrhage (DAH) is a rare, life-threatening condition that has either immune or non-immune etiologies1. DAH caused by capillaritis can be immune-mediated (IM-DAH), e.g. anti-neutrophil cytoplasmic antibody (ANCA) vasculitis and systemic lupus erythematosus, but DAH may also result from anticoagulation, heart failure, drugs or inhaled toxins. Since IM-DAH has specific therapies available, we hypothesized that patients with IM-DAH would have a better prognosis.
Objectives: We did a retrospective analysis of all DAH cases seen at our university hospital in the last 12 years to investigate the predictors of adverse outcomes.
Methods: Using Epic radiant and Agfa Radiology Information System databases, we queried electronic medical records of all patients admitted to our university between Jan 2007 to Jan 2019 who had the words "diffuse alveolar hemorrhage" in their chest x-ray report. We manually reviewed charts of all these patients to confirm true DAH. True DAH was defined as suspicion of DAH on chest x-ray plus inclusion of DAH on the discharge problem list. We did a detailed chart review of true DAH cases to extract information regarding demographics, baseline disease characteristics, physical/serology/imaging findings, treatment received, and outcomes. The outcomes of interest were death, intubation, shock, need for hemodialysis (HD), and red blood cell transfusions. We compared IM-DAH with non IM-DAH cases using descriptive statistics, t-test, and chi-squared tests. We used logistic regression models to assess the influence of baseline characteristics on outcomes. A p-value < 0.05 was considered statistically significant.
Results: There were 88 cases of DAH (M:F 54:34, median age 57) fulfilling inclusion criteria (Table 1). The non-immune etiology was diagnosed in 63%, while 36% were IM-DAH (18% ANCA associated, 9% SLE, 2% decompensated heart failure, the rest were others). No clear etiology for DAH was found in 37.5% cases. Death within 90 days of onset of DAH occurred in 37.5%, 5.6% had recurrent DAH, and 56.8% had sustained remission. Non-IM DAH cases had worse outcomes such as death and were less likely to experience sustained remission (Chi-squared = 19.1, p < 0.001), though IM-DAH were more likely to receive HD (Chi-squared = 7.5, p-value 0.01). Presence of extrapulmonary findings (e.g. nephritis) was a risk factor for adverse outcome, and was statistically significantly correlated with the amount of blood products received, need for HD and likelihood of death, which did not reach statistical significance. Shock and intubation were associated with a higher likelihood of death (p = 0.02 and p = 0.001, respectively).

Table 1. Comparison of Clinical Characteristics of Immune versus Non-Immune Cases of Diffuse Alveolar Hemorrhage

Variable	Immune cases (N = 32)	Non-immune cases (N = 56)	Statistical comparison
Age (years)	51.09	55.91	P = 0.196
%Female	43.8	35.7	P = 0.510
%presenting with hemoptysis	8 (25%)	14 (25%)	P = 0.101
%extrapulmonary findings	20 (62.5%)	1 (1.7%)	P = $6.9*e^{-10}$
pANCA positive	16 (50%)	2 (3.6%)	P = 0.0004
% on anticoagulation	9.4	2.5	P = 0.090
Mean Creatinine	2.38	1.89	P = 0.507
Mean hospital length of stay (days)	16.69	23.27	P = 0.139
Drop in Hemoglobin prior to DAH and day of DAH	0.24	1.17	P = 0.070
%Bronchoscopy-confirmed DAH	62.5	75.0	P = 0694
Mean units of blood transfused	1.91	2.66	P = 0.448
%Need for hemodialysis	37.5	12.5	P = 0.010
%Shock (any kind)	21.9	32.1	P = 0.338
%Need for intubation	43.8	62.5	P = 0.122
%Death within 90 days	12.5	52.7	P = 0.0009

Conclusion: DAH, a life-threatening condition, has both immune and non-immune etiologies. Our 12-years, single-center, university hospital experience showed that IM-DAH has a better prognosis than non IM-DAH. Presence of extrapulmonary manifestations was associated with worse outcomes.
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SAT0248

PATTERNS OF DRUG TREATMENT FOR MAINTENANCE PHASE OF ANCA-ASSOCIATED VASCULITIS (AAV) IN REAL WORLD PRACTICE IN EUROPE – PROLONGED GLUCOCORTICOID USE IS COMMON AND VARIOUS TREATMENT REGIMES ARE USED

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	Maintenance start	6 months	12 months	18 months	36 months
Remission full/partial %	43 / 50	59 / 38	67 / 30	72 / 25	74 / 22
Receiving GC %	65	61	53	46	39
5mg or less	19	40	58	68	72
5-10mg	34	41	35	27	23
10-20 mg	25	16	6	4	4
More than 20mg	22	3	2	1	1
Receiving RTX %	21	21	19	17	14
RTX alone	10	10	10	11	8
RTX + GC	10	10	8	5	5
RTX + other + no GC	1	1	1	1	1

RTX maintenance schedules varied - 375mg/6 monthly 22%, 500mg/6 monthly 36%, 1000mg/6 monthly 31%, 375mg/12 monthly 1%, 500mg/12 monthly 4% and 100mg/12 monthly 3%. 32% had RTX initial regime adjustments on basis of B cell counts (44%), age (34%) or immunoglobulin levels (22%). Over 36 months 28% patients relapsed, 18% minor and 10% major (who then left follow up in this study). This led to greater GC use in the minor relapse patients at 36 months compared to those maintaining remission without relapse (48% vs 38%).

Background: Maintenance therapy following remission induction in ANCA associated vasculitis (AAV) is required to prevent relapse but patients are also still at risk from long term organ damage. This can be due to disease activity and also adverse events from therapy in particular high dose and prolonged use of glucocorticoids (GC).
Objectives: This retrospective study aimed to examine clinical outcomes and in particular the drug treatment used for maintenance in AAV patients managed in routine clinical practice in Europe.
Methods: 1478 AAV patients (France, Germany, Italy, Spain and UK) managed by 493 physicians (37% Rheumatologists) who completed induction therapy for organ or life threatening AAV and initiated maintenance therapy between 2014-16 were studied. Data were collected at the time maintenance was determined to begin by the physician and then at 6, 12, 18 and 36 months. 49% had granulomatosis with polyangiitis,; mean age 54.2 years with 56% male. 49% had incident AAV and 51% were studied from a relapse. 70% received cyclophosphamide and GC and 30% received rituximab (RTX) and GC for remission induction therapy.
Results: Definition of maintenance start from the time of incidence/relapse and initial maintenance therapy varied between incident patients (mean time 4.7 months, GCs 66%, Azathioprine 38%, RTX 19%, Cyclophosphamide 11%) and relapsed patients (mean time 6.5 months *, GCs 63%, Azathioprine 30% *, RTX 24% *, Cyclophosphamide 20% *, $p<0.05$ vs incident). RTX use was notably higher in relapsing patients in Italy, Spain and UK compared to incident patients. Control of AAV activity varied over follow up and prolonged GC use was common even after 36 months including in RTX treated patients.
Conclusion: Maintenance therapy regimes used in clinical practice in Europe are variable including on basis of incident vs relapsing disease yet full remission is often not maintained. Many patients remain on GCs for long periods placing the patients at higher risk of GC related adverse events and organ damage. Even minor relapse increases the prolonged use of GCs. The high burden of prolonged GC use in AAV should be more clearly recognized and new therapeutic approaches explored.
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SAT0249

A PROBABILITY-BASED DIAGNOSTIC ALGORITHM FOR SUSPECTED GCA

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Background: Clinical presentation of GCA is protean. It is vital to make a secure diagnosis, exclude mimics urgently and avoid inappropriate steroids to minimise side effects. Fast track GCA clinics (FTC) provide rapid specialist assessment with temporal and axillary US (1). EULAR recommendations support US as first-choice test. A pre-test probability score (PTPS) stratifies patients to low (LC), intermediate (IC) and high-risk (HC) categories.
Objectives: To validate a diagnostic GCA algorithm based on stratification by PTPS, with sequential US and additional tests (AT), if necessary
Methods: For the algorithm (Figure) retrospective data was extracted from case records of cases seen in 2019. PTPS overall showed median (Q2) score of 9,75th percentile (Q3) score 12. Based on this and reported cut-off 9.5 (2) we classified LC as PTPS <9, IC 9-12 and HC >12 (Graph). GCA diagnosis was by modified GiACTA including US (Halo), CRP > 5 mg/L and AT if necessary. The algorithm performance was assessed overall and in individual categories.
Results: Of 187 consecutive cases, 13 were excluded for incomplete data (tertiary referrals). In remaining 174, GCA confirmed 33%, mean age 72.4 years, 69% females,45% LC, 35% IC, and 20% HC. 130 (75%) had US whereas 44 did not (41 LC, 3 IC) (Figure)
In HC, 25/31 (81%) were US +ve, 19 treated as GCA without AT, 6 with AT (Table 2). Of 6 US -ve 3 had GCA confirmed by AT (PET-CT 2, TAB 1). US in HC showed sensitivity 89%, specificity 75%, accuracy 87%, GCA prevalence 87%, mean CRP 65.52 (SEM+/- 8.67).
In LC, 38 (49%) were US - ve, of whom 5 had AT. US not done on 39 (50%) for either PTPS very low or urgent alternative diagnosis. 1 went on to AT. 1 was US positive and had GCA excluded with AT. US in LC showed specificity 99%, sensitivity 0/0 (undefined), accuracy 99%, GCA prevalence 0%, mean CRP 21.79 (SEM+/- 3.80)

Graph-1: Categories according to the probability score

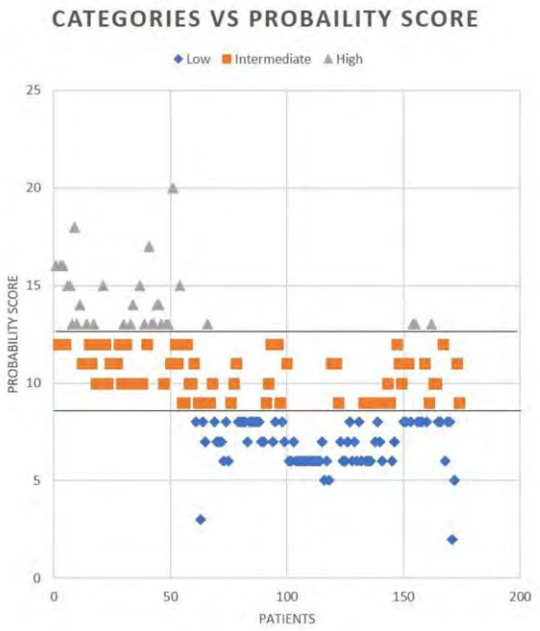


Table 1. US performance with PTPS

Category (n)	US	GCA, n	Non-GCA, n	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Prevalence (%)	Accuracy (%)
HC (31)	+	24	1	24/27 (89)	3/4 (75)	24/25 (96)	3/6 (50)	27/31 (87)	(24+3)/31 (87)
	-	3	3						
IC (65)	+	30	0	30/30 (100)	35/35 (100)	30/30 (100)	35/35 (100)	30/65 (46)	(30+35)/65 (100)
	-	0	35						
LC (78)	+	0	1	0/0 (undefined)	77/78 (99)	0/1 (0)	77/77 (100)	0/78 (0)	(0+77)/78 (99)
	-	0	77						
Total (174)	+	54	2	54/57 (95)	115/117 (98)	54/56 (96)	115/118 (97)	57/174 (33)	(54+115)/174 (97)
	-	3	115						

Abbreviations: GCA, Giant cell arteritis; NPV, Negative predictive value; PPV, Positive predictive value; US, Ultrasound

Table 2. US, AT & confirmed diagnosis

Category	Ultrasound			No of AT	Type of AT	Final Diagnosis
	+ve	Not done	-ve			
LC (78)	1	39	38	7	1x TAB (-), CTB (-)	Fibromyalgia
					1x TAB (-), MRA (-), MR neck (+)	Tongue cancer
					1x CTA (+)	Stroke
					1x CTCAP (-)	IA
					1x PET (-)	PMR
					1xTAB (-)	NA AION
					1x PET (-)	CVA
IC (65)	30	3	32	15	5x TAB (-), 2x PET (-)	Not GCA
					2x TAB (+), 6x PET (+)	GCA
HC (31)	25	0	6	10	1x PET (-)	URTI
					1x TAB (-)	NAAION
					2x PET (+)	
					1x TAB (+)	
					1x CTA (+)	
					1x MRA (+)	GCA
					1x PET (-)	
					2x CTA (-)	
					1x CTCAP (-)	

Abbreviations: AT, Additional test; CTA, Computed tomography angiogram; CTB, Computed tomography of brain; CTCAP, Computed tomography of chest, abdomen and pelvis; GCA, Giant cell arteritis; IA, Inflammatory arthritis; MRA, Magnetic resonant angiogram; NA AION, Non arteritic anterior ischemic optic neuritis; PET, Position emission tomography; TAB, Temporal artery biopsy; URTI, Upper respiratory tract infection

In IC, 30/65 (46%) were US +ve 8 had AT (all GCA confirmed) while on treatment. 32 (49%) US negative where 7 had AT (all GCA excluded). 3 did not have US. Sensitivity, specificity, accuracy of US was all 100%, GCA prevalence 46%, mean CRP 39.05 (SEM+/- 5.04)

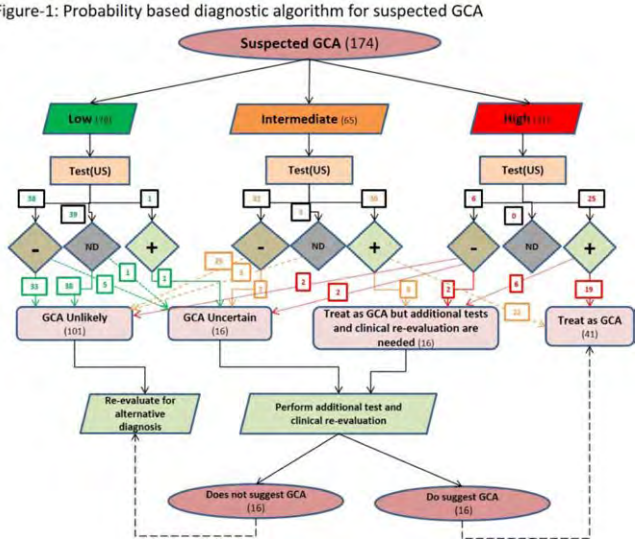
US test performance overall sensitivity 95%, specificity 98%, accuracy 97%

Conclusion: PTPS successfully stratifies GCA, excludes mimics and enhances US performance. The algorithm interprets correctly US findings and choice of AT.

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Figure-1: Probability based diagnostic algorithm for suspected GCA



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SAT0250 CLINICAL CHARACTERISTICS AND THE DISEASE ACTIVITY OF BEHCET'S DISEASE IN CHINA: A STUDY BASED ON SMART SYSTEM OF DISEASE MANAGEMENT (SSDM)

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Background: Behcet´s disease (BD) is a systemic autoimmune disease that affects multiple organ systems with recurrent oral ulcers, genital ulcers and skin lesions. Behcet´s Disease Current Activity Form (BDCAF) and Electronic Medical Record-based Activity Index (EMRAI) are commonly used internationally to evaluate the disease activity of BD.

Objectives: This study aimed to analyze the clinical characteristics, the level of disease activity, and the incidence of anxiety and depression for Chinese BD patients. Patients can perform self-management of disease with SSDM.

Methods: SSDM is a series of doctor-patient interactive applications for self-management of patients with chronic diseases. Patients can perform self-assessment with SSDM and upload the data to their authorized doctors. The SSDM patients' application system integrates the BDCAF and EMRAI into one scoring system. Patients could obtain scores of BDCAF and EMRAI by responding to one questionnaire through SSDM.

Results: From Apr 2017 to Jan 2020, 719 BD patients from 166 hospitals used SSDM, with a mean age of 38.97±12.71 (14~81) years old, and median disease duration of 20.8 months. 719 patients performed BDCAF and EMRAI self-assessment 1321 times, 252 patients repeat assessments for 855 times. The mean score of BDCAF and EMRAI are 3.57±2.17 and 3.44±1.90, respectively. The matching degree of the two score was 0.8747.

The most common clinical characteristics were oral ulcers (83.73%), ocular symptoms (62.03%), joint pain (50.07%). The comparative study between males and females revealed significant difference in the aspects of epididymitis (10.94% vs 0, p<0.001), genital ulcer (35.09% vs 44.93%, p=0.01), headache (24.15% vs 33.92%, p=0.01) and superficial thrombophlebitis (24.15% vs 33.92%, p=0.01). Table 1.

Table 1. Clinical Characteristics of different systems in Chinese BD patients.

Presence of clinical characteristics	Total	Males	Females	P value
Oral ulcer	83.73% (602)	86.42% (229)	82.16% (373)	0.14
Genital ulcer	41.31% (297)	35.09% (93)	44.93% (204)	0.01*
Epididymitis	4.03% (29)	10.94% (29)	0 (0)	<0.001**
Erythema	29.49% (212)	29.43% (78)	29.52% (134)	0.98
Skin lesions	26.84% (193)	28.68% (76)	25.77% (117)	0.4
Superficial thrombophlebitis	30.32% (218)	24.15% (64)	33.92% (154)	0.01*
Headache	30.32% (218)	24.15% (64)	33.92% (154)	0.01*
Joint pain	50.07% (360)	51.32% (136)	49.34% (224)	0.61
Arthritis	14.60% (105)	14.72% (39)	14.54% (66)	0.95
Gastrointestinal involvement	24.90% (179)	27.92% (74)	23.13% (105)	0.15
Ocular symptoms	62.03% (446)	62.64% (166)	61.67% (180)	0.79
Nervous involvement	23.78% (171)	25.66% (68)	22.69% (103)	0.37
Vascular involvement	15.72% (113)	18.11% (48)	14.32% (65)	0.18

*P values are for the comparison between the males and females.

Conclusion: Chinese BD patients can effectively perform BDCAF and EMRAI self-assessment with SSDM. The results of the assessment conducted by the two scoring systems are similar. The clinical characteristics of Chinese BD were different depending on gender.

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SAT0251 ANGIOGRAPHIC PROGRESSION OF DISEASE IN LARGE-VESSEL VASCULITIS

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Background: Angiography is essential to detect vascular disease in patients with large-vessel vasculitis (LVV). Guidelines differ on the role of periodic angiography to monitor patients with LVV, in part because there is limited prospective data characterizing the natural history of angiographic disease. Development of new areas of arterial damage, even in periods of apparent clinical remission, has been reported in LVV; however, whether this is a common or rare phenomenon is unknown.

Objectives: To characterize angiographic progression of disease over time in Takayasu's arteritis (TAK) compared to giant cell arteritis (GCA).

Methods: Patients with GCA or TAK were recruited into a prospective, observational cohort. Patients fulfilled the 1990 American College of Rheumatology (ACR) Classification Criteria for TAK or modified 1990 ACR Criteria for GCA.

All patients underwent baseline magnetic resonance angiography (MRA) and a follow-up MRA at least one year after baseline per a standardized imaging protocol. The presence of angiographic lesions, defined as stenosis, occlusion, or aneurysm, was evaluated by visual inspection by a single reader who was blinded to clinical status. Angiographic lesions were evaluated in 4 segments of the aorta and in 13 branch arteries. On follow up angiography, the development of new lesions was recorded, and existing lesions were characterized as improved, worsened, or unchanged.

Results: 782 arterial territories were evaluated from 46 patients with LVV (TAK=28; GCA=18). Baseline characteristics were as follows: Age [TAK=24.8 years (18.6-34.9), GCA=64.8 years (57.8-73.9)], Female gender [TAK=21 patients (78%), GCA=16 patients (84%)], Disease duration [TAK=2.3 years (0.6-4.9), GCA 1.2 years (0.4-2.9)], Active clinical disease [TAK=12 patients (44%), GCA 12 patients (63%)]. The median time from initial MRA to follow up MRA was 2.4 years (1.5-3.1) for GCA and 1.6 years (1.3-3.3) for TAK.

There were 159 territories affected at the baseline visit in 41 patients [TAK: 108 territories in 26 patients, GCA: 51 territories in 15 patients]. The development of new territory involvement was infrequent and only occurred in patients with TAK (8 new lesions out of 352 baseline unaffected territories (2.3%) in 5 patients).

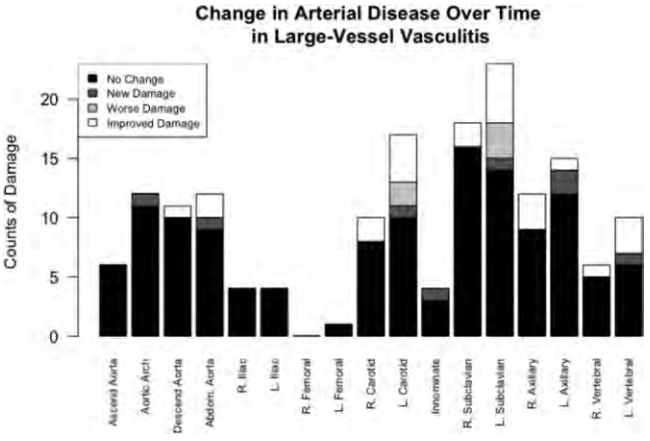
At follow up, existing arterial lesions improved in 25 (15.7%) territories, worsened in 6 (3.8%) territories, and stayed the same in 128 (80.5%) territories. There were no significant differences in angiographic progression of disease between the two diseases: improved - TAK 19 (17.6%), GCA 6 (11.8%); worsened - TAK 5 (4.6%), GCA 1 (1.9%); unchanged - TAK 84 (77.8%), GCA 44 (86.3%). Change in the branch arteries was more dynamic than change in the aorta **(Figure).**

Improvement in angiographic disease was observed in 8 (17%) patients (TAK=6, GCA=2). Worsening of disease was seen in 3 (7%) patients (TAK=2, GCA=1). In 5 (11%) patients (TAK=5, GCA=0), there were areas of improvement and other areas of worsening disease within the same patient.

Conclusion: Dynamic change in arterial lesions is observed in patients with TAK and GCA. Improvement and worsening of arterial lesions can be observed over time, even within the same patient. This observation suggests that both local factors at the level of the artery and systemic factors (e.g. treatment response) are likely associated with angiographic progression. The development of new angiographic lesions was infrequent, and only occurred in patients with TAK. These data may inform future guideline recommendations for angiographic monitoring in LVV.

References: N/A

Figure.



Disclosure of Interests: None declared

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SAT0252

INCREASED MORTALITY FOR INDIVIDUALS WITH GIANT CELL ARTERITIS: A POPULATION-BASED STUDY

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Background: Individuals with giant cell arteritis (GCA) are at increased risk of serious morbidity including cardiovascular disease and stroke. Yet the risk of mortality among individuals with GCA have produced conflicting reports[1].

Objectives: Our aim was to evaluate excess all-cause mortality among individuals with GCA relative to the general population over time.

Methods: We performed a population-based study in Ontario, Canada, using health administrative data among all individuals 50 years and older. Individuals with GCA were identified using a validated case definition (81% PPV, 100% specificity). All Ontario residents aged 50 and above who do not have GCA served as the General Population comparators. Deaths occurring in each cohort each year were ascertained from vital statistics. Annual crude and age/sex standardized all-cause mortality rates were determined for individuals with and without GCA between 2000 and 2018. Standardized mortality ratios (SMRs) were calculated to measure relative excess mortality over time. Differences in mortality between sexes and ages were also evaluated.

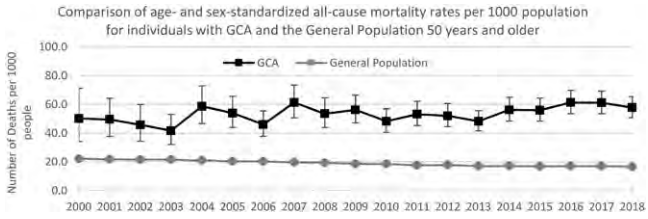
Results: Population denominators among individuals 50 years and older with GCA and the General Population increased over time with 12,792 GCA patients and 5,456,966 comparators by 2018. Annual standardized mortality rates among the comparators steadily declined over time and were significantly lower than GCA morality rates (Figure). Annual GCA mortality rates fluctuated between 42-61 deaths per 1000 population (with overlapping confidence intervals) during the same time period. SMRs for GCA ranged from 1.28 (95% CI 1.08,1.47) at the lowest in 2002 to 1.96 (95% CI 1.84, 2.07) at the highest in 2018. GCA mortality rates and SMRs were highest among males and younger age groups.

Conclusion: Over a 19-year period, mortality has remained increased among GCA patients relative to the general population. GCA mortality rates were higher among males and more premature deaths were occurring at younger age groups. In our study, improvements to the relative excess mortality for GCA patients over time (mortality gap) did not occur. Understanding cause-specific mortality and other factors are necessary to inform contributors to premature mortality among GCA patients.

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Figure.



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Disclosure of Interests: Lillian Barra: None declared, Janet Pope Grant/research support from: AbbVie, Bristol-Myers Squibb, Eli Lilly & Company, Merck, Roche, Seattle Genetics, UCB, Consultant of: AbbVie, Actelion, Amgen, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Eicos Sciences, Eli Lilly & Company, Emerald, Gilead Sciences, Inc., Janssen, Merck, Novartis, Pfizer, Roche, Sandoz, Sanofi, UCB, Speakers bureau: UCB, Priscila Pequeno: None declared, Jodi Gatley: None declared, Jessica Widdifield: None declared

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SAT0253

ANTI-NEUTROPHIL CYTOPLASMATIC ANTIBODIES PREDATE SYMPTOM ONSET OF ANCA-ASSOCIATED VASCULITIS. A CASE-CONTROL STUDY

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Background: Presence of anti-neutrophil cytoplasmatic autoantibodies (ANCA) is important for the diagnosis of ANCA-associated vasculitis (AAV) and reflects on-going immune processes. The timing of the antibody development and its contribution to disease is not well established.

Objectives: To investigate the presence of proteinase 3 (PR3)- and myeloperoxidase (MPO)-ANCA in blood samples collected from healthy individuals who subsequently developed AAV.

Methods: The Swedish National Patient Register of inpatient care and the Swedish Cause of Death Register were used to identify individuals assigned ICD codes for AAV (1) in the discharge summary or cause of death, respectively. The resulted cohort was then linked to the registers of 4 different biobanks to identify those with available predating blood samples. Diagnoses of AAV were confirmed and time point for onset of symptoms was identified by reviewing all available case records (1); 68 were classified as granulomatosis with polyangiitis (GPA), 14 as microscopic polyangiitis (MPA), and 4 as eosinophilic GPA (EGPA). The 86 cases (36 males, 50 females) had a mean (SD) age of 51.9 (16.9) years at sampling, with ≥1 sample (26% plasma, 74% serum samples). The sampling time point before onset of symptoms was mean (SD); 4.4 (3.1) years. Serum and plasma control samples (n=198; 82 males, 116 females; mean age (SD); 52.0 (16.5) years) were identified and matched for sex, age and date of sampling. The samples were first screened for ANCA using high sensitive ELISA (ORGANTEC diagnostika, Germany) and samples close to or above cut-off level were further analysed for capture PR3- and capture MPO-ANCA (ELISA; SVAR Life Science,

Sweden). For each case one control sample was included for the ANCA specificity tests. Statistical calculations were performed using SPSS software.
Results: In ANCA-screen 36.0% of the cases and 2.6 % of controls tested positive (p<0.001). 23/52 (44.2%) of the cases were PR3-ANCA positive (OR 56.3; 95% CI 7.26-436.62) and 8/52 (15.4%) were MPO-ANCA positive (OR 4.18; 95% CI 1.05-16.62). The mean (SD) predating time for PR3-ANCA positivity was 3.73 (3.49) years and for MPO-ANCA positivity 2.11 (1.46) years. Cases with positive predating PR3-ANCA were younger (46.0±19.4 vs 65.6±12.0 years; P<0.001) than cases with a negative predating PR3-ANCA. MPO-ANCA positive vs. MPO-ANCA negative pre-dating cases had more often severe disease (kidney/lung/peripheral nervous system) (OR 15.08; 95% CI 1.68—135.54) at disease onset. Furthermore, predating MPO-ANCA positive vs predating PR3-ANCA positive cases had significantly more often severe manifestations at disease onset (87.5% vs 28.6%; p<0.05). Cases positive vs. negative for MPO-ANCA in predating samples were less often classified as GPA (37.5% vs 86.4%; p<0.01) and more often as MPA (62.5% vs 13.6%; p<0.05).
Conclusion: The production of both PR3 and MPO-ANCA starts already years before onset of symptoms of AAV. Presence of MPO-ANCA appeared closer to symptom onset and with more severe disease presentation. Differences in the disease phenotype and disease severity were evident between the two ANCA serotypes.
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Acknowledgments: : Vasculitis Foundation, USA
Disclosure of Interests: Ewa Berglin: None declared, Aladdin J Mohammad Speakers bureau: lecture fees from Roche and Elli Lilly Sweden, PI (GiACTA study), Johanna Dahlqvist: None declared, Catharina Eriksson: None declared, Johanna Sjöwall: None declared, Solbritt Rantapää Dahlqvist: None declared
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SAT0254 PROSPECTIVE ANALYSIS OF THE PREVALENCE OF GIANT CELL ARTERITIS IN CONSECUTIVE PATIENTS WITH POLYMYALGIA RHEUMATICA

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Background: Giant cell arteritis (GCA) is the most common form of systemic vasculitis affecting people aged 50 years and older.[1] Although it is known, that GCA often coexists with polymyalgia rheumatica (PMR)[2], prevalence of GCA in consecutive patients with PMR has not been investigated
Objectives: To prospectively examine the prevalence of GCA in consecutive patients with PMR by vascular ultrasound (US).
Methods: Patients with newly diagnosed PMR fulfilling the ACR /EULAR classification criteria[3] were included. Vascular US examination of the extracranial arteries typically involved in GCA, such as axillary arteries, vertebral arteries, common carotid arteries, superficial temporal arteries with both frontal and parietal branches, occipital arteries, facial arteries and the central retinal arteries was performed in all PMR patients. Diagnosis of GCA was made, if intima-media thickness (IMT) was above respective cut-off values.[4]
Results: Fifty patients with diagnosis of PMR underwent vascular US. Twenty-three patients (46%) had PMR without GCA (PMR-group). The mean age in this group was 71 years (SD ± 10) with seventeen (73%) females. In twenty-seven PMR patients (54%) GCA was diagnosed (GCA-PMR group); the mean age in this group was 74 years (SD ± 9) with ten (37%) females respectively. Mean C-reactive protein (CRP) values were 29.4 mg/l (SD±24.5) in the PMR-group and 52.2 mg/l (SD±43.2) in the GCA-PMR-group. Although different mean values between the PMR-group and the GCA-PMR-group were observed, CRP values did not differ significantly between the two groups (p = 0.1432). Ten (37%) patients of the GCA-PMR group did not have GCA symptoms and diagnosis of GCA was only determined by ultrasound examination. Symptoms and numbers of patients with respective symptoms are depicted in Table 1 and 2.

Table 1. Symptoms and signs in both groups

Symptoms and signs	Group	
	PMR-group	GCA-PMR-group
Morning stiffness	22 (95%)	23 (85%)
≥1 shoulder with synovits or bursitis trochanterica	12 (52%)	13 (48%)
≥1 shoulder or hip with synovitis or bursitis	11 (48%)	14 (51%)
hip pain	23 (100%)	23 (85%)
No other joints affected	22 (95%)	26 (96%)

PMR-group: patients with diagnosis of polymyalgia rheumatica only
GCA-PMR-group: patients with diagnosis of polymyalgia rheumatic and giant cell arteritis

Conclusion: Prevalence of GCA in patients with PMR in our cohort was 54%. Ten (37%) patients with GCA and PMR did not have any GCA symptoms. Performing vascular US in patients with PMR can be useful to diagnose a clinical inapparent GCA. Prompt onset of the respective therapy could prevent complications of GCA and improve disease outcome.
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Table 2. Number of patients in each group with symptoms of giant cell arteritis

Symptoms	Group	
	PMR-group	GCA-PMR-group
Visual symptoms	2 (9%)	8(30%)
Headache	2 (9%)	9 (33%)
Jaw claudication	4 (18%)	10 (38%)
Scalp tenderness	0 (0%)	5 (19%)
No GCA symptoms	15 (65%)	10 (37%)

PMR-group: patients with diagnosis of polymyalgia rheumatica only
GCA-PMR-group: patients with diagnosis of polymyalgia rheumatic and giant cell arteritis

Disclosure of Interests: None declared
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SAT0255 THE RATE OF RELAPSE AMONG PATIENTS WITH LARGE VESSEL VASCULITIS AND THE SYSTEMIC INFLAMMATORY RESPONSE AS A POSSIBLE PREDICTOR FOR RELAPSE

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Background: Large vessel vasculitides are known relapsing diseases. However, the rate of relapses has been seldom addressed and there are only few data on relapse predictors.
Objectives: We conducted the present study to investigate the prevalence of relapses in the first year after diagnosis and the overall relapse among patients with large vessel vasculitis. Furthermore, we aimed to identify if the systemic inflammatory response (SIR) is a possible predictor for relapse among patients with large cell vasculitis.
Methods: The systemic inflammatory response (SIR) has been described as a potential clinical and serological score predicting the risk for relapses[1]. SIR estimates the systemic inflammatory activity at the time point of first diagnosis[1]. It was defined as follows: Temperature >38°C, weight loss >4kg, Haemoglobin <11 g/dl and erythrocyte sedimentation rate >85 mm/h. For each of the above-mentioned criteria one point was attributed, leading to a range from 0 to 4 points. Patients with 3 to 4 points were considered having a highly inflammatory response and patients with an SIR ≤ 2 were considered having a low inflammatory response and thus a lower risk for relapses. Relapses are defined as reappearance of disease-related symptoms requiring treatment adjustment. The study cohort included 75 patients with large cell vasculitis (Giant Cell Vasculitis, Takayasu Vasculitis, inflammatory non-infections Aortitis), longitudinally followed by the authors over a mean period of 5.2 ± 3.3 years (range 1-14 yr).
Results: The study-cohort includes 71 patients with a mean age at diagnosis of 63.5 (16 – 85) years. Almost three quarters (73%) of the patients were women. Most of the patients were suffering from GCA (73.2%), followed by Takayasu arteritis (16.9%) and inflammatory non-infections Aortitis (9.8%). 38 patients (53.5%) relapsed at least once during the follow up, and 17 patients had two or more relapses. The vast majority of relapses (86.8%) were observed within the first year following diagnosis. Most of the patients, 54 patients (76%), were considered having a low inflammatory response (SIR <=2). The relapse rate in this group was 59.2%. On the other hand, there were 17 patients having an SIR higher or equal to 3 points. The relapse rate in this group was 33%.
Conclusion: In conclusion, the results of this preliminary study reveal that the relapse rate among patients with large vessel vasculitis high is. The SRI appears to be an inadequate predictor for relapse in this cohort.

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Disclosure of Interests: Vasile-Mihai Coroian: None declared, Sebastian Saur: None declared, Ann-Christin Pecher: None declared, Theodoros Xenitidis: None declared, Jörg Henes Grant/research support from: Novartis, Roche-Chugai, Consultant of: Novartis, Roche, Celgene, Pfizer, Abbvie, Sanofi, Boehringer-Ingelheim,
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SAT0256 THE ROLE OF FAST-TRACK ULTRASOUND IN PREVENTING EARLY COMPLICATIONS AND RELAPSES IN GIANT CELL ARTERITIS

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Background: Giant Cell Arteritis (GCA) is the most common form of primary systemic vasculitis, mainly affecting adults over 50 years old. Permanent visual loss (PVL) is one of the most feared complications, occurring in about 20% of cases, typically prior to initiation of high-dose glucocorticoid (GC) therapy. Color-duplex sonography (CDS) of temporal arteries (TAs) and large vessels (LVs) is recognized as a first-line diagnostic tool for patients with suspected GCA. A fast track approach (FTA), incorporating CDS has been associated to a significant reduction of PVL in two retrospective studies[1,2].
Objectives: To assess the impact of FTA on PVL and risk of relapses during follow-up compared to conventional care prior to the introduction of the FTA in our rheumatology clinic.
Methods: Patients with new-onset GCA evaluated in our department from January 1998 to September 2019 were included in the study. The FTA approach for GCA was implemented since October 2016. The diagnosis of GCA was based on positive TAs and/or LVs CDS and/or a positive TA biopsy and clinical signs and symptoms of GCA. All patients were clinically examined by the same rheumatologist who performed the CDS. PVL was defined as total visual impairment in one or both eyes. Data on baseline clinical features and later outcomes were collected.
Results: 153 patients were included: 115 females (75.2%), mean age at diagnosis 71.6±8.2 years. Of these, 112 patients (73%) were evaluated conventionally and 41 (27%) with FTA. Patients in the FTA group were older (P=0.0002), presented more frequently with polymyalgia rheumatica symptoms, weight loss, jaw or tongue claudication and scalp tenderness (P<0.05 for all comparisons). The median duration of follow-up in the FTA group was shorter compared with the conventional group (1.5 vs 5.8 years). PVL occurred in 22 (19.6%) patients in the conventional group compared to 5 patient (12.2%) in the FTA, leading to a reduction of 37.9% in the relative risk of PVL with the FTA approach. Cumulative incidence of relapses and time to first relapse did not change after FTA introduction (P>0.05) (Fig. 1).

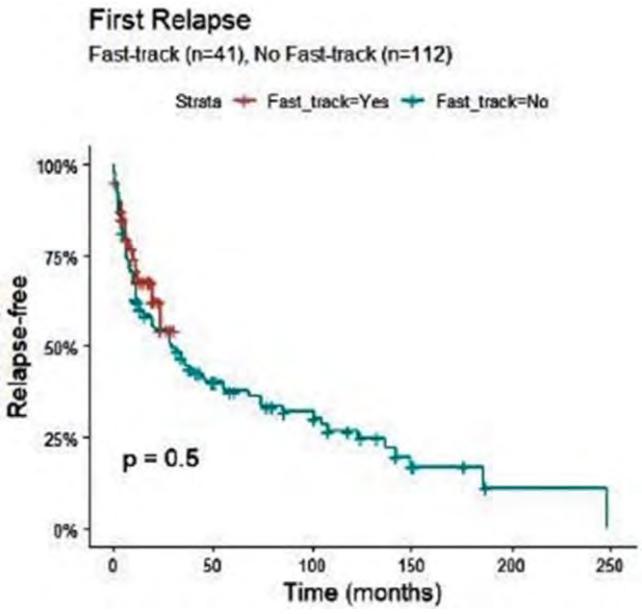


Fig. 1. Time to first relapse in patients with GCA and evaluated with a FTA compared to conventionally approached patients.

Conclusion: The application of a FTA in GCA resulted in a significant reduction of PVL. However, the relapse rate did not seem to be influenced by the FTA, highlighting the need to implement further management strategies, besides earlier diagnosis and prompt initiation of GC, that would impact the course of the disease during long-term follow-up
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Disclosure of Interests: None declared
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SAT0257 IMAGING MANIFESTATIONS OF PULMONARY INVOLVEMENT IN TAKAYASU ARTERITIS

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Background: Takayasu arteritis (TA) is a form of chronic large vessel vasculitis. Recently, we found that some patients had lung manifestations and abnormal computed tomography (CT) results that cannot be explained by other causes. And so far, the prevalence of pulmonary features of TA is uncertain.
Objectives: To investigate the imaging findings of lung involvement in patients with TA by high-resolution CT (HRCT) at a single center of China, and analyze the associations with mortality.
Methods: A retrospective study was carried out of TA patients (n = 237, 200 women) who had routine HRCT scanning performed at the time of diagnosis from 2008 to 2018 at Xijing Hospital, Xi'an (China). Radiological manifestations of pulmonary involvement were evaluated from the HRCT images by two experienced radiologists. Patients with a confirmed diagnosis of pulmonary disorder (i.e., infections, tumors, except tuberculosis) have been excluded.
Results: The median age of patients was 33 years (range 18-74), and the duration of disease was 66±55 months. Of all the patients, 57.8% (137/237) had abnormal lung HRCT results. Among them, 29.2% (40/137) of patients had pulmonary arterial involvement, including artery stenosis or occlusion. Mild pulmonary interstitial hyperplasia was the most common abnormal HRCT findings (27.4%, 65/237) observed in TA patients. Moreover, the frequencies of stripe/patchy shadows and nodule were 22.7% (53/237) and 15.6% (37/237), respectively. Pleural effusion was rare in these patients (10/237). Additionally, there are 9 cases of active pulmonary tuberculosis, 14 cases of suspected tuberculosis, and 9 cases of obsolete pulmonary tuberculosis. The common symptoms associated with lung were dyspnea (42%), cough (14%), chest pain (9.1%), and hemoptysis (4.9%). In a Cox regression model, there was no significant correlation between pulmonary involvement and mortality (P = 0.001).
Conclusion: Pulmonary abnormalities on HRCT scanning is common among patients with TA. Apart from tuberculosis-related lesions and pulmonary arterial involvement, these manifestations are probably part of non-specific systemic inflammation of TA.
Disclosure of Interests: None declared
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SAT0258 DRUG RETENTION RATE AND PROGNOSIS AFTER DISCONTINUATION OF INFLIXIMAB IN PATIENTS WITH BEHÇET SYNDROME

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Background: Infliximab (IFX) has become an important treatment option for all manifestations of Behçet syndrome (BS). Adverse events, loss of efficacy, lack of patient compliance and cost may limit its sustained use in patients with BS.

Objectives: We aimed to evaluate the drug retention rates, causes of discontinuation and outcome after cessation of IFX.
Methods: We reviewed the charts of 850 patients with BS who were registered in our clinic between 2009 and 2013 and identified those who had used IFX. The charts of these patients were surveyed for demographic features, the reasons for IFX use, previous and concomitant drugs, IFX duration, reasons for discontinuation and time to flare after discontinuation of IFX. We defined flare as disease activity in the organ involvement that necessitated IFX use. New major organ involvement that developed during or after discontinuation of IFX were also be noted.
Results: A total of 50/850 patients were treated with IFX (40 men, mean age 40±9.5 years), for uveitis (n=29), vascular involvement (n=11), parenchymal neurologic involvement (n=8), arthritis (n=1) and venous ulcer (n=1). Of these 50 patients, 22 (43%) are still receiving IFX for a median duration of 40 (IQR: 25-83) months. The remaining 28 (47%) patients had discontinued IFX after a median follow-up of 12 (IQR: 7-30) months. Reasons for discontinuation were remission in 7 patients, adverse events in 10, primary lack of efficacy in 2, and lack of patient compliance in 9 patients. Among the 7 patients who discontinued IFX due to remission, only 1 patient with uveitis had a flare, 11 months after discontinuation, while on azathioprine. The remaining 6 did not experience any flares during a median follow-up of 29.5 (IQR: 4-24) months. Five of these patients used azathioprine and 1 used mycophenolate mofetil for maintenance. Among the 10 patients who discontinued due to adverse events, IFX was switched to adalimumab in 3 patients and none experienced flares under adalimumab. The remaining 7 patients continued to receive azathioprine or mycophenolate mofetil without a biologic. Among these, 1 patient with uveitis 1 with arthritis experienced flares 6 months after discontinuing IFX. Among the 9 patients who discontinued IFX due to lack of patient compliance, 3 patients (2 with uveitis and 1 with arthritis) had flares after 5 months, 1 year and 1.5 years. IFX was re-initiated in all. The remaining 6 patients did not experience any flares after a mean follow up of 5±1.5 years. Two with uveitis and 2 with venous thrombosis used azathioprine for maintenance, while 2 patients did not receive further treatment. New major organ involvement was not observed. New BS manifestations developed in 2 patients under IFX, arthritis in one patient and both epididymitis and erythema nodosum in the other.
Conclusion: Almost half of our patients with BS remained on IFX during a median follow-up of 5.4 years (IQR:2.4-7). Main reasons for discontinuation were adverse events, remission and lack of patient compliance. Our observations further support the efficiency of IFX in managing patients with BS.
Disclosure of Interests: Sinem Nihal Esatoglu: None declared, Beyza Tukek: None declared, Sıtkı Safa Taflan: None declared, Yilmaz Ozyazgan: None declared, Didar Ucar: None declared, Emire Seyahi: None declared, Melike Melikoglu: None declared, Vedat Hamuryudan Speakers bureau: Pfizer, AbbVie, Amgen, MSD, Novartis, UCB, Ugur Uygunoglu: None declared, Aksel Siva: None declared, Izzet Fresko: None declared, Sebahattin Yurdakul: None declared, Hasan Yazici: None declared, Gulen Hatemi Grant/research support from: BMS, Celgene Corporation, Silk Road Therapeutics – grant/research support, Consultant of: Bayer, Eli Lilly – consultant, Speakers bureau: AbbVie, Mustafa Nevzat, Novartis, UCB – speaker
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SAT0259 ANCA-ASSOCIATED VASCULITIS WITH RENAL INVOLVEMENT: THE ROLE OF A COMBINED HISTOPATHOLOGICAL ASSESSMENT AS PREDICTOR OF PATIENTS' PROGNOSIS

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Background: Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis often affect the kidney and renal involvement has a considerable clinical impact on patient's prognosis. Currently used histopathological classifications are basically focused on the glomerular damage and assessing chronic damage progression, but their prognostic role presented some limitations.
Objectives: To combine the Berden Classification, the ANCA Renal Risk Score (ARRS) and the Mayo Clinic-Renal Chronicity Score (RCS) with the inflammatory interstitial infiltrate and to evaluate the prognostic value of the combined assessment in patients with AAV
Methods: We included 19 AAV patients with renal involvement (mean age 63±13.2 years; disease duration 4.9±5.2 months) who underwent renal biopsy. Patients were classified according to age, sex, disease duration, ANCA positivity. The histopathological evaluation was performed assessing the Berden category, Risk group (low, medium, high) according to the ARRS and Chronicity class according to the RCS; we also assessed the % of inflammatory interstitial infiltrate. Each patient was followed-up for 12 months; we considered the stage IV (eGFR < 30 ml/min/m^2) of the *KDIGO CKD* Classification as renal outcome.
Results: 8 (42.1%) AAV patients were p-ANCA and 11 (57.9%) c-ANCA. 12 months after renal biopsy, 8 patients (42.1%) had a GFR <30 ml/min. According to the ARRS, 10 (52.6%) patients were in low, 7 (36.8%) in medium and 2 (10.5%) in high risk group. According to the RCS, 2 (10.5%) biopsies had minimal, 10 (52.6%) mild and 7 (36.8%) moderate chronic changes, no one presented severe chronic changes. According to the Berden classification, 6 (31.6%) samples represented the focal, 2 (10.5%) the crescentic and 11 (57.9%) the mixed category, no one represented the sclerotic class. The mean % of inflammatory infiltrate was 37.4±25.2. The interstitial inflammatory infiltrate showed a direct correlation with the severity of the Berden category (R=0.51; p=0.025), the % of sclerotic glomeruli (R=0.6; p=0.007) and the number of fibrocellular crescents (0.46; p=0.05) and an inverse correlation with the GFR at 12 months (R=-0.48; p=0.045). A ROC curve study identified a 22.5% cut-off of inflammatory infiltrate to predict the outcome of GFR at 12 months < 30 ml/min (sensitivity 88%, specificity 97.5%). Patients in focal class developed less frequently a GFR<30 (χ2=9.1; p=0.003), but there were no differences in the outcomes between the crescentic and mixed class. ARRS could differentiate risk group with regard to the renal outcome stage IV (χ^2=9.0 e p=0.01) as well as the chronicity Score (χ^2=8.1; p=0.017). Finally, we built a matrix combining the different histopathological scores and the % of inflammatory infiltrate to predict the outcome; we found that an inflammatory infiltrate wider than 22.5% characterizes most of patients developing stage IV chronic renal failure at the 12th month. In fact, more than 75% of patients with eGFR < 30 ml/min had inflammatory infiltrate wider than 22.5% at biopsy, despite they were in the low risk class (ARRS) and in minimal changes class (RCS).
Conclusion: Our results underline the importance of the inflammatory infiltrate in renal outcome and histology. Despite the limited number of patients, our data suggest that a combined histological score assessing the chronicity and activity of renal disease from both glomerular and interstitial perspective could better predict patients' global and renal prognosis.
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Disclosure of Interests: Laura Gigante: None declared, Pier Giacomo Cerasuolo: None declared, Gisella Vischini: None declared, Francesco Federico: None declared, Dario Bruno: None declared, Alessia Musto: None declared, Stefano Costanzi: None declared, Silvia Laura Bosello Speakers bureau: Abbvie, Pfizer, Boehringer, Elisa Gremese Speakers bureau: Abbvie, BMS, Celgene, Jannsen, Lilly, MSD, Novartis, Pfizer, Sandoz, UCB
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SAT0260 PENTOXYFILLINE GEL FOR ORAL ULCERS IN PATIENTS WITH BEHÇET'S SYNDROME

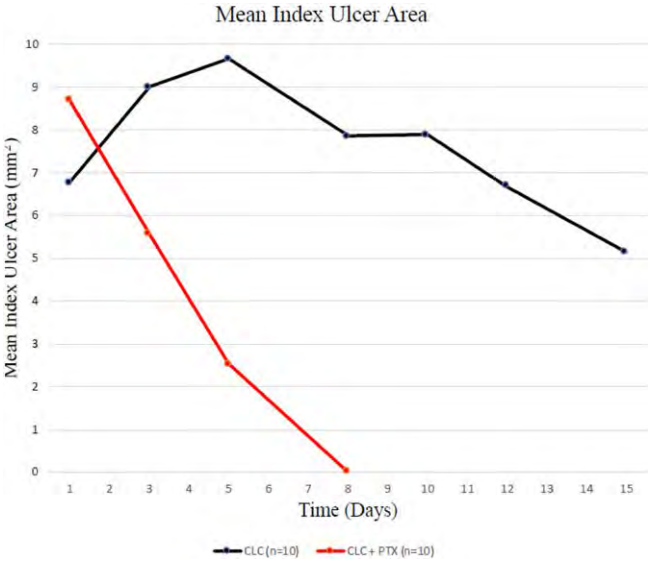
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Background: Oral ulcers, the hallmark lesion of Behçet's syndrome (BS) can be disabling and impair eating, drinking and speaking. Despite recent advances in systemic medications for the treatment of oral ulcers, some patients do not achieve complete remission. Topical agents may help such patients by decreasing the pain and duration of oral ulcers. Pentoxyfilline (PTX) is a methylxanthine derivative that inhibits phosphodiesterase and is thought to have immunomodulatory effects in addition to improving blood flow which is its main reason for use in peripheral vascular disorders.
Objectives: The aim of this study is to assess the efficacy and safety of PTX gel for oral ulcers in patients with BS. We also aimed to explore the best tools for the assessment of treatment response to topical agents in randomized controlled trials (Clinicaltrial.gov ID: NCT 03888846).

Methods: This was an open-label, randomized, parallel group study comparing PTX gel in addition to colchicine (PTX-COL) with colchicine alone (COL). Patients with BS who were treated with colchicine and not using any other systemic medications for BS, having at least one oral ulcer that appeared during the last 48 hours were included. PTX 5% gel with a dose of 1000 mg/day was applied in 4 divided doses per day for 14 days. Patients were contacted daily for 14 consecutive days. Photographs were taken every 24 - 48 hours and graphical processing software was used to calculate the area of the index ulcer. Duration of the index ulcer, time to start of index ulcer shrinkage, time to 50% reduction in oral ulcer pain on a 10 mm visual analog scale (VAS), change from baseline in the area of the index ulcer over time, total number of oral ulcers and adverse events were evaluated.

Results: A total of 41 patients were randomized, 39 patients (18 in the PTX-COL group and 21 in the COL group) completed the study and 2 patients in PTX-COL group withdrew from the study due to unacceptable dysgeusia and nausea. Mean duration of index ulcer, time to start of index ulcer shrinkage, time to 50% reduction in oral ulcer pain, and number of patients with no detectable ulcers on day 4 in each group were lower in the PTX-COL group as presented in the Table. Change from baseline in the area of index ulcer and pain score over time is shown in the Figure. There were no serious adverse events. Fifteen (75%) patients reported nausea, 11 (55%) reported dysgeusia and 2 reported vomitting in the PTX-COL group, while 2 patients (10%) reported nausea in the COL group.

Conclusion: This pilot phase 2 open label, randomized controlled study supports the hypothesis that topical PTX in addition to colchicine accelerates the healing of BS oral ulcers compared to colchicine alone. A phase 3 controlled study with a higher number of patients is planned with improving the taste for tolerability of the product.



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SAT0261 FEATURES AND RISK FACTORS OF SERIOUS INFECTIONS IN ANCA ASSOCIATED VASCULITIS: LONG TERM FOLLOW UP OF 186 PATIENTS

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Background: Serious infections (SI) are one of the main complications in patients with ANCA associated vasculitis (AAV).

Objectives: We planned to investigate the prevalence, features and risk factors of SI in our AAV cohort during follow-up.

Methods: Outpatient and hospital data of patients diagnosed with granulomatous polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic granulomatous polyangiitis (eGPA) between 1999 and 2019 according to Chapel Hill Consensus Criteria and followed up at least 6 months in our vasculitis clinic were evaluated. Development of sepsis, requirement for intravenous (IV) antibiotherapy and / or hospitalization during infection episodes were considered as SI. Chi-square, student's t-test and logistic regression analysis were used for statistical analysis.

Results: Study was conducted with 186 (53.6% female) patients with adequate follow-up data. Mean age of diagnosis was 54.3±14,5 (23-79), mean follow-up duration was 86,4 ± 54,3 (6-251) months. Number of GPA, MPA and eGPA patients were 132 (71%), 42 (22,5%) and 12 (6,5%), respectively. IV cyclophosphamide (CYC) was used in 148 (79,6%), azathioprin in 105 (56,5%), rituximab (RTX) in 69 (%37,1), methotrexate in 29 (15,6%) and mycophenolate mofetil in 14 (7,5%) patients. Number of patients developed SI was 66 (34.7%), total SI episode was 86, patients who had multiple episodes was 15. All SI is shown in Table-1. Bacterial pneumonia was the most common diagnosis and 26 of SI (30.2%) were considered as opportunistic (systemic viral, parasite, fungus) infections. Thirty-one of patients developed SI (40,7%) in the first year after diagnosis. SI were observed more frequently in the presence of major organ involvement (kidney, lung, neurological) (65/173 vs. 1/13 p = 0.02 OR = 8.7 95% CI 1.06-64.4). Diffuse alveolar hemorrhage (DAH) was associated with SI in multivariate analysis (12/52 vs. 0/34 p=0.007 OR=1.6 95% CI 1.3-1.96). Cumulative CYC dose was significantly higher in patients with SI (14,2±21 vs. 8.2±13.9 p=0.045). During maintenance, patients treated with RTX had significantly more SI (18/53 vs. 17/99 p=0.19 OR=3,3 95% CI 1,55- 7,07). Hypogammaglobulinemia (HIgG) (IgG<700 mg/dL) was present in 12 (14%) SI episodes. HIgG was associated with SI in RTX-treated patients (5/13 vs. 7/47 p=0.03 OR=4.2, CI=1-16.5). Hospitalization need for SI was 65%. Disease flares (34/128 vs. 32/62 p = 0.001 %95 CI = 2.9 95% CI 1.6-5.6) and organ damage presence were more common (64/65 vs. 109/125 p = 0.01 95% OR= 8.9 95% CI 1.1-68.9) in patients with a history of SI in multivariate analysis. SI was confirmed as cause of death in three cases.

Conclusion: Long-term follow-up results of a single center cohort of AAV patients revealed that approximately one third of patients developed SI, most frequently in the first year of treatment. During the maintenance period, the risk of SI continues. Cumulative CYC dosage and maintanence with RTX is associated with SI, especially in patients who developed hIgG. Major organ involvement, disease flares and organ damage are significant risk factors for SI. In this regard, protection measures (vaccination, prophylaxis) should be reviewed and the quality of follow-up should be improved.

Table 1. Serious infections in AAV patients.

BACTERIAL	N	FUNGAL	N	VIRAL	N	PROTOZOAN	N
Pneumonia	37	PJP	7	Zoster Zona	3	Intramuscular abscess (Nocardiosis)	1
Urinary Tract Infection (UTI)	8	Aspergilloma	1	CMV Pneumonia	1		
Gr (-) sepsis	2	Invasive Fungal Infection	3	CMV Colitis	1		
Perianal abscess	2	Candida Eosephagitis	4	CMV Gastritis	1		
Intraabdominal abscess	2	Candidemia	2	HSV Eosephagitis	1		
Catheter infection	2	UTI	1				
Sellulitis	1	Fungal otitis	1				
Orbital sellulitis	1						
Maxillary sinüs abscess	1						
Mastoiditis	1						
Prosthesis infection	1						
Septic artrhitis	1						
Lung tuberculosis	1						

Disclosure of Interests: None declared

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SAT0262 PROPOSAL FOR OPTIMIZATION OF DIAGNOSTIC IMAGING FOR GIANT CELL ARTERITIS USING THREE-DIMENSIONAL COMPUTED TOMOGRAPHY ANGIOGRAPHY IMAGE AND CONSTRUCTING VASCULAR MAPPING FROM VASCULAR ULTRASONOGRAPHY AS REFERENCES

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Background: The development of rapid and accurate methods of diagnosing giant cell arteritis (GCA) is critical to prevent blindness and stroke, which may develop rapidly in patients with GCA. In 2018, EULAR published recommendations that the first imaging modality for GCA should be vascular ultrasonography without biopsy. However, many institutions still consider biopsy to make an important contribution to the diagnosis of GCA.

Objectives: Our purpose is to eliminate blindness and stroke among GCA patients by optimizing diagnostic imaging and method to diagnose GCA employed by vascular ultrasonography (V-US), CT Angiography (CTA), MRI/A, and PET/CT without biopsy.

Methods: We evaluated the clinical and serological characteristics of 20 patients who were diagnosed with GCA at our hospital from 2012 to 2018, and compared the image and biopsy findings of these patients. We then evaluated the effect of optimizing diagnostic imaging and methods for patients with suspected GCA who visited our hospital during 2019. Vascular mapping was carried out using V-US for 3DCTA and other imaging methods as references.

Results: Table 1 shows the clinical characteristics of the study population. The sensitivity of CTA for GCA was 85.7% (12 of 14 patients), which was the highest of the studied imaging methods. All biopsy-positive cases were diagnosed as GCA, and we compared these cases with cases with positive imaging findings. This revealed that CTA findings were correct (i.e., positive) in 66.7% (four of six patients), MRI/A findings were correct in in 33.3% (three of nine), V-US findings were correct in 50.0% (three of six). Therefore, CTA exhibited the highest sensitivity for positive findings. Comparison of biopsy-positive cases with cases in which imaging findings were negative revealed that CTA findings were correct (negative) in 33.3% (two of six patients), MRI/A findings were correct in 55.6% (five of nine), V-US was correct in 50.0% (three of six). Thus, CTA had the lowest sensitivity for negative findings. Comparison of CTA findings of positive cases with other imaging modalities which reported positive findings revealed MRI/A findings to be correct in 44.4% (four of nine patients), PET/CT findings to be correct in 50.0% (one of two), V-US to be correct in 63.3% (five of eight). Thus, V-US had the highest agreement with CTA. We carried out vascular mapping by V-US using 3DCTA and other imaging methods and produced references to improve the accuracy of diagnosis. Using these references, we diagnosed five cases of GCA among the 20 patients; the positive predictive value of V-US was 80% (four of five patients) and negative predictive value was 86.7% (13 of 15 patients).

The number of biopsies performed decreased from 50% (10 of 20 patients) from 2012 to 2018 to 15% (3 of 20 patients) in 2019. Two cases in the present study had positive findings in both biopsy and V-US; in one case, biopsy, CTA, and MRI/A were negative while V-US revealed positive findings. No patients with GCA developed blindness or stroke during 2019.

Age (years)	average 74.7 (median 74.5)
Female (%)	80.0
Cranial type (%)	60.0
LV type (%)	10.0
Cranial + LV type (%)	30.0
First symptom	Temporal 25%,Occipital 20%, Arthritis and myalgis 10%
Duration to diagnosis (days)	average 82.1
Ocular findings(%) (blindness)	30.0 (15)
PMR (%)	50.0
Jaw claudication(%)	50.0
Headache (%)	85.0
Cerebral infarction(%)	10.0
CRP (mg/dl)	average 8.18 (median 7.14)
ESR (mm/hr)	104.5 (median 104.6)
RF positive (%)	10.0
CCP Ab positive (%)	0.0
ANA positive (%)	80.0 (average 25x)
SS-A Ab (%)	0.0
Clβ 2GP1 Ab positive (%)	30.0
TAB (%)	50 (giant cell positive 56)

Table 1. Baseline characteristics of the study sample

Conclusion: We propose that V-US should be performed as the first examination for the diagnosis of GCA by the creation of vascular mappings when GCA is suspected in order to prevent blindness and stroke.

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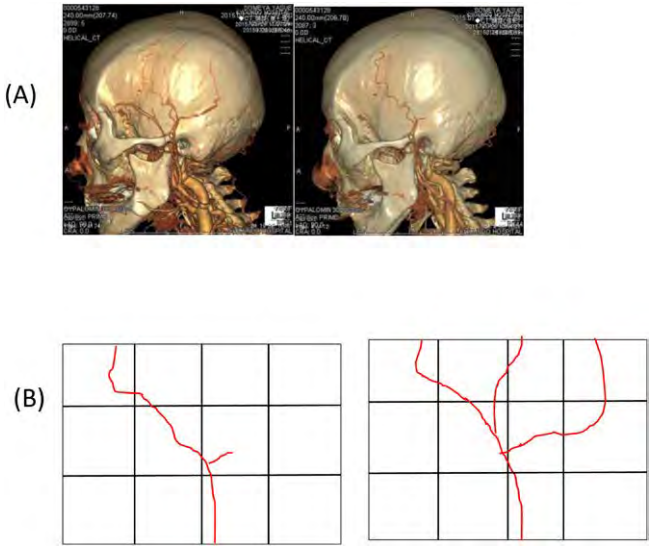


Figure 1. Left side is before, right side is after thrapy. (A) 3DCTA finding, (B) determination of V-US arrangement with vascular location to evaluate wall thickening of V-US, compression sign, stenosis and stoppage of vessels.

Disclosure of Interests: None declared

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SAT0263

LOW-DOSE IL-2 THERAPY EFFECTIVELY PROMOTES THE BALANCE BETWEEN TREG CELLS AND PRO-INFLAMMATORY LYMPHOCYTES IN PATIENTS WITH BEHCET'S DISEASE

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Background: Behcet's disease (BD) is a chronic multisystemic disease. Several studies have shown that immune mechanisms play an important role in the development of the disease and limited options of therapeutic medicines for BD. Low dose IL-2 has been reported to selectively promote the expansion of Treg.

Objectives: To evaluate the significance of Treg cells and cytokines in the pathogenesis and the changes of peripheral lymphocyte subsets and clinical indexes in patients with BD after low dose IL-2 therapy.

Methods: Absolute number of CD4+CD25+FOXP3+Treg, CD4+IL17+T (Th17) and other subsets in peripheral blood (PB) from 177 patients with BD and 160 healthy donors were characterized by flow cytometry combined with an internal microsphere counting standard. And cytokines were analyzed by cytometric beads array. Thirty-nine patients were treated with daily subcutaneous injections of 0.5 million IU of human IL-2 for five consecutive days, and then its effects were analyzed.

Results: As compared to healthy controls, the number of Treg cells were significantly decreased in BD patients (median:22.32 cells/ul VS median:33.12 cells/ul, $P<0.001$), while there was no difference about Th1, Th2 and Th17 cells. Accordingly, the median ratios of Th17/Tregs cells in patients were greatly higher than those of healthy volunteers. Besides, the circulating NK cells in the patients appeared to be lower than the proportion in the healthy donors. While no difference was observed for that of T, B, CD4+T, CD8+T cells between groups. Further, the correlation analysis showed that circulating Treg levels were negatively correlated with ESR, CRP and BDCAF respectively, suggesting an important role of Tregs in sustained high disease

activity. While no obvious correlation was seen in Th1, Th2, Th17 and NK cells. Then the results showed there was a statistically significant decrease in the secretion of IL-10 in the BD patients (P = 0.004), not for IFN-γ, IL-4, IL-17 and IL-6.

To evaluate the effects of IL-2 on lymphocytes in vivo, we examined 39 inpatients who received daily low-dose IL-2 at the dosage of 50 WIU for 5 days. It showed that, besides NK cells, total T cells, B cells, CD4+ T cells, CD8+ T cells, Th1 cells, Th2 cells, and Th17 cells were all increased after IL-2 treatment. But only Treg cells were amplified more dramatically, with the four-fold increase. Accordingly, the ratio of Th17/Treg was decreased significantly in patients with IL-2 treatment, tended to balance and had no difference with healthy individuals. At the same time, we found that the symptom were mitigated obviously and disease activity including ESR and CRP were both decreased distinctly without observed side effects.

Conclusion: Absolute decrease of PB Tregs in patients with BD was associated with disease activity,which might be the major reason for imbalance of Th17/Tregs. It is speculated that BD is an autoimmune disease triggered by the defect of immunotolerance. More importantly, low-dose IL-2 proposes a selective biological treatment strategy by restoring immune tolerance and promoting rapidly remission.

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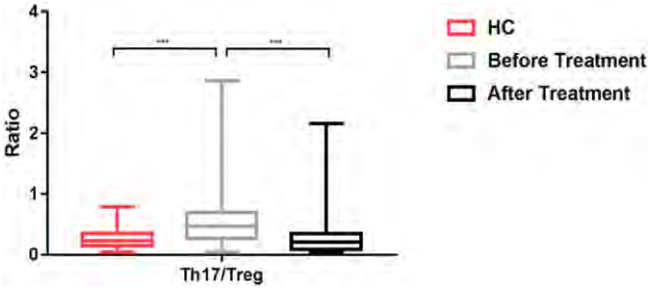


Figure 1. The ratios of Th17/Treg among Healthy controls(HC), Before treatment and After treatment.

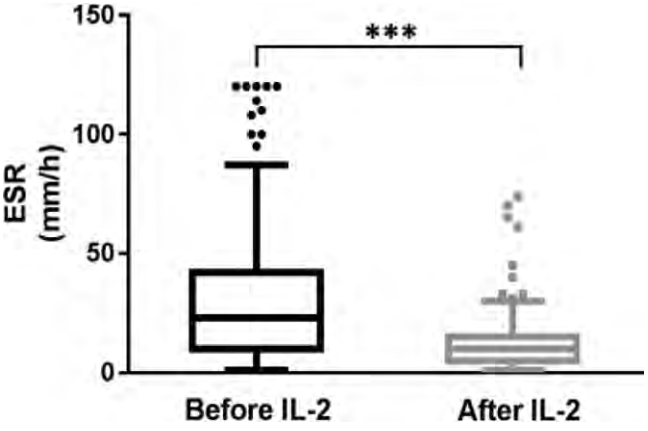


Figure 2. The changes of disease activity in BD patients after low-dose IL-2 treatment.

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Disclosure of Interests: None declared
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SAT0264

LONG TERM FOLLOW-UP AND OPTIMIZATION OF INFLIXIMAB IN REFRACTORY UVEITIS DUE TO BEHÇET'S DISEASE. MULTICENTER STUDY OF 103 CAUCASIAN PATIENTS

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Background: Biologic therapy has improved prognosis of Behçet Disease (BD) uveitis (1-5). Although infliximab (IFX) is approved in Japan, most data in Caucasian patients comes from small series. No data on optimization has been published

Objectives: In a large series of Caucasian patients with refractory uveitis of BD, we assess: **a)** long-term efficacy and safety; **b)** IFX optimization when ocular remission was achieved

Methods: Multicenter study of IFX-treated patients with BD uveitis refractory to conventional immunosuppressants.103 patients were treated with IFX as 1st biologic as follows: 3-5 mg/kg i.v. at 0, 2, 6 and every 4-8 weeks. The main outcomes were anterior chamber cells, vitritis, retinal vasculitis, macular thickness, visual acuity, and glucocorticoids sparing effect; analysed at baseline, 1st week, 1st and 6th months and 1st and 2nd years. After remission, IFX optimization was performed

Results: In whole series (n=103), main outcomes showed a rapid and maintained improvement, reaching remission in 78 patients after a mean IFX duration of 31.5 months. Severe side-effects were observed in 9 patients.

Comparative study between optimized and non-optimized groups showed: **a)** no differences in clinical baseline characteristics; **b)** similar maintained improvement in most ocular outcomes; **c)** lower severe adverse events and **d)** lower IFX cost in optimized group (4826.52 vs 9854.13 euros/patient/year) **(Table)**

Conclusion: IFX seems effective and safe in Caucasian patients with refractory BD uveitis. IFX optimization is effective, safe, and cost-effective

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Table.

	Optimized N=18	Non Optimized N=42	P
Patients/eyes affected, n/n	18/34	42/77	
Age, mean (SD), years	39.5 (9.8)	38.8 (10.5)	0.82
Men, %	55.6	59.5	0.78
Duration of uveitis before IFX, median [IQR] months	38 [18-119]	35 [10-48]	0.11
Ocular features at time of IFX onset			
-AC cells count, median [IQR]	2 [1-4]	2 [1-2]	0.29
-Vitritis, median [IQR]	2 [1.5-3]	2 [1-2]	0.02
-BCVA, mean (SD)	0.32 (0.21)	0.37 (0.26)	0.51
-OCT, mean (SD)	303.5 (23.3)	397.7 (155.7)	0.12
-Retinal vasculitis, n (%)	9 (50)	26 (66.7)	0.23
Uveitis pattern, n (%)			
-Bilateral/unilateral	16/2 (88.9/11.1)	35/7 (83.3/16.7)	0.71
-Anterior	0 (0)	6 (14.3)	0.17
-Posterior	5 (27.8)	8 (19.0)	0.50
-Panuveitis	13 (72.2)	28 (66.7)	0.67
Prednisone dose at IFX onset, mean (SD), mg/d	40.3 (20.6)	41.4 (15.5)	0.81
IFX therapy			
Monotherapy/combined treatment, n (%)	15 (83.3)	30 (71.4)	0.33
-AZA	5 (27.8)	4 (9.5)	0.11
-CsA	9 (33.3)	8 (19.0)	0.32
-MTX	4 (22.2)	15 (35.7)	0.30
Follow-up on IFX therapy, median [IQR], months	48 [33-60]	24 [6-60]	0.007
-Relapses, median (IQR)	0 [0-1]	0 [0-2]	
-Remission, %	100	75.6	0.46
-Severe side effects, n (per 100 patients/year)	0 (0)	3 (0.78)	0.02
-Cost (mean), euros per year	4826.52	9854.13	0.55 –

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MSD and Roche, Speakers bureau: AbbVie, Lilly, Celgene, Grünenthal, UCB Pharma, Emma Beltrán: None declared, Alfredo Adan: None declared, Elena Aurrecoechea: None declared, Santos Castañeda: None declared, Miguel A González-Gay Grant/research support from: Pfizer, Abbvie, MSD, Speakers bureau: Pfizer, Abbvie, MSD, J. Luis Hernández: None declared, Ricardo Blanco Grant/research support from: AbbVie, MSD, and Roche, Speakers bureau: AbbVie, Pfizer, Roche, Bristol-Myers, Janssen, and MSD

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SAT0265 RISK FACTORS FOR INFECTIOUS COMPLICATIONS FOLLOWING RITUXIMAB TREATMENT – MULTICENTER POLISH EXPERIENCE

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Background: Rituximab (RTX) is a B cell depleting monoclonal antibody with proven efficacy in the treatment of ANCA-associated vasculitis (AAV). The infectious complications occur in 15-25%.

Objectives: We aimed to assess the frequency and risk factors of infections in patients with AAV receiving RTX among Polish patients.

Methods: 7 tertiary referral centers experienced in the treatment of vasculitis completed a questionnaire regarding AAV patients treated with RTX.

Results: Among 49 patients included in the analysis (47 with GPA, 2 with MPA; 36/73% men; mean age at diagnosis 42,45±14,9 yrs., mean age on RTX initiation 46,14±14,72 yrs.,) at least one infection occurred in 20 patients (40.82%) after mean time of 16,65±16,01 weeks since the administration of RTX. Patients were followed for a mean time of 26,88±21,94 months. There were no differences in the incidence of infectious complications by gender, age, BMI, smoking status, severity of the disease, activity of the disease (BVAS), time from diagnosis to RTX initiation, carriage of staphylococcus aureus in the upper respiratory tract, total dose of CYC before RTX treatment. We didn't observe severe hypogammaglobulinemia or neutropenia after RTX treatment. 40% of the observed infections occurred during the first month, 35% between second and sixth month of follow-up, while 25% were observed between 6 and 12 months after the RTX initiation. Of the 20 patients who developed infection, 12 (24.5%) had further infections. Antibiotic prophylaxis with trimethoprim–sulfamethoxazole was administered in 40 out of 49 (81.63%). Upper respiratory tract infection was the most common infectious complication (n=11), followed by lower respiratory tract (n=4), soft tissues (n=4) and urinary tract infections (n=4), lacrimal gland abscess (n=2) and abdomen (n=1). In cases with a positive microbial result Staphylococcus aureus (n=4), Klebsiella pneumoniae (n=2), Pseudomonas aeruginosa (n=1), Candida (n=1) and others (n=6) were identified. No fatalities were recorded and only 3 patients had severe infection with the necessity of prolonged treatment.

Conclusion: Despite the high number of infections in our group treated with RTX, most of them were not severe. Upper respiratory tract was the most common site of infection.

Disclosure of Interests: None declared

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SAT0266 FAMILIAR AGGREGATION OF LONGEVITY IN GIANT CELL ARTERITIS AND POLYMYALGIA RHEUMATICA

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Background: The long-term mortality in giant cell arteritis (GCA) and polymyalgia rheumatica (PMR) is unexpectedly decreased (1,2,3,4) or at least not increased regardless increased mortality risk factors that these diseases share with other systemic inflammatory disorders.

Objectives: We aimed to test the hypothesis on aggregation of increased longevity in families of PMR/GCA patients because the family members of long-lived subjects have a survival advantage.

Methods: After questioning our patients we compared age of death of 358 parents of 179 PMR and GCA patients with corresponding data retrieved from 506 parents of 235 randomly collected age and sex matched controls.

Results: We found the number of nonagenarian (≥90 year old) mothers of PMR/GCA patients significantly higher vs controls. Both nonagenarian parents were found in 6 patients (3.35%) and in none of the controls. Decreased number of nonagenarian fathers of our patients remains unexplained.

Conclusion: Confirming our findings in a wider studies would imply a need of including some genetic or behavioural factors to explain PMR/GCA survival advantage.

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Table 1. Number of nonagenarians (≥90 years olds) in parents of PMR/GCA patients

	Parents age	PMR/GCA (N=179)	Controls (N=253)	OR	95%CI	p
Mothers	<90	148 (82.68%)	243 (96.05%)			
	≥90	31 (17.32%)	10 (3.95%)	2.34	1.11-11.95	<0.0005
Fathers	<90	161 (89.94%)	203 (80.24%)	0.45	0.24-0.83	0.0064
	≥90	18 (10.06%)	50 (19.76%)			
One of parents	<90	136 (75.98%)	193 (76.28%)	1.02	0.63-1.63	0.9412
	≥90	43 (24.02%)	60 (23.72%)			
Both parents	<90	173 (96.65%)	253 (100.00%)	8.77	2.26-405.10	0.003
	≥90	6 (3.35%)	0 (0%)			
Mothers of female patients	<90	105 (84%)	149 (97%)	7.1	2.27-29.19	0.0001
	≥90	20 (16%)	4 (3%)			
Mothers of male patients	<90	43 (80)	94 (94%)	4.01	1.25-13.97	0.0066
	≥90	11 (20%)	6 (6%)			

N - number of all parents

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SAT0267 ROLE OF AGGRESSIVE IMMUNOSUPPRESSION ON SUBGLOTTIC STENOSIS IN GRANULOMATOSIS WITH POLYANGIITIS: RETROSPECTIVE ANALYSIS OF A MONOCENTRIC COHORT

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Background: Subglottic stenosis (SGS) is defined as airway narrowing below the vocal cords and is a common and potentially life-threatening manifestation of Granulomatosis with Polyangiitis (GPA), with an estimated prevalence of 16-23% (1). Balloon catheter dilation is effective in GPA-related SGS, but relapses are frequent. Little is known about the role of immunosuppression in this setting.

Objectives: to analyse the clinical characteristics of a monocentric GPA cohort, describe phenotype differences among patients with and without SGS and investigate the role of surgical and medical treatments on relapse risk and general outcome.

Methods: Biopsy-proven patients with SGS were identified by review of medical charts among a cohort of patients with GPA, classified according to the algorithm of the European Medicine Agency (2). The clinical characteristics

of patients with SGS were retrospectively collected over a median follow-up time of 15.9 years and compared to those of patients without SGS.

Results: Fourteen patients with SGS-GPA were identified, with a female to male ratio of 1:1 and a prevalence of 29.2% among the cohort. The mean ± SD age at GPA onset was 30.8 ± 14.4 years, with a mean time from GPA diagnosis to SGS onset of 4.7 ± 4.2 years. ANCA were positive in 78.6% (54.0% anti-PR3, 18.1% anti-MPO and 27.9% IFI only). The mean Birmingham Vasculitis Activity Score (BVAS) at onset was 10.0 ± 5.6. The main clinical manifestations associated with SGS were crusty rhinitis (100%), sinusitis (78%), pulmonary disease (72.7%), otitis/mastoiditis (50%), glomerulonephritis (42.9%), orbital pseudotumor (28.6%). Six patients (42.9%) received medical treatment only, other six (42.9%) had one to three balloon dilations and two (14.2%) underwent four or more procedures. Eight patients had no SGS relapse (maximum one dilation) and they all received immunosuppression with rituximab (RTX), cyclophosphamide (CYC) or azathioprine (AZA). All patients who received no immunosuppression, methotrexate (MTX) or mycophenolate (MMF) had at least one relapse. Patients treated with MTX or MMF had a mean relapse-free survival of 13.1 months, which was comparable to the one of patients not receiving medical treatment (40.2 months; p=NS) and shorter than the one of patients receiving CYC or RTX (153.2 months; p=0.032). CYC use also inversely correlated with the number of surgical procedures (r=-0.691, p=0.006). Compared to patients without SGS (31 consecutive patients with at least 4 years of follow-up), patients with SGS-GPA had an earlier disease onset (mean age 30.8 vs 50.4 years; p<0.001), but with lower BVAS (mean 10.0 vs 15.3; p=0.013) and showed a higher prevalence of crusty rhinitis (100% vs 67.7%; p=0.019). No difference was observed in damage accrual over time between the two groups.

Conclusion: Subglottic stenosis is highly prevalent in patients with GPA and may define a milder disease subset occurring more frequently in younger patients. MTX and MMF might be insufficient to prevent SGS relapses requiring balloon dilation. Aggressive immunosuppression (CYC or RTX) might have a non-redundant role in this setting and reduce the risk of relapses.

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SAT0268 COMPLEMENT ACTIVATION VIA ALTERNATIVE PATHWAY IN ANCA-ASSOCIATED VASCULITIS

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Background: There is increasing evidence that the complement system, in particular the alternative pathway, plays a crucial role in the pathogenesis of ANCA-associated vasculitis (AAV) [1]. Efficacy of C5a receptor antagonists indicates that chemoattraction mediated by C5a plays a key role in the inflammatory process observed in AAV [2]. Another promising research object are regulatory proteins such as factor B [3].

Objectives: To study complement activation via the alternative pathway in patients with active ANCA-associated vasculitis.

Methods: 59 patients with newly diagnosed (n=35) or relapsing GPA or MPA (n=24) were enrolled in this prospective study. Median BVAS v.3 at the time of AAV onset was 16.5 (9.5; 20). In 28 patients activation of complement was reassessed during sustained remission (BVAS v.3 = 0) after a median of 16 months. Thirty six age-and gender-matched healthy volunteers comprised the control group. Levels of complement components (C3, C5, C3a, C5a, vitronectin, factor B and factor P) were measured by ELISA (Cloud Inc.). Data were not normally distributed, therefore, values are given as medians and IQRs and nonparametric statistical tests were used.

Results: The concentrations of C5, C3, vitronectin and CFB were significantly higher in patients with active AAV than control group. There were no significant differences in the levels of factor P in patients with active AAV and control group (388000 (371960; 417150)) vs 416000 (400200; 437000), ng/ml, p >0.05) (Fig. 1).

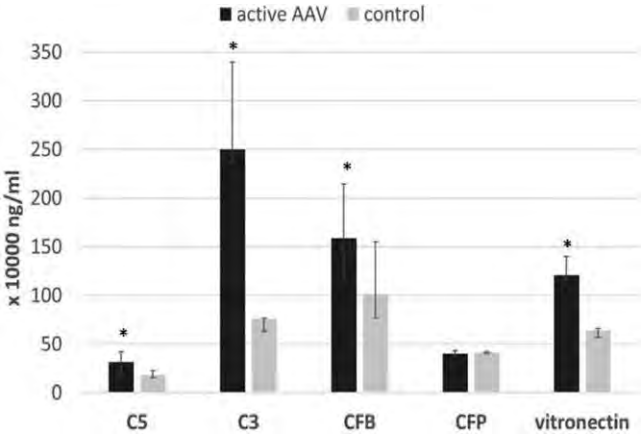


Fig 1. Concentration of complement components in patients with active AAV and healthy controls (*p<0.05)

Serum level of C5a and C3a were higher in patients with active AAV than in healthy controls (22.9 (14.4; 33.0) vs 3.0 (0.35; 6.73), ng/ml, p<0.001; 21436 (11395; 21436) vs 1224.5 (798.5; 1947.7), ng/ml, p<0.001). Patients with active AAV had significantly higher MAC levels than healthy controls (24646 (15342; 46681) vs 3305.5 (2780.2; 3777.5), mAU/ml, p<0.001).

The levels of complement components were similar in PR3-ANCA and MPO-ANCA disease, and severe and non-severe AAV. C5a/C5 and C3a/C3 ratios were not influenced by disease activity, severity or ANCA type.

After immunosuppressive treatment concentrations of C5, C3, and their activated products, C5a, C3a significantly decreased (Fig. 2). However, concentrations of regulatory proteins such as factor B, factor P and vitronectin were unaffected. Interestingly, that there was no significant difference in MAC levels before and after immunosuppressive treatment (24646 (15342; 46681) vs 20057.4 (19709.3; 41477.6), mAU/ml, p=0.925).

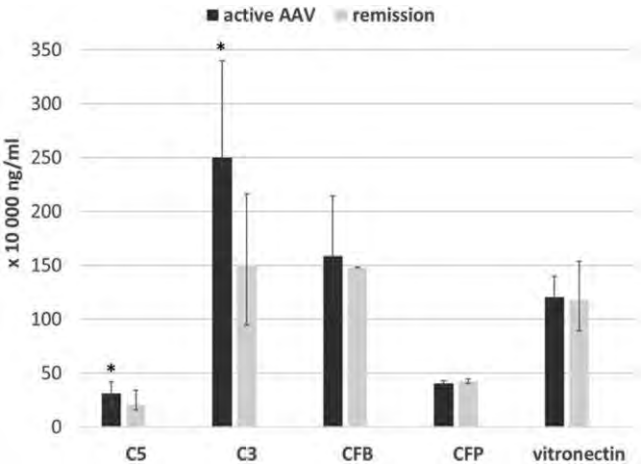


Fig 2. Concentration of complement components in patients with active disease and remission (*p<0.001)

Conclusion: The complement system plays an important role in AAV. While treatment affects some component, some remain unchanged and are not dependent on AAV severity or ANCA serotype.

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SAT0269 TAKAYASU ARTERITIS AND INFLAMMATORY BOWEL DISEASE. COEXISTENCE AMONG NORWEGIAN PATIENTS

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Background: Takayasu arteritis (TAK) and inflammatory bowel disease (IBD), consisting of ulcerative colitis (UC) and Crohn's disease (CD), are uncommon diseases. The incidence rates of TAK is 22.0/million and IBD 193/million in Norway (1, 2). UC in patients with TAK has previously been reported with a prevalence between 0,21% and 6.4% and may be explained by shared genetic disposition (3). Epidemiological data are mainly based on one Asian study (3), one Canadian study (4) and case reports.
Objectives: We investigated the coexistence of TAK and IBD and compared clinical characteristics between TAK patients with- and without IBD.
Methods: We analysed the prevalence of TAK with IBD in a population-based cohort of patients based on the Norwegian Systemic connective tissue disease and Vasculitis Registry (NOSVAR). The diagnoses of TAK were based on either 1990 ACR classification criteria (5) or the modified Ishikawa diagnostic criteria (6). The distribution of vasculitis was recorded in accordance with the angiographic classification of the 1994 International TAK Conference in Tokyo (7). The diagnoses of IBD were based on gastroenterological investigations and conclusions recorded in hospital charts.
Results: Among 116 patients with TAK, living in Southern part of Norway (2.5 mill inhabitants) 5 patients (4.3%) had IBD, 3 with UC and 2 with CD. All patients had onset of IBD prior to TAK and intestinal involvement of colon (Table 1). Moreover, patients with TAK and IBD were younger at TAK onset than in those without IBD (Table 2).

Table 1. Patients with the combination of Takayasu arteritis (TAK) and Inflammatory bowel disease (IBD); ulcerative colitis (UC) or Crohn's disease (CD)

Patients	IBD	Gender F/M	IBD extension	Age at disease onset (years) IBD	TAK	Vascular complication	Distribution of vasculitis (4)
1	UC	F	Total	12	27	Stenosis and Occlusions	I
2	CD	F	Colon	32	34	Stenosis	V
3	UC	M	Total	11	16	Stenosis and Aneurisms	IIB
4	CD	K	Colon	30	40	Stenosis	I
5	CD	K	Ileocecal+ colon	20	22	Stenosis	IIb

Table 2. Comparison of Takayasu arteritis (TAK) with- and without IBD

	TAB/IBD	TAK/non-IBD	p
Number of patients (n%)	5	111	
Females (n%)	4	90 (94)	
Age at TAK onset (years)	27	39 (17)	0.043
Disease duration (years)	1.1	1.4	0.46
Arterial distribution (n%)			
	I	2	17 (15)
	IIa	0	30 (27)
	IIb	2	16 (14)
	III	0	0
	IV	0	2 (2)
	V	1	29 (26)
Arterial complications* (n%)			
	Stenosis	5	85 (85)
	Occlusions	1	30/110 (27)
	Aneurisms	1/5 (20)	19/132 (14)
	Carotidynia	2	29 (26)
	Myocardial infarction	1	5/106 (5)
	Deceased (n%)	0	23 (16)

*Based on CTA, MRA or PET/CT.

Conclusion: The presence of IBD in Norwegian patients with TAK is higher than expected by chance. This is comparable to previously reported data from Asian patients (3). Strikingly, onset of IBD preceded TAK in all our cases. The patients with IBD were younger at onset of TAK, but vascular distribution and complication rate did not seem to differ between TAK with and without IBD.
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SAT0270 TOCILIZUMAB IN REFRACTORY TAKAYASU ARTERITIS. OPEN-LABEL NATIONAL MULTICENTER STUDY OF 53 PATIENTS OF CLINICAL PRACTICE

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Background: Tocilizumab (TCZ) was recently approved for Takayasu Arteritis (TAK) in Japan based on the results of the TAKT trial **(1).** However, data in clinical practice in Europe and America are scarce **(2).**
Objectives: To assess efficacy and safety of TCZ in TAK of clinical practice in Spain.
Methods: Observational, open-label multicentre study of 53 TAK patients treated with TCZ due to refractoriness or adverse events of previous therapy. Outcomes variables were improvement of clinical features, acute phase reactants and glucocorticoid-sparing effect.
Results: 53 patients (46w/7m); mean age, 40.6±14.6 years at TCZ onset. TCZ was started after a median of 12 [3.0-48.0] months from TAK diagnosis. In addition to systemic corticosteroids and before TCZ they received conventional immunosuppressant drugs (n=42) and biologic therapy (n=14). TCZ was prescribed as standard I.V. (n=42;

79.2%) or subcutaneous (n=11; 20.8%). The initial dose was 8 mg/kg/IV/4 weeks or 162 mg/SC/week, respectively. TCZ was used in monotherapy or combined with immunosuppressants (n=32; 60.4%): methotrexate (n=27), azathioprine (n=2), cyclosporine (n=3). Main clinical features at TCZ onset were: malaise (n=30),limb claudication (n=22), headache (n=18), fever (n=14), abdominal pain (n=10), and chest pain (n=9). Most of the patients experienced a rapid and maintained clinical, analytical improvement **(TABLE).** After a median follow-up of 18.0 [7.0-45.0] months, TCZ was discontinued in 20 patients due to: sustained remission (n=6), relapse (n=6), adverse event (n=5), gestation (n=3). Most relevant adverse side effects were serious infections: pneumonia (n=2), herpes zoster (n=1), abdominal sepsis (n=1).

Table.

	Basal (N=53)	Month 1 (N=53)	Month 3 (N=46)	Month 6 (N=44)	Month 12 (N=34)
Clinical improvement, n/N(%)					
Complete		17/53 (32.1)	19/46 (41.3)	23/44 (52.3)	26/34 (76.5)
Partial		30/53 (54.6)	26/46 (56.5)	18/44 (40.9)	8/34 (23.5)
No improvement		6/53 (11.3)	1/46 (2.2)	3/44 (6.8)	0/34 (0.0)
Analytical markers,					
ESR (mm/1st h), *median [IQR]*	35.0 [16.0-52.0]	7.5 [3.0-14.0] *	3.5 [2.0-8.0]*	5.0[2.0-6.0]*	5.0 [2.0-8.5]*
CRP (mg/dL), *median [IQR]*	1.7 [0.6 -3.5]	0.21 [0.05-0.6]*	0.14 [0.05-0.5]*	0.14 [0.04-0.4]*	0.10 [0.03-0.30]*
Hb (g/dL), *mean ± SD*	12.3±1.5	12.8±1.2*	12.9±1.3*	12.9±1.4*	12.9±1.4*
Prednisone dose (mg/day), *median [IQR]*	30.0 [15.0-50.0]	20.0 [10.0-37.5]*	10.0 [5.0-20.0]*	5.0 [5.0-12.5]*	5.0 [0.0-7.5]*

*Wilcoxon test p < 0.001.

Conclusion: TCZ appears to be effective and safe in patients with refractory TAK in clinical practice.

References:

[1] Nakaoka Y et al. Ann Rheum Dis. 2018;77:348-354

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SAT0271

THE "GOLD STANDARD" DIAGNOSTIC TEST FOR GCA IS THE WHOLE GCA FAST TRACK PATHWAY COMBINED

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Background: We have been developing a rheumatologist-led ultrasound driven giant cell arteritis (GCA) fast-track pathway (FTP), which in year 3 had the following structure:

1. **Rapid access to rheumatology assessment (RAS)** to establish clinical probability of GCA (CP-GCA). No referral criteria required
2. **Temporal and axillary artery ultrasound (TAUS)** if GCA not excluded with RAS. TAUS considered positive if bilateral (halo score ≥2/8[1,2] at >1 temporal artery)
3. **Second test in selected patients:** GCA diagnosed in those with mod-high CP-GCA and +ve TAUS and excluded in those with low CP-GCA and -ve TAUS. All others had biopsy (TAB) or large vessel imaging (LVI), presentation depending
4. **Protocolised withdrawal of prednisolone:** Patients only treated for GCA if ≥1 of: high CP-GCA, +ve TAUS, TAB or LVI
5. **Rapid access** if symptoms recurred on steroid withdrawal for RAS + TAUS

Objectives:

- To compare security of GCA diagnosis, sight loss rate and TAB rate in Year 3 to previous years
- To assess sensitivity and specificity of all components of the Yr 3 FTP for diagnosis of GCA

Methods: As in Yr 2, TAUS was performed by VQ with an Esaote Mylab7, 6-15MHz probe for axillaries, 22MHz for temporal arteries (TAs). In Yr 1 VQ used a GES8 with ML6-15 for axillaries, 18MHz probe for TAs. Year 3 audit data were compared to previous audits

Results:

Year 3 Luton GCA FTP compared to previous years

	Traditional Model	Year 1	Year 2	Year 3
Audit period	2015 12 months	1/1/16-31/3/17 15 months	1/4/17-31/3/18 12 months	1/4/18-31/3/19 12 months
Pathway structure	No rapid access to RAS TAB, no TAUS service	Patients seen ad-hoc for RAS + TAUS TAB requested in all appropriate cases to compare TAUS to TAB	Rapid access for RAS + TAUS, 2 slots/wk 2nd test in selected patients	Rapid access for RAS + TAUS, 3 slots /wk 2nd test in selected patients Protocolised withdrawal prednisolone
No. referrals with suspected GCA/yr	NK	50.4	70	90
Cases GCA /yr	9	24	18	25
Cases GCA excluded /yr	NK	26.4	52	65
% GCA patients with imaging/TAB +ve GCA	44.4	63.3	83.3	92
% GCA patients with clinical GCA (high CP-GCA, no +ve test)	55.6	36.7	16.6	8
% referred where GCA excluded on clinical grounds alone	NK	11.1	5.7	5.6
% referred where TAUS performed and TAB avoided	NA	NA	38.6	50.0
% referred who had TAB	NK (total 27)	84.1	42.8	31.1
% referred where TAUS, then LVI performed instead of TAB	NA	4.8	12.8	13.3
Mean days on prednisolone for GCA before TAUS (median, range)	NA	10.6 (7, 0-81)	4.4 (2, 0-54)	5.9 (3, 0-57)
% GCA patients with permanent sight loss due to GCA	33	23.3	11.2	8

NA: Not applicable NK: not known

Performance of components of Year 3 Luton GCA FTP compared to final diagnosis at >6 months*

Diagnostic Tool	No. pts**	Sensitivity %	Specificity %	PPV %	NPV %
Rheumatologist CP GCA (High)***	90	60	98.3	93.8	86.1
Rheumatologist CP GCA (Moderate & High)***	90	88	63.5	48.9	93
Any halo on TAUS	85	81.5	91.4	81.5	91.4
Bilateral positive TAUS	85	59.3	98.3	94.1	83.8
TAB	28	69.2	100	100	78.9
LVI (CT or CTPET)	12	80	100	100	87.5
Combined diagnostic tests in the whole FTP (bilateral positive TAUS +/or positive TAB +/or positive LVI)	88	92	98.3	95.8	96.7

*using patient record to Oct 2019 **2 patients passed through twice ***before imaging/TAB

Conclusion: Unlike Yr 2, the higher secure diagnosis rate in Yr 3 could not be attributed to shorter time on prednisolone or better equipment. The increase was likely due to several factors including further improved sonographer skill and increased confidence to withdraw steroids in insecure cases with low/moderate CP-GCA. This approach did not increase sight loss. Further reduction in TAB rate financially justified a 3rd FTP slot/wk created in Yr 3.

Each component of the FTP was an inadequate diagnostic tool. Combinations of diagnostic tools are needed to obtain the highest sensitivity and specificity for GCA diagnosis. FTPs limit tests to the minimum required for secure diagnosis. The "gold standard" diagnostic test for GCA is the whole FTP combined.

References:

[1] Schäfer et al *Rheum (Ox)* 2017:56(9);1479-83

[2] van der Geest et al *ARD* doi: 10.1136/annrheumdis-2019-216343

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SAT0272 THE VALUE OF CLINICAL AND LABORATORY FEATURES TO PREDICT EXTENT OF LARGE VESSEL VASCULITIS ON PET CT

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Background: Giant cell arteritis (GCA) is an idiopathic vasculitis affecting large and medium-sized vessels. The pattern of arterial involvement is heterogeneous with two overlapping categories recognised: classical cranial GCA and extra-cranial GCA (or large vessel vasculitis – LVV) that predominantly affects the aorta and its proximal branches. Although LVV is present in around 80% of patients with cranial GCA, and around one third will develop large vessel complications, there are no guidelines for which patients should be screened for it (1). We sought to investigate whether clinical and laboratory features were a useful guide to the severity of LVV on FDG PET-CT.

Objectives: To retrospectively analyse whether baseline patient characteristics are able to predict the extent of large vessel vasculitis on PET-CT.

Methods: Clinical data for 65 patients referred for a PET-CT scan by Rheumatology at the Freeman Hospital, Newcastle between January 2015 and May 2018 were retrospectively analysed. The most recent full blood count and inflammatory markers prior to the scan were used. Scans were reviewed by a consultant radiologist and trainee. The arterial network was split in to ten potentially involved territories (aortic arch, thoracic aorta, abdominal aorta, iliac vessels, axillary, brachiocephalic, subclavian, carotid, vertebral and femoral arteries. Both the value of highest standardised uptake value (SUV max) and the territory affected was recorded for each positive scan.

Results: In the period analysed 65 PET-CT scans were requested, mostly (77%) as baseline investigations for symptoms with LVV in the differential diagnosis. Of these 22 (34%) were positive for LVV and in that group the majority of patients (64%) were female. In those with a negative scan, 47.5% were on concurrent steroid treatment compared to 9% with a positive scan. Regression analysis suggested that the number of systemic features (weight loss, pyrexia, polymyalgia) was weakly correlated with the number of affected territories (p=0.04). In contrast there was no correlation between laboratory tests ((CRP (p=0.91), ESR (p=0.46), Hb (p=0.44), platelets (p=0.74)) and the number of territories affected. The aortic arch (47%) was most commonly the territory with the highest degree of FDG uptake (SUV max) followed by the abdominal aorta (21%) and thoracic (10%) and femoral arteries (10%). There was no correlation between SUV max and laboratory tests ((CRP (p=0.55), ESR (p=0.89), Hb (p=0.82), platelets (p=0.17)) or the number of systemic features (p=0.7). There was no significant difference in the number of territories affected between those on steroid treatment at the time of the scan and steroid-naïve patients, albeit the number of positive scans in those on steroid treatment was low (n=5).

Conclusion: These results suggest that clinical and laboratory features are a poor guide to predicting the maximal severity and extent of disease on FDG PET-CT.

References: [1]Koster MJ, Matteson EL, Warrington KJ. Large-vessel giant cell arteritis: diagnosis, monitoring and management. Rheumatology (Oxford). 2018;57(suppl_2):ii32-ii42.

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SAT0273 PROGNOSTIC FACTORS FOR POOR OUTCOME IN BEHÇET'S SYNDROME WITH NEUROLOGICAL INVOLVEMENT: RESULTS FROM A CLINICAL LONG-TERM FOLLOW-UP OF A SINGLE CENTRE

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Background: Behçet's Syndrome (BS) is a vasculitis of unknown cause. Neurological disease is a type of its serious involvement and causes morbidity and mortality.

Objectives: In this study, we aimed to describe the clinical characteristics of neuro-Behçet Syndrome (NBS) and to define prognostic factors that were associated with poor outcome.

Methods: Among 2033 patients with BS, we performed a retrospective analysis of 94 patients (52.1% male; mean age 36.1 (11.9) years), who fulfilled the ISG-1990 for BS. We divided patients into two subgroups, either parenchymal (p-NBS) or non-parenchymal (np-NBS). Clinical, laboratory, and imaging characteristics of the patients were defined. We described the poor outcome as a modified Rankin score (mRS) >= 3 at last follow-up and/or death, and assessed the predictor factors associated such kind of outcome.

Results: In total, 52 (55.3%) patients presented with p-NBS, of whom 15 (28.8%) had progressive course, and 42 (44.7%) presented with np-NBS (Table.1). Ocular involvement was more common in p-NBS than np-NBS (59.6% vs. 39.1% respectively, p=0.04), whereas vascular involvement excluding sinus vein thrombosis was more frequent in patients with np-NBS (15.4% vs. 50.0%, respectively, p=0.001). Headache and papilledema were frequently observed in np-NBS (p<0.001), whereas paresis, sensory symptoms, pyramidal and cerebellar signs were significantly common in p-NB (<0.001). Twenty-five patients (26.6%) experienced at least one relapse. After a median of 54 (IQR 79.4) months, 11 patients (11.7%) had disabling

Table 1. Clinical characteristics of the patients in each subgroup

	All n= 94	Parenchymal NBS n= 52	Non parenchymal NBS n= 42	p value
Gender (male, %)	49 (52.1)	29 (55.8)	20 (47.6)	0.43
Age at Behçet diagnosis	29.2 ± 9.52	29.93 ± 9.49	28.26 ± 9.60	0.40
Age at NBS diagnosis	36.1 ± 11.9	37.02 ± 11.43	35.00 ± 12.61	0.42
Initial mRS ≥3	33 (35.1)	28 (53.8)	5 (11.9)	**<0.001**
Oral aphtae	94 (100.0)	52 (100.0)	42 (100.0)	-
Genital ulcer	71 (75.5)	40 (76.9)	31 (73.8)	0.73
Skin involvement (PPE+EN)	72 (76.6)	35 (67.3)	37 (88.1)	**0.018**
Musculoskeletal involvement	46 (48.9)	28 (53.8)	18 (42.8)	0.29
Ocular involvement	47 (50)	31 (59.6)	16 (38.1)	**0.038**
Vascular involvement (except SVT)	29 (30.9)	8 (15.4)	21 (50)	**<0.001**
Gastrointestinal involvement	5 (5.3)	2 (3.8)	3 (7.1)	0.65
HLA B51 positivity (n=32)	14 (43.8)	6/12 (50)	8/20 (40)	0.58
Pathergy positivity (n=51)	26 (51.0)	13 (54.2)	13 (48.1)	0.67
Clinical characteristics				
Headache	73 (77.7)	32(61.5)	41 (97.6)	**<0.001**
Fever	6 (6.4)	5 (9.6)	1 (2.4)	0.22
Paresis	26 (27.7)	24 (46.2)	2 (4.8)	**<0.001**
Pyramidal signs	34 (36.2)	31(59.6)	3 (7.1)	**<0.001**
Sensory symptoms	34 (36.2	30 (57.7)	4 (9.5)	**<0.001**
Cerebellar signs	19 (20.2)	18 (34.6)	1 (2.4)	**<0.001**
Cranial nerve involvement	13 (13.8)	9 (7.3)	4 (9.5)	0.28
Papilledema	24 (25.5)	3 (5.8)	21 (50)	**<0.001**
Relapse	25 (26.6)	16 (30.8)	9 (21.4)	0.31
Total follow-up time (mo)	54.01(IQR: 79.4)	64.8 (IQR: 90.2)	44.0 (IQR: 68.1)	0.12
Last mRS≥3	16 (16.8)	15 (28.8)	1 (2.4)	**0.001**
Death	5 (5.3)	5 (9.6)	0 (0)	*0.06*

mRS: Modified Rankin Score, PPE: Papulopustular eruption, EN: Erythema nodosum, SVT: Sinus Vein Thrombosis

Table 2. Characteristics of patients with and without poor outcome

	With Poor Outcome n= 16	Without Poor Outcome n= 78	p value
Gender (male, %)	9 (56.3)	40 (51.3)	0.72
Type of neurological involvement, p-NBS	15 (93.8)	37 (47.4)	**0.001**
Age at Behçet diagnosis (year)	30.7 ± 11.0	28.9 ± 9.2	0.50
Age at neurological involvement (year)	38.9 ±12.2	35.5 ±11.9	0.307
Initial mRS ≥ 3	14 (87.5)	19 (24.4)	**<0.001**
Genital ulcer	10 (62.5)	61 (78.2)	0.21
Skin involvement (PPE+EN)	12 (75)	60 (76.9)	1.00
Musculoskeletal involvement	10 (62.5)	36 (46.2)	0.23
Ocular involvement	10 (62.5)	37 (47.4)	0.27
Vascular involvement (except SVT)	1 (6.3)	28 (35.9)	**0.019**
Gastrointestinal involvement	1 (6.3)	4 (5.1)	1.00
HLA B51 positivity (n=32)	1 (50)	13 (43.3)	1.00
Clinical characteristics			
Headache	6 (37.5)	67 (85.9)	**<0.001**
Fever	0 (0)	6 (7.7)	0.585
Paresis	12 (75)	14 (17.9)	**<0.001**
Pyramidal signs	14 (87.5)	20 (25.6)	**<0.001**
Sensory symptoms	11 (68.8)	23 (29.5)	**0.003**
Cerebellar symptoms	7 (43.8)	12 (15.4)	**0.017**
Cranial nerve involvement	3 (18.8)	10 (12.8)	0.69
Convulsion	1 (6.3)	2 (2.6)	0.43
Papiledema	2 (12.5)	22 (28.2)	0.23
Nausea-vomiting	3 (18.8)	20 (25.6)	0.753
Treatment			
Colchicine	16 (100)	73 (93.6)	0.584
Anticoagulation	5 (31.3)	26 (33.3)	0.87
Azathioprine	15 (93.8)	70 (89.7)	1.00
Cyclophosphomide	9 (56.3)	13 (16.7)	**0.002**
Pulse steroid	13 (81.3)	27 (34.6)	**0.001**
Oral steroid	16 (100)	59 (75.6)	**0.036**
Interferone	1 (6.3)	8 (10.3)	1.00
Cyclosporine	2 (12.5)	12 (15.4)	1.00
Methotrexate	1 (6.3)	1 (1.3)	0.313
Acetylsalicylic acid	5 (31.3)	34 (43.6)	0.36
Diazomide	1 (6.3)	13 (16.7)	0.451
Total follow-up time (month)	66.84 (IQR: 67.3)	49.4 (IQR: 80.7)	0.36

mRS: Modified Rankin Score, PPE: Papulopustular eruption, EN: Erythema nodosum, SVT: Sinus Vein Thrombosis

sequela and a total of 5 (5.3%) deaths occurred. Characteristics of patients with and without poor outcome are presented in table 2. In multivariable logistic regression analysis, factors associated with poor outcome were initial mRS (OR 24.2 (95% CI 3.16 – 108.67)) and age >= 40 at NBS diagnosis (OR 4.59 (95% CI 1.02 – 20.69)), meanwhile, headache at presentation was associated with a lower risk for poor outcome. (OR 0.22 (95% CI 0.05 – 0.91)).

Conclusion: Neurologic involvement is a detrimental manifestation of BS and causes disability, even death. Patients who have an initial disabling presentation in advanced age are more likely to have poor prognosis. Treatment intensification in this subpopulation might be considered.

References: None

Disclosure of Interests: None declared

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SAT0274 DESCRIPTIVE ANALYSIS OF FLARES DURING THE LONG-TERM FOLLOW-UP OF PATIENTS WITH BEHÇET'S DISEASE INCLUDED IN REGEB COHORT

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Background:

Objectives: To describe the clinical manifestations and treatment of flares during follow-up in patients with Behçet's disease (BD) included in the REGEB cohort over the last decade.

Methods: *The Spanish Registry of BD or REGEB (REGistro* de la Enfermedad de Behçet as Spanish nomenclature) Project Group was created by the Spanish Internal Medicine Society in 2009 with the aim of compiling a large cohort of Spanish patients with this rare disorder. By July 2012, REGEB has collected 635 BD patients with a multicentre, longitudinal and consecutive design. Diagnosis of BD was performed on the basis of the International Study Group criteria for BD. Since inclusion in the registry, patients have been followed prospectively and new flares have been recorded, defined as those clinical manifestations which have required initiation or modification of immunosuppressive treatment, or prednisone dose at or higher than 10mg/d of prednisone during more than 1 month.

Results: A prospective follow-up of 326 patients included in the registry has been analysed. There are 182 women (56%) and their average age (SD) at the time of diagnosis was 33 (13) years. The majority of them were Caucasian (91%). The median follow-up time from BD diagnosis was 180 months, and the prospective follow-up period from the inclusion in the registry was 80 months. The cumulative clinical manifestations until the initial registration were oral ulcers in 100% of patients, genital ulcers in 221 (68%), arthritis in 147 (45%), erythema nodosum in 96 (29%), fever in 82 (25%), thrombosis in 74 (23%), anterior uveitis in 76 (23%), retinal vasculitis in 46 (14%), posterior uveitis in 35 (11%), aseptic meningitis in 32 (10%), and other neurological manifestations in 15 (5%) patients. One hundred and fifty-six (48%) patients received immunosuppressants and 47 (14%) biological therapy.

During follow up (period from the inclusion in the REGEB to the last visit) 68 (23%) patients presented at least a severe outbreak. The median time from the BD diagnosis to the first flare were 170 months. The main clinical manifestations were oral-genital ulcers in 43 (63%) patients, uveitis in 31 (45%), arthritis in 13 (19%), neurological in 16 (24%), vascular in 10 (15%), and gastrointestinal in 3 (4%) patients. Immunosuppressants were used in 37 (54%) patients and biological therapy in 14 (21%). Biological therapy was mostly used due to refractory disease, the majority of cases because ocular manifestations. There were no differences in terms of age, sex, race and previous clinical manifestations between patients who suffered from flares and those who did not. Flares were more frequent in patients who have received previous immunosuppressive or biological treatment (35% vs 13% and 48% vs 19%, respectively) (p<0.001 in both cases), probably reflecting a more severe disease.

Conclusion: The long-term follow-up of BD patients from REGEB cohort showed that 10 years after diagnosis, a fifth of them may continue to present severe flares requiring systemic treatment. The use of biological therapy increased over time and their main indication was refractory disease.

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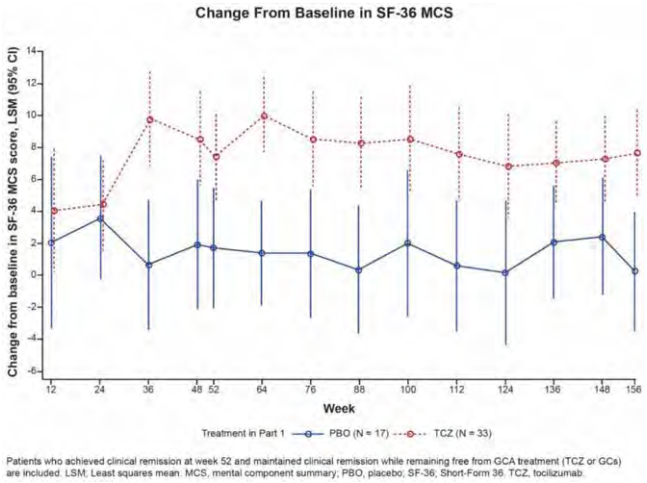
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SAT0275 MAINTAINED BENEFIT IN HEALTH-RELATED QUALITY OF LIFE OF PATIENTS WITH GIANT CELL ARTERITIS TREATED WITH TOCILIZUMAB PLUS PREDNISONE TAPERING: RESULTS FROM THE OPEN-LABEL, LONG-TERM EXTENSION OF A PHASE 3 RANDOMIZED CONTROLLED TRIAL

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Background: In part 1 of the 52-week, double-blind GiACTA trial, patients with giant cell arteritis (GCA) who received weekly tocilizumab (TCZ) plus prednisone tapering reported improvement in the 36-item Short-Form Health Survey (SF-36) Mental Component Summary (MCS) and Physical Component Summary scores and FACIT-Fatigue scores that were statistically significant and clinically meaningful compared with patients who received prednisone alone.[1]

Objectives: To analyze whether benefit in SF-36 MCS was maintained in patients originally assigned to TCZ compared with those originally assigned to placebo (PBO) plus a 26- or 52-week prednisone taper among patients who achieved clinical remission at week 52 and maintained treatment-free clinical remission in the 2-year, long-term extension of GiACTA.
Methods: At the end of part 1, patients entered open-label part 2, in which GCA therapy (including initiation/termination of open-label TCZ and/or GCs) was given at the investigator's discretion according to disease status. Change from baseline in SF-36 MCS score was compared for combined original TCZ (n = 33) and PBO (n = 17) patients who achieved clinical remission at week 52 and maintained treatment-free (no TCZ or GCs) clinical remission in part 2 using a repeated-measures model. The minimal clinically important difference (MCID) for SF-36 MCS is >2.5.[2]
Results: During treatment, SF-36 MCS scores in all 50 patients who maintained treatment-free clinical remission in part 2 had diverged between the TCZ and PBO groups as early as 36 weeks after baseline, with greater improvements evident in the TCZ group (Figure). The difference in least square means (LSM) change between TCZ and PBO was statistically significant at week 52 ($p = 0.016$) and maintained at weeks 100 ($p = 0.023$) and 156 ($p = 0.002$). The LSM difference (95% CI) between TCZ and PBO at weeks 52, 100, and 156 was 5.6 (1.1-10.2), 6.5 (0.9-12.1), and 7.4 (2.9-11.9), respectively, exceeding the MCID.
Conclusion: Among patients who maintained treatment-free clinical remission during part 2 of GiACTA, those originally assigned to receive TCZ plus a prednisone taper during part 1 maintained statistically significant and clinically meaningful improvements in SF-36 MCS up to week 156 compared with those originally assigned to receive PBO plus a prednisone taper in part 1. This was true even though neither of the patient groups received TCZ or GC treatment after they achieved clinical remission at week 52.
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SAT0276 CARDIAC MAGNETIC RESONANCE IMAGING IN PATIENTS WITH BEHCET'S DISEASE: A PILOT STUDY

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Background: Behçet's disease is a multisystemic vasculitis characterized by mucocutaneous, ocular, arthritic, and vascular manifestations.[1] However, the incidence and nature of cardiac involvement in Behcet's disease have not been clearly documented yet.
Objectives: This study aimed to assess the cardiac involvement in patients with Behçet's disease using cardiac magnetic resonance imaging (MRI).
Methods: This cross -sectional descriptive study was carried out on thirty consecutive patients with Behçet's disease (21 males,9 females) with mean age 32.3±8.9 years and with no evidence of cardiac disease. They underwent cardiac MRI to determine morphological and functional changes of the heart and to detect areas of hyperenhancement after IV administration of gadolinium.
Results: At least one abnormality on cardiac MRI was observed in 20/30 patients (66.67%). Myocardial oedema was observed in 3 patients (10.0%) and late gadolinium enhancement in only 1 patient (3.3%). Pericardial effusion was found in 3 patients (10.0 %), global hypokinesia in 6 patients (20.0%) and intra-cardiac thrombosis in only 1 patient (3.3%). Pulmonary artery was dilated in 4 patients (13.3%). Left ventricular and right ventricular end diastolic volume were altered in 4 patients (13.3 %) and 7 patients (23.3%) respectively. Also, left ventricular and right ventricular end systolic volume were abnormal in7 patients (23.3%) and 5 patients (16.7%) respectively. Moreover, there was aortic valve regurge in 2 patients (6.7%), tricuspid valve regurge in 9 patients (30%), and mitral valve regurge in 9 patients (30%).Dilated left main coronary artery in 2 patients (6.7%) and arythmogenic right ventricular dysplasia in only one patient 1 patient (3.3%).
Conclusion: Behçet's disease may cause cardiac abnormalities without clinical manifestations and cardiac MRI may represent a tool for early detection of these subtle abnormalities.
References:
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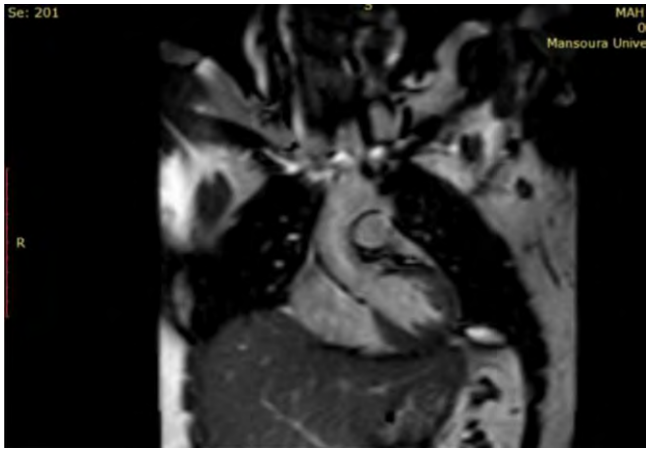


Figure 1. Cardiac MRI in 32 year-old female patient with Behçet's disease for 3 years.

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SAT0277 HEAD AND NECK INVOLVEMENT OF IGA VASCULITIS: A CASE-CONTROL STUDY

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Background: IgA vasculitis (IgAV) is an immune-complex mediated, small-vessel vasculitis which predominantly involves the skin on the lower extremities. Head and neck involvement is rarely reported.
Objectives: To describe the presentation and outcome of a series of patients with head and/or neck involvement in comparison to patients with cutaneous findings isolated to the lower extremities.

Table 1. Baseline characteristics of patients with head and neck involvement of IgA-vasculitis compared to those with lower extremity only

Characteristic, n (%)	H/N-IgAV (N=13)	LE-IgAV (N=26)	*p*-value
Age at diagnosis, years*	38 (24)	38 (24)	1.0
Male	7 (54%)	16 (62%)	0.65
Caucasian	13 (100%)	24 (96%)	0.47
Length of follow-up, years*	2.6 (3.5)	1.3 (2.0)	0.28
Body mass index, kg/m^2*	32 (17)	28 (10)	0.72
Hypertension	2 (15%)	8 (31%)	0.30
Infection within 4 weeks	7 (54%)	11 (42%)	0.50
Antibiotic exposure within 4 weeks	4 (31%)	6 (24%)	0.65
Abdominal ischemic symptoms	2 (15%)	3 (12%)	0.74
Palpable purpura	13 (100%)	26 (100%)	---
Skin ulceration	3 (23%)	0 (0%)	0.01
Any renal involvement	5 (38%)	19 (73%)	0.04
Microscopic hematuria	4 (31%)	17 (65%)	0.04
Proteinuria	4 (31%)	15 (58%)	0.11
C-reactive protein, mg/L*	28 (25)	22 (22)	0.61
Erythrocyte sedimentation rate, mm/hr*	20 (21)	27 (25)	0.80
eGFR (ml/min/1.73m^2)*	87 (41)	95 (42)	0.88

*mean (±standard deviation); H/N, head and/or neck; LE, lower extremity only



Figure 1. A) H/N involvement in IgAV (perioral, nasal, cheeks and neck). B) Severe PP in lower extremities with bullous, ulcerations and skin necrosis.

Methods: Patients with biopsy-proven IgAV from January 1, 1997 through December 31, 2016 were retrospectively identified through direct medical chart review. IgAV was diagnosed in accordance with the American College of Rheumatology (ACR) and the European League Against Rheumatism/ Paediatric Rheumatology European Society/Paediatric Rheumatology International Trials Organisation (EULAR/PRINTO/PRES) criteria. Among this cohort, patients with documented clinical, photographic, or histologic descriptions of vasculitic skin lesions affecting the head or neck were compiled. Each patient with head/neck (H/N) involvement of IgAV (case) was matched to two age- and sex-matched control patients with IgAV for which the cutaneous features were isolated to the waistline or distal. Baseline characteristics, laboratory parameters, treatments and outcome were collected by a physician abstractor.

Results: Thirteen patients with H/N-IgAV involvement were identified. Baseline characteristics of the cases and controls are demonstrated in Table 1. H/N involvement included facial (cheeks, forehead) [n=6], perioral/oral/lip [n=6], auricular [n=2], nasal [n=2], and neck [n=1]. All patients in both groups had evidence of purpuric skin lesions. Patients with H/N-IgAV involvement more frequently had evidence of skin ulcerations (23% vs. 0%; p=0.01) [Figure 1]. Overall baseline renal involvement and microscopic hematuria were less commonly observed in patients with H/N-IgAV. Among H/N-IgAV cases, at last follow-up all had resolution of H/N lesions but 3 of 13 had persistent skin lesions on the lower extremities despite ongoing treatment. Long-term outcome between cases and controls did not identify any significant differences in the development of end-stage renal disease, time to resolution of hematuria or proteinuria, time to complete IgAV response, or time to first IgAV relapse.

Conclusion: This study reports the largest series of patients with head/neck involvement of IgA, a rarely reported entity. In this cohort, patients with H/N-IgAV had less frequent renal involvement compared to IgAV patients with lower extremity only skin lesions. Clinicians should be aware of atypical locations of IgAV involvement. Additional research is needed to further understand this clinical subset.

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SAT0278 LOW-DOSE IL-2 RESTORES TREG-MEDIATED IMMUNE TOLERANCE IN PATIENTS WITH ANCA-ASSOCIATED VASCULITIS

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Background: Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a group of autoimmune disease that can cause systemic organ damage, including granulomatosis with polyangiitis(GPA), microscopic polyangiitis (MPA), and eosinophilic granulomatosis with polyangiitis(EGPA)[1]. Several observations have showed that the breakdown of immune tolerance was involved in the pathogenesis of AAV [2], furthermore, a single, open and clinical trial demonstrates that IL-2 can be used to treat patients with GPA [3]. But there is still a lack of understanding of the relationship between Th17 / Treg and AAV and evidence for the therapeutic effect of IL-2 on AAV, which needs further exploration.

Objectives: We first measured the absolute number of CD4+T subsets in peripheral blood of patients to explore the pathogenesis of AAV, and then investigated the effects of short-term and low-dose recombinant human IL-2 (rhIL-2) on CD4+T subsets of patients to analyze the regulatory effect of IL-2 on AAV.

Methods: 49 patients with AAV, hospitalized at the Second Hospital of Shanxi Medical University from the May 2016 to the November 2019 were enrolled, including 36 patients who were only received conventional glucocorticoids and DMARDs, and other 13 patients who were not only received these treatments but were also injected subcutaneously rhIL-2(50WIU/day for a 5-day course). 31 age and gender-matched healthy adults were selected as controls. The absolute number of Th17 and Treg cells in peripheral blood of health controls and the patients before and after treatment was detected by flow cytometry.

Results: There was significant decreased level of Treg cells in the patients with AAV compared with healthy controls (P<0.001) leading to a higher Th17/Treg ratio in the patients with AAV, but there was no statistically significant in the absolute number of Th17 cells between the patients and healthy controls. After the treatment of short-term and low-dose IL-2, there was a significant increase in the absolute number of Treg cells (P<0.01) leading to a decrease in the ratio of Th17 and Treg (p<0.05).The absolute number of Th17 had a trend towards higher values but was not statistical significance.

Conclusion: The difference of Treg cells between the patients and healthy controls suggested that the decreased number of Treg cells failed to control autoimmune inflammatory response contributing to the pathogenesis of AAV. After the treatment of short-term and low-dose rhIL-2, there was a more significant increase in the absolute number of Treg cells showing that IL-2 could selectively stimulate the growth of Treg cells and restore the Treg-mediated immune tolerance in patients with AAV to achieve disease remission.

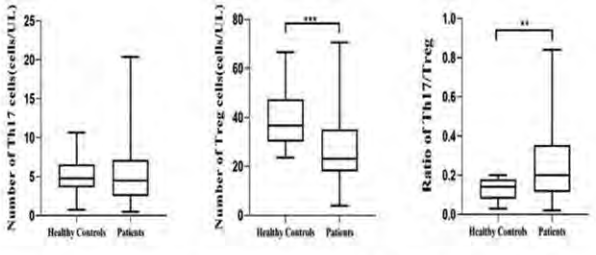


Figure 1: Characteristics of the absolute number of Th17 cells and Treg cells in peripheral blood of health controls (n=31) and the patients with AAV (n=49). The absolute number of Th17 cells and Treg cells was detected by flow cytometry. There was significant decreased level of Treg cells in the patients with AAV compared with healthy controls leading to a higher Th17/Treg ratio in the patients with AAV, but there was no statistically significant in the absolute number of Th17 cells between the patients and healthy controls. Statistical analyses were performed by the Mann-Whitney U test. *P<0.05,**P<0.01, ***P<0.001.

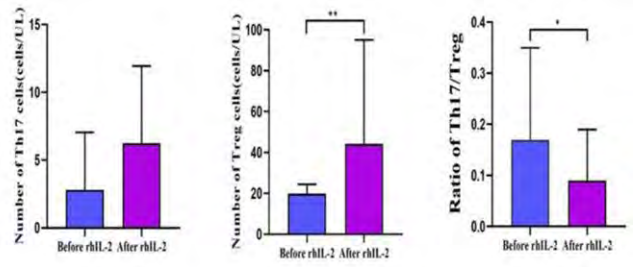


Figure 2: The absolute number of Th17 and Treg cells in peripheral blood of the patients before and after treatment were detected by flow cytometry. After the treatment of short-term and low-dose rhIL-2(50WIU/day for a 5-day course), there was a more significant increase in the absolute number of Treg cells leading to a decrease in the ratio of Th17 and Treg ($p<0.05$). Data are presented as medians with 95%CI. Statistical analyses were performed by the Wilcoxon signed rank test. *p<0.05,**p<0.01,***p<0.001. CI: Confidence intervals.

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SAT0279

FACTORS PREDICTIVE OF POSITIVE TEMPORAL ARTERY BIOPSY IN TWO AUSTRALIAN COHORTS

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Background: Temporal artery biopsy (TAB) is widely recognised as the diagnostic gold standard for GCA despite having a poor sensitivity due to the presence of 'skip' lesions. There is, however, a lack of consensus guiding TAB practice, particularly in relation to optimal length, need for bilateral specimens, and number of segments examined.

Objectives: To investigate the impact of factors such as total biopsied length, laterality, segment number, and referral centre on histopathological outcomes in an Australian setting.

Methods: Reports for all available biopsy specimens labelled "temporal artery" were extracted from the pathology service records of two rheumatology referral centres with adjacent geographic catchments. Each histopathology report was manually reviewed to establish length of biopsied artery, laterality, and number of segments, along with patient demographics such as age, sex, and referral centre. Key histopathological findings including intimal hyperplasia, disruption of the internal elastic lamina, presence of giant cells, and adventitial inflammation were recorded. Multivariable logistic regression with site-varying intercept was performed.

Results: TAB reports from a total of 577 patients were captured, with results available from the two centres from 1999-2019 and 2010-2019 respectively. The mean age in this group was 73, and 69% were female (Table 1). A bilateral TAB was performed in 29%, and the mean total biopsy length was 2.5cm. Of these patients, 122 had positive biopsies (21%), with intimal hyperplasia reported in 100 (17%), giant cells in 83 (14%), and adventitial findings in 68 (12%). Positive biopsy weakly correlated with increased total length of biopsy in centimetres (OR 1.25 [1.06-1.47]) (Figure 1) and increased age in years (OR 1.02 [1.00-1.05]) but not laterality or sex (Table 2). There was a substantial difference between the two centres, which was incompletely accounted for once corrected for total biopsy length and calendar year of biopsy, suggesting either unmeasured differences in patient demographics or a difference in clinical practice. This change was preserved across analysis of different histopathological subtypes.

Table 1. Patient characteristics by biopsy result.

	Negative (n = 455)	Positive (n = 122)	Total (n = 577)
Age (years)			
Mean (SD)	72 (± 11)	75 (± 8.9)	73 (± 10)
Sex			
Female	310 (68%)	88 (72%)	398 (69%)
Male	145 (32%)	34 (28%)	179 (31%)
Maximum biopsy length (cm)			
Mean (SD)	1.8 (± 0.86)	2.0 (± 1.10)	1.9 (± 0.92)
Total biopsy length (cm)			
Mean (SD)	2.4 (± 1.6)	2.8 (± 2.1)	2.5 (± 1.7)
Mean biopsy length (cm)			
Mean (SD)	1.7 (± 0.78)	1.9 (± 0.97)	1.7 (± 0.83)
Laterality			
Bilateral	130 (29%)	39 (32%)	169 (29%)
Unilateral	325 (71%)	83 (68%)	408 (71%)

Table 2. Associations with positive TAB on multivariable logistic regression.

	Overall positive finding	Intimal hyperplasia	Giant cells	Adventitial inflammation
Total biopsy length (cm)	1.25 (1.06-1.47)	1.18 (0.98-1.40)	1.21 (1.00-1.46)	1.07 (0.87-1.31)
Unilateral (vs. bilateral)	1.56 (0.82-3.07)	1.12 (0.56-2.30)	1.28 (0.61-2.77)	0.82 (0.38-1.82)
Age (years)	1.02 (1.00-1.05)	1.02 (1.00-1.04)	1.03 (1.00-1.05)	1.00 (0.98-1.03)
Male (vs. female)	0.83 (0.52-1.29)	0.63 (0.37-1.05)	0.59 (0.32-0.92)	0.75 (0.41-1.31)
Centre 2 (vs. centre 1)	0.54 (0.34-0.84)	0.41 (0.24-0.68)	0.55 (0.32-0.92)	0.46 (0.25-0.82)

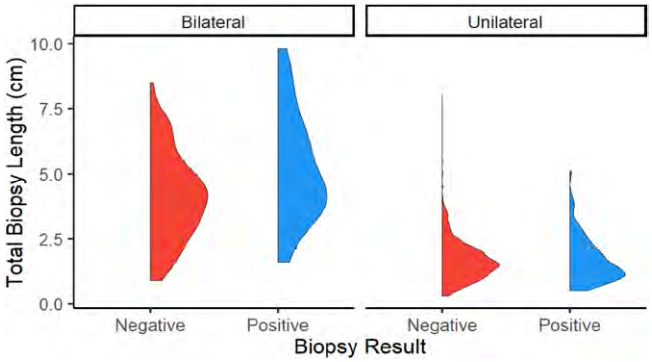


Figure 1. The effect of total biopsy length on result, stratified by laterality.

Conclusion: Total biopsy length was weakly associated with a positive TAB result, but differences in results between referral centres independent of biopsy length suggest other selection factors may be important in determining TAB yield. Examination of differences in results between a greater number of referral centres would assist in determining the extent of this variability.

Disclosure of Interests: None declared

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SATURDAY, 06 JUNE 2020

Systemic sclerosis, myositis and related syndromes - etiology, pathogenesis and animal models

SAT0280

IMPACT OF PLACENTAL FACTORS ON PREGNANCY AND FETAL OUTCOME IN SYSTEMIC SCLEROSIS

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Background: Systemic Sclerosis (SSc) is one of the rheumatic diseases burdened with obstetrical complications. An Italian multicenter study showed that women with SSc have a higher-than-normal risk of intrauterine growth restriction, preterm delivery, very-low birth weight babies and pregnancy should be discouraged in patients with severe organ damage. However, with a multidisciplinary management, patients with SSc can have successful outcomes[1]. Little is known about the pathogenesis of obstetrical complications, as studies on placenta are case reports or description of a few cases[2,3].

Objectives: The aim of this study was to analyze the placental alterations with a focus on the role of inflammation in the pathogenesis of obstetrical complications in SSc, including the study of the atypical chemokine receptor 2 (ACKR2), involved in immune modulation and known to be highly expressed in circulating leucocytes in SSc patients[4-6].

Methods: Eight SSc pregnant patients were compared with 16 patients with other rheumatic diseases (ORD) and 16 healthy controls (HC), matched for gestational age. Clinical data were collected. Placentas biopsies were obtained for histopathological analysis and immunohistochemistry for CD3, CD20, CD11c, CD68 and ACKR2. Frozen placenta samples from 4 SSc, 8 ORD and 8 HC were analyzed by qPCR for ACKR2 gene expression and proteins were extracted for multiplex assay for cytokines, chemokines and growth factors involved in angiogenesis and inflammation. Statistical analysis was performed with parametric or non-parametric tests depending on samples distribution.

Results: The number of placental CD3 ($p<0.05$), CD68 ($p<0.001$) and CD11c+ ($p<0.001$) cells was significantly higher considering the group of patients affected by rheumatic diseases (SSc+ORD) compared to HC. The SSc group alone did not show significance due to the lower sample size. No differences were observed between groups in terms of vascular alterations or fibrosis. The percentage of stained area for ACKR2 and the ACKR2 transcripts levels were comparable between groups. Hepatocyte growth factor (HGF), involved in angiogenesis, was significantly increased in the group of rheumatic diseases patients (SSc+ORD) compared to HC ($p<0.05$), while the chemokine CCL5 was significantly higher in SSc patients compared to patients affected by ORD ($p<0.05$) and to HC ($p<0.01$). CCL5 levels directly correlated with the number of all inflammatory cells considered and higher levels were associated to histological villitis ($p<0.01$).

Conclusion: The higher number of placental inflammatory cells and the alterations in the levels of HGF and especially CCL5 could play a role in the pathogenesis of the obstetrical complications in SSc. ACKR2 does not seem involved in the obstetrical complications of SSc.

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Disclosure of Interests: None declared
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SAT0281 BIOSAMPLES FROM AT RISK SSC PATIENTS SHOW CLASSIC PATHOLOGICAL SIGNS OF SCLERODERMA: OPPORTUNITY FOR DIAGNOSIS OF PRE-CLINICAL SSC

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Background: The VEDOSS study has recently indicated that more than 80% of patients affected by Raynaud's phenomenon (RP) with specific SSc auto-antibodies and capillaroscopy changes satisfied ACR/EULAR 2013 criteria within 5 years. These data suggest that there is a window of opportunity for early detection of SSc in these patients.

Objectives: Here we aimed to determine whether sera, skin biopsies and skin fibroblasts cultured from these patients showed any biomarker sign of SSc.

Methods: Fifty-nine at risk patients identified by having RP and SSc auto-antibodies or capillaroscopy pattern (or both) were enrolled in the Kennedy national inception cohort. Sera were tested for IFN inducible chemokines (CXCL-9,10 and 11 and CCL2, 8 and 19) and biomarker of extracellular matrix turnover (ELF test), all previously shown to be increased in SSc. Further, two 3mm skin biopsies were taken from the forearms from 3 ACA+ve (anti-centromere antibodies), 3 SCL70+ve patients. One biopsy was subjected to histology analysis, including haematoxylin and eosin staining and immunohistological staining for Collagen Type 1, alpha-SMA, Caveolin 1 and CD31 as endothelial marker. The other biopsy was used to explant fibroblasts cultures. mRNA and protein were isolated from primary fibroblasts and processed for RT-qPCR and western blotting analyses.

Results: Sera from at risk patients showed overall higher IFN inducible chemokines and ELF test ($P<0.05$) with bimodal distribution among patients. Skin biopsies from both ACA or SCL70+ve patients showed decreased number of CD31+ cells, increased number of myofibroblasts and increased collagen bundles within the dermis, as usually seen in SSc, compared to healthy controls. In vitro, fibroblasts from both ACA or SCL70+ve patients showed average 10-fold higher collagen mRNA levels and 31-fold increased collagen protein levels
compared to healthy control fibroblasts. Furthermore, fibroblasts from ACA or SCL70+ve patients showed limited TGF-beta induced increase in collagen and SMA expression, similar to SSc fibroblasts.

Conclusion: Although pilot in nature, this study suggests that patients "at risk" already show biomarker signs of SSc both in their sera, at skin biopsy and fibroblast level. Longitudinal studies on patients at this stage of pre-clinical disease may inform on the stratification strategies for imminent progression to clinical manifestations, and offer both insights on pathogenesis of clinical signs and a window of opportunity for delaying the onset clinical intervention trials.

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SAT0282 ASSOCIATION BETWEEN A VARIANT OF THE SRP55 SPLICING FACTOR GENE AND SYSTEMIC SCLEROSIS IN AN ITALIAN POPULATION

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Background: In systemic sclerosis (SSc), alternative splicing of the last exon (exon 8) of vascular endothelial growth factor (VEGF)-A pre-mRNA is a key element in the switch from proangiogenic to antiangiogenic VEGF-A isoforms. The mRNA-binding protein serine/arginine protein 55 (SRp55, also known as SFRS6) is a key regulatory splicing factor that promotes distal splice-site selection in the exon 8 region of VEGF-A pre-mRNA and subsequent upregulation of the exon 8b-containing $VEGF_{165}b$ antiangiogenic isoform. Overexpression of both $VEGF_{165}b$ and SRp55 has been implicated in SSc-related angiogenesis impairment and peripheral vascular damage. Moreover, differential splicing of the VEGF-A gene has been shown to be critical for development of pulmonary fibrosis. Of note, previous studies reported the lack of sequence variations in the VEGF-A alternatively spliced region, while a single nucleotide polymorphism (SNP) in the *SRp55* gene (rs2235611) has been associated with susceptibility to disturbed ocular angiogenesis in proliferative diabetic retinopathy.

Objectives: This case-control pilot study examined the possible implication of *SRp55* rs2235611 SNP in the genetic predisposition to SSc susceptibility and clinical phenotype.

Methods: A total population of 872 white Italian individuals (414 SSc patients, 458 controls) was studied. All patients were classified as limited and diffuse cutaneous SSc (lcSSc and dcSSc, respectively) and were clinically evaluated for the presence of autoantibodies (anticentromere, anti-Scl70 antibodies), pulmonary fibrosis and digital ulcers. The *SRp55* rs2235611 SNP was genotyped by TaqMan Real-Time PCR.

Results: *SRp55* rs2235611 genotype distribution and allele frequency were similar in SSc and healthy controls, though a trend toward significance was observed for genotype distribution ($p=0.07$). The *SRp55* rs2235611 AA genotype significantly influenced the predisposition to SSc (OR 2.55, 95% CI 1.11 to 5.57,

p=0.03), and to both lcSSc (OR 2.80, 95% CI 1.16 to 6.84, p=0.02) and dcSSc (OR 3.42, 95% CI 1.20 to 9.72, p=0.02) subtypes. The *SRp55* rs2235611 A minor allele and AA genotype showed a significant risk association with susceptibility to SSc-related pulmonary fibrosis (A allele: OR 1.39, 95% CI 1.00 to 1.93, p=0.046; AA genotype: OR 3.95, 95% CI 1.48 to 10.54, p=0.006). A trend toward an association between the AA genotype and anti-Scl70 antibody-positive SSc was also found (OR 2.82, 95% CI 0.95 to 8.37, p=0.06). Both rs2235611 A allele and AA genotype were significantly associated with the SSc subset without digital ulcers (A allele: OR 1.33, 95% CI 1.01 to 1.75, p=0.04; AA genotype: OR 3.26, 95% CI 1.32 to 8.03, p=0.01).

Conclusion: The *SRp55* rs2235611 polymorphism is associated with susceptibility to SSc and, in particular, with SSc-related pulmonary fibrosis and peripheral vascular phenotype, consistent with a role of VEGF-A pre-mRNA alternative splicing in the development of pulmonary fibrosis and impairment of angiogenesis. Further replication studies are warranted to confirm our findings in independent SSc cohorts.

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SAT0283 SOLUBLE GUANYLATE CYCLASE REDUCED THE GASTROINTESTINAL FIBROSIS IN BLEOMYCIN-INDUCED MOUSE MODEL OF SYSTEMIC SCLEROSIS

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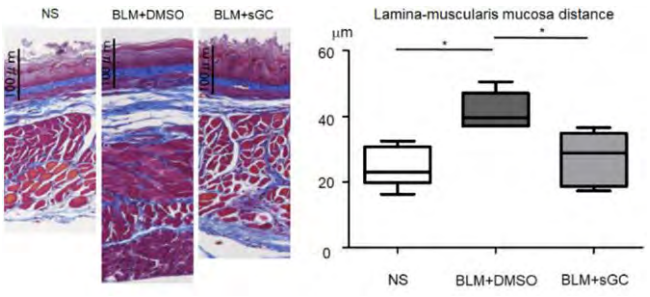
Background: Systemic scleroderma (SSc) is a chronic autoimmune-mediated connective tissue disorder. Although the etiology of the disease remains undermined, SSc is characterized by fibrosis and proliferative vascular lesions of the skin and internal organs. SSc involves the gastrointestinal tract in more than 90% of patients[1]. Soluble guanylate cyclase (sGC) is used to treat pulmonary artery hypertension (PAH), and has been shown to inhibit experimental skin fibrosis[2].

Objectives: The aim of this study is to investigate whether bleomycin (BLM)-treated mice show gastrointestinal fibrosis, and find a therapeutic strategy to the lesion.

Methods: Female C57BL/6J mice were treated with BLM or normal saline by subcutaneous implantation of osmotic minipump. These mice were sacrificed on day 28 or day 42. Gastrointestinal pathologies were examined by Masson Trichrome staining. The expression of fibrosis-related genes in gastrointestinal tract were analyzed by real-time PCR, and the levels of collagen in the tissue was measured by Sircol collagen assay. To evaluate peristaltic movement, the small intestinal transport (ITR%) was calculated as [Dyeing distance×(Duodenum- Appendix)] -1 ×100 (%). We treated BLM-treated mice with soluble guanylate cyclase (sGC) or DMSO orally and analyzed them on day 42.

Results: Histological examination revealed that fibrosis from lamina propria to muscularis mucosa in the esophagus was significantly increased in BLM-treated mice, suggesting that BLM induces esophageal fibrosis in C57BL/6J mice. In addition, the levels of Col3a1 and CTGF were significantly increased in BLM-treated mice. More severe fibrosis was observed in the mice sacrificed on day 42 than the mice sacrificed on day 28. The ITR% was found to be significantly lower in BLM-treated mice, suggesting that gastrointestinal peristaltic movement was reduced in BLM-treated mice. Furthermore, we demonstrated that sGC treatment significantly reduced fibrosis of esophagus and intestine in BLM-treated mice, by histological examination and Sircol collagen assay.

Esophagus (Masson's trichrome stain×100)



* One way ANOVA Newman-Keuls

Conclusion: These findings suggest that BLM induces gastrointestinal fibrosis in C57BL/6J mice, and treatment with sGC improves the BLM-induced gastrointestinal lesion.

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SAT0284 EPIGENETIC DEREGULATION OF AUTOPHAGY PROMOTES FIBROSIS IN SYSTEMIC SCLEROSIS

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Background: Autophagy is catabolic process allowing cells to degrade unnecessary or dysfunctional cellular organelles. Failure of appropriate regulation of autophagy, however, can severely perturb tissue homeostasis. Several stimuli present in fibrosis such as pro-fibrotic cytokines are known to activate autophagy.

Objectives: The objective of this work was to characterize the regulation of autophagy in systemic sclerosis (SSc) and to decipher its role in the pathogenesis of SSc.

Methods: Activation of autophagy in SSc skin and matched tissue samples from healthy individuals was assessed by immunofluorescence staining for ATG7, BECLIN1 and P62. We generated *Atg7*$^{fl/fl}$x *Col1a2*;*Cre*ER mice to selectively disable autophagy in fibroblasts. The role of the autophagy was investigated in the model of bleomycin- and TβRIact-induced dermal and pulmonary fibrosis. Overexpression of Myst1 was achieved by adenovirus encoding for *Myst1*. Collagen release and protein expression were measure by Western blot. Target genes were analyzed by RT-PCR. Co-immunoprecipitation and reporter assay were performed to study physical and functional interactions between MYST1 and SMAD3. To monitor the autophagic flux *in vitro* and *in vivo* we generated adenoviral vectors encoding for tandem fluorescent-tagged LC3 (mRFP-EGFP-LC3).

Results: Transforming growth factor-β (TGFβ) activates autophagy by an epigenetic mechanism to amplify its profibrotic effects. TGFβ induces autophagy in fibrotic diseases by SMAD3-dependent downregulation of the H4K16 histone acetyltransferase MYST1, which regulates the expression of core components of the autophagy machinery such as ATG7 and BECLIN1. Activation of autophagy in fibroblasts promotes collagen release and is both, sufficient and required, to induce tissue fibrosis. Forced expression of MYST1 abrogates the stimulatory effects of TGFβ on autophagy and re-establishes the epigenetic control of autophagy in fibrotic conditions. Interference with the aberrant activation of autophagy inhibits TGFβ-induced fibroblast activation and ameliorates experimental dermal and pulmonary fibrosis. These findings link uncontrolled TGFβ signaling to aberrant autophagy, deregulated epigenetics in fibrotic diseases and may open new avenues for therapeutic intervention in fibrotic diseases.

Conclusion: We demonstrate that the epigenetic control of autophagy is disturbed by a TGFβ-dependent downregulation of the H4K16 histone acetyltransferase MYST1. The increased activation of autophagy induces fibroblast-to-myofibroblast transition and promotes fibrotic tissue remodeling. Re-expression of MYST1 prevents aberrant autophagy, limits the profibrotic effects of TGFβ and ameliorates experimental fibrosis. Restoration of the

epigenetic control of autophagy might thus be a novel approach to ameliorate fibrotic tissue remodeling.

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SAT0285 VISUALISATION OF THE ACTIVE CALCIFICATION PROCESS WITH 18-F SODIUM FLUORIDE PET/CT IN LIMITED CUTANEOUS SYSTEMIC SCLEROSIS WITH CALCINOSIS CUTIS IS FEASIBLE: A PILOT STUDY

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Background: Calcinosis cutis is a major daily challenge to patients with long-standing systemic sclerosis (SSc), negatively affecting their quality of life. Unfortunately, treatment options are very limited due to lack of understanding of the pathogenetic process. Currently, calcinosis cutis is only detected at its irreversible end-stage. Early detection of calcinosis cutis could putatively allow early disease-modifying interventions and monitor treatment effects.

Objectives: The aim of the current study is to assess the feasibility of visualising "active" micro-calcifications with 18-F Sodium Fluoride (NaF) PET scanning, compared to low-dose CT in patients with clinically overt calcinosis cutis.

Methods: This was a cross-sectional, observational, pilot study. All patients met 2013 ACR/EULAR criteria for SSc. Patients underwent a whole body NaF PET/low-dose CT scan, scanned 90 minutes post-injection. (Sub)cutaneous calcifications were described and assessed on NaF PET, which was compared to CT images by two independent investigators.

Results: A total of 10 female patients with limited cutaneous SSc [median age 56 years (IQR 52-66), median disease duration 17 years (8-19), PAH 10%, ILD 20%] were included, and compared to 10 controls [70 years (65-73)]. NaF uptake showed normal distribution throughout the skeletal bones, arterial tree, and visceral organs, which was comparable between patients and controls. Additionally, NaF uptake was visible in the skin of all SSc patients, but in none of the controls. Cutaneous NaF uptake largely correlated with clinical calcifications. Most common sites of cutaneous NaF uptake were fingers (6 patients) and knees (7 patients). Only 5% of the NaF positive lesions were not accompanied by visible calcifications on CT. Furthermore, of all calcified lesions seen on CT, 51% showed uptake on NaF PET. Small lesions (<1 cm), were generally only visible on CT, due to lower resolution of NaF PET.

Conclusion: Imaging of "active" calcinosis cutis in limited cutaneous systemic sclerosis is feasible using NaF PET scanning. Most clinically overt calcifications and half of those seen on CT were positive for NaF uptake. Whether these "active" calcifications behave differently in terms of faster progression, clinical complaints, and infection risk, and whether these are potentially suitable for disease modifying interventions is subject to future study.

Fig. 1 Clinical calcinosis cutis with corresponding images of 18F-NaF PET/CT-scan



Disclosure of Interests: None declared

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SAT0286 BIOLOGICAL CORRELATES OF RADIOGRAPHIC FEATURES OF INTERSTITIAL LUNG DISEASE IN SYSTEMIC SCLEROSIS: AN IN DEPTH ANALYSIS OF BRONCHOALVEOLAR PROTEINS OF SCLERODERMA LUNG STUDY I PARTICIPANTS

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Background: Systemic sclerosis-related interstitial lung disease (SSc-ILD) involves a combination of inflammation, fibrosis and vascular pathology that is typically assessed on CT imaging as a mixture of ground-glass opacification (GGO) and fibrotic changes. We hypothesized that proteins recovered from bronchoalveolar lavage (BAL) could be used to probe the underlying pathobiology associated with GGO and fibrotic changes.

Objectives: (1) To assess the relationship between 68 unique BAL proteins measured in participants of Scleroderma Lung Study (SLS) I[1] and radiographic and physiologic measures of ILD; (2) To identify inter-correlations among specific proteins to enlighten our understanding of how specific biological pathways contribute to SSc-ILD.

Methods: Bronchoscopy was performed on 144 of the 158 participants in SLS I with 103 BAL samples available for analysis. BAL was lyophilized, concentrated 10X and used in a multiplex protein analysis for 68 different cytokines, chemokines and other factors. Kendall tau correlations were performed to assess the relationship between individual proteins and baseline measures of pulmonary function and quantitative CT scores for fibrosis, GGO and total ILD. Those proteins found to correlate significantly with at least 2 clinical measures of ILD were entered into a cluster analysis with inter-correlations expressed as a heatmap.

Results: Significant correlations were observed between fibrosis scores and several biologic pathways including pro-fibrotic factors (transforming growth factor beta [TGF-β], platelet-derived growth factor [PDGF]), proteins involved in tissue remodeling (Matrix metallopeptidase [MMP]-1,7,8,9; Hepatocyte growth factor [HGF]), and those involved in monocyte/macrophage migration and activation (Monocyte chemoattractant protein [MCP]-1,3; macrophage colony-stimulating factor [MCSF]). These same pathways correlated with the diffusing capacity for carbon monoxide (DLCO). In contrast, GGO scores correlated primarily with immune and inflammatory mediators (interleukin [IL]-5,8,13,15, IL-1 receptor antagonist and interferon gamma) with only limited overlap to proteins that related to fibrosis. Vascular endothelial growth factor (VEGF) levels were lower in patients with more extensive GGO, fibrosis and diffusion impairment, suggesting that vascular changes are a central feature of SSc-ILD. Specific proteins were highly correlated with one another in a pattern suggesting biologically-related networks (Figure) that might provide additional insight regarding disease pathogenesis.

Conclusion: Combining a diverse analysis of BAL proteins with the rich dataset available from SSc-ILD patients participating in SLS I, the study findings suggest the involvement of distinct biologic pathways, inter-related networks, and specific biologic signatures associated with unique radiographic features of ILD. The relationship of these factors to other SSc disease features, patient outcomes and as predictors of treatment responses will be studied in future analyses.

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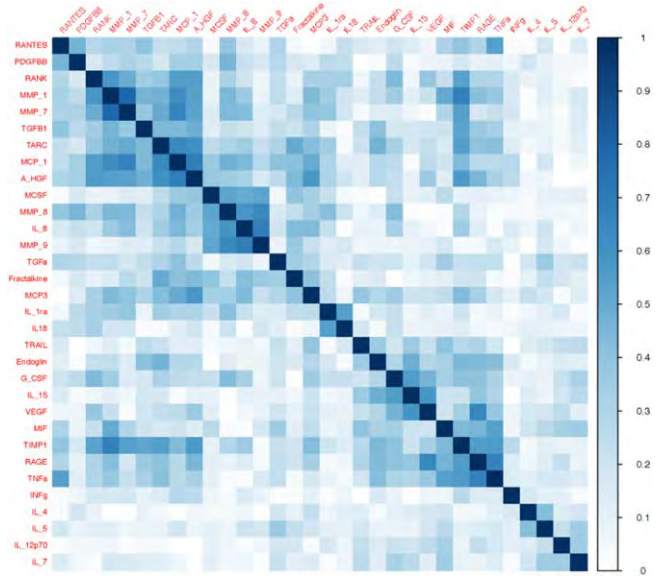


Figure. Correlation heatmap of BAL proteins associated with at least 2 clinical measures of ILD in SSc patients. Absolute correlations are depicted, and darker colors signify stronger correlations.

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SAT0287 AMPLIFICATION OF THE PRO-FIBROTIC JAK2-STAT3 SIGNALING AXIS BY TGFB-INDUCED EPIGENETIC SILENCING OF SOCS3

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Background: Tissue fibrosis caused by a pathological activation of fibroblasts is a major hallmark of systemic sclerosis (SSc). Epigenetic gene silencing of anti-fibrotic genes is thought to play a central role to establish the persistently activated phenotype of fibroblasts independent of external stimuli such as TGFβ, which has been identified as key-mediator of fibroblast activation.

Objectives: The aims of the present study were to investigate whether the aberrant activation of JAK2-STAT3 signaling in fibrosis might be caused by epigenetic silencing of SOCS expression and whether re-establishment of the endogenous, SOCS-dependent control of JAK / STAT signaling may prevent aberrant fibroblast activation and ameliorate tissue fibrosis.

Methods: The methylation status of SOCS3 in fibroblasts was evaluated by methylation-specific PCR and MeDIP assays. 5-aza-2-deoxycytidine (5-aza) and siRNA was used to inhibit DNA methyltransferases (DNMTs) *in vitro* and *in vivo*. Knockdown and overexpression experiments served to analyze the mechanism of action in cultured fibroblasts. Fibroblast-specific knockout mice were additionally used to analyze the role of SOCS3 and DNMTs *in vivo*.

Results: Chronically increased levels of TGFβ reduced the expression of SOCS3 in normal fibroblasts to a level also found in SSc fibroblasts. Consistently, the expression of SOCS3 was severely downregulated in skin of SSc patients compared to healthy individuals with only minor differences between limited and diffuse cutaneous SSc. Methylation analyses demonstrated a prominent promoter hypermethylation of SOCS3 in SSc fibroblasts and in normal fibroblasts exposed to persistently high levels of TGFβ. Increased DNMT activity and a time-dependent induction of DNMT3A and DNMT1 expression upon chronic exposure to TGFβ resulted in promoter hypermethylation of SOCS3. Knockdown of SOCS3 induced an SSc-like phenotype in normal dermal fibroblasts with increased activation of JAK2-STAT3 signaling, enhanced expression of myofibroblast markers, increased collagen release, and aggravated experimental tissue fibrosis with increased activation of JAK2-STAT3 signaling. This effect was mimicked by overexpression of mutant JAK2 with mutations in the SOCS3 binding motif. Vice versa, forced overexpression of SOCS3 reduced TGFβ-mediated fibroblast activation and ameliorated the endogenous activation of SSc fibroblasts. Pharmacological inhibition or selective knockdown of DNMTs restored the normal expression of SOCS3, reduced fibroblast activation and collagen release, blocked STAT3-responsive transcription, and exerted potent antifibrotic effects in bleomycin- and $TBRI^{act}$-induced dermal fibrosis. In addition, treatment with 5-aza or knockdown of either DNMT1 or DNMT3A induced regression of established fibrosis.

Conclusion: These findings identify a novel pathway of epigenetic imprinting of fibroblasts in fibrotic disease with translational implications for the development of new targeted therapies in fibrotic diseases. We demonstrate that the chronic activation of TGFβ signaling in fibrotic diseases perturbs the epigenetic control of STAT signaling by DNMT-induced silencing of SOCS3 expression. Our data might thus strengthen the scientific rational for targeting DNA methylation in fibrotic diseases.

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SAT0288 CHARACTERIZATION OF ANTI-AMINOACYL TRNA SYNTHETASE AUTOANTIBODIES IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

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Background: Idiopathic inflammatory myopathies (IIM) are rare chronic inflammatory diseases associated with high mortality and morbidity [1]. One sub-group of IIM, anti-synthetase syndrome (ASS), is characterized by the presence of autoantibodies that target aminoacyl transfer(t) RNA synthetases (aaRS), together with specific clinical manifestations such as myositis, interstitial lung disease (ILD), arthritis, mechanic's hand, Raynaud's syndrome and fever [2]. The most common anti-aaRS autoantibody, anti-Jo1 targeting histidyl tRNA synthetase (HisRS), is present in up to 20-30% of patients with IIM, and up to 90% of patients with myositis and ILD [3, 4]. Besides Jo1, there are today seven other identified autoantigens within the aaRS family.

Objectives: A large part of patients with IIM, including individuals with clinical manifestations indicating ASS, test seronegative to all known myositis specific autoantibodies. However, these patients could potentially harbor autoantibodies

against targets not tested for in clinic. In this study, we aimed at extending the detection of autoantibodies by including all cytoplasmic aaRS in the analysis of patients with IIM. We hypothesized the existence of new potential autoantigens within this protein family.

Methods: The presence of anti-aaRS autoantibodies was determined using a multiplex suspension bead array assay on 242 IIM patients from the Karolinska University Hospital myositis cohort. A panel of 186 recombinant constructs, representing 57 proteins that included full-length or partial sequence overlaps between constructs of all cytoplasmic aaRS as well as other myositis related proteins, were coupled to magnetic color-coded beads and each plasma sample was tested against the complete antigen panel.

Results: By the use of this multiplex method we identified patients with autoantibodies against many of the tested aaRS. Autoantibodies binding to HisRS have previously been shown to bind with higher reactivity to the WHEP domain of HisRS and this was also confirmed in this study. We confirmed reactivity against three of the other aaRS tested for in the clinic (PL-12, PL-7, and EJ). In addition, we identified patients positive for anti-Zo, -KS and -HA, autoantibodies usually not screened for in routine. Finally, our data indicates that there are autoantibodies binding to other aaRS than the previously known eight autoantigens, which will be presented.

Conclusion: In this study, we could detect autoantibodies in plasma from patients with IIM, both against the most common aaRS autoantigens, but also against other aaRS that are usually not tested for in clinic. We conclude that it is important to continue the studies of anti-aaRS autoantibodies, and their correlation to clinical manifestations, and in the long run also include more aaRS autoantigens in clinical practice.

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SAT0289 THE INS AND OUTS OF EPIDERMAL DYSFUNCTION IN SYSTEMIC SCLEROSIS (SSC): RESULTS FROM A NOVEL TISSUE ENGINEERED EPIDERMAL EQUIVALENT FROM SSC KERATINOCYTES

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Background: Skin fibrosis is a hallmark of systemic sclerosis (SSc). It is commonly accepted that vascular damage, immune system activation and, abnormal fibroblasts-to-myofibroblasts differentiation are pathological capital features. Nevertheless, recent evidence portrays a potential role of the epidermis in the pathogenesis of SSc skin fibrosis (1, 2). This new angle on skin fibrosis pathogenesis is particularly attractive as the epidermis is an easy to access therapeutic target.

Objectives: To dissect the potential epidermal dysfunction in SSc and its effect on dermis homeostasis, using a novel epidermal equivalent reconstituted from SSc keratinocytes.

Methods: Primary keratinocytes and fibroblasts cell lines were generated from skin biopsies obtained from 6 SSc and 6 healthy donors (HD), upon informed consent and ethical approval. Epidermal equivalents (EE) were generated from 4 SSc and 6 HD keratinocytes. Skin and EE expression of the mitotic marker Ki67, of the differentiation markers (K10, involucrin, filaggrin, loricrin), and activation markers (K6, K16) was evaluated by immunohistochemistry. The transcriptomic profile of SSc keratinocytes in monolayer or stratified in EE was identified by RNAseq analysis. EE conditioned medium was used to stimulate fibroblasts. The fibroblast production of interleukin (IL)-6, IL-8, matrix metalloproteinase (MMP)-1, type-I collagen (col-I), and fibronectin was assessed by ELISA.

Results: Compared to HD, immunohistochemistry revealed that SSc epidermis is characterized by aberrant premature differentiation and enhanced expression of activation markers associated with a lower mitotic rate of basal keratinocytes. Of interest, EE reconstituted from SSc keratinocytes reproduced most of the abnormalities observed in SSc epidermis. RNAseq analysis revealed that SSc keratinocytes, either cultured in monolayer or in EE, have a distinct transcriptomic profile compared to their HD counterpart, characterized by the downregulation of genes from the HOX family.

The supernatant of EE enhanced the production of IL-6, IL-8, MMP-1, col-I, and fibronectin by HD fibroblasts ($p<0.05$). Except for col-I and fibronectin, this effect was 2-fold higher in the presence of supernatant from EE reconstituted by SSc keratinocytes. Neutralization experiments indicated that IL-1 was, at least in part, responsible for keratinocyte-dependent fibroblasts activation.

Conclusion: We established a novel epidermal equivalent tissue engineered from SSc keratinocytes, that recapitulates the *in vivo* characteristics of SSc epidermis. Our preliminary data suggest that SSc keratinocytes have an intrinsic altered program of differentiation, possibly due to the downregulation of some HOX genes. This altered phenotype is associated with increased production of mediators that stimulate fibroblasts production of inflammatory cytokines. In this scenario, we may hypothesize that SSc epidermis participates in modifying the dermis environment, favoring the development of chronic inflammation and fibrosis.

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Disclosure of Interests: Barbara Russo: None declared, Julia Borowczyk-Michalowska: None declared, Wolf-Henning Boehncke Consultant of: WHB received honoraria as advisor or invited speaker from Abbvie, Almirall, BMS, Celgene, Leo, Lilly, Novartis, UCB., Speakers bureau: WHB received honoraria as advisor or invited speaker from Abbvie, Almirall, BMS, Celgene, Leo, Lilly, Novartis, UCB., Nicolò Brembilla: None declared, Carlo Chizzolini Consultant of: Boehringer Ingelheim, Roche

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SAT0290 HIGH SERUM MYOSTATIN LEVELS SUGGEST ACCELERATED MUSCLE SENESCENCE IN ACTIVE IDIOPATHIC INFLAMMATORY MYOSITIS

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Background: Inflammation is the forerunner to fibrosis and premature ageing in various systemic diseases. Hence it seems plausible that idiopathic inflammatory myopathies (IIM) may exhibit accelerated senescence too.

Objectives: Hence we investigated the Myostatin: Follistatin system in the serum as a reflection of early senescence in myositis as compared with healthy and diseased controls.

Methods: Patients with inflammatory myositis (ACR/EULAR criteria) presenting to the wards and outpatient clinic between December 2017 to August 2019 were recruited. Those with active infection, pregnancy, renal dysfunction or chronic kidney disease were excluded. Apart from patient and disease variables, activity and damage were assessed using standard IMACS score set measures. Patients in inception cohort were additionally followed up at 1 and 6 months. Myostatin and Follistatin were estimated in sera using ELISA (R&D systems, USA). Juvenile myositis and young adults (18-40 years) were subsequently analyzed separately. Non-parametric tests were used for paired and unpaired analysis. Results expressed as median.

Results: 95 myositis (8 Juvenile myositis, 26 DM, 10 PM, 29 Overlap, 2 NAM 1 CAM and 19 ASS) patients (23 Male and 72 Female) with median age 38 (24.5-46.0) years and disease duration 0.9 (2.3-5.1) years were included. Serum Myostatin was lower in IIM than in healthy control (HC) (153.5 vs. 243.6 $p<0.0001$, Fig 1A) but higher in IIM as compared with disease controls (153.5 vs 86.1 $p=0.0174$ Fig. 1B). Serum myostatin was comparable between juvenile and adult myositis and in the various subsets of adult myositis (Fig. 1 C and D). Myostatin levels were higher in active as compared with inactive myositis in young adults (211.7 vs. 158.9, $p=0.0149$, Figure 1E). Serum Myostatin correlated with height (r 0.3, $p=0.003$) and weight (r 0.2, $p=0.047$) but not MMT8 or muscle enzymes.

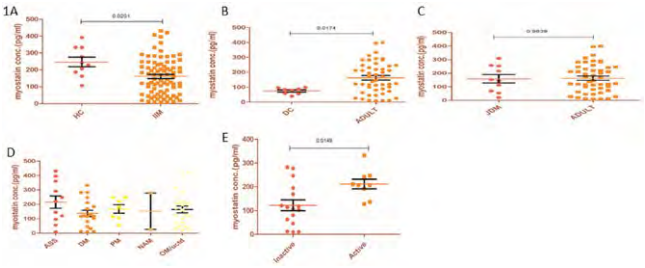


Figure 1. Serum Myostatin levels in IIM as compared with healthy controls (A) and disease controls (B). Levels in juvenile myositis as compared with adult IIM (C) and in various subsets of IIM (D). Serum Myostatin levels in active and inactive disease (E).

Although Follistatin was lower in IIM than HC (198.4 vs 243.6, p=<0.0001), the neither Follistatin nor Myostatin: Follistatin ratios differ between subsets, and in active versus inactive disease Figure 2 A-D). On follow-up, the serial Myostatin estimation paralleled change in disease activity.

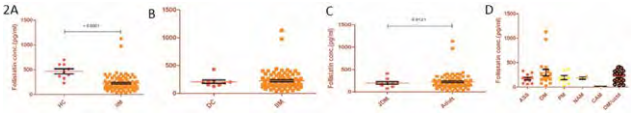


Figure 2. Serum Follistatin levels in IIM as compared with healthy controls (A) and disease controls (C). Levels in juvenile and adult IIM (D) and in various subsets of IIM (D).

Conclusion: Elevated serum Myostatin levels in active myositis raise the possibility of accelerated senescence in the inflamed muscle tissues which need further investigation.

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SAT0291 THE ROLE OF X-LINKED INHIBITOR OF APOPTOSIS PROTEIN (XIAP) IN SYSTEMIC SCLEROSIS

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Background: Pathologic activation of fibroblasts is a central feature of fibrotic tissue disease in Systemic Sclerosis (SSc). Although individual key signaling pathways of fibroblast activation such as transforming growth factor β (TGFβ) and WNT/β-catenin signaling have been identified, the consequences of the concomitant upregulation of these pathways and their crosstalk are incompletely characterized. Given the high medical need, the identification of mutual activation and amplification loops of profibrotic signals is essential to identify novel candidates for antifibrotic therapies. XIAP (X-linked inhibitor of apoptosis protein) is a ubiquitously expressed member of the IAP protein family which are implicated in the regulation of various cellular functions and tissue turnover. XIAP was recently described to be implicated in WNT/β-catenin signaling and TGFβ signaling.

Objectives: The aim of this study is to characterize the role of XIAP in fibrotic disease.

Methods: XIAP-expression was analyzed by qPCR, IF and Western blot. XIAP was targeted pharmacologically and with siRNA. The activation of WNT/β-catenin signaling was assessed by analyses of WNT target genes, by TOPflash/FOPflash luciferase reporter assay and in reporter mice. *In vivo,* XIAP inhibition was analysed in two different models of fibrosis.

Results: The expression of XIAP is increased in the skin of SSc patients compared to matched healthy individuals with a particular prominent expression in fibroblasts. The overexpression of XIAP is more pronounced in SSc patients with diffuse and active skin fibrosis compared to SSc patients with limited and inactive disease. The overexpression of XIAP is also reflected in several experimental fibrosis models: the model of sclerodermatous graft versus host disease, the model of bleomycin induced skin fibrosis and Topoisomerase I induced fibrosis (TopoI) mice. TGFβ induces the expression of XIAP in vitro and in vivo and treatment with the TGFβ1 receptor antagonist SD208 reverses the TGFβ induced expression of XIAP. Inhibition of XIAP with embelin or siRNA reduces the TGFβ induced activation of fibroblasts with reduced collagen release and reduced expression of myofibroblast markers. In addition, XIAP inhibition reverted the activated fibroblast phenotype in SSc fibroblasts with reduced expression of stress fibers and αSMA. The antifibrotic effects of XIAP inhibition occurred in non-toxic doses as demonstrated by MTT and by TUNEL staining. In vivo, inhibition of XIAP reduced skin fibrosis in the models of bleomycin induced skin fibrosis and in TopoI-induced skin and lung fibrosis as demonstrated by analysis of dermal thickening, dermal hydroxyproline content and by analysis of myofibroblast differentiation. Mechanistically, XIAP inhibition reduced the activation of WNT/β-catenin signaling as demonstrated by TOPflash reporter assays and by the analysis of WNT target genes.

Conclusion: XIAP is upregulated in SSc fibroblasts and murine SSc models in a TGFβ-dependent manner and promotes fibroblast activation by fostering canonical WNT signaling. Our data suggest that XIAP mediates an amplification loop between TGFβ and WNT/β-catenin signaling. Inhibition of XIAP may thus be a novel approach to target aberrant WNT/β-catenin signaling in fibrotic diseases.

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SAT0292 INTEGRATIVE TRANSCRIPTOMIC AND FUNCTIONAL ANALYSIS REVEALS A ROLE OF DIMETHYL-A-KETOGLUTARATE IN TGFB-DRIVEN CYTOSKELETON REGULATION AND MYOFIBROBLAST DIFFERENTIATION

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Background: Myofibroblasts are the orchestrators of aberrant extracellular matrix (ECM) remodelling in fibrosis. Actin cytoskeleton is a central hub that integrates mechanical signals to promote myofibroblast differentiation and ECM remodelling. Targeting these pathways could represent a novel antifibrotic strategy. We have recently shown that metabolic intermediate dimethyl-α-ketoglutarate (dm-αKG) blocks TGFβ-driven myofibroblast differentiation in dermal fibroblasts (DF).

Objectives: To investigate the mechanisms by which dm-αKG regulates TGFβ-driven myofibroblast differentiation and inflammatory responses in DF.

Methods: DF from healthy controls and patients with systemic sclerosis (SSc) were treated with TGFβ (10 ng/ml) and/or dm-αKG (6 mM) for 24h, 48h and 72h. RNA sequencing (Illumina 2000, n=3 per experimental group) was followed by the analysis of differentially expressed genes (DeSEQ2, log2 fold ≥ |0.5|, p_{adj} < 0.01), pathway enrichment analysis (GO terms) and supervised PCA analysis (ClustVis). Protein amounts (fibronectin, αSMA, IL-6), cell contraction and apoptosis were measured with Western blot (n=6), ELISA (n=4), collagen gel contraction assay (n=4) and real time Annexin V assay (n=6). Significance (p<0.05) was determined by one-sample t-test or ANOVA with Tukey's correction for multiple comparisons.

Results: TGFβ (24h) altered the expression of 4076 genes in DF as determined by RNA-seq, among which 1864 genes were upregulated. The upregulated genes were enriched in GO biological processes/molecular functions/cellular compartments related to ECM organization (p=1e-07), Wnt signalling (p=5e-06), actin binding (p=3e-07), focal adhesion (p=1e-10), stress fibers (p=3e-07) and actin cytoskeleton (p= 3e-06). Dm-αKG altered the expression of 589 genes in TGFβ-treated DF compared to TGFβ only. The most downregulated pathways in DF treated with dm-αKG + TGFβ compared to TGFβ only included actin binding (p=5e-05), muscle contraction (p=0.001), ECM organization (p=0.008), focal adhesion (p=0.01), Z disk (p=0.01) and stress fibers (p=0.03). Specifically, dm-aKG significantly (p<0.01, log2>-0.5) decreased the expression of many TGFβ-induced genes involved in actin organization and focal adhesion (*NEXN, FRMD5, ANTXR1, ACTC1, LIMCH1, SORBS2, TGM2, CSRP2, CAP2, LMO7, FZD2*), muscle contraction (*SNTB1, LMOD1, ANKRD1, SULF1, JPH2, CAVIN4, OXTR, DYSF, FBXO32*) and ECM organization (*COL10A1, COL11A1, HAPLN1, MMP14,*

MMP3, SPINT2, GREM1, MATN3, ADAMTS4). The PCA analysis revealed that the experimental treatment (PC1, Fig 1A) accounted for 61% variability in the expression of these genes, while 19% was attributed to interdonor variability (PC2). Dm-αKG diminished TGFβ-induced production of αSMA protein (72h, p=0.02, mean O.D. ± SD in TGFβ + dm-αKG vs. TGFβ: 0.34 ± 0.38 vs. 3.1 ± 2.3) and repressed TGFβ-driven secretion of fibronectin protein (72h, p=0.047, 0.5 ± 0.1 vs. 1.2 ± 0.6). Dm-αKG reduced the contractile capacity of TGFβ-stimulated DF in collagen gel contraction assay (p=0.003, 0 vs. 67.1 ± 5.4%). Additionally, dm-αKG decreased TGFβ-driven production of IL-6 transcripts (24h, p=0.05, 2.9 ± 0.6 vs 1.9 ± 0.3) and protein (24h, p=0.0005, 5.9 ± 1.2 vs 3 ± 0.7, Fig 1B), but did not increase the apoptosis of DF (24h, 48h, 72h).

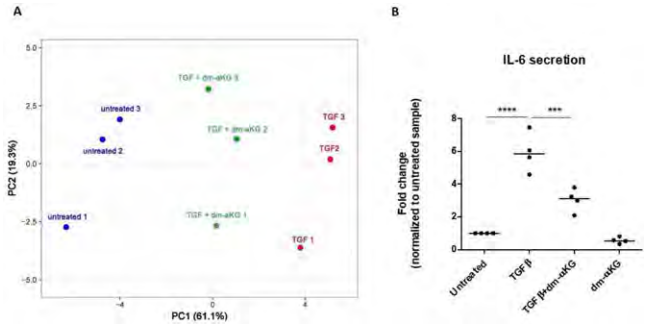


Fig 1. A Supervised PCA analysis of RNA-seq data. B. IL-6 secretion (ELISA).

Conclusion: Dm-αKG counteracted TGFβ-induced myofibroblast differentiation by regulating the cytoskeleton organization and ECM dynamics in DF and blocked the TGFβ-induced IL-6 production. This closely links metabolism to inflammatory and pro-fibrotic responses in DF. Therefore, regulating intracellular αKG might offer a novel strategy in combating the inflammatory and fibrotic stages of skin fibrosis in SSc.

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SAT0293 EXOSOMES DERIVED FROM PLASMA OF SYSTEMIC SCLEROSIS (SSC) PATIENTS AND FROM SSC CULTURED FIBROBLASTS CONTAIN PRO-FIBROTIC MIRNA SIGNATURES AND COULD INDUCE MYOFIBROBLAST DIFFERENTIATION IN VITRO

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Background: Exosomes generated great resonance in the last few years due to their important roles in different biological pathways and diseases, including systemic sclerosis (SSc) (1). They are lipid-like nanovesicles containing biomarkers, such as proteins, lipids, macromolecules and nucleic acids, including microRNA (miRNA) (2). Exosomes are implicated in intercellular communication by fusing and releasing their cargo into the target cells (3).

Objectives: In the present study, we evaluated the potential of exosomes deriving from plasma of SSc patients or generating from cultured SSc fibroblasts to drive the fibrotic signaling in the disease.

Methods: Exosomes were isolated from plasma of n=10 SSc patients and from n=10 control subjects. Exosomes were also purified from cell culture supernatants of SSc fibroblasts and of control fibroblasts. Exosome size and concentration were assessed by Nanosight Particle Tracking Analysis (NTA) and by transmission electron microscopy (TEM). The content of anti-fibrotic (let-7a, 146a, 200a, 223a) and pro-fibrotic (150, 155) miRNAs was assessed in all the plasma-derived and cell culture-derived exosome populations by semiquantitative real time PCR. Finally, isolated exosomes were used to stimulate control dermal fibroblasts in culture. Gene expressions (COL1A1, ACTA2 and TAGLN) were assessed by quantitative real time PCR (qRT-PCR) and protein levels (type-I-collagen, α-SMA and SM22) by immunofluorescence (IF).

Results: Exosomes isolated from SSc plasma samples showed higher concentration ($3.3x10^{10}$±$1.1x10^{10}$ particles/mL) compared to those isolated from control plasma ones ($1.5x10^{10}$±$0.4x10^{10}$ particles/mL) (p<0.01). The exosome size did not differ between SSc and control plasma samples and ranged from 50nm to 150nm. Similar results were obtained with exosomes generated from fibroblast cultures: the concentration was higher in SSc fibroblasts ($1.1x10^{10}$±$0.2x10^{10}$ particles/mL) than in control ones ($0.4x10^{10}$±$0.1x10^{10}$ particles/mL) (p<0.05) with no significant differences in size distribution. The content of all anti-fibrotic (let-7a, 146a, 200a, 223a) miRNAs was decreased in exosomes coming from both SSc plasma samples and from SSc fibroblasts with respect to control plasma samples (p<0.05) and to control fibroblasts (p<0.05). On the contrary, the pro-fibrotic (150, 155) miRNAs were significantly upregulated in exosomes deriving from SSc plasma samples and from SSc fibroblasts, with respect to control plasma samples (p<0.05) and to control fibroblasts (p<0.05). Finally, only exosomes coming from SSc plasma samples or SSc fibroblast cultures were able to induce pro-fibrotic gene (COL1A1, ACTA2 and TAGLN) and protein (type-I-collagen, α-SMA and SM22) expression in control fibroblasts. No pro-fibrotic induction was seen in presence of exosomes isolated from control plasma samples or control fibroblast cultures.

Conclusion: This study demonstrates that plasma from SSc patients contains higher concentration of exosomes compared to plasma from control subjects and SSc-derived exosomes contain specific pro-fibrotic miRNA signatures that can induce myofibroblast differentiation *in vitro*. These results suggest that exosomes could be fibrotic drivers towards non-affected areas *in vivo*, and they might represent novel targets for precision medicine treatments in SSc.

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SAT0294 IL33 ACTIVATES FIBROBLASTS AND INDUCES SKIN FIBROSIS IN SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a chronic immune-mediated autoimmune disease that is characterized by fibrotic changes of the skin and internal organs, which in turn leads to distortion of tissue structure and gradual loss of organ function. So far, there is still no treatment allows full recovery from this severe disorder. Therefore, it is of great social significance to study the pathogenesis of this disease and find new targets for treatment. Interleukin 33 (IL-33), which is a potent inducer of type 2 immune response, has been confirmed to be involved in the development and progression of multiple fibrotic diseases. However, the role and mechanism of IL-33 in SSc-related fibrosis remains unclear.

Objectives: To clarify the role of interleukin 33 (IL-33) and its receptor Suppression of tumorigenicity 2 (ST2) in the skin fibrosis of SSc, so to provides a new target for the treatment of fibrosis in patients with SSc.

Methods: The levels of IL-33 and ST2 was analysed in human samples, murine models of SSc and in cultured fibroblasts by immunohistochemistry and immunofluorescence. The functional role of IL-33 was evaluated by detecting changes

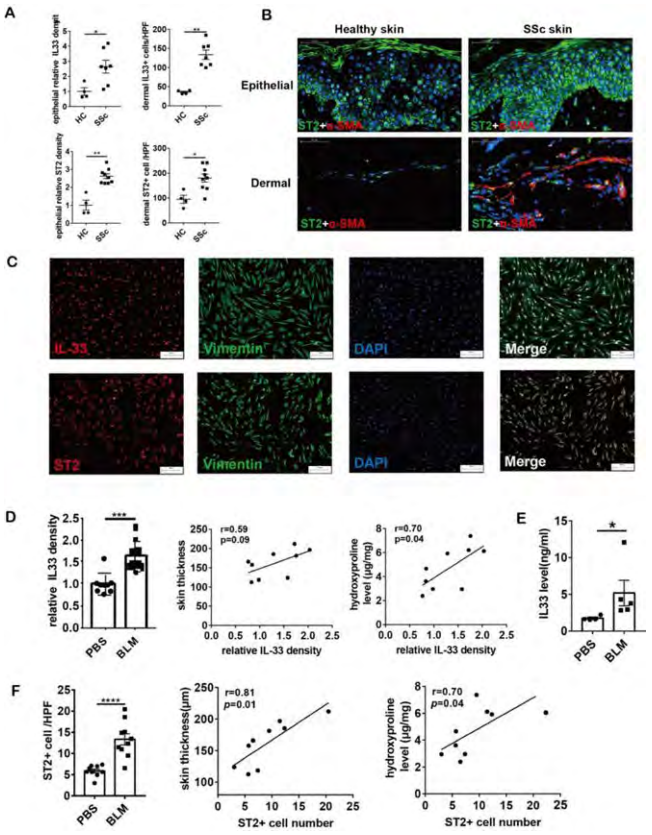


Fig 1. Increased expression of IL33, ST2 in SSc patients and bleomycin-treated mice.

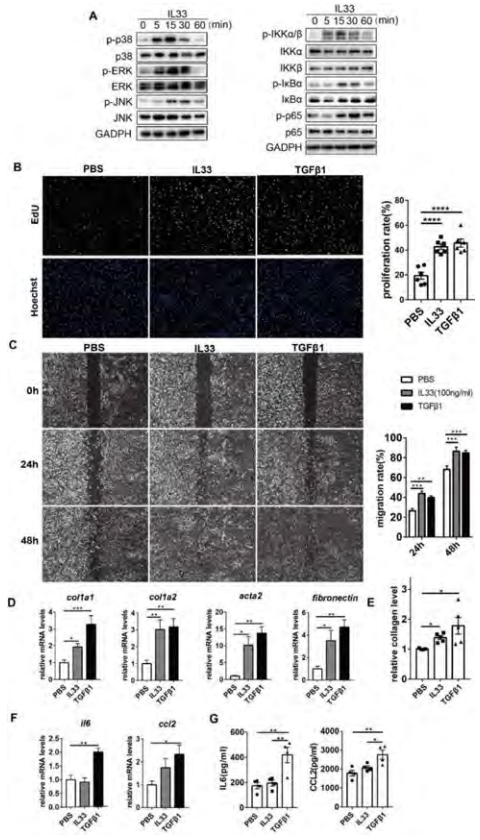


Fig 2. IL33 induces MAPK and IκBα activation in human dermal fibroblast, and and promote proliferation, migration and production of collagen of human dermal fibroblasts.

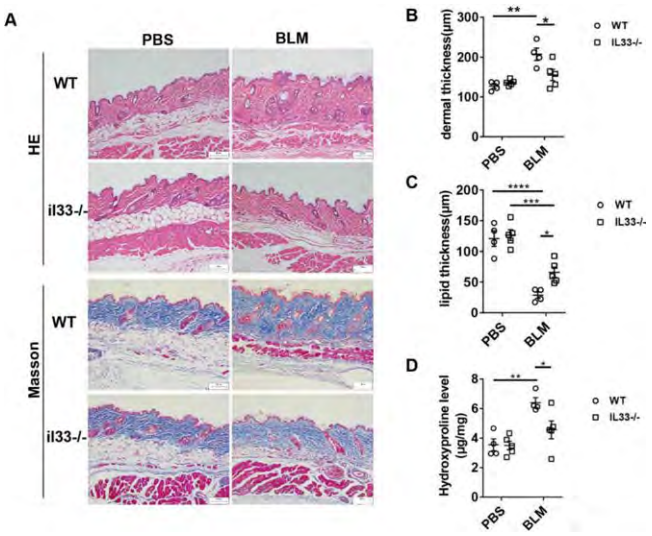


Fig 3. Mice deficient for IL33 are protected from bleomycin-induced dermal fibrosis.

in proliferation, migration, and activation of fibroblasts stimulated with recombinant IL-33 protein. MAPK and NF-κB signallings of fibroblasts were assessed by western blotting and analyses of target genes. The role of IL-33 in skin fibrosis was analysed in IL-33 deficient mice (il33–/–) and wild-type controls injected with bleomycin or NaCl.

Results: The expression of IL-33 and its receptor ST2 were up-regulated in skin lesions of SSc patients (Fig 1 A-C) and bleomycin-treated mice(Fig1 D-F). Compared to the healthy skin, the skin from SSc patients expressed more ST2 on fibroblasts membrane(Fig 1 B-C). IL33 induces MAPK and IκBα activation in human dermal fibroblast(Fig 2 A), and promote proliferation, migration and production of collagen of human dermal fibroblasts, but not the release of inflammatory factors(IL-6, MCP-1)(Fig2 B-G). Mice deficient for IL33 are protected from bleomycin-induced dermal fibrosis (Fig3).

Conclusion: IL33 promotes skin fibrosis by activating fibroblasts, and IL33/ST2 may be an important target for the treatment of fibrosis in patients with SSc.

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SAT0295

GLUCAGON-LIKE PEPTIDE-1 RECEPTOR AGONIST AMELIORATED MUSCLE WEAKNESS AND INFLAMMATION IN EXPERIMENTAL POLYMYOSITIS

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Background: Polymyositis (PM) is a chronic inflammatory myopathy that impairs muscle functions. While the treatment with glucocorticoids (GC) has been the cornerstone of the treatment for PM to suppress immune-mediated muscle injury, some patients suffer from glucocorticoid-induced myopathy during the treatment, which further deteriorates the muscle weakness. It has been reported that significant disability and muscle weakness persist in a quarter of the patients even after successful treatment with the immunosuppressive therapy[1]. Ultimately, new therapeutic strategies to preserve and recover muscle strength as well as to

suppress immune-mediated muscle injury are needed. Glucagon-like peptide-1 (GLP-1) is a peptide hormone with a variety of functions. Although GLP-1 receptor (GLP-1R) agonists have been developed as an anti-diabetic therapy to promote insulin secretion, emerging data suggest that they have pleiotropic actions including anti-inflammatory effects and suppression of muscle wasting[2]. We presumed that GLP-1R agonists have beneficial effect on PM to preserve and recover muscle strength.

Objectives: To examine the effect of a GLP-1R agonist on C protein-induced myositis (CIM), a murine model of polymyositis[3], in monotherapy or in combination with prednisolone (PSL).

Methods: Muscle specimens of PM patients and CIM were examined with immunohistological staining for the expression of GLP-1R. The therapeutic effect of PF1801 (ImmunoForge), a GLP-1R agonist (5 mg/kg body weight (BW)/day), in monotherapy or in combination with PSL (20 mg/kg BW/day) on CIM was examined for grip strength, muscle weight and histological muscle inflammation.

Results: GLP-1R was expressed on the plasma membrane of muscle cells of PM patients and CIM. The expression levels were high in the area where inflammatory infiltrates were observed. The treatment of CIM with PF1801 in monotherapy or in combination with PSL suppressed the CIM-induced decrease in grip strength on day 14. The combination therapy with PF1801 and PSL ameliorated the CIM-induced muscle weight loss in quadriceps, while the monotherapy with PF1801 or PSL did not. The histological analysis of muscle specimens on day 14 of CIM revealed that the muscle inflammation was suppressed by the treatments with PF1801, PSL, or the combination of PF1801 and PSL. None of the mice in the combination therapy group developed histologically evident myositis, while the myositis was observed in 90%, 40% and 40 % of the mice in vehicle treated group, PF1801 treated group, and PSL treated group, respectively. The necrotic area of the muscle in CIM was also reduced in the mice treated with PF1801, PSL, or the combination of PSL and PF1801. The CIM-induced increase in spleen weight was suppressed by PF1801, PSL, or the combination of PSL and PF1801. The additive effect of PSL and PF1801 on the suppression of CIM-induced increase in spleen weight was observed.

Conclusion: PF1801 ameliorated CIM-induced muscle weakness and muscle inflammation in CIM. The combination therapy with PF1801 and PSL ameliorated CIM-induced muscle weight loss. PF1801 could be a novel therapy to recover muscle weakness and to suppress muscle inflammation in PM.

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SAT0296 SERUM LEPTIN LEVELS IN SYSTEMIC SCLEROSIS PATIENTS WITH ELECTROCARDIOGRAPHIC ABNORMALITIES

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Background: Electrocardiographic (ECG) abnormalities are described in 25-75% Systemic Sclerosis (SSc) cases and they are associated with other systemic manifestations as well as with a worse prognosis. There is an increasing need for clinical and laboratory biomarkers to ameliorate the diagnostic and therapeutic approaches to patients with ECG abnormalities, due to their actual low sensitivity and specificity. Adipokines are circulating proteins that appear dysregulated in SSc and leptin in particular is synthesized in response to inflammatory conditions and seems to play a proinflammatory and pro-fibrotic action in SSc. Interesting, many studies in the last years have underlined its role in the cardiac remodeling mechanisms and in the development of cardiac fibrosis in other chronic diseases.

Objectives: Aim of our study is to evaluate the role of leptin in the development of cardiac rhythm disorders (CRD) during SSc. Furthermore, by the analysis of the clinical and demographical parameters of our SSc patients, we tried to define other possible features associated with increased serum leptin concentration.

Methods: We included eighty-five SSc patients, fulfilling the 2013 ACR/EULAR classification criteria, attending the Regional Rare Disease Center of Policlinico Umberto I of Rome. Fifty presented significant CRD at non-invasive diagnostic techniques (12 Lead ECG, 24-hour Holter ECG). Demographic, clinical, conventional cardiovascular risk factors were examined; instrumental and laboratory assessments were obtained, together with ECG recordings. Thirty-five SSc patients without pathologic finding at ECG traces, matched for demographic and clinical features, were recruited as the control group. In all cases, after obtaining written informed consent, blood samples were taken to measure serum levels of leptin using an ELISA assay (Life Technologies-Italia).

Results: The fifty SSc patients with CRD (mean age 51±15 years; F:M 41:9) had pulmonary fibrosis (PF) in 32 cases (64%) and a BMI >25Kg/m^2 in 22 (44%) while in the control group of thirty-five SSc patients (mean age 49±16 years; F:M 33:2) PF was found in 15 (43%) and a BMI >25Kg/m^2 in 9 (35%); We detected significantly higher median values of serum leptin in SSc patients with CRD compared to the control group (12027 pg/ml IQR 12314 versus 6392 pg/ml IQR 7103; *p 0,0009*). Additionally, SSc patients with a BMI> 25 kg/m^2 (31 cases) as well as those with PF (47 cases) showed a significantly higher median serum leptin levels compared to those with BMI <25 kg/m^2 (13161 pg/ml IQR 13610 versus 8187 pg/ml IQR 8255; *p 0,0008)* and those without PF (11740 pg/ml IQR 11940 versus 7616 pg/ml IQR 7855; *p 0,0079*).

Conclusion: To our knowledge this is the first report on high serum levels of leptin in SSc patients with CRD that also confirms its increase in those cases with a BMI >25 kg/m^2 and with PF, according to scientific literature data. The role of leptin in the pathogenesis of SSc remains unclear although it is already known its involvement in the development of cardiac fibrosis during other chronic diseases. On the basis of these results we speculate on leptin involvement in the pathogenesis of CRD during SSc, although further studies are needed with larger cohort of patients.

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Disclosure of Interests: Greta Pellegrino: None declared, Katia Stefanantoni Consultant of: Italfarmaco
Boehringer Ingelheim, Fausta Facioni: None declared, Carlotta Angelelli: None declared, Antonietta Gigante: None declared, Roberto Badagliacca: None declared, Carmine Dario Vizza: None declared, Sergio Morelli: None declared, Edoardo Rosato: None declared, Valeria Riccieri: None declared

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SAT0297 DIFFERENTIAL PHENOTYPES OF DISEASE-SPECIFIC AUTO-REACTIVE B CELL RESPONSES IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Systemic Sclerosis (SSc) carries the highest mortality burden among the rheumatic diseases. >95% of SSc patients harbor autoantibodies. Anti-topoisomerase antibodies (ATA) and anti-centromere antibodies (ACA) are most prevalent, mutually exclusive in individual patients, associate with distinct disease phenotypes and predict disease. Whether and how these auto-reactive B cell responses contribute to disease, however, is currently unclear.

Objectives: To delineate phenotypic and functional characteristics of anti-topoisomerase and anti-centromere specific B cell responses in individual patients with SSc.

Methods: Peripheral blood mononuclear cells (PBMC) obtained from ATA- and ACA-positive SSc patients were cultured without stimulation or in the presence of CD40L-expressing fibroblasts, IL-21 and BAFF. In addition, PBMC were depleted of circulating plasmablasts (CD19+CD20-CD27++) by fluorescence activated cell sorting (FACS), and isolated plasmablasts were cultured separately. ATA- and ACA-IgG and -IgA were measured in culture supernatants by ELISA. B cell

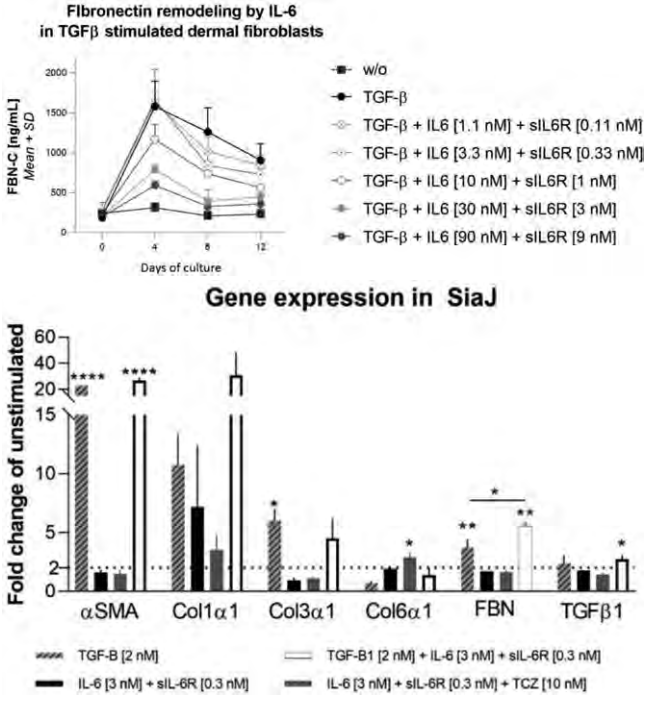
subsets were defined by flow cytometry. Healthy donors and patients with rheumatoid arthritis served as controls.
Results: We observed that ATA- and ACA-positive SSc patients harbour circulating B cells that secrete either ATA-IgG or ACA-IgG upon stimulation, depending on their serotype. In addition, we noted spontaneous secretion of ATA-IgG and, more remarkably, extensive secretion of ATA-IgA in ATA-positive patients. This degree of spontaneous, antigen-specific IgA secretion was specific for the ATA response in ATA-positive patients, while spontaneous ACA-IgA secretion was undetectable in the ACA-positive patient group. FACS experiments showed that spontaneously ATA-IgA secreting B cells were primarily present in the plasmablast compartment.
Conclusion: Our findings demonstrate that ATA-positive SSc patients harbour an activated ATA-IgG and ATA-IgA B cell response, as indicated by the spontaneous secretion of both ATA isotypes by circulating plasmablasts. Remarkably, the ACA B cell response was far less active and lacked the active IgA component which suggests a difference in the triggers driving these autoreactive B cell responses in patients. Moreover, the remarkable ATA-IgA secretion points towards a potential mucosal origin of the ATA response.
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SAT0298 IS INTERLEUKIN 6 A FACTOR OF FIBROGENESIS IN DERMAL FIBROBLASTS?

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Background: Interleukin 6 (IL-6) is known to have both pro- and anti-inflammatory properties, depending on the receptor activation. The classical IL-6 signaling via the membrane bound receptor is mainly anti-inflammatory, whereas signaling through the soluble receptor (sIL-6R) is pro-inflammatory/pro-fibrotic. However, the direct fibrotic effect of IL-6 stimulation on dermal fibroblasts is unknown.
Objectives: We investigated the fibrotic effect of IL-6 + sIL-6R in a dermal fibroblast model and assessed fibrosis by neo-epitope biomarkers of extracellular matrix proteins.
Methods: Primary healthy human dermal fibroblasts were grown for up to 17 days in DMEM medium with 0.4% fetal calf serum, ficoll (to produce a crowded environment) and ascorbic acid. IL-6 [1-90 nM]+sIL-6R [0.1-9 nM] alone or in combination with TGFβ [1 nM] were tested in three different donors. TGFβ [1 nM], PDGF-AB [3 nM] and non-stimulated cells (w/o) were used as controls. Tocilizumab (TCZ) with TGFβ + IL-6 + sIL-6R stimulation was tested in one donor. Collagen type I, III and VI formation (PRO-C1, PRO-C3 and PRO-C6) and fibronectin (FBN-C) were evaluated by validated ELISAs (Nordic Bioscience). Western blot analysis investigated signal cascades. Gene expression of selected ECM proteins was analyzed. Statistical analyses included One-way and 2-way ANOVA and area under the curve analysis.
Results: formation by the end of the culture period. The fibronectin and collagen type VI signal were consistent between the three tested donors, whereas the formation of type III collagen was only increased in one donor, but in several trials. Type I collagen formation was unchanged by IL-6 + sIL-6R stimulation. The gene expression of type I collagen was induced by IL-6 + sIL-6R. Western blot analysis validated trans-signaling by the IL-6+sIL-6R stimulation as expected.
IL-6 + sIL-6R stimulation in combination with TGFβ decreased fibronectin levels compared to TGFβ alone but did not reach the level of unstimulated fibroblasts. The formation of collagen type IV was generally unchanged with IL-6 + sIL-6R + TGFβ compared to TGFβ alone. Collagen type I and III formation was more scattered in the signals when IL-6 + sIL-6R was in combination with TGFβ, as the biomarker level could be either decreased or increased compared to TGFβ alone. In two studies the type I collagen level was synergistic increased by IL-6 + sIL-6R + TGFβ, whereas another study found the level to be decreased compared to TGFβ alone. The gene expression of fibronectin and type I collagen was increased with TGFβ +IL-6+sIL-6R compared to TGFβ alone.
Inhibition of IL-6R by TCZ in combination with IL-6 + sIL-6R did only decrease the fibronectin level with the lowest TCZ concentration (p=0.03). TCZ alone decreased the fibronectin level in a dose-dependent manner (One-way ANOVA p=0.0002).
Conclusion: We investigated the fibrotic response of dermal fibroblasts to IL-6 + sIL-6R stimulation. IL-6 modulated the fibronectin level and modulated the collagen type III formation level in a somewhat dose-dependent manner. In combination with TGFβ, IL-6 decreased collagen type I and IV formation and fibronectin. However, in this study inhibition of IL-6R by TCZ did not change the fibrotic response of the dermal fibroblasts. This study indicated that IL-6 did not induce collagen formation in dermal fibroblasts, except type III collagen formation with high IL-6 concentration.

Figure:



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SAT0299 PROLIFERATION, MIGRATION AND CONTRACTION ARE DIFFERENT BETWEEN TGFB AND PDGF STIMULATED DERMAL FIBROBLASTS

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Background: Systemic sclerosis has vascular, inflammatory and fibrotic components, which may be associated with different growth factors and cytokines. Platelet derived growth factor (PDGF) is associated with the vasculature, whereas tumor necrosis factor beta (TGFβ) is associated with inflammation and fibrosis. We have developed a fibroblast model system of dermal fibrosis for anti-fibrotic drugs testing, but the effect of the fibroblasts mechanistic properties are unknown.
Objectives: We investigated different mechanical capacities of PDGF and TGFβ treated human healthy dermal fibroblasts in the SiaJ setting.
Methods: Primary human healthy dermal fibroblasts were grown in DMEM medium containing 0.4% fetal calf serum, ficoll (to produce a crowded environment) and ascorbic acid for up to 17 days. A wound was induced by scratching the cells at 0, 1, 3 or 7 days after treatment initiation. Wound closure was followed for 3 days. Contraction capacity was tested by creating gels of human fibroblasts produced collagens containing dermal fibroblasts and contraction was assessed at day 2 by calculating the percentage of gel size to total well size. Collagen type I, III and VI formation (PRO-C1, PRO-C3 and PRO-C6) and fibronectin (FBN-C)

were evaluated by validated ELISAs (Nordic Bioscience). Gene expression was analyzed after 2 days in culture. Statistical analyses included One-way ANOVA and student's t-test.

Results: Generally, PDGF closed the wound in half the time of w/o and TGFβ, when treatment and cells are added concurrently or scratched one day after treatment initiation. When treatments were added 3 or 7 days prior to scratch, the cells treated with PDGF had proliferated to a higher degree than w/o and TGFβ. A consequence of this, was that when cells were scratch the sheet of cells produced was lifted from the bottom and fold over itself, leaving a much greater scratch than in the other treatments. However, despite this increased gap the PDGF treated cells closed the wound at the same time as w/o and TGFβ, confirming the results of the cells scratched at day 0 and 1.

Inhibition of contraction by ML-7 of otherwise untreated cells inhibited contraction significantly compared to untreated cells alone (p=0.0009). Contraction was increased in both TGFβ and PDGF treated cells compared to untreated cells (both p<0.0001). TGFβ+ ML-7 inhibited the contraction to the level of w/o (p=0.0024), which was only 35% of ML-7 alone. In the contraction study the cells were terminated after 2 days of culture, thus prior to when biomarker of ECM remodeling is usually assessed. However, FBN-C was detectable and a significant release of fibronectin by TGFβ and PDGF compared to w/o was found in the supernatant (both p<0.0001). The gene expression of FBN was only increased with TGFβ (p<0.05) and not PDGF. ML-7 alone tended to decrease FBN-C and in combination with TGFβ the FBN level was significantly decreased compared to TGFβ alone (p<0.0001). However, the level of TGFβ+ML-7 was significantly higher than ML-7 alone (p=0.038).

TGFβ increased the gene expression of most genes assessed, except Col6a1. PDGF increased the gene expression of Col3a1, Col5a1 and Col6a1 above the critical fold change of 2, but only significantly in Col5a1 and Col6a1 (both p<0.05).

Conclusion: This study demonstrates that TGFβ and PDGF have different mechanical capacities in human healthy dermal fibroblasts; TGFβ increased gene expression of ECM related genes, such as collagens and have increased FBN release in the supernatant already 2 days after initial treatment. PDGF has increased contraction, proliferation and migratory capacities and less expression of ECM related genes and proteins.

Disclosure of Interests: Anne Sofie Siebuhr Employee of: Nordic Bioscience, Sofie Falkenløve Madsen: None declared, Morten Karsdal Shareholder of: Nordic Bioscience A/S., Employee of: Full time employee at Nordic Bioscience A/S., Anne-Christine Bay-Jensen Shareholder of: Nordic Bioscience A/S, Employee of: Full time employee at Nordic Bioscience A/S., Pernille Juhl Employee of: Nordic Bioscience

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SAT0300

SERUM FROM "EARLY" SYSTEMIC SCLEROSIS PATIENTS ALREADY INDUCES THE ALTERNATIVELY ACTIVATED MACROPHAGE PHENOTYPE (M2) IN CULTURED HUMAN MONOCYTES

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Background: Alternatively activated (M2) macrophages seem to play a role in the fibrotic process of systemic sclerosis (SSc) as potential inducers of tissue fibrosis through their secretion of specific cytokines and chemokines, such as interleukin-10 (IL-10), macrophage derived chemokine (CCL-22) and pro-fibrotic metalloproteases (i.e. MMP9) (1-3).

Objectives: To investigate the presence of circulating cells belonging to the monocyte lineage showing an M2 phenotype in SSc patients (pts) and possible correlation with the clinical parameters of the disease. Moreover, to investigate if the treatment of cultured monocytes isolated from healthy subjects with serum derived from early SSc pts may induce their *in vitro* polarization into M2 macrophages.

Methods: Fifty female SSc pts (mean age 64±13 yrs), fulfilling the EULAR/ACR criteria, and 27 gender-matched healthy subjects (HSs, mean age 57±7 yrs) were considered at the Rheumatology Division of Genoa University after written informed consent. Nailfold videocapillaroscopy (NVC), serum SSc-related antibodies and skin involvement were investigated. Circulating cells belonging to the monocyte populations ($CD45^+$and $CD14^{+-}$ cells) were characterised by flow cytometry using specific surface markers of M2 phenotypes (CD204, CD206, CD163). Each SSc pt had been under stable treatment regimen for at least six months. Cultured monocytes, isolated by negative selection from peripheral blood mononuclear cells (PBMCs) of 8 HSs, stimulated for 48 hrs with 10% of serum of lcSSc pts with "Early" NVC pattern, as well as serum of dcSSc pts with "Active" and "Late" NVC patterns. Cultured monocyte human cell line (THP1) was differentiated into macrophages (5ng/ml of phorbol myristate acetate) and then stimulated with SSc sera. The expression of CD204, CD206 (M2 markers) and CD68 was investigated by immunocytochemistry, whereas MMP9 secretion was investigated by zymography. Statistical analysis was performed using Mann-Whitney and Kruskal-Wallis tests, and correlations were explored by bivariate Pearson's analysis.

Results: In SSc pts the percentage of circulating M2 cells ($CD14^+CD204^+CD163^+CD206^+$cells) was significantly increased compared to both HSs and SSc pts not under immunosuppressive treatment (p<0.05) However, no correlation with skin involvement and SSc-related antibodies was observed. Cultured macrophages stimulated with SSc serum expressed CD204 and CD206 markers compared to the macrophages stimulated with HS serum (CD204 and CD206 double negative cells). Of note, the ability to express M2 markers was already evident in cultured macrophages stimulated with "Early" NVC SSc serum and their expression even increased in macrophages stimulated with "Active" and "Late" NVC sera together with the secretion of MMP9. Same results were observed also in cultured THP1-derived macrophages.

Conclusion: The study confirmed that SSc pts are characterized by a significant increase of circulating M2 cells, suggesting their possible involvement in the pathogenesis of the disease. Interestingly, results insinuate that sera from SSc patients already in an "Early" NVC condition (sera known to contains specific profibrotic molecules such as cytokines, growth factors like TGFb1 or endothelin-1) seem able to induce *in vitro* a profibrotic M2 macrophage phenotype.

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Disclosure of Interests: Stefano Soldano: None declared, Samuele Tardito: None declared, Sabrina Paolino: None declared, Massimo Patanè: None declared, Emanuele Gotelli: None declared, Claudio Corallo: None declared, Carmen Pizzorni: None declared, Greta Pacini: None declared, Federica Goegan: None declared, Alberto Sulli Grant/research support from: Laboratori Baldacci, Carlotta Schenone: None declared, Vanessa Smith Grant/research support from: The affiliated company received grants from Research Foundation - Flanders (FWO), Belgian Fund for Scientific Research in Rheumatic diseases (FWRO), Boehringer Ingelheim Pharma GmbH & Co and Janssen-Cilag NV, Consultant of: Boehringer-Ingelheim Pharma GmbH & Co, Speakers bureau: Actelion Pharmaceuticals Ltd, Boehringer-Ingelheim Pharma GmbH & Co and UCB Biopharma Sprl, Maurizio Cutolo Grant/research support from: Bristol-Myers Squibb, Actelion, Celgene, Consultant of: Bristol-Myers Squibb, Speakers bureau: Sigma-Alpha

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SAT0301

CIRCULATING FIBROCYTES FROM SYSTEMIC SCLEROSIS PATIENTS AS POSSIBLE TARGET OF CTLA4-IG TREATMENT: AN IN VITRO STUDY

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Background: muscle actin (aSMA)$^+$cells involved in the overproduction of extracellular matrix proteins, primarily fibronectin (FN) and type I collagen (COL1) at the level of damaged tissues (1). These cells may originate from different cell types including fibroblasts, endothelial and epithelial cells, and fibrocytes (1). Circulating fibrocytes are bone marrow progenitor cells expressing specific markers of hematopoietic (CD34, CD45, and MHC class II) and stromal cells (COL1 and COL3), chemokine receptors (CCR2, CCR7), and CXCR4 (2). CXCR4 regulates fibrocyte migration into injured tissues allowing their differentiation into fibroblasts/myofibroblasts (2).

In vitro, fibrocytes differentiate from circulating CD14$^+$monocytes showing an antigen-presenting capability through the expression of HLA-DR and costimulatory molecule CD86 (2). CTLA4-Ig fusion protein (abatacept) interacts with CD86 on cell surface of antigen presenting cells (APCs), such as macrophages and endothelial cells (3,4).

Objectives: To investigate the possible effect of CTLA4-Ig treatment on cultured human fibrocytes and skin fibroblasts isolated from the same systemic sclerosis patients (SSc pts).

Methods: Fibrocytes isolated from the peripheral blood mononuclear cells of SSc pts and healthy subjects (HSs) were cultured on fibronectin-coated plates in DMEM at 20% of FBS; for further 8 days (T8) to allow their complete differentiation. Differentiated fibrocytes were maintained in growth medium or treated with CTLA4-Ig at different concentrations (10, 50, 100, and 500µg/ml) for 3 hours. Fibroblasts were isolated from the skin biopsies of the same patients and HSs, cultured until the 3rd passage in RPMI at 10% FBS and then treated with CTLA4-Ig for 24 and 48 hours. Fibrocytes were characterized as CD45$^+$CXCR4$^+$COL1$^+$cells and the expression of CD86 and HLA-DR was also evaluated. The gene expression of aSMA, COL1, CXCR4, TGFb1 and CD86 was investigated by quantitative real-time polymerase chain reaction in cultured fibrocytes and skin fibroblasts. In cultured skin fibroblasts, COL1 and fibronectin synthesis was evaluated by Western blotting.

Results: Treatment with CTLA4-Ig for 3 hours significantly downregulated aSMA and COL1 gene expression in cultured SSc fibrocytes at T8 ($p<0.01$, $p<0.05$ vs. untreated fibrocytes), whereas no modulatory effect was observed on the TGF-beta1 and CXCR4 gene expression. In cultured SSc skin fibroblasts, CTLA4-Ig did not induce any significant effect on CD68, TGFb1, COL1 and FN gene expression as well as COL1 and FN protein synthesis, both after 24 and 48 hours. Of note, these cultured SSc skin fibroblasts showed a low expression of CD86.

Conclusion: Due to their high expression of CD86, circulating fibrocytes seem to be more responsive to CTLA4-Ig treatment than the skin fibroblasts isolated from the same SSc patient.

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SAT0302

INNATE LYMPHOID CELLS INDUCE A FIBROTIC PHENOTYPE OF FIBROBLASTS

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Background: Fibrotic diseases are characterized by excessive extracellular matrix production as a result of immune-mediated permanent fibroblast activation. Innate lymphoid cells type II (ILC2) are an only recently discovered cell type involved in barrier integrity and tissue homeostasis. There is upcoming evidence that ILC2s play a central role in mediating fibrotic diseases.

Objectives: The aim of the study was to further elucidate the role of ILC2s in fibrotic tissue remodeling and fibroblast activation.

Methods: Skin biopsies of patients with systemic sclerosis (SSc) or sclerodermatous chronic graft versus host disease (scGvHD) as well as lung biopsies of patients with idiopathic pulmonary fibrosis (IPF) were analyzed by immunofluorescence (IF) staining. Single cell RNA-sequencing (scRNA-seq) was performed on ILCs from fibrotic skin and lung of bleomycin-challenged mice. Further characterization of ILC2 phenotypes in fibrosis models was done by flow cytometry. *In vitro* culture of fibroblasts and ILC2s was used to study cellular interaction and fibrotic activation. Quantitative realtime-PCR, western blot, IF staining and ELISA were used as readouts.

Results: Two different subtypes of ILC2s were found in skin of SSc and scGvHD patients as well as in lungs of IPF patients with one subpopulation being particularly increased in fibrotic tissue. Single cell RNA-sequencing confirmed the existence of two major populations of ILC2s in experimental fibrosis. One subtype showed features of immature ILC2 progenitors and was actively recruited from the bone marrow during fibrotic tissue remodeling. The other ILC2 subset was highly activated and expressed pro-fibrotic cytokines. These profibrotic ILC2s directly interacted with fibroblasts in a cell contact dependent manner. Semaphorin 4A (SEMA4A) expressed by ILC2s bound to Plexin D1 (PLXND1) on fibroblasts. This interaction resulted into fibrotic imprinting with high expression levels of the transcription factor PU.1 which was recently described as central regulator of the pro-fibrotic gene expression program (Wohlfahrt et al. 2019). Signaling through Jagged 1 (JAG1) and Notch receptor 2 (NOTCH2) was identified as a second mechanism of interaction between fibroblasts and ILC2s. JAG1 expressed by fibroblasts activated NOTCH2 signaling in ILC2s which emphazised the secretion of pro-fibrotic cytokines.

Conclusion: We identified a bidirectional interaction between ILCs and fibroblasts incorporating a vicious circle of fibrotic tissue remodelling. As ILCs are still not accessible as therapeutic targets these results might contribute to the development of new strategies for anti-fibrotic therapies.

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SAT0303

SINGLE-CELL DECONVOLUTION OF SKIN FIBROBLAST HETEROGENEITY IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Fibroblast heterogeneity and homeostasis has long been recognized in patients with systemic sclerosis (SSc). However, there is no common consensus on fibroblast subtypes, lineages, biological properties, signaling, and plasticity, which severely hampers our understanding of SSc pathogenesis.
Objectives: This study is aimed to comprehensively classify skin fibroblast populations from SSc patients.
Methods: We applied single-cell RNA sequencing on skin fibroblasts from two SSc patients and two health control (HC) with matched age and sex. Cell clustering were mainly determined by UMAP with batch effect correction. Differently expressed genes in each cell cluster was analyzed by Gene Set Enrichment Analysis (GSEA).
Results: With an unbiased approach, single-cell transcriptome analyses showed classified and defined eight fibroblast types in SSc skin and six in normal skin. The cell types seldom overlapped between the patients and HC. Extracellular interaction and collagen production were remarkably stronger in SSc fibroblasts. A subgroup of dramatic cell proliferation and activation was defined only in SSc fibroblast. Two subtypes responding inflammatory stimuli were only found in SSc patients. Furthermore, delineation of their differentiation trajectory was achieved by a machine learning method.
Conclusion: This collection of single-cell transcriptomes and the distinct classification of fibroblast subsets provide a new resource for understanding the fibroblast landscape and the roles of fibroblasts in SSc.
References: N/A
Disclosure of Interests: None declared
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SAT0304

TOFACITINIB INHIBITS TGF-Β1-INDUCED ACTIVATED CELL FUNCTIONS OF MYOFIBROBLAST IN HUMAN LUNG FIBROBLAST POPULATIONS

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Background: Connective tissue disease-associated interstitial lung disease (CTD-ILD) is a class of refractory diseases.Non-specific treatment with hormone and immunosuppressive agents is mostly used at present, but the effect is limited and the long-term survival rate is not improved [1],while anti-fibrosis treatments (such as Pirfenidone and Nintedanib) have only recently been approved, the long-term efficacy is still unknown.
Tofacitinib(TOFA), a JAK inhibitor, has recently been used to treat patients with severe dermatomyositis related interstitial pulmonary disease, with significantly improved survival rate [2-4].A basic study showed that TOFA improved interstitial pulmonary disease in mice by promoting the proliferation of myelogenic inhibitory cells [5].However, whether TOFA can affect the migration and invasion of human lung fibroblasts and further research to reveal the mechanism of its inhibition of pulmonary fibrosis has not been reported.
Objectives: To investigate the anti - fibrosis effect of TOFA in CTD-ILD.
Methods: Cell migration and invasion Assays
HLFs were incubated with TOFA for 72h, followed by TGF- β1 for 24h.DMEM serum-free medium was used to determine the cell density to 5. 0 × 10^7/L, 600 uL medium containing 10% fetal bovine serum was added to the lower compartment of Transwell chamber, and 200 uL cell suspension was added to the upper compartment.Incubate in incubator for 12 h.After fixation, staining and sealing, the cells were observed and counted under a microscope. At least 5 random field transmembrane cells were counted in each hole, and the mean value was taken. For the invasion assays, Transwell chamber coated with matrigel was used, and the cell incubation time was 16 h.
Results: 1. Effect of TOFA on HLFs migration function (Figure 1)
The number of cells passing through the biofilm in the three groups was counted. It can be seen that TGF-β1 group significantly increased compared with control group ($^*P < 0.0001$), and TOFA group significantly decreased compared with TGF- β1 group ($^\#P < 0.0001$), suggesting that TOFA can significantly inhibit TGF-β1- induced HLFs migration.
2. Effect of TOFA on HLFs invasion function (Figure 2)

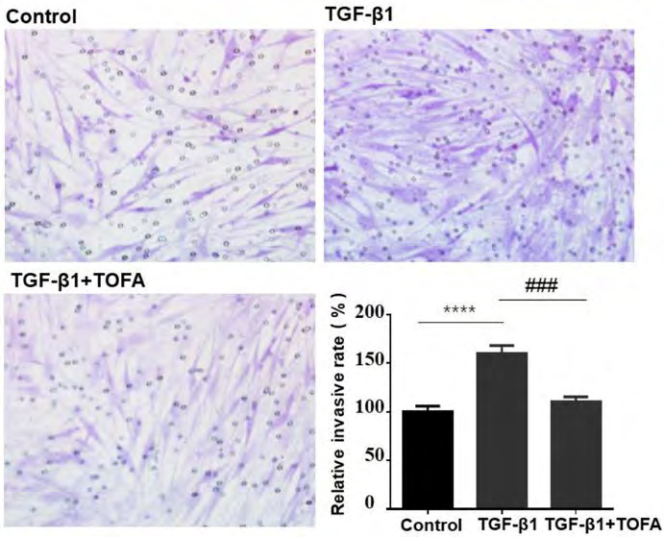


Figure 2. Effect of TOFA on HLFs invasion function(×200).Mean ± SEM. n = 5.

The number of cells passing through the matrigel in the three groups was counted.It can be seen that TGF-β1 group was significantly higher than the control group ($^*P < 0.0001$), and TOFA group was significantly lower than TGF-β1 group ($^\#P < 0.001$), suggesting that TOFA can significantly inhibit the invasion function of HLFs induced by TGF-β1.
Conclusion: TOFA can effectively inhibit the function of HLFs migration and invasion. Although further studies are needed to elucidate the mechanism by which TOFA inhibit the function of HLFs migration and invasion, our study suggests that TOFA has a potential therapeutic effect for CTD-ILD.
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DOI: 10.1136/annrheumdis-2020-eular.1139

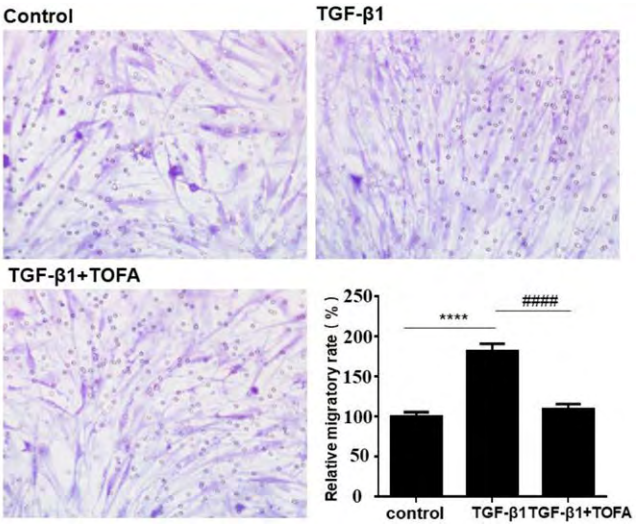


Figure 1. Effect of TOFA on HLFs migration function(×200).Mean ± SEM. n = 5.

SATURDAY, 06 JUNE 2020

Scleroderma, myositis and related syndromes

SAT0305 PERFORMANCE OF HIGH FREQUENCY ULTRASOUND IN THE ASSESSMENT OF SKIN INVOLVEMENT IN SYSTEMIC SCLEROSIS

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Background: The modified Rodnan skin score (mRSS) is the current gold standard for skin assessment in systemic sclerosis (SSc) both in clinical trials and practice. High frequency ultrasound (HFUS) has been suggested to offer a quantitative assessment of skin thickness in SSc by several studies, however results are inhomogeneous with regards to the machine used, number of imaged sites, as well as the various stages of skin involvement.
Objectives: Aim of this cross-sectional study was to compare performance of HFUS in the assessment of skin involvement in diffuse cutaneous SSc (dcSSc) patients, at different disease stages, as compared with healthy controls (HC).
Methods: Dorsal finger, hand, forearm and upper arm skin of consecutive dcSSc patients, at different disease stages, and of matched-HC were scanned bilaterally using HFUS. Two investigators, expert in MSK ultrasound, blinded to the clinical details, measured skin thickness using Esaote MyLab70 equipped with a 22 MHZ probe. Clinical involvement was assessed by a blinded operator using the mRSS and results were compared with imaging data. Statistical analysis was performed using GraphPad Prism software V.7.0.
Results: A total of 704 HFUS images were obtained from 22 dcSSc patients [20 Female, mean age 49 (±11) years, 12 with ≤ 5 years disease duration] and 22 HC [20 Female, mean age 50.7 (±6.7) years]. Skin thickness was significantly higher in SSc patients than in HC at fingers ($p<0.0001$) and hands ($p<0.0001$), while no significant difference was found at the forearms and upper arms ($p>0.05$). HFUS showed a good discriminative ability between SSc and HC skin at fingers and hands (AUC 0.91, 0.81, 0.6 and 0.65 for fingers, hands, forearms and upper arms respectively). When analysing the subgroup of SSc patients with ≤5 years disease duration, HFUS showed a slightly lower performance in discriminating between SSc without clinical skin involvement (site mRSS=0) and HC (AUC 0.68, 0.57, 0.68 for hands, forearms and upper arms respectively). Mean HFUS skin thickness significantly correlated with mRSS at site of analysis (hand: $r=0.78$, $p=<0.0001$; forearm: $r=0.47$, $p=0.0013$; upper arm: $r=0.52$, $p=0.0003$) and total mRSS (hand: $r=0.53$, $p=0.0002$; forearm: $r=0.63$, $p<0.0001$; upper arm: $r=0.63$, $p<0.0001$). No significant correlation was found between finger skin thickness and mRSS (both local and total, $p>0.05$). Interobserver reliability for skin thickness was good to excellent at all sites with intraclass correlation coefficient ranging between 0.79 and 0.94.
Conclusion: HFUS of the skin is a reliable measure of skin involvement in SSc. Studies with higher number of patients with different clinical features are needed to explore the potential of HFUS to discriminate between healthy and SSc skin, including sites at a preclinical stage of involvement.
Disclosure of Interests: None declared
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SAT0306 SEMIQUANTITATIVE AND QUANTITATIVE ANALYSIS OF LUNG CT IN THE ASSESSMENT OF INTERSTITIAL LUNG DISEASE IN IDIOPATHIC INFLAMMATORY MYOPATHIES WITH A FOCUS ON ANTISYNTHETASE.

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Background: Interstitial lung disease (ILD), is common in patients with idiopathic inflammatory myopathies (IIM) and strongly impact on patients' morbidity and mortality. Patients with anti-aminoacyl-transfer RNA-synthetases (anti-ARS) antibodies are associated with an increased risk of ILD.
Objectives: Defining the radiological characteristics of IIM patients, with special focus on serological groups, through qualitative, semiquantitative and quantitative analysis of lung CT.
Methods: This was a prospective study conducted from 2016 to 2019. Ninety-eight IIM patients (35 men, 63 women) were included. Myositis specific autoantibodies (MSA) were assessed with Myositis Prophyle III (Euroimmune, Lubeck).
Each patient had a baseline CT; the total score of Warrick (WS) was obtained at semiquantitative analysis. The radiological scores ILD% (interstitial lung disease %) and PVRS% (pulmonary vascular related structure) were the result of quantitative analysis in 61 patients (CALIPER). Pulmonary function tests (PFTs) included TLC%, FVC% and DLCO% (65 patients). The analysis was conducted in the whole group and divided in subgroups based on their MSA pattern: in particular anti-ARS (Group 1) and patients negative to MSA (Group 2) were analysed.
Results: Positive correlations between ILD% and PVRS% ($Rho=0.916$; $\rho=0.000$), WS and ILD% ($Rho=0.663$; $\rho=0.000$) and WS and PVRS% ($Rho=0.637$; $\rho<0.001$) were found.
The most relevant inverse correlations were found between ILD% and DLCO% ($Rho=-0.590$; $\rho=0.001$), PVRS% and DLCO% ($Rho=-0.549$; $\rho<0.001$) and WS and DLCO% ($Rho=-0.471$; $\rho<0.001$).
Statistically significant higher values of WS, ILD% and PVRS% were found in Group 1 (WS=15, ILD%=11 and PVRS%=3.5), compared to Group 2 (WS=2.5, ILD%=0.84 and PVRS%=2.2). NSIP pattern resulted dominant represented in the two groups (80% Group 1, 75% Group 2). No statistically significant differences of DLCO%, FVC% and TLCO% were found.
Conclusion: The inverse correlations between the radiological scores and the functional data TLC% and DLCO% ($\rho<0.001$) confirm the role of lung CT in the clinical management of ILD in IIM patients, and may represent a promising tool for clinical trials. For the first time anti-ARS and serological negative patients were defined through qualitative, semiquantitative and quantitative analysis of lung CT. Further study should be conducted in order to define the prognostic value of the quantitative analysis of lung CT in the follow up of IIM patients.
Disclosure of Interests: None declared
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SAT0307 PROGRESSION OF SUBCLINICAL MYOCARDIAL INVOLVEMENT IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a progressive autoimmune disease affecting the skin as well as internal organs, including the heart. A few studies have identified a subclinical heart involvement in patients with no pulmonary hypertension. Changes in myocardial deformation are consistent with the idea of SSc-related cardiomyopathy as a primary condition affecting the heart globally through microvascular dysfunction and subsequent myocardial fibrosis.
Objectives: The aim of the present study is to describe the progression of myocardial deformation in patients with SSc and no overt cardiac disease.
Methods: Prospective longitudinal study enrolling consecutive SSc patients referred to the Clinica Medica, University Hospital 'Ospedali Riuniti', Ancona, Italy, from February 2016 to December 2018. All patients fulfilled the 2013 ACR/EULAR classification criteria for SSc. Patients with structural heart disease, heart failure, atrial fibrillation or pulmonary hypertension were excluded. Disease subset, antibodies pattern, cardiovascular risk factors and involvement of other organ systems were recorded for each patient. An echocardiographic exam was performed for all patients at baseline and during their follow-up evaluation. Standard and speckle-tracking derived variables for the systolic and diastolic function of the left ventricle (LV) and right ventricle (RV) were acquired. Speckle tracking analysis software (EchoPAC 13.0; GE Medical Systems, Milwaukee, USA) was used to assess the GLS of the left and right ventricle, excluding the ventricular septum from right ventricular GLS calculations.
Results: Seventy-two patients (68 females, age 56.6±15.4 years) were enrolled. Common echocardiographic parameters of left and right systolic function were within normal range at baseline and did not change during follow-up. Mean GLS, however, worsened for both left (from -19.8±3.5% to -18.7±3.5%, p=.034) and right ventricle (from -20.9±6.1% to -18.7±5.4%, p=.013) during a median follow-up of 20 months (1st-3rd quartile 12-24 months). The increased impairment registered in SSc patients was homogenous across endocardial layers (LV from -22.5±-3.9 to -21.4±3.9, p=.041; RV from -24.2±6.2 to -20.6±5.9, p=.001), mesocardial layers (LV -19.7±3.6 to -18.7±3.5, p=.043; RV from -21.3±5.9 to -18.8±5.7, p=.012) and epicardial layers (LV from -17.1±3.0 to -16.4±3.1, p=.112, RV -18.8±6.3 to -16.0±8.4, p=.035), as well

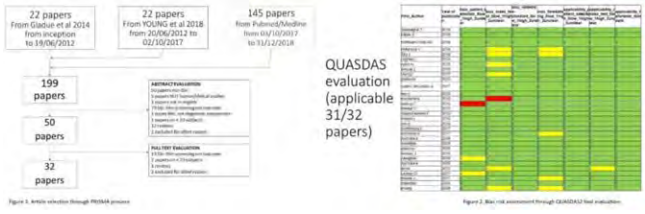
as myocardial segments. No difference in progression rate was observed stratifying patients according to disease subset or other clinical parameters.
Conclusion: GLS impairment progressed over a 20-month follow-up period in a cohort of SSc patients without clinically overt cardiac involvement. Further studies are needed to assess the significance of subclinical heart involvement and its progression in patients with SSc.
Disclosure of Interests: : None declared
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SAT0308 SCREENING TOOLS FOR PULMONARY ARTERIAL HYPERTENSION (PAH) IN SYSTEMIC SCLEROSIS (SSC): A SYSTEMATIC LITERATURE REVIEW (SLR).

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Background: in SSc, PAH has a high morbidity and mortality burden. Therefore, screening and early detection are pivotal to achieve an early diagnosis of PAH.
Objectives: to search the literature for all screening modalities for SSc-PAH in reference to right heart catheterization as diagnostic gold standard.
Methods: papers from 2 previously published SLRs [22 from *Glaude et al* (1) – from inception to 19/06/2012 - and 22 from *Young et al 2018* – from 20/06/2012 to 02/10/2017] were included. The articles' database was integrated with a systematic search on Pubmed, EMBASE, Web of Science for papers published from 03/10/2017 to 31/12/2018. A total of 199 papers were reviewed and 32 were finally extracted. Bias risk was assessed through QUADAS2 tool.
Results: 167 papers were excluded from data extraction mainly for PAH screening non as main focus or for non-including SSc patients. The 32 papers extracted presented a low bias risk according to QUADAS2. Screening methods reported were:

- Echocardiographic parameters in 31/32 studies, in particular systolic pulmonary arterial pressure (sPAP) in 22 papers; 40 mmHg was the most frequently used cut-off (in 12/22 papers); sPAP was part of a composite algorithm in 9/22 papers. Among others, tricuspid regurgitation velocity (TRV) was used in 6/31 (as part of composite 5/6) and right atrial pressure (RAP) in 3/31 papers.
- Pulmonary function tests parameters in 22/32 papers, with % predicted Lung diffusion for carbon oxyde (DLco) in 21 papers, with a 50% cut-off in 11/21 and as part of composite algorithm in 13/21 studies. Moreover, walked distance at six minutes walking test was a screening parameter in 3/32 papers.
- Serum biomarkers in 12/32 papers, with anti-centromere antibodies (6/12), NT-proBNP (6/12) and uric acid (5/12) being the most frequently reported.
- Clinical parameters in 15/32 papers, with unexplained dyspnoea in 9/15 and telangiectasias in 5/15 papers.
- Composite algorithms were used in 18/32 manuscripts: among them, DETECT (5/18), ESC/ERS 2009 (4/18) or 2015 (3/18) guidelines, ASIG (2/18) e ITINERair (1/18). In different cohorts, DETECT and ASIG showed higher sensitivity and negative predictive value than ESC/ERS 2009.



Conclusion: in the literature, the screening of SSc-PAH is largely investigated by echocardiographic parameters. In particular, sPAP and TRV, both as single items or part of a composite algorithm, including also serum biomarkers, clinical and functional parameters, are the most frequent parameters evaluated.
(supported by an Actelion Pharmaceuticals unrestricted research grant)
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Disclosure of Interests: Cosimo Bruni Speakers bureau: Actelion, Eli Lilly, Giacomo De Luca Speakers bureau: SOBI, Novartis, Celgene, Pfizer, MSD, Maria Grazia Lazzaroni: None declared, Elisabetta Zanatta: None declared, Gemma Lepri: None declared, Marco Matucci-Cerinic Grant/research support from: Actelion, MSD, Bristol-Myers Squibb, Speakers bureau: Acetelion, Lilly, Boehringer Ingelheim
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SAT0309 CARDIAC MAGNETIC RESONANCE IMAGING ELEVATED NATIVE MYOCARDIAL T1 IS PREDICTIVE FOR THE DEVELOPMENT OF MYOCARDIAL DYSFUNCTION IN SYSTEMIC SCLEROSIS

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Background: All patients included in the study fulfilled the ACR/EULAR classification criteria for SSc. We prospectively included patients who underwent at least two CMR at 1.5T, including native T1 and T2 mapping (which give account for myocardial fibrosis and myocardial edema respectively), left and right ventricles morphology and functional assessment, and Late Gadolinium Enhancement (LGE) as a part of routine follow-up between 2015 and 2019.
Objectives: To evaluate the prognostic value of initial abnormal T1 mapping.
Methods: All patients included in the study fulfilled the ACR/EULAR classification criteria for SSc. We prospectively included patients who underwent at least two CMR at 1.5T, including native T1 and T2 mapping (which give account for myocardial fibrosis and myocardial edema respectively), left and right ventricles morphology and functional assessment, and Late Gadolinium Enhancement (LGE) as a part of routine follow-up between 2015 and 2019.
Results: Sixty-three patients underwent at list two CMR during the study period. Forty-three patients were women. Mean age was 52.5±15.5 years old. Follow-up duration between the initial and the follow-up CMR was 14.5±11.5 months. Forty-one had diffuse SSc. The mean native T1 was 1066.8 ±44.6 ms. Twenty-one patients suffered from cardiac clinical manifestations. Nine patients died during the follow-up. Thirty patients (47.6%) had elevated T1 (ET1) with mean T1 1105.4±36.7 ms at the time of initial CMR. Initial ET1 was clearly correlated with: 1/ alteration of Left Ventricle (LV) Ejection fraction (EF) (r=0.5, p<0.0001) during the study period, 2/LV dilatation at initial screening and follow up (r=0.22, p=0.03 and r=0.3, p=0.02). Regarding Right ventricle, initial ET1 was correlated with initial Right Ventricle (RV) dilatation (r=0.3, p=0.02) but neither with RV volume nor RVEF at follow-up. Interestingly, initial ET1 correlated with pericardial effusion (r=0.3, p=0.003) which is known to be a pejorative prognostic factor. Seventeen patients (28%) had LGE but the ET1 at initial screening and follow-up was not correlated with LGE.
Six patients had elevated T2 (ET2) which correlated with initial and follow up LV dilatation (r=0,32, p=0.002 and r=0.5, p<0.0001 respectively) but not with LVEF during the period study. Among other parameters, initial increased BNP was correlated with follow up ET1 LVEF and RVEF (r=0.4, p=0.01; r=0.35, p=0.007; r=0,37, p=0.005 respectively). In the same way, initial Pulmonary Arterial Hypertension (PAH) was correlated with follow up ET1 (r=0.3, p=0.02). Initial ET1 did not correlate with age, sex, cardiovascular risk factors, cardiac manifestations or death.
Conclusion: Assessment of diffuse myocardial fibrosis by native T1 is predictive of the occurrence of cardiac dysfunction at the follow-up as initial ET1 was associated with decreased left ventricular function and LV and RV dilatations). These data highlights the potential role of CMR with T1mapping in initial screening and at the follow-up and provides new insights in the cardiac SSc follow up strategy.
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SAT0310

ANTI-CENTROMERE ANTIBODY ISOTYPE LEVELS AS BIOMARKER FOR DISEASE PROGRESSION IN SUBJECTS AT RISK TO DEVELOP SYSTEMIC SCLEROSIS

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Background: Presence of anti-centromere antibodies (ACA) generally associates with a better prognosis than many other systemic sclerosis (SSc) associated autoantibodies. However, presentation of the disease can be very heterogeneous and prediction of the disease course is challenging. Some older studies suggest a possible association between clinical characteristics and isotypes of ACA in patients with SSc. It is unknown whether ACA can serve as biomarker for future SSc development.

Objectives: To evaluate the clinical course of very early SSc and to assess whether ACA isotype levels can identify subjects that will progress to definite SSc.

Methods: ACA IgG+ patients with very early SSc (defined as presence of ACA IgG AND Raynaud and/or puffy fingers and/or abnormal nailfold capillaroscopy but not fulfilling ACR 2013 criteria) from five prospective SSc cohorts (Leiden, Zurich, Oslo, Bordeaux, Ghent) were included. Presence and levels of ACA IgG, IgM and IgA were determined at first clinical assessment and clinical course was evaluated annually. Disease progression to definite SSc, which was defined as fulfillment of the ACR 2013 criteria for SSc, and included any development of: digital ulcers (DU), interstitial lung disease (ILD) assessed by high resolution chest tomography, pulmonary arterial hypertension assessed by right heart catheterization, gastro-intestinal involvement, renal crisis or myocardial involvement was determined. ACA response characteristics were compared between very early SSc patients that progressed to definite SSc and those who did not. Logistic regression was performed to determine whether ACA response characteristics can predict progression to definite SSc, with adjustment for age and follow-up duration.

Results: In total 92 subjects were included with median follow-up (FU) of 3 years (table 1); 39% progressed to definite SSc, mostly based on the development of skin involvement (77%). Twenty-three percent of patients developed lung involvement, 11% DU, 17% gastro-intestinal involvement and 4% myocardial involvement. Progression on more than one organ system was present in 31% of the very early SSc patients. In the multivariable logistic regression, with adjustment for age and follow-up duration, ACA IgG levels at baseline were significantly associated with progression to definite SSc (OR 3.0 (1.1-8.8)). Likewise, a trend was observed for higher ACA IgM levels (OR 1.8 (0.9-3.5)) in the very early SSc patients progressing to definite SSc (figure 1).

Table 1. Baseline characteristics and ACA isotype levels in patients with very early SSc, and between progressors and non-progressors. * p value < 0.05.

	Progressors (n=35)	Non-progressors (n=57)
Female, n(%)	32 (91)	50 (91)
Age, mean (SD)	56 (14)	53 (13)
Disease duration since non Raynaud phenomenon, median(IQR) in years	3 (0.8-10)	2 (0.6-7)
Follow-up duration in years, median (IQR)	**4 (2-6)**	**2 (1-3)***
Abnormal Nailfold videocapillaroscopy, n(%)	17 (65)	27 (60)
IgA level [aU/mL], median (IQR)	63 (34-120)	75 (35-144)
IgM level [aU/mL], median (IQR)	131 (32-585)	79 (18-391)
IgG level [U/mL], median (IQR)	**342 (162-720)**	**195 (93-488)***

Conclusion: In this study we illustrate that 39% of the ACA positive very early SSc subjects progress to definite SSc within median 4 years. We identified higher ACA IgG level as a predictive biomarker for progression to definite SSc indicating that it might be a useful biomarker for risk stratification in clinical practice.

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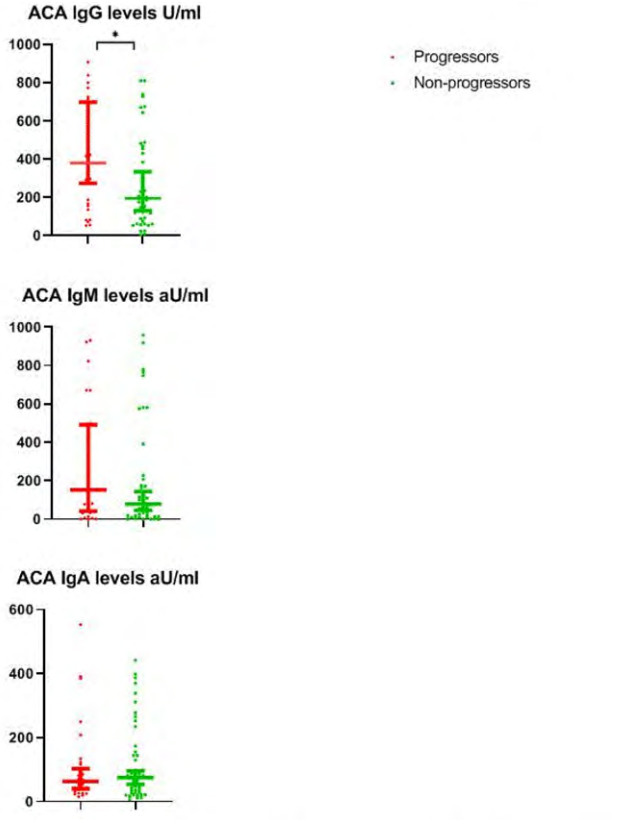


Figure 1. ACA isotype levels in the progressors and the non-progressors. ACA IgG levels were significantly different between the two groups (*p =0.02). On the X-as the two groups (progressors vs. non-progressors are shown) on the Y-axis the levels of ACA isotypes are shown in U/ml for ACA IgG, aU/ml for ACA IgM and ACA IgA.

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SAT0311

BIOELECTRICAL IMPEDANCE VECTOR ANALYSIS FOR NUTRITIONAL STATUS ASSESSMENT IN SYSTEMIC SCLEROSIS AND ASSOCIATION WITH DISEASE CHARACTERISTICS

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Background: Bioelectrical impedance vector analysis (BIVA) is a common non-invasive method for estimating body composition which ultimately allows to obtain information on subject's nutritional status. So far no data about the use of BIVA in patients with systemic sclerosis (SSc) have been published.

Objectives: We used BIVA in a cohort of SSc patients in order to assess their nutritional status and any correlation with the various clinical characteristics of the disease, also evaluating the differences with the general population.

Methods: We collected data from consecutive patients diagnosed with SSc according to EULAR/ACR criteria and from healthy controls (HC) matched for age and sex. Patients underwent BIVA for the assessment of fat mass (FM), free fat mass (FFM), total body water (TBW), extracellular water (ECW), body cellular mass (BCM), basal metabolic rate (BMR) and ECM/BCM ratio, an early index of protein catabolism. Data included anthropometric and clinical features, Body Mass Index (BMI) and specific organ involvement with particular attention to gastrointestinal symptoms. Laboratory parameters, including haemoglobin and albumin levels, were also collected. Additionally, patients completed the UCLA GIT 2.0 questionnaire.
Results: Data from 50 SSc patients (92% female; mean age 61.1±12.5 years; mean disease duration 13.4±10.2 years) and from 50 HC were compared. BIVA revealed that SSc patients presented a significant reduction in BMR, BCM and ECW values compared to HC (p<0.001 for all). The former also exhibited a higher ECM/BCM ratio (p<0.001). No significant differences regarding FM, FFM, TBW and BMI were found between the two groups. Among the cohort of SSc patients, a direct correlation was found between age and ECW (p=0.001; ρ=0.473) and between disease duration and FM (p=0.023; ρ=0.325), whereas age inversely correlated with BMR (p=0.012; ρ=-0.357). Patients with anaemia and/or hypoalbuminemia had significantly reduced BMR, BCM and TBW values; those with hypoalbuminemia also had elevated ECW levels (p=0.001). No other significant associations with BIVA values were found among the laboratory findings and among the gastrointestinal complaints. Results showed relevant interrelations between BIVA parameters and the SSc-related involvement of different organs, e.g. digital ulcers, interstitial lung disease and pulmonary arterial hypertension (See Table 1). In addition, a higher skin involvement inversely correlated with FM (p=0.038; ρ=-0.387). The only correlation that emerged from the UCLA GIT 2.0 questionnaire was the inverse relationship between TBW and GIT-reflux (p=0.017; ρ=-0.385). Four patients died during the study: they had significantly lower BMR and BCM, with an increased ECW.

Table 1.

	Ongoing digital ulcers	History of digital ulcers	Interstitial lung disease	Pulmonary arterial hypertension	Heart involvement
FM	p=0.006	ns	p=0.042	ns	ns
FFM	p=0.019	p=0.046	ns	ns	ns
TBW	p<0,001	ns	p=0.007	ns	ns
ECW	ns	ns	p=0.015	p=0.004	p=0.02
BCM	p=0.01	p=0.047	p=0.016	p=0.013	p=0.03
BMR	p=0.002	p=0.036	p=0.004	p=0.015	ns
ECM/BCM	ns	ns	p=0.034	ns	ns

Conclusion: BIVA has shown that SSc patients have a worse nutritional status than HC. The parameters obtained with BIVA in SSc patients correlate with serological malnutrition markers (haemoglobin and albumin), with various organ-specific SSc manifestations (cardiopulmonary involvement and digital ulcers) and with mortality. BIVA could therefore play a role in the prognostic stratification of SSc patients.
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SAT0312 SUBCLINICAL ATHEROSCLEROSIS IN SYSTEMIC SCLEROSIS AND RHEUMATOID ARTHRITIS: A COMPARATIVE MATCHED-COHORT STUDY

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Background: Systemic autoimmune inflammatory disorders confer a higher risk of cardiovascular (CV) disease leading to increased morbidity and mortality compared to the general population. CV risk in Systemic Sclerosis (SSc) has not been studied so extensively as in other diseases, such as Rheumatoid Arthritis (RA), and the real impact of CV disease on SSc prognosis remains unknown. Surrogate markers of atherosclerosis namely carotid intima media thickness (cIMT) and pulse wave velocity (PWV) are impaired in some but not all studies in SSc patients.
Objectives: The aim of the study was to investigate the prevalence of subclinical atherosclerosis assessed by cIMT and PWV between two well-characterized SSc and RA cohorts.
Methods: Consecutive SSc patients attending the Scleroderma Clinic were compared with RA patients recruited in the Dudley Rheumatoid Arthritis Co-morbidity Cohort (DRACCO), a prospective study examining CV burden in RA. Cardiovascular risk was assessed using the QRisk3 and cIMT, Augmentation Index (AIx75) and central systolic and diastolic blood pressure were measured in all participants. Propensity score matching, was utilized to select patients from the two cohorts with similar demographic characteristics, CV risk factors (smoking, hypertension, obesity, dyslipidemia, diabetes) and inflammatory load. Unpaired t-test and Chi-square test of independence were applied.
Results: Fifty five age- and sex-matched SSc and RA patients with similar distribution of CV risk factors were included. No difference was demonstrated between SSc and RA regarding cIMT and AIx75% (0.65 vs 0,61mm p=0,17 and 33.4 vs 31,7 p=0,397 respectively). However average QRisk3 score was significantly higher in the RA compared to the SSc group (P<0.05).
Conclusion: The results of this comparative study show that subclinical atherosclerosis is comparable between individuals with SSc and RA, a systemic disease with well-defined high atherosclerotic burden. RA patients have higher CV risk (QRisk3 algorithm) suggesting that disease-specific factors such chronic high-grade inflammation may influence the CV risk in this population.
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Table 1. Demographic and cardiovascular risk factors of the matched patients

	RA	SSc	P
	N=55	N=55	
Age	63.6 (14.8)	61.3 (10.9)	0.140
Female	49 (89.1%)	53 (96.4%)	0.438
Smoking	10 (18.2%)	13 (23.6%)	0.5
Diabetes	0 (0.00%)	1 (1.82%)	0.364
Hyperlipidemia:	7 (12.7%)	6 (10.9%)	1.000
Hypertension:	23 (41.8%)	19 (34.5%)	0.441
ESRD	20.4 (18.4)	22.0 (19.1)	0.666
CRP	8.38 (11.6)	6.65 (30.2)	0.692

Table 2. Comparison of IMT, AIx75, Framingham and QRISK3 between matched patients

	RA	SSc	P
	N=55	N=55	
IMT right average	0.65 (0.17)	0.61 (0.12)	0.175
IMT left average	0.67 (0.15)	0.64 (0.13)	0.214
IMT average	0.66 (0.14)	0.63 (0.10)	0.137
AIX 75% (%)	33.4 (9.23)	31.7 (10.8)	0.397
Framingham risk			**< 0.001**
< 10%	9 (31.0%)	37 (74.0%)	
10 – 20%	12 (41.4%)	9 (18.0%)	
20 – 30%	3 (10.3%)	4 (8.00%)	
>30%	5 (17.2%)	0 (0.00%)	
QRISK3	18.2 (15.3)	11.1 (10.6)	**0.006**

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SAT0313 CORRELATION BETWEEN PROGRESSION OF SKIN FIBROSIS AND PROGRESSION OF INTERSTITIAL LUNG DISEASE (ILD) IN PATIENTS WITH SSC-ILD: DATA FROM THE SENSCIS TRIAL

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Background: In the SENSCIS trial in patients with SSc-ILD, nintedanib reduced the rate of decline in FVC over 52 weeks vs placebo, with no difference between groups in change in mRSS.
Objectives: Analyse correlation between progression of skin fibrosis and progression of SSc-ILD in the SENSCIS trial.
Methods: Patients with SSc-ILD were randomised to receive nintedanib or placebo until the last patient reached week 52 but for ≤100 weeks. We calculated Spearman correlation coefficients between FVC (mL) at baseline and change from baseline in mRSS, mRSS at baseline and change from baseline in FVC (mL), and changes from baseline in mRSS and FVC at weeks 52 and 100 in all patients. We analysed the rate of decline in FVC (mL/year) in patients who did and did not have progression of skin fibrosis (relative change from baseline in mRSS >25% and absolute change from baseline >5 points) at week 52.
Results: In the nintedanib (n=288) and placebo (n=288) groups, respectively, mean (SD) baseline FVC (mL) was 2459 (736) and 2541 (816) and mRSS was 11.3 (9.2) and 10.9 (8.8); 53.1% and 50.7% had dcSSc;18.4% and 16.0% had progression of mRSS at week 52. No meaningful correlations were observed in analyses between mRSS and FVC (Table). The mean (SE) annual rate of decline in FVC in the placebo group was similar in patients who did and did not have progression of mRSS (-95.2 [27.1] and -91.4 [15.7] mL/year, respectively). The effect of nintedanib vs placebo on reducing the rate of decline in FVC was numerically more pronounced in patients who did not have progression of mRSS vs those who did (difference [95% CI] 44.3 mL/year [0.6, 88.1] vs 24.6 [-53.7, 102.9]), but the interaction p-value (0.66) did not indicate heterogeneity in treatment effect between subgroups.
Conclusion: In the SENSCIS trial, the proportion of patients who had progression of skin fibrosis over 52 weeks was low, without significant differences between placebo and nintedanib. No meaningful correlations were observed between skin fibrosis at baseline or progression of skin fibrosis and progression of SSc-ILD. The rate of decline in FVC was similar between patients who did and did not have progression of mRSS. These findings suggest that in the overall patient population in the SENSCIS trial, progression of skin fibrosis and progression of ILD were distinct manifestations of disease progression.

Table:

	FVC at baseline and change from baseline in mRSS		mRSS at baseline and change from baseline in FVC		Changes from baseline in mRSS and FVC	
	N	Correlation*	N	Correlation*	N	Correlation*
Week 52						
Nintedanib	247	0.11 (-0.01, 0.23)	241	-0.08 (-0.20, 0.05)	238	-0.07 (-0.19, 0.06)
Placebo	254	0.12 (-0.00, 0.24)	257	-0.15 (-0.27, -0.03)	252	0.03 (-0.09, 0.15)
Week 100						
Nintedanib	73	0.21 (-0.02, 0.42)	73	-0.06 (-0.29, 0.17)	70	0.06 (-0.17, 0.30)
Placebo	66	0.28 (0.04, 0.49)	73	0.04 (-0.19, 0.27)	66	-0.14 (-0.37, 0.10)

*Spearman correlation coefficient (95% CI)

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SAT0314 TIMED FUNCTION TESTS ARE AN ALTERNATIVE TO MMT8 AND FI-2 IN INFLAMMATORY MYOSITIS - AN OBSERVATIONAL COHORT STUDY

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Background: Inflammatory myositis are heterogenous group of diseases affecting skeletal muscles and multiple different organs[1]. Manual muscle testing (MMT) is the common tool used for assessment of muscle strength. Its limitations include poor sensitivity to change, floor/ceiling effect, and under representation of certain important muscle groups[2]. Functional index 2(FI-2) is an objective measure of dynamic repetitive muscle function at 11 proximal and distal muscle groups which correlates well with patient-reported physical function[3]. Since MMT8 is inadequate and FI-2 takes longer time to administer, several timed tests to assess muscle function, endurance and fatiguability like the 2- minute walk test (2MWT) or 30s raise from a chair test and 30s arm rise test are viable alternatives to be tested. Data looking at the performance of these tests are limited to small controlled studies.
Objectives: To study correlation of timed tests with MMT8 and FI-2 in assessing muscle strength, endurance at baseline and at 3 months of therapy.
Methods: An observational cohort study, included 19 patients with polymyositis and dermatomyositis attending OPD and IPD service of tertiary center. Patients with nclusion body myositis, overlap myositis, chronic kidney disease, coexisting myocarditis, sepsis, malignancy, pregnancy were excluded. MMT8, FI-2 and Timed function tests were done at baseline and after 3 months.
Results: The study had 19 patients of which 6 were polymyositis and 13 were dermatomyositis. Male to female ratio was 1:2.1. Anti-cell antibody was positive in 16 patients. The mean MMT8 of the study group at baseline was 60.84±16.77 and after 3 months was 67.05±11.7. Out of 19 patients, all received prednisolone as induction agent followed by Methotrexate in 13, cyclophosphamide in 9, azathioprine in 5, Rituximab by one patient. Mean scores of 30s arm lift, 30s rise from chair test and 2 min walk test were 11.7±6.39,14±7.29,101.5± 46.48 respectively at baseline and 13.05±6.5,15.6±7.1,117.84±38.4 after 3 months.

Table 1. Spearman Rho Correlation between timed function tests and MMT8, FI-2, patient and physician VAS

	Δ 30s rise from chair test	Δ 30s arm lift test	Δ 2 min walk test
Δ MMT8	0.382	0.337	**0.724****
Δ FI-2			
Hip flexion right	0.388	0.413	0.314
Hip flexion Left	**0.503***	0.416	0.422
Neck flexion	**0.600****	**0.590****	**0.610****
Shoulder flexion right	0.183	0.300	0.239
Shoulder flexion left	0.393	0.222	0.207
Shoulder abduction right	0.236	0.222	0.348
Shoulder abduction left	0.182	0.236	0.273
Step test right	**0.744****	**0.489***	0.326
Step test left	0.840	**0.500***	0.378
Heel rise	0.442	0.294	0.388
Toe rise	0.446	0.291	0.419
Δ Physician VAS	**-0.508***	**-0.506****	-0.215
Δ Patient VAS	**-0.600****	**-0.597****	-0.249

Δ → change from baseline to 3 months *→ Correlation is significant at the 0.05 level **→ Correlation is significant at the 0.01 level

Conclusion: Timed function tests correlated well with MMT 8 and parameters with in FI-2. Thus these tests are good alternatives in assessing disease activity and response assessment in inflammatory myositis.

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SAT0315 INHIBITION OF MICROSOMAL PROSTAGLANDIN E SYNTHASE-1 (MPGES-1) BY GS-248 REDUCES PROSTAGLANDIN E2 BIOSYNTHESIS WHILE INCREASING PROSTACYCLIN IN HUMAN SUBJECTS

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Background: Microsomal prostaglandin E synthase-1 (mPGES-1) catalyzes the formation prostaglandin (PG) E_2 from cyclooxygenase derived PGH_2 [(1, 2)]. Inhibition of mPGES-1 leads to reduction of pro-inflammatory PGE_2, while in vessels there is a concomitant increase of vasoprotective prostacyclin (PGI_2) via shunting of PGH_2 [(3,4)]. Apart from relieving symptoms in experimental animal models of inflammation, inhibitors of mPGES-1 cause relaxation of human medium sized arteries[(4)] and resistance arteries[(5)]. The prostaglandin profile following mPGES-1 inhibition, explains the anti-inflammatory effects and also opens for the possibility of treating inflammatory diseases with concomitant vasculopathies. GS-248 is a potent and selective inhibitor of mPGES-1 exhibiting sub-nanomolar IC_{50} in human whole blood *ex vivo*.

Objectives: To evaluate safety, tolerability, pharmacokinetics and pharmacodynamics of GS-248.

Methods: Healthy males and females (age 18–73 years) were included in the study. Six cohorts were administrated single oral doses of 1-300mg GS-248 (n=36) or placebo (n=12), three cohorts were administered once daily doses of 20-180mg GS-248 (n=18) or placebo (n=12) over ten days. In addition, 8 subjects were treated in a separate cohort with 200mg celecoxib bid for ten days. Blood samples were drawn for measurement of GS-248 exposure and production of PGE_2 after LPS incubation *ex vivo*. The content of PGE_2 and PGI_2 metabolites was measured in urine. All analyses were performed by LC-MS/MS.

Results: GS-248 was safe and well tolerated at all tested dose levels. Maximum plasma concentration was achieved 1 - 2.5 hours after dosing, and half-life was about 10 hours. Induced PGE_2 formation *ex vivo,* catalyzed by mPGES-1, was completely inhibited for 24 hours after a single low dose (40mg) of GS-248. In urine, GS-248 dose-dependently reduced the excretion of PGE_2 metabolite by more than 50% whereas the excretion of PGI_2 metabolite increased more than twice the baseline levels. In the celecoxib cohort urinary metabolites of both PGE_2 and PGI_2 were reduced with approx 50%.

Conclusion: GS-248 at investigated oral doses was safe and well tolerated. There was a sustained inhibition of LPS induced PGE_2 formation in whole blood. In urine, there was a metabolite shift showing reduced PGE_2 and increased PGI_2, while celecoxib reduced both PGE_2 and PGI_2 metabolites. This suggests that selective inhibition of mPGES-1 results in systemic shunting of PGH_2 to PGI_2 formation, leading to anti-inflammatory and vasodilatory effects, while preventing platelet activation. The results warrant further evaluation of GS-248 in inflammatory conditions with vasculopathies such as Digital Ulcers and Raynaud's Phenomenon in Systemic Sclerosis.

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SAT0316 ANTI-PM/SCL ANTIBODIES IN SYSTEMIC SCLEROSIS: CLINICAL ASSOCIATIONS IN THE RESCLE COHORT

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Background: Anti-PM/Scl antibodies are associated to systemic sclerosis (SSc) but are not specific to SSc. The true prevalence of anti-PM/Scl antibodies in SSc is unknown, ranging from 2.5% to 12.5%. An association between anti-PM/Scl antibodies with muscular involvement, pulmonary fibrosis, calcinosis, and a relatively benign prognosis have been described.

Objectives: To compare the clinical manifestations and prognosis of SSc patients according the presence of anti-PM/Scl antibodies in the cohort of RESCLE (*Spanish Scleroderma Registry)*.

Methods: From the Spanish Scleroderma Study Group database, we selected patients in whom anti-PM/Scl antibodies had been tested. We compared demographic features, clinical manifestations, laboratory characteristics, and survival data between patients according the anti-PM/Scl antibodies status.

Results: 72 out of 947 (7%) patients tested positive for anti-PM/Scl antibodies. As presenting SSc manifestations, patients with anti-PM/Scl antibodies had higher prevalence of puffy fingers (11% versus 2%; p=0.002) and arthralgias (11%

versus 4%; p=0.03), and lower prevalence of Raynaud's phenomenon (65% versus 82%, p=0.002). Regarding cumulative manifestations, myositis (51% versus 15%; p<0.001), arthritis (43% versus 22%; p=0.001), and interstitial lung disease (ILD) (60% versus 45%, p=0.014) were more prevalent in patients with anti-PM/Scl antibodies. In fact, those patients with anti-Pm/Scl antibodies presented with FVC (77.4% ± 23.1% versus 85.8% ± 23,1%; p=0.006) and more severe ILD defined as FVC <70% (41% versus 24%; p=0.004). Death rate was similar in patients with and without PM/Scl antibodies (18% versus 17%; p=0.871). *We did not find differences in terms of death rate nor in the causes of death (SSc and non-SSc related) according to the anti-PM/Scl antibodies profile.* The 5- and 10-years survival rates of patients with anti-PM/Scl antibodies were 91% and 82% respectively, without differences with those without these antibodies (93% and 85%, respectively).

Conclusion: In Spanish SSc patients, the presence of anti-PM/Scl antibodies confer a distinctive clinical profile. However, anti-PM/Scl antibodies do not play a role in the prognosis of these patients.

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SAT0317 HDL-CHOLESTEROL EFFLUX CAPACITY IS DOWNREGULATED IN PATIENTS WITH SYSTEMIC SCLEROSIS.

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Background: It is well established that patients with systemic sclerosis (SS) show a disrupted lipid profile and an increased cardiovascular risk. Cholesterol efflux capacity (CEC) is the ability of high-density lipoprotein (HDL)-cholesterol to accept cholesterol from macrophages. CEC has been linked to cardiovascular events in the general population and to subclinical atherosclerosis in patients with rheumatoid arthritis and systemic lupus erythematosus.

Objectives: The main purpose of our study was to assess, for the first time, whether CEC is disrupted in patients with SS compared to controls. We also aimed to identify patients' characteristics that could explain such potential CEC disturbance.

Methods: Cross-sectional study that encompassed 188 individuals; 73 SS patients and 115 age- and sex-matched controls. CEC, using an *in vitro* assay, and lipoprotein serum concentrations were assessed in patients and controls. A multivariable analysis was performed to study the differences in CEC between patients and controls, and if SS-related data could explain CEC differences.

Results: CEC was downregulated in SS patients as compared to controls (beta coefficient -6 [95%CI -10- -2] %, p=0.002). This occurred independently of traditional cardiovascular risk factors, statin use or other variations in the lipid profile produced by the disease. Demographics and lipid profile were, in general, not related with CEC in both patients and controls. In this sense, only abdominal circumference showed a positive association with CEC in patients (beta coefficient 0.09 [95%CI 0.03-0.14], p=0.002) but not in controls. Similarly, no traditional cardiovascular risk factors were related with CEC in both populations. Regarding lipid profile, no correlations were identified between the standard lipid profile molecules and CEC. Remarkably, the use of statins was not related to CEC in both patients and controls. Lastly, concerning SS related data, a negative association between mRSS and CEC was identified (beta coef. -1.08 [95%CI -2.03- -0.12] %, p=0.028).

Skin thickness through modified Rodnan (mRSS) was positively related to age and the presence of hypertension, but negatively associated with apolipoprotein B, apo B:A1 ratio, and CEC when univariate correlations were assessed (Table 4). When the relation of mRSS to these lipid-related molecules was adjusted for traditional CV risk factors, the statistical significance of mRSS with those molecules was maintained. Moreover, when the relation between mRSS and CEC was additionally adjusted for other lipid-related molecules, its significance was conserved (beta coef. -1.35 [95%CI -2.62- -0.08]) %, p=0.038)

Conclusion: CEC is downregulated in SS patients independently of other inflammation-related lipid profile modifications that occur in the disease. Skin thickness is independent and inversely associated with CEC in SS patients.

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SAT0318 GENERALIZED INDICATOR OF RAYNAUD'S PHENOMENON EXPRESSION FOR EVALUATION OF CLINICAL EFFICACY OF PROSTANOID THERAPY

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Background: Raynaud's phenomenon (RP) secondary to rheumatic diseases (RD) can progress to irreversible tissue damage with digital ulceration, scarring and, rarely, gangrene requiring amputation[1]. Current medical treatments for RP are far from ideal: they are often either ineffective and/or poorly tolerated, thus a significant proportion of patients discontinue drug therapy[2].

Objectives: To determine RP expression levels and to evaluate the long-term efficacy of iloprost and alprostadil in RP patients with RD.

Methods: Indicated therapy with intravenous iloprost (n=10), alprostadil (n=17) or their combinations (n=13) was carried out for three years in patients with secondary RP in RD. Frequency of Raynaud's attacks, digital ulcers (DU) formation and pain intensity on visual analogue scale (VAS) were evaluated. A control group included 30 patients with RP in RD who did not receive prostanoid therapy. By factor analysis method a generalized index of RP expression was identified, on the basis of which levels of RP expression were determined.

Results: "RP expression" scale, revealed as an indicator of RP generalized manifestation, was an average value of two subscales: (1) consisted of 4 indices "DU", "digital pitting scars", "phalange amputation" and "frequency of Raynaud's attack", (2) included 3 indicators: "intensity of pain", "duration of illness", "whitening of fingers". Correlation of subscales showed their reliability (r=0.294, p=0.053). RP final expression (severity) was 1.51±0.86. A low level of RP expression had values below 0.65, a high level – over 2.37. At baseline, the high level of RP severity was defined in 16 (22.9%) patients, medium – in 43 (61.4%), low – in 11 (15.7%).

RP treatment with iloprost was effective in the healing of DU in 100% of patients and led to decrease of RP expression generalized index from 2.25 [1; 3] to 1.75 [1; 2] (p=0.012). Alprostadil therapy reduced pain intensity on VAS (p<0.05) and numbness during Raynaud's attacks (p<0.01) and decreased RP expression from 1 [1; 2] to 1 [0.5; 1.5] (p=0.038). Patients on prostanoids combination had new DU and amputations; pain intensity reduced by 47% (p<0.05), RP expression generalized indicator did not change.

Conclusion: Based on RP clinical manifestations in RD patients, a generalized index of RP expression was identified and levels of RP severity were determined. Treatment with iloprost or alprostadil has significant effects on reducing the clinical manifestations of RP with a corresponding decrease in its severity. Iloprost is indicated in patients with medium and high levels of RP expression index, alprostadil – with medium and low index and non-effectiveness of calcium channel blockers.

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SAT0319 SUBCLINICAL ATHEROSCLEROSIS IN INDIAN PATIENTS WITH SCLERODERMA – CLINICAL AND SEROLOGICAL ASSOCIATIONS

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Background: Scleroderma has been associated with increased risk of cardiovascular events, however,studies on this from India are sparse.We evaluated clinical and serological factors associated with subclinical atherosclerosis in Indian patients with scleroderma, in a cross-sectional design.
Objectives: To compare carotid intima-medial thickness (CIMT, mean value of both carotids) as a measure of subclinical atherosclerosis (SCA) between patients with scleroderma (n=61) fulfilling 2013 ACR/EULAR criteria, and healthy controls (n=41).
- To compare clinical (body mass index – BMI, waist-hip ratio – WHR, fasting lipid profile) and serological factors (microparticles, endothelial microparticles, inflammatory cytokines associated with increased cardiovascular risk) between patients with scleroderma and healthy controls.
- To identify factors associated with SCA in scleroderma patients.
Methods: Subclinical atherosclerosis(SCA) was defined by presence of carotid plaques, or increased CIMT >2 standard deviations compared with Indian reference standards for age and sex. Total microparticles (TMP) were measured of plasma after ultracentrifugation as per previously described protocol using microbeads of 3 µm size (TMP were of size 0.1-1 µm); of these, microparticles positive for CD31 and CD142 were endothelial microparticles (EMP). Serum cytokines (IL-1, IL-6, TNF-α, IL-17) were measured by ELISA using manufacturer instructions. Linear regression was used to identify the determinants of CIMT in scleroderma. Binomial logistic regression was used to identify factors associated with subclinical athersclerosis in scleroderma.

Variable	Patients with sclero-derma (n=61)	Healthy controls (n=41)	p value
Age	37.8 ± 11.92	35.37 ± 6.69	0.2375
Gender (M:F)	11:50	6:35	0.6516
Diabetes/Hypertension/Tobacco use	1/2/0	0/0/0	NS
Body mass index (kg/m2)	20.11 ± 3.82	24.38 ± 4.45	<0.0001
Waist-hip ratio	0.86 ± 0.11	0.89 ± 0.07	0.1251
Total cholesterol (mg/dL)	142.5 ± 30.7	147.3 ± 39.5	0.4948
Triglycerides (mg/dL)	99.4 ± 37	121.4 ± 46	0.0087
HDL cholesterol (mg/dL)	46.9 ± 4.9	46.1 ± 4.2	0.4029
LDL cholesterol (mg/dL)	93.6 ± 10.5	93.3 ± 7.5	0.8520
VLDL cholesterol (mg/dL)	19.9 ± 7.4	24.7 ± 9.7	0.0057
Carotid intima-medial thickness (mm)	0.68 ± 0.10	0.53 ± 0.03	<0.0001
Total microparticles (per ±L)	12913 ± 2493	6272 ± 1533	<0.0001
Endothelial microparticles (per ±L)	2623 ± 1032	829 ± 439.5	<0.0001
Serum IL-1± (pg/mL)	38.19 ± 13.46	31.38 ± 18.29	0.0326
IL-6 (pg/mL)	176.6 ± 85.74	128.9 ± 53.61	0.0020
IL-17 (pg/mL)	56.3 ± 20.45	53.89 ± 20.51	0.5611
TNF± (pg/mL)	49.65 ± 26.71	42.09 ± 30.41	0.1879

Results: Despite lower BMI, triglycerides and VLDL cholesterol, CIMT was significantly higher in patients with scleroderma. Patients with scleroderma had significantly higher total microparticles and endothelial microparticles in plasma, and serum IL-1± and IL-6 (Table 1). On multivariable regression, age was the only significant determinant of CIMT. 28 (45.9%) patients had SCA; 13 (21.3%) had carotid plaques. Patients with SCA had higher proportion of males (9/28 in those with SCA vs 2/33 in those without SCA). Binomial logistic regression did not identify any other significant predictors of SCA.

Table 1. Comparison between patients with scleroderma and healthy controls

Serum IL-1± (pg/mL)	38.19 ± 13.46	31.38 ± 18.29	0.0326
IL-6 (pg/mL)	176.6 ± 85.74	128.9 ± 53.61	0.0020
IL-17 (pg/mL)	56.3 ± 20.45	53.89 ± 20.51	0.5611
TNF± (pg/mL)	49.65 ± 26.71	42.09 ± 30.41	0.1879

Conclusion: Patients with scleroderma had significant burden of subclinical atherosclerosis, which could not be explained by traditional or novel cardiovascular risk factors.
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SAT0320 BONE MINERAL DENSITY AND FRACTURE RISK IN A COHORT OF PORTUGUESE SYSTEMIC SCLEROSIS PATIENTS

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Background: Although poorly understood, patients with Systemic Sclerosis (*SSc)* seem to have higher prevalence of low bone mineral density (BMD) and an increased spine fracture risk.
Objectives: We aim to determine, by conventional densitometry (DXA) and using the fracture risk assessment tool (FRAX), the prevalence of low BMD and the fracture risk, respectively, in our SSc cohort and its potential determinants.
Methods: Observational transversal study was performed including consecutive patients with the diagnosis of SSc. We collected data regarding demographics, BMD (lumbar spine and femoral neck) and occurrence of fracture. Ten-year risk of osteoporotic fracture was estimated using FRAX *v4.1* with the Portuguese population reference. Statistical analysis was performed using SPSS 23.0; p<0.01 was considered statistically significant.
Results: Median age of patients (n=97) was 62 years old [56, 70], 88.7% females (n=86). Seventy-eight patients (80.4%) had limited cutaneous form, 5 (5.2%) presented a diffuse cutaneous form and 13 (13.4%) an overlap syndrome. Regarding clinical features: digital ulcers in 30 patients (30.9%), interstitial lung disease (ILD) in 16 (6.5%), gastrointestinal involvement in 16 (16.5%), miositis in 4 (4.1%) and pulmonary arterial hypertension in 3 (3.1%). Anti-topoisomerase I antibody (anti-Scl70) positivity was present in 15 patients (15.5%) and anti-centromere antibody (ACA) positivity in 63 (64.9%). Nine patients (9.3%) were smokers and 6 (6.2%) reported an alcohol consumption of 3 or more units/day. Median body mass index (BMI) was 25.4 Kg/m^2 [21.4, 29.1], with 5 patients (5.2%) being underweight. Vitamin D insufficiency was reported in 19 patients (19.6%). Twenty-one patients (21.6%) have been exposed to oral glucocorticoids (GCT) for more than 3 months at a dose of 5mg daily or more. Eleven patients (11.3%) had previous low impact fractures: 10 of which were vertebral and 1 wrist fracture. Regarding the prescribed anti-osteoporotic treatment (AOP), we found: alendronate (n=7, 7.2%), zoledronic acid (n=7, 7.2%), denosumab (n=2, 2.1%) and teriparatide (n=1, 1%).
Low BMD was present in 45 patients (46.4%); median femoral neck BMD (FN-BMD) was 0.827 [0.709, 0.893].Ten year probability of fracture (%) was: median risk for major fracture was 5.1 [3.5, 9.7] and 3.8 [2.5, 8], with and without FN-BMD, respectively; for hip fracture the estimated risk was 1.2 [0.6, 3.1] and 1.0 [0.4, 2.5], with and without FN-BMD, respectively. According to FRAX thresholds for the Portuguese population, 25 patients (25.8%) met criteria to start AOP treatment. Among them, only 10 patients (40%) started it, as the agreement between the indication to treat by FRAX and the onset of treatment was weak (*k*= 0.338). A strong agreement was found between FRAX risk threshold with DXA and World Health Organization (WHO) threshold for starting AOP (*k*= 0.814) and no agreement was found between FRAX risk without DXA and WHO threshold.
FN-BMD presented a weak correlation with BMI (r = 0.393), a moderate inverse correlation with major fracture risk with and without FN-BMD (r = -0.704,

r=-0.412, respectively) and with hip fracture risk with and without FN-BMD (r = -0.799, r=-0.412, respectively). Major fracture risk with and without FN-BMD presented a moderate correlation with spine fractures (r = 0.350; r=0.397, respectively).

No correlation was found between WHO threshold and spine fractures. No correlations were found between FN-BMD or fracture risk estimated by FRAX and disease manifestations, anti-Scl70 or ACA positivity, vitamin D insufficiency, smoking or GCT use.

Conclusion: In our cohort, low BMD was prevalent and had correlation with BMI. FRAX appears to be an useful instrument as it correlated with spine fractures, contrary to what was verified when we used the WHO threshold. Early monitoring of BMD and estimating fracture risk using FRAX appear to be useful tools for the prevention of fractures in this population.

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SAT0321 CURRENT PATIENT REPORTED OUTCOMES (PROS) POORLY REFLECT CHANGES IN LUNG FUNCTION IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Lung involvement is very common is systemic sclerosis (SSc). Approximately one quarter of patients develops pulmonary problems within the first 3 years of diagnosis and still represents the leading cause of death in these patients. In a recent clinical trail, the reduction of FVC was not accompanied by a benefit with respect to health-related quality of life and patient-reported outcomes (PROs).

Objectives: To assess how the change in Pulmonary Function Test (PFTs) parameters correlates with the Patient Reported Outcomes (PROs) in an observational cohort of patients with Systemic Sclerosis (SSc).

Methods: We conducted a retrospective study of 330 clinic episodes from 121 unselected patients diagnosed with systemic sclerosis according to EULAR/ACR 2013 criteria, in annual follow-up (for a total of 165 patients/year) with PFTs, Health Assessment Questionnaire Disability Index (HAQ-DI), Scleroderma Health Assessment Questionnaire (sHAQ), Modified Borg Dyspnea Scale (Borg) and Cochin Hand Function Score (CHFS). We assessed the correlation between the HAQ and the Visual Analogical Scale 1-7 at baseline (VAS1 pain, VAS2 disease severity, VAS3 arthritis activity, VAS4 intestinal problems, VAS5 dyspnea, VAS6 Raynaud's phenomenon, VAS7 digital ulcers). We evaluated the correlation of PFTs with PROs at every time period and the correlation between the change of PFTs parameters (δFVC, δDLCO) with the change of the PROs over a year of follow-up. Following analysis of distribution, Spearman or Pearson Test were used to determine correlation coefficients, as appropiate (Prism 7).

Results: The median disease duration was 5 years (IQR 3-10). The median of 12 months δFVC% and δDLCO% were 0 (IQR -5.81 to 3.28) and -2.439 (IQR -8.76 to 5.98), respectively. The analysis evidenced a strong positive correlation between VAS1-7 and HAQ. We observed also significant correlation between FVC%, DLCO% and HAQ-DI (r= - 0.355 and -0.266, respectively; p<0.0001 for both), Borg (r= -0.403 and -0.379, respectively; p<0.0001) and CHFS (r = -0.355 and -0.256, respectively; p<0.0001). Nevertheless, in longitudinal setting there was no significant correlation between δPROs and changes lung function, as continuous variables, neither there was any significant PROs difference in patients that did or did not lose more than 10% of FVC and DLCO over a year of follow-up.

Conclusion: This analysis of a monocentric non-selected population evidenced that the current commonly used PROs in SSc while showing a good correlation with lung function are poorly sensitive to change or to reflect changes in lung function over 12 months. In this sense, prudent interpretation of the lack of correlation between FVC and patient-reported outcomes in studies of phase 3 is warranted.

References:

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SAT0322 PREVALENCE AND RISK FACTORS FOR LEFT VENTRICULAR DIASTOLIC DYSFUNCTION IN SYSTEMIC SCLEROSIS: RESULTS FROM RESCLE REGISTRY

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Background: Left ventricular diastolic dysfunction (LVDD) is a very common finding in heart involvement in Systemic Sclerosis (SSc).

Objectives: To determine the prevalence, risk factors and mortality associated with LVDD in a cohort of patients with SSc.

Methods: A retrospective study was conducted with data from the multicentre Spanish Scleroderma Registry (RESCLE). A case-control study was performed to identify factors associated with LVDD.

Results: Out of 1517 cases of SSc, 319 (21%) developed LVDD. Basal characteristics are shown in Table 1. In multivariate analysis, LVDD was associated to older age at diagnosis of SSc [54 vs 44 years, OR 1.05 (1,04-1.06)], presence of telangiectasia [67 vs 59%, OR 1.42 (1,88-1.08)], and treatment with calcium channel blockers [50 vs. 45%, OR 1.55 (1.16-1.96)], and inversely correlated to treatment with ACE inhibitors [74 vs. 83%, OR 0.59 (0.44-0.8)]. Mortality was increased in patients with LVDD (24 vs 17%, OR 1.4, p = 0.01). Kaplan–Meier cumulative survival for the SSc cohort, according to the presence or absence of LVDD showed significant differences in 30 years from the first SSc symptom (59 vs. 70%, p = 0.04).

Table 1.

Number of patients	*1517*	*319 (21%)*	*1198 (79%)*	**P**
Limited SSc	923 (61%)	201 (63%)	722 (60%)	0.438
Diffuse SSc	304 (20%)	51 (16%)	253 (21%)	0.041
Sine Sclerodema SSc	174 (11%)	47 (15%)	127 (11%)	0.048
Age at disease onset *(years)* med±SD	46.4±16.5	54.1±15.9	44.5±16.1	<0.001
Arterial hypertensión	491 (33%)	148 (48%)	343 (30%)	<0.001
Digital ulcers	615 (41%)	108 (34%)	507 (42%)	0.006
Telangiectasia	918 (61%)	212 (67%)	706 (59%)	0.011
Interstitial lung disease	645 (43%)	153 (48%)	492 (41%)	0.021
Pulmonary hypertension	139 (9.2%)	34 (11%)	105 (8.8%)	0.325
Capillaroscopy Slow pattern	673 (51%)	130 (46%)	543 (53%)	0.038
Centromere Antibodies	679 (49%)	154 (55%)	525 (48%)	0.032

Conclusion: In our cohort, LVDD is relative common in SSc patients, and it is associated with older age at diagnosis, treatment with calcium channel blockers and telangiectasia. ACE inhibitors could play a protective role against the development of LVDD. Mortality is higher in SSc patients with LVDD, and is more significative over time.

References:

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SAT0323

MYOSITIS-SPECIFIC AND MYOSITIS-ASSOCIATED AUTOANTIBODIES IN A LARGE INDIAN COHORT OF INFLAMMATORY MYOSITIS REVEAL NOVEL CLINICO-PHENOTYPIC PATTERNS

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Background: Idiopathic Inflammatory Myositis (IIM) are heterogenous, with distinct autoantibodies reflecting upon possible clinical evolution and outcomes. Ethnicity has major influence on both antibody prevalence patterns as well as phenotypic behaviours linked to them.
Objectives: Thus we sought prevalence and co-existence of myositis specific autoantibodies (MSAs) and myositis associated autoantibodies (MAAs) and associated clinical characteristics in a large cohort of patients with IIM.
Methods: Adult patients with a physician diagnosis of IIM as per ACR/EULAR classification criteria were investigated for the presence of MSAs/MAAs by Line immunoassay (G4, Euro-Immune, Lubeck, Germany). Anti-Nuclear Antibody (ANA) was tested by Immunofluorescence assay (IFA), and patterns in various antibody subsets explored. Prevalence and associations of different antibodies were assessed in disease subsets and clinical phenotypes.
Results: MSA and MAAs were tested in 250 IIM patients (F:M 3.8:1) of median age 37 (25-47) and disease duration 6 (3-17) years. Dermatomyositis (DM) was seen in most patients 83 (33.2%) followed by overlap myositis (OM), juvenile DM, Anti-synthetase syndrome (ASS), polymyositis (PM), and cancer associated myositis (CAM). MSAs/MAAs were found in 148 (59.2%) of patients, of which 95 (64.2%) had an MSA and 53 (35.8%) had MAAs (**Fig, 1A**). 93 (62.8%) of autoantibody positive patients were positive for a single antibody, and only 2 (0.8%) of total had more than one MSA (Table 1).

Table 1. Multiple antibodies positive upon testing for MSA and MAA by the LIA

AutoAntigen	Auto-Ab (n)	None	Jo-1	PL-7	PL-12	MDA5	SAE	Mi2	NXP2	TIF1γ	SRP	Ku	Pm/Scl	Ro52
Jo-1	21	3			1									17
PL-7**	4	1										1**	1	1
PL-12**	7	0	1										1**	5
MDA5*	14	8								1*				5
SAE*	5	3					1*							1
Mi2	19	17					1							1
NXP2	9	8										1		
TIF1Y	12	9				1								2
SRP**	5	0											1**	4
Pm/Scl	12	11		1										
Ro52	72	33	17	1	5	5	1	1		2	4	3		
Ku	10	6						1						3

Note: ** PL-7 co-exists with Ku + Pm/Scl, **PL-12 co-exists with Pm/Scl + Ro52, **SRP co-exists with Pm/Scl + Ro52

The most frequently detected MSA was anti-Jo-1 (8%), with a further 9 specificities each found in 0.5–7.0% of patients. Amongst the autoantibody positive patients, 21% (n=53) had isolated MAA positivity, anti-Ro52 (33, 62.3%) being the most common, followed by anti-Pm/Scl (11, 20.8%) and anti-Ku (9, 17.0%) (Fig. 1**B**).

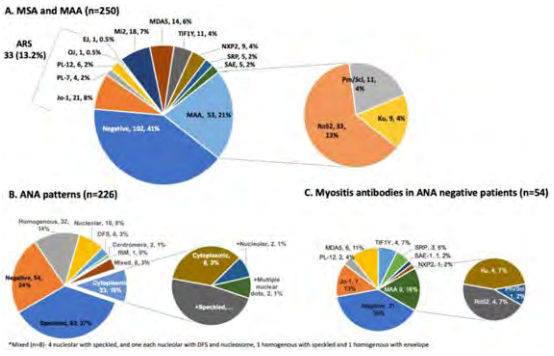


Figure 1. A. MSA and MAA in Indian cohort of myositis B. ANA patterns in myositis C. MSA in ANA negative IIM

On ANA, 76.0% (172 of 226) were positive, with speckled being the most common pattern (37%,Fig. 1**C**). Of those ANA negative (n=54), 61% had either MSA or MAA (Fig 1**D**). 18 (54.6%) had autoantibodies associated with cytoplasmic patterns suggesting that cytoplasmic ANA may be underreported.
Clinical presentation akin to DM was seen with all MSA except anti-SRP. PM group was heterogenous, and included ASS, OM and necrotizing phenotype (Fig. 2**A**). On occasion, anti-SRP, anti-Mi-2 and anti-MDA5 presented with clinical phenotype of ASS. (Fig 2**A,C**). Patients with ARS or anti-SAE were often clinically amyopathic (Figure 2 **B,C**)

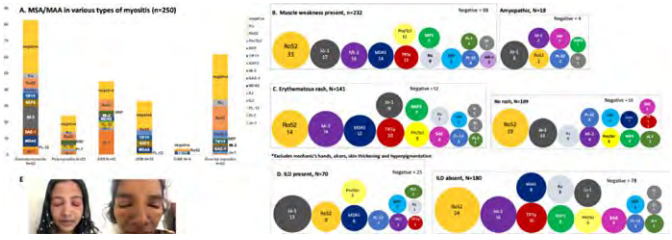


Figure 2. A. Phenotypic associated with various antibody subsets B,C,and D. MSA/MAA in muscle weakness, rash and ILD phenotype. E. Unique feature of eye-lid edema in some patients with MDA-5 positive myositis

ARS were associated with mechanic's hand (p<0.0001,OR 7.6), ILD (p<0.0001,OR 4.4), and arthritis (p=.002,OR 2.6) though there was no difference between Jo-1 and non-Jo-1 ASS. Anti-MDA-5 associated with fever (p=0.003,OR 12) and weight loss (p=0.008,OR 10.2) and unique phenotype of eye-lid edema in some adults (Figure 2**E**) and arthritis in children (p=0.01, OR 11.5). Anti-TIF-1γ associated with alopecia (p=0.007,OR 5.9) and malignancy (p= <0.0001,OR 34) in adults but not children.
Conclusion: Myositis autoantibodies are seen in two-thirds IIM and identify distinct clinical subsets as well as unique phenotypes. MSA/MAA are positive in two-thirds of those negative on ANA, adding diagnostic value. MSAs are nearly always mutually exclusive and thus useful as biomarkers for diagnosis.
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SAT0324

SEXUAL HEALTH IN WOMEN AND MEN WITH SYSTEMIC SCLEROSIS: A CROSS-SECTIONAL STUDY

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Background: Systemic sclerosis (SSc) is a chronic multisystem disease that may affect all aspects of life including sexual function.
Objectives: To assess sexual function, pelvic floor function in 80 women and 14 men with SSc compared to age-/sex-matched healthy controls (HC) and to analyze the potential impact of clinical features on sexual health.
Methods: In total 80 women (mean age: 49, disease duration: 6.1 years, lcSSc/dcSSc: 53/27, mRSS: 9.3, ESSG activity index: 2.1) and 14 men with SSc (mean age: 51.6, disease duration: 3.1 years, lcSSc/dcSSc: 6/8, mRSS: 12.9, ESSG activity index: 2.2) who fulfilled the ACR/EULAR 2013 criteria, filled in 12 well-established and validated questionnaires assessing sexual function, pelvic floor function, quality of life, fatigue, physical activity and depression. Full names of questionnaires are listed in Table 1. These questionnaires were also completed by 80 healthy women and 14 healthy men with identical age. Data are presented as mean±SEM.

Table 1

Clinical parameter	Correlated parameters	r	p-value
ESSG diseases activity index	FSFI Arousal domain	-0.300	p<0.0001
	IIEF EF	-0.597	p=0.0240
CRP	IIEF Orgasmic Function	-0.668	p=0.0081
mRSS	MSHQ Sexual Desire	0.555	p=0.0613
FIS	BISF-W	-0.410	p=0.0002
MAF	FSFI	-0.399	p=0.0002
BDI-II	BISF-W	-0.381	p=0.0002
	IIEF EF	-0.801	p=0.0005
HAP	SQoL-F	0.383	p=0.0006
	BISF-W	0.456	p<0.0001
	IIEF EF	0.639	p=0.0062
SHAQ	FSFI	- 0.409	p<0.0001
	BISF-W	-0.451	p=0.0002

Name of Questionnaires/Acronyms: FSFI: Female Sexual Function Index; BISF-W: Brief Index of Sexual Function for Women; SQoL-F/M: Sexual Quality of Life Questionnaire-Female/Male; PISQ–12: Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire short form; PFIQ7: Pelvic Floor Distress Inventory Questionnaire; IIEF: International Index of Erectile Function; MSHQ: Male Sexual Health Questionnaire; FIS: Fatigue Impact Scale; MAF: Multidimensional Assessment of Fatigue; BDI-II: Beck's Depression Inventory II; HAP: Human Activity Profile; SHAQ: Scleroderma Health Assessment Questionnaire; ESSG: European Scleroderma Study Group; CRP: C-reactive protein; mRSS: modified Rodnan skin score

Results: Compared to HC, women with SSc had significantly higher prevalence and greater severity of sexual dysfunction [FSFI total score (SSc: 16.4±1.3, HC: 25.6±1.2, p<0.0001) as well as in all subscales (p<0.0001 for all), BISF-W total score (SSc: 17.2±2.3, HC: 32.0±1.9, p<0.0001)], dysfunction of pelvic floor [(PISQ-12 (SSc: 3.6±0.7, HC: 8.9±0.6, p<0.0001), PFIQ7 (SSc: 33.4±5.6, HC: 6.8±1.4, p<0.0001)], and worse sexual quality of life [SQol-F (SSc: 55.3±3.3, HC: 82.1±2.1, p<0.0001)]. Men with SSc also reported more severe sexual dysfunction: [IIEF - Erectile function (EF) (SSc: 15.4±3.0, HC: 26.2±2.1, p=0.004), IIEF - Orgasmic function (SSc: 6.4±1.2, HC:9.0±0.6, p=0.045), IIEF - Intercourse satisfaction (SSc: 9.7±1.8, HC: 15.7±1.3, p=0.008), MSHQ - Erectile Function (SSc: 9.0±1.2, HC: 12.9±0.9, p=0.005), MSHQ - Satisfaction (SSc: 19.2±2.1, HC: 26.8±0.9, p=0.001)] and worse sexual quality of life [SQol-M (SSc: 68.5±7.4, HC: 86.7±6.2, p=0.023)]. According to the IIEF classification, 71 % of SSc men reported mild to severe erectile dysfunction. No significant differences were found in pelvic floor function. Significant associations with major clinical parameters are presented in Table 1.

Conclusion: Both women and men with SSc reported significantly impaired sexual function compared to HC with identical age. Worse scores in SSc were associated with disease activity, increased systemic inflammation, health status, physical activity, fatigue and depression.

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SAT0325 STELLATE BLOCKADE COMBINED TO ILOPROST AS SUPPORTIVE TREATMENT OPTION IMPROVES PAIN AND ISCHAEMIC SYMPTOMS IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Peripheral ischaemia is a common symptom in systemic sclerosis (SSc) patients with risk of development of digital ulcers (DU). For its treatment, intravenous iloprost is the most effective option. Accompanying pain symptoms worsen the ischaemic symptoms, so a combination with anaesthetic procedures may improve ischaemic status and the subjective sensation of raynaud and pain. The aim of this study was to observe the impact of a combined treatment of iloprost with stellate blockade (ILOST) in improvement of ischaemic symptoms compared to iloprost treatment only (ILO).

Objectives: To evaluate efficacy of the ILOST treatment on changes in vascularisation and sensation of patients with SSc and indication for vasodilatative treatment with Iloprost.

Methods: Twenty SSc-patients with indication for ILO-treatment (prophylactic or due to digital ulcerations (DU)) will be included in a prospective observational study. Patients will be offered to combine ILO with stellate blockade (ILOST). Beside documentation of disease activity characteristics (mRSS, number of DU, capillary microscopy at baseline, after ILO-treatment and at week 12), patients are assessed using fluorescence-optical imaging (FOI) as innovative method for illustration of changes in microvascularisation and patient reported outcomes (DASH, VAS) at week 12.

Results: This interims analysis includes the result of the first 11 patients treated. Mean baseline characteristics (age and gender) are well balanced. Iloprost treatment was initiated due to prophylactic treatment to avoid DU in all patients. 100% of the patients in the ILOST-group were diagnosed as limited SSc compared to 60% in the ILO-group (diffuse type with 40%). All patients showed abnormalities in capillary microscopy (ILOST group: 83,3% late pattern 16.7% active pattern; ILO group: 80% late pattern, 20% early pattern). MRSS was low in both groups with 1.8, the disease duration in mean 15.3 years in the ILOST-group compared to 13.2 in the ILO-group, respectively. In both groups, no new DU occurred in the 12-week follow-up. Improvement in VAS pain was reported in 83% of the patients in the ILOST group compared to 60% in the ILO group. DASH improved with a mean of 5.5 points in the ILOST group compared to 3 points in the ILO group. FOI was compared individual at both arms in the ILOST group only. The arm with stellatum blockade showed a pronounced increase of FOI signals of 5% in mean whereas the opposite site showed a decrease of the signal shortly after ILO treatment indicating a pronounced increase of vascularisation in the ILOST treated body site.

Conclusion: A new treatment approach to improve acute ischaemic symptoms was tested by combining stellate blockade to iloprost treatment. No new DU occurred up to 12 weeks after treatment in all patients of both groups indicating the relevance of iloprost as effective vascular dilatative therapy in SSc. The additional intervention was well tolerated and asked to repeat. Subjective sensation on pain of the hands as well as DASH was improved in the combined group. FOI showed a relevant increase in vascularisation in the blockade arm compared to the opposite site in which signals decreased indicating a stronger effect of the combined treatment for improvement of vascularisation.

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SAT0326 SYSTEMIC SCLEROSIS WITHOUT ANTINUCLEAR ANTIBODIES: A MULTI-CENTER STUDY OF EUSTAR COHORT IN CHINA

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Background: The presence of circulating antinuclear antibodies (ANAs) is a hallmark of immune dysregulation and malfunction in patients with systemic sclerosis (SSc) [1]. A variety of ANAs [2], including anti-centromere antibody, anti-topoisomerase I antibody, and anti-RNA polymerase III antibody, are associated with unique sets of disease manifestations and widely used in routine clinical practice for diagnosis, clinical subgrouping, risk stratification and prediction of future organ involvements and prognosis in SSc patients [3,4].

Objectives: This study aimed to investigate the clinical features of SSc patients with negative ANAs in a European League Against Rheumatism Scleroderma Trials and Research Group (EUSTAR) and Chinese Rheumatism Data Center (CRDC) multi-center cohort in China.

Methods: Patients were prospectively recruited between April 2008 and June 2019 based on the EUSTAR database and CRDC multi-center cohort from 154 clinical centers nationwide, all of whom fulfilled the 2013 ACR/EULAR classification criteria for systemic sclerosis. Antinuclear antibody testing result was intensively collected. Demographic, clinical, and laboratory data were compared between ANA-positive SSc patients and those with negative ANAs. T-test and chi-square analysis were performed in the comparisons.

Results: Antinuclear antibodies were detected in 2129 out of 2809 systemic sclerosis patients enrolled in the multi-center cohort and 4.2% of them were negative. There was significant difference between patients with negative and positive ANAs based on gender (29/60 vs 294/1746, p<0.001). The presence of Raynaud's phenomenon is less common (71.8% vs 99.8%, p<0.001) in the ANA-negative patients. In addition, compared with ANA-positive patients, the incidence of certain critical organ involvements, including gastroesophageal reflux (5.6% vs 18.5%, p=0.002), interstitial lung disease (65.2% vs 77.9%, p=0.015) and pulmonary arterial hypertension (11.5% vs 29.0%, p=0.006) were significantly lower in ANA-negative patients than in the positive group. The proportion of IgG elevation, an indicator of disease activity and severity of inflammation, was significantly lower in the ANA-negative patients than that in the positive group (14.3% vs 41.2%, p<0.001), while no significant differences were found in other inflammatory indicators and skin scores.

Conclusion: This study describes the clinical features of SSc patients with negative ANAs, which have been rarely mentioned or focused in existing studies. Antinuclear antibody is proved to be strongly associated with the clinical manifestations of systemic sclerosis patients and ANA-negative SSc patients tend to be in relatively milder conditions, including a less common involvement of critical organs and a more temperate inflammatory severity.

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SAT0327 SEXUAL DYSFUNCTION IN FEMALE SCLERODERMA PATIENTS AND ITS CORRELATION WITH VASCULAR INVOLVEMENT

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Background: Systemic Sclerosis (Scleroderma, SSc) is an autoimmune disorder characterized by multi-organ dysfunction, which ultimately leads to multiple clinical and psychological complications. Among various complications of scleroderma, sexual dysfunction can be named as a major issue in both male and female patients, which has great impact on quality of life of the patients.

Objectives: Investigating the sexual dysfunction in scleroderma patients and its relation to their vascular involvements.

Methods: A case control study was done on 80 married female scleroderma patients with age between 20-60 years old. Eighty normal individuals adjusted for age, place of living and socioeconomic status were also recruited. Sexual performance in both groups was assessed using FSFI standardized questionnaire, which evaluated it in 6 domains of desire, arousal, lubrication, orgasm, satisfaction, and pain. Micro and macro-vascular involvements of the patients were also determined using Raynaud Condition Score, Echocardiography, physical exam for assessing their digital ulcers and reviewing their medical records for presence of past or present history of renal crisis and thromboembolic events.

Results: The total score of FSFI in the case group was significantly lower compared to control one (16.68 ± 6.35, 19.69 ± 6.01, P-value <0.001). The score was significantly lower in all domains of sexual dysfunction except for pain and lubrication. Moreover, the mean score of FSFI was also found to be significantly lower in limited form of the disease compared to diffuse one (14.6 ± 6.9, 18.1 ± 5.5, P-value 0.01). No significant association was found between vascular complications and sexual impairment of the scleroderma patients.

Conclusion: This study can be named as the first survey investigating the sexual dysfunction in Iranian female scleroderma patients and assessing its relation with vascular complication of the disease. Thus, it can be a guide for future studies on sexual dysfunction especially in societies with cultural limitations in discussing this issue.

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SAT0328 OUTCOME OF INTERSTITIAL LUNG DISEASE (ILD) IN ANTI-PM/SCL PATIENTS WITH SYSTEMIC SCLEROSIS: RESULTS FROM AN EUSTAR CASE-CONTROL STUDY.

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Background: The main clinical associations of anti-PM/Scl in Systemic Sclerosis (SSc) so far reported include calcinosis, myositis and interstitial lung disease (ILD). Nevertheless, data regarding the long-term outcome of ILD in these patients are lacking. A single centre Spanish cohort reported a better functional outcome in 14 SSc-ILD patients anti-Pm/Scl+ as compared to 49 anti-Topo I after a mean follow-up of 7 years (1).

Objectives: To analyze the long-term outcome of ILD in a large multicentre EUSTAR study dedicated to anti-Pm/Scl SSc patients.

Methods: A case-control study within the EUSTAR cohort collected 165 anti-PM/Scl+ SSc cases and 257 anti-PM/Scl- SSc controls, matched for sex, cutaneous subset, disease duration, and age at onset. Data for ILD at HRCT were available for 162/165 cases and 249/257 controls. Data for pulmonary function tests (PFT) at the baseline (T0), 1 year after diagnosis (T1) and at the last visit (LV) were analyzed.

Results: A significantly higher frequency of ILD was reported in anti-Pm/Scl+ cases vs anti-Pm/Scl- controls (62.3% vs 39.4%, p:<0.0001, OR 95%, CI 2.55, 1.70-3.83). Complete PFTs data were available for 81/101 ILD anti-Pm/Scl+ cases and 78/98 anti-Pm/Scl- ILD controls, with similar age at onset and female/male ratio and disease duration at LV (112±81 months vs. 115±64 months, p:0.77). Diffuse cutaneous involvement was less frequent in cases than in controls (27.2% vs. 44.9%, p:0.03).

In ILD cases, %pFVC tended to improve from T0 (85.1±18.3) to T1 (89.5±16.5, p:0.045) and to LV (87.9±16.9, p:0.057), while in ILD controls remained stable from T0 (90.4±18.5) to T1 (91.1±16.5, p:0.38) and significantly declined to LV (85.0±18.0, p:0.0002). %pDLCO remained stable from T0 (60.5±16.8) to T1 (60.1±17.6, p:0.87) and to LV (60.4±16.9, p:0.77) in ILD cases, while significantly declined from T0 (67.0±18.9) to T1 (62.7±18.2, p:0.0016) and to LV (59.6±18.4, p<0.0001) in the control group. Mean %pFVC and %pDLCO at the 3 time points were not significantly different between the two groups.

Delta %pFVC (LV-T0) was 2.85±11.3 for the anti-Pm/Scl+ group vs -5.42±13.4 in the control group (p:0.0004) with a significant smaller proportion of patients with FVC loss ≥10% from T0 to LV in the anti-PM/Scl group (12.3% vs. 39.7%, p:0.0001). Delta %pDLCO (LV-T0) was -0.13±10.8 for the anti-PM/Scl+ group vs -7.38±14.6 in the control group (p:0.0015), with a significant smaller proportion of patients with DLCO loss ≥10% from T0 to LV in the anti-PM/Scl+ group (13.6% vs. 42.3%, p<0.0001).

Conclusion: In this multicenter real-life study, the long-term pulmonary functional outcome in SSc-ILD patients with anti-Pm/Scl positivity seems to be more favorable than in patients without anti-Pm/Scl antibodies.

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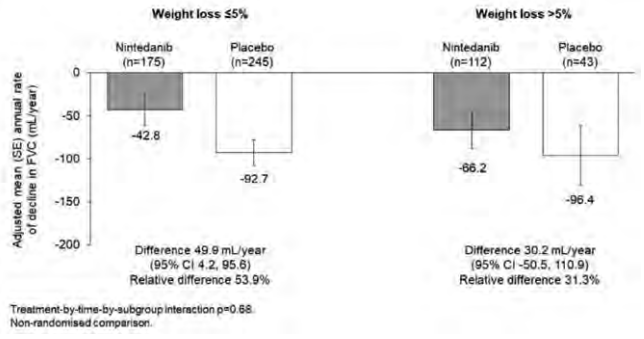
SAT0329 IS THE RATE OF LUNG FUNCTION DECLINE THE SAME IN PATIENTS WITH SYSTEMIC SCLEROSIS-ASSOCIATED ILD (SSC-ILD) WHO EXPERIENCE WEIGHT LOSS? DATA FROM THE SENSCIS TRIAL

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Background: In the SENSCIS trial, nintedanib reduced the progression of SSc-ILD vs placebo, as shown by a lower rate of decline in forced vital capacity (FVC). The adverse event (AE) profile of nintedanib was characterised mainly by gastrointestinal (GI) events, including weight loss.
Objectives: Assess FVC decline and AEs in subgroups by weight loss ≤5% vs >5% over 52 weeks in the SENSCIS trial.
Methods: Patients with SSc-ILD with first non-Raynaud symptom <7 years before screening and ≥10% fibrosis of the lungs on an HRCT scan were randomised to nintedanib or placebo. In a non-randomised comparison, we analysed the rate of decline in FVC (mL/year) and AEs over 52 weeks in subgroups by weight loss (≤5% vs >5%) over 52 weeks.
Results: In the nintedanib (n=288) and placebo (n=288) groups, respectively, 112 (38.9%) and 43 (14.9%) patients had weight loss >5% over 52 weeks. At baseline, patients with weight loss >5% over 52 weeks had a higher mean age (57.0 vs 52.9 years), greater proportion of females (81.3% vs 72.9%), and similar mean BMI (26.5 vs 25.7 kg/m^2, respectively) and FVC % predicted (71.0% vs 73.1%, respectively) vs patients with weight loss ≤5%. In the placebo group, the mean (SE) annual rate of decline in FVC was similar between patients who had weight loss ≤5% and >5% over 52 weeks (-92.7 [14.7] mL/year and -96.4 [34.9] mL/year, respectively). The estimated annual rate of decline in FVC was lower in patients treated with nintedanib than placebo, with between-group differences in patients who had weight loss ≤5% and >5% of 49.9 mL/year [95% CI 4.2, 95.6]) and 30.2 mL/year [95% CI -50.5, 110.9]), respectively, with no evidence of heterogeneity between subgroups by weight loss (p=0.68 for interaction). Standardised differences in baseline values of potential confounders were <0.2 (indicating negligible differences). The most frequent AEs in patients treated with nintedanib were diarrhoea (74.4% and 77.7% of patients with weight loss ≤5% and >5%, respectively), nausea (30.1% and 33.9%, respectively) and vomiting (19.3% and 33.3%, respectively). In the nintedanib and placebo groups, respectively, AEs leading to discontinuation of study drug occurred in 17.0% and 8.6% of patients with weight loss ≤5%, and 14.3% and 9.3% of patients with weight loss >5% over 52 weeks.
Conclusion: In the SENSCIS trial in patients with SSc-ILD, a greater proportion of patients treated with nintedanib than placebo had weight loss >5% over 52 weeks. The rate of decline in FVC was numerically lower in the nintedanib group than in the placebo group both in patients with weight loss ≤5% and >5% over 52 weeks. AEs leading to discontinuation of nintedanib were not more frequent in patients with weight loss >5% vs ≤5%.

References:

Figure. Rate of decline in FVC in subgroups by weight loss over 52 weeks in the SENSCIS trial



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SAT0330 NEW IMMUNOMODULATORY COMBINATION THERAPIES IN PATIENTS WITH SYSTEMIC SCLEROSIS: A RETROSPECTIVE CROSS-SECTIONAL STUDY

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Background: Systemic sclerosis (scleroderma, SSc) is a rare complex connective tissue disease associated with high mortality and high morbidity[1]. Active SSc

are typically treated with immunosuppressants, which may create a variety of severe side-effects, especially for long-term treatment[2]. As the pathogenesis of SSc is still a matter of debate, growing evidences have focused on the immune disorders[3]. However, the quantitative status of lymphocyte subsets in SSc patients are unclear and effects of immunomodulatory combination therapies (avoiding side-effects of conventional therapy) on the lymphocyte subsets are unknown.

Objectives: To investigate the quantitative status of peripheral lymphocyte subpopulations and CD4+T subsets in SSc patients for the exploration of SSc pathogenesis and evaluate the effects of new immunomodulatory combination therapies on those cells.

Methods: From July 2014 to December 2019, total 166 patients with SSc and 206 healthy controls (HCs) were enrolled in this study, in which, 79 follow-up patients received immunomodulatory drugs (IMiDs) such as low-dose interleukin-2, rapamycin, metformin, retinoic acid and coenzyme Q10. The absolute numbers of T, B, NK, CD4+T, CD8+T, Th1, Th2, Th17 and Tregs in peripheral blood of these subjects were detected by flow cytometry combined with standard absolute counting beads.

Results: Patients with SSc had lower absolute counts of total T, NK, Th2, Th17 and Tregs as compared with those of HCs (P<0.05) (Figure 1). After immunomodulatory combination treatments, there were increases in a various of peripheral lymphocyte subsets such as T, B and CD8+T (P < 0.05). Moreover, the increased level of Tregs was much more dramatical than those of other lymphocyte subsets, resulting in the decrease ratios of Teffs/Tregs such as Th1/Tregs and Th2/Tregs and rebuilding immunologic equilibrium (Figure 2).

Conclusion: This cross-sectional study clarified the abnormal status of lymphocyte subsets in SSc patients, suggesting lymphocyte subsets, especially Tregs, might be relevant and play a crucial role in the pathogenesis of SSc, thus providing a potential therapeutic target for SSc patients. Immunomodulatory combination therapies effectively increase the level of Tregs as well as other lymphocytes to some degree and maintain the immunologic equilibrium, which may help for SSc patients' symptom remission.

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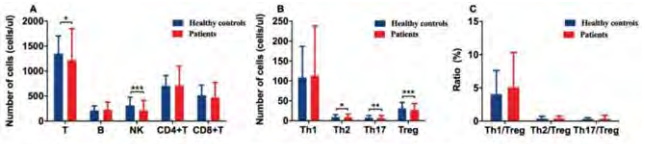


Figure 1: Comparison of absolute numbers of peripheral lymphocyte subsets between patients with SSc (n=166) and healthy controls (n=206). All the lymphocytes subpopulations were analyzed by detected by flow cytometry combined with standard absolute counting beads. Data were presented as mean±SD and statistical analysis was determined by two-tailed unpaired t-test. Patients had lower levels of T, NK, Th2, Th17 and Tregs compared with those of healthy controls. *P < 0.05, **P < 0.01, ***P < 0.001

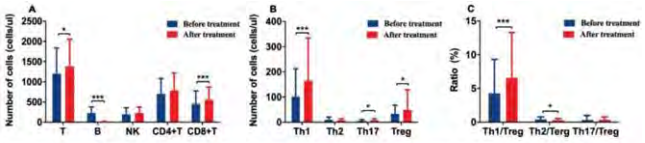


Figure 2: Changes of peripheral lymphocyte subsets after immunomodulatory combination treatments (n=79). Data were presented as mean±SD and statistical analysis was determined by two-tailed paired t-test. Absolute numbes of T, B, CD8+T, Th1, Th17 and Tregs in SSc patients were significantly increased after immunomodulatory combination treatments. *P < 0.05, **P < 0.01, ***P < 0.001.

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SAT0331

CHIPPING AWAY AT POLYMYOSITIS: A RETROSPECTIVE REVIEW AT A TERTIARY MYOSITIS CENTRE

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Background: Since first described, our understanding of polymyositis (PM) has evolved substantially. Patients previously diagnosed with PM may now be better described as having an alternative diagnosis, including immune-mediated necrotizing myopathy (IMNM), connective tissue disease overlap myositis (CTD-OM), anti-synthetase syndrome (ASS) or inclusion body myositis (IBM).

Objectives: To apply the current understanding of IIM subtypes to retrospectively review the diagnosis of patients classified as PM at our centre.

Methods: We reviewed a cohort of 255 patients from a UK tertiary myositis clinic, with 37 patients classified as PM according to the EULAR/ACR IIM criteria and expert opinion (1). Consensus decisions made as to whether reclassification as an alternative IIM subtype would be appropriate in each case.

Results: Thirty-seven patients with PM diagnosis according to EULAR/ACR IIM criteria and expert opinion were included in the analysis. Twenty-six patients (26/37, 68.4%) were female. The mean age at diagnosis was 57 years (SD 16.25) and mean follow up was 5.2 years (SD 4.8).

After consensus discussions, ten patients (27%) retained classification as PM, representing 3.9% (10/255) of the original cohort of 255 patients. The remaining 27 were reclassified as follows: 7 CTD-OM (18.9%), 6 IMNM (16.2%), 6 unspecified myopathy (16.2%), 2 DM (5.4%), 1 IBM (2.7%), and 1 non-inflammatory myopathy (2.7%, myofibrillar myopathy). Four patients (10%) had insufficient data available to allow for a defined diagnosis.

Of the 10 patients retaining classification as PM, 7 (70%) were female and mean age at diagnosis was 58.9 years. Clinical characteristics are represented in table 1. Mean CK at diagnosis was 2321 IU/L. Four patients (40%) were ANA positive, 8 patients (80%) were tested for the complete myositis antibody panel and 8 (80%) were specifically tested for the presence of HMGCR antibodies (figure 1). EMG revealed a myopathic pattern in 6/7 patients tested, while MRI demonstrated muscle oedema compatible with myositis in 3/5 of the patients that were tested. A complete muscle biopsy report was available in 8/10 PM-classified patients (80%), diffuse HLA-1 upregulation was present in 5 patients (50%), endomysial inflammatory infiltrates in 5 (50%) and perimysial infiltrates (in conjunction with endomysial infiltrates) in 3 (30%). No other specific features were found.

Table 1. Clinical features.

	PM (n=10)	CTD-OM (n=7)	IMNM (n=6)	All (n=37)
Pyrexia	0	0	0	1 (2.7 %)
Weight loss	2 (20%)	2 (28.6%)	2 (33.3%)	6 (16.2 %)
Cutaneous rash	0	1 (14.3%)	0	2 (5.4 %)
Mechanic's hands	1 (10%)	2 (28.6%)	0	4 (10.8 %)
Sclerodactyly	0	1 (14.3%)	0	1 (2.7 %)
Periungual erythema	0	1 (14.3%)	0	2 (5.3 %)
Raynaud's	0	5 (71.4%)	0	8 (21.6 %)
Arthralgia	0	5 (71.4%)	0	8 (21.6 %)
Arthritis	0	2 (28.6%)	0	5 (13.5 %)
Muscle weakness	10 (100%)	7 (100%)	6 (100%)	36 (97.2%)
Myalgia	3 (30%)	5 (71.4%)	3 (50%)	20 (54 %)
Dysphagia	3 (30%)	5 (71.4%)	1 (16.7%)	13 (35.1 %)
Interstitial lung disease (ILD)	0	3 (42.9%)	0	4 (10.5 %)
Malignancy	1 (9.1%)	0	2 (33.3%)	3 (8.1%)

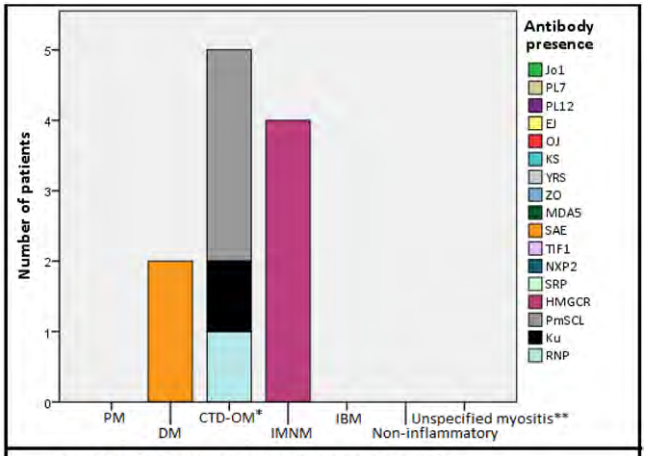


Figure 1. Antibody status according to consensus diagnosis.
* CTD-OM: Additionally 3 patients were anti-Ro52 positive and 1 patient was anti-Ro60 positive.
** Unspecified myositis. Additionally 2 patients were anti-Ro52 positive

Conclusion: This study confirms that PM can now be considered a rare IIM subtype. A thorough examination, complete myositis antibody panel including HMGCR testing and careful interpretation of the biopsy results is recommended to accurately classify these patients.

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SAT0332 ANTIBODIES AGAINST CYTOSOLIC 5'-NUCLEOTIDASE 1A IN SPORADIC INCLUSION BODY MYOSITIS: ASSOCIATION WITH CLINICAL AND MRI FEATURES

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Background: Autoantibodies directed against cytosolic 5´-nucleotidase 1A (cN1A) have been identified in sporadic inclusion body myositis (sIBM) and other connective tissue diseases. Anti-cN1A antibodies may support the diagnostic process for sIBM as well as potentially provide clues for disease pathogenesis. Nevertheless, the utility of anti-cN1A autoantibody testing in clinical practice remains unclear and requires validation.

Objectives: To investigate the association between anti-cN1A antibody status and clinical and MRI features in patients with sIBM.

Methods: Data for patients fulfilling European Neuromuscular Centre (ENMC) 2011 criteria for sIBM were obtained from a natural history study database. Demographic, clinical, functional assessment, and muscle MRI data in patients with sIBM who had anti-cN1A autoantibody testing were collected and analysed. Comparisons between subgroups with anti-cN1A antibody status were performed with the Mann-Whitney or Fisher's exact tests, as appropriate.

Results: Forty-nine patients with sIBM had anti-cN1A autoantibody testing, of whom 17 (34.7%) were positive. Twelve patients had muscle MRI performed (seropositivity=5). Demographics, disease duration at antibody testing and overall disease pattern were closely matched in antibody positive and negative cohorts. Dysphagia was more common in the seropositive subgroup (77% vs 47%, p=0.070). Antibody positive patients were more severely affected with a trend to lower IBM functional rating scale (IBMFRS) scores (22.4±8.4 vs 26.7±6.4, p=0.09) with significantly worse ability to climb stairs (0.9±0.9, 1.7±1.1, p=0.02). On T1-weighted MRI more fatty infiltration was found in seropositive patients (Mercuri score: 3.0±0.8 vs 1.7±0.7, p=0.03). Short tau inversion recovery (STIR) hyperintensity was more conspicuous in seropositive patients (STIR extent score: 2.4±0.6 vs 1.4±0.7, p=0.04).

Conclusion: There was a trend for more dysphagia and severity of dysphagia in seropositive patients. Differences in upper limb involvement were not seen according to IBMFRS and Medical Research Council (MRC) strength grades. Seropositive patients were more severely affected at the lower limb level, in terms of muscle weakness, physical function, MRI fatty infiltration and muscle inflammation. These results suggest positive antibody status is associated with a worse phenotype. These results have potential implications in clinical trials: whether antibody status influences treatment response should be assessed.

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SAT0333 SERUM METABOLITES AS BIOMARKERS IN SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE

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Background: In fibrotic diseases, metabolic processes are altered with a tendency towards an anabolic state, which is partially reflected in serum. Circulating biomarkers for interstitial lung disease (ILD), the leading cause of death in systemic sclerosis (SSc), are still sparse and not established in routine care.

Objectives: To assess the potential of serum metabolites as biomarkers for the presence and progression of SSc-ILD.

Methods: Age and sex matched serum samples of SSc patients from the Zurich cohort and of healthy controls (HC) were analyzed. Progressive SSc-ILD was defined as either a relative decrease in forced vital capacity (FVC) >10%, a decrease in FVC of 5-9% and a concomitant decrease of carbon dioxide diffusion capacity >15%, or an increase of the extent of lung fibrosis on computed tomography from <20% to ≥20% compared to the last visit (mean follow-up interval = 14 months (range = 9-26)). Sera of HC, non-ILD SSc and stable vs. progressive SSc-ILD patients (n = 12 per group; total n = 48) were screened for 110 metabolites by targeted liquid chromatography coupled to tandem mass spectrometry (LC-MS/MS). Peak areas were analyzed with R 3.6. For univariate analysis, FDR-corrected one-way ANOVA was used. In multivariate group-wise partial least squares discriminant analysis (PLS-DA), variable importance in the projection (VIP) scores ≥2 were considered significant.

Results: In total, 85 metabolites were detected. Univariate analysis of all groups were suggestive of changes for 1-methyladenosine, L-tryptophan, L-tyrosine, L-leucine and xanthosine (p = 0.077, 0.028, 0.077, 0.028 and 0.032, respectively). In PLS-DA, HCs and SSc patients differed in their levels of L-tyrosine and L-tryptophan, while levels of L-threonine, 3-aminoisobutyric acid, adenosine monophosphate and xanthosine were changed when comparing non-ILD and SSc-ILD patients. Receiver operating curve (ROC) analysis of significant metabolites from uni- and multivariate testing resulted in separation of SSc patients from HCs by L-tyrosine (area under the curve (AUC) = 0.81, 95% confidence interval (CI): 0.67-0.96), L-tryptophan (AUC = 0.86, CI: 0.75-0.97) and 1-methyladenosine (AUC = 0.82, CI: 0.71-0.94). Progressive SSc-ILD patients were separated from stable patients by their levels of L-isoleucine, L-leucine, adenosine monophosphate and xanthosine (AUC = 0.83, 0.85, 0.79 and 0.77; CI: 0.66-1.00, 0.70-1.00, 0.60-0.97 and 0.55-0.99, respectively). Validation of increased values of the branched-chain amino acids L-leucine and L-isoleucine in progressive SSc-ILD vs. stable ILD using an enzymatic assay resulted in similar results as LC-MS/MS analysis, with higher values detected in progressive vs. stable patients (mean = 286.5 and 235.5 nM, respectively; p = 0.005). In ROC analysis (AUC = 0.81, CI: 0.62-1.00), a cut-off value of 250.3 nM separated stable from progressive patients with a sensitivity of 72.7% and a specificity of 83.3%.

Conclusion: This study in SSc(-ILD) patients suggested alterations in serum metabolite levels corresponding with their current state of disease, indicating the potential use of serum metabolites as discriminating biomarkers upon further confirmation in larger multicenter studies.

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SAT0334 PERICARDIAL INVOLVEMENT IN SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is an autoimmune rheumatic disease characterized by visceral and skin fibrosis, vascular dysfunction, and immune dysregulation. Regarding cardiac manifestations, pericardial disorder is one of the most frequent but often asymptomatic.

Objectives: To analyze clinical manifestations, diagnostic tools and treatments of a patient cohort with SSc and pericardial involvement associated.

Methods: A descriptive, observational, cross-sectional study was carried out. We included all patients between 1975 and 2019 with diagnosis of SSc. Demographic, clinical and analytical data; imaging tests; treatments; and mortality rate were collected.

Results: 158 patients were included, 142 (89.9%) women and 16 (10.1%) men. 144 (91.1%) were Caucasians. Mean age at diagnosis was 57 years (range: 17-86). Type of scleroderma, clinical manifestations and autoimmunity profile were shown in table 1 and 2, respectively.

Table 1. Clinical manifestations

Clinical manifestations	n (%)
Cutaneous	
- Limited	104 (66.5%)
- Diffuse	40 (25.3%)
- Sine	13 (8.2%)
Raynaud's phenomenon	156 (98.7%)
Digital tip ulcers	63 (39.9%)
Telangiectasia	111 (70.3%)
Calcinosis	29 (18.4%)
Tendon friction rubs	3 (1.9%)
Joint involvement	44 (27.6%)
Musle involvement	13 (8.2%)
Interstitial Lung Disease	46 (28.9%)
Gastrointestinal	100 (62.9%)
Pulmonary hypertension	22 (13.8%)
Renal	1 (0.6%)

15 (9.4%) patients developed a pericardial disorder, 3 of them (1.8%) an acute pericarditis. In the majority of the patients (11, 73.3%) pericardial involvement appeared later than diagnosis of SSc with a mean time of 8 years (maximum period of time: 20 years), and the remaining 4 (2.5%) presented the pericardial involvement prior to SSc onset (up to 4 years before). Regarding to cutaneous involvement, limited SSc was the most frequent (13 patients, 86.6%), followed by diffuse SSc (3 patients, 13.4%). In relation to antibody profile, 11 (73.3%) patients were AC positive and 4 (26.6%) AT positive. Seven (46.6%) of the 15 patients with pericardial involvement had a prior pulmonary hypertension associated. Eleven (73.3%) were asymptomatic, 4 (26.6%) referred chest pain and 4 (26.6%) dyspnea. 100% of the pericardial effusions were detected through the performance of an echocardiogram, 3 of them (13.4%) with signs of diastolic dysfunction. Regarding to electrocardiographical findings, 2 (13.3%) showed low voltages. The size of the pericardial effusion was described as: mild in 9 (60%) patients, moderate in 5 (33.3%) and severe in 1 (6.7%). One Cardiac- Magnetic Resonance Imaging was performed which showed constriction data. None of the patients suffered cardiac tamponade or hemodynamic compromise, due to invasive therapies were not necessary. A spontaneous resolution of the pericardial effusion was registered in 6 (40%) patients, with a mean time of 8 months (range: 2-36 months); and 1 (6.7%) patient after an increment in immunosuppressive dose, without improvement of pulmonary hypertension. No renal crisis or deaths were recorded in these patients.

Conclusion: In our cohort patient with SSc, 9.5% developed a pericardial involvement. This kind of disorder could be the first manifestation of the disease. Pulmonary hypertension is the most frequent underlying pathway, however serositis must also be taken into account. Most part of the pericardial effusions were mild. No hemodynamic compromise was registered, due to an invasive treatment was not required.

Table 2. Antibody profile

Antibodies	n (%)
Anticentromere (AC) +	92 (58.2%)
Anti- topoisomerase I (AT) +	36 (22.8%)
Antinuclear (ANA) +	155 (97.5 %)

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SAT0335

SERUM AND BALF-DERIVED ANTI-JO1 AUTOANTIBODIES EXHIBIT HIGH REACTIVITY TO DISTINCT HISRS DOMAINS AND ASSOCIATE WITH LUNG AND JOINT INVOLVEMENT IN PATIENTS WITH IIM/ASS

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Background: Autoantibodies that target aminoacyl transfer(t) RNA synthetases (aaRS) represent the serological marker of the anti-synthetase syndrome (ASS), a major subgroup of the idiopathic inflammatory myopathies (IIM) (1). Among the anti-aaRS, anti-histidyl tRNA synthetase (HisRS) autoantibodies (anti-Jo1) are the most common. Up to 90% of IIM/ASS patients diagnosed with interstitial lung disease (ILD) harbor anti-Jo1 autoantibodies (2).

Objectives: Reactivity and affinity of anti-Jo1 autoantibodies from serum and broncheoalveolar lavage fluid (BALF) were investigated against HisRS autoantigen. Associations with clinical data from patients IIM/ASS were addressed.

Methods: Total IgGs were purified by affinity chromatography. Samples and clinical data were obtained from: i) 26 anti-Jo1$^+$ patients (19 at diagnosis, 16/19 at follow-up, 7 BALF/matching serum at baseline; ii) 29 anti-Jo1$^-$ (25 serum at diagnosis, 4 BALF/matching serum at baseline); iii) 24 age/gender matched healthy controls. Anti-Jo1 IgG and IgA response against HisRS was evaluated by ELISA and western blot. Affinity was measured by surface plasmon resonance. HisRS full-length (HisRS-FL), two HisRS domains (ABD and CD), and two HisRS splice variants (WHEP and WHEP + ABD splice variant (SV)) were tested. Correlations between autoantibody reactivity and clinical data, at baseline and over disease course, were evaluated.

Results: Anti-Jo1 autoantibodies from serum and lung bound HisRS-FL, WHEP and SV with high reactivity and affinity already at diagnosis and recognized both conformational and linear HisRS epitopes (Fig. 1). Levels of autoantibodies (against HisRS-FL, -domains and -splice variants) varied among patients and overtime. Patients with ILD, arthritis and less skin involvement presented higher anti-Jo1 titers compared to those with lower anti-Jo1 titers and to the anti-Jo1 negative group (Fig. 2). Anti-WHEP reactivity in BALF strongly correlated with poor pulmonary function.

Conclusion: High reactivity and affinity at time of diagnosis indicates that autoimmunity against HisRS is most likely initiated before IIM/ASS diagnosis. Reactivity to specific splice variants of HisRS may be employed as diagnostic and prognostic markers.

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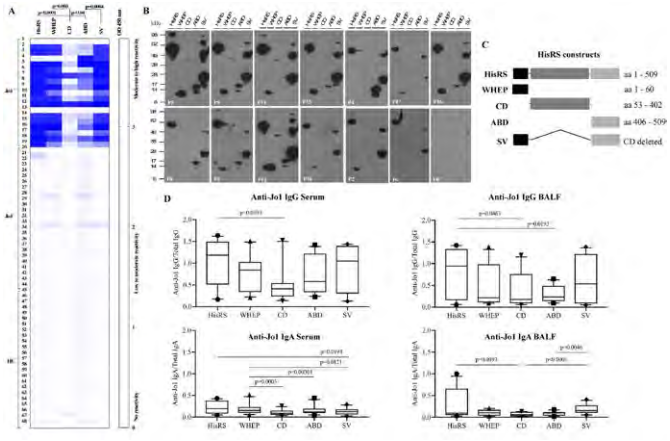


Fig. 1. Anti-Jo1 reactivity in total IgG purified from the first available serum sample

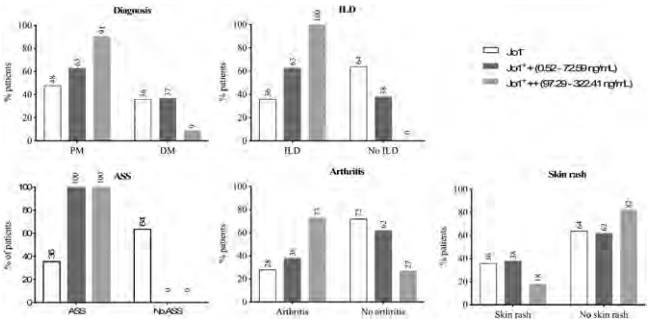


Fig. 2. Reactivity of total anti-Jo1+ IgG purified from the first available serum close to IIM/ASS diagnosis in relation to clinical data

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SAT0336 SYMPTOMS OF AUTONOMIC DYSFUNCTION IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Objectives: This study aims to assess prevalence, severity and clinical correlates of symptoms of autonomic dysfunction in patients with SSc
Methods: Fifty five consecutively recruited SSc patients were included in this study. Thirty seven (67.3%) patients had limited (lcSSc), whilst 18 (32.7%) patients had diffuse cutaneous SSc (dcSSc). Anticentromere antibodies (ACA) were positive in 31 (56.4%) of patients, whilst 20 (26.4%) patients had anti-topoisomerase I antibodies (ATA). All patients completed the Composite Autonomic Symptom Score (COMPASS-31) questionnaire, which consists of 31 items, quantifying six autonomic domains: orthostatic intolerance (OI), vasomotor (VD), secretomotor (SD), gastrointestinal (GD), bladder (BD) and pupillomotor dysfunction (PD). The total score ranges from 0 to 100, whilst scores for particular domains range as follows: 0-40 for OI, 0-5 for VD, 0-15 for SD, 0-25 for GD, 0-10 BD, and 0-5 for PD. Higher values representing more severe symptoms. Differences in total COMPASS-31 score and domain-specific scores were assessed with respect to disease form, antibody status, capillaroscopic findings, lung diffusing capacity and joint involvement. Moreover, we assessed the correlation between COMPASS-31 scores, disease status (assesed using the Scleroderma Assessment Questionnaire – SAQ) and severity of gastrointestinal symptoms (assessed using the UCLA SCTC GIT 2.0 questionnaire)
Results: Percentage of SSc with a score >0 in particular domains of the COMPASS-31 were as follows: OI – 32/55 (58.2%), VD – 49/55 (89.1%), SD – 36/55 (65.5%), GD – 40/55 (72.7%), BD - 26/55 (47.3%), PD – 30/55 (54.5%). The COMAPSS-31 score did not correlate with age or disease duration. There was no relationship between the COMPASS-31 total or subdomain scores and SSc subtype or autoantibody status. Similar mean values for total and subdomain scores were found among patients with different capillaroscopic patterns. Patients with DLCO < 80% had significantly higher mean values of GD, BD and PD scores, compared to patients with DLCO≥80% (4.42 vs 2.75, 1.51 vs 0.38, 1.93 vs 1.09, respectively). Moreover, the total COMAPSS-31 score was significantly higher in patients with decreased DLCO (16.24 vs 11.34, p=0.008). Patients with joint involvement had higher COMPASS-31 score than patients without (17.74 vs 9.85, p=0.012). We have found a statistically significant (p<0.001) correlation between the COMPASS-31 score and the Index of disease status (IDS), as well as the the total UCLA SCTC GIT score (rho=+0.45, rho=+0.51, respectively).
Conclusion: Symptoms of dysautonomia are common in SSc patients. Patients with a more severe disease, especially decreased lung diffusing capacity, joint pain, and severe gastrointestinal involvement, report more symptoms of autonomic dysfunction.
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SAT0337 EVALUATION OF BODY COMPOSITION AND BONE STATUS ACCORDING TO MICROVASCULAR INVOLVEMENT IN SYSTEMIC SCLEROSIS PATIENTS

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Background: Systemic sclerosis (SSc) is a complex autoimmune connective tissue disease, characterized by autoimmune inflammatory microvascular damage with progressive loss of capillaries, fibrosis and ischemia of skin and internal organs. (1) Nailfold videocapillaroscopy (NVC) is a safe toll for early diagnosis of SSc, it identify morphological changes of vessel that are predictive for clinical disease progression and organ involvement.(2) About clinical complication the loss of bone mass and body composition abnormalities, particularly muscle mass and strength loss (sarcopenia), are recognized in advanced disease.(3)
Objectives: To evaluated in SSc patients, the body composition and the bone status according to the microvascular condition, assessed and scored by nailfold videocapillaroscopy (NVC, "Early","Active","Late" patterns).
Methods: Body composition and bone mineral density (BMD) were assessed by DEXA in 35 female SSc patients classified according to the 2013 EULAR/ACR criteria and 32 sex-matched healthy subjects. Clinical, laboratory, body composition and bone parameters were analysed according to the different NVC patterns. Means were compared by the Student's t test or one way analysis of variance; medians were compared by the Kruskall Wallis test; and frequencies by the chi square test.
Results: Higher prevalence of vertebral (26.4%vs 9.3%) and femoral (32.3% vs 9.3%) osteoporosis (OP) was found in SSc. Particularly SSc patients with "Late" NVC pattern showed a significantly higher prevalence of vertebral (p=0.018) and femoral OP (p=0.016). Regional assessment of bone mass (BM) in 7 different body areas showed a significant lower BMD only at the total spine (P=0.008) and femoral neck (p=0.027) in advanced microvascular damage. Patients with "Late" NVC pattern showed lower whole body lean mass (LM) compared to "Early" and "Active" NVC patterns, particularly at upper limbs. To note, in all body sites, BMD correlate with LM and BMC according to NVC pattern severity.
Conclusion: SSc patients with most severe microvascular damage show a significantly altered body composition and bone status suggesting a strong link between microvascular failure and associated muscle/bone sufference.
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SAT0338 CONTRAST-ENHANCED ULTRASONOGRAPHY IN THE EVALUATION OF MYOSITIS

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Background: contrast-enhanced ultrasonography (CEUS) has been proposed as a tool to assess myositis, but data in the literature are still scarce (Radiologe 2018;58:579).
Objectives: to evaluate CEUS as a tool to assess myositis patients and its accuracy in differentiating myositis from common mimickers.
Methods: 16 patients with myositis (4 polymyositis, 6 dermatomyositis, 2 immune-mediated necrotizing myopathy, 1 inclusion body myositis, 2 overlaps Sjøgren's syndrome - myositis and 1 Enterovirus-reactive myositis) and

4 controls (2 peripheral neuropathy, 1 limb girdle muscle dystrophy, and 1 metabolic myopathy) underwent after rest CEUS (Esaote MyLab, linear probe 13-5 MHz, Sonovue®) at a room temperature of 20° of the vastus lateralis and medialis muscles. CEUS was performed by 2 ultrasonographists with an expertise in muscle US blinded to the clinical data of the patients. CEUS muscle signal was expressed on a 0-4 scale as described in J Rheumatol 2001; 28:1271 per each muscle group and the global score was divided by four. Creatine kinase (CK), manual muscle test (MTT) and MRI of the thigh muscles were performed within maximum one month from the CEUS. MMT was expressed using the 0-5 Medical Research Council scale; intermediate points were converted into decimals as detailed in Kendall FP et al, Muscle Testing & Function: Testing and Function with Posture and Pain. 5th ed., Lippincott Williams & Wilkins, 2005. MRI of the thigh muscles was considered positive if it showed muscle edema. Myositis was defined active if CK was raised above the reference range and/or MMT showed progressive worsening. Results were expressed as median (range). Between-group comparison was performed with Mann-Whitney test. Statistical analysis was performed with SPSS version 20. The study was approved by the Ethics Committee and all patients provided their written consent.

Results: Median (range) age was 38 (69) years in the myositis and 41 (45) years in the control group (p=0.89). Disease duration in the myositis group was 60 (334) months. CEUS muscle score was 0.5 (3) in the myositis group and 2 (3) in the control group (p=0.99). In the myositis group, CEUS score did not differ between treated and untreated patients (p=0.84). CK values were 361 (6442) in the myositis group and 363 (799) in the control group (p=0.68). MMT was significantly lower in the myositis group [4.33 (2)] than in the control group [4.94 (0)] (p=0.038). CEUS was 77% (47-05 95% confidence interval) sensitive and 67% (9-99% 95% confidence interval) specific for a diagnosis of myositis. CEUS was positive in 10/13 patients and negative in 3/13 with active myositis, while was negative in 2/3 patients and positive in 1/3 with inactive myositis. Statistically, CEUS did not discriminate between active and inactive myositis (Fisher's exact test p= 0.21). All controls had a positive CEUS. No association was found between MRI edema and a positive CEUS (intraclass correlation coefficient p=0.5). No correlation was found between CEUS score, on the one hand, and CK levels or MMT, on the other (Spearman's rho p>0.05).

Conclusion: CEUS has moderate sensitivity for a diagnosis of myositis, but does not discriminate between myositis and some of its common mimickers. Larger studies are required to better evaluate the role of CEUS in patients with myositis.

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Investigator for the gevokizumab in myositis Servier study (2014), the sirukumab in GCA GSK study (2016), PI for the ToReMy AIFA funded (2017) study and for the FOREUM funded (2018) GCA study

, Speakers bureau: Guest speaker at UCB-sponsored meetings: (Immunology Summits, Prague, 2012, 2013 & 2014, MACRO Meet the expert at the ACademy of RheumatOlogy, Bologna 13 - 14 April 2012, GRAPPA Workshop, Milan 29 January 2016 and Rome 30 November 2017), Fininvest (Catania 2016), Aim Group (Reggio Emilia 2018), I&C (Cologna, 2018), Alfa-Wassermann sponsored meeting (Rhewind, Bologna, February 2016 and 2019)

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SAT0339 NERVOUS SYSTEM INVOLVEMENT IN SYSTEMIC SCLEROSIS: A COHORT STUDY

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Background: Nervous system involvement is considered to be rare in systemic sclerosis (SSc). Its prevalence is highly variable in SSc cohort studies and its prognosis is not well established.

Objectives: To determine the frequency, clinical characteristics, associations, and outcomes of different types of peripheral nervous system (PNS) and central nervous system (CNS) disease in a cohort of systemic sclerosis patients.

Methods: We have carried out a retrospective observational study by systematically analyzing the medical records of patients diagnosed with SSc in Toulouse University Hospital and Ducuing Hospital, south west France. We included patients who met the following inclusion criteria: being over 18 years of age on diagnosis, meeting the ACR /EULAR 2013 classification criteria, being diagnosed after 01/01/1966 and before 31/12/2018, at least 12 months of follow-up. Patients were followed until 31/12/2019. Nervous system involvement associated with SSc was included when there was involvement on or after diagnosis and after exclusion of all other causes. Only symptomatic clinical involvement was included. Ischemic or hemorrhagic strokes were excluded. We calculated the incidence of CNS and/or PNS disease during the follow-up period per 1,000 person-years. Kaplan-Meier curves were plotted to determine the cumulative incidence of nervous system disease. We evaluated associated factors of CNS and/or PNS disease using multivariable Cox regression.

Results: Of 447 SSc patients, 79.8% were female, 68 (15%) were diffuse cutaneous SSc, 342 (77%) were limited cutaneous SSc and 37 (8%) were sine scleroderma SSc. The mean ± SD age at diagnosis was 52.9 ± 14.3 years.

During the study period, 82 (18%) patients experienced a PNS disease, 29 (6%) a CNS disease. The incidence was 28 per 1,000 patient-years of any nervous system disease, with 22 per 1,000 patient-years and 6 per 1,000 patient-years of PNS disease and CNS disease, respectively. The most frequent were carpal tunnel syndrome (63%) and polyneuropathies (12%) for PNS disease, and headache (45%) and seizures (10%) for CNS disease.

Three significant independent associated factors with PNS disease occurrence were identified using multivariable Cox regression: BMI>23.1kg/m^2 (HR = 1.06 [1.01-1.12]), joint involvement (HR = 2.7 [1.3-5.5]), and an alteration in the left ventricular ejection fraction (HR = 3.8 [1.4-10.3]).

Four significant independent associated factors with CNS disease occurrence were identified: age > 54 years (HR = 2.5 [1.1-6.0]), positive anti-PmScl testing (HR = 6.4 [1.5-28.2]), Caucasian origin (HR = 0.2 [0.1-0.5]) and hemoglobin < 12g/dl (HR = 0.2 [0.04-0.8]).

Nervous system disease occurrence did not appear to have a negative impact on the survival of SSc patients (log-rank p=0.56).

Conclusion: This study shows that specific nervous system disease in SSc is not uncommon and does not appear to increase mortality, but it could have an impact on functional prognosis and needs to be monitored.

Disclosure of Interest: None declared

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SAT0340 A REDUCED NUMBER OF CAPILLARIES AND AN INCREASED NUMBER OF MEGACAPILLARIES PREDICT THE DEVELOPMENT OF SYSTEMIC SCLEROSIS IN RAYNAUD'S PHENOMENON PATIENTS AT RISK

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Background: Undifferentiated connective tissue disease at risk for systemic sclerosis (UCTD-risk-SSc) is a condition characterised by Raynaud's phenomenon and either SSc marker autoantibodies or typical capillaroscopic findings or both, unsatisfying classification criteria for SSc and evolving into definite SSc in about 30-50% of cases (1,2). Recently, we developed a weighted score based on a baseline IF-ANA titer ≥1:320, marker autoantibody positivity and presence of avascular areas at videocapillaroscopy identifying patients who will evolve with a 91.3% sensitivity and a 73.2% specificity (3).

Objectives: To improve the predictivity of the score assessing the role of marker autoantibody ELISA titer and further capillaroscopic items.

Methods: The 102 UCTD-risk-SSc patients investigated for the development of the previous score were reassessed for anti-Scl-70 and anti-centromere antibody titers detected by ELISA and for the mean number of capillaries observed in the same capillaroscopic field (Cs) and the total number of giant capillaries (GC) by videocapillaroscopy (4). Each patient was evaluated every 6 months to assess disease progression. Risk prediction was assessed by Cox regression analyses. The predictive value of the score was determined by receiver operating curve (ROC) analysis.

Results: Table 1 shows the resulting predictive variables in multivariate Cox analysis and their relative weight in a 10-point scale. No increase in the predictivity was detected by adding the anti-Scl-70 and anti-centromere antibody ELISA titers. However, a mean number of Cs≤5/mm and GC>5 improved the score. At ROC analysis (Figure 1) a score >3.25 predicted evolution to SSc with a sensitivity of 93.5% and a 75% specificity (AUC=0.91).

Table 1. Indipendent predictive variables in multivariate regression analysis and the resulting weighted prediction model *

Variable	β	HR	95% CI	*P*	Weight
Anti-Scl70	2.9553	19.21	4.87-75.76	<0.001	3.25
Cs≤5/mm	1.9093	6.75	2.07-22.00	0.001	2
ANA ≥ 1:320	1.7402	5.70	1.42-22.85	0.01	2
ACA	1.6740	5.33	1.51-1.90	0.01	1.75
GC>5	1.0049	2.73	1.44-5.17	0.002	1

*β: regression coefficients; HR: hazard ratio; 95% CI: 95% confidence interval; Cs: Capillaries; ANA: anti-nuclear antibodies; ACA: anti-centromere antibodies; GC: giant capillaries

Conclusion: Assessing the mean number of capillaries/mm and the total number of giant capillaries instead of avascular areas at videocapillaroscopy, resulted in improving the sensitivity and specificity of the score recently developed to predict the evolution of UCTD-risk-SSc into definite SSc.

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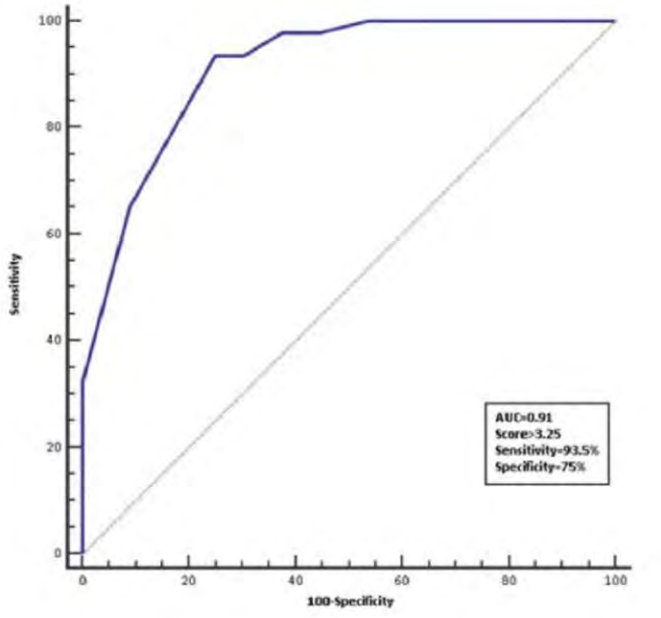


Figure 1. ROC analysis identify the score with the highest sensitivity and specificity. A score>3.25 predicted evolution to SSc with 93.5% sensitivity and 75% specificity.

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SAT0341

PREDICTORS TO PROGRESSION TO SYSTEMIC SCLEROSIS IN A GROUP OF SECONDARY RAYNAUD PHENOMENON OBSERVED IN A LARGE SINGLE BRAZILIAN COHORT

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Background: The 2013 ACR/EULAR classification criteria for systemic sclerosis (SSc) allowed the inclusion of a subset of patients without skin involvement, emphasizing the need of early diagnosis of SSc.

Objectives: In this setting, the objective of this study was to classify, according to ACR/EULAR SSc criteria, patients with Raynaud phenomenon (RP) and at least one SSc manifestation, except for skin involvement, and analyze predictors for development of SSc.

Methods: This is a cross-sectional single-center analysis of consecutive patients presenting RP and a characteristic SSc manifestation (SSc autoantibody, SSc visceral involvement or SD pattern at nailfold capillaroscopy - NFC), without skin involvement, who attended a scleroderma outpatient clinic between 2010 and 2019. Patients were classified as SSc (according to ACR/EULAR SSc criteria) or undifferetiated connective tissue disease (UCTD) in their last medical visit and compared. Additionally, a longitudinal retrospective analysis of both groups was performed to find predictors for development of SSc. Data were obtained from an electronic register database. Statistical significance was set up as p<0.05.

Results: Among 217 patients, 153 (70.5%) were classified as SSc, at the last medical visit, including 65 (30%) after the first investigation. During a comparable median follow-up [4.9±3.8 vs. 4.6±3.0 years;p=0.90], patients with SSc presented more frequently puffy fingers (PF:73% vs. 6.3%;p<0.01), pitting scars (87.4% vs. 4.7%;p<0.01), digital ulcers (25.2% vs. 1.6%;p<0.01), telangiectasias (52.3% vs. 7.8%;p<0.01), interstitial lung disease (ILD:66.7% vs. 34.4%;p<0.01), pulmonary hypertension (PH:18.3% vs. 7.9%;p=0.049) and esophageal dismotility (ED: 58.9% vs. 43.8%:p=0.02) than secondary RP patients without SSc. Moreover, SSc patients had more SD pattern at NFC (83.4% *vs*. 57.8%;p<0.01), anti-Scl70 antibody (16.6% *vs*. 3.1%;p<0.01), and nucleolar ANA pattern (22.5% *vs*. 10.9%;p=0.048). Furthermore, SSc patients were more frequently treated with immunosuppressive therapy (80.1% *vs*. 37.5%;p<0.01) and presented an increased death rate (9.9% *vs*. 1.6%;p<0.01 and Figure 1). For the analysis of the predictors to SSc, patients who had already fulfilled SSc criteria at baseline were excluded and 152 patients were analysed: 88 progressed to SSc and 64 remained as UCTD. After multivariate analyses, puffy fingers (OR=4.48; 95%CI 1.17-17.17;p=0.029) and a higher SSc score, both at baseline, (OR: 1.97; 95%CI 1.33-2.92;p<0.001) were predictors to SSc, while esophageal symptoms (OR=0.18; 95%CI 0.05-0.67; p=0.01) and absence of clinical symptoms (OR=0.08; 95%CI 0.01-0.40; p=0.002) were negative predictive factors. When analyzing the combination of SSc features, RP + PF + positive ANA (OR=15.5; 95%CI 4.5-53.1;p<0.001), RP + PF + positive ANA + SD-NFC (OR=12.3; 95%CI 2.8-54.2;p<0.001), RP + PF + SD-NFC (OR=12; 95%CI 2.79-54.1;p<0.01), and RP + lung disease (ILD/HAP) + SD-NFC (OR=3.0; 95%CI 1.1-10.5;p<0.04) were associated with classification as SSc, while combinations without non-RP clinical symptoms, as RP + SD-NFC (OR=0.027; 95%CI 0.003-0.210;p<0.001) and RP + anticentromere + SD-NFC (OR=0.050; 95%CI 0.007-0.440;p<0.001) were not associated with SSc.

Conclusion: Among patients with RP and SSc features, but without skin involvement, those with SSc had a more severe disease with worse prognosis than UCTD with RP. Puffy fingers and a higher baseline SSc score, especially in combinations including PF or lung disease were predictors of SSc, reinforcing the strength of the ACR/EULAR classification criteria and the presence of specific non-RP symptoms.

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SAT0342

INNATE LYMPHOID CELLS ARE PREDICTORS OF DISEASE PROGRESSION IN SYSTEMIC SCLEROSIS: A 3-YEARS FOLLOW-UP STUDY

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Background: Activation of the immune system is a characteristic feature of SSc. Numerous studies have suggested that type 2 are key drivers of progressive fibrosis. Recently, innate lymphoid cells (ILC) are emerging as an important cellular source of type 2 cytokines triggering fibrotic tissue remodeling independently of the adaptive immune system. Increased levels of ILC2 were found in patients with SSc. However, the contributive role of ILC2 in pathogenesis of SSc is not completely understood.

Objectives: We aim in our 3 years observational study to evaluate the predictive role of ILC2 in SSc patients.
Methods: We conducted an observational retrospective study on 52 patients with SSc fulfilling the 2013 ACR/EULAR classification criteria. Yearly clinical, laboratory and investigational data according to EUSTAR recommendations were collected. Blood samples collected between 15.09.2014 and 15.01.2015 were analyzed by flow cytometry and ILC2 counts were measured. The predictive value of ILC2 during a 3-year follow-up was analyzed using SPSS 21.0.
Results: 52 patients were included in the study, 78% female, 63% limited cutaneous SSc with a mean follow-up time of 2.85 ± 1.28 years. At baseline we have shown that circulating ILC2s are significantly increased compared to gender and age-matched healthy controls. Increased numbers of ILC2s significantly correlated with worsening of mRSS calculated by five point increase in mRSS or 25% increase from baseline ($p < 0.001$; 95% CI 1.39 – 3.26). ILC2 counts also correlated with 5% decrease of diffusion capacity of carbon monoxide (DLCO) during the follow-up time ($p < 0.0001$; 95% CI 1.83 – 3.49). Worsening of forced vital capacity (FVC) assessed as 5% decrease over 2 years was also significantly correlated with an increased number of ILC2s ($p < 0.0001$; 95% CI 1.27 – 3.04). In contrast, we did not find any correlation regarding increase in pulmonary arterial pressure assessed by echocardiography. Although new appearance of digital ulcers could not be predicted by ILC2 counts, increased numbers of ILC2s were correlated with digital ulcers at follow-up.
Conclusion: Here, we provide first evidence for a role of ILC2s as potential prognostic marker of disease progression in SSc.
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SAT0343 NUTRITIONAL STATUS OF SYSTEMIC SCLEROSIS PATIENTS: A PILOT STUDY

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Background: Gastrointestinal involvement (GI) in systemic sclerosis (SSc) is one of the major disease burdens. Its consequences on the nutritional status of SSc patients and their quality of life is poorly evaluated during routine check-ups. Since malnutrition is an important cause of morbidity and mortality, addressing this issue seems necessary.
Objectives: The aim of this study was to evaluate the risk of malnutrition in SSc patients and to identify potential associations between the risk of malnutrition and clinical features or laboratory parameters.
Methods: All patients aged >18 years old with a definite diagnosis of SSc according to the 2013 ACR/EULAR classification criteria from the EUSTAR Center 16 and ERN ReCONNET cohort of the County Emergency Clinical Hospital Cluj-Napoca were included in the study. Patients with localized scleroderma, scleroderma sine scleroderma, overlap syndromes and mixed connective tissue disease were excluded. Clinical and laboratory data was collected from the EUSTAR database and medical charts. A telephone survey was conducted and patients were interviewed using the Malnutrition Universal Screening Tool (MUST) questionnaire.
Results: 75 patients were eligible for the study. Female to male ratio was 10:1 with an almost equal distribution among limited (57%) and diffuse (43%) SSc subtypes. The most prevalent autoantibodies were anti-TOPO-I and anti-centromere. GI symptoms were reported in 48.6% patients out of which 86% SSc patients underwent further evaluation by upper GI endoscopy. Abnormal endoscopic findings, such as esophagitis, Barret esophagus and gastritis were identified in 80% patients. Most patients had a low risk of malnutrition (93%) with only a minority carrying a medium (6%) or high (1%) risk. No significant association was demonstrated between MUST score and the extend of cutaneous involvement (limited SSc versus diffuse SSc; p=0.39), presence of GI symptoms (p=0.35), presence of abnormal endoscopic findings (p=0.45) or presence of anemia (p=0.83).
Conclusion: The majority of SSc patients from this cohort exhibited a low risk of malnutrition. These results are contradictory to previous literature reports. A possible explanation is that the MUST score is a dynamic screening tool and therefore interviewing patients with a stable disease (outpatient care) versus patients with active disease (inpatient care) might lead to different results. Another limitation of this study is the small number of patients included. This is a pilot study. We aim to further extend the study population to the other EUSTAR cohorts and to prospectively evaluate these patients in an inpatient care setting.
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SAT0344 LIMITED JOINT MOBILITY OF HAND IN SYSTEMIC SCLEROSIS PATIENTS BY USING "PRAYER" AND "TABLE TOP" SIGNS

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Background: Limited joint mobility (LJM) is a musculoskeletal disorder caused by flexion contractures of hand is a common complication in systemic sclerosis (SSc) patients. The distal parts of the upper limb (hands and fingers) is the most involved site in SSc.
Objectives: In this study, we aimed to evaluate LJM in SSc patients and to determine the relationship between the clinical features of the disease.
Methods: A total of 113 patients (>18 years old) diagnosed with diffuse cutaneous systemic sclerosis (DcSSc) and limited cutaneous systemic sclerosis (LcSSc) and 104 healthy controls were included in this study. LJM was evaluated with "prayer sign" and "table top sign" tests. LJM staging was done by Rosenbloom classification method(1, 2). LJM (+) and LJM (-) patients were compared in terms of demographic findings (gender, age and duration of disease), laboratory results (ESR, CRP, ANA, anti-topoisomerase I and anti-centromere) and modified Rodnan Skin Score (mRSS) results.
Results: In our study, a total of 113 patients diagnosed with SSc and 104 healthy controls with similar age and gender distribution were included. While LJM (+) was detected in 75 (66.4%) (LcSSc = 38, DcSSc = 37) of the patients diagnosed with SSc, LJM (mild) (+) was detected in 3 (2.8%) of the control group. One of these people had right 2nd DIF joint contracture due to osteoarthritis, and 1 patient was found to have simple contractures due to minor hand injury previously (Table 1). A statistically significant difference was observed in between LcSSc and DcSSc patients according to the presence of LJM ($p<0.001$) (Table 2). There was a moderate positivity relationship between LJM and mRSS (LcSSc: $r=0.449$ ve $p<0.001$, DcSSc: $r= 0.565$ ve $p<0.001$) (Figure 1).

Table 1. Comparison of demographic findings between SSc and Control group

	SSc Group (n=113)	Control Group (n=104)	p value
Age, year	57.02 ± 11.58	58.47 ± 11.26	0.061
Gender (F / M)	98 (86.7) / 15 (13.3)	65 (62.5) / 39 (37.5)	0.064
CRP (mg/L)	5.45 ± 5.39	2.14 ± 1.12	**<0.001**
ESR (mm/hr)	25.19 ± 18.9	14.46 ± 10.09	**0.024**
Smoking, n (%)			
Smoker	89 (78.8)	70 (67.3)	0.464
Non-Smoker	24 (21.2)	34 (32.7)	
LJM (Absent / Present)			
Present	75 (66.4)	3 (2.8)	**<0.001**
Absent	38 (33.6)	101 (97.2)	
Rosenbloom classification	**LcSSc (n=71) (%)**	**DcSSc (n=42) (%)**	**Total (n=113) (%)**
Normal	46.5	11.9	33.6
Mild	22.5	14.3	19.5
Moderate	23.9	33.3	27.4
Severe	7.1	40.5	19.5

Table 2. Comparison of demographic and clinical findings LJM(-) and LJM(+) in SSc

	LJM (-) (n=38)	LJM (+) (n=75)	p value
Age, year	54.16 ± 11.82	58.47 ± 11.26	0.061
SSc Type	n (%)	n (%)	
LcSSc, n (%)	33 (56.8)	38 (50.7)	**<0.001**
DcSSc, n (%)	5 (13.2)	37 (49.3)	
Gender, F/M (%)	37 (97.3) / 1 (2.7)	61 (81.3) / 14 (18.7)	**0.018**
Raynaud's (symptom duration), month	148 (44-456)	150 (35-588)	0.990
Non-raynaud (symptom duration), month	108 (28-458)	138 (38-447)	0.132
mRSS, median	2 (0-14)	8 (0-36)	**<0.001**
CRP (mg/L)	4.21 ± 4.48	6.08 ± 5.71	0.069
ESR (mm/hr)	19.74 ± 10	27.95 ± 21.6	0.270
Renal crisis, n (%)	1 (2.6)	4 (5.3)	0.662
PAH, n (%)	8 (21.1)	14 (18.7)	0.762
ANA positivity, n (%)	36 (94.7)	70 (93.3)	1
Anti-centromere positivity, n (%)	18 (47.4)	19 (25.3)	**0.01**
Anti-topoisomerase-1, n (%)	8 (21)	34(45.3)	**0.01**
Smoking, n (%)	n (%)	n (%)	
Non-smoker	30(78.9)	59 (78.7)	0.970
Smoker	8 (21.1)	16 (21.3)	

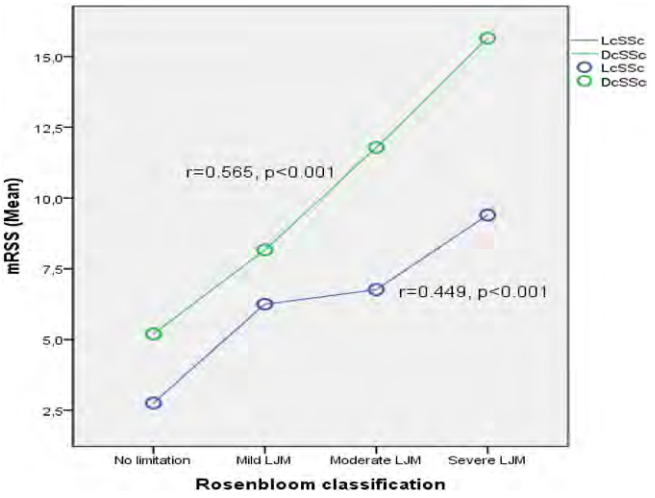


Figure 1.

Conclusion: In our study, it was found that LJM staging positively correlated with mRSS and DcSSc patients had more severe LJM findings than LcSSc. We conclude that "prayer sign" and "table top sign" tests used in hand evaluation in SSc patients have similar clinical results with mRSS and can be easily performed in daily practice in about 3 minutes.

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SAT0345

IS THERE A DIFFERENCE BETWEEN THE SEXES IN THE RATE OF PROGRESSION OF SYSTEMIC SCLEROSIS-ASSOCIATED ILD (SSC-ILD)? DATA FROM THE SENSCIS TRIAL

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Background: Previous studies suggested that male sex may be associated with a greater rate of decline in FVC in patients with SSc-ILD. In the SENSCIS trial, nintedanib reduced the rate of FVC decline over 52 weeks vs placebo.

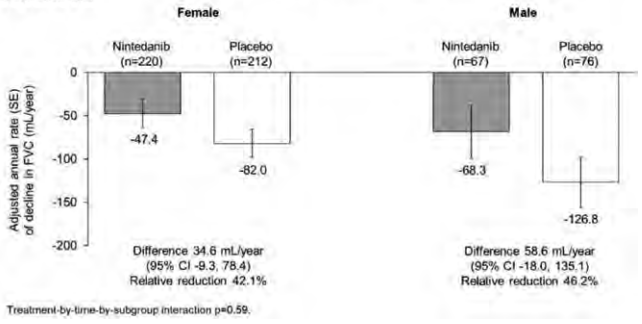
Objectives: Analyse the rate of decline in FVC and the efficacy and safety of nintedanib in the SENSCIS trial in subgroups by sex.

Methods: Patients with SSc-ILD with first non-Raynaud symptom <7 years before screening and ≥10% fibrosis of the lungs on HRCT were randomised to nintedanib or placebo. We analysed the rate of decline in FVC (mL/year) and adverse events over 52 weeks in male and female patients.

Results: Of 576 patients, 433 (75.2%) were female. Compared with males, the female subgroup included a smaller proportion of White patients (64.7% vs 74.8%), a smaller proportion on mycophenolate at baseline (46.9% vs 53.1%), a greater proportion of ATA positive patients (63.3% vs 53.1%), and had a lower mean weight at baseline (66.6 vs 79.1 kg). FVC % predicted (72.8% vs 71.7%) and mRSS (11.2 vs 10.8) were similar in females and males. The adjusted annual rate of decline in FVC in the placebo group was numerically greater in male than female patients (-126.8 [SE 29.0] vs -82.0 [16.2] mL/year). The estimated effect of nintedanib vs placebo on reducing the rate of decline in FVC was numerically more pronounced in males than females (difference: 58.6 [95% CI -18.0, 135.1] vs 34.6 [-9.3, 78.4] mL/year), but the interaction p-value did not indicate heterogeneity in the treatment effect between subgroups (p=0.59). Among nintedanib-treated patients, diarrhoea was reported in similar proportions of females and males (74.7% vs 79.1%); nausea, vomiting and liver test abnormalities were reported in greater proportions of females vs males (35.3% vs 19.4%, 28.1% vs 13.4%, and 15.4% vs 9.0%), while serious adverse events were more frequent in males (32.8% vs 21.3%). In the nintedanib and placebo groups, respectively, adverse events leading to treatment discontinuation were reported in 16.7% and 8.5% of females and 13.4% and 9.2% of males.

Conclusion: In the SENSCIS trial in patients with SSc-ILD, the annual rate of decline in FVC in the placebo group was numerically greater in male than female patients. The rate of FVC decline was lower with nintedanib than placebo both in males and females. The safety profile of nintedanib was similar between males and females.

Figure. Rate of decline in FVC (mL/year) over 52 weeks in subgroups by sex in the SENSCIS trial



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Bristol-Myers Squibb, Boehringer-Ingelheim, Lilly and Novartis, Consultant of: Lilly, Novartis, Janssen, Boehringer-Ingelheim, Amgen, Pfizer and Abbvie, Speakers bureau: Sandoz, Celltrion, Lilly, Novartis, Janssen, Boehringer-Ingelheim, Amgen, Pfizer and Abbvie, Sindhu Johnson Grant/research support from: Boehringer Ingelheim, Corbus Pharmaceuticals, GlaxoSmithKline, Roche, Merck, Bayer, Consultant of: Boehringer Ingelheim, Ikaria, Christian Stock Employee of: Employee of Boehringer Ingelheim, Martina Gahlemann Employee of: Employee of Boehringer Ingelheim, Lizette Moros Employee of: Lizette Moros is an employee of Boehringer Ingelheim, Margarida Alves Employee of: Employee of Boehringer Ingelheim, Maureen Mayes Grant/research support from: Maureen Mayes has received grants from Boehringer Ingelheim, Corbus, CSL Behring, Eicos, and Galapagos, Consultant of: Maureen Mayes has acted as a consultant for Boehringer Ingelheim, Eicos, and Galapagos. She was a member of the SENSCIS trial Steering Committee (Boehringer Ingelheim)
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SAT0346 THE EFFICACY AND SAFETY OF RITUXIMAB IN 27 CASES OF TREATMENT RESISTANT SYSTEMIC SCLEROSIS WITH SEVERE DISEASE ASSESSED BY ACTIVITY SCORES

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Background: Treatment options for systemic sclerosis (SSc) remain limited especially in severe skin, lung and musculoskeletal involvements. B-cell targeted therapy with anti-CD20 Rituximab (RTX), is widely available, reports from case series are encouraging as a a rescue therapy and might have an improving effect on organ involvement in SSc.
Objectives: We aimed to retrospectively analyze the efficacy and safety of rituximab (RTX) courses in patients with severe systemic sclerosis who were refractory to standard immunosuppressive treatment.
Methods: Twenty-seven SSc patients fulfilling ACR/EULAR classification criteria (2013) who received RTX treatment due to acive disease despite treatment with immunosuppresives were analyzed. Disease activity was evaluated by using EScSG/EUSTAR activity scores prior to and after RTX treatment. Disease severity was also assessed at baseline by Medsger's index.
Results: The demographics and characteristics of SSc patients were as follows: the median age of 50 (30-70), duration of Raynaud's 10 (3-26) and non-Raynaud symptom 8.5 (3-18) years and summarised in table 1. RTX was given as a single cycle (2 infusions of 1000 mg) in 12 cases, 2 cyles in 5 cases, ≥3 cyles in 10 cases. DMARDs were prescribed in 19 (73%) patients (14 MMF, 5 MTX) concomitantly with RTX. The main RTX indications were skin and lung involvement (n=9), skin and arthritis (n=6), skin(n=5), lung (n=3), myositis (n=2), cardiac involvement (n=1) and digital vasculopathy (n=1). Medsger severity score was 7.39±3.091(3-13) at baseline.

Table 1. Prevelance of Characteristics of SSc Patients

	n(%)
female/male	25 /2
diffuse/limited cutaneous SSc	22 (81.5) / 5 (19,2)
Clinical Characteristics	
synovitis / flexion contractures	12(44,4) / 10 (37,1)
tendon friction rubs / myositis	7 (26,9) / 4 (15,4)
renal crisis	1 (3,8)
GI involvement	19 (69,2)
lung involvement	16 (61,5)
Serology	
ANA	23 (85,2)
Anti-Scl70 / Anti-sentromer	16(61,5) / 1(3,8)
Anti-Ro	6 (22,2)
Previous Immunosuppressives	
CYC / MMF	19 (73,1) / 19 (73,1) 12 (46,2) / 16 (61,5) 27 (100)
AZA / MTX Low dose steroids	

Disease activity and severity scores prior to and after RTX were summarised table 2. Disease activity scores were improved after RTX in patients who had a median follow-up period of 1 year (0,5-5 years). After RTX treatment, according to EscSG /EUSTAR scores 13 (%46.2) and 10 (%34.6) patients out of 26 were assessed as inactive.

Table 2. Disease activity scores prior to and after RTX treatment

	Prior to RTX (n=26)	After RTX (n=18)	median Δ Change (n=18)
EscSG activity score	4,89±1,82 (2,0-9,0)	2,37±1,10 (0,50-4,50)	-2,00 (P<0,001)
EUSTAR activity score	4,57±2,68(1,0-10,0)	2,30±2,15 (0,0-7,25)	-2,00 (P=0,002)

There were severe infecions in 4 patients (Pneumonia in 2, infected digital ulcers in 2) and an episode of sinusitis in one during treatment period. One patient was deceased because of pneumonia and sepsis after the first cycle of RTX.

Conclusion: In our SSc cohort, RTX treatment was used in severe patients, who had predominantly diffuse cutaneous disease with lung and joint involvements, severe vasculopathy and anti-Scl-70 positivity. Concomitant DMARDs were used in three-forth of the patients in addition to RTX cycles. Disease activity scores that assessed retrospectively were shown to be improved after RTX and 37-48% of the cases were assessed as inactive by using activity scores. Serious infections like pneumonia and infected digital ulcers were observed in 14,8% of cases during the follow-up. The addition of RTX treatment can be effective in selected patients with active disease despite immunosuppressive therapy.
Disclosure of Interests: None declared
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SAT0347 AUTOANTIBODIES TO UNCOUPLED RO52 PROTEIN IN PATIENTS WITH ANTI-SYNTHETASE SYNDROME; A POTENTIAL MARKER FOR SUBCLASSIFICATION.

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Background: Anti-Ro/SS-A (anti-SS-A) antibody is one of myositis-associated antibodies, and is found in patients with anti-synthetase antibodies[1]. Anti-SS-A antibody targets the complex consisting of Ro52 and Ro60 proteins coupled with cytoplasmic non-coding Y-RNAs. Autoantibody against Ro52 uncoupled with Y-RNAs (anti-uncoupled Ro52) is also present in patients with a variety of connective tissue diseases, including myositis[2]. However, the majority of previous studies used enzyme-linked immunoassay (EIA) for detection of anti-Ro52 antibodies, resulting in failure to discriminate between anti-Ro52 antibodies coupled and uncoupled with Y-RNAs. The prevalence and clinical significance of anti-uncoupled Ro52 antibodies still remain unclear in patients with anti-synthetase antibodies.
Objectives: To elucidate clinical relevance of anti-uncoupled Ro52 antibodies in a cohort of anti-synthetase syndrome employing RNA immunoprecipitation assay (RNA-IP) in combination with EIA.
Methods: This is a single-center, cross-sectional study involving 80 patients positive for anti-synthetase antibodies by RNA-IPP. Complete clinical information was obtained from a medical chart review. Serum samples were obtained at first visit and stored at -20°C until use. Anti-SS-A and anti-SS-B antibodies were detected by RNA-IP, and anti-Ro52 and anti-Ro60 antibodies were measured by commercial EIA kits (ORGENTIC, Mainz, Germany). Autoantibodies that immunoprecipitated Y-RNAs regardless of results of anti-anti-Ro52 or anti-Ro60 EIAs were regarded as anti-SS-A antibody, while antibodies that did not immunoprecipitate Y-RNAs but reacted with anti-Ro52 antibodies by EIA were regarded as anti-uncoupled Ro52 antibody. Student's t-test, Mann-Whitney's U test, and Fisher's exact test were employed to compare the clinical features between each group. Cumulative survival rates were compared using log-rank test.
Results: In our cohort of 80 patients with anti-synthetase antibody, mean age at diagnosis was 61 ± 12 years, and 76% were female. Clinical diagnosis was classic dermatomyositis (cDM) in 11, clinically amyopathic dermatomyositis (CADM) in 21, polymyositis (PM) in 11, systemic sclerosis (SSc) in 3, myositis-SSc overlap in 5, interstitial lung disease (ILD) alone in 29, and unclassified in 3. The antigenic specificity of anti-synthetase antibodies included Jo-1 in 19, PL-7 in 12, PL-12 in 9, EJ in 21, OJ in 4, and KS in 16. Anti-SS-A anti-SS-B antibodies were found in 14 (17%) and 2 (2.5%) patients, respectively. The presence of anti-Ro60 and anti-SS-A antibodies was almost concordant ($P < 0.0001$), although the presence of anti-Ro52 and anti-SS-A antibodies was not correlated ($P = 0.8$). This was primarily because of high prevalence (40%) of autoantibodies to uncoupled Ro52. Interestingly, prevalence of anti-uncoupled Ro52 antibodies was different among antigenic specificities of anti-synthetase antibodies: high in Jo-1 (58%) and EJ (55%), and low in PL-7 (8%) and OJ (0%). Gottron's sign/papule was more frequent in patients with anti-uncoupled Ro52 than in those without (61% versus 28%, $P = 0.005$), resulting in clinical diagnosis of cDM or CADM more common in patients with anti-uncoupled Ro52 than in those without (59% versus 26%; $P = 0.003$). The prevalence and extent of ILD tended to be greater in anti-uncoupled Ro52-positive versus negative patients, but difference did not reach statistical significance. There were no differences in cumulative survival rates between patients stratified by the presence or absence of anti-uncoupled Ro52 antibodies.
Conclusion: Autoantibodies to uncoupled Ro52 were commonly found in patients with anti-synthetase antibodies. Anti-Ro52 positivity might be useful for subclassifying anti-synthetase syndrome.
References:
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[2] Schulte-Pelkum J et al. *Autoimmun Rev*. 2009; **8**(7): 632-7.
Disclosure of Interests: Akira Yoshida: None declared, Yuka Okazaki: None declared, Takahisa Gono Speakers bureau: Astellas, and Medical and Biological Laboratories, Masataka Kuwana Grant/research support from: Acetelion, Consultant of: Acetelion,

Bayer, Chugai, Corbus Pharmaceuticals, CSL Behring and Reata Pharmaceuticals. He was a member of the SENSCIS trial Steering Committee (Boehringer Ingelheim)
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SAT0348

CLINICAL SPECTRUM TIME COURSE OF ANTISYNTHETASE SYNDROME PATIENTS POSITIVE FOR ANTICENTROMERE ANTIBODIES

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Background: ASSD is characterized by antisynthetase antibodies (ARS) and the triad arthritis/myositis/Interstitial Lung Disease (ILD). ASSD and systemic sclerosis (SSc) may share features, like Raynaud's phenomenon (RP), capillaroscopic alterations, and also some SSc specific autoantibodies.
Objectives: To evaluate the characteristics of ASSD + for anticentromere antibodies (ACA).
Methods: Retrospective analysis of clinical and laboratory characteristics of ACA + ASSD. Patients were identified in an established international cohort, randomly matched 1:1 for sex, age, disease duration and ARS positivity with a group of ACA - ASSD.
Results: 18 ACA + ASSD (15 females, 83%, 15 anti-Jo1, 2 anti-PL7, 1 anti-PL12 ARS) patients were identified. In comparison to ACA - group, no differences were observed in disease clinical presentation and evolution. Though, 9 ACA + patients (50%) satisfied the ACR/EULAR 2013 classification criteria for SSc and only 1 in ACA - group (p=0.007) (Table 1).
An incomplete ASSD (lack of at least one triad finding) was observed in 15 patients in both ACA + and – group (p=1). Among these patients, 13 ACA + and 11 ACA – developed de-novo triad finding during disease course (p=0.651). In ACA + group, a de-novo arthritis was observed in 4 patients (vs 1, p=0.565), a de-novo myositis in 8 (vs 5, p=1), and a de-novo ILD in 7 (vs 10, p=1). The prevalence of complete forms was similar between ACA + and – group at both disease onset (3 vs 3, 17%, p=1) and last follow-up, (10 vs 11, 56% vs 61%, p=1). Of note, only 1 patient (6%) for each group died (p=1).
Conclusion: The clinical spectrum time course of ACA+ and - ASSD is similar, even when ACA + patients could be classified as SSc. By considering the high prevalence of arthritis and myositis we observed, we suggest that ACA+ patients with arthritis and myositis, should be tested for ARS antibodies even when an ASSD is not clearly suspected.
References:
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Table 1. Patients characteristics. IQR, interquartile range; ILD, interstitial Lung Disease; SSc, systemic sclerosis

	ACA+ (18)	ACA - (18)	p
Age (years) at disease onset (median, IQR)	*47 (37-63)*	*47 (39-63)*	0.834
Disease duration (months) (median, IQR)	*81 (62-169)*	*77 (58-165)*	0.486
anti Ro52 *antibody (%)*	12 *(67)*	11 (61)	1
Arthritis onset	10 (56)	13 (72)	0.489
Arthritis last follow-up (%)	14 (78)	14 (78%)	1
Myositis onset (%)	7 (39)	11 (61)	0.318
Myositis last follow-up (%)	15 (83)	16 (89)	1
ILD onset (%)	9 (50)	6 (33)	0.5
ILD last follow-up (%)	16 (89)	16 (89)	1
Complete form onset (%)	3 (17)	3 (17)	1
Complete form last follow-up (%)	10 (56)	11 (61)	1
Raynaud phenomenon (%)	13 (72)	9 (50)	0.305
Mechanic's hands (%)	6 (33)	7 (38)	1
Teleangectasias (%)	2 (11)	0 (0)	0.486
Cutaneous sclerosis (%)	5	1	0.177
Acral ulcers (%)	1 (6)	0 (0)	1
Scleroderma pattern at NVC	8 (44)	7 (39)	1
Pulmonary arterial hypertension (%)	3 (17)	2 (11)	1
2013 ACR/EULAR SSc classification criteria	9 (50)	1 (6)	0.007

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SATURDAY, 06 JUNE 2020

Spondyloarthritis - etiology, pathogenesis and animal models

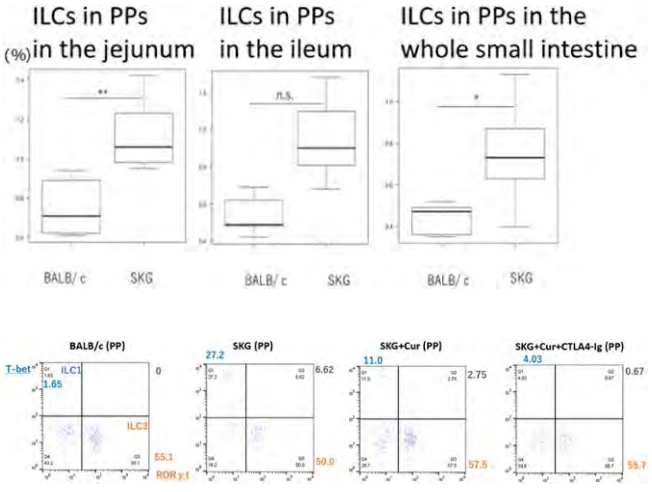
SAT0349

CTLA4-IG DECREASES TH17 CELL LEVELS BUT MAINTAINS ILC3S WITH AN INCREASE IN THE ILC3/ILC1 RATIO IN THE GUT OF SKG MICE AS A MODEL OF SPONDYLOARTHRITIS.

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Background: SKG mice have been known for their autoreactive Th17 cells resulting from the insufficient thymic negative selection due to a Zap70 mutation[1,2]. Under specific pathogen-free conditions, they acquire features of spondyloarthritis (SpA) by intraperitoneal injection of curdlan, a (1,3)-β-glucan[3]. Several reports have shown that Th17 cells also increase in human SpA[4]. However, CTLA4-Ig, which ameliorates rheumatoid arthritis by suppressing pathogenic cells such as effector T cells, was unable to show adequate efficacy as much as expected in SpA patients[5]. Around the same time, innate lymphocytes began to be focused on, in the pathogenesis of SpA, including innate lymphoid cells (ILCs), which abundantly reside in the gut[6].
Objectives: This study aimed to clarify the effects of CTLA4-Ig on the pathogenesis of SpA by using curdlan-treated SKG mice, focusing on type 3 immunity such as Th17 cells and ILC3s.
Methods: Two- to three-month-old female SKG mice were injected intraperitoneally with 3mg of curdlan or PBS at the beginning and with 500 µg of CTLA4-Ig or PBS every other week (n=5 per group). The body weight and arthritis score were measured weekly for a month. Then, the changes in the proportion of T cells and ILCs in the spleen and Peyer's patches (PPs) were analysed by flow cytometry (FCM). BALB/c mice, without treatment, were also examined by FCM as a control cohort. In addition, a next-generation analysis of their feces was performed on 16S ribosomal coding genes before curdlan and CTLA4-Ig treatment.
Results: SKG mice contained not only more Th17 cells but also more ILC1s and ILC3s than BALB/c mice, in their guts (the PPs). The feces of SKG mice intrinsically showed a decrease in the number of bacterial species, suggesting a dysbiosis. Then, in curdlan-treated SKG mice, CTLA4-Ig administration decreased the proportion of both Th17 cells and ILC3s in the spleen, but did not decrease the proportion of ILC3s in the PPs. Moreover, the ILC3/ILC1 ratio in the PPs was from low to high in the order of SKG mice without treatment, SKG mice injected with curdlan, and SKG mice injected with both curdlan and CTLA4-Ig. The phenotype corresponding to SpA features, in curdlan-treated SKG mice, continued after repeated CTLA4-Ig administration.
Conclusion: Curdlan provoked SpA features in SKG mice with an intrinsic dysbiosis. Additional CTLA4-Ig injection decreased the proportion of Th17 cells but maintained that of ILC3s with increased ILC3/ILC1 ratio in the gut. This result supports the hypothesis that in the SpA pathophysiology, a weakened acquired immunity in the gut might lead to ILC3 activation, via dysbiosis, and its continuous disease progression, suggesting that ILC3s are a promising therapeutic target in SpA.
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SAT0350 A ROLE FOR IL-17A IN THE SUPPRESSION OF SPINAL ENTHESEAL MESENCHYMAL STEM CELL ADIPOGENESIS WHILST SIMULTANEOUSLY FACILITATING OSTEOGENESIS.

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Background: Fat formation in the bone adjacent to the enthesis is an important but poorly characterised intermediate stage in new bone formation that occurs in the spine in AS. We and others have previously reported that IL-17A can increase mesenchymal stem cell (MSC) mediated osteogenesis in normal and AS spinal tissue (1, 2).
Objectives: Herein we investigate the impact of IL-17A & TNF on MSC adipogenesis from spinal enthesis tissue.
Methods: Samples from healthy spinous process and interspinous ligament (n=14, median age = 53) were separated into the peri-entheseal bone (PEB) and entheseal soft tissue (EST) & enzymatically digested. Minimally passaged (<p3) MSCs were cultured in a complete adipogenic media, with some cultures supplemented with either IL-17A (50ng/ml), TNF (1ng/ml) or IL-17A & TNF for 3 weeks. Adipogeneis was quantitatively assessed by Oil Red O staining at day 21. IL-17A's effect on adipogeneis was further investigated by RNA extractions at Day 0, 3, 5, 7, 15 & 21 with supporting Oil Red O staining. 48 adipogenic and IL-17A target genes were used to investigate adipogenic progression and IL-17A effects on it over 21 day adipogenic differentiation.
Results: EST MSCs have a significantly higher adipogenic potential than matched PEB MSCs (n=14, $p<0.001$). TNF and IL-17A both cause significant decreases (all $p<0.01$, n=5) in adipogenesis for both PEB and EST MSCs. EST MSCs produced lipid vesicles by day-3 post-induction, with significant inhibition by IL-17A ($p<0.01$, n=4) seen from day 15 onwards. IL-17A caused a significant decrease in overall Oil Red O staining, and it changed the morphology of lipid vesicles with a majority of cells consistent with immature pre-adipocytes. This was supported by gene expression data, which indicated significant decreases in transcripts encoding vesicle fusion proteins (CIDEC $p<0.05$, PLIN1 $p<0.01$). PLIN1 also aids protection against lipolysis (4). Transcripts associated with osteogenesis (CEBPβ (3)) and MSC stromal support (CXCL12) were significantly upregulated in adipogenically-induced cultures stimulated with IL-17A when compared to control adipogenic media. TNF & IL-17A combination demonstrated that IL-17A drove the vesicle morphology changes, with TNF alone not showing the same vesicle changes.
Conclusion: Given the inverse link between MSC mediated osteogeneis & adipogenesis, these findings reveal a role of IL-17A especially on EST MSCs. The rapid formation of adipocytes seen in EST MSCs may be relevant to MRI determined peri-entheseal bone "shiny corners" due to post inflammation fat accumulation. Elevated transcripts associated with pre-adipocytes & undifferentiated MSCs support the idea of plasticity between early osteogenesis & adipogenesis. Downregulation of transcripts for proteins associated with protection against lipolysis allows for the rationalising of the gradual loss of the shiny corners seen in AS preceding subsequent new bone formation.
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SAT0351 CHEMOKINE PATHWAYS ARE ENRICHED IN PSORIATIC ARTHRITIS (PSA) SKIN LESIONS WITH INCREASED EXPRESSION OF ATYPICAL CHEMOKINE RECEPTOR 2 (ACKR2)

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Background: Skin in people with psoriasis has been comprehensively studied; uninvolved skin has abnormal gene expression. Less is known specifically about skin in PsA, the assumption being that it is identical to psoriasis. Chemokines and ACKR2 are among the upregulated genes in uninvolved psoriasis compared

to healthy skin[1]. ACKR2 is a scavenging receptor of inflammatory CC chemokines and has been proposed as a regulator of cutaneous inflammation in psoriasis. It has not been studied in PsA.

Objectives: To compare the transcriptome of PsA lesional, PsA uninvolved and healthy control skin and evaluate ACKR2 expression in PsA.

Methods: Biopsies were taken from healthy control (HC) skin and paired lesional and uninvolved skin from patients with PsA. Libraries for bulk RNA sequencing were prepared from polyA selected RNA and sequenced on NovaSeq 6000. Sequencing data were analysed using Searchlight2. ACKR2 mRNA expression was validated by qPCR. RNAscope was used to localise ACKR2 expressing cells and sections were co-stained with podaplanin or stained in serial sections with CD45. Chemokine protein expression in skin was evaluated using Luminex technology.

Results: Nine HC and 9 paired skin samples from patients with PsA were sequenced. The PsA skin lesions (PsA L) formed a distinct population in the transcriptomic principal component analysis (PCA) plot while HC and PsA uninvolved skin (PsA U) were overlapping. Only 15 genes were differentially expressed between HC and PsA U and none coded for chemokines. There were however significantly upregulated chemokines and receptors in PsA L. Unexpectely, ACKR2 was the 2nd most upregulated chemokine receptor in PsA L with unchanged expression in PsA U compared with HC (PsA L vs HC log2fold 3.38, p.adj=9.51E-41; PsA L vs PsA U log2fold 3.58, p.adj=3.24E-45; PsA U vs HC log2fold -0.2, p.adj=0.732).

The upregulation of ACKR2 in PsA L and unchanged expression in PsA U was confirmed by qPCR. RNAscope demonstrated strong expression of ACKR2 in the suprabasal layer of the epidermis in PsA L. In HC and PsA U, only occasional ACKR2 positive cells were seen in the epidermis. ACKR2 was expressed in lymphatic vessel walls but was not observed in CD45+ leukocytes.

Provisional skin chemokine protein expression data showed poor correlation between mRNA levels and protein expression for the ACKR2 ligands CCL2, CCL3, CCL7, CCL8, CCL11, CCL13 and CCL22 in HC and PsA U, with negative correlation between ACKR2 mRNA expression and CCL2, CCL8 and CCL11 protein expression. In PsA L, chemokine mRNA correlated with protein expression, but protein expression of chemokine ligands did not correlate with ACKR2 expression.

Conclusion: This data set shows expected upregulation of chemokines and their receptors in PsA L but relatively unchanged gene expression in PsA U, which contrasts to previous studies in psoriasis. Notably, this study demonstrates a strong upregulation of ACKR2 in keratinocytes in PsA L, with unchanged expression in PsA U. The RNA expression and preliminary protein data suggest that ACKR2 has little effect on the levels of its ligands in PsA skin lesions. However, this study may have missed local effects of ACKR2 in the epidermis.

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SAT0352

AN UNSUPERVISED ANALYSIS IDENTIFIES A SPECIFIC IMPACT OF BIOLOGICS ON T LYMPHOCYTE PHENOTYPES.

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Background: It is currently not known if TNF or IL-17A inhibitors have an impact on immune cell frequencies in axial Spondyloarthritis (AxSpA). This question is important to understand the impact of biologics on the immune system. Data from clinical trials didn't show significant modification on immune cells and especially on lymphocytes. But regarding the risk of infections linked to these treatments lymphocyte cell subsets are certainly disturbed. Moreover, biologics could affect subsets of cells with an unusual phenotype.

Objectives: To identify the phenotype of cell subsets affected by biologics.

Methods: We used an "unsupervised approach" to analyze CD4+ T cells and CD8+T cells subsets. Contrary to a "supervised approach", this strategy takes advantages of the fluorescence emitted by all of the surface markers used to characterize the cells at the same time. The objective was on the one hand to overcome statistical problems related to the number of patients and the repetition of the tests and on the other hand to increase the sensitivity of the analysis by identifying and analyzing new cell populations. The first step was to cluster the cells based on a selection of 12 T cells markers characteristic of the classical cell subsets and the stage of maturation to obtain cell clusters with a phenotype based on the combination of these 12 markers. Then, we were able to describe "a posteriori" the change of frequency of the clusters identified. The second step was to create a visualization of the cells affected to confirm their existence in a classical flow cytometry gate. With this pipeline, we analyzed CD4 and CD8 T cells isolated from a group of AxSpA patients (n=7) before and after 3 months of TNF therapy and a group of patients (n=6) before and after 4 months of IL-17A therapy.

Results: We observed that after biologics CD4 and CD8 T cells frequencies did not change but there was a redistribution of the different clusters analyzed. Specifically, we identified for CD4+T cells after anti TNF treatment an increase of 2 clusters (CD4+CD27+CD45RA+Va7.2intCD161int and CD4+CD27-CD45RA-CCR6+CD161int) and a decrease of 3 clusters (CD 4+CD27+CD45RA+CRTH2intCD161int, CD4+ CD27+CD45RA+CXCR3+, CD4+CD27+CD45RA+gdint CD161int) and for CD8+T cells a decrease of 1 cluster after treatment (CD8+ CD27+CD45RA+CD161+CXCR3+) and an increase of 1 cluster (CD8+ CD27+CD45RA+). The clusters affected by anti-IL-17A therapy were different. For CD4+T cells, we identified a decrease of 2 clusters (CD4+CD27+CD45RA+CXCR5+ CD161+ and CD4+CD27+CD45RA-CXCR3+CCR6+CD161+) and an increase of 2 clusters (CD4+CD27+CD45RA+gdintCD161+, CD4+CD27+ CRTH2intCCR6+) and for CD8+T cells a decrease of 1 cluster (CD8+CD27+CD45RA+ CXCR3+CRTH2intCD161int) and an increase of 1 cluster (CD8+CD27+CD45RA+CXCR3intCD161-).

Conclusion: We identified 5 different clusters in CD4+T cells affected by anti TNF and 4 by anti-IL-17A. We identified 2 clusters in CD8+T cells affected by anti TNF and 2 by anti-IL-17A. The phenotypes of these clusters were unexpected and raised new questions about the effect of biologics in AxSpA. We were also able to create a visualization of these cells affected by biologics in a "classic gating view" which will help us to perform scRNAseq. With this unique approach, we show an impact of biologics on the frequency of very specific subset of CD4+ and CD8+ T cells in AxSpA

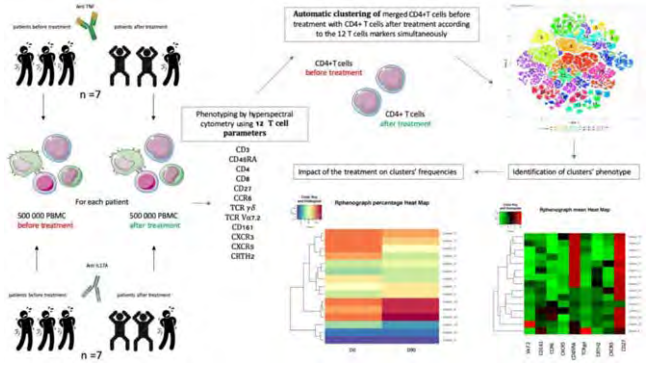


Figure 1.

Disclosure of Interests: None declared

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SAT0353

STAT3 PHOSPHORYLATION IS INVOLVED IN THE DEVELOPMENTS OF INFLAMMATORY ARTHRITIS, ENTHESITIS, AND NEW BONE FORMATION IN ANKYLOSING SPONDYLITIS

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Background: Ankylosing Spondylitis (AS) is a chronic inflammatory rheumatic disease, which is characterized by the enthesitis, peripheral arthritis, and chronic inflammation of the spine, leading to bony ankylosis. Signal transducer and activator of transcription (STAT) family proteins are latent cytoplasmic transcription factors that convey signals to the nucleus. It is activated by IL-6, IL-23, and IL-22 through JAK-mediated phosphorylation. Moreover, genetic studies implicate interleukin-23 (IL-23) receptor signal, including STAT3 in the development of AS. IL-17A has recently emerged as a potential target that regulates the extensive inflammation and abnormal bone formation observed in AS. It was reported that STAT3 is a regulatory factor that induces Th17 cell development from naive CD4 T cells.

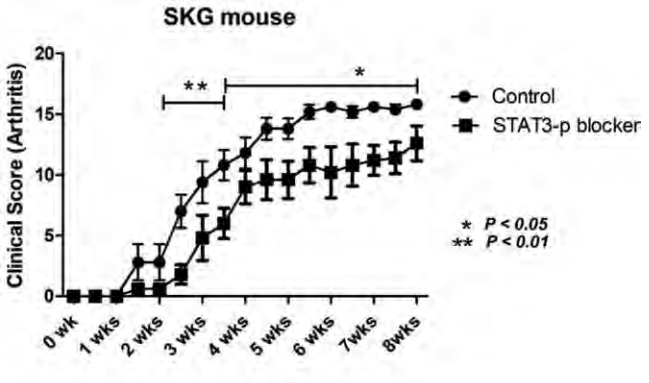
Objectives: The aim of this study is to investigate whether the STAT3 phosphorylation (stat3-p) inhibitor has a therapeutic effect on inflammation and new bone formation in AS.

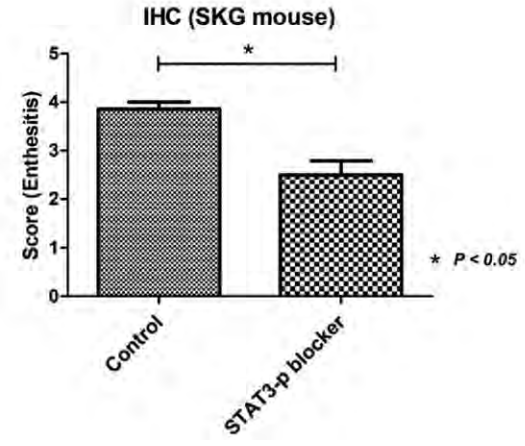
Methods: Eight weeks after curdlan injection, SKG mice were treated with stat3-p inhibitor or mock as a control. Clinical and histologic scores for arthritis and enthesitis were evaluated. Synovial fluid mononuclear cells (SFMC) samples were obtained from AS patients. Inflammatory cytokine producing cells were analyzed using flow cytometry. Bone tissue samples were obtained from the facet joints of patients with AS at surgery. Primary bone-derived cells (BdCs) were isolated and cultured. The osteogenic differentiation was assessed in vitro for 3 weeks using ALP activity, Alizarin red S (ARS), Type I collagen, von kossa, *and hydroxyapatite* stains. Statistical analysis was performed using Prism 5.0 Software. A $p < 0.05$ was considered statistically significant.

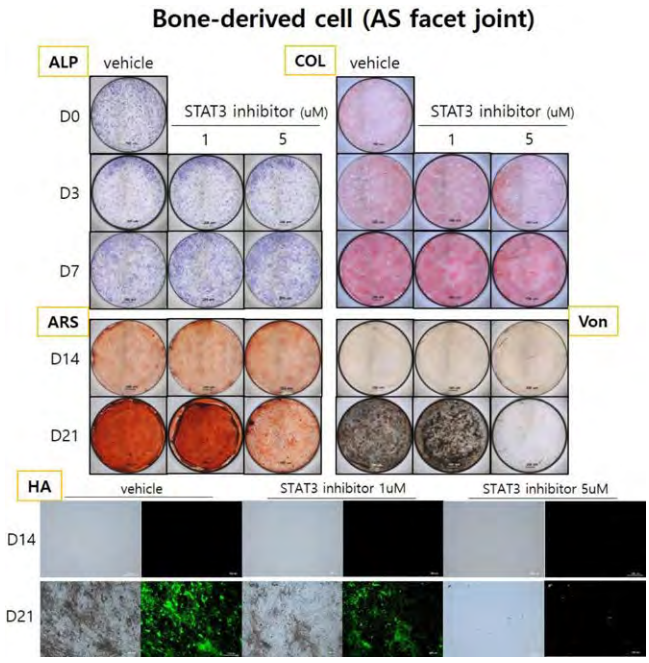
Results: The stat3-p inhibitor significantly suppressed peripheral arthritis and enthesitis in SKG mice (figure 1). Inflammatory infiltration around the tendon–bone insertion site and along the tendon, as well as bony involvement were all reduced in stat3-p inhibitor-treated mice compared to control mice. We found that the levels of IFN-±, IL-17, TNF-± were higher in AS Synovial fluid. A significantly decreased frequencies of IFN-±, IL-17, TNF-± producing cells in AS SFMC were shown after stat3-p inhibitor treatment ($P < 0.01$).

In vitro experiment of bone formation, the stat3-p inhibitor suppressed ALP activity. In addition, there were significant decrease in Alizarin red S (ARS), Type I collagen, von kossa staining scores due to stat3-p inhibitor at a concentration of 5 μM. *Light intensity of hydroxyapatite* staining was also decreased by stat3-p inhibitor in a dose dependent manner (figure 2). Intriguingly, the stat3-p inhibitor suppressed osteogenesis in both early phase and late phase in AS-BdCs, down-regulating osteoblast-involved genes.

Conclusion: The stat3-p inhibitor had beneficial effects on reducing inflammation and new bone formation in AS animal model. In addition, stat3-p inhibitor suppressed bone formation in vitro experiment. These findings suggest that the stat3-p inhibitor could be a potential therapeutic agent for AS.







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SAT0354

TYPE 3 INNATE LYMPHOID CELLS ARE KEY DRIVERS OF PSORIATIC ARTHRITIS

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Background: Psoriasis (PsO) and psoriatic arthritis (PsA) are two types of chronic inflammatory diseases that share a similar cytokines profile. About 30% of PsO patients also develop a joint involvement, but the underlying mechanism is still unclear. Innate lymphoid cells (ILC) and specifically the type 3 ILCs (ILC3s) have raised increasing interest as possible player in the pathogenesis of both diseases, as they produce the pathological key cytokine IL-17A.

Objectives: We addressed the contribution of ILC3s to the pathogenesis of PsO and PsA in patients as well as murine *in vivo* models.

Methods: 130 patients satisfying the Classification Criteria for Psoriatic Arthritis (CASPAR), 40 patients with PsO and 35 healthy volunteers were enrolled in the study. Information regarding clinical features, laboratory parameters were collected and psoriasis area severity index (PASI), disease activity score 28 (DAS28), disease activity in psoriatic arthritis (DAPSA), minimal disease activity score (MDA) were calculated. Magnetic resonance imaging (MRI) and high-resolution peripheral CT (HR-pQCT) were taken and PsA MRI score (PsAMRIS) was assessed. Flow cytometric analysis was performed and IFNγ-producing ILC1s, IL-4/IL-5-producing ILC2s and IL-17/IL-22-producing ILC3s were identified

among ILCs. Multivariate linear regression and Receiver-Operating Characteristic (ROC) Curve analysis was performed using the IBM SPSS Statistics software. Different in vivo models were used to assess functional implications of ILCs at different time points of the disease. Joint inflammation was assessed through MRI and H&E staining of ankle areas. Peripheral blood was obtained from mice of each group and flow cytometry analysis was performed. High dimensional analyses including RNA-seq was performed to identify phenotypic characteristics of ILCs implemented into the pathogenesis of the disease.

Results: Total number of circulating ILCs were increased in PsA patients compared to PsO and healthy controls (p<0,001). Linear regression analyses of the relationship between disease activity and circulating ILCs counts showed strongest correlation between ILC3s counts and DAPSA score. ILC3s counts also correlated with imaging signs of inflammation such as enthesitis, synovitis, erosions and/or ostoeproliferation as assessed by MRI and HR-pQCT. Musculoskeletal inflammation in mice was predominantly associated with p19 expression and IL-23R-signaling as assessed by RNA-seq. These effects were also accompanied by a strong upregulation of IL-17-producing lymphocytes within the inflamed joint niche with a dominant presence of ILC3s. Multi-channel immunofluorescence and confocal laser scanning microscopy revealed not only upregulation of ILC3 induced IL-17 production within the synovial membrane but also in peri-articular areas of the inflamed joints.

Conclusion: ILC3s not only correlate with various facets of PsA manifestations but also functionally contribute to synovitis and enthesitis suggesting them as interesting target for upcoming treatment strategies in the near future.

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SAT0355 WNT SIGNALING CAN PLAY AN IMPORTANT ROLE IN VASCULAR CALCIFICATION IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Vascular calcification is highly correlated with atherosclerosis. Ankylosing spondylitis (AS) is associated with a process of accelerated atherosclerosis. Wnt signaling plays an important role in the pathogenesis of vascular calcification. However, there has been no study of the role of Wnt signaling in vascular calcification in patients with AS.

Objectives: We investigated the relationship between vascular calcification and Wnt signaling in patients with AS.

Methods: Sixteen male patients aged over 20 years with AS were enrolled. They fulfilled the modified New York criteria and each of their ankylosing spondylitis disease activity score was more than 2.1. Sex and age matched nineteen healthy controls were also recruited.

Mouse MOVAS vascular smooth muscle cell line (American Type Culture Collection, ATCC® CRL-2797™) were stabilized in maintain media for 24 hours. Then media were exchanged for the 10% serum of patients with AS or controls in maintain media. Cells were stimulated for another 72hours. We exchanged this medium with calcification medium. Cells were cultured until 2 weeks then stained with Alizarin Red S and the optical density (OD) was measured.

For Western blotting and RT-qPCR, cells were stabilized for 24 hours and stimulated for another 72 hours through the same procedure as that of Alizarin Red S staining. After cell stimulation, the level of mRNA and protein were measured by RT-qPCR and western blot, respectably. We measure the level of Low-density lipoprotein receptor-related protein (LRP)5, LRP6, Dickkopf-related protein 1, Wnt3a, matrix metalloproteinase-7(MMP-7), beta-catenin for canonical Wnt signaling; Receptor Tyrosine Kinase Like Orphan Receptor 2, Wnt5a, Runt-related transcription factor 2 (RUNX2) for non-canonical Wnt signaling. We also checked the level of Alkaline phosphatase (ALP), IL-17, IL-23 and TNF-a.

Results: The level of OD of MOVAS cells treated with serum from AS patients (19.503 ± 6.422, mean ± SD) was significantly higher than that from controls (10.994 ± 4.291) (P=0.000, Mann-Whitney test). The protein level of MMP-7 and beta-catenin of MOVAS cells treated with serum from AS patients (1.881 ± 0.687; 1.301 ± 0.342) was significantly higher than that from controls (0.779 ± 0.48; 0.854 ± 0.285) respectively (P=0.005,: P=0.002, Mann-Whitney test). The mRNA level of RUNX2, ALP, IL-17 and IL-23 of serum from AS patients (2.697 ± 1.46; 2.687 ± 1.753; 2.253 ± 1.128; 2.574 ± 1.142) was significantly higher than that from controls (1.396 ± 0.587; 1.696 ± 0.637; 1.358 ± 0.473; 1.386 ± 0.714) respectively (P=0.000; P=0.037; P=0.044; P=0.007, Mann-Whitney test). There was positive correlation between the mRNA level of WNT5a and RUNX2 (rho=-0.705, p=0.002, Spearman rank correlation coefficient) and the protein level of WNT5a and ALP, MMP-7 and TNF-a, MMP-7 and IL-17, MMP-7 and IL-23 (rho=-0.601, p=0.039; rho=-0.769, p=0.026; rho=-0.828, p=0.011; rho=-0.777, p=0.003), respectively.

Conclusion: 1. Vascular smooth muscle cell calcification was increased in patients with ankylosing spondylitis than those of the control group.

2. The level of several molecules(i.e. Beta-catenin, RUNX2, MMP-7) related to Wnt signaling of vascular smooth muscle cells treated with serum of patients with AS was elevated significantly compared to those of controls and positively related.

3. Wnt signaling can play an important role in vascular calcification in patients with ankylosing spondylitis.

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Disclosure of Interests: None declared

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SAT0356 THE ROLE OF IL-36 AS A POTENTIAL NOVEL THERAPEUTIC TARGET IN SPONDYLARTHROPATHY ASSOCIATED PATHOLOGY DUE TO ITS UPSTREAM INDUCTION OF IL-23/IL-17 PATHWAY CYTOKINES AND STROMAL ACTIVATION IN AN IN VITRO ENTHESITIS MODEL.

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Background: Enthesitis, defined as inflammation of anchorage points of tendons, ligaments and joint capsules to bones, is now understood to be the cardinal pathogenic lesion in spondyloarhtopathies (SpA). Evidence from genetic studies, animal models, and therapeutic studies firmly implicates the IL-23/IL-17 axis in the pathogenesis of SpA. We have recently confirmed the presence of IL-23 myeloid cells and IL-17 producing T cells populations in the human enthesis (McGonagle, ARD 2019). The upstream drivers of these key cytokines in the enthesis is, however, not defined. Emerging evidence suggests that IL-36 may be critical in regulating the IL-23/IL-17 axis in various organs. Also IL-38 SNPs have been associated with SpA which is of interest given that IL-38 is an IL-36 antagonist. Further, IL-36α is upregulated in the joints of psoriatic arthritis patients and deficiency of the IL-36 receptor antagonist (DITRA) results in generalized pustular psoriasis with comorbid arthritis in at least third of patients. Thus, we hypothesised that IL-36 could be an upstream regulator of the IL23/17 axis at the enthesis.

Objectives: To confirm the induction of IL-36 at the human enthesis and to test the effect of IL-36 on resident innate and adaptive immune cell populations and enthesis stromal cells.

Methods: Entheseal spinous processes from patients undergoing elective orthopaedic surgeries was obtained and mechanically digested. Peri-entheseal bone (PEB), and entheseal soft tissue (EST) digests were stimulated with fungal and bacterial adjuvants and IL-36 measured by ELISA. Disease relevant compounds such as methotrexate and PDE4i were assessed for their ability to attenuate IL-36 secretion. IHC was used to confirm the presence of IL-36R+ cells in the enthesis. Digested PEB was stimulated with IL-36, and IL-6, IL-8, IL-23, and TNF-alpha were analysed by ELISA and Flow Cytometry. As the IL-36 cytokines require protease mediated post translational processing for full activation, these were measured in enthesis digests. Entheseal fibroblasts were isolated and stimulated with IL-36 and ICAM-1 measured by Flow Cytometry and genes by qPCR.

Results: TLR ligands induced the production of IL-36 at the enthesis. Further cell sorting, revealed CD11+ myeloid cells were the predominant entheseal producer of IL-36. Induced IL-36 could be significantly attenuated by PDE4i but not by methotrexate. IHC confirmed the presence of IL-36R+ in the enthesis. Stimulation of enthesis digest with IL-36 significantly upregulated the production of IL-6, IL-8, TNF-a, and IL-23. Stimulation of enthesis fibroblasts with IL-36 upregulated surface ICAM-1 and secretion of IL-6, CCL2 and CCL20. Enthesis digests showed high basal expression of IL-36 activating protease including cathepsin S and G.

Conclusion: IL-36 is inducible from enthesis myeloid cells and IL-36R+ cells are present at the enthesis. Enthesis stimulation with IL-36 results in the upregulation

of several disease relevant mediators such as TNF, IL-23 and CCL20 in both immune and stromal lineage cells. This is the first demonstration of IL-36 production in human enthesis. Given its pleiotropic effect and relation to IL-23/IL-17 axis, IL-36 is a potential novel therapeutic target in SpA.

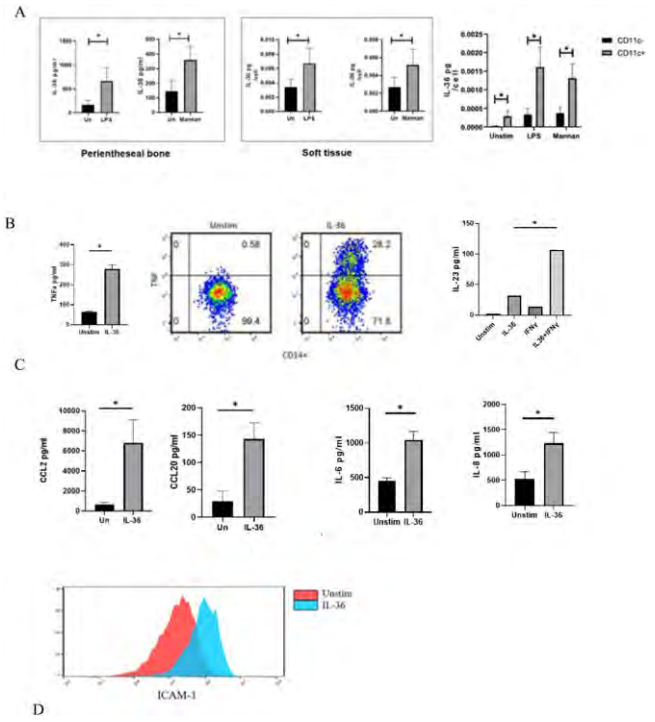


Figure 1. Expression and role of IL-36 at the enthesis. (**A**). IL-36 is induced by stimulation with lipopolysaccharide (LPS) and Mannan. (**B**) IL-36 is predominantly produced by CD11c+ cells. (**C**) IL-36 stimulation of PEB resulted in increased TNF-alpha production by CD14+ cells, and increased production of IL-23 (**D**) IL-36 stimulation of stromal cells increased ICAM-1 expression, and CCL2, CCL20, IL-6 and IL8 secretion

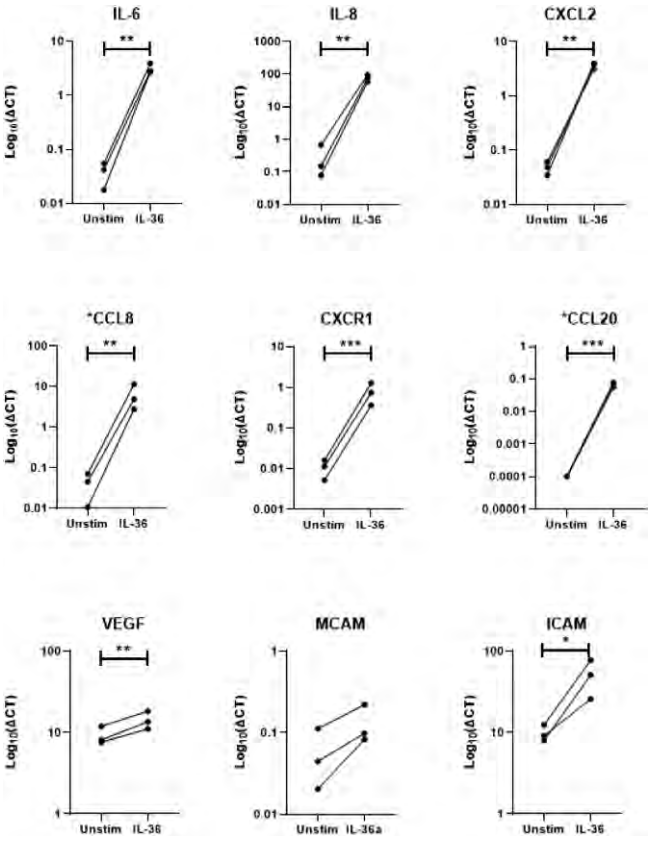


Figure 2. Gene expression by qPCR following stromal cell stimulation by IL-36

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SAT0357

LEVELS OF PERIPHERAL LYMPHOCYTE SUBPOPULATIONS IN PATIENTS WITH ANKYLOSING SPONDYLITIS AND THEIR CHANGES AFTER RECEIVING IMMUNOREGULATORY COMBINATION THERAPIES

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Background: Ankylosing spondylitis is an immune-mediated inflammatory disease involving of the axial skeleton, joints, and entheses[1]. Although the homeostatic balance of effector T cells (Teffs) and regulatory T cells (Tregs) is considered to play an important role in the pathogenesis of ankylosing spondylitis(AS) [2], it is unclear whether the levels of peripheral blood lymphocyte subpopulations in patients with ankylosing spondylitis are abnormal or not.

Objectives: To explore the differences of lymphocyte subpopulations of peripheral blood (PB) between AS patients and healthy controls (HCs), and further evaluate the therapeutic effect of immunoregulatory drugs on the lymphocyte subpopulations.

Methods: Total 1141 patients with AS and 206 healthy individuals were enrolled in the study and donated their blood to measure the levels of T, B, NK, $CD4^+$T, $CD8^+$T, Th1, Th2, Th17 and Tregs by flow cytometry combined with standard absolute counting beads. And 456 patients received immunoregulatory combination treatments which includes low-dose interleukin-2, rapamycin, metformin, retinoic acid etc. and donated their PB after the therapies. Data were expressed as mean ± standard deviation to the distribution. Independent-samples T test and paired-samples T test were applied. *P* value <0.05 were considered statistically significant.

Results: Compared with HCs, AS patients had a lower absolute number of Tregs but higher numbers of peripheral T, B, $CD4^+$T, $CD8^+$T and Th17 cells ($P<0.05$). Further, there was a significant increase in the percentage of B, $CD4^+$T and the ratios of Teffs/Tregs such as Th1/Tregs, Th2/Tregs and Th17/Tregs compared with HCs ($P<0.05$)(Figure 1). Although, after receiving the immunoregulatory combination treatments, the absolute numbers of various peripheral lymphocyte subpopulations such as T, B, NK, $CD4^+$T, $CD8^+$T, Th1, Th17 and Tregs and the percentage of Tregs, Th1 and $CD8^+$T significantly increased ($P<0.05$), the ratios of Th2/Tregs significantly decreased ($P<0.05$)(Figure 2), suggesting a rebalance of immune systems.

Conclusion: The insufficiency of Tregs may involve in pathogenesis of AS. Immunoregulatory combination therapies could promote the proliferation of Tregs as well as other lymphocytes to some degree, which may be a new target for AS treatment.

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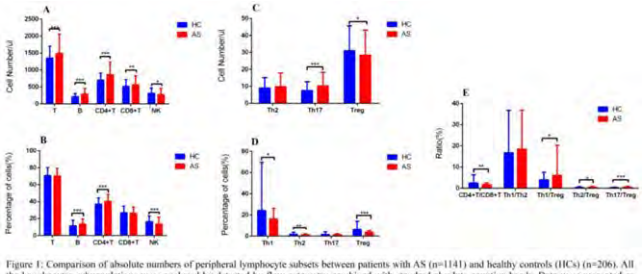


Figure 1: Comparison of absolute numbers of peripheral lymphocyte subsets between patients with AS (n=1141) and healthy controls (HCs) (n=206). All the lymphocytes subpopulations were analyzed by detected by flow cytometry combined with standard absolute counting beads. Data were presented as mean±SD and statistical analysis was determined by two-tailed unpaired t-test. AS patients had a lower absolute number of Tregs but higher numbers of peripheral T, B, $CD4^+$T, $CD8^+$T and Th17 cells compared with HCs. *P < 0.05, **P < 0.01, ***P < 0.001.

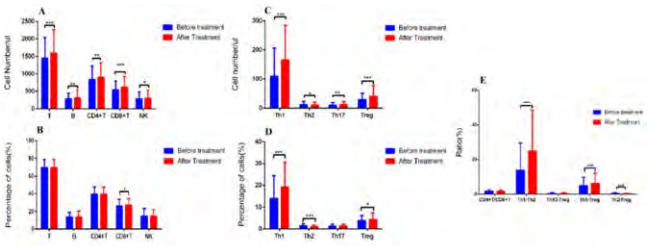


Figure 2:Changes of peripheral lymphocyte subsets after immunomodulatory combination treatment (n=456). Data were presented as mean±SD and statistical analysis was determined by two-tailed paired t-test. the absolute numbers of various peripheral lymphocyte subpopulations such as T, B, NK, $CD4^+T$, $CD8^+T$, Th1, Th17 and Tregs and the percentage of Tregs, Th1 and $CD8^+T$ significantly increased. *P < 0.05, **P < 0.01, ***P < 0.001.

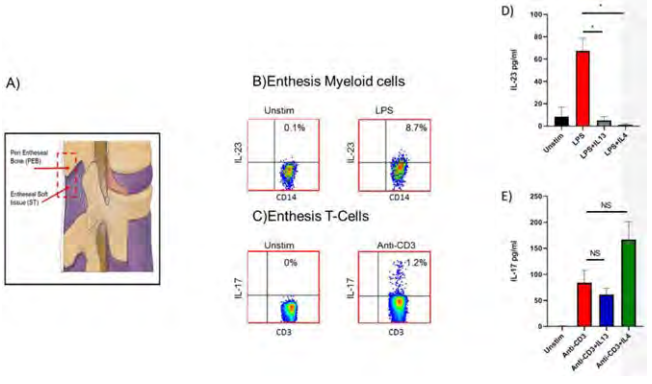
Disclosure of Interests: None declared
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SAT0358 A ROLE FOR IL-4 AND IL-13 IN MODULATING THE IL-23/IL-17 AXIS IN ENTHESITIS

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Background: IL-4 and IL-13 are related Th2 cytokines, with documented roles in allergic inflammation such as atopic dermatitis (AD). Psoriatic Arthritis (PsA) is typically thought to be a result of Th1/Th17 driven response, and blockage of this pathway (IL-23, IL-17 and TNF) has proven successful. Despite this, there is a strong genetic risk association for IL-13 and PsA(1), however, the precise role of IL-13 in PsA is presently unknown. The enthesis is the region where tendons or ligaments attach to bone, and inflammation of this site (enthesitis) is thought to be the cardinal lesion of PsA, whereas as Rheumatoid Arthritis inflammation is more synovial centric. Dupilumab is a monoclonal antibody that works by blocking the common receptor chain (IL-4α) shared by both IL-13 and IL-4. Recent studies have reported that AD patients receiving dupilumab have developed clinical enthesitis(2).
Objectives: To investigate whether IL-4 and IL-13 could modulate IL-23production from entheseal myeloid cells and IL-17 production from enthseal T-cells.
Methods: Healthy enthesis samples from patients undergoing surgery for non-inflammatory conditions such a lumbar decompression or scoliosis were obtained. Enthesis samples were digested and stimulated (Fig 1A) with LPS and anti-CD3 to induce IL-23 and IL-17 respectively. Samples were pre-treated with IL-4 and IL-13 to ascertain whether this modulated entheseal cytokine production.
Results: Both IL-23 and IL-17 were readily induced from enthesis samples with IL-23 coming predominantly from entheseal myeloid resident cells (Fig 1B) and IL-17A from T-cells (Fig 1C). Pre-treatment of entheseal digested material with either IL-4 or IL-13 attenuated IL-23 secretion (Fig 1D). Neither IL-4 nor IL-13 was able to significantly attenuate IL-17 secretion from enthesis T-cells, however IL-13 trended downwards and IL-4 surprisingly trended upwards (Fig 1E).
Conclusion: Our clinical and vitro data point towards a previously unknown role for IL-4 and IL-13 having a protective role in entheseal induction of IL23/17 axis cytokines. These findings point towards a novel explanation for IL-13 pathway SNPs in PsA and also a molecular explanation for why anti-IL4/13 therapy may induce entheseal pathology.
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SAT0359 THE ASSOCIATION BETWEEN IMAGING SUB-PHENOTYPES OF PSORIATIC ARTHRITIS AND GENE EXPRESSION PROFILES

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Background: Heterogeneity is a hallmark of psoriatic arthritis (PsA), which is reflected in diverse clinical, imaging and molecular features that may reflect disease course and response to treatment. We hypothesized that specific molecular pathways underlie the various manifestations of PsA.
Objectives: To create a model for accurate and biologically meaningful sub-phenotyping of PsA using imaging and molecular data. Specifically, we aimed to identify imaging sub-phenotypes in patients with PsA and determine their association with whole blood mRNA expression markers.
Methods: 55 patients with PsA ready to initiate treatment for active disease were prospectively recruited. An ultrasound assessment of the extent of musculoskeletal inflammation in 64 joints, 34 tendons and 16 entheses was performed. Sonographic inflammation (in greyscale and Doppler) of the following domains was graded for: a) synovitis; b) peri-tendonitis; c) tenosynovitis; and d) enthesitis. A global inflammatory score was calculated for each tissue domain. Peripheral blood was profiled with RNAseq, and gene expression data were obtained. Analyses were performed in two stages: 1) Unsupervised cluster analysis was performed using hierarchial and k-means to define imaging sub-phenotypes in PsA that reflected the predominant tissue involved; 2) Principal component analysis with ellipses was used to determine the association between imaging-defined clusters and peripheral blood gene expression profile.
Results: The patients could be divided into 3 groups based on unsupervised hierarchical and k-means clustering of images indicating the predominant involved tissue (Figure 1): 1) Enthesitis predominant (N=13 [24%]); 2) Peri-tendonitis predominant (N=11 [20%]); 3); Synovitis predominant (N=31 [56%]). Patients in the synovitis predominant group had more nail involvement, while those in the peri-tendonitis group had the highest number of clinically active joints (Table 1). Unsupervised clustering of gene expression data identified three clusters that partially overlapped with the imaging clustering (Figure 2). Overall, 344 genes were differentially expressed (p<0.05) in two of the three comparisons between the imaging clusters.

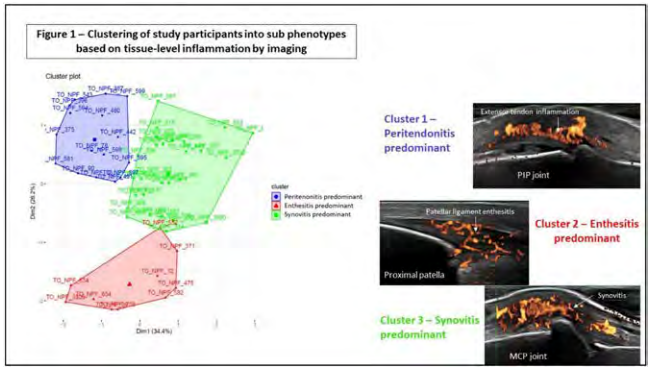
Table 1. Clinical Features by Imaging Clustering

Variable	Enthesitis predominant cluster (N=13)	Peritendonitis predominant cluster (N=11)	Synovitis predominant cluster (N=31)
Age (years)	47 (14)	49 (16)	45 (20)
Sex: Female	8 (61.5%)	5 (45.5%)	15 (48.4%)
PsA duration (years)	1.2 (1.5)	1.6 (11.5)	0.8 (3.7)
BMI	29.4 (6.8)	25 (8.1)	26.1 (8.4)
Nail lesions	**3 (23.1%)**	**5 (45.5%)**	**17 (54.8%)**
PASI	1.2 (2.7)	1.2 (3.2)	2.8 (7.8)
Tender joint count	**6 (9)**	**11 (5)**	**3 (6)**
Swollen joint count	**2 (6)**	**10 (7)**	**3 (6)**
Dactylitis	3 (23.1%)	4 (36.4%)	7 (22.6%)
Enthesitis count	**3 (3)**	**1 (4)**	**0 (2)**
Enthesitis	**12 (92.3%)**	**7 (63.6%)**	**15 (48.4%)**
hsCRP	2.9 (8.8)	8.5 (21.5)	3.6 (9.4)

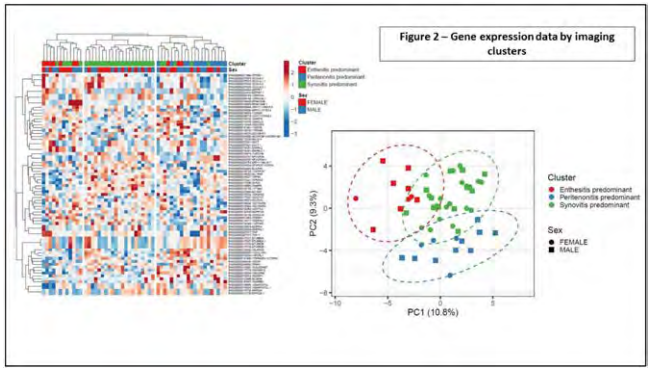
Median (IQ range) and frequencies (%)
Bolded=Statistically different between the 3 groups (p<0.05)

Conclusion: We identified three different imaging clusters based on the predominant tissue involved in patients with active PsA. Distinct gene expression profiles may underlie these imaging clusters seen in PsA.

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SAT0360 BACTERIAL TRANSLOCATION IN THE ADJUVANT INDUCED ARTHRITIS MODEL: PRELIMINARY STUDY AND IMPACT OF NSAIDS

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Background: In patients with spondyloarthritis, the presence of intestinal inflammation and an increase in digestive permeability responsible for bacterial translocation has been described. No data are available on the effect of non-steroidal anti-inflammatory drugs (NSAIDs) on this bacterial translocation in patients with spondyloarthritis. Zonulin and lipopolysaccharide (LPS) have been described as good biomarkers of intestinal permeability and bacterial translocation, respectively. Adjuvant-induced arthritis (AIA) is a model of recent arthritis characterized by ossification and ankylosis in the post arthritis period. This model can be considered as a model of reactive arthritis in which our previous work has reported a clear efficacy of NSAIDs with differences between molecules at the structural and vascular levels.

Objectives: To test the hypothesis that there is an increase in digestive permeability and bacterial translocation in the AIA model and to show the influence of different NSAIDs on these two parameters.

Methods: Adjuvant-induced arthritis (AIA) was induced in 6-week-old male Lewis rats by an injection at the base of the tail of Mycobacterium butyricum. A group of non-AIA (control) rats received saline. At the first signs of arthritis, the AIA-rats were evaluated (arthritis score 0-6) and treated daily intraperitoneally with naproxen (10 mg/kg/day), diclofenac (5mg/kg twice daily), celecoxib (3 mg/kg/day) or saline solution (AIA-vehicle group). After 21 days of treatment, the rats were sacrificed and serum levels of zonulin and LPS were evaluated by ELISA and liquid chromatography-mass spectrometry, respectively. Circulating levels of TNF-α and IL1-β and paw radiographic score were measured.

Results: Compared to the control group, there was a significant increase in zonulin concentration ($p < 0.001$) in the AIA group. There was no significant difference in the concentration of LPS between the two groups. The levels of zonulin were correlated with the TNF-α levels (R= -0.42; p=0.032) and the arthritis score (R=0.45; p=0.013) but not with the level of IL1-β (R=; p-0.018; p=0.39). Treatment with NSAIDs significantly and equivalently decreased the arthritis score in each group. Compared to the vehicle group, treatment with naproxen significantly decreased the radiographic score ($p<0.001$), TNF-α, IL1-β ($p < 0.01$), zonulin ($p<0.001$) and LPS ($p < 0.05$). Celecoxib decreased radiographic score ($p < 0.001$), IL1-β ($p < 0.01$), TNF-α ($p < 0.01$) but increased zonulin levels ($p < 0.05$) without effect on LPS. Diclofenac also decreased radiographic score ($p < 0.001$), TNF-α ($p < 0.01$), and IL1-β ($p < 0.01$) but increased both zonulin ($p < 0.01$) and LPS ($p < 0.001$).

Conclusion: We have demonstrated an increase in serum zonulin levels in the AIA model and a beneficial effect of naproxen on intestinal permeability and bacterial translocation in contrast to celecoxib and diclofenac. Moreover, the plasmatic zonulin levels were correlated with TNF-α supporting a pivotal role of TNF-α on the tight junctions in this model.

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SAT0361 HEALTHY HUMAN SPINAL PROCESSES PERI-ENTHESEAL T-CELLS EXHIBIT A TR1 RATHER THAN A FOXP3 REGULATORY PHENOTYPE

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Background: We have previously reported that the normal spinal enthesis has populations of conventional T-cells including CD4+ & CD8+ T-cells that could be induced to produce IL-17A and TNF following anti-CD3/CD28 stimulation. The biology of such cells in health including their normal function and antigen reactivity is completely unknown. The purpose of this work was to define the phenotype, functionality and TCR reactivity of such T-cells in health.

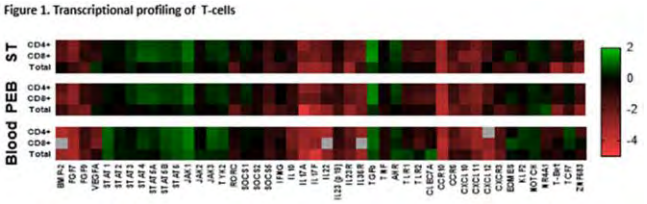
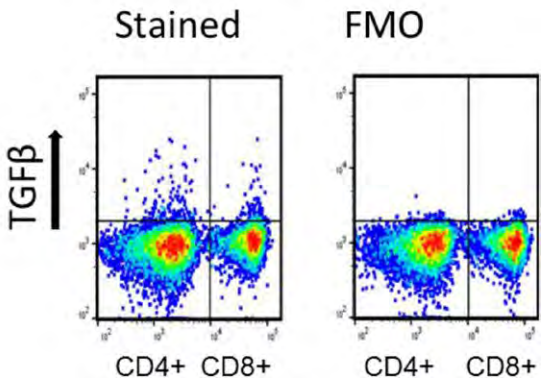


Figure 2. TGFβ from secretion enthesis T-cells



Objectives: To investigate whether the T-cells at the normal enthesis were regulatory in nature and to determine the type of regulatory T-cell as Tr1 or FOXP3 regulatory T-cell and to determine T-cell reactivity.
Methods: Healthy interspinous ligament and spinous process with matched peripheral blood were harvested from patients undergoing elective spinal surgery (n=20). Entheseal soft tissue (EST) & peri-entheseal bone (PEB) was enzymatically digested and then sorted. Tr1 and Treg phenotypes were investigated using flow cytometry. Analysis of cytokines, growth factors and chemokines was performed by qRT-PCR, ELISA and flow cytometry. TCR sequencing was performed and a search for putative T-cell reactivity was done using TCR3 database.
Results: Pro-inflammatory cytokine transcripts including IL-17A, IL-17F, IL-22, IL-23 (p19) & TNF were very low or undetectable in the Enthesis T-cells (Fig 1). Flow cytometry confirmed entheseal T-cells had a Tr1 phenotype (CD4+ LAG3+ CD49b+). Intracellular flow cytometry showed enthesis T-cells had very low FOXP3 expression, when compared to their blood counterparts. Intracellular flow cytometry and gene expression showed high basal expression of growth factors and regulatory proteins such as IL-10 & TGFβ, when compared to blood T-cells. RNA-Seq data, showed 13 potential TCR clonal sequences the most common of which are predicted to be reactive viral infection was CMV present in 8 sequences and Influenza A virus present in 2 sequences.
Conclusion: The healthy human enthesis has regulatory T-cells of a Tr1 phenotype rather than a FOXP3 Treg phenotype. Many clones have antigen specificity indicating reactivity to prior infection. These findings suggest that conventional entheseal T-cells have a role in enthesis immune homeostasis.
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SAT0362 ASSOCIATION OF GUT DYSBIOSIS WITH STRUCTURAL DAMAGE AND ACTIVITY IN AXIAL SPONDYLOARTHRITIS PATIENTS. DATA FROM THE COSPAR REGISTRY.

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Background: The etiopathogenesis of axial spondyloarthritis (AxSpA) is multifactorial. The possible role of alteration in gut microbiome (dysbiosis) has been recently suggested. However, the association of dysbiosis with structural damage is still unknown and further studies are needed to assess its association with disease activity.
Objectives: To determine the alterations in the gut microbiota in AxSpA patients. To evaluate whether changes in the gut microbiota in AxSpA patients are associated with structural damage or disease activity.
Methods: Fifteen AxSpA patients and 15 healthy donors (HDs) were included in a cross-sectional study. Disease activity variables such as C-reactive protein and ESR were measured. Structural damage was determined by lateral X-rays of the cervical and lumbar spine to establish the mSASSS index. Axial mobility was evaluated using the BASMI index and the enthesis affectation was evaluated using ultrasound to obtain the MASEI index. Gut microbiota was measured using the Ion Torrent S5 platform and sequences were processed using the QIIME2. Chi-square and Mann-Whitney U were used, and correlations were determined using the Spearman Rho test. Significant differences were considered $p < 0.05$.
Results: Alpha diversity indicators, such as the number of observed OTUs group and the faith index, showed a greater richness in AxSpA compared to HDs (p=0.03 and p=0.01). A significant decrease in family Bacteroidaceae (p=0.006) and an increase in families Synergistaceae and Bifidobacteriaceae were found in the microbiota of AxSpA (p=0.036, p=0.049). According to genera, Bacteroides decreased in AxSpA (p=0.006), while Dialister and Bifidobacterium increased (p=0.010 and p=0.046). Positive correlation among lumbar mSASSS (r=0.508, p=0.019) and Synergistaceae was found. This family was also increased along with the increase in enthesis damage (MASEI index (r=0.656, p=0.028)) and axial mobility by the BASMI index (r=0.529, p=0.011). Correlation studies between the decrease in Bacteroidaceae and Bacteroides with disease activity measured by ASDAS (r=-0.697, p=0.025; r=-0.770, p=0.009) was also significant. Positive correlation was observed between Dialister with mSASSS (r=0.549, p=0.010) and BASMI (r=0.512, p=0.015).
Conclusion: 1) AxSpA patients had a significant alteration of the gut microbiota. 2) These alterations are associated with radiographic damage, disease activity, affectation of enthesis and axial mobility.
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SAT0363 DELPHINIDIN DOSE-DEPENDENTLY DIMINISHES PERIPHERAL IL-17 AND IFN-Γ PRODUCING LYMPHOCYTES IN PSORIATIC ARTHRITIS

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Background: Delphinidin, a dietary anthocyanidin and powerful anti-oxidant from pigmented fruits and vegetables, has broad anti-inflammatory properties. In a human skin model of psoriasis, delphinidin reduced expression of proliferative and inflammatory markers (1).
Objectives: The rationale of our study was to assess whether delphinidin can in vitro suppress IL-17 and IFN-γ production in peripheral blood mononuclear cell (PBMC) subsets from patients with psoriatic arthritis (PsA).
Methods: PBMCs were obtained from 24 patients with PsA attending the outpatient clinic of the Department of Rheumatology/clinical Immunology at the University General Hospital of Larissa, Greece. 16 age- and sex-matched healthy volunteers were also included in the study. Delphinidin was supplemented at a concentration ranging from 1 to 50μg/ml, one hour prior to cell stimulation. Cell viability (Annexin V staining) and innate/adaptive lymphocyte subpopulations were assessed by flow cytometry with a panel of fluorochrome-conjugated antibodies against CD56, CD3, CD4 and CD8. Intracellular expression of IL-17 and IFN-γ was measured following PMA/ionomycin stimulation for 5 hours using standard cell permeabilization protocols and monoclonal antibodies against IL-17 and IFN-γ
Results: Delphinidin at concentration ≥10 μg/ml sharply diminished IL-17-production by CD4(+) T cells (Th17) and CD56(+)CD3(+) (NKT) cells from patients with psoriatic arthritis and normal controls ($p \leq 0.05$). IFN-γ producing T (CD4 and CD8) cells, as well as NK and NKT cells were also dose-dependently suppressed following delphinidin pre-incubation in both patients and healthy controls. Inhibition of IFN-γ(+) cells ranged from 27 to 69% and peaked at delphinidin concentration 20-50μg/ml. The inhibitory effect of delphinidin on IL-17 and IFN-γ producing lymphocytes was not due to compromised cell viability, as assessed by annexin V binding.
Conclusion: Delphinidin exerts, in a dose-dependent manner, a profound in vitro inhibitory effect on T cell and NKT cell IL-17 and IFN-γ production in PsA, and therefore, it may be used as a dietary immunosuppressant, complementary to standard treatment.
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Disclosure of Interests: ATHANASIOS MAVROPOULOS: None declared, Sotirios Tsiogkas: None declared, Dimitrios Skyvalidas: None declared, Christos Liaskos: None declared, Aggeliki Roussaki-Schulze Grant/research support from: Received a grant to support the educational and research activities of the

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SATURDAY, 06 JUNE 2020

Spondyloarthritis - clinical aspects (other than treatment)

SAT0364

DATA TO BE COLLECTED FOR AN OPTIMAL MANAGEMENT OF AXIAL SPONDYLOARTHRITIS IN DAILY PRACTICE: PROPOSAL FROM AN EVIDENCE BASED AND CONSENSUAL APPROACHES

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Background: Standardization of clinical practice has been proven to be effective in management of chronic diseases. This is particularly true at the time where the concept of treat to target is becoming more and more important in the field of axial spondyloarthritis (ax-SpA).

Objectives: To propose a list of variables to be collected at the time of the diagnosis and over the follow-up of patients with axial spondyloarthritis (ax-SpA) for an optimal management in daily practice.

Methods: The process comprised (1) the evaluation of the interest of 51 variables proposed for the assessment of axSpA via a systematic literature research, (2) a consensus process involving 78 hospital-based or office-based rheumatologists, considering the collection of the variable in a 4 grade scale from "potentially useful" to "mandatory", (3) a consensus on optimal timeline for periodic assessment of the selected variables on a 5 grade scale from "at each visit" to "never to be re-collected".

Results: The systematic literature research retrieved a total of 14,133 abstracts, of which 213 were included in the final qualitative synthesis. Concerning the data to be collected at the time of the diagnosis and during follow-up, we proposed to differentiate the results based on a) the way of collection of the variables (e.g. questionnaires by the patient, interview by the physician, physical examination, investigations) b) the usefulness these variables in daily practice based on the opinion of the rheumatologists " c) the optimal timeline between 2 evaluations of the variable based on the opinion of the rheumatologists. In the initial systematic review, symptoms of heart failure history of inflammatory bowel disease, psoriasis or uveitis, patient global visual analogic scale, spine radiographs, modified Schöber test, coxo-femoral rotations, swollen joint count, urine strip test, BASDAI and ASDAS global scores were considered very useful and nocturnal back pain/ morning stiffness, sacro-iliac joints radiographs and CRP were considered mandatory (**Figure 1**). Timeline between 2 evaluations of variables to collect in the periodic review are summarized in **Figure 2**.

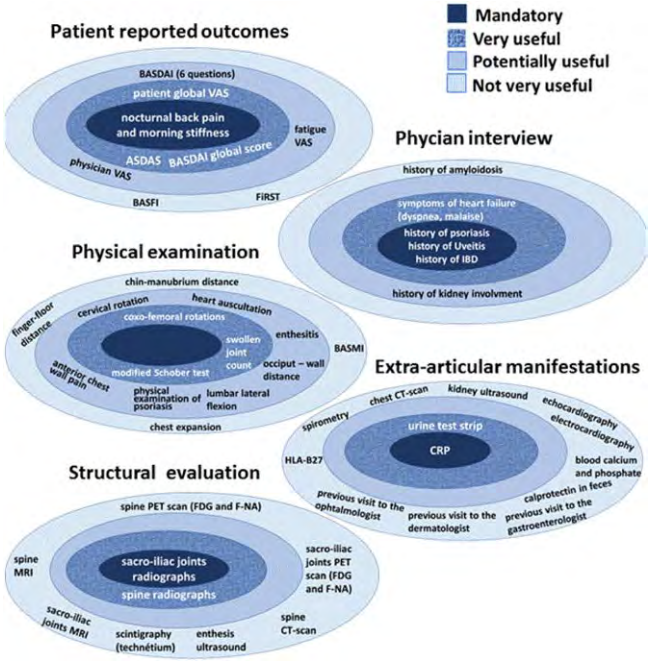


Figure 1. Core sets of items to collect and report in the systematic review in axial spondyloarthritis management in daily practice ASDAS=Ankylosing Spondylitis Disease Activity Score, BASDAI=Bath Ankylosing Spondylitis Disease Activity Index, BASFI=Bath Ankylosing Spondylitis Functionnal Index, BASMI=Bath Ankylosing Spondylitis Metrology Index, CRP=C Reactive Protein, CT=computerized tomography, FIRST=Fibromyalgia Rapid Screening Tool, HLA=Human Leukocyte Antigen, MRI=Magnetic resonance imaging, PET=positron emission tomography.

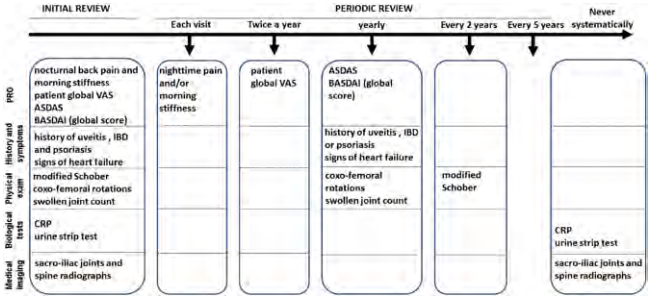


Figure 2. Periodic review timeline of variables to collectASDAS=Ankylosing Spondylitis Disease Activity Score, BASDAI=Bath Ankylosing Spondylitis Disease Activity Index, Spondylitis Metrology Index, CRP=C Reactive Protein, IBD = inflammatory bowel diseases, PRO = Patient Reported Outcomes

Conclusion: Using an evidence-based and an expert consensus approaches, this initiative defined a core set of variables to be collected and reported at the time of the diagnosis and during follow-up of patients with ax-SpA in daily practice.

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SAT0365

EFFECTS OF ANTI-TNF-THERAPY ON OSTEOBLASTIC ACTIVITY IN ANKYLOSING SPONDYLITIS – RESULTS FROM A PROSPECTIVE STUDY USING PET-MRI OF SIJ AND SPINE

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Background: The clinical efficacy of tumor necrosis factor inhibitors (TNFi) in patients with axial spondyloarthritis (axSpA) is well established but its effect on new bone formation is still unclear (1). Positron emission tomography (PET) using bone-seeking ^{18}F-Fluoride [18F]F in combination with magnetic resonance imaging ([18F]F /MRI) has been shown to depict not only bone marrow edema (BME) but also shows the quantity of tracer uptake in the late phase of perfusion suggestive of remodeling and osteoblastic activity, not only in radiographic axSpA (r-axSpA) (2).

Objectives: Assess the effect of TNFi on bone remodeling processes in the axial skeleton of r-axSpA patients using [18F]F/MRI prior (baseline, BL) and 4 months after (follow-up, FU) treatment.

Methods: Patients (11 male, 5 female, mean age 38.6±12.0 years) with clinically active r-axSpA (BASDAI>4, failure of NSAIDs, no previous biologics) prospectively underwent 3-Tesla and [18F]F PET/MRI (40 minutes after injection of a mean activity of 157 MBq [18F]F). Images of the SIJ (n=16 patients) and the whole spine (n=10 patients) were performed at BL and FU. Three readers (1 for [18F]F/MRI and 2 for conventional MRI) evaluated all images independently and blinded to timepoint allocation. Only lesions on which all readers agreed on were used for further analyses. Inflammation (bone marrow edema, BME), structural lesions (fat deposition (FD), sclerosis, erosions and ankylosis) and focal [18F]F uptake were recorded on the level of SIJ (SIJ-Q) and vertebral quadrants (V-Q), with each SIJ or vertebral body consisting of 4 VQs (superior and inferior sacral and iliac for the SIJ, and superior and inferior, anterior and posterior for the vertebral bodies).

Results: A total of 128 SIJ-Q and 920 VQs were analyzed at both BL and FU. In the SIJs, 75 (58.6%), 120 (93.8%), 69 (53.9%), 99 (77.3%) and 16 (12.5%) SIJ-Q showed BME, FD, sclerosis, erosions and ankylosis, while 111 (86.7%) SIJ-Q showed focal [18F]F-uptake at BL. Association with increased [18F]F-uptake was found most frequently in SIJ-Q with BME (70/75 SIJ-Q, 93.3%), sclerosis (65/69 SIJ-Q, 94.2%) and FD (105/120 SIJ-Q, 87.5%). At FU, 37 SIJ-Q still showed BME (improvement by 50.7%), while almost no changes were observed in chronic lesions. In comparison, improvement of focal [18F]F-uptake was found in all lesion combinations, with improvement of focal [18F]F-lesions associated with BME by 62.9%, with sclerosis by 33.8% and with FD by 22.9% of SIJ-Q.

In the spine, only 41 (4.5%), 61 (6.6%), 14 (1.5%) V-Q showed BME, FD and sclerosis, respectively, while 77 V-Q (8.4%) showed focal [18F]F-uptake. An association to increased [18F]F-uptake was found most frequently with sclerosis (7/14 V-Q, 50%) and FD (25/61 V-Q, 41%). At FU, 12 V-Q still showed BME (improvement by 70.7%), while, similar to SIJ, almost no changes were observed in the chronic lesions. The largest improvement was found in focal [18F]F-lesions associated with BME 81.8% and with FD by 22.9% of V-Q.

Conclusion: In this first prospective study on whole spine and SIJ [18F]F/MRI in patients with r-axSpA, a significant decrease of osteoblastic activity was observed over 4 months of continuous anti-TNF treatment. The effect of treatment was observed not only at sites with inflammatory lesions (BME) but also at sites with pre-existing chronic structural lesions, while some osteoblastic activity remained visible at 4 months. These data support a short-term effect of anti-TNF treatment on osteoblastic activity, while the long-term effects need to be further studied.

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SAT0366 CLINICAL RESPONSE TO BIOLOGIC DMARDS IN AXIAL SPONDYLOARTHRITIS AND AXIAL PSORIATIC ARTHRITIS. DIFFERENT DISEASES, SAME OUTCOMES?

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Background: Patients with psoriatic arthritis may present predominant axial involvement. Currently, it is unclear whether these patients should be considered as axial spondyloarthritis (axSpA) with psoriasis or psoriatic arthritis with axial involvement –also known as axial PsA (axPsA). Data comparing medium-term treatment response to biological drugs in axSpA and axPsA would add relevant information to answer this question.

Objectives: To compare the clinical response and predictor factors after one year of biological therapy in patients with axSpA and axPsA.

Methods: One-year follow-up data from all patients (pts) with axSpA or axPsA (defined by the treating rheumatologist) included in a prospective cohort of pts receiving biological therapy from la Paz University Hospital between 2002 and 2019 were analysed. Demographic information, laboratory tests, concomitant treatments and disease status were collected at baseline. Clinical disease activity was measured by PhGA and ASDAS criteria at baseline, 6 and 12 months. According to ASDAS, disease activity was defined as: inactive disease (ID) (ASDAS <1.3), low disease activity (LDA) (ASDAS 1.3-2.1), high disease activity (HDA) (ASDAS 2.1-3.5) and very high disease activity (VHDA) (ASDAS >3.5). Clinical important improvement and major improvement were defined by ASDAS (delta-ASDAS ≥ 1.1 and ≥ 2.0, respectively). According to PhGA, disease activity was assorted by consensus of 3 expert rheumatologists in: ID with PhGA<5, LDA with PhGA 5-30, HDA with PhGA >30-60 and VHDA with PhGA >60. Clinical improvement by PhGA was defined as an improvement of 30 % compared to baseline. In the statistical analysis, the frequency of pts achieving each clinical activity status and clinical improvement at 6m and 12m were compared using Fisher test, separately for axSpA and axPsA. Baseline predictor factors for achieving clinical response and clinical improvement were identified using univariable and multivariable binary regression.

Results: Out of 352 included pts, 287 (81.5%) had axSpA and 65 (18.5%) axPsA. Sixty percent were males, 158 (45%) smokers, with mean (SD) baseline disease activity of ASDAS (bASDAS): 3.3 (0.9) and PhGA: 39.1 (21.5). Biological therapies initiated included TNF inhibitors in 93.8 % and secukinumab in 6.2%. In comparison to axPsA, pts with axSpA were more HLA B27 positive (p<0.001) and had better PhGA at baseline (p=0.02). They also had more uveitis (p=0.03) and were more radiographically affected (p<0.001).

Response rates at 6m and 12m in both diseases according to ASDAS are shown in Figure 1, and to PhGA in Figure 2. Both diseases presented a similar clinical response, and no statistically significant differences were observed for any disease activity interval between them for ASDAS or PhGA. There were no differences between both diseases on clinical improvement, regardless the type of measurement.

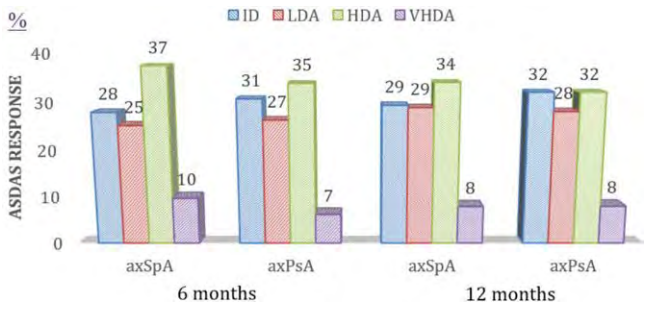


Figure 1. Response rates (in percentage) by ASDAS at 6m and 12m in axSpA and PsA

In the group of axSpA, the univariate analysis observed that LDA (by ASDAS) at 12m was associated with bASDAS (OR=0.67, p=0.02), male gender (OR=2.8, p=0.001) and HLA B27 positive (OR=2.3, p=0.01). In the multivariate analysis, these variables remained significantly associated with LDA (bASDAS: OR= 0.67; p<0.05; male gender: OR=2.7, p<0.01; and HLA B27 positivity OR=2.6, p<0.01). In the group of axPsA, the univariate analysis showed a tendency that male pts achieved LDA more frequently at 6m (OR=3.0, p=0.05) and at 12m (OR=2.75, p=0.09). In the multivariable analyses, none of the factors was significantly associated neither with clinical improvement nor with LDA in pts with axPsA.

Conclusion: In clinical practice, pts with axSpA and axPsA present a similar clinical response to biological therapy within the first year of treatment. Male pts seem to have better medium-term outcomes in both diseases, and HLA B27 pts respond better in axSpA.

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SAT0367 EXTRA-ARTICULAR MANIFESTATIONS IN EARLY AXIAL SPONDYLOARTHRITIS: WHAT IS THEIR FREQUENCY? A SYSTEMATIC LITERATURE REVIEW INCLUDING 2854 PATIENTS

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Background: Extra-articular manifestations (EAMs): psoriasis, uveitis and inflammatory bowel disease (IBD) are common in patients with established spondyloarthritis (SpA), with prevalences reported around 9%, 26% and 7 % respectively (1). However, data on the prevalence of EAMs are lacking in early axial SpA (axSpA).
Objectives: The aim was to assess the prevalence of EAMs in early axSpA in the published literature.
Methods: Systematic literature search on Pubmed MEDLINE up to 31.12.2019 with keywords referring to EAMs (*uveitis and synonyms, psoriasis and synonyms or IBD and synonyms*) and early axSpA (*recent, young adult, young, untreated, inception*) and selection by one reader of all full-text publications in English, describing the prevalence of at least one of the EAMs in patients with early axSpA, defined here as patients fulfilling ASAS, ESSG or Amor criteria and symptom duration of less than 6 years (as this was defined by authors as early disease). Patients' age, axSpA symptom duration, sex, HLA-B27 status, and number of patients with EAMs were recorded by one reader using a predefined extraction sheet. For longitudinal studies, baseline data was recorded. Description of patients was analysed using weighted means. Prevalences in each study according to symptom duration were graphically reported, and pooled prevalences were calculated by meta-analysis of proportions, using a random-effects model and the DerSimonian & Laird method to derive the summary estimate.
Results: Of 667 articles, 17 were relevant to the research question with prevalence data of psoriasis, uveitis and IBD available in 16, 17 and 15 articles, respectively (and most studies reporting several EAMs). Of the 17 articles, 14 were cohort studies and 3 were trials in early axSpA. A total of 2854 patients with early SpA was analyzed: weighted mean age 32.3±9.1 years (range 21-42 years), weighted mean axSpA symptom duration 20.7±11.1 months (range 8-68), 40.3 % were female, and 65.1% carried HLA-B27.
The pooled prevalences of psoriasis, uveitis and IBD were respectively 8.9 % (95% CI 5.0, 13.8), 13.4% (95% CI 9.5, 17.8) and 3.5% (95% CI 1.7, 5.9) (**Figure 1**). There was a trend towards higher prevalences in patients with longer disease duration (**Figure 2**).

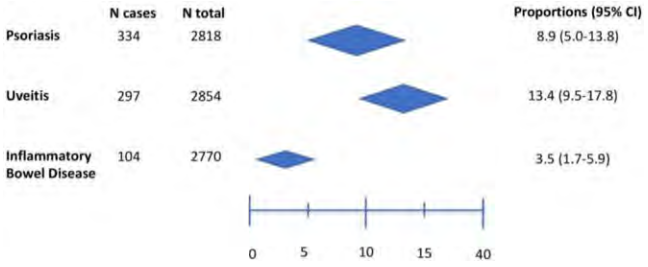


Figure 1. Meta-analysis of prevalence of each EAM

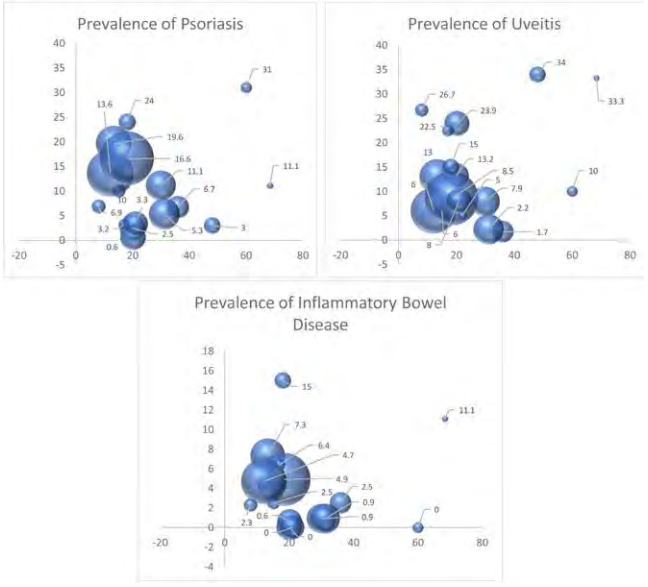


Figure 2. The prevalence of each EAM according to the symptom duration in early axSpAX axis: mean symptom duration (months). Y axis: prevalence (%) of an EAM. Diameter of bubbles is proportional to sample size of each article.

Conclusion: Over the first years of axSpA, EAMs are frequent, in particular psoriasis and uveitis, with prevalences up to 30% in some studies. Compared to established axSpA, the EAM which was much less frequent was uveitis, which suggests the appearance of new cases over follow-up. Physicians need to screen carefully for EAMs right from the time of diagnosis, and need to repeat this screening over follow-up.

References:
[1] Stolwijk C et al. Prevalence of extra-articular manifestations in patients with ankylosing spondylitis: a systematic review and meta-analysis. *Ann Rheum Dis*. 2015;74(1):65–73

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SAT0368 PREGNANCY IN WOMEN WITH SPONDYLOARTHRITIS: WHO ARE THE PATIENTS AT RISK OF DISEASE FLARE?

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Background: Patients with Spondyloarthritis (SpA) can experience flares during pregnancy and postpartum even though the available data are limited and not conclusive.
Objectives: To assess disease activity and treatment modification during pregnancy and postpartum in patients with SpA and to identify risk factors for disease flare.
Methods: Data on SpA pregnancies prospectively-followed in a pregnancy clinic from 2010 to 2019 were retrospectively analysed. Disease activity was assessed during each trimester and postpartum using ASDAS-CRP or DAS28-CRP. Flare was defined as an increase of disease activity leading to treatment modification (introduction or increase ≥5mg/day of prednisone, introduction of cDMARD or bDMARD)[1].
Results: Data on 50 pregnancies in 46 patients were collected (mean age at conception 33±4.7 years; median disease duration: 60 months (IQR 24-132); 33 psoriatic arthritis, 6 axialSpA, 2 reactive arthritis, 2 IBD-related SpA; 6 undifferentiated SpA, 1 juvenile idiopathic arthritis). Six pregnancies ended in miscarriage, so they weren't considered for the analysis of flares during pregnancy (table 1). Fifteen out of 44 (34%) pregnancies had at least one flare during pregnancy (6, 7 and 4 during 1st, 2nd and 3rd trimester respectively; 2 pregnancies had multiple flares). A higher rate of flare was observed in pregnancies of patients with axial involvement (p=0.01), on treatment with bDMARDs at preconceptional visit (p=0.03) and who stopped TNFi at positive pregnancy test (p=0.03). Peripheral involvement was associated with a lower rate of flares (p=0.02). Medications resumed during pregnancy were steroids (in 6 pregnancies), cDMARDs (2 sulfasalazine, 1 cyclosporine) and bDMARDs (4 certolizumab, 4 etanercept). During postpartum period flares were recorded in 46% of patients.

Table 1. clinical features, medication and disease activity in pregnancies with flare *vs* without flare

CLINICAL FEATURES	FLARE (15)	NO FLARE (29)	*p*
Axial involvement, n (%)	11/15 (73)	9/29 (31)	0.01
Peripheral arthritis, n (%)	8/15 (53)	26/29 (90)	0.02
Enthesitis, n (%)	5/15 (33)	14/29 (48)	ns
Dactilitis, n (%)	3/15 (20)	8/29 (28)	ns
Psoriasis, n (%)	6/15 (40)	17/29 (59)	ns
IBD, n (%)	2/15 (13)	0	ns
Uveitis, n(%)	1/15 (7)	3/29 (10)	ns
HLAB27 +	7/11 (64)	5/12 (42)	ns
MEDICATION HISTORY			
bDMARDs, n (%)	11/15 (73)	7/29 (24)	0.003
bDMARDs at preconception visit, n (%)	8/15 (53)	6/29 (21)	0.04
bDMARDs stopped at positive pregnancy test, n (%)	7/15 (47)	4/29 (14)	0.03
cDMARDs, n (%)	12/15 (80)	25/29 (86)	ns
DISEASE ACTIVITY			
ACTIVE DISEASE* preconception visit, n(%)	3/14 (21)	4/23 (17)	ns
ACTIVE DISEASE 1st trimester, n(%)	6/15 (40)	1/29 (3)	0.004
ACTIVE DISEASE 2nd trimester, n(%)	8/15 (47)	2/29 (7)	0.001
ACTIVE DISEASE 3rd trimester, n(%)	2/15 (13)	1/29 (3)	ns

*DAS28-CRP>3.2 or ASDAS-CRP≥2.1

Conclusion: In our cohort of prospectively-followed SpA pregnancies, 34% experienced a flare during pregnancy and 46% during postpartum. Flares

occurred especially in those patients who discontinued TNFi early in pregnancy and with axial involvement. When resumed during pregnancy, TNFi was able to control the disease. At preconception counselling, the continuation of TNFi during pregnancy should be considered to ensure a better control of disease.

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Disclosure of Interests: : None declared

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SAT0369 SPINAL RADIOGRAPHIC PROGRESSION IN EARLY SPONDYLOARTHRITIS: SIX-YEAR RESULTS FROM THE ESPERANZA COHORT

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Background: There are few studies focused on the development of structural damage over time in patients with early SpA

Objectives: The aim of this study is to analyze the mSASSS radiographic progression of spine in patients with early spondyloarthritis (SpA) in the Esperanza cohort.

Methods: In this longitudinal study, 49 patients of the Spanish early spondyloarthritis (SpA) Esperanza cohort were included. Every patient had a baseline and a six years lateral X-Ray of the cervical and lumbar of spine. The assessment of spine structural damage was done by the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS). Nine readers, blinded for the diagnosis, participated in the reliability exercise, all of them experienced rheumatologists and members of the Spanish spondyloarthritis working group (GRESSER). The mSASSS progression and development of new syndesmophytes was analyzed. The gold standard of every elemental lesion of the mSASSS and the total mSASSS score was the agreement achieved by the independent categorical opinion of at least five of the nine readers. For reliability, intraclass correlation coefficient (ICC) two-way mixed, absolute agreement was used.

Results: Forty-nine patients were included, 69 % were males and 49%, HLA B27 positive. Mean ± SD baseline ESR, CRP, BASDAI, BASFI and mSASSS were 10.7±11.7, 5.4±7.1, 3.7±2.5, 2.1±2.0 and 0.326±0.85, respectively. Inter-reader ICC reliability of the 9 readers was 0.812 (CI 95%; 0.764-0.857). The mSASSS score at the six-year visit was 0.67 ± 1.6: thirty-nine patients did not present any changes in this score at the end of the follow-up, two patients had Δ mSASSS of – 1 and eight patients, an increase in this score (four patients, +1; three patients, +2 and one patient, +9 points).

At baseline, five patients presented one syndesmophyte; at the six-year visit, seven had one syndesmophyte; one patient, two syndesmophytes and another one, one bone bridge. Only 2/5 patients (40%) with syndesmophytes at baseline showed an increase in Δ mSASSS; the two patients with a Δ mSASSS of -1 did not have syndesmophytes at baseline. Five out of eight patients (62.5%) with an increase of the Δ mSASSS presented this lesion at the six-year visit but only two of them showed syndesmophytes at baseline. On the other hand, two of the three patients who showed an increase of the ΔmSASSS without syndesmophytes at baseline presented an erosion in the anterior vertebral corner and the patient with the bone bridge had a previous syndesmophyte. Our results indicate that in early SpA much of the progression appears in patients without previous syndesmophytes.

Conclusion: Spinal radiographic progression was very low in our early SpA cohort, with a mean progression of 0.3 mSASSS units. Only eight patients (16.3%) presented spinal structural progression, most of them not showing syndesmophytes at baseline. It is reasonable to consider that an early diagnosis and monitoring could result in a low radiographic progression.

Disclosure of Interests: Eugenio de Miguel Grant/research support from: Yes (Abbvie, Novartis, Pfizer), Consultant of: Yes (Abbvie, Novartis, Pfizer), Paid instructor for: yes (AbbVie, Novartis, Pfizer, MSD, BMS, UCB, Roche, Grunental, Janssen, Sanofi), Speakers bureau: yes (AbbVie, Novartis, Pfizer, MSD, BMS, UCB, Roche, Grunental, Janssen, Sanofi), Jose Francisco Garcia LLorente: None declared, Claudia Urrego-Laurín: None declared, Maria Luz García-Vivar: None declared, Cristina Fernández-Carballido Consultant of: Yes, I have received fees for scientific advice (Abbvie, Celgene, Janssen, Lilly and Novartis), Speakers bureau: Yes, I have received fees as a speaker (Abbvie, Celgene, Janssen, Lilly, MSD, Novartis), María del Carmen Castro Villegas: None declared, Beatriz Joven-Ibáñez Speakers bureau: Abbvie, Celgene, Janssen, Merck Sharp & Dohme, Novartis, Pfizer, Xavier Juanola-Roura: None declared, Carolina Tornero: None declared, E. Galindez: None declared

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SAT0370 TUMOUR NECROSIS FACTOR INHIBITOR THERAPY DOES NOT REDUCE THE INCIDENCE OF COMORBIDITIES AND EXTRA-ARTICULAR MANIFESTATIONS IN ANKYLOSING SPONDYLITIS: AN ANALYSIS OF THREE US CLAIMS DATABASES

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Background: Comorbidities and extra-articular manifestations (EAMs) substantially increase disease burden and mortality risk in patients (pts) with ankylosing spondylitis (AS).[1,2] Tumour necrosis factor inhibitors (TNFi) are highly efficacious and effective in AS treatment (tx), and are used after inadequate response to non-steroidal anti-inflammatory drugs.[3,4] However, the impact of TNFi on the incidence of comorbidities and EAMs in pts with AS is unknown.[5]

Objectives: To determine the incidence of comorbidities and EAMs in TNFi vs non-TNFi treated pts with AS in the US.

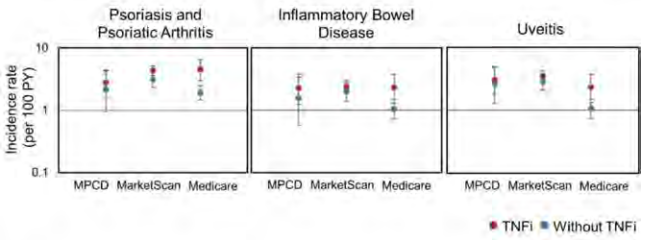
Methods: This was a retrospective, observational cohort study using data from 3 healthcare insurance claims databases: Multi-Payer Claims Database (MPCD Optum Insight; 2007–2010), Truven MarketScan® (2010–2014) and US Medicare Fee-for-Service Claims database (2006–2014). Eligible pts: ≥20 years (yrs) for MarketScan/MPCD or ≥65 yrs for Medicare, had an AS diagnosis (≥2 International Classification of Disease, 9th version [ICD-9] diagnosis codes of 720.0 from a rheumatologist) and ≥12 months' continuous medical and pharmacy enrolment prior to AS diagnosis (AS index date). Pts with AS not receiving tx were excluded. Tx exposure was reported from the first date of a new prescription/administration of an AS tx (no prior exposure) after the AS index date. Crude incidence rates (IR; shown as cases/100 pt-yrs) were calculated for EAMs (uveitis, psoriasis [PSO], psoriatic arthritis [PsA], inflammatory bowel disease [IBD]), with follow-up until the earliest of: death, lost medical/pharmacy coverage, study period end, first outcome occurrence, tx switch/discontinuation. Hazard ratios (HRs) of comorbidities (hospitalised infection, solid cancers) and EAMs for propensity score (PS)-matched pt groups were calculated using Cox proportional hazard regression models. Pts with the specific comorbidity/EAM of interest prior to AS index date were excluded. PS analyses assessed probability of TNFi initiation vs non-TNFi tx and adjusted for factors including comorbidities and demographics. HRs with confidence intervals crossing 1 are not reported.

Results: 20,460 pts with AS were eligible (MPCD: 2,384; MarketScan: 9,032; Medicare: 9,044). In all databases, crude IR of EAMs were higher for TNFi vs non-TNFi treated pts (**Figure 1**). In the PS-matched cohort, incidences of hospitalised infections were lower in TNFi vs non-TNFi treated pts from the MarketScan and Medicare databases (**Figure 2**). Higher incidences of solid cancers and EAMs were observed in TNFi vs non-TNFi treated pts; Medicare data (**Figure 2**). A higher risk of PsA and PSO was seen in TNFi vs non-TNFi treated pts; MarketScan data (**Figure 2**). PS-matched cohort data from the MPCD database were non-significant.

Conclusion: Despite strong efficacy in treating AS-related signs and symptoms, similar incidence of comorbidities and increased incidence of some EAMs (IBD, PSO/PsA, uveitis) was seen in TNFi vs non-TNFi treated pts in the PS-matched analyses. This may be due to channelling of pts with more severe AS to receive TNFi, despite the PS-matched analysis aiming to overcome this. Moreover, prior medical history of Medicare pts may not be captured in the database, as pts are typically older with longer disease durations. While these results confirm previous findings,[6] a prospective observational study is required to generalise to pts outside the US.

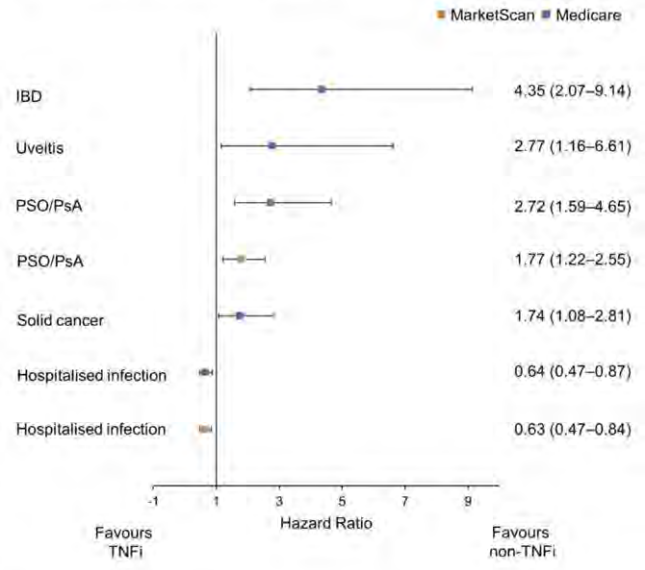
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Figure 1. Crude incidence of EAMs by treatment exposure in patients with AS using TNFi and without TNFi treatment (95% CIs included)



AS: ankylosing spondyloarthritis; CI: confidence interval; EAM: extra-articular manifestation; MPCD: Multi-Payer Claims Database; PY: patient-years; TNFi: tumour necrosis factor inhibitor.

Figure 2. Propensity score-weighted hazard ratios of comorbidities and EAMs by treatment exposure in patients with AS using TNFi and without TNFi treatment



The forest plot shows propensity score-weighted hazard ratios and 95% CIs. Some data have been excluded due to a lack of events recorded in the dataset. All propensity score-weighted hazard ratios with CIs crossing one were deemed non-significant and were therefore not included; this includes all relevant data from the MPCD database. AS: ankylosing spondylitis; CI: confidence interval; EAM: extra-articular manifestation; IBD: inflammatory bowel disease; MPCD: Multi-Payer Claims Database; PsA: psoriatic arthritis; PSO: psoriasis; TNFi: tumour necrosis factor inhibitor.

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SAT0371 ARE ENGLISH-LANGUAGE VIDEOS ON YOUTUBE A USEFUL SOURCE OF INFORMATION FOR SPONDYLOARTHRITIS?

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Background: Spondyloarthritis (SpA) is a family of chronic inflammatory disorders. Social media, such as YouTube, is a popular online platform where patients often visit for information. However, the validity of the content uploaded onto YouTube is not known.

Objectives: This study aimed to evaluate the content, reliability and quality of the most viewed English-language YouTube videos on SpA.

Methods: Keywords "spondyloarthritis", "spondyloarthropathy" and "ankylosing spondylitis" were searched on YouTube on October 7th, 2019. The top 270 videos were screened. Videos were excluded if they were irrelevant, in non-English language or if they had no audio. Total number of views, duration on YouTube (days), video length, upload date, number of likes, dislikes, subscribers and comments were recorded for videos. A modified 5-point DISCERN tool[1] and the 5-point Global Quality Scale (GQS) score[2] were used to assess the reliability and quality of the videos, with higher scores indicating greater reliability and quality respectively.

Results: Two hundred of 270 videos were included in the final analysis [61.5% from healthcare professionals, 37.0% from patients, 1.5% from news channels]. Of the 200 videos, 15 were uploaded within the last year and 112 in the last five years. 120 (60%) were categorized as useful information (Group 1), 6 (3%) as misleading information (Group 2), 52 (26%) as useful patient opinion (Group 3) and 22 (11%) as misleading patient opinion (Group 4). Useful videos were mainly from healthcare professionals or patients (86%). Useful videos (Group 1 and 3) had higher median (IQR) number of subscribers [2700 (14700) vs 211 (457), $p < 0.01$], reliability scores [3 (1) vs 2 (1), $p < 0.01$] and GQS scores [3 (1) vs. 2 (1), $p < 0.001$] compared to misleading videos (Group 2 and 4), respectively.

Videos uploaded by healthcare professionals tended to have more useful information [94% (116 of 123) vs. 66% (49 of 74), $p < 0.001$] and had higher median (IQR) reliability scores [3 (1) vs 2 (1), $p < 0.001$] and GQS scores [3 (2) vs 2 (1), $p < 0.001$] compared to patient uploaded videos respectively. Of the 5 (out of 123) videos from healthcare professionals that had misleading information, it was because of outdated information on diagnosis (3 videos) and treatment (5 videos) of SpA. Of the 22 videos that had misleading patient opinion, 9 (41%) wrongly described the clinical features for SpA and 14 (64%) portrayed the current evidence based treatment options as ineffective and described alternative treatment plans (i.e. diet restrictions, complementary and alternative medicine).

Conclusion: The majority of English language YouTube videos have useful information on the topic of SpA, however, 31% of patient opinions have inaccurate information on the clinical features and treatment options, and viewers need to be cognisant of these "fake news".

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SAT0372 PATIENTS WITH PSORIATIC ARTHRITIS SHOW HIGHER BONE DENSITY COMPARED TO AGE AND GENDER MATCHED PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: The prevalence of osteoporosis in inflammatory rheumatic diseases such as psoriatic arthritis (PsA) has not been sufficiently clarified yet, and the data in the literature are heterogeneous. In addition, it is still unclear to what extent patients with PsA differ in terms of bone density from patients with other forms of spondyloarthritis such as ankylosing spondylitis (AS).

Objectives: In an interim analysis of the Rh-GIOP Study (ClinicalTrials.gov Identifier NCT02719314), we observed that PsA patients demonstrated more frequently normal bone density than any other patient group analyzed (suffering from e.g. rheumatoid arthritis or systemic sclerosis). The main objective of this investigation was to compare bone density data from patients with PsA and

AS, as both diseases belong to the spondyloarthritis group. 1100 patients with inflammatory rheumatic diseases provided the basis of Rh-GIOP, a prospective study monitoring glucocorticoid (GC)-induced osteoporosis in patients with rheumatic diseases. Rh-GIOP was established in 2015 at the Charité University Hospital. Bone mineral density data were measured by dual x-ray absorptiometry (DXA).

Methods: 92 patients with PsA (65% female) were compared with 51 patients suffering from AS (35% female). Potential risk and protective factors (e.g. data on GC treatment, anti-rheumatic therapy), laboratory parameters (e.g. Vitamin D, alkaline phosphatase, calcium and inflammatory markers) and functional status (e.g. Health Assessment Questionnaire, sporting activities, back pain) were compared between these groups. Statistical analysis was performed descriptively using mean and standard deviation, t-tests for metric variables, and chi-square tests for nominal variables. Due to the heterogeneous gender distribution, an additional statistical matching was performed to compare patients matched by age and gender.

Results: Patients with PsA displayed significantly higher minimal T-scores than patients with AS (p=0.003) even though patients with AS were younger and more often male (p<0.001). AS patients showed a higher frequency of osteopenic bone densities (p<0.05), however, no differences in the frequency of osteoporotic bone densities were found. Body-mass-index (BMI) was significantly higher (p<0.001) in PsA patients. PsA patients demonstrated a higher frequency of csDMARD use (p<0.001). Additional analyses among PsA patients with and without csDMARDs revealed also significantly higher minimal T-scores in PsA patients taking csDMARDs (90% Methotrexate), and both groups showed the same average of age and gender distribution. Furthermore, AS patients complained significantly more often of back pain (96 % vs. 74%, p=0.001) than PsA patients. No differences in GC use or cumulative GC dose were found. All results could be confirmed when groups were matched by age and gender.

Conclusion: Our results demonstrate that patients with PsA display higher bone density compared to age and gender matched patients with ankylosing spondylitis. Possible influencing factors could be the higher frequency of csDMARD use, higher BMI or the lower frequency of back pain in PsA patients. Multivariate tests and additional biomarker investigations in larger cohorts are necessary to corroborate these findings and to identify underlying pathogenic differences which could serve for an explanation.

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SAT0373 QUANTITATIVE ASSESSMENT OF RESPONSIVENESS IN SACROILIAC JOINTS MRI OF PATIENTS WITH AXIAL SPONDYLOARTHRITIS: A PILOT STUDY.

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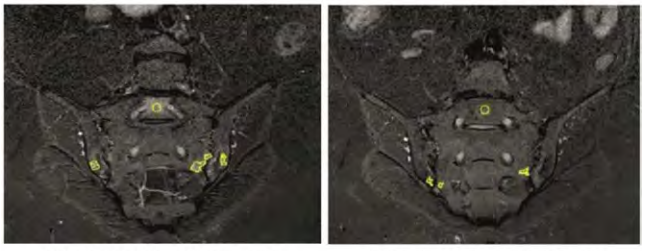
Background: The presence of inflammatory signals in sacroiliac joints (SIJ), using MRI, is used for early diagnosis of axial spondyloarthritis (axSpA)[1]. Some studies also demonstrate that this inflammation can be suppressed quite dramatically by TNF-α blockers. Different scoring methods to quantify inflammatory changes in SIJ using MRI have been defined and validated: SPARCC, Leeds, Berlin, and ASSpiMRI-a. However, its use is complex and subjective. Recently Zarco et al[2] developed a method to measure bone marrow edema (BME) in MRI images from SIJ. This method, in a semiautomatic procedure, allows to measure the area affected by inflammation and the signal intensity to produce an index: the SCAISS. A simplified version, the s-SCAISS, using only a semi-coronal slide, has been proposed with good validity and reliability results.

Objectives: To assess responsiveness of inflammation in SIJ of axSpA patients, treated with TNF-α inhibitors, using a novel score method: the s-SCAISS.

Methods: Two rheumatologists independently quantified SIJ images from axSpA patients by three methods (s-SCAISS, SPARCC and Berlin) on a single semi-coronal MRI slide (STIR). Patients were assessed before TNF-α therapy (PRE) and 3 months later (POST). Spearman correlations was used to analyze relationship between variables, Wilcoxon signed-rank test for significant differences and Cohen's d for calculating the effect size of improvement. Figure shows MRI images of a patient before and after treatment.

Results: 9 axSpA patients were recruited from the COSPAR cohort (44% female, age 47±13 years, disease duration 18±14 years, BMI 29±4). Results PRE and POST are shown in Table: mean values (sd), statistical significance (NS, not significant; *, p<0.05; **, p<0.01), and Effect Size. In the first rows, different scoring system for MRI inflammation appears: Area analyzed by s-SCAISS, s-SCAISS, Berlin and SPARCC (using only a semi-coronal slide). Activity and functional indexes were lower with significant differences and a large effect size. Correlations of s-SCAISS with Berlin (rho=0.78;p<0.05) and SPARCC (rho=0.96;p<0.001) were good; with clinical disease activity outcomes were poor, except with BASDAS (rho=0.70;p<0.05). The best correlation according improvements appeared comparing reduction of ASDAS with reduction of s-SCAISS (rho=0.57) but this difference was not significant. Although improvements in BASMI was not significant, a good correlation was found between improvement in s-SCAISS and BASMI (rho=-0.72;p<0.05).

	PRE	POST	Sign	E.S.
Area	71.33 (66.71)	20.89 (39.02)	**	0.86-Large
s-SCAISS	118.67 (114.6)	27.78 (51.09)	**	0.98-Large
BERLIN	2.33 (1.66)	0.67 (1.12)	**	1.14-Large
SPARCC	3.11 (2.26)	0.78 (1.39)	**	1.18-Large
CRP	13.1 (9.4)	4.1 (3.2)	**	0.90-Large
BASDAI	6.5 (1.7)	4.4 (2.7)	*	0.84-Large
BASFI	6.3 (2.6)	4.1 (3.4)	*	0.69-Medium
ASDAS	3.6 (1.0)	2.3 (1.2)	**	1.15-Large
BASDAS	3.7 (1.1)	2.6 (1.3)	*	0.96-Large
BASMI	3.6 (1.5)	3.3 (1.3)	NS	



PRE: Area= 178; s-SCAISS=234 Berlin = 4 Sparc = 7

POST: Area= 72; s-SCAISS=100 Berlin = 3 Sparc = 2

Conclusion: Different methods exist for quantifying inflammation in MRI images of SIJ in axSpA patients. According to our preliminary results, all of them had significant improvements in axSpA patients treated with anti tnf-α. The s-SCAISS index show good responsiveness, with similar features to validated indexes, but with an accuracy assessment of the BME area.

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Disclosure of Interests: Cristina Garrido-González: None declared, María del Carmen Castro Villegas: None declared, MLourdes Ladehesa Pineda: None declared, Juan L. Garrido-Castro: None declared, Rafaela Ortega Castro: None declared, Cristina Gonzalez-Navas: None declared, Pedro Zarco-Montejo Speakers bureau: Abbvie, MSD, Novartis, Pfizer., RAQUEL ALMODOVAR Speakers bureau: Abbvie, Celgene, Janssen, Lilly, Novartis, Pfizer.
, Angel Bueno: None declared, Luis Miguel Molinero: None declared, Eduardo Collantes Estevez Grant/research support from: ROCHE and Pfizer, Speakers bureau: ROCHE, Lilly, Bristol and Celgene

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SAT0374 ONSET OF AXIAL SPONDYLOARTHRITIS REPERCUSSIONS ON PATIENTS' SOCIAL AND FAMILY LIFE: RESULTS FROM THE EUROPEAN MAP OF AXIAL SPONDYLOARTHRITIS (EMAS)

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La Paz, Madrid, Spain; [4]*Cardiff University, Cardiff, United Kingdom*; [5]*Axial Spondyloarthritis International Federation (ASIF), London, Spain*; [6]*Cyprus League Against Rheumatism, Nicosia, Cyprus*; [7]*Novartis Pharma AG, Basel, Switzerland*; [8]*Charité – Universitätsmedizin Berlin, Berlin, Germany*; [9]*German Rheumatism Research Centre, Berlin, Germany*

Background: Axial Spondyloarthritis (axSpA) is associated with a high degree of functional limitation in daily life activities. However, few studies have evaluated the social and family burden from the patient's perspective.
Objectives: To describe the impact of axSpA on social and family life since disease onset, and the associated PROs.
Methods: Data from 2,846 unselected patients of the European Map of Axial Spondyloarthritis (EMAS) study through an online survey (2017-2018) across 13 European countries were analysed. The impact of axSpA on social and family life were assessed through four PROs: i) Impact on relationships with the spouse, family, friends, neighbours, and work colleagues since disease onset (5 point Likert scale; 1 "much better" – 5 "much worse"; ii) Frequency of social activities including outings to bars/restaurants, cinema/theatre/museums, practising sports, travel/excursions, and intimate relations since disease onset (5 point Likert scale; 1 "much more" – 5 "much less"); iii) Adaptations made to cope with axSpA since disease onset (yes/no question); iv) The degree of functional limitation in 18 daily activities (3 point Likert scale). Self-reported BASDAI (0-10), spinal stiffness (3-12), functional limitation (0-54), and psychological distress (GHQ-12) were analysed using Pearson's correlation comparing the impact on relationships and frequency of social activities since disease onset.
Results: Among 2,846 participants, mean age was 43.9 years, 61.3% were female, 48.1% had a university degree. The greatest impact on relationships (sum of 'worse' and 'much worse') since disease onset were those with work-colleagues (44.5%), friends (35.6%), and spouse (30.4%). Sport was the activity they reduced the most since disease onset (64.2%), followed by travel/excursions (57.3%) and intimate relationships (56.4%) (Fig. 1). 55.5% had purchased comfortable shoes (N = 2748) and 43.9% had made adaptations to their workplace (N = 2651). For those who reported their level of functional limitation in daily activities, the greatest limitations were in physical exercise (85.5%), cleaning the house (84.4%) and using stairs (79.2%) (Fig. 2). In the correlation analysis, BASDAI, spinal stiffness, functional limitation, GHQ-12 were associated with a worsening in all of relationships and social activities ($p < 0.001$) (Table 1).

Table 1. Pearson's correlation between social and family life changes and PROs

Relationships: 1 much better – 5 much worse	BASDAI	Spinal Stiffness	Functional Limitation	GHQ-12
Spouse	0.157*	0.130*	0.167*	0.258*
Family	0.162*	0.133*	0.138*	0.206*
Friends	0.211*	0.173*	0.180*	0.282*
Neighbours	0.210*	0.165*	0.112*	0.229*
Work colleagues	0.229*	0.153*	0.213*	0.334*
Frequency activities: 1 much more – 5 much less				
Bars / restaurants	0.261*	0.246*	0.314*	0.316*
Cinemas / theatres / museums	0.291*	0.243*	0.299*	0.338*
Do sports	0.271*	0.213*	0.240*	0.242*
Travel / excursions	0.308*	0.218*	0.307*	0.362*
Intimate relations	0.284*	0.254*	0.288*	0.321*

*p <0.001

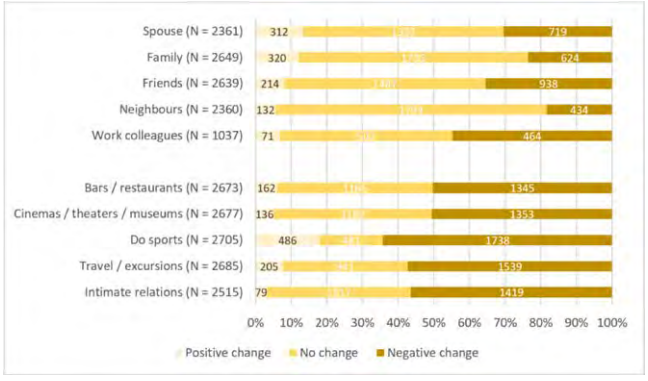


Figure 1. Reported social and family live changes since disease outset

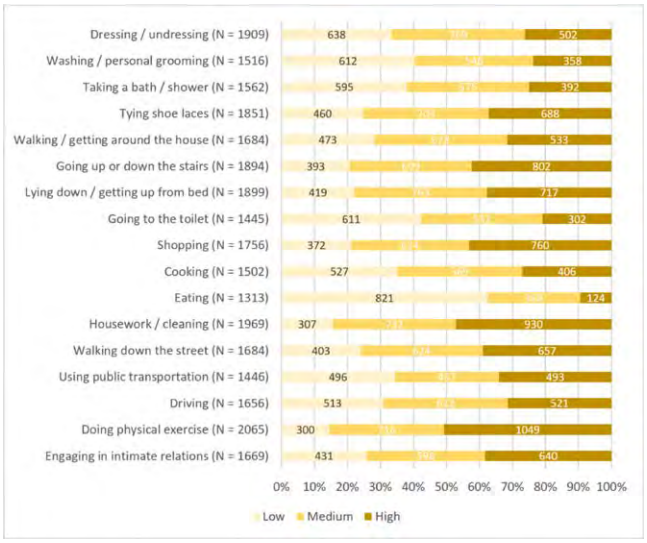


Figure 2. Reported level of functional limitation in daily live activities

Conclusion: For most participants the onset of axSpA marked the worsening of personal relationships in different areas, as well as the reduction of social, leisure, and entertainment activities.
Acknowledgments: Funded by Novartis Pharma AG
Disclosure of Interests: Marco Garrido-Cumbrera: None declared, Victoria Navarro-Compán Consultant of: Abbvie, Lilly, Novartis, Pfizer, UCB, Speakers bureau: AbbVie, MSD, Lilly, Novartis, Pfizer, UCB, Christine Bundy Grant/research support from: Has received unrelated honoraria from Abbvie, Celgene, Janssen, Lilly, Novartis, and Pfizer., Raj Mahapatra: None declared, Souzi Makri: None declared, Sergio Sanz-Gómez: None declared, Laura Christen: None declared, Carlos Jesús Delgado-Domínguez: None declared, Denis Poddubnyy Grant/research support from: AbbVie, MSD, Novartis, and Pfizer, Consultant of: AbbVie, Bristol-Myers Squibb, Eli Lilly, MSD, Novartis, Pfizer, Roche, UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, MSD, Novartis, Pfizer, Roche, UCB
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SAT0375

DETERMINANTS OF PATIENT'S GLOBAL ASSESSMENT OF WELL-BEING IN EARLY AXIAL SPONDYLOARTHRITIS; 5-YEAR LONGITUDINAL DATA FROM THE DESIR COHORT.

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Background: A framework has been proposed to explain which disease outcomes impact quality of life or well-being in patients with axSpA; this was based on cross-sectional data and patients with radiographic axSpA.[1]
Objectives: To investigate the determinants of patient's well-being over time, and the influence of contextual factors on these relationships in patients with early axSpA.
Methods: Five-year data from DESIR, a cohort of early axSpA, were analysed. Clinical data were collected every 6 months up to 2 years and annually thereafter. X-rays and MRI of the spine and SIJ were performed at baseline, 2, and 5 years. The outcome was BAS-G, the patient's global assessment of the disease impact on well-being. Generalized estimating equations (GEE) were used to test the relationship between potential explanatory variables from 5 domains (disease activity, physical function, spinal mobility, structural damage, spinal and SIJ inflammation) and BAS-G over 5 years. Longitudinal relationships were analysed using an autoregressive GEE model. Contextual factors (patient's educational level, gender and age) were tested as potential effect modifiers or confounders.
Results: A total of 708 patients were included, mean age 33.7 (SD 8.6) years, 46% male, 41% lower educated. Higher scores of the individual questions of BASDAI on fatigue (Q1) (β [95% CI]: 0.17 [0.13-0.22]), back pain (Q2) (0.51 [0.46-0.56]), peripheral joint pain (Q3) (0.08 [0.04-0.12]) and severity of morning stiffness (Q5) (0.08 [0.03-0.13]), and BASFI (0.14 [0.08-0.19]) were independently associated with a higher BAS-G over time (Table 1). In the autoregressive GEE model, all variables except for the BASDAI Q5 showed true longitudinal

associations with BAS-G. Age, gender and educational level were neither effect modifiers nor confounders.

Table 1. Factors associated with BAS-G over time.

	Multivariable GEE model	Multivariable autoregressive GEE model §
	Coefficient (95% CI)	Coefficient (95% CI)
BASDAI Q1 (fatigue, 0-10)	**0.17 (0.13 to 0.22)***	**0.15 (0.10 to 0.20)***
BASDAI Q2 (back pain, 0-10)	**0.51 (0.46 to 0.56)***	**0.54 (0.47 to 0.60)***
BASDAI Q3 (peripheral joint pain, 0-10)	**0.08 (0.04 to 0.12)***	**0.13 (0.08 to 0.19)***
BASDAI Q4 (enthesitis, 0-10)	0.03 (-0.01 to 0.07)	0.02 (-0.04 to 0.08)
BASDAI Q5 (severity of morning stiffness, 0-10)	**0.08 (0.03 to 0.13)***	0.06 (-0.01 to 0.13)
BASDAI Q6 (duration of morning stiffness, 0-10)	0.03 (-0.01 to 0.07)	0.05 (-0.01 to 0.11)
SJC28 (0-28)	0.01 (-0.11 to 0.13)	0.10 (-0.11 to 0.31)
TJC53 (0-159) ¶	-0.01 (-0.02 to 0.01)	-0.01 (-0.03 to 0.01)
MASES (0-39)	0.00 (-0.02 to 0.02)	-0.00 (-0.03 to 0.02)
CRP (mg/L)	0.01 (-0.00 to 0.01)	0.00 (-0.01 to 0.01)
Any EAM (presence vs absence)	-0.05 (-0.21 to 0.11)	-0.09 (-0.28 to 0.10)
BASFI (0-10)	**0.14 (0.08 to 0.19)***	**0.08 (0.00 to 0.16)***
BASMI linear (0-10)	-0.07 (-0.16 to 0.02)	-0.10 (-0.22 to 0.02)
mNY grading (0-8)	0.01 (-0.03 to 0.06)	**0.06 (0.01 to 0.12)***
mSASSS (0-72)	-0.01 (-0.04 to 0.02)	0.00 (-0.03 to 0.04)

* p-value < 0.05

¶ Each joint graded 0-3

§ **Adjusted for the outcome (i.e. BAS-G) one year before, in order to disentangle the cross-sectional and longitudinal relationships between outcomes and allow the interpretation of a longitudinal relationship**

Conclusion: A higher level of back pain was associated with a worsening of the patient's well-being in early axSpA, as were, though to a lesser extent, higher levels of fatigue, morning stiffness, peripheral joint pain and physical disability. Contextual factors like age, gender and educational level did not have an impact on these relationships. Thus, the previously proposed framework of disease outcomes also applies to patients with early axSpA and to outcomes over time.

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Disclosure of Interests: Fumio Hirano Paid instructor for: Ono pharmaceuticals, Astellas Pharma Inc, Sumitomo Dainippon Pharma, Chugai Pharmaceutical Co., Ltd., Désirée van der Heijde Consultant of: AbbVie, Amgen, Astellas, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Cyxone, Daiichi, Eisai, Eli-Lilly, Galapagos, Gilead Sciences, Inc., Glaxo-Smith-Kline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB Pharma; Director of Imaging Rheumatology BV, Floris A. van Gaalen: None declared, Robert B.M. Landewé Consultant of: AbbVie; AstraZeneca; Bristol-Myers Squibb; Eli Lilly & Co.; Galapagos NV; Novartis; Pfizer; UCB Pharma, Cecile Gaujoux-Viala: None declared, Sofia Ramiro Grant/research support from: MSD, Consultant of: Abbvie, Lilly, Novartis, Sanofi Genzyme, Speakers bureau: Lilly, MSD, Novartis

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SAT0376 DOES SUPPRESSION OF IL-4 AND IL-13 LEAD TO THE DEVELOPMENT OF NEW ONSET SPONDYLOARTHRITIS IN SUSCEPTIBLE PATIENTS?

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Background: Enthesitis is a key feature of peripheral Spondyloarthritis (SpA). Several pro-inflammatory cytokines including Interleukin-17 and Interleukin-23 are found within the enthesis (1). Dupilumab is a recombinant human monoclonal antibody that inhibits signalling of Interleukin-4 and Interleukin-13, approved for use in patients with moderate- to –severe atopic eczema. Here we describe a cohort of patients with severe atopic eczema who have developed a new peripheral SpA/ enthesitis after receiving Dupilumab.

Objectives: To describe the clinical and imaging details of this cohort.

Methods: All patients in St John's Institute of Dermatology who exhibited new arthralgias on Dupilumab therapy were referred for assessment in Guy's Rheumatology Department. These patients had a focussed history, examination, ultrasound and/or MRI of affected joints and entheseal sites.

Results: To date we have seen 12 patients with a history of new inflammatory peripheral SpA type symptoms following onset of Dupilumab therapy. There were 7 males and 5 females all of whom have longstanding severe atopic Eczema. All patients had raised baseline IgE levels of mainly >10000. All patients exhibited a positive response to Dupilumab with a marked improvement in eczema as measured by the EASI score. All patients had normal inflammatory markers and negative immunological screening bloods. Musculoskeletal symptom onset was between 2 and 20 weeks after starting treatment. Typically, these patients had inflammatory symptoms affecting both the small joints and the entheseal sites. 2/12 patients developed inflammatory sounding spinal pain. 2/12 patients had ultrasound evidence of arthritis. 11/12 patients had radiological findings of enthesitis as seen on MRI or ultrasound (power doppler ultrasound signal). 9/12 patients were treated with non-steroidal anti-inflammatories with variable improvement.1 patient required no treatment and 1 patient received low dose prednisolone.

Conclusion: In our centre approximately 200 patients have received Dupilumab. These musculoskeletal findings have not been reported previously in clinical trials. We hypothesise that the profound inhibition of IL- 4/13 may allow an inflammatory response at the enthesis presenting with a peripheral SpA pattern. IL-4 has been shown to suppress delayed type hypersensitivity reactions (DTHRs) and psoriasis in both human and mice studies (2). These findings and the demonstratation that IL-23 transcription and secretion can be suppressed by IL-4 with resultant reduction in Th17 function (3) may be key factors as to why a SpA type response is seen in certain subjects.

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Disclosure of Interests: Catherine Hughes Speakers bureau: Lilly, Bina Menon Speakers bureau: Novartis, Richard Woolf: None declared, Zena Willsmore: None declared, Catherine Smith: None declared, Andrew Pink: None declared, L Bruce Kirkham Grant/research support from: Eli Lilly Novartis, Consultant of: Eli Lilly Gilead Janssen Novartis

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SAT0377 ASSESSMENT OF ANKYLOSING SPONDYLITIS ACTIVITY DURING PREGNANCY USING DIFFERENT ACTIVITY INDICES

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Background: Currently, there is no consensus on the effect of pregnancy on the activity of ankylosing spondylitis (AS). Moreover, in the absence of a pregnancy modified AS activity index, it remains unclear which of the commonly accepted tools can most adequately assesses AS activity during gestation.

Objectives: To assess the dynamics of AS activity during pregnancy, using Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) и Ankylosing Spondylitis Disease Activity Score CRP (ASDAS- CRP).

Methods: The study group included 36 pregnant women with confirmed AS (modified New York criteria, 1984). Patients' mean age was 31.6±4.8 years, mean age at AS onset was 21.8±10.9, and disease duration - 134.9±89.3 months. Activity was assessed using BASDAI and ASDAS-CRP at 10-11, 20-21, and 31-32 weeks of pregnancy. BASDAI at the time of conception was assessed retrospectively at the first visit.

Results: BASDAI values in the month of conception and in the trimesters of pregnancy were 2.3 ±1.9; 2.8 ±1.72 (p<0.05 compared to the month of conception); 3.2 ±1.9 and 3.3 ±2.1. Analyzed dynamics of individual BASDAI components is indicative of increasing fatigue from the month of conception (2 [1; 3,5]) and up to 10-11 weeks of pregnancy (5 [3; 7]; p<0.05); the statistical differences with month of conception remained in the II and III trimesters. In the II trimester a tendency to growing back pain (3 [2; 4]) and entheses pain (2 [0; 4]) as compared to the month of conception (2.5 [1; 4] and 1 [0; 2], respectively) was documented. There was an increase in the intensity and duration of morning stiffness in the III trimester (3.5 [1; 7] and 2.5 [1; 5], respectively) compared to the month of conception (1.5[0; 4] and (2 [0; 3], respectively; p<0.05).

ASDAS-CRP values by trimesters of pregnancy were as follows: 1.9 ±0.7; 2.3 ±0.9 and 2.2 ±0.8. There was a tendency to increasing CRP levels in the II (8.0 [2.1;9.6] mg/l) and III trimesters (7.9 [2.0;9.2] mg / l) compared to the I trimester (5.7 [1.6;6.2] mg/l).

Patients' distribution by grades of AS activity is presented in the Table.

Disease activity	BASDAI				ASDAS – CRP		
	month of conception	trimester 1	trimester 2	trimester 3	trimester 1	trimester 2	trimester 3
inactive/low	57,8%	33,3%	25,7%	35,3%	16,7%	14,3%	14,7%
mild	30,6%	36,1%	40%	26,5%	42,2%	28,6%	32,4%
high	11,1%	30,6%	31,4%	31,4%	33,3%	48,6%	41,2%
very high	5,6%	0	2,9%	2,9%	2,8%	8,9%	11,8%

When dividing patients into two groups depending on AS activity in the I trimester (group 1-low activity, group 2-moderate, high and very high activity), no significant change in the values of both BASDAI and ASDAS – CRP was identified in each group during pregnancy.

Conclusion: A tendency of increasing AS activity during the first half of pregnancy with no reverse until the end of gestation based on BASDAI and ASDAS – CRP values and CRP levels was found. There was a discrepancy in degree of activity assessed by the tools used: moderate and high disease activity was identified in greater number of AS patients based on ASDAS-CRP scores compared to BASDAI during the entire pregnancy. It is deemed necessary to continue research so that to identify the most adequate index for AS activity assessment during pregnancy.

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SAT0378 THE RELATIVE DIAGNOSTIC UTILITY OF INFLAMMATORY BACK PAIN CRITERIA IN AN INCEPTION COHORT OF PATIENTS WITH PSORIASIS, IRITIS, AND COLITIS PRESENTING WITH UNDIAGNOSED BACK PAIN

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Background: Clinicians rely on the elicitation of features of inflammatory back pain (IBP) for diagnosis of axial spondyloarthritis (axSpA) but the utility of IBP criteria in patients presenting with extra-articular features of axSpA remains unclear. Assessment of utility should include not only rheumatologist diagnosis as benchmark but imaging to address the circularity between elicitation of IBP and clinical diagnosis.

Objectives: To assess the diagnostic utility of all criteria for IBP in patients with psoriasis, iritis, or colitis and undiagnosed back pain using the rheumatologist diagnosis and imaging as benchmarks.

Methods: Consecutive patients (n=246) with undiagnosed back pain ≤45 years of age, ≥3 months, with any one of psoriasis (n=46), acute anterior uveitis (AAU) (n=73), or colitis (n=127) had diagnostic evaluation by a rheumatologist. Majority central reader assessment of MRI indicative of axSpA and diagnosis by the rheumatologist were external standards for testing the utility of these IBP criteria: ASAS, Berlin, Calin, rheumatologist global for IBP >5 (0-10 scale).

Results: AxSpA was diagnosed in 44.4%, 61.6%, and 41.8% of patients with psoriasis, iritis, and IBD, respectively. Diagnostic utility for all IBP criteria was comparably poor (Table 1). MRI was indicative of axSpA in 21.2%, 43.5%, and 19.7% of patients with psoriasis, iritis, and IBD. The utility of the IBP criteria was even worse using MRI as the external reference (Table 2), especially in patients with psoriasis. Only 14% of psoriasis patients with a positive MRI reported "improvement with exercise but not rest" as compared to 70% and 62% of patients with iritis and IBD, respectively.

Table 1. Rheumatologist diagnosis as external reference.

	Sensitivity	Specificity	LR+	LR-
Psoriasis				
ASAS IBP	65.00%	52.00%	1.35	0.67
Berlin IBP	80.00%	36.00%	1.25	0.56
Calin IBP	80.00%	28.00%	1.11	0.71
All 3 criteria sets	60.00%	56.00%	1.36	0.71
IBP global >5	85.00%	36.00%	1.33	0.42
AAU				
ASAS IBP	84.44%	42.86%	1.48	0.36
Berlin IBP	80.00%	57.14%	1.87	0.35
Calin IBP	93.33%	17.86%	1.14	0.37
All 3 criteria sets	77.78%	60.71%	1.98	0.37
IBP global >5	86.67%	57.14%	2.02	0.23
IBD				
ASAS IBP	78.43%	45.07%	1.43	0.48
Berlin IBP	82.35%	52.11%	1.72	0.34
Calin IBP	84.31%	19.72%	1.05	0.80
All 3 criteria sets	70.59%	57.75%	1.67	0.51
IBP global >5	80.39%	66.20%	2.38	0.30

Table 2. Central assessment that MRI is indicative of axSpA as external reference.

	Sensitivity	Specificity	LR+	LR-
Psoriasis				
ASAS IBP	28.57%	38.46%	0.46	1.86
Berlin IBP	42.86%	15.38%	0.51	3.71
Calin IBP	71.43%	23.08%	0.93	1.24
All 3 criteria sets	14.29%	42.31%	0.25	2.03
IBP global >5	85.71%	23.08%	1.11	0.62
AAU				
ASAS IBP	75.00%	26.92%	1.03	0.93
Berlin IBP	70.00%	38.46%	1.14	0.78
Calin IBP	90.00%	15.38%	1.06	0.65
All 3 criteria sets	65.00%	38.46%	1.06	0.91
IBP global >5	75.00%	38.46%	1.22	0.65
IBD				
ASAS IBP	92.31%	37.74%	1.48	0.20
Berlin IBP	76.92%	39.62%	1.27	0.58
Calin IBP	92.31%	16.98%	1.11	0.45
All 3 criteria sets	76.92%	45.28%	1.41	0.51
IBP global >5	92.31%	47.17%	1.75	0.16

Conclusion: All IBP criteria have poor diagnostic utility for diagnosis of axSpA, especially in patients with psoriasis. This reinforces the desirability of less subjective assessment tools, especially imaging.

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SAT0379 C-REACTIVE PROTEIN TO ALBUMIN RATIO IS ASSOCIATED WITH DISEASE ACTIVITY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: C-reactive protein to albumin ratio (CAR) has emerged as a significant biomarker to evaluate and predict systemic inflammation[1]. However, the role of CAR in patients with axial spondyloarthritis (axSpA) remains unknown.

Objectives: The aim of this study was to investigate the relationship between CAR and disease activity of axSpA.

Methods: A total of 241 patients and 61 healthy controls from Guangdong Second Provincial General Hospital from December 2015 to August 2019 were retrospectively recruited in this study. Patients were divided into two groups, with 176 patients in remission group (BASDAI<4) and 65 patients in active group (BASDAI≥4). Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), albumin (ALB), CAR, neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR) and monocyte-lymphocyte ratio (MLR) were detected. The correlations between CAR, NLR, PLR, MLR and disease activity were analyzed by the Spearman's correlations analysis. Receiver

operation characteristic (ROC) curves were performed to evaluate the discriminative utility of these parameters for disease activity of axSpA. Furthermore, the evaluation of the risk factors of axSpA was conducted using binary logistic regression analysis.

Results: CAR, ESR, CRP, NLR, PLR and MLR in axSpA patients were significantly higher than those in the control group (p<0.05 for each), while ALB was significantly lower (p<0.001). Similarly, CAR in remission group was higher than that in control group (p<0.001) and was lower than that in active group (p<0.001). Besides, there were significantly positive correlations between CAR and ESR (r=0.702, P<0.001), CRP (r=0.996, P<0.001), BASDAI (r=0.329, p<0.001) and BASFI (r=0.328, P<0.001). Furthermore, ROC suggested that the area under the curve (AUC) of CAR was 0.701, which was the highest. The optimal cutoff point of CAR was 0.3644, with sensitivity and specificity of 58.5% and 79.0%. Logistic analysis results revealed that elevated CAR and MLR were independent risk factors for axSpA (EXP (B) =15.546, 95%CI: 5.898-40.979, P<0.001; EXP (B) =2.206, 95%CI: 1.077-4.519, P=0.031, respectively).

Conclusion: CAR was increased in axSpA patients especially in active group, and significantly correlated with disease activity. CAR may serve as a novel inflammatory marker of monitoring disease activity in patients with axSpA.

References:

[1] He, Y., et al., Correlation between albumin to fibrinogen ratio, C-reactive protein to albumin ratio and Th17 cells in patients with rheumatoid arthritis. Clin Chim Acta, 2020. 500: p. 149-154.

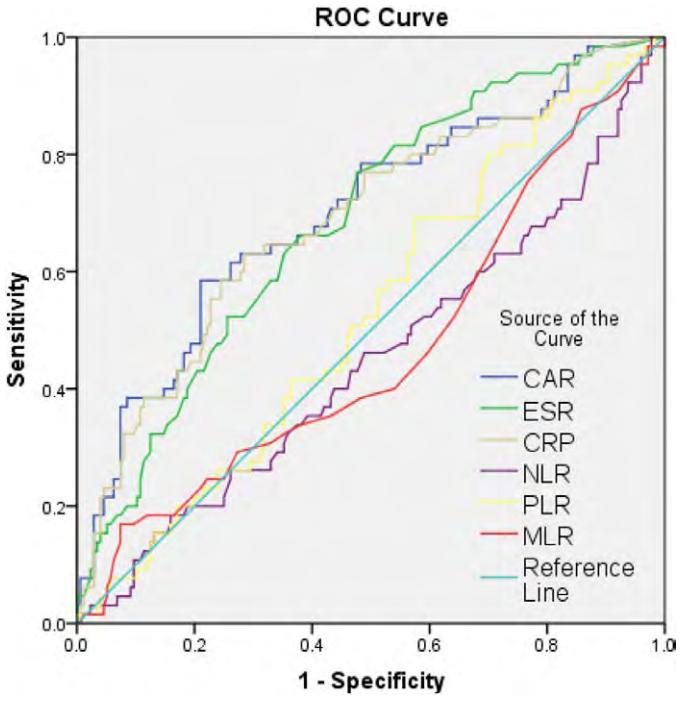


Fig 1. ROC curve analysis of the discriminative values of the parameters for disease activity of axSpA

Table 1. Discriminative values of the parameters for disease activity of axSpA

	AUC	95% CI	Optimal cutoff point	Specificity	Sensitivity
CAR	0.701	0.623-0.778	0.3644	79.0%	58.5%
NLR	0.450	0.365-0.534	3.165	84.1%	18.5%
PLR	0.528	0.448-0.608	127.385	42.6%	69.2%
MLR	0.468	0.384-0.553	0.385	92.6%	16.9%
ESR	0.685	0.612-0.758	15.5	52.3%	76.9%
CRP	0.691	0.614-0.769	10.85	71.6%	63.1%

CAR, C-reactive protein to albumin ratio; NLR, neutrophil-lymphocyte ratio; PLR, platelet-lymphocyte ratio; MLR, monocyte-lymphocyte ratio; CRP, C reactive protein; ESR, erythrocyte sedimentation rate; AUC, areas under the ROC curve

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SAT0380 ENHANCING RHEUMATOLOGY REFERRALS AMONG INFLAMMATORY BOWEL DISEASE PATIENTS WITH SUSPECTED AXIAL SPONDYLOARTHRITIS

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Background: Axial spondyloarthritis (axSpA) is associated with inflammatory bowel disease (IBD). In IBD patients, the clinical probability of axSpA increases in those with chronic back pain (CBP) whose symptoms started before the age of forty-five years old. In practice, this should trigger a rheumatology review especially if accompanied by other symptoms suspicious of inflammatory disease. However, in any health system, the goal of identifying all possible cases need to be balanced with the practical realisation of the finite resources available.

Objectives: The study aimed to define the clinical characteristics of a subgroup of IBD patients who are routinely managed in secondary care who have an increased clinical probability for axSpA. Identification of these characteristics may help improve the quality and specificity of referrals to Rheumatology from Gastroenterology clinics.

Methods: An analytical cross-sectional study was undertaken. Consecutive IBD patients attending routine Gastroenterology clinics were sent a modified validated back pain questionnaire. The questionnaire included the presence or absence of a previous diagnosis of axSpA; components of validated inflammatory back pain criteria; diagrams to indicate the location of back pain and other musculoskeletal pain; personal and family history of known axSpA manifestations; and details of their IBD course, activity and treatment.

IBD patients, with back pain duration > 3 months with onset before 45 years were considered to have a medium diagnostic probability (MDP) for axSpA. MDP-positive IBD patients were compared with MDP-negative IBD patients and logistic regression was used to model the association with clinical features.

Results: Four hundred and seventy consecutive IBD patients (mean age 54 years; 46% male) were surveyed. Two hundred and nine patients (59%) replied, of whom 191 patients (69%) consented to participate. One hundred and seventy-three (91%) of those who consented had a valid completed questionnaire and were included for data analysis. Of these, 74% had Ulcerative Colitis and 26% had Crohn's disease. Their mean age was 58 years, 39% male. Mean age at IBD diagnosis was 39 years, mean IBD disease duration 19 yrs. CBP (back pain greater than three months) was reported by 76%. Inflammatory back pain fulfilling Calin, Berlin, ASAS criteria was seen in 23%, 29%, and 15% respectively. In addition, 80% reported peripheral musculoskeletal pain. Self-reported personal history of enthesitis, reactive arthritis (ReA), acute anterior uveitis (AAU), skin psoriasis (PSO) and dactylitis were 50%, 30%, 24%, 15% and 0% respectively. Self-reported family history of IBD, ReA, PSO, axSpA and AAU were 60%, 36%, 22%, 11%, and 1% respectively. Ninety-one (53%) patients were MDP-positive and 82 (47%) patients were MDP-negative. The clinical characteristics associated with MDP (adjusted for age at invitation) were: the presence of inflammatory back pain using ASAS criteria [OR 8.84 (1.61,48.67); p=0.01], longer interval between symptom onset and gastroenterologist diagnosis of IBD [OR 1.09 (1.03,1.16); p=0.005], and use of rectal topical 5-aminosalicylic acid [OR 3.27 (1.11,9.68); p=0.03].

Conclusion: Chronic back pain and peripheral musculoskeletal pain are common in a secondary care IBD population. In IBD patients, with back pain duration > 3 months and onset before 45 years, the presence of inflammatory back pain, longer diagnostic delay of IBD and the use of rectal topical 5-aminosalicylic acid were associated with a higher clinical probability of axSpA. The identification of these clinical features may not only improve the quality and specificity of Rheumatology referrals from Gastroenterology in this subgroup of patients but also lends real world evidence to current ASAS-endorsed recommendations for early referral of patients with a suspicion of axial spondyloarthritis.

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SAT0381 UNDERSTANDING JOINT REPLACEMENT SURGERY IN AXIAL SPONDYLOARTHROPATHY

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Background: Axial spondyloarthropathy(axSpA) is a form of inflammatory arthritis that primarily affects the axial skeleton and sacroiliac joint, but can be associated

with a peripheral arthritis. Rapid advances in the field of axSpA has led to faster detection, diagnosis and treatment of this disease. This improved management has led to improved level of function and quality of life for patients, despite this a proportion of patients are still requiring joint replacement surgery. The Ankylosing Spondylitis Registry of Ireland (ASRI) is a source of epidemiological data on patients with axSpA in Ireland. Given the large size of the ASRI to date, this is a prime opportunity to analyze patients with axSpA requiring joint replacement surgery.

Objectives: Detailed analysis of a large cohort of patients with axSpA with a focus on those who underwent joint replacement to determine trends in disease and baseline demographics.

Methods: The patient population registered in the ASRI was analysed using IBM SPSS version 26. Analysis was performed by comparing patients who underwent joint replacement surgery to the rest of the ASRI cohort. Mean age, disease duration, delay to diagnosis and scores of disease activity (BASDAI, BASFI, HAQ, ASQoL and BASMI) were compared between these two groups. Differences between the groups was tested for significance using an independent two tailed t-test. Further analysis on gender, HLA-B27 status, co-morbidities and medication exposure was done using a chi-squared test for independence. A p value of less than 0.05 was deemed significant.

Results: At present 860 patients are currently enrolled in the ASRI with 76.6% (659) males and 23.4% (201) females. Average age of patients is 45.8 years, mean disease duration of 19.4 years with 95.5% (821) of patients listed as Caucasian. Mean scores were BASDAI 4.02, BASFI 3.7, BASMI4.02, HAQ 0.55, and ASQoL of 6.51. In total 33 (3.8%) of patients underwent joint replacement surgery. These patients were noted to be significantly older than the rest of the rest of the cohort (55.3 years old vs 45.1, p<0.01), with a longer disease duration (31.6 years vs 18.3, p<0.01) and higher rates of HLA-B27 positivity (94.7% vs 80.2%, p<0.01). No significant differences were noted between gender(table 1). No significant difference was found between medication exposure rates, although the joint replacement population did have higher rates of NSAID, sDMARD and biologic therapy usage than the rest of the population although this did not reach significance. These patients also scored worse in all measures of disease activity, although this only reached significance in the BASFI (5.67 vs 3.64, p<0.01), HAQ (0.9 vs 0.54, p<0.01) and the BASMI (6.07 vs 3.94, p<0.01).

Table 1.

	Joint replacement (n=33)	No Joint Replacement (n=827)	*p value*
Age	55.3	45.1	**<0.01**
Disease duration	31.6	18.31	**<0.01**
Delay to dx	6.97	7.97	0.51
HLA-B27+	94.7% (18)	71.9% (491)	**<0.01**
Males	78.8% (26)	64.7% (535)	0.76
Females	21.2% (7)	19.3% (160)	0.76
Mean Scores			
BASDAI	4.91	4.06	0.06
BASFI	5.67	3.64	**<0.01**
HAQ	0.9	0.54	**<0.01**
ASQoL	7.42	6.67	0.45
BASMI	6.07	3.94	**<0.01**
Medications			
NSAIDs	51.5% (17)	47% (389)	0.21
Bio tx	72.7% (24)	57.2% (473)	0.9
DMARDs	33.3% (11)	15.7% (130)	0.1

Conclusion: Patients requiring joint replacement surgery, although few in number, represent a cohort with significantly impaired function and quality of life. This is likely due to the fact that these patients were older with more established disease. It is therefore not surprising that this cohort had significantly worse spinal mobility. As registries continues to develop, it will be interesting to see if rates of joint replacement surgery will decline with increased use of biologic therapy at an earlier stage of disease. This will help to differentiate patients requiring joint replacement surgery due to underlying inflammatory arthritis and those with osteoarthritis.

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SAT0382

THE SAME BUT DIFFERENT? ANALYSIS OF A COHORT OF PATIENTS WITH LATE ONSET ANKYLOSING SPONDYLITIS

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Background: Ankylosing spondylitis(AS) has long been described as presenting in the third decade of life with the onset rarely occurring over the age of 45 years old. Previous research has shown there are small numbers of patients being diagnosed with AS later in life. These studies have been limited to small numbers limiting the ability to detect patterns in disease. The Ankylosing Spondylitis Registry of Ireland (ASRI) is an epidemiological data source on patients with AS in Ireland. Large registries, such as this, are an opportunity to further study this subtype in large numbers with greater power to detect differences between late and typical onset.

Objectives: The purpose of this study was to examine late onset AS in a large, well characterized cohort.

Methods: Patient registered in ASRI were analysed on the basis of their age of symptom onset using IBM SPSS version 26. Patients were divided into two groups with an age over 45 years old at symptoms onset categorized at late onset. Mean BASMI, BASFI, BASDAI, HAQ, and ASQoL scores were compared between the two groups and tested for statistical significance using an independent two tailed t-test. Further analysis looking at differences in gender, HLA B27 status, sacroiliitis on MRI, medication use and extra-articular manifestations(EAMs) was also performed using a chi-squared test for independence.

Results: A total of 851 patients with AS were included in the analysis. Of these patients 659(77.4%) were males, with 192(22.6%) females, mean age of 45.8 years and mean disease duration of 19.4 years (means: ASQoL 6.52, HAQ 0.54, BASDAI 4.03, BASFI 3.7, BASMI 4.03). Patient population was made up of 797 patients(93.7%) categorized as typical onset, 54 patients(6.3%) categorized as late onset(table 1). Males had a higher rate of late onset AS than females, but this did not reach significance (6.8% vs 4.7%, p=0.19). Patients with late onset AS were noted to have higher BASFI (5.53 vs 3.58, p<0.01), HAQ (0.75 vs 0.53, p<0.01) and ASQoL scores (7.68 vs 6.44, p<0.01). Late onset patients also had lower rates of HLA-B27 positivity (76.5% vs 91.2%, p<0.01). No significant difference was detected in BASDAI or BASMI scores. No difference was detected between groups regarding rates EAMs. The late onset AS patients were noted to have lower rates of biologic therapy use (50% vs 72%, p<0.01). No significant difference was detected in rates of NSAID use.

Table 1.

	Onset < 45 years (n=797)	Late Onset (n=54)	*p* value
Males (n=659)	93.2% (614)	6.8% (83.3)	0.19
Females (n=192)	23% (183)	16.6% (9)	
HLA B27+ (n=580)	90.5% (554)	76.5% (26)	<0.01
Enthesitis (n=146)	16.9% (135)	20.4% (11)	0.45
Dactylitis (n=54)	6% (48)	11.1% (6)	0.21
Arthritis (n=256)	29.7% (237)	35.2% (19)	0.4
MRI Sacroiliitis (n=384)	45.3% (361)	42.6% (23)	0.69
Bilateral sacroiliits (n=668)	79% (628)	74% (40)	0.07
BASDAI	4.02	4.19	0.6
BASFI	3.58	5.53	<0.01
BASMI	3.96	4.97	0.12
HAQ	0.53	0.75	<0.01
ASQoL	6.44	7.68	<0.01
Uveitis	28.5% (227)	24.1% (13)	0.07
IBD	9.9% (79)	14.8% (8)	0.32
Psoriasis	16.4% (131)	18.5% (10)	0.54
Smokers (ever)	57.3% (457)	64.8% (35)	0.01
Alcohol consumption (ever)	82% (654)	75.9% (41)	0.53
Biologic tx	69.1% (551)	48.1% (26)	<0.01
NSAID tx	54.2% (432)	61.1% (33)	0.2

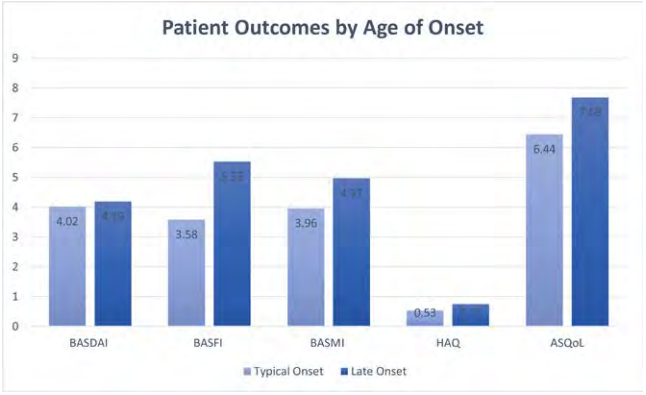


Figure 1.

Conclusion: This analysis shows that late onset AS does occur in up to 6.3% of patients with AS. Patients with late onset disease were noted to have similar patterns of disease, EAMs and radiological findings consistent with current

classification criteria for AS. Less patients with late onset disease were HLA-B27 positive, the reason for this is unknow. These patients had worse functional outcomes, which could reflect the older age of symptom onset. It is notable that patients with late onset AS are being treated with less biologic agents, and have a slightly higher rate of NSAID usage. Additional registry studies into this subgroup would help to understand these variations in medication usage and prescribing practices.

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SAT0383 ENHANCED PERFORMANCE OF THE ASAS CLASSIFICATION CRITERIA BY DELETION OF NON-DISCRIMINATORY CLINICAL ITEMS: DATA FROM THE SCREENING IN AXIAL SPONDYLOARTHRITIS IN PSORIASIS, IRITIS, AND COLITIS COHORT

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Background: The ASAS classification criteria for axial spondyloarthritis (axSpA) have overall sensitivity/specificity of 82.9%/84.4% but component imaging and clinical arms differ in performance (66.2%/97.3% and 56.6%/83.3%, respectively)[1].
Objectives: We aimed to demonstrate that a data-driven elimination of SpA clinical features that were non-discriminatory in comparisons of patients diagnosed with and without axSpA in a prospective cohort of patients with undiagnosed back pain could enhance the performance of the criteria.
Methods: We used data from the prospective multicenter Screening for Axial Spondyloarthritis in Psoriasis, Iritis, and Colitis (SASPIC) Study. Consecutive patients ≤45 years of age with ≥3 months undiagnosed back pain with any one of psoriasis, AAU, or colitis undergo routine diagnostic evaluation by a rheumatologist for axial SpA, including imaging assessed by central readers. Univariable and multivariable logistic regression analysis was performed to determine which clinical SpA features were/were not discriminatory for the final diagnosis of axSpA. We then compared the sensitivity and specificity of the ASAS criteria with and without these features.
Results: A total of 246 patients were recruited, 47.6% being diagnosed with axSpA (61.5% male, age 33.7 years, symptom duration 7.6 years, B27 positive 52.1%). The following clinical SpA features were non-discriminatory between axSpA/not axSpA: NSAID response, family history of SpA, heel enthesitis, peripheral arthritis, dactylitis. Specificity of the clinical arm and the overall criteria increased from 82.2% to 86.8% without impacting sensitivity. This effect was particularly noteworthy in patients with lower degree of symptomatology (back pain severity <5/10, specificity increases from 76.7% to 90.7%), short symptom duration (<5 years, specificity increases from 78% to 84.7%), and in females (specificity increases from 80.6% to 86.1%).

Patient Category	Number	ASAS criteria		Imaging arm		Clinical arm	
		Sen	Spec	Sen	Spec	Sens	Spec
All patients	246	65	82.2	36.8	97.7	50.4	82.2
High confidence in diagnosis	190	73.8	84.5	47.5	98.2	56.3	84.5
Patients with back pain ≥5/10	165	63.3	84.9	34.2	98.8	51.9	84.9
Patients with back pain <5	81	68.4	76.7	42.1	95.3	47.4	76.7
Patients with symptom duration ≥5 years	103	71.2	85.7	35.6	97.1	56.2	85.7
Patients with symptom duration <5 years	143	54.5	78	38.6	98.3	40.9	78
Males	129	68.1	84.2	47.2	98.2	48.6	84.2
Females	117	60	80.6	20	97.2	53.3	80.6
After deletion of 'NSAID response', 'Family Hx SpA', 'heel enthesitis', 'peripheral arthritis', 'dactylitis' SpA features							
All patients	246	65	86.8	36.8	97.7	50.4	86.8
High confidence in diagnosis	190	73.8	87.3	47.5	98.2	56.3	87.3
Patients with back pain ≥5/10	165	63.3	84.9	34.2	98.8	51.9	84.9
Patients with back pain <5	81	68.4	90.7	42.1	95.3	47.4	90.7
Patients with symptom duration ≥5 years	103	71.2	88.6	35.6	97.1	56.2	88.6
Patients with symptom duration <5 years	143	54.5	84.7	38.6	98.3	40.9	84.7
Males	129	68.1	87.7	47.2	98.2	48.6	87.7
Females	117	60	86.1	20	97.2	53.3	86.1

Conclusion: In a prospective cohort with a high pre-test probability of axSpA certain clinical SpA features were not helpful in discriminating a diagnosis of SpA from not-SpA. Deletion of these features from the list of SpA features used in the ASAS classification criteria enhanced the performance of the criteria, especially in female patients and those with early disease.

References:
[1] Rudwaleit et al. Ann Rheum Dis 2009;68: 777-83

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SAT0384 REPLACEMENT OF RADIOGRAPHIC SACROILITIS BY MRI STRUCTURAL LESIONS: WHAT IS THE IMPACT ON CLASSIFICATION OF AXIAL SPONDYLOARTHRITIS IN THE ASAS CLASSIFICATION COHORT?

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Background: Classification of axial spondyloarthritis (axSpA) is based on either an imaging or clinical arm. Radiographic or MRI evidence of sacroiliitis can be applied for the imaging arm. However, it is well-established that reliability and sensitivity of radiographic sacroiliitis is inadequate.
Objectives: To assess the impact of replacing radiographic sacroiliitis with MRI structural lesions (MRI-S) typical of axSpA on the number of patients classified as having axSpA in patients with undiagnosed back pain recruited to the ASAS Classification Cohort (ASAS-CC).
Methods: MRI images of the sacroiliac joint (SIJ) were available from 217 cases in the ASAS-CC, which also had clinical, laboratory, and radiographic data. Seven central readers from the ASAS-MRI group recorded MRI lesions in an eCRF that included active (MRI-A) and structural (MRI-S) lesions typical of axSpA. MRI-A was deemed to be present according to majority agreement (≥4/7) of central readers. MRI-S was deemed to be present according to the majority (majority reader MRI-S) and also according to at least 2 central readers (≥2-reader MRI-S). We calculated the number of patients that were classified differently after replacement of radiographs by MRI-S for overall fulfillment of the ASAS criteria and for the imaging arm.
Results: In total, 119 (54.8%) cases fulfilled the axSpA criteria based on local reading of radiographic sacroiliitis and central reading of active inflammation on MRI. This changed to 125 (57.6%) and 118 (54.4%) of cases after replacement of radiographic sacroiliitis by ≥2-reader and majority reader MRI-S, respectively (Table). A total of 13 (6.0%) and 7 (3.2%) cases who were classified as not having axSpA were re-classified as having axSpA after replacing radiographic sacroiliitis with ≥2-reader and majority reader MRI-S, respectively. Conversely, 7 (3.2%) and 8 (3.7%) cases were re-classified as not having axSpA after substitution by ≥2-reader and majority reader MRI-S, respectively. When fulfillment of the imaging arm was the primary consideration (irrespective of the clinical arm), the number of patients reclassified from not axSpA to axSpA was 25 (11.5%) by ≥2-reader and 13 (6.0%) by majority reader MRI-S, while 8 (3.7%) and 11 (5.1%) were reclassified from axSpA to not axSpA.
Conclusion: The number of patients classified as having axSpA does not change substantially when MRI-S replaces radiographic sacroiliitis. However, it remains possible that MRI structural lesions can influence the final diagnosis, the gold standard for assessment of the performance of the ASAS criteria.

Impact of Replacement of Radiographic Sacroiliitis by MRI Structural Lesions on SpA Classification in cases with all clinical, radiographic, and central and local MRI inflammation data available (n=217)

MRI assessment used	SpA Classification=Yes N(%)	SpA Classification=No N(%)	Imaging Arm SpA Classification=Yes N(%)	Imaging Arm SpA Classification=No N(%)
Radiographic Sacroiliitis + Majority Central Reader MRI Inflammation Positive	119 (54.8%)	97 (44.7%)	83(38.2%)	134 (61.8%)
Replace Radiographic Sacroiliitis with ≥2 Central Reader MRI Structural Positive	125 (57.6%)	92 (42.4%)	100 (46.1%)	117 (53.9%)
Replace Radiographic Sacroiliitis with Majority Central Reader MRI Structural Positive	118 (54.4%)	99 (45.6%)	85 (39.2%)	132 (60.8%)

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SAT0385

CAN MISCLASSIFICATION BETWEEN SPONDYLOARTHRITIS (SPA) AND RHEUMATOID ARTHRITIS (RA) OCCUR? SPA-RELATED CLINICAL MANIFESTATIONS AMONG RA AND SPA PATIENTS - A SYSTEMATIC LITERATURE REVIEW

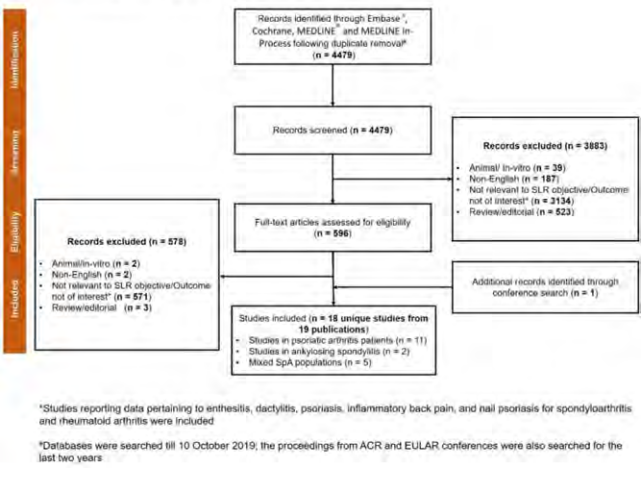
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Background: Delayed diagnosis is associated with worse outcomes and poor treatment responses in patients with SpA, including psoriatic arthritis (PsA) and axial spondyloarthritis.[1] Misclassification may be associated with this delay, as SpA and RA, especially seronegative RA, may present with similar manifestations such as joint pain, swelling, fatigue, and disability. Key features that typically distinguish SpA from RA include spine pain, dactylitis, enthesitis, psoriasis, and nail psoriasis.[2] Increased physician awareness of the potential overlap and distinctions between SpA and RA manifestations is needed for the early diagnosis and appropriate treatment for SpA.
Objectives: To identify and summarise the published literature on the prevalence of SpA-related clinical manifestations among patients with RA and SpA.
Methods: Publications were retrieved from Embase®, Cochrane, MEDLINE®, and MEDLINE® In-Process databases. Studies were included if they were non-interventional, recruited patients with RA and SpA, or patients with seronegative/seropositive RA, and reported the following manifestations: enthesitis, dactylitis, axial symptoms, psoriasis, or nail psoriasis. Two reviewers assessed each citation against predefined eligibility criteria, with discrepancies reconciled by a third independent reviewer.
Results: Of the 4479 publications retrieved, 18 studies were included (Figure 1). All studies compared SpA populations to patients with RA. Of the 18 studies, 11 studies reported patients with only PsA, 2 studies reported patients with only ankylosing spondylitis (AS), and 5 studies reported mixed SpA populations. Three studies each reported data pertaining to seropositive/seronegative RA and early RA, defined as symptom onset <1 year. The majority (N=12) of studies used ultrasound imaging to identify manifestations of interest. Enthesitis (N=17) was the most frequently evaluated manifestation while axial symptoms (N=2) was least evaluated. Of the studies reporting enthesitis, the majority (N=14) reported a higher prevalence of enthesitis in the SpA cohort compared to the RA cohort. The remaining studies (N=3) reported no significant difference in enthesitis between the SpA and RA cohorts. Notably, these 3 studies comprised of the 2 studies evaluating only AS patients, and all 3 studies evaluated late RA patients. In contrast, the 3 studies that reported early RA and PsA patients found a significantly higher prevalence of enthesitis in early PsA vs. early RA cohort. Two of the 3 studies reporting RA serostatus found a higher prevalence of enthesitis, psoriasis, and/or nail psoriasis in the SpA population compared to seronegative and seropositive RA cohorts. All studies reporting axial symptoms, dactylitis, psoriasis, and nail psoriasis found a higher prevalence of the corresponding manifestation in the SpA vs. RA cohort.
Conclusion: While this review found a higher prevalence of key SpA-related clinical manifestations in SpA vs. RA, overlap was present suggesting that misclassification could occur. Differences in the prevalence of manifestations were also seen in the early vs. late RA populations as well as by RA serostatus. This suggests that an earlier and comprehensive evaluation, including advanced imaging of peripheral manifestations such as enthesitis, dactylitis, axial symptoms, and skin signs such as psoriasis and nail disease, among RA and SpA patients may reduce misclassification and inappropriate treatment. Further research is needed to confirm these findings.

References:

[1] Seo et al. Clin Rheumatol. 2015;34:1397-1405.
[2] Merola et al. RMD. 2018;4:e000656.

Figure 1: PRISMA diagram for study selection



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SAT0386 USEFULNESS OF THE FECAL CALPROTECTIN AS SCREENING TOOL FOR INFLAMMATORY BOWEL DISEASE IN PATIENTS WITH SPONDYLOARTHRITIS AND NO DIGESTIVE SYMPTOMS

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Background: Fecal calprotectin (FC) is a biomarker of bowel inflammation widely spread in diagnosis and follow-up of inflammatory bowel disease (IBD). It is classically estimated that 5% of patients with axial spondyloarthritis (SpA) also have IBD; coexistence of both conditions has definite impact in clinical decisions. Proactive detection of both diseases should be advisable, though appropriate screening tools are still lacking.
Objectives: To evaluate the usefulness of FC for the diagnosis of IBD in patients diagnosed with SpA with no clinical suggestive manifestations or previous diagnosis of IBD.
Methods: Patients from a Rheumatology clinic diagnosed with SpA who met ASAS criteria and did not present digestive symptoms suggestive of IBD were consecutively included. Demographics, clinical and analytical data of SpA (uveitis, HLA B27, acute phase reactants) at the time of inclusion, and treatment history were collected. Patients with a positive FC (> 50 mg/Kg) underwent ileocolonoscopy with biopsies of colon and terminal ileum. Patients who were recommended to avoid NSAIDs 2-4 weeks before stool collection and endoscopy.
Patients with no endoscopic findings underwent a second determination of fecal calprotectine. If persisted positive, capsule endoscopy was performed to evaluate small intestine.
Results: 98 patients included; 47% male, mean age 46.1 (20-74) years. BASDAI 3.6 ± 2.5. HLA B27 positive in 78% of patients, high ESR in 31.6%, high CRP in 9.2%. FC positive in 49 patients (50%): mean 147 mg/kg (range 0-3038).
47 underwent ileocolonoscopy: In 13 cases (26.5%), endoscopic findings were suggestive of IBD (7 Crohn's disease and 1 ulcerative colitis). Microscopic inflammation was found in 2 additional cases. Among those 34 patients with normal ileocolonoscopy, 16 patients refused further investigations; among the remining 18 patients, a second FC was positive in 16. Capsule endoscopy showed findings suggestive of small intestine IBD in 6 additional patients.
In patients with high FC levels, **those with high CRP and ESR were more likely to have IBD** (29% v 16% and 29% v 12% respectively). Patients with a history of **uveitis** (18% vs 12%) or **psoriasis** (33% v 16%) also had a higher prevalence of IBD, although none of those differences reached statistical significance.
FC was higher in **smokers** (72%v 44%; p=0.03). There were no significant differences regarding HLA B27. No statistically significant differences were found in FC between patients with high FC who were diagnosed with IBD and those who were not.
Conclusion: In our study, patients with SpA and no clinical feature suggestive of IBD who showed FC> 50 mg/kg had high prevalence of IBD, which could indicate the **usefulness of FC as screening tool for IBD in patients with SpA.**
Patients with SpA and other immune-mediated condition or elevated CRP, seem to be more likely to have subclinical IBD.
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SAT0387 ROLE OF HLA-B27 IN THE COMORBIDITIES OBSERVED IN AXIAL SPONDYLOARTHRITIS: DATA FROM COMOSPA

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Background: Comorbidities have merged as an important field in Spondyloarthritis, however there is few data about its relationship to genetic factors such as HLA-B27.
Objectives: To analyze the potential association between the presence of HLA-B27 and the different comorbidities observed in axSpA patients.
Methods: A comparative cross-sectional study including axSpA patients from COMOSPA registry. COMOSPA is a worldwide registry that includes a wide set of anthropometric and clinical variables from 3984 patients with spondyloarthritis. The registry also includes the most frequent comorbidities observed in spondyloarthritis such as obesity, hypertension, diabetes, hyperlipidemia, heart ischemic disease, stroke, renal failure, neoplasms, peptic ulcer, diverticulitis, chronic obstructive pulmonary disease, and the presence of osteoporosis. A descriptive analysis and a multiple logistic regression model was performed including all variables assessed.
Results: 2370 patients fulfilled ASAS criteria of axSpA patients and were included in the study. 1858 (78.4%) of them were HLA-B27 positive. HLA-B27 positive axSpA patients presented significantly higher percentage of male sex, longer disease duration, higher percentage of definite Ankylosing Spondylitis, higher CRP levels, and were also more frequent tobacco consumers and excessive alcohol intakers compared to the negatives. However, disease activity measured by BASDAI, BASFI and ASDAS-CRP were all significantly higher in the HLA-B27 negative patients compared to the positive ones.
The only association observed between any comorbidity and presence of gen HLA-B27 was the presence of osteoporosis. This association was independently significant even after adjusting in the multivariate analysis for all variables assessed.
Conclusion: The association observed between the gen HLA-B27 and the presence of osteoporosis in axSpA patients could be of great relevance given the impact of osteoporosis in the phenotypical frame of axSpA patients.
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SAT0388 CHROMOENDOSCOPY AND MAGNIFICATION COLONOSCOPY: ANALYSIS OF THE MUCOSA OF THE COLON AND ILEUM IN PATIENTS WITH SPONDYLOARTRHITIS AND GASTROINTESTINAL SYMPTOMS WITHOUT INFLAMMATORY BOWEL DISEASE

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Background: Digital chromoendoscopy with magnification is a technique that identify microscopic inflammation, with a better characterize, highlighting specific gastrointestinal findings showing a good correlation with histopathological features. Spondyloarthritis (SpA) patients with the presence of non-specific gastrointestinal symptoms, subclinical intestinal inflammation is defined by endoscopic and histological techniques
Objectives: To detect early structural inflammatory changes by chromoendoscopy and magnification colonoscopy in colonic/ileum digestive mucosa and establish its association with clinical variables in patients with SpA and gastrointestinal symptoms

Methods: In total, 180 patients with SpA (ASAS/criteria) were assessed by rheumatologists, of which (n=35) (19.4%) had an indication by a gastroenterologist to perform the chromoendoscopy, magnification colonoscopy and histological analysis. The association between clinical and colonoscopy variables were evaluated using the Chi square or Fisher's exact test. (Ethical/Code. 2017-023)
Results: The average age of the patients included for colonoscopy was 45.4±10.3 years, 57.1% were men and 42.9% presented the HLA-B*27 allele. Axial involvement (91.4%), inflammatory back pain (68.6%) and use of biological therapy (71.4%). High levels of calprotectin (25.7%), CRP>3 (14.3%), positive ESR (22.9%) and positive ANCA (8.6%) was observed. Regarding outcome measures of function and activity, BASDAI >4 (60%) and ASDAS-PCR >2.1 (80.0%) was observed
The loss of vascular pattern in the ileum was associated with high levels of calprotectin levels (p=0.002). At microscopic level, 80% of the patients who presented acute inflammation in the ileum had elevated calprotectin (p=0.013). Cryptitis (77.8%) in the ileum was associated with axial involvement (p=0.017). Ulcers and erosion in the ileum were associated with positive ESR (p=0.003). All patients who presented ulcerations and inflammation (64.3%) in ileum were HLA-B27 positive (p=0.029) and (p=0.052) respectively. The 50% of patients with atrophy of villi in ileum were receiving biological treatment (p=0.035)
Conclusion: Digital chromoendoscopy and augmentation colonoscopy provided an improved and detailed contrast of the surface of the gastrointestinal mucosa. The tissue sampling showed the loss of vascular pattern as main finding in ileum with interesting associations with fecal calprotectin levels in patients with SpA. The interest of proposing the active search for symptoms, signs and biomarkers of gastrointestinal involvement in patients with SpA without IBD is to define subclinical gastrointestinal involvement and early remission through an endoscopic evaluation and objective histological and propose a specific clinical and therapeutic treatment.
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SAT0389

FREQUENCY OF DISEASE FLARES UNDER LONG-TERM ANTI-TNF THERAPY IN PATIENTS WITH EARLY AXIAL SPONDYLOARTHRITIS: RESULTS FROM THE ETANERCEPT VERSUS SULFASALAZINE IN EARLY AXIAL SPONDYLOARTHRITIS TRIAL

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Background: Disease flares in axial spondyloarthritis (axSpA) might occur even in patients with otherwise stable disease receiving highly effective anti-inflammatory therapy such as TNF inhibitors. The frequency of disease flares, especially in patients with axSpA receiving long-term stable therapy, and factors associated with flares are not sufficiently investigated.
Objectives: The objective was to assess the frequency of disease flares and to identify factors associated with flares in patients with early axSpA receiving continuous long-tem (up to 10 years) treatment with a TNF inhibitor etanercept.
Methods: In the ESTHER (etanercept versus sulfasalazine in early axial spondyloarthritis trial), patients with early axSpA (symptom duration ≤5 years) were treated with ETN (n=40) versus sulfasalazine (n=36) for 48 weeks [2]. After one year all patients were treated continuously with etanercept (n=17 patients temporarily interrupted treatment in the 2nd year to assess time to flare and were then (re-)treated with etanercept, except 4 patients who completed the study in sustained remission) for up to 10 years in total. Only patients who were continuously treated with etanercept for at least 6 months were included in the current analysis. The disease flare was defined as a worsening of the ASDAS by ≥0.9 as compared to the value obtained at the previous visit. Univariate and multivariable cox-regression analyses were performed to analyze the predictors of flares.
Results: Out of 76 patients who entered the study at baseline, 62 patients (n=32 with radiographic (r-) axSpA and n=30 with non-radiographic (nr-) axSpA) fulfilled the criterion of the continuous etanercept treatment. A total of 22 patients (35%) experienced at least one flare over the entire treatment period 10 patients (31.3%) in the r-axSpA and 12 patients (40%) in the nr-axSpA subgroup) - figure. A total of 81 flares occurred (33 and 48 in the r- and nr-axSpA subgroups, respectively) in the 10 years of follow-up. None of the documented disease flares resulted in a direct study withdrawal. The majority of flares occurred within first 4 years of treatment (figure). There were also no statistically significant differences between nr- and r-axSpA in the time until the first flare (p=0.4, Log-rank test). In the multivariable Cox regression analysis normal CRP values (≤5mg/l), HLA-B27 negativity, higher physician global assessment, a longer symptom duration at study entry, higher spinal ankylosis and higher fatty degeneration in the sacroiliac joints but lower spinal osteitis scores and lower ankylosis scores in the sacroiliac joints at baseline MRI were associated with a higher risk for flares.
Conclusion: Disease flares according to the ASAS definition of clinically important worsening in axSpA based on ASDAS occurred ~1/3 of patients with early axSpA who received a treatment with etanercept for up to 10 years without major differences between r- and nr- forms of axSpA. HLA-B27 negativity, normal CRP, higher spinal ankylosis scores, higher fatty degeneration scores but lower ankylosis scores in the SIJ´s at baseline MRI were associated with a higher risk for flares.

		all	≥1 flare	no flare
patients	n (%)	62 (100)	22 (35.5)	40 (64.5)
male	n (%)	38 (61.3)	16 (72.7)	22 (55)
age	mean (SD)	34.1 (8.3)	32.6 (7.8)	35 (8.6)
BASDAI	mean (SD)	2.7 (2)	1.8 (1.8)	3.2 (1.9)
ASDAS	mean (SD)	1.6 (0.8)	1.3 (0.7)	1.7 (0.8)

Figure 1. Baseline characteristics of all patients with with continous ETC treatment.

		all	≥1 flare	no flare
patients	n (%)	62 (100)	22 (35.5)	40 (64.5)
male	n (%)	38 (61.3)	16 (72.7)	22 (55)
age	mean (SD)	34.1 (8.3)	32.6 (7.8)	35 (8.6)
BASDAI	mean (SD)	2.7 (2)	1.8 (1.8)	3.2 (1.9)
ASDAS	mean (SD)	1.6 (0.8)	1.3 (0.7)	1.7 (0.8)

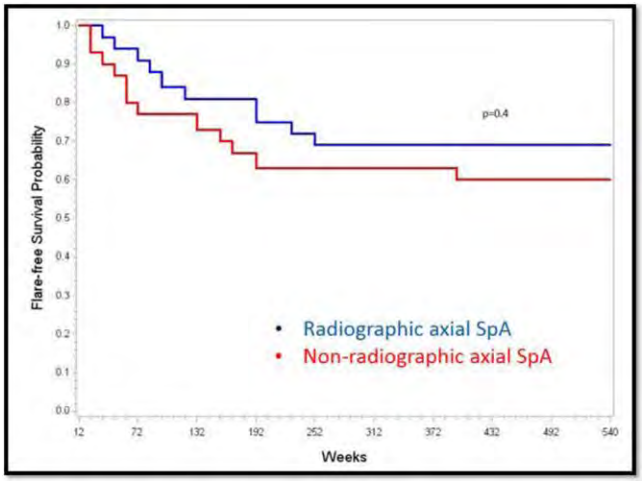


Figure 2. Kaplan-Meier curves indicating time to first flare and flare free survival propability.

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BMS, Celgene, Lilly, MSD, Novartis, Pfizer, Roche, UCB, Speakers bureau: Consultancy / speaker fees from: Abbvie, BMS, Celgene, Lilly, MSD, Novartis, Pfizer, Roche, UCB, Murat Torgutalp: None declared, Anja Weiß: None declared, Mikhail Protopopov Consultant of: Novartis, Valeria Rios Rodriguez Consultant of: Abbvie, Novartis, Hildrun Haibel Consultant of: Abbvie, Jansen, MSD, and Novartis, Speakers bureau: Abbvie, Jansen, MSD, and Novartis, Kay Hermann: None declared, Christian Althoff: None declared, Olaf Behmer Employee of: Pfizer Pharma GmbH, Joachim Sieper Consultant of: AbbVie, Boehringer Ingelheim, Eli Lilly and Company, Janssen, Merck, Novartis, Pfizer, Roche, and UCB Pharma, Speakers bureau: AbbVie, Boehringer Ingelheim, Eli Lilly and Company, Janssen, Merck, Novartis, Pfizer, Roche, and UCB Pharma, Denis Poddubnyy Grant/research support from: AbbVie, MSD, Novartis, and Pfizer, Consultant of: AbbVie, Bristol-Myers Squibb, Eli Lilly, MSD, Novartis, Pfizer, Roche, UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, MSD, Novartis, Pfizer, Roche, UCB

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SAT0390 PROPROTEIN CONVERTASE SUBTILISIN/KEXIN TYPE 9 IN THE INFLAMMATION-RELATED DYSLIPIDEMIA OF PATIENTS WITH SPONDYLOARTHRITIS

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Background: Proprotein convertase subtilisin/kexin type 9 (PCSK9) is a serine protease that regulates cholesterol metabolism through low-density lipoprotein receptor degradation and that has been linked with cardiovascular (CV) risk. Patients with spondyloarthritis (SpA) are prone to an increased and premature prevalence of atherosclerosis that has been linked to an atherogenic lipid profile among these individuals.

Objectives: The purpose of the present study was to examine whether PCSK9 levels are related to both abnormalities in the lipid profile and the severe atherosclerosis that occur in patients with SpA.

Methods: Cross-sectional study that encompassed 545 individuals; 299 patients with SpA and 246 statins intake-matched controls. PCSK9 and lipoproteins serum concentrations, standard lipid profile and carotid intima-media thickness and carotid plaques were assessed in patients and controls. A multivariable analysis, adjusted for standard CV risk factors, was performed to evaluate the influence of PCSK9 on SpA related dyslipidemia, disease related data, and subclinical carotid atherosclerosis.

Results: Lipid profiles showed that most lipid panel parameters (total cholesterol, HDL- and LDL-cholesterol, lipoprotein A and apoliprotein A1) were lower in SpA patients compared to controls. Contrary, Apo B:Apo A1 and LDL:HDL cholesterol ratios were higher in SpA. The mean PCSK9 serum levels were significantly lower in SpA patients compared to controls (249 ± 105 vs. 199 ± 74, ng/ml, p=0.000) in the univariate analysis. An additional multivariable analysis adjusting for demographics and CV risk factors plus all the lipid-related molecules (that were found to be different between patients and controls) disclosed that PCSK9 (beta coef. -44 [95%CI -60- -27] % mg/dl, p=0.000) conserved its downregulation in SpA patients.

Traditional CV risk factors were not related to PCSK9 in controls and patients. Concerning lipid profile, some correlations were found between lipid-related molecules and PCSK9. In this sense, triglycerides were positively associated with PCSK9 in both patients and controls; total cholesterol and apolipoprotein A1 serum levels were associated with PCSK9 in patients but not in controls and; Lipoprotein (a) was related to PCSK9 only in controls (Table 1).

Regarding disease-related data, disease duration (log beta coef. 10 [0-20], p=0.043), and ASDAS-CRP (12 [95%CI 4-20], p=0.004) and BASFI (log beta coef. 12 [95%CI 0-25], p=0.049) scores,were positively related to PCSK9. Moreover, patients in the very high disease activity ASDAS-CRP category disclosed higher serum levels of PCSK9 compared to those in the remission category (32 [95%CI 2-63], p=0.038). Remarkably, while patients on current prednisone showed higher serum levels of PCSK9 (55 [95%CI 24-8]) ng/ml, p=0.001), patients under anti-TNF alpha therapies exhibited inferior levels (beta coef. -26 [95%CI -43- -9], p=0.003). PCSK9 in SPA patients with carotid plaque was higher compared to patients without plaque, however, this difference was lost after multivariable analysis.

Conclusion: PCSK9 is downregulated in SpA patients independently of other inflammation-related lipid profile modifications that occur in the disease. Disease activity is positively associated with PCSK9 serum levels. PCSK9 is univariately related to the presence of carotid plaque.

Disclosure of Interests: Juan Carlos Quevedo-Abeledo Speakers bureau: Abbvie, Laura de Armas-Rillo: None declared, Vanessa Hernández-Hernández Speakers bureau: Pfizer, Abbvie, MSD, delgado frias esmeralda Speakers bureau: Pfizer, Abbvie, MSD, Antonia de Vera-González: None declared, Alejandra Delgado-González: None declared, Jose Antonio García-Dopico: None declared, Iván Ferraz-Amaro Grant/research support from: Pfizer, Abbvie, Speakers bureau: Pfizer, Abbvie, MSD.

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SAT0391 DEPRESSIVE SYMPTOMS ARE ASSOCIATED WITH HIGHER DISEASE ACTIVITY AND WORSE FUNCTIONAL STATUS IN AXSPA: A CROSS-SECTIONAL ANALYSIS FROM RABBIT-SPA

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Background: Axial spondyloarthritis (axSpA) is a potentially severe chronic inflammatory disease with impact on function and quality of life. About 20-30% of axSpA patients show symptoms of depression or are diagnosed with depression [1]. Depression may influence outcome, especially patient reported outcomes.

Objectives: To assess differences in baseline characteristics and outcome parameters between patients with and without symptoms of depression using WHO-5 score.

Methods: RABBIT-SpA is a prospective longitudinal cohort study including axSpA patients enrolled at start of a new conventional treatment (including NSAID) or bDMARD. WHO-5 score was used to identify depressive symptoms categorised into 3 groups using validated cut-offs: moderate to severe depressive symptoms <=28, mild depressive symptoms 29-50, good well-being >50. Baseline values of patients categorised as having moderate to severe depressive symptoms were compared with the rest of the patients using t-test. Spearman correlation coefficient was calculated to analyse the relationship between WHO-5 score and other outcome parameters.

Results: A total of 848 axSpA patients were included in this analysis (table 1). Moderate to severe depressive symptoms were found in 221 patients (30%), 226 (31%) had mild depressive symptoms and 285 (39%) reported a good well-being. Percentages of patients with inflammatory back pain, peripheral arthritis or enthesitis as well as the number of affected joints (44 JC) and entheseal sites (using SPARCC) were higher in the group of patients with moderate to severe depressive symptoms.

Table 1.

Parameter	WHO-5 (<=28) Moderate severe N=221	WHO-5 (29-50/>50) Mild/well-being N=511
Age, mean	43.8	44.1
Female, n (%)	100 (45.2)	229 (44.8)
Disease duration, years, mean	6.8	6.5
Inflammatory back pain, n (%)	195 (88.6)	416 (81.6)
Enthesitis, n (%)	49 (22.3)	78 (15.4)
Peripheral arthritis (44 JC), n (%)	64 (29.1)	134 (26.3)
Uveitis, n (%)	45 (20.4)	76 (15)
IBD, n (%)	13 (5.9)	31 (6.1)
Psoriasis, n (%)	35 (15.8)	58 (11.4)
CRP positive (≥5mg/l), n (%)	115 (59)	243 (55.1)
HLA-B27, n (%)	151 (72.6)	354 (74.2)
BMI≥30, n (%)	66 (30)	117 (23.6)
Comorbidities ≥3, n (%)	50 (22.6)	89 (17.4)
Current smoking, n (%)	102 (47.2)	185 (36.7)

Table 2.

Parameter	WHO-5 (<=28) Moderate severe N=221	WHO-5 (29-50/>50) Mild/well-being N=511	p-value
PhysGA (NRS 0-10)	6.2 (1.6)	5.4 (1.9)	0.0001
ASDAS	6.1 (1.6)	4.2 (1.8)	0.0001
BASDAI (NRS 0-10)	3.5 (0.8)	2.9 (0.9)	0.0001
BASFI (NRS 0-10)	5.5 (2.2)	3.2 (2.2)	0.0001
ASAS-HI (0-17)	9.8 (3.1)	5.8 (3.1)	0.0001
PatGA (NRS 0-10)	7 (1.8)	5.4 (2.3)	0.0001
PatPain (NRS 0-10)	6.9 (1.9)	5.2 (2.3)	0.0001
PatSleep (NRS 0-10)	7.2 (2.4)	4.6 (2.9)	0.0001

Results are presented as mean ± SD.

All analysed outcome parameters (e.g. ASDAS, ASAS-HI, BASDAI, BASFI, patient global, physician global, pain, sleep) were significantly worse in the group of patients with moderate to severe depressive symptoms versus the other patients (table 2). This includes physician-reported, patient-reported and composite scores.

WHO-5 was highly correlated with all outcome parameters regardless of gender. Figure 1 shows the correlation of BASDAI and WHO-5 stratified for gender.

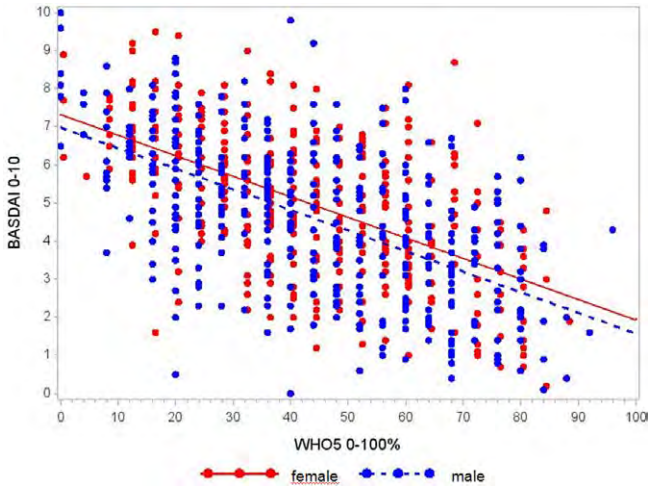


Figure 1.

Conclusion: Almost one third (30%) of axSpA patients in this analysis reported scores indicative of depressive symptoms and depression. The strong correlation of WHO-5 scores with patient and physician reported outcomes may be relevant for the management of patients with axSpA.

References:

[1] Redeker I, et al. Ann Rheum Dis 2018;0:1–8. doi:10.1136

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SAT0392 DIAGNOSIS OF AXIAL SPONDYLOARTHRITIS IN DAILY CLINICAL PRACTICE – A SURVEY AMONG DUTCH RHEUMATOLOGISTS

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Background: Since publication of the ASAS classification criteria for axial spondyloarthritis (axSpA) in 2009[1] and the development of ASAS-endorsed recommendation for early referral of patients with a suspicion of axSpA,[2] awareness for non-radiographic (nr-) axSpA besides Ankylosing Spondylitis (AS) has increased. Still there is limited information of how nr-AxSpA is addressed in daily clinical practice.

Objectives: To get insight into the diagnostic phase of axSpA in daily rheumatologic practice in the Netherlands, and to explore if nr-axSpA is addressed differently from AS.

Methods: We set up a 21 multiple choice question survey for rheumatologists in the Netherlands with 5 general questions about their practice and 16 questions addressing the diagnostic phase of axSpA. The questionnaire was taken by representatives of the medical department of Novartis NL during structured face-to-face interviews. Rheumatologists in the Netherlands were invited to participate, aiming to get a sample of rheumatologists varying in geographical location and hospital type, as well as a mix of SpA-experts and non-SpA-experts. Rheumatologists gave approval for anonymous use of the data, which were entered in a database and subsequently analyzed using descriptive statistics.

Results: From October 15th 2019 until January 16th 2020, 36 Dutch rheumatologists participated in the face-to-face survey; 6 from university hospitals, 27 from general hospitals and 3 from private care centers. Most of axSpA patients (61%) were referred by the general practitioner and mean time between referral and first visit was 2-6 weeks. More than 50% of rheumatologists reported a mean symptom duration of >1 year and in 30% even >2 years before first visit. For diagnosing axSpA rheumatologists performed in almost all cases X-pelvis (mean 100% (SD 0%) for both AS and nr-axSpA), CRP/ESR (91% (26%) for AS; 94% (22%) for nr-axSpA) and HLA-B27 (74% (40%) for AS; 86% (26%) for nr-axSpA. MRI of the SI joints was performed in 31% and 82% of patients, respectively, and about 60% of the rheumatologists used of classification criteria for diagnosing axSpA. In addition, rheumatologists marked the level of importance of several (SpA) clinical features for making the diagnosis AS or nr-axSpA (Figure 1). Most rheumatologists graded inflammatory back pain, arthritis/enthesitis/dactylits and uveitis as very important for contributing to the diagnosis. Functional impairment of the spine and male sex were mostly graded neutral or not important for making a diagnosis of axSpA. All features were graded of similar importance for the diagnosis AS and nr-axSpA, except for backpain starting before the age of 45, which was considered more important for diagnosing AS.

Conclusion: This survey among Dutch rheumatologists showed that in 30% of patients referred with possible suspicion of axSpA, symptom duration still was >2 years. Almost 60% of rheumatologists make use of the ASAS classification criteria for diagnosing nr-axSpA. Therefore, for early referral awareness of axSpA in first line should enhance. Furthermore, rheumatologists should become aware that classification criteria are not similar to diagnostic criteria and cannot be used as a tick box for diagnosis.

References:

[1] Rudwaleit M et al, Ann Rheum Dis 2009;68:777-83, 2. Poddubnyy D et al, Ann Rheum Dis 2015;74:1483–7

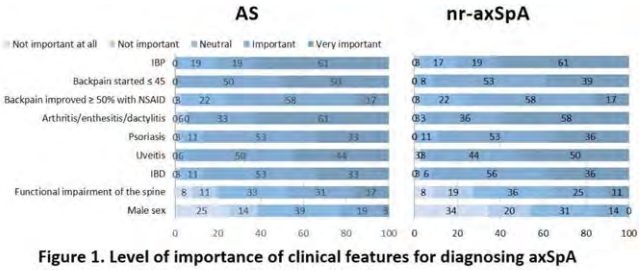


Figure 1. Level of importance of clinical features for diagnosing axSpA

Values given as % of responders (total of 100% per feature)

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SAT0393 DISCREPANCY IN THE CARDIOVASCULAR RISK SEVERITY CALCULATED USING DIFFERENT RATING SCALES IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: Cardiovascular risk (CVR) in patients (pts) with axial spondyloarthritis (axSpA) exceed the populational level. However, it remains unclear, which of the cardiovascular risk assessment systems is the most accurate in cases of chronic inflammation..
Objectives: of the current study were to assess the CVR in pts with axSpA and to compare different cardiovascular risk scales in these pts.
Methods: The study included 118 patients at the age of 25-65 years with diagnosis of axSpA fulfilling ASAS criteria (2009) from St. Petersburg' axSpA register. Three indices of cardiovascular risk evaluation (Systematic COronary Risk Evaluation (SCORE) with increasing coefficient 1.5 for inflammatory diseases, Reynolds Risk Score (RRS), and the third modification of QRESEARCH Cardiovascular Risk Algorithm (QRISK3) were calculated. For the pts below 40 years old only QRISK3 was calculated.

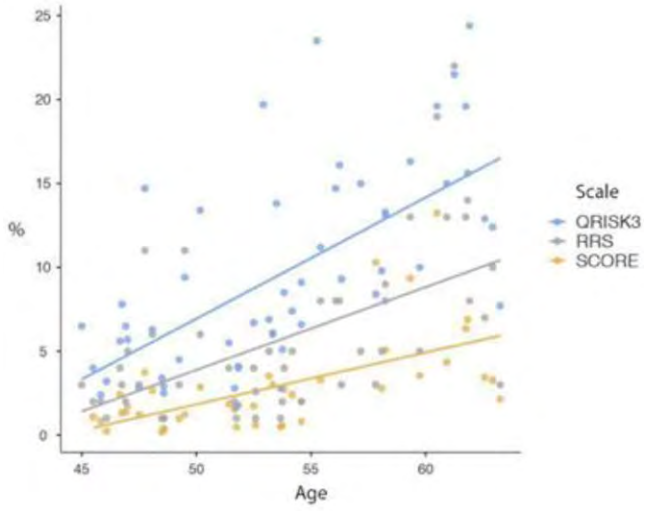


Figure 1. Cardiovascular risk evaluation indices in patients with axial spondyloarthritis, n=118 for QRISK3, n=72 for SCORE and RRS.

Results: Mean age of the pts was 44.3±11.1 years; 91(77.1%) pts were males, HLA-B27 positive – 83 (70.3%) of the pts; mean disease duration 13.0±8.3 years. Mean value of SCORE was 2.78±1.89%, of RRS – 5.28±3.31%, of QRISK3 – 7.91±3.8% (figure 1). Cronbach's alpha for the scales was 0.873.

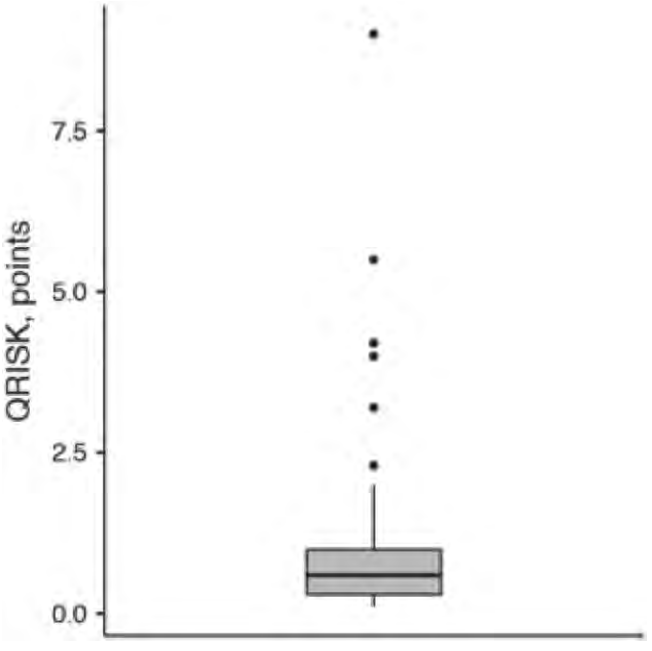


Figure 2. QRISK3 index in axSpA patients 25-40 years old, n=46

High CVR (≥5 %) was found in 14 (11,7%) of the pts according to the SCORE, in 65 (55,1%) of the pts according to the RRS, and in 81 (69%) of the pts according to the QRISK3. Ranking of CVR severity did not match in SCORE and QRISK3 indices in 83.72% of cases, in SCORE and RRS – in 51.16% of cases, and in QRISK3 and RRS in 8% of cases. The SCORE index showed the lower values of the expected risk as compared to the QRISK3 and RRS (figure1).In axSpA pts at age 25-40 years old (n=46, mean age 32.6±4.0 years, males 36 (78.3%)), mean value of QRISK3 was 1.16±0.99 %; in 14 from 46 (30.4%) of those pts increased CVR was registered (figure 2).
Conclusion: There was a discrepancy in the severity of CVR calculated using different rating scales in axSpA patients. The SCORE index showed lower values of CVR as compared to the QRISK3 and RRS, which hypothetically could be the consequence of CVR underestimation. QRISK3 demonstrated the highest CVR and was the only index useful in pts below 40 years old. To exclude hyper- or underestimation of CVR calculation more data about CVR calculations and frequency of CV events, occurring in axSpA patients are needed.
Disclosure of Interests: Elizaveta Vasilenko: None declared, V Mazurov: None declared, Ruzana Samigullina: None declared, Anna Dadalova: None declared, Inna Gaydukova Grant/research support from: JSC BIOCAD, Speakers bureau: Pfizer, Novartis, AbbVie, JSC BIOCAD, Celgene, MSD, Sanofi
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SAT0394

CAN FECAL CALPROTECTIN PREDICT FUTURE DEVELOPMENT OF INFLAMMATORY BOWEL DISEASE IN AXIAL SPONDYLOARTHRITIS PATIENTS? – TREASURE REAL-LIFE DATA

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Background: Patients with active inflammatory bowel diseases (IBD) fecal calprotectin (FC) levels are high and FC can be used for diagnosis [1].
Objectives: This study aimed to investigate whether fecal calprotectin levels could predict future development of IBD in axSpA patients.
Methods: This study was practiced in three centers using TReasure database and that are able to measure FC. Fecal calprotectin levels were measured in 137 axSpA patients as of September 2018 and FC level ≥200 µg/g was considered significant. All study subjects were evaluated for IBD symptoms (loose defecation, mucous diarrhea, bloody defecation, bloody diarrhea, abdominal pain, obstruction, or pseudo-obstruction) at beginning of the study and every 3 months for the first year. 25 RA patients and 24 healthy volunteers were included as a control group. Disease activity was evaluated by the ASDAS CRP, BASDAI, *BASFI*, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), visual analog scale (VAS)-pain, VAS-fatigue, and tender and swollen joint count for axSpA patients.
Results: This study included 137 axSpA patients and all patients followed for 1 year. Of the 137 axSpA patients 33.6% were females and median (Q1-Q3) age was of 43 years (33-50 years), median (Q1-Q3) disease duration was 8.9 years (5.0-13.9 years). The median (Q1-Q3) fecal calprotectin level was 48 µg/g (30-122 µg/g) and FC level was ≥200 µg/g in 23/137 (16.8%) in axSpA patients. FC level was elevated in 15/24 (62.5%) RA patients and none of the healthy volunteers. Patients median (Q1-Q3) BASDAI was 2.2 (1.0-3.6) / 1.4 (0.4-2.2), median (Q1-Q3) BASFI 1.55 (0.4-3.4) / 1.5 (0.3-3.0) and median (Q1-Q3) ASDAS CRP 1.63 (1.3-2.2) / 1.5 (1.3-1.9) at baseline and first year respectively and there was no difference regarding fecal calprotectin level. In 1 year follow-up 9 (6.5%) patient had abdominal pain, 2 (1.4%) had bloody defecation, 1 (0.7%) had loose defecation and Crohn disease developed in an axSpA patient with high FC (266 µg/g) (Table 1). IBD occurrence rate was 0.73/100 patient-year for all SpA patients, and IBD occurrence rate was 4.34/100 patients year for SpA patients with ≥200 µg/g FC level.

Table 1. IBD symptom inquiry and development of IBD in the first year

	n (%)
Loose defecation	1 (0.73)
Mucous diarrhea	0
Bloody defecation	2 (1.45)
Bloody diarrhea	0
Abdominal pain	9 (6.56)
Obstruction	0
Pseudo-obstruction	0
Inflammatory bowel disease	1 (0.73)

Conclusion: In one year follow-up, IBD occurrence rate was 0.73/100 patient-year, at a similar rate with DESIR cohort [2]. However, FC level may be a predictor for the development of IBD in SpA patients (occurrence rate 4.34/100 patients year). Further follow up duration and more patients may be needed to make conclusion in these field.

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[1] Simioni, J., et al., *Fecal Calprotectin, Gut Inflammation and Spondyloarthritis.* Arch Med Res, 2019. **50**(1): p. 41-46.

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SAT0395 SOCIAL ISOLATION IS INDEPENDENTLY ASSOCIATED WITH MORE SEVERE DISEASE IN AXIAL SPONDYLOARTHRITIS

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Background: Social isolation has negative impacts on health and wellbeing at different stages of life. It is associated with longer sickness absence and increased mortality in the general population [1]. Reducing social isolation is a growing governmental priority in many countries such as the UK. The effects of social isolation on patients with rheumatic diseases have not been studied.

Objectives: To examine whether living alone impacts disease severity and quality of life among axial spondyloarthritis (axSpA) patients.

Methods: We conducted a single-centre cross-sectional study of consecutive patients meeting the ASAS axial SpA criteria in Liverpool, UK. Patients answered questionnaires including whether they lived alone, which we used as a proxy for social isolation. Disease assessment measures included BASDAI, spinal pain, BASFI, quality of life (EuroQol), global health and fatigue. We separately extracted self-reported anxiety or depression from the EuroQol questionnaire (as absent, moderate, severe) since it is an important associated factor. Patient characteristics were compared between patients who lived alone and those who did not, using descriptive statistics. The association between social isolation and each disease measure were assessed using multivariable linear models, adjusted for age, gender, post-code derived deprivation index, BMI, anxiety/depression and smoking status.

Results: A total of 353 patients (68% male, mean age 46 years) were studied; 82% met the modified New York criteria for ankylosing spondylitis. 58 (16%) patients reported living alone. These patients were older (49 vs 43 years, P=0.006), more frequently male (83 vs 65%, P=0.008), and more frequently current smokers (53 vs 31%, p=0.009). They were otherwise similar in the proportion meeting criteria for AS, HLA-B27 positivity, and BMI (Table 1). Self-reported anxiety or depression was not significantly different between the two groups. Regression models showed that patients living alone had 1 unit higher BASDAI, pain and BASFI than those who did not, independent of potential confounders (Table 2). Living alone was also associated with poorer quality of life, but not fatigue or global health.

Table 1. Patient characteristics compared according to whether they live alone.

	Do not live alone	Live alone	P value
N (%)	295 (83.6%)	58 (16.4%)	
Mean age, years (SD)	43.4 (14.0)	49.0 (12.4)	0.006
Males, n (%)	192 (65.1%)	48 (82.8%)	0.008
Meeting mNY criteria	238 (80.7%)	48 (82.8%)	0.712
HLA-B27 positive	109 (54.0%)	25 (71.4%)	0.054
Mean BMI, (SD)	28.17 (5.6)	29.40 (6.8)	0.196
Smoking status			
Current	87 (31.4%)	30 (52.6%)	0.009
Ex	52 (18.8%)	8 (14.0%)	
Never	138 (49.8%)	19 (33.3%)	
Self-reported anxiety or depression			
Absent	145 (49.2%)	22 (38.0%)	0.229
Moderate	120 (40.7%)	27 (46.6%)	
Extreme	30 (10.2%)	9 (15.5%)	
Deprivation Index, median (IQR)	2 (1, 5)	2 (1, 4)	0.190

Table 2. Impact of social isolation (living alone) on disease severity measures in axial spondyloarthritis.

BASDAI	1.0 (0.2 to 1.8)
Spinal pain	1.0 (0.03 to 1.9)
BASFI	1.0 (0.1 to 1.9)
Quality of life	-0.13 (-0.24 to -0.02)
Fatigue	0.1 (-0.7 to 0.9)
Global health	-0.03 (-0.8 to 0.7)

Data shown as coefficient (95%CI). Quality of life assessed using EuroQol. All other indices are on a scale of 0 (best) to 10 (worst).

Conclusion: Living alone - as a proxy for social isolation - was associated with more severe disease and poorer quality of life in axSpA patients, independent of depression and other confounders. Further studies are needed to examine the direction of causation, and whether lack of social support influences their ability to seek and/or benefit from healthcare provision.

References:

[1] Cornwell EY, Waite LJ. Social disconnectedness, perceived isolation, and health among older adults. J Health Soc Behav. 2009;50(1):31–48.

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SAT0396 INFLUENCE OF SMOKING AND OBESITY ON THERAPEUTIC RESPONSE IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: A SYSTEMATIC LITERATURE REVIEW

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Background: Biological therapies have substantially improved the prognosis of patients with Spondyloarthritis (SpA). However, a satisfactory clinical response is not achieved in all patients and it is essential for the clinician to identify all those factors that predict treatment response. Although they are supposed as unfavorable and potentially avoidable factors, the influence of smoking and obesity as predictors of treatment response in SpA is unknown.

Objectives: To determine if smoking and obesity are factors of worse therapeutic response in patients with axial spondyloarthritis (axSpA).

Methods: Systematic review of the literature in MEDLINE and EMBASE until June 30, 2019 based on the PICO design method. Population (P): patients with axSpA. Intervention (I): smoking or obesity. Comparator (C): non-smokers and normal weight. Outcome (O): any of the response criteria currently validated for axSpA. A specific excel form was used for data collection, EndNote software for the management and organization of papers and the Oxford 2009 level for evidence evaluation.

Results: 1873 citations were recovered, 46 studies were selected for full-text review and 12 for data extraction: 6 for smoking and 6 for obesity. The design

INFLUENCE OF OBESITY IN THE RESPONSE TO BIOLOGICAL THERAPY IN RADIOGRAPHIC AND NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS

Author	Design. Country. Total Patients. Treatment.	Patients per group	Outcomes	Influence. Evidence level.
Ottaviani 2012	Longitudinal observational (Retrospective cohorts) France 155 patients; iTNF	BMI 25 63 BMI 25-0 54 BMI 30 38	- 6 months: BASDAI 50;VAS 50; NSAID 50	Yes 2b
Gremese 2014	Longitudinal observational (Retrospective cohorts) Italy 170 patients, iTNF	BMI<25 92 BMI 25-0 55 BMI>30 23	- 12 months: BASDAI50; BASDAI	Yes 2b
Micheroli 2017	Longitudinal observational (Retrospective cohorts) Switzerland 624 patients, iTNF	BMI<25 332 BMI 25-0 204 BMI>30 88	- 6 months: ASAS 40; ASAS remission; BASDAI 50; ASDAS	Yes 2b
Rosas 2017	Cross-sectional Spain 57 patients, iTNF	BMI <25 17 BMI 25-0 25 BMI>30 15	BASDAI; ASDAS; BASFI	Yes 4
Hernandez-Breijo 2019	Prospective observational Spain; Holland 180 patients, iTNF	BMI<25 78 BMI>25 102	- 1 year: Δ BASDAI ≥ 2 Δ ASDAS ≥ 1.1; Clinical remission	Yes 2b
Hernandez 2019	Longitudinal observational Spain 147 patients, iTNF	BMI<25 27 BMI 25-0 61 BMI>30 15 30 Not reported 29	- Withholding of treatment after 5 years of onset	No 2b

INFLUENCE OF SMOKING IN THE RESPONSE TO BIOLOGICAL THERAPY IN RADIOGRAPHIC AND NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS

Glintborg 2016	Longitudinal observational (Retrospective cohorts) Denmark 1425 patients , iTNF	Smokers 614 Past smokers 233 Non Smokers 578	- 3 y 6 months: BASDAI 50/20mm	Yes 2b
Ciurea 2016	Longitudinal observational (retrospective cohorts) Switzerland 698 patients, iTNF	Smokers 268 Past smokers 167 Non smokers 263	- Every year: BASDAI 50/20m; ASDAS; ASAS 40	Yes 2b
Kydd 2015	Longitudinal observational (retrospective cohorts) Australia 422 patients, iTNF	Smokers 206 Past smokers 187 Non smokers 234	- 2 years: HRQoL, SF-36, ASQoL, HAQ-S	No 2b
Zhao 2019	Longitudinal observational (retrospective cohorts) United Kingdom 627 patients, iTN	Smokers 206 Past smokers 187 Non smokers 234	- ASDAS, BASDAI, BASFI, BASG, Chalder Fatigue Scale, Sleep; Evaluation.HADS, BASDAI50/20mm	No 2b
Zhao 2019	Longitudinal observational (retrospective cohorts) United Kingdom 598 patients, iTNF	Smokers 197 Past smokers 177 Non smokers 224	- iTNF discontinuation	No cause Discontinuation in smokers 2b
Hernandez 2019	Longitudinal observational Spain 147 patients, iTNF	Smokers 46 Past smokers 10 Non smokers 76 Not reported 17	- Withholding of treatment after 5 years of onset	No 2b

BMI: body mass index; ASDAS: Ankilosing Spondylitis disease activity score; AQoL, assessment of quality of life; ASQoL, Ankilosing Spondylitis quality of life questionnaire; BASDAI: Bath Ankilosing Spondylitis disease activity index; BASDAI50: 50% reduction BASDAI; BASDAI50/2, 50% reduction or 2 units BASDAI; BASFI, Bath Ankilosing Spondylitis functional index; BASMI: Bath Ankilosing Spondylitis metrology index; BASG: Bath Ankilosing Spondylitis Global Score; HAQ-S, health assessment questionnaire for spondylitis; iTNF: TNF inhibitor, SF-12/36: 12- or 36-item short form health survey

of all studies was observational and longitudinal with data from national registries except one cross-sectional. In total, these studies included 5291 patients (3917 patients for smoking and 1333 patients for obesity), all treated with a TNF inhibitor (iTNF). The Oxford level of evidence for all studies was 2b except the cross-sectional study, which was 4. Regarding smoking, the evidence found is not consistent. Two of the studies concluded an unfavorable effect on the response to the iTNF (Glintborg and Ciurea) but the remaining 4 studies found no differences in the clinical response to iTNF (Zhao), the cause of discontinuity of the iTNF (Zhao, Hernandez) or quality of life indexes (Kydd). For obesity, the evidence is more consistent, so that 5 of the 6 studies observed a negative influence on the therapeutic response to iTNF (Ottaviani, Gremese, Micheroli, Hernández-Breijo and Rosas).

Conclusion: According to scientific evidence in patients with axSpA, obesity is associated with a worse therapeutic response to iTNF. However, this negative effect is not clearly evidenced for smoking.

Disclosure of Interests: Pablo Zurita-Prada: None declared, Claudia Urrego-Laurín: None declared, Carlos Guillén-Astete: None declared, Victoria Navarro-Compán Consultant of: Abbvie, Lilly, Novartis, Pfizer, UCB, Speakers bureau: AbbVie, MSD, Lilly, Novartis, Pfizer, UCB

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SATURDAY, 06 JUNE 2020

Psoriatic arthritis

SAT0397

GUSELKUMAB, AN IL-23 INHIBITOR THAT SPECIFICALLY BINDS TO THE IL23P19-SUBUNIT, FOR ACTIVE PSORIATIC ARTHRITIS: ONE YEAR RESULTS OF A PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF PATIENTS WHO WERE BIOLOGIC-NAÏVE OR TNFA INHIBITOR-EXPERIENCED

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Background: Guselkumab (GUS), a monoclonal antibody that specifically binds to the p19-subunit of IL-23, is approved to treat PsO. At Week24 (W24) of the Phase 3, double-blind, PBO-controlled trial in pts with active PsA who

Fig 1. NRI and Observed ACR20 (A & B), ACR50 (C & D), and ACR70 (E & F) responses through W52 (Note: patients randomized to PBO crossed over to GUS Q4W at W24)

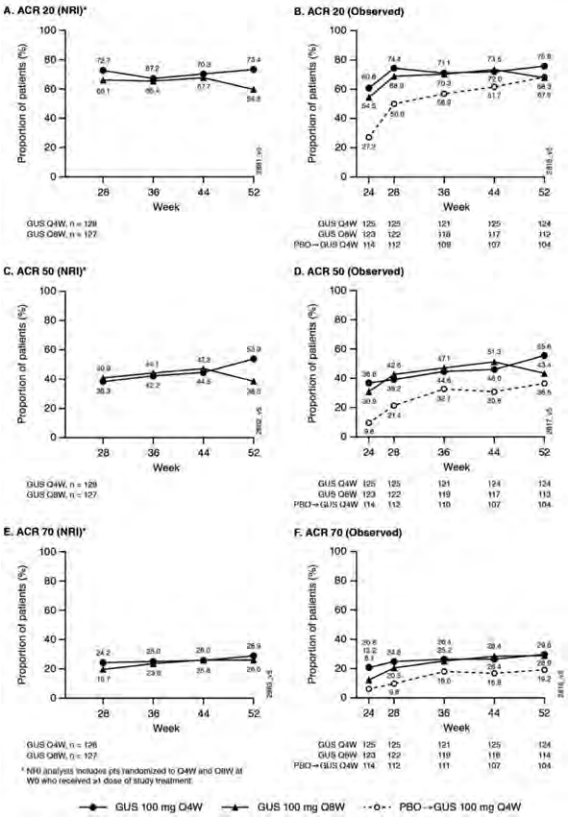
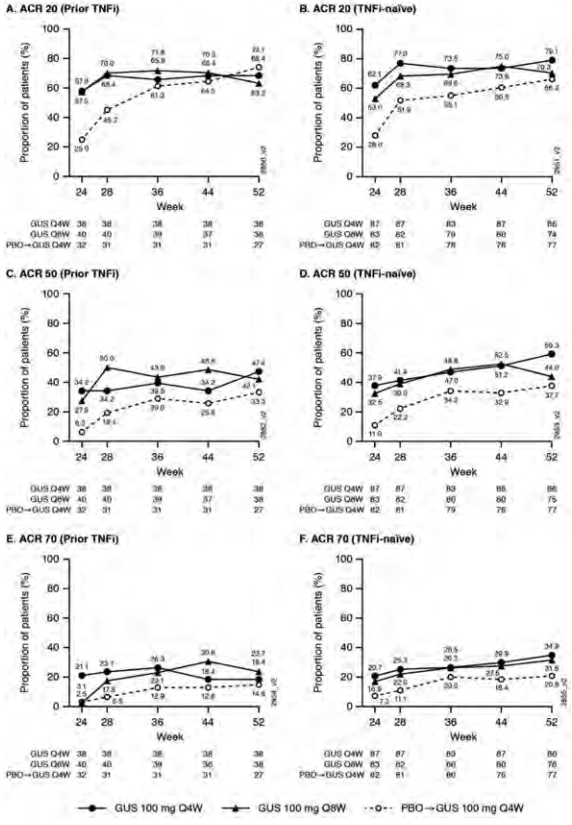


Fig 2. Observed ACR20 (A&B), ACR50 (C&D), ACR70 (E&F) response rates from W24 through W52 by prior TNFi use (Note: patients randomized to PBO crossed over to GUS Q4W at W24)



were biologic-naïve or prior TNFα inhibitor (TNFi)-treated (DISCOVER-1), GUS 100 mg, given every 4/8 weeks (Q4W/Q8W), demonstrated efficacy for joint & skin symptoms, physical function & quality of life vs PBO; AEs were consistent with GUS safety in PsO.

Objectives: Assess GUS efficacy & safety in PsA through 1 year.

Methods: Adults with active PsA (≥3 swollen+≥3 tender joints; CRP ≥0.3mg/dL) despite standard therapies were eligible. Approx. 30% of pts could have previously received ≤2 TNFi. Pts were randomized 1:1:1, stratified by W0 DMARD [Y/N] & prior TNFi (Y/N) use, to GUS 100mg Q4W; GUS 100 mg at W0, W4 & Q8W; or PBO. At W24, PBO pts crossed over to GUS 100 mg Q4W (PBO X Q4W). W48 marked the last dose of study agent. ACR response rates at W52, based on nonresponder imputation (NRI) for missing data and as observed in pts still on study agent at W24, are shown. Observed data for additional endpoints are shown. AEs through W60 are reported.

Results: 362/381 (95%) randomized pts continued study agent at W24 (125 Q4W, 123 Q8W, 114 PBO X Q4W), 347/381 (91%) pts completed treatment & 343/381 (90%) completed study. NRI ACR20 response rates were maintained at W52 (Q4W 73%, Q8W 60%; Fig 1A). Similar responses patterns were seen for the more stringent ACR50/70 criteria (Fig 1C,E). Observed ACR responses, overall (Fig, 1B,D,F) and in pts with (Fig 2A,C,E) & without (Fig 2B,D,F) prior TNFi use, were also maintained at W52. Improvements in other clinical outcomes were also maintained at W52, and responses for pts crossing over from PBO X Q4W at W24 were generally consistent with other GUS-treated pts by W52 (Table 1). Through W24, 4 (2%) GUS- and 5 (4%) PBO-treated pts had serious AEs; no GUS-treated and 2 (2%) PBO-treated pts had a serious infection. Through W60, serious AEs and serious infections occurred in 4% & 1%, respectively, of all 369 GUS-treated pts; no GUS-treated pt died or had IBD, opportunistic infections or active TB, or anaphylactic or serum sickness-like reactions.

Table 1. Observed Efficacy[1]

	GUS Q4W	GUS Q8W	PBO (W0-24) X Q4W (W24-52)
Data are % unless otherwise stated	**W24**	**W52**	**W24**	**W52**	**W24**	**W52**
Dactylitis at W0, n	37	37	49	44	47	43
Resolution	64.9	78.4	67.3	79.5	61.7	81.4
Enthesitis at W0, n	71	70	71	64	71	63
Resolution	49.3	62.9	40.8	56.3	31.0	69.8
≥3% BSA psoriasis, IGA ≥2 at W0, n	88	88	81	75	68	66
IGA 0/1 + ≥2-grade decrease	76.1	83.0	58.0	69.3	17.6	81.5[2]
PASI75	87.5	94.3	76.5	80.0	20.6	84.8
PASI90	63.6	76.1	50.6	66.7	13.2	72.7
PASI100	45.5	64.8	25.9	48.0	7.4	62.1
HAQ-DI, n	125	124	123	114	114	104
Mean change	-0.4	-0.5	-0.3	-0.4	-0.1	-0.4
SF-36 scores, n (mean change)	124	124	123	114	114	104
Physical Component - PCS	6.6	8.5	6.5	7.3	2.7	6.9
Mental Component - MCS	3.8	4.9	3.0	5.1	1.8	4.2
MDA, n	125	124	123	112	114	103
MDA response	31.2	40.3	23.6	33.9	12.3	31.1
VLDA, n	125	124	123	114	113	104
VLDA response	9.6	16.9	4.1	12.3	1.8	14.4

[1]Randomized pts still on study agent at W24; **2**n=65

Conclusion: GUS Q4W & Q8W maintained improvements in joint symptoms through 1 year in pts with active PsA who were biologic-naïve or previously TNFi-treated. In pts continuing in the study, improvements in skin symptoms, dactylitis, enthesitis, physical function & quality of life were also maintained through 1 year. GUS 100 mg Q4W & Q8W were safe and well-tolerated through study completion and consistent with GUS safety in PsO.[1]

References:

[1] https://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/TREMFYA-pi.pdf.

Acknowledgments: None

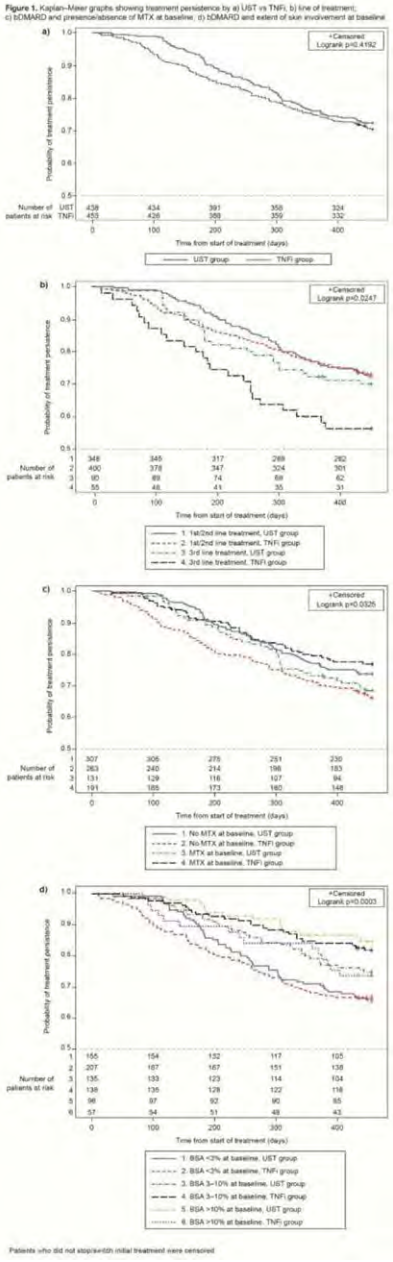
Disclosure of Interests: Christopher T. Ritchlin Grant/research support from: UCB Pharma, AbbVie, Amgen, Consultant of: UCB Pharma, Amgen, AbbVie, Lilly, Pfizer, Novartis, Gilead, Janssen, Philip Helliwell: None declared, Wolf-Henning Boehncke Grant/research support from: Janssen Research & Development, LLC, Consultant of: Janssen, Elizabeth C Hsia Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Alexa Kollmeier Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Ramanand A Subramanian Employee of: Janssen Research & Development, LLC, Xie L Xu Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Shihong Sheng Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Yusang Jiang: None declared, Bei Zhou Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Atul Deodhar Grant/research support from: AbbVie, Eli Lilly, GSK, Novartis, Pfizer, UCB, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myer Squibb (BMS), Eli Lilly, GSK, Janssen, Novartis, Pfizer, UCB, Speakers bureau: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myer Squibb (BMS), Eli Lilly, GSK, Janssen, Novartis, Pfizer, UCB

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SAT0398

PERSISTENCE OF USTEKINUMAB (UST) OR TNF INHIBITOR (TNFI) TREATMENT IN PSORIATIC ARTHRITIS (PSA): INSIGHTS FROM THE LARGE, PROSPECTIVE, MULTINATIONAL, REAL-WORLD PSABIO COHORT

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Background: Several biologic DMARDs (bDMARDs) exist for PsA, TNFi and UST being the earliest on European markets. When bDMARDs are insufficiently effective, later-line bDMARDs typically have shorter persistence. Treatment persistence reflects a mix of effectiveness and adverse events (AEs), and persistence data are limited in PsA.

Objectives: Comparative analysis of 1-year persistence of UST and TNFi within the prospective PsABio cohort.

Methods: PsABio is an observational, multinational study of PsA patients (pts) treated with 1st to 3rd line UST or TNFi at their rheumatologist's discretion.[1] Treatment persistence (up to 15 months of follow-up) was defined as time between start of first bDMARD treatment in PsABio, and either stop or switch to another bDMARD, or withdrawal.

Persistence of UST and TNFi is shown by Kaplan-Meier curves and compared using Cox regression analysis, with propensity score (PS) to adjust for baseline imbalanced demographic and disease-related covariates (age, sex, bDMARD line, BMI, Clinical Disease Activity index for PSoriatic Arthritis [cDAPSA], 12-item PsA Impact of Disease [PsAID-12], Fibromyalgia Rapid Screening Tool [FiRST] score, co-treatments with MTX, NSAIDs, glucocorticoids, cardiovascular/metabolic comorbidities, dactylitis, enthesitis and body surface area [BSA]). Factors including concomitant MTX use and skin involvement: <3%, 3–10% and >10%, were added to the Cox model to investigate their impact on the PS-adjusted treatment effect.

Results: Of 438 and 455 pts who started UST and TNF, respectively, 121 (28%) and 134 (29%) stopped or switched treatment before Month 15, with differences (as expected) according to treatment line (Fig. 1a, b). Reasons for stop/switch were related to safety/AEs in 12% (UST) and 28% (TNFi), and effectiveness (joints, nails or skin) in 77% (UST) and 69% (TNFi) of pts.

The observed mean time on drug was 397 days for UST and 385 days for TNFi pts (1st line 410/397 days, 2nd 390/382 days, 3rd 381/338 days). Fig. 1b shows similar persistence for all drugs and treatment lines, except for lower persistence in TNFi 3rd line vs 1st/2nd. In PS-adjusted Cox analysis, no statistically significant difference between UST and TNFi persistence was seen; hazard ratio (HR; 95% CI) for stop/switch bDMARD (UST vs TNFi) was 0.82 (0.60, 1.13). In the model, bDMARD monotherapy (without MTX) and extensive skin involvement (BSA >10%), showed significantly better persistence for UST (HR 0.61 [0.42, 0.90] and 0.41 [0.19, 0.89] respectively; unadjusted Kaplan-Meier graphs shown in Fig. 1c, d). MTX co-therapy and low BSA did not affect the PS-adjusted treatment effect. Other factors added to the PS-adjusted Cox model did not show significant effects.

Conclusion: In this real-world PsA cohort undergoing bDMARD treatment, persistence was generally comparable for UST and TNFi, but some clinical situations led to better drug persistence with UST compared to TNFi – particularly monotherapy, more extensive skin involvement, and in 3rd-line treatment. Our data emphasise the importance of skin involvement for pts with PsA.

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SAT0399 RISK OF OSTEOARTHRITIS IN AN INCIDENT COHORT OF PEOPLE WITH PSORIATIC ARTHRITIS: A POPULATION-BASED COHORT STUDY

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory arthritis that causes pain, stiffness and swelling around the joints. PsA is reported to affect between 10 and 40% of individuals with psoriasis[1] and in the majority of patients presents after, or synchronously with, psoriasis onset.[2] Osteoarthritis (OA) is a common form of non-inflammatory arthritis related to joint degeneration and typically commences late in the fifth decade. PsA and OA have long been considered two distinct arthropathies, however they do have some overlapping features and symptoms and in certain circumstances it can be difficult to differentiate between them, particularly in the small joints of the hands or spine.[3]

Objectives: To determine the risk of a diagnosis of osteoarthritis in psoriatic arthritis patients compared to patients with psoriasis and a general population cohort.

Methods: Incident PsA patients aged 18-89 years at diagnosis were identified from the UK Clinical Practice Research Datalink between 1998 and 2014. All PsA patients were matched to a cohort of patients with psoriasis and a general population cohort (with no psoriasis or PsA) at a 1:4 ratio based on index date, year of birth, sex and general practice. The baseline prevalence of OA of any site was calculated as a percentage for each study cohort and then those prevalent cases were excluded from the numerators and denominators of the incident calculations. The incidence of OA was calculated and relative risks (RR_{adj}), adjusting for body mass index (BMI), were calculated using conditional Poisson regression.

Results: In total, 6,783 incident PsA patients were identified. The baseline prevalence of OA ranged from 22.1% (CI_{95}21.1-23.1) in the PsA cohort to 12.6% (CI_{95}12.2-13.0) and 11.0% (CI_{95}10.6-11.3) in the psoriasis and general population cohorts respectively. The incidence of OA was significantly higher in the PsA cohort compared to the psoriasis and general population cohorts after adjusting for BMI (RR_{adj} 1.68 CI_{95}1.46-1.93 and RR_{adj} 1.86 CI_{95}1.62-2.14 respectively) (Tables 1 and 2).

Conclusion: An increased risk of OA was observed in patients with PsA compared to patients with psoriasis alone and those in the general population. Further work is needed to determine whether this reflects a true increase in OA risk or misdiagnosed PsA and the extent to which it can be explained by differences in the opportunity for OA diagnosis between cohorts.

Table 1. Incidence of osteoarthritis in the PsA, psoriasis and general population cohorts

	Cases	Median age (years) at diagnosis (IQR)	Person years	Incidence rate per 10,000 person years	CI_{95}
Any OA†					
General population	1374	59 (51 - 66)	125,798	109.2	(103.5 - 115.0)
Psoriasis	1432	59 (53 - 67)	122,279	117.1	(111.0 - 123.2)
PsA	464	59 (51 - 66)	28,574	162.4	(147.6 - 177.2)

†including spondylosis

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Table 2. Risk of osteoarthritis in patients with PsA compared with patients in the general population and patients with psoriasis

	PsA compared with a general population cohort						PsA compared with a psoriasis cohort					
	Unadjusted			Adjusted†			Unadjusted			Adjusted†		
	RR	CI_{95}	*P*	RR	CI_{95}	*P*	RR	CI_{95}	*P*	RR	CI_{95}	*P*
OA	1.87	1.67-2.10	<0.0001	1.86	1.62-2.14	<0.0001	1.68	1.50-1.88	<0.0001	1.68	1.46-1.93	<0.0001

† adjusted for BMI taken as the closest entry within 3 years of the index date

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SAT0400

EVIDENCE FOR "DEEP KOEBNERISATION" AT BOTH THE ENTHESIS AND VASCULAR BIFURCATIONS AS A NOVEL MECHANISTIC LINK BETWEEN PSORIATIC ARTHRITIS AND CARDIOVASCULAR DISEASE- RESULTS OF PILOT ULTRASOUND STUDIES OF JOINTS AND ARTERIES

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Background: The association between PsA and cardiovascular disease is generally thought to be greater than the risk between psoriasis and cardiovascular disease. Vascular calcifications (VC) are considered an early marker of atherogenesis and accurate VC scores including Carotid, Aortic and Lower limbs vascular Calcifications (CALC) were published[2]. PsA localises to entheses that are sites of high physical stressing, analogous to artery bifurcations which are sites of high vascular stress. Entheseal calcification is a feature of the post-inflammatory changes. We hypothesised that there may be common "deep koebernisation" responses in the entheses and vessels in PsA as a common biomechanical response specifically linking PsA with cardiovascular disease

Objectives: To quantify non-coronary VC in a consecutive series of PsA patients using CALC score (CALCs) and compare PsA patients with CV risk factors to the group without. To independently evaluate sonographic entheseal changes including new bone formation and to determine if the magnitude of vascular and entheseal lesions was linked

Methods: 122 adult PsA patients diagnosed according to the CASPAR criteria underwent US assessment for the presence of VC according to CALCs. Carotids arteries intima-media thickness (IMT) was also measured. Blinded to this US assessment, further US imaging of 12 large entheseal sites was performed. The presence of enthesophytes was scored dichotomously for each site and summed up to generate the ARES score. Enthesophytes were scored semi-quantitatively in a 0-3 scale according to previous studies[3] to generate RESS score. Enthesal inflammatory changes were identified according with OMERACT definitions

Results: Overall, 83 patients were female (68%), mean age 58.6±10.3 y and mean PsA duration 9.5±7.0 y. PsA with obesity, metabolic syndrome and hypertension presented higher IMT values. The IMT scores correlated significantly with entheseal thickness (p< 0.001). A statistical significant correlation was found between CALCs with enthesophytes scores ARES and RESS (spearman rho = 0.665, p < 0.001 and 0.634, p < 0.001 respectively). CALCs, ARES and RESS were significantly increased in patients with CV risk factors or an history of CV events, compared with patients without (table 1). No significant correlation was found between CALCs and PsA duration (Spearman rho = 0.132, p = 0.135)

	PATIENTS, N. (%)	CALCs	ARES	RESS
Hypertension	50 (41%)	8.18 ± 6.20 **	6.55 ± 2.59 **	12.06 ± 5.91 **
No hypertension	72 (59%)	3.82 ± 4.24 **	4.79 ± 2.61 **	8.05 ± 5.40 **
Positive history of CV events	16 (13%)	11.5 ± 5.34 **	7.56 ± 2.50 *	13.56 ± 4.97 *
No CV events	106 (87%)	4.70 ± 5.02 **	5.16 ±2.64 *	9.06 ± 5.86 *
Obesity	31 (25%)	6.55 ± 5.03	6.63 ± 1.86 *	12.03 ± 4.96 *
No obesity	91 (75%)	5.48 ± 5.77	5.32 ± 2.85 *	9.17 ± 6.07 *
Hyperuricemia	14 (11%)	11.86 ± 8.15 *	7.43 ± 2.56 *	15.00 ± 5.33 **
No hyperuricemia	108 (89%)	4.65 ± 4.55 *	5.23 ± 2.68 *	8.97 ± 5.69 **
Dyslipidemia	54 (44%)	7.47 ± 6.43 **	5.90 ± 2.70	10.84 ± 6.13 *
No Dyslipidemia	68 (56%)	3.92 ± 4.03 **	5.11 ± 2.73	8.59 ± 5.58 *
Diabetes	11 (9%)	10.09 ± 7.29 *	7.18 ± 2.14 *	14.55 ± 5.20 *
No diabetes	111 (91%)	5.08 ± 5.16 *	5.31 ± 2.73 *	9.14 ± 5.79 *

* = p<0.05, ** = p<0.001

Conclusion: In PsA patients vascular and entheseal calcifications are significantly correlated. Patients with CV risk factors and/or history of CV events have higher values of CALCs, ARES and RESS. This suggests possible commonalites between entheses and vessels that might represent a deep Koebnerisation response in arteries and entheses. This raises the possibilities that the primary joint inflammatory responses and what is viewed as a comorbidity are closely linked

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SAT0401

SWOLLEN JOINTS ARE ASSOCIATED WITH ULTRASOUND POWER DOPPLER SYNOVITIS, WHEREAS TENDER JOINTS IN THE ABSENCE OF SWELLING ARE NOT: AN ANALYSIS OF AGREEMENT AND CORRELATION IN VERY EARLY DMARD NAÏVE PSORIATIC ARTHRITIS

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Background: Ultrasound (US) is an imaging adjunct to clinical joint examination adding sensitivity and objectivity to the assessment of inflammation. Previous studies in PsA have shown disparity between ultrasound and clinical findings with significant subclinical joint inflammation. A clinical challenge in PsA is to interpret tender joints (TJ) that are not swollen (SJ). As US is not widely used, alignment of clinical with US assessment is needed to determine its future role.
Objectives: To determine how joint clinical examination relates to US findings in very early DMARD naïve PsA.
Methods: Newly diagnosed DMARD naïve PsA patients, fulfilling CASPAR criteria, were recruited into the Leeds Spondyloarthropathy Register for Research and Observation (SpARRO), a prospective observational cohort study. US examination of 48 joints per patient was conducted by trained ultra-sonographers, blinded to clinical details with semi-quantitative scoring (0-3) for gray scale (GS) and power Doppler (PD). TJ and SJ counts were independently recorded. Cross-sectional baseline analysis was performed. The prevalence-adjusted and bias-adjusted kappa (PABAK) was calculated to determine agreements between clinical and US parameters. Spearman's rank correlation coefficient was calculated to identify permutations of TJ/SJ correlating with GS ≥2, PD≥1 or both.
Results: A total 5927 joints were scanned in 155 PsA patients. The mean age was 44.4 years, (SD 12.8), median disease duration 5.1 weeks (0.4-13.1); median TJC=7 (3-14) and SJC=2 (1-7). Oligoarthritis was present in 63.9% (99/155). US GS≥2 was frequently detected in the feet at MTPs1-4 (37.4- 53.6 %) and wrists (26.5- 33.6%). PD was most prevalent at wrists (17.5%) and MTP1 (12.6%) but observed less in other joints. Erosions were less frequent, the commonest site being MTP5 (17/310, 5.4%).
Overall, SJ demonstrated high agreement (p<0.001) with US synovitis (GS ≥2 and/or PD ≥1). High agreement was equivalent between combined GS ≥2 and PD ≥1 compared with PD ≥1 alone (p<0.001) indicating it was predominantly driven by PD. Agreement with TJ and US was consistently lower yet still significant (p<0.001). Combinations of TJ/SJ were explored with US synovitis (table 1). Correlation was significant for T+ S+ and PD≥1 at wrists, MCP1-5, PIP2-5, MCP3-4 (p<0.001); DIP2 (p<0.05), knees and ankles (p<0.01) but weaker correlation in MTP3,4. In contrast, poor correlation was observed in the T+ S- group for most joints.

Table 1. Agreement between TJ or SJ with GS≥2 & PD ≥1 and correlations for tender with/ without swollen combinations for right sided hand/feet joints.

	Tender		Swollen		T+ S-	T+ S+
Joint (Right)	A (%)	PABAK	A (%)	PABAK	r	r
Wrist	75.5	0.51*	89.1	0.78*	-0.09	0.35*
MCP1	84.1	0.68*	87.5	0.75*	0.09	0.44*
MCP2	77.7	0.55*	83.1	0.66*	0.08	0.35*
MCP3	79.1	0.58*	84.5	0.69*	0.005	0.50*
MCP4	78.4	0.57*	86.4	0.72*	0.07	0.22†
MCP5	87.8	0.76*	95.6	0.91*	-0.03	0.49*
MTP1	69.8	0.40*	83.9	0.68*	-0.03	-
MTP2	79.1	0.58*	90.5	0.81*	0.06	0.11
MTP3	77.0	0.54*	88.5	0.77*	0.05	0.22‡
MTP4	77.7	0.55*	87.2	0.74*	-0.002	0.23‡
MTP5	79.9	0.60*	89.9	0.80*	0.15	0.09

T+= tender, S+ =swollen, S- = not swollen, A=agreement (%), r =coefficient, † p<0.05, ‡ p<0.01, *p<0.001.

Conclusion: Swollen joints demonstrate higher agreement with US synovitis (PD≥1 alone or GS ≥2 & PD ≥1 combined) than tender joints in early PsA. In addition, joints that are tender but not swollen have poor correlation with US synovitis at the individual joint level indicating that swelling is a better clinical discriminator of active synovitis, and factors other than synovial inflammation may drive tenderness in very early, DMARD naïve PsA. These results suggest re-appraisal of clinical joint counts is needed to refine treatment decision making in early PsA.
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SAT0402

EFFICACY AND SAFETY OF GUSELKUMAB, A MONOCLONAL ANTIBODY SPECIFIC TO THE P19-SUBUNIT OF INTERLEUKIN-23, THROUGH WEEK 52 OF A PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY CONDUCTED IN BIOLOGIC-NAÏVE PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS

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Background: Guselkumab (GUS), a monoclonal antibody that specifically binds to the p19-subunit of IL-23, is approved to treat psoriasis. Through Week24 (W24) of the Ph3, double-blind, placebo (PBO)-controlled trial in biologic-naïve pts with active PsA (DISCOVER-2), GUS every 4 or 8 weeks (Q4W or Q8W) demonstrated efficacy for joint & skin symptoms and inhibition of structural damage progression (Q4W), and was well tolerated.
Objectives: Assess GUS efficacy and safety through W52.
Methods: Biologic-naïve adults with active PsA (≥5 swollen+≥5 tender joints; CRP ≥0.6mg/dL) were randomized (1:1:1) to GUS 100 mg Q4W; GUS 100 mg at W0, W4, Q8W; or PBO. At W24, PBO pts crossed over to GUS 100 mg Q4W (PBO X Q4W). ACR response rates at W52, based on nonresponder imputation (NRI) for missing data and as observed in pts who continued study agent at W24, are shown. Observed data for additional endpoints, including PsA-modified van der Heijde Sharp (vdH-S) scores derived from blinded radiographic images collected at W0, W24, W52 (or at d/c) and scored in a new Read Campaign, are shown.
Results: 712/739 (96.3%) randomized & treated pts continued study agent at W24; 689/739 (93.2%) completed Wk52. NRI ACR20 response rates continued to increase after W24, and at W52 were 70.6% for GUS Q4W and 74.6% for GUS Q8W (Fig 1A). Similar response patterns were observed for the more stringent ACR50/70 criteria (Fig 1C,E). Observed ACR (Fig, 1B,D,F), IGA, PASI & MDA/VLDA responses; dactylitis & enthesitis resolution; and mean improvements in HAQ-DI and SF-36 PCS/MCS scores were also sustained through W52 in pts receiving Q4W & Q8W; W52 data for PBO X Q4W pts were generally consistent with other GUS-treated pts (Fig 1, Table 1). Changes in vdH-S scores were

Table 1. Observed Efficacy[1]

	GUS	Q4W	GUS	Q8W	PBO X (W0-24)	GUS Q4W (W24-52)
Data are % unless otherwise stated	**W24**	**W52**	**W24**	**W52**	**W24**	**W52**
Dactylitis at W0, n	116	111	107	105	95	93
Resolution	68.1	81.1	60.7	81.9	41.1	78.5
Enthesitis at W0, n	165	160	151	148	172	168
Resolution	45.5	60.0	57.6	65.5	32.6	67.3
≥3% BSA psoriasis, IGA ≥2 at W0, n	176	173	172	170	176	172
IGA 0/1 + ≥2-grade decrease	71.0	84.4	72.1	77.1	19.9	84.3
PASI75	81.8	91.9	80.8	88.8	23.3	88.4
PASI90	63.6	81.5	70.3	77.1	10.2	76.7
PASI100	46.6	61.3	46.5	54.7	2.8	55.2
HAQ-DI, n	234	229	238	234	237	230
Mean change	-0.4	-0.5	-0.4	-0.5	-0.2	-0.4
SF-36 scores, n (mean change)	234	229	238	234	237	230
Physical Component - PCS	7.2	9.0	7.8	9.5	3.8	8.1
Mental Component - MCS	4.1	4.1	4.5	4.5	2.2	4.3
MDA/VLDA, n	234	228	238	234	238	231
MDA	19.7	36.8	26.5	32.9	6.3	31.6
VLDA	5.1	12.2[2]	4.6[3]	17.1	1.3	6.9

[1]Randomized pts still on study agent at W24; [2]N=229; [3]N=237

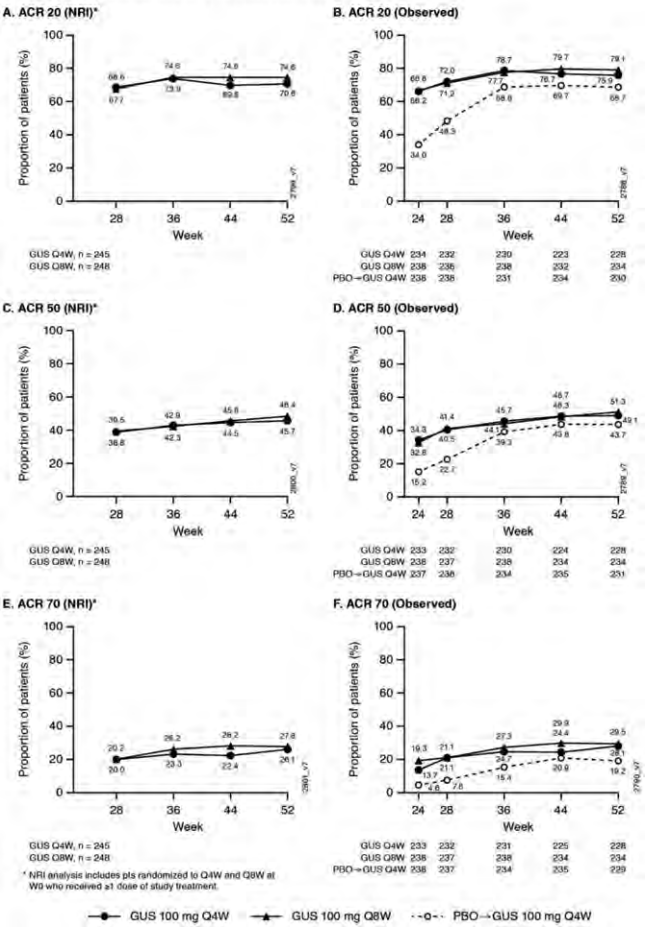
similar for W24-52 (0.62) and W0-24 (0.46) for Q4W; less radiographic progression occurred from W24-52 v W0-24 for Q8W (0.23 v 0.73) & PBO X Q4W (0.25 v 1.00). In 731 GUS-treated pts, 4.2% had SAEs; 1.2% had serious infections; no pt died; and no pt had IBD, opportunistic infections or active TB, or anaphylactic or serum sickness-like reactions.

Conclusion: In biologic-naïve pts with active PsA, GUS elicited sustained improvements in joint & skin symptoms; inhibition of radiographic progression & improvements in physical function, quality of life & composite indices through W52. GUS safety in PsA was similar at W24[1] & W52 and consistent with GUS safety in psoriasis.

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Fig 1. NRI and Observed ACR20 (**A & B**), ACR50 (**C & D**), and ACR70 (**E & F**) responses through W52 (Note: patients randomized to PBO crossed over to GUS Q4W at W24)



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SAT0403

EFFICACY AND SAFETY OF 108 WEEKS' BIMEKIZUMAB TREATMENT IN PATIENTS WITH PSORIATIC ARTHRITIS: INTERIM RESULTS FROM A PHASE 2 OPEN-LABEL EXTENSION STUDY

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Background: Bimekizumab (BKZ), a monoclonal antibody that selectively neutralises IL-17A and IL-17F, has shown clinical improvements in skin and joint outcomes over 48 weeks (wks) in patients (pts) with active psoriatic arthritis (PsA).[1]

Objectives: To report 2-year interim results from a phase 2b dose-ranging study (BE ACTIVE; NCT02969525) and open-label extension (OLE; NCT03347110) of BKZ in pts with PsA.

Methods: Design of the dose-ranging study is described elsewhere.[1] Pts who completed 48 wks' BKZ treatment without meeting withdrawal criteria were eligible for OLE entry. All OLE pts received BKZ 160 mg Q4W, irrespective of prior dosing regimen.

Data are presented from dose-ranging study baseline (BL) to OLE Wk 60 (Wk 108 total). Efficacy outcomes are reported for the full analysis set (FAS): pts who received ≥1 dose BKZ (specifically those randomised to 160 mg, 160 mg with 320 mg loading dose [LD], or 320 mg at BL), with BL efficacy measurements to allow subsequent determination of ACR50. Outcomes include ACR20/50/70, body surface area (BSA) 0%, minimal disease activity (MDA), and enthesitis/dactylitis resolution. Rates of treatment-emergent adverse events (TEAEs) are reported for the Safety Set (SS; pts who received ≥1 dose BKZ in the dose-ranging study).

Results: BL mean (SD) tender/swollen joint counts were 21.7 (15.7) and 11.2 (8.4). 80 (65.0%) pts had BSA ≥3% and dactylitis/enthesitis were present in 41 (33.3%) and 68 (55.3%) pts. Over 108 wks' BKZ treatment, improvements were observed in skin/joint outcomes: ACR50 (66.7%), BSA 0% (75.4%), MDA (65.6%), and resolution of dactylitis (65.9%) and enthesitis (77.9%) (Table). Serious TEAEs occurred in 9.3% pts (Table); no deaths or major adverse cardiac events were reported. Oral candidiasis occurred in 16 (7.8%) pts (no serious cases).

Conclusion: BKZ leads to long-term efficacy for skin/joint manifestations of PsA, with >50% pts achieving high thresholds of disease control (ACR50, BSA 0%, MDA) after 108 wks' treatment. The safety profile reflects previous observations.[1]

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Table. Outcomes at OLE Wk 60 (Wk 108 total)

	BKZ 160 mg [a] (N=82)		BKZ 320 mg [a] (N=41)		BKZ total (N=123)	
	OC	NRI	OC	NRI	OC	NRI
Efficacy (FAS) n (%)						
ACR20	53/62 (**85.5**)	53 (**64.6**)	29/37 (**78.4**)	29 (**70.7**)	82/99 (**82.8**)	82 (**66.7**)
ACR50	41/62 (**66.1**)	41 (**50.0**)	25/37 (**67.6**)	25 (**61.0**)	66/99 (**66.7**)	66 (**53.7**)
ACR70	34/62 (**54.8**)	34 (**41.5**)	19/37 (**51.4**)	19 (**46.3**)	53/99 (**53.5**)	53 (**43.1**)
BSA 0% [b]	35/42 (**83.3**)	–	14/23 (**60.9**)	–	49/65 (**75.4**)	–
MDA [c]	43/61 (**70.5**)	43 (**52.4**)	20/35 (**57.1**)	20 (**48.8**)	63/96 (**65.6**)	63 (**51.2**)
Dactylitis resolution	–	16/27 (**59.3**)	–	11/14 (**78.6**)	–	27/41 (**65.9**)
Enthesitis resolution [c]	–	34/45 (**75.6**)	–	19/23 (**82.6**)	–	53/68 (**77.9**)

Safety (SS) **n (%) [EAER]**	**BKZ 160 mg** [d] **(N=198)**	**BKZ 320 mg** [d] **(N=80)**	**BKZ total** [d, e] **(N=204)**
Any TEAE	163 (82.3) [160.9]	57 (71.3) [299.8]	179 (87.7) [181.1]
Study discontinuation due to TEAEs	17 (8.6)	1 (1.3)	18 (8.8)
Permanent withdrawal of study drug due to TEAEs	16 (8.1)	2 (2.5)	18 (8.8)
Drug-related TEAEs	72 (36.4)	29 (36.3)	92 (45.1)
Serious TEAEs	19 (9.6) [4.8]	0	19 (9.3) [4.1]

[a] BKZ 160 mg pts received this dose continuously to Wk 108 (includes those originally assigned to 160 mg with LD); BKZ 320 mg pts were dose-reduced to 160 mg at OLE entry; [b] Pts with BSA ≥3% at BL; [c] Data from OLE Wk 72 (Wk 120 total); [d] Dose received at TEAE onset (pts may be counted in multiple columns); [e] Includes pt time on BKZ 16 mg. EAER: exposure-adjusted event rate; NRI: non-responder imputation; OC: observed case.

Consultant of: UCB Pharma, Amgen, AbbVie, Lilly, Pfizer, Novartis, Gilead, Janssen

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SAT0404 INCIDENCE OF PSORIATIC ARTHRITIS FROM 2000-2017: A POPULATION-BASED STUDY

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory musculoskeletal disease with an estimated prevalence of 0.05% to 0.25% in the population and 6% to 41% in psoriasis patients. There is disparity in the reported incidence patterns in the general population in more recent years, with increasing incidence seen in Denmark, but relatively stable rates seen in Canada. However, no studies in the US have looked at the recent incidence patterns, and it would be important to see how newer therapies for psoriasis have impacted the incidence of PsA. Variability in the estimates of incidence and prevalence across different studies has been attributed to differences in case ascertainment and most studies have used ICD codes to identify PsA patients.

Objectives: To determine the annual incidence of PsA (2000-17) and compare it to incidence of PsA in previous years (1970-1999)[1] in the Olmsted County, Minnesota, USA population.

Methods: A retrospective, population-based cohort of PsA patients ≥18 years of age from Olmsted County, MN meeting CIASsification of Psoriatic ARthritis (CASPAR) criteria for PsA (2000-17) was identified from the Rochester Epidemiology Project (REP). REP ensures virtually complete ascertainment and follow-up of all clinically diagnosed cases of PsA in a geographically-defined area. The date of fulfillment of CASPAR criteria was taken as the PsA incidence date. Age- and sex-specific incidence rates, adjusted to 2010 US white population, were reported. Our previously reported cohort from REP (1970-1999)[1] also used the same CASPAR criteria, and trends from the current study were compared to the previous years.

Results: There were 170 incident cases of PsA, with a mean age of 46.7 (SD=12.3) years and 47% females from 2000-17. The overall age and sex adjusted annual incidence of PsA per 100,000 population was 8.8 (95% CI 7.5-10.1), and higher in males (9.7, 95% CI 7.7-11.7) than females (8.0, 95% CI 6.2-9.8). Overall incidence was highest in the age range 40-59 years (Table 1). The incidence rate was relatively stable in the recent years 2000-2017 compared to 1970-1999[1] where a rise in incidence was observed (3.6 to 9.8 per 100,000 persons from 1970-79 to 1990-99, p<0.001) (Figure 1).

Table 1. Annual incidence rate, IR (per 100,000) of psoriatic arthritis by age and sex between 2000-17 in Olmsted County, MN.

	Male		Female		Total	
Age Group, yrs	N	IR	N	IR	N	Rate
18-29	9	4.1	4	1.6	13	2.8
30-39	24	13.4	14	7.3	38	10.2
40-49	24	13.9	26	14.0	50	14.0
50-59	21	13.5	28	16.2	49	14.9
60-69	7	6.9	8	7.1	15	7.0
70-79	3	5.0	0	0.0	3	2.2
80+	2	6.0	0	0.0	2	2.2
Total (95% CI)	90	9.7 (7.7-11.7)†	80	8.0 (6.2-9.8)†	170	8.8 (7.5-10.1)††

† Age-adjusted to the 2010 US White population. †† Age- and sex-adjusted to the 2010 US White population

Conclusion: In the Olmsted County population, the increasing PsA incidence seen in previous years 1970-1999[1] seems to have leveled off after 2000. This is in contrast to increasing incidence in recent years reported from Denmark, Taiwan and Israel. However, similar to our study, incidence rates for PsA from 2008-2015 were reported to be stable in Canada.

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SAT0405 CLINICAL AND PSYCHOLOGICAL PREDICTORS OF GASTROINTESTINAL INTOLERANCE TO METHOTREXATE IN PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Methotrexate (MTX) is a first-line treatment for psoriatic arthritis (PsA). Gastrointestinal intolerance (GI) to the drug is a common adverse event

that limits its use and can be mediated by autonomic dysfunction or classical conditioning phenomena to repeated drug exposure. Anxiety and depression could promote these processes.

Objectives: To assess the prevalence of GI to MTX and its association with anxiety and depression in PsA patients.

Methods: One hundred unselected PsA patients in stable MTX treatment were characterized by disease characteristics, adherence to treatment by Morisky Medication Adherence Scale (MMAS-8) and comorbidity by Rheumatic Disease Comorbidity Index (RDCI). Depressive and anxious symptoms were assessed by Hospital Anxiety and Depression Scale (HADS). The presence and the severity of nausea, vomiting, abdominal pain and diarrhoea after administration (associative symptoms) and just before or even at the thought of taking MTX (anticipatory symptoms) were recorded.

Results: Patients had a mean age of 56.9±12.0 years and a disease duration of 9.5 years (0.1-58.0 years). They were male, smokers and overweight in 40.0%, 20.0% and 65.0% of cases, respectively. The prevalence of both significant anxious and depressive symptoms was 42.0%. DAPSA showed remission, low disease activity (LDA), moderate disease activity (MDA) and high disease activity (HDA) in 24.0%, 41.0%, 32.0% and 3.0% of patients, respectively. MTX was taken orally by 15.0% of patients and associated with another conventional or biological DMARD in 14.0% and 35.0% of cases, respectively. Symptoms of GI to MTX were complained by 69.3% of patients. Specifically, the prevalence of nausea, diarrhea, vomiting and abdominal pain was 59.0%, 23.0%, 21.0% and 30.0% with associative pattern and 43.0%, 12.0%, 10.0% and 16.0% with anticipatory pattern, respectively. Patients with anxious symptoms experienced more frequently moderate to severe associative nausea (71.4% vs 50.0%, p=0.032) and abdominal pain (42.9% vs 20.7%, p=0.017), and anticipatory nausea (42.9% vs 19.0%, p=0.009), vomiting (14.3% vs 6.9%,p=0.046), and abdominal pain (26.2% vs 8.6%, p=0.018) than non-anxious patients. Patients with depressive symptoms more commonly had associative diarrhea (33.0% vs 15.5%, p=0.037), with no difference in the prevalence of anticipatory symptoms. The presence of associative and anticipatory nausea was associated with higher anxiety scores (p=0.006 and p=0.02 respectively) without differences in the depression score. Associative nausea characterized younger patients (p=0.001), female (p=0.02), with lower BMI (p=0.02) and treated with higher MTX doses (p=0.05). Anticipatory nausea was associated with a lower age (p=0.02), a lower BMI (p=0.005), a longer disease duration (p=0.028), a lower DAPSA (p=0.02), an higher MTX doses (p=0.02) and a lower comorbidity burden (p=0.03). The anticipatory and associative nausea determined lower compliance according to MMAS-8 (p=0.007 and p=0.001, respectively). An anxious profile characterized patients with moderate to severe associative nausea also in the logistic regression model corrected for age (≥65 years), gender, BMI (≥25 kg/m2) and MTX dose (≥0.2mg/kg/week) (OR 3.0, IC 1.1-8.4, p=0.036), and patients with anticipatory nausea also in the model corrected for age (≥65 years), gender, BMI (≥25 kg/m2) and MTX dose (≥0.2mg/kg/week) and disease duration (≥6 years) (OR 3.0, IC 1.1-8.0,p=0.027).

Conclusion: Up to two-thirds of patients with PsA who have been treated with MTX experienced symptoms of GI, leading to reduced therapeutic adherence. Associative and anticipatory symptoms characterize patients with a specific clinical and psychological profile.

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SAT0406 THE ASSOCIATION BETWEEN PERIPHERAL ENTHESITIS SCORES AND NAILFOLD VIDEOCAPILLAROSCOPY FINDINGS IN PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Enthesitis is one of the key feature of psoriatic arthritis (PsA), it is usually overlooked in the asymptomatic patients. Nail disease often precedes PsA and nailfold videocapillaroscopy (NVC) is a useful technique for evaluating changes in microcirculation of nail that is considered to play an important role for early detection of enthesitis and PsA [1-4].

Objectives: To investigate the link between NVC findings and severity of peripheral enthesitis scores in patients with PsA.

Methods: In this cross-sectional single center study, 34 consecutive PsA patients and as control group (healthy controls - HC), 22 subjects without rheumatic diseases were involved. Psoriasis area severity index (PASI) was used to express severity of psoriasis (Ps) and percentage of affected area. Leeds enthesitis index (LEI) comprised assesment of lateral epicondyles of humerus, medial condyles of femur, and the insertion of the Achilles tendon. Madrid Sonographic Enthesitis Index (MASEI) was applied to quantify the extent of sonographic entheseal abnormalities. MASEI-inflammatory, MASEI-damage and as a sum of these MASEI-total scores were recorded. NVC was performed on eight fingers in each subject.

Results: We enrolled 34 patients with PsA (median age=47.74 years, median disease duration=6.91 years) and 22 HC (median age=46.77 years). There were no significant differences between two groups concerning age, gender distribution and body mass index. Ps and PsA disease duration in terms of years were not correlated with MASEI and NVC scores. PASI score associated with MASEI-inflammatory score (r=0.40, p=0.01). There were significant correlation between the NVC score and MASEI-inflammatory (r=0.53, p=0.001) and MASEI-total scores (r=0.35, p=0.04) (Table 1). No association was found between LEI and NVC scores (p=0.34). MASEI enthesitis and NVC scores were significantly higher in the patient group (p=0.00).

Table 1. Correlation between the capillaroscopy findings and MASEI-inflammatory and MASEI-total scores in patients with psoriatic arthritis

MASEI	Capillaroscopy	
	PsA	HC
MASEI-inflammatory		
r	0.53**	0.7
p	***0.001***	0.75
MASEI-total		
r	0.35*	0.19
p	***0.04***	0.38

Spearman's Correlation Coefficient; ** Correlation is significant at the 0.01 level (2-tailed), * Correlation is significant at the 0.05 level (2-tailed).
p< 0.05 statistic significance
MASEI: Madrid Sonographic Enthesitis Index, PsA: psoriatic arthritis, HC: healthy controls

Conclusion: NVC may objectively reflect the peripheric enthesopathy severity and give opportunity for early diagnosis of PsA.

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SAT0407 FOLLOW-UP EXAMINATION FOR THE DETECTION OF POTENTIAL PSORIATIC ARTHRITIS BY FLUORESCENCE OPTICAL IMAGING – IN COMPARISON TO MUSCULOSKELETAL ULTRASOUND

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Background: Up to 30% of all plaque-type psoriasis patients develop psoriatic arthritis (PsA) (1). Early diagnosis of PsA can be difficult due to its heterogenous manifestation and the lack of disease- specific biomarkers, but it is crucial for disease outcome. Recently, our group has shown that fluorescence optical imaging (FOI) can be a helpful diagnostic tool for early PsA diagnosis since it can differentiate between patients with confirmed PsA and suspected PsA (2).

Objectives: To follow-up patients by FOI with confirmed and suspected PsA with special focus on the group of patients in which PsA could be confirmed between baseline and follow-up – and to compare with the findings of musculoskeletal ultrasound (US).

Methods: Patients included in our previous study (1) were re-evaluated by FOI of both hands in a standardized manner using the predefined phases 1-3 (p1-p3) and the PrimaVistaMode (PVM). US in greyscale (GS) and power Doppler (PD) were performed of the clinically dominant hand (for tenderness and/or swelling)

in the dorsal and palmar view at wrist, MCP, PIP and DIP 2-5 joint levels for synovitis and tenosynovitis.
Subsequently, a comparison of the findings in the affected joints was performed using US as the reference method. Furthermore, AUC was calculated to show the extent to which a new joint inflammation was associated with a change in diagnosis.
Results: Of the 60 patients initially examined (1), 30 patients (dropout rate 50%) were followed-up approximately 3 years later. The patients were newly divided into 3 groups: Diagnosed PsA (n=14, Group I), still suspected PsA, (n=6, Group II) and in-between diagnosed PsA (n=10, Group III). Patients with a change in the diagnosis from suspected to diagnosed PsA (Group III) showed a significantly increased prevalence of joints with pathological findings in FOI (46% at baseline, 88% at follow-up; p=0.046), with an unchanged joint distribution pattern, i.e. with a dominant involvement of the DIP joints. Compared to baseline, patients of group III were three times more common to show enrichment in p3 in FOI at follow-up (1.7% vs. 7.0%; p=n.s.). Newly detected pathologic joints by FOI (PVM, p2) and US at follow-up were positively associated with the change of diagnosis from suspected PsA to confirmed PsA (FOI: AUC 0.78; GSUS: AUC 0.77).Using US in greyscale as reference, inflammatory changes in the joints were diagnosed in all 3 cohorts by means of FOI in P1 and P3 with high specificity (Group III: 90.6%, Group II: 97.5%, Group I: 94.2%) and low sensitivity (Group III: 24.4%, Group II: 20.3%, Group I: 19.8%).
Conclusion: FOI appears to be helpful to differentiate between acute and chronic disease stages. Furthermore, it is specific for detecting inflammatory changes in the joints of the hands in PsA – in comparison to US. FOI could thereby become a helpful tool as a "dermatological-screening" method to select psoriasis patients with indication for further rheumatological evaluation.
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SAT0408 UTILITY OF CAROTID ULTRASOUND AND FRAMINGHAM RISK SCORE ON DISCRIMINATING CORONARY ARTERY DISEASE IN PATIENTS WITH PSORIATIC ARTHRITIS (PSA)

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Background: While carotid ultrasound (US) has been advocated for cardiovascular (CV) risk screening in patients with rheumatoid arthritis as various traditional scores underestimate CV risk, whether subclinical carotid atherosclerosis (SCA) is associated with coronary atherosclerosis on coronary computed tomography angiography (CCTA) in patients with psoriatic arthritis (PsA) remains uncertain.
Objectives: This study aimed to identify carotid US parameters which can discriminate PsA patients with coronary artery disease (CAD) and obstructive CAD (O-CAD), and determine the utility in combination with Framingham Risk Score (FRS).
Methods: Ninety-one PsA patients (56 males; age: 50±11years, disease duration: 9.4±9.2years) without overt CV diseases were recruited. Carotid intima-media thickness (cIMT), presence of plaque and total plaque area (TPA) were determined by high-resolution US. CAD was defined as the presence of any coronary plaque on CCTA. O-CAD was defined as >50% stenosis of the lumen. FRS <10% indicates low CV risk, 10-19% indicates intermediate risk while ≥20% indicates high risk (1).
Results: Thirty-five (38%) patient had carotid plaque. Fifty-five (60%) patients had CAD and 9 (10%) patients had O-CAD. 53 (58%), 25 (17%) and 13 (14%) were classified as low, moderate and high CV risk according to the FRS respectively. FRS underestimated the CV risk as only 11/55 (20%) of subjects with CAD were correctly identified as having high CV risk by FRS (Figure 1). Fifteen patients out of 53 (28%) with low CV risk based on FRS were reclassified as high CV risk by the presence of carotid plaque. Nine out of these 15 (60%) had CAD and 1/15 (6.7%) had O-CAD. Concerning the carotid ultrasound parameters, cIMT (mean and maximum) and TPA were increased in both the CAD+ and O-CAD+ group compared to those without CAD or O-CAD (Table 1). Multivariate logistic regression analysis revealed that mean cIMT (OR=1.06, 95% CI:1.01-1.11, *p*=0.013) was an independent explanatory variables associated with CAD. Meanwhile, mean cIMT (OR=1.06, 95%CI: 1.01-1.11, *p*=0.013) maximum cIMT (OR=1.06, 95%CI: 1.00-1.13, *p*=0.043), and TPA (OR=1.55, 95%CI: 1.01-2.36, *p*=0.043) were independent explanatory variables associated with O-CAD after adjusting for covariates. Based on Receiver Operating Curve (ROC) analysis, an optimal cut off for FRS at 5% and mean cIMT at 0.62mm yield 63% sensitivity and 73% specificity for the presence of CAD (AUC: 0.71, *p*=0.001).

Table 1. Relationship between carotid ultrasound parameters and the presence and extent of coronary artery disease on coronary computed tomography angiography.

	Coronary artery disease		
	No (n=37)	Yes (n=54)	*p*
Mean carotid IMT, mm	0.63 ± 0.12	0.69 ± 0.1	**0.017**
Maximum carotid IMT, mm	0.77 ± 0.17	0.84 ± 0.14	**0.040**
Carotid Plaque, n, %			
Absence	26 46.4%	30 53.6%	0.156
Presence	11 31.4%	24 68.6%	
Total plaque area, mm^2	0.0 [0,6]	0.0 [0, 10.8]	0.059
	Obstructive coronary artery disease		
	No (n=82)	Yes (n=9)	*p*
Mean carotid IMT, mm	0.65 ± 0.12	0.76 ± 0.07	**0.011**
Maximum carotid IMT, mm	0.80 ± 0.16	0.93 ± 0.14	**0.020**
Carotid Plaque, n, %			
Absence	53 93.0%	4 7.0%	0.235
Presence	29 85.3%	5 14.7%	
Total plaque area, mm^2	0.0 [0, 7.0]	6.0 [0, 15.3]	0.103

IMT-intima media thickness; coronary computed tomography angiography.

Conclusion: Increased cIMT and TPA were associated with CAD and O-CAD in PsA patients while the presence of carotid plaque alone was insufficient to discriminate patient with or without CAD. A combination of US parameters should be considered for CV risk stratification in patients with PsA.
References:
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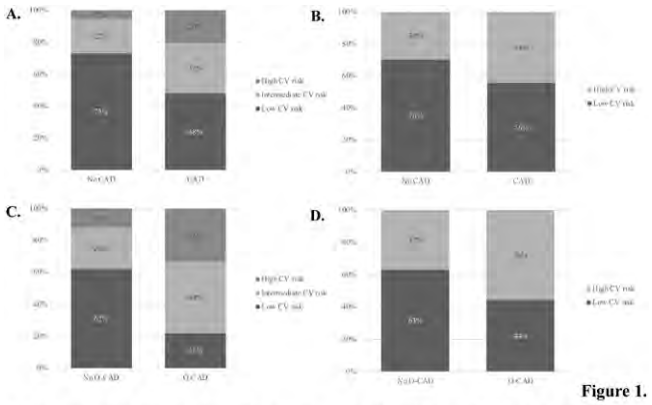


Figure 1.
CV Risk classification based on Framingham risk score (FRS) (A&C) (high CV risk: FRS ≥20%; intermediate CV risk: FRS 10-19%; low CV risk: FRS<10%) and CV Risk classification based on the presence of carotid plaque (high CV risk) and absence of carotid plaque (low CV risk) (B&D) in patient with or without CAD/.O-CAD

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SAT0409 BIOLOGIC TREATMENT IN PSORIATIC ARTHRITIS AND AXIAL SPONDYLOPATHY REDUCES SICKNOTES ISSUED BY GPS, DESPITE DELAYS IN DIAGNOSIS: A REAL-LIFE STUDY IN WALES.

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Background: Seronegative inflammatory arthritis including psoriatic arthritis (PsA) and axial spondyloarthropathies (AxS) are chronic inflammatory diseases associated with significant morbidities. The National Institute of Health and Clinical Excellence (NICE) has produced several pieces of guidance on disease management including the use of biologic therapies which have been shown to improve patient outcomes and quality of life. However, there are limited real-life data on patient journey from symptom onset to diagnosis and treatment including with biologics in the UK.

Objectives: The purpose of this study is to examine the real-life patient journey from symptom onset to diagnosis and treatment.

Methods: Data from the Secure Anonymised Information Linkage (SAIL) databank in Wales, which holds over a billion anonymised records, were used to assess the treatment of patients with PsA or AxS, aged 18 years or over with at least one READ code present for PsA or AxS in their primary care records. We examined the drug use of patients across primary, secondary care and specialist rheumatology clinics to explore the use of NSAIDs, DMARDs and biologics in the real-life setting while exploring demographics, comorbidities and surgical procedures of 1829 PsA and 908 AxS patients.

Results: The AxS patients were significantly younger at diagnosis and were predominantly male. Typical delays in diagnosis of 8-9 years from symptom onset were observed. The rate of stopping or switching a biologic medication was similar for AxS and PsA patients (Table 1). There was a significant reduction in sicknotes issued following biologic initiation for PsA (Difference: 14.6%, 95% CI: 8.7% to 20.4%) and AxS (Difference 16.9%, 95% CI: 10.5% to 23.3%)

Table 1. Characteristics of treatment of PsA and AxS patients

	PsA (n=1829)	AxS (n=908)	Difference (95% CI)
Female (%, n)	55.1% (1007)	29.1% (264)	26 (22.2 to 29.6)*
Mean age at diagnosis (years, SD)	46.9 (14)	43.5 (14.4)	3.4 (2.3 to 4.5)*
BMI (Index, SD)	30.3 (6.3)	28 (5.8)	2.3 (1.8 to 2.8)*
Time from symptom to diagnosis (years, SD)	8.9 (5.5)	8.0 (5.6)	0.9 (0.5 to 1.3)
Hypertension at diagnosis (%, n)	24.2% (442/1829)	19.4% (176/908)	4.8 (1.5 to 8.0)*
Time from diagnosis to biologic (years, SD)	6.3 (4.7)	6.1 (5.0)	0.2 (-0.9 to 0.5)
Used a Biologic (%, n)	23% (420/1829)	36.8% (334/908)	13.8 (10.2 to 17.5)*
NSAIDs used pre-biologic (SD)	11.3 (3.2)	11.6 (3.2)	0.3 (-0.2 to 0.8)
Number of DMARDs used pre-biologic (SD)	3.1 (1.5)	2.5 (1.7)	0.6 (0.4 to 0.8)*
Biologic treatment change/ failure (%, n)	21.6% (92/425)	22% (74/336)	0.4 (-6.4 to 5.5)
Sicknotes issued by GP[ɪ] pre-biologic (SD)	33.9% (144/425)	33.6% (113/336)	0.3 (-6.5 to 7.0)
Sicknotes issued by GP [ɪ] post-biologic (SD) (%, n)	19.3% (82/425)	16.7% (56/336)	2.6 (-2.9 to 8.0)
Hospitalised for serious infection pre- diagnosis (%, n)	7.2% (131/1829)	6.3% (57/908)	0.9 (-1.2 to 2.8)
Hospitalised for serious infection post- diagnosis (%, n)	10.4% (190/1829)	11.6% (105/908)	1.2 (-1.3 to 3.8)
Hospitalised for serious infection post- biologic (%, n)	5.6% (24/425)	6.3% (21/336)	0.7 (-2.8 to 4.2)

* Significant at p<0.05

ɪ General practioner/Primary care physician

Conclusion: Patients with PsA and AxS were treated with NSAIDs and DMARDs prior to receiving biologic medication in accordance with NICE guidelines. However, there was a long delay from symptom onset to diagnosis. Biologic treatment reduced sicknotes issued by GPs confirming the benefit of biologic treatment on work productivity observed in clinical trials.

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SAT0410 EFFICACY AND SAFETY OF IXEKIZUMAB IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS BASED ON CONCOMITANT CONVENTIONAL DISEASE-MODIFYING ANTIRHEUMATIC DRUGS (CDMARD) USE: RESULTS FROM SPIRIT-P1 AND SPIRIT-P2

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Background: Biologic disease-modifying antirheumatic drugs such as ixekizumab (IXE), a high-affinity monoclonal antibody that selectively targets interleukin (IL)-17A, are commonly prescribed to patients with psoriatic arthritis (PsA) in combination with conventional synthetic disease-modifying antirheumatic drugs (cDMARDs). Previous studies have shown that, after 24 weeks of treatment, IXE is efficacious with or without concomitant cDMARD therapy in patients with active PsA.[1,2] However, there is limited evidence demonstrating efficacy and safety after 3 years of treatment.

Objectives: To evaluate the long-term (3-year) efficacy and safety of IXE in patients with active PsA from SPIRIT-P1 (NCT01695239) and SPIRIT-P2 (NCT02349295) based on concomitant cDMARD use.

Methods: Patients were subdivided into the following subgroups: 1) no cDMARD use for 3 years (ixekizumab monotherapy); 2) methotrexate (MTX) use without interruption (i.e., ≤14-day gap of not using MTX), but allowing a change of MTX dose; and 3) any cDMARD (MTX, sulfasalazine, leflunomide, ciclosporin, hydroxychloroquine) use during 3 years without interruption (i.e., ≤14-day gap of not using cDMARDs), but allowing a switch of cDMARD type and/or change of dose. The post-hoc integrated analysis assessed efficacy and safety up to 3 years by three subgroups. Efficacy outcomes included the American College of Rheumatology (ACR) 20/50/70, Psoriasis Area and Severity Index (PASI) 75/90/100, Health Assessment Questionnaire-Disability Index (HAQ-DI) ≥0.35-point improvement. Missing data were imputed using modified non-responder imputation. The IXE 80 mg every 4 weeks (IXEQ4W) dose data are reported here.

Results: Overall, IXE-treated patients showed improvement in all efficacy outcomes over 156 weeks, regardless of concomitant cDMARD use. ACR response rates by concomitant cDMARD use at 156 weeks are highlighted in Figure 1. Patients treated with IXEQ4W in the no cDMARD use, MTX, and any cDMARD use subgroups had similar ACR20 (59.1%, 67.0%, and 66.1%, respectively), ACR50 (46.2%, 47.4%, and 46.8%, respectively), and ACR70 (30.7%, 28.4%, and 28.1%, respectively) response rates at 156 weeks. Patients treated with IXEQ4W in the three subgroups also had similar PASI75 (65.5%, 60.8%, and 59.8%, respectively), PASI90 (53.6%, 49.7%, and 48.0%, respectively), and PASI100 (42.2%, 46.2%, and 42.4%, respectively) response rates at 156 weeks. The proportion of patients achieving HAQ-DI improvement ≥0.35 in the three subgroups (51.9%, 45.0%, and 47.5%, respectively) was comparable. The safety profile of IXEQ4W was consistent with that previously reported.[1,2] A similar proportion of IXEQ4W-treated patients in the three subgroups reported ≥1 treatment-emergent adverse events (TEAEs) regardless of the addition of MTX or other cDMARDs (91.0%, 84.1%, and 83.2%, respectively), and the majority of TEAEs were mild or moderate in all three subgroups.

Conclusion: IXEQ4W provided sustained improvements in the signs and symptoms of active PsA. While there are some numerical differences in ACR20/50/70 as well as PASI75/90/100, the overall responses with or without the addition of MTX or other cDMARDs were similar. In this post-hoc analysis, it appears that, for sustained responses over time, IXEQ4W does not require the addition of MTX or other cDMARDs. Addition of MTX or other cDMARDs to IXEQ4W did not negatively impact its favorable long-term safety profile.

References:

[1] Coates LC, Kishimoto M, Gottlieb A, et al. RMD Open 2017.

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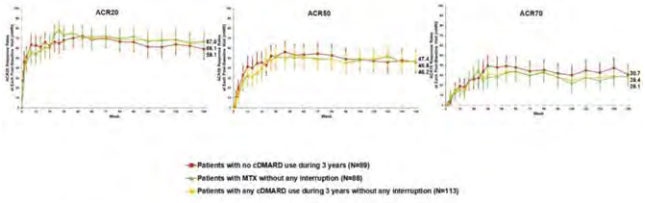


Figure 1. ACR20, ACR50, and ACR70 Response Rates (IXEQ4W treatment) at Each Post-Baseline Visit by Concomitant cDMARD Use. Abbreviations: ACR, American College of Rheumatology; AE, adverse event; cDMARD, conventional synthetic disease-modifying antirheumatic drugs; IXEQ4W, ixekizumab 80 mg every 4 weeks; mNRI, modified non-responder imputation.

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SAT0411 EFFICACY AND SAFETY OF IXEKIZUMAB IN PATIENTS WITH PSORIATIC ARTHRITIS AND INADEQUATE RESPONSE TO TNF INHIBITORS: THREE YEAR RESULTS FROM A PHASE 3 STUDY (SPIRIT-P2)

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Background: Ixekizumab (IXE) is a high affinity monoclonal antibody that selectively targets interleukin-17A. In the SPIRIT-P2 study, IXE every 4 (Q4W) or 2 (Q2W) weeks was superior to placebo (PBO) in improving the signs and symptoms of psoriatic arthritis (PsA) at Week 24 in patients (pts) with prior inadequate response or intolerance to 1 or 2 tumor necrosis factor inhibitors (TNFi).
Objectives: To determine efficacy and safety of IXE treatment up to 3 years in pts with PsA.
Methods: In SPIRIT-P2 (NCT02349295), 310 pts entered the extension period where pts maintained their original ixekizumab dose, and placebo pts received IXEQ4W or IXEQ2W (1:1). Pts failing to demonstrate ≥20% improvement in both tender and swollen joint counts at Week 32, or any subsequent visit, were discontinued (mandatory discontinuation criteria). Efficacy outcomes were ACR20/50/70 response, Psoriasis Area and Severity Index (PASI) 75/90/100 response, Leeds Enthesitis Index (LEI), Leeds Dactylitis Index-Basic (LDI-B), Minimal Disease Activity (MDA), and Disease Activity in Psoriatic Arthritis (DAPSA). Ad-hoc efficacy data are presented for intent-to-treat (ITT) pts initially randomized to IXE at Week 0. Observed and modified non-responder imputation (mNRI; missing data treated as non-response for pts discontinued due to lack of efficacy or adverse events [AEs]) was applied to categorical measures. Observed and modified baseline observation carried forward (mBOCF) was applied to continuous efficacy measures. Safety was analysed in pts exposed to at least one dose of IXE.
Results: Of the 245 pts initially randomized to IXE at Week 0 (ITT), 64 (26.1%) pts discontinued due to lack of efficacy and 22 (9.0%) pts due to mandatory discontinuation criteria. Efficacy results are summarized below (Figure 1). Pts in SPIRIT-P2 who received IXEQ4W and IXEQ2W for 156 weeks reported sustained improvement in ACR responses and manifestations of PsA, including enthesitis, dactylitis, and skin outcomes. Treat-to-target measures such as MDA and DAPSA (Low Disease Activity or Remission) were achieved by 30.8% and 47.7% of pts, respectively on IXEQ4W, and by 29.2% and 40.7% of pts, respectively on IXEQ2W. Incidence rates (IR) of treatment-emergent adverse events (TEAEs) are provided below (Figure 2). Most TEAEs were mild or moderate in severity, and 38 out of 337 (5.9%) pts (safety population) discontinued due to AEs. The most common TEAEs were infections (IR=33.1) and injection site reactions (IR=5.4). Three deaths were reported in the study.

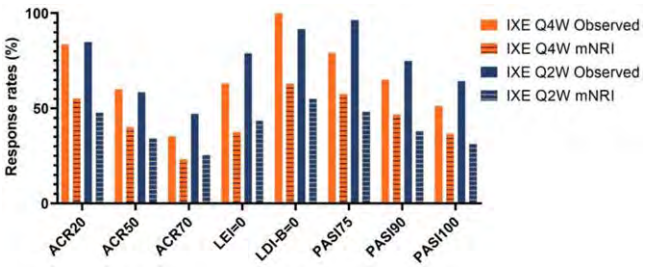


Figure 1. Efficacy Outcome Measures at Week 156 (Intent-to-treat Population). ACR=American College of Rheumatology; IXE=ixekizumab; LEI=Leeds Enthesitis Index; LDI-B=Leeds Dactylitis Index-Basic; mNRI=modified non-responder imputation; PASI=Psoriasis Area and Severity Index; Q2W=every two weeks; Q4W=every four weeks.

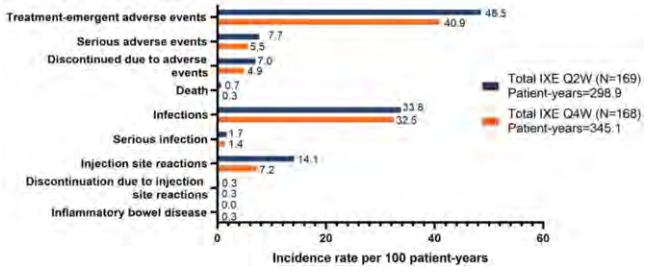


Figure 2. Safety Outcome Measures (Weeks 0-156). Safety was analysed in patients exposed to at least one dose of ixekizumab. During the double-blind treatment period (Weeks 0-24), one patient reported serious adverse events of anal fistula and anal abscess, which were considered by the sponsor to be IBD; however, an independent adjudication committee of external experts reviewed the case and determined the events to be "Not IBD."

Conclusion: In pts treated with IXE who had prior inadequate response or intolerance to 1 or 2 TNFi, improvements in the signs and symptoms of PsA persisted up to 3 years. No unexpected safety signals were observed, and the safety profile was consistent with previous studies of IXE.
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SAT0412 ACCURACY OF AN INSTRUMENT FOR SCREENING PSORIATIC ARTHRITIS AMONG PSORIATIC PATIENTS: RESULTS FROM THE MULTICENTRE ITALIAN STUDY HERACLES (SCREENING STRATEGIES FOR RHEUMATOLOGICAL REFERRAL OF PSORIATIC SUBJECTS AIMED TO DISCLOSE PSORIATIC ARTHRITIS)

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Background: Identifying psoriatic arthritis (PsA) among people with psoriasis is often challenging due to low specificity of symptoms at early PsA stage and/or delayed referral to the rheumatologist. Screening instruments -assisting the dermatologist to decide when rheumatological assessment is beneficial- have potential to reduce the diagnostic delay.

Objectives: To evaluate the accuracy of a dermatologist-filled-out questionnaire designed for screening PsA among psoriatic patients under dermatology care.

Methods: HERACLES is a multicentre, cross-sectional study running at 9 Italian dermatology and rheumatology tertiary centres. All participants were under dermatology care for skin psoriasis. Previous diagnosis of PsA precluded eligibility. Dermatologists at each site assessed consecutive psoriatic subjects, filled in the specifically-designed HERACLES questionnaire (HQ, Figure 1) and finally referred the participants to rheumatologists for clinical evaluation. All participants filled in the ToPAS, PASE, PEST and EARP questionnaires. Rheumatologists assessed the participants regardless of the questionnaires' scores. The gold standard applied to assess the instruments' accuracy was the diagnosis of PsA as established by the rheumatologists. ROC curve analysis evaluated the performance of the scores associated with the clinical criteria listed in the HQ, estimating the sensitivity and specificity of different cut-off levels. Further exploratory ROC curve analysis compared HQ performance to that of the other four questionnaires tested.

Final set of clinical referral criteria: model of a form

CENTRE NAME

PATIENT'S DETAILS	Surname Name	Date of birth Age Sex	Date of collection
	Psoriasis form	Age at psoriasis onset	Nail psoriasis YES NO
	Familial history for psoriasis	Familial history for rheumatoid arthritis, ankilosing spondylitis or psoriatic arthritis	Height Weight Current PASI score
	Current dermatological therapies	Previous dermatological therapies	

The patient complains of musculo-skeletal discomfort **YES** **NO**

	ITEM	DETAILS	YES	NO	ITEM SCORE
1	**The patient complains of arthralgias**	Pain in one or more articular sites, continuous for at least 6 weeks, not due to trauma. The complain may be spontaneous or elicited	1	0	
2	**The patient complains of spinal pain**	Mostly at night, continuous, improves with exercise, insidious onset, for at least 8 weeks	1	0	
3	**The patient reports history of heel discomfort**	Entheses are the sites of insertion of tendons, ligaments and muscles on bones. The most important sites are the plantar fascia and Achilles' tendon at the heels	1	0	
4	**The dermatologist sees joint swelling**	Articular swelling, usually associated with pain, warmth and redness, not due to trauma	1	0	
5	**The patient reports history suggestive of dactylitis OR The dermatologist sees digital swelling**	Finger(s) or toe(s) are swollen, appearing as "sausages". There may be redness and pain, the onset may be insidious or acute. Rule out trauma. Comparison of the involved finger/toe with the other side is usually very helpful.	2	0	
6	**The dermatologist sees joint deformity**	Alteration of joints profiles, telescoping fingers/toes	1	0	
7	**The dermatologist sees the patient limping**	The patient comes to visit limping. Rule out trauma. Investigate elective surgery	1	0	
		TOTAL SCORE (0-8)			

If total score is 2 or more, consider referral to rheumatologist

Figure 1.

Results: Out of 759 subjects enrolled, 524 (69%) attended rheumatology assessment. Rheumatologists diagnosed PsA in 73/524 patients (13.9%, Figure 2). Mean age was 53 (SD 16) years and 46% were female. Mean psoriasis duration was 20 (SD 19) years. The area under the ROC curve of HQ was 0.775. The HQ score cut-off value of 2 yielded a sensitivity of 92% and a specificity of 47%; a cut-off value of 3 yielded a sensitivity of 66% and a specificity of 75%. The comparison between the ROC curve of the HQ and those of the other four questionnaires evaluated did not show any significant difference (p=0.523 versus TOPAS; p=0.201 versus PASE; p=0.345 versus PEST and p=0.240 versus EARP).

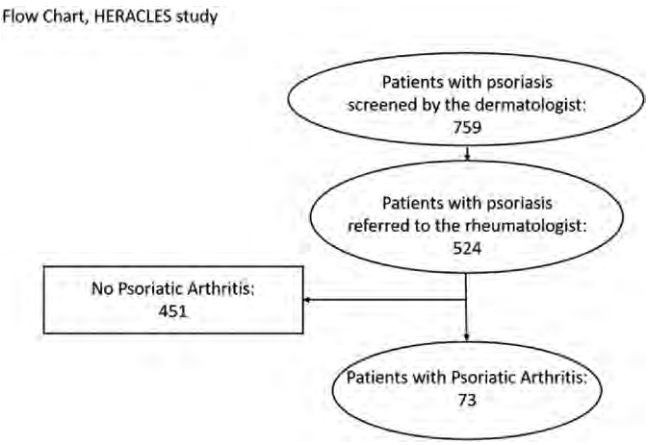


Figure 2.

Conclusion: The HERACLES questionnaire, a tool designed for dermatologists, showed good sensitivity and specificity in identifying PsA cases among subjects with cutaneous psoriasis.

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SAT0413

DACTYLITIS IS ASSOCIATED WITH DISEASE SEVERITY AND ULTRASOUND DEFINED EROSIVE DAMAGE IN VERY EARLY, DMARD NAÏVE PSORIATIC ARTHRITIS

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Background: Dactylitis is a hallmark feature of Psoriatic arthritis (PsA) and Spondyloarthritis (SpA) defined as a uniform swelling of a digit ("sausage digit"). Dactylitis is associated with radiographic damage in chronic PsA. However, there are a paucity of data on the significance of dactylitis and its potential impact in disease burden in early PsA.

Objectives: To characterize a very early DMARD naïve PsA cohort based on clinical presence or absence of dactylitis at disease onset.

Methods: PsA subjects fulfilling the CASPAR classification criteria, were recruited into a prospective observational cohort, the Leeds Spondyloarthropathy Register for Research and Observation (SpARRO) after providing informed written consent. Clinical data including tender (TJC) and swollen joint counts (SJC) were independently assessed. Dactylitis was recorded per digit (finger or toe) as tender (hot) or non-tender (cold). Differences in baseline characteristics were evaluated using percentages to describe categorical variables and means and standard deviations for continuous variables, p value of the mean/proportion difference was calculated. Ultrasound (US) examination was conducted by trained ultra-sonographers blinded to clinical details. Bone erosions were defined on US if intra-articular discontinuity was present in two perpendicular planes at any of 46 joints: wrists, MCP1-5, PIP2-5, DIP2-5, MTP1-5, knees, ankles, subtalar, talonavicular.

Results: A total of 177 PsA patients were recruited. Dactylitis was seen in nearly half the cohort [n=83 (47%)]. Patients with dactylitis had significantly more early morning stiffness, higher TJC and SJC, compared with non-dactylitis (Table 1). A total of 211 digits with dactylitis were recorded in 83 patients. Dactylitis of multiple digits was seen in 47/83 (57%) patients whilst a single dactylitic digit occurred in 36/83 (43%). Foot involvement was more prevalent (141/211, 67%) than hands (70/211, 33%). "Hot" or tender dactylitis was more frequently detected (153/211,

72.5%) than "cold" or non-tender dactylitis (58/211, 27.5%). The most prevalent sites for hot dactylitis were toes 2-4th and fingers 2-3rd.

Table 1.

Variable	No Dactylitis (n=94)	Dactylitis (n=83)	P value
Age, mean (SD) years	44.4 (12.8)	43.7 (13.2)	>0.05
Male	38 (40.4%)	42 (50.6%)	>0.05
Disease duration, median (IQR) weeks	4.7 (0.0-11.4)	5.2 (1-22.4)	>0.05
Early Morning stiffness, mean (SD) mins	82.8 (145.4)	170.5 (230.2)	0.0025*
TJC (78), mean (SD)	8.3 (10.9)	13.7 (14.0)	0.004*
SJC (76), mean (SD)	2.2 (3.2)	8.4 (8.0)	<0.001*
Psoriasis	94/94 (100.0%)	76/83 (91.6%)	0.004*
PASI, mean (SD)	3.6 (4.0)	3.0 (4.1)	>0.05
Nail Dystrophy	51/94 (54.3%)	41/83 (49.4%)	>0.05
mNAPSI, mean (SD)	4.9 (7.1)	7.5 (14.0)	>0.05
MASES, mean (SD)	1.6 (2.9)	1.5 (2.4)	>0.05
BMI, mean (SD)	29.1 (6.4)	28.6 (5.6)	>0.05
Smoker	19.0 (20.2%)	9.0 (10.8%)	>0.05
Elevated CRP (>10 mg/L)	24 (25.5%)	36 (43.4%)	>0.05
PsAQoL, mean (SD)	6.2 (6.6)	6.2 (6.1)	>0.05
HAQ, mean (SD)	0.79 (0.71)	0.84 (0.65)	>0.05
US Erosions (n=154)	12/83 (14.4%)	21/71 (29.5%)	0.023*

US defined erosions were significantly more prevalent in the dactylitis group: 34 erosions in 21/71 patients (29.5%) versus 16 erosions in 12/83 (14.4%) patients in non-dactylitis. Sites prone to erosive damage in both groups were the wrists, MCP1,2 and MTP4,5. The right MCP2 (n=6) and MTP5 (n=6) were most commonly eroded in the dactylitis group, but erosions corresponding at the dactylitic digit level were overall low.

Conclusion: This study identifies a more severe phenotype in very early DMARD naïve PsA presenting with dactylitis with higher prevalence of ultrasound erosions. Longitudinal follow up will determine whether dactylitis represents a poor prognostic factor in very early PsA, which may be a useful discriminator for risk stratification in future PsA management recommendations.

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SAT0414 THE PERFORMANCE OF A MULTI-MARKER GENETIC TEST TO IDENTIFY PATIENTS WITH PSORIATIC ARTHRITIS AMONG PSORIASIS PATIENTS

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Background: Improved understanding of the complex genetic architecture of psoriatic arthritis (PsA) along with the reduction in the cost of genetic testing provide an opportunity to assess the application of genetic testing for PsA diagnosis in clinical setting.

Objectives: The study aimed to assess the performance of the multi-SNP genetic test in predicting a clinical diagnosis of PsA by a rheumatologist among psoriasis patients with musculoskeletal symptoms.

Methods: 328 patients with psoriasis and musculoskeletal symptoms that were referred to a rapid access clinic for suspected PsA were enrolled. Patients with a prior diagnosis of PsA were excluded. A rheumatologist evaluated all patients and classified them as "PsA" or "not PsA" All patients who were classified as not PsA at baseline were reassessed 1 year later to determine whether they have developed PsA. We tested 2 outcomes: 1) diagnosis of PsA at baseline; and 2) diagnosis of PsA at baseline or at 1 year. A custom multi-SNP genetic assay was genotyped on a MassARRAY system (Agena Biosciences). The custom PsA weighted genetic panel included 42 variants in or near 20 genes based on genome-wide significance in PsA studies. We tested the ability of each genetic maker individually to predict PsA using logistic regression models adjusted for age and sex. Machine-learning methods including logistic regression, naïve bayes and random forest were used to identify the optimal prediction model. Age and sex were included in the prediction models.

Results: 78 patients were classified as PsA (PsA-baseline) and the remaining 250 patients as not PsA. After 1 year, 17 additional patients developed PsA resulting in 95 patients with PsA at 1 year (PsA-1 year). The association between the tested SNPs and PsA is shown in Table 1. 5 SNPs located at LCE3A (rs10888503), TNIP1 (rs146571698) and IL-23R (rs4655683, rs2201841 and rs12044149) were associated with PsA-baseline or PsA-1 year (all p<0.05). Of the three machine-learning methods used, logistic regression was found to have the best prediction properties (highest AUC). Overall, the performance of prediction models to classify patients as PsA was modest (see Table 2). The AUC, sensitivity and specificity of the models to predict PsA **at baseline** were: 0.62, 0.15, 0.97, respectively and **at 1 year**: 0.62, 0.15, 0.94.

Table 1. The association between (selected top markers)

Chrom	SNP	Gene	PsA diagnosis at baseline (N=78)			PsA diagnosis at 1 year (N=95)		
			OR	95% CI	P value	OR	95% CI	P value
1	rs10888503	LCE3A	**1.78**	**1.21, 2.62**	**0.003**	**1.52**	**1.06, 2.17**	**0.02**
6	rs12191877	HLA-C	**0.52**	**0.31, 0.89**	**0.017**	0.63	0.39, 1.01	0.057
6	rs2894207	HLA-C*6	**0.57**	**0.35, 0.93**	**0.025**	**0.62**	**0.39, 0.99**	**0.045**
6	rs13214872	HLA-C	**0.57**	**0.34, 0.96**	**0.035**	0.65	0.41, 1.05	0.078
6	rs12189871	HLA-C	0.55	0.30, 1.01	0.055	0.68	0.40, 1.17	0.169
6	rs4406273	HLA-C	0.57	0.32, 1.02	0.057	0.67	0.40, 1.12	0.122
5	rs146571698	TNIP1	2.03	0.97, 4.24	0.061	**2.07**	**1.02, 4.18**	**0.044**
1	rs4655683	IL-23R	1.42	0.97, 2.08	0.069	**1.52**	**1.06, 2.17**	**0.022**
1	rs2201841	IL-23R	0.72	0.50, 1.05	0.087	0.68	0.48, 0.96	0.054
1	rs12044149	IL-23R	1.34	0.88,2.06	0.167	**1.60**	**1.07, 2.39**	**0.021**

Table 2. Performance of the genetic assay in predicting PsA

2A. Prediction of PsA at baseline (N=78)

Method	TP	TN	FP	FN	Accuracy	Sensitivity	Specificity	AUC
Logistic Regression	12	242	8	66	0.77	0.15	0.97	0.62
Naïve Bayes	27	203	47	51	0.70	0.35	0.81	0.61
Random Forest	14	237	13	64	0.77	0.18	0.95	0.56

2B. Prediction of PsA at 1 year (N=95)

Method	TP	TN	FP	FN	Accuracy	Sensitivity	Specificity	AUC
Logistic Regression	15	218	15	80	0.71	0.15	0.94	0.62
Naïve Bayes	21	203	30	74	0.68	0.22	0.87	0.62
Random Forest	16	204	29	79	0.67	0.17	0.88	0.55

Conclusion: Despite the association of several genetic markers with PsA, genetic testing has marginal effect on predicting a diagnosis of PsA among patients with psoriasis and musculoskeletal symptoms.

Disclosure of Interests: Lihi Eder Grant/research support from: Abbvie, Lily, Janssen, Amgen, Novartis, Consultant of: Janssen, Speakers bureau: Abbvie, Lily, Janssen, Amgen, Novartis, Quan Li: None declared, Dana Jerome: None declared, Chandra Farrer: None declared, Tanya Burry: None declared, Proton Rahman Grant/research support from: Janssen and Novartis, Consultant of: Abbott, AbbVie, Amgen, BMS, Celgene, Lilly, Janssen, Novartis, and Pfizer., Speakers bureau: Abbott, AbbVie, Amgen, BMS, Celgene, Lilly, Janssen, Novartis, Pfizer

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SAT0415 AGE RELATIONSHIP WITH ULTRASOUND ARTICULAR AND ENTHESEAL INVOLVEMENT IN PSORIATIC ARTHRITIS: CROSS-SECTIONAL STUDY

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Background: Detection of subclinical enthesitis and synovitis in psoriatic arthritis (PsA) is prevalent and ultrasound (US) examination is informative tool for it diagnosing. Aging positively affects degenerative changes.

Objectives: To study relationship between US articular and entheseal findings with age in patients with PsA.

Methods: 57 patients were enrolled to study with fulfilled PsA criteria (CASPAR, 2009). Data collection: demographical, clinical (current psoriasis, axial

involvement, enthesitis, dactylitis), US (synovitis count (by Grey Scale), Power Doppler(PD)+ synovitis), thickening and hypoechogenicity at enthesis, PD+ enthesitis, entheses with structural components); biological (high sensitive C-reactive protein (hsCRP), Erythrocyte Sedimentation Rate (ESR).

US examination included 798 joints and 3078 entheses (bilateral shoulders, acromioclavicular joints, elbows, wrists, hips, knees, ankles; entheses at the projection of these joints (total number - 54). US entheseal findings were fixed according to consensus-based US definition and scoring for enthesitis in spondyloarthritis and PsA (OMERACT US)[1].

Results: In all 57 patients: male - 25 (43.9%), mean age 43.4±10.3(SD) years (y), PsA duration was 7 (3;10) y, Ps duration 10 (8; 22) y; 53 (41.1%) had axial involvement, 42 (73.7%) dactylitis, 8 (14%) clinical enthesitis, and 56 (98.2 %) skin psoriasis, Psoriasis Activity and Severity Index score 6.4 (2;14.4), Disease Activity in PsA score 18.1 (10.2;26.1), hsCRP 10.1(2.4;21.4), ESR 20 (11.3;31.5). Synovitis count increased with age noticeably (r=0.508, p<0.01), and weak correlation of PD+ synovitis (r=0.262, p=0.049) and age was found. The entheseal thickening and hypoechogenicity and structural findings increased with age respectively (r=0.345, p=0.009; r=0.337, p=0.01). There was no correlation between PD+ enthesitis and age. The assosiation between PD+ enthesitis and blood biomarkers of inflammation (hs-CRP (r=0.364, p=0.008); ESR (p=0.358, p=0.008) was found.

Conclusion: Our study found significant relationship between age and US synovitis. Association between age and US entheseal involvement was noted. Only PD+ enthesitis was not related with age in comparison with other US entheseal findings. The presence of PD US signal at enthesitis in association with increased inflammatory blood biomarkers can be evaluated as the sign of disease activity regardless of age and not as age-related lesion in PsA patients.

References:

[1] Balint PV, Terslev L, Aegerter P et al. Reliability of a consensus-based ultrasound definition and scoring for enthesitis in spondyloarthritis and psoriatic arthritis: an OMERACT US initiative. Ann Rheum Dis.;2018;77(12):1730-1735.

Disclosure of Interests: None declared

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SAT0416 ENTHESITIS AND CLINICAL RESPONSE IN PSORIATIC ARTHRITIS: REAL-LIFE DATA

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Background: Psoriatic arthritis (PsA) is an inflammatory arthritis that is characterized by a broad spectrum of clinical conditions, including axial skeletal involvement, enthesitis, dactylitis, uveitis and arthritis. Among those, enthesitis, the inflammation of the junction where the tendon, ligament or joint capsule inserts into the bone, is assigned to be the hallmark, affecting 35–50% of patients. Several clinical methods have been developed to measure it, including The Maastricht AS Enthesitis Score (MASES) index, which tests 13 entheses and the Spondyloarthritis Research Consortium of Canada (SPARCC) index that assesses 16.

Objectives: To assess the relationship between enthesitis and clinical response in psoriatic arthritis.

Methods: Retrospective study including all the patients with PsA meeting the CASPAR criteria, beginning first-line biologic therapy at our centre. Demographic and clinical data including age, gender, body mass index (BMI), smoking status, physical examination findings such as presence of enthesitis, dactylitis, chronic back pain, tender and swollen joint counts (TJC/ SJC), ESR, CRP, DAS 28 4vESR, BASDAI, BASFI, BASMI, ASDAS, HAQ, patient VAS score, MASES and SPARCC were collected from the Portuguese database Reumapt. Statistical analysis was performed with SPSS. Continuous variables were analysed through Spearman correlations.

Results: We included 119 patients with PsA (60 female), of which 14.9% were active smokers. The mean age of patients was 46.3 ± 1.03 years. The median disease duration was 6.8 (0.3-33.8) years and the mean BMI was 26.8 ± 0.5 Kg/m2. Enthesitis, dactylitis, inflammatory back pain, peripheral arthritis, ungueal distrophy, and psoriasis were present in 53 (45.7%), 45 (38.8%), 76 (65.5%), 109 (94%), 45 (38.8%), 104 (89.7%) patients, respectively.

At baseline, mean (SD) disease activity parameters were: DAS 28 4vESR 4.9 (0.2), ESR 33.2 (2.3) mm/h; CRP 2.35 (0.3) mg/dL, HAQ 1.3 (0.1), BASDAI 6.6 (0.2), ASDAS 3.9 (0.1), BASMI 3.7 (0.2), BASFI 5.8 (0.3), MASES 1.9 (0.3), SPARCC 2.3 (0.3). Median (min-max) values of TJC, SJC and patient VAS score at baseline were 4 (0-28), 3 (0-19), 76 (0-100), respectively.

There were statistically significant positive correlations (0-12 months) between ΔMASES and ΔDAS 28 4vESR (p=0.02, rho=0.432), Δpatient VAS score (p=0.027, rho=0.307), ΔHAQ (p=0.02, rho=0.411), ΔBASDAI (p=0.025, rho=0.326), ΔBASFI (p=0.037, rho=0.315), ΔASDAS (p=0.023, rho= 0.331). Correlations between ΔSPARCC and ΔDAS 28 4vESR (p=0.023, rho=0.332), Δpatient VAS score (p=0.003, rho=0.402), ΔHAQ (p=0.012, rho=0.440), ΔBASDAI (p=0.011, rho=0.368), ΔBASFI (p=0.001, rho=0.445), ΔASDAS (p=0.002, rho= 0.437), ΔCDAI (p=0.039, rho=0.320) and ΔSDAI (p=0.039, rho=0.319), were also significant. However, there weren't strong correlations between ΔMASES neither ΔSPARCC and PsARC response at 12 months.

Conclusion: Our results suggest that enthesitis is correlated with clinical response in PsA, supporting the idea that it is a major determinant of disease activity. It should be given more importance, namely by incorporating it in daily clinical practice, due to its major role, both in establishing an early diagnosis and in assessing treatment response.

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SAT0417 TILDRAKIZUMAB EFFICACY ON PSORIASIS IN PATIENTS WITH PSORIATIC ARTHRITIS—A 52-WEEK ANALYSIS FROM A PHASE 2 STUDY

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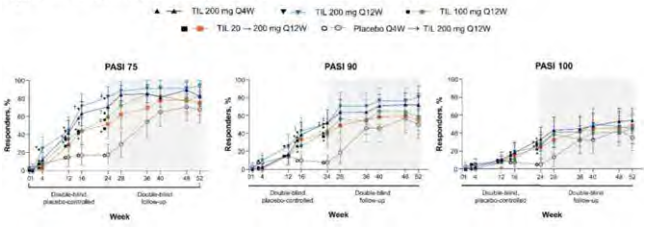
Background: Tildrakizumab (TIL)—a high-affinity anti–interleukin-23p19 monoclonal antibody—is approved in the US, EU, and Australia to treat moderate to severe plaque psoriasis.[1] A randomised, double-blind, multidose, placebo-controlled, phase 2b study (NCT02980692) evaluating the efficacy and safety of TIL for the treatment of psoriatic arthritis (PsA) was recently completed.

Objectives: To evaluate the proportion with 75%/90%/100% improvement in Psoriasis Area and Severity Index (PASI 75/90/100) among patients (pts) with PsA and measurable psoriasis (≥3% of the body surface area [BSA] affected at baseline) over 52 weeks of treatment.

Methods: Pts ≥18 years old with PsA[2] and ≥3 tender and ≥3 swollen joints, stratified by prior anti-TNF use and baseline body weight (≤90 kg and >90 kg), were randomised 1:1:1:1:1 to receive TIL 200 mg every 4 weeks (Q4W) to week 52 (W52), TIL 200 mg every 12 weeks (Q12W) to W52, TIL 100 mg Q12W to W52, TIL 20 mg Q12W to W24→TIL 200 mg Q12W to W52, or placebo (PBO) Q4W to W24→TIL 200 mg Q12W to W52. PASI 75/90/100 were prespecified endpoints and were assessed by an independent assessor. Pts who received ≥1 dose of study drug were analysed. Safety assessments included treatment-emergent adverse event (TEAE) monitoring.

Results: Overall, 391/500 pts screened met inclusion criteria; 235 (60.1%) had ≥3% BSA involvement at baseline (41–55/treatment arm). Demographics and baseline disease characteristics were generally consistent across treatment arms. Mean (standard deviation [SD]) age was 48.8 (12.6) years, average body mass index was 29.7, 96.7% of pts were White, and 23.3% were anti–tumour necrosis factor (TNF)-experienced. At baseline, the mean (SD) PASI score was 6.8 (8.2) and mean (SD) BSA affected was 10.5% (14.3%) overall. Among pts with baseline BSA ≥3%, TIL treatment significantly increased the proportion of PASI 75/90/100 responders vs PBO at W24; the proportion of responders continued to increase thereafter and was sustained through W52 (**Figure**). Similarly, in pts switching from PBO→TIL 200 mg Q12W or escalating from TIL 20→200 mg Q12W after W24, PASI 75/90/100 response rates increased through W36 and remained stable through W52. From W0→W24/W25→W52, 50.4%/39.9% pts experienced a TEAE. The most frequent TEAEs were nasopharyngitis (pooled TIL arms 5.4%/4.2% vs PBO 6.3%/3.8%) and upper respiratory tract infection (pooled TIL arms 3.8%/4.2% vs PBO 1.3%/0.0%). One pt (0.3%) discontinued before 24 weeks due to hypertension. There were no deaths or major adverse cardiac events during W0→W24 or W25→W52.

Figure. PASI 75/90/100 response rates up to week 52 across treatments and time points



Response rates were calculated in patients with BSA ≥3% at baseline.
Black symbols and corresponding p-values were analysed using nonresponse imputation for missing responses.
Error bars represent two-sided 95% CI based on the normal approximation for binomial proportions.
P-values are based on Cochran-Mantel-Haenszel test (with prior anti–TNF use and baseline body weight as stratification factors) for nonresponse imputation dataset.
*P <0.05, †P <0.001; ‡P <0.0001 vs placebo.
BSA, body surface area; CI, confidence interval; PASI, Psoriasis Area and Severity Index; Q4W, every 4 weeks; Q12W, every 12 weeks; TIL, tildrakizumab; TNF, tumour necrosis factor

Conclusion: PASI75/90/100 response rates progressively improved with treatment; PASI 75 responses were significantly improved vs placebo as early as W4 (TIL 200 mg Q12W), and all response rates were significantly improved vs placebo at W24. Response rates continued to improve through W36 and were sustained through W52. These results demonstrate TIL significantly reduced psoriasis disease activity and was generally well tolerated in a mixed population of anti–TNF-naïve and -experienced patients with PsA and BSA ≥3% through W52.

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[1] Reich K, et al. *Lancet.* 2017;390(10091):276–88.
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SAT0418 EFFECT OF TOFACITINIB TREATMENT ON ACTIVE MRI SACROILIITIS AND DISEASE ACTIVITY REDUCTION IN PSORIATIC ARTHRITIS PATIENTS. DATA FROM CLINICAL PRACTICE

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Background: Axial involvement in psoriatic arthritis (PsA) is quite common. Tofacitinib (TOFA) is an oral Janus kinase inhibitor. There is no data on the use of TOFA in PsA patients (pts) with axial involvement, nor is there any data on its effect on active MRI sacroiliitis (MRI-SI). There are only preliminary results of a randomized clinical trial on TOFA efficacy on active SI in AS (1).

Objectives: To study the effect of TOFA therapy on active MRI-SI in PsA pts.

Methods: 40 pts (F/M – 23/17) with active PsA fulfilling the CASPAR criteria were examined. No patients with inflammatory back pain (IBP) were specifically selected. Median (Me) age 41.0 [35.0; 50.0] yrs, Me PsA duration 6.0 [3.0; 10.0] yrs. Pts underwent a standard clinical examination of PsA activity: Me tender joint count 19 [12; 24], swollen joint count 11 [8; 16], patient's global disease activity measured by Visual Analogue Scale (VAS) 70 [50; 80], patient's pain VAS 65 [50; 75], Me activity indixes: DAPSA 44.2 [37.8; 55.3], BASDAI 6.0 [4.2; 7.0], ASDAS 3.8 [2.8; 4.4]. Me CRP 21.3 [3.2; 72.3] mg/L, ESR 28 [12; 52] mm/h. Enthesitis was observed in 65.9% of pts, dactylitis in 53.7% of pts. Apart from a standard clinical examination, all 40 pts underwent sacroiliac joint (SIJ) MRI on scanner Siemens General Electric 1.5 TESLA. Bone marrow edema/osteitis on MRI (STIR) with one lesion on two consecutive slices or at least two lesions on a single slice, was considered active MRI-SI. MRI results were evaluated by 2 independent readers (radiologist and rheumatologist). TOFA was given in 5 mg tablets bds over a period of 6 months, after which 35 patients underwent SIJ MRI. Me [Q25; Q75], Pierson-χ^2 tests were performed. All $p<0.05$ were considered to indicate statistical significance.

Results: Prior to TOFA therapy, active MRI-SI was detected in 14 of 40 (35%) pts: bilateral in 9 pts, unilateral in 5 pts. At the end of 6 months therapy, active MRI-SI was detected in 4 of 35 (11.4%) pts observed: in 1 pt with baseline bilateral MRI-SI and in 2 pts with unilateral MRI-SI. 1 pt showed negative dynamics, that is, development of active MRI-SI (absent at baseline). The decrease in number of active MRI-SI patients is statistically significant ($p = 0.017$; Pearson-χ^2). At baseline, inflammatory changes were detected in 23 of 80 (28.8%) SIJs, after 6 months of therapy they were found in 5 of 70 (7.1%) SIJs observed. Decrease in number of SIJs with active inflammation is statistically significant ($p = 0.001$; Pearson-χ^2). At baseline, Me BASDAI 6.0 [4.2; 7.0], Me ASDAS 3.8 [2.8; 4.4]. After 6 months of treatment, Me BASDAI 1.4 [0.6; 3.2], Me ASDAS1.5 [1.0; 2.1] ($p = 0.001$ for both comparisons).

Conclusion: JAK inhibition using TOFA therapy shows high efficacy in reducing active MRI-SI and decreasing activity of axial involvement in PsA. More extensive studies are needed.

References:

[1] van der Heijde D. et al. Ann. Rheum. Dis. 2017;76:1340–47

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SAT0419 ASSOCIATION OF ACTIVE MRI SACROILIITIS WITH DACTYLITIS AND WORK PRODUCTIVITY IMPAIRMENT IN PSORIATIC ARTHRITIS PATIENTS. POSITIVE EFFECTS OF TOFACITINIB TREATMENT. DATA FROM CLINICAL PRACTICE

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Background: Psoriatic arthritis (PsA) is a heterogeneous disease with multiple manifestations and choosing among treatments can be a complex decision. Patients (pts) with axial involvement and pts having dactylitis are more likely to develop a severe disease (1, 2). Tofacitinib (TOFA), an oral Janus kinase inhibitor, showed efficacy in treating PsA pts with dactylitis (3). However, its efficacy in treating PsA pts with active *sacroiliitis* (SI) and dactylitis has not been studied.

Objectives: To study the effect of TOFA therapy in PsA pts having active SI on MRI (MRI-SI) and dactylitis.

Methods: 40 pts (M/F – 23/17) with active PsA fulfilling the CASPAR criteria were examined. Median (Me) age 41.0 [35.0; 50.0] yrs, Me PsA duration 6.0 [3.0; 10.0] yrs. A standard clinical examination of PsA activity was performed: Me tender joint count 19 [12; 24], swollen joint count 11 [8; 16], patient's global disease activity measured by Visual Analogue Scale (VAS) 70 [50; 80], patient's pain VAS 65 [50; 75], Me activity indexes: DAPSA 44.2 [37.8; 55.3], BASDAI 6.0 [4.2; 7.0], ASDAS 3.8 [2.8; 4.4]. CRP 21.3 [3.2; 72.3] mg/L, ESR 28 [12; 52] mm/h. Enthesitis was observed in 65.9% of pts with Me LEI index 1 [0; 1], dactylitis in 53.7% of pts, Me digits with dactylitis 1 [0; 2]. Apart from a standard clinical examination, MRI of sacroiliac joints (SIJs) was performed in all 40 pts using MRI scanner Siemens General Electric 1.5 TESLA. Bone marrow edema/osteitis on MRI (STIR) considered active MRI sacroiliitis (MRI-SI), was evaluated by 2 independent readers (radiologist and rheumatologist). TOFA was given in 5 mg tablets bds over a period of 6 months, after which 35 patients underwent SIJ MRI. Me [Q25; Q75], Pierson-χ^2 tests were performed. All $p<0.05$ were considered to indicate statistical significance.

Results: Prior to TOFA therapy, MRI-SI was detected in 14 of 40 (35.0%) pts. At the end of 6 months therapy, MRI-SI was detected in 4 of 35 (11.4%) pts: in 3 pts with baseline SI; 1 pt showed negative dynamics, that is, development of active SI (absent at baseline). The decrease in number of active MRI-SI pts is statistically significant ($p=0.017$; Pearson-χ^2). Significant differences between baseline symptoms in patients with MRI-SI (n=14) and without it (n=26) were defined **by number of digits with dactylitis:** 2 [0; 4] and 0 [0; 2] (p=0.047), **by ESR**: 47 [26; 76] and 20 [6; 37] mm/h (p=0.025), and by **WPAI overall work impairment due to health index:** 80 [60; 84]% and 20 [0; 60]% (p=0.033), respectively; these parameters were higher in MRI-SI subgroup. After 6 months of therapy number of digits with dactylitis, ESR and WPAI indexes were significantly lower as compared with the baseline ones (Table 1).

Table 1
Dynamics of symptoms in TOFA treated pts with or without MRI-SI

Symptoms	MRT-SI (+) (n=14)			MRT-SI (-) (n=26)		
	Baseline	After 6 months	p	Baseline	After 6 months	p
Number of digits with dactylitis	2 [0; 4]	0 [0; 0]	0.008	0 [0; 2]	0 [0; 0]	0.003
ESR (mm/h)	47 [26; 76]	12 [6; 16]	0.006	20 [6; 37]	8 [6; 16]	0.001
WPAI (%)	80 [60; 84]	0 [0; 20]	0.007	20 [0; 60]	0 [0; 10]	0.128

After 6 months of TOFA therapy, no differences were found between groups of pts with and without MRI-SI in the number of digits with dactylitis (p=0.47), in ESR (p=0.79) and in WPAI (p=0.93).

Conclusion: In PsA pts significant association of active MRI-SI was found with dactylitis, high ESR level and WPAI. Use of TOFA in pts with both active MRI-SI and dactylitis demonstrated its high efficacy in reduction of SI inflammation and dactylitis; it also significantly improved pts' work productivity. These findings are important for personalized approach to treatment of PsA.

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SAT0420

EFFICACY OF NON-TUMOUR NECROSIS FACTOR BIOLOGICS AND TARGETED SYSTEMIC DISEASE MODIFYING ANTI-RHEUMATIC DRUGS IN THE TREATMENT OF PSORIATIC ARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Psoriatic arthritis (PsA) is a systemic, inflammatory condition presenting in approximately 30% of patients with psoriasis and associated with functional impairment and a reduced health-related quality of life. Current treatment guidelines recommend non-steroidal anti-inflammatory drugs, conventional Disease Modifying Anti-Rheumatic Drugs (cDMARDs) and Tumour Necrosis Factor α inhibitors (TNFi). Recent research has focused on alternative biologic medications which target interleukin (IL) 6, 12/23, 17A, 23 and T Cell co-stimulation, as well as targeted synthetic DMARDs (tsDMARDs) including Janus Kinase inhibitors (JAKi) and Phosphodiesterase 4 inhibitors (PDE4i). Evidence of the safety and efficacy, measured using the American College of Rheumatology-20 (ACR20), has been demonstrated leading to the inclusion of several biologics and tsDMARDs in guidelines. However, it can be argued that ACR50, indicating a 50% improvement in disease, is a more clinically relevant outcome measure.

Objectives: To conduct a systematic review and meta-analysis of the efficacy (ACR50 response) of non-TNFi biologics and tsDMARDs in the treatment of PsA.

Methods: A systematic literature search of Embase, MedLine and Web of Science was undertaken to identify randomised controlled trials (RCTs) investigating efficacy and safety of non-TNFi biologics and tsDMARDs published in English from the inception of the databases to September 2019. The Cochrane Risk of Bias tool was used to assess methodological rigour of included trials. A meta-analysis was performed using a random effects model to estimate odds ratios of ACR 50 response vs placebo. A subgroup analysis was performed using patients with previous TNFi exposure.

Results: 21 RCTs were eligible with 6389 participants. Evaluation periods ranged from 12 to 24 weeks. JAKi, PDE4i, IL6i, IL12/23i, IL17Ai and IL23i treatments were more efficacious than placebo for ACR50 response (p<0.001) (Figure 1). Only tofacitinib (JAKi), secukinumab (IL17Ai) and ixekizumab (IL17Ai) were able to demonstrate efficacy at the ACR50 level in participants with prior TNFi exposure (p<0.0001) (Figure 2). All treatments demonstrated an adequate safety profile.

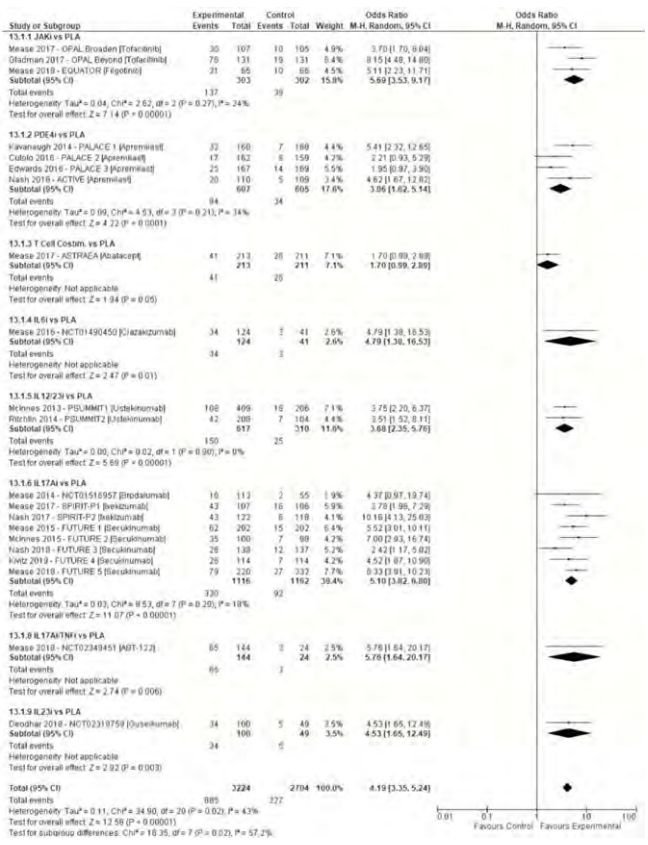


Figure 1. Forest plot of achieving American College of Rheumatology-50 with treatment versus placeboM-H, Mantel-Haenzel; CI, confidence interval; JAKi, Janus Kinase inhibitor; PLA, placebo; df, degrees of freedom; PDE4i, Phosphodiesterase 4 inhibitor; IL6Ai, Interleukin 6 inhibitor; IL12/23i, Interleukin 12/23 inhibitor; IL17Ai, Interleukin 17A inhibitor; TNFi, Tumour necrosis factor inhibitor; IL23i, Interleukin 23 inhibitor

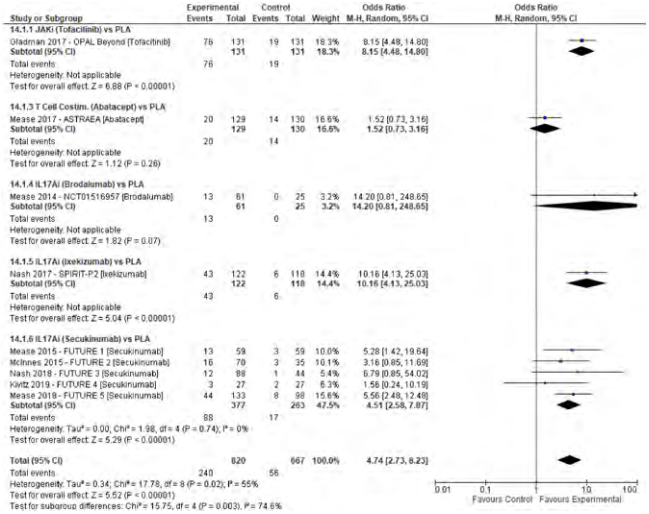


Figure 2. Forest plot of achieving American College of Rheumatology-50 with treatment versus placebo in tumour necrosis factor inhibitor-exposed subgroupM-H, Mantel-Haenzel; CI, confidence interval; JAKi, Janus Kinase inhibitor; PLA, placebo; df, degrees of freedom; PDE4i, Phosphodiesterase 4 inhibitor; IL6Ai, Interleukin 6 inhibitor; IL12/23i, Interleukin 12/23 inhibitor; IL17Ai, Interleukin 17A inhibitor; IL23i, Interleukin 23 inhibitor

Conclusion: Non TNFi biologics and tsDMARDs are able to demonstrate 50% improvement with adequate safety profiles. These therapies are often used in patients who are inadequate responders to TNFi but there is less robust data in this specific patient group. Studies with clinically relevant primary endpoints should be considered in this patient population.

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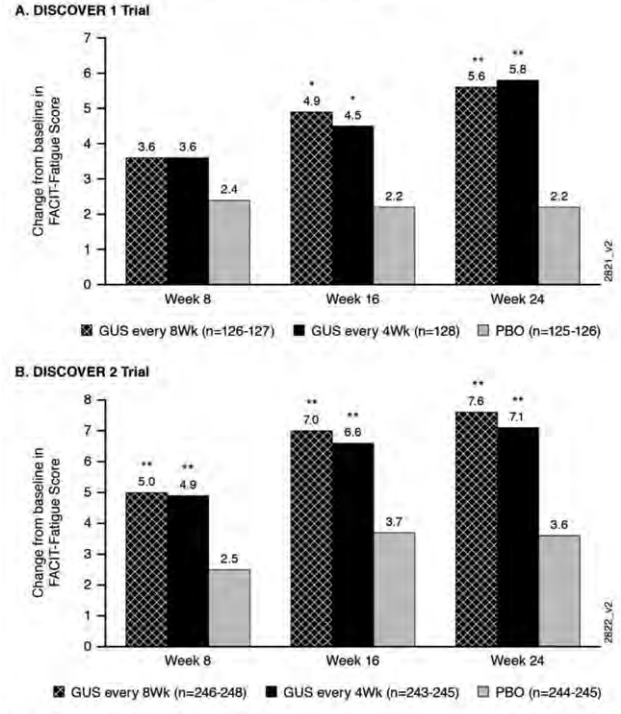
SAT0421

GUSELKUMAB DEMONSTRATED AN INDEPENDENT TREATMENT EFFECT ON FATIGUE AFTER ADJUSTMENT FOR CLINICAL RESPONSE (ACR20) IN PATIENTS WITH PSORIATIC ARTHRITIS: RESULTS FROM PHASE-3 TRIALS DISCOVER 1 & 2

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Background: DISCOVER 1 and 2 are phase-3 trials of guselkumab (GUS, a monoclonal antibody that specifically binds the p19-subunit of IL-23) in patients with psoriatic arthritis (PsA). In both trials, treatment with GUS led to significantly more improvement than placebo (PBO) in the primary endpoint (ACR20) as well as in other measures of arthritis and psoriasis at week (W) 24.[1,2]
Objectives: To evaluate the effect of GUS on fatigue in DISC 1 & 2 using the patient reported outcome (PRO) FACIT-Fatigue, which has demonstrated content validity and strong psychometric properties in clinical trials.[3]
Methods: DISC 1 & 2 enrolled patients with active PsA, despite nonbiologic DMARDS and/or NSAIDS, who were mostly biologic naïve except for ~30% of patients in DISC 1 who had received 1-2 TNFi. Patients were randomized (1:1:1) in a blinded fashion to subcutaneous GUS 100 mg at W0 and W4 then every (q) 8W, to GUS 100 mg q4W, or to matching PBO. Concomitant treatment with select non-biologic DMARDS, oral corticosteroids, and NSAIDs was allowed. The FACIT-Fatigue is a 13-item PRO instrument assessing fatigue and its impact on daily activities and function over the past seven days, with a total score ranging from 0 to 52, higher score denoting less fatigue. A change of ≥4 points is identified as clinically meaningful.[3] Change from baseline in FACIT-Fatigue was analyzed using MMRM (Figure). Independence of treatment effect on FACIT-Fatigue from effect on ACR20 was assessed using Mediation Analysis[4] (Table) to estimate the natural direct effect (NDE) and natural indirect effect (NIE) mediated by ACR20 response.
Results: At baseline in DISC 1 & 2, the mean FACIT-fatigue scores (SD) were 30.4 (10.4) and 29.7 (9.7), respectively, indicating moderate to severe fatigue. In both DISCOVER 1 & 2 trials, treatment with GUS led to improvements in FACIT-Fatigue scores compared with PBO as early as W8 (Figure). 54%-63% of GUS patients compared with 35%-46% of PBO patients achieved clinically meaningful improvement (≥4 points) in FACIT-Fatigue (P≤0.003). Mediation analysis revealed that the independent treatment effects on fatigue after adjustment for ACR20 response (Natural Direct Effect [NDE], Table) were 12-36% in the q8W GUS dosing group and 69% -70% in the q4W GUS group.
Conclusion: In 2 phase-3 trials, treatment with GUS of patients with active PsA led to significant improvements compared to PBO in fatigue, including substantial effects on FACIT-Fatigue that were independent of the effects on ACR 20, especially for the q4W dosing group.

Figure. Week-24 Changes from Baseline in FACIT-Fatigue in the DISCOVER 1 and 2 Trials of Guselkumab in Patients with Psoriatic Arthritis



*P vs. PBO ≤0.013, **P vs. PBO <0.001
FACIT=Functional Assessment of Chronic Illness Therapy, GUS=guselkumab, PBO=placebo, Wk=Week
Analysis of changes from baseline in FACIT-Fatigue scores used Mixed-Effect Model Related Measures (MMRM), with factors including treatment group, baseline use of non-biologic DMARDs, CRP status (>2.0 or ≤2.0 mg/dL), and for DISCOVER 1 only, prior use of TNF inhibitors.

Table. Mediation Analysis of the Effect of ACR 20 Response on Change from Baseline in FACIT-Fatigue Score at Week 24

	Effect	GUS 100 mg q8W vs. PBO Estimate (95% CI)	GUS 100 mg q4W vs. PBO Estimate (95% CI)
DISCOVER 1	NDE	0.36 (-1.7, 2.4)	2.60 (0.6, 4.5)*
	NIE	2.75 (1.4, 4.3)*	1.20 (0.3, 2.3)*
	Total Effect	3.12 (1.0, 5.2)*	3.79 (1.9, 5.4)*
	Proportion Independent	11.7%	68.5%
	Proportion Mediated	88.3%	31.5%
DISCOVER 2	NDE	1.44 (-0.1, 3.0)	2.49 (1.0, 4.1)*
	NIE	2.53 (1.6, 3.6)*	1.09 (0.4, 1.9)*
	Total Effect	3.97 (2.4, 5.5)*	3.58 (2.1, 5.0)*
	Proportion Independent	36.3%	69.7%
	Proportion Mediated	63.7%	30.3%

*P vs placebo<0.02
NDE=Natural Direct Effect (effect on FACIT-F beyond effect on ACR20), NIE=Natural Indirect Effect (effect on FACIT-F mediated by ACR20)
Mediation analysis[4] used linear and logistics regression models with Bootstrapping method

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SAT0422

FIRST-LINE CSDMARD MONOTHERAPY RETENTION IN PSORIATIC ARTHRITIS: METHOTREXATE OUTPERFORMS SULFASALAZINE

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Background: Conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs) are the first-line treatment for psoriatic arthritis (PsA), but there is conflicting data regarding their efficacy and scarce reports describing the duration of use (drug retention) of csDMARD in this population. Their position in treatment recommendations is a matter of growing debate due the availability of alternative treatment options with higher levels of evidence.

Objectives: To study drug retention and predictors for drug retention among PsA patients receiving first-line csDMARD monotherapy.
Methods: Retrospective cohort study in DMARD-naïve adult PsA patients in whom a first csDMARD was prescribed as monotherapy primarily to treat PsA-related symptoms. Main outcome was time to failure of the csDMARD (i.e stopping the csDMARD or adding another DMARD).
Results: 187 patients were included, who were mainly prescribed methotrexate (MTX) (n=163) or sulfasalazine (SSZ) (n=21) (Table 1). The pooled median time to failure was 31.8 months (IQR 9.04-110). Drug retention was significantly higher in MTX (median 34.5 months; IQR 9.60-123) as compared to SSZ treated patients (median 12.0 months; IQR 4.80-55.7)(p=0.016, log-rank test) (**Figure 1**). In multivariable cox-regression the use of MTX and older age were associated with increased retention. The main reasons for treatment failure were inefficacy (52%) and side-effects (28%) (**Figure 2**). Upon failure, MTX treated patients were more commonly, subsequently treated with a biologic DMARD compared to SSZ (p<0.05).

Table 1. Main demographic and clinical characteristics of the study population at baseline. The total cohort (n=187) included 3 patients treated with leflunomide (data not shown separately). Psoriasis area and severity scores were unavailable for most cases and not shown. Descriptive data show the mean ± SD, median (IQR) or N (%).

	Total, N = 187	MTX, N = 163	SSZ, N = 21
Male, N (%)	128 (31.6)	115 (71)	12 (57)
Age (years), mean ± SD*	48.3 ± 13.3	49.1 ± 12.7	39.5 ± 13.4
Body mass index, mean ± SD*	26.7 ± 4.5	27.4 ± 4.4	25.3 ± 3.5
Smoker, N (%)	34/150 (18.2)	31/129 (19.0)	3/18 (14.3)
Disease duration (years), median (IQR)			
PsA	0.4 (0.1 – 3.0)	0.4 (0.1 – 2.9)	0.3 (0.1 – 2.0)
Psoriasis	7.5 (2.1 – 18.4)	7.5 (2.0 – 15.7)	10.8 (3.1 – 26.7)
Psoriasis phenotype, N (%)*			
Vulgaris only	130/185 (69.5)	117/161 (71.8)	10/21 (47.6)
Sine psoriasis	31/185 (16.6)	21/161 (12.9)	10/21 (47.6)
Other types[1]	24/185 (12.8)	23/161 (14.1)	1/21 (4.8)
Nail disease present, N (%)	81/121 (43.3)	72/104 (44.2)	9/17 (42.9)
Swollen joint count, median (IQR)*	4 (2 – 6)	4 (2 – 6)	2 (1 – 3)
Tender joint count, median (IQR)*	4 (1 – 6)	4 (2 – 6)	1 (0 – 3)
Dactylitis present, N (%)	18/161 (9.6)	17/142 (10.4)	1/17 (4.8)
Axial disease present[2], N (%)	27/185 (14.4)	24/161 (14.7)	3/21 (14.3)
CRP, median (IQR)	8.0 (2.9 – 16.0)	8.0 (3.0 – 15.0)	10.0 (1.0 – 26.0)
ESR, median (IQR)	14.0 (6.0 – 27.5)	14.0 (7.0 – 27.0)	16.0 (6.0 – 31.0)
Erosive disease, N (%)	40/156 (21.4)	37/140 (22.7)	2/15 (9.5)

[1] Other psoriasis types included guttate, palmoplantaris, inverse, and mixed types.
[2] Presence/absence of axial disease was based on the clinical diagnosis from the treating physician.
* Clinical parameter is significantly different (P <0.05) between MTX and SSZ.
Abbreviations: MTX = methotrexate. SSZ = sulfasalazine. CRP = C-reactive protein. ESR = erythrocyte sedimentation rate. PsA = psoriatic arthritis.

Conclusion: MTX outperformed SSZ as first-line csDMARD monotherapy in DMARD-naïve PsA patients with respect to drug retention in daily clinical practice.
References: n.a.
Disclosure of Interests: Marleen Jacobs: None declared, Juliette Pouw: None declared, Paco Welsing: None declared, Timothy RDJ Radstake Employee of: TR currently is an employee of AbbVie. At the time of the work described he had no COIs., Emmerik Leijten: None declared

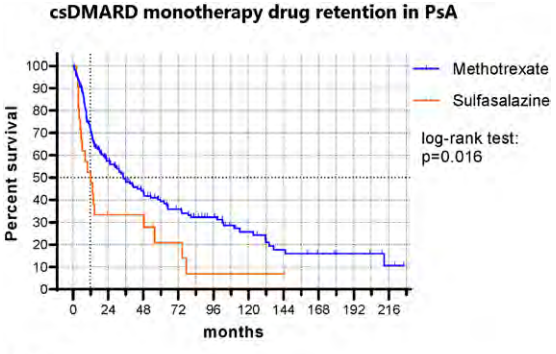
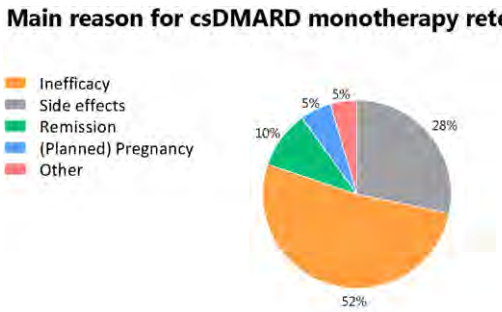


Figure 1
csDMARD monotherapy drug retention. Kaplan-Meier plot shows monotherapy drug retention rate of methotrexate or sulfasalazine prescribed as first-line treatment in DMARD-naïve psoriatic arthritis patients. Ticks indicate censored data. Methotrexate showed significantly higher monotherapy drug retention as compared to sulfasalazine.



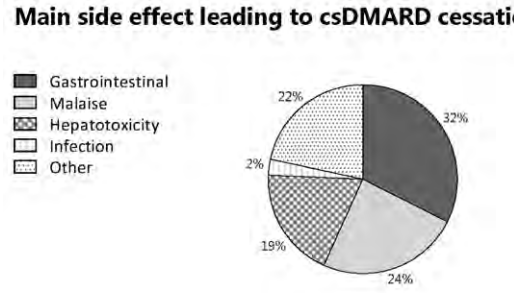


Figure 2
Top: Main reasons for csDMARD monotherapy retention failure (non-censored cases, n=132).
Bottom: Major side effect reported at stop date for patients in whom the primary reason for csDMARD cessation was side effects (non-censored data, n=37).

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SAT0423

LONG-TERM SURVIVAL OF THE FIRST BIOLOGIC TREATMENT IN PSORIATIC ARTHRITIS AND THE EFFECT OF THE SELECTED TREATMENT ON DRUG SURVIVAL; TURKBIO REGISTRY

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Background: Currently, biologic treatments are used effectively in patients with psoriatic arthritis (PsA).
Objectives: The aim of this study was to evaluate and compare long-term drug survival of the first biologic treatments including adalimumab, certolizumab, etanercept, golimumab, infliximab, secukinumab and ustekinumab in patients with PsA.
Methods: PsA patients, electronically registered at each visit in the TURKBIO database between 2011 and 2019 were included in the study. PASW 18.0 for Windows was used for statistical analysis. Drug survival rates were calculated by Kaplan Meier method.
Results: 355 patients (227 women; axial PsA = 48, peripheral PsA = 307) were included in the study (Table 1). Adalimumab was the most commonly used first biologic treatment (n=125; 37.6%). The rate of drug survival was found to be 0.75 at month 60 in patients receiving the first biologic treatment (Figure 1). There was no significant difference in drug survival rate between tumor necrosis factor alpha inhibitor (TNFi) and non-TNFi biologic drugs (p=0.56). No difference was also found in drug survival rates between each biologic treatment.

Table 1. Initial demographic and clinical datas of patients with PsA

	PsA Patients (n=355)
Females, n (%)	227 (63,9)
Age of diagnosis, years*	34,6 (27-42)
CRP baseline*	6 mg/ L (3-15)
ESR baseline*	24 mm/h (10-38)
Smoking, n (%)	
Current	99 (28,5)
Never	192 (55,3)
Previous	56 (16,2)
HLA B27 positivity,n (%)	41 (26,4)
First biologic agent, n (%)	
-TNFi	332 (95,4)
Adalimumab	125 (37,6)
Etanercept	80 (24,1)
Golimumab	52 (15,6)
Certolizumab	44 (13,3)
Infliximab	31 (9,4)
- Other biologic agents	16 (4,6)
Secukinumab	13 (81,3)
Ustekinumab	3 (18,7)

*** median (min-max)**

Conclusion: The results of this study establish that more than half of patients with PsA can remain in their initial biologic treatment over a long term. It has been observed that the choice of biologic treatment did not effect the drug survival in PsA.

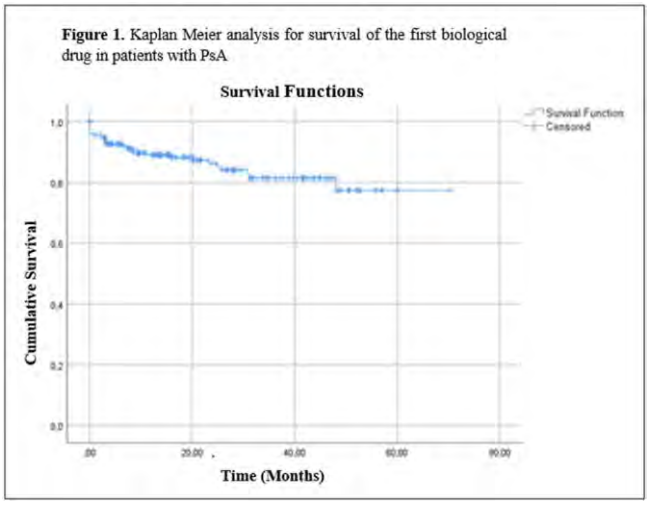


Figure 1. Kaplan Meier analysis for survival of the first biological drug in patients with PsA

Disclosure of Interests: None declared
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SAT0424

OBESITY LINKS TO PSORIATIC ARTHRITIS (PSA) ACTIVITY, HIGHER PREVALENCE OF CARDIOMETABOLIC DISORDERS AND WORSE PATIENT REPORTED OUTCOMES (PROS): DATA FROM THE RUSSIAN PSA REGISTRY (RU-PSART)

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Background: PsA patients (pts) have an increased risk of cardiovascular (CV) and metabolic (Met) disorders due to the combination of inflammation and increased prevalence of traditional CV risk factors. Only limited data are available on Russian PsA pts. Data was collected from 25 rheumatology clinics of the Russian Federation
Objectives: to study, in clinical practice, the prevalence of obesity and its association with PsA activity, CV/Met comorbidities and PROs
Methods: 614 (M/F=331(54%)/283(46%) PsA pts fulfilling the CASPAR criteria were included from the RU-PsART cohort. Mean age 45.2±0.52 yrs, PsA duration 5.7±0.27 yrs, PsO duration 15.71±0.56 yrs, DAPSA 28.79±0.75. At baseline (BL) PsA activity was evaluated by Tender Joint Count (TJC68), Swollen Joint Count (SJC66), PGA, physician global assessment by Visual Analog Scale (VAS), DAPSA; PROs according to PtGA VAS, PtPain VAS, HAQ, Work Productivity and Activity Index (WPAI) and Body Mass Index (BMI, kg/m^2) were calculated. All pts were split into three groups by BMI (kg/m^2): normal<25 (I group), overweight 25-30 (II group), obese>30 (III group). M±m, %, Me [Q25; Q75], χ^2 or Fischer's exact tests were performed
Results: At BL the BMI was 27.7±0.23 kg/m^2 with the following BMI categories: normal - 213 pts (34.7%), overweight - 214 pts (34.8%) and obese - 187 (30.5%). Increased BMI was observed in 65.3% of PsA pts. In all groups, comorbidities were found in 297 out of 614 pts (48%): arterial hypertension in 190 (64%), diabetes mellitus in 44 (14.8%), Met syndrome in 36 (12.1%), Coronary Heart Disease in 22 (7.4%). CV and Met disorders were significantly more common in obese pts with BMI>30 compared to overweight pts and to normal BMI pts; female prevailed (Table 1).

Table 1. CV/Met comorbidity in three groups, n (%).

	I group BMI<25 kg/m^2	II group BMI 25-30 kg/m^2	III group BMI>30 kg/m^2	p
Arterial hypertension	28(13.2)	55(25.7)	85(46.5)	p<0.0001*
Diabetes mellitus	0	15(7)	25(14)	p<0.0001**
Metabolic syndrome	0(0)	6(2.8)	23(12.8)	p<0.0001**
Coronary heart disease	2(0.9)	6(2.8)	10(5.6)	p<0.026***

*III vs I and II groups, ** III vs II, *** III vs I group
At BL pts with BMI>30 had higher PsA activity by DAPSA, HAQ, daily activity impairment by WPAI, PtPin compared to I and II groups (table 2).

Table 2. PsA activity and PROs based on BMI categories.

	I group BMI<25 kg/m^2	II group BMI 25-30 kg/m^2	III group BMI>30 kg/m^2	p
DAPSA	22.7 [14.7; 35.8]	24.9 [13.5; 38.5]	27 [17.2; 44.4]	p<0,05*
HAQ	0.9 [0.5; 1.3]	0.9 [0.5; 1.3]	1 [0.8; 1.6]	p<0,05*
Daily activity impairment	0.3 [0; 0.5]	0.3 [0; 0.5]	0.4 [0; 0.6]	p<0,05*
PtPain, mm VAS	50 [30; 66.5]	50 [30; 68]	50 [40; 70]	p<0,05**

*p<0.05 III vs I and II groups, ** p<0.05 III vs II group

Conclusion: In clinical practice, BMI increase was found in the majority of PsA pts. Obesity was associated with higher PsA activity, more prevalence of CV/Met disorders and worse PROs. Obesity requires a change of the pts' lifestyle, nutrition correction and a right choice of therapy
Disclosure of Interests: Yulia Korsakova: None declared, Elena Loginova Speakers bureau: Janssen, ELENA GUBAR: None declared, Elizaveta Vasilenko: None declared, Aleksey Vasilenko: None declared, Natalia Kuznetsova: None declared, Irina Patrikeeva: None declared, Tatiana Korotaeva Grant/research support from: Pfizer, Consultant of: Abbvie, BIOCAD, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Merck Sharp & Dohme, Novartis, Novartis-Sandoz, Pfizer, UCB, Speakers bureau: Abbvie, BIOCAD, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Merck Sharp & Dohme, Novartis, Novartis-Sandoz, Pfizer, UCB, Alexander Lila: None declared, Evgeny Nasonov: None declared
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SAT0425

NOVEL COMPUTER-ASSISTED METHODOLOGY FOR QUANTITATIVE ASSESSMENT OF MRI TREATMENT RESPONSES TO APREMILAST IN PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Response to treatment in psoriatic arthritis (PsA) can be captured using the OMERACT PsA Magnetic Resonance Imaging Score (PsAMRIS). While reliable and valid, PsAMRIS interpretation requires a trained reader to assess inflammatory lesions such as synovitis and flexor tenosynovitis on a discrete scale ranging from 0 to 3, which might not have sufficient sensitivity to capture early and subtle changes in inflammation in small cohorts.

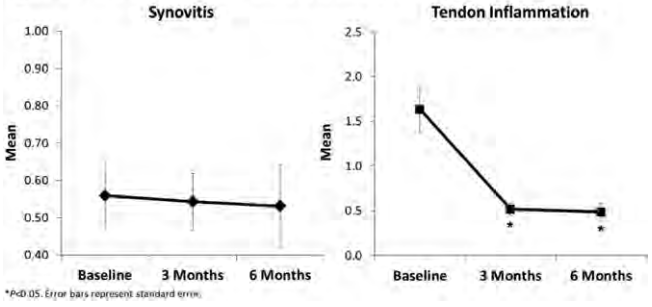
Objectives: To propose a novel computer-assisted imaging quantitative methodology to assess early response to treatment on a continuous scale and compare its results with those of PsAMRIS.

Methods: Patients with active PsA in the hand and wrist were treated with apremilast 30 mg twice daily after a 5-day titration period. A total of 29 patients underwent MRI scans at baseline and months 3, 6, and 12. Images were scored for synovitis using the PsAMRIS interpreted by an experienced reader and were read in blinded sequences. Images for 13 patients with involvement of the wrist and metacarpophalangeal (MCP) joints and MRI available at baseline, 3 months, and 6 months were further processed using a novel computer-assisted imaging quantitative methodology. Images were scored concurrently, with the reader blinded to the order of visits. An experienced reader pre-defined regions of interest (ROIs) around the wrist, MCP joints (MCP-2 to MCP-5), and flexor and extensor tendons of the fingers and wrist (as applicable) with adjacent blood vessels and possible artifacts excluded from ROIs. From these ROIs, the normalized volume of inflammation (NormI) was calculated in each joint and tendon. This was done by automatically counting the pixels that were enhanced above the intensity level of a muscle. Each enhanced pixel was given a weight corresponding to the degree of enhancement, allowing differentiation of areas of residual inflammation and high perfusion. This method has been validated, tested, and implemented in the CE/FDA510-cleared software package Dynamika (IAG, Image Analysis Group). PsAMRIS responses were compared with those of the computer-assisted imaging quantitative methodology at baseline, 3 months, and 6 months. A heat map of normalized intensities was produced, highlighting areas of perfusion higher than that of healthy muscle. Changes from baseline were tested for significance using a *t*-test. Patients with non-missing data were included in the final statistical analysis.

Results: The generated NormI map highlighted a reduction in wrist inflammation activity after 3 and 6 months of treatment with apremilast. In all cases, a downward trend in inflammatory activity in the wrist and MCP joints was observed at 3 months, indicating a reduction following treatment with apremilast (Figures 1 and 2). Similar improvements were observed in tenosynovitis (Figures 1 and 2).

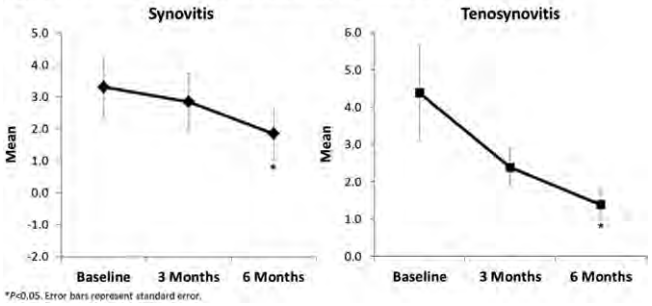
Conclusion: In this pilot assessment, apremilast was associated with improvements in synovitis and tenosynovitis over a period of 6 months using PsAMRIS. Assessment of images using NormI, a methodology allowing quantification of inflammatory activity within a joint or tendon, demonstrated the same trends over 6 months. Further studies are planned to determine the sensitivity of this novel computer-assisted imaging quantitative methodology relative to that of PsAMRIS and whether it could be used to provide early indications of treatment response in small cohorts of patients.

Figure 1. NormI Mean Intensity Values at Baseline, 3 Months, and 6 Months



*P<0.05. Error bars represent standard error.

Figure 2. PsAMRIS Mean Values at Baseline, 3 Months, and 6 Months



*P<0.05. Error bars represent standard error.

Disclosure of Interests: Paul Bird Consultant of: AbbVie, Celgene Corporation, Eli Lilly, Janssen, Novartis, Pfizer – advisor, Speakers bureau: AbbVie, Celgene Corporation, Eli Lilly, Janssen, Novartis, Pfizer, Mikael Boesen Consultant of: AbbVie, AstraZeneca, Eli Lilly, Esaote, Glenmark, Novartis, Pfizer, UCB, Paid instructor for: IAG, Image Analysis Group, AbbVie, Eli Lilly, AstraZeneca, esaote, Glenmark, Novartis, Pfizer, UCB (scientific advisor)., Speakers bureau: Eli Lilly, Esaote, Novartis, Pfizer, UCB, Mark Hinton: None declared, Eser Sanverdi Employee of: Image Analysis Group – employment, Romiesa Hagoug Employee of: Image Analysis Group – employment, Christoper Sabin Employee of: Image Analysis Group – employment, Priscila Nakasato Employee of: Amgen Inc. – employment; Celgene Corporation – employment at the time of study conduct, Benoit Guerette Employee of: Amgen Inc. – employment; Celgene Corporation – employment at the time of study conduct, Olga Kubassova Shareholder of: IAG, Image Analysis Group, Consultant of: Novartis, Takeda, Lilly, Employee of: IAG, Image Analysis Group

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SAT0426

CAN BIOLOGICS "PREVENT" THE DEVELOPMENT OF PSORIATIC ARTHRITIS IN PSORIASIS PATIENTS? DATA FROM A LARGE UNIVERSITY HOSPITAL COHORT IN ARGENTINA

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Background: As psoriasis (Pso) commonly precedes psoriatic arthritis (PsA), an important unanswered question is whether treatment of Pso might influence the development of PsA in patients with psoriasis

Objectives: The objective of this study was to analyze the incidence of PsA in a large cohort of patients with PsO according to different treatments, with the hypothesis that treatment with biologics might prevent the development of PsA.

Methods: Patients with PsO without PsA followed at a University Hospital were included in this retrospective cohort study. Data was obtained from the Hospital Electronic Medical Record (EMR). Patients were classified according to their treatment in topics group (topic and phototherapy), conventional DMARDs (cDMARDs) group (Methotrexate (MTX) and cyclosporine (Cyc)), and biologic DMARDs group (bDMARDs) (TNFi, IL17i, and IL12-23i). Patients contributed time since beginning of the corresponding treatment until diagnosis of PsA, lost of follow up, end of treatment or end of study. Incident cases of PsA were attributed to one treatment if developed during the administration of that treatment and up to 6 months after its discontinuation if no other treatment was started. Incident cases that developed more than one year after discontinuation of treatment were disregarded (3 cases). Incidence rate was calculated for the whole population and for each one of the treatment groups and compared with chi2test, and rate ratios were calculated as well. A multivariable logistic model for the development of PsA was analyzed by treatment groups, adjusting by other variables.

	Topics, n= 599	cDMARDs, n=106	bDMARDs, n=92	Total group, n=797
Mean age at PsO diagnosis (SD)	43.6 (20.6)	46.2 (20.7)	35.1 (18.9)	42.9 (20.6)
Female, n (%)	314 (52)	53 (50)	36 (39)	403 (50.5)
Plaque PsO, n/N (%)	514/578 (89)	93/103 (90)	85/90 (94)	692/771 (90)
BMI, n; Mean (SD)	498; 27.6 (5.4)	80; 28.5 (5.6)	91; 30 (7)	659; 28 (5.7)
N Developed PsA (%)	68 (8.5)	3 (0.38)	1 (0.13)	72 (9)
Follow up (patient/years)	9153	316	548	10017
Incidence rate/1000 Patient/years (95% CI)	7.4 (5.8-9.4)	9.5 (1.9-27.5)	1.81 (0.04-10)	7.2 (5.6-9)
Median years between PsO and PsA (IQR)	10 (2-21)	Patient 1: 23 Patient 2: 11.7 Patient 3: 24.7	Patient (1): 9.6	10.5 (2-20.8)

Results: 797 patients, contributed a total of 10017 patient/years. Patient's characteristics are shown in table 1. 599 (75%) patients were treated only with topics or phototherapy, 106 (13%) with cDMARDs (81% MTX and 19% Cyc) and 92 (11.5%) with biologics (TNFi: 64: etanercept: 44, adalimumab:23, infliximab:6; IL17i: 43: 14 Ixekizumab, 29 Secukinumab; IL12-23i: (Ustekinumab) 16; some patients received more than one biologic). During follow-up 72 patients developed PsA (68 under topics; 3 under cDMARDs (2 MTX and 1 Cyc) and 1 under biologics (1 Secukinumab): Global incidence rate: 7.2 per 1000 patient/years (table 1). Although numerically the incidence of PsA in PsO patients treated with biologics was lower, the difference was not statistically significant. In Cox regression analysis, after adjusting by sex, age, and BMI, treatment with biologics was significantly associated with a reduced risk of developing PsA: Hazard ratio (95% CI): 0.1 (0.013 – 0.7); p= 0.021.

Conclusion: Treatment with biologics in patients with PsO seemed to reduce the risk of PsA and preventing its development in this retrospective single center cohort.

Acknowledgments: This study was awarded with the PANLAR stimulus award 2019

Disclosure of Interests: Luciano Lo Giudice: None declared, Maria Laura Acosta Felquer: None declared, Maria Laura Galimberti: None declared, Luis Mazzuoccolo: None declared, Enrique Soriano Grant/research support from: AbbVie, Eli Lilly, GlaxoSmithKline, Novartis, Pfizer Inc, Sandoz, Consultant of: AbbVie, Eli Lilly, GlaxoSmithKline, Novartis, Pfizer Inc, Sandoz, Speakers bureau: AbbVie, Amber, Bristol-Myers Squibb, Eli Lilly, Novartis, Pfizer Inc, Roche
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SAT0427

COMPARATIVE EFFECTIVENESS OF TOFACITINIB (TF) AND ADALIMUMAB (ADA) IN PSORIATIC ARTHRITIS (PSA) PATIENTS IN REAL CLINICAL PRACTICE.

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Background: Tofacitinib (TF) is an oral Janus kinase inhibitor approved for PsA treatment. It has demonstrated comparable to ADA efficacy in RCT in reducing PsA clinical symptoms [1,2]. There is currently no data concerning comparative effectiveness of TF and ADA in clinical practice. The Russian PsA RegisTry (RU-PsART) collected data from 43 rheumatology centers of the Russian Federation.
Objectives: to study responses to TF or ADA over a period of 6 months (mo) treatment in patients (pts) with active PsA in real clinical practice.
Methods: 77 (M/F=43/34) PsA pts fulfilling the CASPAR criteria from the RU-PsART cohort were divided into two groups according to the treatment given. 41pts (M/F=24 (58.5%)/17 (41.5%), mean age 42.4±10,3 years (yrs), median (Me) PsA duration 72 [35;120] mo were treated with TF 5 mg twice daily. 36 pts (M/F=19 (52.8%)/17 (47.2%), mean age 44±11.5 yrs, Me PsA duration 59 [22;102] mo were treated with ADA 40 mg/2 weeks, subcutaneous, as a first-line bDMARD. In TF/ADA groups 89%/52.8% pts accordingly were given combination therapy with Methotrexate (MTX). At baseline (BL) and at 6 mo of therapy PsA activity by DAPSA, BASDAI, the number of pts (NPts) with dactylitis, enthesitis by LEI, BSA, HAQ were evaluated in both groups. At 6 mo of therapy the NPts who achieved remission by DAPSA (≤4)/Low activity (LA)≤14) and Minimal disease activity (MDA, 5 of 7) were calculated in both groups. M±SD, Me [Q25; Q75], Min-Max, %, t-test, Pierson-χ^2, Manna-Whitney, Wilcoxon tests were performed. All p<0.05, were considered to indicate statistical significance.
Results: At BL TF pts had higher PsA activity by DAPSA compared to ADA group: 44.2[37.8; 55.3]/35.8 [21.1; 52] accordingly (p=0.03). At 6 mo of treatment DAPSA significantly decreased in TF/ADA groups - to 11 [4,3; 17,3]/9,1[6; 19,6] (p<0,001) accordingly. At 6 mo of therapy there were no significant differences between groups in achieving MDA, DAPSA LA/Remission (table 1). At 6 mo of treatment in TF-treated group the NPts with dactylitis significantly decreased from 22 (53,7%) to 5 (13,2%) pts (p<0.001), and in ADA-treated group no significant differences were found in NPts with dactylitis [despite a quantitative decrease from 13 (36,1%) to 6 (20%) pts (p=0.15)]. The NPts with enthesitis in both TF/ADA groups decreased significantly: from 27 (69,2%) to 12 (30,8%) (p<0,002) and from 16 (72,7%) to 5 (38,5%) (p<0.046) pts accordingly. In TF/ADA-treated pts BASDAI improved from 6 [4.2;7] to 1.4 [0.6; 3.2] (p<0.001)/from 4.4 [1.9;5.8] to 3 [0.8;4.5] accordingly (p<0.046); HAQ significantly decreased from 1 [0.625;1.5] to 0,5 [0; 0.875] and from 0.875 [0.5;1.38] to 0.5 [0; 0.875] accordingly. The NPts with BSA>3% significantly reduced in the TF group: from 20 (51,3%) to 8 (26,7%) pts (p<0,002), but not in the ADA group.

Table 1. MDA, DAPSA LA/Remission in TF/ADA at 6 mo

	TF		ADA			
Study	Events	Subjects	Events	Subjects	OR (95% CI)	P
DAPSA remission abs, % achieved	11 (26,8%)	41	6 (20,8%)	29	1,406 (0,453-4,366)	0.556
DAPSA LA abs, % achieved	15 (36,6%)	41	13 (44,8%)	29	0,710 (0,269-1,872)	0.489
MDA abs, % achieved	16 (40%)	40	9 (30%)	30	1,556 (0,569-4,249)	0.389

Conclusion: In real clinical practice TF and ADA demonstrated comparable effectiveness in all clinical domains of active PsA and showed equal result in achievement of MDA/LA/Remission according to DAPSA.
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SAT0428

IMPACT OF DOSE ESCALATION OF SECUKINUMAB IN PATIENTS WITH PSORIATIC ARTHRITIS IN REAL-WORLD SETTING.

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Background: Secukinumab (SEC) has provided efficacy in clinical trials in patients with psoriatic arthritis (PsA). In PsA patients, a gain in response has been suggested by dose escalation from 150 to 300 mg in the open phase of the FUTURE study[1].
Objectives: To analyze the usefulness of dose escalation of SEC from 150 to 300 in patients with non-responding PsA to 150 mg in real-world setting.
Methods: Multicentric observational, longitudinal, retrospective study conducted in a tertiary hospital between January 2016 and December 2019. Patients with PsA (CASPAR criteria) receiving at least one dose of SEC were included. Medical records were reviewed to collect demographic and clinical data related to PsA (including activity assessment and treatment). Descriptive statistics and a comparative analysis of the efficacy of SCK by the Student *t* test in the different dose groups and by the ANOVA test to compare the response between the three dose groups were performed.
Results: 98 patients with PsA treated with SEC, of which 69(70%) female were included. Mean age was 54 y.o (SD12) and average duration of the disease was 9 (SD 7) years. Three groups were made according to the dose received, SEC150, SEC300 and SEC150-300 (non-responders after SEC150 onset increasing to 300 mg). The SEC150 group includes 58(59%) patients of whom 32(55%) had received at least one biological (16 one biological, 8 two biological and 10 three or more). The survival of SEC was 1.3 (SD1) years and was suspended in 24(41%) patients, due to primary failure in 9, secondary failure 10, adverse events 4 and allergy to latex 1. The SEC300 group includes 12 (12%) patients of whom 10 (83%) had received at least one biological (1 one biological, 3 two and 6 three or more). The survival of the SEC was 1.6 SD (1.3) years and was suspended in 8 (67%) patients, due to primary failure in 2, secondary failure 5 and remission 1. Finally, the SEC150-300 group includes 28 (29%) patients of whom 17 (61%) had received at least one biologic (7 one biologic, 2 two and 8 three or more). The survival of the SEC was 1.6 (SD0.9) years and was suspended in 13 (46%) patients, all due to secondary failure. 54%, therefore, maintains the SCK after responding to the dose increase. The average time of dose increase to 300 mg was 9(SD6) months. In the three treatment groups, a significant decrease in the values of CRP, ASDAS-CRP and DAPSA was observed at 6 months of SEC (Table 1). However, when comparing the difference of means obtained during follow-up (ΔCRP, ΔASDAS and ΔDAPSA) between the 3 dose groups, no significant differences were found (p=0.76 for CRP, p=0.86 for ASDAS and p=0.35 for DAPSA).

Table 1. Disease activity assessment at 6 months of SEC therapy.

	Baseline	6 months after SEC	Mean difference	p value
CRP300 (mg/L)	9±8,3	4,7±3,7	-4,3 (IC95% -8,9 a 0,2)	p=0,06
CRP150 (mg/L)	7,3±9,1	4,0±4,7	-2,9 (IC95% -4,7 a -1,3)	p=0,0009
CRP150-300(mg/L)	9,9±11	6,0±7,4	-3,9 (IC95% -6,9 a -8,5)	p=0,0142
ASDAS-CRP300	2,3±0,7	1,6±0,6	-0,6 (IC95% -0,9 a -0,3)	p=0,0014
ASDAS-CRP150	2,3±0,6	1,6±0,7	-0,7 (IC95% -0,8 a -0,5)	p<0,0001
ASDAS-CRP150-300	2,2±0,6	1,6±0,7	-0,6 (IC95% -0,8 a -0,4)	p<0,0001
DAPSA300	33,7±19,3	16,9±10,6	-16,8 (IC95% -29,6 a -3,9)	p=0,01
DAPSA150	27,4±11,4	15,4±10,4	-11 (IC95% -14,4 a -7,6)	p<0,0001
DAPSA150-300	28±9,9	15,8±8,7	-12,2 (IC95% -15,3 a -9,1)	p<0,0001

CRP300: C-reactive protein in patients with SCK 300 mg, CRP150: in patients with SCK 150, CRP150-300: in patients with dose escalation from 150 to 300 (same for ASDAS-CRP and DAPSA), SEC: secukinumab

Conclusion: There are no significant differences in the response evaluated by CRP, ASDAS-CRP and DAPSA between the dose of 150 and 300 mg of SEC. However, both doses of treatment provided efficacy in clinical practice with significant reduction of activity parameters. In the case of patients not responding to SEC150 mg and prior failure to TNFi, increasing the dose to 300 mg could be an effective option.

References:
[1] Mease PJ, et al. ACR Open Rheum.2020 Jan;2(1):18-25.
Disclosure of Interests: MARIA MARTIN LOPEZ: None declared, Beatriz Joven-Ibáñez Speakers bureau: Abbvie, Celgene, Janssen, Merck Sharp & Dohme, Novartis, Pfizer, José Luis Pablos: None declared
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SAT0429 SECUKINUMAB IMPROVES CLINICAL AND PATIENT-REPORTED OUTCOMES AT 6 MONTHS AMONG PATIENTS WITH PSORIATIC ARTHRITIS IN THE US-BASED CORRONA PSORIATIC ARTHRITIS/SPONDYLOARTHRITIS (PSA/SPA) REGISTRY

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Background: Secukinumab, an interleukin-17 antagonist approved for the treatment of PsA, improves all PsA manifestations in the GRAPPA-OMERACT core domain set.[1] Few US-based studies have evaluated the real-world effectiveness of secukinumab in patients with PsA.
Objectives: To examine clinical and patient-reported outcomes (PROs) in patients with PsA enrolled in the Corrona PsA/SpA registry initiating secukinumab with ≥ 1 follow-up visit.
Methods: Included were adult patients with PsA in the Corrona registry who initiated secukinumab after April 1, 2017 and remained on secukinumab at their 6-month (window, 5-8 months) follow-up visit. The primary outcome was achievement of minimal disease activity (MDA) at 6 months among patients not in MDA at secukinumab initiation. MDA was defined as meeting 5 of the 7 following criteria: tender joint count (TJC) ≤ 1, swollen joint count (SJC) ≤ 1, psoriasis affected body surface area (BSA) < 3%, patient assessment of pain on visual analog scale (VAS) ≤ 15, patient global assessment VAS ≤ 20, HAQ-DI ≤ 0.5, and tender entheseal points ≤ 1 using the Leeds Enthesitis Index (LEI). Secondary outcomes included the proportion of patients who achieved resolution (0 sites) of TJC, SJC, enthesitis (using the LEI), and dactylitis among those with ≥ 1 site at initiation and improvement from baseline in clinical outcomes (BSA, nail psoriasis, physician global assessment, TJC, SJC, and DAPSA) and PROs (patient-reported pain, patient global assessment, HAQ-DI, and Work Productivity and Activity Impairment questionnaire) at 6 months. Outcomes were evaluated in the overall population and in potentially recalcitrant patients with failure of or intolerance to ≥ 3 previous biologics to examine if the later line biologic could be adequately effective.
Results: A total of 100 patients with PsA who initiated and maintained secukinumab after 6 months were included. The mean (SD) age was 51.6 (11.6) years, 54.3% were male, and 96.8% were white. The mean (SD) symptom and disease duration were 10.8 (9.7) and 7.0 (7.0) years, respectively. Thirty patients (30.0%) initiated secukinumab 150 mg and 70 (70.0%) initiated secukinumab 300 mg. Most (83.0%) were biologic experienced; 17 patients initiated secukinumab as a 1st biologic, 34 as 2nd, 26 as 3rd, and 23 as ≥ 4th. At initiation, 75/90 patients (83.3%) were not in MDA; 26/71 (36.6%) of those with follow-up data available achieved MDA at 6 months (Figure 1). In the overall population, 28 patients (41.2%) with TJC ≥ 1, 24 (44.4%) with SJC ≥ 1, 17 (60.7%) with enthesitis, and 9 (75.0%) with dactylitis at initiation achieved resolution at 6 months (Table 1). Improvement was observed at 6 months in clinical outcomes and PROs in the overall population (**Figures 1 and 2**) and in patients who initiated secukinumab as a ≥ 4th-line biologic.

Table 1. Resolution of Peripheral Arthritis, Enthesitis, and Dactylitis at 6 Months Among Patients With ≥ 1 Site at Initiation

Secondary Outcomes	Initiation, Mean (SD) [n]	6-Month Follow-Up, Resolution (Count = 0), n (%)
TJC (1-68)	9.0 (9.7) [68]	28 (41.2)
SJC (1-66)	4.7 (4.2) [54]	24 (44.4)
Enthesitis (1-6)	1.9 (1.1) [28]	17 (60.7)
Dactylitis (1-20)	2.1 (1.3) [12]	9 (75.0)

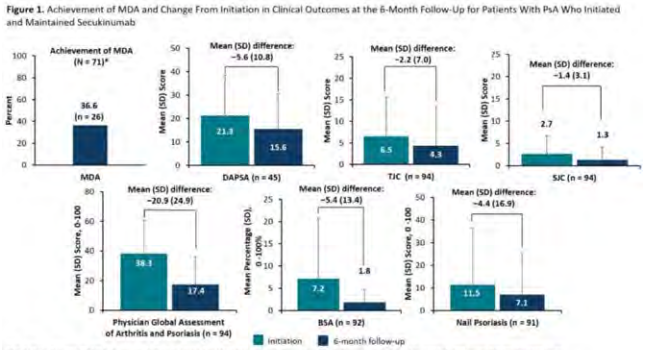


Figure 1. Achievement of MDA and Change From Initiation in Clinical Outcomes at the 6-Month Follow-Up for Patients With PsA Who Initiated and Maintained Secukinumab

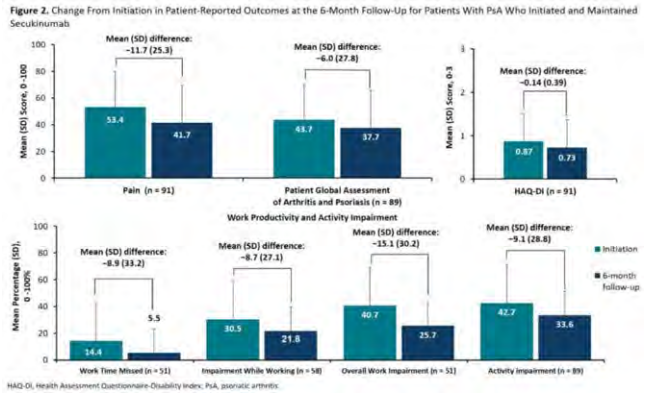


Figure 2. Change From Initiation in Patient-Reported Outcomes at the 6-Month Follow-Up for Patients With PsA Who Initiated and Maintained Secukinumab

Conclusion: In the Corrona registry, most secukinumab initiators with PsA were biologic experienced and were not in MDA at time of initiation. Consistent with clinical trials, real-world patients treated with secukinumab achieved MDA as well as improvement in clinical manifestations, PROs, and work productivity.
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[1] Orbai AM, et al. *J Rheumatol.* 2019 Oct 15. [Epub ahead of print].
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SAT0430 SECUKINUMAB EFFECTIVENESS IN 1543 PATIENTS WITH PSORIATIC ARTHRITIS TREATED IN ROUTINE CLINICAL PRACTICE IN 13 EUROPEAN COUNTRIES IN THE EUROSPA RESEARCH COLLABORATION NETWORK

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Background: There is a lack of real-life evidence on secukinumab effectiveness in psoriatic arthritis (PsA) patients.

Objectives: To assess the real-life 6- and 12-month secukinumab retention rates and proportions of patients in remission/low disease activity (LDA) overall, and by prior biologic disease-modifying anti-rheumatic drug (bDMARD)/targeted synthetic (ts)DMARD use.

Methods: Data from PsA patients treated with secukinumab in routine care from 13 countries in the European Spondyloarthritis (EuroSpA) Research Collaboration Network were pooled. Patients started secukinumab ≥12 months before date of datacut. Crude and LUNDEX adjusted (crude value adjusted for drug retention) 28-joint Disease Activity index for PSoriatic Arthritis (DAPSA28) and 28-joint Disease Activity Score with CRP (DAS28CRP) remission and LDA rates were calculated. Group comparisons between b/tsDMARD naïve, 1 prior and ≥2 prior b/tsDMARD users were done with ANOVA, Kruskal-Wallis, Chi-square or Kaplan-Meier analyses with log-rank test, as appropriate.

Results: A total of 1543 PsA patients were included (Table 1). b/tsDMARD naïve patients had shorter time since diagnosis, higher baseline disease activity, a higher proportion were men and a higher proportion achieved remission. Overall 6/12-month secukinumab retention rates were 86%/74% and significantly higher in b/tsDMARD naïve patients at 12, but not 6 months (Table 2, Figure). Overall, crude 6- and 12-month DAPSA28≤4/DAS28CRP<2.6 were achieved by 13%/34% and 11%/39% of the patients, respectively.

Table 1.

	All patients (n=1543)	b/tsDMARD naïve (n=287)	1 prior b/tsDMARD (n=333)	≥2 prior b/tsDMARDs (n=923)	p *
Age (years), mean (SD)	52 (11)	49 (12.3)	51 (11)	53 (11)	<0.001
Male, %	42%	49%	46%	39%	0.003
Years since diagnosis, mean (SD)	9 (8)	7 (8)	8 (7)	10 (8)	<0.001
Current smokers, %	19%	21%	22%	18%	0.23
CRP (mg/L), median (IQR)	5 (2-12)	7 (2-19)	4 (2-8)	5 (2-11)	<0.001
DAPSA28, median (IQR)	26 (18-37)	28 (19-38)	22 (13-32)	27 (19-38)	<0.001
DAS28CRP, median (IQR)	4.2 (3.3-5.0)	4.4 (3.5-5.2)	3.8 (2.6-4.5)	4.2 (3.4-5.0)	<0.001

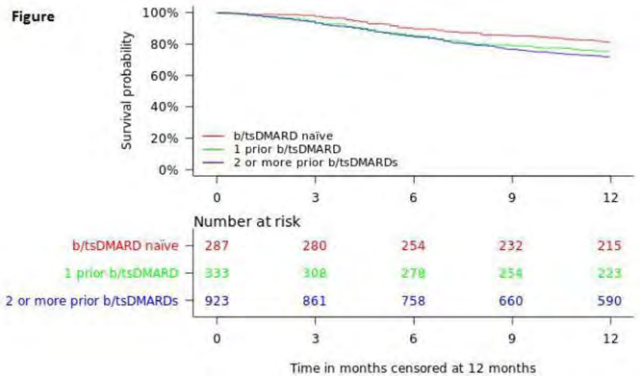
*Comparisons across number of prior b/tsDMARD were done with ANOVA, Kruskal-Wallis or Chi-square test, as appropriate

Table 2.

	Months	All patients (n=1543)	b/tsDMARD naïve (n=287)	1 prior b/tsDMARD (n=333)	≥2 prior b/tsDMARDs (n=923)	p *
Secukinumab retention rate, % (95%CI)	6	86% (84-87%)	89% (86-93%)	85% (81-89%)	85% (82-87%)	0.11
	12	74% (72-76%)	81% (76-86%)	76% (71-80%)	72% (69-75%)	0.006
DAPSA28≤4						
Crude	6	13%	25%	11%	11%	<0.001
LUNDEX		11%	22%	9%	9%	<0.001
Crude	12	11%	22%	11%	8%	<0.001
LUNDEX		7%	17%	7%	5%	0.001
DAS28CRP<2.6						
Crude	6	34%	51%	33%	30%	<0.001
LUNDEX		29%	45%	27%	24%	<0.001
Crude	12	39%	55%	41%	34%	<0.001
LUNDEX		26%	41%	27%	21%	<0.001
DAPSA28 >4 and ≤14						
Crude	6	33%	42%	32%	30%	0.04
LUNDEX		27%	37%	27%	25%	0.02
Crude	12	35%	48%	36%	32%	0.009
LUNDEX		24%	36%	24%	20%	0.004
DAS28CRP ≤3.2						
Crude	6	52%	69%	53%	47%	<0.001
LUNDEX		43%	61%	45%	38%	<0.001
Crude	12	55%	72%	55%	50%	<0.001
LUNDEX		37%	54%	37%	32%	<0.001

*Comparisons across number of prior b/tsDMARDs were done with Kaplan-Meier with log-rank test or Chi-Square test, as appropriate

Figure



Conclusion: In this real-life study of 1543 patients with PsA in 13 European countries 12-month secukinumab retention was high, and significantly higher for b/tsDMARD naïve patients. Overall, a higher proportion of bionaïve than previous b/tsDMARD users achieved remission, regardless of remission criteria.

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SAT0431 PROPORTIONS OF PATIENTS ACHIEVING A MINIMAL DISEASE ACTIVITY STATE UPON TREATMENT WITH TILDRAKIZUMAB IN A PSORIATIC ARTHRITIS PHASE 2B STUDY

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Background: Tildrakizumab (TIL) is a high-affinity anti–interleukin-23p19 monoclonal antibody approved in the US, EU, and Australia to treat moderate to severe plaque psoriasis. A randomised, double-blind, placebo-controlled, multiple-dose, phase 2b study evaluating the efficacy and safety of TIL was recently completed (NCT02980692).

Objectives: To characterise and evaluate the rate of minimal disease activity (MDA) up to week (W)52 from the phase 2b study.

Methods: Patients (pts) ≥18 years old with active psoriatic arthritis (PsA)[2] and ≥3 tender and ≥3 swollen joints were randomised 1:1:1:1:1 to receive TIL 200 mg every 4 weeks (Q4W) to W52, TIL 200 mg Q12W to W52, TIL 100 mg Q12W to W52, TIL 20 mg Q12W to W24→TIL 200 mg Q12W to W52, or placebo (PBO) Q4W to W24→TIL 200 mg Q12W to W52. MDA was assessed throughout the study; an MDA response was achieved when 5 of 7 criteria were met.[3] Safety was assessed throughout the study and included treatment-emergent adverse event (TEAE) monitoring.

Results: Of 500 pts screened, 391 were randomised and received ≥1 dose of study drug. At baseline (BL), mean age was 48.8 years, 55% were female, 97% were White, mean body mass index was 29.7 kg/m^2, and pts had PsA for a median (range) of 4.4 (0–42.8) years since diagnosis. Baseline disease characteristics related to MDA varied little between study arms (**Table**).

By W24, MDA state was achieved in significantly more pts receiving TIL vs PBO (24%–39% vs 7%; p<0.02 for all groups); the proportion further increased with continued TIL treatment to W52 (45%–64%), including pts who switched from PBO to TIL (47%) (**Figure**).

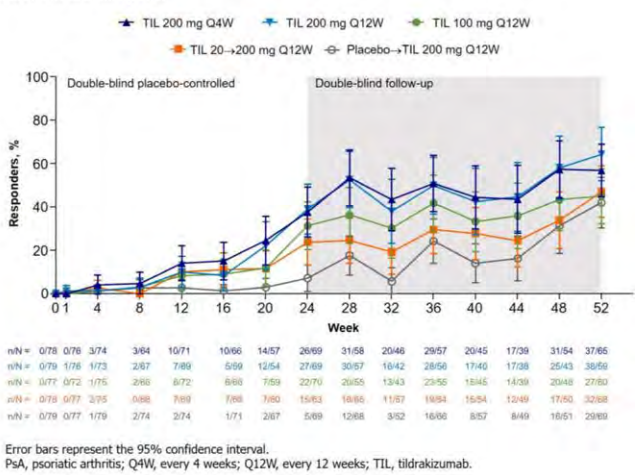
Among the overall pt population from BL→W24/W25→W52, 50.4%/39.9% and 2.3%/1.0% experienced a TEAE and serious TEAE, respectively. From BL→W24, 1 serious infection (chronic tonsillitis) was reported for TIL 20 mg→200 mg Q12W arm. From W25→W52, there was 1 malignancy (TIL 20→200 mg Q12W). There were no reports of candidiasis, uveitis, inflammatory bowel disease, major adverse cardiac events, or deaths from BL→W24 or W25→W52.

Table. Baseline disease characteristics related to minimal disease activity

	TIL 200 mg Q4W n = 78	TIL 200 mg Q12W n = 79	TIL 100 mg Q12W n = 77	TIL 20→200 mg Q12W n = 78	PBO→TIL 200 mg Q12W n = 79
Swollen joint count	10.4	10.0	11.0	9.4	11.8
Tender joint count	16.6	19.5	21.3	19.0	19.7
Patient GADA score	57.8	61.1	60.3	61.9	65.2
Patient pain assessment	55.4	59.6	59.2	60.9	64.2
Enthesitis (LEI) score*	1.9	1.5	2.2	2.2	1.5
PASI†	7.6	6.2	8.8	6.6	5.0
HAQ-DI score	1.0	1.0	1.0	1.1	1.2

Data are reported as mean.
*Total patients analysed (n) = 76, 79, 76, 78, 78, respectively.
†Total patients analysed (n) = 75, 79, 76, 75, 75, respectively.
GADA, global assessment of disease activity; HAQ-DI, Health Assessment Questionnaire Disability Index; LEI, Leeds Enthesitis Index; PASI, Psoriasis Area and Severity Index; PBO, placebo; Q4W, every 4 hours; Q12W, every 12 hours; TIL, tildrakizumab.

Figure. Minimal disease activity response rates from baseline to week 52 in PsA patients across treatments and time points



Error bars represent the 95% confidence interval.
PsA, psoriatic arthritis; Q4W, every 4 weeks; Q12W, every 12 weeks; TIL, tildrakizumab.

Conclusion: TIL produced clinically meaningful improvement in pts with PsA, resulting in a large proportion of pts achieving MDA by W52, and was well tolerated through W52.

References:
[1] Reich, et al. *Lancet* 2017;390:276–88.
[2] Taylor, et al. *Arthritis Rheum* 2006;54:2665–73.
[3] Coates, et al. *Ann Rheum Dis* 2010;69:48–53.

Disclosure of Interests: Peter Nash Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Gilead, Janssen, MSD, Novartis, Pfizer Inc, Roche, Sanofi, UCB, Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, MSD, Novartis, Pfizer Inc, Roche, Sanofi, UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, MSD, Novartis, Pfizer Inc, Roche, Sanofi, UCB, Michael E Luggen Grant/research support from: AbbVie; Amgen; Eli Lilly; Genentech; Nichi-Iko; Novartis; Pfizer; R-Pharm; and Sun Pharmaceutical Industries, Inc., Consultant of: AbbVie; Amgen; Eli Lilly; Genentech; Nichi-Iko; Novartis; Pfizer; R-Pharm; and Sun Pharmaceutical Industries, Inc., Speakers bureau: AbbVie; Amgen; Eli Lilly; Genentech; Nichi-Iko; Novartis; Pfizer; R-Pharm; and Sun Pharmaceutical Industries, Inc., Luis Espinoza: None declared, Ferran J García Fructuoso Grant/research support from: AbbVie, Eli Lilly, Gedeon Richter, MedImmune, Nichi-Iko, Pfizer, Sanofi-Aventis, Takeda, and UCB, Consultant of: AbbVie, Eli Lilly, Gedeon Richter, MedImmune, Nichi-Iko, Pfizer, Sanofi-Aventis, Takeda, and UCB, Speakers bureau: AbbVie, Eli Lilly, Gedeon Richter, MedImmune, Nichi-Iko, Pfizer, Sanofi-Aventis, Takeda, and UCB, Richard C Chou Consultant of: Sun Pharmaceutical Industries, Inc, Alan M Mendelsohn Shareholder of: Johnson and Johnson, Employee of: Sun Pharmaceutical Industries, Inc, Stephen Rozzo Employee of: Sun Pharmaceutical Industries, Inc, Iain McInnes Grant/research support from: Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Janssen, and UCB, Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Gilead, Janssen, Novartis, Pfizer, and UCB

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SAT0432 EFFECT OF SEX ON DISEASE CHARACTERISTICS AND DISEASE IMPACT IN PATIENTS WITH PSORIATIC ARTHRITIS (PSA): INSIGHTS FROM THE REAL-WORLD, OBSERVATIONAL MULTINATIONAL PSABIO COHORT

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Background: Female sex has been associated with more severe disease and poorer treatment outcomes in PsA. These observations are often based on small populations or national cohorts/registries.

Objectives: To investigate the effects of sex on disease characteristics and disease impact in PsA, using data of 929 consecutive patients (pts) from PsABio.

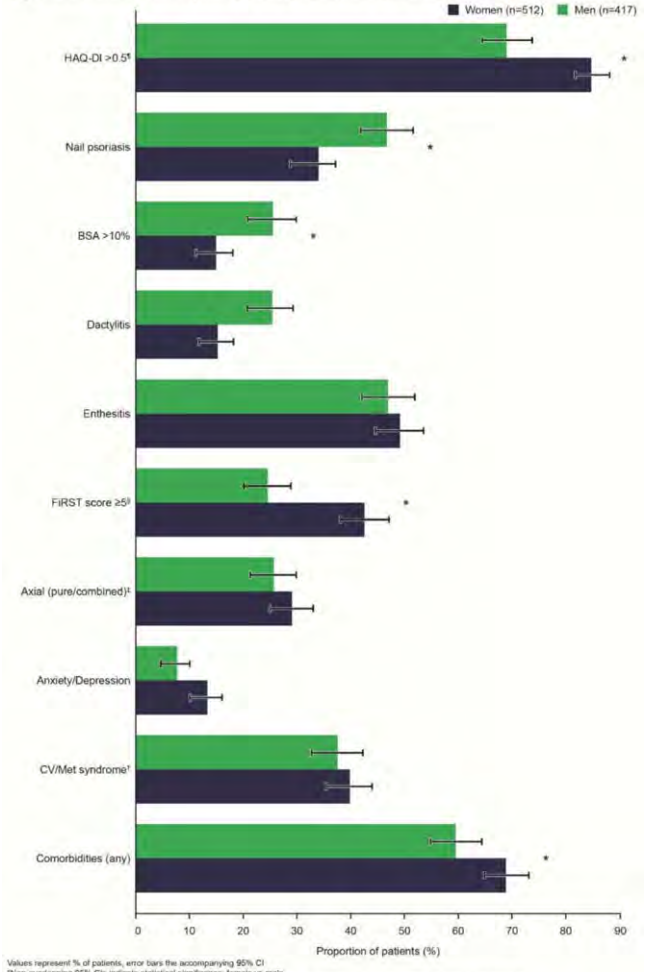
Methods: PsABio is a real-world, non-interventional European study in PsA pts treated with UST or TNFi based on their rheumatologist's choice. Observed male and female baseline (BL) data were described and compared using 95% CI.

Results: Women in PsABio (n=512 [55%]) were numerically older than men (mean [SD]: 50.5 [12.7] / 48.7 [12.3] years, respectively). Women were more obese (BMI >30), % (95% CI): F: 35 (30, 39), M: 24 (20, 29), men more overweight (BMI >25–30): F: 31 (27, 36), M:51 (46, 57). Age at diagnosis, delay from first symptom to diagnosis, and disease duration were similar for both sexes.

Women entered PsABio more often on 3rd line treatment, whereas men started on 1st-line biologic treatment more often (F/M 1st line 47%/55%; 2nd line 34%/33%; 3rd line 20%/12%). Numerically, concomitant MTX was given more often to women vs men (32% vs 27%). At BL, 60% of women and 64% of men were on NSAIDs; 7.9% and 2.5% on antidepressant drugs. Women had significantly more comorbidities, with numerically more cardiovascular disease and anxiety/depression, and 3 times more IBD.

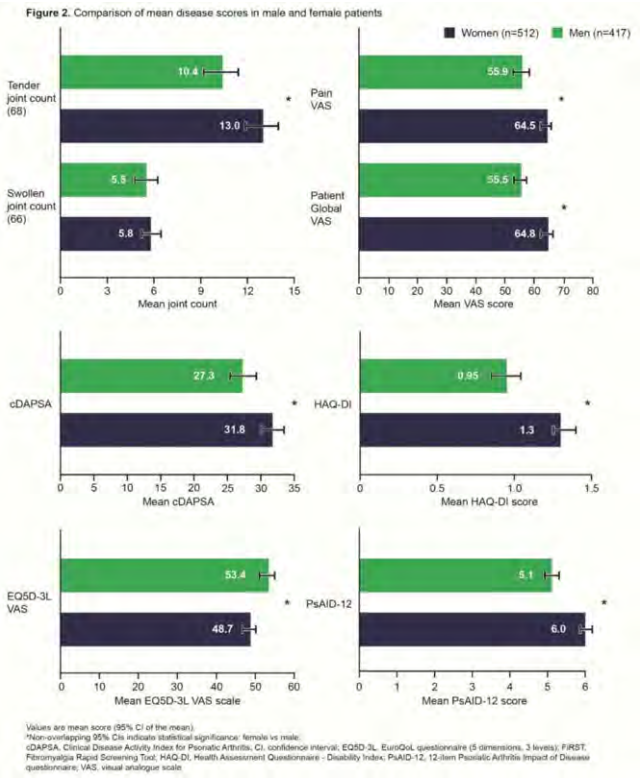
Women had significantly higher 68 tender joint counts (TJC): 13.0 vs 10.4, while 66 swollen joint counts were not significantly different: 5.8 vs 5.5. Axial or combined axial-peripheral disease was similarly frequent, in 29% of women and 26% of men (Figs. 1, 2).

Figure 1. Comparison of the observed percentages of male and female patients with selected disease characteristics



Values represent % of patients, error bars the accompanying 95% CI
*Non-overlapping 95% CIs indicate statistical significance: female vs male
[1]CV/Met syndrome defined as one or a combination of the following: hypertension, myocardial infarction, congestive heart failure, stroke or transient ischaemic attack, angina pectoris, peripheral vascular disease, hyperdyslipidaemia, type 1 or 2 diabetes or obesity, defined as BMI >30kg/m²
[2]According to the investigator's categorization; to be categorized as axial disease, the following was required: axial disease according to the investigator AND presence of inflammatory back pain
[3]FIRST score of ≥5 is potentially indicative of overlapping chronic widespread pain or fibromyalgia
[4]HAQ-DI score >0.5 indicates abnormal physical function
BSA, body surface area; CI, confidence interval; CV/Met, cardiovascular/metabolic; FIRST, Fibromyalgia Rapid Screening Tool; HAQ-DI, Health Assessment Questionnaire – Disability Index

Figure 2. Comparison of mean disease scores in male and female patients



Values are mean score (95% CI of the mean).
*Non-overlapping 95% CIs indicate statistical significance: female vs male.
cDAPSA, Clinical Disease Activity Index for Psoriatic Arthritis; CI, confidence interval; EQ5D-3L, EuroQoL questionnaire (5 dimensions, 3 levels); FIRST, Fibromyalgia Rapid Screening Tool; HAQ-DI, Health Assessment Questionnaire - Disability Index; PsAID-12, 12-item Psoriatic Arthritis Impact of Disease questionnaire; VAS, visual analogue scale

Clinical Disease Activity index for PSoriatic Arthritis (cDAPSA) was higher in women (31.8 vs 27.3); pt-reported levels of pain, global disease activity (VAS scales) and higher TJC contributed to this. While enthesitis prevalence (based on Leeds Enthesitis Index) was comparable, men had significantly more frequent dactylitis, nail disease and worse skin psoriasis. At BL, 3.4% of women vs 7.1% of men, were in MDA.

Regarding physical functioning (HAQ-DI), impact of disease (PSAID-12) and quality of life (EQ5D-3L health state), women with PsA starting a biologic (b) DMARD, expressed significantly greater negative impact and more limitations due to their disease (Fig. 2).

Conclusion: In routine care, women with PsA starting a bDMARD presented with worse outcomes over a range of assessments compared with men (higher pt-reported pain and disease activity, TJC, and worse physical functioning and QoL), while men had worse dactylitis and psoriasis. Follow-up analysis will report whether the effects of biologic therapy are different in both sexes. The increased prevalence of associated features related to pain and impact on functioning and QoL may indicate the need for a more comprehensive treatment approach for women to avoid unnecessary and premature bDMARD stop or switch.

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Merck Sharp & Dohme, Novartis, Pfizer, Tatiana Korotaeva Grant/research support from: Pfizer, Consultant of: Abbvie, BIOCAD, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Merck Sharp & Dohme, Novartis, Novartis-Sandoz, Pfizer, UCB, Speakers bureau: Abbvie, BIOCAD, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Merck Sharp & Dohme, Novartis, Novartis-Sandoz, Pfizer, UCB, Wim Noel Employee of: Janssen Pharmaceuticals NV, Petros Sfikakis Grant/research support from: Grant/research support from Abvie, Novartis, MSD, Actelion, Amgen, Pfizer, Janssen Pharmaceutical, UCB, Elke Theander Employee of: Janssen-Cilag Sweden AB, Josef S. Smolen Grant/research support from: AbbVie, AstraZeneca, Celgene, Celltrion, Chugai, Eli Lilly, Gilead, ILTOO, Janssen, Novartis-Sandoz, Pfizer Inc, Samsung, Sanofi, Consultant of: AbbVie, AstraZeneca, Celgene, Celltrion, Chugai, Eli Lilly, Gilead, ILTOO, Janssen, Novartis-Sandoz, Pfizer Inc, Samsung, Sanofi, Laure Gossec Grant/research support from: Lilly, Mylan, Pfizer, Sandoz, Consultant of: AbbVie, Amgen, Biogen, Celgene, Janssen, Lilly, Novartis, Pfizer, Sandoz, Sanofi-Aventis, UCB

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SAT0433 TRIAL SIMULATION TO INFORM ENROLLMENT CRITERIA AND OUTCOME MEASURES FOR PRAGMATIC TRIALS IN PSA

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Background: Randomized controlled trials (RCTs) in psoriatic arthritis (PsA) have traditionally enrolled a homogenous subgroup of patients with more polyarticular disease, and the outcome measure used in PsA RCTs (ACR20) may not be ideal to measure differences between two active therapies nor capture change in patients with lower joint counts.
Objectives: We conducted a simulation study to determine how changing the inclusion criteria and the primary outcome measure would impact the outcome of a future RCT.
Methods: We used the Tight Control of PsA (TICOPA)[1] trial to inform simulation of two hypothetical head-to head trials comparing MTX to TNFi with 100 patients per arm. Within TICOPA, we identified MTX and TNFi new users; the visit at drug initiation became the hypothetical trial baseline visit, and the follow up visit was 12 weeks later. These data informed prediction models to simulate enrolled patients. We utilized propensity score-adjusted outcome models to account for potential confounding by indication. Trial 1, modeled after the SEAM-PsA trial,[2] used typical enrollment criteria (≥3 tender joint count (TJC) and ≥3 swollen joint count (SJC))[2]; Trial 2 required ≥1 TJC/SJC.[1] For each trial, five binary outcomes were simulated: ACR20, Disease Activity in PsA (DAPSA), clinical DAPSA (cDAPSA), Routine Assessment of Patient Index Data (RAPID3), and PsA Disease Activity Score (PASDAS), where low disease activity was the cutoff for continuous measures. Each hypothetical trial was simulated 1000 times, and the distribution of estimated effects was summarized using standard summary statistics and graphs.
Results: Among 188 patients in TICOPA, 179 patients initiated MTX, and 43 patients initiated TNFi within the first 36 weeks. Among these, 107 MTX initiators and 15 TNFi initiators had ≥3 TJC and ≥3 SJC at drug initiation. Baseline characteristics of those in the "severe" (≥3 TJC and ≥3 SJC) and not severe (not meeting ≥3 TJC and ≥3 SJC) are shown in Table 1. Among "severe" patients, the mean probability of achieving ACR20 across simulations was approximately 0.27 in both arms and the observed relative risk (RR) TNFi vs MTX severe cohort across simulations was 1.0, IQR 0.84-1.17 (the RR in the SEAM trial at 24 wks was 1.20, 95%CI:1.05-1.35). In the "full cohort," the median RR was 1.0, IQR 0.81-1.04. Trials using PASDAS, cDAPSA, and RAPID3 were more likely to differentiate between TNFi and MTX in the severe cohort (figure) but in the full cohort the results favored MTX.

Table 1. Observed characteristics at drug initiation

	Severe (n=148)			Not Severe (n=75)		
	MTX (n=127)	TNFi (n=21)	SMD	MTX (n=52)	TNFi (n=23)	SMD
TICOPA Arm (no. (%))						
Standard Care	57 (45%)	4 (19%)	0.58	28 (54%)	3 (13%)	0.96
Intensive Management	70 (55%)	17 (81%)		24 (46%)	20 (87%)	
Female (no. (%))	65 (51%)	11 (52%)	0.02	22 (42%)	12 (52%)	0.20
TJC (mean (SD))	17.8 (15.3)	19.1 (17.3)	0.08	3.5 (4.6)	16.4 (19.1)	0.93
SJC (mean (SD))	9.2 (7.4)	10.2 (12.1)	0.10	2.4 (3.4)	2.2 (2.4)	0.05

Severe = ≥3 tender and ≥3 swollen joints
Not-severe = <3 tender or <3 swollen joints
*Pseudo-baseline characteristics were at the time of drug initiation. In cases where the patient started a TNFi between visits, these were the values at the previous visit.
Abbreviations: SMD = standardized mean difference, TJC=tender joint count, SJC=swollen joint count

Conclusion: Including patients with lower joint counts in an RCT reduced the ability to detect change with therapy. Additionally, among the outcome measures used to detect a difference between two active therapies, PASDAS, cDAPSA, and RAPID3 outperformed ACR20.

References:
[1] Coates et al. Lancet 2015; 2. Mease et al. Arthritis Rheumatol 2019

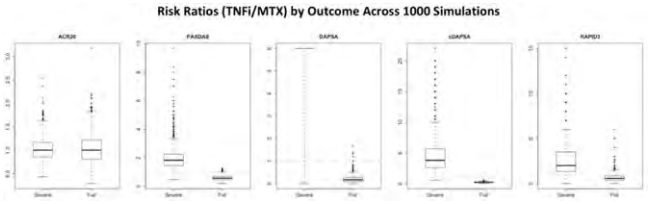


Figure 1. Risk Ratios (TNFi vs MTX) by Outcome Across 1000 Simulations

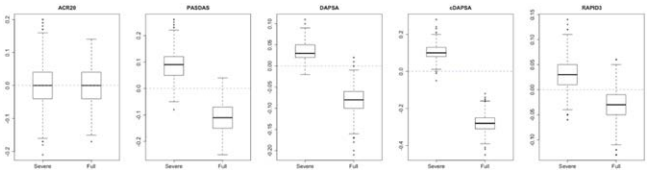


Figure 2. Risk Differences (TNFi – MTX) by Outcome Across 1000 Simulations

Disclosure of Interests: Alexis Ogdie Grant/research support from: Pfizer, Novartis, Consultant of: Abbvie, Amgen, BMS, Celgene, Corrona, Janssen, Lilly, Pfizer, Novartis, Sarah Weinstein: None declared, Laura C Coates: None declared, Philip Helliwell: None declared, Alisa Stephens-Shields: None declared
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SAT0434 MINIMAL CLINICALLY IMPORTANT DIFFERENCE IN OUTCOME MEASURES FOR USE IN CLINICAL CARE AND PRAGMATIC TRIALS IN PSA

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Background: While several outcome measures have been studied for use in clinical studies of psoriatic arthritis, little is known about thresholds of meaning such as minimal clinically important improvement (MCII).
Objectives: To investigate the distribution of scores for candidate outcome measures for pragmatic trials in PsA and to calculate the MCII for each outcome measure.
Methods: We performed a longitudinal cohort study within the Psoriatic Arthritis Research Consortium (PARC), a multi-center study based in the US. Patients completed validated PROs (patient reported outcomes) and rheumatologists completed skin, joint, enthesis and dactylitis scores at therapy initiation and follow up 12-16 weeks later. In addition, patients completed a global assessment of response at the follow up visit, categorizing their status as improved, stayed the same, or worsened and then ratied the importance of the change on a scale from 0-7.[1] We then calculated and plotted the change in each of the following measures: Routine Assessment of Patient Index Data (RAPID3), clinical Disease Activity of Psoriatic Arthritis (cDAPSA), Patient Reported Outcome Measure Information System (PROMIS) Global Health short form (10a) physical health (PH) subscore, patient pain assessment, patient global assessment (0-10 NRS), and physician global assessments (0-10 NRS) of the joints and overall. We calculated the MCII as the mean change in score (with 95% confidence interval) among patients who reported improvement and rated the level of improvement as "almost none/hardly at all" or "a little important." Additionally, we calculated Spearman's correlation coefficients between the measures and the global assessment of response.
Results: Among 148 unique patients, 233 therapy change visits were eligible for analysis. The average age was 52.5 years, 52% were female and mean BMI was 29.6. Baseline RAPID3 was 11.1 (SD 6), cDAPSA 17.9 (SD 13.9), PROMIS PH 42 (SD 8), patient global 4.2 (SD 2.5), TJC 5.9 (SD 7.5), and SJC 2.9 (SD 4.5). TNFi comprised 61% of drug initiations, 21% were IL17i and the remainder were other biologics and oral systemic therapies. At follow up, 63 (27%) patients rated themselves as improved whereas 103 (44%) stayed the same and 67 (29%) reported

worsening. The mean change in each measure by patient-reported response (improved, stayed the same, or worsened) are shown in Figures 1A & B. In general, the mean score increased from 'improved' to 'worsened' as expected (with the exception of PROMIS PH which declines given a different direction of scoring). The MCII for each measure was as follows: RAPID3 -1.8 (-4.1 to 0.5), Patient Global -0.6 (-1.6 to 0.4), Physician Global -1 (-1.9 to -0.1), cDAPSA -5.7 (-9.8 to -1.7), and PROMIS PH 1.9 (-2.1 to 5.8). Correlation for each measure with the global assessment of response were: RAPID3 0.48, Patient Global 0.37, Physician Global 0.39, cDAPSA 0.51, and PROMIS PH 0.39.

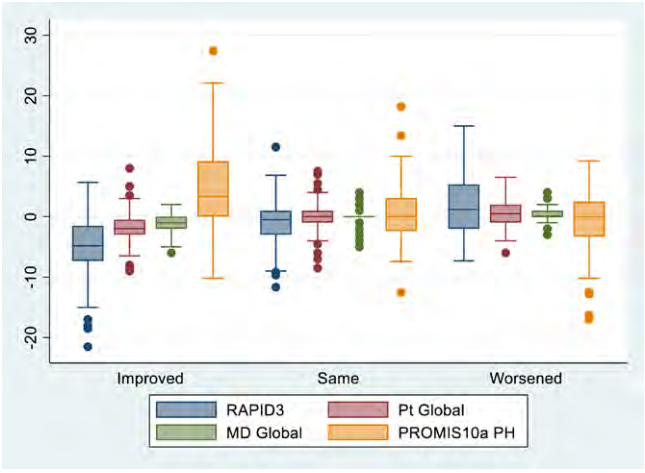


Figure 1 A. Distribution of change (median, IQR) in RAPID3, Physician Global, Patient Global, PROMIS10a physical therapy by patient reported response.

Conclusion: This is the first study to test thresholds of meaning for these particular measures in PsA. The MCII values are relatively low for all outcome measures. This may be related to the relatively low disease activity at baseline but is consistent with patients seen in clinical practice initiating therapy.[2]

References:

[1] Ward MM et al. J Clinical Epi 2014; [2]Ward MM et al. J Clinical Epi 2015

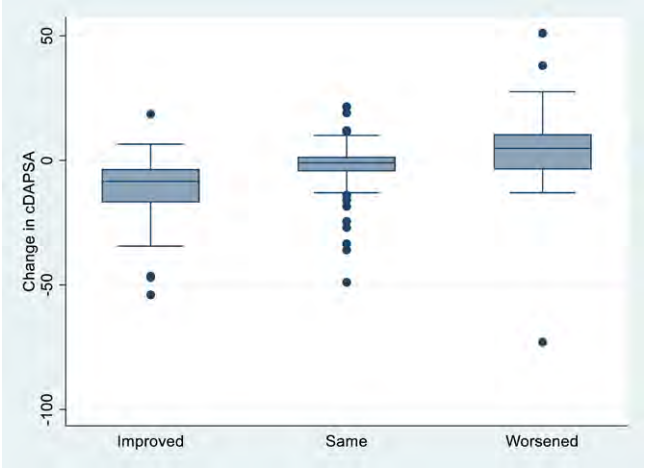


Figure 2 B. Distribution of change (median, IQR) in clinical DAPSA by patient reported response.

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SAT0435 SECUKINUMAB EFFICACY IN PSA PATIENTS IS DEPENDENT ON PATIENTS' BODY MASS INDEX

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory arthritis burdened by a series of metabolic comorbidities. Among them, obesity is very common in PsA, with a prevalence of 27%, as confirmed by a recent Spanish work (1). Obesity in PsA has been associated with higher disease activity and a worse effectiveness of biologic treatment in PsA. This has been certainly proven for anti-TNF-α as demonstrated by different studies reporting, in obese patients, a reduced treatment response and adherence. In particular, results coming from DAN-BIO and ICE-BIO registries, (2) point out that obesity is a risk factor for anti-TNF withdrawal due to poor response. Although a recent multi-centric, retrospective study in Spain has shown that obese subjects with psoriasis have a poor therapeutic response to secukinumab, (3) no data are currently available for secukinumab in PsA obese patients.

Objectives: Our studies focused on the relationship between BMI and clinical response to secukinumab in PsA.

Methods: We, retrospectively, analysed clinical data of 100 patients with PsA (57% female, median age 53 (49.2-55 years)) satisfying CASPAR criteria (4) for PsA, afferent to our clinic, who were treated with secukinumab. Patients were divided into 2 groups based on BMI (BMI<25 normal weight and BMI≥25 overweight/obese).

Results: In the normal weight group 75% were female, median age was 50.5 (41-54.6), median BMI was 22 (20.2-23.3) and median DAPSA was 19.19 (15.6-24.2). The features of the overweight/obese patients were similar to the normal weight group (48% were female, median age 54 (50-59), median BMI 29 (27.4-30.1) and median DAPSA 21.2 (19-24.4)). Clinical response to therapy, evaluated as the achievement of low disease activity or remission according to DAPSA, was recorded 6 months after starting treatment. After 6 months of treatment, the variation of the DAPSA was inversely related to BMI: overweight/obese patients had in fact a better response to secukinumab compared to normal weight patients. By using a correlation coefficient (SPSS), to analyze the degree of association between BMI and DAPSA, we observed that BMI and DAPSA are inversely related in our PsA patients (p=0.05). Interestingly, analysis of serum levels of IL-17 in 20 obese patients compared to 20 non-obese patients, showed significantly higher serum levels of IL-17 in the former (Figure 1), indicating IL-17 as a key cytokine driving inflammation in PsA obese patients.

Conclusion: These are the first data about clinical response to secukinumab in obese PsA patients. Our results support the relevance of IL-17 in driving systemic inflammation in obese PsA patients, also providing evidence that obese patients may have a better response to secukinumab compared to non-obese patients. Interestingly, this effect was not

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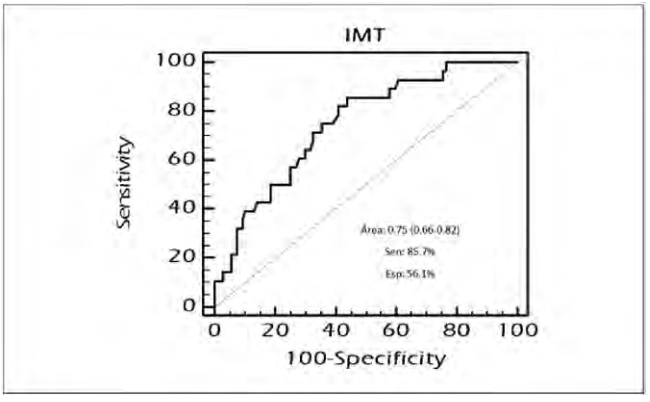
Disclosure of Interests: Ilenia Pantano: None declared, DANIELA IACONO Speakers bureau: PFIZER, BRISTOL MAYERS SQUIBB, SANOFI, ENNIO GIULIO FAVALLI: None declared, GIUSEPPE SCALISE: None declared, Luisa Costa: None declared, Francesco Caso: None declared, Giuliana Guggino Grant/research support from: Pfizer, Celgene, Speakers bureau: Celgene, Sandoz, Pfizer, Raffaele Scarpa: None declared, francesco ciccia Grant/research support from: pfizer, novartis, roche, Consultant of: pfizer, novartis, lilly, abbvie, Speakers bureau: pfizer, novartis, lilly, abbvie
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SAT0436

PATIENTS WITH PSORIATIC ARTHRITIS WHO ACHIEVE THE MDA RESPONSE SHOW LESS SUBCLINICAL ATHEROSCLEROSIS THAN THOSE IN DAPSA REMISSION

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Background: Although the MDA response and DAPSA remission are treatment objectives proposed by EULAR for a proper management of psoriatic arthritis (PsA), there is no clear consensus on which of the two is the most advisable in clinical practice. Some studies suggest that patients who reach a sustained MDA have less subclinical atherosclerosis, but whether the same applies to DAPSA remission is unknown at present.
Objectives: To compare the frequency of subclinical atherosclerosis in patients with PsA that reach the MDA response versus those who achieve DAPSA remission.
Methods: One hundred-forty consecutive patients with PsA (CASPAR criteria) treated with biological and non-biological systemic agents were included. SCORE risk charts were used to estimate cardiovascular risk (CVR). The presence of plaques and / or carotid intima-media thickness (cIMT) > 0.9 mm in carotid ultrasound defined subclinical atherosclerosis. These findings were analyzed in patients in MDA and in those in DAPSA remission.
Results: According to the SCORE tables, 42.8%, 35.7% and 21.5%, had low, moderate and high-very high CVR, respectively. There was a linear association between cIMT values and the SCORE risk categories (p <0.0005). The best cut-off point to define a high CVR (by SCORE plus carotid plaques) corresponded to a cIMT > 0.63 mm, with an area under the ROC curve of 0.75 (0.66-0.82), sensitivity 85.7%, specificity 56.1% (Figure 1). Ninety-seven of the 140 patients (69.3%) were in MDA situation, while 60 (42.8%) were in DAPSA remission. The average value of the cIMT was 0.64 ± 0.12 mm. One in 4 patient had atheroma plaques, while 19 (13.6%) had a cIMT> 0.9 mm. There were no differences in cIMT values of patients with (0.66 ± 0.12 mm) and without (0.63 ± 0.12 mm) DAPSA remission. An identical percentage (25%) of patients with and without DAPSA remission had carotid atheroma plaques. On the other hand, there were differences between patients with (6.2%) and without (30.2%) MDA in terms of cIMT values > 0.9 mm, p <0.05. 32.6% of non-MDA and 23.7% of MDA patients had carotid plaques, p NS.
Conclusion: Patients who achieve an MDA response show less subclinical atherosclerosis than those in DAPSA remission. These findings suggest that the MDA response better discriminates the presence of subclinical atherosclerosis, and therefore, it could be a more complete therapeutic target than DAPSA remission.



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SAT0437

GENDER DIFFERENCES IN PSA OUTCOME PARAMETERS AND THEIR CORRELATION WITH SKIN INVOLVEMENT: A CROSS-SECTIONAL ANALYSIS OF RABBIT-SPA PATIENTS

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Background: PsA is a complex disease characterised by a heterogeneous pattern including different clinical symptoms of musculoskeletal (MSK) inflammation like arthritis, enthesitis, dactylitis and axial involvement as well as skin and nail involvement. There are differences in these disease patterns between female and male patients which need to be taken into account.
Objectives: To assess the differences between female and male PsA patients in the extent of psoriatic skin (body surface area, BSA) and joint (tender joint count 68, TJC68; swollen joint count 66, SJC66;) disease, composite scores (disease activity in PsA, DAPSA; disease activity score 28, DAS28), and patient-reported outcomes (PROs) and to correlate the extent of skin disease with PROs.
Methods: RABBIT-SpA is a prospective longitudinal cohort study including PsA patients enrolled at start of a new csDMARD, bDMARD or tsDMARD. Gender specific differences in outcome parameters are compared using Wilcoxon resp. t-test at baseline visit. Spearman correlation coefficient was calculated to analyse the relationship between BSA and outcome parameters.
Results: 722 PsA patients were included in this analysis. Women were slightly older (52 vs 50 yrs), had longer disease duration (7 vs 5.8 yrs), more comorbidities and were more often obese. Men had a significantly higher skin involvement than women measured by BSA and physician skin assessment (physSk, table 1). Women had significantly higher joint involvement as measured by TJC68, DAPSA, DAS28, and patient muskuloskeletal assessment (patMSK). Impact of disease as measured by PSAID and patient global assessment (patGA) was more severe in women than in men and also physical function (HAQ) was lower in women than in men (table 1). Despite the higher skin involvement in men, the DLQI was equally high in women and men with more than 50% of patients in reduced quality of life state (table 1).

Table 1.

Parameter	Female N=424	Male N=298
SJC66	3.4 (5)	2.7 (3.8)
TJC68	7.9 (8.7)	5.7 (7)
BSA (0-100)	6.6 (13)	10.8 (16.5)
physGA (NRS 0-10)	5.3 (1.9)	5.2 (2)
physSk (NRS 0-10)	3.1 (2.7)	3.7 (2.6)
physMSK (NRS 0-10)	5.2 (2.1)	4.9 (2.3)
DAPSA	24.2 (13.8)	20.1 (12.3)
DAS28-CRP	3.7 (1.2)	3.4 (1.2)
patGA (NRS 0-10)	5.5 (2.1)	4.9 (2)
patSk (NRS 0-10)	3.9 (3.1)	3.9 (2.8)
patMSK (NRS 0-10)	5.8 (2.2)	5 (2.5)
DLQI (0-30)	6.1 (6.8)	5.3 (5.7)
HAQ (0-3)	1.1 (0.6)	0.7 (0.6)
PSAID (0-10)	4.8 (2.3)	3.9 (2.2)

Results are presented as mean ± SD.

BSA was not correlated with SJC66 or TJC68, DAPSA, DAS28, phys MSK, patGA and patMSK neither in men nor in women. BSA was however positive correlated with DLQI, patSk, and physSK and slightly with physGA in both genders. The PSAID is correlated to BSA in women only.
Conclusion: Women and men show differences regarding many PsA criteria. Men have a more severe skin involvement, while women have higher burden of joint involvement. In addition in the patient reported parameters women show significantly higher values than men except for the skin specific parameters. Notably, although skin involvement is not correlated with most PsA activity parameters, around 50% of patients in specialised rheumatologic care are negatively affected in their quality of life by psoriatic skin disease. Therapeutic decisions need to take into account the complexity of the patients' symptoms as well as gender differences.
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SAT0438

REAL-WORLD TREATMENT PERSISTENCE WITH BIOLOGIC DISEASE MODIFYING ANTIRHEUMATIC DRUGS AMONG GERMAN PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Persistence rates of biologic disease modifying antirheumatic drugs (bDMARDs), which refer to the duration of time from initiation to discontinuation or switch of therapy, have been shown to vary considerably depending on the country, types of health centers, as well as the specific drug being investigated. Evidence on treatment persistence of psoriatic arthritis (PsA) patients in Germany is scarce.
Objectives: Our aim was to study drug survival of bDMARDs in a German real-world cohort of adult biologic-naïve psoriatic arthritis patients.
Methods: We utilized the German "Institut für angewandte Gesundheitsforschung Berlin" (InGef) research database consisting of about 4 million covered lives structured to represent the German population in terms of age and gender according to the Federal Office of Statistics (DESTATIS). Thereof, 2.9 million patients were continuously enrolled in the study period spanning from January 1st, 2013 and December 31st, 2018. For the analysis of persistence rates, the study population was identified based on the International Classification of Diseases, German Modification (ICD-10-GM) and claims records of biologic prescriptions based on ATC codes. Adult patients who had a diagnosis of psoriasis arthritis (L40.5 in combination with M07.0 or M07.1 or M07.2 or M07.3) in the inpatient or outpatient setting, and a claims record of biologic treatment licensed for psoriasis arthritis between January 1st, 2014 to December 31st, 2017 were included. Patients with Crohn's disease (K50), ulcerative colitis (K51), ankylosing spondylitis (M45), and rheumatoid arthritis (M05-M07) were excluded. Biologic-naïve patients were identified as those who had no prior record of bDMARDs prescription during the 12 months before the index date ('washout'). The index date was defined as the first claim for a biologic agent. Non-persistence occurred if a treatment gap exceeding the days of supply plus 60 days or a switch to a bDMARD other than the index therapy was observed. Days of supply were calculated based on the daily defined doses defined by the WHO for the respective bDMARDs. Kaplan-Meier curves were plotted to show the persistence of different biologics. The log-rank test was used to test for differences in the 1-year persistence rate.
Results: Among 10,954 patients with a diagnosis of PsA, 348 biologic-naïve patients aged 18 years or above were identified. The one-year overall persistence rate was 57.5% for all bDMARD compounds. Reasons for non-persistence were switches to a different bDMARD agent in 15.8% of patients and 26.7% discontinued treatment. The highest persistence rate was observed for ustekinumab (81.3%), which was significantly higher than the respective rates for adalimumab (58.1%), certolizumab pegol (51.7%), etanercept (51.0%), or secukinumab (54.7%).
Conclusion: Persistent rates for a real-world cohort of German PsA patients are modest with significant variations among different bDMARD therapies.
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Rheumazentrum Rhein-Ruhr, Consultant of: AMGEN GmbH AbbVie Deutschland GmbH & Co. KG Biogen GmbHBristol-Myers Squibb Celgene GmbH Chugai Pharma arketing Ltd. / Chugai Europe GmbHHexal Pharma Janssen-Cilag-GmbH Johnson & Johnson Deutschland GmbHLilly Deutschland GmbH / Lilly Europe / Lilly Global Novartis Pharma GmbH Pfizer Deutschland GmbH Roche Pharma Rheumazentrum Rhein-Ruhr Sanofi-Genzyme Deutschland GmbH Swedish Orphan Biovitrum GmbH UCB Pharma GmbH, Speakers bureau: AMGEN GmbH AbbVie Deutschland GmbH & Co. KG Biogen GmbHBristol-Myers Squibb Celgene GmbH Chugai Pharma arketing Ltd. / Chugai Europe GmbHHexal Pharma Janssen-CilagGmbH Johnson & Johnson Deutschland GmbHLilly Deutschland GmbH / Lilly Europe / Lilly Global Novartis Pharma GmbH Pfizer Deutschland GmbH Roche Pharma Rheumazentrum Rhein-Ruhr Sanofi-Genzyme Deutschland GmbH Swedish Orphan Biovitrum GmbH UCB Pharma GmbH, Kathrin Borchert Consultant of: Janssen-Cilag GmbH, Dominic Meise Consultant of: Janssen-Cilag GmbH, Jörg Mahlich Shareholder of: Janssen-Cilag GmbH, Employee of: Janssen-Cilag GmbH
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SAT0439

POWER DOPPLER ULTRASOUND ASSESSMENT OF A1 PULLEY. A NEW TARGET IN PSORIATIC ARTHRITIS?

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Background: In the last few years annular pulleys inflammation has been highlighted as a possible key pathogenetic factor in psoriatic dactylitis, first with magnetic resonance imaging (MRI)[1], then, in a very recent paper[2], with power Doppler (PD) ultrasound (US). However, the prevalence of PD US inflammation of annular pulleys in psoriatic arthritis (PsA) patients compared to rheumatoid arthritis (RA) patients has not been investigated yet.
Objectives: To determine the prevalence of PD US findings indicative of A1 pulley inflammation in PsA patients and in controls with RA and to preliminarily investigate the correlation between A1 pulley inflammation and disease activity (DAPSA).
Methods: Consecutive patients with PsA and RA were included in this cross-sectional single-centre study. A rheumatologist recorded demographic and clinical data and in the same day another rheumatologist performed the US examination using a MyLab ClassC (Esaote, Genova, Italy) equipped with a 10-22 MHz linear probe. A1 pulleys of fingers 2nd to 5th were assessed bilaterally adopting longitudinal and transverse scans. The following pathological US findings were recorded: inflammation of the pulley (defined as the presence of PD signal within a thickened pulley) and tenosynovitis of the digital flexor tendons at finger level according to OMERACT definition.
Results: Sixty patients were enrolled: 30 with PsA and 30 with RA. Inflammation of A1 pulley was found in 15 out 240 fingers (6.3%) of 8 (26.7%) PsA patients and in 1 out of 240 fingers (0.4%) of 1 (3.3%) RA patients ($p<0.01$ and $p=0.03$ respectively). Both pulley inflammation and tenosynovitis were correlated with DAPSA (Rpb=0.56, $p<0.01$ and Rpb=0.48, $p<0.01$). In fact, 7 out 8 (88%) PsA patients with at least one inflamed A1 pulley had a moderate/high disease activity score. The regression linear analysis (R2=0.36, adjusted R2=0.31) showed that A1 pulley inflammation was correlated with higher DAPSA scores ($\beta=0.43$, $p=0.03$). No significant association was reported between A1 pulley inflammation and past or current episodes of dactylitis ($p=0.09$). However, the only current dactylitis assessed showed A1 pulley inflammation.
Conclusion: This pilot study demonstrated that ultrasound A1 pulley inflammation, defined as the presence of power Doppler signal within a thickened pulley, is relatively common at patient level in psoriatic arthritis and seems to be characteristic of PsA compared to RA. In psoriatic arthritis patients, a positive significant correlation was found between ultrasound A1 pulley inflammation and disease activity.
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SAT0440

METHOTREXATE SURVIVAL RATE IN PATIENTS WITH PSORIATIC ARTHRITIS FROM PSORIATIC ARTHRITIS –INTERNATIONAL DATABASE (PSART-ID) COHORT

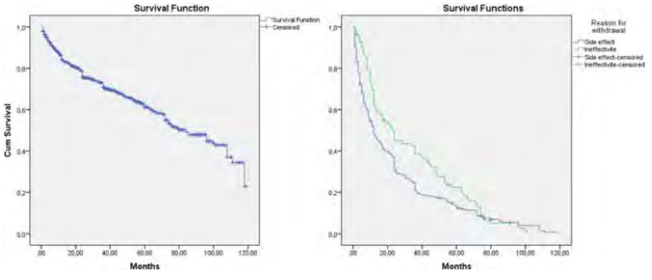
D. Solmaz[1], U. Kalyoncu[2], I. Tinazzi[3], O. Bayindir[4], E. Dalkılıç[5], A. Dogru[6], C. Özişler[7], G. Kimyon[8], G. Yildirim Cetin[9], A. Omma[10], E. F. Tarhan[1], L. Kılıç[2], S. Akar[1], S. Yılmaz[11], M. Can[12], S. Yavuz[12], O. Küçükşahin[7], S. Bakırcı[13], S. Aydin[14]. *[1]Izmir Katip Celebi University School of Medicine, Izmir, Turkey*; *[2]Hacettepe University School of Medicine, Ankara, Turkey*; *[3]Ospedale Sacro Cuore, Verona, Italy*; *[4]Ege University, Izmir, Turkey*; *[5]Uludag University, Bursa, Turkey*; *[6]Suleyman Demiral University, Isparta, Turkey*; *[7]DisKapi Yildirim Beyazit Education and Research Hospital, Ankara, Turkey*; *[8]Mustafa Kemal University, Hatay, Turkey*; *[9]Kahramanmaraş Sutcu Imam University, Kahramanmaras, Turkey*; *[10]Ankara Numune Education and Research Hospital, Ankara, Turkey*; *[11]Selcuk University, Konya, Turkey*; *[12]Marmara University, Istanbul, Turkey*; *[13]Antalya*

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Background: Methotrexate (MTX) is the most common first-line disease-modified anti-rheumatic drugs in psoriatic arthritis (PsA), despite the controversies.
Objectives: In this study, we aimed to determine the rate of withdrawal rate of MTX in PsA and reasons for discontinuing.
Objectives: In this study, we aimed to determine the rate of withdrawal rate of MTX in PsA and reasons for discontinuing.
Methods: A large prospective international multicenter PsA registry was used for this study. Data were collected either at enrolment, based on history, or prospectively if there was a follow up. We analyzed the frequency of MTX usage, discontinuation and the reason for discontinuation. The time on MTX was compared according to the reason of discontinuation (inefficacy vs side effects) using Kaplan-Meier and Cox regression analyses to identify risk factors for discontinuation.
Results: At the time of analyses, 1670 patients had been recruited to the registry and 1359 PsA patients had used MTX during the course of the disease (81.3%). Within these, 942 (69.3%) were still on MTX at the time of analysis, and 417 (30.7%) patients have discontinued (Table). The most common reasons for withdrawal were side effects (219/417, 52.5%) and ineffectiveness (88/417, 21.1%). Other reasons included pregnancy, remission, self-decision (11.9% for all). For 60 patients (14.3%), the reason could not be identified. In patients who were still on MTX, the median duration of MTX therapy was 31 months (IQR=59) compared to 17 months (IQR=43) in the withdrawal group. The most common side effects were gastrointestinal symptoms (47%) and abnormal liver function tests (25%). There was a significant difference in survival plots (Log-rank p=0.026) with discontinuing due to side effects occurring earlier than inefficacy (Figure 1). In cox regression model, longer disease duration was found as an independent predictor of MTX discontinuation due to all reasons [Hazard Ratio (HR)=1.01, 95% Confidence interval (CI)=1.0-1.02; p=0.003].
Conclusion: MTX is frequently used on PsA treatment, despite the controversies in the literature. One third of patients with PsA discontinue MTX, most commonly due to side effects or inefficacy. Patients discontinue MTX earlier in case of having side effects. Longer disease duration is linked to MTX discontinuation.

Table. Demographics and disease characteristics of study groups

	All patients n=1359	Still on MTX n=942	Withdrawal MTX any reason n=417	p
Age, mean (SD)	46.4 (13.4)	46.1 (13.4)	47.7 (14.0)	**0.038**
Male gender, n (%)	523 (38.5)	360 (38.2)	163 (39.1)	0.761
Ever smoking, n (%)	569/1258 (46.2)	390/861 (45.3)	179/397 (45.1)	0.966
Psoriasis duration (years), mean (SD)	14.2 (11.7)	14.0 (11.2)	16.4 (12.7)	**0.003**
Polyarthritis, n (%)	657/1343 (48.9)	471/931 (50.6)	186/412 (45.1)	0.066
Axial disease, n (%)	388/1343 (28.9)	267/931 (28.7)	121/412 (29.4)	0.797
Nail involvement (ever), n (%)	644 (47.8)	435 (46.6)	209 (50.5)	0.191
Swollen Joint Count, mean (SD)	1.5 (2.6)	1.4 (2.6)	2.0 (3.2)	**<0.001**
Tender Joint Count, mean (SD)	3.0 (4.4)	3.5 (5.0)	4.2 (5.4)	**<0.001**
HAQ, mean (SD)	0.6 (0.6)	0.7 (0.7)	0.8 (0.7)	**0.035**
BASDAI,mean (SD)	37 (22)	39 (23)	46 (25)	**0.001**



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SAT0441 BODY COMPOSITION AND FAT DISTRIBUTION IN PATIENTS WITH PSORIASIS OR PSORIATIC ARTHRITIS.

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Background: Obesity is a leading comorbidity in both psoriasis (Pso) and psoriatic arthritis (PsA) and is associated with common metabolic complications and increased cardiovascular (CV) risk. Obesity is also a risk factor for the onset of these diseases. Body composition and fat distribution have been rarely evaluated in Pso and PsA.
Objectives: In this study, we aimed to characterize the fat mass distribution in patients with Pso or PsA compared to a control group, with a special emphasis on the android/visceral region.
Methods: case-control study (NCT02849795). Patients with Pso (plaque psoriasis) or PsA (CASPAR criteria) were evaluated. Each patient was paired to a control subject, recruited in the same outpatient population, and matched for sex, age and body mass index (BMI) category. Clinical assessment included BMI, anthropometric measurements (waist circumference, waist /hip ratio), disease activity (PASI for Pso, CPDAI for PsA) and the SCORE CV risk score. Laboratory parameters of inflammation (ESR, CRP, IL-6), lipid parameters (total cholesterol, LDL and HDL cholesterol, triglycerides), metabolic parameters (glycemia, insulin, HOMA), serum adipokines (total and high molecular weight [HMW] adiponectin, leptin, resistin and retinol binding protein 4 [RBP4]) were measured. Body composition (lean mass, fat mass) and fat distribution (android/gynoid regions and visceral fat) were evaluated (DEXA, Lunar GE, CoreScan). Our primary criteria was the fat mass in the android/visceral region. Comparisons between patients and controls were performed with paired t tests, between all groups with ANCOVA (adjusted for age, sex, and BMI category) and Tukey post-hoc tests. Pearson correlations between CV risk and fat mass were calculated within groups.
Results: 52 patients with Pso and 52 patients with PsA and their respective paired-control were evaluated. Total fat mass was increased in Pso but not in PsA. Android fat and visceral fat were found higher in Pso ($p<0.05$) while the fat mass measurements did not differ between the patients with PsA and their controls. Waist circumference was higher in patients with Pso compared to their controls. Leptin, leptin/fat mass ratio, and total adiponectin were elevated in PsA while only the HMW/total adiponectin ratio was decreased in Pso. Insulin levels and HOMA were increased in both Pso and PsA groups. Finally, RBP4 was higher in both Pso and PsA patients compared to their respective controls. In patients with Pso, android and visceral fat were correlated with SCORE ($r=0.3$, $p=0.02$ and $r= 0.6$, $p < 0.0001$ respectively). In ANCOVA analysis, visceral fat was higher in Pso patients ($p=0.0029$), with a trend toward higher android fat ($p=0.055$), compared to PsA patients.
Conclusion: visceral fat is increased in patients with Pso but not in PsA. In parallel, both groups showed an elevation of circulating RBP4. Patients with Pso and PsA were also characterized by metabolic disturbances as showed by the increase in HOMA, and specific adipokine changes. In the Pso group, visceral fat is associated with CV risk evaluated by SCORE. Weight control and reduction of fat mass, especially visceral fat mass, may thus be an important concern in patients with Pso and appears less relevant in PsA.
Disclosure of Interests: None declared
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SAT0442 EVOLVEMENT OF SWOLLEN JOINTS IN THE FIRST YEAR OF EARLY PSORIATIC OLIGOARTHRITIS.

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Background: Oligoarthritis and polyarthritis are the predominant phenotypes in PsA. Previous we have shown that patients with oligoarthritis suffer a similar loss in quality of life as polyarthritis patients.[1] Although oligoarthritis is one of the most prevalent form, ample data is available on this phenotype.[2-5]
Objectives: To evaluate the evolution of swollen joint count over the first year since diagnosis and to assess baseline difference in those groups that evolved differently over time.
Methods: Our study is embedded in the Dutch south-west Early Psoriatic Arthritis (DEPAR) prospective cohort study. We described patient characteristics using simple descriptive analysis techniques. For the comparison across groups univariable multinomial logistic regression was used in STATA15. Oligoarticular disease was defined as 2, 3 or 4 swollen joints,
Results: 175 patients had a complete 12-month evaluation as of February 2019 (80% of all included patients with oligoarthritis). Baseline characteristics are shown in table 1. In total 63 percent of the patients (111/175) had resolution of swollen joints at 1 year. (figure 1). Over the first year, 27 patients had consistently no swollen joints since their 3 month evaluation, 26 had no swollen joint from 6 months and 12 from 9 months and 11 at 12 months. 65 of the 175 (37%) had inconsistently no swollen joints (intermittent) during the first year. In 8% of the patients values were missing to determine to which group they belonged. Univariable multinomial logistic regression of baseline characteristics showed that the group that had resolution of swollen joints 'early' (within 6 months) compared to (i) the group that 'never' had resolution differed in having fewer tender joints; (ii) the group having 'late' resolution of swollen joints (after 6 months) showed little difference and;(iii) the 'intermittent' group varied in smoking status, fatigue, being female and age. Multivariable analysis may reveal other patterns, but requires a larger sample than that currently available.

Table 1. Baseline characteristics of oligo arthritis patients with complete follow-up at 1 year.

n=	175
sex (% female)	45%
age	51 (39-61)
symptom duration (months)	10.0
BMI	28 (24-32)
current smoking	23%
paid employement	70%(n=136)
tender joint count	3.0 (2.0-7.0)
PASI	2.0 (0.4-4.5)
entheses	44%
dactylitis	9%
VASglobal	42 (21-65)
VASpain	49 (25-68)
HAQ	0.63 (0.25-1.13)
fatigue (BRAF)	18 (10-30)

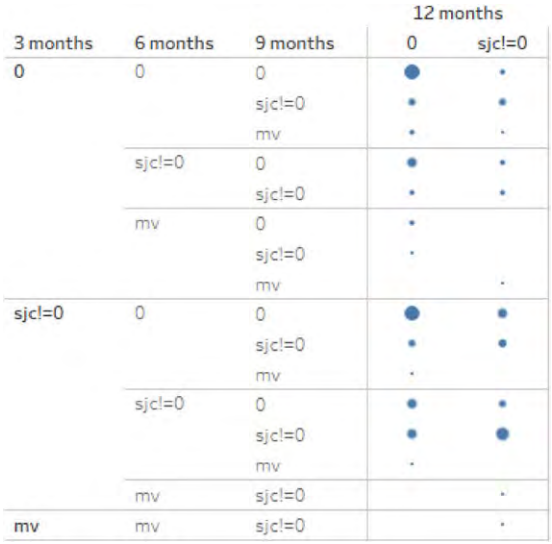


Figure 1. Evolution of swollen joint count in psoriatic oligo arthritis (n=175) over time expressed in a binary swollen joint count (yes: 0 / no: sjc!==0; mv= missing value),

Conclusion: In our set of real world data, about one third of the PsA patients with oligoarticular disease had no resolution of swollen joints at 1 year. About half of these patient had consistently inflamed joints over time. Another third of the PsA patients had intermittently inflamed joints. At baseline these groups seems comparable in clinical presentation, demographics and PROMs, although some variation existed between early versus never and early versus intermittent resolution of swollen joints. Both indices provide room for improvement in the management of oligoarticular disease in PsA.

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SAT0443 CONCOMITANT PSORIATIC ARTHRITIS AND INFLAMMATORY BOWEL DISEASE IN THE PSA BIOLOGICAL REGISTRY: HUR-BIO REAL LIFE RESULTS

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Background: Patients with spondyloarthritis (SpA) have 3 important extra-articular involvement; psoriasis, uveitis and inflammatory bowel disease (IBD). Psoriatic arthritis (PsA) patients may have IBD, as well, and clinical features of PsA + IBD patients do not assess comprehensively, yet.
Objectives: The purpose of this study is to determine the frequency and clinical features of concomitant PSA and IBD in a PsA biological DMARD cohort.
Methods: Hacettepe University Rheumatology Biologic (HUR-BIO) is a single center biologic registry since 2005 and include 469 psoriatic arthritis patients to date. Demographics, clinical features, co-morbidities, laboratory and disease activity parameters collected from the database. The diagnosis of IBD was accepted with colonoscopy findings and pathology.
Results: Overall, 469 PsA patients (70% females) with the mean age 47.7±12.4 years and [median (IQR)] disease duration 7 (3-11) years included in the study. Overall, 10/469 (5 male) PsA patients (2.1%) had IBD (7 (70%) with ulcerative colitis and 3 (30%) Crohn's disease). Mean age of the patients was 53.3±10.0 years and mean disease duration was 9.0 ± 6.1 years. Six of ten patients were diagnosed with IBD before PsA and 4 of them were diagnosed with PsA first. Patients were followed-up for 3.7±2.8 years and bDMARD switch were made in 4 patients mostly due to primary inefficacy. bDMARD was discontinued in 2 patients (one for Crohn disease with fistula and one for drug induced SLE). According to DAPSA score 44% of the patients had low disease activity and 56% of the patients had moderate disease activity at last visit (9 patients were available). Sacroiliitis (70%) and severe radiographic hip (20%) involvement were common in PsA patients with IBD. Disease characteristics and demographic data are given in table 1.

Table 1. Disease characteristics and demographic data of PsA patients with IBD

Age (years) /sex	Disease duration (years)	IBD type	Sacroiliitis	Last visit treatments
61/M	16	Crohn's disease	(+)	Azathioprine, GC
50/M	5	Ulcerative colitis	(+), hip	Adalimumab, GC
59/F	3	Ulcerative colitis	(+)	Certolizumab, methotrexate
40/F	10	Ulcerative colitis	-	Adalimumab, methotrexate
71/M	19	Ulcerative colitis	-	Infliximab
62/M	13	Crohn's disease	(+), hip	Azathioprine, GC, sulphasalazine
50/F	1	Ulcerative colitis	-	Adalimumab, GC
59/M	12	Crohn's disease	(+)	Secukinumab, GC
45/F	9	Ulcerative colitis	(+)	Adalimumab, methotrexate, GC
36/F	5	Ulcerative colitis	(+)	Infliximab, methotrexate, GC

Conclusion: In our single center biological registry, relatively small portion of PsA patients had concomitant IBD, however, those cases may have severe axial involvement, particularly in hip involvement, and further studies needed for these subgroup. Physician should be aware those SpA subgroup, because treatment choices, particularly IL-17 inhibitors may have some cautions patients with PsA and IBD.

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Levent Kılıç: None declared, Omer Karadag: None declared, Ali Akdoğan: None declared, Şule Apraş Bilgen: None declared, Ali İhsan Ertenli: None declared, Sedat Kiraz: None declared, Umut Kalyoncu Consultant of: Abbvie, Amgen, Janssen, Lilly, Novartis, UCB

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SATURDAY, 06 JUNE 2020

Osteoporosis

SAT0444 PREVALENCE OF VERTEBRAL FRACTURES BY BONE FRAGILITY IN PATIENTS BEFORE AND 1 YEAR AFTER LIVER TRANSPLANTATION

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Background: Bone fragility is frequent in patients awaiting orthotopic liver transplantation (OLT) for severe liver disease, leading to a high prevalence of fractures, particularly vertebral ones. During the year following OLT, there is an early decrease in bone density and a high incidence of new vertebral fractures (VF).

Objectives: To determine the prevalence of VF due to bone fragility during the year after OLT in a large population of patients.

Methods: We conducted a cohort, prospective, descriptive, monocentric study including all the patients with severe chronic liver disease and awaiting OLT. Patients were seen during the pre-transplant period and one year after OLT. At each visit demographic, clinical, biological (including bone remodeling markers) and bone mineral density (BMD) data with VFA (Vertebral fracture Assessment) were collected. We estimated the incidence of VF after OLT. We compared biological and morphological data.

Results: We have seen 272 patients before OLT (median age 59 years [Interquartile Range IQR: 53; 64], 75% male). Hepatopathy was due to alcoholic disease for 187 patients (69%). Before OLT, 12% had T-score<-2.5 SD (Standard Deviation) at lumbar spine site, 10% at total hip site and 10% at femoral neck site. Among the 272 patients, 31 had at least one VF (for a total of 49 VF). After OLT, we have seen 101 patients (median of 14 months [IQR: 5; 40] after OLT). For those 101 patients seen before and after OLT: we noted 18 VF for 12 patients (11.8%) before OLT and 29 VF for 18 patients (17.8%) after OLT on VFA. The VF incidence was 8.8 for 100 patients-years. During the year following OLT, there was a significant decrease of T-score at femoral neck and total hip sites. The number of osteoporotic patients was 13/101 (12.8%) at femoral neck and 14/101 (13.8%) at total hip. There was no significant change at the lumbar spine. Bone remodeling markers were significantly higher after OLT than before: CTX (µg/L) from 0.350 [IQR: 0.260; 0.501] before OLT to 0.490 [IQR: 0.279; 0.762] after OLT and osteocalcin (mg/mL) from 17 [IQR: 12; 22] to 30 [IQR: 19; 43], p<0.001. Fifteen of those 101 patients had an anti-osteoporotic drug prescribed before OLT despite being justified for 30 patients.

Conclusion: Despite bone fragility and a high fracture risk, patients undergoing OLT are not enough treated for osteoporotic disease. It seems justified to offer a systematic rheumatology visit to detect bone damage before OLT and 6 months after OLT when the damage is the most significant. The drug prescription should be systematically proposed in a situation of fracture before OLT and/or in case of low bone parameters after OLT.

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SAT0445 TRABECULAR BONE SCORE IMPROVES FRACTURE RISK STRATIFICATION IN PATIENTS WITH REDUCED BONE MINERAL DENSITY

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Background: Trabecular bone score (TBS) is a textural index of bone microarchitecture and has been found to be related to 3D bone structure. A number of cohort studies have demonstrated the value of TBS as an independent fracture risk in clinical trials. Yet, very little is known about the performance and clinical value of TBS in real life practice.

Objectives: To investigate the sensitivity and specificity of TBS in identifying prevalent fractures when compared with bone mineral density (BMD) measured by DXA. To evaluate the added value of TBS in fracture risk prediction above that obtained from DXA.

Methods: Consecutive patients aged ≥ 18 with BMI 15-37 attnding a DXA plus TBS assessment were considered eligible. Sensitivity, specificity, and area under the curve (AUC) for prevalent major osteoporotic fracture (MOF) and clinical vertebral fractures (VF) were assessed for the following parameters: BMD lowest T-score ≤-2.5 (neck of femur, total hip, or spine), TBS T-score ≤-2.5, and either TBS or BMD T-score ≤-2.5. BMD categories (normal, osteopenia, and osteoporosis) were stratified by TBS T-score: normal (T-score ≥-1), moderate (-1≥T-score≥-2.5), and degraded TBS (T-score ≤-2.5) resulting in 9 risk groups. Odds ratios were calculated for all risk categories and fracture prevalence was compared between the best and worst TBS strata at each BMD level using chi-square test.

Results: 540 patients (87% females, 68.1 ± 11.6 years) were included. 238 (44%) had MOF including 81 (15%) clinical VF. For MOF, BMD had higher sensitivity (49.6% vs 30.7%), lower specificity (68.2% vs 82.1%), and similar AUC (0.59 vs 0.56) versus TBS. For VF, the sensitivity, specificity and AUC for BMD were 60%, 64%, and 0.62 respectively versus 42%, 79.7%, and 0.61 for TBS. Combining TBS and BMD (either T-score ≤ -2.5) increased the sensitivity to 63% for MOF and 75.3% for VF without affecting AUC (0.6 and 0.64 respectively). Patients with osteoporosis and degraded TBS had the highest OR of 2.65 for MOF and 3.8 for VF. The fracture risk increased at the same level of BMD when TBS was degraded. Numerically, the risk of MOF increased steadily from strata 1 to 9 and was statistically significant for osteoporosis with degraded TBS and osteoporosis with moderate TBS. When both TBS and BMD were normal, the risk of fracture was significantly reduced. In the osteopenia and osteoporosis BMD categories, patients with degraded TBS had significantly higher prevalence of fracture compared to those with normal TBS in the same BMD category.

Conclusion: Fracture risk stratification can be improved when TBS is added to BMD. The sensitivity of predicting fracture may also improve when TBS and BMD are combined. Patients with both normal TBS and BMD have the lowest fracture risk, whereas those with degraded TBS and osteoporosis have the highest risk of fracture and should be targeted for early or more aggressive treatment.

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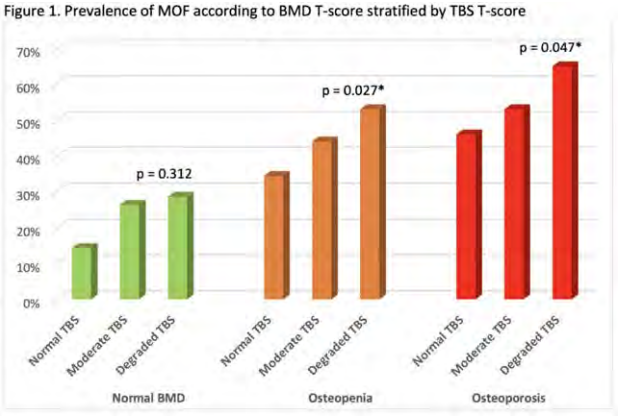
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Table 1. Prevalence and risk of MOF and VF according to BMD stratified by TBS T-score

	Patients within category	Number of MOF	OR for MOF	Number of VF	OR for VF
Normal BMD & TBS	49	7 (14.3%)	0.19 (0.08-0.43)*	0	0.83 (0.80-.87)*
Normal BMD moderate TBS	19	5 (26.3%)	0.44 (0.16-1.24)	2 (10.5%)	0.66 (0.15-2.9)
Normal BMD degraded TBS	7	2 (28.6%)	0.50 (0.1-2.6)	1 (14.3%)	0.94 (0.11-7.9)
Osteopenia normal TBS	96	33 (34.4%)	0.61 (0.39-0.97)	7 (7.3%)	0.39 (0.18-0.88)*
Osteopenia moderate TBS	98	43 (43.9%)	0.99 (0.64-1.54)	11 (11.2%)	0.67 (0.34-1.32)
Osteopenia degraded TBS	57	30 (52.6%)	1.47 (.085-2.55)	11 (19.3%)	1.41 (0.7-2.86)
Osteoporosis normal TBS	39	18 (46.2%)	1.1 (0.57-2.1)	6 (15.4%)	1 (0.42-2.6)
Osteoporosis moderate TBS	112	59 (52.7%)	1.55 (1.02-2.35)*	21 (18.8%)	1.42 (0.82-2.45)
Osteoporosis degraded TBS	63	41 (65.1%)	2.65 (1.53-4.59)*	22 (34.9%)	3.8 (2.12-6.83)*
Total	540	238		81	

Figure 1. Prevalence of MOF according to BMD T-score stratified by TBS T-score



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SAT0446 RISK OF ACUTE MYOCARDIAL INFARCTION (AMI) AMONG NEW USERS OF BISPHOSPHONATES: A NESTED CASE-CONTROL STUDY

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Background: Evidence suggest that bisphosphonates (BF) may inhibit atherosclerosis and vascular calcification. In several small-scale clinical trials, BF improved some intermediate targets of atherosclerosis. Observational studies found a lower risk of Acute Myocardial Infarction (AMI) or stroke among BF users compared to non-users. While this epidemiological evidence suggests that BF may protect against cardiovascular events a "prevalent user bias" cannot be excluded.
Objectives: To analyze the hypothesis that BF reduce de risk of AMI in new users and assess whether the effect depends on the duration of treatment.
Methods: Case-control study nested in a primary cohort composed of patients aged 40 to 99 years, with at least one year of follow-up in the BIFAP database during the 2002-2015 study period. From this cohort of patients, we identified incident cases of AMI and randomly selected five controls per case, matched by exact age, gender, and index date. Adjusted odds ratios (AOR) and their corresponding 95% confidence interval (CI) were calculated through an unconditional logistic regression. Only new users of BF were considered.
Results: A total of 23,590 cases of IAM and 117,612 controls were included. The mean age was 66.8 (SD 13.4) years and 72.52% were male, in both groups. 584 (2,47%) cases and 2,892 (2.46%) controls used or had used some bisphosphonate. The use of BF was not associated with a lower risk of IAM (**AOR 0.97; 95%CI: 0.84–1.13**). Nor was it associated with the duration of treatment (**AOR less than 1 year = 0.91; 95%CI: 0.72-1.15**); **AOR more than 1 year= 1.01; 95%CI: 0.84-1.21**). The stratified analysis by age and sex also did not show either a protective effect of BF. Detailed results by BF type are shown in the following table:

	Cases (%)	Controls (%)	Non-adjusted OR	Adjusted OR
	N=23590	N=117612	(95% CI)	(95% CI)
Bisphosphonates				
Non users	23006 (97.52)	114720 (97.54)	1 (Ref.)	1 (Ref.)
Current	276 (1.17)	1458 (1.24)	0.93 (0.81-1.06)	0.97 (0.84-1.13)
Recent	109 (0.46)	478 (0.41)	1.13 (0.92-1.40)	1.11 (0.89-1.40)
Past	199 (0.84)	956 (0.81)	1.04 (0.89-1.21)	1.01 (0.86-1.20)
Alendronic acid				
Non users	23338 (98.93)	116421 (98.99)	1 (Ref.)	1 (Ref.)
Current	88 (0.37)	469 (0.40)	0.91 (0.72-1.15)	0.97 (0.76-1.24)
Recent	46 (0.19)	201 (0.17)	1.17 (0.84-1.61)	1.18 (0.83-1.66)
Past	118 (0.50)	521 (0.44)	1.12 (0.91-1.37)	1.13 (0.91-1.40)
Alendronic acid+VitD				
Non users	23509 (99.66)	117155 (99.61)	1 (Ref.)	1 (Ref.)
Current	34 (0.14)	207 (0.18)	0.81 (0.56-1.17)	0.89 (0.60-1.31)
Recent	15 (0.06)	77 (0.07)	0.94 (0.54-1.63)	0.71 (0.40-1.29)
Past	32 (0.14)	173 (0.15)	0.92 (0.63-1.35)	0.83 (0.56-1.25)
Alendronic acid (all)				
Non users	23274 (98.66)	116057 (98.68)	1 (Ref.)	1 (Ref.)
Current	122 (0.52)	671 (0.57)	0.89 (0.73-1.08)	0.95 (0.77-1.18)
Recent	58 (0.25)	261 (0.22)	1.11 (0.83-1.48)	1.03 (0.76-1.39)
Past	136 (0.58)	623 (0.53)	1.08 (0.89-1.31)	1.05 (0.86-1.29)
Ibandronic acid				
Non users	23504 (99.64)	117174 (99.63)	1 (Ref.)	1 (Ref.)
Current	41 (0.17)	216 (0.18)	0.96 (0.68-1.34)	1.00 (0.70-1.42)
Recent	18 (0.08)	69 (0.06)	1.24 (0.74-2.09)	1.38 (0.80-2.36)
Past	27 (0.11)	153 (0.13)	0.87 (0.57-1.31)	0.88 (0.57-1.35)
Risedronic acid				
Non users	23355 (99.00)	116446 (99.01)	1 (Ref.)	1 (Ref.)
Current	102 (0.43)	527 (0.45)	0.95 (0.76-1.18)	0.99 (0.79-1.25)
Recent	47 (0.20)	186 (0.16)	1.27 (0.92-1.75)	1.17 (0.83-1.66)
Past	86 (0.36)	453 (0.39)	0.94 (0.75-1.19)	0.93 (0.72-1.19)

Conclusion: Our results do not support a cardioprotective effect of BF, regardless of the duration of treatment, age, sex or background cardiovascular risk.
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SAT0447 CORRELATES OF RADIAL BONE MICROARCHITECTURES IN OLDER ADULTS

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Background: Weight, dietary patterns, vitamin D, physical activity and grip strength have been suggested to be associated with bone loss in older adults. However, studies have yet been performed to investigate the associations between these factors and radial bone microarchitecture.
Objectives: This study aimed to describe the associations of weight, dietary patterns, serum 25-hydroxyvitamin D (25(OH)D) concentrations, physical activity and grip strength with bone measures in older adults.
Methods: Cross-sectional data on 201 older adults (mean age 72 years, female 46%) from a population-based cohort study were analysed. Weight, dietary patterns, serum 25(OH)D concentrations, physical activity (steps per day), grip strength were collected and analysed from baseline to 10-year follow-up. Areal bone mineral density (aBMD) at spine, hip and whole body were measured by dual-energy X-ray absorptiometry (DXA). Radial cortical and trabecular bone microarchitectures were measured by high-resolution peripheral computed tomography (HRpQCT). Multivariable linear regression was used to analyse associations of study factors with bone measures.
Results: Weight was positively associated with radial bone area (total: β=0.18, 95% CI: 0.07, 0.29; cortical: β=0.12, 95% CI: 0.03, 0.21; trabecular: β=0.18, 95% CI: 0.05, 0.32), and was inversely associated with compact cortical volumetric bone mineral density (vBMD) (β= -0.19, 95% CI: -0.37, -0.01) and trabecular thickness (β= -0.25, 95% CI: -0.43, -0.07). Ten-year changes in weight were not significantly associated with bone measures, apart from radial trabecular separation (β= 0.15, 95%CI: 0.009, 0.28). Western dietary pattern scores were inversely associated with radial vBMD (total: β= -0.17, 95% CI: -0.32, -0.01; cortical: β= -0.19, 95% CI: -0.34, -0.04; compact cortical: β= -0.19, 95% CI: -0.34, -0.04; outer transitional zone: β= -0.20, 95% CI: -0.35, -0.06), and were positively associated with cortical porosity (cortical: β= 0.18, 95% CI: 0.03, 0.33; compact cortical: β= 0.19, 95% CI: 0.04, 0.34; outer transitional zone: β= 0.20, 95% CI: 0.06, 0.35). Steps per day were not significantly associated with bone measures, apart from inner transitional zone area and thickness (β= 0.12, 95% CI: 0.003, 0.24; β= 0.19, 95% CI: 0.05, 0.33). Healthy food pattern scores, serum 25(OH)D and grip strength were not significantly associated with radial HRpQCT measures.
Conclusion: Higher weight, but not weight change, was beneficial for radial cortical and trabecular bone area but also associated with worse compact cortical vBMD and trabecular thickness. Higher western dietary pattern scores had adverse effects on radial vBMD and cortical porosity while physical activity had inconsistent associations.
Disclosure of Interests: None declared
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SAT0448

BONE HEALTH IN PATIENTS WITH PSORIASIS ARTHRITIS IN THE SWISS NATIONAL COHORT: A CROSS-SECTIONAL STUDY

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Background: There is much controversy surrounding the loss of bone mass in patients with psoriasis arthritis (PsA).
Objectives: To evaluate the prevalence of osteoporosis (OP) and fracture in patients with PsA in the Swiss Clinical Quality Management (SCQM) cohort, a large national database of patients with inflammatory arthritis; to study different factors influencing bone health and the correlation between disease activity, treatment and occurrence of densitometric osteoporosis or fracture.
Methods: We analyzed all PsA-patients included in the cohort from 2006-April 2019. We evaluated demographic and clinical data: age, gender, BMI, disease duration, smoking/alcohol habits, patient's and physician's global assessment, joint count, HAQ, medication and inflammatory activity measured by ESR, CRP, DAS 28 and DAPSA score. We compared patients with BMD measurement (DXA) with the group without DXA (nDXA). In DXA group we analyzed patients according to osteoporotic status and did subgroup analysis in premenopausal, menopausal women and men.
Results: Of the 2443 patients, 545 had a DXA. Age of scanned patients was 18-84 years. Only 295 BMD data were available for analysis. DXA patients were 6.4 years older (54.2±11,1 vs 47.8±12.4 years, p<0.001), and were more female (67% vs 43%). Duration of the disease was longer (6.6±8.3 vs 5.3±7.1 y, p<0.001) in DXA group. DAS28-CRP and DAS28-ESR were higher in DXA group (3,1 ± 1,2 vs 2,9 ± 1,1, p< 0,04 and 3,2 ± 1,4 vs 3 ± 1,3, p< 0,002, respectively), as was the DAPSA score (32 ± 30 vs 27 ± 20 p<0.04). Patients in DXA group were more exposed to prednisone and conventional DMARDs (15.4% vs 4.7%, p<0.001 and 51.7% vs 43%, p<0.01 respectively). There were more fractures in DXA- than in nDXA group (5.7% vs 1.4%, P< 0.001).
In DXA group 18.4% patients had OP and 50.2% osteopenia. Patient characteristics are shown in Table 1. We confirmed a positive correlation between femoral and lumbar BMD and BMI, and between higher age and lower femoral BMD. Disease duration was inversely correlated with femoral, but not lumbar BMD. Interestingly, other variables, including disease activity, showed no significant correlation with the BMD, but OP patients had higher disease activity.

Table 1. Comparison between patients with and without OP in DXA group. *: statistically significant. Values are expressed as mean and standard deviation unless stated otherwise.

	NO OSTEOPOROSIS (n=244)	OSTEOPOROSIS (n =51)	P
Age	52.9 ± 9,8	56.3 ± 13,4	0,04*
Female %	67.6	68.6	0,88
Disease duration (y)	6,3 ± 8	7,7 ± 9,9	0,339
BMI	26,6 ± 5	22,7 ± 4,8	0,0001*
Smoking %	19,9	29	0,29
Alcohol %	77,2	68,6	0,37
HAQ	0,7 ± 0,5	0,9 ± 0,7	0,03*
PGA	3,8 ± 2,2	4,1 ± 2,5	0,329
ESR	16,6 ± 16,7	20,8 ± 20,9	0,2
CRP	9,1 ± 12,8	16,9 ± 36,2	0,01*
DAS28_ESR	3,2 ± 1,4	3,6 ± 1,3	0,08
DAS28_CRP	3,1 ± 1,2	3,4 ± 0,9	0,04*
DAPSA	29,6 ± 23,6	37,8 ± 43,5	0,04*
Fracture %	2	3,9	0,4
Anti-TNF%	35,7	25,5	0,16
csDMARD %	53,7	54,5	0,6
tsDMARD %	0,4	2	0,22
Prednisone %	15,2	13,7	0,069

Subgroup analysis (Figure 1) showed higher OP prevalence in postmenopausal women (22,6%) vs in men (16.8%) or premenopausal women (10.7%) in concordance with the fracture rate (8.3% vs 6.3% vs 3.9%). BMD was lower and the disease activity was higher in postmenopausal women compared to the others groups.

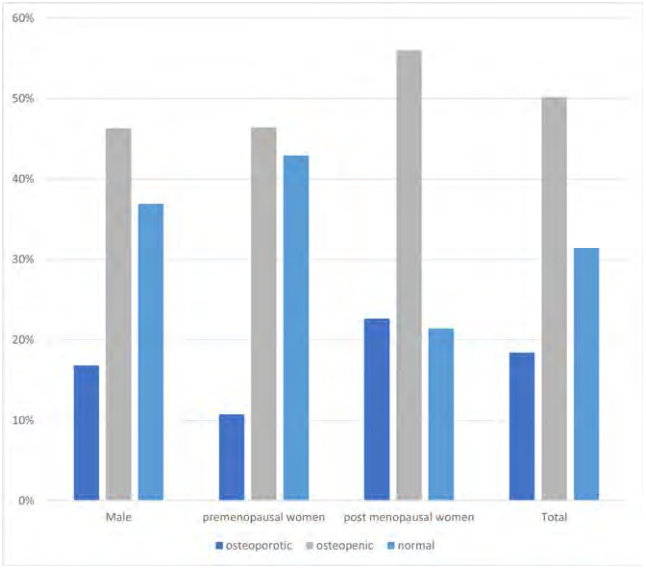


Figure 1. Subgroup analysis on the prevalence of OP and osteopenia

Conclusion: Our data suggest that Swiss clinician are aware of risk of poor bone-health in PsA patients and perform DXA in this population even in younger patients and in men. Interestingly, we describe that the patients with OP had higher disease activity and poorer functional status than patients without OP. Longitudinal studies are needed to evaluate bone quality, fractures, and relationship between bone health in PsA and disease associated factors. They should integrate parameters of bone turnover and use an appropriate control group.
Disclosure of Interests: None declared
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SAT0449

SPONDYLOARTHRITIS AND FRACTURE RISK: DOES DXA REALLY HAVE AN IMPACT IN THE RISK OF FRACTURE ESTIMATED BY FRAX?

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Background: Low bone mineral density (BMD) is common in ankylosing spondylitis (AS). The fracture risk (FR) is increased and its reduction with pharmacologic therapy is not clearly defined in this population. However, early screening and bisphosphonates as first-line treatment are recommended.
Objectives: To investigate the influence of dual-energy X-ray absorptiometry (DXA) in the ten-year risk of fracture assessed by FR Assessment Tool (FRAX) and to determine possible demographic or clinical factors associated with an increased FR in a spondyloarthritis (SpA) population.
Methods: Retrospective study including all the over 40 years-old SpA patients (ASAS classification criteria) followed at our Rheumatology Department and registered in the national database. Demographic, clinical and laboratorial data were collected at the time of the last follow-up visit. Data from the last DXA (until 3 years prior to the last visit) were collected. Indication for pharmacological treatment by FRAX was assessed according to the national recommendations.
Results: A total of 231 SpA patients were included: 126 males (54.5%), 53 (22.9%) smokers; 171 (74%) had AS, 23 (10%) had Inflammatory Bowel Disease Associated SpA and 37 (16%) had Undifferentiated SpA. At the last follow-up visit, the mean age was 52.9 years (±9.6) and the median disease duration was 21.9 years [1.0-55.5]. The mean ASDAS-CRP was 2.5 (±0.9) and the majority of patients had moderate (25.5%) or high (48.5%) disease activity (according to ASDAS). One hundred and thirty patients (56.3%) were taking NSAIDs, 45 (19.5%) were taking glucocorticoids, 85 (36.8%) were under csDMARDs and 170 (73.6%) under bDMARDs [157 (68%) under TNFi, 11 (4.8%) under secukinumab and 2 (0.9%) under ustekinumab].
Eleven patients (4.8%) had previous fragility fractures, 118 (51.1%) had DXA in the last 3 years and 167 (72.3%) were taking calcium and/or vitamin D supplements. Sixteen patients (6.9%) had indication for treatment by FRAX without DXA and 9 of these (56.3%) were already under treatment. Similarly, 16 (6.9%) had indication for treatment by FRAX with DXA and 13 of these (81.3%) were already under treatment. Ten patients (4.3%) were reclassified in FRAX with DXA: 7 (3%) had no indication for treatment by FRAX without DXA but obtained it by FRAX with

DXA and 3 (1.3%) had indication for treatment by FRAX without DXA but they lost it by FRAX with DXA. We found a moderate level of agreement in the indication for treatment between FRAX with and without DXA (kappa=0.595; p<0.001). The use of DXA in FRAX estimated a significant higher median FR, both for major osteoporotic fracture (2.4% [0.8-31.0] vs 1.8% [0.6-20.0]; p<0.001) and for hip fracture (0.5% [0.0-23.0] vs 0.2% [0.0-14.0]; p<0.001).

We found significant correlations between FR and some disease-related variables (table 1).

Table 1. Correlations between the risk of fracture estimated by FRAX and disease-related variables.

			Disease duration	BASDAI	ASDAS-CRP	BASMI	BASFI
Estimated fracture risk by FRAX:	without DXA	major osteoporotic fracture	r=0.352 *p*<0.001	r=0.204 *p*=0.002	r=0.214 *p*=0.001	r=0.301 *p*<0.001	r=0.317 *p*<0.001
		hip fracture	r=0.389 *p*<0.001	r=0.142 *p*=0.034	r=0.170 *p*=0.011	r=0.305 *p*<0.001	r=0.275 *p*<0.001
	with DXA	major osteoporotic fracture	r=0.227 *p*=0.014	r=0.314 *p*=0.001	r=0.356 *p*<0.001	r=0.293 *p*=0.002	r=0.379 *p*<0.001
		hip fracture	n.s.	r=0.197 *p*=0.036	r=0.269 *p*=0.004	r=0.271 *p*=0.004	r=0.258 *p*=0.006

Conclusion: Our results showed that a similar number of patients had indication for pharmacological treatment by FRAX both with and without DXA. Although the inclusion of DXA resulted in a higher estimated FR by FRAX, the observed moderate level of agreement between FRAX with and without DXA suggests that the FR estimation by FRAX, even without DXA, may be a reasonable approach in SpA patients. In line with literature, we found significant associations between the estimated risk fracture by FRAX and some disease activity and function measures.

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SAT0450 GLUCOCORTICOID-INDUCED OSTEOPOROSIS IN PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATIC DISEASES: A MULTIVARIATE LINEAR REGRESSION ANALYSIS IDENTIFYING PREDICTIVE FACTORS FOR LOW BONE MASS

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Background: Rheumatic diseases are associated with increased systemic bone loss and fracture risk related to chronic inflammation, disease-specific, general and demographic risk factors as well as treatment with glucocorticoids (GC). Yet, there is evidence that GCs may, by adequately suppressing systemic inflammation, also have a positive effect on bone mineral density (BMD) and fracture risk[1].

Objectives: The purpose of this study was to investigate the prevalence of osteoporosis and fragility fractures in patients with inflammatory rheumatic diseases and to analyze the impact that treatment with GCs, other known risk factors and preventive measures have on bone health in these patients.

Methods: Rh-GIOP is an ongoing prospective observational study collecting and analyzing disease- and bone-related data from patients with chronic inflammatory rheumatic diseases and psoriasis treated with GCs. In this cross-sectional analysis, we evaluated the initial visit of 1091 patients. A multivariate linear regression model with known or potentially influential factors adjusted for age and sex was used to identify predictors of BMD as measured by dual-energy X-ray absorptiometry (DXA). Multiple imputation was applied for missing baseline covariate data.

Results: In the total cohort of 1091 patients (75% female of which 87.5% were postmenopausal) with a mean age of 62.1 (±13.2) years, the prevalence of osteoporosis by DXA was 21.7%, while fragility fractures have occurred in 31.2% of the study population (6.7% vertebral, 27.7% non-vertebral). Current GC therapy was common (64.9%), with a median daily dose of 5.0mg [0.0;7.5], a mean life-time total GC dose of 17.7g (±24.6), and a mean GC therapy duration of 7.8 years (±8.5). Bisphosphonates were the most commonly used anti-osteoporotic drug (12.6%).

Multivariate analysis showed that BMD as expressed by the minimum T-Score at all measured sites was negatively associated with higher age, female sex and menopause as well as Denosumab and Bisphosphonate treatment. A positive association with BMD was found for body mass index as well as current and life-time (cumulative) GC dose. While comedication with proton-pump-inhibitors significantly predicted low bone mass, concomitant use of non-steroidal anti-inflammatory drugs showed a positive association with BMD. Of the measured bone-specific laboratory parameters, higher alkaline phosphatase levels were determinants of low DXA-values, while the association was positive for gamma-glutamyltransferase.

BMD was neither predicted by duration of GC treatment nor by treatment with disease modifying anti-rheumatic drugs.

Predictive variables for BMD differed at the respective anatomical site. While treatment with Denosumab predicted low bone mass at the lumbar spine and not at the femoral neck, the opposite was true for health assessment questionnaire (HAQ) score. Current and life-time GC-dose as well as direct sun-exposure of more than 30 minutes daily were positively associated with bone mass at the femoral sites only.

Conclusion: This cross-sectional analysis of a prospective cohort study quantified the prevalence of osteoporosis and identified predictive variables of BMD in patients with rheumatic diseases.

Multivariate analyses corroborated low BMD to be predicted by traditional factors like age, female sex and menopause but showed current and well as life-time GC dose to be positively associated with BMD in our cohort of patients with chronic inflammatory rheumatic diseases. This suggests that optimal management of disease activity with GCs might be beneficial in order to avoid bone loss due to inflammation.

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Disclosure of Interests: Edgar Wiebe: None declared, Desiree Freier: None declared, Dörte Huscher: None declared, Robert Biesen: None declared, Sandra Hermann: None declared, Frank Buttgereit Grant/research support from: Amgen, BMS, Celgene, Generic Assays, GSK, Hexal, Horizon, Lilly, medac, Mundipharma, Novartis, Pfizer, Roche, and Sanofi.

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SAT0451 COMPARISON OF PHARMACOKINETIC, PHARMACODYNAMIC AND SAFETY OF A TERIPARATIDE BIOSIMILAR AND REFERENCE TERIPARATIDE

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Background: Intas is developing a biosimilar teriparatide. This teriparatide biosimilar has shown similarity to European Union approved teriparatide (EU teriparatide) and United States approved teriparatide (US-teriparatide) in analytical (structural and functional assays) and animal studies[1].

Objectives: To primarily asses pharmacokinetic (PK) equivalence and to compare pharmacodynamic (PD) and safety profiles of teriparatide biosimilar against EU- and US-teriparatide in healthy men and postmenopausal women with potentially similar in-clinic real-life user profiles.

Methods: In this assessor-blind, three-period study, 105 subjects were randomized (1:1:1) to receive single subcutaneous 20µg dose each of teriparatide biosimilar, EU-teriparatide, and US-teriparatide in a crossover manner on 3 consecutive days. The primary PK endpoints were area under the curve (AUC) from time zero to t (AUC_{0-t}), AUC from time zero to infinity ($AUC_{0-\infty}$), and maximum concentration (C_{max}). Secondary endpoints were total serum calcium level as a pharmacodynamic marker and safety.

Results: The mean age of 48 men was 38.4 years and 57 women was 43.9 years. Mean serum teriparatide concentrations were similar for teriparatide biosimilar, EU- and US-teriparatide (Figure 1). The 90% confidence intervals (CI) of the geometric least square mean ratios (GMR) of C_{max}, AUC_{0-t} and $AUC_{0-\infty}$ of teriparatide biosimilar relative to EU- and US-teriparatide were within the predefined acceptance range of 80.00% to 125.00% (Table 1). The baseline-adjusted and non-adjusted corrected total serum calcium levels were similar (Table 2). A total of 42 adverse events (AE) were reported by 31 (29.52%) subjects (9 subjects, teriparatide biosimilar; 14 subjects, EU-teriparatide; 13 subjects, US-teriparatide), with headache and pain in extremity being the most common AEs. No death or serious AEs were reported.

Table 1. Summary of Statistical Analysis of Pharmacokinetic Parameters of Teriparatide

Parameters	N	GLSM	N	GLSM	Ratio (T/R1) %	90% Confidence Interval
	Teriparatide Biosimilar (T)		EU-Teriparatide (R1)			
lnC_{max} (pg/mL)	104	99.314	104	99.229	100.1	95.50 - 104.89
$lnAUC_{0-t}$ (pg.h/mL)	103	130.402	103	129.067	101.0	96.37 - 105.93
$lnAUC_{0-\infty}$ (pg.h/mL)	103	150.589	103	144.887	103.9	99.19 - 108.90
	Teriparatide Biosimilar (T)		US-Teriparatide (R2)		Ratio (T/R2) %	
lnC_{max} (pg/mL)	104	99.255	104	96.397	103.0	98.74 - 107.37
$lnAUC_{0-t}$ (pg.h/mL)	102	131.212	102	126.837	103.4	98.90 - 108.21
$lnAUC_{0-\infty}$ (pg.h/mL)	102	150.564	102	143.860	104.7	99.88 - 109.67

GLSM: Geometric least squares mean; N: Number of subjects.

Table 2. Summary of Corrected Total Serum Calcium Levels after Administration of Teriparatide

Parameter	Teriparatide Biosimilar		EU-Teriparatide		US-Teriparatide	
	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
Baseline-adjusted						
E_{max} (mg/dL)	101	0.314 (0.142)	101	0.333 (0.179)	102	0.341 (0.153)
$AUEC_{0-t}$ (mg.h/dL)	101	1.764 (1.305)	98	2.051 (1.816)	101	2.253 (1.732)
T_{max} (h)	101	5.457 (4.185)	101	5.023 (2.728)	102	5.252 (3.543)
Baseline non-adjusted						
E_{max} (mg/dL)	104	9.724 (0.268)	104	9.719 (0.272)	104	9.729 (0.261)
$AUEC_{0-t}$ (mg.h/dL)	104	222.215 (13.588)	104	223.389 (9.397)	104	223.972 (9.156)
T_{max} (h)	104	5.406 (4.149)	104	5.022 (2.691)	104	5.266 (3.510)

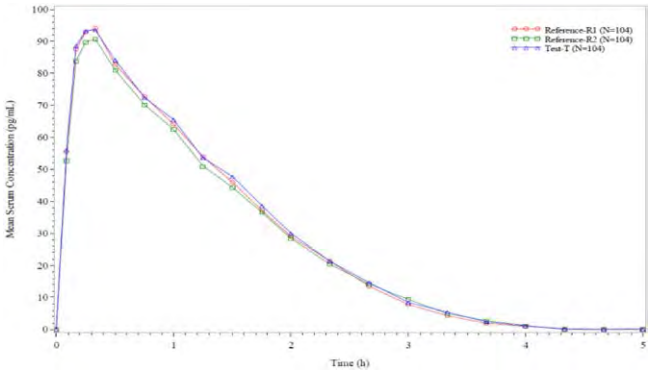


Figure 1. Mean Serum Concentration vs. Time Curve for Teriparatide

Conclusion: This study showed PK equivalence as well as similar PD and safety profiles between teriparatide biosimilar, EU-teriparatide and US-teriparatide in healthy subjects.

References:

[1] Data on file

Disclosure of Interests: Inderjeet Singh Employee of: Intas Pharmaceuticals Limited, Anshul Attrey Employee of: Lambda Therapeutics Research Limited, Ronak Patel Employee of: Lambda Therapeutics Research Limited, Sridevi Khambhampaty Employee of: Intas Pharmaceuticals Limited, Vinu Jose Employee of: Intas Pharmaceuticals Limited

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SAT0452

DIFFERENT PROFILE OF RISK OF FRACTURE IN PATIENTS TREATED WITH ANTI-OSTEOPOROTIC DRUGS IN ITALY USING A NEW ALGORITHM

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Background: A new algorithm for management of patients at low, high and very high risk of osteoporotic fractures has been recently proposed, has been also recommended treating those patients at very high risk of fracture with bone anabolics (1). A similar treatment algorithm has been applied in Italy since 2015, when the "Nota 79", that regulates the reimbursability for osteoporosis medications, has been developed by the Italian Agency for Drugs (AIFA) (2).

Objectives: In the present study, using a new mathematical and computerized algorithm, we seek to investigate the profile of risk of fracture of patients starting treatment with different anti-osteoporotic medications in Italy.

Methods: We retrospectively analyzed the 10-year risk of major osteoporotic fracture calculated with the DeFRAcalc79 tool in postmenopausal women aged over 50 years that were initiating an anti-osteoporotic treatment (fully reimbursed according to the Nota 79). DeFRAcalc79 is a new web-based fracture risk-assessment tool (https://defra-osteoporosi.it) that arithmetically adjusts the risk based on the integration of multiple risk factors contemplated by the AIFA's Nota 79, including: demographic and anthropometric data, femoral and/or lumbar spine BMD T-score, family history of femoral or vertebral fractures, number and site of previous osteoporotic fracture (including vertebral, femoral, and nonvertebral nonfemoral fractures), glucocorticoid treatment (> 3 or > 12 months, ≥5 mg prednisone or equivalent), adjuvant hormone therapy for breast or prostate cancer, and comorbidities that increase the risk (rheumatoid arthritis and other connective tissue diseases, chronic obstructive pulmonary disease, inflammatory bowel diseases, Parkinson's disease, multiple sclerosis, HIV infection, diabetes, or severe physical handicap).

Results: We retrieved data for 10,235 women prescribed with an anti-osteoporotic treatment. **Figure 1** shows the mean 10-year fracture risk estimated with DeFRAcalc79 tool at the time of the treatment initiation. Teriparatide users had the highest 10-year risk of fracture (67.4% Standard Deviation [SD] 21.5%). We found that in 2,231 patients starting denosumab, the 10-year baseline risk of fracture was 38.5%, SD 22.8%. In 5,759 patients initiating alendronate was 25.7%, SD 15.3% and in patients initiating risedronate was 27.9%, SD 26.9%. Patients prescribed with zoledronic acid had a mean 10-year risk of fracture of 35.6%, SD 21.6. P values between means were all <0.01.

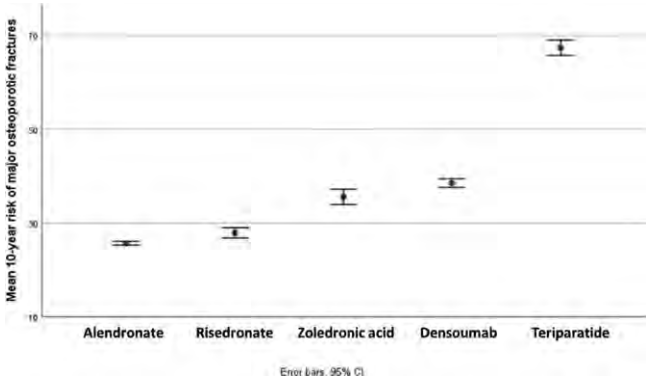


Figure 1. Mean 10-year risk of fracture estimated with DeFRAcalc79 tool at the time of treatment initiation, p< 0.01 between all means.

Conclusion: The risk of fracture of Italian post-menopausal women initiating different anti-osteoporotic medications varies significantly. Teriparatide is prescribed to patients with greater risk of fracture. The Nota 79 correctly individuates patients at very high risk of fracture that merit treatment with a bone anabolic. Denosumab and zoledronic acid are prescribed to patients with a greater risk of fracture compared to oral bisphosphonates.

DeFRAcalc79 is a useful and practical tool for the integrated evaluation of the profile of risk of fracture.

References:

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SAT0453

DELAYED DENOSUMAB INJECTIONS AND FRACTURES RISK AMONG SUBJECTS WITH OSTEOPOROSIS: A POPULATION-BASED COHORT STUDY

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Background: Denosumab is effective for osteoporosis, but discontinuation leads to rapid reversal of its therapeutic effect[1].

Objectives: To estimate the risk for fracture among users of denosumab who delayed subsequent dosages compared with users who received dosages on time.

Methods: Population-based cohort study. We included patients aged over 45 years who initiated denosumab for osteoporosis from UK THIN database, 2010 to 2019. Observational data were used to "emulate a hypothetical trial"[2, 3] with three dosing intervals: subsequent denosumab injection 24-28 weeks after prior dose ("on time"), delay by 4-16 weeks ("short delay"), and delay by over 16 weeks ("long delay"). The primary outcome was a composite of all fracture types. Secondary outcomes included major osteoporotic fracture, vertebral fracture, and hip fracture.

Results: The rate of composite fracture per 1000 person-years was 58.9 for on-time, 61.7 for short delay, and 85.4 for long delay of subsequent denosumab injections. Compared to on-time injections, short delay had a hazard ratio (HR) for composite fracture 1.03 (95% CI 0.63-1.69) and long delay HR 1.44 (95% CI 0.96-2.17; p for trend 0.093). For major osteoporotic fractures, short delay had an HR 0.94 (95% CI 0.57-1.55) and long delay an HR of 1.69 (95% CI 1.01-2.83; p for trend 0.056). For vertebral fractures, short delay had an HR 1.48 (95% CI 0.58-3.79) and long delay 3.91 (95% CI 1.62-9.45; p for trend 0.005).

Conclusion: While delayed subsequent denosumab dosages over 16 weeks was associated with an increased risk of vertebral and major osteoporotic fracture compared to no delay, composite fracture risk was not increased with longer delays.

References:

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Table. Rates and Adjusted Hazard Ratios of Fracture

	On-time	Short delay	Long delay	P for linear trend
Composite Fracture				
Rate (per 1000 person-years)	59	61.7	85.4	-
Unadjusted HR (95 %)	Ref	1.05 (0.62, 1.76)	1.45 (0.95, 2.21)	0.097
Adjusted HR (95% CI) †	Ref	1.03 (0.63, 1.69)	1.44 (0.96, 2.17)	0.093
Major Osteoporotic Fracture				
Rate (per 1000 person-years)	34.8	31.9	58	-
Unadjusted HR (95 %)	Ref	0.92 (0.55, 1.53)	1.67 (0.98, 2.84)	0.074
Adjusted HR (95% CI) †	Ref	0.94 (0.57, 1.55)	1.69 (1.01, 2.83)	0.056
Vertebral Fracture				
Rate (per 1000 person-years)	4.9	7.3	19.4	-
Unadjusted HR (95 %)	Ref	1.47 (0.58, 3.71)	3.93 (1.59, 9.72)	0.006
Adjusted HR (95% CI) †	Ref	1.48 (0.58, 3.79)	3.91 (1.62, 9.45)	0.005
Hip Fracture				
Rate (per 1000 person-years)	10.2	9.6	18.3	-
Unadjusted HR (95 %)	Ref	0.94 (0.43, 2.04)	1.78 (0.80, 3.97)	0.18
Adjusted HR (95% CI) †	Ref	0.97 (0.44, 2.12)	1.75 (0.81, 3.79)	0.173

† Adjusted model: adjusted by age, sex, baseline CCI index, major osteoporotic fracture, oral BP duration (years), 10-year risk of major osteoporotic fracture, prior denosumab doses.

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SAT0454

EARLY CLINICAL EFFICACY OF ROMOSOZUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS AND PRIMARY OSTEOPOROSIS

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Background: Romosozumab (ROM), a monoclonal antibody that binds sclerostin, increases bone formation and decreases bone resorption. And although it is a novel therapeutic agent for osteoporosis, which has shown high effects of increasing bone density and inhibiting fragile fracture in overseas clinical trials. However the clinical efficacy in daily clinical practice is unknown.

Objectives: To evaluate the early clinical efficacy of ROM in patients with osteoporosis between rheumatoid arthritis (RA-OP) and primary osteoporosis (P-OP) for 6 months.

Methods: RA patients diagnosed according to the 2010 ACR/EULAR criteria. RA-OP and P-OP patients met at least one of the following criteria were eligible; a bone mineral density T score of -2,5 or less at the lumber spine or total hip and either one or more moderate or severe vertebral fractures or two or more mild vertebral fractures. All patients were initiated ROM from between March and June, 2019. The total number of patients was 15 cases, including 8 RA-OP and 7 P-OP. All patients received continuous ROM therapy more than 6 months. The DMB dose was 210mg at once every 1 months. In all cases native or activated vitamin D has been used. We reviewed the results for 6 months about the increase and decrease of bone mineral density (BMD) of lumbar spine(LS) and total hip(TH) by DEXA and bone turnover markers, intact n-terminal propeptide type I procollagen(PINP) and tartrate-resistant acid phopshatate form 5b(TRACP-5b).

Results: The gender was all female. The mean age was 71.8 ± 8.7; disease duration of RA-OP patients was 23.0 ± 15.1 years; the body mass index was 19.9 ± 3.2 and the FRAX was 32.5 ± 14.9. Clinical findings related to RA-OP at baseline were as follows; CRP 0.97 ± 0.77; DAS-CRP 3.22 ± 0.41; HAQ 1.41 ± 0.94 in RA-OP patients and in the all patients, bone turnover markers and bone mineral density at baseline were as follows; P1NP 72.2 ± 39.8; TRACP-5b 539 ± 212; LS-BMD and T-score 0.80 ± 0.20 g/cm^2 and -2.75 ± 1.36 and TH-BMD 0.55 ± 0.07 g/cm^2 and -3.18 ± 0.55 g/cm^2. The rate of increased P1NP from baseline to 1, 3 and 6 months were each -96.8 ± 80.8% at 1 month, 106.8 ± 115.6% at 3 month and 90.7 ± 115.7% at 6 month and decreased TRAC-5b were -20.4 ± 20.6% at 1 month, -80.8 ± 19.6% at 3 month and -1.8 ± 50.8% at 6 month. The rate of increased LS-BMD from baseline to 6 months were 11.0 ± 8.0% and TH-BMD were 5.3 ± 3.8% (Fig. 1, 2).

Conclusion: Early clinical efficacy of ROM for RA-OP and P-OP was extremely effective and has the high potential to be an important option in the treatment of osteoporosis.

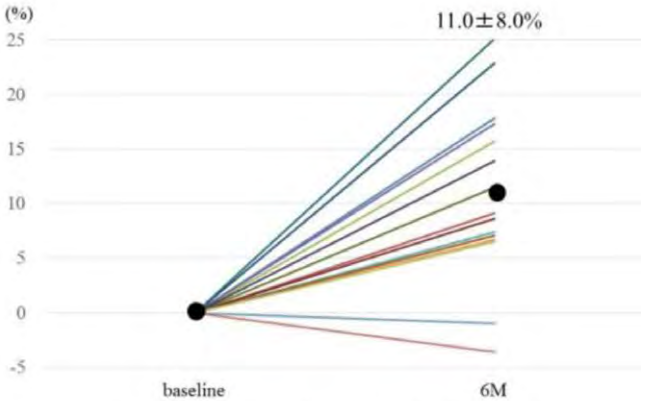


Fig.1: The rate of increased LS-BMD from baseline to 6 month

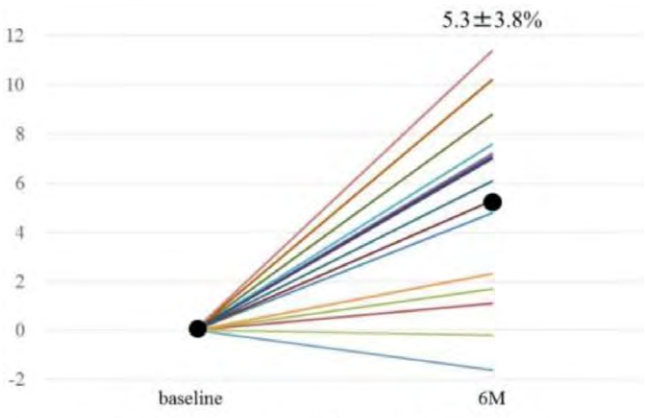


Fig.2: The rate of increased TH-BMD from baseline to 6 month

Disclosure of Interests: None declared
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SAT0455 RADIOFREQUENCY ECHOGRAPHIC MULTI SPECTROMETRY (REMS) FOR THE IDENTIFICATION OF FRAIL BONES

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Background: Radiofrequency Echographic Multi Spectrometry (REMS) is the first clinically available approach for direct non-ionizing measurement of bone mineral density (BMD) at lumbar spine (LS) and femoral neck (FN). Available scientific evidences describe BMD estimated by REMS as an accurate parameter for the diagnosis of osteoporosis [1].
Objectives: To investigate the effectiveness of the T-score values provided by REMS scans at FN and LS in the identification of frail patients at risk for osteoporotic fractures and to compare the performance of REMS with the dual-energy X-ray absorptiometry (DXA) one.
Methods: The patients underwent DXA and REMS scans at FN and at LS. Five clusters of fractures occurred during a median 3.5-year follow-up were identified whether involving the upper limb (forearm, elbow, humerus, wrist, hand), lower limb (tibia, ankle, metatarsus), thorax (shoulder blade, shoulder, rib), hip (femur or pelvis bones), or vertebrae. The ability of REMS and DXA T-score values to assess the incidence and site of fractures was evaluated through an analysis of covariance.
Results: Seven hundred twenty-one Caucasian women were enrolled. Ninety-five fractures occurred, in particular 41 at upper limb, 16 at hip, 15 at thorax, 14 at lower limb, 9 at vertebrae. Patients characteristics are reported in table. Considering subcategories of fractured patients, there were not statistically significant differences for age, height, weight and BMI.
In the analysis of covariance including age and BMI as covariates, the difference of T-score values between fractured and non-fractured patients is statistically significant for REMS and DXA at both sites.
Lower FN T-score values were found for patients with fractures at hip or vertebra with respect to non-fractured patients both for REMS and DXA ($p<0.001$). Considering LS T-score, lower values were found for patients with fractures at hip, vertebra or upper limb with respect to non-fractured patients both for REMS and DXA ($p<0.001$, Figure).
Conclusion: REMS T-score measured at axial sites is an effective parameter for identification of patients at the risk of incident fragility fractures, in particular occurring at hip, vertebra or upper limb in a population-based sample of female subjects.
References:
[1] Diez-Perez, Aging Clin Exp Res 2019;31(10):1375–89

Table 1. Baseline patient characteristics, expressed as median (25^{th} – 75^{th} percentiles).

	Patients with incident fragility fracture	Patients without incident fragility fracture	p-value*
Age [years]	70 (60-73)	59 (54-64)	<0.001
Height [cm]	159 (155-164)	160 (156-165)	0.08
Weight [kg]	63 (58-70)	62 (57-69)	0.42
BMI [kg/m^2]	24.97 (23.13-26.86)	24.24 (22.22-26.59)	0.04
FN REMS T-score	-2.3 (-2.8 – -1.7)	-1.8 (-2.3 – -1.1)	<0.001
FN DXA T-score	-2.2 (-2.8 – -1.6)	-1.7 (-2.3 – -1.1)	<0.001
LS REMS T-score	-3.0 (-3.5 – -2.0)	-2.0 (-2.8 – -1.0)	<0.001
LS DXA T-score	-2.8 (-3.4 – -1.8)	-1.9 (-2.7 – -1.0)	<0.001

* Wilcoxon ranksum test

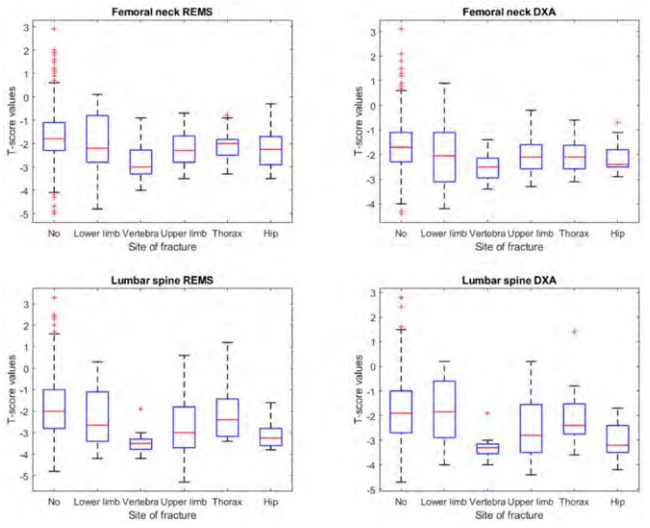


Figure. Boxplot of the distribution of T-score values estimated REMS and DXA at FN and LS among patients without incident fragility fracture and patients with incident fragility fractures at different sites.

Note: **G. Adami, G. Arioli[§], G. Bianchi[§], M.L. Brandi[§], C. Caffarelli[§], L. Cianferotti[§], G. Girasole[§], S. Gonnelli[§], M. Manfredini[§], M. Muratore[§], E. Quarta[§], L. Quarta[§], D. Gatti[§] equal contributors listed in alphabetical order.**

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SAT0456 REAL-LIFE RISK OF FRACTURE AND TREATMENT PREVALENCE IN DRUG-INDUCED OSTEOPOROSIS IN ITALY USING A NEW ALGORITHM

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Background: Glucocorticoid-induced osteoporosis and osteoporosis induced by adjuvant hormone therapy for breast cancer are the most common forms of secondary osteoporosis.
Objectives: The exact real-life prevalence of treatment with anti-osteoporotic drugs in women with drug-induced osteoporosis is not known. In the present study, using a new mathematical and computerized algorithm, we investigate the profile of risk of fracture of women with drug-induced osteoporosis and the prevalence of treatment with anti-osteoporotic drugs.

Methods: We have retrospectively analyzed the 10-year risk of major osteoporotic fracture calculated with the DeFRAcalc79 tool in postmenopausal women aged over 50 years that were initiating an anti-osteoporotic treatment (fully reimbursed according to the Nota 79). DeFRAcalc79 is a new web-based fracture risk-assessment tool (https://defra-osteoporosi.it) that arithmetically adjusts the risk based on multiple risk factors contemplated by the Nota 79, which regulates the reimbursability for osteoporosis medications in Italy (Italian Agency for Drugs, AIFA), including demographic and anthropometric data, femoral and/or lumbar spine BMD T-score, family history of femoral or vertebral fractures, number and site of previous osteoporotic fracture (including vertebral, femoral, and non-vertebral non-femoral fractures), glucocorticoid treatment (> 3 or > 12 months, ≥5 mg prednisone or equivalent), adjuvant hormone therapy for breast cancer, and comorbidities that induce an increased risk of fracture (rheumatoid arthritis and other connective tissue diseases, chronic obstructive pulmonary disease, inflammatory bowel diseases, Parkinson's disease, multiple sclerosis, human immunodeficiency virus infection, diabetes, or severe physical handicap). This is a sub-analysis of the cross-sectional observational study to validate and further develop the DeFRA algorithm for the estimation of the risk of osteoporotic fractures, promoted by Verona hospital with the unconditional support of Amgen Srl.

Results: Among 208 women, 116 (55.8%) were treated with adjuvant hormone therapy for breast cancer and 92 (44.2%) were on glucocorticoid ≥5 mg/day. Women on glucocorticoids had a greater mean 10-year risk of fracture compared to women on adjuvant hormone therapy for breast cancer (67.0% vs 39.1% p<0.01). 50.7% of women on adjuvant hormone therapy for breast cancer used denosumab, 28.0% zoledronic acid and 17.3% alendronate. In glucocorticoid-induced osteoporosis, 17.6% of the women used teriparatide, 37.3% alendronate, 29.4% zoledronic acid and 13.7% denosumab.

Conclusion: In our cohort of patients, treatment with adjuvant hormone therapy for breast cancer was slightly more common than glucocorticoids. Women with glucocorticoid-induced osteoporosis had a greater risk of fracture compared to patients treated with adjuvant hormone therapy for breast cancer. Half of the patients on adjuvant hormone therapy for breast cancer were prescribed with denosumab. One-fifth of the patients with glucocorticoid-induced osteoporosis was treated with teriparatide. DeFRAcalc79 is a useful and practical tool for the integrated evaluation of fracture risk in drug-induced osteoporosis.

Disclosure of Interests: Giovanni Adami: None declared, Angelo Fassio Speakers bureau: Angelo Fassio reports personal fees from: Abiogen and Novartis, outside the submitted work., Alessandro Giollo: None declared, Giovanni Orsolini: None declared, Ombretta Viapiana: None declared, Davide Gatti Speakers bureau: Davide Gatti reports personal fees from Abiogen, Amgen, Janssen-Cilag, Mundipharma, outside the submitted work., Maurizio Rossini Speakers bureau: AbbVie, Abiogen, Amgen, BMS, Eli-Lilly, Novartis, Pfizer, Sanofi, Sandoz and UCB

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SAT0457 PREVALENCE OF OSTEOPOROSIS IN OSTEOARTHRITIC PATIENTS: A SYSTEMATIC REVIEW

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Background: There is controversy regarding the relationship between osteoarthritis (OA) and osteoporosis (OP). While OA may be associated with increased bone mineral density (BMD) due to increased weight, evidence exists that the incidence of OP may be increased in patients with OA.

Objectives: To determine whether the prevalence of OP is increased in patients with OA, compared to age and sex-matched populations.

Methods: We conducted a systematic literature review using the databases PubMed, Embase, Scopus, and Web of Science, including articles that that analysed the frequency, rate, prevalence, incidence, risk, or excess risk of OP in patients with OA compared to age and sex-matched comparison groups (controls). Articles with fewer than 200 participants, and those without controls were excluded. Two reviewers conducted title and abstract screening.

Results: Of 2772 unique articles, 49 articles were chosen for full article screening, and 4 articles met the inclusion criteria of our present study. Data from 2 and 4 studies used OP in men and women, respectively. Other articles reported on BMD and not OP so they were excluded. In women, 998 participants with OA were compared with 1903 controls. The pooled estimate of the odds ratio for prevalence of OP vs general matched population was not statistically different (Figure 1). In men, 136 participants with OA were compared with 682 controls. The results did not show a statistically significant different in the frequency of OP in OA in men (Figure 2).

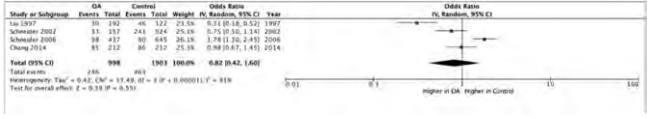


Figure 1. Prevalence of OP in women with OA compared to controls

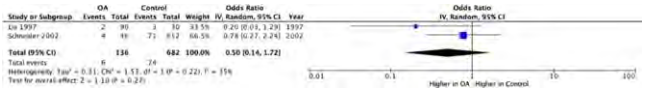


Figure 2. Prevalence of OP in men with OA compared to controls

Conclusion: The frequency of OP in participants with OA was the same in both men and women compared to the matched controls.

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Disclosure of Interests: Ali Ahmadi Pirshahid: None declared, Dongkeun Kim: None declared, Yueyang Li: None declared, Timothy Varghese: None declared, Janet Pope Grant/research support from: AbbVie, Bristol-Myers Squibb, Eli Lilly & Company, Merck, Roche, Seattle Genetics, UCB, Consultant of: AbbVie, Actelion, Amgen, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Eicos Sciences, Eli Lilly & Company, Emerald, Gilead Sciences, Inc., Janssen, Merck, Novartis, Pfizer, Roche, Sandoz, Sanofi, UCB, Speakers bureau: UCB

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SAT0458 THE POLYMORPHISM ON FAT MASS AND OBESITY ASSOCIATED GENE (FTO) WAS ASSOCIATED WITH LOW BONE MASS IN JAPANESE COMMUNITY DWELLING POPULATION.

K. Arima[1], M. Tamai[2], F. Nonaka[3], N. Iwamoto[2], S. Mizukami[1], T. Nishimura[1], Y. Abe[1], T. Origuchi[4], K. Aoyagi[1]. [1]*Nagasaki University Graduate School of Biomedical Sciences, Department of Public Health, Nagasaki, Japan*; [2]*Nagasaki University Graduate School of Biomedical Sciences, Department of Immunology and Rheumatology, Division of Advanced Preventive Medical Sciences, Nagasaki, Japan*; [3]*Nagasaki University Graduate School of Biomedical Sciences, Department of Island and Rural Medical Research, Nagasaki, Japan*; [4]*Nagasaki University Graduate School of Biomedical Sciences, Department of Rehabilitation Sciences, Nagasaki, Japan*

Background: A polymorphism on *FTO* (OMIM 610966) was reported as a causal variant for obesity, plays a critical rule not only in amount of adipose tissue but also in function of mitochondrial thermogenesis1.

Objectives: To examine the association of the genotype on a single nucleotide polymorphism on *FTO* with bone health.

Methods: FTO rs1421085 polymorphism was genotyped in 1,601 community-dwelling Japanese participants. This cross-sectional study was nested in Nagasaki Islands Study, which is a prospective cohort in Goto City, in islands of Japan. Participants were recruited at medical check-ups for community dwelling population.

Bone mass of the calcaneus was evaluated with stiffness index calculated using a quantitative ultrasound measurement. Low bone mass was defined as a stiffness index less than 80 % of the young adult mean.

Sera and peripheral blood mononuclear cells were obtained. The SNP of rs1421085 was genotyped using hydrolysis probe. The chi-squared test was used to determine whether the variants were in equilibrium in that population. Trend for the median of BMI among genotypes was assessed using the Jonckheere-Terpstra test. Potential associations between FTO polymorphism and overweight and between the polymorphism and low bone mass were evaluated using logistic regression. All analyses were carried out using SPSS 23.

Results: Genotype and allele frequencies for the polymorphism were in Hardy-Weinberg equilibrium (minor allele frequency 0.16, p = 0.40) in 1,601 community-dwelling persons (mean age was 68.5 years in men and 68.1 years in women).

There were significant associations between the minor allele and higher median of BMI on dose dependent manner in men (p = 0.04 for trend in men and p = 0.10

for trend in women, respectively), and between the minor allele and overweight (>25 in BMI, OR 1.52, 95%CI 1.07 2.14, p=0.02 in men, OR 1.48, 95%CI 1.16 1.95, p=0.01 in women).
Logistic regression analysis showed a significant protective association in men with carriers of minor allele against low bone mass after an adjustment for age and BMI (OR 0.63, 95%CI 0.44 0.90, p=0.01 in men, not significant in women).
Conclusion: Our study indicated significant associations of the polymorphism on *FTO* with BMI and bone mass among community dwelling men. The polymorphism may play a rule in a part of bone health with higher BMI and other beneficial functions.
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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.4050

SAT0459 EVALUATION OF THE PREVALENCE AND THE MANAGEMENT OF OSTEOPOROTIC FRACTURES IN PATIENTS HOSPITALIZED AT NANCY UNIVERSITY HOSPITAL (FRANCE) IN 2017.

A. Baccichetti[1], P. L. Nguyen-Thi[2], A. Blum[3], D. Mainard[4], F. Sirveaux[4], L. Nace[5], A. Valance[6], T. Civit[7], G. Dautel[8], C. Perret-Guillaume[9], B. Guerci[10], H. Tronel[11], I. Chary Valckenaere[1], D. Loeuille[1]. *[1]CHU Nancy, Rheumatology, Nancy, France*; *[2]CHU Nancy, Medical Evaluation, Nancy, France*; *[3]CHU Nancy, Radiology Guilloz, Nancy, France*; *[4]CHU Nancy, Orthopedic Surgery, Nancy, France*; *[5]CHU Nancy, Emergencies Unit, Nancy, France*; *[6]CHU Nancy, Post Emergencies Unit, Nancy, France*; *[7]CHU Nancy, Neurosurgery, Nancy, France*; *[8]CHU Nancy, Hand Surgery, Nancy, France*; *[9]CHU Nancy, Geriatrics, Nancy, France*; *[10]CHU Nancy, Endocrinology, Nancy, France*; *[11]CHU Nancy, Medical Information, Nancy, France*

Background: Osteoporotic fractures are a major public health concern because of their consequences in morbidity, costs and mortality. In the meantime, historically postfracture osteoporosis medication use rates have been poor.
Objectives: The aim is to analyze the management of osteoporosis in patients hospitalized for osteoporotic fractures (OF) at Nancy University Hospital (France) in 2017.
Methods: Total number of hospitalized patients and hospital stays were extracted by the Department of Medical Information (DIM) which selected departments with at least forty hospitalizations with Medical Unit Summary related to a diagnosis of fracture or osteoporosis. Hospitalizations not concerned by a recent OF were excluded. Data on fractures, patient characteristics, risk factors for OF and fall, management of osteoporosis, discharge status, stay duration, were studied from patient medical records. Prevalence of OF stays, management of osteoporosis and factors associated with duration of stay were analyzed.
Results: Out of a total of 153,840 hospitalizations, 918 hospitalizations (844 patients, mean age 74.5 years ± 13.6, 74.5% women) concern an OF. The prevalence of hospitalizations for OF was 0.6% of total hospitalizations and 17.9% of total hospitalizations for fractures. Among the 844 patients, 85.7% had a severe fracture (vertebral fracture: 56.2%, hip fracture: 24.1%), 16.5% had a non-severe fracture, and 8.5% had a fracture cascade in the year. At discharge from hospital, 11.7% of patients received a specific treatment for osteoporosis. Longer stay duration was associated with age, severe fractures, Groll index and discharge status.
Conclusion: Nearly one hospitalized fracture in five is osteoporotic, while only one in ten patients is treated for osteoporosis. Stay duration increased with age and comorbidities. This encourages the development of early prevention, screening and treatment strategies for osteoporosis.
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Disclosure of Interests: None declared
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SAT0460 INGESTION OF LEMON JUICE MAY MODULATE BONE METABOLISM.

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Background: An association between bone health and consumption of citrus fruits have been previously reported; however, the effect of lemon juice on bone metabolism have not been explored yet.
Objectives: To investigate bone metabolic changes in postmenopausal women assuming lemon juice.
Methods: Participants were postmenopausal osteoporotic women without history of clinical fractures who agreed to enrich their diet with lemon juice (Acti Lemon, Polenghi) over a 2-month period. The daily juice dose of 30 ml we suggested was equivalent to one Sicilian organic lemon. Surrogate markers of bone formation as procollagen type 1 N-propeptide (P1NP) and of bone resorption as C-terminal telopeptide of type I collagen (CTX), but also some regulators of bone metabolism as RANK-L, OPG, RANK-L/OPG ratio and sclerostin were assessed at baseline and then at 1 and 2 months after lemon juice administration. Controls were represented by a placebo group of age-matched osteoporotic postmenopausal women.
Results: 47 participants [mean age 60.2 ± 4.1 yr.] completed the study, without reporting any adverse events. Lemon juice was well tolerated. Over the observation period modifications of bone metabolism occurred: we detected a decreased RANK-L/OPG ratio and increased CTX levels at all time points vs. baseline. Particularly, change at month-1 of sclerostin (versus baseline) has been positively associated with change at month-1 and month-2 of CTX (r=0.46, p=0.01 and r=0.43, p=0.01, respectively). Change at month-1 of OPG was positively associated with change at month-1 of P1NP (r=0.49, p=0.006). Change at month-1 of RANKL/OPG has been related with variation at day 30 of P1NP (r=-0.44, p=0.013). Variation of P1NP at month-1 was related with sclerostin variation at day 30 (r=-0.56, p=0.02) and month-2 vs. baseline value (r=0.44, p=0.017) and with sclerostin variation between month-1 and month-2 (r=0.69, p<0.001). Variation of P1NP between month-1 and month-2 was associated with RANKL change at month-1 (r=-0.35, p=0.05), with sclerostin change at month-1 (r=-0.49, p=0.008) and with sclerostin change between month-1 and month-2 (r=0.41, p=0.028). At a multiple regression analysis the change of P1NP between month-1 and month-2 was independently predicted by the change of sclerostin at month-1 (ß=-1.5, SE 0.5, p=0.006), after correcting for age, BMI and change of RANKL and CTX levels at month-1. No significant modifications raised from controls.
Conclusion: Drinking lemon juice may boost bone metabolic changes involving both bone resorption and bone formation.
Disclosure of Interests: None declared
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SAT0461 SHORT-TERM MONITORING OF DENOSUMAB EFFECT IN BREAST CANCER PATIENTS RECEIVING AROMATASE INHIBITORS USING REMS TECHNOLOGY ON LUMBAR SPINE

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Background: Aromatase inhibitor (AI) therapy in women with estrogen receptor-positive (ER+) breast cancer (BC) causes accelerated bone loss and increased risk of osteoporosis and fractures as side effects. Denosumab (i.e. 60 mg twice a year) is a viable therapy against bone resorption, but the short-term monitoring of bone mineral density (BMD) change with time is still an unmet clinical need, since the current techniques (including dual-energy X-ray absorptiometry, DXA) require 1-2 years between two consecutive measurements [1]. Radiofrequency Echographic Multi Spectrometry (REMS), with high performance in terms of precision and repeatability [2], might be used in this setting of patients for short-term monitoring of bone health-related parameters.
Objectives: The objective is the short-term monitoring of the effect of AIs with/without denosumab on bone health in BC patients using REMS and DXA scans at lumbar spine.
Methods: Post-menopausal ER+ BC patients treated with adjuvant AIs were recruited. Two subgroups were identified, whether receiving also 60 mg of denosumab therapy every 6 months or not (named Group A and Group B, respectively). All patients underwent baseline DXA and REMS lumbar spine scans at

time T0, previous to the first AI therapy, and after 12 months (time T1). REMS scan only was repeated also at 18 months (T2), since a 6-month interval between two consecutive scans is not recommended for DXA. The bone mineral density (BMD) was measured with both techniques.

Results: Overall, 254 ER+ BC patients were enrolled (127 per group). The effect of denosumab on BMD is reported in Table. The BMD values obtained by DXA and REMS were not significantly different at T0 and T1, whereas the difference between Group A and B at T1 was statistically significant (p<0.001) both for REMS and DXA. At T2, REMS confirmed the increasing trend of BMD for Group A and the decreasing one for Group B, and the difference between groups was statistically significant (p<0.001). For each time point and each group, there were not statistically significant differences between DXA and REMS.

Conclusion: Several studies have shown the effect of denosumab on BMD over a period not less than 2 years from the start of treatment. This study showed the feasibility of short-term follow-up using REMS lumbar spine scans at 6-month time steps.

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Table 1. BMD values, expressed as g/cm^2, measured by DXA and REMS for Group A (patients receiving AIs only) and Group B (patients receiving AIs and denosumab) at baseline (T0), 12 months (T1) and 18 months (T2) from the start of therapy. Results are presented as median values with 25th and 75th percentiles. P-values are obtained with a Mann-Whitney test.

	DXA			REMS		
Scan time	**Group A**	**Group B**	**p**	**Group A**	**Group B**	**p**
T0	0.840 (0.719-0.959)	0.867 (0.723-0.958)	0.99	0.833 (0.708-0.949)	0.855 (0.714-0.973)	0.77
T1	0.823 (0.702-0.944)	0.889 (0.749-0.990)	0.003	0.819 (0.691-0.927)	0.887 (0.740-1.018)	<0.001
T2	-	-	-	0.801 (0.679-0.909)	0.899 (0.754-1.020)	<0.001

Note: The authors **D. Ciardo, M. Ciccarese, F. Conversano, M. Di Paola, R. Forcignanò, A. Grimaldi, F.A. Lombardi, M. Muratore and P. Pisani** are listed in alphabetical order

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SAT0462 ASSESSMENT OF BONE MINERAL DENSITY IN INFLAMMATORY BOWEL DISEASE

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Background: Inflammatory bowel disease (IBD), including ulcerative colitis (UC) and Crohn's disease (CD), is considered as a risk factor of low bone mineral density (BMD). In fact, the prevalence of osteoporosis ranges from 17% to 41% in IBD patients. The possible contributing factors may include malabsorption, glucocorticoid treatment and coexisting comorbidities

Objectives: The purpose of our work was to determine the frequency and the determinants of osteoporosis in patients with IBD and to assess whether there is a difference in BMD status between UC and CD.

Methods: This is a retrospective study, over a period of 5 years (from January 2014 to December 2018) and including patients followed for IBD who had a measurement of BMD by DEXA. Clinical, anthropometric and densitometric data (BMD at the femoral and vertebral site) were recorded. The WHO criteria for the definition of osteoporosis and osteopenia were applied.

Results: One hundred and five patients were collected; among them 45 were men and 60 were women. The average age was 45.89 years old. The average body mass index (BMI) was 25.81 kg/m2 [16.44-44.15]. CD and UC were diagnosed in respectively 57.1% and 42.9%. A personal history of fragility fracture was noted in 4.8%. Hypothyroidism was associated in one case. Early menopause was recorded in 7.6%. 46.8% patients were treated with corticosteroids. The mean BMD at the vertebral site was 1.023 g/cm3 [0.569-1.489 g/cm3]. Mean BMD at the femoral site was 0.920g/cm3 [0.553-1.286g / cm3]. The mean T-score at the femoral site and the vertebral site were -1.04 SD and -1.27 SD, respectively. Osteoporosis was found in 25.7% and osteopenia in 37.1%. Osteoporosis among CD and UC patients was found in respectively 63% and 37%. The age of the osteoporotic patients was significantly higher compared to those who were not osteoporotic (52.23 vs 43.67 years, p = 0.01). We found a significantly higher percentage of osteoporosis among men compared to women (35.6% vs 18.3%, p=0.046). The BMI was significantly lower in the osteoporotic patients (23.87 vs 26.48 kg/m2, p=0.035) and we found a significant correlation between BMI and BMD at the femoral site (p=0.01). No increase in the frequency of osteoporosis was noted in patients treated with corticosteroids (27.9% vs 21.6%, p=0.479). Comparing the UC and CD patients, no difference was found in baseline characteristics, use of steroids or history of fracture. No statistically significant difference was found between UC and CD patients for osteoporosis(p=0.478), BMD at the femoral site (p=0.529) and at the vertebral site (p=0.568).

Conclusion: Osteoporosis was found in 25.7% of IBD patients without any difference between CD and UC. This decline does not seem to be related to the treatment with corticosteroids but rather to the disease itself. Hence the interest of an early screening of this silent disease.

Disclosure of Interests: None declared

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SAT0463 SEVERE OSTEOPOROSIS IN COLOMBIAN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Osteoporosis predominantly affects post-menopausal women. There is an important percentage of the population that have additional risk factors that decrease bone mineral density. Patients with Systemic Lupus Erythematosus (SLE) have an increased risk for osteoporosis due to corticosteroid use and chronic inflammation. This population could have a higher prevalence of osteoporosis when compared to post-menopausal women of equal or older age. There is a paucity of information regarding bone mineral density and SLE in Latin America.

Objectives: To describe the prevalence and incidence of osteoporosis and osteoporotic fractures in a Colombian population with Systemic Lupus Erythematosus

Methods: We collected 464 clinical records of patients who met either the American College of Rheumatology 1997 or Systemic Lupus International Collaborating Clinics (SLICC) 2012 classification criteria for systemic lupus erythematosus between January 2015 and June 2019. The clinical and immunoserological characteristics, and damage accrual were monitored for one year. The diagnosis of osteoporosis was confirmed with densitometry by energy x-ray absorptiometry (DXA) and the presence of fragility fractures according to the rheumatologist's report in the clinical history. The description of proportions and incidence rate of osteoporosis and fragility fracture is performed.

Results: The mean age was 45 years, 96.5% were women and the mean disease duration was 12 years. Others clinical characteristics in table 1. The prevalence of osteoporosis was 13.8% with an incidence of 1.1 fractures / 100 person-months in the general population with SLE. In postmenopausal women, over 50 years the prevalence of osteoporosis was 28.4% with an incidence of 0.8 fractures / 100 months person. In the densitometric characteristics, the mean bone mineral density was 0.772 gr / cm2, T-score spine -2.9 and T-score femoral -2.6. SLEDAI mean 1.5 (SD 2.92) and SLICC mean 1.

Table 1. clinical characteristics

	n	%
Active Smoking	83	17.9
Premature gonadal failure	8	1.7
Lupic Nephritis	178	38.4
Proteinuria >2.5grams/24hours	34	7.3
End Stage Renal Disease	16	3.4
Anti-dsDNA	146	31.4
Anti-Sm	110	23.7
Anti-Ro	138	29.7
Prednisone Cumulative Dose	2.8gr	
Antimalarial	57	12

Conclusion: Low bone mineral density and severe osteoporosis are prevalent in our cohort with SLE. We have found a fracture rate of 1080 per 100.000 people, which is well over what has been reported in the general population (53-443 per 100.000 people in women). Osteoporotic fractures are part of damage accrual

and thus have an association with morbidity and mortality. Data regarding osteoporotic fractures are necessary in order to develop guidance and health policy in the region. SLE is an important risk factor for severe osteoporosis and must be kept in mind when developing guidance and health policy

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Disclosure of Interests: Juan camilo Diaz-Coronado: None declared, Sebastian Herrera Speakers bureau: academic conference, Deicy Hernandez-Parra: None declared, Laura Betancur-Vasquez: None declared, Daniel Gonzalez-Hurtado: None declared, Juanita Gonzalez-Arango: None declared, laura Uribe-Arango: None declared, Maria Fernanda Saavedra Chacón: None declared, Jorge Lacouture-Fierro: None declared, Sebastian Guerra-Zarama: None declared, Santiago Monsalve: None declared, Jose David Serna Giraldo: None declared, Juan david Serna: None declared, Julian Barbosa: None declared, Ricardo Pineda.Tamayo: None declared

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SAT0464 MULTIPLE REBOUND-ASSOCIATED VERTEBRAL FRACTURES AFTER DENOSUMAB DISCONTINUATION IN RHEUMATOLOGY CLINIC

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Background: Denosumab, a monoclonal antibody against RANKL, is an effective treatment for osteoporosis. Discontinuation of denosumab has been shown to lead in multiple vertebral fractures in some patients due to a severe acceleration of bone resorption (rebound-associated vertebral fractures-RAVFs). Limited data published during the last 2 years highlighted this issue.

Objectives: The aim of this case series is to describe features of the denosumab-associated RAVFs and the characteristics of these patients.

Methods: Patients from our outpatient rheumatology clinic who were diagnosed with recent vertebral fractures after denosumab discontinuation from January 2019 to December 2019 were included. Diagnosis was based on x-ray and/or magnetic resonance imaging (MRI) of thoracic (T) or lumbar (L) spine. All cases were the result of reduced compliance of the patients to the treatment regimen. A baseline x-ray examination was available in all patients included and was compared in order to exclude prevalent osteoporotic fractures. Demographic and clinical parameters were recorded.

Results: Nine patients (8 females) with a mean±SD age of 71.3±11.9 years were included (Table 1). A total of 32 fractures occurred, affecting median 4 (range 1-6) vertebras (Figure 1). The mean±SD duration of denosumab treatment prior to discontinuation was 54.0±30.1 months, while the mean±SD time that RAVFs occurred after the last denosumab injection was 8.8±2.4 (range 7-12) months. The most commonly affected vertebra was L3 (Table1). Most patients (66.7%) did not have any prevalent osteoporotic fracture. Four patients (44.4%) were receiving drugs that affected bone metabolism (mainly corticosteroids and aromatase inhibitors). Only 33.3% of the patients had a history of previous treatment with bisphosphonates.

Table 1. Characteristics of RAVFs and patients affected. L: Lumbar, T: Thoracic, SD: Standard Deviation

Females (%)	88.9%
Age (years) (mean±SD)	71.3±11.9
Affected vertebras (median, range)	4, 1-6
Treatment duration (mean±SD) (months)	54.0±30.1
Time after last injection (mean±SD) (months)	8.8±2.4
Vertebral fracture site	1 3
T10 T11 T12	2
L1	5
L2	5
L3	8
L4	5
L5	5
Patients with prevalent osteoporotic fractures (%)	33.3
Patients receiving drugs affecting bone metabolism (%)	44.4
Patients with previous treatment with bisphosphonates (%)	33.3

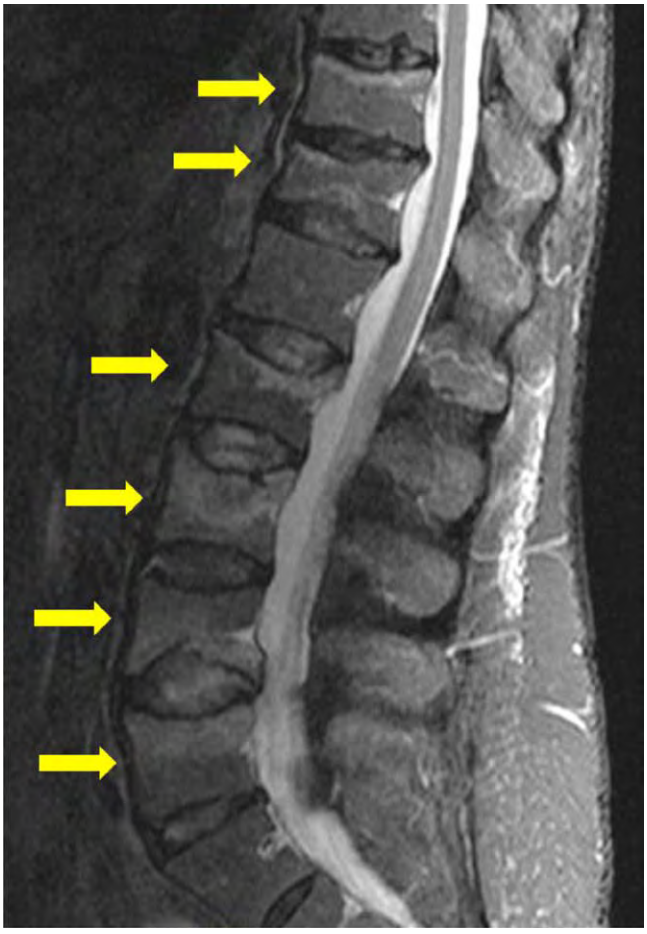


Figure 1. Multiple vertebral fractures (yellow arrows - T11, T12, L2-L5) in a patient 7.5 months after the last denosumab injection. T: thoracic, L: Lumbar

Conclusion: Denosumab-associated RAVFs usually occur within 7-12 months after the last denosumab injection and affect multiple vertebras. Most cases are associated with long-term (>2 years) denosumab administration without previous treatment with bisphosphonates. Rheumatologists should be alert of this complication since the reported compliance in patients under denosumab treatment is only 46% (1) and the expected incidence of RAVFs after denosumab discontinuation has been reported to be 10% (2).

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SAT0465 FRACTURE RISK ASSESSMENT BY FRAX IN A SYSTEMIC LUPUS ERYTHEMATOSUS PORTUGUESE COHORT

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Background: Osteoporosis is commonly seen in patients with Systemic Lupus Erythematosus (SLE), even in pre-menopausal patients. The etiology is multifactorial and chronic glucocorticoid therapy seems to play a central role.

Objectives: To investigate the ten-year risk of fracture assessed by Fracture Risk Assessment Tool (FRAX), with and without dual-energy X-ray absorptiometry (DXA) and to determine possible demographic or clinical factors associated with an increased risk of fracture in a SLE population.

Methods: Retrospective study including all the over 40 years-old patients with the diagnosis of SLE (2012 SLICC classification criteria) followed at our Rheumatology Department registered in our national database. Demographic, clinical and laboratorial data were collected at the last follow-up visit. Data from the last DXA (until 3 years prior to the last visit) were collected. Indication for pharmacological treatment by FRAX was assessed according to the national recommendations: estimated fracture risk, without DXA, ≥11% for major osteoporotic fracture or ≥3% for hip fracture and/or estimated fracture risk, with DXA, ≥9% for major osteoporotic fracture or ≥2.5% for hip fracture.

Results: We included 104 patients, 101 (97.1%) females, aged 54.5±9.9 years, with a median disease duration of 19.3 years [4.3-51.6]. Twelve patients (11.5%) were current smokers, 31 (29.8%) had elevated anti-dsDNA antibodies (≥100 IU/mL) and 27 (26.0%) had complement consumption (C3c<83mg/dL or C4<12mg/dL). 73 patients (70.2%) were taking glucocorticoids with a mean daily prednisolone equivalent dosage of 4.4±5.2 mg/day. Regarding SLE treatment, 69 patients (66.3%) were under hydroxychloroquine, 22 (21.2%) under azathioprine, 16 (15.4%) under mycophenolate mofetil, 5 (4.8%) under belimumab, 4 (3.8%) under methotrexate, 1 (1.0%) under leflunomide and 1 (1.0%) under rituximab.

Ten patients (9.6%) had previous fragility fractures, 54 patients (51.9%) had DXA in the last 3 years and 81 (77.9%) were taking calcium and/or vitamin D supplements.

Sixteen (15.4%) had indication for treatment by FRAX without DXA and 8 of these (50%) were under treatment. Moreover, thirteen (12.5%) had indication for treatment by FRAX with DXA and 8 of these (61.5%) were under treatment.

Five patients (4.8%) were reclassified in FRAX with DXA: 3 patients (2.9%) had no indication for treatment by FRAX without DXA but conquered it by FRAX with DXA and 2 patients (1.9%) had indication for treatment by FRAX without DXA but lost it by FRAX with DXA. We found a good level of agreement in the indication for treatment between FRAX with and without DXA (kappa=0.741; p<0.001).

There was no significant difference in the risk of fracture estimated by FRAX with or without DXA, both for major osteoporotic fracture and for hip fracture. Correlations between fracture risk and some clinical variables can be seen in table 1.

Table 1. Correlations between the risk of fracture estimated by FRAX and disease related features.

			Age at SLE diagnosis	Disease Duration	ESR	SLEDAI
Estimated fracture risk by FRAX:	without DXA	major osteoporotic fracture	r=0.483 *p*<0.001	n.s.	r=0.249 *p*=0.012	r=-0.586 *p*=0.028
		hip fracture	r=0.481 *p*<0.001	n.s.	r=-0.552 *p*=0.041	n.s.
	with DXA	major osteoporotic fracture	r=0.386 *p*=0.005	r=0.299 *p*=0.033	n.s.	n.s.
		hip fracture	r=0.338 *p*=0.015	n.s.	n.s.	n.s.

Conclusion: A higher number of patients had indication for pharmacological treatment by FRAX with DXA in comparison with FRAX without DXA. However, we found no statistically significant difference in the estimated fracture risk with and without DXA. This, together with the good level of agreement between FRAX with and without DXA, suggests that the fracture risk estimation, even without DXA, may be an appropriate approach. The low number of patients with indication for pharmacological treatment by FRAX, with and without DXA, may be explained by their low mean age and the high number of them under vitamin D/calcium supplementation.

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SAT0466

FRAX RISK OF FRACTURE AND ITS CORRELATION WITH BONE MINERAL DENSITY IN MEXICAN PATIENTS WITH RHEUMATIC DISEASES

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Background: Osteoporosis (OP) is characterized by compromised bone strength and deterioration of quality, often leading to fragility fractures (1). Dual-energy x-ray absorptiometry (DXA) is the recommended test for OP screening among patients with rheumatoid arthritis (RA) and other RD (2). However, there are limitations to perform DXA on every patient, and the clinicians use screening tools to identify those patients with higher risk. The opportune identification of the patients at increased risk and early treatment can prevent the loss of bone mineral density (BMD) and reduce the risk of fractures(3).

Objectives: To evaluate the FRAX risk and its correlation with the spine and femoral neck T-score in patients with RD.

Methods: An observational retrospective study was done in the rheumatology clinic of the university hospital "Dr. Jose Eleuterio Gonzalez" in Monterrey, Mexico, between March and November 2019. Patients who had reported DXA from the spine and hip in the medical record were included. The risk factors included in FRAX tool was collected; FRAX tool was used online at https://www.sheffield.ac.uk/FRAX/ (algorithm for Mexicans) and classified as low (<10% for OP or <1% for hip), intermediate (10%-19% for OP or 1%-<3% for hip) and high risk (≥20% for OP or ≥3% for hip); results of DXA of the spine and hip were collected. Results are shown in means or frequency. A chi-square test or one-way analysis of variance was used to compare groups. Pearson's correlation test (r) was done between spine T-score and FRAX risk for OP and between femoral neck T-score and FRAX risk for hip. P<0.05 was considered statistically significant.

Results: 141 patients were included, Patients with OP was older (mean 62.6 years), weight and height were higher in those with normal BMD. There was no difference between the use of glucocorticoids or other risk factors (Table 1). According to FRAX risk for OP, 122 (86.5%) had low risk, 14 (9.9%) had intermediate risk and only 5 (3.5%) had high risk. According to FRAX risk for hip, 81 (57.4%) had low risk, 38 (27.0%) had intermediate risk and only 22 (15.6%) had high risk (Table 2). There was a low negative correlation between spine T-score and FRAX risk for OP (r= -0.396, P=<0.001) (Figure 1), there was a moderate negative correlation between femoral neck T-score and FRAX risk for hip (r= -0.614, P=<0.001) (Figure 2).

Table 1. FRAX score risk factors

	Normal BMD N= 27	Low BMD N= 66	Osteoporosis N= 48	P
Age, years, mean (SD)	46.8 (10.6)	56.5 (11.7)	62.6 (9.1)	<0.001*
Female, n (%)	24 (88.8%)	61 (92.4)	43 (89.5)	0.814
Weight, kg, mean (SD)	76.6 (14.6)	66.4 (12.1)	64.8 (10.6)	0.001*
Height, cm, mean (SD)	156.7 (7.5)	152.3 (6.8)	153.3 (7.1)	0.034*
Previous Fracture, n (%)	-	-	-	-
Parent Fractured Hip, n (%)	-	-	-	-
Current Smoking, n (%)	-	2 (3.0%)	4 (8.3%)	0.060
Glucocorticoids, n (%),	15 (55.5%)	30 (45.4%)	19 (39.6%)	0.411
Rheumatoid arthritis, n (%)	18 (66.6%)	40 (60.6%)	21 (43.7%)	0.040*
Secondary osteoporosis, n (%)	-	-	-	-
Alcohol use, n (%)	1 (3.7%)	2 (3.0%)	1 (2.0%)	0.631
Osteoporosis treatment, n (%)	-	16 (24.2%)	42 (87.5%)	<0.001*

Table 2. BMD and FRAX risk

	Normal BMD N= 27	Low BMD N= 66	Osteoporosis N= 48	P
FRAX risk for OP, n (%)				
Low risk, (n=122)	27 (100%)	63 (95.4%)	32 (66.6%)	<0.001*
Intermediate risk, (n=14)	-	3 (4.5%)	11 (22.9%)	0.001*
High risk, (n=5)	-	-	5 (10.4%)	0.007*
FRAX risk for hip, n(%)				
Low risk, (n=81)	26 (96.3%)	45 (68.1%)	10 (20.8%)	<0.001*
Intermediate risk, (n=38)	1 (3.7%)	18 (25.7%)	20 (41.6%)	0.001*
High risk, (n=22)	-	4 (6.0%)	18 (37.5%)	<0.001*

Conclusion: Most of the patients were classified as low risk for OP and hip, including a high amount of those with OP showing a low and moderate correlation with DXA respectively.

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Figure 1. Lumbar Spine T-score and FRAX risk for OP

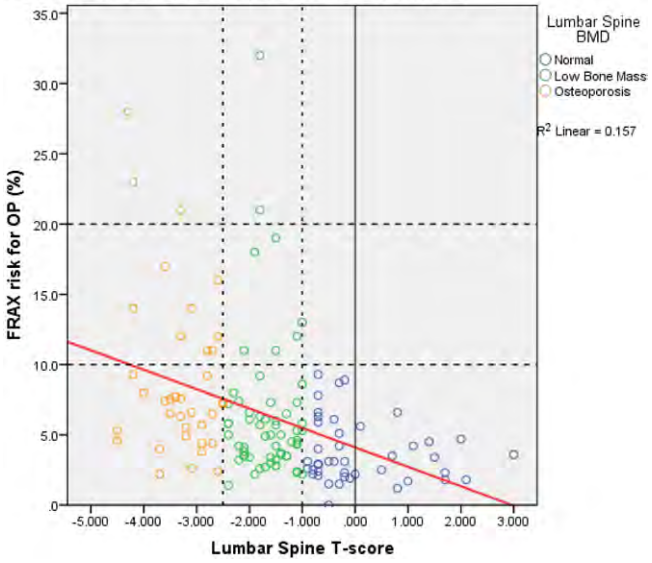
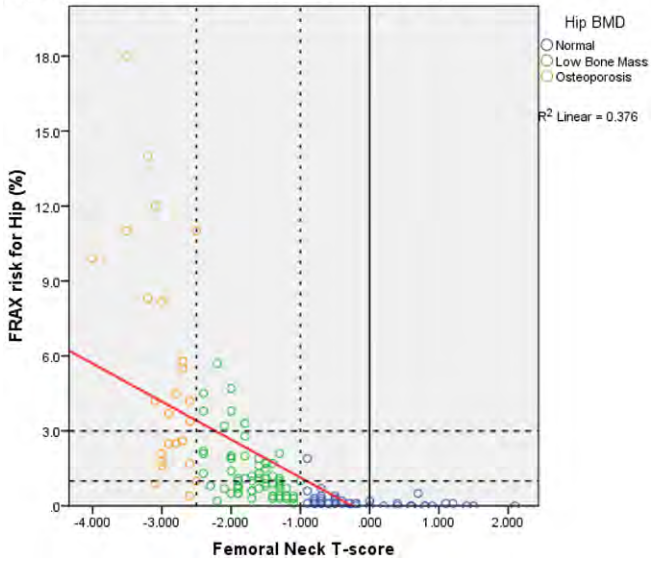


Figure 2. Femoral neck BMD and FRAX risk for Hip



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SAT0467

LOW SERUM OSTEOCALCIN LEVELS ARE ASSOCIATED WITH THE PRESENCE OF DIABETES MELLITUS IN GLUCOCORTICOID TREATED PATIENTS.

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Background: Increasing evidence indicates that osteocalcin (OC) is involved in the regulation of glucose homeostasis. Glucocorticoid (GC) treatment is associated with impaired osteoblast function and decreased OC levels and also with the development of CG-induced diabetes mellitus (GIDM). However, whether decreased OC levels in GC-treated subjects contribute to GIDM is not well known.
Objectives: To analyse whether OC levels in GC-treated patients are associated with the presence of GIDM.
Methods: 127 patients (aged 62±18years, 63% women) on GC treatment for autoimmune diseases (≥5mg/day, >3 months) were included. Clinical and anthropometric data were analysed, including the GC dose and treatment duration, presence of GIDM, fragility fractures, densitometric osteoporosis and bone formation (OC, bone alkaline phosphatase [BAP], PINP) and resorption markers (urinary NTX, serum CTX). The cut-offs of each bone marker for the presence of GIDM were estimated and optimized with the Youden index and included in the logistic regression analysis (adjusted for BMI, age and GC doses).
Results: 17.3% of patients presented GIDM. Diabetic subjects were older (70.5±12.2 vs. 59.6±18.4, p=0.001) and had a higher BMI than non-diabetics (30±5.2 vs. 26±4.2, p=0.002). No differences were observed in GC dose or duration or in the presence of vertebral fractures. Diabetics showed lower levels of OC (7.57±1.01 vs. 11.56±1; p<0.001), PINP (21.48±1.01 vs. 28.39±1; p=0.0048), NTx (24.91±1.01 vs. 31.7±1; p=0.036) and CTX (0.2±1.01 vs. 0.3±1; p=0.0016) with similar BAP values. The best discriminating cut-offs for GIDM presence were: <9.25ng/mL for OC, <24ng/mL for PINP, <27.5nMol/mM for NTX and <0.25ng/mL for CTX. On multivariate analysis OC (<9.25) was the only marker related to the presence of GIDM (OR 6.1; CI95% 1.87-19.89; p=0.001).
Conclusion: Decreased OC levels in GC-treated patients are associated with an increased risk of GIDM, a finding that was not observed with other bone turnover markers, further confirming the involvement of OC in the glucose homeostasis regulation in this entity.
Disclosure of Interests: None declared
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SAT0468

EFFECTS OF ANDROGEN DEPRIVATION THERAPY ON BONE QUALITY (TBS) IN PATIENTS WITH PROSTATE CANCER

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Background: Androgen deprivation therapy (ADT), by inducing severe hypogonadism, leads to a loss of bone mineral density (BMD) and an increased risk of fragility fractures after 6 months of treatment in men with prostate cancer[1]. However, its effect on bone quality has not been described.
Objectives: To evaluate the changes on bone microarchitecture (bone quality) assessed by TBS (trabecular Bone Score) in male patients with prostate cancer after one year of treatment with ADT.
Methods: All patients diagnosed with prostate cancer candidates for long-term ADT admitted to Urology department of Hospital Universitari Parc Tauli (reference population of 450,000 inhabitants) between April 2017 and December 2019 were included. Patients who received chemotherapy, previous hormonal therapy or specific treatment for osteoporosis in the last year or those who had a very impaired functional capacity (Barthel index <30) were excluded.
Demographic, clinical and analytical data (testosterone, calcium, phosphorous, alkaline phosphatase, 25-hidroxyvitamin D, PTH) were collected in all patients. A bone densitometry (GE-Lunar Prodigy) including the measurement of lumbar spine TBS (L1-L4) using Medimaps Software was performed at baseline and at 12 months of treatment with ADT.
Results: 78 patients were included. Mean age 77,9±8,3 years. The median Gleason score was 7,88±1,05. 3 patients had previous fragility fracture (one sacral fracture, one fibula and one multiple vertebral fracture). Baseline analytical values in patients were the following: testosterone11,6±74,9 nmol/L.; 25-hidroxyvitamin D 20,8±10,4 ng/ml; PTH 51,8±23,0 pg/ml; CTX 0,58±0,66. The daily calcium intake was 573±207 mg/day.
According to BMD, 17 patients (21,8%) had osteoporosis before starting ADT, with the following average T-score values: lumbar spine +0,15±1,85, femoral neck -1,75±1,00, and total hip -1,19±1,16. Mean baseline TBS value of the entire cohort was 1,279±0,122. 30,5% of the patients showed very degraded microarchitecture (TBS<1,230), 28,8% had partially degraded microarchitecture (TBS 1,230-1,310) and in 40,7% showed normal microarchitecture (TBS >1,310).
After one year of ADT treatment, TBS mildly worsened in this cohort, with a median value of 1,256±0,131 (p = NS). However up to 43% of patients reached highly degraded microarchitecture, 27% partially degraded and only 29,5% had a normal TBS (p = NS).
Conclusion: Most patients with prostate cancer have an altered bone quality before starting ADT. After 12 months of treatment, the percentage of patients with highly degraded bone microarchitecture increases, although not significantly. More studies are needed to confirm this trend and to evaluate if these patients present more long-term fractures.
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Disclosure of Interests: Silvia Garcia-Cirera: None declared, Enrique Casado Speakers bureau: UCB, Lilly, Amgen, Theramex, Gebro, Gedeon-Richter, Stada,

Jesús Muñoz: None declared, Luis Del Río: None declared, Marta Arévalo: None declared, Menna Rusiñol: None declared, Noemí Navarro: None declared, Víctor Parejo: None declared, Jordi Gratacos-Masmitja Grant/research support from: a grant from Pfizzer to study implementation of multidisciplinary units to manage PSA in SPAIN, Consultant of: Pfizzer, MSD, ABBVIE, Janssen, Amgen, BMS, Novartis, Lilly, Speakers bureau: Pfizzer, MSD, ABBVIE, Janssen, Amgen, BMS, Novartis, Lilly

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SAT0469 PROSPECTIVE STUDY ASSESSING BONE MINERAL DENSITY AND RISK FACTORS FOR OSTEOPOROSIS IN PATIENTS WITH ANDROGEN DEPRIVATION THERAPY. PRELIMINARY CROSS-SECTIONAL RESULTS

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Background: Few studies have analysed the incidence and risk factors for osteoporosis (OP) development in patients with prostate cancer (PC) and androgen deprivation therapy (ADT).

Objectives: To assess risk factors for OP, bone turnover markers (BTM) and bone mineral density (BMD) in a cohort of patients with ADT, as well as the duration of ADT and previous treatments received for PC.

Methods: Ongoing prospective study including patients with ADT for PC. Risk factors for OP, BTM (total ALP, bone ALP, CTx), spinal X-Ray and BMD (Lunar, DPX) were assessed yearly since inclusion in the study (April 2018). Patients with known OP or previous antiosteoporotic treatment were excluded. The study was approved by the ethics committee, and all patients gave their signed consent. Herein we present the preliminary cross-sectional study at inclusion.

Results: Of the 83 patients attended at the Rheumatology Department during the study period, 75 were included with a mean age 75±5years and median ADT duration of 1 year. 18 were receiving concomitant radiotherapy and 7 docetaxel. When assessing risk factors for OP: 28% had previous fragility fractures and 24% had current alcohol intake. After X-Ray assessment, 14% had morphometric vertebral fractures. Mean 25OHD at inclusion was 19±9ng/ml (73% had 25OHD <30ng/ml) and mean testosterone was 82±162ng/dL (75% had levels <50ng/dl). All patients had increased values of CTx and 9% had increased bone ALP levels. BMD showed up to 28% with densitometric OP and osteopenia in 56%. Patients with OP were older (83±7 vs 74±8 years, p=0.021), had lower testosterone levels (16 vs 89 ng/dl, p=0.004), as expected lower BMD (at spine, proximal femur and even distal radius) and had more previous fragility fracture (75 vs 19%, p=0.022). But it should be noted that 16% had high bone mass (HBM) mostly affecting spine BMD (in 6 patients combined with femoral osteopenia). All patients with HBM had high bone metastatic disease, and no differences were observed between patients with/without HBM when comparing BTM or calcium-phosphate metabolism.

Conclusion: Low bone mass (including osteoporosis and osteopenia) is frequent in patients with ADT as well as previous fragility fractures. Up to 16% had high bone mass, being mostly in patients with high volume metastatic disease. Thus, all patients with ADT should undergo a bone health assessment and start antiosteoporotic treatment if required.

Disclosure of Interests: None declared

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SAT0470 FRAX AND DXA-BASED APPROACHES IN DIAGNOSTICS OF OSTEOPOROSIS RISK IN POSTMENOPAUSAL WOMEN WITH RHEUMATOID ARTHRITIS

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Background: Nowadays, the bone mineral density (BMD) measured by DXA and FRAX® are the most important methods for fracture risk assessment. Rheumatoid arthritis is a crucial disease for bone loss and osteoporosis development [1] which is included into FRAX algorithm. Ukrainian version of FRAX [2] is a new one and its value should also be assessed in patients with RA.

Objectives: Our study was aimed to assess the parameters of BMD and FRAX in postmenopausal women with RA.

Methods: We have examined 635 postmenopausal females aged 50-89 years old which were divided into 2 groups: 1st (control, n=313) – without any factors which have influence on bone metabolism, 2d (n=322) – patients with RA. The 10-year probabilities of hip fracture and major osteoporotic fractures were calculated without BMD parameter using the Ukrainian FRAX model [2]. The DXA was used to measure the lumbar spine, femoral neck and total body BMDs; the T-score was calculated (DISCOVERY Wi, Hologic, Inc., USA).

Results: FRAX indexes for major osteoporotic and hip fractures were significantly higher in patients with RA (Me [25-75Q]): 9.7 [6.8-15.0] and 3.1 [1.5-6.2] % compared to 6.0 [3.8-8.5] and 1.2 [0.6-2.4] % in females from the control group (p<0.001). 45.3 % of women with RA required antiosteoporotic treatment according to Ukrainian FRAX threshold ratio without measure of BMD compared to 12.1% of subjects from control group. Only 3.4% of patients with RA had FRAX indexes which were less than low threshold (requirement of additional DEXA measurement) compared to 31.3 % of females from control group.

BMD of femoral neck and distal radius were reliably lower in subjects with RA and consisted 0.65±0.13 and 0.69±0.12 g/cm in 1st and 2d groups, accordingly (p<0.001) and 0.56±0.10 and 0.58±0.09 g/cm (p=0.02) without any significant differences at lumbar spine and total body BMDs. 16.6 % of subjects from the control group and 31.6 % of females with RA had osteoporosis according to DXA parameters (T-score ≤-2.5 SD).

Conclusion: FRAX should be used more widely in clinical practice for detection of risk of osteoporotic fractures in subjects with RA.

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SAT0471 EFFECTS OF ONE YEAR TOFACITINIB THERAPY ON BONE DENSITY AND BIOMARKERS OF BONE TURNOVER IN RHEUMATOID ARTHRITIS

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Background: Oral JAK inhibitor, tofacitinib appeared as a new therapeutic option, beside biological therapies, which has already proven its safety and effectivity in RA, but we lack of knowledge how it affects density of bone structures and bone turnover markers.

Objectives: The aim of this study was to assess the effects of one-year tofacitinib therapy on bone metabolism in patients with RA.

Methods: Altogether 30 RA patients with active disease were recruited and treated with tofacitinib in this 12-months follow-up study. Mean age of patients were 52.8±10.0 years, duration of rheumatoid arthritis were 7.7±5.0 years. Half of the patients haven't received biological treatment prior tofacitinib therapy, other half of the patients switched to tofacitinib therapy after completing washout. 15 patients received 2x5mg and 15 patients received 2x10mg tofacitinib daily for 12 months. On both arms 2-2 patients have discontinued treatment and excluded from the study. Assessments were performed at baseline, month 6 and 12. Levels of CRP and IgM rheumatoid factor (RF) antibodies were measured by quantitaive nephelometry and levels of anti-CCP, sclerostin, osteocalcin (OC), P1NP were assesed by ELISA. Bone density was assesed by DXA (dual-energy X-ray absorptiometry, Lunar) and pQCT imaging techniques. Levels of DKK-1, OPG, RANKL were measured by multiplex microbead immunoassay (BioLegend LEGENDplex). In addition, disease activity (DAS28), age and disease duration were also measured. Correlations were determined by Spearman's analysis. Univariate and multiple regression analysis using the stepwise method was applied to investigate independent associations between DXA measurements (dependent variables) and laboratory parameters (independent variables).

Results: Tofacitinib significantly reduced DAS28 (p<0.001) and HAQ values (p=0.001), also level of CRP (p<0.001) and We (p=0.014). With respect to bone biomarkers we have experienced significant increase in levels of OC (p=0.013), OPG (p=0.006), sclerostin (p=0.026) and vitamin-D (p=0.017) at month 6, also in levels of OPG and vitamin-D (p=0.004, p=0.003) at month 12. We have found decrease in levels of CTX at month 6 (p=0.009) and 12 (p=0.003). When we examined the groups separately, we've found significant increase in levels of P1NP (p=0.027, p=0.005), OPG (p=0.005, p=0.002) and vitamin-D (p=0.001, p=0.004) at month 6 and 12, also in OC at month 6 (p=0.027) in Group A (2x5mg). In Group B (2x10mg) we've experienced a significant decrease in levels of phosphate and CTX at month 6 and 12 (p=0.012, p=0.021, and p=0.005, p=0.007).

Conclusion: One year tofacitinib treatment effectively stabilized bone density in patients with rheumatoid arthritis, and led to the increase of bone turnover markers, which is beneficial for ossification in long term.

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SAT0472 GOAL-DIRECTED TREATMENT OF OSTEOPOROSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS USING DENOSUMAB FOR FIVE YEARS

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Background: Osteoporosis (OP) is frequent complication identified in patients with rheumatoid arthritis (RA). Effective treatment must be provided to treat OP in RA (RAOP). Denosumab (DMB) is one of the promising drugs that are currently being used for the treatment of RAOP. We reported the results of 12-month DMB treatment for RAOP as part of Japanese multicenter registry study (TBCR-BONE) in EULAR2016 [1]. Recently, a treatment goal of OP was reported by the American Society for Bone and Mineral Research and the National Osteoporosis Foundation (ASBMR-NOF) working group [2]. This report advocated that the goal of treatment is a T-score of >-2.5 at the femoral neck, total hip (TH) or lumbar spine (LS) on DXA if the primary reason for starting treatment was a T-score of ≤-2.5 at the abovementioned skeletal sites. The working group noted that it was reasonable to expect that initial treatment should offer at least a 50% chance of achieving the treatment goal within 3 to 5 years of initiating therapy. We have reported the achievement rates of treatment goal in RAOP with 3-year DMB treatment on RAOP in EULAR2019 [3].

Objectives: The aim of this retrospective study was to evaluate whether 5-year DMB treatment can achieve treatment goal of OP using data from TBCR-BONE.

Methods: The study included 46 female patients who had completed 5-year DMB treatment. The LS-BMD analysis included 22 patients with a baseline (BL) LS-BMD T-score of ≤ -2.5. The TH-BMD analysis included 29 patients with a BL TH-BMD T-score of ≤ -2.5. Similar to clinical setting in Japan, 60mg of DMB was administered once every 6 months with a vitamin D3 supplement. BL characteristics, change in T-score over time, and achievement of the treatment goal (T-score>-2.5) were evaluated.

Results: BL characteristics of the 46 female patients included: mean age of 69.1 years and RA duration of 16 years. Prednisolone was administered to 37% of the patients. In the LS-BMD analysis, T-scores improved significantly; the mean value at BL was −3.4, which increased to −3.0 at 1 year, −2.6 at 3 years, and ultimately to −2.5 at 5 years. The fraction of patients who achieved the treatment goal was as follows: 36.4% at 1 year, 40.9% at 2 years, 45.5% at 3 years, 50.0% at 4 years, and 54.5% at 5 years (**Fig. 1A**). The patients who achieved this treatment goal were those who had a significantly lower risk of fracture at BL as determined by FRAX (17.9% vs. 32.2%, p = 0.044), who had significantly higher BL serum TRACP-5b level (572.8 vs. 401.0: p = 0.03), and who had significantly better BL LS-BMD T-scores (−3.0 vs. −3.9, p < 0.01) than the nonachievers. In the TH-BMD analysis, T-scores improved significantly; the mean value at BL was −3.0, and it increased to −3.0 at 1 year, −2.7 at 3 years, and reached −2.7 at 5 years. The fraction of patients who achieved the treatment goal was as follows: 20.7% at 1 year, 31.0% at 2 years, 34.5% at 3 years, 31.0% at 4 years, and 37.9% at 5 years (**Fig. 1B**). The patients who achieved this treatment goal were those who had significantly better BL TH-BMD T-scores (−2.7 vs. −3.2: p < 0.01) than the nonachievers. Cut-off values at BL for achievement of the treatment goal determined using ROC analysis were −3.1 for the LS-BMD (sensitivity 83.3%, specificity 90.0%) and −2.85 for the TH-BMD (sensitivity 100.0%, specificity 81.0%).

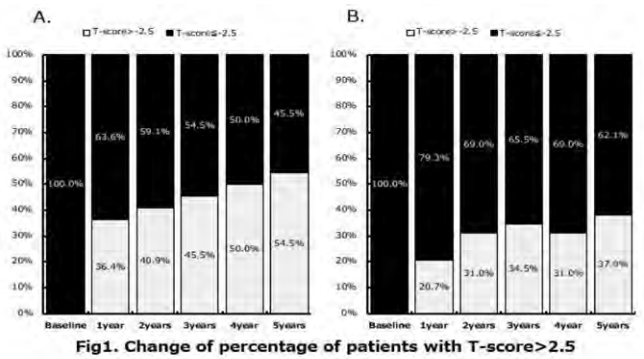


Fig1. Change of percentage of patients with T-score>2.5

A: results of lumbar spine bone mineral density (n=22)
B: results of total hip bone mineral density (n=29)

Conclusion: The results of this study suggested that achievement of the treatment goal was comparatively easy for those with LS-BMD loss; however, it was comparatively difficult for those with TH-BMD loss. Early initiation or longer duration of DMB therapy may be necessary to improve achievement rates. Likewise, other agents, such as romosozumab, may be considered for those with significant TH-BMD loss.

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Disclosure of Interests: Yuji Hirano Speakers bureau: Tanabe-Mitsubishi, Pfizer, Eisai, Abbie, Chugai, Bristol-Meyers, Jansen, Astellas, UCB, Eli-Lilly, Asahikasei, Daiichi-Sankyo, Amgen, Yasuhide Kanayama: None declared, Hironobu Kosugiyama: None declared, Naoki Ishiguro Grant/research support from: AbbVie, Asahi Kasei, Astellas, Chugai, Daiichi-Sankyo, Eisai, Kaken, Mitsubishi Tanabe, Otsuka, Pfizer, Takeda, and Zimmer Biomet, Consultant of: Ono, Speakers bureau: Astellas, Bristol-Myers Squibb, Daiichi-Sankyo, Eli Lilly, Pfizer, and Taisho Toyama, Toshihisa Kojima Grant/research support from: Chugai, Eli Lilly, Astellas, Abbvie, and Novartis, Consultant of: AbbVie, Speakers bureau: AbbVie, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eli Lilly, Janssen, Mitsubishi Tanabe, Pfizer, and Takeda

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SAT0473 COMPARSION OF THE FRACTURE RISK IN WOMEN WITH AND WITHOUT SCOLIOSIS THROUGH DUAL-ENERGY X-RAY ABSORPTIOMETRY

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Background: Osteoporosis is known to be a risk factor for fragility fractures [4, 5]. On one hand, vertebral body fragility fractures often lead to additional spine deformity [2]. On the other hand, it was found that with the progression of the spinal curvature in osteoporotic patients, the fragility fractures develop more frequently. The increased incidence of these fractures could be explained with a predominance of the mechanical forces on the one side of the already weakened osteoporotic vertebrae [3].

Objectives: The aim of this study is to compare the fracture risk (FRAX) for major osteoporotic fractures (MOF) and for hip fractures (HF) in women with and without scoliosis through dual-energy X-ray absorptiomentry (DXA)

Methods: In the current study, 59 women underwent DXA scans. Scoliosis was defined as Cobb's angle ≥ 5◦ according to the Chaklin's classification [6, 7]. Cobb's angle was measured from DXA images with DICOM software. We evaluated the following risk factors: previous fractures, parental hip fractures, secondary osteoporosis, rheumatoid arthritis, use of corticosteroids, current smoking and alcohol consumption more than 3 units daily. We estimated FRAX MOF and FRAX HF on the basis of these risk factors and on the basis of the femoral neck bone mineral density (BMD). The calculations were done through FRAX tool published on the website of the University of Sheffield [1].

Results: The mean age of the women was 63 years (yrs.) ± 10 yrs. (range 43 yrs. – 89 yrs.). Subjects with scoliosis were significantly older (67 yrs.) than those without scoliosis (59 yrs.), (p = 0.004). Mean weight and height didn't differ between the groups with- and without scoliosis. Mean lumbar spine BMD and T-score differed significantly between the groups, (p = 0.02). Women with scoliosis had lower mean BMD (0.786 g/cm2) and lower mean T-score (-2.1 standard deviations (SDs)) compared to those without scoliosis (mean BMD: 0.912 g/cm2 and mean T-score: 0.9 SDs). The mean FRAX MOF (19.3%) and FRAX HF (5.9%) of the subjects with scoliosis were significantly higher than those of the women without scoliosis (FRAX MOF: 14.9% and FRAX HF: 3.1%), (p = 0.004 for FRAX MOF and p = 0.010 for FRAX HF).

Conclusion: Women with scoliosis showed significantly higher fracture risk for major osteoporotic fractures and for hip fractures compared to those without scoliosis.

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SAT0474 WHAT DETERMINES THE EFFECT OF THERAPY WITH DENOSUMAB ON BONE IN WOMEN WITH RHEUMATOID ARTHRITIS AND OSTEOPOROSIS

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Background: RANK-ligand is essential for osteoclast development, activation, and survival and it is a key mediator of increased osteoclast activity in rheumatoid arthritis (RA). Denosumab is a monoclonal antibody that binds RANK-ligand.
Objectives: The aim of this study was to evaluate the effects of denosumab on bone mineral density (BMD) and to define a contribution of factors: anamnesis, clinical/laboratory markers, glucocorticoids (GC) intake, etc. on the response to therapy with denosumab in women with RA and osteoporosis (OP).
Methods: 66 postmenopausal women (mean age 59,6±7,4) with RA (mean duration 17,7±10,4 years) and OP received s/c denosumab 60 mg every 6 months pro 12 months. RF-positive were 72%, ACCP – 74% of patients. 34 (49%) patients continued GC. At baseline and after 12 months it was carried out the dual energy x-ray absorptiometry at 3 sites: lumbar spine (L1-L4), hip neck (HN) and distal forearm (DF) and x-ray of hands and feet (Sharp/van der Heijde (SVH) score). The Statistica 6.0 was used.
Results: After therapy it was noted the increase ($p < 0,05$) of BMD in L1-L4 and HN, a tendency to increase ($p = 0,0529$) in DF. Mean BMD (L1-L4) before\after the treatment was 0,821 ± 0,104 g/cm^2 vs 0,864 ± 0,110 g/cm^2, at HN was 0,625 ± 0,089 g/cm^2 vs 0,639 ± 0,088 g/cm^2, at DF was 0,498 ± 0,090 g/cm^2 vs 0,503 ± 0,089 g/cm^2. The mean change of BMD (%) after 12 months at L1-L4 was +4,6%, at HN +2,8%, at DF +0,7%. Positive response (increase or stabilization of BMD) was noted in 89% patients at L1-L4, 67% - at HN and 60% - at DF. Analysis of influence of various factors (statistically significant) on the response to therapy is presented in the Table.
Conclusion: After 12 months of therapy with denosumab in postmenopausal women with RA and OP it was shown the significant increase of BMD in L1-L4 and HN, a tendency to increase in DF. The mean change of BMD (%) after 12 months was +4,6% at L1-L4, at HN +2,8%, at DF +0,7%. Positive response on denosumab (BMD) was noted in 89% patients at L1-L4, 67% - at HN and 60% - at DF. Analysis of influence of factors on the response to therapy showed that positive response on therapy in NH and DF was associated with RF-positivity. The distinct contribution to the negative response in L1-L4 and HN was associated with GC intake (previous intake more than 3 months in the anamnesis) and purpose of the GC after menopause onset. Also, negative response in DF back correlated with increase in erosion score and total SVH score.

Table. Influence of various factors on the response to therapy with denosumab after 12 months of treatment (n=66)

DXA site	Positive response on therapy is associated with	Negative response on therapy is associated with
L1-L4	–	- GC intake (> 3 months in anamnesis) (p = 0,034); - the beginning of GC intake after menopause (p = 0,023)
Hip neck	- higher concentration of the RF (initially and in dynamics) (p < 0,05); - the beginning of menopause later than RA onset (p = 0,024)	- GC intake (> 3 months in anamnesis) (p = 0,024)
Forearm (distal 1/3)	- RF-positivity (p = 0,02)	- back correlates with increase in erosion score and total SVH score: r = –0,360 (p < 0,05)

Disclosure of Interests: None declared
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SAT0475 DENOSUMAB VERSUS ORAL BISPHOSPHONATE FOR OSTEOPOROSIS IN LONG-TERM GLUCOCORTICOID USERS: A 12-MONTH RANDOMIZED CONTROLLED TRIAL

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Background:
Objectives: To compare the efficacy of denosumab (DEN) and oral alendronate (ALN) on spinal bone mineral density (BMD) in long-term glucocorticoid users.
Methods: Patients receiving long-term prednisolone treatment for medical illnesses were recruited. Inclusion criteria: (1) adult patients ≥18 years of age; (2) prednisolone ≥2.5mg/day for ≥1 year. Exclusion criteria: (1) previous use of DEN, teriparatide; (2) plan for pregnancy; (3) metabolic bone disease or unexplained hypocalcemia; (4) renal insufficiency. Participants were randomized to receive either: (1) DEN (60mg subcutaneously every 6 months); or (2) ALN (70mg/week). Calcium (Caltrate 3000mg/day) and vitamin D3 (cholecalciferol 1000IU/day) was given. BMD (femoral neck, total hip, lumbar spine) at month 0, 6 and 12 months were performed. Markers of bone turnover (serum P1NP and CTX) were also assayed at the same time points. The primary outcome was the difference of lumbar spine BMD change at month 12 between the two groups.
Results: 139 subjects were recruited (age 50.0±12.7 years): 69 assigned DEN and 70 assigned ALN. Underlying medical diseases: SLE (81%), RA (9.4%) and myositis (5%). Prednisolone dose at entry was 5.7±2.1mg/day. 56% of female patients were postmenopausal. 73(53%) of patients were osteoporotic (T score <-2.5) at the hip, femoral neck or lumbar spine. The mean body mass index (BMI) was 23.1±4.1kg/m2 (11% patients had BMI<18kg/m2). 82(59%) patients were naive to bisphosphonates. Pre-existing fragility or vertebral fracture was present in 19 (14%) patients and 18 patients (13%) had a family history of fractures. Baseline demographic data, osteoporotic risk factors, and BMD at various sites were not significantly different between the two groups at entry. At month 12, a significant gain in BMD at the lumbar spine (+3.5±2.5%; p<0.001) and the hip (+0.9±2.8%; p=0.01) was observed in DEN-treated patients, whereas the corresponding change was +2.5±2.9% (p<0.001) and +1.6±2.7% (p<0.001) in the ALN group. The spinal BMD at month 12 was significantly higher in the DEN than ALN group after adjustment for BMD values at baseline, age, sex and other osteoporosis risk factors that included smoking, drinking, cumulative steroid doses in one year, BMI, menopausal status and personal history of fracture (p=0.045). The differences in hip and femoral neck BMD were not significantly different between the two groups after adjustment for the same confounding factors. No new symptomatic fractures occurred in any participants at month 12. Adverse events were similar in frequency between the two treatment arms. Major infective episodes were uncommon (0.06/patient/year) and similar in the two groups. Minor upper gastrointestinal symptoms and non-specific dizziness were numerically more common in the ALN but arthralgia, minor infections (eg. upper respiratory tract) and new hypertension was more commonly reported in the DEN group. Three patients from ALN and 2 patients from DEN group were withdrawn from the study because of non-compliance but none withdrew because of adverse events.
Conclusion: In patients receiving long-term glucocorticoids, DEN is superior to ALN in raising the spinal BMD after 12 months' treatment. Both DEN and ALN were well tolerated.
Acknowledgments: NIL
Disclosure of Interests: None declared
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SAT0476 COMPLIANCE AND PERSISTENCE OF ANTI-OSTEOPOROTIC TREATMENTS IN PATIENTS WITH HIP FRACTURE

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Background: Osteoporotic fractures have a high health and economic impact. The best strategy to minimize the incidence of fractures is, certainly, the prevention of these that includes pharmacological treatments. However, long-term discontinuation treatment and sub-optimal compliance of the treatment are common.

Objectives: The aim of the study is to quantify the therapeutic compliance and permanence of the osteoporosis pharmacological treatments for patients who were discharged from hospitals in Catalonia with hip fracture during 2017.

Methods: From the Hospital Discharge Database of the Catalan Health Service, all patients who had been discharged during 2017 were selected with the main diagnosis of femur fracture, according to the coding CIM-9. The consumption of drugs to assess compliance and permanence was obtained from the Catalan Health Service pharmacy Database. The study period was 18 months from the date of hospital discharge. Patients who died, moved to other areas or switched their treatment were excluded from the study. Good compliance was considered when sufficient drug was obtained to cover 80% of the time since treatment was prescribed until the end of the study period. In the case of denosumab, good post-fracture compliance was considered when the treatment time was remained at least 12 months. Permanence was considered positive if a drug had been obtained during the last three months of the study period. To compare the differences in compliance and permanence between the patients treated with different drugs, the chi-square statistic was used, considering statistically significant differences if p<0.05.

Results: 8,354 patients were discharged with the main diagnosis of hip fracture. Of these, 1,712 patients (20.49%) were treated after been discharged. After applying the exclusion criteria, the final sample was made up of 1,327 patients. 81,54% were women, and the median age was 84,79 years.

The most commonly used treatments were bisphosphonates (69%), denosumab (23%) and teriparatide (7%)

The results of good compliance and permanence of treatment were those described in the table.

	n	Compliance	Permanence
Alendronate	863	63,27%	64,77%
Alendronate+colecalciferol	27	74,07%	81,48%
Ibandronate	3	66,67%	100%
Risedronate	23	39,13%	60,87%
Raloxifene	1	100%	100%
Bazedoxifene	1	0%	0%
Teriparatide	99	76,77% (*)	73,74%
Denosumab	310	76,77% (*)	74,52% (*)

(*) p<0.05 for total bisphosphonates and for alendronate

Conclusion: The results obtained suggest that a small number of patients were treated after a hip fracture (20.49%) in addition the instituted treatments are followed in a suboptimal way. It is necessary to investigate which factors may lead to the detection of potential non-compliant patients. It seems appropriate to consider drugs that facilitate compliance and permanence of treatment.

Our results suggest that denosumab and teriparatide improve compliance compared with oral bisphosphonates.

The introduction of specific plans and cross-sectional health structures between levels of care should lead to improve detection, treatment and compliance in patients with osteoporosis.

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SAT0477 A TWO-YEAR LONGITUDINAL STUDY COMPLETION, LONGITUNEAL STUDY, THE DIFFERENCE IN BONE LOSS IN PATIENTS WITH EROSIVE AND NON-EROSIVE HAND OSTEOARTHRITIS

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Background: Hand osteoarthritis (OA) and its more severe subset erosive hand OA are common causes of pain and morbidity. Some metabolic factors were suggested to be implicated in erosive disease. Few studies investigated differences in systemic bone loss between erosive and non-erosive hand OA.

Objectives: To compare the change of bone mineral density (BMD) between patients with erosive and non-erosive hand OA in a two-year longitudinal study.

Methods: Consecutive patients with symptomatic HOA fulfilling the American College of Rheumatology (ACR) criteria were included in this study. Erosive hand OA was defined by at least one erosive interphalangeal joint. All patients underwent clinical assessments of joint swelling and radiographs of both hands. DEXA examination of lumbar spine, total femur and femur neck was performed at the baseline and after two years.

Results: Altogether, 141patients (15 male) with symptomatic nodal HOA were included in this study and followed between April 2012 and January 2019. Out of these patients, 80 had erosive disease after two years. The disease duration (p<0.01) was significantly higher in patients with erosive compared with non-erosive disease at baseline.

Osteoporosis (T-score <-2.5 SD) was diagnosed in 12.5% (9/72) of patients with erosive hand OA and in 8.06% (5/57) of patients with non-erosive hand OA at baseline. BMD was significantly lowered in patients with erosive compared with non-erosive disease at baseline (lumbar spine: 1.05g/cm2 vs. 1.13 g/cm2, p<0.05, total femur: 0.90 g/cm2 vs. 0.97 g/cm2, p<0.01 and femur neck: 0.86 g/cm2 vs. 0.91, p<0.05). T-scores of lumbar spine (-0.96 vs. -0.41 SD, p<0.05), total femur (-0.69 vs. -0.33 SD, p<0.05) and femur neck (-1.14 vs. -0.88 SD, p<0.05) were also significantly lowered in patients with erosive compared with non-erosive disease.

Two years, the BMD remained also significantly lowered in patients with erosive compared with non-erosive disease (lumbar spine: 1.05g/cm2 vs. 1.14 g/cm2, p<0.05, total femur: 0.92 g/cm2 vs. 0.97 g/cm2, p<0.05 and femur neck: 0.86 g/cm2 vs. 0.91, p<0.05), which was in agreement with the finding for T-scores of lumbar spine (-1.05 vs. -0.39 SD, p<0.05), total femur (-0.74 vs. -0.34 SD, p<0.01) and femur neck (-1.07 vs. -0.72 SD, p<0.01).

Conclusion: These results suggest that patients with erosive hand OA are at higher risk for the development of general bone loss. Over two years patients with erosive disease had significant lower bone mineral density at all measured sites.

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SAT0478 OSTEOPOROSIS TREATMENT IN PORTUGUESE PATIENTS WITH PSORIATIC ARTHRITIS – WHAT IS THE VALUE OF THE FRACTURE RISK ASSESSMENT TOOL (FRAX)?

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Background: Few studies have evaluated the prevalence and treatment of osteoporosis (OP) in patients with psoriatic arthritis (PsA), and many of these patients are not screened using dual-energy X-ray absorptiometry (DXA). FRAX makes it possible to stratify the risk and define which patients may benefit from anti-osteoporotic treatment, but its usefulness in this population is not well established.

Objectives: The aim of this study was to determine whether the application of FRAX changes the indication for anti-osteoporotic treatment in PsA patients, according to the Portuguese guidelines.

Methods: In this cross-sectional study, we evaluated PsA patients from a tertiary hospital, registered in a national database (Reuma.pt), aged between 40 and 90 years and with a last consultation in 2019. FRAX was applied in all of them, regardless of being under anti-osteoporotic treatment and, when DXA was available, the femoral neck bone mineral density was used. Patients were stratified according to the risk of fracture, and those at high risk were considered candidates for anti-osteoporotic treatment, according to national guidelines [FRAX ≥11% for major osteoporotic fracture (MOF) or ≥ 3% for hip fracture (HF) without DXA; FRAX ≥9% for MOF or ≥ 2.5% for HF, with DXA].

Results: We included 100 patients, 52 females, with a mean age of 54,4 ±8,9 years and a median disease duration of 10 (6-17) years. Only 43 had already performed DXA and 6 had OP according to World Health Organization criteria. Seven patients were identified as having a high risk of fracture; applying femoral neck bone mineral density, 2 more patients with indication for treatment were recognized, totalizing 9 patients. There was a low agreement between the indication for treatment based only on DXA and FRAX (Cohen's k 0.066). There was a moderate and significant correlation between percentage of risk of MOF by FRAX with and without DXA (Spearman's ρ 0.804, p <0.001); for the risk of HF by FRAX with and without DEXA the correlation was weaker but still significant (Spearman's ρ 0.439, p = 0.004). There was no association between the indication for treatment by FRAX and the performance of DXA (chi-square test,

p = 0.597), nor the fact of performing DXA significantly affected the risk of MOF (Wilcoxon test, p = 0.185) or of HF (Wilcoxon test, p = 0.785) by FRAX.
Conclusion: In line with Portuguese guidelines, FRAX seems to be, in itself, a very useful tool in patients with PsA, and the performance of DXA does not significantly alter the indication for anti-osteoporotic treatment.
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SAT0479 IMPACT OF TRABECULAR BONE SCORE ON INTERVENTION THRESHOLD FOR BONE SPARING THERAPY IN PATIENTS REFERRED FOR BONE MINERAL DENSITY

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Background: Trabecular bone score (TBS) is an index of skeletal quality that has been validated as an independent risk factor for fracture and incorporated into fracture risk assessment (FRAX). TBS provides information on bone microarchitecture not captured from standard bone mineral density (BMD) measured by dual energy X-ray absorptiometry (DXA). Nonetheless, the clinical implications of using TBS in routine practice are not yet fully understood and warrant further evaluation.
Objectives: To determine whether lumbar TBS can have an impact on clinician's treatment threshold derived from DXA and clinical risk factors: does the addition of TBS to DXA measurements make the clinician more or less likely to recommend bone sparing therapy?
Methods: A cross-sectional study at a tertiary metabolic bone centre in the West Midlands region of England. Three expert metabolic bone physicians, two rheumatologists and one elderly care, assessed consecutive patients referred for a DXA scan ± clinic review and provided treatment recommendations with and without TBS. Patients ≥ 18 years old with BMI of 15-37 who were not on bone sparing therapy were considered eligible. TBS was defined according to T-score as normal (T-score ≥ -1), moderate (-1 > T-score ≥ -2.5) or degraded (T-score ≤ -2.5). TBS groups were stratified by BMD T-scores (normal, osteopenia, or osteoporosis) using minimum T-score of total hip, femoral neck, and spine to identify categories in which TBS may be of more clinical use. The main outcome measure was the proportion of change in clinician's treatment threshold between BMD alone and BMD plus TBS. The difference was assessed for significance using Chi-square test. Additionally, the change in UK National Osteoporosis Guideline Group (NOGG) threshold was also assessed using TBS-adjusted FRAX scores. Correlations between BMD-TBS strata and the change in intervention threshold (yes/no) were carried out using Spearman test.
Results: 540 patients were analysed. The inclusion of TBS resulted in 8.2% change in clinician's treatment threshold (p <0.001) shifting the outcome 6.5 % for and 1.7 % against treatment. More than half of the cases in which the clinical decision was changed were for patients with osteopenia and degraded TBS (significant correlation; P <0.001). NOGG intervention threshold was changed in 7.4% of the cases (P<0.001); 6.1% for and 1.3% against treatment. 37.5% of NOGG changed outcome was related to osteopenia with degraded TBS (p<0.001). Kappa agreement between the clinician and NOGG was fair at 0.42 (p<0.001).
Conclusion: These results demonstrate that using TBS in routine clinical practice is most likely to impact treatment decision in patients with osteopenia who have compromised bone microarchitecture. Incorporating TBS in routine DXA scans may lead to a net increase in bone protective therapy of approximately 5%. It is unknown whether adopting such an approach universally can reduce future fracture risk, and prospective studies are needed to address this question.
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Table 1. Demographic and baseline characteristics (n = 540)

Female	470 (87%)
Age (years)	68.1 ± 11.6
Body mass index (BMI)	26.2 ± 4.6
Femoral neck T-score	-1.80 ± 1.04
Total hip T-score	-1.32 ± 1.07
Lumbar spine T-score	-1.37 ± 1.42
Lumbar spine TBS	1.32 ± 0.13
Major osteoporotic fractures	238 (44%)
Spinal fractures	81 (15%)
FRAX major osteoporotic fracture	14.43 ± 9.03
FRAX hip fracture	4.60 ± 6.20
TBS-adjusted FRAX major osteoporotic fracture	13.82 ± 8.80
TBS-adjusted FRAX hip fracture	4.45 ± 5.73

Table 2. Change in clinician's treatment threshold according to TBS-BMD strata

	Distribution of clinical decision change (%)	P value
Normal BMD with normal TBS¶	0	0.029
Normal BMD with moderate TBS	11.1	0.005
Normal BMD with degraded TBS	4.4	0.79
Osteopenia with normal TBS	6.7	0.048
Osteopenia with moderate TBS	4.4	0.012
Osteopenia with degraded TBS	51.1	<0.0001*
Osteoporosis with normal TBS	6.7	0.916
Osteoporosis with moderate TBS	8.9	0.048
Osteoporosis with degraded TBS	6.7	0.284

*statistically significant

¶ normal TBS: T-score ≥ -1, moderate TBS: -1 > T-score ≥ -2.5, degraded TBS: T-score ≤ -2.5

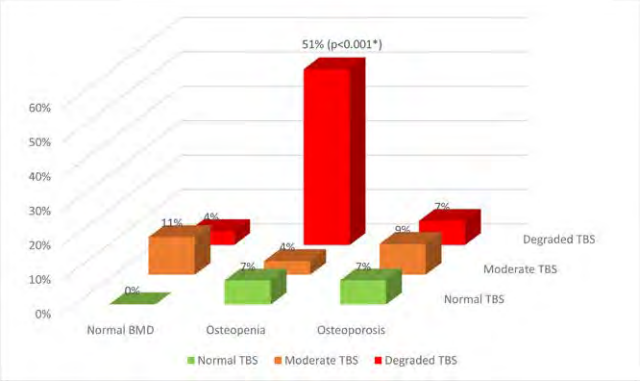


Figure 1. Distribution of changed clinical treatment threshold in normal, moderate, and degraded TBS according to BMD T-score

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SAT0480 ASSESSMENT OF CORONARY ATHEROSCLEROSIS SEVERITY IN MEN WITH CORONARY HEART DISEASE DEPENDING ON BONE MINERAL DENSITY

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Background:
Objectives: Assess the severity of coronary atherosclerosis in men with coronary heart disease (CHD) depending on bone mineral density (BMD).
Methods: 102 of men with verified CHD aged 51-75 (60 .8 ± 6.9) were examined. All patients performed two-energy X-ray absorption of lumbar vertebrae bodies LI-LIV and hip necks (Excell XR-46, Norland, USA) and polyproject coronarangiography (Innova, General Electric, USA). On the basis of results of densitometry on value of T-criterion (the recommendation of ISCD, 2007) estimated BMD condition: normal BMD (T criterion ≥-1), osteopenia (T-criterion from-1 to-2.5) and osteoporosis (OP) (T criterion <-2.5). According to the SYNTAX scale (www.syntaxscore.com), the following degrees of coronary artery (CA) injury severity were isolated to quantify the expression of atherosclerotic injury: low (22 or less), intermediate (23-32) and high (33 or more). According to the result of multispiral computed tomography of CA, calcium index of vessels was determined by the Agatston method using the CaScore program. On the basis of the calcium index value the degree of CA calcinosis was evaluated: 0 - absence of calcinosis, 1-10 - minimal, 11 - 100 - moderate, 101-400 - increased, more than 400 - expressed calcinosis.
Results: According to the results of densitometry, patients were found to have 21 patients (20.6%) with normal BMD, 48 (47.0%) - osteopenia and 33 (32.4%) -osteoporosis. Osteopenic syndrome (OPS) was found in 79.4% of men. All patients tested, depending on the degree of CA calcinosis, were distributed as follows: 57.8% of men had pronounced CA calcinosis, 25.5% - increased, 6.9% - moderate, 2.0% - minimal, 7.8% of patients had no CA calcinosis. In a comparative analysis of the degree of coronary calcinosis in men with CHD depending on the T-criterion, it was found that the majority of patients with OPS (69.7% of patients with OP and 60.4% with OPe) had pronounced CA calcinosis. In men with normal BMD, the prevalence of pronounced CA calcinosis (33.3%) was significantly lower than in patients with OPS ($p < 0.050$). Calcinosis-negative CA was recorded reliably more frequently in patients with normal BMD (28.6%) compared to men with low BMD ($p < 0.050$). The results of the work demonstrated the relationship of the studied parameters of coronary atherosclerosis expression with densitometry indicators in men with CHD. Thus, the inverse correlation of the BMD at the level of the hip neck with the number of significant stenoses of the spacecraft ($r = -0.19$; $P = 0.045$) and the degree of coronary calcinosis ($r = -0.23$; $P = 0.022$) and similar dependence of BMD of vertebral bodies LI-LIV with coronary calcinosis degree ($r = -0.19$; $p=0,046$). A direct correlation between CA calcinosis and FRAX hip fracture risk ($r = 0,24$; $p=0,018$). Inverse correlation of parameters of atherosclerotic damage of CA (number of significant stenoses and degree of calcinosis) with BMD was established, and direct correlation of CA calcinosis degree with risk of hip fracture on FRAX scale in male persons with CHD over 50 years of age was revealed.
Conclusion: The findings suggest in favor of likely common mechanisms for developing atherosclerosis with OP and allow coronary calcinosis to be considered as a condition potentially increasing the risk of hip fracture.
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SAT0481 RELATIONSHIP BETWEEN SARCOPENIA AND BONE MINERAL DENSITY IN MEN WITH CORONARY HEART DISEASE

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Objectives: To study the relationship of indicators of muscle mass, muscle strength and muscle function with bone mineral density (BMD) in men with coronary heart disease (CHD).
Methods: 79 men aged over 50 years with verified CHD were examined (mean age 63 (57; 66) years).
The BMD (g/cm^2) and T-criterion (standard deviation) of the femoral neck and lumbar spine (L1-L4) were evaluated using dual-energy x-ray absorptiometry (DXA) on the lunar Prodigy Primo bone densitometer (USA).
To assess muscle mass, the total area (cm^2) of the lumbar muscles of the axial section at the level of the 3rd lumbar vertebra (L3) was determined using multispiral computed tomography on a 64-slice computer tomograph "Somatom Sensation 64" (Siemens AG Medical Solution, Germany). The ratio of the obtained index of the area of skeletal muscle to the square of the patient's growth index determined the "musculoskeletal index L3" (SMI). The media considered the threshold value to be 52.4 cm^2/m^2. Evaluation of muscle strength was performed using a mechanical wrist dynamometer DC-25. Muscle function was examined using a short physical performance battery (SPPB).
Results: The data obtained from the results of correlation analysis show that there is a reliable direct correlation between BMD and hand dynamometry indicators ($r=0.250$; $p=0.026$ for the right hand and $r=0.247$; $p=0.028$ for the left hand), the T-criterion of the femoral neck and hand dynamometry indicators ($r=0.245$; $p=0.030$ for the right hand and $r=0.242$; $p=0.032$ for the left hand). A similar relationship was established between the BMD of the lumbar vertebra and the parameters of dynamometry ($r=0.237$; $p=0.036$ for the right hand and $r=0.228$; $p=0.043$ for the left hand) and T-criterion for the lumbar region and dynamometry parameters ($r=0.232$; $p=0.039$ for the right hand and $r=0.220$; $p=0.051$ for the left hand). There is no significant relationship between densitometry scores and the result of SPPB tests.
There was a significant direct relationship between the total SPPB score and the area of skeletal muscle at the L3 level ($r=0.249$, $p=0.026$), the total SPPB score and the musculoskeletal index ($r=0.233$, $p=0.039$). A similar relationship was established between the result of the chair lift test and the total area of skeletal muscle at the L3 level ($r=0.262$, $p=0.019$) and the musculoskeletal index ($r=0.220$, $p=0.050$).
A significant negative relationship between walking speed and the musculoskeletal index was found ($r= -0.260$, $p=0.021$). The relationship between muscle mass and strength could not be traced.
Conclusion: A decrease in muscle strength correlates with the severity of bone loss, while a decrease in muscle function correlates with a decrease in muscle mass. The results obtained confirm the probability of common mechanisms in the development of sarcopenia and osteoporosis in patients with CHD.
Disclosure of Interests: None declared
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SAT0482 FRAX 10-YR FRACTURE RISK IN RHEUMATOID ARTHRITIS ASSESSED WITH AND WITHOUT BONE MINERAL DENSITY – ARE WE TREATING OUR PATIENTS UNDER BDMARDS?

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Background: Patients with rheumatoid arthritis (RA) have a higher risk of osteoporosis not only due to chronic inflammation status, but also due to the treatment with glucocorticoids. FRAX is a computer-based algorithm developed by the World Health Organization for estimation of the 10-year risk of a hip or major osteoporotic fracture. Inclusion of femoral neck bone mineral density (BMD) in the estimation is optional.
Objectives: The study aimed to identify the RA patients under treatment with biological disease-modifying antirheumatic drug (bDMARD), who have FRAX scores, calculated with and without BMD, classified as high fracture risk and evaluate if they are receiving treatment for osteoporosis. The authors also investigated the intra-individual agreement between FRAX fracture risk calculated with and without BMD.
Methods: Demographic and clinical data and BMD results from RA patients followed in a tertiary university hospital and registered in the Rheumatic Diseases Portuguese Register were used for analysis. Patients under 40 years of age at the last visit were excluded. McNemar test was applied for the identification of discordance of risk categories. The Wilcoxon test was used to characterize the intraindividual differences between paired FRAX risks with and without BMD. Correlations between pairs of variables were evaluated by the Spearman test. For independent variables Mann-Whitney test was used.
Results: A total of 303 patients were included, 244 were females (80.5%) and 49 current smokers (16.2%). Mean age was 59.5 ± 9.54 years and mean disease duration 18.5 ± 10.4 years. Two hundred and twenty patients (72.4%) and 243 (80.2%) were RF and ACPA positive, respectively, and 51.5% had erosive disease. Mean disease activity score (DAS28-4V-CRP) was 3.08 ± 1.18 and mean femoral neck BMD 0.84 ± 0.12 g/cm^2. One hundred and seventy nine patients (58.9%) were concomitantly treated with conventional synthetic DMARDs and 215 (70.7%) with glucocorticoids. Among all the patients, 35 (11.6%) had previous fractures and 19 (6.3%) have family history of fracture. The median 10-year risk of a major fracture and a hip fracture, calculated without BMD, was 6.0 (1.2-50) and 1.5 (0.1-39), respectively; with BMD it was 6.9 (1.3-61) and 1.7 (0-49). When FRAX score is calculated without BMD (n=303), 76 (25.1%) patients were categorized as high fracture risk. Among them, only 41 (54%) were receiving osteoporosis treatment. FRAX assessment with BMD (n=231) identified 99 (32.7%) patients with high fracture risk, 51 (51,5%) in treatment for osteoporosis. Thirty patients (21%) previously classified as low fracture risk using FRAX without BMD were recategorized as high risk ($p<0.001$). Despite that, there was a strong correlation between fracture risks assessed with and without BMD for both major and hip fracture ($r = 0.867$, $p <$

0.0001 and r = 0.728, p < 0.0001, respectively). ACPA and RF positive patients did not have higher FRAX scores (including or not BMA). Patients with erosive disease had a higher 10-year probability of major fracture evaluated by FRAX when it includes BMD (p=0.041).

Conclusion: It is very important to accurately assess the risk of osteoporotic fractures in RA patients to treat them properly. The authors highlight the high number of patients who are not receiving treatment according to FRAX categorization. In spite of the correlation between estimated fracture risk by FRAX with and without BMD, there is a discordance in fracture risk categorization, as one fifth of patients of low risk were reclassified as high risk. For the RA population treated with bDMARDS, our findings raise the need to request a DXA not only for patients classified as having an intermediate risk of fracture, but also for low-risk patients.

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SAT0483 SAFETY OF INTRAVENOUS IBANDRONIC ACID IN CHRONIC KIDNEY DISEASE: A REAL WORLD EXPERIENCE

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Background: Common forms of intravenous bisphosphonate used at the Royal Derby Hospital are zoledronic acid and ibandronic acid for a variety of indications. In the treatment of osteoporosis, zoledronic acid is preferred due to its convenience of once-yearly dosing; compared to ibandronic acid which is given three-monthly. Zoledronic acid is contraindicated in patients with an estimated glomerular filtration rate (eGFR) of less than 35 due to nephrotoxicity concerns. Ibandronic acid, however, is generally offered with an eGFR of 30 or over and is perceived to be a safer choice in more advanced chronic kidney disease. The potential of extending the use of ibandronic acid to patients with lower eGFR is being explored. However, there is a paucity of real world data and this study will therefore seek to affirm the safety profile in those on treatment.

Objectives: Establish the safety profile of IV ibandronic acid with regards to worsening renal function or significant hypocalcaemia injury in the context of reduced renal clearance.

Methods: The details of patients receiving IV ibandronic acid at Royal Derby Hospital were retrieved from the osteoporosis department register in September 2019. Data was collected anonymously from records using the electronic prescribing and pathology hospital database, together with electronic letters. The first three pre-infusion serum adjusted calcium levels, vitamin D, creatinine and eGFR were recorded. In addition, results from initiation to present were screened for any episodes of hypocalcaemia, acute kidney injury (AKI) or significant decline in renal function.

Results: Treatment duration ranged from 6 months to 6 years. Female:male ratio was 9:1 and the average age was 75 years (range 50-90). Baseline eGFR ranged from 27 to over 60; 3 patients had eGFR≥60, 2 had eGFR 27 while remaining patients (75%) had eGFR 30-59. All patients received a standard 3mg infusion on each occasion. The most common rationale cited for ibandronic acid choice as opposed to zoledonic acid was reduced creatinine clearance or eGFR. Three patients (15%) developed one or more episodes of mild hypocalcaemia (lowest 2.01 mmol/l). No episodes of hypocalcaemia were identified in the first three pre-infusion levels. Four patients (25%) had a decline in eGFR by more than 5 ml/min/1.73m^2 but there was no definitive causal link with ibandronic acid and was most commonly felt to be related to their underlying renal disease. Three patients (15%) had at least one episode of AKI since commencing treatment, each explained by an intercurrent illness. Serum Vitamin D levels were measured pre-infusion in 92% of cases.

Conclusion: This study reaffirms the safety profile of ibandronic acid use in renal function as low as CKD Stage 3b (≥30ml/min/1.73m^2). No episodes of AKI or sustained decline in renal function were causally linked to ibandronic acid.

References: Royal Derby Hospital Proposed Clinical Guideline (2019) – Use of ibandronic acid in CKD 4 at reduced dosage.

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SAT0484 TRABECULAR BONE SCORE IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: Systemic lupus erythematosus (SLE) patients shown an increased risk of low bone mass as a result of multifactorial events: physical inactivity, persistent inflammation, low vitamin D levels (photosensitivity) and glucocorticoid treatment. Trabecular Bone Score (TBS), is an index extracted from the dual-energy X-ray absorptiometry (DXA) that provides an indirect measurement of bone axial microarchitecture and allows to get information about bone quality in several rheumatic diseases (1-4).

Objectives: The aims of this study were to examine the prevalence and risk factors for low bone mineral density (BMD) (osteoporosis or osteopenia) in female patients affected by SLE and to compare with matched healthy subjects (CNT).

Methods: 70 female patients (mean age 41±20 years) affected by SLE and 65 age- matched CNT (mean age 46±7 years) were enrolled. Bone Mineral Density (BMD, g/cm2) of the lumbar spine (L1-L4) was analyzed using a DXA scan (GE, Lunar Prodigy). Lumbar spine TBS was derived for each spine DXA examination using the TBS index (TBS iNsight Medimaps).

Results: The mean BMD±SD was 0.47±0.57 g/cm2 at the lumbar spine and 0.78 ± 0.22 g/cm2 at the hip in SLE patients. The prevalence of osteopenia was 40.0% and was 19.4% of osteoporosis in SLE patients. Most of SLE patients (75%) presented a bone loss that was significantly higher when compared with control group (p<0.001). Lumbar spine TBS score was found significantly lower in SLE patients compared with CNT (0.687±0.675 vs, 1.294±0.809 p<0.001, respectively) and of 0,47±0,94 times lower than expected from the concomitant reference BMD value.

Conclusion: The study shows that the further TBS analysis, independently from the concomitant BMD value, is significatively lower then expected in SLE patients. The detection of the TBS, together with the BMD, may offer a more reliable indication of the real whole bone condition in chronic and systemic inflammatory rheumatic diseases, such as SLE.

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SAT0485 PERCENTAGE BODY FAT HAS A STRONGER ASSOCIATION WITH BONE MINERAL DENSITY AT THE HIP AND SPINE COMPARED TO BODY MASS INDEX

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Background: A decreased body mass index (BMI) is associated with poorer bone health, a decreased bone mineral density (BMD), and an increased fracture risk. Cardiovascular (CVS) data has shown that the waist:hip ratio is a more robust measurement for CVS outcomes than BMI (1). Waist:hip ratio has never been evaluated as an outcome measure for bone health. Dual-energy x-ray absorptiometry (DEXA) has the capacity to measure average percentage fat in the L1-L4 region and at the hip, and directly relates to the measurement of waist:hip ratio.

Objectives: To evaluate the relationship between BMD and average percent fat in a cohort referred for DEXA scanning.

Methods: We analysed data routinely collected from patients referred for DEXA between 2004 and 2010 at the Royal Lancaster Infirmary in the North of England. Data collected for these patients included DEXA scans

of BMD at the left and right hip, and at the lumbar spine, as well as average percent far and other risk factors for osteoporosis, including the FRAX risk factors. We used only the measures collected at baseline (time of first scan). We modelled the T scores of the BMD measurements using a linear regression model including percentage fat and BMI as explanatory variables, and adjusting for gender, age at scan, and other known risk factors for osteoporosis, including the FRAX risk factors. BMI and average percent fat were standardised.

Results: The number of patients included was 33037, (82% female). Results of both regression models are shown in table 1 below. We show the standardised effect size estimates for average percent fat and BMI.

Anatomical location	Effect size estimate for average percent fat (95% confidence intervals)	P value	Effect size estimate for BMI (95% confidence intervals)	P value
Left neck	-0.156 (-0.171, -0.141)	<0.001	-0.0255 (-0.0441, -0.00701)	0.00692
Left total	-0.225 (-0.241, -0.208)	<0.001	-0.0680 (-0.0882, -0.0477)	<0.001
Left Ward's	-0.181 (-0.196, -0.166)	<0.001	-0.0268 (-0.0456, -0.00813)	0.00493
Left trochanter	-0.263 (-0.281, -0.246)	<0.001	-0.0667 (-0.0882, -0.0451)	<0.001
Right neck	-0.139 (-0.154, -0.124)	<0.001	-0.0131 (-0.0317, 0.00549)	0.167
Right total	-0.221 (-0.237, -0.204)	<0.001	-0.0611 (-0.0811, -0.0411)	<0.001
Right Ward's	-0.180 (-0.196, -0.165)	<0.001	-0.0193 (-0.0381, -0.000586)	0.0433
Right trochanter	-0.261 (-0.278, -0.243)	<0.001	-0.0598 (-0.0810, -0.0386)	<0.001
Spine (averaged L1-L4)	0.219 (0.195, 0.242)	<0.001	-0.00846 (-0.0379, 0.0206)	0.563

Conclusion: The analysis shows that average percent fat is a statistically significant predictor for BMD at different anatomical locations, and a larger predictor in comparison to BMI when evaluated in the same model. In the right hip neck and the spine, BMI was not predictive of changes in BMD. Higher average percent fat increases the BMD in the spine, compared to a decline at the hip. Further research is needed to characterise the relationship more precisely and identify whether there is a causal link.

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SAT0486 BONE MINERAL DENSITY IN PATIENT WITH SHRUNKEN PORE SYNDROME IS SIGNIFICANTLY LOWER THAN THAT IN PATIENT WITHOUT, HOWEVER SERUM PARATHYROID HORMONE DOES NOT CORRELATED MUCH WITH IT

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Background: Shrunken pore syndrome (SPS), defined by cystatin C (CysC) based estimated glomerular filtration rate ($eGFR_{CysC}$) < 60% of creatinine (Cr) based eGFR ($eGFR_{Cr}$) in the absence of extrarenal influences on the plasma levels of CysC or Cr, is associated with a higher increase in mortality. SPS often causes reduced bone mineral density (BMD).

Objectives: In this study, relationship between BMD and SPS was investigated.

Methods: Patient with rheumatic diseases who were measured BMD with dual-energy X-ray absorptiometry and at the same time, CysC and Cr were also measured, were picked up. $eGFR_{CysC}$ and $eGFR_{Cr,}$ were calculated, and a patient group with SPS were recruited. Relationship between serum PTH and CysC, or Cr was evaluated with univariate linear regression analysis. Between the SPS groups and the other patient group, statistical difference was evaluated regarding sex, age, Cr, CysC, serum Cr-CysC ratio (Cr/CysC), serum calcium corrected with albumin (Ca), creatinine phosphokinase (CPK), parathyroid hormone (PTH), $eGFR_{CysC}$, $eGFR_{Cr,}$, BMD in the lumbar spine (BMD_LS) and femoral neck (BMD_FN) were evaluated with Mann-Whitney U-test. Relationship between BMD for each bone and sex, age, CPK, PTH, Cr/CysC, $eGFR_{CysC}$, and being SPS was statistically evaluated with multivariate linear regression analysis. Furtherly, sensitivity and specificity regarding being SPS for T-score < -2.5, that is defined as diagnosis criteria of osteoporosis calculated from BMD, was evaluated with chi square test.

Results: A total of 819 participants with 75 males and 744 females joined. Patient with SPS counted 31 and without SPS counted 782. Underlying diseases are shown in Table 1. Average age, CysC, Cr, PTH, $eGFR_{Cr,}$ and $eGFR_{CysC}$ were 76.5, 1.18, 0.76, 42.1, 66.2 and 59.0, respectively. PTH significantly correlated with CyC ($p=0.015$), but not correlated with Cr ($p=0.079$). SPS demonstrated significantly higher ratio for being male ($P<1.0x10^{-10}$), higher age ($p=1.07x10^{-3}$), higher titer of CysC ($p=5.5x10^{-10}$), lower titer of CPK ($p=1.5x10^{-4}$), lower Cr/CysC ($P<1.0x10^{-10}$), lower $eGFR_{CysC}$ ($p=2.8x10^{-7}$), BMD_LS ($P<1.0x10^{-10}$) and BMD_FN ($P<1.0x10^{-10}$), however no significant difference demonstrated for Cr ($2.4x10^{-1}$), PTH ($p=1.7x10^{-1}$) and Ca ($p=6.3x10^{-1}$). BMD_LS demonstrated significant positive correlation with CPK ($p=2.6x10^{-4}$), and negative correlation with being female ($p=4.9x10^{-7}$), age ($p=2.1x10^{-3}$), PTH ($p=2.2x10^{-2}$), $eGFR_{CysC}$ ($p=2.5x10^{-9}$) and being SPS ($p=4.9x10^{-3}$), while BMD-FN demonstrated significant positive correlation with Cr/CysC ($p=7.3x10^{-4}$), and negative correlation with being female ($p=1.5x10^{-6}$), age ($p=4.9x10^{-8}$) and being SPS ($7.3x10^{-3}$). Sensitivity and specificity of T-score < -2.5 in the LS regarding SPS was 50.0% and 74.0% ($p=6.9x10^{-3}$), while in the FN 67.9% and 61.7% ($p=1.7x10^{-3}$), respectively.

Table 1. Number of patients who were picked up in the study
Abbreviations: RA, rheumatoid arthritis; PsA, psoriatic arthritis; AJA, Sjoren Syndrome; SLE, systemic lupus erythematosus; PPP, pustulosis palmaris et plantaris; AS, ankylosing spondylitis; SSc, systemic sclerosis; UA, ulcerative colitis; PM/DM, polymyositis/dermatomyositis; MCTD, mixed connective tissue disease; FMF, Familial Medditeranean fever; PAN, polyarteritis nodosa.

Diseases	Number of patient
RA	512
PsA	110
SJS	67
SLE	66
PPP	17
AS	16
SSc	13
UA	11
Behcet	8
PM/DM	3
MCTD	2
FMF	2
PAN	1
total	828

Conclusion: These results suggested that SPS has serious potential risk of osteoporosis. BMD_LS loss may correlate elevation of PTH due to filtration disorder, however BMD_FN loss is not affected. Split of Cr and CysC is more important.

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SATURDAY, 06 JUNE 2020

Basic and translational science in paediatric rheumatology

SAT0487 PREDICTIVE BIOMARKERS OF I IGA VASCULITIS WITH NEPHRITIS BY METABOLOMIC ANALYSIS

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Background: IgA vasculitis/ Henoch Schönlein Purpura (IgAV/HSP) is the most common vasculitis of childhood and renal involvement is the most serious long-term complication. A better understanding of the pathophysiology of the progression to kidney disease is required for better treatment to be achieved and current biomarkers of Ig A vasculitis with nephritis (IgAVN) lack the predictive value.

Objectives: In this study, an untargeted metabolomics approach was performed to reveal the underlying molecular mechanism of disease pathogenesis and to find potential biomarkers of plasma samples from patients with IgAV and IgAVN.

Methods: IgAV/HSP was diagnosed according to the Ankara criteria in 2008 (1). Forty-five patients, including 39 active IgAV patients (H), 6 IgAVN (N), and 6 age- and

gender-matched healthy controls (C), were enrolled in the study. Plasma samples from subjects were collected on the same day of IgAV(HSP) diagnosis and before steroid or other immunosuppressive treatment initiated. This study has utilized liquid chromatography-mass spectrometry (LC-MS/ Q-TOF) to investigate the alterations in plasma metabolomic profiles. Three separate pools, health controls, active IgAV, and IgAVN were created. Peak picking, grouping, and comparison parts were performed (metabolite profiling) via XCMS (https://xcmsonline.scripps.edu/) software.
Results: Totally 2618 peaks were detected for group H, N and C. Among them 355 peaks were found to be statistically significant and reliable ($p<0.05$) and 155 of these peaks were found to be changed (fold change >1.5) between the groups C and H. On the other hand, 66 peaks were found to be changed (fold change >1.5) between the groups H and N. The number of the peaks on the intersection of the peaks found to be changed between the groups (C and H) and (H and N) was 39. This situation was illustrated in Figure 1. Based on putative identification results, 15 peaks were matched with 24 metabolites. The list of these metabolites is given in Table 1.

Table 1. Putative identification of 15 peaks found to be statistically different and having fold changes.

Peak	Putative Identification	KEGG Codes	rt (min)	N/H
1	5-Aminopentanamide	C00990	2,10	0,36
1	5-Aminopentanoic acid	C00431	2,10	0,36
1	2-Keto-6-aminocaproate	C03239	2,10	0,36
1	(S)-5-Amino-3-oxohexanoate	C03656	2,10	0,36
1	D-1-Piperideine-2-carboxylic acid	C04092	2,10	0,36
2	Oxalureate	C00802	15,52	0,50
3	Porphobilinogen	C00931	14,78	9,62
4	(+)-cis-3,4-Dihydrophenanthrene-3,4-diol	C04468	15,52	0,02
5	(-)-trans-Carveol	C00964	12,69	1,82
6	DHAP(18:0)	C03805	12,70	1,92
6	N-Acetyl-b-glucosaminylamine	C01239	12,70	1,92
7	5-Methyltetrahydrofolic acid	C00440	14,88	2,41
8	N2-Succinyl-L-ornithine	C03415	15,52	0,05
8	N6-Acetyl-LL-2,6-diaminoheptanedioate	C04390	15,52	0,05
9	Estrone	C00468	12,71	1,90
10	N-Acetyl-4-O-acetylneuraminic acid	C04015	14,89	2,41
10	N-Acetyl-7-O-acetylneuraminic acid	C04016	14,89	2,41
11	Oleoyl-CoA	C00510	15,52	0,26
12	Saccharopine	C00449	15,52	0,26
13	Prostaglandin D2	C00696	17,81	2,05
13	Prostaglandin I2	C01312	17,81	2,05
14	Glycocholic acid	C01921	13,78	0,61
15	Galactosylsphingosine	C01747	24,41	0,45
15	Glucosylsphingosine	C03108	24,41	0,45

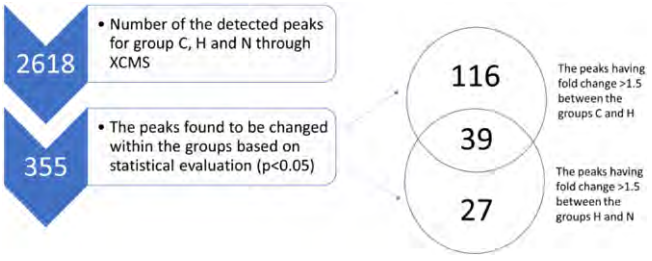


Figure 1. The number of the peaks found on datamining process

Conclusion: Certain differences in metabolites were identified between controls and IgAV patients and between those with and without kidney involvement.
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Paediatric rheumatology

SAT0488 **ETANERCEPT CONCENTRATION IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS**

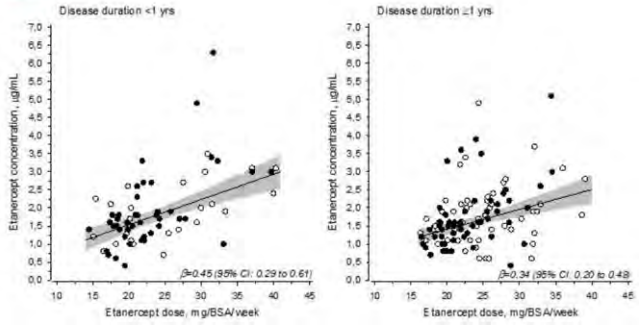
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Background: Etanercept (ETN) is the most used TNF blocker in children with JIA. There is still limited real-life data of etanercept concentrations in children, especially in association with dosing.
Objectives: The aim of the study was to investigate association between ETN dosing and serum trough concentration in children with non-systemic JIA.
Methods: We conducted a multicenter retrospective study of 180 Finnish JIA patients (Table 1) receiving ETN either as monotherapy or in combination with one or more DMARDs (Table 2). Prior biologicals were used by 17 % of the patients. Patients were divided into two groups, ETN started before or after one year of diagnosis (Figure 1). ETN concentration samples (collected 2014-2017) were analyzed using validated enzyme-linked immunosorbent assay (ELISA) in Sanquin Diagnostics, Amsterdam, the Netherlands.
Results: Demographics at etanercept start and diagnoses are shown in Table 1. Duration of the treatment with ETN, ETN doses, concentrations and concomitant medications at the time of concentration measurement are shown in Table 2.
Association between ETN dose and concentration is shown in Figure 1.
Those who started medication early (< 1 year from diagnosis) were younger than those who started later (Table 1) and association between ETN dose and concentration was more obvious (Figure 1).

Table 1	N=68, Disease duration <1 year	N =112, Disease duration ≥1 year	P-value
Girls, n (%)	39 (57)	70 (62)	0.49
Age, mean (SD), years	6.6 (3.8)	8.9 (3.5)	<0.001
BSA, mean (SD)	0.86 (0.32)	1.03 (0.30)	<0.001
Disease duration, mean (SD), months	0.7 (0.2)	3.9 (2.7)	..
Dg n (%)			0.078
Oligoarthritis, persistent	12 (18)	23 (21)	
Oligoarthritis, extended	7 (10)	22 (20)	
Polyarthritis, RF-neg	42 (62)	55 (49)	
Polyarthritis, RF-pos	3 (4)	0 (0)	
Enthesitis-related arthritis	3 (4)	8 (7)	
Psoriatic arthritis	0 (0)	3 (3)	
Undifferentiated arthritis	1 (1)	1 (1)	
HLAB27 pos, n (%)	19 (29)	33 (30)	0.86
ANA pos, n (%)	21 (31)	33 (29)	0.84

Table 2	Disease duration at ETN start <1 year	Disease duration at ETN start ≥1 year	P-value
BSA, mean (SD)	0.98 (0.33)	1.18 (0.31)	<0.001
ETN duration, mean (IQR), months	11.7 (4.3-29.2)	10.9 (4.7-32.9)	0.68
ETN dose (mg/BSA/week), mean (SD)	23.7 (6.4)	23.9 (5.0)	0.90
ETN concentration (ug/ml), mean (SD)	1.91 (1.00)	1.74 (0.85)	0.24
Concomitant treatments, n (%)			
MTX	43 (63)	54 (48)	0.050
LEF	10 (15)	14 (13)	0.67
HCQ	5 (7)	3 (3)	0.16
SSZ	4 (6)	6 (5)	0.88
AZA	0 (0)	1 (1)	0.99
Glucocorticoids	9 (13)	2 (2)	0.003

Figure 1



Conclusion: There was an association between etanercept dose used and serum trough concentration and it was more evident when medication was started early after diagnosis, when the patients were younger and BSA lower.

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SAT0489 CLINICAL COURSE AND THERAPY RESPONSE IN TAKAYASU ARTERITIS: COMPARISION BETWEEN CHILDHOOD AND ADULT ONSET

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Background: Takayasu arteritis (TA) is a granulomatous vasculitis of the large vessels of unknown origin, which mainly affects the aorta and its main branches. TA is a disease of the young age with onset usually before 40 years and in more than 20% of patients the diagnosis is made before 19 years.

Very few clinical series have compared the clinical manifestations, treatment and outcomes between pediatric and adult patients.

Objectives: Objective of our study was to compare childhood and adult onset TA evaluating clinical manifestations, treatment (including biotechnological agents) and outcomes.

Methods: All consecutive patients with childhood-onset TA (onset <18 years) and adult-onset (onset ≥ 18 years) TA followed from 2002 to 2019 in two Italian centers (Genoa Gaslini Hospital and Santa Maria Nuova Hospital of Reggio Emilia) were retrospectively evaluated and compared.

All patients met TA classification criteria (ACR 1990 and EULAR/Printo/PrES 2010 for children).

Clinical, demographic, laboratory, radiological, therapeutic data were collected retrospectively at baseline, at 6-month follow-up and at the last follow-up.

Disease activity at each follow-up visit was evaluated according to NIH criteria.

Results: 58 patients were consecutively enrolled: 18 children (C) and 40 adults (A). In both groups there was a higher prevalence of females (83.3% C vs 77.5% A; p NS).

The diagnostic delay was lower in the pediatric group (median of 5 months VS 10 months in A; p NS).

Fever and headache as presenting manifestations affected more frequently children with statistically significant differences (55,6% C vs 17,5% A, p 0,003; 27,8% C vs 5% A, p 0,025)

Adults had a higher frequency of claudication of the upper limbs and carotid/subclavian bruits (30% and 55% A vs 5,6% and 38,9% C respectively; p NS), while the discrepancy in blood pressure of the four limbs was higher in children (22,2% C vs 12,5% A; p NS).

Hypertension was not significantly different between the two groups at baseline and during the follow-up.

We found a significantly more frequent inflammatory involvement of the aorta (arch, thoracic, or abdominal) in children (72,2% C vs 30% A, p 0.003).

The subclavian arteries were most affected in the adults (65% A vs 38,9% C; p NS), although the difference was not statistically significant.

Treatment regimen were different between the groups: glucocorticoid monotherapy was more frequently used in adults (45% A vs 27,8% C; p NS), glucocorticoids in combination with Cyclophosphamide or anti-TNF were more significantly used to induce remission at the beginning in the pediatric group (22% C vs 0 A, p 0,007 and 22% C vs 2,5% A, p 0,029).

At the last follow-up the disease was significantly more active in children according to NIH criteria (55.6% C vs 27.5% A, p 0,04).

Conclusion: We reported some differences between children and adults. TA in children was characterized by a shorter diagnostic delay, a more frequent inflammatory involvement of the aorta and a more refractory disease. Patients with pediatric TA were treated more aggressively at the beginning.

Disclosure of Interests: None declared

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SAT0490 MATCHED CONTROLLED SURVEILLANCE OF TOCILIZUMAB TREATMENT FOR POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS–AN INTERIM ANALYSIS

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Background: Tocilizumab (TOC) is approved for treatment of polyarticular juvenile idiopathic arthritis (pJIA). Data out of clinical practice are limited.

Objectives: Long-term surveillance of patients initiating TOC treatment compared to a cohort of patients initiating a comparator biologic using the BIKER-registry.

Methods: Baseline parameters, efficacy and safety parameters were compared. Efficacy outcomes were JADAS10 and joint counts. Functional status was determined with the Childhood Health Assessment Questionnaire disability-index (CHAQ-DI). Safety was assessed by adverse events (AE) reports.

Results: Until January 2020, 152 patients have been recruited to each cohort. Patients starting on TOC were older at treatment start (12.1 vs. 10.1 years (y); p<0.0001) and had a longer disease duration (5.4y vs. 3.0y; p<0.0001). TOC was significantly more often a second-line biologic (84% vs 13%, p< 0.0001). Otherwise patients were comparable (Table 1).

Table 1. Comparison of TOC patients and matched controls.

	Tocilizumab N=152	Matched controls N=152	p
Gender female, n (%)	128 (84)	124 (81)	0.65
Disease duration, mean (SD), years	5.4 (4.1)	3.0 (2.9)	**<0.0001**
RF neg. polyarthritis, n (%)	104 (68.4)	92 (60.5)	0.19
RF pos. polyarthritis, n (%)	14 (9.2)	19 (12.5)	0.46
Extended oligoarthritis, n (%)	34 (22.4)	41 (27)	0.42
Pretreatment with biologics, n(%)	127 (83.5)	20 (13.2)	**<0.0001**
Active joint count, mean (SD)	6.7 (7.1)	6.1 (5.1)	0.4
CHAQ DI, mean (SD)	0.63 (0.63)	0.65 (0.64)	0.8
ESR, mm/h, mean (SD)	17.5 (14.9)	20.9 (20.6)	0.1
JADAS10, mean (SD)	16.8 (9.8)	15.1 (5.8)	0.067
Efficacy Month 12	N=87	N=105	
JADAS MDA, n (%)	50 (57.5)	63 (60.0)	0.77
JADAS REM, n (%)	32 (36.8)	39 (37.1)	1.0
JIA ACR 30/50/70/90, %	80/75/61/53	86/84/70/56	0.34/0.15/0.17/0.66
Adverse events	248,65 PY	290.4 PY	RR (95%CI); p
N (rate/100PY; 95%CI)			
AE	145 (58.3; 50-69)	157 (54.1; 46-63)	1.1 (0.9-1.4); 0.5
SAE	12 (4.8; 2.7-8.5)	4 (1.4; 0.5-3.7)	**3.5 (1.1-10.9); 0.03**
Medically important infection	2 (0.8; 0.2-3.2)	12 (4.1; 2.3-7.3)	**0.2 (0.04-0.9); 0.03**
Uveitis event	2 (0.8; 0.2-3.2)	12 (4.1; 2.3-7.3)	**0.2 (0.04-0.9); 0.03**

Upon TOC a substantial response to treatment with a significant reduction in JADAS 10 from 16.8 to 3.4 (p<0.0001) after 12 months was observed. There were no significant differences between patients from the TOC cohort and their matched controls regarding JIA ACR 30/50/70/90 criteria and active joint counts. JADAS 10, JADAS remission (REM) and minimal disease activity (MDA) was reached by comparable numbers in the TOC (37% and 58%) and the control cohort (37% and 60%).

While the total number of AE was comparable between the TOC cohort (58/100PY) and in the control cohort (54/100PY; RR 1.1; 95%CI 0.9-1.4), more serious AE (SAE) were reported with TOC (4.8/100PY compared to 1.4/100PY; RR 3.5; 95% CI 1-10.9). Medically important infections and uveitis events were documented at significantly lower frequency in the TOC-(0.8/100PY) than in the control cohort (4.1/100PY; RR 0.2; 95% CI 0.04-0.9). SAE with TOC were suicidal intent (n=3), depression (n=2), exacerbation of JIA, abscess, gastrointestinal infection, abdominal pain, colitis, bone surgery and fracture (n=1). SAE in the control cohort were depression, osteomyelitis, gastrointestinal infection and superinfected eczema (n=1). No significant differences regarding cytopenia and elevated transaminases were observed. No gastrointestinal perforation, no vascular event, no malignancy and no death occurred.

Conclusion: The efficacy of tocilizumab is comparable to that of alternative biologics. Tolerability was acceptable. As Tocilizumab was given as a second-line biologic in the vast majority of patients, comparisons between the cohorts have to be interpreted carefully. Observation in the registry is ongoing.

Disclosure of Interests: Ariane Klein Consultant of: Celgene, Toni Hospach: None declared, Frank Weller-Heinemann: None declared, Sandra Hansmann Consultant of: Advisory board Novartis Pharma, Jasmin Kuemmerle-Deschner Grant/research support from: Novartis, Sobi, Consultant of: Novartis, Sobi, Speakers bureau: Novartis, Sobi, Maria Fasshauer Consultant of: Shire, CSL Behring, Kirsten Minden Consultant of: GlaxoSmithKline, Sanofi, Speakers bureau: Roche, Ivan Foeldvari Consultant of: Novartis, Christoph Rietschel Consultant of: Pfizer, Abbvie, Novartis, Chugai, and Sobi, Tobias Schwarz: None declared, Ralf Trauzeddel: None declared, Markus Hufnagel: None declared, Dirk Foell Grant/research support from: Novartis, Sobi, Pfizer, Speakers bureau: Novartis, Sobi, Rainer Berendes: None declared, Gundula Boeschow: None declared, Prasad Oommen Consultant of: Novartis, Frank Dressler: None declared, Astrid Helling-Bakki: None declared, Gerd Horneff Grant/research support from: AbbVie, Chugai, Merck Sharp & Dohme, Novartis, Pfizer, Roche, Speakers bureau: AbbVie, Bayer, Chugai, Merck Sharp & Dohme, Novartis, Pfizer, Roche

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SAT0491 PSORIASIS ASSOCIATED WITH MONOCLONAL-ANTIBODY-TNF-A INHIBITORS VS. FUSION PROTEIN ETANERCEPT IN JUVENILE IDIOPATHIC ARTHRITIS PATIENTS - ANALYSIS OF THE BIKER REGISTRY

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Background: Although efficacy of Tumor necrosis factor inhibitors (TNFi) for treatment of psoriasis is well established, patients may develop psoriasis for the first time while on TNFi as a paradoxical effect. Few data are available in patients with juvenile idiopathic arthritis (JIA).

Objectives: To analyze the incidence of psoriasis in TNFi – treated JIA patients and to identify associated factors.

Methods: Safety data from patients registered in the German Biologics registry (BIKeR) were analyzed. Cohorts of patients were grouped by treatment: any or multiple TNFi, single TNFi, biologics other than TNFi and no biologics (control group on methotrexate (MTX) only). TNFi-associated psoriasis was defined as incident diagnosis of psoriasis after starting a TNFi. Patients with personal history of psoriasis prior to TNFi therapy were excluded. Rates and events per 100 patient-years (PY) of exposure were calculated using AEs reported after first dose under therapy and under the age of 18 years. Rates were compared by X2-test, event rates by Wald test.

Results: A total of 4149 treatment episodes with TNFi (Etanercept, Adalimumab, Golimumab, Infliximab), with a total exposure time of 8437 PY, were identified. There were 676 treatments with a non-TNFi- biologic (Tocilizumab, Abatacept, Anakinra, Canakinumab) with a total exposure time of 1112 PY. MTX monotherapy was conducted in 1692 patients with a total exposure time of 3971 PY. In total, 31 patients were diagnosed with incident psoriasis on JIA-treatment (Table 1). The mean duration of therapy until incident psoriasis was 2.2 (± 1.8) years. Multiple psoriatic skin manifestations were observed.

Psoriasis events were significantly more frequent in any or multiple TNFi compared to MTX-monotherapy, and specifically in the subgroup of TNF-antibody treatment (all) or Adalimumab compared to MTX or Etanercept (Table 2). Interestingly, psoriasis events were also observed with non-TNFi at high frequency. At occurrence of the event, patients exposed to biologics received MTX or steroids less frequently compared to the total patient cohort and had a higher JADAS10.

Table 2.

Reference	Psoriasis event n/100 PY	Comparator	Psoriasis event n/100 PY	Risk ratio	P-value
Non-TNFi	0.63	TNFi	0.27	0.4 (0.2 -1.0)	0.052
MTX	0.03	TNFi	0.27	10.8 (1.5-80.1)	0.019
MTX	0.03	ETA	0.11	4.4 (0.5-35.8)	0.165
MTX	0.03	TNF-antibodies	0.75	42.9 (5.8-317)	0.0002
ETA	0.11	TNF-antibodies	0.75	6.8 (2.8-16.5)	0.00002
MTX	0.03	ADA	0.69	27.4 (3.6-2209)	0.001
Non-TNFi	0.63	ADA	0.69	1.1 (0.4-2.7)	0.847
Non-TNFi	0.63	ETA	0.11	0.2(0.1-0.5)	0.0012
ETA	0.11	ADA	0.69	6.2 (0.5-15.6)	0.0001

Conclusion: Our findings demonstrate a higher incidence of psoriasis in monoclonal-antibody-TNFi-treated JIA-patients, whereas in Etanercept-treated JIA patients no significant increase was detected. On average, psoriasis-manifestation occurred more than two years after treatment-initiation. Teenage females with ANA-positivity were most often affected.

Disclosure of Interests: Angela Zimmer: None declared, Ariane Klein Consultant of: Celgene, Gerd Horneff Grant/research support from: AbbVie, Chugai, Merck Sharp & Dohme, Novartis, Pfizer, Roche, Speakers bureau: AbbVie, Bayer, Chugai, Merck Sharp & Dohme, Novartis, Pfizer, Roche

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SAT0492 RAPID IMPROVEMENT AND ACHIEVEMENT OF INACTIVE DISEASE IN CHILDREN WITH SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS UNDER 4 YEARS OF AGE DEPENDING ON DISEASE DURATION ON TOCILIZUMAB TREATMENT

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Table 1

N/PY	TotalCohort* 4792/13519	All TNFi 4149/8437	ADA 1105/1859	ETA 2824/6307	GOL 144/145	INF 76/126	Non-TNFi 676/1112	MTX only 1692/3971
Psoriasis events/rate(%)	31/0.6	23/0.6	13/1.2	7/0.2	2/1.4	1/1.3	7/0.6	1/0.1
Pso**/100 PY (95%CI)	0.2 (0.2-0.3)	0.3 (0.2-0.4)	0.7 (0.4-1.2)	0.1 (0.1-0.2)	1.4 (0.3-5.5)	0.8 (0.1-5.6)	1.0 (0.5-2.1)	0.03 (0.004-0.2)
Age at event Mean ± SD	13.9 (±3.1)	13.9 (± 3.2)	14.0 (±3.0)	13.0 (±4.0)	15.1 (±3.4)	16.4	13.4 (±3.1)	17.3
Female	24 (77%)	18 (78%)	10 (77%)	5 (71%)	2 (100%)	1 (100%)	5 (71%)	1 (100%)
ANA positive	22 (71%)	16 (70%)	10 (77%)	4 (57%)	1 (50%)	1 (100%)	5 (71)	1 (100%)
Treatment duration until event (years) Mean ±SD	2.2 ±1.8	2.4 ±2.3	2.2 ±1.4	2.8 ±2.2	0.6 ±0.5	3.8	1.4 ±2.0	5.6
Concomitant MTX	11 (36%)	6 (26%)	3 (23%)	2 (29%)	1 (50%)	0	4 (57%)	1 (100%)
Concomitant Steroids	4 (13%)	2 (9%)	0	1 (14%)	0	1 (100%)	2 (29%)	0
JADAS10 Median [IQR]***	2.5 (0.6-8.8)	4.2 (1.0-11.0)	2.0 (0.6-10.1)	5.8 (1.5-11.4)	18.0	6.6	1.3 (0.8-3.4)	1.7

*individual therapy numbers add to a sum > the total cohort number, because some patients switched between multiple drugs; ** Pso= Psoriasis event; *** at time of event

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Background: Early-onset form of systemic juvenile idiopathic arthritis (sJIA) often presents severe disease course. Choosing the optimal therapy option as first-line treatment is necessary for rapid improvement of patients' quality of live and prevention of further radiologic progression.
Objectives: To evaluate the long-term effectiveness and safety of tociliizumab (TOC) in sJIA patients depending on the duration of the disease treated in the National Medical Research Center of Children`s health, Moscow, Russia.
Methods: The study was conducted as a subanalysis of the prospective cohort study to evaluate the efficacy of biologics in children with sJIA. Analysis included sJIA patients younger than 4 years of age at the moment of TOC initiation. Patients were divided into 2 groups: with disease duration shorter than 6 month (ShorterDD group, n=35) and more than 6 month (LongerDD group, n= 19). Treatment efficacy was evaluated according to the dynamics of clinical and laboratory signs using the ACRPedi criteria. The Wallace criteria were used to evaluate whether or not remission had been achieved. Treatment safety was evaluated according to the data presented in the Adverse Event Reports.
Results: TOC was first biologics in 34/35 (97.1%) patients in ShorterDD group and 18/19 (94.7%) patients in LongerDD group. Groups were comparable in terms of disease activity at TOC initiation with 100% of patients presented active systemic features. 31/35 (88.6%) patients in ShorterDD group and 17/19 (89.5%) patients in LongerDD group have median 3 (IQR 1: 6) and 5 (IQR 3: 7.5) active joints, respectively (p=0.119). JADAS-71 level was 17.14 ± 6.25 ShorterDD group and 17.36 ± 5.45 in LongerDD group (p=0.895).
TOC showed high efficacy after first months of treatment with only 6/35 (17.1%) patients in ShorterDD group and 7/19 (36.8%) in LongerDD group remained with active systemic features (p=0.181). JADAS-71 level decreased to 0 points 26/35 patients (74.3%) in ShorterDD group and in 11/19 patients (57.9%) LongerDD group (p=0.237). After 3 month of treatment, WID was achieved by 27/35 patients (77.1%) in ShorterDD group and by 9/19 patients (47.4%) LongerDD group (p=0.038). ACR Pedi 50/70/90 was achieved by 88.6%/85.7%/80% of patients in ShorterDD group and by 84.2%/73.7%/68.4% of patients in LongerDD group after 1 months of treatment and in 77.1%/74.3%/74.3% and 84.2%/78.9%/68.4%, respectively, after 3 months of treatment.
Conclusion: Initiation of tocilizumab treatment in sJIA patients under 4 years of age is highly effective. However, early treatment within first 6 month after disease onset had advantages in speed of reaching an inactive disease as soon as after 3 months of therapy.
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SAT0493 CLINICAL PROFILE OF JIA PATIENTS WITH THE CERVICAL SPINE INVOLVEMENT: A SINGLE CENTER RETROSPECTIVE CONTINUOUS STUDY.

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Background: JIA is the most common chronic condition in pediatric rheumatology. The cervical spine (CS) involvement is associated with severe disease activity and disability and has been recognized as a factor of a poor prognosis. Data about the CS involvement is contradictory due to silent CS involvement in some patients.
Objectives: the aim of our study was to provide a clinical profile of the patients with the CS involvement.
Methods: 753 patients for last 10 years with JIA were analyzed. Patients were divided depending on the CS involvement, which was confirmed by clinical (pain, LOM) and radiological features (effusion in the CS joints). We evaluated active joints and routine tests, such as CRP, ESR, ANA-positivity and HLA B27
Results: The CS involvement was in 101 patients (13.4%). The data are in the table. The CS involvement was more frequently associated with joints of upper body, such as TMJ (23.7% vs 2.9%, p=0.000001), shoulder (29.7% vs 2.9%, p=0.000001), elbow (34.2% vs 12.2%, p=0.000001), wrist (61.4% vs 21.8%, p=0.0000001), MCP (43.6% vs 18.4%, p=0.0000001), PIP (52.5% vs 21.3%, p=0.0000001), DIP (23.8% vs 7.1%, p=0.0000001) and hip (44.6% vs 16.6%, p=0.0000001), and ankle (60.4% vs 40.2%, p=0.0001) from lower body.

Parameters	CS, yes (n=101)	CS, no (n=652)	p
Female, n (%)	69 (68.3)	388 (59.5)	0.092
ANA-positivity, n (%)	22/57 (38.6)	190/403 (47.2)	0.226
HLA B27-positivity, n (%)	12/33 (36.4)	88/275 (32.0)	0.613
Onset age, years	5.3 (2.7-10.1)	6.1 (3.0- 10.4)	0.241
ESR, mm/h	12.0 (5.0-31.0)	7.0 (3.0- 18.0)	0.0006
CRP, mg/l	3.9 (0.0- 20.0)	1.1 (0.0-9.2)	0.002
Active joints, n (%)	16.0 (9.0-28.0)	5.0 (3.0-10.0)	0.000000
Time before remission, years	2.9 (1.5-5.1)	2.2 (1.1-4.6)	0.046
Oligoarthritis	5 (5.0)	199 (30.5)	0.0000001
Polyarthritis	48 (48.0)	217 (33.3)	
Psoriatic arthritis	7 (7.0)	33 (5.1)	
Enthesitis-related arthritis	22 (21.8)	164 (25.2)	
Systemic arthritis	19 (18.9)	39 (6.0)	
Uveitis, n (%)	9/76 (11.9)	107/444 (24.1)	0,018
Oral glucocorticosteroids, n (%)	37 (36.7)	115/651 (17.7)	0.00001
Biologic, n (%)	68 (67.3)	283 (43.4)	0.000007
Remission, n (%)	57 (56.4)	428 (65.6)	0.072
Flare, n (%)	10 (9.9)	128/651 (19.7)	0.018

Conclusion: The main risk factors of CS involvement in JIA were polyarthicular and systemic arthritis, high inflammatory activity and involvement of joints of upper body. Patients with CS involvement required more often biologics.
Disclosure of Interests: None declared
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SAT0494 RITUXIMAB IN REFRACTORY PEDIATRIC RHEUMATIC DISEASES: FOCUS FOR THE SAFETY IN REAL CLINICAL PRACTICE

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Background: Rituximab (RTX) is now approved only for pediatric patients (pts) 2 years of age and older with granulomatosis with polyangiitis or microscopic polyangiitis, but it has been used with success to treat another rheumatic diseases (RD) in children despite the status "of label".
Objectives: to analyze the safety of RTX in children with various RD who did not respond to conventional therapy.
Methods: In our retrospective study safety data was analyzed for all pts, who received at least one infusion of RTX. The dose of RTX was established as 375 mg/m^2 of body surface area, administered by intravenous infusion once weekly for 1 to 4 weeks, depending on the CD19 lymphocyte count.
Results: 81 patients with RD, who received RTX, were included: 38 (46.9%) with systemic lupus erythemathosis (SLE), 16 (19.75%) – JIA, polyarthritis (2 pts - RF negative, 14 - RF positive), 9 (11.1%) - systemic JIA (sJIA), 6 (7.4%) – *systemic sclerosis (SSc), 5 (6.2%)* – primary Sjogren's syndrome (pSS), 2 (2.5%) - *juvenile dermatomyositis* (JDM), 4 (4.9%) - mixed *connective tissue disease (MCTD)* and 1 with *livedoid vasculitis* (LV). Most were female – 69 (85.2%). The median age at onset – 11.6 years [interquartile range (IQR) 7.9; 14.3], median age of the starting therapy - 15.2 [IQR 12.5; 16.85] and median disease duration - 2.8 [IQR 1.0; 4.6]. 53 pts (65.4%) reported more than one course of RTX, maximum - 10. The median time between each course was 182 days [IQR 156–315]. The RTX was effective in 95% pts, ineffective in 5% (2 pts with sJIA, 2 pts with SLE and macrophage activation syndrome (MAS)). Adverse events (AE) were recorded in 23 (28.4%) pts, included upper respiratory tract infections – 7 (8.6%), urinary tract infections – 2 (2.5%), short-term infusion reactions that did not require discontinuation of therapy – 2 (2.5%), clinically insignificant neutropenia (grade I-II) – 4 (4.9%), decrease of IgG level was detected in 14 (17.5%) pts (median 5.5 g/l [IQR 4.0; 6.9]). The infection rate in pts with a low IgG level was 35.7%, in pts with neutropenia wasn't recorded. Serious AE were recorded in 16 (19.7%) pts: sepsis – 4, pneumonia – 3, herpes zoster – 1, serious infusion reactions – 2, serious postinfusion reactions within 3 to 10 days – 4 (3 – MAS, 1 – hemorrhagic vasculitis), death – 2 pts with SLE and MAS (therapy of RTX was inefficiency). In general, various AE were registered in 55.6% of pts with sJIA, in 52.6% of pts with SLE, 50% of pts with SSc and JDM, and 80% of pts with pSS. Discontinuation of therapy due to SAE was observed in 15 pts (18.5%).

Conclusion: Our study demonstrated that RTX is highly effective in children with RD, the majority with SLE, but the safety data obtained indicate the need for careful monitoring of therapy, primarily taking into account the frequency of infections. A decrease in IgG level was observed in a small proportion of pts and did not correlate with the incidence of infections. The frequency of serious infections was low.

Disclosure of Interests: None declared
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SAT0495 **LONG TERM OUTCOME OF JUVENILE IDIOPATHIC ARTHRITIS IN ADULTHOOD; THE MONOCENTRIC EXPERIENCE OF 520 PATIENTS FOLLOWED FOR 20 YEARS IN A TRANSITION TERTIARY CLINIC OF PEDIATRIC RHEUMATOLOGY.**

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Background: Juvenile Idiopathic Arthritis (JIA) is a chronic pediatric inflammatory disease that shows many differences compared to adult-onset arthritis. The different clinical manifestations, the assessment and the management of JIA is the reason that the transition from childhood to adulthood is an important multidimensional process that emphasizes a lot of aspects.
Objectives: To describe the long-term outcome of JIA.
Methods: Five-hundred and twenty patients affected by JIA and referred to a transition care rheumatology tertiary centre were considered between 1999 and 2019. The outcome assessment included remission, disease duration, medications, number of prosthesis implantation, pregnancies, mortality and social integration (employment status and educational level).
Results: A hundred and thirty-eight (26%) males and 382 (73%) females were included; 157 (30%) patients were lost to follow up. The mean age of the patients was 27 (18-57) years, with a mean age at onset of 8 years and an average disease duration of 19 years. Subtypes of JIA at disease onset included 252 (48%) oligoarthritis, 134 (26%) polyarthritis, 64 (12%) systemic arthritis, 22 (4%) psoriatic arthritis, 43 (8%) enthesitis related arthritis and 1 (0.1%) undifferentiated arthritis. Ninty-three (18%) patients suffered of uveitis. Ninty-five implant prosthesis and 16 arthrodesis were recorded. At follow up 198 (38%) patients were on remission of which 107 (20%) off medication. Among the 322 patients still on medication, 84 (16%) were under treatment with oral steroids, 226 (43%) with sDMARDs and 249 (40%) with bDMARDs. Five deaths (1%) occurred in this cohort. Two hundred and thirty-five subjects had a higher educational level, 327 had an employment. We have data of twenty-nine pregnancies. The transition age was considered after the age of 16 years old. The key word for the management of this cohort was the multidisciplinary approach towards each patient, with the collaboration of other specialists (ophthalmologist, orthopedic, dermatologist, gastroenterologist, obstetric and psychologist).
Conclusion: In the era of biologic therapy the long-term outcome of JIA underwent an outstanding improvement regarding a lot of variables. Two hundred and thirty-two patients were still followed, not only because of the continuation of the biological therapy, but also for a multidisciplinary care even during remission. JIA often persists over the adulthood, therefore the long term follow-up and care of these patients needs to be conducted by a rheumatologist expertized in JIA in collaboration with other specialists.

Disclosure of Interests: None declared
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SATURDAY, 06 JUNE 2020

Basic and translational science in paediatric rheumatology

SAT0496 **INTERROGATING THE CIRCULATORY IMMUNE ARCHITECTURE OF ENTHESITIS-RELATED ARTHRITIS**

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Background: Enthesitis-related arthritis (ERA) is one of the most common subtype of juvenile idiopathic arthritis (JIA) in Asia[1]. It carries a poor prognosis, but limited knowledge of its pathogenesis hampers clinical diagnosis and treatment.
Objectives: We hypothesise multiple aberrations from the healthy immunome culminating in an imbalance between the immune effector and regulatory cell subsets as key for driving ERA pathogenesis. Thus, we employed a comprehensive high-dimensional interrogative strategy using mass cytometry to assess the ERA immune architecture[2].
Methods: We examined peripheral blood mononuclear cells from 30 ERA patients (15 with active sacroilitis, 15 without active sacroilitis) within the first two years of disease and 30 healthy paediatric controls with mass cytometry, using two extensive antibody panels encompassing key lineage and functional markers. Dimensional reduction and unsupervised clustering were performed to identify immune cell subsets differentially present in ERA patients. Manual gating was performed to further describe observed differences in subset frequencies. These subsets were statistically evaluated with reference to the healthy cohort and their association with disease activity determined.
Results: We identified broad differences in the ERA circulatory immune architecture that involved both innate and adaptive immune cell populations, notably with the enrichment of naive CD4+ T cells as well as depletion of cytolytic NK cells ($CD56^{dim}CD16+$). The chemotactic profiles of their subsets also differed in ERA patients, which underscores their migratory capacity and hence potential effector role in the ERA arthritic microenvironment. In addition, there were some dissimilarities in the circulatory immunome of ERA patients with active sacroiliitis as compared to those without, which alludes to a possible mechanistic basis behind the disease complication.
Conclusion: This is the first study, via deep parameterisation afforded by mass cytometry, to demonstrate a concomitant dysregulation of both innate and adaptive immune cell subsets in ERA patients. Further mechanistic studies of these immune cell subsets and their functional networks will inform the development of diagnostic and prognostic markers that can reliably predict clinical fate in ERA, thereby complementing clinical assessment in the care of ERA patients.

References:
[1] Arkachaisri et al. Paediatric rheumatology clinic in Southeast Asia: are we different? *Rheumatology (Oxford)*. 2017.
[2] Tay et al. Immunomics in pediatric rheumatic diseases. *Front Med (Lausanne)*. 2019.

Disclosure of Interests: None declared
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SAT0497 **A PILOT PROTEOMIC ANALYSIS OF PLASMA BIOMARKERS IN IGA VASCULITIS**

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Background: IgA vasculitis/ Henoch Schönlein Purpura (IgAV/HSP) is the most common vasculitis of childhood, characterized by the IgA1 immune deposits in the small vessels. Although it is very common, the understanding of its molecular pathogenesis is still very limited.
Objectives: We aimed to analyse plasma proteomes of IgAV/HSP patients using nano liquid chromatography – tandem mass spectrometry (nLC-MS/MS) to investigate the disease pathogenesis.
Methods: IgAV/HSP was diagnosed according to the Ankara criteria in 2008 (1). Five active IgAV/HSP patients and two age and gender-matched health controls were enrolled in this pilot study. Serum samples from subjects were collected on the same day of IgAV/HSP diagnosis and before steroid or other immunosuppressive treatment initiated. Sample preparation was carried out using PreOmics İST Kit. We investigated the alteration of serum proteome using the nano LC-MS/MS approach. Bruker raw files were analyzed using the proteomics software Max Quant (1.6.7.0). The human reference proteome set from UniProt was used to identify proteins. Proteomic data were analyzed with Perseus 1.6.7.0.
Results: The data file includes peptide and protein identification, accession numbers, protein and gene names, sequence coverage and label free quantification (LFQ) values of each sample. 345 proteins were reported per sample. Identifications from the reverse decoy database, identified by site only and known contaminants were excluded. Data were log transformed. Two sample T-test was performed between groups. We identified 23 significantly different expressed proteins (Table 1). Mainly the differentially expressed proteins were in the Ig and complement pathway, innate immune inflammatory,

and were among the structural cytoskeletal filaments. The levels of Complement C3, Apolipoprotein E, Glyceraldehyde-3-phosphate dehydrogenase, Filamin-A, Alpha-1B-glycoprotein, Tubulin beta-1 chain, Lipopolysaccharide-binding protein, Ig mu chain C region were significantly higher in IGAV patients.

Table1. List of differentially expressed proteins identified in IgAV compared to healthy controls

Majority protein IDs	Protein names	Gene names	p-value
O75822	Eukaryotic translation initiation factor 3 subunit J	EIF3J	0,004
P05106; H3BM21	Integrin beta-3	ITGB3	0,008
P02743	Serum amyloid P-component	APCS	0,015
A0A0J9YX35	unknown		0,015
A2NJV5; A0A075B6S2	unknown	IGKV A18; IGKV2D-29	0,021
P02679	Fibrinogen gamma chain	FGG	0,022
A0A0C4DH36	unknown	IGHV3-38	0,024
P0DP03; P01768	Ig heavy chain V-III region CAM		0,024
O14791	Apolipoprotein L1	APOL1	0,025
P01024	Complement C3	C3	0,030
P02675	Fibrinogen beta chain; Fibrinopeptide B	FGB	0,030
P01860	Ig gamma-3 chain C region	IGHG3	0,031
A0A075B7D8	unknown	IGHV3OR15-7	0,034
P02649	Apolipoprotein E	APOE	0,035
P04406	Glyceraldehyde-3-phosphate dehydrogenase	GAPDH	0,037
A0A075B6R2; A0A087WW49	unknown	IGHV4-4	0,039
P21333	Filamin-A	FLNA	0,043
P04217	Alpha-1B-glycoprotein	A1BG	0,045
P02790	Hemopexin	HPX	0,046
A0A0C4DH25	unknown	IGKV3D-20	0,047
Q9H4B7	Tubulin beta-1 chain	TUBB1	0,049
P18428	Lipopolysaccharide-binding protein	LBP	0,049
P01871	Ig mu chain C region	IGHM	0,050

Conclusion: This pilot proteomic study may provide us a perspective in the pathogenesis of IgAV (HSP).

References:

[1] Ozen S, Pistorio A, Iusan SM, Bakkaloglu A, Herlin T, Brik R, et al. EULAR/PRINTO/PRES criteria for Henoch-Schonlein purpura, childhood polyarteritis nodosa, childhood Wegener granulomatosis and childhood Takayasu arteritis: Ankara 2008. Part II: final classification criteria. Ann Rheum Dis 2010;69(5):798e806.

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SATURDAY, 06 JUNE 2020

Paediatric rheumatology

SAT0498

ENTHESITIS-RELATED ARTHRITIS (ERA) IN SOUTHEAST ASIA: A DECADE OF SINGAPORE EXPERIENCE

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Background: ERA is the most common Juvenile Idiopathic Arthritis (JIA) subtype in Singapore (1), but less common in the West. Clinical characteristics and treatment of ERA in the region is not well-described thus impede the diagnosis and management plan which could lead to poorer outcomes.

Objectives: To describe the clinical characteristics, joint manifestation and treatment of ERA in a large monocentric cohort in Singapore over 10-year period

Methods: Children diagnosed with ERA according to ILAR criteria with a minimum follow-up of 3-month duration were recruited from our registry, from 2009 to 2019, at KK Women's and Children's Hospital, Singapore. Nonparametric descriptive statistics including median (IQR) were used to described data. Kaplan-Meier survival analyses were used to estimate the probability of ever sacroiliitis development. Multivariate logistic and Cox regression analyses were used to determine predictors as appropriate. The significant level was set at < 0.05.

Results: A cohort of 147 ERA out of 439 JIA patients (male 88%; Chinese 80%) were included. Median age at onset was 11.9 yrs (IQR9.4-14.0) and disease duration was 6.0 yrs (3.1-8.9). Median lag period was 2.9 mo (1.2-7.4). Family history of HLA-B27 related diseases was positive at 8%. Acute uveitis occurred only 3%. Joint distribution at diagnosis and cumulative involvement were shown in Fig 1. Hip, sacroiliac and knee were the three most common joints involved. 24% presented with enthesitis and Achilles tendon enthesis were the most common. Majority presented with pauciarthritis (84%) while 12% of patients had no peripheral joint involvement. 40% of patients presented with sacroiliitis (SIs) with 59% had bilateral involvement. Median duration to develop SIs was 7.6 mo (IQR 2.0-26.9). Probability of SIs development was 36%, 55% and 70% at 1, 5 and 10 yrs after onset, respectively. Interestingly, neg HLA-B27, female and older age at onset predicted SIs (p=0.001-0.044). Hip arthritis increased (p=0.043) but tarsitis decreased (p=0.031) the risk of SIs. Again, female, hip arthritis at diagnosis and neg HLA-B27 had a shorter time to SIs (p=0.004-0.007). Fig 2 showed medication used in our ERA cohort. Methotrexate (MTX) remained the most common DMARD used. However, 76% required anti-TNF therapy (aTNF) due to MTX failure. For SIs patients, 86% were on MTX but 85% of these, as compared to patients without axial disease, 60%, failed MTX. Only 10% of patients had aTNF without MTX.

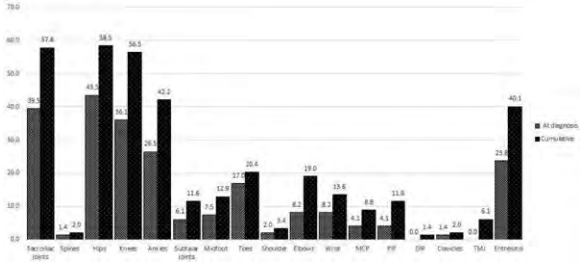


Fig 1. Proportion of joint involvement at onset and cumulative involvement during the course of disease (%)

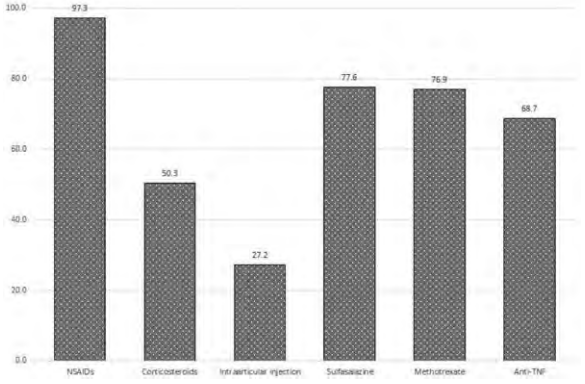


Fig 2. Proportion of medications used in ERA cohort during the course of disease (%)

Conclusion: Our ERA cohort had less uveitis and family history of HLA-B27 associated diseases, but comparable gender and age at onset as compared to reports elsewhere(2). Up to 40% of our patients presented with SIs and/or enthesitis. Majority of SIs developed within the first 5 yrs (88%) for which over one-half developed within the first year. When considering only ERA patients, interestingly that female, neg HLA-B27 and older age increased risk of SIs development. 77% of patients were treated with MTX, but 76% of the patients required aTNF later. As for SIs, concurred with adult AS data, 85% failed MTX. About one-half of non-axial disease patients failed MTX which is less response rate as compared to other JIA subtypes.

References:
[1] Arkachaisri T, Tang SP, Daengsuwan T, Phongsamart G, Vilaiyuk S, Charuvanij S, et al. Paediatric rheumatology clinic population in Southeast Asia: are we different? Rheumatology. 2017;56(3):390-8.
[2] Mistry RR, Patro P, Agarwal V, Misra DP. Enthesitis-related arthritis: current perspectives. Open access rheumatology: research and reviews. 2019;11:19-31.

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SAT0499 PREVALENCE OF ULTRASOUND FINDINGS SUGGESTIVE OF INFLAMMATORY ARTHRITIS IN CHILDREN WITH SKIN PSORIASIS (CHILDECHOPSO)

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Background: The prevalence of psoriasis (PsO) in children is estimated between 0.5-1% (1), and can be associated with muskuloskeletal involvement, although the prevalence and typology of such involvement is unknown. (2)
Over the last years ultrasound associated with Doppler (PDUS) has become an important tool for evaluating joint involvement in children with Juvenile Inflammatory arthritis (JIA). Several studies have shown the high sensitivity of this technique for detecting joint involvement, as well as high acceptability, due to the lack of radiation or of sedation (3).
Objectives: To evaluate the prevalence of joints and entheses involvement in children affected by PsO.
Methods: Observational cross-sectional study aiming at evaluating 150 consecutive children (≤16 years) affected by skin PsO and addressed by a dermatologist. For each child a standardized clinical and ultrasound evaluation of joint and entheses is performed at the following bilateral sites: a) Entheses: quadriceps tendon, proximal and distal patellar ligament, Achilles tendon, plantar fascia and extensor elbow tendon), b) joints: metacarpophalangeal, proximal and distal interphalangeal, wrist, elbow, knee, ankle, and metatarsophalangeal. PDUS evaluation is performed by an independent examiner, blinded to the clinical assessment of each subject.
Results: 41 patients were included until now, where 9 patients presented some kind of symptom (painful joint or enthesis), 24 patients have family history of psoriasis and none of them had family history of psoriatic arthritis. Demographic and clinical characteristics are shown in table 1, whilst PDUS findings in Table 2.

Table 1. Demographic and clinical characteristics:

	Total (n=41)	Asymptomatic (n=32)	Symptomatic (n=9)	p
Males	22 (53.7%)	18 (56.3%)	4 (44.4%)	NS
Age	9.4 ± 3.9	8.91 ± 3.5	11.3 ± 4.6	NS
Pso duration (years)	**3.5 ± 3.4**	**2.9 ± 2.9**	**5.6 ± 4.5**	**<0.05**
PASI	5 ± 4.3	4.8 ± 4.5	5.7 ± 3.56	NS
BSA	4.3 ± 3.9	4.47 ± 4.3	4.1 ± 2.26	NS
Nail involvement	25 (61%)	19 (59.4%)	6 (66.7%)	NS
Plaques psoriasis	20 (48.8%)	14 (43.8%)	6 (66.7%)	NS
TJC ≥1, n/tot (%)	**9 (22%)**	**0 (0)**	**9 (100%)**	**<0.001**
SJC ≥1, n/tot (%)	**2 (4.9%)**	**0 (0)**	**2 (22.2%)**	**<0.05**
Entheseal pain, n/tot (%)	**6 (14.6%)**	**0 (0)**	**6 (66.7%)**	**<0.001**
Dactylitis	0	0	0	NA

PASI: Psoriasis area severity index. BSA: Body surface area. TJC: Tender Joint Count. SJC: Swollen Joint Count.

Conclusion: This study shows that the presence of ultrasound abnormalities was higher in the symptomatic group and considering the fact that the most frequent inflammatory ultrasound finding was enthesitis, we might consider the enthesis as a possible landmark for developing juvenile psoriatic arthritis.
References:
[1] Michalek et al. J Eur Acad Dermatol Venereol, 2017
[2] Petty et al. J Rheumatol, 2004
[3] Buchmann et al. Radiol Clin N Am, 2004
Acknowledgments: This research was conducted while Luis Coronel was a PARTNER Fellow
Disclosure of Interests: None declared

Table 2 PDUS Findings:

Patients	Total (n=41)	Asymptomatic (n=32)	Symptomatic (n=9)	p
≥1 ultrasound abnormality, n/tot (%)	19 (46.3%)	13 (40.6%)	6 (66.7%)	NS
≥1 joint effusion, n/tot (%)	11 (26.8%)	9 (28.1%)	2 (22.2%)	NS
≥1 synovitis, n/tot (%)	3 (7.3%)	1 (3.1%)	2 (22.2%)	NS
≥1enthesitis, n/tot (%)	**7 (17.1%)**	**3 (9.4%)**	**4 (44.4%)**	**<0.05**
≥1 tenosynovitis, n/tot (%)	0 (0)	0 (0)	0 (0)	NA
≥1 nail with modified structure, n/tot (%)	22 (53.7%)	19 (59.4%)	3 (33.3%)	NS

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SAT0500 HOW THE ADULT CRISS WORKS IN PEDIATRIC JSSC PATIENTS - RESULTS FROM THE JUVENILE SCLERODERMA INCEPTION COHORT

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Background: The Composite Response Index in Systemic Sclerosis (CRISS) was developed by Dinesh Khanna as a response measure in patients with adult systemic sclerosis. CRISS aims to capture the complexity of systemic sclerosis and to provide a sensitive measure for change in disease activity. The CRISS score is based on a two-step approach. First, significant disease worsening or new-onset organ damage is defined as non-responsiveness. In patients who did not fulfill the criteria of part one, a probability of improvement is calculated for each patient based the Rodnan Skin Score (mRSS), percent predicted forced vital capacity (FVC%), patient and physician global assessments (PGA), and the Health Assessment Questionnaire Disability Index (HAQ-DI). A probability of 0.6 or higher indicates improvement.
Objectives: The objective of this study was to validate the CRISS in a prospectively followed cohort of patients with juvenile systemic sclerosis (jSSc).
Methods: Data from the prospective international inception cohort for jSSc was used to validate the CRISS. Patients with an available 12-months follow-up were included in the analyses. Clinically improvement was defined by the anchor question about improvement (much better or little better versus almost the same, little worse or much worse) in patients overall health due to scleroderma since the last visit provided by the treating physician.
Results: Forty seven jSSc patients were included in the analysis. 74.2% had diffuse subtype. The physician rated the disease as improved in 34 patients (72.3%) since the last visit. No patient had a renal crisis or new onset of left ventricular failure during the 12-months follow-up. Three patients (3.4%) each had a new onset or worsening of lung fibrosis and new onset of pulmonary arterial hypertension. In total, 6 patients resulted in a rating of not improved based on the CRISS in part I. The mRSSS, FVC%, CHAQ and PGA significantly improved during the 12-months follow-up in patients who were rated as improved. The predicted probability based on the CRISS algorithm resulted in an area under curve of 0.77 predicting the anchor question of improvement. In summary, 33 (70.0%) patients were correctly classified by the adult CRISS score resulting in an overall area under curve of 0.7.
Conclusion: The CRISS score was evaluated in a pediatric jSSc cohort for the first time. It showed a good performance. However, it seems that the formula of part II of the CRISS score needs a calibration to pediatric jSSc patients.
Disclosure of Interests: Jens Klotsche: None declared, Ivan Foeldvari Consultant of: Novartis, Ozgur Kasapcopur: None declared, Amra Adrovic: None declared, Kathryn Torok: None declared, Valda Stanevicha: None declared, Jordi Anton Grant/research support from: grants from Pfizer, abbvie, Novartis, Sobi. Gebro, Roche, Novimmune, Sanofi, Lilly, Amgen, Grant/research support from: Pfizer, abbvie, Novartis, Sobi. Gebro, Roche, Novimmune, Sanofi, Lilly, Amgen, Consultant of: Novartis, Sobi, Pfizer, abbvie, Consultant of: Novartis, Sobi, Pfizer, abbvie, Speakers bureau: abbvie, Pfizer, Roche, Novartis, Sobi, Gebro, Speakers bureau: abbvie, Pfizer, Roche, Novartis, Sobi, Gebro, edoardo marrani: None declared, Maria T. Terreri: None declared, Flávio R. Sztajnbok: None declared, Cristina Battagliotti: None declared, Lillemor Berntson Consultant of: paid by Abbvie as a consultant, Speakers bureau: paid by Abbvie for giving speaches about JIA, Despina Eleftheriou: None declared, Gerd Horneff Grant/research support from: AbbVie, Chugai, Merck Sharp & Dohme, Novartis, Pfizer, Roche, Speakers bureau: AbbVie, Bayer, Chugai, Merck Sharp & Dohme, Novartis, Pfizer, Roche, Farzana Nuruzzaman: None declared, Nicola Helmus: None declared
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SAT0501

EARLY START OF BIOLOGICAL TREATMENT IN JUVENILE IDIOPHATIC ARTHRITIS: DOES A THERAPEUTIC WINDOW EXIST IN REAL LIFE?

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Background: Biological therapy (BT) has changed the treatment and perspectives of JIA patients but little is known about when is the best moment to start BT and the impact of this prompt iniciation.
Objectives: To analyze the response to BT of Juvenile Idiophatic Arthritis (JIA) patients according to the time when the BT was started.
Methods: A retrospective, descriptive study was conducted on JIA patients followed up in a referal hospital that started BT up to 24 months after diagnosis from 2000 to 2018. Disease activity was measured, at 2 years after diagnosis, according to Wallace criteria for remission (absence of: active arthritis, active uveitis, fever, rash or any other manifestation attributable to JIA, normal CRP and ESR, PGA indicating no active disease) for at least 6 months.
Results: 55 JIA patients that started BT up to 24 months from diagnosis were analyzed. 69,1% were girls with a median age at diagnosis of 8 years old IQR(3-13), median age at the start of BT of 9 years old IQR(3-13). Regarding JIA categories: 25,5% were Oligoarticular Persistent (OligP), 18,2% Systemic JIA (sJIA), 16,4% Entesitis related Arthritis (ERA), 12,7% Psoriatic Arthritis (APso) and Polyarticular RF- (PolyRF-), 5,5% Oligoarticular Extended (OligE) and Polyarticular RF+ (PolyRF+), 3,6% Undifferentiated (Und). 20% of patients had uveitis during followup. Conventional DMARD (cDMARD) was indicated in 83,6% of patients (95,7% Methotrexate) at diagnosis [median 0 months IQR(0-2,3)]. At the end of followup (2 years) only 30,9% of patients continued with cDMARDs. The main causes of discontinuation were: adverse events (46,7%), remission (36,7%). TNF inhibitors were precribed in 81,8% of patients and 18,2% of patients recieved two BT during the first 2 years from diagnosis. 54,5% of BT were indicated during the first 6 months from diagnosis, 27,3% from 7 to 12 months, 12,7% from 13 to 18 months, 5,5% from 19 to 24 months. After 2 years from diagnosis, 78,2% of patients were on remission and 21,8% active. Among patients with active disease: 75% had arthritis, 16,7% had uveitis and 8,3% had both. There were no differences regarding disease activity among patients with uveitis and neither taking cDMARDs. Regarding JIA categories: 66,7% of OligE, 57,1% of PolyRF- and 57,1% of APso patients were active at 2 years from diagnosis when compared to the other categories (p=0.004).
Patients on remission at 24 months from diagnosis started sooner the BT than active patients [CI 95% (0,46-8,29) p=0,029]. The time when the BT was started was correlated to the activity at 2 years (K= 0,294 p=0,029). When the BT was prescribed after 7,5months from diagnosis it was correlated, in a COR curve, with a higher probability of active disease at 2 years (S= 0,67 E= 0,63). There was a correlation, among patients on remission at 2 years, between prompt start of BT and less time to reach remission (K= -0,345 p=0,024). Patients with active disease at 2 years, regardless of moment of BT iniciation, required more BT during follow-up (p=0,002).
Conclusion: Prompt iniciation of BT was correlated with a better outcome. JIA patients that started BT early after diagnosis had a higher probability of remission after 2 years. Starting BT after 7,5 months was correlated with a higher probability of active disease at 2 years. Active disease at 24 months was correlated with persistent active disease during follow-up.
Disclosure of Interests: None declared
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SAT0502

LONG-TERM OBSERVATIONAL SAFETY SURVEILLANCE OF GOLIMUMAB TREATMENT FOR POLYARTICULAR JUVENILE IDIOPATHIC ARTHIRTIS—AN INTERIM ANALYSIS

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Background: Golimumab (GOL) is approved for treatment of polyarticular juvenile idiopathic arthritis (pJIA) in patients 2 years and older. Data on long-term safety in this indication are limited.
Objectives: Prospective monitoring of long-term safety and effectiveness of GOL in routine care using the German BIKER registry.
Methods: In this non-interventional study baseline and safety parameters were compared between patients initiating GOL and contemporary matched control cohorts starting either an alternative TNF inhibitor (TNFi) or methotrexate (MTX) without exposure to a biologic. Efficacy outcomes were JADAS10, JIA ACR scores, joint counts and Childhood Health Assessment Questionnaire disability-index (CHAQ-DI). Safety assessments were based on adverse event (AE) reports.
Results: From 2016 to 2019, 55 patients initiating GOL have been recruited and matched to 110 patients starting alternative TNFi and 47 biologic-naïve patients. Patients starting GOL had a longer disease duration (6.8y vs. 4.1 y and 1.0y; p<0.0001) and use of GOL was significantly more often second-line (85% vs 31% and 0%, p<0.0001). Disease activity was lower at baseline compared to MTX patients as indicated by active joint counts, JADAS10 and concomitant steroid use. Otherwise they were comparable with patients treated with other TNFi (Table 1).

Table 1 Comparison of GOL cohort with (1) other TNFi cohort and (2) MTX cohort.

	GOL N=55	Other TNFi N=110	MTX N=47	p-value # GOL vs TNFi/MTX
Gender female, n (%)	44 (80)	86 (78)	34 (72)	0.8/0.5
Age at baseline, mean (SD), years	13.6 (2.8)	13.6 (3.0)	13.1 (3.4)	1.0/0.4
Disease duration, mean (SD), years	6.8 (4.5)	4.1 (3.8)	1.0 (1.6)	**<0.0001**
RF neg. polyarthritis, n (%)	28 (51)	53 (48)	29 (62)	0.7/0.3
RF pos. polyarthritis, n (%)	6 (11)	18 (16.4)	11 (23.4)	0.5/0.1
Extended oligoarthritis, n (%)	20 (36.4)	37 (33.6)	6 (12.8)	0.7/**0.007**
Psoriatic arthritis	1 (1.8)	2 (1.8)	1 (2.1)	1.0/1.0
Pretreatment bDMARD n(%)	47 (85.5)	34 (30.9)	0	**<0.0001**
Concomitant steroids, n (%)	9 (16.4)	26 (23.6)	25 (53.2)	0.3/**0.0001**
Active joint count, mean (SD)	4.6 (4.0)	5.4 (6.1)	9.7 (6.5)	0.4/**<0.0001**
CHAQ DI, mean (SD)	0.4 (0.4)	0.5 (0.6)	0.6 (0.7)	0.3/0.07
ESR, mm/h, mean (SD)	20.4 (27.6)	15.4 (18.6)	21.4 (18.6)	0.2/0.8
JADAS10, mean (SD)	11.3 (6.0)	12.4 (5.8)	16.9 (5.4)	0.3/**<0.0001**
AE, n (rate/100PY; 95%CI)	45 (96; 72-128)	106 (114; 94-138)	39 (107; 78-146)	0.3/0.6
SAE, n (rate/100PY; 95%CI)	2 (4.2; 1.1-17)	5 (5.4; 2-13)	1 (2.7; 0.4-19)	0.8/0.7
Infectious AE, n (rate/100PY; 95%CI)	6 (12.8; 5.7-28)	11 (11.8; 6.5-21)	9 (24.5; 13-47)	0.9/0.2
Serious infections, n (rate/100PY; 95%CI)	0	2 (2.2; 0.5-8.6)	0	n.a.
Uveitis new manifestation	1 (2.1; 0.3-15)	2 (2.2; 0.5-8.6)	0	1.0/n.a.

In GOL treated patients a marked clinical response was noted at 6 months and beyond demonstrated by a significant decrease of the mean JADAS 10 from 11.3 to 6.4 (p=0.0008), as well as JIA ACR 30/50/70/90 response rates of 56/56/35/21%. JADAS remission and minimal disease activity was observed in 18% and 47% after 6 months and in 29% and 43% of patients after 12 months.
Rates of AE, SAE and infectious AE were comparable between the GOL cohort (96, 4.2 and 12.8/100PY), the alternative TNFi cohort (114, 5.4 and 11.8/100PY) and the MTX cohort (107, 2.7 and 24.5/100PY). SAE reported in the GOL cohort were uveitis and JIA flare (each 1). Two serious infections, both influenza, were reported in the alternative TNFi cohort, none in the GOL cohort. No case of pregnancy, malignancy or death was reported.
Conclusion: Interim results from this ongoing safety surveillance study indicate acceptable safety and tolerability of GOL in pJIA that is comparable to treatment with alternative TNFi or MTX. The long-term effectiveness data reinforce the established efficacy of GOL in pJIA treatment.
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SAT0503

SERIOUS INFECTION RISK IN PEDIATRIC PATIENTS WITH LOW IMMUNOGLOBULIN LEVELS FOLLOWING RITUXIMAB TREATMENT FOR GRANULOMATOSIS WITH POLYANGIITIS (GPA) OR MICROSCOPIC POLYANGIITIS (MPA)

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Background: Low immunoglobulin (Ig) levels can occur after rituximab treatment, but the clinical significance is not completely understood. Not all patients (pts) who develop low Ig levels after rituximab are at an increased risk of serious infection (SI), but factors such as pre-existing low Ig levels, prior biologic therapies, history of SI and other disease and age-related factors may increase the risk.
Objectives: To assess the risk of SI in pediatric pts with prolonged low IgG or IgM serum concentrations following rituximab treatment for GPA or MPA in a global clinical trial.
Methods: In the Phase 2a PePRS study (WA25615), pts aged ≥ 2 to ≤ 18 yrs with GPA or MPA received 4 weekly intravenous rituximab infusions of 375 mg/m^2 body surface area and concomitant oral glucocorticoid taper. After 6 months, pts could receive further rituximab and/or other immunosuppressants at the investigator's discretion during a minimum 12-month follow-up phase. Pts with IgG/IgM levels below age-specific reference ranges at baseline were excluded. Ig levels were measured every 4-12 wks. SI occurrence was assessed during/after low IgG or IgM. Prolonged low Ig was defined as IgG or IgM levels < lower limit of normal (LLN) reference range for age for a ≥ 4-month period.
Results: All 25 pts completed 4 weekly rituximab infusions and the 6-month Remission Induction Phase; 24/25 pts completed ≥ 18 months of follow-up. 17 pts received additional rituximab treatment on or after Month 6. 11 pts received concomitant immunosuppressants (cyclophosphamide, azathioprine, mycophenolate mofetil) during the study. All pts had a decrease in IgG and IgM mostly after the first rituximab infusion. There was no consistent trend in IgG or IgM levels over time and no clear relationship between low IgG or IgM levels and the number of follow-up rituximab treatments. 18 pts (72%) had prolonged low IgG ≥ 4 months, of whom 5 had IgG levels < LLN at screening and/or baseline; in 7 pts, IgG levels returned to within normal range by study end. During or after prolonged low IgG, 6/18 pts experienced a total of 7 SIs. Three pts received treatment with intravenous Ig. 19 pts (76%) had prolonged low IgM, of whom 5 had IgM levels < LLN at screening and/or baseline. During or after prolonged low IgM levels, 6/19 pts experienced a total of 8 SIs. There were no deaths or study discontinuation due to SI. All pts with prolonged low IgG or IgM had past and/or concomitant treatment with steroids and/or immunosuppressants as potential contributory factors. Analysis of SI onset in relation to timing of low Ig was limited due to protocol-defined time points for Ig assessments.
Conclusion: In pediatric pts with GPA/MPA treated with rituximab, there was no consistent pattern in IgG or IgM levels over time. The majority of pts with prolonged low IgG or IgM did not experience any SIs; no increase in the number of SIs was observed over time or with multiple rituximab treatments. While no firm conclusions can be made on a possible relationship between prolonged low IgG or IgM and risk of SI following rituximab due to study limitations (low pt numbers, lack of placebo comparator), these observations are consistent with the known rituximab safety profile in adult pts with GPA/MPA.
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SAT0504 STING-ASSOCIATED VASCULOPATHY WITH ONSET IN INFANCY (SAVI SYNDROME) CAN MIMIC JUVENILE IDIOPATHIC ARTHRITIS.

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Background: STING-associated vasculopathy with onset in infancy (SAVI syndrome) can mimic Juvenile Idiopathic Arthritis.
Objectives: The aim of this study is to describe a detailed cohort of patients with SAVI syndrome and highlight the similarity, in some cases, of the phenotype of this disease with Juvenile Idiopathic Arthritis.
Methods: 3 patients diagnosed with SAVI syndrome from the institution Hospital Universitari Vall d'Hebron were recruited. Written informed parental consent was obtained for the use of clinical data and pictures reported. Demographic, clinical, analytical, lung function and previous and current treatment are described.
Results: Patient 1, a 11-year-old boy, was identified to carry a de novo p.V155M mutation in TMEM173. He presented at first month of life with recurrent bronchial infection and skin vasculitis lesions in nose, cheeks and toes. Arthritis affected hands, toes and knees but no erosions were found at X-Ray. Fever was not reported. High-resolution computed tomography (HRCT) of the lungs identified a nonspecific interstitial pneumonia (NSIP) and a lung biopsy showed lymphoid hyperplasia. Elevated inflammatory markers were reported and rheumatoid factor (RF), ACPA antibodies and antinuclear antibodies (ANA) were also positive. At the age of 6 years Ruxolitinib (RX) was introduced at the initial dose of 5 mg twice daily with an improvement of skin disease and lung function. Arthritis was well controlled and RX was well tolerated.
Patient 2, a 17-year-old girl, was identified to carry a de novo p.V155 mutation in TMEM173. She presented at the age of 3 with a severe polyarthritis of large and small joints. No fever, skin or respiratory symptoms were reported at the beginning of the disease. Laboratory tests were positive for RF and ACPA antibodies. She was diagnosed with Polyarticular JIA and was treated with steroids and Methotrexate without improvement. Few months later she reported dyspnoea with recurrent bronchial infections. HRCT showed NSIP and lymphoid interstitial pneumopathy was found at the lung biopsy. RX was initiated at the age of 17 years but at this time lung fibrosis was stablished. Moreover, RX was not well tolerated due to headache. She requires continuous domiciliary oxygen and has been included to lung transplant.
Finally, patient 3, a 29-year-old man, was recently diagnosed with a de novo p.V155 mutation in TMEM173. He presented at the age of 7 years with symmetrical polyarticular arthritis after a bronchial infection that course with fever. No skin manifestations were objectified. Autoimmune lab test was positive for RF, ACPA, and ANA. With the diagnosis of Polyarticular JIA he received different treatments with no response. Due to recurrent bronchial infections a HRCT was performed showing an ILD at bases and follicular bronchiolitis with NSIP pattern in a lung biopsy. Functional tests were worsening without any response to different treatments. SAVI syndrome was suspected, and genetic test was performed with positive result. RX was initiated but compliance was not good
Conclusion: SAVI syndrome is a rare monogenic autoinflammatory disease with few cases reported in the literature. Disease phenotype could be different in every patient, with no presence of skin vasculitic lesions or fever. Patient 2 and 3, in contrast with patient 1, had severe articular and lung manifestations with no skin involvement. Furthermore, lab tests were positive for RF and ACPA and were misdiagnosed as JIA so genetic test was performed later in the follow-up. Being aware of the distinct phenotype of the disease could help the clinicians to make a PRONTO diagnostic and reassess the patients with these presentations that not respond well to conventional treatments.
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SAT0505 PLUTO TRIAL OF INTRAVENOUS BELIMUMAB IN PAEDIATRIC PATIENTS WITH CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS (CSLE): PATIENT RESPONSES OVER TIME

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Background: Belimumab (BEL) is a human monoclonal antibody that specifically inhibits B-cell activating factor (BAFF). PLUTO is an ongoing trial evaluating efficacy and safety of intravenous (IV) BEL in children ≥5 years of age with cSLE. Efficacy, and safety endpoints of PLUTO have been reported;[1] briefly, numerically more BEL vs PBO pts met the primary and major secondary efficacy endpoints. We present patient (pt) response to BEL over time.
Objectives: To evaluate changes in SLE Responder Index (SRI) 4 and SRI6 responses, and disease activity over 52 weeks, in paediatric pts receiving BEL, or placebo (PBO), plus standard SLE therapy (SST).

Methods: PLUTO (GSK Study BEL114055, NCT01649765) is a Phase 2, randomised, double-blind, placebo-controlled study. Pts 5–17 years of age with active cSLE were randomised to monthly BEL 10 mg/kg IV, or PBO, plus SST. Endpoints assessed: SRI4 and SRI6 response rate, mean percentage and absolute change from baseline in Safety of Estrogens in Lupus Erythematosus National Assessment (SELENA)-SLE Disease Activity Index (SLEDAI) and Physicians' Global Assessment (PGA) scores, and percentage of pts with no new British Isles Lupus Assessment Group (BILAG) 1A/2B organ domain scores compared with baseline, all by study visit. The last-observation-carried-forward (LOCF) principle (missing values imputed using the last available non-missing value) was applied to pts who withdrew or received protocol-prohibited medication or a dose of allowable medication that resulted in treatment failure prior to the Week (Wk) 52 visit. Descriptive statistics were used.

Results: A total of 93 pts (94.6% female, mean [SD] age 14.0 [2.49] years) were randomised for the intention-to-treat (ITT) population: 53 to BEL and 40 to PBO. Mean (SD) BEL and PBO baseline scores were 10.3 (3.34) and 10.4 (3.63) for SELENA-SLEDAI and 1.3 (0.43) and 1.4 (0.42) for PGA, respectively. Pt number with at least BILAG 1A/2B organ domain involvement at baseline was 37 (69.8%) for BEL and 29 (72.5%) for PBO. SRI4 and SRI6 responses over 52 weeks were mostly numerically higher with BEL than PBO; more BEL than PBO pts were SRI4 and SRI6 responders at Wk 52 (**Figure 1**). Unadjusted mean (SE) percentage changes from baseline over time in SELENA-SLEDAI and PGA scores generally favoured BEL over PBO, as did unadjusted mean (SE) absolute changes (**Figure 2**). Wk 52 adjusted mean (95% CI) percentage treatment difference vs PBO was -4.0% (-21.8, 13.9) for SELENA-SLEDAI and -6.1% (-23.9, 11.7) for PGA, while Wk 52 adjusted mean (95% CI) treatment difference vs PBO was -0.7 (-2.4, 1.1) for SELENA-SLEDAI and -0.1 (-0.3, 0.1) for PGA. Over the study duration, numerically more BEL than PBO pts had no new BILAG 1A/2B organ domain scores (**Figure 2**).

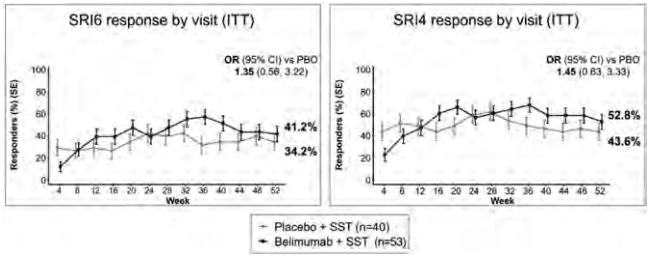


Figure 1. SRI4 and SRI6 response by study visit

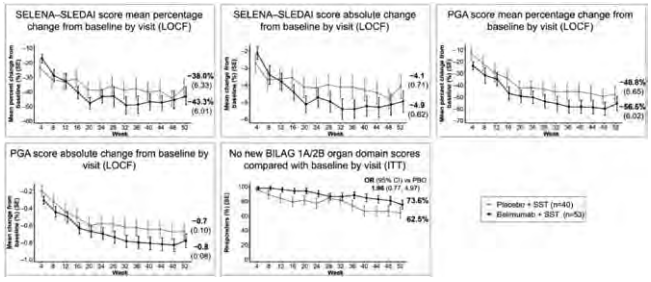


Figure 2. SELENA-SLEDAI and PGA score mean percentage and absolute change from baseline, and no new BILAG 1A/2B organ domain scores compared with baseline, all by study visit

Conclusion: In line with the main analyses performed at Wk 52,[1] further analyses of responses over time in SRI4, SRI6 and disease activity generally favoured BEL over PBO. Combined, these results continue to support the efficacy profile of IV BEL in the treatment of children with cSLE.

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SAT0506 MULTIPLE PATTERNS OF 'RESPONSE' TO METHOTHREXATE IDENTIFIED IN A NATIONAL JUVENILE IDIOPATHIC ARTHRITIS COHORT

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Background: Disease activity following treatment for JIA is currently understood in terms of 'response' or 'non-response'. This state is usually defined using composite measures such as the ACR Pedi scores or cut-offs on the Juvenile Arthritis Disease Activity Scores (JADAS). However, response is a complex state and it is likely that separate, identifiable clusters of children and young people (CYP) have different, varying levels of response across the individual measures of JIA disease activity. Identifying these clusters may facilitate stratified medicine in JIA.

Objectives: To identify clusters of CYP with distinct patterns of change across the individual JADAS components following MTX initiation for JIA.

Methods: MTX-naïve CYP enrolled into the MTX cohorts of the British Society for Paediatric and Adolescent Rheumatology Etanercept Cohort Study or the UK Biologics for Children with Rheumatic Diseases registers before January 2018 were selected. JADAS components (active joint count to 71, physician global assessment (0-100mm), parent global evaluation (0-100mm) and ESR (mm/hr)) were collected at MTX start and at (approximately) 6- and 12-month follow-ups. Outcomes were Log1p transformed for analysis and all outcome data were censored following start of a biologic. CYP were excluded if they had clinically inactive disease at MTX initiation, initiated a biologic within a month of MTX or had no available JADAS data at any time point.

Multivariate group-based trajectory models explored MTX response clusters over the first year following MTX initiation using censored-normal models. Linear, quadratic and cubic polynomials were tested, with one to ten trajectories tested within each polynomial group. Optimal models within each polynomial group were selected using Bayesian Information Criteria, after excluding those with groups representing <1% of the cohort, average posterior probability for assigned group <70% or relative entropy <0.5.

Results: Of 657 CYP, the majority were female (69%) and of white ethnicity (85%), with RF-negative polyarticular JIA the most common disease category (33%).

The optimal model identified multiple patterns of disease activity following MTX initiation, with greater complexity than the traditional 'response' or 'non-response' paradigm. Although there were no substantial differences in ESR trajectories between the groups, there were differences in initial disease severity and speeds of improvement across active joint counts, physician and parental global assessments over time. In addition, individual JADAS components did not always change in parallel over time, even within the same cluster of CYP.

Conclusion: There are multiple patterns of disease activity following MTX initiation for CYP with JIA. This suggests that a simple response/non-response analysis at a single time point may be inadequate. Understanding clinical or biological factors associated with these clusters could facilitate stratified medicine in JIA.

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SAT0507

CLINICAL CHARACTERISTICS AND TREATMENT RESPONSE IN JUVENILE GOUT PATIENTS: A SINGLE CENTER EXPERIENCE

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Background: The incidence of juvenile gout is increasing in China. The clinical manifestations of juvenile gout and treatment strategies to reduce uric acid levels in children are not well described due to the limited number of cases in the past.
Objectives: We aim to describe the clinical characteristic of children with gout and study the treatment response to febuxostat.
Methods: These studies were approved by the Institutional Review Board of Guangdong Second provincial General Hospital. We performed a retrospective analysis on 98 juvenile gout patients (age ≤ 18 years) evaluated in our hospital from Jan 2016 to Dec 2019. We analyzed clinical parameters, laboratory data and treatment response.
Results: The average age of disease onset in children with gout was 15.2 ± 2.0 years and the youngest patient was 9 years old. The majority of patients were male (94/98) and mean serum uric acid (sUA) level were 705.8 ± 145.7 μmol/L (reference range <420 μmol/L). More than half of the cohort had normal body mass index (mean 24.7 ± 4.7 kg/m^2; range 14.9 to 36.1 kg/m^2). Renal function was generally normal in these children (serum creatinine 96.9 ± 17.8 μmol/L). In terms of joint manifestations, juvenile gout preferentially affected finger joints (29%), ankles (28%) and metatarsal joints (MTP; 20%). The most frequent sites of initial gout attack were ankles (45%), MTP (39%) and fingers (6%). In addition, tophi can occur in pediatric patients and typically develop in the finger joints (54%). Tophi was observed in about 25% of juvenile gout patients, typically within the first two years of disease onset (mean duration 1.7 ± 0. 9 years). We have found tophi in children as young as 10 years of age.
For treatment for chronic hyperuricemia, 32 patients (32.7%) were started on febuxostat and 5 patients (5.1%) received allopurinol. A decrease in sUA was observed in both groups after the first month of treatment (febuxostat: baseline 690.4 ± 99.7 μmol/L to 482.7 ± 140.8 μmol/L vs. allopurinol: baseline 728.8 ±112.8 μmol/L to 565.0 ± 116.7 μmol/L, P=0.477). Serum uric acid of 6 patients in the febuxostat group (none in the allopurinol group) dropped below 360 μmol/L. There were no statistical differences in Cr, AST and ALT between the groups. During follow-up after 3 months, further decline in sUA level were observed in patients treated with febuxostat (409.5 ± 83.4, compared with baseline P<0.001).
Conclusion: Juvenile gout has a different pattern of joint involvement and is less associated with elevated BMI compared to gout in adults. We show that febuxostat is effective in reducing uric acid levels in juvenile gout. These findings will help clinicians better understand the clinical manifestations and treatment response in juvenile gout.

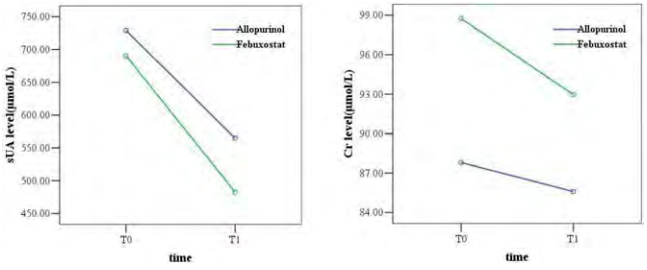


Figure 1 Compared treatment response with allopurinol and febuxostat

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SATURDAY, 06 JUNE 2020

Other orphan diseases

SAT0508

DIAGNOSIS OF BEHÇET'S DISEASE: COMPARISON OF TWO SETS OF CLASSIFICATION CRITERIA. APPLICATION IN 111 PATIENTS OF A WELL-DEFINED POPULATION

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Background: Behçet's disease (BD) is a systemic, chronic, relapsing vasculitis with no pathognomonic diagnostic test. The most widely used classification criteria are those of the International Study Group (ISG) for BD (1). These criteria were repeatedly found to have low sensitivity. Therefore, the International Criteria for Behçet's Disease (ICBD) were published in 2014 (2).
Objectives: To compare the ISG with ICBD diagnostic criteria for BD.
Methods: The study included all consecutive 111 patients diagnosed with definitive or possible BD by expert rheumatologists. They were diagnosed at a well-defined population in Northern Spain between 1980 and 2019. The ISG and ICBD diagnostic criteria for BD were applied to and compared among all patients.
Results: We studied 111 patients (62 Women/49 Men), mean age 36.8±13.2 years. BD was diagnosed in 65 (58.5%) by ISGBD criteria and in 86 (77.5%) by ICBD criteria. No significant differences were observed between both criteria ($p < 0.001$). The overall concordance was fair (Kappa 0.3; $p<0.001$). Sensitivity was 58.6% for ICBD criteria and 80.2% for ISG. **(TABLE-1)**
Conclusion: ICBD criteria exhibit higher sensitivity than ISG criteria. Thus, the application of these new criteria can achieve a more correct and earlier diagnosis of BD.

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[1] Criteria for diagnosis of Behcet's disease, International Study Group for Behçet's Disease,The Lancet, Volume 335, Issue 8697, 1078 – 1080
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TABLE 1

	Expert diagnosis (N=111)	ISG criteria -(N=65)	ICBD criteria (N=86)
Age, mean (SD)	36.7 (13.2)	36 (12.8)	36.7 (13)
Gender, men/women, N (%)	49/62 (44.1/55.8)	29/36 (44.6/55.4)	38/48 (44.2/55.8)
Oral aphthosis	110 (99)	65 (100)	85 (100)
-Recurrent (3 times/year)	91 (87.2)	61 (93.8)	74 (86)
Genital aphthosis	59 (53.1)	42 (64.6)	56 (65.1)
Skin manifestations	76 (68.4)	56 (86.15)	71 (70.9)
-Pseudofolliculitis/	51 (67.1)/ 27 (35.5)	38 (58.5)/ 21 (32.3)	42 (68.8)/
Erythema nodosum			22 (36.1)
Ocular lesions	39 (35.1)	32 (49.2)	39 (45.3)
-Anterior/ Posterior/	17 (43.6);	16 (50)/ 8(25)/	17 (45.6); 0;
Panuveitis	12 (30.8)/ 0	7 (21.9)	12 (30.8)
-Retinal vasculitis	4 (10.3)	1 (3.1)	4 (10.6)
Joint manifestations	76 (68.5)	43 (66.1)	58 (67.4)
-Arthralgias / Arthritis	69 (92.8)/ 45 (60)	39 (90.7)/ 24 (55.8)	52 (89.6)/
			33 (56.9)
Neurological manifestations	20 (18)	11 (16.9)	16 (18.6)
-Peripheral / Central	11 (55)/ 14 (70)	7 (63.6)/ 7 (63.6)	12 (75)/
			10 (62.5)
Vascular manifestations	9 (8.6)	7 (10.8)	10 (11.6)
-Arterial/ Vein thrombosis/	0/ 5 (55)/ 1 (11.1)	0/ 4 (57.1)/ 1 (14.3)	1 (12.5)/
Phlebitis			5 (62.5)/0
Gastrointestinal features	4 (4.5)	4 (6.1)	4 (4.6)
Pathergy test positive (available data; %)	6 (28; 21.4)	4 (19; 21)	4 (25, 16)
HLA B51 positive (available data; %)	38 (86; 44.2)	19 (47; 40.4)	28 (63; 44.4)

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SAT0509

MYCOPHENOLATE MOFETIL VERSUS AZATHIOPURINE FOR THE MAINTENANCE TREATMENT OF CONNECTIVE-TISSUE RELATED INTERSTITIAL LUNG DISEASE FOLLOWING CYCLOPHOSPHAMIDE TREATMENT

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Background: Cyclophosphamide (CYC) had a good response rates when used as an induction regimen for the treatment of connective tissue related interstitial lung disease (CTD-ILD). But the safety profile of CYC necessitates the usage of a second line treatment for maintenance

Objectives: To compare the effect of mycophonetil (MMF) and azatiyopurin (AZA) for maintanance therapy following cyclophsphomide treatment in CTD-ILD

Methods: Between 2009 and 2019 all interstitial lung disease patients admitting rheumatology or pulmonology department were retrospectively evaluated and patients treated with cyclophospamide as an induction regimen and having not progression were selected. Among those, as a second line regimen treated with MMF or AZA were included. Primary end point was treatment responses at 6th months

Results: 68 patients treated with CYC for the first line treatment. 46 patients treated with either MMF (n:22) or AZA (n:24) for the maintenance. Scleroderma patients were the largest group and consituted 63% of the population. MMF group had worse FVC values and more involvement in lung paranchyme at the begining of the treatment. In univariate analysis FVC (lt) values and lung involvement (%) on HRCT at the start of the treatment, and disease subtype were associated significantly with treatment responses.After adjusted with these factors, in multivariate analysis, AZA treatment was associated with the increased risk of progression (odds ratio 5,8, 95% CI 1,061-31,09) as compared with MMF treatment

Conclusion: MMF had better results compared to AZA in the treatment of CTD-ILD,after the usage of CYC treatment.

References:

[1] Barnes, H., et al., *Cyclophosphamide for connective tissue disease-associated interstitial lung disease.* Cochrane Database Syst Rev, 2018. **1**(1): p. Cd010908.

Table 1. Patient and disease characteristics at the start of the treatment and treatment responses at the 6th months of the treatment: FVC forced vital capacity

	MMF (22)	AZA (24)	p
Lung involvement (%)	36%	23,3%	**0,022**
FVC (lt)	1,96	2,55	**0,021**
FVC (%)	71%	81%	**<0,001**
FVC change at 6th month (lt)	-,02	-0,19	**0,051**
FVC change at 6th month (%)	-0,42	-5,81	0,068
Progression	23,8%	50%	**0,118**

Disclosure of Interests: None declared

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SAT0510 LONG-TERM EFFECTIVENESS OF CANAKINUMAB IN AID – INTERIM ANALYSIS OF THE CAPS SUBGROUP FROM THE RELIANCE REGISTRY

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Background: In the treatment of monogenic autoinflammatory diseases (AID), a heterogeneous group of diseases with excessive interleukin (IL)-1β release and severe systemic and organ inflammation, the anti-IL-1 inhibitor canakinumab (CAN) has been associated with rapid remission of symptoms in clinical trials as well as in real-life.[1-3]

Objectives: The aim of the RELIANCE registry is to explore long-term effectiveness and safety of CAN under routine clinical practice conditions in pediatric and adult patients with CAPS (cryopyrin-associated periodic syndromes, including Muckle-Wells syndrome [MWS], familial cold autoinflammatory syndrome [FCAS], neonatal onset multisystem inflammatory disease [NOMID]/ chronic infantile neurological cutaneous and articular syndrome [CINCA]), FMF (familial Mediterranean fever), TRAPS (tumor necrosis factor receptor-associated periodic syndrome) and HIDS/MKD (hyperimmunoglobulinemia D syndrome/ mevalonate kinase deficiency).

Methods: This prospective, non-interventional, observational study is based in Germany with a 3-year follow-up and enrolls pediatric ≥2 years and adult patients with clinically confirmed diagnoses of CAPS, FMF, TRAPS and HIDS/MKD routinely receiving CAN. In 6-monthly visits, clinical data and patient-reported outcomes are assessed. Study endpoints are long-term effectiveness and safety of CAN. Here, the CAPS cohort was analyzed.

Results: This 18-month interim-analysis includes 78 CAPS patients (49% females) enrolled by September 2019. Mean age at baseline was 25 years and mean duration of prior CAN treatment was 5.7 years. 64 patients (82%) had MWS, 2 FCAS, 7 NOMID/CINCA, 3 atypical CAPS and 2 lacked subtype diagnosis. Disease activity, fatigue and social impairment by patients' assessment, days absent from school/work, inflammatory markers, and remission by physician assessment were evaluated at 6-monthly intervals starting at baseline with last update at 18 months of follow-up (table 1). The results demonstrate sustained remission and disease control as evaluated parameters remained stable over time. Serious adverse events were reported for 9 patients including papillitis, pyrexia, tonsillitis (n=2), appendicitis, chest pain, circulatory collapse, skin disorders, and preterm delivery.

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

	Baseline	6 months	12 months	18 months
Number of patients, N	78	51	42	29
Mean age, years (SD)	25 (4; 79)	22 (4; 79)	20 (4; 58)	22 (4; 54)
Patient's assessment of disease activity 0-10, mean (min; max)	2.2 (0; 7)	1.8 (0; 7)	2.4 (0; 7)	2.8 (0; 8)
Patient's assessment of fatigue 0-10	2.9 (0; 9)	2.4 (0; 8)	2.8 (0; 8)	1.7 (0; 7)
Number (%) of patients without impairment of social life by disease	16 (49)	29 (76)	20 (61)	14 (67)
Number (%) of patients with days absent from school/work	25 (32.5)	11 (22)	14 (34)	15 (52)
Inflammatory markers, CRP/SAA, mean (mg/dL)	0.4 3.2	0.4 2.1	0.3 0.8	0.2 0.5
Number (%) of patients in disease remission (physician assessment)	55 (72)	38 (76)	29 (71)	22 (76)

Conclusion: The 18-month interim analysis of the RELIANCE study, the longest running real-life CAN registry, demonstrates that long-term CAN treatment is safe and effective in CAPS patients.

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SAT0511 CYTOKINES, CHEMOKINES AND INFLAMMATORY BIOMARKERS IN NEUROSARCOIDOSIS

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Background: Sarcoidosis is characterized by granulomatous inflammation, which in rare cases can affect the central nervous system, neurosarcoidosis (NS).

Objectives: The aim of this study was to estimate levels of cytokines, chemokines, and vascular biomarkers in patients with NS.

Methods: In this observational, cross-sectional study, cerebrospinal fluid (CSF) and plasma were collected from biopsy-proven sarcoidosis patients with clinical suspicion of NS. They were categorized into either a NS group (n=14) or a non-NS group (n=5) depending on fulfilment of NS criteria. The results were

compared to a healthy control group (HC, n=11). Samples were analysed with Electrochemiluminescence, Mesoscale®.

Results: The level of INF γ was significantly higher in NS group compared to non-NS group in CSF (median 11.3 pg/mL vs. 3.3 pg/mL) and in plasma (median 21.6 pg/mL vs. 4.5 pg/mL)

In CSF and not in plasma, the level differs significantly in NS group compared to non-NS group, IL12/IL23p40 (median 54.05 pg/mL vs. 3.61 pg/mL), IL16 (median 8.7 pg/mL vs. 4.3 pg/mL), IL17A (median 1.37 pg/mL vs. 0.19 pg/mL), TNF β (median 0.37 pg/mL vs. 0.02 pg/mL), IL8 (median 55.4 pg/mL vs. 37.8 pg/mL), CCL11 (median 36.1 pg/mL vs. 16.4 pg/mL, CCL26 (median 6.7 pg/mL vs. 3.7 pg/mL), CXCL10 (median 4981 pg/mL vs. 771 pg/mL), CCL13 (median 24.5 pg/mL vs. 10.0 pg/mL), CCL22 (median 129.8 pg/mL vs. 22.6 pg/mL), CCL3 (median 54.1 pg/mL vs. 20.7 pg/mL), CCL17 (median 54.0 pg/mL vs. 6.9 pg/mL), ICAM1 (median 13901 pg/mL vs. 7327 pg/ml), and VCAM1 (median 18594 pg/mL vs. 12132 pg/mL)

A cut-off level for each cytokine was set at 20% above the maximum values of both non-NS group and HC. Using this, the ratio of patients in NS group over were:

-INF γ, 57% had level over 6.2 pg/mL in CSF, and 50% had level over 21.6 pg/mL in plasma.

-IL12/IL23p40, 71% had level over 16.7 pg/mL in CFS.

-CXCL10, 79% had level over 1614 pg/mL in CFS.

-CCL22, 79% had level over 49.8 pg/mL in CFS.

Conclusion: In NS patients, INF γ was elevated in both CSF and plasma, and multiple cytokines, chemokinves and vascular biomarkers were elevated in CSF.

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SAT0512 OCULAR INVOLVEMENT AND TREATMENT IN SARCOIDOSIS. STUDY OF 41 PATIENTS OF A SERIES OF 383 PATIENTS FROM A SINGLE UNIVERSITY HOSPITAL

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Background: The eye is a common and potential severe complication of sarcoidosis. Topical and systemic corticosteroids are the first-line treatment. Conventional and biological immunosuppressants (IS) are frequently needed **(1-5).**

Objectives: To assess the frequency, clinical and treatment of ocular involvement of sarcoidosis.

Methods: Study of a large cohort (n=383) of systemic sarcoidosis from a single university hospital. All consecutive patients diagnosed with sarcoidosis from January 1,1999 to January 1,2019 according the ATS/ERS/WASOG criteria *(Eur Respir J 1999;14:735–737)* were included.

Results: 41 (22 women/19 men) of 383 (10.7%) patients had ocular involvement, mean age 44.8±16 years. Uveitis (n=34; 82.9%) was the most common ocular manifestation, especially anterior uveitis (n=18; 52.9%). Ocular surface and eye orbit may also be affected **(Table)**. In addition to topical and systemic corticosteroids, conventional (n=23; 56.1%) and biologic (n=14; 34.1%) IS drugs were required. Adalimumab and Infliximab were the most used biologic treatments **(Table).** Cystoid macular edema (CME) and Retinal Vasculitis was observed in both cases in 3 (7.3%) patients, 2 of them (66.7%) required biological treatment. Papilitis appeared in 7 (17.1%) cases, biological treatment was needed in 3 (42.9%) patients. The most frequent sequels were cataract (n=9, 21.9%), intraocular hypertension (n=5; 12.2%) and pupil alterations (n=4; 9.7%). The average of the best corrected visual acuity was 0.6±0.3 at diagnosis and 0.7±0.3 after one year follow up.

Conclusion: Ocular involvement of sarcoidosis is a relative frequent and potential severe complication, especially if panuveitis is presented.

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SAT0513 ASSOCIATION OF SERUM OMENTIN LEVELS WITH COLCHICINE RESISTANCE IN FAMILIAL MEDITERRANEAN FEVER

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Background: Omentin is an anti-inflammatory adipokine, which plays important roles in the adjustments of glucose metabolism, cardiovascular homeostasis, atherosclerosis (1).

Objectives: To investigate the omentin levels in Familial Mediterranean fever (FMF) patients and to assess the association with markers of subclinical inflammation in FMF patients such as serum amyloid A (SAA), erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP).

Methods: This cross-sectional study included 54 consecutive adult FMF patients (27 male, 27 female) and 28 healthy individuals (16 male, 12 female). The demographic and clinical features and MEFV gene mutations were recorded. The FMF patients were separated into 3 groups: 1) attack-free group, 2) active attack group and 3) colchicine-resistant group. Serum omentin levels were compared between the FMF patients and the healthy control group.

Results: Serum omentin and SAA levels were higher in the study group than in the control group (108.05(19.97-343.22) vs. 199.5(42.98-339.41) $p<0.05$, 3.69(1.18-22.75) vs. 1.31(0.95-3.16) $p<0.001$) (Table 1). When the FMF patients were examined as separate groups, serum omentin values were lower in the colchicine resistant group than in the groups without resistance (Table 2). The correlation analysis showed a negative correlation between omentin and SAA levels ($r = -0.240$, $p = 0.030$).

Table. Ocular manifestations of sarcoidosis and treatment with corticosteroids, conventional and biological IS.

		CONVENTIONAL IS									BIOLOGICAL IS					
OCULAR INVOLVEMENT	**Cases**	**TCS**	**OCS**	**MD of OCS**	**IVMP**	**CIS**	**MTX**	**AZA**	**CFM**	**MMF**	**BT**	**ADA**	**IFX**	**TCZ**	**GLM**	**ETN**
SURFACE n(%)	3(7.3)	2(66.7)	2(66.7)		2(66.7)	2(66.7)	2(66.7)	2(66.7)	1(33.3)	0(0)	2(66.7)	2(66.7)	2(66.7)	0(0)	0(0)	0(0)
-CG/N, n(%)	1(33.3)	1(100)	0(0)		0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
-PUK, n(%)	2(66.7)	1(50)	2(100)	60	2(100)	2(100)	2(100)	2(100)	1(50)	0(0)	2(100)	2(100)	2(100)	0(0)	0(0)	0(0)
UVEITIS n(%)	34(82.9)	25(73.5)	28(82.3)		10(29.4)	19(55.6)	18(52.9)	7(20.6)	1(2.9)	1(2.9)	12(35.3)	11(32.3)	4(11.8)	3(8.8)	2(5.9)	1(2.9)
-Anterior uveítis, n(%)	18(52.9)	11(61.1)	13(72.2)	30	1(5.5)	5(27.8)	5(27.8)	1(5.5)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
-Posterior uveítis, n(%)	4(11.7)	2(50)	3(75)	60	1(25)	3(75)	2(50)	2(50)	0(0)	0(0)	2(50)	1(25)	0(0)	0(0)	1(25)	0(0)
-Panuveítis, n(%)	12(35.3)	12(100)	12(100)	60	8(66.7)	11(91.7)	11(91.7)	4(33.3)	1(8.3)	1(8.3)	10(83.3)	10(83.3)	4(33.3)	3(25)	1(8.3)	1(8.3)
EYE ORBIT n(%)	4(9.7)	2(50)	3(75)		2(50)	2(50)	2(50)	2(50)	0(0)	0(0)	2(50)	1(25)	1(25)	1(25)	0(0)	0(0)
-Proptosis, n(%)	2(50)	1(50)	1(50)	30	1(50)	1(50)	1(50)	1(50)	0(0)	0(0)	1(50)	1(50)	0(0)	1(50)	0(0)	0(0)
-Strabismus, n(%)	2(50)	1(50)	2(100)	60	1(50)	1(50)	1(50)	1(50)	0(0)	0(0)	1(33.3)	0(0)	1(33.3)	0(0)	0(0)	0(0)
TOTAL, n(%)	41(100)	29(70.7)	33(80.5)	50±15.5	14(34.1)	23(56.1)	22(53.7)	11(26.9)	2(4.9)	1(2.4)	14(34.1)	14(34.1)	7(17.5)	3(7.3)	2(4.9)	1(2.4)

TCS: topical corticosteroids; **OCS:** oral corticosteroids; **MD:** maximum dose; **IVMP:** intravenous methylprednisolone; **CIS**: conventional immunossupresors; **BT:** biologic therapy; **CG/N:** conjunctival granuloma/nodule; **PUK:** peripheral ulcerative keratitis

Table 1. Laboratory results of the FMF and the control group

Variables	FMF patients (n=54)	Control (n=28)	P value
Omentin, pg/mL	108.05(19.97-343.22)	199.5(42.98-339.41)	0.03
SAA, ng/mL	3.7 (1.18-22.75)	1.31(0.95-3.16)	<0.001
ESR, mm/h	15(2-68)	12(7-17)	<0.001
CRP, mg/L	12(1-194)	2.5(1-8)	<0.001

Variables were given as median (IQR).
Calculated using Mann-Whitney U test for non-normal distribution.
FMF=Familial Mediterranean fever, SAA=serum amyloid A, ESR=erythrocyte sedimentation rate, CRP=C-reactive protein, IQR=interquartile range.

Table 2. Laboratory results of FMF patients with and without colchicine resistance

Variables	With resistance (n=16)	Without resistance (n=38)	P value
Omentin, pg/mL	76.64(19.77-224.33)	186.47(28.41-343.21)	0.006
SAA, ng/mL	3.69(1.18-22.75)	3.77(1.18-21.49)	0.784
ESR, mm/h	25.5(2-68)	15(2-60)	0.835
CRP, mg/L	11(1-67)	19(1-194)	0.111

Variables were given as median (IQR).
Calculated using Mann-Whitney U test for non-normal distribution.
FMF=Familial Mediterranean fever, SAA=serum amyloid A, ESR=erythrocyte sedimentation rate, CRP=C-reactive protein, IQR=interquartile range.FOM

Conclusion: FMF patients with colchicine resistance are associated with decreased omentin concentrations, probably mediated by inflammation-driven mechanisms.

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SAT0514 FATIGUE IN FAMILIAL MEDITERRANEAN FEVER

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Background: Fatigue is an important and common symptom in rheumatologic diseases. It causes disability and worsens patients quality of life. Familial Mediterranean Fever (FMF) is a hereditary autoinflammatory disease characterized by recurrent episodes of fever and serositis. Mutations in the MEFV gene that encodes pyrin protein are responsible for the disease. Most frequent mutation is M694V and FMF patients with M694V/M694V genotype have more severe disease.

Objectives: The aim of this study is to investigate fatigue and its impact on quality of life of FMF patients who are attack-free for more than one year.

Methods: Seventy-seven FMF patients and 70 age and sex matched healthy controls were enrolled in the study. Fatigue severity scale (FSS) was used to evaluate fatigue level. Disease severity was evaluated via FMF disease severity score. Short form-36 (SF-36) was used to evaluate the quality of life of the participants and Beck depression inventory (BDI) was used to evaluate depression.

Results: No statistically significant difference was found when FMF group and healthy controls were compared for demographic variables and laboratory markers (complete blood count, erythrocyte sedimentation rate, c-reactive protein levels, liver and kidney function tests). All of the subscale scores of SF-36 were lower in FMF group when compared with the control group. BDI and FSS scores were higher in the FMF group.(Table 1)

Table 1. Comparison of FMF and control groups for fatigue, depression and quality of life

	FMF group (n: 77) median(min-max)	Control group (n: 70) Median (min-max)	p
Fatigue severity scale (FSS)	31(27-47)	28 (24-37)	p<0.05
Beck depression inventory (BDI)	15 (0-35)	12 (0-19)	p<0.05
SF-36 Physical functioning	80.00(25.00-100.00)	95.00 (50.00-100.00)	p<0.01
SF-36 Social functioning	55.50 (40.00-88.80)	77.70 (22.20-88.80)	p<0.01
SF-36 Role physical	25.00 (0.00-100.00)	100.00 (0.00-100.00)	p<0.01
SF-36 Role emotional	33.30 (0.00-100.00)	100.00 (0.00-100.00)	p<0.01
SF-36 Mental health	56.00 (24.00-88.00)	72.00 (24.00-100.00)	p<0.01
SF-36 Pain	55.50 (0.00-100.00)	77.70 (33.30-100.00)	p<0.01
SF-36 Vitality	45.00 (15.00-95.00)	65.00 (5.00-100.00)	p<0.01
Sf-36 General health	40.00 (5.00-92.00)	67.00 (20.00-100.00)	p<0.01

Twenty-three of FMF patients had M694V/M694V genotype and those patients had higher disease severity scores (p<0.01), higher FSS (p<0.01) and higher BDI scores (p<0.05) when compared with other FMF patients. Regarding the quality of life, patients with M694V/M694V genotype had lower scores in social functioning, role physical, role emotional and pain subscales of SF-36. In the correlation analysis depression and fatique were found to be the major determinants of quality of life in FMF. Disease severity or duration were not strongly correlated with the SF-36 scores (Table 2).

Conclusion: Despite being attack-free for more than one year, FMF patients had poor quality of life and fatigue when compared with the healthy controls. The quality of life in FMF patients, whose attacks are well controlled, is mainly determined by fatigue and depression rather than disease severity.

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SAT0515 COMPLEX HYPERMOBILITY EHLERS-DANLOS SYNDROME (HEDS): MAPPING THE PATIENT'S JOURNEY OVER 40 MONTHS IN A TERTIARY REFERRAL CENTRE

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Background: Ehlers-Danlos Syndromes are heritable connective tissue disorders.They are multisystemic and patients can present with several symptoms such as joint pain and instability, visceral and autonomic dysfunction, as well as significant psychosocial sequela. Managing this cohort of young patients is usually challenging as many patients present late due to delayed diagnosis, often with several complications, problems with mobility and opioid use. Furthermore, there is often a prolonged lack of coordinated healthcare and access to social care services. A recent parliamentary debate in the U.K. highlighted that hEDS services are excluded from specialist Rheumatology commissioning services. In order to ascertain the relevance and utility of specialist services in this population, we conducted this study.

Objectives: The objective of this study was to map the patient experience following a referral to the specialist clinic in order to assess the need for an integrated, multidisciplinary approach to treating patients with hypermobility EDS.

Methods: We retrospectively reviewed the records of 50 patients with the diagnosis of hypermobility EDS who were seen in a specialist hypermobility clinic at University College Hospital UCLH between January 2016 and March 2016. Relevant data was collected regarding their medical care in our hospital up to October 2019.

Results: The median age was 37 (range 21-59). We had 10 males and 40 females. The diagnosis of hypermobility EDS was based on the 1997 criteria as these patients were seen prior to the 2017 classification. Overall, the study yielded 6 key themes: 1. All patients experienced chronic pain, with 36% reporting use of opioids for pain management. 2. Patients were referred to multiple

Table 2. Correlation of fatigue, depression, disease severity and duration with quality of life in FMF patients

	Physical functioning	Social functioning	Role Physical	Role emotional	Mental health	Vitality	Pain	General health
FMF disease severity scale	r= -0,223	r= -0,319**	r= -0,313**	r= -0,184	r= -0,124	r= -0,188	r= -0,191	r= -0,351**
Beck Depression Inventory	r= -0,418**	r= -0,554**	r= -0,461**	r= -0,470**	r= -0,660**	r= -0,594**	r= -0,308**	r= -0,576**
Fatigue severity scale	r= -0,391**	r= -0,426**	r= -0,475**	r= -0,324**	r= -0,650**	r= -0,739**	r= -0,410**	r= -0,521**
Disease duration	r= -0,40**	r= -0,218	r= -0,232*	r= -0,287*	r= -0,026	r= -0,211	r= -0,189	r= -0,109

** p<0.01
*P<0.05

medical specialities within the same hospital trust, (22% patients were referred to ≥5 specialities). 3. Patients required a high number of follow up appointments (28% of patients required ≥20 follow-up visits). 4. Failed discharges were common; patients were often referred back to the Rheumatology Clinic despite being discharged to primary care. 5. Patients had a significant number of comorbidities, reflected by polypharmacy. (36% of patients were prescribed ≥5 medications). 6. Disability was high (20% of patients reported severe mobility problems).

Conclusion: This study shows that patients with hEDS referred to UCLH have significant levels of disability, opioids use and polypharmacy especially for a relatively young population of patients. They need a complex interdisciplinary approach in a timely manner. In order to minimise delays and allow earlier diagnosis and intervention, we have recently adopted a multidisciplinary team approach, including pain specialists, rheumatologists, psychologists, physiotherapists, nurse specialists, urogynaecologists and neurogastroenterologists. This allows more coordinated and efficient care and incorporates an EDS-specific pain management programme. Specialised services for complex hEDS cases should be established and adequately resourced. Moreover, it would be cost effective to commission a patient-centred "one-stop-shop" service, where patients, who often travel from long distances with severe disabilities, can be seen by multiple specialities in a single visit.

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SAT0516 CLINICAL CHARACTERISTICS AND PROGNOSTIC FACTORS IN PATIENTS WITH SECONDARY HEMOPHAGOCYTIC SYNDROME

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Background: The Hemophagocytic Syndrome (HPS) had a mortality rate between 20% and 90%. The mortality of HPS secondary to autoimmune diseases (AID) is lower than hemato-oncological diseases (HOD). In general, the HOD, thrombocytopenia, age, and a prolongation of prothrombin are considered to be an adverse prognostic factor.(1)

Objectives: To describe and identify differences between patients who survived and did not survive to HPS during hospital admission to a tertiary hospital between 2005 and 2019.

Methods: This is a retrospective observational study. All patients who met the diagnostic criteria for LHH were included, or who presented haemophagocytic cells in the bone marrow biopsy, or who had diagnosis of HPS in the hospital discharge report.(2) Demographic, clinical, analytical, etiological, underlying disorder and prognosis variables were collected. Continuous variables are described with the mean or median according to the degree of normality. Kruskal Wallis, Fisher test and Mann-Whitney U test were used for the bivariate analysis, and also a multivariate logistic regression analysis was performed.

Results: Thirty patients with HPS were included. They were distributed in 5 subgroups (Table 1). Overall mortality was 43.3%, statistically significant higher in the HOD [8 patients (66.7%); p 0.029]. Also, they were divided into 2 groups (survivor vs. non-survivor; Table 2). In the multivariate model the age and INR prolongation were confirmed to be independently associated with the outcome of mortality.

Table 1. Etiology of HPS

Etiology	n = 30	Mortality
AID	**10**	**n = 1**
Systemic lupus erythematosus	5	1
Adult Still's Disease	3	No
Rheumatoid arthritis	1	No
Sclerosing Disease IgG4	1	No
HOD	**12**	**n = 8***
Non-Hodgkin's lymphoma	3	1
Myelodysplastic syndrome	3	2
Acute leukemia	3	3
Extranodal NK cell lymphoma	1	1
Multiple Myeloma	1	No
Probable lymphoproliferative process	1	1
Infectious diseases	**2**	**n = 1**
Pneumocystis carinii in patient with H.I.V.	1	1
Campylobacter yeyuni	1	No
Glyoblastoma multiforme with temozolomida	**1**	**n = 0**
HPS without defined aetiology	**5**	**3**

HIV: Human Immunodeficiency Virus, NK: Natural Killer. *p = 0,029

Table 1. Etiology of HPS

Etiology	n = 30	Mortality
Myelodysplastic syndrome	3	2
Acute leukemia	3	3
Extranodal NK cell lymphoma	1	1
Multiple Myeloma	1	No
Probable lymphoproliferative process	1	1
Infectious diseases	**2**	**n = 1**
Pneumocystis carinii in patient with H.I.V.	1	1
Campylobacter yeyuni	1	No
Glyoblastoma multiforme with temozolomida	**1**	**n = 0**
HPS without defined aetiology	**5**	**3**

HIV: Human Immunodeficiency Virus, NK: Natural Killer. *p = 0,029

Table 2. Characteristics and differences between survivor and non-survivor groups

	Total		Non-survivor		survivor		
n	**30**		**13**		**17**		**p<0,05**
Age	55,5	±18,3	68	58,2-74,5	40	34-57	**0,043**
Women	16	53,3%	7	61,5%	9	47,1%	1,00
Comorbidities (≥ 2)	5	16,7%	2	15,4%	3	17,6%	1,000
Hospital stay	35,5	20-60,8	29	15,5-39	13	8-17	0,563
Splenomegaly	16	53,3%	7	53,8%	9	52,9%	1,000
Hepatomegaly	10	33,3%	5	38,5%	5	29,4%	0,705
Hb (g/dL)	7,1	6,4-7,9	710%	6,2-7,8	7,1	6,6-7,8	0,094
Pt (x10^9/L)	13 500	5 000-52 500	16 000	11 000-44 000	12 000	5 000-99 000	0,281
Pt ≤ 100 000	25	83,3%	13	100%	12	70,6%	**0,052**
Leu (x10^9/L)	1 250	238-3 153	1 300	150-3 940	1 400	200-3 340	0,457
Neu (x10^9/L)	615	0-1 550	1 290	20-3 300	650	0-1 400	0,805
Fb (mg/dL) (n=24)	171	111-358	167,00	106-253	169,00	103-451	0,796
Fer (ng/mL) (n=28)	15 330	5 434-38 284	29 063	5 728-74 604	13 225	8 287-28 729	0,108
Tg (mmol/L)	341	226-438	254,00	184-382	471,00	341-604	**0,053**
GOT (U/L)	139	77,5-406,3	133,00	101-513	179,00	101-512,5	0,483
GPT (U/L)	162	46-389	109,00	41-333	199,00	99-298	0,198
INR (n=29)	1,5	1,1-1,9	2,1	1,2-3,7	1,5	1,1-1,6	**0,028**

Hb: Hemoglobin, Pt: platelets, Leu: leukocytes, Neu: neutrophils, Fb: fibrinogen, Fer: ferritin, Tg: triglycerides, GOT: aspartate aminotransferase, GPT: alanine aminotransferase

Conclusion: The HOD presented higher mortality. The non-survivor group presented a longer INR prolongation and a higher age at the time of diagnosis.

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SAT0518 CANAKINUMAB TREATMENT IN ADULT PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER: A SINGLE-CENTER STUDY

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Background: Familial Mediterranean Fever (FMF) is the most common autoinflammatory disease characterized by recurrent, self-remitting attacks of fever, serositis, arthritis, and erysipelas-like erythema. Canakinumab is an Interleukin-1β inhibitor that is shown to be effective and safe in treating colchicine resistant FMF patients.

Objectives: The main objective of this study is to present the single tertiary center experience of adult FMF patients who received Canakinumab.

Methods: The study is a retrospective analysis conducted at a tertiary rheumatology center experienced in FMF. The patients who had a clinical diagnosis of FMF and who were treated with at least a single subcutaneous injection of canakinumab were

included. Patients with amyloidosis and pregnancy were excluded. In order to evaluate the disease status, acute phase reactants and patient-reported disease severity visual analog scale (VAS) scores were analyzed. Acute phase reactants were evaluated during attack-free periods. The VAS score was reported on a scale of 0-10, 10 meaning the disease at its most severe form, and 0 meaning the least.

Results: Fifty-two patients (21 male, 31 female) with the mean age of 35.88±12.4 years, were included in this study. The presenting signs and symptoms of the patients are shown in Figure 1. The mean age of initial symptoms and diagnosis were 12.84±10.06 and 20.39±12.35 years in respective order. The treatment information of the patients before and during Canakinumab injections was shown in Table 1. The mean Erythrocyte Sedimentation Rate (ESR) decreased from 25.31±20.64 to 11.52±9.78 mm/hour. The mean C-reactive Protein (CRP) decreased from 28.18±47.04 to 2.02±2.31 mg/L (both p<0.0001). The mean VAS score decreased from 8.04±1.9 to 1.4±1.73 (p<0.0001). Canakinumab treatment was terminated in 33 patients, 22 of which was due to successful remission. The termination of the treatment was because of pregnancy or will of pregnancy in 4 patients, inadequate treatment response 3 patients, treatment noncompliance in 2 patients, chronic hepatitis C related cirrhosis in 1 patient, and change to a different biologic agent in 1 patient. The only side effect experienced was hallucinations in one patient who was already under remission.

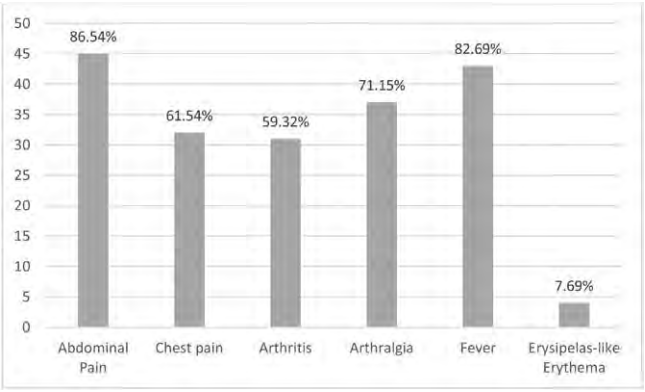


Figure 1. The Presenting Signs and Symptoms of the Patients

Table 1. The Treatment Information of the Patients

Initial Mean Daily Colchicine Dose, mg (mean± standard deviation)	1.68±0.46
Mean Daily Colchicine Dose before Canakinumab Treatment, mg	1.63±0.6
The Mean Injection Number, n	17.5±17.8
Canakinumab Treatment Indication, n (%)	
Inadequate Response to Previous Treatment	38 (73.08)
Side Effect to Previous Treatment	8 (15.38)
Poly Arteritis Nodosa	2 (3.85)
Recurrent Pericarditis	1 (1.92)
CNS Vasculitis	2 (3.85)
Poor Anakinra Treatment Adherence	1 (1.92)
FMF Encephalopathy	1 (1.92)

Conclusion: Canakinumab seems effective in controlling the subclinical inflammation and raising the quality of life of the patient. It has a favorable side effect profile. According to our single-center, real-life data, Canakinumab can be used as an alternative treatment method in colchicine resistant patients.

Disclosure of Interests: None declared

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SAT0519

DRUG RETENTION RATES OF BIOLOGICAL AGENTS IN ADULT ONSET STILL'S DISEASE IN THE PRE-CANAKINUMAB ERA

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Background: Adult onset Still's disease (AOSD) is a rare systemic inflammatory disease. Glucocorticoids represents first-line therapy and conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) play a central role as steroid-sparing agents. Patients refractory to csDMARD may require the introduction of a biological DMARD (bDMARD). There is paucity of data about the efficacy and drug retention rate (DRR) of bDMARDs used in the treatment of AOSD.

Objectives: To retrospectively evaluate DRR and reasons for discontinuation of five different bDMARDs in a monocentric cohort of AOSD patients in a real-world setting.

Methods: AOSD patients followed at our Center who received at least one bDMARD were selected. Data about disease duration, number of bDMARDs, reasons for bDMARDs discontinuation, concomitant csDMARDs were collected. Survival curves were determined by the Kaplan-Meier method and compared using a stratified log-rank test. 24-month DRRs were then calculated. Hazard ratio (HR) for previous bDMARDs was also evaluated.

Results: We identified 42 patients and 79 bDMARD-courses (**Table 1**). Anakinra (ANK, n = 41) was the most used bDMARD, followed by tocilizumab (TCZ, n=21) and Tumor Necrosis Factor inhibitors (TNFi, n = 17). At bDMARDs initiation, all patients were being given prednisone (mean dose, 23 ± 18 mg/day) and 76% were on concomitant csDMARD therapy. 36 (46%) treatment courses were stopped by 24 months; discontinuation causes are shown in **Table 2**. 14 treatment courses were started in the previous 24 months (ANK = 9, TCZ = 5), without being stopped before the study time but not reaching 2-year treatment duration. Overall retention rates at 24 months were the following: TCZ, 62.5%; ANK, 53.1%; TNFi, 11.8% (p = 0.021). Survival curves are shown in **Figure 1**. DRRs of ANK and TCZ were statistically comparable (p = 0.576), and they were both significantly higher than the DRR of TNFi (p = 0.015). Previous bDMARDs therapy showed no effect on DRR (HR 0.73, 95% CI = 0.40 - 1.31, p = 0.288).

Table 1. Clinical characteristics at initiation of biologic agents in adult onset Still's Disease. TNFi = Tumor Necrosis Factor inhibitors

	Anakinra (n=41)	Tocilizumab (n=21)	TNFi (n=17)	p - value
Age (years)	38 ± 16	43 ± 19	38 ± 13	0.601
Female sex (%)	61%	48%	35%	0.443
Mean disease duration (months)	49 ± 60	72 ± 75	61 ± 64	0.445
Systemic disease (%)	61%	38%	29%	0.213
C-reactive protein (mg/l)	99 ± 84	111 ± 100	66 ± 52	0.445
Erythrocyte sedimentation rate (mm/h)	71 ± 32	65 ± 27	77 ± 41	0.617
White blood cells (cells/ul)	14640 ± 4540	14116 ± 3724	16870 ± 5504	0.361
Ferritin (ng/ml)	10114 ± 18657	6327 ± 8061	6295 ± 9573	0.591
Previous therapy (%)	100%	100%	100%	1.000
csDMARD (%)	88%	90%	94%	0.973
bDMARD (%)	22%	81%	59%	**0.003**
Mean prednisone dose (mg die)	20.3 ± 18.1	15.8 ± 14.4	27.3 ± 14.4	0.252
Concomitant csDMARD therapy (%)	71%	71%	59%	0.865

Table 2. Causes of treatment discontinuation of biologic agents in adult onset Still's Disease. TNFi = Tumor Necrosis Factor inhibitors

	Anakinra (n=41)	Tocilizumab (n=21)	TNFi (n=17)	Total (n=79)
Inefficacy	24%	14%	65%	30%
Adverse events	10%	10%	24%	13%
Other reasons	2%	5%	0%	3%
Total	37%	29%	88%	46%

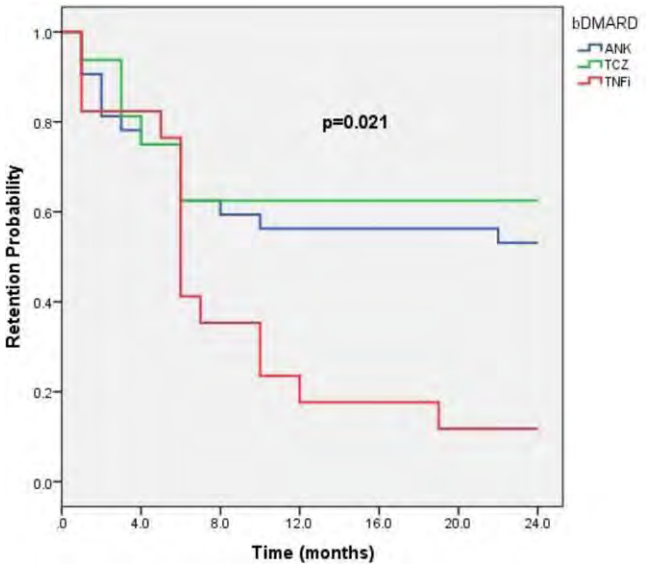


Figure 1. Kaplan-Meier curves comparing anakinra (ANK), tocilizumab (TCZ) and Tumor Necrosis Factor inhibitors (TNFi) at 24 months in adult onset Still's disease.

Conclusion: In our AOSD cohort, DRRs at 24 months of TCZ and ANK were not statistically different, and they were both significantly higher than the DRR of TNFi. Previous use of biologic agents was found to have no effect on bDMARDs retention probability.

References:

[1] Efficacy and safety of biological agents in adult-onset Still's disease; Cavalli et al; Scand J Rheumatol. 2015;44(4):309-14.

Disclosure of Interests: Nicola Farina: None declared, Alessandro Tomelleri: None declared, Corrado Campochiaro Speakers bureau: Novartis, Pfizer, Roche, GSK, SOBI, Giacomo De Luca Speakers bureau: SOBI, Novartis, Celgene, Pfizer, MSD, Giulio Cavalli Speakers bureau: SOBI, Novartis, Pfizer, Elena Baldissera Speakers bureau: Novartis, Pfizer, Roche, Alpha Sigma, Sanofi, Lorenzo Dagna Grant/research support from: Abbvie, BMS, Celgene, Janssen, MSD, Mundipharma Pharmaceuticals, Novartis, Pfizer, Roche, SG, SOBI, Consultant of: Abbvie, Amgen, Biogen, BMS, Celltrion, Novartis, Pfizer, Roche, SG, and SOBI

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SAT0520 CONTROVERSY ON DIAGNOSIS AND TREATMENT OF ADULT PATIENTS WITH SAPHO SYNDROME: MULTI-DISCIPLINARY INTERNATIONAL SURVEY

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Background: Synovitis, acne, pustulosis, hyperostosis, osteitis (SAPHO) is a rare disease involving skin and skeleton, with a potentially complicated and severe course, optimal management of which seems to require a collaborative rheumatology and dermatology care. Diagnostic criteria for SAPHO remain preliminary and lack validation. There are no evidence-based treatment algorithms in SAPHO due to lack of clinical trials in this rare medical condition.

Objectives: This study aimed to investigate the current practice in the diagnosis and treatment of SAPHO syndrome among the international rheumatology and dermatology communities.

Methods: We conducted a survey among the members of the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) combining international rheumatologists and dermatologists as well as members of the Japanese and Israeli Societies of Rheumatology.

Results: A total of 78 physicians participated in the survey: rheumatologists (83%, n=65), dermatologists (11.5%, n=9), and orthopedics (3.8%, n=3). SAPHO was considered a subtype of spondylarthritis by 48.7% (n=38), a subtype of psoriatic arthritis by 19.2% (n=15), a separate entity by 25.6% (n=20), and a subtype of reactive arthritis by 6.4% (n=5). Palmoplantar pustulosis was the most prevalent cutaneous manifestation (n=44, 56.4%) and anterior chest pain - the most prevalent osteoarticular manifestation (n=66, 84.6%). The majority (84.6%, n=66) voted for the update of the present diagnostic criteria by Khan 1994. Magnetic resonance imaging was considered the preferred imaging modality for the diagnosis of SAPHO by 41% (n=32). Conduction of bone biopsy for diagnosis of non-infectious osteitis was supported only by 10.3% (n=8). Patient-reported outcomes were considered the most appropriate measure for the assessment of disease activity by 47.4% (n=37). The treatment approach was overall similar among the rheumatology and dermatology communities, including non-steroidal anti-inflammatory drugs, bisphosphonates, conventional disease-modifying anti-inflammatory drugs, and biologics (Table 1).

Table 1. Preferences in the treatment choice of SAPHO

Treatment	% of responders
NSAIDs	76.6%
Glucocorticoids	32.5%
Conventional DMARDs	57.1%
Bisphosphonates	48.1%
Anti-TNF biologic therapy	75.3%
Other biologic therapy	20.8%
Antibiotic	14.3%
Tonsillectomy	5.1%
Isotretinoin	5.2%
Topical therapy	10.4%
Intra-articular steroid injection	7.8%

Legend: NSAIDs – non-steroidal anti-inflammatory drugs; DMARDs – disease modifying anti-rheumatic drugs

Conclusion: Our study underlines the controversy on diagnosis and treatment of SAPHO syndrome among specialists in rheumatology and dermatology and emphasizes an unmet need for update and validation of diagnostic criteria and treatment approach.

Acknowledgments: GRAPPA, Japanese Society of Rheumatology, Israeli Society of Rheumatology

Disclosure of Interests: Victoria Furer: None declared, Mitsumasa Kishimoto: None declared, Shigeyoshi Tsuji Grant/research support from: Eli Lilly, Speakers bureau: AbbVie, Asahi Kasei, Chugai, Daiichi Sankyo, Eli Lilly, Eisai, Mitsubishi Tanabe, Celgene, and Novartis Pharma K.K., Yoshinori Taniguchi: None declared, Yoko Ishihara: None declared, Tetsuya Tomita Consultant of: Eli Lilly and Company, Ori Elkayam Speakers bureau: AbbVie, BMS, Pfizer, Roche, Sanofi-Aventis, Novartis, Jansen

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SAT0521 EVALUATION OF LIPID PROFILE IN PATIENTS WITH AVASCULAR NECROSIS

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Background: Avascular necrosis (AN) is a disabling disease affecting predominantly young men. It steadily progresses to secondary osteoarthritis. The rate of disability is high, because hip joint is most commonly affected by AN; moreover, the rate of bilateral hip joint involvement is also high. The key event in the pathogenesis of AN is circulation disorder which results in ischemia and, furthermore, death of bone tissue.

Nowadays the data about lipid metabolism in patients with AN. Besides, there is contradictory data about the role of homocysteine in the risk of cardiovascular events. Based on these, it is topical to investigate lipid metabolism and endothelial function in patients with AN.

Objectives: The aim of the present study was to investigate lipid metabolism and endothelial function in patients with different stages of AN in order to find risk factors for incidence and progression of this disease.

Methods: We recruited 41 patients with AN of the femoral head or femoral condyles aged 51 (35-64) years, 56,1% (n=23) were male. The inclusion criteria was diagnosis of AN confirmed by X-Ray, CT or MRI. The exclusion criteria were: traumatic AN, Legg-Calve-Pertes disease, connective tissue systemic diseases. Also we divided patients into subgroups with early (39% (n=16)) and late (61,0% (n=25)) stages of AN.

Patients of the control group (n=32) were comparable by age and gender. The data was proceeded using non-parametric and descriptive statistics. We evaluated the following parameters: homocysteine, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, very low-density lipoprotein cholesterol, cholesterol ratio, apolipoprotein A1, apolipoprotein B.

Results: In patients with AN we observed higher level of homocysteine (12,119 (7,771-14,38) vs. 7,911 (6,612-10,54) mcmol/l, p=0,05). The results are consistent with the data that higher homocyseine level is associated with higher risk for cardiovascular events (1). There is literature data about elevated homocysteine level in patients with AN, which was associated with lower levels of vitamin B12 and folic acid. Thus, interpretation of homocystene significance is more reliable in association with vitamin B12 and folic acid levels.

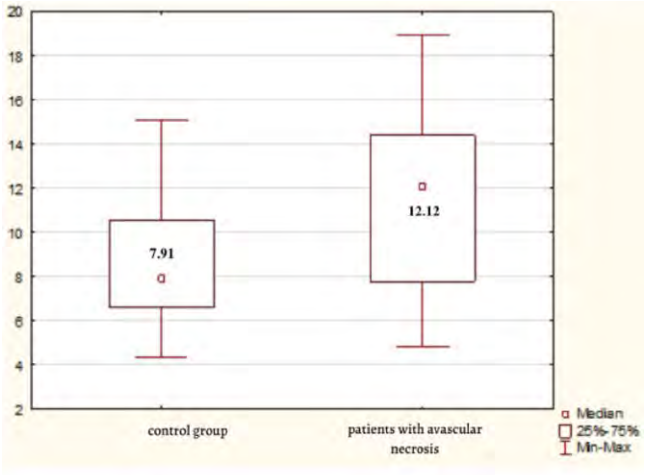


Figure 1. Homocysteine levels in patients of control group and in patients with avascular necrosis

Also, we observed that level of HDLP-C is higher in patients with early stages than in pate stages of AN (1,55 (1,31-1,57) vs. 1,23 (1,04-1,36) mmol/l, p=0,04). Thus, HDLP-C can be interpreted as a protective factor against contralateral joint involvement in AN patients. The data obtained is consistent with the existing data that HDLP-C lowers the risk for cardiovascular events.

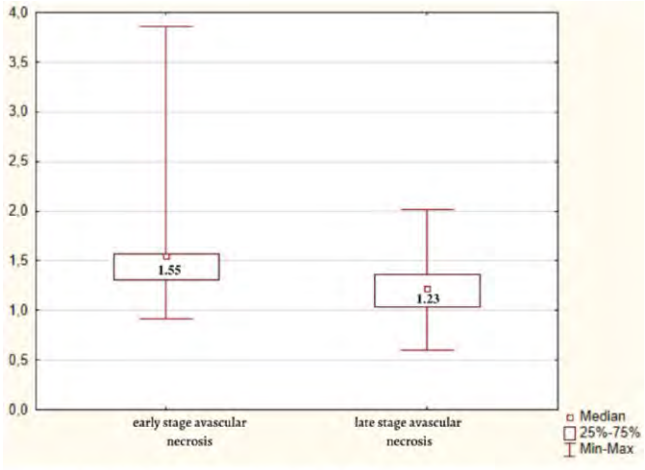


Figure 2. HDLP-C levels in patients with early and late stages of avascular necrosis

Conclusion: The data obtained indicate a significant role of dyslypidemia in the pathogenesis of AN in the context of vascular theory.

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[2] Narayanan, A., Khanchandani, P., Borkar, R.M. *et al.* Avascular Necrosis of Femoral Head: A Metabolomic, Biophysical, Biochemical, Electron Microscopic and Histopathological Characterization. *Sci Rep* 7, 10721 (2017). https://doi.org/10.1038/.

Disclosure of Interests: Katsiarina Gudkevich: None declared, Natalia Martusevich Shareholder of: k, Elena Dashkevich: None declared

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SAT0522 PROGRESSION OF VISION-RELATED QUALITY OF LIFE AND IDENTIFICATION OF RISK FACTORS IN NON-INFECTIOUS UVEITIS PATIENTS

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Background: Uveitis are characterized by inflammation of the middle layer of the eye wall. In developed countries uveitis are the second major treatable cause of blindness in those 20–65 years of age. Additionally, more than 50% of the subjects affected with these conditions will develop complications related to the uveitis, and more than 30% will suffer visual impairment. As a result, these conditions are associated with an important burden. The assessment of the patient's quality of life (QoL) through standardized and validated questionnaires allows us to evaluate objectively the burden of the disease. Several studies have shown that the QoL of uveitis patients is reduced when compared with that of general population. Moreover, several socio-demographic and clinical related characteristics have been associated with impaired QoL. However, no longitudinal analysis of the vision-related (VR) QoL in clinical practice has been carried out.

Objectives: To describe VR-QoL in non-infectious uveitis (NIU) patients during a follow-up period of two years. Furthermore, to analyse the influence of socio-demographic, clinical and treatment factors on the progression of VR-QoL.

Methods: Longitudinal prospective study which includes patients examined in a multidisciplinary tertiary uveitis clinic, with a diagnosis of NIU. In each of these patients a yearly determination of VR-QoL was carried out following the VFQ-25 questionnaire, finally including all those who had completed at least an initial questionnaire and a second one after two years of follow-up. Analysis of risk factors at baseline in repeated VFQ-25 measurements was carried out by generalized estimating equations (GEE) models. Variables related to demographic, clinical and treatment factors with a determination of p-value <0.15 were included in multivariable models, which were then compared using the *Quasi Akaike Information Criteria* (qAIC). A local Ethics Committee approved the execution of this project.

Results: 128 patients were included, 117 of which also had an evaluation after the first year of follow-up. 55.5% were female with a median age of 34 years at the start of symptoms and of 37 years at the moment of attending our clinic for the first time. First evaluation of VR-QoL was determined a median (p25-p75) of 6.1 (1.8-13.1) years after that first visit. The most frequent locations of NIU were anterior (41.1%), panuveitis (27.4%), posterior (16.1%) and intermediate (15.3%). At our first evaluation, 27.3% of patients were receiving treatment with topical steroids, 22.3% oral, 49.2% immunosuppressant drugs (both synthetic and/or biological) and 19.05% biological therapies. The median (p25-p75) VFG25 determinations at baseline, first and second years of follow-up were 0.87 (0.78-0.93), 0.88 (0.80-0.93) y 0.89 (0.81-0.94), with no significant differences (first year vs. Baseline p = 0.54; 2 years vs. Baseline p = 0.61).

In the GEE multivariable models the presence at baseline of permanent incapacity due to NIU, concomitant thyroid disease, worse visual acuity, unilateral pattern, cataracts, retinal vasculitis, epiretinal membrane and use of azathioprine were independently associated with a worse VR-QoL (**Table 1**).

Table 1. Risk factors related to VR-QoL in patients with NIU

Variables	Coef. (IC 95%)	p-value
Visual acuity	23.6 (12.3 - 34.8)	<0.01
Permanent incapacity	-24.8 (-33.7 - -15.9)	<0.01
Unilateral NIU	-2.9 (-5.7 - -0.006)	0.05
Cataracts	-5.2 (-10 - -0.3)	0.037
Vasculitis	-13.3 (-23.4 - -3.1)	0.011
Epiretinal membrane	-6.8 (-12.7 - -0.8)	0.026
Azathioprine	-7.5 (-14.7 - -0.3)	0.041

Conclusion: During these two years of follow-up, no significant changes have taken place regarding VR-QoL in patients with NIU assessed at a tertiary centre. Other than visual acuity at baseline, certain ocular manifestations and clinical comorbidities have also been shown to have an independent effect on the VR-QoL of these patients.

Disclosure of Interests: None declared

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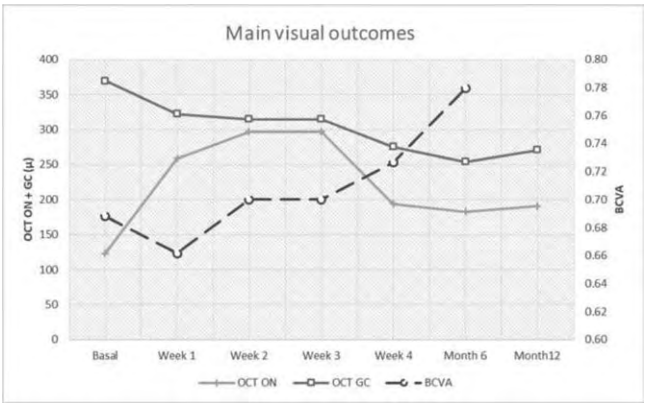
SAT0523 BIOLOGICAL THERAPY IN REFRACTORY ATYPICAL OPTIC NEURITIS. MULTICENTER STUDY

A. Herrero Morant[1], C. Álvarez Reguera[1], V. Calvo del Rio[1], O. Maíz Alonso[2], A. Blanco[3], J. Narváez[4], S. Castañeda[5], E. Vicente[5], S. Romero-Yuste[6], R. Demetrio-Pablo[7], A. Urruticoechea-Arana[8], J. L. García Serrano[9], J. L. Callejas Rubio[9], N. Ortego[9], J. Sánchez[10], P. Estrada[11], I. Rua-Figueroa[12], D. Martínez-López[1], J. L. Martín-Varillas[1], M. Á. González-Gay[1], R. Blanco[1]. [1]*H. U. M. Valdecilla, Rheumatology, Santander, Spain*; [2]*H. Donostia, Rheumatology, Santander, Spain*; [3]*H. Donostia, Ophthalmology, San Sebastián, Spain*; [4]*H. Bellvitge, Rheumatology, Barcelona, Spain*; [5]*H. La princesa, Rheumatology, Madrid, Spain*; [6]*H. Pontevedra, Rheumatology, Pontevedra, Spain*; [7]*H. U. M. Valdecilla, Ophthalmology, Santander, Spain*; [8]*H. Can Misses, Rheumatology, Ibiza, Spain*; [9]*H. San Cecilio, Rheumatology, Granada, Spain*; [10]*H. 12 de Octubre, Rheumatology, Madrid, Spain*; [11]*H. Moises Broggi, Rheumatology, Barcelona, Spain*; [12]*H. Dr. Negrín, Rheumatology, Gran Canaria, Spain*

Background: Optic Neuritis (ON) is an inflammation of the optic nerve. Its most common presentation is demyelinating typical ON. Atypical ON is rare, severe, non-demyelinating and can be isolated or associated to different diseases including autoimmune diseases. If it is not treated, it can lead to devastating visual results. Conventional treatment includes systemic corticosteroids and conventional immunosuppressants (CIS).

Objectives: Our aim was to assess the efficacy of biological therapy in atypical ON refractory to conventional treatment.

Methods: Open-label multicenter study including 19 patients diagnosed with atypical ON refractory to systemic corticosteroids and at least one CIS. The main outcomes assessed were Best Corrected Visual Acuity (BCVA) and optic nerve and ganglionar cells Optical Coherence Tomography (OCT). These outcome variables were recorded at baseline, 1 week, 2 weeks, 1 month, 3 months and 6 months and 1 year after biological therapy onset.



FIGURE

Results: We studied 19 patients (12 women/7 men); mean age of 34.8 ± 13.9 years. The underlying diseases were idiopathic (n=7), Behçet´s disease (n=5), systemic lupus erythematosus (n=2), neuromyelitis optica (n=3), sarcoidosis (n=1) and relapsing polychondritis (n=1) **(TABLE).** Before biological therapy and besides systemic corticosteroids, patients had received different CIS. Biological therapy was adalimumab (n=6), rituximab (n=6), infliximab (n=5) and tocilizumab (n=4). After biological therapy, an improvement in ocular parameters was observed: BCVA [0.7±0.3 to 0.8±0.3; p= 0.03], optic nerve OCT [123.2±58.3 to 190.5±175.4; p= 0.11], and ganglionar cells OCT [369.6±137.4 to 270.7±23.2; p= 0.03] at one year **(FIGURE)**. After a mean follow-up of 29.1 ±19.2 months, there were no severe adverse effects observed.

Conclusion: Biological therapy may be effective in patients with refractory atypical ON.

Disclosure of Interests: Alba Herrero Morant: None declared, Carmen Álvarez Reguera: None declared, Vanesa Calvo del Rio Grant/research support from: MSD and Roche, Speakers bureau: Abbott, Lilly, Celgene, Grünenthal, UCB Pharma, Olga Maíz Alonso: None declared, Ana Blanco Speakers bureau: Abbvie, J. Narváez: None declared, Santos Castañeda: None declared, Esther Vicente Speakers bureau: BMS, Roche., Susana Romero-Yuste: None declared, Rosalía Demetrio-Pablo: None declared, ANA URRUTICOECHEA-ARANA: None declared, J. L. García Serrano: None declared, J. L. Callejas Rubio: None declared, Norberto Ortego: None declared, Julio Sánchez: None declared, Paula Estrada: None declared, Iñigo Rua-Figueroa: None declared, David Martínez-López: None declared, José Luis Martín-Varillas Grant/research support from: AbbVie, Pfizer, Janssen and Celgene, Speakers bureau: Pfizer and Lilly, Miguel Á. González-Gay Grant/research support from: AbbVie, MSD and Roche, Speakers bureau: AbbVie, MSD and Roche, Ricardo Blanco Grant/research support from: Abbvie, MSD and Roche, Consultant of: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen and MSD, Speakers bureau: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen, Lilly and MSD

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SAT0524

THE INCIDENCE RATE OF ADULT ONSET STILL'S DISEASE IN SLOVENIA

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Background: Adult Onset Still's disease (AOSD) is an uncommon systemic inflammatory disease.

Objectives: To determine for the first time the incidence rate of AOSD in our population.

Methods: We retrospectively collected AOSD cases diagnosed between 1 January 2010 and 31 December 2019 at our secondary/tertiary rheumatology centre, which is the only referral centre for an average population of 704,000 adults. AOSD cases were identified by searching the electronic medical database both for ICD-10 code M06.1 and a full text search for »AOSD«. Patients' records were analyzed and descriptive statistics was used to describe our study group. The adult population was obtained from the national statistics institute database. The annual incidence rate for AOSD was calculated.

Results: During the 10-year observation period we identified 22 incipient AOSD cases. All 22 cases fulfilled Yamaguchi classification criteria for AOSD[1]. Five cases were excluded from analyses since they were referred to our department from regions served by other secondary/tertiary centres. Hence, we finally analyzed 17 AOSD cases (11 females; median (IQR) age 38.9 (29.9; 56.5) years, range 20-71 years), resulting in the average annual incidence rate of 2.4 (95%CI 1.5-3.8) cases per 10^6 adults. Age specific incidence rate of AOSD is presented in Figure 1. Clinical characteristics of AOSD cases at presentation are shown in Table 1. AOSD was complicated with macrophage activating syndrome in 4/17 (23.5%) cases, and with pulmonary hypertension in one case. Patients were followed for a median (IQR) 31 (20; 58) months. Twelve (70.5%), 2 (11.8%), and 3 (17.6) patients had monophasic, relapsing, and chronic disease course, respectively.

Table 1. Clinical characteristics of AOSD at presentation

Characteristic	AOSD (%)	Characteristic	AOSD (%)
Female gender	64.7	Lung infiltrates	23.5
Age*	38.9 (29.9;56.5)	Pericardial effusion	23.5
Fever	94.1	Abdominal pain	17.6
Weight loss	64.7	Lymphadenopathy	52.9
Skin rash	76.5	Splenomegaly	41.2
Throat pain	88.2	Hepatomegaly	17.6
Arthralgia/Arthritis	88.2/47.1	Leukocytosis	88.2
Myalgia	29.4	Elevated AST/ALT	88.2
Pleural effusion	23.5	Ferritin >1000ng/ml	94.1

Legend: *median (IQR);

TABLE

Case	Gender/ Age	Underlying disease	Laterality	IV steroids dose (g)	Maximum prednisone oral dose (g)	Conventional immunosuppressants	Biological therapy	Adverse effects
1	F/29	Idiopathic	Unilateral	4	60	AZA	TCZ	No
2	F/26	Idiopathic	Bilateral	5.5	30	AZA	TCZ	No
3	F/13	Idiopathic	Bilateral	-	10	MTX	ADA	No
4	F/25	Idiopathic	Bilateral	4	60	MTX	IFX, TCZ	No
5	F/24	Idiopathic	Bilateral	0.5	60	MTX, AZA	ADA	No
6	M/14	Idiopathic	Bilateral	-	10	MTX	ADA	No
7	F/30	Vasculitis ANCA+	Unilateral	3	60	AZA, MMF, LFM, CFM	RTX	Yes
8	M/21	Behçet	Bilateral	-	60	MTX, AZA	ADA	Nausea Vomits
9	M/25	Behçet	Unilateral	0.5	60	MTX, CyA	ADA	No
10	M/39	Behçet	Unilateral	3	80	MTX, MMF	IFX	No
11	M/40	Behçet	Unilateral	-	80	MMF	IFX	No
12	M/37	Behçet	Unilateral	-	60	CyA	IFX	No
13	F/68	NMO	Unilateral	2.5	30	CFM, AZA	RTX	No
14	F/41	NMO	Unilateral	3	60	CFM	RTX	Infection
15	F/43	NMO	Bilateral	5	60	AZA	RTX	Infusion reaction
16	F/56	SLE	Unilateral	-	60	HCQ, MMF, CFM	RTX	No
17	F/47	SLE	Unilateral	5	60	HCQ, MMF	RTX	No
18	F/43	Relapsing polychondritis	Bilateral	3	60	MTX, CFM	IFX, TCZ	No
19	M/41	Sarcoidosis	Bilateral	3	40	AZA	ADA	No

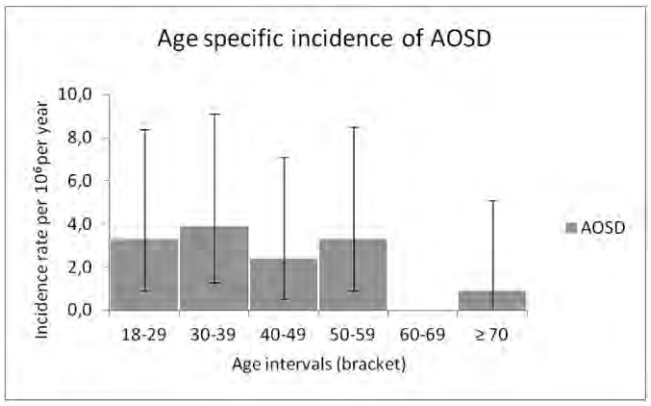


Figure 1. Age specific incidence rate of AOSD

Conclusion: AOSD is rare in our population, with an average annual incidence rate of 2.4 cases per 10^6 adults.

References:

[1] Yamaguchi M, Ohta A, Tsunematsu T, Kasukawa R, Mizushima Y, Kashiwagi H, et al. Preliminary criteria for classification of adult Still's disease. J Rheumatol. 1992;19(3):424-30.

Acknowledgments -

Disclosure of Interests: ALOJZIJA HOCEVAR: None declared, Ziga Rotar Consultant of: Speaker and consulting fees from Abbvie, Amgen, Biogen, Eli Lilly, Medis, MSD, Novartis, Pfizer, Roche, Sanofi., Speakers bureau: Speaker and consulting fees from Abbvie, Amgen, Biogen, Eli Lilly, Medis, MSD, Novartis, Pfizer, Roche, Sanofi., Monika Krosel: None declared, Martina Plešivčnik Novljan: None declared, Sonja Praprotnik: None declared, Matija Tomsic: None declared

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SAT0525

EFFICACY AND SAFETY OF MZR FOR IGG4-RELATED DISEASE.

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Background: IgG4-Related Disease (IgG4RD) is known to cause multiple organ lesions with infiltration of IgG4-positive plasma cells, and patients often have relapses with tapering treatments despite an initial good response to glucocorticoids therapy. Mizoribine (MZR) is an immunosuppressant working as an inhibitor of purine synthesis, which mechanism of action is similar to mycophenolate mofetil. Data regarding the efficacy and safety of MZR on IgG4RD is limited although some previous case reports[1] showed effectiveness for IgG4RD.

Objectives: This study aims to assess the efficacy and safety of MZR in patients with IgG4RD.

Methods: We retrospectively reviewed charts of IgG4RD patients who used MZR between January 2004 and December 2019 at Immuno-Rheumatology Center in St. Luke's International Hospital, Tokyo, Japan. We investigated basic demographics, involved organs, results of blood tests including IgG and IgG4 titer, and medications used including glucocorticoid and other immunosuppressants (IS). We followed IgG4 titer, dose of glucocorticoid, flare of disease and retention of MZR at the beginning, 6 and 12months after starting MZR. We compared changes in PSL (prednisolone) doses and IgG4 titers over time using Friedman test with Bonferroni correction. We also checked adverse events during follow up.

Results: Twenty-two patients with IgG4RD who used MZR were included. Median age was 62 years old, and 15 (68.2%) patients are male. Lacrimal and salivary glands, pancreatitis and retroperitoneal fibrosis were common lesions. All patients were initially treated with glucocorticoids. Flare was observed in 5 (22.7 %) patients before initiation of MZR. The number of patients who continued MZR without flare are 19 (86.4 %) at 6 months, and 14 (73.7 %) at 12 months. IgG4 titer significantly declined at 6 and 12 months from baseline although significant consecutive decrease in PSL dose (Figure 1, 2). Liver dysfunctions are commonest adverse events (n=16, 72.7%) but mild (grade1; n=15, 68.2%) and most cases are apparently due to other reasons. Serious infection (SI) occurred in 3 (13.6%) patients in total follow up, however no SI were observed during 1 year after MZR treatment.

Conclusion: MZR can be safely used in patients of IgG4RD with high retention rate, and seemed to have steroid-sparing effect. Prospective comparative studies are needed.

References:

[1] Nanke Y, Kobashigawa T, Yago T, Kamatani N, Kotake S. A case of Mikulicz's disease, IgG4-related plasmacytic syndrome, successfully treated by corticosteroid and mizoribine, and then by mizoribine alone. Intern Med 49: 1449-1453, 2010.

Table 1. Patient characteristics

Factor	Overall (n=22)
Age	62 [60-69]
Male (%)	15 (68.2)
Biopsy proven (%)	14 (63.6)
Follow up after treatment (days)	1425.5 [589.0-2519.8]
Days to MZR treatment from initial treatment	68.5 [14.0-178.3]
Days to MZR treatment from flare up or initial treatment	22.0 [13.0-107.0]
Follow up after initiation of MZR treatment (days)	1159.0 [365.5-2387.5]
Number of flare before MZR treatment(%)	5 (22.7)
with Methotrexate (%)	1 (4.5)
Initial MZR dose (mg/day)	150 [150-150]
Last MZR dose (mg/day)	200 [150-300]
Involved organs	
Number of involved organs	3.0 [2.0-3.0]
Multiple lesion(%)	15 (68.2)
Lacrimal gland (%)	11 (50.0)
Salivery gland (%)	11 (50.0)
Sinus (%)	2 (9.1)
Thyroid gland (%)	1 (4.5)
Lung (%)	4 (18.2)
Pancreatitis (%)	9 (40.9)
Biliary duct(%)	0 (0.0)
Retroperitoneal fibrosis (%)	8 (36.4)
Kidney (%)	1 (4.5)
Orbital lesion(%)	0 (0.0)
Periaortitis (%)	3 (13.6)
Arteritis (%)	4 (18.2)
Prostatitis (%)	1 (4.5)
Joint (%)	1 (4.5)
Skin (%)	0 (0.0)
Lymphodadenopathy (%)	7 (31.8)
IgG (mg/dL)	1722.0 [1354.0-3429.0]
IgG4 (mg/dL)	184.5 [164.0-665.3]
Concommitant immunosuppressnts	
Until 12 months after MZR treatment	6 (27.3)
Azathioprin (%)	1 (4.5)
Methotorexate (%)	4 (18.2)
Tacrolimus (%)	2 (9.1)
Over all	
Azathioprin (%)	1 (4.5)
Methotorexate (%)	8 (36.4)
Tacrolimus (%)	2 (9.1)

Table 2. Disease and treatment status before and after initiation of MZR

	At PSL treatment initiation	At MZR initiation	At 1 month after MZR treatment	At 6 months after MZR treatment	At 12 months after MZR treatment	At latest visit
Number of followed-up patient (%)	-	-	22 (100.0)	22 (100.0)	19 (86.4)	22 (100.0)
No flare and retention of MZR (%)	-	-	22 (100.0)	19 (86.4)	14 (73.7)	9 (40.9)
Flare after treatment with MZR (%)	-	-	0 (0.0)	3 (13.6)	5 (26.3)	8 (36.4)
Retention of MZR (%)	-	-	22 (100.0)	22 (100.0)	19 (100.0)	15 (68.2)
PSL dose (mg/day)	35.0 [20.6-43.8]	12.5 [10.0-23.1]	10.0 [7.8-18.8]	5.6 [4.6-7.9]	3.0 [2.3-5.0]	2.0 [0.6-3.8]
IgG (mg/dL)	1722.0 [1354.0-3429.0]	1301.0 [1172.8-1560.5]	1213.0 [1108.0-1378.0]	1275.5 [1082.0-1573.8]	1381.0 [1195.5-1617.0]	1372.5 [1130.8-1510.0]
IgG4 (mg/dL)	184.5 [164.0-665.3]	122.0 [94.2-203.0]	102.0 [91.6-246.0]	92.2 [45.8-194.0]	147.0 [69.1-191.0]	122.5 [69.8-252.5]

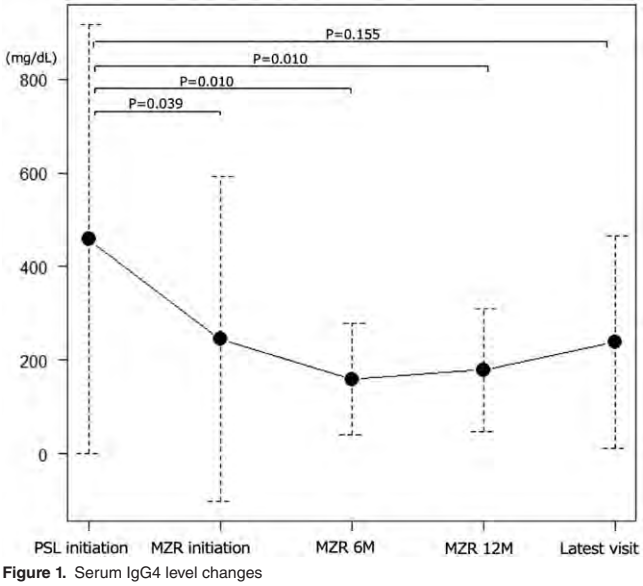


Figure 1. Serum IgG4 level changes

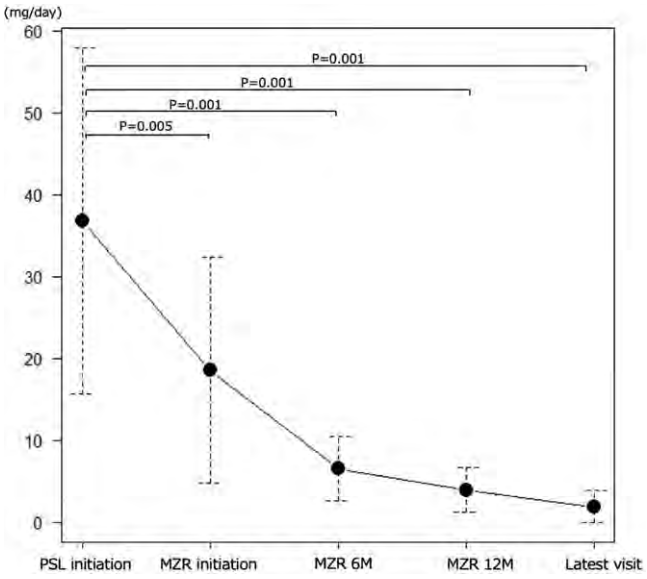


Figure 2. Changes in the PSL dose over time

Disclosure of Interests: None declared
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SAT0526

COMPARISON OF INFLAMMATORY MARKERS AS DIAGNOSTIC TOOL IN PATIENTS WITH ADULT-ONSET STILL'S DISEASE

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Background: The diagnosis for adult-onset Still's disease (AOSD) is still based on nonspecific symptoms and laboratory data, and had necessity to rule out several infectious, autoimmune or malignant diseases.

Objectives: This study aimed to elucidate the efficiency of inflammatory markers, including systemic immune-inflammation index (SII); C-reactive protein (CRP)-to-albumin ratio (CAR), albumin-to- glubulin ratio (AGR), prognostic nutritional index (PNI), and ferritin-to-ESR ratio (FER) for evaluation of diagnostic or prognostic factors in AOSD.

Methods: The medical records of patients with suspected AOSD between January 1999 and June 2019 were collected and retrospectively analyzed. Among 225 patients, 61 patients received another diagnosis, such as infection and malignancy, and 164 patients were newly diagnosed to AOSD. The values of SII, CAR, AGR, PNI, and FER were compared with AOSD and non-AOSD groups. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic significance of inflammatory markers. Correlations between inflammatory markers and disease activity index were analyzed.

Results: A total of 164 patients who diagnosed AOSD had higher values of SII, CAR, and FER as well as lower values of AGR and PNI. For AOSD diagnosis, the area under the curve (AUC) obtained from the ROC curve were 0.859 (95% CI=0.806-0.911) for SII, 0.769 (95% CI=0.702-0.837) for CAR, 0.749 (95% CI=0.615-0.782) for AGR, 0.699 (95% CI=0.675-0.823) for PNI, and 0.764 (95% CI=0.693-0.834) for FER with cut-off value of 2195.7, 1.80, 1.38, 48.8 and 17.0, respectively. The SII had the largest AUC, and FER and SII each had the highest sensitivity (70.9%) and specificity (91.5%). In correlation analysis, there were no strong correlations between inflammatory markers and disease activity indices except CAR and CRP.

Table 1. Demographic and baseline characteristics of patients with adult-onset Still's disease(AOSD)

	AOSD patients (N=164)	Initially suspected AOSD but not diagnosed (N=61)	P-value
Age, years	42.6 ± 15.7	42.1 ± 14.4	0.805
Fever	162 (98.8)	56 (91.8)	0.017
Sore throat	93 (56.7)	18 (29.5)	<0.001
Skin rash	131 (79.9)	26 (42.6)	<0.001
Lymphadenopathy	63 (38.4)	10 (16.4)	0.002
Hepatomegaly	25 (15.2)	1 (1.6)	0.004
Arthritis	79 (48.2)	22 (36.1)	0.132
SII	4601.7 ± 6406.8	1105.6 ± 970.0	<0.001
CAR	3.37 ± 2.82	1.22 ± 1.58	<0.001
AGR	1.15 ± 0.35	1.38 ± 0.39	<0.001
PNI	41.94 ± 6.70	48.85 ± 8.43	<0.001
FER	139.19 ± 372.12	28.39 ± 70.80	0.006

Table 2. Discriminatory ability of inflammatory markers for predicting AOSD diagnosis

Variables	AUC	P-value	Cut-off	Sensitivity	Specificity	+LR	-LR
SII	0.859	<0.001	2195.7	64.6%	91.5%	7.60	0.39
CAR	0.769	<0.001	1.80	65.2%	74.6%	2.57	0.47
AGR	0.700	<0.001	1.38	54.1%	82.3%	3.06	0.56
PNI	0.752	<0.001	48.8	52.5%	86.0%	3.75	0.55
FER	0.764	0.006	17.0	70.9%	74.6%	2.76	0.39

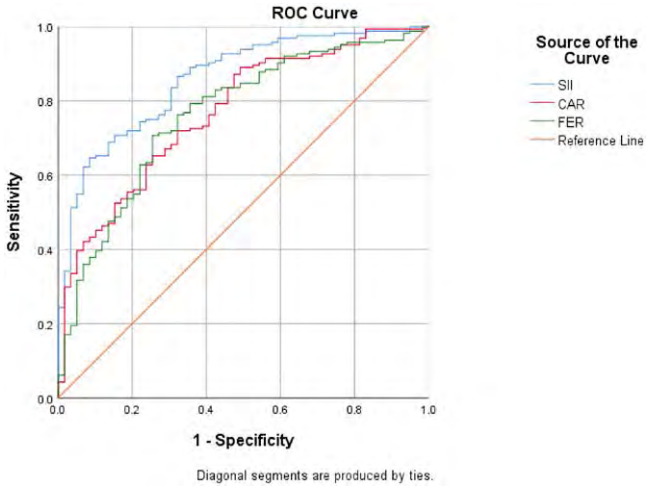


Figure 1. Receiver operating characteristic (ROC) curves for SII, CAR and FER in AOSD and non-AOSD patients (Initially suspected AOSD but not diagnosed).

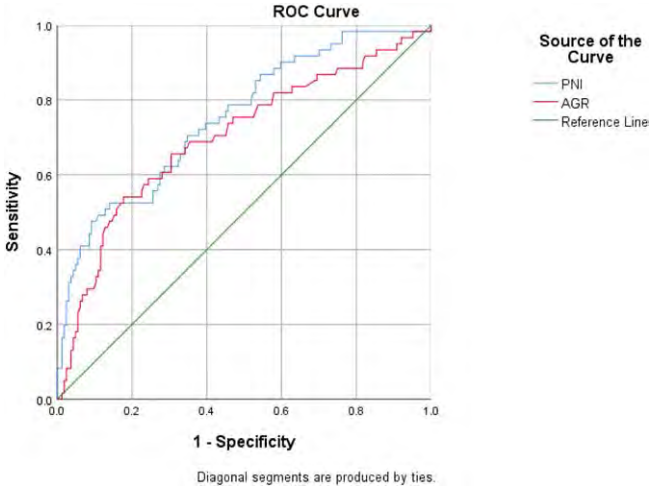


Figure 2. Receiver operating characteristic (ROC) curves for AGR and PNI in AOSD and non-AOSD patients (Initially suspected AOSD but not diagnosed).

Conclusion: SII, CAR, AGR, PNI and FER were can be used as a practical tool for diagnosing AOSD. Among the inflammatory markers, SII was revealed as most powerful marker for diagnosis.

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[1] Yamaguchi M, Ohta A, Tsunematsu T, et al. Preliminary criteria for classification of adult Still's disease. J Rheumatol 1992;19:424-30.

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Disclosure of Interests: None declared

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SAT0527

COMBINED EFFECT OF COMMON VARIANTS IN EXON 2 OR EXON 3 AND A PATHOGENIC MUTATION IN EXON 10 OF THE MEDITERRANEAN FEVER GENE ON INFLAMMASOME ACTIVATION IN JAPANESE PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER

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Background: Familial Mediterranean fever (FMF) is an autoinflammatory disease that is caused by Mediterranean fever (*MEFV*) gene mutations. It is characterized by recurrent and self-limiting febrile attacks within a short period. Although the pathologic significance of *MEFV* exon 2 or exon 3 common variants in patients with FMF is modest and these variants are usually associated with less severe clinical presentations of FMF (1, 2), their combined effects with pathogenic mutation in exon 10 remain to be evaluated.

Objectives: To determine the combined effect of common variants on clinical manifestations and inflammasome activity, we compared the clinical and laboratory characteristics between the coexistence and non-coexistence of *MEFV* exon 2 or exon 3 variants in patients with FMF that had a heterozygous *MEFV* exon 10 mutation.

Methods: We excluded patients with FMF that had two *MEFV* exon 10 mutations in one or more alleles and those with *MEFV* variants in exons other than in exons 2, 3, or 10. Finally, we reviewed 131 Japanese patients with FMF that had a heterozygous *MEFV* exon 10 mutation, and they were divided into the groups with and without *MEFV* exon 2 or exon 3 variants of 34 and 97, respectively. All enrolled patients had only a heterozygous M694I mutation in exon 10 of the *MEFV* gene. We measured serum IL-18 levels at remission without febrile attacks in the groups with and without *MEFV* exon 2 or exon 3 variants of 9 and 31, respectively.

Results: In the univariate analysis, the group with variants in exon 2 or exon 3 had significantly earlier onset (16.0 years v.s. 20.5 years, p = 0.04), a higher percentage of thoracic pain with febrile attacks (68% v.s. 44%, p = 0.02), a higher frequency of attack (1.0/month v.s. 0.5/month, p = 0.02), and a higher IL-18 level in the serum at remission (606.3 pg/ml v.s. 168.4 pg/ml, p = 0.04, Figure 1) compared to the group without these variants. Importantly, multivariate analyses showed that the coexistence of *MEFV* exon 2 or exon 3 variants and an exon 10 mutation was independently and significantly associated with earlier onset of FMF (p = 0.049) and thoracic pain (p = 0.03).

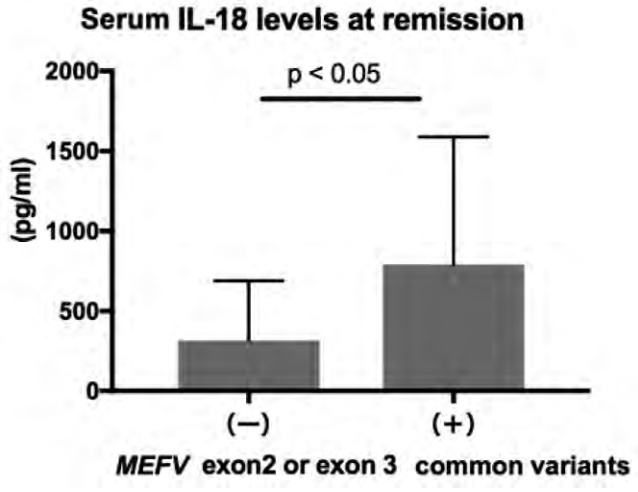


Figure 1.

Conclusion: Our results suggest that the coexistence of *MEFV* exon 2 or exon 3 variants and a *MEFV* exon 10 mutation has combined effects on inflammasome activation in the Japanese population.

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[1] Migita K, Uehara R, Nakamura Y, et al. Familial Mediterranean fever in Japan. Medicine (Baltimore). 2012 Nov;91(6):337-43.

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Disclosure of Interests: None declared

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SAT0528

CLINICAL PHENOTYPES OF IGG4-RELATED DISEASE REFLECT DIFFERENCES IN EPIDEMIOLOGICAL FEATURES, SEROLOGICAL FINDINGS, AND PROGNOSTIC OUTCOMES

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Background: Four clinical phenotypes of IgG4-Related Disease (IgG4-RD) have been recently identified by Latent Class Analysis (LCA) - Pancreato/biliary (Group 1); Retroperitoneum/Aortitis (Group 2); Head-and-neck limited (Group 3); Mickulicz/Systemic (Group 4) - but the relevance of this classification for patient management remains unknown (1,2).

Objectives: We aimed to assess whether clinical judgment can replicate LCA classification and to evaluate potential differences in epidemiological features, serological findings, and disease outcomes between disease phenotypes.

Methods: The study included 179 patients. Four IgG4-RD experts were asked to classify a validation cohort of 40 patients according to published LCA derived phenotypes based on clinical judgment. Agreement between LCA and clinical clustering was calculated. To assess differences among disease phenotypes, the following variables were recorded on additional 139 patients: serum IgG4 and IgE; inflammatory markers; eosinophils; plasmablasts; IgG4-RD Responder Index (RI); history of atopy, diabetes, osteoporosis, relapses, and tumors; cumulative dose of glucocorticoids and use of rituximab.

Results: Clinical judgment recapitulated LCA classification with strong agreement between IgG4-RD experts (κ= 0.841, p < 0.0005). Group 1 showed the highest levels of serum IgG4 and IgE. Group 2 and 4 had the lowest and highest IgG4-RD RI, respectively (Table 1). Increased cumulative doses of glucocorticoids and higher relapse rate were observed in Group 3 (Fig 1). A higher incidence of diabetes mellitus was observed in Group 1 and 4.

Table 1 Clinical and serological characteristics of patients cohort.

	Group 1 (59 pts - 45%)	Group 2 (29 pts - 22%)	Group 3 (25 pts - 19%)	Group 4 (18 pts - 14%)	P value
Female n° (%)	12 (20%)	8 (28%)	11 (44%)	5 (28%)	0.18
Age	67 (61-73)	61 (56-70)	52 (40-62)	57 (51-62)	<0.0001
Serum IgG4 (mg/dL)	331 (184-575)	155 (49-258)	150 (80-255)	282 (166-460)	0.0009
IgG4-RD RI	9 (6-9)	6 (6-9)	9 (6-12)	9 (6-13)	0.004
Definite diagnosis n° (%)	20 (34%)	18 (62%)	20 (80%)	10 (55%)	0.0008
Probable diagnosis n° (%)	1 (0.59%)	0 (0%)	1 (0.19%)	1 (0.14%)	0.6
Possible diagnosis n° (%)	38 (64%)	10 (34%)	4 (16%)	7 (39)	0.0003
Emergency Department n° (%)	37 (63%)	14 (48%)	7 (28%)	10 (55%)	0.03
History of atopy n° (%)	7 (12%)	4 (14%)	7 (28%)	6 (23%)	0.09
ESR (mm/h)	20 (8-39)	40 (14-59)	38 (14-54)	12 (8-21)	0.04
CRP (mg/L)	5 (2-8)	10 (3-52)	8 (3-28)	3 (2-6)	0.03
Eosinophils (cell/mm^3)	200 (200-500)	200 (100-275)	300 (200-475)	200 (100-500)	0.3
IgE (U/mL)	283 (97-723)	69 (28-264)	120 (41-412)	219 (54-657)	0.02
Plasmablast (cell/mL)	1765 (627-4000)	1890 (1020- 4000)	2000 (370- 4780)	2690 (140-5130)	0.99
Diagnostic delay (months)	4 (2-9)	7 (4-12)	10 (3-18)	11 (2-38)	0.04
Starting prednisone dose (mg, range)	60 (37-70)	50 (40-75)	65 (40-90)	40 (30-70)	0.8
Diabetes at disease onset	10 (17%)	1 (3%)	2 (8%)	2 (11%)	0.09

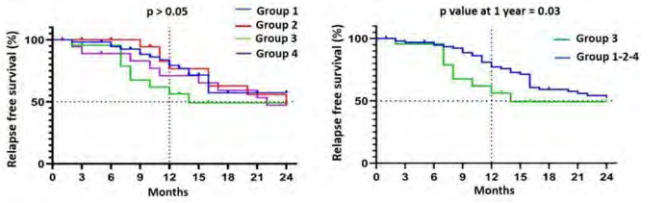


Figure 1. Relapse free survival of the four different IgG4-RD phenotypes.

Conclusion: Clinical phenotypes of IgG4-RD reflect differences in epidemiological features and prognostic outcomes.

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Disclosure of Interests: Marco Lanzillotta: None declared, Emanuel Della Torre: None declared, Corrado Campochiaro Speakers bureau: Novartis, Pfizer, Roche, GSK, SOBI, Gaia Mancuso: None declared, Lorenzo Dagna Grant/research support from: The Unit of Immunology, Rheumatology, Allergy and Rare Diseases (UnIRAR) received unresctricted research/educational grants from Abbvie, Bristol-Myers Squibb, Celgene, Janssen, Merk Sharp & Dohme, Mundipharma Pharmaceuticals, Novartis, Pfizer, Roche, Sanofi-Genzyme, and SOBI., Consultant of: Prof Lorenzo Dagna received consultation honoraria from Abbvie, Amgen, Biogen, Bristol-Myers Squibb, Celltrion, Novartis, Pfizer, Roche, Sanofi-Genzyme, and SOBI.

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SAT0529 CLINICAL CHARACTERISTICS AND TREATMENT PATTERNS IN A PATIENT GROUP WITH INTERSTITIAL LUNG DISEASE.

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Background: Diffuse interstitial lung disease (ILD) is frequently associated with connective tissue diseases (CTD) and is one of the main causes of morbidity and mortality in these patients. Recently, the concept of Interstitial Pneumonia with Autoimmune Features (IPAF) has been defined to characterize ILD associated with systemic manifestations limited to subtle serological and clinical autoimmune abnormalities and not fulfilling the international criteria for the diagnosis of a given CTD.

Objectives: The objective of this study is to describe the clinical, serological and radiological characteristics, as well as the treatment patterns of patients with ILD referred to a Rheumatology Service for suspected CTD

Methods: Observational, cross-sectional study of 43 patients with ILD referred for evaluation to the medical consultation of CTD of the Rheumatology service at the Reina Sofía Hospital. Patients were classified as patients with defined CTD, patient with IPAF and patients with other types of pneumopathy. We conducted a descriptive study of all patients and compared the clinical-analytical-radiological characteristics and treatment patterns of the first two groups.

Results: Of the 43 patients, 67.40% were women with a mean age at diagnosis of 65.65 (10.42) years and 53.50% of smoking patients

Of the total of patients, 16 (37.2%) were included in the CTD group, 17 (39.5%) met criteria for IPAF and 10 (23.3%) had another type of pneumopathy.

In the CTD group scleroderma was the most frequent disease (6/16), followed by inflammatory myopathy (4/16), Sjögren's syndrome (3/16), rheumatoid arthritis (2/16) and polymyalgia rheumatic (1/16). In this group of patients, the most common symptom was Raynaud's phenomenon (RP) (7/16), followed by arthritis (7/16) and mechanic's hands (3/16). Regarding the most frequently antibodies were ANA (100%), anti-RO (41.7%), anti-citrullinated protein antibodies (30%) and rheumatoid factor (RF) (28.6%).

In patients with IPAF, as in the CTD group, the most observed clinical criterion was RP (5/17), followed by arthritis (1/17) and mechanic's hands (1/17). Among the serological criteria the most common antibodies were ANA (100%), followed by anti-RO (33.3%), anti-RNA synthetase (28.6%) and RF (22.2%).

Regarding the radiological pattern, in both groups the most frequent was nonspecific interstitial pneumonia, followed by the indeterminate pattern and usual interstitial pneumonia (UIP) in third place. There were no significant differences by gender and age, between the group of CTD and IPAF, observing in both groups a predominance of women with a similar mean age, being the upper smoking habit in the IPAF group (70.6% vs 31.5%, p= 0.02). Regarding the treatment used, the use of immunosuppressants (IS) was more frequent in CTD group (56.3% vs 11.8%, p = 0.007).

Conclusion: The clinical-serological and radiological characteristics were similar among patients with IPAF and CTD, which supports the notion of a similar pathophysiology in both groups. In our cohort patients with CTD received IS more frequently than IPAF group, however, future work would be necessary to assess whether the response to treatment is similar in these populations and if IS can benefit patients with IPAF to long term. In addition, it could be useful to include the UIP pattern within the IPAF classification criteria, not currently included, since it is the third most frequent radiological pattern.

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Disclosure of Interests: Rafaela Ortega Castro: None declared, Pérez Sánchez Laura: None declared, Font Ugalde Pilar: None declared, Jerusalem Calvo Gutierrez: None declared, Antonio Requejo-Jimenez: None declared, Simona Espejo-Pérez: None declared, Teresa Gonzalez-Serrano: None declared, María del Carmen Castro Villegas: None declared, Gómez García Ignacio: None declared, Alejandro Escudero Contreras: None declared, Eduardo Collantes Estevez Grant/research support from: ROCHE and Pfizer, Speakers bureau: ROCHE, Lilly, Bristol and Celgene, Maria A Aguirre: None declared

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SAT0530 DESCRIPTION AND OUTCOMES OF A SERIES OF 21 PATIENTS WITH INTERSTITIAL PNEUMONIA WITH AUTOIMMUNE FEATURES IN A MULTIDISCIPLINARY UNIT.

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Background: A significant proportion of patients with idiopathic interstitial pneumonia shows autoimmune features, but do not meet the criteria to be classified as a systemic autoimmune disease. In 2015, a joint working group of the European Respiratory Society (ERS) and the American Thoracic Society (ATS) proposed classification criteria for the category called interstitial pneumonia with autoimmune features (IPAF).

Objectives: To evaluate the clinical, serological and morphological characteristics of a series of 21 patients with IPAF as well as the treatment that was applied and the evolution they presented.

Methods: A retrospective cohort study was conducted. The patients who met ERS/ATC IPAF classification criteria in the period from 2012 to 2019 were collected from our interstitial lung disease (ILD) database, including 546 patients. All cases were systematically assessed in a multidisciplinary committee. Clinical, serological, morphological, as well as treatment and outcome variables were collected. A Descriptive analysis is shown.

Results: 21 patients were included in the study, 12 of them (57.1%) women. The mean age at diagnosis was 61.6 years (SD 14.0), and the median follow-up time was 2.9 years (IQR 4.9). All showed ILD by HRCT, 10 (47.6%) patients had autoimmune features at the moment of the diagnosis, and 20 (95.2%) were positive for some auto-antibody. 12 (57.1%) fulfilled two of the three domains, and 9 (42.9%) fulfilled the three IPAF domains. Characteristics are described in Table 1. Lung biopsy was performed in 9 cases (42.9%). The mean FVC at diagnosis was 70.4% (DS 21.0) and DLCO 46.7% (DS 21.5). Regarding the treatment during the disease, mofetil mycophenolate (MMF) was used in 8 (38.1%) patients, cyclophosphamide (CYC) in 3 (14.3%), rituximab (RTX) in 2 (9.5%) and azathioprine in 2 (9.5%). In 1 case (4.8%), CYC and RTX were used in combination. Oral glucocorticoids (GCC) were prescribed in 14 patients (66.7%), 4 of them alone, and 6 cases (28.6%) required high-dose methylprednisolone in 250-1000 mg regimens. Antifibrotic drugs (nintedanib or pirfenidone) were used in 5 cases (23.8%) in combination with immunosuppressants and/or GCC. Five patients (23.8%) required home oxygen supplementation. Outcomes to date: 7 (33.3%) patients had readmissions due to ILD acute exacerbation; 2 (9.5%) required lung transplantations, and 3 (14.3%) died during follow-up, 1 (4.8%) due to respiratory causes.

Table 1.

CLINICAL DOMAIN			SEROLOGIC DOMAIN			MORPHOLOGIC DOMAIN		
	n	%		n	%	**MORPHOLOGY**		
						RADIOLOGY	n	%
Raynaud's phenomenon	7	33,3	ANA ≥ 1:320 (mottled, diffuse, homogeneous)	12	57,1	NSIP	15	71,4
Inflammatory arthritis/ polyarticular morning joint stiffness ≥ 60 min	4	19	Anti-Ro	11	52,4	UIP	5	23,8
Digital oedema	4	19	ANA nucleolar	3	14,3	LIP	1	4,8
Mechanic hands	1	4,8	ANA centromere	1	4,8	Others	0	0
Distal digital ulceration	1	4,8	Anti-PM-Scl75	4	19	HISTOPATHOLOGY	n	%
Palmar telangiectasia	1	4,8	Anti-SRP	2	9,5	NSIP	4	19
Gottron's sign	1	4,8	Anti-PM-Scl100	2	9,5	Interstitial lymphoid aggregates with germinal center	2	9,5
Others	0	0	Rheumatoid factor≥ 2 ULN	2	9,5	Diffuse lymphocytoplasmic infiltration	1	4,8
			Anti-Jo1	1	4,8	UIP	1	4,8
			PL-7	1	4,8	Others	0	0
			PL-12	1	4,8	MULTICOMPARTIMENTAL AFFECTION	n	%
			Anti-Mi2A	1	4,8	Pulmonary vasculopathy	5	23,8
			Anti-CENPA	1	4,8	Pleural effusion	1	4,8
			TIF1-gamma	1	4,8	Intrinsic airways disease	1	4,8
			Others	0	0	Unexplained pericardial effusion	0	0

Conclusion: IPAF was more frequent in women; ANA were the prevalent antibodies; NSIP was the most repeated radiological and pathological pattern; and the combination of GC plus MMF was the most used treatment scheme. Despite our low numbers, acute exacerbations, requirement of lung transplantation and deaths have occurred, which demonstrates the severity of the disease.

References:

[1] Fischer A, et al. An official ERS/ATS research statement: interstitial pneumonia with autoimmune features. Eur Respir J. 2015 Oct;46(4):976–87.

Disclosure of Interests: María del Carmen López González: None declared, ESTER NOFUENTES: None declared, Sandra Ruíz Alcaraz: None declared, Ignacio Gayá García-Manso: None declared, Raquel García Sevila: None declared, Paloma Vela-Casasempere: None declared, Mariano Andrés Grant/ research support from: Grünenthal, Consultant of: Grünenthal, Menarini, Speakers bureau: Grünenthal, Horizon

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SAT0531

NEXT GENERATION SEQUENCING AND AUTOINFLAMMATORY SYNDROMES: CLINICAL AND GENETICAL CORRELATION ON AN ADULT POPULATION FROM A REFERRAL THIRD-CARE CENTRE

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Background: Systemic autoinflammatory diseases (sAID) are a group of conditions with recurrent episodes of inflammation in absence of infection or autoimmune response. Its physiopathology mainly lies on mono/poligenic mutations involving genes related to the innate immune system response. Next Generation Sequencing (NGS) platformss have been a big step forward on sAID diagnosis, although a clinical and genetic correlation is still needed.

Objectives: To review the sAID related gene panel variants identified using NGS sAID gene panel on a cohort of adult patients screened for sAID from a referral third-level hospital.

To correlate genetic and clinical findings for sAID related variants identified in order to the clinical suspicion diagnosis of sAID.

Methods: A retrospective review of a cohort of adult (≥ 16 yo) patients with available NGS sAID related gene panel (MiSeq Illumina sequencing platform including intron and exon variants from up to 17 sAID genes, with coverage depth > x100) among 2014 and 2019 was performed.

Demographic, clinical and genetic data were collected in a database.

Genetic variants were classified according to the American College of Medical Genetics/Association for Molecular Pathology classification as benign/likely benign/ variable of unknown significance (VUS)/likely pathogenic/pathogenic. In case of polymorphisms or lack of genetic data, the variants were named as unclassified.

A description of the cohort and an analysis of the correlation assessment between clinical data and genetic findings were performed.

Results: 246 out of 299 (82%) patients with NGS sAID gene panel had clinical data available. 170/246 (69%) were adult patients. The medium age was 48 yo, and the M/F ratio was 2.46. 87/170 (51%) adult patients presented 122 variants involving sAID genes (60/87 patients with a single variant). All the variants out of 7 seven were heterozygous variants.

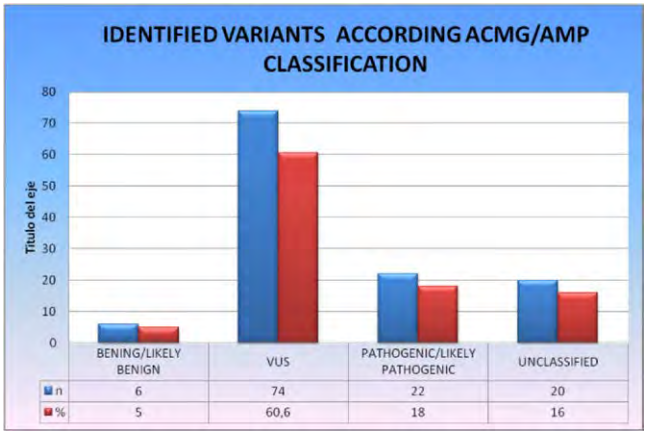
Variants were classified according to ACMG/AMP as follow: pathogenic/probably pathogenic: 22/122 (18%), unknown significance: 74/122 (60.6%), benign/ probably benign: 6/122 (4.91%). 20/122 (16.4%) were unclassified variants or polymorphisms.

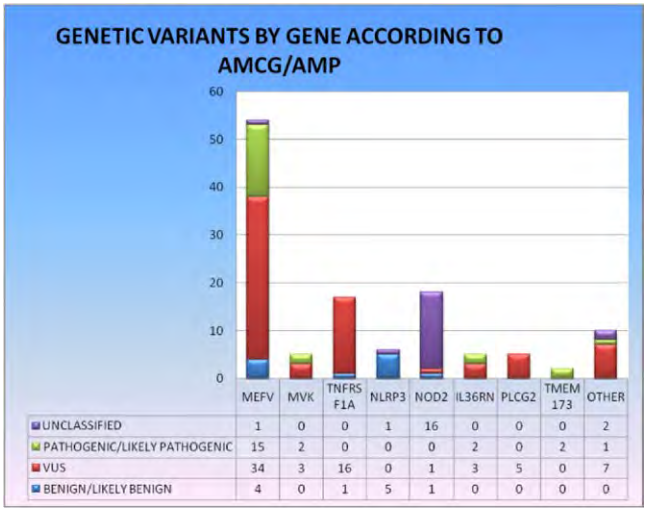
The most frequent variants identified involved MEFV (54/122), NOD2/CARD15 (18/122) and TNFRSF1A (17/122 including 12 p.Arg121Gln variants) genes.

37/122 (30%) variants correlated with the clinical picture in 33 patients, allowing to confirm the suspected diagnosis. Among the 122 variants, 7 not previously communicated variants were identified.

No somatic variants were found.

Conclusion: NGS sAID related gene panel is a useful tool for sAID diagnosis. In this cohort of 170 adult patients from a referral third-level hospital, genetic tests identified sAID related variants in almost half of them.





20% of patients who underwent genetic NGS sAID related gene panel studies were finally diagnosed with sAID.

The identification of a genetic variant (even pathogenic / likely pathogenic variant) is not diagnostic for sAID if there is not a suggestive clinical picture.

Despite genetic findings, a careful evaluation of clinical – genetic correlation is needed to confirm the suspicion diagnosis, especially for low penetrance variants like TNFRSF1A p. Arg121Gln.

References: Diagnostic utility of a targeted next-generation sequencing gene panel in the clinical suspicion of systemic autoinflammatory diseases: a multi-center study. Karacan I, Balamir A, Uğurlu S, et al. . Rheumatol Int. 2019 May;39(5):911-919. doi: 10.1007/s00296-019-04252-5. Epub 2019 Feb 19.

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SAT0532

POSITIVE DISEASE-SPECIFIC AUTOANTIBODIES LOWER DIAGNOSTIC SENSITIVITY BUT HAVE LITTLE CLINICAL SIGNIFICANCE IN DIAGNOSING IGG4-RELATED DISEASE USING THE 2019 ACR/EULAR CLASSIFICATION CRITERIA IN DAILY CLINICAL PRACTICE

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Background: Recently, the 2019 ACR/EULAR classification criteria for IgG4-related disease (IgG4-RD) were published mainly to identify more homogeneous subjects for inclusion in clinical trials and observational studies [1]. However, although their high specificity is presumed to be useful to differentiate IgG4-RD from various mimickers, their value in daily clinical practice needs to be evaluated.
Objectives: This study aimed to clarify the usefulness of the 2019 ACR/EULAR classification criteria for IgG4-RD and characteristics of false-negative patients in daily clinical practice.
Methods: We retrospectively reviewed the medical records of 162 patients with IgG4-RD and 130 consecutive non-IgG4-RD patients (mimickers) diagnosed by experts whose serum IgG4 levels were measured at a single center in Japan. Using the collected data, we calculated sensitivity, specificity, and fulfillment rates for the entry criteria, exclusion criteria, and threshold of inclusion criteria points. In addition, to clarify the characteristics of false-negative cases in IgG4-RD, we performed an intergroup comparison of their clinical features including disease-specific autoantibodies.
Results: Both the patients with IgG4-RD and mimickers were relatively old (66 and 65 years) with male predominance (67% and 60%). The final diagnoses of mimickers mainly consisted of cancer, lymphoma, vasculitis, sarcoidosis, multicentric Castleman's disease, and atherosclerotic or infectious aortic aneurysm. The classification criteria had a sensitivity of 72.8% and a specificity of 100%. Of the 44 false-negative cases, one did not fulfill the entry criteria, 20 fulfilled one exclusion criterion, and 27 did not achieve sufficient inclusion criteria points. Compared with the true-positive cases, the false-negative cases had significantly fewer affected organs, lower serum IgG4 levels, higher serum CH50 levels, and lower prevalence of salivary/lacrimal gland and renal parenchymal lesions. They were also less likely to have had biopsies (61% vs 97%). Of note, positivity of disease-specific autoantibodies including SSA/Ro antibody, ANCA, ds-DNA antibody, and ACPA was the most common exclusion criterion fulfilled in 18 patients, only 2 of whom were diagnosed with a specific autoimmune disease (rheumatoid arthritis) complicated by IgG4-RD. The remaining 16 patients had no specific clinical symptoms related to such autoantibodies. In addition, compared with IgG4-RD patients without disease-specific autoantibodies, the 18 patients with them had almost equal serum IgG4 and complement levels, number of affected organs, and histopathology and immunostaining scores despite higher serum IgG and CRP levels.
Conclusion: The present study suggests that the 2019 ACR/EULAR classification criteria for IgG4-RD has excellent diagnostic specificity and moderate sensitivity in daily clinical practice. Positive disease-specific autoantibodies alone, which lowered the sensitivity in this study, may have little clinical significance concerning the diagnosis of IgG4-RD.

References:

[1] Wallace ZS et al. The 2019 American College of Rheumatology/European League Against Rheumatism classification criteria for IgG4-related disease. Ann Rheum Dis. 2020 Jan;79(1):77-87.

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SAT0533

ADULT ONSET STILLS DISEASE AND IDIOPATHIC RECURRENT PERICARDITIS: ARE THE MORE SIMILARITIES OR DIFFERENCES?

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Background: Adult onset Stills disease (AOSD) and Idiopathic recurrent pericarditis (IRP) are currently considered auto-inflammatory diseases. Common features of these disorders are symptoms such as fever, leukocytosis, serositis, increased acute phase reactants.
Diagnosis of IRP is based on ESC 2015 diagnostic criteria, while AOSD is defined according to 3 sets of classification criteria. A detailed study shows that modern criteria for these nosologies overlap and do not allow distinguishing one from the other.
Objectives: We have not found any data on the comparison of the two groups in the literature. We compared the two groups of patients according to several parameters, such as clinical features, laboratory testing, genetic analysis to identify common patterns.
Methods: We enrolled 22 newly identified subjects (13 patients with AOSD, 9 patients with IRP) to our prospective, monocenter study. The mean age of patients with AOSD was 31 [22; 39], the mean age of patients with IRP was 46 [35;54]. Blood sampling in all patients was performed in the flare.
We quantified the serum levels of ferritin and its glycosylated fraction in both groups. Mutations of the MEFV, TNFRSF1A genes were studied. As more sensitive imaging methods for lymphadenopathy and serositis, we performed the following instrumental studies for all patients: transthoracic echocardiography, ultrasound of the abdominal cavity and pelvis, chest high-resolution computed tomography.
Results: One subject with a heterozygous missense variant was found in exon 2 of the MEFV gene (E148Q) in the IRP group. The patient was excluded from our study. Elevated white blood cell (WBC) count and C-reactive protein (CRP) were observed in all patients in 2 groups, however, the level of WBC greater than 10,000/mm^3 was found only in 10 patients from the AOSD group and 5 – from the IRP. Elevated ferritin level in both groups was detected. The number of subjects with high level of ferritin in the AOSD group reached 12 (n=13), in the IRP group – 7 (n=8).
The ferritin level appeared to be more significant in the AOSD group compared to the IRP group (1521 ng/ml vs 408 ng/ml p=0.0159) Figure 1.In turn, lower glycosylated ferritin was recorded in 9 patients with AOSD (n=13), and 7 – with IRP (n=8). We have demonstrated a more significant decrease of glycosylated ferritin level in patients with AOSD in comparison to patients with IRP, which amounted (11% vs 37% p = 0.0286) reference value (38.6%-84.7%). Figure 1.
Abnormal liver function tests were found in the majority of patients with AOSD and IRP (61% vs 75%).
We have also shown that, if the patient had pericardial effusion, the fluid was present in the pleural cavity, regardless of the group.
The number of AOSD patients with polyserositis was 5 (n=13).
Other symptoms are presented in Table 1

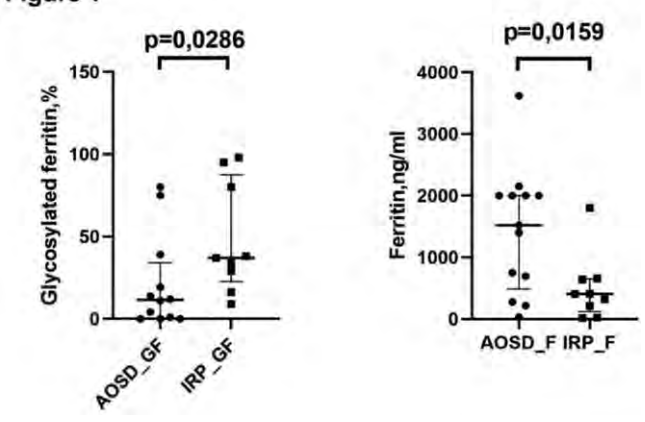
Table 1

Symptom and sign	AOSD (n=13)	IRP (n=8)
CRP mg/L, mean, %	123 [69;164], 100%	151[65; 226], 100%
Pericarditis	38%	100%
Pleuritis	38%	100%
Leukocytosis ≥10,000/mm3	77%	62%
Abnormal liver function tests	61%	75%
Fever >39 °C	100%	100%
Rush	77%	0 %
Arthralgia	100%	75%
Arthritis, lasting 2 weeks or longer	100%	12.5%
Sore throat	54%	0%
Recent lymphadenopathy	85%	25%
Hepatomegaly or splenomegaly	54%	62%
Elevated ferritin	92%	87%
Glycosylated ferritin ≤20%	69%	25%

Conclusion:

1. The level of ferritin in the IRP group was lower, which can be explained by a less generalized process, the absence of such symptoms as arthritis, rash, splenomegaly.
2. Diagnostic and classification criteria of both disorders do not allow distinguishing between the diseases.
3. There might be no differences between the diseases; further research (on more representative groups) is needed. We consider the comparison of the gene-expression analysis in these patients to be of great importance.

Figure 1



Disclosure of Interests: None declared
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SAT0534

RITUXIMAB FOR REFRACTORY IDIOPATHIC RETROPERITONEAL FIBROSIS: A SINGLE TERTIARY CENTER EXPERIENCE

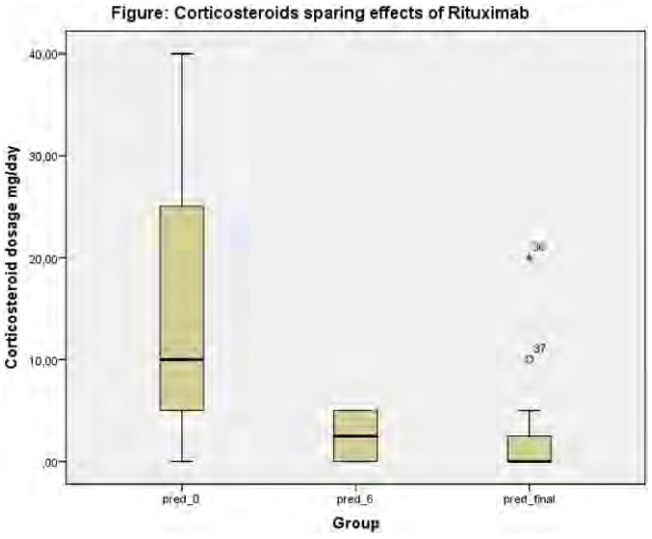
M. Oztas[1], E. Cerme[1], S. Ugurlu[1]. [1]*Istanbul University-Cerrahpasa, Department of Medicine, Division of Rheumatology, Istanbul, Turkey*

Background: Idiopathic retroperitoneal fibrosis (RPF) is a progressive disorder of the retroperitoneum which is often idiopathic. Although prednisolone is the mainstay approach to treating RPF, the remission rates range between 75% to 95% (1-2).
Objectives: Here, we report the outcomes and steroid-sparing effect of Rituximab (Rtx) therapy in 14 patients with RPF.
Methods: This retrospective study was conducted at a tertiary rheumatology center. Patients were diagnosed with RPF and had at least a course of 0.5-1 mg/kg prednisolone treatment previously. These patients were switched to Rtx due to inadequate response or side effects while on prednisone, tamoxifen, azathioprine or cyclophosphamide therapy. Patients were treated with Rtx in order to be included in this study. Involvement and activation of RPF was shown via PET-CT either before or at least 6 months after the therapy. Daily prednisolone dose was noted before rituximab initiation and 6 months after the therapy. All of the patients reported, except two, were followed for at least 6 months after the Rtx treatment. The final disease status of the three patients were not included in the study.
Results: Fourteen patients (7F) received at least 2 cycles (1 gr for each) of Rtx. The age of diagnosis was 54.3 ± 11.0 years, follow-up duration was 46.0 ± 37.2 months. The previous treatments, number of the cycles of Rtx and final disease status were shown in the Table. The Control PET-CT revealed metabolic and radiologic remission in 3 patients. In 6 patients, the disease remained stable. In 2 patients there was disease progression hence they were treated with the second course of Rtx. One of the two patients had the progression two years after the first cycle but then, was lost to follow-up. The mean prednisolone dose decreased from 15.5 ± 12.4 mg to 2.2 ± 2.2 mg/day after 6 months of Rtx initiation. Final prednisolone dose was 2.6 ± 5.5 mg/day (Figure). Rtx treatment was ceased in 6 patients with sustained remission.
Conclusion: The present study shows that Rtx could be a therapeutic option after gluocorticoid or DMARD failure. The steroid sparing effect of Rtx is essential and further prospective studies are needed to assess the Rtx efficacy more objectively in RPF treatment.

Table. Characteristics and final disease status of the patients

Number	Age of Rituximab Initiation	Sex	Previous Treatments	Number of Rituximab Cycle(s)	Final Pet-CT
1	49	M	Pred, Mtx	1	Stable disease
2	54	M	Pred,Mtx	1	Stable disease
3	46	F	Pred,Aza,Tmx,Mmf	2	Progression
4	40	M	Pred,Aza,Mtx	4	Remission
5	63	F	Pred,Tmx	10	Stable disease
6	47	F	Pred,Mtx	2	Stable disease
7	30	F	Pred	1	Stable disease
8	52	M	Pred,Aza	2	Progression
9	54	M	Pred	1	N/A
10	59	M	Pred,Aza,Mtx	1	N/A
11	30	F	Pred, Mtx	6	Remission
12	40	F	Pred,Aza,Tmx;Cyc	3	Stable disease
13	50	M	Pred	2	N/A
14	45	F	Pred,Aza	3	Remission

Pred:Prednisolone, Aza:Azathioprine,
Tmx:Tamoxifen,Mtx:Methotrexate,Cyc:cyclophosphamide



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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.6419

SAT0535

CLINICAL COURSE IN PATIENTS WITH INTERSTITIAL PNEUMONIA WITH AUTOIMMUNE FEATURES (IPAF) IN A MULTIDISCIPLINARY CONSULTATION.

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Background: A proportion of patients with Interstitial Lung Disease (ILD) show autoimmune characteristics but do not completely meet the classification criteria for a definitive connective tissue disease. In order to unify the nomenclature and criteria to define this condition, the classification of patients with Interstitial Pneumonia with Autoimmune Features (IPAF) has recently been adopted (Fisher, et al).
Objectives: To describe the sociodemographic, clinical, functional characteristics and therapeutic management of IPAF patients in clinical practice and to evaluate the incidence rate of functional respiratory impairment over time.
Methods: A longitudinal observational study was performed. Patients with IPAF classification criteria (Fischer et al) were included from the time of ILD diagnosis (Feb 2017 to Sept 2018) and followed until loss of follow-up or end of the study (Oct 2019), in a multidisciplinary team, carried by a pneumologist and a rheumatologist in a Tertiary Hospital in Madrid. Main outcome: relative functional respiratory impairment: defined as decline in percent predicted forced vital capacity (FVC%) of ≥ 5% compared to the previous visit. Respiratory function was measured at baseline and every 6 months. Covariates: a) sociodemographic, b) clinical, c) radiological pattern (non-specific interstitial pneumonia [NSIP]; usual interstitial pneumonia [UIP], others); d) FVC%, DLCO%; e) laboratory tests; f) therapy used (glucorticosteroids, disease modifying antirheumatic drugs (DMARDs) and Biologic Agents). Statistical analysis: description of the sociodemographic, clinical, radiological, functional and treatment characteristics of the patients. Survival techniques were used to estimate the incidence rate (IR) of relative functional respiratory impairment, expressed per 100 patient-semester with their respective confidence interval [95 % CI].
Results: 17 patients were included with a mean follow-up of 3 ± 1.5 years, 70.6% were women with a mean age of 65±10 years. The most frequent IPAF classification criteria were: a) clinical: arthritis (50%), Raynaud`s phenomenon (33%) and mechanical hands (17%); b) serological: 65% had ANA ≥1/360; 31% FR> 40; 30% Anti-Ro positive; c) morphologic: 59% presented NSIP pattern and 29.4% was UIP. The baseline median FVC% and DLCO% were 89 [83-107.7] and 63 [50-79.8] respectively. During the study period, 94% received treatment: 87.5% glucorticosteroids, 68.5% mycophenolate, 56% azathioprine, 18.7% cyclophosphamide iv and 33% antifibrotics. During the follow-up (104.6 patient - semester), 15 patients presented relative functional respiratory impairment, with an IR of 23.8 [16.1-35.3]. After 14 months from IPAF diagnosis 50% of the patients had relative functional respiratory impairment. At the end of the follow-up, 50% showed a worsening of the DLCO%.
Conclusion: IPAF patients are mostly women in their sixties. The most frequent clinical criteria are arthritis and Raynaud`s phenomenon and the serological were FR and ANAs. The most frequent radiological pattern was NSIP. The therapeutic management is mainly with glucorticosteroids, mycophenolate and azathioprine. At the beginning, patients have a slightly diminished lung function. These patients have significant functional impairment over time that will impact in their prognosis. Longitudinal and multicenter studies are necessary to advance in the knowledge and management of these patients.

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SAT0536

IMMUNE CHECKPOINT INHIBITOR THERAPY IN PATIENTS WITH PREEXISTING SARCOIDOSIS

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Background: Immune checkpoint inhibitors (ICI) have changed the treatment landscape of many cancer types, but are also associated with development of immune-related adverse events, including *de novo* sarcoid like reactions. However, little is known about the use of ICI therapy in patients with preexisting sarcoidosis as patients with preexisting autoimmune diseases have been systematically excluded from clinical trials of ICI therapy due to concerns of heightened toxicities. Emerging research suggests that ICI therapy can be considered in some patients with autoimmune diseases.[1]

Objectives: To determine the risk of sarcoidosis exacerbation or flare in patients with preexisting sarcoidosis receiving ICI therapy.

Methods: We conducted a retrospective cohort study of patients seen at The University of Texas MD Anderson Cancer Center between 2016-2019. Patients were included in the cohort if they received one of 7 ICI therapies (ipilimumab, nivolumab, pembrolizumab, durvalumab, avelumab, atezolizumab, or cemiplimab) and had an International Classification of Disease version 10 code of sarcoidosis (D86.*), prior to the ICI initiation, with diagnosis confirmed in medical record by treating physicians. A sarcoidosis diagnosis was considered "possible" if the medical record documented a history of sarcoidosis, "probable" if a history of biopsy proven sarcoidosis was mentioned, and "definitive" if histological evidence was available. Frequency of flares and outcomes of patients after receiving ICI were collected.

Results: During the study timeframe a total of 32 patients with preexisting sarcoidosis received ICI therapy. Nine patients (28%) had a definitive diagnosis of sarcoidosis, 12 (37%) had a probable diagnosis and 11 (35%) had a possible diagnosis of sarcoidosis. The mean time between diagnosis of sarcoidosis and initiation of ICI therapy was 13 years (range: <1 to 51 years). Twenty-seven patients (84%) received monotherapy and five patients (16%) received combination or sequential ICI therapy. Of the 32 patients, one patient with a 20-year remote history of sarcoidosis, never treated, developed a clinically symptomatic exacerbation of sarcoidosis one month after the initial dose of atezolizumab, with increased hilar nodules on imaging, skin nodules, arthritis and uveitis. Biopsy of a lymph node showed non-necrotizing granulomas, and biopsy of the skin panniculitis. The patient also developed colitis thought to be an immune-related adverse event. Atezolizumab was discontinued after 3 doses. Patient was treated with prednisone and azathioprine.

Conclusion: Patients with a remote history of stable sarcoidosis at the time of ICI therapy infrequently develop a flare of their sarcoidosis. The risk of flares in patients with active sarcoidosis requiring immunosuppression at the time of ICI initiation is unknown.

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[1] Kennedy LC, Bhatia S, Thompson JA, Grivas P. Preexisting autoimmune disease: implications for immune checkpoint inhibitor therapy in solid tumors. Journal of the National Comprehensive Cancer Network. 2019 Jun 1;17(6):750-7.

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SAT0537 ANALYSIS OF ADULTS PATIENTS WITH NOD2-ASSOCIATED AUTOINFLAMMATORY DISEASE

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Background: More than 100 mutations of the NOD2 gene have been described, some of which have been related to diseases such as Crohn's disease, Blau syndrome, early-onset sarcoidosis and NOD2-associated autoinflammatory disease (NAID), the latter of polygenic character. The inflammatory disease associated with a NOD 2 gene is characterized by periodic fever, dermatitis, polyarthritis, gastrointestinal symptoms and symptoms similar to those of the dry syndrome and currently associated with the NOD2 variants.

Objectives: Describe the clinical characteristics and genetic variants of a cohort of patients in adulthood with autoinflammatory disease associated with the NOD2 gene with follow-up in a third level hospital in southern Spain

Methods: Retrospective descriptive study of patients in adulthood with diagnostic suspicion of autoinflammatory disease and with genetic mutation in NOD2 gene. Patients with follow-up from 2013 to the present and in which another diagnosis of autoimmune disease (inflammatory bowel disease, sarcoidosis, etc.) were excluded. Data were obtained by review of medical records.

Results: 17 patients with alterations in the NOD2 gene were included. 14 cases (76.4%) were women. The mean age at diagnosis was 34.3 years (± 13.2). In the 17 patients, 19 mutations were found at the level of the NOD2 gene, the most frequent was with 9 cases (47.3%) the mutation in exon 4 (R702W), followed by mutation in exon 11 (1007finsC) with 5 cases (26.3%) and mutation in exon 4 (P268S) with 3 cases (15.4%). Other mutations obtained were mutation in exon 4 (R311w), mutation in exon 6 (M863V) and mutation in exon 11 (G908R) with a single case in each of them. In 6 cases (35.3%) there were first-degree relatives with a similar clinic, although not in all cases they were studied. Regarding the clinical manifestations, joint involvement (arthralgia and / or arthritis) with 12 cases (70.6%) was the most frequent followed by rash skin involvement with 10 cases (58.9%) and nonspecific abdominal pain with 9 cases (52.3%). Other less frequent manifestations were evening predominance fever and the elevation of acute phase reactants (CRP and ESR) with 8 cases (47.1%), oral thrush present in 5 patients (27.8%) and diarrhea with 4 cases (23.5%).

Conclusion: The autoinflammatory disease associated with the NOD2 gene is an entity that can occur in adulthood and that can occur in a similar way to other auto-inflammatory diseases of a monogenic nature and in which the joint, cutaneous and abdominal involvement may predominate. We must maintain a high degree of suspicion and always include inflammatory bowel diseases in the differential diagnosis.

Disclosure of Interests: None declared

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SAT0538 CLINICAL PROFILE OF AUTOIMMUNE UVEITIS NOT ASSOCIATED WITH HLA B27: A RETROSPECTIVE SINGLE CENTER STUDY

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Background: Autoimmune uveitis is frequently referred to a rheumatologist for evaluation & treatment. While clinical characteristics of HLA B27 associated uveitis are well documented, scanty information is available on non HLA-B27 associated autoimmune uveitis. We have described the clinical characteristics of our patients of non-B27 uveitis and compare the same with patients of Asian Indian HLAB27 uveitis.

Objectives: To describe and compare the clinical characteristics of non HLA-B27 associated autoimmune uveitis.

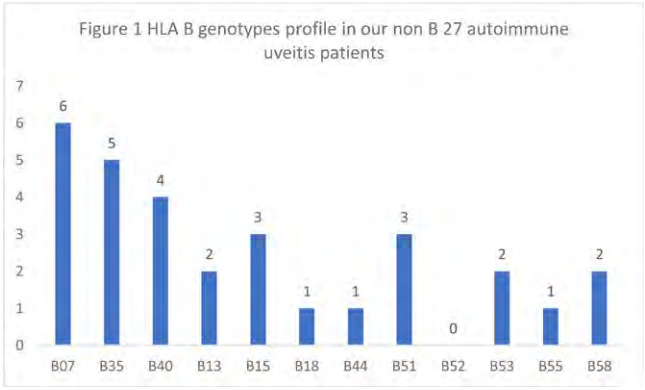
Methods: Retrospective review of records from hospital's electronic medical record database and included all cases of autoimmune uveitis that were referred to rheumatology from January 2017 and December 2018. Among these, those who did not have HLA B tissue typing record or were HLAB27 positive; were excluded. Pertinent details like age, sex, no. of episodes, unilateral or bilateral, location of uveitis (anterior, posterior or pan uveitis, association of synechiae & vasculitis), baseline CRP & ESR levels along with the HLA B profile(SSP-PCR) & nature of treatment received (systemic steroids, DMARD initiation) were collected. For comparison, clinical features of a HLA B27+ve uveitis series from the same ethnic Asian-Indian population were used[1]. Subgroup analysis was also done between the common non B27 HLA genotypes. Descriptive statistics were summarized using mean & percentage. Chi square & Fischer's test was used to compare the groups and subgroups.

Results: Out of total 210 patients screened, 17 cases were HLA B27 negative on HLA B tissue typing. The key demographic and clinical features of our patients of autoimmune uveitis not associated with HLA B27 in comparison with the B27 +ve uveitis group are given in table 1.

Table 1 Comparison of clinical features of our patients versus B27 +ve uveitis

	Non HLA B27 Autoimmune Uveitis (N=17)	Ninan et al (N=25)	P value
Age (years) at disease onset			
16-35	4	15	
More than 35	13	7	**0.009**
Onset not known	0	3	
Sex			
Male	6	21	**0.002**
Female	11	4	
Region of uveitis			
anterior	9	24	**0.001**
posterior & pan-uveitis	8	1	
Biochemical parameters			
CRP (mg/L)	6.45 + 8.39	N.A	-
ESR (mm/hr)	24.75 + 18.80	N.A	
Associated complications			
synechiae formation	4 of 17	4 of 25	0.69
retinal vasculitis	4 of 17	0 of 17	-

Recurrent uveitis was seen in 11 out of 17 patients in our patients as compared to 15 out of 22 (p 0.81) in HLA B27 +ve patients.



HLA B7 and HLA B35 were the most frequent genotypes (figure 1). Sub group analysis showed that 87.5% of patients with a component of posterior uveitis were HLA B7 or HLA B35 positive. It was noted none of 5 cases of HLA B35 +ve uveitis needed second line DMARD initiation after a tapering course of systemic steroids. There was no other significant difference in the clinical or treatment parameters noted in the subgroup analysis between the HLA genotypes.

Conclusion: Autoimmune uveitis not associated with HLA B27 tends to have older age of onset, female predominance, more common involvement of posterior uvea and association of vasculitis than HLAB27 autoimmune uveitis. Among non HLA B27 uveitis, HLA B07 and HLA B35 are the most common serotypes in our Asian south Indian group. Therapeutic stratification for a delayed initiation of second line DMARD therapy needs to be studied further particularly in HLA B35 +ve uveitis.

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SAT0539 MUCKLE-WELLS SYNDROME IN RHEUMATOLOGY PRACTICE, FAMILY CASES: FEDERAL CENTER EXPERIENCE.

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Background: Muckle-Wells syndrome (MWS) is a monogenic autoinflammatory disease caused by a NLRP3 gene mutation. It is the most common variant of cryopyrin-associated periodic syndromes (CAPSs) and can be observed in rheumatology practice. It manifests itself in fever, urticaria-like rash, arthralgias/arthritides, conjunctivitis/uveitis, sensorineural hearing loss, acute-phase markers (ESR, CRP). The disease's onset usually takes place in infancy. There are examples of family cases. Targeted therapy: interleukin-1 inhibitors (anakinra, canakinumab).

Objectives: to provide characteristics of MWS patients, family cases in the rheumatology practice of the Federal Rheumatology Center in Russia.

Methods: in a 10-year period (2009 to 2019), MWS was diagnosed in 42 outpatient and inpatient patients, among them were 24 children, 18 adults, and 9 family cases. All of them underwent a standard rheumatology examination, including a ECR, CRP, ophthalmologist examination, and an audiogram. A molecular genetic test of the NLRP3 gene was carried out for all patients, the diagnosis was confirmed in all of them.

Results: Out of 18 adult patients aged between 19 and 59 years, women were prevalent (16 to 2), the onset age was 0 to 53 years, in 88,9% cases the onset took place before a patient was 18 years old. When diagnosed, the disease duration varied from 6 to 46 years. Most patients demonstrated fever, urticarial-like rash, arthralgias/arthritides, which were observed in 16 patients (88.9%), conjunctivitides were observed in 15 patients (83,3%), sensorineural hearing loss – in 8 patients (44,4%), abdominal pain, nausea, vomiting – in 4 patients, headache, dizziness – in 6 patients. There also were rare manifestations, such as: recurrent oral ulcers (8), genital ulcers (3), erythema nodosum (3), sore throat and raids on the tonsils (PFAPA-like phenotype) was observed in 2 patients. In 3 patients manifestations were triggered by cold temperature. All patients had an increased ESR and C-reactive protein concentration. Eight family cases of MWS were identified (in total 26 family members aged between 2.5 and 62 years) with a number of affected in one family ranging from 2 to 6 people of different age (8 children, 18 adults, out of which 20 were female, and 6 were male). Most patients had fever (17), urticarial-like rash (18), conjunctivitides (12), oral ulcers (7), articular syndrome (14), sensorineural hearing loss (5), and 2 patients died of renal insufficiency (probably due to amyloidosis of the kidneys). The heterozygous mutations in NLRP3 have been identified in pts: T348M (3 families), R262W (2 families), A439V (1), V198M (1), Pro294Ser (1). Ten patients received canakinumab for a period of 6 months to 6.5 years, and 5 patients received anakinra before canakinumab.

Conclusion: MWS is an orphan autoinflammatory disease, however it sometimes can be observed in rheumatology practice. It is very important to acquire family medical history to identify affected family members and prescribe therapy in a timely manner. IL-1 inhibitors are an effective and safe treatment option for MWS patients.

Disclosure of Interests: None declared

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SAT0540 ONE-YEAR OUTCOMES AFTER RHEUMATIC IMMUNE-RELATED ADVERSE EVENTS FROM CHECKPOINT INHIBITORS

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Background: Description and initial management of rheumatic immune-related adverse-events (irAEs) from cancer immunotherapies have been reported by several groups but to date, few studies have evaluated the long-term outcomes and management of rheumatic irAEs (1).

Objectives: To describe the long-term management and assess the one-year outcomes of patients who experienced rheumatic immune-related adverse events (irAEs) due to immune checkpoint inhibitors (ICI).

Methods: This was a single-centre prospective observational study including patients referred for musculoskeletal symptoms while treated with ICI. After baseline rheumatological evaluation defining the clinical entity presented, follow-up visits were organised according to the type and severity of irAE. At one year, persistence of irAE, ongoing treatment, as well as cancer outcomes were assessed.

Results: 63 patients were included between September 2015 and June 2018. 24 patients (38%) presented with non-inflammatory musculoskeletal conditions managed with short-term symptomatic treatment and did not require specific follow-up. 39 patients (62%) experienced inflammatory manifestations, mimicking either rheumatoid arthritis (RA, n=19), polymyalgia rheumatica (PMR, n=16), psoriatic arthritis (PsA, n=3) and one flare of a preexisting axial spondyloarthritis. Overall, 32 patients (82%) received systemic glucocorticoids, with a median rheumatic dosage of 15mg/day (range: 5-60mg/day). None of the patients had to permanently discontinue ICI therapy for rheumatic irAE. 20 patients (67%) were still receiving glucocorticoids at one year, with a median dosage of 5mg/day (range: 2-20mg/day). Glucocorticoids were more frequently discontinued for patients with RA-like condition (44%) than PMR-like condition (23%), but no other predictive factor of glucocorticoids withdrawal could be identified. At one year, overall survival and progression-free survival were comparable between patients who were still receiving glucocorticoids for rheumatic irAE and patients who have discontinued. Eight patients required csDMARDs.

Conclusion: At one year, a majority of patients required long-term low-dose glucocorticoids for chronic rheumatic irAE, which seems not altering oncological control.

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Disclosure of Interests: None declared

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SAT0541 THE SEVERITY OF FMF MAY BE ASSOCIATED WITH CO-MORBIDITIES

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Background: Familial Mediterranean fever (FMF) is an auto inflammatory disease with recurrent attacks of serositis. Frequent attacks and disease related sequels may be associated with co-morbidities in FMF patients.

Objectives: One of the tools for evaluating the FMF severity is the international severity scoring system for FMF (ISSF) [1]. This score includes disease related sequels, acute phase measurements, attack features and exertional leg pain.

Therefore, more severe disease may be link with subclinical inflammation, amyloidosis and frequent, prolonged and widespread attacks. All these components may augment the frequency of non-disease related co-morbidities.

Methods: We enrolled 158 FMF patients who fulfilled modified *Tel-Hashomer* Diagnosis *Criteria2. The patients dichotomized based upon disease severity (mild disease or severe disease). Patients with ISSF scores lower or equal to 2 were accepted to have mild disease. Then, we compared frequency of non-disease related co-morbidities between the groups. These co-morbidities are* hypertension, hypothyroidism, hyperthyroidism cardiovascular diseases, coronary artery diseases, cerebrovascular diseases, chronic renal disease (non-FMF related), chronic obstructive pulmonary diseases, and diabetes mellitus. This study was approved by the Local Research Ethics Committee and carried out in compliance with the Helsinki Declaration. All the patients gave written informed consent. P-value lower than 0.05 was considered as statistically significant.

Results: Demographic features, disease duration, smoking history and body mass index (BMI) were similar between the groups. Frequency of co-morbidity in severe disease group was statistically higher than mild disease group (p=0.02). Most frequent co-morbidity was hypertension in both groups.

Table. Features of mild and severe FMF groups

	Mild (n=135)	Severe (n=23)	p
Gender (M/F)	47/88	11/12	0.23
Age	36.4±11.3	36.5±14.3	0.68
Smoking (%)	38 (28.1)	5 (21.7)	0.52
BMI (kg/m^2)	24.3±9.2	24.0±8.9	0.34
Disease duration (year)	7.7±11.3	8.6±14.3	0.09
Amyloidosis (%)	2 (1.4)	3 (13.0)	**0.02**
Exon 10 homozygote (%)	35 (25.9)	9 (39.1)	0.19
Colchicine dosage (mg/day)	1.2±0.4	1.4±0.5	**0.02**
ISSF scores	0.7 ±0.7	3.4±0.5	**<0.001**
Co-morbidity (%)	25 (18.5)	9 (39.1)	**0.02**

Conclusion: In our FMF patient cohort, we found that severity of the disease may be associated with higher frequency of co-morbidities. Therefore, clinicians should be aware of the high possibility of co-morbidities in patients with more severe FMF and addressed these co-morbidities timely and properly.

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Disclosure of Interests: None declared

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SAT0542 UTILITY OF QUANTITATIVE ANALYSIS OF 18FDG-PET/CT IN IGG4-RELATED DISEASE

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Background: In IgG4-related diseases (IgG4-RD), usefulness of ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) imaging for detecting the organ involvement of IgG4-RD have been shown and, ^{18}FDG PET/CT was more accurate and appeared to be more sensitive as compared to other imaging technics[1,2]. However, until now, the studies regarding about quantitative analysis of PET/CT imaging in IgG4-RD were few. To avoid unnecessary biopsy and select suitable lesion for biopsy on multi-organ involvement disease such as IgG4-RD, the information which lesion is suspected as disease-involvement lesion in a non-invasive test is important.

Objectives: The purpose of this work is to evaluate the usefulness of ^{18}FDG-PE/CT imaging in management of IgG4-RD using quantitative analysis of PET/CT imaging.

Methods: 21 patients with IgG4-RD, in whom PET/CT was undertaken at the time of diagnosis between December 2009 and July 2018, were enrolled. We retrospectively investigated the association between histological findings in which biopsy was performed for diagnosis of IgG4-RD and findings of PET/CT. ^{18}FDG uptake was assessed in site of major organ involvement of IgG4-RD which could be differentiated from the normal uptake of background tissue with ^{18}FDG-PET/CT. For quantitative analysis, we measured the highest standardized uptake value (SUV) of the pixels within the region of interest (ROI) (SUV_{max}) and the average SUV within ROI (SUV_{mean}). We also measured SUV_{mean} of liver as reference tissue. Then, we calculated ratio between SUV_{mean} of ROI and SUV_{mean}/liver.

Results: The age at diagnosis was 64.5 ± 11.9 years, serum IgG4 was 743.8 ± 584.1 mg/dl, and biopsy was performed at 24 sites (Submandibular gland 10, prostate gland 4, pancreas 2, thyroid gland 1, lung 1, retroperitoneum 1, kidney 1). Histological findings were consistent with IgG4RD (positive) at 19 sites.

Although SUV_{max} at the biopsy site was not correlated with the biopsy results, SUV_{mean} at the biopsy site were significantly higher in the biopsy-positive group (figure 1). As similar, SUV_{mean} /liver SUV_{mean} were also higher in the biopsy-positive group (2.17 vs 1.52, respectively P<0.05). To establish cut-off value of SUV_{mean} to consider biopsy, A receiver operating characteristics (ROC) curve was constructed. ROC curve analysis indicated SUV_{mean}=4.074 as cut-off value which discriminate IgG4-RD related lesion.

Conclusion: Our present study suggested that quantitative analysis of ^{18}FDG-PET/CT imaging is useful for selecting the biopsy site in IgG4-related disease.

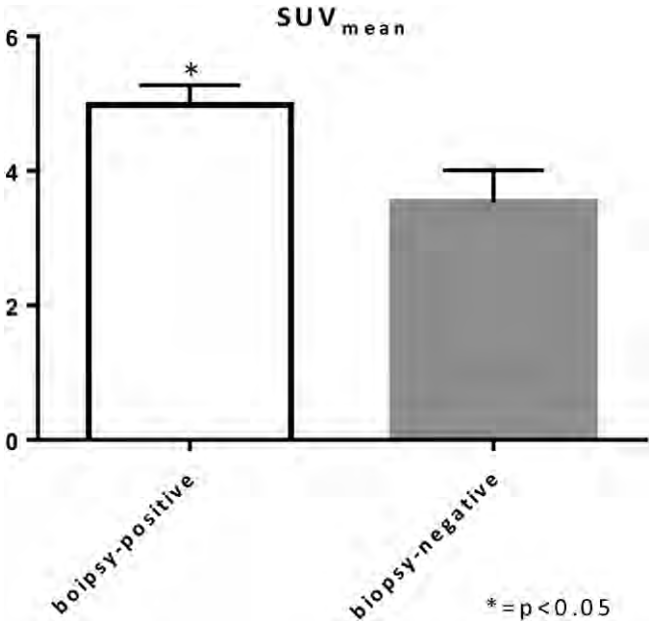


Figure 1. XXXXX

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Disclosure of Interests: None declared

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SAT0543 PREVALENCE OF FABRY'S DISEASE IN MILD AND SEVERE FMF PATIENTS

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Background: Fabry disease (FD) is a rare metabolic disorder caused by the mutations in the α-galactosidase A (GLA) gene. FD patients present with heterogeneous clinical manifestations, which may overlap with systemic diseases including familial Mediterranean fever (FMF). Recurrent episodes of fever,

abdominal pain, and arthralgias can be observed in both disorders and this may lead to misdiagnosis.

Objectives: To investigate FD prevalence in mild and severe FMF patients.

Methods: A total of 66 FMF patients, according to the Tel-Hashomer criteria, were included in the study. Patients were grouped into mild (Group 1) and severe (Group 2) subsets according to the severity score. α-GLA enzyme activity and mutations in the GLA gene were performed. Demographic features, clinical findings, MEFV mutations and treatments were recorded.

Results: The clinical and demographical characteristics of the patients were given in Table 1. In severe form, 27 patients were using biological drug and 40.7% had amyloidosis. Symptoms related to FD including hypohidrosis, acroparesthesias, and painful neuropathies, were not different between the groups. Only one patient in group 1 had a low GLA enzyme activity (0.1 nmol/h/ml;Normal >2.5) which also had mutations in the GLA gene but MEFV mutation test was negative. (Table 2). This patient was a 39-year-old female with recurrent abdominal pain, distal extremity pain and the presence of fever during the attacks. She was heterozygous for R301Q. In detailed history, she reported mild acroparesthesias, hypohidrosis, and tinnitus.

Table 1. Demographic and clinical findings

	All patients n: 66	Group 1 n: 32	Group 2 n: 34	p-value
Age, median (min./max.)	34 (17/64)	27 (17/59)	36 (18/64)	0.192
Male, n (%)	36 (54.5)	14 (43.8)	22 (64.7)	0.137
Disease duration, median (min./max.)	20.5 (1/57)	12.5 (2/50)	25 (1/57)	**0.006**
Family history of FMF, n (%)	41 (62.1)	22 (68.8)	19 (57.6)	0.443
Alpha-galactosidase A (nmol/h/ml), median (min./max.)	5.9 (0.1/16)	5.6 (0.1/9.6)	6 (3.1/16)	0.330
Abdominal pain, n (%)	58 (87.9)	31 (96.9)	27 (79.4)	**0.030**
Fever, n (%)	54 (81.8)	25 (78.1)	29 (85.3)	0.532
Arthritis, n (%)	34 (51.5)	10 (31.3)	24 (70.6)	**0.003**
Pleuritis, n (%)	31 (47)	19 (59.4)	12 (35.3)	0.083
Painful neuropathy, n (%)	23 (34.8)	13 (40.6)	10 (29.4)	0.440
Acroparesthesias, n (%)	9 (13.6)	6 (18.8)	3 (8.8)	0.240
Angiokeratomas, n (%)	0 (0)	0 (0)	0 (0)	-
Cardiac abnormalities	1 (1.5)	1 (3,1)	0 (0)	0.485
Tinnitus, n (%)	4 (6.1)	3 (9.4)	1 (2.9)	0.274
Hearing loss, n (%)	2 (3)	2 (6.2)	0	0.086
Hypohydrozis, n (%)	2 (3)	1 (3.1)	1 (2.9)	0.965
Cornea verticillata, n (%)	0 (0)	0 (0)	0 (0)	-
Proteinüria, n (%)	13 (19.7)	2 (6.3)	11 (32.4)	**0.012**
Colchine dosing (mg/day), median (min./max.)	2 (1/3)	1 (1/2)	2 (1/3)	**<0.001**

Table 2. MEFV mutant alleles and GLA mutations

	All patients n: 66	Group 1 n: 32	Group 2 n: 34
Alpha -galactosidase A (*GLA*) gene mutations, n (%)	1 (1.5)	1 (3.1)	0 (0)
M694V mutations, n (%)	47 (35.6)	17 (26.5)	30 (44.1)
Non-M694V mutations, n(%)	36(27.2)	20 (31.2)	16 (23.5)

Conclusion: In this study, we showed the following: 1) the FD rate in the total FMF group was 1.5% (3.1% in group 1), 2) none of the patients in the severe FMF subset had abnormal enzyme activity or mutations related with FD, 3) symptoms related with FD such as hearing loss, hypohidrosis, acroparesthesias, and painful neuropathies also noted in FMF patients particularly in the milder group. Based on our results, FD should be considered in the differential diagnosis of FMF particularly in patients with atypical symptoms.

Disclosure of Interests: None declared

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SAT0544

USE OF BIOLOGICAL DMARDS IN PATIENTS WITH ADULT-ONSET STILL'S DISEASE: RESULTS FROM TURKBIO REGISTRY

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Background: Adult-onset Still's disease (AOSD) is a rare multisystemic inflammatory disorder, and is diagnosed by exclusion. AOSD is generally treated with nonsteroidal antiinflammatory drugs, corticosteroids, and conventional disease modifiying antirheumatic drugs (cDMARDs). Biological disease modifiying antirheumatic drug (bDMARD) therapy are recommended in AOSD patients who are refractory to tradional therapy, and bDMARDs is becoming increasingly important in AOSD treatment.

Objectives: To evaluate the use of bDMARDs and drug survival in AOSD patients.

Methods: TURKBIO registry is the Turkish version of Danish DANBIO rheumatological database which has been established in 2011. All patients with AOSD who received biological agents registered in TURKBIO registry between dates of October 2011 and October 2019 were included in this study. The demographic data, response of therapy, frequency of using and switching biological agents were collected.

Results: As of October, 21 AOSD patients were recruited. Mean age of patients was 34.6±7.3 (min-max: 24-49) years, mean disease duration was 9.3±7.4 (min-max: 1-22) years, and 57.1% of patients was female. Mean duration from onset to start of bDMARDs was 7±6.1 (min-max: 0.5-21) years. It was observed that 13 patients (61.9%) received tocilizumab (TCZ), 6 patients (28.6%) received IL-1 inhibitors (5 anakinra and one canakinumab), 2 patients (9.5%) received certolizumab and one patient (4.8%) received etanercept as a first-line bDMARDs. The most frequently used biological agents in current treatment were as follows: 52.4% of patients received TCZ and 33.3% received IL-1 inhibitors (4 anakinra, 3 canakinumab), and the most frequently used concomitant drugs were methotrexate (47.6%) and hydroxychloroquine (14.3%). The switching rate was 33.3%, and in half of them the reason of switching was adverse events. The median drug survival for bDMARDs was 28.6 months (Table).

Table. Demographic, laboratory features and management of AOSD

(median;25-75)	n=21
Age (year)	34.7 (28.3-40.6)
Gender (Female) n(%)	12 (57.1)
Disease duration (year)	8 (2-17)
Duration from onset to start of bDMARs (year)	6 (1.5-10)
ESR (on onset)	44 (21-66)
CRP (on onset)	65 (3.1-108)
Current bDMARDs n(%)	
Tocilizumab	11(52.4)
IL-1 inhibitors	7 (33.3)
Etanercept	1 (4.8)
Certolizumab	2 (9.5)
Concomitant cDMARD n(%)	
Methotrexate	10 (47.6)
Leflunomide	4 (19)
Sulfasalazine	1 (4.8)
Hydroxychloroquine	3 (14.3)
bDMARDs Survival (months)	28.6 (5.5-75)
Switching Rate n(%)	7 (33.3)
Adverse Event n(%)	3 (14.3)

Conclusion: This is the first evaluation of AOSD patients who used biological agents from TURKBIO registry. According our data, TCZ and anti-IL1 agents were the most frequent biological choices. The limitation of this study was the low number of the patients with AOSD who used biological agents.

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SATURDAY, 06 JUNE 2020

Diagnostics and imaging procedures

SAT0545

ULTRASONOGRAPHIC ENTHESEAL AND JOINT INVOLVEMENT IN PATIENTS WITH ACUTE ANTERIOR UVEITIS: A MONOCENTRIC CROSS-SECTIONAL STUDY.

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Background: Few studies have been investigating ultrasonographic (US) changes at peripheral entheses and joints in patients with anterior acute uveitis (AAU)[1] and none has been comparing non granulomatous uveitis (AANGU) with granulomatous uveitis (AAGU).

Objectives: To investigate prevalence of US entheses and joints abnormalities in a consecutive series of AAU patients and to compare US findings in AANGU HLA-B27 positive and HLA-B27 negative, with AAGU patients.

Table 1. US findings at the patient level

	Total n = 121	AAGU n = 20	AANGU n = 101	AANGU B27– n = 40	AANGU B27+ n = 61	AANGU vs AANGU	AAGU vs AANGU B27-	AAGU vs AANGU B27 +	AANGU B27- vs AANGU B27+
Entesophyte, n. (%)	109 (90,1%)	16 (80%)	93 (92,1%)	39 (97,5%)	54 (88,5%)	0,111	**0,038**	0,451	0,142
Entheseal erosion, n. (%)	12 (9,9%)	0	12 (11,9%)	5 (12,5%)	7 (11,5%)	0,213	0,159	0,184	1
Hypoechogenicity, n. (%)	5 (5,1%)	0	5 (5%)	3 (7,5%)	2 (3,3%)	0,589	0,544	1	0,382
Thickened enthesis, n. (%)	118 (97,5%)	19 (95%)	96 (98%)	37 (97,4%)	59 (97,3%)	0,440	1	0,440	1
Doppler signal at enthesis, n. (%)	32 (26,4%)	1 (5%)	31 (30,7%)	13 (32,5%)	18 (29,5%)	**0,024**	**0,023**	**0,032**	0,750
Active enthesitis, n. (%)	10 (8,3%)	0	10 (9,9%)	5 (12,5%)	5 (8,2%)	0,211	0,159	0,326	0,512
Structural damage, n. (%)	109 (90,1%)	16 (80%)	93 (92,1%)	39 (97,5%)	54 (88,5%)	0,111	**0,038**	0,451	0,142

Results are presented as number and percentage of patients having at least 1 entheseal abnormality, with significance

Methods: 121 consecutive patients diagnosed with AAU [91 AANGU (40 B27-, 61 B27+) and 20 AAGU, M/F 32/29, mean age 45.4± 12.8 y, mean disease duration 44± 84 m] from the Immunology Eye Unit (AUSL-IRCCS Reggio Emilia, Italy) entered the study. Patients with Fuchs uveitis were enrolled as controls (AAGU group). A complete rheumatological examination, including 68/66 peripheral joint count, entheses and bone spine mobility evaluation, was conducted. Using an Esaote MyLabClass, 18-6MHz linear multifrequency transducer both in B-mode and PD-mode, 6 entheses were evaluated bilaterally for the presence of any elementary lesion, structural damage and active enthesitis, according to OMERACT definitions[2]. The following sites were studied: lateral epicondyle of humerus, distal quadriceps insertion into the patella, proximal and distal patellar tendon insertions, calcaneal insertion of Achilles tendon and plantar fascia. Knee and ankle joints, were evaluated for synovial hypertrophy, effusion and PD signal. Extensor and flexor tendons of the foot and ankle were also examined for tendon sheath effusion, synovial hypertrophy and PD signal.

Results: Abnormal US findings, consisting in the presence of at least one entheseal abnormality, were detected in 110/121 patients (90.2%), the mean number of abnormal entheses per patient was 6.71±5.46. At the enthesis level, structural damage was significantly higher in AANGU, as compared with AAGU (30.9% vs 21.7%, p<0.001) and in AANGU B27+ as compared with B27- (27% vs 36%, p < 0.001). The presence of PD signal at enthesis was significantly increased in AANGU vs AAGU (7.1% vs 0.4%, p < 0.001) but also among AANGU B27+ vs AANGU B27- pts (5.9% vs 9%, p = 0.040). Analysis based on patient-level data showed a significantly higher percentage of patient in AANGU group having at least one enthesis exhibiting PD signal, when compared with AAGU (31% vs 5%, p = 0.023) (Table 1). The prevalence of US joint and tendon sheath alterations was negligible in the entire AAU population (<1%) without any difference between groups.

Conclusion: US entheseal structural damage is frequent in AAU patients, whereas US active enthesitis has a low prevalence. At the patient level, the presence of PD signal at enthesis seems to be associated with AANGU, without apparent influence of HLA-B27 positivity.

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SAT0546 COMPARISON OF SHEAR WAVE ELASTOGRAPHY AND CONVENTIONAL ULTRASONOGRAPHY OF SALIVARY GLANDS IN PATIENTS WITH PRIMARY SJOGREN'S SYNDROME: CAN SHEAR WAVE ELASTOGRAPHY CAPTURE LESIONS THAT ARE DIFFICULT TO DIAGNOSE WITH CONVENTIONAL ULTRASONOGRAPHY?

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Background: Sjögren's syndrome (SS) is a chronic inflammatory autoimmune disease characterized by lymphocyte infiltration in salivary and lacrimal glands. Recently, salivary gland ultrasonography (US) proved valuable for assessing salivary gland involvement in SS and seemed to exhibit good diagnostic properties. In the literature, studies conducted by the scoring of the structural changes according to B-Mode US of salivary glands showed a wide variability regarding sensitivity and specificity. Our previously study demonstrated that although conventional B-mode US findings were useful for the diagnosis of SS with low salivary flow they were not for subclinical SS with normal salivary flow (EULAR 2016). Recently, we reported that the tissue elasticity was decreased due to structural changes in the submandibular glands (SG) at the advanced stage of the disease and the shear wave elastography (SWE) is useful to distinguish pathological changes of the SG in patients with SS (EULAR2018).

Objectives: The aim of this study was to compare the usefulness of SG conventional B-mode US and SWE findings in non-SS and SS patients classified by salivary flow.

Methods: Twenty-two non-SS patients and 99 SS patients who fulfilled the American College of Rheumatology (ACR) / European League Against Rheumatism (EULAR) classification criteria for SS were studied. SS patients were divided into three groups according to salivary flow using gum test (VL/SS <5mL/10min. (n=38), L/SS 5-10mL/10min. (n=41) and N/SS >10mL/10min. (n=20)). All patients were examined SGUS by a single investigator who was blinded to device (TUS-A300; Canon Medical Systems, Tokyo, Japan) with a linear transducer (7.5-10MHz). The examination consisted of conventional B-mode US (US staging score), pulsed wave Doppler US (PD grading score) and SWE with quantitative assessment. US staging scores were assessed by glandular size, inhomogeneity and contrast of diagastric muscle (stage 0 to 3). PD grading scores were graded by pulsed wave pattern in pulsed wave Doppler US at the internal SG facial arteries (grade 0 to 2). With the region-of-interest (ROI) placed over the stiffest areas of the lesion on SWE, the quantitative means of the elasticity values were measured by shear wave velocity (Vs; m/s) and elasticity (E; kPa) for each lesion.

Results: The US staging score, the PD grading score, the values of Vs and E were significantly higher in patients with SS than in non-SS group (SS vs non-SS; US staging score 2.10±1.07 vs 0.86±0.99, p<0.0001, PD grading score 1.17±0.83 vs 0.23±0.61, p<0.0001, Vs 1.75±0.34 vs 1.57±0.29m/s, p=0.02, E 9.64±4.02 vs 7.81±2.27kPa, p=0.04). However, there was no significant difference between non-SS and N/SS in early-stage SS by US staging score (N/SS vs non-SS; 0.95±0.89 vs 0.86±0.99) and PD grading score (N/SS vs non-SS; 0.40±0.15 vs 0.23±.061). In contrast, the values of Vs and E were highest in N/SS as compared with all groups, and were significantly higher in N/SS than in non-SS (N/SS vs non-SS; Vs 2.02±0.24 vs 1.57±0.29m/s, p<0.01, E 12.58±3.16 vs 7.81±2.27kPa, p<0.01).

Conclusion: The present study demonstrated that although the tissue elasticity was decreased due to structural changes at the advanced stage, it increased due to inflammation and high viscosity in the SG at the subclinical SS with normal salivary flow comparing that in non-SS patients. The SWE may be a useful tool for the differential diagnosis between patients with non-SS and subclinical SS with normal salivary flow, which is difficult to distinguish by conventional B-mode US.

Disclosure of Interests: None declared

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SAT0547 RADIOGRAPHIC IMAGING IN ASSESSMENT OF FLUOROSCOPIC GUIDED INJECTION OF RHEUMATOID ATLANTOAXIAL JOINT INFLAMMATION

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Background: Rheumatoid spondylitis is a feature of long-lasting Rheumatoid arthritis (RA) that is presented by neck pain, headache and sleep disturbance. Atlantoaxial joint (AAJ) is the commonest cervical spine joint that affected in patients with RA. When it is involved, it can be associated with dangerous complications. Magnetic Resonance Imaging (MRI) can be used for assessing the disease activity, the amount of cartilage destruction, associated cervical myelopathy and differentiating synovial fluid from inflammatory pannus (Taniguchi D, et al., 2008).

Objectives: This study aimed to evaluate the efficacy of intra-articular steroid injection of inflamed AAJ in RA patients, regarding neck pain, headache and sleep quality using pre and post-interventions MRI.

Methods: A prospective case control study. Patients with inflamed AAJ were recruited. Group 1 (AAJ group, n = 30), received intraarticular AAJ steroid injection, guided by fluoroscopy and Group 2 (control group, n = 30), received systemic steroids. Both groups were assessed with: Visual Analogue scale (VAS) for

nocturnal neck pain and headache. Pittsburgh sleep quality index (PSQI) was used for sleep disturbance. Pre and post contrasts enhanced MRI interventions were done for both groups during the period of follow up (three months).

Results: Nocturnal neck pain, headache and sleep disturbance have significantly decreased, during follow up visits (3 months), in AAJ group in comparison to the control group. The Pre-intervention nocturnal pain score was 60.3 ±17.1 in AAJ group & 58.5 ±17.9 in control group. Pain has significantly decreased after 2weeks in AAJ group with continuous improvement till 3 months' post-intervention 6.9 ±4.65 & 51.26 ±10.54 respectively. The pre-intervention headache was 22.68 ±16.74 in AAJ group & 45.17 ±15.83 in control group decreased to 7.54 ±5.23 & 48.52 ±11.98 respectively post intervention. The percentage of patients who had sleep disturbance at baseline was 66.7% & 73.3% in AAJ and control groups respectively which has significantly decreased to 6.7% & 43.3% after 3 months. Regarding MRI, AAJ group had *a statistical significant decrease* in the percentage of patients with MRI synovial enhancement, inflammatory *pannus,* fibrosis and bone marrow edema in comparison to control group 3 months post intervention. All post-procedural side effects resolved within thmonth without further medical intervention, and no long-term sequelae were identified

Conclusion: Fluoroscopic guided intra-articular steroid injection of inflamed atlantoaxial joints is considered a beneficial therapeutic option in rheumatoid arthritis patients regarding clinical and radiological assessments.

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SAT0548

DEVELOPMENT AND VALIDATION OF THREE PRELIMINARY MRI SACROILIAC JOINT COMPOSITE STRUCTURAL DAMAGE SCORES IN A 5-YEAR LONGITUDINAL STUDY OF PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: In axial spondyloarthritis (axSpA), MRI reliably detects structural lesions in the sacroiliac joints (SIJs). The SPARCC SIJ Structural Score (SSS) (1) is a reliable and validated method to assess the individual structural lesions of the SIJs, i.e. fat lesion, erosion, backfill (fat metaplasia in an erosion cavity) and ankylosis. Several MRI studies have indicated that bone destruction, i.e. erosion, is often followed by formation of new bone in the erosion cavity (backfill), ultimately leading to ankylosis(2).

Objectives: The aim was to combine SPARCC SSS for erosion, backfill and ankylosis into a composite score for SIJ structural damage and to test this score in a 5-year follow up study.

Methods: Thirty-three patients fulfilling ASAS criteria for axSpA were followed for 5 years after initiation of TNF inhibitor in the BIOSPA study(3). T1-weighted and STIR MRI sequences of the SIJs acquired at week 0, 46 and year 2, 3, 4, 5 were evaluated with SPARCC SSS. In each of 5 slices of each SIJ, erosion is scored 0-1 per joint quadrant (score range 0-40), backfill 0-1 per joint half (score range 0-20) and ankylosis 0-1 per joint half (score range 0-20). Based on the scores for erosion, backfill and ankylosis 3 versions of a preliminary Composite axSpA MRI SIJ Structural Damage Score (CSDS) were calculated:

CSDS–A: (erosion score x0.5) + backfill score + ankylosis score

CSDS–B: (erosion score x1) + (backfill score x4) + (ankylosis score x6)

CSDS–C: (erosion score x1) < (backfill score x4) < (ankylosis score x6)

The "<" indicates a hierarchical order, meaning that erosion was not scored if backfill was present in the same joint half and erosion and backfill were not scored if ankylosis was present in the joint half.

Results: Patients were divided into two groups: patients with almost complete bilateral ankylosis (baseline SPARCC SSS Ankylosis ≥18, n=10) and patients with no/minor ankylosis (baseline SPARCC SSS Ankylosis ≤7, n=23). At baseline patients with no/minor ankylosis were younger, had shorter symptom duration, lower BASMI, higher SPARCC SIJ Inflammation, lower SSS Fat, Erosion, Backfill and Ankylosis, as compared with patients with almost complete ankylosis.

At baseline, CSDS-A, -B and -C correlated positively with SPARCC SSS Fat and Ankylosis and modified New York criteria grading, and negatively with BASDAI and SPARCC inflammation. Change in CSDS-B and -C over 5 years correlated positively with change in SSS Fat and Ankylosis and negatively with change in SPARCC Inflammation. There was no change in the group with almost complete ankylosis.

The annual progression for CSDS-B and -C was statistically significantly larger in year 1 compared with year 4 (p=0.01) and numerically larger compared with year 2 (p=0.075), 3 (p=0.382) and 5 (p=0.073). Figure 1 shows the annual change in patients with no/minor ankylosis.

Figure 1

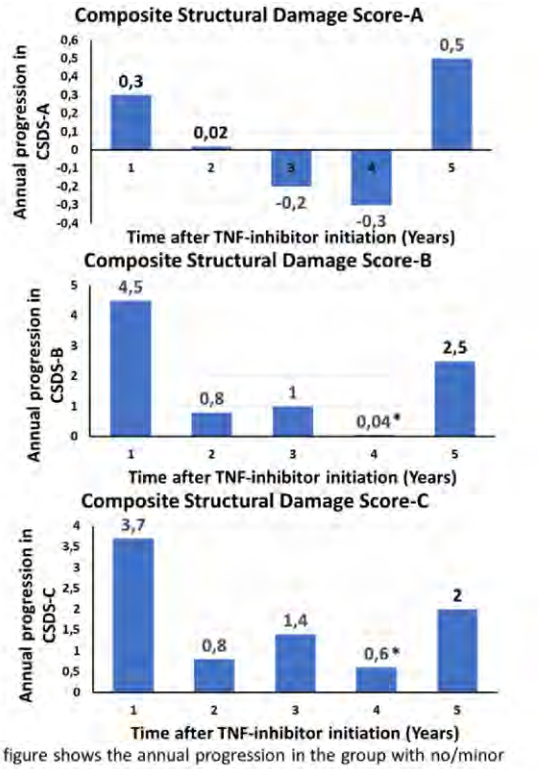


Figure 1. The figure shows the annual progression in the group with no/minor ankylosis at baseline in CSDS -A, -B and -C. Data are shown as mean. Annual progression was calculated as the change between MRI scans divided by the exact interval (years) between MRI assessments. Comparison of annual progression year 1 (week 0-46) with the other time intervals were calculated with Wilcoxon signed rank test. *p<0.05.

Conclusion: Three preliminary Composite Structural Damage Scores for MRI assessment of the SIJs in patients with axSpA, which allows scoring of MRI progression of erosion through backfill to ankylosis, were introduced. Progression was most pronounced the first year after TNF inhibitor initiation. This novel approach may be useful for monitoring structural progression in axSpA. We suggest that these methods are further tested for responsiveness and ability to differentiate between different therapies in randomized controlled trials.

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SAT0549

A SEMI-QUANTITATIVE MRI SCORING SYSTEM FOR INFLAMMATION IN JOINTS AND ENTHESES IN THE LOWER EXTREMITIES DEMONSTRATES GOOD RELIABILITY AND VALIDITY: POST-HOC ANALYSIS OF DATA FROM THE CRESPA TRIAL

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Background: MRI allows an objective assessment of signs of inflammation in peripheral joints and entheses and is therefore of potential interest as outcome measure in trials. No knowledge exists on the reliability and validity of semi-quantitative MRI scores in the setting of peripheral spondyloarthritis (pSpA).
Objectives: To describe the reliability of a semi-quantitative lower-extremity MRI scoring system, to investigate correlation with known measures of disease activity and ability to capture patients with improvement during treatment.

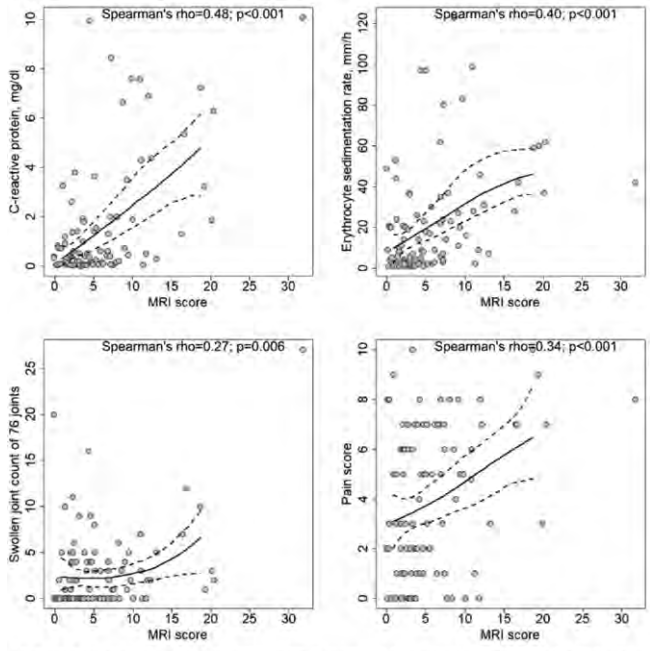


Figure 1. Validity demonstrated by positive relations between MRI score and established measures of disease activity, using data from both timepoints. Scatter plots, loess curves with bootstrap 95% confidence intervals and Spearman's rho with p-values.

Methods: In a post-hoc analysis, scores from 3 readers (LJ, MØ, SK) who independently assessed MRI images of pelvis (except sacroiliac joints), knees and ankles in the CRESPA trial blinded to chronology and all clinical data, were further analyzed. Entheses were scored 0-3 (none/mild/moderate/severe) for soft tissue inflammation (19 sites) and 0-3 for bone marrow edema (24 sites), joints were scored 0-3 for effusion/synovitis (10 sites) and 0-3 for bone marrow edema (22 sites). MRI score was defined as the sum of scores from all joints and entheses (i.e. all 75 sites). The CRESPA trial (NCT01426815) included 60 patients with early pSpA, defined as a symptom duration of <12 weeks. All patients fulfilled the Assessment of SpondyloArthritis international Society criteria for pSpA; data from 56 patients with available MRI images at baseline were included in this analysis, 46 had available MRI images at follow-up. Follow-up MRI was only performed if sustained clinical remission was reached. Reliability was assessed using two-way intra-class correlation coefficient (ICC) models by absolute agreement, single-measure (relevant when using scores from 1 reader) and average-measure (relevant when using averaged scores from 3 readers).
Results: MRI scores at baseline were mean 7.2 (median 5, inter-quartile range 3 to 9, range 0 to 32). MRI change scores were mean –3.1 and (median –1, IQR –4 to 0, range –18 to 2). MRI status scores at baseline (n=56) had single measure ICC 0.78 (95% CI: 0.66-0.87) and average measure ICC 0.92 (0.85-0.95). MRI change scores (n=46) had single measure ICC 0.73 (0.57-0.84) average measure ICC 0.89 (0.80-0.94).
MRI status scores correlated significantly with CRP, ESR, swollen joint count and pain score.
Patients with PSpARC40 response (n=34) (≥40% improvement in disease activity according to the Peripheral SpA Response Criteria) had larger decreases in MRI scores compared to patients without PSpARC40 response (n=11), mean –3.4 vs. –1.0, p=0.03.
When using all MRI data from pelvis, knees and ankles combined, more patients could be identified to have improvement, as compared to only taking one of three parts into account.

	MRI scores of pelvis, knees and feet combined	MRI scores of pelvis only	MRI scores of knees only	MRI scores of ankles only
Number of patients with improvement in MRI score > SDC	15 (33%)	9 (20%)	12 (26%)	14 (30%)
Number of patients with improvement in MRI score ≥ 50%	21 (46%)	10 (22%)	20 (43%)	17 (37%)
Net number of patients with improvement in MRI score*	24 (52%)	6 (13%)	21 (46%)	15 (33%)
Number of patients with improvement in MRI score as assessed by 3 readers	17 (37%)	3 (7%)	11 (24%)	13 (28%)

*Patients with improvement minus patients with worsening.

Conclusion: The semi-quantitative lower-extremity MRI score showed acceptable reliability and validity. The ability to capture response was best when combining information from all available areas that were imaged, i.e. both pelvis, knees and ankles.
*First authorship is shared between SK and TR.
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SAT0550

SPINAL AND PELVIC MDCT USING "IDOSE5" ITERATIVE RECONSTRUCTION ALGORITHM IN PATIENTS WITH PSORIATIC SPONDYLOARTHRITIS: DIAGNOSTIC CAPABILITIES AND IMAGE QUALITY IN RELATION TO RADIATION EXPOSURE

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Background: Psoriatic spondyloarthritis (PsSpA) is an inflammatory arthritis related to psoriasis, whereas a large number of patients may have persistent inflammation developing gradual and in some cases extensive joint involvement of the axial skeleton.
Conventional radiographs (CRs) have been used for the detection of structural damage (syndesmophyte formation, paravertebral ossification, sacroiliitis, ankyloses and erosions), facilitating as an important measure of efficacy of various therapies. However overlapping of anatomic structures of pelvis and spine as well as limited capabilities to visualize soft tissue have led to the development of newer imaging technologies (1). Multidetector CT technology (MDCT), it is now possible to perform low dose CT (ldCT) of the entire vertebral column, viewed in multiple planes and without overprojection with a low radiation dose. (2) Still, the capabilities of ldCT algorithms in the diagnosis and progression of PsSpA has not been fully explored.
Objectives: The aim of this study is to examine the effect of "iDose5" iterative reconstruction algorithm on radiation dose, diagnostic capabilities and image quality in spine-pelvis (S-P) CT scanning compared with CRs, in detection of findings suggestive of PsSpA.
Methods: Thirty-nine patients with PsSpA (26 females and 13 males, age range: 23 to 70 years old) were prospectively studied with "iDose5" CT of spine and pelvis on a 64-row MDCT scanner. Multiplannar reformats followed. All patients satisfied the Psoriatic Arthritis (CASPAR) classification criteria and had undergone standard AP and lateral CRs of the cervical, thoracic and lumbar spine and AP radiographs of the pelvis within one months of the iDose CT. Twenty-five patients underwent, additional MR imaging (MRI) of the same anatomic areas. Written consent was obtained from all patients. Two musculoskeletal radiologists read and scored CT scans and CRs in consensus, according to the PASRI criteria and the CTSS score. CT image quality and effective dose for CT and radiographs were assessed.
All data were analyzed using SPSS 24.0 statistical software.

Results: CT revealed erosions and ankyloses of the sacroiliac joints, fusion of the posterior elements of vertebra especially in the thoracic spine, enthesophytes, not seen with CRs, in 26 patients (p<0,05).
Level of diagnostic confidence was higher when interpreting CT compared to CRs, in cases of erosions and ankyloses, in 35 patients (p<0,05).CT was slightly superior in the detection and characterization of syndesmophytes, enthesopathy and calcifications.
Effective dose for "i-Dose 5" CT was 1.20 ± 0.26 mSv and for CR =1.07 ± 0.21 mSv. The difference was not statistically significant (p=0.588).
Conclusion: iDose CT of spine and pelvis at an effective dose, lower than previously published, seems to perform better than radiographs in the detection of structural changes of PsSpA. Further studies are needed to document the capabilities of iDose CT for the imaging assessment of PsSpA in daily clinical practice.
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Disclosure of Interests: None declared
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SAT0551 WHOLE BODY MACROPHAGE PET IMAGING THAT INCLUDES THE FEET CAN PROVIDE ADDITIONAL INFORMATION TO CLINICAL ASSESSMENT IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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Background: Clinical assessment of arthritis is the cornerstone in the diagnosis and treatment of rheumatoid arthritis (RA). Nevertheless, reliable determination of (sub)clinical arthritis can be difficult, especially in the feet. Advanced imaging techniques may contribute to early diagnosis and therapy monitoring through sensitive detection and (quantitative) monitoring of synovitis. Previously, it has been demonstrated that macrophage imaging using (*R*)-[^{11}C]PK11195 positron emission tomography (PET) allows for highly sensitive and specific imaging of RA disease activity in the hands. [1,2] Whole body macrophage PET imaging that includes the feet has not yet been evaluated in RA.
Objectives: To compare whole body macrophage PET imaging to clinical assessment of arthritis activity in clinically active, early RA patients.
Methods: Thirty-five previously untreated RA patients (age 54 ± 12, 51% male) with at least two clinically inflamed joints were included. They underwent a whole body (*R*)-[^{11}C]PK11195 PET/computed tomography (CT) scan in addition to standard clinical assessment of number of tender and swollen joints (TJC and SJC, respectively). Two readers blinded to clinical assessment (GZ and CvdL) visually scored intensity of uptake in joints on a 0 to 3 scale. A PET positive joint score was defined at ≥ 1. Additionally, (*R*)-[^{11}C]PK11195 uptake in joints was assessed quantitatively as standardized uptake values (SUV). Visual parameters were compared to clinical parameters using Cohen's kappa, and quantitative parameters were analyzed using an independent T-test.
Results: All patients showed enhanced tracer uptake in one or more joints (Figure 1). A total of 168 joints were visually PET positive, with the following distribution: 16% in the wrists, 14% in the metacarpophalangeal joints, 25% in the proximal interphalangeal joints, 4% in the ankles, 37% in the metatarsophalangeal joints. Positivity in other large joints was rare (4%). The number of discrepant findings between PET and clinical outcome (TJC and/or SJC) varied based on anatomic localization; more joints were clinically active in the hands, and more joints were active on the PET scan in the feet. Consequently, agreement between visual PET positivity and clinical activity was low, with only moderate agreement found in the ankles (κ = 0.46 and 0.41 for SJC and TJC respectively). Quantitative PET data showed a trend towards higher SUV values in joints that were clinically tender and/or swollen, reaching a significant difference in the feet (ankles + MTPs) versus SJC (Figure 2; 0.7 vs 1.0, $p < 0.001$). However, parts of the clinically non-affected joints also depicted moderately increased SUV values, and vice versa.

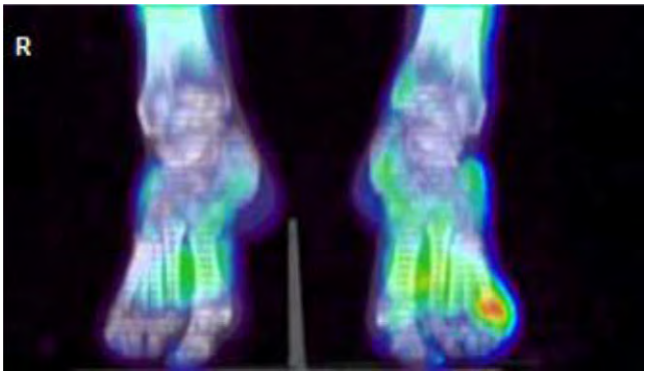


Figure 1. Visual PET uptake in the left MTP5-joint.

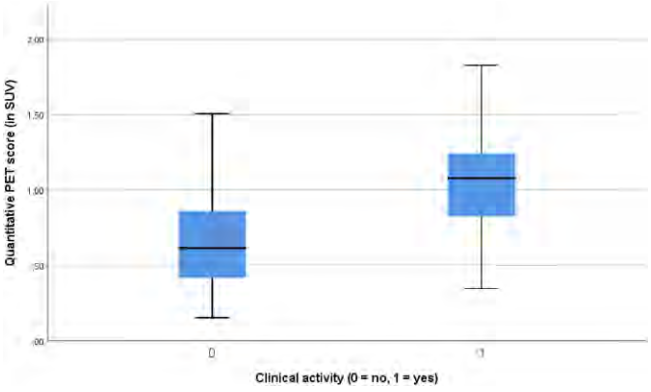


Figure 2. (R)-[11C]PK11195 (SUV) in both clinically affected and non-affected feet joints (defined as swollen yes or no).

Conclusion: Whole body macrophage PET imaging showed clear uptake of (*R*)-[^{11}C]PK11195 in several joints of clinically active, early RA patients, especially in MTP-joints. The best correlation between quantitative PET data and clinical assessment of swelling was observed in the feet. In general, however, PET also provided distinct information from clinical assessment, which may provide a means for detecting subclinical synovitis. We are performing longitudinal studies to further assess the value of macrophage PET in RA.
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SAT0552 IMAGING OF CORTICAL INTERRUPTION IN THE METACARPOPHALANGEAL JOINTS WITH HIGH-RESOLUTION PERIPHERAL QUANTITATIVE COMPUTED TOMOGRAPHY SHOWS HIGH RELIABILITY AND ACCEPTABILITY FOR PATIENTS WITH RHEUMATOID ARTHRITIS.

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Background: High-Resolution peripheral Quantitative Computed Tomography (HR-pQCT) has been proposed as a modality for assessment of disease severity in inflammatory arthritis. The excellent resolution (82μm^3) and the inherent contrast between bone and soft tissue makes it a gold standard reference for the detection of bone damage in vivo. However, the nine minutes acquisition

time for the metacarpophalangeal (MCP) joints might yield some disadvantages. Having the hand and arm immobilised for this long might discomfort the patients, thereby reducing acceptability, resulting in poor adherence. The longer imaging time might also increase the risk of motion-induced image degradation.
Objectives: The objective of this study was two-fold. Firstly, we investigated motion-induced image degradation of 2nd and 3rd MCP joints for two methods of standardised positioning of the hand. Secondly, the acceptability of HR-pQCT imaging was explored for patients with established Rheumatoid Arthritis (RA).
Methods: Fifty patients with RA had their 2nd and 3rd MCP joints imaged by HR-pQCT. The patients were scanned two times, using a custom-made positioning splint, with and without an inflatable immobilisation device. In order to investigate acceptability, the patients were afterwards given a questionnaire regarding their procedure experience of HR-pQCT imaging with and without the inflatable hand immobilisation device. For each acquisition, the image quality was graded, and the number, width, depth and length of cortical interruptions were measured. Twenty percent of the acquisitions were reevaluated to determined intrareader reliability using the intraclass correlation coefficient (ICC).
Results: The acceptability regarding HR-pQCT imaging was high, with only 6% preferring conventional X-ray compared to 40% of the patients preferring HR-pQCT imaging. The remaining 54% were indifferent to the modality. Seventy-four percent found it hard to keep their fingers at rest during the imaging. Fifty percent of the patients thought the inflatable hand immobilisation device helped keep their fingers at rest compared to only 6% who believed it impaired their ability to keep their fingers at rest. This was not observable in the image quality, however, as the overall image quality was high and no clinically relevant difference of the visual grading between the acquisitions with and without the inflatable hand immobilisation device was observed. The number, width, depth and length of cortical interruption all indicated excellent reproducibility as shown in table 1. No discernible difference between the two acquisitions was observed.

Table 1. Intraclass correlation coefficients for the number, width, depth and length of cortical interruptions, with and without the inflatable hand immobilization device.

	Acquisition 1	Acquisition 2
Cortical interruptions number	0.99 (0.94 to 1.00)	0.98 (0.91 to 1.00)
Average cortical interruption width	0.98 (0.92 to 0.99)	0.99 (0.95 to 1.00)
Average cortical interruption depth	0.98 (0.92 to 0.99)	0.97 (0.89 to 0.99)
Average cortical interruption length	0.93 (0.75 to 0.98)	0.98 (0.94 to 1.00)

Acquisition 1 - Without the inflatable hand immobilization device.
Acquisition 2 - With the inflatable hand immobilization device.
Data presented as mean (95% confidence intervals).

Conclusion: The high acceptability signifies the feasibility of the novel HR-pQCT imaging; this was evident by the fact that more patients preferred HR-pQCT imaging compared to conventional X-ray examination. The inflatable hand immobilisation device did not reduce motion-induced image degradation as the overall image quality was high for imaging of the MCP joints in both acquisitions. Our result, however, shows that the patients are more than capable of keeping their fingers at rest for the long acquisition time.
Disclosure of Interests: Rasmus Klose-Jensen: None declared, Kresten Krarup Keller: None declared, Bente Langdahl Grant/research support from: Amgen, NovoNordisk, Consultant of: Amgen Inc., Eli Lilly, UCB Pharma, Ellen Margrethe Hauge: None declared
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SAT0553 QUANTITATIVE ANALYSIS OF IMAGING FEATURES AT CHEST CT OF PULMONARY ARTERIAL AND VENOUS COMPONENTS IN SYSTEMIC SCLEROSIS-INTERSTITIAL LUNG DISEASE (SSC-ILD).

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Background: Interstitial lung disease (ILD) and pulmonary arterial hypertension carry a negative impact on SSc prognosis. Chest CT is the gold standard in assessing ILD and helps in evaluating associated vascular involvement.
Objectives: As qualitative analysis of CT scans is limited by low reproducibility and time constraints, we aimed at evaluating parenchymal and vascular features in SSc-ILD by quantitative analysis (QA) of CT scans and testing the relationship with clinical-functional data.
Methods: We prospectively enrolled 80 patients who underwent PFTs and chest CT scan spirometry gated at TLC on the same day. Clinical, lung functional and diffusion data, as well as disability indexes were collected. CT images were analyzed by a computational platform for texture analysis of ILD patterns (CALIPER), through Imbio LTA. It quantified the extent of normal pattern (NP %), ground glass opacities (GG %), reticulation (RET %), honeycombing (HC %), total ILD extent (ILD EXT %) and hyperlucent (HL %). Low density areas, representing emphysematous area, were also quantified (LDA %). For lung vessel analysis, a software program developed by the Ludwig Boltzmann Institute for Lung Vascular Research was used. This software determined total, arterial, and venous vascular volumes (TV, AV, VV), and relative volumes (TV%, AV%, VV%), as well as density and number for total, arterial and venous vessels.
Results: 43/80 patients/CT scans were eligible for both software analyses, while 36/43 for arterial and venous separation. TV% and total vessel density were correlated positively with mRSS and negatively with %FVC (r=-0.537 and r=-0.382) and %TLC (r=-0.511 and r=-0.648), while vessel tortuosity correlated positively with %DLco. This was confirmed when separately analyzing arterial vessels, while VV% negatively correlated with %FVC, %TLC and %DLco. There was a positive correlation between %ILD patterns and %vascular volumes, being significant for TV%-AV%, total vessels and arterial density. Conversely, %ILD patterns were negatively correlated with VV and number of veins detected, despite positive correlation between VV% and ILD_EXT%. When clustering patients according to %FVC and %DLco with 80% normal cutoff, %FVC allowed clustering according to significantly different ILD patterns extents and vascular features, while %DLCO for vascular features only. Moreover, the consecutive addition of functional impairment and worsening of ILD (from both normal %FVC and %Dlco, to %DLco impairment only to both %FVC and %Dlco impairment), there was a significant increase in %TV, % AV and %VV, with the exception of decrease in %VV and venous density in patients with double impairment versus DLco single impairment.
Conclusion: This is the first study showing in SSc a direct correlation between ILD and the increase in lung vascular volume, which is characterized by increase in arterial volume and density and reduction in venous volume and number. These results might be explained by the reduction of pulmonary volume due to fibrosis. However, also a para-physiological mechanism of redistribution of blood flow in lung areas, less involved by ILD, might be considered. Further studies on lung vessel quantification and distribution are ongoing.
Disclosure of Interests: Cosimo Bruni Speakers bureau: Actelion, Eli Lilly, Mariaelena Occhipinti Consultant of: Imbio, Gianna Camiciottoli: None declared, Maurizio Bartolucci: None declared, Michael Pienn: None declared, Gemma Lepri: None declared, Alessio Fabbrizzi: None declared, Alessandra Tottoli: None declared, Giuglia Ciardi: None declared, Dilia Giuggioli: None declared, Giovanna CUOMO: None declared, Francesco Masini: None declared, Horst Olschewski: None declared, Federico Lavorini: None declared, Linda Calistri: None declared, Marco Matucci-Cerinic Grant/research support from: Actelion, MSD, Bristol-Myers Squibb, Speakers bureau: Acetelion, Lilly, Boehringer Ingelheim
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SAT0554 SONOGRAPHIC ASSESSMENT OF CALCIUM PYROPHOSPHATE DEPOSITION DISEASE AT WRIST. A FOCUS ON THE SCAPHO-LUNATE LIGAMENT.

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Background: Only few articles evaluated the wrist in calcium pyrophosphate deposition disease (CPPD), although it is the second most frequent target of CPPD. Very recently, in a computed tomography (CT) study ligamentous calcifications were reported as a highly specific feature of CPPD at wrist level (1).
Objectives: i) to determine the prevalence and distribution of the ultrasound (US) findings indicative of calcium pyrophosphate (CPP) crystal deposits at the wrist, with a particular focus on the dorsal aspect of the scapho-lunate ligament (SLL); ii) to investigate the diagnostic accuracy of US and conventional radiography (CR) in the evaluation of CPP crystal deposits at wrist level, iv) to assess the agreement between the different imaging techniques.
Methods: Consecutive patients with a "definite" diagnosis of CPPD according to the Ryan and McCarty criteria and disease controls were prospectively included in this cross-sectional single-centre study. Dorsal part of the SLL, triangular fibrocartilage complex (TFCC), and volar recess of the radio-lunate joint were explored using US (according to EULAR standard scans and OMERACT definitions), CR and CT.
Results: Sixty-one CPPD patients and 39 disease controls were enrolled. Two-hundred wrists were evaluated using both CR and US. CT data of 26 (13.0%) wrists were available: 20 wrists in CPPD patients and 6 wrists in controls. CPP crystal deposits were found by US in at least one wrist in 95.1% of CPPD patients and in 15.4% of controls (p<0.001). SLL calcification was reported in 83.6% of CPPD patients and in 5.1% of controls (p<0.001). CPP crystal deposits were

observed by US at the SLL and/or radio-lunate joint in 5.7% of wrists and 6.6% of CPPD patients, but not at the TFCC of the same wrist. On CR, calcifications were found in at least one wrist in 72.1% of CPPD patients and in 0% of controls (p<0.001). Using the Ryan-McCarty criteria as a gold standard, the sensitivity, specificity and diagnostic accuracy were 0.72 (0.59-0.83), 1.0 (0.91-1.0) and 0.83 (0.74-0.90) for CR and 0.95 (0.86-0.99), 0.85 (0.69-0.94) and 0.91 (0.84-0.96) for US. Table 1 shows the agreement between the different imaging techniques.

Table 1. Agreement between US and the other imaging techniques in the evaluation of CPP crystal deposits at the wrist.

	US-CR (n=200)	US-CT (n=26)
TFCC	0.55 (0.43-0.67)	0.70 (0.43-0.97)
SLL	0.23 (0.07-0.39)	0.69 (0.41-0.97)
RLJ	0.25 (0.09-0.41)	0.46 (0.12-0.80)

Legend. **n**: number of the wrists, **RLJ**: volar recess of the radio-lunate joint. Values in brackets are the 95% confidence intervals of the Cohen's kappa.

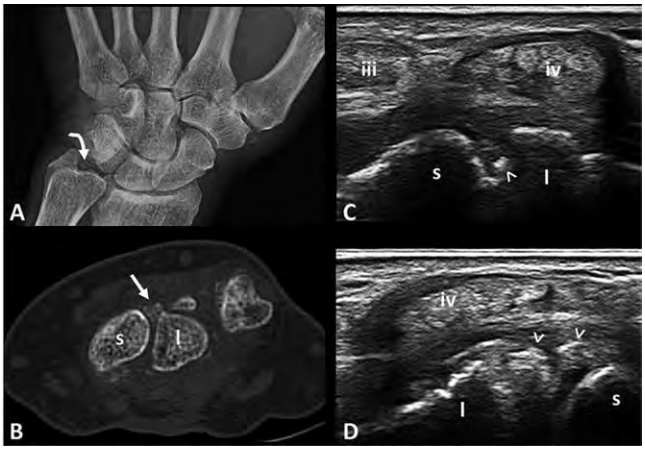


Figure 1 provides a pictorial evidence of the appearance of CPP crystal deposits in the SLL.**A**: CPP crystal deposits (curved arrow) at the TFCC. The SLL is not assessable due to superimposition of other bones.**B**: in the same patient of figure 1A, CT scan shows the presence of a calcification of the dorsal aspect of the SLL (arrow).**C**: dorsal longitudinal scan of the SLL: isolated hyperechoic spot (arrowheads) inside the ligament.**D**: dorsal longitudinal scan of the SLL showing the presence of a large aggregate extending towards the extensor tendons and hyperechoic spots (arrowheads) within it.**Legend**. **iii**: third extensor compartment, **iv**: fourth extensor compartment, **l**: lunate bone, **s:** scaphoid bone.

Conclusion: This study supports the diagnostic accuracy of US in evaluating wrist involvement in CPPD patients. SLL calcifications are a specific US finding of CPPD at wrist level.

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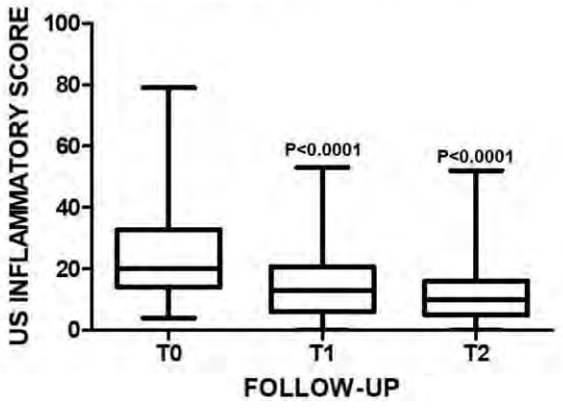
SAT0555

MUSCULOSKELETAL ULTRASOUND IN MONITORING RESPONSE TO JAKI IN RHEUMATOID ARTHRITIS PATIENTS: RESULTS FROM A LONGITUDINAL STUDY

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Background: Therapeutic approach of rheumatoid arthritis (RA) patients has been enriched by the introduction of small molecules. In particular Jak inhibitors (JAKi), baricitinib and tofacitinib, demonstrated their efficacy in patients naïve or resistant to biological treatments in randomized controlled trials. Moreover, these drugs seem to be able to prevent radiographic progression. To date few data are available from the real life context. Ultrasonographic (US) assessment has became a valid imaging tool in the management of RA patients in clinical practice, allowing the evaluation of joint inflammatory status. Together with clinimetric assessment, US could provide a comprehensive assessment of drug response.
Objectives: In the present study we aimed at assessing the early response to JAKi treatment by using musculoskeletal US.
Methods: In this prospective longitudinal study, we collected data about all consecutive active RA patients starting treatment with JAKi. RA was diagnosed according to the 2010 ACR/EULAR criteria. At each visit, clinical and laboratory data were collected in a standardized and computerized form, including demographics, past medical history, co-morbidities, previous and concomitant treatments. According with study protocol, all patients underwent clinical and US assessment at the following time-points: baseline (T0), 4 weeks (T1) and 12 weeks (T2). Clinical evaluation included tender and swollen joint counts (0-28), patients global health assessment. C-reactive protein (CRP) levels were registered and disease activity was calculated by disease activity score (DAS) in 28 joints by using CRP (DAS28-CRP). A systematic multiplanar grey-scale and power Doppler (pD) US examination was performed by using MyLab Eight Exp Machine (Esaote, Florence, Italy) at level of 22 joints (bilateral I-V metacarpophalangeal, I-V proximal interphalangeal, wrist). According with OMERACT definitions (1) we assessed the presence of synovial effusion, hypertrophy and pD, that were scored according to a semi-quantitative scale (0-3). A total US inflammatory score (0-198) was obtained by their sum.
Results: We enrolled 91 patients [F/M 77/14; median age 60.0 years (IQR 15.5); median disease duration 144 months (IQR 126)]. Of these patients, 54 (59.3%) were treated by baricitinib and the remaining 37 by tofacitinib. At baseline we found a median US inflammatory score of 20 (IQR 18.7) and a median DAS28-CRP of 5.0 (IQR 1.56). US assessment demonstrated significant reduction in the median values of inflammatory score already at T1 [median 13 (IQR 14.7), p<0.0001], that was maintained at T2 [median 10 (IQR 11), p<0.0001]. These results are represented in figure 1. Similar to US inflammatory score, a significant reduction was registered for DAS28-CRP median values [T1 3.5 (IQR 1.73), p<0.0001; T2 3.3 (IQR 1.8), p<0.0001]. No significant differences were found when subgrouping patients according with different JAKi drug, in terms US and clinimetric assessment.
Conclusion: In the present study, specifically designed to evaluate the US-detected efficacy of JAKi in RA patients, we demonstrated in a real life setting a significant, early and sustained improvement of inflammatory joint status.

Figure 1. Box and whiskers plot (median, quartiles, range) of US inflammatory score of 91 RA patients at baseline (T0), after 4 weeks (T1) and 12 weeks (T2) of treatment with JAKi. P values were referred to the comparison with baseline.



References:

[1] Wakefield et al, J Rheumatol 2005

Disclosure of Interests: enrica cipriano: None declared, Fulvia Ceccarelli: None declared, Francesca Romana Spinelli Grant/research support from: Pfizer, Consultant of: Novartis, Gilead, Lilly, Sanofi, Celgene, Speakers bureau: Lilly, Cristina Garufi: None declared, Ilaria Duca: None declared, Silvia Mancuso: None declared, cristiano alessandri Grant/research support from: Pfizer, Manuela Di Franco: None declared, Roberta Priori: None declared, Valeria Riccieri: None

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SAT0556

FINE STRUCTURE ANALYSIS OF THE INTER-RELATION BETWEEN TOPHUS DEPOSITION AND BONE LESIONS IN GOUT USING A COMBINATION OF DUAL ENERGY AND HIGH-RESOLUTION CT

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Background: Deposition of uric acid crystals cause an inflammatory reaction, which can lead to structural bone changes, if such deposits form adjacent to cortical bone [1, 2]. Both erosions and bony spurs can form in conjunction with tophus deposition. The exact spatial inter-relation between tophi and structural bone lesions in humans in vivo is not fully characterized.

Objectives: To spatially relate structural bone changes (erosions, osteophytes) to the deposition of monosodium urate crystals in the first metatarsophalangeal (MTP1) joint in patients with tophaceous gout.

Methods: Tophaceous gout patients with clinically detected tophi at the MTP1 joint underwent simultaneous dual energy computed tomography (DECT) and high-resolution peripheral quantitative computed tomography (HR-pQCT) of the feet. Tophi detected by DECT and erosions and osteophytes detected by HR-pQCT were overlayed to define their exact anatomical relation. Furthermore, feet of sex- and age-matched healthy controls (HC) were scanned to define the normal architecture of the MTP1 joint.

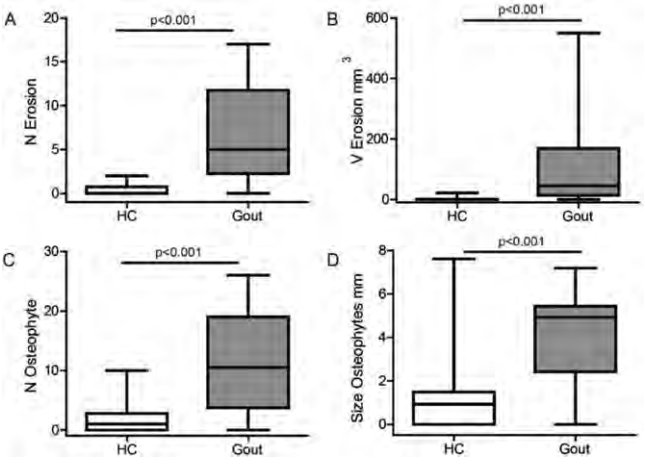
Results: Gout patients (N=20) had significantly higher numbers (5 (0–17 vs. 1 (1– 2)) and volumes (45.32 mm^3 (7.26–550.32) vs. 0.82 mm^3 (0.15–21.8)) of bone erosions as well as significantly higher numbers (10.5 (0-26) vs. 1 (0-10)) and sizes of osteophytes (4.93 mm (0.77-7.19 mm vs. 0.93 mm (0.05-7.61 mm)) than healthy controls (N=20). Erosions were in direct spatial relation to bone erosions, while osteophytic responses were more widespread and affected bone regions on the MTP1, which were not directly adjacent to tophi. Median tophus volume detected by DECT (0.12 mm^3 (0.01–2.53)) was associated with the total volume of erosions (r=0.597, p=0.005).

Conclusion: This study demonstrates that bone changes in gout are substantial and not only include erosions but also widespread architectural bone remodeling associated osteophyte formation. While there is a direct spatial relation between tophi and bone erosions the anabolic bone responses in gout are more widespread.

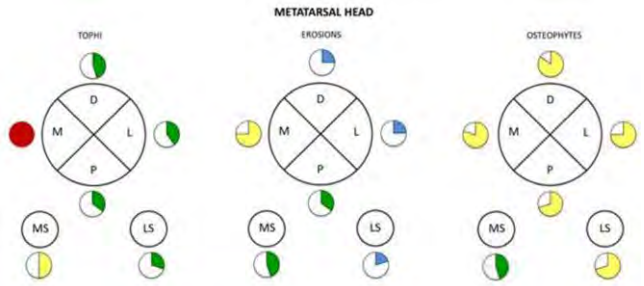
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Data are based on high-resolution peripheral quantitative computed tomography (HR-pQCT) of metatarsophalangeal joints I in gout patients (grey boxplots) and healthy controls (white boxplots). (A) number of bone erosions, (B) volume of bone erosions, (C) number of osteophytes and (D) size of osteophytes. Data are shown as medians and inter-quartile ranges (boxes).



Distribution of (A) tophi based on dual-energy computed tomography (DECT) as well as (B) bone erosions and (C) osteophytes based on high-resolution peripheral quantitative computed tomography (HR-pQCT) of metatarsophalangeal (MTP) I head in gout patients. Data are shown for the different regions of the MTPI head including the plantar, medial, dorsal and lateral region of the metatarsal head, as well as the medial and lateral sesamoid bones. Data indicate percentage of patients with tophi, erosions and osteophytes in respective region.

Disclosure of Interests: Sara Bayat Speakers bureau: Novartis, David Simon Grant/research support from: Else Kröner-Memorial Scholarship, Novartis, Consultant of: Novartis, Lilly, Caroline Pecherstorfer: None declared, Hanna Ellmann: None declared, Camille Figueiredo: None declared, Matthias Englbrecht: None declared, Axel Hueber Grant/research support from: Novartis, Lilly, Pfizer, EIT Health, EU-IMI, DFG, Universität Erlangen (EFI), Consultant of: Abbvie, BMS, Celgene, Gilead, GSK, Lilly, Novartis, Speakers bureau: GSK, Lilly, Novartis, Arnd Kleyer Consultant of: Lilly, Gilead, Novartis,Abbvie, Speakers bureau: Novartis, Lilly, Jürgen Rech Consultant of: BMS, Celgene, Novartis, Roche, Chugai, Speakers bureau: AbbVie, Biogen, BMS, Celgene, MSD, Novartis, Roche, Chugai, Pfizer, Lilly, Georg Schett Speakers bureau: AbbVie, BMS, Celgene, Janssen, Eli Lilly, Novartis, Roche and UCB

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SAT0557

RESIDUAL DISEASE ACTIVITY IN ADULT-ONSET STILL'S DISEASE: QUALITATIVE AND QUANTITATIVE ANALYSIS OF A SERIES OF 18F FDG-PET/MR

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Background: Adult-onset Still's disease (AOSD) is a systemic autoinflammatory disorder characterized by episodes of spiking fever, the presence of an evanescent pink-salmon rash, arthritis/arthralgias, sore throat and increased inflammatory serum markers. The diagnosis is clinical and needs the exclusion of potential mimickers such as infections and lymphoproliferative disorders. Currently, a specific diagnostic test to assess the disease activity is not available.

Objectives: To define the residual disease activity in AOSD and establish a possible response to therapy through ^{18}F-FDG PET/MR imaging technique.

Methods: 23 patients affected by AOSD and 24 controls underwent ^{18}F-FDG PET/MR between 2014 and 2018. A total of 54 ^{18}F-FDG PET/MR were analysed. AOSD patients were diagnosed according to the Yamaguchi's criteria and were in follow-up at the Rheumatology Unit of Padova University Hospital. The controls were chosen among non-AOSD patients with a previous diagnosis of solid tumors (lymphomas excluded). A *qualitative analysis* of PET/RM carried out by a Nuclear Medicine Specialist and a *semiquantitative analysis* carried out by measuring SUVs-to-liver (Standardized Uptake Value) for spleen, bone marrow (BM), lymph nodes and pharynx were performed. A SUVmax BM/SUVmean liver higher than 2.09 was set up as significant area of uptake for each organ considered. This threshold was calculated by adding the standard deviation multiplied by 2 at the mean ratio between SUVmax BM and SUVmean liver of the control group. The Pouchot score for disease activity was calculated for each subject. The distribution of the variables was investigated by Shapiro-Wilk test. The analysis of the association between the variables was carried out using the Mann-Whitney U test.

Results: AOSD patients present areas of focal ^{18}F-FDG uptake mainly in BM, lymph nodes, pharynx, spleen and salivary glands. Sites of uptake in spleen were found in 3.3% of PET/MR, in BM in 23.3%, in lymph nodes in 23.3% and in pharynx in 36.6% of PET/RM respectively. Eleven/thirty (47.8%) patients were

defined as "positive" since the uptake was higher than liver, and twelve/thirty (52.2%) were defined as "negative" since the uptake was lower than liver, regardless of SUVs and clinical manifestations. A semi-quantitative analysis assessed whether the values of the SUVmax BM/liver were higher than the cut-off of 2.09 in "positive" PET/MR and lower in the "negative" ones and if the clinical manifestations were present or absent in agreement with the evaluation of SUVs for each patient. BM was found to be active (SUVmax ratio > of 2.09) in 7 out of 11 patients when the PET/MR was defined "positive", while only in 1 case out of 12 BM SUVmax was >2.09 when the exam was "negative". Clinical manifestations were present in 10 out of 11 AOSD with a "positive" scan and in 7 out of 11 with both a "positive" scan and a SUV max BM/liver >2.09. Clinical manifestations were present in 1 out of 12 patients with a "negative" scan, while in 10 out of 12 cases with both a negative scan and a SUV max BM/liver <2.09 were absent. Six patients repeated PET/MR during follow-up. The values of the SUVmax BM/liver significantly decreased after anti IL-1β treatment with anakinra. In two cases in which anakinra was deferred, the BM SUVmax values exceeded the cut-off of 2.09 despite the patients did not complain any symptom or inflammation markers increase.

Conclusion: ^{18}F FGD-PET/MR could be able to evaluate the disease activity in AOSD when clinical manifestations and serum markers are not sufficient to establish it. The uptake on BM seems quite sensitive in pointing out the disease severity and in assessing the response to anti IL-1β therapy. ^{18}F PET/MR is an accurate and repeatable method, however further studies are required to validate its applicability in routinary clinical practice.

Disclosure of Interests: None declared

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SAT0558 THE IMPACT OF A STANDARDIZED TRAINING PROGRAM FOR IMPROVING THE RELIABILITY AND AGREEMENT – A STUDY OF VASCULAR ULTRASOUND FOR DIAGNOSING GIANT CELL ARTERITIS IN DENMARK

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Background: Due to a high level of evidence of good test performance, accessibility, minimal invasiveness, low cost, and good overall performance, EULAR recommends ultrasound (US) of the temporal and axillary arteries as primary diagnostic imaging test in patients suspected of Giant Cell Arteritis (GCA) (1).

Despite the growing body of evidence supporting the utility of US in GCA, standardized training programs and their impact on reliability are lacking(1). In TABUL study (2), the only US study published to date using a standardised US training program, the interobserver agreement by 12 different sonographers was only moderate, illustrating the challenges presented in the education for US in GCA.

Objectives: To evaluate the impact of a standardized training program including equipment adjustment on the agreement and reliability of US in the diagnosis of GCA for experienced musculoskeletal (MSK)ultrasonographers, without previous experience on vascular US.

Methods: Five rheumatologists with long-standing experience in MSK US were trained by a standardized training program including equipment adjustment (Box 1) prior to a prospective, non-interventional observational study in patients suspected having GCA.The rheumatologist performing the US subsequently evaluated the images blinded to the patients data. Thereafter the images were evaluated by a blinded external expert (i.e. considered the gold standard).

Results: In three Danish centers 112 patients were included, 59% females, mean age 72.4 (SD) 7.9 years and median CRP 55 (IQR 21-100)mg/l. Median duration of prednisolone treatment prior to US examination was 0 (IQR 0 to 1) days. 92% of the patients reported a newly emerged localized headache.

The reliability between the performing ultrasonographer and the US expert for the overall GCA diagnosis, as for the diagnosis of cranial (c-GCA) and large-vessel GCA (Lv-GCA) was excellent. In addition, excellent reliability was also found for the US examination of all examined arteries (Table 1). According to the US expert, vasculitis changes were found in 66 patients with the pathological findings distributed as presented in table 1.

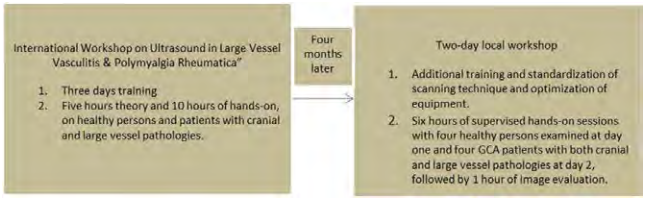
Tabel 1

Variables	Pathological findings (%)	Interobserver agreement (%)	Interobserver Reliability Kappa Coefficient	95% Confidence Limits
US positive for GCA	59% 66/112	96%	0.93	0.85-0.99
US positive for cGCA	53% 59/112	95%	0.89	0.81-0.98
US positive for Lv-GCA	19% 21/112	96%	0.89	0.78-0.995
Halo sign TA, all segments	51% 57/112	96%	0.91	0.83-0.99
Compression sign TA, all segments	48% 51/107	94%	0.89	0.80-0.98
Halo sign FA	20% 23/112	96%	0.87	0.75-0.98
Compression sign FA	16% 17/107	96%	0.86	0.73-0.99
Halo sign AA	18% 20/112	97%	0.91	0.81-1.00
Halo sign AC	4% 6/11	100%	1.00	1.00-1.00

TA: Temporal; FA: Facial; AA: Axillary; AC: common Carotid, artery

Conclusion: Our training program resulted in excellent reliability of US findings in patients suspected of having GCA and for the final diagnosis. The training program could be used when implementing vascular US in clinical practice.

Box 1



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SAT0559 INCREASED FREQUENCY OF INTER- AND SUBMETATARSAL BURSITIS AND MORTON'S NEUROMA IN RHEUMATOID ARTHRITIS: RESULTS OF A LARGE CASE-CONTROLLED MRI STUDY OF FOREFEET IN PATIENTS WITH EARLY ARTHRITIS AND HEALTHY CONTROLS

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Background: The forefoot is a preferential location for tendon and joint inflammation in rheumatoid arthritis (RA). Some imaging studies suggested that intermetatarsal and submetatarsal pathology (such as bursitis and Morton's neuroma) are also involved in RA, but these studies were small and its association was not thoroughly explored.

Objectives: To determine whether intermetatarsal bursitis (IMB), Morton's neuroma (MN) and submetatarsal bursitis (SMB) occur more often in early RA, compared to patients with other early arthritides and healthy controls. Contrast-enhancement in the subcutis that has been described as diffuse submetatarsal alterations (DSMA) were also included.

Methods: In this cross-sectional cohort-study, consecutive patients with RA, other arthritides and healthy controls underwent MRI of unilateral forefoot. Two readers, a trained PhD-student an experienced MSK-radiologist, scored IMB, MN, SMB and DSMA in consensus, and measured transverse and dorsoplantar

diameters of IMB, MN and SMB. Logistic regression models determined their association with RA, and test characteristics for RA were calculated. Lesion-sizes were plotted.

Results: 634 participants underwent MRI: 157 consecutive patients with RA (109 women; age 59±11SD), 284 with other early arthritides (158 women; age 56±17SD), and 193 healthy controls (136 women; age 50±16SD). Univariably, IMB, MN and SMB were more prevalent in RA (all P<0.001), DSMA was not (P=0.16). Multivariably, MB, SMB and MN were all associated with RA independent of each other (P<0.016). IMB was most frequent (sensitivity 69%), followed by SBM and MN (25% and 19%), specificity was high (70%, 96%, 94% respectively compared to other arthritides and 84%, 99% and 97% compared to healthy controls).

Although IMB, MN and SNB were more frequent in RA, the lesion-size was mainly similar in all groups. For MN a dorsoplantar diameter >6mm or transverse diameter >5mm was highly specific (specificity 100% compared to healthy controls), however it was infrequent (sensitivity 12% and 13%, respectively). For IMB and SMB no cut-off size could be distinguished with high specificity.

Conclusion: Intermetatarsal bursitis, Morton's neuroma and submetatarsal bursitis are increased prevalent in early RA and could be considered as disease features.

Disclosure of Interests: None declared

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SAT0560 THE PROGNOSTIC VALUE OF ULTRASONOGRAPHIC FINDINGS IN INDIVIDUALS WITH ASYMPTOMATIC HYPERURICEMIA

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Background: Chronic and steady asymptomatic hyperuricemia (AHU) can eventually lead to the deposition of monosodium urate crystals in joints and soft tissues. The rate of progression from AHU to clinically evident gout varies and mainly depends on serum uric acid levels. However, little is known about the prognostic value of ultrasonographic findings in individuals with AHU in detail.

Objectives: To explore the prognostic value of ultrasonographic findings in individuals with asymptomatic hyperuricemia.

Methods: We analyzed the ultrasonographic findings (snowstorm sign, double-contour (DC) sign, tophi, bone erosion, and abnormal blood flow) of bilateral knees, ankles and the first metatarsal-phalangeal joints (1st MTP) of individuals with AHU at Peking University People's hospital between June 2014 and May 2016. All individuals were followed up for two years.

Results: Among 218 individuals with AHU, the prevalence of snowstorm sign, DC sign, tophi, bone erosion and abnormal blood flow was 41%, 23%, 4%, 9% and 13%, respectively. Gout attacked in 36 patients during 2-year follow-up with 4.5 years of HU duration. The first attack affected the 1st MTP in 60%, the ankle in 31%, and the knee in 11% of the patients with gout. Patients with gout attack has longer hyperuricemia duration compared with individuals with AHU without gout attack. DC sign, tophi, and bone erosion on ultrasound were more frequently presented in patients with gout attack compared with individuals with AHU without gout attack. However, the prevalence of snowstorm sign and and abnormal blood flow on ultrasound has no significant differences between patients with gout attack and individuals with AHU without gout attack.

Conclusion: Longer hyperuricemia duration, DC sign, tophi, and bone erosion on ultrasound in individuals with AHU could be associated with gout attack.

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Disclosure of Interests: None declared

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SAT0561 METATARSOPHALANGEAL JOINT MEDIAL COLLATERAL LIGAMENT MEASUREMENT, A NOVEL ULTRASOUND FEATURE OF MONOSODIUM URATE DEPOSITION IN THE JOINT.

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Background: Acute gouty arthritis most commonly initially affects the first metatarsophalangeal joint (MT1). (1) Musculoskeletal ultrasound (US) is a reliable tool for detecting monosodium urate crystal (MSU) deposition in gout and hyperuricemia with validated, ultrasound features of double contour (DC) sign, tophus, and erosions. (2, 3) The collateral ligaments of MT1, which originate on the medial and lateral epicondyles of the metatarsals and extend to the proximal phalanx, function to stabilize the joint. (4) While tophus deposition typically occurs between the medial collateral ligament (MCL) and head of MT1, small MSU aggregates may be indistinguishable from surrounding tissue. In this study using US, we propose that an increased vertical depth between the superficial surface of the MCL to cortical surface of MT1 (dMC-MT) is indicative of MSU deposition (see figure 1). The aim was to evaluate associations of dMC-MT with serum uric-acid level (sUA) in a cohort of individuals with hyperuricaemia and non-episodic foot pain. We propose a novel sonographic feature of MSU crystal deposition in the MT joint.

Objectives:

1.)To evaluate the association between sUA and dMC-MT

2.)To record the presence/absence of classical features of MSU deposition including; double contour sign, erosions and tophi in a cohort of patients with hyperuricaemia and foot pain.

3.)To evaluate the associations between sUA and dMC-MT in those with\without classical features of MSU deposition (DC, erosion, tophi).

Methods: Following informed consent, hyperuricaemic patients (n = 52) underwent bilateral US of the 1MT using LogiqE9 at 15 MHz. Features of MSU deposition including DC sign, tophus and juxta-articular erosion were recorded. The dMC-MT was measured as the mean of the perpendicular distance between the superficial surface of the midpoint of the MCL to the MT1 head. Statistical analysis was performed using SPSS V.25 software. Data presented as MEAN ± S.E unless otherwise indicated.

Results: DC sign, tophus and erosion occurred in 31%, 20.7% and 19% of cases, respectively. Mean sUA was higher in tophus positive (540 ± 36) versus non tophus (470 ± 16) ($p<0.01$) and erosion positive (522 ± 32) versus non erosion (477± 17) patients. dMC-MT was significantly greater in tophus positive patients (0.34cm ± 0.17cm) versus non tophus (0.27cm ± 0.01cm) ($p < 0.01$). dMC-MT was significantly greater in erosion positive patients (0.31cm ± 0.18cm) versus non erosion (0.28cm + 0.01cm) ($p < 0.05$). In DC negative patients dMC-MT was significantly correlated with increasing sUA ($r = 0.34$ $p = <0.05$). No correction between dMC-MT and sUA was seen in DC positive patients.

Conclusion: dMC-MT is significantly greater both in patients with tophus and erosions indicating its role as an additional marker of MSU crystal deposition. Furthermore a significant association between dMC-MT and sUA in DC negative patients suggests that dMC-MT may be a more sensitive indicator of early urate deposition in a subset of patients where the earliest site of urate deposition has not occurred directly on to articular hyaline cartilage. dMC-MT may therefore be a sensitive tool for very early urate deposition. Further studies clarifying a role for dMC-MT are now required.

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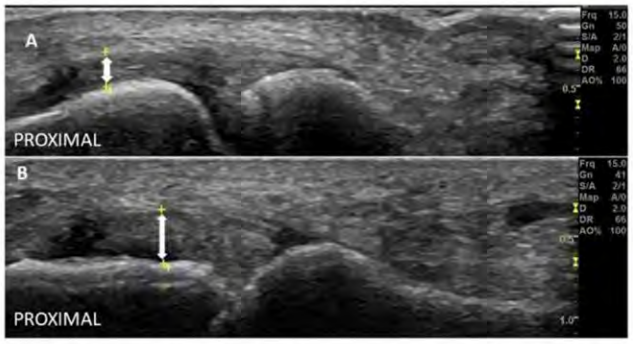


Figure 1. Medial Longitudinal Ultrasound of 1st MTP Joint in Patients with Hyperuricaemia. (A) Normal dMC-MT (0.22cm – block arrows.) (B) Large dMC-MT & tophus (0.33cm – block arrows.) Greyscale images obtained using Logiq E9 at 15mHZ.

Disclosure of Interests: None declared
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SAT0562 ADDITIONAL BENEFIT OF ULTRASOUND TO THE EARLY DIAGNOSIS OF PSORIATIC ARTHRITIS

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Background: Being an inflammatory disease of joint, spine or enthesis is the premise of the CASPAR diagnostic criteria for psoriatic arthritis (PsA). Traditionally, the assessment of local inflammation in joint, enthesis and tendon relies on physical examinations. But multiple studies have demonstrated that ultrasound (US) is capable of detecting subclinical inflammation as well as non-inflammatory lesions.
Objectives: To compare the capabilities of physical examination and US findings in the diagnosis of early PsA, and further identify the US features which are most valuable for the diagnosis of PsA.
Methods: 66 patients with suspected PsA or early PsA (disease duration< 2 years) due to psoriasis with joint pain or seronegative inflammatory arthritis were enrolled and further assessed by both physical examination and ultrasound (US). Tender and swollen joint counts based on 68/66 joints, tender tendons, enthesitis (14 entheses) and dactylitis (20 digits) count were collected by physical examination. Abnormalities of peripheral joints, entheses and tendons were also evaluated by US. New bone formation was evaluated by hand X-ray. The diagnostic capacity of CASPAR criteria based on US and based on physical examination were compared. The diagnosis value of US features as well as clinical characteristics were analyzed. The clinical diagnosis of PsA by the expert panel was taken as the standard.
Results: CASPAR criteria based on US showed a higher specificity than those based on physical examination (96.7% vs. 53.3%) with a bit decrease of sensitivity (91.7% vs. 97.2%). 36 patients were eventually diagnosed as PsA and 30 patients were non-PsA. Gender distribution, mean age and disease duration were equally distributed in two groups of patients. Dermatology Life Quality Index (DLQI) was higher in PsA patients than non-PsA patients. Significantly more patients had nail change and new bone formation on hand X-ray in PsA patients than in non-PsA patients (69.4% vs. 26.7%, P=0.001 and 66.7% vs. 13.3%, P<0.001 respectively). Significantly higher frequencies of synovitis/synovium hypertrophy, tenosynovitis and enthesitis were found in PsA patients than non-PsA patients (58.3% vs 20.0%, P=0.002, 38.9% vs 3.3%, P=0.001 and 52.8% vs 13.3%, P=0.002, respectively). Logistic regression analysis showed that nail change (OR=25.1, P=0.007), new bone formation on X-ray (OR=33.1, P=0.003), tenosynovitis on US (OR=149.1, P=0.003) and enthesitis on US (OR=39.2, P=0.008) were independent risk factors for predicting the diagnosis of PsA.
Conclusion: US increased the specificity of CASPAR criteria compared with physical examination. Combined nail change, new bone formation on X-ray, tenosynovitis and enthesitis on US improved the diagnosis of early PsA.
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SAT0563 SINGLE-PHOTON EMISSION COMPUTED TOMOGRAPHY-COMPUTED TOMOGRAPHY IS EQUIVALENT TO MAGNETIC RESONANCE IMAGING IN THE EARLY DIAGNOSIS OF SPONDYLOARTHRITIS: A RETROSPECTIVE STUDY

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Background: SpA has historically been a difficult clinical diagnosis, especially early diagnosis. Two imaging techniques that address this problem are magnetic resonance imaging (MRI) and Single-Photon Emission Computed Tomography-Computed Tomography (SPECT-CT). Their accuracies have not been adequately compared.
Objectives: The purpose of this study is to compare the sensitivities and specificities of SPECT-CT and MRI in SpA.
Methods: This retrospective study assessed all patients who underwent SPECT-CT of the sacroiliac joint to assess for SpA. The results of SPECT-CT were compared against MRI for all patients in the cohort who underwent an MRI within 4 weeks of the SPECT-CT. A diagnosis of SpA in the discharge summary was considered the reference standard, and was based on a combination of clinical scenario, response to therapy, imaging,, patient history or lab index.
Results: 200 patients (173 men; average 22±4 years of age) were included SpA was diagnosed in 189 (AS patients=99 and excluded in 11. SPECT-CT and MRI had similar (P >0 .05;k ¼ 0.74) sensitivities (0.94 vs 0.94),specificities (1.00 vs 1.00),positive predictive values (1.00 vs 1.00),negative predictive values (0.94 vs 0.80),and accuracies (0.97 vs 0.95) when compared to the reference standard.
Conclusion: Although MRI remains the initial modality of choice in early diagnosing SpA, SPECT-CT appears diagnostically equivalent and should be considered a viable supplementary or alternative imaging modality particularly if there is contra-indication or inaccessibility to MRI.
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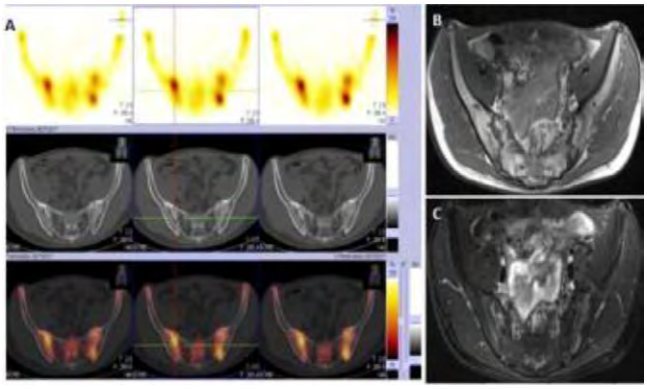


Figure 1. An 20-years-old man with 5 years of low back pain and spine malformation. (A) SPECT-CT showed an abnormal concentration of radioactivity in SIJ. (B–C) In SIJ, MRI showed a high signal on T1-WI, and a high signal on STIR.

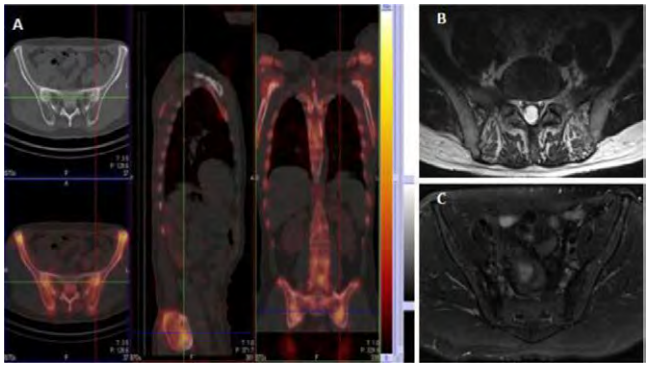


Figure 2. An 37-year-old man with 20 years of low back pain and spine malformation. (A) SPECT-CT showed an abnormal concentration of radioactivity in SIJ. (B–C) In SIJ, MRI showed a high signal on T1-WI, and a low signal on STIR.

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SAT0564 BONE TEXTURE ANALYSIS WITH DEEP LEARNING IN HAND RADIOGRAPHS FOR ASSESSING THE RISK OF RHEUMATOID ARTHRITIS

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Background: Conventional x-rays are essential to identify radiographic changes of rheumatoid arthritis (RA) in structure and bone texture. Limited evidence suggests that the bone texture analysis may quantify the radiographic changes in RA;[1] however, current techniques such as the fractal dimension characterize fixed texture features. Deep learning offers novel methods to 'learn' radiographic texture features relevant to RA.
Objectives: To develop a deep learning model to assess the radiographic bone texture in the distal metacarpal bone relevant to RA.
Methods: We collected 3,738 conventional hand radiographs from 2,128 individuals (RA, n = 908; non-RA, n = 1220). The second, third, and fourth metacarpal bone images were segmented using a curve Graph Convolutional Network (GCN), and the distal third was used as the input to train a texture model to classify RA. The texture model was based on the Deep Texture Encoding Network (Deep-TEN) architecture (figure 1),[2] which put an encoding layer on top of a pre-trained 18-layered residual network (ResNet18). The vectors produced by the model represent the orderless texture features that were used to generate a texture score for RA. Five texture models are trained using 5-fold cross-validation and are ensembled during inference by averaging the model outputs to produce the final score. We then validate the model using hand radiographs of 166 RA patients and 166 non-RA patients. Overall model performance was measured by area under the curve of the receiver operator curve (AUROC). Multivariate logistic regression was used to estimate the odds ratio (OR) and 95% confidence interval (CI) of RA.

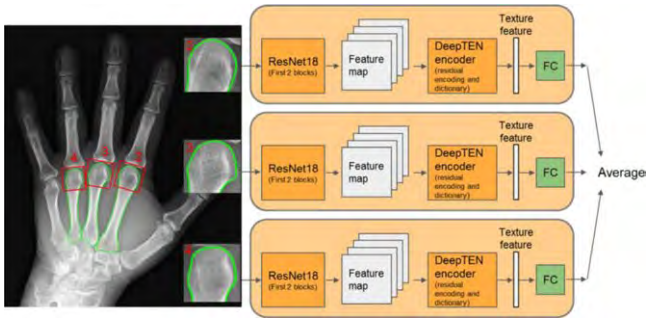


Figure 1. Schematic representation of deep learning models to extract and encode texture features for RA classification.

Results: We included 140 women and 26 men with RA (mean age, 55.9±1.8 years) and 166 non-RA individuals (F: M, 140:26; mean age, 55.5 ± 1.8 years). The mean texture score was 0.49 (95% CI, 0.48–0.50) in RA patients, which is significantly higher than non-RA patients (0.42, 95% CI, 0.40–0.43; p<0.01). The AUROC of the model was 0.68. In the multivariate logistic regression model, a high texture score (>0.43) is associated with an OR (95% CI) of 3.42 (2.48–4.72) for RA, adjusted by age and sex.
Conclusion: This study indicates that the texture model can delineate radiographic changes in texture relevant to RA and, coupled with automatic joint detection and segmentation, it has the potential to aid early RA diagnosis and monitor radiographic progression.
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Disclosure of Interests: None declared

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SAT0565 MODIFIED ULTRASONOGRAPHY SCORING SYSTEM BASED ON ORAL MUCOSA AND MAJOR SALIVARY GLANDS IMPROVING THE DIAGNOSTIC SPECIFICITY OF PRIMARY SJÖGREN'S SYNDROME

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Background: Primary Sjögren's syndrome (pSS) is a chronic autoimmune disease that affects exocrine systems. Xerostomia is one of representative clinical features which contributes to an accelerated destruction of the mucosal epithelium. Atrophic lesions of the oral mucosa is a common observation in pSS cases.
Objectives: To develop a modified ultrasonography scoring system which included the buccal mucosa and major salivary glands in patients with pSS and assess the ultrasonography characteristics of buccal mucosa.
Methods: Ultrasonography of buccal mucosa and major salivary glands were conducted for 53 pSS patients and 44 patients with SS-related manifestation but without pSS. The thickness of buccal mucosa and the echogenicity of the buccal mucosa were scored using the 0-2 scoring system. The sonographic features of major salivary glands were scored using the 0-16 scoring system. Differences of buccal mucosa thickness between groups were compared with Mann-Whitney test. The 2 methods (0-16 scoring system, modified 0-18 scoring system) were compared and statistical cutoffs were identified using receiver operating characteristic (ROC) curve analysis.
Results: The thickness
r the pSS group was significantly thinner than that for the non-pSS group (p < 0.001), and the best score cut-off was 0.38mm. The echogenicity of buccal epithelium was heterogeneously hyperechoic in 32 (60.4%) of the 53 patients, and was 5(11.4%) of the control group. The optimal cutoff point to distinguish between pSS and non-pSS was 7 in the modified scoring system (sensitivity 79.2%, specificity 95.5%), and it was 6 in the 0-16 system (sensitivity 81.1%, specificity 86.4%). Compared with the 0-16 system, modified scoring system improved the diagnostic specificity.
Conclusion: The thickness of the oral mucosa in patients with pSS is thinner and the echogenicity in buccal epithelium increases compared with that of non-pSS.

The modified ultrasonography scoring system integrated oral mucosa and major salivary glands is able to improve the diagnostic specificity of patients with pSS.

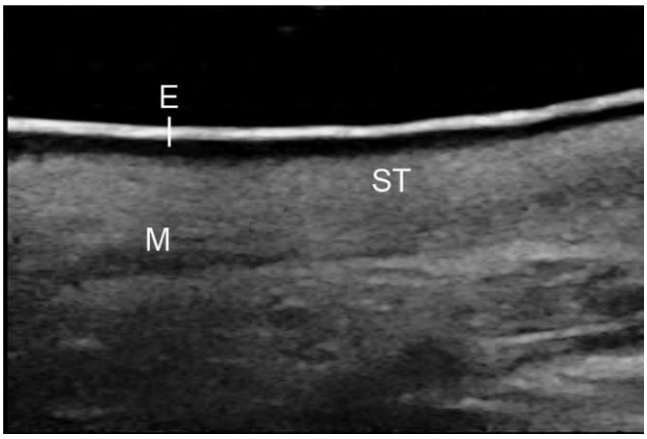


Figure 1. Ultrasonography image of the normal buccal tissue. E = epithelial membrane of buccal mucosa; ST = subepithelial connective tissue; M = buccinator muscle.

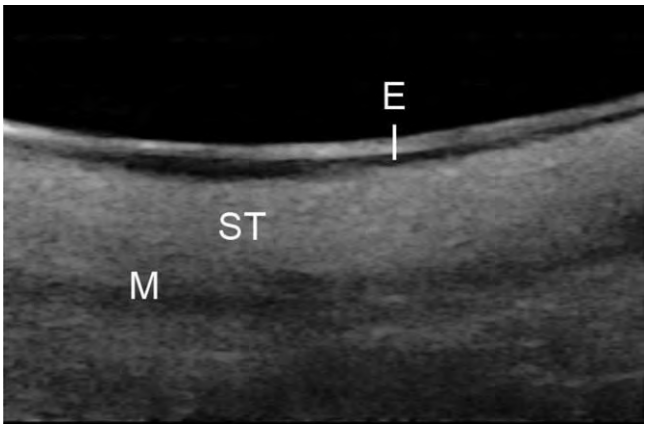


Figure 2. Ultrasonography image of pSS patient reveals decreased thickness and heterogeneous hyperechogenicity of buccal mucosa. E = epithelial membrane of buccal mucosa; ST = subepithelial connective tissue; M = buccinator muscle.

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Disclosure of Interests: None declared

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SAT0566 ULTRASOUND DOPPLER MASEI SHOWS SENSITIVITY TO CHANGE AFTER BIOLOGICAL THERAPY IN SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS PATIENTS

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Background: The assessment of activity in spondyloarthritis (SpA) and psoriatic arthritis (PsA) involves several domains, including enthesitis. Clinical enthesitis has shown low sensitivity, specificity and reliability. The MAdrid Sonographic Enthesitis Index (MASEI) is a feasible and reliable ultrasound score, but its responsiveness to treatment has not yet been evaluated.

Objectives: The main objective of this study was to investigate the sensitivity to change of MASEI in active SpA and PsA patients.

Methods: Longitudinal study in patients with SpA and PsA with active disease (defined as patients who were going to start or switch biologic disease modifying antirheumatic drugs (bDMARD) therapy according to physician criteria and in agreement with clinical guidelines). MASEI evaluation was performed at baseline, 3- and 6-months visits. MASEI and Outcome Measures in Rheumatology (OMERACT) enthesitis Power Doppler (PD) definitions were checked. Each enthesis was scanned in both the longitudinal and transverse planes, and 5 second videos were recorded for reliability. An inter-reader analysis by three readers was performed. For statistical analysis t-Student test was used to determine changes between visits and kappa test was used for reliability.

Results: A total of 72 US evaluations of 25 patients were included, of whom 13(52%) were ankylosing spondylitis (AS) patients, 9(36%) PsA, and 3(12%) non radiographic axial spondyloarthritis (nr-axSpA). Mean age was 51.2±14.1 years and 13(52%) were females. Mean DAS28 (3.5±1.2) for peripheral involvement, mean BASDAI (5.8±2) for axial involvement, and CRP values (13.1±13.6) reflect moderate-high disease activity at baseline. US parameters at baseline and at the 3- and 6-month follow-up visits are shown in Table 1. Global MASEI score was responsive at the 3- and 6-month follow-up visit (-4.9 and -5.7, respectively) ($p<0.05$) and both MASEI and OMERACT PDUS definitions of active enthesitis improved significantly at 3- (-0.6 and -1.1) and 6-month follow-up visits (-0.7 and -1.1) ($p<0.05$). Reliability of PD MASEI definition among the three readers was excellent (kappa = 0.918).

Table 1. MASEI evaluation at baseline, 3- and 6-month follow-up visits

Parameter	Baseline n=25	3 months n=25	P[a]	6 months n=22	P[a]
MASEI score	28±9.3	23.2±7.6	**0.002**	24.7±8.1	**0.01**
PD US MASEI score	1.8 ±1.3	1.1±1.1	**0.046**	1±0.9	**0.004**
PD US OMERACT score	1.6±1.2	0.9±0.9	**0.024**	0.8±0.9	**0.006**

[a]t-Student test for comparison to baseline

Conclusion: MASEI score significantly improves at 3 and 6 months of follow up in patients under bDMARD treatment and both MASEI and OMERACT Doppler definitions of active enthesitis reflects treatment response. These findings support the usefulness of PD US in the assessment of bDMARD treatment response in SpA and PsA.

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SAT0567 USE OF THERMOGRAPHY OF HANDS AND MACHINE LEARNING TO DIFFERENTIATE PATIENTS WITH ARTHRITIS FROM HEALTHY SUBJECTS

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Background: The early diagnosis of rheumatic diseases improves their prognosis. However, patients take several months to reach the rheumatologist from the beginning of the first symptoms. Thermography is a safe and fast technique that captures the heat of an object through infrared photography. The inflammation of the joints causes an increase in temperature and, therefore, can be measured by thermography. Machine learning methods have shown that they are capable of analyzing medical images with an accuracy similar or superior to that of a healthcare professional.

Objectives: Develop an algorithm that, based on thermographic images of hands and machine learning, differentiates healthy subjects from patients with rheumatoid arthritis (RA), psoriatic arthritis (PA), undifferentiated arthritis (UA) and arthritis of hands secondary to other diseases (SA).

Methods: Multicenter observational study conducted in the rheumatology and radiology service of two hospitals. Patients with RA, PA, UA and SA who attended the followup visit and healthy subjects (companions and healthcare proffesionals) were recruited. In all cases, a thermal image of the hands was taken using a Flir One Pro or Thermal Expert TE-Q1 camera connected to the mobile and an ultrasound of both hands. The degree of synovial hypertrophy (SH) and power

doppler (PD) was assessed for each joint (score from 0 to 3). Inflammation was defined as the presence of SH> 1 or PD> 0. Machine learning was used to classify patients with RA, PA, UA and SA with inflammation evidenced by ultrasound and healthy subjects from thermographic images. The evaluation of the classifier was performed by leave-one-out cross-validation and the area under the ROC curve (AUCROC) in those subjects whose thermal image was performed with the Thermal Expert TE-Q1 camera. The study was approved by the Clinical Ethics and Research Committee of the centers.

Results: 500 subjects were recruited from March 2018 to January 2020, of these 73 were excluded due to poor quality in the thermal image (moved or absence of temperature contrast between hand and background). Of the 427 subjects analyzed, 129 corresponded to healthy subjects, 138 to patients without evidence of inflammation and 160 to patients with inflammation evidenced by ultrasound (116 RA and 44 PA, UA or SA). Of these, 42% were taken using the Thermal Expert TE-Q1 camera. An AUCROC of 0.73 (p-value <0.01) was obtained for the healthy classifier vs RA and 0.72 (p-value <0.01) for the healthy classifier vs PA, UA and SA.

Conclusion: A classification model has been developed capable of differentiating patients with RA, PA, UA and SA with evidence of inflammation from healthy subjects. These results open an opportunity to develop tools that facilitate early diagnosis.

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SAT0568 PERSISTENT VASCULAR 18F-FDG UPTAKE DESPITE CLINICAL-ANALYTICAL REMISSION IN PATIENTS WITH LARGE VESSEL VASCULITIS UNDER TOCILIZUMAB THERAPY. SINGLE UNIVERSITARY CENTER EXPERIENCE OF 30 PATIENTS.

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Background: Tocilizumab (TCZ) has shown efficacy in large vessel vasculitis (LVV) **(1-3)**. Disease activity assessed by laboratory markers (ESR,CRP) may be of less value with TCZ. ^{18}F-FDG PET/CT may be useful to monitor LVV disease activity **(4-5)**.

Objectives: To assess **a)** evolution of disease activity in LVV treated with TCZ by PET/CT and **b)** its correlation with clinical/serological markers.

Methods: Single centre study of 30 patients with refractory LVV treated with TCZ who had a baseline and follow-up PET/CT scan. Vascular uptake was assessed quantitatively and qualitatively. Quantitative analysis was assessed as a target to background ratio (TBR)=SUVmax thoracic aorta/SUVmax aortic vascular pool. For qualitative analysis, FDG uptake at vessel wall was visually grading compared to the liver. We defined a total vascular score which included 5 vascular areas (supra aortic trunks, thoracic, abdominal, iliac and femorotibial arteries) ranging from 0 to 15. Clinical improvement (no improvement/partial/complete), analytical (CRP mg/dL; ESR mm/1st hour) and reduction of prednisone dose (mg/day) were also assessed.

Results: 30 patients (24 w/6 m); mean age 65.3 ± 10.6 yrs. TCZ was started after 6.5 [2.0-20.0] months from LVV diagnosis. Most patients received TCZ as intravenous infusions (70%) and almost half of them (46.7%) received combined therapy with MTX. Clinical/analytical evolution and quantitative/qualitative uptake assessment is shown in **TABLE**. After a mean follow-up of 37.0±18.5 months, 92.3% of patients experienced complete clinical/analytical improvement. Complete quantitative normalization of vascular uptake (TBR< 1.34) was achieved in 30.8%. Qualitatively, 23.1% of patients showed normalization (total vascular score =0) at the end of the study period.

Conclusion: Most patients with LVV under TCZ experienced rapid and effective clinical and analytical response. Decrease of vascular uptake was also observed both quantitatively and qualitatively assessed. However, complete normalization of vascular uptake despite clinical remision was only observed in less than one-third of patients.

TABLE.

	Basal (n=30)	6 months (n=9)	12-18 months (n=21)	>18 months (n=13)
Clinical improvement				
Complete, *n (%)*		7 (77.8)	16 (76.2)	12 (92.3)
Laboratory markers				
ESR (mm/1sth), *median [IQR]*	24.0 [9.8-53.0]	2.0 [2.0-3.0] *	2.0 [2.0-4.0] *	2.0[2.0-3.5] *
CRP (mg/dL), *median [IQR]*	1.5 [0.5-2.4]	0.1 [0.1-0.2] *	0.1 [0.1-0.1] *	0.1 [0.1-0.1] *
ESR/CRP normalization, n *(%)*		9 (100)	21 (100)	13 (100)
FDG vascular uptake				
TBR, *mean ± SD*	1.69 ± 0.52	1.56±0.41 *	1.46±0.16 *	1.40 ± 0.18 *
Total vascular score, *mean ± SD*	5.0 ± 2.6	3.7 ± 2.2	3.3 ± 1.7*	2.7 ± 2.4*
Quantitative normalization, n *(%)*		4 (44.4)	5 (23.8)	4 (30.8)
Qualitative normalization, n *(%)*		1 (11.1)	1 (4.8)	3 (23.1)

*test Wilcoxon: p < 0.05. Quantitative normalization when TBR <1.34. Qualitative normalization when total vascular score =0.

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SAT0569 "IMAGES ARE MORE THAN PICTURES, THEY ARE DATA" [1] – EXPLORATION OF RADIOMICS ANALYSIS FOR SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE

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Background: Interstitial lung disease (ILD) affects 60% of patients with systemic sclerosis (SSc) and is the primary cause of death. Medical imaging is an integral part of the routine work-up for diagnosis and monitoring of SSc-ILD and includes high-resolution computed tomography (HRCT). Radiomics is a novel research area that describes the in-depth analysis of tissue phenotypes in medical images with computational retrieval of quantitative, mineable metadata appropriate for statistical analyses.

Objectives: To explore the performance of HRCT-derived radiomic features for the assessment of SSc-associated ILD (i.e. diagnosis, staging, and lung function).

Methods: Radiomics analysis was performed on HRCT scans from 98 SSc patients, including n=33 SSc patients without ILD, n=33 with limited and n=32 with extensive ILD as defined by 0%, <20% and ≥20% visual extent of fibrosis on HRCT, respectively. Following semi-automated segmentation of lung tissue on 3D reconstructed HRCT scans, 1386 radiomic features, including 17 intensity, 137 texture, and 1232 wavelet features were extracted using the in-house developed software Z-Rad (Python 2.7). In order to identify robust features, we conducted intra- and inter-reader correlation analysis (ICC) in a subgroup of patients. Only features with good reproducibility (ICC ≥ 0.75) entered subsequent analyses. We applied the Wilcoxon test, followed by Receiver Operating Characteristic ROC) curve analyses, to identify features significantly different between a) ILD

and non-ILD and b) limited vs. extensive ILD patients. Spearman rank correlation was performed to reveal significant associations of radiomic features from a) and b) with lung function as measured by percentage of predicted forced vital capacity (FVC% predicted).

Results: In total, 1355/1386 radiomic features passed the test of robustness and were eligible for further, exploratory analyses. Radiomic features with good performance (area under the ROC curve (AUC) ≥ 0.7 and p-value ≤ 0.05) were considered as potential candidate discriminators. Under this criterion, we identified 288/1355 (21.3%) radiomic features that were significantly different between ILD and non-ILD patients and 409/1355 (30.2%) features that significantly discriminated between limited and extensive ILD (Fig. 1). For diagnosis, the texture feature *dependence count entropy* was the top parameter to distinguish ILD patients from healthy controls (AUC = 0.89, p = 1.83×10^{-10}), whereas for staging the wavelet feature *HHH long run high grey level emphasis* proved to be best suited to separate limited from extensive ILD (AUC = 0.88, p = 7.76×10^{-9}).

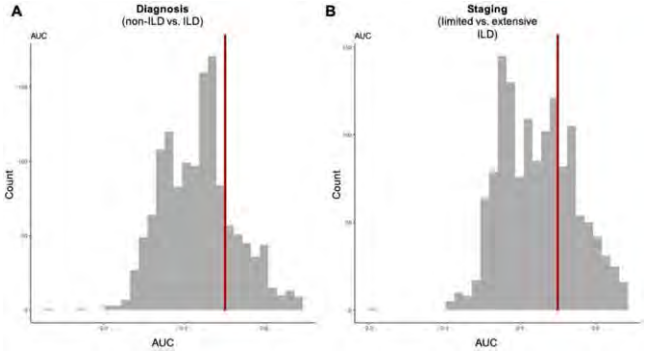


Fig 1.

Correlation analysis of the most significant (best performing) discriminative radiomic features with lung function revealed a significant negative correlation of *dependence count entropy* (rho = -0.51, p = 9.89×10^{-8}) and *HHH long run high grey level emphasis* (rho = -0.51, p = 1.73×10^{-5}) with FVC% predicted.

Conclusion: Our study adds novelty to the field of SSc-ILD showing that radiomic features have great potential as quantitative imaging biomarkers for diagnosis and staging of SSc-ILD and that they may reflect lung function. As the next step, we are planning to build predictive models, using machine learning, for diagnosis, staging, and lung function and validate them in external patient cohorts. If validated such models will pave the way for computer-aided management in SSc-ILD and thus improve patients' outcome.

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SAT0570 CLINICAL SIGNIFICANCE OF FINGER EXTENSOR PARATENONITIS DETECTED BY MUSCULOSKELETAL ULTRASOUND

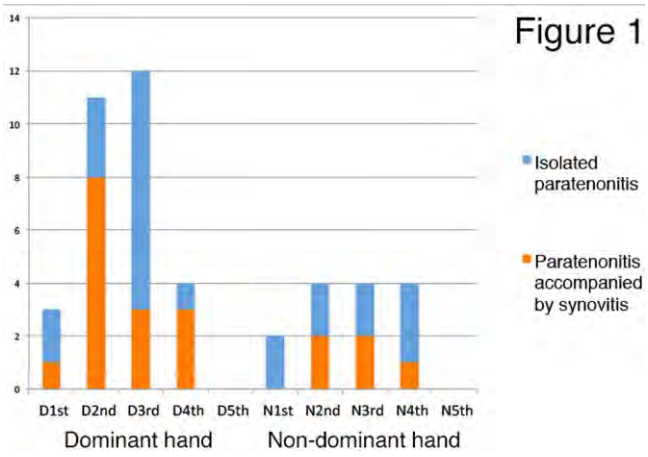
T. Suzuki[1], H. Shirai[1]. [1]*Japanese Red Cross Medical Center, Division of Allergy and Rheumatology, Tokyo, Japan*

Background: The extensor tendons over fingers are devoid of a tendon sheath, so that the term paratenonitis is used to describe extra-articular hyperemia or anechoic fluid collections along the extensor tendons of the fingers. Although the grading of paratenonitis is found in one sonographic scoring system of RA known as German US7, the clinical significance of paratenonitis is not fully understood.

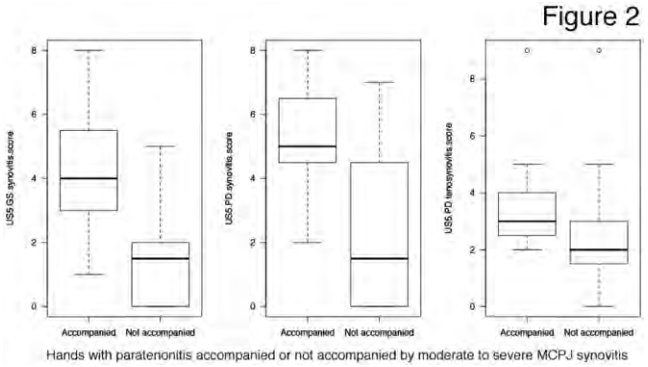
Objectives: To determine the clinical significance of finger extensor paratenonitis detected by ultrasound (US), especially in the patients with RA.

Methods: We reviewed 1200 reports of the US examination underwent in our division since April 2015. The items necessary for scoring US5 scores (the 'hand-limited version' of the German US7) have been routinely recorded. The cases with finger extensor paratenonitis over the dorsal metacarpophalangeal joint (MCPJ) were determined. The severity of articular synovitis in the perilesional MCPJ were subjectively graded for grey-scale (GS) and power Doppler (PD) on a four-step scale (0-3) and scored using EULAR-OMERACT combined scoring system. In RA patients, US5 scores were determined for the involved hands.

Results: Paratenonitis was found in 44 fingers in the 38 hands of the 36 patients with rheumatic diseases/disorders including 25 patients with RA (11 early RA and 14 established RA). Non-RA diseases/disorders included 4 cases of undifferentiated arthritis, 2 cases of PsA, 1 case each of SLE, Sjogren syndrome, reactive arthritis and other disorders.



The 44 fingers were classified according to the absence or presence of articular synovitis in the perilesional MCPJ into "isolated paratenonitis" or "paratenonitis accompanied by synovitis". The distribution of paratenonitis over the 1st-5th fingers of the dominant or non-dominant hands is shown in Figure 1. Paratenonitis was relatively frequently found in the 3rd and 2nd fingers of the dominant hands. Interestingly, articular synovitis in the perilesional MCPJ were found significantly more frequent in the cases of MCP2 in the dominant hands (73%) than in the cases of MCP3 in the dominant hands (25%) (p=0.039).



Among the 27 hands with paratenonitis of 25 RA patients, US5 scores were compared based on the absence or presence of moderate to severe articular synovitis in the perilesional MCPJ (the combined score >1) (Figure 2). GS synovitis score, PD synovitis score and PD tenosynovitis score were significantly higher in those with moderate to severe perilesional MCP synovitis than in those without it (p=0.007, 0.0092 and 0.0458, respectively).

Conclusion: Finger extensor paratenonitis over the dorsal MCPJ tends to occur in the 3rd and 2nd fingers of the dominant hand. In RA patients, paratenonitis accompanied by active perilesional MCPJ synovitis are presumably due to active disease, while isolated paratenonitis can also be caused possibly by degenerative changes due to overuse or deformity. Isolated paratenonitis may be more frequently found in the 3rd finger than in the 2nd finger of the dominant hand.

References: None

Disclosure of Interests: Takeshi Suzuki Speakers bureau: Abbvie, Asahi-kasei, Astellas, Bristol-Myers Squibb, Chugai, Eli Lilly, Mitsubishi-Tanabe, Novartis, UCB, Harumi Shirai: None declared
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SAT0571 OPTICAL SPECTRAL TRANSMISSION TO ASSESS THERAPY RESPONSE IN PATIENTS WITH ARTHRITIS: A COMPARATIVE STUDY WITH CLINICAL, LABORATORY AND ULTRASONOGRAPHIC ACTIVITY MARKERS.

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Background: Valid assessment of disease activity leads to outcome improvement in patients with rheumatoid arthritis (RA) (1). Optical spectral transmission (OST) is a modern diagnostic tool able to assess the blood-specific absorption of light transmitted through a tissue, promising quantification of inflammation in the finger and wrist joints of RA patients (commercial device: HandScan - Hemics, The Netherlands) (2).

Objectives: To our knowledge, there are no data regarding the diagnostic value of OST in the evaluation of inflammatory activity changes during arthitis follow up. Thus, aims of this study were to examine the ability of OST to detect response to anti-inflammatory therapy in patients with arthritis and to explore OST associations with clinical, laboratory and ultrasonographic (US) activity markers.

Methods: OST measurements were performed in patients with active arthritides of the wrist and finger joints before and after administration of glucocorticoids (GC), during a disease flare. For the same points in time (a and b) patients and healthy controls underwent clinical, laboratory and joint US [Grey Scale (GSUS) - Power Doppler (PDUS)] examinations. OST-values before and after therapy were subsequently compared with their corresponding DAS28- and US-values. The distributions of Delta-PDUS und OST-values between the two time points were compared by Bayesian statistics. Moreover, OST diagnostic performance was tested by Receiver Operating Characteristics (ROC).

Results: We recruited 54 patients with active inflammatory arthritis: 39 RA, 4 gout, 7 peripheral spondylarthritides and 4 other miscellaneous arthritides (66.7% females) and 114 controls.

Previous to therapy with GC, median OST was [OST(a): *8.75* (*5.38-16.25*, IQR)] and after therapy [OST(b): *4.75* (*2.38-8.63*, IQR)] (*p<0.05*). Similarly, DAS28 dropped significantly after GC therapy [DAS28(a): *5.12* (*4.33-6.10*, IQR) vs. DAS28(b): *3.85* (*3.40-4.82*), *p<0.05*)]. OST correlated moderately with PDUS at both time points: (a) *rho=0.449* and (b) *rho=0.414*, respectively (both; *p<0.01*). Moreover, OST correlated significantly with swollen joint count at both time points (a) *rho=0.379* and (b) *rho=0.382*, *p<0.01* respectively.

OST and US performed similarly in the assessment of inflammatory changes caused by the administration of GC (same tendency in the change of OST values in *83.2%* of the cases). Furthermore, Bayesian statistic revealed no significant differences between OST and US for all 3 examined joint categories (MCP: *p=0.81*; PIP: *p=0.74*; wrists: *p=0.60*).

In addition, ROC revealed that OST is a very good tool to distinguish patients with arthritis from healthy controls at both examination points [AUC(a): *0.883*(*95% CI=0.83-0.94*) and AUC(b): *0.811*(*95% CI=0.74-0.881*)].

Conclusion: OST was able to assess response to therapy in arthritis patients comparable to US. Moreover, OST correlated with disease activity markers and could effectively differentiate between arthritis patients and controls. Therefore, OST could prove to be a valuable non-interventional time- and resource-saving diagnostic tool to assist arthritis monitoring.

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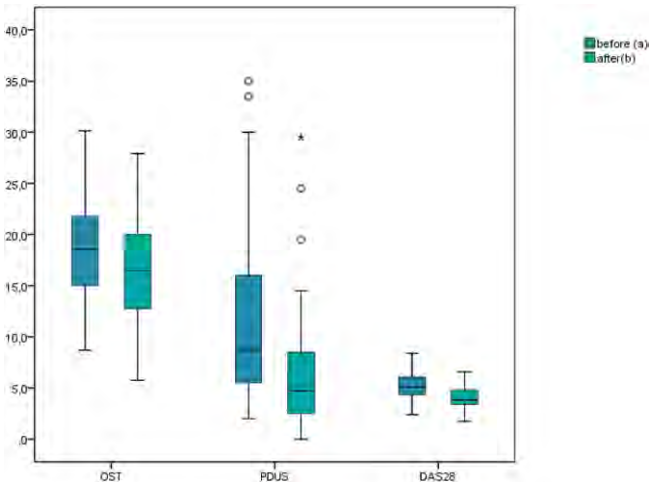


Figure 1. OST-, PDUS- and DAS28- values before and after GC therapy.

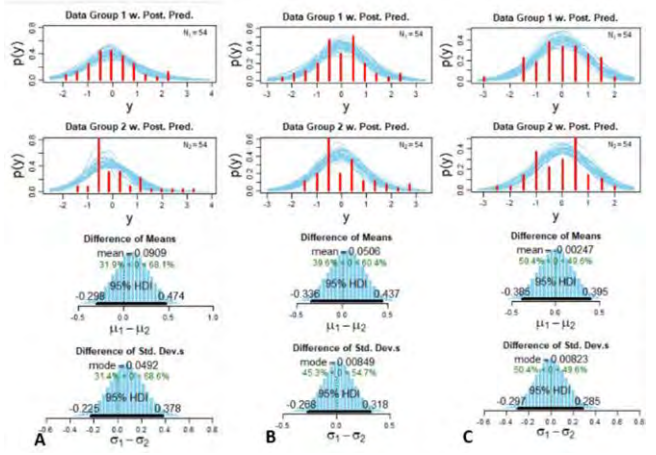


Figure 2. OST- (group 1) und Ultrasound- (group 2) Bayesian distributions, means- and standard deviation-differences for MCP (A), PIP (B) and wrists (C).

Disclosure of Interests: None declared
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SAT0572 CONSTRUCTIVE VALIDITY OF MUSKULOSKELETAL ULTRASOUND MEASUREMENT OF CARTILAGE THICKNESS IN PATIENTS WITH KNEE OSTEOARTHRITIS

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Background: Cartilage thickness is one important measure in describing both OA development and progression. Based on current knowledge, conventional radiography (CR) and magnetic resonance imaging (MRI) have not been demonstrated to be superior over one another. Because of disadvantages of MRI and CR neither can be use in routine daily clinical practice for follow up of OA patients. Diagnostic ultrasound assessment (US) of cartilage thickness offers an alternative measure as a clinically available and more cost-effective source of knee articular cartilage imaging.

Objectives: Our objective was to determine the relationship between US and CR measures of femoral cartilage thickness in patients with knee osteoarthritis because systematic feature- and site-specific cross-comparison between this two methods is still missing in the current literature.

Methods: 120 patients with knee osteoarthritis (240 knees) are recruited for this study. The joint space width (JSW) and Kellgren and Lawrence (K&L) grade were measured using weight-bearing anteroposterior 30° knee semi-flexion knee radiography (with inclusion criteria K&L grade 1-4). Femoral cartilage thickness was measured three times in supine position and with a suprapatellar transverse scan with the knee in maximal flexion at the lateral condyle (LC), medial condyle (MC) and intercondylar notch (IN) by one rheumatologist and arithmetic mean is taken. Pain and

functionality are measured with VAS pain scale, Womac, Lysholm and SF 36 score. The agreement between two methods was evaluated with Bland-Altman analysis.
Results: We found a statistically significant low level of rank correlation between CR and US measurements of mean cartilage thickness; ρ (rho) values between modalities were low (0.263 and 0.273 depending on side (right/left), p=0.005 and p=0.007 respectively). In Bland – Altman analysis, US measurement showed bad agreement with CR. Presence or absence of US features of OA (effusion, synovial hypertrophy, osteophytes and popliteal cysts) didn't influence on cartilage thickness assessed by US (p>0.05). For US assessment, we found correlation only between cartilage thickness and VAS pain scale (ρ (rho) -0.281, p=0.004). We didn't found any statistically significant correlation between CR thickness measures and pain/functionality/HRQoL scores (p>0.05).
Conclusion: These results suggest that ultrasound may be a useful clinical tool to assess relative cartilage thickness. However, the absolute validity of the ultrasound measure is called into question due to the larger CR-based thickness measures and low level of agreement according to Bland-Altman analysis. The use of ultrasound as a complementary imaging tool along with CR may enable more accurate and cost-effective detection, prognosis and follow-up of knee osteoarthritis in routine clinical practice.
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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.3049

SATURDAY, 06 JUNE 2020

Epidemiology, risk factors for disease or disease progression

SAT0573

TUBERCULOSIS INFECTION IN MOROCCAN PATIENTS WITH RHEUMATIC DISEASES UNDER BIOLOGIC THERAPY: A MULTICENTER NATIONAL STUDY

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Background: Tuberculosis (TB) is a major health problem worldwide, occurring mainly in low income countries. Therefore, screening for latent TB infection (LTBI) before initiating biologic therapy is mandated by current guidelines.
Objectives: The aim of this study was to evaluate the prevalence of tuberculosis infection (TB) in Moroccan patients with rheumatic diseases under biologic therapy, and to describe the demographic characteristics of these patients as well as to explore potential risk factors.
Methods: This fourteen-year nationally representative multicenter study enrolled Moroccan patients with rheumatic diseases who had been treated with biologic therapy. Patient medical records were reviewed retrospectively for demographic characteristics, underlying rheumatic diseases, associated co-morbidities, and TB related data.
Results: In total, 1407 eligible patients were studied; 31 cases with active TB were identified at an estimated prevalence rate of 2.3%. The mean age was 42.9±12 years and 75.8% were males. Ankylosing spondylitis (AS) accounted for 84.8% of active TB cases and the majority of cases (31/33) occurred among anti TNF-α users. A total of 8 out of 33 patients were positive at initial Latent TB infection (LTBI) screening by tuberculin skin test (TST) and/ or interferon gamma release assay (IGRA). Consumption of unpasteurized dairy products (odds ratio [OR], 34,841; 95% CI, 3,1-389,7; p=0,04), diabetes (OR, 38,468; 95% CI, 1,6-878,3; p=0,022), smoking (OR, 3,941; 95% CI, 1-159,9; p=0,047) and long biologic therapy duration (OR, 1,991; 95% CI, 1,4-16,3; p=0,001) were identified as risk factors for developing active TB.
Conclusion: Moroccan patients with rheumatic diseases under anti TNF- α agents are at an increased TB risk especially when risk factors are present. Strict initial screening and regular monitoring of LTBI is recommended for patients living in high TB prevalence areas.

Table 1. Risk factors by univariate and multivariate logistic regression.

Variables	Univariate analysis			Multivariate analysis		
	Odds Ratio	95% CI	*p* value	Odds Ratio	95% CI	*p* value
Age	0,999	0,97-1,028	0,929			
Sexe	0,973	0,388-2,443	0,954			
Marital status :						
▪ Married	0,593	0,259-1,357	0,216			
▪ Single	1,685	0,737-3,855	0,216			
Residence :						
▪ Urban	0,778	0,189-3,199	0,728			
▪ Rural	1,286	0,313-5,288	0,728			
Level of education :						
▪ Illiterate	1,313	0,547-3,150	0,542			
▪ Primary	2,370	0,797-7,047	0,121			
▪ Secondary	0,918	0,314-2,683	0,875			
▪ Tertiary	1,123	0,345-3,649	0,847			
Consumption of unpasteurized dairy products	3,571	1,531-8,330	0,03	34,841	3,1-389,7	0,04
Diabetes	5,145	1,140-23,211	0,033	38,468	1,6-878,3	0,022
Smoking	3,667	1,311-10,253	0,013	3,941	1-159,9	0,047
Type of rheumatic disease :						
▪ Ankyosing spondylitis	0,276	0,97-0,781	0,13			
▪ Rheumatoid arthritis	0	-	0,999			
Biologic therapy :						
▪ Adalimumab	1,151	0,511-2,593	0,734			
▪ Infliximab	1,340	0,583-3,079	0,491			
▪ Etanercept	2,29	0,675-7,804	0,183			
▪ Rituximab	0,272	0,033-2,210	0,223			
▪ Toclizumab	0,223	0,033-2,210	0,223			
▪ Golimumab	0,979	0,098-9,751	0,986			
▪ Secukinumab	0	-	0,999			
Duration of exposure to bDMARD (months)	1,462	1,261-1,695	<0,001	1,991	1,4-16,3	0,001

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SAT0574

RISK FACTORS ASSOCIATED WITH OPIOID USE AMONG WORKER'S COMPENSATION: A LITERATURE REVIEW

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Background: To increase recovery and return to work after an occupational accident or injury, a worker's compensation claim provides individualised management plan involving multiple kinds of treatment. These plans can consist of the prescription of opioids to reduce inflammation, provide pain relief and increase functionality within a short period of time to aid return to work. Recently, there have been growing concerns about the misuse of opioids in managing pain symptoms by both the insurance industry and the general community. Studies from North America have indicated the prescription and management of opioid consumption among workers compensation claimants can cause more harm to functionality and reduce recovery to return to work, often leading to misuse, dependency or overdosing (Dembe, Wickizer, Sieck, Partridge & Balchick (2012)].
Objectives: The aims of this abstract are to provide a comprehensive literature review of the studies that have examined: 1) the prevalence of opioid use among worker compensations claimants and, 2) identify predictors of long-term opioid use among the workers compensation claimants.
Methods: A search strategy, with terms associated with "worker compensation", "opioids" "prevalence" and/or "risk factors" were used to search through relevant databases such as CINAHL, Cochrane, Embase, MEDLINE, PsycINFO, Scopus and Web of Science from database inception to January 2020. Duplicates were excluded. Two researchers retrieved, screened for eligibility and reviewed the results accordingly using a staged approach. Systematic review registration number PROSPERO registry number: CRD42013004137.
Results: The search yielded 2857 records. After the initial screening, 125 full-text articles were assessed by two independent reviewers. The inclusion criteria were met by nine studies1-9. All studies conducted retrospective cohort studies using workers compensation claimant's data, ranging from 54,931, to 100,357 reports, either over a short 12-month period to over 11 years, with no reporting of response rate or recruitment rates. All studies examined the association of being exposure to opioids from the date of the workers injury(7), ranging from 30 to 730 days or from 0 days to 4 or more years1 4-9. Carnide et al (2018)2 was the only study to investigate opioid exposure before and after injury as a predictor of future long term use. Among those who examined work-opioid related factors (4) found workers compensation reports with work disability for more than 14 days where more likely to become a long term opioid uses (OR: 2.17 [95% CI:1.52–3.10])1. Kraut et al7 on the other hand, found being a worker's compensation claimant increased the risk of being prescribed ≥ 120 morphine equivalents (ME)

per day (ME/D) (OR: 2.06 [95% CI: 1.58 - 2.69]), than those who were not in workers compensation program. Another study found, initial days of supply of opioids from 5 to 20 or more days was strongly associated with long term use of opioids (OR: 28.94 [95%CI, 23.44-35.72])5. While a study by Heins et al (2015)6 examined receiving opioids within the first month, people with back injuries were less likely to become a long-term opioid user (OR: 0.67 [95% CI: 0.59 – 0.76]), while those with shoulder injury were at risk (OR: 1.29 [95% CI: 1.06 – 1.58]).

Conclusion: There are a number of reliable prevalence studies among workers compensation settings indicating opioid use is below 20 percent however, there remains inconsistencies when examining predictors of long term or persistent opioid use. After reviewing the literature, a validity of studies will be conducted and graded by two authors independently using a standardised checklist to complete a systematic review for publication which will assist with managing opioid use among work compensation claimants and managers.

Disclosure of Interests: None declared

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SAT0575 POSITIVE QUANTIFERON-TB GOLD TEST AND SEROCONVERSION OF QUNATIFERON-TB GOLD TEST IS ASSOCIATED WITH INCREASED RISK OF THE DEVELOPMENT OF ACTIVE TUBERCULOSIS IN PATIENTS WITH ANKYLOSING SPONDYLITIS: RESULTS FROM A REAL-WORLD DATA OVER 20 YEARS

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Background: With the promising efficacy and the prevalent use of anti-tumor necrosis factor-α (TNF) agents in managing AS, the risk for reactivation of latent tuberculosis infection (LTBI) still is a concern. Although guidelines include the screening and treatment of LTBI prior to the initiation of anti-TNF agent by QuantiFERON-TB Gold (QFT-G) or tuberculin test, there is a lack of evidence whether treatment of LTBI before initiation of anti-TNF agent may reduce the risk of reactivation to the same as LTBI patient without anti-TNF agent or anti-TNF agent users without LTBI. Furthermore, evidence on the need for follow-up testing and the association between seroconversion and the development of active tuberculosis is also limited.

Objectives: This study aims to investigate the real-world impact of QFT-G test on the development of active tuberculosis in patients with AS.

Methods: This retrospective study investigated 2,930 patients who had a diagnosis of AS and conducted QFT-G testing during the period of March 1998 to June 2019. 191 patients with history of treatment for LTBI or acute tuberculosis prior to the first QFT-G test and 157 patients whose hospital visits or prescription was less than 3 were excluded. Observational period was defined from the firs QFT-G test to the last hospital visit of development of active tuberculosis. The screening for development of active tuberculosis was conducted by reviewing the diagnosis, prescription of anti-tuberculosis medication, chest images and electronic medical record. Treatment of LTBI was defined when a patient was prescribed isoniazid for at least 220 for 12 months, rifampin for at least 90 days for 6 months, or concurrently prescribed isoniazid and rifampin for at least 70 days for 4 months. Wilcoxon rank-sum test, chi-square test and cox-proportional hazard analysis were performed.

Results: A total of 2687 patients (median age 32.7 years, 78.4% male, anti-TNF agent user 16.7%) were included. Baseline QFT-G was positive in 426 (20.3%) patients, and 15 active tuberculosis was observed [Incidence rate 1.5/1000 person years (PY)]. Compared with baseline QFT-G (-) patients, baseline QFT-G (+) patients were older (41.2 years vs. 31.3 years, p<0.001) and they were accompanied with more active tuberculosis (4.4/1000PY vs. 1.0/1000PY) despite the less usage of anti-TNF agents (38.5% vs 45.8%, p=0.006). The observational period, sex, and medication utilization pattern except anti-TNF agent were similar between two groups. Multivariable analysis showed that QFT-G (+) test increases the risk of active tuberculosis more than 10 times [adjusted hazard ration 17.0, 95% confidence interval (CI) 5.1-56.8, p<0.001] after adjusting age, sex and the usage of anti-TNF agents.

Then we conducted subgroup analysis on 965 patients with baseline QFT-G (-) and follow-up QFT-G tests. Seroconversion was documented in 65 patients (6.7%). Active tuberculosis was observed in 4 patients, and seroconversion was occurred before the development of active tuberculosis in all patients. The incidence of active tuberculosis in seroconversion patients were 10.5/1000PY.

Conclusion: QFT-G (+) and QFT-G seroconversion is associated with increased risk of the development of active tuberculosis in patients with AS.

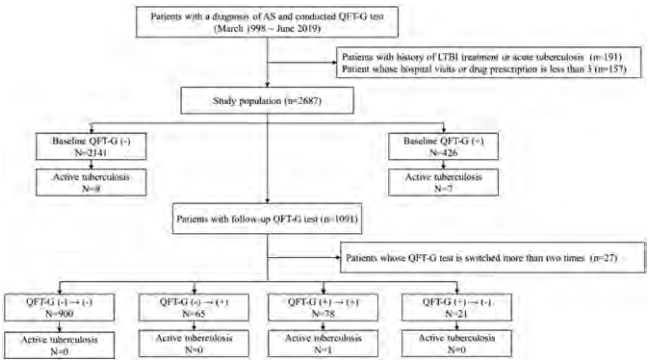


Figure 1. Overview of patient flow

Disclosure of Interests: None declared

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SAT0576 THE PREVALENCE OF RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW OF POPULATION-BASED STUDIES.

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Background: Rheumatoid arthritis (RA) is a heterogeneous disease with unknown aetiology (1). The reported worldwide RA prevalence varies widely (2, 3), and it is unclear whether this is due to inconsistencies in defining populations or methodologies used to identify RA patients (3, 4). Accurate RA prevalence data are required to plan preventative, diagnostic, and management strategies to address raising health care service demands and costs associated with improved lifespan and level of disability (5, 6).

Objectives: To estimate the prevalence of RA from international population-based studies and investigate the influence of prevalence definition, data sources, classification criteria and geographical area on RA prevalence.

Methods: A systematic review of existing literature was performed using the Joanna Briggs Institute approach for the systematic review and Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. A search of ProQuest, MEDLINE, Web of Science, and EMBASE was undertaken to include population-based studies investigating RA prevalence between 1980 and 2019.

Results: Sixty published population-based studies met the inclusion criteria over the study period. The mean point-prevalence of RA was 0.56% (range 0.00% to 2.70%) between 1986 and 2014. The period-prevalence was 0.51% (range 0.05% to 1.9%) between 1955 and 2015. RA point- and period-prevalence was higher in urban settings than rural settings, (0.69% vs 0.48%) and (0.54% vs 0.25%), respectively. The mean point- and period-prevalence were 0.56% (SD=0.52) and 0.57% (SD=0.41) and were lower in sampling population studies than in larger population databases studies (0.60% (SD=0.27) and 0.44% (SD= 0.26)). The highest period-prevalence of RA was observed in linked databases (0.80%, SD=0.1) where RA diagnosis was validated by rheumatologists.

Conclusion: The average point- and period-prevalence of RA were 51/10,000 and 56/10,000 respectively. The RA prevalence was higher in urban areas than rural areas, suggesting an impact of environmental differences. Population database studies were more consistent than sampling studies, and linked databases appeared to provide the best estimate of RA period-prevalence when rheumatologists clinically verified RA.

Table 1. The top five countries for the highest and lowest prevalence of RA in recent global estimate between 1980 and 2019.

Global prevalence of RA	Top five countries	Prevalence (%)
Highest	1-Cuba	2.70
	2-Finland	1.90
	3-Lesotho	1.80
	4-USA	1.07
	5-Lebanon	1.00
Lowest	1-Nigeria	0.00
	2-Taiwan	0.05
	Taiwan	0.10
	Taiwan	0.12
	3-Thailand	0.12
	4-India	0.15
	5-Philippines	0.17

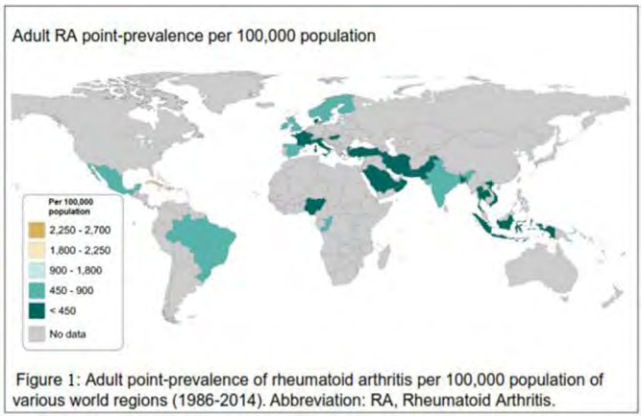


Figure 1: Adult point-prevalence of rheumatoid arthritis per 100,000 population of various world regions (1986-2014). Abbreviation: RA, Rheumatoid Arthritis.

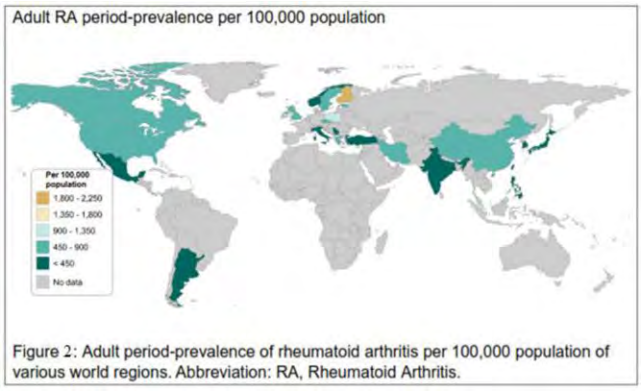


Figure 2: Adult period-prevalence of rheumatoid arthritis per 100,000 population of various world regions. Abbreviation: RA, Rheumatoid Arthritis.

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SAT0577 USE OF CONTRACEPTIVE METHODS IN MEXICAN WOMEN WITH RHEUMATIC DISEASES

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Background: The importance of safe and effective contraception for women with rheumatic diseases has been increasing.[1] Several studies have demostrated that carefully planned pregnancies are related with better outcomes making the use of contraceptive methods (CM) more significant.

Objectives: To describe the use of methods of contraception among Rheumatoid Arthritis (RA) and Systemic Lupus Erythematosus (SLE).

Methods: A Cross-sectional study where women aged 18-45 followed in our CEER outpatient clinic, at Monterrey, Mexico, were questioned about the use of CM. Sociodemographic data was collected from the medical record.

CM were classified as Ineffective (10-25% pregnant each year), effective (6-9% pregnant each year) and highly effective (<1% pregnant each year). Methotrexate, Mycophenolate, Cyclophosphamide, Thalidomide and Leflunomide were considered as teratogenic drugs.

The statistical analysis was performed using SPSS 24.0. A $p<0.05$ was taken to indicate statistical significance.

Results: A total of 91 patients were included, 35 (38.5%) SLE patients with a median age of 30 years (22-39) and 56 (61.5%) RA patients with a median age of 34.5 years (27.25-40). From the total population, 58 (63.7%) reported the use of teratogenic drugs, with a higher use in RA patients (p <.001). Socio-demographic characteristics are listed in **Table 1**.

Table 1. Socio-demographic characteristics.

	RA (n=56)	SLE (n=35)	p
Age, *years, median (IQR)*	34.5 (27.25-40)	30 (22-39)	
Disease duration, *years, median (IQR)*	3.5 (1.25-7.75)	4 (1-7)	
Onset of Sexual activity,n (%)	46 (82.1)	24 (68.6)	.135
Onset of Sexual activity age, median (IQR)	18 (17-20)	14 (17-20)	
Sexually Active, *n (%)**	34 (60.7)	18 (51.4)	.384
Use of teratogenic drugs, *n (%)*	44 (78.6%)	14 (40%)	<.001

RA, Rheumatoid Arthritis; SLE, Systemic Lupus Erythematosus. *Sexual activity in the last month.

Among the patients that had started sexual activity (SLE=24, RA=46), the most common CM was tubal ligation 26 (28.6%) **Graphic 1**. In this group, 49 (70%) patients received contraceptive counseling, however, 21 (42%) patients were using innefective CM.**Table 2**.

According to effectiveness, highly efective were the most frequent method used in patients that had started sexual activity (n=39, 55.7%) **Graphic 2**.

Conclusion: Despite highly effective CM were more frequent in patients that had started sexual activity, 42% of patients that received contraceptive counseling reported the use of inneffective methods. It is neccesary to promote the counseling and use of contraception and provide a multidisciplinary support among rheumatoid patients.

Table 2. Methods according to effectiveness in patients that received contraception counseling.

		GRADE OF EFFECTIVENESS		
n (%)	**Patients That receive Contraceptive counseling**	**Inneffective**	**Effective**	**Higly effective**
RA= 46	30 (65.21)	12 (40)	1(3.3)	17 (56.6)
SLE= 24	19 (79.16)	9 (47.3)	1 (5.2)	9 (47.36)
Total = 70 *	49 (70)	21 (42)	2 (4.08)	26 (53.06)

RA= Rheumatoid Arthritis; SLE= Systemic Lupus Erythematosus. * Total of patients that have started sexual activity.

References:

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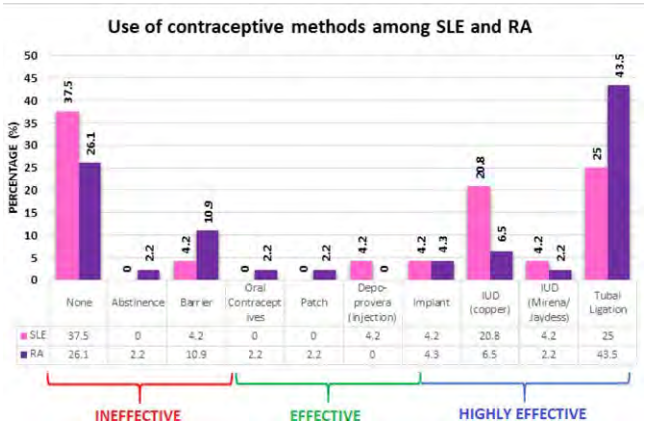


Figure 1. Graphic 1. This graphic shows the frequence in percentage % of contraceptive methods used by Rheumatoid Arthritis (RA) n=56 and Systemic Lupus Erythematosus (SLE) n=35 patients, which are categorized by the grade of effectiveness. Only were included patients that had started sexual activity.

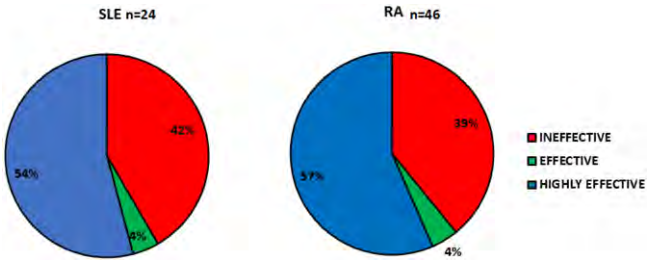


Figure 2. Graphic 2. This graphic shows the percentage of use according to the effectiveness of contracetive methods. RA, Rheumatoid Arthritis; SLE, Systemic Lupus Erythematosus. Only were included patients that had started sexual activity.

Disclosure of Interests: None declared
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SAT0578 RHEUMAL REGISTRY PROVIDES FIRST INSIGHTS INTO MUTUAL INTERDEPENDENCIES BETWEEN RHEUMATIC AND MUSCULOSKELETAL DISEASES AND MALIGNANCIES

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Background: Knowledge about interdependencies between rheumatic and musculoskeletal diseases (RMDs) and malignancies is limited on the clinical and molecular level. Particularly, valid prospective data on the timely association of malignancies in patients with RMDs and treatment of the latter are sparse.
Objectives: Due to the heterogeneous patient population, a registry-based study has been conducted in order to provide insights into mutual interdependencies and novel evidence for suitable clinical management of patients with concomitant RMD and malignancies.
Methods: The RheuMal registry is a long-term, open-end observational study designed to address the specific situation of patients suffering from concomitant RMD and concomitant malignancy and/or premalignant conditions. The RheuMal registry is one of the three subregistries of the MalheuR project, a registry-based study initiated in July 2018 at the at the university hospital Heidelberg, Germany.
Results: Data from the RheuMal registry (n=404) show an earlier onset of gender-specific cancers and malignant melanoma in RMD patients compared to data from the German Cancer Registry Data of the Robert-Koch-Institute: compared to the reference population, in RMD patients breast cancer (n=32) occurred 5.3 years and prostate cancer (n=16) 3.3 years earlier. Onset of malignant melanoma was 2.4 years earlier in females (n=9) and 1.1 years in males (n=7) with concomitant RMD. The mean latency between the initial diagnosis of the RMD and the later occurring malignant condition was 10.2 years. The diagnosis of the malignancy frequently led to a change or interruption of disease-modifying antirheumatic therapy in RMDs.
Conclusion: The RheuMal registry offers first insights into interdependencies between RMDs and malignancies based on demographic data, disease characteristics, clinical management and outcome as well as correlation of specific diagnoses and therapies. The earlier onset of gender-specific cancers and malignant melanoma suggests differences in the epidemiology and course of the malignant disease in RMD patients compared to a healthy reference population, suggesting interdependency between the two disease entities. Future research will focus on further understanding of this interdependency und the underlying molecular mechanisms.
Disclosure of Interests: Karolina Benesova Grant/research support from: Study grants for SCREENED study by Abbvie, Novartis and Rheumaliga Baden-Württemberg, Consultant of: One-time participation in Novartis advisory board., Leonore Diekmann: None declared, Maria Czaja: None declared, Karin Jordan Consultant of: Consultancy and/or speaker fees: MSD, Merck, Amgen, Hexal, Riemser, Helsinn, Tesaro, Kreussler, Voluntis, Pfizer, Pomme-med., Jan Leipe Grant/research support from: Consultancy and speaker fees: Abbvie, AstraZeneca, BMS, Celgene, Hospira, Janssen-Cilag, LEO Pharma, Lilly, MSD, Novartis, Pfizer, Roche, Sanofi, UCB. Scientific support: Novartis, Pfizer., Consultant of: Consultancy and speaker fees: Abbvie, AstraZeneca, BMS, Celgene, Hospira, Janssen-Cilag, LEO Pharma, Lilly, MSD, Novartis, Pfizer, Roche, Sanofi, UCB. Scientific support: Novartis, Pfizer., Speakers bureau: Abbvie, AstraZeneca, BMS, Celgene, Hospira, Janssen-Cilag, LEO Pharma, Lilly, MSD, Novartis, Pfizer, Roche, Sanofi, UCB, Hanns-Martin Lorenz Grant/research support from: Consultancy and/or speaker fees and/or travel reimbursements: Abbvie, MSD, BMS, Pfizer, Celgene, Medac, GSK, Roche, Chugai, Novartis, UCB, Janssen-Cilag, Astra-Zeneca, Lilly. Scientific support and/or educational seminars and/or clinical studies: Abbvie, MSD, BMS, Pfizer, Celgene, Medac, GSK, Roche, Chugai, Novartis, UCB, Janssen-Cilag, Astra-Zeneca, Lilly, Baxter, SOBI, Biogen, Actelion, Bayer Vital, Shire, Octapharm, Sanofi, Hexal, Mundipharm, Thermo Fisher., Consultant of: see above
DOI: 10.1136/annrheumdis-2020-eular.3815

SAT0579 SYSTEMATIC GERIATRIC ASSESSMENT IN OLDER PATIENTS WITH RHEUMATIC DISEASES - THE RHEUMAGIC PILOT STUDY

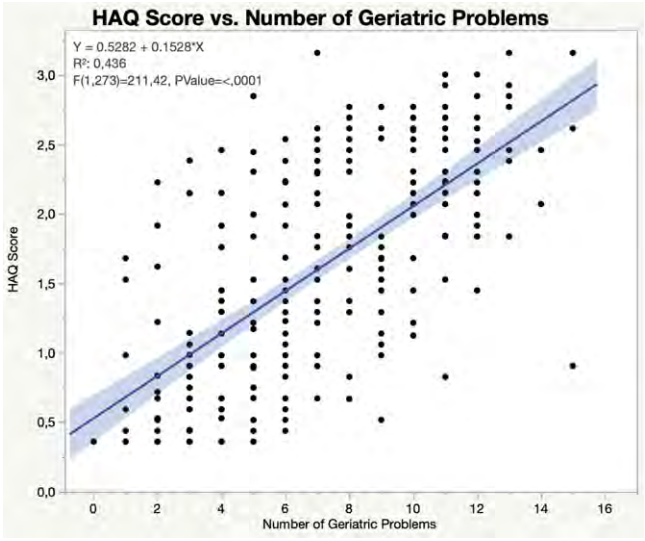
A. Berrisch[1], I. Andreica[1], S. Tsiami[1], D. Kiefer[1], U. Kiltz[1], X. Baraliakos[1], J. Braun[1], B. Buehring[1]. [1]*Ruhr-University Bochum, Rheumazentrum Ruhrgebiet, Herne, Germany*

Background: Current demographic data predict that the number of older adults with rheumatic diseases will considerably increase in the coming years. Geriatric patients differ from younger adults in many ways including their clinical presentation, co-morbidities and response to medication. The management of such patients is often challenging due to the presence of multi-morbidity, polypharmacy and geriatric syndromes (i.e. conditions in which symptoms result from impairments in multiple systems rather than a discrete disease). To systematically assess geriatric patients, specific tools have been developed; however, they are not routinely utilized by rheumatologists. Using these tools could improve patient management and satisfaction in rheumatologic care.
Objectives: To examine the prevalence of 17 common geriatric health problems using validated geriatric assessment tools in older patients with rheumatic and musculoskeletal diseases.
Methods: Adults 65 years and older who presented to a tertiary rheumatologic hospital were included after informed consent. All patients recruited were assessed using the **MA**ngable **G**eriat**rIC** Assessment (MAGIC) which addresses 14 common geriatric health problems. In addition, polypharmacy (≥ 5 medication), muscle function using the Short Physical Performance Battery and frailty applying the Fried definition were assessed. Disability was quantified with the "Funktionsfragebogen Hannover" (FFbH), a validated tool for patients with rheumatologic diseases that can be easily converted to Health Assessment Questionnaire (HAQ) scores. Primary outcome was the frequency of the selected 17 geriatric health problems; the correlation of the total number of problems with HAQ scores was a secondary outcome.
Results: Of the 300 individuals included 67% were female with a mean age of 73±6.6 years; 85% (> 50% with rheumatoid arthritis) had a rheumatologic diagnosis. The remaining participants had either a chronic pain syndrome or degenerative joint/spine disease. On average participants had 7 out of 17 assessed geriatric problems. Females had more such problems than males (8 vs. 6, p<0.0001). Chronic pain and polypharmacy were most common but several others were also seen in more than 50% of patients (see Table). The mean HAQ Score was 1.67±0.79. There was a positive correlation (see Graph) between the number of problems and the HAQ Score (R^2= 0.44, p<0.0001).
Conclusion: A systematic geriatric assessment can be successfully used to discover and quantify geriatric health problems in older patients with rheumatic and musculoskeletal diseases. These problems appear to be very common and importantly, patients with more problems had poorer functional status. Frailty, depression, incomplete vaccination status, cognitive impairment or polypharmacy are all known to negatively impact patient care. Recognizing and addressing geriatric problems has the potential to lead to health care improvements including adherence and medication side effects and might increase patient satisfaction and functional status independent of disease activity.
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Geriatric Problem	% present
Problems with Daily Activities	67
Problems with Vision	28
Problems with Hearing	38
Problems with Falls	11
Problems with Urinary Incontinence	38
Problems with Depression	57

Geriatric Problem	% present
Lack of Social Support	10
Incomplete Vaccinations	53
Problems with Cognition	31
Problems with Chronic Pain	90
Problems with Dizziness	44
Problems with Mobility	41
Problems with Unintentional Weight Loss	30
Inappropriate Medications present	17
Polypharmacy present	81
Frailty present	46
Short Physical Performance Battery low	57



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SAT0580 ANALYSIS OF ANAS/DFS70 PATTERN IN A LARGE COHORT OF AUTOIMMUNE/AUTOINFLAMMATORY DISEASES COMPARED WITH FIRST DEGREE RELATIVES AND HEALTHY CONTROLS EVALUATED IN A SINGLE HOSPITAL FROM COLOMBIA.

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Background: Autoimmune diseases have a broad phenotypic spectrum, with great variability in clinical manifestations. Anti-DFS70/LEDGFp75 (ANAS/DFS70) antibodies have attracted interest as a positive result in patients without clinical evidence of autoimmune systemic rheumatic disease (SARD). It has been proven in non-rheumatic inflammatory diseases and in "apparently healthy" individuals.

Objectives: To assess ANAS/DFS70 performance in a large population with autoimmune/autoinflammatory diseases compared with first degree relatives and healthy controls.

Methods: A cross-sectional study was conducted. We analysed 531 individuals between 18-65 years old, 101 rheumatoid arthritis (RA) patients (ACR/EULAR 2010 classification criteria), 137 relatives from RA, 60 psoriasis (Ps) patients (Colombian classification consensus), 47 Undifferentiated connective tissue diseases(UCTD) patients and 186 healthy controls matched by age and sex. The healthy control group were individuals who lived and work similarly like those patients those criteria of exclusion criteria were to present autoimmune or auto-inflammatory disease, infectious, neoplasms, diabetes, antibiotic treatment, pregnancy or lactation, consanguinity with autoimmune entities. Ethical Committee approved.

The determination of ANAS-HEp2 antibodies (ANA-Hep-2 AESKU.Dignostic®, Autoantiboy test SYSTEM IMCO DIAGNOSTICS REF 1103® and ANA-Hep-2 AESKU.Dignostic®) was carried out. The positive results (standard AC-2) are used as a confirmatory test the determination of ANAS / DFS70: AUTOANTIBOY TEST SYSTEM IMMCO DIAGNOSTICS (Knocked out, for the psip gene) REF 1108® and CytoBead ANA Generic Assays ref 8065 ® by indirect immunofluorescence-IFI technique. In addition, serum levels of C-reactive protein (PCR), erythrocyte sedimentation rate (ESR), IgG/IgA antibodies against citrullinated peptide (ACPA), and rheumatoid factor (RF). Absolute and relative frequencies were established.

Results: 531 participants were included: RA 19%, 25,8% RA relatives, Ps 11,3%, UCTD 8,9%, and 35% healthy controls. RA mean age was 41,8±12,2 years, female 82,2%, with ANA test(+) result 42%. In Ps mean age 49,1±15,7 years, female 53,3%, ANA test(+) 41,7%. UCTD mean age 41,3±15,2 years, female 85,1%, and ANA test(+) 78,7%. Relatives of RA mean age 38,7±12,2 years, female 73%, ANA test(+) 26,3%. And healthy controls mean age 41,3±12,2 years, female 74,7%, and ANA test(+) 26,9%.

ANA/DFS70 was positive in a 6,4% in UCTD, 3,2% in healthy controls, 1,7% in Ps, 1,5% in Relatives of RA, no RA had positive results. These 12 participants were negative for acute phase reactants (ESR[-] 83,3% and CRP[-] 66,6%), as well as they were all negative for RF and two were positive for APCA from UCTD.

Conclusion: ANAS/DFS70 autoantibodies were present in very low frequency in patients with SARD. Thus, patients with a positive result tend to have a mild or non-progressing phenotype of autoimmune/inflammatory diseases, as UTCD. This is the first time ANA/DFS70 are tested in a large population cohort in Latin American countries which coincide with previous results in RA and RA relatives.

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Disclosure of Interests: Consuelo Romero-Sánchez: None declared, Omar-Javier Calixto Employee of: Worked in Janssen Cilag as medical manager from 2016 to 2018, V Romero-A: None declared, A Vargas: None declared, Luis Castro: None declared, Julio Amador: None declared, Pedro Lopez-Mojica: None declared, Daniela Marin: None declared, Diana Acero-M: None declared, M Acevedo: None declared, Diana Rincón-Riaño: None declared, Juan Manuel Bello-Gualtero: None declared

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SAT0581 SERIOUS INFECTION RATES WITH BIOLOGICAL DISEASE MODIFYING ANTI-RHEUMATIC AGENTS (BDMARDS) AND PREDISPOSING FACTORS: A 5-YEAR RETROSPECTIVE REVIEW

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Background: Biological and targeted synthetic disease modifying anti-rheumatic agents (bDMARDs) increase the risk of serious infections (SIs), however there is limited 'real-world' evidence comparing the relative risk of SI for individual bDMARDs. (1,2)

Objectives: This study examines the rates of SIs in a non-select Australian Northern Queensland (NQ) cohort of patients with various rheumatic diseases receiving treatment with a bDMARD, to define predisposing factors and directly compare the bDMARDs.

Methods: A retrospective review was performed for all patients who received a bDMARD through the Townsville Hospital Rheumatology Department over the

5-year period between June 2013 and May 2018. Episodes of a SI were defined as infection requiring admission or use of intravenous antibiotics. For each bDMARD the rate of SI per 100 patient years (PYs) was calculated and patient demographics and comorbidities were analysed. Between group differences were assessed using independent samples t-tests or ANOVA. Where assumptions were violated, Mann-Whitney U tests or Kruskal-Wallis tests were used. For categorical variables, chi-square tests were used, except when assumptions were violated when Fisher's Exact tests were used.

Results: 296 patients received bDMARDs with an overall SI rate of 11.7/100PYs. There was no significant difference in presence of SI by disease type with 24% of patients with rheumatoid arthritis versus 19% with psoriatic arthritis, 14% with ankylosing spondylitis and 29% with "other" (X^2=3.11; df=3; p=0.37). Respiratory tract infections were the most common infection (46%) followed by skin and soft tissue infections (23%). The highest incidence rate of SI occurred with rituximab (29.72 SI/100PYs) followed by certolizumab (22.50 SI/100PYs) and tocilizumab (15.00 SI/100PYs). Duration of time on a bDMARD, disease duration and use of methotrexate or leflunomide were not shown to significantly increase the risk of SI for the entire cohort. The characteristics which were shown to significantly increase SI rates were; prednisone use, increasing age, chronic pulmonary comorbidity and specifically in those with rheumatoid arthritis male gender and total duration of bDMARD use.

Conclusion: In this real-world NQ cohort of patients treated with a bDMARD for a rheumatic disease, we have identified a number of factors potentially contributing to the risk of the development of SIs. This study provides valuable data on SI rates in an Australian 'real-world' cohort that may assist clinicians' choice of bDMARD in patients with a high baseline risk of infection and highlights the importance of minimising prednisone use in patients on bDMARDs.

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SAT0582 RISK OF INTERSTITIAL LUNG DISEASE IN SYSTEMIC AUTOIMMUNE RHEUMATIC DISEASES: A NATIONWIDE, POPULATION-BASED COHORT STUDY

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Background: To date, very few studies had investigated the epidemiology of interstitial lung disease (ILD) among patients with systemic autoimmune rheumatic disease (SARD).

Objectives: To study the risk of interstitial lung disease (ILD) among patients with various systemic autoimmune rheumatic diseases (SARDs) including rheumatoid arthritis (RA), dermatomyositis (DMtis), polymyositis (PM), systemic sclerosis (SSc), systemic lupus erythematosus (SLE), and primary Sjögren's syndrome (pSS).

Methods: Using 1997–2013 claims data from the Taiwanese National Health Insurance Research Database, we identified 63,277 newly diagnosed patients with various SARDs after excluding those with overlapping SARD diagnoses from 2001-2013 and randomly selected 253,108 non-SARD subjects matching (1:4) SARD patients for SARD diagnosis, age, sex and the year of the index date. We calculated the incidence rates (IRs) of ILD (ICD-9 code 515) in various SARD groups and the corresponding non-SARD comparison groups and estimated the IR ratios (IRRs) with 95% confidence intervals (CI) of ILD development. Using multivariable cox regression analyses, we estimated hazard ratios (HRs) with 95% CIs of ILD in various SARD groups compared with their comparison groups after adjusting for age, sex, Charlson comorbidity index, amiodarone use and methotrexate use. Sensitivity analyses were conducted by using a narrow definition of ILD.

Results: As shown in Table 1, the IRs of ILD were greatest in SSc patients (2,523 per 10^5 years), followed by patients with DMtis (2,463 per 10^5 years), PM (1,956 per 10^5 years), SS (601 per 10^5 years), RA (279 per 10^5 years), and SLE (276 per 10^5 years). Multivariable analyses showed that the risks of ILD were significantly increased in patients with SSc (HR, 66.01; 95% CI, 32.73—133.13), DMtis (128.74, 95% CI, 40.19—412.47), PM (HR, 30.39; 95% CI, 11.24—82.15), pSS (HR, 8.76; 95% CI, 7.03—10.90), RA (HR, 4.22; 95% CI, 3.51—5.08), and SLE (HR, 13.98; 95% CI, 9.25—21.14).

Table 1. Comparison of incidence rates of interstitial lung disease among patients with SARD

SARD	Total	Event (%)	Person-years	Incidence rate (/10^5 years)	IRR (95% CI)
SARD					
Control	253,108	781 (0.3)	1,601,941	49	Reference
SARD	63,277	1,660 (2.6)	380,783	436	8.9 (8.2–9.7)
DMtis					
Control	3,716	10 (0.3)	25,508	39	Reference
DMtis	929	116 (12.5)	4,710	2,463	62.8 (32.9–119.9)
PM					
Control	2,828	9 (0.3)	18,647	48	Reference
PM	707	72 (10.2)	3,681	1,956	40.5 (20.3-81.0)
SSc					
Control	6,224	16 (0.3)	40,789	39	Reference
SSc	1,556	205 (12.2)	8,124	2,523	64.3 (38.7–107.0)
SLE					
Control	52,236	81 (0.2)	366,437	22	Reference
SLE	13,059	230 (1.8)	83,346	276	12.5 (9.7–16.1)
pSS					
Control	60,684	191 (0.3)	326,589	58	Reference
pSS	15,171	471 (3,1)	78,406	601	10.3 (8.7–12.2)
RA					
Control	127,420	474 (0.4)	823,970	58	Reference
RA	31,855	566 (1.8)	202,516	279	4.9 (4.3–5.5)

Conclusion: This nationwide, population-based, matched cohort study demonstrated that the risks of ILD were significantly increased in patients with SARDs.

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Disclosure of Interests: None declared

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SAT0583 DIPEPTIDYL PEPTIDASE-4 AND RISK OF PSORIASIS IN PATIENTS WITH TYPE 2 DIABETES

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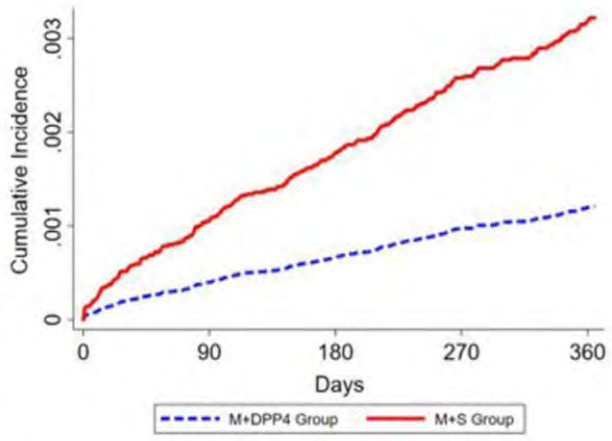
Background: The risk of psoriasis in diabetic patients has rarely been explored.

Objectives: This study aimed to investigate the association between dipeptidyl peptidase-4 (DPP4) inhibitors and the risk of psoriasis in type 2 diabetes mellitus (T2DM) patients.

Methods: We conducted a population-based propensity score-matched cohort study on the basis of Taiwan's National Health Insurance Research Database that included initiators of combination therapy with DPP4i (DPP4i plus metformin) and sulfonylurea (sulfonylurea plus metformin). Psoriasis (PSO) was identified with ≥2 diagnoses. Diabetes complications severity index (DCSI) was calculated. A total of 22721 DPP4 initiator and 227684 sulfonylurea initiator were identified. A 1:10 matched-pair cohort based on propensity score(PS) was created. PS-stratified Cox proportional hazards models compared the risk of PSO in DPP4i versus sulfonylurea initiator within 2 years, controlling for potential confounders.

Results: After propensity score matching, 9962 patients with T2DM starting DPP4i combination therapy and 39848 starting sulfonylurea combination therapy were selected. The incidence rate of PSO was lower in DPP4i group (188/100000 person- years) than in sulfonylurea group (467/100000 person-years). Risks of

incident psoriasis were significantly lower in the DPP4i group versus sulfonylurea with the PS-stratified HR of 0.422 (95% CI 0.273 to 0.716).
Conclusion: DPP4i plus metformin was associated with a reduced risk of psoriasis than sulfonylurea plus metformin. These findings merit further investigation.



Cumulative Incidence Curve of M+DPP4 Group and M+S Group

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SAT0584 SPECIFIC ACPA REACTIVITIES AND INFLAMMATORY BIOMARKERS ALONG WITH ULTRASOUND TENOSYNOVITIS ARE ASSOCIATED WITH ARTHRITIS ONSET IN A POPULATION AT RISK FOR RHEUMATOID ARTHRITIS

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Background: Anti-citrullinated protein antibodies (ACPA) are characteristic markers for rheumatoid arthritis (RA), developing years before disease onset. Early clinical and biological biomarkers could provide useful information on the onset of RA in predisposed individuals.
Objectives: The aim of the study was to investigate whether ACPA along with inflammatory markers and musculoskeletal ultrasound changes could predict arthritis development in individuals at risk for RA.
Methods: ACPA-positive individuals with musculoskeletal complaints were referred from primary care to a rheumatology clinic, recruited in the Risk-RA research program and followed-up for up to 3 years, between April 2014 and October 2019. All individuals lacked arthritis both at clinical examination by a trained rheumatologist and ultrasound assessment of hands and feet and any other symptomatic joints (according to EULAR-OMERACT definition). Blood samples were collected at inclusion and were analyzed for 15 ACPA fine specificities (by custom made peptide array), 92 inflammation-associated protein biomarkers (by multiplex immunoassay with Olink extension technology) and HLA-SE (DR low resolution kit). Statistical analysis used univariate and multivariate models with backwards selection and cox regression.
Results: 268 individuals with a median age of 48 (36-58) were recruited, out of which 212 (79%) were females. 75 (28%) developed arthritis within 11 months of follow-up while the median follow-up for those not developing arthritis was 21 months (14-28). Increased ACPA levels, shorter symptom duration and RF positivity were the main differences between individuals developing arthritis and those who did not. In univariate models, the presence of HLA-SE, specific ACPA reactivities, certain inflammatory markers and ultrasound-detected tenosynovitis were associated with arthritis development. In multivariate analysis the presence of anti-cit-fillagrin (HR 2.1 (95% CI 1.2-3.7, p 0.01), IL6 levels (HR 1.4 (95% CI 1.2-1.7, p 0.0001) and tenosynovitis (HR 2.9 (95% CI 1.7-5.0, p 0.0001) remained significant predictors for arthritis onset.
Conclusion: Certain ACPA reactivities together with inflammatory markers and ultrasound-detected tenosynovitis predict arthritis development in predisposed individuals for developing RA.

Disclosure of Interests: None declared
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SAT0585 GEO-EPIDEMIOLOGY OF AUTOANTIBODIES IN RA: DIFFERENT PREVALENCES IN FOUR ETHNICALLY DIVERSE RA POPULATIONS

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Background: Rheumatoid arthritis (RA) has been described in virtually every ethnic population. Most RA patients harbor anti-modified protein antibodies (AMPAs), including anti-citrullinated protein (ACPA), anti-carbamylated protein (anti-CarP), anti-malondialdehyde acetaldehyde (anti-MAA), and anti-acetylated protein antibodies (AAPA). However, it is unclear whether differences exist in the AMPA response between different ethnic groups. Such differences could provide new clues to genetic and environmental factors contributing to autoantibody development.
Objectives: To investigate the prevalence of different AMPA in four ethnically diverse RA populations, and their association with smoking.
Methods: Enzyme-linked immunosorbent assays were used to measure anti-CarP IgG, anti-MAA IgG (both in-house), and anti-acetylated vimentin IgG (Orgentec) in ACPA-positive sera of Dutch (NL, n=103), Japanese (JP, n=174), Canadian First Nations People (FN, n=100), and black South Africans (SA, n=67) fulfilling the 1987 ACR classification criteria for RA. Ethnicity-matched local healthy controls were used to calculate cohort-specific cut-offs. Logistic regression was used to identify whether ever-smoking was associated with AMPA seropositivity in each cohort, corrected for age, gender, and disease duration. Random-effects meta-analysis was used to pool the resulting odds ratios (OR).
Results: For all three AMPAs, median levels were higher in FN and especially SA than NL and JP patients (Figure 1). The median autoantibody levels in arbitrary units (in % of patients positive) for NL, JP, FN and SA RA patients were: anti-CarP IgG: 1157 (47%), 994 (43%), 1642 (58%) and 2336 (76%) (p<0.001); anti-MAA IgG: 131 (29%), 179 (22%), 251 (29%) and 257 (53%) (p<0.001); AAPA: 133 (20%), 136 (17%), 153 (38%) and 316 (28%) (p<0.001). Prevalence, meaning positivity, also differed significantly between cohorts for all AMPAs (p<0.001). There were also marked differences in total IgG levels in mean (SD) g/L: 13 (4) for NL, 17 (6) for JP, 18 (6) for FN, and 25 (8) for SA (p<0.001). When the autoantibody levels were normalized to total IgG, the differences in became less pronounced between cohorts (Figure 2). The median arbitrary units per g/L Total IgG for NL, JP, FN and SA RA patients were: anti-CarP IgG: 54, 25, 53, and 79; anti-MAA IgG: 6, 5, 8, and 9; and AAPA: 2, 2, 2, and 3, suggesting that autoantibody level differences may partly correspond to cohort-specific differences in total IgG, although the overall trend of higher levels in SA persisted. There was no association between smoking and anti-CarP or anti-MAA positivity, with pooled OR (95% CI) of 1.31 (0.79-2.18) and 0.85 (0.46-1.56), respectively. However, smoking was positively and consistently associated with AAPA positivity in each cohort: pooled OR (95% CI) of 2.01 (1.06-3.81).
Conclusion: In these ACPA-positive ethnically diverse RA populations, levels and prevalence of various AMPAs differ, suggesting that ethnic background and environment may influence the development of the autoantibody response in RA. Despite these differences, our results imply smoking as a consistent risk factor for AAPA across different ethnic backgrounds.

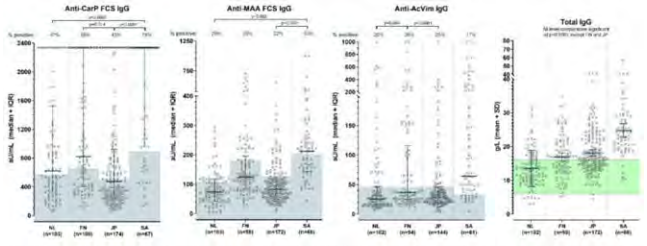


Figure 1: Levels in arbitrary units (aU/mL) for three AMPAs and grams per liter (g/L) for Total IgG in the serum of four ethnically diverse RA populations. Patients clustered at the maximum were above the highest standard of the ELISA. Blue shading indicates the patient falling below the cohort-specific positivity cut-off, green shading is the normal range for Total IgG. Lines indicate median and interquartile range. P-values correspond to Chi-square tests on proportion of patients considered positive, indicated in percentages above graphs.

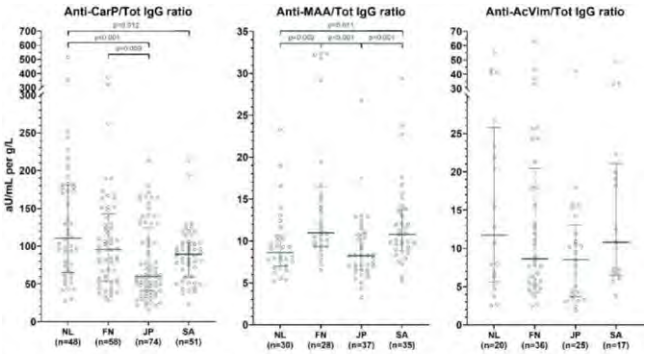


Figure 2: Ratios of levels in arbitrary units (aU/mL) for three AMPAs per grams per liter (g/L) Total IgG in the serum of four RA populations. Ratios are only shown in patients that were positive for the AMPA. Lines indicate median and interquartile range; p-values correspond to Mann-Whitney U tests. The range of aU/mL per g/L are not directly comparable between AMPAs.

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SAT0586

PREVALENCE AND RISK FACTORS FOR CARDIO-METABOLIC ABNORMALITIES IN PATIENTS WITH INFLAMMATORY ARTHRITIS ATTENDING CARDIO-RHEUMATOLOGY PRIMARY PREVENTION CLINICS

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Background: Cardio-metabolic abnormalities are common in patients with inflammatory arthritis (IA) but tend to be under-recognized and under-treated.
Objectives: We aimed to compare the prevalence and risk factors for cardio-metabolic abnormalities between patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS).
Methods: Consecutive patients enrolled in the University of Toronto Cardio-Rheumatology Network from July 2017 to August 2019 were analyzed. This is a primary prevention program that uses structured clinical, laboratory and multimodal imaging to diagnose and treat cardiovascular disease (CVD). Patients with a rheumatologist-confirmed diagnosis of RA, PsA or AS with no known CVD were evaluated. Information about IA diagnosis, medications and comorbidities was recorded. Each patient was evaluated by a cardiologist focusing on CVD risk assessment. We evaluated the prevalence of previously recorded and newly recognized cardio-metabolic risk factors including hypertension, dyslipidemia, obesity and diabetes. The prevalence of these abnormalities was compared between IA diagnoses. Regression models were used to assess the association between diagnosis and cardio-metabolic abnormalities after adjusting for demographics, smoking, BMI, measures of disease activity and medications.
Results: A total of 358 patients (201 RA, 124 PsA, 33 AS) were assessed (mean age 59±10.5 years, 68.7% female). Hypertension was reported in 33%, dyslipidemia in 26.8%, diabetes mellitus in 8.9% and overweight/obesity in 69.7% (Figure 1). Newly detected elevations in lipids were frequent for triglycerides (9.3%,), non-HDL-cholesterol (6%,) and LDL-cholesterol (2.7%). Elevated HbA1c occurred in 1.4% and newly diagnosed hypertension occurred in 9.8%. A total of 32.8% patients required a change or initiation of medications for their cardio-metabolic abnormalities (21.7% lipid-lowering therapy, 14.6% aspirin, 11.1% anti-hypertension therapy). Patients with PsA had the highest prevalence of cardio-metabolic abnormalities including dyslipidemia, obesity and hypertension. Having hypertension (prior or new diagnosis), elevated levels of triglycerides, non-HDL cholesterol, total cholesterol and BMI were associated with PsA vs. RA after adjusting for potential confounders (all p<0.05) (Figure 2). No significant association was found between cardio-metabolic abnormalities and AS vs. PsA or RA.
Conclusion: Dedicated cardio-rheumatology clinics have improved CVD screening and management in an IA population. The burden of cardio-metabolic abnormalities is elevated in PsA and suggests that tailored strategies to reduce adverse CVD events are particularly needed in this subgroup.

Figure 1 – The Prevalence of Cardiovascular Risk Factors (Previously diagnosed and Newly diagnosed)

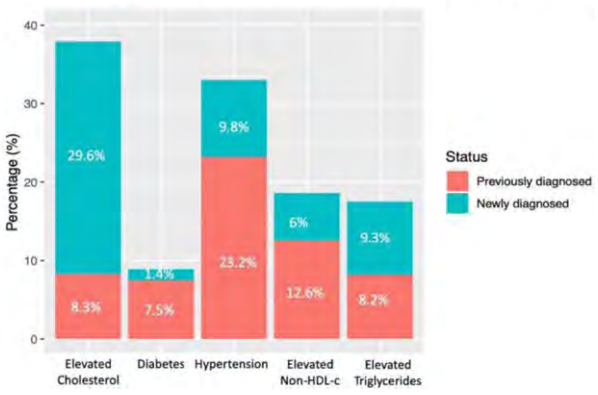
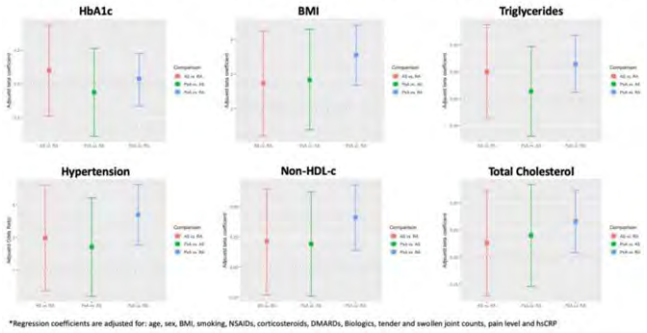


Figure 2 - The Association between Disease Category and Cardiovascular Risk Factors by Adjusted regression coefficients*



*Regression coefficients are adjusted for: age, sex, BMI, smoking, NSAIDs, corticosteroids, DMARDs, Biologics, tender and swollen joint counts, pain level and hsCRP

Disclosure of Interests: Lihi Eder Grant/research support from: Abbvie, Lily, Janssen, Amgen, Novartis, Consultant of: Janssen, Speakers bureau: Abbvie, Lily, Janssen, Amgen, Novartis, Shadi Akhtari: None declared, Paula Harvey: None declared, Kuriya Bindee Grant/research support from: Abbvie, Pfizer, Sanofi, BMS, Consultant of: Abbvie, Eli Lily, Pfizer

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SAT0587

MACHINE-LEARNING DERIVED ALGORITHMS FOR OUTCOMES PREDICTION IN RHEUMATIC DISEASES: APPLICATION TO RADIOGRAPHIC PROGRESSION IN EARLY AXIAL SPONDYLOARTHRITIS

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Background: Axial spondyloarthritis (axSpA) is a chronic rheumatic disease that encompasses various clinical presentations: inflammatory chronic back pain, peripheral manifestations and extra-articular manifestations. The current nomenclature divides axSpA in radiographic (in the presence of radiographic sacroiliitis) and non-radiographic (in the absence of radiographic sacroiliitis, with or without MRI sacroiliitis. Given that the functional burden of the disease appears to be greater in patients with radiographic forms, it seems crucial to be able to predict which patients will be more likely to develop structural damage over time. Predictive factors for radiographic progression in axSpA have been identified through use of traditional statistical models like logistic regression. However, these models present some limitations. In order to overcome these limitations and to improve the predictive performance, machine learning (ML) methods have been developed.
Objectives: To compare ML models to traditional models to predict radiographic progression in patients with early axSpA.
Methods: Study design: prospective French multicentric cohort study (DESIR cohort) with 5years of follow-up. Patients: all patients included in the cohort, i.e. 708 patients with inflammatory back pain for >3 months but <3 years, highly suggestive of axSpA. Data on the first 5 years of follow-up was used. Statistical analyses: radiographic progression was defined as progression either at the spine (increase of at least 1 point per 2 years of mSASSS scores) or at the sacroiliac joint (worsening of at least one grade of the mNY score between 2 visits). Traditional modelling: we first performed a bivariate analysis between our outcome (radiographic progression) and explanatory variables at baseline to select the variables to be included in our models and then built a logistic regression model (M1). Variable selection for traditional models was performed with 2 different methods: stepwise selection based on

Akaike Information Criterion (stepAIC) method (M2), and the Least Absolute Shrinkage and Selection Operator (LASSO) method (M3). We also performed sensitivity analysis on all patients with manual backward method (M4) after multiple imputation of missing data. Machine learning modelling: using the "SuperLearner" package on R, we modelled radiographic progression with stepAIC, LASSO, random forest, Discrete Bayesian Additive Regression Trees Samplers (DBARTS), Generalized Additive Models (GAM), multivariate adaptive polynomial spline regression (polymars), Recursive Partitioning And Regression Trees (RPART) and Super Learner. Finally, the accuracy of traditional and ML models was compared based on their 10-foldcross-validated AUC (cv-AUC).

Results: 10-fold cv-AUC for traditional models were 0.79 and 0.78 for M2 and M3, respectively. The 3 best models in the ML algorithm were the GAM, the DBARTS and the Super Learner models, with 10-fold cv-AUC of: 0.77, 0.76 and 0.74, respectively (Table 1).

Table 1. Comparison of 10-fold cross-validated AUC between best traditional and machine learning models.

Best models	Cross-validated AUC
Traditional models	
M2 (step AIC method)	0.79
M3 (LASSO method)	0.78
Machine learning approach	
SL Discrete Bayesian Additive Regression Trees Samplers (DBARTS)	0.76
SL Generalized Additive Models (GAM)	0.77
Super Learner	0.74

AUC: Area Under the Curve; AIC: Akaike Information Criterion; LASSO: Least Absolute Shrinkage and Selection Operator; SL: SuperLearner. N = 295.

Conclusion: Traditional models predicted better radiographic progression than ML models in this early axSpA population. Further ML algorithms image-based or with other artificial intelligence methods (e.g. deep learning) might perform better than traditional models in this setting.

Acknowledgments: Thanks to the French National Society of Rheumatology and the DESIR cohort.

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SAT0588 PREVALENCE, INCIDENCE, AND THE CARDIOVASCULAR AND CEREBROVASCULAR RISKS OF NONTRAUMATIC AVASCULAR NECROSIS IN SOUTH KOREA

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Background: Due to the shared mechanism of nontraumatic avascular necrosis (AVN) and endothelial dysfunction, the associations of AVN with increased cardiovascular and cerebrovascular events have been suggested in the several population-based studies.

Objectives: This study aimed to estimate the prevalence and incidence of nontraumatic AVN in South Korea from the Korean National Health Insurance Service Sample Cohort Database 2.0 (2006-2015) and to evaluate the risk of major cardiovascular and cerebrovascular events among patients with nontraumatic AVN.

Methods: We defined an incident case as a newly diagnosed and registered patient in the registry in that year, with a 2-year washout period. Prevalent cases were defined as all patients with nontraumatic AVN in the corresponding year. To evaluate the cardiovascular and cerebrovascular risks in patients with AVN, we set AVN group composed of patients with an initial diagnosis of non-traumatic AVN between 2008 and 2010 (n=1,150). The comparison group was composed of randomly selected subject (5 per patient with AVN; n = 5,750) who were matched to the AVN group according to age, sex, resident area, and year of AVN diagnosis. The development of major cardiovascular and cerebrovascular events was tracked in each sampled patient until 2015. Cox proportional hazard regressions were used to calculate the overall risks for the development of major cardiovascular and cerebrovascular events.

Results: From 2008 to 2015, the prevalence of nontraumatic AVN increased gradually, but its incidence did not change, with an annual average incidence of 413 per 1 million population and the male-to-female ratio of 1.2:1. The peak incidence occurred in the 50-59 year age group. The incident AVN was more prevalent in male than in female under 70, but there was female predominance after the age of 70 (Figure 1). The patients with AVN had a higher cumulative incidence of major adverse cardiovascular and cerebrovascular events than controls (19.5% versus 14.9%; p = 0.017). Upon univariate Kaplan-Meier method with the log-rank test, there was a significant difference in major cardiovascular and cerebrovascular events-free survival rates between AVN group and control group (p <0.001). However, after adjusting for potential confounders including hypertension, diabetes, dyslipidemia, and use of steroid or statin, the association between AVN group and major adverse cardiovascular and cerebrovascular events was insignificant (adjusted HR 1.114, 95% CI 0.959-1.295, p=0.158)

Conclusion: In this population-based cohort study, we provided the updated epidemiologic data of Korean patients with nontraumatic AVN. The increased risk for major cardiovascular and cerebrovascular events among AVN patients was not observed in the representative Korean population.

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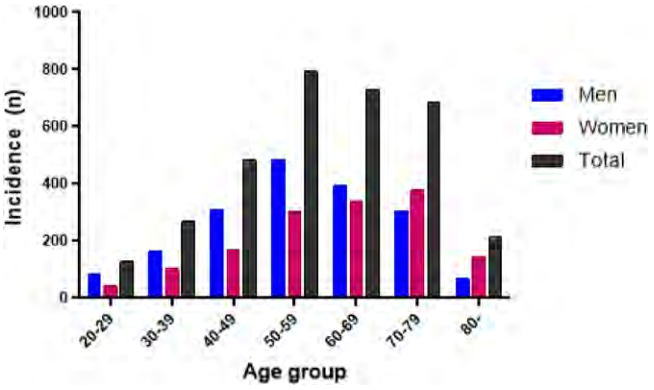


Figure 1. Age- and sex-distributed incidence of patients with nontraumatic avascular necrosis in Korea, 2008-2015

Disclosure of Interests: None declared

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SAT0589 RISK FOR PSYCHIATRIC HOSPITALIZATION FOLLOWING A RHEUMA-RELATED HOSPITALIZATION: RESULTS FROM A CZECH NATIONWIDE, COHORT STUDY

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Background: Cohort studies using nationwide health registers have shown an increased risk for affective and anxiety disorders in people with ankylosing spondylitis (AS) and rheumatoid arthritis (RA) (1-3). Moreover, a nationwide cohort study demonstrated an increased risk for mental disorders in people with rheumatic diseases (4).

Objectives: We aimed to investigate the risk for psychiatric hospitalization following a hospitalization for rheumatic disease.

Methods: Using data from the Czech nationwide register of all-cause hospitalizations, we obtained 4 971 individuals hospitalized (index hospitalization) between 2004 and 2012 for rheumatic diseases - RA, spondyloarthritis (including AS, psoriatic arthritis and undifferentiated spondyloarthritis), systemic lupus erythematosus and systemic sclerodermia, with no history of psychiatric and rheuma-related hospitalization in the previous 10 years from the index hospitalization. On these individuals, we randomly matched (on age, gender and year of index hospitalization) controls that were hospitalized in the same time period for a non-rheumatic disease and have no history of psychiatric and rheumatic hospitalization in the last 10 years from their index hospitalization, in the ratio of 1:5. We employed conditional logistic regression for assessing the risk for psychiatric hospitalization in the subsequent 3 years from the index hospitalization. To strengthen our results, we repeated the matching step 100 times and run the analysis on each resulting dataset

separately, and pooled the results. The findings are expressed as odds ratios (OR) with 95% confidence intervals (95% CI).
Results: We identified an elevated risk for psychiatric (OR = 1.34, 95% CI = 1; 1.78) and for affective disorders (OR = 2.19, 95% CI = 1.17; 4.1) in people hospitalized for rheumatic diseases. We did not find a statistically significant association with organic, psychotic and anxiety disorders.
Conclusion: There is an increased risk for experiencing a psychiatric disorder in the period of 3 years after a rheuma-related hospitalization.
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Acknowledgments: Supported by the project (Ministry of Health Czech Republic) for conceptual development of research organization 00023728 (Institute of Rheumatology).
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SAT0590 ORAL MICROBIOTA IDENTIFIES PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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Background: Several studies have suggested a link between the two chronic inflammatory diseases, rheumatoid arthritis (RA) and periodontitis (PD) [1]. The diseases share similar environmental and genetic risks factors, *e.g.,* smoking [2] and the HLA-DRB1 alleles [3]. Several serum markers used in the diagnosis of RA have also been found to be elevated in PD, *e.g.,* anti-citrullinated proteins antibodies (ACPA) and rheumatoid factor (RF) [4]. The connection between PD and RA has been suggested to be explained by several periodontal pathogens, *e.g., Aggregatibacter actinomycetemcomitans* and *Porphyromonas gingivalis*, which have been suggested to induce the production of autoantibodies [5, 6].
Objectives: To investigate the composition of the concerted saliva microbiota and its role in the development of RA, with the aim of improving the diagnostic tools.
Methods: 16S ribosomal RNA gene sequencing of saliva bacterial DNA isolated from a total of 61 early RA (eRA) patients and 59 healthy controls was made. The eRA (symptoms ≤ 12 months) was diagnosed at an Early Arthritis Clinic (fulfilling the 1987 ARA criteria) and matched with the controls for sex and age, except for two of the elderly cases. None of the individuals included in the study had taken antibiotics during the preceding 3 months. No one of the cases were treated with anti-rheumatic drugs except for corticosteroids in 16 cases the latest month.
Results: All participants were classified into three hierarchical cluster groups based on their saliva microbiota and the distribution of eRA cases versus controls differed distinctly between the cluster groups. The microbiota from the eRA had higher species richness, differed in beta-diversity, and was enriched for species in the Fusobacterium and Porphyromonas genera, and for the Alloprevotella tannerae, Campylobacter gracilis, Capnocytophaga leadbetteri, Filifactor alocis, Fusobacterium nucleatum subsp. polymorphum, Neisseria elongate, Porphyromionas endodontalis and Prevotella pleuritidis species compared to controls. Combining two topped ranked species, *A. tannerae* and *Catonella morbi* significantly predicted eRA with an AUC score of 0.86 and a specificity and sensitivity of 0.80 and 0.85, respectively. The predicted functions of the microbiota in eRA patients were dominated by fatty acid metabolism, ornithine metabolism, glucosylceramidase, sphingolipids, beta-lactamase resistance, biphenyl degradation and 17-beta-estradiol 17-dehydrogenase metabolism.
Conclusion: In this study a difference in oral microbiota diversity between eRA patients and healthy controls could be shown. Some of the eRA-associated oral bacteria have previously been suggested to play an aetiological role in the development of RA, but others have not been recognized earlier, such as A. tannerae, F. alocis, F. nucleatum subsp. polymorphum, and P. endodontalis, and may therefore be useful in RA risk assessment.
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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.2416

SAT0591 REAL-WORLD PATTERNS OF PEGLOTICASE USE FOR TREATMENT OF GOUT IN THE U.S.

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Background: Pegloticase is used in severe refractory gout or in cases of intolerance to other urate lowering therapies but the real-world use of pegloticase since its U.S. Food and Drug Administration approval in 2010 is not known.
Objectives: We sought to evaluate the real-world patterns of pegloticase use in the U.S. and the incidence of safety outcomes with its use.
Methods: We conducted a retrospective descriptive study using data from two U.S. commercial insurance claims databases (MarketScan and Optum, 2010-2018). We identified new initiators of pegloticase with ≥1 gout diagnosis code in the 365-day baseline period prior to pegloticase initiation. We measured the number and duration of pegloticase therapy. We assessed the risk of anaphylaxis, cardiovascular events including myocardial infarction or stroke, hospitalization for heart failure (new onset or exacerbations) while receiving pegloticase therapy.
Results: Among 2.9 million patients with ≥1 diagnosis code for gout, we identified only 483 (179 in Optum and 304 in MarketScan) pegloticase initiators. The mean age and % female was 55.6 years, 10.9% for MarketScan and 60.6 years and 17.3% for Optum (**Table**). Cardiovascular comorbidities were prevalent in both cohorts. Hypertension was present in up to 85%, diabetes mellitus in 38%, chronic kidney disease in 46%, and heart failure in 21% of the patients. As expected, use of gout-related medications at baseline was common. The median duration of pegloticase therapy was 93 days (interquartile range [IQR] 56-186) in MarketScan and 105 (IQR 56-127) in Optum. The median number of pegloticase infusions was 4 (IQR 2-10) for MarketScan and 5 (IQR 2-12) in Optum. In MarketScan, 57 (18.8%) patients switched to allopurinol, 64 (21.1%) to febuxostat, and 2 (0.7%) to probenecid during the mean 0.5-year followup time. Similarly, during the mean 0.5-year followup time in Optum, 38 (21.2%) patients switched to allopurinol, 34 (19.0%) to febuxostat, and 2 (1.1%) to probenecid. During the mean 0.5-year follow-up time on pegloticase, there were 3 (0.6%) anaphylaxis, 7 (1.4%) composite cardiovascular, 31 (6.4%) heart failure hospitalizations, and 3 (0.6%) deaths in both datasets.
Conclusion: Pegloticase is rarely used in gout, and the median duration of pegloticase therapy was 3 months. There were few anaphylaxis events captured in this claims-b ased study, while heart failure hospitalizations were common.

Table. Select baseline characteristics of pegloticase initiators

	MarketScan	Optum
N	304	179
Mean age (SD), years	55.62 (12.83)	60.58 (12.85)
Female sex, %	10.9	17.3
Comorbidities		
Hypertension, %	73.0	84.9
Diabetes mellitus, %	34.9	38.0
Heart failure, %	12.5	20.7
Coronary artery disease, %	12.8	26.3
Chronic kidney disease, %	34.2	45.8
Malignancy, %	10.2	8.4
Medication use		
NSAID/COXIB use, %	51.3	40.0
Colchicine use, %	72.0	65.4
Allopurinol use, %	33.6	47.5
Febuxostat use, %	38.8	36.9
Probenecid use, %	8.2	4.5
Oral steroid use, %	67.1	72.1
Anakinra use, %	5.9	6.7

Disclosure of Interests: Sarah Chen Employee of: After finishing the work for this abstract, she has moved to work for Gilead., Jun Liu: None declared, Seoyoung Kim Grant/research support from: Research grants from Pfizer, AbbVie, Bristol-Myers Squibb and Roche for unrelated studies
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SAT0592

MORTALITY AND CAUSE OF DEATH IN KOREAN PATIENTS WITH RHEUMATOID ARTHRITIS: BASED ON A LARGE COHORT.

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Background: Rheumatoid arthritis (RA) is a common chronic inflammatory disease characterized by arthritis of multiple joints. Although the use of corticosteroid and extra-articular complications may lead increased mortality of patients with RA and it have been confirmed by hundreds of studies, the prognosis of RA has improved over the past decades with the introduction of biologics disease-modifying anti-rheumatic drugs and treat-to-target strategy. Along with the increase of overall survival of RA, the needs for re-assessment of actual life expectancy in patients with RA have also been increased.
Objectives: To investigate the cause and the risk of death of Korean patients with RA in a large RA cohort.
Methods: We analyzed patients in Hanyang BAE RA cohort who fulfilled the American College of Rheumatology criteria. A total of 2,355 patients were enrolled from October 2001 to December 2015. Mortality data were derived by linking with data from the Korean National Statistical Office and date and cause death were identified. Standardized Mortality Ratio (SMR) was estimated by dividing the observed deaths by the expected number of deaths of age- and sex- matched general population. Confidence intervals were calculated based on the Poisson distribution.

Table 1. Comparison of demographic and clinical characteristics of analyzed patients

	Total	Died patients	Survivors	P value
	(n=2,355)	(n=225)	(n=2,130)	
Age at onset	41.8 ± 12.8	49.7 ± 12.7	41.0 ± 12.5	<0.001
Age at enrollment	50.8 ± 12.3	63.3 ± 9.4	49.5 ± 11.8	<0.001
Male	265 (11.3)	42 (18.7)	223 (10.5)	<0.001
Disease duration	18.1 ± 10.4	20.7 ± 10.9	17.8 ± 10.3	<0.001
Observation period	9.0 ± 4.4	7.0 ± 3.6	9.2 ± 4.5	<0.001
Smoking				<0.001
Never smoker	1,953 (83.9)	161 (74.9)	1,792 (84.8)	
Former smoker	212 (9.1)	36 (16.7)	176 (8.3)	
Current smoker	164 (7.0)	18 (8.4)	146 (6.9)	
Comorbidity				
Hypertension	330 (14.0)	63 (28.0)	267 (12.5)	<0.001
Diabetes mellitus	106 (4.5)	24 (10.7)	82 (3.9)	<0.001

*Values are number (%) or mean ± standard deviation. ** Missing data were excluded from analysis.

Results: Over the observation period, 225 deaths were reported. The age at enrollment was 50.8 ± 12.3 years and disease duration was 18.1 ± 10.4 years. The most common cause of death was malignancy (40 cases) followed by respiratory disease (38 cases), cardiovascular disease (32 cases) and musculoskeletal disease (21 cases). Total SMR was increased [1.7, 95% CI 1.5-2.0] but age- and sex- adjusted SMR was not increased [SMR 1.0, (95% CI 0.9-1.1)]. When we classify patients by age conduct subgroup analysis, sex-adjusted SMR was also similar with that of general population by all group: the adjusted SMR in patients aged 15-39, aged 40-59 and aged over 60 were 0.7 (observed death 1, expected death 1.5, 95% CI 0-2.0), 0.9 (observed death 29, expected death 32 95% CI 0.6-1.3), and 0.9 (observed death 195, expected death 221.0, 95% CI 0.8-1.0), respectively. Compared with survivors, patients who died were more likely to be male (18.7% vs. 10.5%, p<0.001) and they had an older age of onset of RA (49.7 years vs. 41.0 years, p<0.001). Died patients were more likely to be current smoker or ever smoker (25.1% vs. 15.2%, p<0.001) and accompanied by more comorbidities including hypertension (28.0% vs. 12.5%, p<0.001) and diabetes mellitus (10.7% vs. 3.9%, p<0.001).
Conclusion: The overall age- and sex- matched SMR of patients with RA was similar with that of general population. However, compared with survivors, patients who died were more likely to be male, diagnosed with RA at older age, more likely to be smoker, and they have more hypertension and diabetes mellitus. Therefore, attention should be paid not only to RA itself but also managing comorbidities to improve the survival of patients with RA.
Disclosure of Interests: None declared
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SAT0593

ANA TESTING IN THE (VERY) ELDERLY: EXPECTATION VERSUS REALITY

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Background: Antinuclear antibodies (ANA) are frequently used as a screening tool for systemic autoimmune rheumatic diseases (SARD), although they are also present in 10-15% of the adult healthy population. SARD have their peak incidence in the young/ middle-aged adult. As age progresses, the incidence of SARD decreases while the prevalence of ANA tends to increase, with some series reporting up to 30% prevalence in older ages[1].
Objectives: To determine the clinical significance and utility of ANA testing in a population over 85 years of age.
Methods: We conducted a retrospective study of patients over the age of 85 who underwent ANA testing due to a SARD suspicion at our hospital autoimmunity laboratory, from 2011 to 2018. Justification for ANA request was collected from patient's clinical records. Patients with pre-established diagnosis of SARD and patients with no justification given for ANA request were excluded from the analysis. ANA titer (positive ≥ 1:160) and cellular staining patterns were assessed by indirect immunofluorescence (Hep-2 cells).
Results: Ages ranged from 85 to 98 years, with 58.8% being females. The prevalence of ANA in this population was 61.5%, mostly in lower titers (1:160 in 45.0%, 1:320 in 31.9%, 1:640 in 20.3% and 1:1280 in 2.7%). Dense fine speckled pattern was by far the most common cellular staining pattern (79.1%). A suspicion of SARD was the reported reason for ANA testing in 34,5% (n=296) of the 854 patients submitted to this test. The main clinical clues justifying SARD suspicion were: arthralgia/arthritis (11.9%), thrombocytopenia (10.0%), pancytopenia (10.0%), spotless fever (8.2%), interstitial lung disease (4.8%), pleural (6.1%) and pericardial (4.1%) effusion. Over a median follow-up of 1.0 year, 10 patients (3.4%) were diagnosed with a SARD, only one being an ANA-related disease: 5 cases of polymyalgia rheumatica, 2 cases of rheumatoid arthritis, 1 case of giant cell arteritis, 1 case of Sjogren syndrome and 1 case of sarcoidosis. In 60% of patients with a confirmed SARD, the main reason for suspicion was the presence of arthralgia/ arthritis. Positive ANA testing showed a 90.0% sensitivity and a 39.6% specificity for SARD. This translates into a positive predictive value of 5.0%.
Conclusion: ANA are highly prevalent in elderly patients under SARD suspicion, while the incidence of SARD is very low, which explains the low positive predictive value of ANA testing. Interestingly, only one among the ten cases of SARD confirmed was indeed an ANA-related disease (Sjogren syndrome).
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SAT0594

LONG-TERM MORBIDITY FOLLOWING IGA VASCULITIS IN CHILDHOOD

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Background: IgA vasculitis (IgAV) in children is considered a mostly self-limiting disease. However, patients may require aggressive initial treatment, are prone to disease relapses and conceivably have a sustained abnormality in mucosal and /or circulating IgA responsiveness, that can predispose to the development of other conditions.
Objectives: To determine whether childhood IgAV predisposes to comorbidity later in life.
Methods: Observational cohort study examining rates of hospitalization, ED visits, procedures and accrual of comorbidity (by Charlson comorbidity index; CCI) comparing 494 IgAV patients <20 years at diagnosis with 1385 non-exposed matched controls over a 20-year period. Maximum likelihood estimates were used to obtain Odds (OR) and Rate ratios per 1000 person-years (RR).
Results: Hospitalization was increased proportionally (73.5 vs 51.5%) and by rate (21.7 vs 18.9; rate ratio 1.15) (both p<0.01) for IgAV patients, who underwent more diagnostic and medical procedures whereas controls had higher rates of surgical interventions. IgAV patients had an higher overall ED attendance (25 vs 16%) and visit rate (10.8 vs 8.43, RR 1.29) (each p<0.01)) and accrued more often peptic ulcer and renal disease and developed severe comorbidity (CCI ≥3) at a higher rate (OR 2.9, 95% CI 0.79-11.6) than controls.
Conclusion: A diagnosis of IgAV in childhood associates with increased risk and rate of subsequent hospital admission, ED attendance and severe comorbidity.

The occurrence of childhood IgAV thus signifies the presence of a sustained predisposition to illness.

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SAT0595 INTERSTITIAL LUNG DISEASE IN SOUTH AFRICAN ADULTS PATIENTS WITH AUTOIMMUNE RHEUMATIC DISEASES

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Background: Interstitial lung disease (ILD) is prevalent in patients with autoimmune rheumatic diseases (ARD), leads to significant morbidity and mortality, and is poorly characterized in South Africa.

Objectives: To describe the clinical, serological and radiological features of ILD associated with ARD in a tertiary referral hospital.

Methods: A cross-sectional study of outpatients attending the rheumatology and respiratory clinics of Groote Schuur Hospital between October 2018 and September 2019. Clinical, serological and radiological features were documented. We compared features of 3 groups of patients: rheumatoid arthritis (RA), systemic sclerosis (SSc) and "Other" autoimmune rheumatic diseases (OARD) which included Idiopathic Inflammatory Myopathies, Mixed Connective Tissue Disease, Systemic Lupus Erythematous, ANCA-associated vasculitis, Sjogren's Syndrome and overlap syndromes. Factors associated with Usual Interstitial Pneumonia (UIP) were sought by univariate and multivariate analysis. P-values ≤ 0.05 were considered statistically significant. Analyses was performed with STATA 14.0 (Stata Corp LP, USA).

Results: Of 124 patients, 29.8 % had RA, 25,8 % SSc and 44.4 % OARD. Most patients were female (86.3%), of mixed racial ancestry (75.0%), and the median (IQR) age was 55 (46-66). Over one-third were smokers, 22.6% had emphysema, and one third had previous pulmonary tuberculosis (PTB) infection. Smoking, emphysema, and previous PTB were higher in RA group but the difference was not statistically significant. All SSc patients and more than two-thirds of RA and OARD patients had gastroesophageal reflux disease (GORD).

Similar to reports elsewhere, Nonspecific interstitial pneumonia (NSIP) was the commonest ILD (63.7 %), followed by UIP (26.6%) and other patterns (9.7%). Contrary to other reports, we found similar frequencies of NSIP and UIP patterns in patients with RA. RA patients were significantly older (median (IQR)) age at ILD onset 62 (55-68) years, compared to SSc (49 (38-56) and OARD (42 (33-56) ($p < 0.001$). The percentage of predicted Forced Vital Capacity (FVC) were significantly worse in SSc and OARD groups and DLCO in OARD. RA diagnosis (OR 3.8, 95% CI 1.5-9.5), older age (0R 1.1, 95% CI 1.0-1.1), COPD (OR 3.2, 95% CI 1.4-8.0), longer ARD-ILD interval, higher FVC (OR 1.0, 95% CI 1.0-1.1) and previous Methotrexate (MTX) use (OR 2.6, 95% CI 1.1-6.0) were significantly associated with UIP. Multivariable analysis showed that only COPD and previous MTX use was associated with UIP (OR 2.8 (95% CI 1.0 – 8.0) and 1.0 (95% CI 1.0 – 1.0) respectively).

Regarding MTX exposure, 37.1% of patients were prescribed MTX before ILD diagnosis, and 33.9% continued, started or restarted after ILD diagnosis. No case of acute pneumonitis was documented.

Conclusion: ILD was most commonly diagnosed in RA and SSc, with NSIP seen most frequently overall. RA patients presented better Pulmonary function tests despite higher frequency of UIP. The use of MTX seems to not be associated with the development of acute pneumonitis in patients with ILD

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SAT0596 ASSOCIATIONS BETWEEN CIRCULATING LIPID MEDIATORS AND INCIDENT INFLAMMATORY ARTHRITIS IN AN ANTI-CITRULLINATED PROTEIN ANTIBODY POSITIVE POPULATION

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Background: Lipid mediators are endogenously derived from the metabolism of omega-3 and omega-6 polyunsaturated fatty acids (PUFAs) and have important roles in promoting and resolving inflammation in the body (1). Epidemiological studies have shown higher omega-3 PUFA status to be associated with a lower risk of both autoimmunity and progression to inflammatory arthritis (IA) (2,3).

Objectives: To determine the association of lipid mediators with progression from rheumatoid arthritis (RA)-related autoimmunity to inflammatory arthritis (IA).

Methods: We conducted a prospective cohort study using data from the Studies of the Etiologies of Rheumatoid Arthritis (SERA). SERA enrolled first-degree relatives (FDRs) of individuals with RA (FDR cohort) and individuals who screened positive for RA-related autoantibodies at health fairs (screened cohort). We followed 133 anti-CCP3.1 positive participants, of which 29 developed IA (22 classified as RA by 2010 ACR/EULAR criteria). We quantified lipid mediators from stored plasma samples via liquid chromatography tandem mass spectrometry methods validated against the collection and storage methods used in the study. A priori, we selected 5S-HETE, 15S-HETE and 17S-HDHA because they are precursors to leukotrienes, Lipoxin A4 and Resolvin D series lipid mediators, respectively. We fit Cox proportional hazard models for each lipid mediator as a time-varying covariate. For lipid mediators significantly associated with progression to IA we then examined IL-1β, IL-6, IL-8 and TNF-α (Bio-Plex Pro™ assay) as potential mediators of this relationship.

Results: Higher plasma 5S-HETE levels were associated with an increased risk of incident IA after adjusting for age at baseline, cohort (FDR or screened), and shared epitope (SE) status (Table 1). The models examining 15S-HETE and 17S-HDHA had the same trend but did not reach statistical significance. We did not find evidence that the association between 5S-HETE and IA risk was mediated by the tested pro-inflammatory cytokines, suggesting a direct role for this lipid mediator in conversion to IA.

Table 1. Hazard ratios and 95% confidence intervals of lipid mediator concentrations associated with IA, n=29 IA cases

Lipid mediator	Crude	Adjusted[b]
5S-HETE	2.10 (1.12, 3.92)	2.41 (1.43, 4.07)
15S-HETE	1.61 (0.88, 2.93)	1.52 (0.87, 2.65)
17-HDHA[a]	1.59 (0.68, 3.74)	1.61 (0.72, 3.56)

[a] dichotomized as <limit of detection (reference) or detected

[b] Adjusted for SE, age at baseline and cohort

Conclusion: In a prospective cohort of anti-CCP positive individuals, higher circulating levels of 5S-HETE, an important precursor to pro-inflammatory leukotrienes, was associated with subsequent IA. Our findings highlight the potential pathologic and prognostic significance of these PUFA metabolites in inflammatory processes in pre-RA populations.

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SAT0597 EARLY DAMAGE AS MEASURED BY SLICC/ACR DAMAGE INDEX IS A PREDICTOR OF HOSPITALIZATION IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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Background: Hospital admissions and re-admissions in lupus patients are common occurrences that can lead to mortality. The predictive factors influencing hospitalizations and mortality are variable in literature.
Objectives: We evaluated the leading causes of hospitalizations and mortality and their predictive factors in the multi-ethnic SLE patients.
Methods: A retrospective study was done on SLE patients from University Malaya Medical Centre and diagnosed for at least 1 year. Data were collected from 1988 until 2019. Demographic and disease details, causes of hospital admissions and mortality were reviewed from electronic medical records. Baseline and latest disease activity (SLEDAI 2K) and SLICC/ACR damage index (SDI) scores were evaluated.
Results: A total of 300 SLE patients, 285 (95%) of whom were females were included in this study. Majority were of Chinese ethnicity 150 (50%), followed by Malays 108 (36%), Indians 39 (13%) and others 3 (1%). The cohort's median age was 48 (18-82) years and median disease duration was 14 (1-72) years. Median age at SLE diagnosis was 27.5 (6-72) years. 133 (44.3%) had SDI score of ≥1 at baseline (early damage). 23% had developed new organ damage during this study period.
There were 222 (74%) patients ever hospitalized and 12 (5.4%) deaths from this cohort. The main cause of hospitalization was lupus flare which included concurrent infection (n=415 admissions, 46%), followed by elective admissions for procedures and others (n=284 admissions, 31.5%). 17% of admissions were due to infections with concurrent flare (8.7% were due to infection alone). Admissions for treatment and disease related complications were 13.8%. Median length of stay for SLE related cause admissions was longer compared to non-SLE related causes, 10 (range 1-113) vs 7.5 (range 1-130) days. Causes of death included SLE flare without features of infection (25%), concurrent lupus flare and infection (25%), and non-SLE causes (50%). Malignancy (33.3%) was the main cause of death in non-SLE deaths. Independent predictive factors for hospitalization and mortality are shown in Table 1 and Table 2.

Table 1. Multivariate logistic regression analysis for the predictors of hospitalization

HOSPITALIZATION			
Parameters	**B Coefficient**	**OR (95% C. I)**	**p value**
Ethnicity			
Malay	2.005	7.428 (0.181-226.883)	0.26
Chinese	1.287	3.623 (0.089-106.163)	0.47
Indian	1.695	5.446 (0.126-177.222)	0.35
Disease Duration	- 0.015	0.985 (0.953-1.020)	0.40
Comorbids ≥ 2	1.673	5.328 (0.843-105.481)	0.14
APLS	1.784	5.956 (1.883-26.685)	0.001*
Serology markers			
Anti-Smith	1.840	6.298 (1.733-40.638)	0.01*
Anti-SSA	1.211	3.360 (1.758-6.640)	<0.001*
ACR			
Serositis	2.656	14.248 (2.555-275.071)	0.01*
Neurological	1.706	5.506(1.403-36.834)	0.01*
SCORES			
SDI Baseline	0.552	1.737 (1.062-3.048)	0.01*

Table 2. Multiple logistic regression analysis of the predictors for mortality

MORTALITY			
Parameters	**B Coefficient**	**OR (95% C. I)**	**p value**
Disease duration	0.095	1.099 (1.031-1.183)	0.001*
Comorbids ≥2	3.161	23.618 (1.997-344.533)	0.01*
APLS	2.556	12.888 (1.592-136.512)	0.01*
SDI			
Renal	2.167	8.734 (1.385-80.528)	0.01*
Malignancy	3.936	51.218 (6.725-616.957)	0.001*
Pulmonary	1.696	5.452 (0.684-41.395)	0.1
SCORES			
SLEDAI latest	0.275	1.316 (1.161-1.556)	0.001*

Conclusion: Early damage in lupus as measured by SDI is of predictive value of hospitalization. Optimization in managing patients with pre-existing damage is crucial to reduce hospitalization risk and subsequent complications.
References:

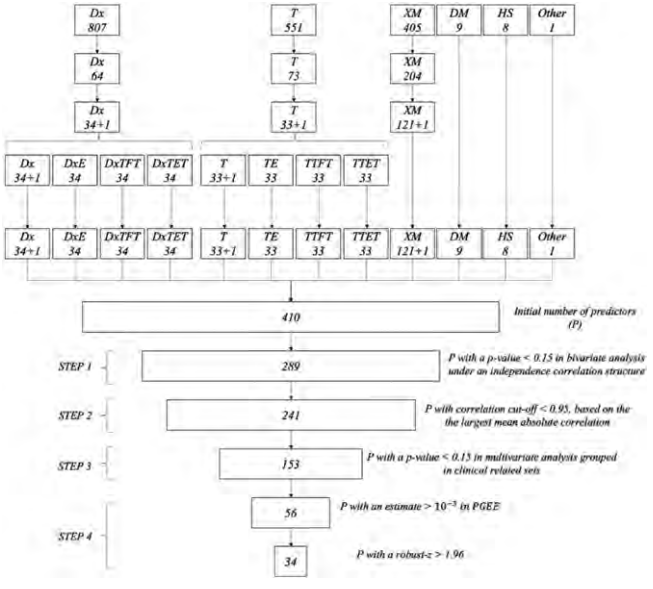
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SAT0598 PREDICTORS OF HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH MUSCULOSKELETAL DISEASES: A LONGITUDINAL ANALYSIS FROM AN ELECTRONIC HEALTH RECORD DATABASE

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Background: Musculoskeletal diseases (MSKs) are the major cause of disability, affecting the patient's daily activities as well as their Quality of Life (QoL).
Objectives: To analyze in a cohort of patients with MSKs the influence of demographic and clinical predictors in repeated measures of Health-Related QoL (HRQoL) obtained from a departmental electronic health record (EHR)
Methods: Patients attending the Hospital Clínico San Carlos rheumatology outpatient clinic (HCSC-MSK cohort) from April 1st, 2007 to November 30th, 2017 who were seen at least twice were included in this study. Visits separated more than one year from previous or next visit were excluded. Our primary outcome was HRQoL collected in each patient's visit using the Rosser Classification Index (it ranges between 0 and 1, the higher value, the higher HRQoL. It is calculated as the combination of two subscales: disability and distress). Demographic and clinical variables, such as diagnoses, treatments, and comorbidities were included as predictors. Variable selection was carried out in 4 steps. First, we developed a bivariate Generalized Estimating Equations model, selecting those variables with a p-value < 0.15. Second, those with a pair-wise absolute correlation < 0.95 were carried to the next step. Third, multivariate GEE analyses were performed including clinical related variables, and those independently associated with our primary outcome were selected with a p-value < 0.15. At least one predictor of each multivariate analyses was included even if none of them had p-value < 0.15. In this case the one, with the lowest p-value was chosen. Fourth, a grid search approach was followed to determine the penalization value and a penalized GEE model was implemented including all selected variables and using an independence correlation structure. Those with an estimate greater than 10^-3 and a z-robust > 1.96 were considered to be independently associated with the HRQoL.



Results: A total of 18,187 patients with 95,960 outpatient visits were included in this study. From the initial 410 predictors, 289, 241, 153, and 34 were selected in the first, second, third, fourth and fifth steps. The median age was 56.4 years. The major part of the patients were women (69.4%), and the median *Rosser* value was 0.986. More common diagnoses, treatments and comorbidities were back pain,

tendinitis, pain in joint; analgesia, gastric protector and NSAIDs; hypertension, dyslipidemia and diabetes respectively. The predictors with a greater negative impact in HRQoL were the use of 3rd level analgesics and azathioprine, a presence of kidney failure, fibromyalgia, and ischemic heart disease. Conversely, use of symptomatic slow action drugs for osteoarthritis, statins, lowering uric acid drugs, a diagnose of mixed connective tissue disease, and better HRQoL in the past six months were independently associated with a positive impact in the HRQoL.

Conclusion: We have identified several diagnoses, treatments and comorbidites independently associated with HRQoL in a cohort of patients followed up in a rheumatology outpatient clinic. This represent a first step in the implementation of value-based care for MSK patients, as we can now review the procedures associated with a worse HRQoL in an attempt to improve them.

References:

Predictor selection. Dx: Diagnoses. DxE: Diagnoses Episode. DxTFT: Diagnoses Total Follow-up Time.

DxTET: Diagnoses Total Episode Follow-up Time T: Treatment. DxE: Treatment Episode. DxTFT:

Treatment Total Follow-up Time. DxTET: Treatment Total Episode Follow-up Time. XM: Comorbidities

and Concomitant Treatments. DM: Demographics. HS: Health Status.

Disclosure of Interests: None declared

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SAT0599 FEET DERMATOLOGICAL CONDITIONS AND DEFORMITIES IN RHEUMATOID ARTHRITIS

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Background: It has been extensively studied the repercussions of rheumatoid arthritis (RA) in hands and in their function. However, the evidence regarding the effect on feet and dermatological problems is scarce[1].

Objectives: Describe risk factors associated with foot deformities (FD) in patients with RA.

Methods: This was a descriptive and observational cross-sectional study. Patients were consecutively recruited. Demographic-clinical data was registered and through physical examination the presence of FD, dermatological problems and pain location were assessed. The Foot Function Index (FFI) survey was used to measure foot functioning. Functional capacity was evaluated using the Health Assessment Questionnaire (HAQ) tool and quality of life with the Rheumatoid Arthritis Impact Disease (RAID) questionnaire. The risk of falling was calculated with Tinetti's scale. An adjusted binary logistic regression was performed to compare patients with and without foot deformities. Models were adjusted for FFI's, HAQ's, RAID's and Tinetti's scores.

Results: We included 76 subjects with RA with a mean age of 52.6 (11.40) years old. The 68.4% presented FD, while 69.7% had dermatological problems. Patients with FD were older (p=.005), had a more affected function of their feet (p=.002), greater risk of falling (p=.002) and worst functional capacity (p=.007) and quality of life (p=.026). Some factors that increased the risk of having FD in patients with RA were: age (OR 1.07, 95%CI: 1.001-1.147; p=.048), pain in toes and in the forefoot (OR 6.194; 95%CI: 1.172 – 32.743; p=.032) and having dermatological conditions in feet (OR 0.244; 95%CI: 0.067 –0.881; p=.031).

Conclusion: Foot deformities and dermatological problems were present in more than the half of our sample. Older patients and subjects with dermatological problems and pain in toes and forefoot had a greater risk of presenting foot deformities.

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Table 1. Demographic characteristics (n=76)

Age, mean (SD)	52.605 +/- 11.40
Women, n (%)	76 (96.1)
BMI*, median (IQR)	27.54 (24.00-30.38)
Disease duration**, median (IQR)	96.00 (24.00 – 210.00)

Table 1. Demographic characteristics (n=76)

Diabetes mellitus, n (%)	19 (25.0)
Arterial hypertension, n (%)	21 (27.6)
DAS28-PCR, mean (SD)	2.99 (1.61)
HAQ-score, median (IQR)	0.81 (0.25 – 1.47)
RAID-score, median (IQR)	4.74 (3.06 – 7.52)
FFI-score, mean (SD)	45.99 (27.37)
Tinetti-score, median (IQR)	22.50 (10.00 – 45.50)
Feet deformities, n (%)	52 (68.4)
Hallux valgus, n (%)	38 (50)
Claw toe, n (%)	23 (30.3)
Hammer toe, n (%)	9 (11.8)
Overlapping toes, n (%)	14 (18.4)
Dermatological problems	53 (69.7)
Ulcerations	1 (1.3)
Plantar hyperkeratosis	30 (39.5)
Plantar corn	6 (7.9)
Onychomycosis	24 (31.6)
Onychocryptosis	5 (6.6)
Subungueal hematoma	1 (1.3)

** kg/m^2 * *months*

Table 2. Comparison between presence and absence of foot deformities.

	Present n=52	Absent n=24	p
Age, mean (SD)	54.88 (11.63)	47.66 (9.31)	.005
Disease duration*, median (IQR)	120 (28.5-246)	54 (12-138)	NS
BMI**, median (IQR)	27.00 (23.95 – 30.40)	28.20 (25.01 – 31.68)	NS
DAS 28, mean (SD)	3.08 (1.61)	2.80 (1.64)	NS
FFI, mean (SD)	52.32 (24.78)	32.26 (28.18)	**.002**
Tinitti's scale, median (IQR)	37.50 (10.75 – 63.00)	12.00 (10 – 21.750)	**.002**
HAQ, median (IQR)	1.19 (0.37 – 1.78)	0.565 (0.00 – 0.910)	**.007**
RAID, median (IQR)	5.75 (3.46 – 7.52)	3.51 (1.27 – 6.81)	**.026**
Pain location, n (%)			**.027**
Absent	7 (13.46)	7 (29.16)	NS
Toes and forefoot	36 (69.23)	8 (33.33)	NS
Midfoot	2 (3.84)	1 (4.16)	NS
Rearfoot	7 (13.46)	8 (33.33)	NS
Pain intensity, mean (SD)	6.308 (3.01)	4.54 (3.50)	**.027**
Dermatological problems, n (%)	42 (80.76)	13 (54.16)	**.003**

**months ** kg/m^2. NS: not significative.*

Disclosure of Interests: None declared

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SAT0600 PNEUMOCOCCAL VACCINATION IN PATIENTS WITH AUTOIMMUNE INFLAMMATORY RHEUMATIC DISEASES, TREATED WITH BIOLOGICAL THERAPY AND WITH A LOW LEVEL OF ANTIBODIES - A COHORT STUDY OF PATIENTS WITH VARYING VACCINATION STATUS.

L. Strandbygaard[1,2], S. Larsen Rasmussen[3], K. Fuursted[4], K. Hay Kragholm[3,5], P. C. Leutscher[3,5], C. Rasmussen[1,2,3,5]. [1]*North Denmark Regional Hospital, Department of Rheumatology, Hjørring, Denmark*; [2]*Danbio Rigshospitalet, Glostrup, Denmark*; [3]*North Denmark Regional Hospital, Centre for Clinical Research, Hjørring, Denmark*; [4]*Statens Serum Institut, København S, Denmark*; [5]*Aalborg University, Institute of Clinical Medicine, Aalborg, Denmark*

Background: Risk of infection is increased in patients with autoimmune inflammatory rheumatic diseases (AIRD)[1]. Furthermore, disease-modifying antirheumatic drug (DMARD) treatment contributes to this risk[2]. To reduce the risk of serious infections, it is recommended that patients are vaccinated against *Streptococcus pneumoniae*[3]. However, some AIRD patients do not develop or maintain an adequate antibody response after pneumococcal vaccination[4].

Objectives: The aim of the study was to examine the proportion of patients with low antibody levels, who achieved a protective level of pneumococcal antibodies after vaccination.

Methods: Pneumococcal antibodies were measured by a serological assay in patients treated with biologics in a rheumatology outpatient clinic. Vaccination with 23-valent-pneumococcal polysaccarid vaccine was then offered to patients with a protective antibody level below the defined threshold and pneumococcal antibody level was measured at follow-up 2-3 months later. The patients continued their DMARD treatment without any changes.

Demographic and clinical data were collected, including age, sex, AIRD diagnosis, duration and activity (high/low), in addition to treatment (biologics, prednisolone, methotrexate) and previous vaccination history.

Results: A total of 248 patients with inadequate antibody level accepted vaccination and among those, 137 patients (55%) had previously been vaccinated, 98 patients had not previously been vaccinated and for 13 patients data on vaccination status could not be obtained.

At follow-up, 84 patients (34%) achieved a protective level of antibodies. Use of methotrexate as part of the DMARD regimen was associated with an unprotected level of pneumococcal antibodies (Figure 1) (p<0,001). There was no similar association with respect to use of biologics.

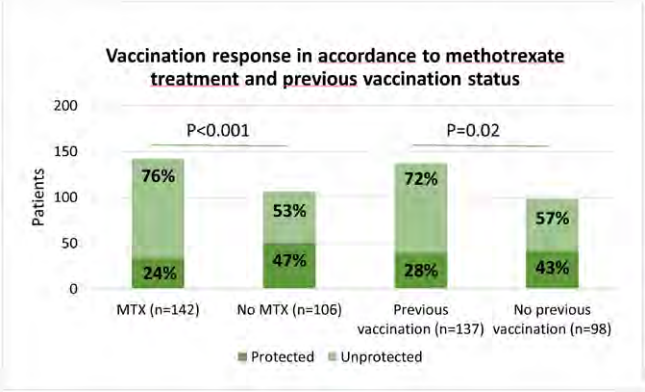


Figure 1

In the group of patients who had previously been vaccinated, time between vaccinations spanned from 20 to 111 months, median 49 months.

There was an association between previous vaccination, and failure in achieving a protective antibody level (Figure 1) (p=0,02), as well as an association between less than 5 years (60 months) between vaccinations and not achieving a protective level.

Conclusion: We found that only one-third of patients achieved a protective pneumococcal antibody level after vaccination. Methotrexate treatment was associated with a decreased antibody response, which was not the case for treatment with biologics or prednisolone.

Among patients who had previously been vaccinated, significantly less achieved a protective level of antibodies, compared to patients who had not been vaccinated. All 248 patients had a low antibody level at baseline, despite 137 being previously vaccinated.

Further studies are warranted to show whether or not a short discontinuation of methotrexate, will better the response to vaccination.

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Disclosure of Interests: None declared

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SAT0601

RELATIONSHIP BETWEEN BODY MASS INDEX AND NAILFOLD CAPILLAROSCOPY IN PRIMARY AND SECONDARY RAYNAUD'S PHENOMENON

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Background: Raynaud's phenomenon (RP) is a diffuse clinical manifestation (3-5% of general population) RP is often secondary to autoimmune systemic diseases, while the condition is classified primary if no underlying disorders can be found. A lower body mass index (BMI) was associated with a greater risk of developing RP, perhaps due to greatest sensivity to cold temperatures
Objectives: The objective of our study was to evaluate the association of BMI with clinical and capillaroscopic features in primary and secondary RP.
Methods: Consecutive patients at the first access to a Rheumatology Outpatient Clinic over a 13 months period were screened to RP; nailfold videocapillaroscopy (NVC)was carried out and qualitative and quantitative assessment was performed. Diagnosis of RP was defined in patients who identified color pictures of witnessed attacks.Patients enrolled were screened for secondary causes of RP. RP was classified as primary when no abnormalities were found. Weight and height were collected in clinical records and patients were divided in 3 groups according to their BMI: underweight (BMI<18.5 kg/m2), normal weight (BMI 18.5–25 kg/m2), and overweight (BMI >25 kg/m2). Chi-square test to compare categorical variable and Parametric Student t-test to comparing mean values of normally distributed data were used. p<0.05 was considered to be statistically significant.
Results: RP was diagnosticated in 100 of 1416 patients (7.06%). Of these, 73 (10 M, 63F) accepted to undergo NVC. An autoimmune disease was found in 35 patients (47.9%), of which 2 were underweight, 14 normal weight and 19 overweight. Of 38 patients with primary RP,3 were underweight, 23 normal weight and 12 overweight. BMI was significantly higher in secondary RP (p=0.03). Overweight patients with secondary RP were older (p=0.01), but with a disease duration not statistically significant longer (p=0.26). In secondary RP, avascular areas and neoangiogenesis were founded only in overweight patients. Moreover,in secondary RP overweight was correlated with decreased capillary density (p=0-04). There was not association between BMI and capillaroscopic abnormalities in primary RP.
Conclusion: In our study BMI was correlated with microvascular changes only in patients with secondary RP. Our findings may suggests a role for obesity in the microcirculatory disfunction in the autoimmune diseases. Further studies are needed to generalize results and to find a causative role.
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Disclosure of Interests: Rosella Tirri: None declared, Marco Barba: None declared, Ranieri Formica: None declared, Rosaria Irace: None declared, francesco ciccia Grant/research support from: pfizer, novartis, roche, Consultant of: pfizer, novartis, lilly, abbvie, Speakers bureau: pfizer, novartis, lilly, abbvie
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SAT0602

INCIDENCE OF INFLAMMATORY ARTHRITIS BEFORE AND AFTER THE INTRODUCTION OF NEW CLASSIFICATION CRITERIA: A SYSTEMATIC REVIEW

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Background: Hallmark in treatment of inflammatory arthritis (IA); rheumatoid arthritis (RA), axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA), is to treat early with intensive regimens to induce remission and prevent disability on the longer term [1,2,3]. To be able to start treatment in an earlier stage of the disease, around a decade ago new classification criteria sets were introduced; 2010 ACR/EULAR for RA, 2009 ASAS for axSpA and 2006 CASPAR criteria for PsA. Compared to old criteria sets for RA, axSpA and PsA these new ones cover a broader spectrum of early disease features [2]. Although classification criteria are not developed for diagnosing, they are widely adopted for use as aids in diagnosing IA [4]. Therefore, the new criteria sets might have led to an increased reported incidence of IA [5].
Objectives: To determine whether the reported incidence of IA has changed after introduction of the new classification criteria this systematic review has been conducted.
Methods: A systematic literature search was conducted using Embase, Medline Ovid, Cochrane Central and Web of Science from database inception to September 2019. For this study only articles that addressed the incidence of IA in adult referrals towards the rheumatologist were included (Fig. 1). A meta-analysis was performed to compare the pooled estimates and 95% confidence intervals (CI) for the incidence of IA before and after the introduction of new classification criteria.

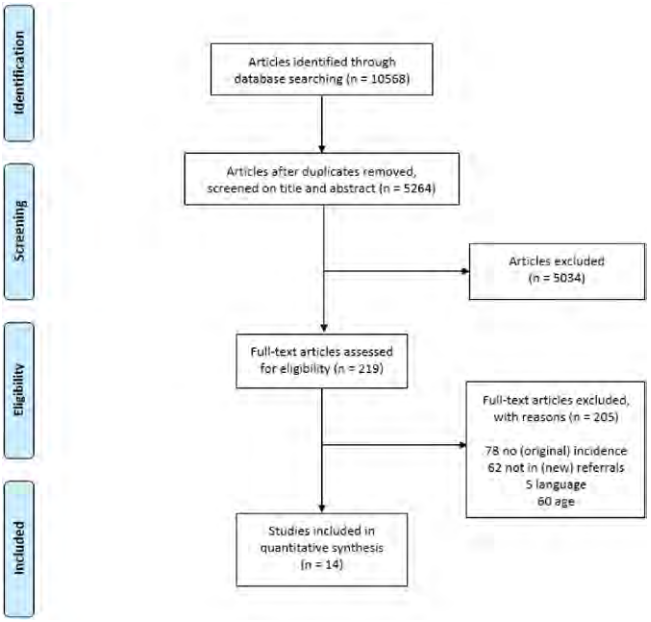
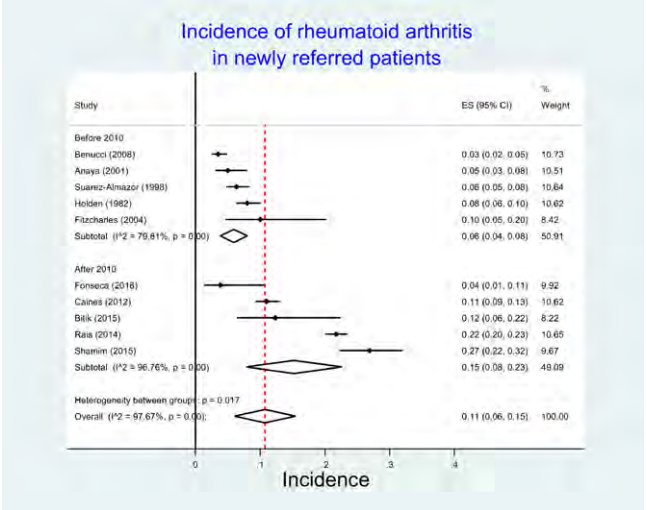


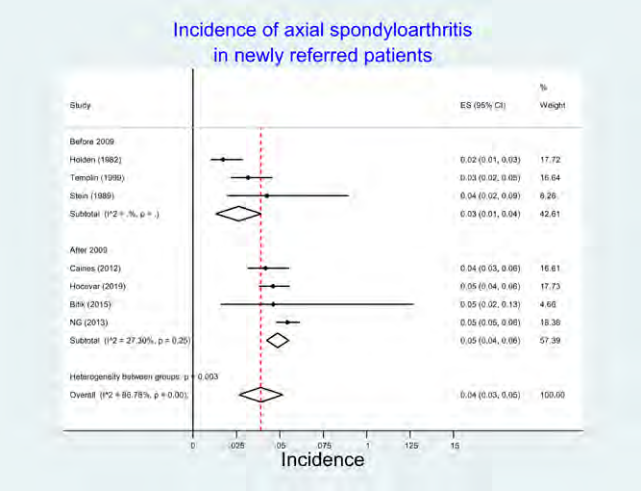
Figure 1. PRISMA flow diagram of study selection



Graph 1. Forest plot of incidence of rheumatoid arthritis compared before and after introduction of new classification criteria in 2010

Results: A total of 14 studies reporting on the incidence of RA (n=10), axSpA (n=7) and PsA (n=4) in adults newly referred towards the rheumatologist were included. Pooled incidences were for RA 11% (95% CI 6-15%); for axSpA 4% (95% CI 3-5%); and for PsA 4% (95% CI 3-5%).
Graph 1 and 2 show a significant increase in incidence of 9% for RA (p=0.019) and 2% for axSpA (p=0.006) after the introduction of the new classification criteria for respectively RA and axSpA. For PsA only one study was included reporting on the incidence of PsA in rheumatology centres before 2006, hence pooled estimates before and after introduction of new criteria could not be compared.

Overall there was a high intragroup heterogeneity (p=0.00) caused by geographical area and study design.



Graph 2. Forest plot of incidence of axial spondyloarthritis compared before and after introduction of new classification criteria in 2009

Conclusion: Rheumatoid arthritis is the most frequent IA diagnosis in newly referred patients, of which the incidence increased over time up to 15%. The introduction of new classification criteria might have introduced higher incidence rates for IA, although heterogeneity could have influenced the results.

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Disclosure of Interests: None declared

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SAT0603 SYSTEMIC SCLEROSIS IS AN INDEPENDENT RISK FACTOR FOR ISCHEMIC HEART DISEASE WITH AN ADDITIONAL RISK IN THOSE POSITIVE FOR CERTAIN ANTI-PHOSPHOLIPID ANTIBODIES: A VERY LARGE CASE-CONTROL STUDY

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Background: A higher prevalence of ischemic heart disease (IHD) in patients with systemic sclerosis (SSc) was reported. However, contrasting findings were published concerning the role of SSc-related autoantibodies in IHD risk which remains controversial.

Objectives: The current study explored the link between SSc and IHD, impact of putative links on SSc mortality and the role of SSc-related and antiphospholipid autoantibodies in disease associated IHD.

Methods: A large cohort study utilising the Clalit-Health-Service (CHS) database was conducted on 2,431 SSc patients and 12,710 age- and sex matched controls. The proportion of IHD was compared between patients diagnosed with SSc and age- and gender-matched controls. The role of SSc-linked and antiphospholipid autoantibodies in disease associated IHD was assessed.

Results: The rate of IHD was significantly higher in SSc than controls (20.4% *vs* 15.0%, p<0.001). At the multivariate analysis, SSc was an independent predictor of IHD with an OR of 1.91 (95%CI 1.57-2.31, p<0.0001). SSc patients with IHD had a higher mortality rate with an HR of 2.67 (95%CI 2.03-3.53, p<0.0001) than those without IHD. SSc patients with positive anti-beta2GPI (IgM-isotype) or anti-cardiolipin (aCL) (IgA-isotype) exhibited a higher risk of IHD than SSc patients without these antibodies with an OR 1.89 (95% 1.04-3.45, p=0.0369) and OR of 3.72 (95% 1.25-11.11, p=0.0184), respectively.

Conclusion: Patients with SSc are at higher risk for developing IHD with an additional risk for the latter in those positive for aCL or anti-beta2GPI. A high degree of suspicion is needed during routine patient follow-up and pre-emptive screening should be considered.

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SAT0604 FAST FOOD HABITS AND SERUM URATE CHANGE IN YOUNG ADULTS: 15-YEAR PROSPECTIVE ANALYSIS

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Background: Fast food consumption has strong positive associations with weight gain and insulin resistance.[1] Obesity and insulin resistance are in turn strongly associated with elevated serum urate (SU) levels, largely mediated by insulin's anti-uricosuric ability.[2]

Objectives: To investigate the relation between fast food consumption and changes in SU over a 15-year period among young black and white adults in the United States.

Methods: Participants for the CARDIA study included 3,122 young (age 18-30 years in 1985-86) black and white adults in the United States who were followed up with repeated dietary and clinical assessments and had both baseline and year 15 SU measurement available. Frequency of fast food consumption (fast food frequency, FFF) was quantified on a semicontinuous scale and classified as <1, 1-2, or >2 times per week. We used multivariable linear regression models to investigate the association of FFF at baseline as well as change in FFF with 15-year changes in SU.

Results: Our analysis included data from 3,122 subjects who had SU data available both at baseline and year 15 (**Table 1**). After adjustment for age, sex, education, baseline height and weight, and baseline SU, baseline FFF (defined as 3 times per week year 0 differences between participants) was independently associated with increases in SU among both black (beta=0.11, p=0.04) and white (beta=0.11, p=0.01) individuals (**Table 2**). Change in FFF (defined as 3 times a week 15-year change within participants) was also independently associated with increases in SU among white (beta=0.09, p=0.01) individuals but not blacks (beta=0.03, p=0.93) (**Table 2**). There was a significant correlation between weight change and SU change (correlation coefficient 0.34, p<0.001). **Figure 1** depicts the joint associations of year 0 FFF and 15-year changes in FFF with change in weight. Compared to the average 15-year SU change among participants with baseline FFF <1 time per week and 15-year FFF change <0 time per week, those with high FFF at both baseline and follow-up had an extra 0.21 mg/dL increase (i.e., 75% of overall population SU increase over 15 years [0.28 mg/dL]) in SU during that time. After adjusting for covariates in model 2, change in weight (beta=0.03, p<0.001) and homeostasis model for insulin resistance (HOMA) (beta=0.05, p<0.001) remained significantly associated with SU change.

Table 1. Participant Characteristics

Characteristic	Blacks (n=1468)	Whites (n=1654)
Age, years (year 0)	24.4 (3.8)	25.6 (3.3)
Male (%)	44	48
Weight, kg (year 0)	72.8 (16.7)	70.0 (14.0)
Weight, kg (year 15)	87.9 (20.9)	80.7 (18.6)
Serum urate, mg/dL (year 0)	5.1 (1.4)	5.4 (1.4)
Serum urate, mg/dL (year 15)	5.6 (1.4)	5.5 (1.4)

All values reported as mean (SD) unless otherwise noted.

Table 2. Mean Adjusted Change in Serum Urate by Baseline and Change in Fast Food Frequency

	Fast Food Variable	Blacks		Whites	
		Beta (SE)	p	Beta (SE)	p
Model 1	Baseline	0.11 (0.04)	0.01	0.11 (0.04)	0.01
	Change	0.003 (0.033)	0.93	0.09 (0.04)	0.01
Model 2	Baseline	0.12 (0.04)	0.01	0.09 (0.04)	0.02
	Change	0.004 (0.03)	0.88	0.08 (0.04)	0.03

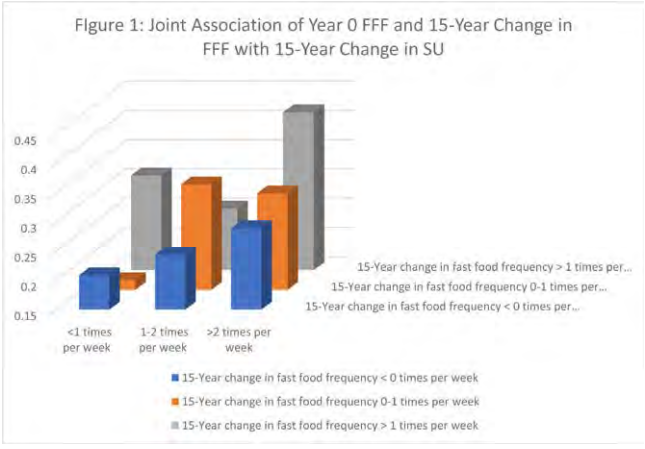
Model 1: age, sex, education, baseline height and weight, baseline SU
Model 2: model 1 + alcohol, physical activity, and smoking (both baseline and year 15 change)

Conclusion: Fast-food consumption has strong positive associations with SU, suggesting that fast food increases the risk of hyperuricemia and gout. The observed association is likely mediated by weight gain and resultant changes in insulin resistance.

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SAT0605

TRENDS OF TOTAL JOINT ARTHROPLASTY AMONG PATIENTS WITH OSTEOARTHRITIS, RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDYLITIS IN BRITISH COLUMBIA, CANADA, 1998-2013

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Background: Total joint replacement or arthroplasty (TJA) is an expensive surgical treatment for severe arthritis when other treatments have failed. Given the substantial changes in the available treatments over the past 2 decades, it is of interest to describe the trends in the use of TJA among patients with different types of arthritis in the general population.

Objectives: The aim of this study was to examine longitudinal trends of TJA including total hip, knee and shoulder replacement performed in British Columbia, Canada, between the year of 1998 and 2013 due to three different types of arthritis conditions: **1) Osteoarthritis (OA), 2) Rheumatoid arthritis (RA) and 3) Ankylosing spondylitis (AS)**.

Methods: We analyzed large, population-based administrative data obtained from Population Data BC that includes patients aged 20+ in B.C., Canada, linked to diagnostic codes of hospitalizations and physician visits. Using the Canadian Classification of Diagnostic, Therapeutic and Surgical Procedures (CCP) procedure codes and the Canadian Classification of Health Intervention (CCI) procedure codes, we identified total joint arthroplasty procedures (TJA) including total hip arthroplasty (THA), total knee arthroplasty (TKA) and total shoulder arthroplasty (TSA) performed among OA, RA and AS prevalent cases. We calculated annual rates of THA, TKA and TSA performed among OA, RA and AS patients. We divided the study period into four equal-length periods and calculated period prevalence rates of THA, TKA and TSA per 100,000 person years as the ratio of the number of cases per period (numerator) to the total follow up time within the same period (denominator). We performed trend tests to test if there are changes in these rates over time.

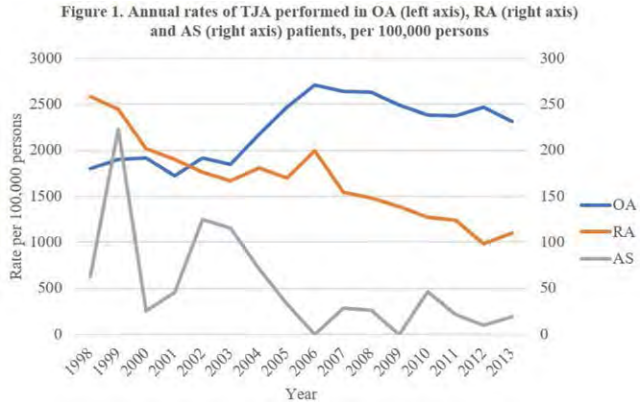
Results: For OA and RA, TKA was the most common types of TJA performed, while THA remained to be the most common types of TJA performed among AS patients. For OA, period prevalence rate of THA, TKA and TSA increased during the study period (**Table 1**.). For RA patients, THA and TKA rates showed a decreasing trend. For AS patients, THA rates decreased and TSA increased. For RA and AS, TSA rates did not show a significant trend.

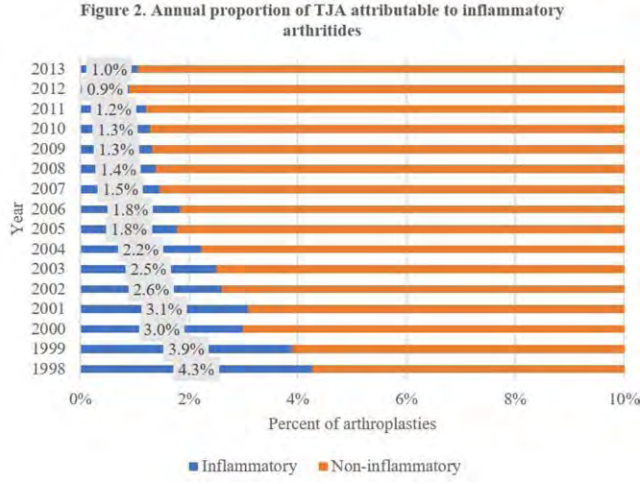
Table 1. Trends in arthroplasty rates (cases per 100,000 person years) among patients with OA, RA and AS by arthroplasty site.

Period	1998-2001	2002-2005	2006-2009	2010-2013	Period Trend (*P*†)
Among OA patients					
THA	816.26	920.62	1035.51	947.03	0.05459 (0.0002)
TKA	1024.7	1244.71	1653.89	1475.44	0.13114 (<0.0001)
TSA	25.96	32.01	43.2	53.92	0.2495 (0.0007)
Among RA patients					
THA	79.53	55.63	46.31	33.11	-0.28321 (<0.0001)
TKA	131.66	111.99	106.08	74.79	-0.16765 (0.0001)
TSA	19.44	16.62	13.77	13.13	-0.1391 (0.221)
Among AS patients					
THA	89.01	76.75	10.02	15.48	-0.6753 (<0.0001)
TKA	<5	<5	<5	7.74	0.6263 (0.0178)
TSA	<5	<5	<5	<5	-0.4196 (0.354)

† *P* values were derived in Poisson regression analysis.

Among patients with OA, annual TJA rates per 100,000 persons show an overall increasing trend. The TJA rates remained relatively flat from 1998 to 2003, started to increase and peaked in 2006, and declined slightly thereafter (**Figure 1**.). Among patients with inflammatory arthritis (RA and AS), annual TJA rates decreased over the study period (**Figure 1**.). Annual proportion of TJA perfromed due to inflammatory arthritides significantly decreased from 1998 to 2013 (4.3% versus 1.0%) (**Figure 2**.).





Conclusion: There have been important changes in the annual rate of total joint replacement in B.C., Canada, during the study period from 1998 to 2013. TJA use increased in OA patients but decreased in patients with inflammatory arthritis (RA and AS). Effective treatment for inflammatory arthritis, such as TNF-α inhibitors

introduced in British Columbia in 2001-2002, may have effectively reduced the need for arthroplasty in RA and AS.

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Disclosure of Interests: None declared

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SATURDAY, 06 JUNE 2020

HPR Epidemiology and public health (including prevention)

SAT0606-HPR

HOW DO THE PATIENTS THAT DECLINE TO PARTICIPATE IN A LIFESTYLE INTERVENTION STUDY DIFFER FROM THOSE WHO ACCEPT? A REGISTER-BASED CROSS-SECTIONAL STUDY.

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Background: A recently conducted randomized controlled trial (Joint Resources Sedentary Behavior Intervention study (JR-SB)) aimed to reduce sedentary behavior and increase light-intensity physical activity in patients with rheumatoid arthritis (RA). Patients were recruited from a rheumatology outpatient clinic and the intervention consisted of three motivational counselling sessions followed by text message reminders. The results showed highly significant between-group differences on behavioral, patient-reported and cardio-metabolic outcomes, both on a short- and long-term basis (1;2). Since a relatively large fraction (58%) of invited patients initially declined to participate in the trial, we decided to explore if and how the declining patients differed from the included patients. The findings may inform which patient characteristics to consider in implementing a lifestyle intervention in clinical practice.

Objectives: To compare socio-demographic, clinical and lifestyle factors between included patients and patients declining to participate in the JR-SB study at the time where study inclusion commenced.

Methods: We conducted a retrospective register-based cross-sectional study. All patients with RA, who had been invited to participate in the JR-SB study during 2013-2014 were identified in the DANBIO registry. Patients' clinical and lifestyle data were also retrieved from DANBIO while data on socio-demography was extracted from Statistics Denmark. Differences between participants and decliners were determined by an independent t-test or chi-square test.

Results: Of invited patients (n=801), a total of 467 (58%) declined participation in the JR-SB study during 2013-2014. See Table 1 for characteristics and comparison of participants and decliners.

Table 1. Participants' and decliners' characteristics; (n (%) unless otherwise stated)

	Participants (n=150)	Decliners (n=467)	P-value (x^2)
Women	121 (80.7)	358 (76.7)	0.30
Age (years), mean (SD)	58.5 (11.7)	60.8 (12.9)	0.045[a]
Living with partner	96 (64)	293 (62.7)	0.78
Working	57 (38)	157 (33.6)	0.15
RA duration (years), mean (SD)	13.8 (11.1)	13.7 (10.8)	0.92[a]
Pain (VAS), mean (SD)	34.4 (21.8)	29.1 (24.5)	0.046[a]
Fatigue (VAS), mean (SD)	44.2 (26.0)	39.5 (28.4)	0.14[a]
Smoking	**(n=61)**	**(n=220)**	0.041
	27 (44.2)	130 (59.1)	
Regular exercise (min 1-2 times/week)	**(n=29)**	**(n=89)**	0.026
	23 (79.3)	50 (56.2)	

VAS – Visual Analogue Scale

Numbers in bold indicate the total number of responders on smoking and exercise status

[a] Determined by an independent t-test

Conclusion: Patients who declined to participate in a randomized controlled trial aiming at reducing sedentary behavior were often smokers, had less regular exercise habits and were older than those who accepted to participate. This indicates that the intervention did not appeal to all patients with RA. The findings should be considered in the implementation of lifestyle interventions in clinical rheumatology practice.

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SATURDAY, 06 JUNE 2020

HPR Service developments, innovation and economics in healthcare

SAT0607-HPR

MULTIDISCIPLINARY CARE CLINIC FOR PATIENTS WITH IMMUNITY MEDIATED INFLAMMATORY DISEASES. FIRST YEAR OF COORDINATED MANAGEMENT

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Background: Patients with immunity mediated inflammatory diseases (IMID) often have clinical manifestations and comorbidity in the field of various medical specialties. A center has been created in our hospital for the comprehensive care of patients with IMID who are being treated with biological therapies (BT) or targeted synthetic molecules (TSM). It is an innovative healthcare model, that incorporate patients into its governance. Physicians, pharmacists and advanced practice nurses (APN), collaborates in consultation or in the day hospital (DH).

Objectives: To analyze the activity developed during the first year of operation of the center, with special attention to effectiveness, efficiency, interdisciplinary relationships and patient satisfaction.

Methods: Observational analysis with indicators of management and monitoring of patients, care activity, effectiveness, adverse effects, resource consumption and patient satisfaction using the hospital's own information systems.

Results: Center staff during 2019: two admission assistants, one nursing assistant, six nurses, seven part-time doctors and three pharmacists. 1,490 patients were included: 694 (46.6%) Rheumatology (Rheu), 585 (39.3%) Digestive (Dig) and 211 (14.1%) Dermatology (Der) generated 11,363 medical consultations, 14,850 APN consultations and 3,920 treatment sessions in the DH. IV treatment 529/1490 (35.5%) patients (45.0% Reu, 53.9% Dig, 1.1% Der). Patients with rheumatic diseases: rheumatoid arthritis: 339/694, 48.8%; Spondyloarthritis: 226/694, 32.6%; psoriatic arthritis: 117/694, 16.9%; and juvenile idiopathic arthritis: 12/694, 1.7%. 217/1490 (14.6%) patients needed multidisciplinary consultations.

Table 1. shows the most relevant indicators and table 2 shows the patient satisfaction survey for 2019.

Table 1. relevant indicators

	RHEU	DIG	DER
On demand consultations 2019 %	21.0%	34.2%	14.3%
Teleconsultations 2019 %	17.8%	41.9%	0.0%
BT, TSM tapering. %			
2019	31.9%	0.2%	45,5%
2018	18.9%	0.2%	13.4%
BT, TSM intensification. %			
2019	5.8%	35.2%	0.5%
2018	2.6%	36.5%	0.5%
Biosimilars %			
2019	43.1%	48.5%	15.9%
2018	30.4%	4.0%	12.1%
Adherence>90% 2019 %	89.4%	91.7%	86.4%
Remission 2019 %	47.8%	67.3%	78.5%
hospital admission, any cause pat-years			
2019	1.4	1.7	0.1
2018	1.5	1.5	0.04
emergency admission, any cause pat-years			
2019	2.1	2.1	1.6
2018	2.1	2.0	1.5

Table 2. patient satisfaction survey

Categoría	Mean and (DS) 1-5
General aspects of the center	4.3 (0.9)
Physicians	4.5 (1.1)
DH and APN	4.5 (1.2)
Pharmacy	4.6 (0.9)
Health proffesional coordinaton	4.4 (0.9)
Hospital global satisfaction	4.3 (0.8)

Conclusion: From previous situation there is an increase in interdisciplinary consultations and HD activity maintenance without an increase in human resources. Efficiency (tapering, biosimilars) and patient and staff satisfaction have improved. However, no improvement in adverse effects has been

observed, which is an area of improvement. Effectiveness is good, waiting to compare with the previous year. Nutrition and preventive medicine consultations has not been evaluated because have been recently established. Other indicators are being analyzed at the end of the submission deadline.

The impact of this pioneering management model, with a holistic approach and incorporating patients into its governance, is difficult to measure until its implementation is completed. Uveitis and psychology consultations and patient school starting in 2020 will improve the quality of IMID patient care, as well as their satisfaction and that of their relatives.

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SATURDAY, 06 JUNE 2020

HPR Interdisciplinary research

SAT0608-HPR

EULAR POINTS TO CONSIDER FOR THE DETECTION, ASSESSMENT AND MANAGEMENT OF NON-ADHERENCE IN PEOPLE WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES

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Background: Non-adherence to medication and non-pharmacological interventions precludes reaching an optimal outcome. 30 to 80% of patients with rheumatic and musculoskeletal diseases (RMDs) do not adhere to their recommended treatment regimens.

Objectives: The objective of this EULAR task force was to establish recommendations/points to consider (PtC) for the detection, assessment and management of non-adherence in people with RMDs.

Methods: A EULAR task force (TF) was established, and the EULAR standardised operating procedures for the development of PtCs were followed. The TF included rheumatologists, health professionals in rheumatology (HPRs), and patient-representatives from 12 countries. A systematic literature review of reviews was conducted in advance to support the TF in formulating the PtC. Agreement was obtained by Delphi technique in three rounds (0-10 rating scale).

Results: A definition of adherence, 4 overarching principles and 9 PtC were formulated (table).

Conclusion: The PtCs can help health-care providers to support people with RMDs to adhere to the agreed treatment plan.

Table. Overarching principles and points to consider.

Definition of Adherence		
Adherence is defined as the extent to which a person's behaviour corresponds with the agreed prescription.		
Overarching principles		**Agreement**
1	Adherence impacts the outcomes of people with RMDs.	99
2	Shared decision making is key, since adherence is a behaviour following an agreed prescription.	96
3	Adherence is influenced by multiple factors.	98
4	Adherence is a dynamic process that requires continuous evaluation.	96
Points to consider		**Agreement**
1	All HCPs involved in the management of people with RMDs should take responsibility for promoting adherence.	99
2	Effective patient-health professional communication should be applied to enhance adherence.	99
3	Barriers and facilitators of adherence of a specific patient to a specific prescription should be appropriately evaluated.	95
4	Patient education should be provided for people with RMDs as an integral part of standard care.	96
5	Care should be tailored to patient preferences and goals to enhance adherence.	98
6	Adherence should be discussed regularly based on open questions and particularly when disease is not well controlled.	99
7	The HCP should explore which factors might negatively influence adherence, including: opportunity (e.g., availability or cost), capability, (e.g., memory problems), motivation (e.g., concerns).	94
8	Together with the patient, the HCP should tailor the approach to overcome individual barriers to adherence, e.g., - simplifying the regimen, - using reminders, - providing education, - discussing the patient's beliefs on treatments.	98
9	When specific expertise or interventions for adherence are needed, they should be made available to patients.	98

HCP, health-care providers; RMDs, rheumatic and musculoskeletal diseases

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SATURDAY, 06 JUNE 2020

HPR Interventions (educational, physical, social and psychological)

SAT0609-HPR

DELPHI CONSENSUS FOR THE OPTIMAL TREATMENT & MANAGEMENT OF COMPLEX RHEUMATOID ARTHRITIS (RA) PATIENTS

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Background: A significant proportion of patients with rheumatoid arthritis (RA) have additional considerations that must be taken into account for managing their disease.[1] These include; co-morbidities, extra-articular manifestations and poor prognostic factors.[2-5] Tailored management could reduce the burden on patients, the health system and wider society.

The 'complex' RA patient group is ill-defined and no specific recommendations exist for their optimal management and treatment.

Objectives: A group of UK Rheumatology experts aimed to provide a set of recommendations to support consistent and high quality management, grounded in current evidence, expert opinion and best practice.

Methods: A steering group meeting identified priority topics associated with complex RA.

Table 1. Topics for consensus

Topic	No. of statements
Definition of 'complex' RA from a medical perspective	19
Definition of patient factors that may contribute to 'complex' RA	3
Outcomes for RA patients with co-morbidities and/or extra articular manifestations	5
Prescribing options for 'complex' RA	8
Evidence vs. best practice requirements	4
Burden of 'complex' RA	4
TOTAL NUMBER OF STATEMENTS	**43**

For each topic, the group defined statements they all agreed with. Delphi methodology was used to ratify these statements with rheumatology peers.

High levels of agreement (over 70%) were achieved in the first round, the group proceeded to formulate the recommendations.

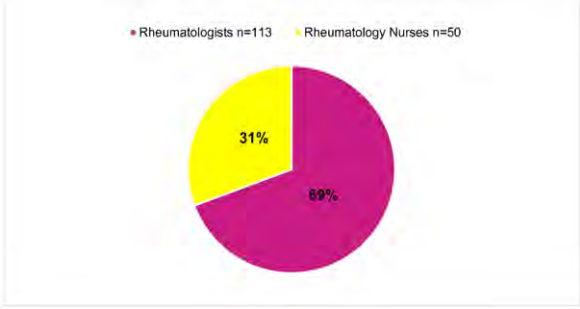


Figure 1. Responses received (n=163)

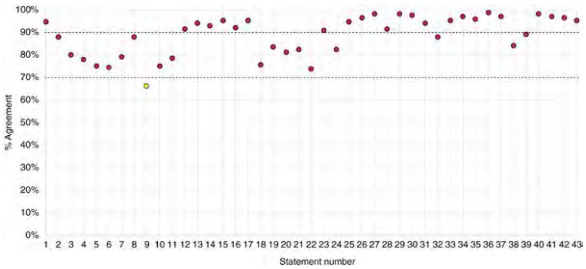


Figure 2. Consensus Plot (total responses n=163)

Conclusion: These recommendations are offered:

1.Healthcare professionals (HCPs) should consider a patient's complexity (including clinical co-morbidities, extra-articular manifestations and poor prognostic factors) prior to making treatment decisions;

2.HCPs should take into account a patient's psychosocial factors and health literacy prior to making treatment decisions;

3.Patient specific outcomes for complex RA should always be proactively agreed with the individual and/or their carers;

4.The local healthcare system should consider the overall costs of complex RA, beyond drug acquisition costs to allow flexibility of prescribing choices, as necessary in this group of patients;

5.Local treatment pathways should reflect that treatments with particular modes of action are more suitable for individual patients with complex RA.

6.Management of complex RA patients should extend beyond guidelines and recognise additional sources of evidence including; clinical studies, Real World Experience (RWE) and post-marketing surveillance.

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SATURDAY, 06 JUNE 2020

HPR Patients' perspectives, functioning and health (descriptive: qualitative or quantitative)

SAT0610-HPR **COHERENT REHABILITATION – EXPERIENCES OF PEOPLE WITH INFLAMMATORY ARTHRITIS**

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Background: 20-40% of patients with inflammatory arthritis (IA) do not tolerate or do not have sufficient effect of the medication and experience considerable problems in their everyday lives. For these patients multidisciplinary rehabilitation and coherence in healthcare are of utmost importance (1). However, only little is known about coherence in healthcare among patients with inflammatory arthritis

Objectives: To explore how persons with IA experience coherence in their rehabilitation pathways

Methods: Semi-structured individual interviews with 11 persons with IA who had experience with rehabilitation across primary and secondary health care. Interviews were conducted in the patients' home before admission to an inpatient rehabilitation stay, during the admission and 2-3 weeks and 4-6 months after discharge. In addition, participant observations and informal interviews were performed during admission. The analysis involved case descriptions (2) and interpretation in a thematic analysis (3).

Results: The analysis derived a main theme *"a person centered approach"*, representing the importance for the person to meet professionals who listen and

acknowledge the persons own views rather than focusing on the "system", regulations and standards. In addition, 4 sub-themes were identified: 1)*"empowerment and disempowerment",* covering how most patients want to be in control and take action but they may lack the energy and ability to express their needs and thus give up; 2) *"Lack of communication and coordination"*, involving processes between the staff in the same department, between departments or sectors. Patients feel forced to take on coordinating tasks themselves, which they do not feel qualified to perform; 3) *"Interventions meant as help may be felt as restrictions"*, which encompass i.e. free physical therapy delivered at times not appropriate for the patient and types of support which can lead to a feeling of social control, and finally, 4) *"The system is difficult to get through".* Information about possible support are provided at random and some ask for a coordinating person.

Conclusion: Facilitators for coherent pathways among people with IA encompass dedicated professionals working with a person-centered approach aiming to empower people. This encompass to provide relevant knowledge and enable the person to ask for the right type of help. A coordinator may facilitate coherence.

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SATURDAY, 06 JUNE 2020

HPR Professional education, training and competencies

SAT0611-HPR

LOW ADHERENCE TO RECOMMENDED PHYSICAL THERAPY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: A MIXED-METHOD CONTENT AND UTILIZATION ANALYSIS.

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Background: Patients with axial spondyloarthritis (axSpA) encounter limitations during daily activities and societal participation which seriously impart health-related quality of life. Optimal management of axSpA consists of combined pharmacological and non-pharmacological treatment modalities, including the encouragement of exercise and the consideration of physical therapy given the latter's superior efficacy[1]. Few studies investigated the use of physical therapy and the alignment of treatment content with practice recommendations among patients with axSpA.

Objectives: 1) To estimate physical therapy use in patients with axSpA in a real life cohort; 2) to quantitatively and qualitatively describe the content of these physical therapy sessions; 3) explore possible determinants of physical therapy use and content.

Methods: This cross-sectional study included 197 patients diagnosed with axSpA (Males/Females: 62.4/37.6%; mean±SD, age 42.6±12.0, BASDAI 3.7±2.1, BASFI 3.6±2.4, BASMI 3.1±1.8) and recruited during their routine consultation. The mixed-method approach included questionnaires (physical therapy use and content, medication, depression/anxiety (HADS), fear (TSK), physician global disease activity (PGDA)) and an in-depth qualitative interview (content of physical therapy). Interviews were analyzed using the Qualitative Analysis Guide of Leuven by two physical therapists. Spearman's Rho correlations guided the exploration of determinants of physical therapy use and content.

Results: Less than half (42.6%, n=84) of the axSpA of patients were in treatment with a physiotherapist. Most patients (40.0%) reported a physical therapy frequency of 1x/week. Session duration was typically 30 minutes (51.7% of the sample) and longer in fewer cases (30.0%). Exercise was in only 31.7% the cornerstone of their sessions. The majority of subjects (53.3%) were classified as receiving 'passive therapy only', with 10% of cases in the 'exercise only' and 36.7% in the 'combination therapy' groups. Interviews also revealed a lack of clear patient-centered treatment goals. We found moderate associations between physical therapy use/content parameters and medication, spinal mobility, fear, anxiety, depression, physician's global disease activity versus (p<.05), but no relationship with patient-reported pain or disease activity.

Conclusion: Despite the importance of exercise and the added value of physical therapy in axSpA, few patients engaged in physical therapy sessions that include exercise training of adequate dosage. Remarkably, physical therapy utilization seems to be predominantly guided by psychological factors. Professional education for physical therapists should therefore include skills training in the management of complex clinical presentations[2]. Last, future research should prepare the evidence-based implementation of state-of-the-art physical therapy guidelines in axSpA.

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SATURDAY, 06 JUNE 2020

Rehabilitation

SAT0612

TEAM-REHABILITATION BENEFITS BODY COMPOSITION AND FUNCTIONAL OUTCOME BEYOND TIME OF THE REHABILITATION PERIOD IN INFLAMMATORY ARTHRITIS, OF WHICH BODY COMPOSITION IS LINKED TO CHANGE IN LEVEL OF CARDIORESPIRATORY FITNESS, WHEREAS MUSCLE MASS AND STRENGTH ARE LINKED TO PHYSICAL FUNCTIONING

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Background: Low physical activity, accumulated disability and disease chronicity contribute to adverse body composition and reduced cardiorespiratory fitness in patients with chronic inflammatory diseases. In the general population, physical exercise improves body composition, muscle strength and aerobic capacity but in inflammatory diseases it is not well established.

Objectives: To investigate whether 1) exercise intervention in patients with arthritis affects body composition, physical and aerobic capacity, and whether 2) body composition and physical capacity could explain outcomes as HAQ and aerobic capacity.

Methods: Consecutive patients with inflammatory arthritis and a clinical need for rehabilitation, ages 18-80 years, participated in a team-rehabilitation program for 4 weeks. Anthropometry, body composition assessed with bioelectrical impedance analysis, muscle force with hand grip strength and Times sit-to-stand test (TST), activity limitation with the HAQ score and cardiorespiratory fitness with the Åstrand 6-minute cycle test for VO2 max were measured pre-rehabilitation and after 3 and 12 months. The ANOVA model with Bonferroni correction, adjusted for age, sex and baseline measures, was used for the pairwise comparisons of repeated measures overtime. Association between body composition, physical functioning, and the course of HAQ and cardiorespiratory fitness for 12 months was determined with linear mixed models adjusted for age, gender and comorbidity.

Results: The study evaluated 149 patients with rheumatoid arthritis (RA), psoriasis arthritis, spondylarthritis and juvenile idiopathic arthritis, aged mean (SD) 53(13) years, 74% women, disease duration 21(13) years, HAQ 1.1(0.6) at inclusion and DAS28 4.1(1.3) for those with RA.

There was a statistically significant reduction of BMI between pre-rehabilitation and after 3 months, reduction of waist circumference, body fat, fat mass and the fat mass index after 3 and 12 months, adjusted p<0.05. The muscle mass of total body, arms and legs did not change significantly post-rehabilitation compared to pre-rehabilitation. Hand grip strength and TST improved together with reduction of HAQ and increased VO2 max after 3 and 12 months, adjusted p<0.05 adjusted for age, sex and baseline measures.

The HAQ overtime was independently associated with total body muscle mass, legs muscle mass, hand grip strength, and TST pre-rehabilitation, but not to the change of body composition overtime.

The course of VO2 max overtime was independently associated with pre-rehabilitation BMI, waist circumference, muscle mass of total body, arms and legs, fat mass, body fat, the fat mass index and TST, as well as with change of BMI, waist circumference, fat mass and the fat mass index between pre-rehabilitation and after 3 and 12 months.

Conclusion: We observed benefits of intervention with a team-rehabilitation program for 4 weeks on body composition profile, functioning, physical limitation and cardiorespiratory fitness, which were presented beyond the time of the rehabilitation period for up to 12 months. Different aspects of body composition and physical capacity were associated with levels of disability measured with HAQ and with cardiorespiratory fitness. This study indicates that in patients with inflammatory arthritis, muscle mass and strength were linked to HAQ over time, whereas the measures of body composition could be more linked to cardiorespiratory fitness than to HAQ.

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SATURDAY, 06 JUNE 2020

HPR Interventions (educational, physical, social and psychological)

SAT0613-HPR

EFFECT OF CERVICAL STABILIZATION EXERCISES ON CERVICAL POSITION ERROR IN PATIENTS WITH SPONDYLOARTHRITIS: A RANDOMIZED CONTROLLED TRIAL

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Background: Proprioception sense might be deteriorated due to joint related diseases. Different exercise programs were shown beneficial for improving proprioception sense. However, the effect of exercise on cervical position error was not investigated in patients with axial spondyloarthritis (axSpA).

Objectives: To investigate the effect of cervical stabilization exercises on cervical position error in patients with axSpA.

Methods: Thirty-nine patients with axSpA were randomly allocated into two groups as exercise group (n: 20, 11 males) and control group (n: 19, 12 males). All patients were evaluated regarding to physical characteristics (age, body-mass index), disease activity (Bath Ankylosing Spondylitis Disease Activity Index), functional status (Bath Ankylosing Spondylitis Functional Index), and spinal mobility (Bath Ankylosing Spondylitis Metrology Index). Cervical position error was evaluated in flexion, extension, rotation and lateral flexion directions and was calculated using a special formula (1). All evaluations were performed at baseline and after six weeks. Exercise group performed a progressive home-based cervical stabilization exercise program, while the control group did not receive any exercise intervention. Exercise adherence control and exercise progression was delivered by sending messages and video instructions via a freeware and cross-platform messaging service (WhatsApp Messenger) in a weekly basis.

Results: Baseline physical and disease related characteristics were similar between groups (p>0.05, table 1). Exercise group showed significant improvements in all directions related to cervical proprioception following six weeks (p<0.05, Table 2), however, no improvements were observed in the control group (p>0.05, Table 2).

Table 1. Comparison of the Groups at Baseline

	Exercise Group (n: 20) Median (IQR 25/75)	Control Group (n: 19) Median (IQR 25/75)	p*
Physical Characteristics			
Age (years)	40.5 (36.0/52.5)	44.0 (39.0/49.5)	0.496
Body-Mass Index (kg/m^2)	27.5 (24.5/30.2)	26.8 (23.6/29.3)	0.569
Disease Related Characteristics			
BASDAI (score)	2.0 (1.0/3.3)	1.8 (1.3/2.5)	0.687
BASMI Total (score)	2.9 (1.7/4.1)	2.3 (1.8/3.1)	0.127
BASFI (score)	1.8 (0.6/2.9)	1.2 (1.0/2.2)	0.496

*Mann-Whitney U Test, IQR 25/75: Interquartile range 25/75, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, BASMI: Bath Ankylosing Spondylitis Metrology Index, BASFI: Bath Ankylosing Spondylitis Functional Index, p<0.05.

Table 2. In-Group Comparison of Cervical Position Sense Error

	Before Median (IQR 25/75)	After Median (IQR 25/75)	p*
Exercise Group (n: 20)			
Flexion (°)	4.9 (2.2/7.0)	2.8 (1.7/3.8)	**0.033**
Extension (°)	4.5 (3.3/6.4)	3.1 (1.8/4.8)	**0.040**
Right Rotation (°)	5.2 (3.0/8.9)	3.7 (1.9/4.7)	**0.006**
Left Rotation (°)	4.3 (2.5/5.0)	2.8 (2.2/3.3)	**0.017**
Right Lateral Flexion (°)	4.9 (3.3/6.8)	2.3 (1.8/3.7)	**0.009**
Left Lateral Flexion (°)	4.3 (2.1/6.7)	2.0 (1.5/3.4)	**0.010**
Control Group (n: 19)			
Flexion (°)	6.3 (3.5/7.3)	5.2 (3.8/7.0)	0.856
Extension (°)	5.5 (4.5/7.3)	4.1 (3.3/8.2)	0.809
Right Rotation (°)	6.4 (4.3/9.0)	5.5 (3.0/8.5)	0.472
Left Rotation (°)	5.4 (3.5/7.9)	5.0 (3.5/7.2)	0.778
Right Lateral Flexion (°)	5.9 (3.6/8.4)	4.3 (2.7/7.7)	0.717
Left Lateral Flexion (°)	3.8 (2.4/5.6)	4.9 (2.9/5.7)	0.904

*Wilcoxon Signed Rank Test, IQR 25/75: Interquartile range 25/75, °: degree, p<0.05.

Conclusion: A six-week cervical stabilization exercise program is beneficial for impaired cervical proprioception sense in patients with axSpA.

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SAT0614-HPR

IDENTIFYING AND OPTIMISING MULTIPLE INTERVENTION COMPONENTS AND THEIR DELIVERY WITHIN A SELF-MANAGEMENT SMARTPHONE APP FOR PEOPLE WITH SJÖGREN'S SYNDROME: A QUALITATIVE STUDY

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Background: Sjögren's syndrome (SS) is an autoimmune rheumatic disease with diverse symptoms including mental and physical fatigue, dryness, pain and sleep disturbances. These symptoms are interconnected and rarely occur in isolation. Improving symptoms and quality of life requires people with SS to navigate multiple interventions and engage in self-management. Smartphone applications (apps) can deliver multiple cognitive and behaviour-based interventions in users' everyday daily lives and are readily accessible. However, delivering several therapeutic interventions together within a single coherent self-management app requires systematic and evidence-based selection of intervention components, and an understanding of existing self-management approaches and their associated challenges for those living with SS.

Objectives: To identify theory-based intervention components for inclusion in a SS self-management app. To understand the self-management approaches and challenges of those living with SS to inform in-app component delivery.

Methods: First, to identify intervention components within the app, existing interventions that target each symptom of fatigue, dryness, pain, sleep disturbance were identified through a literature search. Their content was coded by the research team using behaviour change techniques and the Theoretical Domains Framework[1]. The content was grouped to form five intervention components which target multiple symptoms.

Second, to understand SS self-management approaches and challenges, 13 people living with SS took part in a series of qualitative focus groups (n=6) and design workshops (n=7). Focus groups involved participants discussing their own self-management experiences and approaches (e.g. when and how they employed a variety of techniques). In design workshops participants sketched metaphors to explain these experiences and used craft materials to create "Magic Machines"[2] addressing their self-management challenges. Focus groups and design workshops were audio-recorded, transcribed, thematically analysed as a single data set, and findings mapped to the self-determination theory[3] dimensions of capability, autonomy, and relatedness.

Results: Intervention components identified were: i) SS psychoeducation, ii) relaxation techniques, iii) activity pacing and goal setting, iv) assertiveness and communication skills, and v) sleep and dryness tips. Participants tackled complex symptom patterns (i.e. symptom interrelatedness and flares) using different self-management approaches; reactively (focusing on the most severe symptom) or systematically (one symptom at a time). Knowing which intervention techniques to choose was felt to be challenging; however the availability of multiple interventions techniques provided a sense of optimism

and motivation. Participants were enthusiastic about accessing several intervention techniques via an app, but warned that smartphones and technology can exacerbate mental fatigue and eye dryness. The invisible nature of symptoms, and highly visible nature of management techniques (e.g. applying eye drops), presented further self-management challenges relating to their interactions with other people.

Conclusion: Promising components to include in an SS app were identified but should be tested in an optimisation trial. The in-app delivery of component modules should be designed to support diverse self-management approaches, choice and autonomy, yet provide module recommendations and guidance when needed, and be simple to use to reduce mental fatigue and dry eye symptoms. A self-management app should also be designed to enable users to share information about SS with other people.

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SATURDAY, 06 JUNE 2020

HPR Patients' perspectives, functioning and health (descriptive: qualitative or quantitative)

SAT0615-HPR FACTORS ASSOCIATED WITH PATIENT ACTIVATION IN PEOPLE WITH RHEUMATIC CONDITIONS

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Background: Patient activation describes the skills, abilities and confidence someone uses to actively manage their health. Patient activation abilities in rheumatology are unclear, and there is little knowledge about factors that explain variation in patient activation. Therefore, understanding these factors can contribute to the development of appropriate, rheumatology-specific interventions targeting activation. The Patient Activation Measure (PAM) captures patient activation and provides people with both a score and a level to describe how able they are to actively manage their health.

Objectives: To explore longitudinal changes to patient activation (measured using the PAM) (Hibbard *et al*., 2005), and the PAM's associations with related constructs (including self-efficacy, health literacy and health beliefs) in a sample of participants with inflammatory arthritis.

Methods: A postal survey was administered at two time points that were nine months apart. This survey captured the PAM and a range of clinical, demographic and psychosocial variables in a sample of rheumatology patients from 6 NHS sites in England. The measures included in the survey had been selected based on both theory and prior qualitative research and the survey pack was designed in collaboration with a patient partner. Following data collection, candidate variables for a multiple regression analysis were initially identified using univariable analysis. These variables were included in a forced entry multiple regression at each time point, and the variables that were statistically significant contributors at a 0.1 level were included in the final models. Changes to PAM scores over time were investigated using a Wilcoxon matched-pair signed rank test.

Results: 251 participants completed the first survey and 154 participants completed both full surveys. Self-efficacy, illness beliefs, health literacy and health locus of control were consistently associated with variance in PAM scores. The first three factors were also predictive of variance in PAM levels. With the 154 participants who fully completed both surveys, there was a statistically significant difference in participants' PAM scores between the two surveys.

Conclusion: The findings suggest factors that may be targets for interventions that aim to increase patient activation. The changes to PAM scores across the data collection period also suggest that when using the PAM as a clinical tool, healthcare professionals would benefit from incorporating regular reviews and preparations for any increases or reductions in patient activation.

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SAT0616-HPR IMPLICATED FACTORS IN THERAPEUTIC ADHERENCE OF PATIENTS WITH RHEUMATOID ARTHRITIS: THE PATIENT´S PERSPECTIVE

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Background: Therapeutic adherence has become a topic of growing interest for medical research. Studies have reported non-adherence rates of 20-50% in rheumatoid arthritis (RA) patients (1). Poor adherence has a negative impact on disease outcomes and implies an economic burden for the health system (2). Identifying the potential risk factors for non-adherence is essential to develop intervention strategies to solve this problem

Objectives: To establish the contribution of illness and medication beliefs to therapeutic adherence in RA. To explore the association of treatment adherence with other patient and disease factors.

Methods: RA patients ≥ 18 years old from a military hospital diagnosed with RA based on ACR /EULAR 2010 criteria were included in a cross-sectional study. Compliance Questionnaire Rheumatology (CQR) was used to assess treatment adherence. Unsatisfactory compliance was defined as taking correct dosing < 80%. Illness and medication beliefs were evaluated using the "Brief Illness Perception Questionnaire "(IPQ-b) and the "Beliefs about medicine questionnaire" (BMQ). Demographic data and clinical characteristics were collected by standardized clinical interview and revision of medical records.

Results: 144 patients were included the study, 106 (73.6%) women, with a mean age of 62 years (SD 12) and median disease duration of 5 years (interquartile range 25-75: 2-11). 113 (78.4%) patients showed good treatment adherence. No differences were observed regarding demographics and clinical characteristics. Strong beliefs about drugs potential damage was associated with poor compliance (13±5 vs. 11±3, p= 0.013), meanwhile increased belief in medication necessity was associated with good compliance (21±3 vs. 20±3, p= 0.015). From the illness perception measures, adherent patients had increased feeling of treatment control (8.8± 1.5 vs 7.7± 2.1,p= 0.008) and greater emotional response (6.2±3.1 vs 4.8±3.4,p= 0.042). In a multivariate analysis was found that for each unit of increase in the score of BMQ´s damage domain, adherence was reduced by 20% (CI 95% 0.7-0.9, p= 0.001); for each unit of increase in the treatment control item of the IPQ-b, adherence increased 1.42 times (CI 95% 1.1-1.8,p= 0.006); and for each unit of increase in the emotional response item of the IPQ-b, adherence increased 1.2 times (CI 95% 1.08-1.46,p= 0.002).

Conclusion: Illness and medication beliefs could influence compliance to treatment in patients with RA.

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SAT0617-HPR QUALITATIVE STUDY EXPLORING THE BARRIERS AND FACILITATORS TO HOME-BASED EXERCISE PROGRAMS ADHERENCE WITH KNEE OSTEOARTHRITIS: THE PERSPECTIVES PHYSIOTHERAPISTS AND PATIENTS.

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Background: Home exercise programs are widely used in the treatment of knee osteoarthritis (OA). However, adherence to these exercises decreases in the long term due to different factors. In recent years, new approaches are being developed to increase exercise adherence (EA) for patients with OA. Although it is known that EA is low in Turkish patients, there is no study that examines the

barriers of adherence to home exercise programs in patients with OA by qualitative research methods.

Objectives: Aim of our study was to investigate the barriers and facilitators for adherence of home-based exercises for knee osteoarthritis management from the perspective of physiotherapists and patients.

Methods: A Qualitative study by using focus groups discussions and semi-structured interviews were designed to investigate the barriers and facilitators to home-based exercise program adherence for OA. Two researchers facilitated focus group interview. Participants of focus group members were eight physiotherapists (PT) working with OA with different experience levels. Third researcher conduct the interviews which lasted 30-60 minutes with patients (patients with knee OA, n=5 ages>50). Data were audio recorded, transcribed verbatim and thematically analyzed with NVIVO 12 software. Three researchers conducted the thematic analysis to ensure the validity.

Results: In total, 25 main themes from the focus group discussions and interviews were determined. Major barrier themes from focus group were (a) beliefs to exercise benefits (b) patient education and (c)fear avoidance beliefs on exercise; from the interviews were (a)negligence of self-management (b) fatigue and (c)patient education. Patients and therapists all agreed for patient education is one of the most important factors for home EA. Patients wanted to get education on arthritis management. A patient said: *"Actually, the clinicians should give information more deeply. I don't know which is correct for me after therapy, resting or moving?"* Major facilitator themes from the focus group were (a)motivation from PT (b)client-centred exercise (c)digital technology; from interviews were (a) motivational approaches of therapists (wats-up messages) (b) having pain and (c)patient education for disease management. Therapists agreed on that personalized exercise is the most important facilitator. A therapist commented, *"If the personalized exercise given the patient with correct intensity and repetitions, I don't think that patients would not do their home exercises."*

Conclusion: This is the first qualitative study about exercise adherence in knee osteoarthritis in Turkey. It has been determined that the lack of education and motivation are the most important barriers. More studies are needed to examine the factors affecting EA for patients with OA. In future studies, implementations to increase home EA on Turkish patients with OA should be investigated by qualitative research methods.

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SAT0618-HPR PATIENTS WITH INFLAMMATORY MYOPATHIES WHO DO NOT REACH HEALTH ENHANCING LEVELS OF PHYSICAL ACTIVITY REPORT HIGHER LEVELS OF ANXIETY AND DEPRESSION - A CROSS-SECTIONAL STUDY OF SELF-REPORTED DATA

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Background: The adult idiopathic inflammatory myopathies (IIM) comprise dermatomyositis (DM), polymyositis (PM), immune-mediated necrotizing myopathy (IMNM), antisynthetase syndrome (ASS), overlap myositis and inclusion body myositis (IBM). Impaired physical capacity, self-reported fatigue and pain are common features in IIM. Quality of life is reduced compared to population-based reference values. To our knowledge self-reported levels of physical activity has not been studied in patients with IIM. Further, anxiety and depression are common in other rheumatic diseases, such as SLE, but is less studied in IIM, and not previously in relation to levels of physical activity. There is evidence for symptom reducing effects of exercise for patients suffering from depression (1).

Objectives: The objective of this study is to assess the levels of self-reported physical activity, depression and anxiety amongst adult patients with IIM. A further aim is to evaluate differences in anxiety/depression based on levels of physical activity as well as to analyze relationships between physical activity and anxiety/depression.

Methods: All patients with IIM visiting the Rheumatology clinic at Karolinska University Hospital in Solna between February 2019 and January 2020 where asked to fill in questionnaires about their levels of physical activity for the last seven days using the International Physical Activities Questionnaire – short form (IPAQ), and anxiety and depression using Hospital Anxiety and Depression Scale (HADS). The myositis team nurse distributed the questionnaires. Spearman's rho was used for correlation analysis. Kruskal-Wallis test and post-hoc adjustment with Bonferroni correction was used to analyze group differences. HADS is scored in two separate scales, one for depression (HADS-D) and one for anxiety (HADS-A). The cut-off value for probable depression or anxiety is ≥8 of a maximum of 21 per scale (2). IPAQ-results was scored as 1 (low, < 150 min/w), 2 (moderate, ≥ 150 min/w – health-enhancing levels of physical activity, HEPA, according to WHO) and 3 (high, ≥ 300 min/w).

Results: A total of 61 patients answered the questionnaires. 52 (85 %) of the patients reported to reach HEPA and 24 of these patients reported to be active on a high level. 22 patients (36 %) scored probable anxiety or depression, with six scoring ≥8 for both depression and anxiety. Patients with low levels of physical activity (IPAQ-1) scored significantly higher anxiety and depression compared to those reaching HEPA (IPAQ-2 and IPAQ-3) p<0.0001 – 0.020. The correlation between physical activity and depression (Fig. 1) was rs=-0.48 (-0.66; -0.26) and between physical activity and anxiety (Fig. 2), rs=-0.27 (-0.49; -0.02).

Conclusion: Self-reported data indicates that most patients with IIM in this sample reached HEPA level or higher. Patients who do not reach HEPA score significantly higher anxiety and depression compared to those reaching HEPA. However, levels of physical activity correlates moderately to depression and weakly to anxiety. The number of patients who reached HEPA is high compared to studies in rheumatoid arthritis or the general population. This could be explained by frequent visits to physical therapists early in the disease and yearly check-ups with a focus on exercise and physical activity. Further the inter-professional myositis team also has a focus on exercise and the importance of everyday physical activity. This is cross-sectional, self-reported data and longitudinal studies are needed also including objective measures. This is preliminary data with data collection ongoing throughout 2020.

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SAT0619-HPR AN AUDIT OF GLUCOCORTICOID PRESCRIPTION IN PATIENTS WITH GIANT CELL ARTERITIS

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Background: Giant cell arteritis (GCA) is treated with high dose glucocorticoids and progressively reduced over months to years.

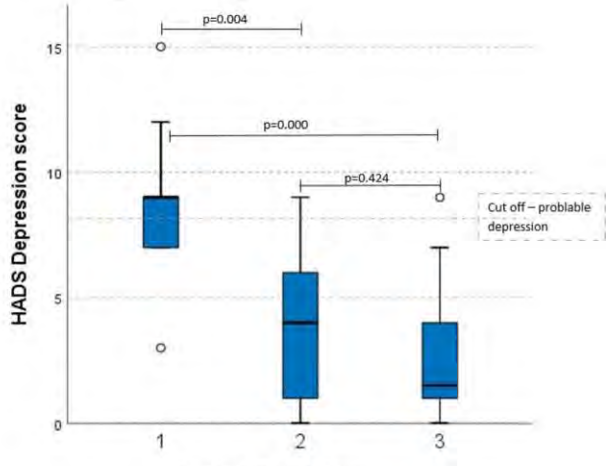


Figure 1. IPAQ level
1-low physical activity, not reaching health-enhancing levels of physical activity (HEPA), 2-moderate physical activity, reaching HEPA, 3-high physical activity, surpasses HEPA

Objectives: We undertook an audit to evaluate self-reported adherence to the original recommended glucocorticoid course and explored reasons for any variation.

Methods: We recruited patients attending a single rheumatology department over 18 months. Respondents were given two self- administered questionnaires

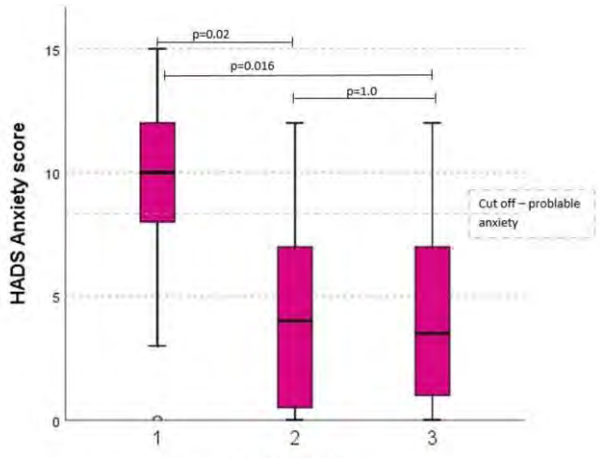


Figure 2. IPAQ level

1-low physical activity, not reaching health-enhancing levels of physical activity (HEPA), 2-moderate physical activity, reaching HEPA, 3-high physical activity, surpasses HEPA

to record information regarding their use of glucocorticoids during the "last 7 days" and during the "last 6 months". We retrieved 132 questionnaires (of whom 6 were discarded as incomplete). All data was analyzed using SPSS Statistics v22.
Results: Of the 126 patients (mean age 74.9 ± 7.7 years), 59% were female. The mean duration of disease was 22.5 ± 19.1 months in patients with GCA and 32.9 ± 29.9 months in those with GCA and polymyalgia rheumatica (PMR). The mean daily number of medications taken was 9.2 ± 5.2 (range: 1 - 30); the mean number of types of daily tablets taken was 5.0 ± 2.1 (range: 1 - 10). The mean daily number of glucocorticoid tablets taken was 3.2 ± 2.6 (range: 0 - 12), with a mean daily dose of 11.1 ± 10.3 mg (range: 0 - 60 mg). Overall, in the last 7 days, 22% and in last 6 months, 40% of patients were not following their original recommended steroid regimens (Table 1). The total mean glucocorticoid dose in the "last 7 days" group (n=81) was 77.8 ± 70.1 mg/week (11.1 ± 10.1 mg/day) whilst the total mean glucocorticoid dose in the "last 6 month" group (n=45) was 1782.0 ± 1543.3 mg/6 month (9.9 ± 8.6 mg/day). Most respondents stated their glucocorticoid non-adherence was due to medical advice; other reasons included forgetting, fear of side e ects, or confusion about di erent preparations of prescribed glucocorticoids. The presence of PMR did not influence glucocorticoid adherence.

Table 1. Glucocorticoid used compared to original regimen in GCA

	Last 7 days (%)	Last 6 months (%)
Higher than prescribed	16	22
Lower than prescribed	6	18
Same as prescribed	78	60

Conclusion: There is significant variation in the use of glucocorticoids compared to the original starting regimen in patients with GCA, with or without PMR. However, the amount of the discrepancy is small. The commonest reason for non-adherence was medical advice received from either primary or secondary care.
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SAT0620-HPR INACTIVITY BEHAVIOR AND EXERCISE BARRIERS IN PATIENTS WITH BEHÇET'S DISEASE

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Background: Behçet's Disease (BD) is a chronic, inflammatory, rheumatic disease that is characterized by mucocutaneous lesions and can be seen major organ involvement such as eyes, musculoskeletal system, gastrointestinal system and central nervous system. Impaired quality of life, aerobic capacity, respiratory function and life satisfaction, sleep disorders, depression, anxiety and fatigue are seen commonly in BD patients like the other rheumatic diseases. Considering that regular physical activity effects survival for patients and healthy people, it is important to determine the factors affecting physical activity level and exercise barriers.
Objectives: The aim of this study is to investigate physical activity level and exercise barriers in patients with BD.
Methods: 45 patients were included in the study. Physical activity level, exercise barriers, fatigue, depression, pain, quality of life and aerobic capacity were evaluated with International Physical Activity Questionnaire (IPAQ), Exercise Barriers and Benefits Scale (EBBS), Fatigue Severity Scale (FSS), Beck Depression Inventory (BDI), Visual Analog Scale (VAS), Behçet's Disease Quality of Life Questionnaire (BDQoL) and 6 minutes walk test, respectively. Spaerman's Correlation Coefficient were used to investigate the relationships between exercise barriers and other parameters.
Results: IPAQ demonstrated that 22 (48.8%) of the patients had low level physical activitiy. Additionally, physical activity levels significantly correlated with both exercise barriers (rho= -0.345) and exercise benefits (rho= 0.320) ($p<0.05$). BDQoL scores also correlated significantly with exercise barrier scores (rho= 0.338), ($p<0.05$). No significant relationships were observed for other parameters.
Conclusion: Exercise and physical activity are of great importance because of its positive contribution to the musculoskeletal system for BD patients' rehabilitation. Thinking of negative effects of physical inactivity, patients with Behçet disease should be encouraged to exercise. Also, reasons of physical inactivity should be investigated and treated.
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SAT0621-HPR EVALUATION OF THE SOCIAL IMPACT OF THE DISEASE IN PATIENTS WITH REUMATOID ARTHRITIS, ANQUILOSING SPONDYLITIS, AND SYSTEMIC LUPUS ERYTHEMATOSUS.

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Background:
Objectives: To describe the impact of the disease on patients with rheumatoid arthritis (RA), systemic lupus erythematosus (SLE) or ankylosing spondylitis (EA) on the social health of people who suffer from it.
Methods: Cross section of a consecutive sampling of patients with AS, RA or SLE. Selection criteria: age ≥18 years with AS (ASAS criteria), AR (EULAR / ACR 2010 criteria) and SLE (ACR-EULAR criteria) able to understand and willing to perform the questionnaires. Protocol: All patients who attended a consultation between October and December 2019 were offered to participate in the study. After their approval and verification of the inclusion criteria, they conducted a battery of PROMIS platform questionnaires focused on assessing their social health. Likewise, data on their disease, comorbidities and socio-labor profile were collected. All participants signed an informed consent and the study was approved by the CEIC of the referral hospital.
Main outcomes: The variables collected by the questionnaires evaluate social health in several areas: mobility, depression, satisfaction with social relationships, social isolation, company, ability to participate in social activities, emotional support, instrumental support and support through information. Statistical analysis: Descriptive, bivariate analysis using t-student, ANOVA and $\chi 2$;, followed by multivariate linear regression (RLM) (Vd: ability to participate in continuous social activities 7-35).

Results: 151 patients participated: 50 with RA (90% women, mean age 55.12 ± 13.64 years), 51 with AS (51% women, 52.59 ± 12.15 years) and 50 patients with SLE (96 % women, mean age 47.14 ± 11.3 years). The most frequent comorbidities were: arthritis, visual impairment, anxiety and depression (table 1). These results present a greater tendency to depression and anxiety patients of SLE. No significant differences were observed in most of the social questionnaires analyzed between groups (table 2), except in a worse mobility in patients with RA and AD compared to SLE (p = 0.017). About half of the patients in all groups had depression (43%) and reduced mobility (63.6%). All groups are satisfied with their social role 128 (85.3%), have the capacity to participate in social activities 140 (94%) and feel accompanied 147 (97.4%). On the contrary, the social isolation figure is 42 (28%). Social isolation implies an affectation of the serious social role in patients who claim to be accompanied, so it is not secondary to loneliness or lack of family support.

In the multivariate analysis it was observed that the independent variables that were associated with the ability to participate in social activities were satisfaction with social relations (β = 0.349 [p = <0.001]), mobility (β = 0.309 [p = < 0.001]), depression (β = -0.186 [p = <0.011]) and social isolation (β = -0.195 (p = 0.001)). This model would explain 32% of the variability in the ability to participate in social activities. (R2 = 0.32).

Conclusion: The predictors of the ability to participate in social activities in patients with RA, AD and SLE were: depression, mobility deficit, social isolation and satisfaction with social activities. Patients with RA, AD and SLE present similar data, so there are no differences due to pathologies in the social role, highlighting that they have a good social support and despite this there is social isolation being able to be associated with the deficit in mobility and high rates of depression.

Disclosure of Interests: None declared

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SAT0622-HPR SAFETY IN PATIENTS WITH RHEUMATOID ARTHRITIS IN BIOLOGICAL TREATMENT OVER 65 YEARS OF AGE

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Background: A bias has been described with the lowest prescription of biologic treatments (bDMARD) in patients with rheumatoid arthritis (RA) in the elderly, despite presenting activity rates comparable to young population and higher risk of functional disability. This could be due to concerns about co-morbidities and polypharmacy1.

Objectives: 1) To define the characteristics of patients with RA ≥65 years and bDMARD to follow up in the Day Hospital of University Assistance Complex of León during the last year. 2) To record the incidence rate (IT) and ratio of incidence rates (RDI) of infections, neoplasms and cardiovascular events (CD) during the course of your therapy.

Methods: Observational, retrospective study of patients diagnosed with RA according to ACR 1987 and/or ACR 2010 criteria in intravenous biological treatment during 2019 with ≥65.

Results: 40 patients with an average age at diagnosis of 55.9±15.76 years were included, 67.5 % of them were women. The average duration of the disease was 17.65±13.15 years. 40% had a history of smoking, 35% hypertension, 20% dyslipemia and 20% diabetes mellitus. A 97.5% were positive FRRA, 57% positive ACPA, 37.5% nodular and 65% erosive. As for pre-treatment, 70% had been with conventional (cDMARD) ≥2DMARD (Methotrexate (MTX) (92.5%) and Leflunomide (60%)). The mean dose of prednisone was 8.79 ±10.14 mg/day. The incidence rate of infections was 1.5%, and neoplasms and CD were 0.75% per person-years. The age at the beginning of the first bDMARD was 67.45 ± 8 years, the second (n=20) 67.98±6.64 and the third (n=7) 71.79±7.49. The first biological was a 52.5% anti-TNF, 5% anti-CTLA4, 30% anti-CD20 and 12.5% antiIL6 (25% monotherapy and combined with MTX 57.5%). The second was 30% anti-TNF, 25% antiCTLA4, 15% antiIL6 and 30% antiCD20 (50% in monotherapy and 40% methotrexate); with the third anti-TNF 42.85%, antiCTLA4 14.29%, antiIL6 14.29% and antiCD20 28.57% (42.86% in monotherapy and 42.46 with methotrexate). The mean doses of prednisone were 6.08±6.82, 4.38±7.21 and 6.95±5.94 mg/day respectively. The IT of bDMARD infections were 8.81%, 19.81% and 7.4% person-years; of neoplasia 1.04%, 0 and 0; and EC 3.63%, 0 and 1.85 person-years. The RTIs with first, second and third biological infections were: 5.88, 13.25, 4.95; with neoplasms 1.38; with EC 1.38, 0 and 0.69. The mean total accumulated corticosteroid dose was 17.69±15.01 mg/day.

Conclusion: 1) Patients over 65 years old receiving bDMARD in our Day Hospital in 2019 were long-standing RA with aggression data, who had not responded to ≥2 cDMARD and required medium-high doses of prednisone.

2) In our sample there is a link between incidence of infection and the introduction of biological therapy, which is maintained with the increasing age of our patients, and it is not so clear with neoplasms and CD. These data are consistent with the existing literature[1,2,3].

3) Larger, comparative studies with RA under 65 years are needed, but it is reasonable to conclude that if bDMARD is required, elderly patients could be a high-risk group for infections, requiring special monitoring and follow-up.

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SAT0623-HPR THE LIVED EXPERIENCES OF COGNITIVE DYSFUNCTION IN ADULTS WITH FIBROMYALGIA: A QUALITATIVE SYSTEMATIC REVIEW

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Background: Adults with fibromyalgia frequently report symptoms of cognitive dysfunction, often referred to as fibrofog. However primary research exploring cognitive dysfunction in the lives of adults with fibromyalgia is very limited (Kravitz and Katz, 2015).

Objectives: The aim of this review was to (i) synthesise the qualitative literature on the lived experiences of cognitive dysfunction in adults with fibromyalgia, (ii) develop common themes through thematic analysis and (iii) identify knowledge gaps to inform future research and clinical practice in this area.

Methods: Seven electronic databases (MEDLINE, Embase, CINAHL, PsycINFO, Amed, Scopus and OpenGrey), reference lists of key articles and two high impact qualitative journals were searched from 1990 to November 2018. Articles were eligible for inclusion if they reported primary qualitative data exploring the experiences of cognitive dysfunction in adults with fibromyalgia. Included studies were appraised using the Critical Appraisal Skills Programme (CASP) qualitative checklist and extracted data analysed using narrative synthesis. SD conducted critical appraisal and data extraction on all included studies. FC, JL and ED reviewed five papers each. All papers were reviewed by two co-authors. Of the 1413 records identified, 15 studies were selected for inclusion.

Results: These studies included 208 women and 22 men with fibromyalgia, aged 18 to 72 years and representing seven different countries. Duration of diagnosis was four months to 34 years. Fourteen studies used interviews and one used focus groups. None of the included studies focussed exclusively on cognitive function in adults with fibromyalgia. Three studies identified themes specific to cognitive dysfunction and fibromyalgia symptoms. The remaining 12 studies presented relevant data intertwined with the overall lived experiences of fibromyalgia.

Cognitive dysfunction, as a part of fibromyalgia, was often unpredictable. Problems with memory and concentration that were most commonly reported were emotionally distressing and affected functional and vocational activities. Participants found communication effortful, with a negative impact on work, leisure and social activities. Stress, fear and worry around perceived cognitive changes were commonly expressed. Lost employment or changed work roles and relationships, due to cognitive difficulties, had negative impacts for many participants. The terms cognitive dysfunction and fibrofog were used interchangeably within the studies, but lacked common definition. This introduced uncertainty around whether participants and authors were describing the same phenomenon.

Conclusion: Adults with fibromyalgia experience unpredictable and emotionally impactful difficulties related to cognitive dysfunction. Functional impact was broad-reaching, particularly around work ability and lost employment opportunities. It is unclear how cognitive symptoms in fibromyalgia related to co-morbid symptoms such as pain, fatigue and poor sleep. Further research focusing on the full impact of cognitive function on the lives of adults with fibromyalgia is recommended to inform clinical practice. Research to establish clarity of definition of the terms cognitive dysfunction and fibrofog within fibromyalgia is highly recommended.

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SAT0624-HPR THE IMPACT OF PSORIATIC ARTHRITIS ON FOOT HEALTH AND INDICATION OF PODIATRY NEED IN A SECONDARY CARE SETTING

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Background: Psoriatic Arthritis (PsA) is a rheumatic disease affecting 0.19% of the UK population (1). It is characterised by asymmetric oligoarticular or polyarticular peripheral arthritis or axial disease with or without associated peripheral arthritis (2). Foot manifestations of synovitis, enthesitis, dactylitis and skin and nail involvement (3) are reported. Hyslop et al. have previously reported high levels of foot involvement but low current access to foot care (4). Outcome measures that include specific PsA related foot features do exist, e.g. Leeds Enthesitis Index, Tender Dactylitis Count (5). However there is currently no measure of foot involvement and impact in PsA (6).
Objectives: To identify the impact of PsA on foot health and indication of podiatry need in a secondary care outpatient setting.
Methods: convenience sample was taken from a consultant rheumatologist's outpatient clinic and screened. Only those with a diagnosis of PsA were included. Sampling was conducted over a ten-week period. Screening was done using the Swindon Foot and Ankle Questionnaire (SFAQ) (7), visual Analogue Scale (VAS), clinical judgement of need for podiatric intervention and the trust's eligibility criteria for routine podiatric care.
Results: The sample (n=16) was 31.3% male with a median age of 59 years (range 28-81).

Table 1. Footcare/Podiatric need identified

	Percentage (%)
Orthotic intervention, acute or routine care	81.3
Already being met	25.0
Eligible for care in podiatry primary care service	81.3

Table 2. SFAQ results

	Percentage Yes (%)
During the past week have your feet or ankles:	
Been painful?	68.8
Been Swollen?	62.5
Made walking difficult?	81.3
Made standing up difficult?	50.0
Stopped you going to work?	27.3
Made other daily activities difficult?	42.9
Do your shoes rub the skin on your feet or ankles?	31.3
Do you have callus or hard, dry skin?	50.0
Have you had your footwear adapted or insoles made?	25.0
Have you had surgery, or are you waiting for surgery, on your feet or ankles?	18.8

Conclusion: Of this patient group, 81.3% had a variety of foot care needs but these were being met in a limited number of cases (25%). Far more patients (81.3%) were eligible for care in the local trust's primary care podiatry service but were not engaging with this. 50% of the sample reported difficulty standing in the past week and 27.3% found their foot pain stopped them from going to work, indicating a clear need for foot health intervention.
Recommendations:
-Raise awareness of availability of podiatric care for PsA patients among patients and secondary care staff.
- Ensure adequate resources are allocated to manage this cohort of patients at a service provision level.
- Further research involving PsA patients referred into podiatry to assess the impact of podiatric intervention.
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Disclosure of Interests: None declared
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SAT0625-HPR FATIGUE AND CONTRIBUTING FACTORS IN CHINESE PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Ankylosing spondylitis (AS) is a systemic chronic inflammatory disease, which most likely occurs in young men. It mainly affects sacroiliac joints, axial skeleton, thoracic cage and seriously decreasing quality of life in AS patients[1,2]. In recent years, fatigue of AS patients has been paid more and more attention[3]. Fatigue is a complex feeling, diseased individuals describe fatigue as a sense of tiredness at rest, exhaustion with activity, lack of energy which affects daily work, inertia or lack of endurance, or as loss of vitality. It has been confirmed that fatigue is not only a symptom but may also be quantified by fatigue scores and can be modified by various measures depending on the underlying cause[4]. However, there has been no study about fatigue in AS patients in China.
Objectives: This study aimed to evaluate the predictors of fatigue and the effects of fatigue on HR-QoL among patients with AS.
Methods: A total of 150 AS patients were involved in the study. A series of questionnaires included: Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Metrology Index (BASMI), Bath Ankylosing Spondylitis Functional Index (BASFI), the 10 cm Visual Analog Scale (VAS), the Self-Rating Anxiety Scale (SAS), the Self-Rating Depression Scale (SDS), the Pittsburgh Sleep Quality Index (PSQI), the Health Assessment Questionnaire-Disability Index (HAQ-DI), the Short Form 36 Health Survey (SF-36) and the Fatigue Severity Scale(FSS). Independent samples t-test, Mann–Whitney U-test, Chi-square analysis, Pearson /Spearman correlation and binary logistic regression were used to analyze the data.
Results: The results demonstrated that 48.7% individuals with AS suffered from fatigue. Compared with AS patients without fatigue, AS patients with fatigue showed higher WHR(P<0.05), increased BASDAI (P<0.01) and poorer BASFI (P<0.05). Meanwhile, AS patients with fatigue tended to have more severe pain(P<0.05), higher degree of anxiety(P=0.001), more serious functional disability(P=0.001) and worse sleep quality(P=0.001). Binary logistic regression indicated that WHR (OR=1.78, P<0.05), BASDAI (OR=1.34, P=0.01), sleep disturbance (OR=2.35, P<0.05) were independent predictors of fatigue in AS patients**.** Additionally, the occurrence of fatigue significantly reduced the quality of life in AS patients both physically and psychologically.
Conclusion: These findings suggested that medical personnel should pay more attention to AS patients with fatigue and take effective measures to relieve fatigue.
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SAT0626-HPR

EXPLORING THE RELATION BETWEEN PAIN AND ACTIVITY AND PARTICIPATION BASED ON ICF IN CHILDREN AND ADOLESCENTS WITH JUVENIL IDIOPATIK ARTRIT: A PILOT STUDY

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Background: Functional limitation and inactivation are the most important problems in children with Juvenil Idiopatik Artrit (JIA).

Objectives: The aim of this study was to link and allocate items of Childhood Health Assessment Questionnaire (CHAQ) with activity and participation based on International Classification of Functioning, Disability and Health (ICF). The other aim was to examine the relationship between the pain and activity and participation determined on the basis of CHAQ with Juvenil Idiopatik Artrit (JIA).

Methods: Thirty-seven children and adolescents (26 girls, 11 boys, mean age=11.75±4.04 years) were included. The mean BMI of the participants was 19.61±4.52 kg / cm^2. Inclusion criteria: To be diagnosed with JIA according to ILAR classification. Being in the 6-18 age range. To be stable in drug use for at least 3 months or longer. Exclusion criteria:The presence of another disease. Intraarticularsteroid injection or surgery in any joint in last 3 months. Evaluations were made by the same pediatric rheumatologist and physiotherapist (PT) by face to face interview method. Pain was evaluated by use of Numeric Rating Scale (NRS) (0=no, 10=worst) and disability by CHAQ. As CHAQ score increases, disability increases. CHAQ has 8 categories. The highest score for any question determines the score for that category. The items of CHAQ were linked with ICF codes and allocated with the ICF components by three PT. Original scoring of CHAQ allocated to ICF components was used in order to calculate scores of activity and participation in accordance with clinical data for 37 JIA. The 20th item in the "Reach" category is not included in the calculation as it contains the body function component of ICF. The data was analyzed using Pearson's correlation coefficient.

Results: Mean score of NRS was 3.52±2.34. Mean activity and participation score of CHAQ was 0.51±0.58, 0.70±1.10, respectively. Based on expert distinction, activity and participation categories of ICF were covered 24 and 5 items of CHAQ, respectively. Pain had moderate correlation with activity (r=0.595; p=0.002) and participation (r=0.604; p=0.001) for CHAQ. Activity had high correlation with participation (r=0.702; p=0.000).

Conclusion: Pain in children and adolescents with JIA is an important parameter affecting activity and participation. Pain should be evaluated in all aspects due to the limitation of both activity and participation. CHAQ largely contains the activity component of ICF. The development of new questionnaire is needed to assess the participation of JIA children and adolescents in more detail.

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Table 1. Linking and allocating items of CHAQ

Items	ICF Code	ICF Component
DRESSING & GROOMING Dress, including tying shoelaces and doing buttons?	d5402	A
Shampoo his/her hair?	d5100	A
Remove socks?	d5403	A
Cut fingernails?	d520	A
ARISING Stand up from a low chair or floor?	d4103	A
Get in and out of bed or stand up in crib?	d4100	A
EATING Cut his /her own meat?	d550	A
Lift a cup or glass to mouth?	d4402	A
Open a new cereal box?	d440	A
WALKING Walk outdoors on flat ground?	d450	A
Climb up five steps?	d4551	A
HYGIENE Wash and dry entire body?	d510	A
Take a tub bath?	dd410	A
Get on and off the toilet or potty chair?	d4103	A
Brush teeth?	d5201	A
Comb/brush hair?	d5202	A
REACH Reach and get down a heavy object from just above his/her head?	d4452	A
Bend down to pick up clothing or a piece of paper from the floor?	d4105	A
Pull on a sweater over his/her head?	d5400	A
Turn neck to look back over shoulder?	b7101	Body Function
GRIP Write or scribble with pen or pencil?	d170	A
Open car doors?	d4450	A
Open jars which have been previously opened?	d4453	A
Turn faucets on and off?	d4402	A

Table 1. Linking and allocating items of CHAQ

Items	ICF Code	ICF Component
Push open a door when he/she to turn a door knob?	d4453	A
ACTIVITIES Run errands and shop?	d6200	P
Get in and out of car or toy car or school?	d4702	P
Ride bike or tricycle?	d4750	P
Do household chores	d6402	P
Run and play?	d9201	P

A:Activity, P:Participation

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SAT0627-HPR

SEXUAL QUALITY OF LIFE IN 39 FEMALE PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

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Background: Symptoms related to idiopathic inflammatory myopathies (IIM) such as weakness of skeletal muscles, pulmonary and articular involvement may have a negative impact on all aspects of life including sexual life.

Objectives: To assess sexual functioning in female IIM patients compared to age-/sex-matched healthy controls (HC) and to analyze the potential impact of clinical features on sexual health.

Methods: In total, 39 women (29 currently have a partner) with IIM [mean age: 54.7, disease duration: 11.8 years, dermatomyositis (DM, 19)/ polymyositis (PM, 16)/ necrotizing myopathy (IMNM, 3)/ inclusion body myositis (IBM, 1)] and 39 healthy controls (30 currently have a partner, mean age: 54.7 years) without rheumatic diseases filled in 11 well-established and validated questionnaires assessing sexual function (FSFI, SFQ28, BISFW), quality of sexual life (SQoL-F), pelvic floor function (PISQ-12, PFIQ-7), fatigue (FIS, MAF), physical activity (HAP), and depression (BDI-II). A standard laboratory testing was performed. Data are presented as mean ± SEM.

Results: Patients with IIM reported significantly higher prevalence and greater severity of sexual dysfunction (FSFI, BISF-W, SFQ28) and worse sexual quality of life (SQoL-F) compared to HC (table 1). Worse scores in IIM patients were associated with increased inflammation [CRP: FSFI (r=-0.378, p=0.0190), SFQ-28 Satisfaction domain (r=-0.346, p=0.0356), SQoL-F (r=-0.331, p=0,0479], greater muscle weakness of m. gluteus maximus/ m. gluteus medius/ m. iliopsoas [FSFI: (r=0.426, p=0.0368), (r=0.370, p=0.0368), (r=0.394, p=0.0252), SQoL-F (r=0.504, p=0.0044), (r=0.421, p=0.0204), (r=0.462, p=0.0100)], greater fatigue [FIS: FSFI (r=-0.358, p=0.0154), BISF-W (r=-0.415, p=0.0084), SQoL-F (r=-0.327, p=0.0481)], more severe depression [BDI-II: FSFI Arousal domain (r=-0.357, p=0.0299)], deteriorated quality of life [HAQ: BISF-W (r=-0.464, p=0.0033)], and worse ability to perform physical activities [HAP: FSFI (r=0.405, p=0.0105), BISF-W (r=0.480, p=0.0019)]. No associations were found with disease duration, prednisone dose or serum levels of muscle enzymes.

Table 1.

Questionnaire: score range (meaning)	IIM (n=39)	HC (n=39)	p-value
FSFI: Female Sexual Function Index: 2(worst)-36(best)	15.7±2.1	20.7±2.0	p=0.0421
BISF-W: Brief Index of Sexual Function for Women: -16 (worst)-75(best)	14.6±2.8	24.5±3.0	p=0.0134
SFQ28 Desire domain: Sexual Function Questionnaire: 5(worst)-31(best)	11.7±1.0	14.7±1.0	p=0.0457
PISQ–12: Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire short form: 0(best)-48(worst)	14.9±0.8	10.1±1.0	p=0.0005
SQoL-F: Sexual Quality of Life Questionnaire – Female: 0(worst)-100(best)	31.8±5.1	80.7±2.5	p<0.0001
PFIQ7: Pelvic Floor Distress Inventory Questionnaire – short form 7: 0(best)-300(worst)	24.7±6.3	10.1±2.7	*p=0.0820*
FIS: Fatigue Impact Scale: 0(best)-160(worst)	55.3±5.5	33.2±4.3	p=0.0025
MAF: Multidimensional Assessment of Fatigue Scale: 1(best)-50(worst)	22.0±2.0	15.7±1.4	p=0.0021
BDI-II: Beck's Depression Inventory II: 0(best)-63(worst)	12.8±1.5	6.6±0.9	p=0.0013
HAP: Human Activity Profile – adjusted activity score: 0(worst)-94(best)	51.0±3.5	80.2±1.6	p<0.0001
HAQ: Health Assessment Questionnaire: 0(best)-3(worst)	1.1±0.1	0.1±0.1	p<0.0001

Conclusion: Women with IIM reported significantly impaired sexual function and sexual quality of life compared to age-matched healthy controls. Worse scores in IIM were associated with disease activity, physical activity, fatigue, depression and quality of life.

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SAT0628-HPR "IT IS THE NEVER ENDING QUEST, HOW TO MOTIVATE PEOPLE" – HEALTH PROFESSIONALS' PERSPECTIVES ON SUPPORTING PHYSICAL ACTIVITY MAINTENANCE IN THOSE LIVING WITH AXIAL SPONDYLOARTHRITIS

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Background: Physical activity (PA) has been identified as a primary treatment option for people living with axial spondyloarthritis (axSpA) [1]. Yet, people living with axSpA can find it difficult to maintain PA at levels required to gain the evidenced benefits [2]. Intensive rehabilitation programmes harness the benefits of physical activity, but little is known about how to support PA maintenance when patients return to everyday life. The perspectives' of health professionals involved in rehabilitation programmes can provide important and rich insights into how people living with axSpA could be helped to maintain their PA.

Objectives: To explore health professionals' experiences of supporting PA maintenance during and after a rehabilitation programme for those living with axial spondyloarthritis.

Methods: A qualitative study was conducted using semi-structured interviews. Nine health professionals (i.e., 4 physiotherapists; 1 clinical nurse specialist; 1 rheumatology SpR; 1 psychologist; 1 occupational therapist; and 1 podiatrist) who contribute to a rehabilitation programme were recruited from the Royal National Hospital for Rheumatic Diseases in Bath, UK (*M* time contributing to course = 6.79 yrs, range 1-19.25 yrs; contact time over course range = 1 to 45 hrs). Interviews were audio recorded, transcribed verbatim, and a thematic analysis employed [3].

Results: Maintaining a physically active lifestyle is a challenge for those living with axSpA and is an issue that is currently not being addressed. Health professionals' perspectives on supporting PA maintenance was illustrated through four main themes: (1) Social environment (group dynamic, importance of others with the same condition, immersion of the disease, external peer groups); (2) Re-framing (education, ownership, exercise off the pedestal, combating fear, routine and habit); (3) PA support (enjoyment and interest, PA as flexible, encouragement and importance, balance and realistic expectations, internal and external feedback); and (4) Challenges for health professionals (training, resources, knowledge of transition process to everyday life, difficulty motivating). The reasons why people engage in PA play a key role within each of these themes.

Conclusion: Results emphasize the current lack of support for the maintenance of PA and the complexities and challenges involved in maintaining PA for people living with axSpA. Interventions to support PA maintenance should pay particular attention to the importance of socially supportive environments, the need for enjoyment, and the use of internal and external feedback. The challenges faced by health professionals in motivating those living with axSpA to engage in PA regularly suggests a need for more training opportunities in motivation and health behaviour change.

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SAT0629-HPR FACTORS ASSOCIATED WITH USE OF BIOLOGICAL THERAPIES FOR AXIAL SPONDYLOARTHRITIS IN CANADA. RESULTS FROM THE IMAS SURVEY.

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Background: Biologics have revolutionized the treatment of axial spondyloarthritis (axSpA). However, there is limited knowledge about factors associated with their use in Canada.

Objectives: To evaluate sociodemographic, healthcare and patient-reported outcomes (PROs) associated with the use of biologics in Canadian axSpA patients.

Methods: The International Map of Axial Spondyloarthritis (IMAS) is a cross-sectional online survey of non-selected patients with self-reported axSpA, conducted in 21 countries and endorsed by the Axial Spondyloarthritis International Federation (ASIF). IMAS captures the patients' perspective of the burden of axSpA. The Canadian adaptation included a review of the survey by an advisory board of axSpA patients and a national steering committee composed of the Canadian Spondylitis Association, rheumatologists and patients. Participants were recruited between August 2018 and February 2019. Sociodemographic and healthcare-related variables, as well as PROs (disease activity [BASDAI, 0–10], spinal stiffness [3–12], functional limitation [0–54] and psychological distress [GHQ-12]) were collected. Respondents were divided in 2 groups 1) biologic and 2) NSAIDs or no treatment, based on reported pharmacologic treatments. Statistical analyses were performed to assess associations between variables and biologic use (bivariate) and the relative weight of these associations (multivariate).

Results: 542 axSpA patients were recruited. Mean age was 44.3±13.9 years, 63.1% were female, 66.4% married and 81.0% educated to university/college level. 22.8% of patients lived >50 km from their rheumatologist. Mean BASDAI was 5.3±2.1 and mean GHQ-12 score (mental health) was 4.0±3.8. Nearly half (49.6%) were currently on a biologic. Reported incidence of side effects was lower for patients having biologics (42.5%) vs. a NSAIDs (53.7%) as part of their treatment armamentarium. Only 15.7% of patients had discontinued biologic therapy, the main reasons for withdrawal being physician recommendation (50%), side effects (50%) and personal choice (34%). Variables associated with biologic use included: membership of a patient support group (p<0.001), non-manual work (p=0.008), higher income level (p=0.039), having a combination of public and private insurance schemes (p<0.001) and diagnosis by a rheumatologist (p<0.001). Associated PROs were spinal stiffness (p=0.011) and diagnostic delay (p=0.030). In the multivariate analysis, all variables except income and diagnostic delay were associated with biologic use (Table 1).

Table 1. Analysis of sociodemographic and clinical variables in relation to pharmacologic treatment

Variable	Univariate linear regression		Multivariate stepwise linear regression	
	B	95% CI	B	95% CI
Income level	0.001	1.000–1.000	NA	NA
Employment—manual worker	**–0.761**	**0.266–0.822**	**–0.838**	**0.228–0.820**
Member of a patient support group	**0.937**	**1.797–3.628**	**1.116**	**1.754–5.309**
Health insurance scheme—combination	**0.209**	**1.162–1.307**	**0.215**	**1.132–1.357**
Diagnostic delay	0.009	0.993–1.026	NA	NA
Spinal Stiffness (3–12)	**0.099**	**1.022–1.193**	**0.220**	**1.090–1.424**
Diagnosed by rheumatologist	**0.535**	**1.412–2.067**	**0.335**	**1.041–1.877**

B, B coefficient; NA, [not applicable]

Conclusion: Canadian axSpA patients with greater social status, disease awareness, and insurance options are more likely to receive biologic therapy. Furthermore, Canadian physicians are more inclined to prescribe biologics to patients with increased spinal stiffness.

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SAT0630-HPR EFFECTS OF GOLIMUMAB ON WORK PRODUCTIVITY AMONG WORK-ACTIVE ANKYLOSING SPONDYLITIS, NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS PATIENTS IN GREECE: THE 'GO-UP' STUDY

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Background: Golimumab is a tumor necrosis inhibitor (TNFi) approved for the treatment of axial SpA (axSpA) and psoriatic arthritis (PsA), both falling under the Spondyloarthritis (SpA) domain. Real-world data regarding its effect on work productivity (WP) and activity impairment (AI) are limited

Objectives: To assess the impact of golimumab on WP and AI over 12 months of treatment in patients with SpA, overall, and in the axSpA and PsA subpopulations

Methods: A 12-month non-interventional, multicenter, prospective study performed in the routine clinical care. Data were collected at baseline (BL: prior to treatment onset), 3, 6 and 12 months. Adult work-active consented patients with axSpA [ankylosing spondylitis (AS) or non-radiographic axSpA (nr-axSpA)] or PsA, newly initiated on golimumab as per approved label, were concequetively enrolled by 20 sites. Patients prior in >1 biologic agent, or switched from another TNFi due to primary non-response or safety were excluded. WP and AI was assessed with the Work Productivity and Activity Impairment: Specific Health Problem (WPAI:SHP) instrument

Results: Between Apr-2017 and May-2018, 121 (51: PsA, 70: axSpA) eligible patients (mean age: 45.4 years; 49.6% males; 69.0% overweight/obese; median disease duration: 11.3 months), (Figure 1), were enrolled. Median study duration participation: 11.9 months. Overall, 60.3% of the patients had previously received disease-modifying antirheumatic drugs and 16.5% biologics. At BL, the mean (standard deviation: SD) DAS28-ESR of the SpA population and PsA and axSpA subpopulations was 4.0 (1.3), 4.5 (1.2), and 3.6 (1.2), while the mean (SD) BASDAI score of patients with axSpA was 5.6 (1.9). At BL 94.1 and 96.7% of the SpA population reported WP loss and AI due to their SpA respectively, and at 3 months 87.3, and 88.0% respectively. In SpA population, the median BL WP loss and AI were 70.0% and 65.0% and decreased by a median of 31.4% and 40.0% at 3 months, by 44.2% and 40.0% at 6 months and by 50.0% and 50.0% at 12 months, respectively (Table 1). Improvements in WP loss and AI were noted in patients with PsA, axSpA, AS and nr-axSpA (Table 1). 12-month golimumab retention rate: 91.7%. No new safety signals emerged

Table 1. Decreases from BL at 3, 6 and at 12 months in WP loss and overall AI with the WPAI:SHP instrument

	WP loss (%)			AI (%)		
	Decrease from BL, median (n)			Decrease from BL, median (n)		
	3 months	6 months	12 months	3 months	6 months	12 months
Overall SpA population[a]	31.4[a] (n=102)	44.2[a] (n=94)	50.0[a] (n=87)	40.0[a] (n=107)	40.0[a] (n=101)	50.0[a] (n=92)
PsA	31.4[b] (n=46)	51.4[a] (n=42)	53.6[a] (n=40)	40.0[a] (n=47)	50.0[a] (n=44)	60.0[a] (n=40)
axSpA	33.0[b] (n=56)	30.4[b] (n=52)	45.5[b] (n=47)	40.0[a] (n=60)	40.0[b] (n=57)	40.0[b] (n=52)
AS[c]	25.1 (n=35)	29.9 (n=32)	39.8 (n=29)	20.0 (n=39)	30.0 (n=37)	30.0 (n=34)
nr-axSpA[c]	47.4 (n=21)	55.4 (n=20)	53.2 (n=18)	50.0 (n=21)	55.0 (n=20)	50.0 (n=18)

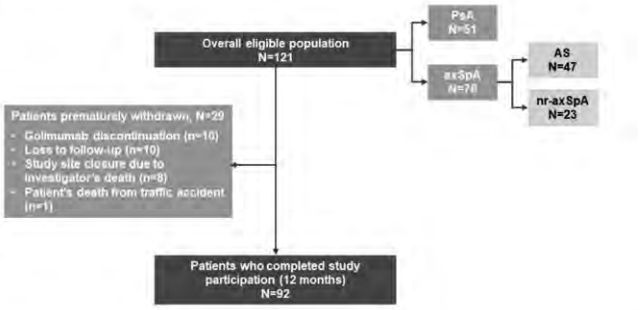
[a]Significant decreases (p<0.001; Wilcoxon signed-ranked test)
[b]Significant decreases (p<0.001; t-test)
[c]Statistical significance of the change from baseline was not examined due to the small observations' number

Conclusion: Patients in the SpA population and axSpA and PsA subpopulations treated with golimumab in a routine care setting experienced significant improvements in work productivity and daily activities at 3, 6 and 12 months after treatment initiation

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Figure 1. Study flow-chart and patient disposition per spondyloarthritis indication



AS: ankylosing spondylitis; axSpA: axial spondyloarthritis; nr-axSpA: non-radiographic axial spondyloarthritis; PsA: psoriatic arthritis; SpA: spondyloarthritis

AbbVie, Novartis, Genesis pharma, Consultant of: MSD, Bristol-Myers Squibb, UCB pharma, AbbVie, Speakers bureau: MSD, Bristol-Myers Squibb, Pfizer, Alexandros Garyfallos Grant/research support from: MSD, Aenorasis SA, Speakers bureau: MSD, Novartis, gsk, Maria Tektonidou Grant/research support from: AbbVie, MSD, Novartis and Pfizer, Consultant of: AbbVie, MSD, Novartis and Pfizer, GEORGIOS VOSVOTEKAS Grant/research support from: MSD, Janssen, Consultant of: MSD, Novartis, Roche, UCB pharma, Bristol-Myers Squibb, AbbVie, Speakers bureau: UCB pharma, Menarini, Bristol-Myers Squibb, MSD, Evangelia Petrikkou Employee of: MSD, Bristol Myers Squibb, Vianex SA, Gkikas Katsifis Grant/research support from: UCB Pharma, Janssen, Abbvie, Novartis, MSD, Aenorasis, Genesis Pharma, Pfizer, Roche, Consultant of: UCB Pharma, Janssen, Abbvie, Novartis, MSD, Aenorasis, Genesis Pharma, Pfizer, Roche, Speakers bureau: UCB Pharma, Janssen, Abbvie, Novartis, MSD, Aenorasis, Genesis Pharma, Pfizer, Roche

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SAT0631-HPR WHEN CAN I STOP MY STEROIDS? THE PATIENT PERSPECTIVE ON GLUCOCORTICOID USAGE IN ADULT INFLAMMATORY MYOPATHY

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Background: Glucocorticoids (GC) are long established as a first line treatment in patients with idiopathic inflammatory myopathy (IIM), in which high dose, long duration treatment is often required. GC usage is associated with a wide range of adverse effects (AEs). The patient perspective on the risks and benefits of GCs is not well studied and no prior studies assesses this issue in IIM patients (1).

Objectives: To describe the perspective of IIM patients on GC treatment.

Methods: We deployed an online survey distributed using the Myositis UK page on Healthunlocked.com, an online social network for health, with approximately 450 patients registered. Patients with diagnosed IIM were invited to take part on an anonymised basis. Respondents were asked to grade the severity on a Likert scale (1 to 5) of all AEs experienced in relation to GC. Additionally, respondents were asked to write about their concerns and to rate their overall experience with GC treatment.

Results: In total, 122 completed surveys were received. Forty five percent (55/122) of respondents had dermatomyositis, 27% (33/122) polymyositis, 10% (12/122) anti-synthetase syndrome, 18% (22/122) other inflammatory myopathies. Seventy-nine percent (96/122) of respondents were female and the mean age overall was 50 years (SD [standard deviation] 14).

The median reported current daily dose of prednisolone was 15 mg and median treatment duration was 5.3 years at the time of survey completion. Females were more likely to stay on GCs for longer than males (5.4 *vs* 4.7 years, p=0.046).

Table 1. Mean severity and frequency for each adverse effect.

	All respondents (n=122)	Male (n=26)	Female (n=96)	<60 years (n=89)	≥60 years (n=33)
Moon face	3.3 (1.9)	2 (2.1)*	3.6 (1.7)*	3.5 (1.8)	2.7 (2)
Weight gain	3.4 (1.7)	3.1 (1.6)	3.4 (1.8)	3.5 (1.7)	3.1 (1.9)
Acne	1.1 (1.5)	1 (1.5)	1.2 (1.6)	1.3 (1.6)	0.7 (1.2)
Hair loss	2 (1.8)	0.8 (1.4)*	2.4 (1.8)*	2.2 (1.8)**	1.5 (1.9)**
Facial hair	2.1 (1.8)	0.7 (1.3)*	2.5 (1.8)*	2.3 (1.8)	1.7 (1.8)
Thin skin	2.2 (1.9)	1.8 (2)	2.3 (1.8)	2.2 (1.9)	2.3 (1.9)
Bruising	2.2 (1.7)	2.1 (1.9)	2.2 (1.7)	2.2 (1.7)	2 (1.9)
Stretch marks	1.3 (1.9)	0.9 (1.5)	1.4 (1.8)	1.5 (1.9)**	0.6 (1.2)**
Nausea	1.4 (1.7)	1.6 (1.8)	1.4 (1.6)	1.5 (1.6)	1.2 (1.7)
Heartburn	1.9 (1.8)	1.8 (1.9)	1.9 (1.8)	2 (1.8)	1.5 (1.8)
Hunger	2.8 (1.7)	2.2 (1.9)*	3 (1.6)*	3 (1.6)	2.4 (2)
Mood swings	2.7 (1.6)	2.1 (1.8)	2.7 (1.5)	2.8 (1.6)	2.6 (1.6)
Sleep disturbances	3.1 (1.5)	2.9 (1.7)	3.2 (1.4)	3.2 (1.5)	3 (1.5)
Cataracts	0.6 (1.3)	1.1 (1.8)	0.5 (1.1)	0.5 (1.2)	1 (1.6)
Glaucoma	0.4 (1.1)	0.6 (1.5)	0.3 (0.9)	0.4 (1)	0.4 (1)
Hypertension	1.6 (1.7)	1.8 (1.7)	1.5 (1.7)	1.5 (1.7)	1.8 (1.8)
Diabetes	0.8 (1.6)	1 (1.6)	0.8 (1.6)	0.7 (1.5)	1 (1.8)
Water retention	2.2 (1.7)	1.7 (1.6)	2.3 (1.8)	2.3 (1.8)	1.9 (1.6)
Infections	2.2 (1.7)	2.2 (1.8)	2.2 (1.7)	2.2 (1.7)	2.1 (1.7)
Fractures	0.5 (1.1)	0.5 (1.2)	0.5 (1.1)	0.5 (1.6)	0.5 (1.1)

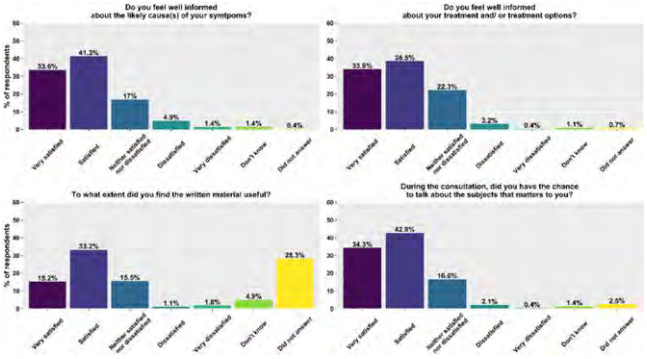
Mean severity on a Likert scale (0-5), mean (SD); *p<0.05, male vs female; **p<0.05, <60 years vs ≥60 years.
Frequency (number of patients reporting adverse effect as present), heatmap: White (0-33%), light grey (33-66%), dark grey (66-100%).

The mean number of reported AEs to GC treatment per patient was 12 (SD 5). Female respondents reported a greater number of AEs compared to males (12.6 *vs* 10.1, p=0.019). The three most commonly experienced AEs were: sleep disturbance (93%), mood swings (86%) and weight gain (86%). Only 54% of respondents agreed that the information given about the potential risks of GC treatment was adequate. Mean severity and frequency of AEs is represented in table 1.
Conclusion: Adverse effects are common, and those rated more severe by patients were physical and behavioural (such as weight gain or sleep disturbance). Female patients reported more severe AEs compared to men.
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SAT0632-HPR PATIENTS VIEW ON CONSULTATION IN OUTPATIENT CLINIC – FROM SATISFACTION TO DEMAND OF GUIDANCE INTO MORE SELF-MANAGEMENT

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Background: Patients with rheumatic diseases, routinely consult the outpatient clinic 1-2 times a year to see their rheumatologist. Many of the patients also attend nurse-led consultations to receive instructions, regarding treatment in association to their intravenous treatment, or DMARD dispensing in the clinic. As clinicians we have an assumption of what the "good practice" is in relation to the patients, but we have little insight, into the patients' own experience and satisfaction.
Objectives: To investigate the patients views on the level of information, and their experience and satisfaction with the doctor and nurse-led consultations in the outpatient clinic.
Methods: The approach of the survey was both quantitative and qualitative. A questionnaire was designed with four questions on a matrix scale concerning *their information level on their disease/symptoms*; *their treatment*; *if they had received written material and if so, it's value*; and *their possibility to talk about subjects that matters for them during consultations*. To gain a qualitative approach with focus on the patients' experiences and comments, every question was constructed with space for comments. Comments were transcribed, indexed, analysed, and thematically divided. The inclusion of patients were all patients visiting the clinic within a specific week in January 2019.
Results: The results from the four questions, are shown in the figures below, measured in percentage. In total, 283 participated (response rate 60%).



Four themes covered from the analysis of patients' comments. *"Seeking own answers", "Own coping – effort", "Conversation with doctor/nurse"* and *"Treatment/medication".* Comments revealed many descriptions and stories of patients, showered with all types of suggestions of taking control or managing the disease by them self, from their family or media. It also revealed their interest in discussing, these subjects and matters with the doctor/nurse, without being rejected. The feeling of rejection resulted in some patients trying other treatments or introducing changes in their lifestyle, without involving the doctor. The patients also called for more knowledge about physical training, and not only medical treatment.
Conclusion: In general, the patients had a very positive perception towards the consultations, and the information from the outpatient clinic. Despite that, the themes indicated a pattern, that needs to be considered, so clinicians acknowledge the patients wish for guidance, besides the medical treatment. To support the patient, without leaving them with a feeling of being rejected, we need to consider how to articulate the subjects the patients are exposed to outside our clinic, so the patients feel free to inform or involve the clinic instead of being silent, in risk of counteracting the medical treatment.
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SAT0633-HPR AN EXPLORATION INTO THE CONVERSATIONS AROUND SEXUAL FUNCTIONING THAT MALES WITH SJÖGREN'S SYNDROME HAVE ON AN INTERNET FORUM.

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Background: Sjögren's Syndrome (SS) is an autoimmune rheumatic disease that targets secretion glands throughout the body, causing symptoms of oral, ocular and genital dryness (van de Merwe, 2010). A small body of literature has investigated the impact of SS on women's sexual functioning, however, no research currently exists that has explored this topic in males with SS. Gathering a snapshot of issues may prove difficult given the sensitivity of the topic. Therefore, data must be gathered from sources where individuals may have the confidence to talk openly. Research has shown that many patient groups turn to internet forums to discuss sensitive issues under the cloak of anonymity (White & Dorman, 2001). Analysing this source of data allows us to explore the conversations pertaining to sexual functioning that males with SS may not feel comfortable discussing in a traditional qualitative setting, and may be instrumental in guiding future intervention strategies.
Objectives: To explore the conversations around sexual functioning that male users with SS have on an internet forum.
Methods: A large publicly accessible internet forum that individuals with a diagnosis of SS used to discuss issues and share experiences with other users was selected. Thread names and post content were scraped using a web scraping tool, and posts identified as containing relevant keywords were exported into Excel. Braun & Clarke's (2006) thematic analysis was used to analyse post content.
Results: A total of 78 posts were identified as being pertinent to the topic of male sexual functioning. Conversations were predominately centred on symptom presence in the reproductive organs. Forum users discussed having fluctuating pain in the testicles, scrotum, groin, anus, and rectum. They also reported experiencing

feelings of dryness at the base of the penis, around the testicles, under the foreskin, around the glans of the penis and in the anus. Discussions were also had about changes in the volume and consistency of seminal fluid released either prior to or during ejaculation. Another conversation theme revolved around how the symptoms they experienced affected their ability to engage in sexual intercourse. Forum users discussed how pain and dryness made sexual intercourse painful, resulting in them withdrawing from sexual activity indefinitely. Discussions were also had about the lack of information available to help understand and manage sexual dysfunction. Forum users discussed how feelings of embarrassment about the nature of the symptoms and the stigma of it being "a woman's disease" kept them from seeking medical assistance. Those who had sought medical assistance shared their belief that health professionals (HPs) were misdiagnosing their symptoms and were prescribing ineffective treatments. They also reported that their HPs were dismissive of symptoms and unwilling to assist further.

Conclusion: Utilising conversations from an internet forum was an effective method to use to gain insight into some of the issues that males with SS experience with sexual functioning. The absence of accessible information and lack of support from HPs for males with SS is hinted at in this research. Future research should focus on identifying issues surrounding male sexual functioning as this will both guide future intervention strategies and allow HPs to publish material to better support males with SS.

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SAT0634-HPR PATIENT-REPORTED OUTCOMES REGARDING TWO FORMS OF METHOTREXATE AUTOINJECTORS IN RHEUMATOID ARTHRITIS: AN INTERNATIONAL CROSS-OVER SURVEY.

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Background: Several types of methotrexate (MTX) autoinjectors (AI) are currently marketed in rheumatoid arthritis (RA), yet comparative data are scarce.

Objectives: Investigate respective perceptions of patients regarding two marketed forms of MTX AI *via* a survey conducted by a global market research company.

Methods: Patients with moderate to severe RA treated by one of the two forms of MTX AI were recruited. In each participating country (France, Ireland, United-Kingdom, Spain), the respective proportions of recruited patients were approximately aligned on local market shares. The two investigated devices were: A-AI/ The first MTX AI marketed in Europe: bigger size, with an activation button, without double injection sound-control, with a larger window; B-AI/ The second MTX AI commercialized in Europe: smaller and thinner size, without activation button, with double injection sound-control and a smaller window. Each patient was interviewed during 30 minutes on his or her satisfaction level with the currently used device. Then, they were presented the alternative AI and they could test it on skin-mimicking pads. After this step, the patients were interviewed on the alternative device.

Results: 100 patients were enrolled over one-month period (A-AI users, n=65; B-AI users, n=35). Overall, 61% of A-AI users reported that B-AI was "better" or "much better" whereas 43% of B-AI users judged A-AI as "better" or "much better". When B-AI users were asked to evaluate convenience elements of A-AI, recognition of injection ending, general design and ease of use were the indicators that were the most poorly judged (60%, 54%, and 46% respectively). When A-AI users were cross-tested for B-AI, injection mode, general feeling, and ease of use were the three items providing the greatest satisfaction (80%, 77%, and 75%, respectively). When they were asked about the characteristics of their usual device, the button, the design of the device and discomfort associated with the injection were the most dissatisfactory elements (30%, 31%, 34% respectively). Also, 73% of A-AI users reported being interested in trying B-AI while 26% of B-AI users replied being so.

Last, 95% of B-AI users declared being "very satisfied" or "totally satisfied", with ease of use and recognition of injection ending being the most attractive items (94% and 95% of high or full satisfaction respectively).

Conclusion: In this international cross-over survey, the newest autoinjector on the market, B-AI has shown to exhibit better reported outcomes with respect to ease of use and recognition of the end of the injection and other tested indicators.

Treatment of patients with RA should aim at the best care and must be based on a shared decision between the patient and the rheumatologist.[1] In this scope, the shared decision making is permitted when the patient agrees with the choice of treatment (medication, administration route, device, etc.). Patient's involvement in decision making is assumed to lead to improvement in health outcomes such as a better adherence to the treatment.[2]

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SAT0635-HPR THE BURDEN OF SCLERODERMA FROM PATIENTS' PERSPECTIVE

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Background: Scleroderma can significantly impair daily functioning by leading to multi-organ involvement and profound fatigue. Recent studies suggest that objective measures of the disease severity may not necessarily correspond with the patients' perception[1].

Objectives: To evaluate the degree of disability and fatigue in patients with scleroderma, distinguish the most troublesome activities and assess which clinical symptoms had mostly impact on daily functioning.

Methods: An online questionnaire was created and distributed to English-speaking patients with scleroderma by means of online support groups. The questionnaire contained inquiries about demographical data, clinical symptoms as well as the Scleroderma Health Assessment Questionnaire (SHAQ, comprised of HAQ-DI and specific VAS scales) and Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F). Standard and Alternative Disability Indexes (SDI and ADI) were counted based on answers in HAQ-DI part. Degrees of disability and fatigue, reflected by SDI, ADI and FACIT-F scores, were compared between subgroup of patients with and without particular clinical symptoms. Responses were analysed statistically.

Results: Questionnaire was completed by 85 responders (mean age 48,93±14,4; 98,82% were female). Mean SDI was 1.09±0.66 with 41.18% of patients fulfilling the criteria of mild to moderate difficulty (SDI<1), 50.59% classified as moderate to severe disability (1≤SDI<2) and 8.24% being severely or very severely disabled (SDI≥2). Mean value of ADI was 0.93±0.61. 56.47 % of responders needed aid of the caregivers while gripping/opening, 31.76% while reaching and 29.41% while running errands and chores. Most frequently used facilitating devices included devices for gripping/opening (32.94%) and for maintaining hygiene (21.18%). Mean value of overall disease severity was estimated by VAS as 52.06±0.66. The mean values of VAS assessing the impact on daily living were respectively 48.16±29.28 for pain related to the disease, 43.34±34.94 for Raynaud's, 41.86±34.59 for gastrointestinal problems, 31.60±31.38 for breathing difficulties and 20.85±33.47 for finger ulcers. Mean FACIT-F score was 23.62±11.88 yet 71.76% of patients fulfilled the criteria of severe fatigue. Both SDI and ADI correlated with FACIT-F score (respectively r=-0.5684, p<0.0001 and r=-0.5711, p<0.0001). SDI, ADI and FACIT-F correlated with VAS scores for overall disease severity, pain, gastrointestinal and breathing problems. Patients with symptoms such as arthralgia, muscle weakness, dysphagia, blurred vision, hair loss, unintentional weight loss and hoarseness were statistically more disabled and fatigued as compared to patients without such symptoms. Responders with skin ulcers/non-healing wounds (other than finger ulcers), Raynaud's or erythema/rash were more disabled than responders without such symptoms, yet no differences were observed in the degree of fatigue.

Conclusion: Majority of patients with scleroderma are moderately to severely disabled yet cope with the impairments with the widespread use of facilitating devices or aid of caregivers. Profound fatigue, observed in the majority of patients, may contribute to the high overall perception of disease severity.

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SAT0636-HPR PATIENT EXPERIENCE WITH THE PRESCRIPTION, INFORMATION AND USE OF METHOTREXATE

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Background: Methotrexate (MTX) is currently a mainstream drug in the treatment of rheumatic diseases. However, the response to MTX is not universal and

may be conditioned by a number of factors, among which adherence could be crucial.
Objectives: The aim of this study is to explore adherence to MTX in patients with rheumatic diseases, facilitators and perceived when taking and maintaining the prescription.
Methods: A qualitative study of content analysis was performed. Focus groups with patients taking either oral or subcutaneous MTX (being the main or coadjuvant treatment) for any rheumatic disease was performed. The groups were moderated by a rheumatologist that was unknown for the patients. The speech was recorded and transcribed. Subsequently, an inductive coding was performed with the help of Atlas.ti and main themes and sub-themes were extracted, with examples of verbatim anonymized speech.
Results: Three focus groups were conducted, with a total of 12 participants, of whom eight were women, seven had rheumatoid arthritis, three had psoriatic arthritis, one had spondyloarthritis, and one had systemic lupus erythematosus. All patients reported an adequate adherence to treatment. The barriers identified were: information in the leaflet, technical language in the consults, difficult access to doctor´s appointment, social environment, side effects and the subcutaneous device. As facilitators, the following aspects were discussed: good predisposition of the physician, reliable graphic information, role of associations and partners support.
The unmet needs detected were: problems with travelling, protocols for eventualities, absence of a plan of care, neglection of "non-physical" symptoms, disinformation on side effects and training in complementary aspects.
Conclusion: Getting reliable information was the main barrier identified. The environment and side effects may also negatively impact on adherence. Shared decision making is a goal to be achieved in the future in these patients.
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SAT0637-HPR IMPAIRED HEALTH-RELATED QUALITY OF LIFE AND PHYSICAL FUNCTION IN NORWEGIAN PATIENTS WITH TAKAYASU ARTERITIS.

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Background: Takayasu arteritis (TAK) is a rare vasculitis of large vessels in young women. We have previously reported a point prevalence of 25.6/10^6. The disease most prevalently limited to the aortic arch and its branches (Type 1) among North Europeans.
Early symptoms of TAK include fever, myalgia and loss of appetite. Later, the inflammation of blood vessel may lead to irreversible vascular damage and ischemic symptoms with claudication of the extremities. We have recently found that TAK may reduce life expectancy, mainly due to cardiovascular complications. The median age among those deceased was only 58 years. These findings clearly indicate that TAK may have severe impact on the wellbeing of the patients and their physical capacity.
It is widely accepted to include patients' perspectives related to their health condition and treatment to better understand the burden of the disease and the impact on their daily life activities. However, studies of health-related quality of life (HRQol) in TAK has rarely been undertaken, and we are not aware of any studies from the Northern part of Europe.
Objectives: (i)To compare HRQol in Norwegian TAK with age– and sex matched Norwegian normative data. (ii) To assess patients reported disease symptoms (iii). To evaluate the impact of disease symptoms on HRQol and functional status.
Methods: Patients with TAK from "The Norwegian Systemic Connective Tissue Disease and Vasculitis Registry" (NOSVAR) were included. All patients had to fulfill the American College of Rheumatology classification criteria and/or the modified Ishikawa diagnostic criteria for TAK and return three sets of questionnaires: 1) The SF 36 was applied to measure HRQL. Age- and sex-matched normative data were obtained from a former study and consisted of 2471 randomly selected Norwegian citizens (1162 women) who were >20 yrs. of age. 2) Questions from the Modified Health Assessment Questionnaire (MHAQ). 3) Patients answered questionnaires regarding disease symptoms, employment and assessment of general health status Disease duration was defined as the time from diagnosis to date of registration. Pearson correlation tests were used to explore associations between disease symptoms and HRQL.
Results: A total of 33 female patients were included. Their mean age at diagnosis was 32 yrs. and they had a disease duration of median, 8,9 yrs. at inclusion. The SF-36 results adjusted for age, indicated significantly impaired HRQoL in the patients compared with normative data on 6 of eight subscales, with the largest differences observed for role physical (51 vs. 80, p < 0.001) and general health (51 vs. 78, p< 0.001) (Fig. 1). Symptoms of claudication in legs correlated strongly to moderately with activities as running or jogging 3 km (.538, p<0.001), walking outdoor on flat ground (.542, p=0.002), climbing stairs (.564, p=0.001) and run errands and shop (.417, p=0.016) assessed by MHAQ. The most frequently reported symptoms were dyspnea at physical exertion (67%), claudication of arms (63%) and myalgia (55%). A moderate correlation was found between claudication of legs (-.572, p<0.001), pain (VAS) (-.585, p<0.001), fatigue (-.493 P<0.002), dyspnea (-.471, p<0.002) and physical function as reported in SF36. Similarly, a moderate negative correlation was present between pain (VAS) (-.553, p<0.001), fatigue (VAS) (-.482, p<0.002) and mental health in SF36.
At the time of diagnosis, 89 % were employed, compared to only 21% at registration. Patients self-perceived health status was reported in 39 %, compared to 79% in a share of the Norwegian population aged 16 or over (The data from the EU Statistics on Income and Living Condiions(EU SILC).
Conclusion: Patients with TAK reported reduced QoL compared to data from our general population. The most frequently reported disease symptoms were dyspnea at exertion, claudication of arms and myalgia. Pain, fatigue and dyspnea at exertion had a significant impact on HRQol. Claudication of legs correlated significantly with impaired walking activities reported in MHAQ.
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SAT0638-HPR CHARACTERIZING THE IMPACT OF AXIAL SPONDYLOARTHRITIS ON DAILY LIFE: GENDER AND PATIENT-REPORTED OUTCOMES ASSOCIATED WITH FUNCTIONAL LIMITATION IN CANADA. RESULTS FROM THE IMAS SURVEY

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Background: Understanding the most limiting daily activities reported by patients is important for a holistic healthcare approach.
Objectives: To evaluate the degree of functional limitation on daily activities and its association with PROs in Canada.
Methods: The International Map of Axial Spondyloarthritis (IMAS) is a cross-sectional online survey of non-selected patients with self-reported axSpA conducted in 22 countries and endorsed by the Axial Spondyloarthritis International Federation. IMAS captures the patients' perspective of the burden of axSpA. The Canadian adaptation included a review of the survey by an advisory board of axSpA patients and a national steering committee composed of the Canadian Spondylitis Association, rheumatologists and axSpA patients. Canadian participants were recruited from 2018 to 2019. Socio-demographics variables, BASDAI and mental health (GHQ-12) data were collected. Degree of functional limitation in 18 daily activities was evaluated using a 3-point Likert scale. Bivariate analysis was performed to assess activities associated with poorer BASDAI and mental health status.

Table 1. BASDAI and mental health (GHQ-12)- impact on daily activities (N = 542)

	BASDAI Mean ± SD			GHQ-12 Mean ± SD		
	Low limitation	Medium + High Limitation	p-value	Low limitation	Medium + High Limitation	p-value
Dressing / undressing	5.5 ± 2.0	6.4 ± 4.4	**<.001***	4.4 ± 3.8	5.7 ±4.0	**.007***
Washing / personal grooming	5.6 ±2.0	6.3 ± 2.0	**.002***	4.7 ± 4.1	5.6 ± 4.1	.099
Taking a bath / shower	5.6 ±2.0	6.6 ±1.8	**<.001***	4.2 ± 4.0	5.9 ± 4.0	**.002***
Tying shoe laces	5.4 ± 2.0	6.1 ± 2.0	**.005***	4.3 ± 3.8	5.2 ± 4.1	**.044***
Walking / getting around the house	5.5 ± 2.0	6.4 ± 1.9	**<.001***	4.2 ± 3.9	5.6 ± 4.1	**.005***
Stair climbing	5.1 ±1.9	6.3 ±1.8	**<.001***	3.4 ± 3.4	5.4 ± 4.0	**<.001***
Lying down / getting up from bed	5.2 ± 2.0	6.3 ± 1.9	**<.001***	3.6 ± 3.6	5.5 ± 4.1	**<.001***
Going to the toilet	5.4 ± 2.0	6.7 ± 1.9	**<.001***	4.3 ± 4.2	5.6 ± 3.9	**.024***
Shopping	5.6 ± 1.8	6.2 ± 1.9	**.003***	4.1 ± 3.7	5.3 ± 4.1	**.025***
Cooking	5.6 ± 1.9	6.3 ± 1.8	**.008***	3.7 ± 3.6	5.8 ±4.2	**<.001***
Eating	5.9 ± 2.1	6.9 ± 1.9	**.024***	5.0 ± 4.4	5.8 ± 3.9	.282
Housework / cleaning	4.9 ± 2.0	6.0 ± 1.8	**<.001***	3.7 ± 3.6	4.8 ± 4.0	**.021***
Walking down the street	5.4 ± 1.9	6.1 ± 2.0	**.005***	4.4 ± 3.8	5.1 ± 4.1	.228

Table 1. BASDAI and mental health (GHQ-12)- impact on daily activities (N = 542)

	BASDAI Mean ± SD			GHQ-12 Mean ± SD		
	Low limitation	Medium + High Limitation	p-value	Low limitation	Medium + High Limitation	p-value
Using public transportation	5.6 ± 1.9	6.1 ± 1.9	.180	4.4 ± 4.0	5.3 ± 4.0	.155
Driving	5.5 ± 2.0	6.1 ± 2.1	**.021***	4.2 ± 3.9	5.3 ± 4.2	.050
Doing physical exercise	4.7 ± 2.1	5.8 ± 1.9	**<.001***	3.4 ± 3.7	4.7 ± 4.0	**.002***
Engaging in intimate relations	5.2 ± 1.9	6.0 ±1.9	**<.001**	4.0 ± 3.8	5.1 ± 4.0	**.015***
Caring for children / grandchildren	5.2 ± 1.9	6.0 ± 2.0	**.003**	3.7 ± 3.8	5.2 ± 4.1	**.005**

* p≤.05

Results: 542 axSpA patients participated. Mean age was 44.3±13.9 years and 63% were female. Mean BASDAI was 5.3±2.1, mean GHQ-12 score was 4.0±3.8 and 50% were on biologics. 94% reported ≥1 limitation in daily activities, of which physical exercise (30%), house cleaning (22%), intimacy (21%) and stair climbing (21%) were most commonly severely impacted (high limitation). Women reported significantly higher limitations in house cleaning, stair climbing, driving, moving around the house and caring for young children (p<.05 for all activities vs men). Compared with low limitation, medium–high limitation in most activities was significantly associated with higher disease activity and worsened mental health for the overall population (Table 1).

Conclusion: Canadian axSpA patients, particularly women, are limited in daily life activities beyond those captured by other validated scales. Strong association between functional limitation, disease activity and mental health emphasizes the need for holistic evaluation of axSpA patients.

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SAT0639-HPR HOW DO PEOPLE WITH AXSPA PERCEIVE THE IMPACT OF DISEASE AND PHYSICAL ACTIVITY?

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Background: The Ankylosing Spondylitis Association of Switzerland (SVMB) offers weekly group exercise therapy for people with axial Spondyloarthritis (axSpA) supervised by physiotherapists (PTs). Given the EULAR physical activity (PA) recommendations [1] and recent research [2, 3], the SVMB has implemented a new concept including assessments evaluating all fitness dimensions, daily PA and disease activity. Based on its results, individual exercise-coaching by the group PT is provided to support the adherence to exercising in correct mode and dose. PTs use the visual-tactile instrument PRISM (Pictorial Representation of Illness and Self Measure) [5] to explore patients' perceived burden of disease (BD) and importance of PA as starting-point for the exercise-coaching.

Objectives: To measure to what extent the perceived BD and importance of PA, measured with PRISM, change over time and to evaluate if the PRISM results are associated with established measures of disease activity and daily PA across four pilot groups including four PTs and 30 people with axSpA.

Methods: Each participant had three exercise-coaching sessions within six months. Each session was started by applying the PRISM, which is a white A4 board with a yellow disk at the bottom right hand corner. The participant was asked to imagine that the board represented his/her life and the yellow disk represented his/her "Self". Then, a red disk, representing axSpA, and later a blue disk, representing PA, were handed and the participant was asked to place the disks where they represented best their importance in the participant's life. The distances between Self and the red and blue disk respectively were measured in centimeters to quantify BD/importance of PA, and correlated with the Bath Ankylosing Spondylitis Disease Activity Inventory, BASDAI (measuring disease activity) and weekly METs (measured with the International PA Questionnaire, IPAQ) by means of spearman rank correlation. The analysis was based on the first session at baseline (T0) and the third session after six months (T1) and paired t-test was applied, to identify changes between sessions.

Results: Complete data were available for 23 participants. Neither BD (distance to Self at T0: 13.7±7.2cm; T1: 12.1±6.2cm; t=0.386, p=0.703) nor importance of PA (distance to Self at, T0: 7.3±5.3cm; T1: 7.0±4.5cm); t=0.246, p=0.808) changed within six months. The perceived importance of PA correlated with IPAQ measured METs at T1 (r=0.572, p=0.00), no correlation between BD and METs was found.

Conclusion: The stable perceived BD could be explained by long disease duration of participants and established disease management. The stable importance of PA could be due to the sample, as for group exercise participants PA may already be important. The correlation between importance of PA and MET at T1 could indicate that people learned more about the meaning of PA leading to a better understanding of the importance of PA. Future research should evaluate factors influencing the perceived importance of PA as well as further explore the use of PRISM in the context of exercise-coaching.

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SAT0640-HPR RHEUMATOLOGY CARE OF MIGRANTS FROM SUB-SAHARAN AFRICA; A QUALITATIVE PILOT STUDY OF PATIENTS' PERSPECTIVES

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Background: Rheumatological diseases are common in Sub-Saharan Africa [1] but specialist healthcare is limited and there are less than 150 rheumatologists currently serving 1 billion people in Sub-Saharan Africa [2]. Rheumatologists practising in the UK NHS are likely to be exposed to migrant patients. There is therefore, an unmet need for health care providers to understand the differences in rheumatology healthcare provision between Sub-Saharan Africa and the UK and the barriers which migrants face in their transition of rheumatology care.

Objectives: To gain an understanding of the experiences of patients with rheumatological conditions, about their past healthcare in Sub-Saharan Africa and their transition of care to the UK.

Methods: A qualitative study using semi-structured interviews was conducted. Participants were recruited from two rheumatology outpatient clinics in London. Thematic analysis was applied to identify key themes.

Results: Seven participants were recruited. Five had rheumatoid arthritis, one had ankylosing spondylitis and one had undifferentiated inflammatory arthritis. Participants described the significant impact their rheumatological conditions had on their physical and emotional wellbeing, including their social and financial implications. Compared to the UK, rheumatology healthcare in Sub-Saharan Africa was characterised by higher costs, limited access to specialists, lack of investigations and treatments, the use of traditional medicines and poor communication by clinicians. Barriers to transition of rheumatology care to the UK were: poor understanding of rheumatological conditions by the public and primary care providers, lack of understanding of NHS entitlements by migrants, fear of data sharing with immigration services and delayed referral to specialist care. Patient, doctor and public education were identified by participants as important ways to improve access to healthcare.

Conclusion: This study has described, for the first time, patients' perspectives of rheumatology health care in Sub-Saharan Africa and the transition of their care to the UK. These initial findings allow healthcare providers in the UK to tailor management for this migrant population and suggests that migrants need more information about their NHS entitlements and specific explanations on what non-clinical data will be shared with immigration services. To increase access to appropriate care, a concerted effort by clinicians and public health authorities is necessary to raise awareness and provide better education to patients and migrant populations about rheumatological conditions.

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SAT0641-HPR

FACTORS ASSOCIATED WITH COGNITIVE IMPAIRMENT IN KOREAN ADULTS WITH RHEUMATOID ARTHRITIS

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Background: For persons with chronic diseases including rheumatoid arthritis (RA), undamaged cognitive capacity is critical for daily functioning, treatment compliance, and self-management. Disease-specific features of RA such as systemic chronic inflammation or increased comorbid cardiovascular disease (CVD) risk may be closely linked to neurocognitive dysfunction in RA patients [1]. However, the evidence of brain involvement in RA is very rare or even controversial and very little is known about the pathogenic mechanisms of cognitive decline in persons with RA.
Objectives: This study explored the prevalence of cognitive impairment in Korean adults with RA using a set of computerized neurocognitive tests and the factors that were significantly associated with cognitive impairment.
Methods: Individuals with RA were recruited by their rheumatologists during follow-up visits at one university hospital in Korea. After getting signed consents, a trained research nurse assessed participants with a range of physical, psychosocial, and biological metrics. Cognitive function was assessed using a set of 6 computerized neurocognitive tests yielding 18 indices covering a range of cognitive domains. Subjects were classified as 'impaired' if they performed 1 *SD* below age-based population norms on each test [2]. The total cognitive function score was calculated by summing the transformed scores, ranging from 0 (no impairment) to 18 (worst impairment). Multiple linear regression analyses were conducted to identify the significant factors influencing cognitive impairment.
Results: Sixty five subjects with a mean (±*SD*) age of 61.9 (±10.0) years were included. 85% were female, 89% were married, and 76% had less 12 years of education. Mean disease activity score (DAS-28) was 2.3 (±1.3) and mean disease duration was 9.8 (±8.7) years. Mean functional limitations score (HAQ) was 0.3 (±0.5) and mean CVD risk factors were 2.3 (±1.5). Total cognitive function score was 11.1 ± 4.0 (2-18). The proportion of persons who were classified as cognitively impaired on each test ranged from 25% to 92%. The proportion of persons classified as cognitively impaired on the quarter of total subtests (5 or more out of 18 subtests) was 94%. The multivariate regression model was statistically significant and accounted for 39% of the variance in cognitive impairment ($F=5.26$, $p<.001$). Education (β=-0.32, $p=0.010$), family income (β=-0.26, $p=0.040$), and cardiovascular disease risk factors (β=0.27, $p=0.025$) were significantly associated with cognitive impairment controlling for other covariates.
Conclusion: A significant number of RA patients were cognitively impaired. Less education, less family income, and increased cardiovascular disease risk factors were the significant factors affecting cognitive impairment in RA. The findings of this study suggest that the burden of cognitive impairment in RA patients is significant, and future studies identifying specific etiological contributors to cognitive impairment are warranted.
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SAT0642-HPR

CAPTURING THE UNMET NEEDS OF WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND IDENTIFYING THE INFORMATION NEEDED IN PHYSICIAN-PATIENT COMMUNICATION

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Background: Systemic lupus erythematosus (SLE) is known to affect the reproductive health of female patients in various ways. Identifying the unmet information and needs of women with SLE about the impact of the disease on maternal health, pregnancy, family planning and contraception is of paramount importance.
Objectives: Our aim was to understand the information needs of women with SLE and capture the gaps in the knowledge of reproductive issues.
Methods: We interviewed 284 female patients with SLE in three centers all affiliated to Alexandria Faculty of Medicine, using a 41 multiple-choice based questionnaire about pregnancy counselling, contraception and the use of drugs during pregnancy. The disease knowledge index (DKI) created by Andreoli et el.,(1) was applied to assess the global knowledge and information of patients on the impact of SLE on reproductive health.
Results: Forty percent of patients declared to have performed the last gynecological visit since 3 years, versus (49.3 %) patients who have done their last visit within a year. 255 patients reported to have received counselling about contraception; 141 of which provided by gynecologists and not rheumatologists. 114 (40.1%) patients have never been asked about the desire to have children. Regarding the methods of contraception used, 104 (36.6%) patients stated that they don't know there are different forms of pills and have never heard of the progestin-only pills. As for the DKI, patients showed proper knowledge about the possibility for SLE women to fall pregnant, have healthy children and the fact that lupus flares up during pregnancy. 118 (41.5%)of the patients didn't know whether children of women with SLE carry a higher risk of having general health problems or not. Also, a great proportion of patients chose "do not know" for the possibility that children could inherit the mother's disease (49.6%). Concerning the drugs used during pregnancy, surprisingly, (34.2%) patients stated that Hydroquinone shouldn't be used during pregnancy, and (28.9%) didn't know if it is compatible with pregnancy or not. Nearly half the patients who were interviewed didn't know that Methotrexate, Cyclophosphamide and Mycophenolate mofetil are contraindicated in pregnancy. About 80% of the patients stated that SLE influenced the number of the family size they desired in various ways and 134 (47.2%) patients blamed the disease for not being able to take care of their children. Expectedly, SLE impacted patients' marriages in different forms; 27 (9.5%) of the patients claimed that the disease led to their divorce, 52 (18.3%) explained that their spouses constantly complained about their illnesses, and 19 (6.7%) refused to answer this question. A total of 181 (63.7%) patients had spontaneous abortions, among which 181 (63.7%) patients before being diagnosed with SLE, and 134 (74%) of these abortions occurred in the first trimester.
Conclusion: There is a crucial unmet need for women with SLE, identified as a wide gap in communication about reproductive issues. This is influenced by the quality of physician-patient communication, as well as rheumatologist-obstetrician communication.
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SAT0643-HPR

NURSE-LED CARE FROM THE PERSPECTIVE OF PEOPLE WITH EARLY RHEUMATOID ARTHRITIS: A QUALITATIVE SYSTEMATIC REVIEW

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Background: Nurse-led care has been shown to be clinically effective and cost effective in rheumatoid arthritis (RA) but the role of the nurse in early RA is not well defined. Evidence for processes of care in RA is limited and it is not known how well rheumatology nurse-led clinics meet care needs of people with early RA.
Objectives: The aim of this study was to develop an understanding of rheumatology nurse-led care from the perspective of people with early RA.
Methods: A qualitative systematic review was conducted. The review protocol is published in the International prospective register of systematic reviews.
In March 2019, the following databases were searched: MEDLINE, EMBASE, CINAHL, PsycINFO and OpenGrey. Due to lack of studies in early RA this review included adults with early and established inflammatory arthritis, qualitative studies with data on patients' perspectives of nurse-led care, published in peer-reviewed journals in English between 2010 and 2019. Two reviewers screened titles, abstracts and full texts. Data were extracted and managed in tables. Joanna Briggs Institute Critical Appraisal Checklist was used for quality assessment of the included studies. A thematic synthesis was undertaken using the framework of Thomas and Harden.[1]
Results: The search identified 1034 records. After screening and assessing for eligibility, 8 qualitative studies were included in the review (133 patients), 2 studies included people with early RA. Three main themes were identified (Figure 1).

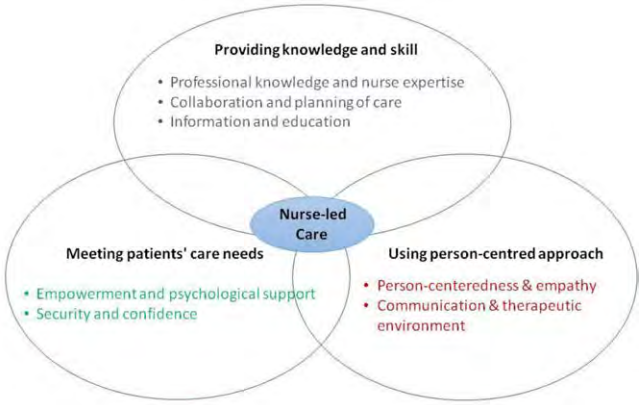


Figure 1. Themes of nurse-led care from the perspective of people with RA

Providing knowledge and skill. This theme delineated rheumatology nursing as providing professional expertise in the planning and delivery of care. The rheumatology nurse-led service included easy access via telephone helpline, consultations with the clinical nurse specialist for assessment of disease activity and care needs, planning of care, disease information and education, supporting self-management, and referral to rheumatologist and the multi-disciplinary team. People with RA highly valued the nurse expertise and specialist knowledge provided at nurse-led clinics. *'She was very good at informing me, so I have only praise for this ... because I have never had it like this before'. (Person with early RA).*

Using a person-centred approach. This theme showed nurse-led care using a person-centred approach combined with empathy and good communication skills, which created a good therapeutic environment. People with RA appreciated the person-centeredness, empathy and involvement of the nurse. '*She is very sensitive. She can see if I am feeling bad and comes straight to me and asks:"How are you today?"...You are treated and taken seriously'. (Person with early RA).*

Meeting patients' care needs. This theme presented nurse-led care as creating a sense of being empowered and psychologically supported in the management of RA and its impact. Nurse-led care made people with RA feel cared for, secure and confident. It added value to rheumatology care and made care complete. *'The thought of sticking a needle into my own stomach... it felt a bit like I would never manage to do that. However, they have been absolutely wonderful here ... and now I can do it myself'. (Person with early RA).*

Conclusion: Nurse-led care for people with RA is characterised by provision of rheumatology expertise using a person-centred approach, and patients' holistic care needs are being met. This study found a dearth of literature on perceptions of nurse-led care in people with early RA, which highlights the need for further research in this population.

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SAT0644-HPR COMPLIANCE OF BIOLOGIC DISEASES MODIFYING ANTI-RHEUMATIC DRUGS (BDMARDS) WITH SYSTEMIC IMMUNO-INFLAMMATORY RHEUMATIC DISEASES (SIRDS). AN ASSESSMENT OF PATIENTS' ADHERENCE AND NON- ADHERENCE CONCERNS.

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Background: Patients with systemic immunoinflammatory rheumatic diseases (SIRDs) are often treated with bDMARDs when the response to conventional disease-modifying antirheumatic drugs (csDMARDs) is inadequate.There are, however, concerns about non-adherence to bDMARDs among patient. The non-adherence to bDMARDs may be caused by the various factors.

Objectives: 1.The main objective of present study was to find out the cause of discontinuation of bDMARDs

2.To find out the adherence and non-adherence rate for bDMARDs.

3.To identify the factors that are modifiable.

Methods: 800 patients with SIRDs prescribed bDMARDs were interviewed to find out the demographic information, their socioeconomic status,and the disease duration.Additional information gathered included the comorbidities, the time for starting bDMARDs, the route of administration of bDMARDs, beliefs and perceptions about treatment efficacy and side effects if any.This was followed by looking at the adherence of bDMARDs; if they had discontinued then efforts was made to find out the reasons for the same.

Based on these findings the patients were classified into adherent and non-adherent categories. The data were analyzed further for

1.Factors that associated with persistence of bDMARDs.

2.Factors that were associated with discontinuation of bDMARDs.

Results: A total of 800 patients were interviewed that included patients with ankylosing spondylitis 430(52.4%), rheumatoid arthritis 300(37.7%), psoriatic arthritis 45(5.2%), and others 25 (0.7%).On analysis 610(76%) patient were compliant but 190(24%) patient had discontinued the bDMARDs on their own. On comparison of both groups

Factors that were significantly related to self-discontinuation were:

- Negative beliefs about biologics (37%)
- Cost (33%)
- Reading side-effect profile on Google search (25%)
- Other co-morbidities (6%)

Factors that were significantly related to persistence of biologic treatment were:

- Good counseling by rheumatologist and rheumatology nurse (60%)
- Faith in the treating rheumatologist (25%)
- Fear of deformities and pain(15%)

On analysis it was found that a good counseling and clarifying the doubts of the patients regarding bDMARDs before starting the treatment encourages the patient to continue the biologic treatment, especially it allays their doubts about the drug adverse effects.

Conclusion: Despite negative beliefs and misconceptions about bDMARDs, patient non-adherence at our center is not alarming.A positive reinforcement counseling appears to be the most significant factor to overcome the negative belief of patients.The affordability of the biologic treatment however remains a limiting factor in our centre as in other parts of India.

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SAT0645-HPR MYTHS AND MISCONCEPTION ABOUT THE ILLNESS AND CONVENTIONAL SYNTHETIC DMARDS (CSDMARDS) IN PATIENTS WITH SYSTEMIC IMMUNO-INFLAMMATORY RHEUMATIC DISEASES (SIRDS): A STUDY BY RHEUMATOLOGY NURSE COUNSELOR

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Background: Myths and misconceptions about illness and conventional disease modifying anti-rheumatic drugs directly influence adherence to the prescribed treatment. It is estimated that 30–50% of patients do not adhere to their prescribed treatment due to various reasons where the beliefs of the patients play a crucial role. At our centre we the specialist rheumatology nurse counsel the patients at every visit and try to remove their myths and negative beliefs about the disease as well as the medications.

Objectives: • To explore the common myths and misconceptions of regarding their disease and regarding the csDMARDs.

• To assess the efficacy of counseling in allaying their unfounded fear.

Methods: A total of 450 patients with SIRDs at least 3 times attended the rheumatology out-patient clinic on csDMARDs were enrolled to complete a questionnaire that, besides demographic information, socio-economic status, and co- morbidities, had the following questions:

1. Self reported adherence to medication
2. Misbelieves regarding food items
3. What kind of health-provider was consulted at the onset of the symptoms
4. Their belief/knowledge regarding:
   A. The need for physiotherapy.
   B. Life style modification requirement
   C. About osteoarthritis
   D. Medication requirement during remission
   E. Pregnancy and DMARDs
   F. The need of vaccination

G. Health hazards of smoking and alcohol use
H. Harms of discontinuing treatment when they felt well

Results: A total of 450 patients included spondyloarthropathy 150(34%), rheumatoid arthritis 200(45.7%), psoriatic arthritis 45(10%), and others 25(5.5%).The following observations was made:
1.Self-reported adherence to medication was in 250 (55%) patients; 200(45%) patient were non-adherent to treatment
2.382/450 (85%) patients had misbelieves regarding different food items.
3.225/450(50)% of the patients were not doing regular physiotherapy they were totally dependent on medications for symptoms relief.
4.387/450 (86%) patients confused the symptoms of osteoarthritis with that of RA.
5.315/450 (70 %) patients did not feel the requirement of continuing drugs during remission.
6.135/450 (30%) patients believed that while on DMARDs they cannot contemplate pregnancy.
7.351/450(78%) patients accept the need for vaccination when staring DMARDs
8.360/450 (80%) patients aware about side effect of smoking in disease but only 40 % were able to quit.
9.273/450 (60%) patients felt that more expensive medicines e.g.bDMARDs have more effects.
10.360/450 (80%) patients believed that DMARDs were 'steroids' and they increased weight. On analysis one patient have more than two myths simultaneously.

Conclusion: Increased awareness of the patient's beliefs about medicines is needed among health care providers. We should encourage patients to express their views about medicines as well as disease in order to optimize and personalize the information process. This can stimulate concordance and adherence to medication and follow up.These myths are deeply rooted in our society, single sitting counseling is not enough, and reinforcement is needed.

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SAT0646-HPR PATTERN AND INFLUENTIAL FACTORS IN PROMOTING TREAT-TO-TARGET (T2T) FOR FOLLOW-UP OF ANKYLOSING SPONDYLITIS (AS) PATIENTS WITH A RHEUMATOLOGIST-PATIENT INTERACTIVE SMART SYSTEM OF DISEASE MANAGEMENT (SSDM): A COHORT STUDY FROM CHINA

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Background: Ankylosing Spondylitis Disease Activity Score (ASDAS) is adopted to evaluate the degree of disease activity and the inflammatory response in AS patients. ASDAS score <= 1.3 represents inactive disease status and achievement of T2T. SSDM is a mobile application for disease management.

Objectives: To evaluate the patterns of T2T and related influential factors among AS patients after applying SSDM in the real world.

Methods: AS Patients were trained to master SSDM by healthcare professionals (HCPs) and to conduct ASDAS self-assessments. Patients were also required for repeating self-assessments after leaving the hospital. After entry by patients, data can be synchronized to the SSDM terminal of authorized rheumatologists. Based on these data, the patients can apply for consultation to their physicians and rheumatologists can provide medical advices to their patients.

Results: From Jan 2015 to Jan 2020, 17,870 AS patients enrolled in SSDM with the mean age of 34.62±10.98 years old and the median disease duration of 3.58 years. Among them, 1,127 AS patients from 150 hospitals were followed up for more than 6 months through SSDM. The results at baseline and in final follow up were summarized in Table 1.

Table 1. The T2T results at baseline and in final follow up.

Baseline\Final follow-up	n	%	x <= 1.3	%	1.3 < x <= 2.1	%	2.1 < x <= 3.5	%	3.5 < x	%
x <= 1.3	315	27.95%	206	65.40%	74	23.49%	26	8.25%	9	2.86%
1.3 < x <= 2.1	340	30.17%	138	40.59%	114	33.53%	75	22.06%	13	3.82%
2.1 < x <= 3.5	363	32.21%	95	26.17%	106	29.20%	133	36.64%	29	7.99%
3.5 < x	109	9.67%	24	22.02%	25	22.94%	42	38.53%	18	16.51%
Total	1,127	100%	463	41.08%	319	28.31%	276	24.49%	69	6.12%

The rate of T2T achievers were 27.95% (315/1,127) at baseline, and improved significantly to 41.08% (463/1,127) after 6 months follow up, p<0.01. Among T2T achievers at baseline, 65.40% (206/315) maintained T2T, 34.60% (109/315) relapsed. Of patients who didn't achieve T2T at baseline, only 31.65% (257/812) achieved T2T after 6 months follow up.

The impact of the online interaction between patients and physicians and the frequency of self-assessment for ASDAS on T2T has been analyzed. Compared with 544 patients who didn't interact online with their physicians and self-assessed less than 3times, 104 patients with online interaction and monthly assessments achieved significant higher improvement rate of T2T (9.19% vs 23.08%, p<0.01). The more frequent of the self-assessments being performed by patients, the higher improvement of T2T rate will be. The improvement of T2T rate(y) was positively correlated with times of self-assessment for ASDAS(x) independently. The regression equation as "y = 0.0304x + 0.0521", r = 0.9107, p<0.01 (Figure 1).

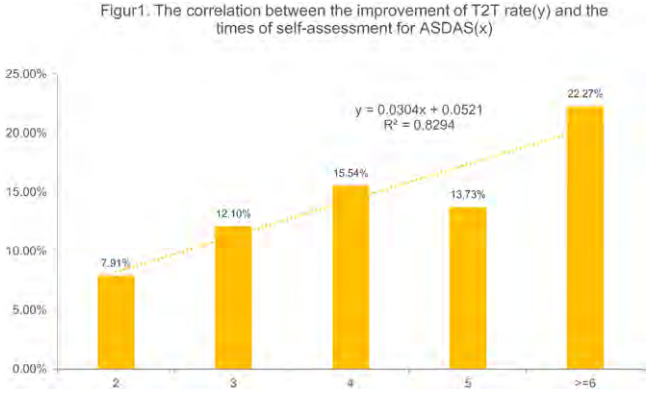


Figure 1.

Conclusion: Significant improvement was observed under applying SSDM through empowering AS patients. After proactive disease management via SSDM for more than 6 months, patients with ASDAS<=1.3 score at baseline had a significantly higher retention rate of inactive disease activity. The patients who performed more frequent self-assessments had lower probability of relapse and higher rate of T2T. Online interaction between patients and physicians contributed to promote the improvement rate of T2T. SSDM is a valuable tool for long term follow-up through empowering patients.

Acknowledgments: SSDM was developed by Shanghai Gothic Internet Technology Co., Ltd.
Disclosure of Interests: None declared
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SAT0647-HPR DEVELOP A MACHINE LEARNING MODEL AND ALGORITHM BASED ON SMART SYSTEM OF DISEASE MANAGEMENT (SSDM) BIG DATA FOR RA FLARE PREDICTION

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Background: Flare, relapse from status of treat-to-target (T2T, DAS28<=3.2), is hard predicted. We try to make it predictable by applying machine learning to a database from smart system of disease management (SSDM). SSDM is an interactive mobile disease management APPs.
Objectives: To develop and validate machine learning algorithms for flare prediction in RA.
Methods: Patients were trained using SSDM and input their data, including demographic, comorbidities (COMBs), lab test, medications and monthly self-assessments, including DAS28, HAQ, SF-36, Hospital Anxiety and Depression Scale (HADS). The data was uploaded to cloud and synchronized to the mobile of authorized rheumatologists. The COMBs were by ICD-9, and medications were listed as cDMARDs, Bio (BioDMARDs), NSAIDs, Steroid, FS (food supplements), MC (medicine for COMBs), TCM (Traditional Chinese Medicine), and combinations.
Results: From Jan of 2015 to Jan of 2020, 8811 RA patients, 85% female and 15% male, used to reach T2T. 4556 were flare-free and 4255 suffering at least one flare. The average 160 attributes were extracted from each flare-free patient at time of reaching T2T, and each flare patients at time of 3 months before the flare. Patients were randomly assigned as model setup (training) group (70%) and validation (testing) group30%.
For training, data were processed using Python with statistical analyses in R. In R, random forests were implemented. Logistic regression via glm in base R. The random forest comprises a set of decision trees. "Splits" in the decision trees reflect binary (i.e., yes/no) respect to attributors. Bootstrapping was used to assess, quantify, and adjust for model optimism. Model performance was evaluated using AUC, precision and recall metrics. Brier scores for accuracy of probabilistic predictions ranged from 0 to 1 (0 is perfect discrimination).
The testing showed model performance for prediction windows are 0.78 for AUC (95% CI), 0.71 for Recall (sensitivity), 0.195 for Brier score, and 0.68 for precision (true positive 893, false positive 417, false negative 367, true negative 966).
Based on weighing in the random forest, the top 10 pro-flare attributes were CRP, swollen joint count (SJC), tender joint count (TJC), HAQ, DAS28, morning stiffness, gout, MCTD, OA, duration; while top 10 anti-flare attributes were cDMARDs+Bio, cDMARDs+steroid+NSAIDs, stable on HAQ, on morning stiffness, on SJC, medicine on COMBs, cDMARDs+TCM, stable on TJC, on ESR, income at 100-200k (Fig.1). The top weighing COMBs for pro-flaring were gout (0.81), MRD (0.75), OA (0.56), AS (0.48). The monotherapies with either Bio or NSAIDs, or steroid, or TCM was pro-flare; while with cDMARDs was anti-flare (-0.21).

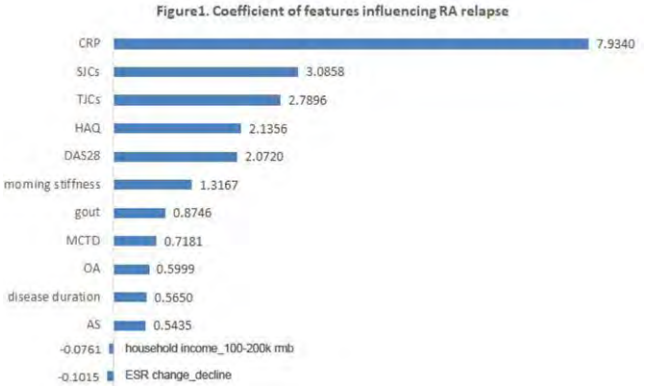


Figure 1.

Conclusion: The attempt to develop a machine learning algorithm for RA flare prediction is successful. The discrimination was acceptable. The attributes of both pro-flare and anti-flare are identified, which may inspire the proactive intervention.
Acknowledgments: SSDM was developed by Shanghai Gothic Internet Technology Co., Ltd.
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SATURDAY, 06 JUNE 2020

HPR Service developments, innovation and economics in healthcare

SAT0648-HPR CAN A SPECIALIST NURSE REPLACE A CONSULTANT - AN INNOVATIVE MODEL FOR OSTEOPOROSIS CARE

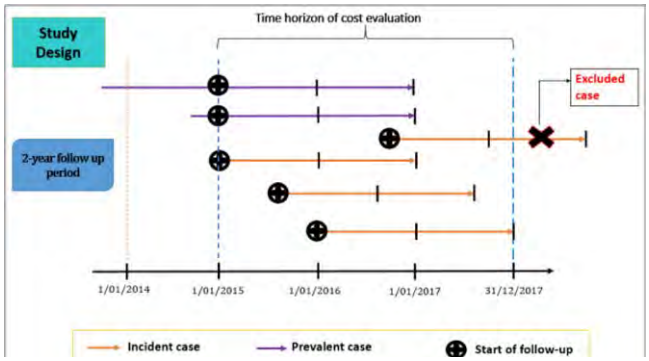
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Background: Specialist services are heavily reliant on a consultant reviewing a patient and discussing management options. However this can significantly delay treatment pathway owing to lack of sufficient consultant appointments. Clinical nurse specialists (CNSs) are an integral part of a multidisciplinary team employed to provide effective care for the diverse needs of patients with chronic conditions such as osteoporosis.
Objectives: We designed an innovative proof-of-concept osteoporosis service with patients only consulting a metabolic bone CNS and a consultant providing remote oversight. The aim of the project was to improve the efficiency of the service by eliminating consultant appointments and reducing unnecessary hospital visits whilst continuing to deliver a high-quality and safe service.
Methods: A new pathway was implemented where a consultant rheumatologist and a CNS virtually triaged post menopausal women over the age of 65 into the service. A dedicated proforma provided the template for the CNS to undertake new patient telephone consultation. Relevant investigations were requested during the telephone clinic and treatment related information was despatched to help with shared decision making. All patients were then reviewed in a consultant-CNS virtual MDT. Appropriate parenteral treatment option was agreed and confirmed to each individual. The CNS worked through a safety checklist and provided further advice and support to the patient as necessary. Using the database, we compared the timelines for patient journey to conventional pathway, obtained the number of consultant follow-up appointments saved by implementing this service and calculated total savings.
Results: In the proof-of-concept phase, 60 patients were triaged into the new service. It was a combination of 25 new referrals and 35 patients pulled from the consultants' waiting list. Mean age of participants was 77.2 years (65-92). Referral to virtual triage took median 20 days (0-62). Median time for triage to new patient CNS telephone consultation was 18 days (6-87). Time to virtual MDT for treatment authorisation was median zero days (0-76 days). 19 patients had anabolic therapy commenced via home care. Remaining had anti resorptive therapy. No patient requested face-to-face review. Only one patient fed back that they would've preferred to see the consultant once. Sixty new patient consultant appointments were saved and median delay in treatment commencement was reduced from 84 to 38 days.
Conclusion: To our knowledge, this is the first successful example of an innovative service wholly provided by CNSs for commencing parenteral anti-osteoporotic therapy with only remote consultant supervision. Our service redesign has significantly improved the efficiency of the parenteral osteoporosis pathway with reduction in treatment delay and a more streamlined patient journey. A nurse-delivered osteoporosis treatment pathway is highly effective, safe and provides an innovative solution to thinly stretched health care needs of people with chronic conditions.
Disclosure of Interests: Julie Begum: None declared, Joanne Fourmy: None declared, Muhammad Khurram Nisar Grant/research support from: Muhammad Nisar undertakes clinical trials and received support (including attendance at conferences, speaker fees and honoraria) from Roche, Chugai, MSD, Abbvie, Pfizer, BMS, Celgene, Novartis and UCB
, Consultant of: Muhammad Nisar undertakes clinical trials and received support (including attendance at conferences, speaker fees and honoraria) from Roche, Chugai, MSD, Abbvie, Pfizer, BMS, Celgene, Novartis and UCB
, Speakers bureau: Muhammad Nisar undertakes clinical trials and received support (including attendance at conferences, speaker fees and honoraria) from Roche, Chugai, MSD, Abbvie, Pfizer, BMS, Celgene, Novartis and UCB
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SAT0649-HPR DIRECT COSTS OF SYSTEMIC LUPUS ERYTHEMATOSUS IN COLOMBIA

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Background: Treatment burden of Systemic Lupus Erythematosus (SLE) is considered high. There are no studies in Colombia that includes the estimation of an incremental cost associated to SLE.
Objectives: To estimate the direct cost associated to SLE in contributory healthcare scheme in Colombia. To estimate prevalence and characterize SLE population affiliated in the contributory healthcare scheme in Colombia. To estimate the direct healthcare cost in patients with and without SLE and the effect of being diagnosed with SLE in the total direct cost during a period of two years.



Methods: The present study was carried out with an administrative database that includes all the enrollees in the contributive health scheme for a period of 4 years. It was established an operative definition to identify individuals with the disease in order to make the descriptive analysis and calculation of prevalence. every patient was aged 18 or older on index date. Additionally, as the length of follow-up period was fixed to two years, all patients whose index 14 date had been greater than 1st January 2016 were excluded from the study sample (Figure 1). The variables considered in this part of the study were demografiphc), clinical (Charlson Comorbidity Index) and cost-related variables, which was the outcome variable of the study, this cost was made up of the sum of all medical costs, regardless of whether they were related or not to SLE. Costs were adjusted for inflation, to values in 2017. To evaluate the effect of having SLE vs. not having, on the direct cost in health, propensity scores analysis was used to reduce differences in the baseline characteristics. Three groups were formed based on disease severity: high (patients who had renal failure), medium (patients in intensive care unit at least once but without renal failure) and low (remaining SLE patients) (See table 1).

Table 1. Incremental cost by degree of severity

Degree of Severity	Average adjust incremental cost per year (in COP)	Confidence interval construction method	Confidence interval (95 %) (in COP)
High	$ 19,930,931.67	t-interval	$16,525,728.01, $ 23,336,135.32
		Bootstrap	$17,088,627.49, $ 23,068,518.89
Medium	$7,248,201.04	t-interval	$2,123,742.99, $12,372,659.09
		Bootstrap	$3,460,932.89, $11,688,205.25
Low	$ 885,300.40	t-interval	$642,925.6, $ 1,127,675.2
		Bootstrap	$ 688,197.5, $ 1,098,098.2

Results: From 2014 to 2017, 21,993 SLE patients were identified. Women represented 87.4% of the cases, 5428 patients were selected to make up the sample of SLE patients. the number of patients without diagnosis of SLE was 19,419,540. From this population was drawn randomly a 10% size sample, to make up the potential control sample. To estimate the incremental cost of having SLE it was used multivariate regression through a GAM model. The estimated average annual total cost of a patient with SLE was $6,139,046 COP vs. non-SLE patient cost of $4,113,191 COP. Meanwhile the adjusted incremental cost of SLE vs non-SLE was $2,025,855 COP. Subsequently, adjusted incremental cost was estimated taking into account the levels of severity. In the Table 1 are presented the mean values of incremental costs and 95% confidence intervals.

Conclusion: Although the prevalence of SLE in Colombia is relatively low, the direct costs generated for this disease might be very high. The annual cost for a SLE patient was $2,025,855 COP greater than the cost of a non-SLE patient. When considering the severity levels of the disease, it was found a $ 19,930,931.67 incremental cost estimate for high level of severity. In the medium level, the estimate was $ 7,248,201.04. Meanwhile, a patient in the low severity level had a $ 885,300.40 incremental cost.

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SAT0650-HPR WHAT CAN WE LEARN FROM A ROUTINE FRAILTY ASSESSMENT IN RHEUMATOLOGY? A SERVICE EVALUATION OF 170 NEW PATIENT REFERRALS TO A SINGLE RHEUMATOLOGY CENTRE.

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Background: Frailty is common among patients with rheumatological diseases, and there is increasing evidence that it is associated with poorer outcomes. Frailty scores worsen during the course of chronic inflammatory arthritis (IA) and connective tissue disease (CTD). Existing tools such as the Rockwood Clinical Frailty Scale (a nine-point scale from 1 very fit- 9 severely frail) allow for rapid frailty assessment by doctors and nurses. Frailty assessment is recommended by NHS England as an important public health opportunity for targeted interventions for both primary and secondary care. We have limited understanding of frailty in rheumatology new patient cohorts, and it is not routinely assessed in most centres. We report the feasibility and utility of frailty scores in patients referred to rheumatology, and association with final diagnosis.

Objectives: This service evaluation assesses the utility and feasibility of implementing the Rockwood Clinical Frailty Score for new patient referrals at a single UK centre.

Methods: New patient assessments at a rheumatology consultant general new patient clinic were prospectively coded over 9-months (March- December 2019). Anonymised coded demographic data included: age, gender, referral source, history of depression, RFCS and clinical diagnosis (coded against established categories, those requiring further tests coded 'awaiting investigations'). RCFS coding was assisted by an online validated pictorial aide memoir for coding.

Results: Of the 181 referrals, 11 (6%) were excluded for incomplete data. The mean age of the remaining 170 patients was 53 years (SD 16.8; range 17-87), predominantly female (123/170; 72%). Most referrals, 57% (97/170) were from primary care, 23% (39/170) from musculoskeletal integrated triage services, 5% (9/170) from orthopaedics, 4% (7/170) from gastroenterology; 18 were from 12 secondary-care specialties. The RCFS was: mean 2.6 (median 2, range 1-7) with depression in 61/170 (36%), but no effect of this on mean RCFS (2.6 in both). RCFS increased with age (70-79, n=21, mean 2.9; >80, N=12, 4.3). The majority of patients had non-inflammatory (NI) diagnoses (119/170, 70%) e.g. osteoarthritis, fibromyalgia. Overall 19% (32) 'inflammatory arthritis' (IA; rheumatoid arthritis, psoriatic, undifferentiated inflammatory arthritis, gout); 4% (6) were diagnosed with a form of connective tissue disease (undifferentiated CTD; SLE; Sjogren's syndrome); 8% (13) were awaiting further investigations. Patients in both the NI and IA category were found to have an average RCFS of 2.6 (SD, NI 1.1; IA 0.9). Patients who received a diagnosis of CTD had an average RCFS of 3.5 (SD 1.8). We identified 30 patients who scored four or more (vulnerable/ at risk) for targeted intervention by therapy and allied health professionals. The RCFS was positively evaluated by clinicians.

Conclusion: RFCS was simple to introduce to our centre and has provided us with additional data to plan our service provision for primary and secondary care support for our cohort. Our new patients with CTD, and who were elderly had higher frailty scores, we found no association between frailty and depression or presence of IA or NI. The RCFS was easy to use and can be integrated into routine clinical practice for new and follow up patients. Further studies are required to support these findings.

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SAT0651-HPR BARRIERS IN DIAGNOSING RHEUMATOID ARTHRITIS – A FOCUS GROUP STUDY ON THE GENERAL PRACTITIONERS' PERSPECTIVES

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Background: Early treatment, before three months from symptom onset of rheumatoid arthritis (RA), is essential to increase the likelihood of remission and to

prevent permanent joint damage (1). However, it has been shown that only 20% of the patients are seen within the first three months, and the median delay in general practice has been estimated to 4 months (range 2–9) (2).

Objectives: To explore the barriers in diagnosing RA from the general practitioners' (GPs) perspective.

Methods: We conducted a qualitative study based on focus group interviews. We recorded the interviews digitally and transcribed verbatim. The transcribed interviews were analyzed based on content analysis (3), by using Nivo 12. Sample size was determined by thematic saturation.

Results: In total ten GPs participated in three different focus groups. 40 % were female, mean age was 53 years (range 37-64), and mean year since specialist authorization as GP was 16 years (range 5-23). 60 % of the GPs worked in a practice located within the referral area of a university hospital; the remaining within the referral area of a regional hospital.

Four themes emerged in the analysis: 1*) When the patient is not a text book example*, referring to the difficulty of identifying relevant symptoms among all clinical manifestations from the joints as described by the patients, 2) *The importance of maintaining the gatekeeper function*, referring to the societal perspective, and the GPs responsibility to refer the right patients to secondary care, 3) *Difficulties in referral of patients to the rheumatologist,* referring to perceived differences in the collaboration with rheumatologists. The GPs experienced that it was sometimes difficult to be assisted by rheumatologists, especially when the clinical picture was not 'clear cut'. Finally, (4) *Para-clinical testing, can it be trusted?* referring to challenges on the evaluation of especially biomarkers.

The overarching theme was: *Like finding a needle in a haystack*, covering the GPs difficulties in detecting RA among the many patients in general practice who appear to be well and at the same time have symptoms very similar to RA.

Conclusion: The GPs experienced that RA was a difficult diagnosis to make. The immediate challenge was that RA patient's initial symptoms often resembled those of more common and less serious conditions, and that investigative findings such as biomarkers can be negative at the early state of the disease. At the same time, the collaboration with rheumatologists was sometimes seen as a hurdle, when the clinical picture was not 'clear cut'.

In order to facilitate earlier diagnosis of RA in general practice, the GPs and rheumatologists need to focus on these barriers by strengthening mutual information and collaboration.

Physicians should remain vigilant to patients who have conditions that do not resolve as expected with treatment, who have symptoms that persist, or who do not look well despite negative investigative findings.

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Disclosure of Interests: Anne Sofie Lundberg: None declared, Bente Appel Esbensen: None declared, Ellen-Margrethe Hauge Speakers bureau: Fees for speaking/consulting: MSD, AbbVie, UCB and Sobi; research funding to Aarhus University Hospital: Roche and Novartis (not related to the submitted work)., Annette de Thurah Grant/research support from: Novartis (not relevant for the present study)., Speakers bureau: Lily (not relevant for the present study).

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SAT0652-HPR CHRONIC DISEASE MANAGEMENT AND HEALTH TECHNOLOGY READINESS OF PATIENTS WITH SYSTEMIC SCLEROSIS IN SWITZERLAND – A CROSS-SECTIONAL STUDY

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Background: People living with systemic sclerosis (SSc) often lack access to coordinated, specialized care and self-management support from qualified healthcare professionals. Such gaps lead to significant unmet health needs and inability to get preventive services. The Chronic Care Model (CCM) has been used to guide disease management across a wide range of chronic conditions. The CCM often uses e-health technologies to address self-management problems, connect patients with clinicians and reduce patient travel requirements.

Objectives: To evaluate current SSc care practice patterns and elicit patient health technology readiness to define relevant aspects and resources needed to improve SSc chronic disease management.

Methods: We employed a cross-sectional survey using the 20-item Patient Assessment of Chronic Illness Care (PACIC) instrument to assess how aspects of SSc care align with key components of the CCM.[1] Six items drawn from the '5A' (ask, advise, agree, assist, and arrange) model of behavioural counselling were included (all 26 items scored on 5-point scale, 1=never to 5=always). Acceptance of health technology was evaluated by adapting and combining questionnaires from Vanhoof[2] and Halwas[3]. German and French speaking SSc patients (>18 years) were recruited from university/cantonal hospitals and the Swiss scleroderma patients' association. Participants completed anonymous paper/online questionnaires. Data were analysed descriptively.

Results: Of 101 SSc patients, most were female (76%), spoke German (78%) and had a median age of 60 years (IQR: 50-68). Median disease duration was 8 years (IQR: 5-15), spanning a range of severity (31% limited SSc, 36% diffuse SSc, 3% overlap syndrome). One-quarter (25%) did not know their disease subset.

The mean overall PACIC score was relatively low (2.91±0.95) indicating that care was 'never' to 'generally not' aligned with the CCM. Lowest mean subscale scores related to Follow-up/ Coordination (2.64±1.02), Goal setting (2.68±1.07) and Problem-solving/Contextual Counselling (2.94±1.22). The single items 'Given a copy of my treatment plan' (1.99±1.38) and 'Encouraged to attend programs in the community' (1.89±1.16) were given the lowest ratings. The '5A' summary score was 2.84±0.97.

In terms of technology readiness, 43% completed the survey online. Most participants owned a smartphone (81%), laptop (63%) and/or desktop computer (46%). The overwhelming majority of patients (91%) reported using the Internet in the last year – primarily for communication (e.g. emails, text messages). Participants indicated relatively little experience with e-health applications and participating in SSc online forums or self-help groups.

Conclusion: To improve chronic disease management of SSc patients in Switzerland, current care practices warrant reengineering taking CCM components into account. Specific unmet needs relate to self-management support, help patients set individualized goals, and coordinate continuous care. Web-based technologies incorporating user-centred design principles may be a reasonable option for improving care.

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SAT0653-HPR COMMUNITY RHEUMATOLOGY SERVICE IN THE UK – WHO BENEFITS THE MOST?

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Background: Community rheumatology (CR) in the UK is a new form of rheumatologic service provision established in the last few years and run by few organisations such as Connect Health Ltd.

CR is based on the principle of sharing the management of rheumatologic patients between community service and secondary care aiming to reduce the

unreasonable referral flow from primary care to secondary care and to share the care of stable inflammatory patients between the services.
In the traditional service model patients are referred by General Practitioners (GP) to the secondary care with a wide spectrum of conditions: from fibromyalgia through soft tissues rheumatisms to inflammatory or connective tissue diseases. Many of these patients will be discharged from the specialist service after their first visit with fibromyalgia, osteoarthritis, chronic pain syndrome or MSK diagnoses. The proportion of these patients versus those who have an inflammatory rheumatologic condition or connective tissue disease (CTD) varies significantly and can contribute to oversaturated specialist rheumatologic services with long waiting time where specialists deal with less relevant cases.
Objectives: To determine how CR can improve quality of care and decrease the waiting time for appointment in secondary care rheumatology services. To set standards for referral pathways and measured outcomes of effectiveness in patient care.
In the UK the regional Clinical Commissioning Groups would accept a maximum waiting time from the referral until patient treatment of up to 18 weeks and specialist services often breach that limit. This long interval may have a significant negative impact for the care of patients with rheumatological condition, reducing patient satisfaction and/or jeopardize patient safety. The solution to the above problem is the creation of CR service.
Methods: Extensive search about the available resources within UK NHS system in regards CR service creation and set up. Web search, literature review in relation to CR in the UK
Results: From the research different models of CR can be identified and one of these will be presented in details based on the experience of one of the largest organisation running CR services in the UK (Connect Health Ltd). This service is organised within community care set up and can accept patients referred by the primary care physicians with non-inflammatory symptoms (e.g. osteoarthritis, Ehlers - Danlos Syndrome, fibromyalgia) or PMR or gout. The service also can review stable inflammatory patients who are treated with DMARDs and are transferred from the secondary care service by their consultant. This presentation will demonstrate how CR provides safer, faster and more accessible services to the patients assisting the specialist services and allowing them to concentrate on the inflammatory and CTD patients who need faster access to these services than it is possible now. Particularly the presentation will emphasise on:

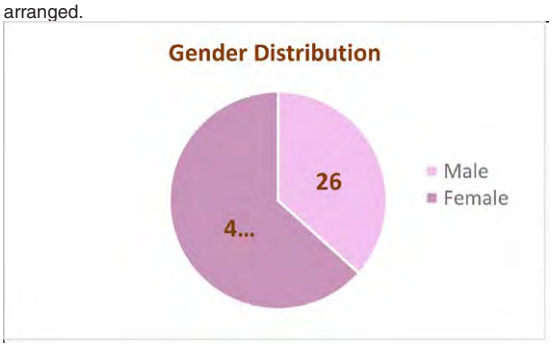
•Patient population cover
•Team structure, their experience and training
•Referral criteria and IT set up for multidisciplinary connection
•Time interval for appointment and patient feedback
•Impact on the secondary care rheumatology service
•Cases of misdiagnosis and inappropriate referrals
•Cost effectiveness of the CR
•Challenges in the CR service

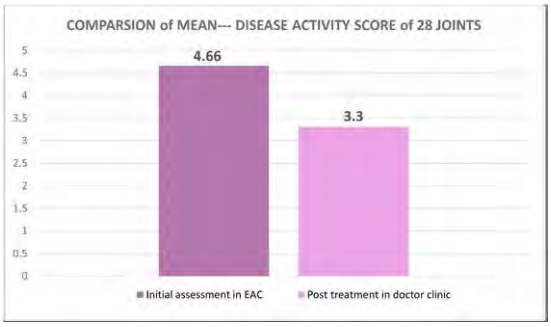
Conclusion: The CR service can be a safe addition to the specialist services taking over significant workload and provide new career opportunities for a wide range of Allied Health Professionals (AHP) for the bigger satisfaction of the patients who can access rheumatology service earlier and easier.
Disclosure of Interests: None declared
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SAT0654-HPR AN OUTCOME EVALUATION FOR THE NURSE-LED EARLY ARTHRITIS CLINIC ON THE DIAGNOSIS AND MANAGEMENT OF RHEUMATOID ARTHRITIS AT CARITAS MEDICAL CENTRE IN HONG KONG

D. K. H. Ng[1], Y. L. J. Yu2, P. Y. K. Lin2on behalf of DOCTOR. *[1]Hong Kong, CARITAS MEDICAL CENTRE, HONG KONG, Hong Kong (SAR)*; *[1]Hong Kong, CARITAS MEDICAL CENTRE, HONG KONG, Hong Kong (SAR)*

Background: Rheumatoid Arthritis (RA) is a chronic, autoimmune, inflammatory disease that may cause progressive joint damage and deformity, leading to functional disability and reduced quality of life. However, there is often a long waiting time for the first assessment in Rheumatology Clinic by doctor. Development of rheumatology nurse-led clinic allows early assessment by qualified rheumatology nurse for patients with suspected RA. It may potentially facilitate the decision and treatment plan in the first doctor clinic. A nurse-led Early Arthritis Clinic (EAC) for RA patients had been established in Caritas Medical Centre (CMC) since January 2018.
Objectives: To determine the effectiveness of the EAC by early identification of new cases of RA and to facilitate decision in early initiation of disease-modifying anti-rheumatic drugs (DMARDs) during the first doctor clinic assessment.
Methods: New cases were screened and recruited by Rheumatology nurse from January to December 2018 to nurse-led EAC. The recruited new cases were seen in EAC around 1 to 4 weeks before the first doctor clinic. Rheumatology nurse performed nursing assessment in EAC according to the 2010 ACR-EULAR Classification of RA. These cases will be reviewed by Rheumatologist during the first doctor clinic for confirmation of diagnosis and formulation of treatment plan. If urgent problems were identified during assessment in EAC, patients would be prioritized to have an earlier doctor clinic appointment or hospitalization may be arranged.





Results: A total of 128 patients with articular symptoms were seen in nurse-led EAC during the study period. Nursing assessment revealed that 71 patients were required further evaluation for the diagnosis of RA (26 males and 45 females, mean age for males: 51, mean age for females: 56) and they were recruited into the study. 36 of these 71 patients were confirmed with the diagnosis RA by rheumatologist during the first consultation of doctor clinic. 13 of 36 patients were prescribed with DMARDs on the same day of consultation. Before the establishment of EAC, the mean time of confirmation of RA by rheumatologist was 8 weeks (range from 4 to 12 weeks). Therefore, EAC facilitates both the early diagnosis of RA and the prompt initiation of treatment after confirmation of diagnosis. Reduction in disease activity was also noted after treatment. The mean Disease Activity Score of 28 joints (DAS 28) during the assessment in EAC was 4.66 (range 3.22 to 6.54) while post treatment after EAC and the first doctor clinic was 3.30 (range 2.08 to 5.16) with mean difference of -1.36 ($p<0.01$). Other diagnoses were also made among the 71 patients. 8 patients were diagnosed of Spondyloarthropathy, 2 patients were diagnosed of psoriatic arthritis and 2 patients were diagnosed of systemic lupus erythematosus. 3 of these 71 patients were identified urgent medical problems required early intervention. Among these 3 cases, two patients with liver function derangement and one of them needed hospital admission for assessment of acute hepatitis. Another patient was arranged hospitalization to rule out sepsis due to raised total white cell count and erythrocyte sedimentation rate.
Conclusion: Rheumatology nurse assessment in EAC is effective in assessing patients with suspected diagnosis of RA. It shortened the time to confirm the diagnosis of RA, and facilitated the decision on treatment plan. It effectively improved the disease activity of patients due to the prompt initiation of DMARDs by Rheumatologist.
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Acknowledgments: DR DANIEL KAM HUNG NG
Disclosure of Interests: None declared
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SATURDAY, 06 JUNE 2020

Patient information and education

PARE0001 **DIET, NUTRITION AND ARTHRITIS – A WORKSHOP FOR YOUNG PEOPLE WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES (RMDS).**

M. Voeten[1], W. Olsder[1]. [1]*Youth-R-Well.com, Nieuwegein, Netherlands*

Background: The impact of diet and nutrition on RMDs is a growing topic with lots of ongoing research and remaining questions. Youth-R-Well.com, the organization for young people (18-30 years) with rheumatic and musculoskeletal diseases (RMDs) in the Netherlands, recognized that young people want to know more about this theme. Therefore, Youth-R-Well.com organized the workshop "Diet, Nutrition and Arthritis" to inform young people with RMDs about the facts and myths of the impact of diet and nutrition on RMDs.
Objectives: The main objective of this project was to inform young people with rheumatic and musculoskeletal diseases about the impact of diet and nutrition on RMDs. Youth-R-Well.com wanted to offer the knowledge of proven research and studies, and provide all the recent facts and fables about this topic. By becoming well-informed about the impact of healthy cooking, young people are able to improve the self-management of their disease. Besides providing information about the impact of diet and nutrition, the objective was to offer tips and tricks about ergonomic cooking. With the right tools for cooking, the participants might be inspired by a less painful and more suitable way of cooking, which also increases the self-management of their disease.
Methods: To make sure the event was consistent with the needs of young people, Youth-R-Well.com organized a cooking workshop, that consisted of two parts: informative presentations and a fun healthy cooking workshop. For the first part, we invited a professor and a dietitian specialized at this specific topic to provide the correct and up-to-date information. For the second part, we invited an occupational therapist to provide information about ergonomic cooking. The kick-off of the day was by two informative presentations: the professor, who focused on recent studies, and the dietitian, who focused on the practical side. Both the presentations ended up in a question and answer component, where the participants showed lots of interaction. After the first session, the practical side of the workshop could be started. Several nutrient full and healthy recipes were made in teams to interact with other participants. An occupational therapist facilitated the participants by presenting the less painful and correct technique for preparing food. The workshop is filmed and shared through YouTube, to make sure the information reaches more young people with RMDs.
Results: It was a successful workshop where over 40 participants were present. The educational and helpful presentations were well received and created more realization of the impact of an appropriate and altered diet. The survey, which was filled up by the participants, has shown that over 91% rated the event by the highest-ranking "good". Also, in the second part of the workshop, the practical cooking was very good and useful; it was rated as the most favorite part. The workshop was filmed and shared online, we reached over 1300 people with enthusiastic and lovely comments.
Conclusion: Based on the questions of young people around the impact of diet and nutrition on RMDs, Youth-R-Well.com organized the workshop: "Diet, Nutrition and Arthritis". Through the combination of informative presentations and a fun cooking workshop, Youth-R-Well.com managed to inform young people about this growing topic. We will continue to spread the information through our online video on our online channels to reach more young people with RMDs.
Disclosure of Interests: None declared
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PARE0002 **IMPACT OF SERVICE DOGS ON THE BURDEN OF ARTHRITIS**

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Background: Assistance dogs support humans with different physical disabilities: 1. Service dogs for people with diverse mobility impairments 2. signaling dogs for humans diagnosed with diabetes, hearing impairments, seizure, or posttraumatic stress disorder 3. guide dogs for people with visual impairments. Definitions and terms are not consistent over Europe; Austrian terminology is used in the following. These specially trained dogs support people in their everyday lives and make it possible that less help is required from personal assistants or caregivers. Diverse studies show this positive impact of assistance dogs on the quality of life of disabled people. There are just a few case reports from United States about service dogs for people diagnosed with any inflammatory rheumatic disorder. Dogs are trained individually for about 1.5 years before team training and the concluding team assessment through Austrian authorities take place. Since 2015, there has been an adapted legislation for service dogs in Austria which brings significant improvements in many areas. In comparison to the model set by Austria, there is no corresponding legal basis at EU level or in other European countries.
Objectives: Case-report about my own situation diagnosed with juvenile idiopathic arthritis (JIA) in 2001 and my service dog May. May supports my every day live in private and business affairs since 2019
Methods: May was trained for less than two years before team assessment. May is able to pick up things I dropped. These include coins, my key, my mobile phone, clothes, towels and lots of other things I want her to pick it up for me. May opens and closes doors, empties the washing machine, pulls the laundry basket and even helps me put on and take off clothes. In general, she carries many things which I instruct her to carry. I am able to learn her more new things in a short time. Furthermore May acts safe on public transport and even airplanes. Due to special training May is allowed to move without dog leash or muzzle. A muzzle or leash would handicap the dog's work. As a result of May's help I need less personal assistance.
Results: May's physical and psychological support gives me greater independence and increases my self-confidence. She was trained to specifically meet the needs of my disability. Beside her skills, May helps to reduce pain and burden of arthritis.
Conclusion: My aim is to spotlight the great support of service dogs to severely affected arthritis patients. Austria had realized legislation for assistance dogs to guarantee certain permissions the owner's needs (e.g. access to working place, hospital). I would love to raise awareness about assistance dogs to improve the knowledge about those animals to implement European legislation.
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Acknowledgments: I am very grateful to Kati Kohoutek, May's trainer and the efforts of Austrian's long lasting dog trainers and Karl Weissenbacher, the leader of Messerli Institute/ department of Veterinary University Vienna.
Disclosure of Interests: None declared
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PARE0003 **MY RA STORY - PERSONAL ACCOUNTS OF LIVING WITH RHEUMATOID ARTHRITIS**

B. Lynch[1]. [1]*Dublin, Dublin, Ireland*

Background: Over 2,000 people are diagnosed with rheumatoid arthritis (RA) in Ireland each year; three in four are of working age. In total, RA affects some 45,000 people in the country; 70 per cent of whom are women.
For someone newly diagnosed with RA, coming to terms with the news can seem overwhelming.
Such a dramatic shift in life circumstances can impact one's physical and mental well-being. While there is no shortage of information available about the condition, it can be overwhelming trying to filter this, assess what is trustworthy and reliable.
Objectives: •To provide information and hope to people newly diagnosed with RA, and to give a voice to those living with the condition;
•To increase awareness and understanding of RA – encourage engagement with HCPs, contributing to early diagnosis and better outcomes;
•To increase awareness of work of Arthritis Ireland as a patient organisation.
Methods: Arthritis Ireland approached best-selling author and RA patient, Sinead Moriarty, to front an RA awareness campaign, called My RA Story.
The purpose of the campaign was to increase awareness and understanding of rheumatoid arthritis, of what it is like to live with this chronic condition with its invisible pain and life-changing impact. In so doing, Arthritis Ireland wanted to give a platform to people to tell their own story, so that they could be heard. We then wanted to publish these experiences in book form.
In April 2019, we launched a video on social media featuring Sinead Moriarty speaking about her experience of living with RA. The video generated lots of engagement across social media and also helped garner national and regional media coverage in print and broadcast.

The call for RA stories received a fantastic response from the public and the reading panel had a tough job in selecting the contributions which would feature in the published volume. Once the successful contributions were chosen, Arthritis Ireland proceeded to design a book, which could be sold in the book trade and online.

Results: In September 2019, Arthritis Ireland published My RA Story: Personal accounts of living with rheumatoid arthritis. Launched in the National Library of Ireland by Sinead Moriarty, the 46 contributions touched upon themes of pain, fatigue, emotional impact, disability, surgery, education, career, family, goal-setting, self-management, connecting with others, hope, etc.

The contributors came from people who were living with RA for over 40 years, as well as from those who were more recently diagnosed.

The book is a hugely valuable contribution to health literature. Arthritis Ireland now plans to make the book available for sale internationally, through Amazon and other retail channels, as well as promoting it more extensively in rheumatology clinics.

In October, one of the contributors was interviewed on national television about her RA story, as part of a feature on World Arthritis Day.

Conclusion: This campaign gave people living with RA a platform to write about and share about their condition. Fronted by an RA champion with significant name recognition and an enormous audience in her own right, best-selling author, Sinéad Moriarty, the book, My RA Story. Crucially, the book is a valuable resource for people who are newly diagnosed with the disease and uncertain of what the future holds.

Acknowledgments: This project was supported by an educational grant from MSD.

Disclosure of Interests: Brian Lynch Grant/research support from: Arthritis Ireland received a grant from MSD to develop this patient education programme. Brian Lynch has not benefited personally in any way.

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PARE0004 PATIENT PERSPECTIVE ON THE EFFICACY AND RISKS OF GLUCOCORTICOIDS IN RHEUMATOID ARTHRITIS – AN INTERNATIONAL SURVEY OF 1344 PATIENTS

T. Santiago[1,2], M. Voshaar[3], M. De Wit[4], P. Carvalho[5,6,7], F. Buttgereit[8], M. Cutolo[9], M. Boers[10], J. A. P. Da Silva[1,2]. [1]*Centro Hospitalar e Universitário de Coimbra, Rheumatology Department, Coimbra, Portugal*; [2]*University of Coimbra, Faculty of Medicine, Coimbra, Portugal*; [3]*University of Twente, Department of Psychology, Health and Technology, Enschede, Netherlands and Stichting Tools Patient Empowerment, Amsterdam, Netherlands*; [4]*Stichting Tools Patient Empowerment, Amsterdam, Netherlands*; [5]*Department of Rheumatology, Centro Hospitalar Universitário do Algarve, Faro, Portugal*; [6]*Lisbon Academic Medical Centre, Lisbon, Portugal*; [7]*Algarve Biomedical Center, Faro, Portugal*; [8]*Department of Rheumatology and Clinical Immunology, Charité University Medicine Berlin, Berlin, Germany*; [9]*Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genova, IRCCS Polyclinic Hospital San Martino, Genova, Italy*; [10]*Department of Epidemiology and Biostatistics; and Amsterdam Rheumatology and immunology Center, Amsterdam University Medical Centers, Vrije Universiteit, Amsterdam, Netherlands*

Background: The Glucocorticoid Low-dose Outcome in Rheumatoid Arthritis Study (GLORIA) is an international investigator-initiated pragmatic randomized trial designed to study the effects of low-dose glucocorticoids (GCs) in elderly patients with Rheumatoid Arthritis (RA).

The research team is also committed to promote a better understanding of the risks and benefits of these drugs among health professionals and patients. In order to achieve these goals, it is important to assess the current ideas and concerns of patients regarding GCs.

Objectives: To evaluate the current patient perspective on the efficacy and risks of GCs in RA patients who are or have been treated with GCs.

Methods: Patients with RA completed an online survey (with 5 closed questions regarding efficacy and safety) presented in their native language. RA patients were recruited through a variety of patient organizations representing three continents. Patients were invited to participate through national patient organizations. In the USA, patients were also invited to participate through MediGuard.org. Participants were asked for their level of agreement on a 5-point Likert scale.

Results: 1344 RA patients with exposure to GCs, from Brazil, USA, UK, Portugal, Netherlands, Germany and 24 other countries** participated: 89% female, mean age (SD) 52 (14) years and mean disease duration 13 (11) years. The majority of participants (84%) had ≥10 years of education. The duration of GCs exposure was 1.6 (4.2) years. The majority of participants had read articles or pamphlets on the benefits or harms of GC therapy.

Regarding GCs efficacy (table 1), high levels of endorsement were found: about 2/3 of patients considered that GCs as very useful in their case, more than half considered that GCs were effective even at low doses, and agreed that GC improved RA symptoms within days.

Regarding safety (table 1), 1/3 of the participants reported having suffered some form of serious adverse events (AEs) due to GCs, and 9% perceived this as "life-threatening. Adverse events had a serious impact on quality of life, according to about 1/3 of the respondents.

Conclusion: Patients with RA exposed to GC report a strong conviction that GCs are very useful and effective for the treatment of their RA, even at low doses. This is accompanied by an important prevalence of serious AEs. Understanding the patient perspective can improve shared decision-making between patient and rheumatologist.

References: **Funding statement:** This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 634886.

Table 1 – Results of the surveys, across different countries, concerning patient perspective on the efficacy and risks of glucocorticoids in patients with RA.

	All	Brazil	USA	UK	Portugal	Germany	NL	Others**
GCs are or have been very useful to me								
Agree	58	64	56	52	42	51	68	54
Slightly agree	20	20	21	11	12	30	10	18
Neutral	6	4	8	7	5	6	6	10
Slightly disagree	3	4	5	1	4	0	3	3
Disagree	4	3	7	3	1	4	3	3
Missings	9	6	1	15	25	9	9	12
At a GC dose ≤7.5mg/day:								
- Are very effective in the control of signs and symptoms of RA								
Agree	41	48	42	40	31	28	46	38
Slightly agree	25	25	15	20	26	45	20	12
Neutral	12	11	24	8	12	12	16	12
Slightly disagree	3	7	6	6	4	0	4	4
Disagree	5	4	7	6	1	6	6	7
Missings	12	6	3	19	25	9	9	15
- Improve RA symptoms within days								
Agree	41	45	44	37	34	37	44	39
Slightly agree	22	23	19	19	20	33	23	24
Neutral	12	12	18	8	13	6	12	9
Slightly disagree	6	6	7	7	7	6	6	7
Disagree	8	8	89	10	1	3	5	7
Missings	11	6	3	19	25	9	9	15
I have suffered very SAEs due to GCs								
Agree	29	40	44	13	15	18	18	29
Slightly agree	3	0	0	0	0	0	32	18
Neutral	14	15	12	15	17	4	7	11
Slightly disagree	1	0	0	0	0	0	7	2
Disagree	44	40	43	56	43	58	27	41
Missings	9	6	1	15	25	9	9	12
N (% of total)*	432 (100)		104 (24)	211 (49)				117 (27)
How serious do you consider these SAEs								
Life threatening	9	NA	55	32	NA	NA	NA	13
Serious impact in my QoL	36	NA	39	38	NA	NA	NA	23
Minor impact in my QoL	27	NA	28	52	NA	NA	NA	17
Mild and well tolerated	29	NA	18	50	NA	NA	NA	32

Numbers indicate %.
***Others (% of total):** Italia 1.9%; Spain 1.7%; Romania and Canada, each one 1.4%; Belgium 0.6%; France, Australia and Venezuela, each one with 0.2%; Algeria, Angola, Argentina, Belize, Cyprus, India, Ireland, Japan, Mauritius, Mexico, Mozambique, Moldova, Nicaragua, Norway, Sweden and Switzerland each one with 0.1%.
*The Portuguese, Germany and Deutschland version as well as the English survey through MediGuard.org. didn't have this question due to legal constraints (% of answers per frequency category).

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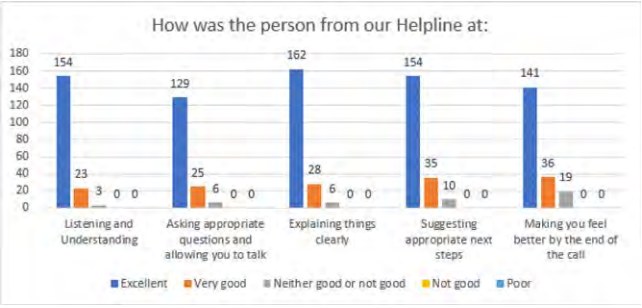
DOI: 10.1136/annrheumdis-2020-eular.3164

PARE0005 INTEGRATED REFERRAL OF NEWLY DIAGNOSED RHEUMATOID ARTHRITIS PATIENT TO EDUCATION AND SUPPORT RESOURCES DELIVERED BY PATIENT LED ORGANISATION

I. Mcnicol[1], A. Bosworth[1], C. Jacklin[1], J. Galloway[2]on behalf of Ailsa Bosworth MBE, James Galloway, Clare Jacklin. [1]*National Rheumatoid Arthritis Society, Maidenhead, United Kingdom*; [2]*King's College Hospital, London, United Kingdom*

Background: NRAS follows best practice, evidence-based standards in all we do. Whilst huge strides have been made in the diagnosis and treatment of RA, the impact on quality of life can be significant and for many this disease remains hard to come to terms with. NRAS services and resources can improve the outcomes of people with RA/Adult JIA through a framework of supported self-management resources tailored to individual need. It is particularly important to provide the right support at the beginning of a person's journey with RA, when unhelpful health beliefs, anxiety and incorrect information can influence how someone responds to prescribed

medication and treatment thus impeding their ability to achieve the best outcomes. We know, for example, that many people do not take their medication as prescribed which reduces their chances of achieving remission or low disease activity state.
Objectives: To demonstrate that by referring patients online as part of a quality improvement programme to NRAS Right Start Service, we can show improved outcomes for patients with early RA when measured by the MSKHQ. Referred patients will benefit by: a) Better understanding what RA is; b) knowing how it can affect them; c) getting the right support; d) feeling more in control; receiving a tailored pack of information that meets their personal needs; e) be able to talk to a like-minded person who has lived with RA. It's a 4 step process which starts with the health professional referring their patient to NRAS on line. NICE Quality Standard 3 states that "Adults with rheumatoid arthritis are given opportunities throughout the course of their disease to take part in educational activities that support self-management." Our service enables health professionals to meet their responsibilities against this national quality standard.
Methods: In preparation for the introduction of this service at BSR congress 2019, an audit of the NRAS helpline service was undertaken at the end of 2018 and remains on going. Currently we have 224 responses which have been analysed against specific criteria. An Advisory Board comprising 7 clincians, from different hospitals was appointed to work with NRAS on this important research.
Results: In the helpline audit, when asked 'how concerned are you about your disease'?, alarmingly, 78% of those surveyed scored their level of concern about their disease at 7 or higher out of 10, while only 8% scored it at 5 or below. When asked about the emotional effects of their RA, 62% scored it as 7 or more where 10 was the worst possible impact. 94% of survey respondents said that they would definitely or very likely recommend NRAS and its services to another person. These results led to the development of New2RA Right Start launched in 2019, whereby health professionals across the UK can refer their patients directly to NRAS via a consented online referral which is fully GDPR compliant. To date (31st Jan, 2020), we have made calls to 101 patients, from 24 referring hospitals of which 55 have been successfully completed, 34 have had information sent through the post although our helpline team were unable to speak to them, and 12 remain open. Data analysis on the service is being carried out by King's College Hospital London, comparing the results of patients who have been referred to Right Start within the national audit who have completed a baseline and 3 month follow up MSKHQ and patients in the audit who have not participated in Right Start.



Conclusion: Anecdotally, we have had a tremendous response to this service from both patients and referring health professionals. We await data from King's on the above figures, which we will have within the next 2 months and further data, should this abstract be accepted, will be available prior to June 2020. Right Start enables health professionals to comply with QS3 above, of the NICE Quality Standards in RA, one of the key standards against which they are being audited in the NEIAA national audit. Once data and write up in a peer review journal has been published we plan to roll this service out to people with more established disease.
References:
[1] To be done, not included in word count.
Acknowledgments: I would like to thank Ailsa Bosworth MBE, Clare Jacklin, and James Galloway
Disclosure of Interests: Iain McNicol Shareholder of: GSK, Ailsa Bosworth Speakers bureau: a number of pharmaceutical companies for reasons of inhouse training, advisory boards etc., Clare Jacklin Grant/research support from: NRAS has received grants from pharmaceutical companies to carry out a number of projects, Consultant of: I have been paid a speakers fee to participate in advisory boards, in house training of staff and health professional training opportunities, Speakers bureau: Various pharma companies, James Galloway: None declared
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SATURDAY, 06 JUNE 2020

Work and rehabilitation

PARE0006 **WORK PRODUCTIVITY LOSS IN PATIENTS WITH INFLAMMATORY ARTHRITIS**

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Background: Limited data exist of work productivity loss in patients with Rheumatoid Arthritis (RA), Psoreatic Arthritis (PsA) and Spondyloarthritis (axSpA).
Objectives: The objective of this research was to assess productivity loss and absenteeism in patients with RA, PsA and axSpA.
Methods: The study was designed as a cross-sectional study aimed to collect patient-reported outcomes from patients with RA, PsA and axSpA in Denmark via a nurse administered questionnaires and patient journals. Patients ≥18 years with RA, PsA or axSpA were consecutively recruited for the study over a 6-month period via routine visits to outpatient rheumatology clinics. Descriptive statistics were analyzed using SAS.
Results: Of 488 respondents, 62% were women and mean age was 53.5 years (RA:57.4; PsA:52.6; axSpA:43.6). Average time since diagnosis was 11-15 years, however, for PsA and axSpA most patients answered 6-10 and 0-5 years, respectively. 280 (57%) answered that they had a job and completed the WPAI questionnaire (RA: 149 (51%); PsA: 48 (56%); axSpA: 83 (75%)). Average work hours was 31.9 in the last week (RA:31.2; PsA:33; axSpA:32.4). Average missed work hours were 4.3 in the last 7 days ((RA:4.0; PsA:4.2; axSpA:4.8), of which 32% was missed due to their inflammatory arthritis (RA:30%; PsA:38%; axSpA:32%). Mean absenteeism was highest for patients with PsA (mean=6.8; SD=17.7) followed by patients with axSpA (mean=5.4; SD=15.1) and with RA (mean=3.4; SD=12.2). Mean productivity loss was 20.5 (SD=23.8) for patients with RA, 27.6 (SD=25.8) for PsA and 26.3 (SD=25.8) for axSpA
Conclusion: We found that patients with PsA or axSpA miss more hours of work compared with patients with RA and when they are at work they have a higher absenteeism/lower productivity. This even though that both the group of patients with PsA and the axSpA were younger and had lived less time with their diagnosed disease compared with the group with RA.
Disclosure of Interests: Trine Pilgaard Shareholder of: Pfizer, Employee of: Pfizer, Bente Appel Esbensen: None declared, Sandra Elkjær Stallknecht Consultant of: Pfizer
DOI: 10.1136/annrheumdis-2020-eular.1497

SATURDAY, 06 JUNE 2020

RMD research

PARE0007 **PATIENT AND PUBLIC INVOLVEMENT IN CLINICAL TRIAL DESIGN**

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Background: Patient and public involvement (PPI) is gaining increasing recognition as important in ensuring research is relevant and acceptable to participants. Rheuma Tolerance for Cure (RTCure) is a 5 year international collaboration between academia and industry; focusing on earlier detection and prevention of rheumatoid arthritis (RA) through the use of immune-tolerising treatments.
Objectives: To bring lived experience and insight into scientific discussions; and to evolve collaboration between lay representatives and academia/industry.
Methods: 9 Patient Research Partners (PRPs) from 5 European countries were recruited via the EULAR PARE Network and institutions within the RTCure Consortium (8 PRPs with RA and 1 'at risk'). They were asked to enter into a legal agreement with the Consortium. PRPs participated in teleconferences (TCs) and were invited to attend face-to-face (F2F) meetings at least annually. Requests for input/feedback were sent from researchers to PRPs via the project's Patient Engagement Expert [SK].
Results: PRP involvement has given researchers and industry partners a new perspective on patient priorities, and focused thought on the ethics of recruitment for

and participation in clinical trials of people 'at risk' of developing RA. PRPs have helped define the target populations, given their thoughts on what types of treatments are acceptable to people 'at risk' and have aided the development of a survey (sent to EULAR PARE members) regarding the use of animal models in biomedical research. Positive informal feedback has been received from researchers and industry regarding the contribution of PRPs to the ongoing project (formal evaluation of PPI in RTCure will be carried out in 2020 and at the project end in 2022).

Challenges: *Legal agreements* **-** Many PRPs refused to sign the Consortium's complex PRP Agreement; feeling it unnecessary, incomprehensible and inequitable. After extensive consultation with various parties (including EULAR and the Innovative Medicines Initiative) no similar contract was found. Views for its requirement even varied between legal experts. After 2 years of intense discussion, a simple non-disclosure agreement was agreed upon. Ideally any contract, if required, should be approved prior to project onset.

Meeting logistics - Other improvements identified were to locate the meeting venue and accommodation on the same site to minimise travel, and to make it easier for PRPs to take breaks when required. This also facilitates informal discussions and patient inclusivity. We now have agreed a policy to fund PRPs extra nights before and after meetings, and to bring a carer if needed.

Enabling understanding – Future annual meetings will start with a F2F meeting between PRPs and Work Package Leads. Researchers will be encouraged to start presentations with a summary slide in lay language. Additionally, an RTCure Glossary is in development.

Enabling participation – SK will provide monthly project updates and PRP TCs will be held in the evening (as some PRPs remain employed). PRPs will be invited to all project TCs and F2F meetings. Recruitment is underway to increase the number of 'at risk' PRPs as their viewpoint is vital to this study.

Conclusion: Currently PPI in RTCure is an ongoing mutual learning process. Universal guidance regarding what types of contracts are needed for PPI would be useful. Communication, trust and fruitful discussions have evolved through F2F meetings (both formal and informal) between PRPs, academia and industry. It is important that all parties can be open with each other in order to make PPI more meaningful.

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SATURDAY, 06 JUNE 2020

Involvement and innovation in healthcare

PARE0008 MOBILE APPLICATION "MOJRA" FOR MONITORING PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: In Serbia, regular examinations with a rheumatologist are scheduled on average every 3 to 4 months. With this in mind, there is a real possibility that many patient data during this period may not be presented to the doctor during the examination, either because the patient forgets them or because they may focus on other issues and may not highlight key facts

Objectives: To overcome this problem, the Association of Patients with Rheumatic Diseases of Serbia-ORS in cooperation with an IT firm developed the application "MojRA", which was presented at the annual rheumatology congress of Serbia held in September 2019. The application "MojRA" is intended for patients suffering from rheumatoid arthritis - RA. The application enables efficient storage and systematization of data, allows doctors to monitor the condition of their patients between two examinations and have a medical history. "MojRA" is available for now from smartphones running the android operating system on the google play store. The privacy of patient information is guaranteed.

Methods: Patients with RA will be able to record and store information about important moments during treatment in a simple and transparent way. At each subsequent visit they will be able to describe what happened to their illness in the meantime. The application can create different types of reports and views.

At the same time, the doctor can use the app to inform the patient about her/his condition in real time, which will contribute to better and more meaningful communication. All this would improve the quality of health care, preserving work capacity and improving the quality of life.

Results: In order to simplify biotherapy committee approval procedure for patients of RA, the "Charger" has been developed in association with ORS and URes. The "Charger" will connect data collected by MojRa to the registry of RA patients, making the whole approval procedure more efficient and transparent. Testing of the second version of this application is underway, meetings are held between the patients using the application and the IT company that created it. Plans are to expand the app to other types of arthritis in the near future, too, and will soon be completed for devices running Apple operating systems.

Conclusion: In addition to being of great benefit to patients and doctors, it can in the future be of immeasurable importance for the savings in the overall health care system of the Republic of Serbia.

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Disclosure of Interests: None declared

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PARE0009 COMMUNITY ADVISORY BOARD INPUT CAN MAKE LAY SUMMARIES OF CLINICAL TRIAL RESULTS MORE UNDERSTANDABLE

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Background: Under European Union (EU) Clinical Trial regulations,[1] clinical research sponsors (CRSs) must ensure all studies performed in the EU are accompanied by a trial summary for laypersons, published within 1 year of study completion. These lay summaries should disseminate clinical trial results in an easy-to-understand way for trial participants, patient and caregiver communities, and the general public. The European Patients Forum (EPF)[2] and European Patients' Academy on Therapeutic Innovation (EUPATI)[3] encourage CRSs to engage with patient organisations (POs) in the development of lay summaries. This recognises the patients' contribution to clinical research and supports the development of patient-focused material.

Objectives: We share learnings from a collaboration between scleroderma POs and a CRS to create the SENSCIS® trial (NCT02597933) written and video lay summaries.

Methods: A community advisory board (CAB), comprising representatives from 11 scleroderma POs covering a range of countries/regions, was formed based on the EURORDIS charter for collaboration in clinical research.[4] Through three structured meetings, over a seven-month period, the CAB provided advice on lay summary materials (written and video) drafted by the CRS' Lay Summary Group (Fig. 1). At each review cycle, the CAB advice was addressed to make content more understandable and more relevant for patients and the general public.

Results: The CAB advised that the existence of lay summaries is not well known in the patient community and also recommended the development of trial-specific lay summary videos to further improve understandability of the clinical trial results for the general public. Videos are a key channel of communication, enabling access to information for people with specific health needs and lower literacy levels. Following CAB advice, the CRS developed a stand-alone video entitled *"What are lay summaries?"* and a trial-specific lay summary video. Revisions to lay summary content (written and video) included colour schemes, iconography and language changes to make content more understandable. For videos, adjustments to animation speed, script and voiceover were implemented to improve clarity and flow of information (Fig. 2). Approved final versions of lay summary materials are publicly available on the CRS website. Translation into languages representing trial-site countries is in progress to widen access to non-English speakers and, where possible, local versions are being reviewed by the patient community.

Conclusion: Structured collection and implementation of CAB advice can make lay summary materials more understandable for the patient community and wider general public.

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Fig. 1. Summary of iterative process to gather and collate CAB advice to make lay summary materials more understandable

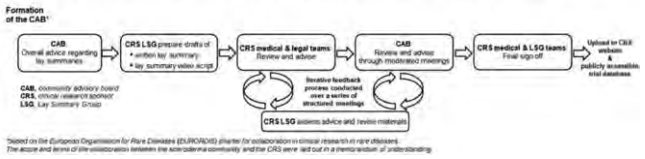
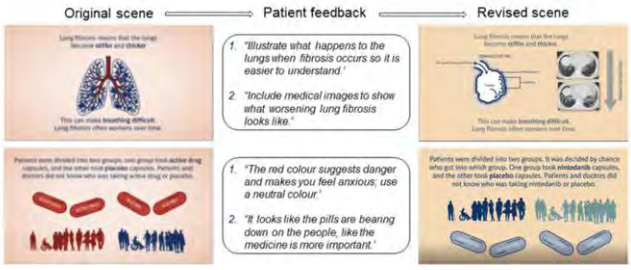


Fig. 2. Examples of revisions to the trial-specific lay summary video made in response to CAB advice



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PARE0010 THE VR DOCTOR – THE IDEAL DOCTOR'S APPOINTMENT

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Background: With new technology available, health care is evolving quickly, and new solutions are constantly being presented. Although few of these solutions focus on patient-participation and patient empowerment. That's what we wanted to create! Using virtual reality, we figured we could prepare and empower patients before meeting their doctor – and also giving doctor's a chance to see what it's like sitting across the table.

Objectives: The main objective was to show an example of how an ideal visit to the doctor could look like, to empower patients. By knowing their rights and what kind of care they are entitled to, we wanted to make patients more prepared and feel safer and more comfortable before a doctor's appointment. The experienced is based on the Swedish Patient Act. We also wanted to be able to show health care professionals what it's like being a patient, and giving them the opportunity to try it out.

Methods: We teamed up with fellow patient organizations Proud Bellies (Stolta Magar) and Youth with Psoriasis (Ung med Psoriasis), pharmaceutical company AbbVie and e-health company Cambio to create the virtual reality experience. Together we workshopped what the ideal doctor's appointment would be like, based on the Swedish Patient Act, and wrote the script. Our example doctor's visit is generic, meaning all of our three organizations could use it even though we represent different diseases and diagnoses. But we also created three other virtual reality experiences. They are disease specific, and one is for RA. In the film, you get to go inside the joint to see what happens when you have rheumatism, while a speaker explains it to you.

Results: We launched the VR Doctor in January of 2019 with a great event. Patients, health care professionals, press and others were gathered and got to try a visit to the VR Doctor. It was very-well received, especially by other patients. Since then, we have used the tool during our member activities such as summer camps, to empower our members. And we have introduced the tool for health care professionals at several rheumatology clinics throughout Sweden.

Conclusion: With new technology comes great opportunities to simplify complicated matters. The VR Doctor is essentially a crash course in the Swedish Patient Act, making it a very useful tool for both patients and health care professionals. By giving an example of what an ideal doctor's appointment could be like, we are letting patients take matters into their own hands and bringing them a sense a power and control over a situation that normally could be tough and sometimes intimidating. With empowered patients who feel safe, we are one step closer full patient-participation and in the long run a better health care system for all.

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Disclosure of Interests: None declared

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SATURDAY, 06 JUNE 2020

Work and rehabilitation

PARE0011 AFLAR'S (FRENCH LEAGUE AGAINST RHEUMATISM) NEW ACTIONS TO HELP PEOPLE WITH RHEUMATIC DISEASES TO GET AND STAY EMPLOYED.

L. Carton[1,2], L. Grange[2], F. Alliot Launois[2], G. Chales[2], B. Liesse[2], C. Jandard[2]. [1]*Paris, Paris, France*; [2]*AFLAR, Paris, France*

Background: Accessing jobs and being able to stay in a paid work position are a personal issue for people with rheumatic diseases, as well as for society. AFLAR, French league against rheumatism, has been acting towards patients and employers since 2014 in this field.

Objectives: After a preparatory work with a panel of all types of professionals and institutions working on the subject, key messages on means to improve the professional situation of people with rheumatic diseases have been published. These messages were used as a basis for an awareness training designed for human resources training and employers' managers, and in a guidance booklet designed for patients and published in 2016: «At work, even if affected by chronic rheumatic diseases ». This booklet, rather than gathering administrative and social resources in favour of patients, was based on patients' and experts' expression, written with them and proposed gradual guidance along their path from their professional choices to the disabled worker certification when needed. Two new actions have been seen as necessary in 2019 in order to go on with our actions: updating our booklet after 2 new laws had been issued in the field of labour law, and additions seemed necessary because of new work methods are developing (distant work from home, independent work); and the need of a new widely spreadable tool to accompany patients from the diagnosis stage, especially on the diagnosis disclosure to the work group issue.

The specific characteristics of rheumatic diseases: diversity, growing invisibility of diseases' effects and aftereffects to new treatments such as biologics and early rehabilitation, variation in time and personal impact, make them hard to understand by employers and even untrained social workers. This is what we noted from our experience in patient education workshops. Patients have a tendency to hide their pathology, and thus cannot benefit from social advantages as disabled workers, with motivation based on keeping personal image and an idea of normality, and fear of negative reactions from the work group, such as depreciation, pity, idea of negative impact on team's productivity).

Patients have to build a real strategy, taking into account these criteria and their personal choices, while preparing their job's adaptation or social requests when needed. AFLAR chose to create a new patient information tool: free short widely spreadable videos, available on line. These will also invite patients to get in touch with expert patients on the specialized hotline, participate to chats of patient education workshops.

Methods: Videos will show witness patients and experts, who will be asked about their experience and advice based on four questions:

- Should we speak about our disease (and when, how?), or not speak about our disease at work?
- What means « disablement », « being disabled » for you as a person affected by a rheumatic disease?
- What have you been able to do to get a paid position, or keep your job, that you could quote as an advice for other people in the same situation?
- If you had been given, or were given now a magic wand to make it easier to get or keep a job, or get/keep the job you dreamed of, what would you change?

At the end, videos will deliver further advice, tools and resources taken from the booklet, such as a model of decisional scale, or reference institutional website addresses.

Results: AFLAR wishes to contribute actively to rheumatic patients', and especially young people's information on the topic thanks to these more innovative and interactive tools.

Conclusion: Furthermore, wishes, solutions and ideas of witness patients and users will be gathered for advocacy towards employers, institutions and decision makers.

Disclosure of Interests: None declared

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SATURDAY, 06 JUNE 2020

Campaigning

PARE0012 **AWARENESS CAMPAING "LUPUS.GR 2020"**

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Background: LUPUS GR 2020

Objectives: To sensitize and educate the wide public about lupus

To contribute to the process of de-stigmatization as the rigid problem of prejudice and stigma prevails.

Methods: The campaign "LUPUS GR 2020" consists of photographs, each of which has a different message for Lupus and 2 TV spots. The well know artists participated did not take any fee.

The campaign consists of

Press Announcements in digital and off digital media, in Social Media (Instagram - Twitter - Facebook), in Eleana Site and in YouTube

Post of the artists in their personal social media pages

Press Conference

Direct mail in international NGOs e.g. Lupus Europe, PAIN ALLIANCE EUROPE, AGORA PLATFORM, etc.

Results: We announced the campaign on January 24, 2020. Until end of January, we have 36 press clipping, 3 TV interviews, more than 35.000 views of the post in our fb and increase of telephone calls in our help line about lupus

Conclusion: The campaign has a high impact in the wide public as well as in all the stakeholders.

Figure:





Disclosure of Interests: None declared

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SATURDAY, 06 JUNE 2020

Patient information and education

PARE0013 **'FIND A NUDGE' AND OTHER TIPS TO MAINTAIN YOUR LEVEL OF PHYSICAL ACTIVITY FOR A LONGER TIME**

R. Geenen[1]. [1]*Utrecht University, Department of Psychology, Utrecht, Netherlands*

Background: Pain, fatigue, physical disability, reduced well-being and sleep problems are common consequences of Rheumatic and Musculoskeletal Diseases (RMDs). Paradoxically, these consequences may all lead to a reduction of physical activity, while physical activity actually is an antidote against these consequences. This is acknowledged by experts that included physical activity and exercise into recommendations for management of RMDs [1-3]. Indeed, after programs aimed at a gradual build-up of exercise, many people with a RMD showed an increase of physical activity. However, it is hard to maintain a higher level of physical activity for years as part of daily routine [4-5].

Objectives: To identify and present tips, applications and illustrations that support people with an RMD to maintain their level of physical activity for a longer time.

Methods: Theoretical considerations and empirical findings guided the identification of tips. Care was taken that the tips and illustrations were translated into layman language and fitted in daily life of common people.

Results: Ten tips were found:

1) break the habit,
2) make sure you can do the exercise activity,
3) use aids if needed,
4) believe in a good outcome,
5) choose a physical activity that fulfils personal goals,
6) find a physical activity that you enjoy,
7) stop moving while it's still fun,
8) find a buddy,
9) make an action plan, and
10) find a nudge.

A "nudge" is a little push in the right direction that makes a person unconsciously perform physical activities. Examples are an outdoor photography hobby, a dog that comes to you with a dog leash in his mouth, or grandchildren that persuade you to go with them to the playground nearby. If a person with a RMD manages to find a nudge that stimulates instinctive moving without feeling the effort, then physical activity may be maintained. People differ a lot and must discover for themselves which tips help them to maintain physical activity. They must be aware that it may take up to two months for changed habits to stick.

Conclusion: The presented tips will help to maintain your level of physical activity. Nevertheless, be aware that effort and perseverance are needed to keep on moving. A challenge for the future is to get more knowledge of natural and pleasurable physical activities. Peers with successful experiences and

behavior change experts can help. For the time being, a main advice to maintain a higher level of physical activity with less effort is to find your own nudges.

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PARE0014 CANNABIS – HOW TO NAVIGATE BETWEEN PRESSURE FROM PATIENTS, LEGISLATION AND NEED FOR EVIDENCE

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Background: Around the world, focus on cannabis has been increasing immensely the last couple of years. Patients with RMD very often experience pain and many of these patients do not get adequate relieve from ordinary painkillers. Therefore, the pressure from patients wanting to try cannabis in order to ease their pain, is very understandable but also a difficult field to navigate in for a rheumatism association. Mainly because there are so many different interests in cannabis from many sides.
Objectives: The Danish Rheumatism Association has taken a very active role in unfolding knowledge of the positive and negative effects of cannabis to patients with RMD. We want to show, that we are aware of our patients needs and interests and we wish to give independent information to patients with RMD about suitable pain relief also when this involves the use of cannabis.
Methods: In order to get more knowledge about the need of the patients, the Danish Rheumatism Association has registered every inquiry from patients to our professional helpline in 2018 regarding cannabis. This information has been used in our political work with the Danish Ministry of Health and has given us a deeper understanding of the RMD-patients background and motivation for using cannabis. The Danish Rheumatism Association has supported cannabis research financially, and we have taken part in the public debate with editorials. On our website, we have fact sheets regarding cannabis along with a theme about cannabis in our magazine. The Danish Rheumatism Association has been very active politically in order to get RMD-patients to be part of a national project with medical cannabis to different groups of patients. We have an ongoing contact with the Danish Ministry of Health regarding RMD-patients experience in using cannabis and we pass on RMD-patients difficulties in even getting cannabis legally. In addition, to continuously gain knowledge about RMD-patients' experience with cannabis, we have also conducted questionnaires and surveys both in collaboration with other patient organizations and through our own channels.
Results: We have made it clear that we take an active role in the public debate regarding the use of cannabis and that we understand the desire from patients to have as many options as possible to choose from when it comes to relieve their pain. However, we also acknowledge the fact, that we need more evidence when it comes to the use of cannabis as an actual option for patients with RMD-related pain. We are a reliable partner that politicians and other stakeholders take very seriously.
Unfortunately, patients with RMD did not get to be part of the national project in Denmark with medical cannabis, but nevertheless many of these patients are using cannabis and most of the patients buy it illegally.
Conclusion: The use of cannabis is still a very "hot topic" in many countries and the legislation can vary a lot from country to country. It is important that the rheumatism associations across Europe have knowledge about cannabis so that they can advise patients with RMD in a serious, objective and evidence-based manner.

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PARE0015 UNDERSTANDING THE NEEDS OF PATIENTS WITH OSTEOARTHRITIS TO INFLUENCE THE DEVELOPMENT OF RELEVANT PATIENT-CENTERED PRODUCTS & TREATMENTS

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Background: Osteoarthritis (OA) is the most common form of arthritis and affects over 30 million adults in the United States of America.[1] There is no cure for osteoarthritis, and unlike other forms of arthritis where great treatment advances have been made in recent years, progress has been much slower in osteoarthritis. [2] However, there is increasing interest in removing barriers to treatment development, and the U.S. Food & Drug Administration has adopted and implemented new patient-focused drug development meetings to ensure the patient voice is informing new treatments.[3]
Objectives: To gain a robust understanding of the barriers, needs and hopes of patients with OA to influence the development of relevant patient-centered products and treatments.
Methods: A 34-question web-based survey was distributed between November 1 - 10, 2019. Survey invitations were sent via e-newsletters and e-mails to patients engaged with the Arthritis Foundation. The first survey question screened out patients who had not been diagnosed with OA.
Results: 2,437 patients diagnosed with OA completed the survey. There are 5 key findings:
1.Patients would like pain (90%) addressed more than any other symptom. Other symptoms such as fatigue (50%), sleep (39%), ability to walk (35%), stiffness (32%), ability to stand (16%), and ability to go up & down the stairs (14%) were ranked significantly below pain.
2.Patients use a variety of techniques to manage their OA and related symptoms. Physical activity (62%) and heat & cold interventions (62%) are the most prevalent. Approximately half of the patients use topical cream (53%), supplements & vitamins (51%), NSAIDS (50%), and/or acetaminophen (48%). Approximately one-third of patients utilize diet/nutrition (39%), assistive devices (38%), cortisone injections (36%), and/or physical therapy (34%). Other methods, including surgery (26%), were utilized less frequently.
3.41% of respondents reported they were "very interested" in participating in OA clinical trials; 40% reported "somewhat interested." Only 19% reported they were "not interested." The top 2 reasons patients were not interested included fear of possible risks/unknow effects (48%) and potential impact on other health problems (44%).
4.Primary care physicians are diagnosing (44%) and treating (48%) OA patients more than any other health care provider.
5.Many daily living tasks are difficult, and patients are interested in in tools/equipment to help. Yard work (66%), opening jars (64%), and cleaning the house (63%) are the most difficult. Over half of patients reported that physical activity (57%) and getting up and down from a chair (54%) are difficult. Patients would like tools/equipment to help them clean the house (54%) and help with physical activity (50%).
Conclusion: OA patients use a variety of management techniques yet are still in pain and have difficulty doing everyday tasks. These findings, along with other patient data, will be used to influence product developers to create easier to use products, to inspire researchers to focus on addressing patients' most pressing needs, and to encourage government agencies to remove barriers and facilitate new patient-centered treatments.

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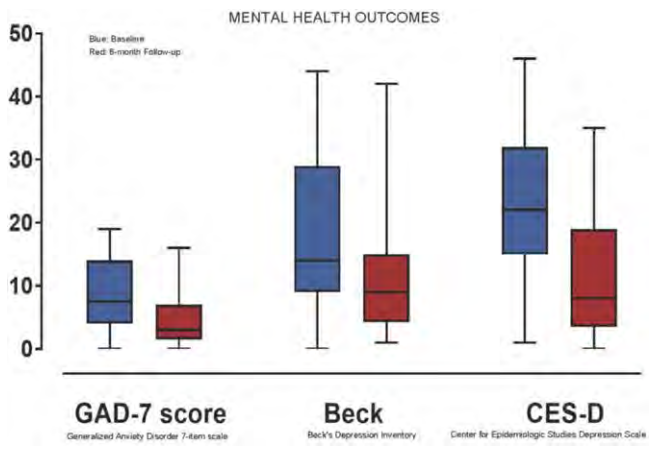
SATURDAY, 06 JUNE 2020

Involvement and innovation in healthcare

PARE0016 **MINDFULNESS-BASED STRESS REDUCTION TO IMPROVE DEPRESSIVE SYMPTOMS AND RHEUMATOID ARTHRITIS-RELATED CLINICAL OUTCOMES: RESULTS FROM A FEASIBILITY AND ACCEPTABILITY TRIAL**

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Background: Despite available highly effective pharmacological treatments, up to 30% of current rheumatoid arthritis (RA) patients remain in quasi-remission, where inflammation is controlled but patients still report unacceptable levels of negative impact of RA (high Patient Global Assessment (PGA) on a 0-10 visual analog scale). PGA levels correlated with depressive symptoms assessed by Center for Epidemiologic Studies- Depression (CES-D) scores. Mindfulness-Based Stress Reduction (MBSR) is relatively inexpensive and reduces both anxiety and depression in several conditions.
Objectives: To complete a feasibility and acceptability study paving the way for a randomized controlled trial (RCT) of MBSR to improve depressive symptoms and clinical outcomes in RA patients in quasi-remission.
Methods: A standardized 8-week MBSR program in adults with controlled inflammatory disease (stable SJC ≤ 2/66 and normal CRP; stable treatments) but high CES-D scores (2 groups), high CES-D or anxiety scores (1 group), or PGA higher than Physician Evaluation of Disease Activity (EVA) by ≥2 (1 group). Feasibility was documented using process indicators. Outcomes were measured at baseline and 6 months after the end of MBSR. Disease activity scores (SDAI) and questionnaires on depressive symptoms (CES-D), HAQ, sleep (VAS), fatigue and pain (SF-36), anxiety (GAD-7), PGA were collected. Qualitative interviews based on a theoretical framework of acceptability were conducted following the post-MBSR evaluation.
Results: We report on the first 21 patients (mean age 59, 91% females) having completed their 6-month follow up evaluation. Factors leading to higher recruitment rates were 1) using pragmatic scores to identify eligible patients (e.g. EVA and PGA), 2) no formal clinical evaluation of mental health and no emphasis on depression in the recruitment material.
MBSR had a highly significant positive impact on depressive symptoms (p=0.003) and anxiety (p=0.025) (Figure), and positive impact on quality of sleep and HAQ. No change in SDAI or joint counts was noted.
During a qualitative interview of 13 participants, most reported that MBSR helped them control their reactions to daily stressful situations. Perceptions were almost uniformly positive towards MBSR, and most appeared to have integrated some part of it in their daily life. No side effects were reported.
Conclusion: Although recruitment was challenging, a MBSR trial in RA patients in quasi-remission was found acceptable and feasible. Positive impacts on mood and on clinical outcomes were observed. Anxiety and depression scores appear the most sensitive to change and are recommended as the primary outcome for an eventual RCT. MBSR added to conventional treatments might help empower RA patients towards self-management.



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UCB Canada (CATCH, Clinical nurse)
BMS (CATCH, Clinical nurse, Observational Study Protocol IM101664. SERO-POSITIVITY IN A LARGE CANADIAN OBSERVATIONAL COHORT)
Janssen (CATCH)
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Eli Lilly (Registry of biologics, Clinical nurse), Consultant of: Eli Lilly, Janssen, Novartis, Pfizer, Speakers bureau: Merck, BMS, Pfizer
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PARE0017 **THE DREAMCATCHER – AN INNOVATIVE TOOL FOCUSING ON POSSIBILITIES INSTEAD OF LIMITATIONS**

C. Helin Hollstrand[1], K. Nilke Nordlund[1]. [1]*The Swedish National Organization for Young Rheumatics, Stockholm, Sweden*

Background: With the launch of The Swedish Young Rheumatics Report in April of 2018, we also presented new way of thinking and a tool called the Dreamscale, our complement to the traditional VAS scale used to assess pain. In October of 2018, we organized a workshop together with communication consults where we invited some of our members in different ages and health care professionals working with children, youths and young adults with rheumatic diseases, to try and reach a joint definition of what the Dreamscale is and could be, as we saw its huge potential. This is where the idea of the Dreamcatcher was born.
Objectives: The objective is to create an innovative digital tool for young people with rheumatic disease. It takes its starting point in what is healthy and what is possible, rather than focusing on sickness and limitations. Using behavioral science, nudging and social functions, the Dreamcatcher has the potential to lower the barriers to living an active lifestyle, while also serving as a tool for dialogue with health care professionals, resulting in more efficient meetings, better resource planning and the gathering of valuable data to the national quality registers. It is also a digital tool with a big potential for development thanks to its open source code and its focus on enabling activity and participation, there is an obvious potential to develop its functions to also serve other actors and patient groups.
Methods: We teamed up with communication bureau Gullers Grupp, pharmaceutical company Pfizer, and two health care clinics in Stockholm, one for children and youths with rheumatic disease and one for adults, and received funding for one year of development from Vinnova, the Swedish innovation authority, in April of 2019. We started the project by conducting a study to try and narrow down what focuses the Dreamcatcher should have. The pilot study contains both workshops with patients, both children, youths and young adults, and with teams of health care professionals, as well as more in-depth interviews with both patients and health care professionals. Based on the study, we will develop a prototype of what the Dreamcatcher could look like, and it will most likely be an application used for smartphones.
Results: The study narrows down the Dreamcatcher into three things: the Dreamscale, Dream data, and the Dream collective. **The Dreamscale** is as previously explained a complement to the traditional pain-scale and a tool for patients to set goals towards their dreams, and for patients and health care professionals to co-plan care and medical treatment based on what's most important to the patient. **Dream data** is where patients can self-track their disease, data which is also available for the health care to view and therefore to be better prepared before meeting with the patient. It is also a goal to have the Dream data transferred to the national quality registers. **The Dream collective** is a social function where patients using the app can connect and get inspired by each other. It is a place to share your dreams and build a community to show that rheumatic disease isn't something that should ever stop you from going after your dreams!
Conclusion: The prototype of the Dreamcatcher will be presented in May of 2020 and we think this it has great potential to help shift focus withing health care, to not just focusing on sickness and limitations but rather on dreams, joy of life and possibilities!
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Disclosure of Interests: None declared
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SATURDAY, 06 JUNE 2020

Psychosocial support

PARE0018 **WEBSITE FOR PARENTS OF CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS REDUCES PARENTING STRESS.**

K. Mulligan[1,2], S. Hirani[1], S. Clarke[3], N. Evans[4], C. Flood[5], J. Taylor[1], L. Wedderburn[6,7,8], S. Newman[1]on behalf of WebParC Investigator Group. *[1]City, University of London, London, United Kingdom*; *[2]East London NHS Foundation Trust, London, United Kingdom*; *[3]Brighton and Sussex University Hospitals NHS Trust, Brighton, United Kingdom*; *[4]Lancaster Associates Ltd, London, United Kingdom*; *[5]London Southbank University, London, United Kingdom*; *[6]UCL GOS Institute of Child Health, University College London, London, United Kingdom*; *[7]Centre for Adolescent Rheumatology Versus Arthritis, London, United Kingdom*; *[8]NIHR Biomedical Research Centre at GOSH, London, United Kingdom*

Background: Having a child with JIA presents many challenges. Many parents experience considerable stress. Parental distress and functioning have been found to be related to child outcomes (Cousino, 2013), therefore interventions that help parents to manage their child's illness are important for both parents and child. We developed a website for parents of children with newly diagnosed JIA to help increase parental confidence in managing their child's arthritis and reduce parenting stress.

Objectives: To evaluate the efficacy of a web-based tool 'WebParC' for parents of children with JIA.

Methods: *Design:* Multi-centre randomised controlled trial conducted in 16 tertiary paediatric rheumatology centres in England.

Participants: Parent(s) of children aged ≤12 years, diagnosed with JIA within the previous six months.

Procedures: Parents were enrolled when they attended the rheumatology service and were randomised by household to either the intervention arm (I) who were given access to the website in addition to their child's standard care or the control arm (C) who received standard care alone.

The primary outcome was parenting stress, measured with the Pediatric Inventory for Parents (PIP) (Streisand, 2001), which parents completed prior to randomisation and at 4-months and 12-months post randomisation.

Website content was developed by a multidisciplinary team including rheumatology, physiotherapy, ophthalmology, social work, podiatry, occupational therapy, clinical and health psychology along with parents of children with JIA. It includes information about JIA and its treatment plus a 'toolkit' for parents. The toolkit is based on cognitive-behavioural principles to develop skills for managing JIA-related issues.

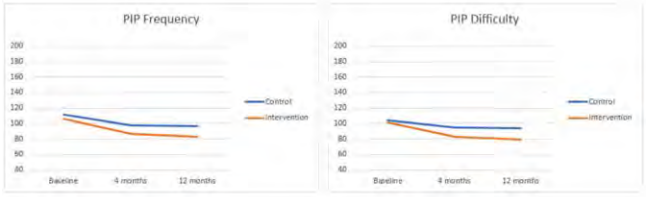
Analysis: We conducted linear mixed models to examine the main effect of trial arm (I vs C), main effect of time (between 4M and 12M scores), and interaction between trial arm and time on PIP scores, after controlling for baseline scores.

Results: A total of 220 parents (183 mothers, 37 fathers) of 203 children were randomised, 106 intervention and 114 controls. Parents mean (SD) age was 36.5 (6.5). Their children with JIA were mostly female (137/203, 67.5%), mean (SD) age of 6.1 (3.4) years. There were 107 (52.7%) with oligoarthritis, 65 (32%) polyarthritis, 8 (3.9%) systemic and 23 (11.3%) other JIA subtypes. Seventy (34.5%) were prescribed methotrexate.

Trial arms did not differ significantly at baseline except for parent education, which was higher in the intervention group and was controlled for in the analysis. Follow-up assessments were completed by 133 (I60, C73) at 4M and 124 (I58, C66) at 12M.

We found significant main effects of trial arm on PIP Difficulty (p=0.022, Control (Mean=93.62, SE=2.717) > Intervention (Mean=84.23, SE=3.025)) and PIP Frequency (p= 0.008, Control (Mean=95.78, SE=2.400) > Intervention (Mean=86.23, SE=2.622), with Controls reporting significantly greater frequency and difficulty of stressful events than the Intervention group (Fig 1).

Figure 1. Pediatric Inventory for Parents (PIP) - measure of childhood illness-related parenting stress



A higher score is worse, reflecting more frequent stressful events / greater difficulty experienced

Conclusion: This trial found that a website for parents of children with JIA can help to reduce parenting stress.

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SATURDAY, 06 JUNE 2020

Work and rehabilitation

PARE0019 **DON'T DELAY - TIME2WORK**

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Background: Employment process of people with RMD is very sensitive and tough subject, especially in Republic of Serbia. For people with RMD it is very hard to get employed or to find a suitable job. Based on study 33% of the total health care costs was allocated to employers.

Objectives: Raise awareness about employment of people with RMDs and identify barriers and bottlenecks of the process of employment. Connect with all relevant stakeholders and figure out a way to ease the whole process of employment.

Methods: A round of surveys were conducted, one for employers and the other for people with RMDs.A round table was organized with participants from various relevant institutions.A series of articles were published online and in writing. A series of interviews were emitted on various TV stations.

Results: Total of 136 persons with RMD took the survey and a total of 75 companies took the survey for employers.56.7% are employed. 31% of people with RMDs that took the survey said that they did not get the job because they have RMD. 37.1% are missing from work just when they are feeling really bad. 87.1% are open for prequalification and retraining. 90% is not familiar with process of qualifying for disability act. 42.60% are looking for a job via Internet. 45% does not get help at the workplace from their colleague when they are not feeling well. 42.3% met the difficulty of employer not understanding disease and it's forecast. 39.7% does not get any feedback after interview. 40% of employers are not familiar with benefits from the state when employing person with disability act. 68% have not used any benefit provided by state. 2/3 of employers are giving advantage to work experience and probation impression over other when deciding about employment of person. Active communication between round table participants and our organization. Employment brochure, digital and hard copies.

Conclusion: People with RMDs are more than interested and willing to take courses and prequalification in order to get employed. More than half that are not employed at the moment are actively seeking for a job opportunity. Employers are willing to employ people with RMDs and also send them for prequalification. They are not familiar with benefits that they can get when employing person with RMD. More than 2/3 of employers that took the survey stated number of benefits that they would see fit them when employing person with disability act, and 95% of those benefits are already on benefit list provided by Republic of Serbia. If more people with RMDs are employed causes less health care cost to the state, more funds for new medicines, more people on innovative drugs, which results in more people getting employed. The other thing that needs raise of awareness is the process of getting act of disability, since people with RMD in Serbia are not familiar with it.

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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.3207

PARE0020 **REUMAWERKT - PROMOTING PROFESSIONAL REINTEGRATION OF PEOPLE WITH A RHEUMATIC DISEASE**

A. Marchal[1]. [1]*ReumaNet vzw, Zaventem, Belgium*

Background: In Belgium, people with Rheumatic and Musculoskeletal Diseases (RMDs) are a large group of patients on sick leave receiving an allowance as their condition does not allow them to remain at work. In order to reduce costs, the Belgian National Institute for Health and Disability Insurance (NIHDI) has reached out to social partners to jointly start up projects to promote the professional reintegration of people with RMDs. ReumaNet is one of these partners and has, in close collaboration with the NIHDI, started up a research project '*ReumaWerkt*' to promote professional reintegration of people with a rheumatic disease.
Objectives: Via the 'ReumaWerkt' research, ReumaNet wanted to identify, as from a patient's perspective, which support patients need in order to stay at work or to start working again:
1. Information: identify and assess patients' available information about professional reintegration
2. Resources: evaluate resources people with RMDs have at their disposal to stay at work and/or to return to work
3. Assess if a Patient Expert (a trained patient) is an added value in supporting peers in their professional reintegration
4. Assess if a certified return to work coordinator is an added value in supporting people with RMDs towards professional reintegration
Methods: - Surveys questioning people with RMDs to assess their satisfaction regarding available information flows, resources and support (127 respondents)
- Survey questioning stakeholders (rheumatologists, health professionals) about information on professional integration they use and share (79 respondents)
- Coaching and supporting people with RMDs via personal contacts, mail, skype, phone calls,… in order to jointly define tailored answers on professional reintegration
Results: 1. There is a discrepancy between where patients expect to find information about professional reintegration and where information is given. There is plenty information available, but not customized, sometimes inconsistent, mostly too general and the legislation is too complex.
2. People with RMDs do experience physical obstacles at work. In addition, the Belgian government provides financial support, which is unfortunately (a) not well known and (b) too limited.
3. 80% of the respondents rated 7/10 and more as satisfaction rate. 82% of the respondents (N=127) would recommend the support of a Patient Expert to other patients.
4. The certified return to work coordinator applies disability management principles, focusing mainly on job retention and stimulating professional reintegration, taking into account each patient's personal bio-psycho-social context.
Conclusion: 1. People with RMDs, and their health professionals, are in need for straightforward and correct information about professional reintegration possibilities. Information flows need to be improved and provided information needs to be more specific, i.e. disease related.
2. People with RMDs have specific needs to allow them to return to or stay at work such as flexible working hours, functional adaptations in their working environment and financial support.
3. Patient expertise is an added value in supporting people with RMDs: respondents felt more understood by a peer, appreciated the opportunity for a more open, candid dialogue and felt encouraged to return to work.
4. Working via the principles of disability management is an added value: it is important to support people with RMDs as soon as possible and provide personalized tailored information on professional reintegration opportunities.
Disclosure of Interests: None declared
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SATURDAY, 06 JUNE 2020

Patient information and education

PARE0021 **TARGETED INITIATIVE TO FACILITATE THE IMPLEMENTATION OF EXISTING EFFECTIVE GOUT TREATMENT IN SWEDEN**

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Background: Gout is a very painful rheumatic condition origin from excess uric acid in the bloodstream, which results in an accumulation of uric acid crystals in the joints and a severe local inflammatory response. Gout is treated in primary care and the current treatment has satisfactory results on disease management, thus patients can expect a controlled disease without flares. In Sweden however, only 30-40 % (1) of the patients receives adequate urate lowering treatment and prevent the disabling flares.
Objectives: As a patient association, the Swedish Rheumatism Association (SRA) has identified an opportunity to use scientific evidence and data to improve awareness in both patients and physicians in order to make the existing treatment available and to shift the gout treatment from flare management to prevention.
Methods: With SRA funding we created the Gout network, consisting of researchers, health professionals and patient research partners. Through meetings and operational support developed strategies to educate patients suffering from gout and to alert physicians in the primary care of the most recent research to aid the management of gout. We also fund a specific research project aimed to create an implementation plan to establish a treatment routine for gout in primary care with already existing resources.
Results: A high quality patient education material is under development and consists of an information video lecture and a comprehensive online patient school providing information about the diagnosis, preventive treatment, possible life style change along with other resources that will support the gout patient, both for self-care and in relation to healthcare. For the healthcare profession we have together with a clinical research expert and a patient research partner developed a fact sheet with the latest scientific updates on gout.
Conclusion: Accessible, high quality diagnosis information about gout is currently missing in Sweden. This collaboration initiative provides high quality facts to raise the general awareness and to educate and empower patients to get the effective therapy that is available today.
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Disclosure of Interests: Li Alemo Munters: None declared, Ingela Loell: None declared, Suzanna Jansson: None declared, Lennart T.H. Jacobsson Consultant of: AbbVie, Eli Lilly, Janssen, Novartis and Pfizer, Mats Dehlin: None declared
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PARE0022 **TARGETING FATIGUE IN RHEUMATOID ARTHRITIS: A SELF-HELP BOOKLET**

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Background: Fatigue in rheumatoid arthritis (RA) is prevalent, intrusive, and disabling [1-3]. It has been shown that fatigue can be reduced, in at least some people with rheumatoid arthritis, using group interventions based on cognitive-behavioral principles [1]. However, the vast majority of the (about 40% [2]) severely fatigued people with rheumatoid arthritis does not have or does not want access to group therapy.
Objectives: To develop a self-help booklet aimed at targeting fatigue in rheumatoid arthritis based on cognitive-behavioral principles.
Methods: Based on the assumption that the most strongly influencing factors of fatigue differ between people [3], a comprehensive patient-centered approach was chosen. The booklet should be easy to read (big fonts,

text boxes, bulleted text, and illustrations). Needed materials should be included.

Results: In the booklet, factors that may influence fatigue are demonstrated by a hanging mobile toy, a device with stars or other figures hanging from the ceiling. If one piece moves, all the other pieces move as well. Every individual piece that is part of the mobile influences the other. However, every mobile is different. The large differences in balance between components of mobiles can be compared to the large variety of influences on fatigue in people. Patients first need to identify which factors seem especially important influencers of their own fatigue by sorting seven cards that are included in the booklet. They put the factor of which they think that it most influences their fatigue at the top and the factor that least influences their fatigue at the bottom. The seven cards are:

1) severe overweight,
2) disease activity,
3) day-night rhythm and sleep,
4) physical activity,
5) emotions and negative thoughts,
6) pain, and
7) another influence.

Interventions targeting these factors are discussed in separate sections of the booklet. Users are invited to start reading the sections with advice regarding the factors that most influence their fatigue. The foldable back cover of the booklet includes the set of seven cards of influencing factors, a diagram to make a 7-day 24-hours day-night rhythm schedule, and instructions to make an action plan.

Conclusion: In the Netherlands, the text can be obtained online and as a booklet in rheumatology departments of hospitals and through a national patient association, free of charge. The booklet was translated into English, which makes it accessible to a larger group of patients. It may take up to two months to successfully change lifestyle. It's an, as yet not empirically verified, hope that the booklet will be more successful than a traditional educational brochure.

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PARE0023

ORAL HEALTH IN RHEUMATOID ARTHRITIS: LISTENING TO PATIENTS

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Background: Rates of periodontal disease and tooth loss are increased in rheumatoid arthritis (RA). Periodontal disease may exacerbate RA inflammation and complicate RA care. Understanding factors that contribute to the increased burden of periodontal disease in RA is critical to improving oral health and possibly arthritis outcomes. People with RA may have unique needs and/or barriers to maintain oral health.

Objectives: To determine from people with RA what are their experiences and perceptions about their oral health, their most important questions relating to oral health, and how they wish to receive oral health information.

Methods: Semi-structured interviews were conducted with RA patients. Recorded interview transcripts underwent iterative content analysis. Transcripts were initially reviewed to develop a coding guide. Latent content, or larger themes, were then applied to the transcripts. Constructs were considered saturated when no new themes were identified with subsequent interviews. We report identified themes with representative quotes.

Results: Interviews with 11 RA (10[91%] female; all on RA medication) averaged 19 minutes (range 8-31 minutes) and were mostly conducted face-to-face. Many believed RA medication contributed to dry mouth. Most participants had not previously considered other links between oral health and RA. Themes identified included the need for complicated oral health routines, barriers of cost and access to dental care, and shame relating to oral health (Table 1). Participants preferred to receive oral health education from their rheumatologists or dentists over printed or online resources.

Conclusion: RA patients have unique needs relating to oral health and report poor oral quality of life. Strategies to optimize oral health in RA may include educational tools for optimizing oral self-care appropriate for RA, and improved access to oral care professionals who are aware of the needs of arthritis patients.

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PARE0024

AWARENESS ABOUT FAMILY PLANNING AND PREGNANCY EXPECTATION AMONG PATIENTS WITH CHRONIC INFLAMMATORY DISEASE OF THE SKIN OR JOINTS

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Background: Patients affected by chronic inflammatory diseases of the skin or joints (CIDs; including psoriasis [PSO], rheumatoid arthritis [RA], juvenile idiopathic arthritis [JIA], psoriatic arthritis [PsA], non-radiographic axial spondyloarthritis [nr-axSpA; reported in the survey as 'axSpA'], or ankylosing spondylitis [AS]) may be challenged in their attempts to have children. A multinational survey conducted in Europe and the US, including 969 patients, revealed that most

Table. Thematic analysis and quotes

Theme	Description	Quote
Oral-RA links	RA medications caused dry mouth	The medications, really, really are awful on your mouth, in particular prednisone. I get very raw gums… it [was] painful to brush my teeth. We don't have saliva to wash things away. We have a different mouth flora
Complicated oral care	Time-demanding oral care routines. Multiple oral health care tools and adaptations used depending on current oral health, and RA activity.	The severe pain made it very hard to open my mouth to brush my teeth. The joint damage [makes it] really hard to handle a toothbrush. We have to have toothbrushes with a wide handle… and different attachments when we need them. Even with those [special] products, the pain sometimes was just overwhelming. I'm dedicated about brushing my teeth, but boy, it was a struggle. It took me a long time to brush my teeth.
Access to professional oral care	Lack of dental insurance and costs of care Logistical access: multiple dental visits. Physical access: attending appointments; prolonged sitting in a dental chair.	I have a hygienist, and a dentist, and a gum dentist and a bunch of dentists with fancy names. I see them every 3 months. Dental offices have dental hygienists. And some of them are an A+, and some of them are C-…it's important that hygienists are trained, that they really understand the tools. When I go back in the [dental] chair, it was uncomfortable [when first diagnosed]. I struggled. I couldn't keep my mouth open.
Shame due to oral health	Shame relating to poor oral health. Seeking oral care possibly considered unusual for their age.	I would feel ashamed. Something's wrong. Everyone around me has these beautiful teeth. I don't, and something is wrong. I'm getting braces. At my age, I'm getting braces.

patients' concerns regarding family planning and pregnancy (FPP) were inadequately or inconsistently addressed.[1]

Objectives: To investigate the general level of information on FPP and the potential concerns among Danish patients with CIDs.

Methods: An online survey to identify FPP issues was designed, and CID patients aged 18–50 years (yrs) were included. Respondents were recruited through patient organisations providing their members with a link to the questionnaire. In addition to demographics, information relating to time of diagnosis, treatments received, pregnancies, and course of disease were collected along with access to and concerns regarding FPP. Descriptive statistics were applied.

Results: Eligible patients included 368 with rheumatological diagnoses (RA, PsA, JIA, nr-axSpA, or AS; 304 [83%] female, mean age: 40 yrs; 64 [17%] male, mean age: 42 yrs) and 95 with dermatological diagnoses (PSO or PsA; 64 [67%] female, mean age: 37 yrs; 31 [33%] male, mean age: 42 yrs). Among the rheumatic patients, 43% of females and 53% of males were currently receiving systemic treatment and 37% of females and 22% of males had received >3 different systemic treatments (other than painkillers and non-steroidal anti-inflammatory drugs [NSAIDs]). Lack of access to FPP information was consistent across age groups, but higher in those with dermatological diagnoses (**Table**).

In total, 68% of patients with rheumatological and 73% with dermatological diagnoses had biological children and among these 18% and 23% of patients, respectively, indicated their disease had affected how many children they had or planned to have. The most frequent concerns among patients with rheumatological diagnoses were the potential physical impact of a pregnancy, disease worsening, heredity and being able to take care of the child (19, 16, 16 and 13%, respectively), whilst disease worsening and heredity (12 and 16%, respectively) were the most frequent concerns in those with dermatological diagnoses. Many patients experienced disease worsening during or after pregnancy (rheumatologic diagnoses: 16% and 34%; dermatologic: 20% and 59%, respectively).

Conclusion: Danish CID patients of reproductive age have concerns related both to their disease and to FPP, which affect their decisions around family planning. The majority of patients responding to this survey reported limited access to information about FPP, pointing to a need for healthcare professionals to provide standardised family planning information.

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Table. Proportion of patients with rheumatological or dermatological diagnoses who reported having little or no access to FPP information, stratified by age

Age	Rheumatological diagnosis N (%)	Dermatological diagnosis N (%)
18–29 yrs	19 (49)	14 (74)
30–39 yrs	61 (58)	16 (73)
40–50 yrs	134 (60)	34 (63)

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SATURDAY, 06 JUNE 2020

RMD research

PARE0025 "RA - DON'T GIVE UP" - LIFE WITH RHEUMATOID ARTHRITIS FROM PATIENTS' PERSPECTIVE

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Background: Rheumatoid arthritis (RA) as chronic and progressing to disability disease decreases a quality of life of every person suffering from it. Knowledge about this influence from patient perspective is important to limit burden of RA and organize appropriate care for patients.

Objectives: RA has input on every area of individual and social lives. Recognition of patients' situation in daily life, professional life, participation in treatment, taking life decision gives possibilities to better understanding of diseases and starting activities to change lives with RA. Aim of research was to learn attitudes, knowledge and experiences of people living with RA.

Methods: The study was initiated by KnowPR in partnership with Polish Rheuma Federation 'REF'. Main researcher was Tomasz Sobierajski PhD., sociologist from Warsaw University. The first stage of the study was a workshop with patients with RA organized by REF. It was brainstorming to identify main problems, appropriate understand life with RA and discussion on questionnaire. After small pilot study on questionnaire, research was made by CAWI technique. Questionnaire had been linked on professional websites, facebook, Twitter, health forums. The data had been completed during one month - January 2019.

Results of survey were presented in booklet with comments. Opinions introducing results were done from persons represented patronages of project: minister of patient rights, president of Polish Society for Rheumatology, national consultant in rheumatology, directors of National Institute of Geriatrics, Rheumatology and Rehabilitation. Publication was enriched by stories of people with RA living full lives. Publication was launched during press conference and disseminated in hard copies and on-line with free access.

Results: In survey took part 619 respondents with RA - mostly women (90%). The biggest group of respondents (34%) was in age 46-60 years old. Duration of disease was different – from few months to more than 40 years. More than half of respondents are suffering from RA more than 10 years. Disease influences of every life area. Only 38% of respondents participate in decision about their treatment and took it together with rheumatologist. There are different opinions about way of taking medication. There are not differences among age groups and duration of disease in this. Majority of patients suffer from pain (73%), from limited abilities (68%) and from permanent fatigue (69%) in everyday lives. Rheumatologist has the biggest confidence among patients like a source of information about disease (73%). Other health professionals have lower confidence (35-40%). Majority of respondents (68%) note his knowledge about diseases like rather good and better. Respondents didn't connected their decision of having a child with disease how it has been before (59%). Part of respondents had to change or resign of professional work (30%). Part of them resigned from social life and hobbies before disease. In opinion of 57% of respondents RA changed totally their lives (57%).

Conclusion: Results of survey was used like a tool in lobbying for accessibility in newest treatment in RA. Further recognize of quality of life in RA is needed. Interviews of focus groups and individuals are planned.

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PARE0026 WHICH PATIENT-REPORTED OUTCOMES DO RHEUMATOLOGY PATIENTS FIND IMPORTANT TO TRACK DIGITALLY? A REAL-WORLD LONGITUDINAL STUDY IN ARTHRITISPOWER

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Background: Development of a standardized approach to assess key elements of disease activity in rheumatology clinical trials has been the goal of Outcome Measures in Rheumatology Clinical Trials (OMERACT), American College of

Rheumatology (ACR), and European League Against Rheumatism (EULAR).[1,2,3] The core sets of measures developed include assessments and composite indices incorporating use of patient-reported outcomes (PROs) and clinical measures and clinicians' assessments to quantify disease activity over time.[2] PROs are important indicators of disease activity and variability, and they are increasingly used to evaluate treatment effectiveness. Little is known about PROs that patients with rheumatic conditions find most important to convey their experience with their condition and its treatment.

Objectives: To examine PROs selected by patients with rheumatic conditions in the ArthritisPower registry to identify symptoms they found most important to track digitally.

Methods: Adult US patients within the ArthritisPower registry with rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis (AS), systemic lupus erythematosus (SLE), osteoporosis (OP), osteoarthritis (OA), and fibromyalgia syndrome (FMS) were invited via email to participate in this study. Enrolled participants (pts) were prompted to select ≤10 PRO symptom measures they felt were important to track for their condition at baseline via the ArthritisPower app. At 3 subsequent time points (Month [m] 1, m2, m3), pts were given the option to continue tracking their previously selected PRO measures or to add, remove and/or select different measures. At m3, pts completed an exit survey to prioritize ≤5 measures from all measures selected during study participation and to specify other symptoms not available that they would have wanted to track. Measures were rank-ordered based on number of pts rating the item as their 1st, 2nd, 3rd, 4th or 5th choice and weighted by multiplying the rank number by its inverse for a single, weighted summary score for each measure. Values were summed across all pts to produce a summary score for each measure.

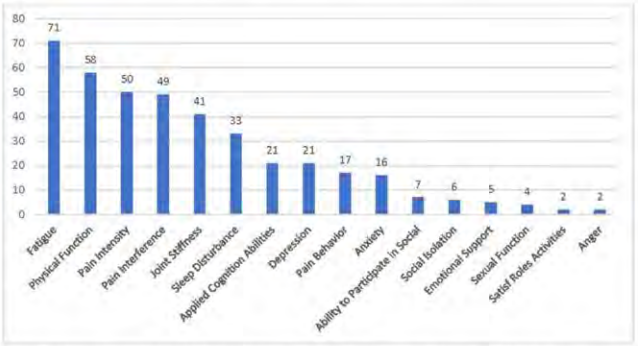
Results: Among pts who completed initial selection of PRO assessments at baseline (N=253), 184 pts confirmed or changed PRO selections across m1-3. Mean (SD) age of pts was 55.7 (9.2) yrs, 89.3% female, 91.3% White, mean disease duration of 11.6 (10.6) yrs. The majority (64.8%) self-reported OA, followed by RA (48.6%), FMS (40.3%), PsA (26.1%), OP (21.0%), AS (15.8%) and SLE (5.9%), not mutually exclusive, and were similar to the overall ArthritisPower population. The average number of instruments (SD) selected for baseline completion was 7.0 (2.5), 7.1 (2.4) at m1, 7.2 (2.4) at m2, and 7.0 (2.5) at m3. The top 5 PROs ranked by pts overall as most important (weighted summary score) for tracking were Fatigue (71), Physical Function (58), Pain Intensity (50), Pain Interference (49), Duration of Morning Joint Stiffness (41) (Figure 1). Fatigue, Physical Function, and Pain were consistently in the top 5 across diseases while Depression was more frequent among pts with OA, AS and FMS. Pts' PRO selections showed stability over time except for the RA Flare measure which decreased from 70.5% of RA pts at baseline to 13.6% at m3.

Conclusion: The symptoms prioritized by pts included fatigue, physical function, pain, and joint stiffness. Pts' choices were consistent over time. These findings provide insights into symptoms rheumatology patients find most important and will be useful to inform design of future patient-centric clinical trials and real-world evidence generation.

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Figure 1. Overall Participant Ranking of PRO Selections (weighted summary score) at Study Conclusion (m3)*



*Considering all PROs selected during the 3-month study, participants selected their first through fifth choice by importance; only those participants who completed the 3 months of the study (N=184). Weighted summary scores were generated based on rankings overall. Measures were rank ordered based on number of pts rating the item as their 1st, 2nd, 3rd, 4th or 5th choice and weighted by multiplying the rank number by its inverse to achieve a single weighted summary score for each measure. For instance, a measure scored 1/1 if ranked as the most important, 1/2 if rated second most important, and so on.

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PARE0027

PATIENT PERSPECTIVE ON INTRA-ARTICULAR THERAPIES IN RMDS: RESULTS FROM A EUROPEAN SURVEY

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Background: Intra-articular therapy (IAT) is routinely used in rheumatic and musculoskeletal diseases (RMDs). In order to improve the effectiveness and safety of IAT, it is essential to understand patients' perceptions and needs.

Objectives: To assess the perspective of persons who have experienced IAT, including perceptions on benefits and safety.

Methods: A steering committee (including a patient research partner) prepared a 44-item questionnaire based on the information needs of a Taskforce on IAT in adult patients with RMDs. The questionnaire was translated into 11 languages and disseminated via EULAR PARE associations and social media. Persons who had experienced at least two IAT procedures were eligible for the survey. Descriptive statistics were used to summarise results as well as inductive codification of open-ended questions.

Results: The survey was answered by 200 individuals diagnosed with rheumatoid arthritis (66%), osteoarthritis (21%), spondyloarthritis (10%), psoriatic arthritis (9%), and others (16%). The mean number of IATs received was 7 (SD 8), mainly in the knee (66%), shoulder (42%), and wrist (28%), and primarily with corticosteroids (83%) or hyaluronic acid (16%). Twenty-seven percent had not been informed about benefits or potential complications of IAT, and 73% had not been asked whether they wanted local anaesthetic. Consent was deemed necessary by 82 (41%). Most (65%) had never received an ultrasound (US)-guided injection, and of those who had experienced blinded and guided injections, 42 (63%) preferred US-guided because of increased perceived accuracy and confidence in the procedure. Only 50% reported a clear benefit of IAT, mainly in terms of reduced pain and increased joint mobility, but also perceived reduced inflammation, with effect from immediate to 36 hours or even 3 weeks post-injection, and that lasted from as little as less than one week to years. Regarding safety, 40 (20%) had experienced some complications from IAT, including but not limited to increased pain, impaired mobility, rashes, or swelling.

Finally, the respondents suggested improvements in the procedure, including: (1) wider availability; (2) less painful procedures; (3) greater efficacy, faster and longer-lasting; (4) fewer side effects; (5) a clear diagnosis beforehand; (6) better shared decision-making, including better information; (7) follow-up, (8) better accuracy; and (9) more expertise.

Conclusion: The survey has identified gaps in the IAT procedures, such as a need for clearer information. Patients perceive IAT as relatively safe, though painful, and with varying effect. Suggestions for improving the procedure, including more expertise, should be relayed to professionals and relevant organisations.

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SATURDAY, 06 JUNE 2020

Involvement and innovation in healthcare

PARE0028 LEAD PATIENTS – A RESOURCE FOR IMPROVEMENT OF THE HEALTH CARE SYSTEM

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Background: The project "Lead Patients – a new resource for health", led by researcher Sara Riggare at Karolinska Institutet and financed by Vinnova, the Swedish innovation authority, launched in 2017 and the Swedish National Organization for Young Rheumatics was one out of 14 partners. One of our tasks was to develop training courses for health care staff, and to try out what happens when lead patients are giving the opportunity to educate. We developed and produced nine different courses, and during the Autumn of 2019, we had the chance to try out two of them within the project.

Objectives: The aim was to switch the perspective and see what would happen when patients' expertise and knowledge is used to educate health care professionals and challenge the norm about health care professionals being superior. The objective with first training course, "Teams that enable self-realization", was to create conditions and find new methods for the health care professionals to better support patients with what actually matters to them. The objective with the second training course, "Anti-oppressive pedagogy and language impact", was to create new knowledge as a group and find methods for inclusion and anti-discrimination.

Methods: "Teams that enable self-realization" was conducted as an interactive lecture with a concluding workshop. The lecture was based on results from the Swedish Young Rheumatics Report, teamwork and the Swedish Patient Act. The workshop consisted of a case, where the participants were supposed to come up with a plan for a first meeting and treatment of a patient. "Anti-oppressive pedagogy and language impact" was conducted in two parts, with one week in between the two occasions. The first one was mainly a lecture with background and theory about anti-oppressive pedagogy, norms and power structures, followed by a workshop where the participants analyzed the organizations' own value principals. The second occasion was a deepened discussion with the purpose of identifying new methods for work and strategies to move forward.

Results: The main goal with the training was to highlight positive examples and create creative conditions to be able to identify these new methods and tools. And during the training, there was a great will from the staff to work in a more patient-centered way and let what is most important fort the patient to be what is directing the meeting. Some suggested that the patient should be considered a part of the health care team, but that methods are missing for making it work today. There was also a great will to reflect over what consequences the current health care system might have, and to discuss possible changes. It was exciting to see the traditional hierarchy, where patients are seen as passive receivers of care, being challenged for real and letting patients not only talk about "what it's like to live with a chronic disease" but actually be seen as capable and qualified educators.

Conclusion: If lead patient-led training becomes an obvious and vital part in building and develop the health care system, it will lead to new opportunities and possibilities to better form the health care based on patients' needs, both strategically and operational. Because converting to a patient focused care isn't just about changing old attitudes and organizational culture, it's also about building new adapted structures and methods for governing the health care system.

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PARE0029 THE JOURNEY FROM PATIENT AND PUBLIC ENGAGEMENT (PPE) TO INVOLVEMENT: FACILITATING PATIENT PARTNER RESEARCH WORKSHOPS WITH A FOCUS ON FIBROFOG IN FIBROMYALGIA

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Background: The Bath Institute for Rheumatic Diseases (BIRD), a registered charity in the United Kingdom (UK), supports research, education and patient engagement for the benefit of people with rheumatic diseases. Event feedback from two Fibromyalgia Information Days showed patients valued the sessions and were keen to be involved in research. Fibrofog in fibromyalgia was identified by patients as one topic of interest.

Objectives: To facilitate Patient Research Partner Workshops to generate research questions and inform the design of clinical research into fibrofog in fibromyalgia.

Methods: Three Patient Research Partner Workshops, focusing on fibrofog in fibromyalgia, were run between January 2018 and April 2019. All were co-facilitated by a clinician, SD, and BIRD Patient and Public Engagement (PPE) lead,MB. Ethical approval was not required[1]. Patients were invited to participate by email. A Patient Partner Information Sheet accompanied the workshop invitation. Audio recordings of the discussions were made to aid data capture, following informed written consent by all workshop participants. Travel expenses were offered to all participants.

Results: 25 (n=25) women with fibromyalgia attended the workshops. Workshop 1 (n= 5) explored, 'What areas do you think we should research around fibrofog in fibromyalgia'? Patient partners felt research into fibrofog in fibromyalgia was needed to identify and validate symptoms, and to inform discussions with healthcare professionals. They also called for research into coping strategies to help with fibrofog symptoms. This reflected similar patient calls for research into fibrofog in fibromyalgia[2].

Workshop 2 (n=10) and Workshop 3 (n=9) explored 'How do you think we should research fibrofog in fibromyalgia'? Both workshops identified a broad range of research questions and designs, reflecting individual experiences, knowledge and symptom severity. Suggested research questions included: How severe is fibrofog for each person? What triggers fibrofog? How does fibrofog affect daily tasks? How does fibrofog affect work? What do people with fibromyalgia, their partners, family members and healthcare professionals understand about fibrofog?

Suggested data collection methods included interviews, focus groups and questionnaires. Use of online surveys or interviews had mixed responses. This reflected computer literacy skills and access to hardware. Discussions around recruitment of participants to future studies revealed a wealth of local knowledge including access to community venues and healthcare facilities, support groups and local networks.

Participants were very satisfied with the workshops, finding them helpful, informative and thought provoking. All wanted to continue their involvement in research.

Conclusion: Patient Research Partner Workshops are integral to the generation and delivery of clinical research into fibrofog in fibromyalgia. Research designs need to offer multiple methods of data collection to be as inclusive as possible. Next steps will be to formally recruit Patient Research Partners to co-develop a research grant application to explore fibrofog in fibromyalgia.

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PARE0030 PEER SUPPORT OF PATIENT AND PUBLIC INVOLVEMENT AND ENGAGEMENT IN RESEARCH: THE 'RUG-BUDDY'

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Background: Since 2006, The School of Primary, Community and Social Care, Keele University has a long standing commitment to Patient and Public Involvement and Engagement (PPIE) in research. The School's Research User Group (RUG) has 133 members in January 2020, compared to 80 members in September 2016. Supporting the practical and emotional needs of a growing number of RUG members to support their long-term involvement is of prime importance.
Arising from Keele's role as a test bed site for the new UK Public Involvement Standards, a new peer support role (the 'RUG-Buddy') was co-produced to facilitate the support of RUG members.
Objectives: The RUG-Buddy is a peer support and mentoring scheme. More experienced RUG members attend research meetings with less experienced members to provide support and reassurance. The scheme aims to provide:
•A welcoming and friendly environment for RUG members
•Extra support for all RUG members before, during and after research meetings
•Help new RUG members ease into public involvement
•Support with discussions between researchers and RUG members, e.g. avoiding research jargon
••Reassurance to new members - learning from those with greater experience of public involvement
•Someone to talk to and confide in from people who have personal experience of PPIE
•Practical advice on completing payment forms, parking issues, etc.
Methods: Peer support is provided by a panel of existing RUG members who have substantial experience of PPIE in research. This is an additional method of supporting the RUG members alongside support provided by the School's PPIE team. RUG-Buddies will be supported in their role by the PPIE team and provided with an induction and training. RUG-Buddies are offered payment for their time and have their travel expenses reimbursed. The RUG-Buddies scheme will be piloted during an initial 6-month period, after which it will be reviewed, with feedback from RUG-Buddies and RUG members.
Results: A role description for the RUG-Buddy role has been coproduced by Keele's PPIE team and its RUG Steering Group (Table 1). A panel of 10 RUG members have been recruited for the RUG-Buddy role and have received an induction and training (e.g. Health and Safety, Information Governance). RUG-Buddies have provided support to and attended research meetings with other RUG members. The RUG-Buddy role will be reviewed in September 2020.

Table 1. Summary of the RUG-Buddy role description

Qualities of a RUG-Buddy	RUG-Buddy responsibilities	PPIE team responsibilities
Willing to share personal experience	To attend up to the first three PPIE meetings of a research project	To provide a training session for all RUG-Buddies
Friendly and approachable	To introduce new member to RUG members and research team	To meet RUG-Buddies every two months to provide review/ feedback of the role
Enthusiastic and knowledgeable about PPIE in research	To encourage contribution to the meeting	To have a named PPIE lead for any questions/queries that may arise

Table 1. Summary of the RUG-Buddy role description

Qualities of a RUG-Buddy	RUG-Buddy responsibilities	PPIE team responsibilities
Be reliable and punctual	To provide support and respond to RUG members' questions	To work alongside RUG-Buddy to meet and greet public members

Conclusion: The RUG-Buddy is an innovative peer support scheme to support the involvement of patients and the public in research. The support provided by RUG-Buddies offers a different perspective from people with real-life experience of involvement in research. It is anticipated that this additional support will enrich the experience of RUG members and facilitate a more welcoming and conducive environment for active and meaningful public involvement. Furthermore, it has also provided an opportunity for the RUG-Buddies to gain valuable new skills and also give something back to the PPIE team and researchers who have supported their own involvement for many years.
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PARE0031 AN MHEALTH TOOL FOR SHARED DECISION MAKING FOR PATIENTS WITH RHEUMATISM AND ARTHRITIS

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Background: Patient empowerment is a key element of patient-centred healthcare according to WHO. In the same direction, the Institute of Medicine in the United States supports actions to engage patients in their health care decision in a new patient-centered care model. Patient-centred care models have demonstrated better quality of care as well as potential long-term cost-efficiencies. However, nowadays, many patients are still struggling to become equal partners in care. Patients with chronic conditions, such as rheumatoid arthritis, are often referred to as the most under-used resource in the health system. Shared decision making is a collaborative process enabling a clinician and patient to participate jointly in making a health decision about the treatment having discussed the options, benefits and harms, while considering also the patient's values and experiences.
Objectives: The objective of the current research was to design a tool that will facilitate the shared decision making regarding the treatment approach, based on real life evidences from the patient. The focus of the application is on the pain assessment of patients suffering from rheumatism and arthritis. The proposed solution utilizes the latest technological innovations to support patients and clinicians on their decisions and assessment strategy on a more accurate base.
Methods: The design process followed a user-centered approach by involving a multidisciplinary team of experts (an mHealth expert, a behavioural scientist, and two physicians). An iterative design process focused on the different end-users (patients and clinicians) and their actual needs on the topic concerned. In each phase, the experts involved the end-users to create a highly usable tool. The aim was to capture and address the whole user experience. An evaluation phase took place for three months.
Results: The design team brought the users into every stage of the design process. Twenty patients and three physicians (one pathologist, one general surgeon and an expert in pharmacology and clinical pharmacology) participated and evaluated the modules implemented. The final solution consists of an application running on Android operating system in any smart phone. The final application supports the patient to enter all necessary information about: (i) the pain he/she is feeling, (ii) the medication he/she is receiving, and (iii) his/her life style.
Conclusion: After a three months period of continuous use of the application from the participants during the evaluation phase, they reported very encouraging results. In terms of usage, the patients found it user friendly, easy to learn, easy to use, and easily accessible. They also consider it really useful in order to keep track of their progress and assess the treatment and medications they receive relevant to the pain they feel. The physicians involved in the evaluation of the application found it very useful and with significant potential for daily use by clinical staff to evaluate the therapies given to their patients. All users concluded that the developed app can help towards a more accurate and acceptable treatment based on shared decision, exploiting the collected evidences.

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PARE0032 **STRENGTHENING SELF-MANAGEMENT TO IMPROVE THE QUALITY OF LIFE AND HEALTH STATUS OF PATIENTS WITH INFLAMMATORY ARTHRITIS AND OSTEOPOROSIS IN SWITZERLAND**

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Background: Previous UK studies suggest that people with arthritis taking part in self-management programmes feel more confident in their ability to manage and control their symptoms. These patients may also visit the doctor less frequently and have shown improved physical and clinical outcomes (1, 2). Based on this evidence, self-management has become an essential component of care for patients with arthritis, or generally with chronic diseases. However, there is still a huge gap regarding such self-management services and support programmes in rheumatology in Switzerland.
In the Swiss National Strategy "Musculoskeletal Diseases" 2017–2022, strengthening patients' empowerment is one of the main strategic pillars. Considering that approximately 500,000 people are suffering in Switzerland from inflammatory arthritis (IA) and osteoporosis (OP) alone, there is huge potential to strengthen patients' self-management capacity and thus improve their quality of life (3).
Therefore, the SLR has developed a self-management programme for IA and OP patients. In this programme medical assistants in outpatient rheumatology clinics are trained to consult patients in self-management. This programme is part of a two-year pilot project (2019–2020) that is supported by a consortium of important stakeholders in rheumatology in Switzerland.
Objectives: The ultimate objective is to increase the quality of life and the health status of people with IA and OP in Switzerland by enhancing their capacity for self-management. Furthermore, this pilot project aims at closing an important gap in the Swiss healthcare system by creating an innovative model that can potentially be replicated for other chronic diseases.
Methods: To measure the quality of life, the health status as well as the change in behaviour in patients, the study design includes both qualitative and quantitative methods. Patients enrolled in the programme are asked to answer a questionnaire at three points in time; at enrolment, after the last session and two months after completing the programme. It is expected that at least 45 patients will be enrolled. For a qualitative assessment, in-depth interviews will be conducted with rheumatologists and their medical assistants as well as some of the programme participants.
The training material for the medical assistants was developed by the SLR and will be evaluated by the programme participants. All patients will also evaluate the quality of the consulting provided by the medical assistant, answering a questionnaire after the last session.
Results: Within the first year of implementation, ten outpatient clinics, with twenty-four rheumatologists and twelve medical assistants, were enrolled in the pilot project. Four medical assistants were trained in 2019 and eight are in the process of receiving training in spring 2020. Only after the completion of training will patients be enrolled in the self-management programme. Therefore, outcome-related results cannot be expected until the beginning of 2021.
Conclusion: This pilot project provides an innovative approach to closing an important gap in the Swiss healthcare system and to providing a missing component of care for patients with IA and OP. However, it has been challenging to enrol enough clinics in the pilot project. The way the programme is embedded in the current healthcare system, it demands a cultural change within outpatient clinics, allowing medical assistants to step into a new role as consultant.

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SATURDAY, 06 JUNE 2020

Psychosocial support

PARE0033 **I'M HERE BUT I'M NOT: A PHOTOVOICE STUDY OF THE LIVED EXPERIENCE OF SELF-MANAGING RHEUMATOID ARTHRITIS**

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Background: Rheumatoid arthritis (RA) is a widespread chronic disease affecting about 1% of the population in the West. It is characterised by pain, fatigue and inflammation that can flare-up without warning. This makes the condition difficult to predict and manage. Bury (1982) introduced the concept of chronic illness as a disruptive experience to one's self-identity. This is often an invisible part of managing the illness and taken for granted by others, such as family members, friends and health care professionals. Thus, there is a need to raise awareness of the patients' lived experiences of self-managing this long-term chronic illness.
Objectives: We aimed to collaborate with people with RA to (i) record and reflect the community's strengths and concerns; (ii) raise awareness of the lived experience of self-managing RA (iii) spark a dialogue among key stakeholders around the self-management of RA.
Methods: A purposeful sample of people with RA (n=12) was recruited. An innovative qualitative methodology, Photovoice, was used (Wang & Burris, 1997). A series of small group workshops took place. Participants were provided with cameras and appropriate training. They were asked to take photographs of the *"challenges and solutions to living with RA"* over approximately two weeks. Semi-structured interviews were conducted incorporating photo elicitation. As a group, the participants, a visual artist and researcher co-created a photo exhibition for the public.
Results: Participants selected 32 photographs for the exhibition. They carried out a thematic analysis of the photos identifying four themes:
•*I'm Here but I'm Not* – this theme reflected feelings of alienation and social isolation.
•*Medicine in all its forms* – this theme captured attitudes towards medication and devices, as well as the creative ways people coped with RA.
•*Visible illness* – this concerned the recognition of RA. It captures the experience of RA as a "contested illness" and the challenge of gaining medical and cultural legitimacy.
•*Mind yourself* – this theme highlighted the value of self-care, often closely connected with the natural world and engagement with social activities.
Exhibitions were held at a community arts centre and a large central hospital in Dublin city. A plain language report was also collaboratively produced.
Conclusion: This study shows how participatory methods can be used to explore the hidden experience of living with an invisible illness. This research design enabled participants to use photographs to reflect on their experiences and the meaning they intended to convey, thereby increasing trustworthiness of the findings through individual and group member checking. This

approach extends beyond traditional written and verbal responses to share the worldview of participants. It demonstrates how to work with patients to create opportunities to improve awareness and spark dialogue among those who play a role in supporting the self-management of chronic illness. The integration of creative arts and participatory methods can have a positive impact for those involved in research and can enhance public engagement with research.

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SATURDAY, 06 JUNE 2020

Campaigning

PARE0034 **PUTTING A FACE TO RHEUMATISM: MULTICHANNEL AWARENESS CAMPAIGN FOR RHEUMATIC DISEASES**

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Background: Although one in four Europeans are affected by rheumatism, the various disease patterns and the consequences for patients are still largely unknown to the general public. Furthermore, it is still widely believed that rheumatism affects only older people. Patients often cite the lack of comprehension of rheumatic diseases as a major hurdle in their daily private and professional lives (1). Therefore, it is imperative to find effective means for providing essential information to patients about the disease and improving their quality of life by raising awareness among the general public. One strategy for reaching this goal was implemented in 2018, when the Swiss League against Rheumatism (SLR) founded a patient council consisting of around ten members affected by rheumatic diseases. The council members advise the SLR on the specific needs and wishes of rheumatic patients. Most members are open to sharing their experiences with the disease with the interested public.

Objectives: The overall goal of our campaign is to raise awareness for rheumatic diseases among the general public. By showcasing patients and their struggles, rheumatism is made tangible to the general public and prejudices and barriers are reduced. The campaign focuses especially on the fact that rheumatism also affects young people. Additionally, the work carried out by the SLR and its services for patients are to be publicised among patients and in their environment. The campaign was aimed at the following target groups: patients, patients' families, health professionals, multipliers and the general public.

Methods: In order to put a specific face to rheumatism and to show that anyone, even young people, can be affected by a rheumatic disease, the SLR asked the members of the patient council to share their story for a multichannel outreach campaign. By the end of 2019 portraits had been taken and, in close collaboration with each council member, concise statements had been chosen in order to illustrate what patients struggle. The main focus was to give patients a voice and to showcase their struggles both in mainstream media such as local newspapers and on social media channels. The combination of pictures of apparently healthy people with a quote about their struggle with rheumatism creates an unexpected discrepancy in the reader's mind. Starting in 2020 the ads were distributed in several formats to editorial offices (tabloid press, local newspapers, specialist media) across Switzerland, asking the editors to publish them for free (as filler ads, when ads cannot be sold). The campaign was launched simultaneously on our social media channels and linked with existing content on our website.

Results: The first ads have already been placed and the analysis of their impact is currently being evaluated. We are still in the process of distributing our ads to an even broader audience. We expect to see a rise in media coverage and the number of free ads as well as an increased number of visitors on our website and social media channels. At a qualitative level we have received very positive feedback from our patient council, patients, and health professionals as well as journalists.

Conclusion: Featuring authentic patients and telling their stories facilitates media activities and aids in removing the barriers surrounding rheumatism. It helps to dispel misconceptions surrounding the topic, especially the notion that only people aged 60 and over are affected by rheumatism.

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"My struggle is not just against pain and limitations, but also for acceptance." Sarah, 31 years old



"I'm young and live with rheumatism. Many people find that hard to believe." Isabella, 20 years old

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PARE0035 **WHAT IS YOUR HEALTH ACTION IN 2020?**

T. Saarela[1]. [1]*The Finnish Rheumatism Association, Helsinki, Finland*

Background: At the turn of the year and decade, it is a time when magazine columns and social media channels are full of New Year's resolutions. We are thinking about weight control, fewer kilos, healthier lifestyles, increased mobility, mental well-being, more time with family and friends, learning new things, etc. For many New Year's resolution is related to well-being, often a healthier diet and exercise.

What if these promises were properly inspired? What if we encouraged people to make especially good decisions supporting musculoskeletal health and do good deeds?

The Finnish Rheumatism Association and its partners started this project to encourage people make health promoting new year resolutions and tell them publicly.

Objectives: The aim of the project is to promote the musculoskeletal health of the population and to raise citizens' awareness of musculoskeletal health and illness. The purpose of the project is to inspire people to make promises and do deeds to support of musculoskeletal health. The project utilized people's tendency to make New Year's resolutions.

Even small actions and everyday life changes are going in the right direction. Anyone can participate and have successful experience.

Methods: The project is online at www.tinjanhuoltamo.fi The website briefly describes the background of the project. It includes links to additional information and reliable sources, and provides guidance on how people with RMD's can have a healthier life.

The project utilized the social media and participants were encouraged to make #Ipromise updates for various social media channels. Campaign started at the beginning of December 2019. The radio campaign focused on Christmas holidays. Promises were made for the New Year´s Eve and some of them during January.

We sent materials and tasks every week for online groups and email lists. Tinja's Service Station acted as a personal trainer but online. We took advantage of a modern, interactive online environment where people shared their habits and experiences.

All those who kept their promises till 2/29/2020 participated in a competition, where the prize was the winner's choice of a welfare event, or a season ticket to a sports club or a local Rheumatism Organisation exercise group.

Results: The Service Station turned out to be more interesting than expected. The Facebook group had 450 members and the email-group 75 people. The quantities exceeded our expectations.

Physical exercise attracted the promises most. Good second was nutrition.

Our social media campaign was not as successful as we had hoped for. It may be that people are too cautious of making public New Year's Resolutions. The radio campaign managed to bring some more people to the email group, not so many for the Facebook group. It seemed a good idea to expand the campaign from social media to radio. The radio campaign reached people nationwide and there was a small peak in the Rheumatism Association website visits.

Conclusion: This was quite nice and different project. It seemed that one act of health easily led to another and created a positive vicious circle. We start the project with good will and without blame. Changing one's own activities and promoting future health require will and motivation. Motivation was the initiator of the action. A clear and realistic goal setting and a decision to reach the goal helped motivate.

At the end of the March we will sum up the final results and pick up good examples for musculoskeletal health actions. It is already certain that we will renew the project at the end of the year. A service station is a great low-threshold place where you can, in a good spirit, get support for your lifestyle changes.

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Genomics, genetic basis of disease and functional genomics

AB0001 PLASMA miRNA PROFILE IN PATIENTS WITH HAND OSTEOARTHRITIS

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Background: MicroRNAs (miRNA) are short non-coding RNAs that can be involved in diverse physiological processes[1]. Aberrant miRNA profiles have been shown in various diseases including osteoarthritis (OA)[2]; for instance, miR-21-5p or miR-140 are known for their altered expression in osteoarthritic cartilage [3,4]. However, no screening of circulating miRNAs has been done in patients with hand OA (HOA) so far.
Objectives: Our aim was to profile circulating miRNAs in plasma of patients with HOA in screening and validation cohort.
Methods: We screened the expression of miRNA profiles in 4 patients with erosive (3 females, mean age=63.7±7 yrs) and 4 patients with non-erosive (3 females, mean age=62.4±6 yrs) HOA, and 4 control subjects (3 females, mean age=63.5±7 yrs). The validation cohort included 10 patients with erosive (7 females, mean age=67.5±7 yrs) and 10 patients with non-erosive (6 females, mean age=67.6±8 yrs) HOA, and 10 control subjects (8 females, mean age=64.3±8 yrs). Circulating miRNA screening were performed using TLDA and selected miRNAs were validated by qRT-PCR.
Results: Profiling circulating plasma discovered 42 miRNAs from 754 analysed miRNAs with different concentration among subjects, including miR–23a–3p (1.7 fold), –222–3p (2.0 fold), and –30e–3p (13.0 fold) to be elevated in patients with HOA compared to control subjects. In addition, six miRNAs were distinctive between erosive and non-erosive HOA, e.g. hsa-miR-24-3p was 2.3 times lower and hsa-miR-576-5p was 3.4 times higher in erosive compared to non-erosive disease.
Out of these selected miRNAs, qRT-PCR validated 42 miRNAs and confirmed 11 miRNAs (e.g., miR–23a–3p or –222-3p) with different concentration between patients and controls. However, no miRNAs distinguished between erosive and non-erosive HOA, although miR-101-3p (4.5 fold) and -320b (13.7 fold) almost reached statistical significance.
Conclusion: Based on our study, we identified 11 miRNAs that may have a potential as biomarkers of HOA. However, further studies on larger cohorts are needed.
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AB0002 CONGENITAL DEFECTS IN A COHORT OF PREGNANT WOMEN FROM A CLINIC OF RHEUMATIC DISEASES AND PREGNANCY

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Background: Some studies have suggested an increased risk of adverse health outcomes for the child of patients with Rheumatic Diseases (RD), including neurodevelopmental disorders, congenital heart defects, hematological malignancies and autoimmune diseases. It is well known that 2 to 3% of live births have a congenital defect. About 7 % of all newborn deaths are due to birth defects.
Objectives: Describe Genetical Evaluation in a cohort of pregnant patients with RD
Methods: We included 22 women from February to December 2019 from a Clinic of Pregnancy and Rheumatic Diseases in Hospital Universitario in Monterrey, Mexico. All spontaneous pregnancies (21 singletons, 1 double twin), with adequate prenatal control. Ten Rheumatoid Arthritis, Antiphospholipid Syndrome in 4 cases; 5 Systemic Lupus Erythematosus, 2 Sjögren's Syndrome and a case of Dermatomyositis. In the perinatal genetics approach, medical and familial history was obtained, and pedigree was developed; ultrasound information of 12 and 22 weeks of gestation was integrated, risks for aneuploidies were adjusted according to maternal age. At birth, the dysmorphological description was made, somatometry is performed, and the newborn screening were evaluated (metabolic, hearing, cardiac). Thus, giving genetic counseling for each case.
Results: Two patients were excluded, so 20 women with follow-up, 12 (60%) were born without complications or birth defects; in 3(15%) there were adverse events (a spontaneous abortion at 12 weeks-of-gestation [wg]; a fetal death in the case of twin pregnancy, at 34.1 wg, with facial asymmetry, intrauterine growth restriction; and a premature delivery, at 36.5 wg; no defects; there were 5(25%) congenital defects: a preauricular appendix, with normal renal ultrasound. A congenital heart disease (transposition of large vessels, tricuspid stenosis). A case of macrosomia (diabetic fetopathy); a heart block with perinatal pacemaker placement (mom with lupus). And in the latter case, Krabbe disease, even without confirming it. Table 1.

Table 1.

Maternal diagnosis	Effects on fetus/neonate	N (%)
Congenital Defects		5 (25%)
Antiphospholipid syndrome	Congenital Heart Disease	
Lupus erythematosus systemic	Heart Block with Perinatal Pacemaker Placement	
Rheumatoid arthritis	Krabbe Disease	
Rheumatoid arthritis	Preauricular appendix	
Sjögren Disease	Diabetic Fetopathy	
Adverse events		3 (15%)
Rheumatoid arthritis	Spontaneous Abortion	
Antiphospholipid syndrome	Fetal death	
Rheumatoid arthritis	Premature delivery	

Conclusion: One out of every 4 pregnancies of women with rheumatic diseases presented a congenital defect, of which, the heart diseases (CHD) have been described as of greater presentation in these groups.
It is very important that women with rheumatic diseases are well attached to a comprehensive clinic in which, in addition to receiving proper attention of their rheumatic disease, they have adequate preconception and prenatal control of their pregnancies, since there is a greater risk of congenital alterations and of perinatal adverse events, as shown by this cohort. Further research is needed to fully elucidate the potential disease-related factors that might lead to the increased risk of adverse health outcomes in offspring, as well as to improve the monitoring and control of their rheumatic diseases.
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AB0003 SINGLE-NUCLEOTIDE POLYMORPHISMS (RS28493229 AND RS2290692) IN ITPKC GENE IN CHILDREN WITH KAWASAKI DISEASE

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Background: Kawasaki disease (KD) is an acute medium vessel vasculitis manifesting with mucocutaneous lesions and cardiac complications especially coronary artery lesions (CALs). Inositol 1,4,5-triphosphate 3-kinase C *(ITPKC)* gene polymorphisms are have been shown to be associated with susceptibility to KD and CAL.
Objectives: This study was designed to investigate the association of single nucleotide polymorphisms (SNPs) of the *ITPKC* gene with KD and CAL in Indian children.
Methods: Two SNPs of the *ITPKC* gene (rs28493229 and rs2290692) were studied in 50 cases of KD and 50 healthy controls. The Deoxyribonucleic acid

(DNA) samples from test subjects and controls were analysed for the two polymorphisms by polymerase chain reaction (PCR) and restriction fragment length polymorphism (RFLP). The allele, genotype, and haplotype frequencies were compared in different groups. A meta-analysis was also performed for the CC and GG genotype of both SNPs of interest.

Results: No significant differences were found in frequencies of C allele, CC genotype and C carriers of rs28493229 and rs2290692. Combined CG+GG genotype frequency of rs2290692 was found to be significantly associated with susceptibility of KD (95% Confidence interval (CI) = 1.38-13.83, p = 0.015). A meta-analysis did not show a significant association of SNP rs28493229 (Odds ratio = 1.46, CI = 0.96-2.23) and rs2290692 (OR = 1.07, 95% CI = 0.663-1.731) of *ITPKC* and susceptibility to KD.

Conclusion: Combined CG+GG genotype of SNP rs2290692 at 3' UTR of the *ITPKC* gene was found to be significantly associated with susceptibility to KD. Our study did not show a significant association of any allele or genotype with susceptibility to KD. The meta-analysis combining our study with previous studies on these 2 SNPs also failed to show a significant association of different genotypes and susceptibility of KD.

Table:

Table 1. Allele, genotype and carrier frequencies of single nucleotide polymorphisms of rs28493229 and rs2290692

Allele, genotype and carrier frequencies of SNP rs28493229 of *ITPKC* (n = 100) Allele/ Genotype	KD patients (n = 50) n (%)	Controls (n = 50) n (%)	Odds ratio (95% C.I.)	*P* value
G allele	89 (89%)	92 (92%)	-	-
C allele	11 (11%)	8 (8%)	1.42 (0.49-4.26)	0.468
GG genotype	39 (78%)	42 (84%)	-	-
CG genotype	11 (22%)	8 (16%)	1.48 (0.54-4.19)	0.446
CC genotype	0 (0%)	0 (0%)	-	-
Frequencies of allele and genotype of rs2290692 SNPs in KD patients and controls (n = 100)				
Allele/ Genotype	KD patients (n = 50) n (%)	Controls (n = 50) n (%)	Odds ratio (95% CI)	*P* value
G allele	63 (63%)	56 (56%)	-	-
C allele	37 (37%)	44 (44%)	0.747 (0.41-1.36)	0.313
GG genotype	19 (38%)	20 (40%)	-	-
CG genotype	25 (50%)	16 (32%)	1.64 (0.68-4.04)	0.272
CC genotype	6 (12%)	14 (28%)	0.45 (0.14-1.37)	0.173

C.I. Confidence interval, KD- Kawasaki disease

Figure:

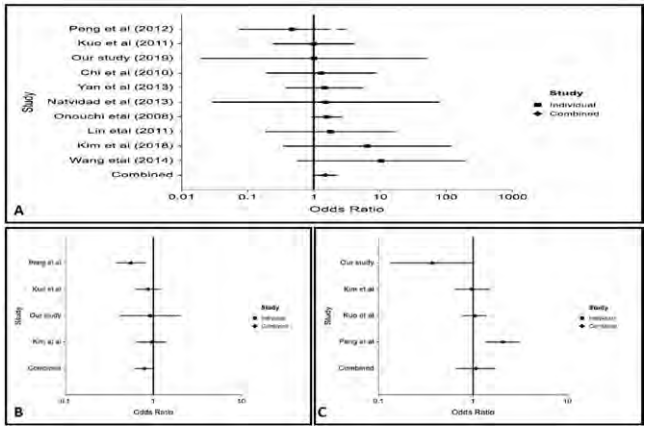


Figure 1. Forest plot for the association between (A) CC genotype of rs28493229 and risk of having KD (B) GG genotype of rs2290692 and risk of having KD (C) CC genotype of rs2290692 and risk of having KD

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AB0004 TLR10 SINGLE NUCLEOTIDE POLYMORPHISMS ARE ASSOCIATED WITH HIDRADENITIS SUPPURATIVA IN A CAUCASIAN SPANISH POPULATION (NORTHERN SPAIN)

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Background: Hidradenitis suppurativa (HS) is a chronic, relapsing inflammatory cutaneous disease affecting terminal hair follicles in apocrine-gland bearing skin. The pathogenesis of HS is still unknown, although increasing evidence suggests that the immune system plays an important role. In order to study the role of innate immunity we analyzed several Toll Like Receptors (TLRs) functional single nucleotide polymorphisms (SNPs). To date, only one previous study focused about the role of TLR4 SNPs in HS showing no association with this disease.

Objectives: The main goal of this study was to analyze the role of several TLRs functional SNPs in HS patients and healthy controls, in a Caucasian population from Cantabria (northern Spain).

Methods: Through a case-control study, we analyzed the allele and genotype distribution of the SNPs in 106 patients with HS and 278 age and sex matched healthy control subjects for the following SNPs (TLR1 rs5743611 and rs4833095, TLR2 rs5743704 and rs5743708, TLR6 rs5743810, and TLR10 rs11096955, rs11096957 and rs4129009, by Real-Time PCR using a TaqMan assay.

Results: We did not find any significant difference in the allelic distribution of the different SNPs between HS patients and controls. Regarding genotypes, only TLR10 rs11096955 (dominant, codominant and overdominant), rs11096957 (dominant, codominant and overdominant) and rs4129009 (codominant and overdominant) showed significant differences between HS patients and controls. However, no association was found when we analyzed the different TLR10 haplotypes.

Conclusion: To the best of our knowledge, this is the first study showing an association of TLR10 SNPs with HS.

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AB0005 HLA CLASS II CONFERS RESISTANCE OR SUSCEPTIBILITY TO HIDRADENITIS SUPPURATIVA IN A CAUCASIAN SPANISH POPULATION (NORTHERN SPAIN)

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Background: Hidradenitis suppurativa (HS) is a chronic inflammatory cutaneous disease affecting terminal hair follicles in apocrine glands bearing skin. The pathogenesis of HS remains unknown, although increasing evidence suggests that the immune system plays an important role. To date, two previous studies, did not find any association between *HLA* and HS.

Objectives: Our aim was to analyze the association of HLA class II with HS in a Caucasian population from Cantabria (northern Spain).
Methods: In this study we analyzed the *HLA-A, -B, -C, DRB1, -DQA1 and –DQB1* allele distribution in 106 HS patients and 262 age- and sex-matched controls from a Caucasian population of Cantabria (northern Spain).
Results: *HLA-A**29 and *B**50 were significantly more frequent in HS patients and *A**30 and *B**37 in controls, but these associations disappeared after correction. On the other hand, *DRB1**07, *DQA1**02 and *DQB1**02 were significantly more frequent in controls (*p* 0.026, *p* 0.0012 and *p* 0.0005 respectively), and the *HLA* allele *DQB1**03:01 was significantly more frequent in HS patients (*p* 0.00007) all of them after Bonferroni correction. Furthermore, the *DRB1**07; *DQA1**02; *DQB1**02 haplotype was significantly more frequent in controls (*p* 0.0005).
Conclusion: This is the first study showing an association of HLA-class II with HS. Our results suggest that HLA-II alleles (*DRB1**07, *DQA1**02, *DQB1**02 and *DQB1**03:01) and the *DRB1**07~*DQA1**02~*DQB1**02 haplotype could influence on resistance or susceptibility to HS.
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Disclosure of Interests: Monica Calderón-Goercke: None declared, J. Gonzalo Ocejo-Vinyals: None declared, Miguel A González-Gay Grant/research support from: Pfizer, Abbvie, MSD, Speakers bureau: Pfizer, Abbvie, MSD, Marcelo A. Fernández-Viña: None declared, Juan Cantos-Mansilla: None declared, Iosune Vilanova: None declared, Ricardo Blanco Grant/research support from: AbbVie, MSD, and Roche, Speakers bureau: AbbVie, Pfizer, Roche, Bristol-Myers, Janssen, and MSD, Marcos González-López: None declared
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AB0006 HYPOMETHYLATION OF THE PROMOTER REGION OF TLR4 GENE AT A SYSTEMIC LEVEL IN PATIENTS WITH RHEUMATOID ARTHRITIS AND PERIODONTITIS

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Background: Periodontitis (PD) has long been linked with Rheumatoid arthritis (RA) [1]. Epigenetic modifications are being recently explored to explain such associations, DNA methylation being one such important mechanism.
Objectives: To study the effect chronic generalized periodontitis on systemic methylation of TLR4 genes in comparison to only RA and RA with PD patients.
Methods: Twenty-three RA patients, among which 11 patients had chronic generalized PD, 20 patients with only PD and 15 healthy individuals recruited. DNA was isolated from PBMCs of the participants blood, then were first bisulphite converted and then methylation specific PCR were performed using primers for methylated and um-methylated promoters of TLR4. The DNA amplifications were checked in horizontal gel electrophoresis. The methylation signatures were verified by DNA sequencing (Sanger) of the amplified products.
Results: The anti-CCP, DAS-CRP and HAQ DI were higher in patients with both RA and PD (220±40, 5.7±0.2, 1.5±0.1 respectively, p<0.05). Control samples had shown amplification bands for methylated primers of TLR4 but not for un-methylated primers of TLR4. However, only RA, only PD and RA with PD samples, had shown amplification for un-methylated primers and not for methylated primers. These results together with DNA sequencing indicated that 4 CpG sites in the promoter ofTLR4 genes were hypo-methylated in the PBMCs of patients whereas those remain methylated in healthy individuals.
Conclusion: The observations indicated that though PD is a localised disease of the gingiva there is a systemic involvement of TLR mediated pathways in them which is similar to those in RA. However, further validation in larger cohort and down-stream signalling molecules needs to be studied.
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AB0007 VALUE OF ULTRASOUND IN ASSESSMENT OF ACTIVE SACROILIITIS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: The inflammatory of the sacroiliac joints (SIJs) called sacroiliitis, is a characteristic of axial Spondyloarthritis (axSpA). The detection of sacroiliitis is meaningful to prevent irreversible changes. The tool of assessment of sacroiliitis including radiographs, computed tomography (CT) and magnetic resonance imaging (MRI). Ultrasound (US) has also been used in the evaluation of sacroiliitis in recent years.
Objectives: We aimed to evaluate the value of US in the assessment of active sacroiliitis in axSpA patients.
Methods: Fifty-one patients fulfilling Assessment of SpondyloArthritis International Society (ASAS) 2009 criteria for the classification of axSpA were recruited[1]. All the patients underwent MRI and US evaluation of bilateral SIJs. MRI was performed using the sequences of T1WI, T2WI and fat suppression T2WI (FS-T2WI). MRI sacroiliitis was defined according to ASAS criteria of active sacroiliitis[2]. The Spondyloarthritis research Consortium of Canada (SPARCC) scoring was used to evaluate the inflammatory lesions in SIJs[3]. US were performed by an ultrasonographer with 10 years of experience in musculoskeletal ultrasound, and resistive index (RI) value was recorded. The US sacroiliitis was defined as the presence of more flow signals at SIJ with an RI ≤ 0.75. The HLA-B27, erythrocyte sedimentation rate (ESR) and hypersensitive C-reactive protein (hsCRP) were also evaluated. Consistency rate, sensitivity, specificity, positive predictive values (PPV) and negative predictive values (NPV)for the diagnosis of sacroiliitis by US were calculated, using MRI as the gold standard.
Results: Of the 51 patients, 24 were female and 27 were male. The HLA-B27 positive rate was 90.2% (46/51). The consistency rate of US and MRI sacroiliitis was 55.88 (57/102). The sensitivity and specificity of US for the diagnosis of sacroiliitis were 55.93 (33/59) and 55.81 (24/43) respectively. The PPV and NPV were 63.46 (33/52) and 48 (24/50) respectively. There was no significant difference in ESR and hsCRP between the US positive sacroiliitis and the others (P= 0.7477 and 0.2268, respectively). The SPARCC scores have no significant difference between the US positive sacroiliitis and the others (P= 0.2206). The RI was not significantly associated with the MRI SPARCC score (P=0.4236).
Conclusion: US may be an optional method for preliminary screening sacroiliitis. But its reliability as a diagnostic method needs further verification.
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AB0008 THE IMPACT OF STAT4 RS7574865, IL6 RS1800795, IL6R RS2228145 AND RS4845618 ON RHEUMATOID ARTHRITIS SUSCEPTIBILITY IN BELARUSIAN POPULATION

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Background: Rheumatoid arthritis (RA) is a chronic systemic disorder of the connective tissue of still unknown aetiology and complex autoimmune pathogenesis that primarily affects small joints. HLA alleles provide for 11-37% of the RA heritability, suggesting the substantial role of the non-HLA loci in genetic predisposition to RA. Among non-HLA loci, *IL6, IL6R* and *STAT4* genes attract attention, however, the data concerning their influence on RA risk are somewhat contradictory.
Objectives: The aim of the study was to analyze the involvement of four SNPs (*STAT4* rs7574865, *IL6* rs1800795, *IL6R* rs2228145 and rs4845618) in RA susceptibility.
Methods: 187 patients diagnosed with RA (mean age 58.2 ± 11.9), and 380 healthy blood donors (mean age 37.18 ± 10.69 years) were included into the

study. DNA extraction from peripheral blood samples was performed using the phenol-chloroform method. SNPs were genotyped using the real-time PCR with fluorescent probes. The allele and genotype frequencies were compared using the χ2 test. Odds ratios (ORs) and 95% confidence intervals (95% CIs) were calculated using the VassarStats online tool.

Results: Utilizing recessive genetic model we found an association between TT genotype of *STAT4* rs7574865 (OR = 2.362; 95%CI [1.0378 – 5.376], p = 0.038) and RA. For *IL6* rs1800795, it was found that CC genotype had significantly higher frequency among patients with rheumatoid arthritis as compared to that in controls (OR = 1.52; 95%CI [1.02 – 2.27], p = 0.0456). No associations of *IL6R* rs2228145 and rs4845618 SNPs with risk of RA were found in the total group of patients vs. controls. It was also shown that *IL6* rs1800795 CC genotype frequency was significantly higher among the patients with RF-negative status (p = 0.0019).

Conclusion: Thus, we provide evidence for association of the *STAT4* rs7574865 and *IL6* rs1800795 variants with risk of RA in the Belarusian population, some features of interplay being revealed between gene polymorphisms analyzed and RA antibody status. Abovementioned SNPs may contribute to RA genetic susceptibility in the Belarusian population.

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AB0009 ASSOCIATION BETWEEN POLYMORPHISMS OF BANK1 AND MANIFESTATIONS OF SLE

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Background: *BANK1* encodes an adapter/scaffold protein primarily expressed in B cells, which is involved in cell signaling and activation. Genome-wide association studies (GWAS) have identified different *BANK1* single nucleotide variants (SNVs) associated with SLE primarily in European or Asian-derived populations. Interestingly, we recently have documented an association between this gene and susceptibility to systemic lupus erythematosus (SLE) in Mexican population.

Objectives: To determine whether the *BANK1* R61H (rs10516487G/A) and A383T (rs3733197G/A) SNVs are associated with clinical and immunological manifestations in SLE.

Methods: Our study included 123 Mexican women with SLE (SLICC 2012 criteria). Genotyping of the two *BANK1* SNVs were obtained by TaqMan probes and real-time PCR. An association study was performed between the alleles and genotypes of *BANK1* R61H and A383T with the clinical and immunological manifestations included in the SLE SLICC classification criteria. Hardy-Weinberg equilibrium and an association study was performed using Finetti, a p value ≤ 0.05 indicated association.

Results: We identify an average age of 38.5±12. Cases and controls remained in Hardy-Weinberg equilibrium. An association with susceptibility to SLE was found between genotypes of the two *BANK1* SNVs and joint manifestations (rs1051487G/A; AA + GA vs GG, OR 4.45, p=0.004, rs3733197G/A; AA + GA vs GG, OR 2.66, p=0.032, respectively), as well as with protection for neurological and renal involvement (rs1051487G/A, OR 0.16, p=0.02, rs3733197G/A; OR 0.40, p=0.02, respectively) (Table 1a and b). No association was found with other clinical manifestations.

Conclusion: Our data in the Mexican population show that both *BANK1* R61H and A383T SNVs are risk factors for synovitis. On the other hand, these *BANK1* R61H and A383T variants are protective factors for neurological and renal damage, respectively.

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Disclosure of Interests: None declared

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AB0010 TRIPLE DMARD TREATMENT IN EARLY RHEUMATOID ARTHRITIS INCREASE SYNOVIAL ACTIVATED NATURAL KILLERS AND RESTING MAST CELLS BUT DECREASE PLASMA CELLS AND M1 MACROPHAGES

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory joint disease with cartilage and bone damage as well as disability and its optimal therapeutic success depends on understanding the underlying pathophysiology[1]. Since RA is a heterogenous disease, there is an urge to characterize new molecular mechanisms to aid the development of more effective and personalized therapy [2]. Genome-wide transcriptional effects of tDMARD in early RA synovial tissues showed alterations in gene expression of T cell activation and plasmablast/plasma cell differentiation[3].

Objectives: Using publicly available synovial tissue transcriptomic data to compare the immune cells infiltration at baseline and after 6 months of tDMARD to identify subgroups that might not respond well to tDMARD.

Methods: RNAseq dataset (GSE97165) of synovial biopsies taken from 19 early RA patients at baseline and after 6 months of tDMARD treatment were retrieved and reanalyzed. The raw RNAseq data were used for in silico prediction of the immune cells' infiltration the synovial tissue using CIBERSORT analytical tool to evaluate the pre versus post tDMARD changes in immune population and/or activation status. Then, patients were divided according to the level of alteration in immune cells percentage after the treatment. Differentially expressed genes between the subgroups were defined and gene set enrichment analysis was performed to identify the underlying pathways in each group using BioJupies tools.

Results: 4 immune cells populations showed significant changes after 6 months of tDMARD indicating their role in disease pathophysiology or in response to the therapy. Resting mast cells and activated natural killer (NK) cells were increased in 84% and 74% of patients, respectively. On the other hand, M1 macrophages and plasma cells were decreased after treatment in 68% and 58% of patients, respectively. GSEA of differentially expressed genes between patients who showed increased activated NK cells in comparison to those who showed decreased or no change in NK cells after treatment identify novel pathways that can explain the heterogeneity in response to treatment specifically genes related to WNT signaling, estrogen metabolism and IL17 signaling.

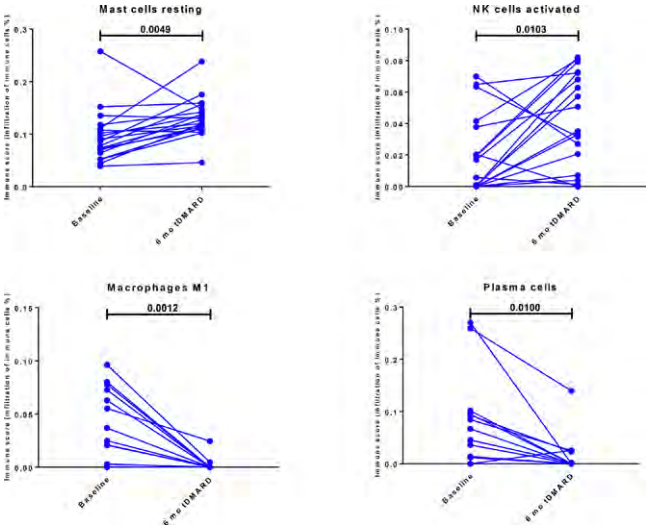


Figure 1. Percentage of infiltrating immune cells in the synovial tissue at baseline and after 6 months of tDMARD therapy in 19 early RA patients using CIBERSORT tool.

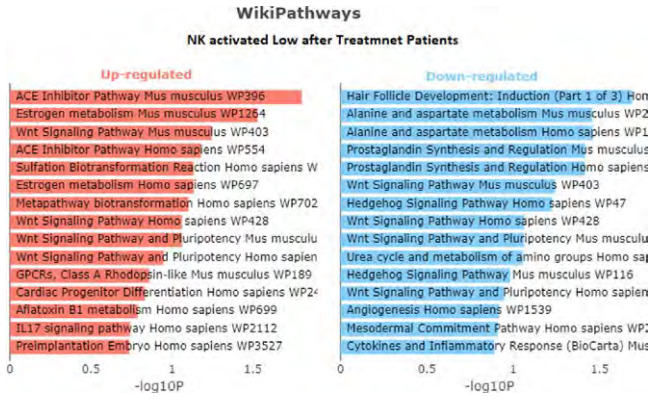


Figure 2. Top wikiPathways enriched in the patients with decreased percentage of synovial infiltrating activated NK after 6 months of tDMARD therapy compared to those who showed increased or unchanged percentage.

Conclusion: Synovial tissue NK cells, resting mast cells, plasma cells and M1 macrophages play major role in response to tDMARD. Genes related to WNT signaling, estrogen metabolism and IL17 signaling can help stratification of patients for a more effective personalized medicine in RA.

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AB0011 INFLUENCE OF IL17A GENE ON THE PATHOGENESIS OF IMMUNOGLOBULIN-A VASCULITIS

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Background: Cytokines signaling pathway genes represent a key component of the genetic network implicated in the pathogenesis of Immunoglobulin-A vasculitis (IgAV) [1], an inflammatory vascular pathology. *Interleukin (IL)17A* is a genetic risk *locus* for autoimmune diseases, such as giant cell arteritis [2] and spondyloarthritis [3].

Objectives: To determine the potential influence of *IL17A* on IgAV.

Methods: Five *IL17A* tag polymorphisms (rs4711998, rs8193036, rs3819024, rs2275913 and rs7747909) were genotyped in 360 Caucasian patients with IgAV and 1,003 sex and ethnically matched healthy controls.

Results: No statistically significant differences between patients with IgAV and healthy controls were observed when each *IL17A* genetic variant was analyzed independently. Similarly, no statistically significant differences between patients with IgAV and healthy controls were found when the five *IL17A* polymorphisms were evaluated combined conforming haplotypes. In addition, there were no statistically significant differences in genotype, allele and haplotype frequencies of *IL17A* when patients with IgAV were stratified according to the age at disease onset or to the presence/absence of gastrointestinal or renal manifestations.

Conclusion: Our results do not support an influence of *IL17A* on the pathogenesis of IgAV.

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Disclosure of Interests: Fernanda Genre: None declared, Sara Remuzgo Martinez: None declared, Verónica Pulito-Cueto: None declared, D. Prieto-Peña: None declared, Belén Atienza-Mateo: None declared, Belén Sevilla: None declared, Javier Llorca: None declared, Norberto Ortego: None declared, Leticia Lera-Gómez: None declared, Maite Leonardo: None declared, Ana Peñalba: None declared, María Jesús Cabero: None declared, Luis Martín-Penagos: None declared, Jose Alberto Miranda-Filloy: None declared, Antonio Navas Parejo: None declared, Diego de Argila: None declared, Maximiliano Aragües: None declared, Esteban Rubio-Romero: None declared, MANUEL LEON LUQUE: None declared, Juan María Blanco-Madrigal: None declared, E. Galindez: None declared, Javier Martin Ibanez: None declared, Santos Castañeda: None declared, Ricardo Blanco Grant/research support from: Abbvie, MSD and Roche, Consultant of: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen and MSD, Speakers bureau: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen, Lilly and MSD, Miguel A González-Gay Grant/research support from: Pfizer, Abbvie, MSD, Speakers bureau: Pfizer, Abbvie, MSD, Raquel López-Mejías: None declared

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AB0012 ROLE OF IRF5 GENE ON THE PATHOGENESIS OF IMMUNOGLOBULIN-A VASCULITIS

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Background: Interferon signaling pathway plays a relevant role in autoimmunity. Genetic variants in the *interferon regulatory factor (IRF) 5* gene, that encodes the major regulator of the type I interferon induction [1], have been related to the development of several inflammatory diseases [2].

Objectives: To determine the influence of *IRF5* on Immunoglobulin-A vasculitis (IgAV), an inflammatory vascular disease.
Methods: Three *IRF5* polymorphisms (rs2004640, rs2070197 and rs10954213) representative of 3 different haplotype blocks were genotyped in 372 Caucasian patients with IgAV and 876 sex and ethnically matched healthy controls.
Results: No statistically significant differences between patients with IgAV and controls were observed when each *IRF5* polymorphism was analyzed independently. Similarly, no statistically significant differences between patients with IgAV and controls were found when *IRF5* polymorphisms were evaluated combined conforming haplotypes. Additionally, there were no statistically significant differences in genotype, allele and haplotype frequencies of *IRF5* when patients with IgAV were stratified according to the age at disease onset or to the presence/absence of gastrointestinal or renal manifestations.
Conclusion: Our results do not support an influence of *IRF5* on the pathogenesis of IgAV.
References:
[1] Nat Immunol 2011; 12: 231-8;
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Acknowledgments: This study was supported by European Union FEDER funds and "Fondo de Investigaciones Sanitarias" (grant PI18/00042) from 'Instituto de Salud Carlos III' (ISCIII, Health Ministry, Spain). RL-M is a recipient of a Miguel Servet type I programme fellowship from the ISCIII, co-funded by the European Social Fund (ESF, `Investing in your future´) (grant CP16/00033). SR-M is supported by funds of the RETICS Program (RD16/0012/0009) (ISCIII, co-funded by the European Regional Development Fund (ERDF)). VP-C is supported by a pre-doctoral grant from IDIVAL (PREVAL 18/01). LL-G is supported by funds of PI18/00042 (ISCIII, co-funded by ERDF).
Disclosure of Interests: Sara Remuzgo Martinez: None declared, Fernanda Genre: None declared, Verónica Pulito-Cueto: None declared, D. Prieto-Peña: None declared, Belén Atienza-Mateo: None declared, Belén Sevilla: None declared, Javier Llorca: None declared, Norberto Ortego: None declared, Leticia Lera-Gómez: None declared, Maite Leonardo: None declared, Ana Peñalba: None declared, María Jesús Cabero: None declared, Luis Martín-Penagos: None declared, Jose Alberto Miranda-Filloy: None declared, Antonio Navas Parejo: None declared, Javier Sanchez Perez: None declared, Maximiliano Aragües: None declared, Esteban Rubio: None declared, MANUEL LEON LUQUE: None declared, Juan María Blanco-Madrigal: None declared, E. Galindez: None declared, Javier Martin Ibanez: None declared, Santos Castañeda: None declared, Ricardo Blanco Grant/research support from: Abbvie, MSD and Roche, Consultant of: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen and MSD, Speakers bureau: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen, Lilly and MSD, Miguel A González-Gay Grant/research support from: Pfizer, Abbvie, MSD, Speakers bureau: Pfizer, Abbvie, MSD, Raquel López-Mejías: None declared
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AB0013

HLA ASSOCIATION WITH SYSTEMIC SCLEROSIS (SSc) IN NORTH INDIAN POPULATION AND FAMILIAL INHERITANCE PATTERNS

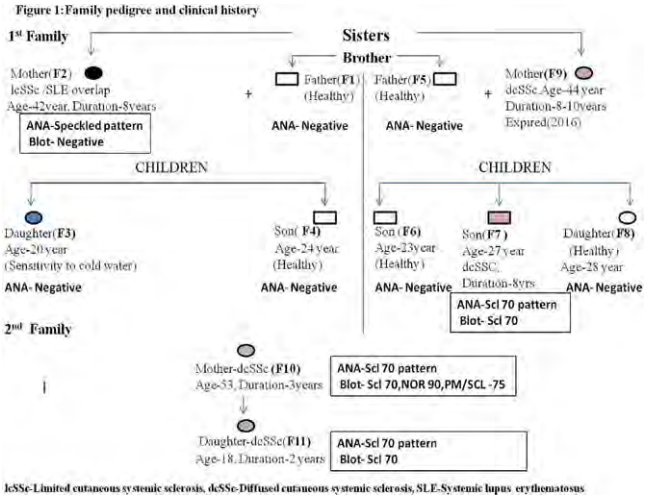
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Background: It is widely believed that SSc develops in an individual with a permissive genetic makeup.Genetic influences have long been suspected to impact SSc. In families with a history of SSc, the incidence of disease can range from 1.5 to 1.7% (1). There are several reports of familial occurrence and certain alleles of the HLA system have been associated with the disease (2).No Indian data pertaining to genetic basis of systemic sclerosis is present. Understanding the genetic basis of the disease will help us in defining the biomarkers of the disease in the population that can help in early diagnosis and prognosis.
Objectives: To study HLA association with Systemic sclerosis (SSc) in North Indian Population and its genetic susceptibility to familial systemic sclerosis.
Methods: A total of 150 SSc patients diagnosed by following ACR and EULAR criteria and 150 control subjects, were genotyped for HLA-A, B, DRB1, DQB1 loci by Luminex® 200 Instrument (USA). The association of alleles with disease susceptibility was tested by Chi-square test and Fisher's exact test.
HLA Typing for HLA class I (A, B, C) and II(DR,DQ,DP) for familial study of systemic sclerosis in 2 families was performed by Next Generation Sequencing(NGS) with illumina MiniSeq using MIA FORA NGS Kits from IMMUCOR. Antinuclear patterns (ANA) and specific antibodies were detected by indirect Immunofluorescence and Immunoblot (Euroline, Germany).
Results: Strong disease associations were observed for haplotypes A*24(OR=1.7;< 0.02), A*32(OR=2.8;< 0.02), B*35(OR=1.7;< 0.03), DRB1*11(OR=2.1;< 0.007). The reduced frequencies of haplotypes A*68(P< 0.05), DRB1*10(P< 0.05), DRB1*12 (P<0.00) among patients suggested a protective association. There was no statistical association found with HLA DQB*1.
Through NGS we observed that in the 1st family haplotypes HLA –A*11, 32, 24; B* 51, 55, 35; C*-14, 04; DRB1*15, 04; DQB1*05, 03; DPB1*04, 26 appears in affected family members with serological abnormalities.In the 2nd family both mother and daughter had same set of haplotypes except DQB1 with serological abnormalities. The haplotypes DPB1*04 was present in all the diseased individuals of both the families (Fig. 1 and table 1).

Table 1. NGS HLA typing report

	A	B	C	DRB1	DQB1	DPB1
F1	11 24	35 15	04 04	15 15	05 05	02 26
F2	11 32	51 55	14 04	15 04	05 03	04 04
F3	11 24	35 55	04 04	15 15	05 05	26 04
F4	32 11	51 15	14 04	15 04	05 03	02 04
F5	24 33	35 44	04 07	15 07	05 02	26 14
F6	11 24	35 55	04 04	15 15	05 05	04 26
F7	11 24	35 55	04 04	15 15	05 05	04 26
F8	24 32	51 35	14 04	04 15	03 05	26 04
F9	11 32	51 55	14 04	15 04	05 03	04 04
F10	11 33	44 52	07 12	11 07	02 03	04 13
F11	11 33	44 52	07 12	11 07	03 03	04 13

Fig. 1



Conclusion: The risk alleles A*24, 32; B*35; DRB1*11 were found to be associated with North Indian cohort of SSc, while the protecting alleles were A*68; DRB1*10, 12.These risk alleles were present in the SSc affected family members and the protective alleles were absent in the same. Surprisingly, even healthy members carried the same risk alleles but did not manifest the disease or have serological evidence of the same. We have not excluded occurrence of disease at a later age, as presently the healthy siblings are young. Thus our study indicates that though HLA association are found with SSc but many other factors like HLA (HLA *C, DPB1*) or non HLA genes as wells as epigenetic factors might also play a role in disease manifestation and severity.
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AB0014

GENETIC MARKERS OF METHOTREXATE HEPATOTOXICITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Methotrexate (MT) is a first-line drug in the treatment of rheumatoid arthritis (RA). The effectiveness and tolerability of the use of MT largely determines the prognosis of the course of the disease, the speed of achieving remission The development of hepatotoxicity (HT) is the most common adverse reaction, it is noted in 5-12.5% of cases and often requires the abolition of MT. In this regard, predicting the development of HT seems to be an important area of research.
Objectives: to study genetic predictors of HT development in patients with RA using MT.
Methods: 44 patients with a reliable diagnosis of RA were included in study. All of the patients used MT at a dose of 15.0 (12.5-17.5) mg/week in combination with folic acid 3-5 mg / day outside of MT. The average age was 46.7 ± 12.3 years; females- 81.8% (n = 36); mail 18.2% (n = 8). The duration of RA is 5.3 ± 2.2 months. All patients were divided into two groups: the first study group (n = 17) included patients with RA who developed a HT reaction to MT, which required the abolition of MT; in the second- (n = 27) - comparison group - patients with good efficacy and tolerability of MT.
Genotypes for polymorphic alleles were analyzed in all patients: C677T (rs1801133) and A1298C (rs1801131) of the methylenetetrahydrofolate reductase gene (MTHFR); 347C> G single-nucleotide polymorphism of the gene of aminoimidazole-carboxamidoriboside transformylase / inosine monophosphate cyclohydrolase (ATIC); c.80G> A locus of the SLC19A1 gene encoding the folate transporter membrane carrier protein.Groups were compared according to possible inheritance models: dominant, recessive, codominant. Statistical data processing was carried out using the SATISTICA 10.0 software package using descriptive and nonparametric statistics methods.
Results: The frequency of occurrence of various mutations in genes that affect the metabolism of MT among patients with RA in the study and comparison groups are presented in table 1

Table 1. The frequency of occurrence of various mutations in genes that affect the metabolism of MT

Genetic option	Study group ГТ+, n=17	Comparison group ГТ <<->>, n=27
MTHFR-A1298C		
CC	5	6
CA	2	8
AA	10	13
MTHFR -C677T		
CC	7	9
CT	8	17
TT	2	1
347C>G ATIC		
CC	9	6
CG	6	19
GG	2	2
SLC19A1c80A>G		
AA	11	22
AG	6	4
GG	0	0

ГТ- hepatotoxicity

When analyzing inheritance models, it was found that differences in hepatotoxicity for comparing genotypes (MTHFR-A1298C, MTHFR-C677T, SLC19A1c80A> G) were not statistically significant. A statistically significant increase in the risk of hepatotoxicity was found for dominant (2.18 (1.06-4.47), x2 = 4.38, p = 0.03) and codominant (0.42 (0.19-0.92), x2 = 5.23, p = 0.02) models for the 347C> G ATIC gene.
Conclusion: Thus, an increase in the risk of hepatotoxicity for the dominant and codominant models for the 347C>G ATIC gene allows recommending genotyping of the alleles of this gene before MT administration in order to reduce the risk of hepatotoxic reactions.
Disclosure of Interests: Natalia Martusevich Shareholder of: k, E. Aksenova: None declared, Katsiarina Gudkevich: None declared
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AB0015

IDENTIFICATION OF KEY GENES TO SUPPORT SYSTEMIC LUPUS ERYTHEMATOSUS, RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDYLITIS DIAGNOSIS BY TRANSCRIPTOMIC APPROACH

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Background: Early diagnosis of inflammatory rheumatic diseases (IRD), as Systemic Lupus Erythematosus (SLE), Rheumatoid Arthritis (RA) and axial Spondyloarthritis (axSpA) represents in our days a major clinical challenge. Increasing evidence has determined that early diagnosis, prompt treatment initiation and early achievement of remission are the best predictors of long-term clinical, functional and radiographic outcomes. Therefore, identification of sensitive biomarkers to support an early diagnosis to enable early therapy is of utmost importance [1,2].
Objectives: This study aims to identify novel genes that may improve the current clinical diagnosis approach for early SLE, RA and axSpA.
Methods: A cross-sectional study was conducted on 44 participants, 12 with axSpA (according to ASAS criteria), 11 with RA (according to ACR/EULAR criteria for RA), 10 with SLE (according to ACR classification criteria for SLE) and 11 Healthy Controls (HC), gender and age matched. Patients with co-occurrence of other IRD or having received biological therapies were excluded. Peripheral blood samples were collected into PAXgene tubes and stored in -80°C. mRNA profiling by RNA-seq was performed. Unpaired t-tests with multivariate permutation correction were applied to identify differentially expressed genes (DEGs) between patients and HC for each disease and within diseases. Enrichment analysis, Gene ontology (GO) and Kyoto Enrichment of Genes and Genomes (KEGG) analysis were also performed. DEGs that allow to distinguish each disease from HC and between diseases. The top DEGs (axSpA n=2, RA n=2, SLE n=3) identified were confirmed by quantitative RT-PCR.
Results: For axSpA, genes involved in negative regulation of cytokines by JAK/STAT pathway and in osteoblast differentiation through STAT3 pathway, were confirmed. In SLE, genes involved in trap for immune complexes in peripheral blood and involved in nucleosome regulation, were also confirmed. Regarding RA, no genes were confirmed.
Conclusion: Our work provides new insights into IRD pathogenesis, and discloses new biomarkers, which may be useful as either predictive biomarkers for diagnosis or therapeutic targets to improve IRD approach.Further validation are needed in different cohorts.
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AB0016

ASSOCIATION OF PTPN22 GENETIC VARIANTS WITH DISEASE SUSCEPTIBILITY AND CLINICAL VARIABLES IN PRIMARY SJÖGREN SYNDROME

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Background: Primary Sjögren's syndrome (pSS) is a systemic autoimmune disease characterized by dysfunction of exocrine glands secondary to lymphocytic infiltration. Lymphoid tyrosine phosphatase (LYP) regulates T and B lymphocyte activation. *PTPN22* gene encodes LYP; multiple polymorphic variants have been described as genetic risk factor of autoimmune diseases.
Objectives: The aim was to analyze the *PTPN22* rs2488457G>C, rs33996649G>A, and rs2476601C>T genetic variants relationship with the development risk of pSS in the western Mexico population.
Methods: One hundred and eighty healthy subjects (HS) and 150 pSS patients, classified according to EULAR 2016 criteria, were included. The genetic variants and mRNA expression were determined through PCR-RFLP and qPCR assays.

Results: The frequency of heterozygote rs33996649GA genotype was higher in pSS patients than HS [OR=3.143 (1–10.234), p=0.046], and also, rs33996649GA genotype was associated with high SSDAI score (p=0.01). The pSS patients showed 44-fold more mRNA expression in comparison with HS (p=0.002), and mRNA expression correlates with SSDAI (r^2=0.512, p=0.006).

Conclusion: The rs33996649G>A genetic variant of the *PTPN22* gene is associated with increased development risk of pSS in the western Mexican population. The expression mRNA correlates with disease activity in pSS.

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AB0017 CONSTANT GENETIC MARKER IL1B T-31C IS ASSOCIATED WITH ANAMNESIS OF BIOLOGICAL DRUGS TREATMENT IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is chronic progressive joint disease with erosions formation. Timely and effectiveness treatment is important due to quickly structural damage and progressive losing of active motion. Synthetic DMARDs didn't have a sufficient effect. Using biological drugs seemed like a panacea, but according to investigations at least 30-40% RA-patients lost treatment efficiency. Biological drugs act through immune cascade, that's why mutation in regulatory region of cytokine genes may partly determine treatment failure.

Objectives: The objective of our study was to analyze the frequency of *IL1 T-31C* single nucleotide polymorphism in patient with rheumatoid arthritis and its association with biological drugs prescribing.

Methods: One hundred two Caucasian RA-patients (age – 56 yrs [45; 61]; DAS28 4.7 [3.8; 5.9]) were enrolled in our study. All of them had American College of Rheumatology (ACR)-defined RA (1987 classification criteria) and gave written inform consent. Single nucleotide polymorphisms *IL1B T-31C* (rs1143627), *IL4 C-590T* (rs2243250), IL10 C-592A (rs1800872), *IL10 A-1082G* (rs1800896) were determined by restriction fragment length polymorphism. Descriptive statistics, Chi-squared test were used for data analysis. Results are presented as median and 25th/75th percentiles (Me [25th percentile; 75th percentile]).

Results: The most of SNPs analyzed had corresponded to the Hardy Weinberg equilibrium (HWE). The only exception was IL1B T-31C – the frequencies were differed statistically significant from HWE (p=0,03). Forty seven (46.1%) patients were treatment with biological drugs. Homozygotes IL1b -31CC were founded more frequently beside patients with biological treatment compare with other group (13 from 47 (27,7%) vs. 6 from 52 (11.5%), p=0,042). Other SNPs didn't demonstrate any associations.

Conclusion: Single nucleotide polymorphism *IL1B T-31C* (rs1143627) may be used for prognosis of basic anti-inflammatory therapy inefficiency and the needing for prescribing biological therapy.

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AB0018 TNFA RS1800629 POLYMORPHISM: WHAT ABOUT ITS ASSOCIATION WITH CLINICAL MANIFESTATIONS AND ANTI-TNFA THERAPY? DATA FROM A SERIES OF ITALIAN PATIENTS WITH BEHÇET SYNDROME

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Background: Tumor Necrosis Factor-alpha (TNF-α) is a pleiotropic cytokine with a critical role in the pathogenesis of Behçet syndrome (BS). Anti-TNF-α therapy is useful for patients with refractory, severe BS, in particular for ocular, central nervous system, and gastrointestinal manifestations. However, although biological treatment with anti-TNF-α agents are effective in BS, not all patients are definite responders. Non-responders patterns could be due to: alternative non-TNFα related pathway of inflammation; anti-drug antibodies presence or development; polymorphic alleles of *TNFα* gene. *TNFα* rs1800629 (-308G>A) is a drug-response single nucleotide polymorphism (SNP) located within the gene promoter. Poor and conflicting data are currently available about the association of this polymorphism and clinical manifestations of BS, as well as about the responsivness to the TNFα blockers in BS patients [1-3].

Objectives: Aims of this study were to investigate in a cohort of Italian patients with BS the frequency of rs1800629 genotypes and its association with clinical features and anti-TNFα therapy response.

Methods: Consecutive patients with BS were recruited. Patients demographic and clinical data were collected by medical records and analyzed. Home-made specific primer pairs were used for rs1800629 coverage. gDNA was isolated and amplified using PCR. Good-quality amplicons were sequenced (Sanger method). *In silico* analysis was downstream performed using specific software for query-subject similarity analysis.

Results: 130 BS patients (64M:66F; mean age: 45.8±12.3 years) were included in the study. Patients predominant lesions were oral aphtosis (100%), eye involvement (86.2%), skin lesions (72.3%) and genital ulcers (57.7%). *TNFα* rs1800629 wild-type GG genotype was found in 106/130 BS patients (81.5%); the heterozygous genotype (GA) was identified in 24/130 patients (18.5%). No statistically significant differences were found in genotypes frequencies when the patients were stratified for presence and absence of each clinical manifestation (p>0.05), while statistical significant differences were found when the patients were compared for therapy (anti-TNFα drugs) response. In detail, 73/130 patients (56.2%) were treated with anti-TNFα agents. We found 16/73 (21.9%) non-responders patients (NRP). In NRP group, we identified 9/16 patients (56.3%) with GG genotype and 7/16 (43.7%) with GA genotype, while 8/57 (14.0%) responder patients showed GA genotype and 49/57 responder patients (86.0%) showed GG genotype (p=0.0093; OR: 0.21, CI: 0.06-0.729).

Conclusion: Here we described a low frequency of *TNFα* rs1800629 SNP-containing allele and the lack of association between SNP and BS clinical hallmark, as previously reported in literature [1-4]. We also found higher percentage of GG genotype in case of therapy response than GA genotype. The SNP is a promoter polymorphism that could affect the auto-inflammatory response and the therapy responsivness, as suggested by our preliminary data of pharmacogenomics. Analyses of a larger cohort of patients are need to confirm the study findings and to explain the SNP role as outcome predictor.

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AB0019 GENETIC POLYMORPHISM OF THE INFLAMMATORY MARKER SAA1 RS12218 (-13 T/C) IS ASSOCIATED WITH AN APTITUDE TO CLINICAL PHENOTYPES OF JUVENILE IDIOPATHIC ARTHRITIS

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Background: Juvenile idiopathic arthritis (JIA) is one of the most widely-spread immuno-inflammatory diseases of an unknown etiology, the leading manifestation of which is chronic joint inflammation, occuring in children under the age of 16. The disease is a complex of chronic arthropathies with various phenotypic manifestations.

Objectives: To verify the hypothesis about the role of SAA1 rs12218 T / C gene polymorphism in the aptitude to various clinical JIA phenotypes.
Methods: The study included 132 children, of whom 66 were diagnosed with JIA and 66 were healthy unrelated volunteers (the college students) as a control group, comparable by gender and age. The group of patients with JIA consisted of 44 girls and 22 boys, with an average age of 11.7 ± 4.2 years and an average disease duration of 4.8 ± 3.8 years. The diagnosis and classification of JIA was established according to ILAR-2004 criteria. The JIA group included 30 (45%) patients with oligoarthritis (oJIA), of which 20 patients (67%) were positive for the HLA-B27 antigen (JIA-B27 +) and 10 (33%) patients with anterior uveitis (uJIA); 20 (30%) patients were assigned to the group with the polyarticular variant (pJIA), while all of them were seronegative for the rheumatoid factor; 16 (24%) patients were diagnosed with JIA with a systemic onset (sJIA). The frequencies of the T / C polymorphism of the SAA1 gene were assessed using an allele-specific polymerase chain reaction in a real time mode (RT-PCR).
Results: In the group of patients diagnosed with oJIA and (JIA-B27 +), the frequency of the C allele was significantly higher compared to the control (53.3% and 57.5% versus 37.1%, p = 0.035 and 0.022, respectively). No significant differences were detected in the frequencies of the mutant C allele between sJIA and pJIA and the control group. The logistics analysis of the frequency distribution of the alleles of the SAA1 gene demonstrated an increased risk of the C allele in formation of an aptitude to the oJIA variant (OR 1.94, 95% CI 1.00-3.76, p = 0.035). In the oJIA-B27 (+) group, the risk of an aptitude was also increased compared to the control (OR 2.29, 95% CI 1.05-5.04, p = 0.022).
Conclusion: The data obtained confirm for the first time the involvement of the rs12218 polymorphism of the SAA1 gene in an aptitude to the oligoarthritis JIA clinical phenotype. The presented results require further replication researches using an enlarged number of patients from different population groups.
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AB0020 CORRELATION BETWEEN SERUM AND SYNOVIAL CONCENTRATION OF IL-17A AND MIRNA EXPRESSION IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Interleukin 17 (IL-17) is a proinflammatory cytokine, which overproduction promotes the autoimmune reaction in rheumatoid arthritis (RA). Posttranscriptional regulation of IL-17 by specific microRNAs (miRNAs) is of great interest in the recent years. 146a was associated with IL-17 expression in IL-17 producing T-cells in the synovium when miR-155 enhanced Treg and Th17 cells differentiation and IL-17A production by directly targeting the suppressor of cytokine signaling (SOCS) 1 [1, 2]. It has been shown that IL-17 production in lymphocytes or its function could be regulated by miR-223 by targeting Roquin ubiquitin ligase or its receptors [3].
Objectives: To examine a possible correlation between systemic and local concentrations of IL-17A and systemic and local miR-146a, miR-155 and miR-223 expression in RA patients.
Methods: Expression levels of three miRNAs were determined in matched peripheral blood (PB) and synovial fluid (SF) samples of RA patients by relative quantitation method $2^{-\Delta\Delta Ct}$. As reference control for normalization RNU6B gene was used. Concentrations of IL-17A were compared between matched serum and SF samples from 20 RA patients by Human IL-17A ELISA kit (Gene probe, Diaclone, France). Healthy donors were used as controls.
Results: miR-146a, miR-155 and miR-223 showed overexpression in RA SF when compared to HCs SF (in 70.83%, p=0.007; in 79.17%, $p=1.63x10^{-4}$ and in 79.17%, $p=1.64x10^{-3}$, respectively). The ROC curve analysis showed diagnostic accuracy for miR-146a in SF with AUC=0.769, p=0.006, AUC for SF miR-155 was 0.858, $p=2.3x10^{-4}$ and AUC for SF miR-223 was 0.841 $p=4.6x10^{-4}$. SF levels of miR-146a and miR-155 were overexpressed in 52.17% and in 76.09% of the RA patients compared to its systemic levels. SF miR-223 was underexpressed in 58.7% of the patients compared to its systemic levels. Levels of IL-17A were higher in RA SF compared to serum (8.645 pg/ml versus 0.315 pg/ml, p=0.012). ROC curve analysis for SF IL-17A showed area under the curve (AUC) = 0.885, p<0.000.
Conclusion: The difference between the systemic and local concentration of IL-17A and miRNAs expression shows that the inflammatory disease process leads to their altered expression with a possible role of these molecules in the disease pathogenesis. The higher local levels of miR-155, miR-146 and IL-17A confirm the data about the possible role of these miRNAs in regulating IL-17A production. The opposite changes of IL-17A and miR-223 systemic and local levels confirm the data about the possible role of miR-223 in regulating IL-17 function. Further analysis with larger sets is needed to confirm these results.
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AB0021 VARIABILITY OF THE RS333 IN LUPUS ERYTHEMATOSUS PATIENTS FROM THE POLISH POPULATION

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Background: There are several subtypes of *Lupus Erythematosus* (LE), which may be limited to the skin (eg. *Discoid Lupus Erythematosus*, DLE) or involve multiple organ dysfunctions (*Systemic Lupus Erythematosus*, SLE). LE is an autoimmune disease that is influenced by genetic and environmental factors. Despite some genetic changes between DLE and SLE were previously shown, the complete genetic background of DLE is still unresolved [1]. Functional C-C chemokine receptor 5 (CCR5) receptor can be associated with the inflammation in LE patients. Importantly, the 32 base pairs (bp) deletion in *CCR5* gene (rs333) leads to a nonfunctional receptor. Previous studies have shown that this mutation may have a protective effect on the development and progression of SLE [2, 3]. Thus it was important to investigate whether 32 bp deletion in rs333 is also associated with DLE development.
Objectives: The aim of this study was to investigate the variability of the *CCR5* gene, within a polymorphic *locus* rs333 in SLE and DLE patients from the Polish population.
Methods: 120 LE patients (77 SLE patients and 43 DLE patients) and 100 healthy persons were recruited to the study from the Polish population. DNA was isolated from blood or buccal swabs. rs333 was genotyped by using polymerase chain reaction (PCR). Statistical significance of the differences between patient and control groups in both allele and genotype frequencies were calculated using Chi-Squared test with Yates correction or two tailed Fisher's exact test.
Results: Deletion allele of the rs333 was significantly less frequent among DLE patients than healthy persons (p = 0.0171). Also the heterozygotes occur significantly less frequent within DLE patients group than in healthy individuals (p = 0.0375). Moreover, homozygotes without deletion in rs333 were found significantly more frequent in persons diagnosed with DLE than in healthy volunteers (p = 0.0214). In contrast, the differences in allele or genotype frequencies between SLE patients and healthy controls were not statistically significant (p > 0.05). Moreover, the rs333 variability was not associated with clinical symptoms of LE patients (p > 0.05).
Conclusion: Summarizing, the results obtained in this study suggest that the 32 bp deletion within rs333 could be a protective factor, that reduce the risk for DLE but not SLE development in the Polish population. However, due to the low statistical power of the obtained results, further studies on larger groups of patients and controls are needed to acquire more reliable data.
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AB0022 INTERRELATIONS OF INCREASED AXIAL SPONDYLOARTHRITIS ACTIVITY AND THE SERUM CONCENTRATION OF IMMUNOGLOBULIN A TO CD74 WITH GENETIC POLYMORPHISMS OF INTERLEUKIN 17 ALLELES

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Background: Genetic predisposition takes one of the main parts at pathogenesis of axial spondyloarthritis (axSpA). Currently, HLA-B27 is a single genetic marker that used in classification criteria of axSpA. However, the presence of HLA-B27 does not affect the activity of the disease. An alternative biomarker of axSpA activity could be an immunoglobulin (Ig) A antibody to an invariant chain peptide associated with class II human leukocyte antigen (HLA) (anti-CD74).

Objectives: The goal is to determine genetic polymorphisms of IL17 alleles prevalence in patients (pts) with axSpA and their interrelations with the disease activity and concentration of IgA to CD74.

Methods: In 48 patients with a reliable diagnosis of axSpA, aged 18 to 69 years ASDAS, BASDAI, BASFI were calculated. The polymorphisms of alleles of interleukin (IL)-17A197 a/g, IL-17F7 histidine (His)/arginine (Arg), IL-17F11139 c/g, HLA-B27 were evaluated. Serum concentration of IgA to CD74 was measured (the normal reference interval according to the instructions for the laboratory kit for serum IgA to CD74 is 0-12.0 U/L).

Results: The mean age of pts was 45.1±14.2 years, male 72.9%, BASDAI 2.99±0.28, ASDAS 2.29±0.16 (Cronbach's alpha for the scales – 0.830), IgA to CD74 16.9±11.0 mg/L. The most often found polymorphisms of interleukin-17 alleles demonstrated in **table 1**.

Table 1. Interleukin-17 alleles' polymorphisms in patients with axial spondyloarthritis, n=48

Indicator	Pts with presence of polymorphism, n	Indicator	Pts with presence of polymorphism, n
IL-17A-197 AA	14	IL-17F7 his/his	45
IL-17A-197 GG	18	IL-17F7 his/arg	2
IL-17A-197 GG	16	IL-17F7 arg/arg	1
IL-17F-11139 CG	26	IL-17F-11139 CC	22

Exceeded levels of IgA to CD74 were identified at 96 pts (70.1%). The factor analysis showed a relationship between ASDAS (R=0.857), BASDAI (R=0.842), BASFI (R=0.857) and level of IgA to CD74 (R=0.667**), (table 2).**

Table 2. Interrelations between serum concentration of IgA to CD74, the activity indices and genetic polymorphisms of interleukin-17 alleles in axSpA patients (factor loads), n=48

Indicator	Factor loading (R)		
Factor	Factor 1	Factor	Factor 1
IgA anti-CD74	0.525	0.925	0.667
BASDAI	0.734	0.816	0.842
ASDAS	0.657	0.576	0.857
BASFI	0.545		0.820
IL-17 F7 His/His	-0.421		
IL-17F7 His/Arg	0.631	0.544	

An increase in the factor load indices for IgA to CD74 (R=0.925) was established, provided that the IL-17F genotype is homozygous for the his / arg allele (R=0.544). The genotypes IL-17F his/his showed an inverse interrelation with the increase in serum IgA to CD74 level (R=-0.421).

Conclusion: Serum concentration of IgA to CD74 exceeded normal reference level in axSpA patients in 70.1% of cases that was associated with ASDAS and BASDAI levels. Presence of heterozygote IL-17F polymorphism in his/arg allele was associated with increasing serum concentration of IgA to CD74 and with increased disease activity (ASDAS and BASDAI). Decreasing of serum IgA to CD74 concentration, less axSpA activity (ASDAS and BASDAI) were found in patients with presence of heterozygote IL-17F polymorphism in his/his allele.

Disclosure of Interests: Elizaveta Vasilenko: None declared, Maxim Korolev: None declared, Sergey Lapin: None declared, Irina Kholopova: None declared, Anna Dadalova: None declared, V Mazurov: None declared, Inna Gaydukova Grant/research support from: JSC BIOCAD, Speakers bureau: Pfizer, Novartis, AbbVie, JSC BIOCAD, Celgene, MSD, Sanofi

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AB0023 ASSOCIATION OF NCF2, NCF4 AND CYBA GENES POLYMORPHISMS WITH RHEUMATOID ARTHRITIS IN A CHINESE POPULATION

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Background: Recent studies have focused on the special roles of NADPH-oxidase, which is composed of gp91phox, p22phox, p47phox, p67phox, p40phox encoded by *CYBB*, *CYBA*, *NCF1*, *NCF2*, *NCF4* genes, in multiple autoimmune diseases. Nevertheless, the association of genetic variation in NADPH-oxidase genes with rheumatoid arthritis (RA) was not extensively studied in Chinese population.

Objectives: We performed this study to examine the association of *NCF2*, *NCF4*, *CYBA* genes polymorphisms with RA susceptibility in a Chinese population.

Methods: Six single nucleotide polymorphisms (SNPs) (*NCF2* rs10911363, *NCF4* rs1883112, rs4821544, rs729749, *CYBA* rs3794624, rs4673) were genotyped in a cohort composed of 593 RA patients and 596 normal controls. All patients were consecutively enrolled from the Department of Rheumatology at the First Affiliated Hospital of University of Science and Technology of China and the First Affiliated Hospital of Anhui Medical University, and the normal controls was enrolled from the same region. Improved multiple ligase detection reaction (iMLDR) was used for genotyping. Chi-square (χ^2) test was used to analyze the association of the genotype and allele frequencies of above SNPs and RA. Odds ratios (*OR*) and 95% confidence interval (*CI*) were also evaluated using Logistic regression analyses, and haplotype analysis was assessed using SHEsis software.

Results: There were 101 males and 492 females in RA group with a mean age of 51.59±6.68 years, and the normal control group included 97 males and 499 females with an average age of 52.32±12.63 years. We observed that *NCF4* rs4821544 CT genotype, C allele frequencies in RA patients were significantly decreased when compared to controls (CT vs. TT: $P = 0.043$; C vs. T: $P = 0.031$), and rs4821544 polymorphism was significantly associated with an increased RA risk under the dominant model (TT vs. CT+CC: $P = 0.031$). Moreover, our results also indicated that rs729749 CT genotype frequency was significantly lower in RA patients than that in controls (CT vs. CC: $P = 0.033$). No significant association between *NCF2*, *CYBA* genes polymorphisms and RA susceptibility was observed. There were no significant differences in allele, genotype frequencies of above SNPs between RA patients with RF-positive and with RF-negative, as well as anti-CCP-positive RA patients and anti-CCP-negative RA patients.

Conclusion: In summary, *NCF4* rs4821544, rs729749 polymorphisms might contribute to RA susceptibility, while *NCF2*, *CYBA* genes polymorphisms were not associated with RA susceptibility.

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Table 1. Genotype and allele frequencies of *NCF2, NCF4, CYBA* genes polymorphisms in RA patients and controls [n(%)]

SNP	Analyze model		RA (N = 593)	Control (N = 596)	*P value*
NCF2					
rs10911363	Genetypes	GG	125	144	0.371
		GT	304	289	0.747
		TT	164	163	
	Alleles	G	554	577	0.408
		T	632	615	
NCF4					
rs1883112	Genetypes	GG	57	56	0.972
		GA	248	255	0.754
		AA	288	285	
	Alleles	G	362	367	0.888
		A	824	825	
rs4821544	Genetypes	CC	4	7	0.323
		CT	117	146	0.043
		TT	472	443	
	Alleles	C	125	160	0.031
		T	1061	1032	
	Dominant model	TT	472	443	0.031
		CT+CC	121	153	
rs729749	Genetypes	TT	104	102	0.445
		CT	266	302	0.033
		CC	223	192	
	Alleles	T	474	506	0.219
		C	712	686	
CYBA					
rs3794624	Genetypes	AA	14	15	0.929
		GA	160	147	0.368
		GG	419	43	
	Alleles	A	188	177	0.498
		G	998	1015	
rs4673	Genetypes	AA	1	5	0.140
		GA	85	90	0.673
		GG	507	501	
	Alleles	A	87	100	0.34
		G	1099	1092	

Acknowledgments: no
Disclosure of Interests: None declared
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AB0024

ASSOCIATION OF IL6 RS1800795 BUT NOT IL6R RS2228145, RS4845618 AND STAT4 RS7574865 POLYMORPHISMS WITH CHLAMYDIA-ASSOCIATED RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA), associated with Chlamydial Infection, has some clinical and immunological particulars that interfere with the early diagnosis and require significant changes in treatment strategy [1].
Objectives: To estimate the distribution of some non-HLA genetic markers such as STAT4 rs7574865, IL6 rs1800795, IL6R rs2228145 and rs4845618 in Chlamydia positive and negative RA patients and healthy controls.
Methods: We examined 380 healthy blood donors and 187 RA patients classified according to the ACR/EULAR 2010 criteria for RA [2]. Twenty-three of the RA patients were positive for Chlamidia trachomatis (n=17) or Chlamidia pneumonia (n=6) persistence. DNA from peripheral blood samples was extracted by phenol-chloroform method. SNPs were genotyped by the real-time PCR with fluorescent probes. Statistical significance of SNPs' frequency was estimated by two-way Fisher exact test (F, $p_{2\text{-}t}$) with Bonferroni correction for multiple comparisons (p_{cor}). Moreover, diagnostic odds ratio (dOR), the likelihood ratio of positive (LR^+) and negative (LR^-) tests and corresponding confidence intervals (CI) were calculated.
Results: We revealed statistically significant increase of genotype CC frequency (IL6 rs1800795) in Chlamydia-associated RA (60.9%) vs healthy donors (20.7%): $p_{2\text{-}t}$=0.000065; p_{cor}=0.00026; dOR=5.95 ($CI_{95\%}$ 2.53-13.94); LR^+=2.94 ($CI_{95\%}$ 1.90-3.29); LR^-=0.49 ($CI_{95\%}$ 0.28-0.75) as well as in Chlamydia-associated RA (60.9%) vs Chlamydia-negative RA (23.9%): $p_{2\text{-}t}$=0.00051; p_{cor}=0.002; dOR=4.99 ($CI_{95\%}$ 2.04-12.16); LR^+=2.56 ($CI_{95\%}$ 1.60-3.57); LR^-=0.51 ($CI_{95\%}$ 0.29-0.78). Significant differences in STAT4 rs7574865, IL6R rs2228145 and IL6R rs4845618 distribution between studied groups were not found.
Conclusion: Our data suggest the association between CC genotype of IL6 rs1800795 and Chlamydia-associated RA.
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Disclosure of Interests: Tatiana Zybalova: None declared, Viktor Yagur: None declared, Roza Goncharova: None declared, Nikolaj Soroka Grant/research support from: JSC BIOCAD, Natalia Dostanko: None declared, Valery Apanasovich: None declared, Anastasiya Tushina: None declared
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Adaptive immunity (T cells and B cells) in rheumatic diseases

AB0025

B-CELL SUBSETS AS ADDITIONAL DIAGNOSTIC TOOL FOR PRIMARY SJOGREN'S SYNDROME AND SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) and primary Sjögren's syndrome (pSS) are chronic complex disorders with an autoimmune background, multifactorial etiology, multiple circulating antinuclear antibodies and damage of various organs. SLE and pSS have several similar clinical and serological aspects; likewise, SLE and Sjögren's syndrome may coexist (so-called secondary Sjögren's syndrome). However, applied classification criteria do not differentiate SLE and pSS. It is known that humoral immunity plays significant part in pathogenesis of those diseases; hereby, we can expect imbalances in B cell subset frequencies during SLE and pSS.
Objectives: To investigate clinical utility of B cell subsets in distinguish SLE and pSS during diagnosis.
Methods: A total of 25 SLE patients, 25 SS patients and 49 healthy volunteers (HV) were included in the study. The diagnosis of SLE was performed according to the 2019 EULAR – ACR classification criteria, the diagnosis of pSS - according to the 2016 EULAR – ACR criteria. Phenotyping of blood B cell subsets was done using flow cytometry. Total peripheral blood B cells were identified using CD19 expression, distinct B cell subsets were characterized by IgD, CD38 and CD27 expression. All of the statistical analysis of data was performed with STATISTICA Version 12.0 Inc. (USA).
Results: We evaluated the percentages of circulating B-cell subsets using three major classification schemes based on the relative co-expression of either IgD/CD38 (so-called "Bm1-Bm5" classification), IgD/CD27 and CD38/CD27. A discriminant analysis was performed for all B cell classifications. Analysis of CD38 and CD27 co-expression demonstrated most significant separation between patients with SLE and pSS (fig. 1). Moreover, discriminant analysis carried out by using a forward stepwise model demonstrated that the top significance was documented while assessing the percentage of plasmoblasts (CD27hiCD38hi), resting memory B-cells (CD27dimCD38low), mature active B-cells (CD27dimCD38dim), naive mature B-cells (CD27dimCD38low), as well as counting the absolute numbers of transitional B-cells (CD27lowCD38hi), model percent correct was 78,6% (p <0,05, tab.1).

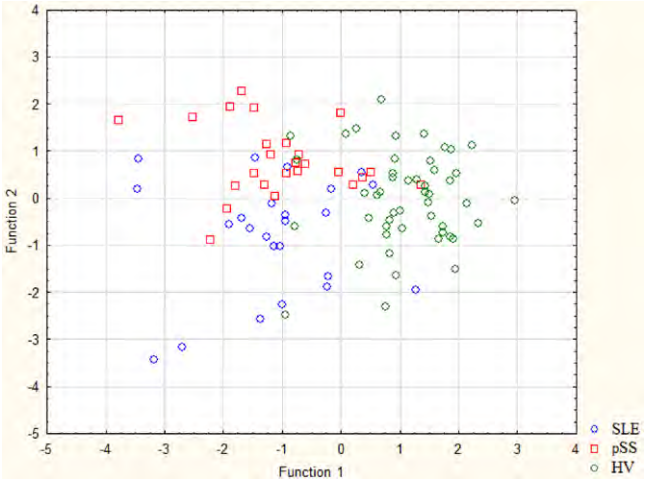


Figure 1. Graphic distribution of SLE and pSS patients as well as HV analyzed by discriminant analysis.

Conclusion: B cell subsets might provide a useful diagnostic tool for distinction SLE and pSS. More research needed to investigate clinical value of B-cell subsets in autoimmune rheumatic diseases.

Table 1. Peripheral B-cell subset composition in SLE and SS patients vs. HV group assessed by discriminant analysis.

Parameter	F-test	p-level
Plasmoblasts (CD27hiCD38hi), %	7,93	<0.001
Resting memory B-cells (CD27dimCD38low), %	13,72	<0.001
Transitional B-cells (CD27lowCD38hi)	29,74	<0.001
Mature active B-cells (CD27dimCD38dim), %	5,20	<0.001
Naive mature B-cells (CD27dimCD38low), %	3,10	0.049
Double negative (CD27lowCD38low), %	1,98	0,14
Resting memory B-cells (CD27dimCD38low)	1,02	0,36
Double negative (CD27lowCD38low)	2,32	0,10
Plasmoblasts (CD27hiCD38hi)	1,02	0,36
Naive mature B-cells (CD27dimCD38low)	1,03	0,36
Mature active B-cells (CD27dimCD38dim)	1,02	0,36
Transitional B-cells (CD27lowCD38hi), %	1,03	0,36

Disclosure of Interests: None declared

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AB0026 SELECTIVE INHIBITION OF TYROSINE KINASE 2 WITH AN ORAL AGENT, BMS-986165, COMPARED WITH JANUS KINASE INHIBITORS

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Background: BMS-986165 is an oral, selective inhibitor of tyrosine kinase 2 (TYK2) with a unique mode of binding to the pseudokinase domain of the enzyme rather than the active site within the kinase domain. This unique mode of binding provides high functional selectivity for TYK2 versus other tyrosine kinases (TYKs) in cellular and other in vitro assays.[1] This approach may provide robust efficacy with a differentiated safety profile due to decreased off-target activity on other kinases. In a 12-week, placebo-controlled Phase 2 trial in patients with moderate to severe plaque psoriasis,[2] BMS-986165 had a favorable safety profile, and 67%–75% of patients achieved Psoriasis Area and Severity Index 75 (PASI 75) after 12 weeks at doses ≥3 mg twice daily versus 7% with placebo. BMS-986165 is currently under investigation in multiple autoimmune disorders such as psoriatic arthritis, psoriasis, and systemic lupus erythematosus.

Objectives: To understand the selectivity of BMS-986165 compared with JAK inhibitors, such as tofacitinib (Tofa), upadacitinib (Upa), and baricitinib (Bari), at clinically relevant doses and plasma concentrations.

Methods: In vitro whole blood assays were developed to measure the activity of common pairings of JAKs (JAK 1/3, JAK2/2, and TYK2/JAK2) and concentrations providing half-maximal inhibition (IC_{50}) for BMS-986165, Tofa, Upa, and Bari were determined. The whole blood IC_{50} values were plotted against pharmacokinetic profiles of these agents at approved doses and/or doses evaluated in their respective Phase 2/3 trials. The time that concentrations were >IC_{50} and projected average daily inhibition were evaluated.

Results: At clinically relevant doses and exposures, BMS-986165 plasma concentrations were higher than the TYK2 whole blood IC_{50} value for a considerable part of the dosing interval. Additionally, the maximal plasma concentration (C_{max}) of BMS-986165 was approximately >9- to 18-fold lower than the JAK 1/3 whole blood IC_{50} value and >52- to >109-fold lower than JAK2/2 whole blood IC_{50}, indicating lack of meaningful inhibition of the JAK 1-3 pathways by BMS-986165 at therapeutic doses. At clinically relevant doses, projected C_{max} values of Tofa, Upa, and Bari were many-fold lower than TYK2 IC_{50}, indicating minimal or no meaningful inhibition of the TYK2 pathway. As expected, Tofa, Upa, and Bari had varying degrees of inhibition against JAK1/3 (daily average inhibition range: 70%–94%) and JAK2/2 pathways (daily average inhibition range: 24%–67%) at clinically relevant doses and exposures.

Conclusion: These results demonstrate the high TYK2 functional selectivity of BMS-986165 at clinically relevant doses and plasma concentrations compared with Tofa, Upa, and Bari and indicate that BMS-986165 is in a different class compared with JAK 1–3 inhibitors. Ongoing studies in psoriasis and other conditions may confirm the expected safety of BMS-986165 based on the above results. The daily average inhibition of JAK1 and JAK2 likely explains some common laboratory observations and adverse events reported for the JAK1–3 inhibitors.

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Disclosure of Interests: Anjaneya Chimalakonda Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, James Burke Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Lihong Cheng Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Joann Strnad Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Ian Catlett Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Aditya Patel Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Jun Shen Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Ihab Girgis Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Subhashis Banerjee Shareholder of: AbbVie, Bristol-Myers Squibb, Lily, Pfizer, Employee of: Bristol-Myers Squibb (current); AbbVie, Lily, Pfizer (past), John Throup Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb

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AB0027 B CELL SYNOVITIS IN RELATION TO DIAGNOSIS AND CLINICAL PHENOTYPE: COMPARISON BETWEEN RHEUMATOID AND PSORIATIC ARTHRITIS

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Background: Rheumatoid arthritis (RA) and psoriatic arthritis (PsA) are both characterized by significant heterogeneity in terms of clinical presentation and outcomes. Furthermore, RA and PsA may share some overlapping features such as autoantibody-negativity, polyarticular involvement, response to certain therapies and pattern of joint damage. The pathobiological bases underlying the intra-disease heterogeneity and the inter-disease similiarities between RA and PsA are however unkown.

Objectives: Aim of the current study was to investigate the relationship between the synovial immune phenotype and different clinical subsets in patients with RA and PsA.

Methods: The study population included 96 patients undergoing ultrasound-guided synovial biopsy of the knee and serum sampling on the same day. Patients were recruited according to defined clinical subtypes: anti-citrullinated positive (ACPA) RA (n=26), ACPA-negative RA (n=32), polyarticular (≥5 involved joints) PsA (n=15), and oligoarticular PsA (n=23). Patients were compared for: (i) demographic and clinical features; (ii) synovial histopathological characteristics including CD68-positive infiltrating macrophages, CD3-positive T lymphocytes, CD20-positive B lymphocytes (semi-quantitative scores 0-3); (iii) serum levels of the lymphoid chemokine CXCL13 as a marker of germinal centre activity.

Results: Collectively, ACPA-positive RA patients, ACPA-negative RA patients and patients with polyarticular PsA presented comparable demographic and clinical features including gender distribution, age, number of involved joints and levels of acute phase reactants. Patients with oligoarticular PsA were instead younger, more frequently males, and with lower levels of acute phase reactants. The degree of macrophage and T cell infiltration correlated with the erythrocyte sedimentation rate (rho 0.38, p=0.001 and rho 0.24, p=0.04 respectively) and C-reactive protein levels (rho 0.38, p=0.001 and rho 0.28, p=0.01 respectively) irrespective of diagnosis, and was significantly lower in oligoarticular PsA (**Figure 1 A**, **B**). In contrast, the degree of B cell infiltration showed significant differences in relation to the disease subtype: the lowest levels were found in oligoarticular PsA, the highest levels in ACPA-positive RA, whilst ACPA-negative RA and polyarticular PsA presented with intermediate and comparable levels between the two extremes (**Figure 1 C**). Serum levels of CXCL13 correlated with the synovial B cell score (rho 0.30, p=0.03) and, similarly to synovial B cell infiltration, were differentially increased according to the clinical phenotype, with again similarities between ACPA-negative RA and polyarticular PsA (**Figure 1 D**).

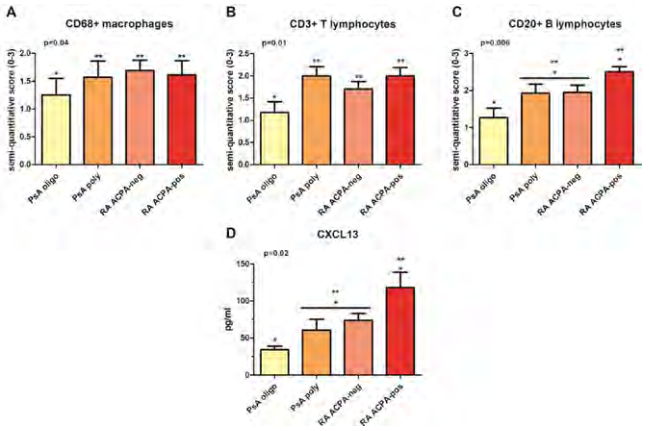


Figure 1.

Conclusion: In patients with chronic inflammatory arthritis, synovial B cell infiltration and systemic markers of germinal centre activity are heterogeneously increased irrespective of disease diagnosis. ACPA-positive RA and oligoarticular PsA appear located at the extremes of a pathobiological continuum, whilst ACPA-negative RA and polyarticular PsA present with intermediate and comparable degrees of B cell involvement. Collectively, our findings open the interesting perspective of a tailored management of patients with inflammatory arthritis based on the disease pathotype rather than on clinical diagnosis.

Disclosure of Interests: Ludovico De Stefano: None declared, Serena Bugatti Speakers bureau: Bristol-Myers Squibb, Sanofi, Lilly, Novartis, Pfizer, Abbvie, Silvia Rossi: None declared, Carlomaurizio Montecucco: None declared, Antonio Manzo Speakers bureau: Bristol-Myers Squibb, Abbvie, Pfizer

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AB0028 IMBALANCES OF TH17/TREG IN CARDIOVASCULAR EVENTS OF PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Ankylosing spondylitis (AS) is a common inflammatory joint disease affecting articulations of axial skeleton and asymmetrical peripheral arthrosis. It has been highlighted that patients with AS exhibit an increased risk of cardiovascular diseases (CVD) compared to the general population [1]. However, little is known about the relationship between cardiovascular burden in AS patients and Th17/Treg imbalance.

Objectives: We aimed to investigated the relationship between cardiovascular events in AS patients and the status of T cell subsets. Furthermore, we want to identify other clinical and/or laboratory features which are associated with the cardiovascular risk in AS patients.

Methods: The study included 32 AS patients with cardiovascular diseases and 32 age-matched AS patients as controls. All the AS patients were hospitalised at the Second Hospital of Shanxi Medical University and met the diagnostic criteria for AS revised in New York in 1984. We collected demographics, laboratory features [erythrocyte sedimentation rate (ESR), c-reactive protein (CRP), DD (D-dimer), PLT (platelet count)], and absolute counts of lymphocyte and CD4+ T cell subset. The absolute numbers of lymphocytes and CD4+ T cells in peripheral blood were measured by Flow Cytometer.

Results: 1. There was statistically significant decrease in Th17 levels (P=0.012) in the AS with CVD group compared to the AS group, while the Treg cells number (P=0.426) and the ratio of Th17/Treg (P=0.202) have no statistically significant differences; 2. DD was significantly increased in AS patients with CVD; 3. The use of NSAIDs between the two groups is significantly different(P=0.013). 86.7% of the AS group have received NSAIDs, while only 58.1% of the AS patients with CVD have received the NSAIDs.

Conclusion: The findings suggested that the cardiovascular events of AS patients correlated with imbalanced T cell subsets and the decreased Th17 cells may be a laboratory feature of AS patients with CVD. Patients with high DD level might have a higher risk of CVD. Monitoring of Th17 cells and DD could be beneficial in cardiovascular burden of patients with AS. However, current studies indicate that Th17 cells mediate the inflammatory response and play a crucial role in the development of CVD [2]. One explanation is that the AS patients with CVD in our study had a long disease duration and immunomodulatory therapy might have an impact on the status of T cell subsets. Meanwhile, the different disease activities of AS patients can be additional factors.

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Table 1. Absolute lymphocyte and CD4+ T cell subset counts (cells/μL) in the AS with CVD group and AS group

Cell count (cells/μL)	AS with CVD	AS	*P*-value
Total T	1447.97±11.49	1442.49±11.49	0.970
Total B	217.06 (144.55- 324.97)	291.27 (171.13-321.16)	0.262
NK	268.09 (171.51-396.99)	277.71 (167.08- 462.45)	0.858
Th1	137.23 (69.8-185.45)	127.04 (76.9-197.26)	0.693
Th2	8.42 (5.56-10.47)	8.03 (5.50-9.95)	0.848
Th17	5.77 (4.00-8.61)	8.89 (5.91-13.88)	0.012*
Treg	29.64 (17.07-47.19)	34.51 (23.26-47.19)	0.426
Th1/Th2	14.99 (10.50-24.21)	17.36 (12.71-25.98)	0.430
Th17/Treg	0.23 (0.12-0.39)	0.31 (0.18-0.52)	0.202

*P<0.05 **p <0.01. Data with a normal distribution and homogeneity of variance are presented as mean±standard deviation. Data without a normal distribution are presented as the median (interquartile range)

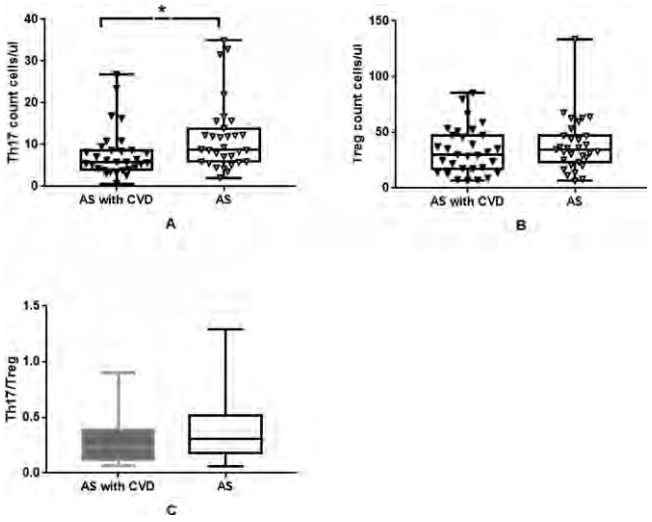


Figure 1. Differences in Treg, Th17 cell counts and Th17/Treg between AS with CVD group and AS group. There was statistically significant decrease in Th17 levels(P=0.012) in the AS with CVD group. * P < 0.05 **P < 0.01. Data were compared using the Wilcoxon's rank sum test.

Disclosure of Interests: None declared

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AB0029 INHIBITION OF EFFECTOR B CELLS BY IBRUTINIB IN SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a connective tissue disease with significant morbidity and mortality. Effective treatment is still missing, and clinical control of the disease remains challenging. In particular, the development of pulmonary and cardiac fibrosis and pulmonary hypertension are severe complications responsible for excessive mortality. Currently available treatment strategies – besides aggressive autologous stem cell transplantation which is an option only for selected patients – only alleviate symptoms and slow disease progression. Previous attempts of immunomodulating therapies addressing B cell pathology like rituximab and tocilizumab in SSc showed mixed efficacy[1,2]

Objectives: Here, we investigated the therapeutic potential of ibrutinib, a Bruton's tyrosine kinase (BTK) inhibitor used in B cell malignancies, to alter B cell pathology in SSc in an *in vitro* model of autoimmunity.
Methods: PBMCs and sorted B cells of 24 patients with SSc were used for functional testing after stimulation with hypomethylated DNA fragments (CpG) to induce an innate immune response. The effects of ibrutinib on cytokine production, autoantibody release and activation of the transcription factor NFκB were evaluated via multiplex cytokine assay, ELISA and flow cytometry.
Results: Ibrutinib was able to reduce the production of the profibrotic hallmark cytokines IL-6 and TNF-α, which are mainly released by the effector B cell population, in response to TLR9-stimulation. Importantly, small doses of ibrutinib (0.1 μM) preserved the production of immunoregulatory IL-10 and IFN-γ while effectively inhibiting the cardinal cytokines of hyperactivated profibrotic effector B cells in SSc. Intracellular cytokine staining of IL-6 in B cell subsets further endorsed the potential of ibrutinib to inhibit B cells in a subset-specific manner, reducing IL-6$^+$ naïve B cells significantly but not IL-6$^+$ memory B cells. The subset specificity was abolished when high doses of ibrutinib (10 μM) were applied. In a flow cytometry analysis of phosphorylated NFκB, an important transcription factor in the induction of innate immune responses in B cells, significantly less activation was observed with ibrutinib treatment (0.1 μM). Higher doses of ibrutinib were unable to further reduce the abundance of pNFκB.
Conclusion: Our data could pave the avenue for a clinical application of ibrutinib for patients with SSc as a novel treatment option for the underlying pathogenetic immune imbalance contributing to disease onset and progression.
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Disclosure of Interests: Jakob Einhaus: None declared, Ann-Christin Pecher: None declared, Elisa Asteriti: None declared, Hannes Schmid: None declared, Kathy-Ann Secker: None declared, Silke Duerr-Stoerzer: None declared, Hildegard Keppeler: None declared, Reinhild Klein: None declared, Corina Schneidawind: None declared, Jörg Henes Grant/research support from: Novartis, Roche-Chugai, Consultant of: Novartis, Roche, Celgene, Pfizer, Abbvie, Sanofi, Boehringer-Ingelheim,, Dominik Schneidawind: None declared
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AB0030 INCREASED CIRCULATING CD19+CD24HICD38HI REGULATORY B CELLS ARE BIOMARKERS OF RESPONSE TO METHOTREXATE IN EARLY RHEUMATOID ARTHRITIS

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Background: The protagonism of regulatory B cells seems to vary along the course of the disease in murine models of inflammatory conditions. Decreased numbers of circulating regulatory CD19+CD24hiCD38hi transitional B cells (cTrB) have been described in patients with longstanding RA.
Objectives: To examine the frequency and evolution of cTrB cells in the peripheral blood of early RA (ERA) patients.
Methods: Freshly isolated PBMCs from 48 steroid and DMARD-naïve ERA patients with a disease duration below 24 weeks and 48 healthy controls (HC) were examined by flow cytometry. Cocultures of isolated memory B cells were established with autologous T cells, in the absence or presence of TrB cells.
Results: As compared with HC, ERA patients demonstrated an increased frequency of cTrB cells. cTrBs of ERA and HC displayed an anti-inflammatory cytokine profile and were able to downregulate T cell IFNγ and IL-21 production, together with ACPA secretion in autologous B/T cell cocultures. Basal frequencies of cTrBs above the median value observed in HC were associated with a good EULAR response to MTX at 12 months (RR=2.91; 95% CI, 1.37-6.47). A significant reduction of cTrBs was observed 12 months after initiating MTX, when the cTrB cell frequency was no longer elevated but decreased, and this was independent of the degree of clinical response or the intake of prednisone.
Conclusion: An increased frequency of regulatory cTrB cells is apparent in untreated ERA, and the baseline cTrB cell frequency is associated with the clinical response to MTX at 12 months.
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Disclosure of Interests: Paula Fortea-Gordo Grant/research support from: BMS, Alejandro Villalba: None declared, Laura Nuño: None declared, Maria-Jose Santos-Bornez Grant/research support from: BMS, Diana Peiteado: None declared, Irene Monjo: None declared, Amaya Puig-Kröger: None declared, Paloma Sanchez-Mateos: None declared, Emilio Martín-Mola Grant/research support from: BMS, Roche, Alejandro Balsa Grant/research support from: BMS, Roche, Consultant of: AbbVie, Gilead, Lilly, Pfizer, UCB, Sanofi, Sandoz, Speakers bureau: AbbVie, Lilly, Sanofi, Novartis, Pfizer, UCB, Roche, Nordic, Sandoz, Maria-Eugenia Miranda-Carus Grant/research support from: BMS, Roche
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AB0031 T HELPER 17 CELLS WERE SIGNIFICANTLY DECREASED BY MITOCHONDRIAL ELECTRON TRANSPORT CHAIN COMPLEX INHIBITOR IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Reactive oxygen species (ROS) and T helper 17 (TH17) cells have been known to play an important role in the pathogenesis of rheumatoid arthritis (RA). However, the interrelationship between ROS and TH17 remains unclear in RA
Objectives: To explore whether ROS affect TH17 cells in peripheral blood mononuclear cells (PBMC) of RA patients, we analyzed ROS expressions among T cell subsets following treatment with mitochondrial electron transport chain complex inhibitors.
Methods: Blood samples were collected from 40 RA patients and 10 healthy adult volunteers. RA activity was divided according to clinical parameter DAS28. PBMC cells were obtained from the whole blood using lymphocyte separation medium density gradient centrifugation. Following PBMC was stained with Live/Dead stain dye, cells were incubated with antibodies for CD3, CD4, CD8, and CD25. After fixation and permeabilization, samples were stained with antibodies for FoxP3 and IL-17A. MitoSox were used for mitochondrial specific staining.
Results: The frequency of TH17 cells was increased by 4.83 folds in moderate disease activity group (5.1>DAS28≥3.2) of RA patients compared to healthy control. Moderate RA activity patients also showed higher ratio of TH17/Treg than healthy control (3.57 folds). All RA patients had elevated expression of mitochondrial specific ROS than healthy control. When PBMC cells were treated with 2.5uM of antimycin A (mitochondrial electron transport chain complex III inhibitor) for 16 h, the frequency of TH17 cells was significantly decreased.
Conclusion: The mitochondrial electron transport chain complex III inhibitor markedly downregulated the frequency of TH17 cells in moderate disease activity patients with RA. These findings provide a novel approach to regulate TH17 function in RA through mitochondrial metabolism related ROS production.
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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.3441

AB0032 ABNORMAL STATUSES OF PERIPHERAL CD4+T CELL SUBSETS IN PATIENTS WITH GOUT AND THEIR CHANGES AFTER RECEIVING COMBINED IMMUNOMODULATORY THERAPY

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Background: Gout is a chronic systemic inflammatory disease that results from the deposition of monosodium urate crystals in joints and the associated activation of the innate immune system associated with hyperuricemia[1]. As the pathogenesis of gout is still a matter of speculation and debate, accumulating evidence converges on inflammasome activation and immunological dysregulation[2]. However, the detailed statuses of lymphocyte subsets in patients with gout are unknown and influence of immunomodulatory combination therapies on the lymphocyte subsets remain to be clearly evaluate[3].

Objectives: To evaluate the quantitative statuses of peripheral CD4$^+$T subpopulations in patients with gout and further investigate the effects of immunomodulatory combination therapies on those cells.
Methods: Total 247 patients who met the clinical criteria of gout from the American College of Rheumatology and 206 healthy controls (HCs) were enrolled in this retrospective cross-sectional study. Among those patients, 70 follow-up patients donated their peripheral blood after receiving immunomodulatory drugs (e.g., low-dose interleukin-2, rapamycin, metformin, retinoic acid, etc). The absolute numbers of Th1, Th2, Th17 and Tregs in peripheral CD4$^+$T subsets were detected by flow cytometry combined with standard absolute counting beads.
Results: Compared with HCs, the absolute numbers of Th1 and Th17 were evidently increased in gout patients (P<0.001), while the level of Tregs was significantly decreased (P<0.05) (Figure 1). After immunomodulatory combination treatments, there were dramatical increases in a wide variety of CD4$^+$T subsets such as Th1, Th17 and Tregs (P<0.05). Interestingly, the increased amount of Tregs was much more than that of other Teffs, leading to the decrease ratios of Teffs/Tregs such as Th2/Tregs, restoring immune homeostasis (Figure 2).
Conclusion: This cross-sectional study clarified the abnormal statuses of CD4$^+$T subsets in gout patients, suggesting that CD4+T subsets, especially Tregs, might be relevant and play a crucial role in the pathogenesis of gout, thus providing a potential therapeutic target for gout patients. Immunomodulatory combination therapies effectively increase the number of Tregs and may help for gout patients' symptom remission.

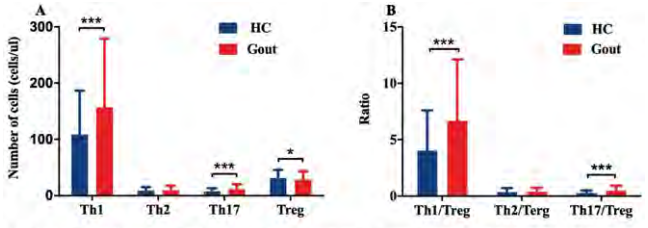


Figure 1: Comparison of absolute counts of peripheral CD4+ lymphocyte subsets between patients with gout (n=247) and healthy controls (n=206). All the CD4+ lymphocyte subpopulations were analyzed by detected by flow cytometry combined with standard absolute counting beads. Data were presented as mean±SD and statistical analysis was determined by two-tailed unpaired t-test. Patients had lower levels of Tregs and Teffs such as Th1 and Th17 compared with those of healthy controls. *P < 0.05, **P < 0.01, ***P < 0.001.

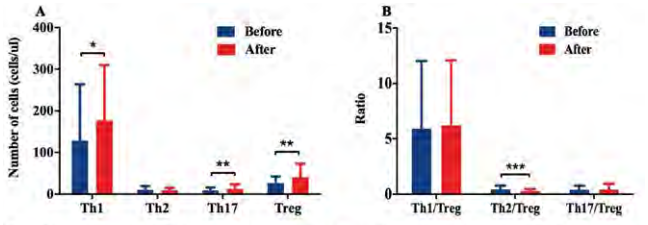


Figure 2: Changes of peripheral CD4+ lymphocyte subpopulations after immunomodulatory combination treatments (n=70). Data were presented as mean±SD and statistical analysis was determined by two-tailed paired t-test. Absolute counts of Tregs and Teffs such as Th1 and Th2 in gout patients were significantly increased after immunomodulatory combination treatments. *P < 0.05, **P < 0.01, ***P < 0.001.

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Disclosure of Interests: None declared
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AB0033 CHARACTERIZATION OF THE PERIPHERAL B CELL COMPARTMENT IN PATIENTS WITH EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS

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Background: Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare form of systemic vasculitis, which is characterized by bronchial asthma, hypereosinophilia, and systemic vasculitis. B-lymphocytes play a key role in EGPA as producers of IgE and anti-neutrophil cytoplasmic antibodies (ANCAs). Indeed, the neutrophils that are targeted by these antibodies are widely described as the mechanism of endothelial damage in this disease. On the other side, the therapeutic response to rituximab in EGPA patients provides evidence for a role of B-cells in the pathogenesis of EGPA. Therefore characterizing B cell subpopulations may help in understanding the disease and the treatment.
Objectives: To characterize the peripheral B cell compartment in patients with EGPA and to analyze the in vivo potential of B lymphocytes to class-switch to IgE and to assess in vitro the differentiation potential of naïve B cells of EGPA patients into IgE-secreting plasmablasts.
Methods: Clinical characteristics of the patients, including organ involvement and treatment regimen were evaluated. Laboratory work-up included ANCA-status, eosinophils, IgE, IgG, IgA, IgM, and peripheral CD19$^+$ B-cell count. For immunophenotyping isolated PBMCs were stained with monoclonal or polyclonal antibodies and B cells were classified into: naïve, marginal zone, class-switched memory B cells, unconventional memory B cells, transitional and plasmablasts. Furthermore, the expression of IgG+ and subclasses IgG1-4, IgA$^+$, IgE$^+$ B cells, BAFFR and TACI was quantified. For in vitro differentiation assays magnetically isolated B lymphocytes from EGPA patients and age-matched healthy controls were stimulated with CD40L, IL-21 and IL-4. Starting the culture with equal number of B cells, the absolute number of plasmablasts, and IgE class switched cells after 9 days was determined by counting the events in the CD27highCD38high gate or the IgG/A/D-IgE$^+$ gate by flow cytometry. IgE secretion in the supernatant was measured by ELISA. JAK-STAT signalling pathway was analyzed in response to IL-4 and IL-21 stimulation and phosphorylation of STAT5 and 6 measured by flow cytometry.
Results: 34 patients with EGPA diagnosed according to ACR and CHC-criteria were included into the study. Ten of these patients were analysed separately because they received rituximab therapy. Peripheral B cell numbers in EGPA patients were markedly diminished. B cell subpopulation phenotyping showed in average 57.9% naïve B cells, 12.5 % marginal zone like B cells and 19.2% switched memory B cells. Plasmablasts constituted in average 1.15% of the peripheral B cell compartment, transitional B cells 2.0%. Interestingly, the expression of BAFF receptor and TACI in the memory B cell subset was significantly decreased in EGPA patients when compared with healthy donors. In vitro assays of isolated B cells from EGPA patients demonstrated an increased proportion of IgE-class-switched B cells after 9 days of culture under IL4 stimulation compared with controls. However, no differences were observed in the phosphorylation of STAT5 and STAT6 after stimulation with IL-4 or IL-21.
Conclusion: In the EGPA-patients we observed markedly diminished B-cells despite of normal lymphocyte counts. B cells showed a reduced expression of BAFF-R and TACI. Class switch to IgE is enhanced in EGPA patients.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.5944

AB0034 EARLY IMMUNIZATION AGAINST TREATMENT IS ASSOCIATED TO POOR CLINICAL RESPONSE AT 6 MONTHS AND LOW NUMBER OF TRANSITIONAL B CELLS AT BASELINE IN RHEUMATOID ARTHRITIS PATIENTS TREATED BY ADALIMUMAB

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Background: Circulating anti-drug antibodies (ADAs) are detectable approximatively in 33% of adalimumab treated rheumatoid arthritis (RA) patients, often within the first 6 months of therapy[1-2]. Classically, circulating ADAs associate with their specific drugs to form immune complexes, increasing drug clearance, and by this mechanism reducing therapeutic effect[3]. B cell involvement leading to ADAs production is not yet well established.

Objectives: To study early ADAs formation according to clinical response to an adalimumab therapy in RA patients and the relationship between ADAs and circulating B cell subsets.
Methods: 28 RA patients and 13 healthy controls were included. Patients all presented inadequately controlled RA under conventional treatment, were naive of biotherapies, and started an adalimumab treatment at baseline (M0). Responder status was determined according to the DAS28CRP score (<or>3.2) at 3 (M3) and 6 months (M6). ADAs plasma concentration >10pg/mL at M3 defined the immunized patient group. Circulating B cell subsets were quantified by flow cytometry at M0 and M3.
Results: 11 (42.3%) patients were immunized at M3. Among them, 4 (36.4%) were responders at M6 and 7 (63.6%) were non-responders. Presence and concentration of ADAs at M3 was associated to non-responder status at M6 (p=0.043; p=0.042). Immunized patients had lower transitional B cells count at M0 compared to non-immunized patients (p=0.031).
Conclusion: A high but classical proportion of RA patients developed ADAs after only 3 months of adalimumab treatment. This immunization was associated to non-responder status at M6 and to a low blood transitional B cells count at baseline. Our results suggest transitional B cells implication in
RA activity and biotherapy resistance due to immunization. Low concentrations of transitional B cells could be an early biomarker of immunization process against adalimumab.
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Table. Patients characteristics at baseline

Characteristics	All RA patients (n=28)	M6 responders (n=16)	M6 non-responders (n=10)
Age (years)	60.5 [47-78]	65.5 [47-76]	54 [47-78]
Sex ratio M/F (% of F)	0.4 (71,4%)	0.5 (68.8%)	0.3 (80.0%)
Disease duration, (years)	5.6 [0.7-43.0]	6.8 [1.0-43.0]	2.9 [0.7-31.0]
Oral steroid use, (%)	18 (64,3%)	9 (56.2%)	8 (80.0%)
Oral steroids, dose (mg/day)	5.0 [2.0-15]	5.0 [4.0-12.5]	8.5 [2.5-15.0]
Methotrexate use, (%)	24 (50.9%)	14 (87.5%)	8 (80.0%)
Methotrexate, dose (mg/week)	20 [10-25]	20 [10-25]	15 [10-20]*
Leflunomide use, (%)	3 (10.7)	1 (6.3%)	2 (20.0%)
Leflunomide, dose (mg/day)	20 [20-20]	20 [20-20]	20 [20-20]
CRP, (mg/dL)	5.5 [1.0-57.0]	6.6 [1.0-46.8]	3.6 [1.0-57.0]
DAS28CRP score	4.3 [3.3-5.7]	4.1 [3.3-5.2]	4.5 [3.4-5.7]
RF positive, (%)	20 (71.4%)	12 (75.0%)	6 (60.0%)
RF, (U/mL)	116 [19-640]	88 [21-640]	181 [19-336]
ACPA positive, (%)	25 (89.3%)	15 (93.8%)	8 (80.0%)
ACPA, (U/mL)	340 [11-340]	340 [14-340]	340 [11-340]

Values are medians with ranges and frequencies with percentages. *p=0.050.

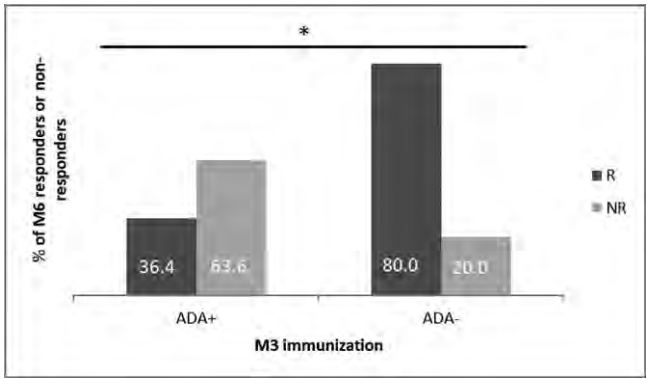


Figure 1. Graph 1 Immunization against treatment at 3 months and clinical response at 6 months in RA patients (n=26). Presence of ADAs at 3 months is associated to non-responder status at 6 months. Fisher exact test.R, responders at 6 months; NR, non-responders at 6 months; ADA+, immunized patients at 3 months; ADA-, non-immunized patients at 3 months.

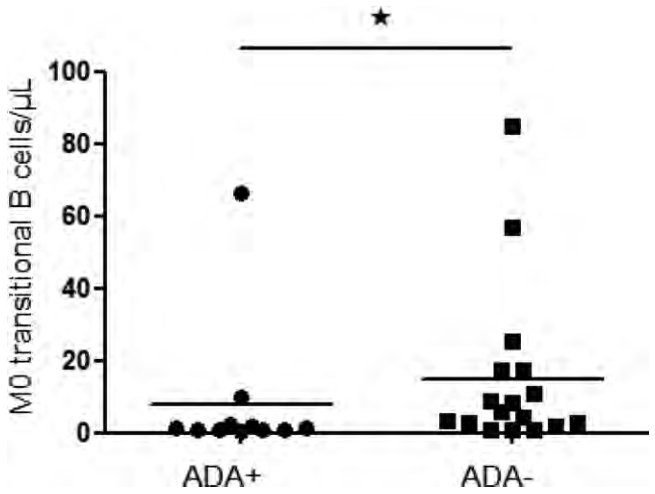


Figure 2. Graph 2 Absolute number of transitional B cells at baseline in RA patients (n=28) according to immunized status at 3 months. Immunized patients at 3 months had lower transitional B cells at baseline than non-immunized patients. ADA+, immunized patients at 3 months; ADA-, non-immunized patients at 3 months. Data represent the mean; *p<0.05 by Mann-Whitney U test.

Disclosure of Interests: None declared
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AB0035 **TWO DIFFERENT ABNORMAL BEHAVIORS IN CD4+T LYMPHOCYTES IN FIBROMYALGIA PATIENTS AND FIBROMYALGIA ASSOCIATED TO SJÖGREN'S SYNDROME**

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Background: Primary fibromyalgia syndrome is a prevalent rheumatic condition characterized by widespread pain and whose etiopathogenesis is not well understood. Fibromyalgia can also be secondary to other rheumatic diseases like Sjogren's syndrome; however, its relation to this disease is unknown. It has been suggested that the immune system is involved in their pathogenesis. The role of activation stages and cytokines profiles of CD4+T lymphocytes in fibromyalgia or fibromyalgia secondary to Sjogren´s syndrome are completely unclear and could play a key role in the pathophysiology of these diseases.
Objectives: The objective of this study is to investigate the counts and distribution of the CD4+T lymphocyte activation subsets and their pattern of cytokine production in women with primary fibromyalgia, fibromyalgia secondary to Sjogren´s, Sjogren´s syndrome and healthy controls (HC). The counts and distribution of naïve (T_N), central memory (T_{CM}), effector memory (T_{EM}) and effector (T_E) CD4+T lymphocyte subsets were analyzed in these diseases. Furthermore, we investigated their pattern of IL-4, IL-10, IL-17A, IFNγ, and TNFα production.
Methods: Counts and distribution of CD4+T subsets (T_N, T_{CM}, T_{EM}, $T_{E)}$ and their cytokine producing capacity were measured using multiparametric flow cytometry in peripheral blood mononuclear cells (PBMC) from 20 primary fibromyalgia, 15 fibromyalgia associated to Sjögren and 15 primary Sjögren patients and 15 female controls. Fibromyalgia and/or Sjögren's syndrome were diagnosed based on ACR criteria. CD4+T cell activation stages were analyzed by the expression of the CD3, CD4, CD45RA, CD27 and CCR7 antigens. Cytokine CD4+T producing cells subsets were assayed stimulating PBMC during 6 hours, fixed, permeabilized and simultaneously stained with IL-4, IL-10, IL-17A, IFNγ, and TNFα intracellular cytokines.
Results: Fibromyalgia patients showed a significant increase in the CD4+T, T_N and T_{CM} cells counts with compared to fibromyalgia secondary to Sjogren, Sjogren´s syndrome and HC. The counts of IL-17A, IL-4 and IFNγ producing

CD4+T cells were increased in fibromyalgia patients with respect to HC. However, only IL17A and IFNγ, but not IL-4 producing CD4+T lymphocytes were increased with respect fibromyalgia secondary to Sjogren. These alterations were due to an increment of T_{EM} IL-17A, T_{CM} and T_{EM} IL-4 and T_N T_{CM} and T_{EM} IFNγ producing CD4+T cell subsets in fibromyalgia patients. Furthermore, IFNγ producing CD4+T cells were decreased in fibromyalgia secondary to Sjogren´s with respect to fibromyalgia patients and HC. Counts of T_N TNFα producing CD4+ T cells were increased in fibromyalgia with respect fibromyalgia secondary to Sjogren. IL-10 producing CD4+T cells were normal in fibromyalgia but decreased in fibromyalgia secondary to Sjogren.

Conclusion: Fibromyalgia patients show an abnormal circulating activation stages of CD4+T cells, as well as, express unusual elevated counts of CD4+T cells producing IL-17A, IL-4 and IFNγ. These alterations could differentiate two different pathologic and inflammatory behaviors of the T cell compartment between fibromyalgia and fibromyalgia secondary to Sjogren patients.

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Disclosure of Interests: None declared

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AB0036 CHILDREN WITH EXTENDED OLIGOARTICULAR AND POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS HAVE A CYTOKINE PATTERN FAVOURING B CELL ACTIVATION IN CIRCULATION

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Background: Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease in children. The majority of polyarticular JIA (pJIA) and a large fraction of extended oligoarticular JIA (oJIA) patients fulfil classification criteria for rheumatoid arthritis (RA) in adulthood. B-cells play several important roles in RA pathogenesis, but it is still unclear if the pattern of B-cell involvement in pJIA and extended oJIA follows what has been described for adults with RA.

Objectives: The main goal of this study was to determine the concentration of cytokines potentially relevant for B-cell activation in serum from children with pJIA and extended oJIA when compared to children with persistent oJIA, adult JIA, early and established RA.

Methods: Serum samples were collected from children with extended oJIA (n=8), persistent oJIA (n=6), pJIA (n=6), adult JIA (n=8), untreated early RA (<1 year of disease duration, n=12), established RA patients treated with synthetic disease-modifying anti-rheumatic drugs (DMARDs) (n=10) and two groups of age- and sex-matched healthy donors (children, n=6 and adults, n=10). A proliferation-inducing ligand (APRIL), B-cell activating factor (BAFF), interleukin (IL)-6 and IL-21 serum levels were measured by enzyme-linked immunosorbent assay (ELISA).

Results: Children with extended oJIA, early and established RA patients had significantly higher BAFF serum levels when compared to controls, but no significant differences were observed in children with persistent oJIA, pJIA and adult JIA when compared to all groups included. APRIL serum levels were significantly increased in early and established RA patients when compared to both controls and children with persistent oJIA. No significant differences were found in APRIL concentrations between children with JIA, adult JIA and controls. IL-6 serum levels were significantly increased in children with extended oJIA, pJIA, early and established RA when compared to controls, but no significant differences were found in children with persistent oJIA and adult JIA patients. IL-21 serum levels were significantly increased in early RA when compared to controls, but no significant differences were observed between any of the other groups included.

Conclusion: The similarity in B-cell cytokine pattern found between extended oJIA, pJIA, early and established RA patients, contrarily to what was observed in persistent oJIA, suggests an early B-cell involvement in the pathogenesis of extended oJIA and pJIA as described for RA.

Disclosure of Interests: None declared

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AB0037 EXPRESSION OF NEGATIVE CHECKPOINT MOLECULES BTLA AND HVEM IS DYSREGULATED IN AUTOIMMUNE DISEASES

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Background: Immune checkpoint blockade with agents targeting CTLA4 and PD-1/PD-L1 alone or in combination has demonstrated exceptional efficacy in multiple cancer types by "unleashing" the cytotoxic action of quiescent, tumor-infiltrating T cells. However, the therapeutic action of these immunotherapies goes hand in hand with the loss of immune tolerance and appearance of immune-related adverse events such as colitis, arthralgia and inflammatory arthritis in responsive patients. Therefore, immune checkpoint molecules have been proposed as targets for the treatment of autoimmune diseases.

Objectives: Herein, we interrogate the potential of BTLA/HVEM axis as a target for restoring immune homeostasis in rheumatoid arthritis (RA), Systemic Lupus Erythematosus (SLE) and Sjogren's Syndrome (SjS) by examining their expression patterns in autoimmune disease tissues.

Methods: Message and protein expression of BTLA and HVEM were examined in RA and SLE synovial tissues, SLE cutaneous lesions, SjS salivary glands and peripheral blood samples of autoimmune disease by RNA sequencing and flow cytometry.

Results: Tissue dysregulation of the BTLA-HVEM axis was observed: Increased BTLA RNA level in RA synovium, SLE-affected skin, and SjS salivary gland samples, whereas HVEM level was affected only in the RA synovium when compared to unaffected tissues. Detailed immunophenotyping of B, T, and myeloid cell populations in RA, SLE, SjS and healthy control PBMCs revealed differential modulation of the BTLA+ or HVEM+ immune cell subsets in a disease-context dependent manner. SjS patients showed an overall decrease in memory B cells and most of the BTLA+ B cell subsets while a decrease in HVEM+ B cells was observed only in SLE PBMC samples and not RA and SLE samples. Immunophenotyping with a T cell panel exhibited decreased BTLA and HVEM expression on T cell subsets in SjS and SLE but not in RA patients. In addition, protein levels of HVEM were differentially decreased in SLE myeloid cell subsets. Finally, we demonstrate tissue-specific surface expression patterns of BTLA in RA and SLE samples: higher surface BTLA levels on RA and SLE PBMC B cells than matched tissue-derived B cells.

Conclusion: Our results demonstrate a dysregulation of the BTLA/HVEM axis in either lesional tissue or peripheral blood in an autoimmune disease context-dependent manner. These results also indicate the potential of targeting BTLA-HVEM axis for the treatment of multiple autoimmune diseases.

Disclosure of Interests: Sunil Nagpal Shareholder of: Janssen Pharmaceuticals, Employee of: Janssen Pharmaceuticals, Suzanne Cole Shareholder of: Janssen Research & Development employee, Employee of: Janssen Research & Development employee, Achilleas Floudas: None declared, Mihir Wechalekar Grant/research support from: Grant from Janssen Research & Development, Qingxuan Song Shareholder of: Employee of Janssen Research, Employee of: Employee of Janssen Research, Tom Gordon: None declared, Roberto Caricchio Grant/research support from: Financial grant from Janssen Research & Development, Douglas Veale: None declared, Ursula Fearon: None declared, Navin Rao Shareholder of: Janssen Pharmaceuticals, Employee of: Janssen Pharmaceuticals, Ling-Yang Hao Shareholder of: Employee of Janssen Research, Employee of: Employee of Janssen Research

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AB0038 IMMUNE PHENOTYPING OF ERDHEIM-CHESTER DISEASE THROUGH MASS CYTOMETRY

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Background: The understanding of Erdheim-Chester Disease (ECD) pathogenesis has been greatly improved these past few years with the discovery of activating MAPK pathway mutations in most of ECD patients. However, the inflammatory phenotype of ECD remains widely unknown.
Objectives: We aimed to explore the inflammatory phenotype of Erdheim-Chester disease (ECD) using mass cytometry.
Methods: We analyzed peripheral blood mononuclear cells from 13 ECD patients and 11 healthy donors (HD) using mass cytometry with 29 metal-conjugated antibodies.
Results: Compared to HD, untreated ECD patients had increased proportion of classical monocytes (90.8 [87.1-96.5] vs 81.6 [76.2-87.5] %, p=0.02) and decreased proportion of non-classical monocytes (4.7 [3.4-9.7] vs 11.8 [6.6-17.2] %, p=0.047). Untreated ECD patients had more circulating Th17 cells compared to HD (3.3 [3-5.3] vs 1.3 [0.4-2.3] %, p=0.015) and ECD patients treated with BRAF or MEK inhibitors (3.3 (3-5.3] vs 1.9 [0.6-2.4] %, p=0.005). Moreover Treg cells were lower in ECD patients than HD, with an increased Th17/Treg ratio (1.37 [0.74-1.9] vs 0.34 [0.19-0.43], p=0.0004). There was no difference regarding Th1 cells, Th2 cells, B cells, NK cells and circulating dendritic cells.
Conclusion: ECD monocyte profile seems similar to what have been described in CMML. Inflammation observed in ECD may be driven through Th17 cells, and might be targeted with specific treatment.
Disclosure of Interests: None declared
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AB0039 ROLE OF MESENCHYMAL STEM CELLS ISOLATED FROM DENTAL PULP (DPSCS) IN IMMUNOREGULATION PROCESSES MEDIATED BY PROGRAMMED DEATH-LIGAND 1 (PD-L1)

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Background: Stem cells isolated from dental pulp (DPSCs) are characterized by a high rate of proliferation, low immunogenicity and a high ability to differentiate in different lineages (i.e. osteogenic, chondrogenic, adipogenic, myogenic and neural commitment). Their multipotency can be attributed to the peculiar embryological origin from the neural crest. DPSCs represent a promising stem cell resource since they hold a low ethical impact and can be easily isolated through routine dental procedures. These cells own immuno-modulatory properties, exerted through the activation of different mechanisms, including the Fas / FasL pathway, as well as through the release of soluble factors. Currently, other molecular mechanisms are under consideration such as PD-1 / PD-L1 (Programmed Death 1 and its Ligand) which are supposed to be involved in the induction and / or maintenance of immune tolerance.
Objectives: The aim of this research was to investigate whether the stimulation of PD-L1 in DPSCs can affect the immunomodulatory effects of these stem cells on peripheral blood mononuclear cells (PBMCs). Furthermore, the expression of PD-L1 was also assayed after the induction of osteogenic differentiation of DPSCs in order to evaluate a possible application of DPSCs in autoimmune inflammatory osteo-erosive diseases.
Methods: Immuno-selection was performed on DPSCs, isolated from waste material, against the stemness markers c-Kit and STRO-1, to obtain a pure stem cell population. Then, STRO-1+/c-Kit+ DPSCs, were co-cultured either directly and indirectly with peripheral blood mononuclear cells (PBMCs) from healthy adult donors, previously activated by anti-CD3 and anti-CD28 antibodies. Co-cultures of PBMCs with amniotic fluid stem cells (AFSCs) and bone marrow mesenchymal stem cells (BM-MSCs) were also set up. The expression of PD-1 in PBMCs as well as of PD-L1 in DPSCs, AFSCs, BM-MSCs and PBMCs, was evaluated by Western Blot (WB) and immunofluorescence (IF) analyses, before and after osteogenic differentiation. Osteogenic differentiation of DPSCs, after 30 days of induction, was verified by IF and WB, of osteopontin, osteocalcin and RUNX2 markers. Interleukin-2 (IL-2) expression levels in PBMCs were analyzed by Real-Time PCR analysis.
Results: Our data highlight that, after direct and indirect co-culture with activated PBMCs, PD-L1 expression was up-regulated not only in DPSCs, but also in BM-MSCs and AFSCs (Figure 1), thus suggesting that 1) this is a common ability of mesenchymal stem cells and 2) this event can be also mediated by soluble factors release. Moreover, when evaluating the effects of DPSCs co-culture on PBMCs an increased expression of cleaved caspase 3 was observed, together with a decreased expression of IL-2 - a growth factor essential for the proliferation and survival of T cells (Figure 2). These findings showed how DPSCs can modulate the immune system by PD-L1 up-regulation. On the other hand, it is noteworthy that, after reaching osteogenic commitment, DPSCs down-regulated the expression of PD-L1, allowing to hypothesize that PD-L1 expression is strictly related to the maintenance of stemness.

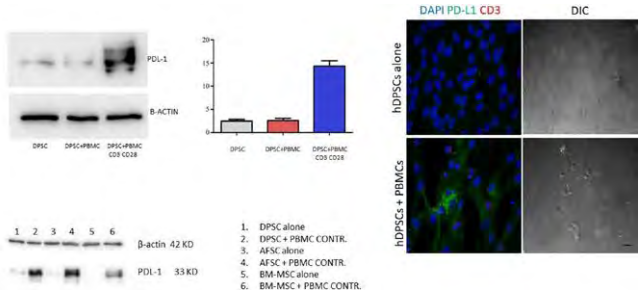


Figure 1.

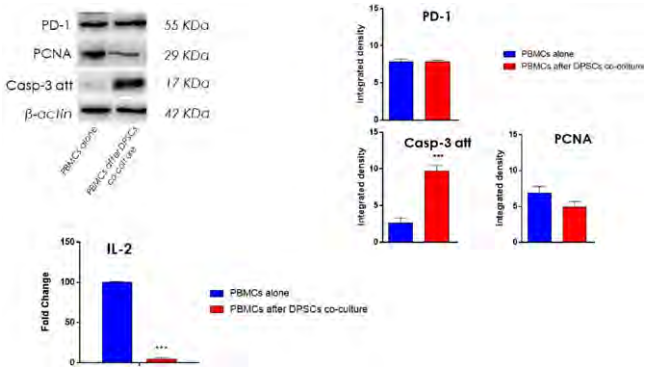


Figure 2.

Conclusion: Taken together, our findings suggest that the expression of PD-L1 in DPSCs is involved in the modulation of immune response and pave the way for further investigations on the role of PD-1/PD-L1 pathway in controlling inflammation and immune response when applied to the treatment of autoimmune inflammatory diseases.
References:
[1] Keir ME, et al. PD-1 and its ligands in tolerance and immunity. Annu Rev Immunol. 2008
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AB0040 IMPAIRED REGULATORY T CELL FUNCTIONS IN PATIENTS WITH PSORIASIS ARTHRITIS ELIGIBLE TO SWITCH TO ANTI-IL-17 TREATMENT

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Background: A dysbalance between Th17 and regulatory T cells (Treg) has been suggested for several T cell-mediated autoimmune disorders. Inhibitors of IL-17 are successfully used for treatment of psoriasis arthritis (PsA). However, so far reconstitution of Treg functions has not been studied in detail in PsA eligible for switching to anti-IL-17 treatment.
Objectives: The project aims to analyze the reconstitution and maintenance of regulatory T cell (Treg) function after inhibition of inflammatory Th17-inducing pathways mediated by IL-1, IL-6, IL-17 and TNFalpha in a longitudinal manner.
Methods: Therefore, Treg derived from 12 PsA patients switching to Th17 inhibition and healthy controls were phenotypically characterized by flow cytometry.

Function was investigated by analysis of suppressive activity of Treg on proliferation of autologous effector T cells in vitro utilizing suppression assays.
Results: First results at the time-point of switching to anti-IL-17 treatment demonstrated PsA to be an IL-17-driven T cell-mediated autoimmune disorder, as proportions of T cells with Th17 phenotype were increased in PsA compared to controls (CCR6+IL-17+4.9% vs. 0.8% of CD4+) and FoxP3+ Treg cells (CD25brightFoxP3+0.2% vs. 0.4% of CD4+) were decreased. Higher proportions of FoxP3+ T cells expressing the Th17-characteristic chemokine receptor CCR6 were found in PsA (4.8% vs. 2.7% of CD4+), as well as higher proportions of pro-apoptotic CD95-expressing FoxP3+ T cells (9.8% vs. 2.8% of CD4+). Less suppression of autologous effector T cells co-cultured with CD25+ Treg cells was found in PsA compared to controls (22.2% vs. 28.3% reduction of proliferative activity), whereas CD25- helper T cells did not contribute to the suppression of effectors in PsA and only minimally in controls. Intracellular IL-10 production in Tregs, a key cytokine of Treg-associated regulation of inflammation, was similar between PsA and controls, although a trend to lower CTLA-4 expression involved in inhibition of co-stimulation was found in PsA.
Conclusion: The current results indicate a skewed T cell balance towards Th17 cells and Treg cells showing Th17-like features in samples of PsA unsuccessfully pre-treated with different biologics recommending them for a switch to a therapy with selective inhibition of IL-17. Longitudinal results regarding the reconstitution and maintenance of Treg function in those PsA patients have to be awaited.
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AB0041 CD8+ T CELLS HAVE AN ELEVATED PROLIFERATIVE CAPACITY IN GIANT CELL ARTERITIS

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Background: Giant cell arteritis (GCA) is the most frequent form of systemic vasculitis affecting the large- and medium-sized vessels. The involvement of innate immune cells and CD4+ T cells in the pathogenesis of GCA has been extensively studied. Interestingly, recent findings suggest a role for CD8+ T cells in disease development (1). However, CD8+ subsets and their functional capacities have not yet been studied in detail.
Objectives: This study aims to characterize the phenotype and proliferative capacity of CD8+ T cells in newly diagnosed GCA patients and GCA patients in remission compared to healthy age- and sex- matched controls.
Methods: To determine the phenotype of CD8+ T cells in GCA, newly diagnosed, untreated GCA patients (baseline, n=14), GCA patients in stable glucocorticoid-free remission (GC-FR, n=10) and age- and sex-matched healthy controls (HCs, n=18) were enrolled. Peripheral blood mononuclear cells (PBMCs) were stained with fluorochrome-conjugated antibodies directed against CD3, CD4, CD8, CCR7, CD45RO, Ki-67, CD69 and CD25 and analyzed by flow cytometry. The following differentiation subsets were defined: CD8+ T naive (CD45RO-CCR7+), central memory (T_{CM}, CD45RO+CCR7+), effector memory (T_{EM}, CD45RO+CCR7-) and effector memory re-expressing CD45RA (T_{EMRA}, CD45RO-CCR7-) cells. Secondly, the proliferative capacity of CD8+ T cells was determined in isolated CD3+ T cells of 10 GCA baseline, 10 GCA GC-FR patients and 19 HCs after 5 days of stimulation with plate-bound anti-CD3 or anti-CD3 plus soluble anti-CD28 using a dye-based proliferation assay.
Results: A reduced frequency of CD8+ T_{EM} cells was found in GCA baseline patients compared to HCs (p=0.025). Furthermore, a higher frequency of Ki-67+ cells was detected among CD8+ T_{EM} cells in GCA baseline patients than in HCs (p=0.0007), suggesting a higher proliferative activity *in vivo.* In addition, *in vitro* stimulation with anti-CD3 and anti-CD3+anti-CD28 led to higher percentages of divided CD8+ T cells in GCA baseline and GC-FR patients than in HCs (p<0.05). Moreover, the frequencies of CD8+ T_{EMRA} cells and the percentage of divided CD8+ T cells upon CD3 stimulation strongly correlated in GCA baseline patients (R=0.79, p=0.009) and GCA GC-FR patients (R=0.67, p=0.039) but not in HCs (R=0.31, p=0.25).
Conclusion: GCA baseline patients demonstrate a higher frequency of proliferating circulating CD8+ T_{EM} cells, defined by Ki-67 expression, than HCs. In addition, functional data on induced proliferative capacity suggest that CD8+ T cells from GCA baseline patients are more rapidly activated by crosslinking CD3 and CD3+CD28, suggesting either reduced regulation in these patients or more intrinsic threshold changes. Furthermore, the induced proliferative capacity is also elevated in patients in stable glucocorticoid-free remission. Whether the increased proliferative capacity of total CD8+ T cells in GCA patients is causally linked to the increased frequencies of CD8+ T_{EMRA} cells in these patients requires further investigation.
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Disclosure of Interests: Rosanne Reitsema: None declared, Rebeca Hid Cadena: None declared, Wayel Abdulahad: None declared, Annemieke Boots Consultant of: Grünenthal Gmbh until 2017, Peter Heeringa: None declared, Elisabeth Brouwer Consultant of: Roche (consultancy fee 2017 and 2018 paid to the UMCG), Speakers bureau: Roche (2017 and 2018 paid to the UMCG)
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AB0042 CYTOKINE NETWORK ELUCIDATED BY THE QUANTIFICATION OF MULTIPLE CYTOKINES IN THE SERUM SEQUENTIALLY SAMPLED FROM RA PATIENTS WHO WERE TREATED WITH BIOLOGIC DMARDS

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Background: Biologic disease modifying anti-rheumatic drugs (DMARDs) have demonstrated that proinflammatory cytokines such as interleukin (IL-) 6 and tumor necrosis factor (TNF) play important roles in the pathogenesis of rheumatoid arthritis (RA). Other cytokines, such as type I interferons (IFNs), are also implicated in its pathogenesis (ref 1). However, the complete picture of the cytokine network involved in RA remains to be elucidated.
Objectives: By quantifying sets of cytokines in the serum of RA patients before and after treatment with various biologic DMARDs, we sought to determine the effects of drugs on (A) type I IFNs, (B) soluble IL-6 receptors, and (C) other cytokines.
Methods: 52 patients with RA were treated with various biologic DMARDs (tocilizumab (TOC): 16, abatacept (ABT): 15, and TNF inhibitors (TNFi): 21). Serum samples were obtained (1) before, (2) approximately 4 weeks after (3) and approximately 12 weeks after the initiation of treatment. A suspension bead-array system was used for analysis; Bio-Plex Human Cytokine 17-plex Assay kits and Express Custom Panels (Bio-Rad), including IFN-β, IFN-α2, soluble IL-6 receptor α (sIL6Rα) and gp130 were used.
Results: (1) As expected, the disease activity score 28-joiny count (DAS28) using the erythrocyte sedimentation rate (ESR) significantly decreased in all three groups (TOC, ABT and TNFi) by 12 weeks.
(2) IFN-α2 was barely detected in the serum samples. IFN-β seemed to increase slightly in the ABT group, but the increase was not statistically significant.
(3) The levels of sIL6Rα did not change substantially. Those of gp130 decreased slightly but significantly in the TOC group by 12 weeks.
(4) The levels of IL-6 decreased significantly in the ABT group by 12 weeks. Those in the TNFi group decreased significantly at 4 weeks but not 12 weeks (Fig. 1A).
(5) The levels of IL-7 decreased significantly only in the TOC group (Fig. 1B).
Conclusion: (1) The biologic DMARDs tested in this study did not significantly affect the serum levels of type I IFNs in this study.
(2) The decrease in gp130 in the TOC group may imply that gp130 is induced by IL-6, although whether this level of decrease has physiological significance is open to question.
(3) Serum IL-6 was significantly decreased in the TNFi group at 4 weeks but not 12 weeks. TNF has been reported to induce IL-6 (ref 2), but negative feedback loop(s) may be present. Such a feedback system might make the discontinuation of TNFi difficult, even if patients are in remission.
(4) IL-7 may be a target of IL-6. A higher level of IL-7 has been reported to be present in the joints of RA patients compared with osteoarthrosis and it is a cytokine implicated in the differentiation of osteoclasts (ref 3). This may partly explain the effect of TOC on preventing bone erosion in RA.
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[1] Ann Rheum Dis. 2007; 66: 1008–14
[2] Rheumatology 2007; 46: 920-6
[3] Rheumatology 2008; 47: 753-9

Fig. 1A

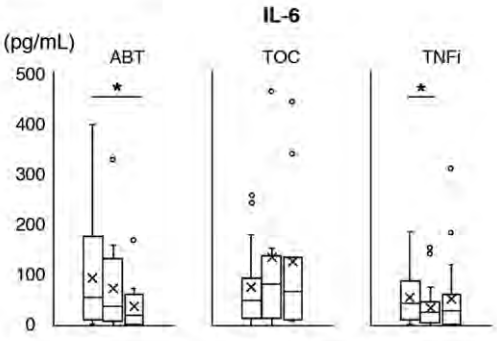
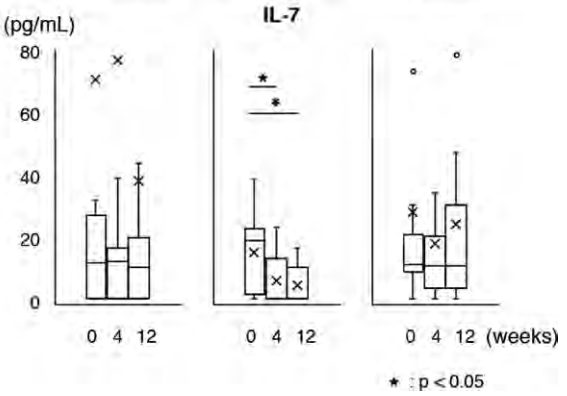


Fig. 1B



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AB0043

THE IMBALANCE OF T FOLLICULAR REGULATORY CELL AND T FOLLICULAR HELPER CELL IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease which can lead to severe joint damage and disability.The relationship between antibodies and rheumatoid arthritis has long been well established. Recently, many studies have found that T follicular regulatory cells(Tfr) and T follicular helper cells (Tfh) are closely related to antibody generation on lymphoid follicular germinal centers (GCs)[1-2]. Tfr cells can inhibite the GC reaction and suppress production of high-affinity antibodies. The dysregulation of Tfh cells can lead to the production of autoantibodies by B cells.

Objectives: To examine the expression of circulating T follicular regulatory cell (Tfr) and T follicular helper cell and its subsets(Tfh1 Tfh2 Tfh17) in RA patients and healthy control group.

Methods: Level of Tfr and Tfh1,Tfh2 and Tfh17 cells in the peripheral blood of 17 new RA patients, 30 treated RA patients and 18 healthy controls were deceted by flow cytomery. All patients were hospitalised at the Department of Rheumatology, Second Hospital of Shanxi Medical University.

Results: We found that the level of Tfr (CD3+CD4+CD25+CXCR5+FOP3+) percent(P=0.020), in the peripheral blood in RA patients were significantly decreased compared with healthy controls. The percent of Tfh (CD3+CD4+CXCR5+CD45RA-) (*P*=0.039)and Tfh17 (CD3+CD4+CXCR5+CD45RA-CXCR3-CCR6+) (*P*=0.000)were increased, but there are no statistical difference about Tfh1(CD3+CD4+CXCR5+CD45RA-CXCR3+CCR6-)(*P*=0.558) and Tfh2 (CD3+CD4+CXCR5+CD45RA-CXCR3-CCR6-) percent(*P*=0.079). We compared the above indicators between new and treated RA patients, and the results indicated that the Tfr(*P*=0.013),Tfh (*P*=0.002) and Tfh1(*P*=0.034) were significantly increased in the new RA patients compared to the treated RA patients, there were no differences between the two groups in Tfh2(*P*=0.419) and Tfh17 percent(*P*=0.124).

Conclusion: Our results indicated that disorder of Tfr and Tfh subsets were involved in RA, restoring the Tfr/Tfh balance may be the potential therapeutic targets.

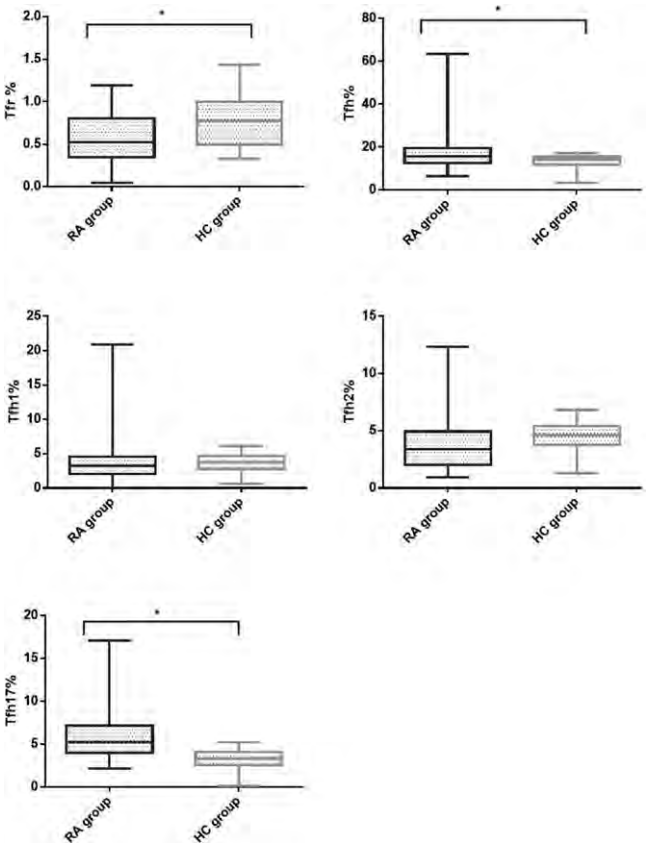


Fig. 1. Comparison of Tfr, Tfh and its subsets(Tfh1 Tfh2 Tfh17) percent among the RA patients (n = 47) and healthy control group (n = 18) (*P < 0.05).

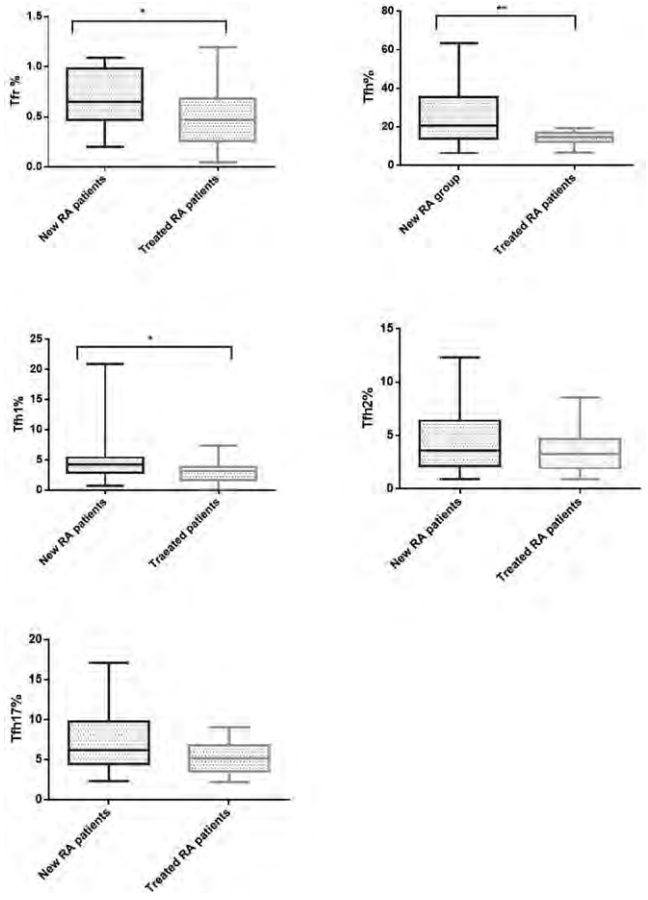


Fig. 2. Comparison of Tfr,Tfh and its subsets(Tfh1 Tfh2 Tfh17) percent among the new RA patients (n = 17) and treated RA patients(n = 30) (*P < 0.05).

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Disclosure of Interests: None declared
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AB0044 ESTABLISHED RHEUMATOID ARTHRITIS PATIENTS HAVE INCREASED FREQUENCIES OF FOLLICULAR REGULATORY T CELLS IN PERIPHERAL BLOOD

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Background: Several studies have demonstrated that an immune dysregulation affecting both B and T cells occurs in rheumatoid arthritis (RA). Follicular helper T (Tfh) cells are crucial for B cell maturation, activation and class-switching as well as for germinal center (GC) formation, whereas follicular regulatory T (Tfr) cells can modulate the GC reaction by suppressing Tfh and B cells.
Objectives: The main goal of this study was to analyze the phenotype and frequency of circulating follicular T cell subsets in established RA patients.
Methods: Blood samples were collected from established RA patients with active disease, treated with methotrexate (n=32) and from a group of age and sex-matched healthy donors (n=11). Peripheral blood mononuclear cells (PBMC) were isolated and Tfh (CD4+CXCR5+CD45RO+) and Tfr (CD4+ CXCR5+CD25+FoxP3+) cells, as well as their three major subsets [CXCR3+CCR6- (Th1-like), CXCR3-CCR6- (Th2-like) and CXCR3-CCR6+ (Th17-like)] were evaluated by flow cytometry.
Results: The frequency of circulating Tfh cells was similar between established RA patients and controls. Nonetheless, RA patients had a decreased frequency of Th1-like Tfh cells, and an increased frequency of Th2-like Tfh cells when compared to controls. No significant differences were observed in the frequencies of Th17-like Tfh cells between both groups. The frequency of circulating Tfr cells was significantly increased in RA patients in comparison to controls. Furthermore, Tfr cells from RA patients had significantly increased CD69 median fluorescence intensity (MFI) values when compared to controls. No significant differences were found in the percentages and MFI values of PD-1, ICOS, CD28, CTLA-4, CD40-L and HLA-DR expressed by Tfh and Tfr cells in RA patients when compared to controls.
Conclusion: Established RA patients have increased circulating frequencies of Tfr cells, with higher CD69 expression levels, when compared to healthy controls. These results suggest a pre-activation state of Tfr cells in RA and a potential role in the disease physiopathology.
*RA Moura, JE Fonseca and L Graca are joint senior authors.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.5077

AB0045 ULTRASOUND GUIDED BIOPSIES OF RA JOINTS AT TIME OF CLINICAL DIAGNOSIS CONTAIN PROFOUND T CELL CLONALITIES

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Background: Rheumatoid arthritis (RA) is a disease characterized by synovial joint inflammation, mainly affecting small joints. Histological findings in synovial biopsies ranges from inflammatory infiltration including ectopic lymphoid structures, to a cell sparse fibroid phenotype. T cells in affected joints are non-naïve and have by flow cytometry approaches been shown to have a wide TCR-beta chain gene usage. New technologies allow for analyses of paired TCR sequences and their antigen-specificities.
Objectives: To study the alpha/beta-T cell receptor repertoire in single sorted T cells from synovial biopsies at time of RA-diagnosis.
Meth ods: Synovial biopsies were taken, primarily using an ultrasound guided technique, from seventeen patients (12 ACPA+, 5 ACPA-) with rheumatoid arthritis. Fresh biopsies were enzymatically digested, followed by mild mechanical treatment, prior to flow cytometry cell sorting. Single cell index sorting of T cells was made into 384-well plates with PCR-buffer followed by a nested PCR and deep sequencing of the TCR amplicons. TCR-receptor sequences showing clonal expansion from four ACPA+ HLA-DRB1*0401 patients were further cloned into SKW3 cells for studies of their reactivity by *in vitro* stimulation with peptides of viral and citrullinated origin from the literature. A positive response, as measured by CD69-up regulation or IL-2 production, was used to define specificity.
Results: Fourteen of the assessed joints were small (1 MTP, 4 MCP and 8 wrists), whereas the remaining three were large joints (2 knees and 1 ankle), table 1. Individual T cells could be isolated from all of these biopsies, with a variating CD4:CD8 ratio. Based on the flow cytometry phenotyping we could identify CD4 T cells of both Treg and T peripheral helper phenotype already at this early time point. Productive alpha/beta-TCR sequences could be retrieved from 16 out of 17 patients and clonal expansion (>1 copy/TCR) was seen in all but one of these patients, with clone sizes ranging between 2 – 34 copies of each TCR.

Table 1. Patient characteristics.

Patients	Gender (F/M)	HLA-SE alleles	Joints	Joint swelling prior to biopsy (months)	Stiffness specific joint (median VAS)	Pain specific joint (median VAS)
ACPA+ (n = 12)	9/3	*0401, *0404, *0408, *01 and *10	1 MTP, 4 MCP, 6 wrists, 1 knee	4 (1-12)[a]	46 (0-84)	45 (22-99)
ACPA- (n = 5)	3/2	*0401	1 MCP, 2 wrists, 1 ankle, 1 knee	5 (0.25-7)	59 (15-73)	47 (33-81)
SKW3 cell lines (patients n = 4)	4/0	*0401/0404 n=2 *0401 n=2	1 MTP, 3 wrists	2 (1-6)	50.5 (42-84)	50 (40-99)

[a] Data not available for one patient. One patient with prior RA-diagnosis, but after 9 months of treatment remission lasting for 20 years.

Artificial T cell lines were generated from the expanded clones of HLA-DRB1*04:01 RA subjects. Our *in vitro* stimulation protocol identified virus specific CD4 T cells in all samples. So far, no citrulline reactivity has been found. HCMV, followed by HHV were the most commonly found viral reactivities, whereas others were found only in one donor (e.g. JCV, EBV). The majority of clones are thus "orphans", to which we are still seeking the driving antigen.
Conclusion: Clonally expanded T cells are found in the synovium of early RA patients and include virus-specific CD4+ T cells. Our data show that the local T cell repertoire is broad already at the time of RA diagnosis
Disclosure of Interests: Sara Turcinov: None declared, Erik af Klint Paid instructor for: Abbvie (courses and lectures), An De Bondt Employee of: Janssen., Muhammad Sohel Mia: None declared, Anca Catrina: None declared, Frederik Stevenaert Employee of: Janssen, Vivianne Malmström Grant/research support from: VM has had research grants from Janssen Pharmaceutica
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AB0046 NO EVIDENCE FOR DISTURBED TH1 AND TH17 FREQUENCIES IN GCA AND PMR PATIENTS - A STUDY IN THE GRONINGEN GPS COHORT

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Background: Giant cell arteritis (GCA) is an aging-associated inflammatory disease of the large-sized arteries. GCA clinically and pathogenically overlaps with polymyalgia rheumatica (PMR), which affects the shoulders and hips. In the inflamed tissues, infiltrated CD4+ T-cells display a disturbed Th cell distribution, that may contribute to the development of the diseases. GCA arteries contain pro-inflammatory T-helper 1 (Th1) and Th17 cells, but almost no Th2 cells or regulatory T-cells. In addition to CD4+ T-cells, macrophages are dominant in GCA and PMR tissue infiltrates. We previously found an altered distribution of monocyte subsets, the precursors of macrophages, in the blood of GCA and PMR patients. Others reported changes in the distribution of Th cells in the blood of treatment-naive GCA and PMR patients as well.
Objectives: We sought to replicate previous studies showing a disturbed Th cell distribution in the blood of GCA and PMR patients. Next, we aimed to link the disturbed Th cell distribution to the altered monocyte subset counts.
Methods: To assess the capacity of circulating T cells to produce lineage cytokines, PBMCs were cultured for 4 hours in the presence of 50 n g/mL PMA, 1.6 µg/mL calcium ionophore and 10µg/mL BFA. Cells were then intracellularly stained for IFNγ (Th1 cells), IL-17 (Th17 cells) and IL-4 (Th2) by flow cytometry. In

addition, monocyte subset counts were determined, based on CD14 and CD16 expression. To obtain absolute counts, proportions determined by flow cytometry were corrected by the total CD4+ T-cell and monocyte counts. Th1, Th17 and monocyte subsets were determined in 21 GCA patients, 19 PMR patients and 19 healthy controls (HC). Th2 cells were determined in 10 GCA patients, 10 PMR patients and 10 HC. All GCA and PMR patients were newly-diagnosed and treatment-naive. HC were age- and sex-matched and without any immunomodulatory medication.

Results: Both absolute counts and percentages of peripheral Th1 cells, Th17 cells and Th2 cells did not differ between GCA/PMR patients and HC. The monocytosis in GCA and PMR was mainly attributed to an expansion of the classical monocyte subset. Counts of monocyte subsets were not strongly correlated with counts of either Th1 or Th17 cell counts. In GCA patients, the ESR correlated positively with counts of intermediate monocytes (R= 0.63), but this was not observed in PMR patients.

Conclusion: Compared to most previous work, we report similar circulating Th1 and Th17 cell counts in HC, but lower counts in treatment-naive GCA patients then previously reported (Table 1). Furthermore, numbers of Th1 and Th17 cells in peripheral blood showed no relationship with monocyte subsets. As our protocol for defining Th1 and Th17 cells appears to be similar to the other studies, we propose differences in patient selection. Alternatively, Th1 and Th17 skewing should be studied at the site of inflammation, since Th1 and Th17 skewing cytokines are all highly expressed by macrophages at the inflammatory site. This study shows the importance of replicating previous research, as key concepts of disease pathology are derived from data on disturbed Th cell distribution.

Table 1. Observed median percentages of circulating Th1 and Th17 cells in GCA patients and age-matched HC. Shown are outcomes from several previous studies as well as the present study. Deng et al, Terrier et al and Saadoun et al found elevated Th1 cell percentages in GCA, whereas Samson et al found them lower. All four previous studies showed elevated Th17 percentages in GCA.

	Th1%		Th17%	
Reference	**GCA**	**HC**	**GCA**	**HC**
Deng et al., *Circulation*, 2010	20	12	2.2	0.4
Terrier et al., *Arthritis Rheumatol*, 2012	22	12	2.5	0.5
Saadoun et al., *Arthritis Rheumatol*, 2015	22	17	2.5	0.6
Samson et al., *Arthritis Rheumatol*, 2012	10	14	0.7	0.3
This study	**11**	**12**	**0.6**	**0.5**

Disclosure of Interests: Yannick van Sleen: None declared, Elisabeth Brouwer Consultant of: Roche (consultancy fee 2017 and 2018 paid to the UMCG), Speakers bureau: Roche (2017 and 2018 paid to the UMCG), Minke G. Huitema: None declared, Wayel Abdulahad: None declared, Maria Sandovici: None declared, Annemieke Boots Consultant of: Grünenthal Gmbh until 2017, Kornelis van der Geest Speakers bureau: Roche (2019)

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AB0047 T-CELL IMMUNOGLOBULIN AND MUCIN DOMAIN–CONTAINING PROTEIN 3 EXPRESSION IN REGULATORY T CELLS OF ANKYLOSING SPONDYLITIS PATIENTS AND THE CORRELATION WITH DISEASE ACTIVITY

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Background: Ankylosing spondylitis (AS) is a chronic inflammatory autoimmune disease. Regulatory T cells have been found in peripheral blood of AS patients. However, there is a controversy regarding the relative number and function of regulatory T cells in AS. T-cell immunoglobulin and mucin domain–containing protein 3 (Tim-3) is a negative immune regulator that participates in immune responses and widely expresses on a variety of immune cells. Many studies have shown that Tim-3 participates in tumors, infections, hematological system diseases and autoimmune diseases (such as systemic lupus erythematosus, rheumatoid arthritis, autoimmune hepatitis, etc). While there has not yet clinical trials with large samples to verify whether or not Tim-3 is involved in the incidence of AS and the relationship between the disease activity of AS and the expression of Tim-3 in regulatory T cells.

Objectives: The present study aimed to identify the Tim-3 expression in regulatory T cells in AS patients, and the association between Tim-3 and the disease activity of AS.

Methods: There were 47 patients diagnosed as AS and 51 age- and sex-matched healthy controls (HCs) from Guangdong Second Provincial Central Hospital enrolled in the study. The clinical information of the AS patients was recorded in detail and the disease activity was calculated. The positive expression rates and medium fuorescence intensity (MFI) of Tim-3 in regulatory T cells were examined by fow cytometry. Statistical approaches were used to analyze the experimental data of patients and controls.

Results: The Treg cells level was significantly decreased in AS patients compared to the healthy controls (5.14±0.27 vs 4.38±0.23, P = 0.032, Fig 1 A). Tim-3 expression in regulatory T cells was lower in AS patients than the HCs (63.29±2.39 vs 52.56±3.49, P = 0.013, Fig1 B). And Tim-3 MFI in regulatory T cells was significantly decreased too(1355.04±171.44 vs 859.19±105.11, P = 0.016, Fig1 C).

The Treg cells ratio negatively correlated with BASDAI (r=-0395, p=0.014) and BASFI (r=-0391, p=0.015) in AS patients. However, the Tim-3 expression in the Treg cells has no correlation with diseases activity in patients.

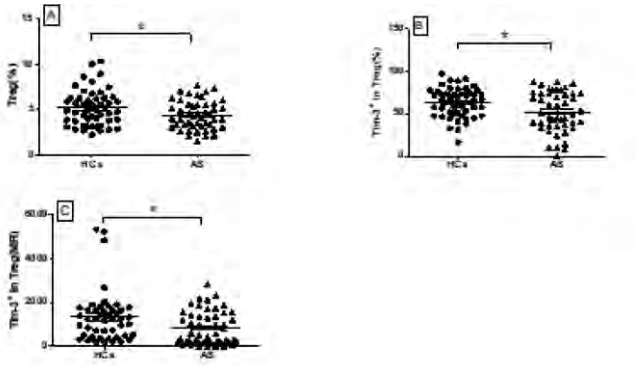


Figure1 The Treg cells frequency, Tim-3 expression and MFI in AS patients compared to the healthy controls.

Conclusion: According to the test results, we could confirm that regulatory T cells participate in the progression of AS, and it has negative relationship with disease activity. Tim-3 can express in Treg, but whether Tim-3 can be used as a potential target for AS treatment in future need further verified.

Disclosure of Interests: None declared

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AB0048 THE EXPRESSION OF T LYMPHOCYTE SUBSETS IN PERIPHERAL BLOOD OF PATIENTS WITH AUTOIMMUNE UVEITIS AND THE SHORT-TERM EFFICACY AND SAFETY EVALUATIONS OF LOW-DOSE IL-2 COMBINED THERAPY

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Background: Autoimmune uveitis is a group of inflammatory diseases that affect the uveal tract such as iris, cilia and choroid. In addition to diabetic retinopathy and age-related macular degeneration, uveitis is one of the main causes of blindness in developed countries[1].The disease is autoimmune-mediated, and abnormal immune responses are induced by pathogenic antigens such as retinal soluble antigens and retinal interphotoreceptor retinoid-binding protein (IRBP), and autoimmune inflammation is caused by specific cytotoxic effects, immune complex responses and delayed hypersensitivity reactions.It has been found that the disorder of lymphocyte subsets, mainly due to the number and function defects of regulatory T cells (Tregs), may be involved in the development of uveitis.IL-2 is a key cytokine in T cell differentiation. As a new type of immunomodulator, IL-2 has achieved preliminary efficacy in the treatment of systemic lupus erythematosus, ankylosing spondylitis, Sjogren's syndrome and other diseases[2-4], but there is no clinical evidence of IL-2 in the treatment of autoimmune uveitis.The purpose of this study was to investigate the expression of T lymphocytes in patients with autoimmune uveitis and the effect of low dose IL-2 on their immune status.

Objectives: To investigate the expression of peripheral blood lymphocyte in patients with autoimmune uveitis and evaluate the short-term efficacy and safety of low-dose IL-2 combined with methylprednisolone.

Methods: A total of 108 patients with autoimmune uveitis and 93 healthy subjects who visited our hospital from January 2016 to April 2019 were collected.Twenty-three patients were treated with a low dose of IL-2 (50WIU/day for 5 consecutive days) on the basis of conventional treatment

(methylprednisolone and/or DMARDs), and the changes in the patients' condition and lymphocyte subsets were observed. The t-test of two independent samples was used when the measurement data conformed to the normal distribution and the variance was homogeneous, and Manil-Whitney rank sum test was used when the measurement data did not conform to the normal distribution.

Results: Among 108 patients, 58 were males and 50 were females, with an average age of 41 + 14 years. Compared with the normal control group, total T cells, total B cells, Th cells, Ts cells, Th1 cells, Th17 cells, Th1/Th2, Th17/Treg in patients with autoimmune uveitis were higher than those in healthy control group ($P < 0.05$), while Th1 cells and Treg cells were lower than those in healthy control group ($P < 0.05$). After IL-2 treatment, the number of Treg cells increased from 21.90±15.29 /ul to 51.54±41.86 /ul ($P < 0.05$), the Th17/Treg ratio decreased back from 0.44±0.27 to 0.33±0.23 ($P < 0.05$), and both serum sedimentation rate and CRP decreased compared with before treatment ($P < 0.05$).

Conclusion: Treg cells are involved in the pathogenesis of autoimmune uveitis. Low dose of IL-2 selectively elevates Treg cells, regulates Th17/Treg balance and improves the condition of the disease.

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Disclosure of Interests: None declared
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AB0049 IMMUNE DYSFUNCTION IN ANKYLOSING SPONDYLITIS (AS) AND THE POTENTIAL OF TUMOR NECROSIS FACTOR-A (TNF-α) INHIBITOR ANBAINUO AS AN EFFECTIVE TREATMENT

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Background: Studies into ankylosing spondylitis (AS) and its relationship with immune function are controversial, and the correlation between the efficacy of TNF-α inhibitor and changes in immune function is unclear.

Objectives: We conducted a prospective study of T-cell and B-cell subset distribution and analyzed lymphocyte function in AS patients to further clarify changes to the immune system caused by AS and to explore resistance that could contribute to relapse after treatment.

Methods: A total of 40 immune cells were tested with flow cytometry, and the results of 105 HC (healthy control) subjects, 177 active-stage AS patients, and 23 AS cases before and after 12 weeks of Anbainuo therapy were analyzed.

Results: Compared with the HC group, the proportion of immune cells, such as naïve and central memory CD4+T cells, in AS increased ($p<0.0001$), but effector memory and terminally differentiated CD4+T cells were decreased ($p<0.01$ and 0.0001, respectively). Naïve, central memory, and effector memory CD8+T cells were increased ($p<0.0001$, 0.001, and 0.01, respectively), but terminally differentiated CD8+T cells were decreased ($p<0.0001$). Th1 cells (helper T cells-1), Tfh1 cells (follicular helper T cells-1), Tc1 cells (cytotoxic T cells-1), and Tregs (regulatory T cells) were lower ($p<0.01$, 0.05, 0.0001, and 0.001, respectively), but Th17 cells, Tfh17 cells, and Tc cells were higher ($p<0.001$, 0.0001 and 0.001, respectively). The proportions of total B cells and class-switched B cells were increased ($p<0.05$), but non-switched B cells, plasma cells, memory B cells, and immature Bregs (regulatory B cells) were lower ($p<0.01$, 0.0001, 0.0001, and 0.0001, respectively). After Anbainuo therapy, the percentage of Tregs and B10 cells (IL-10-producing regulatory B cells) had increased ($p<0.01$and 0.05, respectively), and the increase in Tregs was positively correlated with the decrease in CRP (C-reactive protein) ($r= 0.489$, $p=0.018$).

Conclusion: We found that, in terms of both innate and acquired immunity, active-stage AS patients have an immunity imbalance involving multiple types of immune cells, including CD4+T cells, CD8+T cells, Th cells, Tfh cells, Tc cells, Tregs, Bregs, and B cells. Anbainuo can not only help to inhibit disease activity and partial immune function imbalance in AS but can also increase the number of negative regulatory cells in inflammation.

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AB0050 EXTENDED POLYDIMENSIONAL IMMUNOME CHARACTERISATION (EPIC) PLATFORM AS A TOOL FOR TRANSLATIONAL RESEARCH

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Background: We created a high dimensionality healthy human Immunome atlas by interrogating the peripheral blood mononuclear cells (PBMC) of >200 healthy subjects (cord blood to adult) with 63 unique mechanistic and phenotypic markers per cell by mass cytometry (CyTOF). This database is built with an open source, web-based bioinformatics toolkit, enabling its mining and uploading of datasets for comparison with the EPIC healthy database.

Objectives: Here, we demonstrate the platform's ability to identify the immunological differences of mechanistically important cell subsets in the uploaded data in comparison with EPIC.

Methods: CyTOF data from 37 healthy elderly (>60 years old) was uploaded onto the EPIC Discovery tool where down-sampling, normalising and FlowSOM (Flow analysis with Self-Organising Maps) clustering were done with the EPIC database for comparison. Online visualisation outputs include cluster frequency boxplots, correspondence analysis (CA) plot and markers expression heat-map. The CA 2-dimensional plot depicts the global differences in immune cells composition between subjects with proximity between points (subjects) denoting similarity. Kruskal-Wallis test was done to identify age groups differences.

Results: Increasing distances on the CA plot with age were observed with the elderly being farthest from the new-borns. Notably, we observed significant changes in naive $CD4^+$ $IL8^+$ T cells ($p<1\times10^{-20}$), memory $CD4^+$ $IL17A^+$ T cells ($p<1\times10^{-20}$) and type 2 innate lymphoid cells (ILC2) (Lin^- $CD7^+$ $CD25^+$ $CD127^+$ $CD161^+$, $p<1\times10^{-17}$) with increasing age. The naive $CD4^+$ $IL8^+$ T cells (median: 0.68%, interquartile range: 0.415 to 1.055% of CD45+ PBMC) and ILC2 (0.09%, 0.065 to 0.12%) were lowest and memory $IL17A^+$ T cells (0.58%, 0.41 to 0.905%) highest in the elderly. Significantly, the memory $IL17A^+$ T cells and ILC2 have been implicated in the pathogenesis of auto-immune conditions[1,2].

Conclusion: With EPIC, we have created an online tool enabling data uploading for comparison to a healthy database, allowing the holistic characterisation of immunological changes in different clinical scenarios. Using it, we were able to identify mechanistically important differences in immune cells composition in a distinct clinical cohort (elderly) compared to the younger ages. Translationally, the EPIC platform can be utilised similarly to catalyse the discovery process in auto-immune diseases interrogated with the EPIC antibody panels.

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Disclosure of Interests: None declared
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Innate immunity in rheumatic diseases

AB0051 SERUM AMYLOID A AND PENTRAXIN 3: INNATE IMMUNE RESPONSE AND DISEASE ACTIVITY IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic Lupus Erythematosus (SLE) is an autoimmune disease that involves several molecular patterns with a wide spectrum of clinical manifestations and symptoms. Inflammation and related pathway play a role in SLE pathogenesis. The pentraxin superfamily including long and short pentraxin, C Reactive Protein CRP, Serum amyloid A (SAA), Pentraxin 3 (PTX3) are key components of innate immune system and induce a variety of inflammation associated pathway. However Literature provides several evidences that CRP serum levels not correlated with clinical and immunological manifestations. This situation affected clinical practice and the patient follow up. PTX3 have been identified as a component of inflammatory status in several autoimmune conditions. SAA is an acute phase protein secreted in large quantity during inflammation.
Objectives: We want to evaluated SAA, PTX3 and CRP concentrations, their correlation between SLE Disease Activity Index (SLEDAI), that including complement fractions C3, C4.
Methods: We enrolled fifty patients that fulfilled the SLE American College of Rheumatology criteria and fifty healthy subjects. The SLE disease activity was classified with the SLEDAI (0 to 12). Patients were divided into two groups according to SLEDAI score: inactive group (Group 1, 25 patients, 50%: SLEDAI < 4) and active group (Group 2, 25 patients, 50%: SLEDAI 5 to 12). PTX3 concentration was measured by a sandwich ELISA kit (Hycult) with 2.8 ng/mL cut-off point. SAA concentration was detected by nephelometry performed on a BN ProSpec System (Siemens, Germany), with assay kit based on polyclonal antibodies (Siemens Healthcare Diagnostics Products, Germany, 6.5 mg/L cut-off point). High sensitive CRP concentrations were determined using the ci8200 platform (Abbott Laboratories Chicago, Illinois).
Results: Plasma PTX3 and serum SAA levels was significantly higher in SLE patients than in the healthy subjects (PTX311.5 ± 7.3 ng/mL vs 2.3 ± 1.1; p < 0.001; SAA: 87 ±77 mg/L vs 2.6±2.5; p < 0.001). These differences were not evident in CRP levels (8.5 ± 7.8 mg/L vs 6.2± 2.5). Considering two groups, there were statistical differences in PTX3 level (Group 2: 14.9 ± 12 ng/mL vs Group 1: 2.16 ±0.5 ng/mL, p<0,05) and SAA concentration (Group 2: 114 ± 89 ng/mL vs Group 1: 3.6 ±1.7 ng/mL, p<0,05) but not in CRP concentration (Group 2: 11.5 ± 8.4 mg/L vs Group 1: 9.5 ±3.5). There was a significantly negative correlation between C3, C4 fractions, PTX3 and SSA levels (respectively r = −0.74, p=<0.05, and r = −0.79, p<0.05). No statistical correlation were appeared between C3, C4 fractions and CRP serum levels (r= −0,12., p= 0.82, and r= −0.18, p= 0,21). We noted a positive significant correlation between SLEDAI, PTX3 and SAA concentration (r = 0.79, p < 0.05, 0.83, p < 0.05, respectively) an increase in PTX3 and SAA levels followed the lupus flare and symptoms. No significant correlation appeared between SLEDAI and CRP (r= 0.15, p=0.89)
Conclusion: PTX3 and SAA concentration was significantly higher in SLE patients than the healthy control subjects and their levels reflected disease activity. We showed a direct correlation between PTX3 and SAA. In SLE patients PTX3 and SAA concentrations were correlated with SLEDAI. We suggest an integrate viewpoint in witch SAA and PTX3 may play a role as a biomarker of disease activity, with synergic work during SLE events. Evidences suggested that PTX3 and SAA could trigger the same molecular pathway, by TLR4, via NF-kB.
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Disclosure of Interests: None declared
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AB0052 ROLE OF TRAINED IMMUNITY AND IMMUNOMETABOLISM IN THE PATHOGENESIS OF ERDHEIM-CHESTER DISEASE

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Background: Erdheim-Chester disease (ECD) is a chronic inflammatory disease characterized by infiltration of bone and other tissues by foamy macrophages. These cells exhibit activating mutations along the MAPK pathway, most commonly BRAFV600E, and increased production of pro-inflammatory cytokines. Although this dual neoplastic-inflammatory nature of ECD has long fascinated scientists, the mechanistic link between these two features remains elusive. We hypothesized that Trained Immunity (TI), a pro-inflammatory cell program physiologically elicited in monocytes/macrophages upon activation of the MAPK pathway, might represent the missing link between oncogenic transformation and pro-inflammatory activation in ECD.
Objectives: In this study, we aimed at determining the role of TI in the pathogenesis of ECD, and to evaluate the therapeutic potential of targeting this mechanism for the treatment of inflammation.
Methods: We developed innovative models to study ECD pathogenesis *in vitro* (based on lentiviral transduction and ectopic expression of BRAFV600E in primary human monocytes), as well as *ex vivo* (3D culture of ECD tissue biopsies in bioreactor). Functional and mechanistic features of TI, including typical changes in cell energy metabolism and epigenetics, were investigated by assessing I) cytokine and lactate production; II) mitochondrial respiration with Seahorse flux analyzer; III) glucose, glutamine and cholesterol metabolism with unbiased and targeted metabolomics analyses; IV) epigenetic changes with ChIP PCR; V) transcriptome changes with RNA sequencing.
Results: Activation of the MAPK pathway induced by BRAFV600E in macrophages induces changes in the epigenetic and gene expression landscape, cell energy metabolism, and cytokine production characteristic of TI. In particular, changes in cell energy metabolism of macrophages are characterized by increased glycolysis, glutamine metabolism, and cholesterol synthesis. This metabolic rewiring is needed to sustain rampant, constitutive production of pro-inflammatory cytokines.
Conclusion: A role emerges for TI in the pathogenesis and pro-inflammatory activation of ECD. However, maladaptive activation of this mechanism is likely common to the pathogenesis of other inflammatory and rheumatologic diseases. Since drugs targeting TI programs are already entering the clinical arena, the identification of this mechanism in the pathogenesis of inflammatory and rheumatologic conditions may promptly translate into novel, effective treatment options for affected patients.
Disclosure of Interests: Riccardo Biavasco Employee of: Bluebird, Raffaella Molteni: None declared, Davide Stefanoni: None declared, Marina Ferrarini: None declared, Elisabetta Ferrero: None declared, Simone Cenci: None declared, Simone Cardaci: None declared, Alessandra Boletta: None declared, Laura Cassina: None declared, Gianfranco Di Stefano: None declared, Jorge Dominguez Andres: None declared, Claudio Doglioni: None declared, Travis Nemkov: None declared, Ivan Merelli: None declared, Angelo D'Alessandro: None declared, Eugenio Montini: None declared, Mihai Netea: None declared, Lorenzo Dagna: None declared, Giulio Cavalli Consultant of: SOBI, Pfizer, Sanofi, Novartis, Paid instructor for: SOBI, Novartis, Speakers bureau: SOBI, Novartis
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AB0053 BERGENIN, ACTING AS AN AGONIST OF SIRT1, REDUCE SERUM URATE IN MICE THROUGH THE UPREGULATION OF ABCG2

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Background: About 20% of individuals in the USA have asymptomatic hyperuricaemia[1]. However, Urate-lowering therapy in asymptomatic hyperuricaemia condition is still controversial considering the benefit and side effects[2]. Therefore, safe and effective anti-hyperuricemia therapies are necessary.
Objectives: Bergenin, the major bioactive ingredient isolated from Saxifraga stolonifera, could activate SIRT1. In this study, we identify the effect of bergenin on hyperuricemia, and explored the related mechanisms.
Methods: Significant hyperuricemia was established in C57BL/6N mice treated with oxonate and yeast polysaccharide. Bergenin was administered to the mice at the same time. The serum uric acid and creatinine levels, clearance of uric acid and creatinine, the intestinal uric acid excretion, and renal pathological lesions were determined were used to evaluate the anti-hyperuricemic effects. The location and expression levels of ABCG2 in the kidney and intestine were analyzed. HK-2 and Caco-2 cell lines were exposed to soluble uric acid with or without the treatment of Bergenin. Then the expression of ABCG2 and underlying mechanisms were explored.
Results: The administration of bergenin decreased serum uric acid in hyperuricemic mice by the promotion of uric acid excretion both in kidney and intestine. Bergenin recued the downregulation of ABCG2 in the kidney of hyperuricemic mice and upregulated the expression of ABCG2 in the jejunum and ileum. In

vitro, Bergenin significantly increased the expression of ABCG2 as well as activated SIRT1, which was reversed by addition of PPARg antagonist GW9662 and siPPARg.

Conclusion: These findings suggest bergenin increases uric acid excretion both in the kidney and intestines, which may be related to the upregulation of ABCG2 via SIRT1- PPARg pathway.

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AB0054 SYNOVIAL CD163+ MACROPHAGES ARE ASSOCIATED WITH RADIOGRAPHIC JOINT DESTRUCTION IN RHEUMATOID ARTHRITIS

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Background: CD163, a hemoglobin scavenger receptor, has been identified as a marker of M2 macrophages, it can promote the release of IL-10 and carbon oxide. Researches on inflammatory diseases and tumors have suggested that CD163 plays anti-inflammatory effect and promotes tumor growth and metastasis. Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by chronic synovitis with inflammatory cells infiltration including considerable macrophages. However, little is known about the role of CD163+ macrophages in RA synovium.

Objectives: To investigate the expression and clinical significance of synovial CD163+ macrophages in RA.

Methods: Seventy-five RA patients were recruited and clinical data including disease activity, HAQ and Sharp/van der Heijde-modified Sharp score of bilateral hands and wrists were collected. Synovial tissues were obtained by needle biopsies or arthroscopy of knee joints. Eighteen osteoarthritis (OA) and seventeen orthopedic arthropathies (orth.A) patients were included as controls. All synovium were stained with H&E and immunohistochemically for CD163, CD3, CD20, CD38, CD68, and CD15. Histologic changes of synovitis in H&E stained sections were graded with Krenn's synovitis score.

Results:

1. Positive CD163 expression were found in both lining synoviocytes and sublining inflammatory cells. Both densities of lining and sublining CD163+ macrophages in RA synovium were significantly higher than that in OA or Orth.A synovium (140.47±66.93 vs. 17.85±7.70 vs. 19.76±5.26 and 417.92±249.62 vs. 27.58±14.19 vs. 29.87±9.33, all P<0.001, Figure 1).
2. According to Krenn's synovitis score, there were 68% RA patients showing high synovitis (score>4). Both lining and sublining synovial CD163+ macrophages were significantly higher than those showing low synovitis (lining: 158.40±62.91 vs. 122.06±66.74, sublining: 462.96±62.91 vs. 371.65±271.54, both P<0.05). Meanwhile, the densities of lining and sublining CD163+ macrophages were both positively correlated with Krenn's synovitis score (r=0.238 and 0.343, both P<0.05).
3. For clinical relationship in RA, the density of sublining CD163+ macrophages was positively correlated with total Sharp score (mTSS) (r=0.399, P<0.001), joint space narrowing subscore (r=0.248, P=0.032) and joint erosion subscore (r=0.457, P<0.001). While the density of lining CD163+ macrophages was positively correlated with mTSS (r=0.319, P=0.005) and joint erosion subscore (r=0.358, P=0.002). Meanwhile, the densities of sublining and lining CD68+ macrophages were also positively correlated with mTSS (r=0.253 and 0.242, both P<0.05), of which the correlation was weaker than that of CD163+ macrophages (Figure 2). There were no significant correlation between the density of CD163+ macrophages and disease activity or HAQ (all P>0.05).

Conclusion: Synovial CD163+ macrophages are associated with radiographic joint destruction, which imply that CD163+ macrophages may play role in the pathogenisis of joint destruction in RA.

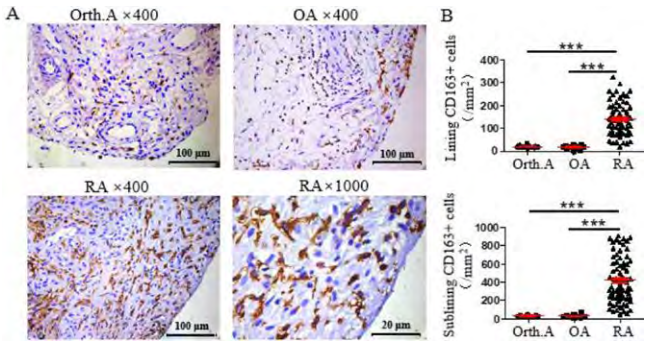


Figure 1. Representative immunohistochemical findings of synovial CD163 expression. (A) Synovial CD163 expression in an Orth.A patient, an OA patient and a RA patient. (B) Densities of lining and sublining CD163+ macrophages in Orth.A, OA and RA patients.

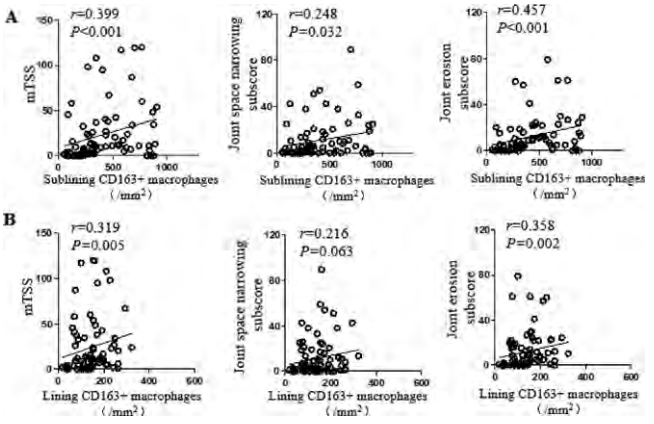


Figure 2. Spearman's rank correlation analysis for synovial macrophages and mTSS in RA. (A) Correlation between sublining CD163+ macrophages and mTSS, joint space narrowing subscore, joint erosion subscore. (B) Correlation between lining CD163+ macrophages and mTSS, joint space narrowing subscore, joint erosion subscore.

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Figures:

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AB0055 SOLUBLE TREM-1 LEVELS IN FAMILIAL MEDITERRANEAN FEVER RELATED AA-AMYLOIDOSIS

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Background: Triggering Receptor Expressed on Myeloid cells-1 (TREM-1) is a monocyte and neutrophil receptor functioning in innate immunity. TREM-1 produces proinflammatory cytokines and serves for neutrophil degranulation. TREM-1 activity is well known in the pathogenesis of sepsis; hence it can be also present in autoinflammatory diseases such as the most common monogenic one, Familial Mediterranean Fever (FMF).

Objectives: The objective of this study is to measure soluble TREM-1 (sTREM-1) activity in severe FMF cases complicated with systemic AA-Amyloidosis.

Methods: The cohort of the study includes regularly followed FMF related AA-Amyloidosis patients in a tertiary center outpatient rheumatology clinic. Soluble TREM-1 levels were measured using enzyme-linked immunosorbent assay (ELISA). In addition, demographic data, renal function tests, acute phase reactants, and medical prescription history was also noted and analyzed. None of the FMF diagnosed patients had an attack during the collection of the blood samples.

Results: The patients were categorized into 4 groups: FMF related AA-Amyloidosis patients (A(+) FMF(+)), FMF unrelated AA-Amyloidosis (FMF(-) A(+)),

FMF patients without Amyloidosis diagnosis (FMF(+) A (-)), and healthy controls (HC). The mean ages, TREM-1, C - reactive protein (CRP), and Creatinine levels of each group are shown in Table 1. TREM-1 levels were found to be significantly higher in A(+) FMF(+) group than FMF(+) A (-), and healthy control groups (p= 0.001 and 0.002). Nevertheless, this difference was not found in between A(+) FMF(+) and FMF(-) A(+) (p= 0.447). In addition, the TREM-1 levels of FMF(+) A (-), and healthy control groups were not different (0.532). In A(+) FMF(+) group, 36 patients used colchicine with the mean dose of 1.9±0.8 mg/day, 14 patients used anakinra, and 9 patients used canakinumab. In FMF(+) A (-) group all 20 patients used colchicine with the mean dose of 2.8±0.9 mg/day, 1 patient used anakinra, and 2 patients used canakinumab.

Table 1. Clinical Features of Patients and TREM-1 levels

	A(+) FMF(+) (n= 42)	FMF(-) A(+) (n=5)	FMF(+) A (-) (n=20)	HC (n=20)
Age	43.9±12.9	54.8±19	35.3±9.64	35.4±6.57
TREM-1	735.3±566.5	1247.1±1349.2	414.3±142.3	439.2±104.6
CRP	11.1±14.2	51.3±98.3	25.8±54	1.8±1.7
Creatinine	1.6±1.8	3.28±4.17	0.7±0.15	0.7±0.15

Conclusion: In conclusion, TREM-1 is a proinflammatory marker found significantly high in AA-amyloidosis patients regardless of their FMF diagnosis. TREM-1 may be useful in AA-amyloidosis follow-up and early diagnosis since currently there is a deficit of an early diagnostic marker of amyloidosis. This study is a cross-sectional one so it is hard to reach a conclusion on the effectiveness of TREM-1 during regular FMF follow-up for the secondary prevention of amyloidosis. However, the sensitivity of TREM-1 as a marker cannot be denied in amyloidosis.

Disclosure of Interests: None declared

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AB0056 NATURAL ANTIBODIES AGAINST PHOSPHORYLCHOLINE AND MALONDIALDEHYDE DURING THE FIRST TWO YEARS OF LIFE: IMPLICATIONS FOR RHEUMATIC DISEASE

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Background: Antibodies against phosphorylcholine (anti-PC) have potentially protective properties in both atherosclerosis and rheumatic disease. IgM anti-PC could play a role in SLE being associated with protection, also in relation to atherosclerotic plaques and vulnerable plaques in SLE[1] and being a non-responder to biologics in RA. [1] We reported potential mechanisms by which anti-PC could be protective: 1:anti-inflammatory; 2: inhibits uptake of oxLDL in macrophages, 3: inhibits cell death.[1] 4: anti-PC (and anti-MDA) increases clearance of human dead cells which could be of importance not especially in SLE;[2] 5: anti-PC increases T regulatory cells in SLE-patients´ T cells from a low level and also in atherosclerosis, with implications for both conditions.[3] Also antibodies against malondialdehyde (anti-MDA) have interesting properties

Objectives: It is not known how these antibodies develop early in life and what may cause low levels. The objective is to determine this.

Methods: Antibodies were studied by ELISA in healthy pregnant women (n=105; Born into life study) and their newborn children. Women were recruited before conception. Informed consent, questionnaires from parents and plasma sample was collected from children at birth from cord blood, at 1-year and 2 years after birth. Extracted antibodies were compared using a proteomics de novo sequencing approach.

Results: Children were born with very low levels of IgM anti-PC, while IgM anti-MDA was present at birth,. Both IgM anti-PC and anti-MDA increased during the first two years of life, but IgM anti-PC in contrast to IgM anti-MDA was still significantly lower than mothers´. IgG anti-PC decreased after 1 year, but reached similar levels as mothers´ after 2 years while IgG anti-MDA reached similar levels as mothers´ already after one year. Proteomics peptide sequencing analysis indicates large peptide sequence variation without specific clone expression during early stage of life compared to the adult stage for which specific peptide sequences dominated.

Conclusion: IgM anti-PC levels develop much slower than anti-MDA and are still relatively low at 2 years. We hypothesize that anti-PC is developed by a combination of pre-programming and exposure to the external world, where infectious agents may play a role. For anti-MDA pre-programming is likely to play a major role and at an earlier stage than for anti-PC.

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Disclosure of Interests: Divya Thiagarajan: None declared, Susanna Lundström: None declared, Göran Pershagen: None declared, Catharina Almqvist Malmros: None declared, Ellika Andolf: None declared, Anna Hedman: None declared, Oscar Berg: None declared, Nina Oparina: None declared, Johan Frostegård Grant/research support from: Unconditional competitive grant from Amgen, related only to PCSK9, not the topic of this abstract

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AB0057 THE ROLE OF NON-INFLAMMATORY MACROPHAGES INITIATING AND RESOLVING THE INFLAMMATORY RESPONSE OF MONOSODIUM URATE IN MICE

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Background: Gout is the most common chronic inflammatory arthritis around the world which is associated with many conditions that affect longevity and well-being, such as metabolic syndrome, cardiovascular diseases, and renal diseases. [1]

Objectives: Gout is the most common inflammatory arthritis around the world. Innate immunity has been implicated in gout inflammation in recent years. However, the phenomena of maintenance of 'asymptomatic' hyperuricemia, the spontaneous resolution of acute gouty arthritis and non-inflammatory tophus and its association with immune regulation are still elusive. We propose that resident macrophages may be a key player in the suppression of gouty inflammation. To address this hypothesis, we used non-inflammatory macrophages to explore the role played in initiating or resolving the inflammatory response.

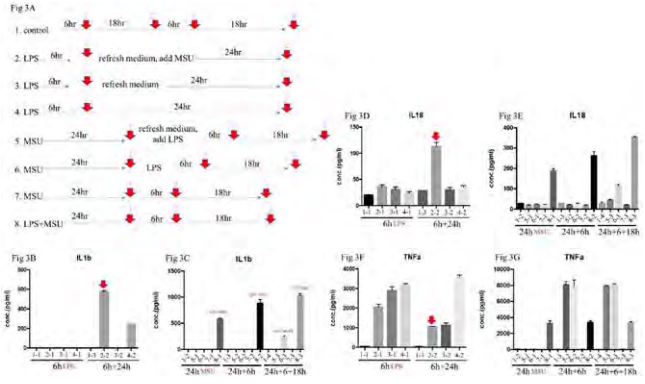
Methods: Bone marrow-derived macrophages (BMDM) were stimulated with monosodium rate (MSU), then analyzed the expression of RNA and protein of inflammatory cytokines, including IL-1β, IL-18 and TNF-α. In addition, we also observe the ability of macrophage to phagocyte and hydrolyze MSU crystal.

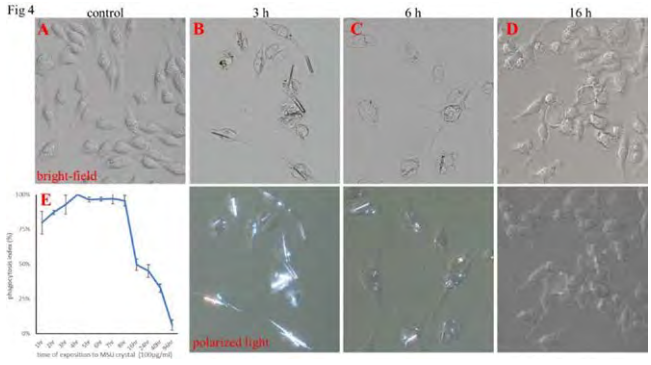
Results: Our results indicate that MSU alone could not induce IL-1β, IL-18, and TNF-α mRNA expression and protein production. However, when macrophages were pre-stimulated with lipopolysaccharide (LPS) or MSU, as well as in combination the production of IL-1β and IL-18 were significantly increased. Furthermore, MSU maybe amplifies LPS-induced protein production of IL-1β and IL-18 but not in TNF-α. A temporal delay in the correlation between mRNA expression and protein production was shown. The results also indicated that macrophages could not only phagocytize MSU crystals but may also hydrolyze MSU crystals.

Conclusion: These data indicate that MSU crystal alone is insufficient to induce pro-inflammatory cytokines production, however, when exposed to an infectious source of infection, it will amplify the inflammatory response and there is a synergistic effect between MSU and LPS. This may explain the diverse clinic phenomena of 'asymptomatic' hyperuricemia, non-inflammatory tophus and acute gouty arthritis. The high efficiency of phagocytosis and hydrolyzed MSU crystals of macrophages may explain the spontaneous regression of acute gouty arthritis. These findings may provide a new therapy for the prevention and treatment of acute gout attacks.

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AB0058

CELL-TYPE SPECIFIC REGULATION OF IL-1R SIGNALING BY R835, A DUAL IRAK1/4 INHIBITOR

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Background: Interleukin-1 beta (IL-1b) is a key mediator of the inflammatory response and is known to exacerbate damage during chronic disease and acute tissue injury. Through association with the adaptor protein Myd88, interleukin receptor associated kinases (IRAK)1 and 4 initiate signaling downstream of IL-1Rs resulting in the activation of the NFkB and MAPK pathways and the production of proinflammatory cytokines (1). IL-1Rs are broadly expressed across cell types and little is known about differences in signaling between cell types and the role of IRAK1 and IRAK4 kinase activity.
Objectives: We have identified a potent and selective IRAK1/4 inhibitor, R835, that substantially suppressed the elevation of LPS (TLR4 agonist)-induced serum cytokines in healthy human volunteers in a recent phase 1 study. The aim of this study was to evaluate the effect of R835 on IL-1R signaling in primary human fibroblasts and endothelial cells.
Methods: Human dermal fibroblasts, lung fibroblasts or endothelial cells were stimulated with IL-1b and the effect of R835 on the signaling pathway was evaluated by western blotting. Human dermal fibroblasts were stimulated with different amounts of IL-1b to evaluate both the signaling pathways activated and the cytokines produced. The ability of R835 to inhibit cytokine production induced by high or low amounts of IL-1b in dermal fibroblasts was assessed.
Results: In human endothelial cells, inhibition of IRAK1/4 kinases with R835 resulted in a block of IL-1b-induced IRAK4 phosphorylation, IRAK1 degradation and downstream NFkB, p38 and JNK activation. In contrast, in both human primary dermal and lung fibroblasts stimulated with IL-1b, we observed potent inhibition of IRAK4 phosphorylation, IRAK1 degradation, and downstream JNK phosphorylation, but no inhibition of NFkB pathway proteins and only weak inhibition of p38. Upon titration of IL-1b we observed that dermal fibroblasts produced IL-8 and GRO in response to low levels of IL-1b (20pg/ml), and produced additional cytokines including G-CSF and GM-CSF with higher levels of IL-1b (400pg/ml). In the presence of low levels of IL-1b (20pg/ml), we observed a weak activation of NFkB pathway proteins and p38, compared to a very robust NFkB, p38 and additional JNK activation in the presence of higher levels of IL-1b (400pg/ml). Consistent with these results, in dermal fibroblasts, R835 showed little to no inhibition of IL-8 and GRO induced by low levels of IL-1b, but potently inhibited G-CSF and GM-CSF induced by high levels of IL-1b where JNK was activated.
Conclusion: This study has elucidated signaling differences between cell types downstream of the IL-1R. In endothelial cells, as in myeloid cells, the kinase activity of IRAK1 and IRAK4 is required for the activation of all downstream signaling. Unexpectedly, in human fibroblasts, IRAK1/4 kinase activity appears to primarily regulate the JNK pathway, and not the NFkB pathway. Concomitant with that, only the cytokines induced by the additional activation of JNK in fibroblasts are regulated by a dual IRAK1/4 inhibitor. Clinically, an IRAK1/4 inhibitor may show select inhibition of IL-1b-induced cytokines depending on the tissue and cell type involved in inflammation.
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Disclosure of Interests: Sylvia Braselmann Shareholder of: Shareholder of Rigel Pharmaceuticals, Employee of: Employee of Rigel Pharmaceuticals, Ernest Tai Shareholder of: Rigel Pharmaceuticals, Employee of: Rigel Pharmaceuticals, Roy Frances Shareholder of: Rigel Pharmaceuticals, Employee of: Rigel Pharmaceuticals, Chi Young Shareholder of: Rigel Pharmaceuticals, Employee of: Rigel Pharmaceuticals, Vadim Markovtsov Shareholder of: Rigel Pharmaceuticals, Employee of: Rigel Pharmaceuticals, Esteban Masuda Shareholder of: Rigel Pharmaceuticals, Employee of: Rigel Pharmaceuticals, Vanessa Taylor Shareholder of: Rigel Pharmaceuticals, Employee of: Rigel Pharmaceuticals
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AB0059

CLINICAL SIGNIFICANCE OF CIRCULATING MYELOID-DERIVED SUPPRESSOR CELLS IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Myeloid-derived suppressor cells (MDSCs) represent heterogeneous population of immature myeloid cells with immunosuppressive functions. The important role of MDSCs is indicated for cancer, but their role in autoimmune pathology is currently controversial. Considering the clinical heterogeneity of ankylosing spondylitis (AS) and involvement of innate immunity in AS pathophysiology the investigation of the MDSC role in AS is of great interest.
Objectives: The aim of our study is to investigate the number of MDSC subsets in AS patients with different clinical manifestations, activity, disease duration, and treatment options and to evaluate the ability of MDSCs to mediate immunosuppressive function in AS patients.
Methods: The study included 34 patients with AS. Ankylosing Spondylitis Disease Activity Score (ASDAS) was used to assess disease activity and high activity was determined as ASDAS≥2.1. The frequencies of monocytic (M-MDSC) (HLADR-CD14 +), granulocytic (G-MDSC) (lin-HLADR-CD33+ CD66 +) and early-stage (eMDSC) (lin-HLADR-CD33 + CD66-) MDSCs and biomarkers of MDSCc functional activity including of Arg-1, IDO, PDL1 were determined in the peripheral blood by flow cytometry.
Results: We found significant elevation in the frequency of both M-MDSC and G-MDSC in the total group of patients compared to healthy controls (HC) (P=0.00006 and P=0.008 respectively), while eMDSCs did not differ from HC. Analysis of MDSCs populations in patient subgroups showed expansion of G-MDSCs in patients with axial plus peripheral damages (P=0.004), while M-MDSCs were elevated regardless of the presence (P=0.002) or absence (P=0.001) of peripheral manifestations. Moreover, the percentage of M-MDSCs was positively correlated with ASDAS in patients with axial disease only (R=0.8; P=0.03). Patients with low activity of disease demonstrated significant elevation of only M-MDSCs compared with HC (P=0.001). Patients who had high activity of disease had increase in both M-MDSCs and G-MDSCs (P=0.008 and P=0.005 respectively). By comparing the frequency of MDSCs in patient groups with different AS duration we showed increase in percentage of both M-MDSCs and G-MDSCs in patients with relatively short duration of disease (< Me=11.5 years) (P=0.002 and P=0.005 respectively) and elevation in M-MDSCs only in patients with longer AS duration (P=0.0003). Compared with patients receiving conventional therapy (NSAIDs, csDMARDs), patients who received biological agents (TNFα inhibitors) had lower disease activity but despite this showed elevated frequencies of M-MDSCs and PMN-MDSCs, comparable to patients receiving conventional therapy. Of note, M-MDSCs in AS patients had increased expression of PDL-1 and IDO (P=0.04 and P=0.02 respectively) and similar to HC expression of Arg-1. The expression of Arg-1, IDO, PDL1 in patients G-MDSCs did not differ from HC.
Conclusion: The data obtained indicate that both M-MDSCs and G-MDSCs are elevated in AS patients. However, the increase of G-MDSCs is associated with peripheral manifestations of AS, high activity, longer duration, and the percentage of M-MDSCs was positively correlated with activity in patients with axial disease only. The unchanged expression of Arg-1, PDL-1 and IDO in G-MDSCs and enhanced expression of PDL-1 and IDO in M-MDSCs suggest MDSCs capacity to mediate immunosuppressive function in AS patients.
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AB0060

STING AND PROINFLAMMATORY CYTOKINES IN SYNOVIAL FLUID OF PATIENTS WITH DIFFERENT ARTHRITIDES

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Background: STING (stimulator of interferon genes) is a cytosolic protein that is found in endoplasmic reticulum (ER) membrane, mitochondria and mitochondria-associated membranes. Although it is well established that STING plays an important role in innate immune responses, its potential involvement in rheumatic disease processes remains to be clarified (1).
Objectives: The aims of this study were to evaluate the levels of STING and its relationship with local inflammation in the synovial fluid (SF) of patients with psoriatic arthritis (PsA), rheumatoid arthritis (RA), gout, calcium pyrophosphate (CPP) crystal-induced arthritis (CPP-IA), osteoarthritis (OA) and OA with CPP crystals (OA+CPP).
Methods: SF was collected from the knees of 60 untreated patients: 10 with PsA, 10 with RA, 10 with gout, 10 with CPP-IA, 10 with OA and 10 with OA+CPP. SF was examined under optical light microscopy. White cell count (WBC) and the polymorphonuclear cell (PMN) percentage were determined in SF according to standard procedures. SF IL-8, IL-6, IL-1β and extra- and intra-cellular STING levels were assayed by ELISA.
Results: The levels of WBC were higher in SFs from gouty patients (27.7±20.56 $10^3/mm^3$), while OA and OA+CPP patients showed the lowest WBC count (0.34±0.3 $10^3/mm^3$, 0.3±0.28 $10^3/mm^3$). SFs from inflammatory arthritis contained elevated percentages of PMN (gout: 85.5±10.86%, CPP-IA: 84±11.31%, RA: 80.33±8.14%, PsA: 42.6±35.97%). Extracellular STING was determined in OA (440±413.31 pg/ml), OA+CPP (225±205.06 pg/ml) and CPP-IA (475±7.07 pg/ml) SF, while was not detectable in RA, PsA and gout. Intracellular STING levels were similar and the highest in SFs from gout (96.4±35.44 pg/ml) and RA (90.64±23.13 pg/ml), while remained under detection limit only in SFs from PsA. SF concentration of IL-6 was lower in OA (354.87±377.56 pg/ml) and OA+CPP (389.56±104.14 pg/ml) as compared with inflammatory arthritides (PsA: 3807.14±489.86 pg/ml; RA: 17354±2334.87 pg/ml; gout: 19359±84.85 pg/ml; CPP-IA: 20389.56±104.14 pg/ml). The patients with gout and RA had the highest levels of IL-8 (2159.54±347.09 pg/ml; 2039.6±97.74 pg/ml) and IL-1β (35.93±20.46 pg/ml; 44.36±23.16 pg/ml), while OA showed the lowest concentrations (IL-8: 23.21±11.32 pg/ml; IL-1β: 0.47±0.13 pg/ml). In the total group of patients, we found a negative correlation between extracellular STING and IL-8 (r=-0.53; p=0.004) and IL-1β (r=-0.47; p=0.012). There was a positive correlation between intracellular STING and IL-8 (r=0.54; p=0.017), IL-1β (r=0.77; p<0.001) and IL-6 (r=0.69 p=0.009).
Conclusion: This study is the first to define the presence of STING in SF of different arthritides. The high levels of extracellular STING in OA, OA+CPP and CPP-IA SFs may be due to the activation of factors that reduce its interaction with the ER. The effect of downregulating factors in PsA might explain the low concentration of intracellular STING in these patients.
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AB0061 INVOLVEMENT OF CELL-FREE DNA IN THE DIFFERENTIATION OF OSTEOCLASTS – IMPLICATIONS FOR CLINICAL RESEARCH

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Background: Cell-free DNA (cfDNA) is a molecule with undisputable immunogenic potential[1]. Its role is well established in etiopathogenesis of systemic lupus erythematosus and many reports suggest it may play an important role in other rheumatic diseases[2]. Patients suffering from rheumatic diseases are at higher risk of osteoporosis[3], which may be a consequence of increased generation of osteoclasts (OC). Traditionally, increased formation of OC is attributed to changes in cytokine network[4]. It is not yet known whether cfDNA can also act on mononuclear precursors and influence their differentiation into OC.
Objectives: The aim of this study was to assess role of cfDNA in differentiation of bone resorbing cells in rheumatic diseases. For this purpose, deoxyribonuclease I (DNAse) was employed to eliminate cfDNA from sera of patients and healthy controls (HC) used for cell culture.
Methods: In order to evaluate effects of cfDNA on osteoclastogenesis, an *in vitro* experiment of peripheral blood monocytes (PBM) cultures was designed. Axial spondyloarthritis (AxSpA) was chosen as a model of rheumatic disease. Sera of AxSpA patients (total n=13) and healthy controls (total n=13) were collected and subsequently used in cell cultures. PBM of 13 healthy donors were cultured in presence of 25 ng/ml macrophage colony-stimulating factor (M-CSF), 0,5 ng/ml receptor-activator of nuclear factor kappa B ligand (RANKL) and 10 % of pooled AxSpA or HC sera, respectively. Serum counterpart treated with DNAse was used in parallel. After 14 days, cells were stained for tartrate-resistant acid phosphatase (TRAP) and counted. TRAP positive cells with 3 or more nuclei were recognized as OC.
Results: On average, differentiation of OC in presence of AxSpA sera led to higher osteoclastogenesis compared to DNAse-treated counterpart (137 vs. 61; $p < 0.01$). In a similar way, treatment of HC sera with DNAse greatly diminished osteoclastogenesis compared to untreated sera (17 vs. 111; $p < 0.05$). Overall, the effect of cfDNA depletion in HC sera regarding OC differentiation was more than 2,5× higher than the effect of cfDNA depletion in AxSpA sera ($p < 0.001$).
Conclusion: Results of our pilot study indicate possible involvement of cfDNA in osteoclastogenesis. Decrease in number of OC after cfDNA depletion in both AxSpA sera and HC sera suggests that cfDNA effect in osteoclastogenesis is non-specific with respect to healthy condition and may represent universal link between innate immunity and bone metabolism. Lower effect of cfDNA depletion in AxSpA sera on osteoclastogenesis is very possibly owing to presence of other inflammatory molecules, which influence osteoclastogenesis. Future research might identify cfDNA as useful therapeutic target to decrease osteoporosis risk not only in patients with rheumatic and autoimmune diseases, where pathological bone resorption is imminent, but also in general aging population.
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AB0062 CHARACTERIZATION OF IL-12 AND IL-23 REDUCTION BY TOFACITINIB IN MDCS

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory auto-immune disease characterized by an excessive production of pathogenic mediators that cause inflammation of the skin, peripheral joints, entheses and the spine. Among these, interleukin (IL)-23, IL-12, the IL-17 family and TNF constitute key players in PsA pathogenesis.[1,2] IL-23, consisting of IL23A (IL-23p19) and IL12B (IL-12p40) subunits, is predominantly produced by myeloid dendritic cells (mDCs). While the p19 subunit is unique to IL-23, the p40 subunit is shared with IL-12. Together, IL-12 and IL-23 play a crucial role in promoting the differentiation of naïve T lymphocytes into T helper (Th) interferon (IFN)-γ-producing Th1 or IL17-producing Th17 cells, respectively.[3]
Small-molecule inhibitors, such as the JAK/STAT inhibitor Tofacitinib, have recently shown promising therapeutic potential in PsA clinical trials.[4] The inhibition of JAKs by Tofacitinib results in the direct suppression of multiple intracellular signaling pathways which constitute key hubs in the cytokine network. [5] However, whether Tofacitinib is able directly target IL-12/IL-23 production by mDCs has not yet been documented. Suppression of these canonical inflammatory pathways would provide further evidence that Tofacitinib is an effective drug in halting both innate and adaptive immune responses.
Objectives: To evaluate the transcriptional and molecular events underlining IL-12 and IL-23 regulation by Tofacitinib in mDCs.
Methods: Peripheral blood mononuclear cells from healthy donors were isolated by Ficoll gradient. Monocytes and myeloid dendritic cells (mDCs) were isolated by using magnetic beads on autoMACS. Monocytes were cultured for 6 days in the presence of IL-4 and granulocyte-macrophage colony-stimulating factor (GM-CSF) to generate monocyte-derived dendritic cells (moDCs). MoDCs were harvested, washed and put to rest for 1 day prior to stimulation, while mDCs

were stimulated on the same day of isolation. Both moDCs and mDCs were pre-treated with Tofacitinib and then stimulated with either lipopolysaccharide (LPS) or combination of LPS with IFN-γ for 4 hours. Cytokines were measured using enzyme-linked immunosorbent assay (ELISA) and gene expression was assessed using quantitative polymerase chain reaction (qPCR).
Results: Treatment of both mDCs and moDCs with Tofacitinib led to a decreased mRNA expression of IL-12 p40 (*IL12B*) in the presence of TLR4 and IFNγ co-stimulation. The decreased *IL12B* mRNA expression also resulted in lower production of IL-12 p40 and IL-23 proteins in mDCs.
Conclusion: In this work, we demonstrated for the first time that Tofacitinib can suppress the production of IL-23/IL-12 p40 subunit in mDCs, upon the condition that an active type II IFN signalling is also present in these cells. This observation indicates that specific factors, such as endogenous IFN-γ levels in the serum of PsA patients, can possibly predict differential responses to Tofacitinib treatment.
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OA, aetiology, pathology and animal models

AB0063 **AGING CARTILAGE IN WILD-TYPE MICE: AN OBSERVATIONAL STUDY**

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Background: Many animal models of osteoarthritis (OA) have been used to study the pathogenesis of cartilage degeneration[1]. In mice, spontaneous OA can occur in wild-type or genetically modified animals. The first report of spontaneous OA developing in wild-type mice was published in 1956 [2] and changes affecting the knee joint were further related to OA by using ultrastructural- histochemical analyses. However, a quantitative assessment of age-related evolution of OA-type cartilage lesions is lacking. The OA Research Society International (OARSI) grading score was adapted to semi-quantify histopathogical changes occurring in OA animal models, including mice [3]. The OARSI score has been used to describe changes occurring in induced or genetic OA mouse models but not to describe spontaneous age-related evolution of OA-type cartilage lesions in wild-type mice.
Objectives: We aimed **t**o describe the spontaneous evolution of age-related changes affecting knee joint articular cartilage, walking speed and a serum biomarker of cartilage remodeling in C57BL/6 wild-type male mice.
Methods: Histological changes were assessed by the OARSI score in newborn, 1-week- and 1-, 3-, 6-, 9- and 12-month-old C57BL/6 wild-type male mice, walking speed by the Locotronic system, and serum C-terminal telopeptide of type II collagen (CTX-II) content by ELISA in 1-, 3-, 6-, and 9-month-old C57BL/6 wild-type male mice.
Results: Mean (SD) OARSI score increased from 0.2(0.3) to 1.3(0.6) (p=0.03) between 1 and 3 months of age and from 1.3(0.6) to 3.3(0.6) (p=0.04) between 3 and 6 months of age. Mean walking speed was stable between 1 and 6 months of age but decreased from 11.4(1.8) to 3.2(0.8) cm.s-1 (p=0.03) between 6 and 9 months of age. Serum CTX-II content was maximal at 1 month of age, then decreased from 12.2(8.5) to 2.4(8.4) pg/ml (p=0.02) between 1 and 3 months of age, remaining low and stable thereafter.
Conclusion: C57BL/6 wild-type male mice showed continuously increasing osteoarthritic changes but delayed decreasing walking speed with age. These variations were maximal between 3 and 9 months of age. Maximal serum CTX-II content preceded these changes.
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Table 1. Evolution of cartilage changes, walking speed and serum C-terminal telopeptide of type II collagen (CTX-II) concentrations in wild-type C57BL/6 male mice.

Age	New-born	1 week	1 month	3 months	6 months	9 months	12 months
OARSI score (0 to 6)	0.0 (0.0)	0.0 (0.0)	0.2 (0.3)	1.3 (0.6)*	3.3 (0.6)*	3.7 (0.6)	4.3 (0.6)
Walking speed ($cm.s^{-1}$)	-	-	10.5 (1.5)	11.3 (4.3)	11.4 (1.8)	3.2 (0.8)*	-
CTX-II concentrations (pg/ml)	-	-	12.2 (8.5)	2.4 (8.4)*	1.1 (4.0)	4.0 (3.8)	-

N ≥ 3 per timepoint. All results are means (standard deviation). *p<0.05 as compared to the previous timepoint using the non-parametric Mann-Whitney U-test.

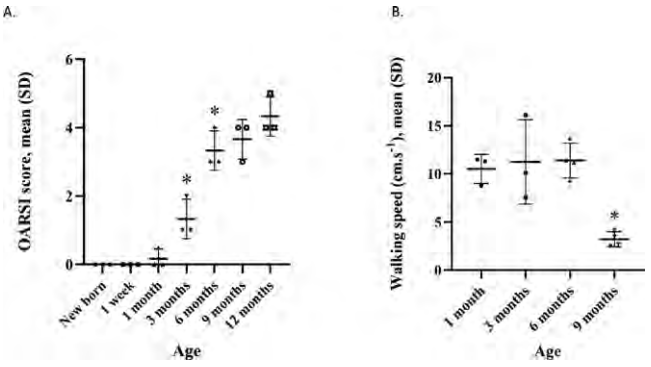


Figure 1. (A) New born,1-week- and 1-, 3-, 6-, 9- and 12-month-old wild-type C57BL/6 male mice (N=3 per timepoint) knees were evaluated for cartilage changes following OARSI recommended guidelines by 3 independents readers. Each point represents the mean of OARSI score per mice as scored by 3 independent readers. **(B)** 1-, 3-, 6- and 9-month-old wild-type C57BL/6 male mice were evaluated for walking speed using the Locotronic® system. Each point represents the mean of 3 measures of walking speed per mice. All results are means (SD). *p<0.05 as compared to the previous timepoint using the non-parametric Mann-Whitney U-test.

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AB0064 **CHANGES IN THE VASCULAR ENDOTHELIAL GROWTH FACTOR A (VEGFA) SPLICING AXIS IN HUMAN SYNOVIUM ARE RELATED TO INFLAMMATION IN ARTHRITIS**

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Background: VEGF-A is a key regulator of rheumatoid (RA) and osteoarthritis (OA). During articular inflammation in OA and RA there is increased synovial angiogenesis and upregulation of angiogenic growth factors such as VEGF-A. VEGF-A comprises two splice variant families, VEGF-A_{xxx}a and VEGF-A_{xxx}b (xxx represents the number of amino acids, from 121 to 206), resulting from alternative splice site selection in exon 8. This site selection is controlled by Serine/Arginine Rich Splicing Factor Kinase 1 (SRPK1), which phophorylates Serine/Arginine Rich Splicing Factor 1 (SRSF1), inducing it to translocate to the nucleus. In most normal tissues, VEGF-A_{xxx}b isoforms predominate, with anti-nociceptive and anti-angiogenic functions. I contrast, in pathological conditions such as inflammation and solid tumours, VEGF-A_{xxx}a isoforms predominate, with pro-nociceptive and pro-angiogenic functions. VEGF-A has been proposed as

a therapeutic target in RA and OA. To date, there are no published data on the functionally distinct VEGF-A splice variants in either RA or OA.
Objectives: To determine the patterns of, and relationships between, VEGF-A, SRPK1, and SRSF1 expression and activation and synovial inflammation in human RA and OA.
Methods: The study was approved by the Nottingham Research Ethics Committee 1 (05/Q2403/24) and Derby Research Ethics Committee 1 (11/H0405/2). Tissues were selected from age- and sex-matched cases in the University of Nottingham joint tissue repository. Post-mortem (PM) samples of healthy knee synovium (n=14, no history of arthritis or knee pain in the 12 months prior to death, no significant articular or synovial pathology) and arthroplasty-derived synovium samples from OA (n=35) or RA (n=14) patients were compared. OA samples were selected to represent the variety of inflammation levels, from low to high grade (0-3, Haywood et al., 2003). 8um thick sections were stained for SRSF1, SRPK1, total VEGF-A and $VEGF_{xxx}b$ via immunohistochemistry. Expression was estimated as fractional area, relative staining intensity ($VEGF\text{-}A_{xxx}b$), and SRSF1 activation quantified by the degree of nuclear localisation. Statistical analyses were performed using Kruskal-Wallis followed by Dunn's tests and Spearman's rank correlations.
Results: SRPK1 expression was similar across all conditions. SRSF1 showed significantly higher expression in the OA tissue compared to PM ($H(2)= 11.29$, $p=0.002$; OA median=0.2, IQR(0.15, 0.28); PM median=0.09, IQR(0.07, 0.16)), and significantly higher nuclear localisation (indicating activation) in RA vs. OA, and in both RA and OA vs PM ($H(2)=37.65$, $p<0.0001$ RA cf. PM; $p=0{,}007$ OA cf. PM; RA median=89, IQR(83, 93); OA median=36.1, IQR(29, 42); PM median=19.8, IQR(14,21)). Nuclear SRSF1 was significantly correlated with inflammation score ($r= 0.52$, $p<0.05$). Total VEGF-A expression was significantly increased in RA compared to PM and OA ($H(2)=23.3$, $p<0.001$ RA cf. PM; RA median=0.4, IQR(0.37,0.59); PM median=0.18, IQR(0.15,0.2)) and was also correlated with the severity of inflammation ($r=0.47$ $p<0.05$). $VEGF\text{-}A_{xxx}b$ showed no changed in expression in OA or RA, although $VEGF\text{-}A_{xxx}b$ staining intensity was significant higher in RA samples, compared to controls ($H(2)=7.2$ $p=0.02$; RA median=2.3(1, 4); PM median=0.9 (0.7, 1.4)).
Conclusion: Increased levels of SRSF1 activation, and the association of total VEGF-A expression with inflammation score, support the hypothesis that there is activation of alternative splicing in inflamed synovium in RA and OA. Targeting this pathway could be a novel therapeutic strategy in OA & RA.
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2017: Consultancy to Pfizer Ltd; personal financial disclosure
2017: Consultancy to Pfizer Ltd through Nottingham University; non-personal financial disclosure (payment to University).
2015: Consultancy to GSK Consumer Healthcare; personal financial disclosure., Speakers bureau: 2019: Irish Society of Rheumatology: speaker fees (personal pecuniary), Lucy Donaldson Shareholder of: LFD is a co-inventor on patents protecting alternative RNA splicing control and VEGF-A splice variants for therapeutic application in a number of different conditions. LFD is also a founder equity holder in, and consultant to, Exonate Ltd, and Emenda Therapeutics Ltd. Both companies have with a focus on development of alternative RNA splicing control for therapeutic application in a number of different conditions, including ophthalmology (www.exonate.com), analgesia and arthritis (www.emendatherapeutics.com)., Consultant of:
LFD is a co-inventor on patents protecting alternative RNA splicing control and VEGF-A splice variants for therapeutic application in a number of different conditions. LFD is also a founder equity holder in, and consultant to, Exonate Ltd, and Emenda Therapeutics Ltd. Both companies have with a focus on development of alternative RNA splicing control for therapeutic application in a number of different conditions, including ophthalmology (www.exonate.com), analgesia and arthritis (www.emendatherapeutics.com).
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AB0067 CHONDROCALCINOSIS IS ASSOCIATED WITH A SPECIFIC EFFECT ON THE CHONDROCYTE PHENOTYPE THAT MARKEDLY DIFFERS FROM OA

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Background: Calcification of cartilage with BCP crystals is a common finding during osteoarthritis (OA) and is directly linked to the severity of the disease and hypertrophic differentiation of chondrocytes. Chondrocalcinosis (CC) is associated with CPPD crystal formation. There is only little knowledge about the effect of CPPD crystals on chondrocytes.
Objectives: The aim of this study was to investigate the chondrocyte phenotype in CC cartilage and the effect of CPPD crystals on chondrocytes.
Methods: Cartilage samples of patients with CC were used and compared with samples of severe OA patients without chondrocalcinosis and healthy cartilage samples served as control. Radiological presence of chondrocalcinosis was evaluated using standard X-ray pictures, as well as macroscopically inspection. The cartilage samples were stained using von Kossa/Safranin-orange staining. These stainings were used for OA severity scoring using the Chambers-Score. FTIR analyses was performed to distinguish CPPD and BCP crystals in cartilage. Chondrocyte differentiation markers were evaluated using Collagen 2 and X, as well as Sox9 and aggrecan as markers for chondrocyte hypertrophic differentiation in immunohistochemistry and qRT-PCR. TUNEL staining was performed to investigate cell death. In vivo results were validated using qRT-PCR for the expression of the respective genes after stimulation of C28 chondrocytes with CPPD and BCP crystals.
Results: Radiologically detectable cartilage calcifications were evident in chondrocalcinosis patients, but absent in OA patients without CC. CPPD crystals were detected on the cartilage surface, whereas BCP crystals were detected in the pericellular matrix of hypertrophic chondrocytes. CC cartilage exhibited an increased collagen X expression compared to healthy cartilage, as well as to severe OA cartilage containing BCP calcification. Interestingly, aggrecan and collagen 2 were not reduced in CC cartilage, but markedly reduced in OA cartilage. TUNEL positive cells were significantly increased in CPPD cartilage compared to OA cartilage, although the histological OA severity was lower. qRT-PCR indicated no relevant influence of CPPD crystals on hypertrophic marker genes, whereas BCP crystals significantly induced hypertrophic differentiation.
Conclusion: BCP and CPPD crystals seem to trigger differential effects on the chondrocyte phenotype. BCP crystals induce hypertrophic differentiation, which is not induced by CPPD crystals.
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Disclosure of Interests: Franziska Meyer: None declared, Miriam Bollmann: None declared, Uwe Kornak: None declared, Jessica Bertrand Grant/research support from: Pfizer, Speakers bureau: Pfizer
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AB0068 NOVEL CHONDROPROTECTIVE AND ANTI-INFLAMMATORY EFFECTS OF THE SELECTIVE HUMAN MELANOCORTIN MC3 RECEPTOR AGONIST PG-990 ON SNAP ACTIVATED CHONDROCYTES

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Background: Osteoarthritis (OA) is a degenerative joint disease that affects over 250 million people worldwide [1] with treatments focussing on the symptoms rather than the cause of the pathology [2, 3]. Thus, this degenerative joint disease requires novel treatment options [3, 4].
Therefore, the melanocortin system [4] could provide a novel avenue to explore given its ability to exert anti-inflammatory effects and chondroprotection [5], although the receptor subtype involved is unclear.

Objectives: This study aims to assess the chondroprotective and anti-inflammatory effects of the selective human melanocortin MC1 receptor agonist BMS-470539 dihydrochloride and the selective human MC3 receptor agonist PG-990 on S-Nitroso-N-acetyl-DL-penicillamine (SNAP) activated chondrocytes.
Methods: The human chondrocytic cell-line C-20/A4 was seeded at 25.0 x 10^6 viable cells/ml (5 µl droplet was transferred into individual wells of a 96-well plate). Micromass cultures [6] were stimulated with SNAP (1.0 mM) and after 2h treated with Dexamethasone (1.0 µM), selective human melanocortin MC1 receptor agonist BMS-470539 dihydrochloride (10.0 µg/ml) or selective human melanocortin MC3 receptor agonist PG-990 (10.0 µg/ml) for 6h. Cell viability was determined by MTT assay, Caspase -3 and -7 activity determined by Caspase-Glo 3/7 apoptosis assay. Glycosaminoglycan (GAG) content determined by alcian blue staining and anti-inflammatory heme-oxygenase-1 (HO-1) protein expression was determined by western blot. Data are expressed as Mean ±S.E.M of n=4 samples repeated in triplicate. #$p \leq 0.05$ *vs* control or *$p \leq 0.05$ *vs* stimulus.
Results: Cell viability analysis showed SNAP stimulation caused a maximal cell death of 23% (#$p \leq 0.05$), Dexamethasone, BMS-470539 dihydrochloride and PG-990 inhibited cell death by 2%, 98% and 129% respectively (*$p \leq 0.05$). SNAP stimulation caused a significant increase in Caspase -3 and -7 activity, which was inhibited by Dexamethasone, BMS-470539 dihydrochloride and PG-990 by 8%, 5% and 19% respectively (*$p \leq 0.05$). GAG content was significantly reduced by SNAP by 29% (#$p \leq 0.05$), which was inhibited by Dexamethasone, BMS-470539 dihydrochloride and PG-990 by 1%, 3% and 14% respectively (*$p \leq 0.05$). SNAP also caused a significant decrease in HO-1 protein expression, which was increased by Dexamethasone, BMS-470539 dihydrochloride and PG-990 by a 1.0-fold, 1.1-fold and 2.1-fold increase respectively (*$p \leq 0.05$).
Conclusion: The selective human melanocortin MC3 receptor agonist PG-990 exhibited enhanced chondroprotection and modulation of inflammatory and tissue destructive mediators following SNAP activation compared to Dexamethasone and the selective human melanocortin MC1 receptor agonist BMS-470539 dihydrochloride. This suggests that melanocortin peptides display enhanced chondroprotective and anti-inflammatory effects at the MC3 receptor sub-type in this cell line.
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Disclosure of Interests: None declared
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AB0069 LORECIVIVINT (SM04690), AN INTRA-ARTICULAR, SMALL-MOLECULE CLK/DYRK1A INHIBITOR THAT MODULATES THE WNT PATHWAY, AS A POTENTIAL TREATMENT FOR MENISCAL INJURIES

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Background: Meniscal injuries, associated with pain, stiffness, and localized swelling, are the most common pathology of the knee with a prevalence of 61 per 100,000.[1] Meniscal damage is a frequent finding on MRI images of knee osteoarthritis (OA) [2]; while a meniscal tear can lead to knee OA, knee OA can also lead to a spontaneous meniscal tear.[3] Efforts to repair meniscal damage have been largely unsuccessful and do not prevent the progression of degenerative changes that lead to knee OA.[4] The Wnt signaling pathway has been shown to be regulated during meniscal development,[5,6] suggesting that manipulation of this pathway may influence the regenerative capacity of the meniscus. Lorecivivint (LOR; SM04690) is an intra-articular (IA), small-molecule CLK/DYRK1A inhibitor that modulates the Wnt pathway.
Objectives: LOR was evaluated in preclinical studies to determine its protective and anabolic effects in ex vivo explants and in a rat model of chemically induced inflammatory meniscus degeneration.
Methods: Effects of LOR (30 nM) on expression of matrix metalloproteinases (MMPs) in cultured rat menisci treated with IL-1B were measured by qPCR. In vivo, LOR activity was evaluated in a rat model of monosodium iodoacetate (MIA) injection-induced inflammatory meniscus degeneration. A single IA injection of MIA was immediately followed by a single IA injection of LOR (0.3 ug) or vehicle. Knees were harvested on Days 1, 4, and 11 and menisci were isolated. Anti-inflammatory effects were evaluated by measuring *TNFA* and *IL6* expression by qPCR. Meniscus protection was evaluated by qPCR for MMPs and aggrecanase and anabolic effects by qPCR for collagens.
Results: In ex vivo meniscal explants, LOR inhibited expression of *MMP1*, *MMP3*, and *MMP13* compared to DMSO (P<0.01). In vivo, LOR significantly decreased expression of these MMPs and aggrecanase (P<0.05) compared to vehicle in the rat model of inflammatory meniscus degeneration at Day 4 after MIA injection. In addition, LOR reduced expression of inflammatory cytokines *TNFA* and *IL6* at Day 4 compared to vehicle. Finally, LOR increased expression of collagen types I, II, and III at Day 11 after MIA injection.
Conclusion: LOR exhibited protective effects in the meniscus ex vivo and in vivo by reducing the expression of catabolic enzymes compared to control. Anti-inflammatory effects of LOR were demonstrated by inhibition of inflammatory cytokine expression. Compared to vehicle, LOR increased expression of collagens in vivo, indicating potential meniscal anabolic effects. These data support further investigation of LOR as a potential disease-modifying therapy for meniscal injuries.
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Disclosure of Interests: Tim Seo Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Vishal Deshmukh Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Yusuf Yazici Shareholder of: Samumed, LLC, Grant/research support from: Bristol-Myers Squibb, Celgene, and Genentech, Consultant of: Celgene and Sanofi, Employee of: Samumed, LLC
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AB0070 LORECIVIVINT (SM04690), A POTENTIAL DISEASE-MODIFYING TREATMENT FOR KNEE OSTEOARTHRITIS, DEMONSTRATED CARTILAGE-PROTECTIVE EFFECTS ON HUMAN OSTEOARTHRITIC EXPLANTS

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Background: Wnt pathway upregulation contributes to knee osteoarthritis (OA) through osteocyte differentiation, cartilage thinning, and inflammation. Lorecivivint (LOR; SM04690), a novel, small-molecule CLK/DYRK1A inhibitor that modulates the Wnt pathway, demonstrated disease-modifying potential for knee OA in preclinical studies.[1] However, the specific mechanisms by which LOR protects cartilage in knee OA are unclear.
Objectives: To evaluate the cartilage-protective effects of LOR on human OA explants from total knee replacement (TKR) donors.
Methods: Knee joint tissue from 22 TKR donors was obtained. IRB approval was obtained from Scripps Health. Cartilage was scored using the Outerbridge classification system based on gross appearance (grade 1=least-damaged tissue, grade 4=most-damaged tissue). Cartilage explants (4 mm in diameter) with Outerbridge grades 2–3 were harvested and cultured for 48 hours to reach metabolic stability. They were then treated with LOR (10 nM, 30 nM) or DMSO and stimulated with either IL-1β (10 ng/ml) or TNF-α (20 ng/ml)+oncostatin M (OM) (10 ng/ml) or left unstimulated. After 72 hours, supernatants and explants were collected. Gene expression of matrix metalloproteinases (MMPs) 1, 3, and 13 was measured by qPCR and protein levels of MMP-1, MMP-3, MMP-13, and thrombospondin-motif-containing disintegrins/metalloproteinases ADAMTS-4 and ADAMTS-5 were measured in supernatants by ELISA. Glycosaminoglycan (GAG) and nitric oxide (NO) levels were measured in supernatants using the dimethylmethylene blue assay and Griess assay, respectively. One-way ANOVA was used for multiple group comparisons.
Results: Treatment with IL-1β or TNF-α+OM led to statistically significant increases in gene expression of *MMP1*, *MMP3*, and *MMP13* and increased secretion of GAG, MMP-1, MMP-3, MMP-13, ADAMTS-4, ADAMTS-5, and NO in supernatants compared to unstimulated control. Treatment with LOR decreased both IL-1β-stimulated and TNF-α+OM-stimulated gene expression of *MMP1*, *MMP3*, and *MMP13* and secretion of GAG, MMP-1, MMP-3, MMP-13, ADAMTS-4, ADAMTS-5, and NO in supernatants compared to treatment with DMSO.
Conclusion: LOR demonstrated potent inhibition of cartilage catabolism enzyme production in human OA explants compared to controls. These cartilage-protective effects support the development of LOR as a potential disease-modifying treatment for knee OA. Human trials are ongoing.
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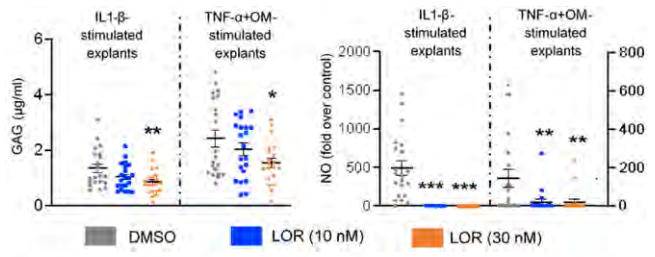


Figure 1. Effects of LOR on the quantity of the cartilage catabolism end products glycosaminoglycan (GAG) and nitric oxide (NO) in supernatants. Knee cartilage explant cultures stimulated with pro-inflammatory cytokines were subsequently treated with DMSO (control) or LOR as shown. N=22; *P<0.05, **P<0.01, ***P<0.001 vs. DMSO by one-way ANOVA.

Disclosure of Interests: Vishal Deshmukh Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Shawn Grogan: None declared, Tim Seo Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Deepti Bhat Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, William Bugbee: None declared, Darryl D'Lima: None declared, Yusuf Yazici Shareholder of: Samumed, LLC, Grant/research support from: Bristol-Myers Squibb, Celgene, and Genentech, Consultant of: Celgene and Sanofi, Employee of: Samumed, LLC
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AB0071 THERAPEUTIC EFFECTS OF BONE MARROW MESENCHYMAL STEM CELLS-DERIVED EXOSOMES ON OSTEOARTHRITIS

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Background: Mesenchymal stem cells (MSCs) have shown chondroprotective effects in clinical models of osteoarthritis (OA)[1].
Objectives: The study aimed to investigate the therapeutic potential of exosomes from human bone marrow MSCs (BM-MSCs) in alleviating OA.
Methods: The anterior cruciate ligament transection (ACLT) anddestabilization of the medial meniscus (DMM) surgery were performed on the knee joints of a rat OA model, followed by intra-articular injection of BM-MSCs or their exosomes. The beneficial effects were evaluated by histological staining, OARSI scores and micro-CT. Furthermore, BM-MSCs-derived exosomes were administrated to primary human chondrocytes to observe the functional and molecular alterations. In addition, lncRNA MEG3 were investigated in chondrocytes to explore the biological contents accounting for anti-OA effects of BM-MSCs-derived exosomes.
Results: Based on the observation in the rat OA model, both of BM-MSCs and BM-MSCs-derived exosomes alleviated cartilage destruction, reduced joint damage and restored the trabecular bone of OA rats. In addition, *in vitro* assays showed that BM-MSCs- exosomes could maintain the chondrocyte phenotype by increasing collagen type II synthesis and inhibiting IL-1β- induced senescence and apoptosis. Furthermore, exosomal lncRNA MEG3 also reduced the senescence and apoptosis of chondrocytes induced by IL-1β, indicating that lncRNA MEG3 might partially account for the anti-OA effects of BM-MSC exosomes.
Conclusion: The exosomes from BM-MSCs exerted beneficial therapeutic effects on OA by reducing the senescence and apoptosis of chondrocytes, suggesting that MSCs-derived exosomes might provide a candidate therapy for OA treatment.
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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.6040

AB0072 A MULTICOMPONENT MEDICATION PROMOTES CHONDROGENESIS AND REDUCES MMP-13 IN PRIMARY ARTICULAR CHONDROCYTES FROM KNEE OSTEOARTHRITIS PATIENTS IN VITRO

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Background: HE-1100 is a multicomponent medicinal product. Initial preclinical data potentially suggest a preventive effect on cartilage degradation.
Objectives: This study aims to understand the mode of action of HE-1100 on OA chondrocytes *in vitro*.
Methods: Primary chondrocytes were obtained from 10 knee osteoarthritis (OA) patients undergoing knee replacement surgery. The cultures were treated with 20% (v/v) HE-1100 or placebo. Samples were collected for subsequent RNA extraction using standard methods. The reads were generated with Illumina NextSeq5000 sequencer and aligned to the human reference genome (UCSC hg19) to generate the transcriptome. Differential expression analysis between HE-1100 and placebo was made in R using the DESeq2 package to identify the differentially expressed genes in the OA-associated regulatory pathways. The protein production of the selected genes was quantified by ELISA in 10 independent human OA chondrocytes cultures.
Results: According to the DESeq2 analysis, HE-1100 significantly modified the expression of 13 genes in OA chondrocytes by at least 10% with an adjusted p-value < 0.05: EGR1 (+93%), FOS (+87%), NR4A1 (+43%), DUSP1 (+18%), ZFP36 (+18%), ZFP36L1 (+14%), NFKBIZ (+16%) and CYR61 (+14%) were upregulated and ATF7IP (-10%), TXNIP (-11%), C10orf10 (-12%), CLEC3A (-12%) and MMP13 (-18%) were downregulated after 24h HE-1100 treatment. HE-1100 significantly increased (2.3 fold +/-1.2 after 24h, p=0.0444 and 2.3-fold +/-1.0 after 72h, p=0.0239) the CYR61 protein production by human OA chondrocytes. After 72h, HE-1100 slightly but not significantly increased aggrecan production by 14 ± 19 % (p=0.1117) and significantly increased type II collagen pro-peptide production by 27 ± 20 % (p=0.0147). For both time points CYR61 production by OA chondrocytes was positively and significantly correlated with aggrecan (r=0.66, p=0.0004) and type II collagen pro-peptide (r=0.64, p=0.0008) production. In alginate beads culture, pro-MMP-13 was significantly decreased by HE-1100 treated cultures from day 7 to day 14 (from -16 to -25 %, p<0.05) and from day 17 to 21 (-22 %, p=0.0331) in comparison to controls.
Conclusion: HE-1100 significantly modified the expression of DUSP1, C10orf10, ZFP36/L1 and CLEC3A, which are pathway mediators involved in MMP-13 expression and activation. Further, long-term (28 days) treatment with HE-1100 significantly reduced the production of pro-MMP-13, the inactive precursor of the metalloproteinase MMP-13 involved in type II collagen degradation. HE-1100 also promoted extracellular matrix formation probably through CYR61 production, a growth factor well correlated with type II collagen and aggrecan production.
References: /
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AB0073 BOSWELLIA SERRATA EXTRACT AND CURCUMIN INCREASE GDF15 PRODUCTION BY HUMAN PRIMARY OSTEOARTHRITIS CHONDROCYTES: A NEW MECHANISM OF ACTION

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Background: Boswellia serrata extract (BSE) and curcumin are used to relief symptoms in osteoarthritis (OA).
Objectives: This study aims to better understand the mode of action of these compounds on OA chondrocytes *in vitro*.
Methods: Therapeutic plasmatic concentrations of the different components of BSE correspond to an *in vitro* range from 25 to 100 µg/ml of total BSE (100 µg/ml of BSE corresponds to 9.2 µM of 11-keto-β-boswellic acid (KBA), 5.2 µM of acetylKBA, 22 µM de αBA, 34 µM de βBA, 4.4 µM de acetylαBA and 13.2 acetyl βBA), and between 2 to 10 µM for bioavaibility-increased curcumin. BSE (5-100 µg/ml) and curcumin (0.04 to 4 µg/ml corresponding to 0.1 to 10 µM) were tested separately on primary chondrocytes from 3 OA patients. Lactate Deshydrogenase LDH, nitrite (NO_2), interleukin (IL)-6 and Growth Differentiation Factor (GDF)15 were quantified in 72h-treated supernatant using enzyme activity, Griess reaction and ELISAs, respectively.
Results: No mortality was observed at the tested concentrations. BSE and curcumin both decreased concentration-dependently NO_2 and IL-6 production, and increased GDF15 production. For NO_2 production, the decrease was observed from 0.2 µg/ml of curcumin and 10 µg/ml of BSE. For IL-6 production,

the decrease was observed from 1 µg/ml for curcumin and 10 µg/ml for BSE. For GDF-15, the increase was observed from 2 µg/ml for curcumin and 50 µg/ml for BSE. Maximal effect was observed at 4 µg/ml for curcumin: -67% NO_2 ($p<0.0001$), -71% IL-6 ($p=0.0001$) and +80% GDF15 ($p<0.0001$) and at 100 µg/ml for BSE: -40% NO_2 ($p=0.0003$), -70% IL-6 ($p=0.0003$) and +73% for GDF15 ($p=0.0017$).

Conclusion: At therapeutic plasmatic concentrations, BSE and curcumin decreased the production of NO_2 and IL-6, two inflammatory mediators. Furthermore, BSE and curcumin enhanced GDF-15 production, an anti-inflammatory growth factor. GDF15 was first identified as Macrophage inhibitory cytokine-1 or NSAID-activated gene-1 (by a prostanoid-independent manner), and is known as a regulator of inflammatory, cell repair and apoptosis pathways. GDF-15 has pro-apoptotic and anti-tumorigenic activity in vitro and in vivo. It could represent a new pathway explaining the beneficial effects of BSE and the curcumin on synovium inflammation and cartilage degradation.

Disclosure of Interests: christelle sanchez: None declared, Jérémie Zappia: None declared, Yvan Dierckxsens Shareholder of: Tilman SA, Employee of: Tilman SA, Jean-Pierre Delcour: None declared, Yves Henrotin Grant/research support from: HEEL, TILMAN

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AB0074 KRÜPPEL-LIKE FACTOR 10 IS A IMPORTANT MODULATORY FACTOR OF CHONDROCYTE HYPERTROPHY IN DEVELOPING SKELETON

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Background: To investigate the functional role of KLF10 as a modulator of chondrocyte hypertrophy in developmental skeleton, the developmental characteristics in the long bone of KLF10 knockout mice and characteristics of MSCs from KLF10 KO mice were investigated regarding chondrogenesis and osteogenesis. Delayed long bone growth and delayed formation of primary ossification center were observed in an early embryonic stage in KLF10 KO mouse along with very low Ihh expression in epiphyseal plate. While the chondrogenic potential of mMSCs appeared normal or slight decrerased in KLF10 KO mice, osteogenesis and hypertrophy were extensively suppressed. KLF10 was found to be a mediator of chondrocyte hypertrophy in developing skeleton. Suppression of KLF10 may be considered as a new strategy for preventing hypertrophy in cartilage regeneration using MSCs.

Objectives: Investigated the functional role of KLF10 to present new insights into the transcriptional network regulating skeletal development and provide a novel strategy for preventing aberrant hypertrophic differentiation in cartilage regeneration strategies using MSCs.

Methods: Generation of KLF10 KO mice and genotyping / Skeletal preparations, embryo heights, and mineralized bone length measurements / Histological and Fluorescent Immunohistochemical Analysis / ALP staining and activity / Alizarin red staining / Von Kossa staining and calcium salts quantification / Isolation and Establishment of Mouse Clonal MSC Lines / Chondrogenic pellet culture and differentiation of mMSCs / DNA Quantification and GAG Contents Analysis / Rq-PCR Analysis / Statistics

Results: The overall results showed that mMSCs from KLF10 KO mice have significantly decreased osteogenic potential with very low Ihh expression while an increase in chondrogenic potential was not significant. In addition to Ihh promotor demonstrated in our previous study, KLF10 can activate Runx2 expression through its proximal-promoter region. Thus, KLF10 may indirectly stimulate Ihh expression upstream of Runx2 or directly bind to Ihh promoter and activate Ihh expression. As shown in this and out previous study, KLF10 also enhances Wnt/β-catenin signalling in MSCs. KLF10 modulates β-catenin sub-cellular localization and enhances Wnt signalling in osteoblasts.

Conclusion: In conclusion, primary ossification in KLF10 KO mice was critically delayed during early endochondral bone development. KLF10 KO inhibited hypertrophy via reduced Ihh expression in developing skeleton. TGF-β-induced hypertrophy was inhibited during chondrogenesis of KLF10 KO mMSCs. Our findings present new insights into the transcriptional-network system of skeletal development and provide a novel strategy for suppressing hypertrophy in cartilage tissue engineering.

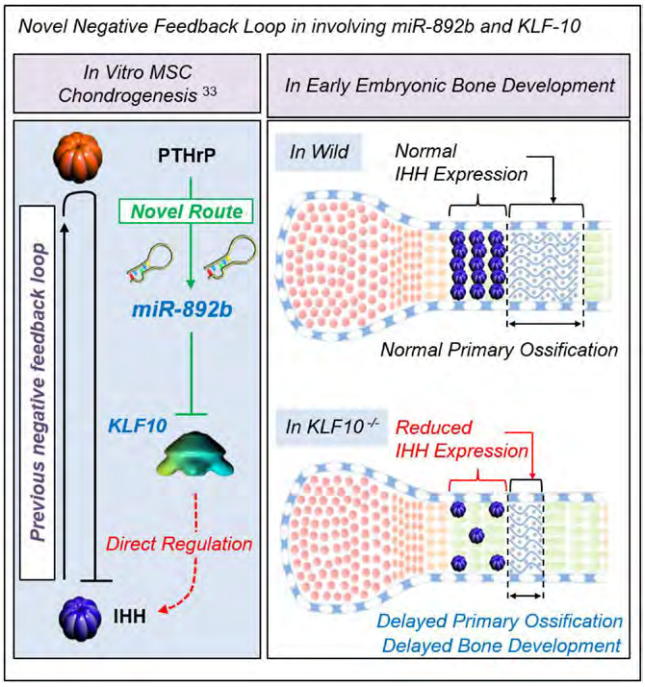


Figure.

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Disclosure of Interests: None declared

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AB0075 SYNOVIAL TISSUE MACROPHAGES ARE DOMINANTLY ALTERNATIVELY ACTIVATED IN PATIENTS WITH MATURE OSTEOARTHRITIS

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Background: Macrophages are abundant inflammatory cell type in the synovial membrane of knee osteoarthritis (OA) (1). Their quantity is associated with radiographic severity of knee OA and joint symptoms (2), while their functions are set in response to micro-environmental signals (3). Classically activated macrophages M1 support T helper 1 (Th1) driven pro-inflammatory reactions, while alternatively activated macrophages M2 strengthen Th2 inflammatory processes (3).

Objectives: To investigate activation status of synovial tissue macrophages in patients with mature OA in terms of M1 / M2 polarization.

Methods: Synovial tissue samples (6) with abundant lymphocyte infiltration were obtained during aloarthroplasty. Double immunofluorescence labeling was performed on paraffin-embedded synovial tissue sections using primary rabbit anti-macrophage CD68 mAb in combination with mouse anti-human antibodies directed toward CD3, arginase-1, TNF-alpha and IL-15. CD206 and CD163 were single labelled.

Results: CD68+ macrophages mostly co-expressed arginase-1 (4/6 samples), indicating their M2 orientation. Macrophages were placed in lining synovial tissue and nearby tissue-resident CD3+ cells. M2 markers CD206 and CD163 were

found in the area of macrophage interaction with T cells. CD68+ cells co-expressing TNF-alpha or IL-15 M1 markers were in minority in these synovial tissues. Lymphocyte infiltration was less abundant in remaining (2/6) synovial tissue samples.

Conclusion: Mature synovial tissue macrophages, equipped dominantly with arginase-1 are M2 oriented and might support Th2 immune response in surrounding T cells.

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Disclosure of Interests: None declared

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AB0076 SPATIAL VARIATIONS OF BONE MICROARCHITECTURE AND MINERALIZATION IN HIP OSTEOARTHRITIS AND OSTEOPOROSIS

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Background: The pattern of changes in bone microarchitecture and mineralisation are distinctly different in osteoarthritis (OA) and osteoporosis (OP). However, the pathogenesis of OA is closely related with OP, making subchondral bone a promising target for OA treatment [1]. A detailed comparison of subchondral bone in OA and OP may help understand the relationship of the two diseases.

Objectives: To carry out a comprehensive analysis of regional and compartmental variations in subchondral bone architecture and mineralisation in OA and OP.

Methods: Femoral heads were collected from patients undergoing hip arthroplasty surgeries for hip OA (N=16) or osteoporotic fracture (N=7). For OP group, osteochondral plugs were collected from fixed sites: anterior, posterior and superior. For OA group, an optimised sampling procedure, based on a new macroscopic grading method and modified OARSI microscopic grading system, was used to collect plugs from regions with varying severity of cartilage degradation. Plugs were scanned by micro CT (voxel size 4.88µm). Regions of interest for cortical plate (Ct) and trabecular bone (Tb) were segmented from reconstructed images using semi-automatic approach. Densitometric (tissue and bone mineral density: TMD and BMD) and architectural parameters (cortical plate thickness (Ct.Th), trabecular bone volume fraction (BV/TV), trabecular thickness (Tb.Th), etc.) were measured using commercially available software. Unmatched intergroup regional comparisons were made between OA microscopic grades (1 to 4) and OP. Matched intra-sample regional analysis was made between 'mild' (Grade 1 and/or 2) and 'severe' (Grade 3 and/or 4) OA. TMD was also subjected to paired comparison between cortical (Ct.TMD) and trabecular (Tb.TMD) compartments. Correlations between densitometric and architectural parameters were also explored.

Results: Regional analysis showed that Tb.TMD in OA Grade 3 and 4 was significantly lower than in OP and Grade 1 and 2, while Tb.TMD in OP was not significantly different from OA Grade 1 and 2 (Fig 1A, F). Ct.TMD in OA Grade 4 was significantly lower than in OP, but no difference was found in other comparisons (Fig 1B, G). For BMD of trabecular bone (Tb.BMD) and architectural parameters including BV/TV and Ct.Th, values for OA Grade 3 and/or 4 were significantly higher than OP and Grade 1 and/or 2, but the difference between OP and Grade 1 and 2 was not significant (Fig 1C-E, H-J). Compartmental analysis showed that Ct.TMD was significantly lower than Tb.TMD in all groups (Table I). Tb.TMD was inversely correlated with Tb.BMD and BV/TV in both OA and OP; Ct.TMD and Tb.TMD were inversely associated with Ct.Th and Tb.Th respectively in OA (Table II).

Conclusion: In both OA and OP, material density (TMD) of cortical plate was lower than trabecular bone. In hip OA, densitometric and architectural changes of subchondral cortical and trabecular bone were related to severity of cartilage degradation. In OA trabecular bone, the decrease in material density was compensated by increased bone volume, leading to higher apparent density (BMD); while in OP, loss of bone volume was correlated with, but not compensated by increased mineralisation, leading to lower apparent density.

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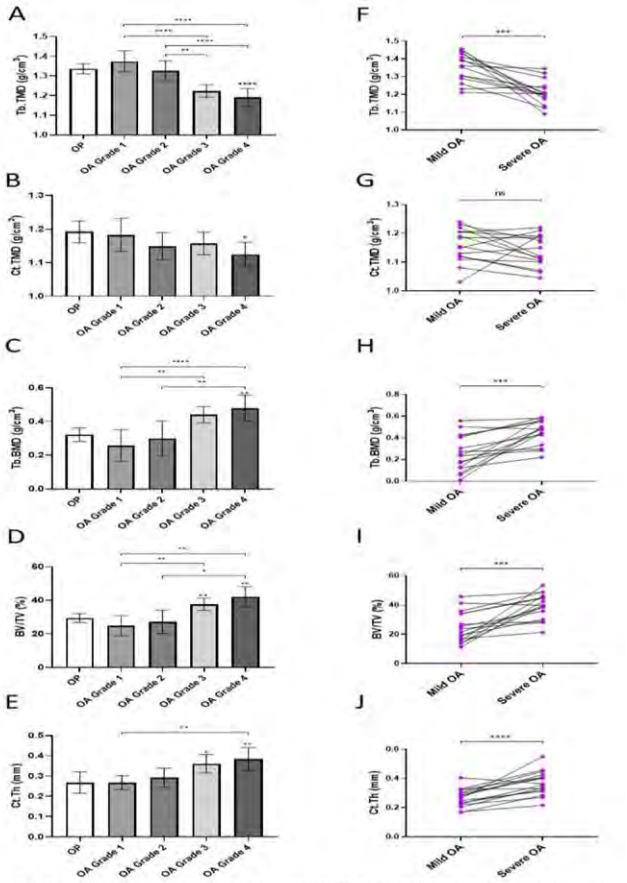


Figure 1. Regional comparisons of densitometric and architectural parameters. Left panel: unmatched inter-group (one-way ANOVA) analysis. Right panel: matched intra-sample (Paired T test) analysis. Significance level is indicated by * as follows: * P < 0.05; ** P < 0.01; *** P< 0.001; **** P < 0.0001.

Table 1. Compartmental comparison of TMD

	OP	OA Grade			
		1	2	3	4
Ct.TMD	1.19±0.07	1.18±0.09	1.15±0.06	1.16±0.06	1.12±0.07
Tb.TMD	1.34±0.06****	1.37±0.10****	1.33±0.07****	1.22±0.06*	1.19±0.09*

Table 2. Correlation analysis

	OP			OA		
	P	R^2	Slope	P	R^2	Slope
Tb.TMD - BV/TV	< 0.0001	0.69	-0.01	< 0.0001	0.84	-0.01
Tb.BMD - BV/TV	< 0.0001	0.95	0.02	< 0.0001	0.96	0.01
Tb.BMD - Tb.TMD	< 0.0001	0.60	-1.25	< 0.0001	0.81	-1.37
Ct.TMD - Ct.Th		ns		0.0009	0.19	-0.33
Tb.TMD - Tb.Th		ns		< 0.0001	0.55	-1.97

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AB0077 CONTRIBUTION OF NOTUM TO THE DEVELOPMENT OF OSTEOARTHRITIS

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Background: Osteoarthritis (OA) is a degenerative disease characterized by altered homeostasis of joint cartilage and bone, the functionality of which relies on chondrocytes and osteoblasts, that leads to the formation of a defective extracellular matrix (ECM). The ECM plays an essential role in bone biology as it provides the structure of cartilage which serves as a template for bone formation. Collagen X, main component of the ECM, has been described by our group as down-regulated in OA [1]. Our data also points to an important role of the Wnt pathway in OA [1,2]. Furthermore, Wnt proteins have been reported to inhibit chondrogenesis [3], and the Wnt pathway and its modulators have gained attention [4]. Glypicans (GPC1 to GPC6) and NOTUM, among others, have been identified as modulators of this pathway [5,6]. Notably, due to its highly specific inhibition of the Wnt pathway, NOTUM has been proposed as a therapeutic target in conditions with a high activity of the Wnt pathway is involved, such as OA [7].

Objectives: We hypothesize that modulators of the Wnt pathway are involved in the development of OA. The aim of this study is to evaluate the presence of Glypicans and NOTUM in the serum of OA patients and healthy individuals in order to determine whether significant differences exist and could clarify their likely involvement in OA.

Methods: Peripheral blood samples were obtained from OA patients during routine rheumatologist hospital visits. OA diagnosis was established according to the ACR criteria. Samples from healthy individuals were obtained from the local Blood Bank. In both cases, blood samples were centrifugated (2000*g*, 15 minutes, 10°C) and serum was obtained.

Quantitative ELISA assays for GPC1-6 and NOTUM were carried out using commercial kits (Human GPC1 ELISA Kit, #E-EL-H1710, Elabscience; Human GPC2 ELISA Kit, #E-EL-H1711, Elabscience; Human GPC3 ELISA Kit, #E-EL-H1712, Elabscience; Human GPC4 ELISA Kit, #E-EL-H1713, Elabscience; Human GPC5 ELISA Kit, #ELH-GPC5, RayBiotech; Human GPC6 ELISA Kit, #CSB-EL009708HU, Cusabio; Human Protein NOTUM homolog ELISA Kit, #EK3787, Sab Biotech) and measured in a plate reader (Heales MB-580,Shenzhen Heales Technology Development Co. Ltd.). Protein concentration in serum was calculated using GraphPad Prism 7 software. Differences between samples were analysed with Mann-Withney U test. Significance level set was $p<0.05$.

Results: Serum from 40 OA patients and 40 healthy donors were included in the study. There were no differences between groups (Table 1).

Table 1. Cohort description

	Control group (n=40)	OA group (n=40)
Age	66,82±5,75	69,59±11,24
Women (%)	32 (80%)	30 (75%)

Out of 7 proteins analyzed, only NOTUM showed a significant difference between healthy and OA groups ($Median_{OA}$=0.4451ng/mL, $Median_{CONTROL}$=0.8263ng/mL, p=0.0013). Besides, GPC4 showed an approaching formal significance ($Median_{OA}$=0.1254ng/mL, $Median_{CONTROL}$=0.1596ng/mL, p=0.0767). The rest of Glypicans analyzed showed no significance differences between groups (GPC1, $Median_{OA}$=0.1346ng/mL, $Median_{CONTROL}$=0.1190ng/mL, p=0.2379; GPC2, $Median_{OA}$=2.593ng/mL, $Median_{CONTROL}$=2.955ng/mL, p=0.7489; GPC3, $Median_{OA}$=2.024ng/mL, $Median_{CONTROL}$=1.422ng/mL, p=0.3574; GPC5, $Median_{OA}$=3.663ng/mL, $Median_{CONTROL}$=5.529ng/mL, p=0.8829; GPC6, $Median_{OA}$=0.3922ng/mL, $Median_{CONTROL}$=0.3558ng/mL, p=0.3212).

Conclusion: Our results suggest that low levels of NOTUM may contribute to the development of OA. The lack of this inhibitor promotes the activation of the Wnt pathway, high activity of which has been related with OA.

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AB0078

ANTI-FIBROTIC EFFECT OF DIFFERENT FUCOIDANS IN OSTEOATHRITIC FIBROBLAST-LIKE-SYNOVIOCYTES

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Background: Synovial fibrosis is a pathological process observed in several musculoskeletal disorders that contributes to articular pain and stiffness. It is characterized by the excessive deposition of extracellular matrix, as well as cell migration and proliferation, being TGF-β main inductor of these processes. Fucoidans are sulfated polysaccharide obtained mainly from various species of brown algae and brown seaweed such as Fucus vesiculosus, Undaria pinnatifida, or Macrocystis pyrifera. Recent studies show that fucoidans are promising candidates to address the symptoms of OA. Although a wide spectrum of biological activities has been registered in these polysaccharides, their properties vary between fucoidans from different species.

Objectives: Our aim was to evaluate and to compare the anti-fibrotic effects of different fucoidans on fibroblast-like synoviocytes (FLS).

Methods: FLS were isolated from OA patients. Primary cultured cells were treated with fucoidans from Fucus vesiculosus (FF), Undaria pinnatifida (FU) and Macrocystis pyrifera (FM) at 5, 30. To activate pro-fibrotic pathways, cells were stimulated with TGF-β and cell viability and proliferation were analyzed by MTT and BrdU assay, respectively. Then gene expression of extracellular matrix proteins, collagen I and III and fibronectin, as well as plod2b, gene coding for alterative splice-variant of lysyl hydroxylases LDH2b, were evaluated by RT-qPCR. The presence of fibrotic maker, alpha smooth muscle actin (α-sma), was analyzed by immunocytochemistry and intracellular collagen levels were assessed by picrosirius red staining. Wound-clousure and transwell cell invasion assay were also performed to evaluate the capacity of cell motility and invasiveness.

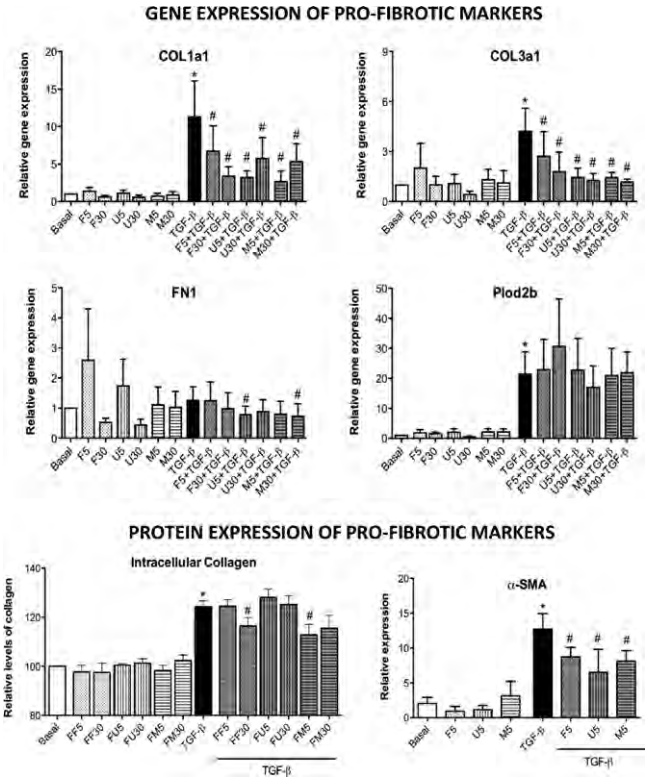


Figure 1. Measurement of expression of pro-fibrotic markers

Results: TGF-β induced a clear pro-fibrotic response (*Figure 1*). Cell proliferation induced by TGF-β was attenuated in the presence of all tested fucoidans. These polysaccharides also reduced the gene expression of TGF-β-elicited collagen I and III ($p< 0.05$), although FF failed to downregulate fibronectin levels and none of them showed modulation of plod2b expression. Results were confirmed at protein level. FF30 and FM5 reduced intracellular collagen accumulation induced by TGF-β ($p< 0.05$). Likewise, the expression of a-sma in TGFb-activated FLS was significantly diminished in the presence

of all fucoidans (p< 0.05). By scratch wound assay, we observed that TGF-b induced cell mobility to close the scratch, which was inhibited by all fucoidans. Similarly, FU and FM were also able to attenuated cell invasion after TGF stimulation. Additionally, we also detected that fucoidans showed anti-inflammatory effects in FLS as they reduced the NO production and IL-6 expression induced by IL-1.

Conclusion: Our results indicate a protective effect of fucoidans against activated pro-fibrotic pathways in fibroblast-like synoviocytes. However, we detected that these beneficial activities vary between fucoidans from different species and further studies are warranted.

Disclosure of Interests: Carlos Vaamonde García: None declared, Herminia Domínguez: None declared, Francisco J. Blanco Grant/research support from: Sanofi-Aventis, Lilly, Bristol MS, Amgen, Pfizer, Abbvie, TRB Chemedica International, Glaxo SmithKline, Archigen Biotech Limited, Novartis, Nichi-iko pharmaceutical Co, Genentech, Jannsen Research & Development, UCB Biopharma, Centrexion Theurapeutics, Celgene, Roche, Regeneron Pharmaceuticals Inc, Biohope, Corbus Pharmaceutical, Tedec Meiji Pharma, Kiniksa Pharmaceuticals, Ltd, Gilead Sciences Inc, Consultant of: Lilly, Bristol MS, Pfizer, Rosa Meijide Failde: None declared

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Bone diseases, including osteoporosis and osteoimmunology: aetiology, pathology and animal models

AB0079 ANGIOPOETIN-LIKE PROTEIN TYPE 3 AS AN INDICATOR OF RHEUMATOID INFLAMMATION AND RESORPTION OF BONE TISSUE IN RHEUMATOID ARTHRITIS

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Objectives: to study the role of type 3 angiopoietin-like protein (ANGPTL3) in the development of osteoporotic processes associated with inflammation in rheumatoid arthritis (RA).

Methods: 88 patients with RA were examined (women - 100%, average age - 54.2 ± 12 years old, disease duration - 11.2 ± 8.7 years, positive for rheumatoid factor (RF-IgM) - 72.7%, positive for anti-citrullinated protein antibody (ACPA) - 67%), DAS28 activity: remission - 21.6%, minimal - 11.4%, medium - 59.1%, high - 7.9%.), functional class: 0 - 1.1%, I - 25%, II - 65.9%, III - 8%). The study was conducted on a bone X-ray densitometer LUNAR DPX (GE, USA). Most of the patients (96.6%) were residents of cities, and 67 (76.1%) people lived in the metropolis (number of inhabitants more than 1 million people).

The concentration of ANGPTL3 in serum was determined by enzyme immunoassay using a commercial test system "Human Angiopoietin-like Protein 3 ELISA" ("Bio Vendor").

Results: Osteoporosis is found in 52 (59%) people. Increased ANGPTL3 values (> 445 ng / ml) were determined in 80.7% of cases. A significant positive correlation was found between the level of ANGPTL3 and the age of patients (r = 0.23, p = 0.032), the functional class (r = 0.214, p = 0.046), the presence of osteoporosis (r = 0.36, p = 0.039), living in the metropolis (r = 0.214, p = 0.046) and smoking (r = 0.31, p = 0.036), as well as a negative relationship with the duration of walking per day (r = -0.314, p = 0.003) and weekly (r = - 0.319, p = 0.002) was determined. The level of ANGPTL3 correlated with the activity of RA calculated by the DAS28-CRP index (p = 0.037), but not by the DAS28-ESR index (p = 0.135).

It is noteworthy that ANGPTL3 is closely related to changes in bone mineral density (BMD) in the femoral neck (BMD Total: r = -0.33, p = 0.042; BMD Troch: r = -0.36, p = 0.038; BMD Wards: r = -0.44, p = 0.009), but not in the spine (L1-L4) (p> 0.05). The lack of connection of ANGPTL3 with ACPA (p = 0.128) may indicate different mechanisms of influence on systemic BMD in patients with established RA.

Conclusion: ANGPTL3 can be used as an indicator of pathological processes associated with rheumatoid inflammation and the development of osteoporosis. Living in a metropolis, smoking and low physical exertion has an additional negative effect on resorptive processes in bone tissue in women with active RA.

Disclosure of Interests: None declared

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AB0080 A SYSTEM-LEVEL APPROACH IDENTIFIES A CRITICAL REGULATOR OF CHONDROSARCOMA PROGRESSION

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Background: Chondrosarcomas are cartilaginous tumors that constitute one-third of skeletal system cancers. Chondrosarcomas are capable of transitioning to highly metastatic and treatment-refractory states, resulting in significant patient mortality. However, the molecular events accompanying this behavior remain unknown.

Objectives: We aimed to uncover the molecular pathway underlying such tumor progression that confers a higher malignancy to chondrosarcoma.

Methods: We conducted unsupervised gene co-expression network analyses using transcriptomes of patients with chondrosarcoma and extracted a characteristic transcription network underlying chondrosarcoma malignancy. By implementing a system-level upstream analysis of this gene network, we identified the transcriptional factor as a key regulator governing chondrosarcoma progression. We unraveled the functional roles of the identified factor in promoting tumor growth and metastasis of chondrosarcomas in the context of their unique microenvironments.

Results: By conducting system-level upstream analysis, we identified a factor as a transcriptional regulator that governs the malignancy gene module. The identified factor was upregulated in chondrosarcoma biopsies associated with a high histological grade and conferred chondrosarcoma cells invasiveness and tumor-initiating capacity. In an orthotopic xenograft mouse model, the identified factor modulated local outgrowth and pulmonary metastasis of chondrosarcoma. Pharmacological inhibition of the identified factor in conjunction with the chemotherapy agents such as cisplatin or doxorubicin synergistically enhanced chondrosarcoma cell apoptosis and abolished malignant phenotypes of chondrosarcoma in mice.

Conclusion: Our study provides a proof of concept evidence that inhibiting the identified factor suppresses progression of chondrosarcoma and improves the efficacy of chemotherapy in cellular and pre-clinical levels. Taken together, we believe that our findings provide novel molecular insights for the development of new anti-cancer therapies to target chondrosarcomas.

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Disclosure of Interests: None declared

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AB0081 THE ROLE OF LOCAL BISPHOSPHONATES IN THE PRESERVATION OF THE BMD IN THE ZONE OF SURGICAL BONE DEFECT (ANIMAL STUDIES)

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Background: One of the reasons for failures in Arthroplasty is the preservation in the postoperative period in the bone adjacent to the implant of the prevalence of resorption over bone formation. The possibility of inhibition of resorption by bisphosphonates, including their local use in the composition of the biocomposite material, aggravates the situation due to the simultaneous oppression of bone formation. A low level of remodeling in these cases leads to a further loss of bone mass in the intervention zone.

Objectives: To evaluate in the experiment the effect of bisphosphonates in the biocomposite material on the bone mass both in the surgical intervention zone and in the segment as a whole.

Methods: The study was conducted as a comparison with the control. 60 females of white non-linear rats, body weight 130-150 g. were divided into 6 groups. In 3 groups, the defect of the tibia was filled with a biocomposite material in the form of a gel (patent No. 2325170) connected to various bisphosphonates Ibandronic acid (Bonviva), zoledronic acid (Aklasta), alendronate sodium (Fosamax) was used in conjunction with a non-demineralized lyophilized bone implant. Groups, the defect was filled with a non-demineralized lyophilized bone implant with biocomposite material without bisphosphonate, in the second control group, non-demineralized lyophils th e bone implants without biocomposite matreiala in tretey- defect is not filled.

Assessment of bone mineral density (BMD) in the intervention area and in the segment as a whole was performed using X-ray densitometry (Hologic, Small Animals Program Performing and Analyzing Small Animal Studies). Results Comparison (simple dispersion analysis) of the MIC of all groups using

bisphosphonates on the one hand, with the MIC of all control groups on the other hand, revealed significant differences (p <0.002).
Results: The analysis, using the paired t-test, the average MIC values in the combined group using bisphosphonates and the pooled control group, confirmed that the BMD in the zone of intervention in the bisphosphonate group was significantly higher than in the control: 0.320 ± 0.008 g / cm2, respectively, versus 0.285 ± 0.019 g / cm2 (p = 0.002). If the group was excluded from the analysis, where the defect was not filled, the tendency to differences remained: 0.320 ± 0.008 g / cm2 vs. 0.308 ± 0.002 g / cm2 (p = 0.11).
Mean BMDs of the whole segment with the use of bisphosphonates also proved to be significantly higher than in the control, both with the inclusion in the analysis of the group without replacement of the defect, and with its exception. Thus, when all control groups were included in the analysis, the mean MIC values in the group with bisphosphonates were 0.30 ± 0.01 g / cm2 vs. 0.272 ± 0.12 g / cm2 (p <0.001). When excluding from the analysis of the group without replacement of the defect, the MIC values were respectively: 0.307 ± 0.01 g / cm2 versus 0.285 ± 0.01 g / cm2 (p = 0.01).
Conclusion: Relative to the control, an increase in BMD in the group using bisphosphonates excludes the possibility of their negative impact on the process of bone formation. The marked positive bone balance confirms the ability of bisphosphonates to maintain the remodeling mechanism at the physiological level.
References: Local application of bisphosphonates, osteoplastic materials, biocomposite material, bone implant reconstruction, bone formation.
Disclosure of Interests: None declared
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Rheumatoid arthritis - aetiology, pathogenesis and animal models

AB0082 INHIBITION OF TGFβ SIGNALING USING SB-505124 BLOCKS TH17 DIFFERENTIATION AND RESTORES THE TH17/TREG BALANCE IN VIVO, BUT DOES NOT SUPPRESS EXPERIMENTAL ARTHRITIS

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Background: TGFβ is an important growth factor that promotes the differentiation of T helper 17 (Th17) as well as regulatory T-cells (Treg). Due to its dual role, the potential of TGFβ as therapeutic target is unclear.
Objectives: In this study we aimed to investigate the effect of inhibition of TGFβ signaling with the ALK5 inhibitor SB-505124 on human Th17 differentiation *in vitro*, on cytokine production by human rheumatoid arthritis (RA) synovial explants, and study the effects of local SB-505124 treatment *in vivo* during innate immune and Th17-driven experimental arthritis models.
Methods: Magnetic sorted naïve human T cells were differentiated into Th17 cells with CD3/CD28 activation beads, IL-2, TGFβ, IL-1β, IL-23, αIFNϒ and αIL-4 for 6 days. Human RA synovial biopsies were cultured for 24h w/o 5μM SB-505124, and supernatant was analyzed by Luminex. T cell-independent SCW arthritis and Th17-driven IL-1/mBSA arthritis were induced in C57Bl6, and mice were treated with SB-505124 by daily intra-articular injections from day 0-4.
Results: SB-505124 potently reduced human Th17 differentiation *in vitro* by decreasing IL-17 and RORϒt gene expression and IL-17 protein production. SB-505124 significantly suppressed IL-6 and TNFα protein production by human RA synovial explants. In addition, SB-505124 did not affect acute joint inflammation during SCW-arthritis (T-cell independent model). Interestingly, SB-505124 reduced Th17 levels in draining lymph nodes (dLN) during IL-1/mBSA arthritis while increased levels of Tregs were observed. Surprisingly, despite this skewed Th17/Treg balance, this did not result in suppression of joint inflammation and destruction in this Th17-driven arthritis model, whereas anti-IL-17 antibody treatment showed significant therapeutic effects.
Conclusion: We revealed suppressive effects of SB-505124 on human Th17 differentiation and the Th17/Treg balance in arthritic mice. However, SB-505124 did not suppress joint inflammation and destruction. This indicates that despite the importance of TGFβ in Th17 differentiation, targeting TGFβ signaling is not enough to suppress experimental arthritis.
Disclosure of Interests: None declared
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AB0083 STUDY OF THE ROLE OF ANGIOPOIETIN-LIKE PROTEIN TYPE 4 IN METABOLIC DISORDERS CAUSED BY INFLAMMATION IN RHEUMATOID ARTHRITIS

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Background:
Objectives: To assess the potential role of angiopoietin-like protein type 4 (ANGPTL4) in metabolic disorders caused by inflammation in rheumatoid arthritis (RA).
Methods: The study included 88 patients with significant RA, 64 patients with other rheumatic diseases (RD) (36 patients with osteoarthritis (OA); 28 patients with psoriatic arthritis (PsA); 17 patients with ankylosing spondylitis (AS)) and 32 healthy individuals. Estimation of ANGPTL4 was carried out by enzyme immunoassay using the commercial test system "RayBio Human ANGPTL4 ELISA Kit" (RayBiotech, USA) in blood serum. Levels of ESR, CRP, RF, antibodies to cyclic citrullinated peptide (anti-CCP) and modified vimentin (anti-MCV) in the ELISA test were determined for all patients with RA.
Results: The level of ANGPTL4 in the blood serum of patients with RA was significantly higher than in healthy people (p <0.001) and patients with other RD (p = 0.012 compared with OA; p = 0.046 with PsA; p = 0.008 with AS). ANGPTL4 indices in patients with RA correlated with the age of onset of RA (r = -0.658, p <0.001), disease activity according to DAS-28 (r = 0.449, p = 0.001), level of education (r = 0.235, p = 0.029), dose of glucocorticoid hormones (r = 0.321, p = 0.009) and methotrexate (r = -0.496, p = 0.05), the presence of osteopenia (r = 0.44), signs of kidney damage - proteinuria (r = 0.309, p = 0.037) and hypoalbuminemia (r = 0.386, p = 0.022), as well as with CRP levels (r = 0.488, p = 0.003), ESR (r = 0.458, p = 0.002), serum vitamin D (r = -0.417) and urinary calcium when recalculated to creatinine (r = 0.797, p = 0.032).
Patients with RA showed a high frequency of insulin resistance (according to the HOMA-IR index) (1.27 [0.84–1.62] in patients with RA; 0.76 [0.44–1.02] in healthy individuals; p <0.001) and the presence of coronary heart disease, as well as a positive correlation between disease activity (according to DAS-28) and insulin resistance (according to the HOMA-IR index) (p = 0.033).
Higher values of C-reactive protein (p = 0.04) and serum ANGPTL4 levels (p = 0.042, compared with patients with RA without type 2 diabetes; p = 0.026, compared with healthy individuals) were determined in the group of patients with RA with the presence of type 2 diabetes. ANGPTL4 acts as an inhibitor of lipoprotein lipase. His contribution to the development of dyslipidemia in RA can be demonstrated by the results we obtained when comparing groups of patients with / without signs of metabolic syndrome (MS). A positive correlation between ANGPTL4 and triglyceride levels (r = 0.42, p = 0.018) was found. An increase in the level of ANGPTL4 in blood serum of patients with RA with MS (p = 0.027 compared with RA without MS) can predict the development of cardiac pathology in this group of patients.
Conclusion: ANGPTL4 is directly involved in the regulation of glucose homeostasis, lipid metabolism, and insulin sensitivity. Cardiovascular diseases associated with atherosclerosis, insulin resistance and metabolic syndrome are known as the most common extraarticular manifestations of RA; the study of the role of ANGPTL4 in metabolic disorders caused by inflammation can show a new direction in the development of laboratory and therapeutic technologies in RA.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.4558

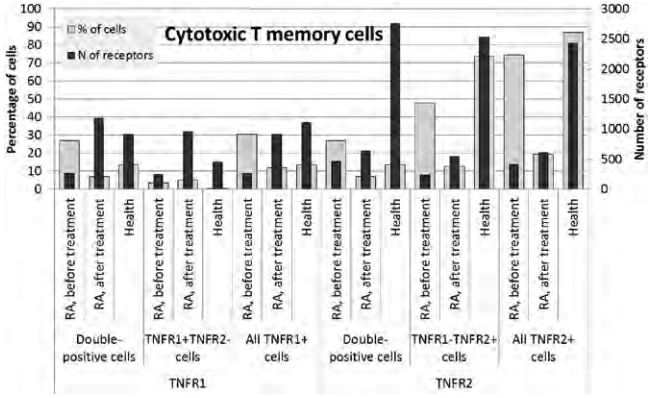
AB0084 TNF RECEPTORS PROFILE CHANGES ON CYTOTOXIC T CELLS SUBSETS IN RHEUMATOID ARTHRITIS ARE ASSOCIATED WITH EFFECTIVE TREATMENT

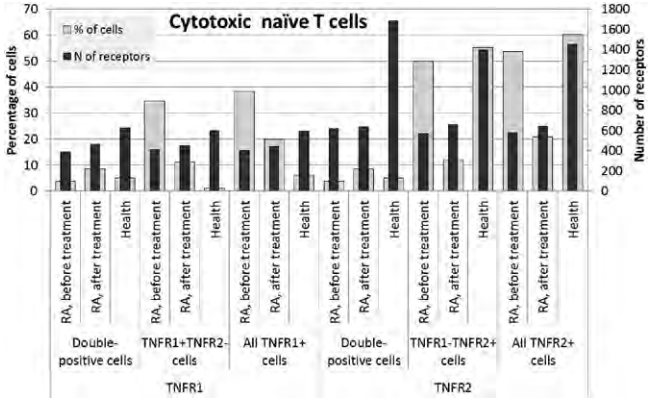
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Background: Previous studies of co-expression profile of receptors to tumor necrosis factor alpha (TNF) in rheumatoid arthritis (RA) have revealed a number of indicators associated with diseases activity with 93% sensitivity and 90% specificity. However, the ratio of receptors to cytokines remains poorly understood. However, the question of therapy effect and its effectiveness in various alteration of cytokine receptors balance remains under investigated.
Objectives: To evaluate the dynamics of co-expression and quantitative expression of type 1 and 2 receptors for TNF in the subpopulations of CD3+CD8+ cells associated with changes in disease severity before and after effective basic therapy.

Methods: Subanalysis of patients with high disease activity level successfully treated with methotrexate and oral glucocorticoids (n = 9) was performed. As a control group, we used data from 43 healthy donors, comparable by sex and age distribution. Subpopulations of cytotoxic T cells were studied, which were included in the final diagnostic models for differentiating different degrees of severity of RA: naive T cells and memory T cells. The dynamics of changes in the indicators of receptors number and proportion of cells expressing the corresponding receptor were compared.

Results: For naïve cytotoxic T cells, the main revealed feature was the relative stability of the number of expressed receptors (both TNFR1 and TNFR2), regardless of the therapy, while this number did not significantly differ from healthy ones for TNFR1 and was significantly lower for TNFR2 ($p < 0.05$ for all three fractions). At the same time, in terms of cell percentage, on the contrary, the therapy led to a change in total proportion of TNFR1 + cells closer to healthy donors indicators, and the proportion of TNFR2 + cells in the opposite direction.





For cytotoxic T memory cells, it was demonstrated that after successful treatment a significant increase in the number of type 1 receptors was observed, with a decrease in TNFR1+ cells proportion, while these indicators were close to the values of healthy donors. At the same time, healthy donors were characterized by a significantly higher expression of type 2 receptors in terms of cell density of receptors. It is noteworthy that with successful therapy, a slight increase in the number of TNFR2 was observed with a sharp decrease in the proportion of TNFR2+ cells ($p = 0.043$).

Conclusion: The balance of TNF receptor expression on cells actively involved in immunopathological processes affects both the density distribution of receptors on cells and co-expression in a subpopulation. Effective treatment of RA leads to equalization of the expression profile either by the percentage of cells or by the number of receptors, approaching the indicators of healthy donors, but not simultaneously.

Disclosure of Interests: None declared

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AB0085

MODULATION OF CIRCULATING SKELETAL STAMINAL CELLS IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH TOFACITINIB

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Background: Rheumatoid arthritis (AR) is an autoimmune systemic inflammatory disease characterized by chronic synovial inflammation resulting in bone damage and erosions, with consequently functional disability. Currently, attempts for regenerative therapies for osteo-cartilage pathologies have proved unsuccessful. Recently, a "pool" of skeletal stem cells (*hSSCs*: human skeletal stem cells) able to generating bone cells, has been identified in human bone (1).

Objectives: In light of these observations, we aim at characterizing skeletal stem cells in peripheral blood from RA patients candidate to Tofacitinib treatment.

Methods: In this pilot study 4 RA patients [4F; mean age 65 years; mean disease duration 19 years] candidate to Tofacitinib treatment and 4 healthy donors (HD), matched by gender and age, were enrolled. Blood samples were collected from each subject of the study, at baseline (T0) and for RA patients, after 1 month of Tofacitinib (T1), to evaluating *hSSC* (CD45-, CD146-, CD73+, PDPN+, CD164+) by flow cytometry. For this purpose, we performed on whole blood a negative magnetic selection for CD45 cells. Then, the eluate was labeled with antibodies anti CD146-PE, anti CD73-APC, anti CD164 - FITC and anti-Podoplanin (PDPN) PerCP/Cyanine5.5. The acquisition was performed using a FACS Calibur, which included 100,000 events per sample (Figure 1).

Results: The *hSSCs* percentage was significantly lower in RA patients than in HD ($p = 0.0286$). At T1, after treatment with Tofacitinib, mean *hSSCs* percentage significantly increased from 1.8% to 4.2 % ($p = 0.016$ vs RA T0) (Figure 2A). Correlation analysis showed a significant indirect relation between the percentage of *hSSC* and disease activity measured by $DAS28_{ESR}$, SDAI and CDAI (Figure 2B).

Conclusion: The results of this study demonstrate, for the first time, circulating skeletal stem cells and their reduced expression in active RA patients. Tofacitinib treatment leads to a significant increase in *hSSCs* percentage. This evidence opens up new perspectives on bone repair mechanisms and on deepening of current therapeutic strategies.

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Figure 1

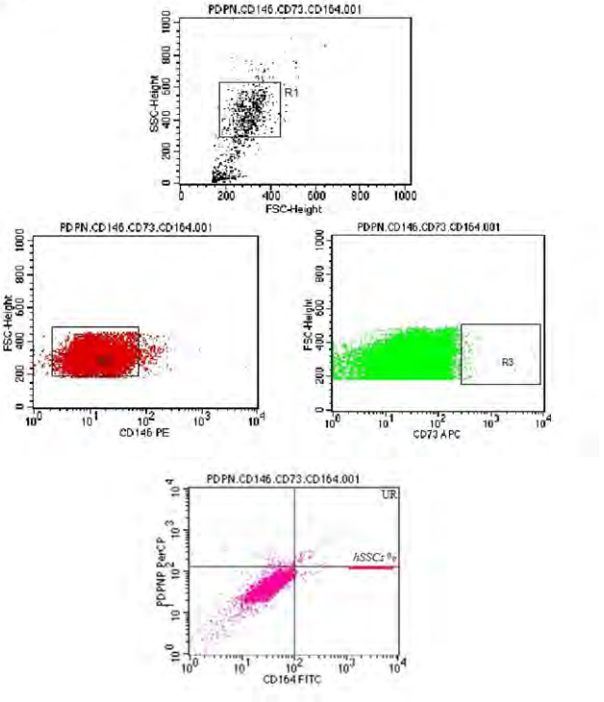


Figure 1. Flow cytometric strategy for hSSC analysis. Top panel represents the morphology of hSSCs (CD45-) cells. CD146- (R2) cells have been identified within of R1 region; CD73 + (R3) cells have been identified within of R2 region; CD164 + / PDPN + (%hSSCs in UpRigtht (UR) quadrant) cells have been identified within of R3 region.

Figure 2

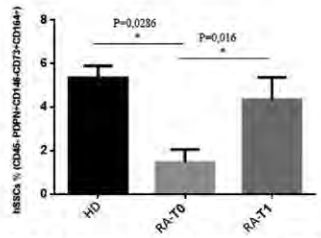


Figure 2A. Characterization of circulating skeletal stem cells. The histogram shows higher *hSSCs* percentage in HD than AR patients at T0. 1 month later Tofacitinib, *hSSCs* percentage increased significantly.

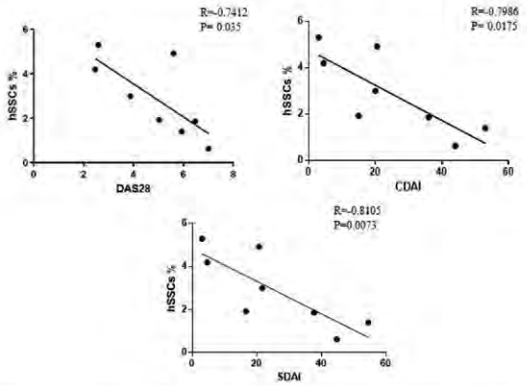


Figure 2B. Correlation between the percentage of *hSSC* cells and clinical parameters. The graphs show, in RA patients, a statistically significant inverse correlation between the percentage of circulating skeletal stem cells and disease activity indices.

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Disclosure of Interests: cristiana barbati: None declared, Francesca Romana Spinelli Grant/research support from: Pfizer, Consultant of: Novartis, Gilead, Lilly, Sanofi, Celgene, Speakers bureau: Lilly, cristina garufi: None declared, Ilaria Duca: None declared, fulvia ceccarelli: None declared, Tania Colasanti: None declared, Marta Vomero: None declared, cristiano alessandri Grant/research support from: Pfizer, Guido Valesini: None declared, fabrizio conti Speakers bureau: BMS, Lilly, Abbvie, Pfizer, Sanofi

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AB0086 NEW METHOD TO ASSESS SKELETAL MUSCLE ATROPHY IN COLLAGEN INDUCED ARTHRITIS (CIA) MODEL

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Background: Muscle quality in rheumatoid arthritis (RA) is a new concept that involves morphological features and function. A measurement that associates cell morphology with clinical and physical parameters has not been reported in the literature. CIA is a RA mice model characterized by loss of muscle mass similar to human RA, thereby it is a convenient model to study the disease impact in muscle physiology.

Objectives: Develop an index to measure the morphometry of muscle fibers and correlate the morphological features with the muscle functional performance in CIA.

Methods: 18 DBA/1J mice were induced using complete Freund's adjuvant and a booster after 18 days induction. Along experimental phase, we evaluated muscle strength using grip strength test and clinical disease score after onset of disease. 16 healthy mice were used as control. After 25 days CIA induction, 8 CIA and 8 controls were euthanized for muscle evaluation in mild disease and, at day 50, 8 CIA and 8 control mice were euthanized for evaluation in severe disease. Tibialis anterior were collected for myofiber histological analysis. Using the Image Pro Plus software (Media Cybernetics, China), we segmented muscle fibers and assessed its area and its regularity (the last through an index named Muscle Fiber Irregularity Index, MFII). The index works as a threshold to set to screen the degree of normal, atrophic and hypertrophic based on the morphometry if muscle fibers. Values are compared to area and shape of control (healthy) fibers. Frequency analysis and Pearson Correlations were used and statistical significance was considered as $p<0.05$.

Results: We found 1.5% atrophic muscle fibers in control animals. Mild CIA showed the same atrophic muscle fibers percentage compared to control. However, severe CIA showed 11.8% of atrophic muscle fibers. Decrease muscle strength in CIA over time were associated with a greater atrophic muscle fiber proportion ($r=-0.8$, $p=0.021$) and increased disease score ($r=-0.8$; $p=0.019$).

Conclusion: Here we developed a new, objective method applied to screen for muscle quality through the morphometry of muscle fibers. Muscular Morphometric Analysis (MusMA) has potential to be used in combination with clinical parameters in several human pathophysiological analysis. Besides that, we can speculate that although muscle strength is associated with atrophic cell percentage, loss of strength does not only depend of atrophy, but disease activity also seems to influence muscle strength reduction.

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Disclosure of Interests: Bárbara Bartikoski: None declared, Jordana Miranda de Souza Silva: None declared, Eduardo Chiela: None declared, Ricardo Xavier Consultant of: AbbVie, Pfizer, Novartis, Janssen, Eli Lilly, Roche

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AB0087 FEATURES OF ANTIPHOSPHOLIPID ANTIBODIES SPECTRUM IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Currently, some data have been accumulated on the participation of antiphospholipid antibodies (aPL) in the development of thrombotic complications in patients with autoimmune rheumatic diseases (ARD), in particular, in patients with systemic lupus erythematosus (SLE). The most studied aPL in this pathology are IgG and IgM antibodies to cardiolipin (aCL), anti-β2-glycoprotein 1 antibodies (aβ2-GP 1), lupus anticoagulant (LA). The participation of IgG and IgM antibodies to prothrombin (aPT) and to annexin V (aAnV), antibodies to oxidized low density lipoproteins (aOxLDL) in hypercoagulation and the development of thrombosis is also discussed. However, the studies focusing on the investigation of aPL in patients with rheumatoid arthritis (RA) are few.

Objectives: To estimate the levels and the frequency of occurrence of aPL in patients with RA in comparison to the SLE patients and the control group.

Methods: The study included 85 female patients with ARD (RA (n=45), mean age 43,0 (33,0; 52,0) years old, disease duration 9,0 (5,0; 13,0) years, disease activity (DAS28= 5,37 (4,69; 5,89) points) and SLE (n=40), mean age 33,5 (27,5; 44,5) years old, disease duration 8,0 (5,0; 14,5) years, disease activity SLEDAI-2K 7,0 (4,0; 11,5) points). Fifty four healthy women (mean age 38,5 (35,0; 46,0) years old) formed the control group.

The levels of antiphospholipid antibodies (IgG/IgM aCL, aβ2-GP 1, aAnV and aPT, aOxLDL) were determined with ELISA according to the instruction of a manufacturer. LA was determined by one-stage clotting assay using reagents for screening and confirmation (Technoclot LA Screen and Technoclot LA Confirm, Austria).

Results: The frequency of occurrence of elevated levels of all investigated aPL in patients with RA was similar to SLE patients and was revealed in 57,8% of cases for IgG/IgM aCL, 44,4% for IgG/IgM aβ2-GP-1, 26,7% for IgG/IgM aAnV, 8,9% for aPT, 52,6% for LA, 64,4% for aOxLDL. The patients with SLE had an increased levels of IgG/IgM aCL in 60,0% of cases, IgG/IgM aβ2-GP-1 in 57,5%, IgG/IgM aAnV in 15,0%, IgG/IgM aPT in 17,5%, high levels of LA in 68,8%, of IgG aOxLDL – in 80,0% of cases. The control group had a high levels of IgG/IgM aCL in 1,8%, IgG/IgM aβ2-GP-1 in 3,7%, IgG/IgM aAnV in 5,6%, IgG/IgM aPT in 1,8%, high levels of IgG aOxLDL – in 42,6% of cases. None of the controls had an increased level of LA. The frequency of occurrence of elevated levels of aPL and their mean levels in both groups of patients with ARD was higher as compare to the control group ($p<0,05$).

The mean levels of IgG aβ2-GP-1, LA, aOxLDL in SLE patients and mean levels of LA, aOxLDL in RA patients were above standard values but were similar in both groups. Moreover, the mean levels of IgG aCL, IgM aβ2-GP-1, IgG/IgM aAnV and aPT were comparable in patients with SLE and RA. However, the mean levels of IgM aCL in RA patients was higher than in SLE patients. This may indicate an increased autoimmune activity.

Simultaneous elevation in four types of aPL levels was observed in 4,4% patients with RA, in 2,5% - with SLE; simultaneous elevation in three types of aPL was reveled in 11,1% patients with RA, in 17,5% - with SLE; two types of aPL were increased in 35,6% patients with RA and 27,5% - with SLE. Only one type of elevated aPL levels (12,9%) was indentified in the control group.

Conclusion: Thus, patients with RA are characterized by a wide range of aPL. Qualitative and quantitative changes in the levels and types of autoantibodies in patients with RA have been established similar to those in SLE patients.

In patients with autoimmune rheumatic pathology, the presence of simultaneously elevated several types of aPL have been proved.

Disclosure of Interests: None declared
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AB0088 N6-METHYLADENOSINE-MODIFIED CIRC_0088194 PROMOTES MIGRATION AND INVASION OF RHEUMATOID ARTHRITIS FIBROBLAST-LIKE SYNOVIOCYTES THROUGH MIR-766-3P/MMP2 AXIS

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Background: Circular RNAs (circRNAs) participate in the initiation and progression of various diseases by miRNA sponges including postmenopausal osteoporosis[1], bladder cancer[2], and osteoarthritis (OA)[3]. However, the activity of circRNAs as "miRNA sponges" in rheumatoid arthritis (RA) has not been studied.

Objectives: To investigate whether circRNA acts as competing endogenous RNA to regulate pathological processes of RA, and whether the N6-methyladenosine (m^6A) modification affects Circ_0088194 stability in RA fibroblast-like synoviocytes (RA-FLSs).

Methods: CircRNA microarray analysis was conducted to characterize the expression profiles of circRNAs in 3 RA-FLSs and 3 osteoarthritis fibroblast-like synoviocytes (OA-FLSs). Methylated RNA immunoprecipitation was performed to validate the level of m^6A modification on Circ_0088194 in RA-FLSs and OA-FLSs. Dual-luciferase reporter assay, bioinformatics analysis, protein array analysis, and fluorescence in situ hybridization were employed to evaluate the interaction between Circ_0088194 and miR-766-3p, and between target miR-766-3p and matrix metalloproteinase 2 (MMP2).

Results: Overexpression of Circ_0088194 promoted the migration and invasion of RA-FLSs and increased MMP2 expression. The expression and function of miR-766-3p were inversely correlated with Circ_0088194, which sponged miR-766-3p to upregulate MMP2 expression. Although m^6A modification of Circ_0088194 exists in RA-FLSs and OA-FLSs, their level did not differ.

Conclusion: This study presents an important role of this novel circRNA as a sponge of miR-766-3p to promote RA-FLS migration and invasion by targeting MMP2. However, the modification might not affect Circ_0088194 stability in RA-FLSs and OA-FLSs. Therefore, Circ_0088194 may contribute to RA development and represent as an auspicious therapeutic target.

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Disclosure of Interests: None declared
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AB0089 THE ANALYSIS FOR THE INHIBITION OF ANGIOGENESIS BY JAK INHIBITOR

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Background: Many blood vessels are generated in the hyperplastic synovial tissue of patients with rheumatoid arthritis (RA), and lead to chronic tissue inflammation and joint destruction [1]. Janus kinase (JAK) family consisting of JAK1, JAK2, JAK3 and tyrosine kinase 2 (TYK2) are chain receptors which phosphorylate signal transducers and activators of transcription (STAT) and mediate inflammatory diseases including RA [2]. Nowadays, several JAK inhibitors such as Tofacitinib (TOF), Baricitinib (BAR) and Peficitinib (PEF) have been developed and demonstrated to have the inhibitory effects on inflammatory arthritis [3-5]. However, there were few reports concerning their effects on angiogenesis in vitro.

Objectives: The purpose of the present study is to investigate the influence of JAK inhibitors on angiogenesis of human umbilical vein endothelial cell (HUVEC) activated by vascular endothelial growth factor (VEGF).

Methods: The cell line of HUVECs were used for this study. The activity of proliferation and tube formation were analyzed by counting assay and tube formation assay, respectively.

In counting assay, HUVECs (5×10^4 cells/ml) were seeded onto 96-well cell culture plate with 20 ng/ml VEGF including various doses (0.1μM, 1μM, 5μM) of TOF, BAR or PEF. After 48 hours incubation at 37°C in a humidified atmosphere containing 5% CO_2, cell proliferation of each groups was assessed using cell counting kit. In tube formation assay, HUVECs (5×10^4 cells/ml) were treated with 20ng/ml VEGF including various dose (0.1μM, 1μM, 5μM) of TOF, BAR or PEF for 00 hours, then seeded onto 48-well plate applied with Matrigel. After 24 hours incubation on Matrigel, the capillary-like tube formation of each well was photographed using phase contrast microscopy. Tube formation were quantitated by measurement of the length of branch.

Results: HUVECs were activated in proliferation and tube formation by VEGF treatment. And, the proliferation and tube formation of HUVECs activated by VEGF were suppressed by All of TOF, BAR and PEF. In particular, TOF and PEF could suppress them highly.

Conclusion: This study showed the inhibitory effect of JAK inhibitors on proliferation and tube formation of HUVECs activated by VEGF. In particular, the angiogenesis of HUVECs activated by VEGF was highly suppressed by TOF and PEF. VEGF is reported to regulate the angiogenesis through multi JAK-STAT signaling pathways [6]. The inhibitory effects on angiogenesis of TOF, BAR and PEF might depend on the differences in their affinity for JAKs. VEGF has been shown to a have a central involvement in the angiogenic process in RA [7]. JAK inhibitors might suppress the angiogenesis in RA synovial tissues by inhibiting VEGF signaling.

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AB0090 DEATH RECEPTOR 3 REGULATES THE GENE EXPRESSIONS OF VARIOUS KEY MOLECULES IN RHEUMATOID SYNOVIAL FIBROBLASTS

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease that causes hyperplasia of synovial tissue. Death receptor 3 (DR3) is a tumor necrosis factor receptor and binds to TL1A, a member of the TNF family. DR3 is involved in the mechanism of cell proliferation and apoptosis through NF-κB signaling. Suppression of DR3 in rheumatoid synovial fibroblasts (RA-FLS) is associated with hyperplasia of rheumatoid synovial tissue [1]. We previously revealed the expression profiles regulated by TL1A, suggesting that TL1A might affect the pathogenesis of RA, including proliferation, regulation of B cells and T cells, inflammation, and cytokine processing [2].

Objectives: In this study, we investigated the gene expression profiles regulated by DR3 in RA-FLS to reveal how DR3 is involved in the pathogenesis of RA.

Methods: RA-FLS were from patients with RA. Four individual lines of primary cultured RA-FLS were incubated either with 1000 ng/ml of human DR3-Fc

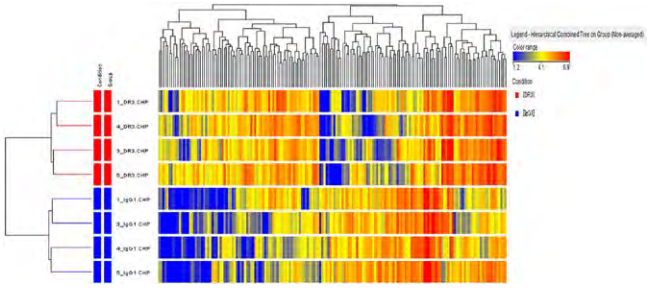
protein or 1000ng/ml of human IgG1 as a control for 12h. Gene expressions were detected by microarray assay.

Results: Microarray data analysis revealed that DR3 up-regulated or down-regulated the expression of various genes in RA-FLS (Figure). The function of regulated genes included protein-L-isoaspartate (D-aspartate) O-methyltransferase activity, carboxyl-O-methyltransferase activity, protein carboxyl O-methyltransferase activity, regulation of cilium assembly, O-methyltransferase activity, regulation of plasma membrane bounded cell projection assembly, regulation of cell projection assembly, regulation of organelle assembly, protein methyltransferase activity, and S-adenosylmethionine-dependent methyltransferase activity. The most up-regulated 2 genes by DR3 were KIAA1109 (KIAA1109), and adhesion G protein-coupled receptor A3 (ADGRA3). The most down-regulated 2 genes by DR3 were RNA exonuclease 2 (REXO2), and family with sequence similarity 120A (FAM120A).

Conclusion: In this study, we first revealed the expression profiles of genes regulated by DR3 in RA-FLS. KIAA1109/TENR/IL2/IL21 gene is strongly associated with RA in European descent populations [3]. ADGRA3 is a member of G protein-coupled receptors (GPCRs). GPCRs associates with the regulation of cytoskeletal organization, the cell adhesion and migration, cell proliferation and apoptosis, and cell differentiation [4]. Loss of REXO2 affects cell growth and morphology [5], and REXO2 was identified as a target gene for inflammatory bowel disease-associated variants [6]. FAM120A regulates activity of Src kinase to protect cells from oxidative stress-induced apoptosis [7]. DR3 regulates the gene expressions of various key molecules in RA-FLS and may affect the pathogenesis of RA by regulating gene expression of RA-FLS.

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AB0091 PD-1 AND GAL3 REGULATE OSTEOCLAST DEVELOPMENT IN RHEUMATOID ARTHRITIS

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Background: Bone erosions in rheumatoid arthritis (RA) is a major complication. Despite improved treatment, erosions still occur and progress. Therefore, a continuous investigation of the interplay between bone regulation and immune activity is needed.

Co-inhibitory receptors, like CTLA-4, participate in modulating osteoclast activity[1], and blocking these receptors in cancer treatment results in autoimmune disease[2]. Programmed death 1 (PD-1) is a central co-inhibitory receptor, also present in a soluble (s) form. We have previously shown that sPD-1 is associated with disease activity and reduced bone erosions in RA[3]. PD-1 and its ligands are glycosylated and the glycosylation affects signaling through the PD-1 pathway[4,5]. Galectins (GAL) bind to specific glycosylation patterns on glycoproteins by their carbonrecognition domain. Gal-3 can bind to multiple immune receptors shaping the immunological response[6].

Objectives: We aimed to investigate if PD-1 and GAL-3 modulate osteoclastogenesis in RA.

Methods: Plasma and synovial fluid (SF) samples were collected from patients with chronic (c) RA (>8 years of disease, n=14) SF and blood samples were obtained when patients presented with disease flare. Soluble PD-1 and GAL-3 were investigated by ELISA. GAL-3:PD-1 complexes were captured in an optimized ELISA using both GAL-3 and PD-1 antibodies. Surface plasmon resonance was used to evaluate on the binding properties between GAL-3 and PD-1, on a Biacore 3000. Lactose was used to block the potential binding. Cells from the synovial fluid (SFMC) were differentiated into osteoclasts with M-CSF and RANKL, recombinant human (rh) PD-1 and rhGAL-3 were added and osteoclast formation evaluated by TRAP in the supernatant.

Results: Soluble PD-1 and GAL-3 were present in both plasma and SF from cRA patient, and the ratio (PD-1/GAL-3) was increased in SF. PD-1:GAL-3 complexes were detected in both plasma and SF, with the highest concentration in SF. The binding between PD-1 and GAL-3 was confirmed by surface plasmon resonance analyses, with an estimated Kd of 5uM. Binding could be blocked by addition of lactose, confirming the binding to be glycan dependent. In SFMC osteoclast cultures, rhPD-1 and rhGAL-3 slightly decreased osteoclast formation evaluated by TRAP. However, combining rhPD-1 and rhGAL3 further potentiated the reduction in osteoclast formation by 37%.

Conclusion: We confirm glycan depended binding between the co-inhibitory receptor PD-1 and GAL-3. Both sPD-1 and Gal-3, and the PD-1:GAL-3 complexes, are upregulated in the inflamed joint at site of erosions. I*n vitro* RA culture demonstrates that GAL-3 potentiate the functions of PD-1 and reduces osteoclastogenesis. These findings indicate that the binding between Gal-3 and PD-1 could provide a novel target to control erosions in RA. Future *in vivo* studies on this interaction is needed.

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AB0092 FIBRIN ADHESION IS A PANNUS-INDEPENDENT MECHANISM OF CARTILAGE DEGENERATION IN RHEUMATOID ARTHRITIS

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Background: Current concepts of cartilage destruction in inflammatory arthritis include pannus infiltration by inflamed synovial tissue as well as direct detrimental effects of inflammatory cytokines and proteinases. Fibrin maintains chronic inflammatory processes in arthritis but has never been shown to be directly involved in cartilage damage occurring in rheumatoid arthritis (RA).

Objectives: To investigate fibrin-mediated cartilage degradation and the possible underlying mechanisms in arthritis.

Methods: Human cartilage samples were obtained from patients with RA undergoing joint replacement and investigated by H.E. and immunohistochemistry for cartilage damage and fibrin deposition. Cartilage explants from RA patients were incubated *in vitro* with autologous synoviocytes and assessed by immunohistochemistry for cell-adhesion and colocalization with fibrin. Experimental RA was studied in the RA murine model of adjuvant-induced arthritis (AIA), in wildtype (WT) and fibrinogen deficient ($Fg^{-/-}$) mice. Cartilage damage and chondro-synovial adhesion were analyzed by safranin-O staining and fibrin deposition by immunohistochemistry. Fibrinogen expression (*Fgα, Fgβ, Fg*$_{\gamma}$) was studied in murine primary chondrocytes by qRT-PCR. Cartilage explants were stained with alizarin-red staining and assessed for colocalization of calcific deposits and fibrin. Calcification of murine primary chondrocytes stimulated with secondary calciprotein particles (CPP) and treated with purified human plasma fibrinogen (100 µg/ml) was assessed by alizarin red staining and gene expression for chondrocytic differentiation (*Agg, Coll2, Coll10, Sox9, Runx2*), calcification (*Alpl, Ank, Anx5, Pc1, Pit1, Pit2*), and extracellular matrix remodeling (*Adamts4, Adamts5, Mmp3, Mmp13, Comp*) by qRT-PCR.

Results: Abundant fibrin deposition on cartilage co-localized and positively correlated with cartilage damage in knee joints of patients with RA. In the AIA model,

absence of fibrin deposition in $Fg^{-/-}$ mice was accompanied by significantly lower synovial inflammation, chondro-synovial adhesion and cartilage damage than in WT mice. Chondro-synovial adhesion correlated with cartilage damage in the WT and led to apparent mechanical stripping of the superficial cartilage, whilst this phenomenon was not observed in the $Fg^{-/-}$ mice. *In vitro*, autologous RA synoviocytes adhered to cartilage explants exclusively in the presence of fibrin deposition. Fibrinogen chains were not expressed by primary chondrocytes, indicating passive deposition from synovial fluid or tissue. In human RA cartilage explants, we found colocalization and a significant positive correlation between fibrin and calcific deposits. Fibrinogen caused exacerbated calcification in CPP-treated primary murine chondrocytes and induction of genes involved in chondrocyte calcification (*Pc1, Pit1*). Cartilage-oligomeric matrix protein (*Comp*) gene was also highly induced suggesting a pro-catabolic role of fibrinogen.

Conclusion: Fibrin deposition is an active trigger of cartilage degeneration in RA via induction of chondro-synovial adhesion (mechanical aspect) and induction of calcification (catabolic aspect). Newer therapeutic approaches may not merely focus on fibrinolysis but protect cartilage from fibrin-induced adhesion or calcification e.g. by fibrin-targeted immunotherapy.

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AB0093 PORPHYROMONAS GINGIVALIS - PERIODONTAL PATHOGEN WITH POTENTIAL ROLL IN RHEUMATOID ARTHRITIS

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Background: In recent literature, a strong association between periodontal disease (PD) and rheumatoid arthritis (RA) has been reported. PD is a common, progressive inflammatory disease, initiated by a bacterial infection that engages the supporting structures of the teeth and leads to tooth loss. A number of common features have been identified between PD and RA.One of the most important associations is the process of citrullination, which is caused by the production of PG specific enzyme so called Porphyromonas Gingivalis Peptydil Deminase (PPAD)

Objectives: The aim of the study was to show the incidence of PG in RA patients, and to compare it with patients with osteoarthritis (OA) and healthy controls (HC) and to evaluate the possible correlation between the presence of PG in patients with RA and the positivity of anti CCP and anti MCV antibodies in RA patients.

Methods: The study included 30 patients with RA which fulfilled RA classification criteria from 2010, 26 patients with osteoarthritis (OA) and 24 healthy controls. All participants were genetically analyzed for the presence of PG by Chelex®100 method and polymerase chain reaction (PCR), by isolating amplified sequences of DNA in a sub gingival biofilm taken from the deep periodontal pockets. The presence of anti CCP and anti MCV autoantibodies was detected in the sera of RA patients with ELISA test.

Results: The average ages of the patients in the 3 groups were as follows -51 years for RA, 52 for OA and 58 years for HC. Seventy two percent of RA patients were females.

Significantly higher levels of PG were found in the periodontal pockets of.RA patients.

Eighty percent of RA patients (80% or 24 RA patients) were PG positive in comparison with 35% of OA patients and 2% healthy controls.

Of the PG-positive RA patients, 83% had positive and 17% had anti-CCP negative test, while of the PG-negative patients, a positive anti-CCP test was present in 33% and a negative anti-CCP test was present in 67%.Accordingly, in PG-positive RA patients positive anti-MCV test was present in 79% and negative anti-MCV test was present in 21%, and in PG-negative RA patients anti-MCV test was positive in 17% and negative in 83% patients.

Table 1.

Patient's groups	RA	OA	HC	Significance
Porphyromonas gingivalis positive	24 (80%)	9 (35%)	7 (29%)	RA→OA ($p < 0.0001$)
Porphyromonas gingivalis negative	6 (24%)	17 (65%)	17(71%)	RA→HC ($p < 0.0001$)
				OA→HC (p 0,65)
Total	30	26	24	

Conclusion: The results of our study indicate that PG is found more frequently in periodontal pockets of patients with rheumatoid arthritis, which implies the important role of oral microbioma in RA pathogenesis, treatment and prevention.

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AB0094 FUNCTIONAL TREG CELLS MAY BE CONVERTED INTO T EFFECTOR PHENOTYPE ON EXPOSURE TO INFLAMMATORY MILIEU IN RHEUMATOID ARTHRITIS (RA) SYNOVIAL FLUID: IN-VITRO STUDY

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Background: The debate on functional versus numerical difference in T regulatory cell population among patients with Rheumatoid arthritis (RA) is not clear. Tregs expressing Inflammatory subset phenotype markers, such as Th1(cxcr3, Tbet) and Th17(ccr6,Rorϒ) are reported. (1) Though the reported numbers of synovial fluid tregs are higher in RA, (2) the fate of Tregs on entering the synovial inflammatory milieu from peripheral blood (PB) has not yet been investigated.

Objectives: To compare Treg frequencies in PB and synovial fluid between osteoarthritis (OA) and RA

To compare cytokine levels in PB and SF between OA and RA

To study the effect of autologous synovial fluid on RA and OA Treg isolated form peripheral blood

Methods: The Peripheral Blood (PB) and synovial fluid (SF) of RA (n=80) and OA (n=30) patients were analyzed for CD4+T-cell subset frequencies and phenotypes by flow cytometry. Cytokine concentrations in plasma and SF were measured by cytometric bead array. Tregs from 5 RA-PB and 5 OA-PB were isolated and cultured in autologous synovial fluid for 24 hrs. Phenotypic expression of Th1 and Th17 chemokines on the cell surface were analyzed by flow cytometry and expression levels of T-bet, RORγ and FOXP3 in those Treg cells were measured with quantitative real-time PCR (RT-qPCR).

Results: The PB and SF frequencies of Th1, Th17 and Tregs are shown in Table 1. The pro-inflammatory cytokines were high in the plasma and SF of RA but the anti-Inflammatory cytokines were similar (Fig 1.A&B). Treg cells were isolated from RA and OA PB and cultured in autologous SF for 24 hrs. RA Treg showed increased cell surface expression of CXCR3+ and CCR6+ (Fig 1C) and there was no difference in OA Treg. Gene expression studies showed an increased expression of T-bet, RORγ and decreased expression of Foxp3 in RA Tregs while there was no difference in OA Tregs before and after in-vitro culture (Fig 1D).

Table 1. Tcell subsets in Rheumatoid Arthritis and Osteoarthritis.

CD4 subtype	RA		OA	
	PB	SF	PB	SF
	N=80	N=30	N=30	N=30
Th1	26.65 ± 5.59	34.99 ± 1.30	25.97 ± 7.24	26.45 ± 1.87*
Th2	5.19 ± 1.9	16.36 ± 1.73	5.24 ± 2.15	1.44 ± 0.10*
Th17	14.05 ± 3.29	21.18 ± 2.04	10.81 ± 2.78*	2.45 ± 0.23*
Treg	10.68 ± 2.47	12.53 ± 2.10	11.162.95	13.04 ± 2.57

*P<0.05

Conclusion: Tregs in RA may be converted to Th1 and Th17 phenotype on exposure to inflammatory cytokine in the synovial fluid, thus losing their regulatory functions. Understanding factors influencing stability of Treg cells may help improve future therapeutics.

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Disclosure of Interests: None declared

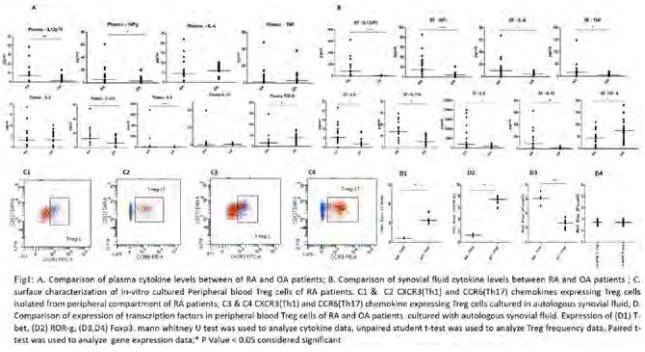


Fig1: A. Comparison of plasma cytokine levels between of RA and OA patients; B. Comparison of synovial fluid cytokine levels between RA and OA patients ; C. surface characterization of in-vitro cultured Peripheral blood Treg cells of RA patients. C1 & C2 CXCR3(Th1) and CCR6(Th17) chemokines expressing Treg cells isolated from peripheral compartment of RA patients; C3 & C4 CXCR3(Th1) and CCR6(Th17) chemokine expressing Treg cells cultured in autologous synovial fluid. D. Comparison of expression of transcription factors in peripheral blood Treg cells of RA and OA patients cultured with autologous synovial fluid. Expression of (D1) T-bet, (D2) RORγt, (D3,D4) Foxp3. mann whitney U test was used to analyze cytokine data, unpaired student t-test was used to analyze Treg frequency data, Paired t-test was used to analyze gene expression data;* P Value < 0.05 considered significant

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AB0095 PRECLINICAL CHARACTERIZATION OF CJ-15314, A HIGHLY SELECTIVE JAK1 INHIBITOR, FOR THE TREATMENT OF AUTOIMMUNE DISEASES

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Background: Janus kinases (JAK1, JAK2, JAK3, and TYK2) play critical roles in mediating various cytokine signaling, and has been developed as a target for autoimmune diseases such as RA. Tofacitinib, oral Pan-JAK inhibitor, demonstrated efficacy in RA patients, but its widespread use is limited by safety issues. Baricitinib, JAK1/2 inhibitor, is also known to interfere with the hematopoiesis system, such as anemia and thrombocytopenia associated with suppression of JAK2 signals. Therefore, it is necessary to develop a new potent compound that selectively inhibits JAK1 over JAK2, 3

Objectives: To identify the pharmacological characteristic based on efficacy of CJ-15314 as potent and selective JAK1 inhibitor for treatment of autoimmune disease.

Methods: In vitro, cell-based, kinase panel, Kd value and human whole blood assay were performed to determine the inhibition potency and selectivity for JAK subfamily kinases. In vivo therapeutic potential was evaluated by RA model including rat Adjuvant-Induced Arthritis (AIA) and collagen-induced arthritic (CIA). To confirm the possibility of further expansion into the autoimmune disease, BioMAP® Diversity PLUS® Panel was performed by discoverX.

Results: In vitro assay, CJ-15314 inhibited JAK kinase family in a concentration-dependent manner with IC50 values of 3.8 nM against JAK1, Selectivity for JAK1 over JAK2, 3 was approximately 18, 83 fold greater for CJ-15314. In 1mM ATP condition, CJ-15314 has been confirmed to have the highest JAK1 selectivity over competing drugs, under 1 mM ATP condition that reflects the physiological environment in the body. Similarly, Kd values has also confirmed the selectivity of JAK1, which is 10 fold higher than JAK2, 3. Accordingly, in human whole blood assays, CJ-15314 is 11 fold more potent against IL-6 induced pSTAT1 inhibition through JAK1 (IC50 value: 70 nM) than GM-CSF-induced pSTAT5 inhibition (JAK2) whereas baricitinib and filgotinib exhibited only 2 fold and 7 fold respectively.

In vivo efficacy model, CJ-15314 inhibited disease severity scores in a dose dependent manner. In the rat AIA model, CJ-15314 at 30 mg/kg dose showed 95.3% decrease in arthritis activity score, 51.2% in figotinib at 30 mg/kg, 97.7% showed baricitinib at 10 mg/kg. CJ-15314 showed superior anti-arthritic efficacy than filgotinib. CJ-15314 also minimally affected anemia-related parameters but not bricitinib end of the 2-week treatment. In the rat CIA model, like 10 mg/kg of bricitinib, 30 mg/kg of CJ-15314 also has a similar effect, with a significant reduction in histopathological scores.

In biomap diversity panel, CJ-15314 inhibited the expression of genes such as MCP-1, VCAM-1, IP-10, IL-8, IL-1, sTNF-α and HLA-DR confirming the possibility of expansion into other diseases beyond arthritis.

Conclusion: CJ-15314 is a highly selective JAK1 inhibitor, demonstrates robust efficacy in RA animal model and is good candidate for further development for inflammatory diseases.

* CJ-15314 is currently conducting a phase I trial in south Korea.

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AB0096 FCER1G GENE METHYLATION AND MIR-106/MIR-17 AS A NEW POTENTIAL EPIGENETIC MARKERS IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease that leads to joints destruction. One of the most important cytokine responsible for this process is interleukin 6 (IL-6). Fc receptor gamma chain (FcRγ), encoded by *FCER1G* gene, is responsible for neutrophils activation, phagocytosis, cell surface signaling pathway as well as IL-4, IL-6, IL-10 and tumor necrosis factor production. Epigenetic factors, including DNA methylation and micro-RNAs (miRs) expression regulate the genes expression on transcriptional and post-transcriptional mechanisms. There are miRs responsible for cytokines production, for example GU rich miRs, miR-106b and miR-155 were reported as associated with IL-6 overproduction.

Objectives: The aim of our study was to evaluate *FCER1G* gene methylation and miR-17 family members as epigenetic markers associated with RA, disease activity and IL-6 expression.

Methods: Bioinformatics analysis were applied to select the miRs with a possible target sites in a promoter region of *FCER1G* gene. The MiR-17 family members, including miR-17, miR-93 and miR-106b were selected for investigation.

A total of 74 individuals, 50 RA patients, 84% female, aged 53,7±12,3 years (mean±SD) and 24 healthy controls (HC), 87,5% female, aged 53±8,49 years were enrolled. RA patients were selected based on DAS-28 scoring. RA patients with high disease activity (DAS28 >5,1; 58%) and remission (≤2,6; 42%) were included in the analysis. DNA was extracted from a whole blood and miRs were extracted from plasma. Quantitative real-time PCR was use for analyze both methylation and expression levels. In a randomly selected samples (16 from high

disease activity group; 9 from remission and 19 from HC) the level of IL-6 in serum was evaluated.

Results: Patients with RA in comparison to HC have had a lower *FCER1G* methylation (0.98 [0.73-1.46] vs 1.96 [1.44-3], p<0.00001; median [interquartile range]) and miR-106b (0.79 [0.49-1.68] vs 1.54 [0.88-2.51], p=0.008) and miR-17 (1.26 [0.41-2.04] vs 2.44 [2.09-3.47], p=0.0001) expressions. No difference in methylation between high and remission RA groups was found. MiR-106b and miR-17 expressions were different between RA patients with high disease activity and remission (p=0.009 and p=0.003, respectively), however a high disease activity group was not different to HC (p=0.82 and p=0.12, respectively). Detailed results are presented in Table 1. A strong correlation between IL-6 levels and *FCER1G* methylation (r_s= -0.46) was found.

Table 1. Methylation and expression between patients divided by disease activity in compare to controls.

	High disease activity, n=29	Remission, n=21	HC, n=24
FCER1G methylation	1.11 [0.83-1.52]	0.96 [0.61-1.18]	1.96 [1.44-3]
miR-106b expression	1.36 [0.63-1.76]	0.54 [0.19-1.19]	1.54 [0.88-2.51]
miR-93 expression	0.63 [0.49-1.21]	0.59 [0.15-1.5]	1.03 [0.65-1.38]
miR-17 expression	1.46 [1.05-2.54]	0.34 [0.11-1.26]	2.44 [2.09-3.47]

Data are given by median [interquartile range]. FCER1G, Fc receptor gamma chain gene; HC, healthy controls; miR, micro-RNA; RA, rheumatoid arthritis patients.

Conclusion: *FCER1G* methylation was found as a new epigenetic marker of RA, which is independent of disease activity and may be associated with IL-6 production. Plasma miR-17 and miR-106b can be considered as a novel molecular biomarkers of disease severity in RA.

FcRγ may plays a significant role in RA pathogenesis and *FCER1G* gene methylation was found as a new, epigenetic and promising marker of RA.

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AB0097 TISSUE CYTOKINES AS NEW DIAGNOSTIC BIOMARKER OF BONE METABOLISM DISORDERS IN RHEUMATOID ARTHRITIS

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Background: Bone mineral density and proteins/peptides determination in blood and urine as markers of bone resorption and formation are currently used to diagnose osteoporosis (OP) and metabolic bone diseases. Recent evidence suggests that in RA changes in the secretion of hormones of white adipose tissue can be revealed [1,2,3,4].

Objectives: To study the clinical and diagnostic value of serum fetuin A, nesfatin, hemerin, leptin, adiponektin, resistin, visfatin determination in RA patients complicated by OP.

Methods: We examined 88 women with documented diagnosis of RA and mean disease duration of 6.56±0.88 years. We used EULAR/ARA 2010 criteria to diagnose the patients. Female patients with II degree of disease activity (DAS28), Steinbrocker stage II (erosive), rheumatoid factor- and anti-cyclic-citrullinated peptide antibody-positive were prevalent. We excluded patients who had surgery or developed an infection within the last 8 weeks, pregnant and breast-feeding women, those with severe heart, liver or kidney disease, immune deficiency, leukopenia or chronic infection.

A control group of 45 healthy females aged of 25 and 59 years were included in the study. There were no reported findings of joint pain and RA symptoms in the group. The groups were adjusted for age (p>0.05) and showed no statistically significant differences.

We measured serum fetuin A, nesfatin, hemerin, leptin, adiponektin, resistin, visfatin levels (μg/ml) using ELISA commercial test systems. We used spectrophotometer with wavelength of 450 nm to detect the test results («Multiskan» immunoenzyme analyzer, Finland). We plotted a curve using computer software. We diagnosed OP using dual-energy X-ray absorptiometry with LUNAR DPX PRO (GE, USA).

Results: At the first stage, the level of pro-inflammatory cytokines was studied in a group of healthy individuals. Then, the reference values of these indicators were measured as M ± 2δ. Patients with OP and RA had significantly higher levels of serum pro-inflammatory cytokines (p<0.001). For example, mean serum Adiponectin levels in RA patients who had normal bone density and had no OP were 35.21±0.6 μg/ml. Mean serum Adiponectin levels in RA/OP patients with low bone mineral density were 52.42±0.69 μg/ml. Adiponectin levels of 44 μg/ml and higher were associated with osteoporosis. Adiponectin levels of 43.9 μg/ml and lower were associated with normal bone density. Other pro-inflammatory cytokines have demonstrated similar dynamics of level serum.

Conclusion: Thus, we revealed that fetuin A, nesfatin, hemerin, leptin, adiponektin, resistin, visfatin levels depend on osteoporosis presence in RA patients. The test may be used to reduce the risk of low-energy fractures and to improve the quality of life in RA.

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AB0098 THE EFFECT OF MALT1-DEFICIENCY ON THE EFFECTOR PHASE OF EXPERIMENTAL AUTOIMMUNE ARTHRITIS

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Background: The paracaspase Malt1 is a cysteine protease, which forms a complex leading to the activation of the in proinflammatory transcription factor NF-κB in lymphocytes with CARMA1 and Bcl10. Previously, we showed that the myeloid equivalent of CARMA1, Card9 is important in neutrophils in Fcγ receptor-mediated cytokine release together with Bcl10 and Malt1. In line with these findings, we observed a significant decrease in the severity of autoantibody-triggered arthritis in the absence of Card9 and Bcl10.

Objectives: Our aim was to directly investigate whether the genetic deficiency of Malt1, the third component of the complex altered the process of the K/BxN serum transfer arthritis (that resembles to the effector phase of rheumatoid arthritis).

Methods: We used wild type and Malt1$^{-/-}$ mice for our experiments. Autoantibody-mediated arthritis was induced by a single intraperitoneal injection of K/BxN serum. Clinical signs of joint inflammation were scored on a scale based on the cardinal inflammatory clues for two weeks. Ankle thickness was measured by a spring-loaded caliper.

Results: Similar to the deficiency of the other two components of the complex, Malt1$^{-/-}$ mice showed a partial, but significant decrease in the macroscopic joint inflammation compared to arthritic serum-treated wild type animals during the entire experimental process. In line with this phenomenon, Malt1$^{-/-}$ animals had reduced autoantibody-triggered ankle thickening.

Conclusion: Our results show that Malt1 seems to be an important molecule in the development and progression of experimental autoantibody-induced arthritis in mice, highlighting the role of the molecule as a potential therapeutic target in the future.
Disclosure of Interests: None declared
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AB0099 METHOTREXATE REDUCES THE INVASIVE ACTIVITIES OF PRIMARY RA SYNOVIAL FIBROBLASTS

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Background: Rheumatoid Arthritis synovial fibroblasts (RASFs) are key player in tissue destruction via the production of a wide range of chemical reactions in the joint with high growth rate and resistance to mortality [1]. Methotrexate (MTX) is a dihydrofolate reductase inhibitor that attenuates inflammation within joints resulting in reduced cartilage and bone damage and is the anchor therapy for RA. Its mechanisms of action are thought to differ from its anti-proliferative effects and are known to include increased adenosine release (2), but may also involve alterations in intracellular methyl donor status resulting in alteration in DNA methylation and gene expression.
Objectives: To investigate the effects of MTX on RASFs auto-aggressive activities, including invasion, migration, proliferation and apoptosis.
Methods: RASF were derived from knee biopsies of RA patients taken at arthroscopy (n=9). Matrigel chambers were used to measure invasive activities. The cells were incubated with DMSO (control), 1μM or 10μM MTX for 96 hours. Wound healing (scratch assays) were used to measure migration. Proliferation and apoptosis was determined using BrdU and caspase-3/7 assays respectively. Significance was determined via repeated measures ANOVA using SPSS software.
Results: Incubation with MTX resulted in significantly reduced invasive activity compared with DMSO control; 1μM (35%, p=0.006) and 10μM (58%, p=0.002) in paired samples. However MTX did not have significant effects on RASF migration, apoptosis or proliferation at either concentration.
Conclusion: Our data reveals that MTX reduces the invasive potential of RASFs in vitro, this effect may contribute to the clinical efficacy of this agent. Further investigation will involve epigenome-wide methylation to determine if the DNA methylome of RASFs is altered by MTX.
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AB0100 PHENOTYPIC AND FUNCTIONAL CHARACTERIZATION OF SYNOVIAL FLUID-DERIVED FIBROBLAST-LIKE SYNOVIOCYTES IN RHEUMATOID ARTHRITIS

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Background: Fibroblast-like synoviocytes (FLS) are central cellular components in persistent inflammatory joint diseases such as rheumatoid arthritis (RA). Pathological subsets of FLS have been identified from synovial tissue. However, the synovial tissue obtained from arthroplasty procedures is acquired at late disease stages and the cellular yield obtained from synovial tissue biopsies is fairly low. Collectively, challenging the robustness of human RA *in vivo* and *in vitro* models. FLS obtained from the synovial fluid (SF-FLS) are proposed as an alternative source of FLS, but a detailed phenotypical and functional characterization of FLS subsets from the synovial fluid has not been performed.
Objectives: The aim of this study was to determine the phenotypical and functional characteristics of synovial fluid-derived fibroblast-like synoviocytes in rheumatoid arthritis.
Methods: In the present study, paired peripheral blood mononuclear cells (PBMC) and SF-FLS from patients with RA were obtained (n=7). FLS were isolated from the synovial fluid by a strict trypsinization protocol[1] and their cellular characteristics and functionality were evaluated at passage 4. Monocultures (SF-FLS) and autologous co-cultures (SF-FLS and PBMC) were established from five patients with RA and subsequently evaluated by flow cytometry, Western blotting and multiplex immunoassays. Human cartilage-sponges (n=3) with SF-FLS and without SF-FLS (n=3) were co-implanted subcutaneously in SCID mice (n=15), mice with only cell-free human cartilage-sponges were used as controls (n=12). After 45 days, the implants were evaluated using stained sections to determine the SF-FLS invasion score based on perichondrocytic cartilage degradation. Data are expressed as median (25-75 percentile). P-values <0.05 were considered statistically significant.
Results: The homogeneous subpopulations of FLS, isolated from the synovial fluid, were negative for CD34 and CD45 [98.9%, (97.5-99.7]) and positive for Thy-1 and PDPN [94.6%, (79.9-97.4]). Without stimulation, RA SF-FLS showed high and comparable levels of NFκB related pathway proteins and secreted multiple pro-inflammatory cytokines and chemokines dominated by IL-6 [2648 pg/mL, (1327-6116)] and MCP-1 [2458 pg/mL, (692-8719)]. SF-FLS increased their ICAM-1 and HLA-DR expression after encountering autologous PBMCs (p<0.01), (p<0.05). Further, SF-FLS and PBMC interacted synergistically in a co-culture model of RA and significantly increasing the secretion of several cytokines (IL-1β, IL-2, IL-6, (p<0.01)) and a chemokine (MCP-1, (p<0.01)). The invasion score of the human SF-FLS *in vivo* was at primary site, [1.6, (1.3-1.7)] and contralateral implantation site [1.5, (1.1-2.2)]. The invasion score of the human SF-FLS-containing implants both at primary and contralateral site were significantly higher compared with cartilage-sponges evaluated from SF-FLS-free control mice (p<0001).
Conclusion: This phenotypical and functional characterization of SF-FLS, acquired and activated at the site of pathology, lays a foundation for establishing *in vivo* and *in vitro* FLS models. These FLS models will be beneficial in our understanding of the role of this cellular subset in arthritis and for characterization of drugs specifically targeting this pathological RA FLS subset.
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Disclosure of Interests: Ditte Køster: None declared, Johanne Hovgaard Egedal: None declared, Malene Hvid: None declared, Martin Roelsgaard Jakobsen: None declared, Ulf Müller-Ladner Speakers bureau: Biogen, Bent Deleuran: None declared, Tue Wenzel Kragstrup Shareholder of: iBio Tech ApS, Consultant of: Bristol-Myers Squibb, Speakers bureau: TWK has engaged in educational activities talking about immunology in rheumatic diseases receiving speaking fees from Pfizer, Bristol-Myers Squibb, Eli Lilly, Novartis, and UCB., Elena Neumann: None declared, Morten Aagaard Nielsen: None declared
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AB0101 ASSOCIATION OF FETUIN-A SERUM LEVEL AND GLUCOCORTICOIDS INTAKE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Fetuin-A (FA) is a pluripotential glycoprotein, which plays an important role in bone turnover [1], inflammation, metabolic diseases [2] and etc. Several studies demonstrated association between FA serum level and rheumatoid arthritis (RA) severity and disease activity [3], however, there was made a suggestion that observed associations were due to glucocorticoids intake [4].
Objectives: To study the association of serum FA levels, glucocorticoids intake and RA activity.
Methods: 81 patients with RA verified by ACR/EULAR 2010 criteria were enrolled in our study. 43 patients were under glucocorticoid therapy with mean cumulative dose 7899±9029,4 mg (hereinafter M±SD) and 38 patients were not. DAS28 index was calculated to determine RA activity. FA serum concentrations were measured by ELISA. Correlations between serum FA levels and RA activity were assessed in each group. Statistic analysis was performed using software package "Statistica 10.0".
Results: The mean level of serum FA was 760,72±112,56 µg/ml. There was a negative correlation between FA serum level and DAS28 index (r=-0,433; p<0,0001) when calculated among all patients. We observed positive correlation between FA serum level and cumulative dosage of glucocorticoids (r=0,297; p=0,008). At the same time FA serum level and DAS28 index were correlated negatively in patients who were under glucocorticoid therapy (r=-0,419; p<0,0001) and were not (r=-0,559; p=0,001).
Conclusion: Serum FA level correlates with RA disease activity and glucocorticoids intake. However, the association between FA serum level and RA disease activity was independent of glucocorticoids intake in our study.
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AB0102 SPECIALIZED PRO-RESOLVING MEDIATOR RECEPTORS AS INFLAMMATORY RESOLUTION BIOMARKERS IN RHEUMATOID ARTHRITIS

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Background: The regulation of inflammation is a dynamic process involving several molecules as lipid mediators. The Specialized Pro-resolving Mediators (SPMs), such as Resolvin (RvD and RvE), Protectins, Maresins and Lipoxin A4 (LXA4), are bioactive metabolites of omega-3 and omega-6 fatty acids which drive inflammatory resolution phase and promote tissue repair. ERV, ALX/FPR2 and BLT1 are SPM receptors. Although in Rheumatoid Arthritis (RA) lipid mediators role within pathophysiology is under definition, studies on SPMs receptors role are still lacking in this disease.
Objectives: Purpose of this study is to define ERV, ALX/FPR2 and BLT1 expression in blood derived leukocytes and synovial cells and to correlate it to disease activity to define SPM receptors ad inflammatory resolution biomarkers in RA patients.
Methods: A cohort of 52 RA patients was enrolled in the study of which 40 with active disease (DAS28= 5,35 (5,18-6,40)) and 12 in sustained remission status (DAS28= 2,1 (1,83-2,42)). Each enrolled patient underwent peripheral blood (PB) drawing and 46 of them underwent US-guided synovial tissue (ST) biopsy. FACS gating strategy was used for PB and ST processing to evaluate percentage of positive cells and the mean fluorescence intensity (MFI) of ERV$^+$, ALX/FPR2$^+$ and BLT1$^+$ in CD45$^+$CD3$^+$, CD45$^+$CD19$^+$ for PB and ST, CD45$^+$CD14$^+$ and neutrophils for PB only and CD45$^-$CD90$^+$, CD45$^+$CD64$^+$CD11b$^+$ macrophages (distinct in CD206$^+$ and CD206$^-$ subpopulations) for ST only. Each included ST was stained with haematoxylin/eosin and categorized by a pathologist, blinded to clinical characteristics, using the Krenn Score (KS) to assess ST inflammation degree. As control group, 11 undifferentiated peripheral inflammatory arthritis (UPIA) patients were enrolled in the study.
Results: Considering the whole RA cohort, DAS28 inversely correlated with BLT1$^+$ positive cells on ST-derived CD45$^+$ (r= -0.48; p= 0.048), CD3$^+$ (r= -0.56; p= 0.019) and CD19$^+$ (r= -0.49; p= 0.042) cells, in contrast with CD90$^+$ (r= 0.50; p= 0.041) cells. Similarly, both DAS28 and KS inversely correlated with ALX/FPR2$^+$ positive cells in ST-derived CD45$^+$ (r= -0.42, p= 0.050 and r= -0,41, p= 0,046 respectively) cells. Evaluating the MFI levels of the SPM receptors along all RA stages (naïve-to-treatment, resistant-to-treatment, sustained remission) compared with UPIA control group, interestingly ST-derived CD45$^+$ cells of remission RA were depleted of ERV1 compared to naïve-to-treatment RA (p=0.04), despite comparable ST inflammation. Furthermore, highest ERV1 expression was found in ST-derived CD45$^+$CD3$^+$ and CD45$^+$CD19$^+$ cells in naïve-to-treatment RA compared with UPIA patients (p= 0,045 and p= 0,012 respectively). Moreover, the lowest BLT1 level was found in remission RA CD3$^+$ cells compared with UPIA and naïve-to-treatment RA patients (p= 0,008 and p= 0,023 respectively).
Conclusion: SPM receptors expression seem to be tightly related to disease activity in the synovial tissue, suggesting an important involvement in the inflammatory process in RA patient.
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AB0103 THE AMBIGUOUS ROLE OF TISSUE CYTOKINES IN THE PATHOGENESIS OF RHEUMATOID ARTHRITIS

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Background: Cytokines stimulate the inflammatory response in the synovial membrane with rheumatoid arthritis (RA), initiate apoptosis of chondrocytes, activation of osteoclasts. The progression of comorbid diseases is also associated with the influence of cytokines. At the same time, anti-inflammatory cytokines are produced in various tissues. Their role in the pathogenesis of RA and its complications is ambiguous.
Adiponectin (A) and Fetuin A (FA) are classified as negative acute phase proteins. Their concentration decreases with an increase in the level of pro-inflammatory cytokines: TNF-α, IL-1 and IL-6. Molecules A and FA, regardless of various factors and from each other, have similar effects in relation to pro-inflammatory cytokines, lipid and carbohydrate metabolism.
Visfatin (V) and Nesfatin-1 (N-1) are pro-inflammatory adipokines. B is produced by cells of the mononuclear phagocytic system and connective tissue. N-1 - is produced by the cells of the intermediate and medulla oblongata and by the cells of the gastric mucosa.
Objectives: to study the correlation of B, H-1, A and FA with the severity of inflammation in RA
Methods: 60 patients with RA and 30 healthy individuals were examined. The level of cytokines was determined by an indirect enzyme-linked immunosorbent assay using commercial test systems (Bio Vendor, cat No. RD195023100, Bio Vendor Human Fetuin-A, RaiBiotech, cat No. EIA-VIS-1, RaiBiotech, cat No. EIA-NESF). All patients underwent a full examination. Diagnosed with 2010 EULAR / ACR recommendations.
Results: A decreased level of A (less than 0.8 µg/ml) was detected in 15 patients (25%), F-A (less than 653.55 µg/ml) in 16 (27%), a high level of V (more than 39 ng/ml) - in 55 (91%), N-1 (more than 37.95 ng/ml) - in 36 (60%), which is significantly more often than in healthy individuals. No significant difference in the levels of determined adipokines was found depending on the gender and body weight of patients with RA. The level of cytokines in RA is associated with high activity according to DAS 28, positivity by Anti-CCP, extraarticular manifestations of RA. The greatest correlation with extraarticular manifestations is with

cutaneous and cerebral vasculitis. The levels of FA and N-1 also correlated with more pronounced radiological changes (X-ray stage III). FA circulating inhibitor of ectopic calcification. N-1 level is positively correlated with systolic blood pressure.

Conclusion: A low level of A and FA, a high level of V and N-1 is characteristic of RA with the presence of high activity and positivity in the RF and Anti-CCP. An increased level of B is determined by more than 90% of patients, which indicates its high pro-inflammatory activity. The level of F and N-1 is also associated with the degree of damage to bone tissue (stage III, a lot of erosion). A positive correlation of level V and N-1, negative A and FA with the severity of inflammation in RA confirms the involvement of these proteins in the pathogenesis. A high level of A and V increases the risk of developing cardiovascular diseases and their complications, the effect of N-1 and FA is being studied. The effect of cytokines on osteoclasts and osteoblasts in RA is ambiguous

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AB0104 CORRELATION OF PLASMA 14-3-3H LEVELS WITH DISEASE ACTIVITY MEASURES IN METHOTREXATE-NAÏVE RA PATIENTS TREATED WITH UPADACITINIB MONOTHERAPY IN THE SELECT-EARLY PHASE 3 STUDY

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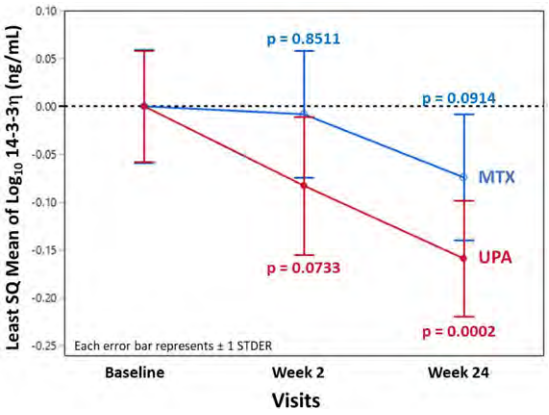
Background: Early diagnosis and treat-to-target strategies in RA improve clinical and radiographic outcomes. 14-3-3η is a soluble diagnostic biomarker that is involved in the pathogenesis of RA (1) including the potent activation of key signalling cascades such as the JAK-STAT pathway and whose initial expression coincides with a transition to synovitis. In undifferentiated arthralgia, 14-3-3η independently predicts the development of RA. In confirmed RA, 14-3-3η levels decrease with treatment response (2) and those changes are associated with clinical and radiographic outcomes, including the prediction of joint damage progression in patients who have achieved clinical remission. Upadacitinib (UPA), an oral JAK1-selective inhibitor, demonstrated significant and clinically meaningful improvements in RA vs. methotrexate (MTX) in the SELECT-EARLY phase 3 study (3).

Objectives: To determine the impact of treatment with UPA monotherapy 15 mg QD on the levels of plasma 14-3-3η and to explore its relationship with clinical measures in early MTX-naïve RA patients.

Methods: Patients from the SELECT-EARLY study were randomly selected (UPA n = 100; MTX n = 100) from the pool of patients with available plasma samples. 14-3-3η tests were performed at Augurex according to standard operating procedures. Concentrations (ng/mL) were log-transformed for analysis. Non-parametric correlations between biomarker data and clinical end points were derived using the Spearman method. Changes in 14-3-3η over time were compared using a Repeated Measure Mixed Linear Model. All statistical analyses were conducted in JMP 14.1 (SAS Institute).

Results: At baseline, 79% of patients were 14-3-3η positive (≥ 0.19 ng/mL) with similar levels in both arms. Baseline levels of 14-3-3η correlated significantly with baseline disease activity measures (CDAI ρ = 0.164, p = 0.042; DASCRP ρ = 0.222, p = 0.004; and SDAI ρ = 0.177, p = 0.028) but not with baseline mTSS (ρ =-0.021, p = 0.787); of note baseline mTSS were relatively low in this subset of early RA patients (median = 2, IQR [0 – 9.5]). Over time, 14-3-3η levels tended to be lower in both the UPA and MTX groups. However, only treatment with UPA for 24 weeks resulted in a significant decrease in circulating 14-3-3η (p = 0.0002) (Figure 1). In addition, at week 24 in the UPA arm, changes in 14-3-3η levels correlated significantly with changes in concurrent disease activity measures (Δ CDAI ρ = 0.264, p = 0.030; Δ DASCRP ρ = 0.267, p = 0.021; and Δ SDAI ρ = 0.267, p = 0.028) but not with change in mTSS (ρ =-0.186, p = 0.111). In contrast to UPA, the relatively small changes in 14-3-3η induced by MTX did not correlate with any clinical measures.

Figure 1



Conclusion: This study demonstrates that treatment with UPA 15 mg QD monotherapy for 24 weeks significantly reduces the levels of circulating 14-3-3η in MTX-naïve RA patients and that these changes correlate with clinical measures of disease activity. Although we were not able to detect a clear relationship between changes in 14-3-3η and rate of structural damage progression, we would like to hypothesize that the superior clinical activity of UPA over MTX on joint damage may be related to the significant reduction in 14-3-3η induced by UPA; this hypothesis should be tested in a larger RA cohort with a larger proportion of joint damage progressors.

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AB0105 CHECKPOINT MOLECULES AND PREGNANCY: ENHANCED SPD-L1 PREDICTS FLARE IN RA PREGNANCY AND POSTPARTUM

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Background: Rheumatoid arthritis (RA) is a female-predominant autoimmune disease that may affect women in childbearing age, making family planning an important issue for their life. There is a need for better understanding the mechanisms modulating RA in pregnancy and develop prognostic marker regarding adverse pregnancy outcome such as reduced birth weight and preterm delivery. As a crucial organ for peripheral tolerance during pregnancy, the placenta is expressing constitutively programmed cell death ligand 1 (PD-L1), major ligand of the inhibitory receptor PD-1 (Zhang et al, 2015). We hypothesize that the PD-1 pathway plays a central inhibitory role in regulating the course of the disease and pregnancy outcome in RA.

Objectives: To investigate the relationship between PD-1 pathway, disease activity during pregnancy/postpartum and pregnancy outcome in RA.

Methods: We measured soluble PD-1 and PD-L1 levels by ELISA in serum samples of 27 pregnant RA patients and 25 healthy pregnant controls at different time points during pregnancy and postpartum. As for pregnancy controls, we analyzed serum samples from 28 non-pregnant RA patients and 18 non-pregnant healthy controls. The data was analyzed in correlation with disease activity (measured by DAS28-CRP) and pregnancy outcome (defined as preterm delivery and birth weight). Statistics were calculated by Mann-Whitney U test and Wilcoxon test, correlations by Spearman rank test.

Results: In healthy pregnancy, sPD-L1 increases significantly in the 1st trimester (p = 0,0198) and decreases significantly postpartum (p = 0,0029). sPD-L1 values are higher in non-pregnant RA patients compared to non-pregnant healthy controls (p = 0,047) and there are no significant changes during RA pregnancy. Postpartum sPD-L1 values are significantly higher in RA patients compared to healthy controls (p = 0,0014), Fig. 1. Notably, regarding disease activity, we noticed a significant positive correlation between the overall sPD-L1 values in

RA and DAS28-CRP (p= 0.0104), Fig. 2. No significant correlation was seen between sPD-L1, birth weight and preterm delivery. For sPD-1 we focused on 3rd trimester and postpartum, however, there was no difference between healthy controls and RA patients and no correlation with disease activity or pregnancy outcome.

Conclusion: In healthy pregnancy, we observed an increase of sPD-L1, which decreases after delivery. This supports the hypothesis, that PD-1 pathway may be involved in shaping the physiological fetal-maternal tolerance. In RA higher sPD-L1 values are measured already in non-pregnant patients compared to healthy controls and there is no physiological decrease postpartum. Intriguing, sPD-L1 correlates positively with RA disease activity, reflecting a possible functional antagonism towards the inhibitory function of membrane bound PD-L1 molecules. However, the detailed function of sPD-L1 need to be further delineated. Nevertheless, sPD-L1 may have the potential to serve as prognostic marker for flares in RA pregnancy. Regarding the rather rarely observed adverse pregnancy outcome, larger cohorts need to be investigated.

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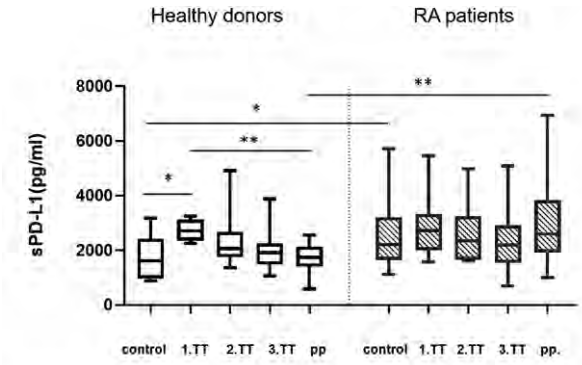


Fig.1 sPD-L1 in pregnant healthy donors and RA patients compared with controls (non-pregnant healthy donors and RA patients). Control = non pregnant; 1.TT = 1st trimester; 2.TT = 2nd trimester; 3.TT = 3rd trimester; pp =postpartum. * p ≤ 0,05; ** p ≤ 0,01

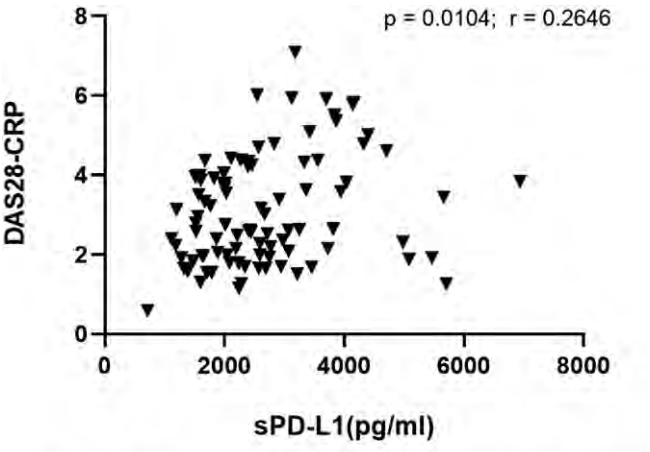


Fig. 2. sPD-L1 correlates positively with DAS28-CRP in RA pregnancy and postpartum.

Disclosure of Interests: Ana-Luisa Stefanski: None declared, Klara Eriksson: None declared, Astrid Zbinden: None declared, Peter Villiger Consultant of: MSD, Abbvie, Roche, Pfizer, Sanofi, Speakers bureau: Roche, MSD, Pfizer, Frauke Förger Grant/research support from: Unrestricted grant from UCB, Consultant of: UCB, GSK, Roche, Speakers bureau: UCB, GSK

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AB0106

THE SERUM N-ACETYLGLUCOSAMINE CONCENTRATIONS IN RHEUMATOID ARTHRITIS PATIENTS ARE ASSOCIATED WITH JOINT DESTRUCTION AND RELATED METABOLISM MORE THAN INFLAMMATORY CONDITION

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Background: In rheumatoid arthritis (RA) patients, synovitis causes severe articular cartilage damage. N-acetylglucosamine (NAc-Glc) is a component of gluglucosaminoglycans (GAG) such as hyaluronic acid (HA) and keratan sulfate (KS), heparan sulfate (HS). NAc-Glc concentration in plasma is thought to reflect the balance between biosynthesis and destruction of articular cartilage, however, few studies had examined the relationship between plasma NAc-Glc conncentration and RA activity.

Objectives: NAc-Glc concentrations in RA patients were measured, and association with clinical indicators was assessed.

Methods: A cross-sectional study was carried out including 60 RA cases. Using N-acetylglucosamine-d3 as standard, the serum of subjects were deproteinized by protein precipitation method with acetonitrile, then concentration of NAc-Glc was measured with high-speed liquid chromatography mass spectrometer (LC-MS / MS). Clinical evaluation items: basic metabolism, presence or absence of exercise habit, Larsen score of knee and wrist joint, therapeutic agents (csDMARDs, biologics and PSL), DAS28, CRP, MMP-3, modified HAQ score (mHAQ). Statically analyzed by Spearman non parametric test.

Results: The age of 60 RA cases was 59.7±16.4 years, and the duration of the disease was 10.4±8.7 years. Biologics were used in 29 cases (TNF inhibitors in 16 cases, IL-6 inhibitors in 4 cases, Abatacept in 9 cases), MTX in 32 cases, and prednisolone in 15 cases.

Plasma NAc-Glc concentration was 113±41 (ng/dl), DAS28CRP was 3.04±1.2, and mHAQ was 0.863±891. Plasma NAc-Glc concentration showed positive correlation with age (correlation coefficient 0.644), knee joint destruction (0.425), HAQ score (0.340), BUN (0.412), and RF (0.287). Plasma NAc-Glc concentrations also negatively correlated with eGFR (-0.597), MTX use (-0.389), basal metabolism (-0.313), and sex difference (-0.272). There was no correlation between plasma NAc-Glc concentration and body weight, BMI, DAS28, CRP, MMP-3, NTX, serum creatinine, hand joint disease, and transaminase.In this study, plasma NAc-Glc concentration had increased with age, and had have a negative correlation with basal metabolism. Considering these results, it is unlikely that NAc-Glc is released into plasma as a metabolite of synthesis promotion. Further, since NAc-Glc had a negative correlation (-0.389) with MTX as a folic acid inhibitor, it was supposed to be affected by protein synthesis reduction. Because no correlation between NAc-Glc and inflammation or bone metabolism markers was observed, NAc-Glc may represent removal of GAG from the cell membrane (shedding).

In previous GAGs studies, in RA patients, HA, KS, CRP, DAS28, was very associated with arthritis, such as MMP-3.The concentration of NAc-Glc in plasma was more relevant to dysfunctions such as destruction and HAQ due to arthritis such as HAQ than inflammatory indicators such as DAS28, MMP-3 and CRP. It is appearing in the plasma by destruction by shedding, as an index to see the joint destruction, it was presumed to be a better indicator than the GAGs. It was also thought that there is a possibility that MTX affects cartilage substrate metabolism.

Conclusion: Serum NAc-Glc concentration in rheumatoid arthritis patients may represent cartilage metabolism and joint destruction.

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Disclosure of Interests: None declared

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AB0107

INVESTIGATION OF THE EFFECTS OF KYNURENIC ACID ANALOGS IN RHEUMATOID ARTHRITIS

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Background: The investigation of anti-inflammatory and immunosuppressive functions of kynurenic acid (KYNA) is now in focus. Previously, we demonstrated the opposite effects of KYNA and different KYNA analogs on tumor necrosis factor-α (TNF-α) production and tumor necrosis factor-stimulated gene-6 (TSG-6) expression in U-937 monocytic cells. The potential effect of KYNA analogs on further immune mediators including alarmins (S100A12=EN-RAGE and S100A8/9=calprotectin), and on human neutrofil peptide 1-3(α-defensin) production has not been investigated.
Objectives: Therefore, in the present study, we compared the effects of newly synthesized KYNA analog on the TNF-α, alarmins and α-defensin production, correlation with the effects on the TSG-6 expression in rheumatoid arthritis (RA).
Methods: 93 RA patients were involved and divided subgroups based on DAS28 activity score. Peripheral blood mononuclear cells (PBMC) was isolated from RA patients and healthy controls. As cytokine inducers heat inactivated *Staphylococcus aureus* (SA1) were used. In parallel in vitro experiments, the SA1 induced PBMCs were pretreated with a newly synthesized KYNA analog (compound SZR-72 was synthesized by direct amidation of KYNA). The concentrations of the above mentioned inflammatory mediators in the supernatants were quantified by using ELISA kits and the TSG-6 expression was also determined by RTqPCR method.
Results: The SA1 induced TNF-α, EN-RAGE, calprotectin and α-defensin production was significantly higher in RA patients' group than in healthy controls. KYNA analog attenuated the SA1 induced TNF-α, EN-RAGE, calprotectin and α-defensin production, and increased TSG-6 production and TSG-6 mRNA expression in PBMC cells from RA patients. The SA1 induced TNF-α and TSG-6 production correlated with the DAS28 activity score. The TNF-α inhibitory effect of the KYNA analog correlated inversely with the TSG-6 stimulatory effect in all subgroups of RA patients based on DAS28 activity score.
Conclusion: TSG-6 expression could participate in the suppression of inflammatory cytokines, such as TNF-α, EN-RAGE, calprotectin and α-defensin. We suppose that the elevation of the TSG-6 expression by KYNA and especially by new KYNA analogs might be one of the mechanisms that are responsible for their suppressive effect on TNF-α production as a feedback mechanism in RA. KYNA and KYNA analogs have an important role in influencing TSG-6 expression, and there is a possible benefit with potential therapeutic consequence of targeting TSG-6 expression by kynurenines in inflammatory conditions in RA.
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Disclosure of Interests: None declared
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AB0108 IRAK4 INHIBITION SUPPRESSES PROINFLAMMATORY CYTOKINE PRODUCTION FROM HUMAN MACROPHAGES STIMULATED WITH SYNOVIAL FLUID FROM RHEUMATOID ARTHRITIS PATIENTS

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Background: Rheumatoid arthritis (RA) is characterized by chronic, uncontrolled joint inflammation and tissue destruction. Macrophages are thought to be key mediators in both the initiation and perpetuation of this pathology.[1,2] The RA synovium contains a complex inflammatory milieu that can stimulate macrophage-dependent production of proinflammatory cytokines through multiple signaling pathways.[1,2] Existing evidence indicates that toll-like receptors (TLRs) and interleukin-1 receptors (IL-1R) along with their agonists, damage-associated molecular patterns (DAMPs) and IL-1β, are highly expressed in RA joints and are important mediators of synovial macrophage activation and proinflammatory cytokine production.[1-9] IRAK4 (interleukin-1 receptor-associated kinase 4) is a serine/threonine kinase that facilitates TLR and IL-1R signaling in many cell types, including macrophages.[10] IRAK4 inhibition represents an opportunity to reduce proinflammatory cytokine production in the joints of patients with RA.
Objectives: To investigate the effect of a highly selective IRAK4 inhibitor on proinflammatory cytokine production from human macrophages stimulated with synovial fluid from patients with RA.
Methods: Primary human monocytes from 2 independent donors were differentiated for 6 days with granulocyte-macrophage colony-stimulating factor (GM-CSF) to generate human monocyte-derived macrophages (hMDMs). hMDMs were then pretreated with an IRAK4 inhibitor for 1 hour and subsequently stimulated for 24 hours with RA synovial fluid from 5 patients. Culture supernatants were then assessed for secretion of proinflammatory cytokines by MesoScale Discovery.
Results: RA synovial fluid stimulation of hMDMs resulted in the production of several proinflammatory cytokines, including IL-6, IL-8, and TNFα. Pretreatment of hMDMs with an IRAK4 inhibitor resulted in the dose-dependent inhibition of IL-6, IL-8, and TNFα production, with an average EC_{50} ± SD of 27 ± 31, 26 ± 41, and 28 ± 22 nM, respectively. Maximal percent suppression ± SD of IL-6, IL-8, and TNFα were 76 ± 8.8, 73 ± 15, and 77 ± 13, respectively. To evaluate the specific IRAK4-dependent signaling pathways mediating this response, hMDMs were pretreated with inhibitors of TLR4 (TAK242) and IL-1R (IL-1RA) prior to stimulation with RA synovial fluid. Both TAK242 and IL-1RA inhibited proinflammatory cytokine production. For TAK242, maximal percent suppression ± SD of IL-6, IL-8, and TNFα were 39 ± 25, 48 ± 24, and 50 ± 21, respectively. For IL-1RA maximal percent suppression ± SD of IL-6, IL-8, and TNFα were 18 ± 18, 20 ± 23, and 16 ± 18, respectively. The broad range of inhibition across each stimulation highlights the complexity and variability in the signaling pathways mediating proinflammatory cytokine production from hMDMs stimulated with RA synovial fluid, but demonstrates that RA synovial fluid can stimulate proinflammatory cytokine production in hMDMs, at least partly, through IRAK4-dependent pathways.
Conclusion: This work demonstrates that IRAK4 inhibition can suppress proinflammatory cytokine production from macrophages stimulated with synovial fluid from patients with RA and supports a potential pathophysiological role for IRAK4 in perpetuating chronic inflammation in RA.
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Disclosure of Interests: Adam Yadon Employee of: Gilead, Debbie Ruelas Employee of: Gilead, Gundula Min-Oo Employee of: Gilead, James Taylor Employee of: Gilead, Matthew R. Warr Employee of: Gilead
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AB0109 THE ROLE OF CD70 IN THE DEVELOPMENT OF RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a progressive, chronic inflammatory autoimmune disease. Pro-inflammatory molecules, activated lymphocytes, and the migration of inflammatory cells are important in the development of RA. There are many unknown causes of RA. And there are many patients who are refractory to treatment with known disease-modifying anti-rheumatic drugs. So, unknown cause of RA needs to be elucidated.
CD70 is a member of the tumor necrosis factor (TNF) superfamily and a ligand for CD27. The interaction of CD70 with its receptor CD27 promotes expansion and differentiation of memory and effector T cells as well as B-cell expansion and plasma cell differentiation. Hypoxia is an important micro-environmental factor in RA synovium. Hypoxia induces activation of hypoxia inducible factor (HIF). The expression of HIF-2α is up-regulated in human RA synovium. Reactive oxygen species (ROS) has been implicated in the pathophysiology of RA.
Objectives: In this study, we tried to examine the presence of CD70 in RA synovium and investigate the role of CD70 in the development of RA associated with HIF-2α and ROS.
Methods: Fibroblast-like synoviocyte (FLS), peripheral blood (PB) and synovial fluid (SF) were used for experiments. FLS was stimulated with recombinant human (rh)-IL-17 and rh-TNF-α. N-acetyl-L-cysteine (NAC) was used as a ROS scavenger. HIF-2α inhibitor (PT-2385) was used for examine the effect of HIF-2α in RA-FLS. RT-PCR, qPCR, western blotting, flow-cytometry, ELISA, cell migration assay, and scratch wound assay were performed.
Results: CD70 mRNA is present and elevated by stimulation with IL-17 and TNF-α in both RA-FLS and osteoarthritis (OA)-FLS (Fig 1). CD70 also expresses on the surface of RA-FLS and OA FLS (Fig 2). CD70 expression on the surface of FLS is elevated by stimulation with IL-17 and TNF-α in both

RA and OA. Soluble CD27 is present higher in the supernatant of RA-SF than OA-SF (Fig 3). HIF-2α mRNA, HIF-2α protein, and the amount of ROS were all elevated after treatment with IL-17 and TNF-α in RA-FLS (Fig 4, Fig 5). CD70 expression and the amount of ROS were lowered by treatment with HIF-2α inhibitor in RA-FLS (Fig 6). Decreased amount of ROS results in decreased CD70 expression on the RA-FLS (Fig 7). CD70 influenced on cell migration directly or by HIF-2α (Fig 8).

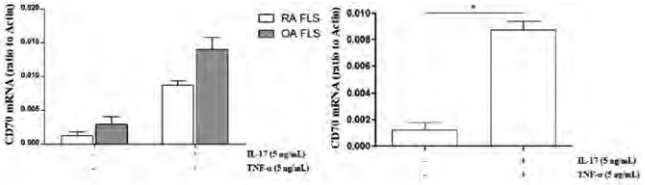


Figure 1. CD70 mRNA in RA-FLS and OA-FLS

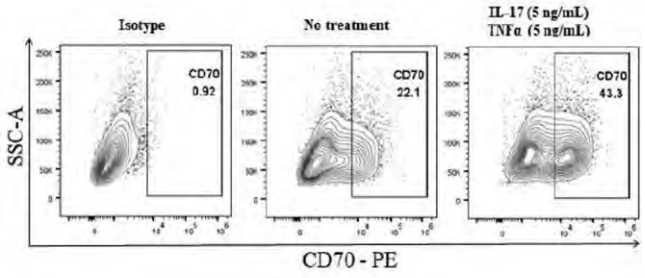


Figure 2. CD70 expression on the surface of RA-FLS

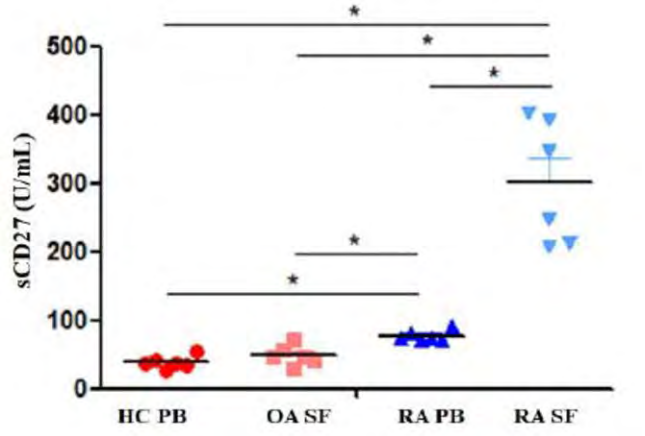


Figure 3. The amount of sCD27 by ELISA

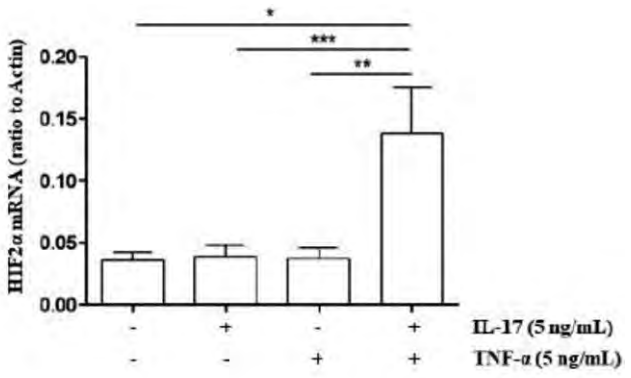


Figure 4. HIF-2α mRNA in RA-FLS

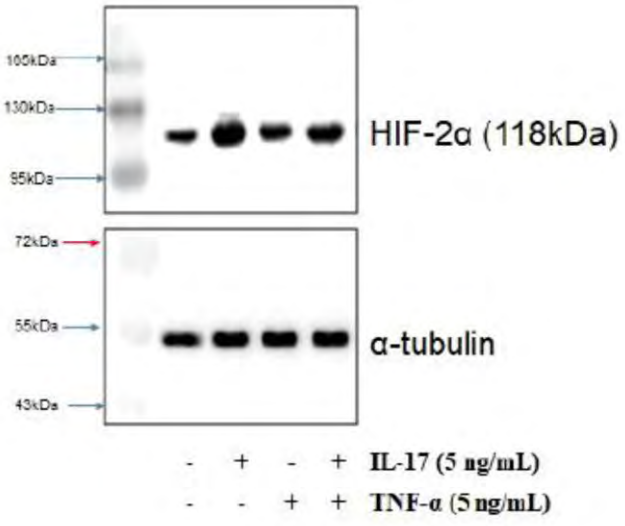


Figure 5. HIF-2α protein in RA-FLS

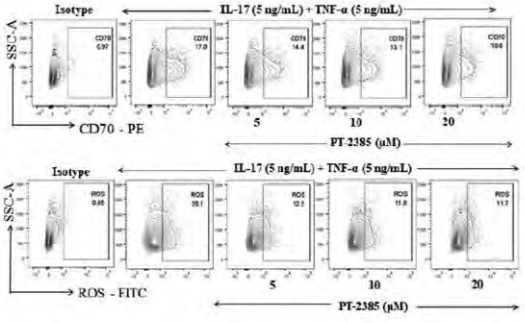


Figure 6. CD70 expression and ROS on the surface of RA-FLS by treatment with HIF-2α inhibitor.

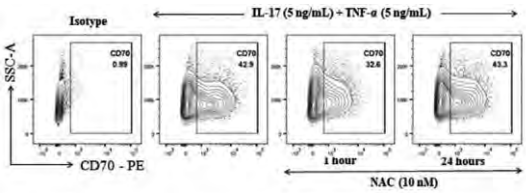


Figure 7. CD70 expression on the surface of RA-FLS by treatment with ROS scavenger

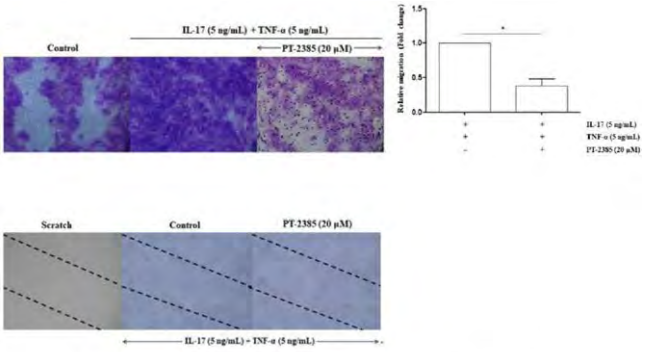


Figure 8. Cell migration in RA-FLS by treatment with HIF-2α inhibitor

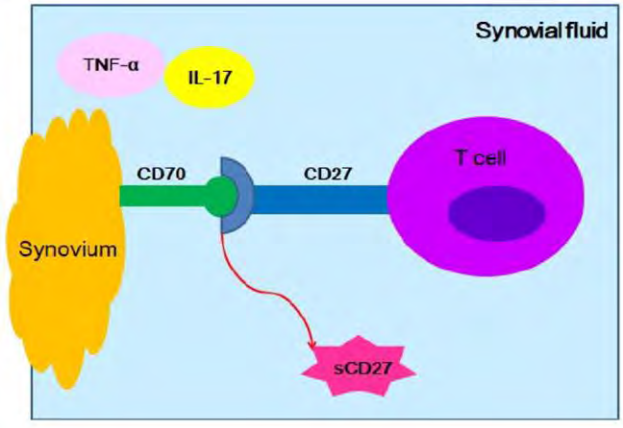


Figure 9. CD70-CD27 interaction on RA-FLS

Conclusion: In this study, we found the function of CD70 in RA-FLS associated with HIF-2α and ROS. First, CD70 on RA-FLS interacts with CD27 in the RA-SF and this interaction produces sCD27 (Fig. 9) and CD70 has an influence on the migration of RA-FLS. Second, IL-17 and TNF-α are critical factors to trigger the expression of CD70, HIF-2α and ROS in RA synovium. Third, CD70 is regulated by HIF-2α associated with ROS. From these results, we suggest that CD70 may be a new therapeutic target of RA. And sCD27 also may be an important diagnostic maker of RA.

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AB0110

ADIPONECTIN INDUCES PRO-INFLAMMATORY CHEMOKINE AND CYTOKINE PRODUCTION BY PERIPHERAL BLOOD MONONUCLEAR CELLS AND FIBROBLAST-LIKE SYNOVIOCYTES FROM NON-INFLAMED SUBJECTS

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Background: Adiponectin is a cytokine mainly secreted by the adipose tissue[1], whose circulating levels are paradoxically low in subjects with obesity and associate with a beneficial metabolic profile[2]., Recent studies have shown that adiponectin levels are elevated in both serum and synovial fluid collected from patients with rheumatoid arthritis (RA)[3,4]. Moreover, adiponectin is able to induce the production of interleukin (IL)-6, tumor necrosis factor (TNF), CXCL1 and CXCL8 by lymphocytes from healthy subjects[5], and of IL-6 and CXCL8 by fibroblast-like synoviocytes (FLS) from patients with RA[6]. However, it is not clear if adiponectin is able to initiate the inflammatory processes associated with the preclinical phase of RA.

Objectives: We aim to determine if adiponectin is able to induce inflammatory responses in peripheral blood mononuclear cells (PBMCs) and FLS from non-inflamed subjects.

Methods: Human PBMCs were collected from healthy donors, whereas non-inflamed FLS from non-arthritic patients who underwent diagnostic arthroscopy due to previous trauma. PBMCs (1×10^5 cells/well in 96-well plate) and FLS (5000 cells/well in 96-well plate) were stimulated using 5 μg/ml recombinant human total adiponectin protein, and the supernatants were collected 48 hours after stimulation. Phytohemagglutinin (PHA) and TNF were used as positive controls to activate PBMCs and FLS, respectively. Using multiplex assay and ELISA, we screened the production of 13 chemokines and 12 cytokines from healthy human PBMCs and non-inflamed FLS.

Results: Adiponectin was able to stimulate a distinct profile of chemokines and cytokines in PBMCs and FLS. In both healthy PBMCs and non-inflamed FLS adiponectin induced the production of CXCL1, CXCL5, CXCL8, CCL2 and IL-6. Moreover, CCL3, CCL20, CCL4, CCL17, TNF, IL-10 and GM-CSF were induced by adiponectin only in healthy PBMCs, whereas CXCL10, CCL5 and CCL11 only in non-inflamed FLS (Fig. 1 and 2).

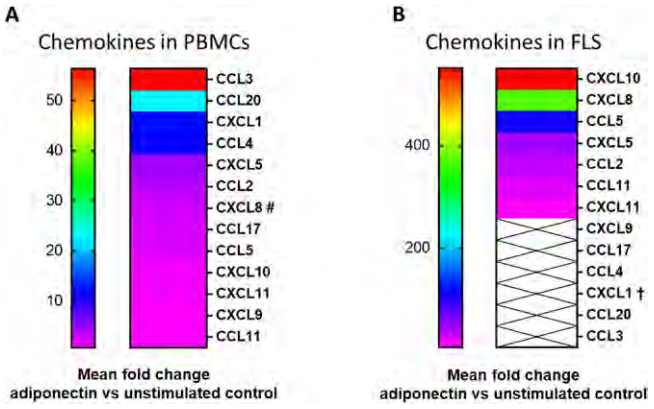


Figure 1. Adiponectin induces the production of various chemokines from PBMCs (A) and FLS (B). CXCL8 (#) was measured using ELISA, and other chemokines were measured using multiplex assay. The fold change of CXCL1 in FLS (†) was not calculated because its level before stimulation was undetectable.

Conclusion: We here report that adiponectin has pro-inflammatory properties as it induced chemokine and cytokine production from human healthy PBMCs and non-inflamed FLS. As adiponectin is able to induce pro-inflammatory responses from non-inflamed cells, we suggest that this adipokine might be implicated in the preclinical phase of RA pathogenesis.

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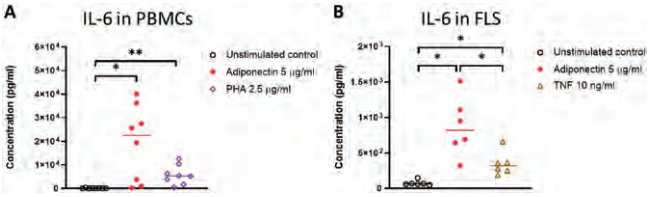


Figure 2. Adiponectin induces the production of IL-6 PBMCs (A) FLS (B) measured using ELISA.

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AB0111 THE COMPARISON OF SYNDECAN-4 LEVEL IN SERA, SYNOVIAL FLUID AND SYNOVIUM OF RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS

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Background: Syndecan-4, one of the members of heparan sulphate proteoglycans (HSPGs), has been shown to be involved in regulating inflammatory responses, angiogenesis, and cell migration. Its role has been proved in animal arthritis models, however not clearly elucidated in rheumatoid arthritis (RA) patients
Objectives: To investigate the role of Syndecan-4 in the pathogenesis of RA, by detecting Syndecan-4 expression in the serum, synovial fluid and synovium of RA patients and comparing with osteoarthritis (OA) patients
Methods: The concentrations of syndecan-4 in sera and synovial fluid of RA and osteoarthritis (OA) patients were detected by ELISA. The expression of syndecan-4 in synovium of RA and OA patients was detected by immunohistochemistry. In another cohort of 60 RA patients, the association analysis was performed. All the RA patients were with disease duration more than 6 months and with DAS28-CRP>3.2 although after csDMARDs (including MTX and/or leflunomide) treatment for more than 3 months. The RA patients were treated with tumour necrosis factor α (TNFα) inhibitor (TNFi) and MTX 10mg per week for 12 weeks. The correlations between sera Syndecan-4 and disease activity of RA as well as therapeutic response to TNFi were analyzed.
Results: The serum Syndedcan-4 level of RA patients [637.1 (483.6-1069.6) pg/mL] was significantly higher than that of OA patients [345.0 (287.9-421.1) pg/mL] and healthy controls [195.6 (165.0-225.2) pg/mL](P<0.001, P<0.001, respectively). The serum concentration of Syndecan-4 is also higher in OA patients than that in healthy controls (P<0.001). It was also higher in RF-positive RA patients than in RF-negative ones [603.0 (100.0-8879.1) pg/mL vs 460.3 (178.7-2468.9) pg/mL, (p=0.026)]. The Syndedcan-4 level in synovial fluid and synovia were comparable between RA and OA patients. No correlation was found between serum Syndedcan-4 and disease activity of RA. TNFi treatment did not change the serum Syndecan-4 level significantly. The baseline serum Syndecan-4 did not show predictive value for TNFi response.
Conclusion: Syndecan-4 can be expressed in the synovia of RA and OA patients. The serum Syndecan-4 is higher in RA patients than in OA patients and healthy controls, and significantly higher in sero-positive RA patients than in sero-negative ones. Syndecan-4 may participate in the pathogenesis of RA.
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AB0112 THE PREDICTIVE VALUE OF SERUM SOLUBLE ICAM-1 AND CXCL13 IN THE THERAPEUTIC RESPONSE IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Tumor Necrosis Factor-α (TNFα) inhibitors (TNFi) have greatly improved the prognosis of RA, but not all these patients respond well to TNFi. So far there has been no definite biomarker to predict the response to TNFi yet.
Objectives: The aim of current study was to explore the predictive value of sICAM-1 and CXCL13 on the response to TNFα receptor fusion protein in RA patients who have poor response to conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs).
Methods: 60 RA patients with disease duration more than 6 months and at least low disease activity definded by DAS28-CRP>3.2 although after csDMARDs treatment for more than 3 months were included. They were further treated with TNFα receptor Fc fusion protein and MTX 10mg per week for 12 weeks. Soluble ICAM-1 (sICAM-1) and CXCL13 concentrations in sera from 60 RA patients and 20 healthy controls were tested by ELISA right before and at the end of 12 weeks of TNFi therapy. The correlation between sICAM-1 and CXCL13 with disease activity and their predictive values for TNFi response were analyzed.
Results: The mean age of the 60 patients were 54.8±11.6 years. Serum sICAM-1 and CXCL13 concentration was higher in RA patients than heathy controls, higher in seropositive RA patients than in seronegative ones, and higher in RA patients with higher disease activity (table 1). Serum sICAM-1 and CXCL13 levels were decreased after TNFi therapy, especially in good responders (table 2). Baseline sICAM-1 concentration was independently associated with EULAR response (p=0.033, OR=1.014, 95% CI=1.003-1.026). The sICAM-1^{high}/$CXCL13^{high}$ patients had the highest response rate, which was significantly higher than the sICAM-1^{low}/$CXCL13^{low}$ group (OR=8.143, 95%CI:1.040-75.482, p=0.045).

Table 1. The correlation between serum sICAM-1 and CXCL13 concentrations and disease activity at baseline and 12 weeks after treatment.

	Baseline sICAM-1 (ng/mL) CXCL13 (pg/mL)				Week 12 sICAM-1 (ng/mL) CXCL13 (pg/mL)			
	r	p	r	p	r	p	r	p
DAS28-ESR	**0.396**	**0.002**	0.233	0.073	**0.315**	**0.014**	0.150	0.254
DAS28-CRP	**0.360**	**0.005**	0.191	0.143	0.250	0.054	0.062	0.639
SDAI	**0.278**	**0.032**	0.138	0.292	0.220	0.091	0.042	0.750
CDAI	**0.277**	**0.032**	0.116	0.377	0.182	0.163	0.009	0.943

Table 2. The comparisons of sICAM-1 and CXCL13 concentrations at baseline and 12 weeks based on different response criteria.

	EULAR responder / EULAR non-responder						ACR 20 achieved ACR / 20 not achieved					
	Baseline	Week 12	p	Baseline	Week 12	p	Baseline	Week 12	p	Baseline	Week 12	p
sICAM-1 (ng/ml) (mean±SD)	388.5±94.0	325.3±83.7	**0.001**	302.1±56.1	334.3±61.5	0.270	390.5±95.8	329.6±87.6	**0.004**	345.7±85.3	329.3±67.9	0.513
CXCL13 (pg/ml) (median, min-max)	190.6 (50.1-2081.4)	103.3 (4.8-1497.8)	**0.003**	120.4 (18.8-1909.4)	144.7 (18.4-2155.0)	0.546	199.7 (57.9-2081.4)	103.8 (8.9-2155.0)	**0.011**	136.0 (18.8-1909.4)	102.2 (4.8-767.33)	0.531

Conclusion: sICAM-1 and CXCL13 are elevated in RA patients and correlated with disease activity. sICAM-1 is an independent predictor of TNFi response in csDMARDs refractory RA patients.

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7. Spondyloarthritis - etiology, pathogenesis and animal models

AB0113 ANTIBODIES AGAINST HELICOBACTER PYLORI ANTIGENS IN PATIENTS WITH PSORIATIC ARTHRITIS AND PSORIASIS

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Background: Psoriasis (Ps) and Psoriatic Arthritis (PsA) are inflammatory diseases of unknown etiology. Helicobacter pylori (Hp) infection has been hypothesized as one of the microbial agents that can lead to development of immune-mediated psoriatic disease, but the nature of the specific Hp antigens involved remains unclear.

Objectives: To asses antigen specific antibody responses against immunodominant Hp antigens in patients with psoriatic diseases.

Methods: Ninety-one patients with Ps (35 females; median age 51.9, age range 25-87), 47 patients with PsA (25 females; median age 52.9, age range 25-87) and 60 demographically matched healthy controls (HC) were studied. Reactivity to Hp-specific antigens were tested by Western immunoblotting (in combination with line immunoassay for anti-CagA and anti-VagA antibody testing) (Euroimmun AG, Lübeck, Germany).

Results: Positivity against Hp was comparable between PsA (38.3%), Ps (39.6%) and HCs (50%). Anti-p66-UreB, anti-p54-flagelin and anti-p29-UreA abs were more frequent in psoriatic patients compered to healthy controls (p66: 94.4% in Ps vs 69.7% in HC, p=0.017; p54: 66.7% in Ps vs 33.3% in HC, p=0.012; p29 72.2% in Ps vs 45.5% in HC, p=0.044) and anti-p29-UreA abs were detected in higher frequency in PsA patients compered to HC (94.4% vs 45.5%, p=0.002). Reactivities against the remaining Hp antigens were comparable between Ps and PsA patients and HC.

Conclusion: Antibody responses against p66-UreB, p29-UreA, and p54-flagelin are more prevalent in patients with psoriatic disease, suggesting their potential involvement in PsA and Ps.

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AB0114 IL12P40/IL23P40 BLOCKADE WITH USTEKINUMAB DECREASES THE INFLAMMATORY INFILTRATE AND MODULATES MOLECULAR PATHWAYS IN THE SYNOVIUM OF PSORIATIC ARTHRITIS PATIENTS

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory joint disease within the spondyloarthritis (SpA) spectrum. TNF and IL17/IL23 pathways play a key role in SpA pathogenesis. Blocking of IL12p40/IL23p40 has been shown to effectively reduce disease activity in PsA [1,2]. It is however incompletely understood how IL12p40/IL23p40 blockade affects local inflammatory processes.

Objectives: To investigate the cellular and molecular pathways affected by IL12p40/IL23p40 blockade with ustekinumab in PsA patients (pts).

Methods: Eleven male PsA pts with at least 1 inflamed knee or ankle joint, who were scheduled to start ustekinumab treatment, were included in a 24-week single-center open-label study. All pts received ustekinumab 45 mg/sc according to standard care at week (W) 0, 4 and 16. Besides clinical outcomes, needle arthroscopic synovial tissue (ST) biopsy samples were obtained from an inflamed knee or ankle joint at baseline (BL), W12 and W24. ST samples were analyzed by immunohistochemistry (IHC), RNA sequencing and real-time quantitative polymerase chain reaction (qPCR) analysis.

Results: Paired BL and W12, and paired BL, W12 and W24 ST samples were available of 9 and 6 pts, respectively. Two pts only underwent BL ST sampling (pt refusal; withdrawal after the W12 clinical visit). Two pts were excluded after W12 because of treatment adjustments. Of 1 pt no ST was obtained at W24 due to technical difficulties. Eight pts finished 24 weeks of clinical follow-up. No serious adverse events were observed. At W12 6/11 pts met ACR20, 2/11 met ACR50 and 1/11 met ACR70 improvement criteria, at W24 this was 3/8, 2/8 and 1/8 pts, respectively. Significant improvements between BL and W12 and/or W24 were seen in clinical (TJC, PASI, BASDAI) and serological markers (CRP and ESR), Table 1. IHC showed a significant decrease in sublining macrophages, a sensitive biomarker of an inflammatory response in peripheral SpA, of BL 2[1-3] vs W12 1.5[0-2]p=0.020, but not W24 1[0.5-2.5]ns. Other synovial infiltrating cells were not significantly decreased. Significant downregulation of MMP3 (p=0.047) and IL-23p19 (p=0.046), but not IL6, TNF or IL12p40 were seen with qPCR analysis at W12. RNA seq analysis showed 178 significantly differentially expressed genes between BL and W12 (FDR 0.1). Gene ontology and KEGG terms enrichment analyses identified overrepresentation of MAPK and PI3K-Akt signalling pathways among the down-regulated genes and WNT signalling pathway among the up-regulated genes. Gene expression was confirmed by qPCR analysis.

Table 1.

	Baseline (n=11)	Week 12 (n=11)	Week 24 (n=8)	p-value*	p-value**
TJC	1 (0-5)	1 (1-2)	0 (0-0.75)	0.168	0.034
SJC	2 (1-3)	2 (1-3)	1.5 (1-2)	0.394	0.715
VAS patient global	28 (16-55)	22 (12-46)	45 (2.8-50.5)	0.423	0.779
PASI	3.2 (1.2-7.4)	0.8 (0-1.8)	0 (0-2.4)	0.028	0.046
BASDAI	3.2 (2.4-4.7)	1.9 (1-3.8)	2.1 (0.4-4.2)	0.008	0.161
CRP (mg/L)	8.5 (1.7-16.4)	1.6 (0.6-3)	1.0 (0.6-7.0)	0.008	0.012
ESR (mm/hr)	20 (8-35)	6 (2-17)	8 (2-20.5)	0.008	0.017

TJC/SJC tender/swollen joint count; VAS visual analogue scale; PASI psoriasis area severity index; BASDAI Bath Ankylosing Spondylitis Disease Activity Index; CRP C-reactive protein; ESR erythrocyte sedimentation rate;

All values are presented as median (IQR) p-value for the comparison of baseline and week 12 (*) or week 24 (**)

Conclusion: Ustekinumab treatment reduced synovial inflammation and modulated specific molecular pathways, however inflammation was not completely resolved. Future studies comparing histological and gene expression data between different treatments targeting IL17/IL23 axis will show which changes are treatment-specific and which reflect downregulation of local inflammation.

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AB0115 SECUKINUMAB THERAPY DOES NOT AFFECT NEUTROPHIL HOST DEFENCE IN PSORIATIC ARTHRITIS

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Background: Biologic therapies have revolutionised therapy in inflammatory diseases such as psoriatic arthritis (PsA), driving major improvements in outcomes. Th17 cells appear to play a key role in the pathogenesis of PsA, and IL-17 can trigger the release of chemoattractants such as CXCL8 and CCL20, leading to the further infiltration of other immune cells including neutrophils. Infiltrating activated neutrophils can themselves generate a range of chemoattractants which may amplify and sustain the inflammatory response. Therapeutic targeting of IL-17 with biologics such as secukinumab offers great benefit in PsA by blocking this inflammatory cycle: however the interaction of this agent with neutrophils, key components of host defence as well as potential mediators of this disease, is not known.
Objectives: This study aimed to measure key aspects of neutrophil function to determine: a) changes in the functions of circulating neutrophils in PsA patients pre-therapy, compared to age- and sex-matched healthy controls and b) if these functions changed in PsA patients 12-weeks post-secukinumab therapy.
Methods: Neutrophils were isolated from venous blood of 16 PsA patients and 10 healthy controls. Key neutrophil functions were measured at baseline and 12 weeks: reactive oxygen species (ROS) production, apoptosis (+/- TNF and GM-CSF), phagocytosis, receptor expression and chemotaxis. Changes in gene expression pre- and 12-weeks post-therapy (n=5 PsA) were measured using RNAseq.
Results: PsARC response was observed in 70.6% of participants on secukinumab therapy at 12 weeks. There were no significant differences in ROS production, phagocytosis or chemotaxis in PsA patients at baseline (compared to healthy controls) or during therapy. Chemotaxis towards IL-8 in PsA patients at baseline was decreased compared to that of healthy controls, but this difference did not reach statistical significance. Surface levels of activation markers CD11b/CD18 and CD63 were increased in PsA patients at 12-weeks compared to baseline, while surface levels of CD16 decreased. RNA-seq analysis indicated down-regulation of pathways mediated by IL-17A, oncostatin M, TWEAK (TNFSF12) and CCL2 during therapy, but up-regulated expression of pathways involving *de novo* protein biosynthesis.
Conclusion: Therapy with secukimumab in PsA did not significantly affect neutrophil host defence functions. The changes that were seen in circulating neutrophils indicate selective up- and down-regulation of functions that may reflect potential alterations in local or systemic cytokines, and/or an increase in the circulating pool of activated neutrophils that are no longer recruited into sites of inflammation because of the down-regulation of the local IL-17/CXCL8 signalling network.
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AB0116 DECREASED SERUM LEVEL OF IRISIN IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Irisin, exercise-mediated myokine, is one of the most recently discovered hormones. Irisin has been shown to play multifunctional roles including anti-inflammation by suppressing secretion of NF kß, TNF-α, IL-6, and other pro-inflammatory cytokines from macrophages and adipocytes [1]. Thus, several attempts have been made to investigate irisin in chronic inflammatory rheumatic diseases. And recent evidences show that serum irisin concentration is lower in patients with osteoarthritis, rheumatoid arthritis, and behcet disease than health individuals [2-4]. Furthermore, one study showed that serum irisin level was negatively correlated with radiographic severity of knee osteoarhtiritis [2]. However, no previous study has investigated irisin in patients with ankylosing spondylitis (AS).
Objectives: To assess the serum level of irisin, and evaluate the possible relationship of irisin with disease activity in patients with AS.
Methods: Male patients with AS fulfilled the modified New York criteria (n=119), and healthy male controls (n=30) were enrolled. Serum irisin level was measured by ELISA (Cusabio, CSB-EQ027943HU). Disease activity was assessed by acute phase reactants, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), and modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS). Clinical characteristics and serum irisin level of the AS group were compared with those of the control group using Student t-test for normally distributed continuous measures and Mann-Whitney U test for non-normally distributed continuous measures. To evaluate the correlations of serum Irisin level and AS disease activity, Spearman's correlation test was used. AS patients were grouped into the high BASDAI group (BASDAI ≥ 4, n=45) and the Low BASDAI group (BASDAI < 4, n=74). And serum irisin level was also compared between two groups.
Results: AS group had lower serum irisin concentration compared with healthy control group (60.50 [23.68-131.15] vs. 124.69 [79.58-192.90], p=0.013), while age and body mass index were not significantly different between groups. There was no significant correlation between irisin level and disease activities. However, High BASDAI group showed significantly lower irisin level than low BASDAI group (44.64 [18.13-85.89] vs. 65.68 [31.81-165.31], p=0.011).
Conclusion: AS patients have lower serum irisin concentrations than healthy controls. AS patients with severe symptoms tend to have lower serum level of irisin than those with less severe symptoms.
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AB0117 HLA B27*SUBTYPES FREQUENCIES IN COLOMBIAN PATIENTS WITH SPONDYLOARTHRITIS AND HEALTHY SUBJECTS TYPED IN HIGH-RESOLUTION TECHNIQUE

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Background: HLA-B*27 has been identify as a susceptibility and prognostic factor associated to axial spondyloarthritis. HLA-B*27 allele has been described to be present in about 90% of patients with ankylosing spondylitis, and with a different frequency in patients with other subtypes of SpA. In contrast, this allele has been observed to be present only in 7–8% in general population. A remarkable heterogeneity in HLA-B*27 alleles has been reported. They have been determined at DNA sequence and some subtypes have been associated increasing the risk to develop the disease
Objectives: To establish the frequencies of HLA-B27 subtypes in a group of Colombian patients with SpA and healthy population
Methods: In total, 61 Blood samples from Colombian mestizo individuals with SpA according to ASAS classification-criteria were evaluated by Sequencing Technology: Illumina Sequencing/PacBio Sequencing with analysis of the second and third exon. Results reported with six digits (including null alleles). In total, 294 results of peripheral blood from healthy individuals without joint symptoms were analyzed. Frequencies were obtained for demographic and genetic variables. Ethic Committee approval code 2018-020/2017-023
Results: The SpA group had a mean age of 45,88 ± 11,67, 62.3% of them were male, 6.6% reported current smoking and 37.7% reported smoking sometime in life. In total, 67.2% had inflammatory back pain, 14.8% had dactylitis, 63.9% enthesitis and 57.4% arthritis. Thirty patients were HLA-B*27 positive with a genotypic frequency of 50.8% and an allelic frequency of 24.6%. In this group of patients, the mean age was 43,5 ± 11,8, 76.6% were male, 86.7% of them were subtype B*27:05:02g and 13.3% presented the B27:02:01g. None of the SpA patients had both B*27 alleles.
On the other hand, the healthy individuals were men in 51.0% and the mean age was 37±15.4 years. Ten subjects were positive for the HLA-B*27 allele with a genotypic frequency of 3.4% and an allelic frequency of 1.7%. In this group of individuals 50.0% were male gender with a mean age of 38.4±17.9. No individuals were found to have the two alleles or homozygous for the B*27 allele. In all of them the subtype B*27:05:02g was observed in high-resolution sequencing

Conclusion: The SpA group had a mean age of 45,88 ± 11,67, 62.3% of them were male, 6.6% reported current smoking and 37.7% reported smoking sometime in life. In total, 67.2% had inflammatory back pain, 14.8% had dactylitis, 63.9% enthesitis and 57.4% arthritis. Thirty patients were HLA-B*27 positive with a genotypic frequency of 50.8% and an allelic frequency of 24.6%. In this group of patients, the mean age was 43,5 ± 11,8, 76.6% were male, 86.7% of them were subtype B*27:05:02g and 13.3% presented the B27:02:01g. None of the SpA patients had both B*27 alleles.

On the other hand, the healthy individuals were men in 51.0% and the mean age was 37±15.4 years. Ten subjects were positive for the HLA-B*27 allele with a genotypic frequency of 3.4% and an allelic frequency of 1.7%. In this group of individuals 50.0% were male gender with a mean age of 38.4±17.9. No individuals were found to have the two alleles or homozygous for the B*27 allele. In all of them the subtype B*27:05:02g was observed in high-resolution sequencing

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Disclosure of Interests: None declared

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AB0118 FREQUENCY OF INTESTINAL PARASITES AND THEIR ASSOCIATION WITH CLINICAL DISEASE ACTIVITY AND TREATMENT-DECISION IN PATIENTS WITH SPONDYLOARTHRITIS

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Background: Studies of human intestinal microbiota have focused mainly on bacteria and scarce information on how eukaryotic parasites fit in the gut context or its role in human health and disease.

Objectives: This is an approach to explore if intestinal parasites represent a significant factor concerning the treatment-decisions or disease activity in inflammatory conditions such as SpA

Methods: A Cross-sectional study including 65 patients with SpA according to ASAS classification criteria was performed. Clinical evaluation was made by rheumatologists and gastroenterologists. Stool samples were collected and microscopically analyzed by direct saline, Mini Parasep concentration and Kato Katz. Most prevalent protozoa in Colombia were also analyzed using PCR/qPCR. Lab tests included fecal calprotectin, CRP, ESR, and HLA-B*27. The association between intestinal parasite infection and clinical/treatment variables were evaluated using the Chi-square or Fisher's exact test. (Ethical/Cod.2017-023)

Results: SpA patients had a mean age of 43.9±11.5 years, 61.5% were male, 52.5% were positive for HLA-B*27 and 87.7% had axial involvement. In total, 67.7% of the patients were receiving biological treatment, 64.6% had ASDAS-CRP ≥2.1. In total, 75.4% of patients were positive for ≥2 gastrointestinal symptoms with a predominance of abdominal pain (66.2%), abdominal inflammation (63.1%), diarrhea (47.7%) and intolerance to some food (58.5%). Interestingly, 21.3% have high levels of calprotectin, 20% of patients with high calprotectin were receiving biological treatment against IL-17 (p=0.086) and 80% of these patients had BASDAI >4 (p=0.017) and ASDAS-VSG >2.1 (p=0.03).

The parasites found in SpA patients were *Endolimax nana* (98%), *Blastocystis* ssp. (63.8%), *Entamoeba coli* (8.6%), *Entamoeba histolytica* (6.9%), *Chilomastix mesnili* (6.4%), *E. dispar*/*moshkovskii* (1.7%) and *Giardia intestinalis* (3.7%). Patients positive for *E coli* (80%) were treated with NSAIDs (p=0.003). 3/4 of patients positive for *E histolytica* presented HLAB*27:05:02 positive. Likewise, the only patient who was positive for *G intestinalis* expressed this allele. 5/7 of patients treated with Sulfasalazine presented *Blastocystis* ssp and 33.3% *E coli*. The presence of intestinal parasites in SpA patients was not associated with gastrointestinal symptoms, either disease-activity measures.

Conclusion: The intestinal parasitism in the tropical countries as Colombia have shown an interesting pattern in SpA patients. The treatment may modulate the presence of some parasites; however, the presence of intestinal parasites in SpA does not seem to influence clinical disease activity

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AB0119 SERUM LEVELS OF INTERLEUKIN-22 ARE HIGH IN ANKYLOSING SPONDYLITIS, PARTICULARLY IN SMOKERS, BUT DO NOT CORRELATE WITH RADIOGRAPHIC BONE FORMATION NOR WITH DISEASE ACTIVITY

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Background: Elevated serum levels of interleukin (IL)-22 were reported in patients with ankylosing spondylitis (AS).[1] IL-22 was also reported to drive the osteogenic differentiation of mesenchymal stem cells. [2]

Objectives: To confirm the fact that serum levels of IL-22 are elevated in AS patients and to examine the relationship between concentrations of IL-22 and degree of radiographic progression in AS patients.

Methods: Seventeen male patients with established AS of more than 4 years duration signed the informed consent and donated 10 ml of peripheral blood. Demographic data was collected from patient's charts. Disease activity indices were calculated for all patients and radiographic disease progression was calculated as mSASS. A control group included 6 healthy persons and 4 patients with advanced diffuse idiopathic skeletal hyperostosis (DISH). Serum levels of IL-22 were tested using enzyme-linked immunosorbent assay. Intergroup differences were examined using the Mann-Whitney test, while correlations were calculated using Pearson correlation coefficient.

Results: Serum IL-22 levels were remarkably elevated in patients with AS, comparing to healthy individuals and patients with DISH (p=0.005). However, increased concentrations of IL-22 did not correlate with the degree of radiographic progression or AS disease activity indices, nor with disease duration or patient's age. Presence of diarrhea, psoriasis, uveitis, or elevated levels of C-reactive protein did not influence the levels of IL-22 as well. More AS patients with elevated serum IL-22 were smokers (p=0.05).

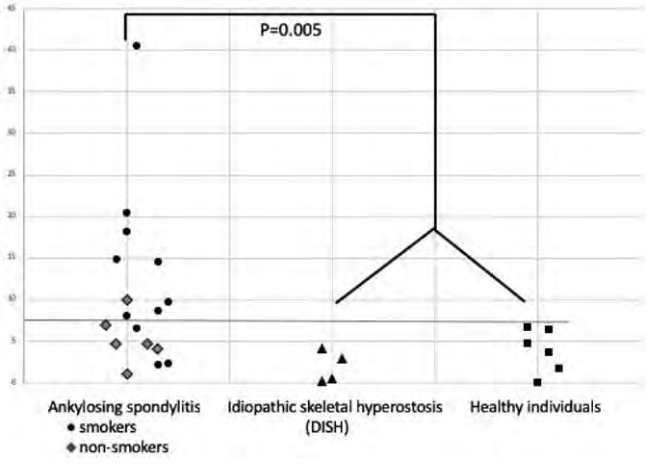


Fig. 1. Serum levels of interleukin 22 (pg/ml)

Conclusion: The serum levels of IL-22 are elevated in patients with AS. It seems that smoking can be related to the elevated levels of serum IL-22 in AS. The significance of this data is unclear and further research is needed.

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to new bone formation in spondyloarthropathies. Rheumatology. 2016 Dec 10;56.

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AB0120 THE EFFECT OF INFLAMMATORY SERA FROM DIFFERENT FORMS OF AXIAL SPONDYLOARTHRITIS ON THE OSTEOCLASTOGENIC POTENTIAL OF MONONUCLEAR PRECURSORS IN BLOOD

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Background: Spondyloarthritis (SpA) is characterized by pathological bone resorption and higher risk of osteoporosis. Inflammation accompanying the disease may activate mononuclear precursors in blood that are able to differentiate into osteoclasts, bone resorbing cells[1,2], and thus substantially contribute to bone resorption and aggravation of symptoms characteristic for this chronic disease.
Objectives: The aim of this pilot study is i) to figure out whether the inflammatory factors present in blood sera of SpA patients activate the osteoclastogenic potential of peripheral blood monocytes (PBM) derived from healthy subjects; ii) to find out whether this effect differs among sera from three forms of SpA, short-term non-radiographic (nr-axSpA) and radiographic (r-axSpA) SpA, and long-term ankylosing spondyloarthritis (AS), and finally iii) to assess whether the stimulatory effect of serum from SpA patients on osteoclastogenesis of healthy PBM reflects the altered clinical markers of inflammation and bone metabolism.
Methods: To simulate inflammatory condition characteristic for nr-axSpA, r-axSpA or AS, we created pool of 10 AS sera together with age- and sex-matched pools of nr-axSpA, r-axSpA and AxC (sera from healthy subjects). Disease duration of nr-axSpA and r-axSpA was set up to less than 2 years. The ASDAS score of AS form was significantly higher compared to the score of short-term forms of disease ($P < 0.05$). PBM from 6 healthy donors were cultured for 14 days in DMEM supplemented with 25 ng/ml macrophage colony-stimulating factor (M-CSF), 0.5 ng/ml receptor-activator of nuclear factor kappa B ligand (RANKL) and in parallel with 10% pooled human sera nr-axSpA, r-axSpA, AS and AxC. TRAP positive cells with 3 or more nuclei were recognized as osteoclasts and counted.
Results: Cultivation of PBM in the presence of both, diseased and healthy human sera increases number of osteoclasts in comparison to cultures without human sera. The strongest osteoclastogenic capacity develop PBM affected by pooled AS sera (2.9 times increase in osteoclast number compared to culture without human sera, $P < 0.05$), the lowest osteoclastogenic potential was detected in culture with pooled sera from healthy donors (2.1 times, P = NS). Pooled nr-axSpA, r-axSpA and AS sera do not appear to differ significantly among each other in size of their effect on PBM; nevertheless, trend to lowest numbers of osteoclasts can be seen in culture with r-axSpA sera (P = NS).
Conclusion: Cytokine milieu in human sera seems to have a pro-osteoclatogenic effect regardless of its origin with respect to healthy condition. However, inflammatory factors present in the sera of SpA patients enhance the osteoclastogenic potential of PBM, as documented especially in AS sera presenting with significant, 7fold increased serum CRP levels (P = 0.003), and thus may contribute to aggravation of the osteoporotic condition of SpA patients.
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AB0121 ASSESSMENT OF GLOBAL DNA METHYLATION IN PERIPHERAL BLOOD CELL SUBPOPULATIONS OF PATIENTS WITH AXIAL SPONDYLOARTHRITIS: PRELIMINARY RESULTS

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Background: Axial spondyloarthritis (ax-SpA) corresponds to a group of chronic inflammatory disease mainly affecting the axial skeleton. TNFα and IL-17A have been identified as key inflammatory mediators driving the inflammatory process of ax-SpA. Epigenetics refers to different mechanisms that alter gene expression without involving changes in DNA sequence. The mechanisms of epigenetics include microRNA, histone modifications or DNA methylation. DNA methylation is associated with a repressed chromatin state and inhibition of gene expression. It is recognized that aberrant DNA methylation can result in immune cell autoreactivity.
Objectives: Epigenetics have been rarely evaluated in ax-SpA. We previoulsy reported that patients with ankysloing spondylitis (AS) had an imbalance between HAT and HDAC activities. In this study, we aimed to evaluate the global DNA methylation of patients with ax-SpA.
Methods: Case-control study (NCT03092583). Patients with radiographic (AS) or non radiographic (nr) ax-SpA (ASAS criteria) and healthy controls (HC) were evaluated. All the patients were biologic naïve and under NSAIDs. Disease activity was evaluated by BASDAI and ASDAS. CD4+T cells and CD14+ monocytes were isolated form peripheral blood and then DNA was extracted (E.Z.N.A. Blood DNA kit, Omega Bio-Tek). Global DNA methylation (5-mC) was determined using MethylAmp global DNA methylation quantification kit (Epigentek) using 150ng of total DNA.
Results: 25 patients with AS (18 M; mean age ± SEM: 48.9 ± 3.5 y; mean disease duration: 14.9 ± 2.2 y; B27+: 84%), 21 with nr-axSpA (11 M; age: 42 ± 3.3 y; disease duration: 7.9 ± 2.3 y; B27+: 68%) and 11 HC (7 M; age: 48.4 ± 3.9 y) were evaluated. Patients had active disease (BASDAI and ASDAS in AS and nr-axSpA: 5.1 ± 0.4 and 5.4 ± 0.5; 4.7 ± 0.4 and 5 ± 0.4, respectively). In CD4+ T lymphocytes, global DNA methylation was lower in the whole group of patients (AS and nr-ax-SpA) compared to HC (0.91 ± 0.26 *vs* 1.08 ± 0.19 % of 5-mC) (NS). Conversely, DNA methylation was higher in monocytes from patients compared to HC (1.43 ± 0.16 *vs* 1.15 ± 0.5 % of 5-mC) (NS). When analysing the results between ax-SpA subgroups, an hypomethylation was more evident in the CD4+T lymphocytes from patients with nr-axSpA compared to AS and HC, a result that was not observed in the monocyte subpopulation (Figures).
Conclusion: A global DNA hypomethylation is observed in patients with ax-SpA, especially in the nr-axSpA subgroup. These results are more evident in T CD4+ lymphocytes. Additional analysis on a larger series of patients is required to confirm these preliminary results. In addition, we aim to examine the specific DNA methylation status of the TNF promoter gene.
References:

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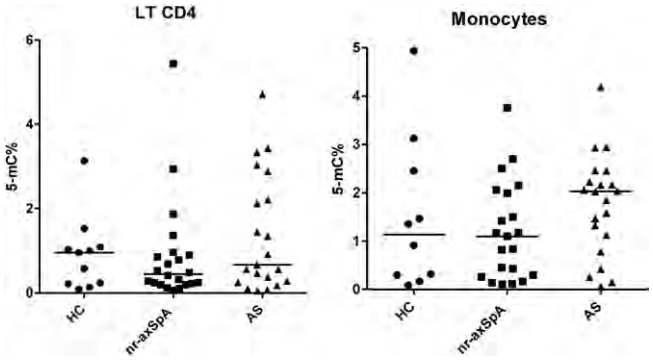


Figure. global DNA methylation of CD4+ T lymphocytes and monocyctes from patients with ankylosing spondylitis (AS), non radiographic axial spondyloarthritis (nr-ax-SpA) and healthy controls (HC)

Disclosure of Interests: None declared
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8. SLE, Sjögren's and APS - etiology, pathogenesis and animal models

AB0122 **DETECTION OF CIRCULATING M3 MUSCARINIC ACETYLCHOLINE RECEPTOR REACTIVE TH17 CELLS IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME**

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Background: Sjögren's syndrome (SS) is an autoimmune disease which is characterized by lymphocytic infiltration including $CD4^+$IL-17 producing helper T (Th17) cells to the lacrimal and salivary glands. We previously detected anti-M3 muscarinic acetylcholine receptor (M3R) antibodies (1) and M3R reactive $CD4^+$IFNγ producing helper T (Th1) cells (2) in SS patients. Moreover, we clarified that M3R reactive Th1 and Th17 cells had pathogenic roles in the development of auto-immune sialadenitis in SS mouse model (3).

Objectives: The purpose of this study was to identify circulating M3R reactive Th17 cells among primary SS (pSS) patients, and to determine functional properties of those cells.

Methods:

1) Peripheral blood mononuclear cells (PBMCs) were isolated from whole blood of 10 pSS patients, age gender matched 10 healthy controls (HC), and 5 IgG4-related disease (IgG4-RD) patients. According to their HLA-DRB1 typing, top 10 ranked 20 mer peptides from the full length of M3R, which were highly predicted to bind to each HLA molecules according to the immune epitope database website, were selected for each subjects. PBMCs were stimulated with these selected M3R peptides mixed for 40 hours, and M3R peptide reactive IL-17 secreting cells were detected by IL-17 enzyme-linked immunospot assay (ELISpot).
2) PBMCs from 5 pSS patients who were positive for M3R specific IL-17 secreting cells, were stimulated with selected 12-20 mer M3R peptides separately, to identify the dominant M3R peptides responsible for IL-17 secretion by ELISpot.
3) To identify whether detected IL-17 secreting cells were Th17 cells or not, isolated $CD4^+$ T cells from 3 pSS patients who were positive for M3R specific IL-17 secreting cells, were co-cultured with auto-monocyte derived dendritic cells (DCs), and stimulated with the dominant IL-17 secreting M3R peptides detected in method 2.
4) Anti-M3R antibodies were examined using ELISA method.
5) Clinical features were compared between M3R specific Th17 cells positive and negative pSS patients.

Results:

1) 5 of 10 (50%) pSS patients, while none of 10 (0%) HC, and 5 (0%) IgG4-RD patients, showed significantly increased IL-17 positive spots against selected M3R peptides mixed stimulation compared with non-stimulation in ELISpot (Figure 1). M3R specific IL-17 secreting cells were detected significantly more frequently in pSS (5/10, 50%) than in HC (0/10, 0%) (p=0.03).
2) All 5 pSS patients, who were positive for M3R specific IL-17 secreting cells, showed significantly increased IL-17 positive spots against M3R AA76-95 peptides.
3) Co-culturing CD4+ T cells with DCs, stimulated with identified dominant M3R peptides in method 2, showed significantly increased spots, clarifying that IL-17 secreting cells were peripheral M3R reactive Th17 cells.
4) Titers of anti-M3R antibodies were significantly higher among M3R reactive Th17 cells positive pSS patients than negative pSS patients.
5) 5 pSS patients positive for M3R reactive Th17 cells had significantly higher disease activity score (ESSDAI: 8.0±4.3) than 5 negative pSS patients (2.8±1.7) (P=0.01).

Conclusion: We detected circulating M3R reactive Th17 cells in pSS patients using ELISpot, whose T cell epitopes were shown to be included in M3R AA76-95. Moreover, M3R reactive Th17 cells might correlate with higher disease activity and production of anti-M3R antibodies in pSS patients.

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Figure 1

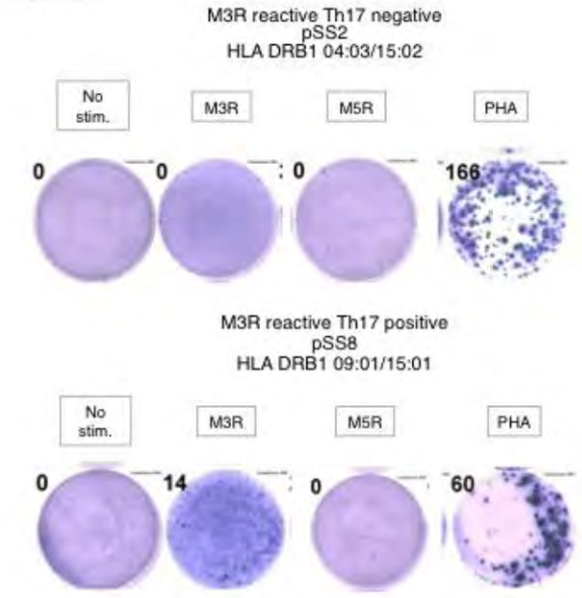


Figure1: Representative photomicrographs of IL-17 ELISpot assay. Significantly increased spots compared with non-stimulation were detected after incubating with selected M3R peptides mixture in M3R reactive Th17 cells positive patient (pSS8: lower row), whereas no spots were detected in those negative pSS patient (pSS2: upper row). M5R; control peptide, PHA; positive control

Disclosure of Interests: None declared
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AB0123 **CHANGES IN CELLULAR GLYCOSYLATION AS A KEY FACTOR IN THE IMMUNOPATHOGENESIS OF SYSTEMIC LUPUS ERYTHEMATOSUS**

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Background: Systemic Lupus Erythematous (SLE) is one of the most challenging autoimmune diseases as it may be presented as a severe, relapsing and disabling immune-mediated disorder still remaining incurable (1,2).
Protein glycosylation is an essential post translational modification that participate in the correct recognition of cells by the immune system (3–5). Moreover, glycosylation changes in T cells (specifically loss of branched *N*-glycans mediated by GnTV, encoded by *MGAT5* gene) have been shown to impact its intrinsic function and activity in a diverse panel of autoimmune diseases (3,4,6)

Objectives: To evaluate the impact of glycans in the cellular and molecular mechanisms underlying the loss of immune-tolerance, envisioning the identification of a new targeted-specific mechanism.

Methods: We have analysed the profile of cellular glycosylation of a subset of biopsy-proven lupus nephritis from SLE patients and normal kidney tissue (from two Porto Centre Hospitals), through immunohistochemistry (IHC) as well as by real time PCR using RNA extracted from paraffin tissues. Blood samples were collected and were analysed by flow cytometry. *Mgat5* null mice with 15-months old were monitored for autoimmune signs by evaluating proteinuria, weight loss and colon and kidney tissues were analysed by IHC and FACS.

Results: SLE patients revealed a significant decreased expression of complex *N*-glycans in the renal parenchyma, when compared to healthy kidney. In addition, we have identified in lupus nephritis patients a unique subset of circulatory $CD3^+$T cells with an abnormal glycosignature and displaying an increased expression of specific glycan-binding receptors. Interestingly, *Mgat5* null mice develop clinical signs compatible within autoimmune-like syndrome together with an increased infiltration of specific $CD3^+$T cells subset identified in SLE patients.

Conclusion: These findings point towards the identification of a novel immune player with increased ability to sense abnormal *N*-glycans, modulating the surrounding immune response. We propose glycosylation as a regulatory mechanism that tips the balance between homeostasis/self-tolerance and autoimmunity opening a potential novel targeted-specific mechanism in SLE pathogenesis.

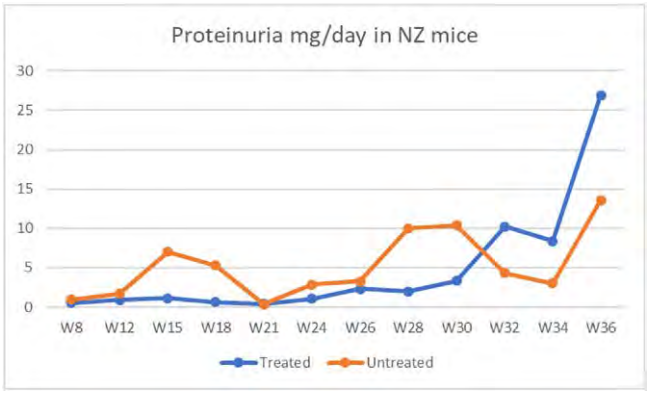
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AB0124 NO EFFECTS OF HIGH DOSE 25OH-VITAMIN D SUPPLEMENTATION ON LUPUS NEPHRITIS IN AN ANIMAL MODEL OF SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: 25OH Vitamin D (25-OH-D3) is a fat-soluble steroid-derived molecule involved in the calcium homeostasis. Low levels of 25-OH-D3 are commonly found in patients with systemic lupus erythematosus (SLE) and have been correlated to higher disease activity and severity. Several recent studies have demonstrated that high dose Vitamin D may influence several aspects of the innate and adaptive immune response and some authors hypothesized that high dose 25-OH-D3 may have a role in the treatment of SLE. Despite these observations, the immunomodulatory effect of high dose 25-OH-D3 *in vivo* still needs to be demonstrated.
Objectives: The aim of our study was to identify the effect of 25-OH-D3 on proteinuria, survival and renal biopsy in New Zealand Black/White F1 mice (NZ), that develop a disease very similar to human SLE nephritis.
Methods: We administered to 20 NZ mice a diet enriched with high dose 25-OH-D3 10,000 UI/Kg starting from 8 weeks of age. Mice were divided in 7 experimental groups (5 mice each). The first group was sacrificed before the start of the treatment (8 week of age), three groups were treated (treated mice – TM) with 25-OH-D3 and sacrificed at 16, 26 and 36 weeks of age. The other three groups were enrolled as controls and sacrificed at 16, 26 and 36 weeks of age respectively (untreated mice – UM). The parameters collected included: total urinary protein and kidney histology for the evaluation of lupus nephritis (LN): glomerulonephritis, interstitial nephritis and vascular lesions according to a 5 points scale to obtain a total score (ranging from 0 to 12).
Results: In UM, proteinuria tended to increase over 1 mg/day at 12 weeks of age (1.7±0.43mg/day) and further increased until to reach a plateau after 28 weeks of age (10±2.0 mg/day).
In TM, a significant increase in proteinuria over 1 mg/day was observed at 24 weeks, when the mean proteinuria was 1.7±1.33 which was lower than controls at the same age although without statistical significance (2.9±2.6); thereafter proteinuria started to increase also in treated mice and at week 30 was higher in TM compared with UM (10,3±8.8 vs 4.3±3.5 p=0.05). Figure 1. Kidney histology showed, in mice sacrificed before the start of the treatment no signs of LN. In mice sacrificed at 16 weeks minimal interstitial nephritis (score 1) was identified in 2 mice only in UM. At 26 weeks of age, a higher total LN score was identified in TM compared with UM (3.4±3.8 vs 0.4 ±0.9) with higher score for all three parameters analyzed. At 36 weeks of age, the TM group maintained a higher total LN score compared to UM (6.5±1.7 vs 6.0±2.6) with higher score for glomerulonephritis and interstitial nephritis.
In the TM group, three mice spontaneously died at 26, 30 and 32 weeks of age, while in the UM only one mouse died at 36 weeks of age.
Conclusion: Our data suggest that, in this animal model of SLE, 25-OH-D3 administration seems to delay the onset of proteinuria, although has no effect on the overall disease control. In addition, it may have a negative effect on renal histology and survival with earlier development of LN.

Figure:



Disclosure of Interests: None declared
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AB0125 EXPRESSION OF INTERFERON TYPE I- AND TYPE II-INDUCED GENES IN PATIENTS WITH SJÖGREN'S SYNDROME WITH AND WITHOUT EXTRAGLANDULAR INVOLVEMENT

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Background: It is well known that Sjögren's syndrome (SjS) is characterized by an upregulation of interferon (IFN)-induced genes. Namely, IFN type I signature has been reported in peripheral blood mononuclear cells (PBMCs) and in salivary glands of patients with this disease. However, few data are available on possible variability of IFN-induced gene upregulation in different clinical phenotypes of SjS.
Objectives: To verify whether upregulation of IFN-induced genes is comparable in patients with SjS characterized by different clinical phenotypes, i.e., patients with systemic extraglandular manifestations (EGMs) versus patients with a disease limited to glandular features (GFs) and with widespread pain (WP).
Methods: The study population was composed by 11 patients with SjS and EGMs (1 male, age range 18-78 years), and 10 patients with only GFs and WP (all females, age range 46-81 years), all classified according to ACR-EULAR criteria. The prevalence of anti-SSA(Ro) antibodies was 11/11 and 8/10, respectively. Lip biopsy was positive in all cases. Six healthy normal subjects were also included in the study as control population.
Four IFN type I- and 5 IFN type II-induced genes were chosen for the study on the basis of previous literature data. Total RNA from each patient and control was isolated from purified PBMCs, followed by cDNA preparation and real time quantitative-PCR (RQ-PCR) analysis, using specific primer/probe sets. For calculation of relative expression, all samples were normalised against expression of a household gene (beta actin). A further normalization was performed against the mean value of relative expression obtained in the normal controls. Final fold change values were determined from the double-normalised values using the $2^{-\Delta\Delta CT}$ method (Applied Biosystems).
Results: Fold change values of gene expression of both IFN type I- and type II-induced genes in PBMCs were different in the two clinical phenotypes of SjS. Fold change values of IFN type I-induced genes appeared strongly higher in patients with EGM, and some of them only moderately increased in those with only GF and WP. The expression of some of IFN type II-induced genes were slightly increased in patients belonging to both clinical phenotypes. Results are detailed in the table.

Table. Fold change values of gene expression in patients with SjS plus EGMs, in patients with disease limited to GF and WP, and in controls.

Gene	MX1	IFIT1	IFT3	IFI44	IDO1	GRP1	MIG	IP-10	P2RY14
SjS-EGMs	85.9	38.5	24.4	40.4	25.1	8.3	4.5	1.5	5.5
SJS-GF-WP	4.2	1.7	2.0	4.8	4.1	1.2	0.6	0.3	1.3
Controls	2.1	1.6	1.1	1.5	1.4	1.3	1.5	1.3	1.4

Legend. IFN type I-induced genes: MIX, IFN-induced GTP binding protein 1; IFIT1, IFN-induced protein with tetratricopeptide repeats 1; IFIT3, IFN-induced protein with tetratricopeptide repeats 3; IFI44, IFN-induced protein 44.
IFN type II-induced genes: IDO1, indolamine-deoxygenase 1; GBP1, guanylate binding protein 1; MIG, C-X-C chemokine 9 (CXCL9); IP-10, C-X-C chemokine 10 (CXCL10); P2RY14, purinergic receptor 14.

Conclusion: The present data indicate that IFN type I- and, to a lesser degree, type II-induced genes are upregulated in patients with SjS, but this phenomenon is consistently stronger in patients with systemic EGMs. In patients with only GFs IFN-induced gene upregulation is milder in PBMCs, and then probably more restricted to the exocrine target tissues.

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AB0126

EXPRESSION CHARACTERISTICS OF ADENOSINE DEAMINASES ACTING ON RNA-1 IN SYSTEMIC LUPUS ERYTHEMATOSUS AND ITS CORRELATION WITH SERUM IFN-A

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Background: SLE is a multisystem autoimmune disease characterized by the production of multiple autoantibodies and loss of immunity against autoantigens in various tissues. SLE patients have significantly elevated RNA editing levels and the potential to produce new autoantigens.[1] ADAR1 is an RNA A-I editing enzyme that converts adenine to hypoxanthine and contributes to SLE pathogenesis.[2]
Objectives: Dama demonstrated the upregulation of ADAR1p150 expression in SLE T cells, B cells, PBMCs, and NK cells;[3] however, the following issues were not reported in detail: 1. specific alterations in ADAR1 expression in PBMCs collected from SLE patients with varying degrees of the disease and its correlation with serum IFN-α levels; 2. association between ADAR1 and clinical indicators; and 3. ADAR1 expression in renal tissue of LN patients. Our study therefore aimed to elucidate the abovementioned points.
Methods: We used qRT-PCR to determine ADAR1 expression levels in PBMCs and renal tissues of controls and SLE patients. We also conducted immunohistochemical studies to detect positive ADAR1 expression rate in renal cells of controls and LN patients.
Results: ADAR1 expression was higher in PBMCs of SLE patients than in those of controls and was positively correlated with SLEDAI. When serum IFN-α levels in SLE patients decreased <260.0 pg/mL, ADAR1 expression in PBMCs increased with the increase in IFN-α concentration, and serum IFN-α may regulate ADAR1 level in PBMC in SLE patients, which may require the participation of serum IgG antibody and related immune complex. However, there was no significant difference between the expression in renal tissues in all patients.
Conclusion: There was a certain correlation between ADAR1 expression and serum IFN-α levels in PBMCs of SLE patients.
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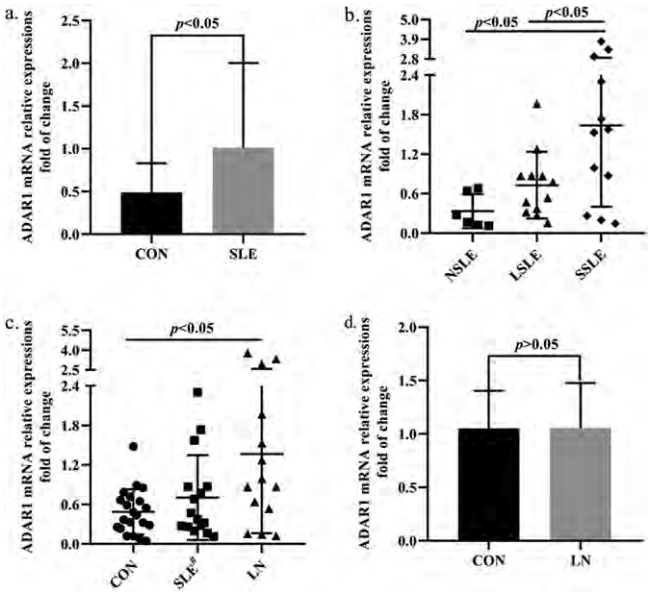


Figure 1. Analysis of ADAR1 expression levels. a. The ADAR1 expression in PBMCs was higher in SLE patients (n=30) than in healthy controls (n = 30) (p <0.05). b. SLE patients were divided into three groups: NSLE (SLEDAI 0–4, n = 6), LSLE (SLEDAI 5–9, n = 12), and SSLE (SLEDAI ≥10, n = 12) according to SLEDAI score. c. Based on the effect of the disease on the kidneys, the patients were divided into the SLE# group (#:SLE patient group without the kidney involved, n = 17) and LN group (lupus nephritis group, n = 13). d. There was no significant difference observed between the renal tissues of controls (n = 5) and LN patients (n = 10) (p >0.05).

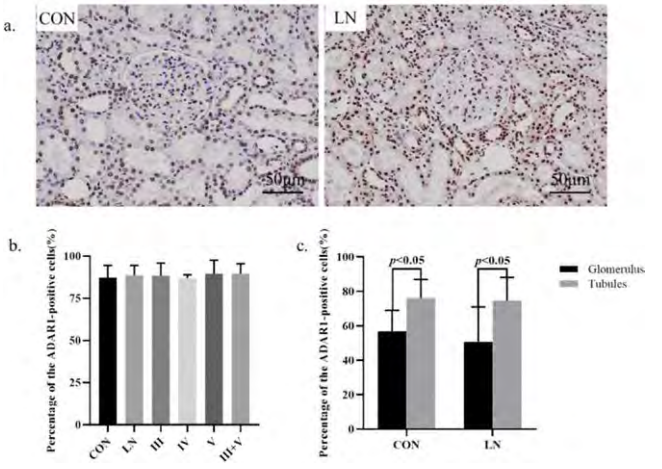


Figure 2. a. Immunohistochemical image of renal tissues from the two groups (200×). b. There was no significant difference in the ADAR1 cell positive rate between controls (n = 5), LN patients(n = 20), and different pathological subgroups (class III, n = 5; class IV, n = 5; class V, n = 5; class III+IV, n = 5) (p >0.05). c. The positive expression rate of ADAR1 in renal tubular cells was higher than that in glomerular cells both in the two groups (p <0.05).

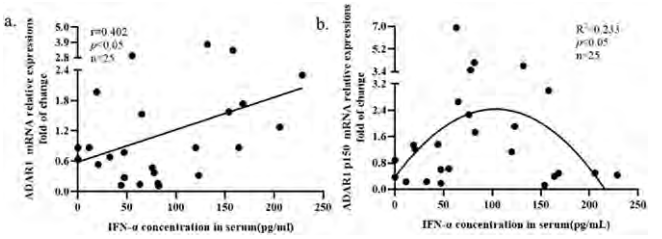


Figure 3. a. Correlation between ADAR1 and serum IFN-α levels in PBMCs of SLE patients. b. Correlation between ADAR1p150 and serum IFN-α levels in PBMCs of SLE patients.

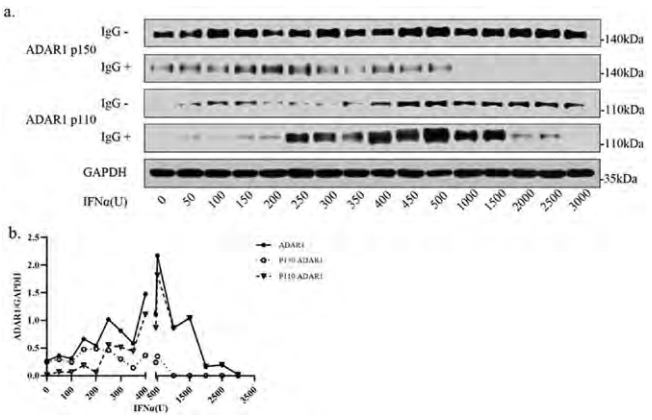


Figure 4. *In vitro* PBMCs assay. a. Western blot (WB) analysis of ADAR1p150 and ADAR1p110 in PBMCs using different concentrations of IFN-α, combined with 1.5 mg/mL IgG purified from the serum of SLE patients or without it, and cultured for 24 hours. b. The line graph depicts the trend of ADAR1, ADAR1p150, and ADAR1p110 expression with increase in IFN-α concentration *in vitro* PBMCs co-cultured with serum IgG from SLE patients.

Disclosure of Interests: None declared
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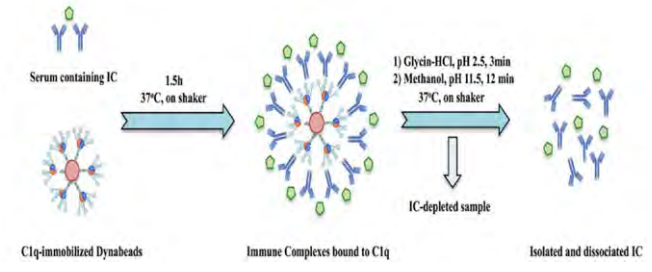
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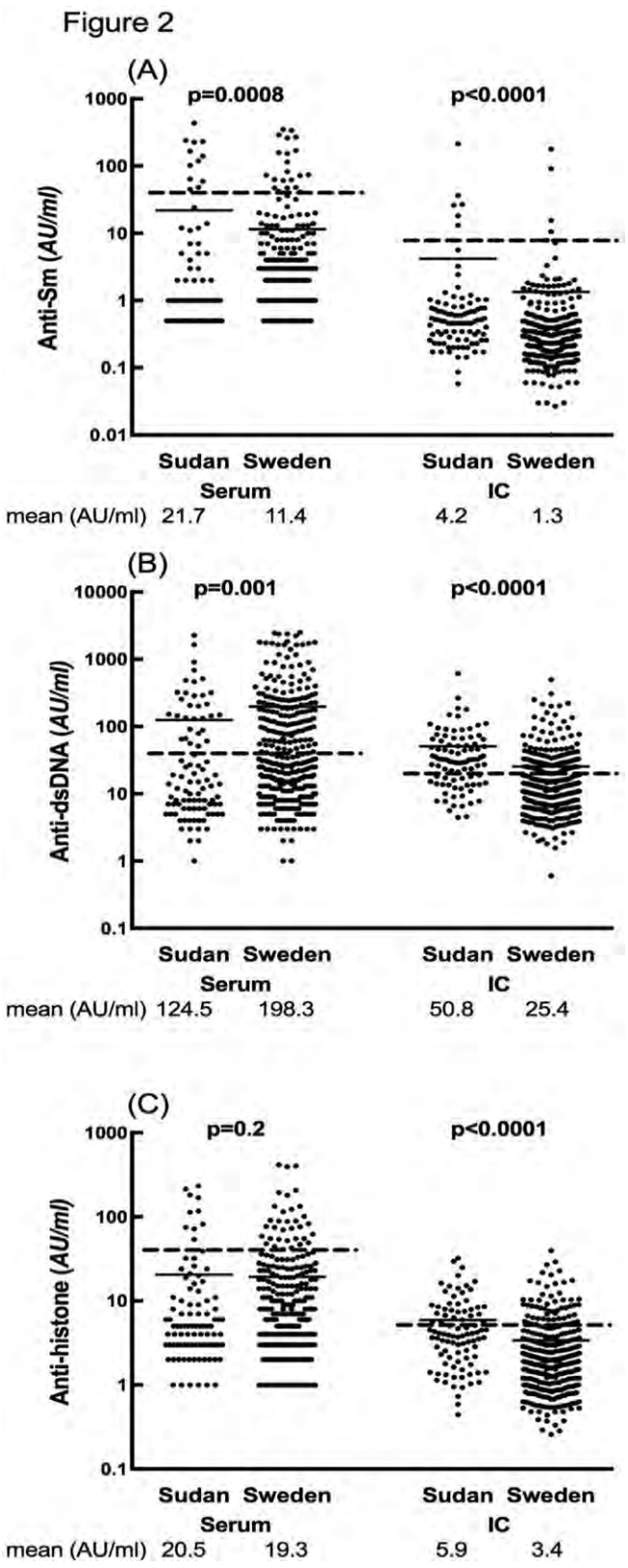
ACCUMULATION OF ANTI-NUCLEAR ASSOCIATED AUTOANTIBODIES IN CIRCULATING IMMUNE COMPLEXES IS MORE PROMINENT IN SLE PATIENTS FROM SUDAN COMPARED TO SWEDEN

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Background: Systemic Lupus Erythematosus (SLE) is a systemic immune complex (IC)-mediated disease associated with autoantibodies targeting multiple nuclear specificities (ANA). SLE has an aggressive nature among African populations. The role of SLE-related autoantibodies in the formation of IC has only been studied to a limited extent, and not at all in African SLE patients.
Objectives: To quantify ANA specificities present in circulating IC in Sudanese and Swedish SLE sera and to compare to corresponding serum levels
Methods: 93 Sudanese and 337 Swedish SLE patients who fulfilled the 1982 ACR classification criteria were included. IC were captured using magnetic microparticles coated with purified human C1q, then separated by a two-step elusion procedure (Figure 1). ANA-associated autoantibodies against dsDNA, Sm, the Sm/U1RNP complex, U1RNP, SSA/Ro52, SSA/Ro60, SSB/La, ribosomal P antigen, proliferating cell nuclear antigen (PCNA) and histones were quantified in sera and corresponding IC using a bead-based multiplex immunoassay. The IC purification technique has been developed and validated in our laboratory (Sohrabian ARD 2018), and previously used to study treatment responses to belimumab in Swedish SLE patients (Sohrabian ART 2019). Occurrence of ANA specificities in serum was determined using manufacturer's suggested cutoffs. These cutoffs were used in regression formulas to determine cutoffs for ANA levels detected in the corresponding IC.

Figure 1 SCHEMATIC ILLUSTRATION OF IMMUNE COMPLEX PURIFICATION PROCEDURE FROM SLE PATIENTS' SERA Sohrabian A et al. Number of individual ACPA reactivities in synovial fluid immune complexes, but not serum anti-CCP2 levels, associate with inflammation and joint destruction in rheumatoid arthritis. Ann Rheum Dis. 2018;77(9):1345-53.





Results: Swedish patients had higher serum levels of anti-Sm, anti-dsDNA and anti-ribosomal P antibodies compared to Sudanese patients. On the contrary, IC levels of all ANA specificities except anti-SSA/Ro52 and anti-SSA/Ro60 were higher in Sudanese patients (Table 1 and Figure 2). Sudanese patients were more often positive for anti-Sm, anti- Sm/U1RNP, anti-dsDNA and anti-histone antibodies in IC, whereas a borderline statistical significance was found for only anti-Sm in corresponding serum samples (Table 1).

Table 1.

Levels median/mean	Sudan serum	Sweden serum	P	Sudan IC	Sweden IC	P
SSA/Ro52	16/52.1	17/52.3	0.8	2.9/14.4	2.4/10.7	0.07
SSA/Ro60	2.0/47.2	3.0/48.7	0.2	1.5/14.6	1.3/12.5	0.7
SSB/La	2.0/22	2.0/22	0.6	1.1/4.2	0.8/5.5	**0.02**
Sm	1.0/21.7	1.0/11.4	**0.0008**	0.5/4.2	0.3/1.3	**<0.0001**
SmRNP	1.0/20.5	1.0/16	0.2	3.7/8.6	2.0/4.6	**<0.0001**
U1RNP	6.0/43.8	7.0/40.2	0.9	1.0/3.5	0.6/2.2	**0.0005**
dsDNA	14.0/124.5	28.0/198.3	**0.001**	32.1/50.8	12.4/25.4	**<0.0001**
Ribosomal P	1.0/9.3	2.0/11.7	**0.0006**	1.7/3.3	1.4/2.9	**0.005**
Histone	5.0/20.5	6.0/19.3	0.2	4.0/5.9	1.9/3.4	**<0.0001**
PCNA	5.0/8.4	5.0/8.9	0.6	11.1/14.2	7.0/11	**<0.0001**
Occurrence n(%)	**serum**	**serum**	**P**	**IC**	**IC**	**P**
SSA/Ro52	30(32.2)	105(31.7)	0.9	18(19.3)	55(16.6)	0.5
SSA/Ro60	34(36.6)	122(36.9)	0.9	27(29)	89(26.8)	0.7
SSB/La	15(16.1)	64(19.3)	0.5	9(9.7)	38(11.4)	0.3
Sm	12(12.9)	21(6.3)	**0.04**	6(6.4)	5(1.5)	**0.008**
SmRNP	15(16.1)	42(12.7)	0.4	17(18.3)	33(9.9)	**0.03**
U1RNP	20(21.5)	69(20.8)	0.9	22(23.7)	55(16.6)	0.1
dsDNA	31(33.3)	147(44.4)	0.055	64(68.8)	105(31.6)	**<0.0001**
Ribosomal P	4(4.3)	20(6)	0.5	2(2.1)	9(2.7)	0.8
Histone	10(10.7)	34(10.3)	0.9	34(36.6)	58(17.5)	**<0.0001**
PCNA	1(1.1)	10(3)	0.3	20(21.5)	45(13.5)	0.06

Conclusion: ANA-associated autoantibodies are more accumulated in circulating IC from Sudanese than Swedish SLE patients. The clinical significance of these findings is yet to be investigated in our upcoming analyses

Disclosure of Interests: None declared

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AB0128 CXCL5 DAMPENS INFLAMMATION IN THE PRE-CLINICAL MODEL OF SYSTEMIC LUPUS ERYTHEMATOSUS VIA THE ORCHESTRAL EFFECT OF REGULATING NEUTROPHIL TRAFFICKING AND SUPPRESSING HELPER T CELL-MEDIATED IMMUNE RESPONSE

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Background: Patients with systemic lupus erythematosus (SLE) suffer from severe morbidity and mortality[1-4], either from the disease itself or from side effects of immunosuppression[5]. Discovery of novel effective therapies with less toxicity is an urgent need.

Objectives: The aim of this study is to elucidate the therapeutic potential and working mechanism of cytokine CXCL5 in lupus mice.

Methods: Treatment with CXCL5, bone marrow (BM)-MSCs, standard of care (SOC) with combination of methylprednisolone and cyclophosphamide was given to 16-week-old Fas^{lpr} mice. Mice were monitored for 10 weeks. Splenic immune cell subsets were measured by flow cytometry. Circulating cytokine and immunoglobulin were detected by Luminex technology. Renal function was evaluated by urinary spot albumin creatinine ratio. In situ renal immune cell infiltration and complement 3 deposition were detected by Haematoxylin and Eosin (H&E) staining and immunohistochemistry.

Results: CXCL5 demonstrated consistent and potent immunosuppressive capacity in suppressing SLE with reduced autoantibody secretion, lymphoproliferation and preserved kidney function. With further exploration, we proved that CXCL5 reduced the proliferation of helper T cells (T_H1 and T_H2) in the *in vitro* functional assay. When we administrated CXCL5 to lupus mice, it promoted the proliferation of regulatory T cells and reduced the proliferation of T_H17 cells, macrophages and neutrophils. Multiple proinflammatory cytokines including IL-2, IL-6, IL-12, IL-17A, KC/CXCL1, MIP-1β/CCL4 and TNF-α were also reduced. When combined with SOC, CXCL5 boosted its therapeutic effect and reduced the relevant indices of disease activity. When we correlated the effect of four different treatment groups (CXCL5, BM-MSCs, SOC, and CXCL5 plus SOC) on mice survival and target cell changes, we found that T_H17 cells were the key effector cells involved in the pathogenesis of SLE.

Conclusion: These findings demonstrated that CXCL5 dampens inflammation in the pre-clinical model of systemic lupus erythematosus via the orchestral effect of regulating neutrophil trafficking and suppressing helper T cell-mediated immune response. Administrating exogenous CXCL5 might be an attractive option to treat patients with lupus.

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Disclosure of Interests: None declared

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AB0129 PCSK9 IS ASSOCIATED WITH DISEASE ACTIVITY AND IMPLICATED IN IMMUNE ACTIVATION IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: LDL-levels are increased by Proprotein convertase subtilisin kexin 9 (PCSK9) which targets the LDL-receptor (LDLR). We reported that PCSK9 has immune modulatory properties in addition to LDL-lowering and ameliorates dendritic cell (DC) activation by oxidized LDL (OxLDL) [1], which is abundant in atherosclerotic plaques. OxLDL is also raised and associated with cardiovascular disease (CVD) in SLE.[1-3]

Objectives: We here investigate the role of PCSK9 in SLE both in a clinical context and in experimental ex vivo studies. The objective is to investigate if PCSK9 and its inhibition could be of relevance in SLE in addition to LDL-level related properties

Methods: PCSK9-levels were determined by ELISA among SLE patients (n=109) and age- and sex-matched population-based controls (n=91). Common carotid intima-media thickness (IMT) and plaque occurrence were determined by B-mode ultrasound. Plaques were graded by echogenicity. Human peripheral blood monocytes from SLE patients or controls were differentiated into DCs. Effects of PCSK9 and its inhibition by silencing were studied.

Results: PCSK9-levels were non-significantly higher among SLE-patients as compared to controls but associated significantly with SLE disease activity, as determined by SLAM (0.020) or SLEDAI (0.0178). There was no association between PCSK9-levels and atherosclerosis as determined by IMT, prevalence of plaques or echolucent (potentially vulnerable) plaques. PCSK9 levels were significantly associated with CVD among SLE-patients but not after adjustment for age.

OxLDL induced PCSK9 in DCs and DC-maturation with increased expression of CD86 and HLA-DR. The effects were significantly stronger in DC from SLE patients than from controls. Silencing of PCSK9 abolished OxLDL-induced DC-maturation.

Conclusion: PCSK9 is associated with disease activity in SLE. One underlying cause could be OxLDL, promoting DC-activation which depends on PCSK9. OxLDL induces PCSK9, an effect which is higher among SLE-patients. PCSK9 could play an unexpected immunological role in SLE and inhibition of PCSK9 could potentially play a role in disease amelioration, pending on clinical studies.

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AB0130 SERUM ATHEROGENICITY IN WOMEN WITH UNTREATED SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is associated with an unexplained increase cardiovascular risk. The nature of the factors that contribute to progression of atherosclerosis were identified using the method for determining the atherogenicity of blood serum in cell culture in cell culture (in vitro). The term "atherogenicity" is meant as the ability of the serum and/or its components to induce intracellular accumulation of cholesterol in cultured cells.
Objectives: To compare atherogenicity of blood serum in women with untreated SLE and healthy women.
Methods: Thirty seven women (median age 30[21;39] years) with active SLE (median disease duration 45[3;102] months; SLADAI 17 [8;34]) were enrolled in the study. Lupus nephritis are defined in 15 (41%), Antiphospholipid syndrome (APS) – in 8 (22%) of 37 SLE patients (pts). The control group consisted of 30 women, median age 31[25;39] years.
Atherogenicity of blood serum was determined in the culture of murine macrophages. Peritoneal macrophages were isolated from the ascitic fluid of the line mice according to the generally accepted method J. Goldstein et al (1979y). Serum atherogenicity was determined by the accumulation of intracellular cholesterol induced by 10% of the blood serum of the patients, and expressed as a percentage of the content of cholesterol in the control cells.
Results: Elevated atherogenicity of blood serum was detected more frequently in SLE pts (24/72 (65%) vs healthy controls (5/30 (17%), p<0,01). The blood serum of SLE pts caused a 3-7-fold accumulation of intracellular cholesterol, which significantly differed from healthy women (203±136% vs 127±42%, p<0,001). The ability to stimulate the accumulation of cholesterol esters in murine macrophages was not associated with age, duration of the disease, lipid spectrum and was the highest in pts with nephritis (305±141% vs 180±52%, p<0,05) and APS (253±130% vs 119±75%, p<0,05).
Conclusion: Serums of women with untreated SLE may stimulate the accumulation of cholesterol in mouse macrophages unlike of healthy women.
The highest atherogenicity was found in blood serum of SLE pts with nephritis and APS.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.5116

AB0131 RESPIRATORY TRACT POLY(I:C) STIMULATION ACCELERATES SALIVARY GLAND IMMUNE DYSFUNCTION IN SPONTANEOUS SJOGREN'S SYNDROME ANIMAL MODEL

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Background: Sjogren's syndrome is one of the most common autoimmune diseases, with a prevalence of 0.33% to 0.77% in Chinese people, characterized by focal infiltration of lymphocytes in glands and the production of multiple autoantibodies. Studies have shown that virus infection may play a crucial role in the occurrence and development of this disease.
Objectives: It has been shown that airway stimulation with poly(I:C) can mimic respiratory tract viral infection to some extent. Thus, this study was aimed to investigate the dynamic immune responses in salivary gland after respiratory tract poly(I:C) stimulation in NOD mice.
Methods: The 5-week-old NOD mice were given respiratory tract poly(I:C) stimulation to mimic the respiratory virus infection once every other day for a total of 5 times (the total dose is 100μg), and the control group were given the same dose of sterile PBS. After 8 weeks, the mice were sacrificed to obtain and analyze the salivary gland tissues.
Results: We found that the salivary gland flow rate was decreased and the blood glucose was influenced by the Viroid stimulation during the early stage in poly(I:C) stimulated group compared with that in PBS group. Accordingly, the pathological injury of salivary gland tissues in poly(I:C) stimulated group was more serious, including decreased volumes of the salivary glands, increased number of pathological focus score and the increased area of lymphocyte infiltration. Furthermore, we found that the expression of IL-33 in salivary glands of poly(I:C) stimulated NOD mice was increased, especially the expression of IL-33 in the acini and ducts. Moreover, the expression of IFN-I and IFN-II is up-regulated in salivary glands.

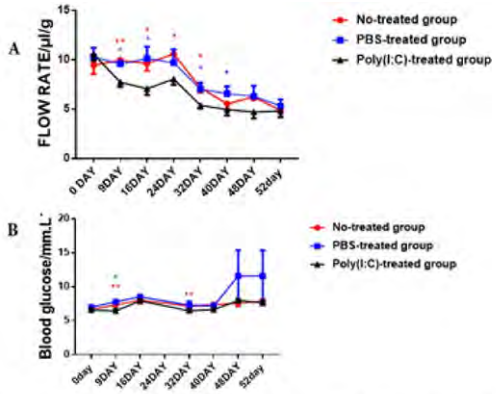


Figure1: Functional change of the NOD mice in different groups.
A. The dynamic change of the salivary gland flow rate; B. The dynamic change of the blood glucose

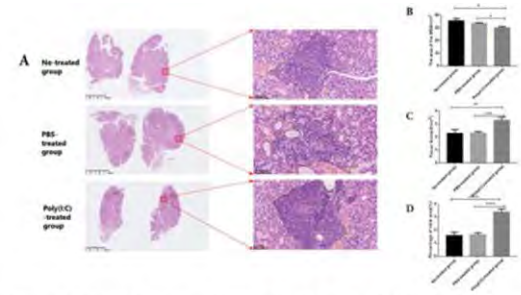


Figure2: Pathological changes of salivary glands in mice after different treatments.
A. The pathological changes of different groups; B. The quantitative analysis of the volume of salivary glands in different groups; C. The quantitative analysis of the numbers of pathological lesions of salivary glands in different groups; D. The quantitative analysis of the areas of pathological lesions of salivary glands in different groups.

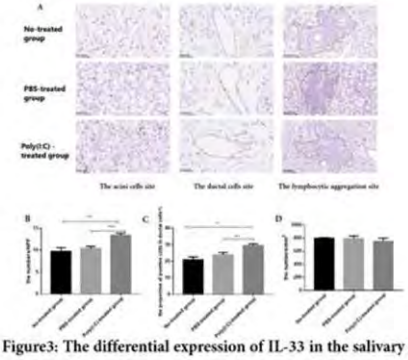


Figure3: The differential expression of IL-33 in the salivary glands.
A. The expression of IL-33 in different sites of salivary glands; B. The quantitative analysis of the expression of IL-33 in the acini cells site; C. The quantitative analysis of the expression of IL-33 in the ductal cells site; D. The quantitative analysis of the expression of IL-33 in the lymphocytic aggregation site.

Conclusion: The results of this study suggest that respiratory tract poly(I:C) stimulation accelerates salivary gland immune dysfunction in spontaneous sjogren's syndrome NOD mice, which mechanisms need to be further investigated.
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AB0132 ALTERATIONS IN PERIPHERAL T-CELLS AND B-CELLS SUBSETS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND SJÖGREN'S SYNDROME UNDERGOING THERAPEUTIC PLASMA EXCHANGE OR IMMUNOADSORPTION

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Background: Systemic lupus erythematosus (SLE) and Sjögren's syndrome (SS) are systemic autoimmune diseases characterized by a broad spectrum of clinical manifestations and disease course. Alternative therapies such as therapeutic plasma exchange (TPE), immunoadsorption are recommended to the patients who lack a good response to standard therapy [1].
Objectives: Our observational study was to explored whether abnormalities in T-cells, B-cells and their subtypes were present in the patients who had TPE or immunoadsorption in patients with SLE and SS compared with healthy controls (HC).
Methods: Demographic, clinical variables and autoantibodies were recorded. Flow cytometry was used to establish the frequencies of lineage subsets. Monoclonal antibodies against 21 surface markers such as CD3, CD4, CD8, were used to distinguish and evaluate T-cells' and B-cells' subpopulation. SLE acvity was measured using systemic lupus erythematosus disease activity index (SLEDAI). Comparisons between subgroups were undertaken using paired T-test, Mann-Whitney U test and ANOVA.

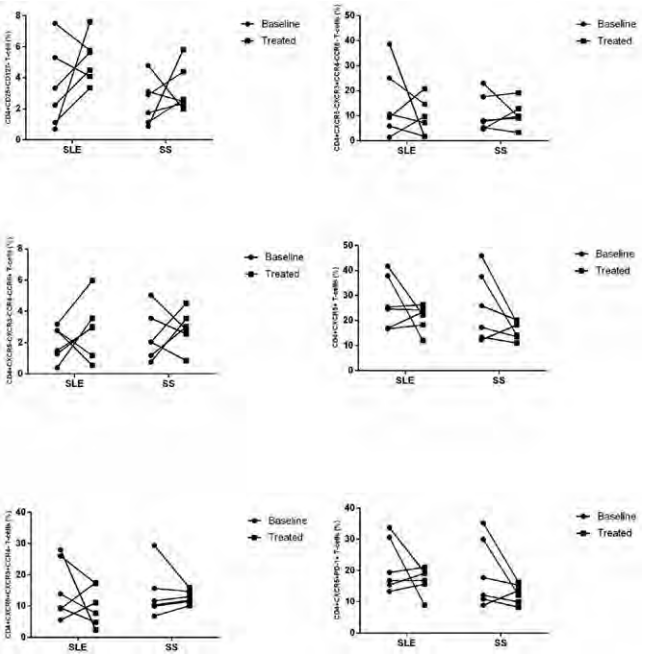


Figure 1. Altered expression of CD4+ T-cell subsets in the patients with SLE and SS after treated with plasma exchange or immunoadsorption

Results: 6 SS patients and 1 SLE patient underwent immune adsorption, while the other 5 SLE patients had plasma exchange all for three times. There was no significant difference among SLE, SS and HC in the proportion of T-cells and B-cells. The proportion of CD3-CD19+CD27+IgD+ B-cells were reduced in SLE, while CD3+CD4+CD25+CD127- T-cells were elevated in SS. The proportion of CD3+CD4+CD45RA+CCR7+T-cells were increased (p= 0.045), while CD3+CD4+CD25+CD127- T-cells were declined (p= 0.027) and CD3+CD4+CXCR5+PD-1+ T-cells went down after the therapies ($p \leq$ 0.030). The proportion of CD3-CD19+IgD-IgM-CD27+CD38+ B-cells was also reduced after TPE or immunoadsorption (p= 0.032) with ANA titers and IgG decreasing dramatically. SLEDAI scores were reduced after the therapy in SLE patients.
Conclusion: The T-cell and B-cell's profiles were proved to have alteration after TPE or immunoadsorption which shed light on the complicated mechanisms of these relatively novel therapy in SLE and SS.

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AB0133 INCREASED SOLUBLE SEMAPHORIN 4D/CD100 IN THE PLASMA OF SJÖGREN'S SYNDROME AND ITS EFFECTS ON HUMAN SALIVARY GLAND CELL AND CD4+ T CELL

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Background: Semaphorin 4D (SEMA4D) / CD100, known as a subfamily of axonal guidance proteins, has also been reported to act as an immunoregulator in several infectious and inflammatory diseases [1]. Sjögren's syndrome (SS) is a systemic autoimmune disease that primarily affects the exocrine glands by infiltrated lymphocytes resulting in dryness of mouth and eyes. IL-17 was reported to impair the integrity of tight junction barrier and attenuate the expression of aquaporin 5 (AQP5), causing salivary gland dysfunction in SS [2].
Objectives: This study was aimed to evaluate the role of SEMA4D in patients with SS and investigate the effect of SEMA4D on human salivary gland epithelial cell (SGEC) and T cell.
Methods: Soluble SEMA4D levels in plasma were measured by enzyme-linked immunosorbent assay (ELISA) from patients with SS, non-SS sicca and healthy controls. Immortalized human SGECs, originated from acini (NS-SV-AC) and duct (NS-SV-DC), were used to evaluate the effects of SEMA4D. $CD4^+$ T cells from human peripheral blood were isolated to determine the secretion of cytokines in response to SEMA4D. IFN-γ and IL-17 were used to determine the effects on AQP5 expression of SGEC.
Results: The levels of soluble SEMA4D in plasma were increased in patients with SS (median [interquartile range]: 1221.3 [393.5] pg/mL) compared to non-SS sicca (940.2 [355.1] pg/mL, p = 0.006) or healthy controls (909.5 [108.0] pg/mL, p < 0.0001). The levels of soluble SEMA4D in plasma were correlated with the levels of several autoantibodies including anti-SSA (Spearman's rho = 0.358, p = 0.006), anti-SSB (rho = 0.350, p = 0.007), and anti-muscarinic receptor 3 (M3R) Ab (rho = 0.495, p < 0.001), and also correlated with total IgG (rho = 0.431, p = 0.002). SEMA4D-stimulated SGECs showed decreased expression of tight junctions such as occludin and Zo-1. $CD4^+$ T cells secreted IFN-γ (p = 0.025), IL-17 (p = 0.028), and IL-21 (p = 0.007) with SEMA4D stimulation. IFN-γ and IL-17 decreased AQP5 expression in SGECs.
Conclusion: SEMA4D contributed to decreased expression of tight junction in SGECs. SEMA4D induced production of IFN-γ and IL-17 in $CD4^+$ T cells and these cytokine decreased AQP5 expression in SGECs.

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AB0134

SERUM LL-37, GALECTIN-3, AND TOLL-LIKE RECEPTORS-3 LEVELS DECREASE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is a systemic inflammatory disease characterized by heterogeneous clinical manifestations (1). Although there are significant developments with its pathogenesis, it is still not fully known. In recent years, pathways such as NETosis and plasmacytoid dendritic cell (pDC) activation have been emphasized in the pathogenesis of SLE (2, 3).
Objectives: In our study, we aimed to investigate serum LL-37, Galectin-3, and Toll-like receptors-3 (TLR)-3 levels, which are thought to be related to pathogenetic pathways in SLE patients.
Methods: 17 SLE patients and 33 healthy controls were included in the study. The clinical and laboratory features of the patients were determined. Serum LL-37, Galectin-3, and TLR-3 levels were determined by ELISA (enzyme-linked immunosorbent assay) method using the appropriate commercial kit, and the results were evaluated according to the manufacturer's instructions.
Results: The clinical and laboratory features of the groups are described in Table 1. In our study, serum LL-37, Galectin-3, and TLR-3 levels were decreased statistically significantly in SLE patients compared to healthy control (p = 0.007, p = 0.002, and p = 0.008, respectively).

Table 1. Clinical and laboratory features of the groups in the study

	Healthy control (n=33)	SLE (n=17)	p
Age (years)	34.1 ± 3.7	40 ± 11.4	0.05
Sex (n; female/male)	33/0	17/0	
LL-37(ng/ml)	78.6 ± 92.6	14.2 ± 19.3	0.007
Galectin-3 (ng/ml)	25.5 ± 23.2	6.7 ± 7.6	0.002
Toll-like receptors-3 (pg/ml)	7893.4 ± 1041.3	916.2 ± 469.7	0.008

Conclusion: It is suggested that LL-37, galectin-3, and TLR-3 levels have various effects on NEtosis and pDc activation pathways in SLE pathogenesis. In our study, low levels of serum LL-37, galectin-3, and TLR-3 in SLE patients suggest that they are associated with SLE pathogenesis.
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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.5782

AB0135

THE MITOCHONDRIAL-RETICULAR NETWORK (MRN) OF NEUTROPHILIC LEUKOCYTES OF SYNOVIAL FLUID (SF) OF PATIENTS WITH SLE AND RA

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Background:
Objectives: It has been established that in cells, in particular in neutrophilic leukocytes of SF, mitochondria form a mitochondrial-reticular dynamic spatial network (MRN). MRN is the epicenter of apoptosis, reflecting structural and functional changes in the immuno-complex pathology in SLE and RA.
Methods: SF was analyzed in patients: 10 SLE (43 ± 2.3 years), 13 RA (45 ± 1.6 years) and 8 donors (42 ± 3.7 years, postmortem). Neutrophilic leukocytes from the SF were isolated by standard methods and resuspended in a composition medium: 70 mM NaCl; 140 mM sucrose; 5.6 mM KCl; 10 mM pyruvate; 8 mM MOPS; pH = 7.4. The cell suspension was centrifuged for 5 min at 800 g. MRN was isolated by centrifuging the resulting supernatant for 15 min at 12 000 g. The resulting MRN fragments were resuspended in citrate-phosphate buffer (pH = 7.4) and used in experiments. The activity of adenosine monophosphate-activated protein kinase (AMPK) was evaluated by Western blotting. Quantitative determination of cytochrome C (Cyt C) was carried out by enzyme immunoassay method using the Human Cytochrome c Platinum ELISA kit (eBioscience, USA). Active forms of oxygen free radicals (AFRF) were registered by EPR. The swelling rate of MRN fragments was determined spectrophotometrically at 540 nm. The electrophoretic mobility (EM) of MRN fragments was determined by the automatic microscope "Parmoquant-2".
Results: MRN of neutrophilic leukocytes of the SF undergoes significant adaptive rearrangements during the development of SLE and RA (tab.1). On average, the expression of biochemical indicators of autophagy (AMPK), apoptosis (Cyt. C), necrosis (level of oxygen free radicals, low-amplitude swelling rate) increases by 2-3 times compared with the conventional norm. Particular attention should be paid to pathological changes in the electrokinetic potential of MRN, which determines the functional state of the SF as a whole as a colloidal system. Obviously, in SLE and RA, depletion of the energy of MRN (a sharp increase in the activity of AMRK), activation of free radical processes, disruption of intracellular ion homeostasis due to an increase in the rate of swelling of MRN as a manifestation of a compensatory-adaptive reaction. It ultimately leads to a decrease in electrokinetic properties of MRN. Thus EM is an integral indicator of physico-chemical properties and architectonics of MRN pointihg to the development of autoimmune pathology.

Table 1. EXPRESSION OF INDUCTORS OF AUTOPHAGY, APOPTOSIS, NECROSIS AND ELECTROPHORETIC MOBILITY OF MRN FRAGMENTS OF NEUTROPHILIC LEUKOCYTES OF SF IN SLE AND RA

Experience Terms	AMPK, cond.unit/mg protein	Cyt C, ng/ml	AFRF, unit/mg protein	Swelling rate of MRN, /min · mg protein	EM, m/v · sec
Donor (8)	0,51±0,05	23,7±5,4	7,3±2,4	0,177± 0,004	1,58± 0,07
SLE (10)	1,73±0,04**	49,3±6,5*	21,3±5,1**	0,435±0,005***	0,35±0,05***
RA (13)	1,25±0,07**	47,8±4.8*	15,7±4,3*	0,410±0,007***	0,41±0,07***

Notes: differences with the control norm: * - p <0.05; ** - p <0.01; *** - p <0.001.

Conclusion: Endoplasmic stress occurs in SF cells during the development of SLE and RA, blocking of autophagy and apoptosis leads to a breakdown of neutrophilic leukocyte MRN, accumulation of high molecular products of tissue decay - phlogogens in the intercellular space, among which the expression in the context is characterized by proteins - chaperones Hsp 60-100. These processes are accompanied by a shift in the bioelectric homeostasis of MRN neutrophilic leukocytes, an increase in their swelling rate and a significant decrease in their electrokinetic potential. The described MRN reactions of neutrophilic leukocytes of the SF should be taken into account when developing pharmacologically induced apoptosis as a new approach in the treatment of autoimmune diseases
References:
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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.1258

AB0136

THE SUSTAINED POSITIVITY FOR ANTI-DSDNA ANTIBODIES FOSTERS THE ESTABLISHMENT OF AN ATHEROTHROMBOTIC STATUS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background:
Objectives: 1. This study, developed within the Innovative Medicines Initiative Joint Undertaking project PRECISESADS framework, aimed to identify specific molecular profiles involved in the enhanced CV-risk present in SLE patients and to analyze the relevance of the sustained positivity for anti-dsDNA on the establishment of their atherothrombotic status.
Methods: One hundred and twenty-four SLE consecutive patients (not including patients with associated antiphospholipid syndrome), belonging to the PRECISESADS project, were evaluated for the presence of CVD and its association with positivity for anti-dsDNA antibodies. A second cohort of 62 SLE patients was included, of which endothelial dysfunction, lipid profile, the presence of atheroma plaques (identified by a pathologic increase in the carotid intimae media thickness -CIMT-), and the frequencies of anti-dsDNA positivity for 7 years, were evaluated. Serum inflammatory and oxidative stress biomolecules, and

NETosis-derived bioproducts were further evaluated by multiplex assay and specific commercial kits, respectively. Besides, miRNnomes were identified using next-generation sequencing. Clinical significance of the biomolecules analyzed was explored by correlation/association studies with immunological and CV-risk features.

Results: A significant relationship among the incidence of CVD (i.e. thrombosis or cardiac involvement) and the positivity for anti-dsDNA antibodies was recognized in the first SLE cohort. Accordingly, in the second SLE cohort, significantly impaired micro-vascular endothelial function (identified by reduction of hyperemia post-occlusion area), increased atherogenic index and pathologic increase in the CIMT were assessed in patients positive for anti-dsDNA in relation to anti-dsDNA negative patients. Around a 65% of SLE patients displayed a sustained positivity for anti-dsDNA antibodies for more than 7 years. These patients showed a distinctive and specific molecular profile compared with patients that had remained negative for anti-dsDNA, including increased inflammatory profile (IL1B, IL2, IL6, IL17, EOTAXIN, FGF, GMCSF, IFNγ, IP10, RANTES, TNF), enhanced oxidative status (lipoperoxides), and higher NETosis (nucleosomes, elastase). Levels of those biomolecules were closely interconnected and associated to their regulatory miRNAs, which accordingly exhibited differential expression in SLE anti-dsDNA(+) *vs* anti-dsDNA(-) patients. Finally, the frequency for positivity of anti-dsDNA significantly correlated both with markers of endothelial dysfunction and with the presence of atheroma plaques in SLE patients, pointing at the direct involvement of anti-dsDNA-Abs in the development of these processes.

Conclusion: 1. Positivity for anti-dsDNA antibodies confers a specific molecular profile linked to an enhanced CV-risk in SLE patients. 2. Moreover, the sustained positivity for anti-dsDNA antibodies fosters the establishment of an atherothrombotic status in these autoimmune patients.

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Disclosure of Interests: Alejandra M. Patiño-Trives: None declared, Maria A Aguirre: None declared, Carlos Pérez Sánchez: None declared, Pérez Sánchez Laura: None declared, María Luque-Tévar: None declared, Iván Arias de la Rosa: None declared, Rafaela Ortega Castro: None declared, Maria del Carmen Abalos-Aguilera: None declared, Mario Espinosa: None declared, Pedro Seguí Azpilcueta: None declared, Jacques-Olivier Pers: None declared, Nuria Barbarroja Puerto Grant/research support from: ROCHE and Pfizer., Speakers bureau: ROCHE and Celgene., Marta Alarcon-Riquelme: None declared, Eduardo Collantes Estevez Grant/research support from: ROCHE and Pfizer, Speakers bureau: ROCHE, Lilly, Bristol and Celgene, Chary Lopez-Pedrera Grant/research support from: ROCHE and Pfizer.

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AB0137 DIVERSITY ANALYSIS OF INTESTINAL FLORA IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is a multiple systemic autoimmune disease and its pathogenesis is still not fully understanding. In recent years, there has been reports on the relationship between SLE and intestinal flora.

Objectives: To study the diversity and the intestinal flora intestinal microbes in patients with SLE and further provide new ideas for clinical treatment.

Methods: The stool samples of 28 patients with SLE and 125 normal healthy adults were collected. The 16S rRNA in the specimen was sequenced using the Roche/45 high-throughput sequencing platform, and the differences between the two groups were compared at the level of the phylum and genus.

Results: In SLE patients, as the picture show, the levels of fusobacteria, proteobacteria and TM7 were significantly higher (P<0.05) and the number of firmicutes was significantly decreased (P<0.05) than that of healthy controls at the phylum level.The percentage of bifidobacterium, collinsella, enterococcus, leuconostoc, streptococcus, bilophila were significantly higher (P<0.05) and the number of lachnospira, roseburia, gemmiger, devosia, desulfovibrio were significantly decreased (P<0.05) than that of healthy participants at the genus level.

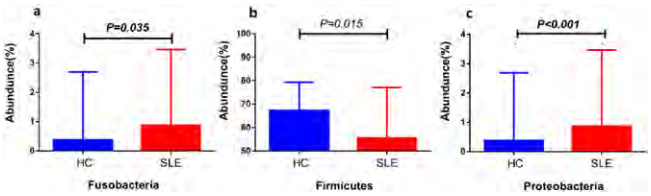


Figure 1. the differences between patients with SLE and normal healthy adults were compared at the level of the phylum

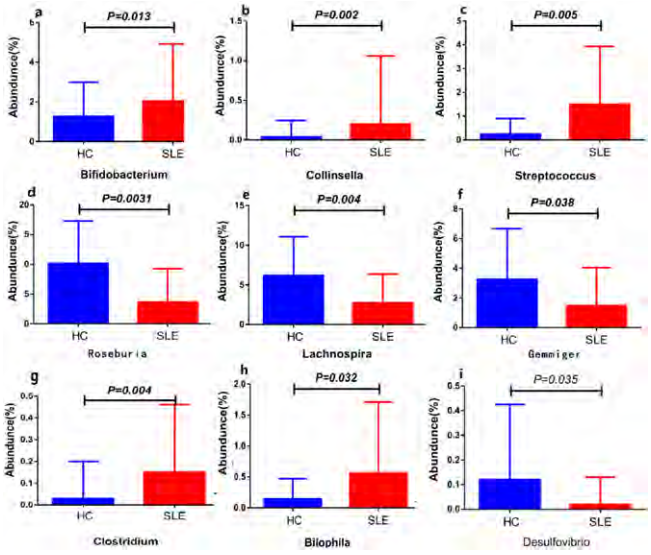


Figure 2. the differences between patients with SLE and normal healthy adults were compared at the level of the genus

Conclusion: The diversity of intestinal flora in patients with SLE altered from that of normal population. The differences are likely to be one of the pathogenesis of lupus, which might provide theoretical foundation for the regulation of intestinal flora to treat autoimmune diseases such as lupus.

Disclosure of Interests: None declared

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AB0138 INCREASED CD38 EXPRESSION LEVELS ON IMMUNE CELL SUBSETS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Plasma Cells (PCs) are implicated in the pathogenesis of Systemic Lupus erythematosus (SLE) and their targeting proved a promising treatment modality. As there is a monoclonal therapeutic antibody targeting CD38 licensed for clinical use in multiple myeloma, plasma cell depletion via CD38 seems to represent a promising path in SLE treatment. While CD38 Is highly expressed on plasmacells, it is present on the surface of subsets of T and B lymphocytes as well as myeloid cells.

Objectives: Here we aim to identify the differential expression of CD38 on peripheral blood leukocytes in SLE compared to healthy controls (HC) investigate the function of CD38+ T lymphocytes

Methods: We performed flow cytometry to investigate the expression of CD38 on peripheral blood mononuclear cells of SLE patients (n=36) and HCs (n=20). We additionally analyzed the expression of T lymphocytes within the urine of patients with lupus nephritis as well as the skin of SLE patients. We investigated the

inflammatory potential of CD38 positive memory T lymphocytes after stimulation and performed single-cell RNA sequencing analyses.
Results: CD38 Expression is increased on certain immune cell subsets: Plasmablasts and unswitched Memory B cells, as well as plasmacytoid dendritic cells and CD16+ non-classical monocytes. We observed a drastic increase CD38 in both memory CD4 and CD8 T lymphocytes in SLE patients. These cells were mostly effector T cells (and not regulatory T cells) and expressed other markers of T cell activation and proliferation. We found an enrichment of CD38+ memory T cells in the urine of patients with lupus nephritis. After polyclonal stimulation of T cells, CD38+ produced less inflammatory cytokines. Preliminary single-cell sequencing results indicate that CD38+ CD8+ T-lymphocytes have decreased clonal diversity and that these cells express genes associated with exhaustion and type 1 interferon response.
Conclusion: Increased CD38 expression on various lymphocyte subsets provides an additional rationale for investigating CD38-directed therapies in SLE. Targeting CD38 could not only deplete plasma cells but also has the potential to target interferon alpha producing plasmacytoid dendritic cells and modulate inflammatory T cell functions.
Disclosure of Interests: Lennard Ostendorf: None declared, Philipp Enghard: None declared, Pawel Durek: None declared, Frederik Heinrich: None declared, Mir-Farzin Mashreghi: None declared, Gerd Rüdiger Burmester Consultant of: AbbVie Inc, Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB Pharma, Speakers bureau: AbbVie Inc, Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB Pharma, Andreas Radbruch: None declared, Falk Hiepe: None declared, Tobias Alexander: None declared
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AB0139 T FOLLICULAR HELPER CELLS MAY BE INVOLVED IN THE LUPUS DEVELOPMENT IN HIGH FAT DIET-INDUCED OBESITY MICE

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Background: System lupus erythematosus (SLE) is an autoimmune disease that is associated with skin rash and multiple organs lesion. It is known that obesity is a major factor contributing to the onset and progression of autoimmune diseases including SLE. Our previous study showed that circulating T follicular helper (Tfh) cells played an important role in autoantibody production in SLE patients. A recent study showed that Tfh cells promote B cell production of IgA antibodies, which help shape the composition of the gut microbiota and may modulate obesity.
Objectives: By establishing an obesity-associated lupus mouse model, we investigated the pathophysiologic link of obesity, SLE and Tfh cells using MRL/lpr lupus prone mice.
Methods: Twenty MRL/lpr mice (10 male and 10 female) were randomized equally fed with a regular diet (RD) or high fat diet (HFD, 60% calories comprised of fat). Their body weights were recorded weekly as an indicator of obesity achievement. SLE progression was monitored weekly by development of skin lesion and urine protein levels assessed by Bradford assay. Blood was collected for IgG, anti-dsDNA and anti-nuclear antibody (ANA) detection. At the endpoint of week 14, spleen was measured and weighted. Spleen, kidney, and dorsum of neck skin were collected and embedded for H&E, PAS, Masson's staining, and immune complex staining to detect active histopathological lupus lesions and be quantified as histological skin score and kidney index. Tfh cells in spleen was identified by immunohistochemistry (IHC) staining glomerulus of kidney.
Results: Obesity was achieved with a significant difference of mouse body weight between the RD and HFD groups by week 3 and continued until week 14 ($p<0.05$ to $p<0.01$). Evidence of SLE development, such as skin rash on the dorsal neck and back in HFD group showed up as earlier as week 6 and occurred in 55.6% of the HFD group vs 11.1% of the RD group ($p<0.05$), with a higher histological score of skin in HFD group ($p<0.05$). Proteinuria was increased from 11 to 14 week in male HFD group with an elevated kidney index and immune-complex deposits in their glomerulus of kidney. There was an increase trend of anti-dsDNA and IgG titer in HFD group, but no difference of ANA was observed between these two groups. Splenomegaly was observed in the HFD mice ($p<0.05$). The Tfh cells in the spleen of HFD group were higher than RD group.
Conclusion: Our results show accelerated and greater severity of lupus development in MRL/lpr mice with HFD compared to mice on RD, indicating HFD-induced obesity exacerbates lupus development in mice. Tfh cells may be involved in the relation of SLE and obesity. This model could be used to investigate the mechanism underlying the link between obesity and SLE development. Interventions to reduce body weight or target Tfh cells may improve both lupus symptoms and outcomes in genetically predisposed SLE patients.
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AB0140 BAFF NEUTRALIZATION HAS JANUS-FACED EFFECT ON ATHEROSCLEROSIS ASSOCIATED WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Cardiovascular diseases (CVD) are the leading cause of death in systemic lupus erythematosus (SLE). B cells play a key role in the pathogenesis of lupus and anti-BAFF therapy has been approved in SLE. Since mature B cells also promote atherosclerosis, BAFF neutralization is expected to have an atheroprotective effect in SLE.
Objectives: The aim of our study was to test this hypothesis using a new mouse model with a mix susceptibility to lupus and atherosclerosis that received or not an anti-BAFF treatment, and in a cohort of SLE patients in whom we monitored carotid plaques, the B cell compartment and BAFF levels.
Methods: The effect of BAFF on atherosclerosis associated with lupus was investigated in the atherosclerosis- and lupus-prone *Apoe°D227K* mouse model and in a cohort of SLE patients. Mice were treated with a blocking anti-BAFF monoclonal antibody (Ab), while fed with a standard chow diet. Carotid plaque and carotid intima media thickness were assessed by ultrasound at baseline and during follow-up in SLE patients asymptomatic for CVD.
Results: Anti-BAFF Ab in *Apoe°D227K* mice i/ induced a B cell depletion, ii/ efficiently treated lupus, *iii/* improved atherosclerosis lesions in mice that had low plasma cholesterol levels but worsened the lesions in mice with high cholesterol levels. In that case, the atheroprotective effect of the BAFF-BAFFR signaling inhibition on B cells was counterbalanced by the proatherogenic effect of the BAFF-TACI signaling inhibition on macrophages. In SLE patients, BAFF blood levels were associated with subclinical atherosclerosis. Anti-BAFF Ab treatment had a differential effect on the intima media thickness progression in SLE patients depending on the body mass index
Conclusion: Depending on the balance between metabolic- and B cell-induced proatherogenic conditions, anti-BAFF could be respectively detrimental or beneficial on atherosclerosis development in SLE
Acknowledgments: Guillaume Even, Yasmine Lamri, Anh-Thu Gaston,
Disclosure of Interests: Fanny Saidoune Grant/research support from: supported by a research partnerships between the academic and GlaxoSmithKline France. Anti-BAFF mAb (IgG1, clone 10F4B) in mice was provided by Glaxosmithkline, Nicolas Charles: None declared, Julie Chezel: None declared, Brigitte Escoubet: None declared, Thomas Papo: None declared, Antonino Nicoletti: None declared, karim sacre: None declared
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AB0141 MYCOPHENOLATE MOFETIL, INHIBITOR OF INOSINE-5'-MONOPHOSPHATE DEHYDROGENASE, REGULATES DIFFERENTIATION, MATURATION AND FUNCTION OF HUMAN DENDRITIC CELL SUBSETS

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Background: Systemic lupus erythematosus (SLE) is a heterogeneous disease in which excessive inflammation, autoantibodies, and complement

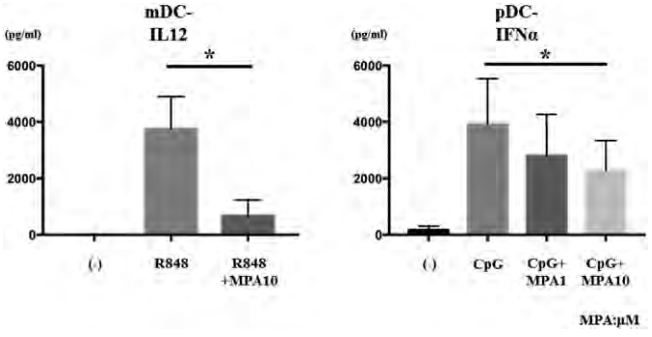
activation lead to multisystem tissue damage. Plasmacytoid dendritc cells (pDCs) play a central role in the pathogenesis of SLE through dysregulated type I IFN production, together with activated myeloid DCs (mDCs), amplifying vicious spiral of autoimmune disorders(1). Therefore, control of the aberrant DC activation may provide an alternative treatment strategy against SLE.

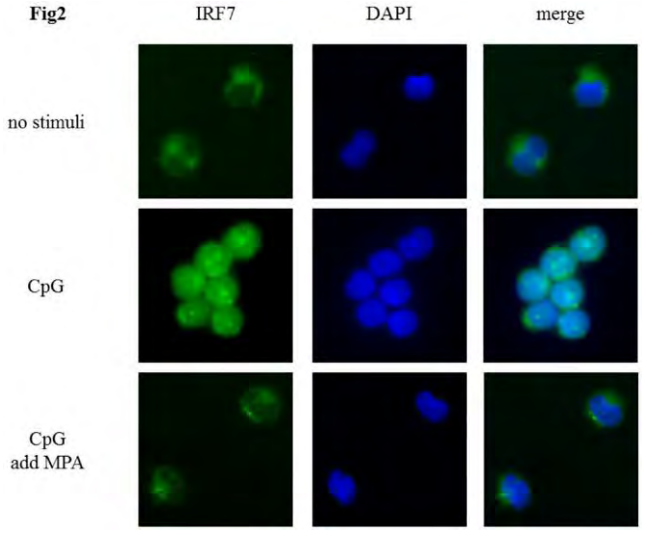
Objectives: Mycophenolate mofetil (MMF), which has been used to treat lupus nephritis, specifically blocks proliferation of B and T lymphocytes by inhibition of inosine-5-monophosphate dehydrogenase (IMPDH). In addition, although there is evidence indicating the immunosuppressive effects of MMF on human monocyte-derived dendritic cells(2.3), there are no reports showing its effects on human blood DC subsets. Here we focused on the effects of MMF on the functions of the blood pDCs and mDCs.

Methods: We isolated human blood DCs from healthy donors using cell sorting(4) and examined the function of mycophenolic acid (MPA), which is metabolic products of MMF, on DC subsets in response to TLR-ligands and serum from patients with active SLE. Written informed consent was obtained from all healthy adult donors and SLE patients.

Results: We found that therapeutic plasma concentration range of MPA down-regulated expression of CD40, CD80 and CD86 dose-dependently on mDCs and pDCs without inducing apoptosis, in response to R848(TLR7/8 agonist) and CpG2216(TLR9 agonist), respectively. Of note, MPA profoundly suppressed IL-12 production and STAT4 expression in the mDCs and IFN-α production and IRF7 expression in the pDCs(Fig 1). We also obserbed inhibition of nuclear translocation of IRF-7 in pDCs treated with MPA by confocal microscopy(Fig 2). Furthermore,we identified that MPA had an inhibitory effect on SLE serum-induced IFN-α production by human PBMCs.

Conclusion: Our data suggest that MMF can drive a wedge into the vicious spiral of autoimmune disorders through regulating the function of not only lymphocyte but also DC subsets. Thus, we unveiled a part mechanism of the therapeutic ability of MMF against SLE.





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AB0142 ANTIPHOSPHOLIPID SYNDROME AND ATHEROSCLEROSIS

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Background: Antiphospholipid syndrome (APS) is a systemic autoimmune disease with unknown etiology and complex pathogenesis. Recent studies have shown that the pathogenesis of the atherosclerotic process is related to the inflammatory component of the immune response, as well as to elements of autoimmunity. A number of autoimmune rheumatic diseases, including rheumatoid arthritis (RA), SLE and APS, are characterized by accelerated atherosclerosis and therefore at increased risk of cardiovascular disease and mortality. The risk of early atherosclerosis in patients with autoimmune disease is determined by traditional risk factors, chronic generalized inflammation, and target-specific autoimmune processes. These processes are complemented by the chronic use of drugs, such as KS, which worsen BMI, lead to hyperglycemia and hyperlipidemia.

Objectives: The aim of this study is to investigate the incidence of atherosclerosis at selected typical sites in patients with APS.

Methods: We examined 139 patients devided in to three groups: APS, SLE and healty controls. We performed US examination of carotid atheries with IMT measeurement and Calcium score of coronary artheries and aorta. All the patients were tested for: CBC, lipid panel, liver probes, ESR, anti-CL, anti-b2GPI anti-Prothrombin antibodies and ANA screen and ANA-profile as well.

Results: With the Kruskall-Wallis analysis, we found a statistically significant difference in IMT between the study groups for left (p = 0.005) and right (p = 0.014) carotid arteries. Comparative analysis between the groups showed that pathological levels of IMT (> 900 μm) in the right carotid artery were the highest in patients with antiphospholipid syndrome 15 (26.3%). In healthy controls, 3 (7.3%) were identified and no cases were reported for patients with SLE. The data for the left carotid artery (LCCA) are similar. 15 (26.3%) were registered for AFS, 4 for healthy controls (9.2%), and no patients with pathological values for IMT were registered in the SLE group. We compared the results for intima-media ticking between groups with the Chi-square test, finding a statistically significant correlation for the two carotid arteries - IMT-RCCA p = <0.001 for IMT-LCCA p = 0.002. Descriptive statistics show that the highest frequency of positive calcium score is characterized by the APS group 12 (31.6%), in patients with SLE they are 3 (15%), in healthy controls the case is 3%.

In our study, the AFS group had the highest incidence of positive CaScore, and its maximum values were significantly higher than the other two groups. The maximum agatson score for patients with antiphospholipid syndrome is 908 HU (Hounsfield Units), for SLE it is 2.1 HU, for healthy controls it is 233HU.

With the Kruskall-Wallis statistical analysis we examined the relationship of calcium score with the individual groups. Aortic aortic valve score was negative in all subjects. We find statistically significant differences between the calcium score groups.

Conclusion: The APS group is statistically significant in both pathologic IMT and higher plaque incidence compared to healthy controls and patients with SLE without the presence of anthophospholipid antibodies.

Based on the data obtained we can conclude that the antiphospholipid antibodies tested and their serum levels did not directly influence the values of the coronary artery and aortic Agatson score.

Disclosure of Interests: None declared

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AB0143 EXPRESSION OF HERV-E CLONE 4.1 GAG TRANSCRIPTS IN PERIPHERAL BLOOD MONONUCLEAR CELLS OF SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: Human endogenous retrovirus (HERV)-E clone 4.1 *gag* transcripts have been detected in peripheral blood mononuclear cells (PBMCs) of systemic lupus erythematosus (SLE) patients and seem to be associated to autoantibody production. To date, no study aimed to investigate whether their expression in

cytokine-stimulated vs. unstimulated PBMCs of SLE patients could be related with clinical manifestations.

Objectives: We aimed to correlate the expression of HERV-E clone 4.1 *gag* transcripts of unstimulated and phyto-haemoagglutinin (PHA) and interleukin-2 (IL-2)-stimulated PBMCs of SLE patients and healthy controls (HCs) and to evaluate the association between their expression and the demographic and clinical data of the SLE cohort.

Methods: PBMCs were isolated from 18 SLE patients and 22 age- and gender-matched controls. Cells from 10 SLE patients and 15 HCs were harvested for RNA isolation, HERV-E clone 4.1 *gag*- and RPL-13-selective cDNA synthesis and SYBR Green RT-PCR analysis. The expression of *gag* transcripts was normalized to that of the housekeeping gene RPL-13, using the Pfaffl method. PBMCs of the remaining patients and HCs were stimulated with PHA/IL-2 and HERV- E clone 4.1 *gag* expression assessed as described before. Statistical analysis was carried using a SPSS software, version n.23.

Results: Table 1 presents the demographic data of patients. The normalized mean ± SD *gag* expression was 1.6 ± 2.2 and 0.80 ± 0.79 in unstimulated PBMCs of SLE patients and HCs, respectively; and 1.1 ± 0.7 and 1.1 ± 0.4 in stimulated SLE and HC PBMCs, respectively. No significant difference emerged between patients and controls and between stimulated and unstimulated PBMCs (fig. 1). *Gag* transcripts expressed in PHA/IL-2-stimulated PBMCs of SLE patients significantly correlated with oronasal ulcers and high titers of anti- dsDNA antibodies (p=0.01 and p=0.004, respectively), while *gag* transcripts of unstimulated SLE PBMCs were significantly associated to the number of ACR criteria fulfilled (p=0.02).

Table 1 Demographic and clinical characteristics of SLE patients

Overall cohort of SLE patients (n.18)	Unstimulated conditions	Stimulated conditions	P
Number of patients	10	9	>0.05
Gender	Female	Female	>0.05
Mean age ± SD at diagnosis (years)	40.6 ± 14.6	26.4 ± 6.5	0.001
Mean disease duration ± SD (years)	12.9 ± 6.3	11.8 ± 7.6	>0.05
Mean SLEDAI ± SD	8.0 ± 5.8	5.7 ± 4.6	0.004
Mean SLICC ± SD	2.3 ± 2.3	1.6 ± 1.4	>0.05
Central nervous system involvement (n.,%)	1, 10%	1, 11.1%	>0.05
Renal involvement (n.,%)	0, 0%	1, 11.1%	>0.05
Cutaneous involvement and photosensitivity (n.,%)	9, 90%	8, 88.8%	>0.05
Oronasal ulcers (n., %)	3, 30%	3, 33.3%	>0.05
Joint involvement (n.,%)	8, 80%	6, 66.6%	>0.05
Hematologic involvement (n., %)	4, 40%	6, 66.6%	0.003
Serositis (n., %)	1, 10%	4, 44.4%	0.046
Anti-nuclear antibodies (n., %)	10, 100%	9, 100%	>0.05
Anti-double stranded DNA antibodies (*10^3IU/L), mean ± SD	15.4 ± 16.7	26.8 ± 74.3	>0.05
Mean C3 ± SD levels (g/L)	0.88 ± 0.12	1.2 ± 1.1	0.001
Mean C4 ± SD levels (g/L)	0.11 ± 0.03	0.16 ± 0.08	>0.05
Chloroquine (n., %)	5, 50%	8, 88.8%	>0.05

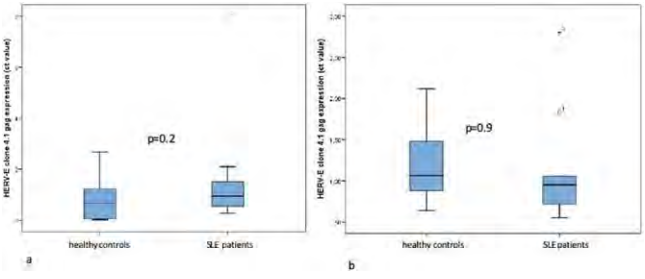


Figure 1. HERV-E clone 4.1 *gag* transcript normalized expression in unstimulated (a) and PHA/IL-2- stimulated (b) PBMCs of SLE patients and controls

Conclusion: According to these preliminary findings, the expression of HERV-E clone 4.1 *gag* transcripts in unstimulated and stimulated PBMCs does not significantly differ between SLE patients and controls. The significant association with some clinical variables in SLE patients needs to be confirmed on wider cohorts.

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Disclosure of Interests: None declared

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AB0144 STRATIFICATION OF PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME BY MEASURING B-CELL HEALTH

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Background: Primary Sjögren's syndrome (pSS) is a heterogeneous immune disorder with broad clinical phenotypes that can arise from a large number of genetic, hormonal, and environmental causes. B-cell hyperactivity is considered to be a pathogenic hallmark of pSS. However, whether B-cell hyperactivity in pSS patients is a result of polygenic, B cell-intrinsic factors, extrinsic factors, or both, is unclear. Despite controversies about the efficacy of rituximab, new B-cell targeting therapies are under investigation with promising early results. However, for such therapies to be successful, the etiology of B-cell hyperactivity in pSS needs to be clarified at the individual patient level.

Objectives: To measure naïve B-cell function in pSS patients and healthy donors using quantitative immunology.

Methods: We have developed standardised, quantitative functional assays of B-cell responses that measure division, death, differentiation and isotype switching, to reveal the innate programming of B cells in response to T-independent and dependent stimuli. This novel pipeline to measure B-cell health was developed to reveal the sum total of polygenic defects and underlying B-cell dysfunction at an individual level. For the current study, 25 pSS patients, fulfilling 2016 ACR-EULAR criteria, and 15 age-and gender-matched healthy donors were recruited. Standardized quantitative assays were used to directly measure B cell division, death and differentiation in response to T cell-independent (anti-Ig + CpG) and T-cell dependent (CD40L + IL-21) stimuli. Naïve B cells (IgD^+CD27^-) were sorted from peripheral blood mononuclear cells and were labeled with Cell Trace Violet at day 0 to track cell division until day 6. B cell differentiation was measured at day 5.

Results: Application of our standardized assays, and accompanying parametric models, allowed us to study B cell-intrinsic defects in pSS patients to a range of stimuli. Strikingly, we demonstrated a hyperresponse of naïve B cells to combined B cell receptor (BCR) and Toll-like receptor (TLR)-9 stimulation in pSS patients. This hyperresponse was revealed by an increased mean division number (MDN) at day 5 in pSS patients compared with healthy donors (p=0.021). A higher MDN in pSS patients was observed at the cohort level and was likely attributed to an increased division burst (division destiny) time. The MDN upon BCR/TLR-9 stimulation correlated with serum IgG levels (r_s=0.52; p=0.011). No difference in MDN of naïve B cells after T cell-dependent stimulation was observed between pSS patients and healthy donors. B cell differentiation capacity (e.g., plasmablast formation and isotype switching) after T cell-dependent stimulation was also assessed. At the cohort level, no difference in differentiation capacity between groups was observed, although some pSS patients showed higher plasmablast frequencies than healthy donors.

Conclusion: Here, we demonstrate defects in B-cell responses both at the cohort level, as well as individual signatures of defective responses. Personalized profiles of B cell health in pSS patients reveal a group of hyperresponsive patients, specifically to combined BCR/TLR stimulation. These patients may benefit most from B-cell targeted therapies. Future studies will address whether profiles of B cell health might serve additional roles, such as prediction of disease trajectories, and thus accelerate early intervention and access to precision therapies.

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AB0145 EFFECTS OF IMMUNOSUPPRESSIVE MEDICATION ON TYPE I INTERFERON ACTIVATION: IN VITRO ANALYSIS SHOWS A DOWNREGULATING EFFECT ON IFN ACTIVATION OF HYDROXYCHLOROQUINE AND ASPIRIN

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Background: Systemic Lupus Erythematosus (SLE) is prototypic Interferon (IFN) driven autoimmune disease characterized by an increased expression of type-I IFN stimulated genes, known as the IFN signature. The inhibitory effects of various drugs like Hydroxychloroquine and more recently Aspirin on IFN inducing pathways (1, 2) led to the idea that some standard of care drugs might decrease the IFN score in patients. Data on the in vitro effect of immunosuppressive medication on IFN activation are limited. Testing immunosuppressive agents for their effect on IFN activation in vitro will give insight into the mechanisms of IFN activation in vivo and the effect of immunosuppressive medication on this activation.
Objectives: To study the effect of immunosuppressive medication on the type-I IFN signature in an *in vitro* model
Methods: Freshly isolated human PBMCs were stimulated for 24 hours with or without CpG-A or Imiquimod (IQ) or transfected with the cGAS agonist G3-YSD to induce IFN upregulation through the TLR7/9- and DNA Sensing Receptor-pathway respectively. To assess the direct role of the medication on the downstream pathway of the IFNAR PBMCs were stimulated with IFN-a2b. Aspirin, diclofenac, HCQ, Mycophenolate Mofetil (MMF) and prednisone were added separately to these cultures followed by analysis of MxA by qPCR as a readout for IFN type I activation. Cell viability in all culture conditions was above 85%.
Results: The type I IFN activation induced by CpG-A, IQ, G3-YSD and IFN-a2b was significantly reduced after addition of Aspirin. Addition of diclofenac showed a trend towards reduced levels in all conditions. HCQ was able to significantly reduce the TLR7/9 induced IFN activation by CpG-A and IQ while MMF and prednisone did not show an effect in any of the culture conditions.
Conclusion: The IFN activation induced by the stimulation of various IFN inducing pathways was significantly reduced by Aspirin and HCQ in an in vitro model. Combining both clinical and *in vitro* data from our longitudinal cohort of childhood-onset SLE patients will elucidate the effect of different immunosuppressive drugs on the type-I IFN signature in these patients.
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AB0146 DRUG DEPENDENT ALTERATIONS IN B-CELL REPERTOIRE IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITH LOW DISEASE ACTIVITY

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Background: B-cells play a major role in the pathogenesis and perpetuation of the immune response in systemic lupus erythematosus (SLE). So far, B-cell subtypes have been studied well, but the precise mechanisms of the B-cell alterations during disease activity and during remission, depending on different medication, are still unclear.
Objectives: The aim of our study was to investigate the drug dependent alterations in the B-cell repertoire of SLE patients with low disease activity (SLEDAI – 2K ≤4).
Methods: Peripheral blood samples from 39 patients suffering from SLE (mean±SD; age 43±13 years, 87.2% females, disease duration 11.1±7 years) were drawn over 2 years. All SLE patients were in remission or low disease activity (median±SE, SLEDAI of 2.0±1.5). B-cells were characterized using CD19, CD20, CD5, CD27 antibodies and were grouped in naïve (IgD^+27^-), non-switched memory (IgD^+, $CD27^+$), memory (IgD^- $CD27^+$), B1 ($CD5^+27^-$) and MBL-like ($CD5^{++}$) B-cells. A quantitative flow cytometric bead-based assay (QuantiBRITE PE kit from Becton Dickinson) was used for the estimation of CD19 antibodies bound per cell. Further, CD38 and CD86 antibodies were used to characterize the B-cell subsets. All cytometric measurements were performed using a standardized BD LSR Fortessa platform. After 3 years of follow-up, patients' data about disease activity and current medication were obtained.
Results: 22 SLE patients were treated with hydroxychloroquine (85.8%) and 19 patients received mycophenolate mofetil (MMF; n=14; 54.6%) or azathioprine (AZA; n= 5; 19.5 %). 5 patients were treated with other DMARDs. Independently of hydroxychloroquine and/or MMF, no significant differences were seen in naïve, non-switched memory, post-switched memory, plasma blasts, B1- or MBL-like B-cells. Patients treated with AZA had significantly lower naïve B-cells (mean±SD, 39.3±6.7vs. 73.1±19.3 %; p = 0.028), but had significantly higher IgD-post switched B-cells (31.2±9.1 vs.12.5 ±9.2 %; p = 0.028, respectively) compared with no AZA-treatment. Interestingly, activated B-cells (5.5±1.5 vs. 1.8±1.1%; p = 0.009) were significantly higher in AZA-treated. After 3 years of follow-up, almost all patients were in remission (median±SE, SLEDAI of 2.0±2.0), except of 3 patients with a SLEDAI of ≥ 6. Interestingly, those patients had at baseline, statistically higher naïve B-cells (p = 0.041) and lower B1-like B-cells (p =0.020) compared with patients with low disease activity.
Conclusion: Our results suggest that independently of hydroxychloroquine and/or MMF treatment, all patients with low disease activity had similar normal B-cell subsets. Interestingly, in the small group of patients who were treated with AZA, a reduced regeneration of B-cells was shown. Patients with higher disease and high naïve B-cells showed an increased disease activity after three years.
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Disclosure of Interests: None declared
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AB0147 GENE EXPRESSION PROFILES OF PRIMARY SJÖGREN'S SYNDROME ASSOCIATED THROMBOCYTOPENIA IN B-LYMPHOCYTE USING HIGH-THROUGHPUT SEQUENCING

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Background: Primary Sjögren's syndrome(pSS) is a classical systemic autoimmune disease. Thrombocytopenia is one of the hematological manifestations of pSS with great challenges in clinic.
Objectives: To identify the candidate genes and functionally enriched pathways in the immune genesis and progression of primary Sjögren's syndrome (pSS) associated thrombocytopenia.
Methods: High-throughput sequencing was performed on 3 patients with pSS, 3 patients with pSS associated thrombocytopenia and 3 healthy individuals. The differentially expressed genes (DEGs) were identified, and function enrichment analyses were processed. The protein-protein interaction network (PPI) was constructed, followed by calculation of topological characteristics and sub-module analysis in order to obtain hub DEGs. The expression of some hub genes was verified by Real-Time PCR in 24 pSS patients.
Results: A total of 19 DEGs were identified. The enriched functions and pathway of the DEGs include Toll-like receptor signaling pathway, Salmonella infection, Viral protein interaction with cytokine and cytokine receptor, NF-kappa B signaling pathway and Human cytomegalovirus infection. Seven hub genes (TNF, IL1B, CXCL8, CCL3, CCL4, CCL3L1, CCL4L1) were identified and pathway enrichment analysis revealed that these genes were mainly enriched in toll-like receptor pathway. The relative expression of the CXCL8 mRNA in B-lymphocytes in patients with pSS associated thrombocytopenia was higher than that in the pSS without thrombocytopenia group. No differences were observed in the IL-1β or TNFα expression between these two groups.
Conclusion: PSS associated thrombocytopenia might be a subset characterized by a systemic inflammatory state. The identification of upregulated genes involved in thrombocytopenia of pSS provides insight in disease pathogenesis and opens avenues for the design of novel therapeutic strategies.
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Table 1. Differentially expressed genes among patients with pSS associated thrombocytopenia, pSS without thrombocytopenia, and healthy controls

Gene	LogFC in group2	FDR in group 2	LogFC in group1	FDR in group 1
TNF	4.96	1.29E-03	4.55	4.98E-05
CXCL8	8.88	1.29E-03	9.74	3.23E-05
CCL3	5.65	4.54E-03	5.61	1.70E-05
G0S2	7.38	4.54E-03	12.33	1.09E-05
LILRA3	8.42	7.23E-03	10.26	4.31E-05
IER3	5.44	9.53E-03	7.71	2.98E-06
DUSP2	3.50	9.53E-03	3.91	8.12E-05
TNFAIP3	2.63	9.53E-03	2.24	1.36E-03
CCL4	4.53	1.19E-02	5.42	3.35E-06
CCL4L2	6.72	1.40E-02	8.92	5.19E-05
CCL4L1	4.72	1.40E-02	5.94	3.94E-06
IL1B	5.54	1.66E-02	10.23	3.27E-06
METRNL	3.55	1.80E-02	4.02	2.08E-04
ID2	2.93	2.43E-02	3.78	6.57E-03
PER1	2.33	2.99E-02	2.42	7.68E-04
EGR1	2.98	3.09E-02	2.93	1.80E-04
CCL3L1	5.86	3.20E-02	6.66	5.94E-03
FFAR2	4.94	4.09E-02	8.40	1.34E-05
FOSB	3.23	4.86E-02	3.49	1.39E-03

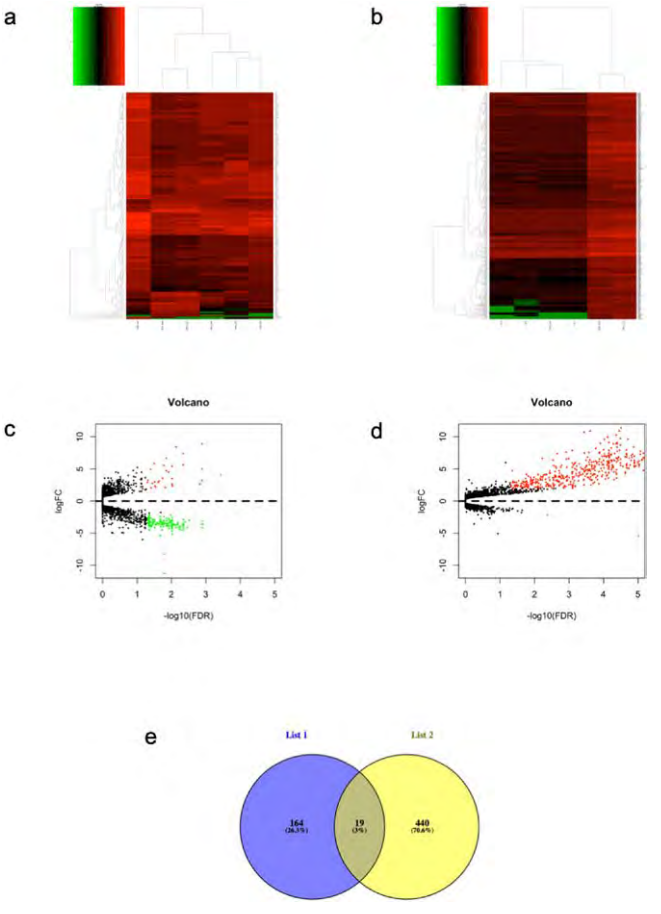


Figure 1. DEGs in pSS associated thrombocytopenia. 183 DEGs (31 up- and 151 down- regulated) between pSS patients with and without thrombocytopenia(a, c). 459 DEGs between pSS associated thrombocytopenia patients and healthy individuals were identified (2up- and 457 down- regulated) (b, d). The overlap among the 2 groups contained 19 genes represents the DEGs specified in pSS associated thrombocytopenia (e).

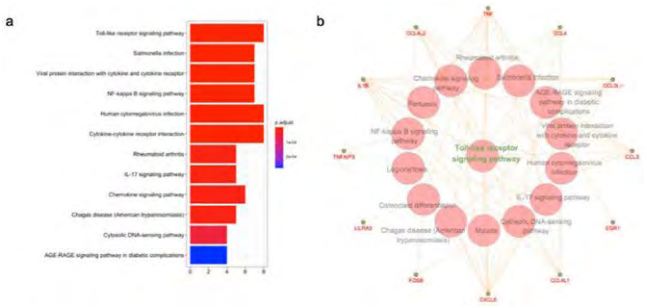


Figure 2. KEGG pathway analysis.

Acknowledgments: The authors apologize to all colleagues whose work has not been separately cited or discussed here due to limitations in space or knowledge.
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AB0148

ANALYSIS OF DIFFERENTIALLY EXPRESSED GENES AND MICRORNAS OF B CELLS IN PRIMARY SJOGREN'S SYNDROME BY RNA SEQUENCING

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Background: Primary Sjogren's syndrome (pSS) is a chronic autimmune disease mainly characterized by the inflammation of exocrine glands. There two key insights into pSS pathogenesis, which included "IFN signature" and hyperactivity of B cells. mRNA and microRNA (miRNA) are very important to control the gene expression.
Objectives: In this research, we analyzed the differentially expressed genes (DEG) and miRNA of B cells in pSS patients by RNA-sequencing. And we aim to preliminarily screen out some special miRNAs and target gene loci that may be involved in transcription regulation of B cells of pSS.
Methods: Peripheral blood samples from 3 pSS patients and 3 age-matched healthy controls (HC) were collected. $CD19^+$ B cells were sorted by Magnetic cell sorting method. Total RNA was extracted and cDNA of transcriptome or miRNA analysis were prepared and RNA-sequencing was performed to screen the DEG and miRNA. The GO Terms was used to uncover the biological function of DEGs, and the KEGG pathway enrichment was used to find out the related signal pathway. The mRNA-miRNA conjoint analysis was also performed.
Results:
1. There were a total of 73 significantly DEGs in B cells of pSS patients compared to HC, including 51 upregulated DEGs (such as *IFI44L*, *IFI44*, *IFIT1*, *IFITM1*, *IFIT3*, *IFIT2*, *IRF7*, *IFI6* and *ISG15*)and 22 downregulated DEGs (such as *ESR2* and *EGR1*). GO Terms and KEGG pathway analyses showed that most of the upregulated DEGs were enriched in IFN signaling and IFN regulatory pathway, and also showed the relationship with microbial infection, such as influenza A virus, hepatitis C virus, measles and herpes simplex virus.
2. There were five significantly differentially expressed miRNAs, including hsa-miR-4485-3p, hsa-miR-144-5p, hsa-miR-144-3p, hsa-miR-451a, hsa-miR-4732-3p. GO Terms and KEGG pathway analyses showed that most of the target genes which regulated by those miRNAs were enrichment on herpes simplex virus and TGF-β signaling pathway.
3. DEG and differentially expressed miRNAs conjoint analysis showed that the target DEGs which regulated by those miRNAs participated in cytoskeleton formation and modification of DNA or RNA, such as *RASD2*, *CKAP4*, *SPARS2L METTL*.

Conclusion: There were 51 upregulated DEGs and 22 downregulated DEGs in B cells of pSS patients. GO Terms and KEGG pathway analyses showed that most of the upregulated DEGs were enriched in IFN related signaling pathway, and also showed the significant relationship with microbial infection.
Conjoint analysis showed that the target DEGs which regulated by differentially expressed miRNAs participated in cytoskeleton formation and modification of DNA or RNA. There maybe more than one regulatory methods lead to DEGs in B cells of pSS patients.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.5684

9. Systemic sclerosis, myositis and related syndromes - etiology, pathogenesis and animal models

AB0149 **PERIPHERAL T HELPER SUBSET PROFILING DIFFERS IN VARIOUS SUBSETS OF IDIOPATHIC INFLAMMATORY MYOSITIS**

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Background: There is dearth of biomarkers in Idiopathic Inflammatory Myositis(IIM) to identify ongoing inflammation in the muscle and distinguish it from inactivity or damage.

Objectives: Since myositis is autoantibody mediated and tertiary lymphoid organogenesis (TLO) reported in the diseased muscles, we investigated peripheral blood T helper subset profiling as a reflection of ongoing muscle inflammation.

Methods: Twenty-six patients of IIM (ACR EULAR criteria) were compared with 15 healthy controls (HC) and 21 patients with sarcoidosis (Table 1). Peripheral blood mononuclear cells were stained with combinations of antibodies to identify Th1, Th17, Th17.1 and Treg cells after stimulation assays (BD Biosciences). Myositis Specific and Associated autoantibodies were tested by the line immunoassay (Euroimmune, Germany).

Table 1. Baseline characteristics of patients with inflammatory myositis

Characteristics	Demographic details (n, % or median, IQR)	Healthy Control (median, IQR)
Age	37±25.25	26.0±32
Gender(M:F)	5 vs. 21	12 vs. 3
Diagnosis		
PM	3	
DM	15	
OM	4	
ASS	4	
Disease course		
Monocyclic	5	
Polycyclic	7	
Chronic continuous	1	
Undefined	13	
Clinical Profile		
Myositis	4 (15.3%)	
ILD	5 (19.23%)	
Rash	3 (11.53%)	
Arthritis	6 (23.07%)	
Other	16 (23.69)	
Disease duration (years)	1.3 ± 6.91	
Disease activity		
Active	12 [PM(1), OM(1), ASS(4), DM(5)]	
Inactive	14 [PM(2),OM(2),ASS(0),DM(8)]	
Antinuclear Antibodies		
Positive		
Nuclear		
Speckled	9 (34.61%)	
Homogenous	4 (15.38%)	
Nucleolar	1 (3.8%)	
Other	5 (19.23%)	
Cytoplasmic	3 (11.53%)	
Negative	4 (15.38%)	
Myositis Specific Antibodies		
Positive		
ARS	2(7.6%)	
Mi-2	3(11.53%)	
SAE-1	2(7.6%)	
NXP2	2(7.6%)	
MDA5	0	
MAA		
Ku	1(3.8%)	
dsDNA	0	
U1RNP	0	
Ro52	4(15.38%)	
Negative	12(46.15%)	

Results: All T helper subsets were higher in myositis as compared with healthy controls (figure 1A a-d). Between various IIM subsets, polymyositis had higher Th1 and Treg cells (Figure 1B b, c) while Th17 and Th17.1 cells(c) were higher in Overlap Myositis (Figure 1B a, d) as compared with healthy controls. Patients with sarcoidosis had similar subset profiling as myositis. (Figure 5a-f)

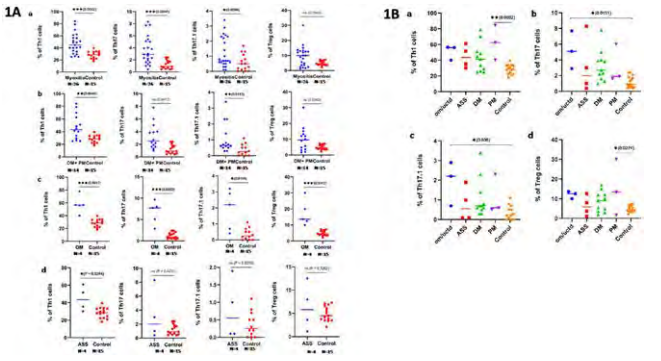


Figure 1 A. **Representative plot depicting all T helper subsets quantified were higher in myositis as compared with healthy controls1B: Representative plot comparing %T cell subsets in various subsets of myositis with healthy controls showing that % Th1 cells (a) and Tregs (d) are highest in Polymyositis than controls while % Th17 (b) and % Th17.1 cells (c) are higher in Overlap Myositis**

Patients who were had either arthritis or were positive for myositis specific autoantibodies had higher Th17.1 cells (Figure 3 a(iii) & b(iii)) than those negative for MSA. There was no difference in T cell profile between the various autoantibody subsets (Figure 6a-d).

There was no difference in subsets between active and inactive disease although active disease had lower Th1/Treg, Th17/Treg and Th17.1/Treg ratios.

Conclusion: T Helper cell subsets are distinct from HC but similar to sarcoidosis patients. However, they differ in various subsets of myositis, suggesting different pathogenic mechanisms are operative. Autoantibody positivity is associated with elevated Th17.1 population suggesting plasticity in TLO which needs to be explored further. However, T cell profiling cannot distinguish active from inactive disease limited predictive potential as a biomarker.

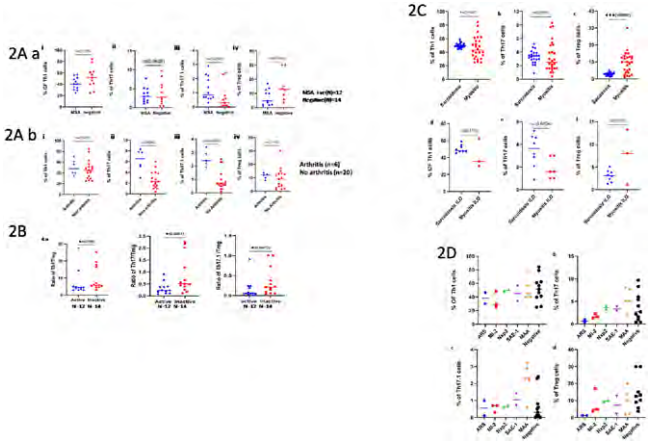


Figure 2 A. **Comparisons between various phenotypic subsets suggest patients positive for MSA had higher Th17.1 cells (Figure 2A a(iii)) than those negative for MSA. Similarly, patients with arthritis had higher Th17.1 cells(Figure 2A b (iii)). 2B Representative dot plot of T cell subsets ratio (Th1, Th17 & Th17.1) with Treg subsets (a) Th17/Treg ratio observed higher in lower cells in active as compared with inactive disease. 2C Representative dot plot T cell subsets in Sacodosis and myositis2D Representative dot plot comparing percentage of T cell subsets in various antibody subsets of myositis**

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Disclosure of Interests: None declared

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AB0150 **ADAPTOR PROTEINS ACTIVATE FIBROBLASTS IN SYSTEMIC SCLEROSIS**

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Background: Systemic sclerosis (SSc) is a chronic autoimmune disease characterized by microangiopathy and fibrosis. In physiological wound healing, fibroblasts are transiently activated for tissue repair. In contrast, fibroblasts are persistently activated during fibrosis and thus resulted in progressive matrix deposition and tissue remodeling. However, the pathogenesis of the fibrotic process is not fully understood.
Objectives: We aimed to identify molecules that play a role in chronically activated fibroblasts.
Methods: To identify molecules specifically upregulated in human fibrotic fibroblasts, RNA-sequencing was performed. Identified adaptor proteins were further validated in skin biopsy samples of patients with limited cutaneous SSc (lcSSc) and diffuse cutaneous SSc (dcSSc), and evaluated correlation between expression levels and clinical parameters. Respective overexpression and siRNA knockdown were further addressed *in vitro*. Functional effects were assessed by qPCR, hydroxyproline, proliferation and migration assays. Mouse models of systemic sclerosis were used to functionally validate adaptor proteins *in vivo*.
Results: We identified adaptor proteins as significantly upregulated molecules in chronically active fibroblasts of skin biopsy samples from SSc patients compared to fibroblasts from healthy controls. Expression levels were correlated with the modified Rodnan skin score in the skin of SSc patients. We observed higher expression levels also in the mouse model of topoisomerase I induced skin fibrosis. This result was also observed in bleomycin induced lung fibrosis model suggesting important functions of adaptor proteins during fibrotic tissue remodeling across different organs. Fibroblast-specific knockout resulted into significantly attenuated bleomycin-induced fibrosis. Upon bleomycin challenge, hydroxyproline content was diminished in mice with genetic deficiency of adaptor proteins. In addition, COL1A1, COL1A2 and Lum mRNAs and also the number of myofibroblasts were significantly lower in knockout mice compared to wild type mice. *In vitro*, knockdown of adaptor proteins resulted into a significant alteration of the migratory potential of fibroblasts.
Conclusion: Our results demonstrate that adaptor proteins play an essential role in the pathogenesis of systemic sclerosis. Understanding the molecular mechanism of adaptor proteins may lead to a novel therapeutic intervention in human SSc and related disorders.
Disclosure of Interests: Yuko Ariza Employee of: Ono Pharmaceutical Co., Ltd., Stefanie Weber: None declared, Nils Neise: None declared, Alexander Kreuter: None declared, Georg Schett Speakers bureau: AbbVie, BMS, Celgene, Janssen, Eli Lilly, Novartis, Roche and UCB, Jörg Distler Grant/research support from: Boehringer Ingelheim, Consultant of: Boehringer Ingelheim, Paid instructor for: Boehringer Ingelheim, Speakers bureau: Boehringer Ingelheim, Andreas Ramming Grant/research support from: Pfizer, Novartis, Consultant of: Boehringer Ingelheim, Novartis, Gilead, Pfizer, Speakers bureau: Boehringer Ingelheim, Roche, Janssen
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AB0151 PRELIMINARY RESULTS SHOW AN INCREASED EXPRESSION OF COINHIBITORY RECEPTORS IN SYSTEMIC SCLEROSIS

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Background: Recent studies suggest dysregulation in T cell activation in systemic sclerosis (SSc). Co-inhibitory-receptors (Co-IRs) such as TIM-3, PD-1 and LAG-3 play a crucial role in controlling excessive T cell activation and in maintaining immune homeostasis. Engagement of these receptors by their ligand's limits cytokine production in response to TCR or activating NK receptor stimulation and hence limit tissue damage from excessive immune activation. However, chronically increased expression of multiple Co-IRs is a hallmark of immune exhaustion. We evaluate the role of these soluble Co-IRs in diffuse SSc (dcSSc).
Objectives: Establish the role of CiR and their ligands in diffuse systemic sclerosis.
Understand how immune regulatory mechanisms influence the development of fibrosis.
Provide a better understanding of the disease and fibrosis in general.
Methods: PBMC's(Peripheral blood mononuclear cells) and dermal fibroblasts from SSc patients were isolated and investigated for markers of T cell inhibition. These cells were analysed using flow cytometry in a 10 colour panel. Cells were stained for PD1, TIM3, TIGIT, LAG3, CD3, CD8, CD4 and CD19 along with a Live/dead marker. Co-cultures of fibroblasts and PBMCs will be setup, and treated with various drugs that act on the Co-IRs.
Results: The proportion of CD4+ T cells expressing PD1 were markedly increased in SSc patients compared to healthy volunteers and Rheumatoid Arthritis patients.
There was increased expression of both TIGIT and TIM3 in the CD4+ T cells. (Figure 1)
Similarly, the co-expression of these receptors on the CD4+ T cell population was elevated compared to healthy volunteers. (figure 2)
Conclusion: Soluble co-inhibitors are differentially expressed in early dcSSc compared to healthy volunteers and other autoimmune diseases. Our preliminary data indicates that these co inhibitors could play an important role in unravelling the pathogenesis of systemic sclerosis. Inhibition or activation of these receptors through different treatment modalities can be utilized as a novel patient centric treatment strategy.
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Figure 1 CD3+CD4+ T cells Co inhibitor Receptor Expression

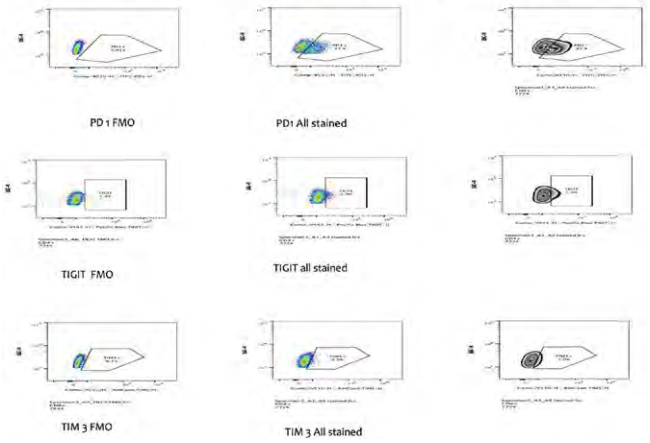
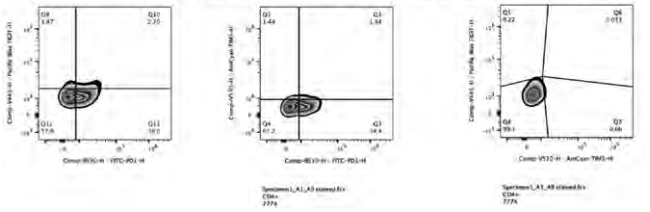


Figure 2 CD3+CD4+ T cells showing Co- expression of Co inhibitor Receptors



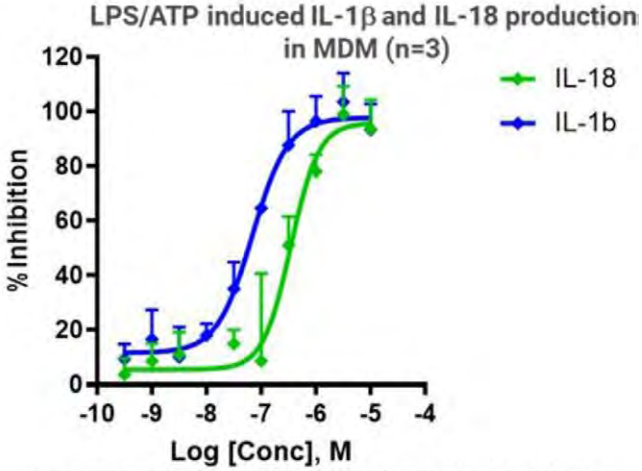
Acknowledgments: FOREUM: Foundation of Research in Rheumatology
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.5997

AB0152 LENABASUM, A CB2 AGONIST, INHIBITS INFLAMMASOME ACTIVATION

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Background: Upregulation of the innate immune response via the activity of Toll-like receptors and the NLRP3 inflammasome have been suggested as initiating events that can drive fibrosis in systemic sclerosis (SSc) (Pharmacol Ther. 2018;192:163). Lenabasum, a cannabinoid receptor type 2 agonist, is known to activate the resolution phase of acute human innate immune responses triggered through Toll-like receptor activation, favoring production of pro-resolving lipid mediators, reducing inflammatory infiltrates, and increasing bacterial clearance (Clin Pharmacol Ther. 2018;104:675). Given the potential importance of inflammasome activation in the pathogenesis of SSc, the question remained whether lenabasum inhibits inflammasome activation.
Objectives: Assess effects of lenabasum on IL-1β and IL-18 production induced by inflammasome activation.
Methods: Primary human macrophages were derived from monocytes, stimulated with LPS and ATP to active inflammasomes and cultured with lenabasum. Levels of IL-1β and IL-18 were measured in cell supernatants by ELISA. Separately, human PBMC were activated with 0.1 μg/ml LPS ± 10 μM lenabasum for 24 hours, and effects of lenabasum on the levels of IL-1β and other pro-inflammatory cytokines were measured.
Results: Lenabasum significantly inhibited IL-1β and IL-18 secretion by monocyte-derived macrophages, with IC_{50} = 66.73 ± 3.92 nM and 349.23 ± 21.27 nM, respectively. A control inflammasome activation inhibitor, MCC950, which showed IC_{50} = 18.33 ± 1.22 nM for IL-1 β inhibition and IC_{50} = 21.43 ± 0.81 nM for IL-8 inhibition.
Conclusion: Lenabasum inhibits inflammasome activation, which could contribute to potential therapeutic efficacy in SSc and other autoimmune diseases.
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Figure



Lenabasum showed a dose-dependent inhibition of IL-1β and IL-18 secretion.

Disclosure of Interests: Subba Chintalacharuvu Shareholder of: Corbus Pharmaceuticals, Inc., Employee of: Corbus Pharmaceuticals, Inc., Ping Zang Employee of: Corbus Pharmaceuticals, Inc., Barbara White Shareholder of: Corbus Pharmaceuticals, Inc., Employee of: Corbus Pharmaceuticals, Inc., Sergei Atamas Shareholder of: Corbus Pharmaceuticals, Inc., Employee of: Corbus Pharmaceuticals, Inc.
DOI: 10.1136/annrheumdis-2020-eular.1854

AB0153 ADIPOSE-DERIVED STROMAL/STEM CELLS FROM SYSTEMIC SCLEROSIS PATIENTS SUCCESSFULLY EXERT A PARACRINE ANTI-FIBROTIC ACTIVITY AND INDUCE A PRO-ANGIOGENIC PHENOTYPE OF SCLERODERMA FIBROBLASTS IN VITRO

N. Del Papa[1], M. Lorini[2], V. Carbonelli[2], A. Minniti[1], F. Pignataro[1], W. Maglione[1], G. Di Luca[3], N. Montano[2], R. Caporali[1]. *[1]ASST Gaetano Pini-CTO, Dept of Rheumatology, Milan, Italy; [2]Ca' Granda IRCCS Foundation, Ospedale Maggiore Policlinico, Department of Clinical Sciences and Community Health, Milan, Italy; [3]ASST Gaetano Pini-CTO, U.O.S Vascular Surgery, Milan, Italy*

Background: Adipose-derived stromal/stem cells (ADSCs) are multipotential non-hematopoietic progenitor cells with anti-inflammatory, immunomodulatory and regenerative effects. They have the advantage of accessibility and potent pro-angiogenic effects when compared with other stem cells, such as bone-marrow derived stem cells. Recent studies have shown that autologous fat grafting may be effective in the treatment of fibrotic and vascular complications in systemic sclerosis (SSc), despite a pro-fibrotic signature.
Objectives: Aim of the study was to better characterize the proliferative and secretive profile of ADSCs in normoxic and hypoxic conditions, and to evaluate the mechanisms by which ADSCs exert these observed clinical effects.
Methods: Adipose tissue samples were obtained by liposuction from 12 SSc patients and 10 healthy donors (HD). ADSCs were purified according to their adherence to the plastic and characterized to express specific MSC surface antigens by flow cytometry analysis. Proliferation of ADSCs from SSc patients and normal controls was evaluated in normoxic and hypoxic conditions. Fibroblasts and ADSCs derived from SSc patients were co-cultured in direct and indirect culture systems and compared to HD. Fibroblasts proliferation, mRNA expression and protein secretion of VEGF and known fibrotic mediators including TGF β-1, TGFR, CTGF, Collagen type I (Col I) were analyzed in the same conditions.
Results: Normoxic and hypoxic culture conditions did not modify the proliferation rate of both normal and SSc ADSCs. Hypoxia significantly increased mRNA expression of VEGF by HD and SSc ADSCs but had no effect on the mRNA expression of pro-fibrotic mediators, ie TGFβ and TGFR. Normal and SSc fibroblast proliferation was significantly reduced in both co-culture systems ($p < 0.001$) and by treatment with normoxic and hypoxic conditioned medium (CM) ($p=0.001$ and $p=0.002$). In the same conditions, mRNA expression and protein secretion of TGF-β1, CTGF and Col I were significantly reduced ($p = 0.003$, $p = 0.02$, $p=0.04$). These results were confirmed when normal and SSc fibroblasts were cultured in the presence of ADSCs normoxic and hypoxic CM ($p=0.02$ and $p=0.01$). Furthermore, a significant increase in mRNA expression and production of VEGF was observed in SSc fibroblasts cultured in the presence of normoxic and hypoxic CM ($p = 0.002$ and $p< 0.0001$, respectively).
Conclusion: We found that treatment with the medium from normoxic and hypoxic preconditioned ADSCs has an anti-fibrotic effect through both the inhibition of fibroblast proliferation and key mediators of fibrosis. The increased expression of VEGF by SSc fibroblasts in the presence of normoxic and, even more, hypoxic ADSCs CM, suggests that ADSCs can induce a paracrine pro-angiogenic phenotype, even in fibroblasts with a pro-fibrotic signature. Altogether these data show that ADSCs may exert their anti-fibrotic and pro-angiogenetic effects on SSc fibroblasts by the secretion of paracrine factors, partly explaining the mechanisms underlining beneficial clinical results of fat graft in SSc patients.
Disclosure of Interests: Nicoletta Del Papa: None declared, Maurizio Lorini: None declared, Vincenzo Carbonelli: None declared, Antonina Minniti: None declared, Francesca Pignataro: None declared, Wanda Maglione: None declared, Gabriele Di Luca: None declared, Nicola Montano: None declared, Roberto Caporali Consultant of: AbbVie; Gilead Sciences, Inc.; Lilly; Merck Sharp & Dohme; Celgene; Bristol-Myers Squibb; Pfizer; UCB, Speakers bureau: Abbvie; Bristol-Myers Squibb; Celgene; Lilly; Gilead Sciences, Inc; MSD; Pfizer; Roche; UCB
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AB0154 MERTK AND THE RESOLUTION OF INFLAMMATION IN IGG4-RELATED DISEASE

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Background: IgG4-Related Disease (IgG4-RD) is characterized by fibrotic lesions, serum IgG4 elevation, and prompt response to glucocorticoids. B and T lymphocytes are considered the initiators of tissue inflammation in IgG4-RD, but the prominent stromal reaction observed at disease sites suggest that a dysregulation of processes involved in the resolution of inflammation could be pathologically relevant as well. Mer receptor tyrosine kinase (MerTK) and its ligands protein S (Pros1) have a pivotal role in the resolution of inflammation through the activation of a well-characterized signaling pathway that ultimately dampens the immune response and promotes the recovery of tissue function. MerTK and the processes involved in the resolution of inflammation have never been addressed in IgG4-RD.

Objectives: To investigate MerTK involvement in the pathogenesis of IgG4-RD by evaluating (a) the expression of MerTK and of its endogenous ligands in IgG4-RD tissues; (b) the presence of circulating precursors of MerTK+ cells infiltrating IgG4-RD lesions in the peripheral blood of IgG4-RD patients; (c) the effects of immunosuppressive therapies on MerTK expression in IgG4-RD tissues.
Methods: Three distinct cohorts of IgG4-RD patients were included in this study. 8 active patients were used for immunohistochemistry studies for MerTK expression. 16 IgG4-RD and 14 Sjögren syndrome patients, together with 6 control tonsils, were used for multicolor immunofluorescence studies and TissueQuest software quantification of the expression of MerTK, CD68, CD163, Pros1, Gas6, CD4, SLAMF7, CD19, IgG4, cleaved caspase-3. 10 untreated IgG4-RD patients were used to evaluate MerTK expression in circulating monocytes subsets and fibrocytes by flow cytometry.
Results: MerTK was highly expressed in IgG4-RD affected organs. MerTK+ cells accounted on average for 16% (range 5-35%) of all cells in the tissue, and the majority of them expressed CD68,reflecting a monocyte-macrophage origin. 33.5 % (interquartile range (IQR) 26-41%) of MerTK+ cells co-expressed CD68 and CD163, while 30.5% (IQR 19-41.5%) expressed CD68 but not CD163. CD68+MerTK+ cells displayed two main morphological appearances, compatible with those of macrophages and of myofibroblasts. In addition, MerTK+ cell number was significantly increased in salivary glands from IgG4-RD patients compared to Sjögren syndrome ($p < 0.0001$). Circulating precursors of CD68+MerTK+ cells infiltrating IgG4-RD lesions were identified by flow cytometery in the peripheral blood of patients with active IgG4-RD as MerTK+ populations of intermediate monocytes, nonclassical monocytes and collagen expressing fibrocytes. MerTK ligand Pros1 was exposed on 52% (IQR 42-57%) of infiltrating B lymphocytes, 74% (IQR 54-89%) of infiltrating T lymphocytes, and, likely, on apoptotic cells that were detected in IgG4-RD tissues. CD68+MerTK+ cells were found in physical contact with Pros1+ cells in IgG4-RD lesions and their number decreased by 56% after successful treatment with rituximab.
Conclusion: MerTK is abundant in IgG4-RD affected organs and is preferentially expressed on CD68+ macrophages and myofibroblasts that infiltrate IgG4-RD lesions. MerTK+ cells might interact with apoptotic cells and Pros1 expressing T and B lymphocytes in IgG4-RD tissues, leading to the persistent activation of processes involved in the resolution of inflammation and promoting the development of tissue fibrosis.
Disclosure of Interests: None declared
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AB0155 THE ULTRASTRUCTURAL FEATURES OF INTERSTITIAL LUNG TISSUE INVOLVEMENT DUE TO SYSTEMIC SCLEROSIS: ANIMAL EXPERIMENTAL STUDY

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Background: Systemic sclerosis (SSc) - is an autoimmune connective tissue disease, which crucial role is played by inflammation and fibrosis development. This pathology is characterized by multiple symptoms that occur due to alterations of the vascular wall, limited or widespread fibrosis of the dermis and visceral organs, dysregulation of cellular and humoral immunity, followed by the formation of autoantibodies specific to the structures of the organism. Although external manifestations of SSc certainly lead to a decrease in the functional activity and patient's quality of life up to disability, the real danger is a violation of the functions of the internal organs and systems.
Objectives: The aim of our study was to determine changes in the morphological structure of lung interstitial tissue at the subcellular level of the structural organization, which were achieved by modeling of this autoimmune pathology in laboratory animals.
Methods: The main concept of modeling process was based on the previously described method of SSc induction [1,2] however with some differences from original model. Into the study were involved 30 pubescent Wistar rats (220-240g) who underwent a three times a week subcutaneous administration of 0.5ml of 5% sodium hypochlorite (NaClO) solution with active chlorine concentration of 190 g/dm^3 for 6 weeks in a row; control group (20 rats) that received injections with an equal volume of sterile saline solution. After 8 weeks from the beginning of the experiment animals were sacrificed under thiopental anesthesia, lung tissue specimens were obtained, fixed alternately in 2.5% glutaraldehyde and in 1% solution of osmium tetroxide. After dehydration, the material was embedded in Epon-Araldite. Sections were obtained on an ultramicrotome (Tesla BS-490) magnification x9600 was performed on high-resolution microscope (PEM-125K).
Results: The ultrastructural study of lung specimens reviled the fibroblasts with high amounts of collagen fibers in the interstitial tissue of the alveoli wall. Fibroblast nuclei were characterized by irregular shape and numerous invaginations of the nuclear envelope and marginal aggregation of chromatin granules. Fig. 1 depicts the fragment of the alveolar wall of the lungs of white Wistar rats in 8 weeks after the start of the experiment. On the Fig. 1 could be distinguished the lumen of the alveoli (1), fibroblast (2) with increased quantity of collagen fibers (3) and a peripheral part of alveolocyte I type (4).

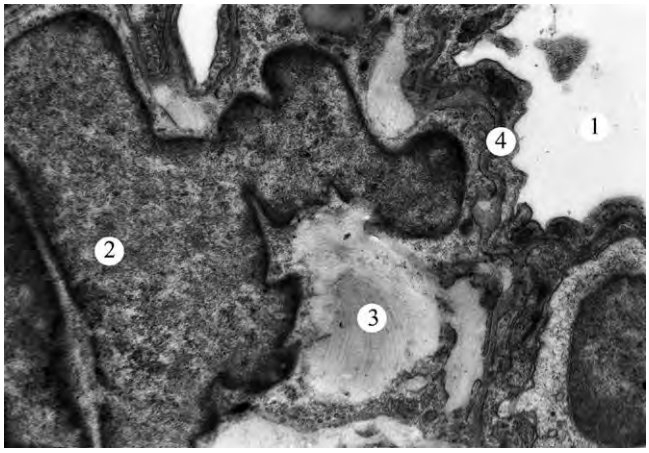


Figure 1.

Conclusion: The current findings confirm the efficacy of NaClO chemical model of reproduction of interstitial lung tissue involvement within SSc pathogenesis; this model could contribute to the further investigation of peculiarities of autoimmune origin interstitial lung disease (ILD).
References:
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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.2542

AB0156 NMR-BASED MUSCLE METABOLOMICS IN INFLAMMATORY MYOSITIS- UNDERSTANDING CHANGES IN SERUM AS A REFLECTION OF THE MUSCLE

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Background: We have previously found promise in NMR as a tool to distinguish sera of active from inactive inflammatory myositis (IIM)1. To understand the changes previously found in sera and urine we studied muscle tissue of patients with myositis.
Objectives: To identify differences in metabolome on inflamed muscle tissues of patients with active myositis from that of healthy controls and infectious polymyositis.
Methods: Muscle (n=17) from patients classifiable as myositis by the ACR-EULAR criteria [34 years (23.5 - 50.5 IQR), M/F 1:3] were compared with healthy controls [n=11, age= 44 (35-50) years, M/F-1:1]. Two disease controls with infectious polymyositis were also compared. Findings were applied to muscle biopsy tissues of two patients with established myositis and superadded infections (HBV, Histoplasmosis) to assess discriminatory potential.

Metabolic profiles were obtained at 800 MHZ NMR spectrometer and compared using multivariate partial least-squares discriminant analysis (PLS-DA). The discriminatory metabolites were identified based on variable importance in projection (VIP) statistics and further evaluated for statistical significance (p-value <0.05). Paired T tests, ANNOVA and correlation of individual metabolites were done after normalizing for formate.

Results: Metabolomics profiles in IIM were distinct from healthy controls (**Fig. 1A).** Of the various discriminatory metabolites (**Fig. 1B**), Succinate had the highest discriminatory potential (AUC 0.8, P=0.01) followed by citrate, glycine, glycerol, glucose, creatine and lactate. (**Fig. 1C**) Both glucose and creatine were decreased in IIM (**Fig. 1D,E**) and this was uniform across all types of IIM. However, glycine levels differed across different myositis subsets supporting the fact that they might differ in pathogenesis. (**Fig. 1E**) Amongst various serum biomarkers of muscle disease and damage, serum Aspartate Transaminase correlated with glutamate (r=0.6, p=0.01), and serum creatinine correlated negatively with glycerol (r-0.8, p=0.04),

Biopsies of infectious polymyositis suggested difference in spectra from IIM (**Fig. 2A**). Trends were observed towards lower succinate and higher citrate levels suggesting metabolomics could possibly be useful to differentiate the two. Muscle of both patients with IIM with superadded infectious polymyositis also exhibited low succinate and elevated citrate.

Conclusion: Muscle metabolomics of active myositis is distinctive. Amino acids and creatine are lower in diseases muscle suggesting active breakdown and loss, in turn explaining previous findings of low levels in serum in active disease. Certain metabolite composition differ in different types of myositis supporting different pathogenesis.

Infectious polymyositis might exhibit different metabolome from IIM with potential as a biomarker though this needs to be confirmed in larger numbers.

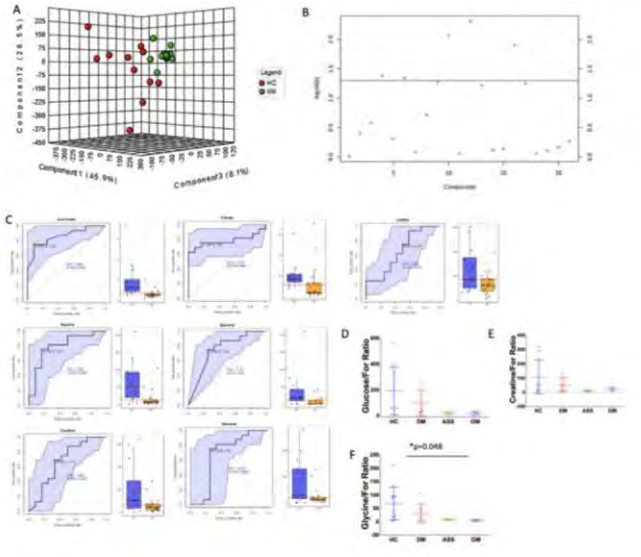


Figure 1: Muscle metabolomics- IIM versus healthy
(A) 3D score plot obtained from PCA analysis of 1D ^{1}H CPMG NMR based serum metabolic profiles showing clustering and separation between healthy control and inflammatory myositis patients **(B)** Screening of metabolites responsible for the group separation in the score plot identified based on variable importance in projection (VIP) score > 2.0 **(C)** Representative ROC curves of discriminatory metabolites **(D,E)** Comparisons suggesting lower glucose and creatine in all active IIM subgroups as compared with healthy controls **(F)** ANNOVA showing lower glycine in anti-synthetase and overlap myositis sub-group as compared with dermatomyositis.

Disclosures: Funded by APLAR research grant 2017 awarded to Dr Latika Gupta.

References:

[1] Gupta L, Kumar D, Gulerai A, Kumar U, Misra R. "NMR-Based Serum, Urine and Muscle Metabolomics in Inflammatory Myositis for Diagnosis and Activity Assessment: Serum Metabolomics Can Differentiate Active from Inactive Myositis" Oral presentation at the ACR, Atlanta 2019.

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Disclosure of Interests: None declared

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AB0157

IGG FROM PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND SYSTEMIC SCLEROSIS HAVE AN INFLUENCE ON COAGULATION FACTORS IN HUMAN CEREBRAL MICROVASCULAR ENDOTHELIAL CELLS IN-VITRO

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Background: Endothelial cells from the microvasculature (hBMEC) of the brain show significant morphological and functional differences compared to EC from other anatomical areas. They are characterized by tight junctions, are not fenestrated and show less active transport mechanisms. On the other hand, the mitochondrial density is relatively high in hBMEC due to the high cerebral glucose metabolism.

It could be already observed that interferon-α from SLE-sera induces the expression of MHC class I molecules on human dermal microendothelial cell line, but it is not known whether this also occurs on hBMEC. hBMECs can synthesize pro-inflammatory cytokines and chemokines such as IL-1β, but in lower concentrations than human umbilical vein endothelial cells.

Patients suffering from systemic lupus erythematosus (SLE) or systemic sclerosis (SSc) show a wide spectrum of central nervous symptoms. Both, SLE and SSc, are characterised by different autoantibodies and endothelial vascular damage, especially in microvessels. 10-40% of patients with SLE suffer from lupus vasculopathy. Vascular dysfunction is one of the earliest pathological changes in SSc. Anti-endothelial autoantibodies (AECA) appear in SLE as well as in SSc and other connective tissue diseases. Research within the last years revealed that AECA play a critical role within the vascular pathogenesis of SLE and SSc. So far there is no evidence that AECA bind to hBMEC and it is not clear whether they have an effect on this special endothelial class.

Objectives: In this project, we investigated if autoantibodies against hBMEC are detectable in SLE and SSc patients and if they have an influence on the activation of the endothelium by inducing adhesion molecules and on haemostasis by inducing factors of the clotting cascade.

Methods: HiTrap Protein G HP antibody purification columns were used to purify IgG antibodies. Flow cytometry was used for analysis of autoantibodies against human cerebral microvascular endothelial cell line (hCMEC/D3). 26 sera of patients with SLE and 29 sera of patients with SSc were tested for presence of autoantibodies against hCMEC/D3. To analyse in vitro effects on hCMEC/D3, we measured changes in the expression of the following surface proteins: ICAM-1, VCAM-1, MHC class I and II, tissue factor, von-Willebrand-Factor, E-Selectin, P-Selectin, Thrombomodulin, CD73 and t-PA, each before and after three- and 24-hours incubation with IgG-fractions. IgG fractions of 12 SLE patients, 13 SSc patients and 13 healthy control persons (HC) were tested.

Results: Autoantibodies against hCMEC/D3 were found in 21 of 26 patients with SLE (81%) and in 19 of 29 patients with SSc (66%) ($p > 0.05$) but not in healthy donors. After three hours incubation of hCMEC/D3 IgG-fractions, an upregulation of tissue factor by SSc-IgG (6.7% ± 5.2%) compared to HC-IgG (1.1% ± 2.8%, $p < 0.01$) and to SLE-IgG (1.6% ± 3.9%, $p < 0.05$), was detectable.

There was no significant correlation between changes in surface protein expression and detection of ANA or of anti-hCMEC/D3 antibodies ($p > 0.05$).

No change in expression of ICAM-1, VCAM-1, MHC class I and II, von-Willebrand-Factor, E-Selectin, P-Selectin, Thrombomodulin, CD73 and t-PA could be detected after incubation with IgG-fractions.

Conclusion: Both, patients with SLE and patients with SSc showed autoantibodies against hBMEC. IgG fractions of patients with SSc, but not with SLE, induced an upregulation of tissue factor on the cell surface of hCMEC/D3. This could be an indicator for a direct pathogenic effect of AECA on hBMEC and might have an influence on haemostasis by activating the clotting cascade. Inhibition of these antibodies could reduce cerebral involvement of SSc.

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Disclosure of Interests: Rebecca Hasseli: None declared, Magdalena Maria Fürst: None declared, Pratibha Singh: None declared, Ulf Müller-Ladner Speakers bureau: Biogen, Manfred Kaps: None declared, Franz Blaes: None declared, Tibo Gerriets: None declared, Marlene Tschernatsch: None declared

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AB0158

IMPACT OF JAK INHIBITORS ON MACROPHAGE POLARISATION: PERSPECTIVES FOR SYSTEMIC SCLEROSIS

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Background: Macrophage can adopt various phenotypes and activation states according to their surrounding microenvironment. M1 or inflammatory macrophages are generated under IFNɣ/LPS signaling and express the membrane marker CD86. Different subtypes of M2 macrophages are also described: M2a macrophages (generated under IL4/IL13 signaling) and characterized by a high expression of CD206 and pro-fibrotic properties and, M2c macrophages (generated under IL10 and/or glucorticoid signaling), considered as anti-inflammatory resolving macrophages. There is growing interest in the role of macrophages in the pathogenesis of Systemic Sclerosis (SSc). Recent studies highlight that macrophages from fibrotic tissues such as lung or skin from SSc patients have a M2 phenotype whereas, in blood-monocytes derived macrophages (MDM), SSc MDM have a mixed signature associating M1 and M2 characteristics. Jak inhibitors are treatments used in rheumatoid arthritis and that can variously target signals that could be involved both in M1 and in M2 polarisation.
Objectives: This study evaluates the impact of three Jak inhibitors on the polarisation state of human MDM in vitro.
Methods: Blood monocytes form healthy donors (HD) were differentiated with M-CSF (for 7 days) in MDM and pre-treated by ruxolitinib (Jak2-Jak1 inhibitor), tofacitinib (Jak3 inhibitor) or itacitinib (Jak1 inhibitor) (1µM for all). They were then polarised into M1i (IFNɣ, 20µg/mL), M1Li (IFNɣ+LPS, 20µg/mL), M2a (IL4+IL13; 20µg/ML), M2c (IL10, 20µg/mL) and M2c(dex) (IL10+dexamethasone, 10 nM). The impact of each Jak inhibitor on phenotype (flow cytometry), gene expression (qPCR) and cytokine secretion (ELISA) was evaluated in each polarisation state.
Results: Concerning phenotypes, all Jak inhibitors reduced the expression of the M1i and M1Li marker CD86, but ruxolitinib had a higher effect. Only ruxolitinib reduced the expression of the M1i marker MHCII. All Jak inhibitors reduced the expression of CD206 in M2a. They had no impact on the expression of CD163, CD204 in any M2 conditions. Key M1 genes were repressed by all Jak inhibitors, such as CXCL10, IL6 or TNFα with a more significant effect of ruxolitinib. All Jak inhibitors reduced the gene expression of CXCL13 and SOCS3 in M2c. Secretion levels of IL6 and CCL18 were also repressed, with a more significant effect of ruxolitinib.
Conclusion: Jak inhibitors can limit M1 and M2 polarisation state in vitro, with a more significant effect of the Jak2-Jak1 inhibitor ruxolitinib. The relevance of these results in MDM from SSc patients and in vivo models of SSc is still to be determined.
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AB0159

INTERLEUKIN-16 PLAYS A ROLE IN THE PATHOGENESIS OF SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is an autoimmune disorder with chronic and persistent inflammation. Interleukin-16 was originally described as a factor that could attract activated T cells in humans [1]. Elevated amounts of IL-16 have been demonstrated in SSc [2].
Objectives: This study was undertaken to find out if IL-16 is associated with clinical characteristics of SSc.
Methods: IL-16 was measured by Elisa in serum of patients with SSc (n=119) and healthy controls (n=50). Further, the presence of active IL-16 in mononuclear cells from peripheral blood of SSc patients (n=10) was examined by Western blot. Statistical analyses were done employing Graph Pad prism software (v 8). Patients with SSc were characterized based upon epidemiological and clinical parameters.
Results: The serum concentration of IL-16 was higher in patients with SSc than in healthy controls (272.7±165.4 vs 172.8±64.84 pg/ml, p<0.0001). Further, the difference in the IL-16 serum concentration was more prominent in females (265.6±174.2 vs 160.1±53.37 pg/ml, p=0.0002) than in males (287.1±144.1 vs 187.6±74.64 pg/ml, p=0.0034). In addition, the concentration of IL-16 was elevated in patients with diffuse SSc compared to limited SSc (p=0.0206). The concentration of IL-16 in serum of SSc patients positively correlated with CRP (n=115, r=0.49, p<0.0001). There was a weak positive correlation between IL-16 in serum of SSc patients and the mRSS (n=112, r=0.22, p=0.0175). Noteworthy, the concentration of IL-16 was heightened in SSc patients with lung fibrosis compared to SSc patients without lung fibrosis (p=0.009). The ROC value of SSc patients with lung fibrosis was 0.64 (95%CI: 0.58-0.83). Moreover, active IL-16 derived from peripheral blood mononuclear cells (PBMC) of SSc patients with lung fibrosis was present in higher amounts compared to PBMC of SSc patients without lung fibrosis (5 vs 5, p=0.0557).
Conclusion: Our results confirm and extend previous data by showing not only an increased concentration of IL-16 in the circulation of SSc patients, but new findings pointing towards a role of IL-16 for contributing to lung fibrosis in SSc.
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AB0160

CARDIAC AUTONOMIC NEUROPATHY PREVALENCE IN A COHORT OF SYSTEMIC SCLEROSIS (SSC) PATIENTS

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Background: Systemic sclerosis is a rare disease determining a damage to the connective tissue and, consequently, an involvement of several organs. Besides the damage of the connective tissue, preminent is also the small vessels injury, detectable by videocapillaroscopy. Some authors report that the vascular damage may be also responsible of a cardiovascular impairment as cardiac autonomic disease (CAN) and heart rate variability [1].
Objectives: Our study aims to assess the presence and entity of CAN in patients with systemic sclerosis (SSc).
Methods: This is a pilot prospective cohort study. We enrolled 28 patients in a period of six months, from May 2019 to November 2019, afferent to the outpatient clinic of internal medicine and immunology of the Primo Policlinico of Naples, with definite SSc diagnosis in absence of other comorbidities. All patients underwent diagnostic tests for autonomic cardiac neuropathy (NAC) and videocapillaroscopy. In particular, four test were performed to search for the presence of NAC: orthostatic hypotension, deep breathing, lying to standing and Valsalva maneuver. Each test was corrected for age and diagnosis was made in the case at least two tests resulted positive. Primary endpoint of the study was the assessment of the prevalence of autonomic cardiac neuropathy in the study population.
Results: Our cohort was mainly characterized by females (92.9%), with a median age of 58.5 years [IQR: 49-64.8 yrs.] and a median duration of the disease of 4 years [IQR 2-13 yrs.]. The observed prevalence of NAC was equal to the 46.4% (13 cases). In addition, we evaluated the potential association of NAC with age, duration of disease, gastrointestinal dysmotility, sicca syndrome, cutaneous involvement and type of videocapillaroscopy pattern, from which no statistically significant result emerged. Hence, a further analysis, by using a time-dependent Cox regression model (with the duration of disease as time covariate), was performed on the same variables. From this model a

significant association emerged in particular between the presence of NAC and the active videocapillaroscopy pattern (OR 6.23; 95% CI: 1.058-36.71, p=0.043).

Conclusion: Though current data in the literature on this topic are poor, cardiac autonomic neuropathy is among the clinical manifestations of SSc. In our study population, though the limited sample size, we observed a high percentage of patients with autonomic cardiac neuropathy, which seems much more frequent with the increase in the duration of disease and based on the type of videocapillaroscopy pattern.

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AB0161 CLONAL HEMATOPOIESIS IS INCREASED AND NOT RELATED TO AGING IN SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is an autoimmune disease characterized by fibrosis, microangiopathy and immune dysfunctions including dysregulation of proinflammatory cytokines. Clonal hematopoiesis of indeterminate potential (CHIP) is defined by the acquisition of somatic mutations in hematopoietic stem cells leading to detectable clones in the blood. Recent data have shown a higher risk of cardiovascular disease in patients with CHIP resulting from increased production of proinflammatory cytokines and accelerated atherosclerosis. Eventual links between CHIP and autoimmune diseases are undetermined.

Objectives: The aim of our study was to evaluate the prevalence of CHIP in SSc patients and its association with clinical phenotype.

Methods: Forty-one genes frequently mutated in myeloid malignancies were sequenced in peripheral blood mononuclear cells from 90 SSc patients and from 44 healthy donors.

Results: A total of 15 somatic variants was detected in 13/90 SSc patients (14%) and 4 somatic variants in 4/44 (9%) HD (p=0.58). The prevalence of CHIP was significantly higher in younger SSc patients than in HD: 25% (6/24) vs 4% (1/26) (p=0.045) under 50 years and 17% (7/42) vs 3% (1/38) (p=0.065) under 60 years. The prevalence of CHIP in patients over 70 years was similar in SSc patients and healthy donors

For SSc patients the most common mutations occurred in *DNMT3A* (7 variants). Other variants involved *ATM*, *SF3B1, SETBP1, TET2*, *TP53*, *NF1* or *CBL*. The distribution of gene mutations was overall comparable in SSc patients and in previously described CHIP series (3)

In most SSc patients, we identified a single CHIP mutation. Several mutations were detected in two SSc patients: *SETBP1* and *NF1* in one and, *TET2* and *ATM* in the other Clonal mutations included missense (n=10), nonsense (n=3), frameshift (n=1) and a single splice site mutation. In all HD we detected a single CHIP mutation which occurred in *DNMT3A,TP53 and CSF3R*

Variant allele frequencies (VAF) of CHIP mutations ranged from 2 to 18.6% and did not differ between genes (*DNMT3A* or others). Mean age was the same in patients with *DNMT3A* mutations or with other mutations. However, C>T transversions, that have been associated with ageing were more frequent in *DNMT3A* variants than in other genes, suggesting distinct mechanisms for mutation acquisition or clonal selection No major differences in clinical and laboratory data were observed between SSc patients with or without CHIP. SSc subtypes, disease duration, different organ involvements and the prevalence of ischemic events were not associated with the presence of CHIP, except less frequent pyrosis in patients with CHIP than those without. SSc patients with CHIP had significantly more anti-RNA polymerase III antibodies than those without CHIP (p=0.045) At the time of analysis, 45 SSc patients had received a treatment for SSc which consisted in low-dose steroids, hydroxychloroquine, mycophenolate mofetil, cyclophosphamide or methotrexate. SSc patients with CHIP were significantly more exposed to cyclophosphamide (3/13 vs. 3/77) (p=0.04) (5, 6.5 and 11 gram respectively between 5 years to 8 years before the NGS sequencing analysis), but among these cyclophosphamide-exposed SSc the age was over 65 in 2/3 of them. When considering all immunosuppressive drugs (cyclophosphamide, methotrexate and mycophenolate mofetil) SSc patients with CHIP were not more exposed than those without CHIP (p=0.75) No patient developed any hematologic malignancy and no cytopenia during the median follow-up of 13 months (0-24 months). One SSc patients with CHIP developed a small lung cancer few months after NGS testing.

Conclusion: Whether CHIP increases the risk to develop SSc or is a consequence of a SSc-derived modified bone marrow micro-environment remains to be explored.

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AB0162 THE SIGNIFICANCE OF M1 AND M2 MONOCYTES IN SYSTEMIC SCLEROSIS

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Background: Recently, the relation between M2 macrophage and fibrosis have been reported in several diseases including systemic sclerosis (SSc). Similar with macrophages, monocytes can be classified into M1 and M2 subset, and the relation of imbalance of these monocytes with disease such as rheumatoid arthritis have been reported[1,2].

Objectives: In this study, we attempted to investigate relationship among M1 or M2 monocytes in SSc.

Methods: This study included 23 SSc patients and 20 healthy donors. Using fluorescence-activated cell sorting, we defined CD14, CD68 and CCR2 positive cells as M1 monocytes and CD14, CX3CR1 and CD163 positive cells as M2 monocytes. We examined the ability of cytokines/chemokines secretion of CD14 positive cells from SSc by multiplex bead array assay using MAP human cytokine/chemokine Magnetic Bead Panel which can measure 38 cytokines/chemokines. We next extracted M2 monocytes from CD14-positive cells using FACS, and we used the rest of the CD14 positive cells as M1-dominant monocytes. Then, we evaluated their ability of TGF-β production by multiplex bead array assay.

Results: SSc patients had higher M2/M1 ratio as compared with healthy control (7.00 vs 1.63, P<0.05). And, there was tendency that M2/M1 ratio was higher in SSc patients complicated with interstitial pneumonia. Beads array analysis revealed that CCL4 and MCP-1 production from CD14 positive cells which consists M2>M1 (M2/M1 ratio>1) were higher than that from CD14 positive cells which consists M2<M1. Furthermore, the ability of TGF-β secretion of M2 monocytes was higher than that of M1-dominant monocytes.

Conclusion: Our present study suggested that the imbalance of M1/M2 monocytes might contribute to pathogenesis of SSc.

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AB0163 ANTI-KU ANTIBODIES: MUCH MORE THAN SCLEROMYOSITIS

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Background: Initially, anti-Ku antibodies (Ab) were described in patients with overlap syndrome with systemic sclerosis (SSc) and inflammatory myophaty (scleromyositis), although later they have been linked to a wide variety of systemic autoimmune diseases (SAD) questioning its diagnostic value. Recently, the possible existence of 2 different clinical phenotypes associated with these Ab has been described: one with myositis and high risk of intersticial lung disease (ILD) and another with positive anti-dsDNA Ab and glomerulonephritis.

Objectives: To analyze the clinical relevance and the main diagnosis of a serie of patients with positive anti-Ku Ab.

Methods: Descriptive observational study of patients with anti-Ku Ab in two third level hospitals between 2011 and 2019. Their determination was made at the criteria of the requesting physician.

Results: Twenty-three patients (20 women) with a median age of 59 ± 14 years (range, 24-83) and a follow up time (median) of 37 months (1-208) were identified. The main clinical and analytical characteristics, as well as the final clinical

diagnosis of these patients are shown in Table 1. In the cluster analysis we could not identify clinical phenotypes, perhaps because of the small sample size. Only 50% of patients with myositis developed ILD. Regarding the final diagnosis, only 1 patient (5%) was diagnosed of scleromyositis. Besides detecting them in patients with SSc (39%) and idiopathic inflammatory myopathy (9%), anti-Ku Ab were detected in other SAD, the most frequent were systemic lupus erythematosus, rheumatoid arthritis (RA) and overlap syndrome of SSc + RA.

Table 1. Main clinical-analytical manifestations and final diagnosis of pacientes with anti-Ku Ab.

FINAL CLINICAL DIAGNOSiS
Scleromyositis: 1
Idiopahtic inflammatory myopathy: 1
Systemic sclerosis (SSc): 6 (Pre-scleroderma: 3, limited SSc: 3).
Systemic lupus erythematosus: 2
Rheumatoid arthritis: 2
Overlap syndrome RA + limited SSc: 2
Primary Sjögren's syndrome: 1 (Secondary Sjögren's syndrome: 3)
Mixed connective tissue disease: 1
Polymyalgia rheumatica: 1
Undifferentiated connective tissue disease: 1
Acute hepatitis due to HEV: 1
Autoimmune thrombocytopenia (ITP): 1
Drug-induced fibrosing ILD: 1
Systemic graft versus host disease (GVHD) in a patient with acute lymphoblastic leukemia who received and autologous haematopoietic progenitor transplant: 1
Primary biliary cirrhosis: 1
CLINICAL MANIFESTATIONS *(patients could have more than one):*
Raynaud's phenomenon: 61% (14/23).
Inflammatory arthralgia/arthritis: 52% (12).
Lung involvement: 30.5% (7: NSIP 3, UIP 2, other patterns 2).
Serositis: 26% (6: pericarditis 4, pleuritis 1, pleuropericarditis 1).
Cardiac involvement: 26% (6: PHT by echocardiogram 3, myocarditis 2, arrhytmia 1).
Dry syndrome: 17% (4)
Myositis: 17% (4).
Esophageal involvement: 17% (4).
Autoimmune cytopenias: leucolinfopenia: 17% (4) / thrombocytopenia: 13% (3).
Telangiectasias: 13% (3).
Photosensitivity: 13% (3).
Other: non-androgenic alopecia: 9% (2); sensory-motor polyneuropathy: 4.5% (1); *Puffy hands*: 4.5% (1); fever: 4.5% (1); lymphadenitis: 4.5% (1); cold sores: 4.5% (1), and retinal hemorrhage: 4.5% (1).
OTHER ASSOCIATED ANTIBODIES:
ANA: 91% (21/23)
anti Ro60/SSA Ab: 30.5% (7)
Anti Ro52 Ab: 30.5% (7)
Anti RNP Ab: 22% (5)
Anti-dsDNA: 17% (4)
Anti-La/SSB Ab: 17% (4)
Anticentromer Ab: 17% (4)
Anti Mi-2 Ab: 13% (3)
Other: anti Sm Ab: 9% (2); anticardiolipin Ab(IgG): 4.5% (1); PM/Scl: 4.5% (1); nucleosomes: 4.5% (1); Scl70: 4.5% (1); PL12: 4.5% (1); anti-U1-RNP: 4.5% (1) and NOR90: 4.5% (1).

Conclusion: Anti-Ku Ab are related to a great variety of SAD, without being a specific marker of any of them, nor being associated with any specific clinical manifestation. We couldn't confirm the existence of clinical phenotypes associated with the presence of these antibodies.
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AB0164 ACTIVITIES OF THE OXIDATIVE-RELATED ENZYMES IN SYSTEMIC SCLEROSIS

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Background: The oxidative-related enzymes are involved in the pathogenesis of various stages of systemic sclerosis (SSc). SSc is a chronic autoimmune disorder that is intimately associated with vascular damage and therefore with chronic perfusion/reperfusion and oxidative organ injury. Mesenchymal cell activation in SSc is now also considered to be mediated primarily through oxidative burst. Regulation of oxidative stress by specific enzymes including several purine metabolism enzymes is likely to play an important role in SSc progression.
Objectives: to characterize interrelationships among circulating xanthine oxidase (XO), xanthine dehydrogenase (XDH), superoxide dismutase (SOD) activities and SSc activity.
Methods: The study was performed according to bioethical standards. 51 patients with verified SSc and 30 healthy controls were included in the study. The diagnosis was verified according to ACR/EULAR 2013 criteria. We assessed SSc activity in compliance with the original activity scale that is commonly used in Russia [Guseva N.G., 1993] and by the 2001 European Scleroderma Study Group Activity Index. XO (EC 1.17.3.2), XDH (EC 1.17.1.4), and SOD (EC 1.15.1.1) plasma activities were measured using spectrophotometric techniques as previously described [Dubinina E.E., 1986; Karpova O.V., 2006]. Results are expressed as mean±SD. The Mann-Whitney U test and Spearman's correlation coefficient were used for statistical analysis.
Results: Mean age of patients was 42.8±1.3 years, mean SSc duration was 7.9±0.7 years. Mean enzymatic activities in normal controls were 3.43±0.56 nmol/ml min (for XO), 5.19±0.71 nmol/ml min (for XDH), and 5.40±1.03 units (for SOD). The respective enzymatic activities in SSc group were 3.91±0.62 nmol/ml min, 7.10±0.71 nmol/ml min, and 7.10±2.19 units. All these mean activities were significantly higher in SSc patients comparing to healthy individuals ($p<0.001$). XO and XDH activities positively correlated with SSc activity ($r=0.499$, $p<0.001$, and $r=0.741$, $p<0.001$, respectively). The opposite but weaker trend was observed for SOD activity and SSc disease activity ($r=-0.190$, $p=0.188$).
Conclusion: SSc is characterized by an increase in the intensity of oxidative and antioxidant processes, more pronounced in high disease activity. A close relationship between function of prooxidant/antioxidant enzymes and some of the key SSc pathogenetic mechanisms, especially vascular disease and fibroblast activation, is widely considered. Overall increase of oxidative stress in patients with higher disease activity, as well as depletion of antioxidant capacity can be also linked with disturbance of purine metabolism through XO and XDH modulation. Pathogenetic influence of this imbalance can also be mediated through initial phase of neutrophil extracellular traps (NETs) formation, an eventual source of nucleoprotein containing autoepitopes.
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AB0165 THE ROLE OF CXCL4, CXCL8 AND GDF-15 IN SYSTEMIC SCLEROSIS

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Background: Systemic Sclerosis (SSc) is an autoinmune disease that can affect several organs and its mortality is fundamentally related to its pulmonary involvement.
It is mandatory to seek for biomarkers that help us with early diagnosis and that are also useful for predicting organic involvement, so that we can adjust the diagnostic and therapeutic approach.
Objectives: Our aim was to check if the presence of CXCL4, CXCL8 and GDF-15 is greater in the disease than in healthy population, and also their involvement in organic damage.
Methods: Observational and cross-sectional study, with a prospectively performed protocol, of patients diagnosed of SSc according to ACR/EULAR 2013 criteria. Demographic, clinical, analytical, activity (EUSTAR index), severity (Medsger scale and modified Rodnan index), health perception (SF36) and disability (HAQ and Cochin test) variables were collected. Moreover, Videocapillaroscopy (VCL) and Respiratory Function Test were made, as well High Resolution Lung Tomography and Echocardiography in order to describe pulmonary features. Serum levels of CXCL4, CXCL8 and GDF-15 were measured in SSc patients and in healthy controls.
Results: A total of 42 patients (95.4% women) were included, with an average age of 59.2 years. The median of years since diagnosis was 4, by 6 since the first non-Raynaud symptom. 20 patients were diagnosed with limited SSc, 20 patients diffusely and 2 patients with SSc without scleroderma. 42 healthy controls were also included.
We found significantly higher levels of GDF-15 in patients with SSc ($P<0.001$), without significant differences in CXCL4 and CXCL8 levels between patients with SSc and healthy controls.
The presence of GDF-15 was associated with diffuse SSc ($P=0.009$), pulmonary arterial hypertension ($P=0.038$), interstitial lung disease ($P=0.004$), decreased forced vital capacity (FVC), ($P=0.002$), high serum titles of antiScl70 ($P=0.006$), increased disease activity measured by EUSTAR index ($P=0.001$), as with capillary dilations in Capillaroscopy ($P=0.015$).
Moreover, we found an association between CXCL4 levels and the consumption of complement C3 fraction ($P=0.008$) and skin involvement (higher Rodnan modified score), ($P = 0.001$); not finding association with lung involvement or other features (spirometric or analytical changes, capillaroscopy or functional tests).

Attending to CXCL8, it was associated to consumption of the C4 fraction of complement (P=0.013) and the presence of tortuosities in capillaroscopy (P=0.02) with no other significant findings.

Conclusion: The presence of GDF-15 is associated with diffuse SSc, lung impairment, disease activity and changes in capillaroscopy. In addition, CXCL4 was only associated with skin involvement, while CXCL8 was not related to any organic damage in our patients.

Disclosure of Interests: None declared

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AB0166 IMMUNOGLOBULIN G DERIVED FROM PATIENTS WITH SYSTEMIC SCLEROSIS IMPRINTS A PRO-INFLAMMATORY AND PRO-FIBROTIC PHENOTYPE IN MONOCYTE-LIKE THP-1 CELLS

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Background: Regulatory IgG autoantibodies directed against diverse G protein-coupled receptors (GPCR), *i.e.* antibodies with agonistic or antagonistic activity are abundant in human serum. The serum titers of autoantibodies targeting angiotensin II receptor 1 (AT_1) and endothelin receptor A (ET_A) are specifically altered in autoimmune diseases such as systemic sclerosis (SSc). Disease-promoting mechanisms regulated by anti-AT_1 and anti-ET_A IgG are still elusive, but induction of pro-inflammatory and pro-fibrotic chemokines (CXCL8, CCL18) has been suggested to be one of them.

Objectives: To determine the cytokine and phospho-kinase profiles induced in monocyte-like cells by IgG derived from SSc patients (SSc-IgG) enriched with anti-AT_1 and anti-ET_A antibodies in comparison to IgG derived from healthy donors (IgG-HD).

Methods: A monocyte-like cell line (THP-1) was cultured *in vitro* and stimulated with IgG (1 mg/ml) derived from SSc patients or HD in the presence of various inhibitors/blockers for 24h. Then, supernatants were analyzed by a human cytokine/chemokine array. Data were analyzed using bio-mathematical tools such as generalized t-test including the robust regression method from R/Bioconductor package LIMMA. In addition, THP-1 cells were cultured *in vitro* and stimulated with IgG (1 mg/ml) derived from SSc patients or HD for up to 30 minutes. Thereafter, cell lysates were assayed for the kinome employing a human phospho-kinase array. To validate potential effects of transcription factor inhibition, release of CXCL8 and CCL18 into the supernatant was measured by Elisa.

Results: In general, SSc-IgG induced the release of most cytokines by THP-1 cells more pronouncedly than HD-IgG. The bio-mathematical analysis suggested that stimuli, responsible for the shift of the THP-1 cell cytokine profile, are more abundant in SSc-IgG than in HD-IgG. Based upon these findings a gene set enrichment analysis for transcription factors yielded the transcription factors NF-κB, AP-1, and PRDM1 (Blimp-1) as putative major regulatory hubs for the response of THP-1 cells to SSc-IgG. Further, SSc-IgG altered the phosphorylation status of several proteins, indicative of an involvement of MAPK and/or JAK/STAT pathways. Interestingly, a role for AP-1 was also proposed by the inhibition of CXCL8 and CCL18 release following pretreatment of THP-1 cells with an AP-1 blocker.

Conclusion: Herein, we demonstrate that IgG of SSc patients, enriched with anti-AT_1 and anti-ET_A autoantibodies drives THP-1 cells towards a general pro-inflammatory and pro-fibrotic phenotype, which is reflected by broad changes in the secretome and kinome of these cells. Furthermore, our results highlight AP-1 as critical regulator of gene transcription of CXCL8 and CCL18 in a monocyte-like cell line.

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AB0167 TOFACITINIB AND NINTEDANIB MODULATE COLLAGEN FORMATION IN DERMAL FIBROBLASTS

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Background: Dermal fibroblasts are responsible for the excessive extracellular matrix (ECM) formation observed in the skin of systemic sclerosis (SSc) patients and fibroblasts are therefore an obvious target for anti-fibrotic treatments. TGFβ, PDGF and IL-6 are known to be central cytokines in systemic sclerosis. Nintedanib, a tyrosine-kinase inhibitor approved for treatment of idiopathic pulmonary fibrosis, did not show effect on dermal fibrosis only on pulmonary fibrosis in SSc patients with interstitial lung disease (ILD). Tofacitinib, as Pan JAK inhibitor, has shown to inhibit dermal fibrosis in mouse models and shown positive indications in patients.

Objectives: We investigated the direct effect of Nintedanib and Tofacitinib on ECM production from human dermal fibroblast using translational biomarkers of type I, III and VI collagens and fibronectin.

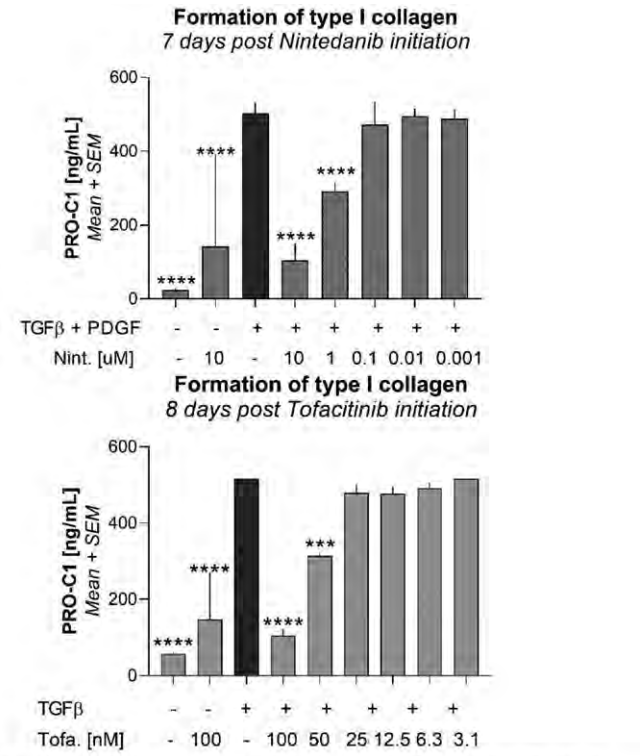
Methods: Primary healthy human dermal fibroblasts were grown in DMEM media containing 0.4% fetal calf serum, Ficoll (to produce a crowded environment) and ascorbic acid for up to 17 days. The cells were stimulated with PDGF [3 nM] and/or TGFβ [1 nM] in combination with Nintedanib [1 nM-10 μM] treatment initiated at day 0 or 7 or Tofacitinib [3-100 nM] treatment initiated at culture start together. Media and treatments were changed twice a week. Non-activated cells (w/o) were used as control. Type I, III and VI collagen formation (PRO-C1, PRO-C3 and PRO-C6, respectively) and fibronectin (FBN-C) were evaluated by validated ELISAs (Nordic Bioscience). Statistical analysis included 1-way and 2-way ANOVA, AUC and Mann-Whitney U-test.

Results: PDGF significantly increased collagen type III and VI formation and collagen type I formation minimally. PDGF did not induce changes in fibronectin levels. TGFβ increased collagen type I and VI formation but did not induce formation of collagen type III. TGFβ increased fibronectin levels, where PDGF did not. Nintedanib (≥100 nM) added either from day 0 or 7 reduced PDGF induced collagen type III and VI formation to the levels of w/o throughout the remainder of the study. In TGFβ treated fibroblasts, Nintedanib added either from day 0 or 7 reduced collagen type I and VI formation. The fibronectin levels were dose-dependently reduced by Nintedanib. The biomarker levels were at study end at the level of w/o. Nintedanib at a concentration of 1 uM and higher significantly decreased the biomarker levels. Nintedanib (≥100 nM) in fibroblasts stimulated with both TGFβ and PDGF significantly reduced collagen type I, III and VI collagen and fibronectin.

A Tofacitinib concentration of 100 nM was toxic to the dermal fibroblasts as the cell viability was minimal at culture end. However, the viability of Tofacitinib (100 nM) in combination with TGFβ was decreased at study end, but only to half the viability of untreated cells. Tofacitinib dose-dependently decreased the TGFβ induced type I and III collagen formation and fibronectin in the dermal fibroblasts. Tofacitinib (100 nM) decreased the level of collagen type I and III formation to the level of w/o, where as the level of fibronectin was lowered by 80 % of TGFβ. Tofacitinib as low as 12.5 nM significantly lowered the collagen type I formation and fibronectin (both $p<0.05$) and Tofacitinib of 25 nM decreased collagen type III formation significantly ($p<0.0001$).

Conclusion: Tofacitinib decreased the formation of the collagens and fibronectin. Nintedanib inhibited ECM production differently in PDGF and TGFβ induced dermal fibroblast, but in the combination of TGFβ and PDGF Nintedanib significantly decreased the ongoing fibrosis. In PDGF induced fibrosis, Nintedanib acted as an on-off switch, whereas the inhibition was dose-dependent in TGFβ induced fibrosis. This cell study indicates that Nintedanib and Tofacitinib inhibits collagen production in dermal fibroblasts.

Figure:



Inhibition of type I collagen by Nintedanib and Tofacitinib in dermal fibroblast stimulated with PDGF and/or TGFβ 8 and 7 days after Nintedanib and Tofacitinib initiation.

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AB0168 NINTEDANIB (TYROSINE-KINASE INHIBITOR) INHIBITS THE TRANSITION OF CIRCULATING FIBROCYTES ISOLATED FROM SYSTEMIC SCLEROSIS PATIENTS INTO MYOFIBROBLASTS: AN IN VITROSTUDY

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Background: Systemic sclerosis (SSc) is a chronic connective disease characterized by microvascular alterations, dysregulated immune response and fibrosis [1,2]. Myofibroblasts are alpha-smooth muscle actin (alphaSMA)$^+$ cells and play a crucial role in fibrosis, through the excessive synthesis and deposition of extracellular matrix (ECM) proteins, in particular fibronectin (FN) and type I collagen (COL1) [3]. Despite myofibroblasts primarily derive from resident fibroblasts transition and differentiation, another important source is represented by circulating fibrocytes [4]. Nintedanib is a tyrosine kinase inhibitor approved for the treatment of idiopathic pulmonary fibrosis that interferes with the signalling pathways involved in the pathogenesis of fibrosis [5].
Objectives: To investigate the possible effects of nintedanib in contrasting the ability of cultured mature fibrocytes from SSc patients to differentiate into profibrotic myofibroblasts.
Methods: Circulating fibrocytes were obtained from peripheral blood mononuclear cells isolated from 5 limited cutaneous SSc patients (mean age 68 +/- 10 years) and then plated on FN-coated tissue culture dishes in growth medium (DMEM at 20% of fetal bovine serum, 1% of penicillin-streptomycin and 1% L-glutamine), to allow the adhesion of fibrocyte precursors. Adherent cells were maintained in growth medium for 8 days in order to allow their differentiation into fibrocytes. Differentiated fibrocytes were treated with nintedanib at the concentrations of 100nM and 1000nM for 3 and 24 hours (hrs) or maintained in growth medium without any treatment. The differentiation of fibrocytes into myofibroblasts was determined evaluating the gene expression of alphaSMA, fibroblast specific protein-1 (S100A4) COL1, FN and CXCR4 by quantitative real-time polymerase chain reaction, and the protein synthesis of alphaSMA, COL1 and FN by western blotting.
Results: Nintedanib inhibited alphaSMA and S100A4 gene expression already at the concentration of 100nM in cultured fibrocytes and after 3 hrs of treatment, when compared with untreated cells. Furthermore, both concentrations of nintedanib (100nM and 1000nM) reduced the gene expression of COL1 and FN, whereas only 100nM downregulated the CXCR4 gene expression. At protein level, nintedanib 100nM and 1000nM reduced the synthesis of alphaSMA and COL1 after 24 hrs of treatment, whereas FN synthesis was reduced only by the nintedanib concentration of 1000nM.
Conclusion: The preliminary results show that nintedanib may inhibit the *in vitro* transition of SSc fibrocytes into myofibroblasts and their profibrotic activity, through the reduction of specific myofibroblast phenotype markers and ECM protein production. The results seem to suggest fibrocytes as further possible target of the antifibrotic action of nintedanib in SSc.
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Disclosure of Interests: Stefano Soldano: None declared, Giulia Martinelli: None declared, Samuele Tardito: None declared, Sabrina Paolino: None declared, Massimo Patanè: None declared, Emanuele Gotelli: None declared, Claudio Corallo: None declared, Carmen Pizzorni: None declared, Alberto Sulli Grant/research support from: Laboratori Baldacci, Carlotta Schenone: None declared, Vanessa Smith Grant/research support from: The affiliated company received grants from Research Foundation - Flanders (FWO), Belgian Fund for Scientific Research in Rheumatic diseases (FWRO), Boehringer Ingelheim Pharma GmbH & Co and Janssen-Cilag NV, Consultant of: Boehringer-Ingelheim Pharma GmbH & Co, Speakers bureau: Actelion Pharmaceuticals Ltd, Boehringer-Ingelheim Pharma GmbH & Co and UCB Biopharma Sprl, Maurizio Cutolo Grant/research support from: Bristol-Myers Squibb, Actelion, Celgene, Consultant of: Bristol-Myers Squibb, Speakers bureau: Sigma-Alpha
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AB0169 ENHANCED PLATELET ACTIVATION AMONG PATIENTS WITH SYSTEMIC SCLEROSIS

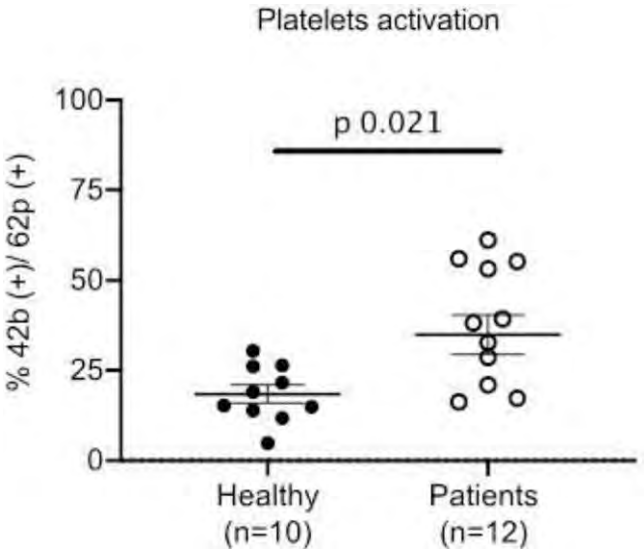
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Background: The function of platelets (PLT), which can serve as reservoirs of transforming growth beta, leads to the question whether they are activated in systemic sclerosis (SSc) to such an extent as to associate with clinical severity.
Objectives: To compare the level of PLT activation in SSc and to correlate with physical findings
Methods: Blood was sampled from 12 patients participating in the randomized clinical trial LIGHT (ClinicalTrials.gov NCT040045743) evaluating the safety and efficacy of bermekimab in SSc. Patients had to meet the 2013 ACR/EULAR classification criteria and have a modified Rodnan skin score (mRSS) between 15 and 40. Sampling was done before allocation to treatment. Nil patient was on DMARDs. Ten healthy donors were used for comparison. Citrated whole blood was exposed to 0.1 mM adenosine diphosphate (ADP) to stimulate PLT. Total platelet populations were defined as CD42b-positive population; P-selectin (CD62p) served as an activation marker.
Results: Expression of 42b(+)/62p(+) PLT was greater among patients (Figure 1). Mean fluorescence intensity (MFI) of 42b(+)/62p(+) PLTs was 0.16 +/- 0.08 in comparators and 0.51 +/- 0.07 in patients (p= 0.015). Negative correlation was found between the expression of 42b(+)/62p(+) on PLT and mRSS (r= -0.73, p= 0.028). Patients with grade 2 findings at capillaroscopy had greater expression of 42b(+)/62p(+) than patients with grade 3 findings (45.9 +/- 7.2 % vs 27.2 +/- 6.7 %; p: 0.041).

Conclusion: PLTs are greatly activated in SSc and this is associated with disease progression. Findings suggest that this activation is greater at less severe patients.

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Disclosure of Interests: None declared

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AB0170 PHENOTYPIC CHARACTERIZATION OF ENDOTHELIAL PROGENITORS CELLS OF SYSTEMIC SCLEROSIS (SSC) PATIENTS: ROLE IN ENDOTHELIAL-TO-WMESENCHIMAL TRANSITION PROCESS

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Background: Endothelial-to-mesenchymal transition (EndoMT), a newly recognized type of cellular transdifferentiation, seems to be involved in Systemic Sclerosis (SSc) pathogenesis. In this process endothelial cells lose their specific markers, and acquire a mesenchymal phenotype, thus expressing cell products such as alpha smooth muscle actin (α-SMA) (1,2).Circulating endothelial progenitors cells (EPCs) derive from bone marrow stem cells and contribute to *de novo* vessels formation. Several studies, although with conflicting results, have shown that EPCs in the peripheral blood of patients with SSc are impaired in their number and function (3).

Objectives: to assess phenotypic characteristics of EPCs fromSSc patients and from patients with Very Early Diagnosis of SSc (VEDOSS) compared with healthy controls (HC). In particular we want to evaluate the expression of α-SMA, as marker of a pro-mesenchymal switch (EndoMT) in:

1. Circulating Early (CD34+KDR+CD 133+) and Late EPCs(CD34+KDR+) in the peripheral blood using flow cytometry
2. Cultured EPCs using Western blot analysis

Methods: we enrolled 11 patients (6 SSc and 5 VEDOSS), classified according to the classification criteria for SSc (4) and for VEDOSS not fulfilling SSc criteria (5), and 5 HC. Phenotypic characterization was performed as previously described by Vasa et al. using a FACS Calibur (BD Immunocytometry Systems). EPCs number was expressed as a percentage of cells within the lymphocyte gate. 5*106 PBMCs were plated on human fibronectin-precoated (10 µg/ml Sigma-Aldrich) 6-well plates and cultured for 7-12 days to obtain EPCs. PBMCs from one HC were also cultured with 20% SSc patient serum. Collected EPCs were lysed and a Western blot analysis for α-SMA detection was performed.

Results: we found a significant higher percentage of α-SMA positive Early EPCs in all patients respect to HC (0,06% ±0,03 vs 0,03% ± 0,01; p=0,0149) particularly in VEDOSS patients (0,07%±0,01 vs 0,03%±0,01 p=0,008). Similarly we found a significant higher expression of α-SMA protein in all patients and VEDOSS patients respect to HC (0,1895±0,16 vs 0,07± 0,06 p= 0,0342; 0,3075 ± 0,14 vs 0,07± 0,06 p=0,0159). After the incubation of HC PBMCs with SSc serum, the α-SMA protein expression seems to be increased respect to its expression in thePBMCs of the same HC cultured without SSc serum (0,33 vs 0,1).

Conclusion: we found higher percentage of Early α-SMA positive EPCs and a higher expression of α-SMA protein in cultured EPCs in patients group (SSc and VEDOSS) than in HC. So we hypothesized a predominant pro-mesenchymal phenotype of this kind of EPCs. This could be considered the expression of the involvement of EPCs in the EndoMT process and it better explain the controversial role of EPCs in SSc pathogenesis. Moreover the modified expression of α-SMA in HC EPCs co-cultured with 20% SSc serum could suggest the presence of a factor inducing the EndoMT process in the disease.

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Disclosure of Interests: Katia Stefanantoni Consultant of: Italfarmaco Boehringer Ingelheim, cristiana barbati: None declared, Tania Colasanti: None declared, Carlotta Angelelli: None declared, Greta Pellegrino: None declared, cristiano alessandri Grant/research support from: Pfizer, Guido Valesini: None declared, Valeria Riccieri: None declared

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AB0171 THE IMMUNOMODULATORY AND ANTI-INFLAMMATORY EFFECTS OF BOSENTAN IN SYSTEMIC SCLEROSIS

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Background: Plasma endothelin-1 (ET-1) levels are increased in patients with systemic sclerosis (SSc), playing a central role in the development of fibrosis, vasoconstriction and inflammation[1]. While the beneficial effect of Bosentan, the endothelin receptor antagonists, have been demonstrated on vasoconstriction and fibrosis, its potential anti-inflammatory and immunomodulatory activity needs to be further investigated.

Objectives: To assess whether Bosentan can modulate the gene expression profile of immune cells in sample of patients with limited and diffuse SSc and active digital ulcers.

Methods: We enrolled 34 patients affected by SSc. Twenty-four patients were affected by limited SSc and 12 by diffuse SSc. Blood samples were collected from patients before and after 24 weeks of treatment with Bosentan, in the absence of immunosuppressive therapies. All patients received Bosentan 125 mg twice a day for 24 weeks. Gene expression profiles were assessed by GeneChip® Human Transcriptome Array 2.0 microarray technology. Significantly (p-value<0.05) and differentially (|FC|>1.5) expressed genes pre/post treatment were obtained by paired t-statistics, as implemented in Partek Genomics Suite ver. 6.6. These genes were subjected to functional enrichment analysis by Ingenuity Pathway Analysis. The effect of Bosentan on patients was studied on the "diffuse" and "limited" sub-cohorts, individually, as well as on the whole cohort.

Results: Contrary to the limited cohort where differentially expressed genes resulted to be all non-coding genes which are almost all over-expressed before treatment, the diffuse cohort was characterized by 19 differentially expressed genes that enrich biological functions and pathways related to the immune system and its organic response (in particular T-cells). Comparing the limited to the diffuse cohort, pre- and post- treatment, a distinct genetic fingerprint emerges, that characterizes the response to Bosentan by the latter cohort as increased apoptosis of lymphocytes (z-score=3.28) and a decreased quantity of antigen presenting cells (from z-score=1.06 (pre) to -0.75 (post)).

Conclusion: The presence of an inflammatory microenvironment, as occur in SSc, influence the relative expression of ET-1 receptors on immune cells, which in turn further contribute to the amplification of cellular responses to inflammation. The observed difference response to therapy between the two cohorts of patients was attributed to influence of ET-1 levels on the relative expression of ET-1 receptors on immune cells surface. Interestingly Bosentan, beside the already-known effect on promoting antigen presenting cells apoptosis, seem to exert its immunomodulatory activity also by deregulating functions that mainly involves the T cells and by promoting their apoptosis, which in turn reflect also its anti-inflammatory proprieties.

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AB0172 **PGC-1A REGULATES AUTOPHAGY TO PROMOTE FIBROBLAST ACTIVATION AND TISSUE FIBROSIS**

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Background: Peroxisome proliferator-activated receptor gamma coactivator-1α (PGC-1α) is the best studied member of the family of coactivators. PGC-1α was initially identified through its interaction with PPARγ in brown adipose tissue. Recent evidence further indicates that PGC-1α may also modulate the transcription of autophagy-related genes, which has recently been shown to be required for fibroblast-to-myofibroblast differentiation under fibrotic conditions. However, the role of PGC-1α in the pathogenesis of SSc has not been investigated.
Objectives: The aim of the present study was to evaluate the role of the coactivator PGC-1α on autophagy and to evaluate its role in the pathologic activation of fibroblasts in SSc.
Methods: Expression of PGC-1α was analyzed by RT-PCR, Western blot and immunofluorescence. Modulation of autophagy was analyzed by reporter studies by expression of autophagy related genes. The effects of PGC-1α knockdown on collagen production and myofibroblast differentiation were analyzed in cultured human fibroblasts and in two mouse models with fibroblast-specific knockout of PGC-1α.
Results: PGC-1α overexpression was detected by immunohistochemistry in skin sections of SSc patients and in experimental fibrotic murine skin, particularly in fibroblasts. Knockdown of PGC-1α inhibited the stimulatory effects of TGFβ on fibroblast activation with impaired induction of collagen as compared to control fibroblasts. Fibroblasts specific knockout of PGC-1α ameliorates experimental fibrosis in bleomycin-induced and adTBR-induced murine dermal fibrosis with decreased dermal thickness, hydroxyproline and myofibroblast counts compared to wild-type fibrotic mice. Incubation of dermal fibroblasts with TGFβ activated autophagy in control fibroblasts with increased expression of the autophagy-related genes ATG7 and BECLIN-1, enhanced conversion of LC3 I to LC3 II and decreased ratios of ILC3 I EGFP to LC3 II RFP in LC3 reporter assays. The expression levels of ATG7, BECLIN-1 and ILC3 II of TGFβ-stimulated PGC-1α knockout fibroblasts decreased compare to TGFβ stimulated wild-type fibroblasts. The ratio of ILC3 I EGFP to LC3 II RFP of TGFβ-stimulated PGC-1α knockout fibroblasts in reporter assays were comparable to unstimulated fibroblasts.
Conclusion: PGC-1α is upregulated in SSc and promotes autophagy to foster TGFβ-induced fibroblast activation. Targeting of PGC-1α prevents aberrant autophagy, inhibits fibroblast activation and tissue fibrosis.
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Disclosure of Interests: Yun Zhang: None declared, Katja Dreißigacker: None declared, Diana Distler: None declared, Andrea-Hermina Györfi: None declared, Christina Bergmann: None declared, xiang zhou: None declared, Lichong Shen: None declared, Ingo Ludolph: None declared, Raymund Horch: None declared, Andreas Ramming Grant/research support from: Pfizer, Novartis, Consultant of: Boehringer Ingelheim, Novartis, Gilead, Pfizer, Speakers bureau: Boehringer Ingelheim, Roche, Janssen, Georg Schett Speakers bureau: AbbVie, BMS, Celgene, Janssen, Eli Lilly, Novartis, Roche and UCB, Jörg Distler Grant/research support from: Boehringer Ingelheim, Consultant of: Boehringer Ingelheim, Paid instructor for: Boehringer Ingelheim, Speakers bureau: Boehringer Ingelheim
DOI: 10.1136/annrheumdis-2020-eular.3603

10. Basic and translational science in paediatric rheumatology

AB0173 **ALLELIC POLYMORPHISM OF PROINFLAMMATORY CYTOKINE GENES AS A BASIS FOR THE FORMATION OF PHENOTYPES OF JUVENILE IDIOPATHIC ARTHRITIS**

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Background: The pathological process of juvenile idiopathic arthritis (JIA) largely depends on pro-inflammatory cytokines, the polymorphism of the alleles of some genes of which we have the opportunity to study. No studies have been conducted on the dependence of certain features of the pathological process of JIA on the polymorphism of the IL-6(G-174C) and TNF(G308A) genes.
Objectives: To reveal the dependence of JIA phenotypes and its course on genetic polymorphism of alleles IL-6 and TNF.
Methods: Polymorphism of the IL-6 and TNF genes was studied by PCR-method using allele-specific primers 44 patients 1-17 y.o. (24f, 20m) with JIA. The level of IL-6 and TNFα in the serum was determined using ECLIA and CLIA methods.
Results: There were 73% cases with an unfavorable course of the disease (UCD) of the patients with the CC allele of the IL-6 gene, for most patients average activity was JADAS27 13.5±1.6. oJIA (50%) & uveitis (30%) were the most frequent among subgroups. The level of serum IL6 was 74.1±69.5 pg/ml, TNFα 27.4±17.3 pg/ml (ratio IL6/TNFα=4.3±2.1). Among patients with GC IL6 70% female, 79% with UCD. More often pJIA (36%, including all RF+) and eJIA (35%) were noted with the largest frequency of inclusion of the hip joints (33%), spine (35%), detection of secondary osteoporosis (43%). The metabolic changes were registered on the ECG in 82% cases. The serum IL-6 level was 11.35±2.95 pg/ml, TNF 241.75 pg/ml (IL-6/TNFα=0.047, p<0.05 vs CC allele). Children with GG IL-6 (wild allele) with a more favorable course of the JIA (31%, less than in the CC and GC groups (p<0.05), only 8% had the highest disease activity), the largest number of patients with sJIA (25%) was registered in this group. The detection of HLA B27 was significantly lower (p<0.05) than in other alleles, while 60% cases were ANA+ (more than in the group GC, p<0.05). The highest level of serum IL6 (35.3±18.9 pg/ml) & the highest average number of mutations in folate metabolism genes (4±0.51) were revealed in this group. The wild allele GG prevailed (n=32) among the TNF gene alleles, sex ratio 1:1, UCD in 70%. The number of active joints, ESR, CRP, ANA-positivity (50%), HLA B27+ (53%) were unsignificantly higher than in GA TNF allele, while serum IL6 level (22.8±9.8 pg/ml) & TNFα (12.3±4.1 pg/ml) were lower. In patients with the GA TNF gene allele, an UCD (73%), eJIA (36%) were noted slightly more often. By such parameters as the patient's gender, the presence of uveitis, damage to the hip joints, the type of synovitis, metabolic changes on the ECG, indicators were observed comparable with the wild allele group. IL6 level was 48.3±39.2 pg/ml, TNFα 636.5±420.1 pg/ml, IL6/TNFα=0.07±0.06 (vs 1.9±0.5 in GG group, p<0.05). The genotype of two wild alleles TNF GG with IL6 GG expectedly showed the smallest proportion of the UCD (33%, p <0.05), the most frequency of ANA-positivity (71%), with no uveitis and RF+pJIA in this group. All cases of RF+pJIA had TNF GA and IL6 GC. oJIA prevailed (57%) in the TNF GG&IL6 CC group, there was not a single case of sJIA, and the AJ number was the smallest (2.86±0,5). The largest group was TNF GG & IL6 GC (n=14). 91% of cases had UCD, AJ=6.6±2.4, damage to the hip joints in 40%, ESR 23.7±6.7 mm/h, CRP 14.5±5.4 mg/l, metabolic changes on the ECG in 100%, but ANA+ only at 13%. In general, there was no correlation between the cytokine content in the blood serum during of active disease in the examined children with features of allelic polymorphism of these genes.
Conclusion: Depending on the allele polymorphism of the IL-6 and TNF genes, certain phenotypes of the JIA course may be distinguished. Thus, revealing the polymorphism of these alleles in patients at the onset of the disease, we can predict to some extent its course and take this into account when choosing treatment tactics.
Disclosure of Interests: None declared
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AB0174 **T REGULATORY CELLS LEVEL IN PERIPHERAL BLOOD OF PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS AND ITS RELATION WITH DISEASE ACTIVITY**

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Background: The most important T-cell subtype in maintenance of immune tolerance is T regulatory cells (Treg). These are characterized by CD4 and CD25 receptors on surface, and by showing FoxP3 regulatory factor, which is necessary for maintaining the suppressive activity of Treg cells in peripheral blood (PB). Previous studies have studied Treg cells in PB and synovial fluid in patients with Juvenile Idiopathic Arthritis (JIA). However, there was insufficient evidence to draw robust conclusions about Treg implication in JIA, due to small simple size and variable results across studies. A deeper understanding of regulatory mechanism in JIA may increase comprehension on variability among JIA subtypes and may help to stablish prognosis on the follow up.
Objectives: To analyze Treg cells level in PB of JIA patients and its relation with disease activity.
Methods: Descriptive, cross-sectional, observational study conducted in a regional reference centre for Pediatric Rheumatology. We included consecutive patients with JIA diagnosed by ILAR criteria. The primary variable was the Treg percentage in PB measured by flow cytometry. To assess JIA activity, we used disease activity indexes (JADAS10, 27, 71 – CRP/ESR and cJADAS), Wallace remission criteria, VAS disease activity by patient/parents and physicians, morning stiffness, multidimensional evaluation (JAMAR) and acute phase reactants (CRP and ESR). Assessment of long-term damage was evaluated with JADI. Association analyses among study variables and Treg levels were performed by Pearson's correlation coefficient and Mann Whitney's U test.
Results: Ongoing study, we present a preliminary analysis with first 50 JIA patients. Mean age (SD) was 11.3 yr (4.6), being females 60%. Most common JIA subtype was persistent oligoarticular (42%) followed by RFneg polyarticular (24%). 42% patients were treated by csDMARD and 46% by biological agents. Mean levels of CRP and ESR were 0.18 mg/dl (0.3) and 6.3 mm/hr (5.4), respectively. At the time of the study, 84% of patients were in remission (Wallace criteria). Mean of JADAS 27-VSG, JADAS 27-PCR and cJADAS were 3.6 (5.1), 3.7 (5.1), and 3.7 (5.5), respectively. Mean long-term damage scores were 0.48 (1.1) for JADI-A and 0 for JADI-E. Mean levels of Treg cells in PB were 2.11% (1.1). The table shows the association between clinical variables and % of Treg. We can observe a significant, inverse and moderate correlation between Treg levels and disease activity by patient/parents, disability and quality of life (global and the physical component). Close to statistical significance, we found inverse and moderate correlation between Treg cells and all JADAS scores, cJADAS, disease activity by physician and morning stiffness. There was no association between Treg and acute phase reactants. Furthermore, there were no differences in Treg cells in Wallace remission (p=0.692) and regarding use of conventional or biological DMARD (p=0.984 and p=0.386, respectively).
Conclusion: According to our preliminary data, higher levels of Treg cells in PB of patients with JIA could be related with lesser disease activity and better quality of life. Larger studies are needed to confirm whether this Treg-mediated regulatory mechanism can have prognostic implication JIA.

Variables	r	p value
CRP (mg/dl)	-0.24	0.099
ESR (mm/hour)	-0.15	0.314
VAS-disease activity (patient / parents)	-0.28	0.049
VAS-disease activity (physician)	-0.25	0.081
JADAS10 (VSG)	-0.27	0.064
JADAS27 (VSG)	-0.27	0.064
JADAS71 (VSG)	-0.27	0.064
JADAS10 (PCR)	-0.28	0.054
JADAS27 (PCR)	-0.28	0.054
JADAS71 (PCR)	-0.28	0.054
c JADAS10	-0.26	0.065
Disability (JAFS – JAMAR)	-0.34	0.021
Quality of lyfe (PRQL – JAMAR)	-0.39	0.007
Quality of life physical (PRQLPh – JAMAR)	-0.46	0.001
Quality of life psychosocial (PRQLPs-JAMAR)	-0.21	0.156
Morning Stiffness	-0.27	0.066

Disclosure of Interests: None declared
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11. Basic and translational pain science

AB0175 INNOVATIVE PREPARATION OF CURCUMIN NANOPARTICLES TO IMPROVE ANTI-INFLAMMATORY EFFECT IN RHEUMATIC DISEASE

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Background: Curcumin (Cur) as a natural compound can be used in the wide spectrum of healthy functions and pharmacological activities [1-4]. It shows great promise for medication of various pro-inflammatory chronic illnesses [5]. In this study, we evaluate the ability of poly(lactide-co-glycolide)(PLGA) and different grads of PVA (polyvinyl alcohol) and lecithin as a drug delivery system for poorly soluble Cur
Objectives: The goal of this study was to prepare and characterize Cur encapsulated PLGA and different grads of PVA and lecithin as an efficient nanocarrier for improve anti-inflammatory effect in rheumatic disease
Methods: The PLGA nanospheres were formulated and then characterized for percent yield, encapsulation efficiency, surface morphology, and in vitro drug release profiles. At first, 6 mg of Cur was added to the organic phase including 24 mg of polymer dissolved in 5 mL of dichloromethane to constitute 1:4 (drug-to-polymer) ratios. Then, a mixture of PVA-lecithin (at about 5 cc) was added to maintain the stability of double emulsion droplets. The emulsion was continuously stirred at 300 rpm for 24 hours (at temperature of 37.5 ˚C) to evaporate the solvent, leaving behind the colloidal suspension of the drug-encapsulated nanoparticle in aqueous phase. The encapsulation of Cur into PLGA was characterized by Fourier transform infrared spectroscopy (FT-IR) and Transmission electron microscopy (TEM).
Results: Our studies achieved the successful formation of smooth surface and spherical shape Cur encapsulated into PLGA nanoparticles by the TEM image confirmed. The particle size distribution demonstrated a range of 30 nm to 100 nm, with the mean particle size being 45 nm. FTIR study implies successful loading of Cur into the nanoparticles. We show high drug-loading efficiency about 98 ± 0.5% for 6% of Cur weight in total ingredients weight of PLGA (w/w). It was also seen that a slower sustained release of 10% CUR in 48 hours is observed with biocompatible PLGA in phosphate buffered saline (pH = 7.4). The MTT assay of the Cur-PLGA exhibited no cytotoxic effect on Normal mouse fibroblast cells (L-929) cell line. IC50 of Cur -PLGA increased 99.5% against Cur nanoparticles (33.57 ±0.62 μM) ($P < 0.05$).
Conclusion: In this study, we constructed a novel preparation of curcumin nanoparticles with PLGA and different grads of PVA (polyvinyl alcohol) and lecithin to improve the bioavailability of CUR and PLGA exhibited no cytotoxic effect on L-929 cell line
References: In this study, we constructed a novel preparation of curcumin nanoparticles with PLGA and different grads of PVA (polyvinyl alcohol) and lecithin to improve the bioavailability of CUR and PLGA exhibited no cytotoxic effect on L-929 cell line
Disclosure of Interests: None declared
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12. Rheumatoid arthritis - prognosis, predictors and outcome

AB0176 RISK OF ANTI-CITRULLINATED PEPTIDE ANTIBODIES AND RHEUMATOID FACTOR IN MALE SMOKERS: DATA FROM KUWAIT REGISTRY FOR RHEUMATIC DISEASES (KRRD)

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Background: Smoking has been proposed to be associated with the development of anti-citrullinated peptide antibodies (ACPA) in rheumatoid arthritis (RA) patients.
Objectives: To study the relationship between smoking and ACPA as well as smoking and RF in patients with RA in Kuwait Registry for Rheumatic Diseases (KRRD).
Methods: Data on RA patients were extracted from KRRD from four major hospitals from February 2013 through December 2019. As females rarely smoke in Kuwait with a smoking prevalence of 3% in female RA patients in KRRD, females were excluded from the study population to reach the minimum statistical percentage needed to perform chi square test and assess the association between smoking and other variables. Statistical tests were applied where appropriate. Logistic regression was conducted to adjust for possible confounders including

age, disease duration, comorbidities, family history of a rheumatic disease, ANA, treatment agents and disease activity and quality of life assessment tools.
Results: A total of 863 RA male patients were studied with a mean age of 53.9±12.5 years and a mean disease duration 7.3±5.5 years. 652 (75.6%) had positive RF and 624 (72.3%) had positive ACPA. 431 (50%) had at least one comorbidity. 640 (74.2%) were on conventional disease modifying agents (cDMARD's) and 223 (25.8%) were on biologic therapy. 183 (21.2%) were smokers. After adjustment of other factors, logistic regression showed that smokers were significantly different than non-smokers in terms of a positive ACPA (β=-1.051, p<0.001, odds=4.019) and a positive RF (β=-0.804, p=0.019, odds=2.517).
Conclusion: Smokers have a higher risk of expressing a positive RF and a positive ACPA in a male population. Smoking should be considered as a possible risk factor for RA and efforts should be done to educate the population to cease smoking to possibly lower that risk.
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AB0177 RHEUMATOID ARTHRITIS SAUDI DATABASE (RASD): A SINGLE CENTER EXPERIENCE

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Background: National Registries are essential to direct current practice and design appropriate management strategies[1]. Rheumatoid arthritis (RA) registries in the middle east and north Africa remain scarcely represented[2].
Objectives: Our objective is to describe the Saudi RA population and to compare the findings to internationally reported data.
Methods: This is a cross sectional, analytical study that was conducted at Doctor Soliman Fakeeh Hospital (DSFH). The study ran from December of 2014 and concluded in December of 2018 using a pool of 433 patients. Inclusion criteria included adults older than 18 years of age who fulfilled the 2010 American College of Rheumatology criteria for diagnosis of RA[3]. Data were collected from patients and entered in a specially designed program for this registry. They included main demographic details,, lag times to final disease diagnosis. Disease Activity Score-28-C Reactive Protein (DAS-28-CRP) was calculated on presentation and on subsequent visits with intervals ranging from three to six months between them. Multiple regression model was used to assess the predictors of disease activity. We charted the lines of medications given, including conventional and biologic disease modifying antirheumatic drugs (DMARDs), following treat to target strategies[4].
Results: Out of 430 patients, 76.68% were female, while only 23.32% were male and the mean age was found to be 49.26 years with SD±11.
At initial presentation, 45.5% had demonstrated active disease (moderate or high disease activity) based on DAS-28-CRP scores while 54.5% were in remission or low disease activity. Out of the total number of clinic visitors, 330 had regular follow ups for more than 1 year while 103 patients were either irregularly visiting the rheumatology clinic or had lost follow up. The remission rates after 1 year had increased to 79.7% (263 patients), while 9.7% (32 patients) had low disease activity and no patients had sustained high disease activity at the end of follow up. It was also found that the female gender, higher Health Assessment Questionnaire-Disability Index (HAQ-DI) and a longer lag1/lag2 period were associated with higher disease activity in our population. Biologic medications had been used by 129 patients (29.7%) while conventional DMARDs were given to 304 patients (70.3%).
Conclusion: We described a population of RA patients in a single center in SA. We detected higher remission rates at one year of follow up. This could be attributed to many factors, including good referral systems and treat to target strategies with easier access to biologic medications.
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AB0178 PERIARTICULAR OSTEOPHYTE FORMATION PROTECTS AGAINST TOTAL KNEE ARTHROPLASTY IN RHEUMATOID ARTHRITIS PATIENTS WITH ADVANCED JOINT DAMAGE

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Background: New medications including biologics and aggressive treatment strategies can halt the inflammatory and destructive disease processes in patients with rheumatoid arthritis (RA), and in some cases repair damaged joints. In the process of damaged joint repair, periarticular osteophyte formation might be detected radiographically (1). However, little is known about the clinical and functional role of osteophyte formation in RA joints. Total joint arthroplasty, a common procedure for treating damaged large joints, can serve as a surrogate for the long-term outcome of large joint destruction in patients with RA.
Objectives: To determine the influence of periarticular osteophyte formation on the incidence of total knee arthroplasty (TKA) in patients with RA.
Methods: This retrospective longitudinal study used data from a registry of patients with RA starting biologics. A flow chart summarizing the study design is shown in Figure 1. A total of 130 symptomatic (tender and/or swollen) knee joints in 80 patients were studied with a median follow-up of 12 years. All data were analyzed using the knee joint as the statistical unit of analysis. The cumulative incidences of TKA were estimated using Kaplan-Meier curves, and compared according to the presence or absence of osteophyte on plain anteroposterior radiograph [osteophyte (+/-)] and the extent of advanced joint damage as defined by Larsen's grading system (0-II vs. III-V).
Results: Baseline characteristics of all subjects included in this study are shown in Table 1. A total of 42 knees underwent TKA during the follow-up period. There was no significant difference in the cumulative incidence of TKA between the osteophyte (+) and osteophyte (-) groups (31% vs. 34% at 10 years, P=0.718) (Fig. 2A). The cumulative incidence of TKA was significantly higher for the Larsen grade III-V group compared to the Larsen grade 0-II group (56% vs. 10% at 10 years, P<0.001) (Fig. 2B). While no significant difference was observed in the cumulative incidence of TKA between the osteophyte (+) and osteophyte (-) groups in the Larsen grade 0-II group (9% vs. 10% at 10 years, P=0.774) (Fig. 2C), the cumulative incidence of TKA was significantly lower for the osteophyte (+) group compared to the osteophyte (-) group in the Larsen grade III-V group (38% vs. 74% at 10 years, P=0.010) (Fig. 2D). Multivariate analysis using Cox proportional hazards models revealed that older age [hazard ratio (HR): 1.04

per 1 year, 95% confidence interval (CI): 1.01-1.08] and osteophyte formation (HR: 0.39, 95% CI: 0.19-0.79) independently predicted TKA in the Larsen grade III-V group, whereas none of the assessed variables predicted TKA in the Larsen grade 0-II group.

Table 1. Baseline characteristics by presence or absence of osteophyte formation

	Total		Osteophyte (+)		Osteophyte (-)		
Characteristics	n = 130		n = 44		n = 86		*P* value
Age, years	57	(41-63)	59	(52-65)	56	(39-63)	0.051
Sex, female, n (%)	108	(83)	40	(91)	68	(80)	0.137
Body mass index	21.3	(19.0-23.8)	21.3	(18.9-24.4)	21.2	(19.0-23.7)	0.744
Disease duration, years	8	(3-12)	9	(5-18)	7	(3-11)	0.007
Larsen grade, n (%)							<0.001
Grade 0-II	66	(51)	11	(25)	55	(64)	
Grade III-V	64	(59)	33	(75)	31	(36)	
Osteophyte formation, n (%)	44	(34)	-		-		-
RF or ACPA positive, n (%)	85	(83)	35	(90)	50	(78)	0.183
CRP, mg/dl	3.2	(1.5-4.9)	2.9	(1.0-4.1)	3.4	(1.8-5.2)	0.172
First biologic agent, n (%)							1.000
Infliximab	57	(44)	19	(43)	38	(44)	
Etanercept	73	(56)	25	(57)	48	(56)	
Use of methotrexate, n (%)	98	(75)	33	(75)	65	(76)	1.000
Methotrexate dose, mg/week*	8	(6-10)	8	(6-9)	8	(6-10)	0.104
Use of glucocorticoids, n (%)	79	(61)	22	(50)	57	(66)	0.088
Glucocorticoid dose, mg/day*†	5.0	(5.0-7.5)	5.0	(5.0-5.0)	5.0	(5.0-7.8)	0.204

Data are presented as median (interquartile range) or number of subjects (percentages). *Median among subjects receiving the drug. †Prednisolone equivalent (mg/day).

Conclusion: Osteophyte formation reduces the incidence of TKA in patients with RA who have advanced joint damage.

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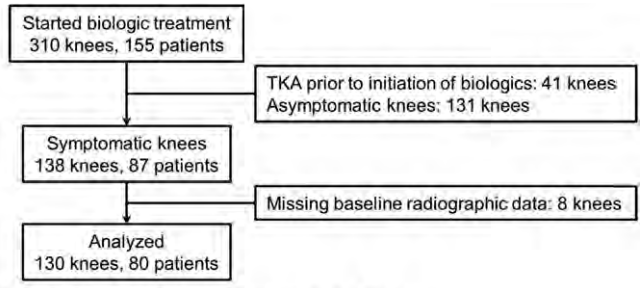


Figure 1. Flow chart summarizing the study design.

Disclosure of Interests: Shuji Asai Speakers bureau: AbbVie, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eisai, Janssen, Takeda, and UCB Japan, Nobunori Takahashi Speakers bureau: AbbVie, Asahi Kasei, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eisai, Eli Lilly, Janssen, Mitsubishi Tanabe, Ono, Pfizer, Takeda, and UCB Japan, KENYA TERABE: None declared, Toshihisa Kojima Grant/research support from: Chugai, Eli Lilly, Astellas, Abbvie, and Novartis, Consultant of: AbbVie, Speakers bureau: AbbVie, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eli Lilly, Janssen, Mitsubishi Tanabe, Pfizer, and Takeda, Naoki Ishiguro Grant/research support from: AbbVie, Asahi Kasei, Astellas, Chugai, Daiichi-Sankyo, Eisai, Kaken, Mitsubishi Tanabe, Otsuka, Pfizer, Takeda, and Zimmer Biomet, Consultant of: Ono, Speakers bureau: Astellas, Bristol-Myers Squibb, Daiichi-Sankyo, Eli Lilly, Pfizer, and Taisho Toyama

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AB0179

BEYOND DISEASE ACTIVITY, PAIN, "TIME" AND "TIMING" ACCOUNT FOR DISABILITY IN PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS FROM A REAL-LIFE COHORT

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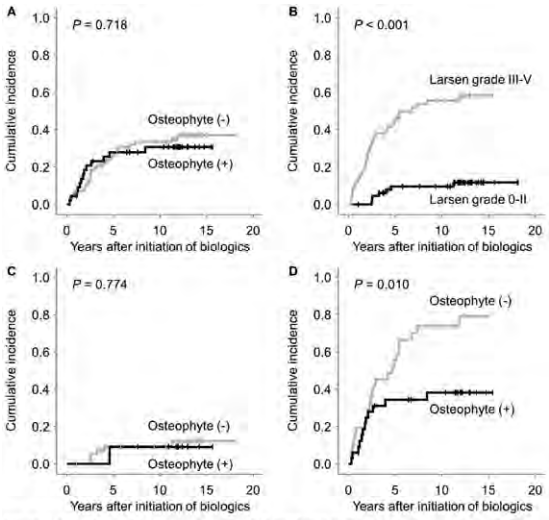


Figure 2. Kaplan-Meier estimates of cumulative incidence of total knee arthroplasty stratified by osteophyte formation (A) and Larsen grade (B) in overall subjects, and by osteophyte formation in the Larsen grade 0-II group (C) and the Larsen grade III-V group (D).

Background: Patients with rheumatoid arthritis (RA) suffer from joint pain, stiffness and fatigue and are therefore limited in their physical activities. Since functional disability is a major determinant of quality of life in patients with RA, an optimized approach should focus on the maintenance of functional ability.

Objectives: To evaluate self-reported disability in RA patients and to identify its influencing clinical and demographic factors in a real-life cohort of patients with RA.

Methods: Cross-sectional study of consecutive patients with RA fulfilling the ACR/EULAR 2010 and/or ACR 1987 RA classification criteria, followed in a Portuguese tertiary care centre. Variables collected included socio-demographic and clinical variables (disease duration; time from symptoms onset to diagnosis, classified as short (≤ 2 years) and long (> 2 years); time of diagnosis, categorised as <2000, 2000-2009, ≥2010); DAS28-CRP-3V and its individual components; pain assessed through visual analogue scale (0-100 mm) and self-perception of anxiety/ depression through EQ5D dimension 5. Disability was assessed through Health Assessment Questionnaire (HAQ) score and categorised as none-to-mild (<1) or moderate-to-severe (1-3). Comparison between groups was assessed through chi-square or T-student test, as adequate. Variables with p<0.1 and others clinically relevant in the researcher's perspective were included in a multivariable logistic regression model. Previously to the analysis, all the assumptions were verified. Given the implementation of new strategies regarding diagnosis and treatment of RA in the last decade, a subgroup analysis was performed for patients with diagnosis performed after 2010).

Results: A total of 251 patients were included (78.9% female, aged 62.0±12.1 years, disease duration 16.7±11.2 years), with a mean DAS28-CRP-3V of 2.24 ±0.87, with 65.3% being in remission or low disease activity. The mean HAQ score was 1.2±0.8. Over half of the patients (56.2%) reported moderate-to-severe disability. In the univariate analysis, moderate-to-severe disability was more frequent in female patients (60.6% vs 39.6%, p<0,006), in patients with moderate-to-severe self-perception of anxiety/depressive symptoms (67.2% vs 44.2%, p<0.001) and in patients with diagnosis before the year 2000, 2000-2009 than ≥2010 (71.4% vs 63.1% vs 36.7%; p< 0.001). In addition, patients with moderate-to-severe disability tended to be older (65.05 vs 57.98, p<0,001), to have longer disease duration (20.07 vs 12.39, p <0.001), to report more pain (VAS 58.08 vs 28.62, p<0.001) and to have higher disease activity (2.48 vs 1.95, p=0.001). In the multivariable analysis, pain (OR=1.04; 95%CI 1.03-1.06, p<0.001), disease activity (OR=1.51; 95%CI 1.01-2.26, p=0.049), and time of diagnosis (OR=0.553, 95%CI 0.38 -0.81, p=0.002) remained as independent factors associated with moderate-to-severe disability (R2: 0.40, p<0,001). In the subgroup of patients diagnosed after 2010, a longer time to diagnosis (>2 years) (OR=7.97, 95%CI 1.88-34.06; p=0.005) and pain (OR=1.05, 95%CI 1.03-1.08; p<0,001) remained as independent factors (R2= 0.44, p=<0.001).

Conclusion: Functional disability remains a major problem in our patients with RA, despite clinical remission. Beyond non-modifiable factors, disease activity and pain are associated with higher disability. Moreover, in the subgroup of patients diagnosed after 2010 a long time to diagnosis was the major predictor of disability. However, a large variance of the reported functional disability remains unexplained. Hence, other factors should be properly evaluated in our patients in order to achieve a more holistic approach aiming at reducing functional disability.

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AB0180 VITAMIN D SUPPLEMENTATION ON DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis(RA) is a chronic inflammatory autoimmune disease with unknown etiology that primarily affects the peripheral joints and, over time, leads to loss of mobility if untreated.1 The prevalence of RA in Myanmar was 1.3% in 2004.2 According to Rheumatology outpatient clinic records of Mandalay General Hospital, there were 402 old patients and 104 new RA patients in 2017 and 453 old patients and 102 new RA patients attending in 2018. In addition to the main effects of vitamin D (vit D) on bone and calcium metabolism, it has other roles in the body, including modulation of cell growth, neuromuscular and immune function, and reduction of inflammation .3 Due to difference in ethnic origins and geographical distribution, the results may be varied when it is done in sunshine rich area such as Myanmar. In the present study, vitamin D supplementation on the disease activity of RA by DAS28 was determined.

Objectives: 1.To compare DAS28 score before and 12 weeks after vitamin D loading dose supplementation in RA patients with vitamin D deficiency

2.To compare DAS28 score before and 12 weeks after vitamin D 1000 IU per day supplementation in RA patients with normal serum vitamin D level

Methods: 58 patients with RA attending to medical unit I, II, III and Rheumatology outpatient clinic of Mandalay General Hospital were recruited. Disease activity was assessed according to DAS28. Patients with DAS28 ≥ 2.6 were assessed for serum vitamin D status. Those with vitamin D level < 20 ng/ml were defined as vitamin D deficient and vitamin D_3 5, 000 IU per day for 8 weeks, then 1, 000 IU per day for 4 weeks were given orally for a total of 12 weeks duration. Patients with normal Vit D level (≥ 20 ng/ml) were provided with Vit D 1000 IU per day for 12 weeks.

Results: Before 12 weeks of Vit D supplementation, 53.45% of patients with RA (2 male and 29 female) were Vit D deficient and 46.55% of patients (1 male and 26 female) had normal serum Vit D level. The largest age group was between 46-55 years in both groups which comprised 41.38% of patients. In patients with Vit D deficiency, mean serum Vitamin D level was 10.32 ± 4.26 ng/ml and, in patients with normal Vit D level, mean serum Vitamin D level was 36.51 ± 17.76 ng/ml.

After 12 weeks of Vit D supplementation, out of 31 patients with Vit D deficiency, serum Vit D level of 23 patients became ≥ 20 ng/ml although only 3 patients were still Vit D deficient. Both groups showed improvement in clinical and biochemical parameters such as VAS, ESR, tender and swollen joint counts.

Before 12 weeks, more than 40% of patients had high or moderate disease activity in each group. After 12 weeks of Vit D supplementation, in Vit D deficient group, most patients (54.84%) had disease remission and 22.58% of patients were found to have moderate disease activity. Disease activity of 19.35% of patients became low. Only one patient had high disease activity.

After 12 weeks of Vit D supplementation, in Vit D normal group, disease activity of most patients (48.15%) became low and 33.33% had remission. 18.52% of patients with RA were found to have moderate disease activity. No patient had high disease activity.

Although there was no correlation between serum Vit D level and DAS28, DAS28 score was significantly decreased from 5.27 to 2.79 (*P* 0.0000) after 12 weeks of Vit D loading dose supplementation in RA patients with Vit D deficiency. Similarly, DAS28 score of RA patients with normal Vit D level was significantly decreased from 5.04 to 2.71 (*P* 0.0000) after 12 weeks of Vit D 1000 IU supplementation.

Conclusion: The present study revealed that Vitamin D supplementation was effective in reducing disease activity in patients with Rheumatoid arthritis. These findings may be helpful in the treatment of Rheumatoid arthritis.

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AB0181 COULD TITERS OF ACPA PREDICT THE SEVERITY OF RHEUMATOID ARTHRITIS, ANALYSIS OF DATA DURING A 3-YEARS FOLLOW-UP?

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Background: Rheumatoid Factor (RF) and/or Anti Citrullinated Protein Antibodies (ACPA). Are included in classification criteria of Rheumatoid arthritis (RA); their presence correlates with RA severity. The influence of ACPA titer on RA course and outcome in long-term follow-up is limited.

Objectives: To check the correlation between ACPA titers at the time of RA diagnosis to RA features and severity during 3 years follow-up.

Methods: We performed a retrospective study on patients treated at our institution during the years 2006-2015 with known ACPA titers at RA diagnosis, who completed at least 3 years of follow-up. Patients (pts) were divided according to ACPA titer: A - seronegative (<15 U/ml), B - weak positive (15-49 U/ml) and C - strong positive (>50 U/ml) with subdivision to C-1 - moderately high (50-99 U/ml), C-2 - high (100-299 U/ml) and C-3 - very high (>300 U/ml). Patient's data including DAS28, bone erosion on hands and/or foot X-rays, treatments with corticosteroids and DMARDs and hospitalizations due to flares. Chi-Square and Mann-Whitney method were used for statistical analysis; p<0.05 was considered statistically significant.

Results: Among 850 pts with RA, 133 (mean age 55 years, 65% female) met the inclusion criteria: group A: 55 (42%) pts, group B: 18 (13%) pts, group C: 60 (45%) pts [C1- 10 pts, C2-21 pts and C3-29 pts]. Most of the characteristics were similar between the groups (including C subgroups). There were no significant differences between the groups in terms of tender and/or swollen joints, acute phase reactants, bone erosions, need for corticosteroids or DMARDs, hospitalizations, number of DMARDs and number of biologicals. There was significant correlation between ACPA titers and positive RF (p<0.0001); it was consistent in all patients groups. Higher ACPA titers were associated with greater percentage of patients with positive RF. The percentage of male was higher in subgroup with highest ACPA: 25% in ACPA-negative group compared to 45% in the strong positive group (group C-3); it correlated with current or ever smoking. DAS28 was high in all groups without significant difference; over 80% of patients had DAS28 higher than 3.2 and 50-60% had a value higher than 5.2. During the 3-year follow-up, 95% of pts received prednisone with an average daily dose of 14.8 mg (SD, 8.9 mg), 50% of pts received more than 15 mg prednisone daily. The average number of synthetic and biological DMARDs was 2.5 (SD 0.73) and 0.56 (SD 0.84) per patient; methotrexate was prescribed in 89% of cases. There were no correlations between negative (group A) or positive ACPA (group B and C) and the variables defined as representing the severity of RA: the percentage of pts with DAS28>3.2 (p=0.136) and DAS28>5.2 (p=0.774). The percentage of pts receiving prednisone dosage higher than 15 mg/day (p=0.828) or at least two synthetic (p=0.846) or biological DMARDs (p=0.668) or their combination (p=0.770) were not significantly different. There was no correlation between ACPA titer and bone erosions (87 pts, p=0.883) during 3 years of follow-up. Finally, there was no correlation between ACPA titers and the number of hospital admissions (p=0.951).

Conclusion: In our cohort of RA pts, higher ACPA titers were observed in males with smoking history. Higher ANCA titers correlated with RF positivity but were not identified as predictive factor for RA severity.

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AB0182 EVALUATION OF THE SOCIO-PROFESSIONAL IMPACT OF ANKYLOSING SPONDYLITIS AND RHEUMATOID ARTHRITIS IN TUNISIA: DATA FROM THE BINAR REGISTRY

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Background: Rheumatoid arthritis (RA) and ankylosing spondylitis (AS) are disabling and common chronic inflammatory rheumatic diseases.

Objectives: The aim of our study was to evaluate the socio-professional impact of RA and AS.
Methods: Using the Biological National Registry (BINAR) data, which includes ten tunisian rheumatology centers,we identified patients≥18 years with AS and RA according to the ACR and EULAR 2010 criteria(RA) and ASAS 2009 (AS), receiving biotherapy for less than two years.
Results: 298 patients were included in the study. The percentage of patients with RA was 58.7 % and those with AS 41.3%. The sex ratio was 0.6. The average age of the onset of the disease was 49.1 years ± 14.1 years [18–79]. For marital status, 72% were married, single (25%), widowed (2.6%) and divorced (0.4%). 22.4% of patients were illiterate, 32.7 % (primary), 28.3% (secondary) and 16.6% had an university level. For the RA population, a high disease activity (DAS28-ESR >5.1) was detected in 36% of patients, an erosive arthritis in 73.1% and 7.2% had a coxitis. In the AS group, an elevate BASDAI (BASDAI≥4) was detected in 56.9% of patients and 39% had coxitis. All patients have received Biological therapy concomitant with corticosteroids (59.1%), methotrexate (42.6%), salazopirine (20.8%) and leflunomide (4.7%). 54% of patients had a comorbidity, of which 1.7% was depression. More than half of our patients (54.3%) were unemployed, 40 % were professionally active, and 5.7% were retired due to the rheumatic condition. Absence from work was observed in 15.1% of cases with a total duration exceeding three months in 55.5% of cases. 37.9 % of patients were physically active: regularly (9.8%), irregularly (28.1%) and (62.1%) were sedentary. For the functional impact, HAQ score was 1.31± 0.7 for RA and BASFI was 5.2 ± 4.8 for AS. The working abandonment is significantly associated to: marital status (p=0.039), low level of education (p=0.04),-depression (p<0.001), high activity of AS (p=0.004) and BASFI>4 (p=0,001).
Conclusion: RA or AS requiring biotherapy have a high socio-economic impact and are responsible for absenteeism at work and even for early working abandonment. Early therapeutic management and a global assessment are essential in order to improve quality of life and working conditions. Longitudinal studies are needed to assess the effect of biological therapy on the socio-professional impact of these chronic inflammatory rheumatic disease.
Disclosure of Interests: None declared
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AB0183 EARLY RA PATIENTS SEEN IN PRACTICE WHO HAVE CO-EXISTENT NON-ARTICULAR PAIN HAVE SIGNIFICANT WORSENING OF PROMIS® 29 DOMAIN SCORES. RESULTS FROM THE CATCH US STUDY

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Background: Non-articular pain (NAP) can co-exist with synovitis in RA. Its presence is associated with higher pain and worse function per legacy patient reported outcomes (PROs) both of concern to people with RA. It is not known if the presence of NAP significantly changes PROMIS 29 health domains.
Objectives: To determine if co-existing NAP (both regional or widespread pain) is associated with important differences in PROMIS 29 domain scores for symptoms and impacts.
Methods: Patients (pts) with early RA, were recruited from two practice settings in the Consortium of early arthritis cohorts, USA (CATCH-US) (New York and Baltimore) between Jan 2015-Dec 2019 (n=96). Data were from baseline (bl) visits; pts must have completed a body pain diagram (BPD) (CHOIR Bodymap®) and the PROMIS-29V.1, and provided legacy PRO and clinical measures. Pts were grouped as i) no-NAP and ii) NAP based on presence of pain in non-articular regions (1-3 regions - regional, 4-5 -widespread). PROMIS 29 domain scores were compared between groups, as were related legacy PROs and clinical outcomes routinely used to assess disease activity. Data are descriptive; continuous variables were compared using t-tests.
Results: Pts (n=96) had a mean age(sd) of 47.9 (14.9), 83% female, 67% white, 13% smokers, 21% obese, 82% seropositive, 51% mod/high CDAI, symptom duration 7.3 (5.4 months) and a comorbidity index (RDCI) of 0.7 (1.0). At study entry most had started RA treatments: 32% csDMARD with MTX, 22% non-MTX csDMARDs, 40% oral steroids, 13% biologics or JAKi's; 28% were treatment naive. Patients reporting NAP were more often white, smokers, obese, but did not differ otherwise. MDSJC28 was higher, mostly effected small joints, and affected regions on BPD were excluded for NAP classification. All but one (anxiety) of PROMIS 29 domain scores differed significantly between groups; similar differences were seen in legacy PRO scores and in some clinical outcomes (Table). Most clinical measures did not differ between groups.
Conclusion: In this cohort of early RA patients almost 1/3 with co-existent NAP unrelated to synovitis had significantly worse legacy PRO and PROMIS scores. These data provide rationale for using generic PROMIS measures as they identify symptoms and impacts, that may be unrelated to synovitis, providing information that could improve patient-oriented care in clinical practice. Clinicians should assess for and treat NAP as part of target-based care. Reasons for (injury, mechanical, disuse) and best treatment of NAP require further research.

Table. PROMIS Scores differ between patients with and without NAP as do Legacy PROs in real world early RA patients.

	NAP Any Pattern (n=26)	No Co-existing NAP (n=70)	p-value
Baseline Characteristics			
Age	50.2 (14.1)	47.1 (15.1)	0.356
Female sex	84%	81%	..
Current Smoker	19%	5%	..
RF+ / ACPA+	57% / 62%	62% / 76 %	..
BMI	27.2 (6.7)	26.1 (6.4)	0.236
RDCI (0-9)	0.68 (1.03)	0.69 (0.97)	0.963
Symptom Duration, mos	7.4 (1.3)	7.4 (0.6)	0.979
Legacy PROs and Clinical Measures			
ESR mm/hr	22.5 (6.8)	16.7 (2.3)	0.425
CRP (mg/dl)	1.03 (0.260)	1.02 (0.19)	0.965
Pain (0-10)	4.5(2.4)	3.0 (2.5)	0.009
Pt global (0-10)	4.5 (2.6)	2.6 (2.3)	0.002
Stiffness (0-10)	5.1(2.5)	3.07 (2.90)	0.002
MDHAQ (0-3)	2.2 (1.7)	0.9 (1.2)	0.001
RAPID 3 (0-10)	2.8 (2.3)	1.8 (1.8)	0.036
ESR mm/hr	22.5 (6.8)	16.7 (2.3)	0.425
CRP (mg/dl)	1.03 (0.26)	1.02 (0.19)	0.965
MDTJC 28	4.1 (5.4)	2.9 (3.8)	0.290
MDSJC 28	6.9 (6.3)	3.4 (3.9)	0.013
MD Global (0-10)	4.1 (2.3)	3.4 (2.0)	0.183
DAS28 ESR	4.14 (2.25)	3.14 (1.39)	0.123
CDAI	19.6 (13.6)	12.2 (9.5)	0.015
PROMIS Scores			
Function	44.03 (8.79)	49.47 (7.02)	0.007
Anxiety	53.2 (10.5)	50.4 (9.4)	0.238
Depression	52.6 (9.2)	47.1 (8.0)	0.012
Sleep Disturbance	55.3 (8.4)	50.3 (8.4)	0.013
Fatigue	58.3 (7.9)	49.3 (9.5)	<.001
Social Participation	43.7 (9.9)	50.7 (10.4)	0.004
Pain Interference	60.2 (8.0)	52.7 (8.9)	0.007

Data are mean(sd) unless noted

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AB0184 ADHERENCE TO TREATMENT IN AN ITALIAN COHORT OF PATIENTS AFFECTED BY CHRONIC INFLAMMATORY ARTHROPATHIES TREATED WITH BIOLOGIC AGENTS

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Background: The lack of adherence to treatment in patients affected by chronic diseases, such as rheumatic diseases, remains a relevant issue. Indeed, "inefficacy" or "intolerance" to therapies prescribed could hide a scarce compliance of a considerable percentage of patients.
Objectives: We aimed to evaluate the adherence to treatment in a series of patients affected by chronic inflammatory arthropathies treated with biologic agents.
Methods: We recruited 175 consecutive patients (M/F: 56/120; mean age 52.6±12.3 years) affected by rheumatoid arthritis (98), psoriatic arthropathy (45) or ankylosing spondylitis (32) treated with subcutaneous biologic agents. All patients completed the Morisky Medication Adherence Scales (MMAS-8)[1], in order to estimate their adherence to therapy. Moreover, we achieved from all cases the Patient Global Assessment (PGA), the Visual Analogue Scale (VAS) for articular pain, the Health Assessment Questionnaire (HAQ), and the report of eventual adverse events.
Results: Considering MMAS-8, 23/175 (13.1%) patients were low adherent to treatment (score <6), and 59/175 (33.7%) presented medium-grade adherence (score 6-7).
Adherence to treatments tended to be higher in males (mean MMAS-8 7.3±1.1 vs. 6.9±1.6; p=0.073), while it was not associated with age, education level, type of articular disease, presence of adverse events, or treatment with the type of traditional or biologic DMARDs.
Higher mean levels of PGA (51.3 vs. 38.8; p=0.012), VAS (52.6 vs. 44.3; p=0.08), and HAQ (0.9 vs. 0.5; p=0.001) was reported in low-adherent patients compared with full adherent subjects.

Conclusion: Our study confirmed that the percentage of patients showing low adherence to therapy is relevant. Moreover, the association of lower adherence to treatments with higher values of the subjective clinimetric indexes suggests to pay attention to the apparent ineffectiveness or loss of efficacy of therapy.

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AB0185 PROSPECTIVE PROFILE OF URINE METABOLOME IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by increased mortality and associated with metabolic disorders. Since the metabolomic profile is known to vary in response to different inflammatory conditions, metabolome analysis could substantially improve diagnosis and prognosis of RA.
Objectives: To analyze the urine metabolome profile in RA patients and correlate it with disease activity changes over 12 months
Methods: Seventy-nine RA patients, according to ACR/EULAR 2010 classification criteria, between 40 and 70 years old, were recruited and followed for 12 months. Metabolome analysis was performed by Nuclear Magnetic Resonance spectroscopy (NMR), resulting in the identification of 93 metabolites in urine collected at the baseline and after 12 months. Frequency analysis, Pearson Correlation and Multivariate data analysis with orthogonal projections to latent structures (OPLS) method were performed and a statistical significance was considered as $p<0.05$.
Results: The study population was characterized by the majority of women (86.7%), mean age of 56 years old, around 80% with positive anti-CCP or Rheumatoid Factor. During the one year of follow-up, there was no substantial variation in the DAS28 measurement (baseline: 3.8, after 12 months: 4.0). There was no significant correlation between the metabolome pattern and DAS28 score ($p>0.05$) over time. However, multivariate analysis (OPLS-DA) demonstrated an adequate differentiation of the population with 0.92 of accuracy (Q2: 0.72 and R2: 0.89).There was a significant increase of L-cysteine, choline, L-Phenylalanin, creatine, L-histidine, oxalacetic acid and xanthine, and a decrease of L-threonine, taurine, butyric and gluconic acid ($p<0.05$) during the follow-up, metabolites that are involved in the skeletal muscle metabolism.

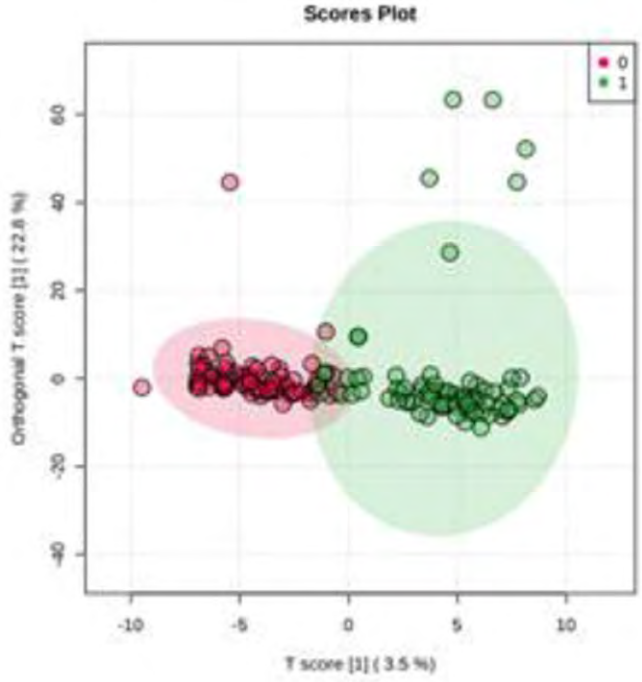


Figure 9: OPLS-DA score plot of all metabolite features.

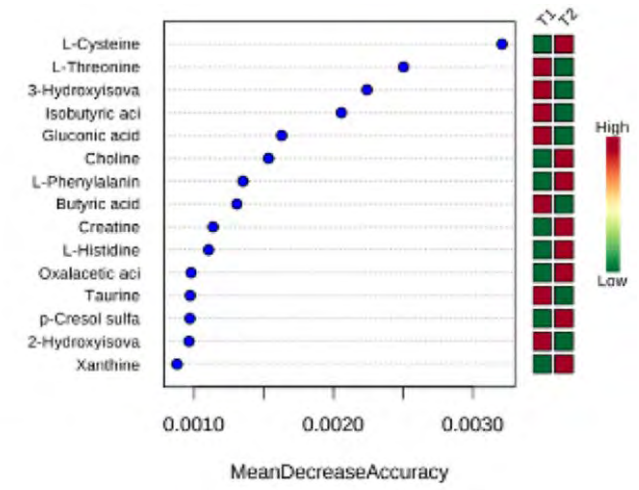


Figure 32: Significant features identified by Random Forest. The features are ranked by the mean decrease in classification accuracy when they are permuted.

Conclusion: The observed biomarkers indicate,as expected, that the RA metabolic profile is associated with inflammation injury and skeletal muscle amino acid metabolism. Correlations with disease activity changes was compromised by the stable disease status during the 12 months. More studies evaluating correlations with skeletal muscle function and mass are underway.
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AB0186 NO PREDICTIVE VALUE OF ADALIMUMAB SERUM LEVELS AND ANTI-ADALIMUMAB ANTIBODIES AT TIME OF ADALIMUMAB FAILURE FOR PREDICTION OF RESPONSE TO THE NEXT BDMARD

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Background: After adalimumab treatment failure, TNFi and non-TNFi bDMARDs are equally viable as subsequent treatment in RA. However, preliminary data suggest that anti-drug antibodies (ADA) and adalimumab serum levels (ADL) predict response to a subsequent TNFi [1].
Objectives: To assess the association of presence of ADA and/or low ADL with response to a subsequent TNFi bDMARD or non-TNFi bDMARD.
Methods: A retrospective cohort study to assess the predictive value of ADA and ADL for response to a subsequent TNFi or non-TNFi bDMARD in RA patients.
All RA patients who received adalimumab (standard dose, ≥ 3 months) and subsequently switched to another TNFi or a non-TNFi (rituximab, tocilizumab, abatacept) in the Sint Maartenskliniek or Radboud University Medical Centre between January 2012 and January 2018 were considered for inclusion in the current study. Further inclusion criteria were the availability of (random timed) serum samples between ≥8 weeks after start, and ≤2 weeks (for ADL) or ≤12 weeks (for ADA) after discontinuation of adalimumab, and clinical outcome measurements (DAS28-CRP/BSE) between 3-6 months after treatment switch. Serum samples were derived from a period of biobanking at every visit of RA patients and an observational cohort study including consecutive bDMARD starters.
The primary outcome of this study was the association between ADL or ADA and EULAR good response (DAS28-CRP/ESR based) to the subsequent bDMARD. When DAS28-based response was unreliable due to glucocorticoid use, or low baseline DAS28 (if switching due to adverse effects), judgement of the rheumatologist was used.
A drug-tolerant competitive enzyme-linked immunosorbent assay (Sanquin, the Netherlands) was used to quantify ADA, and thereafter, ADL was determined via an ELISA. Reference values were ≥5 µg/ml for ADL and <12 AU/ml for ADA [2,3]. Treatment was blinded for ADL and ADA levels.

Prediction of response were assessed using the area under the receiver-operator characteristic (AUROC) and sensitivity/specificity. Sub-analyses were performed for primary and secondary non-responders. Correlations between ADL and ADA presence and clinical variables were also cross-sectionally explored.

Results: 137 patients were included, 47 of whom switched to a second TNFi and 90 to a non-TNFi. Sensitivity and specificity of the proposed ADA and ADL reference values were low (table 1). The AUROC did not differ appreciably or significantly from 0.5. Results were similar for both primary and secondary non-responders to adalimumab.

Table 1. predictive values of ADA and ADL for response to a subsequent bDMARD in TNFi and non-TNFi switchers.

	sensitivity (%)	specificity (%)	AUC	CI
	TNFi switchers			
ADA presence (>12AU/mL)	18	75	0.46	0.32-0.59
low ADL (<5mg/L)	32	69	0.50	0.29-0.71
	non-TNFi switchers			
ADA presence (>12AU/mL)	33	70	0.52	0.42-0.63
low ADL (<5mg/L)	50	52	0.50	0.34-0.65

Higher ADL (Spearman's ρ = -0.68, p = 0.00) but not ADA (ρ = 0.23, p = 0.28) presence was associated with a lower DAS28 at the time of switching to a subsequent bDMARD, but not with follow-up DAS28 after starting the subsequent bDMARD (ρ = -0.29, p = 0.17, and ρ = 0.10, p = 0.65, respectively). In addition, higher ADL were associated with lower baseline CRP (ρ = – 0.67, p = 0.00) and ESR (ρ = – 0.546, p = 0.006) and higher ADA correlated with higher baseline ESR (ρ = 0.49, p = 0.01).

Conclusion: No predictive value for response to a second TNFi or non-TNFi was found for either ADA or random timed ADL. Limitations of this study are the retrospective design and random timed serum sampling. An ongoing randomized blinded test-treatment trial will provide more definitive answers [4].

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AB0187 ASSESSMENT OF ADHERENCE TO TREATMENT OF PATIENTS WITH RHEUMATOID ARTHRITIS (RA)

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Background: Rheumatoid arthritis (RA) is the most common chronic immune inflammatory disease. The effectiveness of RA therapy largely depends on adherence to treatment. Non-compliance with the recommendations of the doctor leads to increased disease activity, a greater risk of complications and the increase in the cost of treatment.

Objectives: To determine predictors of adherence to treatment of patients with RA.

Methods: The study included 82 women with reliable RA according to the criteria of ACR1987 and / or EULAR / ACR2010 (mean age 53.3 ± 10.2 years, the age at the onset of the disease is 42.4 [36;51] years, mean duration of RA - 10.8 [6;14] years, DAS28 - 5.03 [4.3;5.8]). Treatment adherence was assessed according to the questionnaire "Quantitative Evaluation of Adherence to Treatment (KOP - 25)" [1]. The following indicators were calculated: adherence to drug therapy, adherence to medical support, adherence to lifestyle modification and their integral index. For all indicators, the level of values in the range up to 50% is interpreted as "low" («non-adherence to treatment»), from 51 to 75% - as "medium", more than 75% - as "high"(«adherence to treatment»). The functional ability of patients was assessed by the Health Assessment Questionnaire (HAQ). The severity of pain was determined by VAS. Statistical processing was performing using the program STATISTICA 10.0.

Results: Adherence to drug therapy in women with RA was determined: low adherence in 32 (39%) patients, average in 34 (41.5%) patients and high in 16 (19.5%) patients; adherence to medical support: low in 26 (31.7%) patients, average in 40 (48.8%) patients, and high in 16 (19.5%) patients; adherence to lifestyle modification: low in 55 (67%) patients, average in 25 (30.5%) patients and high in 2 (2.5%) patients. According to the integral indicator of adherence to treatment, 34 (41.5%) patients were not adherent to treatment, average adherence was recorded in 42 (51.2%) patients, and high in 6 (7.3%) patients.

The HAQ functional impairment was absent in 7 (8.5%) patients, minimal impairment occurred in 26 (31.7%), moderate - in 40 (48.8%) and severe - in 9 (11%) patients.

Severe pain in the VAS was noted by 29 (35.4%) patients, moderate - 39 (47.6%), in 14 (17%) patients the pain syndrome was weakly expressed.

The relationships of adherence to treatment was established with age (r = -0.29, p <0.05), age at the onset of the disease (r = -0.28, p <0.05), HAQ index (r = -0.27, p <0.05), the number of swollen joints (r = -0.3, p <0.05).

Patients under age of 39 years were the most adherence to drug therapy.

In patients with medium and high adhering to treatment, the severity of pain according to VAS was significantly lower than in non-adherent patients (50.6 [34;66] and 60.4 [46;73], respectively, p = 0.04), In patients with treatment adherence, activity was significantly lower than in non-treatment adherents (DAS 28 (4.7 [3.5;5.4] and 5.3 [4.7;5.9], respectively, p = 0.04).

Conclusion: Low treatment adherence has 41,5% of RA patients. Predictors of adherence to treatment are the young age patients, the onset of the disease before age of 39 years. Non-treatment patients with RA have a higher activity of RA according to DAS28, pain intensity according to VAS, the worst functional status. To increase the effectiveness of treatment, constant interaction between the patient and the physician is necessary, explaining to patients the consequences of non-compliance with recommendations.

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AB0188 COMPARISON OF COMPOSITE INDICES FOR DETECTING REMISSION ON ULTRASOUND

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Background: Several studies have shown the greater sensitivity of ultrasound (US) to detect B-mode synovitis and synovial Doppler activity in a high percentage of rheumatoid Arthritis (RA) patients in clinical remission, assessed by different composite indices.

Objectives: The aim of the study was to compare the accuracy of composite indices to detect remission in ultrasound B-mode and power Doppler (PD) in RA patients that are in remission according to the DAS28 ESR.

Methods: Cross-sectional study including patients with RA in clinical remission defined by: DAS28ESR ≤ 2.6, without disease flare or changes in therapy in the previous 6 months. Each patient underwent B-mode and PD assessments of 36 joints and 20 tendons in the Rheumatology Department over a period of 6 month. B-mode and PD signal for synovitis and tenosynovitis were defined according to the Outcome Measures in Rheumatology Clinical Trials (OMERACT). A global score for B-mode and a global score for PD signal were calculated for each patient. The DAS28, CDAI, SDAI and the Boolean 2010 ACR/EULAR remission criteria were compared.

Results: Thirty two patients were enrolled, the mean age was 53.7±13.4 and the sex ratio M/F was 0.3. The mean disease duration was 15.0 years ± 8.8. According to the SDAI, 68.8% of patients were in remission. These were lower for the CDAI (62.5%) and the Boolean criteria (23.3%). Synovial hypertrophy and tenosynovitis in B mode was detected in 100% with the Boolean remission criteria, in 93.8% with a DAS28, in 90.9% with a SDAI ≤ 3.3 and in 90% with a CDAI ≤ 2.8 (p>0.05). The PD signal was detected in 62.5% with a DAS28, in 59.1% with a SDAI ≤ 3.3, in 57.1% with the Boolean remission criteria and in 55.1% with a CDAI≤ 2.8 (p>0.05). The mean B-mode global score was higher for the DAS28 ESR (8.2±6) and lower for the Boolean remission criteria (6.2 ±5.4). For a CDAI ≤ 2.8, the mean global score for B-mode was 7.6 ±5.9 and for a SDAI ≤ 3.3, it was 7.4±5.7. The median PD global score was similar for the DAS28, SDAI≤ 3.3 and Boolean remission criteria (1[0-12]). It was higher for a CDAI ≤ 2.8 (1.5 [0-12]). The global score for PD signal was correlated with DAS28 ESR (r: 0.42 p: 0.02). There were no significant correlations between the other indices and the mode B and PD global scores.

Conclusion: The CDAI least detected subclinical synovitis and tenosynovitis in B mode and in power Doppler signal but it showed higher scores of power Doppler.

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AB0189 ASSESSMENT OF POWER DOPPLER SYNOVITIS IN RHEUMATOID ARTHRITIS PATIENTS WITH CLINICAL REMISSION

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Background: Ultrasound-detected synovitis, mainly synovial Doppler signal, has shown predictive value in relation to radiographic damage progression and disease flare or relapse in rheumatoid arthritis (RA) patients with clinical remission.
Objectives: The aim of the study was to analyze the correlation between power Doppler scores and clinical/laboratory and radiographic data in clinical remission RA patients.
Methods: Cross-sectional study including patients with RA in clinical remission defined by: DAS28ESR ≤ 2.6, without disease flare or changes in therapy in the previous 6 months. Each patient underwent ultrasound: B-mode and PD assessments of 36 joints and 20 tendons in the Rheumatology Department over a period of 6 month. Synovitis and tenosynovitis were defined and scored according to the Outcome Measures in Rheumatology Clinical Trials (OMERACT). Radiological measurements included the modified Sharp/van der Heijde method (SHS). Functional capacity was assessed by the Health Assessment Questionnaire (HAQ).
Results: Thirty two patients were enrolled, the mean age was 53.7±13.4 and 75% were female. The mean disease duration was 15 years ± 8.8. Subclinical synovitis were the most frequent in wrist (56.3%), 2nd metacarpophalangeal joints (28.1%) and 2nd metatarsophalangeal joints (29%). The mean subclinical synovitis/ tenosynovitis numbers was 4±3.1 per patient. Synovial hypertrophy and B mode tenosynovitis were detected in 93.8%: 71.3% had a grade = 2 and 9.8% had a grade= 3. Total B mode score was correlated only with the SHS score in the feet (r: 0.4, p: 0.03). PD signal was detected in 62.5% of patients: 37.5% had a grade =2 and 9.4% had a grade= 3. Total PD score was correlated with DAS28 (r:0.42, p:0.02), the SHS score in the hands (r:0.39, p:0.03) and in the feet (r:0.5, p:0.007), synovial hypertrophy (r:0.6, p:0.0001) and HAQ (r:0.32, p:0.06). No correlation was found with CDAI, SDAI, swollen joint counts, tender joint counts, patient global health assessment, erythrocyte sedimentation rate, C-reactive protein, rheumatoid factor and anti-cyclic citrullinated peptide, biologic treatment.
Conclusion: Synovial hypertrophy and PD signal were frequent in RA remission. PD signal was associated with RA activity, radiologic damage and functional capacity.
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AB0190 DO IT FAST! EARLY ASSESSMENT BY A RHEUMATOLOGIST INCREASES THE CHANCES OF RHEUMATOID ARTHRITIS BEING TREATED WITHIN THE "WINDOW OF OPPORTUNITY"

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Background: The current concept of treating rheumatoid arthritis RA patients emphasizes the importance of early diagnosis and early initiation of disease-modifying drugs (DMARD) for a better prognosis of these patients.
Objectives: To evaluate the impact of rheumatologic evaluation on the diagnosis of RA patients, as well as on the initiation of DMARD and on the clinical control of disease activity of these patients under real-life conditions.
Methods: The REAL study included RA patients attending eleven public hospitals, from different regions of Brazil. All subjects met the ARA (1987) or ACR/EULAR (2010) RA classification criteria. Subjects were submitted to clinical interview with physical exam and review of medical records. Specialized assessment was defined as sequentially "early", when the rheumatologist was the 1st or 2nd consulted physician, and sequentially "late", when the rheumatologist was consulted after two or more other doctors. Welch's *t*, Mann-Whitney's U, chi-square and Spearman's rho tests were used to test hypotheses, at significance level of 0.05. The study was approved by local ethics committees and all participants granted informed consent.
Results: 1057 RA patients were assessed; 89.4% (n=945) female; 56.5% (n=597) white; mean (SD) age of 56.9 (11.5) years; mean (SD) disease duration of 173.1 (114.5) months. Median [IQR] delay from symptoms onset to RA diagnosis and to the first DMARD both equaled 12 [6, 36] months. Only 28.7% received a DMARD within 6 months of symptoms onset, and 13.1% within 3 months. Most patients (64.6%) sought a general practitioner first, but 80.7% were finally diagnosed only upon rheumatologist consultation. For 28.8%, the rheumatologist was consulted after two or more other doctors. Early specialized assessment resulted in higher chances of receiving a DMARD within 6 months (OR 2.77; 95%CI [1.93, 3.97]) and within 3 months (OR 2.57; 95%CI [1.54, 4.27]) of RA onset. Late assessment was associated with lower chances of being in remission or low disease activity upon study inclusion (OR 0.53; 95%CI [0.39, 0.72]). Patients assessed early by the rheumatologist, compared to those assessed late, showed lower (mean [SD]) HAQ scores (0.877 [0.715] vs. 1.074 [0.857]; p<0.001) and DAS28-CRP scores (3.20 [1.32] vs. 3.45 [1.48]; p=0.02), and shorter delays to RA diagnosis (26.9 [46.7] vs. 44.6 [60.1] months; p<0.001) and to use the first DMARD (32.5 [58.5] vs. 50.6 [69.9] months; p<0.001). The delay to initiate a DMARD was strongly correlated to that of diagnosing RA (rho 0.816; p < 0.001).
Conclusion: Most RA patients missed the window of opportunity to early treatment. Treatment delay strongly correlated with delay in diagnosis, which critically depended on the input from the rheumatologist. Late rheumatologist assessment was associated with lower chances of early RA treatment and with worse outcomes. Failure in direct transition from primary to specialized care was a common problem that needs to be solved.
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Pfizer, Bristol-Myers Squibb, UCB, Eli-Lilly, AbbVie, Abbott and EMS, Consultant of: Has received consulting fees, speaking fees and supporting for internationals congresses from Roche, Pfizer, Bristol-Myers Squibb, UCB, Eli-Lilly, AbbVie, Abbott and EMS, Paid instructor for: Has received consulting fees, speaking fees and supporting for internationals congresses from Roche, Pfizer, Bristol-Myers Squibb, UCB, Eli-Lilly, AbbVie, Abbott and EMS, Speakers bureau: Has received consulting fees, speaking fees and supporting for internationals congresses from Roche, Pfizer, Bristol-Myers Squibb, UCB, Eli-Lilly, AbbVie, Abbott and EMS, Sebastião Radominsky Grant/research support from: Has received consulting and speaking fees from Abbvie, Janssen, Pfizer, Roche and UCB, Consultant of: Has received consulting and speaking fees from Abbvie, Janssen, Pfizer, Roche and UCB, Paid instructor for: Has received consulting and speaking fees from Abbvie, Janssen, Pfizer, Roche and UCB, Speakers bureau: Has received consulting and speaking fees from Abbvie, Janssen, Pfizer, Roche and UCB, Licia Mota Grant/research support from: Has received personal or institutional support from AbbVie, Janssen, Pfizer and Roche; has delivered speeches at events related to this work and sponsored by AbbVie, Janssen, Pfizer, Roche and UCB., Speakers bureau: Has received personal or institutional support from AbbVie, Janssen, Pfizer and Roche; has delivered speeches at events related to this work and sponsored by AbbVie, Janssen, Pfizer, Roche and UCB., Geraldo Castelar-Pinheiro Grant/research support from: Has received consulting fees from AbbVie, Bristol-Myers Squibb, Eli Lilly, Glaxosmithkline, Janssen, Pfizer, Sanofi Genzyme and Roche, Consultant of: Has received consulting fees from AbbVie, Bristol-Myers Squibb, Eli Lilly, Glaxosmithkline, Janssen, Pfizer, Sanofi Genzyme and Roche, Speakers bureau: Has received consulting fees from AbbVie, Bristol-Myers Squibb, Eli Lilly, Glaxosmithkline, Janssen, Pfizer, Sanofi Genzyme and Roche

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AB0191

DECREASING DELAY TO DIAGNOSIS AND TREATMENT OF RHEUMATOID ARTHRITIS: STILL DIFFICULT TO TREAT WITHIN THE WINDOW OF OPPORTUNITY

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Background: The need for early rheumatoid arthritis (RA) treatment for better outcomes is widely accepted. Is that goal being achieved in real-life settings?

Objectives: To evaluate changes in the delay to RA diagnosis and treatment, and in the proportions of patients being treated early along the last decades in Brazil.

Methods: This study was drawn from the REAL cohort, designed to assess RA management under real-life conditions. Patients ≥ 18 years old attending public hospitals in Brazil and meeting RA classification criteria were included. Subjects were stratified according to the year their symptoms began. Delays from symptoms onset to RA diagnosis and treatment were inquired. Early RA diagnosis and treatment was assessed using three different cut points: ≤3, ≤6 and ≤12 months of symptoms onset. Mann-Kendall's trend test, chi-square tests, Welch's ANOVA and Games-Howell's post-hoc tests were used to test hypotheses, at 0.05 significance level.

Results: 1116 RA patients were included; 89.4% female; 56.8% white; mean (SD) age 57.1 (11.5) years. A downward trend was found in the delay to RA diagnosis (tau = -0.677, $p < 0.001$) and treatment (tau = -0.695, $p < 0.001$) from 1990 to 2015 (Figures 1 and 2). The year of symptoms onset was associated with the frequency of early treatment for all defined cut points: ≤3 months ($\chi^2 = 11.25$, $p = 0.001$), ≤6 months ($\chi^2 = 34.84$, $p < 0.001$), and ≤12 months ($\chi^2 = 64.79$, $p<0.001$). The more recent the year of symptoms onset, the higher the proportions of individuals treated early (Table 1). Groups stratified according to successive periods of symptoms onset differed in the mean delay to RA treatment [$F(5, 372.8) = 41.9$; $p < 0.001$]. Patients with symptoms initiated more recently (2011-2015) had significantly lower delays compared to all other groups. Nonetheless, only 36.3% of these patients with more recent disease started treatment within 6 months of symptoms onset, and 17.2% within 3 months.

Table 1. Proportions of individuals with RA receiving the first DMARD within different time intervals from symptoms onset, according to the year their symptoms began.

Symptoms beginning (year)	Interval from symptoms onset to first DMARD			N
	≤ 3 months	≤ 6 months	≤ 12 months	
≤ 1990	8.5%	14.9%	33.3%	141
1991 – 1995	5.3%	15.8%	34.7%	95
1996 – 2000	12.3%	24.7%	44.5%	146
2001 – 2005	11.5%	26.3%	49.8%	217
2006 – 2010	17.2%	38.9%	61.1%	239
2011 – 2015	17.2%	36.3%	72.0%	157

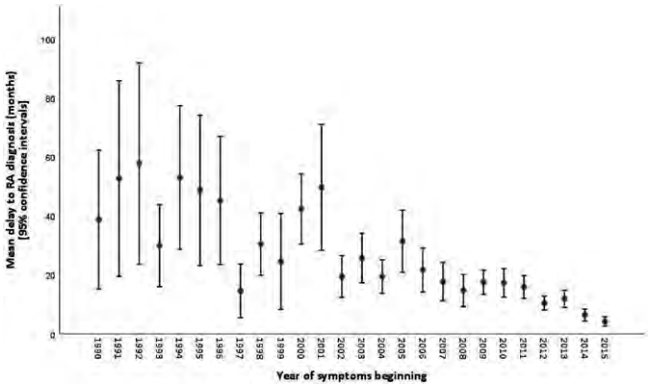


Figure 1. Rheumatoid arthritis diagnostic delay according to the year of symptoms beginning, from 1990 to 2015 in Brazil

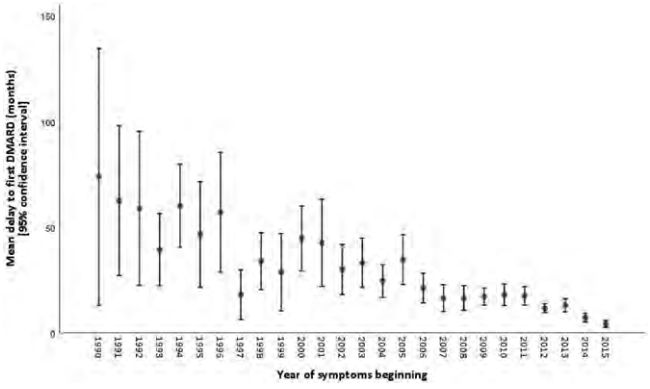


Figure 2. Rheumatoid arthritis treatment delay according to the year of symptoms beginning, from 1990 to 2015 in Brazil.

Conclusion: Delays to RA diagnosis and treatment have decreased, and more patients have been treated within defined windows for early RA management in the last decades in Brazil. Despite all improvements, it was still difficult to attain early RA treatment. Additional efforts are warranted in pursuit of that goal.

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AB0192 RHEUMATOID ARTHRITIS: IS IT WORTH IT TO ADD LEFLUNOMIDE TO METHOTREXATE IN REFRACTORY DISEASE?

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Background: In refractory rheumatoid arthritis (RA), adding other classic synthetic disease-modifying antirheumatic drug (csDMARD) such as leflunomide (LFN) to methotrexate (MTX) is one suitable option [1,2]. Yet, there are safety issues to consider which may limit this strategy, but also regarding its true effectiveness in avoiding exposure to biological DMARDs (bDMARD) or target synthetic DMARDs (tsDMARD).

Objectives: To assess the effectiveness and safety of adding LFN to MTX and to evaluate the predictors of drug retention, toxicity and inefficacy.

Methods: A retrospective clinical record review of adult RA patients followed on our rheumatology department in whom LFN was added to MTX was done. Sociodemographic information, comorbidities, disease related information, adverse reactions and disease activity according to Disease Activity Score 28 – C reactive protein (DAS28) were recorded at baseline and after 3, 6 and 12 months of combination therapy (3_DAS28; 6_DAS28; 12_DAS28, respectively). Information regarding toxicity (need to dose adjustment/suspension) and inefficacy (add/switch to bDMARD/tsDMARD) were recorded. Follow-up was considered until last medical record available. SPSS was used for statistical analysis. Kaplan Meier and Cox-regression were used for univariate and multivariate analysis, respectively, significant level was 2-sided $p<.05$.

Results: In total, 77 patients were included, 66.20% females, with a mean age of 56±11 years old. There was a significant reduction of DAS28 only after 3 months of therapy (4.01±1.01 to 2.57±1.52, $p=.003$; ΔDAS28 = 1.58±1.17). However, during a median follow up time of 64 (IQR 39-83) months, 58.44% of patients needed to change treatment strategy, 66.67% due to toxicity (median time to toxicity 13 months, IQR 2-16) and 33.33% due to inefficacy (median time to inefficacy of 10 months, IQR 5.84-17.64). Gastrointestinal intolerance was the main reported toxicity (46.15%). In univariate analysis, anti-citrullinated protein antibodies (ACPA) positivity, alcohol consumption, lack of comorbidities, hepatic toxicity, higher 6_DAS28, swollen joint count and tender joint count on the 6th month were associated to lower retention rates.

In multivariate analysis, lack of comorbidities (HR=3.3, CI 95% 1.4-7.8, $p=.006$) and higher 6_DAS28 (HR=0.32, CI 95% 0.14-0.72, $p=.006$) were independent predictors of suspension of combination therapy. Moreover, both male gender (HR=2.87, 95%CI 1.2-6.56, $p=.016$) and positivity to ACPA (HR=0.1, 95%CI 0.01-0.73, $p=.024$) were independent predictors of toxicity. There was also higher tendency to toxicity, but without statistical significance, in alcohol consumers ($p=.08$). Regarding inefficacy, smoking habits (HR=0.15, 95%CI 0.04-0.52) and 3_DAS28 (HR=0.15, 95%CI 0.04-0.53) were independent predictors.

Conclusion: Addition of LFN to MTX showed an early positive response. However, it was frequently associated to toxicity, and less than half of the patients continued with this therapeutic strategy after 5 years of follow up. Male gender, smoking habits and positivity to ACPA were predictors of worse outcome, as already reported in literature [1]. Lack of comorbidities was an independent predictor of suspension. This can be explained by the fact that physicians tend to adopt a more aggressive strategy on patients without comorbidities, switching earlier to bDMARDs/tsDMARDs.

This study also showed that early response to combination therapy is an independent predictor on drug retention, suggesting that decisions on treatment strategy should be made early after the beginning of MTX/LFN.

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AB0193 ROLE OF DICKKOPF-1 IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is characterized by persistent synovitis that leads to structural joint damage causing deformity and disability. Dickkopf-1(DKK-1) was shown to be a major regulator of joint remodeling, which is associated with subchondral bone erosion in RA. Dickkopf-1 is a secreted glycoprotein that also acts as a potent negative regulator of wingless signaling. Current therapies used to treat RA are not able to effectively repair damaged bone. There is a strong relationship between Wnt signaling pathway, RA and DKK-1 so; this relationship may be a therapeutic point of interest

Objectives: To assess the correlation between Dickkopf-1 and RA disease activity, disability, severity and functional status.

Methods: Fifty patients fulfilled the 2010 ACR -EULAR criteria for RA were included. Twenty five healthy age and sex matched individuals served as a control (for assessment of serum DKK-1 level). Excluded from the study, patients with Paget disease, Multiple myeloma, Breast cancer, Bone metastasis, Diabetes mellitus, Hyperthyroidism, patients on medication that influence bone metabolism as: heparin, anticonvulsant or thyroxin.

All patients were subjected to full history and examination. Disease activity measures as disease activity score (DAS 28-ESR), Visual analogue scale (VAS) and Disease disability indices including ACR criteria of functional status in RA and Health assessment questionnaire disability index (HAQ-DI). Erythrocyte sedimentation rate (ESR), C-Reactive protein (CRP), Rheumatoid factor (RF), Anti citrullinated peptide antibody (ACPA) and Serum dickkopf-1 level. Simple erosion narrowing score (SENS) and Ultrasound DAS (US DAS) were done

for all patients. Ultrasound DAS included 28 joints, Power Doppler ultrasound (PDUS) examination of 22 joints and gray scale ultrasound (GSUS) examination for Effusion/Hypertrophy (E/H) of 28 joints. Ultrasound erosion count (USEC) and Ultrasound erosion rate (USER) were assessed.

Results: Dickkopf-1 level in RA patients ranged from 66 to 453 ng/ml while in the control group ranged from 15 to 87 ng/ml with statistically significant difference. RA patients were grouped in to: group 1 included 15 (30%) patients with normal DKK-1 level and group 2: included 35 (70%) patients with elevated DKK-1. The differences between both groups were highly significant regarding clinical and laboratory measures (duration of morning stiffness, DAS 28, VAS, ESR, CRP, RF and ACPA), and regarding HAQ-DI, SENS and US DAS. We found significant positive correlation between DKK-1 level and laboratory measures (ESR, CRP, RF, ACPA), radiographic parameters (SENS and erosion score), ultrasonographic parameters (US DAS, USEC and USER) and with HAQ-DI and functional status.

Conclusion: Serum level of dickkopf-1 was elevated in RA patients and the results demonstrated the relationship between increased dickkopf-1 level and increased disease activity, decreased functional capacity and chronic structural damage suggesting its important role in the pathogenesis of RA.

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AB0194

VITAMIN D TRAJECTORIES IN EARLY DIAGNOSED, AGGRESSIVELY TREATED RHEUMATOID ARTHRITIS PATIENTS: A 10 YEAR LONGITUDINAL COHORT STUDY BASED ON THE DANISH CIMESTRA TRIAL

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Background: Low vitamin D levels are common in Rheumatoid Arthritis (RA)[1], and possibly associated with disease course,[2] but data on vitamin D levels during long-term disease course has not been reported previously.

Objectives: To describe vitamin D trajectories from time of diagnosis through 10 years follow-up in early diagnosed RA patients.

Methods: The CIMESTRA trial included 160 newly diagnosed RA-patients, treated aiming at remission with methotrexate and intraarticular steroid, further randomized to ciclosporine or placebo. Vitamin D supplementation was recommended according to national guidelines. Vitamin D_{total} was measured at diagnosis, and year 1, 5 and 10 using LC-MS/MS. $1,25(OH)_2D$ was measured at diagnosis and year 1 using RIA. Linear mixed effects models were used to study vitamin D levels serially. We had fixed effects for time, and patients modelled as a random effect. We tested the hypothesis that percentage of patients achieving $D_{total} \geq 50$ nmol/l during follow-up was 90%. Analyses of associations between D_{total} and DAS28-CRP during the disease-course were adjusted for age, sex, symptom-duration prior to diagnosis and season of diagnosis.

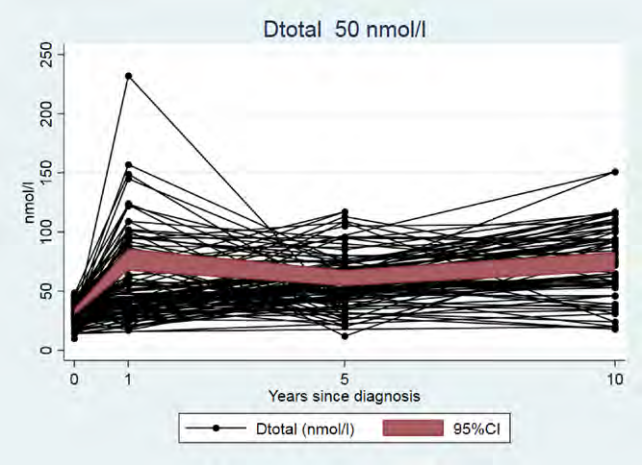
Results: Median D_{total} at baseline was 53 nmol/l (IQR 36-567.8). D_{total} increased significantly during follow-up, independently of level at diagnosis ($p<0.001$). Individuals achieving $D_{total} \geq 50$nmol/l during follow-up was 80-87%, but not as high as 90% at year 1 and 5, $p<0.002$. DAS28-CRP during disease-course was inversely associated with D_{total} trajectories only in crude (β-coefficient (β) -0.0034, 95%CI (-0.007; -0.0002) p=0.039) and partially adjusted analyses (β -0.003, 95%CI (-0.007; -0.002) p=0.04). Estimate was left insignificant in fully adjusted analyses (β -0.003, 95%CI (-0.0006; 0.0001) p=0.06). $1,25(OH)_2D$ levels did not change significantly during follow-up (p=1.00).

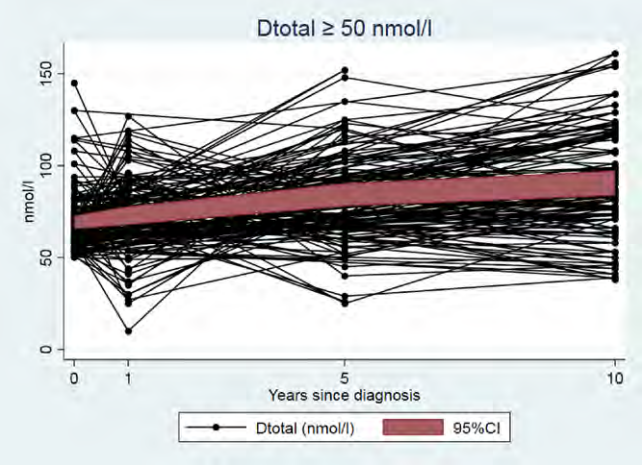
Conclusion: D_{total} increased significantly during follow-up, but fewer than 90% achieved the recommended 50 nmol/l at year 1 and 5. Disease activity during follow-up was associated with D_{total} trajectories only in partially adjusted analyses, while adjustment for possible confounders left estimates insignificant. Results suggest vitamin D supplementation to be recommended in all RA patients.

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AB0195

FACTORS RELATED TO RADIOGRAPHIC PROGRESSION IN PATIENTS WITH RHEUMATOID ARTHRITIS-RELATED INTERSTITIAL LUNG DISEASE

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Background: Interstitial lung disease is an important cause of mortality and morbidity for RA. Lung computerized tomography (CT) is a valid method for the detection of interstitial lung disease (ILD) in rheumatoid arthritis (RA) patients. Besides, CT may have a role in the detection of progression in RA-ILD.

Objectives: To compare the clinical and radiological features of RA-ILD patients with and without radiographic progression according to lung CT.

Methods: From the hospital database, all patients recorded as having RA according to ICD-10 code and had a lung CT examination were recruited. RA was confirmed in 822 of 2305 (35.6%) records. Three radiologists re-evaluated lung CTs and 156/822 (18.9%) patients with had RA-ILD. Of these 156 patients, 101 (64.7%) had at least 1 follow-up long CT and these patients were included to analysis. Demographic and clinical data of the patients were recorded. ILD was divided into 3 main groups by radiologists: Usual interstitial pneumonia (UIP), non-specific interstitial pneumonia (NSIP) and airway disease (AD) (bronchiectasis and/or bronchiolitis without parenchymal involvement). Avila et al reported a grading system to assess the severity of ILD using HRCT (1). In our study we utilized a similar method using interlobular septal thickening, ground glass opacities, reticulations, traction bronchiectasis and honeycomb appearance as elementary findings to evaluate the RA associated ILD. Septal thickening, reticulations and ground glass opacities were considered as relatively mild features whereas traction bronchiectasis and honey comb appearance were considered as severe findings as those frequently result from advanced fibrosis. The lungs were divided into upper, middle and lower zones each with equal number of slices. Progression was defined as involvement of more zones in vertical extent by the same elementary findings or emergence of more severe findings (i.e traction bronchiectasis or honey comb appearance) in the same zones compared to previous exam. For the multivariate analysis, the possible factors identified with univariate analyses were further entered into the logistic regression analysis to determine independent predictors of radiographic progression.

Table. Comparison of demographic, clinical and radiographic characteristics of patients with and without radiographic progression

	Radiographic Progression (+)	Radiographic Progression (-)	p
n (%)	42 (41.5)	59 (59.5)	
Male n (%)	19 (45.2)	15 (25.4)	**0.038**
Age at RA diagnosis [year] (SD)	57.0 (11.0)	54.5 (11.2)	0.25
Age at ILD diagnosis [year] (SD)	62.3 (8.0)	61 (9.0)	0.63
Elapsed time between RA and ILD [year] (SD)	4.3 (6.9)	6.1 (7.2)	0.22
RA disease duration [year] (SD)	10.4 (7.5)	11.8 (7.8)	0.77
ILD disease duration [year] (SD)	5.7 (3.5)	5.4 (3.8)	0.67
Smoking (current or ever) n (%)	21/36 (58.3)	27/52 (51.9)	0.55
Rheumatoid factor (+) n (%)	37/40 (92.5)	55/58 (94.8)	0.64
Anti-CCP (+) n (%)	14/22 (63.6)	28/37 (75.7)	0.32
Dyspnea n (%)	21 (53.8)	22 (41.5)	0.24
ILD patern			
- UIP	30/42	30/59	0.12
- NSIP	9/42	22/59	
- AD	3/42	7/59	
ILD at lung X-Ray n (%)	36/40 (90.0)	33/49 (67.3)	**0.011**
Rheumatoid Lung Nodule n (%)	20 (47.6)	26 (44.8)	0.78
CT findings			
- Ground Glass Opacities, n (%)	40 (95.2)	44 (74.6)	**0.006**
- Bronchiectasis, n (%)	29 (69.0)	40 (67.8)	0.89
- Reticular densities, n (%)	37 (88.1)	46 (78.0)	0.19
- Interseptal thickening, n (%)	18 (43.9)	20 (33.9)	0.31
- Honeycombing, n (%)	26 (62.0)	24 (46.1)	**0.03**
Treatment			
- Methotrexate (ever), n (%)	25 (59.5)	49 (83.1)	**0.008**
- Leflunomide (ever), n (%)	29 (69.0)	49 (83.1)	**0.10**
- Biologic DMARD (ever) n (%)	18 (43.0)	25 (42.4)	0.98
- Anti TNF (ever) n (%)	11 (26.2)	13 (22.0)	0.62
- Rituximab (ever) n (%)	13 (31.0)	12 (20.3)	0.22
Death n (%)	15 (35.7)	12 (20.3)	0.085

Results: In this study, 101 patients with 215 lung CT were included to analysis. 67 (66.3%) patients had 3 CTs, 30 (29.9%) patients 4 CTs and 17 (16.9%) patients had 5 CTs. Mean duration between first and last CT was 47.7±38.8 months. Of 101 patients, radiographic progression was seen in 42 (41.6%) patients. Univariate comparison of demographic, clinical and radiographic features of patients with or without radiographic progression were given in Table. In multivariate analysis (adjusted for ILD disease duration) *having ground-glass opacity* (aOR 8.6; CI: 1.65-44.9; p=0.011), *male gender* (aOR 2.9; CI: 1.13-7.4; p=0.026) were found as independent risk factors radiographic progression, while *taking methotrexate (ever)* (aOR 0.21; CI: 0.07-0.6; p=0.04) was found as an independent protector factor for radiographic progression.

Conclusion: The prediction of ILD progression in RA patients were a challenge for clinicians. According to lung CT, baseline ground-glass opacities looks like prominent factor for ILD progression, particularly at male RA patients. Using methotrexate in ILD patients is a dilemma in routine practice, our results demonstrate that methotrexate (not other cs or bDMARDs) is protective drugs for ILD progression, however these results should be confirmed in the further studies.

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AB0196

THE ASSOCIATION BETWEEN OSTEOPOROSIS AND FUNCTIONAL IMPAIRMENT EVALUATED BY THE LOCOMO25 IN RHEUMATOID ARTHRITIS

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Background: Locomotive syndrome is a condition in which activities of daily living are affected by impairment of the motor organs, most often due to rheumatoid arthritis (RA). Locomo25 is a new index developed for the early detection of locomotive syndrome. It consists of 25 items associated with pain, physical activity, and subjective state of health, with a score of 7 points or higher classed as Grade 1 locomotive syndrome and a score of 16 points or higher as Grade 2. In RA, joint impairment causes the appearance of problems affecting motor organs as a whole, as well as progressive functional impairment. As functional impairment progresses, it causes increasing immobility, which raises the risk of osteoporosis.

Objectives: Locomo25 was used to investigate functional impairment and its association with RA disease activity and osteoporosis indicators.

Methods: The subjects were 105 patients with RA (24 men and 81 women) with a mean age of 68.7 (28–91) years. In terms of staging, 25 were Stage I, 22 Stage II, 17 Stage III, and 41 Stage IV, and their motor disability was Steinbrocker Class 1 in 68 cases, Class 2 in 27, Class 3 in 9, and Class 4 in 1. Disease activity according to the Disease Activity Score 28 with erythrocyte sedimentation rate (DAS28 ESR) was assessed as remission in 44 cases, low disease activity in 24, moderate in 33, and high in 4. The associations between the Locomo25 score and disease activity indices, bone mineral density (BMD), and bone turnover markers (TRACP-5b, NTX, urinary DPD, BAP, total P1NP, and 25(OH)D) were investigated.

Results: Locomo25 grade was 0 in 37 cases (35.2%), 1 in 24 (22.9%), and 2 in 44 (41.9%). Locomo25 grade was significantly associated with Steinbrocker class (r = 0.4299, Spearman's rank correlation coefficient, p < 0.0001). DAS28 ESR and Health Assessment Questionnaire scores increased as locomotive syndrome progressed. There was no significant difference in eGFR between groups, but bone resorption markers (TRACP-5b, NTX, and urinary DPD) and a bone quality marker (pentosidine) decreased significantly as locomotive syndrome progressed. There were no significant differences in BMD or other bone turnover markers.

Conclusion: The Locomo25 score was useful for evaluating functional impairment in RA. The prevalence of Grade 2 locomotive syndrome in the general population is reported to be around 25%, and many patients with RA had advanced locomotive syndrome. Although there was no significant difference in BMD, elevated bone resorption and deteriorating bone quality were associated with progressive functional impairment, suggesting that RA patients with advanced locomotive syndrome may be at risk of increasingly severe osteoporosis as a result of immobility.

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AB0197 INCREASED CIRCULATING ADIPONECTIN IS AN INDEPENDENT DISEASE ACTIVITY MARKER IN PATIENTS WITH RHEUMATOID ARTHRITIS: A CROSS-SECTIONAL STUDY USING THE KURAMA DATABASE

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Background: Adiponectin is a major adipokine with pleiotropic effects on inflammatory conditions including rheumatoid arthritis (RA). Adiponectin generally has anti-atherogenic effects, and its serum level inversely correlates with body mass index (BMI) and visceral fat area (VFA). On the other hand, several studies have indicated a deleterious role of adiponectin in RA progression [1]. Recently, both low BMI and increased serum adiponectin have been reported as poor prognostic factors of RA [2, 3]. However, large-scale surveys have not been done focusing on both BMI and serum adiponectin, and it is unclear which factor provides further contribution to RA disease activity. In addition, the effects of biological disease-modifying antirheumatic drugs (bDMARDs) and Janus kinase (JAK) inhibitors on serum adiponectin are largely unknown.
Objectives: To clarify the relationship among serum adiponectin, body composition, current disease activity and therapeutic agents of RA.
Methods: We conducted a cross-sectional study in RA patients under treatment with agents including bDMARDs and JAK inhibitors. A total of 351 subjects from the Kyoto University RA Management Alliance cohort (KURAMA) were enrolled. We classified the participants into five body composition groups (overweight with or without visceral adiposity, normal with or without visceral adiposity, and underweight), according to the cut-off points for obesity and visceral fat used in Japan: BMI, 18.5 kg/m^2 for underweight and 25.0 kg/m^2 for obesity, and VFA, 100 cm^2 for visceral adiposity. Differences of continuous variables among the five groups were assessed by the Steel-Dwass test or one-way analysis of variance (ANOVA). We adopted a multiple standardized linear regression model to analyze effects of serum adiponectin level on DAS28-ESR.
Results: Serum adiponectin levels (20.9±12.5 vs. 14.7±8.4 μg/ml, $p < 0.001$) and DAS28-ESR (3.04±1.0 vs. 2.63±0.9, $p = 0.017$) in the underweight group were significantly higher than those in the others. In multiple regression analysis, serum adiponectin level, but not BMI, was positively correlated with DAS28-ESR (estimate = 0.0127, $p = 0.0258$). Subanalysis also showed that the use of bDMARD or JAK inhibitor did not have an obvious influence on circulating adiponectin.
Conclusion: In the multiple regression analysis we revealed a positive and independent correlation between serum adiponectin and DAS28-ESR in Japanese RA patients. Thus, serum adiponectin is an potential marker reflecting high disease activity of RA regardless of current medications.
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AB0198 SMOKING AND POSITIVITY OF RHEUMATOID FACTOR AND ANTI-CYCLIC CITRULLINATED PEPTIDE ANTIBODY IN THE GENERAL POPULATION

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Background: It is well known that rheumatoid arthritis (RA) occurs due to environmental risk factors in addition to genetic risk factors. Rheumatoid factor (RF) and anti-cyclic citrullinated peptide antibody (ACPA) are strongly associated with RA, and these biomarkers could turn to be positive before development of clinical symptoms. While smoking, particularly Brinkman index (BI) is well known as a risk factor for RA and ACPA positivity, it is still unclear whether smoking intensity or smoking duration contribute more to positive RF and ACPA.
Objectives: This study aims to evaluate risk factors for RF and ACPA positivity in the general population. It also describes whether smoking intensity, duration, and BI are significant.
Methods: This is a cross-sectional, observational, single center study. We reviewed the baseline characteristics of the general population who checked RF and ACPA at Preventive Medicine Center in St. Luke's International Hospital, Tokyo, Japan from January 2004 to December 2018.
The data for basic demographics, dietary habit, smoking intensity, smoking duration, BI, and blood tests including RF and ACPA were extracted. The data was analyzed statistically.
Results: A total of 127472 people who checked RF are included. Of these 127472 people, 64504 (50.6%) are male and the mean age was 44.9 years. RF was positive in 11477 people (9.0%). Among these, 1667 (1.2%) were checked for ACPA, and 21 people (1.3%) had positive ACPA. None of variables demonstrated significant association with RF positivity. In contrast, BI and smoking duration was significantly associated with an increased risk of ACPA positivity (13.3 years vs 7.49 years, p value = 0.023), although the number of cigarettes smoked was not. The smoking duration for 10 years or more was associated with an increased risk of ACPA positivity even after adjusted for age and sex (adjusted hazard ratio: 2.47 [95% confidence interval: 1.04-5.87]; p=0.04).
Conclusion: In this study, no significant risk factor for positive RF was found. Even smoking was not associated with RF positivity. On the other hand, smoking duration, not smoking intensity was significantly associated with an increased risk of ACPA positivity.
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Table 1. Patient characteristics with RF and ACPA positivity

	RF positive (n=11477)	RF negative (n=115995)	p value	ACPA positive (n=21)	ACPA negative (n=1646)	p value
Age	44.86 (12.32)	44.94 (12.47)	0.54	37.90 (9.07)	45.26 (12.58)	0.008
Male (%)	5659 (49.3)	57309 (49.4)	0.845	11 (52.4)	834 (50.7)	1
Body Mass Index	22.33 (3.38)	22.35 (3.40)	0.521	21.64 (3.28)	22.34 (3.37)	0.346
Smoker, total (%)	4509 (39.3)	45738 (39.4)	0.772	12 (57.1)	642 (39.0)	0.115
Current smoker (%)	1959 (17.1)	20483 (17.7)	0.114	8 (38.1)	277 (16.8)	0.017
Previous smoker (%)	2550 (22.2)	25255 (21.8)	0.271	4 (19.0)	365 (22.2)	1
Brinkman index	144.8 (299.3)	145.2 (313.8)	0.897	280.9 (409.7)	145.3 (300.3)	0.041
Number of cigarettes (/day)	17.7 (18.5)	17.4 (13.3)	0.166	19.8 (12.0)	17.4 (12.1)	0.511
Smoking Duration (years)	7.43 (11.68)	7.45 (11.66)	0.851	13.33 (14.11)	7.49 (11.68)	0.023
Alcohol Drinker (%)	6972 (60.7)	70010 (60.4)	0.418	10 (47.6)	1005 (61.1)	0.261
Alcohol Intake (g/day)	13.67 (21.88)	13.58 (21.32)	0.676	16.70 (26.89)	14.06 (22.16)	0.59
Exercise ≥3 times/week (%)	2792 (24.3)	28293 (24.4)	0.882	5 (23.8)	402 (24.4)	1
White blood cell (103/μL)	5.32 (1.46)	5.35 (1.50)	0.13	5.59 (2.05)	5.37 (1.54)	0.52
Hemoglobin (g/dL)	13.82 (1.44)	13.82 (1.45)	0.753	14.12 (1.03)	13.83 (1.43)	0.36
Creatinine (mg/dL)	0.73 (0.20)	0.73 (0.25)	0.194	0.76 (0.16)	0.73 (0.18)	0.586
AST (U/L)	21.89 (9.39)	21.93 (11.65)	0.782	20.95 (6.02)	21.68 (8.29)	0.69
LDL cholesterol (mg/dL)	115.41 (30.90)	115.48 (30.77)	0.815	112.62 (33.26)	115.36 (31.03)	0.688
Triglyceride (mg/dL)	97.63 (78.46)	97.70 (80.36)	0.929	100.57 (63.40)	97.85 (78.37)	0.874
Uric Acid (mg/dL)	5.32 (1.42)	5.33 (1.42)	0.623	5.76 (1.34)	5.34 (1.42)	0.172

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AB0199

GENES PREDICTIVE ON THE EFFICACY OF INFLIXIMAB IN THE TREATMENT OF RHEUMATOID ARTHRITIS: A PROSPECTIVE, MULTI-CENTRE, CLINICAL PERFORMANCE EVALUATION STUDY FOR AN IN-VITRO DIAGNOSTICS MEDICAL DEVICE

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Background: Approximately 30% of rheumatoid arthritis (RA) patients fail to respond to first biological therapy, thus treatment selection of biologic therapy for patients with RA is of high importance. The lack of biomarkers to predict specific biological treatment response, in the case of non-responder (NR) patients leads to unnecessary exposure, delay of adequate therapy, progression of the disease and therapy cost increase. Predicting the patient's responsiveness to the first biological therapy is still an unmet need in the clinical setting. Predictive in vitro testing would have a significant effect on the administration of biological therapy, on the real life implementation of cost effective personalized therapy.
Objectives: The purpose of this in vitro diagnostic medical device study was to demonstrate that particular gene expression profiles as genomic biomarkers (i.e. the IVD medical device) predict therapeutic response to infliximab, discriminate between responders and non-responders to infliximab treatment. Responders were defined if they reached DAS target value DAS28≤3.2 at 6 month (M6).
Methods: 110 bionaive patients were enrolled with moderate-high activity RA (DAS28-CRP >3.2), who have responded inadequately to DMARDs (including methotrexate), after they have been assigned to infliximab treatment. All patients received commercially available infliximab, procured according to SmPC, local guidelines and regulations in this non-interventional clinical study. The clinical response was evaluated according to the change from baseline in disease activity at M6. Clinical characteristics (RA duration, smoke, steroid treatment, etc.) and serological parameters (RF, ACPA, aCVM) were collected. A 3rd visit scheduled around week 22 (M6) and change of DAS28-CRP value from the baseline has been evaluated. Gene expression profiling was performed from blood samples taken at month 0 (M0); - just before the first infliximab infusion. Global gene expression profiling was performed to identify differentially expressing genes using RNA sequencing. The set of differentially expressing genes were further reduced with a combination of machine learning modelling and various feature elimination methods. The expression of the reduced gene set was confirmed and further analysed using reverse-transcription and quantitative real-time PCR.
Results: A total of 250 genes were identified by a combination of differential gene expression analyses, feature elimination techniques and various machine learning modelling methods of which 44 genes showed significant differences between NR and good responder groups. Preliminary interim analysis identified associations between gene expression and clinical response/ non-response to infliximab therapy.

Table. Three models containing gene expression + clinical data sets illustrates some statistical characteristics

Modell building_ID	Accuracy	Sensitivity	Specificity	Modell Verification	Accuracy	Sensitivity	Specificity
00232	100.00	100.00	100.00	00232	88	88.89	87.50
00249	98.82	96.55	100.00	00249	84	77.78	87.50
00270	98.82	96.55	100.00	00270	88	77.78	93.75

Conclusion: Our preliminary analysis shows that this set of genes and selected clinical parameters are predictive markers for infliximab specific response in RA patients. Ongoing work involves the clinical validation of these results in an independent patient cohort (n=60). This approach provides the opportunity to develop an in vitro diagnostic test method for the prediction of infliximab treatment responsiveness in bionaive rheumatod arthritis patients, hence to personalize infliximab therapy for these patients.
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AB0200

SHORT AND MID-TERM OUTCOME OF FOREFOOT SURGERY FOR PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Patients with rheumatoid arthritis (RA) have frequently painful foot deformities. These deformities including hallux valgus, dorsal dislocation of the metatarsophalangeal (MTP) joints and hammer toe deformity of the lesser toes are associated with disability in daily activities.
Objectives: The aim of this study is to investigate short and mid-term outcome of forefoot surgery for patients with RA.
Methods: We investigated 28 patients with 39 foots who underwent forefoot surgery between January 2010 and December 2018 and followed for more than one year after surgery. Swanson implant arthroplasty or metatarsal osteotomy was performed for big toe, and shortening oblique osteotomy (SOO) was performed for the II-V toes. Examination items were as follows; plain X-ray changes in the angle of hallux valgus (HVA), the angle between the first and second metatarsal bones (M1/2), and the angle between the first and fifth metatarsal bones (M1/5) after surgery. The progress of painful hyperkeratosis and bunion, Japanese Society for Surgery of the foot standard rating system (JSSF scale), the recurrence of deformity and bone fusion, complications, and patient satisfaction were also examined.
Results: The patients followed were 24 women with 34 feet and 4 men with 5 feet, and average age at the time of surgery was 66.1 years. HVA improved from average of 39.7 degrees to 20.2 degrees one month after surgery, but increased slightly to 23.5 degrees one year after surgery. Painful hyperkeratosis and bunion tended to disappear one month after surgery, and JSSF scale significantly improved at the final observation. One year after surgery, the bone fusion rate of big toe was 100%, but 7.8% of the metatarsal bone underwent SOO had non-union. The complications after surgery were one infection at the surgical site, one necrosis at the tip of the toe, and one infection of Swanson implant. Patient satisfaction at the final observation was high
Conclusion: Forefoot surgery for RA has problems such as recurrence, non-union, and infections, but it is considered to be a useful treatment because that pain by hyperkeratosis and bunion disappears and ADL improves.
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AB0201 **IMPACT OF TREATMENT INITIATION DELAY ON DISEASE ACTIVITY DURING RHEUMATOID ARTHRITIS**

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Background: During rheumatoid arthritis (RA), initiating conventional synthetic Disease Modifying Anti-Rheumatic Drug (csDMARD) at the early stages of the disease is a mandatory condition to achieve DMARD-free sustained remission (1). Limited data studying the relationship between RA treatment delay and disease activity are available.
Objectives: The aim of this study was to assess the impact of csDMARD initiation delay during RA on disease activity.
Methods: This is a cross-sectional study including patients with RA (ACR/EULAR criteria).Delays were collected from patients' interview and were represented respectively by D1, D2 and D3. D1 stands for the lag time separating the first RA symptom onset and rheumatologist consultation. D2 stands for the lag time separating the first RA symptom onset and RA diagnosis. D3 stands for lag time separating the first RA symptom onset and csDMARD initiation. Disease activity was evaluated by: Visual Analogue Scale for pain (VAS), number of tender joints, number of swollen joints, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and Disease Activity Score28 (DAS28).The data were analyzed with descriptive statistics, Student's t test, chi (2) test, and Spearman correlation using the SPSS statistical package. A p value < 0.05 was considered significant.
Results: The study included 100 RA patients (86 women and 14 men), with a mean age of 56.5 ± 12.4 years. The mean age at the onset of RA was 47.5 ± 12.4 years. Median D1, D2 and D3 were respectively 12 months [0-242], 15.7 months [2-252] and 18 months [2-270].Methotrextate was prescribed in 86% of cases. At RA diagnosis, the median values for the following parameters were: VAS 80 [30-100], number of tender joints 10[0-28], number of swollen joints 5 [0-17], ESR 43mm/hour [6-133], CRP 14.1 mg/l [1-120], DAS28 (ESR) 5.22 [2-7.52] and DAS28 (CRP) 4.6 [1-6.93]. After one year of follow-up, the median parameters of the disease activity were respectively: VAS 60 [0-100], number of tender joints 6[0-28], number of swollen joints 2 [0-22], ESR 32 mm/hour [2-106], CRP 7.5 mg/l [1.2-94], DAS28 (ESR) 4.1 [1.4-7.1] and DAS28 (CRP) 3.7 [1.68-6.22]. Significant positive correlation was found between delays in csDMARD initiation and DAS28 (CRP) scores over the first year (p=0.02, r=0.29).
Conclusion: In this study, delays in treatment were associated with higher DAS28 (CRP) scores after one year of follow-up. Our results suggest that early identification and treatment of RA leads to improved outcomes and even improved rates of drug-free remission.
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AB0202 **GENETIC SUSCEPTIBILITY AND PHENOTYPE OF RHEUMATOID ARTHRITIS IN DANISH AND TURKISH PATIENTS**

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Background: Previous studies indicate that genetic susceptibility and phenotype of rheumatoid arthritis (RA) differ between the populations.
Objectives: To compare the clinical, serologic expression and the presence of shared epitopes (SE) of incident RA in two different populations, one from Northern and the other from Southern Europe.
Methods: Data on incident RA patients fulfilling EULAR/ACR 2010 classifications criteria for RA were collected at Rheumatology Departments in Denmark and Turkey in 2015-2016. Patients were assessed using the same standardized protocol in both populations. SE carrier status were assigned, according to the du Montcel classification based, into six allele groups: *S1*, S2, *S3D*, *S3P* and *X*, where S2 and S3P are RA risk-enhancing alleles and S1 and S3D are RA protective alleles of the shared epitope(*1*).
Results: 109 incident RA patients from Denmark and 114 incident RA patients from Turkey were enrolled. Genetic data were available from 87% of the patients.

Table 1. Characteristics of incident rheumatoid arthritis patients in Denmark and Turkey

	Danish patients n=109	Turkish patients n=114	P-value
Age at diagnosis, years	60 (49-69)	52 (43-64)	0.003
Female, %	64	74	0.12
Symptom duration, months	7 (4-21)	6 (2-22)	0.6
Smoking status			
Never smoker, %	43	44	0.98
Former smoker, %	28	31	0.68
Current smoker, %	29	25	0.54
VAS pain (0-100 mm)	45 (28-66)	60 (41-72)	0.01
VAS fatigue (0-100 mm)	51 (29-69)	50 (20-70)	0.32
VAS global, patient (0-100 mm)	60 (31-80)	60 (41-73)	0.77
Swollen joint count (0-28)	7 (4-11)	3 (1-6)	<0.00001
Tender joint count (0-28)	7 (3-11)	5 (2-8)	0.04
HAQ score (0-3)	0.75 (0.34-1.25)	1.0 (0.25-1.75)	0.02
DAS28	4.7 (4.1-5.5)	4.3 (3.3-5.2)	0.01
CRP, mg/l	7 (3.0-18.5)	8 (3.1-22.6)	0.54
IgM RF positive, %	70	66	0.58
ACPA positive, %	63	75	0.1

Medians (interquartile range) for continuous variables
VAS – Visual Analog Scale, HAQ - Health Assessment Questionnaire, DAS28 - Disease Activity Score 28 joints, CRP – C-reactive protein, RF – Rheumatoid Factor, ACPA - Anti-Citrullinated Protein Antibodies.

Table 2. Shared epitope allele carrier frequencies.

Allele	Danish patients n=98	Turkish patients n=95	P-value
S1, % (n)	19 (37)	22 (42)	0,43
S2, % (n)	26 (51)	8 (16)	<0,00001
S3D, % (n)	6 (12)	21 (39)	0,000029
S3P, % (n)	27 (52)	29 (56)	0,52
X, % (n)	22 (44)	19 (37)	0,47

We found no associations between the risk-enhancing alleles and the presence of IgM rheumatoid factor or ACPA.
Conclusion: The Turkish patients were younger and had lower disease activity than Danish at the time of diagnosis. Our study found an enhanced genetic susceptibility to RA in Danish compared to Turkish patients with a higher prevalence of risk-enhancing RA alleles and a lower prevalence of protective alleles.
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AB0203 **LUNG DISEASE CHARACTERISTICS IN MOROCCAN RHEUMATOID ARTHRITIS PATIENTS**

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Background: Pulmonary involvement is the most common extra-articular Rheumatoid Arthritis (RA) manifestation. Interstitial lung disease is an important and early feature and can increase the mortality risk in RA patients. In Morocco no previous studies have been carried out to identify the prevalence of lung disease in RA patients nor have the risk factors for development of interstiel lung disease (ILD).
Objectives: The aim of this study was to investigate the prevalence of lung disease and analyse the ILD associated risk factors, in Moroccan patients with rheumatoid arthritis.
Methods: This was a retrospective analysis of 288 patients diagnosed with RA between January 2014 and December 2019. Exclusion criteria were: pregnant women, history of other autoimmune disease than RA, pulmonary tuberculosis diagnostignosed before lung exploration, any drugs known to cause pulmonary changes (such as Amiodarone). Clinical, and laboratory features were recorded simultaneously with the period of pulmonary exploration. Lung involvement was

assessed by High-resolution computed Tomography (HRCT). Statistical analyses were performed using SPSS 20.0. The *t*-test was employed to compare means of continuous variables, whereas chi-square test was used to compare frequencies. Variables that were significantly associated with ILD using univariate analyses, were included in multivariate logistic regression model. Statistical significance was considered if ***p<0.05***.

Results: The majority (89.2%) of patients were female. Mean age was 52.6±12.53 years and disease duration was 11.2±9.3 years. A total of 48 (16.7%) patients were noted to have respiratory symptomatology. Lung involvement was documented in 189 (65.6%) patients. In each compartment of the lung, abnormal HRCT findings suggestive of ILD were detected in 134 (70.8%) cases, bronchiectasis in 37 (19.5%) and then pleural effusion in 11 (5.8%) (Table 1).

Table 1. Frequency of subtype's pleuropulmonary involvement detected on HRTC (n=189)

Lung abnormal types N (%)	Lung abnormal Sub-types N (%)	N (%)
Interstitial lunge disease	Usual interstiel pneumonia	113(59.7%)
134 (70.8%)	Non-specific interstiel pneumonia	23(12.1%)
	Cryptogenic organizing pneumonia	3(1.5%)
	Acute interstiel pneumonia/diffuse alveolar damage	0(0%)
	Fibrosis	18(9.5%)
Airways respiratory disease	Bronchiectasis	37(19.5%)
50(26.4%)	Follicular bronchiolitis	10(5.2%)
	Obliterative Bronchiolitis	2(1.05%)
Pleural damage	Effusion	11(5.8%)
20(10.5%)	Pleural thickening	6(3.17)
	Nodules	3(1.5%)

In multivariate analysis, ILD was associated with male older age (OR=1.43, 95% IC [1.202-1.952], ***p=0.037***), advanced age at RA onset (OR=2.17, 95% IC [1.151-1.874], ***p=0.007***), extra-articular manifestations (OR=10.8, 95% IC [5.312-12.300], ***p<0.001***), disease activity (OR=2.68, 95% IC [1.463-1.715], ***p<0.001***) and low methotrexate dose (OR=1.03, 95% IC [1.003-1.106], ***p=0.031***).

Conclusion: ILD was the most prevalent manifestation of RA lung involvement, it was associated to male gender, older age active and severe RA.

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AB0204 A NEW INFLAMMATORY MARKER ASSOCIATED WITH DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS: PLATELET TO ALBUMIN RATIO

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Background: Rheumatoid arthritis (RA) is an inflammatory autoimmune disease characterized by disordered immunity and dysregulated cytokine. Neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) have been defined as inflammatory markers to evaluate disease activity of RA. Recently, platelet to albumin ratio (PAR) was reported as a new prognostic index in patients with cancer. However, similar studies have not been displayed in RA.

Objectives: This study was to explore the role of PAR in RA and its association with disease activity.

Methods: This retrospective study enrolled 136 RA patients and 87 age- and gender-matched healthy controls. Neutrophil, lymphocyte, monocyte, platelet, hemoglobin, albumin, NLR, neutrophil to hemoglobin ratio (NHR), neutrophil to albumin ratio (NAR), monocyte to lymphocyte ratio (MLR), monocyte to hemoglobin ratio(MHR), monocyte to albumin ratio(MAR), PLR, platelet to hemoglobin ratio (PHR), PAR, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) and Disease Activity Score of 28 joints - ESR (DAS28-ESR) were detected. Receiver operation characteristic (ROC) curve was used to discriminate RA patients from healthy individuals. Relationships between PAR and DAS28-ESR as well as other laboratory data were measured by the Spearman's correlations analysis.

Results: RA patients showed higher levels of NLR, NHR, NAR, MLR, MHR, MAR, PLR, PHR PAR and lower levels of albumin than healthy controls. PAR and other inflammatory parameters were also raised along with increased disease activity in RA patients ($P < 0.05$) except NHR ($P = 0.098$). Similarly, albumin was decreased in RA patients as the disease activity increased ($P = 0.001$). ROC showed that area under curve (AUC) of PAR (0.887, 95%CI: 0.843-0.931) was higher than NLR (0.818, 95%CI: 0.762-0.874), NHR(0.839, 95%CI: 0.787-0.890), NAR(0.829, 95%CI: 0.776-0.882), MLR (0.794, 95%CI: 0.734-0.854), MHR(0.817, 95%CI: 0.760-0.874), MAR(0.814, 95%CI: 0.757-0.872), PLR (0.832, 95%CI: 0.779-0.886), PHR(0.884, 95%CI: 0.838-0.930) and albumin(0.860, 95%CI: 0.813-0.908). Besides, PAR was positively correlated with DAS28-ESR ($r = 0.429$, $P < 0.001$), CRP ($r = 0.540$, $P < 0.001$) and ESR ($r = 0.492$, $P < 0.001$), yielding a highest relevance than other inflammatory indexes.

Conclusion: This study demonstrated that PAR was elevated in RA patients and increased with the disease activity. PAR may be a novel marker to assess the disease activity of RA patients.

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AB0205 PREDICTORS OF ULTRASOUND DETECTED INFLAMMATORY FINDINGS IN PATIENTS WITH INFLAMMATORY ARTHRALGIA

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Background: Patients with inflammatory arthralgia (IA) are considered to be at increased risk for progression to RA. US has shown high sensitivity to detect synovitis compared with physical examination. Thus, US is recommended to identify subclinical synovitis in patients without clinical signs of inflammation.

Objectives: The objective of our study is to determine the frequency and pattern of US detected inflammatory findings in patients with IA and investigate factors contributing to predict these findings.

Methods: An US clinic is scheduled in an academic center running three days every week. A retrospective analysis of our US unit cohort during a period of 6 months was undertaken. Patients with IA and no previous diagnosis of inflammatory arthropathies were included for analysis. Inclusion criteria of IA definition included: severe symptoms presenting in the morning, duration of morning stiffness ≥60 min, symptoms predominantly located in MCP joints and abscense of clinically detected synovitis by the referral rheumatologist. The following routinely collected variables were included in the analysis: demographics, clinical features and laboratory tests. Patients underwent bilateral US examination in GS and PD mode of hands and/or feet according to the European League Against Rheumatism (EULAR) guidelines. The presence of synovitis, tenosynovitis and enthesitis was assessed on a semi quantitative scale (0–3) for Grey Scale(GS)/Power Doppler(PD) or using enthesitis OMERACT definition, respectively. Patients were stratified in two groups based on the presence of US inflammatory findings (synovitis, tenosynovitis or enthesitis with PD signal). First, differences between groups were tested using chi-squared and Student-t tests in the univariate analysis. Second, multivariate logistic regression models were employed to investigate the association between possible predictive factors of US detected inflammatory findings.

Results: A total of 57 patients were included in the analysis. Mean age was 55.8±15.2 years, 41 (71.9%) were females, and mean symptoms duration was 11.4±10.4 months (Table 1). A total of 42 (73.7%) patients presented with a polyarticular arthralgia pattern. US inflammatory findings were present in 20 (35.1%) patients (26.3% PD synovitis, 21.1% PD tenosynovitis and 3.5% PD enthesitis). Hands were most commonly involved with PD synovitis at wrists in 19.3% and at MCP in 12.3% of patients (Table 2). For PD tenosynovitis, the flexor MCP 2-5 (5.3%) and compartment IV tenosynovitis (1.8 %) were the most frequent affected locations. Only two patients had PD enthesitis at feet and 6 (10.5%) had erosions in hands or feet at baseline examination. In the univariate analysis, the higher ESR values and the shorter time from symptoms onset were significantly associated with US detected inflammatory findings (p=0.044 and 0.049, respectively). In the multivariate analysis, only ESR values (OR=1,04; 95%CI 1,002-1,078), remained significantly associated with the presence of US inflammatory findings (Table 3).

Table 3. Independent predictors of US detected inflammatory findings

	p	Odds ratio	95% C.I.	
			Lower	Upper
ESR (mm/h)	0.039	1.04	1.002	1.078
Time (months) from symptoms onset	0.1	0.924	0.841	1.015

		Total n= 57	US inflammatory findings n= 20	Non US inflammatory findings n=37	p
Age		55.8 ± 15.2	53.9±14.5	59.5±16.2	0.2
Sex	Female	41 (71.9%)	13 (65%)	28 (75.7%)	0.3
Smoking	Non smoker	27 (47.4%)	10 (55.6%)	17 (50%)	
n= 52	Smoker	20 (35.1%)	6 (33.6%)	14 (41.2%)	0.8
	Former smoker	5 (8.8%)	2 (11.1%)	3 (8.8%)	
	Monoarticular	7 (12.3%)	3 (15%)	4 (10.8%)	
Extension	Oligoarticular	8 (14%)	5 (25%)	3 (8.1%)	0.9
	Polyarticular	42 (73.7%)	12 (60%)	30 (81.1 %)	
Time (months) from symptoms onset		11.4 ± 10.4	7.3±6.2	13.5±11.5	0.049
ESR (mm/h)		19.1 ± 21	29.3±28.4	14.5±14.8	0.044
CRP (mg/dL) n=47		0.6 ± 1.4	1.1±1.9	0.4±0.9	0.15
RF (IU/mL) n=53		64.3 ± 321.6	21±53.7	88.5±399.7	0.5
CCP (IU/mL)		52.2 ± 231.4	104.8±360.5	22.3±103.6	0.2

Table1. Baseline characteristics of patients with IA

Conclusion: PD US inflammatory findings are found in 1 over 3 patients with IA being PD synovitis the most common finding, specially at the wrists and MCP joints. Higher ESR values were significantly associated with the presence of US inflammatory findings. Our data highlights how the use of PD US may be useful to detect subclinical synovitis in patients with IA.

		US synovitis	PD positive
Hands		14 (24.6%)	11(9.3%)
	Wrist	14 (24.6%)	11 (19.3%)
	MCP	7 (12.3%)	7 (12.3%)
	PIP	1 (1.8%)	0 (0%)
Feet		8 (14%)	4 (7%)
	Ankle	4 (7%)	3 (5.2%)
	Tarsal joints	1 (1.8%)	1 (1.8%)
	MTP	3 (5.3%)	0(0%)
		US tenosynovitis	PD positive
Hands		4 (7%)	3 (5.3%)
	2nd, 3rd, 4th or 5th flexor	3 (5.3%)	3 (5.3%)
	4th extensor	1 (1.8%)	1 (1.8 %)
	6th extensor	0 (0%)	0 (0%)
Feet		1 (1.8%)	1 (1.8%)
	Tibialis anterior	0 (0%)	0 (0%)
	Posterior tibialis	1 (1.8%)	1(1.8%)
	Peroneus	0 (0%)	0 (0%)
		US enthesitis	PD positive
Feet		2 (3.5%)	2(3.5%)
	Achilles	2 (3.5%)	2 (3.5%)
	Plantar Fascia	1 (1.8%)	0 (0%)

Table 2. US findings of patients with IA

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AB0206 CIRCULATING CENTROMERE PROTEIN F AUTOANTIBODIES FOR PREDICTING CLINICAL RESPONSE TO INFLIXIMAB IN RHEUMATOID ARTHRITIS

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Background: One third of patients with rheumatoid arthritis (RA) respond poorly to TNF inhibitors and related studies are inconsistent in predictive biomarkers. The identification of biomarkers that predict the treatment response prior to drug exposure is a current priority on the RA field. ACPA and RF are ubiquitously tested in RA patients, but other autoantibodies exist and may provide additional information on RA treatment response.
Objectives: This study aimed to identify circulating autoantibodies for predicting response to infliximab (IFX) in RA.
Methods: We profiled the autoantibody repertoire of baseline sera from 155 biologic naïve RA patients treated with IFX. The sera were provided by three independent clinical sources and distributed in one exploratory cohort (N=20) collected from Hospital Clínico Universitario of Santiago de Compostela (Spain), one replication cohort (N=61) collected from Hospital Universitario de A Coruña (Spain) and samples from the Swedish Farmacotherapy (SWEFOT) trial (Sweden) (N=74) for clinical validation. The presence of autoantibodies and their levels in serum were analysed in association with EULAR clinical response at 6 months follow-up: good response (GR, N=56), moderate (MR, N=55) and non-response (NR, N=44). A suspension bead array platform built on protein fragments within Human Protein Atlas and selected from an initial untargeted screening using an array containing 42000 antigens was employed to identify the IgG and IgA autoantibodies on the exploratory cohort. A replication and validation phases were carried out on the other two serum sample cohorts. Meta-analysis and Receiver Operating Curves were performed in order to assess the clinical relevance of the findings observed.
Results: Meta-analysis revealed that the levels in serum of IgG autoantibodies against Centromere protein F (CENPF) are significantly increased in responders (good responders and moderate responders; N=111) to IFX compared to non-responders (N=44) (P=0.018). CENP-F is a proliferation-associated and cell cycle-dependent centromere autoantigen that might be involved in the increased or abnormal cell proliferation that occurs during RA process. The combination of the anti-CENPF antibodies with clinical variables (age, sex, DAS28-ESR) resulted in the best model to discriminate the patients that will respond to IFX, showing an AUC of 0.756 (95% CI [0.639-0.874], P=0.001).
Conclusion: High serum levels of IgG anti-CENPF antibodies might be potentially useful to identify RA patients more likely to benefit from IFX

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AB0207 CLINICAL IMPACT OF ANTI-CARP ANTIBODIES IN RHEUMATOID ARTHRITIS

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Background: Antibodies directed against carbamylated proteins (anti-CarP) have been recently introduced for the first time as a new biomarker in rheumatoid arthritis (RA) (1). Their presence is predictive for the development of RA (2). Anti-CarP antibodies are associated with the development of more severe forms of the disease in overall and anti-citrullinated peptide antibodies negative

population of patients with RA (3). In the literature is still current the research which associate these antibodies with disease activity and functional status of patients.

Objectives: This study investigated the incidence of anti-CarP positive findings in patients with RA on synthetic and biologic disease-modifying therapy (DMT) and the relationship between anti-CarP antibody status and both disability and disease activity.

Methods: It was an open-label, observational, cross-sectional study. The trial included 70 patients with RA diagnosed on the basis of ACR 1987 and ACR / EULAR 2010 criteria, on treatment with synthetic and biological DMT, who attended the Clinic of Rheumatology, Military Medical Academy, from September to December 2018.The control group consisted of 18 healthy individuals. After approval of the institutional Ethical Committee and after patients have signed Informed Consent,the study was conducted. Disease activity score (DAS28) was determined for the assessment of RA activity, and the assessment of patients' functional ability was performed using the Health assessment questionnaire disability index (HAQ-DI). Concentration of anti-CarP antibodies was determined by commercial ELISA anti-CarP quantitative sandwich immunoassay. The methods of descriptive and analytical statistics were used in statistical data processing.

Results: Based on the cut-off value (5.9 ng / ml), no one in the control group had positive anti-CarP antibodies, while 34.7% of the subjects with RA were positive. The positive correlation was found between anti-CarP antibody concentration and DAS28 in all RA patients (p = 0.0003; Pearson r = 0.4829). The positive correlation was also found between anti-CarP antibody concentration and HAQ-DI in all RA patients (p = 0.0003; Pearson r = 0.4253).

Conclusion: Anti-CarP antibodies were present in a significant number of patients with RA. This study demonstrated that patients with RA with higher concentrations of anti-CarP antibodies have higher disease activity and impaired functional status. It is undisputed that further and larger studies are needed to better determine the clinical significance of these antibodies.

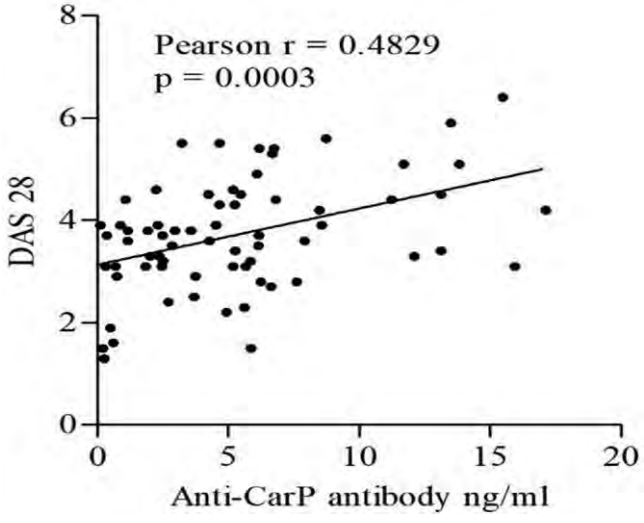
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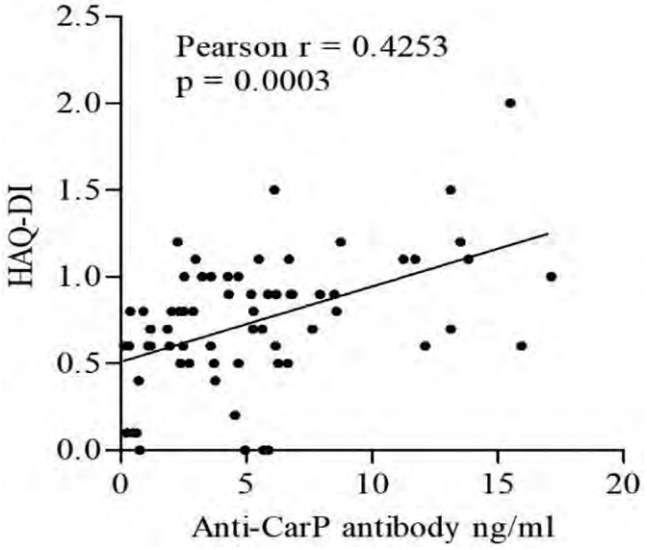
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Graphs 1 and 2. Correlation of anti-CarP antibody concentration with DAS28 and HAQ-DI in all RA patients





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AB0208 **ASSOCIATION OF RHEUMATOID FACTOR, HLA-DRB1 SHARED EPITOPE (SE) AND SMOKING WITH RADIOGRAPHIC OUTCOME IN RHEUMATOID ARTHRITIS**

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Background: Genetic and environmental factors interact in aetiopathogenesis of Rheumatoid Arthritis (RA). However, it remains unclear whether current smoking, presence of Rheumatoid factor (RF) and HLA-DRB1 SE influence the radiographic outcome.

Objectives: To clarify the possible associations between radiographic outcome, HLA-DRB1 SE, RF and smoking status in patients with longstanding RA.

Methods: An observational study of 240 consecutive Greek patients with RA, whose mean age and mean disease duration was 65.31±12.5 and 12.7±11.8 years respectively. Among them 74.17% were female, 40% were smokers, 60.42% had positive RF and 68.33% possessed at least one SE allele. HLA-DRB1 alleles were typed by molecular techniques (PCR-SSOP and SSP). X-rays of hands and feet were performed and scored by the Sharp-van der Hejde score (SHS) method.

Results: Results were stratified by RF and smoking status and analyzed by multivariate logistic regression. Overall, the mean SHS was significantly higher in RF positive than RF negative patients and in smokers than non-smokers (52.76±31.1 vs 38.4±31.96, p: 0.0007, 55.33±38.56 vs 26.8±22.32, p <0.0001, respectively). Furthermore, patients that possessed at least one SE allele had higher SHS than SE negative (35.49±24.76 vs 25.74±19.22, p: 0.0013). An association between radiographic severity and SE was found in RF positive patients. More specifically, seropositive patients carrying at least one SE allele had higher SHS than those lacking SE (40.85±33.21 vs 29.23±24.72, p: 0.037). On the other hand, smokers with at least one SE allele had higher SHS when compared to smokers without SE (29.27±25.20 vs 20±17.22, p: 0.048). Among RF negative and non-smokers RA patients, no significant association was found between the presence of HLA-DRB1 SE and radiographic severity.

Conclusion: Our data indicate that in longstanding RA there is an association between RF positivity, the presence of SE, current smoking status and radiographic outcome.

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AB0209

PREDICTORS OF ACHIEVING STRINGENT REMISSION IN PATIENTS WITH ESTABLISHED RHEUMATOID ARTHRITIS IN CLINICAL REMISSION FOLLOWING A TREAT-TO-TARGET STRATEGY

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Background: Achieving remission according to stringent criteria such as Simplified Disease Activity Index (SDAI) and ACR/EULAR Boolean remission is associated with a better long-term outcome in patients with RA[1]. Possible predictors of achieving stringent remission in patients in clinical remission, following targeted treatment strategies, have not been investigated.

Objectives: To investigate the predictive value of clinical, radiographic and MRI variables on achieving more stringent remission in RA patients in clinical remission, following MRI and conventional treat-to-target (T2T) strategies.

Methods: In this post-hoc study, data were used from 171 RA patients in clinical remission (DAS28-CRP< 3.2 and no swollen joints) on conventional synthetic DMARDs, included in the IMAGINE-RA randomized clinical trial[2], where they followed an MRI T2T strategy (targeting absence of osteitis) combined with clinical remission (DAS28-CRP≤3.2 and no swollen joints) or a conventional T2T strategy (targeting clinical remission only). Baseline contrast-enhanced MRIs of the dominant wrist and 2nd-5th MCP joints and radiographs of hands and feet were evaluated according to the OMERACT RAMRIS scoring system and Sharp/van der Heijde method, respectively, by two experienced readers. Potential clinical, radiographic and MRI baseline predictors of remission were first tested in univariate logistic regression analyses with achievement of Clinical Disease Activity Index (CDAI), SDAI, and ACR/EULAR Boolean remission at 24 months as dependent variables. Variables with p<0.25 were subsequently tested in multivariate logistic regression analyses with backward selection, adjusted for age, gender and strategy group. Missing values of covariates were imputed using chained equations.

Results: Based on the univariate analyses, tender joint count, patient VAS global, VAS pain, VAS fatigue, physician VAS global, HAQ, MRI osteitis, radiographic and MRI erosion and joint space narrowing scores were included in multivariate analyses (Table).

Following the MRI T2T strategy was a positive predictor and high patient VAS global a negative predictor of achieving all definitions of remission. Furthermore, high patient VAS pain was negatively associated with achieving SDAI and ACR/EULAR Boolean remission and high tender joint count negatively associated with achieving CDAI and SDAI remission.

Multivariate logistic regression analyses with backward selection, final models

	Dependent variables, remission at 24 months								
	CDAI			SDAI			ACR/EULAR Boolean		
	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
Covariates									
MRI T2T strategy group	2.94	1.25-7.52	0.013	2.46	1.03-6.35	0.043	5.47	2.33-14.11	<0.001
Female	0.90	0.36-2.25	0.82	0.80	0.31-2.05	0.64	0.80	0.32-1.97	0.63
Age	1.02	0.98-1.07	0.32	1.02	0.98-1.07	0.33	1.03	0.99-1.07	0.15
Tender joint count (0-28)	0.33	0.12-0.86	0.023	0.29	0.10-0.78	0.013			
Patient VAS global	0.91	0.88-0.94	<0.001	0.93	0.88-0.97	<0.001	0.93	0.88-0.98	0.003
Patient VAS pain				0.95	0.91-1.00	0.049	0.92	0.87-0.98	0.004

Conclusion: In RA patients in clinical remission, poor patient reported outcomes and tender joint count were associated with decreased chance of achieving stringent remission, while following an MRI T2T strategy predicted stringent remission across all definitions thereof.

References:

[1] Smolen et al. Ann Rheum Dis 2017
[2] Møller-Bisgaard et al. JAMA 2019

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AB0210

ACREULAR: AN R PACKAGE FOR THE CALCULATION AND VISUALISATION OF ACR/EULAR RELATED RHEUMATOID ARTHRITIS MEASURES

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Background: The American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) individually and collaboratively have produced/recommended diagnostic classification, response and functional status criteria for a range of different rheumatic diseases. While there are a number of different resources available for performing these calculations individually, currently there are no tools available that we are aware of to easily calculate these values for whole patient cohorts.

Objectives: To develop a new software tool, which will enable both data analysts and also researchers and clinicians without programming skills to calculate ACR/EULAR related measures for a number of different rheumatic diseases.

Methods: Criteria that had been developed by ACR and/or EULAR that had been approved for the diagnostic classification, measurement of treatment response and functional status in patients with rheumatoid arthritis were identified. Methods were created using the R programming language to allow the calculation of these criteria, which were incorporated into an R package. Additionally, an R/Shiny web application was developed to enable the calculations to be performed via a web browser using data presented as CSV or Microsoft Excel files.

Results: acreular is a freely available, open source R package (downloadable from https://github.com/fragla/acreular) that facilitates the calculation of ACR/EULAR related RA measures for whole patient cohorts. Measures, such as the ACR/EULAR (2010) RA classification criteria, can be determined using precalculated values for each component (small/large joint counts, duration in days, normal/abnormal acute-phase reactants, negative/low/high serology classification) or by providing “raw” data (small/large joint counts, onset/assessment dates, ESR/CRP and CCP/RF laboratory values). Other measures, including EULAR response and ACR20/50/70 response, can also be calculated by providing the required information. The accompanying web application is included as part of the R package but is also externally hosted at https://fragla.shinyapps.io/shiny-acreular. This enables researchers and clinicians without any programming skills to easily calculate these measures by uploading either a Microsoft Excel or CSV file containing their data. Furthermore, the web application allows the incorporation of additional study covariates, enabling the automatic calculation of multigroup comparative statistics and the visualisation of the data through a number of different plots, both of which can be downloaded.

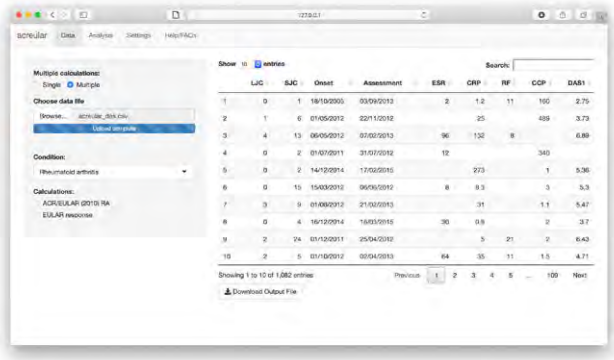


Figure 1. The Data tab following the upload of data. Criteria are calculated by the selecting the appropriate checkbox.



Figure 2. A density plot of DAS28 scores grouped by ACR/EULAR 2010 RA classification. Statistical analysis has been performed and shows a significant difference in DAS28 score between the two groups.

Conclusion: The acreular R package facilitates the easy calculation of ACR/EULAR RA related disease measures for whole patient cohorts. Calculations can be performed either from within R or by using the accompanying web application, which also enables the graphical visualisation of data and the calculation of comparative statistics. We plan to further develop the package by adding additional RA related criteria and by adding ACR/EULAR related measures for other rheumatic disorders.

Disclosure of Interests: Fraser Morton: None declared, Jagtar Nijjar Shareholder of: GlaxoSmithKline plc, Consultant of: Janssen Pharmaceuticals UK, Employee of: GlaxoSmithKline plc, Paid instructor for: Janssen Pharmaceuticals UK, Speakers bureau: Janssen Pharmaceuticals UK, AbbVie, Carl Goodyear: None declared, Duncan Porter: None declared

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AB0211 DIFFERENTIAL INFLUENCE OF CDAI COMPONENTS BASED ON DISEASE STATE IN RHEUMATOID ARTHRITIS PATIENTS: REAL-WORLD RESULTS FROM THE ONTARIO BEST PRACTICES RESEARCH INITIATIVE (OBRI)

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Background: Treat-to-target recommendations for rheumatoid arthritis (RA) dictate that remission or low disease activity should be aimed. Although numerous composite indices are available, the clinical disease activity index (CDAI) is commonly used in routine clinical care due to its simplicity and non-reliance on acute phase reactants.

Objectives: The purpose of this analysis was to evaluate the CDAI properties both cross-sectionally and longitudinally in a cohort of RA patients followed in Canadian routine care.

Methods: RA patients enrolled in the Ontario Best Practices Research Initiative (OBRI), with available follow-up for ≥6 months and data on CDAI, disease activity score based on 28 joints (DAS28), health assessment questionnaire (HAQ), and ACR/EULAR Boolean remission were included. For both the CDAI score and its change from baseline to 6 months, construct validity was assessed with principal component analysis, internal consistency with the Cronbach's alpha coefficient (α), correlational validity with the Spearman's rho coefficient, agreement in disease state classification with percent concordant pairs and the kappa statistic. Stratified analysis by presence of CDAI low disease activity (LDA) or remission was performed.

Results: 1,582 patients met the inclusion criteria. Principal component analysis showed that CDAI could be reduced to a single component when CDAI is >10 with SJC28 accounting for most variance in score and patient global assessment (PtGA) the least; whereas, when CDAI is ≤10, two distinct components were identified, the first comprising PtGA and physician global assessment (PhGA) and the second SJC28 and TJC28. In terms of internal consistency, high levels were observed for both CDAI at baseline (α=0.83) and its change from baseline to 6 months (α=0.81); however, the consistency between CDAI components was very low when CDAI is ≤10 (α=0.23).

Overall, a strong positive correlation was observed between CDAI and DAS28 (rho=0.86) and their changes (rho=0.87) while its correlation with HAQ was weak. When stratifying by CDAI levels, the correlation of CDAI with DAS28 was moderate when CDAI is ≤10 and very weak when CDAI is ≤2.8. Similarly, agreement in the classification of LDA between CDAI and DAS28 or HAQ was fair to moderate, and agreement in classification of remission was poor to fair.

Conclusion: CDAI and DAS28 correlate well when disease activity is moderate or high and poorly in LDA or remission. PtGA had a stronger influence on CDAI at LDA or remission state compared to moderate or high disease state. Thus, careful interpretation of PtGA is necessary particularly in patients who are identified as CDAI non-remitters.

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AB0212 FLARE RISK AFTER DISCONTINUING LONG-TERM METHOTREXATE TREATMENT IN PATIENTS HAVING RHEUMATOID ARTHRITIS WITH LOW DISEASE ACTIVITY

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Background: Several recent studies have reported that MTX could be discontinued in patients with low disease activity who are taking biologic DMARDs or tofacitinib. However, there are limited studies on whether MTX could be discontinued in patients with low disease activity who have taken MTX for a long term.

Objectives: We investigated the disease flare rate in patients with rheumatoid arthritis (RA) who achieved low disease activity following long-term methotrexate (MTX) treatment and the factors related to flare.

Methods: This retrospective longitudinal cohort study included patients with RA and low disease activity who were exposed to MTX for >10 years. Disease flare was defined as an increase in DAS28 of >1.2 within 6 months of discontinuation of MTX. Logistic regression analysis was performed to identify the factors associated with flare.

Results: In total, 97 patients with RA were included in the study. The mean baseline DAS28 was 1.96 ± 0.56. The median cumulative MTX dose was 11.7g; the median duration of exposure to MTX was 19 years. Following MTX discontinuation, flare occurred in 43 (44.3%) patients; the mean time to flare was 98 ± 37.7 days. According to univariable logistic regression analysis, C-reactive protein, erythrocyte sedimentation rate (ESR) at discontinuation, the average ESR in the 6 months before discontinuation of MTX, a weekly dose of MTX before discontinuation, and use of other conventional synthetic DMARDs were associated with a higher risk of disease flare. In multivariable analysis, a weekly dose of MTX before discontinuation (OR, 1.014; 95% CI, 1.014–1.342; p = 0.031) was significantly associated with flare risk.
Conclusion: Among patients with RA who achieved low disease activity with long-term treatment with MTX, more than half of the patients remained flare free after MTX discontinuation. A higher MTX dose before discontinuation was associated with a high flare risk.
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AB0213 THE USE OF MUSCULOSKELETAL ULTRASOUND AND PATIENT REPORTED OUTCOMES TO IDENTIFY THE FACTOR TO GIVE RESIDUAL SYMPTOMS AMONG PATIENTS WITH RHEUMATOID ARTHRITIS IN SDAI-REMISSION OR LOW DISEASE ACTIVITY.

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Background: The goal of treatment in rheumatoid arthritis (RA) is to achieve remission. There is the patient with residual symptoms in the Japanese RA patient who achieved clinical remission. There are not many studies to examine the relation between everyday life, social activity and evaluation of disease activities using musculoskeletal ultrasound (MSKUS).
Objectives: To identify the factor to give residual symptoms of RA patients in SDAI-remission (REM) or low disease activity (LDA), using MSKUS.
Methods: 300 patients were enrolled. The synovitis evaluated gray scale (GS) and power doppler (PD) with 22 both hands joints by MSKUS. We evaluated age, sex, the number of tender joint (TJ) and swelling joint (SJ), the serologic characteristics (CRP, ESR, CCP, RF, MMP-3), Patient Reported Outcomes (PROs) (morning stiffness (MS), pain-VAS, fatigue-VAS), HAQ and EQ5D-5L.
Results: (1). Stratified analysis was performed between HAD/MDA group (N=106) and LDA/REM group (N=194). As a result of single variable analysis, many factors were extracted with significant difference. As a result of the multivariate analysis, MTX dose, number of TJ and SJ, MS, fatigue-VAS, HAQ, EQ5D-5L, and GS≧2 were extracted with a dominant difference. (2). For the stratified analysis in GS≧2, the ratio was low, and the disease duration was short significantly in the LDA/REM group. (3). Next, stratified analysis was performed between Low group (N=95) and REM group (N=99). As a result of single variable analysis, number of TJ and SJ, MTX dose, HAQ, EQ5D-5L, MS, pain-VAS, fatigue-VAS, EGA, GS≧1, GS≧2, GS total score, PD≧1 and PD total score were extracted with significant difference. As a result of the multivariate analysis, number of TJ and fatigue-VAS were extracted with a dominant difference.
Conclusion: (1). It became clear that the factor which participated in the achievement with SDAI-remission or low disease activity was enough quantity of MTX dose, use of b/t DMARD, US-GS level, residual symptoms (lassitude · pain joint) to be caused by RA. Particularly, the ratio of GS≧2 was low, and the disease was short. (2). In the LDA patients (who do not achieve clinical remission), they had residual symptoms (fatigue and TJ). (3). In the REM patients, remaining inflammation was not seen in MSKUS. The conclusion is that the induction of remission is important from the viewpoint of not only the prevention of joint destruction but also improvement and maintenance of long-term QoL.
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AB0214 4-YEAR EXPERIENCE OF AN OUTPATIENT CLINIC OF PATIENTS WITH CLINICALLY SUSPECTED ARTHRALGIAS OF EVOLVING TO ARTHRITIS

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Background: Although genetic and serological risk factors have been extensively studied in rheumatoid arthritis (RA), the phase of symptoms without clinical arthritis is poorly characterized.
Objectives: To identify baseline clinical and immunological markers in patients with clinically suspicious arthralgia (CSA) progressing to chronic arthritis.
Methods: Prospective longitudinal study of a cohort of patients with CSA. Patients are were followed up for at least 2 years, with clinical and analytical data collection by means of standardized protocols every 6 months. Inclusion criteria were an onset of symptoms ≤ 12 months, inflammatory arthralgias involving small joints of hands or feet (predominantly in nights or mornings, improving throughout the day or with movement, and morning stiffness ≥30 min). Patients with clinical synovitis, diagnosis of fibromyalgia or osteoarthritis at baseline visit were excluded from the study.
Results: 45 patients were recruited from November 2015 in our CSA clinics. The majority were women (42 patients), with a mean age at entry of 44 ± 13 years, a mean duration of symptoms before entry of 32.3 ± 15.1 weeks, and a mean follow-up time of follow-up of 17.2 ± 13.3 months. A third (30%) of patients had a family history of autoimmune diseases, 18.6% were seropositive, an average body mass index (BMI) of 27.6 ± 6.6, and 14 (31.3%) were smokers or ex-smokers. Most patients reported a progression of arthralgia over time (53%) and a joint swelling (57%). Out of 45 patients, 18 (40%) developed clinical arthritis or autoimmune disease (11 RA, 2 undifferentiated arthritis, 3 spondyloarthritis, 2 undifferentiated connective diseases), after 7 ± 8.6 months of follow-up. Among patients with ≥ 6 months follow-up, 47.1% progressed to a clinical arthritis (CA). CA patients had a longer follow-up time (22.4 ± 13.9 vs. 16.8 ± 13 months; p = 0.015), and a higher frequency of smoking (60 vs. 21.7%; p = 0.037). Likewise, CA patients presented a higher age at baseline, family history of autoimmune disease and higher baseline scores of HAQ, PGA and VAS pain, although without statistical significance (Table 1). In the subset of patients with a final diagnosis of RA, patients presented a significantly longer follow-up, and higher scores of baseline VAS pain compared to non-progressors (Table 2).

Table 1. Baseline characteristics of patients

	Arthritis (N=18)	No arthritis (N=27)	p
Age at onset (years)	48.5±12.1	41.2±12.5	0.06
Time of follow-up (months ± SD)	22.4±13.9	16.8±13.0	0.02
FR and / or ACPA (+)	5 (31.3%)	7 (31.8%)	0.70
Smokers / former smokers	9 (60%)	5 (21.7%)	0.04
Familial history of autoimmune disease	5 (27.8%)	4 (15.4%)	0.65
HAQ	6.5±7.0	3.6±4.5	0.20
VAS pain	46.6±35	33.4±18.5	0.17
PGA	40.2±30.5	29.6±23.2	0.28
BMI	24.3±4.2	27.1±7.4	0.18
Increased levels of acute phase reactants	31.3%	31.8%	1.00

VAS: visual analogue scale; PGA: patient global assessment; BMI: body mass index

Table 2. Baseline characteristics of patients with RA vs. no arthritis

	RA (N=11)	No arthritis (N=27)	p
Age at onset (years)	48.9±11.4	41.2±12.5	0.09
Time of follow-up (months ± SD)	25.5±15.6	12.8±10.9	0.01
FR and / or ACPA (+)	36.4%	16.7%	0.23
Smokers / former smokers	44.4%	21.7%	0.23
Familial history of autoimmune disease	22.2%	17.4%	1.00
HAQ	8.5±8.1	3.8±4.5	0.08
VAS pain	58.2±31.9	33.4±18.5	0.02
PGA	49.7±23.7	29.6±23.2	0.08
BMI	24±4.9	27.1±7.4	0.25
Increased levels of acute phase reactants	36.4%	16.7%	0.23

VAS: visual analogue scale; PGA: patient global assessment; BMI: body mass index

Conclusion: In our CSA clinic, 40% of the patients progressed to clinical arthritis, while almost half of those who were followed for more than 6 months progressed.

PROs are important to consider as markers of future development of RA. It is necessary to expand the number of patients recruited to obtain more robust conclusions.
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AB0215 EARLY IMPROVEMENT OF THE POWER DOPPLER SIGNAL CAN PREDICT TO CONTINUE THE BIOLOGICAL DMARDS AFTER 1 YEAR.

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Background: In rheumatoid arthritis (RA), biologics treatment is one of the effective treatment options. On the other hand, the effects of biologics cannot be obtained satisfactorily in all patients, and there are some cases in which treatment is interrupted due to ineffective or adverse events. However, the useful predictive markers of the biologics have not been found in the early phase of treatment in RA. Recently, ultrasound (US) has played a role of sensitive imaging modality in the diagnosis and follow-up of patients with RA.
Objectives: In this study, we investigated whether continuation of biologics treatment can be predicted by ultrasonographic findings in the early phase.
Methods: Fifty-four RA patients who started the first biologics from September 2016 to December 2018 were included. All the patients were performed clinical examination, blood tests and US examination of hand and foot at baseline, 4, 12, 24, 36 and 52 weeks. US examination was performed on MCP joints, PIP joints, wrist and MTP joints.
Results: Among 54 cases, 42 cases were able to continue treatment until one year later, and the continuation rate was 80.8%. Of the 12 patients who discontinued first biologics treatment, 5 were changes to other biologics due to inadequate response, 4 were their wishes, and 3 were adverse events. Multiple regression analysis was performed with treatment continuation as the dependent variable and improvement of CRP, MMP-3, DAS28-CRP, grayscale score and power Doppler score in 4 weeks as explanatory variables. Only improvement of power Doppler score was extracted as a significant predictor ($p = 0.045$). In the continuation group, the improvement of the power Doppler signal at week 4 was 36% compared with the baseline, compared with 10% in the discontinuation group.
Conclusion: The early improvement of power Doppler signal in 4 weeks could be a predictive factor for the continuation of 1-year biological treatment.
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Table 1. Multivariate regression analysis of predictive factors for continuation of biologics treatment in 1-year.

Improvement ratio of 0 to 4 weeks	beta	P value
CRP	-0.122	0.465
MMP-3	0.228	0.103
DAS28 CRP	0.280	0.103
Ultrasound grey scale score	-0.342	0.119
Ultrasound power Doppler score	0.442	0.045

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AB0216 POWER DOPPLER SCORE IS USEFUL TO PREDICT JOINT DESTRUCTION OF HAND AND WRIST JOINT IN RHEUMATOID ARTHRITIS PATIENTS.

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Background: Several studies demonstrated that total power Doppler (PD) signal can predict radiographic progression as a change in total van der Heijde-modified total Sharp score (mTSS) in rheumatoid arthritis (RA) patients. However, in some studies, radiographic progression was observed in a different joint compared with the site of a positive PD signal at baseline in many cases.
Objectives: The aim of this study was to identify the clinical factor of RA patients in association with radiographic progression of hands and wrists and to investigate which joint showed radiographic progression in RA patients. We focused on the correlation of the site of a positive PD signal and the site of radiographic progression.
Methods: We examined retrospectively of 70 RA patients (67 women, three men) who underwent ultrasonography (US) examination at 32 regions on bilateral hands and wrists from 2014 to 2016. Radiographs of the hands were taken at baseline and at least one year after US (mean, 19.9 months), and radiographic progression was assessed using mTSS system. We performed multivariate logistic regression analysis to investigate the association between baseline factors and radiographic progression. The relationships between radiographic progression of the individual joint and total/each joint PD score were assessed by ROC analysis and Fisher's exact test.
Results: Nineteen patients (37.3%) experienced progression of mTSS of hands and wrists. DAS28-CRP (P=0.02) and total PD score (P=0.01) were associated with radiographic progression, and total PD score was significantly associated with radiographic progression (OR 1.22; 95% CI 1.04-1.36; P=0.006) by multivariate logistic regression analysis (Table 1).

Table 1. Association between the demographic and clinical findings at baseline and radiographic progression over 12 months

a.univariate analysis	No radiographic progression (n = 51)	Radiographic progression (n = 19)	P-value
Age, years	63.4 ± 12.7	58.1 ± 10.6	0.61
Duration of RA, years	24.4 ± 13.6	20.0 ± 5.0	0.28
Usage of Bio, %	42.2	40.4	0.57
Amount of MTX, mg/week	4.8 ± 3.3	4.5 ± 4.3	0.77
Amount of PSL, mg	1.5 ± 2.1	1.8 ± 2.2	0.73
DAS28-CRP	2.5 ± 0.7	2.9 ± 0.6	0.02*
CRP, mg/dl	0.4 ± 0.5	0.7 ± 0.7	0.10
Total PD score	2.4 ± 3.3	6.6 ± 6.1	0.01*
b.multivariate analysis	**odds ratio**	**95% CI**	**P-value**
DAS28-CRP	1.63	0.72 - 3.71	0.238
Total PD score	1.19	1.04 - 1.36	0.010*

Predictive performance of total PD score was good for radiographic progression of MCP joint (AUC-ROC 0.91) and wrist joint (AUC-ROC 0.85), although poor for PIP joint (AUC-ROC 0.57).
PD score of wrist joint, MCP joint, and PIP joint were significantly associated with radiographic progression of each joint (P<0.01). The sensitivity, specificity, positive predictive value, and negative predictive value of wrist joint PD score were 100%, 57.0%, 8.0%, and 100%, MCP joint PD score were 85.7%, 90.5%, 8.0%, 99.8%, and 8.3%, and PIP joint PD score were 30.0%, 97.2%, 13.6%, and 99.0%, respectively.
Conclusion: Total PD score of hands and wrists was a strong predictor of radiographic progression, especially in MCP and wrist joint. Evaluation of PD signal in individual joint is a clinically useful method to predict radiographic progression of the same joint, however there are some differences in sensitivity and specificity.

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Disclosure of Interests: Shunji Okita: None declared, Ryuichi Nakahara: None declared, Minami Matsuhashi: None declared, Masahito Watanabe: None declared, Yoshihisa Nasu: None declared, Keiichiro Nishida Grant/research support from: K. Nishida has received scholarship donation from CHUGAI PHARMACEUTICAL Co., Eisai Co., Mitsubishi Tanabe Pharma and AbbVie GK., Speakers bureau: K. Nishida has received speaking fees from CHUGAI PHARMACEUTICAL Co., Eli Lilly, Janssen Pharmaceutical K.K., Eisai Co. and AYUMI Pharmaceutical Corporation., Toshifumi Ozaki: None declared
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AB0217 IMPACT OF THE BODY-MASS-INDEX ON DISEASE ACTIVITY, FUNCTIONAL ABILITY AND QUALITY OF LIFE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Objectives: This study aims to assess differences in disease activity, functional ability and quality of life among underweight, normal weight, overweigth and obese patients with rheumatoid arthritis (RA).
Methods: 715 patients with RA (609 women and 106 men) were included in this study. According to their Body-Mass-Index, all patients were divided into four subgroups: underweight (BMI <18,5), normal weight (BMI between 18,5 and 24,9), overweight (BMI between 25,0 and 29,9) and obesitas (BMI ≥ 30,0). Mean values of DAS_{28}, CDAI and SDAI (measures of disease activity), HAQ-disability index (measure of functional ability) and RAQoL index (measure of qualitiy of life) were compared among four subgroups of patients.
Results: 28 (3,9%) RA patients were underweight, 310 (43,4%) had normal weight, 268 (37,5%) were overweight, whilst 109 (15,2%) patients were obese. Among these subgroups, no difference in mean age, disease duration, percentage of seropositive patients, and patients treated with glucocorticoids, csDMARDs or biologics, was noticed. There were no statistically significant differences in mean values of DAS_{28}, CDAI und SDAI in four subgroups of patients. However, mean value of the HAQ disability index was significantly higher ($p<0.05$) in underweight (1.32) and obese patients (1.27), compared to normal (0.87) and overweigth patients (1.08). The mean value of the RAQoL-Index was also somewhat higher in underweight and obese patients (8.8 and 8.1, respectively) than patients who are overweight or have normal weigth (7.0 and 6.5, respectively), but the difference was not statistically significant.
Conclusion: Underweight and obese RA patients have worse physical function than normal and overweight patients. However, worse disability can not be explained by higher disease activity.
Disclosure of Interests: None declared
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AB0218 FUNCTIONAL DISABILITY AND PAIN BUT NOT DISEASE ACTIVITY ARE ASSOCIATED WITH POOR HEALTH-RELATED QUALITY OF LIFE IN A COHORT OF RHEUMATOID ARTHRITIS PATIENTS

A. R. Prata[1], H. Assunção[1], M. Luis[1], L. Brites[1], F. Costa[1], J. Dinis de Freitas[1], S. Silva[1], J. A. P. Da Silva[1,2], C. Duarte[1,2] on behalf of 'Promoting Happiness Through Excellence of Care' Group. [1]*Centro Hospitalar Universitário de Coimbra, Rheumatology, Coimbra, Portugal;* [2]*Faculty of Medicine, University of Coimbra, Coimbra, Portugal*

Background: Rheumatoid Arthritis (RA) is a systemic autoimmune disease that presents with joint pain and inflammation leading to significant disability and poor health-related quality of life (HRQoL) (1,2). Optimizing long-term HRQoL is the primary goal of disease management in RA (3).
Objectives: To evaluate HRQoL and identify its influencing clinical and demographic factors in a Portuguese RA population.
Methods: This is a cross-sectional study including consecutive patients fulfilling the ACR/EULAR 2010 and/or ACR 1987 RA classification criteria, followed at a tertiary Rheumatology Department. Sociodemographic and clinical variables were collected. HRQoL was assessed using the EuroQoL 5-Dimensional Descriptive System (EQ-5D) total score (normal range from -0.496 to 1.000, lower values indicating poorer HRQoL). Independent t-test and Pearson's correlation coefficient were performed to evaluate EQ-5D differences between groups and examine its relationships with continuous variables, respectively. Variables with $p<0.1$ in univariate analysis were included in a stepwise multiple linear regression analysis to evaluate the independent association of variables with the EQ-5D score.
Results: 358 RA patients were included (80.20% female, mean age ± SD: 63.22 ± 0.66 years old). Mean EQ5D total score ±SD was 0.48 ± 0.01. Based on EQ-5D domains, 0.60% reported extreme problems with mobility, 3.40% extreme problems with self-care, 2.50% extreme problems with usual activities, 12.0% extreme pain or discomfort, and 7.30% extreme anxiety or depression symptoms (Fig. 1). There was a significant difference in EQ-5D scores between male (M=0.55, SD=0.24) and female gender (M=0.46, SD= 0.27); t (356) = -2.41, p=0.016. EQ-5D was weakly correlated with DAS-28-CRP (r=-0.32; $p<0.001$), moderately correlated with patient's global assessment of disease activity (r=-0.54; $p<0.001$) and pain-visual analogue scale (pain-VAS) scores (r=-0.58; $p<0.001$) and strongly with Health Assessment Questionnaire (HAQ) score (r=-0.72; $p< 0.001$). After multivariate analysis, HAQ-score (β=-0.57 [95% CI -0.24 to -0.17]; $p<0.001$) and pain-VAS ((β=-0.25 [95% CI -0.003 to -0.002]; $p<0.001$) remained as independent predictors of EQ-5D ($R2=0.56$, $p<0.001$).
Conclusion: Greater functional impairment and pain are associated with poor HRQoL in RA patients, and thus special attention must be given to treatment strategies providing the best patient-centred outcomes.
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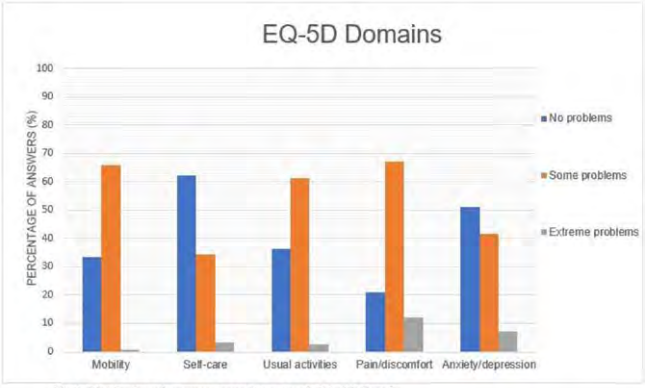


Fig.1. Distribution of answers according to each EQ-5D domain.

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AB0219 PREDICTIVE FACTORS FOR THE PROGRESSION OF EARLY INFLAMMATORY ARTHRITIS TO RHEUMATOID ARTHRITIS

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Objectives: To identify factors predicting the progression of early inflammatory arthritis (EIA) to rheumatoid arthritis (RA)
Methods: This was a prospective longitudinal study of inflammatory rheumatism that could not be classified according to defined rheumatism criteria. Demographic, biological, immunological and radiographic data were collected at the time of inclusion in the study. Disease activity as determined by the Disease Activity Score 28-CPR (DAS28-CPR: 4 variables), functional handicap as calculated by Heath Assessment Score (HAQ), and bone and joint damage as evaluated by Sharp-Van der Heijde (SVDH) score. ultrasound joint imaging were evaluated at the beginning of the study and then 1 year later. Logistic regression was performed to identify predictive factors for progression to RA.
Results: One hundred seventy two patients were included (24 men, 148 women), with an mean age 43.13±14.07 years and an mean time to diagnosis 10.24±6.84 months The mean ESR was 46.81±31.16 mm/1st hour, and the mean CRP level was 22.84±39.8 mg/l. Rheumatoid factors (RFs) and anti-citrullinated protein antibodies (ACPAs) were present in 48.8% and 53% of patients, respectively. The erosion, joint space narrowing, and total SVDH scores were 3.38±3.48, 5.08±3.32, and 5.95±4.94, respectively. One hundred sixty one patients were followed up for 12 months. Multivariate regression analysis showed that a DAS28-CRP level >5.2 (OR=28.6; CI95% 8.7-94.5), an RF level >60 IU/L (OR=11.2; CI95% 4.3-87.5), and an ACPA

level >60 IU/L (OR=5.4; CI95% 1.9-15.3) were predictive for progression to RA.

Conclusion: Our study suggests that clinical evaluation of EIA by DAS28-CRP from the time of diagnosis, as well as evaluating the presence of RA auto-antibodies, can predict progression to RA.

Disclosure of Interests: None declared

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AB0220 TENOSYNOVITIS AS THE PRESENTING FEATURE OF FLARE IN RHEUMATOID ARTHRITIS

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Background: The importance and relevance of tenosynovitis (TS) has long been recognised in rheumatoid arthritis (RA), but it is not usually considered in disease activity assessments. The significance of TS in early arthritis (EA) has also been recognised and, using ultrasound (US) it has recently been identified as a precursor to RA[1]. The ongoing BIO-FLARE (BIOlogical Factors that Limit sustAined Remission in rhEumatoid arthritis) observational study aims to investigate the pathogenesis of flare in RA. Patients with RA in remission stop their disease modifying anti-rheumatic drug medication (DMARDs: methotrexate, sulfasalazine and/or hydroxychloroquine) and are closely followed for 6 months, in anticipation that approximately 50% will experience a flare. We investigated whether TS occurrence was a frequent herald of flare in this cohort.

Objectives: To review the case notes of 49 patients in the BIO-FLARE study with confirmed flare to date, seeking evidence of US tenosynovitis prior to or concurrent with flare.

Methods: Patients in the study who are deemed to be in remission based on a disease activity score (DAS28-CRP) < 2.4 stop their DMARD medication and attend regularly for review over 6 months, with provision for ad-hoc appointments if symptoms return between visits. Patients are defined as having a flare if their DAS28-CRP ≥ 3.2 at any point or two consecutive DAS28-CRP ≥ 2.4. Targeted US assessment occurs at baseline only for patients that consent to an optional baseline ultrasound-guided synovial biopsy. If a flare occurs, US of symptomatic joints is undertaken, to assess suitability for a synovial biopsy. Following this, the patient receives a steroid injection and restarts their DMARD medication.

Results: To January 2020, 120 patients had been recruited into the study and 49 experienced a flare. Seven patients had a flare predominantly or initially characterised by TS or paratenonitis, the results of which are summarised in Table 1.

Table 1. Tenosynovitis in BIO-FLARE

	DMARD stopped	Time to TS, weeks	Tendon involved	Time to flare, weeks	Joints involved
1	Methotrexate, sulfasalazine, hydroxychloroquine	12	Extensor carpi ulnaris	12	Shoulders and PIPJs, no synovitis suitable to biopsy
2	Methotrexate	7	Bilateral extensor carpi ulnaris	7	Shoulders, wrists, knees, PIPJ with no accompanying synovitis
3	Methotrexate	5	Tibialis posterior	5	No joints flared, no synovitis but treated as a flare due to severity of TS
4	Methotrexate	8	Tibialis posterior – attributed to increase in patient activity	22	MCPJ, PIPJs, mid tarsal and MTPJ
5	Methotrexate and hydroxychloroquine	7	Extensor policis longus	8	Polyarticular flare
6	Methotrexate and hydroxychloroquine	2	Extensor carpi ulnaris – attributed to overuse	6	Polyarticular flare
7	Methotrexate	12	Extensor paratenonitis at PIPJ4 & 5	12	MCPJ synovitis

Conclusion: Although highlighted as a precursor of RA in early arthritis[1], the occurrence of TS in the context of flare – and the prodrome heralding this – has not been studied. Our findings show that TS in early flare is reminiscent of the features sometimes seen in EA or clinically suspect arthralgia[2]. Further data are required to determine the role of periarticular inflammatory phenomena, such as TS, as risk factors for joint synovitis. Our study did not entail formal US assessments, therefore the rate of TS in this population may be under estimated. Careful study of RA patients in early phase of disease flare may pose an opportunity to characterise the nature and chronology of this association in greater depth.

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[1]Sahbudin I et al. Rheumatology. 2018;57(7):1243-1252

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AB0221 ULTRASOUND ASSESSMENT OF INFLAMMATORY ARTHRALGIA: PREDICTORS FOR CHRONIC ARTHRITIS DEVELOPMENT

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Background: Inflammatory arthralgia (IA) onset is a common rheumatology consultation. Identifying predictors for chronic arthritis (CA) development by ultrasonography (US) may provide early diagnosis and treatment in order to prevent progression of the disease.

Objectives: Establishing US findings that can be related to CA development in patients with inflammatory arthralgia without arthritis. Assess the link among US, clinical and biochemical parameters.

Methods: A prospective longitudinal study of a cohort of patients with IA. Patients with less tan one year of AI evolution and involvement of at least one small joint from hands or feet were included. Patients with arthritis, osteoarthritis, fibromyalgia and those treated with DMARDs or steroids were excluded. We made a 6-monthly evaluation for 2 years and recorded the CA development during that period. The number of painful joints (PJC) and biochemical data (CRP, ESR) were assessed at the first visit. A blind US exploration was made using a MyLabTwice (Esaote) equipment with a 5-13MHz probe for greyscale (GS) and Power Doppler (PD), examining 36 joints (radio-carpals, MCP, IPP, 2nd-5th MTP, elbows, shoulders and knees) and 14 tendon compartments (2nd, 4th and 6th wrist extensors, 3rd and 4th finger flexors and posterior tibial and fibularis tendons), giving an overall score of GS, PD (0-3) and number of erosions by rating the presence of sinovitis on each location.

We performed a descriptive analysis based on the frequencies of qualitative variables and mean±SD/median (IQR) of quantitative variables, comparing the characteristics between patients with and without CA progression by Chi-Square and Mann-Whitney U tests. Also, the possible relationship of those variables and the disease progression was assessed by a univariate binary logistic regression analysis.

We designed a reduced US examination (RUE) selecting the most affected locations and those with greatest differencies between groups in the statistical analysis.

Results: Of the 49 patients included, 21 (42.9%) progressed to CA. 87% were females and 71.4% non-smokers with a mean age of 44 ± 12 years. The median of PJC was 4 (1-9). RF and/or CCPA were positive in 18.4% and 34.7% had high CRP/ESR. The suggested RUE included carpi, 2nd-4th MCP, 2nd-3rd IPP, 2nd and 5th MTP, 4th and 6th wrist extensors and fibularis tendons. Scores and comparative analysis within subgroups are listed in Table 1. The RUE score was significantly greater in both GS (OR 1.4, CI 95%) and PD (OR 1.3, CI 95%) on patients that progressed to CA.

Table 1. GS and PD scores compared by main locations and RUE-Score [showed as median (IQR)].

Score	No progression (n=28)	Progression to IA (n=21)	P
GS global	5.5 (2-11)	11 (7-15)	0.005*
PD global	2 (1-3.25)	6 (2-10)	0.002*
ERO global	0 (0-0)	0 (0-0)	0.59
Carpi GS	1 (0-2)	3 (2-3)	0.002*
Carpi PD	1 (0-2)	1 (0-3)	0.16
MCP GS	1 (0-3.25)	2 (0-5)	0.08
MCP PD	0 (0-1)	1 (0-2)	0.03*
IPP GS	0 (0-1.25)	2 (0-3)	0.03*
IPP PD	0 (0-0.25)	0 (0-1)	0.3
MTP GS	0.5 (0-3)	2 (0-7)	0.08
MTP PD	0 (0-0)	0 (0-1)	0.02*
Wrist extensors GS	0 (0-0)	0 (0-1)	0.1
Wrist extensors PD	0 (0-0)	0 (0-0)	0.01*
Fibularis GS	0 (0-0)	0 (0-0)	1
Fibularis PD	0 (0-0)	0 (0-0)	0.06*
RUE GS	5 (2-6.25)	7 (5-10)	0.01†
RUE PD	2 (1-3.5)	5 (2-7)	0.01†

* Medians compared by Mann-Whitney U test. Statistical significance at a 95% CI. † Logistic regression analysis. Statistical significance at a 95% CI.

There were no significant associations between RF/CCPA positivity or CRP/ERS levels and US findings.

Conclusion: Patients with IA without arthritis that progressed to CA had significant higher GS and PD scores, hence showing the utility of US to predict disease progression. A RUE of 8 joints and 3 tendon compartments could be enough to achieve this goal.

Disclosure of Interests: Pablo Rodríguez-Merlos: None declared, Diana Peiteado: None declared, Irene Monjo: None declared, Laura Nuño: None declared, Alejandro Villalva: None declared, Marta Novella-Navarro: None declared, Torres Jenny Gabriella: None declared, Maria-Eugenia Miranda-Carus Grant/research support from: BMS, Roche, Paula Fortea-Gordo Grant/research support from: BMS, Eugenio de Miguel Grant/research support from: Yes (Abbvie, Novartis, Pfizer), Consultant of: Yes (Abbvie, Novartis, Pfizer), Paid instructor for: yes (AbbVie, Novartis, Pfizer, MSD, BMS, UCB, Roche, Grunental, Janssen, Sanofi), Speakers bureau: yes (AbbVie, Novartis, Pfizer, MSD, BMS, UCB, Roche, Grunental, Janssen, Sanofi), Alejandro Balsa Grant/research support from: BMS, Roche, Consultant of: AbbVie, Gilead, Lilly, Pfizer, UCB, Sanofi, Sandoz, Speakers bureau: AbbVie, Lilly, Sanofi, Novartis, Pfizer, UCB, Roche, Nordic, Sandoz

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AB0222 HEALTH STATE UTILITY VALUES IN RHEUMATOID ARTHRITIS BY SEX, AGE AND DISEASE ACTIVITY: REFERENCE DATA FROM A COLOMBIAN COHORT OF 1,545 PATIENTS

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Background: As the basis for quality-adjusted life years (QALYs) calculation, health state utilities are essential for health technology assessment and economic evaluation.

Objectives: To provide a reference value set of health state utility for patients with rheumatoid arthritis.

Methods: A cross-sectional study was conducted in 1,545 patients diagnosed with rheumatoid arthritis. Disease activity was evaluated with the DAS-28 score. Health state utility (HSU) was estimated with the EUROQOL-5D-3L, using as reference the Spanish-speaking Hispanic predicted preference weights for 243 EQ-5D health states. Mean HSU differences were analyzed with the generalized linear model. A p-value <0.05 was considered statistically significant.

Results: Patients mean age was 58.2 years (SD = 12.5), 82.4% were female. Disease activity was high in 137 (8.9%), moderate in 305 (19.7%) and low in 231 (56.4%) patients; 872 (56.4%) patients were in remission. HSU differed significantly by sex age and disease activity. Figures 1a (women) and 1b (men) shows the HSU by age and disease activity.

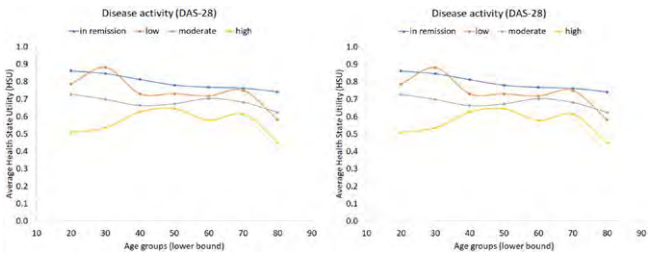


Figure 1. Health State utilities by sex, age and disease activity

Conclusion: The way patients value different health states according to their sex, age and disease activity must be considered in health technology assessment and economic evaluations of interventions for rheumatoid arthritis patients. We provide a reference set for Latin-American patients.

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Disclosure of Interests: None declared

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AB0223 PHYSICIAN'S GLOBAL ASSESSMENT OF DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS IS A RELIABLE AND RESPONSIVE TOOL IN CLINICAL PRACTICE

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Background: Physician's global assessment of disease activity (PhGA) is highly influential upon treatment decisions taken by rheumatologists, surpassing the impact of DAS28. [1, 2]. However, data regarding its psychometric properties are scarce.

Objectives: To evaluate the reliability and responsiveness of PhGA.

Methods: We included two consecutive visits of RA patients followed in a Tertiary Rheumatology Department. Socio-demographic (age and gender) and clinical data were collected including tender (TJ28) and swollen (SJC28) joints in 28 count, C-Reactive Protein (CRP), Erythrocyte Sedimentation Rate (ESR), Disease activity Score (DAS28-3v-CRP, DAS28-3v-ESR, DAS28-4v-CRP, DAS28-4v-ESR), PhGA and Patient Global Assessment of disease Activity (PGA) through a Visual Analogic Scale (VAS) 0-100mm. Changes (Δ) between the two visits were calculated. Only patients without missing data were included. Correlations between ΔPhGA and change of other variables were assessed using Pearson's correlations. Reliability was evaluated through Intraclass Correlation Coefficient (ICC) between two consecutive appointments in a subgroup of patients with stable disease activity (Δ DAS28-4vESR [-0.6 to 0.6]. An ICC above 0.8 was considered indicative of excellent reliability. Sensitivity to change was assessed in the subgroup of patients who improved their disease activity at least 0.6 on DAS28-4V-ESR, through Standardized Response Mean (SRM). The respective intervals of confidence were obtained through bootstrapping procedures. SRM above 0.8 were considered large. Independent factors associated with ΔPhGA were identified through multivariate linear regression analysis. p<0.05 was considered statistically significant

Results: 121 RA patients (84.3% female and 64.0±12.6 years) were included. Δ PhGA was weakly correlated with ΔCRP (r=0.23), Δ PGA (r=0.31) and Δ pain (r=0.37). Moderate to strong correlations were observed with Δ DAS28-3V-ESR (r=0.55), Δ SJC28 (r=0.56), Δ DAS28-3V-CRP (r=0.58), Δ DAS28-3V-CRP (r=0.60), Δ TJ28 (r=0.62) and Δ DAS28-4V-CRP (r=0.63). ICC between two consecutive visits was 0.7, [95%CI:0.47-0.83] and SRM was -1.01 [95%CI:-1.26-(-0.73)]. In the multivariate regression analysis, ΔSJC28 (β=4.01; 95% CI:3.07 to 4.96) and Δ Pain (β=0.18; 95%CI: 0.07 to 0.28) remained as independent factors associated with ΔPhGA (R2:0.49, p<0.01)

Conclusion: In this study, PhGA showed a high reliability and sensitivity to change regarding disease activity, in clinical practice. Changes in SJC had the strongest association with change in PhGA scoring, but Δ Pain was also significantly correlated (graph 1).

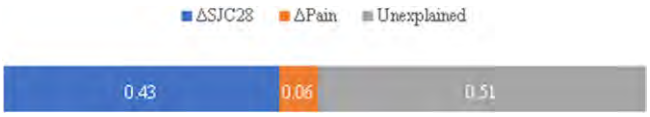


Figure 1. Graph 1 – Explicative model to variations on PhGA

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AB0224 ASSOCIATIONS BETWEEN JOINT REPLACEMENT HISTORY AND CYCLIC CITRULLINATED PEPTIDE ANTIBODY TITERS IN RHEUMATOID ARTHRITIS PATIENTS

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Background: High titers of cyclic citrullinated peptide antibodies (anti-CCP) are predictive of poor prognosis in the treatment of rheumatoid arthritis (RA). The 2010 ACR/EULAR classification criteria for early RA assign a high point value to cases having highly positive anti-CCP titers. Previous reports have claimed that osteoarthritic damage is more severe and advanced in RA patients who test positive for anti-CCP than in their negative counterparts.
Objectives: To retrospectively investigate whether anti-CCP titers were associated with the extent of osteoarthritic damage in RA patients treated at our institution.
Methods: Data were analyzed for 422 RA patients who received biologic agents due to resistance to methotrexate or other conventional antirheumatic drugs. Associations were explored between joint replacement history-i.e. total knee replacement (TKR), total hip replacement (THR), or lack thereof—and anti-CCP positivity rates and titers.
Results: The sample consisted of 90 men and 332 women. On average, patients were put on biologics at 58.6 years of age (range: 22–85), and had a disease duration of 9.3 years. The first biologic agent chosen was infliximab (IFX) in 154 cases, etanercept (ETN) in 76, adalimumab (ADA) in 61, tocilizumab (TCZ) in 70, abatacept (ABT) in 41, golimumab (GLM) in 18, and certolizumab pegol (CZP) in 2. In total, 331/422 patients (78.4%) tested positive for anti-CCP. TKR was performed in 46 cases (M:F ratio: 7:39, mean age: 64.7 y, mean disease duration: 15.1 y), of which 46 were positive for anti-CCP (100%). THR was performed in 18 cases (M:F ratio: 2:16, mean age: 62.3 y, mean disease duration: 18.5 y), of which 17 were positive for anti-CCP (94.4%). The mean anti-CCP titer among all positive patients (n=331) was 152.9 IU/ml. This value was significantly higher in patients who underwent either joint replacement procedure than those who did not (215.4 v. 142.8 IU/ml, p<0.0005).
Conclusion: With one exception, all RA patients who underwent joint replacement were positive for anti-CCP, and their titers were higher than non-surgical cases. Practitioners should be aware of this trend, and pay attention to the progression of damage in the knee and hip joints when treating RA patients with high anti-CCP titers.
Disclosure of Interests: None declared
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AB0225 THE NATURAL COURSE OF EARLY RA WITH LATE ONSET IN EVERYDAY CLINICAL PRACTICE ACCORDING TO THE RUSSIAN RA PATIENT REGISTER OREL

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Background: The opinion about the severity and prognosis of rheumatoid arthritis (RA) with late onset balanced between more favorable and more severe over various periods of rheumatology development. We studied this group of patients according to the Russian RA Patient Register OREL.
Objectives: To study clinical, laboratory and radiological characteristics in patients with early RA with late onset of the disease (50 years and older) who are DMARD (disease modifying antirheumatic drugs), biological DMARD and glucocorticoid (GC) (systemic administration) – naive.
Methods: All patients were included in the OREL register in the period from 01.01.2014 to 12.31.2018. There were 151 patients in the study (M:41, W:110; average age 60 ± 7.0 years). There were 73 patients (48%) with the duration of RA up to 3 months, 45 (30%) - 4-6 months, 33 (22%) - 7-12 months. The ratio of men and women was only 1: 2.8 (50 -64 years = 1:3.8; 64 years and older = 1: 1.8).
Results: 99/151 (66%) patients had high disease activity (according to DAS-28), 52/151 (34%) – medium activity.
22/151 (15%) patients had II functional class (FC), 103 (68%) – III FC, 26 (17%) – IV FC.
Table 1 illustrates that with an increase in the duration of the disease, a gradual increase in the frequency of detection of radiological erosion in the hands and distal parts of the feet is noted: 1.5 - 3 months - 33/73 (45%) patients; 4-6 months - 22/45 (49%) patients and in the period 7-12 months - 23/33 (70%) patients.

Table 1. X-ray Stage and RA duration

X-ray Stage		Duration of disease (months)					
		<3	4	5	6	7-12	Total
Non Erosive RA	I	11(1*)	6(1*)	3(1*)	1	5	26(3*)
	II	29(1*)	5	5	3	5	47(1*)
Erosive RA	II	31	8	7	4	20	70
	III	2	1	1	1	3	8
	IV	-					
Total		73(2*)	20(1*)	16(1*)	9	33	151(4*)

* - Erosion according to MRI of the hands

Table 2. illustrates higher incidence of joint erosions in the presence of RF and / or anti-CPA antibodies (ACPA) compared to patients who are seronegative for RF and ACPA. Таблица 2. X-ray-Stage and RF and ACPA Detection Frequency

X-ray-Stage	The frequency of RF and ACPA detection			
	RF (+) ACPA (+)	RF (+) ACPA (-)	RF (-) ACPA (+)	RF (-) ACPA (-)
Non-erosive RA: Stages I and II	30%	20%	22%	58%
Erosive RA: II, III and IV stages	70%	80%	78%	42%

The frequency of RF and ACPA detection in non-erosive patients, in all patients with radiological erosion and in patients with advanced stages only (III and IV) was 67% (RF) -78% (ACPA), 75% -90% and 100% -100%, respectively.

Conclusion: Everyday clinical practice (OREL register) shows that in patients aged 50 years and older with early clinical stage of RA who are naive about the treatment of DMARD, biological DMARD and GC, the detection of RF, ACPA and erosive changes in the joints are often observed in the onset of the disease. RF and ACPA are markers of early joint destruction.
Disclosure of Interests: None declared
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AB0226 USING 3 TESLA MRI WITH A HIGH-RESOLUTION 16-CHANNEL HAND COIL TO DIFFERENTIATE BETWEEN RHEUMATOID AND PSORIATIC ARTHRITIS: A PILOT STUDY

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Background: The differentiation between rheumatoid arthritis (RA) and psoriatic arthritis (PsA) is sometimes a challenge for rheumatologists in daily clinical practice. Imaging techniques such as MRI could be a helpful tool for this purpose.
Objectives: To examine the value of 3 Tesla (T) magnetic resonance imaging (MRI) with a high-resolution 16-channel hand coil for the differentiation between RA and PsA.
Methods: A total of 17 patients with active PsA and 27 patients with active RA were evaluated by 3T MRI. Images were analyzed by three readers according

to the outcome measures for RA clinical trials (OMERACT) and RA and PsA MRI scores for the presence and intensity of the following MRI features: synovitis, flexor tenosynovitis, bone edema, bone erosion, periarticular inflammation, bone proliferation, and joint space narrowing. A receiver operating characteristics (ROC) curve was established for a calculated prediction model comprising age, gender, and the imaging features 'periarticular inflammation' and 'erosion' of the metacarpophalangeal (MCP) joint of the 5th finger.

Results: PsA could be differentiated from RA by extracapsular inflammatory changes (PsAMRIS sub-score 'periarticular inflammation'), with a minimal odds ratio (OR) for the outcome 'not RA' of 0.06 ($p < 0.01$) at all MCP joints. The calculated ROC curve had an area under the curve (AUC) of 98.1%.

Conclusion: 3T MRI showed a strong association of extracapsular inflammatory changes with PsA at the MCP joint level, and consequently allowed differentiation between PsA and RA.

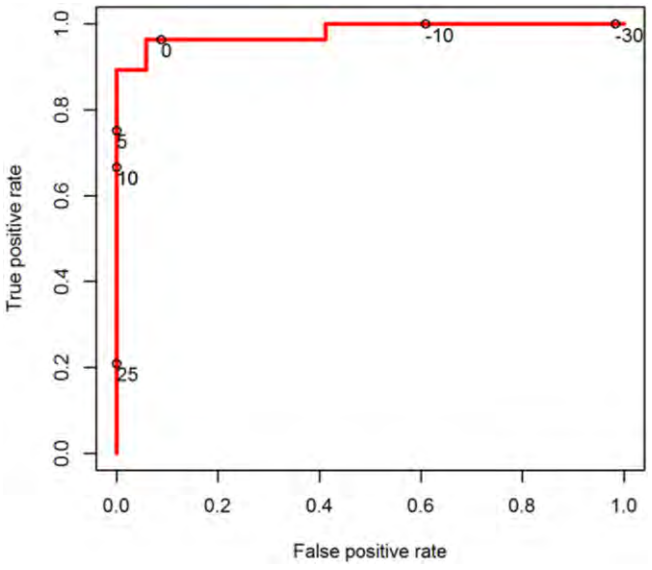


Figure 1. Receiver operating characteristics (ROC) curve with different thresholds for the calculated prediction model for the outcome RA. Area under the curve (AUC) = 98.1%.

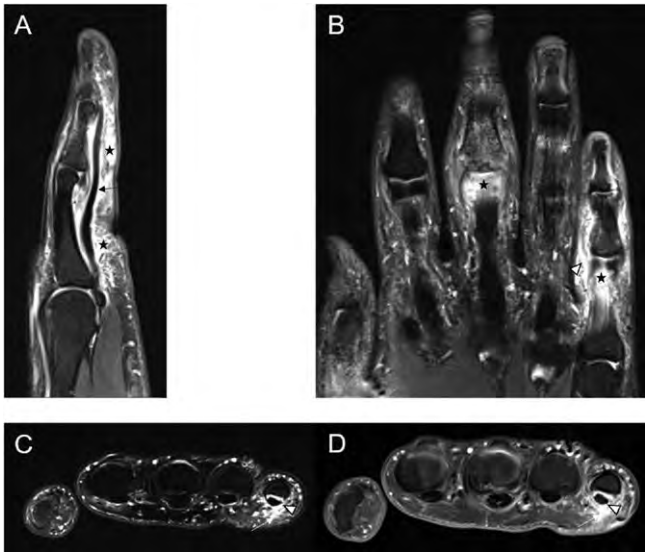


Figure 2. 51-year-old female patient with PsA. MR images show flexor tenosynovitis (FS), synovitis (Syn), and periarticular inflammation (PI). A. Sagittal PD fat-saturation of D5. PI at the volar and dorsal aspects at the MCP, PIP, and DIP levels. FS at the PIP and DIP joint levels. Black asterisks indicate PI. Black arrow points to FS. B. Coronal STIR with bone edema (BE) at the proximal portion of PIP3 and 5 accompanied by PI at PIP3 and MCP, PIP and DIP5. Asterisks indicate BE. Arrowheads point to PI. C. Transversal T2 fat-saturation with FS and PI at MCP5. Arrowhead indicates FS, arrow points to volar PI. D. Transversal T1 fat-saturation following iv contrast, with FS and PI at MCP5. Arrowhead indicates FS, arrows points to volar PI.

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AB0227

BASELINE SYNOVIAL LEVELS OF MATRIX METALLOPROTEINASES-9 IN EARLY RHEUMATOID ARTHRITIS-THE ASSOCIATION WITH INITIAL RADIOGRAPHIC CHANGES

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Background: Matrics metalloproteinases (MMPs) are the key enzymes responsible for the joint destruction in rheumatoid arthritis (RA).

Objectives: The aim of this study was to examine the association of baseline levels of metalloproteinases-9 (MMP-9) in serum and synovial fluid (SF) with structural damage of hand and feet joints in patients with early RA and also with imunoserological markers of the disease.

Methods: The study enrolled 134 subjects with knee synovitis: 72 patients with early DMARD-naïve RA (symptom duration ≤12 months) and 62 patients with osteoarthritis (OA), as control group. Synovial fluid was obtained by an arthrocentesis of the knee joint. Joint damage was estimated by hands, knee and feet radiography. With regard to the presence of destructive joint changes on initial x-ray, RA patients were classified as erosive and nonerosive form of disease. ELISA assay was used for the detection of MMP–9 activity in serum and SF as well for the imunoserology tests: rheumatoid factor RF (IgG) and anti-CCP antibody (ACPA).

Results: MMP–9 activity in serum and SF of RA patients was significantly higher compared to its activity in serum and SF of control group ($p<0.01$ and $p <0.001$ respectly) (table 1).

Table 1. MMP–9 activity (ng/ml) in serum and SF of RA and control group patients

Group	MMP-9 activity in BP (ng/ml); mean±SD	MMP-9 activity in SF (ng/ml) mean±SD
RA (n=72)	18.28±7.54**	15.07±13.24***
Controls -OA (n=62)	13.58±3.07	0.65±0.41

RA – rheumatoid arthritis; SD – standard deviation; n – number of subjects; ** – p<0.01, *** p<0,001

We did not establish a significant correlation between the activity of MMP 9 in serum and SF in the RA and control groups (Spearman's rank correlation coefficient in RA was 0,02 and 0,06 in control group).

Most of the subjects from RA group (52–72.22%) had verified radiographic erosive changes in joints. Nonerosive arthritis was present in remaning 20 (27.78%) of RA patients. No differences were obtained according to the sex, age or disease duration between erosive and nonerosive RA patients.

Table 2 represents MMP–9 activity in serum and SF of patients with erosive and nonerosive RA. The values of MMP–9 activity measured in serum were higher in nonerosive compared to erosive RA (20.35±10.30 vs. 17.46±6.25), but the difference was not statistically significant ($p>0.05$). However, MMP–9 activity in SF

was significantly higher in erosive compared to nonerosive RA (17.53±12.87 vs. 8.76±7.72; p<0.05).

Table 2. MMP–9 activity (ng/ml) in serum and SF of patients with erosive and nonerosive RA

MMP-9 activity	Erosive RA (n=52) [ng/ml]	Nonerosive RA (n=20) [ng/ml]
Serum	17.46±6.25	20.35±10.30
Synovial fluid	17.53±12.87*	8.76±7.72

RA – rheumatoid arthritis; SD – standard deviation; n – number of subjects; * p<0.05;

We also examined the correlation of MMP 9 activity in serum and SF with standard imuno serological markers of disease (RF and ACPA). Our results indicate that there is a significant correlation of MMP 9 activity in SF with ACPA level in RA group (Spearman's rank correlation coefficient is 0,48), but not with RF (Spearman's rank correlation coefficient is 0.06).

Conclusion: MMP–9 activity in serum and synovial fluid of patients with early RA is significantly higher compared to patients with osteoarthritis. High activity of MMP–9 in synovial fluid of patients with early RA correlated with ACPA level and may be a predictor of rapid radiographic progression of disease.

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Disclosure of Interests: None declared

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AB0228 **COMPREHENSIVE RHEUMATOID HAND ASSESSMENT THROUGH PATTERN OF DEFORMITIES USING CLUSTER ANALYSIS**

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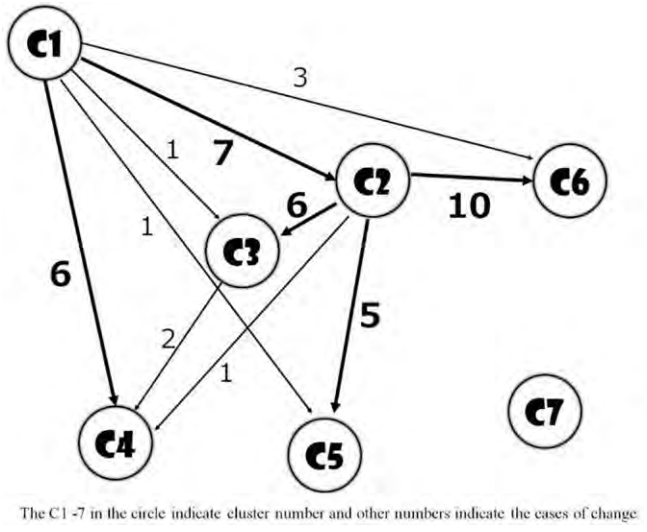
Background: The treatment of rheumatoid hand, which is characterized by thumb deformity, finger deformities, and ulnar drift (UD), is challenging. Its pathophysiology is complex, and a comprehensive understanding of the optimal intervention for this condition requires high technical skill and extensive clinical experience. Moreover, the natural course of rheumatoid hand itself remains unclear.

Objectives: This study was performed to comprehensively evaluate rheumatoid hand through the specific parameters of each deformity.

Methods: A rheumatoid hand cohort was established in 2004. In total, 134 hands of 67 patients were registered and underwent clinical evaluations. All hands surgically treated during follow-up were excluded from the study, but the contralateral hands were assessed. Evaluations were repeated in 2009 (100 hands of 52 patients) and in 2015 (63 hands of 37 patients) among all available patients. Therefore, among the data obtained from the 3 study endpoints, 297 hands were available for the cross-sectional analysis and 43 hands were available for the longitudinal analysis. Thumb deformities and finger deformities (swan-neck and boutonnière) were semi-quantitated by the Nalebuff classification score, and UD was quantified using a metacarpophalangeal joint condition scoring method[1)]. A two-step cluster analysis was performed with entered parameters, and the distribution of each parameter was considered to clarify the characteristics of each cluster. The hands with different clusters at each endpoint were recruited for the following longitudinal analysis. The natural course of rheumatoid hand was considered based on the cluster change.

Results: Seven clusters were used in this study to emphasize the impact of thumb deformity on function. The characteristics of each cluster were as follows. Cluster 1: mild finger deformities and various severities of UD; Cluster 2: type 1 thumb deformity and various severities of UD; Cluster 3: type 2 thumb deformity and severe UD; Cluster 4: type 3 or 4 thumb deformity, low or moderate level of swan-neck deformity, and various severities of UD; Cluster 5: various types of thumb deformity, severe boutonnière deformity, and various severities of UD; Cluster 6: type 1 thumb deformity, severe swan-neck deformity, and various severities of UD; and Cluster 7: type 6 thumb deformity.

The longitudinal analysis showed that Cluster 1 mainly changed to Cluster 2 or 4, indicating progression of thumb deformity. Cluster 2 changed to Cluster 3, indicating that thumb type 1 progressed to type 2 (Figure 1). When the affected period was shorter than 10 years, the incidence of severe hand deformity (including two or more affected joint areas and low hand function) was <10%. In contrast, when the affected period was longer than 10 years, the incidence of severe hand deformity was >30% (Figure 2).



The C1 -7 in the circle indicate cluster number and other numbers indicate the cases of change.

Figure 1.

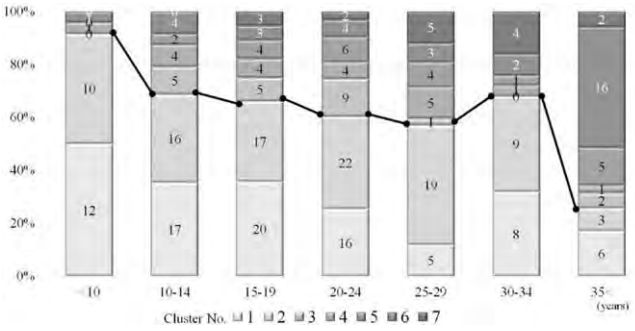


Figure 2.

Conclusion: This study suggests the presence of seven patterns of deformity enabling a comprehensive understanding of rheumatoid hand. Furthermore, the results of the longitudinal analysis suggest a natural course of rheumatoid hand progression. Therefore, from the distribution of parameters of each deformity and its severity, rheumatologists can easily classify rheumatoid hand and determine its pathophysiology to choose the most effective intervention.

References:

[1] Toyama S, Oda R, Tokunaga D et al. A new assessment tool for ulnar drift in patients with rheumatoid arthritis using pathophysiological parameters of the metacarpophalangeal joint. Modern rheumatology 2019, 29: 113-8.

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AB0229

SHORT-TERM EXPOSURE TO OUTDOOR AIR POLLUTANTS AND RHEUMATOID ARTHRITIS ACTIVITY IN METROPOLITAN AREAS IN THE NORTH OF ITALY

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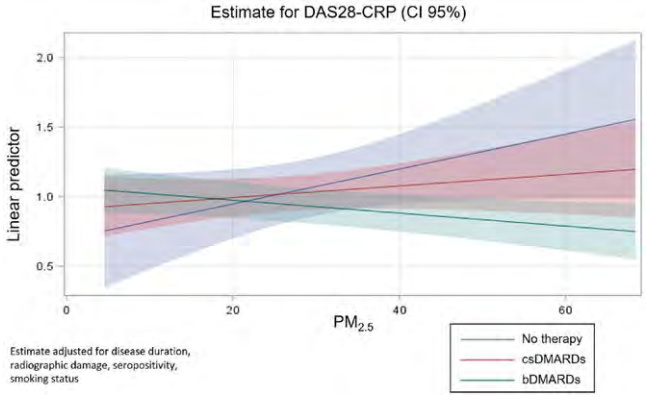
Background: Air pollution is believed to cause oxidative stress and systemic inflammation, that could trigger autoimmunity in rheumatoid arthritis (RA). Several epidemiological studies investigated the possible role of air pollution in the outbreak of RA with controversial results. As far as we know, studies on the effects on disease activity of short-term exposure have not been published.

Objectives: To evaluate the impact of short-term exposure to air pollutants (daily mean PM_{10}, $PM_{2.5}$, NO_2 and O_3) on disease activity in patients with RA.

Methods: Consecutive patients with RA (ACR/EULAR Criteria 2010) resident in Lombardy (Italy) were enrolled. In each patient Disease Activity Score on 28 joints (DAS28), Simple Disease Activity Index (SDAI) were assessed. Daily PM_{10}, $PM_{2.5}$, NO_2 and O_3 concentrations, estimated by Regional Environmental Protection Agency at municipality resolution, were used to assign short-term exposure from day of visit back to 14 days. Multivariable linear regression models were performed to identify the day of the pollutants independently associated with disease activity indices, adjusting for the variables significant at the univariate analysis. β coefficients were reported for 1 $\mu g/m^3$ increments of pollutants' concentrations.

Results: 422 RA patients were enrolled in the study between January and June 2018: 81.5% females, mean age 58.2±13.3 years, mean disease duration 16.1±11.5 years, 27.3% current smokers, 59.5% RF positivity, 54.5% ACPA positivity. Sparse punctual statistically significant negative associations emerged at the multivariate analysis between PM_{10}, $PM_{2.5}$, NO_2 and the outcomes, although with very low estimates, whereas positive associations resulted for O_3.

Afterwards patients were stratified in 3 subgroups according to their ongoing treatment (no therapy, n=25, conventional synthetic Disease Modifying anti-Rheumatic Drugs -DMARDs-, n=108 and biological or targeted synthetic DMARDs, n=289). A statistical significance was found by analysing the influence of therapy on the interaction between $PM_{2.5}$ and DAS28 (Figure below): a positive trend between $PM_{2.5}$ and DAS28 appeared in the first two groups (no therapy, 0.013±0.007, p=0.06 and csDMARDs, 0.006±0.004, p=0.17), whereas a statistically significant inverse association was seen in the b/tsDMARDs group (-0.005±0.002, p=0.01). Therapy interaction was particularly evident in several days before the visit also for O_3.



Conclusion: The changes of the outcome measures related to the increase of the pollutants' levels did not reach the minimal clinically important difference, therefore air pollution seems barely relevant on disease activity once the loss of tolerance is established in RA. O_3 and PM/NO_2 always exhibit an opposite performance having inversely proportional atmospheric concentrations, whereas the biological role of this substance is still matter of debate and will need further understanding. Therapy seems to be able to interact with the relation between air pollutants and the parameters considered.

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AB0230

STATINS TO PREVENT RHEUMATOID ARTHRITIS: INCONCLUSIVE RESULTS OF THE STAPRA TRIAL

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Background: Persons at high risk for developing rheumatoid arthritis (RA) may benefit from a low-risk pharmacological intervention aimed at primary prevention. Statins are safe and widely-used drugs; previous studies demonstrated disease-modifying effects of statins in RA patients[1] as well as an association between statin use and a decreased risk of RA development[2].

Objectives: We designed a multi-center, randomized, double-blind, placebo-controlled trial to investigate if atorvastatin use for 3 years could prevent arthritis.

Methods: Persons at high risk for RA, defined by the presence of arthralgia and anti-citrullinated protein antibody (ACPA) concentration >3xULN or both ACPA and rheumatoid factor (RF), were randomized to atorvastatin 40 mg daily or placebo for 3 years. Eligible participants were ≥18 years, had no indication for lipid-lowering therapy and had no clinical synovitis. The primary endpoint was development of clinical arthritis. Our goal was to include 220 patients, based on an anticipated 30% risk reduction by atorvastatin. Analysis was by intention-to-treat.

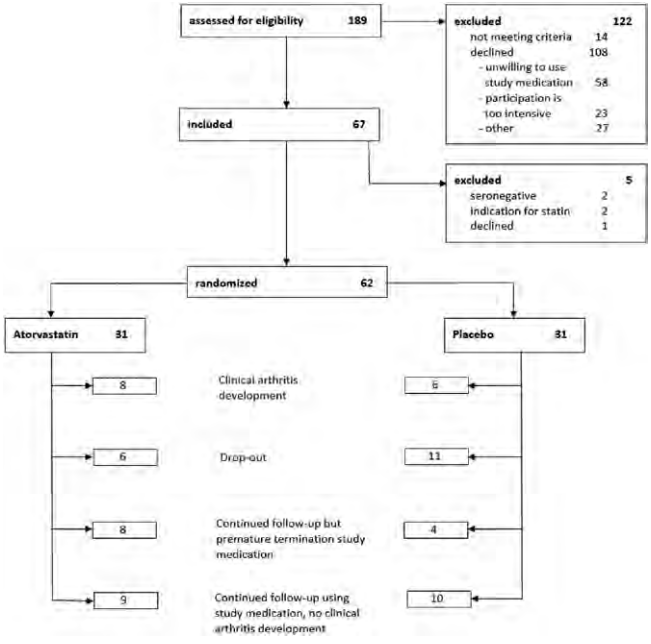
Results: 189 patients were screened, 175 were eligible, but only 67 persons were included of whom 62 were randomized (figure 1). The main reason for non-inclusion was unwillingness to use study medication (n=58, 54%). Inclusion was stopped after 38 months due to the low inclusion rate. Analyses were performed 1 year after inclusion stop. Mean follow up was 18 (0-36) months. Mean age was 48 years and 74% of participants were female. 14 persons (23%) developed clinical arthritis: 8/31 (26%) in the atorvastatin group and 6/31 (19%) in the placebo group (HR 0.8, 95% CI 0.3-2.2) after a median period of 7.5 (IQR 5.3-21.8) months (atorvastatin) and 4 (0-14.8) months (placebo). In the atorvastatin group, 17 persons completed the study according to protocol, 6 dropped out and 8 continued follow-up after prematurely stopping study medication. In the placebo group, 16 persons completed the study according to protocol, 11 dropped out and 4 continued follow-up after prematurely stopping study medication. Median duration of study medication use was 9 (6-26) months (atorvastatin group) and 8 (3-17) months (placebo group).

Conclusion: The results of this trial are inconclusive due to severe difficulties with patient inclusion and low treatment adherence. The difficulty to enter and retain participants in this prevention trial is highly relevant given the current interest in treating RA in an ever earlier phase. At-risk individuals' perceptions should be taken into account when designing preventive trials and will be important in optimizing acceptance and adherence to preventive treatment. Currently we are finalizing research into the motivation and barriers for participation in different primary prevention trials of RA and the willingness to initiate different types of preventive treatment in individuals in the at-risk phase of RA.

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[1] McCary et al. Lancet. 2004; 19;363(9426):2015-21

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AB0231 RHEUMATOID ARTHRITIS PATIENTS TREATED WITH ABATACEPT AT A COMMUNITY RHEUMATOLOGY CLINIC AND WHO ARE POSITIVE FOR ANTICYCLIC CITRULLINATED PEPTIDE ANTIBODIES HAVE MORE SUSTAINED CLINICAL RESPONSES THAN PATIENTS NEGATIVE FOR THE MARKER

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Background: Treating Rheumatoid Arthritis (RA) patients to target (T2T) has been shown to result in better outcomes in patients with RA [1]. There are now a number of therapeutic options to accomplish this goal, but determining which agent to select for each individual has not been defined.
Objectives: The purpose of this post hoc analysis was to assess if Anticyclic Citrullinated Peptide Antibody (anti-CCP) status effects outcomes following treatment of RA patients with Abatacept.
Methods: Patients at a community based rheumatology clinic undergo disease activity measure assessments on a routine basis as part of the implementation of T2T strategy with ongoing assessments on at least a yearly basis. Over the past 15 years there have been 78 patients initiated on treatment with Abatacept at this clinic. Anti-CCP and Rheumatoid factor status is routinely obtained when patients are first seen in the clinic. A patient was considered to be Anti-CCP positive if the test was 20 u/ml or greater. As a comparison, the 53 patients in the clinic started on Tofacitinib were also analyzed.
The difference in sustained clinical response rates between seropositive and seronegative patients were determined for these two groups. Sustained clinical response was defined as remaining on treatment for at least three years. Patients who were lost to follow up or who died, while on treatment for less than three years, were not included. Statistical analysis was performed with IBM SPSS V. 25 using chi square tests and logistic regression incorporating pretreatment gender, DAS28CRP, CDAI, rheumatoid factor, Multi-biomarker disease activity score, and a power Doppler joint count.
Results: Fifty anti-CCP positive patients and twenty-two anti-CCP negative patients treated with Abatacept were clinically assessed and results of the post hoc analysis are shown in Table one. Chi square risk estimate 4.61 Clinical sig p= 0.01. Logistic regression: Unadjusted Risk ratio (95% CI) 4.86 (1.54, 8.18) Clinical sig p= .01. Adjusted Risk Ratio (95% CI) 4.21 (1.23, 7.19.) Clinical sig = 0.03.
Results of the post hoc analysis for patients treated with Tofacitinib are shown in Table two. Chi square risk estimate 1.75 (not clinically significant.) Unadjusted Risk 1.70 (not clinically significant). Adjusted Risk 1.42 (not clinically significant).

CCP * Responder Crosstabulation Abatacept

			Responder		Total
			yes	no	
CCP	ccp positive	Count	29	21	50
		% within CCP	58.0%	42.0%	100.0%
	ccp negative	Count	5	17	22
		% within CCP	22.7%	77.3%	100.0%
Total		Count	34	38	72
		% within CCP	47.2%	52.8%	100.0%

Conclusion: Rheumatoid Arthritis patients who are Anti-CCP positive and who are treated with Abatacept in a community rheumatology clinic have a significantly greater number of sustained clinical responses than patients who are Anti-CCP negative.

CCP * Responder Crosstabulation Tofacitinib

			Responder		Total
			yes	no	
CCP	ccp positive	Count	21	8	29
		% within CCP	72.4%	27.6%	100.0%
	ccp negative	Count	9	6	15
		% within CCP	60.0%	40.0%	100.0%
Total		Count	30	14	44
		% within CCP	68.2%	31.8%	100.0%

This difference for patients treated with Tofacitinib was not clinically significant in this clinic, though a higher percentage of Anti-CCP positive patients treated with Tofacitinib responded (72% vs 60%).
Anti-CCP positivity could be used as a clinical marker to select patients with rheumatoid arthritis to be treated with Abatacept.
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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.2223

AB0232 PAIN SCORE WITH VISUAL ANALOG SCALE OF 30MM OR MORE IS A RISK FACTOR OF WORSENING CLINICAL DISEASE ACTIVITY INDEX (CDAI) AT THREE MONTHS AFTER ATTAINING CDAI REMISSION IN PATIENT WITH RHEUMATOID ARTHRITIS

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Background: In treating with rheumatoid arthritis (RA), it is needless to say essential treatment goal with first priority. On the other hand, patient's pain influences on clinical indices deeply, however, pain score is not been regarded as most important despite that correlates with patient reported outcome.
Objectives: Clinical significance of remnant pain score for clinical outcome although attaining remission in clinical disease activity index (CDAI) statistically.
Methods: RA patient who have attained remission with CDAI were picked up. These patients were divided into two groups whether CDAI at three month after the first CDAI remission attained; namely CDAI-R or CDAI-F. Background data such as sex, age at onset, age, anti-cyclic citrullinated polypeptide antibodies (ACPA), rheumatoid factor (RF), Sharp/van der Heijde Score (SHS), clinical disease activity score (CDAI), C-reactive protein (CRP), modified Health Assessment Questionnaire score (mHAQ), and pain score with visual analog scale (PS-VAS) at first consultation, time span from the first consultation to first CDAI remission were compared between the two groups using Mann-Whitney U-test. CDAI, CRP, mHAQ, PS-VAS, and QOL value calculated from EuroQOL-5 dimension questionnaire (EQ-5D) at the time of CDAI were also statistically compared with Mann-Whitney U-test. Parameters that demonstrated statistical significance within 5% were picked up, and odds ratio for CDAI remission were calculated with binary logistic regression analysis. Moreover, parameters that demonstrated statistical significance with p-value within 5% were evaluated with receiver's observational characteristics (ROC) analysis, and cut-off index (COI) was calculated.
Results: A total of 907 patients with 594 CDAI-R and 313 CAI-F were recruied. Demographic characteristics of the two groups were shown in Table 1. SHS at first consultation and time span from first consultation to CDAI remission attained demonstrated significantly less in the CDAI-R than the CDAI-F group, while the other parameters demonstrated no significant difference. CRP, CDAI, mHAQ, PS-VAS, and QOL at CDAI remission demonstrated significant difference between the CDAI-R and CDAI-F groups. With binary logistic regression analysis, CRP, CDAI, and PS-VAS demonstrated significant regression for CDAI-R with 1.68, 0.71, and 0.78 in odds ratio, respectively. COI for CDAI remission was 0.4, 1.0, and 30 for CRP ($p=2.4 \times 10^{-4}$), CDAI ($p=3.0 \times 10^{-32}$), and PS-VAS ($p=2.4 \times 10^{-4}$), respectively.
Conclusion: PS-VAS at the moment of CDAI remission is suggested to be predictive factor for sustaining CDAI remission at three months thereafter as well as CRP value and the CDAI score.

Table 1. Demographic characteristics of the two groups

	CDAI-R	CDAI-F	p-value
cases	594	313	
sex	430 (72.4%)	313 (80.2%)	5.7×10^{-2}
age at onset	62.2	60.9	1.8×10^{-1}
age at FC	65.8	65.1	4.7×10^{-1}
ACPA at FC	209.3 (83.9%)	227.9 (86.7%)	7.2×10^{-2}
RF at FC	83.8 (92.2%)	92.3 (86.1%)	5.6×10^{-2}
SHS at FC	41.9	66.9	6.0×19^{-5}
CDAI at FC	10.7	11.1	5.5×10^{-2}
CRP at FC	1.3	1.6	1.2×10^{-1}
mHAQ at FC	0.439	0.475	3.2×10^{-1}
PS-VAS at FC	32.6	34.9	2.1×10^{-1}
time span	3.7	4.5	6.4×10^{-4}

Abbreviations: FC, first consultation; ACPA, anti-cyclic citrullinated polypeptide-antibodies; RF, rheumatoid factor; SHS, Sharp/van der eijde Score; CDAI, clinical disease activity index; CRP, C-reacive protein; mHAQ, modified Health Assessment Questionnaire; PS-VAS, pain score with visual analog scale; time span, time span from FC to date first CDAI remission attained.

Disclosure of Interests: None declared
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AB0233 **ATTAINING CDAI REMISSION IS THE FIRST GATEWAY TO ATTAIN BOOLEAN REMISSION**

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Background: Boolean remission is most stringent but most comparable remission status for the patient with rheumatoid arthritis (RA). Clinical remission evaluated with clinical disease activity index (CDAI) is also one of the most popular index for evaluation of RA treatment. These two criteria often overlap, but some are split.
Objectives: Clinical significance of attaining CDAI remission before attaining Boolean remission was investigated.
Methods: Patient with RA were treated in the institute since August 2010 under treat to target (T2T) strategy. In accordance with T2T, RA patients were monitored from the first consultation with parameter such as tenderness joint count (TJC), swollen joint count (SJC), patient's global assessment (PGA), evaluator's global assessment (EGA), C-reactive protein (CRP), modified Health Assessment Questionnaire (mHAQ), pain scale with visual analog scale (PS-VAS), and EuroQOL 5-dimension (EQ-5D). CDAI and Boolean are also evaluated at the same time. Radiographs of bilateral hands and feet are taken once a year from the first consultation, and the Sharp/van der Heijde Score (SHS) is measured.
In patients, a group who attained CDAI remission prior to attaining Boolean remission (CDAI-R), a group who could not attain CDAI remission previously than attaining Boolean remission (CDAI-F), and a group who could not attain Boolean remission despite attaining CDAI remission (Boolean-F) were picked up and divided according to change of disease activity. Among these three groups, mean age, sex, education level, job style, anti-cyclic citrullinated polypeptide antibodies (ACPA), rheumatoid factor (RF), the CDAI score, the HAQ score, PS-VAS and quality of life index (QOL) calculated from EQ-5D were compared with each other using Mann-Whitney U-test. Boolean remission attaining rate whether CDAI remission attained was compared with chi square test.
Results: Patient group configured with 255 of CDAI-R, 160 of CDAI-F, and 28 of Boolean-F. Patient who could not attain none of CDAI nor Boolean remission counted 175. In background factors at baseline, mean age, the HAQ score, and SHS of the Boolean-F were significantly older than the other groups. In the two groups of CDAI-R and CDAI-F, 28-joints disease activity score with C-reactive protein (DAS28-CRP), CDAI and PS-VAS in the CDAI-R were significantly lower than in the CDAI-F, similarly, DAS28-CRP, the CDAI score, the HAQ score, PS-VAS and QOL after Boolean remission attain were significantly higher in the CDAI-F than the CDAI-R. Sensitivity of Boolean remission when attaining CDAI remission previously before Boolean remission is 93.4%, and specificity was 52.2% ($p<1.0x10^{-30}$).
Conclusion: Attaining CDAI remission previously is extremely important, both for attaining Boolean remission and more stable clinical course after attaining Boolean remission. CDAI remission could be the first gateway to send sustainable QOL course.
Disclosure of Interests: None declared
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13. Rheumatoid arthritis - comorbidity and clinical aspects

AB0234 **ASSOCIATION OF HOMOCYSTEINE LEVEL AND CAROTID INTIMA-MEDIA THICKNESS IN PATIENTS WITH RHEUMATOID ARTHRITIS**

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Background: Homocysteine (Hcy) has been implicated in atherogenesis. High homocysteine level can predict cardiovascular events, including death. Atherosclerosis has a high incidence in patients with Rheumatoid Arthritis (RA).
Objectives: The aim of this study is to evaluate the relationship between serum homocysteine levels and carotid atherosclerosis in patients with RA and anti-TNF therapy.
Methods: Our study included 80 RA patients divided into two groups: 45 patients were with anti-TNF-alpha therapy (Adalimumab, Infliximab, Etanercept) and 35 RA patients with disease-modifying antirheumatic drugs (DMARDs). The patients were diagnosed with RA used ACR/EULAR 2010 Classification Criteria. We measured carotid intima-media thickness (CIMT) using high-resolution Doppler ultrasonography at baseline and then at 12 months. CIMT above 0.9 mm is an atherosclerosis marker. We considered high levels of homocysteine in the serum above 15 µmol/L. All patients had treatment with hypolipemiant drugs and antiplatelet agents during the 12 months. Other parameters were analyzed at baseline and after 12 months: age, lipid profile (HDL, LDL, and cholesterol), ESR and disease activity score (DAS28<2.6 means remission; DAS28=2.6-3.2 means low disease activity, DAS28=3.2-5.1 means moderate disease activity; DAS28>5.1 high disease activity).
Results: 45 patients received anti-TNF-alpha therapy (mean age 45.50±9.69 years) and 35 RA patients had treatment with DMARDs (mean age 48.3±8.9 years). High Hcy levels were found on 34% patients in DMARDs group and 21% patients in anti-TNF group. After 12 months of treatment, patients with high levels of Hcy and anti-TNF therapy had a significant decrease in CIMT. In patients with low Hcy level the decrease in CIMT was insignificantly statistic. In DMARDs group atherosclerotic plaque was detected to 26 patients (74.29%) and 21 (46.66%) patients were detected into anti-TNF group. After 12 months CIMT was significantly higher in DMARDs group and the difference was statistically significant compared to baseline and to anti-TNF group (p=0.0002). High DAS28 score was associated with increased CIMT and hyperhomocysteinemia in both groups (p=0.0001).
Conclusion: Increased Hcy levels were associated with increased CIMT values in both groups. In RA patients with anti-TNF therapy and high Hcy levels, reduction of CIMT was statistically higher than in patients with DMARDs treatment.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.2690

AB0235 **DENOSUMAB INCREASE THE BONE MINERAL DENSITY REGARDLESS OF DISEASE ACTIVITY, THE BIOLOGICAL DISEASE-MODIFYING ANTIRHEUMATIC DRUGS, THE CONCOMITANT TYPE OF VITAMIN D, AND PRETREATMENT OF OSTEOPOROSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS.**

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Background: Osteoporosis is one of the major comorbidities in patients with rheumatoid arthritis (RA). There are a lot of evidence that denosumab increase bone mineral density (BMD) in patients with osteoporosis. However, there are few reports investigated the influence of denosumab in patients with RA.
Objectives: We evaluated the BMD change in patients with RA treated denosumab and assessed the effect of various factors, such as disease activity, biological disease-modifying anti-rheumatic drugs (bDMARDs) use, concomitant medications of osteoporosis and pretreatment of osteoporosis.
Methods: This study included 140 consecutive RA patients (135 female, mean age was 70.6 ± 8.6 years) who fullfilled the criteria of osteoporosis and treated with denosumab. BMD at the lumbar spine, proximal femoral and femoral neck were evaluated by dual energy X-ray absorptiometry at baseline and one year after treatment. We evaluated the influence of disease activity, bDMARDs use,

the concomitant type of vitamin D and pretreatment of osteoporosis for BMD change.

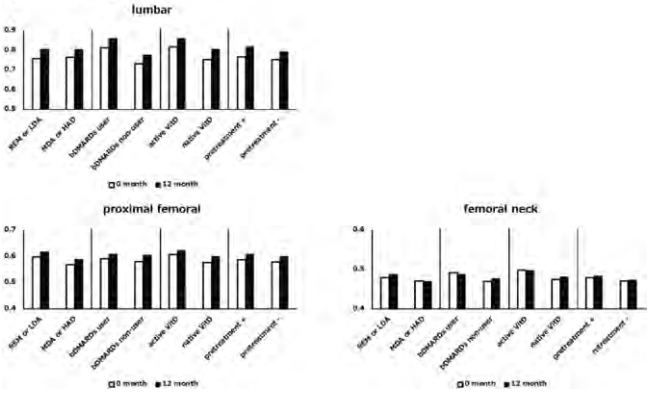
Results: BMD change at the lumbar spine, proximal femoral and femoral neck were 5.9% (p<0.01), 4.0% (p<0.01), and 1.2% (p=0.36) durling one year. There were no differences in improvement ratio of BMD between each parameters (fig 1). Disease activity: 75 patients in remission or low disease activity and 65 patients in moderate or high disease activity were 6.4 vs 5.3% (p=0.91), 3.0 vs 5.1% (p=0.73), 2.0 vs 0.3% (p=0.1). bDMARDs: 45 patients with bDMARDs (anti-tumor necrosis factor inhibitors (TNF): 23, tocilizmab (TCZ): 13, abatacept (ABT): 7, Tofacitinib: 2) and 93 patients without bDMARDs were 6.0 vs 5.8% (p=0.31), 4.3 vs 4.1% (p=0.57), -0.2 vs 1.8% (p=0.18). Type of vitamin D: 47 patients taking active form vitamin D and 60 patients taking native form vitamin D were 5.5 vs 6.8% (p=0.82), 3.1 vs 3.8% (p=0.93), 0.4 vs 1.9% (p=0.14). Pretreatment of osteoporosis: 74 patients with pretreatment of osteoporosis (bisphosphonate:58, teriparatide:16) and 66 patients without pretreatment of osteoporosis were 6.9 vs 5.4% (p=0.41), 0.9 vs 4.0% (p=0.22), 2.0 vs 1.2% (p=0.68). Moreover, BMD change were not different in bDMARDs type, 5.0, 6.4, 0.5% in TNF group, 4.8, 0.7, -1.9% in TCZ group, 9.7, 4.9, 0.2% in ABT group (TNF vs TCZ: p=0.83, 0.98, 0.81, TNF vs ABT: p=0.83, 0.41, 0.97, TCZ vs ABT: p=0.98, 0.43, 0.9). There were no difference between bisphosphonate and teriparatide (6.2 vs 6.9%: p=0.49, 4.8 vs 0.9%: p=0.35, 0.9 vs 2.0%: p=0.49).

Conclusion: Denosumab improved BMD in patients with RA independently regardless of disease activity, bDMARDs, the concomitant type of vitamin D and pretreatment of osteoporosis.

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fig1 : BMD change.



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AB0236 DIFFERENCES AND DETERMINANTS OF PHYSICIAN'S AND PATIENT'S PERCEPTION IN GLOBAL ASSESSMENT OF RHEUMATOID ARTHRITIS

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Background: Patient's Global Assessment of Disease Activity (PtGA) and Physician's Global Assessment of Disease Activity (PhGA) are assessed as part of commonly used measures of disease activity in RA.[1] Both are important measures in treat-to-target strategies in Rheumatoid Arthritis (RA), but often provide discordant results.[2,3] This can provide an erroneous assessment of disease activity in patients under Biologic treatment and mislead treatment decisions, namely switches.

Objectives: To assess differences and determinants of PtGA and PhGA in RA patients under biologic treatment.

Methods: Cross-sectional study, including 46 patients with RA diagnosed according to the ACR/EULAR criteria, under biologic treatment, consecutively evaluated in day-care unit. Participants completed patient-reported outcomes (PROs), including PtGA, and sociodemographic characteristics. Physicians collected comorbidities and parameters of inflammatory activity (erythrocyte sedimentation rate [ESR] and C-reactive protein [CRP]) and completed PhGA and disease activity score 28 with ESR (DAS28). SPSS was used for statistical analysis and significance level was defined as 2-sided p<0.05.

Results: Clinical and laboratory characteristics of patients are shown in table 1. PtGA and PhGA were significantly different (36.1±27.6 mm *vs* 8.7±14.2 mm, p< 0.001) and a positive discordance (PtGA>PhGA, more than 25mm in visual analogue scale [VAS]) was found in 54.3% of cases.

PtGA had a correlation with PROs (Pain VAS, 36-Item Short Form Health Survey [SF-36], Health Assessment Questionnaire [HAQ], Functional Assessment of Chronic Illness Therapy [FACIT], EuroQol [EQ5D] and Hospital Anxiety and Depression Scale [HADS]), CRP, tender and swollen joint counts and an association with comorbidities like fibromyalgia or osteoarthritis (OA). No association was found between PtGA and age, sex, education level, profession, employment status, extra-articular manifestations, positivity of rheumatoid factor, ESR, years of disease evolution or number of biologic treatments. In multivariable analyse including SF-36, CRP, tender joints count and OA (R^2 adjusted= 0.672), the main predictors of PtGA were lower SF36, concomitant OA and higher CRP level.

PhGA had a correlation with PtGA, pain VAS, CRP, tender and swollen joints. No association was found between PhGA and patient or physician age, patient or physician sex, extra-articular manifestations, positivity of rheumatoid factor, ESR level, years of disease evolution or number of biologic treatments. In multivariable analysis including ESR, tender and swollen joints count and CRP (R^2 adjusted= .800), the main predictors of PhGA were swollen joint count and higher CRP level.

Conclusion: This study showed the variability implied on global assessment of RA activity. Overall PtGA is based on function and also in subjective and emotional experience of pain, whereas the PhGA is based on more objective measures, more related to disease activity.

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AB0237 ARE THERE DIFFERENCES IN CLINICAL PROFILE AND TREATMENT AMONG 2 DIFFERENT INTERCONTINENTAL COHORTS OF PATIENTS WITH RHEUMATOID ARTHRITIS-ASSOCIATED INTERSTITIAL LUNG DISEASE?

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Background: Rheumatoid Arthritis (RA) is characterized by persistent joint synovitis causing progressive destruction of the cartilage and bone. Interstitial lung disease (ILD) is a frequent extra-articular manifestation of RA. Clinical profiles of patients with RA-associated ILD may vary.

Objectives: To describe the clinical characteristics and radiological patterns and evaluate the different clinical profile between two different cohorts of patients (pts) with RA- associated ILD.

Methods: Retrospective cohort study. We collected clinical and epidemiological data of pts seen in outpatient clinic from a Hospital from Barcelona, Spain and another from Jacksonville, Florida, USA. Pts who met the RA ACR/EULAR 2010 criteria and the ILD American Thoracic Society /European Respiratory Society 2013 classification criteria were selected. The study was approved by both local committees.

Results: A total of 63 pts were included, 37 from Barcelona and 26 from Jacksonville. Forty-one pts (65%) were women with a median age of 68 years. General characteristics are summarized in Table. Thirty-eight pts (60.3%) were former smokers, but only 9 pts (14.3%) were current smokers. Fifty-two pts (82.5%) were Caucasian, 9.5% Mestizo, 3.2% Maghreb and 1.6% Indian. Most were overweight with mean BMI of 28.6 (SD 5.4). The Barcelona cohort showed more erosive disease than the pts from Jacksonville (26 vs 5 pts, p= 0.00). Seven pts had ILD diagnosis before RA. 4.82 (range 0-33) years was the median evolution from RA diagnosis until ILD diagnosis. Most common type of ILD was usual interstitial pneumonia (UIP) in 40% of pts, followed by nonspecific interstitial pneumonia (NSIP) in 25% of pts. Respiratory bronchiolitis was significantly more common in Barcelona cohort, while unspecific pattern in Jacksonville cohort (Table). A total of 71.4% were under GC treatment, methotrexate was used in 23 pts (36.5%), leflunomide in 14 (22.2%) and hydroxychloroquine in 7 pts (11.1%) prior to diagnosis of ILD. 6 out of 26 pts from Jacksonville were under MMF. TNF-α inhibitors were the most commonly used bDMARD in both cohorts as a first-line option prior to ILD diagnosis. Currently, half of the patients (50.8%) were under bDMARD. Current use of bDMARD was more often in US cohort (80.7%) than in Barcelona cohort (29.7%). Rituximab (RTX) was the most common bDMARD currently used (17 pts). Jacksonville pts were more commonly treated with RTX, while Barcelona pts were more commonly treated with Abatacept.

Conclusion: Globally pts with RA-associated ILD have similar clinical profile in both centers, however, we found some differences in radiological patterns and treatment strategies between both cohorts. Those differences could be explained in part by sociodemographic differences, diagnostic and therapeutic approach and/or access for health care among others.

	Total n=63 %	Barcelona cohort n= 37	Jacksonville cohort n=26	P value
Caucasian, patients (%)	52 (82.5%)	31 (83.8)	21 (77.8)	0,49
Time RA evolution, mean years (SD)	10.58 (8.01)	11.63 (7)	9 (9.24)	0.80
Time ILD evolution, mean years (SD)	3.89 (3.20)	3.86 (3.28)	4 (3.12)	0.28
Erosive disease, patients (%)	31 (49.2)	26 (72,2)	5 (18.5)	0,00
Rheumatoid nodules, patients (%)	8 (12,7)	7 (18,9)	1 (3.8)	0,12
Current scDMARDs treatment, patients (%)	35 (55.55)	31 (49.20)	4 (6.34)	0,002
Current bDMARD treatment, patients (%)	32 (50.8%)	11 (17.5)	21 (33.3)	0,001
ILD type				
Usual interstitial pneumonia (UIP), patients (%)	25 (40.3)	14 (37.8)	11 (44)	0,08
Nonspecific interstitial pneumonia (NSIP), patients (%)	16 (25.8)	14 (37.8)	2 (8)	0,23
Respiratory bronchiolitis–interstitial lung disease (RB), patients (%)	7 (11.3)	7 (18.9)	0	0,039
Cryptogenic organizing pneumonia (OP), patients (%)	4 (6.5)	2 (5.4)	2 (8)	0,43
Unspecific, patients (%)	8 (12.9)	0	8 (32)	0,004

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AB0238

SERUM LEVELS OF E-SELECTIN AND IL-8 DECREASE AFTER 6 MONTHS OF ANTI-INFLAMMATORY THERAPY AND MIRROR FAVORABLE VASCULAR CHANGES IN RHEUMATOID ARTHRITIS

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Background: Accelerated atherosclerosis is a systemic manifestation of rheumatoid arthritis (RA). E-selectin, VCAM-1, MCP1/CCL2 and IL-8/CXCL8 are involved in leukocyte migration through endothelial cells in both atherosclerosis and RA [1]. Therefore, these endothelial function markers might reflect endothelial function and systemic inflammation in RA. If so, such a marker could be used to assess cardiovascular risk in RA patients.

Objectives: The aim of this study was to investigate the effect of 6 months of anti-inflammatory treatment on RA serum levels of endothelial function markers and whether these serum levels are related to prognostic imaging markers for atherosclerosis.

Methods: E-selectin, VCAM-1, MCP1 and IL-8 serum levels were determined at baseline and after 6 months of therapy with MTX monotherapy or in combination with adalimumab for 40 RA patients and 19 osteoarthritis (OA) controls using commercial ELISA kits. Prognostic imaging markers for atherosclerosis were pulse wave velocity (PWV) and augmentation index (AIx) as measured with SphygmoCor tonometry. Parametric analyses were used for E-selectin, VCAM-1 and MCP1 and non-parametric or parametric analyses after log transformation for IL-8.

Results: Baseline VCAM-1 and IL-8 were significantly higher for RA patients than OA controls with and without adjustment for age and sex or traditional risk factors (table 1).

Table 1. Comparison between RA and OA serum levels of endothelial function markers at baseline

	OA	RA	Crude analysis		Adjusted age sex		Adjusted traditional risk factors*	
	Mean ±SD or median (IQR)	Mean ±SD or median (IQR)	Difference OA and RA (95%CI)	p	Difference OA and RA (95%CI)	p	Difference OA and RA (95%CI)	P
E-selectin (ng/ml)	29 ±15	32 ±17	3 (-6-12)	0.49	3 (-6-12)	0.53	3 (-7-13)	0.54
VCAM-1 (ng/ml)	786 ±102	897 ±200	110 (13-208)	0.03	103 (4-202)	0.04	110 (2-218)	0.05
MCP1 (pg/ml)	248 ±248	316 ±165	68 (-15-150)	0.11	71 (-10-152)	0.09	49 (-41-138)	0.28
IL-8 (pg/ml)	15 (10-25)	37 (17-117)	n/a	0.01	n/a	0.01	n/a	0.02

* Age, hypertension, bmi and pack years

After 6 months of anti-inflammatory therapy, E-selectin and IL-8 serum levels significantly decreased (table 2). This decrease was especially present in the RA patients with good EULAR-DAS28 response to the medication and not in patients with no/moderate response (E-selectin: -7, 95%CI -13- -2, p=0.007 versus -0.1, 95%CI -3-2, p=0.925; IL-8: -2, p=0.033 versus -1, p=0.267).

Table 2. Endothelial function markers difference after 6 months of therapy in RA patients

	Difference (95%CI)	p-value
E-selectin (ng/ml)	-4 (-7-1)	0.010
VCAM-1 (ng/ml)	+10 (-56-77)	0.753
MCP1 (pg/ml)	-14 (-34-62)	0.557
IL-8 (pg/ml)	-11 (n/a)	0.014

Furthermore, in the RA patients we found a significant correlation between the difference in PWV after 6 months and the difference in E-selectin (Pearson r=0.450, p=0.018) and IL-8 (Spearman r=0.401, p=0.038). All other possible correlations of the endothelial function markers with PWV and AIx were not significant (data not shown).

Conclusion: Serum levels of E-selectin and IL-8 decreased after 6 months of anti-inflammatory therapy, and both correlated with the PWV changes. This is the first study investigating both serologic as well as imaging markers of endothelial function and atherosclerosis in RA patients undergoing anti-inflammatory therapy. Our study suggests that E-selectin and IL-8 circulatory levels may reflect the best both systemic inflammation as well as endothelial function in RA, and might be therefore useful in the future as markers of cardiovascular risk in these patients.

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AB0239

EFFECTS OF DYSMETABOLISMS AND COMORBIDITIES ON THE EFFICACY, SAFETY AND RETENTION RATE OF BIOLOGICAL DMARDS (BDMARD) IN INFLAMMATORY JOINT DISEASES.

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Background: bDMARDs have an effect on glucose homeostasis (1), lipoproteins profile (2; 3) and blood pressure (4). However, with the exception of obesity (5; 6), there are no clear data on how bDMARDs work in patients who already have or develop metabolic comorbidities and whether these conditions can impact on their efficacy and safety profile.
Objectives: to evaluate, in chronic inflammatory joint diseases, the effect of arterial hypertension (AH), dyslipidemia (DYS) and diabetes mellitus (DM) on efficacy, safety and retention rate of first-line bDMARDs therapy.
Methods: a retrospective observational study on the clinical charts of Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA) or Ankylosing Spondylitis (AS), treated with first on-label bDMARD was performed. Data on adverse events, efficacy and comorbidities at the baseline visit in which the bDMARD was prescribed (BL), the visit performed after 6 months of therapy (6M), and the last visit on treatment (LoT) were collected.
Results: 383 patients (41,8% RA, 33,4% PsA and 24,8% AS) were included in the study, with the predominance of females (F: 67,36%, M: 32,64%; mean age 51,67 ± 15,11 years). Our data show that the presence of comorbidities had no influence on efficacy of bDMARD, while patients who had DYS at BL manifested a higher rate of systemic adverse events either in the first 6 months of therapy (58,9% vs 43,7%, p=0,040) and also later on (80,36% vs. 66,67%, p=0,046). In addition, patients who developed DYS and AH after the 6M visit reported a higher rate of systemic adverse events at LoT visit, compared to others (DYS: 97,8% vs 66,7%, p<0,001; AH: 86,9% vs 65,2%, p=0,031). For what concerns the retention rate, patients who developed DYS or AH during bDMARD treatment continued the drug for a longer period of time (DYS 95,5 vs 19,6 months, p<0,001; AH 72,1 vs 23,4 months, p<0,001). In particular, patients with AH who concomitantly carried out therapy with ACE-inhibitors (ACEi) and/or angiotensin II receptor blockers (ARB) continued bDMARDs for nearly 20 more months than patients who were not exposed to these drugs (40,5 vs 23,4 months, p=0,001) and more frequently maintained the bDMARDS at LoT (59,42% vs. 47,53%). In case of withdrawal in the ACEi/ARB exposed cohort, this was due to well-being and disease remission rather than inefficacy or adverse reaction (p=0,025). In dyslipidemic patients treated with statins, data showed that bDMARDs were continued for a longer time than in DYS patients treated with other anti dyslipidemic therapies (41,09 vs. 26,50 months, p=0,042).
Conclusion: our data suggest that AH and DYS may be associated with higher frequency of adverse events but a better drug retention. The combination of bDMARD and ACEi/ARB may determine a better control of the inflammatory process by inhibition of angiotensin II, favouring the achievement of remission. In AH patients on bDMARDs, ACEi and ARB could therefore represent an useful anti-hypertensive drug choice. Similarly, statins could be the treatment of choice in DYS patients.
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AB0240

EXAMINING THE RELATIONSHIP BETWEEN RHEUMATOID ARTHRITIS, MULTIMORBIDITY AND ADVERSE HEALTH-RELATED OUTCOMES: A SYSTEMATIC REVIEW

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Background: Rheumatoid arthritis (RA) is a chronic autoimmune disorder characterised by inflammation of the synovial joints causing pain, swelling and stiffness. Multimorbidity (the presence of two or more long-term conditions) affects approximately two thirds of people with RA. However, the relationship between RA and multimorbidity is poorly understand, as is the effect of this relationship on mortality and other health-related outcomes, particularly those relating to physical functioning and well-being.
Objectives: To explore existing literature to determine what is known about the effect, if any, of multimorbidity on mortality and other health-related outcomes in people with RA.
Methods: A systematic review was conducted following a protocol prepared using PRISMA-P 2015 reporting guidelines, ensuring the quality of the review. Studies were sourced from electronic medical databases, specifically MEDLINE, Embase, CINAHL, PsycINFO, The Cochrane Library and Scopus, using a pre-defined search strategy. Studies were selected based on specified eligibility criteria and quality appraised using the Cochrane Prognosis Methods Group-developed, Quality in Prognostic Studies (QUIPS) tool. A narrative synthesis of findings was conducted.
Results: In total, 15 studies fulfilled our criteria for inclusion in our review. Of these, 7 studies had mortality as an outcome, with 6 reporting a significant association between multimorbidity and increased risk of all-cause mortality in people with RA. Nine studies had functional status/disability as an outcome, with 2 of these studies also including quality of life. All 9 studies reported significant associations between multimorbidity and the aforementioned health-related outcomes, demonstrating poorer functional status/increased disability and reduced quality of life in people with RA and multimorbidity.
Conclusion: Multimorbidity in people with RA is significantly associated with increased mortality and poor health-related outcomes in current literature. A better understanding of this relationship will provide an important foundation of knowledge to guide future health service design.
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AB0241

PREVALENCE OF ANXIOUS SYMPTOMS AND DEPRESSION IN A SAMPLE OF PATIENTS WITH RHEUMATOID ARTHRITIS (RA) AND OTHER CHRONIC RHEUMATIC DISEASES

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Background: Clinical practice with patients suffering from chronic diseases highlights the presence of psychological symptoms of discomfort fed by biological and non-biological mechanisms linked to disease and treatment. In rheumatic diseases, literature detects the presence of anxious symptoms and depressed mood of clinical and sub-clinical importance with a multifactorial genesis[1].
Objectives: To detect the impact on the state of health of anxious symptoms and depressed mood in a population suffering from RA and other rheumatic diseases in order to implement the effectiveness of psychological intervention through the selection of patients who present critical levels of discomfort.
Methods: Patients afferent to the Rheumatology outpatient clinic of Mauriziano Hospital have been screened from May 2018 to July 2018 with two self-administered questionnaires: HADS-A and HADS-D (Hospital Anxiety and Depression Scale), specifically developed for the evaluation of anxious and depressive symptoms in medical pathologies, and HAQ (Health Assessment Questionnaire) to explore functional disability. Data about rheumatic diagnosis and socio-demographic characteristics were also collected. Data were analyzed with descriptive statistics; the Student Test and the ANOVA test were used to evaluate prevalence and to compare the presentation of symptoms in the different diseases and the Pearson correlation coefficient was used to evaluate the relationship between symptoms and disability.
Results: A total of 427 subjects were screened (317 females and 110 males), aged between 19 and 90 years (mean 60 ± 14 yrs). 156 subjects (36.5%) had a diagnosis of RA, 76 (17.8%) of psoriatic arthritis, 42 (9.8%) of ankylosing spondylitis, 14 (3.3%) of systemic lupus erythematosus and 139 (32.6%) of other rheumatic diseases (including Sjogren, osteoarthritis, fibromyalgia).
A high prevalence of anxious symptoms and depressed mood has been found and the number of subjects reporting scores indicating a clinically relevant

uncomfortable situation (HADS ≥ 11) was also relevant (Table 1); an increased prevalence in female patients was observed. There were no differences in the presentation of symptoms between RA and the other included pathologies (Table 2).

Table 1. Prevalence of anxiety and depression according to the HADS questionnaire in rheumatic diseases

	Mean	SD
HADS-A	7.56	4.63
HADS-D	7.12	4.59
HADS-A Score	N	%
0-7	224	52.4
7-10	84	19.7
11-21	119	27.9
HADS-D Score	N	%
0-7	231	54.1
7-10	92	21.5
11-21	104	24.4

Table 2. Comparison between RA and other rheumatic diseases in anxiety and depression symptoms presentation (ANOVA test).

		N	Mean	SD	SE	CI
HADS-A	RA	156	2.34	5.20	0.41	1.52
	PsA	76	2.30	4.47	0.51	1.28
	AS	42	1.51	3.19	0.49	0.51
	SLE	14	1.77	3.74	1.00	-0.38
	other	139	2.46	5.08	0.43	1.61
HADS-D	RA	156	1.74	3.51	0.28	1.19
	PsA	76	2.03	4.21	0.48	1.07
	AS	42	0.69	0.54	0.08	0.52
	SLE	14	0.93	0.68	0.18	0.54
	other	139	1.68	3.79	0.32	1.04

There was a positive and significant correlation between anxious symptoms or depressed mood and functional disability (0.49 and 0.60 respectively, p<0,01).

Conclusion: The results show a significant presence of uncomfortable situations that could evolve in a psychopathological sense. The discomfort expressed through anxious and depressive symptoms is related to the level of functional disability. Recognizing the presence of psychological distress allows to orient the treatment plan and facilitate the patient's adaptation to the disease condition.

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AB0242 SURVIVAL ANALYSIS IN THE DEVELOPMENT OF SERIOUS INFECTIONS AND SERIOUS RESPIRATORY INFECTIONS IN AR PATIENTS INCLUDED IN A VACCINATION PROGRAM

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Background: Rheumatoid arthritis is an autoimmune disorder in which patients have an increased risk of developement of serious infections. This risk may be augmented due to RA itself and to immunosuppressive drugs, specially biologic therapy. Vaccination programs may change this condition.

Objectives: Our aim in this study was to evaluate the incidence of serious infections in a vaccinate RA patients cohort.

Methods: Prospective study of 401 patients diagnosed with RA who were invited to participate in the vaccination program of the Preventive Medicine department of our hospital from October 2011 to October 2016. The follow up was made until June 2017 with a minimun follow-up period of 8 months and maximun of 5.5 years. Serious infections were defined as those that required hospitalization or at least one dose of intravenous antibiotic treatement at emergency room. Information was retrieved from dthe hospital records.

Only 7 patients refused vaccination (2%). Information was not obtained in 4 of the remaining 394 patients. Therefore, these 4 patients were not incuded in the assessment.

Survival análisis was assessed by Kaplan-Meier method.

Results: We finally studied 390 patients (307♀/83♂) mean age±SD 61,28 ± 12,9 years that participate in the vaccination program and followed-up. The main features at the time of vaccination were: median disease duration (4years), positive rheumatoid factor (56,7%), subcutaneous nodules (4.9%), erosive arthritis (36.9%), pulmonary fibrosis (3.8%), secondary Sjögren syndrome (5.1%), other extraartocular manifestations (14.6%) and rheumatoid vasculitis (5.6%) Most patients had received imunosuppressive drugs before the vaccination program. The most frequently used were systemic corticosteroids (n=228), methotrexate (n=362) and biologic agents (40.3%).

During the follow-up, 42 patients (10.7%) had required hospital admissions due to infections, 17 of them were severe respiratory infections (4.35%). The remaining 25 admissions were in the setting of urinary tract infections (n=12), intraabdominal infections (7), skin and soft tissues (12) and articular (1). Also 12 of these patients had a zoster herpes.

Afeter a median follow-up of 1061,89 ± 417 days, the incidence of serious infection, with a CI (95%), was 4.00 (2.95-5.41) for 100 patients yearly. Concerning to admissions due to serious respiratory infections, with a CI (95%), was 1.55 (0.9-2.47) for 100 patients yearly. **Images 1 and 2.**

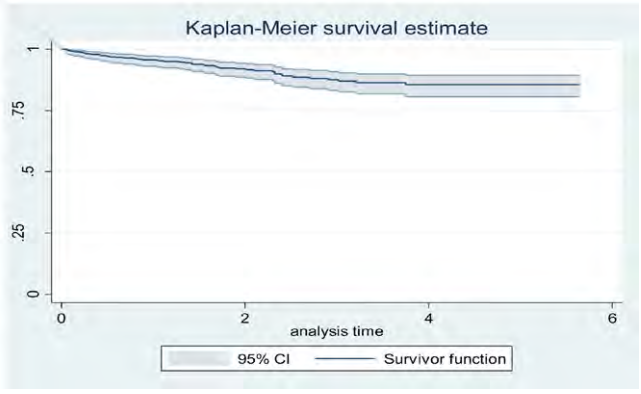


Image 1. Survival analysis on serious infections

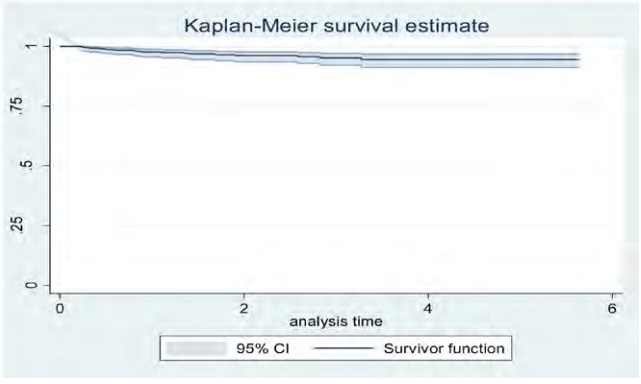


Image 1. Survival analysis on serious respiratory infections

Conclusion: In this stydy we can concluded that our RA vaccinated patients present a dicrease of the incidence of serious infeccions, similar to other published cohorts. The incidence of serious respiratory infections shows a dicrease even lower to other published cohorts. The vaccination program seems to be effective to prevent hospital admissions due to infections.

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AB0243 THE SHORT DISEASE DURATION IS ASSOCIATED WITH WORSE MOOD DISORDER IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is commonly associated with mood disorders, especially depression and anxiety. But the status of mood disorders in RA patients with different courses is unknown.
Objectives: The aims of this study were to investigate the frequencies of depression and anxiety in patients with early RA and non-early RA, and further to identify the risk factors for mood disorders.
Methods: Self-Rating Anxiety Scale (SAS) and Self-Rating Depression Scale (SDS) were applied to all enrolled RA patients to assess their corresponding status of anxiety and depression. Besides clinical assessment, power Doppler and grey-scale ultrasound of 22 joints were also performed. The status of mood disorder was studied in early RA patients compared to non-early RA patients. Multivariate regression was used to identify the risk factor for mood disorders.
Results: 201 RA patients were enrolled, with 76 early RA (disease duration ≤ 2 years) and 125 non-early RA (disease duration > 2 years) patients. Mood disorder (depression and/or anxiety) was found in 20.9% (42/201) patients. Depression was more often observed in early RA patients than non-early RA patients (26.3% vs. 14.4%, *P*=0.036). The similar trend for anxiety was observed also in early RA patients compared to non-early RA patients, although the difference was insignificant (13.2% vs. 5.6%, *P*=0.062). Multivariate logistic regression analysis showed that disease duration (OR 0.991 [95% CI 0.985-0.998]), rheumatoid factor concentration (OR 2.697 [95% CI 1.165-6.241]), Health Assessment Questionnaire Disability Index (HAQ-DI) (OR 1.045 [95% CI 1.001-1.091]) and grey-scale synovitis score (GS score) (OR 1.092 [95% CI 1.032-1.156]) were independent risk factors for predicting depression in RA. Disease duration (OR 0.983 [95% CI 0.970-0.997]), HAQ-DI (OR 1.069 [95% CI 1.002-1.141]) and GS score (OR 1.073 [95% CI 1.005-1.141]) were independent risk factors for predicting anxiety in RA patients.
Conclusion: Mood disorders were almost doubled in frequency in early RA patients than non-early RA patients. RA Patients with short disease duration, high HAQ-DI and high GS score were more likely to be in depression and anxiety. More attention is needed to the psychological status of RA patients, especially those at an early stage, with poor physical function and severe synovitis.
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AB0244 BODY MASS INDEX AND BODY COMPOSITIONS CORRELATES WITH CAROTID INTIMA MEDIA THICKNESS IN RHEUMATOID ARTHRITIS

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Background: Risk of rheumatoid arthritis (RA) had been reported in overweight obese compared with normal weight people. More, obesity is associated with high prevalence of cardiovascular disease (CVD) risk factors in RA. No previous publications have examined the detailed body composition parameters among RA, or its relation to CVD in RA.
Objectives: This study looked at the body composition and the body mass index and correlated it with the subclinical cardiovascular disease as manifested by carotid intima media thickness (cIMT).
Methods: During 2019, a cross-sectional study was carried out to recruit cases that met the 2010 American College of Rheumatology/EULAR criteria for diagnosis of RA. All the patients were free of cardiovascular and or cerebrovascular disease. Patients with clinical diagnosis of hypertension, diabetes, renal disease, dyslipidemia, thyroid disorder and pregnant female were excluded. None of the participants is smoker or had history of smoking.
cMIT ultrasound (US) measures were obtained using a real-time US scanner equipped with a 7.5 MHz linear probe by a single sonographer. Patients underwent a detailed body composition analysis within the same week of the cIMT measurement. The body composition analysis involved assessing the level of total body water, protein, minerals, body fat mass, intra- and extracellular water, basal metabolic rate, waist hip ratio, visceral fat level, obesity degree, bone mineral content, body cell mass, arm and arm muscle circumference, detailed muscle fat analysis, obesity analysis, segmental lean analysis, weight control parameters, and segmental fat analysis.
Results: During 2019, 35 female RA patients were recruited that met the inclusion criteria. The mean (SD) of the age was 52 (10) with a minimum of 20 and maximum of 72 years old. The mean (SD) of cIMT was 0.59 (0.098) mm with a minimum of 0 .38 and maximum of 0.87. The mean (SD) of the BMI was 30.7 (7.0) with a minimum of 20 and maximum of 56.9 Kg/m^2. Mean systolic blood pressure was 126 (19) with a minimum of 91 and maximum of 140 mmHg. Also, the mean diastolic blood pressure was mmHg 74 (11) with a minimum of 49 and maximum of 96.
The correlation of cIMT with the parameters of the body composition in a linear regression analysis showed a positive linear relationship between cIMT and each of the Body fat mass (kg): P=0.045, CI 0.000-0.004), BMI (p=0.029, CI: 0.001, 0 .009), the target weight (p=0.040, CI: 0.000- 0.001), extracellular water (P=0.033, CI: 0.002, 0.034) and bone mineral content (p=0.031, CI: 0.009, 0.192).
The Multiple linear regression analysis showed persistence of the relationship between the cIMT and the age of the participants (p=0.049, CI:0.001-0.007) and the BMI (p=0.031, CI: 0.002- 0.032), with R^2 of the model was 0.38.
Conclusion: To the best of our knowledge, this is the first paper to examine the detailed body composition parameters among RA and found a good correlation with subclinical cardiovascular disease as manifested by cIMT. More research with larger study population is needed to look at the association between body mass index and CVD risk factor in RA.
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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.2423

AB0245 RHEUMATOID ARTHRITIS DISEASE ACTIVITY AND VITAMIN D LEVELS IN A COLOMBIAN COHORT

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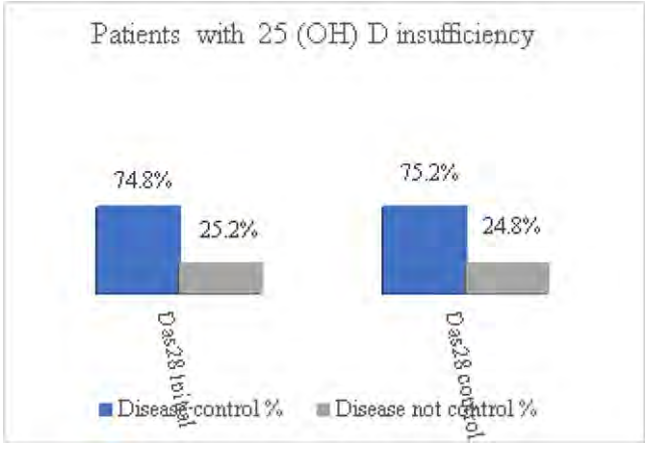
Background: There seems to be a relationship between 25-hydroxyvitamin D [25(OH)D] level and rheumatoid arthritis (RA)(1). It has been proposed that susceptibility for RA exists in selected patients with low 25(OH) with conflicting results (2,3) Regarding disease activity, most of the evidence suggests an inverse relationship of disease activity with 25(OH)D levels(4). To our knowledge, there is only a small study that suggests low 25(oh) D levels as a predictor of disease activity (5) in our region
Objectives: We aimed to evaluate the possible association of low 25(OH) D levels and disease activity in a large cohort of patients with Rheumatoid Arthritis in Colombia
Methods: We evaluated the clinical records of 3576 patients with RA that fulfilled the 2010 EULAR Classification Criteria for Rheumatoid Arthritis and that were managed in our autoimmunity center between 2014 and 2017. Registries that contained both the measurement of 25(OH)D levels and DAS28 VSG with no more than 6 months apart and that also had at least a mean 12-month follow-up were included. We classified 25(OH) D insufficiency as levels ≤ 20ng/ml. We evaluated differences in achieving disease control depending on the 25(OH) D levels with McNemar's test. Disease control was defined as DAS28VSG≤3.2
Results: A total of 880 patients were included, 90% were female and their mean age was 63 years and 24.3% had 25(OH) D insufficiency. The vast majority were seropositive and only 13% were on biologics (Table 1). A 25% of patients who 25(OH)D insufficiency had DAS28 3.2 and a year of follow-up decreased to 24% with medical intervention (p=0,1), while patients without 25(OH)D insufficiency

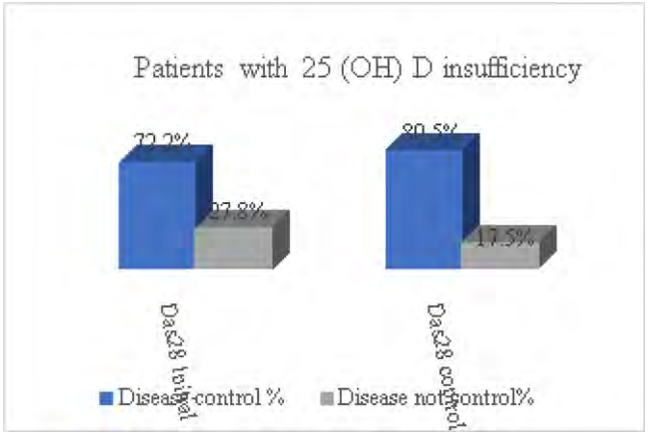
at the beginning of follow-up, 27% had DAS28 3.2 and after one year follow-up decreased to 17% (p=0.001)

Table 1

	Mean (SD)	
Age (years)	63.3 (10.6)	
Disease Duration	14.7 (10.8)	
Age at diagnosis	48.6(13.5)	
	N	%
Sex (Feminine)	793	90.1
Rheumatoid Factor (Positive) N=817	699	85.6
ACPA (Positive) N=366	32.3	77.6
Actual Steroid use	611	69.4
Actual Biologic Therapy	123	13.9
DMARD		
Methotrexate	570	64.8
Leflunomide	682	77.5
Sulfasalazine	218	24.8
Azathioprine	5	0.6
Antimalarials	147	16.7

Conclusion: In Colombian patients with rheumatoid arthritis low 25(OH) D status has an inverse correlation with disease control. Even in an equatorial country, up to 24% of RA patients had low vitamin levels. A strategy of active detection of 25(OH) D insufficiency could have an impact on disease activity and health status





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AB0246

FACTORS ASSOCIATED WITH THE TIME OF PRESENTATION OF CARDIOVASCULAR EVENTS IN A COHORT OF COLOMBIAN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus is a systemic disease characterized by a compromise of vital organs. The autoimmune activity has been linked to accelerated endothelial damage and increased cardiovascular risk and its outcomes such as heart attack, stroke, and peripheral arterial disease(1). Patients with Lupic nephritis have been characterized by requiring aggressive immunosuppressive therapies apart from prolonged and progressive use of corticosteroids, what you have shown can accelerate these outcomes(2). Other factors such as secondary arterial hypertension, dyslipidemia among others are factors to consider (3).

Objectives: To analyze clinical and immunological characteristics associated with time to severe renal involvement in patients with Systemic Lupus Erythematous in a Colombian cohort followed for one year, between January 2015 and December 2018.

Methods: Retrospective follow-up study based on clinical records of patients with SLE diagnosis that fulfilled either 1987 American College of Rheumatology Classification Criteria for SLE or 2011 Systemic Lupus International Collaborating Clinics (SLICC) classification criteria for SLE. Patients with cardiovascular disease outcomes such as angina, acute myocardial infarction, stroke, transient cerebral ischemia and chronic arterial occlusive disease were included. Patients who did not have at least two follow-up measurements or had structural heart disease, valvulopathies, arrhythmias, myocarditis, pericarditis were excluded. The main outcome was defined as the time from diagnosis to cardiovascular diseases.

Clinical and immunological characteristics were analyzed. Descriptive statistical analyses of participant data during the first evaluation are reported as frequencies and percentages for categorical variables, and as medians and interquartile ranges for quantitative variables. Age and sex adjusted survival functions and Hazard Ratios (HR) with 95% confidence intervals and p-values were estimated using parametric Weibull models for interval-censored data. P values < 0.05 were considered statistically significant

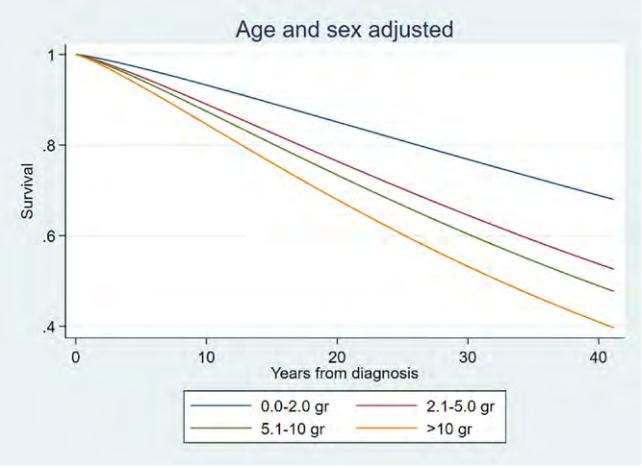
Results: 547 patients were analyzed: 29 were left-censored as they presented renal involvement at entry, 22 were interval censored as outcome occurred between study visits, and 496 were right-censored as involvement was not registered during follow-up. 528 (96.5%) patients were female, median age at entry was 46 (IQR = 23) and median age to diagnosis was 29.4 (IQR = 20.9). Statistically significant age and sex adjusted variables were High Blood Pressure (HBP) HR = 2.0 (95%CI 1.1-3.6; p-value <0.018) and cumulative prednisolone dose (>10 gr vs <2 gr) HR = 2.4 (95%CI 1. 1-5.1; p-value = 0.023). Figure 1 shows the age and sex adjusted survival function for HBP

Conclusion: HBP and cumulative steroid doses accelerate the onset of cardiovascular diseases in patients with lupus more than two times. Maintaining blood pressure in goals and performing early clearance of glucocorticoids could improve outcomes in these patients who are already considered a high cardiovascular risk

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AB0247 LIFE QUALITY AND DEPRESSION LEVEL ASSESSMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Depression is a common and significant rheumatoid arthritis (RA) comorbidity that develops under the influence of severalfactors, the most important being disease activity, pain intensity and degree of disability.
Objectives: The goal of the investigation was to determine existence of depression and assess life quality in patients living with RA.
Methods: The study sample comprised of 150 patients of average age 59.2 years, 79.2% of whom were women and 20.8% were men, who have lived with RA for an average of 9.6 years. For determining disease activity level, Disease Activity ScoreDAS28was utilized. Pain intensity and global disease activity were rated using a visual analogue scale ranging from 1 to 100mm. For functional capacity assessments, Health Assessment Questionnaire(HAQ) index was adopted,depressions severity was determined through Back Depression Inventory (BDI), and Serbian version of the health-related quality of life instrument EQ-5Dwas employed to assess patients' quality of life.
Results: Average DAS28 score for the sample was4.46±1.32, suggesting moderate RA activity. Pain intensity was on average scored at 53.2±18.6, whereas global disease activity was measured at 49.63±20.2, and theHAQ indexof 1.0±0.70 was obtained. According to theBDI, 21.4% of the patients exhibited no signs of depression, whereas 12.9% had mild, 54.3% moderate, and11.4% severe form of depression.Quality of life, as measured by EQ-5D, was compromised in all life domains, withpain/discomfort, anxiety/depression, inability to partake in usual activities, compromised mobility and self-caremost frequently reported. In patients suffering from moderate and severe depression, high statistically significant positive correlation between depression score and HAQ index was noted.BDIscore was statistically significantly positively correlatedwith the ratings on the EQ-5D scales pertaining to self-care, usual activities, pain/discomfort, and anxiety/depression.
Conclusion: Depression symptoms are common in patients with RA and can compromise quality of life in all life domains.When assessing disease severity and general status of patients with RA, depression symptoms should also be considered, given their high prevalence and influence on patients' everyday life.
Acknowledgments: not
Disclosure of Interests: None declared
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AB0248 PREVALENCE OF THYROID PEROXIDASE ANTIBODIES IN THE NORMAL POPULATION AND IN PATIENTS WITH RHEUMATOID ARTHRITIS AND THEIR PREDICTIVE VALUE FOR THE EFFECTIVENESS OF TREATING RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is sometimes associated with autoimmune thyroid disease (AITD)[1]. However the relation between RA autoantibodies and thyroid autoantibodies is doubtful. However, there is no reliable data on whether concomitant positivity of level of anti-TPO in rheumatoid arthritis patients alters the efficacy of RA therapy.
Objectives: To study the presence of level of autoimmune thyroid markers (thyroid peroxidase antibodies -anti-TPO-), in clinically and serologically different forms of RA, compared to serum level of anti-TPO in control population, and to study whether anti-TPO positivity in any RA group influences the risk of high disease activity and also affects the likelihood of achieving DAS-28 remission.
Methods: 1428 patients were included in the retrospective single-center study using the database of the Arthritis Registry of Kecskemét (ARK). 772 RA patients, subclassified according to the presence of RF and anti-MCV into seropositive RA patients (positive to one or both seromarkers), and seronegative RA (negative to both seromarkers), and 656 patients were included as control group without autoimmune diseases.
Results: Elevated level of anti-TPO was found in 199/772 (26%) RA patients, compared to controls 32% (209/656). Furthermore, the level of anti-TPO was similar in seropositive and seronegative groups (24% and 27% respectively). RA patients treated with biological therapy presented higher level of anti-TPO in 28%, similarly to RA patients without biological therapy (24%). There was no relevant difference in level of anti-TPO among the groups with different disease activity (high activity: DAS28 > 5.1; - 24%; moderate activity: DAS28 ≤5.1; > 3.2; - 25%; and in low activity DAS28 ≤ 3.2; - 28% respectively).
Conclusion: Our present data show that the elevated level of anti-TPO is similarly in patients with serologically different forms of RA and in the control group. The presence of anti-TPO antibody does not affect the severity of RA and the results obtained with the treatment, including that anti-TPO positivity does not increase the need for biological therapy.
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Disclosure of Interests: None declared
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AB0249 POSITIVE EFFECT OF ANTIRHEUMATIC THERAPY ON THE COURSE OF CHRONIC HEART FAILURE IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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Background:
Objectives: to evaluate the effect of antirheumatic therapy according to the "treat to target" strategy on the course of chronic heart failure (CHF) in patients with early RA.
Methods: The study included 22 patients CHF with valid diagnosis of RA (criteria ACR / EULAR, 2010), 17 (77%) of women, median (Me) age - 60 years, Me disease duration - 7 months; IgM seropositive for rheumatoid factor 10 (45%) and / or antibodies to the cyclic citrulline peptide 22 (100%), DAS28-5.6 [4,8;6,5]. CHF verified in accordance the recommendations for the diagnosis and treatment of CHF Society of Specialists in Heart Failure (2013). The concentration of NT-proBNP

was determined by electrochemiluminescence. For all patients was started methotrexate (MT) therapy with a rapid increase in the dose to 30 mg per week subcutaneously. If the MT was not effective enough, after 3 months a biological Disease-Modifying Anti-Rheumatic Drug (bDMARDs) was added to the therapy, predominantly TNF-alpha inhibitors. After 18 months, 10 (45%) patients were in remission and low disease activity, 6 (60%) of patients underwent MT therapy in combination with bDMARDs.

Results: In baseline CHF with preserved EF was revealed in 21 (95%) patients, in 1 patient - CHF with reduced EF. After 18 months there was a positive dynamics of improvement of clinical symptoms, echocardiographic indicators (decrease the size of the left atrium (LA) and the index of end-systolic volume of LA, IVRT, E' LV), diastolic function of the left ventricle (LV). There was no decompensation of CHF. LV diastolic function normalized in 7 (32%) patients who reached the target level of blood pressure, remission (n = 5) and low (n = 2) disease activity, mainly in the treatment of MT and bDMARDs. In patients with RA and CHF, the level of NT-proBNP decreased from 192.2 [151.4; 266.4] to 114.0 [90.4; 163.4] pg / ml (p <0.001), normalized in 16 of 22 (73%) patients (p <0.001) with remission or low RA activity. In 5 (22%) patients, the clinical manifestations of CHF regressed, LV diastolic function and NT-proBNP level normalized.

Conclusion: In patients with early RA and CHF anti-rheumatic therapy improves the clinical course of CHF. There were an improvement in the clinical course of CHF, diastolic function of the left ventricle and a decrease in NT-proBNP.

Disclosure of Interests: None declared

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AB0250 OSTEOPOROSIS, VERTEBRAL FRACTURES AND NON-ALCOHOLIC FATTY LIVER DISEASE IN RHEUMATOID ARTHRITIS: ARE THEY ASSOCIATED?

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Background: Non-alcoholic fatty liver disease (NAFLD) is a frequent finding in rheumatoid arthritis (RA). It has been advanced that NAFLD and vertebral fractures (VF) are associated in healthy men recently(1).

Objectives: The aim of this study was to evaluate NAFLD association with BMD and VF in RA population.

Methods: Cross-sectional study was made at our rheumatology department, patients with RA have been assessed for NAFLD with ultrasonography and osteoporosis (hip and lumber BMD) with DXA device. Patients with secondary liver disease (viral, alcoholic) were excluded. Data about osteoporosis risk factors, clinical features and laboratory tests (liver enzymes, lipid profile, hemoglobin, ferritin, etc) were collected. Anterior vertebral fractures (VF) were assessed by lateral spine radiographs. Comparison of patients with and without NAFLD was done by SPSS.20. Multiple regressions were made to explain osteoporosis and VF with models including NAFLD and other risk factors. Significance was defined by p under 0.05.

Results: We have included 172 RA patients, mean age was 55.4±11.9 years. Ninety per cent were females. Their average BMI was 26.8±5.47. Hypertension was diagnosed in 23.8% and 16.3% had diabetes. Forty per cent (40.1) had osteoporosis, 27.3% (47) had NAFLD. RA patients with NAFLD were older (p=0.04), obese (p=0.003), frequently associated to diabetes (p=0.02), Sjogren's disease (p=0.001), higher total cholesterol (p=0.02) and gamma-glutamyl transferase (GGT) (p=0.002). Comparison tests did not reveal any associations with fractures, BMD or osteoporosis. In multiple regression models, patients with NAFLD and altered liver enzymes were associated to VF (p=0.04, OR=4.7[1.05-21.69] but not to BMD when adjusted on age (p=0.02), BMI (p=0.02), diabetes, menopause and Sjogren's disease.

Conclusion: NAFLD was frequent among our RA patients and was associated to VF prevalence in this study but not to BMD.

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AB0251 SARCOPENIA IN MOROCCAN POPULATION WITH RHEUMATOID ARTHRITIS: PREVALENCE AND PREDICTIVE FACTORS

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Background: Patients with rheumatoid arthritis (RA) were at risk for altered body composition with higher prevalence of sarcopenia compared to the general population. Low lean muscle mass may constitute an additional risk factor for altered bone density in RA patients.

Objectives: We aimed to study the prevalence of sarcopenia and to assess its predictive factors in Moroccan patients with RA.

Methods: We conducted a cross-sectional study over two months in our department of rheumatology. All RA patients fulfilled ACR/EULAR 2010 criteria. We performed a whole-body dual-energy X-ray absorptiometry (DXA) to measure lean mass, fat mass and bone mass in the whole body and body parts. The appendicular skeletal muscle mass was assessed using the sum of skeletal muscle mass in the arms and legs. The relative skeletal muscle mass index (RSMI) was calculated from the appendicular skeletal mass divided by the square of the patient's height (kg/m2). According to Baumgartner et al, sarcopenia was defined as a relative SMI <5.5 kg/m^2 on women and <7.26 kg/m^2 on men. Body mass index (BMI) was measured and patients were classified according to World Health Organization. Disease activity and functional disability were measured using the 28-joint Disease Activity Score (DAS28) with CRP and the Health Assessment Questionnaire (HAQ). Comorbidities and medication use including corticosteroids were also recorded. Data was entered and processed using the IBM SPSS Statistics 20. A univariate analysis as well as multivariate regressions were carried out to assess the association between sarcopenia and lumbar spine and femoral neck (FN) bone mineral density (BMD) and RA characteristics.

Results: We included 70 (87.5%) women and 10 (12.5%) men with a mean age of 53.59 ±10.96 years old. They had a mean disease duration of 12.35± 8.68, a mean DAS 28 CRP of 2.64±1.34, a mean HAQ of 0.94±0.63 and a mean RSMI of 5.75±1.17. Women had a mean RSMI of 6.33±1.04 while men had a mean RSMI of 5.66±1.17. The prevalence of sarcopenia in our population was 47.4% (37), of whom 81.1% (30) women.

In univariate regression analysis, sarcopenia was associated with normal BMI (OR: 8.59, 95% CI [3.054-24.182], p= 0.000), DAS 28 CRP (OR: 1.78, 95% CI [1.203-2.657], p= 0.004), HAQ (OR: 2.15, 95% CI [1.165-5.433], p= 0.019), lumbar spine BMD (OR: 0.001, 95% CI [0.00001-0.043], p= 0.0004) and FN BMD (OR: 0.000006, 95% CI [0.000-0.002], p= 0,00008 at right FN and OR: 0.00009, 95% CI [0.000001-0.010], p=0.000 at left FN, respectively).

In multiple regression analysis, sarcopenia was associated with normal BMI (OR: 11.56, 95% CI [2.754–48.598]), p=0.001 and FN BMD (OR: 0.00, 95% CI [0.000–0.084], p = 0.006).

Conclusion: In the present study, sarcopenia was common among RA patients and associated with normal BMI and femoral neck BMD, emphasizing the importance of this modifiable risk factor. Further studies are needed to identify effective means to improve lean muscle mass in patients with RA.

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AB0252 ASSOCIATION OF FAT MASS AND ITS DISTRIBUTION WITH BONE MINERAL DENSITY FOR RHEUMATOID ARTHRITIS PATIENTS.

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Background: Bone mineral density (BMD) and body mass are closely associated. lean mass(LM) and fat mass(FM) account for approximately 95% of body mass[1].

Objectives: We aimed to study the association between body fat mass and its distribution with femoral and lumbar bone mineral density in rheumatoid arthritis (RA) patients.

Methods: The present RA population-based cross sectionnel study done on 2019 was part of our rhumatology departement. Clinical data, femoral and lumbar BMD, body fat mass (BFM), android fat mass(AFM), gynoid fat mass (GFM), visceral fat mass (VFM) measured with dual energy X-ray absorptiometry (DXA: Hologic®) and results of laboratory tests were collected. Our statistical analysis was based on descriptive study and linear regression with SPSS20.

Results: We included 73 RA patients witch mean age of 52.7+/-11.7, their mean of body mass index was 26.6+/5.8, mean of disease activity score was 2.6+/-0.94 and the mean health assessment questionnaire was 1.14+/0.78. In univariable linear regression, we found a significant association between femoral BMD and (BFM) (p=0.001, béta=0.36, IC:[0.000003-0.00001]), (AFM) (p=0.01, béta=0.29, IC:[0.00001, 0.00008]) and (GFM) (p=0.001, béta= 0.38, IC=[0.000005-0.000088]). There wasn't any association between (VFM) and femoral BMD. Also we have found a significant association between lumbar spine BMD and BFM (p=0.0002, béta=0.41, IC[0.000003-0.000011]), AFM(p=0.001, béta=0.38, IC[0.000025-0.000094]), GFM(p=0.000018, béta=0.47, IC[0.00003-0.00007] and VFM (p=0.01, béta=0.28, IC[0.000027, 0.000251]). Adjusted on BFM, GFM, AFM and VFM in multiple regression analysis, it seems that the association between GFM, femoral BMD (p=0.02, béta= 0.38, IC[0.000005, 0.000088]. and lumbar spine BMD(p=0.01, béta=0.85, IC[0.000022, 0.000168]), was more significant.

Conclusion: The finding of this study confirmed previous studies partly, that genoid fat mass has a positive effect of lumbar and femoral BMD.

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AB0253 A REVIEW OF SMOKING CESSATION STRATEGIES AND LUNG CANCER SCREENING PRACTICES IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Smoking rates among patients with rheumatoid arthritis (RA) exceed those reported in the general population. In addition, people with RA who smoke are more likely to develop lung cancer than smokers who do not have RA.

Objectives: To identify smoking cessation strategies and lung cancer screening practices in patients with RA.

Methods: We conducted a review of the literature in electronic databases (i.e., PubMed, EMBASE, Cochrane, Scopus, and Web of Science) from inception until June 2019. We included studies that reported on the results of interventions for smoking cessation or lung cancer screening in patients with RA. We excluded case reports, reviews, guidelines, protocols, or studies on tobacco use not reporting interventions. We included studies published in abstract or full-text format. We extracted study and intervention characteristics including delivery format, timing and results.

Results: We retrieved 394 relevant citations and ultimately included 9 studies evaluating smoking cessation strategies, and one regarding lung cancer screening practices. Five studies were reported in abstract format. There were 3 studies conducted in the United Kingdom, and one each in Croatia, France, Ireland, New Zealand, Sweden, Spain and United States. Two studies were randomized control trials and the remaining were uncontrolled. Follow-up ranged between 1 month and 24 months, however, one study only reported data on the assessment immediately after the intervention. Sample sizes ranged between 20 and 185 current smokers. Smoking cessation strategies included: 1) brief advice and nicotine replacement therapy + smoking cessation counseling for 3 months; 2) information booklet on harms of smoking (i.e., impact on disease and treatment); 3) spoken information on harms of smoking (i.e., impact on disease and treatment) plus advice to quit smoking; 4) advice to quit smoking plus nicotine replacement; 5) smoking cessation support with contact every 4 weeks; 6) spoken information on harms of smoking (i.e., impact on disease and treatment) plus advice to quit smoking plus nurse telephone visit at 3rd month; 6) staff driven tobacco QUIT line referral process; 7) multi-modality intervention with advise to quit smoking plus guidance on safe alcohol use plus dietary advise with booklet and swimming group. The lung cancer screening study reported on a program with nurse evaluation of comorbidities and risk factors, and recommendations for lung cancer screening with a chest X-ray and smoking cessation. Most studies reported benefits when implementing a structured plan to educate, counsel, and offer pharmacological treatment to patients with RA.

Conclusion: There was large heterogeneity among studies in patient characteristics and interventions proposed, and outcomes. Only 2 studies were randomized clinical trials. Additional controlled studies are needed to determine best practices for smoking cessation and lung cancer screening in patients with RA.

Disclosure of Interests: None declared

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AB0254 PATIENT CHARACTERISTICS, COMORBIDITIES, AND INFECTION OUTCOMES AMONG RHEUMATOID ARTHRITIS (RA) PATIENTS IN PUERTO RICO (PR)

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Background: Although the burden of comorbidities and infections in RA patients in the US is well established, [1] there is an evidence gap for RA patients in the US territory of PR.

Objectives: To describe the patient demographics, clinical characteristics, and infection rates in patients with RA in PR

Methods: A retrospective cohort of adults age ≥18 years from PR with ≥2 diagnosis of RA were identified using International Classification of disease codes (ICD-9 or ICD-10) on separate days from Jan 1, 2006 to June 30, 2018 using the Truven MarketScan™ database. Patients were divided into three treatment cohorts: no treatment, conventional disease-modifying anti-rheumatic drugs (csDMARD) user, and biologic DMARD (bDMARD) user. Patients in the no treatment group were followed from their first RA diagnosis date to the date of initiation of any DMARDs. The csDMARD users were followed from the initiation of csDMARD until the initiation of any bDMARD or targeted synthetic DMARDs (tsDMARDs). Patients were censored at the last observed medical claim if treatments were not initiated during follow-up. bDMARD users were followed from the date of initiation of bDMARD or tsDMARD until their last observed medical claim. Crude incidence rates /1000 person-years (PY) were reported for opportunistic infections (e.g. Mycobacterium, Cytomeglavirus, Candidiasis, and Chlamydial infections) and infections requiring hospitalisation.

Results: Of the 623 patients in the cohort of RA patients from PR, majority were women (75.4%), aged 41-64 years (67.1%), employed full time (69.8%), with PPO health plan (89.4%), and with mean length of follow-up of 5.77 years from index RA diagnosis. Our results shows that cardiovascular conditions (CVD, hypertension, and hyperlipidemia) were the most prevalent comorbidities in PR patients with RA (Table 1), followed by diabetes (55.7%) in the total RA patient population. The crude IR/1000 PY for opportunistic infections was 23.35 for patients in the no treatment cohort, 48.52 for patients in csDMARD, and 28.31 for bDMARD users. For hospitalized infections, the crude IR/1000 PY was 26.00 for patients in the no treatment cohort, 22.08 for csDMARD users, and 41.90 for bDMARD users.

Table 1. Patient Clinical Characteristics

Patient Characteristics	Total Patients		No Treatment		csDMARD user		bDMARD user	
	N	%	N	%	N	%	N	%
Total	623	100.0	606	97.3	168	27	94	15.1
CCI Score								
Mean (SD)	2.31 (1.85)		2.39 (1.82)		1.85 (1.47)		2.57 (2.41)	
Comorbidities								
Total Patients	571	91.7%	486	80.2%	130	77.4%	76	80.9%
Asthma	170	29.8%	125	25.7%	33	25.4%	25	32.9%
Chronic Kidney Disease	47	8.2%	32	6.6%	7	5.4%	8	10.5%
COPD	138	24.2%	108	22.2%	22	16.9%	16	21.1%
Cardiovascular disease	357	62.5%	278	57.2%	61	46.9%	55	72.4%
Hypertension	447	78.3%	371	76.3%	87	66.9%	63	82.9%
Hyperlipidemia	418	73.2%	350	72.0%	66	50.8%	47	61.8%
Malignancy	124	21.7%	101	20.8%	18	13.9%	20	26.3%
Peripheral artery disease	74	13%	58	11.9%	10	7.7%	11	14.5%
T2DM	318	55.7%	251	51.7%	58	44.6%	37	48.7%

Note: Comorbidities and CCI was calculated for patients during follow-up in respective cohort

Conclusion: Puerto Rican patients with RA have a significant burden of comorbidities, infections and hospitalisations. Trends indicate a variation in the burden by the type of treatment. Furthermore studies are warranted to better understand the potential healthcare implications of comorbidities in patients with RA.

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Disclosure of Interests: Manasi Suryavanshi Consultant of: Bristol Myers Squibb, Sonick Suri Consultant of: Bristol Myers Squibb, Ying Bao Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Maribelis Ruiz Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Vardhaman PATEL Employee of: Bristol Myers Squibb, Eory Madera-Miranda Employee of: Bristol Myers Squibb

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AB0255 RISK OF FRAGILITY FRACTURE IN A COHORT OF PATIENTS WITH RHEUMATOID ARTHRITIS.

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Background: Rheumatoid Arthritis (RA) is associated with low bone density and hight risk fracture compared to general population.
Objectives: The aim of this study is to assess the effect of some variables on fragility fractures in patients with RA.
Methods: We perform an observational study in a cohort of patients diagnosed of RA according to 1987 and 2010 ACR criteria, to determine the frequency of osteoporotic fractures and associated clinical and densitometric variables. All patients diagnosed of RA were invited to participate in the study between 2013 and 2019, and to perform BMD DXA (GELunarProdigy®). SPSS25 was used to compare variables between patients with fracture and without fracture.
Results: 376 patients with RA were included (78,7% women), mean age 63,3 (±13,2) years old and a mean of evolution of the RA of 118,7(±96,7) months at the moment the BMD was performed. We found bone fracture in 47 (12,6%) patients. Fractures were associated to female gender (OR: 2,93 (1,08-7,93); p=0,02), lower height and weight (p<0,05) and older age (p=0,007).
Table 1 shows the characteristics and differences between patients with and without fragility fractures. Women presented high risk of osteoporosis in lumbar spine [OR=3,89(1,46-10,37); p=0,002] than men, but any differences between gender were found in BMD of femoral neck. Of the fractured patients, BMD T-score was normal in 2 (4,3%), <-1 in 45 (95,7%) and <-2,5 en 25 (54,3%). In the multivariate analysis, the values of T score <-1 and <-2.5 of the hip were associated with fragility fracture, but not the value of T-score in lumbar spine. The risk of fracture decreases 0.008 with each mg/cm2 that increases BMD. The use of corticosteroids was associated with the development of femoral osteopenia [OR 2.04 (1.3-3.2); p = 0.002] but not with an increased risk of fractures. No significant association was found between fractures and the presence of RF, ACPAs, smoking, or treatment with biological therapy.

Table 1.

Characteristics	Patients with fractures (n=47)	Patients without fractures (n=327)	OR (IC 95%); p value
Females	43 (14,7%)	250 (85,3%)	2,9 (1,1-7,8); p=0,02
Age	67,7 (±10,6)	62,7 (±11,6)	P=0,005
Height	152,4 (±9,4)	157,3 (±8,8)	P=0,001
Weight	66,2 (±16)	73,3 (±14,4)	P=0,003
Smokers	8 (12,1%)	58 (87,9%)	0,9 (0,4-2,1) p=0,89
RF (+)	35 (12,2%)	252 (87,8%)	0,9 (0,4-1,7) p=0,66
ACPA+	30 (12,3%)	213 (87,7%)	1,3 (0,6-2,8) p=0,44
Steroids	36 (14,4%)	214 (85,6%)	1,7 (0,8-3,5) p=0,13
Biologics treatment	16 (16,2%)	83 (83,8%)	1,5 (0,8-2,9) p=0,22
Bone mineral density (BMD) in lumbar spine<-1	34 (16,8)	168 (83,2)	2,6 (1,3-5,2) p=0,006
BMD femoral neck CF<-1	43 (17,8)	198 (82,2)	9,0 (2,7-29,6) p<0,001
BMD lumbar spine<-2.5	17 (26,6)	47 (73,4)	3,4 (1,7-6,7) p<0,001
BMD femoral neck<-2.5	20 (29,4)	48 (70,6)	4,4 (2,3-8,5) p<0,001
Major osteoporotic risk (FRAX)	37 (23,6)	120 (76,4)	7,4 (3,2-17,2) p<0,001
Hip fracture risk (FRAX)	34 (24,5)	105 (75,5)	5,9 (2,8-12,5) p<0,001

Conclusion: Women with RA present higher risk of fracture than men. The most sensitive indicator for fracture risk seems to be MBD in femoral neck.
Disclosure of Interests: None declared
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AB0256 INCREASED SERUM PROCALCITONIN CONCENTRATION IN PATIENTS WITH RHEUMATOID ARTHRITIS FREE OF ACTIVE INFECTION

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Background: Rheumatoid arthritis (RA) is the most common inflammatory arthritis, affecting 0.5-1% of the general population worldwide. Patients with RA are often in a relatively immunocompromised status. Previous study have evaluated procalcitonin (PCT) application among autoimmune and autoinflammatory diseases for the diagnosis of systemic bacterial infection (1, 2) To date, the correlation of baseline PCT levels and RA disease activities, different treatment, or the expression of proinflammatory cytokines in patients with RA remained unknown.
Objectives: To investigate the baseline PCT levels among patients with RA without active infection compared with healthy controls and to understand the relationship of PCT with RA disease activity, treatment received by patients, and the expression of proinflammatory cytokines.
Methods: Patients aged 20 years and above, with clinician-confirmed diagnosis of RA were included during regular outpatient visits. RA disease activity was measured using the DAS28-ESR.
Results: A total of 623 patients with RA and 40 healthy subjects were recruited in this study. The mean PCT were significantly higher in patients with RA (6.90 ± 11.81 * 10^{-3} ng/mL) compared with healthy controls (1.14 ± 3.26 * 10^{-3} ng/mL) (p = 0.002). After adjusted for age and sex, the PCT levels remain significantly elevated in patients with RA (p = 0.001). PCT was not significantly correlated with biologic agent, age, sex, disease duration, disease activity, C-reactive protein, conventional synthetic disease-modifying antirheumatic drugs (csDMARD), and comorbidities. Multiple linear regression analysis showed that PCT was inversely associated with the expression of IL-1β (B = –0.883; CI 95% –1.388, –0.378, p = 0.001) and IFN-α (B = –1.197; CI 95% –2.153, –0.242, p = 0.014) after adjusted for age and sex.
Conclusion: Patients with RA have significantly higher baseline PCT compared with healthy controls. The treatment received by patients with RA did not affect the level of PCT. Further investigation is required to determine the optimal cutoff value of PCT among patients with RA before applying it in daily clinical practice.
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AB0257 ASSESSMENT OF PHYSICAL DYSFUNCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO PLANNED PREGNANCY FROM THE IORRA COHORT.

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Background: It has been reported that female rheumatoid arthritis (RA) patients have a longer time to pregnancy than healthy women (1), and that high Disease Activity Score with 28 joint count (DAS28) -CRP in preconception increases the frequency of infertility (2). Before the era of biologics, RA treatment tended to be inadequate from pregnancy planning to the end of lactation. And it was not uncommon for female RA patients to be unable to get pregnant or develop physical dysfunction as a result of insufficient control of the disease. There are some reports of disease activity during pregnancy and postpartum in RA patients, and the effects of RA disease activity on pregnancy and childbirth outcomes (3-5), but there are few reports focusing on the physical function during pregnancy planning of RA patients.
Objectives: To investigate disease activity and physical function in female patients with RA who planned and didn't plan pregnancy.
Methods: The IORRA cohort is a large, single institute-based, observational cohort of RA patients established at the Institute of Rheumatology, Tokyo Women's Medical University, in 2000. We identified female RA patients aged 20-49 years who answered 'pregnant' or 'delivered' in the IORRA survey in 2010-2015 and whose pregnancy and the pregnancy planning time was confirmed in the medical records, and defined them as the pregnancy planning (PP) group. Matched control was extracted at 1:3 ratio from patients without pregnancy plan based on entry time, age, RA disease duration, DAS28-CRP, Japanese version of Health Assessment Questionnaire (J-HAQ) score, and comorbidities. The primary endpoint was J-HAQ at 3years from the baseline,

which was defined as the most recent IORRA survey before planning pregnancy. The mixed-effect model for repeated measures was used to analyze group difference.

Results: There were 40 patients in the PP group (average 32.2 years, disease duration 5.7 years, DAS28-CRP 1.7, J-HAQ 0.26), and 120 patients in the control group (average 32.4 years, disease duration 5.9 years, DAS28-CRP 1.7, J-HAQ 0.21). The proportion of user and dosage of MTX and glucocorticoid (GC) and bDMARDs user at baseline were comparable between the groups (MTX: PP 87.5% [9.8 mg/week], control 85.0% [8.8 mg/week]; GC: PP 32.5% [3.6 mg/day], control 27.5% [4.4 mg/day]; bDMARDs: PP 40.0%, control 27.5%). DAS28-CRP at year 3 of the PP group elevated and was higher than the control group (PP 2.3, control 1.7, p<0.01), while J-HAQ was stable over the observation period and did not differ significantly at year 3 (PP 0.21, control 0.22, p=0.92). At year 3, the proportion of patients taking MTX was lower and taking GC was higher in the PP group than those in the control group (MTX: PP 36.7%, control 76.7%, p<0.01; GC: PP 70.0%, control 25.6%, p<0.01). The proportion of patients taking bDMARDs was not different in both groups (PP 36.7%, control 32.6%, p=0.68).

Conclusion: Physical function in pregnancy planning patients with RA did not deteriorate as well as the control patients in clinical settings.

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AB0258 CAROTID INTIMA-MEDIA THICKNESS AND SERUM BIOMARKERS IN PARAGUAYAN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The mechanism of increased cardiovascular risk in RA is not well understood and is independent of traditional CV risk factors. Intima-media thickness of the common carotid wall measured by ultrasonogram is a safe and useful biomarker of early stage atherosclerosis that correlates with coronary involvement; and it correlates with severity and duration of disease. Several studies have shown a relationship between inflammation markers, endothelial dysfunction markers, and carotid involvement. (1)

Objectives: To determine the presence of inflammation biomarkers and its relationship with subclinical atherosclerosis measured by carotid ultrasound, and with the clinical characteristics in patients with established Rheumatoid Arthritis (RA)

Methods: Descriptive, cross sectional, prospective study, in a Paraguayan cohort of patients with RA meeting ACR/EULAR2010 criteria. This study had two phases: the first one, included a standardized questionnaire according to the variables included in the Cardiovascular Risk project (PINV15-0346), from the National Sciences and Technology Council (CONACYT), and physical examination; the second one included laboratory sample collection performed by a specialized laboratory for serum biomarkers measurement for cardiovascular risk prediction (i.e endothelin, alpha-TNF, E-selectin, homocysteine, apolipoprotein, fibrinogen, and high sensitivity-CRP levels) and carotid ultrasound evaluation by a trained specialist, to evaluate subclinical atherosclerosis. Subclinical atherosclerosis was defined as carotid intima-media thickness (CIMT) >0,9mm and/or presence of carotid plaques. All patients signed informed consent. SPSS 23rd version was used for data analysis. Quantitative variables were presented as means and qualitative as frequencies. Chi square test was performed for comparisons between dichotomous variables and t Student for continuous, and $p \leq 0.05$ for statistical significance.

Results: 100 patients were included, 87% were women, mean disease duration 130.9±102.64 months, 77% were RF positive, and 84.4% were ACPA positive, 43.4% had bone erosions, mean ESR-DAS28 was 3,42±1,1; 30% had remission criteria. 39% had extra-articular manifestations.

Elevated serum biomarkers were found: fibrinogen >400 mg/dL 88.2%, high sensitivity-CRP (hs-CRP) >5mg/dL 42.9%, endothelin >2 ng/mL 20%, alpha-TNF >15,6 pg/mL 13.1%, E-selectin >79,2 ng/mL 6%. 25.3% had CIMT >0,9 mm and mean CIMT was 0.68±0.25mm. 27.14% had carotid plaques. Patients with CIMT>1mm had higher frequency of family history of arterial hypertension (p=0.006), greater mean disease duration (p=0.0007), hip circumference (p=0.014), blood pressure (SBP p=0.038, DBP p=0.027), HAQ levels (p=0,019) and hs-CRP levels (p=0.013), also lower mean height (p=0,04); while carotid plaques were related to higher homocysteine (p=0.026) and hs-CRP levels (p=0.024).

Conclusion: A considerable percentage of patients had subclinical atherosclerosis. Patients with CIMT>0,9mm had a longer disease duration, higher HAQ levels, hip circumference, as well as higher BP. High levels of hs-CRP were more frequently related to the presence of subclinical atherosclerosis

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Disclosure of Interests: None declared

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AB0259 THE RELATIONSHIP BETWEEN MICROVASCULAR DAMAGE AND DISEASE ACTIVITY IN PATIENT WITH RHEUMATOID ARTHRITIS – ASSESSMENT BY VIDEOCAPILAROSCOPY

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Background: Rheumatoid arthritis (RA) is an autoimmune disease characterized by erosive synovitis (causing severe joint damage) and systemic damage.

Rheumatoid vasculitis (RV) is an extra-articular manifestation of rare but serious rheumatoid disease that involves the damage of small and medium sized vessels.

Objectives: The purpose of the study was to evaluate the incidence of damages occurred on cutaneous level in patients diagnosed with RA and to detect capillaroscopic microangiopathy changes in the activity of rheumatoid disease.

Methods: 101 patients were included in the study, all were diagnosed with RA according to the ACR/EULAR 2010 criteria. RV diagnosis was based on the clinical examination. The capillaroscopic evaluation was performed with a 3.0 VideoCap device at a 200x magnification (200x magnification contact lenses). Capillaroscopic examination was performed on fingers II-V of both hands, being considered pathological if the capillaroscopic changes are present in at least two fingers. The activity of disease was calculated using DAS 28 ESR score.

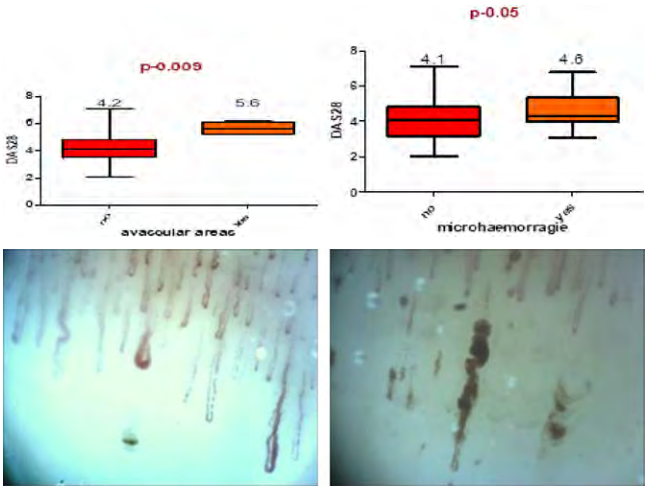
Results: 18% of examined patients was male and 82% female, with the mean age of 56,2years±10.16SD, and the mean duration of the disease in years of illness was 8.65±5.31SD. 3 patients had periungual vasculitis with cutaneous ulceration and gangrene, 12 patients had palpable purpura. 29% of the patients had vasospastic skin changes. The activity score of RA was associated with the capillaroscopic changes in peripheral microangiopathy p-0.037. Capillaries images were heterogenous in aspects and distribution, tortuous capillaries, microhemorrhages, giant/dilated capillaries, avascular areas were observed.

Conclusion: Vascular microangiopathy evidenced by capillaroscopic examination is present in patients with cutaneous vasculitis having a medium, severe activity of rheumatoid diseases.

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Dilated, giant capillaries, microhemorrhage bleedings, avascular area
Reduced blood flow (observed in dynamics)

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AB0260 SARCOPENIA AND RHEUMATOID ARTHRITIS

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Background: Nowadays in the field of syndromes and diseases associated with age, scientists focus especial attention on the problem of sarcopenia, which combines an increased risk of falls, deterioration of life quality, impaired functional activity, reduced life expectancy and increased mortality of patients. In 2016, sarcopenia has been included in the International Classification of Diseases. There are the primary and secondary forms of sarcopenia.

Objectives: The aim of this study was to evaluate the bone mineral density, lean mass, frequency of pre-sarcopenia and analyze correlation among the activity parameters, duration of the disease, life quality and lean mass indices in women with rheumatoid arthritis.

Methods: 461 women aged 40-87 years (age - 57.17 ± 0.71 years) were examined, among them 71 patients with rheumatoid arthritis and 390 controls. We conducted the clinical and laboratory examination. Pain intensity was evaluated by the visual analogue scale, the quality of life – by the HAQ questionnaire. Lean mass, bone mineral density were measured by the X-ray absorptiometry (Prodigy, GEHC Lunar, Madison, WI, USA). Pre-sarcopenia was determined when an appendicular lean mass index was less than 5.72 kg/m2 (V. Povoroznyuk, N. Dzerovych, 2016).

Results: Patients with rheumatoid arthritis had a significantly lower femoral neck mineral density (p = 0.002), lean mass of the total body (p = 0.01) and appendicular lean mass (p <0.01). We didn't find any significant connection among the activity parameters (C-reactive protein, ESR, pain VAS, DAS-28), duration of the disease, life quality and lean mass indices in patients with rheumatoid arthritis. However, a significant correlation was found between the number of swollen joints and lean mass of upper limbs (r=0.67; p=0.02).The frequency of pre-sarcopenia in women with rheumatoid arthritis was 49 %, in the control group – 18 %.

Conclusion: Patients with rheumatoid arthritis had not only bone tissue, but also skeletal muscle tissue disorders, resulting in a significant deterioration of functional capacity and quality of life. Given the significant medical and social significance of the problem, further studies into the mechanisms of pathogenesis, development of diagnostic methods, prevention and treatment of sarcopenia in patients with rheumatoid arthritis are required.

Disclosure of Interests: None declared

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AB0261 IMPACT OF COMORBIDITIES IN THE DISEASE ACTIVITY OF PATIENTS WITH SPONDYLOARTHRITIS AND RHEUMATOID ARTHRITIS: TUNISIAN REGISTRY (BINAR)

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Background: Comorbidities can be associated with rheumatoid arthritis (RA) and spondyloarthritis (SpA). This association can be fortuitous but can also be secondary to rheumatism itself or to the effects of the treatments used. These comorbidities can worsen the disease and even increase patient mortality.

Objectives: To assess the prevalence of comorbidities in RA or SpA patients from the Tunisian BIologics National Registry (BINAR) and to focus on their influence on the disease activity.

Methods: BINAR is a multicenter non-interventional and prospective study, conducted in Tunisia with 80 rheumatologists over a period of three years. It included patients with RA (ACR / EULAR 2010 criteria) or SpA (ASAS 2009 criteria). Data were collected and analyzed through an electronic platform managed by DACIMA. They included demographic data, smoking status and types of comorbidities (cardiovascular disease, diabetes, dyslipidemia, osteoporosis, high blood pressure (HBP), neoplasia, gastrointestinal ulcer, depression and fibromyalgia). RA activity was evaluated by the DAS28-VS score and SpA activity by the BASDAI and ASDAS-CRP scores.

Results: We included 298 patients (175 PR and 123 SpA) making the mean sex ratio 0.6 and mean age 49.18 years ± 14.1 [18-79]. Mean BMI was 27.0 ± 5.5 kg / m^2 [15 -45] and 17.7% of the patients were current smokers. Concerning disease activity, mean DAS28-VS in RA was at 4.9 ± 1.5 [1.1 - 8.1 and mean BASDAI and ASDAS-CRP, in SpA, were respectively 4.1 ± 1.8 and 2.8 ± 1.1. Comorbidities were noted in 54% of patients (62.1% in SpA and 37.9% in RA), with an average of 1.7 comorbidities per patient.

The most common comorbidities were osteoporosis (38.8%), cardiovascular disease (20.1%), diabetes (16.8%), HBP (18.1%), dyslipidemia (6.7%) and GIU (6.0%). Depression, fibromyalgia and neoplasia were mentioned in 1.7%, 1% and 1%, respectively.

No correlation was found between the number of comorbidities and the activity level of RA: DAS28-VS (p=0.12), nor the activity level of SpA: BASDAI(p=0.07), ASDAS-CRP(p=0.15). Correlations were studied between each comorbidity and activity disease parameters of RA and SpA, they are specified in Table 1. We found that only the presence of osteoporosis was associated with SpA activity, (ASDAS-CRP; p = 0.02).

Tableau n°1: Relation between comorbidities and the disease activity parameters of rheumatoid arthritis and Spondyloarthritis

	DAS 28 ESR	BASDAI	ASDAS CRP
Diabetes	p = 0.737	p = 0.633	p = 0.652
High Blood pressure	p = 0.252	p = 0.998	p = 0.323
Obesity	p = 0.565	p = 0.585	p = 0.904
Dyslipidemia	p = 0.332	p = 0.349	p = 0.997
Osteoporosis	p = 0.372	p = 0.989	p = 0.020
Gastrointestinal ulcer	p = 0.829	p = 0.286	p = 0.910

DAS: disease activity score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; ASDAS: Ankylosing Spondylitis Disease Activity Score

Conclusion: According to this study, in patients with RA and SpA associated comorbidities may occur more frequently than expected (54%). However, they had no relation to the activity of the disease according to their frequencies or their types, except osteoporosis which was significantly associated with the SpA activity. Identifying these comorbidities may affect the management and treatment decisions for these patients to ensure an optimal clinical outcome.

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AB0263 SEXUAL FUNCTION IN WOMEN WITH RHEUMATOID ARTHRITIS: A CASE-CONTROL STUDY.

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Background: Sexual dysfunction is defined as a change in any component of sexual activity, which may cause frustration, pain and decreased sexual intercourse[1]. Rheumatoid arthritis (RA) is a systemic autoimmune disease, which may lead to decline in joint mobility, pain, and fatigue; these impairments may influence the sexual health of patients[2].

Objectives: The main aim of this study is to determine if there is an altered sexual function in Mexican women with RA and compare if it occurs in a greater proportion than in healthy women.

Methods: A case-control study that included Mexican women between 18 and 65 years, with RA diagnosis (according to ACR/EULAR 2010 criteria) and age-matched controls was performed. Patients were excluded if they couldn't answer the questionnaires reliably or were currently pregnant. They were asked about their sexual activity in the last month, and the Arizona Sexual Experiences Scale (ASEX), Hospital Anxiety and Depression Scale (HADS) and Functional Assessment of Chronic Illness Therapy (FACIT) self-questionnaires were applied; disease activity was assessed by DAS-28. Variables were compared between groups with student T test for independent samples and chi-square.

Results: We included 102 RA patients and 101 controls. Baseline demographic characteristics between groups are shown in Table 1. Women with RA had less sexual activity than controls (48.03% vs. 90.09%, p <0.001). Out of the total women included, the ASEX was applied only to those that had an active sex life, 49 with RA and 91 controls. Sexual dysfunction (> 18 points) was found in 55.1% of women with RA and in 52.74% of controls, with no significant differences (p = 0.860); the prevalence of severe fatigue was higher in RA than in the healthy group (p = 0.009) (Table 2). Women with RA and sexual dysfunction had higher levels of anxiety (p = 0.024) and fatigue (p = 0.008) than those with RA without sexual dysfunction; however, no significant difference was found in age, depression and level of disease activity between these groups.

Table 1. Comparison of demographic variables between groups.

	RA GROUP (n=102)	CONTROL GROUP (n=101)	P*
Age, years (±SD)	52.98 (+/-13.36)	52.45 (+/- 8.34)	0.738
Sexual activity in the last month, n (%)	49 (48.03%)	91 (90.09%)	<0.001
Civil status			0.456
Single, n (%)	26 (25.5%)	18 (17.82%)	
Married, n (%)	43 (42.2%)	55 (54.45%)	
Divorced, n (%)	15 (14.7%)	11 (10.89%)	
Domestic partnership, n (%)	5 (4.9%)	4 (3.96%)	
Widowed, n (%)	13 (12.7%)	13 (12.87%)	
Menopause, n (%)	70 (68.6%)	72 (71.28%)	0.760
Has children, n (%)	88 (86.3%)	83 (82.17%)	0.447

T de student or Chi-Square test according to type of variable

Table 2. Difference in means of survey scores and frequencies of abnormal scores between groups.

	RA GROUP (n=49)	CONTROL GROUP (n=91)	P*
ASEX score (±SD)	15.65 +/- 4.82	15.45 +/- 5.07	0.819
Sexual dysfunction, n (%)	27 (55.1%)	48 (52.74%)	0.860
HADS-A, anxiety subscale (±SD)	6.53 +/- 3.95	7.15 +/- 3.98	0.378
HADS- D, depression subscale (±SD)	5.34 +/- 4.12	4.32 +/- 3.20	0.108
Fatigue score (FACIT) (±SD)	34.42 +/- 9.52	39.21 +/- 8.37	0.003*
Severe fatigue symptoms, n (%)	17 (34.69%)	13 (14.28%)	0.009*

T de student or Chi-Square test according to type of variable

* Statistically significant difference.

High scores **HADS, ASEX** and low scores in **FACIT** indicate severity.

Conclusion: In this study, women with RA have less sexual activity than healthy women, but no greater sexual dysfunction. Patients with RA and sexual dysfunction have more anxiety and fatigue; but they have no difference in age, disease activity and depression than those with RA and normal sexual function.

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AB0264 ARTERIAL STIFFNESS IN RHEUMATOID ARTHRITIS PATIENTS AS A POTENTIAL PREDICTOR OF EARLY CARDIOVASCULAR AGEING AND MORBIDITY

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Background: Cardiovascular disease (CVD) is one of the most common causes of death in Rheumatoid arthritis patients. Increased arterial stiffness is considered as an independent risk factor of development CVD and a predictor of all-cause morbidity and mortality. Increased arterial stiffness, due to premature vascular ageing, can be observed in patients with chronic inflammatory diseases as well as in RA patients.

Objectives: To evaluate arterial stiffness determined as carotid – femoral pulse wave velocity in rheumatoid arthritis patients. The comparison of traditional and nontraditional risk factor of CVD, disease activity and laboratory findings connected with subclinical atherosclerotic changes.

Methods: We evaluated data of 50 patients with rheumatoid arthritis (39 females, 11male, mean age 57, mean duration of disease of 13years). The arterial stiffness, measured as carotid – femoral pulse wave velocity (PWV), was established with the SphygmoCor system. This non-invasive technique uses the principle of applanation tonometry. Our control group counted 25 heathy male and females with no history of CVD or autoimmune disease. We evaluated the influence of traditional risk factors for CVD as age, smoking, BMI, lipid profile, diabetes mellitus, history of CV and cerebrovascular morbidity to PWV in RA patients. Non-traditional risk factors contained Adiponectin, Fetuin A, Endothelin-1 and Asymmetric dimethylarginine. To measure disease activity was used DAS 28 and inflammatory parameters as a marker of current disease activity. For chronic changes was used X-ray of small joints. Results were correlated with PWV and statistically evaluated.

Results: Mean PWV in Rheumatoid arthritis patients was significantly higher (9.7 m/s) than that in healthy control group (6.7m/s). 49% of RA patients (n= 24) had increased arterial stiffness according to their age. 32% patients (n=16) with PWV over 10m/s that indicates aortal function alteration. We didn´t find correlation between arterial stiffness and traditional and non-traditional CVD risk factors. Increased PWV was not associated with high disease activity. Patients with higher arterial stiffness according to their age had longer RA history, higher level of rheumatoid factor, were more frequently anti-citrullinated protein antibodies (ACPA) negative and were more frequently treated with biological therapy.

Conclusion: Rheumatoid arthritis patients are in increased risk of CV disease. PWV is considered as an independent risk factor of CVD. We proved increased arterial stiffness and vascular ageing in comparison to healthy controls. We did not find correlation between increased arterial stiffness and disease activity. All CVD risk factor intervention is necessary to improve the prognosis of patients. Further investigation is needed to establish the role of increased PWV in RA patients.

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AB0265 REDUCTION OF APPENDICULAR SKELETAL MASS INDEX IS A PREDICTOR OF FRACTURE IN PATIENTS WITH RHEUMATOID ARTHRITIS BASED ON THE THREE-YEAR FOLLOW-UP DATA OF THE CHIKARA STUDY

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Background: Patients with rheumatoid arthritis (RA) have lower muscle mass[1] and a higher risk of fragility fracture[2] compared with healthy individuals. The predictors for fractures among baseline data and the chronological changes of disease activity, body composition, and muscle mass are unknown.

Objectives: The predictors for fractures were investigated over a 3-year period in a longitudinal study.

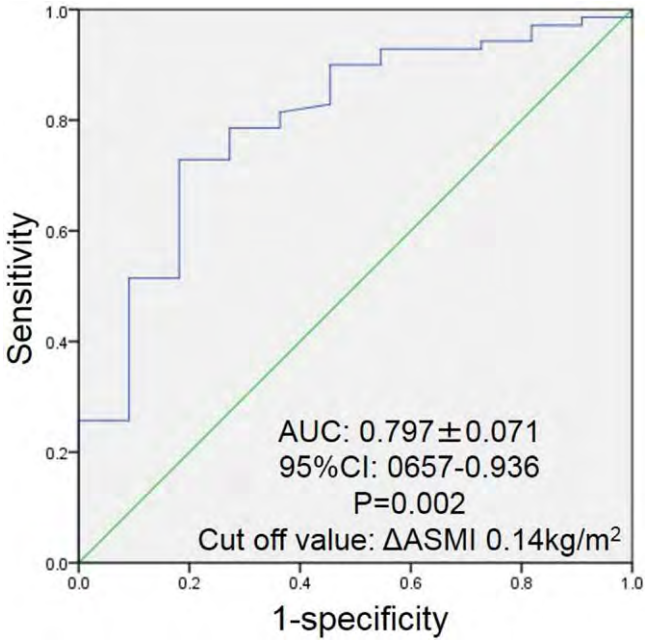
Methods: The 3-year follow-up data from a prospective observational study (CHIKARA study: Correlation researcH of sarcopenIa, sKeletal muscle and disease Activity in Rheumatoid Arthritis) were used. The patients' fractures were counted, and correlations between fractures and disease activity, body composition, and sarcopenia were investigated. Muscle mass, body fat mass, total body water, bone mass, and basal metabolic rate were measured using a body composition analyzer. The fracture-free survival rate was calculated. The relationships between fractures and each parameter at baseline and the changes over the 3-year period (Δ) were investigated by univariate and multivariate analyses.

Results: A total of 100 patients (78 female, average age 68 years) were enrolled in this study; 12 patients (10 female and 2 male) had fractures during the 3-year follow-up, and the fracture-free survival rate was 86.9%. The Δmodified Health Assessment Questionnaire (mHAQ), Δweight, Δmuscle mass, Δestimated bone mass, Δbasal metabolic rate, and Δappendicular skeletal muscle index (ASMI) were predictors for fractures. On the other hand, body composition, disease activity, and sarcopenia at baseline were not correlated with fractures (Table 1). The ΔASMI was an independent predictor for fractures on multivariate analysis (odds ratio:0.015, P=0.026). The estimated cut-off value of the ΔASMI was 0.14 kg/m^2 on receiver operating characteristic curve analysis (Figure). When the ΔASMI decrease was greater than or equal to 0.14 kg/m^2 for three years, the odds ratio of fractures was significantly increased 9.8-fold, compared to a ΔASMI decrease less than 0.14 kg/m^2 (P=0.001).

Table 1. Predictors for fractures in patients with RA

	Univariate	
	R value	P value
Baseline		
Age, year	0.172	0.087
DAS28-ESR	-0.083	0.411
mHAQ	0.077	0.447
Weight, kg	0.021	0.837
Muscle mass, kg	-0.0035	0.728
Estimated bone mass, kg	-0.020	0.845
Sarcopenia	-0.093	0.356
Change of 3-year period		
ΔDAS28-ESR	0.187	0.088
ΔmHAQ	0.224	0.040
ΔWeight, kg	-0.224	0.045
ΔMuscle mass, kg	-0.253	0.023
ΔEstimated bone mass, kg	-0.236	0.034
ΔBasal metabolic rate, kcal/day	-0.248	0.025
ΔAppendicular skeletal muscle index, kg/m^2	-0.352	0.001

Conclusion: The fracture-free survival rate was 86.9% in this 3-year longitudinal study. It was difficult to predict future fractures from the baseline data. Reduction of the ASMI was an independent predictor for fractures. Alleviating muscle mass loss may prevent fractures.



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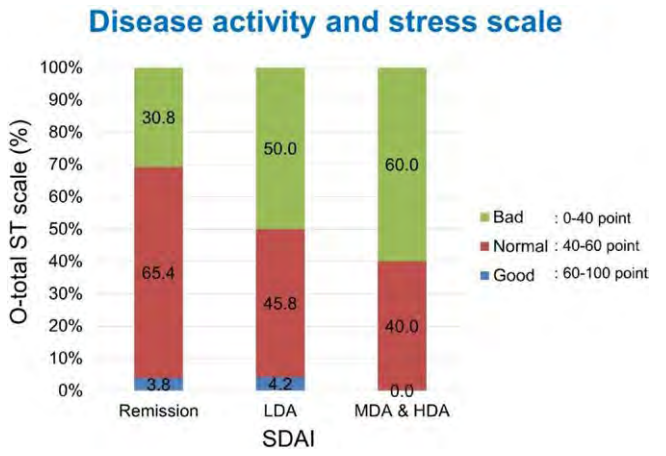
Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.2064

AB0266 ANALYSIS OF STRESS AND FATIGUE IN PATIENTS WITH RHEUMATOID ARTHRITIS USING A DIGITIZING DEVICE

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Background: Stress and fatigue are evaluated subjectively by patients using a visual analog scale (VAS) and questionnaires such as the SF-36 and the FACIT Fatigue Scale. Such evaluations are based on patients' self-reported outcomes. It is difficult to evaluate stress and fatigue objectively. A digitizing device was used to quantify stress objectively.
Objectives: To evaluate the correlations of a digitizing device and a VAS or a questionnaire about stress and fatigue, and the relationships with disease activity of patients with rheumatoid arthritis (RA).
Methods: Data from a prospective observational study (CHIKARA study: Correlation researcH of sarcopenIa, sKeletal muscle and disease Activity in Rheumatoid Arthritis) were used. The study protocol was reported previously[1]. A total of 84 RA patients entered the study and were evaluated using a stress digitizing device (Smart Pulse, MEDICORE Co. LTD). This device evaluates stress based on heart rate variability theory[2]. The objective physical stress score (O-physical ST), mental stress score (O-mental ST), and total stress score (O-total ST) were calculated, ranging from 0 to 100 (higher score indicating greater stress). A questionnaire for stress, the Perceived Stress Scale[3] (PSS) 10 Japanese version (minimum 0, maximum 40), and VAS evaluations of stress (stress-VAS) and fatigue (fatigue-VAS) were carried out. The correlations between subjective and objective methods were analyzed. The relationships between stress, fatigue, and disease activity of RA patients were examined.
Results: The patients' mean age was 68.6 years (women n=66, men n=18), disease duration was 8.8 years, DAS28ESR was 3.24, and modified Health Assessment Questionnaire (mHAQ) was 0.5. The average PSS10 was 26.1, which was higher than in healthy individuals (20.3). The fatigue-VAS was higher than the stress-VAS (41.3 vs 34.5 mm). The O-physical ST score was similar to the O-mental ST score (39.5 vs 37.4). Correlations are shown in Table. The O-physical ST was positively correlated with the fatigue-VAS (R=0.243 p=0.026), and the O-mental ST was also positively correlated with the stress-VAS (R=0.267 p=0.014). However, there was no correlation between the PSS10 and objective stress parameters. The DAS28-ESR was correlated with the fatigue-VAS (R=0.223 p=0.041) and the O-total ST (R=0.329 p=0.002). The stress scale (O-total ST) was worse with moderate and high disease activity than in remission (Figure).
Conclusion: The stress score obtained by an objective digitizing device was correlated with stress- and fatigue-VAS scores. However, there was no correlation with the PSS10 questionnaire. It was found that the fatigue-VAS score and the objective total stress score were high with worse disease control.



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Table. Correlation coefficients of subjective and objective evaluations of stress and fatigue in patients with RA

	PSS10	Stress-VAS	fatigue-VAS	O-physical ST	O-mental ST	O-total ST
PSS10		0.580**	0.404**	0.066	0.055	0.004
Stress-VAS			0.673**	0.007	0.267*	0.023
Fatigue-VAS				0.243*	0.059	0.160
O-physical ST					-0.224*	0.708**
O-mental ST						-0.017
O-total ST						

*: p<0.05, **: p,0.01, Spearman rank correlation coefficient

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.3022

AB0267 BODY COMPOSITION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a complex inflammatory disease that modifies body composition. Using the dual-energy x-ray absorptiometry (DXA) in RA patients could be a method for body composition changes detection.
Objectives: To study the body composition using DXA in patients with RA.
Methods: The study involved 79 women with RA, median age 60 [55; 65] years. The bone mineral density (BMD) was measured by dual-energy x-ray absorptiometry using «Discovery A» (Hologic, USA). Assessment of body composition was carried out, using the program «Whole body». Sarcopenia (SP) was diagnosed as a decrease in appendicular mass index (AMI) <6.0 kg/m^2. Osteoporosis (OP) was diagnosed as a decrease in T-score <-2.5 SD. Osteosarcopenia was determined when T-score was <-1.0 SD, AMI was <6.0 kg/m^2, osteosarcopenic obesity - T-score was <-1.0 SD, AMI was <6.0 kg/m^2 and total fat was >35%.
Results: The mean duration of RA was 9 [3; 11] years. The mean body mass index (BMI) was 27.6±4.8 kg/m^2. Disease activity score in 28 joints-erythrocyte sedimentation rate was 4.5±1.3 points for the group. 39 (49.3%) patients used oral glucocorticoids continuously. Appendicular muscle mass and AMI were on average 17.8±3.0 kg and 6.8±1.0 kg/m^2, respectively. AMI <6 kg/m^2 was detected in 20 (25.3%) patients. 56 (70.9%) women with RA had total fat > 35%, while only 22 (27.8%) of women with RA had obesity according to BMI (BMI >30 kg/m^2). Isolated OP was found in 13 (16.5%), osteosarcopenia in 7 (8.9%) and osteosarcopenic obesity in 13 (16.5%) patients RA. No cases with isolated sarcopenia or sarcopenic obesity were detected. Only 3 (3.8%) patients did not have appendicular muscle mass, AMI and BMD decrease and overfat or obesity.
Conclusion: About 97% women with RA had abnormal body composition phenotype: 16,5% - OP, 8.9% -osteosarcopenia, 16,5% - osteosarcopenic obesity and 54,4% - overfat.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.2318

AB0268 HUMAN T-CELL LEUKAEMIA VIRUS TYPE 1 MAY INVALIDATE T-SPOT.TB RESULTS AMONG RHEUMATOID ARTHRITIS PATIENTS: A RETROSPECTIVE OBSERVATIONAL STUDY

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Background: In clinical rheumatology, interferon-γ release assays (IGRAs) have been reported as a useful diagnostic test for latent tuberculosis infection (LTBI) before beginning the administration of biologics such as anti-TNF therapies (1). CD4-positive T cells are the main target in Human T-cell leukaemia virus type 1 (HTLV-1) infection. Several reports suggest that the reaction of tuberculin skin test (TST) is attenuated in HTLV-1-positive individuals compared with that in HTLV-1-negative individuals (2). However, it remains unclear whether IGRAs are reliable for detecting TB infection among HTLV-1-positive RA patients.
Objectives: The present study aimed to investigate the usefulness of the T-SPOT.*TB* assay in HTLV-1-positive RA patients. In addition, the association between the existence of IFN-γ producing T cells and HTLV-1 proviral loads (PVLs) in HTLV-1-positive RA patients was analysed on the basis of the T-SPOT.*TB* assay results.
Methods: We reviewed the medical records of 75 HTLV-1-negative and 29 HTLV-1-positive RA patients were suspected cases of LTBI and evaluated using the T-SPOT.*TB* assay as a clinical practice from April 2012 to July 2019. The results of T-SPOT.*TB* were collected from medical records, retrospectively. Peripheral blood samples were obtained from HTLV-1-positive RA patients for the analysis of HTLV-1 PVLs values. The study protocol was approved by the research ethics committees of our hospitals.
Results: Approximately 55% of the HTLV-1-positive RA patients showed invalid results for the T-SPOT.*TB* assay ($p < 0.0001$); the cause of invalid results was a spot-forming count of >10 spots in the negative controls of the T-SPOT.*TB* assay among HTLV-1-positive RA patients. Among HTLV-1-positive RA patients, HTLV-1 PVL values were significantly higher in 16 patients who showed invalid results than in 13 patients who did not ($p = 0.003$). There were no between-group differences in female patient ratio, age, RA disease activity and therapeutic regimens. IFN-γ producing cells were detected in the peripheral blood of HTLV-1-positive RA patients without stimulation with TB-specific antigens.

Conclusion: The incidence of invalid results for the T-SPOT.*TB* assay has been reported to be as low as 0.6% (3). The results of this assay for screening of LTBI in HTLV-1-positive RA patients should be interpreted with caution. Furthermore, our results show that an increase in IFN-γ producing T cell numbers due to HTLV-1 infection in RA patients may affect the pathogenesis of RA.

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Disclosure of Interests: Kunihiko Umekita Paid instructor for: Astellas Pharma Inc. Chugai Pharma Inc. Tanabe-Mitsubishi Pharma Inc., Speakers bureau: Bristol-Myers Squibb, Yayoi Hashiba: None declared, Risa Kudou: None declared, Shunichi Miyauchi: None declared, Masatoshi Kimura: None declared, Motohiro Matsuda: None declared, Chihiro Iwao: None declared, Yumi Kariya: None declared, Takeshi Kawaguchi: None declared, Katoko Takajo: None declared, Koushou Iwao: None declared, Yuuki Rikitake: None declared, Ichiro Takajo: None declared, Toshihiko Hidaka Paid instructor for: Astellas Pharma Inc. Chugai Pharma Inc. Tanabe-Mitsubishi Pharma Inc., Speakers bureau: Astellas Pharma Inc. Chugai Pharma Inc. Tanabe-Mitsubishi Pharma Inc., Akihiko Okayama: None declared

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AB0269 THE CHARACTERISTICS OF PERIPHERAL LYMPHOCYTE SUBSETS AND CYTOKINES LEVEL IN RHEUMATOID ARTHRITIS WITH CORONARY ARTERY DISEASE

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Background: Rheumatoid arthritis (RA) is a systemic autoimmune disease. It is characterized by highly disabling polyarthritis, but extra-articular features are also common and portend a poor prognosis. Compared with the general population, the incidence and mortality of cardiovascular disease in RA are significantly increased. Chronic autoimmune inflammation is the common pathogenesis of RA and coronary heart disease(CAD). We've proved that lymphocyte subsets imbalance and high cytokines expression play an important role in the occurrence and development of RA diseases. However, the level of lymphocyte subsets and cytokines of RA patients with CAD are rarely reported[1-2].

Objectives: To explore the clinical characteristic of lymphocyte subsets and cytokines of RA patients with CAD,and make comparisons with simple RA patients and healthy controls.

Methods: The study included 96 patients with a diagnosis of RA according to the 1987 revised criteria of the ACR, including 54 RA patients with CAD and 42 RA patients without CAD and other cardiovascular disease, 40 healthy controls are also concluded. The absolute numbers of lymphocyte subsets and T subsets in peripheral blood were measured by Flow Cytometer (FCM). Serum levels of IL-2, IL-4, IL-6, IL-10, IL-17, INF-γ, and TNF-α were measured by flow microsphere capture chip technique (CBA) for 19 RA patients with CAD and 38 simple RA patients among 96 patients.We also collected relevant clinical information and made DAS28 score, and all patients are in the middle-high disease activity group (DAS28>3.2).

Results: (1) There was no difference in DAS28 scores between the two groups(p=0.572). (2)Compared with RA patients without CAD, the absolute number of total T cell(P=0.035), total B cell (P=0.006), CD4+T cell(P=0.012), Th1 cell(P=0.037), Th17 cell(P=0.033) and CD4+CD25+FOXP3+ Treg(P=0.003) was lower than RA patients with CAD, the number of NK cell(P=0.685), CD8+T cell(P=0.322) and Th2 cell(P=0.770) had no obvious difference between them. (3)Compared with the healthy control, the absolute number of total T cell(P=0.014), total B cell (P=0.006), CD8+T cell(P=0.000) in RA with CAD was evidently lower, but there was no siginificant difference in absolute number of CD4+T cell(P=0.582), Th1 cell(P=0.052), Th2 cell(P=0.595), Th17 cell(P=0.148) and Treg(P=0.176) (Figure 1).(4) In RA patients with CAD,the level of cytokines IL-2(P=0.042), IL-4(P=0.043) and IL-17(P=0.012) was lower, while other cytokines had no difference (Table 1).

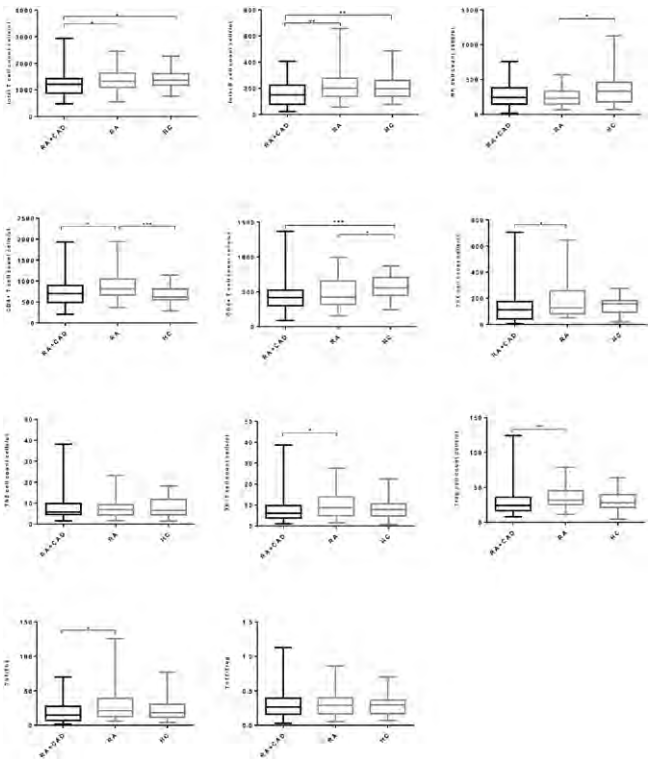


Figure 1. The absolute number of lymphcytes of RA patients with CAD(n=54),RA patients without CAD (n=42) and healthy control (n=40). (*P<0.05,**P<0.01, ***P<0.001).

Table 1. The expression level of cytokines of RA patients with CAD(n=19) and RA patients without CAD (n=38).

Cytokines (pg/ml)	RA and CAD group(A) (n = 19)	RA group(B) (n = 38)	*P* value A vs. B
IL-2	5.50(1.96, 12.82)	6.82(4.45, 14.44)	0.042
IL-4	4.93(1.67, 9.41)	6.28(4.49, 11.88)	0.043
IL-6	23.69(10.93, 73.08)	36.67(15.40, 72.50)	0.636
IL-10	7.76(4.54, 10.50)	7.62(5.69, 19.91)	0.223
IL-17	10.81(4.04, 20.25)	20.68(13.88, 45.58)	0.012
IFN-γ	6.10(3.27, 13.84)	7.13(5.79, 15.83)	0.115
TNF-α	10.49(2.50, 29.04)	14.96(10.03, 30.39)	0.097

Conclusion: Our research shows that there is lymphocyte imbalance and immune disorder existing in RA patients with CAD. Both the number of lymphocyte subsets and cytokine levels decreased in these patients than pure RA patients. It suggests that this group may be in lower immune state, which providing guidance for further clinical treatment of RA patients with CAD.

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Disclosure of Interests: None declared

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AB0270 THE IMPACT OF DIABETES MELLITUS ON OUTCOMES OF RHEUMATOID ARTHRITIS AT 5-YEAR FOLLOW-UP: RESULTS FROM A MULTI-ETHNIC ASIAN COHORT IN SINGAPORE

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Background: Both diabetes mellitus (DM) and rheumatoid arthritis (RA) are prevalent diseases and represent the leading causes of disability and mortality worldwide. Systemic chronic inflammation is recognized as the underlying

etiology of a variety of diseases, including DM and RA [1]. Additionally, cardiovascular and musculoskeletal complications from DM may influence the outcomes of RA patients.

Objectives: To investigate the impact of DM on outcomes of RA patients.

Methods: This is a cross-sectional study including 583 RA patients with 5 years' history after diagnosis in Tan Tock Seng Hospital RA registry, Singapore from 2001 to 2013. Information related to demographics, serologies, clinical features, comorbidities, and outcomes was collected. Independent t-test or Mann-Whitney U test was used to compare continuous quantitative data, while Pearson Chi-square or Fisher Exact test for categorical data. With adjustment for age, gender, ethnicity, smoking and comorbidities, multivariate regressions were performed to analyze the impact of DM on outcomes of RA patients.

Results: DM is more prevalent in Malay and Indian patients than Chinese patients with RA (26%, 24% and 11% respectively, $p = 0.005$). There is no difference of disease activity between DM and non DM patients. There is a tendency that non diabetic RA patients use more methotrexate ($p = 0.052$) and leflunomide ($p = 0.058$). Diabetic RA patients are in higher risk of poor American College of Rheumatology (ACR) functional status ($p = 0.009$), knee arthroplasty ($p < 0.001$) and admissions ($p = 0.006$). Adjusted for age, gender, ethnicity, smoking and comorbidities, multivariate regression analyses showed a trend of poor function status for diabetic RA patients, i.e. ACR functional status (adjusted odds ratio [aOR]: 1.802, 95% confidence interval [CI]: 0.968 – 3.353, $p = 0.063$) and median Health Assessment Questionnaire (HAQ) (β coefficient value: 0.129, 95% CI: -0.010 – 0.267, $p = 0.068$), and higher risk for knee arthroplasty for diabetic RA patients (aOR: 3.480, 95% CI: 1.016 – 11.920, $p = 0.047$).

Conclusion: This is the first report on the impact of DM on RA outcomes in a long term follow-up RA registry in a multiethnic Asian society.

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Acknowledgments: TTSH Rheumatoid Arthritis Study Group

Disclosure of Interests: None declared

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AB0271 EFFECTIVENESS OF DULOXETINE FOR RELIEF OF THE REMNANT PAIN OF RHEUMATOID ARTHRITIS PATIENT WHOSE DISEASE ACTIVITY IS REMISSION

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Background: Pain control in rheumatoid arthritis (RA) patient is an important matter. When pain remains even disease activity is remission, it causes deterioration of activity in daily living (ADL) in past research. In other words, pain affects ADL independently from disease activity, namely the Health Assessment Questionnaire (HAQ) score, a most popular index of ADL for patient with RA[1]. Thus, burden of remnant pain despite clinical remission in RA is serious and pending subject.

Duloxetine, a potent reuptake inhibitor of serotonin and norepinephrine, is developed for the treatment of major depressive disorder [2]. It's effectiveness for pain relief with osteoarthritis is also widely accepted. This drug should be effective not only for chronic pain due to osteoarthritis, but also due to RA. However, effectiveness of duloxetine for remnant pain relief in patient with RA in clinical remission is still unclear.

Objectives: In this study, effectiveness of duloxetine for the remnant pain despite clinical remission in patient with RA was statistically evaluated.

Methods: RA patients whose pain score with visual analog scale (PS-VAS) >30mm despite Clinical Disease Activity Score (CDAI) is <2.8, were picked up for the study. These patients were divided into groups whether duloxetine was administrated (a group without duloxetine: G-C; a group with duloxetine: G-D).

PS-VAS, C-reactive protein, CDAI and simplified disease activity index (SDAI), modified Health Assessment Questionnaire (mHAQ), and QOL value which is calculated from Euro-QOL 5-Dimensions (EQ-5D) were measured at the initiation of duloxetine in the G-D and at the first CDAI remission attained in the G-C, and at week 12 thereafter. Change of these indices were compared with One sample T-test for each group. Patient's global assessment (PGA) at baseline compared to the other components of CDAI was evaluated for each group statistically with One-tailed T-test. Differences between the two groups at each moment were statistically evaluated with Mann-Whitney U-test. Statistical significance was set less than 1%. All statistical analyses were performed using StatPlus:mac® (AnalystSoft Inc., Walnut, CA, USA).

Results: A total of three hundred and six patients were recruited. G-D counted sixty-eight with 18 males and 50 females, while G-C counted 238 with 57 males and 181 females. Average age were 71.3 and 71.5 for G-D and G-C, respectively, with 53.6 months for time span from baseline to initiation in the G-D. 80.8% of the patients in G-D sustained to administrate duloxetine. PGA was 0.6 and 0.5 for G-D and G-C respectively, while the other component of CDAI were below 0.3 in average for both groups and these values were significantly lower than the PGA score in both groups. PS-VAS was 46.4 and 44.0, and significantly decreased to 26.1 and 36.0 in average for G-D and G-C respectively at week 12 when compared to baseline. Reversely, the CDAI score was significantly elevated significantly from 1.16 and 1.19 to 3.25 and 4.34 for G-D and G-C respectively. PGA also significantly increased to 1.5 and 2.4 for G-D and G-C respectively. CRP and the SDAI score also demonstrated same trend significantly as the CDAI score for both groups. mHAQ decreased significantly from 0.430 and 0.495 to 0.393 and 0.487 for G-D and G-C respectively. QOL value increased from 0.800 and 0.817 to 0.811 and 0.840 for G-D and G-C respectively, however no statistical significance demonstrated in both groups.

Conclusion: Duloxetine has been suggested to have effectiveness for the pain relief, for improvement of ADL, and for the contribution to QOL maintenance, however, no effect of disease activity control is expected.

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Disclosure of Interests: None declared

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14. Rheumatoid arthritis - biological DMARDs

AB0272 SWITCHING FROM ETANERCEPT ORIGINAL TO ETANERCEPT BIOSIMILAR. EXPERIENCE IN A TERTIARY HOSPITAL.

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Background: With the arrival of biosimilar drugs and savings policies to make the health system sustainable, hospital managers have chosen to make changes from original molecules to biosimilar drugs.

Objectives: This work aims to reflect what happens when making these switchings.

Methods: We reviewed 235 patients who started Etanercept original in Rheumatology at Navarra Hospital Complex and Henares University Hospital and their switch to Etanercept biosimilar with a follow-up of 6 months.

Results: The switch was performed in 174 patients with psoriatic arthritis (PsA), rheumatoid arthritis (RA), ankylosing spondylitis (AS), juvenile idiopathic arthritis, SAPHO and spondyloarthritis.

9.8% discontinued treatment: 6 RA (8.1%), 5 PsA (9.8 %) and 6 AS (20.7%); all of them in the injection presentation. 12 patient stopped treatment due to ineffecacy, 2 due to reaction at the injection site, 2 due to diarrhea and 1 due to headache. Among 88.2% of patients who returned to Etanercept original, 28.6% did not achieve good response and had to change of treatment. The median time from Etanercept original beginning until the moment of switching was 54 (40-87) months.

Conclusion: In our series, approximately 10% of switching patients failed after a 6-month of follow-up; when trying to return to Etanercept original 28.6% did not achieve response.

The median persistence time in the original molecule and the percentage of failures observed in AS could be two conditions to consider before switching.

A longer-term follow-up and a greater number of patients are necessary to ratify these data.

Table 1

DISEASE	STOPPED CAUSE	BACK TO Etanercept original	CONTINUE Etanercept original	TIME UNTIL SWITCH (meses)
AS	Reaction at the injection site	Yes	Yes	28
AS	Headache	Yes	Yes	54
AS	Ineffecacy	Yes	Yes	126
RA	Ineffecacy	Yes	No	25
AS	Diarrhea	Yes	Yes	87
RA	Ineffecacy	Yes	Yes	37
PsA	Ineffecacy	No	No	43
RA	Ineffecacy	Yes	Yes	54
PsA	Ineffecacy	Yes	No	93
PsA	Ineffecacy	No	No	132
PsA	Ineffecacy	Yes	Yes	62
RA	Ineffecacy	Yes	Yes	142
RA	Reaction at the injection site	Yes	Yes	51
RA	Ineffecacy	Yes	No	56
PsA	Ineffecacy	Yes	No	40
AS	Ineffecacy	Yes	Yes	26
AS	Diarrhea	Yes	Yes	48

Disclosure of Interests: Vicente Aldasoro Speakers bureau: Roche, Abbvie, MSD, UCB, Pfizer, Menarini, Grunenthal, Gebro, Novartis, Janssen, Javier Mendizabal: None declared, Sara Perez Garcia: None declared, Guillen Sada Urmeneta: None declared, Juliana Restrepo Vélez: None declared, Natividad del Val del Amo: None declared, Inmaculada Paniagua Zudaire: None declared, Ricardo Gutiérrez Polo: None declared, Loreto Horcada: None declared, Laura Garrido Courel: None declared, C. Fito-Manteca: None declared
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AB0273 PREDICTORS OF DRUG SURVIVAL OF BDMARDS IN BIO-NAIVE PATIENTS WITH RHEUMATOID ARTHRITIS (RA) DURING THE FIRST YEAR OF THERAPY.

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Objectives: To investigate predictors of drug survival of bDMARDs in previously bio-naive patients (pts) with RA during the first year of therapy.
Methods: 204 adult bio-naive pts (173 women, 84.8%), with active RA, despite the concomitant DMARD therapy, were included into retrospective study. All of them initiated bDMARDs: infliximab (INF) - 65 pts (31.9%), rituximab (RTM) - 39 (19.1%), adalimumab (ADA) - 30 (14.7%), etanercept (ETA) - 28 (13.7%), abatacept (ABA) - 23 (11.3%), tocilizumab (TZ) - 15 (7.4%), certolizumab pegol - 4 (1.9%). The following indicators were used as survival predictors: sex, age and clinical form of RA. Pts were divided by age according to the classification adopted by the World Health Organization: 18-44 years (74 pts), 45-59 years (68 pts), 60-74 years (57 pts), 75 years or more (5 pts). Clinical forms of RA were presented: RA, seropositive by rheumatoid factor (RF), RA, seronegative by RF, RA with extra-articular manifestations, adult-oneset Still's disease, juvenile RA. Predictors of therapy inefficiency or AE were investigated in Cox proportional risk model. Survival on drug was estimated using the Kaplan-Meier method and evaluation of difference significance using log-rank criterion.
Results: A year later, 92 pts (45%) remained on bDMARDs and 112 pts had their treatment discontinued. The reasons of bDMARDs discontinuation during the first year of treatment were: lack of effectiveness (including primary inefficiency) - 50%, adverse events (AE) - 25%, administrative causes - 17%, remission - 6.25%, death due to reasons unrelated to the therapy - 1.75%. By the end of the observation period, the best survival was shown by RTM therapy (69.23% of patients continued treatment for a year), ETA (44.4% of patients) and ABA (43.48% of patients). Discontinuation of bDMARDs due to remission was achieved in 7 patients and proved to be significantly higher in the RTM group (10.26%, $p < 0.05$) compared to the ABA group (8.7%) and ADA group (3.45%). Although the number of women continued after a year was significantly higher than that of men (84.8% and 15.2% respectively), female sex was not a reliable predictor of drug survival. At the same time, the rate of discontinuation due to AE in women was higher (96.55%, $p = 0.03$). After a year, the number of pts continuing treatment in all age groups remained comparable, and the difference between them - statistically not significant: 1 group (18-44 years old, 29 pts) - 31.52% of pts, 2 group (45-59 years old, 36 pts) - 39.13%, 3 group (60-74 years old, 26 pts) - 28.26%, 4 group (75-90 years old, 1 pts). Discontinuation of bDMARDs due to inefficiency was noted in 1 group more often (46.43%, 26 pts, $p = 0.03$), in other groups this indicator was 33.93% (19 pts) in the 2nd group, 19.64% (11 pts) in the 3rd group and 0% in the 4th group. Discontinuation therapy due to AE was also prevalent in 1 group (50%, 14 pts) than in 2 (14.3%, 4 pts), 3 (32.1%, 9 pts) and 4 (3.6%, 1 pts). Discontinuation of therapy due to inefficacy was more common in the group of seronegative RA - 59.1% ($p < 0.05$). In the seropositive RA group 24.8% of pts had interrupted bDMARDs for this reason, in the RA with extra-articular manifestations group it was 18.1%, in the adult-oneset Still's disease group - 30% and in the juvenile RA group - 30%. Discontinuation of therapy due to remission was overwhelmingly observed in seropositive RA group (6 pts, 4%) and was significantly higher than in other groups (1 patient in RA with extra-articular manifestations group, 4.5%).
Conclusion: Female sex, young age (18-44 years), RA, seronegative by RF were associated with less survival of bDMARDs due to lack of effectiveness and/or AE, and RTM and seropositive RA - with more frequency of discontinuation of therapy due to remission.
Disclosure of Interests: Eugenia Aronova: None declared, Galina Lukina Speakers bureau: Novartis, Pfizer, UCB, Abbvie, Biocad, MSD, Roche, Galina Gridneva: None declared, Svetlana Glukhova: None declared, Anastasia Kudryavtseva: None declared
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AB0274 USE OF TNF-INHIBITORS BIOSIMILARS IN CHRONIC INFLAMMATORY ARTHRITIDES: A THREE-YEAR EXPERIENCE IN A LARGE MONOCENTRIC COHORT OF PATIENTS FROM THE NORTH-EAST ITALY

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Background: In recent years several biosimilars (BS) of tumour necrosis factor inhibitors (TNF-i) were introduced. At the Padova University Hospital the first BS of etanercept (bsETN) was available in October 2016 and the BS of adalimumab (bsADA) was available in November 2018.
Objectives: The objectives of the study were to evaluate the rate of bioriginator-biosimilar (BO-BS) switch in all patients with rheumatoid arthritis (RA), psoriatic arthritis (PSA) and axial spondiloarthritis (axSpA) in the cohort of the Padova University Hospital and to examine factors favouring BO-BS switch. Secondly, we investigated survival of BO-BS switch and BO treatment and factors associated with longer treatment survival.
Methods: We considered all patients on ETN originator (boETN) treatment when the first bsETN was available (1st October 2016) and all patients on ADA originator (boADA) when bsADA was available (1st November 2018). Patients were followed until 30 August 2019 and were classified as BO-BS switchers if they underwent a switch from either boETN or boADA to BS during the follow-up, otherwise they were considered as continuing BO treatment. Factors associated with BO-BS switch were tested with a multivariable regression analysis. To test the survival of the BO-BS switch and of the BO treatment, Cox regression analysis was used including all variables achiving a $p<0.10$ in univariate analysis tested with Log-rank test and Kaplan-Meier curves.
Results: Among 1208 patients (553 RA, 433 PSA, 215 axSpA), 560 (46.3%) patients switched to bsETN (391) or bsADA (169). Mean disease duration was 16 (14.2) years and mean duration of the bDMARD treatment was 96.3 (56.8) months. After adjustment for potential confounders, factors associated with BO-BS switch were a longer disease duration, a shorter duration of previous bDMARD treatments and diagnosis (Tab.1) RA patients had almost a 3 fold increased likelihood of being switched to BS compared to PSA and axSPA, while difference between PSA and axSPA was not significant.
Following Cox regression analysis we observed a longer drug survival in BO-BS switchers compared to those continuing with BO (HR 1.38; 95% C.I. 1.2-1.58; $p<0.001$) (Fig. 1). A longer drug survival was also associated with a longer disease duration (≥15years: HR 1.75; 95% C.I. 1.5-2; $p<0.001$), longer mean duration of previous bDMARDs (≥5years: HR 4.1; 95% C.I. 3.5-4.7; $p<0.001$), and diagnosis (RA vs PSA: HR 1.22; 95% C.I. 1.02-1.47; $p=0.030$; RA vs axSpA: HR 0.89 95% C.I. 0.067-0.97; $p=0.023$; PSA vs axSpA: HR 0.66; 95% C.I. 0.57-0.77; $p<0.001$) (Fig 2).
Conclusion: BO-BS switch was undertaken in almost half of the patients. Patients with longer disease duration and longer bDMARD duration, were the most likely to be switched successfully to BS. BO-BS switching does not affect the survival of the treatment, indeed, it provides sustained effectiveness particularly if undertaken in patients with stable disease activity.

Table 1. Factors associated with BO-BS switch, multivariate regression analysis.

		OR (95% C.I.)	p value
Age	per 10 years increase	1.11 (0.98-1.25)	0.102
Disease duration	per 5 years increase	1.19 (1.08-1.32)	0.01
Mean time on bDMARD	per 1 year increase	0.71 (0.66-0.77)	< 0.001
HAQ* per 1 unit increase		1 (1-1)	0.68
Gender (male)		1.07 (0.74-1.56)	0.71
Disease diagnosis			<0.001
RA vs PSA		2,70 (1,79-4,07)	<0,001
RA vs axSPA		2,77 (1,62-4,72)	<0,001
PSA vs axSPA		1,03 (1,62-4,72)	0,925
csDMARD combination		0.77 (0.54-1.11)	0.167
Model Constant			<0.04

OR odds ratio, C.I. confidence interval, * at the time the biosimilar of the ongoing originator was available.

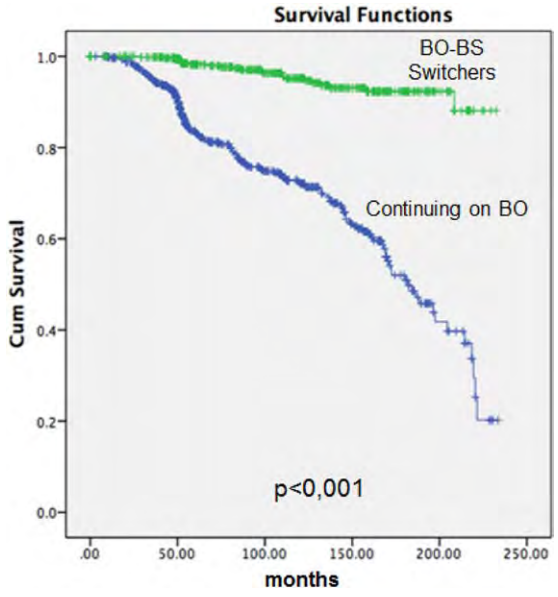


Figure 1. Kaplan-Meier curves for treatment survival, Log-rank test.

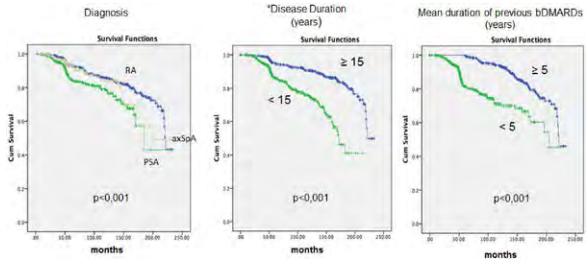


Figure 2. Kaplan-Meier curves for treatment survival in all patients, Log-rank tes

Disclosure of Interests: DAVIDE ASTORRI: None declared, Francesca Ometto: None declared, LARA FRISO: None declared, BERND RAFFEINER: None declared, Costantino Botsios: None declared, Andrea Doria Consultant of: GSK, Pfizer, Abbvie, Novartis, Ely Lilly, Speakers bureau: UCB pharma, GSK, Pfizer, Janssen, Abbvie, Novartis, Ely Lilly, BMS
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AB0275

COMPARATIVE EFFICACY (DAS 28) OF TOCILIZUMAB AND OTHER TARGETED IMMUNE MODULATORS (TIMS) FOR RHEUMATOID ARTHRITIS: A NETWORK META-ANALYSIS (NMA)

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Background: With a 'treat to target' approach in RA, guidelines recommend tailored monitoring of disease activity using validated composite instruments, such as the disease activity score (DAS) 28. While response assessment at 24 weeks is the standard in clinical trials, assessment as early as 12 weeks is recommended. There is limited evidence assessing the relative efficacy of TIMs following a 'treat to target' strategy.

Objectives: To evaluate the relative efficacy of intravenous (IV) and subcutaneous (SC) tocilizumab plus a conventional disease modifying antirheumatic drug (cDMARD) to other TIMs plus a cDMARD in TIM-naïve or mixed (<20% TIM-experienced) adults with moderate to severe RA. Efficacy was defined as achieving remission according to a DAS28 score <2.6 at 12 and 24 weeks.

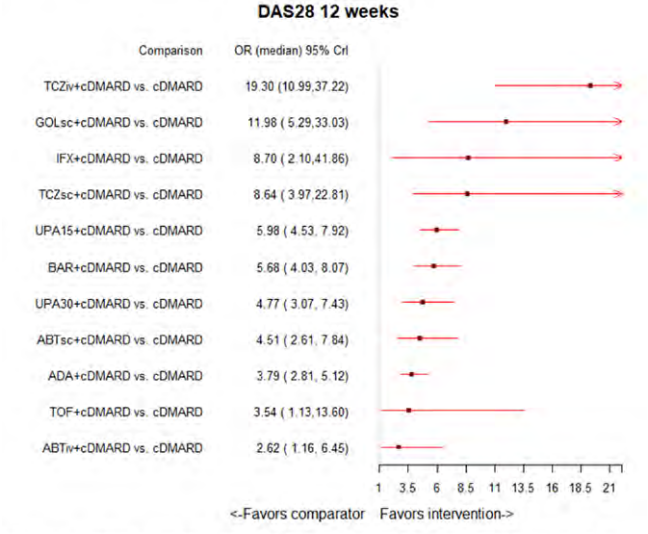
Methods: Randomized controlled trials (RCTs) were selected from a recent systematic literature review conducted by the Institute for Clinical and Economic Review (ICER), as well as from trials for upadacitinib (SELECT-NEXT, SELECT-COMPARE), which were not included in the ICER 2017 report. RCTs that compared TIMs to each other or placebo were included. Treatments included Janus kinase (JAK) inhibitors (upadacitinib, baricitinib, and tofacitinib), tumor necrosis factor alpha inhibitors (TNFi; adalimumab, certolizumab pegol, golimumab, and infliximab), and other non-TNFis (rituximab, sarilumab, tocilizumab, and abatacept). A Bayesian NMA was performed in OpenBUGS and R using a fixed effects model. Model selection was based on deviance information criterion. Forest plots of odds ratios (OR) are presented.

Results: In the 12-week analysis, 15 trials were included with a pooled study population of 9,154 patients. Populations were similar across trials and predominantly female (mean 78%, range 39-87%), with a baseline mean age of 52 years (range 47-56), mean disease duration of 8 years (range 2-11), and mean DAS28 score of 6 (range 5-7). In the 12-week analysis, compared to cDMARD, all TIMs were more likely to achieve remission (statistically significant), but tocilizumab IV showed a substantially greater magnitude of effect (OR=19.3, 95% Crl=10.99, 37.22) which was consistent with raw trial results (Figure 1). In pair-wise comparison, tocilizumab IV was associated with a greater likelihood of achieving remission compared to abatacept IV (OR=7.47, Crl=2.53, 20.89), abatacept SC (OR=4.29, Crl=1.96, 9.94), baricitinib (OR=3.39, Crl=1.74, 7.09), adalimumab (OR=5.10, Crl=2.68,10.42), tofacitinib (OR=5.44, Crl=1.26, 20.57), upadacitinib 15mg (OR=3.23, Crl=1.72, 6.54), and upadacitinib 30mg (OR=4.05, Crl=1.97, 8.85).

In the 24-week analysis, 21 trials were included in the analysis with a pooled study population of 12,180 patients. Patient characteristics were the same as the 12 week analysis. Compared to cDMARD, all TIMs were more likely to achieve remission (statistically significant), with tocilizumab IV and SC showing a greater magnitude of effect (OR=12.08, Crl=8.09-18.30 and OR=11.98, Crl=5.17-35.86, respectively) (Figure 2). In pair-wise comparison, tocilizumab IV and SC were associated with a greater likelihood of achieving remission compared to abatacept IV, adalimumab, baricitinib, infliximab, upadacitinib 15 mg, and sarilumab.

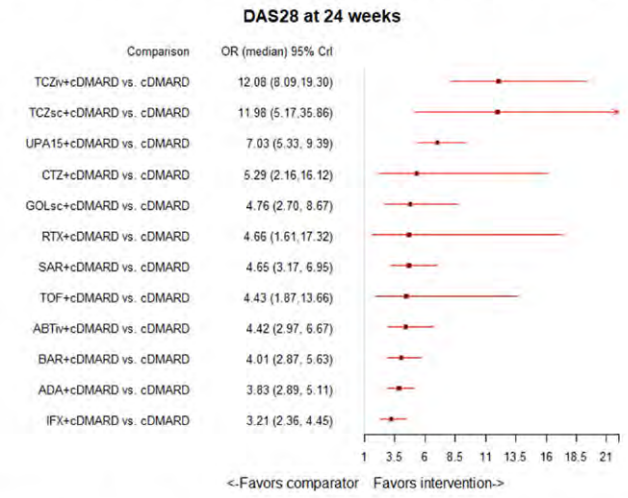
Conclusion: Results of this NMA demonstrate that tocilizumab is associated with a greater likelihood of remission (DAS28 <2.6) at 12 and 24 weeks compared to most other TIMs including new JAK inhibitors, when used in combination with a cDMARD among TIM-naïve/mixed patient populations.

Figure 1. DAS28 at 12 weeks—All TIMs were more likely to achieve remission compared to cDMARD, but tocilizumab IV showed a substantially greater magnitude of effect that was consistent with raw trial data*



Abbreviations- ABT: Abatacept, ADA: Adalimumab, BAR: Baricitinib, cDMARD: Conventional Disease-modifying Antirheumatic Drugs, Crl: credible interval, GOL: Golimumab, IFX: Infliximab, Int: Intensive, iv: intravenous, sc: subcutaneous, TOF: Tofacitinib, TCZ: Tocilizumab, UPA: Upadacitinib (15 or 30 mg)
* 95% Crls that do not overlap with 1 are statistically significant
cDMARDs are defined as systemic agents with broad immunomodulatory effects like methotrexate, leflunomide, hydroxychloroquine, and sulfasalazine.

Figure 2. DAS28 at 24 weeks—All TIMs were more likely to achieve remission compared to cDMARD, but tocilizumab IV and SC had a greater magnitude of effect*



Abbreviations- ABT: Abatacept, ADA: Adalimumab, cDMARD: BAR: Baricitinib, Conventional Disease-modifying Antirheumatic Drugs, CTZ: Certolizumab pegol, CrI: credible interval, GOL: Golimumab, IFX: Infliximab, iv: intravenous, RTX: Rituximab, SAR: Sarilumab, sc: subcutaneous, TOF: Tofacitinib, TCZ: Tocilizumab, UPA: Upadacitinib (15 mg)
* 95% CrIs that do not overlap with 1 are statistically significant
cDMARDs are defined as systemic agents with broad immunomodulatory effects like methotrexate, leflunomide, hydroxychloroquine, and sulfasalazine.

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Disclosure of Interests: Jennie H. Best Shareholder of: Genentech, Inc., Employee of: Genentech, Inc., Jennifer Uyei: None declared, Joseph Dang Shareholder of: Genentech, Inc., Employee of: Genentech, Inc., Yilin Jiang: None declared, Rajpal Singh: None declared, Pinar Bilir: None declared, Andreas Karabis: None declared, Julie Munakata: None declared, William Reiss Shareholder of: Genentech, Inc., Employee of: Genentech, Inc.
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AB0276 DIFFERENCES BETWEEN IMPACT OF BIOLOGICAL THERAPY AND IMPACT OF CONVENTIONAL TREATMENT ON PRODUCTIVITY AND QUALITY OF LIFE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Number of patients with rheumatoid arthritis in Montenegro amounts around 3,000, while 8% of them are on biological therapy. This percent is similar, or even higher in comparison to countries that are highly comparable to Montenegro. However, the percentage is still lower than in European countries.
Objectives: Objective of the study was to identify the differences between impact of biological and conventional therapy on quality of life of RA patients, their work ability and productivity, mental health, emotional state and social inclusion.
Methods: The analysis was based on data gathered from the questionnaires filled by RA patients in Montenegro: 92 patients treated with biological therapy and 78 treated with conventional therapy. More insights and information from examined patients were gathered on two focus groups. Following indicators were used in the study: two indicators that measure work ability and productivity: one monetized – Work Productivity and Activity Impairment Questionnaire General Health V2.0 (WPAI-GH) and one non-monetized – RA Work Instability Scale (RA WIS), and two indicators that measure quality of life – Health Assessment Questionnaire (HAQ-DI) and RAND 36-Item Health Survey (SF-36).
Results: WPAI-GH results are used in evaluation of absenteeism and presentism costs per RA patient per annum, which are caused exclusively by rheumatoid arthritis. WPAI-GH results are presented in the following figure. Total cost of absenteeism and presenteeism of RA patients in Montenegro amounts to 3.8 million EUR per annum. Results of RA WIS indicator suggest that patients treated with biological therapy are characterized by low to moderate level of work instability, and patients treated with conventional therapy by moderate level. Patients treated with biological therapy have shown 25% lower level of work instability. HAQ-DI indicator shows that both groups of patients are characterized by mild difficulties to moderate disability in performing everyday activities. However, patients treated with conventional therapy deal with higher level of difficulties, even though their level of RA progression is lower, on average. SF-36 indicator shows that patients treated with conventional therapy have lower level of physical functioning, followed by 26% higher pain intensity. They are 25% more exposed to limitations due to physical health problems caused by RA, and 20% more to limitations due to emotional problems. Patients treated with biological therapy, on average, rate their health with 50% higher rank in comparison to subjective health rate of patients treated with conventional therapy. They also feel that their health has improved during the past year, or stayed approximately the same, while patients treated with conventional therapy feel that their health condition has aggravated, or stayed unchanged.
Conclusion: Results show that health condition, emotional state and life quality are better among the patients treated with biological therapy. Also, their productivity is higher compared to patients treated with conventional therapy. This conclusion is additionally supported by the fact that there is more progression of disease among RA patients treated with biological therapy, as well as by the fact that the average duration of RA is almost two times longer among examinees who are on biological therapy than among examinees who are on conventional therapy. Accordingly, access to biological therapy for greater number of patients in earlier stage of disease would result in reduction costs of lost productivity and work disability connected to RA, as well as in mitigation of RA impact on lives and functionality of patients.

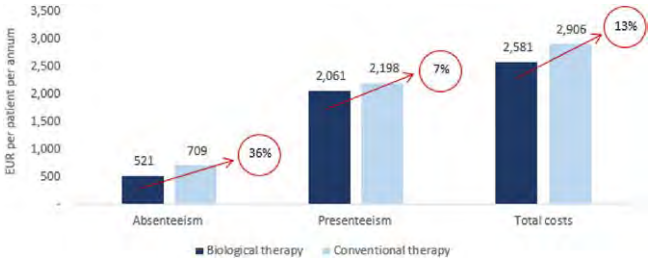


Figure 1. WPAI-GH

Disclosure of Interests: None declared
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AB0277 PREVALENCE OF HEPATITIS MARKERS IN PATIENTS TREATED WITH BIOLOGICAL DISEASE-MODIFYING ANTIRHEUMATIC DRUGS: RESULTS OF THE TUNISIAN REGISTRY BINAR

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Background: In the recent decades, biological disease-modifying antirheumatic drugs (bDMARDs) have significantly improved management and quality of life in patients with rheumatoid arthritis (RA) and spondyloarthritis (SpA).
However, bDMARDs have also a strong influence on the immune system, leading to a risk of serious infection. Reactivation of hepatitis B (HBV) and C (HCV) virus is one of the most redoubtable complications of these immunosuppressive agents.
Objectives: The aims of this study were to determine the screening rate for hepatitis B and C before starting a biological treatment and to examine the prevalence of their markers in patients with RA or SpA.
Methods: Our study evaluated all patients included in the Tunisian registry BINAR (Biologic National Registry) since 2018 who had RA (ACR/EULAR 2010) or SpA (ASAS criteria) aged with more than eighteen years old and receiving their first bDMARDs during the two past years.
The following information were retrieved from the registry: demographic data on the patients, disease parameters, medication, HBV surface antigen (HBs Ag), antibody to HBs Ag (Anti HBs), antibody to HBV core antigen (Anti HBc), HBV-DNA, antibody to HCV (anti HCV) status and liver function tests (AST: aspartate aminotransferase; ALT:alanine aminotransferase).
Results: A total of 298 patients was included, 111 men and 178 women, with a mean age of 49.2 ± 14.1 years old [18-79]. Among them, 58.7% were

diagnosed with RA and 41.3% were diagnosed with SpA. The mean disease duration was 6.7±3.5 years [1-12] in patients with RA and 6.5±3 [1-12] in patients with SpA. The mean Disease Activity Score (DAS28) and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) were respectively of 4.9±1.5 [1-8] and 4.1±1.8 [0-9].
Therapeutically, 167 patients (56%) were on Prednisone at a mean daily posology of 8.2±5.4 mg [4-60] and 70.3% on conventional synthetic disease modifying antirheumatic drug (csDMARD) in association with bDMARDs. It was about Tumor Necrosis Factor alpha antibodies (anti TNF a) in 87.9% of cases, Tocilizumab in 10.4% of cases and Rituximab in 5% of cases.
A screening of HBV was performed in 286 patients (96%). Ag HBs was positive in two cases (0.7%), and anti-HBc was positive in 16 cases (6.4%) which indicate a prior HBV infection. Fifteen patients (6%) were immunized with positive anti HBs. HBV-DNA was measured in 177 cases (66.8%) and was positive in 15 patients (6%). HCV infection was searched in 282 patients (94.6%) and anti-HCV was negative in all cases.
AST and ALT mean rates were respectively of 18.3 [2-108] and 17.9 UI/l [2-74]. A perturbation of these liver function tests was observed in 13 patients (4.4%).
Conclusion: Screening for hepatitis B and C were performed respectively in 96% and 94% of our Tunisian patients before receiving any bDMARDs. This should be systematic to avoid HBV reactivation which can lead to fulminant hepatic failure with a severe prognosis.
Disclosure of Interests: None declared
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AB0278 REAL LIFE EXPERIENCE OF DISEASE ACTIVITY AND QUALITY OF LIFE IN PATIENTS TREATED WITH BIOLOGICAL DMARDS VERSUS TOFACITINIB.

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Background: Assessment of disease activity and quality of life are one of the main indicators for determining the effectiveness of treatment with disease-modifying antirheumatic drugs. In recent years, a new group has entered the market - target synthetic DMARDS, which prove their effectiveness in treating RA comparable to that of biological products.
Objectives: The aim of this study is to evaluate the disease activity and quality of life of patients with rheumatoid arthritis (RA) treated with biological agents in comparison with Tofacitinib (real life data from Bulgarian population) and determine whether or not the benefits of different therapies were sustained over a follow up period of 1 year.
Methods: 164 patients were selected with a mean age 55.34 ± 16SD years, meeting the 1987 ACR and /or ACR/ EULAR (2010) classification criteria for Rheumatoid arthritis (RA). Patients were arranged according to treatment regimens: Tocilizumab (TCL) 30 patients, Certolizumab (CZP) 16, Golimumab (GOL) 22, Etanercept (ETN) 20, Adalimumab (ADA) 20, Rituximab (RTX) 16, Infliximab (INF) 20, Tofacitinib (TOF) 20. Disease activity and quality of life was the primary concern. Independent joint assessor evaluated 28 joints on baseline, 6th and 12th month's thereafter. CRP was used to measure the inflammatory process.
DAS28-CRP, clinical disease activity index (CDAI) and simplified disease activity index (SDAI)were calculated. On baseline all of the patients' groups had severe disease activity (mean DAS28-CRP > 5.2, mean CDAI > 22, mean SDAI > 26. The quality of life was evaluated via EQ-5D.
All of the patients were on stable therapy according to the inclusion criteria, and didn't interrupt any of the medications including biological or target synthetic treatment.
Results: Significant clinical improvement and statistically significant reduction in disease activity were observed in patients treated with bDMARDS and tsDMARDS within 6 months (p <0.005) of treatment and after 12 months of follow-up (p=0.039). The mean value of DAS28-CRP after one year follow up showed an non-inferior effect of Tofacitnib (3.04± 0.81) in comparison to biological treatment (TCL: 3.07 ± 0.73; CZP: 3.06 ± 0.65; GOL: 2.49 ± 0.76; ETN: 2.85 ± 0.55; ADA: 3.15 ± 0.82; RTX: 2.90 ± 0.70; INF: 3.14; ± 0.61; TOF: 3.04± 0.81). An improvement was also observed for the 6 to 12 months of follow-up as we did not detect a significant difference in the activity of the disease assessed by CDAI among the different drug groups.
The mean values showing the change of the SDAI over the study period also outline comparable profiles. All of the treatment groups achieved a rapid reduction in disease activity that continued to decrease through the 6 and 12 months period, respectively, as supported by changes in SDAI.The quality of life evaluated with EQ-5D revealed significant improvement on the 6-th month of follow up as well as after 12th month (p<0.005) without significant difference between the observed groups.
Conclusion: Real-life data show that patients on biological treatment as well as those on Tofacitinib therapy achieve a significant decrease in disease activity after one year of follow-up. This gives us reason to accept the importance of non-inferior effect of jak-inhibitors and their place in treatment of Rheumatoid arthritis.
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AB0279 IMPACT OF DISEASE-MODIFYING DRUGS IN SECOND BIOLOGICAL TREATMENT SURVIVAL IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Several studies have proposed that the immunosenescence of elderly patients with Rheumatoid Arthritis (RA) in treatment with biological therapies could eliminate the need for concomitant immunosuppression with disease-modifying drugs (DMARDs), due to a probable lower production of anti-drug antibodies; however, the evidence is limited.
Objectives: To compare the characteristics of patients with RA who started a second biological agent, according to age groups. To analyse second biological agent survival and its relationship with DMARDs.
Methods: Retrospective, observational and longitudinal study. Patients with RA who started a second biologic between 2000 and 2019, who discontinued a first-line TNF inhibitor, were included. Demographic, clinical and analytical data were obtained. The sample was divided in 2 groups: <70 and ≥70 years old. A comparative analysis was performed. Kaplan-Meier curves and Log-rank were used to conduct the survival analysis.
Results: 156 patients were included. 83.3% were women, with a mean age at the beginning of second biological treatment of 54.64±13.54 years. 22 patients (14.1%) were ≥70 years. Comparative analysis is detailed in table 1: patients ≥70 years presented a longer time from diagnosis to the start of biological treatment, and a higher prevalence of hypertension and diabetes mellitus. The main cause of withdrawal in this group was adverse events (46.67%) while in younger patients was treatment failure (25.27% primary failure, 29.66% secondary failure). The most frequent biological agent in ≥70 years was Rituximab (27.26%) while in <70 years was Etanercept (26.12%). 126 patients (80.8%) had a DMARD associated. In both groups, Methotrexate was the most frequent (table 2). The second biological agent survival analysis showed that patients who received a DMARD presented a higher survival [77 months (55.50-98.55) vs. 51.53 months (41.67-61.40); p=0.023]. After conducting a survival analysis in patients whose withdrawal cause was treatment failure, DMARDs use was associated with an increased biological agent survival in patients <70 years [103.48 months (82.28-124.68) vs. 81.95 months (66.05-97.86); p=0.037]; but statistical differences were not found in patients ≥70 years [117.33 months (82.15-152.52) vs. 65.07 months (40.72-89.42); p=0.291].

Table 1.

Variable	<70 years = 134 (mean ± SD or %)	≥70 years = 22 (mean ± SD or %)	p
Age at diagnosis (years)	40.5 ± 12.3	58.8 ± 8.9	<0.001
Age at the beginning of the treatment (years)	51.28 ± 11.44	75.14 ± 3.5	<0.001
Time since diagnosis (years)	10.65 ± 8.20	16.27 ± 9.09	0.003
Women	113 (84.33%)	17 (77.27%)	0.373
Smokers	29 (21.64%)	2 (9.09%)	0.320
Rheumatoid factor positive	109 (81.34%)	17 (77.27%)	0.770
Anti-CCP positive	114 (90.48%)	14 (82.35%)	0.390
Erosions	92 (70.23%)	16 (76.19%)	0.576
Arterial hypertension	28 (21.37%)	14 (66.67%)	<0.001
Diabetes mellitus	3 (2.24%)	4 (18.18%)	<0.001
Retirement	91 (67.91%)	15 (68.18%)	0.980
Infections	10 (7.46%)	3 (13.64%)	0.397
Second biological agent withdrawal cause			
Primary failure	23 (25.27%)	3 (20%)	0.242
Secondary failure	27 (29.66%)	3 (20%)	
Adverse events	25 (27.47%)	7 (46.67%)	
Remission	2 (2.20%)	0 (0%)	
Exitus	3 (3.30%)	0 (0%)	
Neoplasia	3 (3.30%)	0 (0%)	

Table 2.

Disease-modifying drug	<70 years old	≥70 years old	p
Methotrexate	72 (53.73%)	9 (40.91%)	0.667
Leflunomide	22 (16.42%)	5 (22.73%)	
Sulfasalazine	2 (1.49%)	1 (4.55%)	
Hydroxychloroquine	6 (4.48%)	0 (0%)	
At least two of the above	7 (5.22%)	1 (4.55%)	

Conclusion: DMARD concomitant treatment has been related to a higher second biological treatment survival. This beneficial effect was not observed in RA patients ≥70 years of age whose second biological agent withdrawal cause was failure. In this age group, withdrawal related to adverse events was more frequent.

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AB0280

SURVIVAL ANALYSIS ON SECOND BIOLOGIC THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS OLDER THAN 65 YEARS

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Background: Patients with Rheumatoid Arthritis (RA) ≥65 years old constitute an important and not very well studied group. Even though the course of the disease may be similar to that of younger patients, treatment is usually less aggressive given the limited information on efficacy, especially of biological treatments, in this age group.

Objectives: To describe the characteristics of patients with RA ≥65 years old who started a second biological agent. To compare the survival of this second-line treatment between patients ≥65 and <65 years old.

Methods: Retrospective, observational and longitudinal study. Patients diagnosed of RA, who started a second biological agent between 2000 and 2019, who discontinued a first-line TNF inhibitor, were included. Demographic, clinical and analytical data were obtained. The sample was divided in 2 groups: <65 and ≥65 years old. Kaplan Meier and Log-rank survival analysis were performed, as well as Cox regression to identify related factors.

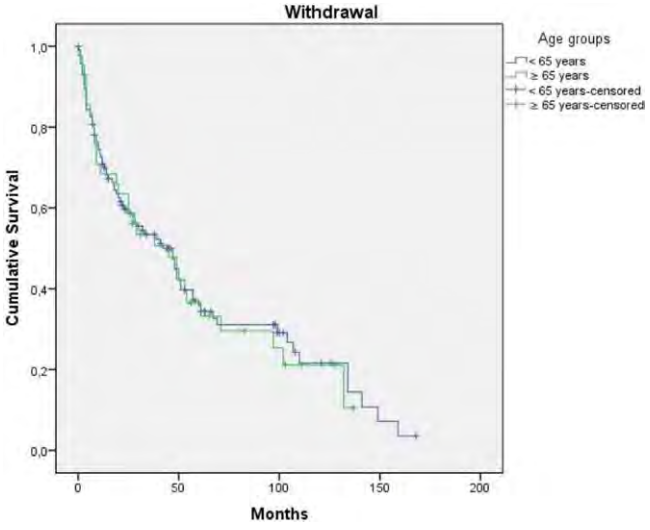
Results: 157 patients were identified, 42 (26.8%) were ≥65 years old. In this group, 73.8% were women, with a mean age at the beginning of second biological treatment of 71.43±4.76 years. Demographic and clinical data of ≥65 years old patients are shown in the table. The most frequent second biological agent was Rituximab (23.8%), followed by Adalimumab (21.4%) and Tocilizumab (19%). 76.2% of patients had a disease-modifying drug associated, being Methotrexate the most frequent (45.2%). Discontinuation of second biological agent occurred in 30 patients (71.42%) ≥65 years old, which is similar to the percentage found in patients <65 years old (66.96%; p=0.70). The main causes of withdrawal of second-line agent in patients ≥65 years were adverse effects (23.8%) and secondary failure (23.8%), whereas in <65 years were primary and secondary failure (18.3% in both). Infections were more frequent in patients ≥65 years (14.3%) in comparison with patients <65 years (6.1%). In the survival analysis of the second biological agent, patients ≥65 years presented a median survival of 45 months (IC-95%=14.10-75.90); while patients <65 years had a median survival of 47 months (IC-95%=29.55-64.46), without statistically significant differences (p=0.803) (See Figure). Among elderly patients no statistically significant differences were found after comparison of survival curves in the subgroups: 65-69, 70-74 and ≥75 years. Rituximab presented a higher survival rate in patients ≥65 years (84.3 months; p<0.001), followed by Abatacept (58.5 months). Smoking (HR=13.96; IC- 95%=2.12-91.93), erosions (HR=7.04; IC-95%=1.05-47.31) and diabetes mellitus (HR=13.37; IC-95%=1.25-143.46) were identified as risk factors for discontinuation of second biologic agent.

Conclusion: The survival of second biological agent after the failure of a first TNF inhibitor in patients ≥65 years is similar to the survival in younger patients, although there was a higher percentage of adverse effects in the first group. Rituximab and Abatacept showed a higher survival in patients ≥65 years. Smoking, erosions and diabetes mellitus were associated with an increased risk for the withdrawal of the second-line biological therapy.

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Variables	n= 42 (mean ± SD or %)
Age at diagnosis (years)	56.48 ± 9.94
Age at the beginning of the treatment (years)	71.43 ± 4.76
Women	31 (73.8%)
Smokers	11 (26.2%)
RF (+)	35 (83.3%)
ACPA (+)	30 (71.4%)
Erosions	29 (69%)
Arterial hypertension	21 (50%)
Diabetes mellitus	4 (9.5%)
Dyslipidemia	11 (26.2%)
Disease-modifying drug	
Methotrexate	19 (45.2%)
Leflunomide	10 (23.8%)
Sulfasalazine	1 (2.4%)
Hydroxychloroquine	0 (0%)
Infections	
Respiratory infection	3 (7.1%)
Skin/Soft tissues infections	2 (4.8%)
Herpes zoster	1 (2.4%)



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AB0281

SAFETY AND RETENTION RATE AFTER SWITCHING FROM ETANERCEPT ORIGINATOR (ETN) TO ETANERCEPT BIOSIMILAR (SB4) IN INFLAMMATORY JOINT DISEASES: DATA FROM REAL LIFE.

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Background: SB4 in now commonly used in the treatment of inflammatory joint diseases, with evidence of efficacy and persistence up to 12 months from switching in both randomized controlled trials in Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA) and Ankylosing Spondylitis (AS).

Objectives: we investigated the safety and retention rate of SB4 at 6, 12 and 18 months after switching from ETN in two rheumatology departments in our region.

Methods: adult patients with RA, PsA, AS, Juvenile Idiopathic Arthritis (JIA) and other rheumatic diseases treated with ETN for at least 6 months, switched to SB4 in stable clinical conditions, were eligible for this retrospective evaluation. Data on adverse events (in particular infectious events), loss of efficacy (articular, cutaneous, ocular or intestinal disease re-activation) and persistence on treatment were collected since latest available follow-up. Retention rate, reason for discontinuation and subsequent management data were collected at 6, 12, 18 months.

Results: 220 patients (142 females, mean age 58+-7 years, disease duration 12+-4 years, ETN duration 7+-4 years) were enrolled, with median follow up of 12.1 (9.7-15.8) months duration; ETN was used in different biologic DMARDs treatment lines (first 76.8%, second 17.7%, third 3.2 %, fourth 2.3%). Study

population was composed of 85 RA, 81 PsA, 33 AS, 14 JIA and 7 other conditions (mostly scleroderma). In the follow-up, 50 patients (22.7%) presented with at least one non-serious adverse event, with 36 (16,4%) disease re-activation (mostly articular) and 30 (13,6% - 11 for safety and 19 loss of efficacy) SB4 interruptions. Retention rates were 99.1 (210/212) at 6, 90.9% (150/165) at 12 and 81.5% (53/65) at 18 months respectively. Back-switch to ETN was performed in 17/30 cases, the remaining cases were managed with change of bDMARD or csDMARD). Age was the only significant predictor of SB4 interruption at 6 months (OR 1.058, 95%CI 1.007-1.112, p=0.026), while disease, bDMARD line, csDMARD combination, gender, disease duration or ETN duration did not influence retention rates at 6, 12 or 18 months.

Conclusion: our real-life data confirm the safety profile of switching from ETN to SB4. In our patients, the data show a higher retention rate, when compared to other-real life registries data (1,2)

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Disclosure of Interests: Cosimo Bruni Speakers bureau: Actelion, Eli Lilly, Stefano Gentileschi: None declared, Marco Capassoni: None declared, Giovanni Pacini: None declared, Marco Bardelli: None declared, Caterina Baldi: None declared, Lorenzo Tofani: None declared, Laura Cometi: None declared, Francesca Nacci: None declared, Francesca Bartoli: None declared, Ginevra Fiori: None declared, Luca Cantarini: None declared, Serena Guiducci: None declared, Bruno Frediani: None declared, Marco Matucci-Cerinic Grant/research support from: Actelion, MSD, Bristol-Myers Squibb, Speakers bureau: Acetelion, Lilly, Boehringer Ingelheim

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AB0282 CLINICAL EFFECTIVENESS OF ABATACEPT MONOTHERAPY OR ABATACEPT CONCOMITANT METHOTREXATE THERAPY IN RHEUMATOID ARTHRITIS PATIENTS PREVIOUSLY TREATED WITH BIOLOGICAL DISEASE-MODIFYING ANTIRHEUMATIC DRUGS (BDMARDS)

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Background: Concomitant use of methotrexate (MTX) in abatacept (ABA) therapy is associated with good clinical response in patients with rheumatoid arthritis (RA) who are naïve to biological disease-modifying antirheumatic drugs (bDMARDs)[1,2]. However, it is unclear when abatacept is used in patients with prior bDMARDs use[3].

Objectives: We compared the effectiveness of abatacept monotherapy versus abatacept combined with methotrexate therapy in rheumatoid arthritis patients with prior bDMARDs use.

Methods: Retrospective cohorts study. Rheumatoid arthritis patients treated with abatacept between 2009 and 2019 (n=86). Socio-demographic, clinical and pharmacological characteristics of patients were collected. We compared clinical effectiveness between ABA monotherapy patients (n=49) and abatacept concomitant methotrexate therapy patients (n=37), prior treated with bDMARDs. The effectiveness was measured according to *The European League Against Rheumatism* (EULAR) response with *Disease Activity Score* (DAS28) like satisfactory (DAS28<3.2) or unsatisfactory (DAS28≥3.2), after 12 months of ABA therapy in RA patients.

Results: 49 RA patients have been evaluated in ABA monotherapy group; 83.67% (41/49) were women, disease duration was 16 (10-22) years and age of RA diagnosis was 48 (38.25-57.00). Concomitants glucocorticoids were administrated in 81.63% (40/49). Rheumatoid factor (RF) was positive in 75.51% (37/49) patients and cyclic citrullinated peptide antibodies (ACPA) in 71.43% (35/49). At 12 months, 40.82% (20/49) of patients had satisfactory EULAR response.

In the combination therapy group, the age of RA diagnosis was 42.5 (35.75-53.50), 75.68% (28/37) were women and the disease duration was 12 (7-21) years. 89.19% (33/37) had concomitants glucocorticoids and the RF was positive in 72.97% (27/37) of patients. EULAR response was satisfactory at 12 months in 43.24% (16/37) of patients. No difference in treatment effectiveness was found in patients receiving abatacept in combination therapy with MTX compared with ABA monotherapy (p=0.829; IC_{95}=0.35-2.35).

Conclusion: Abatacept plus methotrexate therapy did not improve the effectiveness in rheumatoid arthritis patients with prior bDMARDs use, compared with abatacept monotherapy.

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AB0283 REDUCED HOSPITAL ADMISSION IN RA PATIENTS TAPERING BIOLOGIC DMARDS: PRELIMINARY ANALYSIS OF A RETROSPECTIVE STUDY

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Background: bDMARDs are among the most effective therapies in the management of inflammatory arthritides, but they are associated with potentially severe adverse events (AEs), particularly infection. Tapering strategies of bDMARDs for patients in remission/low disease activity (R/LDA) have demonstrated comparable efficacy to standard-dose treatments, but their safety profile has not been studied yet.

Objectives: To compare the number and the causes of hospital admissions in RA patients in R/LDA continuing or tapering bDMARDs.

Methods: Consecutive patients with rheumatoid arthritis (RA) evaluated between 2011 and 2017, were assigned, based on treating physician's discretion, to continue the standard dose (STD) of bDMARDs or to undergo a predetermined tapering strategy (TAP), after being in R/LDA for two consecutive visits at least 3 months apart. Down-titration of bDMARDs was obtained by a stepwise increase of the dosing interval to achieve a reduction of about 30% (e.g. administration of etanercept every 10 days instead of weekly). Demographic, clinical data and concomitant treatments were retrospectively retrieved from the electronic charts of the outpatient clinics. Information about hospital admissions, including main diagnosis, period and duration of hospitalization, and death were retrieved from the Regional Healthcare System Database.

For the STD group, the observation period started with the occurrence of remission and finished with one of these events: loss of remission, switch to another bDMARD, withdrawal of the bDMARD, severe AE, death, end of the study period in (December 2017). For the TAP group, the observation period started with tapering onset and finished with one of these events: reduction of the dosing interval due to either a relapse (according to a DAS28 increase) or to a subjective, symptomatic relapse (according to the patient's definition), switch to another bDMARD, withdrawal of the bDMARD, severe AE, death, end of the study period in (December 2017).

Results: 81 patients were included, of whom 40 underwent TAP. Demographic, clinical and treatment data are shown in table 1. Baseline characteristics were comparable between the two groups, except for the number of previous bDMARDs before observational period entry that was slightly higher in the STD group (STD 1.0±0.9 versus TAP 0.5±0.8, P=0.11).

Table 1. Baseline demographic and clinical characteristics of the patients in remission or low disease activity.

	NO TAPERING (n=41)	TAPERING (n=40)	p value
Mean age (yrs)	57±11	58±13	0.563
Mean disease duration (yrs)	12±9	12±7	0.897
Starting bDMARD to tapering/monitoring (months)	52±45	67±41	0.128
Mean monitoring period (months)	22±24	19±23	0.632
Taking sDMARD at any time ((n (%))	40 (98%)	37 (92%)	0.359
Taking glucocorticoids	29 (71%)	28 (70%)	0.999
Mean prednisone dose (mg/day)	2.5±2.9	2.1±2.7	0.527
DAS28 at the time of tapering or first LDA/REM	2.3±0.8	2.3±0.9	0.863
Previous bDMARDs >1 (n (%))	10 (24.4%)	4 (10%)	0.140

In the STD group, 14 hospital admissions occurred, while in the TAP group there were 7 admissions (p=0.128). The corresponding figures for hospital admission due to infectious diseases were 6 in the STD group and 0 in the TAP group (p=0.026).

Conclusion: Tapering bDMARDs in RA patients in R/LDA is associated with fewer hospital admissions, with a possible protective effect especially toward infections.

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Disclosure of Interests: Dario Camellino Consultant of: I have received consultancy fees from Celgene, Sanofi, Novartis, Janssen-Cilag, Accord, Paid instructor for: I have served as a paid instructor for Mylan, Andrea Giusti Consultant of: UCB, Amgen, Janssen, Eli Lilly, Abiogen, EffRx, Speakers bureau: UCB, Amgen, Janssen, Eli Lilly, Abiogen, EffRx, Alfa-Sigma, Chiesi, Giuseppe Girasole: None declared, Chiara Craviotto: None declared, Paola Diana: None declared, Antonia Locaputo: None declared, Tiziana Caviglia: None declared, Lacramioara Luca: None declared, Gerolamo Bianchi Consultant of: Amgen, Janssen, Merck Sharp & Dohme, Novartis, UCB, Speakers bureau: Abbvie, Abiogen, Alfa-Sigma, Amgen, BMS, Celgene, Chiesi, Eli Lilly, GSK, Janssen, Medac, Merck Sharp & Dohme, Novartis, Pfizer, Roche, Sanofi Genzyme, Servier, UCB

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AB0284 RHEUMATOID ARTHRITIS REFRACTORY TO BIOLOGICAL TREATMENT

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Background: In Rheumatoid arthritis (RA), between 20% and 40% of patients do not achieve a 20% improvement in American College of Rheumatology (ACR) criteria, another similar percentage loses response over time or experience adverse events that forces them to the suspension of treatment. Those patients who have failed one or more therapeutic strategies, are more refractory patients and the response to successive targets is usually lower than naive patients, with 50% ACR20 response percentages.

Objectives: To describe the clinical-analytical characteristics and response to the last treatment, in rheumatoid arthritis (RA) refractory to biological disease modifying anti-rheumatic drugs (bDMARDs) and targeted synthetic DMARDs (tsDMARDs). To identify possible factors related to refractoriness to bDMARDs and tsDMARDs.

Methods: Retrospective multicentre, controlled study of patients with RA refractory to bDMARDs and tsDMARDs. Control group was formed by patients with non-refractory RA; matched by gender, age and diseaseduration. Refractoriness was defined as failure to more than 2 different targets of bDMARDs or tsDMARDs. Demographic, clinical-analytical data and rates of disease activity and physical function were collected. A descriptive analysis, a bivariate analysis and a binary logistic regression were performed to see the variables associated with refractoriness.

Results: A total of 94 patients were selected from HRUM and HCUVV: 47 with refractory RA and 47 with non-refractory RA. The clinical-epidemiological characteristics of both groups are classified in Table 1. The majority were women with a mean age of 57 years. There was a greater proportion of patients with multimorbidity and cardiovascular risk factors among the refractory to FAMEb. All patients affected a significant improvement with the new treatment in activity and physical function at 6 months compared to baseline. Refractoriness is associated with a higher body mass index [OR(IC95%), 7.73 (1.56-8.42); p=0.012], and depression [OR(IC95%), 1.11 (1.24-1.83); p=0.035].

Table 1. Clinical-epidemiological characteristics of patients.

Variable	Refractory RA (N=47)	Non-refractory RA (N=47)	p-value
Sex (female), n (%)	38 (80,9)	38 (80,9)	1,000
Age, means (SD)	57,1 (10,8)	57,4 (10,8)	0,896
Caucasian race, n (%)	45 (95,7)	44 (93,6)	0,646
Body mass index, means (SD)	30,4 (6,8)	26,5 (3,8)	0,002
Non-smoker, n (%)	26 (55,3)	28 (59,6)	
Former smoker>6 months, n (%)	16 (34,0)	7 (14,9)	
Smoker, n (%)	5 (10,6)	12 (25,5)	
Rheumatoid Factor, n (%)	40 (85,1)	42 (89,4)	0,536
Anti-cyclic citrullinated peptide, n (%)	37 (78,7)	38 (80,9)	0,797
Erosions, n (%)	33 (70,2)	28 (59,6)	0,280
Hypertension, n (%)	24 (51,1)	20 (42,6)	0,408
Obesity, n (%)	19 (40,4)	9 (19,1)	0,024
Diabetes Mellitus, n (%)	10 (21,3)	6 (12,8)	0,272
Dyslipidemia, n (%)	20 (42,6)	15 (31,9)	0,286
Neoplasia, n (%)	2 (4,3)	0 (0,0)	0,153
Fibromyalgia, n (%)	4 (8,5)	1 (2,1)	0,168
Depression, n (%)	18 (38,3)	4 /8,5)	0,001
Multicomorbidity, n (%)	17 (36,2)	6 (12,8)	0,008
Comorbidities number, median (IQR)	2,0 (1,0-3,0)	1,0 (0,0-2,0)	0,002

Conclusion: Patients with refractory RA have an adequate response to subsequent treatment lines. These patients have a remarkable percentage of associated comorbidities.

Disclosure of Interests: None declared

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AB0285 RANDOMIZED, OPEN-LABEL, SINGLE-DOSE, PARALLEL-GROUP PHARMACOKINETIC STUDY OF PF-06410293, AN ADALIMUMAB BIOSIMILAR, BY SUBCUTANEOUS DOSING USING A PREFILLED SYRINGE OR A PREFILLED PEN IN HEALTHY SUBJECTS

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Background: Similarity in efficacy, safety, and immunogenicity (IMG) of PF-06410293 (ADL-PF), an adalimumab (ADL) biosimilar, and reference ADL sourced from the European Union (ADL-EU), by subcutaneous (SC) injection using a prefilled syringe (PFS), have been demonstrated in a randomised controlled trial in patients with rheumatoid arthritis (RA) (NCT02480153).

Objectives: To determine if the pharmacokinetics (PK), safety and tolerability of ADL-PF were similar following a single SC dose by prefilled pen (PFP) or PFS in healthy subjects (NCT02572245).

Methods: In this phase 1, 2-arm study, healthy subjects, aged 18–55 years, were randomised (1:1) to receive ADL-PF (40 mg, SC) in the lower abdomen or upper anterior thigh by PFS or PFP. Primary endpoints were maximum observed serum concentration (C_{max}) and area under the serum concentration–time profile from time 0–2 weeks after dosing ($AUC_{0\text{-}2wk}$). Safety, including injection-site reactions (ISRs), and secondary PK endpoints, were also assessed. Bioequivalence between ADL-PF administered by PFS or PFP device was demonstrated if the 90% confidence intervals (CIs) for the test/reference ratios of $AUC_{0\text{-}2wk}$ and C_{max} fell within the 80.00–125.00% pre-specified margin.

Results: A total of 164 subjects, stratified by body weight were randomised and assigned to treatment; ADL-PF PFS (n=81) and PFP (n=83). Baseline characteristics were comparable between treatment arms. 163 subjects were included in the primary PK analysis. The concentration–time profiles were comparable between the ADL-PF PFS and PFP treatment arms, and were characterized by an increase in serum drug concentrations, with the C_{max} achieved at approximately 6-7 days, followed by a multi-phasic decline in drug concentrations. The 90% CIs for test/reference ratios of the geometric means for the primary PK parameters fell within the pre-specified margin (**Table**). In total, 50 and 51 treatment-emergent adverse events (AEs) were reported in 31 (38.3%) and 29 subjects (34.9%), respectively, in the ADL-PF PFS and PFP groups. One subject experienced an unrelated serious AE in the ADL-PF PFS group. Injection-site pain was similar between treatment arms at all time points, and for the 2 injection-site locations. IMG testing was limited to subjects experiencing an ISR and/or rash AE, and a matched control group, with 11 (11/15; 73.3%) and 7 (7/15; 46.7%) subjects, respectively, testing anti-drug

antibody (ADA)-positive. Amongst ADA-positive subjects, a majority (12/18) also tested positive for neutralising ADAs (7/11 [63.6%] and 5/7 [71.4%] subjects, respectively).

Conclusion: This study demonstrated that the PK of ADL-PF was comparable following SC administration using either a PFS or PFP device. ADL-PF by PFS or PFP injection was well tolerated by healthy subjects, with the distribution of AEs, including ISRs, being similar between treatment arms.

Table. Summary of Statistical Comparisons of PK Exposure Parameters between Test and Reference Treatments (PK Analysis Set)

PK parameter (units)	Adjusted geometric means		Ratio[a,b]	90% CI for ratio[b]
	ADL-PF PFP (test)	ADL-PF PFS (reference)		
C_{max} (µg/mL)	4.45	4.13	107.74	99.16–117.06
$AUC_{0\text{-}2wk}$ (µg•hr/mL)	1150	1100	104.89	95.76–114.89
AUC_T (µg•hr/mL)	2040	2100	97.23	86.75 – 108.98
$AUC_{0\text{-}inf}$ (µg•hr/mL)	2200	2150	102.27	91.12 – 114.78
T_{max} (hr)[c]	142 (45.4, 336)	166 (47.7, 674)		

[a] (test/reference) of adjusted means.
[b] Ratios and 90% CIs are expressed as percentages.
[c] Median (range).
ADL-PF, PF-06410293; AUC, area under the serum concentration–time profile; $AUC_{0\text{-}2wk}$, AUC from time 0–2 weeks after dosing; AUC_{inf}, AUC from time 0 extrapolated to infinity; AUC_T, AUC from time 0 to the time point of the last quantifiable concentration; C_{max}, maximum observed serum concentration; CI, confidence interval; h, hour(s); PK, pharmacokinetic(s); PFP, prefilled pen; PFS, prefilled syringe; T_{max}, time of maximum serum concentration.

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Disclosure of Interests: Donna Cox Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Daniel Alvarez Shareholder of: Pfizer, Employee of: Pfizer, Amy Bock Shareholder of: Pfizer, Employee of: Pfizer, Carol Cronenberger Shareholder of: Pfizer, Employee of: Pfizer

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AB0286 EFFICACY AND SAFETY OF INTRA-ARTICULAR INJECTION OF ETANERCEPT IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Refractory mono-oligo-arthritis is still a challenging clinical situation in rheumatoid arthritis. Intra-articular corticosteroids are the first-line therapy; however, their efficacy is rather varying and many patients experience relapses within 6 months after injection. (1) Intra-articular anti-TNF has the potential of being less toxic and cost effective compared to its systemic usage.(2) Recent evidences have shown a reduction in the synthesis of either the T helper 1 cytokines or in the interleukin-6/17 axis cytokines at joint level following intra-articular injection of etanercept. (3)

Objectives: Our aim was to evaluate the safety and efficacy of intra-articular injection of etanercept in patients with rheumatoid arthritis.

Methods: This study included 23 rheumatoid arthritis patients diagnosed according to the American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) 2010 diagnostic criteria for RA (4), who suffered from flare of activity in one joint. Patients were selected from the outpatient clinic and the in-patient section of Physical Medicine, Rheumatology and Rehabilitation Department, Faculty of Medicine, Tanta University Hospitals, Egypt. The degree of swelling and tenderness of the affected joint was evaluated on a score (0-3) and the degree of pain was assessed by using visual analog scale (VAS). Musculoskeletal ultrasound (MSUS) examination was done to assess synovitis which was evaluated on two axes, longitudinal and transverse and was semiquantitivaly scored on a (0-3) scale, synovial vascularity was assessed using power Doppler and it was semi-quantitativaly scored on a (0-3) scale, *Follow-up:* Patients were examined both clinically (degree of swelling, degree of tenderness and VAS), and by MSUS on weeks: 1, 4 and 12 after injection.

Results: No serious or life-threatening adverse effects were noticed in any patient during the follow-up periods and up till the end of the study except for temporary local soreness during the injection, there was a significant improvement of VAS, tenderness and swelling scores after 1-week $p<0.002$ and 1-month $p<0.003$ follow-up periods, but there was insignificant change after 3 months $p=0.116$, by MSUS, there was an insignificant change in synovitis $p=0.112$, but a significant change was found in power Doppler after 1-week $p= 0.046$ and no significant changes were detected further.

Conclusion: Intra-articular injection of etanercept is a safe and an encouraging treatment modality in managing refractory mono-arthritis in rheumatoid arthritis patients. Further researches are needed to study the use of repeated injection of etanercept to get more sustained effects.

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AB0287 HEMATOLOGICAL SIDE EFFECTS OF BIOLOGICAL THERAPY IN RHEUMATOLOGY: DATA FROM THE TUNISIAN REGISTER

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Background: During the last decade, the treatment of chronic inflammatory rheumatism (CIR) has been greatly improved with the advent of biotherapy.However, the use of biological treatment can lead to a number of side effects including abnormalities in the blood count.

Objectives: The aim of this study was to assess the different hematological side effects of biological treatment in patients with rheumatoid arthritis (RA) and spondyloarthitis (SA).

Methods: This study included patients with RA (ACR/EULAR 2010) and SA (ASAS 2009) registred with the Tunisian Biologic National Registry (BINAR). Patients were followed and treated with biologics for 2 years of less. Clinical data relative to biological treatment, including haematological side effects, have been collected.

Results: Two hundred and ninety-eight patients (178 women and 111 men) were included in the study.

The mean age was 49.2 ± 14.1 years. The male/female ratio was 0.6. The mean diseases durations for RA and SA were respectively 6.7 ± 3.5 years and 6.5 ±3.6 years.

Anti-TNFα agents were prescribed in 87.9% of patients (n = 263) with respectively: Infliximab (20.4%) Etanercept (23.1%), Adalimumab (24.6%) and Certolizumab (26.5%).

Tocilizumab and Rituximab were prescribed in 10.4% and 5% of the patients, respectively.

Blood count abnormalities were noted in 15.4 % of patients (n=46).

Neutropenia was the most frequently anomaly met on the hemogram (9.1%) followed by anemia (3.4%) and thrombocytopenia (3%). Pancytopenia was found in 11.4% of patients (n=34).

The median time between biological therapy initiation and the onset of hematologic manifestations was 4.8 months [1-12]. Biological treatment was interrupted in two patients.

In the other cases, the biological treatment was maintained with close monitoring of blood cell count. No case of death related to these hematological disturbances has been reported.

Conclusion: In our registry, hematological side effects of biological treatment were found in 15.4% of cases and were noted with a median delay of 4.8 [1-12] months after the treatment initiation. Further studies are needed to confirm our preliminary results.

Disclosure of Interests: None declared

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AB0288

GLUCOCORTICOID SPARING EFFECT OF THE BIOLOGIC DISEASE MODIFYING ANTI-RHEUMATIC DRUGS IN RHEUMATOID ARTHRITIS IN TUNISIAN REAL LIFE PRACTICE

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Background: Glucocorticoids (GCs) are still widely prescribed in rheumatoid arthritis (RA). Despite their disease-modifying properties, they are associated with significant adverse effects. The international guidelines recommend the lowest effective dose and the lowest duration of GCs. Previous studies have shown that biologic disease modifying anti-rheumatic drugs (bDMARDs) can have a GC-sparing effect in RA.

Objectives: The aim of the study was to assess the impact of the bDMARDs on glucocorticoids use in rheumatoid arthritis Tunisian patients, in real life practice.

Methods: RA patients (according to the American College of Rheumatology criteria) who started their first bDMARDs (Tumour necrosis factor(TNF)α inhibitors, Tocilizumab and Rituximab) between January 2016 and august 2019, were recruited from the BINAR« Biologic National Registry», a prospective national Tunisian biologic registry. Oral prednisone intakewascompared at inclusion (M0), at 3 months (M3)and at 6 months(M6) after bDMARDs initiation.

Results: 175 patients were included (149 females / 26 males). The mean age was 54.1 years ± 12.6 and the mean disease duration was 6.7 years ± 3.5. The TNFαinhibitors, the Tocilizumab and the Rituximab were prescribed, respectively, in 79.4%, 17.7% and 8.6%. The mean DAS28 index activity was 4.9 ± 1.5 at M0, 4.5 ±1.5 at M3 and 4.2 ± 1.1 at M6 (p=0.78). At inclusion, 150 patients (85.7%) were taking oral prednisone and the mean dose was 8.2 ± 5.4 mg/day. Overall, a significant decrease of oral prednisone use was observed at M3 (78%) and M6 (67.6%). The mean daily dose of oral prednisone was 8.9 ± 4.3mg at M3 (p>0.05) and 8.1 ± 2.7 mg at M6 (P>0.05). At M3 and M6, 4% and 2% of patients (p>0.05) had lowered prednisone doses, respectively. Prednisone discontinuation was observed in 17.7% at M3 and 18.1% at M6. Increased prednisone doses were noted in 2.7% at M3 and 2.6% at M6. The bDMARDs use wasn't associated with oral prednisone decrease at M3 (TNFi p=0.51; Tocilizumab p=0.54; Rituximab p=0, 77) and at M6 (TNFi p=0.61; Tocilizumab p=0.39; Rituximab p=0,64).

Conclusion: This study showed a small glucocorticoids sparing-effect of bDMARDs at 3 months and 6 months in rheumatoid arthritis patients with a decrease of oral prednisone use of 18.1% at 6 months.

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Disclosure of Interests: None declared

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AB0289

EFFICACY, SAFETY AND IMMUNOGENICITY IN PATIENTS WITH RHEUMATOID ARTHRITIS COMPARING PF-06410293 (ADL-PF), AN ADALIMUMAB (ADL) BIOSIMILAR, AND REFERENCE ADL: RESULTS FROM WEEK 26–52 OF A DOUBLE-BLIND, RANDOMISED PHASE 3 STUDY INCLUDING PATIENTS WHO SWITCHED FROM ADL-PF TO REFERENCE ADL AT WEEK 26

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Background: PF-06410293 (ADL-PF) is an adalimumab biosimilar approved for the treatment of several inflammatory and autoimmune indications.[1] The efficacy, safety and immunogenicity of ADL-PF and reference adalimumab sourced from the European Union (ADL-EU) in patients with rheumatoid arthritis (RA) have been demonstrated to be similar in a randomised controlled trial up to 26 weeks (wks; treatment period 1 [TP1]).[2]

Objectives: To evaluate the efficacy, safety and immunogenicity of ADL-PF and ADL-EU in patients with moderate to severe RA on longer-term treatment, and following a treatment switch from ADL-EU to ADL-PF in a subset of patients.

Methods: This multinational, randomised, double-blind, parallel-group study compared ADL-PF and ADL-EU in essentially biologic-naïve patients with active RA despite methotrexate (MTX) (NCT02480153). In TP1, patients were randomised (1:1) to ADL-PF or ADL-EU (40 mg subcutaneous injection every 2 wks) for 26 wks while continuing MTX (10–25 mg/wk). The primary endpoint was achievement of American College of Rheumatology response (ACR20) at Wk 12. At Wk 26, the start of treatment period 2 (TP2), patients receiving ADL-EU were blindly re-randomised (1:1) to remain on ADL-EU or switch to ADL-PF for 26 wks while patients receiving ADL-PF continued treatment in a blinded manner. Secondary efficacy endpoints at Wks 26, 30, 36, 44 and 52 (ACR20/50/70, European League Against Rheumatism [EULAR] response, Disease Activity Score [DAS] 28-4[CRP] <2.6 and ACR/EULAR defined remission), safety events and percentage of patients with anti-drug antibodies (ADA) were assessed.

Results: In TP1, 597 patients were randomised to ADL-PF (n=297) or ADL-EU (n=300). At Wk 26, 552 patients were re-randomised for TP2 (continued ADL-PF, n=283; continued ADL-EU, n=135; switched from ADL-EU to ADL-PF, n=134). Patients who demonstrated at least minimal efficacy continued in TP2. Observed ACR20 rates were comparable between treatment groups at all visits during TP2 (**Figure**). Other measures of deep response (ACR70, EULAR good response, DAS28-4(CRP) <2.6 and ACR/EULAR defined remission) showed maintained efficacy during TP2 in all treatment groups. Incidences of treatment-emergent adverse events were comparable between treatment groups (**Table**). Overall, incidences of ADA through Wk 52 were comparable between treatment groups (47.3%, 54.1% and 45.9% for patients who continued ADL-PF, continued ADL-EU or switched from ADL-EU to ADL-PF, respectively). In patients who switched from ADL-EU to ADL-PF compared with patients who continued ADL-EU, the increase in ADA incidence over TP2 was 0.8% (from 45.1% to 45.9%) versus 6.7% (from 47.4% to 54.1%), respectively.

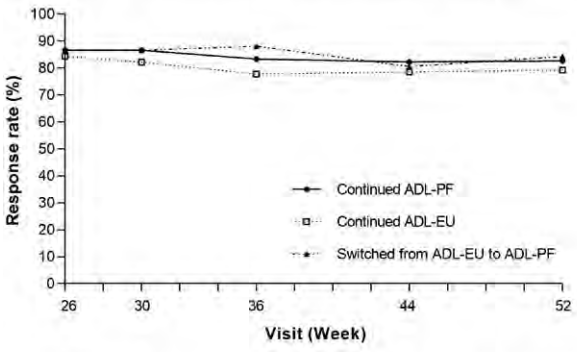
Conclusion: TP2 results demonstrated comparable efficacy, safety and immunogenicity between ADL-PF and ADL-EU was maintained up to Wk 56 and was unaffected by a blinded switch from ADL-EU to ADL-PF at Wk 26.

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Figure ACR20 response rates by visit: Treatment Period 2 (ITT population)



ACR20, ≥20% improvement in American College of Rheumatology response; ADL-EU, adalimumab sourced from the European Union; ADL-PF, adalimumab biosimilar PF-06410293; ITT, intent-to-treat.

Table. All-causality TEAEs: Treatment Period 2 (Safety population)

	Continued ADL-PF (n=283)	Continued ADL-EU (n=135)	Switched from ADL-EU to ADL-PF (n=133)
Number of AEs	243	112	100
Patients with events, n (%)			
AEs	123 (43.5)	60 (44.4)	51 (38.3)
Serious AEs	4 (1.4)	6 (4.4)	3 (2.3)
≥ Grade 3 AEs	7 (2.5)	7 (5.2)	4 (3.0)
TEAEs leading to treatment discontinuation	6 (2.1)	8 (5.9)	2 (1.5)
Deaths	0	0	0

ADL-EU, adalimumab sourced from the European Union; ADL-PF, adalimumab biosimilar PF-06410293; AE, adverse event; TEAE, treatment-emergent AE.

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Genzyme, UCB, Daniel Alvarez Shareholder of: Pfizer, Employee of: Pfizer, Amy Bock Shareholder of: Pfizer, Employee of: Pfizer, Carol Cronenberger Shareholder of: Pfizer, Employee of: Pfizer, Ivana Vranic Shareholder of: Pfizer, Employee of: Pfizer, Wuyan Zhang Shareholder of: Pfizer, Employee of: Pfizer, Rieke Alten Grant/research support from: Pfizer, Galapagos, Galapagos NV, Gilead, Gilead Sciences, Inc., Novartis, Consultant of: Pfizer, Speakers bureau: Pfizer

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AB0290 HERPES ZOSTER INFECTIONS IN RHEUMATOID ARTHRITIS PATIENTS EXPOSED TO BIOLOGICAL AGENTS AND JAK INHIBITORS. REAL-WORLD EVIDENCE.

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Background: The overall occurrence of Herpes zoster (HZ) infections in patients with rheumatoid arthritis (RA) is greater than in the general population although is controversial whether the use of the different disease-modifying antirheumatic drugs (DMARDs) increases this risk.

Objectives: To investigate the incidence and factors associate to HZ infections in patients with RA exposed to biologic agents (BA) and small molecule JAK inhibitors (JAKi), and to describe RA disease features at the moment of HZ infection.

Methods: Retrospective longitudinal study was conducted. We included RA patients seen at the rheumatology outpatient clinic of tertiary hospital, commencing BA (anti-TNF therapy and no anti-TNF therapy) or JAKi from Jan 2007 until Dec 2017, and followed up until end of study (Dec 2019). The outcome of interest was the occurrence of HZ infection, the diagnosis of HZ events was based on the rheumatologist's report. Covariables: sociodemographic, clinical, and concomitant treatments including glucocorticoids, conventional synthetic DMARDs (csDMARDs). Survival techniques were used to estimate the incidence of HZ (IR), per 1000 patient-year (PYs) with the respective Confidence Interval [95%CI]. Cox multivariate regression model to compare the risk of HZ was performed. Results were expressed in Hazard ratio (HR).

Results: 474 RA patients were included, starting 881 different courses of treatment (1954.86 patients-years of follow-up). 382 (80.6%) were women with a mean (SD) age of 56.9 (15.0) years at first BA. Across all groups of treatments, a total 18 HZ were recorded, events were non-serious and involved 1 or 2 dermatomes. The mean age (SD) at moment of the infection was 62 (11) years and 10 cases were on prednisone > 7.5 mg/day. 13 HZ cases (72.2%) occurred on treatment with anti-TNF treatment (6 with adalimumab, 4 with certolizumab and 1 with infliximab), 4 (22.2%) cases were on treatment with rituximab one occurred during tocilizumab prescription. The overall incidence of HZ was 9.20 cases per 1000PYs [5.80-14.61]. The crude IR was similar between gender, increased with age (Patients < 46 years: 2.17 [0.3-15.4]; >70 years 14.1 [5.8-33.8]), was higher with concomitant use of two csDMARDs (IR: 15.68 [7.8-31.7], and was similar between anti-TNF and non anti-TNF therapy. None HZ event was recorded in patients exposed to JAKi. In the multivariate analysis, age (HR: 1.05, p: 0.006), prednisone dose > 7.5 mg/day (HR: 2.83, p: 0.02) and the concomitant use of two csDMARDs (HR: 2.34 p: 0.039) increase the risk for HZ. Lymphopenia (HR: 2.6; p=0.06) achieved a trend and BA therapy dropped from the model.

Conclusion: HZ incidence rate was 9.20 cases per 1000PYs, HZ occurrence in RA patients cannot be attributed solely to the current BA or JAKi treatment and other factors involved must be taking in count as age, concomitant DMARDs prescriptions, and use of glucocorticoids. Our data suggest that preventive strategies for HZ should be developed for patients with RA.

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AB0291 RITUXIMAB MAY DELAY THE MOVEMENT OF RHEUMATOID ARTHRITIS PATIENTS ON CARDIORENAL CONTINUUM: RESULTS FROM A PROSPECTIVE OBSERVATIONAL SINGLE-CENTRE COHORT STUDY

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Background: Similarities in risk factors, initial stages, progression and final stage of both atherosclerotic cardiovascular disease (ACVD) and chronic kidney disease (CKD) allowed formulating a concept of cardiorenal continuum.[1] ACVD and CKD remain the main causes of mortality in rheumatoid arthritis (RA) patients.[2,3]

Objectives: To evaluate the effects of rituximab (RTM) therapy on cardiorenal continuum of RA patients.

Methods: Biologics-naïve RA patients (n=92; age 49.5±9.9) were followed up for 72 months after commencing and continuing RTM therapy (1–10 standard courses) compared with 50 control RA patients (age 49.2±9.8). All control and 63% of RTM patients received methotrexate or leflunomide.

Results: There were no baseline differences between two groups – Table. At year 6, RTM patients have fewer incidences of hypertension, anxiety/depression, atherosclerosis and diastolic dysfunction than controls. RTM decreased prevalence of albuminuria and CKD.

Table. Cardiorenal continuum of rheumatoid arthritis patients (%)

Features	Rituximab group			Control group			p_{RTM-C}
	1 year n=92	3 years n=47	6 years n=31	1 year n=50	3 years n=26	6 years n=16	
Risk factors							
Hypertension	52.2	38.3	25.8 p6–1=0.022	50.0	38.5	50.0	p6=0.032
Dyslipidaemia	44.6	36.2	38.7	48.0	46.2	50.0	>0.05
Pre-diabetes	41.3	36.2	41.9	44.0	34.6	56.3	>0.05
Metabolic syndrome	12.0	6.4	3.2	10.0	7.7	12.5	>0.05
Diabetes mellitus	3.2	0	0	2.0	0	0	>0.05
Anxiety/ depression	78.3	41.5 p3–1=0.005	35.3 p6–1<0.001	76.0	73.1	68.8	p3=0.009 p6=0.008
Initial stages (asymptomatic organ damage)							
Atherosclerosis	34.8	21.3	12.9 p6–1=0.045	36.0	34.6	37.5	p6=0.02
Left ventricular hypertrophy	8.7	4.3	0	8.0	7.7	0	>0.05
Diastolic dysfunction	57.6	38.3	22.6 p6–1=0.018	56.0	50.0	56.3	p6=0.04
Albuminuria	19.6	0	0 p6–1=0.038	12.0	0	6.3	>0.05
Kidney impairment	6.5	2.1	0	6.0	0	0	>0.05
Progression							
Angina	6.5	0	0	4.0	0	0	>0.05
Chronic kidney disease	26.1	8.5	9.7 p6–1=0.042	12.0	0	0	>0.05
End stage							
Myocardial infarction	0	0	0	0	0	0	>0.05
Stroke	0	0	0	0	0	0	>0.05
Heart failure	4.4	0	0	0	0	0	>0.05
Acute/chronic renal failure	0	0	0	0	0	0	>0.05
Death	0	0	0	0	0	0	>0.05

There were no significant differences in frequencies of other risk factors, signs of organ damage and cases of established heart, cerebrovascular and renal diseases/complications.

Conclusion: RTM may be effective in delay of the movement of RA patients on cardiorenal continuum. The clinical implications of RTM for cardiorenal correlations in RA patients need to be confirmed in large-scale clinical outcome trials.

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AB0292

EFFICACY AND SAFETY OF TWO BIOSIMILAR ETANERCEPT AFTER THE SWITCH FROM THEIR CORRESPONDING ORIGINATOR IN THE TREATMENT OF PATIENTS WITH AUTOIMMUNE ARTHRITIS; A RETROSPECTIVE ANALYSIS IN A REAL LIFE SETTING

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Background: The available biosimilars of etanercept are as effective and well tolerated as their bio originator molecule in the naive treatment of chronic autoimmune arthritis. More data about the switching from the bio originator are needed.

Objectives: To compare the clinical outcomes of the treatment with etanercept biosimilars (SB4 and GP2015) naïve and after the switch from their corresponding originator in patients affected by autoimmune arthritis in a real life setting

Methods: We retrospectively analyzed the baseline characteristics and the retention rate in a cohort of patients who received at least a course of etanercept (originator or biosimilar) in our Rheumatology Units from January 2000 to January 2020. We stratified the study population according to biosimilar use. Descriptive data are presented by medians (interquartile range [IQR]) for continuous data or as numbers (percentages) for categorical data. Drug survival distribution curves were computed by the Kaplan-Meier method and compared by a stratified log-rank test. A Cox proportional hazards regression analysis stratified by indication, drug, age, disease duration, sex, treatment line, biosimilar use and prescription year was performed. P values ≤ 0.05 were considered statistically significant.

Results: 477 patients (65% female, median age 56 [46-75] years, median disease duration 97 [40.25-178.75] months) treated with etanercept were included in the analysis. 257 (53.9%) were affect by rheumatoid arthritis, 139 (29.1%) by psoriatic arthritis, and 81 (17%) by axial spondylarthritis. 298 (62.5%) were treated with etanercept originator, 97 (20.3%) with SB4, and 82 (17.2%) with GP2015. Among the biosimilars 90/179 (50.3%) patients were naïve to etanercept treatment. Among the 89 switchers we observed 8 treatment discontinuations: one due to surgical infection complication, three due to disease flare, two due to subjective worsening and one due to remission. The overall 6- and 12-month retentions rate were 92.8% and 80.2%. The 6- and 12-month retention rate for etanercept, SB4 and GP2015 were 92.7%, 93.4% and 90.2%, and 82%, 74.5% and 88.1% respectively, without significant differences among the three groups (p=0.374). Patients switching from originator to biosimilars showed and overall higher treatment survival when compared to naive (12-month retention rate 81.2% vs 70.8%, p=0.036). The Cox proportional hazard regression analysis highlighted that the only predictor significantly associated with an overall higher risk of treatment discontinuation was the year of prescription (HR 1.08, 95% CI 1.04 to 1.13; p<0.0001).

Conclusion: In our retrospective study etanercept originator and its biosimilars (SB4 and GP2015) showed the same effectiveness. Patients switching from originator to biosimilar showed an significant higher retention rate when compared to naive. The only predictor of treatment discontinuation highlighted by the Cox proportional hazard regression analysis was the year of treatment prescription.

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AB0293

FACTORS ASSOCIATED WITH INITIATION OF BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS IN MOROCCAN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a progressive autoimmune disorder of joints that is associated with high health care costs, yet guidance is lacking on how early to initiate biologic disease-modifying antirheumatic drugs (DMARDs). Few studies have examined the factors associated with the transition from non biologic DMARDs to biologic DMARDs in RA patients.

Objectives: to examine the association of patient's comorbidities with initiation of biologic DMARDs (disease-modifying antirheumatic drugs) in rheumatoid arthritis (RA).

Methods: cross-sectional study was designed on a cohort of RA patients. Sociodemographic, clinical data and comorbidities were collected. Logistic regression analysis was used to explore the impact of comorbidities on the initiation of bDMARD. The statistical analysis was done by SPSS. 20, p <0.05 was considered significant.

Results: among the 257 patients, 90.5% were females. Their mean age was 54.66 ± 11.9 years. The most frequent comorbidities in our population were: high blood pressure (22.5%), diabetes (16.6%), history of heart disease (5.1%), history of neoplasia (2.4%) and nephropathies (2%). RA patients with comorbidities were more likely to initiate bDMARD: high blood pressure (p = 0.003 OR=2.36, 95% CI: 1.332- 4.181), history of heart disease (p = 0.036 OR=3.01, 95% IC: 1.073-8.468) and history of neoplasia (p = 0.026 OR= 5.07, 95% CI: 1.219- 21.110). In multiple regression models, high blood pressure was associated to the initiation of biologic agents (p= 0.026, OR= 2.07, 95% CI: 1.090-3.932).

Conclusion: the probability of initiating therapy with biologic agents in patients with RA is affected by different co-morbidities in our context specifically hypertension.

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AB0294

PERSISTENCE WITH ABATACEPT VERSUS TUMOR NECROSIS FACTOR-INHIBITORS FOR RHEUMATOID ARTHRITIS COMPLICATED BY POSITIVE ANTI-CYCLIC CITRULLINATED PEPTIDE/RHEUMATOID FACTOR OR OTHER POOR PROGNOSTIC FACTORS

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Background: Rheumatoid arthritis (RA) treatment usually begins with a non-biologic disease-modifying antirheumatic drug (DMARD), followed by a biologic DMARD (including abatacept or tumor necrosis factor-inhibitors [TNFis]) in non-responsive patients.[1] Since, treatments are switched if disease activity does not improve, it is valuable to understand treatment persistence and switch patterns in RA patients with poor prognostic factors in a real-world setting.

Objectives: To assess 12-month treatment persistence in early-line abatacept versus TNFi treated patients with RA complicated by poor prognostic factors.

Methods: We performed a multi-center retrospective medical record review of adult RA patients with poor prognostic factors treated at 6 United States clinics. Patients were treated with abatacept or TNFi as the first biologic treatment at the clinic. Poor prognostic factors included positive anti-cyclic citrullinated peptide antibodies (ACPA+), positive rheumatoid factor antibodies (RF+), increased C-reactive protein levels, elevated erythrocyte sedimentation rate levels, or presence of joint erosions. TNFis included adalimumab, etanercept, infliximab (and their biosimilars), certolizumab pegol, or golimumab. Data were collected from first biologic treatment for ≥1 year. Patients with Crohn's disease, ankylosing spondylitis, ulcerative colitis, psoriatic arthritis, or anal fistula were excluded. Demographic, disease, and treatment information (start, stop, reason for discontinuation) was abstracted. Treatment persistence (continuation of index treatment with gap ≤60 days) at 12 months and time to discontinuation were reported. Multivariate logistic and Cox regressions were used to compare 12-month persistence and risk of discontinuation between abatacept and TNFi, controlling for demographic and clinical characteristics (age, sex, Charlson comorbidity index [CCI], RA duration), baseline utilization, and clinic. Findings among a subgroup of ACPA+ and/or RF+ patients are reported.

Results: Data on 265 patients (100 abatacept, 165 TNFi) were collected, including 163 ACPA+ and/or RF+ patients (55 abatacept, 108 TNFi). Overall, abatacept patients were older than TNFi patients (67.0 vs. 60.3 years, p<0.001), but there were no statistically significant differences in gender, comorbidities, or duration of treatment at the clinic. At 12 months, 83.0% of abatacept patients were persistent vs. 66.1% of TNFi patients (p=0.003). Persistence was similar among ACPA+ and/or RF+ patients (83.6% vs. 64.8%, p=0.012). Median time to discontinuation was 1,423 days for abatacept vs. 690 days for TNFi (p=0.014) (961 days vs. 581 days among ACPA+ and/or RF+ patients, p=0.048) (Figures 1,2). In the adjusted analysis, risk of all-cause discontinuation was statistically significantly higher among TNFi than abatacept patients (1.7 [95% CI: 1.1-2.6], p=0.012). The odds of TNFi patients being persistent at 12 months was 51% lower than abatacept patients, although not statistically significant

(p=0.071). More TNFi than abatacept patients discontinued index treatment due to disease progression (27.3% vs. 12.0%, p=0.003). Adjusted analyses showed that TNFi patients had a statistically significantly higher risk of discontinuing index treatment due to disease progression (3.4 [95% CI: 1.6-7.2], p=0.001).

Conclusion: In a real-world setting, RA patients with ACPA or RF positivity or other poor prognostic factors are less likely to discontinue abatacept compared with TNFi and are more likely to be persistent on their early line treatment. This difference may be explained by the lower proportion of patients discontinuing abatacept due to disease progression.

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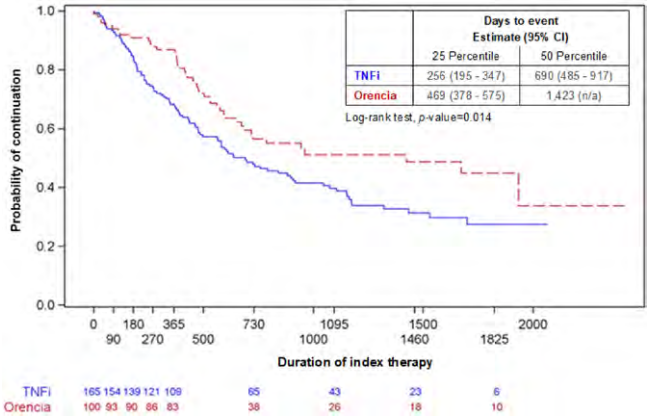


Figure 1. Time to discontinuation of index treatment among all patients (N=265)

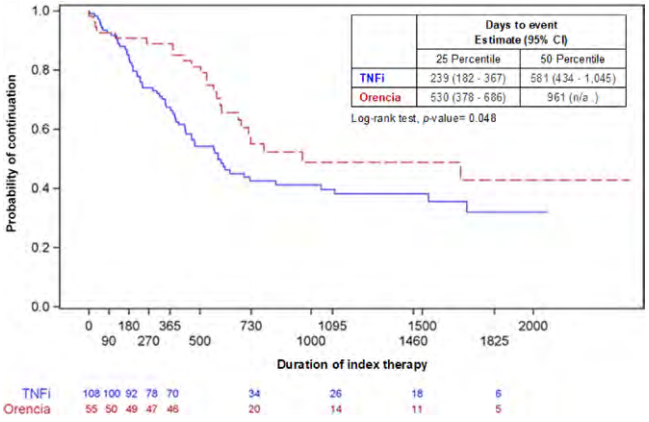


Figure 2. Time to discontinuation of index treatment among ACPA+ and/or RF+ patients (N=163)

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AB0295

CHANGE IN DISEASE ACTIVITY AND TREATMENT RESPONSE AFTER ABATACEPT TREATMENT FOR RHEUMATOID ARTHRITIS: REAL-WORLD EVIDENCE FROM THE UK

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Background: Patients with moderate to severe active rheumatoid arthritis (RA) may be treated with biological disease-modifying antirheumatic drugs (bDMARDs), such as abatacept, after treatment failure with conventional synthetic DMARDs (csDMARDs). Abatacept has shown equivalent efficiency with other targeted therapies for RA in clinical trials and network meta-analyses. However, there is limited real-world evidence on patient outcomes associated with abatacept treatment in UK routine clinical practice.

Objectives: To describe the clinical outcomes of RA patients treated with abatacept in UK real-world clinical practice.

Methods: A multi-centre, retrospective observational study was undertaken in RA patients treated with abatacept at any line of therapy (LOT). Data were extracted from medical records at four UK hospitals. Patients aged 18 years or older who received abatacept between 1 January 2013 and 31 December 2017 were included. The index date was the date of first bDMARD initiation, with follow-up from index date to latest RA clinic visit, death or 31 December 2017, whichever occurred first.

Clinical outcomes (disease activity and response to treatment) were measured using the 28-joint Disease Activity Score based on erythrocyte sedimentation rate (DAS28-ESR) and European League Against Rheumatism (EULAR) response criteria[1-3].

Results: The study included 213 patients (mean age 55.2 years, 71.4% female, 7.0 years mean duration of RA at index date). Where ACPA and RF status were recorded, 66.1% of patients were anti-citrullinated protein antibodies (ACPA) and rheumatoid factor (RF) positive at index. Mean DAS28-ESR at index was 6.2 (SD 1.0) and 80.9% of patients were categorised with high disease activity.

Irrespective of LOT, changes in DAS28-ESR (where recorded) from LOT initiation among patients treated with abatacept versus other bDMARDs were -1.59 vs -1.56 (LS mean (SE): -0.04; 95% CI: -0.45,0.38; p=0.86) at 6 months and -1.98 vs -1.42 (LS mean (SE): -0.56; 95% CI: -1.04,-0.07; p=0.03) at 12 months, respectively. Table 1 shows that compared with other bDMARDs, patients treated with abatacept at any LOT experienced good response to treatment at 6 months (22.8%, n= 21/92 vs 15.9%, n= 24/151) and 12 months (27.9%, n= 17/61 vs 20.5%, n= 24/117) according to EULAR criteria.

Table 1. Treatment response at 6 and 12 months after initiation of any LOT*

EULAR response	6 months		12 months	
	Abatacept, n = 92	Other bDMARDs, n = 151	Abatacept, n = 61	Other bDMARDs, n = 117
Good	21 (22.8%)	24 (15.9%)	17 (27.9%)	24 (20.5%)
Moderate	38 (41.3%)	60 (39.7%)	22 (36.1%)	40 (34.2%)
None	33 (35.9%)	67 (44.4%)	22 (36.1%)	53 (45.3%)

n = number of unique LOTs in which a patient has both a DAS28-ESR collected at initiation and 6 and/or 12 months (a patient may be included in this analysis multiple times)

Patients who received abatacept remained on treatment for significantly longer than patients who received other bDMARDs at LOT1 (median 53.4 vs 17.4 months; p<0.01) (Figure 1) and at LOT2 (median 40.1 vs 17.1 months; p<0.01).

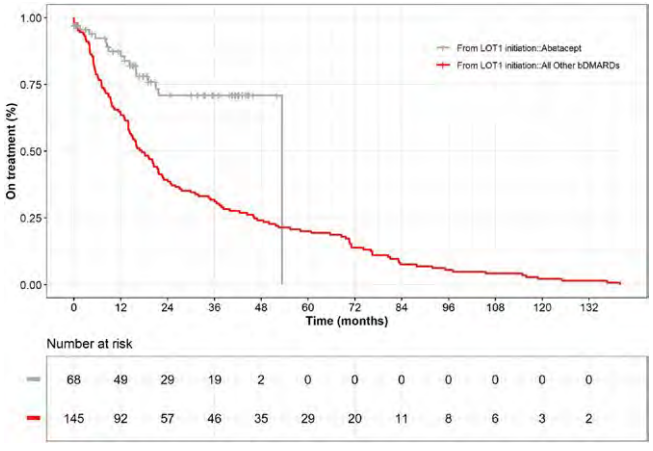


Figure 1. Time on treatment from first LOT initiation, abatacept versus other bDMARDs

Conclusion: RA patients who received bDMARDs, including abatacept, experienced reduced disease activity. These findings are comparable with those from a European, multicentre, observational study on patients receiving abatacept[4].

The mechanisms associated with such clinical benefit should be elucidated in future research.

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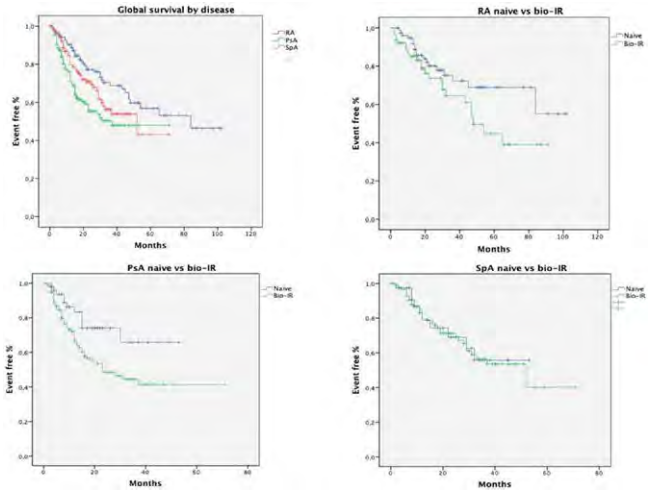
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AB0296 EFFECTIVENESS OF CERTOLIZUMAB IN 506 PATIENTS WITH RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS, AND SPONDYLOARTHRITIS FROM THE APULIAN REGISTRY BIOPURE.

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Background: Little is known about effectiveness of certolizumab (CTZ) in clinical practice, especially in patients with inadequate response to prior biologics.
Objectives: To estimate the survival rate of CTZ in RA, PsA or SpA cohorts from the registry BIOPURE. Secondary endpoint was the changes of clinical outcomes from baseline at 6 and 12 months for each disease.
Methods: We analyzed longitudinal data of consecutive patients, affected with RA, PsA or SpA starting a treatment with CTZ recorded into the web-based Apulian registry BIOPURE. Demographic and disease related characteristics were collected at baseline, 6 and 12 months. Drug survival was evaluated by Kaplan-Meier life table analysis. Estimates hazard ratios (HRs, 95% confidence intervals (CI)) of drug discontinuation adjusted for patient's demographics, disease characteristics and prior biologic treatments were computed by Cox-regression models. Differences of DAS28, DAPSA and BASDAI among baseline, 6 and 12 months were estimated by T-test.
Results: 506 patients were included in this analysis (table 1). Global mean survival time (95% CI) was 58 (52-64) months. Drug survival rate was significantly higher in RA (71.1%) than in PsA (63.5%, p=0.001), while SpA showed 67.5% (Figure 1). Naïve-CTZ patients showed higher survival rates than biologic-inadequate responder (Bio-IR) patients in PsA (naïve 78.4% vs 56.9%, p=0.02), but not in RA (76.9% vs 64.1%, p=0.08), or SpA (73.7% vs 64.8%, p=0.84). The only weak predictor of drug discontinuation was age at baseline for SpA patients (HR 1.04 (95% CI:1.005-1.007) p=0.02) (Figure 1). No baseline covariate, including sex, cDMARDs co-therapy and biologic-naïve status, was found to be associated with CTZ discontinuation for RA and PsA cohorts. A significant improvement of clinical outcomes from baseline was seen at 6 and 12 months, regardless prior biologic therapies. In RA DAS28 dropped from 3.95 ±1.5 to 2.77 ±1.3 at 6 months (p=0.0001) and 2.55 ±1.3 at 12 months (p= 0.0001). In PsA DAPSA decreased from 19.1 ±10 to 10.8 ±8 at 6 months (p=0.0001) and 9.6 ±7 at 12 months (p=0.0001). In SpA DAS28 reduced from 3.66 ±1.4 to 2.85 ±1.3 at 6 months (p=0.0001) and 2.55 ±1.1 at 12 months (p=0.0001). Additionally, in SpA BASDAI dropped from 5.3 ±1.6 to 3.8 ±2.3 at 6 months (p=0.0001) and 2.8 ±1.8 at 12 months (p=0.0001).
Conclusion: In real-life settings CTZ has shown a good effectiveness also in Bio-IR patients. Unlike other TNF-inhibitors, the clinical response and the survival rate were also meaningful in RA patients.
Table:

	RA (nr. 180)	PsA (nr.189)	SpA (nr.137)
Age (mean ± SD)	54.5 ±12	50.6 ±12	52.0 ±11
Female	82.9 %	74.6 %	56.3 %
BMI (mean)	25.9 ± 5	28.4 ± 5	26.7 ± 5
Dis Durat months (mean ± SD)	46 ± 14	106 ± 82	97 ± 92
Naive	53.9 %	32.8 %	28.5 %
Prior biologics	52.9 %	75.0 %	71.1 %
Glucocorticoids	55.9 %	39.7 %	39.4 %
DMARDs	72.4 %	52.4 %	43.8 %
DAS28 (mean ± SD)	4.8 ± 1.5	3.6 ± 1.2	3.7 ± 1.3
BASDAI (mean ± SD)			5.2 ± 2
DAPSA (mean ± SD)		19.7 ±10	
HAQ (mean ± SD)	1.2 ± 0.7	1.1 ± 0.6	1.2 ± 0.7
RF/ACPA +	72.4 %		



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AB0297 THE LONG-TERM OBSERVATION OF PATIENTS WITH RHEUMATOID ARTHRITIS WHO ACHIEVED A BIO-FREE CONDITION WITH ADALIMUMAB.

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Background: Biological disease-modifying antirheumatic drugs (bDMARDs) caused a paradigm shift in the treatment of rheumatoid arthritis (RA). However, their high cost is a burden for patients and the national medical economy.
Objectives: To analyze the long-term outcomes of patients with RA who achieved a bio-free condition (BF) with adalimumab (ADA).

Methods: We followed 25 patients (male 6, female 19) who discontinued ADA with clinical remission (CR), and one female with a low disease activity (LDA), over 19.4 ±7.8 months of ADA treatment[1)]. At the introduction of ADA, the average age was 51.2 ± 11.9 years old, and the average disease duration was 45.1 ± 48.4 months. The disease activity measured by disease activity score based on C-reactive protein (DAS28-CRP) was defined as follows: CR, <2.3; LDA, 2.3 - 2.7; moderate DA, 2.7 -4.1; and high DA, > 4.1, since the DAS28-CRP tends to be lower than the DAS28-based on the erythrocyte sedimentation rate in Japanese patients [2)].

Results: We lost one patient with a transfer to another hospital. Four patients re-started ADA due to flare (DAS28-CRP>2.7) but achieved CR (in BF) again with the intensification of the treatment (dose increase or initiation of prednisolone [PSL] and/or conventional synthetic [cs] DMARDs such as tacrolimus or iguratimode). The DAS28-CRP significantly decreased from 3.45 ± 1.32 at base line (BL) to 1.55 ± 0.41 (p<0.0001) at BF. It remained 1.59 ± 0.59 (n=25) at 24 months after BF, 1.56 ± 0.39 (n= 20) at 48 months, 1.8 ± 0.7 (n=11) at 60 months. At the last observation, every patient remained in CR up to 84 months (n=2, Figure 1). The modified health assessment questionnaire score significantly decreased from 0.42 ± 0.46 (BL, n=19) to 0.02 ± 0.05 (p<0.002) at BF. It remained 0.03 ± 0.07 (n=19) at 24 months and 0.06 ± 0.14 (n=14) at 48 months, 0.04 ± 0.08 at 60 months (n=9). The PSL dose (mg/day) decreased from 3.2 ± 3.3 (BL) to 2.2 ± 2.8 at BF and 2.04 ± 2.13 (n=25) at 24 months, 1.73 ± 1.9 (n=20) at 48 months, and 1.6 ± 2.3 (n=11) at 60 months, but there were no significant changes. The methotrexate (MTX) dose (mg/week) increased from 10.1 ± 2.9 (BL) to 10.6 ± 2.6 (p< 0.78) at BF, 10.4 ± 3.3 (n=25) at 24 months, 10.7 ± 3.4 (n=20) at 48 months, 10.4 ± 3.1 at 60 months (not significant). The number of csDMARDs significantly increased from 0.8 ± 0.6 (BL) to 1.3 ± 0.9 (p<0.001, at BF), 2.56 ± 0.94 (n=25) at 24 months, 1.6 ± 1.01 (n=20) at 48 mnths, and 1.6 ± 2.3 at 60 months (n=11, Figure 2).

Conclusion: BF can be sustained with an adequate dose of MTX and combination of csDMARDs.

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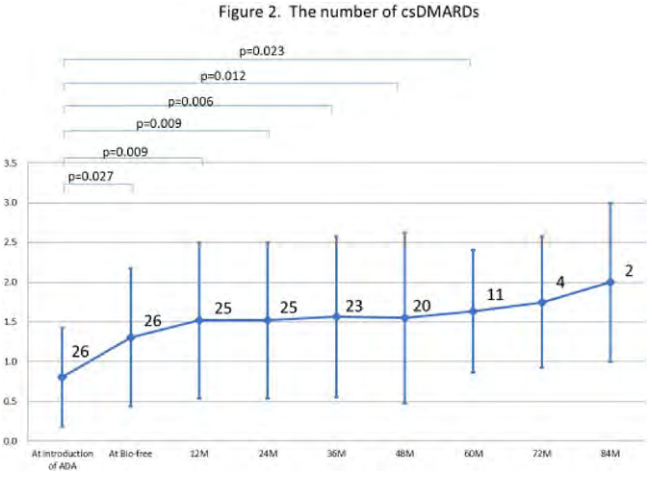
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Figure 1. Change in DAS28-CRP



Figure 2. The number of csDMARDs



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AB0298

LONG-TERM SUPPRESSION OF RAPID RADIOGRAPHIC PROGRESSION AFTER DISCONTINUATION/REDUCTION OF SHORT-TERM BIOLOGIC THERAPY IN PATIENTS WITH EARLY DESTRUCTIVE RHEUMATOID ARTHRITIS ACCOMPANIED WITH EXTENSIVE BONE MARROW EDEMA.

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Background: We reported that short-term (3 or 6 months) treatment with biologics (BIO) group compared with conventional synthetic non-biological disease-modifying anti rheumatic drug (csDMARDs) enhanced group is more effective in the reducing bone marrow edema (BE) and improving structural remission in early destructive RA accompanied with extensive hand BM despite csDMARDs therapy (1).

Objectives: Purpose of this extended study is to investigate whether suppression of RRP will maintain after the discontinuation/reduction of short term biological treatment during over 1 year. Clinical registration number; (UMIN-CTR 000013614)(Figure 1)

Methods: RA disease activity was evaluated by DAS28-ESR after BIO withdrawal/reduction at 12 months. Bone destruction was determined by modified total Sharp scoring (mTSS) using by conventional radiography expressed as yearly progression of mTSS (ΔmTSS/y) at 12 months. Statistical analysis were performed by t-test or Wilcoxon rank sum test using SAS .13.2 software

Results: Fourteen out of 23 patients in BIO group achieved improvement of BM (>70% improvement of baseline BE). Three patient continued BIO. Among 11 patient started to discontinuation/reduction of BIO, 7 patients were successful for discontinuation of BIO. Four patients flared (Table 1). Mean DAS28-ESR, mean ΔmTSS/y at 0, 12 months after discontinuation in 7 patients were 1.77, 2.02 and -0.66,-0.44, respectively (no significant difference between values in 0 and12 month). In contrast, those in 4 flared patients were 1.91, 4.08 and 0, 1.83, respectively (significant difference). Finally, to resolve baseline prognostic factors for improvement of BE for biological treatment, we compared baseline data between 14 BE improved and 9 BE unimproved RA patients. Low DAS28-ESR at 3 or 6 month (P<0.001) are indicated for significant prognostic factor for improvement of BE, although Low DAS28-ESR at baseline (P=0.07) may associate improvement of BE.

Table1. Summary of 1 year clinical data in 11 patients treated in BIO discontinuation/ reduction after improvement of BE by short-term treatment of BIO.

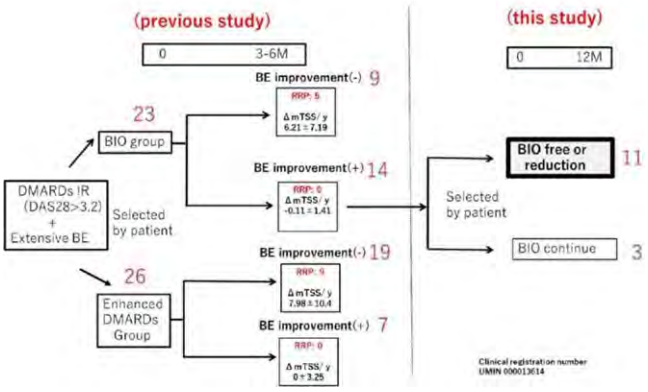
Patient No.	BIO treatment: Dbiologics (+ cs DMARDs)	BIO period (M)	BF/reduction: treatment BF/reduction	BF/reduction(12M)	DAS28-ESR: baseline	BF/R(0M)	BF/R(12M)	ΔmTSS/y: baseline	BF/R(0M)	BF/R(12M)
1	IFX-TAC1.5mg + MTX4mg/w	4	BF	success	3.91	1.66	1.61	30	0	−1
2	ADA + MTX8mg/w	9	BF	success	4.66	2.17	2.31	8.4	0	0
3	ADA + MTX10mg/w	6	BF	success	3.84	1.42	1.74	8.7	0	0
4	ADA + MTX6mg/w	3	BF	success	3.21	1.55	1.09	12	0	−1
5	ADA + MTX8mg/w	12	BF	success	5.03	2.56	3	11	−4.6	0
6	ADA + MTX8mg/w	3	BF	success	3	1.53	2.25	15.1	0	1.3
7	TCZ+MTX6mg/w	5	BF	success	3.12	1.46	3.15	30.8	0	−2.4
Mean					3.83	1.77	2.02	20.1	−0.66	−0.44
8	ABA + MTX12mg	5	BF	flare (11M)	3.59	0.78	3.46	33	0	3.3
9	TCZ + MTX8mg/w	6	reduction	flare (5M)	3.24	1.36	3.92	8.4	0	0
10	TCZ	9	reduction	flare (5M)	3.9	1.56	3.29	16	0	0
11	ABT + BIOG100mg	6	reduction	flare (6M)	4.2	3.3	5.76	10	0	4
Mean					3.73	1.81	4.08	16.8	0	1.83

Conclusion: Results of this study indicated suppression of RRP will maintain during over 1 year after the discontinuation of short term biological treatment in some patients. We recommend that a short-term treatment with biologics for early RA patients, who are resistant to non-bio DMARDs therapy and at high risk to transit to RRP, will be an effective and economical treatment strategy.

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Figure 1 Study Protocol



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AB0299

REAL-WORLD ASSESSMENT OF GP2015 (ETANERCEPT BIOSIMILAR, SDZ-ETN): AN INTERIM ANALYSIS OF DATA FROM THE SELF-INJECTION ASSESSMENT QUESTIONNAIRE IN PATIENTS WITH RHEUMATOID ARTHRITIS IN THE COMPACT STUDY

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Background: COMPACT is a non-interventional study to collect real-world evidence in European countries and Canada on effectiveness, safety and quality of life in rheumatoid arthritis (RA), ankylosing spondylitis or psoriatic arthritis patients (pts) treated with SDZ-ETN (GP2015), an approved etanercept biosimilar. The first effectiveness and safety data from the study have been reported earlier[1].
Objectives: This interim analysis assessed patient usage behaviour and feelings of self-administered injection in general and with the auto-injector device using the Self-Injection Assessment Questionnaire (SIAQ) at Week 12 in pts with RA.
Methods: Pts aged ≥18 years for whom treatment with SDZ ETN were initiated are being enrolled. The SIAQ, a patient questionnaire validated for pts with RA, was developed to assess overall pt experience with subcutaneous self-injection[2]. It assesses the perceived self-confidence on self-injection, potential barriers, as well as satisfaction with self-injection via device before the first self-injection (PRE module) and after dosing (POST module). The POST module used in COMPACT includes 21 items grouped into six hypothetical domains: "feelings about injection," "self-image," "self-confidence," "injection-site reactions," "ease of use of self-injection device (SD), and "satisfaction with self-injection." Descriptive statistics were used to summarise SIAQ POST module data. The results for "ease of use of SD" domain are reported here. The "ease of use of SD" was rated by pts on a 6-point scale: 1 (very difficult) to 6 (very easy).
Results: Of the 430 pts recruited, pts with RA represented the largest group (59.5%, n=256). Majority of pts with RA (77.7%) had comorbidities. Of the 256 pts with RA, 102 (40%) pts who used SD responded to the questionnaire. Majority of the pts found usage of the SD easy or very easy, for each of the domains assessed (Table). 49 % and 14% of the patients were "comfortable" and "very comfortable", respectively using the SD. A majority of patients reported to be bothered by pain at the injection site "not at all" or only "a little" (69.6%), and to be bothered by redness "not at all" or only "a little" (89.2%), respectively.

Table. Overall patient experience with usability of self-injection device at Week 12 (RA population)

Domain: Ease of use of self-injection device

Questions	Category, %						
	Very easy	Easy	Some what easy	Somewhat difficult	Difficult	Very difficult	N/A
Removal of Cap	36.3	34.3	16.7	4.9	3.9	2.0	2.0
To depress the device	34.3	42.2	13.7	2.9	2.0	2.9	2.0
To administer without any help	42.2	35.3	10.8	2.0	2.0	5.9	2.0
Use of self-injection device	38.2	37.3	11.8	3.9	2.9	3.9	2.0

Conclusion: The interim analysis results, although descriptive, show a clear trend for ease of use and good satisfaction with SDZ-ETN SD in pts with RA.
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Disclosure of Interests: Herbert Kellner: None declared, Ayman Askari Speakers bureau: Eli Lilly, Pfizer, Thomas Kupka: None declared, Hilke Friccius-Quecke Employee of: Sandoz Hexal AG, Fabricio Furlan Employee of: Sandoz Hexal AG, Sohaib HACHAICHI Employee of: Sandoz Hexal AG, Marc Schmalzing Consultant of: Paid consultant for Hexal AG
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AB0300

SEVERITY FACTORS IN RHEUMATOID ARTHRITIS AND SPONDYLOARTHRITIS IN NEWLY TREATED PATIENTS WITH BIOLOGICS: SURVEY OF THE BINAR REGISTRY

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Background: Rheumatoid arthritis (RA) and spondyloarthritis (SA) are two heterogeneous diseases but both being major causes of disability in our practice. Biologic treatments have changed miraculously the course of these diseases in the past two decades.
Objectives: To determine severity factors in RA and SA patient newly treated with biologics.
Methods: A survey using results of the Tunisian registry BINAR including ten rheumamtology centers was conducted. Adults of 18 years or more were included. Only those meeting the ACR/EULAR 2010 critera for RA or the ASAS 2009 criterea for SA and treated with biologics for 2 years or less were included.
Results: Two hundred and ninety-eight patientd were enrolled including 111 males and 187 females (sexe ratio H/F of 0.6. The mean age was 49.1 years ± 14.1. The mean disease duration was 6.7 years ± 3.5 for RA and 6.5 years ±3.6 for SA. All patients were prescribed biologics for poor response under NSAIDS or conventional DMARDS. Smoking was reported in 17.7% patients. High disease activity defined as a DAS 28 VS score>5,1 in RA and was reported in 36% of cases. HAQ>2 was present in 14.3%, erosive forms were reported in 73.1% of cases. Rheumatoid factor (RF) and anti cetrullinated peptide antibodies were highly positive (>3x normal rates) in 71,2% and 62.4% of cases respectively. As for AS, active disease was defined by ASDAS CRP or ASDAS VS>2,1 or BASDAI>4 and was reported in 39%, 39.8% and 56.9 % of cases respectively. The functional score BASFI>4 was reported in 54.5% of cases. On the whole, a coxitis was noted in 48.8% of cases and extra articular manifestations (EAM) were present in 59.3 % of cases. Statistical analysis for SA patients didn't show an association between active disease (ASDAS>2,1 and different parameters (genre (p=0.205), smoking (p=0.120), inflammation in biology (p=0.481), uveitis (p=0.241) and the presence of coxitis (p=0.375)). Nevertheless, RA patients with severe disease were more likely men (p= <0.001). Other features for RA patients showed no significant statistical difference (age (p= 0.253), inflammation on biology (p=0.963), positive RF (p=0.789), ACPA positive (p=0.258), présence de EAM (p=0.382), erosive forms (p=0.203) and HAQ≥2 (p =0.219).
Conclusion: It's important to determine clinical, biological and radiographic factors in RA and SA patients as well as activity scores in order to recognize patients potentially at risk of poor progression and for better therapeutic management and biologic treatment may have an influence on these factors.
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Disclosure of Interests: None declared
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AB0301

SARILUMAB AS MONOTHERAPY OR IN COMBINATION WITH CONVENTIONAL SYNTHETIC DMARDS IN PATIENTS WITH RHEUMATOID ARTHRITIS: 12-WEEK TREATMENT RESULTS FROM A MULTICENTER, OPEN-LABEL, PROSPECTIVE, SINGLE-ARM OBSERVATIONAL STUDY

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Background: Due to strict inclusion/exclusion criteria, randomized controlled trials (RCTs) may not represent the heterogeneous rheumatoid arthritis (RA) population encountered in routine clinical practice; longitudinal observational studies are needed to complement learnings from RCTs. The PROspective sarilumab (preFILled syringe/pen) multinational, obsErvational Study (PROFILE) is collecting information on treatment strategies and sarilumab usage patterns and adherence in routine clinical practice for up to 52 weeks in patients with moderate-to-severe RA.

Objectives: In this planned interim analysis, we report baseline characteristics of patients prescribed sarilumab in routine clinical practice and the efficacy and safety of sarilumab after 12 weeks of treatment.

Methods: Adults with RA (2010 ACR/EULAR criteria) can enroll in this multinational, open-label, single-arm, Phase 4 study if, per their treating physicians' judgment, they are to initiate treatment with sarilumab as mono- or combination (with csDMARD) therapy, in accordance with local labeling/prescribing information, ≤4 weeks prior to or ≤8 weeks after study Visit 1 (signed informed consent and disease characteristics documented); 1000 patients are planned for enrollment. Concomitant use of biologic or targeted synthetic DMARDs (b/tsDMARDs) is not permitted. Primary endpoint is change from baseline in Clinical Disease Activity Index (CDAI) score at Weeks 24 and 52. Statistical analyses are descriptive.

Results: This analysis included 291 patients who reached, or discontinued before, the Week 12 visit, of whom 108 (37%) received sarilumab mono- and 183 (63%) received combination therapy. At baseline (BL), the monotherapy group had longer disease duration and a smaller proportion of b/tsDMARD-naïve patients than the combination therapy group (9.7 vs 8.7 years and 39% vs 53%). Baseline and week 12 CDAI values were available in 132 patients. Mean (SD) BL CDAI scores for the monotherapy and combination groups were 26.7 (13.1) and 27.0 (14.4). At Week 12, CDAI scores were improved by –9.1 (17.5) and –10.5 (13.9), and 37% (19/51) of patients receiving monotherapy and 48% (45/93) of those receiving combination therapy had achieved low disease activity (CDAI ≤10). Remission (CDAI ≤2.8) was achieved by 12% (6/51) of monotherapy and 20% (19/93) of combination-therapy patients. Overall, 55 (19%) discontinued sarilumab: 27 (9%) for an adverse event (AE), 19 (7%) for insufficient response, 4 (1%) for noncompliance, 5 (2%) for other reasons. Severe AEs leading to treatment discontinuation were leukopenia and neutropenia (n=1 patient), peripheral swelling (1), lung cancer (1), and fatigue (1). Ten patients (3%) had a treatment-emergent serious AE.

Conclusion: In this planned interim analysis, sarilumab mono- or combination therapy resulted in improved disease outcomes, assessed by CDAI, at Week 12, an important treat-to-target time point. Safety and efficacy were consistent with Phase 3 trial findings, with no new safety signals, although interim results must be interpreted with caution. Future analyses will evaluate efficacy and safety after 24 and 52 weeks of treatment in routine clinical practice.

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Disclosure of Interests: Alan Kivitz Shareholder of: AbbVie, Amgen, Gilead, GSK, Pfizer Inc, Sanofi, Consultant of: AbbVie, Boehringer Ingelheim,,Flexion, Genzyme, Gilead, Janssen, Novartis, Pfizer Inc, Regeneron, Sanofi, SUN Pharma Advanced Research, UCB, Paid instructor for: Celgene, Genzyme, Horizon, Merck, Novartis, Pfizer, Regeneron, Sanofi, Speakers bureau: AbbVie, Celgene, Flexion, Genzyme, Horizon, Merck, Novartis, Pfizer Inc, Regeneron, Sanofi, Jacques-Eric Gottenberg Grant/research support from: Bristol-Myers Squibb, Pfizer, Roche, Consultant of: AbbVie, Bristol-Myers Squibb, Janssen, Lilly, MSD, Pfizer, Roche, UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Gilead, Janssen, Lilly, MSD, Pfizer, Roche, UCB, Martin Bergman Shareholder of: Johnson & Johnson – stockholder, Consultant of: AbbVie, BMS, Celgene Corporation, Genentech, Janssen, Merck, Novartis, Pfizer, Sanofi – consultant, Speakers bureau: AbbVie, Celgene Corporation, Novartis, Pfizer, Sanofi – speakers bureau, Melitza Iglesias-Rodriguez Shareholder of: Sanofi Genzyme, Employee of: Sanofi Genzyme, Gregory St John Shareholder of: Regeneron Pharmaceuticals, Inc., Employee of: Regeneron Pharmaceuticals, Inc., Chunfu Qiu Shareholder of: Sanofi Genzyme, Employee of: Sanofi Genzyme, Hubert van Hoogstraten Shareholder of: Sanofi, Employee of: Sanofi, Louis Bessette Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer, Roche, Sanofi, UCB Pharma, Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer, Roche, Sanofi, UCB Pharma, Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer, Sanofi

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AB0302

USE OF TNF-INHIBITORS BEFORE, DURING AND THE FIRST YEAR AFTER PREGNANCY AMONG WOMEN WITH RHEUMATOID ARTHRITIS

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Background: Treat to target is a goal, also in pregnant women with Rheumatoid arthritis (1). There is increasing evidence on safe use with TNF inhibitors during pregnancy. Adjusted use of TNF inhibitors preconception and throughout pregnancy may stabilize disease activity and prevent flares (2). Low disease activity is also beneficial for the fetus.

Objectives: To study the use of TNF-inhibitors among women with Rheumatic arthritis during and after pregnancy.

Methods: RevNatus is a Norwegian, nationwide quality register that monitors treatment of inflammatory rheumatic diseases before, during and after pregnancy. Data from RevNatus in the period October 2017 to October 2019 was used to map the use of all types of TNF inhibitors among 208 women with rheumatoid arthritis, diagnosed by the ACR/EULAR criteria. The use of medication was reported at the time of visit in outpatient clinic. The frequency of use of TNF inhibitors registered at seven timepoints from pre-pregnancy to twelve months after delivery.

Results: The use of medication was reported at each visit for all the women with rheumatoid arthritis. Most of the women were not using TNF inhibitors before and beyond conception. Most of the women continuing TNF inhibitors beyond conception used certolizumab or etanercept. Adalimumab and infliximab were used in pregnancy (tabell 1**).**

Tabell 1.

	certoliz-umab	etane-rcept	adalim-umab	golim-umab	inflixi-mab	No TNF-inhibitor
Before pregnancy n=105	21% (22)	9% (10)	3% (3)		1% (1)	66% (69)
1.trimester n=81	19% (15)	10% (8)				71% (58)
2.trimester n=88	10% (9)	10% (9)				80% (70)
3.trimester n=91	11% (10)	5% (5)				83% (76)
6 weeks post partum n=96	22% (21)	13% (13)	1% (1)		1% (1)	63% (60)
6 months post partum n=88	24% (21)	18% (16)	4% (4)		1% (1)	53% (46)
12 months post partum n=84	21% (18)	17% (15)	7% (6)		2% (2)	53% (43)

Conclusion: Most of the women with rheumatic arthritis were not treated with TNF inhibitors before or in pregnancy. Women with rheumatic arthritis that continuing treatment with TNF inhibitors through pregnancy were using certilozumab and etanercept.

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AB0303

PREDICTORS OF SERIOUS INFECTIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING TARGET THERAPY.

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Background: The problem of infectious complications in patients receiving bDMARDs deserves special attention. Serious infectious adverse events (SIAE) are a most important issue. To develop measures for their prevention it is necessary to know the predisposing factors.
Objectives: to detect predictors of serious infections among patients with rheumatoid arthritis receiving targeted therapy
Methods: The study includes patients with rheumatoid arthritis from the Moscow Unified Arthritis Registry (MUAR), receiving treatment with biologics or tofacitinib. Search for predictors was carried out in two steps. At first step we selected patient related predictors (confounders) that significantly correlate with risk of SIAE. At the second step in the Cox risk regression model by forward stepwise selection were identified independent significant predictors of risk. which demonstrated significant correlation with development of serious infections. Then data about the treatment was added to the generated model: used targeted DMARDs, doses of glucocorticoids (GC), doses of methotrexate (MTX).
Results: Analysis includes 1052 treatment events in 772 patients. There were 44 serious infections. The mean age was 57,1 ± 12,8 years. The mean observation time – 5.3 years. Independent patient related predictors of SIAE risk were the age RR - 1.12 per year (CI: 1.06-1.19), the age of onset disease RR - 0.94 per year (CI: 0.90-0.98), the year of inclusion in the registry RR - 0.64 per year (CI: 0.49-0.85). The dose of MTX and the doses of GC positively correlate with SIAE risk. RR for MTX is 1.05 per mg (CI: 1.005-1.109), RR for GC - 1.11 per mg (CI: 1.004-1.236).
Used targeted DMARD didn't show any significant correlation with SIAE risk.
Conclusion: Higher doses of methotrexate and glucocorticoids are independent significant predictors of serious infections in RA patients receiving targeted DMARDs.
Disclosure of Interests: Ekaterina Koltsova: None declared, Galina Lukina Speakers bureau: Novartis, Pfizer, UCB, Abbvie, Biocad, MSD, Roche, Evgeniya Shmidt Speakers bureau: MSD, Novartis, Pfizer, Karine Lytkina Speakers bureau: Novartis, Eli Lilly, Pfizer, UCB, Abbvie, Biocad, MSD, Jonson&Jonson, Evgeniy Zhilyaev Speakers bureau: Novartis, UCB, Pfizer, Biocad, Abbvie, MSD, Roche
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AB0304

IMMUNOGENICITY OF BIOLOGIC DRUGS IN THE CLINICAL PRACTICE IN THE BULGARIAN POPULATION OF PATIENTS SUFFERING FROM RHEUMATOID ARTHRITIS

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Background: Biological drugs are protein derivatives that, as such, are highly immunogenic. In recent years there have been many conflicting opinions about the role of drug immunogenicity in clinical practice.
Objectives: To evaluate the drug immunogenicity of TNF-alpha blocking drugs (etanercept and adalimumab) used to treat patients with rheumatoid arthritis. To determine whether their presence can alter the effect of treatment and to evaluate their role in the clinical practice of rheumatologists.
Methods: 121 patients with rheumatoid arthritis, as well as 31 healthy controls, similar in sex and age, were examined. They were all monitored at 0, 6, 12 and 24 months from the start of TNF-alpha blocker treatment. Demographics, vital signs, markers of inflammation such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) and disease activity indices were examined at each visit, respectively. Drug-induced neutralizing antibodies, as well as drug bioavailability in patients treated with adalimumab, were examined by ELISA.
Results: Drug-induced neutralizing antibodies to adalimumab were detected in 11.57% of patients at 6 month, in 17.64% of patients at 12 month, and 24.8% at 24 month. Drug-induced neutralizing antibodies to etanercept were not detected at 6 months, at 7.77% at 12 months, at 9.63% of patients at 24 months. Of the adalimumab patients who were having drug-induced antibodies, 92.59% had low drug bioavailability, while the remaining 7.41% of patients showed normal drug bioavailability despite the presence of drug-induced neutralizing antibodies. In terms of worsening of the disease activity, a positive correlation was found with the presence of drug antibodies - Pearson Correlation = 0.701, p = 0.001. Patients with poor clinical response and available drug antibodies receiving adalimumab were slightly more than those treated with etanercept at 12 and 24 months but the difference is non-significant-U = 0.527, p> 0.05 and U = 0.623, p> 0.05, respectively.
Conclusion: Presence of drug-induced neutralizing antibodies in patients treated with adalimumab and etanercept has been associated with poor clinical response and worsening of the patient's condition. Testing of drug-induced neutralizing antibodies as well as the drug bioavailability of the drug used can be used as reliable biomarkers in clinical rheumatology.
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AB0305

STUDY OF CORRELATION OF B-CELL LEVEL AND PROGRESSION OF BONE DESTRUCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING RITUXIMAB THERAPY

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Background: Rheumatoid arthritis is a chronic autoimmune disease characterised by inflammation of the synovial tissue and destruction of the underlying cartilage and bone. The goal of antirheumatic treatment is not only to attenuate the clinical symptoms of joint inflammation, but also to inhibit the progression of joint destruction. Rituximab - it is a chimeric monoclonal antibody that targets the CD20 molecule expressed on the surface of B cells. It has been successfully used to treat rheumatoid arthritis, and it is worth noting that his antidestructive effect sometimes does not meet the clinical.
Objectives: The aim of our study was to evaluate the correlation between the degree of B-cell depletion and the development of the clinical and antidestructive effects of Rituximab (RTM) therapy in patients with rheumatoid arthritis (RA).
Methods: the study included 108 patients (pts) with rheumatoid arthritis, most are middle-aged women with high disease activity (mean DAS28 6,1±1.04, RF-positive 77%, ACCP-positive 83%) treated with RTX (1000 mgx2 or 500 mgx2). Clinical effect was scored by EULAR criteria, radiographic progression was assessed using Sharp/van der Heijde (SvH) modified scoring method. B-cell level was measured with flow cytometry.
Results: patients who were treated by different doses of RTX (500 x2 or 1000 x2) had good response. After 48 week of treatment RTX clinical improvement was achieved in 65% pts, good and moderate response by EULAR criteria in 23 % and 42 % pts respectively. Noteworthy, after 12 months of treatment RTX radiological progression was absent in 50 % pts with high disease activity. There was no significant difference in the degree of B-cell reduction when assessing the antidestructive effect. However, in assessing the clinical effect, it was noted that depletion of B cells in patients with RA in a state of remission (median 0.05% B cells) was more pronounced than in patients with signs of disease activity (2.03% B cells).
Conclusion: rituximab therapy slows the radiologic progression regardless of the therapeutic effect. Radiologic progression did not show any dependence on the degree of B-cell reduction. The most pronounced depletion of B cells was observed in RA patients in a state of remission.
Disclosure of Interests: Anastasia Kudryavtseva: None declared, Galina Lukina Speakers bureau: Novartis, Pfizer, UCB, Abbvie, Biocad, MSD, Roche, Alexander Smirnov: None declared, Svetlana Glukhova: None declared, Eugenia Aronova: None declared, Galina Gridneva: None declared
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AB0306 EXPERIENCE WITH RITUXIMAB BIOSIMILAR BCD-020 IN PATIENTS WITH RHEUMATOID ARTHRITIS IN REAL-WORLD CLINICAL PRACTICE ACCORDING TO DATA FROM MOSCOW UNIFIED ARTHRITIS REGISTRY (MUAR)

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Background: The introduction of perspective anti-rheumatic biologic agents into clinical practice has not only increased therapy efficacy and improved medical prognosis in patients with rheumatoid arthritis (RA), but also resulted in a dramatic increase in treatment cost and, therefore, in a reduced accessibility of the innovative treatment for patients. For this reason, over the last years, there has been a huge interest towards developing biosimilars [1,2].

Objectives: To assess the effectiveness and safety of switching from reference rituximab (RTX_{ref}) to rituximab biosimilar (RTX_{bs}) BCD-020 in patients with RA in real clinical practice according to the data from MUAR.

Methods: Patients with RA who treated by RTX_{ref} at the onset and then switched to RTX_{bs} (BCD-020) were enrolled in the study. For all patients were performed: swollen and tender joints count, ESR, CRP, biochemistry and immunologic blood analyses. Assessment of dynamic of DAS28, RAPID3, HAQ-DI was performed. The great attention was given to the therapy safety assessment. RTX_{ref} effectiveness and safety profile was assessed at the moment of switching; data for RTX_{bs} (BCD-020) were collected not earlier than 6 months after switching.

Results: 46 patients with RA were enrolled, 80.5% were women; the mean age was 59.5±12.2 years; 91.3% were RF-positive, 63% - ACCPA-positive, the disease activity at the moment of switching was moderate, the mean DAS28 was 3.5. The duration of RTX_{ref} therapy until switching was 36.8 ± 26.8 months; the duration of the follow-up period for BCD-020 biosimilar was 12.1 ± 6.18 months. In 43.5% of patients, previously inefficiency or intolerance of other biologics was discovered. The proportion of patients who received concomitant therapy with glucocorticoids or methotrexate (MTX) was 45.7% and 43.5%, respectively. The mean MTX dose was 13.6 mg/wk. The mean dose of RTX_{ref}/BCD-020 was 1000 mg. The stability dynamic of clinical parameters was retained after switching to biosimilar (Tab.1) without significant difference between the rituximab products ($p>0.05$).

Table 1. Comparison of Efficiency Parameters for the Reference Rituximab and Biosimilar BCD-020

Parameter	Reference rituximab	Biosimilar BCD-020
DAS28 (ESR)	3.39	3.34
HAQ-DI	1.48	1.44
RAPID3	12.9	12.6

The safety profile of RTX_{ref} and RTX_{bs} (BCD-020) was also similar. None of the patients discontinued BCD-020 therapy for reasons related to safety or inefficiency.

Conclusion: Within the framework of routine clinical practice, switching from reference rituximab to BCD-020 biosimilar is not accompanied by a change in efficiency and safety profile of the therapy and does not pose a risk of discontinuation, which is coherent with the results of the registration clinical trial for BCD-020. [3]

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AB0307 DOES FCGR2A, FCGR3A AND FCGR3B POLYMORPHISM CAN PREDICT ANTI-DRUG ANTIBODIES APPARITION IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH TNF-BLOCKERS?

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Background: Fc gamma receptors (FcγRs) play a major role in the regulation of humoral immune responses. Single-nucleotide polymorphisms (SNPs) of FCGR2A and FCGR3A and FCGR3B can impact the expression level, IgG affinity and function of the CD32 and CD16 FcγRs in response to their engagement by the Fc fragment of IgG. It was described in patient treated for rheumatoid arthritis (RA), that such a polymorphism may influence patients response to TNF-blockers.

Objectives: In this study, we aimed to investigate whether the FCGR2A H131R (rs1801274), FCGR3A F158V (rs396991), and FCGR3B NA1/NA2 polymorphisms can be involved in the genesis of anti-drug-antibody ADAb to anti-TNF therapy in RA patients under etanercept (ETA), adalimumab (ADL) and infliximab (INF).

Methods: We included 47 patients treated for RA under TNF-blockers. To assess the association between the FCGR2A H131R (rs1801274), FCGR3A F158V (rs396991), and FCGR3B NA1/NA2 polymorphisms and immunogenicity of TNF-blockers, we used allele contrast, the recessive model, the dominant model, and the homozygote contrast. Quantitative measurements of the ADAbs was carried out by a commercial enzyme-linked immunosorbent assay (ELISA) kit (Promonitor)® after 6 months of treatment.

Results: We involved 18 patients treated with ETA, 13 patients with ADL and 16 under INF. None of the patients under ETA has developed ADAb and respectively 1 and 7 patients developed immunogenicity with ADL and INF. We excluded patients under ETA from statistical study since they didn't develop ADAb.

A significant association was revealed between FCGR2A H131R polymorphism and immunogenicity of INF and ADL (table 1).

Table 1. Association between FCGR2A polymorphism and immunogenicity to INF and ADL

FCGR2A association with ADAb (n=29, crude analysis)				
Genotype	**ADAb=0**	**ADAb=1**	**OR (95% CI)**	**P-value**
H/H	1 (4.8%)	3 (37.5%)	1.00	0.031
H/R-R/R	20 (95.2%)	5 (62.5%)	**0.08 (0.01-0.98)**	

There weren't significant associations between ADAb's development and FCGR3A F158V and FCGR3B NA1/NA2 polymorphism.

Conclusion: FCGR2A R allele carriers show less susceptibility to develop ADAb to ADL and INF with follow-up times of 6 months. Our results provide an explanation for controversies in the relationships between FCGR2A H131R polymorphism and TNF-blockers response. Further studies with larger population of RA patients should be undertaken to confirm this hypothesis.

References: None

Disclosure of Interests: None declared

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AB0308 NO SIGNS OF CONGESTIVE HEART DISEASE PROGRESSION IN PATIENTS WITH RHEUMATOID ARTHRITIS ON IL-6 RECEPTOR ANTAGONIST AFTER 12 MONTHS TREATMENT

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Background: N-terminal pro-brain natriuretic peptide (NT-proBNP) is a known marker of heart dysfunction, mainly described in patients with high activity of rheumatoid arthritis (RA). Further knowledge of the influence of the IL-6 receptor

antagonist, tocilizumab (TCZ), on NT-proBNP levels and systolic heart function is yet to be obtained.

Objectives: Access the effect of 12 months TCZ therapy on NT-proBNP levels, transthoracal ehocardiography results and analyze the association between congestive heart disease progression and RA activity.

Methods: 37 RA patients (pts) (31F/6M); median age 56,5 [48; 63,5] years; disease duration 48 [6; 348] months; DAS28 score 6,15 [5,44; 6,45]; rheumatoid factor (RF)+100%; anti–citrullinated protein antibody (ACPA) + 79,6% were treated in an open-label study with TCZ (8 mg/kg every 4 weeks). Identification of NT-pro-BNT in blood serum, transthoracal ultrasound evaluation of left ventriculum ejection fraction (LVEF), E/A ratio performed at baseline and 12 months.

Results: 11 (29,7%) pts had congestive heart disease (CHD) (II functional class of NYHA), 7 (18,9%) pts having signs of mild left ventricular dysfunction (LVD) as dyspnea, shortness of breath, cardiotropic treatment remained the same in the course of the study. After 12 month TCZ treatment as RA activity lowered (DAS28 2.32 [1,75; 3,15], p<0,05), NT-proBNP levels decreased (100,95 [57.9; 117.6] pg/ml to 90,46 [33.62; 106.6] pg/ml), along with elevation of LVEF (60,75 [60; 70]% to 67,68 [62.5; 73.5], p = 0,001). Increase of E/A (0,97 [0.8; 1.17] to 1,04 [0.7; 1.42] correlated with decrease of NT-proBNP level (r = -0,63, p=0,036). Raise of LVEF over 12 months correlated with decrease of RA activity according to SDAI scale (r= -0,670, p<0,05). No significant relationship between NT-proBNP levels, LVEF, E/A and other scales measuring RA activity was found. Clinically all patients had improvement in evaluation of their health and no signs of CHD or RVD progression were found.

Conclusion: Use of TCZ in patients with active RA showed none to positive influence on heart condition, specifically, lowering NT-proBNP levels, improving LVEF and reducing clinical signs of LVD.

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AB0309 MEASURING THE DIFFERENCE: COMPARISON OF MEASUREMENT OF FREE INFLIXIMAB ANTI-DRUG ANTIBODIES

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Background: Infliximab (IFX) was one of the first TNF alpha inhibitors to be licenced in inflammatory arthritis and is still commonly used today. Studies have shown that approximately 50% of primary IFX responders will suffer from secondary loss of response within the first 12 months of treatment (1). The development of Anti-Drug Antibodies (ADA's) plays a significant role in this treatment failure (2).

Monitoring of ADA's helps identify those patients who fail to respond to treatment due to low IFX trough levels. In this scenario the presence of ADA's can aid decision-making regarding increasing IFX dosing or switching biologic therapy to optimise treatment. (3).

Objectives: Despite their potential importance the detection of ADAs varies widely depending on the type of assays used. The aim of this study was to determine the qualitative concordance of three commercially available ELISA kits for measurement of free ADAs to IFX on the Grifols Triturus analyser.

Methods: 150 patient samples from patients with inflammatory conditions and low IFX trough drug levels (≤0.6µg/ml) were analysed for free ADAs using Promonitor, Lisa Tracker and IDKmonitor kits on the Grifols Triturus automated ELISA analyser.

Results: Kappa coefficient (κ) analysis indicated a moderate agreement between the Promonitor and IDKmonitor assays (κ =0.484 (95% CI, 0.357 to 0.611)) and the IDKmonitor and Lisa Tracker assays (κ = 0.485 (95% CI, 0.348-0.621)) as well as substantial agreement between the Promonitor and Lisa Tracker assays (κ =0.768 (95% CI, 0.667-0.870)). Figure 1 shows the distribution of samples identified as free ADA positive by each kit.

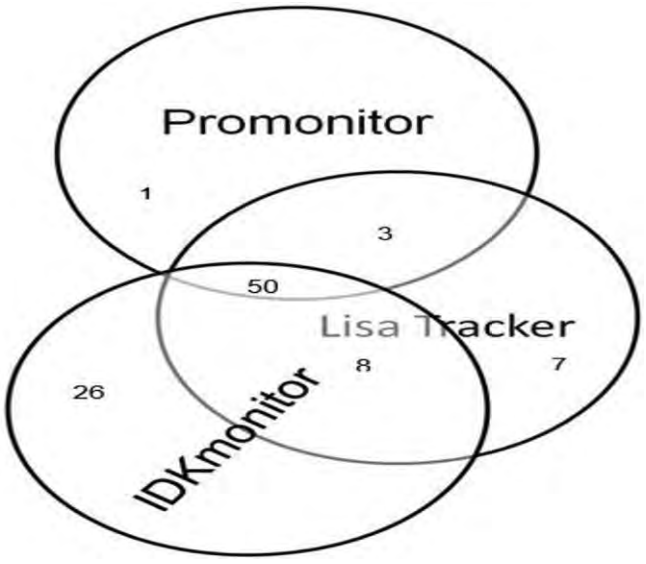


Figure 1. Distribution of samples identified as free ADA positive by Promonitor, Lisa Tracker, and IDKmonitor assays. Fifty samples were considered positive by all assays. Three samples were considered positive by Promonitor and Lisa Tracker, and eight samples were considered positive by Lisa Tracker and IDKmonitor. No samples were considered positive by Promonitor and IDKmonitor. One sample was considered positive by Promonitor only, seven samples were considered positive by Lisa Tracker only, and twenty-six samples were considered positive by IDKmonitor

Conclusion: All kits appear amenable for utilisation in a high-throughput laboratory though a true quantitative comparison between these kits was precluded by the absence of any certified reference material for free ADAs to IFX.

Although broad qualitative agreement was found between the three kits, they should not be used interchangeably for patient management.

Further research is required to estimate the impact of free ADAs on efficiency of IFX treatment and patient management.

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AB0310 TROUGH CONCENTRATION AND ESTIMATED CLEARANCE CAN DETECT IMMUNOGENICITY TO ADALIMUMAB IN RA PATIENTS: A PROSPECTIVE LONGITUDINAL MULTICENTRE STUDY

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Background: Anti-Drug Antibodies (ADA) to adalimumab increase drug clearance in rheumatoid arthritis (RA).
Objectives: To study the ability of drug concentration or estimating clearance to identify ADA to adalimumab.
Methods: Adalimumab concentration was measured with a validated ELISA. ADA was measured using a capture ELISA (Theradiag®) and the Meso scale discovery (MSD) platform. Using a bayesian PK model, adalimumab clearance was estimated at 1, 3, 6 and 12 months. Predictions for ADA presence were calculated, and the correlation between ADA and adalimumab clearance was analysed.
Results: We analyzed 108 samples from 53 RA patients. Serum concentrations and clearance estimates showed good prediction performance for ADA presence (Table 1). There was a correlation between adalimumab clearance and ADA (Figure 1).

Table 1. Immunogenicity prediction of adalimumab, using trough concentration or estimated clearance

Time of visit	ADA method	Adalimumab trough concentration		Adalimumab estimated clearance	
		AUC ROC	p-value	AUC ROC	p-value
Month 1	THER	.55	.6411	.52	.8358
	MSD	.65	.0821	.61	.1872
Month 3	THER	.89	.0006	.91	.0003
	MSD	.73	.0096	.72	.0131
Month 6	THER	.95	.0035	.95	.0035
	MSD	.85	.0004	.84	.0006
Month 12	THER	.87	.0045	.86	.0057
	MSD	.88	.0002	.88	.0002

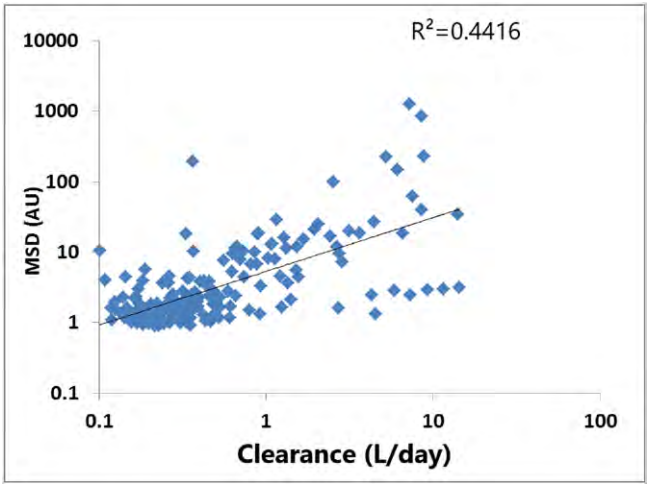


Figure 1. correlation between adalimumab estimated clearance and ADA as provided by the Meso scale discovery (MSD) plateform

Conclusion: Adalimumab concentration and clearance should be considered as reliable predictors for ADA presence in RA patients.
Acknowledgments: Measurement of adalimumab serum concentrations was performed within the 'Centre pilote de suivi biologique des anticorps thérapeutiques' (CePiBAc)– Pilot centre for therapeutic antibodies monitoring platform of Tours University Hospital, which was cofinanced by the European Regional Development Fund (ERDF). We thank Oscar Knight, Delphine Delord and Fabien Giannoni (ABIRISK lab technician), Caroline Brochon and Anne Claire Duveau (CePIBAc), Aliette Decock-Giraudaud (Centre de ressource-Biobank), Sophie Tourdot (ABRISIK Project manager), Aline Doublet (Assistance Publique Hopitaux de Paris, Agnès Hincelin-Méry (Sanofi, Chilly-Mazarin, France). This work has received support from the Innovative Medicines Initiative Joint Undertaking (IMI JU) under grant agreement no. 115303, the resources of which are composed of financial contributions from the European Union's Seventh Framework Programme (FP7/2007-2013) and European Federation of Pharmaceutical Industries and Associations (EFPIA) companies' in-kind contributions.
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AB0311

THE PROPER STUDY: RESULTS OF THE FIRST INTERIM ANALYSIS OF A PAN-EU REAL-WORLD STUDY OF SB5 BIOSIMILAR FOLLOWING TRANSITION FROM REFERENCE ADALIMUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS, AXIAL SPONDYLOARTHRITIS OR PSORIATIC ARTHRITIS

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Background: SB5, a biosimilar to reference adalimumab (ADA), received EU marketing authorisation in August 2017, based on the totality of evidence from pre-clinical and clinical Phase I and III studies that demonstrated bioequivalence, similar efficacy, and comparable safety and immunogenicity to the reference. There are few published data on the transition from reference to biosimilar ADA outside the controlled, randomised, clinical trial setting.
Objectives: To evaluate candidate predictors of persistence on SB5 in EU patients across multiple indications.
Methods: This ongoing observational study will enrol approximately 1200 subjects with rheumatoid arthritis (RA), axial spondyloarthritis (axSpA) or psoriatic arthritis (PsA), who initiated SB5 as part of routine clinical practice following a minimum of 16 weeks' treatment with reference ADA, at clinics in Belgium, Germany, Ireland, Italy, Spain and the UK. Data are captured from clinic records retrospectively for the 24 weeks prior to transition, and prospectively and/or retrospectively for 48 weeks following transition. The primary objective is to evaluate candidate predictors of persistence, and primary outcome measures include baseline clinical characteristics, disease activity scores, clinical management and patient satisfaction over time. This interim analysis provides an overview of baseline characteristics for subjects enrolled and followed up by the data extract date of 20th December 2019.
Results: Of the 123 patients included in this interim analysis, 43 suffer from RA, 42 from axSpA and 38 from PsA.

Table 1. Patient baseline characteristics

	RA (N=43)		axSpA (N=42)		PsA (N=38)	
	Mean (SD)	**Q1, Q3**	**Mean (SD)**	**Q1, Q3**	**Mean (SD)**	**Q1, Q3**
Age (years)	58.7 (11.3)	53, 64	52.3 (13.3)	41, 63	53.7 (14.1)	48, 63
Duration of disease (years)	6.8 (9.5)	1, 6	22.0 (14.4)	12.5, 32.5	13.8 (9.4)	5.5, 22
	n	%	n	%	n	%
Women	31	72.1	16	38.1	16	42.1
Dosing regimen ADA to SB5:						
40mg Q2W: 40mg Q2W	34	85.0	36	85.7	34	89.5
Other*	6	15.0	6	14.3	4	10.5
Stable disease (physician opinion)	34	91.9	27	65.9	30	85.7
Disease Activity Score:	Mean (SD)	95% CI	Mean (SD)	95% CI	Mean (SD)	95% CI
DAS28 (n = 26)	2.71 (0.88)	2.36, 3.06	-	-	-	-
BASDAI (n = 31)	-	-	3.71 (2.89)	2.65, 4.77	-	-
PsA scores (n = 23)					0.3 (0.9)	
Swollen joint					2.9 (5.7)	-0.1, 0.8
Tender joint						0.4, 5.4
Patient Awareness:	n	%	n	%	n	%
Instructed in self-administration	43	100.0	37	90.2	35	94.6
Know to remove SB5 from fridge 30 minutes pre-injection	43	100.0	38	95.0	36	97.3
Know SB5 can be stored out of fridge <25°c for 28 days	42	97.7	33	82.5	28	75.7

DAS-28 Disease Activity Score 28; BASDAI Bath Ankylosing Spondylitis Disease Activity Index; SD standard deviation; Q1 1st quartile, Q3 3rd quartile; CI Confidence Interval
'Other' includes all other reported doses and/or dosing intervals: 40mg QW, 80mg Q2W, and unspecified frequency

Conclusion: This interim analysis provides a first insight into a contemporary cohort of EU patients with established RA, axSpA and PsA, switched from reference to biosimilar ADA in clinical practice. The majority of patients have stable disease at transition, 85% or more of each cohort transitioned to the same dose regimen of biosimilar as received for the reference prior to transition, and most are aware of correct storage and self-administration of their biosimilar medication. With ongoing enrolment and longer follow-up, the study will provide pertinent information about clinical outcomes of transition from reference to biosimilar adalimumab in real-world practice and in indications not investigated in controlled studies.

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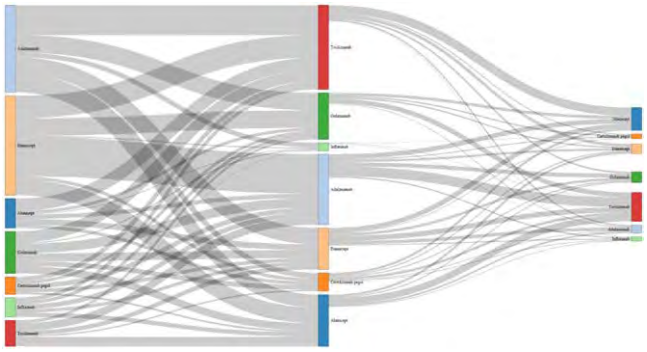
AB0312 REAL-LIFE DATA ON THE USE OF BIOLOGICAL DMARDS IN RHEUMATOID ARTHRITIS IN AUSTRIA WITH SPECIAL ATTENTION TO SWITCHING AFTER FIRST BDMARD FAILURE

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Background: The introduction of biological disease modifying anti-rheumatic drugs (bDMARDs) offered new dimensions in controlling disease progress for patients with Rheumatoid Arthritis (RA). According to the recommendations by EULAR, treatment should be commenced with a conventional synthetic DMARD as soon as diagnosis is made, followed by a bDMARD after treatment failure. The choice of drug is done in respect to comorbidities, preference of the patient and to costs.
Objectives: Drug expenditure data of 2012-2016 were retrieved to evaluate frequency of prescription and drug survival with special focus on switching habits after first bDMARD failure.
Methods: Data were extracted from 11 Austrian social health insurance funds covering 86% of the Austrian population. Only patients with first prescriptions of bDMARDs were included. Absolute and relative frequencies of first bDMARD prescriptions, second and third courses of bDMARDs (switches) and probabilities of drug survival of first line bDMARDs were calculated. Baselines were set individually at the beginning of the first bDMARD course. A Sankey diagram was used to illustrate the relationships between first, second and third courses of bDMARDs (Figure). The first left column represents the first bDMARDs, the second and third columns the second and third switched bDMARDs, respectively. The quantity of the bDMARDs is reflected in the width of the lines.
Results: 7637 RA patients on bDMARD therapy were retrieved in total. With a presumed prevalence of 0.5% (Ref) this would account for 27% of RA patients being treated with a bDMARD. Of these, 3813 were first time prescriptions. The most commonly prescribed drug in bDMARD naïve patients was Etanercept with 26%, followed by Adalimumab with 25%. Third was Tocilizumab followed by Golimumab (16% and 15%), Abatacept with 9% and Certolizumab and Infliximab with both 4%. Tocilizumab showed the longest drug survival with 80% after one and 61% of patients still on the drug after 3 years. Golimumab was clearly favorable among TNF inhibitors with a drug survival of 71% after one and 50% after 3 years compared to Certolizumab showing the lowest with 63% after one year and only 38% after three years. Tocilizumab was the drug most often switched to after first course failure, followed by Adalimumab. The choice of second bDMARD was different: After Adalimumab failure more patients were switched to another mode of action (almost 50%), predominately Tocilizumab. This is also seen after Golimumab failure and is less pronounced in the other TNF inhibitors: they were mostly switched to second TNF inhibitor, mainly Adalimumab. The majority of patients started on Tocilizumab and Abatacept were switched to a TNF inhibitor (74% and 58%, respectively). In third DMARD choice again Tocilizumab is mostly chosen followed by Abatacept, leaving 42% to a TNF inhibitor, mostly Golimumab.
Conclusion: Patients were most often started on a TNF inhibitor as first bDMARD, namely Etanercept and Adalimumab. Golimumab was prescribed less often but showed the longest drug survival among TNF inhibitors. Tocilizumab showed the longest drug survival overall and was the bDMARD most often switched to as second bDMARD. When starting with Adalimumab or Golimumab there was a tendency towards change of mode of action, which was not as pronounced for the other three TNF inhibitors. After failing twice Tocilizumab and Abatacept were the most often prescribed drugs.

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AB0313 CLINICAL PREDICTORS OF MULTIPLE FAILURES TO BIOLOGICAL THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS.

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Background: Biological therapies have improved the clinical course and quality of life of Rheumatoid Arthritis (RA) patients. Despite the availability and effectiveness of these treatments, some patients present multiple failures to biologic disease-modifying anti-rheumatic drugs (bDMARDs), constituting a challenge to clinicians.

Objectives: To determine the frequency of multiple failure to bDMARDs in RA patients and to identify baseline/early features as possible predictors of multiple failure.

Methods: This case-control study involved subjects with RA[1,2] treated with bDMARDs from the RA-Registry at La Paz Hospital between 2000 and 2019. Patients who presented insufficient response to >3 different bDMARDs or >2 bDMARDs with different mechanism of action were considered Multi-refractory (*MR-patients*). Patients who achieved low disease activity or remission (by DAS-28) with the first bDMARD and maintained it in a follow-up period of at least 5 years were considered non-refractory *(NR-patients).* For all patients, demographic, clinical characteristics and laboratory parameters were assessed in the database at baseline visit, just prior to start bDMARD for first time and at 6-months visit.

Descriptive analysis was performed, and using the "refractory status" as the dependent variable, multiple bivariate logistic regression models were performed to identify which variables should be considered in the multivariate analyses. P<0.05 was considered statistically significant. Odds Ratio (OR) and Confidence Intervals (CI) were calculated. IBM SPSS 21.0

Results: In total, 402 RA patients who had ever received bDMARD treatment were identified. According to pre-established inclusion criteria, 112 patients were included: 41 *MR-patients* (10%) and 71 *NR-patients* (18%). No differences in gender, age or age at RA diagnosis were found between both groups. Global time on bDMARD treatment was longer in *MR-patients* (11.7 vs 9.7 years, p=0.01) and survival on first bDMARD was 4.1±3.4 years, which was decreasing with the successive treatments. In *MR-patients*, shorter disease duration between RA diagnosis and starting bDMARD (6.9 vs 10.0; p=0.04) and higher number of previous cDMARDs were observed. Also presence of erosions and extra-articular manifestations were more frequent in *MR-patients (58.5% vs 25.4%, p=0.03 and 29.3% vs 12.7%, p<0.001)*.

Results of variables included in bivariate and multivariate analyses are shown in Table 1. Finally, factors associated with multi-bDMARDs refractoriness in the multivariate analysis were presence of erosions, earlier age at bDMARD start, higher baseline DAS-28 and especially ΔDAS< 1.2 in the first 6 months of treatment (OR 11.12; 95% CI 3.34-26.82).

Table 1.

VARIABLE	Bivariate OR (95%CI)	Multivariate OR (95%CI)
Age at diagnosis	0.99 (0.96-1.0)	-
Sex (Female)	1.67 (0.58-4.73)	5.94 (0.92-38.20)
Age at bDMARD treatment	0.97 (0.93-1.00)	0.95 (0.90-0.99)
Time between diagnosis and bDMARD	0.94 (0.89-1.00)	-
Body mass index	1.01 (0.94-1.09)	-
Erosions (ref yes)	4.07 (1.79-9.26)	3.26 (1.18-9.00)
Extraarticular manifestations (ref yes)	2.81 (1.0-7.52)	2.14 (0.59-7.78)
Metothrexate (ref yes)	1.83 (0.66-5.10)	-
Previous cDMARDs	3.54 (2.05-6.1)	-
CRP baseline	1.02 (0.99-1.05)	-
DAS28 baseline	1.77 (1.2-2.6)	2.29 (1.39-3.76)
ΔDAS-28 (ref <1.2)	0.22 (0.09-0.52)	11.12 (3.34-26.82)
HAQ baseline	1.13 (1.03-1.23)	1.09 (0.92-1.29)

Conclusion: In our cohort, *10%* of patients with RA were observed to have multi-refractoriness to bDMARDs. This study also identified baseline and early clinical characteristics of patients as predictors of multi-refractoriness, especially absence of clinical response during the first 6 months on a first bDMARD.

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AB0314 VIRAL HEPATITIS B REACTIVATION UNDER BIOLOGICAL THERAPY: SCREENING AND PREVENTION MODALITIES IN RHEUMATIC AND INFLAMMATORY BOWEL DISEASE PATIENTS

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Background: Viral hepatitis B reactivation (VHBr) is a serious complication of immunomodulatory therapy and in particular biological therapy (BT), which can be life-threatening, whence the adoption by societies of screening and prevention strategies based on the risk of VHBr which depends on serological status and the treatment used.

Objectives: The objective of our study was to determine the modalities of HBV screening, to describe the prevalence of HBV infection in this group of patients, and to evaluate the VHBr prevention strategies adopted in our country.

Methods: This was a retrospective, 8-year [2011-2018], single-centre, descriptive, retrospective study conducted in two departments: Rheumatology and Hepato-Gastroenterology. Patients under BT were included. Records with missing data were excluded. The modalities of screening and prevention of VHBr were determined and the prevalence of HBV markers was investigated.

Results: One hundred patients were included: 85 followed up for chronic inflammatory rheumatic disease: rheumatoid arthritis (n=40), ankylosing spondylitis (n=41), juvenile idiopathic arthritis (n=4) and 15 patients followed up for inflammatory bowel disease (11 Crohn's disease and 4 ulcerative colitis). The mean age was 44 years with a predominance of females (59%). The BTs prescribed were: anti-TNFα, anti-IL6 and antiCD20 in 83%, 11% and 7% respectively.

HBV screening was done in 89% of cases: HBsAg was tested in 89%, anti-HBc in 64% and anti-HBs in 43%. Complete B serology (HBsAg, anti-HBc and anti-HBs) was performed in 40%.

One patient had chronic hepatitis B on Entecavir for 3 years before starting anti-CD20 (HBsAg(+),anti-HBc(+)). A previous contact with HBV as evidenced by isolated anti-HBs(+) positivity was noted in 13 patients (20%).

A negative B serology was noted in 30 patients (30%). The vaccination rate was 10%.

Prophylaxis with Entecavir was indicated in 2 patients at high risk of viral B reactivation (candidates for anti-CD20 therapy and having anti-HBc(+) with undetectable viral load).One patient at moderate risk of reactivation (candidate for anti-TNF therapy and having anti-HBc(+)) was placed on Lamivudine for prophylaxis. Pre-emptive therapy based on monitoring of alanine aminotransferase (ALT) and HBV DNA levels every 1 to 3 months was indicated in 10 patients (with anti-HBc (+) and candidates for BT other than anti-CD20) but correctly applied in only 2 patients (20%). The remaining eight patients were monitored only for ALT levels. No cases of viral reactivation B were objectified.

Conclusion: In our study, viral hepatitis B screening was done correctly in 40% of the cases. The rate of VHB vaccination was low (10%) despite the low cost of the vaccine. Prophylactic and pre-emptive treatment for viral reactivation were correctly applied in 100 and 20% of cases respectively. This underlines the difficulties encountered in applying pre-emptive treatment when access to HBV DNA level determination is limited and warrants more vigilance prior to the prescription of BT.

Disclosure of Interests: None declared

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AB0315 RETENTION RATE OF ABATACEPT MONOTHERAPY IN AN ITALIAN MULTICENTRIC RHEUMATOID ARTHRITIS COHORT

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Background: EULAR recommendations focus the importance of Methotrexate (MTX) therapy as a key element in the treatment of patients with Rheumatoid Arthritis (RA), alone as first line therapy and in combination with biological Disease Modifying Anti-rheumatic Drug (bDMARDs). Abatacept (CTLA4-Ig) in Europe is approved for the treatment of moderate to severe active RA in combination with MTX. Several patients, however, discontinue MTX for intolerance, side effects or contraindications, and real-life data demonstrate how, even in patients receiving therapy with MTX, compliance could be suboptimal. The only data on the use of abatacept in monotherapy come from the ORA-Registry, where a worse performance is observed in monotherapy patients.

Objectives: To evaluate a multicenter cohort of RA patients treated with Abatacept in patients underwent combined MTX therapy vs monotherapy.

Methods: We retrospectively evaluated RA patients, referring to 2 Italian rheumatology centers, treated with Abatacept monotherapy or in combination with MTX. We compared both persistence in therapy and the rate of remission/low disease activity according to Clinical Disease Activity Index (CDAI) between the 2 groups.

Results: We enrolled 147 patients, out of them 66 patients were on monotherapy with Abatacept due to intolerance or controindications and 81 in therapy with Abatacept plus MTX. The two cohorts appeared homogeneous in age, gender, disease duration and baseline activity indexes, with the only difference being higher baseline Physician Global assessment (PhGA) values in monotherapy patients. During the follow-up (median duration 24±14 months), the retention rate of Abatacept treatment was 71.2% in MTX patients (median duration 27–15.6 months) and 62.1% in monotherapy patients (median duration 25.2–17.5; p=ns). No differences between the two groups in terms of retention rate, low-disease activity and CDAI remission (log rank p=ns), Breslow p=ns) were detected.
Conclusion: In patients with RA with intolerance or contraindication to MTX use, Abatacept monotherapy could be an efficient and safe option even in the long term follow-up.
References: *[1]Abatacept monotherapy compared with abatacept plus disease-modifying anti-rheumatic drugs in rheumatoid arthritis patients: data from the ORA registry.* **Truchetet ME et al. Arthritis Res Ther. 2016 Mar 30;18:72.**
Disclosure of Interests: DANIELA IACONO Speakers bureau: PFIZER, BRISTOL MAYERS SQUIBB, SANOFI, Ilenia Pantano: None declared, domenico birra: None declared, GIUSEPPE SCALISE: None declared, Melania Alessia Coscia: None declared, VALENTINA MESSINITI: None declared, Gabriella Loi: None declared, Anna Merchionda: None declared, Paolo Moscato: None declared, francesco ciccia Grant/research support from: pfizer, novartis, roche, Consultant of: pfizer, novartis, lilly, abbvie, Speakers bureau: pfizer, novartis, lilly, abbvie
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AB0316 MULTIPLE SWITCH BETWEEN BIOSIMILARS DMARDS (BSDMARDS) IN PATIENTS WITH INFLAMMATORY ARTHRITIDES: EXPERIENCE OF A SINGLE ITALIAN CENTRE

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Background: The availability of bsDMARDs since some years represents an opportunity to improve patient access to effective biologic therapy, to better accommodate restraints within healthcare budgets and to improve overall patient outcomes. Different policies are followed in different countries to implement the use of bsDMARDs. Although the latest position paper of AIFA (Agenzia Italiana del Farmaco) envisions the automatic sostitution between the originator and biosimilar, until now the prescriber decision and the patient consent are strongly advised. The question around biosimilar to biosimilar switching is overlooked. Nevertheless different rules are established at regional level and in our Hospital automatic switching between originator/biosimilar and biosimilar/biosimilar was applied.
Objectives: To analyze the efficacy and safety of switch from originator to biosimilar (O/B) and/or biosimilar to biosimilar (B/B) in patients with RA, PsA and SpA.
Methods: We retrospectively analyzed in 63 patients (30 F, mean age 58.3 yr, 21 RA, 26 PsA, 16 SpA), treated with Infliximab, Etanercept and Adalimumab, disease activity (DAS28 CRP for RA, Tender/Swollen joint count for PsA, BASDAI for SpA, CRP for all) and adverse events/infections (AE). The time points considered were 3rd month before the switch and 3rd and 6th month after.
Results: 45 patients underwent sigle switch (35 O/B, 9 B/B) and 18 (28.5%) double switch (O/B/B). 27 B/B switch were done. No differences in disease activity were observed before and after switch (8 RA patients: mDAS28 CRP 2.86>3.23, 11 PsA patients: mTJ count 2.5 > 3.43, 8 SpA patients: BASDAI 2.88 > 2.84). The mean number of swollen joints was very low in PsA group and we decided to exclude this variable. The CRP level was low and stable along all period examined in the three groups. No increase in steroid daily dose, nor in concomitant DMARDs therapy was reported. In the Etanercept B/B switch (14 pts) the number of infections was the same before (3) and after (3). In Infliximab B/B switch (13 pts) 3 infections were reported only before the switch. The severity was mild/moderate with prevalence of respiratory infections (57%). No remarkable variation of transaminases and blood counts were observed.
Conclusion: Althoug the population we examined was eterogeneous and quite small, we observed that the efficay and safety of Infliximab and Etanercept are maintained with biosimilar to biosimilar switch, also after double switch (originator>biosimilar>biosimilar). We also can confirm that the switch from originator to biosimilar Infliximab, Etanercept and Adalimumab is safe in our experience.
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AB0317 BIOLOGIC THERAPY OPTIMIZATION IN RHEUMATOID ARTHRITIS PATIENTS IN COLOMBIA

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Background: The optimization of biological agents (bDMARD), is a strategy that has proven to be cost effective and its use can reduce the risk related to drug exposure (1–3). It is included in the EULAR management guidelines and in the consensus of the Colombian Rheumatology Association.
Objectives: To analyze optimization success of bDMARD therapies in patients with RA.
Methods: Cohort study of RA patients in a specialized multicenter institution in Colombia, followed from January 2015 to December 2019. Patients in remission or low activity for at least 6 months with bDMARD, and with at least two consecutive medical visits, were included. Optimization types were dose decrease, application interval increments, or both. Patients who had disease reactivation (DAS28- CPR >3.2) and returned to standard dose, were considered a failure. By Kaplan-Meier analysis, the optimization failure was estimated according to bDMARD type
Results: 92 patients were included, 78.26% were women, with a median age of 57 years (IQR 50-64), a disease evolution time of 15 years (IQR 10-21), a treatment of 5.6 years (IQR 2.7-8.0), and optimization of 7.75 months (IQR 3.25-15.75). The most commonly used bDMARD therapies were etanercept 36.96%, tocilizumab 30.43% and adalimumab 16.30%. 69.39% (34) were naive for biological treatment. The 53.26% (49) of patients had a follow-up time greater than 6 months.
95.92% remained under optimization scheme without disease activity changes, and 4.08% of patients underwent definitive discontinuation of bDMARD, for sustained therapeutic objective. 8.16% (4) had relapses in the first 6 months after onset, of which 2 patients returned to standard doses. In survival analysis it was observed that patients who were optimized for antiTNF failed faster than the non-antiTNF, although this difference was not statistically significant (Log Rank test 0.003 p value = 0.959). Of the total patients, 28 have been optimized for 12 months or more, of these, 96.43% (27) continue in sustained remission, and 55.56% (15) received combined therapy with s synthetic DMARD (sDMARD).

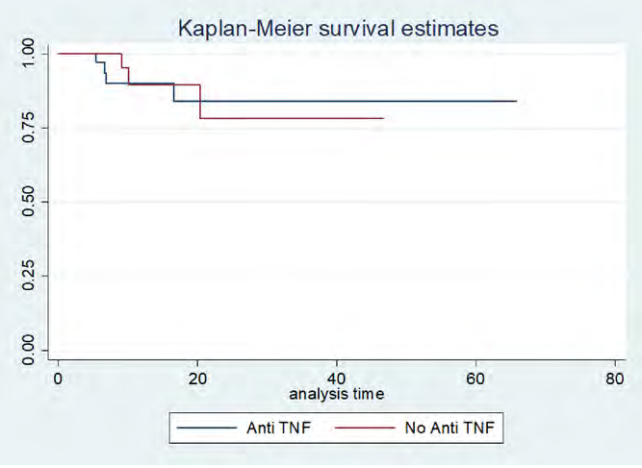


Figure 1. Kaplan Meier

Conclusion: During follow-up, most patients remain in optimization strategy. In those who continued in sustained remission, more than half received sDMARD, this suggests that their use may be a determining factor in preventing disease relapses. More studies are required to evaluate this hypothesis.
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AB0318 CHARACTERISTICS OF PATIENTS WITH RHEUMATOID ARTHRITIS WHO HAVE WITHDRAWN THE LAST BIOLOGICAL DRUG: REAL-LIFE RESULTS FROM A LOCAL REGISTRY

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Objectives: To assess the characteristics of patients with rheumatoid arthritis (RA), who have withdrawn the last biological drug (bDMARD), and to know the reasons for withdrawal of treatment.
Methods: Retrospective and cross-sectional study on December 31, 2019, of patients with RA, treated with any of the bDMARDs, including JAK (JAKi) inhibitor drugs, commonly used, from 1/1/2000 to 12/31/2019. General data were collected from patients, and RA: time of evolution, presence of rheumatoid factor (RF) and anti-citrullinated peptide antibodies (ACPA), type of bDMARD, time in bDMARD, and cause of withdrawal.
Results: Of 252 patients, who have received some bDMARD, 81 (32%) patients had withdrawn on 12/31/2019. 62 (77%) patients were women, with a mean age at diagnosis of RA of 48 years (SD: 16.5 years) and 59.5 (15) years at the beginning of the first bDMARD (F1), with an average evolution of RA 10.2 (2.5) years. 68% and 74% of patients were positive for RF and ACPA, respectively.
In 64 (79%) patients, bDMARD was withdrawn as second to fifth bDMARD received (F2 to F5): as F2: 37/81 (46%) patients, F3: 14 (18%), F4: 8 (10%) and as F5: (6%) patients.
When comparing the last bDMARD received, before the suspension as F1 vs F2-F5, 95% vs. 61% of patients (p <0.0001), the drug was an anti-TNF (TNFi); Abatacept: 1 (1%) vs 9 (14%); Tocilizumab: 0% vs 8 (12%); Rituximab: 1 (1%) vs 5 (8%) and JAKi: 4 (5%) vs 3 (5%). The mean time in treatment with some bDMARD was 2.6 (SD: 3) years in the F1 group vs 1.7 (2) years in the F2-F5 group (p = 0.034). Among the F3-F5 patients, 9 (14%) patients had failed at 2 different previous therapeutic targets and 6 (9%) at 3 targets.
No differences were detected between the F1 group vs F2-F5, regarding the causes of withdrawal of bDMARD: whether it had occurred due to 1) loss of efficacy (25/31% patients vs 19/30%); 2) adverse events (31/38% vs. 29/45%): infection: 18/81 (22%) patients, malignancy: 5 (6%), malaise/pain: 11 (14%), laboratory parameters alteration: 7 (9%), death: 5 (6%), others: 14 (17%); 3) change of address/loss of follow-up (20/25% vs. 7/11%) or by 4) voluntary abandonment of treatment by the patient (5/6% vs. 9/14%).
Conclusion: 1. 32% of patients with RA withdraw the bDMARD. 2. The group treated with TNFi withdraws it significantly higher among the F1 group. 3. Survival of bDMARD is significantly higher in group F1 compared to F2-F5. 4. No differences were detected between the groups regarding the cause of withdrawal of bDMARD. 25% -30% of patients withdraw it due to loss of follow-up or voluntary abandonment of bDMARD.
Acknowledgments: The study was supported by a research grant from the Association for Research in Rheumatology of the Marina Baixa (AIRE-MB).
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AB0319 DRUG SURVIVAL OF BIOLOGICS IN RHEUMATOID ARTHRITIS: PRELIMINARY DATA FROM THE TUNISIAN BINAR REGISTRY

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Background: The arrival of Biotherapy has changed the management and prognosis of rheumatoid arthritis (RA). However, drug survival of the first biotherapy is changing according to the studies.
Objectives: We aimed to report the data on the drug survival of biotherapies in RA, collected from the Tunisian BIologics National Registry (BINAR)
Methods: BINAR is a multicenter non-interventional and prospective study, conducted in Tunisia with 80 rheumatologists over a period of three years. It included patients with RA (ACR / EULAR 2010 criteria) and refractory to conventional background treatments (csDMARDs), who required the use of biological treatment of anti TNF, anti IL6 or Rituximab type. Data were collected and analyzed through an electronic platform managed by DACIMA. Sociodemographic data (age, gender, body mass index (BMI), smoking) and characteristics of RA (duration of evolution, erosive character) were collected. RA activity was studied by the DAS28-VS score and drug survival was evaluated by the duration of the biologics.
Results: We included 175 patients with a sex ratio of 5.7 and a mean age of 54.1 ± 12.6 years [19-79]. Patients were smoking in 6.7% of cases and mean BMI was 27.9 ± 5.2 kg/m^2 [15.1-45.2]. RA was erosive in 73.1% of cases and the mean disease duration was 6.7±3.5 years. Disease activity was moderate (mean DAS28vs: 4.9±1.5). Concerning the treatments, 139 (79.4%) of the patients received TNFα inhibitor, 31 (17.7%) of the patients were on IL6 inhibitor and 15 (8.6%) were on Rituximab.
The mean duration of drug survival for TNFα inhibitor agents was 15.2 months, 18 months for anti IL6 and 16.3 months for Rituximab. The drug was discontinued by 19 patients (10.8%). The causes of discontinuation were primary failure in 31.8% (7 subjects), secondary escape in 9.1% (4 subjects), the occurrence of adverse effects in 31.8% (7 subjects), intolerance to drug in 9.1% (2 subjects), non-compliance for one patient and for other reasons in one case.
The drug survival of TNF inhibitor was not associated with socio-demographic data (gender (p=0.9), age (p=0.4), smoking (p=0.9), BMI (p=0.9)), nor with the characteristics of the disease duration (p = 0.5), DAS28 vs (p = 0.9), association with a csDMARDs (p = 0.2)) except the presence of erosion (p = 0.013).
Also, drug survival of IL6 inhibitor drugs was not associated with socio-demographic parameters (gender (p = 0.1), age (p= 0.6), smoking (p= 0.6), BMI (p = 0.4)) and the characteristics of the disease (duration (p = 0.9), erosive character (p = 0.6), DASvs (p = 0.1), association with a csDMARDs (p = 0.2)).
Similarly, drug survival of Rituximab was not associated with socio-demographic data (gender (p = 0.6), age (p = 0.7), BMI (p = 0.7)) or with the characteristics of RA (duration of evolution (p= 0.5), erosive character (p = 0.6), DASvs (p = 0.08), association with a csDMARDs (p = 0.5))
Conclusion: Our study demonstrated that IL6 inhibitor had the longest duration of drug survival (18 months). The major causes of cessation were dominated by primary failure and the occurrence of an adverse event. Finally, the drug survival of TNF inhibitor agents was associated with the erosive character.
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AB0320 BDMARDS SURVIVAL: THE TUNISIAN DATA

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Background: The advent of biotherapies in the late 90s radically changed the face of inflammatory diseases including rheumatoid arthritis. The survival of these innovative therapies is an indicator, in clinical practice, of their long-term efficacy and safety.
Objectives: The objective of this study was to assess their use in Tunisia through their survival during rheumatoid arthritis as well as to determine the factors that may influence their therapeutic maintenance in real life.
Methods: This is a retrospective study including RA patients (ACR/EULAR 2010 criteria) and putted on biotherapy between 01-01-2014 and 12-31-2016. They were followed until 12-31-2018. The therapeutic maintenance rate at 12, 24, 36 and 48 months as well as the survival curves of biotherapies were analyzed using the Kaplan-Meier survival curves and compared by the Log-rank test. Reasons for interruption and patterns of biological change have been reported. Finally, an analysis of factors influencing survival was performed using Cox regression. A p<0.05 was considered statistically significant.
Results: Three hundred seventy-four patients were included in the study; sex ratio was 0,147. The baseline age was 55 ± 12.5 years [20 – 90] and the average disease duration was 11.7 ± 6.7 years [2 – 41]. Rheumatoid factor and ACPA were positive respectively in 79% and 71% cases. After failure of cDMARD, the first biotherapy prescribed was etanercept in 54%

of cases, adalimumab in 14% of cases, certolizumab pegol 13%, infliximab 6%, tocilizumab 6% and rituximab in 7% of cases, with an average DAS28 at baseline 6.01 ± 0.89 [5,37 – 6,50]. Association with methotrexate was observed in 59,6% case and with corticosteroid in 57.2% case. Drug persistency rate at 12 months was 85.8%; at 24 months, 69.9%; at 36 months, 60.6% and at 48 months, 55.9%. Survival was on average 41.7 months with 95% CI (39.47 - 43.91). The presence of rheumatoid factors, the co-prescription of methotrexate as well as good initial therapeutic response were predictor of a better survival of biologicals at a statistically significant level p<0.01 (Hazard Ratios for pursuit of biotherapy were respectively 1.79, 1.91 and 2,3). The use of glucocorticoids was a negative predictor of retention (Hazard Ratio for therapy pursuit was 0.47 p < 0.001). This first biotherapy was stopped in 39% of cases and ineffectiveness was the major reason of interruption (52.7%). The anti-TNFα cycling was the most adopted therapeutic strategy with 64.6% of cases. The survival rates of the second biotherapy at 12, 24 and 36 months were 91%, 76.4% and 72.1%, respectively.

Conclusion: Our study provides information about biotherapy prescription practices in Tunisia and their effectiveness in "real life". It informs us about the use of these new therapies in our country and has shown an efficacy and a tolerance profile close to those reported in international registers.

Disclosure of Interests: None declared

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AB0321 EFFECT ON RETENTION RATES OF A NOVEL AUTOINJECTOR E-DEVICE IMPLEMENTED IN CLINICAL PRACTICE IN PATIENTS WITH CHRONIC ARTHRITIS TREATED WITH CERTOLIZUMAB PEGOL; A MULTI-CENTRE STUDY

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Background: Anti-tumour necrosis factor (anti-TNF) adherence is suboptimal and impacted by multiple psychological, practical and physical barriers, such as patient needle phobia, lack of confidence in self-administration skills and forgetting injection dates (1,2). ava®, a reusable electro-mechanical self-injection device (e-Device) developed for certolizumab pegol (CZP) administration, aims to overcome some of these barriers.

Objectives: The objective of this study was to explore the clinical retention rate of an e-Device aimed at empowering chronic arthritis patients using CZP.

Methods: Patients treated with CZP were recruited from the Netherlands, Denmark and Sweden through rheumatology clinics to evaluate patient experience with the e-Device. Patients were adults (aged between 18 and 85 years) with RA, axSpA or PsA. After being trained on how to use the e-Device, patients administered 3 consecutive self-injections on their own. Descriptive statistics for baseline characteristics, retention rates and reasons for withdrawal were assessed. Data on physical function (HAQ) are reported for Denmark and Sweden only due to lack of data from Holland.

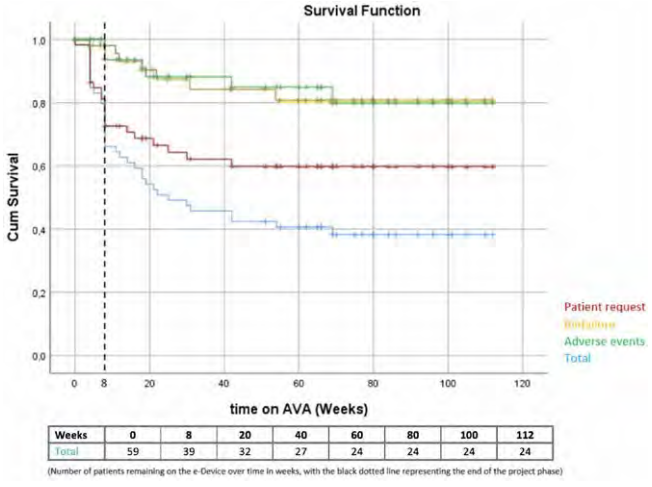


Figure 1. Overall retention rate and reasons for withdrawal

Results: 59 patients participated in the study (Netherlands: 25; Denmark: 15; Sweden: 19). Most patients were women (71%), with a mean age of 55 years [16.2] and an average disease duration of 12 years [8.8]. A total of 42% and 39% had previously been treated with csDMARD(s) or were currently on csDMARD(s), respectively. 12% of the patients were bio-naive. Only 6 (10%) patients started CZP de novo. The remaining switched device. The most used administration form prior to entering the study was pre-filled syringe (78%). At the time of inclusion, patients were mildly disabled with an average HAQ score of 0.5 [0.6] and a moderate VAS-pain score of 32 [25.1] (data not shown).

The overall retention rate was 42% after 52 weeks, declining to 38% after 104 weeks (Figure 1). A sharp decline is seen at week 8 which coincides with the end of the project phase. Between week 32 and 112 only 4 patients withdrew from the study (Figure 1). The primary reason for withdrawal was patient's request (Figure 1). Dropout rates due to lack of efficacy or adverse events were as expected compared to other cohorts of biologic therapies. When stratified by country the analysis showed no significant differences between countries (data not shown).

Conclusion: An initial large drop-out was evident within the first 8 weeks, whereas almost no drop-out was seen in the extension phase (after week 8). The reasons for withdrawal was primarily patient request. Thus, the injection experience must be tailored carefully when selecting patients for new autoinjector e-Devices to enhance retention on device and patient satisfaction. Not one device fits all.

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AB0322 LESSONS LEARNED FROM THE PAST THAT SHOULD IMPROVE THE FUTURE: 18 YEARS OF EXPERIENCE WITH BIOLOGIC THERAPIES IN RHEUMATOID ARTHRITIS IN A TERTIARY RHEUMATOLOGY CENTER IN ROMANIA

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease, which affects approximately 1% of the population. Although diagnostic, monitoring and treatment strategies have improved noticeably over the last decades, allowing an early and sustained clinical and radiological remission, both direct and indirect costs of treatment and disease still create an economic burden for patients and society. The last few years have brought many therapeutic options and knowledge about them, which has led to the 2019 updated EULAR recommendations for the management of RA (1).

Objectives: This study aimed to evaluate the trends in prescribing of biologic therapies in RA over time, the factors that influenced them and the persistence of patients on these treatments.

Methods: In this retrospective study we evaluated patients with RA treated with biologic therapies in the last 18 years, who presented for routine clinical and biological evaluation, performed according to the standard of care principles in RA.

Results: 244 patients were enrolled in this study. Baseline characteristics are presented in Table 1.

Table 1. Baseline characteristics of the 244 patients evaluated

Parameters	RA patients (n=244)
Gender (Female); n(%)	202 (82,8%)
Age (Mean±SD)	61,09±11,86
Age at RA onset (Mean±SD)	46,16±13,12
Disease duration (years); (Mean±SD)	14,93 ±8,78
Number of biologic therapies received; n(%)	
1 line	244 (100%)
2 lines	152 (62,29%)
3 lines	31 (12,70%)
4 lines	2 (0,81%)
5 lines	1 (0,40%)

There is a significant decrease in the persistence period on the first biological therapy after 2010 (60.67 ± 50.53 months before 2010 vs. 37.02 ± 34.92 months after 2010, p <0.001, 95% CI = - 34,464 - -12,838).
There is a significant increase in the period from diagnosis to the initiation of biological therapy after 2012 (6.88 ± 6.75 years before 2012 vs. 9.25 ± 9.33 years after 2012, p <0.001, 95% CI = 0.341-4.406).
Overall, regardless of the therapeutic line in which they were used, persistence on anti-CD20 (44,89±43,02 months (mean±SD)) therapies was significantly higher than that on TNFi (81,85±42,17 months (mean±SD)) (p<0,001, CI=27.806-46.129). (Image 1)

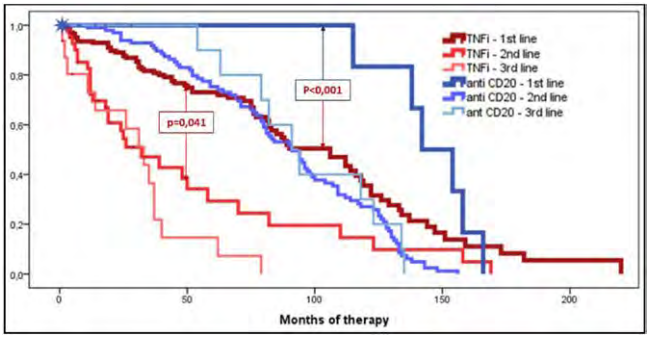


Figure 1. Image 1. Persistence on TNFi and anti CD20 therapies

Conclusion: The two trends observed in this study: the decrease in persistence on biologic therapy, in 2010, and the increase of the period between RA diagnosis and the initiation of a biologic therapy, in 2012, were generated by the appearance of new molecules, thus reducing the boundaries generated by the previously limited number of options, and by the major changes in national health insurance system regulations.
Anti-CD20 therapy proved to be non-inferior to TNFi therapies regarding persistence on therapy and did not result in higher adverse events than TNFi, justifying the inclusion of RTX therapy as one of the biological therapies used in the first line in 2019 RA treatment recommendations.
A limitation of this study is the small number of patients who received other therapies (JAKi, T cell co-stimulation blockers, anti IL6), which did not allow a correct analysis of other therapeutic lines compared to those previously mentioned.

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Disclosure of Interests: None declared

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AB0323

DEMYELINATING DISEASE AFTER EXPOSURE TO TUMOR NECROSIS FACTOR ALPHA INHIBITORS (TNFI): LONG-TERM OUTCOMES FROM A SINGLE CENTER

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Background: TNFi are effective treatments for multiple immune-mediated inflammatory diseases. There are five TNFi's approved for clinical use. Despite their acceptable safety/efficacy profile, serious side effects have been reported, including central and peripheral nervous system demyelinating diseases (DD).[1] Causation remains controversial and there is a paucity of data on the long-term outcomes in these patients.
Objectives: To assess long term outcomes in patients with DD related to TNFi use.
Methods: We conducted a database search and then retrospective chart review to identify patients with potential TNFi related neurologic events at a university medical center between 2006 and 2016. 15 total patients (13 living, 2 deceased) were ultimately identified. Six were able to be contacted by phone to assess their current status. Four of these patients were able to attend a one time-visit to complete a neurologic assessment and musculoskeletal examination. Interviews over the phone or in person were used to complete multiple assessments for disability.
Results: 15 patients with DD were identified from among 4600 patients on TNFi's for various indications (0.3%). Mean duration of follow-up was 6.8 years. Neurologic symptoms occurred >12 months after starting a TNFi in 8/15 (53%) patients. 47% of patients had been exposed to two or more TNFi's. 40% received some form of treatment for their DD, including MS disease modifying therapies, IVIG and immunosuppression. No patients experienced worsening DD after stopping their TNFi except for one patient with MS who experienced a repeat flare. Two of three patients diagnosed with MS after TNFi had a first degree relative with MS. 3/15 (20%) experienced complete resolution of their symptoms. Two patients were deceased; cause of death was thought not directly related to DD on chart review.
Conclusion: Prevalence of DD after TNFi exposure was low at our center, consistent with previously published data. Presentations included both central and peripheral demyelinating events. With the exception of one patient who developed MS, withdrawal of TNFi's appeared to halt further progression or development of new neurologic symptoms. It is unclear if treatment for DD is beneficial after diagnosis and TNFi withdrawal.
Patient Data:

Age	Sex	Indication	TNFi at time of event	Neurologic Presentation/ Diagnosis	Duration of follow-up, years	DD status at last follow-up
32	F	JIA	E	Ataxia, paresthesias, dysarthria, nystagmus, tetraparesis	11	Persistent despite tx
58	M	PsA	G	Paresthesias	9	Improved no tx
38	F	AS	A	Numbness and weakness	5	Resolved, no tx
54	M	PsA	E	Paresthesias, cognitive impairment	10	Persistent, no tx
51	F	AS	A	Incontinence, paresthesias	10	Persistent, no tx
26	F	Crohn's	A	Optic neuritis	11	Resolved, no tx
49	M	PsA	A	Multifocal motor neuropathy	3	Resolved after tx
37	M	PsA	A	Weakness, spasticity, paresthesias, optic neuritis	9	Persistent, on tx
33	F	PsA	A	Optic neuritis, transverse myelitis (MS)	5	Flared, no tx
59	F	PsA	E	Transverse myelitis (MS)	9	Deceased
45	F	AS	I	Transverse myelitis	7	Deceased
70	M	RA	A	CIDP	1	Received treatment but lost to follow-up
34	F	Crohn's	A	Small fiber neuropathy	11	Persistent, no tx
62	F	RA	E	Optic neuritis	<1	Lost to follow-up after initial visit
42	M	Uveitis, retinal vasculitis	A	Paresthesias (MS)	1	Persistent, on tx

Juvenile idiopathic arthritis (JIA), Psoriatic arthritis (PsA), Ankylosing spondylitis (AS), Rheumatoid Arthritis (RA)
Adalimumab (A), Etanercept (E), Golimumab (G), Infliximab (I)
Treatment (tx)

References:

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AB0324

REASONS FOR DISCONTINUATION OF BIOLOGICS IN PATIENTS WITH REFRACTORY RHEUMATOID ARTHRITIS: RESULTS OF A RETROSPECTIVE STUDY

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Background: Refractory rheumatoid arthritis (RRA) is a subtype of rheumatoid arthritis (RA), in which the sequential administration of optimal methotrexate (MT) doses in combination with glucocorticoids (GCs), and at least - two biologic disease-modifying antirheumatic drugs (bDMARDs) with different mechanisms of action during 18-24 months does not lead to a significant decrease in the inflammatory activity of RA.
Objectives: Analysis of the selection strategy and the "survival" of bDMARDs in patients with RRA.
Methods: The retrospective study included data of 95 RRA patients (80 females, 80.8%), aged 23 to 80 years (mean age 57 years), treated with bDMARDs. Mean RA duration was 11.9±7.6 years. All patients were divided into 6 groups depending on the number of the lines of therapy (LOTs) received (from 2 to 7 consecutive bDMARDs). Totally 348 cases of bDMARDs administration were analyzed.
Results: TNF-α inhibitors were most commonly used as the first and second lines of therapy: infliximab (INF) – 43 prescriptions, adalimumab (ADA) – 39, etanercept (ETC) – 25, certolizumab pegol (CZP) – 11, golimumab (GLM) - 6. Abatacept (ABA) was prescribed in 32 cases, rituximab (RTM) in 22 cases, and tocilizumab (TCZ) - in 12 cases. The following reasons for bDMARDs discontinuation were identified: lack of efficacy (LE) (55.2% of cases), adverse events (AE), including serious adverse events (14.8% of cases), administrative reasons (10.0% of cases), persistent remission (2.1% of cases), pregnancy (0.6%), and other (17.3% of cases)
TNF-α inhibitors were also used in third-line bDMARDs therapies, but preference was given to drugs with a different mechanism of action: ABA-20 patients (23.2%), RTM – 20 (21.1%), TCZ – 15 (15.8%), ETC – 22 (23.2%), ADA – 9 (9.5%), INF – 4 (4.1%), CZP – 3 (3.1%). Treatment was discontinued in 74 patients (77.9%). In this cohort the following reasons for bDMARDs withdrawal were identified: LE (54.1%), AE (17.6%), administrative reasons (9.5%), remission (1.3%), and other (17.5%).
The fourth line of therapy was administered in 45 patients: ABA-16 (35.6%), RTM-9 (20%), ADA – 6 (13.3%), TCZ – 5 (11.1%), ETC – 4 (8.9%), CZP – 4 (8.9%), GLM – 1 (2.2%). The reasons for discontinuation (29 patients, 64.4%) were as follows: LE (44.8%), AE (13.8%), other (41.4%).
The fifth bDMARDs was used in 3 patients: TCZ-6 (46.1%), RTM – 3 (23.1%), ABA – 1 (7.7%), ETC – 1 (7.7%), ADA – 1 (7.7%), GLM – 1 (7.7%). Therapy was discontinued in 11 patients (84.6%) for the following reasons: LE (45.5%), AE (18.2%), other (36.3%).
The sixth line of therapy was necessary in 4 patients: ETC (25%), GLM (25%), CZP (25%), ABA (25%) and was discontinued in 3 (75%) of them due to AE (33.3%) and other reasons (66.7%). One patient received TCZ as the seventh line of therapy.
Mean duration of the first line of therapy was 7.6 ± 6.5 months, of the second line - 9.6 ± 7.5 months, of the third line - 11.5 ± 7.1 months, fourth line - 12.5 ± 8 months, fifth line - 13.4 ± 4.8 months, and sixth line - 14.6 ± 4.4 months. Statistical analysis revealed significant differences ($p<0.05$) in the mean duration of therapy (retention on therapy) between the 1st and 3rd, as well as the between the 1st and 4th lines of therapy. There were no significant differences in rates of bDMARDs discontinuation due to LE or AE. The rates of bDMARDs discontinuation did not differ significantly in the study groups.
Conclusion: The mean retention on a drug in the 3rd and 4th lines of therapy in patients with refractory rheumatoid arthritis was significantly longer than on the 1st line of therapy. The most common reason for bDMARDs discontinuation was lack of efficacy. Additional lines of bDMARDs therapy were not associated with increasing rates of adverse events.
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AB0325

FLUORESCENCE OPTICAL IMAGING (FOI) AIDS DIFFERENTIAL DIAGNOSIS OF RHEUMATIC DISEASES AND INCREASES TREATMENT RESPONSE RATE IN RA THROUGH PATIENT STRATIFICATION

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Background: In recent years, indocyanine green (ICG)-enhanced FOI has become clinically available as a novel tool for the early detection of rheumatic diseases, assessment of disease activity and monitoring of treatment response. The high sensitivity of this method allows visualization of slight changes in the microcirculation of the hands as a sign of inflammation. Different rheumatic diseases present characteristic signal enhancement patterns, which may facilitate differential diagnosis. Signal enhancement in metacarpophalangeal (MCP) joints, for example, can frequently be seen in patients with rheumatoid arthritis (RA).
Objectives: We analyzed data of a multicentric clinical study (OPERA, n = 3300) including patients with different rheumatic diseases. Patients were divided into groups using clinical parameters followed by FOI examination to test the hypothesis that this method can improve the diagnosis.
Methods: The present study involved 200 patients with RA (n=200), divided into groups according to Steinbrocker's (STBR) staging system, patients that had degenerative osteoarthritis (OA, n=100), and a control group without clinical symptoms (n=40). RA patients were examined before and during treatment with biologicals, glucocorticoids (GK), or DMARDs. Clinical and laboratory assessments were made by analyses of DAS28, patient questionnaires, rheumatoid factor (RF), anti-citrullinated protein antibodies (ACPA), erythrocyte sedimentation rate (ESR), and x-rays. FOI signal intensity (SI) was defined by ratio of areas with SI in patients and controls. Image sequences were analyzed visually, and MCP joints were judged as positive if in the early phase of ICG inflow, a higher SI in any MCP region was found in comparison to the control group.
Results: Initially, serum factors typical for RA patients were analyzed in the different groups. In 23 % of OA patients RF and/or ACPA were detected in the serum. Surprisingly, in the STBR I group, only 35 % of patients were tested as serum-positive for RF and/or ACPA. After FOI, the patients were subdivided into two groups with and without ICG enrichment in MCPs. In the MCP-positive group, the percentage of RF/ACPA-positive STBRI patients increased to 83%, with only 25 % seropositive patients in the MCP-negative group. In STBRII-IV cohorts, the proportion of RF/ACPA-positive patients was initially higher as in the STBRI group, but also increased after FOI analysis of MCP positivity. In the group treated with biologicals (STBRI-IV), responders were identified both by clinical parameters and FOI. After treatment, 42 % of all analyzed patients were found to respond to treatment. Compared to all patients, the MCP-positive group showed a significantly increased response rate at 71%, while all patients (100%) in the MCP-negative group were identified as non-responders (Figure 1).
Conclusion: The study indicates that FOI is highly effective for the diagnosis of RA, selection of the appropriate therapy, and for the monitoring of therapeutic success. Treatment response rate can be increased (from 42% to 71%) through patient stratification in terms of ICG enrichment in MCP.
Figure.

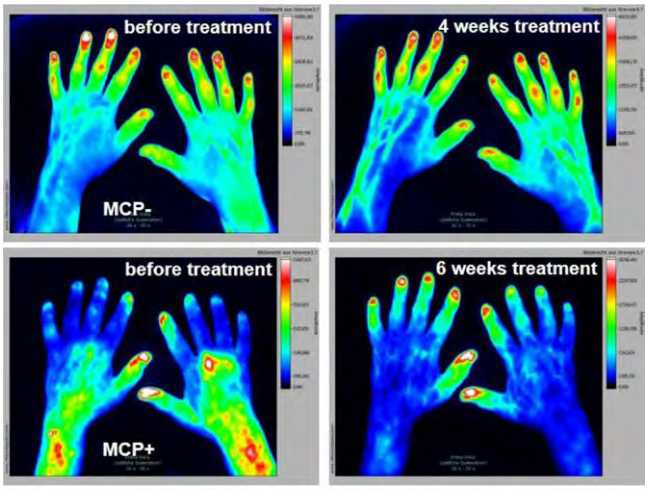


Figure 1: Examples of FOI images in patients with suspected early rheumatoid arthritis before and after treatment with anti-rheumatic biologics

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AB0326

REAL-WORLD EXPERIENCE ON SWITCHING ADALIMUMAB ORIGINATOR TO BIOSIMILAR IN INFLAMMATORY ARTHRITIS – A RETROSPECTIVE STUDY

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Background: The patent for adalimumab originator expired in 2018 in the United Kingdom. Subsequently, four adalimumab biosimilars were launched. National Health Service England undertook a managed market share tender to ensure plurality of suppliers and price competition over the longer term. Each hospital was subsequently allocated a preferred brand of adalimumab biosimilar. Here we describe our experience of switching patients with inflammatory arthritis from adalimumab originator to the biosimilar, ABP 501 in a single centre.
Objectives: To evaluate the proportion of patients successfully switched from adalimumab originator to ABP 501 focusing on drug retention, reasons for remaining on originator and reasons for switching back from biosimilar to originator.
Methods: A retrospective analysis was completed on the cohort of 287 rheumatology patients who were prescribed adalimumab originator prior to the switch to ABP 501. Case notes were analysed to identify whether patients remained on biosimilar 24 weeks after switching from originator.
Results: 99% patients on adalimumab originator (283/287) were switched to ABP 501 within 32 weeks, starting from February 2019. 1% (4/287) remained on originator due to a confirmed latex allergy, as the needle cover of the ABP 501 pre-filled syringe consists of dry natural rubber. 4% (12/283) of patients who switched to biosimilar reverted to originator (1 patient per 2 weeks over 24 weeks). 3% (9/283) of patients who switched to biosimilar were no longer receiving any adalimumab therapy. Reasons for ceasing therapy included recurrent infections (4/9) and progression to the next line of biologics/small molecule therapy (5/9). 93% (262/283) remained stable on ABP 501 (Table). Applications to revert to originator were reviewed by a Biosimilar Steering Group (BSG). The BSG assessment included a review of disease activity, reported symptoms and adverse reactions before and after the switch to biosimilar. Approval to revert to originator occurred in patients who had a clear increase in disease activity or newly reported adverse reactions. If the patient had active disease prior to switch, a change to non-adalimumab therapy would be recommended instead. Of the 12 patients who reverted to originator, 7 (58%) did so due to reduced effectiveness, 3 (25%) due to adverse reactions, and 2 (17%) due to both. Adverse reactions reported within 24 hours of the first injection included nausea, anxiety, insomnia, tinnitus, dizziness, headaches and injection-site reactions. Patients also reported hair loss, fatigue and mouth ulcers. Reported adverse reactions ceased once biosimilar was stopped and/or switching back to originator. All patients who reverted to originator due to reduced effectiveness reported a reduction in disease activity and improvement in symptoms.
Conclusion: The vast majority of patients in our cohort on adalimumab were successfully switched from originator to ABP 501. The adalimumab biosimilar has been generally well-tolerated. 93% remained on biosimilar 24 weeks after switching, 4% have switched back to originator and 3% have either stopped or changed treatment. Reasons for switching back to originator from biosimilar included adverse reactions, most of which occurred within 24 hours, and also worsening of symptoms.

Table. Baseline characteristics and 6-month outcome of patients who have switched from originator to ABP 501

Baseline characteristics/outcome	Total N = 283	RA N = 90 (32%)	SpA N = 108 (38%)	PsA N = 77 (27%)	Other N = 8 (3%)
Mean age (SD)	49.8 (14.6)	58.5 (14.9)	43.6 (11.0)	48.4 (13.2)	46.1 (15.2)
Female, n (%)	126 (45)	67 (74)	29 (38)	26 (34)	4 (50)
Reverted to Originator n (% of patients within subgroup)	12 (4)	4 (4)	6 (6)	1 (1)	1 (13)
Reasons for switching back to Originator					
Inefficacy	7	1	4	1	1
Adverse reactions	3	2	1	0	0
Both	2	1	1	0	0
Switched to another biologic agent n (% of patients within subgroup)	5 (2)	3 (3)	2 (2)	0 (0)	0 (0)
Stopped biologics n (% of patients within subgroup)	4 (1)	1 (1)	1 (1)	2 (3)	0 (0)

Disclosure of Interests: None declared
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AB0327

SERUM IRISIN LEVELS IN HEALTHY WOMEN AND PATIENTS WITH RHEUMATOID ARTHRITIS

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Objectives: to study serum irisin levels in healthy females and patients with rheumatoid arthritis.
Methods: We examined 110 patients with a reliable diagnosis of rheumatoid arthritis (RA). The age of the examined was from 18 to 69 years, all patients were female. The diagnosis of RA was established on the basis of the 2010 EULAR diagnostic criteria. The group of patients included patients with a diagnosis at least one month before the planned screening. As a control group, as well as to create a representation of the normal values irisina level in the blood serum of healthy persons were examined 60 healthy volunteers (all women). In both groups, the level of serum irisin was determined using the enzyme-linked immunosorbent assay by the commercial Irisin ELISA kit.
Results: As a result of measurements in the group of healthy individuals, the average value with the standard deviation used to assess the reliability of the average values was 20.49±4.82 μg/ml (μ±σ). By calculation, a reference interval of 10.85-30.13 μg/ml was determined, defined as μ±2σ. In patients with RA, the level of serum irisin was 14.52±6.99 μg / ml (μ±σ), which is significantly lower than in healthy individuals ($p<0.01$). Then we divided all patients into 2 groups: group 1 with normal values (66 people), group 2 (44 patients) - with a reduced (less than 10.85 μg/ml) level of irisin. In both groups, the dynamics of the level of serum irisin was studied depending on the duration of the disease. Among patients with a disease RA duration of less than 4 years, 16 (24.24%) patients had a normal level of irisin, and 14 (31.82%) had a reduced level (less than 10.85 μg/ml). Among patients with a disease duration of more than 10 years, 36 (54.55%) patients had a normal level of serum irisin, and a low level was determined in 16 (36.36%) patients ($\chi^2=3.568$, $p=0.168$).
Conclusion: According to the data obtained, the normal level of serum irisin in healthy female individuals was 10.85-30.13 μg/ml. In patients with RA, the average level of irisin is significantly lower, however, with an increase in the duration of the disease, it tends to normalize.
Disclosure of Interests: None declared
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15. Rheumatoid arthritis - non biologic treatment and small molecules

AB0328

SIMILAR EFFICACY OF TOFACITINIB THERAPY IN BIOLOGIC NAIVE AND HAD PRIOR BIOLOGIC USE HISTORY PATIENTS WITH RHEUMATOID ARTHRITIS (OREL REGISTER)

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Objectives: To evaluate the efficacy of tofacitinib therapy (TOFA) in biologic naive and had prior biologic use history patients with rheumatoid arthritis (RA) according to OREL register
Methods: Were analyzed the data from Russian national register of patients with RA - OREL treated with TOFA. 138 patients (118 woman, Me;IQR age 55.0 (43.0-63.0) years, disease duration 128.0 (84.0-213.0) months, mean DAS 28 5.5 (4.6-6.2), SDAI 30.5 (21.4-42.9), positive for ACCP (73%)/RF (77%), who were non-responders to MTX at least 15 mg/week and/or other synthetic DMARDs) who received TOFA therapy for more than 1 year were selected for statistical analysis. TOFA used in 26 (18.8%) pts without DMARDs, combination with MTX in 82 (59.4%) pts, leflunomide in 21 (15.2%). Low-dose oral corticosteroids (<10 mg/day prednisone or equivalent) were received by 43 (31.2%) pts. TOFA therapy was started in all pts in dose 5 mg BID per os with dose escalation to 10 mg BID in (86%) pts.
Results: The use of TOFA was accompanied by a decrease in the disease activity and the level of acute phase reactants (CRP and ESR) after 12, 24 and 48 weeks of therapy, $p<0.05$, table 1. Depending on the previous treatment with biological DMARDs, all patients were divided into two groups: had prior biologic use history pts (group 1) (n=51) and biologic naïve pts (group 2) (n=87), table 1.

Table 1. The dynamics of the disease activity during treatment with TOFA

Parameters	Weeks	All patients (n=138)	Had prior biologic use history (group 1) (n=51)	Biologic naive (group 2) (n=87)
DAS28	baseline	5,5 (4,6-6,2)	5,1 (4,5-5,9)	5,7 (4,8-6,5)$
	week 12	4,2 (3,1-4,8)*	3,9 (2,8-4,8)*	4,4 (3,7-4,8)*
	week 24	3,4 (2,7-4,4)*	3,5 (2,4-4,3)*	3,4 (2,8-4,5)*
	week 48	3,3 (2,5-4,4)*	3,2 (2,4-4,2)*	3,4 (2,7-4,4)*
SDAI	baseline	30,5 (21,4-42,9)	28,6 (18,1-36,6)	33,1 (22,6-45,9)
	week 12	14,5 (7,1-23,3)*	13,1 (5,1-19,1)*	16,3 (9,3-25,6)*
	week 24	10,5 (5,1-19,0)*	11,0 (5,5-17,6)*	9,1 (4,7-20,4)*
	week 48	10,3 (4,9-17,7)*	10,2 (3,4-15,8)*	10,9 (6,2-18,1)*
CDAI	baseline	28,2 (20,0-37,1)	25,7 (17,0-33,7)	30,0 (21,5-40,5)
	week 12	14,9 (8,0-22,5)*	13,0 (6,8-18,7)*	16,6 (9,0-24,0)*
	week 24	10,0 (5,0-18,0)*	11,0 (4,7-16,0)*	9,3 (5,0-18,0)*
	week 48	10,1 (5,8-17,0)*	10,4 (4,0-16,0)*	10,0 (6,0-17,0)*
CRP, mg/l	baseline	15,6 (6,5-38,0)	15,6 (6,0-38,1)	15,4 (6,9-36,7)
	week 12	5,5 (1,7-12,1)*	6,4 (2,7-10,4)*	5,2 (1,3-12,8)*
	week 24	4,5 (1,0-10,0)*	5,0 (0,8-9,8)*	4,2 (1,0-10,0)*
	week 48	4,0 (0,7-9,0)*	2,9 (0,6-9,6)*	4,0 (0,8-8,9)*
ESR, mm/h	baseline	32,0 (23,0-48,0)	29,0 (16,0-37,0)	32,0 (23,0-49,0)$
	week 12	21,0 (17,0-33,0)*	20,0 (12,0-33,0)	21,0 (17,0-33,0)*
	week 24	21,0 (12,0-31,0)*	13,0 (9,0-28,0)	21,0 (12,0-31,0)*
	week 48	16,0 (10,0-27,0)*	16,0 (7,0-30,0)*	16,0 (10,0-27,0)*

*p<0.05 from baseline; $p<0.05 between the groups 1 and 2

Patients of the second group had a higher disease activity and ESR before therapy. The use of TOFA was accompanied by a decrease in the disease activity and the level of acute phase reactants (CRP and ESR) in both groups of patients. By week 48 of treatment, no significant difference between the groups according to the disease activity was detected.

In the first and the second group of pts on the 48-th week of therapy remission/low disease activity was achieved on DAS 28 in 51% and 43% (p=0.57), high disease activity on DAS 28 in 12% and 8% (p=0.48).

Conclusion: An analysis of the data from the Russian national register of patients with RA demonstrated similar efficacy of TOFA among patients who received and did not receive previous biological therapy.

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AB0329 PHYSICIANS' PRE-LAUNCH AWARENESS AND CONCERNS WITH PIPELINE JANUS KINASE INHIBITORS (JAKIS) VERSUS TOFACITINIB AND BARICITINIB IN RHEUMATOID ARTHRITIS IN THE UNITED STATES AND EUROPE

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Background: Clinical data regarding use of tofacitinib and baricitinib in rheumatoid arthritis patients have recently posed safety concerns, with regulatory bodies suggesting limiting use of higher dosages. Investigating physicians' awareness and views of each of these products leading up to their launch, as well as the physicians' patient characteristics, may provide evidence of how pipeline JAKis could be received in the treatment landscape once approved.

Objectives: The objective of the study was to investigate awareness and anticipated concerns of upcoming versus already launched JAKis among a sample of treating rheumatologists in the US and EU5 countries, and assess potential correlation between sampled physicians' views on JAKis and their managed patient characteristics.

Methods: A multi-country, multi-center online medical chart review study of patients with RA was conducted across 2011 – 2019 among rheumatologists in hospitals and private practices to collect de-identified data on a sample of patients who were recently treated with a biologic/JAKi in the USA & EU5 (UK, France, Italy, Spain, Germany). Physicians were screened for duration of practice (3-30 years) and patient volume (≥2 RA biologic/JAKi patients per week) and recruited from a large, geographically representative access panel. Patient charts were recorded for the next 5 eligible patients seen during the screening period. Respondents abstracted patient demographics and personal awareness and concerns for drugs in development. Sites waived local ethics review owing to collection of retrospective de-identified data. Data were analyzed using descriptive statistics.

Results: In Q1 19, 56.2% and 56.2% of sampled US physicians were aware of upadacitinib (upa) and filgotinib (filgo), respectively[1]. Prior to US launch, tofacitinib (tofa) and baricitinib (bari) achieved respective awarenesses of 89.9% (Q4 11, n = 109)[2] and 85.2% (Q2 17, n= 101)[3]. Among 262 sampled EU5 rheumatologists, pre-launch awareness in of upa and filgo in Q1 19 was 46.2% and 45.8%[1], while for tofa and bari it was 46.2% and 45.8%, respectively (Q2 16, n= 380)[4]. 'Poor safety profile' was cited as a common anticipated concern for upa and filgo, 9.9% of sampled physicians aware of upa (n=121) and 7.5% of those aware of filgo (n=120)[1], with the respective scores for tofa and bari prior to their launch being 16.9% (n = 296) and 14.5% (n= 227)[4]. Sampled patient characteristics in each physician segment (upa concerned n= 449 patients / non-concerned, n= 155 patients; filgo concerned, n= 454 patients /non-concerned, n= 145 patients) included: (a) age in years 54.6/51, p<0.01; 53.9/51.2, p<0.05 (b) retired employment status 31%/20.6%, p<0.05; 29.5%/20%, p<0.05 [1].

Conclusion: In this sample, upa and filgo achieved lower awareness scores, compared to tofa and bari prior their launch. Sampled EU5 physicians were less concerned with upa and filgo's safety profiles, than for the other two JAKis before launch. Sampled physicians holding concerns with upa/filgo manage significantly older patients and a significantly higher number of retired patients. Further investigation using comparator cohort is warranted.

References:

[1] Ipsos Global Rheumatoid Arthritis Therapy Monitor (Q1 2019, 262 sampled rheumatologists in the EU and 115 sampled rheumatologists in the US reporting on a sample of RA patients seen in their practice; data collected online).

[2] Ipsos Global Rheumatoid Arthritis Therapy Monitor (Q4 2011, 109 sampled rheumatologists in the US reporting on a sample of RA patients seen in their practice; data collected online).

[3] Ipsos Global Rheumatoid Arthritis Therapy Monitor (Q2 2017, 101 sampled rheumatologists in the US reporting on a sample of RA patients seen in their practice; data collected online).

[4] Ipsos Global Rheumatoid Arthritis Therapy Monitor (Q2 2016, 380 sampled rheumatologists in the EU reporting on a sample of RA patients seen in their practice; data collected online).

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AB0330 HIGH REMISSION RATES IN RA – REAL LIFE DATA FROM BARITICINIB

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Background: Recent developments of targeted treatments such as targeted synthetic DMARDs (tsDMARDs) increase the chances of a sustained low disease activity (LDA) or remission state for patients suffering rheumatoid arthritis (RA). tsDMARDs such as baricitinib, an oral inhibitor of the Janus Kinases (JAK1/JAK2) was recently approved for the treatment of RA with an inadequate response to conventional (cDMARD) and biological (bDMARD) therapy. (1, 2).

Objectives: Aim of this study is to analyze the effect of baricitinb on disease activity (DAS28, LDA) in patients with RA in real life, to analyze drug persistance and associate these effects with various baseline characteristics.

Methods: All RA patients were seen in our outpatient clinic. If a patient was switched to a baricitinib due to medical reasons, these patients were included in our prospective, observational study which started in April 2017. Clinical scores (SJC/TJC 76/78), composite scores (DAS28), PROs (HAQ-DI; RAID; FACIT), safety parameters (not reported in this abstract) as well as laboratory biomarkers were collected at each visit every three months. Linear mixed effects models for repeated measurements were used to analyze the time course of disease activity, patient reported outcomes and laboratory results. We estimated the probabilities of continued baricitinib treatment and the probabilities of LDA and remission by DAS-28 as well as Boolean remission up to one year using survival analysis and explored their association with disease characteristics using multivariable Cox regression. All patients gave informed consent. The study is approved by the local ethics.

Results: 95 patients were included and 85 analyzed with available follow-up data until November 2019. Demographics are shown in table 1. Mean follow-up duration after starting baricitinib was 49.3 (28.9) weeks. 51 patients (60%) were on monotherapy. Baricitinib survival (95%CI) was 82% (73% to 91%) at one year. Cumulative number (%probability, 95%CI) of patients that

attained DAS-28 LDA at least once up to one year was 67 (92%, 80% to 97%) and the number of patients attaining DAS-28 and Boolean remission were 31 (50%, 34% to 61%) and 12(20%, 9% to 30%) respectively. Median time to DAS-28 LDA was 16 weeks (Figure 1). Cox regression analyses did not show any sufficiently precise association of remission or LDA with age, gender, seropositivity, disease duration, concomitant DMARD use and number of previous bDMARDs. Increasing number of previous bDMARDs was associated with poor baricitinib survival (HR=1.5, 95%CI 1.1 to 2.2) while this association was not robust to adjustment for baseline disease activity. Favorable changes were observed in tender and swollen joint counts, pain-VAS, patient and physician disease assessment scores, RAID, FACIT and the acute phase response.

Conclusion: In this prospective observational study, we observed high rates of LDA and DAS-28 remission and significant improvements in disease activity and patient reported outcome measurements over time.

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Table 1

Age, yr, mean (SD)		57.8 (12.1)
Sex, n(%)	Male	23 (27.1)
	Female	62 (72.9)
Disease duration, yr, mean (SD)		8.5 (8.2)
RF status,n(%)	Positive	69 (81.2)
ACPA status,n(%)	Positive	66 (77.6)
anti-MCV statu, n(%)	Positive	45 (52.9)
Follow up, weeks, mean (SD)		49.3 (28.9)
Baricitinib use	Monotherapy	51 (60.0)
	Combination	34 (40.0)
TJC (78), mean (SD)		6.6 (6.6)
SJC (76), mean (SD)		4.3 (5.5)
ESR, mm/h, mean (SD)		20.5 (16.4)
CR P, mg/L, mean (SD)		11.7 (12.7)
DAS -28, mean (SD)		4.4 (1.2)
HAQ-DI, mean (SD)		1.2 (0.7)
No. of previous csDMARDs	0	1 (1.2)
	1	27 (31.8)
	2	31 (36.5)
	3	17 (20.0)
	4	8 (9.4)
	6	1 (1.2)
No. of previous bDMARDs	0	28 (32.9)
	1	16 (18.8)
	2	19 (22.4)
	3	8 (9.4)
	4	8 (9.4)
	5	6 (7.1)

Figure 1

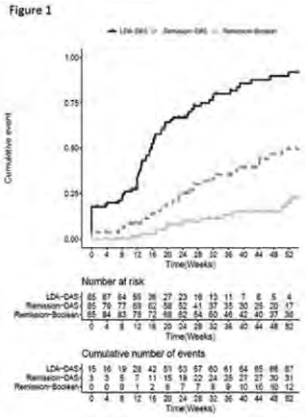


Figure 1. Cumulative probability of low disease activity or remission under treatment with baricitinib.

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AB0331 EFFICACY, RETENTION RATE AND PREDICTORS OF TOFACITINIB EFFICACY AND RETENTION IN RHEUMATOID ARTHRITIS PATIENTS: HUR-BIO REAL-LIFE EXPERIENCE

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Background: Tofacitinib (TOF) is an oral Janus Kinase (JAK) inhibitor and is indicated in the treatment of rheumatoid arthritis (RA). Several interventional or observational studies demonstrated its safety and efficacy, however, its real-life retention rate and related factors need to be elucidated further and its efficacy needs to be approved in real-life.

Objectives: To assess the real-life efficacy, retention rate and related factors of both parameter in rheumatoid arthritis patients under tofacitinib.

Methods: We analyzed all RA patients registered to HURBIO database who received at least 1 dose of tofacitinib (*for drug retention*) and who had at least 1 control visit under tofacitinib (*for efficacy)*. Drug retention rates were calculated using the Kaplan-Meier method and predictors of drug retention were determined by Cox proportional hazard model. Patients were grouped as ''responder" or ''non-responders according" to DAS28 at last control visit: DAS28-CRP≤3.2: ''Responders"; DAS28-CRP>3.2: ''Non-responders". Predictors of response (DAS28-CRP≤3.2 at last visit) were determined by logistic regression analysis. Reasons for switching and discontinuation were also determined.

Results: ***For drug retention;*** a total of 247 (210 (85%) female) patients were recruited. Mean age was 53.1±12.6 years. Mean disease duration was 11.3±8.0 years. Rheumatoid factor and anti-CCP antibodies were positive in 160/240 (66.7%) and 135/207 (65.2%) patients, respectively. Combination with DMARDs was used in 83.3% of patients. 55.5% of patients was biologic-naive. Median follow-up while receiving tofacitinib was 10.2 (IQR:4.0-24.2) months. One-year crude retention rate was 64%. Median duration of drug retention was 24.8 months. Predictors of good tofacitinib retention were (in multivariate analysis): *living in Ankara (where our center is located)* (HR 1.43 (0.96-2.14); 95% CI) and *BMI> 25* (HR 1.46 (0.97-2.29); 95% CI).

For efficacy; a total of 204 (174 (85.4%) female) patients were recruited. Mean age was 53.2±12.5 years. Mean disease duration was 11.5±8.1 years. Rheumatoid factor and anti-CCP antibodies were positive in 135/198 (68.1%) and 115/171 (67.2%) patients, respectively. Detailed demographic and clinical characteristics of participants were given in table 1. Median follow-up while receiving tofacitinib was 11.6 (IQR:5.2-26.2) months. DAS28-CRP levels at baseline and last visit were 4.8 (IQR:3.9-5.4) and 3.3 (IQR:2.5-4.6), respectively (p<0.001). At last visit, 19.6% of patients was in low-disease activity (2.6≤DAS28-CRP≤3.2), 26.0% of patients was in remission (DAS28-CRP<2.6) Predictors of good response to tofacitinib were (in multivariate analysis, adjusted for follow-up duration under tofacitinib): *biologic-navie* (aOR 2.38 (1.30-4.34); 95% CI) and *RF negativity* (aOR 2.12 (1.13-3.95); 95% CI).

The most common cause of drug discontinuation was primary failure (in 36/108 patients, 33.4%).

Conclusion: Tofacitinib seems an effective treatment option for rheumatoid arthritis. Relationship between seronegativity and good response to tofacitinib needs to be elucidated. Also, Clinicians should keep in their mind that in addition to patient characteristics, socioeconomic factors may influence the adherence to the treatment.

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AB0332 IMMUNOSUPPRESSIVE AND IMMONOMODULATING AGENTS IN RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW OF CLINICAL TRIALS AND THEIR CURRENT DEVELOPMENT STAGE

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Background: Rheumatoid arthritis (RA) is the most frequent chronic inflammatory diseases with an incidence of 0.5% to 1%. Therapeutic arsenal of RA has continuously expanded in recent years with the recent therapeutic progress with the arrival of conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs), biological (bDMARDs) and targeted synthetic (tsDMARDs), JAK inhibitors. However, there are still some unmet needs for patients who do not achieve remission and who continue to worsen despite treatments. Of note, only approximately 40% of patients are ACR70 responders, in most randomized controlled trials. For these patients, finding new therapeutic avenues is challenging.

Objectives: The objective of our study was to analyze the whole pipeline of immunosuppressive and immunomodulating drugs evaluated in RA and describe their mechanisms of action and stage of clinical development.

Methods: We conducted a systematic review of all drug therapies in clinical development in RA in 17 databases of international clinical trials. Inclusion criterion: study from one of the databases using the keywords "Rheumatoid arthritis" (search date: June 1, 2019). Exclusion criteria: non-drug trials, trials not related to RA or duplicates. We also excluded dietary regimen or supplementations, cellular therapies, NSAIDs, glucorticoids or their derivatives and non-immunosuppressive or non-immunomodulating drugs. For each csDMARD, bDMARD and tsDMARD, we considered the study at the most advanced stage. For bDMARDs, we did not take into account biosimilars.

Results: The research identified 4652 trials, of which 242 for 243 molecules met the inclusion and exclusion criteria. The developed molecules belong to csDMARDs (n=21), bDMARDs (n=117), tsDMARDs (n=105).

Among the 21 csDMARDs molecules: 8 (38%) has been withdrawn, 4 (19%) are already labelled in RA (hydroxychloroquine, leflunomide, methotrexate and sulfasalazine) and 9 (43%) are in development: 1 (11%) is in phase I/II, 5 (56%) in phase II, 3 (33%) in phase IV.
Among the 117 bDMARDs molecules: 69 (59%) has been withdrawn, 9 (8%) are labeled in RA (abatacept, adalimumab, anakinra, certolizumab, etanercept, golimumab, infliximab, rituximab, sarilumab, tocilizumab) and 39 (33%) are in development: 9 (23%) in phase I, 3 (8%) in phase I/II, 21 (54%) in phase II, 5 (12%) are in phase III, 1 (3%) in phase IV. bDMARDs currently under development target B cells (n=4), T cells (n=2), T/B cells costimulation (n=2),TNF alpha (n=2), Interleukine 1 or his receptor (n=3), Interleukine 6 or his receptor (n=7), Interleukine 17 (n=4), Interleukine 23 (n=1), GM-CSF (n=1), other cytokines or chemokines (n=5), integrins or adhesion proteins (n=3), interferon receptor (n=1) and various other targets (n=4).
Among the 105 tsDMARDs molecules: 64 (61%) has been withdrawn, 6 (6%) JAK inhibitors, have just been or will probably soon be labelled (baricitinib, filgotinib, peficitinib, tofacitinib and upadacitinib), 35 (33%) are in development: 8 (24%) in phase I, 26 (74%) in phase II, 1 (3%) in phase III and. tsDMARDs currently under development target tyrosine kinase (n=12), janus kinase (JAK) (n=3), sphingosine phostate (n=3), PI3K pathway (n=1), phosphodiesterase-4 (n=3) B cells signaling pathways (n=3) and various other targets (n=10).
Conclusion: A total of 242 therapeutic trials involving 243 molecules have been or are being evaluated in RA. This development does not always lead to new treatments since 141 (58%) have already been withdrawn. Hopefully, some of the currently evaluated drugs will contribute to improve the therapeutic management of RA patients, requiring a greater personalization of therapeutic strategies, both in the choice of molecules and their place in therapeutic sequences.
Disclosure of Interests: Julien Blaess: None declared, Julia Walther: None declared, Jacques-Eric Gottenberg Grant/research support from: BMS, Pfizer, Consultant of: BMS, Sanofi-Genzyme, UCB, Speakers bureau: Abbvie, Eli Lilly and Co., Roche, Sanofi-Genzyme, UCB, Jean Sibilia: None declared, Laurent Arnaud: None declared, Renaud FELTEN: None declared
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AB0333 CLINICAL AND ULTRASONOGRAPHIC RESPONSE TO SUBCUTANEOUS METHOTREXATE IN EARLY RHEUMATOID ARTHRITIS. PRELIMINARY RESULTS.

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Background: Metotrexate (MTX) is usually the first line therapy for Rheumatoid Arthritis (RA) because of its favorable efficacy-toxicity ratio. However the exact mechanism and treatment response time in both a clinical and ultrasonographic setting are still uncertain.
Objectives: To describe the clinical and ultrasound response to MTX during the first 6 months of treatment in early RA patients who started subcutaneous methotrexate as the first disease-modifying drug (DMARD).
Methods: Ongoing prospective cohort of patients with early RA (ACR-EULAR 2010 criteria), over 18 years and starting MTX-SC. Patients had a clinical and ultrasonographic evaluation at baseline, 1, 3 and 6 months. We collected demographic data, C-reactive protein [CRP], erythrocyte sedimentation rate [ESR], rheumatoid factor [FR], anti-citrullinated protein antibody [ACPA]), inflammatory activity indexes (DAS28esr and DAS28crp) and EULAR's response to treatment (delta value of -1.2 in DAS28 scores). Joints explored with ultrasound were elbows and wrists (radio-carpal and inter-carpal joint) counted as a single joint, 1st-5th metacarpophalangeal (MCF), proximal interphalangeal (IFP), knees, tibio-talar and subtalar joints and 2nd-5th metatarsophalangeal (MTF) joints. Bone erosions were evaluated in 2nd and 5th MCF, styloid, distal ulna and 5th MTF. Synovitis was graduated semi-quantitatively from 0 to 3 (OMERACT) and calculated on B mode and Doppler.
Results: 35 patients were included (mean age 61.2 years, 65.7% women) with a median of 0.8 (+/-8) months delay to diagnosis. 34 patients (97.1%) started 15mg MTX-SC/weekly. A higher DAS28esr was found in baseline data for the group that had a response by month 1 (DAS28esr baseline 5.5 vs 4.2 p=0.01), no other significant differences were found. During the first month, a significant response was achieved in 13 (41%) patients and remission in 11 (35%) (Table 1). 17 patients have 6th month data. 11 (64.7%) have achieved EULAR response compared to baseline(P=0.0005) out of which 7 (54.5%) had already reached it by month 1. A difference in MTX dose (month1 14.8 vs month6 17.1 p=0.003) was found between month 1 and 6, with no differences in disease activity. In the ultrasonographic baseline data; 8 patients (22.9%) had erosions, with a mean of 2,75 erosions/patient (22 of the 280 locations). During the follow up the global rating lowered, with no differences in B mode but significant differences in Doppler at the 6 month mark (Table 2). As of this report, 10 patients (28.5%) had stopped MTX treatment due to lack on response or adverse effects and 8 (22.9%) are waiting 6th month evaluation.

Table 1. Baseline vs month 1

	Baseline	Month 1	P Value
EULAR response	0	13 (41)	**0.00005**
MTX Dose mg (SD)	14.8 (+/-0.8)	14.8 (+/-1.6)	1
Prednisone Dose mg(SD)	5.9 (+/-6.5)	2.9 (+/-3)	**0.02**
DAS28crp (SD)	4.3 (+/-1.5)	3,4 (+/-1.4)	**0.02**
DAS28esr (SD)	(4.8 (+/-1.5)	3.7 (+/-1.4)	**0.006**
Remission (DAS28<1.2)	3(9.6)	11(35.5)	**0.04**

Table 2. Ultrasound synovitis global rating.

	Baseline N=35	1 month N=31	3 months N=25	6 months N=17
B Mode: Median (interquartile range)	8 (3.5-12)	8 (3-12.5)	6 (4-11)	5 (2-11) p 0,16
Doppler Mode: Median (interquartile range)	2 (0.5-6)	2 (0-6)	2 (0-6)	0 (0-2) **p 0,005**

Conclusion: In this cohort half of the patients that responded to treatment had achieved this by month 1. A higher baseline inflammatory profile was related to the response. Little difference is found between month 1 and 6 on clinical data, however ultrasonographic results suggest that at least 6 months are needed for Doppler improvement. Perhaps MTX has a faster effect over joint pain and lowers DAS28 scores requiring longer to completely suppress inflammatory activity.
References:
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Disclosure of Interests: Liz R. Caballero Motta: None declared, Ana Melissa Anzola Alfaro: None declared, Luis A Torrens Cid: None declared, Christian Y Soleto: None declared, Belén Serrano Benavente: None declared, Iustina Janta: None declared, Juan Molina Collada: None declared, Carlos Gonzalez Consultant of: Gilead, Janssen, Novartis,, Speakers bureau: Abbvie, Celgene, Gilead, Janssen, Novartis, Pfizer, Roche, Indalecio Monteagudo: None declared, Jose Maria Alvaro Gracia: None declared, Juan Carlos Nieto Speakers bureau: Pfizer, Abbvie, MSD, Novartis, Janssen, Lilly, Nordic Pharma, BMS, Gebro, FAES Farma, Roche, Sanofi
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AB0334 COST-EFECTIVENESS OF JAK INHIBITORS IN RHEUMATOID ARTHRITIS IN THE REAL WORL PRACTICE

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Background: The Janus Kinase (JAK) inhibitors Baricitinib (BAR) and Tofacitinib (TOF), both in monotherapy or in combination with methotrexate, are indicated for moderate to severe active rheumatoid arthritis (RA) with inadequate response to conventional synthetic disease modifying anti-rheumatic drugs (csDMARD). Data about cost-effectiveness in a real-world setting are still scarce.
Objectives: To assess the cost-effectiveness (C-E) of BAR and TOF in patients with RA in usual clinical practice.
Methods: Retrospective observational study of adult RA patients who started BAR and TOF between September 2017 and December 2019, in a university hospital. Data were collected from the electronic medical records and the Dominion® External Patient Dispensing program. Demographic, clinical and laboratory parameters [erytrocyte sedimentation rate (ESR), C reactive protein (CRP), Rheumatoid factor (RF), anti-citrullinated peptide antibodies (ACPA)], concomitant csDMARD, previous biological (b) DMARD, DAS28-ESR activity score items, and treatment duration were registered. DAS28-ESR remission or low disease activity (LDA) were used as the effectiveness measure to estimate C-E. The official Spanish prices were considered to calculate the costs of the treatments. Statistical analysis was performed with SPSS v.15 program. Descriptive statistics are shown in proportions, medians and interquartile ranges (IQR).

The Wilcoxon signed ranges test was applied for the changes from baseline of DAS28-ESR and CRP.

Results: 39 patients were included, 87.2% women, median age 62.9 (49.9-74.4) years. 9/39 patients (23.1%) were *naive* to bDMARD, 6 (15.4%) had received 1, 18 (46.1%) 2, and 6 (15.4 %) ≥3 previous bDMARD. Demographic, clinical and effectiveness characteristics are shown by drug in the Table:

	Baricitinib (n=30)	Tofacitinib (n=9)	p value
Sex (women, n, %)	26 (86,7)	8 (88,9)	0,676
Age [med (IQR)]	63,3 (49,7-74,8)	59,7 (49,8-68,6)	0,857
Rheumatoid Factor + (n, %)	23 (76,7)	9 (100)	0,132
ACPA + (n, %)	21 (70,0)	7 (77,8)	0,501
Erosive disease (n, %)	16 (53,3)	6 (66,7)	0,377
Concomitant csDMARD (n, %)	26 (86,7)	8 (88,9)	0,676
bDMARD-*naive* (n, %)	7 (23,3)	2 (22,2)	0,419
Treatment duration (months) [med (IQR)]	8,4 (6,5-20,3)	13,2 (3,9-20,7)	0,909
Baseline CRP (mg/dl) [med (IQR)]	2,2 (0,3-1,0)	1,4 (0,3-1,0)	0,806
Final CRP (mg/dl) [med (IQR)]	0,9 (0,1-0,3)	1,0 (0,1-0,4)	-
Baseline DAS28-ESR [med (IQR)]	5,5 (3,6-4,3)	6,1 (3,8-5,3)	0,315
Final DAS28-ESR [med (IQR)]	3,9 (2,2-2,8)	5,5 (2,6-3,6)	-
DAS28-ESR Remission (n, %)	10 (33,3)	3 (33,3)	0,663
DAS28-ESR LDA (n, %)	8 (26,7)	1 (11,1)	0,316

Regarding BAR, 17 patients (56.6%) continue on treatment and 3 (10%) changed to TOF. The change in DAS28VSG was statistically significant (p = 0.000), as well as difference in CRP (p = 0.008). The total cost per analysed period was € 357,806.40, with 18/30 patients (60%) achieving remission or LDA. The C-E was € 19,878.13. As for TOF, 6 patients (66.6%) remain on drug, with no switch to BAR. Neither the difference from baseline in DAS28VSG nor the CRP changes reached statistical significance (p = 0.08 and p = 0.735, respectively). The total cost per analysed period was € 90,201.72, with 4/9 patients (44.4%) achieving remission or LDA. The C-E was € 22,573.0

Conclusion: In our daily practice, JAK inhibitors are mainly used in combination with csDMARD and commonly after failure to ≥ 1 bDMARD. In this real setting, BAR proves to be cost-effective, while TOF renders less effectiveness. However, results should be addressed with caution because of the smaller sample size of TOF population. Additional studies with greater follow-up and sample size are needed to confirm these findings.

Disclosure of Interests: Alberto Calvo Garcia: None declared, Noelia García Castañeda: None declared, Cristina Valero: None declared, Irene Llorente Speakers bureau: Lilly, Janssen, Novartis, Sanofi, Gebro, Blanca Varas: None declared, Alberto García-Vadillo: None declared, Isidoro González-Álvaro Grant/research support from: Roche Laboratories, Consultant of: Lilly, Sanofi, Paid instructor for: Lilly, Speakers bureau: Abbvie, MSD, Roche, Lilly, Alberto Morell: None declared, Esther Ramirez: None declared, Rosario Garcia de Vicuna Grant/research support from: BMS, Lilly, MSD, Novartis, Roche, Consultant of: Abbvie, Biogen, BMS, Celltrion, Gebro, Lilly, Mylan, Pfizer, Sandoz, Sanofi, Paid instructor for: Lilly, Speakers bureau: BMS, Lilly, Pfizer, Sandoz, Sanofi

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AB0335 PATIENTS IN REMISSION FREE OF DIRECTED BIOLOGICAL / SYNTHETIC DRUG. ANALYSIS OF A COHORT OF PATIENTS TREATED BY OBJECTIVES IN OPTIMIZATION FOR 6 YEARS

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Background: The goal of treatment with biological DMARDs (bDMARDs) should be the use for a limited period of time, during the called "therapeutic window of opportunity" to induce disease remission, followed by the maintenance of low activity with conventional DMARDs. We study if we achieve this goal in a cohort of patients treated by objectives in the last 6 years.

Objectives: To assess the frequency and characteristics of patients with rheumatoid arthritis (RA), spondyloarthropathies (SA) and psoriatic arthritis (PsA)) treated with FB / SD who achieve remission without FB / SD.

Methods: Observational and prospective study, which included a cohort of patients with RA, SA and PsA treated by objectives with FB / SD and optimized from January 2014 to December 2019. Optimization, defined as the reduction or prolongation of the interval of at least one dose, it was indicated when patients had received> 6 months of treatment and were in clinical remission / low activity defined as DAS28 <3.2 for RA and PsA, and BASDAI <4 for SpA. All patients who managed to maintain remission without receiving FB / SD were also collected.

Results: A total of 260 patients (115 RA, 69 SA and 76 PsA) were included in the study. Of the total of these patients, 32.7% received at least two treatments ("switch"). Of all the patients, 53% were optimized and according to the diagnosis: 60.9% had RA, 52.2% SA and 39.4% PsA.

5.3% of the patients were free of FB / SD: 5 patients with RA (4.34%), 8 patients with SA (11.6%) and 1 patient with PsA (1.3%). Among patients who entered clinical remission without FB / SD, 57% had received only one treatment with FB / SD while 43% of the patients had received two or more FB / SD. Only 3 of the patients with RA and 1 patient with PsA managed to be free of treatment without FB / SD or conventional DMARD.

Conclusion: Remission without FB / SD treatment was rare, being higher in SA than in RA and in PsA, maintaining the same severity and frequency patterns in achieving optimization according to different pathologies (EspA> AR> APs). Except in the APs, more than 50% of the patients with RA and SA entered into optimization. Clinical remission without FB / SD was less frequent in the PsA probably because the MDA is more demanding than the other outcome measures and because it is a more complex and heterogeneous disease with domains controlled by various cytokines. Patients with disease-free RA or APs without FB / SD or conventional DMARD were the exception.

Disclosure of Interests: None declared

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AB0336 IMPACT OF SUBJECTIVE INTOLERANCE TO METHOTREXATE ON THE QUALITY OF LIFE OF PATIENTS WITH RHEUMATOID ARTHRITIS: SIDE EFFECTS AND AVOIDANCE COPING STRATEGIES THROUGH SELF-ADMINISTRATION IN THE EVENING OR DURING THE WEEKEND

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Background: Methotrexate (MTX) represents the *anchor drug* for the treatment of rheumatoid arthritis (RA), as well as other rheumatological diseases such as psoriatic arthritis (PsA) and spondyloarthritides (SpA). Despite consolidated clinical efficacy, the use of MTX suffers from relevant limitations. Common issues include subjective intolerance, nausea, malaise, and fatigue, which negatively impact on quality of life and work/social participation.

Objectives: In this study, we evaluated the frequency with which patients on MTX therapy opt for self-administration over the weekend or in the evening hours, in order to minimize interference with daily activities, work productivity, and social participation.

Methods: A cross-sectional, prospective study was performed in two tertiary referral Rheumatology clinics, which included consecutive patients with RA, PsA, or SpA on MTX therapy. Enrolled patients had not previously received instructions by their healthcare provider as to when during the week or day MTX ought to be administered, and were free to choose or change the weekday and time for self-administration. Data on the route and timing of MTX self-administration was collected using dedicated questionnaires, which included queries on the dose and route of administration, day of the week and time of self-administration, reasons for the patient's choice, use of folic acid supplementation, and concomitant therapies. Statistical analyses were conducted using a chi-square test; a p-value <0.05 was considered significant.

Results: A total of 275 consecutive patients treated with MTX were included, mostly with RA (86%). Patients had an average age of 59.8 years (SD 14.0) and an average disease duration of 134.5 months (SD 127.3). The average MTX dose was 15 mg/wk (SD 4.4); MTX was administered subcutaneously in 68.2% of cases, orally in 17.8%, and intramuscularly in 5%. Regarding the timing of MTX self-administration, 157 patients (57.1%) took MTX in the evening and 119 patients (44.3%) took it during the weekend; even among patients taking MTX in the evening, weekend administration was preferred (93/157, 59.2%, p <0.001). The most frequent reasons leading to MTX self-administration during the evening or weekend were gastrointestinal side effects/nausea (85% of cases), fatigue (63%), interference with work activities (36%) and interference with social activities (29%). Patients who opted for MTX self-administration in the evening or over the weekend were significantly younger (p <0.001), with no significant gender differences or disease duration.

Conclusion: The majority of patients with inflammatory arthritis opt for self-administration of MTX in the evening (absolute majority) or during the weekend (relative majority). This choice is dictated by the need to avoid side effects and detrimental repercussions on the individual's social or working life. The adoption of these strategies for minimizing the adverse effects of MTX is more frequent among younger patients, and provides an

indirect, yet powerful indicator of the impact of MTX therapy on patients' quality of life.

Disclosure of Interests: Giulio Cavalli Consultant of: SOBI, Pfizer, Sanofi, Novartis, Paid instructor for: SOBI, Novartis, Speakers bureau: SOBI, Novartis, Martina Biggioggero: None declared, adriana cariddi: None declared, Giacomo De Luca Speakers bureau: SOBI, Novartis, Celgene, Pfizer, MSD, Elena Agape: None declared, nicola boffini: None declared, Elena Baldissera Speakers bureau: Novartis, Pfizer, Roche, Alpha Sigma, Sanofi, Lorenzo Dagna: None declared, Ennio Giulio Favalli Consultant of: Consultant and/or speaker for BMS, Eli-Lilly, MSD, UCB, Pfizer, Sanofi-Genzyme, Novartis, and Abbvie, Speakers bureau: Consultant and/or speaker for BMS, Eli-Lilly, MSD, UCB, Pfizer, Sanofi-Genzyme, Novartis, and Abbvie

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AB0337 TOFACITINIB MONOTHERAPY OR COMBINED WITH METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS SHOW SIMILAR RETENTION OVER FOUR YEARS. REPORT FROM RHUMADATA ®

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Background: Since the introduction of biologic agents around the turn of the century, the scientific evidence shows that the majority of agents, independent of the therapeutic target, have a better outcome when used in combination with methotrexate (MTX). In 2014, tofacitinib (TOFA), an agent targeting Janus kinase 1 and 3, has reached the Canadian market with data showing that the combination with MTX may not be necessary [1,2].

Objectives: To evaluate the efficacy and retention rate of TOFA in real-world patients with rheumatoid arthritis (RA).

Methods: Two cohorts of patients prescribed TOFA was created. The first cohort was formed of patients who were receiving MTX concomitantly with TOFA (COMBO) and the other of patients using TOFA in monotherapy (MONO). MONO patients either never use MTX or were prescribed MTX post-TOFA initiation for at most 20% of the time they were on TOFA. COMBO patients received MTX at the time of TOFA initiation or were prescribed MTX post-TOFA initiation for at least 80% of the time. For all those patients, baseline demographic data definitions. Disease activity score and HAQ-DI were compared from the initiation of TOFA to the last visit. Time to medication discontinuation was extracted, and survival was estimated using Kaplan-Meier calculation for MONO and COMBO cohorts.

Results: Overall, 194 patients were selected. Most were women (83%) on average younger than the men (men: 62.6 ± 11.0 years vs. women: 56.9 ± 12.1 years, p-value=0.0130). The patient's assessments of global disease activity, pain and fatigue were respectively 5.0 ± 2.7, 5.2 ± 2.9, 5.1 ± 3.1 in the COMBO group and 6.2 ± 2.5, 6.5 ± 2.6, 6.3 ± 2.8 in the MONO group all differences being significant across groups. HAQ-DI at treatment initiation was 1.3 ± 0.7 and 1.5 ± 0.7 in the COMBO and MONO groups, respectively, p-value=0.0858. Similarly, the SDAI score at treatment initiation was 23.9 ± 9.4 and 25.2 ± 11.5, p-value=0.5546. Average changes in SDAI were -13.4 ± 15.5 (COMBO) and -8.9 ± 13.5 (MONO), p-value=0.1515, and changes in HAQ -0.21 ± 0.63 and -0.26 ± 0.74, p-value 0.6112. At treatment initiation, DAS28(4)ESR were 4.4 ± 1.4 (COMBO) and 4.6 ± 1.3 (MONO), p-value 0.5815, with respective average changes of -1.06 ± 2.07 and -0.70 ± 1.96, p-value=0.2852. The Kaplan-Meier analysis demonstrated that the COMBO and MONO retention curves were not statistically different (log-rank p-value=0.9318).

Conclusion: Sustainability of TOFA in MONO or COMBO are not statistically different as are the changes in DAS28(4)ESR and SDAI. Despite this result, some patients may still benefit from combination with MTX.

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UCB, Paid instructor for: Abbvie, Speakers bureau: AbbVie, BMS, Pfizer, Roche, Louis Coupal: None declared

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AB0338 EVALUATION OF THE ASSOCIATION OF ALLELES OF INTOLERANCE RISK TO METOTREXATE IN RHEUMATOID ARTHRITIS PATIENTS UNDER TREATMENT WITH BIOLOGIC THERAPIES

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Background: Metotrexate (MTX) is the first-line treatment for rheumatoid arthritis (RA) both in monotherapy and in combination with biologic disease-modifying antirheumatic drugs (bDMARDs), it usually well tolerated but AEs may appear that causing toxicity that requires suspension of the treatment

Objectives: Determine the prevalence of certain polymorphisms among patients that receive bDMARD in monotherapy or in combination with MTX to confirm its relevance as biomarkers of intolerance. Evaluate the influence of certain polymorphisms in the effectiveness of monotherapy or combined treatment in patients, through *"Disease Activity Score 28"* (DAS28), SDAI Simple disease activity index (SDAI), Clinical disease activity index (CDAI) and each one of its components

Methods: Retrospective observational multicentric study (University Hospital Complex, Granada, Carlos de Haya Hospital, Malaga and University Hospital Reina Sofia, Cordoba), of cases-control of 227 patients with RA (criteria ACR/EULAR), of which 120 received MTX and bDMARD combined therapy (cases) and other with only bDMARD (controls). All of them had been or were currently treated with MTX, remained with stable doses of bDMARD, and had a DNA sample stored before the inclusion in the study

DNA was isolated from total peripheral blood and by fluorescent probe HybProbe and/ or Taqman, 10 polymorphisms of 10 protein coding genes were determined involved in the metabolism and toxicity of MTX according to current evidence

Besides the type of polymorphism, data on the activity of the disease were analysed (DAS28VSG, DAS28PCR, SDAI, CDAI, at the start of the MTX income, of the BT, and in the inclusion visit

A descriptive and comparative study was carried out on all that and afterwards an assessment was made through a multiple logistic regression analysis (MLR) on the risk of intolerance to MTX

Results: An analysis was carried out on 227 patients (120 cases and 107 controls) with an average age of 60 (12,1) being women 78,4%, with a time of evolution since diagnosis of 14,84 (7,78) years

48,9% registered adverse events (AE) MTX related, mainly gastrointestinal, hepatobiliary and skin-subcutaneous tissue. The percentage of AE appearance was superior in the monotherapy group than in the group with combined therapy

The most prevalent polymorphism (84,6% (IC95%: 84,09%-85,11%) and in cases (86,0% (IC95%: 79,43%-92,57%) was **homozygous CC (ITPase-c94a)**; in controls **homozygous GG (GGH-T401C)** (87,5% (IC95%:81,58%-93,42%)

There were no significant differences in the parameters of activity between groups, in both, patients were best basally controlled than at the start of the MTX income and/or bDMARD

Being **homozygous-AA for the DHFR gene** was significantly associated ($p<0.05$) with the appearance of AE (none of the 4 homozygous AA patients for that gene had AE)

In MLR, **homozygous GG** (ref. heterozygous AG) in polymorphism **GGH-T401C,** being **homozygous CC** (ref. heterozygous TC) in polymorphism **ABCC2-C24T** and **PCR (mg/dL) at the start of bDMARD** resulted independent predictive factors of MTX intolerance

Conclusion: Polymorphisms T401C for the GGH gene and C24T for the ABCC2 gene and PCR at the start of the bDMARD resulted independent predictive factors of MTX intolerance

. Polymorphism **homozygous AA** for **DHFR gene** was related to significant protection against appearance of AE

Disclosure of Interests: Alejandro Escudero Contreras: None declared, Rafaela Ortega Castro: None declared, Jerusalem Calvo Gutierrez: None declared, Natalia Mena-Vázquez: None declared, Rafael Cáliz Cáliz: None declared, Eduardo Collantes Estevez Grant/research support from: ROCHE and Pfizer, Speakers bureau: ROCHE, Lilly, Bristol and Celgene, Antonio Fernandez-Nebro: None declared, Maria del Carmen Abalos-Aguilera: None declared, Chary Lopez-Pedrera Grant/research support from: ROCHE and Pfizer., Mª Teresa Ruiz Jimenez Employee of: Roche Farma, SPAIN, Font Ugalde Pilar: None declared

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AB0339 THE IMPORTANCE OF THERAPEUTIC COMPLIANCE: ADHERENCE TO METHOTREXATE AND ITS ROLE IN IMMUNOGENICITY

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Background: Immunogenicity against adalimumab leads to loss of response and secondary failure to biologic therapy; however, concomitant use of methotrexate (MTX) seems to reduce the development of anti-drug antibodies (ADAbs) in a dose-dependent manner. Suboptimal adherence to MTX may favour ADAbs appearance.

Objectives: To evaluate the relationship between MTX adherence and ADAbs development.

Methods: Observational study among adult patients with chronic inflammatory arthropathy, followed in a tertiary care centre, who were in treatment with MTX and adalimumab. ADAbs formation in relation to MTX adherence was assessed.

Results: 33 patients were included, with a MTX adherence overall mean of 82.13 (12.45%-100%, median adherence 92.19%). Only 9.09% (n=3) of the patients developed ADAbs, being its MTX adherence mean of 60.95% (46.47%-70%, median adherence 66.39%); ADAbs negative group showed an average MTX adherence of 84.23% (12.45%-100%, median adherence 94.29%). A statistically significant result ($p<0.05$) between groups was found.

	n	Adherence mean	
ADAbs (+)	3 (9.09%)	60.95%	p<0.05
ADAbs (-)	30 (90.91%)	84.23%	
Total	33 (100%)	82.13%	

No statistically significant differences ($p>0.05$) involving MTX adherence and its dose were found.

Conclusion: While the sample is small, this study suggests that ADAbs development may be influenced by MTX adherence, thereby promoting adequate MTX adherence should be a priority in the daily practice of every rheumatologist.

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Disclosure of Interests: Paula García: None declared, Marta González Fernández: None declared, Mayra Nathali Rivas: None declared, Javier Duruelo: None declared, Elena Garmendia: None declared, Javier Arostegui Lavilla: None declared, Fernando Perez-Ruiz Consultant of: Amgen

Lilly, Speakers bureau: Amgen, Alberto Alonso: None declared, Consuelo Modesto: None declared, Boris Anthony Blanco Cáceres: None declared

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AB0340 EFFECT OF BARICITINIB ON RANKL SERUM CONCENTRATION IN RHEUMATOID ARTHRITIS PATIENTS

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Background: RANKL (receptor activator of nuclear factor κB ligand) and osteoprotegerin, the main regulators of bone metabolism, are involved in osteoblasts/osteoclasts balance in inflammatory disease, such as Rheumatoid Arthritis (RA). Janus kinase (JAK) inhibitors (baricitinib and tofacitinib) can reduce the progression of structural damage in patients with moderate to severe RA. Previous studies suggest a link between JAK inhibition, production of RANKL and osteoclastogenesis[1,2].

Objectives: to investigate the effect of baricitinib on RANKL serum concentration in unselected RA patients.

Methods: Patients affected by RA according to 2010 ACR criteria, starting treatment with baricitinib as clinically indicated, were consecutively enrolled. Demographic, clinical and laboratory data were collected at baseline (T0) and after three months of therapy (T3). RANKL serum concentration was analyzed by ELISA at the same timepoints. All patients underwent ultrasound (US) examination at T0 and T3. According with OMERACT definitions, the presence of synovial effusion, hypertrophy and power Doppler were assessed and scored on a semi-quantitative scale (0=absent, 1=mild, 2=moderate, 3=severe), obtaining a total US score (0-198), representing the joint inflammatory status (15); erosions were registered. Data were expressed as median (interquartile range); Mann-Whitney and Spearman tests were performed for comparisons and p values < 0.05 were considered statistically significant.

Results: We prospectively followed up 33 RA patients starting treatment with baricitinib [M/F 8/25; age 58(9) years; disease duration 165(150) months; 22/33 (67%) ACPA-anti-citrullinated protein antibody positive; 24/33 patients (73%) RF-rheumatoid factor positive]. After three months of therapy we observed a significant reduction of $DAS28_{CRP}$, CDAI and SDAI compared to baseline ($p<0.0001$). The US inflammatory score showed a significant improvement at T3 ($p<0.0001$). The serum concentration of RANKL showed a significant decrease after three months of therapy from 44 (25.9) to 27.5 (35.3) pg/ml, $p=0.0256$ (Figure 1). While in 67% of patients RANKL decreased after treatment, in 33% of patients no decrease or an increase of RANKL was detected. Those patients showing an increase of RANKL had similar $DAS28_{CRP}$, CDAI, SDAI, but had significantly less swollen joints, compared to those in which RANKL decreased ($p=0.0364$). At baseline, the concentration of RANKL significantly correlated with the swollen joint count ($p=0.0117$) and ESR ($p=0.0482$), but not with $DAS28_{CRP}$, CDAI, SDAI nor with the US inflammatory score. Nevertheless, the reduction of RANKL was not significantly associated with the achievement of low disease/remission after three months of treatment, with ACPA/RF positivity or the presence of erosions detected by US.

Conclusion: This is the first study demonstrating that baricitinib reduces *in vivo* the serum levels of RANKL, regardless the correlation with disease activity indices. The discrepancy between the levels of RANKL and the clinical response is in line with previous data in the literature, demonstrating that, under treatment with anti-TNF and anti-IL1, the decrease of RANKL did not

influence the local or systemic inflammatory parameters, even if still preventing bone loss[3].

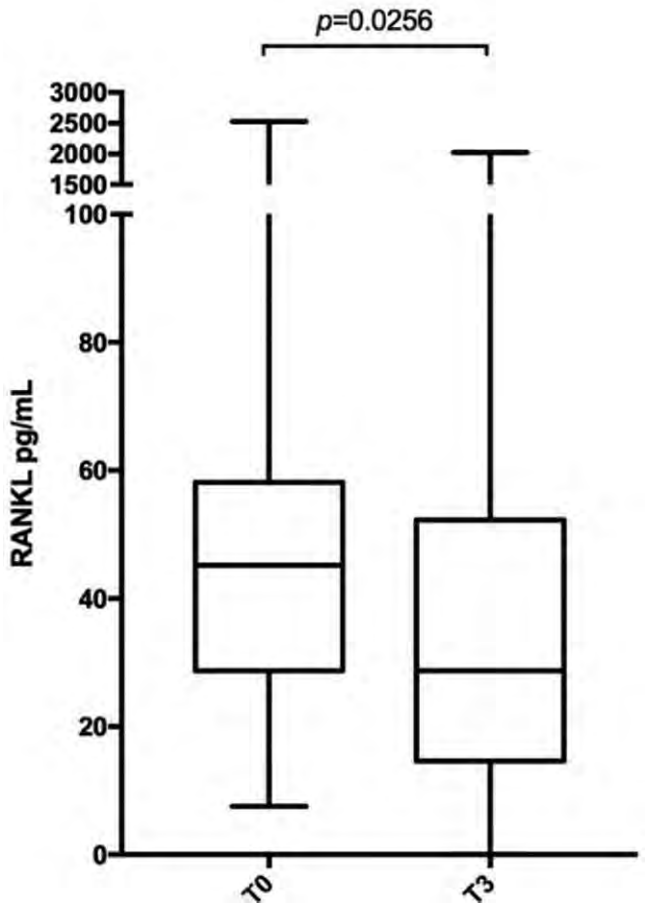
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Figure 1. RANKL levels at T0 and T3



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AB0341

SURVIVAL OF REMISSION OR LOW DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH TOFACITINIB. RESULTS OF RUSSIAN NATIONAL REGISTER

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Background: Tofacitinib is an oral Janus Kinase inhibitor for the treatment of rheumatoid arthritis (RA). The survival of remission or low disease activity (LDA) in RA patients, treated with tofacitinib remain unknown.

Objectives: To evaluate the survival of DAS28 remission or low disease activity in RA patients treated with tofacitinib.

Methods: Data from 102 patients from Russian national register of patients with RA treated with tofacitinib (OREL), achieved DAS28 remission (DAS28<2.6, n=92) or LDA (DAS28<3.2, n=102) were analyzed. Number of patients with increased disease activity, time of disease activation were registered. Statistical analysis performed with statistical programs SPSS2017 and GraphPadPrizm. p-value < 0.05 considered as significant.

Results: Baseline characteristics of the patients are presented in table 1.

Table 1. Baseline characteristics of the patients with RA (n=102).

Parameter	LDA (n=102)	Remission (n=92)
Male, n (%)	19 (18.6)	15 (16.3)
Age, years (mean ±SD)	53.55±13.46	52.45±12.56
Symptoms duration, month (mean±SD)	170±111.92	169±110.93
Positive rheumatoid factor, n (%)	41(40.19)	36 (39.13)
Erosions of hand joints (X-rays), n (%)	43(42.15)	41 (44.56)
BMI, kg/m^2(mean ±SD)	25.67 ± 2.22	26.87 ± 2.19
Smokers (current and in the past), n (%)	9 (8.82)	9 (9.78)

p-value ≥ 0.05 for all the differences.

The remission failed in 45 from 92 patients (48.91%), LDA failed in 65 from 102 of patients (63.72%), table 2.

Table 2. Median for the time of survival of remission or LDA in RA patients treated with tofacitinib.

	Time, month			
	Me	Standard error	95% Confidential Interval	
			from	To
LDA (n=102)	12.000	2.021	8.039	15.961
Remission (n=92)	10.312	6.000	0.796	4.440

Proportions of survival of remission or LDA are presented at figure 1 and figure 2 respectively.

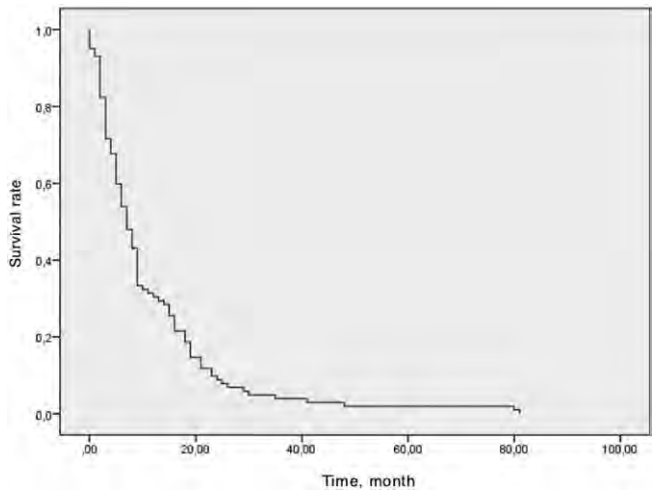


Figure 1. Survival proportion in RA patients achieved LDA on tofacitinib (n=102).

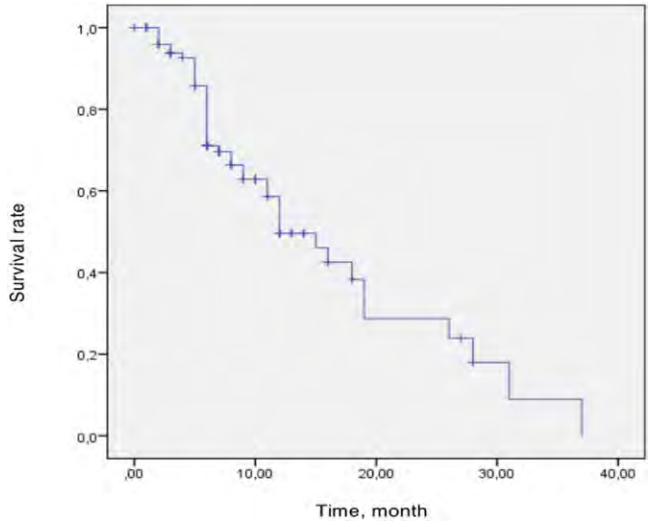


Figure 2. Survival proportion in RA patients achieved remission on tofacitinib (n=92).

In 28 from 45 cases of remission failure (62.22%) and in 34 cases from 65 cases of LDA loss (52.3%) the proposal reasons of treatment effect loss were non-medical (absence of reimbursement, changes in patients accommodation, low treatment compliance, etc.). Medical reasons (side effects, inefficacy, etc.) of decrease in remission or LDA survival rate were registered in 17 from 45 cases of remission loss (37.77%) and in 31 from 65 cases of LDA loss (47.69%).

Conclusion: On-year survival of remission or low disease activity achieved in Rheumatoid arthritis patients treated with tofacitinib is 51.1% and 36.3 % respectively. The main reasons of treatment efficacy loss were associated with non-medical.

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AB0342

EFFICACY AND SAFETY OF TOFACITINIB MONOTHERAPY AND WITH METHOTREXATE COMBINATION. DATA FROM NATIONAL RHEUMATOID ARTHRITIS REGISTER

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Background: Currently it is unclear whether combination of tofacitinib (tofa) with methotrexate (Mtx) more effective and safe than tofa in monotherapy.

Objectives: To compare efficacy and safety of tofacitinib monotherapy with combination of tofa and mtx in RA patients.

Methods: Data from 450 patients from Russian national RA register OREL were included in the statistical analysis. Data from the 1st, 6, 12, 24 and 36 month after baseline were analyzed. Demographical and disease-related characteristics of RA (symptoms duration, DAS28, CDAI, SDAI, number of tender and swollen joints (NTJ, NSJ), erythrocytes sedimentation rate (ESR), C-reactive protein (CRP)) were collected. Statistical analysis performed with SPSS2017.

Results: Baseline characteristics of RA patients involved in the analysis are presented in table 1. Mean dosage of mtx was 15.5±5.5 mg/week.

Table 1. Baseline characteristics of the patients with RA (n=450), mean±SD/n(%)

Parameter	Tofa monotherapy, n=169	Tofa +Mtx, n=281
Male	34 (20%)	51 (18.14)
Age, years	53.0±13.3	49.8±12.8
Symptoms duration, month	149.7±110.1	120.0±96.5
Positive rheumatoid factor (RF)	126 (75)	210 (74.3)
Positive antibodies to cyclic citrullinated peptide (ACCP)	129 (79)	233 (83)

p≥0.05 for all the differences.

Treatment results are presented in table 2.

Table 2. Treatment results in RA patients, received monotherapy of tofacitinib and tofacitinib with mtx, Mean±SD / n (%).

Parameter	1 month*	6 month*	12 month*	24 month*	36 month*
n mono	123 (72.78)	111 (65.68)	90 (53.25)	48 (28.40)	20 (11.83)
n combo	205 (72.95)	222 (79)	150 (53.38)	69 (24.55)	37 (13.16)
CDAI mono	30.14±12.45	14.49±10.76	13.08±8.91	13.54±5.53	11.84±7.89
CDAI combo	28.27±13.12	16.46±10.58	12.78±9.51	9.71±10.62	10.61±10.05
DAS28 mono	5.35±1.16	3.97±1.30	3.50±1.1	3.26±1.00	3.10±0.89
DAS28 combo	5.54±1.26	3.87±1.25	3.63±1.27	3.56±1.18	3.47±1.29
SDAI mono	30.95±13.91	16.84±11.97	14.33±11.39	10.62±5.79	12.95±12.12
SDAI combo	35.05±14.89	15.50±11.15	14.04±10.31	14.31±10.87	12.89±11.39
CRP mono, mg/L	24.01±26.66	8.45±11.80	8.79±14.01	5.90±5.13	8.74±10.46
CRP combo, mg/L	34.48±39.25	11.76±22.36	8.12±12.67	8.54±14.35	10.49±17.51
ESR mono, mm/h	32.96±17.26	22.54±15.45	21.26±15.38	22.83±21.24	21.29±14.02
ESR combo, mm/h	36.68±22.98	24.24±16.89	21.59±15.40	19,52±12.83	22.97±19.36
NTJ from 28 mono	10.73±6.15	6.26±4.65	4.97±5.02	4.13±3.09	3.42±4.01
NTJ from 28 combo	11.75±6.63	5.21±5.36	4.55±4.43	5.73±5.68	3.45±4.15
NSJ from 28 mono	8.0±4.78	2.0±2.94	2.0±2.64	1.0±1.30	0.0±0.45
NSJ from 28 combo	8.26±5.22	2,96±3.49	2.55±3.33	2.54±4.28	1.68±3.00

*from the baseline ± 14 days for 1 and 6 month, ±28 days for 12, 24, and 36 month

p-value ≥ 0.05 for all the differences between monotherapy and combination therapy in all the time points.

No differences were found in safety parameters between groups of tofamonotherapy and tofa plus mtx.

Conclusion: The efficacy and safety of tofacitinib monotherapy is not worth than combination of tofacitinib and methotrexate in RA treatment.

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AB0343 BETTER QUALITY OF LIFE AND ADHERENCE WITH LESS ADVERSE EVENTS WHEN SWITCHING FROM ORAL TO SUBCUTANEOUS METHOTREXATE: RESULTS OF THE SIX-MONTH OBSERVATIONAL PROSPECTIVE STUDY IN CROATIA

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Background: It has been demonstrated that bioavailability of oral (P.O.) MTX reaches plateau at doses ≥15 mg QW, and that subcutaneous (S.C.) form has a better efficacy. Alongside with less side-effects this might translate into improvement in quality of life (QoL) and better adherence.

Objectives: An academic-induced observational longitudinal study of patients with RA and peripheral form of PsA on csDMARDs who were switched from oral (P.O.) to subcutaneous (S.C.) MTX was conducted. Previously we reported on the better efficacy of S.C. compared to P.O. MTX. The objective of this part of the study we are presenting was to evaluate the 6-month changes in quality of life (QoL), adverse events and adherence in these patients.

Methods: Forty-eight consecutive patients (79.2% women) with established diagnosis of RA (77.1%) and peripheral PsA were enrolled from the outpatient clinics in six centres in Croatia. Median age was 61 (39-79) years, and the median of disease duration was 120 (3-528) months. Data were collected at baseline (T0) (on P.O. MTX), at day 90 (±10 days) (T1) and at day 180 (±10 days) (T2), during S.C. MTX treatment. Median dose of MTX remained stable during the study (15mg QW). At each visit QoL was measured using EuroQuol-5D (EQ-5D), adverse events related to MTX use were recorded, and adherence by the number of missed dose.

Results: EQ-5D global health assessment showed significant improvement in quality of life of patients on S.C. MTX during the 6 month follow-up (change from T0 to T2 8.6; 95%CI 4.00, 13.3), and the same trend was observed in each of its five component. Number of patients who experienced adverse events related to MTX use has decrease after switching from P.O. to S.C.MTX – from 52.1% during the last 3 months on P.O. MTX to 33.3% during the first 3 months and 18.2% during the last 3 months of S.C. MTX use. During the follow-up adherence to MTX therapy improved, with 25% of patients who missed dose during the last 3 months on P.O. MTX use, to 6,3% and 2.3% with missed dose in the first and the last 3 months on S.C. MTX, respectively.

Conclusion: In our group of patients with RA and peripheral PsA who switched from P.O. to S.C. MTX there was a consistent improvement in QoL, less adverse-events and better adherence.

Disclosure of Interests: Simeon Grazio Speakers bureau: Abbvie., Roche, MSD, Eli Lilly, Pfizer, Mylan, Amgen, Fresenius Kabi, Stada, Berlin-Chemie, Dijana Perković Speakers bureau: Abbvie., Roche, MSD, Eli Lilly, Pfizer, Mylan, Amgen, Fresenius Kabi, Nadica Laktašić Žerjavić Speakers bureau: Abbvie., Roche, MSD, Eli Lilly, Pfizer, Mylan, Amgen, Fresenius Kabi, Frane Grubisic Speakers bureau: Abbvie., Roche, MSD, Eli Lilly, Pfizer, Mylan, Amgen, Marija Glasnović Speakers bureau: Abbvie, Roche, Pfizer, Ana Gudelj Gračanin Speakers bureau: Abbvie. Roche, MSD, Eli Lilly, Pfizer, Željka Kolak: None declared, Helena Kolar Mitrović: None declared, Jadranka Morovic-Vergles Speakers bureau: Abbvie., Roche, MSD, Eli Lilly, Pfizer, Mylan, Amgen, Fresenius Kabi, Porin Perić: None declared, Petra Šimac: None declared, Iva Žagar Speakers bureau: Abbvie. Roche, MSD, Eli Lilly, Pfizer, Ines Doko Speakers bureau: Abbvie. Roche, Vladimir Trkulja: None declared

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AB0344 FACTORS WHICH CONTRIBUTE PERSISTENCY AND OPTIMAL USE OF TOFACITINIB; LESSONS FROM LONG TERM DAILY CLINICAL USE OF TOFACITINIB

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Background: Recently, tofacitinib treatment in rheumatoid arthritis (RA) is thought to be not inferior to other biologic disease-modifying antirheumatic drugs (bDMARDS) such as TNF-inhibitor. However, approval of tofacitinib for treatment with RA is relatively recent as compared to other bDMARDs, therefore until now, little knowledge about long term efficacy and safety of tofacitinib in real-world settings or about which patients should be initiated tofacitinib are available. Thus, we need evidence from real-world setting for optimal use of tofacitinib.

Objectives: To investigate the efficacy and safety of tofacitinib and to identify factors which contribute persistency and efficacy of tofacitinib treatment during 2 years.

Methods: 148 patients, for whom tofacitinib was initiated until January 2018 were enrolled. All patients received 5 mg of tofacitinib twice daily and were followed for 2 years. Clinical disease activity indicated by disease activity score (DAS)28-ESR as well as adverse events (AEs) were evaluated. Statistical analysis was performed to determine which baseline variables influenced the persistency and efficacy of tofacitinib.

Results: 92 patients (62.2 %) continued tofacitinib for 2 years. Clinical disease activity rapidly and significantly decreased, and this efficacy continued throughout the 2 years: i.e., DAS28-ESR decreased from 5.13 ± 1.42 at baseline to 4.02 ± 1.11 at 4 weeks and 3.91 ± 1.32 at 2 years (P<0.0001, vs. baseline). 55 AEs including 22 herpes zoster infection occurred during tofacitinib treatment. 27 patients discontinued tofacitinib due to lack of efficacy. Multivariable logistic analysis showed that the number of bDMARDs previously used and age were associated with discontinuation of tofacitinib treatment due to lack of efficacy(table 1). Another set of multivariable logistic analysis revealed that lower disease activity at baseline contributed the achievement of DAS-low disease activity(odds ratio= 1.56, 95% confidence interval: 0.48-0.85). In the concomitant use of MTX or without MTX, the Δ values of DAS28-ESR from baseline to 24 months were -1.62, -1.13, respectively(P=0.12). And, the efficacy of patients after switching from tocilizumab(TCZ), which also inhibit IL-6 as same as JAK inhibitor, were not inferior as compared to non-switching from TCZ (Δ DAS28-ESR;-1.07, -1.61, respectively P=0.10).

Table 1.

Univariate Model			Multivariate Model	
	OR(95% CI)	P-value	OR(95% CI)	P-value
Age (per 1-year increase)	0.92(0.88-0.95)	<0.001*	0.91(0.87-0.95)	<0.001*
Disease duration (per 1-year increase)	0.97(0.97-1.02)	0.21		
Concomitant MTX use (yes/no)	0.95(0.39-2.31)	0.91		
Concomitant oral steroid use (yes/no)	1.84(0.76-4.42)	0.16	1.61(0.60-4.34)	0.349
Number of previous use of bDMARDs (per drug)	1.26(0.99-1.62)	0.05	1.39(1.05-1.84)	0.02*
DAS-ESR at baseline (per 1 increase)	1.02(0.76-1.36)	0.92		
LDA achievement at 1 year (yes/no)	0.56(0.76-1.49)	0.23		
RF positive (yes/no)	0.91(0.32-2.56)	0.85		
ACPA positive (yes/no)	0.76(0.27-2.18)	0.62		

OR odds raio, *95% CI* 95% confidence interval, *MTX* methotrexate, *bDMARDs* biologic disease-modifying antirheumatic drugs, *ACPA* anti-citrullinated protein antibodies, *RF* rheumatoid factor *P<0.05

Conclusion: Our present study suggests that tofacitinib is effective in real-world settings even without concomitant MTX. Our results also suggest that for continuous use of tofacitinib without lack of efficacy, use tofacitinib earlier during switching strategy for RA patients who have failed to be treated with bDMARDs is better.

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AB0345 EFFICACY OF JAK INHIBITORS IN REFRACTORY RHEUMATOID ARTHRITIS

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Background: Disease-modifying antirheumatic drugs (DMARDs) have been the main agents for treating rheumatoid arthritis (RA) unless there are serious clinical restrictions or contraindications such as comorbidities. With inefficacy of conventional synthetic DMARDs (e.g., methotrexate), biological DMARDs (bDMARDs) are now available to suppress progression of joint destruction. However, bDMARDs cannot control disease activity in some patients, so JAK inhibitors targeting different cytokines are expected to be beneficial.

Objectives: This study investigated factors associated with the efficacy and continuation of JAK inhibitor therapy in patients with refractory RA for whom disease activity was not adequately controlled even with multiple sequentially administered bDMARDs with different targets.

Methods: We obtained the number of bDMARDs used and the various reasons for discontinuing therapy in our hospital from January 2005 to December 2019. Kaplan–Meier analysis was used to obtain the therapy continuation rate, and the log-rank test was used to examine the difference in therapy continuation rate. Refractory RA was defined as RA with inefficacy with 3 or more bDMARDs with different targets (1 or more tumor necrosis factor inhibitor, a selective costimulation modulator abatacept, and an interleukin 6 receptor inhibitor tocilizumab). We then examined patients with refractory RA who had received tofacitinib (TOF) or baricitinib (BAR) therapy after discontinuation of a series of bDMARDs due to unsatisfactory response. Various statistical tests were performed to identify predictors of ≥ 6-month continuation of JAK inhibitor therapy that achieves low disease activity without increases in prednisolone (PSL) use. Explanatory variables included characteristics of patients at initiation of TOF or BAR therapy: age, sex, disease duration, number of bDMARDs previously used, concomitant methotrexate dose, concomitant PSL dose, DAS28-ESR value, presence of rheumatoid factor or anti-CCP antibodies, and MMP-3 level.

Results: A cumulative number of 782 bDMARDs were administered to 362 RA patients by December 2019. The most common reason for discontinuation was inefficacy (51.8%), followed by adverse events including deaths (30.1%), patients' circumstances such as hospital transfer (9.2%), switch to biosimilars (5.2%), and remission (3.7%). The bDMARDs continuation rate and the number of bDMARDs used were 69.6% and 2.17 for 5 years and 53% and 2.83 for 10 years, respectively, if the switch was considered to be continuous due to insufficient effect. The 6-month continuation rates were not significantly different between TOF and BAR (60 patients [62.3%] vs. 39 patients [81.3%], respectively; P = 0.147). In patients with refractory RA, continuation rates were not significantly different between TOF and BAR (19 patients [42.1%] vs. 11 patients [54.5%], respectively; P = 0.86). Only TOF-treated patients, not BAR-treated patients, showed significant differences in disease duration (226.1 months in the continued group vs. 111.8 months in the discontinued group; P = 0.035) and concomitant PSL dose (0.71 mg vs. 4.0 mg, respectively, P = 0.045).

Conclusion: There are not a few patients with refractory rheumatoid arthritis. These findings, albeit retrospective, suggest that low concomitant PSL dose and long disease duration at the time of TOF therapy initiation were factors for TOF continuation. Therapy continuation rate was decreased in patients with refractory RA, and further study on switching therapy between different JAK inhibitors is anticipated.

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AB0346 THE NUMERAL CHANGES OF PERIPHERAL LYMPHOCYTE SUBSETS IN PATIENTS WITH RHEUMATOID ATHRITIS AND THEIR RESTORATIONS AFTER RECEIVED COMBINED IMMUNOMODULATORY THERAPY

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Background: Rheumatoid arthritis (RA) is an aggressive immune-mediated joint disease with synovial inflammation and joint destruction characterized by abnormal immune responses to self-antigens[1]. An imbalance in pro- and anti-inflammatory lymphocyte subsets has been considered to contribute to the pathogenesis of RA[2]. However, the detailed lymphocyte statuses of RA patients are required clarified and the effect of immunomodulatory therapy on the lymphocyte subsets is unclear[3].

Objectives: To investigate the status of lymphocyte subsets in peripheral blood (PB) of RA patients at relatively large-sample size and the changes of them after our immune regulatory combination treatment.

Methods: This cross-sectional study enrolled 3016 patients with RA who met the ACR's revised RA diagnostic classification in 1987 as well as 206 healthy controls (HCs). Among these participations, 1415 patients have received the treatment of immunomodulatory drugs (IMiDs) such as low-dose interleukin-2, rapamycin, metformin, retinoic acid etc. Flow cytometry (FCM) was used to measure the levels of PB lymphocyte subgroups and CD4+T subsets in RA patients before and after the treatments and HCs. Data were expressed as mean ± standard deviation to the distribution. Independent-samples T test and paired-samples T test were applied. *P* value <0.05 were considered statistically significant.

Results: Compared with HCs, patients with RA had a lower absolute numbers of total T, $CD8^+$T, NK and Tregs ($P<0.05$), decreased percentages of NK, Th1, Th2 and Th17 ($P<0.05$), but higher ratios of Teffs/Tregs such as Th1/Tregs and Th17/Tregs ($P<0.05$), indicating a disturbance of immune systems (Figure 1). After receiving combined immunomodulatory therapy, the absolute numbers of T, B, $CD4^+$T, $CD8^+$T, NK, Th1, Th17 and Tregs were dramatically increased ($P<0.05$) and the percentages of B, Th1, $CD4^+$T and Tregs were also increased ($P<0.05$). Although these subsets increased globally, the ratio of Teffs/Tregs such as Th2/Tregs and Th17/Tregs tended to decrease, suggesting a rebalance of immune systems(Figure 2).

Conclusion: Impaired peripheral lymphocytes especially insufficiency of Tregs might played an important role in pathogenesis of RA. Immunoregulatory combination therapies could promote the proliferation and functional recovery of Tregs in patients and help to alleviate disease activity.

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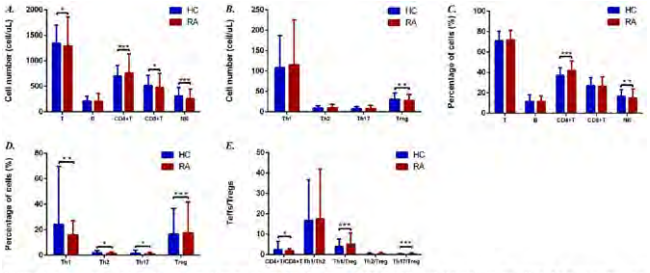


Figure 1: Comparison of lymphocyte subsets in peripheral blood between HCs (n=206) and RA patients (n=3016). All the lymphocytes subsets were analyzed by detected by flow cytometry combined with standard absolute counting beads. Data were presented as mean±SD and statistical analysis was determined by two-tailed unpaired t-test. Patients had lower levels of T, CD8+T, NK and Tregs(A and B), decreased percentages of NK, Th1, Th2 and Th17(C and D), and higher ratios of Teffs/Tregs such as Th1/Tregs and Th17/Tregs in RA compared with those of HCs (E). HC:healthy control*P < 0.05, **P < 0.01, ***P < 0.001.

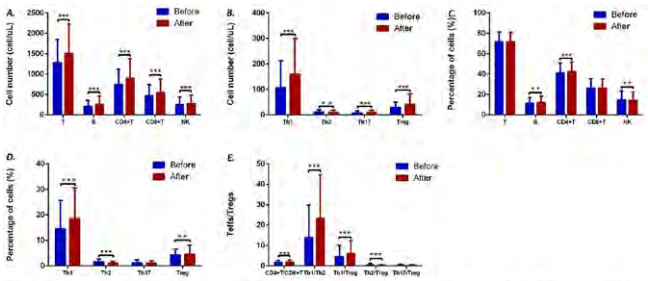


Figure 2: Changes of peripheral lymphocyte subsets after immune new regulatory combination therapies (n=1415). Data were presented as mean±SD and statistical analysis was determined by two-tailed paired t-test. Absolute number of T, B, CD4+T, CD8+T, NK, Th1, Th17 and Tregs were significantly increased (A and B). The proportion of B, Th1, CD4+T and Tregs were also increased (C and D), while the ratio of Teffs/Tregs such as Th2/Tregs and Th17/Tregs had a tendency to decrease after immune new regulatory combination therapies (E). *P < 0.05, **P < 0.01, ***P < 0.001.

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AB0347 INCREASING TO OPTIMAL METHOTREXATE DOSE MIGHT BE A BETTER TRADITIONAL DMARD STRATEGY IN RA TREATMENTS: A RANDOMIZED CASE-CONTROL TRIAL OF HAKKA PEOPLE IN SOUTHERN CHINA

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Background: The optimal methotrexate (MTX) dose is defined as 0.3mg/kg/week or ≥ 20mg/week at 6 months. [1] Considering average weight of Chinese, [2] the optimal MTX should be >15mg/w. However, not more than 30% in 25191 RA cases ever had MTX treatment in CREDIT (Chinese Registry of Rheumatoid arthritis). [3] The biggest concern is side effects of MTX. Our study is to investigate whether increasing MTX would get better results accompanied with more side effects to Chinese people.
Objectives: Hakka people have the purest genes of the majority people-Han in China. It is planned to recruit 160 RA patients in Meizhou, where is a gathering place of Hakka people.
Methods: The RA volunteers had no relief with 10 mg/w oral dose of MTX with/without other 1-2 inadequate dose of DMARDs for at least 3 months. They were randomly divided into 1:1 groups*. The experimental group would be treated with original DMARDs and incremental MTX (gradually increased to the optimal oral dose (0.3 mg/k/w) in the first 12 weeks and folic acid (the dose adjusted on demand with range from 5 mg/w to 5mg tid). While the control group would be treated with original MTX dose(10mg/w) but incremental original DMARDs(gradually increased to the maximum dose in the first 12 weeks). The two groups would keep the treatment at 12th week last to the 36th week, and the efficacy and safety indexes would be evaluated during the whole study.
Results: 1)We planned to recruit 160 RA patients in our study. 46 Hakka RA patients were enrolled in the study so far. 2 of 46 finished the 24th week visit and 24 finished the 36th week visit. The average age is 54.2± 9.3 years old, the average weight is 59.1±11.1kg, and the female to male ratio is 41:5.
2)The average Folic acid dose is 14.4±9.5mg/w in the experimental group at the 12th week.
3)The morning stiffness time, PGA, PhGA, HAQ, DAS28 were better in experimental group after 12 weeks though slightly worse during 0-12 weeks. 100%(12) patients in experimental group, while 66.67%(8/12) in control group reach ACR20.
4) Only 1 case(5.9%,1/23)had adverse event while 6 cases (26%,6/23) occurred adverse events. All events were mild level. 1 case (4.2%,1/23) in control group withdrew from the study because the disease was getting worse during 0-24 weeks.
Conclusion: Hakka patients in China might have better outcomes due to increasing MTX to the 0.3mg/kg/w dose than increasing the other DMARDs. Therefore, We recommended the Chinses patients choose MTX as first incremental DMARD. The appropriate dose of Folic acid plus with the optimal dose of MTX in our study is higher than previous studies (such as 13.0±4.8mg/w reported by Gaujoux-Viala, 2018[1]). We recommended Chinese patients take 15mg/w folic acid to prevent MTX side effects in view of lower folic acid level in Chinese population.[3]
References:

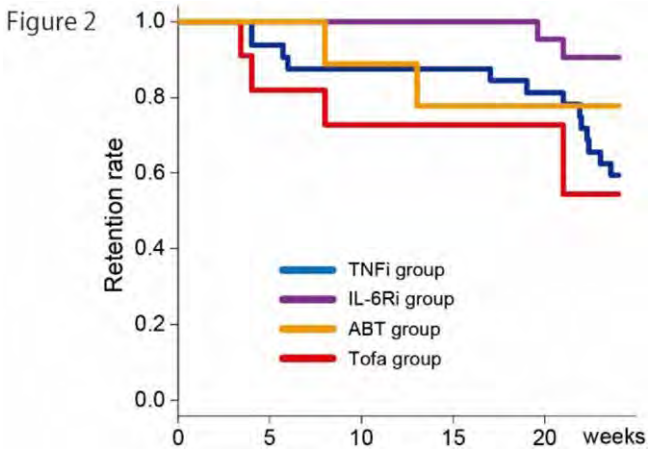
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Disclosure of Interests: None declared
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AB0348 THE EFFECTIVENESS AND SAFETY OF BARICITINIB AFTER INSUFFICIENT RESPONSE TO BDMARDS OR TSDMARDS IN PATIENTS WITH RA FROM JAPANESE MULTI-CENTER REGISTRY: 24-WEEK OUTCOMES

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Background: EULAR has issued updated guidelines for the management of rheumatoid arthritis (RA) using conventional, biologic, and targeted synthetic DMARDs. In the 2019 update, the task force revised the preference of bDMARDs over tsDMARDs. In routine clinical practice, baricitinib is commonly used as second line or after. However, there is little information about the clinical efficacy and safety profile of baricitinib after failure of the previous agent, including another tsDMARD.
Objectives: The aim of this study was to evaluate the short-term effectiveness and safety profiles of baricitinib after insufficient response (IR) to bDMARDs or tsDMARDs in patients with RA in clinical settings.
Methods: RA patients who had been treated with baricitinib after failure of the previous agent were registered in the TBCR, a Japanese multicenter registry for RA patients treated with biologics or JAK inhibitors and followed for at least 24 weeks. Patients were divided into two groups according to the cause of failure of the previous treatment; IR ("After IR" group) and the others ("After non-IR" group). "After IR" group was further divided into four groups according to the previous agent; TNF inhibitor (TNFi group), IL-6 receptor inhibitor (IL-6Ri group), abatacept (ABT group) and tofacitinib (Tofa group). We assessed disease activities by CDAI score and drug retention rates between these groups. Furthermore, discontinuation rates due to IRs and adverse events (AEs) were evaluated.
Results: A total of 86 consecutive RA patients were registered in this study. The previous treatment was as follows; TNF inhibitor: 38 (44.2%), IL-6 receptor inhibitor: 23 (26.7%), abatacept: 11 (12.8%), tofacitinib: 13 (15.1%) and the other: 1 (1.2%).The cause of failure of the previous therapy were IRs (n=74: 86%), AEs:(n=6: 7.0%) and the others (n=6: 7.0%). In "After IR" group, the most common

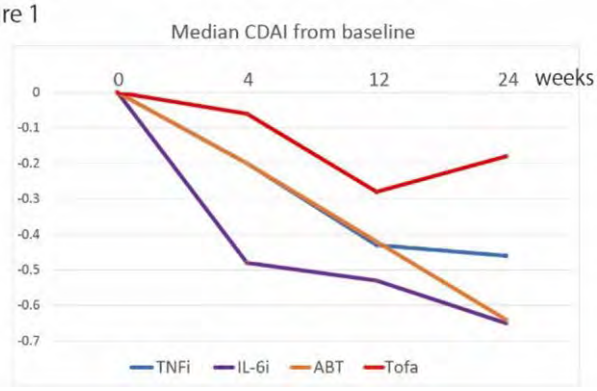


previous agents were TNFis (Table 1). While the percent change in CDAI was decreased at week 12 in all groups, those in Tofa group showed lower rates of improvement in CDAI compared to the others at week 24 (Figure 1). Drug retention rate at 24-week was 59.4% in TNFi group, 90.5% in IL-6Ri group, 54.5% in ABT group and 77.8% in Tofa group (Figure 2). In the present study cohort, seven patients developed herpes zoster. All seven patients were treated with antiviral agents for herpes zoster and restarted baricitinib treatment (these cases were not treated as discontinuation due to AEs in this study). The overall Cumulative discontinuation rate due to IRs and AEs at 24 weeks were 9.7% and 7.3%, respectively.

Table 1

Groups	Cases; n (%)
TNFi group	32 (43.2)
IL-6R group	21 (28.4)
ABT group	11 (14.9)
Tofa group	9 (12.2)
The oter	1 (1.4)

Figure 1



Conclusion: In this study, we demonstrated the short-term effectiveness and safety profiles of baricitinib after insufficient response to bDMARDs or tsDMARDs in patients with RA in the 'real-world' setting. Baricitinib improved disease activity after failure of the previous agent, even after IR to another tsDMARD. With respect to safety, the profile is almost tolerable, although careful observation is necessary for possible complications and AEs including herpes zoster.

Disclosure of Interests: Hanabayashi Masahiro Speakers bureau: Astellas Pharma Inc., Mitsubishi Tanabe Pharma Corporation, Eisai Pharma Corporation, Chugai Pharma Corporation, abbvie, Bristol-Myers Squibb, Pfizer, Janssen Pharmaceutical K.K., Eli Lilly Japan K.K. and UCB Japan, Nobunori Takahashi Speakers bureau: AbbVie, Asahi Kasei, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eisai, Eli Lilly, Janssen, Mitsubishi Tanabe, Ono, Pfizer, Takeda, and UCB Japan, Toshihisa Kojima Grant/research support from: Chugai, Eli Lilly, Astellas, Abbvie, and Novartis, Consultant of: AbbVie, Speakers bureau: AbbVie, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eli Lilly, Janssen, Mitsubishi Tanabe, Pfizer, and Takeda

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AB0349 EFFICACY OF TOFACITINIB THERAPY, DEPENDING ON THE USE OF DMARDS IN PATIENTS WITH RHEUMATOID ARTHRITIS IN A REAL CLINICAL PRACTICE IN RUSSIAN FEDERATION.

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Background:

Objectives: To evaluate how disease-modifying antirheumatic drugs (DMARDs) affects efficacy of tofacitinib (TOFA) therapy in patients with rheumatoid arthritis (RA).

Methods: We analyzed the history of 107 patients (mean age 51,4±12,1 yrs) with RA according to the 2010 ACR/EULAR criteria, from 11 regions Russian Federation, including patients who were treated at the V.A. Nasonova Research Institute of Rheumatology. These patients were non-responders to DMARDs, previously biologic therapy and were treated with TOFA in combination with DMARDs or without. 107 patients (77 woman (72%),tested positive for ACCP (76.5%)/RF (87.3%), the median disease duration was 7,5±6,6 years; the mean DAS28 score was 5,8±1,0, mean SDAI and CDAI score was 35,6±13,4 and 32,1±12,4 respectively) received TOFA for 12 months. TOFA therapy was started in all patients in dose 5 mg BID per os with escalation to 10 mg BID in 17,6% pts.

Results: The use of TOFA was accompanied by a decrease in the disease activity after 6 and 12 months of therapy. All patients were divided into 3 groups, depending on DMARDs therapy: TOFA+ methotrexate (MTX), TOFA+ another DMARDs (leflunomide, hydroxychloroquine, azathioprine), mono-therapy of TOFA. The dynamic of the disease activity in 3 groups is presenting on the table below:

Parameters	Weeks	TOFA+MTX (n=69)	TOFA+ another DMARDs (n=20)	TOFA monotherepy (n=18)
DAS28 (ESR)	baseline	5,9 ±1,0	5,6±1,1	6,0±0,8
	6 months	3,5±1,2*	4,1±1,1*	4,2±1,6*
	12 months	3,3±1,0*	3,5±1,3*	3,8±1,2*
SDAI	baseline	36,2±14,2	32,6±9,5	35,3± 10,3
	6 months	14,4± 10,7*	16,7± 10,2*	27,3±19,1*
	12 months	9,5±8,0*	12,9± 8,6*	15,3±10,2*
CDAI	baseline	32,4±12,1	29,7±8,9	33,2±9,8
	6 months	13,3±10,2*	15,6±9,8*	22,4±16,8*
	12 months	8,7±7,6*	12,6±8,2*	14,4±9,6*

*p<0,05

Patients who received TOFA with MTX had lower disease activity during the therapy. Patients on mono-therapy of TOFA had higher disease activity according to DAS28, SDAI, CDAI.

Conclusion: Tofacitinib is effective ts-DMARDs for active rheumatoid arthritis on the Russian population. It shows better efficacy in combination with methotrexate, than in combination with another DMARDs (leflunomide and other) or in mono-therapy.

Disclosure of Interests: None declared

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AB0350 EFFICACY OF ADDING IGURATIMOD THERAPY IN RHEUMATOID ARTHRITIS PATIENTS WHO HAD INADEQUATE RESPONSE TO BIOLOGIC DMARDS

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Background: Iguratimod (IGU) was newly approved in Japan in June 2012 and recommended by JCR guideline 2014 in the treatment of rheumatoid arthritis (RA). Although there have been efficacy of monotherapy and concomitant MTX in clinical trials, however, there have been no reports of concomitant biologic DMARDs (Bio).

Objectives: we investigated efficacy of concomitant IGU therapy in RA patients who had inadequate response to Bio at the author's institution.

Methods: Subjects were 107 patients adding IGU who had inadequate response to Bio from Janually 2014 to October 2018. Previous treatment Bio. was ADA. And baseline mean concomitant MTX was 12.3 mg/week). And baseline characteristics were Mean age 53.8 years, mean duration of illness 5.5 years, corticosteroid use 9.3%(mean 3.1mg/day).

The course of DAS28, SDAI, CDAI and remission rates were analyzed.

Results: Mean DAS28-ESR, SDAI, CDAI were significantly decreased from the initiation of IGU treatment at 24 weeks (3.1→2.3, 7.1→2.7, 6.5→2.4), at 52 weeks (2.1, 2.4, 2.0). Remission rates of DAS28-ESR, SDAI, CDAI were 69.2%, 68.2%, 70.1% at 24 weeks, 74.8%, 78.5%, 79.4% at 52 weeks. There were no side-effect that must be stopped after adding IGU.

Conclusion: IGU might be a new RA treatment option for aiming remission in patients who had inadequate response to Bio.

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Disclosure of Interests: None declared

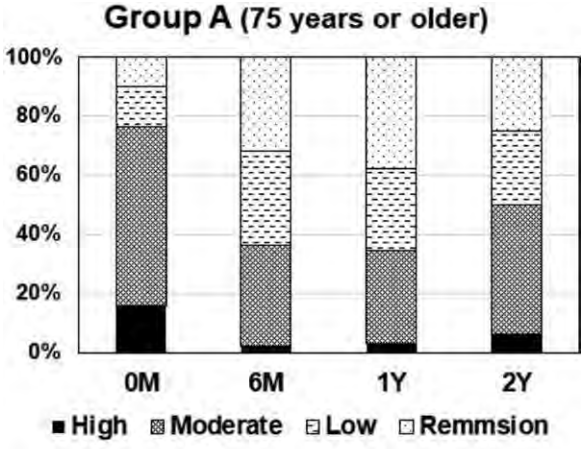
DOI: 10.1136/annrheumdis-2020-eular.459

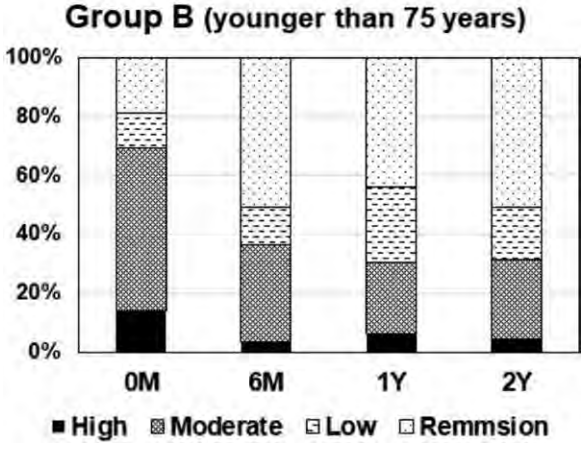
AB0351 EFFICACY OF IGURATIMOD FOR RHEUMATOID ARTHRITIS IN ELDERLY PATIENTS

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Background: Iguratimod (IGU) was started development as new non-steroidal anti-inflammatory drugs (NSAIDs), but it was changed for development as disease modifying antirheumatic drugs (DMARDs) because it showed suppression of inflammatory cytokine and inflammatory parameter which was not to be found in existing NSAIDs in the early stage of pharmacological study of drug efficacy. Although the clinical efficacy and the safety of IGU were already reported, the efficacy for elderly cases was not sufficiently analyzed.

Objectives: In this study, we compared the efficacy of IGU in elderly group with the non-elderly group.
Methods: 190 patients who were able to continuously administer IGU more than three months was included. Cases were divided into two groups. Group A (75 years or older) includes 57 patients, and Group B (younger than 75 years) includes 133 patients. The patients background, the use of methotrexate (MTX) and glucocorticoid, the change of serum CRP, and the DAS28-ESR (before, 6, 12, and 24 months) as an evaluation of the disease activity were compared between two groups. The study protocol was approved by our institutional review board. All the patients were required to give written informed consent.
Results: The average age at the beginning of IGU was 79.9±4.1 years old in Group A, and 59.9±10.6 years old in Group B. The average disease duration was 14.8±16.5 year in Group A and 8.5±10.6 year in Group B ($p<0.01$). Although the rate of concomitant use of MTX was significantly lower in Group A (Group A; 28.1%, Group B; 56.4%), the averaged dose of MTX did not show difference between groups (7.0 and 8.4 mg/week, respectively). Group A showed significantly higher rate of concomitant use of glucocorticoid (56.1%, and 36.1%, respectively), but the averaged dose of glucocorticoid did not show a difference between groups (4.3 and 3.6mg/day, respectively). Similarly, the rate of concomitant use of NSAIDs did not have a difference in two groups. Group A showed significantly higher serum CRP at the beginning of the IGU (Group A; 2.0 mg/dl, Group B; 1.2 mg/dl), but there was no difference after six months. In both groups, serum CRP was significantly decreased when compared at the beginning of IGU. After six months of IGU administration, both groups showed good clinical performance with DAS28-ESR, more than 60% of the cases showed remission or low disease activity. No difference of DAS28-ESR scores between two groups was observed after six months.
Conclusion: From the results of this study, the efficacy of IGU for elderly patients was confirmed and did not show differences with non-elderly people. IGU is an inexpensive drug with enough efficacy and thought to be possible substitute for cases with insufficient reaction with other DMARDs.
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Disclosure of Interests: None declared
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AB0352 **CONSENSUS STATEMENT: USE OF JAKINIB THERAPY IN IMMUNE MEDIATED INFLAMMATORY DISEASES.**

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Background: Janus kinase inhibitor therapy is approved for use in a variety of Immune mediated inflammatory diseases.
Objectives: With 4 agents approved & 1 in development, it is timely to undertake a systematic literature review (SLR) of evidence across indications for efficacy, safety & management issues.
Methods: Existing data was evaluated by a steering committee & subsequently by a 25 person expert committee leading to a consensus statement to assist the clinician once the decision had been made to commence a Jakinib. The Committee included patients, rheumatologists, gastroenterologist, haematologist, dermatologist & infectious disease specialists. SLR of Medline, Embase, Cochrane, abstracts from 2018 EULAR & ACR congresses & Epistemonikos identified 1,178 RA & PsA, 128 SLE, & 1339 "other indications" unique references meeting criteria that included randomized & open label clinical trials, registries, phase 4 trials, & meta-analyses. Warnings from regulators issued after the end of the SLR search date were taken into consideration. Cochrane risk of bias tool was used.
Results: General principles included (1) shared decision making, (2) adherence to T2T principles, (3) reference to disease specific product information & (4) reference to country/region specific treatment algorithms. Mode of action & indications are discussed & consensus was reached on pre-treatment screening, contra-indications, monitoring, treatment dose, co-medications & adverse effects (see Table 1.), with 80-100% agreement. A research agenda was formulated to update the review as new information becomes available.

Table 1. A. Pre-treatment screening

1. Patient history, examination
2. Routine Laboratory testing: FBC diff LFTs Renal function, lipids at wk 12
3. Hepatitis Bs Ag & Ab, core Ab & Hep C ab, & HIV in high risk individuals.
4.TB screening as per national guidelines
5.Assess & update vaccination status
6.Consider VTE risk factors – prior history, familial VTE, use of Cox2 inhibitors
B. Monitoring
1. FBC diff LFTs mth 1, & mth 3 with lipids, repeat periodically
2. Annual skin examination
3. Evaluated response using validated disease specific measures of disease activity – be aware ESR/CRP may be reduced independently of reduction in disease activity or infection
C. Contra-indications (consult label & warnings)
1. Severe active (or chronic) infection, including tuberculosis and opportunist infections
2. Current malignancies
3.Pregnancy & lactation
4. Severe organ dysfunction eg severe hepatic disease (Child-Pugh C) or severe renal disease
5. Allergy to Jak ihibitor
6. History of VTE (relative contra-indication, careful consideration +/_ anticoagulation)

Table 2.

D. Adverse Effects.
1. Serious infections including opportunist infections, TB, Herpes Zoster, are increased. The risk is lowered with reduction or elimination of concomitant corticosteroid
2.Rates of malignancy do not appear elevated although the risk of NMSC may be elevated
3. Lymphopenia, neutropenia, elevated liver transaminases, & lipid changes have been noted
4. An increased risk of VTE has been reported in a safety trial of tofacitinib & in the placebo-controlled trial period of baricitinib in RA patients
5. Elevations of CPK noted but have been rarely associated with clinical events
6. Elevations of creatinine noted but not associated with renal failure or hypertension

Conclusion: The consensus provides an assessment of evidence for efficacy & safety of an important therapeutic class with guidance on practical management issues.
Acknowledgments: Unrestricted grants were provided by Abbvie & Lilly with no input into the planning & development of the recommendations, nor influence or attendance at the meeting nor review of the abstract, with full disclosures from participants & the opportunity to declare any feelings of conflict of interest.
Disclosure of Interests: Peter Nash Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Gilead, Janssen, MSD, Novartis, Pfizer Inc, Roche, Sanofi, UCB, Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, MSD, Novartis, Pfizer Inc, Roche, Sanofi, UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, MSD, Novartis, Pfizer Inc, Roche, Sanofi,

UCB, Andreas Kerschbaumer Paid instructor for: Celgene, Speakers bureau: Andreas Kerschbaumer has received lecture fees from Bristol-Myers Squibb, Gilead, Merck Sharp and Dohme and Pfizer., Désirée van der Heijde Consultant of: AbbVie, Amgen, Astellas, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Cyxone, Daiichi, Eisai, Eli-Lilly, Galapagos, Gilead Sciences, Inc., Glaxo-Smith-Kline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB Pharma; Director of Imaging Rheumatology BV, Josef S. Smolen Grant/research support from: AbbVie, AstraZeneca, Celgene, Celltrion, Chugai, Eli Lilly, Gilead, ILTOO, Janssen, Novartis-Sandoz, Pfizer Inc, Samsung, Sanofi, Consultant of: AbbVie, AstraZeneca, Celgene, Celltrion, Chugai, Eli Lilly, Gilead, ILTOO, Janssen, Novartis-Sandoz, Pfizer Inc, Samsung, Sanofi

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AB0353

COMPARATIVE STUDY OF PATIENT BACKGROUND AND TREATMENT OUTCOME BY BARICITINIB DOSE UNDER REAL CLINICAL CONDITIONS.

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Background: Balicitinib (BAR) is one of the Janus kinase (JAK) inhibitors, which mainly inhibits JAK1 and JAK2 and has an anti-inflammatory effect on rheumatoid arthritis(RA). In Japan, it is necessary to use different doses of BAR depending on the RA patient's estimated glomerular filtration rate (eGFR). The RA-BEACOM and RA-BUILD trials reported the treatment effects by BAR dose at 24 weeks and concluded that there was no difference in DAS(disease activity score)28CRP between BAR 2mg and 4mg. The patient background treated in these double-blind RCTs is uniform even at different BAR doses. There is uncertainty about the difference in the therapeutic effects of BAR dose under the real clinical setting where the patient background differs from that of the trial patients.

Objectives: To compare patient backgrounds and treatment outcome by Baricitinib dose under real clinical setting.

Methods: 113 RA patients taking BAR who were registered in the Nagoya University Orthopedic Surgery Multicenter Study (TBCR) were included in this study. Patient characteristics (such as age, illness duration, combined anti-rheumatic drugs, eGFR) and DAS28CRP, clinical and simplified disease activity index(CDAI, SDAI respectively) up to 24 weeks were compared between BAR 2mg and 4mg groups. The continuation rates, including the discontinuation due to ineffectiveness and adverse events (AEs), were also compared between the two groups. For these comparisons, Student's t-test and Pearson's chi-square test, Kaplan-Meier survival curve were used. Missing data due to discontinuation of BAR was complemented by LOCF method and analyzed statistically. The significance level was set to less than 0.05.

Results: There were 39 subjects (8 males and 31 females) in BAR2mg group and 74 patients (17 males and 57 females) in BAR4mg group. There was a significant difference in mean age (73.5 vs. 62.3 years old, p <0.001), average eGFR (65.1vs 84.8ml / min / 1.73m^2, p <0.001), methotrexete(MTX) use rate (28 vs 58%, p <0.01), average MTX dose (3.0 vs 5.5mg, p <0.01),glucocorticoid(GC) use rate(51.3 vs 33.8%, p<0.01) between the two groups(Table). DAS28CRP improved from week 0 (3.2 vs 3.5) to week 24 (2.5 vs 2.4), and no significant difference was observed between the two groups at each time point (Fig.1-A). The same was true for CDAI and SDAI(Fig.1-B,-C). The rate of DAS28CRP remission and low disease activity was not significantly different at 24 weeks (0.64 vs. 0.69, Fig.1-D). The same was true for CDAI and SDAI(Fig.1-E,-F). Kaplan-Meier analysis showed that there was no difference in discontinuation rate due to ineffectiveness in the two groups. The same was true for the discontinuation rate due to AEs (Figure 2-B,-C). The total continuation rate including discontinuation due to ineffectiveness and AEs was significantly lower in BAR2mg group (0.691 vs 0.843, p <0.05, Fig.2-A).

Conclusion: BAR2mg group under real clinical setting was older and had lower eGFR than BAR4mg group. Although the treatment effect for 24 weeks was similar, safety management was considered more important because the discontinuation rate due to AEs tended to be higher in BAR2mg group.

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Table. Clinical characteristics of the BAR2mg group and the BAR4mg group

	BAR2mg (n=39)	BAR4mg (n=74)	p value
Age, years old	73.5±9.7	62.3±12.6	<0.001
Female	31(79)	57(77)	0.767
Disease duration, year	13.7±11.3	14.2±15.4	0.857
Stage(1/2/3/4)	6/17/8/8	15/24/14/21	0.473
ACPA >4.5U/ml	29(74.4)	59(79.7)	0.629
eGFR, ml/min/1.73m^2	65.1±27.7	84.8±23.2	<0.001
MTX dose, mg/week	3.03±4.83	5.54±5.48	0.018
MTX use	11(28.2)	41(55.4)	0.003
GC dose, mg/day	1.91±2.36	1.32±2.20	0.191
GC use	20(51.3)	25(33.8)	0.007
DAS28CRP	3.42±1.04	3.52±13.0	0.689
CDAI	12.6±7.6	15.1±10.9	0.222
SDAI	14.7±9.7	16.2±11.4	0.279

Values are the mean±SD or the number (%).

Figure1

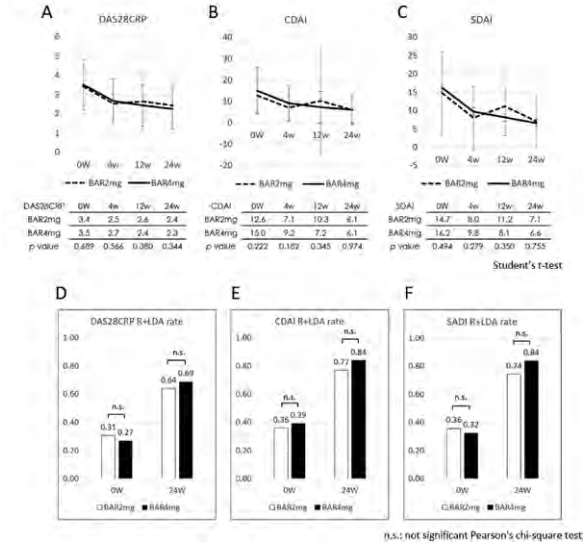
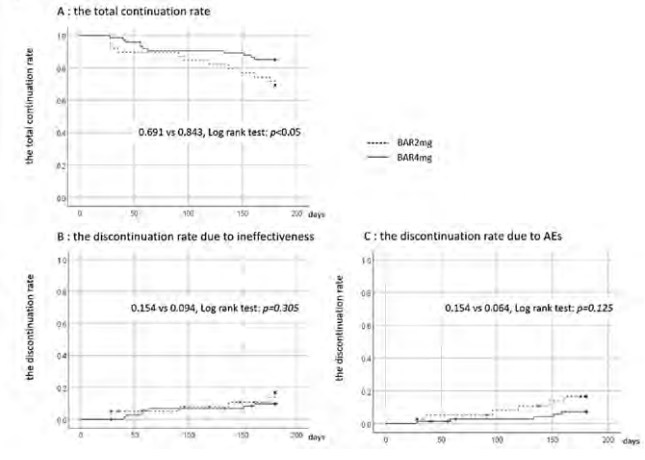


Figure 2



Disclosure of Interests: Tsuyoshi Nishiume: None declared, Nobunori Takahashi Speakers bureau: AbbVie, Asahi Kasei, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eisai, Eli Lilly, Janssen, Mitsubishi Tanabe, Ono, Pfizer, Takeda, and UCB Japan, Toshihisa Kojima Grant/research support from: Chugai, Eli Lilly, Astellas, Abbvie, and Novartis, Consultant of: AbbVie, Speakers bureau: AbbVie, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eli Lilly, Janssen, Mitsubishi Tanabe, Pfizer, and Takeda, Shuji Asai Speakers bureau: AbbVie, Astellas, Bristol-Myers

Squibb, Chugai, Daiichi-Sankyo, Eisai, Janssen, Takeda, and UCB Japan, Kenya Terabe: None declared, Naoki Ishiguro Grant/research support from: AbbVie, Asahi Kasei, Astellas, Chugai, Daiichi-Sankyo, Eisai, Kaken, Mitsubishi Tanabe, Otsuka, Pfizer, Takeda, and Zimmer Biomet, Consultant of: Ono, Speakers bureau: Astellas, Bristol-Myers Squibb, Daiichi-Sankyo, Eli Lilly, Pfizer, and Taisho Toyama
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AB0354 STEPPING UP FOR INFLAMMATORY ARTHRITIS: A PILOT TRIAL TO TEST BEHAVIORAL ECONOMICS STRATEGY TO INCREASE PHYSICAL ACTIVITY IN INFLAMMATORY ARTHRITIS

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Background: Regular physical activity may have benefits for patients with rheumatoid arthritis (RA) and psoriatic arthritis (PsA), but patients with active disease are often reluctant to increase activity. Principles from behavioral economics (BE), a field combining psychology and economics, have been applied to motivate increased physical activity in non-arthritis patients.[1] No published studies have examined the application of BE concepts in rheumatology to promote exercise.
Objectives: To assess the feasibility and efficacy of a loss aversion financial incentive for increasing step counts and improving disease symptoms in RA and PsA patients with active disease.
Methods: A randomized controlled pilot trial was performed among patients with RA and PsA. Participants were required to have active disease defined by having at least one swollen joint and a Routine Assessment of Patient Index Data-3 (RAPID3) score>3 (range 0-30 with <3 indicating remission). The trial included two visits (baseline and 14-week) and weekly check-ins via virtual trial platforms, Way to Health and the ArthritisPower app. Patients were given a Fitbit Alta at baseline and completed a two-week run-in period to assess average step count. Patients were then prompted to select a step count goal and complete a commitment contract. After selection of a goal, participants randomized to the intervention arm received a financial loss aversion incentive (each month, patients started with $75 in their account and lost $2.50 for each day they did not reach their goal). Patients were blinded to the other study arm and investigators were blinded to assignment. All patients received weekly text message prompts providing feedback about their performance over the previous week, completed weekly PROs, and had the opportunity to report adverse events including flares of joint pain. After 12 weeks of the intervention (at week 14), the incentive was removed and patients were followed to 26 weeks to determine how long the effect persisted.
Results: In the pilot trial, 71 patients were verbally consented for screening, 34 underwent screening (of these, two were ineligible), 27 were randomized, and 22 patients completed the 14-week study visit. Mean age of participants was 50 (SD 13), 85% were female, 17(63%) had PsA, mean BMI was 30.6 and mean swollen (0-66) and tender (0-68) joint counts were 6.2 (5.6) and 8.1 (9.1), respectively. Baseline RAPID3 was 10.5 (SD 4.6) and the mean step count at baseline was 5,962. By 28 days, 65% of patients increased their step count. Participants receiving the incentive had an average of 714 more steps per day over the first 14 weeks and a greater probability of reaching 10,000 steps per day during follow-up (30% v. 21%, p=0.41). Among patients who achieved their step count goals more than 50% of days, we observed more improvement in sleep quality, fatigue, and overall well-being (p<0.05) (Figure 1). After adjusting for baseline RAPID3, the 14-week RAPID3 scores were lower in the group that achieved their step goals 50% of the time [B: -3.91 (-11.8, 3.99); a difference that approximates the minimal clinically important difference (MCID) for the RAPID3 (3.6).

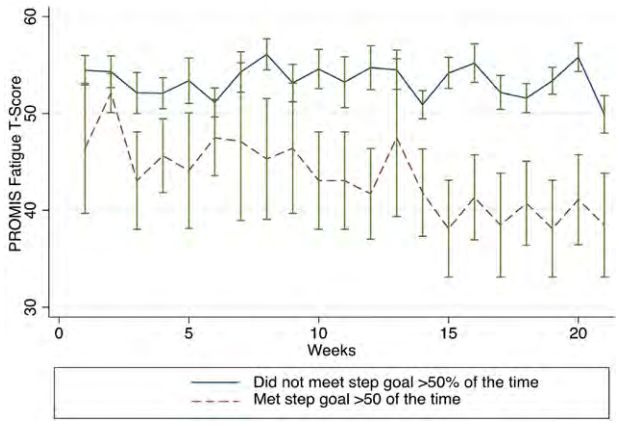


Figure 1. Change in fatigue severity among those with greater adherence to step count goals.

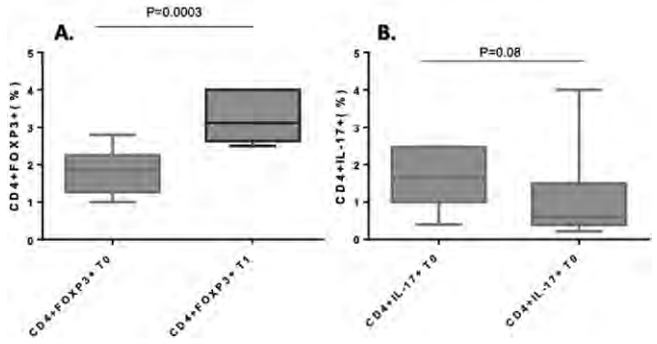
Conclusion: While financial incentives have worked well in patients without arthritis, the estimated effect of the financial incentive in this small study was more modest in patients with RA and PsA. Those that were able to increase their physical activity and meet their step goals had greater improvements in symptoms over the course of the study. These data support further study in this area to promote physical activity by leveraging concepts from behavioral economics.
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[1] Ogdie & Asch. Nat Rev Rheumatol. 2019
Disclosure of Interests: Alexis Ogdie Grant/research support from: Pfizer, Novartis, Consultant of: Abbvie, Amgen, BMS, Celgene, Corrona, Janssen, Lilly, Pfizer, Novartis, Mitesh Patel Shareholder of: Owner, Catalyst Health LLC, Consultant of: Advisory Board Member for Healthmine Services, Life.io, Holistic Industries, Jeffrey Curtis Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Janssen, Lilly, Myriad, Pfizer, Regeneron, Roche, UCB, Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Janssen, Lilly, Myriad, Pfizer, Regeneron, Roche, UCB, Kelly Gavigan: None declared, W. Benjamin Nowell: None declared, Joshua Baker: None declared
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AB0355 EFFECT OF TOFACITINIB IN TREG /TH17 BALANCE IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a systemic chronic autoimmune disease that can cause progressive articular destruction (1). The imbalance between Tregs and Th17-cells - an effector T-cell subset acting as Treg antagonists – is closely linked to autoimmunity (2). A shift in the Th17/Treg balance towards the pro-inflammatory Th17 side has been reported in many autoimmune disorders including RA (4-5). Tofacitinib is the first janus kinases (JAK) inhibitor (JAKi) approved for the treatment of RA and it binds to and competitively inhibits the kinase domain of JAK3, JAK1 and, to a lesser degree, JAK2. Data on JAKi and Th17 cells/regulatory T cells (Tregs) are only available for ruxolitinib, a JAKi registered for myeloproliferative diseases (6).
Objectives: Our project aimed at investigate the possible effect of Tofacitinib on the Treg/Th17 balance in RA patients.
Methods: We isolated Peripheral Blood Mononuclear Cells (PBMCs) from patients affected by RA at baseline (T0) and after one month of Tofacitinib therapy (T1). By flow cytometry we characterized Treg and Th17 at T0 and T1. Clinical and laboratory data of the patients were collected in a standardized, computerized and electronically filled form. We assessed the disease activity by using DAS-28 (CRP). Data were expressed as mean(SD) or median (interquartile range, IQR) according to the variables' distribution. Mann-Whitney and Spearman test were used. The values of $P < 0.05$ were considered statistically significant.
Results: We isolated PBMCs from 9 patients with RA (F:M = 7:2, mean age±SD 60±17.4 years; mean disease duration±SD 20±6.6 years, DAS-28 median at T0 4.14 IQR 1.6; at T1 3.08 IQR 1.3). The median percentage of Treg and Th17 at T0 and T1 were respectively: T0 1.85 IQR 0.98 T1 3.12 IQR 1.37; T0 1.64 IQR 1.4, T1 0.6 IQR 1.1. Treg significantly increased after tofacitinib treatment while Th17 showed a tendency in decreasing without achieving a statistical difference (p= 0.003 and p=0.8, respectively) (figure 1). DAS-28 was negatively correlated with Treg number (r = -0.76565, p = 0.00021) and positively with Th17 numbers (r = 0.5816, p = 0.01135).
Conclusion: This is the first study that investigated the role of JAKi on the Treg/Th17 balance in RA showing and increase in Treg cells with a concurrent tendency in decrease of Th17 cell population. The restore of the Treg/Th17 balance was associated with the reduction of DAS-28 (CRP).
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Figure1. Modification of Treg (A) and Th17 (B) populations at baseline and after one month of Tofacitinib treatment in RA patients.



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AB0356

TARGETING THE RHEUMATOID ARTHRITIS SYNOVIAL FIBROBLAST VIA CYCLIN DEPENDENT KINASE INHIBITION (TRAFIC): A PHASE 1B STUDY TO DETERMINE THE MAXIMUM TOLERATED DOSE OF SELICICLIB FOR REPURPOSING IN RHEUMATOID ARTHRITIS

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Background: Current rheumatoid arthritis (RA) therapeutics target immune inflammation and are subject to ceiling effects, with non-response observed in a third of recipients together with low remission rates. Synovial fibroblasts (SFs) are stromal cells not yet targeted in RA, whose hyperplastic and proliferative properties drive inflammation and tissue destruction. Seliciclib (R-roscovitine) is an orally available cyclin-dependent kinase (CDK) inhibitor that suppresses SF proliferation and ameliorates inflammatory arthritis in rodents.
Objectives: To determine the maximum tolerated dose (MTD) of seliciclib in patients with active RA despite anti-TNF, with or without background conventional disease modifying anti-rheumatic drugs (cDMARDs). Safety and pharmacokinetics (PK) were also evaluated.
Methods: A restricted, one-stage Bayesian continual reassessment method (CRM) determined MTD based on a target dose-limiting toxicity (DLT) probability of 35%. RA patients (DAS28 ≥3.2) were recruited sequentially to cohorts of 3 subjects each. Cohort 1 received 400mg seliciclib daily for 4 consecutive days each week for 4 weeks, added to existing therapy. Each subsequent cohort received a dose determined by the toxicity-based CRM algorithm, calculated upon conclusion of the previous cohort. Safety was assessed through adverse event (AE) monitoring. Associations with relevant PK parameters were sought.
Results: 15 anti-TNF recipients were enrolled, 10 of whom were also taking cDMARDs (median DAS28 4.9). Application of the CRM algorithm prompted one dose increment during the study (to 600mg for cohort 2), but reversion to 400mg for subsequent cohorts (Figure 1*A*). After treatment of 5 cohorts, 400mg was determined the MTD, with a DLT probability of 0.35 (CI 0.18-0.52; Figure 1*B*). 6 patients experienced DLTs, of which two were classified as serious AEs (SAEs) in keeping with the safety profile of seliciclib; these are summarised in Table 1. Of 43/65 total AEs reported at any dose that did *not* contribute to a DLT, 26 were possibly, probably or definitely related to seliciclib; 19 of these 26 were mild, 7 moderate and none severe. The most frequent AE was mild nausea. No relationship of safety and/or tolerability with concomitant cDMARD use or PK was seen.

Table 1. [A]**Outcome of contributory AEs/SAE at close of follow-up.** [B]**SAEs classified as 'expected'. DLT: dose limiting toxicity; N+V: nausea, vomiting.**

DLT	Seliciclib dose (mg)	Doses received	Contributing AEs	Contributing SAEs	Description	Outcome[A]
1	400	8	3	0	Constipation, N+V, liver injury; fatigue.	Resolved
2	600	4	3	0	Constipation, N+V.	Resolved
3	600	1	0	1[B]	Fever, N+V, renal injury.	Resolved
4	400	8	3	1[B]	Constipation, N+V, jaundice, liver injury.	Resolved
5	400	8	4	0	Fever, dizziness, liver injury.	Resolved
6	400	8	9	0	Dizziness, N+V, liver injury, bilirubin rise.	Persistent AST rise

Conclusion: The MTD of seliciclib has been defined for RA. No unexpected safety concerns were identified to preclude ongoing evaluation in patients, which focuses on clinical, radiological and biological indicators of efficacy.

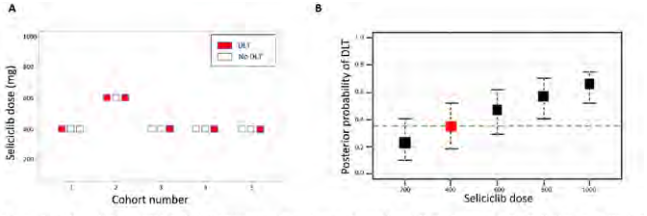


Figure 1. A. Dose limiting toxicity (DLT) occurrence by cohort and dose level (DLTs shown in red). B. Bayesian posterior probability of DLT at each dose level (with 90% confidence interval) following completion of cohort 5. Red point indicates value closest to target of 0.35, and hence maximum tolerated dose (MTD).

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AB0357

USE OF TOFACITINIB AND REASONS FOR DISCONTINUATION IN CLINICAL PRACTICE

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Background: Tofacitinib is an oral JAK 1 and 3 inhibitor for the treatment of moderate to severe active rheumatoid arthritis (RA) or psoriatic arthritis (PsA) in adults with inadequate response or intolerant to one or more conventional disease-modifying antirheumatic drugs (cDMARDs). Since its approval by the European Medicines Agency (EMA), there is limited data about its use in daily practice in Europe.
Objectives: To describe rates and reasons for discontinuation of Tofacitinib in patients with RA and other inflammatory conditions
Methods: We identified patients with a prescription for tofacitinib at our academic center from January 2017 to January 2020. Patients were treated according to their rheumatologist evaluation following standards of care. The following variables were retrospectively collected from the electronic

medical chart: age, gender, diagnosis, date of treatment initiation, date and reasons for treatment discontinuation, the use of concomitant or previous cDMARDs and of biologics. A comparison between patients continuing and stopping tofacitinib was performed through chi^2 or t-test for qualitative and quantitative variables, respectively. Survival analysis was done by Kaplan-Meier method

Results: Ninety patients receiving tofacitinib were identified, 81 with RA, 6 with PsA, 1 with Dermatomyositis, 1 with Sjögren´s and 1 with juvenile idiopathic arthritis. Table 1 shows the baseline characteristics. 84% percent patients were women and the mean (SD) age was 58.5 (14.2) years. 51% patients started tofacitinib in monotherapy. When used, methotrexate was the most frequent cDMARD (61.3%); 10% patients used tofacitinib as first line after cDMARD and the majority used it after 1 or 2 previous biologics (46.7%).

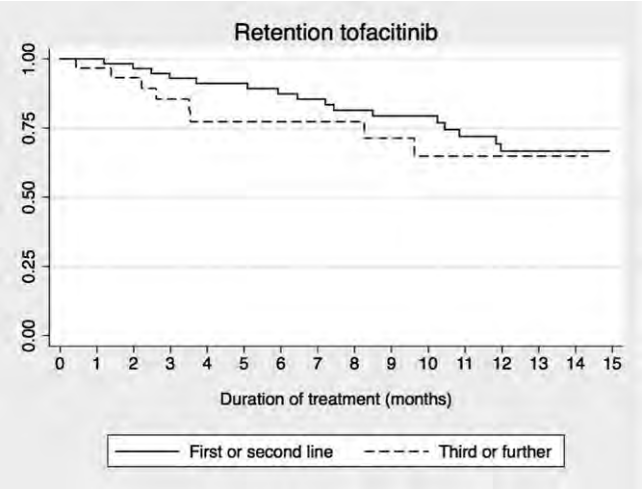
Table 1. Baseline characteristics of the patients

	All patients (n=90, 100%)	Continue Tofacitinib (n=58; 64%)	Not continue Tofacitinib (n=32; 35.5%)	p-value
Female (%)	76 (84.4)	48 (82.7)	28 (87.5)	0.55
Age (year) – mean (SD)	58.5 (14.2)	58 (12.9)	59.5 (16.5)	0.63
Diagnosis				0.66
Rheumatoid arthritis	81 (90)	52 (89.6)	29 (90.6)	
Psoriatic arthritis	6 (6.7)	4 (6.8)	2 (6.2)	
Other	3 (3.3)	2 (3.4)	1 (3.1)	
Treatment duration (months) – mean (SD)	10.6 (6.9)	11.9 (7.3)	8.2 (5.5)	0.02
Prednisone (mg) – mean (SD)	1.75 (3.2)	1.20 (2.5)	2.73 (4.1)	0.03
Monotherapy (%)	46 (51.1)	28 (48.2)	18 (56.2)	0.244
Concomitant csDMARDs (%)	44 (48.8)	30 (51.7)	14 (43.7)	0.62
Methotrexate (%)	27 (30)	17 (29.3)	10 (31.2)	
Leflunomide (%)	10 (11.1)	8 (13.7)	2 (6.2)	
Other (%)	7 (7.7)	5 (8.6)	2 (6.2)	
Prior biologic treatment				0.13
None (%)	9 (10)	6 (10.3)	3 (9.3)	
1-2 (%)	42 (46.6)	28 (48.2)	14 (43.7)	
≥3 (%)	39 (43.3)	24 (41.3)	15 (46.8)	

Survival rates when used as first or second line were 85% at 6 months and 70% at 12 months; when used as third line or further, 76% and 70%, respectively (graphic 1). Factors associated to tofacitinib discontinuation were treatment duration and baseline prednisone dose. In contrast concomitant csDMARD and number of previous biologics were not. Reasons for tofacitinib discontinuation were: lack/loss of efficacy 46.9%, adverse events 50% (including intolerance -22%- herpes zoster -16%-, other infections 12%) and others.

Conclusion: Tofacitinib in our experience is mostly used in RA patients after biologic failure. Overall survival rate at 12 months was good regardless line of therapy. Adverse event rates were similar to other biologic treatments. Herpes zoster was the most common infectious AE.

Graphic 1:



References:

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AB0358

REDUCTION OF WHITE BLOOD CELL COUNT PREDICTS THE EFFICACY OF BARICITINIB, DOES NOT OF TOFACITINIB FOR RHEUMATOID ARTHRITIS.

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Background: Pairing Janus kinase (JAK) 1/JAK3 signaling mediates lymphocyte proliferation and differentiation while pairing JAK2/JAK2 signaling is essential in myelopoiesis, erythropoiesis, and platelet production by facilitating signaling mediated by granulocyte-macrophage colony stimulating factor and erythropoietin. Tofacitinib (TOF) preferentially inhibits JAK1 and JAK3, while baricitinib (BAR) inhibits JAK1 and JAK2 *in vitro* (1). However, the difference in the efficacy and the clinical courses between TOF and BAR in patients with rheumatoid arthritis (RA) remains unclear.

Objectives: The objective of this study was to compare TOF and BAR in efficacy and changes in peripheral blood cell counts. We hypothesized that the efficiency of BAR was related to the decline in the blood cell counts, but that of TOF was not in patients with RA.

Methods: We conducted a multicenter, 24 week-retrospective observational study. All RA patients received TOF (n = 43) or BAR (n = 26) treatment at Tama-Hokubu Medical Center and Tama Medical Center from December 2013 to March 2019 were included.

Results: Baseline characteristics were similar between both groups; age 59.1 and 65.0 years old, disease duration 164.1 and 111.7 months, C-reactive protein 1.98 and 2.22 mg/ml, rheumatoid factor positive 76.7 % and 84.0 %, anti-citrullinated peptide antibody positive 78.9 % and 78.8 %, methotrexate combination 81.4 % and 69.2 %, the number of previous treatment of biologic or targeted disease-modifying antirheumatic drugs were 2.7 and 2.8, for TOF and BAR, respectively (mean).

Simplified Disease Activity Index (SDAI) at baseline were similar between the groups (TOF 20.77, BAR 19.15). There was no significant difference in efficacy between the both groups at week 24 (SDAI remission: TOF 3 (7%), BAR 6 (23.1%), p = 0.054, SDAI low disease activity (LDA): TOF 21 (48.8%), BAR 17 (65.4%), p = 0.181).

Among those who achieved SDAI LDA at week 24 in the BAR group, significant decrement of white blood cell (WBC) counts at week 12 and 24 and of neutrophil counts at week 4, 12 and 24 were observed ($p < 0.05$, Table). These decrements of cell count were not observed in patients who did not achieve LDA or in patients in the TOF group. Platelets and hemoglobin (data not shown) had no significant change in all groups.

Conclusion: Clinical efficacy of TOF and BAR in RA was comparable in our cohort. A significant decrease of WBCs and neutrophils was associated with LDA achievement at week 24 in the BAR group. This could be explained by the inhibition of myelopoiesis through JAK2 signaling.

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Table. Peripheral blood cell counts for each week.

		tofacitinib				baricitinib			
	week	LDA	*p*	not LDA	*p*	LDA	*p*	not LDA	*p*
White Blood Cells [/µl]	0	6821 ± 2402		6041 ± 2612		7994 ± 4309		7886 ± 2513	
	4	6247 ± 1905	.254	6465 ± 2440	.344	6706 ± 2499	.059	7143 ± 1526	.363
	12	6480 ± 1949	.497	5871 ± 2070	.217	6470 ± 2867	.031	7383 ± 2963	.356
	24	6733 ± 2297	.858	6450 ± 3001	.428	6418 ± 2875	.024	6833 ± 1021	.454
Neutrophils [/µl]	0	4888 ± 2399		3982 ± 2300		6221 ± 4085		6221 ± 4085	
	4	4243 ± 1655	.210	4298 ± 2100	.461	4548 ± 2578	.015	5923 ± 2716	.294
	12	4261 ± 1843	.324	3617 ± 1869	.236	4542 ± 3062	.019	5429 ± 3055	.311
	24	4487 ± 2243	.657	4547 ± 2847	.190	4225 ± 2900	.008	4474 ± 1396	.207
Lymphocytes [/µl]	0	1419 ± 651		1305 ± 489		1370 ± 416		1395 ± 485	
	4	1515 ± 544	.357	1502 ± 514	.039	1730 ± 659	.013	1530 ± 652	.484
	12	1537 ± 555	.523	1327 ± 664	.996	1569 ± 572	.011	1453 ± 401	.832
	24	1511 ± 598	.697	1143 ± 378	.092	1792 ± 699	.011	1836 ± 710	.109
Platelets [10^4/µl]	0	26.9 ± 9.1		23.7 ± 6.6		30.3 ± 11.2		26.9 ± 7.4	
	4	25.5 ± 8.9	.291	23.8 ± 6.6	.940	30.5 ± 4.6	.940	27.3 ± 10.8	.798
	12	24.7 ± 7.4	.261	25.6 ± 7.5	.209	33.1 ± 8.3	.209	27.0 ± 9.3	.905
	24	26.3 ± 8.1	.930	23.3 ± 6.1	.961	33.4 ± 6.9	.961	33.0 ± 4.4	.063

Data are mean ± standard deviation. LDA: patients achieved SDAI LDA at week 24. not LDA: patients did not achieve SDAI LDA at week 24. Shown *p* values were calculated by t-test compared to week 0.

Disclosure of Interests: None declared

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AB0359 TNF ALFA THERAPY AND RADIOSYNOVIORTHESIS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The treatment of patients with rheumatoid arthritis (RA) has been spectaculary changed since the 1950's. Introduction of the steroid compounds and their local application, the chemical and radionuclide synovectomy, surgical synovectomy, use of non steroid drugs, the basic treatment and the spread of biological therapy are the most important steps. Introduction of the biological therapy has changed the quality of life for these patients.

Objectives: During biological therapy sometimes 1 or 2 joints could be affected by inflammation. In this cases always the question is how to solve the problem. Change of the biological or basic therapy, use surgical synovectomy or radiosynovectomy (RSO)?

Methods: In our reumatological department 2100 patients with RA were treated with biological therapy between 2002 and 2018. In 100 patients we applied RSO because of the inflammation of the knee joint during biological therapy. We made a long term follow-up in 82 patient. All participants provided written informed consent. 82 participants inflammatory knee joint disease was diagnosed on the basis of the American College of Rheumatology. 70 of 82 patients with rheumatoid arthritis were seropositive, 12 seronegative. Steinbrocker functional stadium II was observed in 72, stadium III in 10. Mean age of 18 male and 76 female patients was 51.4 years (range 24-79) years. In 42 patients the right knee, in 40 the left knee was treated by radiosynovectomy. Mean duration of disease was 8.3 years (range 0.5-25), of synovitis (6.3month (range 3-8) Mean number of punctions of the treated joint prior to radiosynovectomy was 4,2 per patient and of steroid administrations prior to radiosynovectomy 3,0. In 15 patients a systemic steroid therapy has been performed.

Results: During the study period, inflammation decreased. In the first 3 years excellent and good results were recorded in 81,2%. 3 years after radiosynoviorthesis 82.2% of patients did not need another punction.

Before the knee inflammation patients were in complete remission which status has been achieved after RSO as well. DAS: 2,4+-0,4.

Conclusion:

1. RSO is an effective method to treat the inflammation of the knees.
2. The RSO performed during biological tehrapy is as effective as in the case of patients without biological therapy.
3. In case of a successful RSO there is no need for biological or basic therapy neither for surgical synovectomy.
4. However an intraarticular injection has a low risk for infection it is recommended to avoid the biological therapy during the RSO.

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AB0360 EFFICACY AND SAFETY OF THE PROSTAGLANDIN EP4 RECEPTOR ANTAGONIST CR6086 ADDED TO METHOTREXATE IN DMARD-NAÏVE EARLY RA PATIENTS: A PHASE 2 RANDOMIZED CONTROLLED TRIAL

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Background: MTX is the first line treatment in early RA. There is robust evidence from cohort studies, but less from RCTs, that a "window of opportunity" exists over 12-16 weeks symptom duration. CR6086 is a selective prostaglandin EP4 receptor antagonist, with an immunomodulatory profile.

Objectives: To test efficacy and safety of CR6086 added to MTX in early RA, DMARD-naïve patients.

Methods: Patients with RA (ACR/EULAR 2010 criteria), < 1 year from symptom onset and naïve to DMARDs were randomized to oral CR6086 30, 90, 180mg, or placebo bid and oral MTX (20mg weekly) for 13 weeks (NCT03163966). Primary endpoint was the ACR20 response rate: 240 patients were needed to detect a difference among groups, with 50% responders on placebo and 70% on the 90mg CR6086 target dose. Pairwise comparisons of proportions were performed, with nonresponder imputation for withdrawals. A subgroup of patients underwent dynamic contrast-enhanced (DCE) MRI for quantification of synovitis at MCP and wrist joints, evaluated as DEMRIQ-ME and DEMRIQ-vol.

Results: The ITT population included all 244 randomized patients receiving at least one dose of study drugs (59 CR6086 30mg/MTX, 60 CR6086 90mg/MTX, 63 CR6086 180mg/MTX, 62 placebo/MTX). Safety was good with no increased rate of infections or other disorders; however, there were more minor upper GI adverse events (AEs) with CR6086, and increased dropouts due to AEs with the 180mg dose (9/63, 14.3% vs 1.7-3.4% in other groups). There were more ACR20 responders with MTX monotherapy than predicted (59.7%) and thus the 10.3% difference with the 90mg target dose (70.0%) was not significant. The low 30mg dose was no better than placebo (55.9%), while the high 180mg dose did not provide additional benefit compared with 90mg (74.0% net of dropouts). CR6086 90mg and 180mg induced a significant improvement in MRI, compared with placebo (Fig. 1). In a post-hoc analysis in patients < 6 months from symptom onset (ACR definition of early RA: 98/244, 40.2%), MTX monotherapy exerted a large 76% ACR20 response rate that precluded potentiation. Conversely, in patients of 6-12 months disease duration (146/244, 59.8%) ACR20 responders were 48.6% with MTX monotherapy vs 68.4% with 90mg, i.e. a 19.8% difference as postulated, with proportional differences in secondary endpoints (Tab. 1).

Conclusion: There was no benefit demonstrated for CR6086 added to MTX in the study cohort as a whole. However, in a post-hoc analysis, enhanced responses were observed with CR6086 90mg bid added to MTX in patients >6 months disease duration. This generated the hypothesis that addition of CR6086 90mg bid may benefit in RA patients initiating MTX after the window of opportunity, to be tested in further studies.

Table 1. ITT outcomes at week 13

	Symptom onset <12 months (principal analysis)		Symptom onset 6-12 months (post-hoc analysis)*	
	Placebo +MTX (N=62)	CR6086 90mg +MTX (N=60)	Placebo +MTX (N=37)	CR6086 90mg +MTX (N=38)
ACR20, %	59.7%	70.0%	48.6%	68.4%
ACR50, %	33.9%	38.3%	29.7%	39.5%
ACR70, %	17.7%	23.3%	10.8%	28.9%
DAS28 (CRP) <2.6, %	12.9%	20.0%	8.1%	18.4%
CDAI ≤2.8, %	8.1%	11.7%	5.4%	15.8%
SDAI ≤3.3, %	6.5%	10.0%	2.7%	15.8%
Boolean-based remission, %	6.5%	6.7%	2.7%	10.5%

*In patients with symptom onset <6 months, MTX monotherapy exerted a large 76% ACR20 response, and correspondingly high secondary efficacy parameters, precluding potentiation in this subset

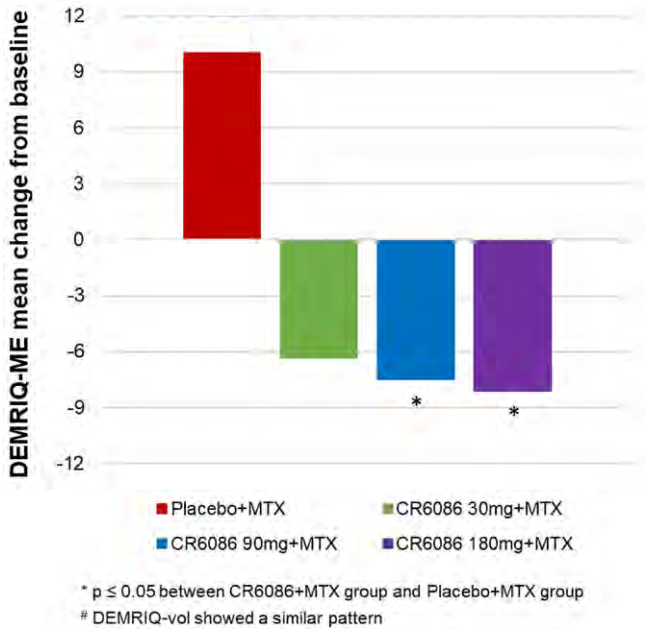


Figure 1. Change in MRI (DEMRIQ-ME#) after 13 weeks

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AB0361

EFFICACY AND SAFETY OF BARICITINIB (BARI) IN RHEUMATOID ARTHRITIS(RA): CLINICAL AND ULTRASOUND EVALUATION IN REAL LIFE

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Background: Remission or low disease activity (LDA) are the ultimate goals of both conventional synthetic (csDMARD), target synthetic and biologic disease-modifying anti-rheumatic drugs (bDMARD) in treating RA. Janus Kinase (JAK) inhibitors are nowadays part of tsDMARDs, with BARI as an oral selective JAK1-2 inhibitor. Ultrasound (US) is a valuable imaging tool for detecting inflammatory joint changes and monitoring RA patients. The US7 score (US7) is a semiquantitative score including grayscale (GS) and power Doppler (PD) measurements of synovitis and tenosynovitis in 7 joints of the clinically dominant hand and foot.
Objectives: to evaluate real life efficacy and safety of BARI 4 mg in RA patients using clinical, clinimetric and US evaluation.
Methods: adult RA patients starting BARI were eligible. DAS28ESR, CDAI, SDAI, painVAS, HAQ, COCHIN, laboratory parameters and US7 were performed/collected at baseline (BL) and after 3 and 6 months. Adverse events (AE) and concomitant medications were recorded. Responder/non responder status was determined using DAS28ESR improvement according to the EULAR Response Criteria at 3 months. Moreover, SDAI clinical remission or LDA (remission: SDAI≤3,3; LDA:3,3<SDAI≤11) were calculated at 3 and 6 months.
Results: 43 patients (12 csDMARD and 31 bDMARD failure) were enrolled, with 30 patients starting BARI in combination with a csDMARDs. BL painVAS was 68±23mm and disease activity was moderate to severe according to DAS28VES, CDAI and SDAI. BARI determined a significant improvement of every disease activity composite score and US7 components, except tendon PD; steroid daily dosage was significantly reduced.
28 patients were considered Responders at 3 months: responders used to have higher disease activity levels and synovitis scores at baseline.
Interestingly, painVAS and steroid dosage significantly decreased both in responders and non-responders, achieving similar value at 6 months. Non-responders showed both synovial and tendon involvement relapse at 6 months, with significantly higher PD score compared to responders. Remission was reached by 12,8% patients at 3 months and 21,6% at 6 months, while LDA patients were respectively 53,8% and 51,3%; combination with csDMARD was the only factor positively associated with remission/LDA at 3 months.
The percentage of dropped-out patients due to AE was aligned with literature data (5% in 6 months) whereas the percentage of Herpes Zoster Virus (HZV) infections was higher (4,6% in 6 months in our population vs 4,3% in 1 year in RCTs). Corticosteroid dosage was directly associated with AE development at 6 months.
Conclusion: Real life data confirmed BARI RCTs efficacy and safety data. Non responders showed both synovial and tendon PD disease relapse, despite painVAS and steroid reduction were comparable to responders. In our population, HZV infection prevalence was higher than in RCTs and corticosteroid dosage was positively associated with AE development at 6 months.

	BL		3M		p value	6M		p value
	R	NR	R	NR		R	NR	
painVAS	67,88±23,37	58,18±22,72	30,19±23,52	45,64±25,48	p=0.0040	30,19±20,42	29,73±22,15	p=0.2105
Daily prednisone equivalent	5,97±5,57	5,45±4,30	2,96±3,02	3,95±3,63	p=0.2248	1,63±2,10	3,03±3,59	p=0.1247
GSS	8,50±5,25	7,00±3,81	3,69±3,63	2,33±2,45	p=0.9334	3,56±3,01	4,22±2,64	p=0.2452
GST	2,88±2,33	3,11±2,09	0,88±0,89	1,56±1,59	p=0.6501	1,00±1,37	2,78±1,72	p=0.0831
PDS	8,00±7,11	3,33±3,46	3,00±3,48	2,44±3,36	**p=0.0066**	3,25±3,13	5,00±4,56	**p=0,0006**
PDT	2,81±2,46	2,44±3,36	0,88±1,54	1,33±1,50	p=0.44990	1,06±1,53	3,78±3,19	**p=0.0156**
Erosions	1,25±2,05	0,44±0,73	1,50±2,03	0,44±0,73	p=0.0736	1,31±2,09	1,11±1,27	p=0.0902

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AB0362 HERPES ZOSTER IN BARICITINIB-TREATED JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS USING REAL-WORLD CLINICAL DATA

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Background: Similar to biologic disease-modifying anti-rheumatic drugs, the association between Janus kinase (JAK) inhibitors and infection is particularly interesting. The incidence of herpes zoster (HZ) among patients treated with JAK inhibitors is twofold to threefold higher in several regions of Asia (e.g., Japan and Korea) as compared with that observed in North America and Western Europe [1].
Objectives: To evaluate the characteristics of patients who developed HZ during baricitinib treatment using real-world, multicenter, clinical data for Japanese population.
Methods: The study enrolled 97 patients with rheumatoid arthritis (RA) who were treated with baricitinib therapy (68 biologic-naïve patients and 29 biologic-experienced patients) were enrolled in the study (observation period: 2–27 months). The severity of HZ infection was determined based on the extent of the rash and the presence or absence of organ damage. We evaluated the characteristics and clinical courses of patients who developed HZ.
Results: Eight patients with HZ. The incidence ratio (IR) was 8.2 per patient-year. Patient data are described in Table 1 and Table 2. The IR was a little higher than that reported in clinical trials [2], which could be attributed to the high average age (i.e., 67.3 years) of the patients in this study. It was reported that adverse events occurred more frequently in elderly patients aged ≥65 years compared with younger patients [3]. The period from baricitinib administration to the onset of HZ varied between 2 months and 16 months. It is suggested that HZ may develop at any time during baricitinib therapy. There were no distinctive patient characteristics, except for age, at the time of initial baricitinib administration between patients who developed HZ and those who did not.

Table 1. Characteristics of patients who developed HZ at initiation of baricitinib

Case-No.	Age (years)	Time (years) from RA onset	Gender Female:F Male: M)	BMI	Bari dose (mg/d)	PSL(mg/d)	MTX (mg/w)	HZ history	Number of prior biologics
1	74	1.5	F	25.6	4	0	12	No	2
2	61	33	F	19.2	2	0	6	No	1
3	61	11.1	F	23.6	4	0	10	Yes	0
4	73	0.5	M	23.3	4	0	8	Yes	0
5	74	21.9	F	20.9	2	0	0	No	0
6	78	1.2	F	19.8	4	0	6	No	0
7	48	23.2	F	24.1	4	4	8	No	0
8	79	5.0	F	22.4	2	2.5	4	No	0

Table 2. Clinical coutcome of patients who developed HZ at initiation of baricitinib

Case No.	HZ incidence period after baricitinib administration (months)	Priod of baricitinib withdrawal (weeks)	Severity (Mild; Mil Moderate: Mod)
1	16	4	Mod
2	2	4	Mod
3	13	1	Mil
4	3	1	Mil
5	8	6	Mod
6	3	4	Mil ~ Mod
7	3	3	Mod
8	20	Discontinuation due to pateient's choice	Mod

None of the patients had severe symptoms, and none of them experienced organ damage. All patients were cured with anti-viral agents. It should be noted that patients who had a history of HZ had milder symptoms than those who had no history of HZ. We noted an interesting finding in one patient (case 2). The half-life of baricitinib in the blood was very short (about 6 hours), and it is reported that the drug is almost fully excreted from the body 24 hours after its administration [4]. However, this patient developed an incidence of HZ at 17 days after the withdrawal of baricitinib for surgery management. Cells may take longer time to regain their original immune status even after excretion of the drug, especially, during intense stress such as in cases of surgical invasion.
Conclusion: The HZ risk in Japanese patients with RA treated with baricitinib in real-world practice was high, especially in elderly patients. It is notable that HZ events were nonserious and that patients could restart baricitinib treatment after healing with antiviral therapy, for the most part.
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AB0363 SAFETY OF JAK INHIBITORS IN PATIENTS WITH ARTHRITIS RHEUMATOID UNDER REAL-LIFE CONDITIONS

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Background: Efficacy and safety profile of new JAK inhibitors have been properly defined by several clinical trials, being tested in many patients with Arthritis Reumatoid. However, real-life conditions studies play an important role in order to know JAK inhibitors behaviour in safety.
Objectives: To describe adverse events of JAK inhibitors in patients with Arthritis Rheumatoid and asses the survival in relation to adverse events.
Methods: Observational, descriptive, retrospective design performed in patients with Arthritis Reumatoid in follow-up by the Rheumatology department of the Hospital de Valme until January 2019. Demographic and clinical data related to safety has been collected
Results: 58 patients were included with a mean age of 57,77 ± 10,78 years. Mean time from diagnosis was 8,7 ± 6,54 years, female predominance (75%). Mean ASDAS at the beginningof JAK inhibitor treatment was 4,76 ± 0,93. Regarding the determination of FR and CCCP 69% and was positive in both cases. Baricitinib was the treatment chosen in 13 patients (22.4%), and Tofacitinib in 45 patients (77.6%). Regarding associated treatments: 84.5% was under low-dose steroids theraphy; 77.6% was under combined therapy with at least 1 DMARD; 15.5% with two of them. Metotrexato was used in 53,4% of patients, leflunomide in 19%, hydroxycloroquine in 13.8%, sulfasalazyne in 12.1%. 72,4% have been before under at least one biologic treatment (frequently antiTNF), 41,1% one of them, 15.5% two of them, 12.1% three and 1.7% four before starting Jak inhibitor therapy. Adverse events has been observed in 17 patients (13 from de Tofacitinib group -28.8%-, and 4 in the Baricitinib group -30.76%). The most common advers events were: herpes zoster infections (4 patients in Tofacitinib group), respiratory infections (3), urinary infections (2), cutaneous (3), caphalea (1), legs oedema (2), toxic hepatitis in 1 patient of Baricitinib group; pulmonary thromboembolism was observed in 1 patient of Tofacitinib group, and atrial fibrillation in other patients of that group. Treatment was interrupted in 24 of 58 patients (mean time 8.92 ± 5.14 months), 16 from Tofacitinib group (35.5% of patients with Tofacitinib) and 8 from Baricitinib group (61.15% of patients with Tofacitinib). In Tofacitinib group, 10 patients stopped therapy for inefficacy reasons and 6 for advers effects related. In Baricitinib group, 5 due to inefficacy, 2 to adverse effects and 1 to clinical remission.
Conclusion: Main adverse effect were mild-moderate infections (involving in-hospital treatment only in one Barictinib group patient). One pulmonary thromboembolism has been detected in a hypertensive 70 years old patient, supporting the recent recommendation of avoiding these drugs in patients over 65 or with cardiovascular risk factors. It is remarkable low survival results due to inefficacy, that could be related to clinical profile of refractory patients in our study, and/or to the small sample that we describe.
Disclosure of Interests: None declared
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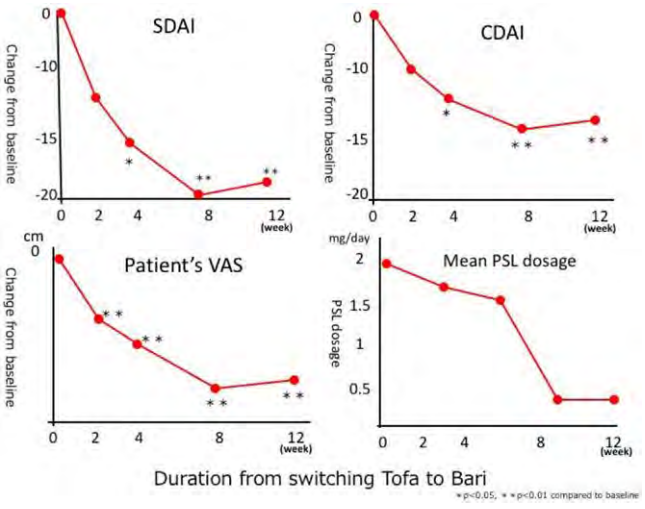
AB0364

EFFICACY OF BARICITINIB (BARI) IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA) WHOSE RESPONSE WAS INADEQUATE TO TOFACITINIB (TOFA).

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Background: Currently, four types of JAK inhibitors are approved for the treatment of RA in Japan, however, they often show differences in clinical efficacies presumably due to their JAK selectivity.
Objectives: To investigate the efficacy of Bari for patients with Tofa-inadequate response (IR), clinical profiles of seven Tofa IR patients were evaluated.
Methods: We performed a single-center retrospective study on seven Tofa IR patients (female:7) who were switched to Bari. Items evaluated were as follows; patient's baseline characteristics, continuation rate of Bari, swollen joint count, tender joint count, C-reactive protein (CRP), matrix proteinase 3 (MMP3), physician's and patient's visual analog scale (VAS), disease activity assessed by Disease Assessment Score of 28 joints - C-reactive protein (DAS 28-CRP), simplified disease activity index (SDAI) and clinical disease activity index (CDAI) at 2, 4, 8, 12 weeks, and the dosage of prednisone (PSL).
Results: Patient's mean age was 56.4 and mean disease duration was 9.2 years. Tofa had administered for 3.4 months (range 1-10) before switching to Bari. All patients were positive for both anti-citrullinated protein antibodies and rheumatoid factor. The number of prior biologics use was 2.3 (range1-4). 3 patients had concomitant MTX use (mean dosage 5.3 mg/week) and 4 had prednisone (mean dosage 3.3 mg/day). Mean swollen joint counts and tender joint counts were 5.0 (range 1-15) and 5.3 (range 1-15), respectively. Physician's and Patient's VAS 0-100 were 71 mm (range 50-90) and 73 mm (range 50-80), mean CRP levels were 1.6 mg/dl (range 0.01-4.3) and MMP3 levels were 357.3 mg/dl (range 27-933). Mean SDAI, CDAI and DAS-28-CRP were 26.3 (range17-50), 24.7 (range17-47) and 4.5, respectively. When enrolled, 4 of 7 patients corresponded to moderate disease activity (MDA) and 3 were in high disease activity (HDA) by all composite measures. After switched to Bari, the patient's VAS significantly decreased at week 2 (P <0.01). CDAI, SDAI and DAS28-CRP also showed a significant improvement at week 4, (P <0.05). At week 4, 2 patients discontinued Bari due to the lack of efficacy or acute exacerbation of interstitial pneumonia. Thus, continuation rate of Bari at week 12 was 71.4%. Among 5 patients who continues Bari, all patients achieved low disease activity (LDA) by SDAI and CDAI at week 12. By DAS 28-CRP, 2 patients achieved MDA, 2 achieved LDA and 1 achieved remission (mean 2.6), respectively, at week 12, 3 of 4 patients taking PSL were able to withdraw that before week 12 (Figure).
Conclusion: Result showed the efficacy of Bari for patients with Tofa IR, representing inadequate improvements of patient's VAS with Tofa. The efficacy of Bari can be expected from the early stage and continued up to 12 weeks after switching. This difference in therapeutic effect may be due to each mechanism of action, Bari inhibits JAK1/2, whereas Tofa mainly inhibits JAK1 /3 (1). JAK2 is important for signal by GM-CSF, which has shown potential as an important therapeutic target in RA (2).Inhibition of JAK2 and GM-CSF may be the reason for Bari efficacy in Tofa IR patients.
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AB0365

COMPARISON OF SUSTAINED CLINICAL REMISSION AND/OR LOW DISEASE ACTIVITY RATE BETWEEN RAPIDLY AND GRADUALLY DE-ESCALATION OF BARICITINIB IN RHEUMATOID ARTHRITIS.

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Background: However baricitinib, an oral selective inhibitor of Janus kinase (JAK) 1 and 2, improved signs and symptoms of rheumatoid arthritis (RA), it is unknown who can taper or stop baricitinib and strategies for de-escalation.
Objectives: We analyze predictors of tapering of withdrawal failure in rheumatoid arthritis (RA) patients treated with baricitinib. This study will assess and compare (1) characteristic of patients who achieve remission (REM) or low disease activity (LDA) as who can taper baricitinib and (2) two de-escalation methods, rapidly and gradually de-escalation in patients who respond first-line therapy.
Methods: Cases were recruited to SHin-yokohama Arthritis REgister (SHARE) between 2015 and 2019 (n=3,674). Patients were diagnosed according to ACR/EULAR 2010 classification criteria, and treated with DMARDs which included baricitinib 2mg/day (n=154). In 154 cases, Clinical Disease Activity Index (CDAI), Health Assessment Questionnaire-Disability Index (HAQ-DI), anti-CCP2 and patients clinical parameters were analyzed. Two de-escalation methods were compared in this study. In rapidly de-escalation methods, baricitinib were stopped in patients with stable REM/LDA over 12 weeks. In gradually de-escalation methods, baricitinib were decreased to 50%, 42%, 28%, 14% in order with stable REM/LDA over 12 weeks.
Results: In 154 (Male25, Female129 cases, RA duration 11.4+/-8.0 years) cases, CDAI at baricitinib-start was 20.6+/-12.4 and titer of anti-CCP2 was 242.6+/-516.5 U/ml. 126 cases (81.8%) were more than 2 years of RA duration and 49 cases (31.8%) had persistency of signs and/or symptoms suggestive of inflammatory RA disease activitiy, despite prior treatment with csDMARDs and at least two biologic DMARDs. 33 cases (21.4%) were biologic DMARDs naive.
(1)"Multivariate logistic regression examined the predictors to detect who can taper baricitinib" However there were no differences in duration of RA, onset age of RA, biologics and/or JAK inhibitors naïve, anti-CCP2 titer and CDAI at the start baricitinib, patients who showed decrease of CDAI at 12 weeks were correlated with achievement of remission (REM) or low disease activity (LDA) in patients treated with baricitinib (OR 0.964, 95%CI 0.934-0.996, p=0.010). ROC analysis of ΔCDAI at 12 weeks is cut-off value of -6.6 (p=0.011).
(2)"Comparison of sustained REM and/or LDA rate between rapidly and gradually de-escalation of baricitinib in rheumatoid arthritis" 11 cases were tapered baricitinib with rapidly de-escalation methods and 60 patients were with gradually de-escalation. Mean times to start taper baricitinib in rapidly and gradually de-escalation group were 4.6+/-1.6 months and 5.9+/-2.2 months respectively. Gradually de-escalation methods showed less relapse rate compared with rapidly de-escalation after tapered baricitinib for 6 months (18.3% vs. 54.5%, p=0.018). There were no differences in clinical features such as anti-CCP2, CDAI and administration period of baricitinib between non-relapse and relapse patients in gradually escalation methods.
Conclusion: A combination of ΔCDAI at 12 weeks and tapering baricitinib using gradually de-escalation methods may help to predict successful baricitinib deduction in RA patients with sustained clinical REM and/or LDA.
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16. SLE, Sjögren's and APS - treatment

AB0366

DIFFUSE ALVEOLAR HEMORRHAGE IN LUPUS NEPHRITIS PATIENTS: MULTICENTER RECTROSPECTIVE STUDY

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Background: Diffuse alveolar hemorrhage (DAH) is a rare and potentially lethal complication of systemic lupus erythematosus (SLE) with a high mortality rate. It occurs more frequently in patients with lupus nephritis (LN).
Objectives: The aim of our study is to explore the characteristics of patients that develop DAH with lupus nephritis, risk factors that predispose DAH, treatment response and outcomes.
Methods: Multicenter retrospective cohort study was undertaken including 6 centers in Saudi Arabia from 2002 to 2018. Systemic lupus erythematosus patients meeting the SLICC criteria with lupus nephritis (biopsy proven or proteinuria or renal impairment due to lupus) presenting with diffuse alveolar hemorrhage (fulfilling a predefined criteria) were included in the study. An identical number of control group with lupus nephritis was also studied. Data was obtained from medical records by using a data sheet: demographics including age, gender, diagnosis, date of diagnosis of lupus, date of presentation of alveolar hemorrhage, clinical presentation, detection of alveolar hemorrhage proved by radiology, lavage or biopsy and laboratory parameters: including level of hemoglobin before and during DAH, sign of activity, treatment and outcome of DAH. Identification of risk factors predisposing to DAH in lupus nephritis patients was analyzed.
Results: We identified 23 cases of DAH with lupus nephritis, all fulfilling the criteria. Mean age at presentation of DAH was 31.09 ± 12.6 years ranging from 14-57 years, of which 87 % were females. 13 patients 56.5% had Class 4 LN and 21.7% had Class 4 and 5 LN on renal pathology. DAH occurred at a mean of 6.5 years ±3.8 in 13/23 patients with LN. Shortness of breath 95%, new chest x ray finding 95.7% and mean drop of haemoglobin of 2.72 gm/dl ±0.97 were more frequent at presentation of DAH with LN patients. High SLE disease activity - SELENA SLEDAI 2K was 38.56 ±19.3 was present at the onset of DAH. All were treated with methyprednisone,15/23 (65.2%) underwent mechanical ventilation and plasmapheresis was done in 21/23 patients (91.3%). Cyclophosphamide was given in 14/21 patients (60.9%), Intravenous immunoglobulins were given in 14/23 patients (65.2%) and dialysis was done in 12/23 patients (52.2%). Mortality occurred 8 patients 34.8 %. In comparison with the LN group, a mean haemoglobin of 7.56 ± 1.3, CNS involvement, vasculitis and fever>38% were of statistically significance P value: <0.001,0.02,0.03 and 0.03 respectively.
Conclusion: In this multicenter cohort series with DAH in LN patients CNS involvement, vasculitis and fever>38 were associated in the occurrence of DAH. Mortality was low in our cohort in comparison to previous series which may be explained by early diagnosis and use of aggressive management.Well designed prospective studies are required to identify high risk patients for preventing this serious complication.
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AB0367 USING UNSUPERVISED CLUSTERING ANALYSIS OF REAL LIFE DATA FROM AN ONLINE COMMUNITY TO IDENTIFY LUPUS PATIENTS' PROFILES REGARDS TO THEIR TREATMENT PREFERENCES

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Background: Lupus is a prototype of a chronic complex autoimmune disease. Non-adherence rate to treatment is surprisingly high and impairs its management. Adherence to drug treatment is a complicated and multifactorial phenomenon, including characteristics of treatment.
Objectives: This study used unsupervised clustering analysis to identify profiles among lupus patients with regards to their treatment preferences (apart from efficiency).
Methods: An online survey among adult lupus patients from Carenity was conducted between August 2018 and April 2019. Multiple Correspondence Analysis (MCA) of a French lupus patient dataset was used with 3 unsupervised clustering methods (hierarchical, kmeans and partitioning around medoids).
Results: The 268 participating lupus patients were mostly female (96%), with a mean age of 44.3 years, and 83% fulfilled the ACR SLE diagnostic criteria. Overall, the preferred galenic form was oral (62%), and the most important characteristic was fewer side effects (32%).
A MCA was performed using 8 profile variables and the best unsupervised clustering method for this dataset (hierarchical clustering) identified 3 clusters (Table 1). Cluster 1, main one (59%), comprised patients with few comorbidities, less capacity to identify coming flares, and that wanted mostly (84%) oral treatments with limited side effects, most of them (83%) already on oral treatments. Cluster 2, the smallest one (13%), comprised younger patients, having already participated in clinical trials, favoring implants and the compatibility of treatments with pregnancy. Cluster 3 comprised patients (28%) that had longer lupus duration but less controlled disease with more comorbidities. A third had injectable treatments, wanting mainly implants and injections and with the main goal of reducing corticosteroids. The robustness of these results was confirmed by external validation and sensitivity analyses.

Table 1. Description of the three clusters

	Overall n=268	Cluster 1 n=158	Cluster 2 n=36	Cluster 3 n=74	p-value
Most represented age group (%)	41-50 (32%)	41-50 (41%)	31-40 (42%)	51-60 (39%)	< 0.001
Comorbidities 0 / ≥ 4	20% / 37%	30% / 4%	14% / 8%	3% / 36%	< 0.001
Ability to identify coming flare	82%	73%	97%	93%	< 0.001
Current lupus control (no or poor)	26%	20%	25%	38%	< 0.05
Current galenic (inj. / oral)	12% / 76%	2% / 83%	8% / 78%	35% / 61%	< 0.001
Trial participation	7%	0%	50%	1%	< 0.001
Ideal galenic oral	62%	84%	50%	20%	< 0.001
implant	19%	9%	33%	32%	
home / auto-inj.	14% / 9%	6% / 2%	11% / 11%	32% / 22%	
hospital inj.	6%	1%	5%	15%	
Top ranked drug characteristics[$] (%)	Side effects (32%)	Side effects (41%)	Pregnancy (55%)	Cortisone sparing (24%)	< 0.001

[$]among the 10 following items: less side effects, compatibility with pregnancy, better long term tolerance, less costly for collectivity, more convenient place for administration, easier administration, less medical follow-up needed, less risk of infection, cortisone sparing effect, shorter time of administration. P-values obtained after $\chi 2$ tests. Inj.: injection.

Conclusion: Most lupus patients preferred a drug galenic favoring the conservation of their autonomy. The identified clusters could help physicians to tailor their therapeutic proposition taking into account patients' preferences and to maximize therapeutic adherence. Our study also highlights the potential of using unsupervised machine learning techniques in combination with direct-access patient community data to provide new a priori knowledge in the field of rare and complex chronic diseases.
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AB0368 TREATMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITH BELIMUMAB – PROSPECTIVE OBSERVATION OVER 2 YEARS

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Background: Systemic lupus erythematosus (SLE) is autoimmune connective tissue disorder of unclear etiology. It is characterized by autoantibody production and a variety of clinical manifestations. The introduction of biological treatment over the past few years provided an opportunity for a disease control.
Objectives: The aim was to assess the effectiveness and safety profile of Belimumab in the treatment programs of SLE patients during a 2 year period.
Methods: We initiated a prospective observational study of SLE patients in the Rheumatology Department in University Hospital St Marina – Bulgaria. The study comprises data from 26 patients at baseline before Belimumab treatment initiation and data after 6, 12, 18 and 24 months of treatment. All patients were with moderate disease activity according to SELENA – SLEDAI index and were on treatment with immunosuppressive drug (azathioprine) and glucocorticoids (GCs). We observed the change in the dosage of glucocorticoids over the observed period, the number of flares of SLE, as well the SELENA – SLEDAI index change. Safety profile of Belimumab was also registered.
Results: We included 26 patients with SLE over a period of 4 years – between 2015 and 2019. The mean age was 45.8 + 11.4 years and 94% were Caucasian females. All patients were on a stable dosage of GCs at least 3 months before the first infusion of Belimumab and azathioprine 100 mg daily. Ninety percent of patients were diagnosed with SLE for more than 6 years according to ACR – SLE criteria. All of SLE patients were with moderate disease activity. Main reasons for biological treatment decision were persistent mucocutaneous manifestations

(20%), polyarthritis (15%), haematological disturbances (35%) and persistent immunological markers (30%). One patient was excluded from the study due to infusion- related flush and severe hypotension reaction while the rest 25 completed the observation. We investigated and analyzed haematological results, ANA, anti – ds DNA, anti – Sm autoantibodies and complement fractions at baseline as well on the 12th and 24th month of treatment. The mean SELENA – SLEDAI index changed from 8.9 to 4.5 after 12 months of treatment and remained unchanged until the end of the study. We observed a mean reduction of GCs daily dosage from 12 mg to 6 mg after 18 months.

Conclusion: Biological treatment with Belimumab added to the standard treatment with GCs and AZA in patients with non-lupus nephritis SLE patients adds additional benefits. Our results show that there is a reduction in SLEDAI index as well as reduction in daily GCs intake. Safety profile is not different from the one reported previously.

Disclosure of Interests: None declared

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AB0369 EFFICACY AND SAFETY OF RITUXIMAB ORIGINATOR AND BIOSIMILAR IN PRIMARY SJÖGREN'S SYNDROME IN A REAL-LIFE SETTING

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Background: Over the last 2 decades rituximab (RTX) has been widely used, albeit off-label, in primary Sjögren's syndrome (pSS). Several studies reported that B-lymphocyte depletion with RTX is effective in this disease not only by reducing disease activity but also by affecting the inflammation and the lymphoid organization that occur in target tissues. With the recent release of several RTX biosimilars (bRTX) on the market, the demonstration of their interchangeability with RTX originator (oRTX) is required.

Objectives: To compare efficacy and safety of oRTX and bRTX in pSS patients in a real-life setting.

Methods: Clinical records of pSS patients referring to a tertiary rheumatology clinic were retrospectively evaluated. Patients having received at least 2 courses of either oRTX or bRTX (1000 mg IV infusion, repeated after 2 weeks -1 course- and the course repeated after 24 weeks) with complete data at baseline and after 3, 6, 9 and 12 months of treatment were enrolled. Disease activity was assessed with the EULAR SS disease activity index (ESSDAI) and its clinical version without the biological domain (ClinESSDAI). Patient-reported symptoms were assessed with the EULAR SS Patient Reported Index (ESSPRI).

Results: Seven patients that received oRTX and 7 patients that received bRTX were enrolled. Baseline clinical features, including ESSDAI and ESSPRI were similar in the 2 treatment groups. Both compounds significantly reduced ESSDAI and ESSPRI as early as 3 months and no difference between the groups was observed at any time point (Figure 1). Of interest, ESSDAI slowly decreased until month 6 when the most pronounced reduction was observed. Conversely, ESSPRI dropped to its lowest values already at month 3. With regard to safety, at 12 months of follow-up no adverse event was observed in any of the treatment groups.

Conclusion: At 12 months of follow-up, oRTX and bRTX display similar efficacy and safety profiles. The improvement of patient reported outcomes is faster than the improvement of disease activity with both compounds. Our data support interchangeability of oRTX and bRTX in pSS.

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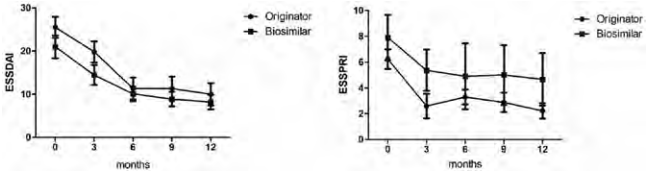


Figure 1 ESSDAI and ESSPRI values at every time point in the 2 treatment groups. Asterisks indicate p values <0.05 compared to the other treatment group at the same time point

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AB0370 SAFETY OF CS20AT04, A HAPLOIDENTICAL ALLOGENEIC BONE MARROW-DERIVED MESENCHYMAL STEM CELLS, IN A PHASE 1 STUDY IN LUPUS NEPHRITIS

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Background: Mesenchymal stem cells are known to have immunomodulatory properties and may potentially have therapeutic effect in lupus nephritis. Mesenchymal stem cells form a haploidentical donor are an attractive cell source

Objectives: CS20AT04, a haploidentical allogeneic bone marrow-derived mesenchymal stem cell, was evaluated in patients with lupus nephritis for safety and tolerability.

Methods: This was a single-arm phase 1 dose-escalation trial of CS20AT04 in adult patients with lupus nephritis (NCT03174587). A 3+3 design was used for dose escalation. The starting dose was 2.0 x 106 cells/kg and was escalated to 3.0 x 106 cells/kg if there no dose-limiting toxicity. The primary objective was to determine the maximum tolerated dose and evaluate the safety and tolerability at 28 days after the infusion.

Results: Seven patients were enrolled in the study. Patients received CS20AT04 through intravenous infusion. The initial dose of 2.0 x 106 cells/kg was administered for the first 3 patients without any dose limiting toxicity. There was 1 patient who were not administered the full 2.0 x 106 cells/kg dose due to technical error during infusion. The patient did not show dose limiting toxicity, but 1 additional patient was enrolled to have 3 patients who received the full 2.0 x 106 cells/kg dose before escalating to the next level dose. The dose of 3.0 x 106 cells/kg was administered for the next 3 patients without any dose limiting toxicity. Three adverse events were reported (1 diarrhea, 1 toothache, and 1 arthralgia) and they were all NCI-CTC grade I events.

Conclusion: CS20AT04 was well tolerated in single dose up to 3.0 x 106 cells/kg in patients with lupus nephritis.

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AB0371 HYDROXYCHLOROQUINE AS VIEWED BY LUPUS PATIENTS – WHAT IMPACT FOR DOCTORS?

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Background: Hydroxychloroquine (HCQ) is recommended for all patients with systemic lupus erythematosus (SLE) and is typically considered as having a good safety profile[1]. Yet, patient organisations observe that concerns about eye impact or "allergies to HCQ" are often raised on social media. This could contribute to the non-adherence, which varies from 3 to 76% in SLE patients depending on assessment method and drug[2].

Objectives: To understand if/how some patients' beliefs impact adherence to HCQ treatment.

Methods: In May 2019, LUPUS EUROPE launched a 29 questions on-line survey in 13 languages including questions on HCQ adherence.

2938 responses were analysed. 67.8% (1990 patients) were current HCQ users, 17.8% had stopped using it, 8.1% never had HCQ (6.4% did not respond to this question). 1820 users reported their adherence level. 314 (17.3%) were classified as "low" adherence as they reported missing/forgetting HCQ "always" (1.8%), "more than twice a week" (5.2%) or "once a week" (10.3%)

Results: The prescribed HCQ dose, kidney involvement or duration of treatment (beyond the 1st year) were found to have no impact on low adherence. Similarly, the user belief that HCQ has significant side effects, without experiencing these, was not found to impact adherence (p=.74).

The following factors were associated with better adherence: (p<.0001)

- The belief that HCQ is "Very important" (12.9% "low") rather than "important" (22.1% "low") or "not important / useless" (33.1% "low").
- Taking many different medications (9.8% "low" for Patients indicating more than 7 medications vs 19.8% for those listing 3 or less)

Childhood onset of the SLE was associated with a lower adherence (30.0% "low" vs. 17.4% for later onset SLE (p<.001)

658 patients (29.6%) reported having experienced side effects. 42.6% of them stopped taking HCQ (patient led 161, doctor led 110, unclear 9). Amongst those continuing HCQ despite experiencing side effects, the proportion of non adherent patients increased to 24.7%, compared to 15.2% in the group of patients that have not experienced side effects (p=.0001). The 232 patients who talked with their Doctor and felt listened to appear to adhere better (22.0% low adherence) than the 84 who did not feel heard (31.0% low adherence), but the significance is only directional (p=<0.15)

523 patients have used HCQ in the past. 206 (39.4%) consider the decision to stop HCQ as doctor initiated, 272 (52.0%) as patient initiated, and 36 (6.9%) as a joint decision.

When stopping was patient initiated, 59.9% was due to experiencing a significant side effect attributed by the patient to HCQ, 6.7% due to concern of a potential side effect, 11.2% "tested" stopping and noticed no difference, 10.0% were not convinced that it worked, 8.2% felt their lupus was less active, 2.6% wanted to reduce pill consumption. (Side effects attributed to HCQ may relate to age, disease activity or other factors).

Conclusion: Doctors can help HCQ adherence by boosting patient's confidence in the importance of HCQ. Better patient education may contribute to avoid up to 40% of patient initiated decision to stop HCQ treatment.

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Disclosure of Interests: None declared

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AB0372 PREGNANCY OUTCOME IN WOMEN WITH SJÖGREN SYNDROME IS OFTEN COMPLICATED BY PLACENTA INSUFFICIENCY

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Background: Chronic inflammatory rheumatic diseases are often associated with a negative effect on pregnancy outcome. Most obstetrical complications are placenta-mediated such as preterm delivery and growths restrictions. In women with Sjögren syndrome, data on placenta- mediated complications are scarce and conflicting (1,2).

Objectives: To analyse neonatal outcome in women with Sjögren syndrome with focus on preterm delivery and growth restriction.

Methods: We retrospectively analysed 23 pregnancies of 16 patients with Sjögren syndrome that were followed at our centre with regard to pregnancy outcome, medication and disease characteristics. Small for gestational age was defined as birthweight percentile <10th. Preterm delivery was defined as delivery before 37, early term as delivery between 37-39 and term as delivery between 39-42 weeks of gestation.

Results: Of 23 pregnancies, one ended in a miscarriage and 22 resulted in live births including one set of twins. Treatment used during pregnancy was hydroxychloroquine (20 pregnancies), prednisone (8), azathioprine (5) and cyclosporine (2). Concomitant treatment with low-dose aspirin was used in 9 pregnancies.

Of the 22 live births, 17 were born at early term and 5 at term. There were no preterm deliveries. Median birth weight was 2820g (range 2095-3845g). Nine newborns (40.9%) were small for gestational age (SGA). Maternal treatment during these pregnancies was hydroxychloroquine in all cases and additional low-dose aspirin in three cases. Elevated CRP levels during pregnancy were found in 57% of the cases with SGA outcome. Only one woman with an SGA infant had positive anti-phospholipid antibodies.

Regarding delivery mode, most patients had caesarean sections.

Conclusion: In our cohort of women with Sjögren syndrome the prevalence of small for gestational age infants was high despite maternal treatment with hydroxychloroquine. Inflammatory markers could help to identify the patients at risk for placental insufficiency, yet prospective studies of larger cohorts are needed.

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AB0373 TREATMENT OF SLE WITH THE IMMUNOPROTEASOME INHIBITOR KZR-616: RESULTS FROM THE FIRST 4 COHORTS OF THE MISSION STUDY, AN OPEN-LABEL PHASE 1B DOSE ESCALATION TRIAL

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Background: Non-specific proteasome inhibitors, such as bortezomib (BTZ), target the constitutive proteasome and immunoproteasome and are approved treatments for multiple myeloma[1]. BTZ has also been used to treat systemic lupus erythematosus (SLE) and lupus nephritis (LN); however, treatment emergent adverse events (TEAEs), such as gastrointestinal (GI) effects, hematologic abnormalities, asthenia and peripheral neuropathy, limit its use as a long-term treatment option for chronic autoimmune disease[2]. KZR-616 is a first-in-class selective immunoproteasome inhibitor and is highly active in murine SLE[3]. Subcutaneous (SC) administration of KZR-616 (30 and 45 mg weekly [QW]) was demonstrated as safe and well-tolerated, and successfully achieved target levels of immunoproteasome inhibition in healthy volunteers[4, 5].

Objectives: We report the preliminary safety and efficacy of KZR-616 in the first 4 cohorts of the Phase 1b portion of Study KZR-616-002 in patients with active SLE (NCT03393013).

Methods: SLE patients (per SLICC Classification Criteria) with SLEDAI ≥4 despite stable background immunosuppressant, anti-malarial, and/or corticosteroid (≤20 mg prednisone equivalent) therapy in this open-label multicentric dose-escalation trial received KZR-616 at doses of 45mg (Cohort 1), 60mg (Cohort 2), or 30mg with escalation to 60mg (Cohorts 2a and 2b) SC weekly through Week 13 (W13) with 12 weeks of follow-up. Efficacy measures included SLEDAI, Cutaneous Lupus Erythematous Disease Area and Severity Index, 28 tender and swollen joint counts, Physicians Global Assessment, Patient Global Assessment, and Patient Assessment of Pain, in evaluable patients (those who received ≥1 month of KZR-616).

Results: As of 16 January 2020, 33 patients had enrolled and received at least 1 dose of KZR-616. The majority of TEAEs have been mild or moderate with no reported peripheral neuropathy, prolonged GI-related AEs, and no clinically significant laboratory AEs. There were 3 treatment emergent SAEs, one each of thrombotic microangiopathy (Cohort 2), localized herpes zoster (Cohort 2a), and systemic inflammatory response syndrome (Cohort 2a) with the latter 2 patients completing the full 13 weeks of treatment after resolution. When compared to baseline, improvement in all measures of disease activity were seen at W13 and maintained or improved during the follow-up period, and 94% of evaluable patients had improvements on at least 2 measures/assessments of disease activity. A single patient with active class IV/V nephritis was enrolled on prednisone 10 mg, leflunomide 10 mg, and hydroxychloroquine 200mg/day; nephrotic-range proteinuria at baseline (3.85 g/day) decreased to 0.6 g/day 4 weeks after the last dose of KZR-616.

Conclusion: Weekly subcutaneous administration of KZR-616 at 45 and 60 mg was safe and well-tolerated. Evidence of disease suppression at W13 in active SLE patients on stable background therapy was observed. In addition, one study participant with active proliferative nephritis was enrolled with significant reduction in proteinuria. The Phase 2 portion of this study in active proliferative LN is open for enrollment.

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AB0374 LUPUS LOW DISEASE ACTIVITY STATE AND MAINTAINING DRUG THERAPY: A RETROSPECTIVE INVESTIGATION

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Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune multisystemic disease, that can begin with a wide range of clinical manifestations, and requires immunosuppressive therapies (1). A treat-to-target strategy leads to a high rate of clinical remission among patients (2). Several "remission" definitions have been provided in the last years and Lupus Low Disease Activity State (LLDAS) seems one of the best tools to evaluate it in clinical practice (3).
Objectives: To evaluate the prevalence of SLE signs and symptoms at onset and the drugs used to induce and maintain the clinical remission, evaluated by LLDAS, in a real-life cohort of SLE patients.
Methods: Thirty female SLE patients (mean age 52±15 years; mean age at disease onset 34±16 years, mean disease duration 18±13 years) in clinical remission have been enrolled (EULAR/ACR 2019 criteria) (4). Remission was defined by LLDAS (SLEDAI-2K < 4 and no activity in major organ systems, no hemolytic anemia; no new features of activity compared with previous assessment, physician global assessment (PGA) ≤ 1, prednisone dose ≤7.5 mg/day, well tolerated and stable therapy with maintenance doses of immunosuppressive drugs). Clinical and serological manifestations, SLEDAI-2K and pharmacological treatments were recorded at baseline and during follow-up.
Results: Mucocutaneous involvement (57%), arthritis (30%), serositis (30%), nephritis (27%), leukopenia (23%), thrombocytopenia (20%), hemolytic anemia (13%), antiphospholipid syndrome manifestations (16%), neuro-psychiatric lupus symptoms (6%) were present in various combinations at disease onset. Baseline mean SLEDAI-2K was 10.5±2.5. Patients were treated with different dosages of glucocorticoids (100%), hydroxychloroquine (HCQ, 73%), cyclofosfamide (20%), mycophenolate mofetile (MMF, 13%), azathioprine (AZA, 13%), methotrexate (MTX, 13%), cyclosporine A (CSA, 6%), rituximab (3%), abatacept (ABA, 3%). Glucocorticoids were prescribed together with a single DMARD in 50% of cases and with two DMARDs in the remaining 50% of patients. Patients reached LLDAS remission after a mean time of 14±12 years, with a mean remission duration of 4.2±3.2 years (mean SLEDAI-2K at last visit 1±1; Mean PGA 0.4±0.1). Maintenance therapies during remission were prednisone ≤ 5 mg/day and/or HCQ ≤ 400 mg/day and/or CSA ≤ 200 mg/day and/or MTX ≤ 10 mg/weekly and/or MMF ≤ 2 g/day and/or AZA ≤ 100 mg/day. In particular, only prednisone 7%, only HCQ 3%, prednisone + HCQ 53%, prednisone + single DMARD (different from HCQ) 7%, prednisone + HCQ + DMARDs 30%.
Conclusion: After reaching the clinical remission by a treat to target strategy, the administration of low dose of prednisone and HCQ in the majority of SLE patients (63%) seems useful to prevent new SLE flares. The retrospective design and the absence of a control group of patients with active disease limit this study.
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AB0375 SAFETY AND BENEFICIAL EFFECTS OF HYDROXYCHLOROQUINE ON PREGNANCY OUTCOMES IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: The use of hydroxychloroquine (HCQ) has long been established in Systemic Lupus Erythematosus (SLE) and especially as applicable drug during pregnancy. Recently, beneficial effects and safety of HCQ have been re-discussed in the light of a change in the summary of product characteristics in some countries. More current studies are required to provide patients with evidence-based advice regarding this essential drug when counselling for pregnancy.
Objectives: To examine the impact of HCQ on pregnancy outcomes of SLE women.
Methods: Pregnancies of women with SLE from an outpatient pregnancy clinic were prospectively evaluated before and throughout gestation. Maternal and fetal outcomes in women without HCQ therapy (group A) were compared to pregnancies under HCQ treatment from 1st trimester on (group B). A multiple logistic regression was performed with adjustment for confounding factors.
Results: We enrolled 184 live births from singleton pregnancies in 145 women (n=77 with HCQ and n=107 w/o HCQ). One neonatal death (group B) occurred after severe preeclampsia at 24 weeks of gestation (w/g) linked to noncompliance in a woman with high-risk aPL profile. One child (group B) was born with mycophenolate mofetil embryopathy.
Women in the HCQ group had a significantly lower rate of preterm births [aOR 0.31 (95%-CI: 0.15-0.64), p = 0.026]. Regarding preeclampsia, we found a tendency towards less incidence with the use of HCQ [aOR 0.49 (95%-CI: 0.23-1.03), p = 0.24]. These improved outcomes are opposed by a higher frequency of risk factors in group B (lupus nephritis, high-risk aPL profile, slightly more hypertension) and a tendency towards more severe SLE (expressed in terms of increased use of Azathioprine) (Table 1). Nevertheless, women with HCQ

Table 1. Patient characteristics & pregnancy outcomes

		All pregnancies (n=184)	No HCQ in pregnancy (n=107)	HCQ during pregnancy (n=77)
	Age (years), median (IQR)	31.0 (28.0-34.0)	31.0 (29.0-34.0)	30.0 (27.0-33.0)
	Hypertension, n (%)	29 (15.8%)	16 (15.0%)	13 (16.9%)
	Preconception counselling, n (%)	122 (66.3%)	69 (64.5%)	53 (68.8%)
SLE disease & therapy characteristics	Disease duration (years), median (IQR)	6.7 (2.9-10.3)	7.0 (3.0-10.0)	6.7 (2.1-11.0)
	Lupus nephritis*1, n (%)	51 (27.7%)	25 (23.4%)	26 (33.8%)
	High-risk aPL profile*2, n (%)	39 (21.3%)	21 (19.8%)	18 (23.4%)
	SLEDAI*1, median (IQR)	2.0 (0-4.0)	2.0 (0.0-4.0)	2.0 (2.0-4.0)
	Anti-dsDNA, n (%)	102 (55.7%)	47 (44.3%)	55 (71.4%)
	Anti-SSA/Ro and/or Anti-SSB/La, n (%)	91 (49.7%)	55 (51.9%)	36 (46.8%)
	Azathioprine*1, n (%)	38 (20.7%)	18 (16.8%)	20 (26.0%)
	Low dose Aspirin*3, n (%)	74 (41.1%)	34 (32.7%)	40 (52.6%)
Obstetrical history	Nulliparous, n (%)	113 (61.4%)	63 (58.9%)	50 (64.9%)
	Previous fetal loss, n (%)	39 (21.2%)	22 (20.6%)	17 (22.1%)
	Previous (pre-)eclampsia or HELLP, n (%)	14 (7.6%)	8 (7.5%)	6 (7.8%)
	Previous congenital heart block, n (%)	1 (0.54%)	-	1 (1.3%)
Pregnancy outcome	(mild-moderate) flare*4, n (%)	44 (29.5%)	30 (34.9%)	14 (22.2%)
	Preterm birth*5, n (%)	46 (25%)	30 (28.0%)	16 (20.8%)
	Preeclampsia, n (%)	24 (13%)	15 (14.0%)	9 (11.7%)
	Intrauterine growth restriction, n (%)	3 (1.7%)	1 (1.0%)	2 (2.6%)
	Congenital heart block, n (%)	1 (0.54%)	-	1 (1.3%)

*1last visit before pregnancy, *2according to the 2019 EULAR recommendations, *3until 16 w/g, *4increase in SLEPDAI ≥ 4 or increase in prednisolone ≥ 5mg/d, *5< 37 w/g

therapy experienced significantly less flares during pregnancy [aOR 0.18 (95%-CI: 0.09-0.38), p = 0.013].

Conclusion: In our cohort, SLE women with additional risk factors achieved a favourable pregnancy outcome. This encouraging result is in part attributable to pregnancy counselling with the advice to continue HCQ throughout gestation.

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AB0376 DETERMINANTS AND PROTECTIVE EFFECTS OF A LOW DISEASE ACTIVITY STATE IN SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS FROM A PROSPECTIVE CHINESE COHORT

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Background: The concept of treat to target in systemic lupus erythematosus has moved forward in recent years. The Lupus low disease activity state (LLDAS) defined by the Asia-Pacific Lupus Collaboration (APLC) in 2016 has been validated prospectively in the APLC cohort itself and retrospectively in multiple other cohorts.

Objectives: The concept of treat to target in systemic lupus erythematosus has moved forward in recent years. The Lupus low disease activity state (LLDAS) defined by the Asia-Pacific Lupus Collaboration (APLC) in 2016 has been validated prospectively in the APLC cohort itself and retrospectively in multiple other cohorts. The aim of this study was to investigate the frequency and determinants of achieving LLDAS, and the influence of LLDAS on short term outcomes including disease flare and damage accrual in Chinese lupus patients.

Table 1-Determinants of achieving LLDAS for at least 50% of follow-up time by univariate and multivariate logistic regression analysis

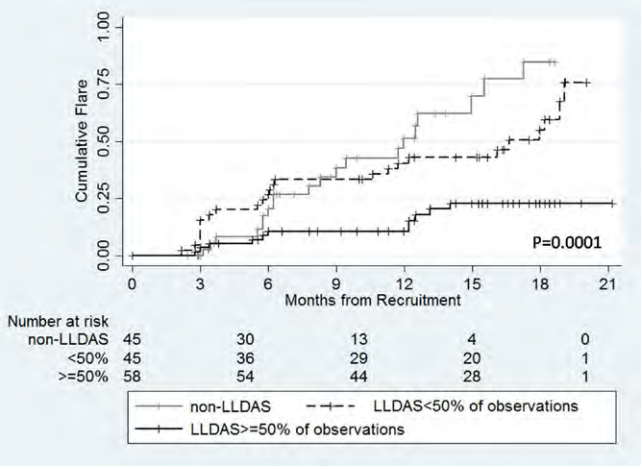
Variables	Univariate analysis			Multivariate analysis		
	OR	95% CI	P value	OR	95% CI	P value
Gender-Female	5.25	0.94-24.02	0.057			
Onset age<30 years old	0.54	0.28-0.99	0.047	0.05	0.01-0.59	0.017
Disease duration at recruitment*	0.98	0.94-1.03	0.434			
Organ involvements∞						
Skin & mucous involvement	0.75	0.38-1.47	0.403			
LN	0.62	0.32-1.21	0.162			
NPSLE	0.84	0.27-2.64	0.764			
AIHA	0.38	0.10-1.44	0.157			
Thrombocytopenia	0.94	0.44-1.98	0.866			
PAH	1.15	0.25-5.34	0.857			
Laboratories at recruitment						
Anti-dsDNA positive	0.67	0.27-1.64	0.382			
C3 (mg/L)	1.003	1.001-1.005	0.002	1.004	1.001-1.008	0.028
UTP (mg)	0.997	0.995-0.999	0.005	0.9992	0.9987-0.9998	0.007
Scr (μmol/L)	0.98	0.97-0.99	0.049	0.98	0.96-1.00	0.094
IS treatment for at least 6 months∞	0.39	0.15-0.96	0.040	0.30	0.02-3.50	0.333

* Years: disease duration at recruitment defined as time from disease onset to recruitment.
∞ Present ever during course of disease.
Abbreviations: LN=lupus nephritis; NPSLE=neuropsychiatric SLE; AIHA=autoimmune hemolytic anemia; PAH=pulmonary arterial hypertension; Scr=serum creatinine; IS: Immunosuppressant.

Table 2 -Determinants of disease flare by univariate and multivariate Cox regression analysis

Variables	Univariate analysis			Multivariate analysis		
	HR	95% CI	P value	HR	95% CI	P value
Gender-Female	0.80	0.38-0.71	0.568			
Age at disease onset (years)	0.97	0.95-0.99	0.004	0.97	0.95-0.99	0.026
Disease duration at recruitment (years)*	1.01	0.98-1.05	0.504			
Organ involvements∞						
Skin & mucous involvement	1.40	0.81-2.43	0.230			
LN	0.76	0.45-1.28	0.298			
NPSLE	0.74	0.29-1.85	0.513			
AIHA	1.10	0.64-1.87	0.735			
Thrombocytopenia	0.88	0.47-1.63	0.683			
PAH	1.13	0.35-3.62	0.842			
Laboratories at recruitment						
Anti-dsDNA positive	1.43	0.82-2.5	0.209			
C3 (mg/L)	0.996	0.995-0.998	0.000	0.997	0.996-0.999	0.001
UTP (mg)	0.998	0.993-1.002	0.450			
Treatments						
Prednisone or equivalent dose at recruitment	1.00	0.99-1.02	0.684			
IS for 6months∞∞	1.21	0.57-2.58	0.614			
Percentage time of LLDAS€	0.10	0.04-0.25	0.000	0.18	0.07-0.48	0.001

* Years: disease duration at recruitment defined as time from disease onset to recruitment.
∞ Present ever during course of disease.
∞∞ Using immunosuppressant for 6 during whole follow-up
€ Percentage time of LLDAS in whole follow-up time
Abbreviations: LN=lupus nephritis; NPSLE=neuropsychiatric SLE; AIHA=autoimmune hemolytic anemia; PAH=pulmonary arterial hypertension.



Methods: The baseline and follow-up data of all consecutive patients in a longitudinal lupus cohort from January 2017 to December 2018 were collected prospectively. SLEDAI-2K, PGA and disease flare were assessed at each follow-up visit, and further compared to the previous routine clinical visits. Irreversible disease damage was captured using the SLICC damage index and the short form (36) health survey for health-related quality of life was completed annually.

Results: One hundred and forty-nine patients were enrolled, with the median disease duration at recruitment of 2.4 (0.9–8.2) years, and median follow-up of 15.4 (10.1-18.2) months. By the end of the study, 104 (69.8%) patients

achieved LLDAS at least once; 59 patients achieved LLDAS for≥50% of observations. Multivariate logistic regression analysis showed that age at disease onset< 30 years (OR=0.05, 95%CI [0.01-0.59], p=0.017), 24-hour urine total protein (UTP) level at recruitment (OR=0.9992, 95%CI [0.9987-0.9998], p=0.007), and C3 level (OR=1.004, 95%CI [1.001-1.008], p=0.024) had independent associations with achieving LLDAS for ≥ 50% of all observations (Table 1). During follow-up, 56 (37.6%) patients experienced disease flare including 14 (9.4%) patients with severe flare. Kaplan-Meier analyses showed significant differences in flare rates according to whether LLDAS was achieved and the percentage follow-up time in LLDAS (Figure 1). Multivariate cox analysis revealed that the percentage time of time in LLDAS was an independent negative determinant of disease flare (HR=0.18, 95% CI [0.07-0.48], p=0.001) (Table 2). There were 16 (15.0%)/107 patients who had damage accrual after one year of follow-up. Multivariate logistic analysis showed a tendency for achieving LLDAS during follow-up being protective for damage accrual (OR=0.27, 95%CI [0.07-1.00], p=0.050).

Conclusion: In this Chinese early disease cohort, LLDAS was an attainable goal in clinical practice. Age at onset, UTP and C3 level at recruitment influenced achievement of LLDAS. LLDAS was negatively associated with disease flare and damage accrual; this needs to be confirmed by future longer follow-up.

Acknowledgments: The data in this cohort was collected and recorded using the framework of the lupus low disease activity status (LLDAS) study from the Asia-Pacific Lupus Collaboration (APLC).

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AB0377 COMPUTATIONAL DISCOVERY AND PRECLINICAL VALIDATION OF THERAPEUTIC LEADS WITH NOVEL MOAS FOR SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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Background: Lupus is a heterogeneous, systemic disease that affects millions of patients globally with a high unmet medical need. We present results from our powerful and efficient computational drug discovery platform that identifies hits with first-in-class mechanisms of action that can advance rapidly and successfully through preclinical validation studies. The twoXAR discovery platform uses an artificial-intelligence framework to integrate diverse patient-derived biomedical data sets to build holistic and unbiased models of human disease biology. The utilization of diverse, proprietary algorithms and deep learning principles provides a highly sensitive platform to elucidate complex disease-specific associations between biology and biomedical data that are integrated with a library of existing drug molecules. This enables the identification of novel, high-value drug discovery hits with known pharmacological properties. The twoXAR platform also preserves interpretable data-driven links to disease biology to facilitate efficient validation and optimization studies.

Objectives: Apply twoXAR's computational drug discovery platform for the discovery of first-in-class lupus therapy hits and perform preclinical characterization of selected hits to identify drug discovery lead molecules.

Methods: Using clinical SLE patient data, we employed the twoXAR platform to build an *in-silico* SLE disease model. Nine molecules with novel mechanisms of action (not previously tested as candidate clinical therapies for lupus) were identified as drug discovery hits and then characterized in preclinical efficacy studies using the MRL mouse model of lupus.

Results: In preclinical validation studies with the MRL mouse model, 2 compounds were differentiated by significant efficacy and excellent tolerability. TXR-711 and TXR-712 increased renal function, decreased renal inflammation and decreased inflammation compared to vehicle-treated control mice. In particular, TXR-711 and TXR-712 significantly decreased serum blood urea nitrogen (BUN) levels, decreased proteinuria levels, and significantly improved kidney histology readouts such as glomerulonephritis and tubule basophilia. Additionally, TXR-711 and TXR-712 treatment resulted in significantly decreased inguinal lymph node weight.

Conclusion: TXR-711 and TXR-712 were identified as SLE drug discovery leads with novel MOAs for further preclinical development. Ongoing studies with TXR-711 and TXR-712 includes pharmacokinetic, pharmacodynamic, and additional MRL mouse efficacy characterization.

Disclosure of Interests: Isaac Hakim Employee of: twoXAR, Inc, Sana Mujahid Employee of: twoXAR, Inc., Aaron C. Daugherty Employee of: twoXAR, Inc., Timothy S. Heuer Employee of: twoXAR, Inc

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AB0378 UPGRADING THERAPY STRATEGY IMPROVES PREGNANCY OUTCOME IN ANTIPHOSPHOLIPID SYNDROME: A COHORT MANAGEMENT STUDY

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Background: While it is generally agreed that pregnant APS patients should receive personalized treatment, evidence-based guidelines for these patients continue to be lacking.

Objectives: The current study was designed as a management cohort study aiming to evaluate the efficacy and safety of different treatment strategies for pregnant APS patients in the attempt to provide some practical suggestions for attending physicians.

Methods: One-hundred-twenty-seven consecutive pregnancies were assessed; 87 (68.5%) with a history of pregnancy morbidity alone were treated with prophylactic low molecular weight heparin (LMWH)+low-dose aspirin (LDA, 100 mg) [Group I] and 40 (31.5%) with a history of thrombosis and/or severe pregnancy complications with therapeutic LMWH+LDA [Group II]. LMWH doses were increased throughout the pregnancies depending on the patients' weight gain, and treatment was switched to a more intensive one at the first sign of maternal/fetal complications. The study's primary outcome was live births.

Results: There were no significant differences in live birth rate between Group I (95.4%) and Group II (87.5%). Even, fetal complication rate was similar in the two groups; the Group II nevertheless had a higher prevalence of maternal and neonatal complications (p=0.0005 and p=0.01, respectively) and registered a significantly lower gestational age at delivery and birth weight (p=0.0001 and p=0.0005, respectively). Two patients in Group I switched to Group II therapy, six patients in Group II switched to a more intensive treatment strategy (weekly plasma exchange+ fortnightly intravenous immunoglobulins in addition to therapeutic LMWH+LDA). Comparison of the clinical and laboratory characteristics between patients who had shifted to a more intensive therapy and those who did not showed a significant prevalence of history of thrombosis ± pregnancy morbidity (p=0.02, OR 5.96, 95% CI 1.33-26.62) previous pregnancy complications (p=0.02, OR 8.32, 95% CI 1.67-41.3), triple aPL positivity (p <0.0001, OR 97.13, 95% CI 10.6-890) and pregnancy complications (p<0.0001, OR 197,7, 95% CI 10.57-3699) in upgrading group, instead single aPL positivity significantly prevailed (p=0.003, OR 0.06, 95% CI 0.008-0.58) in non-upgrading group. Logistic regression analysis demonstrated that triple aPL positivity was an independent factor for switching to a more effective therapy protocol (p <0.0001, OR 98, 95% CI 10.7-897.54). All eight switched patients achieved a live birth.

Conclusion: Using adjusted LMWH doses and upgrading therapy at the first signs of pregnancy complications led to a high rate of live births in a relatively large group of APS patients. The study outlines the criteria for prescribing appropriate therapy for various subsets of these patients and for switching/upgrading the treatment protocol when it is no longer sufficient. Unfortunately, for the moment there are no evidence-based guidelines on the ideal additional treatment in refractory to conventional therapy APS patients. The present results will hopefully help point the direction of future clinical trials investigating the efficacy and safety of the different therapies on large numbers of APS pregnant patients in order to identify the benefits and limits of different treatment strategies administered from the beginning of pregnancy.

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AB0379

IS MYCOPHENOLATE SODIUM (MYFORTIC) SIMILARLY EFFECTIVE AS MYCOPHENOLATE MOFETIL (CELLCEPT) IN TREATMENT OF LUPUS NEPHRITIS? EXPERIENCE FROM NON-MEDICAL SWITCHING REAL WORLD DATA IN TAIWAN

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Background: Lupus nephritis is the most important predictive factor of morbidity and mortality in SLE. Though Mycophenolate mofetil is recommended for induction and maintenance treatment of class III, IV V lupus nephritis, it is not approved by US or Taiwan FDA (TFDA). In previous reports of kidney transplantation, no efficacy differences were observed between mycophenolate sodium (Myfortic) and mycophenolate mofetil (Cellcept). However, no clinical trial was conducted to compare these two widely-used mycophenolic acid derivatives in lupus nephritis. In December, 2016, TFDA approved Mycophenolate sodium in treatment of lupus nephritis. For reimbursement issue, patients treated with mycophenolate mofetil were non-medically switched to mycophenolate sodium in Taiwan.
Objectives: To compare the treatment efficacy of mycophenolate mofetil and mycophenolate sodium in lupus nephritis patients with non-medical switching.
Methods: Between 2016 and 2018, a retrospective observational study enrolled 50 biopsy-proven LN patients in Taichung Veterans General Hospital, Taiwan. All these patients were initially treated with Cellcept for at least one year. Treatment response was evaluated by urinalysis and daily urine protein one year before and after switching to Myfortic.
Results: Before switching, 72% patients were classified as responder if complete remission or partial remission were achieved, while 28% patients were categorized as non-responders (Table 1). After switching to Myfortic, 75% of the responder group achieved or maintained complete remission or partial response. In for non-responder group, 85.7% exhibited complete remission or partial response (Table 2). We did not observe new safety signals after switching.

Table 1. Comparisons demographics and renal pathologies of responder and non-responder groups

	Non-responder (N=14)	Responder* (N=36)	Total (n=50)	*p* value
Age	31.12±11.48	32.58±9.39		0.660
Female	23(88.5%)	20(76.9%)	43(82.7%)	0.465
Daily urine protein (g)	4.44±4.40	4.43±3.81		0.835
Creatine (mg/dl)	1.44±0.92	1.22±1.16		0.212
Renal pathology class				0.649
III	6(23.1%)	4(15.4%)	10(19.2%)	
III+V	2(7.7%)	4(15.4%)	6(11.5%)	
IV	16(61.5%)	15(57.7%)	31(59.6%)	
IV+V	2(7.7%)	3(11.5%)	5(9.6%)	

*complete remission and partial remission.

Table 2. Response rates of non-medical Switch from Cellcept to Myfortic

	Initial treatment with Cellcept		
	Non-responder	Responder	*p* value
Non-medical switch to Myfortic			0.705
Non-responder	2(14.3)	9(25)	
Responder	12(85.7)	27(75)	

Conclusion: This real-world data indicated similar efficacy of Cellcept and Myfortic. Further prospective study is needed to confirm our findings.
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AB0380

THERAPEUTIC CHOICES AND OUTCOMES IN CHINESE PATIENTS WITH SEROLOGICALLY ACTIVE CLINICALLY QUIESCENT SYSTEMIC LUPUS ERYTHEMATOSUS

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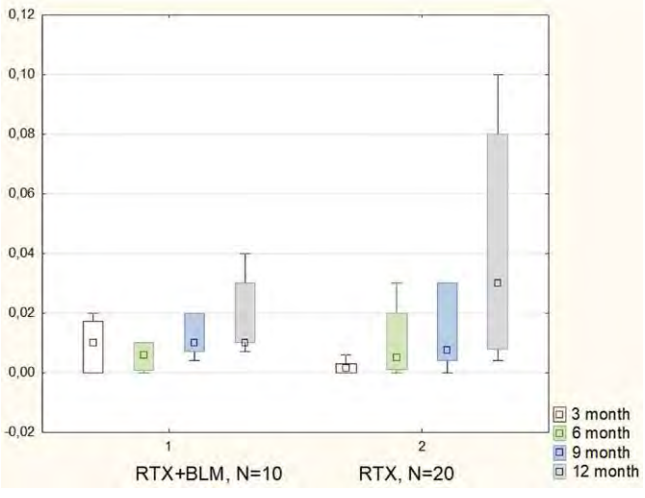
Background: Patients with systemic lupus erythematosus (SLE) who achieved the clinical state as serologically active clinically quiescent (SACQ). It appears to account for 6–12% of all patients with SLE, but there is disagreement about whether such patients are indeed clinically stable [1-3], especially in Chinese patients. And there is no conclusion as to what kind of treatment should be taken for such patients.
Objectives: To clarify the frequency and outcome of SACQ patients in lupus. And to identify factors associated with the flare of disease.
Methods: Clinical data of patients diagnosed as SLE and followed in Peking University First Hospital from 2009 to 2015 were retrospectively reviewed. 682 patients with systemic lupus erythematosus who were followed up for more than 6 months at Peking University First Hospital from January 2007 to December 2015 were summarized. SACQ was defined as an at least a 6-month period with persistent serologic activity and without clinical activity and could be taking a daily dose of prednisone or equivalent less than 7.5 mg. Serologically quiescent clinically quiescent (SQCQ) patients and serologically active clinically active (SACA) patients served as control groups. Data including demographics, initial symptoms, duration to SACQ, treatments before and after SACQ, and characteristics of the flare group were analyzed.
Results: Of the 682 patients, 170 were SACQ patients (24.9%), 187 were SQCQ patients, and 325 were SACA patients (47.7%). SQCQ patients (38.61±15.08 years old) were older at study start than SACQ patients (38.61±15.08 years vs. 32.09±14.35 years, p<0.001), but there was no significant difference between that of SACQ and SACA patients. 56 of the 170 SACQ patients (32.9%) experienced flare. Corticosteroids (OR 1.317, 95% CI 1.131 to 1.534; p<0.001) was an independent risk factor for flare, while antimalarials (OR 0.265, 95% CI 0.118 to 0.599; p=0.001) and immunosuppressants (OR 0.316, 95% CI 0.149 to 0.670; p=0.003) were protective factors.
Conclusion: About one third of SLE patients with SACQ experience flare, more than that of patients with SQCQ. Thus, approach to prevent relapse in SACQ patient is required. Maintenance therapy of hydroxychloroquine and immunosuppressant agents may be protective and beneficial treatment strategy in these patients need further investigation.
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AB0381

THE UTILITY OF HYDROXYCHLOROQUINE (HCQ) THERAPY FOR TWO YEARS AS A SPARING CORTICOSTEROID AGENCY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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Background: Prednisolone (PSL) and HCQ are key drugs in the therapy of SLE. However, since PSL induce many harmful adverse events, PSL is preferred to be reduced especially in the maintenance therapy. The efficacy of HCQ for reducing the dose of PSL has not been revealed yet. So, we focused on the cessation of PSL under the treatment of HCQ with conventional SLE therapy.



Objectives: The aim of this study is to evaluate the efficacy and the safety of HCQ as co-treatment in the standard therapy of SLE.
Methods: SLE patients (n=30) under the maintenance therapy were enrolled in this study. Dose of PSL, titer of anti-DNA antibody, WBC count, serum complement and SLE disease activity index (SLEDAI) were examined retrospectively at 0 and 12 months after administration of HCQ.
Results: Baseline patient-characteristics are as follows (mean±S.E); the age of patients was 54.4±3.2 years old, 21 patients (70%) were female, the disease duration was 108.5±25.2 months, SLEDAI was 4.0±0.9, the dose of PSL was 10.3±1.7 mg/day, the titer of anti-DNA antibody was 7.3±1.8 IU/ml, C3 was 85±4.3 mg/dl and C4 was 18±1.6 mg/dl.
The mean dose of PSL was reduced with statistically significance (pre-administration of HCQ:10.3±1.7 mg/day, 24 months after administration of HCQ:2.2±0.3 mg/day, *p<0.0001*). Furthermore, in this observation period, 6 patients could achieve the cessation of PSL.
SLEDAI was also significantly reduced (4.0±0.9 vs 1.0±0.3, *p<0.01*).
There was no statistical significance between before treatment by HCQ and after treatment in the titer of anti-DNA antibody (7.3±1.8 vs 2.8±1.6 IU/ml, *p=0.06*), WBC count (6208±4.9 vs 5096±3.3 /μl, *p=0.06*) and serum complement level (C3 85±4.3 mg/dl vs 89±4.0 mg/dl, *p=0.52*, C4 18±1.6 mg/dl vs 19±1.4 mg/dl, *p=0.45*). Relapse of SLE was clarified in only one patient.
As for adverse events (AEs), Severe bacterial infection (n=4), herpes zoster (n=1) and patellar tendon rupture (n=1) were revealed. All cases of the AEs were fully recovered.
Conclusion: Our study suggested that co-treatment with HCQ on standard SLE therapy could be enable to prevent the flare of SLE and reduce the dose of PSL with statistical significance. In some cases, we could achieve the cessation of PSL treatment.
References: None.
Disclosure of Interests: None declared
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AB0382 A RITUXIMAB AND BELIMUMAB COMBINATION THERAPY IN SLE PATIENTS.

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Background: Various mechanisms of action of RTM and BLM, in particular their interaction with defined subpopulations of B cells, can contribute to more effective suppression of autoreactive B cells and achieve a therapeutic effect.
Objectives: To assess the efficacy of a rituximab and belimumab combination therapy in pts with active SLE.
Methods: The study included 10 SLE pts (1M/9F) with high (SLEDAI2K≥10 – 8pts.) and moderate (SLEDAI2K<10- 2pts.) disease activity; out of them 2 patients had lupus nephritis, 2- vasculitis. 1 pts both (nephritis and vasculitis), and remaining 5 had predominantly mucocutaneous and articular manifestations of SLE. The dose of oral GCs at baseline did not exceed 20 mg/day in 9 pts, two pts were treated with prednisone 5 mg/day and only 1 received 60 mg. Rituximab (RTM) was administered at 500-2000 mg, with subsequent adding of Belimumab (BLM) 1-6 months later at a standard dosing regimen 10 mg/kg once a month. CD19+ B- lymphocytes counts were obtained before initiation RTM (0), and subsequently after 3 (N=10), 6 (N=10), 9 (N=7), and 12month (N=7). Depletion of CD19+ B- lymphocytes after RTM was assessed as the decrease of B-cell counts < 0,01 10*9/l, where 0 10*9/l was categorized as complete depletion, from 0,001 to 0,01 10*9/l – partial depletion, and >0,011 10*9/l – absence of depletion. The comparison group included 20 pts receiving a sing=ъ500-2000mg dose of RTM with high (SLEDAI2K≥10 – 16pts.) and moderate (SLEDAI2K<10- 4pts.) disease activity (SLEDAI Me 14[10;16])
Results: 6 pts demonstrated the decrease in clinical and laboratory SLE activity, starting from 3mo of follow-up, and by the 6th month the decrease in the activity of the disease was observed in 9 patients (SLEDAI-2K 0 mo–Me 12[10;16], 3mo-Me 8[6;10], 6mo–Me 4[2;6], 9mo–Me 6[4;10], 12mo–Me 2[2;6]) with RTM + BLM combination therapy. The oral GCs dose was reduced to 6,9 [5;10]mg/day by 6mo. One patient managed to completely eliminate glucocorticoids; he continued to receive cytostatic therapy (mycophenolate mofetil). None of the patient required prednisone dose escalation during follow-up. There were no cases of severe infection. The damage index did not increase by 6 and12mo. The combination therapy reduced the absolute counts of CD19+. B-cells. RTM therapy resulted in complete depletion in 3 pts, in partial depletion - in 4. Addition of BLM resulted in slowing down of CD19+ B-cell repopulation (Fig.1) (0mo–Me $0,11x10^9$/l[0,08;0,5], 12mo -Me $0,01x10^9$/l[0,01; 0,03]) vs pts receiving RTM monotherapy (0mo–Me $0,1x10^9$/l[0,08;0,2], 12mo -Me $0,03x10^9$/l[0,008; 0,08]). RTM and BLM combination failure, as well as failure of standard GCS and cytostatic based therapy, was documented in one patient with cutaneous, articular and hematological SLE.
Conclusion: Combination therapy allows to gain control over disease activity in short time, due to the effect of RTM, while added BLM provides further prolongation of the effect achieved, minimizing the risk of exacerbation. This combination may be used as a method of choice in pts with severe SLE involving vital organs, and in persistent cutaneous-articular disease and high immunological activity. In these patients there were no signs of infection.

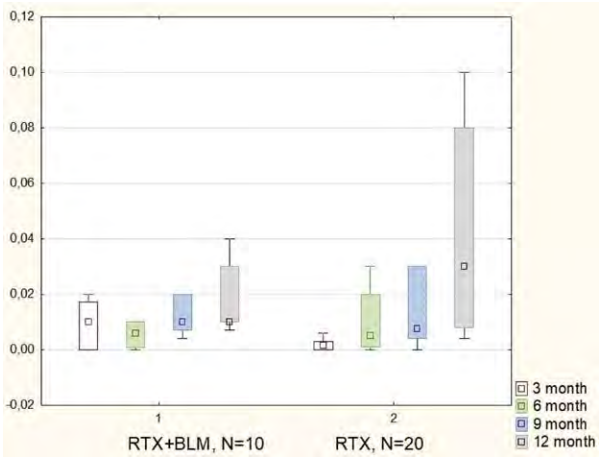


Figure 1.

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AB0383 EXTREME FATIGUE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND NEUROPSYCHIATRIC SYMPTOMS

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Background: Fatigue is commonly described in chronic illnesses, especially auto-immune disorders such as systemic lupus erythematosus (SLE).
Objectives: We aim to study the prevalence of fatigue in SLE patients with NP symptoms and compare fatigue in SLE patients with NP symptoms attributed to major organ involvement due to SLE (NPSLE) with SLE patients with NP symptoms not caused by major nervous system involvement (non-NPSLE).
Methods: All patients visiting the tertiary referral center for NPSLE in the LUMC between 2007-2019 with the clinical diagnosis of SLE and age >18 years that signed informed consent were included in this study. Patients underwent a standardized multidisciplinary assessment, including two questionnaires: SF-36 (2007-2019) and multidimensional fatigue index (MFI, 2011-2019). Patients were classified as NPSLE in this study if NP symptoms were attributed to SLE and immunosuppressive or anticoagulant therapy was initiated, otherwise patients were classified as non-NPSLE. The vitality (VT) domain of the SF-36 domain was used to assess fatigue, which generates a score from 0-100, 100 representing the complete absence of fatigue. Patients with a score more than 1 standard deviation (SD) removed from age-related controls of the Dutch general population were classified as fatigued; patients more than 2 SD removed were classified as extremely fatigued[1]. The MFI was also used, which consists of 5 subdomain scores between 0-20, leading to a total score between 0-100, 100 representing the most extreme fatigue. All scores are presented as mean and standard deviation.
Results: 373 patients fulfilled the inclusion criteria and SF-36 questionnaires of 328 patients were available (88%). The majority of these patients was female (87%) and 98 were classified as NPSLE (30%). In NPSLE patients, average age was 41 ± 13 years and in non-NPSLE the average age was 45 ± 14 years. The average score of the SF-36 vitality domain was 36.0 ± 20.7 in NPSLE vs 33.9 ± 18.8. in non-NPSLE. Overall, 73.5% of the patients were fatigued and 46.9% extremely fatigued in NPSLE vs 77.8% fatigued and 45.7% extremely fatigued in non-NPSLE.
The MFI questionnaire and VAS score were available for 222 patients, of which 65 patients were classified as NPSLE (29.3%). Table 1 depicts the scores of NPSLE and non-NPSLE patients on the MFI subdomains and the VAS score.

Table 1. Fatigue in NPSLE and non-NPSLE patients (N = 222)

	NPSLE (N = 65)	Non-NPSLE (N = 157)
MFI (mean, sd)		
General Fatigue	10.8 (1.8)	11.1 (1.5)
Physical Fatigue	11.4 (2.4)	12.3 (1.9)
Reduced Activity	9.6 (2.9)	10.7 (2.2)
Reduced Motivation	10.7 (2.6)	11.1 (1.9)
Mental Fatigue	9.5 (3.0)	9.8 (2.7)
Total score	51.8 (9.9)	54.9 (6.9)
SF-36 Vitality (mean, sd)	35 (20.7)	32.7 (18.2)

Table 1.

	GC	AM	IS					
			MPh	MPhA	AZA	MTX	CyA	LEF
Overall med survival, days to 25% discontinuation (95%CI)	1048 (938, 1197)	1267 (1113, 1428)	175 (175, 182)	387 (252, 756)	409 (350, 476)	525 (219, 686)	268 (182, 350)	329 (190, 524)
Univariable associations,HR (95% CI) p-value								
Disease activity								
≤4	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
>4 & <10	0.69 (0.56, 0.84) p<0.001	1.15 (0.92, 1.44) 0.2	0.92 (0.80, 1.05) 0.2	1.37 (0.78, 2.42) 0.3	1.16 (0.97, 1.39) 0.11	1.11 (0.72, 1.71) 0.6	1.26 (0.90, 1.77) 0.18	1.88 (1.07, 3.30) 0.03
≥10	0.65 (0.35, 1.21) 0.18	1.56 (0.94, 2.59) 0.08	0.84 (0.45, 1.57) 0.6	1.92 (0.80, 4.63) 0.14	2.69 (1.86, 3.91) p<0.001	1.85 (0.92, 3.71) 0.08	2.66 (1.36, 5.21) 0.004	1.62 (1.13, 2.32) 0.009
LLDAS								
<50%	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
≥50%	1.30 (1.09, 1.55) 0.003	0.67 (0.54, 0.84) <0.001	1.22 (1.08, 1.40) 0.002	0.83 (0.44, 1.57) 0.6	0.83 (0.69, 1.00) 0.054	0.70 (0.46, 1.07) 0.10	1.29 (0.92, 1.83) 0.14	0.43 (1.5, 1.25) 0.12

Conclusion: Nearly half of patients with SLE and NP symptoms are as extremely fatigued as only 2.5% of the general Dutch population. Extreme fatigue is not influenced by major nervous system involvement.

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AB0384 MEDICATION USE IN SYSTEMIC LUPUS ERYTHEMATOSUS – DATA FROM A MULTICENTRE COHORT STUDY

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Background: In the absence of evidence-based treatment guidelines, medication use in SLE is highly variable. Low rates of remission and lupus low disease activity state (LLDAS) suggest that suboptimal responses to standard medications, which include glucocorticoids (GC), anti-malarial (AM) drugs and immunosuppressive (IS) agents, are common. Understanding the utility of current medications will facilitate the selection of patients for advanced therapies as they emerge.

Objectives: To examine medication use patterns in a large multicentre SLE cohort.

Methods: We used 2013-18 data from the Asia Pacific Lupus Collaboration (APLC) cohort in which disease activity (SLEDAI-2K) and medication details were captured at every visit. LLDAS was defined as in Golder *et al.*, 2019 (1). We examined the use of medication (med) categories (GC &/or AM &/or IS) by SLE disease activity and LLDAS at the visit level. Additionally, we performed Cox regression analyses to determine the time-to-discontinuation of meds stratified by SLE disease activity, ranked by time-adjusted mean SLEDAI-2K, and by percent-time spent in LLDAS.

Results: We analysed data from 19,804 visits of 2,860 patients. We observed 8 med categories: no meds; GC, AM or IS only; GC+AM; GC+IS; AM+IS and GC+AM+IS (triple therapy). Triple therapy was the most frequent med pattern (32%); single agents were used in 21% of visits and biologicals in only 3%. Among visits where SLEDAI-2K was ≥10, triple therapy was used in 46%, with median [IQR] GC dose 10 [6, 24] mg/day; in contrast, among visits with SLEDAI-2K≤4 triple therapy was used in 28% (p<0.01). Patients in LLDAS received less combination therapy than those who were not in LLDAS.

Med persistence (survival analysis) varied widely, with lowest survivals for IS. Patients with time-adjusted mean SLEDAI-2K ≥10 had lower discontinuation of GC and higher discontinuation of IS including azathioprine, leflunomide and cyclosporine (Table 1). In contrast, increased time in LLDAS was associated with reduced discontinuation of AM and azathioprine.

Conclusion: In a large multicentre SLE cohort, most patients were receiving combination treatment. AM treatment survival was high and associated with low disease activity, GC survival was high and associated with high disease activity, while IS survival was low. Patients with high disease activity received more medication combinations but had reduced IS survival. These data suggest ongoing unmet need for improved medications for treatment of SLE.

Reference:

Golder, V., et al Lancet Rheum. 2019 1(2):e95-102

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AB0385 TARGETING CD38 IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Depletion of long-lived plasma cells (PC) resembles a novel concept for the treatment of antibody-mediated autoimmune diseases, such as systemic lupus erythematosus (SLE). Therapeutic approaches such as autologuos stem-stem cell transplantation and proteasome inhibition are limited by significant treatment-related toxicity. A novel target for PC depletion is CD38, a surface protein that is highly expressed on plasma cells (PCs) but also activated T-cells and most myeloid cells. Daratumumab is a monoclonal antibody targeting CD38 that is licensed for the treatment of multiple myeloma.
Objectives: Here, we aimed to ascertain clinical safety and efficacy of Daratumumab for the treatment of refractory SLE, as well as to gain insights into effects of Daratumumab on the immune system.
Methods: We treated two SLE patients with life- and organ-threatening SLE with four weekly dosis of 16 mg/kg Daratumumab. We performed integrative analyses of clinical, serological and immunological effects over a follow-up period of 6 months. Using flow cytometry and single-cell RNA and T-cell receptor sequencing we followed CD38 expression and composition of peripheral blood leukocytes with a special focus on memory T cells.
Results: Patient 1, a 50-year old woman, suffered from active biopsy-proven class III lupus nephritis (LN) with nephrotic syndrome, pericarditis, arthritis and skin rash. Upon Daratumumab treatment, her glomerular filtration rate normalized within 3 months and proteinuria gradually declined from 6.4 to 1.9g/g Creatinine during the 180-day follow-up period. Pericarditis, arthritis and skin rash completely resolved. Patient 2, a 32-year-old woman, presented with autoimmune hemolytic anemia requiring blood transfusions, immune thrombocytopenia and cutaneous vasculitis. Her direct antiglobulin test normalized within 3 months and remained negative throughout follow-up with consecutive recovery of the hemolytic anemia. Immune thrombocytopenia stabilized and vasculitic skin lesions completely resolved. Infusions were well tolerated without severe adverse drug reactions. NK cells and Dendritic Cells were transiently depleted, while numbers of T cells, B cells and Monocytes in the peripheral blood remained stable. CD38+ memory T cells that were expanded prior to treatment were virtually undetectable early after treatment. Their single cell transcriptomics demonstrated an upregulation of genes associated with activation, cytotoxicity and type 1 interferon response. CD38+ CD8+ memory T-cells showed marked oligoclonality. These prominent clones persisted upon treatment but their transcription profile gradually normalized.
Conclusion: Daratumumab appears to be a safe and effective treatment for refractory SLE. Further investigations are warranted to establish the efficacy in a clinical trial and to gain further insights into the pathophysiologic mechanism of action.
Disclosure of Interests: Lennard Ostendorf: None declared, Udo Schneider: None declared, Marie Urbicht: None declared, Philipp Enghard: None declared, Frederik Heinrich: None declared, Pawel Durek: None declared, Gitta Heinz: None declared, Henrik Mei: None declared, Mir-Farzin Mashreghi: None declared, Gerd Rüdiger Burmester Consultant of: AbbVie Inc, Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB Pharma, Speakers bureau: AbbVie Inc, Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB Pharma, Andreas Radbruch: None declared, Falk Hiepe: None declared, Tobias Alexander: None declared
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AB0386 RITUXIMAB IN LUPUS NEPHRITIS. REAL CLINICAL PRACTICE

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Background: Lupus nephritis (LN) is a potentially life-threatening complication of systemic lupus erythematosus (SLE). Standard treatment of this entity includes glucocorticoids (GC) and immunosuppressants such as cyclophosphamide (CF), with remission rates between 20 and 70%. Given its pathogenesis, the anti-CD20 antibody rituximab (RTX) may be useful, although the information available in the scientific literature remains controversial.
Objectives: To evaluate the effectiveness and safety of RTX in NL refractory to conventional treatment, under real clinical practice conditions.
Methods: Retrospective descriptive observational study, which included consecutive patients attended in a Rheumatology Unit who met SLICC 2012 criteria for SLE, with renal involvement, and who had received RTX for NL refractory to standard treatment. We collected different epidemiological, clinical (including other manifestations of SLE as well as previous treatments), analytical, RTX-related and adverse event variables. In all cases, renal function prior to the initiation of RTX was determined, as well as the degree of proteinuria and sediment alterations. The therapeutic response was evaluated considering partial response if they presented reduction of proteinuria in >50% compared to initial and stabilization of renal function (± 25%) or improvement of serum creatinine with respect to initial values; and complete response if they presented levels of serum creatinine <1.2mg/dL (or decrease to initial values or ± 15% of the basal value in those with creatinine ≥1,2 mg/dL), proteinuria ≤0,5 g/24h and inactive sediment. A quantitative descriptive analysis has been carried out with the statistical program IBM SPSS 24.0 for Windows.
Results: Thirteen patients (11 women and 2 men) were included, with a mean age of 32.3 years and a mean follow-up time from the start of RTX of 11.09 years. Class IV NL was the most frequent (46.15%), followed by Class III NL (38.46%). Class V NL represented 7.69% and another 7.69% the combination of Class III+V. Renal failure was present in 46.2% of patients at the beginning of RTX, 84.6% hematuria and all patients presented proteinuria, of which 76.9% were confirmed to have nephrotic range and 84.6% showed hypoalbuminemia. With regard to previous treatments, all cases had received high-dose of GC and at least one immunosuppressant: 92.3% had failed to CF, a similar percentage had received azathioprine and 46.2% had failed to mycophenolate. After treatment with RTX, partial or complete response was achieved in 84.61%, infections were identified in 46.15% of patients and allergic reactions in 15.38%; most adverse events were mild and all cases developed favorably.
Conclusion: RTX treatment is effective in SLE and specifically in LN. More than 80% of patients in our study with refractory LN benefited from RTX treatment. Despite the not insignificant incidence of adverse events, most were mild and resolved without sequels or complications, so we can conclude that the safety of RTX is acceptable and should be considered as a treatment option for these patients according to the good risk-benefit profile.
Disclosure of Interests: Consuelo Ramos Giráldez: None declared, Maria Luisa Velloso Feijoo: None declared, Sergio Rodríguez Montero: None declared, Jose Luis Marenco Speakers bureau: ABbvie, Pfzer, lilly
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AB0387 TREATMENT STATUS FOR OSTEOPOROSIS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: CROSS-SECTIONAL ANALYSIS FROM A LUPUS REGISTRY OF NATIONWIDE INSTITUTIONS (LUNA)

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Background: Osteoporosis is one of the most important adverse effects of glucocorticoids in patients with systemic lupus erythematosus (SLE). Because osteoporosis is accelerated by chronic kidney disease (CKD), more attention should be paid to the treatment for osteoporosis in SLE patients with CKD. Many treatment options for osteoporosis have emerged recently, but treatment status in patients with SLE is not elucidated.
Objectives: The purpose of this study is to elucidate the treatment status for osteoporosis in patients with SLE among the CKD stages.
Methods: Using data from lupus registry of nationwide institutions (LUNA), a cross-sectional analysis was performed. We firstly described treatment status for osteoporosis in all enrolled patients. Secondary, treatment status for osteoporosis was compared among CKD stages. Finally, bone damage in Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI) was compared among CKD stages.
Results: The median age (interquartile range [IQR]) of enrolled 917 patients was 44 (34- 57) years and 809 patients (88%) were female. CKD stages were follows: CKD stage 1, 234 (26%); CKD stage 2, 465 (51%); CKD stage 3, 189 (21%); CKD stage 4, 9 (1%); CKD stage 5, 16 (2%). Median (IQR) age, female sex,

and median (IQR) previous maximum dose of prednisolone in patients with and without CKD (≥CKD stage 3) were 56 (46.5-66) and 41 (32-50), 191 (89%) and 615 (88%), and 40 (30-60) and 40 (30-55) mg/day, respectively. Bisphosphonate was administered in 388 (42%) patients, vitamin D supplements in 448 (49%), Ca supplements in 36 (4%), denosumab in 20 (2%) and teriparatide in 14 (2%), respectively. Of enrolled patients, any treatment for osteoporosis was not administered in 226 (25%) patients. In spite of more frequent bone damage in patients with CKD compared to those without CKD (15% vs 10%, p=0.036), treatment status did not differ between patients with and without CKD (bisphosphonate: 41% vs 46%, p=0.29; vitamin D supplements: 50% vs 44%, p=0.14).

Conclusion: About a quarter of patients with SLE did not take any treatment for osteoporosis. Treatment for osteoporosis might be strengthened to prevent bone damage in SLE patients with CKD.

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AB0388 IMPROVEMENT OF PATIENT-REPORTED OUTCOMES IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME UNDERGOING CPAP-TREATMENT

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Background: Fatigue is a frequent symptom in primary Sjögren's Syndrome (pSS) determining health-related quality of life in many patients. Earlier studies could show that sleep apnea syndrome (SAS) is associated with patient-reported outcomes in pSS-patients [1].

Objectives: To investigate whether treatment of an underlying SAS improves disease activity in pSS-patients.

Methods: 14 female pSS-patients from our rheumatology outpatient clinic were enrolled and screened for SAS; continuous positive airway pressure (CPAP)-treatment was initiated in patients with a sleep apnea/hypopnea index >5/h and a respiratory disturbance index >15/h sleeping time (pSS treated with CPAP: pSS+; pSS untreated: pSS-). As controls, 11 SAS-patients (4 female) scheduled for initiation of CPAP-treatment were recruited from pulmonology department. In pSS, ESSDAI, ESSPRI, pain and patient global health on a visual analogue scale from 0-100mm were recorded. In both groups CRP, ESR, depression (PHQ-9), fatigue (FACIT), daytime sleepiness (EPS), and salivary gland ultrasound (SGUS) of the parotid and submandibular glands (PG; SMG) were obtained [2]. Data were collected at baseline (BL) and month 3 (M3). A p-value <0.05 was deemed significant.

Results: 6 pSS-patients were diagnosed with SAS and underwent CPAP-initiation, as well as all SAS-patients. Table 1 shows means ± SD of all assessments. EPS indicated normal sleep propensity in all groups at both time points. Fatigue was severe in all groups at BL. Numerically in SAS and pSS+, fatigue and depression trended towards improvement between BL and M3. Depression scores were moderate in all groups at BL; in SAS, PHQ-9 score showed a trend towards improvement at M3. SGUS grades 0 or 1 (i.e. normal or unspecific SGUS pattern) were found in 46.43% of PG and SMG at BL, in 40.39% at M3 in pSS, and in 100% in SAS at both time points. Grades 2 or 3 (pSS-typical US-pattern or gland destruction) were exclusively found in pSS at BL (53.57%) and M3 (59.62%). pSS-SGUS scores worsened irrespective of CPAP-treatment.

		Baseline (mean±SD)	Month 3 (mean±SD)	p-Values
CRP	pSS+	4.58±2.98	2.79±0.56*	*p=0.014
	pSS-	6.53±5.07	4.08±3.69	
	SAS	4.27±1.80	4.76±3.50*	
ESR	pSS+	30.50±21.92	24.75±10.69+	+p=0.031
	pSS-	34.75±37.92	47.29±37.82^	^p=0.013
	SAS	20.67±17.56	11.67±11.38+^	
ESSDAI	pSS+	10.67±4.97	11.00±6.08	
	pSS-	11.63±3.25	9.43±4.72	
ESSPRI	pSS+	6.75±1.44"	6.47±1.75	"p=0.037
	pSS-	5.18±1.32"	5.46±1.77	
VAS pain	pSS+	55.83±21.61°	54.17±24.60	°p=0.037
	pSS-	27.50±26.33°	34.25±26.87	
VAS PGH	pSS+	58.50±11.67	56.00±19.54	
	pSS-	52.88±30.86	53.00±23.05	
FACIT	pSS+	24.00±6.03	29.00±10.56¥	¥p=0.059
	pSS-	27.88±14.75	30.50±12.54	
	SAS	29.36±10.46Δ	37.82±10.73¥Δ	Δp=0.054
PHQ-9	pSS+	11.50±3.02	9.33±3.88∞	
	pSS-	10.86±5.05	9.00±2.51®	
	SAS	10.11±5.33×	6.55±5.75×®∞	×p=0.059; ®p=0.068; ∞p=0.087

Conclusion: Even though this is only preliminary data of a small fraction of patients who completed M3 so far, there is already a clear tendency towards reduced fatigue, inflammatory markers and depression both in the CPAP-treated pSS and in the SAS-patients compared to the non-CPAP-treated pSS-patients.

References:

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AB0389 GLUCOCORTICOID WITHDRAWAL IN SYSTEMIC LUPUS ERYTHEMATOSUS: ANALYSIS OF 750 SLE PATIENTS FROM THE RUSSIAN AND KYRGYZ COHORTS.

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Background:

Objectives: Glucocorticoids (GCs) have been the mainstream of systemic lupus erythematosus (SLE) treatment for the last 70 years. GCs allow to achieve effective control over SLE activity quite rapidly – both in mild and severe disease. The majority of SLE patients have received GC therapy; in some cohorts up to 80% - 100% of patients continue on low maintenance GCs doses < 7.5 mg/day for many years, perhaps some of them are treated indefinitely. It is clear that cumulative GCs dose is responsible for adverse effects. But it remains still unclear whether GCs should be continued indefinitely and, if not, when and how this treatment should be discontinued. On the other hand, treat-to-target SLE recommendations suggest GC withdrawal where possible as an important target of the treatment plan.

Methods: Patients who attempted GCs withdrawal were included in the Eurasian SLE RENAISSANCE cohort. A retrospective analysis of 350 patients from Russia and 400 patients from Kyrgyzstan was conducted. The following information was assessed during withdrawal attempts: SLE duration, disease activity at the onset and initiation of GCs dose reduction, therapy at SLE onset, the duration of the last flare, activity and therapy at the end of FUP, and duration of remission after GCs withdrawal. Definitions of remission were applied to GCs withdrawal in line with European consensus criteria.

Results: Out of 750 patients with a follow-up of about 6 years (IQR 1-23), GCs withdrawal due to persistent remission was documented in 15 patients (2.0%). In 14 out of these 15, SLE onset was associated with high disease activity based on SLEDAI 2K > 8. High level of anti-DNA and a decrease in C3 \ C4 complement were present in 12, 4 patients had nephritis with preserved renal function, 4 patients manifested signs of CNS damage (convulsions, headaches, sleep disturbances, memory issues, neuropathy, hallucinations), and another 5 had vasculitis. 10 patients were administered pulse therapy with 3 g methylprednisolone due to high disease activity. Initiation of GCs dose reduction with intent to discontinue in 7 patients was substantiated by prolonged clinical remission, meanwhile SLE duration in this group varied from 2 to 20 years, and duration of the last flare - from 6 to 165 months. Acute onset with high disease activity reaching 12-23 scores by SLEDAI 2 K was documented in 8 cases of early SLE with disease duration varying from 1.5 to 6 months. These patients were prescribed the most aggressive induction therapy, including cascade plasma filtration in combination with pulse therapy, cyclophosphamide and Rituximab at 1 g dose. Remission (SLEDAI2K 0-2 scores) was achieved 4-6-8 months later after termination of aggressive induction therapy. The duration of remission after GCs withdrawal in all 15 patients ranged from 3.5 to 240 months. In 8 patients with aggressive induction therapy, remission lasted from 18 to 240 months. In 2

remaining patients, remission lasted for 9 and 16 months after GCs withdrawal. Each flare required intake of low prednisolone doses for 3-4 weeks.
Conclusion: GCs withdrawal is an achievable goal in SLE and may be attempted after a long-term remission, and possibly after aggressive intensive care in the early stages of SLE.
Disclosure of Interests: None declared
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AB0390 ASSOCIATION BETWEEN INITIAL SERUM "TUMOR NECROSIS FACTOR-LIKE WEAK INDUCER OF APOPTOSIS" (TWEAK) LEVEL AND TREATMENT RESPONSE IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) NEPHROPATHY

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Background: SLE is a chronic inflammatory immunologic abnormalities disease which produce a number of antinuclear antibodies. The SLE renal involvement is clinically apparent in approximately 50% patients (Norby et al., 2017). It is very important to introduce the prompt treatment to prevent the permanent end stage renal disease.
Objectives: This study aimed to identify the serum biomarkers that correlate with pretreatment disease activity in patients with SLE nephropathy and predict the treatment outcome so that we may identify the unresponsive cases and switch to the other biologic agents like anti-TWEAK monoclonal antibody in the future.
Methods: This was a hospital-based prospective analytical study conducted from January 2018 to November 2019 in Rheumatology Department, Yangon Specialty Hospital. 88 SLE nephropathy patients with 24-hour urinary protein above 0.5g/day planned to have 6 months course of IV cyclophosphamide were enrolled. The paired serum sample of each patient was analyzed by ELISA twice to get the mean serum TWEAK value. Pretreatment SLE disease activity was assessed by the SLEDAI 2k. After the completion of 6 months of aggressive treatment, the treatment response was assessed by measuring the 24 hour urinary protein.
Results: Among the 88 patients, 63 patients (71.6%) had completed total 6-months course and 25 patients (28.4%) had not completed:11 patients (12.5%) expired and 2 patients (2.27%) had been changed to other DMARD and 12 patients (13.63%) did not attend the follow up clinic. The mean serum TWEAK level was 856 ± 77 pg/ml in 88 patients. According to the range of serum TWEAK level, most of the patients had serum TWEAK level of 601-900 pg/ml (53.4% of the study population). There was positive correlation between pre-treatment SLEDAI 2k score and pretreatment serum TWEAK level (r=0.464 and P <0.001). When the SLEDAI 2k score was grouped into mild, moderate, high and very high disease activity, the serum TWEAK level also had positive association with the different levels of disease activity (p<0.001). Among 63 treatment completed patients, 55 patients (87.3%) were the treatment responders but 8 patients (12.7%) were treatment non-responders. There was significant difference in the pretreatment SLEDAI 2k in terms of disease activity between treatment responder and treatment non-responder (p<0.001). There was significant difference in the pretreatment SLEDAI 2k in terms of reduction in 24-hours urinary protein between treatment responder and treatment non-responder (p<0.001). There was no significant difference in the level of pretreatment serum TWEAK level between treatment responders and treatment non responders (p=1.000). There was also no significant difference in the pretreatment serum TWEAK level between treatment responders and treatment non-responders in terms of reduction in 24 hours urinary protein (p=0.804).
Conclusion: Although the pretreatment serum TWEAK level had a positive correlation with pretreatment disease activity of SLEDAI 2k, it did not reflect the outcome of the responsiveness to the intensive therapy.
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[1] Norby, et al (2017) Outcome in biopsy-proven lupus nephritis: evaluation of biopsies from the Norwegian kidney biopsy registry. *Lupus*; 26:88
Acknowledgments: Prof.Chit Soe, Prof.Hlaing Mya Win
Disclosure of Interests: None declared
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AB0391 EFFECT OF HCQ ON LLDAS ACHIEVEMENT IN SLE PATIENTS

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Background: HCQ for SLE in Japan has been administered in many cases after approval. Therefore, the effect of additional administration of HCQ on low disease activity of SLE was considered to be clearer.
Objectives: To clarify the effect of HCQ treatment on the control of disease activity in SLE patients.
Methods: All SLE patients with low disease activity (LDA) enrolled in this study started additional HCQ treatment from January 2016. All patients with LDA enrolled in this study started HCQ treatment and had been receiving oral HCQ continuously for at least 3 months without using other immunosuppressive treatments or glucocorticoids. Disease activity was evaluated by SLEDAI, CLASI, and LLDAS, and serum complement values, anti-DNA antibodies, and pro-inflammatory cytokines were analyzed as immunological biomarkers before and after HCQ treatment.
Results: 52 of 100 patients were enrolled in this study (M:F; 4:48, average age; 40.6±13.4). 24 lupus nephritis patients were in sustained remission. 29 patients (56%) achieved LLDAS and 3 patients (6%) achieved clinical remission (CR) before HCQ administration.
Of the 20 patients (38%) who did not achieve LLDAS before HCQ administration, the LLDAS achievement rates at 3, 6, and 12 months after additional HCQ were 47%, 59%, and 81% (including 12.5% of CR achievement rates), respectively.
Serum levels of MRP8, MRP14, TNF-α, IL-6, VEGF-A, IL-1ra, MIP-1a and IL-2 decreased significantly 3 months after additional HCQ treatment. In addition, serum levels of MRP8, MRP14, TNF-α, IL-6 and IL-2 also decreased significantly 3 months after additional HCQ treatment despite achieving LLDAS or CR. The expressions of IFN-α didn't decrease significantly in 9 cases that could be detected.
The magnitude of the changes in serum MRP8, MRP14, IL-8 and Il-1ra levels in patients with a history of LN was significantly higher than in those without a history of LN. The magnitude of the reduction in serum MCP-1 levels in patients not achieving LLDAS with a history of LN was significantly higher than in those without a history of LN(p=0.046).
The change of CLASI activity score was correlated with the change in serum levels of MRP14 and MCP-1 with univariate analysis (MRP14: r=-0.41, p=0.017, MCP-1: r=-0.58, p=0.0006). The change of serum C3 levels had a negative correlation with MCP-1(r=-0.33, p=0.022).
The magnitude of the change in serum levels of MRP14, TNF-α, IL-8, MCP-1, MIP-1a and IL-1ra in patients achieving LLDAS were correlated with the change of CLASI activity score with univariate analysis (MRP14: r=-0.49, p=0.041, TNFα: r=0.74, p=0.0038, IL-1ra: r=0.66, p=0.038, MIP-1a: r=0.63, p=0.037, Figure 1). Moreover, the change of serum C3 and C4 levels in them had a negative correlation with the change of serum MCP-1 levels (Figure 2).

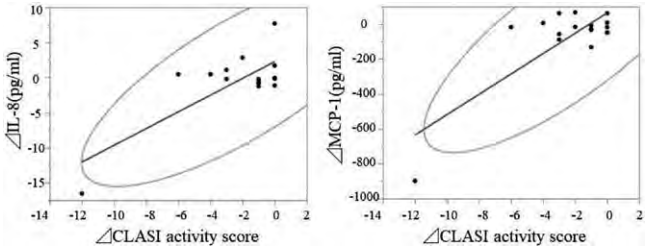


Figure 1. Correlation between change of CLASI activity scores and serum MCP-1 levels in SLE patients with LLDAS (IL-8: r=0.77, *p*=,0.0007, MCP-1: r=0.80, *p*=,0.0001).

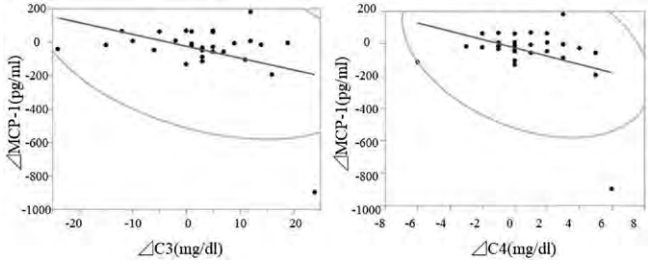


Figure 2. Correlation between change of serum C3 and C4 levels and serum MCP-1 levels in SLE patients with LLDAS (C3: r=-0.40, p=0.028, C4: r=-0.37, p=0.047).

Conclusion: Additional administration of HCQ is useful for cytokine control even in LLDAS-achieved cases, and particularly contributes to the improvement of skin lesion.
In addition, regulation of IL-8 and MCP-1 is important for control of renal lesions of SLE, and more control of the activity of SLE
The effect of HCQ on IL-8 and MCP-1 is related to the control of renal lesions in SLE, so that disease activity of more SLE patients might be more controlled disease activity.

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[1] R Wakiya, et al. Hydroxychloroquine modulates elevated expression of S100 proteins in systemic lupus erythematosus. Lupus. 2019;28:826-833
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AB0392 THE EFFECT OF HYDROXYCHLOROQUINE ON THE RISK FACTORS FOR ATHEROSCLEROSIS DEVELOPMENT

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Background: Systemic lupus erythematosus(SLE) patients, especially patients with lupus nephritis have poor vascular endothelial function and increased cardiovascular(CV) mortality.
Meanwhile, several studies showed hydroxychloroquine(HCQ) has effect on reduction in lipids and thrombosis(1), but the mechanism is unclear.
Objectives: We examined effect of HCQ on adipocytokine expression in SLE patients.
Methods: 52 SLE patients with low disease activity started with HCQ were analyzed before and 3 months after HCQ treatment. 21 SLE patients has past history of lupus nephritis. Serum S100 proteins and adipocytokines were measured by ELISA, and serum inflammatory ctytokine levels were evaluated by Multiplex assay (TNF-α, IL-6, VEGF-A).
Results: Serum adiponectin level was increased significantly 3 months after HCQ treatment compared with those at baseline (mean change 1.35, Figure 1). SLE patients who achieved LLDAS had a greater increase than those who did not. Additionally, the changes of serum adiponectin levels were associated with those of TNF-α, IL-6, VEGF-A and S100A9 protein, which plays an important role of SLE pathogenesis.

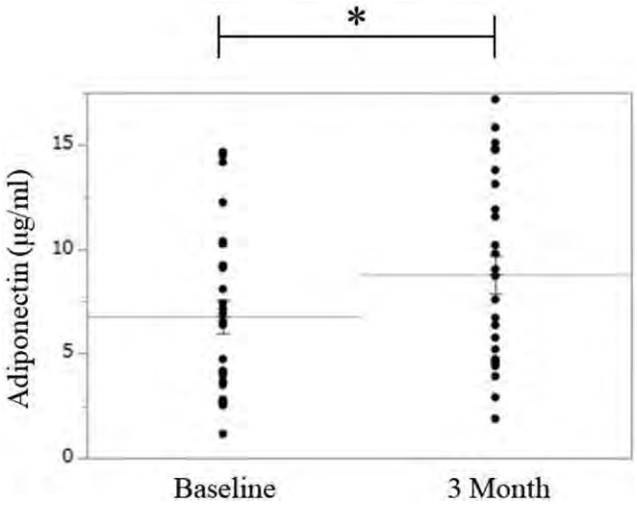


Figure 1. Serum adiponectin levels at baseline were compared with levels after 3 months of HCQ treatment. Serum adiponectin levels significantly decreasing during HCQ treatment in SLE patients.For statistical analyses * $p<0.0001$, P value: Wilcoxon signed-rank test

Conclusion: A HCQ could reduce the risk factors for atherosclerosis along with control of SLE disease activity.
References:
[1] Wallace DJ, et al. Cholesterol-lowering effect of hydroxychloroquine in patients with rheumatic disease: reversal of deleterious effects of steroids on lipids. Am J Med. 1990; 89: 322-6.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.5449

AB0393 EFFICACY OF HYDROXYCHLOROQUINE FOR LUPUS NEPHRITIS IN MAINTENANCE PHASE

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Background: Hydroxychloroquine (HCQ) is an essential drug for systemic lupus erythematosus. But in Japan, chloroquine and HCQ remain unavailable until mid 2015 because of a series of lawsuits about its retinal toxicity in the 1970s. There is insufficient knowledge regarding renal protective effect of HCQ.
Objectives: We aimed to investigate its efficacy of adding HCQ for Lupus nephritis (LN) as a maintenance-phase therapy.
Methods: We conducted an observational retrospective cohort study included patients with LN (n=42) in maintenance-phase in Japan. We reviewed medical records of LN patients aged > 18 years who were initiated HCQ from May 2015 to May 2018. Maintenance phase was defined as stabilization in serum creatinine and urinary segment after induction therapy and who achieved complete or partial remission. The annual change of proteinuria was compared between patients on HCQ who have proteinuria (>0.5g/gCr) or not. Other outcome measures were disease flare, dose of steroids, renal and immunologic features.
Results: A total of 42 patients were analyzed and allocated to two groups based on their amount of daily urine protein level: HCQ with proteinuria as group A (>0.5g/gCr, n=14) and HCQ without proteinuria as group B(≦0.5g/gCr, n=28). Both groups were comparable, with mean (SD) age of 36.1 (12.9) years and 37.5 (13.8), female 78.6% and 92.9% in each group, mean (SD) disease duration until HCQ of 3.5 (3.25) and 3.3 (2.9) years in group A and group B, with prednisolone dose at base line of 10.3 (7.1) mg and 7.9 (4.4) mg, respectively. The mean (SD) proteinuria at base line was 1.38 (1.11) g/gCr in group A and 0.20 (0.09) g/gCr in group B and after 12 months, proteinuria decreased in group A (-1.34 g/gCr in group A vs +0.03 g/gCr in group B; p<.001;95% CI,0.305-0.736). No relapse was experienced in group A during the study period.
Conclusion: In patients with clinically stable LN but with proteinuria, hydroxychloroquine is a good therapeutic option for achievement of complete remission.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.5378

17. SLE, Sjögren's and APS - clinical aspects (other than treatment)

AB0394 DOES HIGH DISEASE ACTIVITY IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS INCREASE THE RISK OF CANCER INCIDENCE?

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Background: Cancer is known as one of the causes of morbidity and mortality in systemic lupus erythematosus (SLE) patients. It has been thought that SLE activity and stimulation of the immune system predisposes the risk of cancer (1).
Objectives: To investigate the correlation between SLE disease activity and the cancer incidence.
Methods: The study included a cohort of SLE patients, diagnosed according to the American College of Rheumatology classification criteria(2) attending the Rheumatology department, Aswan University in the period from January 2018 to June 2019. We used a questionnaire to screen patients who were diagnosed with cancer. We collected demographic and laboratory data on all screened patients and their disease activity using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI)(3). For the patients diagnosed with cancer, we recorded age of onset of SLE, age of diagnosis of cancer, type of cancer, treatment received, immunosuppressive regimen (dosage and duration) and cancer outcomes.
Results: The study included 117 patients (95 female, 22 male), mean age (25.6 ± 6.5) years with mean SLE duration(7.3 ±6.3) years and mean SLEDAI(9± 8.9). 76% had lupus nephritis, 62.2% had hematological abnormalities and 17.8%had neurophsycatric lupus. 91% were on corticosteroids (CCS), 33% on mycophenolate mofetil (MMF), 43% on azathioprine, 14% on cyclosporin. 56.8% were either receiving or had received intravenous cyclophosphamide (CYC) with a mean cumulative dose (7.5 ± 4.7) gm. We found 18 (15.3%) patients (13 female and 5 males) were diagnosed with cancer during the course of SLE with mean age at onset (31±3.7), mean age at cancer diagnosis (39.28±10.77), mean SLE duration(18.17±6.02) and mean SLEDAI (7.39±4.19). Most of SLE patients with cancer had lupus nephritis (89%) and all cancer patients were on a median dose of CCS 10 (2.5- 20) mg daily for median 10 (4-24) years. 83.5% of them had received intravenous CYC prior to the development of cancer with mean total cumulative dose of (6.7±4.6) gm, 67% received MMF, 33% received cyclosporine and 50% received azathioprine. Types of cancer were as follow; 22.2% lymphoma, 16.7% cancer cervix, 16.7% cancer breast, 11.1% colorectal cancer, 11.1% squamous cell carcinoma, 5.6% leukemia, 5.6% bronchogenic carcinoma, 5.6% prostate cancer and 5.6% cancer thyroid. 66.7% of them

had been successfully treated, 27.8% had metastasis, 5.6% had died. There was no significant difference in SLEDAI between patients with cancer and patients without. Whereas malignancy is correlated to longer disease duration (p= 0.01) and older age of SLE onset with significant difference (p= 0.001).

Conclusion: Although we have detected an increasing incidence of cancer in SLE patients in comparison to normal population, our study didn't find a signficant correlation between SLE disease activity and the risk of cancer. We should closely observe SLE patients with old age at onset and/or long disease duration because of their higher risk for cancer development.

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Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.5044

AB0395 SYSTEMIC LUPUS ASSOCIATED MACROPHAGE ACTIVATION SYNDROME – A SINGLE CENTRE EXPERIENCE FROM INDIA

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Background: Macrophage activation syndrome (MAS) is a potentially fatal complication of systemic lupus erythematosus (SLE).(1) Overlapping clinical features of SLE activity with MA makes it a clinical diagnosis. There is limited data from developing countries like India.

Objectives: To study the clinical features, treatment, and outcomes in SLE-MAS.

Methods: This single-centre, retrospective study included patients fulfilling SLICC 2011 criteria for SLE, admitted from January 2017 to November 2019, and diagnosed as MAS by a team of attending physicians. Their demographic and clinical data, treatment, and outcomes were recorded. H score and SLEDAI were calculated. Patients were assessed for HLH classification criteria (2004) and preliminary diagnostic criteria for MAS in childhood SLE (cSLE).

Table 1. Patient characteristics

Characteristic	N=16
Age (years)	26 (19.5 – 30)
Duration of symptoms (days)	60 (18.7 – 90)
Fever	16 (100)
Pancreatitis	1 (6.3)
Renal	7 (43.8)
Neurological	7 (43.8)
Myocarditis	6 (37.5)
Hepatomegaly	7 (43.8)
Splenomegaly	3 (18.8)
Lymphadenopathy	12 (75)
Anaemia	16 (100)
Leukopenia	13 (82)
Thrombocytopenia	14 (88.2)
Coagulopathy	7 (43.8)
Concomitant infection	3 (18.8)
H score	222 (193 – 254)
cSLE-MAS diagnostic criteria	16 (100%)
HLH 2004 (≥5)	7 (43.8)
Corticosteroids	16 (100%)
Cyclophosphamide	8 (50%)
Intravenous immunoglobulin	2 (12.5%)
Cyclosporine	6 (37.5%)
Death	4 (25%)

All data presented as n (%) and median (IQR)
cSLE-MAS – Childhood systemic lupus erythematosus – Macrophage activation syndrome, HLH – Hemophagocytic lymphohistiocytosis

Results: Sixteen patients (median age – 26 years, 15 females) were included. Twelve patients (75%) had MAS as the initial presentation of SLE. The common clinical features were fever (100%) and cytopenias (100%). The mean duration of symptoms was 60 days. The most frequent biochemical abnormalities were high ferritin (>500 ng/ml, 100%) and elevated transaminases (100%, aspartate transaminase > alanine transaminase). Common complications were renal (43.8%), neurological (43.8%), and coagulopathy (43.8%). Seven and 16 patients fulfilled the HLH 2004 and cSLE – MAS preliminary criteria, respectively. The median H score was 222, giving a cumulative probability of 96%. All the patients received high-dose steroids. Cyclophosphamide pulse and cyclosporine were administered to 8 (50%) and 6 (37.5%) patients respectively. There were four (25%) in-hospital mortalities.

Table 2. Laboratory features

Parameter	N = 16
Haemoglobin (g/dL)	6.9 (5.7 – 7.8)
Total leucocyte count (cells/mm3)	1400 (1025 -3175)
<1000	3 (18.8)
1000 – 2500	9 (56.3)
2500 - 4000	1 (6.3)
Platelet (cells/mm3)	57500 (23500 – 95250)
<20000	3 (18.8)
20000 – 50000	3 (18.8)
50000 – 1 lac	8 (50)
Serum ferritin > 500 ng/ml	16 (100%)
Fibrinogen	2.48 (1.6 – 4)
Triglycerides (mg/dL)	375 (294 -470)
AST/ALT (U/L)	153 (113 – 234) / 90 (68 – 170)
Procalcitonin (pg/mL)	0.8 (0.3 – 1.4)
Lactate dehydrogenase (U/L)	1674 (1081 – 2184)
Erythrocyte sedimentation rate (mm in 1st hour)	61 (44 – 69)
C- reactive protein (mg/L)	36 (6.3 – 52)
Bone marrow examination	14 (87.5)
Increased histiocytes with hemophagocytosis	5 (32.5)

All data presented as n (%) and median (IQR)
ALT – Alanine transaminase, AST – Aspartate transaminase

Conclusion: Fever, cytopenia, high ferritin, and elevation of transaminases were the commonest features in this series of SLE-MAS. SLE-MAS carried a high mortality (25%) despite aggressive treatment.

References:

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Acknowledgments: NONE

Disclosure of Interests: None declared

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AB0396 DIAGNOSTIC PROTOCOL INCLUDING MINIMALLY INVASIVE MINOR SALIVARY GLANDS BIOPSY IN SJÖGREN'S SYNDROME IN A SPANISH REFERENCE CENTER

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Background: Sjögren's syndrome (SjS) is a systemic autoimmune disease with a broad clinical presentation from dry syndrome to systemic extraglandular manifestations. The diagnosis can be complex since none of the markers, except anti-Ro, is sufficiently sensitive or specific. Although, minor salivary glands biopsy (MSGB), Schirmer's test and unstimulated whole salivary flows (UWSF) are the hallmark for the diagnosis of this entity, its use is not widespread in some centers.

Objectives: The aim of the study was to analyze the usefulness and safety of the diagnostic protocol for the classification of SjS and the immunological and analytical markers in dry syndrome due to SjS.

Methods: Prospective observational study of a cohort of patients with sicca syndrome from a reference center. The diagnostic protocol (Schirmer's test, UWSF and minimally invasive MSGB) was applied in the same consultation. Demographic, clinical, analytical and histological data were reviewed.

Results: Over a period of 6 months, 48 patients with dry syndrome were analyzed, of which 39 women (81.2%). The main suspicion was SjS (39), followed by sarcoidosis (3), IgG4-related disease (2) and other diagnoses (4). The mean age was 59.1±4.4 years. Almost half (45.8%) reported xerostomia and 41.6% xerophthalmia. Recurrent parotidomegaly was described in 6 patients (12.5%) and arthralgias in 12 (25%). Immunologically, 23 (47.9%) presented anti-nuclear antibodies, 13 (27.1%) anti-Ro, 4 (8.3%) anti-La, 12 (25%) rheumatoid factor and 15 (31.2%) low C4. Schirmer test was positive in 32 patients (66.7%), UWSF in 22 (45.8%) and 9 (18.8%) had a focus score ≥1, although 16 (33.3%) had focal lymphocytic sialadenitis in the MSGB. A total of 21 (43,8%) patients were classified according to the 2016 ACR/EULAR criteria. 12 (57.1%) were seropositive SjS and 9 (42.9%) seronegative SjS. MSGB sensitivity was 71% and specificity 96%. Patient reported symptoms were unhelpful to differentiate SjS from other causes of dry syndrome. The number of protocols needed to diagnose a SjS was 2.28 (5.33 in seronegative SjS). Complications associated with the procedure were low (1 of 48) and mild (self-limited paraesthesia). Patients with SjS, unlike those with dry syndrome of another etiology, had more anemia (p<0.001), lymphopenia (p=0.022), ESR (p=0.030), beta-2 microglobulin (p=0.011), ANA (p<0.001), anti-ENA (p=0.006), anti-Ro (p<0.001), low C4 (p<0.001) and hypergammaglobulinemia (p=0.002).

Conclusion: Immunological and histological manifestations were more predictive than clinical ones to differentiate SjS from other causes of dry syndrome. MSGB is a simple, sensitive, specific and safe procedure. The application of the diagnostic protocol (Schirmer test, UWSF and MSGB) allowed to standardize the classification of SjS and increased the diagnosis of patients with seronegative SjS.

References:

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[2] Guellec D, Cornec D, Jousse-Joulin S, et al. Diagnostic value of labial minor salivary gland biopsy for Sjögren's syndrome: a systematic review. *Autoimmun Rev*. 2013;12(3):416–420.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.4921

AB0397 LUPUS FATIGUE PROBLEMS IN THE RUSSIAN COHORT OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (RENAISSANCE).

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Background:

Objectives: To determine the dependency of fatigue from SLE activity, irreversible organ damage and HRQoL in SLE patients of the Renaissance cohort.

Methods: 328 Russian SLE patients were enrolled in the study (M/F 30/298) who fulfilled SLICC 2012 criteria. The SLEDAI 2K activity, SLICC damage index, Facit Fatigue scale, and health related quality of life (HRQol) using the LupusQol questionnaire were evaluated.

Results: Based on the Facit Fatigue scale scores fatigue was verified in 148 (45%) out of 328 patients with SLE. Following lupus fatigue status patients were divided into two groups - 148 and 168 patients respectively. The groups were perfectly matched in terms of age, duration of the disease, duration of GCs therapy, and damage scores (Table 1)

The SLEDAI 2K activity scores were significantly higher in the group with lupus fatigue - 9.6±6.0 vs 6.7±4.2 (p=0.01) as compared to values in the group without fatigue, as well as the level of antibodies to DNA (p=0.02), 110.2±34.2 and 82.3±20.5, respectively.

There was a significant decrease in HRQoL in patients with lupus fatigue based on scores in all eight scales of the questionnaire (p=0.00),

Table 1. Comparative analysis of 328 SLE patients with and without lupus fatigue

Characteristics mean (SD)	Patients with lupus fatigue (n=148)	Patients without lupus fatigue (n=168)	P (Mann-Whitney)
Age in years	35,31±12,03	33,68±10,68	0,13
Disease durationin in years	9,57±9,47	10,1±9,17	0,6
Duration of glucocorticoid therapy in month	72,81±7158	79,43±75,98	0,6
SLICC Dal, score	1,55±1,37	1,69±1,23	0,44
C3 Mu\ml	0,88±0,33	0,87±0,31	0,75
C4 Mu\ml	0,15±0,12	0,16±0,14	0,36
ANF, hep2	641± 453	550± 402	0,4
Fatigue scores by the Facit fatigue scale	25,16±6,58	42,43±4,56	0,000

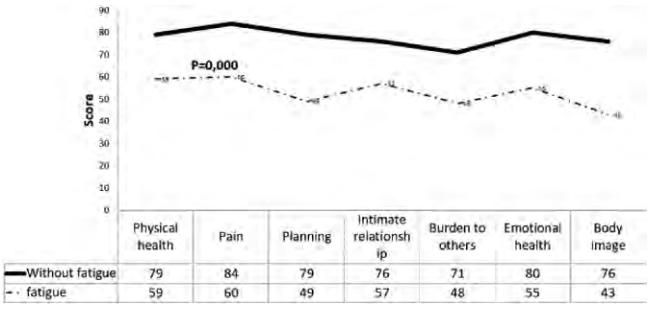


Figure 1. Comparative assessment of HRQoL using the LupusQol questionnaire in 328 SLE patients with and without fatigue.

Conclusion: Almost half (45%) SLE patients in the Russian cohort experience fatigue. It is associated with disease activity on the SLEDAI 2k scale and high levels of antibodies to DNA. All patients experiencing lupus fatigue have significantly worse HRQoL based on scores in all eight scales of the questionnaire LupusQol.

Disclosure of Interests: None declared

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AB0398 TNF-LIKE WEAK INDUCER OF APOPTOSIS / FGF INDUCIBLE MOLECULE 14 PATHWAY IN UNTREATED LUPUS NEPHRITIS: SERUM OR URINE TWEAK LEVELS MORE ACCURATE IN RELATION TO RENAL ACTIVITY?

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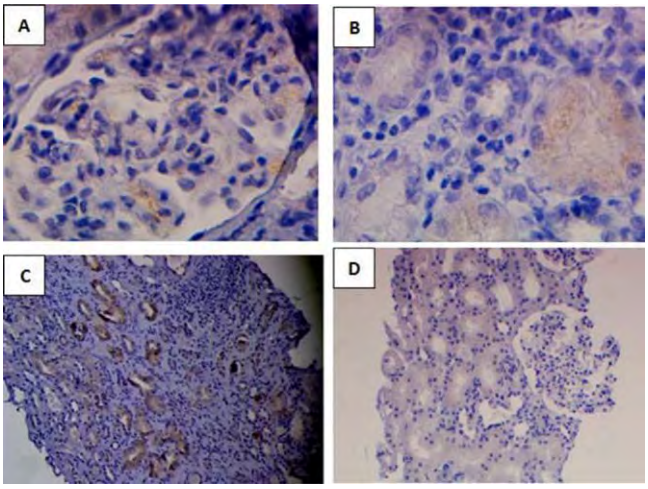
Background: Lupus nephritis (LN) is one of the most serious manifestations of SLE, affecting 70% of patients and the most critical predictor of morbidity and mortality of the disease [1].Tumor necrosis factor-like weak inducer of apoptosis/ fibroblast growth factor inducible molecule 14 (TWEAK/Fn14) activation is involved in various pathological processes that occur locally in kidneys, facilitating the pathogenesis of LN [2].

Objectives: To assess serum and urine TWEAK levels as well as renal Fn14 expression in newly diagnosed patients with LN and its correlation to disease activity.

Methods: The present study included 30 selected newly diagnosed previously untreated SLE patients divided into 2 groups; 15 patients with LN and 15 without LN as well as 30 age and sex matched healthy subjects who served as control group. Written consent was obtained from all patients and

controls after a full explanation of the study. Clinical assessment of disease activity by SLE Disease activity index (SLEDAI) [3]. Lupus nephritis was assessed clinically with the renal SLE disease activity index (rSLEDAI).Indicated renal biopsies were taken from the patients with LN and were classified according to the International Society of Nephrology and the Renal Pathology Society (ISN/RPS) classification [4].Serum and urinary levels of TWEAK were measured for the patients and controls using enzyme-linked immunosorbent assay (ELISA). Fn 14 was examined in renal biopsies from LN group by immunohistochemistry.

Results: A significantly higher uTWEAK level on comparing SLE patients with LN to those without LN and controls (F = 149.2, $P < 0.001$). uTWEAK had a highly significant positive correlation with, proteinuria (r = 0.755, $P < 0.001$), a significant positive correlation with SLEDAI and rSLEADI (r = 0.217, $P < 0.037$) (r = 0.476, $P < 0.024$) respectively. uTWEAK had a significant negative correlation with anti-dsDNA titres, C3 and C4 (r = -0.579, $P < 0.008$) (r = -0.456, $P < 0.011$) (r = -0.552, $P < 0.002$). Although sTWEAK level was higher in SLE patients than controls, it was not found to be associated with the presence of LN (F = 4.963, P =0.012). Fn14 expression was detected in glomerular and tubular cells in LN patients.



Expression of Fn14 in renal biopsies from LN patients was examined. Immunohistochemistry for Fn14 was detected in **(A)** glomerular endothelial cells, **(B, C)** some specimens showed moderate and intense staining for Fn14 in renal tubular cells. In the controls [renal biopsies from patients with renal cell carcinoma **(D)**], there was very slight staining for Fn14 in renal tubular cells.

Conclusion: Urinary TWEAK is a specific and sensitive biomarker for detection of active LN in newly diagnosed untreated SLE patients.

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Disclosure of Interests: None declared

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AB0399

SYSTEMIC LUPUS ERYTHEMATOSUS AND OPPORTUNISTIC INFECTIONS: PREVALENCE, FEATURES OF CLINICAL SYMPTOMS

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Background: Modern therapy for systemic lupus erythematosus (SLE) is associated with long-term treatment with cytotoxic drugs which is often accompanied by activation of comorbid infection, including viral infection.

Objectives: to identify prevalence and specific characteristics of the clinical symptoms of co-infection in SLE.

Methods: 67 patients with SLE were examined, mainly middle-aged women (62) of 33.5 ± 8.1 years old with the disease duration of 1 to 7 years who received "basic therapy".All patients were examined by ELISA for the presence of Herpesviridae viruses.

Results: In 67 patients, ELISA revealed anti-viral antibodies IgG to CMV (86.5%) and VCA IgG of EBV (56.7%), somewhat less frequently than HSV-1 IgG (38.8%) and HSV-2 (26. 8 %). Active CMV and EBV infections were diagnosed in 26 (38.8%) and 19 (28.3%) patients, respectively; moreover, in 11 patients a combination of production of antibodies of the IgM CMV and EA IgG EBV class was revealed. Analysis of anamnestic data and serological examination allowed us to distinguish 3 groups of patients: group I– 35 patients with a viral infection, including 9 with the infection of a mixed viral and bacterial nature; Group II – 14 patients with bacterial infection and Group III – 18 patients without viral and bacterial complications. Analysis of clinical symptoms showed that there is a definite correlation of high titers of antibodies to CMV and EBV with symptoms such as fever ($p<0.01$, r=0.74), polyarthralgia ($p<0.02$, r=0.46) lymphadenopathy ($p<0.01$, r=0.74), carditis ($p<0.05$, r=0.42), hepatomegaly ($p<0.05$, r=0.62), central nervous system damage ($p<0.02$, r=0.46), migratory erythematous/hemorrhagic rash ($p<0.05$, r=0.58), urinary syndrome ($p<0.02$, r=0.41), anti-dsDNA ($p<0.01$, r=0.82), ANA ($p<0.02$, r=0.74); cryoprecipitins ($p<0.01$, r=0.45). Although there were similar clinical manifestations, the presence of CMV and EBV had some organ specificity. Thus, damage to the central nervous system, joints (polyarthralgia) and liver was more common in patients with CMV, and lymphadenopathy and erythematous/hemorrhagic rash – in patients with EBV.

Conclusion: In SLE a comorbid viral infection contributes to clinical picture with a lingering remitting inflammatory process, as well as insufficient effectiveness from corticosteroid and immunosuppressive therapy.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.1444

AB0400

PATIENT-REPORTED OUTCOME MEASURES IN SWEDISH PATIENTS WITH RECENT-ONSET SLE VERSUS RA IN THE FIRST 60 MONTHS AFTER DIAGNOSIS

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Background: Patient (pt)-reported outcome measures (PROMs) provide information on a pt's own perception of disease impact, helping to provide a global perspective of disease when combined with conventional physician assessments. There is a discrepancy in PROMs between pts with rheumatoid arthritis (RA) and those with systemic lupus erythematosus (SLE); improvements in PROMs are often seen within the first year after diagnosis among pts with RA,[1] but not SLE.[2] Whether this discrepancy persists during subsequent years is unknown.

Objectives: To compare changes in PROMs among pts with SLE versus RA within the first 60 months after diagnosis.

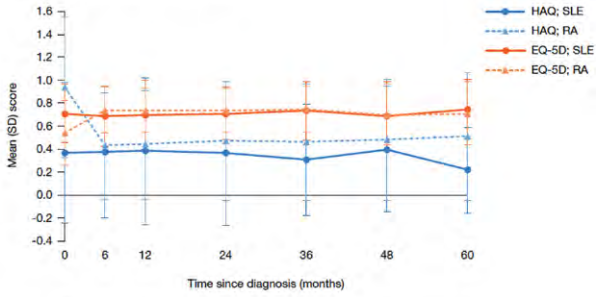
Methods: Pts with SLE with no prior organ damage were consecutively enrolled (2010–2015) from the Clinical Lupus Register in Northeastern Gothia and met the ≥4 of the 1982 American College of Rheumatology (ACR) and/or the 2012 Systemic Lupus International Collaborating Clinics classification criteria. Pts with RA were included from the observational 2nd Management of Early Intervention in RA cohort (TIRA-2; 2006–2009),[3] which enrolled pts with recent-onset RA; 84% of patients fulfilled the 1987 ACR criteria. Pts in both cohorts had symptoms for <12 months prior to diagnosis/inclusion and were treated according to Swedish guidelines. Pts with SLE or RA were followed prospectively after diagnosis. PROMs (quality of life: EuroQoL-5 Dimensions [EQ-5D]; activity limitations: Health Assessment Questionnaire [HAQ]; pain, fatigue, and well-being: Visual Analogue Scale 0–100 mm) were collected at Months 0 (inclusion), 6, 12, 24, 36, 48, and 60. HAQ, pain, fatigue, well-being: higher scores indicate greater severity; EQ-5D: lower scores indicate greater severity.

Table. Patient characteristics at registry entry.

Characteristic	SLE (n=41)	RA (n=522)
Age, median (interquartile range), years	39.0 (18–77)	60.0 (51–68)
Female sex	33 (80.5)	352 (67.4)
White	35 (85.4)	NC
Previous or current tobacco smoking	18 (43.9)	183 (65.6)*
Fulfilled 1982 ACR SLE classification criteria	36 (87.8)	NA
Number of fulfilled ACR SLE criteria, mean (range)	4.7 (3–9)	NA
Fulfilled 2012 SLICC classification criteria	41 (100)	NA
Fulfilled 1987 ACR RA criteria	NA	439 (84.1)

Data are n (%) unless otherwise specified.
*n=279.
ACR=American College of Rheumatology; NA=not available; NC=not collected due to ethics approval; RA=rheumatoid arthritis; SLE=systemic lupus erythematosus; SLICC=Systemic Lupus International Collaborating Clinics.

Figure 1: Mean (SD) HAQ and EQ-5D scores over time

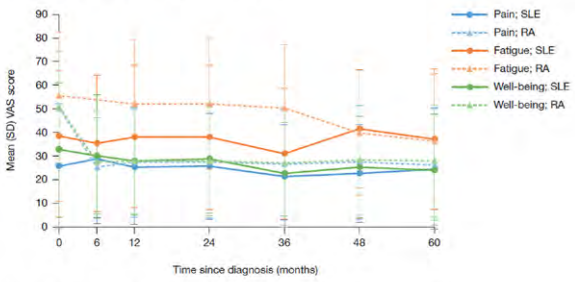


HAQ	SLE, n	39	31	36	36	30	22	19
	RA, n	461	428	430	422	402	367	351
EQ-5D	SLE, n	39	31	36	36	30	22	19
	SLE, n	412	265	272	278	255	80	62

HAQ: higher scores indicate greater severity. EQ-5D: lower scores indicate greater severity.
Patients with missing data were not included in the mean (SD) calculations for that particular time point.
EQ-5D=EuroQoL-5 Dimensions; HAQ=Health Assessment Questionnaire; SD=standard deviation;
RA=rheumatoid arthritis; SLE=systemic lupus erythematosus.

Results: 41 pts with SLE and 522 pts with RA were included in this analysis. Numerical differences between cohorts in age, sex, and tobacco smoking were seen (Table). Baseline PROM scores were generally worse for pts with RA versus SLE (Figs 1 and 2). However, an improvement in PROM scores was seen by Month 6 for pts with RA, but not SLE. Between Months 6 and 60, PROM scores remained largely unchanged for both groups.

Figure 2: Mean (SD) VAS pain, VAS fatigue, and VAS well-being scores over time



Pain	SLE, n	35	30	36	36	30	22	19
	RA, n	489	444	447	443	416	377	363
Fatigue	SLE, n	25	26	32	35	30	22	19
	RA, n	204	NC	201	177	134	71	67
Well-being	SLE, n	35	30	36	36	30	22	19
	RA, n	498	444	448	445	420	382	361

Pain, fatigue, and well-being (VAS ranging from 0–100): higher scores indicate greater severity. VAS fatigue data were not collected for patients with RA at Month 6. Patients with missing data were not included in the mean (SD) calculations for that particular time point.
NC=not collected due to ethics approval; RA=rheumatoid arthritis; SD=standard deviation; SLE=systemic lupus erythematosus; VAS=Visual Analogue Scale.

Conclusion: PROMs in pts with early SLE tended to remain stable in the years following diagnosis compared with the improvement experienced by pts with early RA, indicating a greater unmet need in SLE. The lack of improvement in PROMs in pts with SLE may be due to the disease's impact across multiple organ systems, which may take longer to resolve versus RA symptoms. These results imply there is room for improvement in disease management – both pharmacological and multi-professional interventions. Data should be interpreted with caution due a low number of pts with SLE.

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Acknowledgments: Sreeram Ramagopalan (supervised analysis). Lola Parfitt (medical writing, Caudex; funding: BMS)

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AB0401 **ASSESSMENT OF GENES INVOLVED IN SJÖGREN'S SYNDROME RELATED XEROSTOMIA**

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Background: Sjögren's syndrome (SS) is characterized by decreased saliva secretion. It is regulated mainly by parasympathetic nervous system. The genes involved in xerostomia can play a neuroprotective role [1]. The expression profiling is helpful to understand the mechanisms of SS related xerostomia.
Objectives: We aimed to investigate and compare gene expression in labial salivary glands from SS patients with xerostomia SS(+) and without xerostomia SS(-) and healthy subjects (HS) by microarray analysis and to find genes potentially involved in xerostomia.
Methods: The study group comprised 11 SS patients (3 SS(+) and 8 SS(-)) and 9 HS. Labial salivary gland samples were processed according to the protocol [2]. Database for Annotation, Visualization and Integrated Discovery (DAVID) and Search Tool for the Retrieval of Interacting Genes (STRING10) were used for the interactions between study groups [3].
Results: Among the genes belonging to "secretion" ontology group, expression of Amyloid Beta Precursor Protein (APP) and Cholinergic Receptor Muscarinic 3 (CHRM3) in both SS(+) and SS(-) groups were lower than in HS. The expression of Visinin Like 1 (VSNL1) in SS(+) and SS(-) was higher than in HS. The expression of Serum Amyloid A1 (SAA1) and Amyloid Beta Precursor like Protein 2 (APLP2) were decreased in SS(+) group and increased in SS(-) compared to HS group. There was no differences between the SS(+) and SS(-) in expression of mentioned genes.

Table 1. Fold changes, adjusted p values of differentially expressed genes in SS(+) and SS(-) groups

Gene symbol	Ratio SS(-)	Ratio SS(+)	adjusted p.value.SS(-)	adjusted p.value.SS(+)
APP	-1,230085	-4,00201	0,9824056	0,00029089
SAA1	1,446255611	-2,222329225	0,831872232	0,046639694
APLP2	1,118778	-2,232646	0,9121355	0,01132797
CHRM3	-1,745830276	-5,359431593	0,867931575	0,000023
VSNL1	1,608504852	3,127527026	0,916228964	0,000513257

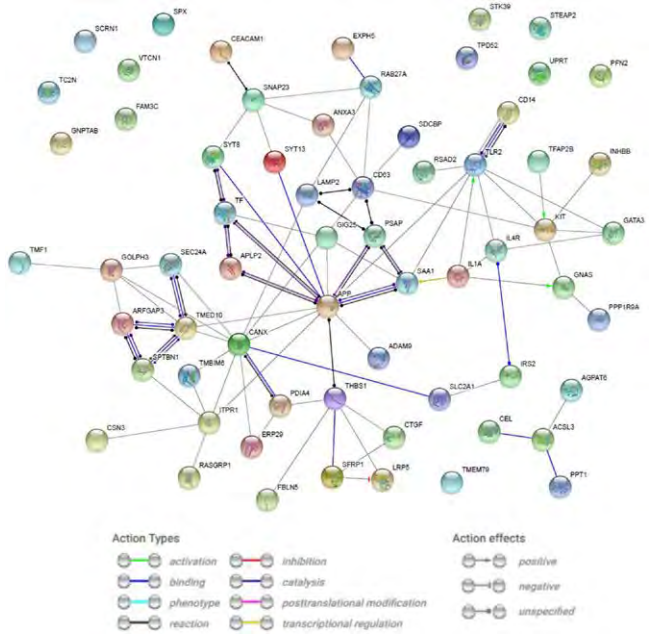


Figure 1. STRING-generated interaction network among differentially expressed genes belonging to the „secretion" ontology group.

Conclusion: Decreased expression of APP, SAA1, APLP2 and CHRM3 in SS(+) sufferers compared to HS can reflect the loss of their neuroprotective function and the cholinergic deficiency in xerostomia. STRING10 software indicates for a cenral role of APP and genes involved in β-amyloid peptide formation and neurodevelopment and for a close relationships between SS and neurodegenerative diseases [4,5].

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AB0402 **DISEASE ACTIVITY AND OBSESSIVE-COMPULSIVE DISORDER IN SYSTEMIC LUPUS ERYTHEMATOSUS**

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Background: Obsessive-compulsive disorder (OCD) is more prevalent in systemic autoimmune diseases when compared to healthy controls. This is in part due to inflammatory mechanisms, common across both conditions. Neuroinflammation and specifically problems within the basal ganglia are associated with OCD.
Objectives: The primary objective of this analysis was to investigate the effects of disease activity in systemic lupus erythematosus (SLE) on OCD. Other variables investigated included psychiatric aspects, inflammatory biomarkers and structural brain abnormalities.
Methods: SLE patients who met ACR or SLICC criteria were recruited. Demographic and clinical data were collected and data measuring disease activity (BILAG and SLEDAI-2K), disease damage (SLICC-DI), depression (MADRS, BDI-II, HADS), anxiety (HADS, STAI), fatigue (FSMC), quality of life (LupusQoL and EQ5D), inflammatory and endothelial activation (EA) biomarkers (IL-6, ESR, TNF-α, MCP-1, hsCRP, BLyS, VCAM-1, VEGF, EMVs) and OCD (OCI-R). MRI FLAIR structural scans were also used to examine signal hyperintensities in the brain. Participants with active disease (SLE-F) also had a 2nd visit approx. 4 months later. Non-parametric correlations with the OCI-R were undertaken for all SLE participants and for the change over time scores for the SLE-F participants (n=11).
Results: 39 participants were included in the analysis and were typical for a SLE population. 6 (23%) patients had scores above the threshold for OCD. OCI-R significantly correlated with disease activity, quality of life, fatigue, depression and anxiety measures for all the SLE participants. Change in monocyte chemoattractant protein-1 (MCP-1) correlated with the OCI-R for the within SLE-F group analysis (Table 1). No significant correlations were found with the full SLE group for inflammatory or EA biomarkers or with either group for the structural brain analysis.
Conclusion: OCD in lupus is strongly related to other psychological co-morbidities, fatigue and quality of life. Our results also support a role for inflammatory pathways in mediating some of these changes and so obsessive-compulsive features should be assessed in SLE patients who flare. A larger study is underway to better understand the mechanisms underlying these associations.
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Disclosure of Interests: : Michelle Barraclough Grant/research support from: This study was partially funded by an unrestricted grant from Sanofi Genzyme., Ben Parker Grant/research support from: GSK and Sanofi Genzyme, Consultant of: GSK, AstraZenaca, UCV, Abbvie, Pfizer, BMS, Celltrion, Shane McKie: None declared, Philip Pemberton: None declared, Alan Jackson: None declared, Rebecca Elliott: None declared, Ian N. Bruce Grant/research support from:

Table 1. Significant correlations with the OCI-R for: a) all SLE participants; b) the SLE-F group only (visit 1 minus visit 2).

Variable	*rs*	p-value
a)All SLE participants, n=39		
Disease activity: BILAG global score	0.408	0.01
Quality of life:		
LupusQoL – Physical	-0.495	0.001
– Pain	-0.535	<0.001
– Planning	-0.586	<0.001
– Intimate	-0.342	0.03
– Burden	-0.504	0.001
– Emotion	-0.397	0.01
– Fatigue	-0.471	0.002
EQ5D: VAS	-0.418	0.01
total	-0.359	0.03
Fatigue measures (FSMC):		
Cognitive	0.521	0.001
Motor	0.448	0.004
Depression measures:		
MADRS	0.467	0.003
HADS – D	0.545	<0.001
Anxiety measure: HADS-A	0.375	0.02
b)SLE-F group (v1-v2), n=11		
Inflammatory marker: MCP-1	0.771	0.006

BILAG The British Isles Lupus Assessment Group index, LupusQoL Lupus quality of life, EQ5D European quality of life, VAS visual analogue scale, FSMC Fatigue scale for motor and cognitive function, MADRS Montgomery Asberg depression rating scale, HADS Hospital anxiety and depression scale, D-depression, A-anxiety score, MCP-1 monocyte chemoattractant protein-1

Genzyme Sanofi, GSK, and UCB, Consultant of: Eli Lilly, AstraZeneca, UCB, Iltoo, and Merck Serono, Speakers bureau: UCB

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AB0403 VALIDATION OF 2019 EULAR/ACR CLASSIFICATION CRITERIA FOR SYSTEMIC LUPUS ERYTHEMATOSUS IN A SOUTH INDIAN COHORT

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Background: New 2019 EULAR/ACR classification criteria for Systemic Lupus Erythematosus (SLE) has been recently published[1]. Before its widespread use in research, this criterion needs to be externally validated in other cohorts. Validation studies for the new criteria were not yet done in the Indian population. Moreover, the new 2019 EULAR/ACR classification criteria for SLE has not been validated in juvenile SLE.

Objectives: To compare the real-world performance of 2019 EULAR/ACR classification criteria when applied to a known cohort of SLE cases, comprising both adult and juvenile SLE, in South Indian population.

Methods: We retrospectively reviewed the electronic medical record of 30,541 patients who visited the Rheumatology department of Amrita Institute of Medical Sciences, Kochi, a tertiary care centre in Kerala, from January 2014 to June 2019. 347 patients diagnosed with SLE by qualified and experienced rheumatologists were included in the study. 44 patients were later excluded as they were found to have an overlap syndrome. From the 30,541 patients, another 303 age-matched patients, who attended the rheumatology department on the first week of each month, from 2014 January to 2019 June, and diagnosed with autoimmune diseases other than SLE, were selected as controls. They were selected regardless of their specific clinical or immunologic manifestations. Patients were excluded if the diagnosis was uncertain. Each patient was evaluated to see if he or she satisfied the 1997, 2012, and 2019 classification criteria, respectively.

Results:

Conclusion: In our cohort, the new 2019 EULAR/ACR criteria attained better sensitivity, PPV, NPV and accuracy when compared to ACR 1997 and SLICC 2012 criteria, and had almost the same specificity as compared to SLICC 2012 and ACR 1997 criteria.

Validation of the 2019 SLE classification criteria

Criteria	Adult (n=196)			Juvenile (n=107)			Total (n=303)		
	1997	2012	2019	1997	2012	2019	1997	2012	2019
Sensitivity(%)	78.1	96.4	98.5	73.8	94.4	96.2	76.6	95.7	97.7
Specificity(%)	92.9	86.2	93.4	100	96.3	98.1	95.4	89.8	95
PPV[#](%)	91.6	87.5	93.7	100	96.2	98.1	94.3	90.3	95.2
NPV[*](%)	80.9	96	98.4	79.3	94.5	96.3	80.3	96.5	97.6
Accuracy(%)	85.5	91.3	95.9	86.9	95.3	97.2	86	92.7	96.4

#PPV- Positive Predictive Value *NPV- Negative Predictive Value

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Disclosure of Interests: None declared

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AB0404 SARCOPENIA AND RELATED FACTORS AMONG PATIENTS WITH PRIMARY SJOGREN'S SYNDROME

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Background: Sarcopenia is the progressive and generalized loss of muscle mass, strength and function especially among elderly population. Inflammation may lead to sarcopenia regardless of age.

Objectives: To evaluate the frequency of sarcopenia and related factors in patients with primary Sjogren's syndrome (SS).

Methods: A total of 44 female patients with SS and 44 age matched female healthy controls were included in this cross-sectional study. Sarcopenia was evaluated by hand grip test, skeletal muscle index (SMI) and 6 meters gait speed (GS) test. According to recommendations of European Working Group on Sarcopenia in Older People (EWGSOP2) 2018, sarcopenia is defined as decrease in results of both hand grip test and SMI, whereas, probable sarcopenia is defined as only decrease in results of hand grip test. Mini Nutritional Assessment Short Form (MNA-SF) was used for evaluating nutritional statement. EULAR SS patient reported index (ESSPRI) and EULAR SS disease activity index (ESSDAI) used for evaluating disease activity. Patient global assessment (PGA) was assessed with visual analogue scale (VAS 0-10 cm). Patients with arthritis in dominant hand and/or ankle joints were excluded from the study.

Results: The mean age of participants was 55.3±10.4 years. Eleven patients (25.0%) had probable sarcopenia in SS group and 2 (4.5%) in control group (p=0.007). Compared with healthy controls, SS patients had lower results of hand grip and 6 meters GS tests (p=0.005 and p<0.001, respectively). According to Mini Nutritional Assessment Short Form (MNA-SF), patients with probable sarcopenia had higher risk for malnutrition compared with patients with no sarcopenia (p=0.043). Patients with probable sarcopenia had higher scores of ESSPRI pain domain and patient visual analogue scale for global disease activity compared with patients with no sarcopenia (p=0.044 and p=0.036, respectively) (Table 1). In multivariate regression analysis ESSPRI pain was associated with hand grip strength (p=0.016, R^2=0.13) and MNA was associated with SMI (p=0.005) (Table 2).

Table 1. Factors associated with probable sarcopenia in Sjogren's syndrome

Sjogren's syndrome group	No sarcopenia (n=33)	Probable Sarcopenia (n=11)	p-value
ESSPRI pain*	5 (0-10)	7 (3-10)	**0.044**[b]
VAS patient*	4 (0-10)	6 (0-10)	**0.036**[b]
MNA SF, n (%)			**0.043**[C]
Normal nutritional status (12-14)	32 (97)	8 (72.7)	
Risk of malnutrition (8-11)	1 (3)	3 (27.3)	

ESSPRI: EULAR Sjogren's Syndrome Patient Reported Index, VAS: Visual Analogue Scale, MNA SF: Mini Nutritional Assessment Short Form. *Variables given as median (minimum-maximum) [a]Independent Samples Student t test,[b]Mann-whitney U,[C] Fisher's Exact test.

Table 2. Multivariate analysis for hand grip strength and SMI in patients with Sjogren's syndrome

	Unstandardized Coefficients		95% Confidence Interval for B		Standardized Coefficients	p-value
	B	Std. Error	Lower	Upper	Beta	
Hand grip strength						
Constant	24,492	1,695	21,071	27,914	–	**<0.001**
ESSPRI pain	-0,707	0,282	-1,276	-0,139	-0,361	**0,016**
SMI						
Constant	5,419	1,705	1,978	8,860	–	**0.003**
MNA	0,380	0,127	-1,276	-0,139	0,419	**0,005**

ESSPRI: EULAR Sjogren's Syndrome Patient Reported Index, SMI: Skeletal Muscle Index, MNA: Mini Nutritional Assessment

Conclusion: Risk of sarcopenia is increased in patients with SS. In the current study, it is shown that pain is related with sarcopenia. ESPPRI pain is a sign of continuing chronic inflammation in patients with SS. Malnutrition, which can indirectly related with SS, may also contribute to this process. Excessive pain may lead to decrease daily activities and nutritional status of patients with SS. Evaluating pain and patient's global disease activity may help physicians to find out patients with increased risk for sarcopenia. Controlling disease activity and pain and preventing malnutrition may reduce the risk for development of sarcopenia.

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Disclosure of Interests: : None declared
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AB0405 ABNORMAL BLOOD LIPID METABOLISM IN PREMENOPAUSAL FEMALE SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS IS RELATED TO HYPERURICEMIA AND PROTEINURIA

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Background: 1. Hyperuricemia is often associated with abnormal lipid metabolism. We reported premenopausal female systemic lupus erythematosus (SLE) patients had elevated blood UA levels[1]. Do these patients also have hyperlipidemia?

2. Estrogen has certain effect on blood lipid metabolism, whether the blood lipid levels of premenopausal female SLE patients who have the background of hyperestrogen function are affected by estrogen and its receptors?

Objectives: To investigate the relationships between blood lipids and serum UA level, estrogen receptors (ERs) as well as ER antibodies in premenopausal female SLE patients.

Methods: 123 premenopausal female SLE patients (SLE group) were divided into normal CH group (n=93) and high CH group (n=30, CH>5.17mmol /l), and 40 healthy premenopausal females served as the control group. The blood lipid levels of the SLE group and the control group were compared, and the blood levels of lipid, UA, estrogen, ERs and ER antibodies were compared between the two SLE subgroups. Linear regression was used to analyze the influencing factors of blood CH.

Results:

1. In SLE group, the blood level of TG was significantly higher than that of the control group (1.67±1.10 vs. 0.87±0.47, P<0.001), while the levels of blood CH, LDL, HDL were comparable to the control group (all with P> 0.05).
2. The mean blood CH level of the SLE patients with hyperuricemia was 5.57 ± 2.44mmol/l, which was significantly higher than that of patients with normal UA level (3.98 ± 1.30mmol / l, P <0.001).
3. The serum UA, CRE, CH, TG, LDL, and 24-hour urinary protein quantification (24h UPRO) in the high CH SLE subgroup were significantly higher than those in the normal CH SLE subgroup (all with P <0.05). There were no significant differences in serum estrogen, ERs and ER antibodies between the two subgroups, Table 1.
4. Linear regression showed that serum UA level and 24h UPRO were the dangerous effects of elevated blood CH in the premenopausal female SLE patients, Table 2.

Conclusion: Compared with healthy female of the same age range, the premenopausal female SLE patients are more likely to have abnormal lipid metabolism, which is related to kidney damage and abnormal UA metabolism.

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Table 1. Some clinical indicators, estrogen, ERs and ER antibodies in the premenopausal female SLE patients

	High CH group (n=30)	Normal CH group (n=93)	P
Age(years)	31.40±7.40	28.12±7.23	0.039
UA(μmol/l)	433.40±192.90	310.10±129.57	0.002
CRE(μmol/l)	112.07±87.09	72.81±91.96	0.039
CH(mmol/l)	7.07±2.05	3.72±0.93	<0.001
TG(mmol/l)	2.27±1.57	1.48±0.84	0.013
LDL(mmol/l)	4.48±1.46	2.29±0.67	<0.001
HDL(mmol/l)	1.02±0.72	1.97±0.43	0.721
Estrogen(pg/ml)	73.53±47.74	69.42±55.48	0.717
ERα(pg/ml)	45.94±31.06	43.34±31.05	0.684
ERβ(pg/ml)	16.65±28.67	13.70±25.09	0.589
Anti-ERα(ng/ml)	59.75±33.87	55.16±31.34	0.496
Anti-ERβ(ng/ml)	89.73±49.03	71.73±41.74	0.052
24h UPRO(g/24h)	2.82±3.82	0.39±0.56	0.002
Positive UBLD(%)	20(66.67)	31(33.33)	0.01
SLEDAI	13.18±4.23	7.39±6.18	0.025

ER, estrogen receptor; 24h UPRO, 24-hour urinary protein quantification; UBLD, urinary blood.

Table 2. Relationships between blood CH level and clinical indicators in in the premenopausal female SLE patients

Variable	Unstandardized Coefficients		Standardized Coefficients	t	P	95%CI
	B	SEM				
24h UPRO	0.353	0.072	0.400	4.932	<0.001	0.211~0.495
UA	0.003	0.001	0.249	3.058	0.003	0.001~0.005
Constant	3.146	0.359		8.754	<0.001	2.434~3.857

UA, uric acid; 24h UPRO, 24-hour urinary protein quantification.

Disclosure of Interests: : None declared
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AB0406 HUMAN PAPILLOMA VIRUS (HPV) VACCINATION SAFETY IN SYSTEMIC LUPUS ERYTHEMATOSUS COHORT - PORTUGUESE UNIVERSITY HOSPITAL SINGLE-CENTER COHORT STUDY

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Background: Cervical cancer is a potentially preventable consequence of Human Papillomavirus (HPV). HPV vaccination is recommended in most countries for all young women, preferentially before sexual activity begins. In Portugal, HPV vaccination is available in either bivalent (genotypes 6, 18) or tetravalent (6, 11, 16 e 18) vaccines. Both have aluminum as an adjuvant, a substance arguably capable of inducing inflammatory adjuvant syndromes. Systemic Lupus Erythematosus (SLE) mostly afflicts women of childbearing age, the very target population for HPV vaccination. There are conflicting reports in the literature regarding both the efficacy and safety of this vaccine in SLE patients. This question is particularly pressing as HPV infection prevalence seems to be increased in SLE patients.

Objectives: To analyze the safety of HPV vaccination in a SLE patient cohort followed at a university hospital.

Methods: Retrospective single-center (35 year long, 436 SLE patient cohort) review of all female SLE patients' local and online national records on HPV vaccination and cervical cancer screening. Data on activity (using SLEDAI-2K scoring) and concomitant drug use were reviewed for the two years before and after vaccination date.

Results: Of the 463 SLE patients, 420 were women (91%), of which 322 had clinical information about yes/no HPV vaccination. Twenty-seven of the patients (8%) had one of HPV vaccines, but only 13 (4%) had full information on activity before and after vaccination. Mean current age was 33,8 years and a minimum of 8,4 years of follow-up after HPV vaccination. Twenty-there (85%) were vaccinated with the tetravalent vaccine. Pre-vaccination mean SLEDAI score of was 5.9: due to arthritis (n= 5; 38,5%), low complement

(n=4; 31%), dsDNA (n=4; 31%); with a medium dose of 10mg prednisolone/day and 265mg/day of hydroxychloroquine. Post-vaccination mean SLEDAI was 5.8: due to arthritis (n=6; 46%), rash (n= 5; 38,5%) and low complement (n=6; 46%); with a medium dose of 8mg prednisolone/day and 288mg/day of hydroxychloroquine. There was not a difference in organ involvement before and after vaccination, but rash was slightly more prevalent after vaccination.

Conclusion: In our population, HPV vaccination didn't significantly change disease activity and organ involvement or mean dose need of prednisolone or hydroxychloroquine. Although it is a small size SLE sample, it suggests that is safe to administer HPV vaccination to SLE patients.

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Disclosure of Interests: : None declared

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AB0407 HUMAN PAPILLOMA VIRUS (HPV) INFECTION AND CERVICAL CANCER PREVALENCE IN A PORTUGUESE UNIVERSITY HOSPITAL SINGLE-CENTER SYSTEMIC LUPUS ERYTHEMATOSUS COHORT

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Background: About 12% of women worldwide are infected with Human Papillomavirus (HPV), the most frequent cause of cervical cancer (CC) - very prevalent (~ 7,5%) and preventable. National screening efforts are in use in several countries, including Portugal. Patients with Systemic Lupus Erythematosus (SLE) are at increased risk of HPV infection and CC when compared to the healthy population.

Objectives: To evaluate the prevalence of HPV infection and rate of incidence of cervical neoplastic lesions in a SLE patient cohort followed at a university hospital.

Methods: Retrospective single-center (35 year long, 463 SLE patient cohort) review of all female SLE patients' local and online national health care records on HPV vaccination and CC screening.

Results: Of the 463 SLE patients, 420 were women (91%), of which 322 had records on of HPV infection or CC developed. Mean patients' current age was 48 years and all had screening for cervical pathology in the last 3 years. Thirty-three patients (11%) had HPV infection diagnosed at a mean age of 44 years. Twenty-seven (8%) of SLE patients were vaccinated for HPV: 8 (22%) of the infected patients had the vaccine, half after the HPV infection. Despite HPV infection, 49 patients (15%) had developed some cervical lesion, of which 41 (84% of cervical lesion) were suggestive of malignancy, and ultimately CC was diagnosed in 20 women (41%; 6% of total women), with a mean age at diagnosis of 45 years. All CC patients had history of HPV infection, but only 3 women (15%; 0,9% of total women) had been vaccinated against HPV, 2 after the diagnoses of CC and 1 before.

Conclusion: In our population the prevalence of HPV was higher than reported for the general population using the World Health Organization database, conforming the higher risk of HPV infection in SLE patients. The prevalence of cervical cancer, however, was similar to the healthy population.

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AB0408 DOES THE PRESENCE IN THE SERUM OF ANTIPHOSPHOLIPID ANTIBODIES CORRELATE WITH SPECIFIC/NON SPECIFIC CAPILLAROSCOPIC ABNORMALITIES?

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Background: Antiphospholipid syndrome (APS) is a systemic autoimmune disease characterized by specific vascular and obstetric manifestations and by antiphospholipid antibodies (aPL) positivity [1].

To date, little is known regarding nailfold videocapillaroscopy (NVC) alterations in APS patients and in asymptomatic aPL-carriers, non-specific abnormalities being the most frequently reported [2,3,4].

Objectives: To retrospectively analyze NVC alterations in APS patients and in asymptomatic aPL-carriers and to correlate NCV alterations with both clinical manifestations and serum aPL profile.

Methods: Thirty-five aPL positive patients having received at least one NCV investigation (mean age 47 years, range 16-81, 31 female and 4 male) were retrospectively included in the study. For each patient complete medical history was collected with a particular attention to past vascular thrombosis and pregnancy morbidity. Patients were classified as affected by APS according to the updated Sapporo classification criteria [5]. Lupus anticoagulant (LAC), IgM and IgG anti-cardiolipin antibodies (ACL) and IgM and IgG anti-Beta2 Glycoprotein 1 (anti-B2GP1) were assessed in each patient according to the recommended procedures [5]. NCV parameters were analyzed in each patient, with a particular interest to hemorrhages or nailfold bed-parallel hemosiderin deposits (*"comb-like"* hemorrhages) presence [2,6]. Statistical analysis was performed by parametric and non-parametric tests.

Results: Seventeen patients (mean age 49 years, range 16-81 years) were asymptomatic aPL-carriers and 18 (mean age 46 years, range 26-71 years) were affected by APS. Within APS patients, 16 had a history of vascular thrombosis and 2 had pregnancy morbidity; in 6 patients APS was secondary to other autoimmune rheumatologic conditions (3 to Systemic Lupus Erythematosus, 2 to vasculitides and 1 to Mixed Connective Tissue Disease).

Among the total number of aPL-carriers and APS patients six patients showed a normal NVC pattern, 24 patients had non-specific NVC abmormalities and 5 patients had a "scleroderma-like" pattern. Interestingly, NCV microhemorrhages were significantly more frequent in APS patients than in asymptomatic aPL-carriers, both in score and in absolute (p=0.05 and p=0.04, respectively). Particularly, in APS patients *"comb-like"* hemorrhages had a statistically significant higher prevalence than isolated hemorrhages (p=0.03). Dilated capillaries score was significantly higher in APS patients than in asymptomatic aPL-carriers (p=0.01). Not any statistically significant difference was observed regarding other capillary parameters (score of giant capillaries, loss of capillaries, or anormal shpaes, i.e. angiogenesis). Not any statistical correlation was observed between NVC parameters and different aPL profile.

Conclusion: The study shows that the total number of microhemorrhages and in particular the *"comb-like"* subtype, are significantly the most frequent specific abnormalities in APL patients when compared to asymptomatic aPL carriers. The presence of the "scleroderma like" NVC pattern may suggest a concomitant overlap syndrome. Not any correlation was found between aPL profile and other NVC parameters. Further studies need to develop a more specific APS NVC pattern for APS patients.

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AB0409 APL PREVALENCE IN WOMEN WITH LATE PREGNANCY COMPLICATION AND LOW-RISK FOR CHROMOSOMAL ABNORMALITIES

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Background: Current guidelines help defining correct pregnancy standard of care for patients with antiphospholipid syndrome (APS) and antiphospholipid antibodies (aPL) carriers, but little is known about the significance of aPL detection during pregnancy and their association with clinical manifestations of the syndrome [1].

Objectives: Investigate the presence of aPL antibodies in a cohort of women who experienced late onset pregnancy complications (LO-PC) and low-risk for chromosomal abnormalities.

Methods: We retrospectively collected clinical, demographic and laboratory data of women ever pregnant from August 2017 to August 2018, who attended the S. Anna University Clinic (Turin, Italy). Inclusion criteria were LO-PC, negative triple test and absence of US foetal abnormalities. 100 patients have been recruited and, as control, 100 women matched for age with normal pregnancy. aPL testing was performed on serum samples derived from pregnancy screening test collected between 15 and 18w of gestation. Criteria and "extra criteria" aPL were tested.

Results: Number of aPL positivity (aPL+) was statistically different between patients and controls: 31 aPL+ vs 10 aPL+, respectively (p-value <0.001; p<0.01) (Graph 1).

Patients' population had a significant higher percentage of single aPL+ (p-value < 0.001; p < .05) and, among single isotypes, of ACA IgG (p-value 0.017; p < 0.05) and aPS/PT IgM (p-value 0.0378; p <0.05). Moreover, patients' population had a significant higher aPL titre of ACA IgG and aPS/PT IgM (p-value <0.0001, p < 0.05; p-value 0.0061, p < 0.05).

When comparing aPL+ and aPL negative (aPL-) patients for median age at conception, mode of delivery, foetal outcomes, maternal and foetal pregnancy complication, maternal and foetal post-partum complication and histology findings (see Table 1), we found that aPL+ patient had a significant higher presence of IUGR (P<0.01) and pre-term birth (34-36+6w; p<0.012). When we granulated data for presence/absence of an underlying disease (UD), we found that 29 women had an UD, mostly arterial hypertension and hypothyroidism (59%, not shown), while 71 were healthy (H).

Table 1. Patient characteristics

Population charachteristics	All patients (100)	aPL positive (31)	aPL negative (69)	Chi square test (p value)
Age at conception, mean (S.D.), years	32.9 (5.3)	33.6 (4.7)	32.6 (5.6)	N/A
Mode of delivery				
Cesarean	52 (52)	14 (45)	38 (55)	0.36
Fetal outcomes				
Live births, n (%)	93 (93)	28 (90)	65 (94)	0.48
Birthweight, mean (S.D.), grams	2448(910)	2505(877)	2423(923)	N/A
Gestational delivery, mean (S.D), weeks	35.5(1.6)	35.3(1.3)	35.6(1.6)	N/A
Mild pre-term birth (34-36+6 gestation w), n (%)	18	10	8	**0.012**
Birthweight below 10 percentile (SGA), n (%)	46 (46)	11 (11)	35 (51)	0.157
Maternal and fetal complications				
Gestational hypertension, n (%)	52 (52)	13 (42)	39 (56)	0.18
Preclamspia, n (%)	47 (47)	11 (35)	36 (52)	0.12
HELLP, n (%)	11 (11)	4 (13)	7 (10)	0.68
IUGR, n (%)	16 (16)	1 (3)	15 (21)	**0.01**
Maternal and fetal postpartum complications				
Hypertensive crisis, n (%)	15 (15)	4 (13)	11 (16)	0.69
Hemorrhage, n (%)	10 (10)	4 (13)	6 (9)	0.51
Placental histology findings				
Placental malperfusion, n (%)	27 (27)	8 (26)	19 (27)	0.85

When comparing aPL+/aPL- in UD patients' subgroub, we found no difference; instead, when comparing aPL+/aPL- in H patients' subgroup we found that aPL+ had a significant higher percentage of pre-term birth (34-36w; p<0. 001).

aPS/PT IgM isotype, alone, allowed the detection 17 patients who tested negative for aPL criteria (Graph 1).

Conclusion: Our results, even if preliminary, suggest a direct correlation between aPL positivity and risk of development of LO-PM. In conclusion, testing for both criteria and "extra criteria" aPL in women with previous LO-PM could improve the diagnostic accuracy identifying women at higher risk in case of future pregnancy.

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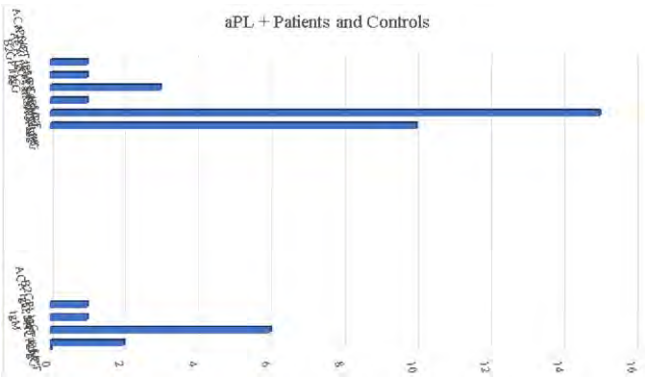


Figure 1. Graph 1. aPL positivity isotype among groups

Disclosure of Interests: : None declared

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AB0410 **COGNITIVE DYSFUNCTION IN PRIMARY SJÖGREN'S SYNDROME AND SYSTEMIC LUPUS ERYTHEMATOSUS**

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Background: Primary Sjögren's syndrome (pSS) and systemic lupus erythematosus (SLE) share several clinical manifestations including neurological involvement. Cognitive dysfunction is a common neuropsychiatric manifestation in both, but evaluation and diagnosis is often challenging and delayed. The Automated Neuropsychological Assessment Metrics (ANAM) is a computerized cognitive screening tool that does not need specialized personnel to apply and is less time consuming than other tests.

Objectives: Assess cognitive function of SLE and pSS patients with a computer-based tool (ANAM) in a single rheumatology clinic, compare its performance, and record their clinical and demographic characteristics

Methods: We recruited patients from the rheumatology clinic of the UANL University Hospital who met the pSS 2002 AECG or ACR-EULAR 2016 classification criteria and SLE patients fulfilling SLICC 2012 criteria. We defined mild cognitive impairment as 1 to 1.9 SD below controls, and moderate-severe cognitive impairment as 2 SD or more below the comparison group (subjects matched by age, sex, ethnicity and educational level by the ANAM program) as previously employed in SLE.

Percentages were used for categorical variables and means (±SD) for numerical ones. To observe differences between groups, chi square and Student´s t were used, p <0.05 was considered significant.

Results: A significant difference was observed in the total ANAM score between SLE and pSS patients (Table 1). In SLE, the most affected domains were simple reaction time, code substitution and delayed memory; in pSS patients, the most affected domains were inhibition and spatial work memory (Table 2).

Table 1. Differences in ANAM performance between pSS and SLE.

Variable	*pSS mean, (SD)*	*SLE mean, (SD)*	*p*
Female, %	92.2	93.5	0.77
Age (years)	56.25 (10.45)	31.99 (13.17)	0.001
Disease duration (years)	6.38 (6.15)	5.61 (6.1)	0.492
ANAM total score	-1.43 (0.85)	-1.87 (0.96)	**0.008**
Simple reaction time	25.5	54.5	**0.001**
Simple reaction time score	148.39 (32.44)	144.13 (52.37)	0.571
Code substitution (Learning)	13.7	9.1	0.411
Code substitution (Learning) score	33.39 (8.42)	38.61 (14.23)	**0.001**
Procedural reaction time-Attention	15.7	27.3	0.125
Procedural reaction time-Attention score	70.29 (12.11)	73.17 (17.68)	0.277
Mathematical processing	11.8	13	0.838
Mathematical processing score	17.92 (11.07)	15.57 (6.63)	0.177
Matching to sample-spatial work memory	21.6	7.8	**0.025**
Matching to sample-spatial work memory score	20.08 (7.66)	22.26 (8.72)	0.139
Code substitution-delayed memory	15.7	7.8	0.161
Code substitution-delayed memory score	26 (11.57)	33.69 (18.99)	**0.005**
Simple reaction time	21.6	32.9	0.165
Simple reaction time score	148.88 (24.82)	166.29 (38.87)	**0.004**
Go/No-Go, Inhibition	21.6	5.2	**0.005**
Go/No-Go, Inhibition score	3.41 (1.57	3.27 (1.68)	0.635

Conclusion: Cognitive impairment was common in both diseases but the cognitive domains affected were different. Rheumatologists should be aware of these differences when evaluating cognitive dysfunction in SLE and pSS patients.

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AB0411 COGNITIVE IMPAIRMENT IN PRIMARY SJÖGREN'S SYNDROME: A CASE-CONTROL STUDY

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Background: Neurological symptoms are common in primary Sjögren's syndrome (pSS) with a prevalence of 8.5 to 70%, focusing on cognitive impairment, information in pSS is scarce.

Many neuropsychological tests are used to diagnose cognitive impairment. The Montreal Cognitive Assessment (MoCA) is a validated, practical, and reliable instrument for screening mild cognitive impairment.

Objectives: To evaluate the prevalence of cognitive impairment with the MoCA test in pSS and compare it with controls.

Methods: Patients of a rheumatology clinic in Northeastern Mexico were recruited, who met the pSS AECG 2002 or ACR-EULAR 2016 classification criteria. Controls, matched by demographic characteristics were included for comparison. All subjects took the MoCA. The test has a range of 0-30 points, the highest score reflects better cognitive function, and explores 6 cognitive domains (Table 2).

Table 1. Demographic and clinical characteristics

Characteristics	pSS n=51	Control n=51
Age, Mean (SD)	56 (10.4)	54 (14)
Sex		
Female n (%)	47 (92.15)	48 (94)
Male n (%)	4 (7.85)	3 (7.3)
Disease duration (years), mean (SD)	6.38 (6.15)	
ESSPRI mean (SD)	4.94 (2.28)	
Years of education, median (q25-q75)	13 (10-17)	12 (10-15)
Employment, mean (%)	19 (37)	29 (56)

Table 2. MoCA subtest analysis by years of education in pSS and control group.

		≤ 9 years of education				≥10 years of education			
	Group	N	mean, SD[1]	Min-max	*p*-value	n	mean, SD[1]	Min-max	*p*-value
MoCA total	pSS	17	25.65 (2.17)	20 - 29	0.248	46	26.67 (2.27)	20 - 30	0.3
	Control	14	24.36 (3.85)	17 - 30		36	27.22 (2.24)	21 - 30	
Visuospatial	pSS	17	3.76 (0.9)	1 - 5	0.505	46	4.17 (1.03)	2 - 5	0.056
	Control	14	4.07 (1.59)	0 - 5		36	4.58 (0.87)	2 - 5	
Naming	pSS	17	2.82 (0.39)	2 - 3	0.831	46	2.96 (0.2)	2 - 3	0.711
	Control	14	2.79 (0.57)	1 - 3		36	2.97 (0.16)	2 - 3	
Deyaled recall	pSS	17	3.06 (1.34)	1 - 5	0.251	46	3.48 (1.31)	0 - 5	0.921
	Control	14	2.43 (1.65)	0 - 5		36	3.44 (1.68)	0 - 5	
Attention	pSS	17	5 (0.79)	3 - 6	**0.041**	46	5.37 (0.77)	4 - 6	0.285
	Control	14	4.29 (1.06)	3 - 6		36	5.53 (0.56)	4 - 6	
Abstraction	pSS	17	1.71(0.68)	0 - 2	0.464	46	1.89 (0.31)	1 - 2	0.79
	Control	14	1.86 (0.36)	1 - 2		36	2 (0.23)	1 - 3	
Orientation	pSS	17	6 (0)	6 - 6	0.999	46	5.93 (0.25)	5 - 6	0.083
	Control	14	6 (0)	6 - 6		36	6 (0)	6 - 6	
Language	pSS	17	2.41(0.71)	1 - 3	0.741	46	2.61 (0.57)	1 - 3	0.878
	Control	14	2.5 (0.76)	1 - 3		36	2.58 (0.84)	0 - 3	

[1]SD: Standard deviation

We defined mild cognitive impairment as a score <26 and moderate-severe cognitive impairment as a score <24 as previously determined in Mexican population.

Results: Demographic and clinical characteristics are described in Table 1. Mild cognitive impairment was present in 13 (25.4%) in pSS group versus 14 (27%) in control group. Moderate-severe cognitive impairment was present in 9 (17%) of pSS group versus 8 (15%) in control (p> 0.05).

Results of the individual domains and comparison between groups are shown in Table 2. Attention was lower in the pSS group with ≤9 years of education compared to the control group (p <0.05).

Conclusion: We did not found a difference in the prevalence of cognitive impairment, either mild or moderate-severe, in pSS subjects with low disease duration versus controls by MoCA. We found a lower attention score in the pSS group with less than 10 of years of education.

The combination of neuropsychological examining and imaging techniques, such as SPECT or brain MRI, seem a more sensitive way to detect cognitive impairment in earlier stages.

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AB0412 URINARY SOLUBLE VCAM-1 IS A USEFUL BIOMARKER OF DISEASE ACTIVITY AND TREATMENT RESPONSE IN LUPUS NEPHRITIS

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Background: The traditional lupus nephritis (LN) biomarkers are not sensitive nor specific enough for detecting ongoing disease activity and early relapse of nephritis and they do not reflect kidney damage nor have prognostic value[1]. Urinary biomarkers are directly excreted by the kidney and are easily obtained. They can also differentiate the renal activity of the disease from other organic manifestations more accurately than the serum biomarkers[2]. Vascular cell adhesion molecule-1 (VCAM-1) is involved in the progression of glomerular and tubulointerstitial injury in LN and its soluble form can be easily assessed in urine (uVCAM-1)[3]. Several studies correlated the uVCAM-1 levels with urine protein-creatinine ratio (UPC), with general disease activity and with active LN[3].

Objectives: To assess uVCAM-1 as a biomarker of disease activity and treatment response in LN.

Methods: This prospective study enrolled patients with class III, IV or V LN diagnosed within the last three years and divided them in two groups: with and without active nephritis at the inclusion. The patients with active nephritis were included before they started a new immunosuppressive treatment. Active LN was defined as proteinuria (UPC≥0.5) plus active urinary sediment (hematuria, leukocyturia or cellular hematic/granular casts). At each visit, a urine sample was collected for uVCAM-1 evaluation and the nephritis status was accessed.

Results: Median uVCAM-1 level was elevated in patients with active compared to inactive LN (p<0.001). The ROC curve of uVCAM-1 demonstrated an AUC of 0.84 and a cutoff of 47.2 ng/mgCr yielded a good sensitivity (74.2%) and specificity (74.2%) for the diagnosis of active LN. A significant correlation was found between uVCAM-1 level and renal activity scores and traditional biomarkers of LN (table 1). The level of uVCAM-1 dropped in patients with active LN who went into remission (p<0.001), increased in patients who went into activity (p=0.002) and did not change in patients who remained inactive (p=0.797) (figure 1). The level of uVCAM-1 peaked during the flare of LN (p<0.05) (figure 2).

Table 1. Correlations between urinary soluble VCAM-1 and other LN biomarkers/disease scores

LN biomarkers/disease scores	VCAM-1
SLEDAI-2k	0.597***
Renal SLEDAI	0.569***
Renal SLAM-R	0.470***
Renal SLICC	0.620***
Anti-dsDNA	0.342**
C3	-0.344**
C4	-0.382**
UPC	0.654***

Spearman's correlation coefficients
*p value <0.05; **p value <0.01; ***p value <0.001
C, complement; LN, lupus nephritis; SLEDAI, Systemic Lupus Erythematosus Disease Activity Index; renal SLAM-R, The renal Systemic Lupus Activity Measure revised; renal SLICC, The Systemic Lupus International Collaborating Clinics renal activity/response exercise; UPC, urine protein-creatinine ratio.

Conclusion: The uVCAM-1 is a reliable biomarker that reflects renal disease activity and is useful for monitoring individual patients with lupus nephritis over time.

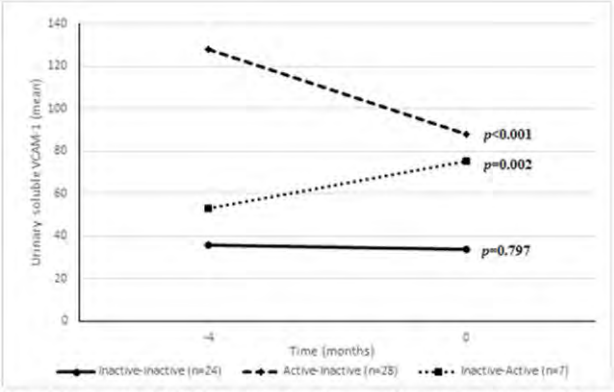


Figure 1. Urinary soluble VCAM-1 levels according to lupus nephritis status. Active LN was defined as proteinuria (UPC≥0.5) plus active urinary sediment (hematuria, leukocyturia or cellular hematic/granular casts).

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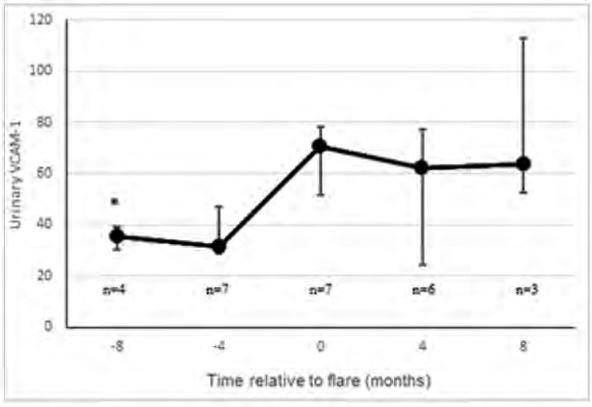


Figure 2. Urinary soluble VCAM-1 levels at different time points relative to a lupus nephritis flare. The levels of uVCAM-1 of seven lupus nephritis patients were evaluated 8 and 4 months before and after a flare, including at the time of the flare itself (time point 0). The number of patients who contributed at each moment was informed. Graph represents median and interquartile range.*p<0.05 compared with level at flare.

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AB0413 INVESTIGATION OF THE ASSOCIATION OF CARDIOVASCULAR EVENTS AND ANTI- SS-A ANTIBODIES AS RISK OF DEVELOPMENT IN PATIENTS WITH LUPUS NEPHRITIS FROM THE LUNA REGISTRY: A CROSS-SECTIONAL STUDY

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Background: Cardiovascular disease(CVD) has been identified as a major cause of morbidity and mortality in patients with lupus nephritis(LN)[1) 2)]. There is a clear causal relationship between the onset of neonatal lupus (cardiac complications) and SS-A antibodies[3) 4)], but no association has been reported in adults. In recent years, there have been reports from overseas that suggest the association between CVD and anti-SS-A antibody in adult systemic lupus erythematosus (SLE) patients[5) 6)]. So far, no studies have not been reported to evaluate the relationship between anti-SS-A antibody and the risk of developing CVD in LN in a large cohort of patients with SLE in Japan.
Objectives: The aim of this study was to evaluate the association between anti-SS-A antibody and the risk of developing CVD in LN patients using a multicenter registration study [Lupus registry of nationwide institution (LUNA)] in Japan.
Methods: We identified 931 patients diagnosed with SLE in the Lupus registry of nationwide institution (LUNA), and further identified 275 LN patients with known the presence or absence of both development of CVD and presence of anti-SS-A antibody. We defined the exposure factor as anti-SS-A antibody, and the outcome as CVD. SELENA-SLEDAI score (at diagnosis), eGFR <60%, HbA1c, BMI, and steroid pulse treatment history were used as confounding factors and we analyzed using logistic regression analysis.
Results: We found 68 patients (24.7%) complicated with CVD, including percarditis (7.3%), cerebrovascular disorder (6.2%), peripheral Arterial Disease (6.2%), Ischemic heart disease (2.9%), *venous thromboembolism (2.9%),* pulmonary hypertension (1.5%), vulvular heart disease (1.1%), and cardiomyopathy (0.4%). In univariate analysis, there was no significant difference in the occurrence of CVD depending on the presence or absence of anti-SS-A antibody (p = 0.32), and the results of multivariate analysis showed no significant difference in anti-SS-A antibody [p = 0.23, odds: 0.41, 95% confidence interval (0.09-1.89)].
Conclusion: The association between anti-SS-A antibody and the development of CVD in LN patients in Japan has not been identified.
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Disclosure of Interests: None declared
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AB0414 ESSPRI COMPONENTS AND SALIVARY FLOW RATE ARE RELATED TO DAILY ACTIVITY IMPAIRMENT IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

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Background: Sjögren's syndrome (SjS) is a chronic systemic autoimmune disease targets primarily the salivary and lacrimal glands, the severe dryness of the mouth and eyes are common manifestations in patients. Therefore, daily life could be affected by these manifestations in patients with SjS.
Objectives: The aim of the study was to assess associations among daily activity impairment and scores of EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI) and major salivary gland ultrasonography (SGUS) in primary SjS.
Methods: In this cross-sectional study, 41 patients with primary SjS (F/M:39/2; mean age: 52,1±10,5) were included. The mean disease duration was 9.5±6,6 years in the group.
Data were collected by clinical examinations and a questionnaire regarding two patients reported outcome measures (PROMs). Firstly, Work Productivity and Activity Impairment (WPAI) questionnaire assessed paid and unpaid work during the last seven days. Scores of WPAI subgroups as absenteeism, presenteeism, overall work impairment as well as daily activity impairment were calculated by using 6 items. Secondly, dryness, fatigue and pain in ESSPRI scale were evaluated by visual analogue scale (VAS; 0-10 points) in SjS. High scores in both PROMs indicates that disease manifestations affect patient 'life poorly.
In addition, structural damage of parotid and submandibular salivary glands were examined by using Milic and Hocevar USG scoring methods. Unstimulated whole salivary flow rate (U-WSFR; as ml/min) were also used to interpret the functional status of major salivary glands. High SGUS score and low U-WSFR reflects that disease activity affects major glands poorly.
Results: Daily activity impairment was calculated as 63,9±31,1 in patients with primary SjS. High scores in ESSPRI-dryness, ESSPRI-fatigue and ESSPRI-pain were also observed in the group (7,5±2,4; 6,4±2,8 and 6,1±3,1, respectively). Daily activity impairment was correlated with scores of ESSPRI-dryness (r:0,55 p=0.000), ESSPRI-fatigue (r:0,38 p=0.014) and ESSPRI-pain (r:0,56 p=0.000) as well as parenchymal inhomogeneity USG scores of right and left parotid glands (r:0,49 p=0.032; r:0,51 p=0.025).
U-WSFR (0.20±0.20 ml/min) was moderately correlated with parenchymal inhomogeneity USG scores of major salivary glands (p<0.05). ESSPRI-dryness score was significantly higher in patients with low U-WSFRs (≤ 0.1 ml/min) than the others (87,5±16,3 vs 68,3±25,1, respectively)(p=0.021).
Conclusion: Firstly, subgroup scores of ESSPRI and low U-WSFR associated to daily activity impairment in patients with primary SjS. Secondly, parenchymal inhomogeneity scores of both parotid glands could give an important clue to clinicians for the disease-related damage. Finally, WPAI with 6-item could be thought as an useful tool to understand the effect of the disease manifestations on patients' daily life.
Disclosure of Interests: : None declared
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AB0415 SERUM RESISTIN LEVEL IN SYSTEMIC LUPUS ERYTHEMATOSUS: RELATION TO LUPUS NEPHRITIS AND DISEASE ACTIVITY

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Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease affecting different organs and systems.. Adipokines have recently been implicated as mediators of immune and inflammatory processes. Human resistin is a cytokine that induces low-grade inflammation by stimulating monocytes
Objectives: The aim of this work is to assess the serum level of resistin in SLE patients and to detect its relation to lupus nephritis, and disease activity
Methods: 40 patients with SLE with age ranged between 18-48 years and 20 healthy age, sex and BMI matched volunteer were enrolled in this study. According to the presence or absence of lupus nephritis (LN), patients were classified into two subgroups Full history, clinical examination and laboratory investigations were performed for all patients including serum resistin level
Results: The level of serum resistin was higher in SLE patients than the controls *(p=0.001).* Also, serum resistin levels were higher in patients with lupus nephritis than those without nephritis *(p= 0.02).* Serum resistin level correlated positively with the levels of ESR *(p< 0.001)*, CRP *(p= 0.005),* Anti-dsDNA *(p= 0.002)* and serum urea *(p= 0.002).* Serum resistin levels correlated negatively with hemoglobin levels *(p= 0.001)* and levels of C3 *(p< 0.001)* and C4 *(p< 0.001).* There was a significant positive correlation between serum resistin level and the presence of albumin *(p= 0.001),* RBCs *(p= 0.003),* pus cells *(p= 0.001)* and casts *(p< 0.001)* in urine and also with the levels of 24 hour urinary protein and protein/ creatinine ratio *(p<0.001).* Serum resistin level was found to be strongly correlated with SLEDAI *(p< 0.001).* No correlation was found between serum resistin levels and ISN/RPS classification of renal biopsy.
Conclusion: Serum resisitin level can be used as a marker of inflammation, nephritis,disease activity in patients with SLE.
Disclosure of Interests: : None declared
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AB0416 ANTIPHOSPHOLIPID SYNDROME IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOUS

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Background: Antiphospholipid Syndrome (APS) is an autoimmune disorder characterized by venous/arterial thrombotic events and pregnancy morbidity in presence of pathogenic autoantibodies known as antiphospholipid antibodies (APL). APS is often associated with systemic autoimmune diseases, especially with Systemic Lupus Erythematous (SLE), being part of the latest criteria of SLE.[1]
Objectives: The aim of this study was to evaluate the impact of Antiphospholipid syndrome in patients with Systemic Lupus Erythematous presented at our Rheumatology Clinic at University Hospital Center Mother Teresa in Tirana, Albania.
Methods: This is an observational case-control study which included patients diagnosed with SLE from 16-51 years old, presented at our clinic during the period from 10 December 2014-10 September 2019.
Seventy-three patients with SLE were included in the study. Patients were classified according to the presence of Antiphospholipid Syndrome or not, according to the current guidelines. The case study (patients with SLE and APS) consisted in 24 patients, and the control group consisted in 49 patients. Besides the usual laboratory tests (complete blood count, erythrosedimentation rate, C3, C4 complement fractions, urinalysis and 24h proteinuria, c-reactive protein), all patients underwent immunological tests for anti-nuclear antibodies, anti-DNA antibodies and antiphospholipid antibodies (Anti-cardiolipin IgM and IgG). If APL were found positive, according to EULAR recommendations, tests were repeated after 12 weeks. Female patients were asked about their pregnancy history and their possible miscarriages/aborts.
Results: After our statistical analysis it resulted that there is a significant difference between C3 complement fraction (patients with APS and SLE tend to have more hypocomplementemia than the other group) (p= 0.006). Thrombocytopenia resulted to be an important feature, statistically significant in the cases' group (p= 0.003). It was seen a statistically significant difference referring to the number of miscarriages/aborts in the history of female patients with APS and SLE in comparison to those with SLE without APS (p= 0.03). Proteinuria it has a tendency to be more marked in patients with APS and SLE, with a significant difference in comparison to the controls (p= 0.04).
Conclusion: In this study was seen that patients with antiphospholipid Syndrome and Systemic Lupus Erythematous tend to have more hypocomplementemia C3, and thrombocytopenia. It resulted a statistically significant relationship with miscarriages or aborts in patients with APS and SLE in comparison to SLE patients. It was seen a significant tendency to have marked proteinuria in patients with SLE and APS compared to controls.
Through this study it was seen a characteristic clinical and laboratory picture that may be useful in the identification of cases with APS in patients with SLE, in their follow-up and treatment.
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Disclosure of Interests: None declared
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AB0417 WORK IMPAIRMENT AND PREDICTORS OF WORK INCAPACITY AMONG PRIMARY SJOGREN'S SYNDROME PATIENTS

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Background: Primary Sjogren's syndrome (PSS) is a prevalent rheumatic disorder affecting exocrine glands but also other systems. It alters quality of life of affected patients and increases work incapacity and general activity impaiment.
Objectives: The purpose of this study was to assess the influence of PSS on work among affected patients and determine predictors of work incapacity.
Methods: A cross-sectional study was conducted in the internal medicine department. Adult patients diagnosed with PSS and fulfilling the EULAR criterea for the diagnosis were included. Clinical and biological data was collected from medical files and during medical visits. Disease activity was calculated using

the ESSDAI score. Work incapacity was assessed by the Work productivity and activity impairment for general health questionnaire (WPAI-GH) from which four dimensions can be calculated and expressed in percentages by the following scores: 1) percent work time missed due to health = Q2/(Q2 + Q4) for those who were currently employed; 2) percent impairment while working due to health = Q5/10 for those who were currently employed and actually worked in the past seven days; 3) percent overall work impairment due to health Q2/(Q2 + Q4) + ((1 - Q2/(Q2 + Q4)) × (Q5/10)) for those who were currently employed; 4) percent activity impairment due to health Q6/10 for all respondents.

Results: Eighty patients were randomly asked to fill out the questionnaire. Response rate was of 62.5%. Total number of enrolled patients was 50. The median age was 56.5 years (min=22, max=60). Patients were mainly women with female to male ratio of 11.5:1. The median age of diagnosis was 50.5 years (min=18, max=59). Mean duration of the disease was 6 years ± 3.76. Sicca syndrome was the most prevalent clinical feature affecting the eyes in 84% of the cases and the mouth in 90% of the cases. Arthralgia was present in 88% of the cases. 65.1% of patients had an active disease. Anti Ro antibodies were positive in 38%, anti La in 28% and rheumatoid factor in 50% of cases. 36% of the patients were unemployed. Percentage of work time missed due to health for those who were employed in the past 7 days was 2.44% (Q1=0;Q2=5.26). Mean percentage of impairment while working due to health for those who were employed and actually worked in the past 7 days was 20.56±18.25%. Percentage of overall work impairment due to health for those who were currently employed and actually worked was 25.87±19.58%, and the percentage of overall activity impairment due to health for all respondents was 26.6±18.36%. Analytic statistics showed no correlation between employment status and age, duration of disease, gender or seropositivity. However, all unemployed patients had ocular symptoms vs 75% of those employed (p value=0.04). The first dimension was correlated with the presence of dry mouth (p value=0.07) but with weak statistical significance. Second and third dimensions weren't associated to any general, clinical or laboratory feature. Fourth dimension was significantly correlated to the presence of dry eyes (p value=0.019) and gender (p value=0.001).

Conclusion: PSS is associated with high unemployment rates in Tunisia, high impairment rates while working and high rates of overall impairment. This high prevalence may be explained by gender and the presence of dry eyes and dry mouths. This work highlights the importance of managing sicca symptoms as they alter different aspects of quality of life like work.

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AB0418 APPLICATION OF ACR (2012), ACR/EULAR (2016) AND RUSSIAN (2001) CRITERIA FOR PRIMARY SJÖGREN'S SYNDROME ON RUSSIAN COHORT OF PATIENTS

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Background: Over the past few years new international criteria have been proposed for the classification of primary Sjögren's syndrome (pSS) from the American College of Rheumatology (ACR) in 2012 and the ACR with European League Against Rheumatism (ACR/EULAR) in 2016 [1, 2]. In real practice in Russia we use Russian criteria (2001).

Objectives: To estimate ACR (2012) and ACR/EULAR (2016) criteria in Russian cohort of patients with pSS patients fulfilling Russian criteria (2001).

Methods: From 2016 to 2019 we examined 110 patients (109 female, 1 male) with newly diagnosed pSS fulfilling Russian criteria with the mean age 50,2±14 years (min 18; max 82). Russian criteria for pSS: I) keratoconjunctivitis sicca (stimulated Schirmer's test <10 mm/5 min or fluorescein staining of the cornea or tear break-up time < 10 sec); II) sialadenitis (sialectasia on parotid sialography (obligatory) +/- stimulated saliva flow test<2,5 ml/ 5min +/- labial salivary gland biopsy with focus score (FS) of ≥2 foci/4mm^2); III) positive antinuclear antibody (ANA) or positive ANA with rheumatoid factor (RF) or anti-SSA (anti-Ro) or/and SSB (anti-La). According it pSS is verified if the first two criteria and at least one of the immunological criteria are presented. We evaluated clinical, laboratory and instrumental features (table 1).

Table 1. Characteristics of Russian cohort of patients with primary Sjögren's syndrome (n = 110)

Parameters	Patients (n / %)
ocular dryness	76 (69%)
oral dryness	88 (80%)
anti-SSA (anti-Ro) positive (>25 IU/ml)	93 (84.5%)
anti-SSB (anti-La) positive (>25 IU/ml)	57 (51.8%)
RF positive >2UNL (>30 IU/ml)	68 (61.8%)
ANA ≥1:320	110 (100%)
(stimulated) Schirmer's test (≤5 mm/5 minutes)	55 (50%)
stimulated SFT <2,5ml/5 min	77 (70%)
OSS ≥5	28 (25.4%)
OSS ≥3	43 (39%)
FS ≥ 1foci/4 mm^2	99 (90%)
Sialectasia on parotid sialography	110 (100%)

In our cohort according to Russian criteria (2001) 94 patients (86%) fulfilled ACR (2012) criteria, 86 (78%) - ACR/EULAR (2016) criteria.

Results: In our cohort, 20-30% of patients, according to Russian criteria did not complain of oral or ocular dryness. In 61% of patients, mild eye damage was detected (OSS<3-5), and in half of the cases, the stimulated Schirmer's test was more than 5.0 mm, but less than 10 mm/5 minutes, while 69% of patients complained of dry eyes. Most patients (84.5%) had positive anti-Ro, just over half (51.8%) had anti-La. All patients had sialectasia of various stages on parotid sialography. Less than 1 FS was detected in 10% of patients.

Conclusion: Using Russian criteria (2001), we can identify pSS at an early stage. Our criteria inclusion complex examination in which an immunological sign must be present to confirm the diagnosis. Patients with pSS according to ACR (2012) and/or ACR/EULAR (2016) criteria seem to be diagnosed without specific antibodies and on the more progressive disease stages.

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[2] Caroline H. Shiboski,1 Stephen C. Shiboski,1 Raphae `le Seror,2 Lindsey A. Criswell,1 Marc Labetoulle,2 Thomas M. Lietman,1 Astrid Rasmussen,3 Hal Scofield,4 Claudio Vitali,5 Simon J. Bowman,6 Xavier Mariette,2 and the International Sjogren's Syndrome Criteria Working Group. 2016 American College of Rheumatology/European League Against Rheumatism Classification Criteria for Primary Sjogren's Syndrome. ARTHRITIS & RHEUMATOLOGY Vol. 00, No. 00, Month 2016, pp 00–00 DOI 10.1002/art.39859.

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AB0419 THE COEXISTENCE OF FAMILIAL MEDITERRANEAN FEVER (FMF) IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) PATIENTS - A CROSS SECTIONAL STUDY

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Background: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease characterized by multisystem inflammatory lesions affecting many organ systems in the body. Familial Mediterranean fever (FMF) is an autosomal recessive disease of chronic autoimmune inflammation characterized by frequently relapsing self-limiting fever and inflammation that may be localized in peritoneum, pleura, joint or skin.[1] Previous studies have described the similarity of clinical symptoms of FMF among SLE patients. However, the literature on this topic is inconsistent and based mostly on case reports.[2-4]

Objectives: To examine the proportions of coexistence of FMF among SLE patients compared to the general population. We hypothesized that the proportion of FMF among SLE patients is higher than the general population.

Methods: This cross-sectional study used the Clalit Health Services database, the largest Health Maintenance Organization in Israel, serving 4,400,000 members. SLE patients were compared to age- and sex-matched controls. Chi- was used for univariate analysis.

Results: The study included *4886 SLE* patients and 24430 age- and sex-matched controls. The SLE group had a significantly higher proportion of FMF patients compared to non-SLE controls (0.68% and 0.21% respectively; p < 0.001).
Table 1. All study population

Table 1. SLE patients and matched controls basic characteristics

	No SLE	SLE	p.overall
	N=24430	*N=4886*	
Age	51.2±16.5	51.2±16.5	1.000
Gender: Female	20100 (82.3%)	4020 (82.3%)	1.000
FMF	52 (0.21%)	33 (0.68%)	<0.001

Table 2. Stratification

Table 2. comparison of FMF patients with and without SLE

	FMF without SLE	FMF with SLE	p.overall
	N=52	*N=33*	
Age	44.6±13.7	50.5±17.7	0.106
Gender: Female	45 (86.5%)	26 (78.8%)	0.523

Conclusion: FMF was found to be more common amongst SLE patients compared to matched controls.The current study results suggest that the occurrence of SLE turn patients with an appropriate genetic and environmental setting to develop also FMF. This cross-sectional study sheds light on the coexistence of these two diseases, autoimmune and autoinflammatory.

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Disclosure of Interests: : None declared
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AB0420 RISK OF DEVELOPING TYPE 2 DIABETES MELLITUS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Patients with systemic lupus erythematosus (SLE) have higher than in general population prevalence of diabetes mellitus (DM). Hyperinsulinemia is a predictor of developing type 2 DM, however routine measurement of insulin levels for DM risk assessment is uncomfortable in daily clinical practice. International Diabetes Federation recommends the use of patient questionnaires to quickly identify people who may be at a higher risk of DM development.
Objectives: To determine the 10-years risk of developing type 2 DM in SLE patients using dedicated questionnaire - Finnish Type 2 Diabetes Risk Assessment Form (FINDRISK) data.
Methods: The study included 92 SLE patients without DM (83 women, 9 men, 39 [34; 47] years old). The median disease duration was 6 [2,14] years, SLEDAI-2K was 4[2;8]. SLE pts were treated with glucocorticoids (GC) (89%) and hydroxychloroquine (78%), immunosuppressive drugs (28%) and biological agents (10%). The control group consisted of 88 subjects without systemic rheumatic diseases, inflammatory arthritis or DM, matched by age and sex with SLE patients. Eight items of FINDRISK questionnaire (age, overweight, abdominal obesity, family history of diabetes, physical inactivity, eating habits, history of antihypertensive drugs treatment, history of hyperglycemia) were taken into account to calculate the total risk score (TS). The risk of developing DM within following 10 years is regarded as low (1%) or slightly elevated (4%) with TS ≤11 points, as moderate (17%), high (33%) or very high (50%) with TS ≥12 points.
Results: The risk of developing DM was low or slightly elevated in 65 (71%) SLE pts and moderate, high or very high in 27 (29%) pts. The difference was significant compared with the control group, in which 76 (86%) subjects had a low or slightly elevated risk and 12 (14%) had a moderate, high or very high risk (p=0,01). The number of risk factors (4[2;5]) and the median TS of SLE pts (9[5;12] points) were higher than values in control subjects (3[2,4] factors and 6[3;9] points, respectively) (p<0,01 for both). DM risk factors profiles were similar in two groups, except for higher prevalence of abdominal obesity (66% vs 41%, p<0,01) and history of antihypertensive drugs treatment (57% vs 17%, p<0,01) in SLE. There were positive correlations between TS and CRP levels (r=0,25, p=0,02), SLICC (r=0,36, p<0,01), HAQ (r=0,29, p<0,01), and negative correlations between TS and SLEDAI-2K (r= -0,32, p<0,01), glomerular filtration rate by CKD-EPI (r=-0,23, p=0,03). Current GC use had no influence on TS values in SLE.
Conclusion: Patients with SLE were more likely than individuals without systemic rheumatic diseases to have a moderate, high and very high risk of developing DM, and therefore, required interventions to prevent the metabolic disease. Increased risk of developing DM was associated with most common traditional factors, especially by abdominal obesity and regular use of antihypertensive drugs that can be considered a kind of equivalent to the presence of hypertension. Curtain contribution of inflammation, lupus activity and irreversible damage index can't be ignored. Clarification of SLE-specific phenomena in DM pathogenesis requires further research.
Disclosure of Interests: : None declared
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AB0421 EFFECT OF BODY WEIGHT ON COMPLEMENT LEVELS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: The complement system is a recognized biomarker for diagnosis or monitoring of disease activity in systemic lupus erythematosus (SLE) patients (pts). But on the other hand, it has been linked to insulin resistance and obesity in general population.
Objectives: To find out whether overweight/obesity can modify C3 or C4 levels in SLE pts.
Methods: A total of 92 SLE pts (83 women, 9 men, 39 [34;47] years old) were enrolled in the study. Median disease duration was 6[2;14] years, and SLE activity using SLEDAI-2K was 4[2;8]. SLE pts were treated with glucocorticoids (89%), hydroxychloroquine (78%), immunosuppressants (28%), biologics (10%). The overweight/obesity status was determined by World Health Organization criteria in patients with body mass index (BMI) ≥25kg/m2.
Results: Overweight/obesity were established in 46% SLE pts. Overweight/obese SLE pts were older than pts with normal BMI (40[36;48] vs 37[31;44] years, p=0,02), and had lower SLEDAI-2K (3[2;6] vs 6[4;8], p<0,01). Lower C3 concentrations were found in 36% overweight/obese pts vs 68% pts with normal weight (p<0,01), decreased C4 levels - in 19% vs 30% pts (p=0,33), median C3 concentrations were 0,98[0,81;1,14] g/l vs 0,84[0,69;0;96] g/l (p<0,01), and C4 levels were 0,15[0,10;0,19] g/l vs 0,12[0,09;0,16] g/l, respectively (p=0,03). C3 and C4 levels negatively correlated with SLEDAI-2K (r=-0,5, p<0,01 for both), the effect was more strongly pronounced in patients with BMI≥25kg/m2 (r=-0,6, p<0,01 for both) than in those with normal weight (r=-0,2, p=0,09 for C3, r=-0,3, p=0,04 for C4).
Conclusion: Overweight/obesity status in SLE pts was associated with increased levels of complement proteins, therefore decreased C3 or C4 levels in patients with BMI≥25kg/m2 are more likely related to disease activity and, can potentially induce SLE flares.
Disclosure of Interests: : None declared
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AB0422 LEFT VENTRICULAR ABNORMALITIES IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS FOLLOWED BY SEQUENTIAL ECHOCARDIOGRAPHY

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Background: Cardiovascular disease (CVD) is detected in up to 50% of systemic lupus erythematosus (SLE) patients[1] and major cause of death[2]. Even clinically silent SLE patients can develop left ventricular (LV) diastolic dysfunction[3]. Proper echocardiographic follow up of SLE patients is required.
Objectives: To clarify how the prevalence of LV abnormalities changes over follow-up period and identify the associated clinical factors, useful in suspecting LV abnormalities.
Methods: 29 SLE patients (24 females and 5 men, mean age 52.8±16.3 years, mean disease duration 17.6±14.5 years) were enrolled. All of them underwent echocardiography as the baseline examination and reexamined over more than a year of follow-up period(mean 1075±480 days) from Jan

2014 to Sep 2019. Patients complicated with pulmonary artery hypertension, deep venous thrombosis or pulmonary embolism and underwent cardiac surgery during the follow-up period were excluded. Left ventricular(LV) systolic dysfunction was defined as ejection fraction (EF) < 50%. LV diastolic dysfunction was defined according to ASE/EACVI guideline[4]. LV dysfunction (LVD) includes one or both of LV systolic dysfunction and LV diastolic function. Monocyte to HDL ratio (MHR) was calculated by dividing monocyte count with HDL-C level.

Prevalence of left ventricular abnormalities was analysed at baseline and follow-up examination. Clinical characteristics and laboratory data were compared among patient groups as follows; patients with LV dysfunction (Group A) and without LV dysfunction (Group B) at the follow-up echocardiography, patients with LV asynergy at any point of examination (Group C) and patients free of LV abnormalities during the follow-up period (Group D).

Results: At the baseline examination, LV dysfunction (5/29 cases, 13.8%), LV asynergy (6/29 cases, 21.7%) were detected. Pericarditis was detected in 7 patients (24.1%, LVD in 3 patients, LV asynergy in 2 patients) and 2 of them with subacute onset had progressive LV dysfunction, while 5 patients were normal in echocardiography after remission induction therapy for SLE. At the follow-up examination, LV dysfunction (9/29 cases, 31.0%, 5 new-onset and 1 improved case), LV asynergy (6/29 cases, 21.7%, 2 new-onset and 2 improved cases) were detected. Though any significant differences were observed between Group A and Group B at the baseline, platelet count (156.0 vs 207.0, p=0.049) were significantly lower in LV dysfunction group (Group A) at the follow-up examination. Group C patients had significantly higher uric acid (p=0.004), monocyte count (p=0.009), and MHR (p=0.003) than Group D(results in table).

Conclusion: LV dysfunction is progressive in most of patients and requires regular follow-up once they developed. Uric acid, monocyte count and MHR are elevated in SLE patients with LV asynergy. Since MHR elevation was reported as useful marker of endothelial dysfunction[5], our future goal is to analyse involvement of monocyte activation and endothelial dysfunction in LV asynergy of SLE patients.

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	GroupC(LV asynergy +,n=8)	GroupD(no abnormality, n=10)	P
Age, (y)	63.0(51.3-71.0)	49.0(45.8-61.8)	ns
SLE duration, (y)	22.9(13.4-33.9)	7.0(4.9-25.6)	ns
SLEDAI	1.0(0.0-2.0)	2.0(0.0-6.3)	ns
White blood cell count, ($x10^9$/L)	7.0(5.4-11.2)	6.1(4.7-7.9)	ns
Lymphocyte count, ($x10^9$/L)	1.2(0.88-2.1)	0.89(0.67-1.2)	ns
Monocyte count, ($x10^9$/L)	0.48(0.29-0.57)	0.24(0.17-0.29)	0.009
Hb, (g/dL)	11.7(10.5-14.2)	13.1(12.3-14.2)	ns
Platelet, ($x10^9$/L)	195.0(157.3-270.8)	225.0(183.3-284.8)	ns
Uric acid, (mg/dL)	7.2(5.8-8.1)	4.5(3.8-6.0)	0.004
IgG, (mg/dL)	1201(807.0-1347)	1260(1034-1786)	Ns
Anti-DNA antibodies, (mg/dL)	0.0(0.0-7.3)	3.0(0.0-26.0)	ns
CH_{50}, (mg/dL)	42.4(38.6-44.4)	39.7(28.9-46.9)	ns
Triglyceride, (mg/dL)	127.0(80.0-156.0)	109.0(75.5-155.0)	ns
HDL-Cholesterol, (mg/dL)	53.0(51.25-62.0)	54.5(42.8-82.7)	ns
LDL-Cholesterol, (mg/dL)	102.0(89.0-103.0)	118.5(82.8-134.3)	ns
MHR	0.0087(0.0063-0.012)	0.0039(0.0026-0.0051)	0.003

Numbers are median (interquartile range), Mann-Whitney u test were performed, p value less than 0.05 was considered statistically significant.

Disclosure of Interests: : None declared

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AB0423 NEUROPSYCHIATRIC OUTCOME OF CHILDREN BORN TO WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) WOMEN AND EXPOSED IN UTERO TO AZATHIOPRINE: A CASE-CONTROL STUDY.

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Background: A possible increase in neurodevelopmental (ND) and learning disorders (LD) in the offspring of mothers affected by SLE have been suggested in some studies, along with the identification of different possible risk factors. Azathioprine (AZA) is commonly used during pregnancy, based on its non-teratogenicity and extended experience in women with different diseases. However, a few small studies suggested an association between in utero exposure to AZA and possible increased frequency of ND/LD in children, indirectly derived from increased request of supportive educational services.

Objectives: To evaluate the medium-long term outcome in terms of ND/LD in children of school age (≥6 years) born to SLE women treated with AZA during pregnancy, as compared to that of children born to SLE mothers not treated with AZA during pregnancy.

Methods: Data from our Pregnancy Clinic registry were collected for prospectively followed pregnancies of SLE women treated with AZA (cases) and compared to pregnancies of SLE women not treated with AZA (controls), that were matched for age at pregnancy, presence of renal involvement and aPL positivity. SLE patients (cases and controls) were interviewed by phone to collect data about their children, focusing on the presence of ND/LD certified by Neuropsychiatrists.

Results: Data were collected for 14 SLE mothers in the AZA group and 31 in the control group, with similar age at pregnancy (30.3±5.21 vs 31.4±4.70 years, p:0.45) and frequency of renal involvement (50.0% vs 44.1%, p:0.77), aPL positivity (33.3% vs 29.4%, p:0.76) and anti-Ro/SSA positivity (27.8% vs. 26.5%, p:0.55). A SLE flare during pregnancy was more frequently recorded in the AZA group (27.8% vs. 2.94%, p:0.02). Other medications included HCQ (55.6% vs. 70.6%, p:0.36) and corticosteroids (100% vs 79.4%, p:0.08).

We collected data for 18 children in the AZA group and 34 children in the control group, that had a similar mean age at the time of the interview (12.7±4.80 vs. 12.9±5.61 years, p:0.91). The two groups had also similar gestational age (37.4±2.20 weeks vs. 38.0±1.29 weeks, p:0.23), birth weight (3003±433 g vs 3011±453 g, p:0.95) and rate of male sex (61.1% vs 44.1%, p:0.38).

We recorded similar frequency of ND/LD in the two groups. In particular, a ND was present in 2/18 (11.1%) of children exposed to AZA vs. 2/34 (5.88%) in the control group (p:0.60). A LD was present in 1/18 cases (5.56%) and 6/34 controls (17.6%) (p:0.40).

Conclusion: The medium-long term outcome of children born to SLE mothers in the whole cohort was characterized by the presence of ND in 4/54 (7.69%) and LD in 7/52 (13.5%). ND/LD do not seem to be related to in utero exposure to AZA.

Disclosure of Interests: None declared

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AB0424 PREDICTORS OF SLE FLARE-UP AND PREMATURE DELIVERY IN PREGNANCY

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Background: Systemic lupus erythematosus (SLE) is a life-threatening autoimmune disease that affects many women of child-bearing age, with potentially severe consequences on pregnancy outcome. SLE flare-ups may occur during pregnancy and the post-partum period. Previous studies documenting the incidence and risk factors of flare-up of SLE during pregnancy and puerperium had partially discordant results.

Objectives: We aimed to delineate the pregnancy complications of women with SLE, as well as neonatal outcomes of their offspring, and hoped to clarify the incidence and risk factors of SLE flare-ups during pregnancy and puerperium.

Methods: We retrospectively reviewed the medical records of SLE patients with previous records of pregnancies in our institution. Flare events during pregnancy and puerperium were documented. The pregnancy outcomes recorded include live births, intra-uterine fetal death (IUFD), premature delivery (< 36 weeks of gestational age), NICU admission, and small for gestational age (SGA, <10^{th} percentile). Univariate logistic regression was performed to determine the factors associated with disease relapse and pregnancy outcomes.

Results: From January, 2000 to December, 2019, a total of 94 SLE patients with 139 pregnancies were identified. The overall live birth rate was 92.4% (134/145). Forty-six (34.3%) of the neonates were delivered prematurely. Forty-six (34.3%) of them were SGA. The admission rate to the neonatal intensive care unit was 25% (30/120). Nine (6.4%) were diagnosed to have SLE during pregnancy. The flare rate during pregnancy was 20% while post-partum 9.4%. The majority of the relapses during pregnancy occurred in the second trimester (46.2%), followed by the first trimester (30.8%), and the third trimester (23.1%). Low complement C3 (C3 < 80mg/dl), thrombocytopenia (PLT < 100*10^3/uL) at conception, and low serum albumin level at the first trimester were associated with antepartum flare. Presence of disease flare and pre-eclampsia in pregnancy, and low serum albumin level at conception were significantly associated with premature delivery.

Conclusion: Low complement C3 and thrombocytopenia at conception, and low serum albumin level at the first trimester were associated with disease flare-up during pregnancy. Patients with relative low serum albumin level at conception, or presence of eclampsia or disease flare-up during pregnancy had a higher risk of premature delivery.

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AB0425

PRELIMINARY EVALUATION OF THE SURAL NERVE USING 24-MHZ ULTRASOUND: A NEW APPROACH TO EVALUATE SURAL NEUROPATHY OF SJOGREN'S SYNDROME PATIENTS

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Background: Peripheral neuropathy is one of the most frequent extraglandular manifestations of primary Sjögren's syndrome (pSS). The diagnosis of peripheral neuropathy complications of pSS is based primarily on careful neurologic examination and electrodiagnostic tests. The value of ultrasound in peripheral nerve has been recognized. However, little clinical researches have focused specifically on cutaneous nerve of pSS.
Objectives: To evaluate the morphological changes of sural nerve in patients with pSS by high-frequency ultrasound.
Methods: The prospective study subjects consisted of 31 consecutive pSS patients underwent sural nerve biopsy and 30 healthy volunteers as controls. The ultrasonic presentations of the fascicle, perineurium, epineurium of sural nerve were observed, and the cross-sectional areas (CSA) of the sural nerves was measured.
Results: Among the 21 sural nerves confirmed by pathology, all showed the thickening of the perineurium and epineurium (Figure 1-2), and abnormal blood flow signal in perineurium or epineurium in 14 cases (Figure 2). The mean CSAs were (1.41±0.44) mm2 for the control group, and (1.58±0.48) mm2 for the case group (P>0.05). In addition, the abnormal blood flow signal in sural nerve correlated with disease activity.
Conclusion: This study indicated that high-frequency ultrasound may be a valuable tool for evaluating cutaneous nerve neuropathy of Sjogren's syndrome patients.
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Figure 1. Transverse sonograms of the sural nerve (arrows)V: indicates lesser saphenous vein

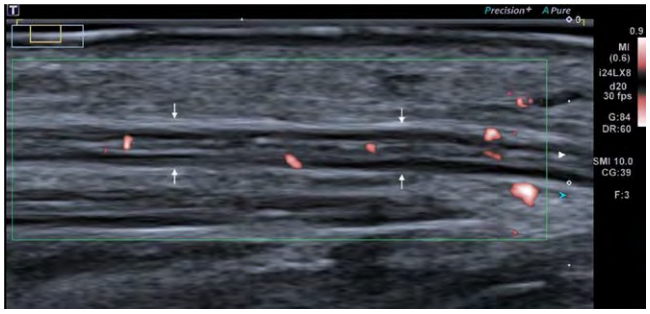


Figure 2. Longitudinal sonograms of the sural nerve (arrows)The sonogram of sural nerve showed abnormal blood flow signal.V indicates lesser saphenous vein.

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AB0426

FIBROSING INTERSTITIAL LUNG DISEASE IN PRIMARY SJOGREN SYNDROME

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Background: Interstitial lung disease (ILD) represents the most frequent pulmonary manifestation of primary Sjogren's syndrome (pSS), with a prevalence ranging between 6-70% in different retrospectives studies. Non-specific interstitial pneumonia (NSIP) is recognized as the most common ILD disorder, followed by organizing pneumonia (OP), usual interstitial pneumonia (UIP) and lymphocytic interstitial pneumonia (LIP), specifically associated with pSS but less frequent.
Objectives: To investigate the prevalence of fibrosing patterns in a monocentric cohort of pSS patients evaluated for lung involvement in a cross-sectional study.
Methods: In a cross-sectional study all patients fulfilling ACR/EULAR classification criteria for pSS and with a known diagnosis of ILD were enrolled; the other patients were carefully investigated for signs or symptoms suggestive for ILD (including the search for velcro crackles with a digital device); when suspect, patients underwent to high resolution computed tomography (HRCT). An expert radiologist re-evaluated all HRCT for classifying the ILD pattern as: UIP, fibrotic NSIP, fibrotic OP, NSIP, OP, LIP, indeterminate.
Results: One hundred and eighty-five pSS patients were enrolled; among them 34 showed ILD (18.4%) with the following features: M/F 3/31, median age 57 (range 24-80), median FVC 90% (39-127%), median DLCO 49% (20-84%). Patients were classified in two groups according to radiologic classification: the group 1 (18 pts 52,9%) included UIP (13 patients, 38.2%), fibrotic NSIP (4, 11.8%), fibrotic OP (1 2.9%); the group 2 (16 pts, 47.1%) included NSIP (6, 17.6%), OP (4, 11.8%), indeterminate (4, 11.8%), LIP (2, 5.9%). No significant differences were observed between the two groups with the exception of anti-SSB positivity more frequently detected in non-fibrosing pattern (p 0,043).
Conclusion: Despite previous observations, our data suggest a high prevalence of fibrosing ILD pattern in pSS patients. We participate at a multidisciplinary team with expert pulmonologists and radiologists and some patients of our cohort firstly referred to pulmonologist for appearance of ILD before the diagnosis of pSS, contributing to the possible selection of more severe lung disease. However, these data suggest first of all that pSS should always be considered in differential diagnosis of fibrosing ILD; moreover, since fibrosing ILD is thought to have a worse response to immunosuppressive drugs, the role of new possible therapeutic strategies such as anti-fibrotic could represent an important field of interest.
Disclosure of Interests: None declared
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AB0427

OCCURRENCE OF NEUROPSYCHIATRIC MANIFESTATIONS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS FROM THE SWISS LUPUS COHORT AND META-ANALYSIS OF THE PERTINENT LITERATURE

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Background: Systemic lupus erythematosus (SLE) is a systemic autoimmune disease, often presenting with neuropsychiatric manifestations. Reports on the frequency and patterns of these manifestations vary substantially and remain incompletely understood.
Objectives: We examined neuropsychiatric manifestations in the prospective nationwide cohort of Swiss SLE (SSCS) patients and conducted a systematic literature review to contextualise our findings.
Methods: We reviewed all patients included in the SSCS from 2007-2019 and classified severe neuropsychiatric manifestations. Searches were performed in relevant electronic databases from 1.1999-1.2020 and by checking reference lists of the pertinent literature. Authors of important papers were contacted to obtain further (unpublished) studies. We included prospective or cross-sectional studies focussing on neuropsychiatric manifestations in SLE, defined according the ACR criteria of 1999. Study selection and data extraction was made in duplicate. We secured salient study characteristics, composition of cohorts, the definitions and the frequencies of neuropsychiatric manifestations. We assessed heterogeneity across reports and investigated sources of variation using meta-regression models.
Results: The frequencies of severe manifestations found in the SSLE were 7.1% (49/688) for cerebrovascular events, 5.3% (37/688) for seizures and 6.5% (45/688) for psychosis. The time-to-event analysis showed a linear relationship between duration of SLE and cumulative incidence of severe neuropsychiatric manifestations. Searches identified 530 studies and authors' contact yielded another unpublished report. We included 28 studies. The mean rates of the most commonly reported severe neuropsychiatric manifestations ranged in the magnitude of 50 percent points. Study characteristics and composition of cohorts could not explain heterogeneity of reported manifestation rates.
Conclusion: The spectrum of neuropsychiatric manifestations in SLE is widely dispersed. The diagnostic work-up and the reporting of manifestations varied substantially across studies which may explain inconsistencies to some extent. We call for concerted efforts and a broad consensus regarding stringent definitions of neuropsychiatric SLE manifestations that allow targeted detection, particularly with view to timely intervention and patient outcomes.
Disclosure of Interests: None declared
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AB0428 ASSOCIATION BETWEEN GEOGRAPHIC AND CLIMATOLOGICAL CONDITIONS AND CUTANEOUS MANIFESTATIONS IN LUPUS PATIENTS FROM THE SPANISH RHEUMATOLOGY SOCIETY LUPUS REGISTRY (RELESSER) AND ARGENTINE RHEUMATOLOGY SOCIETY LUPUS REGISTRY (RELESSAR) COHORT

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Background: Climatological conditions and ethnicity impact on the course of the disease in systemic lupus erythematosus patients.
Objectives: We carry out a study to analyze cutaneous manifestations in SLE patients from Argentina and Spain.
Methods: Patients data from Spanish Rheumatology Society Lupus Registry (RELESSER) and Argentina Rheumatology Society Lupus Registry (RELESSAR) were retrospectively analyzed for presence of cutaneous lesions (alopecia, photosensitivity, malar rash, discoid lesions, oral ulcers and subacute lesions). RELESSER-T and RELESSAR-T are multicenter, hospital-based registries, with retrospective cross-sectional collection of data about patients with SLE attending Spanish and Argentinian rheumatology services from the public national health system. Data about climatological conditions throughout the Spanish and Argentinian geography were provided by the Spanish Meteorological Agency and Argentine Meteorological Services.
Results: A total of 5604 patients were included, median age 44.6 ± 15.3, 90.4 % female. Current smokers were 28,9%. Other climatological, geographical, biological and clinical data are shown in table 1. In the multivariable model, the presence of cutaneous lesion were significantly associated with temperature OR 1.116 (95% CI:1.042-1.196 p=0,002), altitude OR 1.001 (95% CI:1.000-1.001, p=0.012), hemolytic anemia OR 1.401 (95% CI:1.017-1.931 p=0.039) and serositis OR 1.509 (95% CI:1.215-1.875 p=0.000). Negative associations were observed between females OR 0.392 (95% CI:0.297-0.518, p=0.000), latitude OR 0.994 (95% CI:0.988-0.999, p=0.000), oceanic climate OR 0.566 (95% CI:0.381-0.842, p=0.005), leukopenia OR 0.790 (95% CI:0.643-0.970, p=0.025), renal disorder OR 0.761 (95% CI:0.600-0.966, p=0.025), glucocorticoids treatment OR 0.571 (95% CI:0.456-0.715, p=0.000) and antimalarial drugs OR 0.439 (95% CI:0.342-0.563, p=0.000).

Table 1. Geographical, climatological and clinical/laboratory variables.

	No cutaneous manifestations	Cutaneous manifestations	p
Latitude, median (interqualite range)	40.47 (38.35-41.63)	40.37 (-31.41-41.34)	0.001
Altitude, median (interqualite range)	192.0 (37.0-698.0)	156.0 (25.0-609.0)	0.000
Temperature, mean monthly ± SD	15.2 ± 3.5	15.3 ± 3.6	0.000
Humidity, mean monthly ± SD	66.9 ± 7.2	67.4 ± 7.1	0.108
Oceanic climate, n (%)	307 (11)	2406 (89)	0.000
Subhumid/altitude climate, n (%)	17 (7)	240 (93)	0.002
Mediterranean climate, n (%)	292 (17)	1434 (83)	0.000
Arthritis, n (%)	523 (12)	3722 (88)	0,003
Serositis, n (%)	254 (16)	1368 (84)	0,000
Renal disorder, ever, n (%)	206 (11)	1576 (89)	0.015
Hemolytic anemia, n (%)	90 (17)	426 (83)	0,002
Leukopenia, n (%)	345 (11)	2669 (89)	0.000
Thrombocytopenia, n (%)	170 (15)	986 (85)	0.076
Antiphospholipid antibodies, n (%)	293 (15)	1606 (85)	0.000
Anti DNA, n (%)	522 (14)	3279 (86)	0.044
Anti-Ro/SSA, n (%)	189 (11)	1563 (89)	0.000
Hypocomplementemia, n (%)	510 (12)	3736 (88)	0.000
Glucocorticoids mucocutaneous cause, ever, n (%)	499 (11)	3928 (89)	0.000
Antimalarial drug: ever, n (%)	500 (11)	4034 (89)	0.000

Conclusion: In the current analysis, taking RELESSAR and RELESSER data together, we observe positive association between higher temperature and skin lesion and negative association with living in southern hemisphere latitudes.
References: Influence of Solar Radiation in Cutaneous Manifestations of Lupus: Data from the Gladel Cohort [abstract]. Arthritis Rheumatol. 2016; 68 (suppl 10).
Disclosure of Interests: Raúl Menor-Almagro: None declared, Mercedes Argentina García: None declared, Iñigo Rua-Figueroa: None declared, Guillermo Pons Estel: None declared, Maria Auxiliadora Martin-Martinez: None declared, Alejandro Muñoz Jimenez.: None declared, María Galindo-Izquierdo: None declared, Jaime Calvo-Alen: None declared, Antonio Fernandez-Nebro: None declared, Alejandro Olive: None declared, Bernardo Pons-Estel Grant/research support from: GSK, Janssen, Consultant of: GSK, Janssen, Speakers bureau: GSK, Janssen, Jose M Pego-Reigosa: None declared
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AB0429 NEUTROPHIL TO LYMPHOCYTE RATIO INDEPENDENTLY PREDICTS CUTANEOUS MANIFESTATIONS IN PATIENTS WITH SJÖGREN'S SYNDROME

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Background: Various cutaneous manifestations are described in patients with Sjogren's syndrome (SS). However, the predictors for its occurrence are not fully investigated. Recently, data regarding the role of hematological parameters ratios in patients with rheumatic diseases were reported. However, routine hematological parameters and the derived ratios were not studied in SS patients.
Objectives: The aim of this study was to evaluate the predictors for cutaneous manifestations in a large cohort of patients with SS followed in a tertiary center.
Methods: We included 114 patients with SS (mean age: 53.1±12.1; 94.7% female). We divided the patients in group A – patients with cutaneous manifestations and group B – without cutaneous manifestations. The complete laboratory workup [including the calculation of neutrophil to lymphocyte ratio (NLR), mean platelet volume (MPV) to platelet ratio, platelet distribution width (PDW) to platelet ratio], clinical manifestations and treatment were reviewed and the EULAR Sjögren's syndrome disease activity index (ESSDAI) was calculated for each patients.
Results: Cutaneous manifestations were diagnosed in 11 patients (9.6%). The age of the patients, the levels of anti-SSA, complement, inflammatory markers (ESR, CRP), immunoglobulins and vitamin D levels, the ultrasonographic score of salivary glands and the ESSDAI value were similar in both groups. The patients with cutaneous manifestations were more frequently treated with hydroxychloroquine (9/11 vs 49/103, p=0.03) but the mean doses were similar in both groups. The values of anti-SSB were marginally higher in patients with cutaneous manifestations (102.3±83.1 vs 53.6±79.9, p=0.07). The lymphocyte, neutrophil count, MPV and PDW were similar in both groups, while platelet count was lower in patients with cutaneous manifestations (224090.9±59528.9 vs 264339.8±60669.0, p=0.03). The MPV/Plt ratio tended to be higher in patients with cutaneous manifestations (0.051±0.017

vs. 0.043±0.013, p=0.07), but the values of PDW/Plt ratio (0.064±0.022 vs 0.051±0.018, p=0.03) and of NLR (3.82±2.30 vs 2.35±0.92, p=0.001) were found to be significantly higher in these patients. In multivariate analysis, only the NLR remains independently associated with cutaneous manifestations (p=0.001). Using the ROC curve analysis, a cutoff of 2.70 for NLR had a 63% sensitivity and 69% specificity for cutaneous manifestations.

Conclusion: The hematological parameters related to platelets appear to be modified in patients with SS and cutaneous manifestations. However, only neutrophil to lymphocite ratio is independently associated with cutaneous involvement in these patients.

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AB0430 MORTALITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND NEUROPSYCHIATRIC SYMPTOMS

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Background: Little is known about mortality in patients with systemic lupus erythematosus (SLE) presenting with neuropsychiatric (NP) symptoms.

Objectives: We aimed to evaluate all-cause and cause-specific mortality in patients with SLE and NP symptoms.

Methods: All patients with the clinical diagnosis of SLE of 18 years and older that visited the tertiary referral NPSLE clinic of the Leiden University Medical Center between 2007-2018 and signed informed consent were included in this study. Patients were classified as NPSLE if NP symptoms were attributed to SLE and immunosuppressive or anticoagulant therapy was initiated, otherwise patients were classified as non-NPSLE. Municipal registries were checked for current status (alive/deceased). Electronical medical files were studied for clinical characteristics and cause of death. Standardized mortality ratios (SMRs) and 95% confidence intervals were calculated using data from the general Dutch population. In addition, a rate ratio (RR) was calculated using direct standardization to compare mortality in NPSLE with non-NPSLE patients.

Results: 351 patients with the clinical diagnosis of SLE were included, of which 149 patients were classified as NPSLE (42.5%). Compared with the general population, mortality was increased five times in NPSLE (SMR 5.0, 95% CI: 2.6-8.5) and nearly four times in non-NPSLE patients (SMR 3.7, 95% CI: 2.2-6.0), as shown in Table 1. Risk of death due to cardiovascular disease (CVD) was increased in non-NPSLE patients (SMR 6.2, 95% CI: 2.0-14.6) and an increased risk of death to infections was present in both NPSLE and non-NPSLE patients ((SMR 29.9, 95% CI: 3.5 – 105) and SMR 91.3 (95% CI: 18.8 – 266) respectively). However, mortality did not differ between NPSLE and non-NPSLE patients (RR 1.0, 95% CI: 0.5 – 2.0).

Table 1. All-cause mortality in SLE patients presenting with neuropsychiatric symptoms attributed to SLE (NPSLE) or to other causes (non-NPSLE)

	NPSLE (N = 149)	Non-NPSLE (N = 202)
Deaths (N, %)	13 (8.7)	17 (8.4)
Age at death (median, range)	49 (32 – 79)	59 (20 – 89)
Follow-up time (years)	906	1047
Crude mortality rate (per 1000 PY)	14.3	16.2
All-cause mortality*		
Female	5.5 (2.8 – 9.6)	3.4 (1.9 – 5.7)
Male	2.3 (0.1 - 12.8)	6.2 (1.3 – 18.2)
Combined	5.0 (2.6 – 8.5)	3.7 (2.2 – 6.0)

*Standardized mortality ratio, ratio of the observed and expected number of deaths

Conclusion: Mortality was increased in both NPSLE and non-NPSLE patients in comparison with the general population, but there was no difference in mortality between NPSLE and non-NPSLE patients. Risk of death due to infections was increased in both groups.

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AB0431 SALIVARY GLAND ULTRASOUND IN CLINICAL PRACTICE

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Background: Sjogren's syndrome (SS) is characterized by lymphocytic infiltration of the exocrine glands and marked B-lymphocytic cell hyperreactivity involving a variety of serum autoantibodies. [1] Salivary Gland Ultrasound (SGU) is a simple, fast, and well- tolerated examination, wich provides information about glandular structure and has proven to be very useful in the Sjögren Syndrome diagnosis[2]. A prognostic value has also been proposed due to its posible relationship with lymphomas and extra-glandular manifestations.

Objectives: The objective of our study is to evaluate ultrasound results in patients who went through an SGU in clinical practice, its usefulness in the diagnosis of Sjögren's syndrome and the presence of complications (lymphomas, extra-glandular manifestations or factors related to increased lymphoma risk).

Methods: We conducted a retrospective cross-sectional study with review of clinical records that included all those patients coded as SGU in the Ultrasound unit of Rheumatology Department from 2016 to December 2019. Information collected included final diagnosis, laboratory results, clinical manifestations and ultrasound results. We performed an analysis on the frequency of pathological SGU and on the relationship between this lesions in patients with final SS diagnosis and the presence of lymphoma, extra-glandular manifestations and the laboratory values related with increased lymphoma risk (low complement levels, cryoglobulinemia, positive autoimmunity).

Results: SGU was performed in 171 patients in four years, 162 women (94.7%). The previous diagnoses, reason for the request and final diagnosis are shown in Table 1. The vast majority of the SGU were normal, only 28 (16,3%) were pathological, 13 with a grade II and 8 with a grade III. In the other 7 patients grading was not available. Of the 28 patients with pathological SGU, none had lymphoma, only 3 had recurrent parotitis and 15 had had extra-glandular manifestations, mainly arthralgia / arthritis (12). Only 1 patient, with rheumatoid arthritis, had had a lymphoma and the SGU was normal. Antibody positivity was frequent in pathological SGU, 16/23 antinuclear antibodies, 13/22 anti-Ro and 9/23 rheumatoid factor. Of the 86 patients without previous diagnosis, 18 were diagnosed with Sjogren syndrome, 9 with pathological SGU and the rest were normal. No patient diagnosed with a dry non-autoimmune syndrome presented pathological SGU.

Table 1. Previous diagnoses, reason for request and final diagnoses.

Previous diagnoses (n: 171)	Reason for request (n: 171)	Final diagnosis (n: 78)
Without prior diagnosis (n: 86)	Dry non- autoinmune syndrome (n: 127)	Dry non-autoimmune syndrome (n: 60)
Primary Sjögren's syndrome (n: 11)	Primary Sjögren's syndrome (n: 12)	Primary Sjögren's syndrome (n: 18)
Systemic Lupus Erythematosus (n: 9)	Lymphoma (n: 0)	Secondary Sjögren's syndrome (n: 0)
Rheumatoid arthritis (n: 24)	Control (n: 13)	Other diagnoses (n: 7)
Other diagnoses (n: 18)	Other reasons (n: 11)	

Conclusion: The impact of the SGU is low and its use cannot, for now, displace other methods (e.g. salivary gland biopsy) in the diagnosis of SS. Also our low number of patients with pathological SGU together with the low prevalence of the complications studied (e.g. lymphomas = 1) prevents the expected comparisons.

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bureau: Abbvie, Celgene, Gilead, Janssen, Novartis, Pfizer, Roche, Indalecio Monteagudo: None declared, Juan Carlos Nieto Speakers bureau: Pfizer, Abbvie, MSD, Novartis, Janssen, Lilly, Nordic Pharma, BMS, Gebro, FAES Farma, Roche, Sanofi

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AB0432 CLINICAL AND SEROLOGICAL CHARACTERISTICS OF "RHUPUS SYNDROME"

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Background: Systemic lupus erythematosus (SLE) is a multisystemic and chronic autoimmune disorder that typically affects (1). Arthritis is one of the most frequent manifestations in SLE with an incidence reported from 69% to 95% (2). Rheumatoid arthritis (RA) is an articular, inflammatory, chronic disease of autoimmune nature (3). Rhupus syndrome is defined as a patient that meets the classification criteria for RA of the American College of Rheumatology (ACR) of 1987 and for SLE of the ACR of 1982, in addition, necessarily erosive arthropathy with antibodies specific for positive SLE (anti-Sm or anti-DNAdc) (4). With the development of more recent classification criteria for both RA and SLE, which allow us to detect both diseases earlier, they create even more heterogeneity in the definition of rhupus, being a rare entity, the analysis of the clinical and serological characteristics of this population in our clinic would provide data to the few existing.

Objectives: To describe the clinical and serological characteristics of patients with Rhupus.

Methods: An observational, retrospective study was done in the rheumatology clinic of the university hospital "Dr. Jose Eleuterio Gonzalez" in Monterrey, Mexico. The electronic medical record (EMR) was reviewed. In search of the term "rhupus". All the patients were analyzed individually to verify the rhupus diagnosis. The main clinical and serological characteristics were evaluated. The results are shown in descriptive statistics.

Results: 30 patients were obtained from the search in the EMR, 22 patients were included, 8 patients were excluded (5 non-SLE, 3 non-RA) (Figure 1). The mean age was 40.14 (SD 10.86); 20 (90.9%) were females; the onset diagnosis was SLE in 5 (22.7%), RA in 14 (63.6%) and both 3 (13.6%). 17 (77.3%) had general symptoms, 12 (54.5%) had cutaneous manifestations, 14 (66.6%) had renal manifestations, 6 (27.3%) had serositis, 19 (86.3%) had hematologic manifestations, 3 (13.6%) had neuropsychiatric manifestations, 1 (4.5%) had diffuse alveolar hemorrhage. 12 (60%) had anti-dsDNA positive, 4 (23.5%) had anti-Sm positive, 16 (84.2%) had anti-CCP positive (Table 1). The articular manifestations (swollen and tender joints at onset and at last visit) are detailed in Table 2. The treatments were different at the onset of the disease compared with the last visit, except for methotrexate (Table 2).

Table 1. Clinical and serological characteristics.

	N=22
Female, n (%)	20 (90.9)
Age, mean (SD)	40.14 (10.86)
Onset diagnosis	
SLE, n (%)	5 (22.7)
RA, n (%)	14 (63.6)
Both, n (%)	3 (13.6)
Manifestations	
General, n (%)	17 (77.3)
Cutaneous, n (%)	12 (54.5)
Renal, n (%)	14 (66.6)
Serositis, n (%)	6 (27.3)
Hematological, n (%)	19 (86.3)
Neuropsychiatric, n (%)	3 (13.6)
Diffuse alveolar hemorrhage, n (%)	1 (4.5)
Serology	
Anti-dsDNA (N=20), n (%)	12 (60)
Anti-Sm (N=17), n (%)	4 (23.5)
Anti-CCP (N=19), n (%)	16 (84.2)

Table 2. Disease activity and treatment.

	At onset N=22	Last visit N=22
Swollen joints, mean (SD)	9.3 (6.6)	3.0 (4.8)
Tender joints, mean (SD)	8.5 (7.1)	1.59 (3.8)
VAS, mean (SD)	42 (33.6)	17.2 (21.1)
PGA, mean (SD)	38 (32.3)	16.6 (20.3)
Activity scales		
SLEDAI-2k, mean (SD)	8.38 (4.5)	2.9 (3.2)
DAS28-VSG, mean (SD)	5.26 (1.51)	2.89 (0.83)
Treatment		
Glucocorticoid, n (%)	21 (95.4)	15 (68.2)

Table 2. Disease activity and treatment.

	At onset N=22	Last visit N=22
Antimalarials, n (%)	17 (77.2)	11 (50)
Immunosuppressants, n (%)	8 (36.3)	2 (9.1)
Methotrexate, n (%)	16 (72.7)	16 (72.7)
Leflunomide, n (%)	4 (18.2)	5 (22.7)
Sulfasalazine, n (%)	5 (22.7)	0 (0)

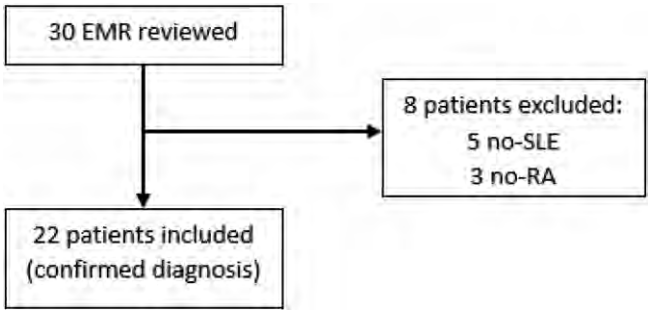


Figure 1.

Conclusion: In our cohort, rhupus affects more frequently females, the hematologic manifestations are very frequent and the neuropsychiatric and diffuse alveolar hemorrhage was rare.

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AB0433 HIGH RISK OF MATERNAL THROMBOTIC AND SEVERE HEMORRHAGIC COMPLICATIONS IN 119 PROSPECTIVE PREGNANCIES ASSOCIATED WITH ANTIPHOSPHOLIPID SYNDROME (GR2 STUDY)

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Background: Women are at higher risk of thrombotic or severe bleeding complications during pregnancy, especially in the postpartum period (around 1%), but no prospective data have been available for women with antiphospholipid syndrome (APS). We report the first results of the French GR2 prospective study of pregnancy and rare diseases.

Objectives: To describe the thrombotic and haemorrhagic events in APS patients included in the GR2 study and to identify risk factors associated with these complications.

Methods: Women with APS and an ongoing pregnancy at 12 weeks of gestation were eligible for prospective inclusion in the GR2 study. Exclusion criteria were proteinuria (ratio > 1 g/g), serum creatinine > 100 µmol/L, or a multifetal pregnancy. Severe bleeding was defined as the need for transfusion, intensive care admission, or invasive treatment. Uteroplacental vascular insufficiency was defined as intrauterine growth restriction, preeclampsia, or HELLP syndrome.

Results: The study included 119 pregnancies in 119 APS patients (53% thrombotic and 47% obstetric only APS). Treatment included aspirin (99%) and heparin (98%, in the therapeutic range for 50%).

Twelve women (10%) had a thrombotic (n=5) and/or a severe haemorrhagic event (n=9).

The thrombotic events included stroke (at 11 weeks; n=1), catastrophic APS (CAPS) (n=2), a pulmonary embolism (n=1), and portal vein thrombosis (n=1) (in the postpartum). Placental insufficiency was also present in 6 of these 12 women.

Among the 22 (18.5%) women with at least one bleeding event (n=28), 9 (7.6%) had events defined as severe. Six of nine (67%) severe haemorrhages occurred in the postpartum and were directly related to the delivery. Two required an intrauterine balloon tamponade, two uterine arterial embolisation, and three surgery, including one hysterectomy.

No women died.

Finally, thrombotic and/or severe bleeding events during the postpartum period (n=9) were more frequent in women with lupus anticoagulant (14% versus 0%; P=0.01), with associated placental insufficiency (29% versus 3%; P=0.001) and with preterm delivery ≤34 weeks (33% versus 4%, P=0.002).

Conclusion: Even though most women in our cohort received treatment based on current recommendations, a substantial number of maternal thrombotic and haemorrhagic events (10%) occurred. Despite several life-threatening complications, including CAPS, no women died.

Most of the thrombotic or haemorrhagic events occurred in the peripartum period, and they were more frequent in women with the lupus anticoagulant, placental insufficiency, and preterm delivery.

Although this morbidity rarely appears preventable, knowledge of the risk factors should increase awareness and help physicians to manage APS patients at particularly high risk.

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AB0434 PREVALENCE OF ANTIPHOSPHOLIPID SYNDROME COMPONENTS IN MEN WITH STABLE CORONARY HEART DISEASE AND POSTINFARCTION CARDIOSCLEROSIS AND CONECTION WITH ECHOCARDIOGRAPHIC EVALUATION OF CARDIAC STRUCTURE AND FUNCTION 1.0.0.20

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Background: Antiphospholipid syndrome (APS) as an independent factor in different forms of coronary heart disease (CHD) has been attracting more attention in recent years [1]. The prevalence of AFS in the general population is low (1-5%) but among patients with acute coronary syndrome it ranges from 6.1% to 43.3%. The persistence of high titers of antiphospholipid (aPL) antibodies, especially antibodies to cardiolipin, accelerates the development of endothelial dysfunction and atherothrombotic lesions of the coronary arteries, worsens the course of acute myocardial infarction. It has been experimentally demonstrated that aPL antibodies can directly affect myocardial status through pro-apoptotic signaling pathways and increased cardiomyocyte apoptosis [2].The impact of aPL antibodies on the course of postinfarction myocardial remodeling in patients with CHD has not been established.

Objectives: To study the prevalence of APS components in men with stable CHD with postinfarction cardiosclerosis and to evaluate the relationship with structural and functional state of left ventricular myocardium.

Methods: 164 patients with CHD with postinfarction cardiosclerosis were examined (100% males at the average age of 53,0±9,14 (M±σ)). The diagnosis of CAD was made according to the recommendations of the ANA / ACC (2014) and ESC (2013). The content of IgG and IgM of aPL antibodies - antibodies to cardiolipin, phosphatidylserine, phosphatidylinositol, phosphatidylacetate and levels of IgG and IgM to β2-glycoprotein I (β2-GP-I) in the blood serum were determined by ELISA. Echocardiography in M-, B- and D-modes was performed.

Results: Among 164 patients with post-infarction cardiosclerosis: 75% had Q myocardial infarction (MI), 10.4% had recurrent MI, 7.9% had a stroke or transient ischemic attack and 4.2% had livedo reticularis. 93 (56.7%) patients had positive levels of total aPL antibodies and antibodies to β2-GP-I of IgG class (58 (35,4%) patients had low positive levels of antibodies, 35 (21.3%) patients had medium positive levels of one or both types of antibodies. Positive levels of aPL antibodies and antibodies to β2-GP-I of IgM were detected in 11.6% of patients. Positive levels of aPL antibodies and antibodies to β2-GP-I were more commonly found in men who had Q MI (OR 2.58 95% CI 1.26 - 5.28) and recurrent MI (OR 2.52 95% CI 0.83 - 7.67). Increases of levels of aPL antibodies and antibodies to β2-GP-I correlated with an increase of left ventricle (LV) mass index (r = 0.259 and 0.331, p <0.001). In patients with positive levels of antibodies of IgG to β2-GP-I in postinfarction LV remodeling was more likely to occur by concentric type of hypertrophy of LV than in patients with negative levels of antibodies to β2-GP-I (OR 6.50, 95% CI 2.49 - 16.9, p <0.001). Hypertension had no significant differences within these groups.

Conclusion: The risk of persisting positive levels of aPL antibodies and antibodies to β2-GP-I in the postinfarction period is significantly increased in men who had Q MI. Patients with CHD with positive antibodies to β2-GP-I of IgG are associated with an increased risk of postinfarction LV myocardial remodeling by concentric type of hypertrophy of LV.

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AB0435 RISK OF SERIOUS INFECTION IN LUPUS NEPHRITIS AND RHEUMATOID ARTHRITIS MEASURED USING THE JAPANESE REAL WORLD HOSPITAL CLAIMS DATABASE

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Background: Patients with lupus nephritis (LN) and rheumatoid arthritis (RA) are at risk of serious infections (SIs) due to the impact of the disease itself and treatments that modulate immune system. Though the epidemiology of RA has been well-established by developing many targeted DMARDs (tDMARDs) including biologics and targeted synthesized DMARDs, LN is a very rare disease. Therefore, a large sample size with a significant number of cases is required to determine the exact risk of SIs in LN.

Objectives: To compare the incidence rates of SIs resulting in an inpatient claim in adult patients with LN compared with RA with or without tDMARDs using hospital claims data in Japan.

Methods: LN and RA were identified using claims data provided by Medical Data Vision Co., Ltd (Tokyo, Japan) between April 2008 and June 2019 which was extracted 5th September 2019. Data between January 2010 and December 2018 was used for analysis. Patients with LN and RA were identified using modifications to algorithms developed before [1, 2]. LN patients were required to have continuous insurance claim for both systemic lupus erythematosus (SLE) and LN for ≥ 6 months after index date and then RA patients had continuous insurance claim for RA for ≥ 6 months after index date. First incident SIs were defined as those that resulted in an inpatient claim for a pre-specified set of ICD-10 code. Incidence rates (IRs) were calculated along with 95% confidence intervals (CI).

Results: The LN, RA, RA treated with tDMARDs and RA treated without tDMARDs cohorts included 6,403, 108,317, 16,450, and 91,867 patients, respectively. As anticipated, the LN and RA cohorts were predominantly female and the RA cohort was generally older than the LN cohorts. IRs per 1,000 person-year(PY) [95% CI] for pneumocystis carini pneumonia were 28.2 [26.0-30.4] in LN, 8.5 [8.2-8.8] in RA, 12.6 [11.7-13.5] in RA with tDMARDs and 7.7 [7.4-8.0] in RA without tDMARDs. IRs per 1,000 PY for septicaemia infection were 23.3 [21.3-25.3] in LN, 12.1 [11.7-12.4] in RA, 13.3 [12.3-14.2] in RA with tDMARDs and 11.8 [11.5-12.2] in RA without tDMARDs. IRs per 1,000 PY for cytomegalovirus infection were 13.4 [11.9-14.9] in LN, 4.4 [4.2-4.6] in RA, 6.2 [5.6-6.8] in RA with tDMARDs and 4.1 [3.8-4.3] in RA without tDMARDs. IRs per 1,000 PY for tuberculosis were 7.2 [6.0-8.3] in LN, 6.7 [6.5-7.0] in RA, 18.2 [17.1-19.3] in RA with tDMARDs and 4.4 [4.2-4.7] in RA without tDMARDs.

Conclusion: In this population-based analysis of claims data from Japan, the IRs of SI such as pneumocystis carini pneumonia, septicemia infection and cytomegalovirus infection were higher in LN than in RA. And also, the incidence of tuberculosis in RA treated with tDMARDs was highest among these cohorts. These findings demonstrate the relative contribution of age, immunosuppressive therapies and disease-related factors in LN and RA.

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Table 1. Description of study population

	LN		RA					
					tDMARDs		Non tDMARDs	
	N	%	N	%	N	%	N	%
Age (years)								
18-34	1700	26.6	9015	8.3	1828	11.1	7187	7.8
35-44	1743	27.2	16662	15.4	2816	17.1	13846	15.1
45-54	1563	24.4	29955	27.7	4452	27.1	25503	27.8
55-64	1397	21.8	52685	48.6	7354	44.7	45331	49.3
Gender								
Female	5385	84.1	78419	72.4	12653	76.9	65766	71.6
Male	1018	15.9	29898	27.6	3797	23.1	26101	28.4

Table 2. IRs per 1,000 PY [95% CI] of SI for LN and RA patients

	LN total PY = 22065	RA total PY = 365033		
			tDMARDs	Non tDMARDs
			total PY = 60999	total PY = 304034
Pneumocystis carini pneumonia	28.2 [26.0-30.4]	8.5 [8.2-8.8]	12.6 [11.7-13.5]	7.7 [7.4-8.0]
Septicaemia	23.3 [21.3-25.3]	12.1 [11.7-12.4]	13.3 [12.3-14.2]	11.8 [11.5-12.2]
Cytomegalovirus infection	13.4 [11.9-14.9]	4.4 [4.2-4.6]	6.2 [5.6-6.8]	4.1 [3.8-4.3]
Tuberculosis	7.2 [6.0-8.3]	6.7 [6.5-7.0]	18.2 [17.1-19.3]	4.4 [4.2-4.7]
Mycosis	5.1 [4.1-6.0]	2.7 [2.6-2.9]	4.6 [4.1-5.1]	2.4 [2.2-2.5]
Aspergillosis	4.7 [3.8-5.6]	2.7 [2.5-2.9]	2.1 [1.7-2.5]	2.8 [2.6-3.0]
Herpes	3.3 [2.5-4.0]	2.4 [2.2-2.6]	2.9 [2.5-3.3]	2.3 [2.1-2.5]

Disclosure of Interests: Mariko Nio Employee of: Chugai Pharmaceutical Co., Ltd., Kosei Tajima Employee of: Chugai Pharmaceutical Co., Ltd., Naofumi Sugaya Employee of: Chugai Pharmaceutical Co., Ltd., Tomoyuki Ishiwata Employee of: Chugai Pharmaceutical Co., Ltd., Tatsuhiko Iwase Employee of: Chugai Pharmaceutical Co., Ltd., hiroyuki kato Employee of: Chugai Pharmaceutical Co., Ltd., Misato Hashizume Employee of: Chugai Pharmaceutical Co., Ltd.

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AB0436 CHANGES OF LYMPHOCYTE SUBSETS AND CLINICAL INDEXES IN PERIPHERAL BLOOD OF PATIENTS WITH ANTI-PHOSPHOLIPID SYNDROME

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Background: Anti-phospholipid Syndrome (APS) is a non-inflammatory autoimmune disease, which can be divided into primary and secondary. Changes in lymphocyte numbers in APS are caused by disruption of the immune balance.
Objectives: The levels of lymphocyte subsets in peripheral blood of patients with anti-phospholipid syndrome were observed and their clinical indexes were analyzed.
Methods: 53 patients with anti-phospholipid syndrome (APS) were collected as the case group and divided into two groups of A, B according to whether primary and 50 health examiners as the healthy control group. The levels of peripheral lymphocyte subsets and laboratory data [erythrocyte sedimentation rate (ESR),

Table 1. Comparison of clinical data of two case groups and healthy control group M (p25, p75)

Groups	Case group A	Case group B	Healthy control group	H value	P value
History of thrombus (case)	4[a]	8[a]	-	13.709	0.001
History of adverse pregnancy (case)	3[a]	19[a]	-	34.596	<0.001
ESR	20.00 (12.25,111.00)[a]	35.00 (14.25,95.00)[a]	9.00 (6.00,13.00)	34.381	<0.001
CRP	15.00 (4.03,37.83)[ab]	7.33 (1.76,21.13)[ab]	2.10 (1.28,2.31)	35.263	<0.001
PLT	228.00 (189.50,573.25)[ab]	197.00 (66.00,260.50)[ab]	258.50 (228.25,272.25)	33.482	<0.001

Note: [a]Comparison with healthy control group $P < 0.05$; [b]Comparison with case group $P < 0.05$.

Table 2. Comparison of lymphocyte subsets in peripheral blood of two case groups and healthy control group M (p25, p75)

Groups	T (ng/ml)	$CD4^+$ T (ng/ml)	$CD8^+$ T (ng/ml)	$CD4^+$ T/$CD8^+$ T
Case group A	1140.22 (878.86,1819.56)[ab]	606.18 (473.50,873.45)[b]	494.55 (252.90,1022.24[b]	1.56 (0.75,2.52)[a]
Case group B	664.89 (281.36,1360.00)[ab]	383.64 (142.46,678.25)[ab]	220.19 (114.43,464.50)[ab]	1.53 (0.94,3.07)[a]
Healthy control group	1250.50 (1070.00,1576.50)	639.00 (543.00,787.50)	422.00 (333.25,526.50)	1.55 (1.24,2.04)
H value	11.444	14.704	6.498	18.607
P value	0.003	0.001	0.039	<0.001
Groups	Th2	Th17 (ng/ml)	Treg (ng/ml)	Th17/Treg
Case group A	10.26 (7.36,14.72)	7.07 (3.65,12.17)	21.98 (18.00,34.25)	0.33 (0.12,0.48)
Case group B	2.78 (1.22,3.56)[a]	7.20 (3.29,10.50)	20.29 (13.03,31.31)[a]	0.31 (0.25,0.38)
Healthy control group	10.80 (5.39,15.83)	5.45 (4.06,7.56)	29.09 (21.63,42.07)	0.18 (0.13,0.33)
H value	10.884	2.452	7.516	2.590
P value	0.004	0.293	0.023	0.274

Note: [a]Comparison with healthy control group$P$ <0.05; [b]Comparison with case group $P < 0.05$.

C-reactive protein (CRP), platelets (PLT)]levels in the three groups were analyzed. The measurement data is not subject to normal distribution using the Median-Quartile method for statistical description; multiple sample comparisons using the Kruskal-Wallis H test; p <0.05 as the difference is statistically significant.
Results: (1) The rates of thrombosis and adverse pregnancy in the two case groups were significantly increased. In the two case groups, the ESR and CRP were higher than those in the healthy control group, and the CRP in group A was higher. (2) Compared with the healthy control group, the levels of $CD8^+$ T, $CD4^+$ T/$CD8^+$ T in case A group were increased,while the levels of total T,$CD4^+$ T, $CD8^+$ T,$CD4^+$ T/$CD8^+$ T,Th2 and Treg cells were decreased. However,there was no significant difference in Th17 cells level and Th17/Treg ratio compared with the healthy control group.
Conclusion: APS patients were more prone to have thrombosis, adverse pregnancy and thrombocytopenia. The changes of lymphocyte subsets were seen in peripheral blood, and the primary and secondary had different directions and different degrees of manifestation.However, whether the secondary factors can aggravate the clinical indicators of APS is still unclear.
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AB0437 RISK FACTORS ASESSMENT FOR SUBCLINICAL ARTHEROSCLEROSIS IN PRIMARY SJÖGREN´S SYNDROME.

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Background: Some autoimmune diseases, including rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE), are considered to be independent risk factors for vascular morbidity and mortality. These pathologies present accelerated atherosclerosis, partly because of a chronic sustained inflammation, greater prevalence of cardiovascular risk factors (CVRFs) and pharmacological therapy. However, regarding primary Sjögren's syndrome (pSS), available data are heterogeneous and proceed from small case series. For this reason, the aim of this study was to provide further information on the identification of atherosclerosis in pSS and its possible association with clinical and analytical parameters of the disease.
Objectives: To assess presence of subclinical atherosclerosis by means of carotid ultrasound in patients with pSS and to analyze clinical, analytical and CVRF along with their potential association with the presence of subclinical cardiovascular affectation.
Methods: This is a cross-sectional study of 38 patients with pSS (all patients met ACR/EULAR[1] classification criteria for pSS) and 38 age and sex matched controls. Demographic variables and classical CVRFs were collected (Hypertension, Diabetes mellitus, dyslipemia, Body Mass Index and smoking habit) and the presence of subclinical atherosclerosis was assessed by carotid ultrasound with carotid intima-media thickness (CIMT) measurement and determination of the presence of atheromatous plaques[2], both in pSS patients and controls. Disease

features were also collected in pSS patients (disease duration, disease activity measured by ESSDAI, glandular vs extraglandular involvement, serological features and treatments received).
Statistical analysis: To evaluate differences between patients and controls, T-test or Wilcoxon test with continuity correction, were used for quantitative features and Fisher test for categorical variables. In order to test the presence of pSS as an independent risk factor for subclinical atherosclerosis, from other features as classic CVRFs or analytical data, first we adjusted logistic binomial regression in a bivariate analysis, to select possible predictors to be included in a multivariate analysis. Statistical significance was p<0.05, and OR CI 95% vas calculated. *R-Statistics v- 3.6*
Results: All of the 76 patients included were women, with a mean age of 53.7 ± 11.7 years. For both groups, no differences between prevalence of classical CVRFs were found. Subclinical atherosclerosis presence was higher in patients with pSS than in controls [OR= 4.17, 95%CI (1.27- 16.54), p<0.001], as well as CIMT values (0.79± 0.43 mm vs. 0.66 ± 0.27 mm; p=0.02). An association of subclinical atherosclerosis with erythrocyte sedimentation rate [OR=1.18, 95%CI (1.05-1.37), p<0.05] and Rheumatoid Factor [OR=1.28, 95%CI (1.63-2.26), p<0.05].
Conclusion: This cohort showed a greater prevalence of subclinical atherosclerosis in patients with pSS, indicating this disease as an independent risk factor for presence of early vascular damage.
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AB0438 MALIGNANCIES IN PATIENTS WITH PRIMARY SJOGREN'S SYNDROME

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Background: Sjogren's syndrome (SS) is a chronic, systemic, autoimmune disease. The risk of developing lymphoproliferative malignancies is high in primary Sjogren's syndrome(pSS).
Objectives: In this study, we planned to present malignancy data in patients who were followed up in our outpatient clinic with a diagnosis of pSS.
Methods: Data of 151 patients diagnosed with pSS between 2004-2019 were retrospectively reviewed and clinical, demographic characteristics of 15 patients diagnosed with malignancy were examined.
Results: All 15 patients with malignancy were female, their mean age was 59 ± 13 years, and the disease duration was 9 ± 1 years.
In this group, 7% of the patients had fever, 13% had weight loss and 7% had night sweats. Dry eye was present in 87%, dry mouth in 93%, LAP in 53% (Table 1). None of the patients had myositis, neuropathy and vasculitis. In 87% of the patients, schirmer was below 5 mm and in 67% of the salivary gland scintigraphy, decreased involvement in the parotid and submandibular gland was detected. Salivary gland biopsy was compatible with pSS diagnosis in 53% of patients. Rheumatoid factor, ANA, SS-A and SS-B were positive in %60, %93, %67 and %53 of patients, respectively.

Table 1. The data of pSS patients with malignancy

	N(%)
Gender (Female)	15(100)
Dry mouth	14(93)
Dry Eye	13(87)
Arthritis	3(20)
Parotitits	4(27)
Raynaud Phenomenon	2(13)
Lymphadenopathy	8(53)
Interstitial Lung Disease	4(27)
Smoking	7(47)

Table 1. The data of pSS patients with malignancy

Hypocomplementemia	4(27)
Malignancy	
Lung Cancer	2(13)
Breast Cancer	4(27)
Thyroid Papillary Cancer	3(20)
Cervical Cancer	2(13)
Vulva Cancer	1(7)
Mycosis Fungoides	1(7)
MALT lymphoma	1(7)
Diffuse Large B Cell Lymphoma	1(7)

Low C3 level was detected in 27% of patients and C4 level was normal in all patients. Hypergammaglobulinemia was detected in%27 patents but data of five patients could not be reached. Malignancy was detected in 10% of the patients who were followed up with the diagnosis of PSS. Two patients had cervical cancer (CA), four had breast CA, three had thyroid papillary CA, one had diffuse large b cell lymphoma, one had MALT (mucous-associated lymphoid tissue) lymphoma, one had mycosis fungoides, one had vulva epithelial carcinoma and two had lung CA. Patients with malignancy and those without were compared in terms of clinical and laboratory findings. There was a significant relationship between presence LAP and smoking with development of malignancy. Subgroup analysis was performed according to titers of C-Reactive protein (CRP) and erythrocyte sedimentation rates (ESH), but there was no significant relationship between laboratory findings and the development of malignancy. (Table 2)
Conclusion: According to 2015 data of Turkey unified database for all age groups, the rate of cancer in woman is 25% for breast cancer, 12% for thyroid CA, 5.1% for lung CA, 2.5% for cervical CA, 2.8% for non-hodgkin lymphoma. Patients with pSS have a 6 to 19-fold increased risk for the development of non-Hodgkin B-cell lymphoma. For these reasons, detailed questioning and physical examination gain importance in the follow-up of patients
References:
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Table-2. Relationship between presence of malignancy and clinical and laboratory findings

N(%)	*Malignancy(±)* **15**	*Malignancy(-)* **136**	*P*	*OR*	*%95 CI*
Hypocomplementemia	4(27)	11/96(12)	0,119	2,81	0,76-10,3
Fever	1(7)	7(5)	0,576	1,31	0,15-11,4
Night Sweats	1(7)	0	*	*	*
Weight Loss	2(13)	10(7)	0,339	1,93	0,38-9,81
Smoking	7(47)	24(20)	0,043	3,6	1,19-10,9
LAP	8(53)	36(27)	0,039	3,17	1,07-9,38
Hypergammaglobulinemia	4/10(40)	26/86(30)	*	*	*
ESH>50 mm/h	2(13)	8(6)	0,260	2,46	0,47-12,8
CRP>3XNormal	2(13)	14(10)	0,662	1,34	0,27-6,56

*No analysis was done because the data was not enough

Disclosure of Interests: None declared
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AB0439 LUNG FINDINGS IN PATIENTS WITH PRIMARY SJOGREN'S SYNDROME

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Background: Sjogren's syndrome (SS) is a systemic, autoimmune disease and can affect many organs and systems.
Objectives: In this study, we planned to present the lung findings of primary SS (pSS) patients who are being followed in our outpatient clinic.
Methods: Chest radiographs and thorax CTs of 151 patients who were admitted to the rheumatology outpatient clinic between 2004 and 2017 and diagnosed as pSS according to the classification criteria of the American-European consensus group Sjogren's syndrome were retrospectively scanned.
Results: In our study, 97% of pSS patients were female and 3% were male and the mean age was 56 ± 12 years, disease duration was 10.5 ± 5 years.
It was observed dry eye in 86% of patients, dry mouth in 88%, parotitis in 17%, arthritis in 29%, vasculitis in 4%, neuropathy in 6%, myositis in 1%, lymphadenopathy in 29% (LAP), and 20% of patients had Raynaud phenomenon. In 50% of the patients, chest radiography was normal, and there were no respiratory complaints. Thorax CT was requested due to suspicious appearance on 50% chest x-ray.

According to CT findings, 23% had nodules in the lung, nodule sizes were less than 1 cm, and patients were followed up for an increase in size. Hiler and subcarinal lymph nodes were present in 6% of patients and their sizes was ranged from 5 mm to 15 mm. Bronchoscopy was performed for two patients due to mediastinal LAP. Biopsy results were evaluated as reactive changes.

Interstitial lung disease (ILD) findings were present in 16 patients. (69% NSIP, 25% LIP, 6% UIP). All patients with ILD received steroid therapy. Two patients received 6 cycles of cyclophosphamide treatment for active alveolitis and azathioprine (AZA) was used in maintenance therapy. Due to ILD, one patient was receiving rituksimab, one patient was receiving mycophenolate mofetil, while nine patients were using AZA.

It was found bronchiectasis in 3% of patients, emphysema in 5%, sequelae fibrotic changes in 13%, and 1% patients had thickening of the pleura. One patient was diagnosed with hypersensitivity pneumonia and two patients had lung cancer (Table-1).

There was a smoking history in 21% of the patients. There was a significant relationship between smoking and development of emphysema and malignancy. The relationship between smoking and lung cancer development could not be assessed due to the absence of lung cancer in the non-smoking group (Table-2).

Conclusion: Lung findings are detected in 9-12% of patients in pSS, which can increase to 75% with the use of tomography, pulmonary function tests and bronchoscopy.

Since pSS has a wide spectrum from airway disease or interstitial lung disease to BALT lymphoma lung involvement of the disease has been emphasized.

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Table 1. Lung Findings of Primary Sjogren's Syndrome Patients

	%(N)
Nodule	23(34)
Mediastinal LAP	9(6)
Interstitial Lung Disease	11(16)
NSIP	69(11)
LIP	25(4)
UIP	6(1)
Bronchiectasis	3(4)
Atelectasis	5(7)
Emphysema	5(7)
Sequelae Fibrotic Change	13(19)
Tuberculosis Sequelae	1(2)
Airway disease	1(1)
Pleural effusion	1(2)
Lung cancer	1(2)

Table 2. Effects of smoking on lung findings

N(%)	Smoker 31(21)	Non-Smoker 107(71)	p	OR	%95 CI
Emphysema	6(19)	1(1)	0,001	25	2,9-220
Interstitial Lung Disease	2(7)	14(13)	0,524	0,458	0,09-2,13
Raynaud	6(19)	22(21)	0,883	0,926	0,33-2,53
LAP	10(32)	32(30)	0,802	1,11	0,47-2,63
Nodule	9(29)	23(22)	0,381	1,49	0,60-3,68
Malignancy	7(23)	8(8)	0,043	3,6	1,19-10,9
Lung Cancer	2(7)	0	-	-	-
Atelectasis	2(7)	3(3)	0,313	2,39	0,38-14,9
Bronchiectasis	0	4(4)	-	-	-

Disclosure of Interests: : None declared

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AB0440

LDL-CHOLESTEROL AS A RISK FACTOR OF PROGRESSION TO ESRD IN PATIENTS WITH LUPUS NEPHRITIS

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Background:

Objectives: There are few data on the effect of dyslipidemia in patients with lupus nephritis (LN). Thus, we investigated the effect of low-density lipoprotein-cholesterol (LDL-C) on the progression to end-stage renal disease (ESRD) in patients with biopsy-proven LN.

Methods: We followed 121 LN patients who underwent kidney biopsy and were subsequently treated with immunosuppressive drugs. Sociodemographic, clinical, laboratory (including lipid profile), and treatment-related data at the time of kidney biopsy and during follow-up were obtained by a review of patients' charts. Patients were divided into two groups related to the mean LDL-C level: <100 mg/dL and ≥100 mg/dL. Cox's proportional regression analysis was performed to identify the independent predictors of progression to ESRD in LN patients.

Results: Seventy-one of 121 biopsy-proven LN patients (58.7%) showed more than 100 mg/dL of LDL-C at the time of LN diagnosis. The higher LDL-C group excreted more 24-hour urine protein (p=0.003), and showed a higher proportion of proliferative LN (p=0.013) and an activity score >12 (p=0.023). During a mean follow-up of 83.0 (range, 12–171) months, ESRD was more frequent in the higher LDL-C group than in the lower group (15.5% vs. 2.0%; p=0.012). In the multivariate Cox's proportional regression analysis, LDL-C ≥100 mg/dL (hazard ratio [HR], 171.340; p=0.012), estimated glomerular filtration rate during the renal biopsy (HR, 0.977; p=0.005), statin exposure during follow-up (HR, 0.163; p=0.031), relapse (HR, 9.752; p=0.036), and complete remission at 1-year of treatment (HR, 0.034; p=0.003) were significant predictors of progression to ESRD in LN patients.

Conclusion: Our findings suggest that dyslipidemia at the onset of LN is an independent risk factor for predicting the development of ESRD in LN patients. Therefore, lipid profile should be monitored carefully and managed aggressively to avoid the deterioration of kidney function in patients with LN.

Disclosure of Interests: None declared

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AB0441

ASSOCIATION OF CO-POSITIVITY FOR ANTI-DSDNA, -NUCLEOSOME, AND -HISTONE ANTIBODIES AND DISEASE ACTIVITY IN PATIENTS WITH LUPUS NEPHRITIS: RESULTS FROM THE KORNET REGISTRY

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Background: Recent studies have shown that the simultaneous positivity of anti-double stranded DNA, -nucleosome, and -histone antibodies (3-pos) is prevalent in lupus nephritis (LN) patients compared to non-renal systemic lupus erythematosus (SLE) patients.

Objectives: The aim of this study was to define the clinical, biologic, histopathologic, and prognostic differences according to the simultaneous reactivity to those antibodies in Korean patients with biopsy-proven LN.

Methods: We studied 102 patients who underwent kidney biopsy prior to the start of induction treatment and who were subsequently treated with immunosuppressives and followed-up for more than 12 months. Sociodemographic, clinical, laboratory, and treatment-related data at the time of kidney biopsy and during follow-up were obtained by a review of patients' charts. Antibodies were detected by immunoblot analysis or ELISA at the time of renal biopsy.

Results: Fifty-eight (35.4%) of the total of 102 LN patients had 3-pos. In comparison with non-3-pos patients, the patients with 3-pos showed a higher SLE Disease Activity Index-2000 score (P=0.002), lower lymphocyte level (p=0.004), higher proportion of proteinuria >3.5 g/24 hr (p=0.005), and higher positivity of urinary sediments (p=0.005) at the time of renal biopsy. In the renal histopathologic findings, the patients with 3-pos had more proliferative LN (p=0.015) and also showed more endocapillary hypercellularity, sub-endothelial hyaline deposits, fibrinoid necrosis/karyorrhexis, and cellular crescents in the disease activity index (p=0.016, p=0.045, p=0.002, and p=0.022, respectively), as well as a higher activity score (p=0.011). After a median follow-up of 83.2 months, rapid glomerular filtration rate decline was frequently observed in patients with 3-pos compared to those without (p=0.012).

Conclusion: Our findings suggest that 3-pos is related to severe LN and, furthermore, that patients with 3-pos show a rapid decline of renal function compared to those without.

Disclosure of Interests: None declared

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AB0442

RISK FACTORS ASSOCIATED WITH THROMBOTIC EVENTS IN KOREAN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background:

Objectives: Up to 30~40% of all patients with systemic lupus erythematosus (SLE) experience thrombosis, presenting as stroke and myocardial infarction, and these thrombotic events cause substantial morbidity and mortality in SLE. We explored the risk factors associated with the occurrence of thrombotic events in SLE patients.

Methods: This study enrolled 259 SLE patients (mean age, 34.0 ± 13.7; 239 females) with available clinical data at the time of SLE onset from the lupus cohort at Chonnam National University Hospital. Sociodemographic, clinical, and laboratory data, and history of concomitant diseases were obtained. Thrombotic events were defined as the presence of arterial or venous thrombosis. The

multivariable Cox's model was performed to investigate the possible risk factors for thrombotic events.
Results: During a mean follow-up of 103.3 months (SD, 53.4), 27 patients (10.4%) developed thrombotic events: stroke in 15 patients, venous thrombosis in five patients, myocardial infarction in four patients, and angina in three patients. In the multivariable Cox's regression analysis, hypertension (hazard ratio [HR], 16.946; P=0.031), antiphospholipid syndrome (APS) (HR, 18.348; P=0.001), cumulative prednisolone >5 mg/day (HR, 14.374; P<0.001), use of ACE inhibitors (ACEi) or angiotensin receptor blockers (ARB) (HR, 0.110; P=0.004), and Systemic Lupus International Collaborating Clinics Group (SLICC) damage index (HR, 1.972; P=0.004) were significant predictors of the development of thrombotic events in patients with SLE.
Conclusion: Patients with SLE showed significant thrombotic events during the course of their disease. Risk factors associated with thrombotic complications were higher cumulative dose of prednisolone, diagnosis of APS, and higher SLICC damage index. On the other hand, the use of ACEi or ARBs was associated with a reduced risk of thrombotic complications in patients with SLE. Our results support the need for increased monitoring of thrombotic complications in SLE patients.
Disclosure of Interests: : None declared
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AB0443

RENAL TRANSPLANTATION IN LUPUS NEPHRITIS. LONG-TERM FOLLOW-UP. STUDY FROM A SINGLE REFERRAL CENTER.

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Background: Lupus nephritis (LN) is a severe complication of systemic lupus erythematosus (SLE). Approximately 10-20% of LN develop end stage renal disease (ESRD) and need replacement therapy. Renal transplantation may be a good option. However, concerns about LN recurrence after renal transplantation have been reported.
Objectives: In a series of 23 patients with first renal transplantation due to LN our aim was to assess **a)** clinical features, **b)** renal transplantation as replacement therapy, **c)** SLE flares after transplantation
Methods: Observational study of unselected all consecutive patients studied in a single reference University Hospital with**: a)** diagnosis of SLE by ACR/SLICC 2012 criteria. **b)** diagnosis of NL by performing biopsy (according to the World Health Organization and International Society of Nephrology/Renal Pathology Society classification), **c)** first renal transplant. Cumulative survival rates after transplantation were estimated by the Kaplan-Meier method.
Results: We studied 23 (16 women/7 men) patients with first renal transplantation due to LN; mean age at SLE diagnosis of 26.37±12.70 years and mean age at kidney transplantation of 39.80±11.27 years. Mean follow-up of 12.18±9.02 years. Demographic baseline characteristics and clinical manifestations of these patients are shown in TABLE 1 **and 1.1.**

TABLE 1. Demographic baseline characteristics and clinical manifestations of patients with renal transplantation due to LN.

DEMOGRAPHIC PARAMETERS	
Sex, n (%)	7 ♂ / 16 ♀ (30.4%/69.06%)
Age at SLE diagnosis (years), mean ± SD	26.37±12.70
Age at renal transplantation, mean ± SD	39.80±11.27
SLE RELATED DATA	
Systemic symptoms	**12.0 (52.17)**
Fever, n (%)	8.0 (34.78)
Weight loss, n (%)	3.0 (30.0)
Asthenia, n (%)	3.0 (30.0)
Articular affection	**12.0 (52.17)**
Joint swelling, n (%)	9.0 (39.13)
Arthralgia, n (%)	3.0 (13.04)
Skin affection	**13.0 (56.52)**
Malar erythema, n (%)	2.0 (8.6)
Discoid lupus, n (%)	0.0 (0.0)
Photosensitivity, n (%)	3.0 (13.04)
Ulcers, n (%)	5.0 (21.73)
Alopecia, n (%)	3.0 (13.04)
Raynaud, n (%)	1.0 (4.34)

The main clinical manifestations at diagnosis were articular (n= 12; 52.17%) and cutaneous (n=13; 56.52%). On the other hand, 16 patients (69.6%) presented impaired renal function at diagnosis. In the other 7 patients (30.4%), this manifestation appeared with a delay of diagnosis from the onset of symptoms of 13.17±7.73 years.
Renal biopsy had been performed in 21 patients with LN: type II LN (n=2; 9.1%), type III (n=8; 36.4%), type IV (n=9; 40.9%) and type V (n=2; 9.1%).
Patient and graft survival function after transplantation is represented in Figure 1 **and 2.**

TABLE 2. 1.1.

SLE RELATED DATA	
Renal involvement	**16.0 (69.56)**
Hematological involvement	**13.0 (56.52)**
Anemia, n (%)	6.0 (26.10)
Leukopenia, n (%)	5.0 (21.73)
Thrombocytopenia, n (%)	2.0 (8.70)
Pericarditis	**2.0 (8.70)**
Nervous system	**6.0 (26.10)**
Peripheral, n (%)	1.0 (4.34)
Central	4.0 (17.40)

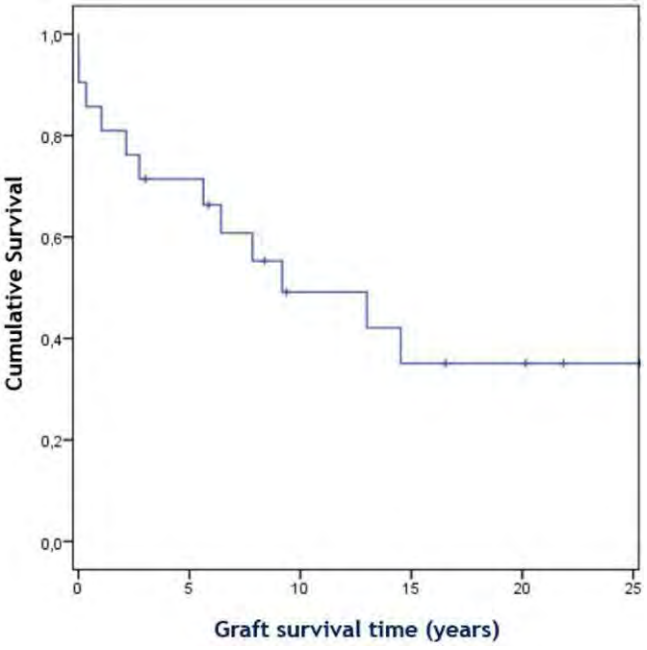


Figure 1.

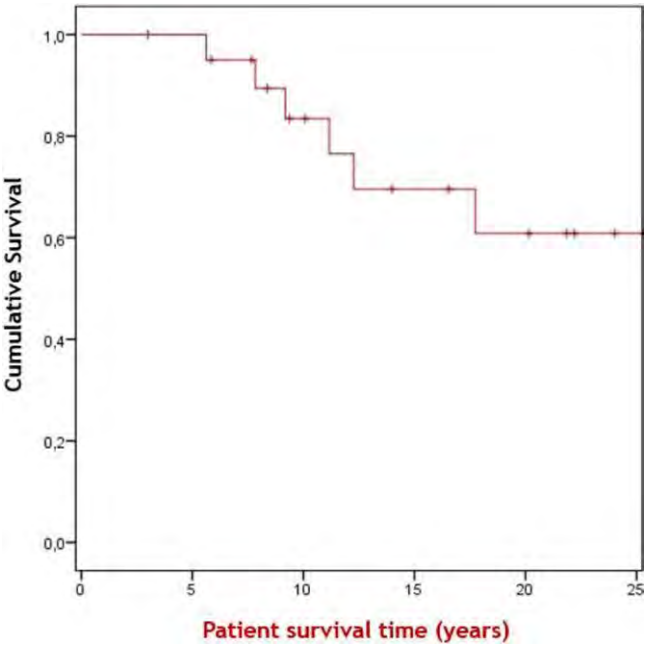


Figure 2.

Regarding lupus flares after transplantation, 3 patients (13.04 %) developed a lupus flare: 2 cases presented as extrarenal disease (one of them was a pneumonitis and the other one was a cutaneous and articular flare) and only 1 case with histological recurrence in the graft (Mean follow-up 15.00±9.84 years).

Conclusion: Renal transplantation is a safe alternative therapy for ESRD in this population and can provide a long-term survival. However, it is very important to consider the occurrence of flares even in the long-term post-transplant.
Figures 1 and 2.
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AB0444

THROMBOTIC MICROANGIOPATHY AND SJÖGREN SYNDROME, AN UNUSUAL ASSOCIATION. PRESENTATION OF CLINICAL CASE AND SYSTEMATIC REVIEW OF THE LITERATURE

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Background: Thrombotic microangiopathy (TMA) is a clinicopathologic diagnosis defined as microangiopathic hemolytic anemia (MAHA) with associated features of thrombocytopenia and end-organ ischemia. Systemic lupus erythematosus, antiphospholipid antibody syndrome, and scleroderma, are within the autoimmune diseases, the more commonly associated with TMA. It has been considered that the association with Sjögren Syndrome (SS) is rare.
Objectives: To describe one patient with TMA and SS, and to review all cases reported in the literature.
Methods: We notified a clinical case of a patient with Sjögren's syndrome and TMA. Then, we searched the medical literature finding a total of 17 cases reported with this association until 2019. Before the data obtained were tabulated by trained staff and descriptive, comparing groups and bivariate analysis was performed. The outcome of interest was the death of the patient. Stata 12.0 software was used.
Results: A 26-years-old Colombian female presented with a 6-week history of petechiae in lower limbs, gingivorrhagia, menorrhagia and jaundice; and previous history of arthritis and xerostomia. On admission, in the context of severe thrombocytopenia and MAHA, MAT diagnosis was made. During hospitalization we confirm the diagnosis of SS with ANA, antiRo and salivary gland biopsy. The patient was treated with steroids (methylprednisolone 500 mg/day, 3 days), plasma exchange therapy (PLEX) and Cyclophosphamide (750 mg), with recovery of hemoglobin and platelet levels; however, the patient died due to a complication of the PLEX catheter removal procedure.
A total of 18 patients diagnosed with de novo or prevalent Sjögren's syndrome who had hospital admission with a diagnosis of TMA were included. The mean age was 54.55 years (Standard deviation (SD): 12.45) and 83.33% of the patients corresponded to the female gender.
At admission, the mean of hemoglobin was 8.45 g/dL (SD: 2.55) and median platelets of 27250/mm3 (interquartile range (IQR) 10500 - 102000) were found. The most frequent clinical manifestations were central nervous system alterations (50%), followed by bleeding in the skin and renal failure (44.44%) and fever (27.78%). The most frequent antibodies found were anti-Ro (100%), anti-nuclear antibodies (80%) and anti-La (75%). The most frequently prescribed treatment was plasma exchange therapy (83.33%), intravenous steroids (61.11%), oral steroids (61.11%) and cyclophosphamide (27.78%). Of the total patients, 38.89% died and 27.7% had some relapse of TMA.
In the group comparison analysis, differences were found in intravenous steroid (81.82% in those who lived vs. 28.57% in those who died p=0.039), use of PLEX (100% in those who survived vs. 57.14% in those who died p = 0.043), fever (9.09% in those who survived and 57.14% in those who died, p = 0.047), admission hemoglobin (7.65 g/dL in those who lived vs. 10.22 g/dL in those who died, p = 0.05), final platelets (148,000 in which who lived and 39,000 in those who died p = 0.02). Then, in the logistic regression analysis, an association was found between mortality and use of intravenous steroids (OR: 0.08, 95% CI 0.009 - 0.83, p = 0.35) and fever at admission (OR: 13.33 95% CI: 1.04 - 169.55, p = 0.046).
Conclusion: While the association between TMA and SS is uncommon, so far 18 cases have been reported in the world medical literature. It is typically a condition of women age close to 50 years. The most frequent manifestations are neurological. Among the variables evaluated, only the use of endovenous steroids was associated with a decrease in the probability of mortality; on the contrary, the presence of fever at hospital admission increased the probability of death. The results should be evaluated with caution, since, due to the limited availability of information, they may not be generalizable to clinical practice. More information on this should be obtained in the future.
Disclosure of Interests: None declared
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AB0446

CLINICAL AND IMMUNOLOGICAL CHARACTERISTICS OF 484 SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS IN XINJIANG OF CHINA: A COMPARATIVE ANALYSIS

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Background: Systemic lupus erythematosus (SLE) is a chronic inflammatory autoimmune disease. Epidemiological studies in SLE have been reported in the literature in many countries and ethnic groups. Although SLE in China has been described in the past, there has not been a detailed evaluation of SLE patients in Xinjiang of China, a largely Uygur population.
Objectives: To describe the clinical featuresand immunological features of 484 SLE subjects.
Methods: 484 adult patients followed in the The People's Hospital of the Xinjiang Uygur Autonomous Region, 211 patients with Uygur SLE as well as 273patients with Han SLE.
Results: Of the 211 Uygur SLE patients, 195 (92.4%) were female and 16 (7.6%) were male (female:male=12.2:1),the mean age at SLE onset was 34.67±11.57 years, mean disease duration was 20.77±35.16 months.Of the 273 Han SLE patients,247(90.5%)were female and 26(9.5%) were male,the mean age at SLE onset was 36.68±14.44 years,mean disease duration was 41.64±61.89 months.(2)between the Uygur and Han SLE patients,the Raynaud phenomenon(χ^2=6.066 P=0.014), Chest pain(χ^2=7.906 P=0.005), headache(χ^2=4.572 P=0.029)has obvious differences(table 1).(3)The anti-nuclear (χ^2=8.108 P=0.004), anti-AHA (χ^2=4.952 P=0.026)were higer in Uygur SLE patients than those in Han SLE patients;the Uygur SLE patients has been anemia(χ^2=6.904,P=0.009), high level of immunoglobulin (χ^2=8.939,P=0.003),decrease of complement(χ^2=6.330 P=0.012). (table 2)

figure 1. Clinical manifestations

Clinical manifestations	Uygur SLE patients(n=211)	Han SLE (n=273)	χ^2	*P*
rash	106(50.2%)	157(57.5%)	2.537	0.111
Photosensitivity	40(19%)	56(20.5%)	0.181	0.670
Alopecia	73(34.6%)	101(37.0%)	0.298	0.585
Oral ulcers	49(23.2%)	64(23.5%)	0.006	0.937
Raynaud phenomenon	28(13.3%)	60(22%)	6.066	0.014
livedo reticularis	5(2.4%)	7(2.6%)	0.020	0.866
arthralgia/arthritis	105(49.8%)	159(58.5%)	3.623	0.057
abnormal liver-function	8(3.8%)	7(2.6%)	0.597	0.440
Chest pain	28(13.3%)	16(5.9%)	7.906	0.005
Suffocation	49(23.2%)	52(19%)	1.256	0.262
palpitation	27(12.8%)	41(15%)	0.487	0.485
Shortness of breath	24(11.4%)	35(12.8%)	0.233	0.630
Ophthalmia	2(0.9%)	6(2.2%)	1.154	0.283
Visual impairment	1(0.5%)	3(1.1%)	0.567	0.457
hemiplegia	1(0.5%)	0(0.0%)	1.297	0.436
Mental disorder	4(1.9%)	11(4.0%)	1.804	0.179
headache	14(6.6%)	7(2.6%)	4.572	0.029
Lower Limb Edem	36(17.1%)	34(12.5%)	2.042	0.153
pleurisy	37(17.5%)	43(15.8%)	0.256	0.613
pericarditis	38(18%)	33(12.1%)	3.273	0.070
pulmonary fibrosis	7(3.3%)	9(3.3%)	0.000	0.982

figure 2. immunological manifestations

manifestations	Uygur SLE patients(n=211)	Han SLE (n=273)	χ^2	*P*
antinuclear antibodies	185(87.7%)	212(77.7%)	8.108	0.004
anti-dsDNA	115(54.5%)	144(52.7%)	0.147	0.701
anti-SSA	101(47.9%)	149(54.6%)	2.147	0.143
anti-SSB	45(21.3%)	63(23.1%)	0.210	0.647
anti-Sm	44(21%)	68(25%)	1.088	0.297
ACL	29(13.8%)	26(9.5%)	2.161	0.142
antiU1-RNP	74(35.1%)	100(36.6%)	0.126	0.723
anti-AHA	60(28.4%)	54(19.8%)	4.952	0.026
Low white blood cell	46(22.1%)	79(29%)	2.938	0.087
anemia	90(42.9%)	85(36.3%)	6.904	0.009
Thrombocytopenia	36(17.1%)	51(18.7%)	0.212	0.645
Urine protein positive	84(39.8%)	114(41.9%)	0.217	0.641
Rise of urine RBC	29(13.7%)	35(12.8%)	0.088	0.766
Increased immunoglobulin	82(38.9%)	71(26.1%)	8.939	0.003
Complement decline	120(57.1%)	124(45.6%)	6.330	0.012

Conclusion: The Uygur SLE patients have their own clinical and immunological characteristics, which has guiding significance in the diagnosis, treatment and prognosis of SLE.

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Disclosure of Interests: None declared
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AB0447 IRREVERSIBLE ORGAN DAMAGE IN PERI- AND POSTMENOPAUSAL WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN REMISSION

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Background: Although the survival of patients with systemic lupus erythematosus (SLE) has improved, irreversible organ damage remains a critical concern. Long-standing inflammation, drug-related side effects and comorbidities may eventually cause permanent organ damage even in remission [1].
Objectives: To describe irreversible organ damage in peri- and postmenopausal women with SLE in remission and low disease activity, to find predictors of damage progression.
Methods: 234 peri- and postmenopausal women with SLE were included (mean age 49,94±9,1 years) in our study. All women were under outpatient observation in St.Petersburg State Clinical Rheumatology Hospital #25 (Russia). Mean disease duration was 8,9±7,5 years. We analyzed treatment regimens and doses of glucocorticoids (GC) based on source medical documents. To assess disease activity, we used SLEDAI-2K and LLDAS. To assess organ damage, we used SLICC damage index (SDI).
Results: 94,3% of women have been taking GC during our study. Median of maintenance dose was 12,5 mg per day. Almost a half of all women (44,8%, n=105) in our study were postmenopausal (mean duration of menopause was 11,1±7,1 years). A half of all patients had low disease activity (44,4%, n=111) or were in remission (18,8%, n=44) according to SLEDAI-2K. 26,5% (n=65) of patients had all 5 criteria and 45,1 % (n=115) of patients had 4 of 5 criteria according to LLDAS. Critical organ damage (SDI>4) was observed in 68,8% (n=161) of women with SLE. Moderate (1≤SDI≤4) and low (SDI=1) damage had 25,6% (n=60) and 6,4% (n=15) of patients respectively. Musculoskeletal damage was on the first place among others: 37,6% (n=88) of patients had osteoporosis with fractures and 34,2% (n=80) had muscle weakness. In 75 women with SLE of osteoporotic fractures occurred in remission or low disease activity (LLDAS). Progression of irreversible organ damage in remission or low disease activity (LLDAS) had 62% (n=145) of women with SLE. Multifactorial logistic regression analysis of factors associated with organ damage in SLE showed that only patients age (p=0.013215), cumulative dose of GC (p=0.000047) and therapy with cyclophosphamide (p=0.041505) were statistically significant.
Conclusion: Progression of irreversible organ damage in peri- and postmenopausal women with SLE may occur despite remission or low disease activity. There are no doubts that organ damage accrual is associated with CG therapy. Correction of GC dose or discontinuation of GC treatment in remission can predict organ damage accrual in SLE including osteoporosis and osteoporotic fractures.
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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.2420

AB0448 IMPACT OF REMISSION ON DAMAGE ACCRUAL IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) PATIENTS: A SYSTEMATIC LITERATURE REVIEW (SLR)

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Authors	Country/ Region	Patients	Remission	Achieving remission (%)	Damage: remission vs not remission	NOS
Zen et al	Italy	224	SLEDAI=0 Serologic= allowed PGA= NR PDN ≤ 5 IS=Yes AM=Yes Duration=5 years	37.5%	Unremitted disease OR=2.53; p=0.008	7
Tani et al	Italy	115	SLEDAI=0 Serologic PGA= NR PDN ≤ 5 IS=Yes AM=Yes Duration=NR	49.6%	ΔSLICC 0.12 vs 0.48,p= 0.018	8
Ugarte-Gil et al	Latin America	1,350	SLEDAI=0 Serologic= not allowed PGA= NR PDN ≤ 5 IS=Yes AM=Yes Duration=NR	20.2%	New damage HR 0.60 p=0.0042 Severe new damage HR 0.32 p=0.0033	8
Tsang-A-Sjoe et al	Netherlands	224	SLEDAI=0 Serologic= allowed PGA= NR PDN ≤ 5 IS=Yes AM=Yes Duration>5 years	37.6%	OR=0.20; p=0.001	8
Mok et al	China	769	SLEDAI=0 Serologic= Allowed PGA<0.5 PDN ≤ 5 IS=Yes AM=Yes Duration≥5years	25.1%	Not being on remission for at least 5 years OR: 2.42; p<0.001	7
Tselios et al	Canada	267	SLEDAI=0 Serologic= Allowed PGA=NR PDN no restriction IS no restriction AM=Yes Duration≥5years	10.1%	SDI after 10 years: 0.96 vs 1.53 (not on remission, not on LDAS), p for trend =0.029	7
Petri et al	US	1,356	SLEDAI=0 Serologic= NR PGA<0.5 PDN ≤ 5 IS=Yes AM=Yes Duration= NR	NR	Rate ratio per percentage of follow-up RR(<25%)=0.54; p<0.0001 RR(25-49%)=0.47; p<0.0001 RR(50-74%)=0.43; p<0.0001 RR(>75%)=0.45; p=0.0019	7
Golder et al	Asia Pacific	1,707	SLEDAI=0 Serologic=Yes PGA<0.5 PDN ≤ 5 IS=Yes AM=Yes Duration= NR	35.8%	HR=0.55; p<0.0001	6

NR: Not recorded. OR: Odds Ratio. HR: Hazard ratio. RR: Rate ratio

Background: Treat-to-target strategy with remission as the target has been proposed for the management of SLE. However, there is not a uniform definition of remission.
Objectives: To determine the protective value of remission state on organ damage accrual in SLE patients through a SLR.
Methods: Two independent reviewers identified studies in Medline and Cochrane Library. Data on remission definitions and rates as well as damage accrual (assessed by the SLICC/ACR damage index [SDI]) were extracted. Definitions of

remission included disease activity indices (SLEDAI and its variants and PGA), serological activity, prednisone (PDN) daily dose (mg/day), immunosuppressive (IS) drugs, antimalarial (AM) use and duration of remission. The quality of the studies was evaluated with the Newcastle-Otawa Scale (NOS).

Results: Eight manuscripts were included comprising more than 6,000 patients from America, Europe and Asia Pacific. All the studies were longitudinal. The majority of the studies reached more than seven out nine points in the NOS. Remission rates ranged between 10 and almost 50%; they tend to be lower in America as compared to Asia Pacific and Europe. All definitions required a clinical SLEDAI=0, and allowed antimalarial use. However, there were differences regarding the inclusion of serological activity, PGA, prednisone or immunosuppressive drug use as well as minimum remission duration required. Even less stringent definition of remission prevented damage accrual. The risk of damage accrual was two to five-fold lower in those patients on remission.

Conclusion: In SLE patients, achieving remission, even with less stringent definitions, prevented damage accrual.

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AB0449

IMPACT OF REMISSION AND LOW DISEASE ACTIVITY (LDA) ON HEALTH-RELATED QUALITY OF LIFE (HRQOL) IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) PATIENTS: A SYSTEMATIC LITERATURE REVIEW (SLR)

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Background: Treat-to-target strategy has been proposed in SLE. Achieving remission/LDAS should prevent damage, reduce mortality and improve HRQoL.

Objectives: To determine the protective value of remission or LDA states on HRQoL in SLE using a SLR.

Methods: Two independent reviewers identified studies in Medline and Cochrane library and extracted data on remission, LDA and HRQoL. Remission and LDA definitions included disease activity (SLEDAI and its variants, SLAM and PGA), serological activity, new organ/system, prednisone (PDN) dose (mg/day), immunosuppressives (IS) drugs, antimalarial (AM) use and remission duration. The quality of the studies was assessed with the Newcastle-Otawa Scale (NOS).

Results: Three manuscripts (1059 patients) for remission and 4 (2385 patients) for LDA were included (America, Europe & Asia Pacific). All the studies reached seven out of nine NOS points. Remission rates ranged 25-39%; and LDA: 42-62%. Even less stringent remission or LDA definitions predicted/were associated with a better HRQoL. Physical rather than mental domains were more associated with remission or LDA.

Conclusion: In SLE patients, achieving remission or LDA, is associated with a better HRQoL.

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Table 2. Association between LDA and HRQoL

Authors	Country/ Region	Patients	LDA	LDA (%)	Domains positively associated or predicted by LDAS
Golder et al*	Asia Pacific	1422	SLEDAI≤ 4 PGA≤ 1 PDN ≤ 7.5 IS=Yes AM=Yes New manifestations: No Duration=NR	42.0	SF-36: Role physical, bodily pain, general health, vitality, social functioning, role emotional, mental health, PCS and MCS
Ugarte-Gil et al#	USA	483	SLAM≤ 3 PGA=NR PDN ≤ 7.5 IS=No AM=Yes New manifestations: NR Duration=NR	NR	SF-36: Physical function, role physical, bodily pain, general health, vitality, social functioning, role emotional, mental health, PCS and MCS
Ugarte-Gil et al#	Peru	243	SLEDAI≤ 4 PGA=NR PDN ≤ 7.5 IS=Yes AM=Yes New manifestations: NR Duration=NR	48.6 at baseline	LupusQoL Physical health, pain, planning, burden to others, emotional health, fatigue
Poomsalood et al*	Thailand	237	SLEDAI≤ 2 Serologic= allowed PGA=NR PDN ≤ 7.5 IS=Yes AM=Yes New manifestations: NR Duration=NR	61.6	SLEQoL Univariable: physical, activities, symptom, treatment, mood, self-image and total. Multivariable: Better global QoL

PCS: Physical component summary. MCS: Mental component summary. *Cross-sectional #Longitudinal

Table 1. Association between remission and HRQoL

Authors	Country/ Region	Patients	Remission	Remission (%)	Domains positively associated or predicted by remission
Mok et al*	China	769	SLEDAI=0 Serologic= Allowed PGA<0.5 PDN ≤ 5 IS=Yes AM=Yes Duration≥5years	25.1	Remission>5 years vs not on remission SF-36: Role physical, bodily pain, general health, vitality, social functioning, role emotional, PCS and MCS LupusPRO: Symptoms, medications, procreation, physical health, pain, emotional, image, HRQoL total
Tsang-A-Sjoe et al#	Netherlands	154	SLEDAI=0 Serologic= allowed PGA ≤2/10 PDN ≤ 5 IS=Yes AM=Yes Duration=NR	39.0 at baseline	Remission on- or off-therapy predicted a better SF-36 PCS but not MCS
Margiotta et al*	Italy	136	SLEDAI=0 Serologic= allowed PGA= NR PDN ≤ 5 IS=Yes AM=Yes Duration>5 years	39.0	Remission >5years vs unremitted or remission<5 years SF-36: Physical health, role physical, bodily pain, general health, social functioning

PCS: Physical component summary. MCS: Mental component summary. *Cross-sectional #Longitudinal

AB0450 DANISH PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS SELF-REPORT HIGH LEVELS OF PHYSICAL ACTIVITY, AND MOST PATIENTS FULFILL THE WHO RECOMMENDATIONS ON PHYSICAL ACTIVITY

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Background: Physical activity is important for enhancing health and the World Health Organization (WHO) recommends that adults aged 18-64 engage in at least 150 minutes of moderate-intensity physical activity throughout the week, or 75 minutes of vigorous-intensity physical activity (1). Swedish patients with SLE reported a lower frequency and capacity of exercise than a control group, and in an Italian study, 60% of the SLE patients did not meet WHO's recommendations for physical activity. Mental health is important for the individual's level of physical activity, and symptoms of depression have been associated with a lower level of physical activity in SLE patients (2).

Objectives: The aim of this study is to describe the pattern of physical activity in a population of Danish SLE patients, and to investigate the association to depression.

Methods: The study was conducted at the Department of Rheumatology at Odense University Hospital, Denmark, in 2018 and 2019. Two questionnaires were handed out before routine outpatient consultation: self-reported physical activity was evaluated using the International Physical Activity Questionnaire (IPAQ), and a continuous variable on energy requirement in the form of the metabolic equivalent (MET) was calculated, and the Major Depression Inventory (MDI) questionnaire was used to screen for depression. Medicine intake was registered, and disease activity and damage were scored using SLEDAI-2K and SLICC/ACR DI.

Results: Two hundred and fifteen patients completed the IPAQ and MDI, 5 were excluded. The population consist of 89.5% women and the mean age was 51.7 ± 15.2 years. The mean disease duration was 16.1 ± 10.1 years.

The SLE patients reported a mean total MET-score of 5319.9 ± 3650 MET-min/week. If divided into categories, 7.6% reported low level, 21.9% moderate and 70.5% of the patients reported a high level of physical activity and 89.5% fulfilled WHO recommendations. The participants reported 363.7 ± 201 minutes per day in sitting time.

Mean MDI score was 12.7 ± 10.1, and if divided into groups, 89.5% were not depressed, 1.9% had a mild depression, 5.3% had a moderate depression and 2.9% had a severe depression. Significantly lower mean MET-scores were observed for the severely depressed patients.

An inverse association was found in the univariate analysis, indication that increasing disease duration and SLICC/ACR DI scores were significantly associated with decreasing total MET-scores. In the multivariate analysis time spent sitting was inversely associated with MET-score.

Our results were similar to a Brazilian study, where 68% of the patients reported, that they were "physical active" according to IPAQ. In contrast, only 22% of the patients in an Italian study reported high level physical activity. Our proportion of active patients were high when comparing with studies on patients with rheumatoid arthritis and spondylarthritis, where only 25-50% fulfilled the WHO recommendations compared to our 89.5%.

A Danish study on registered ICD diagnoses found a prevalence of depression in SLE patients to be 4.3%, which was lower than our prevalence. Foreign studies reported very diverse prevalences of depression, e.g. 16.6% in the Netherlands and 51% in Sweden.

Conclusion: A high portion of the SLE patients reported a high level of physical activity and 89.5% fulfilled the WHO recommendations. Significant predictors for a lower level of physical activity were increasing disease duration, higher SLICC/ACR DI score and longer time spent sitting. However, further studies are needed, where more suitable questionnaires could be considered.

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Disclosure of Interests: None declared

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AB0451 PRIMARY SJOGREN'S SYNDROME IN MEN

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Background: Primary Sjogren's syndrome (PSS) is characterized as an autoimmune exocrinopathy, but this disorder also may involve extraglandular organs, giving rise to multisystem disease. Although the first case reported by Dr Mikulicz was a 42 year old man [1], there are only few reports describing the clinical picture of Sjogren's Syndrome in males

Objectives: To determine whether there were any clinical and biological differences between male and female tunisian patients with primary Sjogren's syndrome (PSS).

Methods: We studied 60 patients with pSS according to American-European Consensus Group (AECG), attending an Internal Medicine departement in Tunisia. The nine (15%) male patients in this cohort comprised the male group described in this study

Results: The average age of men at diagnosis was 53.2 years [31 to 73 years]. Male SSp was revealed by sicca symptoms (55.5%), by extra glandular manifestations (33.3%). Fourty-four percent of our male patients had a positive result for a minor salivary gland biopsy (grade III or IV).

Extraglandular manifestations during the course of the disease were present in 6 cases (66%) of our male patients with pSS. weight loss and raynaud's phenomenon were more common in men. a significantly greater percentage of men had neurological involvement (66.6%vs 23,7) and and pulmonary involvement, notably a restrictive syndrome (66.6% vs 31,1%, p=0.043). The positivity of Anti-nuclear antibodies, anti-SSb and rheumatoid factor were significantly less common in males.

Anemia was significanty more common in the male patients (p=0,049). No cases of Lymphoma in the male patients in our series.

Eighty-eight percent of the men were treated with corticosteroids. In our series, the use of immunosuppressants was not necessary in male patients.

Conclusion: Although pSS is typically a disease affecting women, clinicians should be aware that it may be diagnosed in male patients. Although men were at the same risk for the development of extraglandular complications, there were significant serologic and immunogenetic differences. In Sharp contrast to women with Sjogren's syndrome, men with Sjogren's syndrome were more seronegative in our series.

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AB0452 PREDICTIVE FACTORS FOR INSUFFICIENT RESPONSE TO INITIAL TREATMENT OR RECURRENCE IN PATIENTS WITH LUPUS ENTERITIS

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Background: Lupus enteritis (LE) is a rare but well-known complication of systemic lupus erythematosus (SLE). However, little knowledge about risk factors for insufficient response to initial treatment or recurrence have been reported.

Objectives: To identify prognostic factors associated with poor response in patients with LE.

Methods: Patients diagnosed as having LE at our hospital were consecutively registered from January 2009 to October 2019. The diagnosis of LE was made according to the criteria of BILAG 2004 which is defined as either vasculitis or inflammation of small or large bowel with supportive imaging and/or biopsy findings. Poor response was defined as insufficient response to initial therapy or relapse. We retrospectively compared clinical characteristics collected from medical records of the patients with good vs. poor response, using a non-parametric Wilcoxon signed-rank test for numerical variables and Fisher's exact test for categorical variables.

Results: A total of 12 patients (16 episodes) diagnosed with LE were reviewed. The median age was 44.5 years and 11 were females. Six patients had a history of SLE (median disease duration; 3.0 years), of which 4 had a history of LE prior to the study period. And in the remaining 6 patients, LE was the primary symptom (Table 1). The comorbidities were 4 lupus cystitis, 1 biopsy-proven lupus nephritis, 1 pseudo-obstruction and 1 protein-losing enteropathy. Computed Tomography (CT) imaging of all 16 episodes showed small bowel wall thickening. Dilatation of intestine was observed in 81.3%, ascites in 81.3%, comb sign in 80.0% and target sign in 62.5%. When comparing clinical characteristics between the groups revealed that CT findings were similar in both groups, however serum CH50 levels (median (interquartile ranges (IQR)) 37.2 (25.3-46.9) U/mL vs 17.6 (7.1-21.4) U/mL, p=0.0095) were significantly lower in poor response group. Furthermore, patients who initiated glucocorticoids (GCs) at a lower dose (less than or equal to 0.6mg/

kg prednisolone equivalent dose (PEQ)) was significantly more frequent in poor response group (Table 2).

Table 1. Baseline demographics and outcomes of LE patients

	Variables	N=12
Demographics	Female (%)	91.7
	Age (yrs), median (IQR)	44.5 (34.0-47.5)
	SLE duration (yrs), median (IQR)	3.0 (0-9.0)
Baseline therapy	Prednisolone (mg), median (IQR)	7.0 (0-10.5)
	Cyclosporine (%)	16.7
	Azathioprine (%)	8.3
	Mycophenolate mofetil (%)	8.3
	Tacrolimus (%)	8.3
Outcomes	Follow-up period (yrs), median (IQR)	4.0 (1.9-5.0)
	Poor response to initial therapy (%)	33.3
	Recurrence (%)	33.3
	Need for surgical intervention (%)	8.3
	Death (%)	0

Table 2. Comparison of baseline characteristics and initial treatment between LE patients with good vs. poor response

	Variables	Good response (N=10)	Poor response (N=6)	p value
Comorbidities	Lupus cystitis (%)	30.0	33.3	1.0
	Lupus nephritis (%)	0	16.7	0.38
CT findings	Maximum external diameter of small intestine (mm), median (IQR)	30.8 (22.2-37.9)	25.3 (19.4-29.0)	0.083
	Colon involvement (%)	30.0	66.7	0.30
	Dilatation of intestine (%)	90.0	66.7	0.52
	Ascites (%)	90.0	66.7	0.52
	Comb sign (%)	90.0	66.7	0.52
	Target sign (%)	70.0	50.0	0.61
Laboratory findings	anti-dsDNA Ab (IU/mL), median (IQR)	5.4 (1.6-12.6)	10.1 (3.8-111.5)	0.17
	CH50 (U/mL), median (IQR)	37.2 (25.3-46.9)	17.6 (7.1-21.4)	0.0095
	C4 (mg/dL), median (IQR)	16.0 (10.5-27.3)	10.0 (10.0-13.8)	0.11
	C3 (mg/dL), median (IQR)	66.0 (56.8-79.8)	46.5 (33.0-58.3)	0.10
Initial treatment	Less than or equal to 0.6mg/kg PEQ (%)	10.0	66.7	0.036
	Intravenous cyclophosphamide	10.0	16.7	1.0

Conclusion: Lower level of CH50 and initial treatment with GCs at a lower dose were identified as prognostic factors associated with poor response to initial therapy or recurrence in LE.

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AB0453 CORONARY ARTERY DISEASES IN PATIENTS WITH ANTIPHOSPHOLIPID ANTIBODY SYNDROME: A RETROSPECTIVE COHORT STUDY IN CHINA

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Background: Antiphospholipid syndrome (APS) is an autoimmune disorder caused by pathogenic antiphospholipid antibodies. Coronary artery disease as one of cardiac involvement of APS brings great challenges in clinical practice.
Objectives: To identify the key demographic, clinical, angiography features, risk factors, and prognosis of patients presenting with coronary artery diseases in APS.
Methods: We retrospectively analyzed patients who had been diagnosed with coronary artery disease induced by APS between January 1st, 2012 and June 30th, 2019, to study the clinical features, management, risk factors for prognosis, and long-term outcomes of patients.
Results: Twenty-eight patients (50% female) with APS and coronary artery diseases were included, with average age 46.9 ± 14.4 years. Arterial thrombosis events (78.6%, n=22) were more common than venous events (42.9%, n=12) in this cohort. Twelve patients had stable CAD, while 14 patients had acute coronary syndrome. The most affected arteries were the anterior descending (60.9%), right coronary (39.1%), and circumflex (30.4%). More RCA stenosis (63.6% vs 16.7%, p=0.036) were observed in the primary APS group than in the secondary APS. The age and disease duration of patients differed among groups and was lower in the triple aPL positive group than in double- and single-aPL positive groups, without significant differences among different CAD manifestations. Thrombocytopenia, elevated creatinine, and elevated urea were the risk factors for poor prognosis.
Conclusion: The coronary artery is an important target organ for APS. More RCA stenosis were observed in the primary APS group. APS-related CAD could endanger life and increase the mortality rate, with risk factors of thrombocytopenia, elevated creatinine, and elevated urea level. In addition to the routine use of anticoagulant and antiplatelet drugs, management of this group of patients is not well documented. The best treatment strategy still needs to be found and evaluated.

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Table 1. Coronary artery disease assessment of the patients

	Total	Types of APS		
		pAPS (n=13)	sAPS (n=15)	p
Coronary artery diseases				
sCAD (n, %)	12, 42.9	6, 46.2	6, 40.0	.743
UA (n, %)	2, 7.1	1, 7.7	1, 6.7	1.0
NSTEMI (n, %)	5, 17.9	4, 30.8	1, 6.7	.153
STEMI (n, %)	7, 25.0	2, 15.4	5, 33.3	.396
Other (n, %)	2, 7.1	0, 0	2, 13.3	.484
Coronary artery thrombosis	17, 60.7	8, 61.5	9, 60.0	.934
ECHO (n)	26	13	13	
LVEF (%)	52.2±15.0	46.8±12.0	57.6±15.7	.09
Segmental ventricular wall motion abnormality	21, 80.8	11, 84.6	10, 76.9	1.00
Diastolic dysfunction	11, 42.3	5, 38.4	6, 46.1	1.00
Ventricular enlargement	13, 50.0	7, 53.8	6, 46.1	1.00
Atrial enlargement	14,53.8	7, 53.4	7, 53.4	1.04
CAG or CTA performance (n)	23	11	12	
LM stenosis (n, %)	5, 21.7	3, 27.3	2, 16.7	.640
LAD stenosis (n, %)	14, 60.9	6, 54.5	8, 66.7	.680
LCX stenosis (n, %)	7, 30.4	3, 27.3	4, 33.3	1.00
RCA stenosis (n, %)	9, 39.1	7, 63.6	2, 16.7	.036
aneurysm (n, %)	1, 4.3	0, 0	1, 8.3	1.00

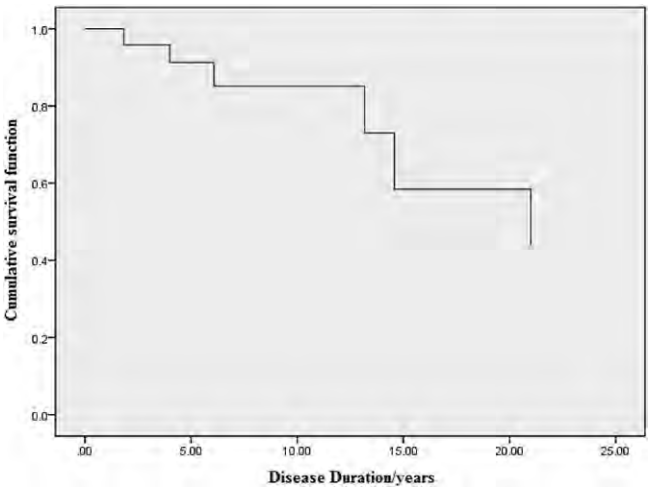


Figure 1. Cumulative survival function figure in APS patients with CAD

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AB0454

CHARACTERISTIC ULTRASOUND FEATURES OF SALIVARY GLAND LYMPHOMA IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

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Background: Lymphoma was one of the most severe complications of primary Sjögren's syndrome (pSS). Lymphomas often developed in organs where pSS is active, such as salivary glands. The enlargement of salivary glands is considered a predictive factor in previous studies. It is clarified that salivary gland ultrasound can visually and clearly demonstrate the parenchyma structure, which is a feasible method for SS diagnosis. However, there are no specific ultrasound features of salivary gland lymphoma and no early ultrasonic alarming system have been reported.
Objectives: To descript the characteristic ultrasound features and assess ultrasonic alarming value of salivary gland lymphoma in patients with pSS.
Methods: We followed a cohort of 63 patients with pSS from March 2017 to September 2019 and salivary gland ultrasound was performed every three months. All patients were examined by grey-scale and color Doppler ultrasound (US). The size, echostructure and vascularity of salivary glands were analyzed. US-guided core-needle biopsy (US-CNB) was used for the diagnosis of salivary gland lymphoma.
Results: In 63 patients with pSS, parotid enlargement occurred in 11 patients and none of them had submandibular gland enlargement. During the follow-up, 2 patients with parotid enlargement demonstrated recovery of size and echostructure improved. The remaining 9 patients had permanent parotid swelling and echostructure unchanged. US-CNB was performed in these 9 patients and histological and immunohistochemical findings of the cores suggested parotid lymphoma. Compared with other patients, these 9 patients revealed marked, permanent parotid enlargement of the unilateral or bilateral or asymmetric parotid. The parotid lymphoma ultrasonography was characterized by multiple, relatively large, well-demarcated hypoechoic (>6mm) with increased vascularity.
Conclusion: Ultrasonographic assessment of salivary gland helped to alarm the occurrence of lymphoma in pSS patients. Marked, permanent and asymmetric parotid enlargement with multiple, relatively large, well-demarcated hypoechoic in echostructure seemed to be characteristic for parotid lymphoma in pSS patients.
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AB0455

HEMATOLOGICAL PARAMETERS AS THE MARKERS OF DISEASE ACTIVITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: As the standard markers of systemic inflammation in autoimmune diseases erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are usually used, but in recent years there have been conflicting results about the potential significance of neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR).
Objectives: Our aim was to investigate the correlation of NLR and PLR with disease activity in patients with systemic lupus erythematosus (SLE).
Methods: The study involved 160 patients with SLE (145 women and 15 men), hospitalized in the Clinic of Rheumatology, Institute „Niška Banja", aged on the average 46.34 ± 10.82 years and with average disease duration of 9.76 ± 8.27 years, in whom the diagnosis was established based on the revised ACR criteria from 1997. In addition to clinical examination and supplementary tests, their disease activity was assessed using the *Systemic Lupus Erythematosus Disease Activity Index* (SLEDAI), together with determination of NLR and PLR.
Results: In SLE patients, there was a positive correlation of NLR with ESR (r=0.212; p=0.010), anti-dsDNA antibodies (r=0.185; p=0.025), and PLR (r=0.601; p<0.001), as well as a negative correlation with complement component 3 (C3) (r=-0.264; p=0.003). Further, there was a positive correlation of PLR with ESR (r=0.329; p<0.001), CRP (r=0.249; p=0.003), anti-dsDNA antibodies (r=0.280; p=0.001), anti-nucleosome antibodies (r=0.263; p=0.026), and values of urinary chemoattractant protein-1 (MCP1) (r=0.263; p=0.043), as well as a negative correlation with C3 (r=-0.276; p=0.002). Our univariate analysis demonstrated that not only the values of ESR, CRP, C3, anti-dsDNA, anti-nucleosome, anti-C1q antibodies, serum and urinary MCP1 (p<0.001) were statistically significantly associated with SLEDAI, but also the NLR (p<0.001) and PLR (p<0.001). Using the method of standard multiple regression analysis, we examined the impact of the above parameters on SLEDAI. The examined model accounted for 21.7% of variance in activity index (corrected r^2=0.217, F=2.525, p=0.017). As the statistically significant risk factors, ESR (Beta=0.394, p=0.020) and serum MCP1 (Beta=0.325, p=0.043) stood out.
Conclusion: NLR and PLR, as hematological parameters available in everyday clinical work, can be significant for disease activity assessment in SLE patients.
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Vasculitis

AB0456

ROLE OF CYTOKINES (INTERLEUKIN 17 AND 23) IN PSYCHIATRIC COMORBIDITIES ASSOCIATED WITH BECHET'S DISEASE

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Background: Behcet's disease (BD) is a chronic multi-systemic autoinflammatory disease associated with increase prevalence of psychiatric comorbidity **(Ilhan et al. 2016)**. Pro-inflammatory cytokines have been reported to be elevated in patients with depression and anxiety. IL-23/IL-17 axis has been shown to play a remarkable role in pathogenesis of BD, depression and anxiety **(Sugita et al. 2012, Gheita et al. 2015)**. However, the relation between the serum level of interleukin (IL)-17 and IL-23 and incidence of cognitive impairment, depression and anxiety in Behcet patients are still unknown.
Objectives: To evaluate the serum levels of IL-17 and IL-23 in Egyptian patients with BD and evaluate the correlations between the level of inflammatory cytokines and psychiatric manifestations as cognitive impairment, depression and anxiety.
Methods: Study design and recruitment
In a case control study, we recruited 45 BD patients, who fulfilled the modified International Criteria for Behçet's Disease **(ITR-ICBD 2014)** from the Rheumatology and Rehabilitation Department, Assiut University hospital. Thirty apparently healthy sex and age matched subjects were recruited, served as controls. This study was approved by the Ethical Committee of the Assiut University, Egypt. Informed consent was obtained from all participants.
Study methodology
All patients and controls were assessed for cognitive impairment, depression and anxiety using memory assessment scale, Hamilton depression rating scale and Hamilton anxiety rating scale respectively.

Serum level of proinflammatory cytokines such as IL-17 and IL-23 were measured by enzyme-linked immunosorbent assay (ELIZA).

Results: Psychiatric manifestations

BD has significant lower score in all components of MAS and high prevalence of depression and anxiety in HDRS and HARS respectively compared with control group (p <0.001). Severe depression was found in 82.9% of BD patients. Moreover, our data showed 46.7% of BD patients have moderate anxiety compared to the control group.

Serum Levels of IL-17 and IL-23

The serum level of IL-17 and IL-23 levels were significantly higher among BD patients than in healthy control (<0.000).

There was no significant correlation between those cytokines and cognitive impairment, depression and anxiety.

Conclusion: Elevated level of IL-17 and IL-23 were observed in BD patients. However, our results do not support an association between serum IL-17 and IL-23 levels and cognitive dysfunction, depression and anxiety.

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AB0457 OBSTETRICAL OUTCOME AND TREATMENTS DURING PREGNANCY IN SERONEGATIVE PRIMARY APS: DATA FROM EUROPEAN RETROSPECTIVE STUDY

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Background:

Objectives: To compare clinical characteristics, pregnancies, and treatments during pregnancies of seronegative and seropositive APS, and analyse factors associated with adverse obstetrical outcomes.

Methods: Inclusion criteria were: (1) thrombotic arterial and/or venous; and /or obstetrical primary clinical APS (Sydney criteria); (2) absence of conventional antiphospholipid antibodies; (3) presence of at least one non-conventional APL among IgA ACL, IgA antiB2GPI, anti-vimentin G/M, anti-annexin V G/M, anti-PE G/M, anti-PS/PT G/M antibodies. The exclusion criteria were: (1) seropositive APS with conventional APS; (2) associated SLE or SLE like (SLE features and / or positive antinuclear autoantibodies); (3) other systemic connective tissue disease (Sjogren's syndrome, systemic sclerosis, myositis).

Results: 187 women (mean 33±5 years) with seronegative APS were included from 12 centers in the world and compared to 285 patients with seropositive APS. Seronegative APS have mostly obstetrical phenotypes rather than venous thrombosis in comparison to seropositive APS. The maternal and fetal outcomes and the rates of live births were not significantly different in seronegative and seropositive APS, except for higher rates of intrauterine deaths (15% vs 5%; p=0.03) and lower live birth term (36±3 vs 38±3 weeks of gestation; p=0.04) in the seropositive APS group. The cumulative incidence of adverse obstetrical events was significantly improved in treated seronegative APS vs untreated ones (log rank<0.05), whereas there was no difference between patients who received aspirin or aspirin-LMWH combination

Conclusion: Patients with clinical manifestations of APS without conventional APL should undergo testing for non-criteria APL. The diagnosis of seronegative APS could be important for a better care of these patients.

Table 1. Characteristics of seronegative and seropositive APS women.

	Seronegative APS N=187	Seropositive APS N=285
APS features		
Thrombotic APS		
Arterial APS (n;%)	0	105 (37)*
Venous APS (n;%)	9 (6)	154 (54)*
Obstetrical APS (n;%)	168 (89)	89 (31)*
Mix APS (n;%)	8 (4)	16 (6)
Non criteria features (n;%)	16 (9)	141 (49)*
Obstetrical history		
Miscarriages (n;%)	66 (35)	18 (6)*
Intrauterine deaths (n;%)	60 (32)	46 (16)*
Prematurity <34 wg (n;%)	43 (23)	31 (11)*

Table 2. Pregnancy outcome and treatment in seronegative and seropositive APS.

	Seronegative APS pregnancies N=108	Seropositive APS pregnancies N=75
Thrombotic APS		
Arterial APS (n;%)	0	20 (27)*
Venous APS (n;%)	8 (7)	42 (56)*
Obstetrical APS (n;%)	93 (86)	36 (48)*
Mix APS (n;%)	6 (6)	18 (24)
Aspirin (n;%) / Aspirin alone	95 (88) / 32 (30)	57 (76)* / 2 (3)*
LMWH isocoagulant amounts (n;%)	63 (58)	39 (52)
Aspirin-LMWH (n;%)	65 (60)	55 (73)
Preeclampsia/HELLP syndrome (n;%)	7 (7)	12 (16)*
IUGR (n;%)	5 (5)	7 (10)
Fetal loss (n;%)	33 (31)	22 (29)
Miscarriage / Intrauterine deaths	23 (21) / 5 (5)	11 (15) / 11 (15)*
Prematurity<34 weeks of gestation (n;%)	6 (6)	9 (12)
Term of fetal loss (weeks gestation)	10±8	13±7
Live births (n;%)	75 (69)	53 (70)
Term of live birth (weeks gestation)	38±3	36±3*

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AB0458 SYSTEMIC TREATMENT IN BEHÇET'S DISEASE ACCORDING TO CLINICAL PHENOTYPES. STUDY OF 111 PATIENTS

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Background: Behçet's disease (BD) is a multisystemic vasculitis. Different clinical phenotypes can be distinguished. Systemic corticosteroids are the most used drugs in BD. Conventional and biological immunosuppressants (IS) may also be used.

Objectives: To evaluate the systemic treatment of BD according to clinical domains.

Methods: Study of all consecutive 111 patients diagnosed with definitive or possible BD by expert rheumatologists in a well-defined population of Northern Spain, between 1980 and 2019. Most of them met the International Criteria for BD (ICBD) (1).

Results: We studied 111 patients (62 women/49 men), mean age at diagnosis 36.8±13.2 years. After a mean follow-up of 81.4±85 months, all patients required systemic treatment (TABLE 1**-2).** Biological therapy (n=28) was indicated by ocular manifestations (n=13; 46.4%) persistent, severe and refractory oral ulcers (n=10, 35.7%), neurological (n=2; 7.1%), musculoskeletal (n=2; 7.1%) or cutaneous involvement (1; 3.6%). Adalimumab and Infliximab were the biological therapy more frequently used.

Conclusion: Most patients with BD required oral corticosteroids and colchicine. Almost half required conventional IS. Up to a third required biologic therapy, especially by ocular involvement. Most patients had clinical improvement.

References:

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AB0459 MORTALITY OF RHEUMATOID VASCULITIS AGGRAVATED BY CLINICALLY LATENT TUBERCULOSIS – A RETROSPECTIVE CLINICOPATHOLOGIC STUDY OF 161 AUTOPSY PATIENTS

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Background: Systemic vasculitis of autoimmune origin (e.g. rheumatoid vasculitis – RV) plays a pivotal role in the pathogenesis of rheumatoid arthritis (RA) [1]. RV may be characterized by *non-specific inflammation* (**nsRV**) with or without *fibrinoid necrosis* (**fnRV**) or by *granulomatous* transformation of blood vessels (**grRV**) [1].

The prevalence and mortality of tuberculosis (**TB**) is higher in rheumatoid arthritis (**RA**) than in the general population.

Objectives: The aim of this study was to assess the influence of dormant (inactive), clinically latentTB (with or without subclinical atypical miliary exacerbation) on the mortality of rheumatoid vasculisit (RV).

Methods: At the National Institute of Rheumatology **9475** patients died between 1969 and 1992; among them **161** with **RA** and all of them were autopsied [1].

RA was confirmed clinically according to the criteria of the **ARA**.

nsRV alone or in combination with **fnRV** or **grRV** was diagnosed at autopsy, and confirmed by a detailed review of extensive histological material [1].

The prevalence fibrous (**fTB)**, fibrocaseous (**fcTB)** or miliary **TB** (mTB) was diagnosed and characterized histologically, reviewing retrospectively the clinical and pathological reports [1].

From each patient a total of 50-100 tissue blocks of 12 organs (heart, lung, liver, spleen, kidneys, pancreas, gastrointestinal tract, adrenal glands, skeletal muscle, peripheral nerve, skin and brain) were studied microscopically.

The possible role of **fTB**, **fcTB** or mTB on the mortality due to **nsRV**, **fnRV** or **grRV** was analyzed with Pearson's chi-squared (χ^2) test.

Results: nsRV complicated **RA** in **33** (**20.49%**) of 161 patients, in combination with **fnRV** in **17** (**51.51** %) or with **grRV** in **10** (**30.30** %) of 33 cases.

The **nsRV** led to death in **19** (**57.57** %) of 33 patients, in combination with **fnRV** in **11** (**64.71**% of 17) or with **grRV** in **7** (**70.0** % of 10) cases; the mortality due to **nsRV**, **fnRV** or **grRV** showed an increasing tendency.

Post-primary **TB** was associated with **RA** in **21** (**13.04%**) of 161 patients, **12** (57.14% of 21) were **fTB**, and **9** (42.86% of 21) **fcTB**. **One** of 12 **fTB** and **5** of 9 **fcTB** were complicated with discrete miliary dissemination (**mTB**) in **6** (3.7% of 161; 28.57% of 21) **RA** patients.

TB (n=21) was associated with **fatal nsRV** in **5**, with **fnRV** in **3**, with **grRV** in **3** of 21 cases.

The **fTB** (n=12) was associated with **fatal nsRV** in **1**, with **fnRV** in **1**, with **grTB** in **1** of 12 cases.

The **fcTB** (n=9) was associated with **fatal nsRV** in **4**, with **fnRV** in **3**, with **grTB** in **3** of 9 cases.

mTB (n=6) was associated with **fatal nsRV** in **3**, with **fnRV** in **2**, with **grTB** in **3** of 6 cases.

There was a significant and positive correlation between **fcTB** and **mortality** of **nsRV** (c: 0.76, χ^2**=9.7593**, **p<0.0017**), between **fcTB** and **mortality** of **fnRV** (c: 0.80, χ^2**=6.5701**, **p<0.0103**), between **fcTB** and **mortality** of **grRV** (c: 0.90, χ^2**=12.5835**, **p<0.00038**), The correlation was also positive and significant between **mTB** and **mortality** of **nsRV** (c: 0.79, χ^2**=5.3406**, **p<0.0208**), between **mTB** and **mortality** of **grRV** (c: 0.95, χ^2**=20.8706**, **p<0.0000049**),

The relationships were not significant between **TB** or **fTB** and **mortality** of **nsRV**, **fnRV** or **grRV**, nor between **mTB** and **mortality** of **fnRV**.

Conclusion: Recognition of indolent **TB** is a great challenge especially before starting immunosuppressive or biological therapy for **RA**.

TB may lead directly to death by arrosion of pulmonary arteries with massive pulmonary bleeding, by hematogenous miliary dissemination (Landouzy typhobacillos) or by canalicular spread as a cavernous chronic process (phthisis tuberculosa), etc. Discrete miliary dissemination may be also lethal caused by circulatory failure [1].

The contribution of **TB** to the mortality of complications of **RA** or of allied disorders is plausible and can never be excluded.

According to our data the risk of mortality due to **nsRV**, **fnRV** or **grRV** showed an increasing tendency, and **fnRV** or **grRV** should be regarded the most severe forms of **nsRV** in **RA**.

The positive and significant correlation between **fcTB** or **mTB** and **mortality** of **nsRV**, **fnRV** or **grRV** represents a positive contribution to the fatal outcome due to **nsRV**, **fnRV** or **grRV**.

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AB0460 INTERLEUKIN-6 INHIBITION WITH TOCILIZUMAB FOR THE TREATMENT OF GIANT CELL ARTERITIS AND POLYMYALGIA RHEUMATICA IN PATIENTS WITH SERIOUS COMORBIDITIES

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TABLE.

CLÍNICAL PHENOTYPES	Cases N (%)	COLCH	COS	Dosis total IS	AZA	MTX	CYA	MMF	TLD	APR	DAP
Oral ulcers	110 (99.1)	85 (77.9)	81 (73.6)	51 (46.4)	30 (27.3)	25 (22.7)	14 (12.7)	2 (1.8)	6 (5.5)	6 (5.5)	3 (2.7)
Genital ulcers	69 (62.2)	56 (81.2)	51 (74)	32 (46.4)	17 (24.6)	16 (23.2)	10 (14.5)	1 (1.5)	5 (7.2)	2 (3.4)	3 (4.3)
Cutaneous lesions	76 (68.5)	58 (76.3)	61 (80.3)	52 (68.4)	32 (42.1)	22 (29)	9 (11.8)	0	5 (6.6)	6 (7.9)	3 (4)
Ocular manifestations	39 (35.1)	27 (69.2)	36 (92.3)	19 (48.7)	17 (43.6)	12 (30.8)	11 (28.2)	2 (5.1)	4 (10.3)	2 (5.1)	2 (5.1)
Neurological involvement	20 (18)	12 (60)	15 (75)	15 (75)	3 (15)	4 (20)	3 (15)	1 (5)	0	0	1 (5)
Vascular manifestations	11 (10)	8 (72.7)	9 (81.8)	5 (45.5)	3 (27.3)	3 (27.3)	1 (9.1)	0	0	0	0
Gastrointestinal involvement	4 (3.6)	2 (50)	1 (25)	1 (25)	1 (25)	0	0	0	0	0	0
TOTAL	111	85 (76.6)	85 (76.6)	51 (46)	30 (27)	25 (22.5)	14 (12.6)	2 (1.8)	6 (5.4)	6 (5.4)	3 (2.7)

TABLE 2.

CLINICAL PHENOTYPES	BT	ADA	IFX	ETN	TCZ	No improvement	Partial improvement	Complete response
Oral ulcers	28 (35.5)	22 (20)	12 (11)	3 (2.7)	2 (1.8)	22 (20)	22 (20)	66 (60)
Genital ulcers	17 (24.7)	13 (18.8)	8 (11.6)	2 (2.9)	1 (1.4)	16 (23.2)	12 (17.4)	41 (59.4)
Cutaneous lesions	21 (27.6)	18 (23.7)	8 (10.5)	3 (4)	2 (2.6)	8 (10.5)	19 (25)	49 (64.5)
Ocular manifestations	19 (50)	16 (42.1)	9 (23.7)	1 (2.6)	2 (5.3)	0	8(21)	30 (79)
Neurological involvement	7 (35)	2 (10)	4 (20)	1 (5)	0	3 (15)	5 (25)	12 (60)
Vascular manifestations	4 (36.4)	3 (27.3)	2 (18.2)	1 (9.1)	1 (9.1)	2 (18.2)	4(36.4)	5 (45.5)
Gastrointestinal involvement	0	0	0	0	0	1 (25)	1 (25)	2 (50)
TOTAL	28 (25.2)	22 (19.8)	12 (10.8)	3 (2.7)	2 (1.8)	22 (19.8)	22 (19.8)	67 (60.4)

Abbreviations: COLCH: Colchicine; OCS: Oral Corticosteroids; IS: Immunosuppressants; AZA: Azathioprine; MTX: Methotrexate; CYA: Cyclosporine A; MMF: Mycophenolate Mofetil; TLD: Talidomide; APR: Apremilast; DAP: Dapsone; BT: Biologic Therapy; ADA: Adalimumab; IFX: Infliximab; ETN: Etanercept; TCZ: Tocilizumab

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Background: Giant cell arteritis (GCA) and polymyalgia rheumatica (PMR) are closely related inflammatory conditions affecting people aged over 50 years.
Objectives: We present our experience of using tocilizumab (TCZ) therapy for management of GCA/PMR aggravated by severe concurrent pathologies that potentially increase the risk of side effects of glucocorticoids (GCs).
Methods: 22 patients were recruited into the prospective study: six patients with GCA, 13- PMR, and three- with both GCA and PMR, 95.5% were females, mean age 72.8±6.5 years. Mean disease duration was 3.5 (0.5-19) months. All patients had active GCA/PMR with mean CRP 30.3±32.7 mg/l. Seven patients had visual ischemic complications, and another one- aortitis. All patients had serious comorbidities, 59% of patients had three and more severe concurrent diseases. All patients were administered TCZ i/v 2.3-8.8 mg/kg Q4W. 50% patients were also treated with prednisone at mean 20 (10-70) mg/day. The follow-up period was 24 (6-60) months.
Results: All patients demonstrated good clinical response to TCZ i/v 2.3-8.8 mg/kg Q4W given for average 4,5 (2-11) months, achieving remission in 100% of cases. Some patients showed a very rapid improvement after initiation of treatment, including TCZ monotherapy. Prednisone dose was discontinued in 6/11, or was reduced to 2.5 (2.5-10) mg in 4/11. There was one relapse after TCZ discontinuation, although this patient managed to regain the remission after resumption of TCZ i/v 4 mg/kg. There was one (4.6%) serious complication (septic olecranon bursitis 1 month after TCZ discontinuation), one patient died of myocardial infarction 12 months later after TCZ discontinuation. Three remaining complications included one case of peripheral artery disease (claudication), one- psoriasis, and one- sural lipodermatosclerosis.
Conclusion: Interleukin-6 inhibitors should be considered as potentially effective and relatively safe treatment for GCA/PMR patients with serious comorbidities, intolerance or contraindications to standard therapy. More data is necessary to identify the optimal dosing regimen and duration of TCZ therapy, as well as cost-effectiveness aspects.
Disclosure of Interests: None declared
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AB0461 ANCA-ASSOCIATED VASCULITIS: CLINICAL FEATURES, RELAPSE, ORGAN DAMAGE AND SURVIVAL IN 197 PATIENTS

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Background: ANCA-associated vasculitis (AAV) is a multisystemic autoimmune disease with high mortality and morbidity.
Objectives: We aimed to present the long-term follow-up results of our cohort.
Methods: Data of patients who fulfilled Chapell Hill Consensus Criteria and followed up at least 6 months between 1999-2019 were analyzed. A standard form including vasculitis damage index (VDI) was used. Multivariable analysis was performed by using logistic regression.
Results: Long-term data was available for 197 patients (%53.8 female) from 208 patient records. Mean age at diagnosis was 49.4 years and mean follow-up was 80.7 months. Granulomatosis with polyangiitis (GPA); microscopic polyangiitis (MPA), eosinophilic GPA (EGPA) were 117 (64.5%), 52 (26.4%), 17 (8.6%), respectively. Relapses are observed in 31.6% of patients. Disease relapses were higher in GPA compared to MPA and EGPA (p = 0.014). Relapse rate was higher in patients with *s.aureus* carriage (p = 0.037). Cyclophosphamide (CYC) (76.6%) was most commonly used drug for induction, whereas azathioprine (57.3%) was used mostly in maintenance. In multivariate analysis relapse was found to be associated with maintenance treatment with rituximab (p <0.001), venous thrombosis (p=0.046) and serious infection (p<0.004). There was no significant association between relapse and mortality. Five-year survival rates were 98.5% for GPA, 88.5% for MPA and 100% for EGPA. Nineteen patients died during follow-up (9.6%). In univariate analysis mortality were high in MPA patients. Low hemoglobin and increased creatinine at baseline, subglottic stenosis, polyneuropathy, and cerebrovascular events (CVE) were associated with increased mortality. In multivariable analysis, mortality was associated with CVE (p=0.047) and anti-MPO positivity (p=0.014). Malignancy was developed in 9 patients (M / F: 7/2; two lung, three bladder, one cervix, one thyroid papillary, one kidney and one of unknown primary). There was no association between malignancy and cumulative dose of CYC. Venous thromboembolism was developed in 12 (6 %) and avascular necrosis (AVN) was detected in 30 patients (15.4%). Most (88.7%) patients developed damage during follow-up. Mean VDI score was 2.6 and VDI score was found to be higher in GPA (p= 0.035). There was no association between VDI score and mortality.
Conclusion: In our AAV cohort, GPA was most frequent. Although survival was improved, permanent organ damage was detected in the majority of patients. Relapse and organ damage were found to be increased in patients with GPA. Relapses are frequent and maintenance with rituximab could not prevent relapses. Also relapses were associated with venous thrombosis and severe infections. Patients should be screened for malignancies especially of the genitourinary tract.

Table 2. Damage findings of AAV patients according to VDI

Organ/system	Number(%)
Steroid myopathy	23 (%11.7)
Osteoporosis	31 (%15.9)
AVN	30 (%15.4)
Cataract	30 (%15.4)
Partial loss of vision	6 (%3.1)
Blindness (one eye)	2 (%1)
Subglottic stenosis	9 (%4.5)
Hearing loss	18 (%9.1)
Nasal septum perforation	21 (%10,7)
Chronic nasal crusting	9 (%4,6)
Chronic ashtma	28 (%14,2)
Chronic dispnea	1 (%0,5)
Hypertension	60 (%30,5)
Coronary artery disease / Angioplasty	10 (%5,1)
Cardiomyopathy	6 (%3)
Valvular heart disease	5 (%2,5)
Myocardial infarction	7 (%3,6)
Deep vein thrombosis	12 (%6)
Chronic renal failure (GFR <50 ml/min)	51 (%26)
End stage renal disease	22 (%10.8)
Cerebrovascular accident	9 (%4,4)
Peripheric neuropathy	39 (%19.8)
Malignancy	9 (%4.5)
Diabetes mellitus	24 (%12.2)
Gonadal failure	2 (%1)

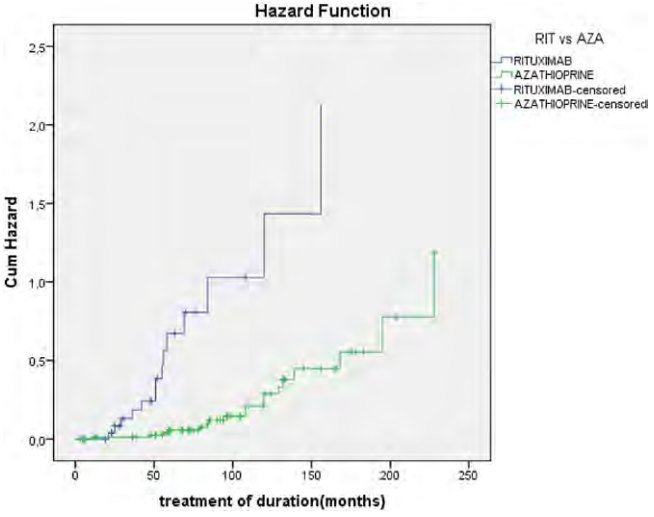


Figure 3. Cumulative Relapse Rate: Hazard ratio of patients treated with Rituximab versus Azathioprine (Log Rank: p<0.001)

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AB0462 BEHCET'S DISEASE: CLINICAL FEATURES AND OFF-LABEL BIOLOGIC TREATMENT STRATEGIES

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Background: The treatment of Behçet's disease (BD) is still mainly based on the evidence derived from case reports, case series, retrospective analyses, and few clinical trials suggesting the safety and potential efficacy of off-label use of biologic agents in refractory cases. [1]
Objectives: To describe clinical manifestations and their management, with particular focus on treatment indications, outcomes and safety of biologic therapy, in a cohort of patients with BD.

Methods: Patients with a diagnosis of BD who visited our outpatient clinic until December 2019 were included in the study. Clinical data were recorded since diagnosis until the latest follow-up visit, analyzing clinical features, flares and therapeutic strategies adopted.
Results: A total of 95 patients were included in the study with a medium follow-up of 108.54 ± 169.59 months. 20 of them (21. 05%) were treated with biologic agents. Patients treated with biologic therapy compared to those on conventional non-biologic therapies had a higher proportion of musculoskeletal (80% vs 46.67%, p = 0.008), neurological (30% vs 10.67%, p = 0.031), intestinal involvement (40% vs 12%, p = 0.004), and they were treated with a higher dose of glucocorticoids at diagnosis (16.84 mg ±14.01 vs 8.89 mg ± 11.76, p = 0.012). The most frequent indications for biologic step-up therapy were musculoskeletal involvement (40%), eye involvement (25%), neurological involvement (15%) and intestinal involvement (10%). Most patients initiated a biologic treatment within the first year of follow-up. TNF-inhibitor (TNFi) were more frequently prescribed (95%) and one patient was treated with 8 therapeutic cycles of Rituximab (500 mg/weekly for 4 infusions to be repeated after at least 6 months) because of recurrent pancytopenia. All patients experienced non-biologic therapy before starting a TNFi. The preferred first-line TNFi was infliximab (50%), followed by adalimumab (40%) and etanercept (5%). As second line treatment were also prescribed certolizumab (10%) and golimumab (5%). 10 patients switched to a second line treatment because of inefficacy of the first biologic agent, mainly because of refractory arthritis, intestinal and mucocutaneous involvement. One patient switched from infliximab to certolizumab during pregnancy with subsequent worsening of arthritis.
85% of patients treated with biologic agents reached a clinical remission by the time of the latest follow up visit without any safety or tolerability issues.
Conclusion: A relevant proportion of patients in our BD cohort were treated with biologic therapy, because of severe or refractory manifestations. The most frequent indications were musculoskeletal, neurological or intestinal involvement. Biologic agents were a generally effective and safe therapeutic approach.
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Table 1. General characteristics and disease involvement at diagnosis

	Biologic therapy		No biologic therapy		p value
	20 (21.05%)		75 (78.95%)		
General characteristics	**Media**	**SD**	**Media**	**SD**	
Age at disease onset (years ± SD)	34.5	± 10.49	38.64	± 13.18	p = 0.1976
Diagnostic delay (months ± SD)	45.28	± 67.48	28.09	± 48.42	p = 0.1996
Glucocorticoids at diagnosis (mg prednisone ± SD)	16.84	± 14.01	8.89	± 11.76	**p = 0.0115**
Glucocorticoids at latest follow up visit (mg prednisone ± SD)	6.38	± 7.76	3.83	± 4.81	p = 0.0707
	N	**%**	**N**	**%**	
F / M	12 / 8	60 / 40	54 / 41	72 / 28	p = 0.3030
Disease involvement at diagnosis					
Oral ulcers	20	100	75	100	
Genital ulcers	11	55	37	49,33	p = 0.6540
Cutaneous lesions	15	75	50	66,67	p = 0.4787
Eye involvement	6	30	27	36	p = 0.6184
Musculoskeletal involvement	16	80	35	46,67	**p = 0.0082**
Neurological involvement	6	30	8	10,67	**p = 0.0311**
Intestinal involvement	8	40	9	12	**p = 0.0039**
Thrombosis	2	10	18	24	p = 0.1747

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AB0463 ETIOLOGY OF PALPABLE PURPURA; A SINGLE CENTER EXPERIENCE

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Background: Purpura are lesions that occur after bleeding on the skin, mucous or serosal surfaces. Purpura can be classified into 2 subgroups; which are linked to thrombocytopenia and non-trombocytopenic purpura. While thrombocytopenic purpura often occurs due to a hematological disease; in non-trombocytopenic purpura etiological causes are very variable, and systemic vasculitis has an important place among them.
Objectives: The demographic features of the patients applying with purpura and the underlying causes and diseases were aimed to be revealed.
Methods: 44 consecutive patients (22 women, 22 men) who were admitted to the hospital in the last 6 months, due to purpura were evaluated. Average age of patients was 49.6 ± 19.6 years. Patients were questioned about a recent infection, drug use, concomitant or underlying diseases. The serological tests and other laboratory tests for etiology were performed and biopsy was taken from the skin lesions which are appropriate.
Results: While 4 (9%) patients had widespread purpura on the trunk-upper-lower extremities, in 22 (50%) patients purpuric lesions were limited only to the lower limb. The period between the onset of the first symptom and the admission to the hospital was longer than 4 weeks in 35 (79.5%) patients, and shorter than 1 week in 9 (20.5%) patients. 24 (54%) patients had an anamnesis of infection 2-3 weeks before purpura, and 20 (45%) patients had an anamnesis of drug use. The most common accompanying symptom was abdominal pain and was present in 15 (34%) patients. Biopsy was performed from the skin lesion in 37 patients. Histopathological examination of all was compatible with leukocytoclastic vasculitis. In indirect immunofluorescence staining, 17 were found to be IgA positive. 2 (4.5%) patients were diagnosed PR3-ANCA positive granulomatosis with polyangiitis. 1 patient had Hepatitis B virus infection was detected in 1 patient (2.2%), HIV infection was detected in 1 patient (2.2%) and malignancy was detected in 1 patient (2.2%).
Conclusion: In our study, the most common reason was found as IgA vasculitis in patients presenting with palpable purpura. Although vasculitic involvement was limited to the skin in most patients, organ-threatening systemic vasculitis was detected in a few patients. Patients applying with Purpura should be questioned for infection and drug use, should be examined for underlying diseases including systemic vasculitis, and closely monitored for organ involvement.
Disclosure of Interests: None declared
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AB0464 THE ROLE OF CYCLOPHOSPHAMIDE CHEMOTHERAPY IN THE TREATMENT OF EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS

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Background: Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare type of ANCA associated Vasculitis (AAVs). Cyclophosphamide (CYC) is generally recommended for the induction of remission in life/organ threatening AAVs in combination with glucocorticoids. However, due to its rarity, randomized controlled trials regarding the efficacy of treatment modalities in EGPA are hard to perform. Therefore, the level of evidence for the use of CYC in the treatment of EGPA is lower when compared to other AAVs (1).
Objectives: The aim of this study is to investigate common therapeutic agents used for the treatment of patients with EGPA.
Methods: Medical records of patients who were followed-up with the diagnosis of EGPA between 2007-2020, in rheumatology clinics of Ankara and Adana Hospitals of Başkent University, were analyzed retrospectively. Treatment outcomes were assessed.
Results: Records of 11 patients (six females) were analyzed. The median age was 47 (19-77) years. The median follow-up time of the patients was 24 (9-156) months. Six patients were diagnosed with asthma. The median time between the diagnosis of asthma and EGPA was 4.5 (1-3) years. Five patients had tissue biopsies. Biopsy locations were terminal ileum, lung, myocardium and nerve. The most common forms of involvement were asthma, eosinophilic pneumonia and / or nodule, cardiovascular involvement, mononoritis multiplex, vasculitic skin rash, arthritis and bowel involvement, respectively. P-ANCA was positive in 8 patients. Three patients had myocarditis and cardiomyopathy, and two patients had isolated valve problems. The median BVAS value at the time of diagnosis and the third month of treatment was 17 (6-27) and 4 (2-7), respectively.
Nine patients used oral 1mg/ kg methylprednisolone (MP) and 500mg CYC every two weeks as an induction therapy. The cumulative median CYC dose was 4.5 g (1.5-8). Neither of the patients developed CYC related side effects. MP was tapered to 2 mg in five patients, and was quited in two patients. Azathioprine (AZA) was used in remission treatment following CYC therapy. Rituximab (RTX) therapy 1 g twice, 2 weeks apart was initiated in two patients due to unresponsiveness to CYC. While RTX was effective in one patient, newly developed renal involvement was detected after the third cycle of RTX therapy in other patient. Two patients had pregnancy plan therefore they used AZA plus MP as induction. A patient had mycophenolate mofetil plus MP due to AZA allergy. All patients are currently in remission except one patient.
Conclusion: In seven out of 11 EGPA patients, long-term remission was achieved with CYC treatment. CYC appears to be an effective and inexpensive method of first-line treatment for organ threatening EGPA.

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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.6481

AB0465 ANALYSIS OF VASCULITIS PATTERNS IN PATIENTS WITH GIANT CELL ARTERITIS COMPARED TO PATIENTS WITH GIANT CELL ARTERITIS AND POLYMYALGIA RHEUMATICA

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Background: Giant cell arteritis (GCA) and polymyalgia rheumatica (PMR) often coexist.[1] The role of modern ultrasound in diagnosis of GCA as well as PMR is well known.[2] To date it is unknown, whether patients with GCA and PMR have a different vasculitis pattern in ultrasound (US) examination than patients with GCA only.
Objectives: To prospectively identify differences in vasculitis patterns in consecutive patients with newly diagnosed GCA and PMR compared to newly diagnosed GCA patients without PMR.
Methods: US examination of the arteries typically affected in GCA, such as axillary arteries, vertebral arteries, superficial temporal arteries with both frontal and parietal branches and facial arteries was performed in patients with GCA and PMR (GCA-PMR-group) as well as in patients with GCA only (GCA-group) at time of first diagnosis. Arteries were defined as pathological, if measured intima-media-thickness by US was above respective cut-off values.[3]
Results: The GCA-PMR-group consisted of 27 patients, the GCA-group of 18 patients. In the GCA-PMR-group, a total of 206 arteries were affected, while in the GCA-group 131 arteries were affected. Mean age and gender distribution was 74 years (SD± 9) with 10 (37%) females in the GCA-PMR-group and 76 years (SD± 9) with 10 (55%) females in the GCA-group. Median values of C-reactive protein (CRP) were 57.2 (IQR 31.7-75.7) in the GCA-group and 48.3 (IQR 17.5-79.9) in the GCA-PMR-group, no significance was observed (p= 0.3577). Mean number of affected arteries per patient was 7.63 and 7.28 in the GCA-PMR-group and GCA-group, respectively. Altogether, no significant difference in vascular pattern between the two groups was observed. Exact numbers, distribution and IMT-values for all measured arteries are depicted in table 1.

Table. Prevalence of vasculitic affection of respective arteries in patients with giant cell arteritis and polymyalgia rheumatica and patients with giant cell arteritis only.

Affected artery	Group					
	PMR-GCA-group (n=27)			GCA-group (n=18)		
	Unilateral	Bilateral	None	Unilateral	Bilateral	none
Axillary artery	9 (33%)	12 (45%)	6 (22%)	5 (28%)	7 (39%)	6 (33%)
Common superficial temporal artery	3 (11%)	21 (78%)	3 (11%)	5 (28%)	13 (72%)	0 (0%)
Frontal branch	6 (22%)	17 (63%)	4 (15%)	3 (17%)	11 (61%)	4 (22%)
Parietal branch	5 (18%)	21 (78%)	1 (4%)	3 (17%)	13 (72%)	2 (11%)
Facial artery	7 (26%)	17 (63%)	3 (11%)	4 (22%)	11 (61%)	3 (17%)

PMR-GCA-group: patients with diagnosis of giant cell arteritis and consecutive polymyalgia rheumatica
GCA-group: patients with diagnosis of giant cell arteritis only

Conclusion: In our cohort, we did not observe a significant difference in vascular patterns between patients with GCA and PMR and GCA only patients.

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[3]Schäfer VS, Juche A, Ramiro S, Krause A, Schmidt WA. Ultrasound cut-off values for intima-media thickness of temporal, facial and axillary arteries in giant cell arteritis. Rheumatology (Oxford) 2017;56:1479–83.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.5469

AB0466 EFFICACY AND SAFETY OF INFLIXIMAB-BIOSIMILAR IN TAKAYASU ARTERITIS (TAKASIM): A MONOCENTRIC, OBSERVATIONAL, PROSPECTIVE, OPEN-LABEL STUDY

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Background: Treatment of Takayasu arteritis (TA) is mainly based on steroids, but, in approximately 50% of patients, disease-modifying antirheumatic drugs(DMARDs) are required.
Objectives: To evaluate efficacy and safety of IFX-biosimilar in TA patients.
Methods: Both bDMARD-naïve and IFX-O treated patients were eligible. Primary endpoint was the number of patients with active disease as assessed by magnetic resonance angiography(MRA), 18FDG PET/CT, ITAS2010 and ITAS-ESR/CRP at month 6. Secondary endpoints were safety and tolerability, number of patients with active disease at month 12, quality of life. Non-parametric statistic tests were used.
Results: Twenty-three patients(21 female) were recruited. At baseline, mean age was 43.8±14.4 years and mean disease duration 95.5±61.3months. Two patients were IFX-O-naïve. Mean time on IFX-O was 51.5±37.9 months. Four patients had been previously treated with other biologics(tocilizumab, 3; adalimumab, 1). Twenty-one patients(91.3%) were on concomitant steroids(mean dose, 4.8±2.0 mg daily) and 82% on concomitant csDMARDs, kept unchanged throughout the study. At baseline, 4 patients(17%) were classified as active according to ITAS2010, ITAS-ESR, and ITAS-CRP; mean HAQ was 3.48±5.26. Over the study period two patients dropped out the study because of poor disease control (1 at month 3 and 1 at month 6). PET/CT was not available for one patient who was on lactation during the study period and 1 patient refused to undergo imaging re-evaluation. At month 6, MRA was available for 21 patients: it was stable in 11(52%), improved in 5(24%), worsened in 5(24%). PET/CT was available for 20 patients: it was negative in 12(65%), improved although still positive in 3(16%), stable in 1(5%), worsened in 3(16%). At month 6, among 22 patients, 4(18%) were clinically active according to ITAS2010, ITAS-ESR and ITAS-CRP; mean steroid dose was significantly lower compared to baseline(4.2±2.0 mg daily, p=0.009); HAQ didn't significantly change(mean, 3.35±6.59, p=0.357). At month 12, MRA was available for 20 patients. It was stable in 9 patients(45%), improved in 8 (40%), worsened in 3(15%). PET/CT was available for 19 patients: it was negative in 14(74%), improved although still positive in 2(10%), stable in 3(10%), worsened in 1(5%). At month 12, 3 patients(14%) were active according to ITAS2010 and 2(9%) according to ITAS-ESR and ITAS-CRP; mean steroid dose was significantly lower compared to baseline(3.4±2.56 mg daily, p=0.034); HAQ didn't significantly change(mean, 3.84±6.34, p=0.919). Nine patients(39%) experienced low-grade side effects related to TNFα-blockade (6, herpes reactivation; 3, urinary tract infection; 1 gastroenteritis). No IFX-B therapy modification was required.
Conclusion: Our study suggests that IFX-B is effective and safe both in IFX-O switch and IFX-O naïve TA patients.
Disclosure of Interests: : Corrado Campochiaro Speakers bureau: Novartis, Pfizer, Roche, GSK, SOBI, Alessandro Tomelleri: None declared, Silvia Sartorelli: None declared, Giacomo De Luca Speakers bureau: SOBI, Novartis, Celgene, Pfizer, MSD, Camilla Sembenini: None declared, Giulio Cavalli Speakers bureau: SOBI, Novartis, Pfizer, Paola Mapelli: None declared, Maria Picchio: None declared, Maurizio Papa: None declared, Elena Baldissera Speakers bureau: Novartis, Pfizer, Roche, Alpha Sigma, Sanofi, Lorenzo Dagna Grant/research support from: Abbvie, BMS, Celgene, Janssen, MSD, Mundipharma Pharmaceuticals, Novartis, Pfizer, Roche, SG, SOBI, Consultant of: Abbvie, Amgen, Biogen, BMS, Celltrion, Novartis, Pfizer, Roche, SG, and SOBI
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AB0467 REMISSION AND LOW DISEASE ACTIVITY STATE IN PATIENTS WITH GRANULOMATOSIS WITH POLYANGIITIS AND MICROSCOPIC POLYANGIITIS: PREVALENCE AND IMPACT ON DAMAGE ACCRUAL

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Background: Granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA) require glucocorticoids (GCs) and immunosuppressants (IS) to induce and maintain remission. At the era of highly active drugs and treat-to-target strategies, defining the goal to achieve in terms of remission could be beneficial for the long-term management.
Objectives: To assess the impact of prolonged remission or low disease activity state (LDAS) in GPA and MPA patients and its relationship with damage accrual.
Methods: Patients diagnosed with GPA and MPA, according to ACR criteria and/or Chapel Hill definitions, seen in two vasculitis centers and followed-up for ≥5 years were included. Disease activity was assessed by BVAS, and damage accrual by the VDI. Three levels of remission were defined: complete remission (CR): BVAS=0 and negative ANCA in GCs-free and IS-free patients; clinical remission off therapy: no disease activity and positive ANCA in GCs-free and IS-free patients; clinical remission on therapy: no disease activity in patients with low dose GCs (≤5 mg/d) and/or IS. LDAS was defined as 0<BVAS≤3 without major organ activity, no new disease activity, low-dose GCs (≤7.5 mg/day) and well-tolerated IS. We defined remission or LDAS as prolonged when lasting ≥2 consecutive years. The effect of prolonged remission and LDAS on damage accrual was evaluated.
Results: 167 patients were included: 128 (76.6%) GPA, mean age 51.0±16.7 years. At 5-years, mean VDI was 2.7±2.0, mainly because of AAV-related items (2.0±1.7) rather than treatment-related items (0.7±1.0). During the 5-year follow-up, 10 (6.0%) patients achieved prolonged CR, 6 (3.6%) prolonged clinical remission off therapy, 89 (53.3%) prolonged clinical remission on therapy, 42 (25.1%) prolonged LDAS and 20 (12.0%) never achieved LDAS. Damage accrual at 5-years in patients with prolonged CR, clinical remission off therapy, clinical remission on therapy, LDAS or those never achieved LDAS was 1.6±1.1, 1.8±1.7, 2.3±1.9, 3.8±2.0 and 3.3±2.0, respectively (P<0.0001). Damage was comparable between patients in prolonged remission off therapy and those in remission on therapy (P=0.3). In contrast, patients in prolonged LDAS or those never in LDAS had significantly more damage accrual (P<0.0001 and P=0.01, respectively) than those in prolonged remission off therapy. Eighty-one patients (49%) reached a VDI ≥3 at 5-years. The inability to achieve prolonged remission was associated with a VDI ≥3 at 5-years (OR 5.07, 95% CI 2.53-9.84, P<0.0001), and considering only prolonged CR or clinical remission off therapy did not had any benefit on damage accrual. In contrast, achieving prolonged LDAS had no benefit compared to spending no time in LDAS (P>0.99). Compared to patients achieving prolonged remission, those not able to achieve prolonged remission were younger (46±16.0 vs. 53.5±16.6, P=0.001), had more frequent GPA (P=0.0003), had more PR3-ANCA (P=0.006), had more ENT and lung involvement (P<0.0001 and P=0.036, respectively).
Conclusion: Sixty percent of GPA and MPA patients achieved prolonged remission, which was associated with a better outcome in terms of damage accrual. In contrast, prolonged LDAS was associated with increased damage and was not a sufficient target to achieve in GPA and MPA.
Disclosure of Interests: : None declared
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AB0468 AGE RELATED DIFFERENCES IN PATIENTS WITH GIANT CELL ARTERITIS

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Background: Few data are available on the epidemiology and management of giant cell arteritis (GCA) in patients over 75 years despite the progressive aging in our societies. In other diseases this subgroup of patients presents important differences in the management and prognosis of their pathologies.
Objectives: To explore this situation by comparing two subgroups of patients, older and younger than 75, assesing possible changes in demographic characteristics, diagnostic tests, treatment and outcome.
Methods: We perform a retrospective review of charts, laboratory data, image studies, treatment and outcome of biopsy-proven GCA in our institution (Complejo Hospitalario Universitario de Vigo) between 1 January 2000 and 30 November 2019.
Results: During study period 124 patients were analysed, 51 in the subgroup of <75 (mean age 64.6 (56-75)) and 73 in the subgroup of >75 (mean age 81.8 (76-89)). There were no differences about sex (female 76.6% vs. 65%) or in the Charlson index between the two groups (0-1 in 72% of patients). Older patients present more frequently with headache (49.2 % vs 32.3%), polymyalgia rheumatica (53.4 % vs 45.1%), weight loss (48% vs 39.2%) and ischaemic manifestations (72.6 % vs 51%), including visual disturbances (26% vs 11.8%). Younger patients present more frequently with fever (33.3% vs 19.2%). Median ESR was similar: 98 vs 96 mm/h; median CPR was slightly higher in younger patients 94.5 mg/dL vs 71.59 mg/dL. PET-TC was performed more frequently at diagnosis in the subgroup of younger patients (29.4% vs 12.3%) and during follow-up period in the other subgroup (3.4% vs 7%) with evidence of involvement of large vessels in 14 of them. Initial treatment consisted of corticosteroids in 100% of patients with the most frequent doses, in both groups, between 40-60 mg/day of prednisone or equivalent. The subgroup of < 75 were treated more aggressively receiving pulses of methylprednisolone (125-250 mg) 12 patients (23.5%), while in the subgroup >75 lower doses were started more frequently (<40mg/day in 21 patients, 28.7%). Lowering corticosteroids to <5 mg/day were slower in the subgroup of patients <75 (47.1% within the first 12 months) with respect to the >75 (58%). During the follow-up period 47 patients had at least one relapse, we did not observe statistical differences between both groups (21 patients <75 and 26 patients >75). Time to first relapse was more frequent within the first year of treatment (12 and 16 patients respectively). We could not identified any factor related to relapses in our multivariate analysis. There was no significant differences between both groups about starting MTX (33.3% and 38%) on relapses. Only two patients started TCZ (one in each group). Twenty-nine patients died during follow-up period (11.7% in <75 vs. 31.5% in >75), but none were related with GCA.
Conclusion: 1. No differences were observed in sex, comorbidities (including cardiovascular risk factors) or laboratory markers between both groups. 2. Younger patients presented with less frequent ischaemic symptoms; however we perform a more powerful treatment, both in doses and duration.
Disclosure of Interests: None declared
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AB0469 CLINICAL DISEASE MIGHT BE DIVIDED INTO TWO PHENOTYPES IN ANCA ASSOCIATED VASCULITIS; RESULTS OF A CLUSTER ANALYSIS

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Background: One of the controversial matters in ANCA associated vasculitis is the definition of disease based on clinical characteristics since there is remarkable overlap between disease groups. For instance, single organ disease like renal limited vasculitis (RLV) is not take place most of the definitions or classification criteria.
Objectives: The aim of this study to determine clinical subgroups that may incorporate different clinical phenotypes including RLV in AAV patients followed up in two tertiary centers.
Methods: Baseline clinical features of AAV patients were studied. To analyse our data and identify sub-groups of AAV patients with similar clinical characteristics, a two-step cluster analysis using log-likelihood distance measures was performed. For clustering we evaluated the following variables: gender, age at symptom onset, the presence of major organ involvement (renal, upper and lower respiratory tract, skin, joint, eye) and ANCA specificity.
Results: In total 165 (87 [53%] male, age at diagnosis 51.6± 15.2 years) out of 238 (126 [53%] male, age at diagnosis 51.3± 15.6 years) AAV patients included in the analysis. Some of the demographic and clinical characteristics were summarized in the table 1. There are two distinct cluster in AAV patients. Of 78% those AAV patients with MPO/pANCA, 56% with renal involvement and 89% without ENT involvement were in Cluster 1. Of 77% those patients with PR3/cANCA, 89% with arthritis, 74% with eye involvement, 83% with skin, 91% with upper, and 60% with lower respiratory tract involvement and 92% of those without renal disease were in Cluster 2. Most of the (89%) patients classified as MPA and all as RLV were repositioned in Cluster 1 and 74% of GPA and 64% of EGPA patients were in Cluster 2.

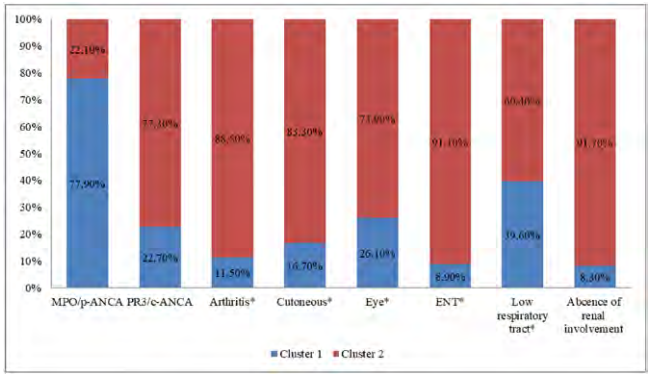
Table 1. Baseline characteristics of 165patients with AAV

Age at diagnosis, mean years ± SD, (n)	51.6 ±15.2, 163
Male, n (%)	87 (52.7)
Labaratory results at diagnosis	
GFR =<60, n (%)	100/145 (69)
MPO-ANCA or p-ANCA /Pr3-ANCA or c-ANCA	68 (41.2)/ 97 (58.8)
Variants of AAVn (%)	
MPA	26(15.8)
GPA	108 (65.5)
EGPA	11 (6.7)
RLV	20 (12.1)
Organ systems involved at diagnosis n (%)	
Cutaneous	24 (14.5)
Eye	23 (13.9)
Ear, nose and throat	90 (54.5)
Low respiratory tract	111 (67.3)
Cardiovascular system	5/163 (3.1)
Gastrointestinal system	10/164 (6.1)
Renal	129 (78.2)
Peripheral nervous system	16 (9.7)

GFR: glomeruler filtration rate; ANCA: antineutrophil cytoplasmic antibodies; Pr3: proteinase 3; MPO: myeloperoxidase; p-ANCA: perinuclear ANCA; c-ANCA: cytoplasmic ANCA; MPA: Microscopic Polyangiitis; GPA: Granulamatosis and Polyangiitis; EGPA:Eosinophilic Granulomatosis with Polyangiitis; RLV: Renal limited vasculitis

Conclusion: Patients with AAV could be separated into two distinct categories. PR3 ANCA specificity and more organ/system involvement determine one and MPO ANCA specificity in renal disease define other subgroup.

Figure. Determining characteristics of ANCA associated vasculitis clusters



Disclosure of Interests: None declared
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AB0470

EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS (EGPA) - ONE-YEAR FOLLOW-UP STUDY USING MEPOLIZUMAB ANTI-IL5 THERAPY AS A STEROID SPARING THERAPEUTIC APPROACH

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Background: EGPA is a small vessel vasculitis characterised by the presence of tissue eosinophilia, necrotising vasculitis and granulomatous inflammation[1]. Typically, a prodromal asthmatic phase, leads to an eosinophilic stage, which can evolve to include the presence of vasculitis with renal manifestations. In the recent randomised, placebo-controlled MIRRA trial for relapsing and refractory EGPA, adjuvant therapy with anti-IL5 mAB Mepolizumab [MEPO] at 300mg s/c monthly, accrued longer times in remission, reduced steroid exposure and reduced relapse rates[2].

Objectives: The aim of our study was to analyse the response and outcome for EGPA patients who received 100mg s/c of MEPO monthly for a minimum of 52 weeks, with particular focus on the steroid minimisation benefits.

Methods: This retrospective, descriptive study analysed 13 patients with EGPA, who received 100mg s/m monthly MEPO therapy under the eosinophilic asthma care-pathway. Time points of assessment included MEPO commencement [M0] and 12 [M12] months.

Results:

Table 1. EGPA patients receiving Mepolizumab therapy for one year [100mg s/c]

Demographics All [n=13]	
Gender ratio M/F	4M:9F
ANCA positive/ negative	ANCA: 3MPO, 1 PR3 positive/ 9 ANCA negative
Age of diagnosis of asthma	35 yrs [IQR 28.5-40]
Age of diagnosis of EGPA	47 yrs [IQR 43.5-53.5]
Median age	51 yrs [IQR 47.5- 60.5]
EGPA disease characteristics N=13 [%]	
Asthma 13 [100]	
Serum eosinophilia or biopsy evidence [N= 12] 12 [100]	
Pulmonary infiltrates, non-fixed 8[61.5]	
Neuropathy, mono/poly 4[30.7]	
Sino-nasal abnormality 12[92.3]	
Glomerulonephritis 3[23]	
Cardiovascular 4[30.7]	

Table 1. EGPA patients receiving Mepolizumab therapy for one year [100mg s/c]

Prior Immunosuppressants N=13 [%]	
Steroids	13[100%]
Cyclophosphamide 6[46%]	
Rituximab	6[46%]
Azathioprine	10[77%]
Mycophenolate mofetil	8[62%]
Methotrexate	4[31%]
Campath 1[7%]	
Response to therapy M0 [%] Post M12 [%]	
Prednisolone dose N= 13	
Mean ±SD 18.925mg ±11.44 10.575mg ± 5.85	
Eosinophil count $X10^9$/L N=13	
Mean ±SD 0.415mg ±0.25 0.035±0.039	
Asthma Control Questionnaire [ACQ] N=5	
Mean ±SD 2.92 ±1.27 1.31± 0.79	
BVAS N= 13	
Mean ±SD 7.307±6.29 2.2307±1.69	
Creatinine N=9	
Mean ±SD 68.44±15.03 69.11±17.84	
Continuation of anti-IL5 therapy N=13 12/13 [92.3%]	

Conclusion: The relapsing nature of EGPA places a potential dependency of therapy on steroids for asthmatic and vasculitic flares. This underscores the importance of targeted pathway specific biologic therapy to minimise steroid exposure, prevent tissue damage and ensure early response to therapy. This study demonstrates that anti-IL5 serves as a favourable model with steroid minimisation, improvement in asthma control questionnaire, reduction in BVAS and eosinophil counts at the 100mg s/c dosage. ANCA positive serology normalised in all four patients, independent of subtype. Well tolerated, it demonstrated considerable clinical benefit, with 12 patients [92.3%] continuing anti-IL5 therapy beyond 12 months.

Long term plan > 12 months N=13 [%] Current Months Adjuvant therapy 12M	
1 Continue	
15 Aza	
2 Switched Benralizumab 26 MMF [+], IVIG [-]	
3 Continue 18	
4 Switched Benralizumab 14	
5 Discontinued Rituximab 12 MTX	
6 Continue 14	
7 Continue 24 MMF Reduced	
8 Continue 18 MTX [+]	
9 Continue 15 MMF [-]	
10 Continue 14	
11 Continue 13	
12 Continue 13 Aza	
13 Continue 12	

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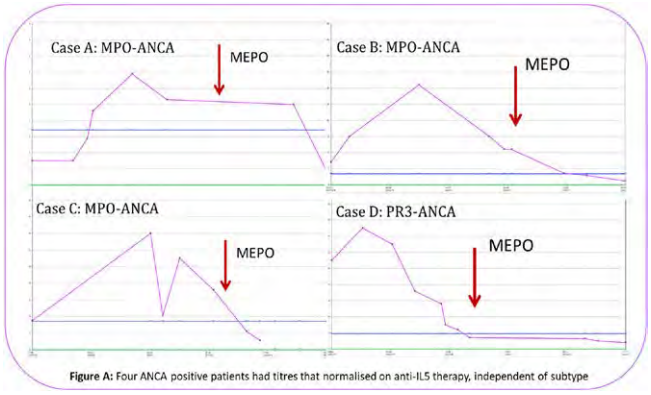


Figure.

Disclosure of Interests: Allyson Egan: None declared, pasupathy Sivasothy: None declared, Robin Gore: None declared, Marcos Martinez Del-Pero: None declared, Caroline Owen: None declared, Lisa Willcocks: None declared, Rona Smith: None declared, Stella Burns: None declared, David Jayne Grant/research support from: ChemoCentryx, GSK, Roche/Genentech, Sanofi-Genzyme, Consultant of: Astra-Zeneca, ChemoCentryx, GSK, InflaRx, Takeda, Insmed, Chugai, Boehringer-Ingelheim

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AB0471 ELEVATED EXPRESSION OF PYRUVATE KINASE M2 IN GIANT CELL ARTERITIS

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Background: Giant Cell Arteritis (GCA) is an inflammatory disease of large and medium vessels. In GCA, expression of interleukin-6 (IL-6), a systemic marker of inflammation, is elevated and it has been shown that treatment with IL-6 receptor blockade (Tocilizumab) is beneficial for GCA patients.[1] To investigate the role of the IL-6 signaling pathway in GCA pathogenesis in more depth, we focused on the metabolic enzyme Pyruvate Kinase M2 (PKM2). PKM2 may exist as a tetramer, a dimer and/or a monomer in the cell. Tetrameric PKM2 acts as a glycolytic enzyme and catalyzes the last steps of glycolysis by converting phosphoenolpyruvate (PEP) to pyruvate and ATP. On the other hand, dimeric PKM2 translocates to the nucleus and mediates gene regulation via its non-canonical protein kinase activity. Dimeric PKM2 regulates hypoxia, IL-1β expression and, phosphorylates signal transducer and activator of transcription 3 (STAT3) which functions downstream of the IL-6 signaling pathway.2

Objectives: To investigate the role of PKM2 in GCA diagnosis and pathogenesis.

Methods: Immunohistochemical staining for PKM2 was performed on inflamed (n=8) and non-inflamed (n=4) temporal artery biopsies (TAB) from GCA patients and on TAB from non-GCA (n=9) patients. To detect soluble, dimeric PKM2 in plasma commercially available dimeric PKM2 specific ELISA kit was used. To determine the modulation of dimeric PKM2 by treatment, samples of GCA patients at baseline (n=44), at 6 weeks (n=32) and at 1 year (n=31) after treatment were compared to samples from age- and sex-matched healthy controls (HC, n=45) As a positive control, samples from melanoma patients (n =8) were used. To investigate the role of dimeric PKM2 in the pathogenesis of GCA, we correlated PKM2 plasma levels with markers of inflammation (CRP, IL-6) and markers of angiogenesis (Angpt2, VEGF, YKL40). Statistical analysis included the Mann-Whitney U test for comparing different groups while the Wilcoxon rank test was used for paired samples. Correlations were assessed by Spearman's rank correlation coefficient.

Results: High expression of PKM2 was found in inflamed and non-inflamed TABs of GCA patients, while in non-GCA TABs PKM2 was sparsely expressed. Circulating levels of dimeric PKM2 were found elevated in melanoma and in GCA patients at baseline/active disease compared to those in healthy controls. Analysis of 6 weeks and 1 year follow up plasma samples showed that plasma levels of dimeric PKM2 significantly decreased upon treatment. Dimeric PKM2 weakly correlated with CRP at baseline (r=0.399, p=0.048) but not with angiogenesis markers.

Conclusion: Dimeric PKM2 plasma levels were found elevated in GCA patients at baseline. PKM2 plasma levels were down modulated by treatment. PKM2 plasma levels weakly correlated with inflammation marker CRP. The data suggest that PKM2 as a marker of glycolysis may have relevance in GCA at diagnosis and for monitoring disease activity. Future studies should aim to validate PKM2 in an independent cohort. Additional studies are needed to determine the molecular mechanism underlying the increase in elevated dimeric PKM2 levels and how this may contribute to IL-6 signaling.

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AB0472 INFECTIOUS PROFILE IN PATIENTS WITH ANCA-ASSOCIATED VASCULITIS: RETROSPECTIVE ANALYSIS IN A REFERRAL CENTRE

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Background: The antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) are rare multisystem autoimmune diseases of unknown cause, characterised by inflammatory cell infiltration causing necrosis of blood vessels. The treatment of AAV requires prolonged immunosuppressive therapy. Infections remain a major cause of morbidity and mortality.

Objectives: The aim of our study was to investigate the prevalence and characteristics of infection, and analyse the factors associated with infection in patients with AAV from Northern of Spain.

Methods: Retrospective, descriptive study of patients with AAV followed in a specific Systemic Autoimmune Diseases and Thrombosis Unit from January 2000 to December 2019. Demographic, laboratory, microbiology, treatment and clinical data were collected from the medical records. AAV was diagnosed according to the definitions of the Chapel Hill nomenclature and designated as granulomatosis with polyangiitis (GPA), eosinophilic granulomatosis with polyangiitis (EGPA), microscopic polyangiitis (MPA) or pauci-immune necrotizing and/or crescentic glomerulonephritis without systemic vasculitis (renal-limited vasculitis, RLV). Disease activity of AAV was evaluated by Birmingham Vasculitis Activity score (BVAS). The infection episode was considered on the basis of clinical, laboratory, microbiology, radiology information, and response to therapy. Different episodes of infection in one patient were independently reflected. Data were analysed using SPSS 25.0

Results: Thirty-six patients of which 20 (55.6%) were males. Median follow-up was 42 months. The mean age at the diagnosis was 61.14 ± 17.49 years and mean BVAS was 18.81 ± 5.96. 15 patients were diagnosed of GPA, 13 of MPA, 5 of EGPA and 3 of RLV. 72.2% MPO, 11.1% PR3. Lung involvement occurred in 75% of patients, upper airways was detected in 41.7%, skin involvement in 16.7%, Nervous system affectation occurred in 33.3%. 30 patients (83.3%) had renal affectation with a mean of 1.93± 1.66 gr/dl of Proteinuria and 2.9±2.17mg/dl of creatinine. We detected hypocomplementemia in 27.8% of patients (C3 in 19.4% and C4 in 16.7%). Regarding induction treatments, all patients received corticoids at high doses, 21 (58.3%) Cyclophosphamide, 3 (20%) Rituximab and 2 (13.3%) patients, Azathioprine. When we analyse infections, we detected 15 patients (41.66%) who presented any infection after the diagnosis of AAV, with a total of 71 episodes of infection. The most frequent were bacterial infections (29 episodes), specifically gram negative pathogens. The most frequent location was the respiratory (56.3%) followed by urinary (22.5%) and Skin (8.5%). Also opportunistic infections were described: 3 patients with Aspergillus fumigatus and one patient with Cryptococcus neoformans. 41 of these episodes needed hospitalisation with a median stay of 11 days. 6 episodes warranted intensive care unit (ICU) admission. Infection related mortality was 2.82%. We made latent tuberculosis screening and Pneumocystis prophylaxis in all our patients. No cases of Tuberculosis or Pneumocystis were recorded. Factors associated with increased risk of hospitalisation with statistical signification in univariated study were MPA, Hypocomplementemia and increased BVAS. But in the logistical regression study, only the value of the BVAS maintained statistical significance. The only factor associated with elevated risk of ICU admission was IgG deficit in the multivariate analysis. Neither immunosuppressive therapy nor age was associated with increased risk of infection in our study.

Conclusion: More than 50% of the episodes of infection needed hospitalisation in patients with AAV. Risk factors for hospitalisation and ICU admission were BVAS and IgG deficit respectively. Bacterial infections were the most frequent but fungal infections were the most severe.

Disclosure of Interests: None declared

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AB0473 "HALO SIGN" IN ULTRASOUND OF TEMPORAL, FACIAL AND AXILLARY ARTERIES: ASSOCIATIONS WITH CLINICAL SYMPTOMATOLOGY AND LABORATORY FINDINGS

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Background: Giant cell arteritis (GCA) has two subtypes, the cranial form ("cranial GCA") and the large-vessel form ("LV-GCA"). GCA can present with "cranial" symptoms (headache, visual symptoms, jaw claudication, scalp tenderness), constitutional symptoms (fever, fatigue), limb claudication and symptoms of polymyalgia rheumatica (PMR) and usually causes increased inflammation markers, anemia and thrombocytosis. Ultrasound (US) of the temporal and axillary arteries

has a well-established role in cranial GCA and LV-GCA diagnosis, respectively. However, it is unknown whether specific clinical and laboratory parameters are linked with US findings suggestive of vascular inflammation ("halo" sign).
Objectives: The aim of this study was to examine possible association between clinical and laboratory characteristics of the patients and detection of vessel wall inflammation in the US.
Methods: Patients ≥50 years old with elevated ESR (≥50mm/h) and/or CRP (≥10mg/L) that presented in our outpatient rheumatology clinics from July 2017 to December 2019 with possible clinical diagnosis of GCA were included. Three groups were compared: Patients with "cranial symptoms" (with or without PMR), patients with PMR symptoms only and patients with increased inflammation markers without specific symptoms indicative of GCA. Temporal arteries and their main branches, as well as facial and axillary arteries were evaluated by US bilaterally for the presence of non-compressible "halo sign" at the vessel wall. Clinical symptomatology and the occurrence of anemia and thrombocytosis were recorded.
Results: 52 patients were included. 71.2% were females, with a mean±SD age of 71.0±10.0 years. 17 patients had "cranial symptoms" (seven patients with concomitant PMR and ten without), 17 patients had PMR symptoms only, while 18 patients had non-specific symptoms (e.g. fever) (Table 1). Among 17 patients with "cranial symptoms", 7/7 (100%) with concomitant PMR had a positive temporal US, while only 3 out of 10 (30%) without PMR had a positive temporal US (p<0.01) and US was indeterminate in 2 of them (20%). Collectively, 10/17 (58.8%) of patients with "cranial symptoms" and systemic inflammation had a US examination compatible with GCA. No patient with "cranial symptoms" had a positive US of axillary arteries. No patient with only PMR symptoms, had "halo sign" in temporal and facial arteries, while 3 out of 17 (17.6%) had a positive axillary US. From the 18 patients with elevated ESR/CRP, one had a positive temporal US and another one had a positive axillary US. Regarding specific symptoms, positive temporal US was associated with new headache (p=0.003), vision impairment (p=0.001), jaw claudication (p=0.05), scalp tenderness (p=0.01) and fever (P=0.002), but not with PMR (p=0.317). Thrombocytosis was associated with an increased risk for "halo sign" detection in temporal (p=0.04) and facial (p=0.007) arteries, but not in axilliary arteries (p=0.52).

Table 1. Symptomatology and ultrasound findings in the patients examined. PMR: Polymyalgia Rheumatica

Ultrasound	Symptoms			
	Cranial (n=17)		PMR only (n=17)	Non-specific symptoms (n=18)
	PMR (+) (n=7)	PMR (-) (n=10)		
Temporal (+)	7	3	0	1
Facial (+)	2	1	0	0
Axilliary (+)	0	0	3	1

Conclusion: 60% of patients with "cranial symptoms" and elevated inflammation markers have US temporal findings indicative of GCA. This is more pronounced in patients with concomitant PMR symptoms and is associated with specific symptomatology. 18% of patients with only PMR symptoms might have LV-GCA, while those with high ESR/CRP without GCA-related symptoms rarely have "halo sign" in US.
Disclosure of Interests: None declared
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AB0474 CAROTID CONTRAST ENHANCED ULTRASOUND IN CASES OF TAKAYASU ARTERITIS COMPLICATED WITH BEHCET'S DISEASE

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Background: Carotid contrast enhanced ultrasound (CEUS) is used for diagnosis and activity determination of patients with Takayasu's arteritis (TA). However, very little is known about the carotid CEUS features of TA complicated with Behcet's disease (BD).
Objectives: This study reports the carotid CEUS features in cases of TA complicated with BD (TBD).
Methods: A total of 10 carotid CEUS examinations were performed on 4 patients of TBD. 10 TA patients complicated with no rheumatoid disease were included as control group. For each carotid artery lesion, the carotid CEUS features was graded as follows: Grade 0, artery wall shows no microbubbles, Grade 1, artery wall shows limited or moderate microbubbles, Grade 2, artery wall shows severe microbubbles.
Results: 2/10 patients in TBD group has oral ulcer during the CEUS examination, while all the other patients included in our study showed no clinical symptoms related to active TA or BD. The carotid wall thickness was greater of CEUS grade 2 than grade 1 in both group(TBD: 2.62±0.74mm vs 1.66±0.22mm, *p*=0.001; TA:1.84±0.31mm vs 1.53±0.5mm, *p*=0.136). The carotid wall thickness was significantly greater in TBD group than TA group, but there was no significant differences between the two groups in clinical data and CEUS grade (table 1).

Table 1. Clinical data and carotid CEUS features of both groups

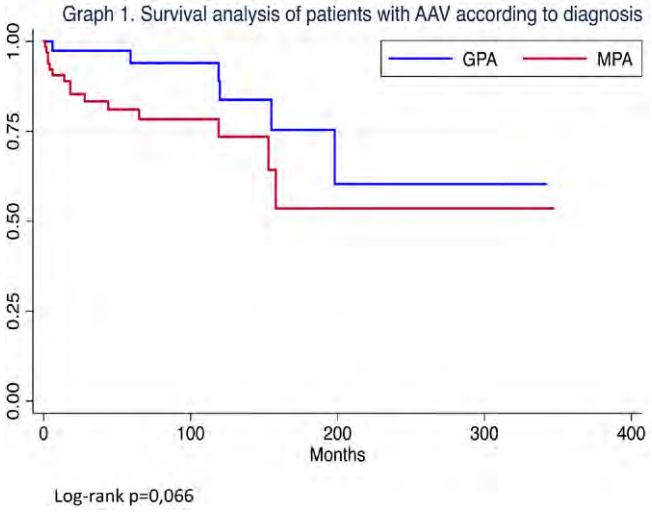
	TBD	TA	*p*
Age (year)	32.5±3.44	30.5±9.2	0.487
Male	3	2	0.605
ESR (mm/h)	4(2, 10)	7(3.5, 11)	0.406
CRP (mg/L)	6.42(0.55, 15.38)	0.58(0.44, 5.05)	0.168
Wall thickness (mm)	2.10±0.70	1.67±0.44	0.030
CEUS grade 2	9	12	0.527

Conclusion: This study first shows carotid CEUS features in cases of TA complicated with BD, which may help with the comprehensive treatments of the disease.
Disclosure of Interests: : None declared
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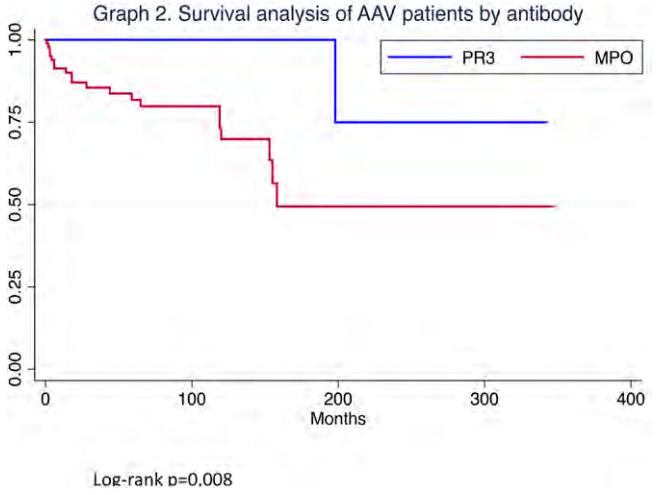
AB0475 CLINICAL RELEVANCE OF CLINICOPATHOLOGICAL PHENOTYPE AND ANTIBODY SPECIFICITY IN ANCA-ASSOCIATED VASCULITIS

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Background: Classification of ANCA-associated vasculitis (AAV) has emerged in order to identify more homogenous subgroups of patients with granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA). However, the exact value of classifying patients according to antibody specificity (proteinase 3 [PR3] or myeloperoxidase [MPO]) is still unclear.
Objectives: To assess demographic, clinical and prognostic differences among subgroups of AAV patients, according to clinicopathological classification (GPA *vs*. MPA) and antibody specificity (PR3 *vs*. MPO) in a single-centre cohort.



Methods: A clinical retrospective (1990-2019) observational analysis was performed. Among all patients with ANCA positivity, we analysed patients with GPA and MPA diagnosed according to 2018 Draft Classification Criteria for AAV[1], who were homogeneously treated and followed by the authors. Demographic, clinical and laboratory data, as well as disease outcomes, particularly BVAS, disease relapses and survival, were reviewed.
Results: Among a total 140 patients with any form of AAV, 32 were excluded for a diagnosis of isolated interstitial lung disease (n=10), cocaine-induced AAV (n=3), ANCA negative or undetermined disease (n=16), atypical ANCA or double PR3/MPO positivity (n=3). Finally, 108 patients with MPA (n=66) or GPA (n=42) were included (83 MPO, 25 PR3). GPA was associated with PR3 in 55% and MPO 45% of patients. MPA was associated with MPO in 97% and PR3 in 3% of patients. GPA patients with PR3 or MPO presented with similar clinical features, disease extent and BVAS. However, compared with GPA/PR3, GPA/MPO were more frequently women (p=0.002). MPA patients presented more frequent with renal involvement (p=0.008) and GPA patients with ENT/ocular involvement (p<0.001). Patients with MPO were older (p=0.028) and more frequently women (p=0.001) than PR3



patients. When antibody specificity was compared, differences on organ-specific manifestations were less clear than between clinical phenotypes (GPA vs. MPA), and were only seen in ENT/ocular involvement (more frequent in PR3 than in MPO patients) and in muscle biopsies disclosing vasculitis (more frequent in MPO than in PR3 patients). GPA and PR3 patients presented more frequent relapsing disease than MPA and MPO patients, respectively (GPA 60% vs. MPA 36%; p=0.018 / PR3 60% vs. MPO 41%; p=0.094). While GPA tended to have a better survival rate than MPA patients (p=0.066) (Graph1), the MPO-associated disease (GPA or MPA) had clearly worse survival prognosis than PR3-AAV (p=0.008) (Graph2), similarly to what occurred in GPA-MPO (compared with GPA-PR3).

Conclusion: A high proportion of GPA patients with MPO-ANCA (45%) is observed in our series. GPA is associated with a more frequent relapsing disease than MPA. MPA and presence of MPO were more frequent in females and older patients. Clinical features were similar in GPA patients with PR3 or MPO. The presence of MPO (in GPA or MPA) seems to be the main factor associated with mortality in AAV.

References:

[1] Robson JC, Grayson PC, Ponte C, *et al.* Draft classification criteria for the ANCA associated vasculitides. Ann Rheum Dis 2018;77 (suppl 2):60-1.

Disclosure of Interests: João Fernandes Serodio: None declared, Sergio Prieto-González: None declared, Georgina Espígol-Frigolé: None declared, Marco Alba: None declared, Javier Marco-Hernández: None declared, Maria C. Cid Grant/research support from: Kiniksa Pharmaceuticals, Consultant of: Janssen, Abbvie, Roche, GSK, Speakers bureau: Vifor, José Hernández-Rodríguez: None declared

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AB0476 GIANT CELL ARTERITIS: A DISEASE WITH DIFFERENT SUBSETS

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Background: Giant cell arteritis (GCA) is the most common form of autoimmune vasculitis in the elderly. Some evidence indicates that GCA is a heterogeneous disease in terms of symptoms, immune pathology and response to treatment[1].

Objectives: To analyze whether the identification by image of cranial vessels (VC) or large vessels (VG) involvement allows to characterize different clinical subsets of the disease.

Methods: Descriptive observational study of the last 87 consecutive patients with a new diagnosis of GCA in our hospital. All patients had a CV and LV CDUS exam that included axillary, subclavian, vertebral and carotid arteries or a Positron Emission Tomography (PET-CT). The OMERACT (Outcome Measures in Rheumatology) definitions of halo sign were used for ultrasound diagnosis and IMT limits were established as ≥ 0.34 mm for superficial temporal arteries and ≥ 1 mm for axillary, subclavian and carotid arteries; a clear halo sign was used in the vertebral arteries. The radiologist's report and the liver/vascular wall index were used for the definition of positive PET-CT. The medical records of these patients were reviewed and their demographic, clinical and laboratory data were compared between the different patterns of GCA. The statistical significance limit was set at $P < 0.05$. Statistical analyses were performed by using SPSS version 25.

Results: Out of 198 patients with suspected GCA who underwent a CDUS or PET-CT between November 2016 and November 2019, 87 were diagnosed of GCA. Three different patterns were detected: 44 patients (50.6%) had an exclusive cranial pattern, 31 (35.6%) had a mixed pattern with involvement of both CV and LV and 12 (13.8%) had an exclusive large vessel pattern. The differences between these 3 subsets are shown in table 1. Patients with a LV pattern had more fever and polymyalgia rheumatica than patients with CV involvement and fewer ischemic visual disturbances than those with mixed pattern, reaching statistical significance. In addition, they tended to have fewer other ischemic symptoms (headache, jaw claudication) and more general symptoms than patterns with CV involvement. Regarding laboratory values, the erythrocyte sedimentation rate was significantly higher in the exclusive CV involvement group and lower in those with only LV involvement.

Table 1. Characteristics of the patients with the different patterns

	Cranial pattern (n = 44; 50.6%)	Mixed pattern (n = 31; 35.6%)	Large vessel pattern (n = 12; 13.8%)	p-value
Age, years (mean, SD)	78 ± 7	76 ± 7	74 ± 11	0.291
Male sex	12 (27.3%)	14 (45.2%)	5 (41.6%)	0.252
ESR, mm/h (mean, SD)	78.7 ± 33.7	63.9 ± 33.0	52.1 ± 33.5	0.031*
CRP, mg/L (mean, SD)	55.8 ± 46.6	68.3 ± 63.6	85.9 ± 89.3	0.801
Headache	36 (81.8%)	25 (80.6%)	8 (66.6%)	0.704
Jaw claudication	12 (27.3%)	5 (16.1%)	1 (8.3%)	0.249
Ischemic visual disturbances	9 (20.4%)	11 (35.5%)	0 (0%)	0.041#
PMR	18 (40.9%)	13 (41.9%)	8 (66.6%)	0,018* 0,029#
General symptoms	17 (38.6%)	13 (41.9%)	8 (66.6%)	0.132
Fever	5 (11.4%)	3 (9.7%)	6 (50%)	0.005*#

SD: standard deviation. ESR: erythrocyte sedimentation rate. CRP: C reactive protein. PMR: polymyalgia rheumatica.
*Statistically significant difference between cranial pattern and large vessel pattern.
#Statistically significant difference between mixed pattern and large vessel pattern.

Conclusion: Imaging in GCA allow us to establish different patterns of involvement (cranial, mixed, large vessel) that correspond to different clinical subsets. The patients with LV subset debut with a lower ESR and have more fever and polymyalgia rheumatica and less ischemic symptoms.

References:

[1] van der Geest KSM, Sandovici M, van Sleen Y, et al. Review: What Is the Current Evidence for Disease Subsets in Giant Cell Arteritis?. Arthritis Rheumatol. 2018;70(9):1366–1376. doi:10.1002/art.40520

Disclosure of Interests: : Elisa Fernández: None declared, Irene Monjo: None declared, Gemma Bonilla: None declared, Diana Peiteado: None declared, Chamaida Plasencia: None declared, Alejandro Balsa Grant/research support from: BMS, Roche, Consultant of: AbbVie, Gilead, Lilly, Pfizer, UCB, Sanofi, Sandoz, Speakers bureau: AbbVie, Lilly, Sanofi, Novartis, Pfizer, UCB, Roche, Nordic, Sandoz, Eugenio de Miguel Grant/research support from: Yes (Abbvie, Novartis, Pfizer), Consultant of: Yes (Abbvie, Novartis, Pfizer), Paid instructor for: yes (AbbVie, Novartis, Pfizer, MSD, BMS, UCB, Roche, Grunental, Janssen, Sanofi), Speakers bureau: yes (AbbVie, Novartis, Pfizer, MSD, BMS, UCB, Roche, Grunental, Janssen, Sanofi)

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AB0477 OVARIAN RESERVE IN PATIENTS WITH RHEUMATIC DISEASES

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Background: Access to assays of circulating anti-Mullerian hormone (AMH) levels has opened a new page in the assessment of ovarian function and fertility in various diseases, including rheumatic diseases (RDs). The definition of AMH as a marker of ovarian reserve significantly simplified its interpretation as well as measuring the contribution of the disease itself to the patients' infertility.

Objectives: To evaluate the effects of the disease and it's treatment on serum AMH levels for Behcet's disease (BD), systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and systemic scleroderma (SSD).
Methods: The study included 73 patients with RDs from 18 to 40 years: 42 patients with BD, 12 with SLE, 11 with RA, 8- with SSD, the control group consisted of 15 healthy women. Enzyme-linked immunosorbent assay (ELISA) was used to measure AMH levels. Parametric and nonparametric statistical methods of Statistica 8.0 package were used for statistical processing of data.
Results: Mean age in BD patients was 30.0 years, in SLE and RA -33.5 years, in SSD - 35.0 years, and 32.0 years in the control group. The average disease duration was 4.5 years, 11.5 years, 4.0 years and 6.0 years, respectively.

	BD, n=42	SLE, n=12	RA, n=11	SSD, n=8	Control, n=15
Mean age, years	30,0 [26;35]	33.5 [29;38]	33,5 [24;36]	35,0 [28;40]	32,0 [26;35]
Average disease duration, years	4,5 [2,6;9,0]	11,5 [2,8;18]	4,0 [4,0;6,0]	6,0 [2,0-10,0]	-
Mean AMH level, ng/ml	2,5 [1,1;3,7]	3,5 [0,4-7,1]	3,35 [2,0;7,6]	2,5 [0,3;7,1]	3,1 [1,9;5,4]

There were no significant differences in the mean AMH levels between the groups. No association between AMG levels and clinical manifestations, disease activity or duration of rheumatic disease was found. Baseline AMH – in treatment-naïve patients before initiation of any DMARDs was assessed in 11 BD patients. A significant (p>0.05) decrease of AMH levels was established in patients with high SLE activity treated with CP. Of notice, all examined patients were additionally receiving a GEBD -Rituximab.

Conclusion: Decreased ovarian function was found in patients with high SLE activity treated with CP with Rituximab.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.3465

AB0478 CORONARY ATHEROSCLEROSIS IN BEHCET'S DISEASE

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Background: Behcet's disease (BD) is systemic vasculitis, which affects all types and sizes of vessels. Increased carotid intima-media thickness (IMT) is parameter associated with subclinical atherosclerosis.
Objectives: To determine the prevalence of atherosclerosis in pts with BD.
Methods: 95 BD pts were evaluated and 45 healthy controls matched for age and gender.
IMT was assessed by high-resolution B-mode ultrasonography. Serum concentration of high-sensitivity C-reactive protein (hs CRP) was measured by immunonephelometric assay (BN-100 Analyzer; Dade Behring). Lipid profile evaluation included total cholesterol, TGs, HDL, LDL and atherogenic index.
Results: The male-to-female ratio was 3,7:1, the mean age of pts was 29.7 (23-35) yrs, the mean age at the disease onset - 19,9 (14-25) yrs, the mean disease duration - 9,6 (4-15) yrs.

	BD, %	Healthy, %	P
Arterial hypertension	22,1	13,3	ns
Smoked	29,5	24,4	ns
Diabetes mellitus	0	0	ns
Lipid abnormalities	76,8	64,4	ns
Total cholesterol	5,0 ±1,40	5,3 ±0,96	ns
TGs	0,91 ±0,65	0,90 ±0,68	ns
HDL	1,18 ±0,39	1,26 ±0,29	ns
LDL	3,40 ±1,46	3,47 ±0,90	ns
Hs CRP	2,42 ±21,0	0,3 ±0,63	<0,00
Mean IMT carotid artery	0,68 ±0,09	0,64 ±0,09	ns
IMT <0,5 mm	31,6	6,6	<0,00
IMT > 0,5-0,89 mm	49,5	86,6	ns
IMT - 0,9 – 1,2 mm	13,68	6,6	ns
IMT > 1,2 mm (plaques)	5,7	0	ns

The mean carotid IMT in BD pts was similar with controls. In pts thinning IMT and concentration of hsCRP was significantly higher compared with controls.
IMT correlated with age of pts, concentration of total cholesterol, LDL and hsCRP but did not correlated with clinical manifestation and disease duration. Carotid atherosclerotic plaques were found in 5 pts with BD – mean age 40,0±8,1, who had traditional cardiovascular risk factors (high body masse index, hypertension) and received long time therapy with glucocorticoids.
Conclusion: Coronary atherosclerosis in BD pts was lower than what we expected. The thinning IMT may be one of the risk factors for aneurysm formation in pts with BD.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.3609

AB0479 PREGNANCY OUTCOMES IN PATIENTS WITH RHEUMATIC DISEASES.

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Background:
Objectives: To evaluate pregnancy outcomes in patients with Behcet's disease (BD), systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and systemic scleroderma (SSD).
Methods: The study included 73 patients with rheumatic diseases (RDs) aged 18 to 40 years signing the informed consent form and completing dedicated thematic chart. The mean age of participants was 30.0 years - for BD patients; 33.5 years - for SLE, 33.5 – for RA; and 35.0 for SSD patients; mean disease duration was 4.5 years, 11.5 years 4.0 years and 6.0 years, respectively. 23 patients (11 BD patients, 5 SLE, 5 RA 5 and 2 SSD 2) out of 73 never had pregnancies, including 15 virgo patients and 4 patients who were planning pregnancy in the near future.158 pregnancies in 50 patients with rheumatic diseases (31 BD patients, 7 SLE, 6 RA, and 6 SSD pts) were retrospectively analyzed.
Results: Outcomes of 159 pregnancies in RD patients were as follows: 95 (60%) on time births of full-term babies; 2 cases (1.2%) of early neonatal death in two BD females (premature deliveries at 28 and 32 gestational weeks of babies with signs of extreme prematurity who died 1 day after birth); 35 pregnancies were terminated before 10 weeks of gestation: 34 pregnancies (in 4 patients) - at the woman's request, 1-for medical reasons (rubella at 7 weeks of gestation).
Totally 27 cases of adverse pregnancy outcomes were documented in 20 patients (40% of 50 patients): 19 cases (in 14 patients) of intrauterine deaths, one case of ectopic pregnancy, 8 cases (in 6 patients) of early miscarriages (at 5, 6 and 10 weeks of gestation).
There were no cases of antiphospholipid syndrome documented.
Pregnancy outcomes in RD patients

	BD, n=31	SLE, n=7	RA, n=6	SSD, n=6
Pregnancy, n	107	16	17	18
Childbirth, n	71	9	9	6
Medical abortion, n	20	2	3	10
Intrauterine deaths, n	12	4	4	0
Miscarriage, n	4	1	1	2

Out of total 95 babies born to RD patients, two had recurrent aphthous stomatitis (in 2 BD patients), and one had congenital glaucoma (born to a mother with neuro-Behcet's).
10 BD and 2 RA are patients multipara mothers who are raising 3 and more children.

Conclusion: Rheumatic diseases are associated with high incidence of adverse pregnancy outcomes.
Disclosure of Interests: None declared
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AB0480 AN OPEN-LABEL, EXPLORATORY STUDY TO ESTABLISH THE EFFICACY AND SAFETY OF 1-YEAR CANAKINUMAB TREATMENT IN BEHÇET'S DISEASE PATIENTS WITH NEUROLOGIC OR VASCULAR INVOLVEMENT

A. Gül[1], M. Kurtuncu[1], M. Erdugan[1], E. Oguz[2], T. Gunduz[2], G. Akman Demir[2], S. Sevgi[3], S. Turgay[4], E. Acar[5]. [1]*Istanbul Faculty of Medicine, Istanbul, Turkey*; [2]*Istanbul Faculty of Medicine, Istanbul, Turkey*; [3]*Novartis Turkey, Istanbul, Turkey*; [4]*Novartis Turkey, Istanbul, Turkey*; [5]*Novartis Turkey, Istanbul, Turkey*

Background: Previous observations in Behcet' s disease (BD) patients receiving anti-IL 1 therapies suggested that dosage and route of administration may be critical in controlling disease manifestations. This was supported by favorable observations with infliximab infusions reaching higher serum trough levels in refractory BD patients compared to other anti-TNF agents.
Objectives: The primary objective was to evaluate the safety and efficacy of intravenous (IV) canakinumab (CAN) on the clinical and inflammatory findings of BD patients with neurologic and vascular involvement.
Methods: Biologic-naïve BD patients, who had a recent attack of large vessel vascular or parenchymal neurologic disease within the last month were enrolled and all received 300 mg CAN IV without a change in other medications. Response was assessed on day 30 as the primary objective; partial

responders were able to take the 2nd 300 mg IV on day 30 and continued the treatment with monthly 150 mg IV 4 times. Others continued the treatment with 150 mg IV monthly. At month 6, patients were able to switch to SC injections or continue 150 mg IV for 6 months. Non-responder patients were dropped out. Prednisolone dosage was ≤20 mg at baseline and not increased during the trial. Complete response was defined as full clinical recovery to pre-attack state, disappearance of MRI lesions, normalization of CSF findings; partial response was defined as partial improvement in clinical findings, which were still worse than pre-attack state, with MRI lesions becoming smaller with no or less enhancement, and a decrease in CSF cell count. Complete response of vascular findings was defined as ≥50% improvement in patient's and physician's global assessments, ≥50% reduction in CRP; along with stable or ≥20% reduced aneurysm size or stable or ≥20% reduced calf swelling; and partial response was an improvement between 20-49% in global assessments, 20-49% reduction in CRP; stable or ≤20% reduced aneurysm size or ≤20% reduced calf swelling.

Results: 9 subjects were screened, and 8 male subjects (5 vascular, 3 neurologic) aged 27.3 ± 2.3 years entered the study. No new attack or worsening of manifestations was observed, and at least a partial response was obtained in all patients on day 30. Two vascular patients (2/5, 40%) and 1 neurologic patient (1/3, 33%) received another 300 mg infusion on day 30; one of them left the study on day 120 because of safety concerns after noticing the use of illicit drugs, and the other required 150 mg IV CAN after day 180 and discontinued the study because of the worsening of pulmonary artery aneurysm, despite favorable response in venous findings. The remaining 3 patients (3/5, 60%) with deep vein thrombosis completed the study with clinical and radiological improvement. 2 patients with parenchymal involvement had lesions in the brain stem and showed complete improvement of clinical findings between 1-3 months and radiologic findings between 3-6 months. Clinical findings of 1 patient with sinus thrombosis improved within 2 months, and the last cranial MRI showed that the vein thrombus was recanalized. Patients experienced other mild manifestations of BD following a switch to SC administration.

Conclusion: Response to CAN without high-dose methylprednisolone treatment suggests that IL-1 antagonism plays a role in acute exacerbations of neurologic and vascular manifestations of BD, and no new safety signal was recorded with IV use. Favorable responses during the early months of the study and development of clinical and laboratory findings after switching to SC administration may suggest that achievement of higher serum trough levels may be critical, and up-titration of the dosages may provide better results in individual patients with higher inflammatory activity.

References: NA

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Disclosure of Interests: Ahmet Gül: None declared, Murat Kurtuncu Grant/research support from: Travel, symposia speaker and Honoraria grants (Novartis, Bayer, Teva, Ali Raif, Gen), Consultant of: (Novartis, Bayer, Teva, Ali Raif, Gen), Speakers bureau: (Novartis, Bayer, Teva, Ali Raif, Gen), Murat Erdugan: None declared, Emin Oguz: None declared, Tuncay Gunduz: None declared, Gulsen Akman Demir Grant/research support from: Novartis, Consultant of: Novartis, Serhan Sevgi Employee of: Novartis, Soner Turgay Employee of: Novartis, Ersen Acar Employee of: Novartis

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AB0481

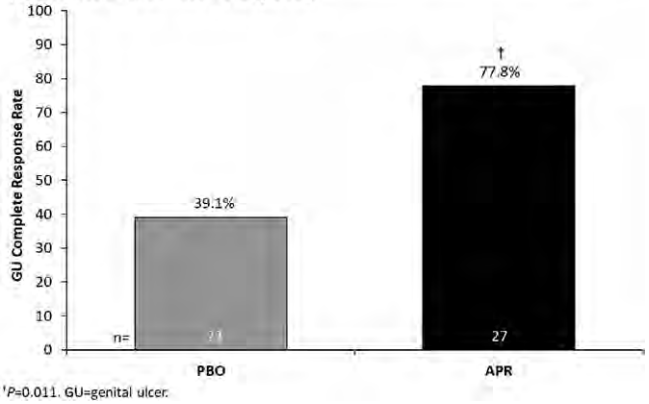
EFFICACY OF APREMILAST FOR THE TREATMENT OF GENITAL ULCERS ASSOCIATED WITH ACTIVE BEHÇET'S SYNDROME: A COMBINED ANALYSIS OF TWO RANDOMIZED CONTROLLED TRIALS

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Background: Behçet's syndrome is a chronic, multi-system inflammatory disorder characterized by painful, recurrent oral ulcers (OU) and genital ulcers (GU).[1] The GU associated with Behçet's syndrome can contribute to difficulties with sexual activity, walking, and sitting[2]; may cause scarring[1]; and may impair quality of life.[1,2] Apremilast (APR), an oral phosphodiesterase 4 inhibitor, has demonstrated efficacy in the treatment of the OU associated with Behçet's syndrome in the phase III, randomized RELIEF study (BCT-002).[3]

Objectives: To describe the efficacy of APR for the treatment of GU associated with active Behçet's syndrome in the RELIEF study and in a pooled data analysis of RELIEF and the phase II study.

Figure 1. Complete Response of GU at Week 12 in Patients With GU at Baseline (Pooled RELIEF and Phase II Study Data)



†*P*=0.011. GU=genital ulcer.

Methods: Adult patients (≥18 years of age) with active Behçet's syndrome and ≥3 OU at randomization or ≥2 OU at screening and randomization, without active major organ involvement, were randomized (1:1) to APR 30 mg twice daily or placebo (PBO). In RELIEF, clinical improvement in GU was assessed by evaluating the time to the first GU recurrence after loss of complete response, the mean number of GU in patients without GU at baseline, and the proportion of patients who were GU-free (complete response) at Week 12 (regardless of baseline GU status). A pooled analysis of patients in RELIEF and a randomized, phase II study[4] were conducted to assess achievement of GU complete response in patients with GU at baseline. In patients with GU complete response before Week 12, the median time to the first GU recurrence after loss of complete response was based on Kaplan-Meier estimates. The mean number of GU was summarized descriptively using data as observed. Between-group differences in the proportion of patients who were GU-free at Week 12 were analyzed by Cochran-Mantel-Haenszel test using non-responder imputation to handle missing data. Statistical tests were 2 sided (α=0.05).

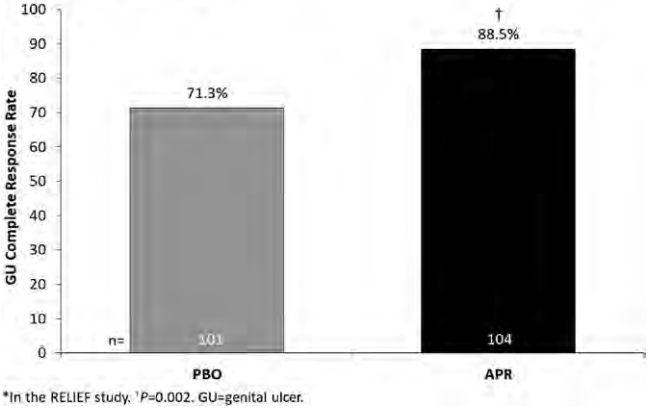
Results: A total of 207 patients were randomized and received ≥1 dose of study medication (APR: n=104; PBO: n=103). In all, 17 patients in the APR group and 17 in the PBO group had GU at baseline, with mean GU counts of 2.9 (APR) and 2.6 (PBO). Among patients with GU at baseline in RELIEF, 12/17 (70.6% [APR]) and 7/17 (41.2% [PBO]) achieved GU complete response at Week 12 (*P*=0.110). The median time to first GU recurrence in these patients occurred earlier with PBO (6.1 weeks) vs. APR (not calculable). In the pooled analysis of RELIEF and the phase II study, a significantly greater proportion of patients with GU at baseline achieved GU complete response at Week 12 with APR vs. PBO (21/27 [77.8%] vs. 9/23 [39.1%]; *P*=0.011) (Figure 1). The proportion of patients who were GU-free was significantly greater with APR (92/104 [88.5%]) vs. PBO (72/101 [71.3%]), regardless of baseline number of GU (*P*=0.002) (Figure 2).

Conclusion: The number of patients with GU was low, but the totality of the data shows a favorable trend in the treatment effect of APR on GU. Greater proportions of APR-treated patients were GU-free at Week 12 vs. patients receiving PBO, and the time to the first GU recurrence occurred earlier with PBO vs. APR.

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Figure 2. Complete Response of GU at Week 12* in Patients Regardless of the Number of GU at Baseline



*In the RELIEF study. †*P*=0.002. GU=genital ulcer.

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AB0482 INFLUENCES OF TIME OF INTRODUCTION OF INFLIXIMAB ON THE FUNCTIONAL DISABILITY AND JOB STATUS OF PATIENTS WITH CHRONIC PROGRESSIVE NEURO-BEHCET'S DISEASE

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Background: Chronic progressive neuro-Behcet's disease (CPNBD) is characterized by progressive neurobehaviour changes leading to disability and death. It has been appreciated that methotrexate is effective for CPNBD. Notably, recent studies have demonstrated that infliximab is effective for patients with CPNBD who had inadequate responses to methotrexate. However, the appropriate timing for introduction of infliximab remains unclear.

Objectives: The current studies examined the effects of intervals before introduction of infliximab on the functional disability and job status of patients with CPNBD.

Methods: Eleven patients (8 males, 3 females, ages 35.2±9.3 [mean±SD]), who met the international classification criteria for BD with CPNBD and received infliximab, were retrospectively followed up. The functional disability of the patients was evaluated by Steinbrocker functional classification as is used in rheumatoid arthritis. Correlation between the patients' functional outcome and the intervals before the introduction of infliximab was analyzed by Spearman's rank correlation test.

Results: All the 11 patients had received methotrexate prior to infliximab. The intervals from the onset to the introduction of infliximab and the follow-up periods were 26.6±35.1 months and 65.2±43.6 months [mean±SD], respectively. Among the 11 patients, 9 patients did not show progression after the introduction of infliximab, whereas 2 patients still progressed and lost job. In the latter 2 patients, infliximab had been discontinued before the final follow-up. No patients improved from the functional disability or gained job even after infliximab treatment. The functional disability grades of the patients after the introduction of infliximab were significantly correlated with the intervals from the onset of CPNBD to the introduction of infliximab (r=0.6177, p=0.0476).

Conclusion: The results indicate that the delay of the introduction of infliximab leads to the irreversible functional disability and job loss of the patients with CPNBD. Thus, it is recommended that infliximab should be administered as soon as possible for the patients with CPNBD with inadequate response to methotrexate.

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Disclosure of Interests: : Shunsei Hirohata Speakers bureau: Tanabe Mitsubishi, Hirotoshi Kikuchi Speakers bureau: Tanabe Mitsubishi, Tetsuji Sawada: None declared, Masataka Kuwana Grant/research support from: Acetelion, Consultant of: Acetelion, Bayer, Chugai, Corbus Pharmaceuticals, CSL Behring and Reata Pharmaceuticals. He was a member of the SENSCIS trial Steering Committee (Boehringer Ingelheim), Yohei Kirino: None declared, Mitsuhiro Takeno Speakers bureau: Esai, Tanabe-Mitsubishi – speaker; Celgene Corporation – advisory board, Yoshiaki Ishigatsubo: None declared

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AB0483 INTERSTITIAL LUNG DISEASE IN PATIENTS WITH ANCA ASSOCIATED VASCULITIS – A PROSPECTIVE SINGLE CENTER STUDY

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Background: Recently, an association between anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) and interstitial lung disease (ILD) has been uncovered.

Objectives: To determine the rate of ILD in our prospective AAV patient cohort and to compare clinical characteristics of AAV patients with and without associated ILD.

Methods: We retrospectively analysed medical records of prospectively diagnosed and followed AAV patients at our secondary/tertiary rheumatology centre between January 2010 and December 2019. The diagnosis of ILD was based on lung HRCT findings.

Results: During the 10-year observation, we identified 94 incipient AAV patients (46 had granulomatosis with polyangiitis, and 48 microscopic polyangiitis). Thirteen (13.8%) patients had ILD (ILD-AAV group). 12/13 had usual interstitial pneumonia (UIP) pattern and 1/13 non-specific fibrosis on HRCT. ILD was diagnosed in tandem with AAV in 9/13 patients, and 9 months to 5 years prior to AAV in 4/17 patients. Characteristics of ILD-AAV, and non-ILD-AAV groups are presented in Table 1. ILD-AAV patients more commonly reported of weight loss, less frequently had ENT involvement, and were predominantly a-MPO ANCA positive (92.3%). Follow up data were available for 85 AAV patients (90.4%; 13 ILD-AAV and 72 non-ILD-AAV). During the median (IQR) follow up of 22.1 (4.8; 50.0) months, 5/13 (38.5%) ILD-AAV patients died, compared to 6 (8.3%) deaths registered in non-ILD-AAV group during 26.4 (11.6; 70.0) months of follow up. The crude mortality rate evaluated by Cox proportional hazards regression was significantly higher for AAV-ILD group (HR 5.6 (95%CI 1.7-18.7), p=0.005).

Table 1. Clinical characteristics of ILD-AAV and non-ILD-AAV group

Characteristic	ILD-AAV (13)	non-ILD-AAV (81)	p	Characteristic	ILD-AAV (13)	non-ILD-AAV (81)	p
Female	46.2	64.2	0.234	ENT	0	60.5	<0.001
Age*	76 (67;77)	66 (55;77)	0.174	Heart	0	7.4	0.591
Smoking	61.5	39.5	0.226	GI tract	15.4	7.4	0.305
Fever	61.5	53.1	0.766	Kidney	53.8	63.0	0.552
Weight loss	84.6	51.9	0.035	PNS	38.5	29.6	0.531
Arthritis	15.4	14.8	1.0	CNS	0	2.5	1.0
Myalgia	15.4	27.2	0.504	ANCA	100	91.4	0.588
Skin	7.7	19.8	0.451	a-MPO	92.3	44.4	0.002
Eye	0	24.7	0.063	a-PR3	7.7	46.9	0.013

Legend: * median (IQR)); ENT ear-nose-throat; GI gastrointestinal tract; PNS peripheral nervous system; CNS central nervous system;

Conclusion: In our incipient AAV cohort 13% of patients presented with ILD. The AAV patients with ILD had a higher mortality rate than the rest of the cohort.

References:

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AB0484 PROTEINASE 3–ANTINEUTROPHIL CYTOPLASMIC ANTIBODY (ANCA)–POSITIVE AND ANCA–NEGATIVE OR MYELOPEROXIDASE–ANCA–POSITIVE PATIENTS WITH GRANULOMATOSIS WITH POLYANGIITIS: DISTINCT PATIENT SUBSETS

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Background: Most patients with clinical diagnoses of Granulomatosis with polyangiitis (GPA) are proteinase 3 (PR3)-ANCA positive, but a significant minority are myeloperoxidase (MPO)-ANCA positive or are negative for ANCA [1]. Several clinical and genome-wide association studies have suggested that classification based on ANCA type, i.e., PR3-ANCA positivity as opposed to MPO-ANCA positivity, may be more relevant clinically than the traditional classification based on specific diagnosis [2].

Objectives: To analyze demographic feature, disease manifestations and laboratory findings of patients with PR3-ANCA positive GPA in comparison with patients ANCA-negative or MPO- ANCA positive GPA.
Methods: This is a retrospective analysis of 37 patients with GPA from a single center in Ukraine observed from 2010 till the end of 2019. The clinical and demographic data, initial Birmingham vasculitis activity score (BVAS/WG), erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were compared between patients with PR3-ANCA positive GPA and ANCA-negative or MPO-ANCA positive GPA.
Results: Of the 37 patients analyzed, 24 (64.9%) had PR3-ANCA–positive GPA, 6 (16.2%) had MPO-ANCA–positive GPA and 7 (18.9%) had ANCA-negative GPA. ANCA–negative GPA patients were younger at diagnosis compared to PR3-ANCA–positive and MPO-ANCA-positive patients (36 versus 47 and 49 years; p = 0.04). The gender ratio was similar in patients with PR3-ANCA–positive GPA and patients with MPO-ANCA–positive GPA or ANCA-negative GPA (33% vs 38% male, p= 0.61). The ocular manifestations - conjunctivitis/episcleritis (15% vs 50%) and ear involvement - otitis, mastoiditis (0% vs 33%) occurred more often in patients with PR3-ANCA–positive GPA (p<0.05), whereas sensory peripheral neuropathy (54 % vs 21%) and Raynaud's syndrome (31 % vs 0%) were more frequent in compared group (p<0.05). ANCA-negative patients with GPA had lower, but no significant, initial BVAS/WG score than PR3-ANCA–positive or MPO-ANCA-positive patients with GPA (17.9 versus 23.5 and 24.8; p=0.20). There were no significant differences between groups in ESR or CRP levels and in the frequency of involvement of other organs and systems.
Conclusion: We demonstrate clinical differences between PR3-ANCA–positive patients with GPA and MPO-ANCA–positive or ANCA-negative patients with GPA. The eye and ear involvement are common for patients with PR3-ANCA–positive GPA. The MPO-ANCA–positive GPA or ANCA-negative GPA is characterized by higher frequency of sensory peripheral neuropathy and Raynaud's syndrome.
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AB0485 INVESTIGATION OF PERMANENT ORGAN DAMAGE IN GIANT CELL ARTERITIS: DISEASE FLARES ARE ASSOCIATED WITH INCREASED DAMAGE SCORES

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Background: Development of organ damage is a major concern in patients with systemic vasculitis. Treatment may also contribute to this important outcome. Scoring systems has been developed to evaluate organ damage in systemic vasculitis and specifically for large vessel vasculitis (1).
Objectives: We aimed to investigate permanent organ damage and determining factors in our giant cell arteritis GCA cohort.
Methods: Organ damage detected at the time of diagnosis and / or follow-up and irreversible for at least 3 months in GCA patients followed up between 1998-2018 were recorded by using Vasculitis Damage Index (VDI) and Vascular Vasculitis Damage Index (LVVID) fom patient records of our vasculitis clinic. In the statistical evaluation, chi-square, students t-test and logistic regression analysis were used.
Results: Eighty-nine patients (64% women, mean age 67.9 ± 9.1) included in the study, the mean follow-up duration was 61.6 ± 58.6 months. All organ damage findings according to both VDI and LVVID are shown in table-1. In this cohort, cardiovascular damage items and diabetes mellitus were prevalent at baseline. At least one damage item was present in 53 (59,5%) according to VDI; 54 (%60,7) according to LVVID and agreement was high between two damage indices (kappa=0.97). Forty-seven of patients (52%) had a damage item presumably with contribution of GC treatment e.g. locomotor system findings, hypertension, diabetes and cataract; 12 (13,5%) had damage items related to disease (total or partial vision loss, ischemic optical neuropathy). Mean time to diagnosis after initial symptoms was longer in patients with permanent vision loss (10,2±4,3 vs. 5,2±1,2 months p=0.006). The presence of damage was associated with flares in univariate and multivariate analysis (29/54 vs. 2/35 p<0,001 OR=19 %95 GA 4,2– 87,9). All patients who had a flare during the first year (n = 15) developed signs of damage at follow-up. No association was found between the development of organ damage and the age of diagnosis, the time between first complaint and diagnosis, presence of cranial, ophthalmologic findings, PET-CT positivity, cumulative steroid dose, and DMARD use.
Conclusion: In our study, permanent organ damage was analysed by using different indices. In this patient population baseline cardiovascular damage and diabetes mellitus were frequent as expected but information for osteoporosis was lacking. More than half of the patients had damage and significant part of the present items was considered due to corticosteroid treatment. The most common damage item developed was osteoporosis. There was a very good agreement between the two indices, despite few specific items in LVVID. The striking relationship of disease flare with damage and frequency of visual problems despite treatment indicate the necessity of new treatment strategies.
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Disclosure of Interests: : None declared
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AB0486 ANALYSIS OF 89 PATIENTS WITH GIANT CELL ARTERITIS FROM TURKEY: PET-CT AS AN EMERGING METHOD FOR DIAGNOSIS AND HIGH FLARE RATE WITH STANDARD CARE

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Background: The prevalence of giant cell arteritis (GCA) in Turkey has been reported lower than other European countries and the information on clinical patterns, diagnostic modalities, treatment and prognosis of GCA are limited (1).
Objectives: We aimed to analyse our GCA cohort from a large outpatient clinic for the last 20 years.
Methods: Data of the GCA patients followed up at least for 6 months in our vasculitis clinic between 1998 and 2018 evaluated retrospectively according to EULAR 2018 GCA clinical research recommendations (2). Chi-square, students t-test, logistic regression analysis and Kaplan-Meier test were used for statistical analysis.
Results: Eighty-nine patients with adequate follow-up data (64% female, mean age 67.9 ± 9.1) were analysed. Median follow up duration was 46 months (3-256) and mean time to diagnosis after presenting symptom (TTD) was 5,9±1,2 months (0-60). Polymyalgia rheumatica was found in 36 (40.4%) patients. The clinical findings of the patients are shown in Table-1. Mean TTD was longer in patients with acute vision loss (AVL) (11±4 vs. 4,8±1,1 months p=0.002). Mean CRP was 90,7±82 (8-343) mg/L and ESR was 103,7±25 (52-138) mm/h at the time of diagnosis. Mean age was lower (63±2 vs 69±1 p=0.01); mean CRP (141,8±107,3 vs. 76,6±67,9 mg/dL p=0.023) and ESR (120,8±25,1 vs. 99,3±24,3 mm/h p=0.004) was higher in patients without cranial symptoms (extracranial GCA group). PET-CT findings compatible with large vessel vasculitis were present in 64% (34/53). Sixteen of 19 (%84,2) patients in the extracranial GCA group had positive PET-CT. Temporal artery (TA) biopsy positivity was 64% (34/53). Sensitivity of ACR 1990 Criteria was 77,5% and GIACTA study inclusion criteria was 58,4% in this cohort at diagnosis. Fullfilment of GIACTA criteria was still present in 12 (13,5%) patients after six months of follow up. Treatment data was shown in table-2. Total flare rate was 34,8% and flare risk was lower in the extracranial GCA group (3/20 vs. 28/69 p=0.035 OR=0.78 %95 CI 0.64 – 0.96). Reduced survival was observed in cases diagnosed older than 65 years (168,8±23,9 vs 209±17,3 months p=0,015).
Conclusion: The analysis of the largest single center cohort from Turkey confirmed that delayed diagnosis is associated with vision loss. A subgroup of patients without apparent cranial symptoms but positive PET-CT findings is delineated. These patients are younger, present with higher inflammatory response and fewer relapses. The sensitivity of ACR criteria in our cohort is less than 80%. High flare rate especially in GCA patients with cranial symptoms and GIACTA criteria fullfilment after 6 months of treatment in more than 10% of the patients show a need for for new treatment options.
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Table 1. Clinical characteristics

Systemic / Extracranial Findings	78 (%87,6)	Cranial Findings	69 (%77,5)	Opthalmologic Findings	20 (%22,5)
Fatigue	72 (%80,9)	*Headache*	60 (%67,4)	*AVL*	16 (%18,8)
Weight loss	47 (%52,8)	*Jaw claudication*	33 (%37,1)	*Unilateral*	12 (%13,5)
Arthralgia	43 (%48,3)	*Scalp / TA Tenderness*	27 (%30,3)	*Bilateral*	4 (%4,5)
Fever	35 (%39,3)	*Decreased pulsation of TA*	11 (%12,4)	*Diplopia*	4 (%4,5)
Arthritis	13 (%14,6)	*CVE*	6 (%6,7)		
Vascular murmur	3 (%3,4)	*Swollen TA*	6 (%6,7)		
Pericardial effusion	2 (%2,2)	*Vertigo*	5 (%5,6)		
Extremity Claudication	1 (%1,1)				

TABLE 2 Treatment data of GCA cohort

Initial glucocorticoid (GC) dosage (mg)	46,7±20,1
Pulse GC treatment	%12,3
12nd month cumulative GC dosage (g)	4,7±2,5
MTX usage	%63,3
bDMARD usage	%6,7
Acetyl salicylic acid usage	%51,7

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AB0487 TAKAYASU'S ARTERITIS: RECOGNIZING AN OLD ENEMY

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Background: Takayasu's arteritis (AT) is a systemic vasculitis that affects large vessels, mainly the aorta, its branches and the pulmonary arteries. There are few data on their behavior in our region.
Objectives: to describe the clinical and angiographic characteristics and outcomes of a group of patients with AT.
Methods: a cross-sectional, retrospective study based on a secondary source taken from two high complexity hospitals in Medellin - Colombia between August 2011 and December 2018.
Results: medical records of 41 patients were evaluated, 87.5% met the 1990 ACR criteria of AT. The majority were women (95.1%), with a median age at the time of diagnosis of 22 years (IR 52), 11 patients (26.8%) were over 40 years old at debut. The median delay in diagnosis was 12 months (IR: 167). Systemic symptoms included general malaise (29.3%), weight loss (29.3%) and fever (19.5%); the main vascular manifestations were hypertension and blood pressure difference (61%), headache (39%), upper limb claudication (31.7%), dyspnea (29.3%), angina (26.8%) and carotidinia (22%). Most frequent findings on physical examination were pulse absence or decrease (78%) and subclavian murmur (53.7%). ESR and CRP were found high in 85.3% and 22%, respectively. Angiographic studies revealed stenosis or occlusion in multiple arterial territories, being the stenosis of the left subclavian artery the most frequent lesion (68.3%), followed by the involvement of the abdominal aorta (58.5%) and thoracic (51%). The distribution according to Hata-Numano classification was: type V (58.5%), type I (17.1%) and type IIa (7.3%), indicating complex vascular lesions and associated serious complications. Abnormalities of the renal arteries, pulmonary arteries involvement, and aortic insufficiency were present in 39%, 14.6%, and 7.3% respectively. Seventy-five percent of patients had active disease, glucocorticoids were the main treatment in 90.2% of the cases, used isolated (2.4%) or in combination with other immunosuppressants (87.8%), including methotrexate (75.6%), azathioprine (26.8%) and cyclophosphamide (14.6%); vascular interventions were performed in 11 patients (26.8%). Most relevant vascular complications were renovascular hypertension (26.8%), stroke (19.5%), chronic kidney disease (19.5%) and chronic heart failure (17.1%). From the clinical point of view, our findings were similar to those shown in series from Brazil, Japan, and Turkey. Contrary to what was reported in other series, carotidinia was a finding that occurred in almost a quarter of our patients (23%) and maybe one of the initial symptoms of the disease. The findings of the vascular physical examination are similar to those reported by the IRAVAS group, where the asymmetry of the pulses was most frequent, followed by the presence of murmurs and the difference in blood pressure, claudication being less frequent in the upper and lower limbs.
Conclusion: patients in this series are characterized by having an extensive disease partly due to a late diagnosis, with a high percentage of complications associated with vascular stenotic compromise, which generates morbidity and impact on the quality of life.
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AB0488 CAN A GCA RISK STRATIFICATION SCORE BE HELPFUL IN CLINICAL PRACTICE?

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Background: Giant cell arteritis (GCA) is the most common type of large vessel vasculitis. Typically it presents in patients over the age of 50 with a combination of temporal headaches, scalp tenderness, jaw claudication, raised inflammatory markers and visual disturbance. The diagnosis of GCA is often challenging and there is a difficult balance of over and under investigation. There have been several proposed scoring systems to help clinicians risk stratify patients who may present with suspected GCA. One such scoring system, published in 2017, showed clinical utility in a large international multi-centre study. Following analysis

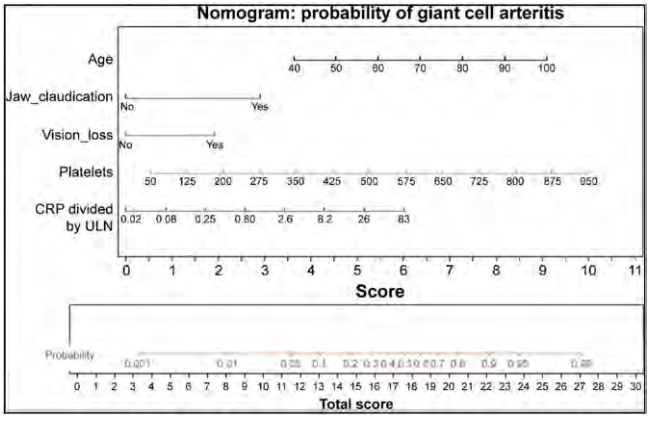


Figure 1. Ing et al's Nomogram of parsimonious model.

by logistic regression on data from 530 biopsies, Ing et al. developed a parsimonious prediction model comprising 5 candidate criteria: age, jaw claudication, ischemia-related loss of visual acuity, platelet count and logCRP (Figure 1). [1]
Objectives: Increasingly, ultrasound doppler imaging is recognised and accepted as satisfactory means of confirming the diagnosis of GCA, with the presence of the halo sign characteristic for GCA. The aim of our study was to determine whether this GCA prediction model accurately predicts positive temporal artery biopsies in a large, real world UK cohort. In addition, we assessed whether this model accurately predicts positive temporal artery ultrasounds.
Methods: A retrospective cohort study was performed using electronic medical records of patients referred for temporal artery biopsy (TAB) and temporal artery ultrasound (USTA) for suspected GCA. All TAB performed at the Royal Wolverhampton NHS Trust between June 2014 - June 2018 and all USTA performed between January 2015 - January 2019 were analysed. Patients who undergo USTA for suspected GCA at our centre routinely have bilateral temporal and axillary arteries scanned. Patients were excluded if they already had a previous diagnosis of GCA (and the clinical question was suspected flare), or if there was insufficient information available.
Results: The total number of patients who underwent a confirmatory diagnostic test (either TAB or USTA) for suspected GCA was 187. Thirteen of these patients met the exclusion criteria, the remaining 174 patients were included for analysis. 126/174 patients underwent a TAB, 63/174 had an USTA. 15/174 had both these were included in the USS cohort because for all these patients the ultrasound was the first diagnostic test performed (Table 1). Our results appear to closely mirror the original multi-centre results with regards to prediction of biopsy positive GCA, with the centiles closely following those in the inception cohort. 0% of the 'low' risk probability biopsy cohort were misclassified - none had a positive biopsy. However, 8% of the 'low' risk probability ultrasound cohort were misclassified - 2 had a positive ultrasound.

Table 1. Investigation outcome summary

Total number of patients who underwent TAB +/ or USS TA for?GCA			
187 - 13 patients rejected			
N = 174			
TAB = 111		USS = 63 Of these 15 patients had *both* USS & TAB	
Positive TAB = 31 (28%)	Negative TAB = 80 (72%)	Positive USS = 24 (38%)	Negative USS = 39 (62%)

Conclusion: Our study, highlights that a probability score for GCA derived from a large multi-centre cohort of patients who were biopsy positive, predicts ultrasound positivity with similar accuracy. Our work reveals that scoring systems are not infallible but can be helpful in guiding clinical decision making

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AB0489 BETA 2 MICROGLOBULIN AS A PROGNOSTIC FACTOR IN CRYOGLOBULINEMIA NON ASSOCIATED WITH HEPATOTROPIC VIRUSES

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Background: Cryoglobulinemia (CG) is a rare phenomenon related to haematological disorders, infections and autoimmune diseases. Age and renal involvement are known prognostic markers.

Objectives: To describe the differential clinical features and the prognostic factors in a cohort of patients diagnosed with CG non-associated with hepatotropic viruses.

Methods: A descriptive, retrospective study of a cohort comprised of 252 cryoglobulin positive samples, obtained from the immunology laboratory database of a tertiary hospital attending 450,000 people over 1 year. 186 patients with CG positive samples were included, 87 of which were not associated with neither hepatitis B nor C virus. Demographic, clinical, serological and pathological data were collected. Nonparametric variables were compared using a Wilcoxon test.

Results: Out of 186 reviewed patients, 87 (46.7%) are included in this study. The mean age at CG diagnosis was 60 (± 16) years. Mixed CG was the predominant subtype, detected in 66 (75.9%) patients, 10 of which (11.5%) were associated with glomerulonephritis (GN) with compatible biopsy, 17 (19.5%) with peripheral neuropathy (PN), 29 (33.3%) with non-erosive arthritis and 10 (11.5%) with leukocytoclastic vasculitis confirmed by skin biopsy. The clinical, epidemiological and serological characteristics of the sample are summarized in Table 1.

Table 1. Clinical, epidemiological and serical characteristics of patients with CG

Sex, female / male, n (%)	65/22 (74.7/25.3)
Age at diagnosis, years ± SD	60 ± 16
CG subtype, n (%)	
- Type 1, n (%)	27 (30)
- Mixed, n (%)	61 (70)
ASSOCIATED DISEASES	
- pSS, n (%)	37 (42,5)
- LES, n (%)	9 (10,3)
- SSc, n (%)	7 (8,05)
CLINICAL CHARACTERISTICS	
- Skin, n (%)	30 (34,5)
- Purpura, n (%)	14(16)
- Ulcers, n (%)	5 (5,7)
- Acral ischemia, n (%)	2 (2,3)
- Acrocyanosis by cold, n (%)	7 (8)
- Raynaud, n (%)	19 (21,8)
- Peripheric Neuropathy, n (%)	17 (19,5)
- Non-erosive arthritis, n (%)	29 (33,3)
- Glomerulonephritis, n (%)	10 (11,5)
LABORATORY	
- β2M +(>1.8 mg/L) mean	3.9
- RCP (mg/L) p50	3.7
- ESR (mm/hour) p50	28
- RF + (>20 UI/mL) p50	124
- Anti Ro52 + /Anti Ro60 + n, (%)	42 (48.3)
- Low C3 n, (%)	48 (55.1)
- Low C4 n, (%)	36 (41.4)

In the comparative analysis of patients with CG and Beta 2 microglobulin (β2M), CG and rheumatoid factor (RF), those with high β2M (>1.8 mg / L) presented significantly more GN (p0.016) and PN (p0.013). However, the association of RF with either GN (p0.948) or PN (p0.645) was not significant. Also, high β2M was significantly related to complement consumption of C4 (p: 0.015) but not of C3 (p: 0.063). In the 30 (34.5%) patients with skin manifestations, high β2M showed no statistically significant association. The main systemic autoimmune diseases associated were primary Sjögren's Syndrome (pSS) 37 (42.5%), Systemic Lupus Erythematosus (SLE) 9 (10.3%) and Systemic Sclerosis (SSc) 7 (8.05%).

Conclusion: A direct association between presence of elevated levels of β2M and the existence of progression to glomerulonephritis and peripheral neuropathy is found in our cohort. No correlation is found between the presence of CG and other serological markers of autoimmunity except low C4. CG with elevated β2M does not associate with greater skin involvement or arthritis.

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AB0490 CIRCULATING REGULATORY T CELLS WERE ABSOLUTELY DECREASED IN TAKAYASU'S ARTERITIS PATIENTS

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Background: Takayasu arteritis (TA) refers to chronic progressive non-specific inflammation that involves the aorta and its main branches, causing stenosis and occlusion of arteries in different parts, and ischemic manifestations in the corresponding parts. A variety of immune dysfunctions are involved in the occurrence and development of TA[(1)] Recent studies have shown that Th17/Treg imbalance plays an important role in the pathogenesis of Takayasu's arteritis, in which T help 17 cells (Th17) cells are up-regulated in TA patients[(2)]. Th17 cells are closely related to Treg cells during differentiation. There are few studies on the expression level of CD4+CD25+FOX3+T lymphocyte (Treg) cells. This study aims to study the clinical significance of Treg cell expression in peripheral blood of patients with Takayasu's arteritis.

Objectives: To analyze the levels of circulating lymphocyte subsets and serum cytokines in patients with takayasu arteritis (TA), and explore the relationship between their changes and TA disease activity.

Methods: A total of 46 TA patients and 43 gender-age-matched healthy controls were enrolled. According to the NIH standard, 30 patients were in active disease. Flow cytometry was used to detect the absolute numbers and ratios of Th1, Th2, Th17 and Treg cells in peripheral blood of all subjects. Magnetic bead-based multiplex immunoassay was used to detect cytokines and statistical analysis was performed.

Results: Compared with the healthy controls, the absolute number and proportion of peripheral Treg cells of TA patients significantly decreased while those of Th17 cells increased significantly, leading to the increased ratio of Th17 / Treg. Compared with the inactive group, the TA active group had significantly increased IL-6 and TNF-α, and there was no significant difference in the expression of Th17 cells and Treg cells.

Conclusion: In peripheral blood of TA patients, Treg cells decreased, while Th17 cells increased as compared with healthay controls, leading to an imbalance between Th17 and Treg cells. The levels of IL-6 and TNF-α were related to disease activity.

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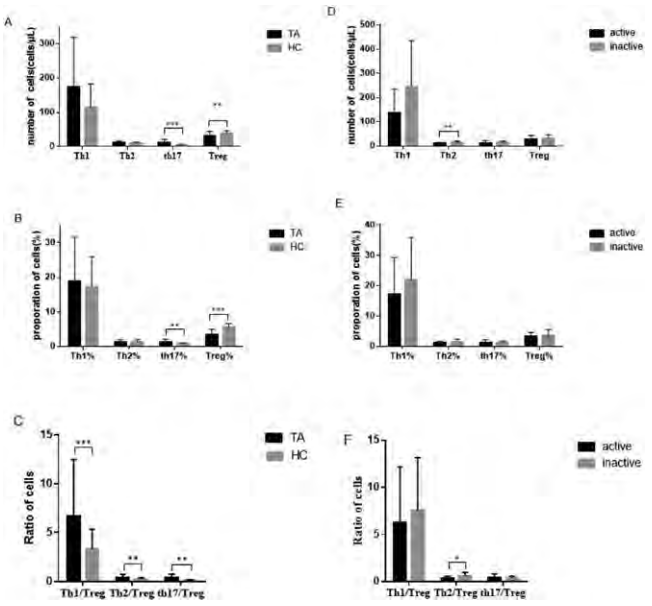


Figure 1. Characteristics of the absolute numbers and proportions of Th1cells,Th2cells,Th17 cells and CD4Treg cells in the PB of patients with TA.(A-C)The levels of Th17 cells and the ratio of Th1/Treg,Th2/Treg,Th17/Treg in PB were significantly increased in patients with TA (n=46). The absolute number and the proportion of CD4Treg cells were significantly decreased in TA(n=46). (D-F) The absolute number of Th2 cells and ratio of Th2/Treg in PB were significantly decreased in active patients with TA (n=30).Neither the absolute number nor proporation of Th1, Th17 and Treg cells was altered significantly between active TA patients(n=30) and inactive TA patients(n=16).*P<0.05; **P<0.001. P<0.05 was considered statistically significant. TA,takayasu arteritis;PB peripheral blood;Tregs, regulatory Tcells.

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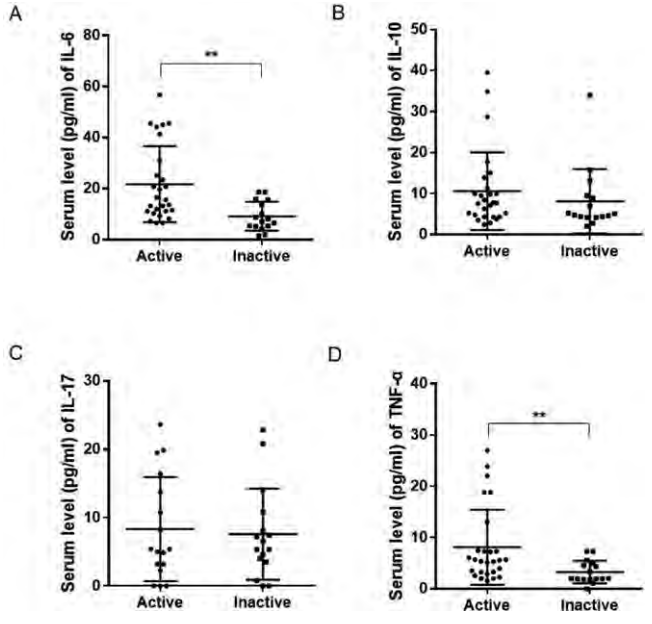


Figure 2. Characteristics of serum concentrations of cytokine (including IL-6, IL-10, IL-17 and TNF-α) between active TA patients(n=30) and inactive TA patients(n=16).(A,D)In terms of cytokines, the concentration of IL-6 and TNF-α was significantly up-regulated,(B,C)but no significant changes in IL-10, and IL-17 were found.*P<0.05; **P<0.001. P < 0.05 was considered statistically significant.

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AB0491 ELEVATED COMPLEMENT 3 INDICATES DISEASE ACTIVITY IN TAKAYASU ARTERITIS

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Background: The disease activity evaluation of Takayasu arteritis (TA) is a critical issue for disease monitoring and treatment. But the previous markers such as Kerr score or ITAS 2010 are not convenient enough.
Objectives: We aim to explore novel biomarkers to assess TA disease activity.
Methods: This cross-sectional study was based on the East China TA (ECTA) cohort. Demographic characteristics, clinical features, laboratory and imaging results were collected. Complements and their combination with other biomarkers in identifying active disease (Kerr >= 2) group were analyzed. Internal and external validation were employed to confirm the accuracy and stability of the results.
Results: 519 patients were enrolled, among which 406 cases (72.2%) were identified as active disease. Higher ESR, CRP, platelet, globulin, IgG, IL-6, complement 3 (C3), complement 4 (C4) and median haemolytic complement (CH50) levels were observed in the active disease group. Logistic regression analysis demonstrated that C3 levels [odds ratio [OR] (95%CI): 10.710(1.825 – 62.835), P = 0.009] and CRP [OR (95%CI): 1.041(1.009 – 1.073), P = 0.011] were independently associated with active disease. The cut-off of C3 to identify active TA was 1.085 g/L, with 69.9% sensitivity, 66.7% specificity. Combining the CRP (cut-off, 10.65g/L; sensitivity, 50.7%; specificity, 82.4%) and C3, the sensitivity and specificity to identify the active disease were 85.1% and 55.0% (parallel test), and 35.4% and 94.1% (serial test), respectively. C3 could significantly improve the diagnostic ability of CRP [net reclassification index: OR (95%CI): 1.728 (1.556–1.990), P = 0.000; integrated discrimination index: OR (95%CI): 0.328 (0.224–0.431), P = 0.000]. The accuracy of the 10-fold cross validation of combining CRP with C3 was over 75%, and the accuracy of the external validation with 53 TA cases was 72.73%.
Conclusion: C3 could reflect the disease activity of TA, and combining CRP with C3 could significantly improve the disease activity evaluation in TA.
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AB0492 INTESTINAL MICROBIOTA COMPOSITION OF PATIENT'S WITH BEHCET'S DISEASE: DIFFERENCES BETWEEN EYE, MUCOCUTANEOUS AND VASCULAR INVOLVEMENT (RHEUMA-BIOTA STUDY)

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Background: Recently, it has been shown that changes in microbiota composition play a role in the etiology and pathogenesis of chronic diseases. Changes in oral and intestinal microbiota diversity and composition are suggested in Behcet disease (BD), however there are no study available about the potential gut microbiota changes among different clinical forms of BD.
Objectives: The aim of this study was to evaluate the intestinal microbiota composition of patient with BD and healthy controls, and also compare BD patients regarding to their eye, mucocutaneous and vascular involvement.
Methods: In this prospective cohort study,27 patients diagnosed with BD and 10 aged and sex matched healthy controls were included. Patients with a body mass index> 35, who have used antibiotics or probiotics in the last 4 weeks, patients with chronic gastrointestinal or other systemic diseases, and those with acute / severe gastrointestinal symptoms requiring medical treatment were excluded from the study. For the intestinal microbiota analysis, gene amplification, library formation, sequence analysis and bioinformatic evaluation of the results were performed with 16SrRNA next generation sequencing methods with Illumina MiSeq.
Results: There was no difference between the BD group and the control group in terms of alpha (Chao-1 and Shannon) and beta (Bray-Curtis) microbiota diversity indices (p> 0.05). *Actinomyces, Libanicoccus, Collinsella, Eggerthella, Enetrohabdus, Catenibacterium and Enterobacter* were significantly higher in BD group compared to the

control group. In addition, *Bacteriodes, Cricetibacter, Alistipes, Lachnospira, Dielma, Akkermansia, Sutterella, Anaerofilum, Ruminococcease-UCG007, Acetanaerobacterium; and Copropaacter* were lower than the control group. There was no difference between the uveitis, mucocutaneous and vascular involvement groups in terms of alpha (Chao-1 and Shannon) and beta (Bray-Curtis) microbiota diversity and wealth indices (p> 0.05) while we obtained a significant p value of the beta diversity between three groups in weighted UniFrac PCoA (p<0.05). When we compared 3 three different system involvement (Eye, Mucocutaneous and Vascular), The LEfSe provides us with cladograms of six-level (from kingdom to genus). We found difference for the genera *Lachnospiraceae NK4A136* in uveitis group, *Dialister, Intestinomonas and Marvinbryantia* in mucocutaneous group and *Gemella* in vascular involvement group.

Conclusion: There was a significant difference in the composition of intestinal microbiota in Behçet's disease compared to healthy adults. We found also found the different clinical forms of Behcet's disease have some different gut microbiota composition. Especially in Behçet's disease, it will be useful to evaluate *Catenibacterium, Collinsella and Eggerthella* increase, *Bacteroides and Akkermansia* decrease in larger series. In addition, due to the increase in the *Eggerthella lenta* strain observed both in the FMF and Behcet patient group, it is useful to make more detailed metagenomic analyzes regarding the role of this agent in the etiopathogenesis and course of rheumatic diseases.

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AB0493 COMPARISON OF EFFICACY AND SAFETY BETWEEN RITUXIMAB AND CYCLOPHOSPHAMIDE IN REMISSION INDUCTION THERAPY FOR JAPANESE ANCA-ASSOCIATED VASCULITIS(AAV) PATIENTS; A SINGLE CENTER RETROSPECTIVE ANALYSIS

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Background: Rituximab(RTX) and Cyclophosphamide(CY) has been indicated for ANCA-associated vasculitis(AAV) as remission induction therapy. However, older age and renal disfunction were independent predictor of treatment related adverse effects in remission induction with CY in recent reports [1)]. Japanese AAV patients are characterized by the predominance of elderly, and the study about comparison of efficacy and safety between RTX and CY in elderly Japanese AAV patients are limited.

Table 1. Comparison of clinical characteristics at baseline between RTX and CY groups.

	RTX (n=20)	CY (n=20)	p value
Age, year	72.3 ± 11.0	74.8 ± 8.01	0.55
female, n (%)	16 (80)	18 (90)	0.33
AAV type			0.14
MPA, n (%)	13 (65)	17 (85)	
GPA, n (%)	7 (35)	3 (15)	
Newly diagnosis, n (%)	7 (35)	4 (20)	0.24
ANCA positivity			
MPO, n (%)	20 (100)	17 (85)	0.12
PR3, n (%)	1 (5)	2 (10)	0.50
negative, n (%)	0 (0)	2 (10)	0.24
eGFR (mL/min)	55.0 ± 29.5	58.1 ± 21.5	0.45
Organ involvement			
General, n (%)	14 (70)	19 (95)	0.046*
Cutaneous, n (%)	1 (5)	3 (15)	0.30
Eyes, n (%)	4 (20)	1 (5)	0.17
ENT, n (%)	5 (25)	5 (25)	1.00
Pulmonary, n (%)	14 (70)	15 (75)	0.50
Renal, n (%)	14 (70)	13 (65)	0.50
Neurologic, n (%)	8 (40)	4 (20)	0.15
BVAS	13.8 ± 6.6	14.1 ± 7.6	0.73

RTX: Rituximab, CY: Cyclophosphamide, ANCA: antineutrophil cytoplasmic autoantibody, AAV: ANCA-associated vasculitis, GPA: granulomatosis with polyangiitis, MPA: microscopic polyangiitis, ENT: Ear, Nose, and Throat, BVAS Birmingham Vasculitis Activity Score, * p <0.05

Table 2. Adverse effects through 12 months. % = patients with 1 effects

	RTX (n=20)	CY (n=20)	p value
Death, n (%)	1 (5)	0 (0)	0.50
Infections, n (%)	7 (35)	8 (30)	0.46
Serious (grade 3), n (%)	4 (15)	3 (10)	0.50
Malignancy, n (%)	1 (5)	0 (0)	0.50
VTE, n (%)	1 (5)	0 (0)	0.50
AMI, n (%)	1 (5)	0 (0)	0.50
Leukopenia, n (%)	3 (15)	3 (10)	0.70
Necrosis of femoral head, n (%)	0 (0)	1 (5)	0.50
Mediastinal emphysema	0 (0)	1 (5)	0.50

VTE: venous thrombotic emboli, AMI: acute myocardial infarction

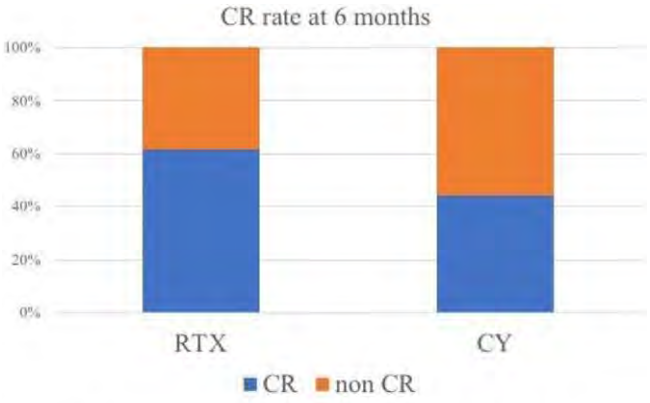


Figure 1. Complete remission rate at 6 month in the two groups. CR: complete remission, RTX: Rituximab, CY: Cyclophosphamide

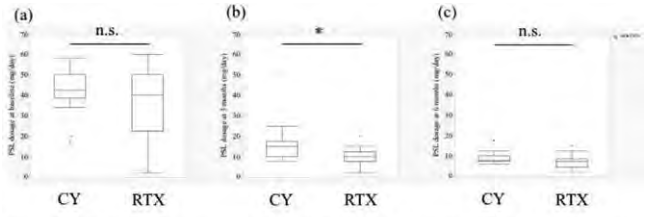


Figure 2. PSL dosage in two groups. (a) PSL dosage at baseline (b) PSL dosage at 3 months (c) PSL dosage at 6 months. PSL: prednisolone, CY: Cyclophosphamide, RTX: Rituximab, n.s. not significant, * p<0.05

Objectives: To compare the efficacy and safety between RTX versus CY as remission induction therapy in Japanese AAV patients.

Methods: We analyzed 40 cases (20 cases received RTX and 20 cases received CY) who received remission induction therapy in our hospital between January 2016 and August 2019. Clinical and laboratory variables at diagnosis, rates of complete remission(CR) at 6 months, defined as Birmingham Vasculitis Activity Score (BVAS)=0 and prednisone 7.5 mg/day, AAV relapse at 12 months, and adverse effects were investigated.

Results: Of 40 patients, mean age was 73.5±9.6 years (6 males and 34 females). Diagnosis of MPA and GPA were 30 cases and 10 cases, respectively. 37 cases (93%) were positive for MPO-ANCA. Treatment regimen was determined by attending physician. Baseline characteristic of each group (RTX group and CY group) are shown in Table1. Baseline charactor, disease activity, organ involvement, and the proportion of patients with relapsing disease were similar in the two treatment groups. At 6 months, there was no difference of remission rate between two groups (RTX: CY = 62%: 44%, p=0.35) (Figure 1). However, mean PSL dosage at 3 months was significantly lower in RTX group (10.0±4.6mg/day) as compared to CY group (15.8±9.5mg/day; p=0.025) (Figure 2). At 12 months, 1 case in CY group and no case in RTX group had relapse. Adverse effects through 12 months are shown in Table 2. 8 infections (30%) in CY group and 7 infections (35%) occurred in RTX group (p=0.64), respectively. 1 case in RTX group had died due to renal failure.

Conclusion: We indicated that PSL was tapered more rapidly in RTX group, although there was no difference of remission rate at 6 months and infection at 12 months between RTX and CY therapy. Therefore, remission induction therapy with RTX might be more safety for elderly Japanese AAV patients.

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AB0494 CHARACTERISTICS OF THE PATIENTS WITH POLYARTERITIS NODOSA IN JAPAN

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Background: Since the number of polyarteritis nodosa (PAN) patients is small not only in Japan but also in the world, the characteristics of PAN have not been fully clarified and appropriate treatment has not been established.
Objectives: This study aimed to describe the epidemiological and clinical features and treatment of patients with PAN in Japan.
Methods: We used the database of the Ministry of Health, Labour and Welfare (MHLW) in 2013 and 2014. Data of 178 patients who fulfilled the diagnostic criteria by MHLW and had registered within a year after onset of PAN was analyzed.
Results: The analysis included 75 males and 103 females, with a mean age of 64.5 ± 20.3 years. PAN was diagnosed by clinical symptoms in 27.6% of the patients, 11.5% of the patients by pathological findings, and the rest of the patients by both. Pathological examination was performed in 71.3% of the patients, of whom 11.2% had evidence of necrotizing vasculitis of the small and medium arteries. As a systemic symptom, fever was observed in 55.2% of cases. As organ symptoms, muscle and joint symptoms (74.7%), skin symptoms (73.0%), neuropsychiatric symptoms (50.0%), respiratory symptoms (32.6%), and renal symptoms (19.7%) were common. Patients aged 65 or older had a higher rate of systemic, renal and respiratory symptoms, and lower rate of skin symptoms compared with the patients younger than 65. Patients with renal symptoms had a high prevalence of respiratory, cardiac and ocular symptoms, while those with respiratory symptoms had a high prevalence of systemic and cardiac symptoms. Laboratory findings showed that MPO- and/or p-ANCA positive rate was 30.5% and PR3- and/or c-ANCA positive rate was 11.0%. The Hepatitis B antigen positive rate was 3.9%. Angiography was performed in 20.7%, among which 27.0% were found to have multiple small aneurysms, wall irregularities and stenosis at the abdominal aortic branches. Glucocorticoids were used for treatment in all cases with an average maximum prednisolone dose of 32.5 mg/day. Concomitant immunosuppressants were used in 28.7%, half of which was cyclophosphamide. In other cases, azathioprine or methotrexate was used. Immunosuppressants have been used more frequently in patients with systemic symptoms and nasal and ear symptoms. Among the immunosuppressants, cyclophosphamide tends to be used for patients with higher CRP or patients with respiratory symptoms, and the maximum dose of glucocorticoids was significantly higher in patients who used cyclophosphamide compared to those who used other immunosuppressants.
Conclusion: PAN developed in middle-aged and elderly people and exhibited various clinical symptoms. We found that common symptoms varied with age, and treatment options were determined depending on the types of organ symptoms and severity. Hepatitis B virus infection was rare in patients with PAN in Japan.
References: None.
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AB0495 SERUM HIGH MOBILITY GROUP BOX-1 LEVEL IN PATIENTS WITH BEHCET'S SYNDROME AND ITS RELATIONSHIP WITH DISEASE ACTIVITY AND CLINICAL FEATURES

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Background: Behcet's Syndrome (BS) is a chronic, multisystemic inflammatory disease. High Mobility Group Box-1 (HMGB-1) is a nuclear protein and acts as a proinflammatory molecule. The serum HMGB-1 levels were found high in various chronic inflammatory diseases.
Objectives: In this cross-sectional study, serum HMGB-1 levels in patients with BS and healthy controls were studied. Also, its association with disease activity scores and clinical findings in BS were evaluated.
Methods: Between March 2018 and March 2019, 90 BS patients and 50 age-sex matched healthy controls were included. Disease activity scores were assessed by using Behcet Disease Current Activity Form (BDCAF) and Behcet Syndrome Activity Score (BSAS). A p-value of <0.05 was considered to be statistically significant.
Results: The demographic and clinical features were summarized in Table 1. Serum HMGB-1 levels were significantly higher in BS than those in control group. (Table 1) The statistically significant corelation of serum HMGB-1 level with current clinical findings was found only in patients having eryhtema nodosum and genital ulcers in the last 1 month. The eye, central nervous system (CNS), gastrointestinal system (GIS), arterial and venous involvements were classified together as major organ involvement (MOI) (n=47). The serum HMGB-1 level was higher in patients with MOI compared to patients without MOI; however,it was not statistically significant.(40.5pg/mL and 37.2 pg/mL, p=0.560) BDCAF and BSAS scores were positively corelated with serum HMGB-1 level (p=0.022, p=0.026 respectively). (Table 2)

Table 1. Demographic features and HMGB-1 levels of study groups with current clinical findings of BS patients

	Behcet Syndrome	Control Group	P value
Age (years) (±SD)	42.1±9.6	39.5±10.6	0.128
Sex (Women) n(%)	51 (56.7)	32 (64)	0.401
Disease Duration (years)	10 (1-37)		
Serum HMGB-1 level (pg/mL)	43.26 (0-221.3)	16.730-41.9)	**<0.001**
Oral Ulcers n(%)	100 (100.0)		
Genital Ulcers n(%)	68 (75.6)		
Erythema Nodosum n(%)	52 (57.8)		
Papulopustuler Eruption n(%)	59 (65.6)		
Patergy pozitivity n(%)	37 (41.1)		
Uveitis n(%)	27 (30.0)		
Retinal vasculitis	2 (2.2)		
CNS involvement n(%)	7 (7.8)		
GIS involvement n(%)	2 (2.2)		
Athralgia n(%)	75(83.3)		
Arthritis n(%)	15 (16.7)		
Arterial disease n(%)	3 (3.3)		
Venous disease n(%)	25 (27.8)		

Table 2. Corelation between Serum HMGB-1 level and inflammatory markers in BD

	HMGB-1	
	r	*p*
ESR (mm/h)	-0,04	0.68
CRP (mg/L)	0,12	0.23
Neutrophil/Lymphocyte	0,14	0.20
Platelet/Lymphocyte	0,02	0.89
BSAS	**0,24**	**0.02**
BDCAF	**0,24**	**0.03**

Conclusion: The two studies evaluating the relationship between serum HMGB-1 level and disease activity in BS found higher levels of serum HMGB-1 level in BS than in healthy controls as in our study[1,2]. This result supports the importance of HMGB-1 in the development of BS through its role in inflammation. De Souza et al. found no association between BDCAF

and serum HMGB-1 level; whereas, we found a positive correlation with both BDCAF and BSAS[2]. This suggests that HMGB-1 can be used as a new disease activity parameter in BS. In conclusion, this study is unique as it involves the largest number of BS patients and uses BDCAF and BSAS together to assess disease activity

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AB0496 AUTOANTIBODIES TARGETING COMPLEMENT RECEPTORS 3A AND 5A1 ARE DECREASED IN ANCA-ASSOCIATED VASCULITIS AND CORRELATE WITH HIGHER RELAPSE RATE.

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Background: Activation of the alternative and final common pathways have been shown in ANCA-associated vasculitis (AAV) (1). Circulating titers of C5a are elevated and correlate with disease activity in AAV. Binding to the corresponding G protein-coupled receptor (GPCR) C5aR1 enhances the influx of neutrophils, leading to ROS generation and severe necrotizing of vascular walls (2). Moreover, subsequent interaction of C5a with C5aR1 may represent a proinflammatory amplification loop (3). Blocking of the receptor is protective in a murine model in AAV (4). In humans, avacopan, a C5aR1-inhibitor showed promising results as glucocorticoid-sparing agent in two randomized phase II and one ongoing phase III clinicals trials in AAV (NCT02994927). Notably, disease-specific anti-GPCR autoantibody (aab) signatures have been found in different autoimmune diseases (5).

Objectives: The aim of the present study was to examine whether (patho)physiological anti-C3aR and anti-C5aR1 aabs correlate with clinical findings in AAV, and whether this is linked to the clinical outcome.

Methods: Sera and plasma of AAV patients [granulomatosis with polyangiitis (GPA), n=64; microscopic polyangiitis (MPA), n=26; eosinophilic granulomatosis with polyangiitis (EGPA), n=11] were measured by Elisa for circulating autoantibodies against complement receptors C3a (anti-C3aR aab) and C5a (anti-C5aR1 aab) and plasma levels of C3a and C5a. Expression of C3aR and C5aR1 on T-cells was determined using flow cytometry. Clinical data were assessed at the time of serum sampling and during follow-up for 48 months

Results: GPA displayed low titers of anti-C3aR aab (GPA:5.33±2.54 *vs*. HD:6.47±2.61, P=0.0031). Anti-C5aR1 aab were decreased in AAV, especially in GPA (GPA:1.02±1.07 *vs*. HD:6.63±2.91, P=<0.0001). Plasma levels of C5a and anti-C5aR aab yielded an inverse correlation in AAV (r=-0.6813, P=0.0127). C5aR1 expression was increased on T-cells in GPA (CD4+C5aR1+T-cells: GPA:10.76±2.55% *vs*. HD:3.44±0.68%, P=0.0021; CD8+C5aR1+T-cells GPA:9.74±2.10% *vs*. HD:4.11±0.92%, P=0.0198). Reduced titers of anti-C5aR1 aab <0.45U/ml displayed an increased relapse risk for major organ involvement in GPA (HR 12.85, P=0.0014).

Conclusion: As potential diagnostic marker, anti-C5aR1 aab titer may additionally be useful to monitor disease activity in AAV.

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AB0497 RENAL INVOLVEMENT IN ANCA-ASSOCIATED VASCULITIS: DO THE PRESENCE OF ANCA AND THEIR TYPE MATTER?

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Background: The role of ANCA type is well established for the risk of relapses of ANCA-associated vasculitis (AAV). However their association with renal involvement and its outcomes is less well understood.

Objectives: To assess clinical and morphological features of ANCA-associated glomerulonephritis (ANCA-GN) and renal survival in ANCA-negative patients, proteinase-3-ANCA (pr3-ANCA) positive and myeloperoxidase-ANCA (MPO-ANCA) positive patients.

Methods: We enrolled 53 patients with AAV, diagnosed according to Chapel Hill Consensus Conference (2012) definition and/or ACR (1990) criteria, with histologically proven renal involvement. There were 13 (24.5%) males, median age at onset was 48 (33; 57) years. Seven patients were ANCA-negative (13.3%), 17 (32.0%) patients were pr-3-ANCA positive and 29 (54.7%) patients were MPO-ANCA-positive. ANCA-associates glomerulonephritis (ANCA-GN) class was established according to Berden et al classification.[1] We retrospectively assessed ANCA renal risk score (ARRS) at disease onset.[2] Twelve patients (22.6%) developed end-stage renal disease (ESRD) after a median of 12 (6.5; 28) months. Renal survival rates were assessed by Kaplan-Meier method and compared by log-rank test.

Results: The only significant difference was median BVAS score which was significantly higher in pr3-ANCA-positive (18 (17;20)) than in MPO-ANCA positive patients (15 (12; 18), p=0.012). Creatinine levels, eGFR, percentage of glomeruli with crescents, global sclerosis, and interstitial fibrosis and tubular atrophy didn't depend on the presence of ANCA or type of the antibodies. The proportion of patients with focal, crescentic, mixed of sclerotic class of ANCA-GN was similar in all groups. There was no significant difference in the numbers of patients with low, medium or high risk of ESRD according to ARRS. One- and three-year renal survival rates were similar in ANCA-negative (81.7% and 60.0% respectively) and ANCA-positive patients (84.2% and 74.6% respectively, Figure 1A). One-year and three-year survival rates were higher in MPO-ANCA-positive (84.4% and 84.4% respectively) than in pr3-ANCA-positive patients (73.1% and 50.1% respectively), however the difference was not statistically significant (Figure 1B).

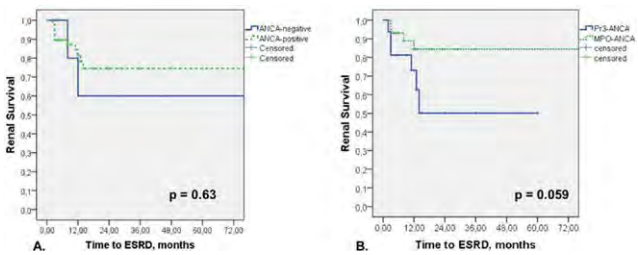


Figure 1. Kaplan-Meier curves showing renal survival in ANCA-positive and ANCA-negative patients (A), and pr3-ANCA-positive and MPO-ANCA-positive patients (B)

Conclusion: Our small study indicates that clinical and morphological features of renal involvement, as well as renal survival are similar in ANCA-negative and ANCA-positive patients and don't depend on the type of ANCA.

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AB0498 CHARACTERISTICS AND OUTCOME OF CORONARY ARTERY LESIONS DUE TO POLYARTERITIS NODOSA: ANALYSIS OF A SINGLE CENTER COHORT IN CHINA

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Background: Polyarteritis nodosa (PAN) is a systemic necrotizing vasculitis that mainly affects medium-sized muscular arteries. The coronary artery could be affected. Some severe cases can lead to spontaneous coronary artery dissection (SCAD) and about 0.02% will die abruptly. Early diagnosis will improve prognosis, but relative studies are all case reports so far.

Objectives: To investigate the clinical characteristics, risk factors and outcome of patients with polyarteritis nodosa (PAN) complicated with coronary artery lesions in China.

Methods: Data of 158 patients with PAN who were admitted to Peking Union Medical College Hospital from September 1986 to September 2019 were retrospective collected. Data were analyzed and compared according to with and without coronary artery lesions due to PAN.

Results: 17 (10.8%) patients with PAN had the coronary artery lesions due to PAN. The age at coronary artery lesion was 36.9±10.3 years. 12 (70.6%) patients were male. There are not statistical differences between two groups in common risk factors of coronary arterial atherosclerosis including smoking, hypertension, diabetes mellitus and hyperlipidemia. Most of them are multi-vessel lesions (8 cases are triple-vessel lesions and 3 cases are bi-vessel lesions). Type of coronary artery affected is shown mainly in stenosis (13 cases). Myocardial infarction are shown in 8 cases (47.1%). Compared to patients without coronary artery lesions, patients with coronary artery lesions had less nervous system involvement (17.6% vs.46.8%) and elevated number of leukocyte (17.6% vs.56%). Besides, patients with coronary artery affected exhibit more cranial and carotid artery involvement(29.4% vs. 5.0%), renal artery involvement (41.2% vs.17.0%), coeliac artery involvement (58.8% vs.27.0%), new onset hypertension (47.1% vs.14.5%), renal infarction (27.3% vs.5.4%,) and higher proportion of 2009 Five-factor score (FFS)≥2 (62.5% vs.15.6%). All patients with coronary artery lesions received at least moderate dose of prednisone and CTX except one refused medication. 3 cases underwent interventional therapy. Stent placement was performed on 2 of them, and in-stent restenosis was appeared in a patient one year later. 2 cases died,one for vascular rupture after coronary aneurysmsutrue plus coronary artery bypass grafting, another for myocardial infarction after stopping immunosuppressant therapy himself.Survival analysis showed patients with digital g angrene had poor prognosis though no significant difference(p=0.055).

Conclusion: PAN with coronary artery lessions are not uncommon. These patients exhibit young age, more proportion of multi-vessel of coronary artery involvement, more combined involvments of other organ arteries and more severe disease.

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AB0499 ABNORMALITY OF PERIPHERAL LYMPHOCYTE SUBSETS IN BECHET'S DISEASE AND EFFECTS OF NEW IMMUNOREGULATORY COMBINATION THERAPIES ON THESE CELLS

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Background: Bechet's disease (BD) is a chronic multisystemic vasculitis. Although its exact etiopathology is unknown, both autoimmune imbalances associated with genetic and abnormal immune response of effector lymphocytes promoted by infectious factors are suggested[1]. The increase of effector T cells (Teffs) and the decrease of regulatory T cells (Tregs) are possibly the involving factors in the pathogenesis of BD[2]. Importantly, we have developed new immunoregulatory combination therapies trying to restore the reduction of Tregs in rheumatic patients.

Objectives: To examine abnormal levels of lymphocyte subsets in BD patients at a relatively large-sample size and to investigate whether the immunoregulatory combination therapies have therapeutic efficacy in BD.

Methods: Total 384 BD patients and 206 healthy controls (HCs) were enrolled in this cross-sectional study. Proportions and absolute numbers of peripheral T, B, NK, $CD4^+$ T, $CD8^+$ T, Th1, Th2, Th17 and Treg subsets were analyzed by flow cytometry (FCM) for all participants. Among these patients,183 cases of BD patients were treated with immunoregulatory combination drugs (IMiDs) such as low-dose interleukin-2, rapamycin, metformin, retinoic acid and coenzyme Q10. The levels of peripheral lymphocyte subsets were measured before and after the treatment. Compared-T test was used to compare continuous measures and to assess effect of these drugs.

Results: Compared to HCs, the absolute numbers of various Teffs such as T, B, $CD4^+$T, $CD8^+$T, Th1 and Th17 cells were significantly increased in BD group (P<0.01), while the level of Tregs in patients with BD was severely decreased (P< 0.05), resulting in increased ratios (imbalance) of Th1/Tregs, Th2/Tregs and Th17/Tregs (P< 0.05) (Figure 1). After the IMiDs treatment, the levels of NK, $CD4^+$T, $CD8^+$T, Th1, Th17 cells as well as Tregs were significantly increased (P<0.05). But the increased Tregs was much more dramatical than those of Teffs, resulting in a decrease in ratios of Teffs/Tregs such as Th2/Tregs (P< 0.001) (Figure 2).

Conclusion: Impaired balance of pro- and anti-inflammatory immune cells, especially insufficiency of Tregs, might be a cornerstone of the pathogenesis of BD. Immunoregulatory combination therapies could promote the proliferation and functional recovery of Tregs in patients with BD and might help to alleviate disease activity.

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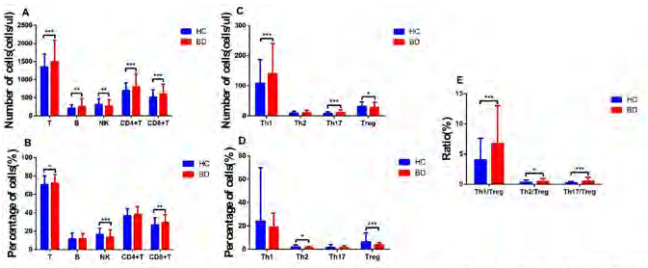


Figure 1: Comparison of lymphocyte subsets in peripheral blood between patients with BD (n=384) and HCs (n=206). All lymphocytes subsets were analyzed by detected by flow cytometry combined with standard absolute counting beads. Data were presented as mean±SD and statistical analysis was determined by two-tailed unpaired t-test. Patients had lower levels of NK, Th2 and Tregs in BD compared with those of HCs. HC: healthy control. *P < 0.05, **P < 0.01, ***P < 0.001.

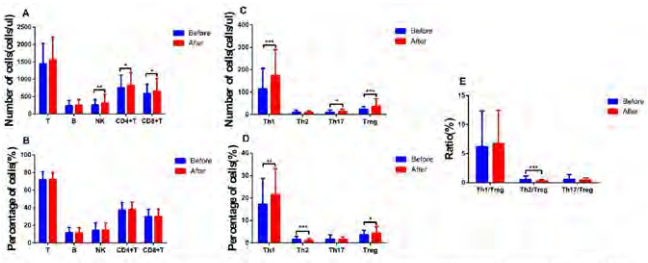


Figure 2: Changes of peripheral lymphocyte subsets after immunoregulatory combination treatment (n=183). Data were presented as mean±SD and statistical analysis was determined by two-tailed unpaired t-test. Absolute numbers of NK, $CD4^+T$, $CD8^+T$, Th1, Th17 and Tregs in BD patients were significantly increased after immunoregulatory combination treatment. *P < 0.05, **P < 0.01, ***P < 0.001.

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AB0500

CLINICAL CHARACTERISTICS AND POTENTIAL BIOMARKERS FOR DISEASE ACTIVITY OF PATIENTS WITH ANCA ASSOCIATED VASCULITIS: A MONOCENTER STUDY IN CHINA

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Background: Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) are a group of multisystem, autoimmune, inflammatory disease characterized by pauci- necrotizing vasculitis affecting small blood vessels. The clinical manifestations of the AAV are diverse and can be confined to one organ, or multiple organs and even life-threatening. However, there has been no specific index for assessing the activity of AAV at diagnosis.
Objectives: The aim of this study was to describe the clinical and serological features of patients with antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) in eastern China using data from a hospital-based study. And looking for indicators that can predict disease activity.
Methods: We retrospectively studied patients with newly diagnosed AAV evaluated from January 1, 2009, to December 31, 2018. In total, 219 patients diagnosed were classified according to the American College of Rheumatology classification criteria and/or revised Chapel Hill 2012 definitions, and their clinical and serological features were evaluated. The association of laboratory data with disease activity was assessed via regression models.
Results: Of 219 incident cases of AAV, 37/219 (16.9%) had granulomatosis with polyangiitis (GPA), 172/219 (78.5%) were microscopic polyangiitis (MPA), and 10/219 (4.6%) had eosinophilic granulomatosis with polyangiitis (EGPA). The mean age at diagnosis of patients with GPA were 51.5 years MPA were 61.7 years, and EGPA were 49.8 years, respectively. Patients with MPA were significantly older than GPA and EGPA at diagnosis (p<0.001). ANCAs tested positive in 207 (94.5%) of cases: 167 (80.7%) were MPO-ANCA and 40 (19.3%) were PR3-ANCA. Lung, skin, nervous system symptoms were the most common in EGPA. For GPA, ear–nose–throat (ENT) symptoms and lungs involvement were the most common. Renal and lung involvement occurs most frequently in MPA. In the multivariable logistic regression analysis, higher anti-MPO antibody (149.4 IU/ml), higher hypersensitive c-reactive protein (hs-CRP, 62.5 mg/L), lower hemoglobin (113.5g/L), and higher complement 4 (C4, >0.215 g/L) were proved to be independent risk factors for active disease. Further research showed that C4 had higher sensitivity (70.0%) and specificity (83.4%) than the other three indicators.
Conclusion: MPO-ANCA-positive MPA is the most common form of AAV in Chinese patients. Serum C4 concentrations at diagnosis might be a useful biomarker of disease activity in AAV.

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AB0501

THREE CASES OF VERTEBRAL ARTERITIS IDENTIFIED ON FDG-PET IN PATIENTS WITH SUSPECTED GCA AT UNIVERSITY COLLEGE LONDON HOSPITAL (UCLH)

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Background: Giant cell arteritis (GCA) may affect both cranial and extra-cranial vessels; where the latter occurs, it can be termed large-vessel GCA (LV-GCA). Large vessel involvement is common: histological evidence has been seen in 80% of autopsies of patients with known GCA, and imaging studies suggest large vessel involvement in over 80%[1]. LV-GCA is important to diagnose due to the risks of vascular complications such as occlusion and ischaemic stroke. The clinical diagnosis can be challenging, and the American College of Rheumatology (ACR) GCA classification criteria often underperform in cases of LV-GCA[1]. F-fluorodeoxyglucose positron emission tomography (FDG-PET) has been found to be useful in the detection of extra-cranial involvement to support the diagnosis of LV-GCA.[2]
Objectives: To appreciate the variability in presentation of cases of LV-GCA, and to further characterise a subgroup of patients with vertebral arteritis.
To explore the use of FDG-PET imaging in GCA patients in addition to or in place of traditional diagnostic tools (temporal artery ultrasound / biopsy).
Methods: Through evaluation of the new GCA fast-track pathway implemented at UCLH, a subgroup of patients diagnosed with vertebral arteritis was identified. The history and presentation of these patients were analysed.
Results: Three patients were diagnosed with vertebral arteritis. All three were male, Caucasian and aged over 70. All were investigated for GCA due to a history of severe headache (frontal in one, occipital in one, bi-temporal in one) with associated red flag symptoms. Two had a history of jaw claudication and visual disturbances (unilateral visual loss in one, transient diplopia in the other). Both of these patients had positive temporal artery biopsies. The third patient had no ischaemic symptoms but a strong history of prominent polymyalgic features and a positive temporal artery ultrasound. Inflammatory markers were raised in two, and normal in one, of the patients. Only one had systemic symptoms (weight loss). All three proceeded to FDG-PET scans which showed vertebral arteritis and were commenced on immunosuppressive treatment.
Conclusion: The cases discussed illustrate the heterogeneity of the presentation of LV-GCA, and the diagnostic challenge this poses. FDG-PET imaging is useful in confirming extra-cranial involvement and therefore guiding treatment.
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AB0502

EVALUATION OF A NOVEL FAST TRACK PATHWAY FOR GIANT CELL ARTERITIS USING PET IN ADDITION TO TAUS AND TAB FOR EARLY DIAGNOSIS

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Background: : Giant Cell Arteritis (GCA) is a common primary systemic vasculitis (1). Its predilection for the temporal artery can result in permanent visual loss if left untreated. Over 25% of patients have involvement of large vessels, such as the aorta, resulting in an increased risk of aneurysm formation and dissection. (3) Diagnosis of GCA is largely clinical and temporal artery biopsy (TAB) has long been the gold standard for diagnosis. In recent years temporal artery ultrasound (TAUS) has emerged as an effective, non-invasive tool to aid diagnosis. Positron-emission tomography (PET) can also be utilised to detect the presence of large vessel involvement but is currently not used in many centres for diagnostic purposes and requires further standardisation and validation (2). The challenge arises from these investigations losing sensitivity in the days following steroid treatment, meaning that rapid access is key to confirm diagnosis.
Objectives: To evaluate the impact of the introduction of a fast track pathway (FTP) on prompt diagnostics and treatment.
To improve our understanding of the use of PET at diagnosis and compare this to the gold standard TAB, and to TAUS, in our institution.
Methods: Cohort 1: 32 patients, all presenting before FTP implementation, identified from outpatient clinics and referrals to the Rheumatology team. Time taken from steroid initiation to TAUS/TAB was extracted from clinical records. Outcomes for this group included number of years on steroid (steroid burden).
Cohort 2: 21 patients all referred after implementation of a new GCA FTP. This group contains all patients referred as query GCA, not just those with positive diagnoses. Time from steroid initiation to TAUS/TAB was recorded. The FTP included the addition of PET imaging within 72 hours.
Results: Cohort 1: 20 (63%) patients had TAB and 3 (9%) had TAUS. The average time from starting steroid to investigation was 5.2 days and 2 days respectively. The average steroid burden in patients with no confirmatory test was 11 years. If patients had just a single diagnostic test this value dropped to 3 years.
Cohort 2: 11 (52%) had TAB, 10 (48%) had TAUS and 11 (52%) had PET. In positive GCA diagnoses, time from steroid start to investigations was 7.2 days, 1 day and 3.2 days respectively. In patients with a negative diagnosis the time frames were 13 days, 1 day and 1.7 days respectively. Sensitivity for TAB was 45.5% and TAUS 40%. Specificity for TAB and TAUS was 100%. These results are comparable to similar studies (4). PET sensitivity was 63.6% and specificity 100%.

Table 1. Sensitivity, specificity, predictive values

	TAB	TAUS	PET CT
Sensitivity (%)	45.5	40.0	63.6
Specificity (%)	100	100	100
PPV (%)	100	100	100
NPV (%)	33.3	57.1	55.6

Conclusion: Prompt diagnostics, best facilitated through a FTP, can reduce steroid burden in GCA even if only one confirmatory test is available. Patients with a low clinical suspicion of GCA and negative TAUS or a high clinical suspicion and positive TAUS stand little to gain from TAB. These findings summarise the first 6 months of our GCA FTP. Continued evaluation of PET in our FTP is needed to understand its role in diagnosis, particularly in patients at risk of vascular complications.
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AB0503

USE OF BIOLOGICAL THERAPY IN A COHORT OF PATIENTS WITH TAKAYASU ARTERITIS IN A THIRD LEVEL HOSPITAL.

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Background: Takayasu arteritis is a granulomatous vasculitis that affects large vassels, specially aorta and its main ramifications. It is a rare disease with an incidence between 0.3 and 1.2 per million inhabitants in Europe. It is more common in women (80%) and it usually occurs before age 40.
Objectives: Describe the characteristics and the use of biological therapy in a cohort of patients with Takayasu arteritis in our Hospital.
Methods: Retrospective descriptive study of patients diagnosed with Takayasu arteritis treated in the Rheumatology and Internal Medicine service in our hospital during 2019. Data have been obtained by reviewing medical records.
Results: 39 patients with takayasu arteritis were included, 33 women (84.4%) and 6 men, withan average age of 48 ±12 years. About treatment, 35 patients received glucocorticoid treatment, of these, 23 patients (65.7%) received treatment with DMARDs. Methotrexato (47.8%) and Ciclophosphamide (43.5%) are the most used. 12.8% (5) of patients received treatment with biological therapy 2 patients received treatment with Rituximab (already retired) and 3 patients maintained the treatment with Tocilizumab. (The characteristics of the patients are in table 1). About the course of disease, 47.8% of patients have achieved clinical remission, 43.6% have a chronic course, and only 3 patients have presented relapse of disease.
Conclusion: The results of our study are consistent with what is published in the literature. The average age of presentation is higher than in other series (48 ±12 years), this is because all patients are European and Caucasian. There is still not much experience on biological treatment in patients diagnosed with sarcoidosis, however the

PATIENT	GENDER	AGE	DIAGNOSIS DATE	BIOLOGICAL THERAPY	START DATE	ADVERSE EFFECTS	RETIRED	TREATMENT TIME	PREVIOUS TREATMENT	COURSE OF DISEASE
1	female	48	2015	Tocilizumab	2018	No	No	13	Corticosteroids, Methotrexate	Chronic
2	female	54	2017	Tocilizumab	2019	Mild AE	No	9	Corticosteroids, Methotrexate	Chronic
3	female	69	2018	Tocilizumab	2018	No	No	18	Corticosteroids, Methotrexate	Chronic
4	female	47	2010	Rituximab	2011	No	Yes	36	Corticosteroids, Ciclophospahmide, Mycophenolate	Chronic
5	male	26	2006	Rituximab	2007	No	Si	48	Corticosteroids	Remission

use of Rituximab, AntiTNFs and Tocilizumab has been described, presenting a good clinical response and with few adverse effects, as has been observed in our patients.
Disclosure of Interests: None declared
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AB0504 THE DIFFERENCES OF IMMUNE CHARACTERISTICS AND ITS RELATIONSHIP WITH DISEASE ACTIVITY IN LARGE VESSEL VASCULITIS PATIENTS

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Background: Large vessel vasculitis(LVV) is a rare refractory disease, giant cell arteritis (GCA) and Takayasu arteritis (TAK) constitute different types of primary LVV. Despite considerable discussion on the potential differences between GCA and TAK, the immunological difference and its relationship to disease activity remains unclear.
Objectives: To investigate the differences of peripheral blood immuno-phenotype between TAK and GCA, and to analyze the correlation between immune metabolism level and disease activity in TAK.
Methods: All patients with TAK and GCA who come to our department from January 2010 to January 2020 were included, all of them met the classification criteria of American college of rheumatology.General information, clinical manifestations, laboratory index, artery involvement and therapeutic schedule were collected.According to the National Institutes of Health criteria, there were 29 active and 23 inactive TAK patients.
Results:
[1] Baseline characteristics, treatment,involvement artery in LVV patients are summarized in Table 1.

Table 1. Clinical characteristics of patients with LVV

Variable	TAK,n=52	GCA,n=4
Age,X±S	29±13	64±7
Female,n(%)	45(86.6)	1(25)
Constitutional symptoms,n(%)	23 (43.4)	3(75)
Cephalic symptoms,n(%)	33 (62.3)	2 (50)
Peripheral limb ischemia,n(%)	22 (41.5)	-
Ocular signs,n(%)	3 (5.7)	2 (50)
Stroke,n(%)	2 (3.8)	-
GC,n(%)	40(76.9)	3(75)
GC dose >7.5mg/day,n(%)	36 (90)	2 (66.7)
Surgical intervention,n(%)	7(13.2)	-
Coronary artery,n(%)	3(5.7)	-
Common carotid artery,n(%)	31(58.5)	-
Subclavian artery,n(%)	23(43.4)	-
thoracic aorta,n(%)	6(11.3)	-
abdominal aorta,n(%)	13(24.5)	-

GC Glucocorticoids,bDMARDS biologic DMARDs
(2)Compared with GCA patients,TAK patients were younger (29±13vs64±7,P=0.015), with higher peripheral blood lymphocyte count of CD8+T cells and lower CD4/CD8(Table 2).

Table 2. Comparison of peripheral immune cells,humoral immunity among TAK and GCA,active and inactive TAK

Variable	TAK,n=52	GCA,n=4	p value	inactive TAK,n=23	active TAK,n=29	p value
Neutrophils	5.5±2.3	5.8±1.1	0.827	4.4±1.6	6.3±2.5	0.009*
Lymphocytes	2.4±0.8	1.0±0.6	0.010*	2.3±0.7	2.4±0.9	0.901
Monocytes	0.5±0.2	0.7±0.1	0.218	0.5±0.2	0.6±0.2	0.431
$CD3^+T$	1959±490	1154±541	0.189	2195±92	1842±585	0.467
$CD4^+T$	1074±305	758±303	0.381	1250±198	987±333	0.376
$CD8^+T$	859±212	297±87	0.048*	945±41	815±258	0.542
$CD4^+CD8^+$	42±27	12±7	0.344	63±2	32±28	0.229
CD4-CD8-	90±75	91±63	0.999	97±74	87±68	0.914
$CD19^+B$	273±97	191±94	0.470	202±106	309±84	0.242
$CD16^+CD56^+$	135±72	104±67	0.709	112±63	146±83	0.639
CD4/CD8	1.25±0.15	2.55±0.51	0.001*	1.33±0.26	1.21±0.10	0.440
IgG	11.7±3.7	8.3±0.5	0.124	10.3±3.4	12.9±3.6	0.025*
IgA	2.6±1.3	2.3±0.8	0.724	2.1±1.3	3.0±1.1	0.021*
IgM	1.7±0.9	0.8±0.2	0.118	1.5±0.8	1.8±0.9	0.202
κ light chain	9.5±3.9	6.6±0.3	0.222	8.1±3.3	10.8±4.0	0.033*
λ light chain	5.2±1.9	3.9±0.3	0.260	4.7±1.9	5.8±1.9	0.086

*P<0.05
(3)The levels of neutrophils, monocytes,IgG, IgA and κ light chain active TAK were higer than inactive TAK, with lower lymphocyte level (Table 2). Further correlation analysis showed that the levels of neutrophils, IgG,IgA and κ light chain were positively correlated with disease activity (r=0.434,P=0.005;r=0.380,P=0.019;r=0.452,P=0.004;r=0.380,P=0.022).

Conclusion: Compared with GCA patients,TAK patients had higer level of $CD8^+$T lymphocytes, consistenting with previous studies.In addition,TAK patients had persistent immune cell involvement,while humoral immunity is related to disease activity.Deeper studies may be required about the role of immune profile in in large vessel vasculitis.
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AB0505 SEASONAL INFLUENCE IN PMR: NOT ONLY SUMMER, BUT WINTER IS COMING TOO

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Background: The cause for polymyalgia rheumatica (PMR) is currently unknown. Disease onset may be triggered by a combination of genetic predisposition and environmental factors such as infection.[1] In different regions of Denmark a simultaneous peak incidence of giant cell arthritis and PMR occurred together with epidemics of Mycoplasma pneumoniae, Chlamydophila pneumoniae and Parvovirus B19.[1] A seasonal epidemics pattern for PMR would be supporting evidence for an infectious cause.[1] However, the current evidence of seasonal effect on the occurrence and disease severity of PMR is limited and show conflicting results.[2,3]
Objectives: To evaluate whether there is a seasonal effect on the risk of developing PMR in the Netherlands
Methods: We retrospectively collected data on patient-, disease,- and treatment characteristics from newly diagnosed PMR patients (clinical diagnosis) who visited our outpatient clinic during April 2012 and September 2017. Exclusion criteria was other concomitant inflammatory rheumatic disease. Based on the onset of PMR (start symptoms, not time of diagnosis) patients were grouped per month. Descriptive statistics were used [mean (SD), median (p25-p75) or n (%) as appropriate]. The Chi square goodness of fit test was used to determine whether the incidence of onset of symptoms was different between months of the year.
Results: In total 448 patients were included and 55 % were female and mean age was 66 years. Other baseline characteristics are described in table 1. The chi-square goodness of fit test to determine whether there was a peak incidence in months was p=0.06. As shown in figure 1 the incidence of onset PMR symptoms is higher in December-January, April through June with a peak in August. The April-June peaks coincides with incidence peaks of Mycoplasma pneumoniae infections and possibly Parvovirus B19 in spring and summer, the December-January peak coincides with Parvovirus B19 infections.[4,5]

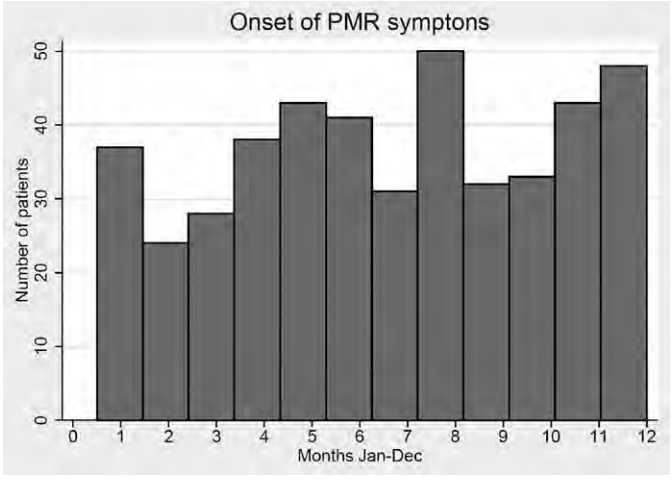
Table 1. Baseline characteristics (n=448)

Characteristic	
Female (%)	247 (55)
Age, years (SD)	66 (8.6)
PMR symptoms before diagnosis, weeks (IQR)	10 (6-16)
Neck pain (%)	205 (46)
Bilateral shoulder pain /stiffness (%)	412 (91)
Bilateral hip pain/stiffness (%)	380 (85)
Morning stiffness>45 min (%)	233 (52)
Peripheral arthritis (%)	35 (8)
Systemic symptoms* (%)	199 (44)
Elevated ESR mm/hour and / or CRP mg/l	309 (87)
ESR mm/hour(IQR)	37 (26-51)
CRP mg/l (IQR)	30 (15-54)

*Fever, night sweats, weight loss, anorexia
** ESR n= 428; CRP n=396

Conclusion: No definitive seasonal effect was found on risk of developing PMR, although a bimodal seasonal pattern compatible with the proposed respiratory infections is suggested.
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AB0506

GIANT CELL ARTERITIS: IS ROUTINE CLINICAL PRACTICE COMPREHENSIVE ENOUGH?

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Background: Recommendations to collect the most relevant information on disease course, treatment and outcomes in giant cell arteritis (GCA) has been proposed by EULAR to facilitate clinical research and to improve clinical care.
Objectives: To assess the quality of data collection in routine clinical practice according to EULAR recommendations and to describe baseline and follow-up characteristics of a retrospective cohort of patients with GCA.

Table 1. GCA-related signs and symptoms, laboratory and therapeutic data.

Item	Performed Baseline	Baseline n=39	Performed Follow-up	Follow-up n=112
Ocular symptoms	35/39 (89.7%)	15/35 (42.9%)	91/112 (81.2%)	29/91 (31.9%)
Permanent ocular symptoms	34/39 (87%)	9/34 (26.5%)	92/112 (82%)	28/92 (30.4%)
Headache	39 (100%)	30/39 (77%)	90/112 (80.4%)	13/90 (14.4%)
Scalp tenderness	31/39 (79.5%)	9/31 (29.8%)	88/112 (78.6%)	4/88 (4.5%)
Jaw claudication	34/39 (87%)	19/34 (55.85)	91/112 (81.2%)	6/91 (6.6%)
Cranial artery abnormality	27/39 (69.2%)	17/27 (63%)	69/112 (61.6%)	3/69 (4.3%)
Constitutional symptoms	35/39 (89.7%)	19/35 (54.3%)	90/112 (80.4%)	11/90 (12.2%)
PMR	35/39 (89.7%)	18/35 (51.4%)	92/112 (82%)	9/92 (9.8%)
ESR mean (SD)	33/39 (84.6%)	58.7 (32.1)	83/112 (74%)	14.6 (18.8)
CRP mean (SD)	31/39 (79.5%)	8.4 (7.9)	70/112 (62.5%)	1.3 (3.3)
Haemoglobin mean (SD)	38/39 (97.4%)	12.0 (1.7)	90/112 (80.4%)	12.9 (1.5)
Peripheral pulses	9/39 (8%)	3/9 (33.3%)	5/112 (4.5%)	2/5 (40%)
Large vessel involvement	8/39 (20.5%)	5/8 (62.5%)	7/112 (6.25%)	3/7 (42.8%)
Glucocorticoids median (IQR)	39 (100%)	102.5 (50-250)	112 (100%)	10.0 (5-15)
Synthetic DMARD	39 (100%)	8/39 (20.5%)	111/112 (99%)	17/39 (43.6%)
Biological DMARD	39 (100%)	0/39 (0%)	111/112 (99%)	3/39 (7.7%)
Antiplatelet agents	39 (100%)	6/39 (15.4%)	110/112 (98%)	25/110 (22.7%)

PMR: polymyalgia rheumatica, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein, SD: standard deviation, IQR: interquartile range, DMARD: disease modifying antirheumatic drugs

Methods: We reviewed medical records of patients diagnosed with GCA in a tertiary academic center between 2004-2018. We included patients with available data at diagnosis and one year of follow-up. Data extraction included: demographics, diagnosis, GCA-related signs and symptoms, laboratory, imaging modalities, comorbidities and treatment. Data in the chart was then compared with the core set of parameters proposed for GCA registries and databases by EULAR. Major relapse, according to the EULAR 2018 definition, was independently assessed by two rheumatologists.
Results: 58 patients were identified, 39 met predefined inclusion criteria with 151 visits during first-year follow-up. Headache (100%; 80.4%), ocular symptoms (89.7%; 81.2%), constitutional symptoms (89.7%; 80.4%), polymyalgia rheumatica (89.7%; 82%) and jaw claudication (87%; 81.2%) were the most frequently collected items at baseline and follow-up. Weight and height (2.6%; 2.6%), peripheral pulses (8%; 4.5%), smoking status (41%; 21%), and blood pressure (61.5%; 4.5%) were the less frequently collected. Most patients lacked differential pressure measurement. Myocardial infarction, malignancy, serious infections, arterial hypertension, diabetes and osteoporosis were collected in every patient (39, 100%). Only 2 mayor relapses were identified (5%). Two (2) patients died during the one-year follow-up period. Table 1 provides information on GCA-related signs and symptoms, laboratory and therapeutic data.
Conclusion: Although data collection in routine care is usually comprehensive enough according to EULAR proposed data set, key components in physical exam mostly those aiming to detect large vessel involvement, should be addressed more carefully.
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Disclosure of Interests: Julia Martínez-Barrio Consultant of: UCB Pharma, Belén Serrano Benavente: None declared, Tamara Del Río Blasco: None declared, Alfonso Ariza: None declared, Juan Ovalles: None declared, Juan Molina Collada: None declared, Teresa González: None declared, Carlos Gonzalez Consultant of: Gilead, Janssen, Novartis,, Speakers bureau: Abbvie, Celgene, Gilead, Janssen, Novartis, Pfizer, Roche, Isabel Castrejon: None declared, Jose Maria Alvaro Gracia: None declared
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AB0507

INVASIVE ASPERGILLOSIS IN ADULT RHEUMATOLOGICAL PATIENTS IN SAINT PETERSBURG, RUSSIA.

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Background: Invasive aspergillosis (IA) is a severe opportunistic infection that is not well understood in rheumatological patients.
Objectives: To study risk factors, etiology, clinical manifestations and results of treatment of IA in adult rheumatological patients.
Methods: Retrospective analysis of 830 patients (1998-2019) with “proven” and “probable” IA (EORTC / MSG, 2019), adults - 699 (84%). The main group included 18 (3%) adult rheumatological patients with IA, a control group included 610 (87%) adult hematological patients. Rheumatological patients were older, the average age was 59 years (21–75) vs 45 years (18–79), p = 0.005, and among them there were more women – 56% vs 42%, p = 0.01.
Results: In rheumatological patients with IA, underlying diseases were ANCA-associated vasculitis (28%), granulomatosis with polyangiitis (22%), periarteritis (11%), systemic lupus erythematosus (22%), rheumatic heart disease (11%) and ankylosing spondylitis (6%). In the control group, underlying diseases were acute leukemia (45%), lymphomas (34%), chronic leukemia (9%), multiple myeloma (7%), myelodysplastic syndrome (3%), and other hematological diseases (2%).
The main risk factors for IA development in rheumatological patients were: systemic steroids use (89% vs 69%), prolonged lymphocytopenia (76% vs 65%, median - 14 vs 12 days), treatment in ICU (44% vs 18%, p = 0.01), acute or chronic renal failure (39% vs 1%, p = 0.0008) and immunosuppressive therapy (28% vs 25%). Severe neutropenia was noted significantly less frequently (18% vs 83%, p = 0.0001). Additional risk factors were decompensated diabetes mellitus (17% vs 2%, p = 0.004), previous surgery (17% vs 1%, p = 0.001) and organ transplantation (6% vs 0%). In rheumatological patients, lung (83% vs 98%, p = 0.0001) and ≥2 organs (6% vs 8%) involvement were less common. Heart (11% vs 0%), sinuses (6% vs 5%) and central nervous system (6% vs 4%) involvement more often developed. In rheumatological patients, respiratory failure (61 vs 37%, p = 0.03), hemoptysis (28% vs 7%, p = 0.0001) and chest pain (17% vs 7%, p = 0, 04) were noted more often, less often - fever ≥38^{0}C (67% vs 85%,

p = 0.01) and cough (61% vs 70%). CT signs of lung damage were similar in both groups, but rheumatologic patients were more likely to show an «air crescent» sign and / or destruction cavity (44% vs 10%, p = 0.0001). In rheumatologic patients, IA was more often confirmed by isolation of *Aspergillus* spp. from BAL (80% vs 45%, p = 0.005) and by histological examination (22% vs 7%, p = 0.01). The main pathogens were *A. fumigatus* (50% vs 43%), *A. niger* (29% vs 32%), and *A. flavus* (14% vs 17%).
Rheumatological patients were less likely to receive antifungal therapy 89% vs 99%, p = 0,0003. The main drug in both groups was voriconazole. The overall 12-week survival did not significantly differ between groups, but was lower in rheumatological patients with IA (69% vs 81%).
Conclusion: In rheumatological patients, invasive aspergillosis more often developed at an older age, mainly in women. The main background diseases were ANCA-associated vasculitis, granulomatosis with polyangiitis, and systemic lupus erythematosus. Typical risk factors were steroids and immunosuppressants use, prolonged lymphocytopenia, ICU stay, and renal failure. The main causative agents were *A. fumigatus*, *A. niger*, and *A. flavus*. The main localization of infection were lungs. Respiratory failure, hemoptysis and heart involvement were typical. The overall 12-week survival of rheumatological patients with invasive aspergillosis was 69%.
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AB0508 EFFICACY AND SAFETY OF TNF-A ANTAGONISTS AND TOCILIZUMAB IN TAKAYASU ARTERITIS: MULTICENTER EUROPEAN RETROSPECTIVE STUDY OF 203 PATIENTS.

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Background: Takayasu arteritis (TA) is a chronic inflammatory large-vessel vasculitis, predominantly affecting the aorta and its main branches
Objectives: To assess safety and efficacy of biologics (i.e. TNF-α antagonists and tocilizumab) in patients with Takayasu arteritis (TA).
Methods: We conducted a retrospective multicenter study in referral centers from Europe and several countries in the world about biological-targeted therapies in Takayasu arteritis during the period from January 2017 to September 2019.
Results: Retrospective multicenter study of characteristics and outcome of 49 TA patients [80% of females; median age 42 [20-55] years] treated by TNF-α antagonists (80%) or tocilizumab (20%)] and fulfilling ACR and/or Ishikawa criteria. Factors associated with complete response were assessed. Eighty-eight percent of TA patients were inadequately controlled with, or intolerant to, conventional immunosuppressive therapy [median number of 3 (1-5)]. Overall response (i.e. complete and partial) to biological-targeted treatments at 6 and 12 months was of 75% and 83%, respectively. There were a significantly lower C-reactive protein levels at initiation of biological-targeted treatments [22 [10-46] mg/l vs 58 [26-76] mg/l, (p=0.006)] and a trend toward lower immunosuppressants drugs used prior biologics (p=0.054) in responders (i.e. complete and/or partial responders) relative to non-responders to biological-targeted treatments. C-reactive protein levels and daily prednisone dosage significantly decreased after 12 months of biological-targeted treatments [30 vs 6 mg/l, p<0.05 and 15 vs 7.5 mg, p<0.05, at baseline and at 12 months, respectively]. The 3-year relapse free survival was of 90.9% (83.5-99) over biologic treatment period compared to 58.7% (43.3-79.7) (p=0.0025) with DMARDs. No difference was found relative to efficacy between TNF-α antagonists and tocilizumab. After a median follow-up of 24 [2-95] months, 21% of adverse effects occurred, with biological-targeted treatments discontinuation in 6.6% of cases.
Conclusion: This nationwide study shows high efficacy of biological-targeted treatments in refractory TA patients with an acceptable safety profile.
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AB0509 SUSPENSIVE EFFICACY OF TOCILIZUMAB IN TREATMENT-NAÏVE PATIENTS WITH TAKAYASU ARTERITIS: TOCITAKA FRENCH PROSPECTIVE MULTICENTER OPEN-LABELLED TRIAL.

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Objectives: To assess long term efficacy of tocilizumab in treatment-naive patients with Takayasu arteritis (TAK).
Methods: In this multicenter, prospective, open-labelled trial, we aim to evaluate the benefit of adding tocilizumab to steroids in treatment-naïve patients with TAK, on discontinuation of steroids after 6 months of tocilizumab treatment, and to assess relapse-free survival following tocilizumab discontinuation.
Results: Thirteen patients with TAK were included, with a median age of 32 years [19-45] and 12 (92%) females. Six (54%) patients met the primary endpoint. Among 11 (85%) patients which achieved remission at 6 months, 6 (54%) have reached primary endpoint.. Among the 5 remaining patients which continued steroids, 3 had a prednisone-equivalent dosage < 5mg/day. A significant decrease of disease activity was observed after 6 months of tocilizumab therapy: decrease of median NIH scale (3 [3-4] at baseline, versus 1 [0-2] after 6 months; p <0.001), ITAS-2010 score (5 [2-7] versus 3 [0-8]; p = 0.002), and ITAS-A score (7 [4-10] versus 4 [1-15]; p = 0.0001)]. All patients discontinued tocilizumab after 7 infusions, and no other immunosuppressive drugs was introduced, except for 1 patient which received methotrexate. After 9 and 12 months, respectively 7 (54%) and 6 (50%) patients achieved remission with less than 7.5 mg/day of prednisone, and 9 (69%) and 9 (75%) with doses <10 mg/day. During the 12 months follow-up after tocilizumab discontinuation, a relapse occurred among 5 patients (45%) out of 11 in which achieved remission after 6 months of tocilizumab.
No severe AEs were considered related to study treatment and none required tocilizumab interruption or dose reduction. No deaths have occurred during the study period.
Conclusion: Tocilizumab seems an effective steroid sparing therapy in TAK but its effect appears to be suspensive.
Disclosure of Interests: Arsene Mekinian: None declared, david Saadoun: None declared, jerome.connault@chu-nantes.fr jerome.connault@chu-nantes.fr: None declared, i-quere@chu-montpellier.fr i-quere@chu-montpellier.fr: None declared, Patrick Jégo: None declared, nicolas.limal@aphp.fr nicolas.limal@aphp.fr: None declared, wxv wxv: None declared, Jacques-Eric Gottenberg Grant/research support from: BMS, Pfizer, Consultant of: BMS, Sanofi-Genzyme, UCB, Speakers bureau: Abbvie, Eli Lilly and Co., Roche, Sanofi-Genzyme, UCB, Mathieu Vautier: None declared, lea.savey@aphp.fr>; lea.savey@aphp.fr>;: None declared, Patrice cacoub: None declared, olivier fain: None declared
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AB0510 INFLIXIMAB IS AN EFFECTIVE GLUCOCORTICOID-SPARING TREATMENT FOR TAKAYASU ARTERITIS: RESULTS OF A MULTICENTER OPEN-LABEL PROSPECTIVE STUDY

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Background: Approximately half of patients with Takayasu Arteritis (TA) have glucocorticoid (GC)-dependency and require the addition of a second-line immunosuppressive treatment.
Objectives: Here, we conducted a multicenter open-label prospective cohort study to assess the efficacy and safety of infliximab originator as a GC-sparing agent in TA.

Methods: A temporary recommendation for use for infliximab in refractory TA was approved by the French National Drug Authorities (April 2014). Infliximab was administered to patients in case of disease activity with a NIH score ≥2 despite conventional therapy. Data regarding patient's clinical, laboratory, imaging and treatments were obtained at baseline, and at each following visit until last visit (October 2017). TA activity was evaluated according to NIH criteria and GC requirement throughout the study.

Results: Twenty-three patients were enrolled, including 19 female. The median age at inclusion was 33 years (Interquartile range, IQR: 23-44 years). At baseline, 17 (74%) patients were treated with GCs, at a median dose of 10 mg/day (IQR: 0-21) of prednisone-equivalent. After a median follow-up of 36.9 months (IQR: 10-58.7), improvement of ≥1 NIH criterion of TA activity was achieved for 14/22 (64%) patients. The median GC dose was 8 mg/day (IQR: 7-10) at 6 months; 5 mg/day (IQR: 0-8) at 12 months and 0 mg/day (IQR: 0-5) at 36 months of follow-up. Overall, infliximab originator had a significant GC-sparing effect between baseline and last follow-up (p=0.009).

Conclusion: This multicenter open-label cohort study suggests that infliximab originator is an effective GC-sparing treatment for TA refractory to conventional therapy.

Disclosure of Interests: None declared

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AB0511 INTERNATIONAL CONSENSUS ON ANCA TESTING AND INTERPRETATION BEYOND SYSTEMIC VASCULITIS

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Background: ANCA can be detected in sera from patients with autoimmune, inflammatory, infectious or neoplastic diseases.

Objectives: To issue a Consensus Statement on ANCA testing and interpretation beyond systemic vasculitis.

Methods: This Statement was prepared by a group of experts, based on the results of a comprehensive search in PubMed.

Results: In certain settings beyond systemic vasculitis, ANCA may have diagnostic, clinical, and/or prognostic relevance. Testing for PR3- and MPO-ANCA by specific immunoassays should be performed in any patient with clinical features suggesting ANCA-associated vasculitis and in patients with anti-GBM disease and idiopathic interstitial pneumonia. Routine ANCA testing is not recommended in patients with connective tissue diseases (CTD), autoimmune liver diseases, inflammatory bowel diseases, infections, and/or malignancy unless there is evidence for small vessel vasculitis. ANCA testing by specific immunoassays may be useful in patients with rheumatoid arthritis, systemic sclerosis or primary Sjögren's syndrome who have kidney disease with a nephritic sediment or in patients with systemic lupus erythematosus if a kidney biopsy shows prominent necrotizing and crescentic lesions or proliferative lupus nephritis. ANCA testing may be justified in patients with suspected autoimmune hepatitis type 1, who do not have conventional disease-related autoantibodies, or in patients with inflammatory bowel diseases in case of diagnostic uncertainty to discriminate ulcerative colitis from Crohn's disease. In these cases, ANCA should be tested by indirect immunofluorescence since target antigens are not well characterized. ANCA against bactericidal/permeability-increasing protein may be a biomarker for deteriorating lung function and a poor prognosis in patients with cystic fibrosis.

Conclusion: ANCA testing is clinically relevant not only in patients with manifestations suggesting systemic vasculitis, but also in patients with certain other disorders, particularly in patients with anti-GBM disease or idiopathic interstitial pneumonia.

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AB0512 ALLERGIC PROFILE AND ALLERGEN-SPECIFIC IMMUNOTHERAPY IN EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS (EGPA): A SINGLE CENTER OBSERVATIONAL STUDY

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Background: Eosinophilic granulomatosis with polyangiitis (EGPA), previously known as Churg-Strauss syndrome, is a systemic disease characterized by late onset asthma associated with small- and/or medium-size vessel vasculitis, besides eosinophil-mediated cytotoxic organ damage. About 20-30% of patients with EGPA displays allergic manifestations related with inhalant sensitization, while prevalence of food and drug allergy is unknown in this context. Moreover, some authors in the past hypothesized in favor of a possible role of allergen-specific immunotherapy (ASIT) as a trigger of disease.

Objectives: Aim of the present study is to establish the prevalence of each category allergen sensitization and to determine whether atopy or specific immunotherapy could influence clinical expression of the disease.

Methods: Our study consisted in a retrospective demographic and clinical data collection regarding EGPA history (including age at diagnosis, organ and tissue involvement, autoantibody profile) and the presence of allergic comorbidities or previous drug hypersensitivity reactions. Patients without either proven allergic reactions or positive tests have been excluded.

Results: Fifty-three (53) patients with definitive diagnosis of EGPA have been included in the analysis among which 25 (47.2%) with chronic respiratory allergy or previous acute allergic reaction. Among allergic patients 15 (60%) resulted sensitized towards inhalants and among them 13 (86.7%) displayed multiple sensitization. Drug allergy affected 13 patients (52%), food 4 (16%). Among 15 patients with respiratory allergy, 13 were eligible to allergen-specific immunotherapy (ASIT). Seven (7) subjects underwent ASIT prior EGPA diagnosis with an average time-to-EGPA of 16.2 years. No statistically significant difference was found in terms of sex, age at diagnosis, positivity for or specificity of anti-neutrophil cytoplasm antibodies (ANCA), eosinophil count at onset, pattern of clinical manifestations comparing allergic vs. non-allergic, ASIT vs. non-ASIT, ASIT vs. allergic, ASIT vs. eligible.

Conclusion: Among patients with EGPA allergies are highly prevalent, particularly towards inhalants and drugs. In the great majority of patients multiple sensitization profile is found. Atopy doesn't seem to be associated with specific patterns of disease presentation. The absence of correlation between inhalant ASIT exposure and variation in mode and time of EGPA onset doesn't support the hypothesis of a its potential role in triggering the disease.

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AB0513 GLOMERULONEPHRITIS IN LEVAMISOLE-ADULTERATED COCAINE VASCULOPATHY (LACIV): A 51-CASE SERIES

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Background: Up to 88% of cocaine is tainted with levamisole, anthelmintic withdrawn from the market due to toxicity. Since 2010 LACIV patients, characterized by retiform purpura, ear necrosis, multisystemic compromise and positivity for multiple autoantibodies, have been reported. Renal involvement is the most serious and heterogeneous clinical manifestation.
Objectives: To describe the renal involvement of patients with LACIV.
Methods: We describe the renal manifestations of a 51 case series with LACIV admitted in four high complexity institutions in Colombia from December 2010 to December 2019.
Results: All patients were mestizos, with median age of 32.5 years (SD 7.8), the male:female ratio was 4.7:1, and the time from symptoms to diagnosis 12 months (IR 32). Nephritis was found in 60.8%, with creatinine elevation in 61%, median 2.0 mg/dl (IR 3), 87% had proteinuria, median 3184 mg/day (IR 5735), 43% in nephrotic-range; 93% had hematuria and 48% pyuria and cilindruria. Biopsy was performed in 21 patients (64%), with immune complex mediated extracapillary glomerulonephritis (35%), immune complex mediated membranoproliferative glomerulonephritis (20%) pauci-immune proliferative glomerulonephritis (20%), membranous glomerulonephritis (15%), focal and segmental glomerulosclerosis (5%) and C3 mediated extracapillary glomerulonephritis (5%). Six patients (19%) developed end-stage kidney disease. Patients with nephritis had more ear necrosis, retiform purpura, leukopenia, lymphopenia, anemia, hypocomplementemia, anti-PR3 and anti-MPO antibodies, compared to patients without nephritis.
Conclusion: Due to the higher abuse of cocaine and its contamination with levamisole, LACIV is an increasingly reported disease. Although skin manifestations are the most characteristic and prevalent, renal involvement is frequent, clinically and histologically heterogeneous, and potentially serious. Cytopenias, hypocomplementemia and antineutrophil cytoplasmic antibodies could identify patients at risk of nephritis
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AB0514 CALF PAIN, KEY POINT IN THE DIAGNOSIS OF POLYARTERITIS NODOSA

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Background: polyarteritis nodosa (PAN) is a primary systemic vasculitis that is becoming a rare disease in part by the decrease in hepatitis B virus (HBV) infection due to widespread vaccination. It is characterized by a full vast constellation of nonspecific clinical manifestations, which sometimes delays and makes it difficult to diagnose. Still, muscle involvement is a feature that could guide the clinician.
Objectives: to describe the main clinical and laboratory characteristics of patients with PAN and to confirm the frequency of muscle involvement.
Methods: retrospective cross-sectional descriptive study of 23 adult patients diagnosed with PAN between January 2011 and December 2018 in two high complexity hospitals in Medellin-Colombia.
Results: twenty-three patients met ACR 1990 classification criteria for PAN, 52% were men with a median age of 51 (IR 36-60), 78.3% were newly diagnosed, and only two patients (8.7%) had HBV infection. General symptoms (found in 95% of the patients), cutaneous (82%), and articular (56%) were the most frequent manifestations. Among systemic symptoms, myalgia, especially calf pain, was the most common characteristic (78.3%), followed by weight loss (73.9%), fatigue (69.3%), and fever (59.3%). Laboratory findings and severity scores are shown in the table. Angiography was performed in 27.3% of patients, finding splanchnic (renal, hepatic and splenic) microaneurysms (17.4%), stenosis (13%), and renal infarction (4.3%). Fourteen patients (61%) had at least one positive biopsy documenting medium-sized artery vasculitis, mainly skin, muscle, nerve, or both; 9 (39%) had normal or inconclusive biopsy findings. All patients received high daily doses of prednisolone (50 ± 16 mg); 52.2% required cyclophosphamide, 30.4% azathioprine, 17.4% methotrexate, 8.7% rituximab, 4.3% dapsone and 4.3% plasmapheresis; acetylsalicylic acid was given to half of the patients and only one required antiviral therapy for HBV. With treatment, 87% improved; 22.7% had an infection, and 8.7% of patients died.
Conclusion: myalgia was the main characteristics of our PAN patients, especially in calves, and its presence in patients with other general, skin or articular symptoms should raise the suspect of this vasculitis.
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Table

Characteristic	PAN patients (n=23)
CRP (mean and SD in mg/dl)	6.3 ± 8.51
ESR (mean and SD in mm/h)	84 ± 38
CPK (median and IR in U/L) normal value < 180	76 (66)
FFS (mean)	1
BVAS (median and IR)	17 (7)

PAN: polyarteritis nodosa; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; CPK: creatine phosphokinase; FFS: five factor score; BVAS: Birmingham Vasculitis Activity Score; SD: standard desviation; IR (interquartile range)

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AB0515 COMPARISON OF THE PERFORMANCE OF THE 1990 ACR CLASSIFICATION CRITERIA AND THE GIACTA INCLUSION CRITERIA FOR THE CLASSIFICATION OF GCA: RESULTS FROM A SINGLE-CENTRE STUDY.

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Background: The classification criteria currently used to define giant cell arteritis (GCA) were developed in 1990 by the American College of Rheumatology

(ACR), and strongly focus on patients with cranial manifestations. Patients with large-vessel GCA (LV-GCA) have less frequently cranial symptoms and a positive temporal artery biopsy, and are less likely to be captured by the ACR criteria. GiACTA, a trial of tocilizumab in GCA, has recognized the concept of GCA as a clinical syndrome, and included patients with cranial and/or polymyalgic symptoms as long as GCA diagnosis was supported by either biopsy or appropriate LV imaging results. However, these inclusion criteria were elaborated by experts and were not validated in patients with GCA.

Objectives: To compare the performance of the 1990 ACR classification criteria and the GiACTA inclusion criteria for the classification of GCA in a single-center cohort of patients with GCA.

Methods: All consecutive patients with a diagnosis of GCA seen between January 2008 and December 2016 in our center were included (GCA cohort). Control cohort consisted of consecutive patients with a negative temporal artery biopsy (TAB) performed in the same time period and a final diagnosis different than GCA. For both study cohort, the final diagnosis was made at the end of the follow-up period by consensus by 2 rheumatologists, who retrospectively evaluated all the medical records from symptoms' onset to December 2019, last visit, or death. Subjects were classified by each of the different criteria. TABs showing inflammation limited to adventitial or periadventitial small vessels were considered negative for both ACR and GiACTA criteria.

Two-by-two classification tables were generated to estimate sensitivity and specificity, and receiver operating characteristic (ROC) curves with corresponding areas under the curve (AUC) were calculated.

Results: 213 patients were included in the study (75% female, mean age 71.7 years). 55 patients had TAB showing transmural inflammation (TMI); 30 patients had TAB showing inflammation limited to adventitial or periadventitial small vessels (PAI); 67 patients had evidence of LV-GCA at imaging (LV-GCA) and 61 patients had TAB without inflammatory changes (negTAB). 1990 ACR and GiACTA criteria were satisfied respectively by 55 (100%) and 51 (93%) TMI, 18 (60%) and 1 (3%) PAI, 23 (35%) and 31 (46%) LV-GCA and 27 (44%) and none (0%) negTAB patients.

After a median follow-up of 52.6 months, 174 of the 213 (84%) patients had a final diagnosis of GCA (55 TMI, 22 PAI; 67 LV-GCA and 30 negTAB) and the remaining 33 patients had a diagnosis different than GCA (2 PAI and 31 negTAB). Sensitivity and specificity of 1990 ACR classification criteria for GCA were 67% and 90%, AUC (95% CI) 0.790 (0.715 – 0.864). Sensitivity and specificity of GiACTA inclusion criteria were 48% and 100%, AUC (95% CI) 0.740 (0.669 – 0.811). By adding systemic symptoms in the symptoms domain of GiACTA inclusion criteria, sensitivity increased to 59% and sensitivity remained 100%, AUC (95% CI) 0.792 (0.730 – 0.854).

Conclusion: Both 1990 ACR classification criteria and GiACTA inclusion criteria showed a good specificity but a low sensitivity in classifying patients with a clinical diagnosis of GCA from this large monocentric cohort. There is an urgent need for new classification criteria for GCA.

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AB0516 INITIAL TREATMENT OF POLYMYALGIA RHEUMATICA PATIENTS: COMPARISONS BETWEEN GENERAL PRACTITIONERS AND THE RHEUMATOLOGIST.

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Background: Polymyalgia rheumatica (PMR) is the most common inflammatory rheumatic disease at persons > 50 years of age. It is clinically characterized by pain and stiffness in the neck, proximal shoulder, and hip girdle. (1)Glucocorticoid (GC) is the cornerstone of PMR treatment; the use is associated with potentially severe side effects (3).According to EULAR-ACR recommendations for the management of PMR, treatment should be individualized using the minimum effective GC dose. (2)

An initial prednisolone dose of > 15mg is associated with significantly higher risk for GCs related side effects (1) and GC doses higher than 25 mg/day are discouraged because of the high risk of adverse events; furthermore, there is no evidence that such doses are more effective than lower doses (2,3).

In most countries, the vast majority of PMR patients are diagnosed and managed primarily by their General Practitioner (GP) (4)

Objectives: To compare the initial GC dose for PMR patients diagnosed by their GP versus an outpatient rheumatological clinic in Denmark.

Methods: All patients with the diagnosis of PMR in South-West Jutland Hospital, Denmark at the period of 2013 to 2018 were identified from an electronic register.

Patients with an already known rheumatic disease before the diagnosis of PMR, GCA symptoms at the diagnosis time or hospitalized at the diagnostic time were excluded.

Clinical and paraclinical data were collected from the patient's electronic journal.

Results: In a period of 6 years, 342 patients with PMR were identified. Of 342 patients 83 were diagnosed by their GP. No significant differences were found regarding demographical, clinical and paraclinical baseline characteristics between the two groups. No differences were identified regarding the treatment response. However the initial prednisone dose in patients diagnosed by the GP's was significantly higher (p<0, 00001) compared to the rheumatological outpatient clinic (Table 1) with an initial dose of ≥25mg at over 50% of newly diagnosed cases (45 patients).

Table 1.

	Diagnosed by GPs N 83	Diagnosed by the rheumatological outpatient clinic N 259	P values
Age (years) ± SD	70,2 ± 8,2	70,58± 7,5	n.s*
Gender-female(%)	62,6%	56,7%	n.s*
Duration of symptoms (weeks) ± SD	12,34 ± 10	12,9 ± 13,4	n.s*
Age over 50 %	98,8%	99,6%	n.s
Bilateral shoulder pain (%)	95,1%	96,5%	n.s
Abnormal CP and/or SR (%)	87,8%	94,2%	n.s*
CRP (mg/lt) ± SD	36,8 ± 32,2	45,8± 36,8	n.s*
SR(mm/hour) ± SD	50,1±26,5	55,1±23,7	n.s*
Morning stiffness	87,9%	91%	n.s*
Hip pain or limited range of motion	66,2%	70,4%	n.s*
RF and aCCP negative %	87,9%	90,2%	n.s*
Absence of other joint involvement	79,5%	71%	n.s*
Initial prednisolone dose(mg) ± SD	25,65 ± 12,1	16,4±4,5	<0,0001
Response to treatment	93,9%	94,1%	n.s

*non-significant

Conclusion: Our study shows that the initial GC dose is significantly higher for PMR patients diagnosed by GPs which may lead to a higher risk of GC related side effects.

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AB0517 USE OF POSITRON EMISSION TOMOGRAPHY IN RHEUMATOLOGY PRACTICE

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Background: Positron emission tomography (PET), which is widely used in oncology, has recently been used as a guide in the diagnosis of vasculitis and activity monitoring.

Objectives: In this study, we aimed to present the desired PET results for the preliminary diagnosis of vasculitis and follow-up.
Methods: PET results requested from the rheumatology outpatient clinic between 2012–2019, clinical findings of patients and other imaging methods were reviewed and evaluated retrospectively.
Results: PET results were achieved of 36 patients (47% male, 53% female). Constitutional symptoms were present in 67% of the patients with a mean age of 51 ± 18 years. The mean erythrocyte sedimentation rate (ESR) was 49 ± 33 mm/h, CRP was 46 ± 33 mg / L, and leukocyte value was 8.8 ± 3 K / mm^3 at the onset of the disease. While 60% of 25 patients with large vessel vasculitis had a murmur in at least one affected area, 48% had no pulse. While 78% of all patients had a finding in favor of vasculitis in non-PET imaging, this rate was 39% in PET(Table-1). Although the most commonly used imaging method is conventional angiography, recently CT and MR angiography have been requested more frequently. Only 32% of patients who are signs of vasculitis in other images had vasculitis in PET.

PET was requested with preliminary diagnosis of vasculitis in 24 patients and vasculitis was detected in 46% of the cases. In twelve of the patients with vasculitis had 25% activity involvement in the desired PET for the presence of activation.

In 5 of 8 patients with a pre-diagnosis of vasculitis who had no evidence of vasculitis in any other imaging modalities, the involvement of vasculitis was detected in the PET, and the diagnosis was confirmed

Before PET, 44% of the patients had not received steroid treatment. In this group, 63% of patients who did not take steroids, had vasculitis findings in PET. In steroid receiving group, the rate of PET involvement was 20%. Presence of vasculitis in PET was significantly higher in patients who did not receive steroid prior to PET (p = 0.009) (Table-2). The mean duration of steroid intake before PET was 28 ± 69 months.
Conclusion: PET is an increasingly used imaging technique in rheumatology practice. The main advantage of PET is that it recognizes other pathologies such as infection and tumor in patients with systemic symptoms. Disadvantage is an expensive test, high radiation rate and misinterpretation of atherosclerosis. Vasculitis is a group of diseases that require rapid diagnosis and treatment. Because of the indisputable contribution of imaging methods at the diagnosis stage, PET was emphasized in this study
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Table-1: Clinical and Demographic Data of Vasculitis Patients

	N(%)
Gender	
Female	**19(53)**
Male	**17(47)**
Diagnosis	
Takayasu Arteritis	**19(53)**
Polymyalgia Rheumatica	**3(8)**
Polymyalgia Rheumatica + Giant Cell Arteritis	**2(6)**
Temporal Arteritis	**4(11)**
Polyarteritis Nodosa	**1(3)**
Granulomatous Polianjitis	**1(3)**
Behcet Disease	**4(11)**
Non-classification vasculitis	**2(6)**
Constitutional Symptoms	**24(67)**
Vasculitis evidence in non-PET imaging	**28(78)**
Imaging method	
MR Angio	**10(28)**
CT Angio	**10(28)**
Arteriography	**16(43)**
Computed Tomography	**12(34)**
Ultrasonography	**3(8)**
Vasculitis evidence in PET	**14(39)**
Steroid use prior to PET	**20(56)**
High CRP at diagnosis> 5 mg / L	**28(78)**
High ESR at diagnosis> 30 mm / h	**23(64)**

Table-2 The effect of findings on PET positivity

	Vasculitis Patients				
N(%)	PET (±) 14	PET (-) 22	p	OR	%95CI
Vasculit in Non-PET Imaging	9(64)	19(86)	0,217	0,28	0,05-1,4
Constitutional Symptoms	11(79)	13(59)	0,292	2,53	0,54-11,7
Murmur	6(43)	11(50)	0,676	0,75	0,19-2,88
Pulselessness	3(21)	9(41)	0,292	0,39	0,08-1,8
High CRP	11(79)	15(68)	0,706	1,7	0,35-8,1
High ESR	11(79)	12(54)	0,143	3,05	0,66-14
Steroid use prior to PET	4(29)	16(73)	0,009	0,15	0,03-0,66
Preliminary diagnosis of vasculitis	11(46)	13(54)	0,292	2,53	0,54-11,7

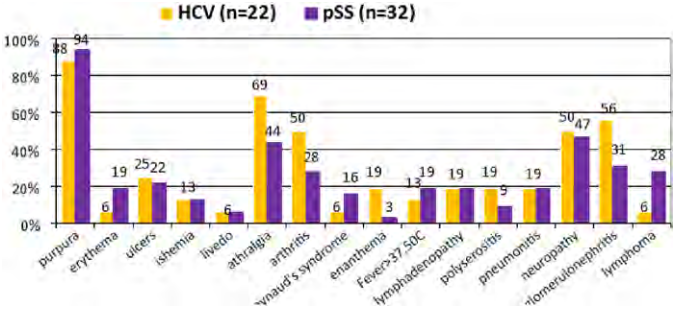
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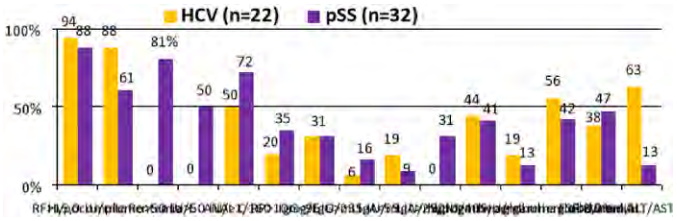
CRYOGLOBULINEMIC VASCULITIS ASSOCIATED WITH HCV INFECTION AND PRIMARY SJOEGREN'S SYNDROME: DATA FROM A SINGLE CENTER EXPERIENCE

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Background: According to some publications [1] cryoglobulinemic vasculitis in different associated diseases varies.
Objectives: To characterize patients with cryoglobulinemic vasculitis (CV) in primary Sjoegren's syndrome (pSS) and chronic hepatitis C virus (HCV) infection
Methods: 54 patients with CV were recruited to this study during 7 years period in our rheumatological center. CV was diagnosed according criteria proposed by Ferri C. [1] and De Vita [2].22 patients had CV associated with HCV (19 women and 3 men) and 32 with pSS (all female). The mean age of patients at the time of inclusion in the study among HCV and pSS patients was 50.4±10.0 years and 55.8±13.5 years, and at CV onset was 42.8± 11.1 years and 47.1±15.3 years (p>0,05).
Results: 19 patients (86%) with HCV-CV had viremia with prevailed 1b genotype (84%). 8 (42%) patients had severe liver fibrosis (F3-4). SS was diagnosed in 6 (28%) patients with HCV-CV (3 with sSS and 3 with pSS). An increase of aRo antibodies (>50 U / ml) was detected in 3patients, ANA>1/320 - in 5/6 patients. 2 patients with SS were diagnosed MALT-lymphoma of the enlarged salivary and lacrimal glands, and 1 marginal zone lymphoma of the spleen in a patient with HCV-CV without pSS. All patients with lymphoma had type II cryoglobulinemia.
Most patients with pSS -CV had late stage and active disease: xerostomia (<0.5 ml/5 min) in 28 (88%), sialoadenitis (>2 foci in MSG), keratoconjunctivitis sicca (in 22 patients, 69%).
Lymphomas were diagnosed in 9 patients with pSS-CV (28%). In all cases, they were non-Hodgkin's lymphomas (NHL): in 7 patients - MALT lymphomas of enlarged parotid salivary (5), lacrimal glands (2), in 5 cases they were accompanied by regional lymph node enlargement. B-cell marginal zone lymphoma of lymph nodes and B-cell large cell lymphoma were observed in 1 case each.
No statistically significant differences were found in 2 groups in clinical manifestations of CV (see Graph.1), although patients with pSS had elevated lymphoma rate (28% compared to 6% for HCV, p=0.08), while in HCV-CV a slightly higher incidence of arthritis (22%, p=0.14), glomerulonephritis (56% vs 31% in pSS, p=0.10), and enanthema (19% and 3%, respectively, p=0.06).
Type II cryoglobulinemia was detected in 68% cases of HCV-CV and in 72% with pSS, less often mixed polyclonal (27% vs 22%) and oligoclonal (5% and 6%) types. There was in 96% (44/46) cases monoclonal IgM with predominant K-light chain mIg (87%, n=40/46).
RF positivity, low C4 complement, increased CRP and the levels of IgG, IgM in 2 groups were almost the same. Obviously pSS-CV group had significantly increased aRo, aLa, ANF titers (p=0.01) and also elevated IgA (p=0.02), lowered CD19+ cell levels (p=0.008) and increased BAFF (p=0.04), while in HCV-CV group high transaminases were typical (p=0.0008). BAFF level (N<0.8 ng/ml) in pSS-CV group was higher (median 2.73 ng / ml (0.66-3.86) than in HCV (median 0.66 ng / ml (0.14 - 0.92), (p=0.04). Patients with pSS-CV had significantly (p=0.008) lowered CD19 + cell count (median 5.3% (2.2-13.6)) if the normal range was 6-19%, in contrast to patients with HCV-associated CV (median 20.5% (13.2-26.0).



Graphic 1. Clinical characteristics of HCV and pSS associated CV



Graphic 2. Laboratory characteristics of HCV and pSS associated CV

Conclusion: Clinical picture of CV, as well as the main immunological parameters are similar in patients with associated pSS and HCV. Immunochemical study of serum and urine proteins is required to determine the type of cryoglobulinemia. SS is not rare in HCV-CV, so appropriate examination with ANA, aRo/La detection is mandatory. Patients with mixed monoclonal cryoglobulinemia had increased risk of hematological malignancies.

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Disclosure of Interests: None declared

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AB0519 PULMONARY INVOLVEMENT IN ANCA ASSOCIATED VASCULITIS (AAV) ACCORDING TO ANTIGENIC SPECIFICITY: A RETROSPECTIVE ARGENTINE COHORT

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Background: The lung in ANCA associated vasculitis (AAV) is one of the most frequently compromised organs (20-80%). The clinical features of pulmonary involvement vary according to the type of vasculitis and some studies have shown its association with the ANCa subtype or antigenic specifity (MPO-ANCA), (PR3-ANCA).

Objectives: A-Describe the clinical features and tomographic findings of pulmonary involvement in vasculitis associated with ANCA and its association according to the ANCA subtypes.

B-Evaluate outcome, relapses and associated mortality.

Methods: Observational, analytical, retrospective study. Data was collected from the medical records and tomographic image files of patient evaluated in rheumatology department in a tertiary level hospital (2007-2019).

Patients diagnosed with AAV, who met criteria for ACR 1990 classification or according to nomenclature of Chapel Hill 2012, with thoracic CT performed and dosage PR3 an MPO antibodies by ELISA technique by a pulmonologist and radiologist.

Demographic data, subtype of vasculitis, concomitant organic involvement, disease activity evaluated by Birmingham Vasculitis Activity Score v 3 (BVAS v3), time of evolution of pulmonary involvement, ERS – PCR, serum creatinine, ANCA determined by ELISA were collected. The following findings in parenchyma were evaluated by thorax CT: Consolidation, Ground glass opacities, Reticulation, Honeycomb, cavitated or not nodules, Central airway compromise (thickening or stenosis), Bronchiectasis,Peribronchial thickening, Pleural effusion and the following patterns of disease:NIU (Usual Interstitial Pneumonia), NINE (Unspecified Interstitial Pneumonia),HAD (Diffuse Alveolar Hemorrhage)

Table 1. shows the main findings in lung parenchyma.

Parenchymal Findings	%
Consolidations	37
Ground glass opacities	72
Reticulation	15
Honeycomb	9
No cavitated nodules	41
Cavitated nodules	20.7
Central airways comp (stenosis)	9.4
Peribronchial thickening	11.3
Bronchiectasis	9.4
Pleural effusion	7.7

According to the pattern of tomographic condition: 36.5 HAD %, 9.6% NIU, 7.8% NINE and, 1.5% Bronchiolitis obliterans.

The presence of positive MPO was significantly associated with the presence of honeycomb (p 0.017) and NIU (p 0.018).

There were no significant associations with the presence of PR3.

Mortality was 17%.

No association was found in relation to mortality or relapse frequency among PR3 or MPO positive patients.

Results: 66/87 patients were included, 59% female, with a mean age of 51 (14 SD) years. GPA 46.9%, MPA 39.4%, EGPA13.6%, median follow-up time of 36 months (RIC 12-77).

According to antigenic specificity: 40.9% PR3 positive, 47.6% MPO positive and ANCA negative 11.5%. 74% of the GPA were positive for PR3, and 58% PAM at MPO.

BVAS basal: 17.8 + 7.5 DS.

Frequency of organic involvement: 81.8% pulmonar, 77% systemic, 57.6% renal, 43% ENT.

54% of patients with pulmonary involvement was present at the onset of their disease.

Conclusion: The frequency of pulmonary involvement in this cohort of patients was 82%, similar to that reported in the literature and was presented at the beginning of the disease in half of the cases. The presence of positive MPO was associated with a higher frequency of usual interstitial pneumonia.

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Disclosure of Interests: None declared

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AB0520 FIVE-YEAR RATE OF HOSPITALIZATIONS IN ANCA-ASSOCIATED VASCULITIDES IN THE ITALIAN REGION OF FRIULI VENEZIA GIULIA (2013-2017)

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Background: ANCA-associated vasculitides (AAV) are a group of systemic vasculitis carrying a high risk of hospitalization because the multiorgan involvement, the acute nature of some clinical manifestations, the chronic but very disabling course of some other manifestations and finally the risk of severe infections due to chronic glucocorticoid and immunosuppressor administration. However, data on hospitalization due to ANCA-associated vasculitis are still scarce.

Objectives: to estimate the rate of the first hospitalization or the death in patients suffering from AAV in the Italian region of Friuli Venezia Giulia (about 1,200,000 inhabitants) from year 2013 to 2017.

Methods: integration of the information coming from many administrative databases were used to this end. The Regional Health Information System of Friuli Venezia Giulia was used as the source of information for this retrospective cohort study. The system covers the entire regional population and includes various electronic health administrative databases that can be linked with one another on an individual basis through a unique encrypted identifier. In particular, the following databases were matched: the database of the regional potential health care beneficiaries (including demographic information and the residential history of all of the subjects living in the region), the hospital discharge database, the database of exemptions from medical charges were used for this study, the database of the different regional laboratories. The population under study was selected based on the following inclusion criteria: patients were residents in Friuli Venezia Giulia and they had to carry the exemption code for AAV, including Granulomatosis with Polyangiitis (GPA), or Eosinophilic Granulomatosis with Polyangiitis (EGPA), or Microscopic Polyangiitis (MPA). This population was observed from 2013 to 2017. The coded event was the occurrence of the first hospitalization or the death. Also, all the hospitalization and their main discharge diagnoses were registered.

Results: 103 patient with AAV were identified. The number of patients with at least one hospitalization/death was 74/103 (71,8%). Seven patients died during the observation period (6,6%). The whole number of hospitalizations was 285 in

74 patients. 55/74 (74,3%) patients experienced more than one hospitalization. In the majority of the hospitalizations (119/285, 41,7%), the cause of hospitalization was directly attributable to the disease itself, while the second cause of hospitalization was the infections (26/285, 9,1%). In 10/103 patients (9,7%), an end stage renal disease was recorded as event. The presence of at least one positivity for ANCA antibodies was documented in 76/103 patients (73,8%), mainly in patients carrying GPA. Globally, the presence of ANCA antibody seems to be associated with greater likelihood of an event (p=0,07, log-rank test). The first event occurred in 50% of ANCA-positive patients within 180 days from diagnosis, while in 50% of ANCA negative patients in 859 days. 6 out of the 7 deaths occurred in ANCA positive patients.

Conclusion: the rate of hospitalization in AAV is very high confirming the high health care burden of illness. The disease itself is often the cause of the hospitalization, as well as the infectious complication, highlighting the need for more effective treatments, and glucocorticoid sparing therapies. ANCA antibody may represent a biomarker of a more serious disease.

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AB0521 COST OF ILLNESS OF ANCA-ASSOCIATED VASCULITIS IN ITALY: DATA LINKAGE ANALYSIS OF MULTIPLE CLINICAL AND ADMINISTRATIVE DATABASES IN THE PROVINCE OF UDINE, ITALY

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Background: ANCA-associated vasculitides (AAV) are a group of systemic vasculitis carrying a high risk of hospitalization because the multiorgan involvement, the acute nature of some clinical manifestations, the chronic but very disabling course of some other manifestations and finally the risk of severe infections due to chronic glucocorticoid and immunosuppressor administration. However, data on cost of illness due to AAV are lacking.

Objectives: to estimate the cost of illness in patients suffering from AAV in the province of Udine (about 500,000 inhabitants), Friuli Venezia Giulia (FVG), Italy, from year 2010 to 2018.

Methods: integration of the information coming from many administrative databases were used to this end. The Regional Health Information System of FVG was used as the source of information for this retrospective cohort study. The system covers the entire regional population and includes various electronic health administrative databases that can be linked with one another on an individual basis through a unique encrypted identifier. In particular, the following databases were matched: the database of the health care beneficiaries (including demographic information and the residential history of all of the subjects living in FVG), the hospital discharge database, the database of exemptions from medical charges, the database of the laboratories. The population under study was selected based on the following inclusion criteria: patients were residents in the province of Udine and they had to carry the exemption code for AAV, including GPA, or EGPA, or MPA. This population was observed from 2010 to 2018.

Results: 57 patients (201 patient-years) with AAV were identified. They were ANCA-positive in 44/57 (77%). GPA, EGPA and MPA was diagnosed in 18 (31,6%), 15 (26,3%), 11 (19,3%) patients, respectively. The mean age at diagnosis was 54,5 (17,5) years. The disease itself was the main cause of hospitalization in almost half of the hospital discharges (60/126, 47,6%). Four patients died during the observation period due to vasculitis itself (1), pneumonia (2), or haematological malignancy (1). Time to the first event (death or hospitalization) was significantly higher in ANCA-negative AAV patients than in ANCA-positive AAV patients (p=0,03, Log-Rank test), ANCA-positive AAV patients having a three-times higher risk (HR 3,38 95%CI 1,13-10,08, p=0,03). Total estimated cost was € 1,215,078, corresponding to € 6,168 patient-year. Costs for ANCA-positive AAV patients were much higher than those for ANCA-negative AAV patients (€ 1,115,253 vs € 99,825, and € 7058 per person-year vs € 2,559 per person-year, respectively). GPA and MPA showed the highest costs if compared to EGPA [GPA: € 239,168 (€ 5199 per person-year) vs MPA: € 281,502 (€ 4771 per person-year) vs EGPA: € 214,287 (2329 per person-year), respectively]. Costs for hospitalization were the highest [€ 734,957 (€ 3731 per person-year) vs other costs € 480,121 (€ 2437 per person-year)].

Conclusion: costs for AAV are very high, confirming the high health care burden of this illness. Management of ANCA-positive patients rather than ANCA-negative patients was burdened by the highest costs. GPA and MPA showed the highest direct costs for hospitalization, which very frequently occurred due to the vasculitis itself.

Disclosure of Interests: Luca Quartuccio Consultant of: Abbvie, Bristol, Speakers bureau: Abbvie, Pfizer, Elena Treppo: None declared, Salvatore De Vita Consultant of: Roche, GSK, Speakers bureau: Roche, GSK, Novartis, Francesca Valent: None declared

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AB0522 GENDER DIFFERENCES IN GIANT CELLS ARTERITIS: ANALYSIS OF A MONOCENTRIC COHORT OF 100 PATIENTS.

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Background: Giant Cells Arteritis (GCA) is the most common primary vasculitis in adults and usually occurs in patients older than 50 years. Epidemiological studies shown a higher prevalence of the disease in women compared to man. However, differences in clinical presentation between men and women have not been demonstrated, even if some distinctions have been suggested (1,2).

Objectives: The purpose of the present study is to analyze differences in the clinical presentation of GCA according to sex.

Methods: We collected retrospectively clinical data of a monocentric cohort of 100 consecutive GCA patients. Mann Whitney test was used to compare continuous variables, while Chi-square test and Fisher's exact test were applied for comparison between qualitative variables.

Results: One-hundred patients with a clinical diagnosis of GCA were enrolled in the study (68 women, 32 men). In all patients the diagnosis of vasculitis was histologically and/or radiologically confirmed. Main clinical data are reported in the table.

Patients were classified according to vascular involvement in three groups: temporal arteritis (C-GCA), extracranial large vessel vasculitis (LV-GCA) and both cranial and extracranial vasculitis (LV-C-GCA). No significant differences in vascular distribution of the disease were found according to sex, even if large vessel involvement seems to be more frequent in women (43% vs 28%; p: ns).

Male and female patients presented at diagnosis a similar clinical picture, with the same frequency of systemic symptoms (fever, fatigue, weight loss), polymyalgia rheumatica, visual symptoms and claudication. However, male patients complained more often temporal headache (90% vs 71%, p: 0.01), even no significant differences were found in the incidence of pathological findings at temporal artery physical examination (38% vs 32%; p: ns) and biopsy (59% vs 50%). On the contrary, in female patients a longer time to diagnosis was recorded (8 (2-49 vs 4 (0-35) months; p: 0.01).

Conclusion: In our cohort of GCA patients, clinical presentation was similar in male and female patients, with no significant differences in clinical, radiological and laboratory findings. However, male patients presented more often temporal headache, the most typical symptom of GCA, and this could explain a shorter time to diagnosis, if compared to female.

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	All GCA (n:100)	WOMAN (n:68)	MAN (n:32)
Age: median (10^{th}-90^{th} percentile)	76 (62-80)	73 (60-83)	76 (62-80)
Time to diagnosis (weeks) *	8 (1-42)	8 (2-49)	4 (0-35)
C-GCA	61 (61%)	38 (56%)	23 (72%)
LV-C-GCA	16 (16%)	13 (20%)	3 (9%)
LV-GCA	23 (23%)	17 (25%)	6 (20%)
New temporal headache*	77 (77%)	48 (71%)	29 (90%)
Visual symptoms	39 (39%)	24 (35%)	15 (47%)
Jaw or tongue claudication	35 (35%)	23 (34%)	12 (38%)
Fever	39 (39%)	24 (35%)	15 (47%)
Fatigue	71 (71%)	48 (71%)	23 (72%)
Weight loss	49 (49%)	34 (50%)	15 (47%)
Polymyalgia rheumatica	43 (43%)	33 (49%)	10 (31%)
Arm or leg claudication	5 (5%)	2 (3%)	3 (9%)
Positive temporal artery biopsy	53 (53%)	34 (50%)	19 (59%)
Pathological findings at temporal artery physical examination	34 (34%)	22 (32%)	12 (38%)
CRP (C-reactive protein)	83 (22-160)	89 (21-159)	78 (23-155)
ESR (erythrocyte sedimentation rate)	72 (34-109)	79 (37-113)	54 (32-100)
FDG-PET activity throughout aorta	32 (32%)	25 (37%)	7 (22%)

*: $p \leq 0.05$

Disclosure of Interests: None declared
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AB0523 TAKAYASU ARTERITIS AND SACROILIITIS: A CASE-CONTROL STUDY

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Background: A possible shared immunopathogenesis between Spondyloarthritis (SpA) and Takayasu Arteritis (TA) has been hypothesized and some clinical cases about SpA in TA patients have been reported (1). In clinical practice the diagnosis of sacroiliitis may be performed by X-ray, Computed Tomography (CT) or Magnetic Resonance Imaging (MRI). In particular, CT findings of sacroiliitis include contour irregularities, joint space alterations, joint erosion, subcondral bone changes (osteoporosis or sclerosis), enthesitis, ankylosis. Meanwhile, TA patients performe routinely FDG-PET/CT scans for monitoring disease activity.
Objectives: This study aims to understand if there is an increased incidence of sacroiliitis in TA patients.
Methods: We collected retrospectively imaging data from FDG-PET/CT scans of 28 TA patients and 28 controls, matched for sex and age. Controls were selected among patients performing FDG-PET/CT in our Nuclear Medicine Unit, excluding patients with bone tumors, bone metastasis and thyroid cancers. The majority of controls were affected by lymphoma in complete remission. An expert rheumatologist read the CT-scans of sacroiliac joints.
Results: No patients or controls demonstrated FDG-uptake in sacroiliac joints. In the control group we detected sacroiliac sclerosis in two cases: one due to degenerative changes, one to sacroiliitis (1/28, 4%). In the TA group four patients presented CT alterations suggestive for sacroiliitis: one bilateral erosion, one bilateral sclerosis, two monolateral sclerosis (4/28, 14%). One of these patients complained an inflammatory back pain.
Conclusion: In our cohort of TA patients we demonstrated an increased prevalence of sacroiliitis, diagnosed by CT scan. Only one patient reported an inflammatory back pain, while three patients had radiological signs of previous sacroiliitis. These findings highlight the importance of looking for spondyloarthropathy in TA patients even if asymptomatic.
References:
[1] Guzel Esen S, Joint Bone Spine, 2019
Disclosure of Interests: None declared
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AB0524 ANCA ASSOCIATED VASCULITIS IN GRAN CANARIA: THE IMPORTANCE OF THE INTERSTITIAL LUNG DISEASE

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Background: ANCA-associated vasculitis (AVV) are a heterogeneous group of systemic diseases that needs a better knowledge and approach due to the high mortality it presents.
Objectives: Describe the clinical characteristics of patients with AAV assessed by the Rheumatology services in two university hospitals in Gran Canaria in the last decade, as well as clinical differences between the AAV subtypes.
Methods: Characteristics of 34 patients diagnosed with AAV between January 2011 - December 2018 were collected retrospectively. The patients met ACR classification criteria and consensus criteria from Chapell Hill-2012. Variables are compared using the $\chi 2$ test for dichotomous variables or the t-Student test for continuos variables. For non-continuous variable, Mann-Whitney U or a logarithmic transformation was used
Results: 21 (61.7%) patients were women. We found 14 granulomatosis with polyangeiitis (GPA 41.2%), 10 microscopic polyangeiitis (MPA) and 10 eosinophilic granulomatosis with polyangeiitis (EGP) (29.4%). They presented an average follow-up time (±SD) of 46.3 months (±26.8). Patients with MPA presented an older age at diagnosis and a higher proportion were diagnosed with age> 65 years (p = 0.003).
The mean (±SD) of the BVAS index of activity at diagnosis was 15,7 (± 7.9). 80,5% of the patients presented positivity against ANCA: 34,4% c-ANCA and 65.5% (Clinical manifestations in Table 1).

TABLE 1. INITIAL CLINICAL MANIFESTATIONS

	ALL THE PATIENTS (n=34)	GPA (n=14)	MPA (n=10)	EGP (n=10)	p value
Otolaryngological involvement		13(92.9%)	2(20%)	6(60%)	0.001
Interstitial lung disease	5 (14.7%)	0	5 (50%)	0	
Renal involvement					0.027
- Reno-pulmonary syndrome	6 (17,6%)	3 (21.4%)	2 (20%)	1 (10%)	
- Renal Involvement - glomerulonephritis	10 (29.4%)	3 (21.4%)	6 (60%)	1 (10%)	
- Basal proteinuria >1 gr/24 hs	13 (38.2%)	4 (28.5%)	7 (70%)	1 (10%)	
Alveolar pulmonary hemorrhage not associated with renal involvement	2 (5.8%)	0	1 (10%)	1 (10%)	
Manifestations Peripheral Nervous System	10 (29.4%)	2 (14.2%)	4 (40%)	4 (40%)	
Cardiomyopathy	3 (8.8%)	0	0	3 (30%)	
Eye involvement (scleritis/conjunctivitis/ keratitis/uveitis)	6 (17.6%)	6 (42.8%)	0	0	0.01

21 (61.7%) patients received cyclophosphamide and 3 (8.8%) patients received rituximab as induction treatment. Azathioprine was the most commonly used maintenance treatment (41,1%). 16 (47%) patients had renal involvement. An improvement in proteinuria was observed, both in GPA (p=0.008) and in MPA (p=0,03) (Renal outcomes in Table 2). No patient received kidney transplant.

TABLE 2. RENAL OUTCOMES

	GPA (n= 6)	MPA (n=8)	p VALUE
Basal serum creatinine, mean (SD), mg/dl	2.07 (1.1)	3.08 (2.06)	0.3934
Basal proteinuria, mean (SD), mg/dl	2264 (1391.5)	2731.2 (1334.7)	0.8348
Last serum Creatinine, mean (SD), mg/dl	2,2 (1.4)	2,1 (1.5)	0.5577
Last proteinuria, mean (SD), mg/dl	485 (457.9)	326 (110.4)	0.4704

Interestingly, 5 patients (14.7%), all of them MPA, presented interstitial lung disease (ILD), 3 of them (60%) prior to systemic involvement (9, 10 and 82 months). 3 patients had an usual interstitial pneumonitis (UIP) pattern, none had a non-specific interstitial pneumonia (NSIP) pattern and two had other patterns.
15 patients had 17 relapses. Five (14.7%) patients had serious infections. Eight (23.5%) patients died: 4 due to progression of ILD, 2 due to vasculitis manifestations.
Conclusion: ILD can be considered a relatively frequent manifestation of this group of diseases. A high percentage of patients had recurrences. Mortality remains high in AAV and in our series ILD is a frequent cause of death.
Disclosure of Interests: Francisco Javier Nóvoa Medina Speakers bureau: I have been paid as a speaker for a few medical talks, Francisco Rubiño: None declared, Beatriz Tejera-Segura Speakers bureau: I have been paid as a speaker for a few medical talks, Beatriz Romero Díaz: None declared, Sergio Machín García: None declared, Iñigo Rua-Figueroa: None declared
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AB0525 NATURAL HISTORY OF CRYOGLOBULINEMIA FROM 2000 TO 2018 FROM THE LABORATORY POINT OF VIEW: AN ANALYSIS OF CRYOGLOBULIN CHARACTERISTICS IN A SINGLE CENTER.

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Background: Big data refers to large amounts of information. With today's ever-improving technologies created by the automation and digitization, it becomes easier to convert data into relevant information, which can be used to provide better patient management, especially when it occurs a rare condition such as cryoglobulinemia (CRG).
CRG is due to an immunoglobulins (Ig) that precipitate at low temperatures. There are 3 types of CRG: type I: monoclonal Ig; type II: monoclonal Ig + polyclonal Ig; type III: 2 polyclonal Ig.

Objectives: The aim of this study was to analyse the available data coming to the Department of Laboratory Medicine of Modena to describe the population of patients suffering of CRG.
Methods: Data from the Modena Labs network were extracted by means of the software "Pagoda", for statistical purposes, directly connected to the Laboratories Information System (LIS). Considered time period 2000-2018
Results: The analysed samples were 28,847, 4901 (17%) of which positive to the cryoglobulins (CR) detection. The typing positive CR were 4190 (85%): type 1 7.8 %, type II 48.54% and type III 43.8% The positive samples belonged to 2528 patients. Patients were 1563 (62%) women, average age 66±16, and 965 (38%) men, average age 62±16. (female/male ratio = 1.62) No statistically significant difference regarding sex and age between the 3 types. The cryoglobulinemia phenomenon is quite complex and the typing of monoclonal, polyclonal components of the Ig classes and chains has made it possible to identify 41 possible combinationsOut of 115 patients with Type 1 cryoglobulin, 73% had a monoclonal IgM and 36% monoclonal IgG; 11.2% both monoclonal IgG and IgM. The κ light chain was the most frequent: 55,6% IgM-k and 23,4% IgG-k vs 29% IgM-λ and 18.2% IgG-λ. Two patients had an IgA-k cryoglobulin.
Patients with Type 2 cryo were 781: monoclonal IgM-k 587 (75.1 %), 126 IgM-λ (16.1 %), 52 IgG-k (6.6 %), IgG-λ (5%), 1 IgA-λ; 2.8% had both IgG and IgM. Out of 1204 patients with Type 3 cryo, 74.8% had both polyclonal IgG and IgM, 13,8% had isolated IgM or IgG (9%); 4.8 % IgG-IgA-IgM together, both IgG and IgA in only 0,5% of patients. Almost the 50% (1255) of the patients had a diagnosis supporting the request of CR:
HCV, 604 (48%); chronic hepatitis, 177 (14%); rheumatologic disorder, 107 (9%); autoimmune diseases, 83 (7%), nephropathy, 80 (7%); others, 204 (15%).
Genotyped HCV+ patients were 290 (48%), with the following results: 1b, 136 (47%); 2a/2c, 65 (22%); 3a, 26 (9%); others 63 (22%).
Conclusion: The data show that CRG is a pathology which affects the elderly and especially women, as in autoimmune and rheumatological diseases. The predominant CRG type is the III and the most frequently related pathology to the request for CR is HCV+ and chronic hepatitis. The most common HCV genotype are 1b and 2a/2c The cryoglobulinemia phenomenon is complex and laboratory typing is intriguing.
Starting from this preliminary descriptive study, it will be possible, with the available data, to perform elaborations that allow to relate CRG with the diagnosis and verify the effect of therapy.
Big Data methods' application represents an undeniable resource for public institutions when carrying out strategic decision-making processes.
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AB0526 DIFFERENCES IN IMMUNOGLOBULIN LEVELS IN PATIENTS WITH ANCA-ASSOCIATED VASCULITIS AND RHEUMATOID ARTHRITIS TREATED WITH RITUXIMAB

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Background: Rituximab (RTX) is a chimeric monoclonal antibody against CD20 receptor, used in the treatment of rheumatic diseases. Hypogammaglobulinemia has been described as an adverse event. It has been reported that hypogammaglobulinemia is more frequent in patients with ANCA-associated vasculitis (AAV).
Objectives: To study the basal characteristics of patients with AAV and rheumatoid arthritis (RA) in treatment with RTX and to analyze the risk factors of hypogammaglobulinemia.
Methods: Retrospective observational study of patients treated with RTX. Patients diagnosed with AAV and RA with immunoglobulin levels prior to treatment and after each cycle were included. Clinical and demographic variables were analyzed. Both populations were compared using t-Student for continuous and chi-squared for categorical variables. The influence of the basal characteristics of the patients was analyzed using univariate and multivariate logistic regression models.
Results: Among the 86 included patients, 10 (11.6%) had AAV and 76 (88.4%) RA. Patient's characteristics stratified by disease are included in Table 1.
The overall sample was divided into two groups, patients who developed hypogammaglobulinemia and patients who did not. Of the 12 patients who developed hypogammaglobulinemia, 4 had RA and 8 AAV (p<0.001). In the univariate analysis, patients who developed hypogammaglobulinemia presented higher age at diagnosis (61 ± 15 vs 43 ± 11 years, OR=1.14 p<0.001), shorter time of disease progression (4.9 ± 8 vs 12.6 ± 9 years, OR=0.86 p0.02) and lower gammaglobulin rates at baseline (744 ± 504 vs 1145 ± 295 OR=0.16 p0.006). There were more severe infections in the group of patients with hypogammaglobulinemia than in the group without it (1/4 [25%] vs 1/74 [1.4%], OR=0.42 p<0.001).

TABLE 1. Characteristics of patients treated with RTX, according to their underlying disease.

	Overall sample n=86	AR n=76	VAA n=10	p
Age at diagnosis, years m±SD	57 ± 12	56 ± 12	63 ± 11	0,11
Disease progression, years m±SD	11,5 ± 9	13 ± 9	1 ± 1	**< 0,001**
Female n/N (%)	66/86 (76,6)	60/76 (78,9)	6/10 (60)	0,18
IGG <725 prior to initiation of treatment n/N (%)	10/86 (11,6)	4/76 (5,3)	6/10 (60)	**< 0,001**
IgG < 600 n/N (%)	12/86 (14)	4/76 (5,3)	8/10 (80)	**<0,001**
IgG <400 n/N (%)	2/86 (2,3)	0	2/10 (20)	**<0,001**
IgM Hipogamaglobulinemia n/N (%)	26/86 (30,2)	17/76 (22,4)	9/10 (90)	**<0,001**
Pretreatment with non-antiTNF biologics n/N (%)	25/86 (29,1)	24/76 (31,6)	1/10 (10)	0,15
Pretreatment with antiTNF n/N (%)	60/86 (69,8)	59/76 (77,6)	1/10 (10)	**<0,001**
Pretreatment with FAMES n/N (%)	80/86 (93)	72/74 (94,7)	8/10 (80)	0,08
Pre-treatment with JAK inhibitors n/N (%)	11/86 (12,8)	11/76 (14,5)	0	0,19
Cyclophosphamide pretreatment n/N (%)	3/86 (3,5)	0	3/10 (30)	**< 0,001**
Infections n/N (%)	21/86 (24,4)	15/76 (19,7)	6/10 (60)	**0,02**
Severe infection n/N (%)	7/86 (4,6)	1/76 (1,3)	3/10 (30)	**< 0,001**
Cumulative dose of steroids one year prior m±SD	2923 ± 3003	2227 ± 1898	6199 ± 4621	**< 0,001**
Cumulative dose of steroids during treatment m±SD	2626 ± 2353	2303 ± 1913	5668 ± 3997	**0,002**

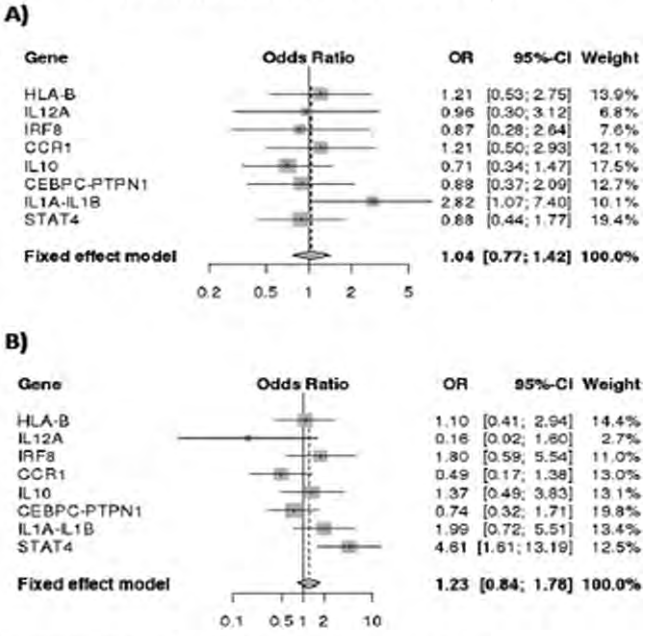
Patients with hypogammaglobulinemia received a higher cumulative dose of steroids during treatment (OR=1,000 p 0.019). Within the RA group, patients with hypogammaglobulinemia also received a higher cumulative dose of steroids (p 0.009).
In the multivariate study, only age at the beginning of treatment (OR=1.1 p=0.020) remained a risk factor for the appearance of hypogammaglobulinemia.
Conclusion: A significantly higher percentage of hypogammaglobulinemia is observed in patients with AAV treated with Rituximab, compared to patients with RA. The development of hypogammaglobulinemia seems to be influenced by age at diagnosis, years of disease progression, IgG levels prior to initiation of treatment and a higher cumulative dose of glucocorticoids (targeted in both the overall sample and the RA group). In addition, there is a higher frequency of severe infections in the hypogammaglobulinemia group. Studies with larger sample sizes are needed to confirm these results.
Disclosure of Interests: María Sanz: None declared, Gemma Bonilla: None declared, Diana Peiteado: None declared, Diego Benavent: None declared, Chamaida Plasencia: None declared, Laura Nuño: None declared, Irene Monjo: None declared, Alejandro Villalva: None declared, Alejandro Balsa Grant/ research support from: BMS, Roche, Consultant of: AbbVie, Gilead, Lilly, Pfizer, UCB, Sanofi, Sandoz, Speakers bureau: AbbVie, Lilly, Sanofi, Novartis, Pfizer, UCB, Roche, Nordic, Sandoz
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AB0527 PHARMACOGENETICS AND PHARMACODYNAMICS OF RESPONSE TO APREMILAST IN A PHASE 3 CLINICAL STUDY IN SUBJECTS WITH ACTIVE BEHÇET'S DISEASE

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Background: Apremilast (APR), an oral phosphodiesterase 4 (PDE4) inhibitor, modulates inflammatory mediators[1] and has demonstrated efficacy in treating oral ulcers in a phase III Behçet's syndrome study (BCT-002 [RELIEF]).[2]
Objectives: To conduct an exploratory analysis of genetic polymorphisms, plasma biomarkers, and blood leukocytes with clinical response in RELIEF.
Methods: Subjects with active Behçet's disease (BD) were randomized (1:1) to APR 30 mg twice daily or placebo (PBO). The primary clinical efficacy endpoint was the area under the curve for the number of oral ulcers through Week 12 (AUC_{Wk0-12}). Among the 207 subjects enrolled, 140 provided consent for DNA genotyping, 116 for plasma biomarker testing, and 96 for leukocyte subset testing. Genotyping was performed on the Illumina Omni2.5 BeadChip (Covance Genomics Laboratory). TNF-α, IL-6, interferon-γ, and IL-17A levels were measured using Simoa Single Molecule Array; IL-8 and IL-23 were measured using the Human DiscoveryMAP multiplex panel (Myriad RBM). Th17,

Figure 1. Forest Plots Showing Association With Response for Each Lead Polymorphism at a Behçet's Disease Genome-Wide Association Study Locus, and Results of a Fixed Effects Meta-analysis



Results for A) APR and B) PBO are plotted separately.

Treg, and CD3 T cells were counted using bisulfite-specific RT-PCR (Epiontis Gmbh). A rank ANCOVA model was used to estimate between-treatment differences (APR vs. PBO) in percent change from baseline for each biomarker/leukocyte subtype over the 12 weeks of treatment. Within each treatment group, the correlation of percent change from baseline at Week 12 in biomarker/leukocyte subtype with the primary efficacy endpoint $AUC_{Wk0\text{-}12}$ was examined using a univariate regression model. A separate regression model was used to assess the interaction between treatment and the biomarker/leukocyte subtype clinical response.

Results: Pharmacogenetic analysis of BD risk variants in HLA-B, IL-10, TLR2, ACE, TNF, GIMAP, PDGFRL, and UBAC2+55 genes associated with PDE4 biology yielded no candidate variants that were significantly associated with response to APR or PBO at a Bonferroni-corrected *P* value of 2×10^{-6}. Clinical response to APR with respect to HLA-B51 yielded an odds ratio (OR) of 1.21 (95% CI, 0.53-2.75), indicating no significant relationship (Figure 1). Pharmacodynamic changes for IL-6, IL-3, IL-17A, IL-23, and TNF-α were not statistically significant. APR treatment was associated with a significant change in interferon-γ (mean: +107.4%; median: −19.2%) vs. PBO (mean: +78.8%; median: +7.9%) (*P*=0.0077). Using a univariate regression model, TNF-α showed strong positive correlation with $AUC_{Wk0\text{-}12}$ in the APR group (*r*=0.90; *P*=0.0140); IL-8 had weak positive correlation with $AUC_{Wk0\text{-}12}$ in the APR group (*r*=0.04; *P*=0.0333). A significant negative correlation was observed between the percent change from baseline in the number of Th17 cells and $AUC_{Wk0\text{-}12}$ in the APR group (*r*=−0.79; *P*=0.0392) and a significant positive correlation was observed with the percent change from baseline in the number of Treg cells and $AUC_{Wk0\text{-}12}$ in the PBO group (*r*=0.94; *P*=0.0182). Of all the biomarkers and leukocyte subtypes examined in a regression model using treatment as a factor, only Treg had a statistically significant treatment interaction (*P*=0.0069).

Conclusion: Although there were no genetic predictors of clinical response to APR treatment, strong correlation was observed between the percent change from baseline in plasma TNF-α with $AUC_{Wk0\text{-}12}$ in the APR group. A negative correlation was observed between percent change from baseline in Th17 cells and $AUC_{Wk0\text{-}12}$ in the APR group and a positive association was observed between Treg cells and $AUC_{W0\text{-}12}$ in the PBO group.

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AB0528

CHARACTERIZATION OF ANTI-MPO POSITIVE INTERSTITIAL LUNG DISEASE. CLINICAL-SEROLOGIC AND RADIOLOGIC FEATURES AND SURVIVAL

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Background: Prevalence of anti-neutrophil cytoplasmic antibody (ANCA) in patient with idiopathic pulmonary fibrosis (IPF) ranges from 1 to 35%, mainly anti-MPO. The presence of ANCA positivity seems to be a poorer prognostic factor in patient with IPF, and some of these patients will develop clinical vasculitis (7-23%).

Unfortunately, the majority of the available studies on this topic are retrospective and the real natural history of the disease remains poorly understood.

Objectives: Aim of the study was to investigate the clinical, serological and radiologic features of patients with interstitial lung disease (ILD) and positivity for anti-MPO, and to evaluate the survival of this population compared with IPF patients.

Methods: We retrospectively analysed 30 patients with ILD and anti-MPO antibodies, without diagnosis of vasculitis, from 3 different rheumatology-pulmonology Italian Center.

For each patient, clinical, radiologic and serological data were evaluated. Treatments were also collected, both immunosuppressants or antifibrotic agents.

Finally, survival of ILD-MPO patients and of 90 unselected idiopathic pulmonary fibrosis (IPF) patients was compared.

Results: Thirty patients were enrolled in the study (see table for the characteristics of the patients).

Fibrosing pneumonia was described in 73.3% of patients (usual interstitial pneumonia [UIP] in 19 patients), and 10 patients (33.3%) received antifibrotic drugs, all with UIP pattern. Of interest, 7 patients were treated with immunosuppressants

Table. Serological, clinical and radiological features of anti-MPO + interstitial lung disease

Number	30
Males/female	15/15
Median age (years + IQR)	68 (17)
Median follow-up (months + IQR)	39.5 (61)
Smoke	36.70%
ILD pattern	
Usual interstitial pneumonia	63.30%
Nonspecific interstitial pneumonia	16.70%
Hipersensitivity pneumonia	10%
Other fibrosing pneumonia	10%
Median FVC (% + IQR)	83 (23)
Median DLCO (% + IQR)	53 (28)
Clinical features	
Raynaud's phenomenon	7.70%
Sicca syndrome	0
Arthralgias	20%
Arthritis	3.40%
Serology	
Antinuclear antibodies	30.80%
Anti-extractable nuclear antibodies (ENA)	8%
Anti-SSA	4%
Rheumatoid factor	21.40%
Therapy	
Immusuppressants	23.30%
Anti-fibrotic drugs	33.30%

(azathioprine, cyclophosphamide, mycophenolate mofetil), independently by the ILD pattern and 21 (70%) low dosage of steroids.
After a median period of 23.5 months (range 11-111), 7 patients developed an ANCA associated vasculitis, while other 3 developed other rheumatic diseases.
Finally, when compared with IPF, ILD-MPO patients had a better survival (81.2%±0.9 vs 54.7±0.7 for ILD-MPO and IPF, respectively; p=0.045)
Conclusion: ILD positive for anti-MPO antibodies are still a not definite condition. We need larger population to identify possible markers for the evolution in an ANCA associated vasculitis, to define the prognosis of disease and the better therapeutic approach.
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Disclosure of Interests: None declared
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AB0529 TEMPORAL ARTERY ULTRASOUND (TAUS) IS A RELIABLE TECHNIQUE TO RULE OUT GCA EVEN IN THE LEARNING PHASE

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Background: Giant cell arteritis (GCA) is an emergency. The initial treatment with high dose glucocorticoids (GC) is often started on clinical suspicion without waiting for Temporal artery biopsy (TAB) results, which can take days to be available. TAUS is a simple, non-invasive test which is readily available. However, like any other ultrasound, it is also operator dependent. A positive halo sign is the most specific abnormality seen on TAUS in GCA patients. The percentage of false positive TAUS in GCA diagnosis is low (1), but it can result in over diagnosis and unnecessary exposure to high dose GC in elderly population.
Objectives: We looked at the reliability of TAUS in ruling out GCA after it was introduced within our rheumatology department one year ago.
Methods: We adopted the quality improvement methodology for assessment. Retrospective data of suspected GCA patients was collected over the last two years. TAUS was introduced regularly to the investigative plan after eleven months. Two Rheumatology consultants were trained in TAUS. Results were compared before and after the introduction of ultrasound as a diagnostic tool. In collecting the data, our main focus for documentation was based on clinical symptoms, TAUS and TAB results. We aimed to increase the awareness of appropriate GCA referrals among the primary and secondary care with the support of teaching sessions.
Results: From January 2018 to November 2019, 101 patients were referred to rheumatology with suspected GCA. Median age of our cohort was 72 years with male to female ratio of 1:3. 35 patients were referred in the first 11 months out of which, 10 (28.6%) were diagnosed with GCA. TAUS and TAB was done in 20% and 49% of patients respectively. 66 patients were referred in the next 12 months after TAUS was introduced. Out of 66, 14 patients (21.2%) were diagnosed as GCA. TAUS and TAB were done in 82% and 38% of the patients respectively. As listed in table 1, only 1 patient was found to have positive TAB after a negative TAUS (false negative). All of patients with positive TAUS were treated as GCA on the basis of clinical grounds, irrespective of TAB results. Despite the regular use of TAUS as a diagnostic tool in the second phase, there is a higher percentage of patients (78.8%) in which GCA was ruled out.

TAUS introduction	Before regular TAUS (Jan 2018 – Nov 2018)	After regular TAUS (Dec 2018 – Nov 2019)
Patients referred	35	66
GCA	10 (28.6%)	14 (21.2%)
Not GCA	25 (71.4%)	52 (78.8%)
TAUS done in	20%	82%
TAB done in	49%	38%
TAUS -ve and TAB +ve	0	1
TAUS +ve and TAB -ve/not done	2	8

Conclusion: After the routine introduction of TAUS, the percentage of patients diagnosed with GCA has declined and clinicians have been able to exclude suspected GCA diagnosis in a larger proportion of patients referred. This is noteworthy as our Rheumatologists are still in the learning phases of determining the significance of utility of TAUS. There is only a small decline in TAB frequency, which is expected to go down further in the coming years. We also noticed that the number of patients referred has almost doubled. This might be due to better education and awareness at the primary and secondary care level which was done as part of the project.
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AB0530 CHARACTERISTICS AND MEDIUM-TERM OUTCOMES OF TAKAYASU ARTERITIS–RELATED RENAL ARTERY STENOSIS: ANALYSIS OF A LARGE CHINESE COHORT

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Background: The incidence of renal artery stenosis in Takayasu arteritis (TA) was 20%–60% according to previous reports. The specific characteristics of patients with TA-related renal artery stenosis and the effect of revascularization procedures on prognosis have not been fully investigated.
Objectives: To investigate the characteristics of patients with TA-related renal artery stenosis and identify the predictors of medium-term adverse outcomes.
Methods: Data for 567 patients registered in a large prospective observational cohort-the East China Takayasu arteritis cohort-up to April 30, 2019, were retrospectively analyzed.
Results: Renal artery stenosis was confirmed in 172/567 (30.34%) patients, with left renal artery involvement seen in 73/172 (42.44%) patients. Renal insufficiency at presentation (HR = 2.37, 95% CI: 1.76-15.83, p = 0.03), bilateral renal artery involvement (HR = 6.95, 95% CI: 1.18-21.55, p = 0.01), and severe (>75%) stenosis (HR = 4.75, 95% CI 1.08-11.33, p = 0.05) were predictors of adverse outcomes. Revascularization was performed for 46/172 (26.74%) patients. Patients without preoperative treatment had higher rate of restenosis (44.44% vs. 15.79%, p < 0.01) and hypertension deterioration (25.93% vs. 10.53%, p < 0.01) after the procedure. Non-receipt of preoperative treatment (HR = 6.5, 95% CI: 1.77-32.98, p = 0.04) and active disease at revascularization (HR = 4.21, 95% CI 2.01-21.44, p = 0.04) were independent predictors of adverse outcomes after revascularization.
Conclusion: Patients with uncontrolled or worsening hypertension or/and renal function may benefit from revascularization. Those who have received preoperative treatment may have more favorable revascularization outcomes. Prognosis appears to be poorer for patients with renal insufficiency at presentation, bilateral artery involvement, and severe stenosis.
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AB0531 GOLIMUMAB IN THE TREATMENT OF SEVERE AND/OR REFRACTORY VASCULO-BEHÇET'S DISEASE: A SINGLE-CENTRE EXPERIENCE IN CHINA

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Background: Vascular involvement is one of the leading causes of mortality and morbidity in Behcet's Disease (BD)[1]. Surgical treatments are difficult for Vaculo-BD (VBD) patients due to the high risk of serious postoperative complications without effective and promptly perioperative immunotherapy[2, 3]. Anti-tumor necrosis factor alpha (TNF-α) therapy has been reported as a potential treatment in severe VBD, e.g. infliximab (IFX) and adalimumab (ADA). However, only few case reports are available regarding the fully humanized monoclonal antibody to TNF-α, golimumab (GOL), in the management of VBD[4].
Objectives: The objective of this study was to report the efficacy and safety of GOL for the treatment of severe and/or refractory VBD.
Methods: We retrospectively analyzed the efficacy and safety profile of patients with severe and/or refractory VBD treated with GOL in our medical center between 2018 to 2020.

Results: Nine VBD patients (8 male and 1 female) were enrolled, with a mean age and median course of 37±8.6 years and 72 months (range 12 to 300), respectively. Cardiac involvements (severe aortic regurgitation secondary to BD) were presented in 7 patients, including 2 patients with post-operative paravalvular leakage (PVL) after aortic valve replacement surgery. Multiple vascular lesions were documented in the other 2 patients, including one patient with life-threatening multiple pulmonary aneurysms, pulmonary thromboembolism and recurrent deep vein thrombosis, and another patient with abdominal aortic pseudoaneurysm and multiple artery stenosis and occlusion. Prior to GOL therapy, all patients experienced disease progression despite high-dose glucocorticoids combined with multiple immunosuppressants. Moreover, seven patients required effective and fast control of inflammation and a decrease of glucocorticoid dose during the perioperative period. They were treated with GOL, 50mg every 4 weeks, in combination with background low-or medium-dose glucocorticoids and immunosuppressants, for a median of 6 (range 3-15) months. After a mean duration of follow-up of 10 (range 2-6) months, all patients achieved improvement both in clinical symptoms and serum inflammation markers. The ESR level [4.88±4.94 mm/h vs 31.13±31.78mm/h, P<0.01] and CRP level [1.9 (0.11-3.73)mg/L vs 24.3 (0.4-85.57)mg/L, P<0.01] significantly decreased. The dosage of glucocorticoid[10 (0-15) vs 40 (0-100)mg/d, P<0.01] effectively tapered, indicating a potential steroid-sparing effect. No newly-onset aneurysm and recurrent venous thrombosis were observed. Also, one patient had a marked reduction in size and number of pulmonary aneurysms. No post-operative PVL was observed in the five patients after Bentall operation with a median follow-up of 10 months. One patient with severe aortic regurgitation remained stable and without surgical intervention with the treatment of GOL for 16 months. No severe complication occurred in one patient after underwent endovascular repair of abdominal aorta for 8 months. GOL was well-tolerated, and no serious adverse event was observed.

Conclusion: Our results suggested that GOL is safe and effective for the treatment of patients with severe and / or refractory VBD. Further controlled studies are warranted to confirm the therapeutic potential of GOL in VBD patients.

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AB0532 CORRELATION WITH THE FREQUENCY OF DISEASE RELAPSES DURING THE FIRST 3 YEARS FROM THE DIAGNOSIS AND DISEASE OUTCOMES IN BEHCET'S SYNDROME

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Background: Beside the organ involvement, a number of demographic factors could considerably influence the long-term and short-term outcomes of Behçet's syndrome (BS): age at disease onset, duration of disease, gender and sex. Younger men patients are more suitable to have a more severe disease, due to an increased frequency both of morbidity and mortality, related to ocular,vascular and neurological involvement

Objectives: The primary aims of the study were to evaluate disease activity in a cohort of BS patients consecutively followed in a BS clinic of a tertiary centre and to explore whether there is a correlation between frequency of relapses in the first 3 years of diseases and disease outcomes.

Methods: One-hundred and sixty-five patients (91 males and 74 females; mean age 39±9 years, mean disease duration 9±5) with a diagnosis of BS according to the ISG criteria were studied. Disease activity has been evaluated by BDCAF and patients were also categorized in major or minor involvement of BS according or not to the presence of ocular, neurological and vascular involvement in the course of disease The numbers of relapses in the first 3 years from diagnosis were correlated with disease outcome and damage.

Results: At time of the evaluation, 47% of BS patients presented an active disease; 69 patients presented muco-cutaneous involvement, 39 ocular disease, 21 joint involvement, 12 neurological impairment and 9 gastro-enteric involvement. Seventy-nine percent of patients presented in the course of the disease a severe BS involvement and the majority was represented by patients characterised by a more frequent relapse in the first 3 years of disease (M/F: 65/48, mean age 43±3 years). Those patients who experienced a more higher number of relapse in the first 3 years compared to the others were also characterised by poor disease outcomes and worse prognosis over time and this correlation was independent by the therapies taken.

Conclusion: The high frequency of relapses during the first three years from diagnosis may be considered an important prognostic factor for disease outcome in BS patients, therefore could be taken into account as a useful element to tailor the management, not only according to the type and severity of symptoms and epidemiological factors.

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AB0533 ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY (ANCA) IN GENERAL POPULATION WITHOUT ANCA ASSOCIATED VASCULITIS

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Background: Currently it is hypothesized that many systemic autoimmune diseases occur due to environmental risk factors in addition to genetic risk factors. Anti-Neutrophil Cytoplasmic Antibody (ANCA) is mainly associated with three systemic autoimmune disease including granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), eosinophilic granulomatosis with polyangiitis (EGPA). It is known that ANCA can be positive before clinical symptoms in patients with known diagnosis of GPA and ANCA titers rise before clinical manifestations appear. However, prevalence of ANCA among general population is not well known. It has not been described as well how many of people with positive ANCA eventually develop clinical manifestations of ANCA associated Vasculitis.

Objectives: This study aims to estimate prevalence of ANCA in general population without ANCA associated Vasculitis. It also describes natural disease course of people with positive ANCA without ANCA associated Vasculitis. Risk factors for positive ANCA are also analyzed.

Methods: This is a single center retrospective study at Center for Preventive Medicine of St. Luke's International Hospital in Tokyo. ANCA was checked among the patients who wished to between 2018 and 2019. St. Luke's Health Check-up Database (SLHCD) was utilized to collect the data. The patients whose serum was measured for ANCA were identified. The data for basic demographics, social habits, dietary habits and laboratory data were extracted. The charts of the patients with positive ANCA were reviewed.

Results: Sera of total 1204 people were checked for ANCA. Of these 1204 people, 587 (48.8%) are male and the mean age was 55.8 years (32.6 to 79). There were total 11 patients with positive ANCA. Myeloperoxidase ANCA (MPO-ANCA) was positive for 3 patients and proteinase 3 ANCA (PR3-ANCA) was positive for 8 patients. Of these 11 patients, 5 were male (45.5%) and the mean age was 54.6 years. Two patients had history of autoimmune disease (primary biliary cirrhosis and ulcerative colitis). Five patients were evaluated by rheumatologists with the median follow-up period of 274 days. None of them developed clinical signs and symptoms of ANCA associated Vasculitis. Four out of five patients had ANCA checked later, two of which turned negative. The prevalence of ANCA in this cohort was 0.9% (95% confidence interval [95% CI]: 0.5% to 1.6%). Univariate analysis was performed to identify risk factors of positive ANCA. The variables analyzed include age, gender, body mass index (BMI), smoking habits, alcohol intake, dietary habits (fruits, fish, red meat), hypertension, dyslipidemia, and laboratory data. None of these variables demonstrated statistically significant differences except for positive rheumatoid factor (ANCA positive group: 33 % vs ANCA negative group: 9.1%, p value = 0.044).

Conclusion: The prevalence of ANCA in this cohort was 0.9% (95% CI: 0.5% to 1.6%). None of them who had a follow-up developed ANCA associated Vasculitis during the follow-up period. Longer follow-up and more patients are necessary to determine natural course of people with positive ANCA.

Disclosure of Interests: None declared

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AB0534 EFFICACY OF TOCILIZUMAB IN LARGE-VESSEL GIANT CELL ARTERITIS: A SINGLE-CENTER REAL-LIFE EXPERIENCE

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Background: In a significant proportion of giant cell arteritis (GCA) patients, large vessels (LV) are affected[1]. GiACTA trial showed tocilizumab (TCZ) to be effective for the treatment of GCA[2] but did not differentiate between patients with and without LV involvement and did not evaluate LV-imaging response.

Objectives: To assess efficacy of TCZ in LV-GCA, evaluating both clinical symptoms and vascular inflammation on PET scan.

Methods: Data from GCA patients followed-up at our Institution between January 2003 and December 2019 were retrospectively collected. Only TCZ-treated patients, with evidence of LV 18F-FDG-uptake at baseline (T0) and who repeated a PET scan after at least 6 months of treatment (T1) were included. All patients received subcutaneous TCZ 162 mg weekly. PET scans were read by 2 physicians blinded with regard to clinical data and to each other's assessment; vascular inflammation was quantified using the PETVAS score[3]. Clinical symptoms, prednisone (PDN) dosage, and PETVAS score between T0 and T1 were compared. Flares and adverse events were recorded. Non parametric tests were used.

Results: 61 TCZ-treated GCA patients were identified. Of these, 28 (45.9%) had evidence of vascular inflammation at T0, and 14 of them (10 female, mean age 66.2±7.4 years) repeated a PET scan during follow-up, after a median of 13 months (IQR, 9.5-17.5). 10 patients started TCZ upon GCA relapse, with a median delay from GCA diagnosis of 7.5 (3-15.8) months; 4 patients were newly diagnosed and started TCZ at diagnosis. At T0, 10 patients had systemic symptoms, 6 patients had cranial symptoms, and 7 had polymyalgia rheumatica (PMR). 12/14 patients were on concomitant steroids, with a median PDN daily dose of 15 (15-25) mg. Erythrocyte sedimentation rate and C-reactive protein levels were respectively 35 (21-39) mm/h and 7.8 (3.2-11) mg/L. Median PETVAS was 7 (3.3-11). At T1, 13/14 patients were asymptomatic; 1 patient had a PMR relapse. No GCA flare was recorded. Median PDN daily dose was 1.25 (0-2.5), p=0.002, and PDN suspension was achieved in 5 patients. Median PETVAS was 0 (0-0.8), p=0.003; only in 1 patient PETVAS increased between T0-T1 (from 2 to 5), in absence of clinical symptoms. This was the patient with the longest delay between diagnosis and TCZ start (124 months) and suspended TCZ for 3 months due to oral aphthosis. No patients had severe infections; 1 patient definitively suspended TCZ at T1 due to severe leukopenia.

Conclusion: In LV-GCA patients, TCZ seems to be effective in obtaining clinical remission and in reducing vascular inflammation on PET scan.

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AB0535

ARE THE NEUTROPHIL/LYMPHOCYTE RATIO (NLR) AND PLATELET/LYMPHOCYTE RATIO (PLR) USEFUL TO COMPARED WITH ACUTE PHASE REACTANTS (ESR/CRP) FOR DIAGNOSIS AND PROGNOSIS OF PATIENTS WITH ACTIVE TAKAYASU'S ARTERITIS (TAK)?: AN ANALYSIS BASED ON ROC AND KAPLAN-MEIER CURVES IN A LATIN AMERICAN POPULATION

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Background: The NIH criteria are the main measure to determine activity in TAK. NLR and PLR appear promising to predict disease activity [(1)]. TAK is one of the most frequent vasculitis in Colombia with a prevalence of 13.3%; however, in more recent years the information is sparse about TAK clinical behavior in our region, which leads to a late diagnosis. Although survival has improved with immunosuppressive treatment, relapses remain high especially in the first year of diagnosis

Objectives: Compare NLR and PLR with ESR/CRP to predict TAK activity
Show survival and relapse in patients with TAK followed to 7 y

Methods: Retrospective cohort of 43 patients with TAK between 2011-2018 with prospective follow-up of relapses and mortality. 88% fulfilled the ACR 1990 criteria. The disease activity was determined according to NIH criteria: active disease (n=34) and inactive disease (n=9). Through bivariate analysis, we compared the clinical and radiologic characteristics between age groups (table 1) using the Pearson test and Wilcoxon range test. Value of p <0.05 was statistically significant. Survival and relapse analysis were performed using Kaplan-Meier plots. Sensitivity (Sn), specificity (Sp) and area under the curve (AUC) were determined for NLR, PLR, ESR and CRP by receiver-operating curves (ROC) compared to NIH criteria.

Table 1. Comparison of Clinical Features in Patients with TAK

	No (%) of Patients		
	Age at diagnosis ≤ 40 y (n=32)	**Age at diagnosis ≥ 40 y (n=11)**	**P value**
Female	30 (94)	11 (100)	0.39
Age at symptom onset (years), median: (Interquartile range –IQR-)	20 (17-25)	52 (47-57)	0.110
Time from symptom onset to diagnosis (months) median (IQR)	9.5 (2-15)	36 (1.5-24)	0.774
Smoking	2 (6)	6 (54)	**0.002**
Dyslipidemia	7 (22)	6 (54)	**0.042**
ACR Criteria 1990			
Claudication of extremities	14 (43)	5 (45)	0.922
Upper extremities blood pressure discrepancy > 10 mmHg	19 (59)	6 (54)	0.779
Decreased brachial artery pulse	24 (75)	9 (82)	0.644
Subclavian artery or aorta bruit	19 (59)	6 (54)	0.774
Arteriographic abnormality	27/27 (100)	11/11 (100)	1.0
ESR (mm/h), median (IQR)	56 (23-115)	38 (33-76)	**0.011**
CRP (mg/dL), median (IQR)	1.35 (0.4-3.4)	3 (1.49-18.5)	**0.020**
Creatinine (mg/dL), median (IQR)	0.72 (0.6-0.83)	0.84 (0.75-1)	0.007
Hata-Numano classification			
I	15%	18%	
IIa	6%	9%	
IIb	6%		
III	6%		
IV	3%	9%	
V	59%	64%	

Results: 41 patients were women (96%) with a median age at diagnosis of 22 y and an interval from the onset of disease to diagnosis of 12 months (IR:1-168 m). The population over 40 years had a greater comorbidities burden (54% had history of smoking and dyslipidemia) and a major interval between the onset of disease and the diagnosis (36 months vs 9.5 months). Most frequent vascular phenotypes were types V (62%) and I (16%). NLR and PLR showed poor performance to predict activity compared with CRP; NLR level of 1.74 showed to be the predictive cut-off value for active TAK (Sn: 85.3%, Sp: 37.5%, AUC = 0.563). PLR level of 112.5 was found to be the predictive cut-off value for active TAK (Sn: 76.5%, Sp: 50%, AUC = 0.517). The CRP was the most accurate biomarker (Sn: 79.4%, Sp: 75%, AUC = 0.761) while the ESR was lower to predict activity (Sn: 63.6%, Sp: 75%, AUC = 0.598) (figure 1). At 5 years, survival was 83% and 50% of patients had presented at least one relapse (figure 2)

Conclusion: Our data does not support the use of NLR or PLR to differentiate relapse and remission in TAK. CRP had better diagnostic performance than ESR in the prediction of activity compared to NIH criteria. The 5-year survival in this cohort is below that reported after 1985 (reported survival: 90-96%) [(2)]

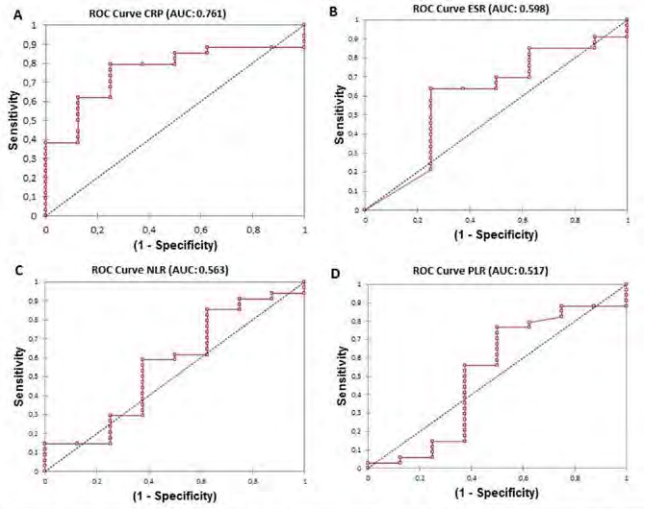


Figure 1: Receiver-operating characteristic (ROC) curves for **A**: CRP, **B**: ESR, **C**: Neutrophil-to-lymphocyte ratio (NLR) and **D**: Platelet-to-lymphocyte ratio (PLR)

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Disclosure of Interests: None declared

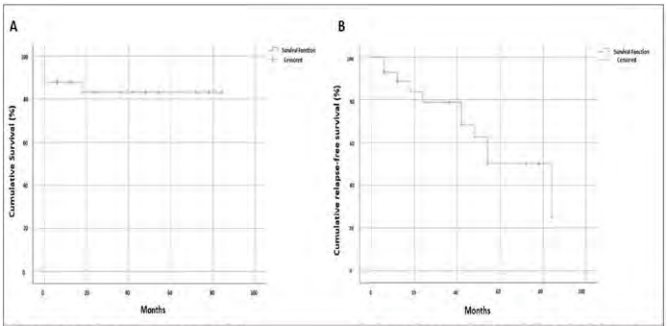


Figure 2: A. Long-term mortality in patients with TAK B. Relapse-free survival in patients with TAK at 7-year follow up.

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AB0536 EFFECT OF HYDROXYCHLOROQUINE TREATMENT IN MUCOCUTANEOUS MANIFESTATIONS IN PATIENTS WITH BEHÇET'S SYNDROME

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Background: Behçet syndrome (BS) is a rare multisystemic vasculitis, most commonly seen in regions along the ancient Silk Road. It runs a relapsing and remitting course. Mucocutaneous disease, consisting of oral ulcers, genital ulcers and skin lesions is often reported. EULAR recommendations advise colchicine and topical agents for the treatment of these lesions.[1] Not all patients respond adequately, thus, it is important to explore alternative treatment options.

Objectives: To study the efficacy of hydroxychloroquine (HCQ) 400 mg daily in patients with mucocutaneous BS.

Methods: Data on all patients who presented at the outpatient Behçet clinic in New York were recorded. Patients with a first prescription with HCQ and a follow-up of 3 months (range: 2.75-41.2 months) were included. Patient reported outcomes BSAS and RAPID3 were used to evaluate the effect of HCQ. Results of all patients and of International Study Group (ISG) positive patients were analyzed separately using Wilcoxon rank tests.

Results: We included 94 patients with a first prescription of HCQ. 72 patients (76.6%) fulfilled ISG criteria. Mean age was 36.1 years (SD 12.5), 76 patients (80.9%) were female and 11 patients (11.7%) were from Silk Road countries.

Mean duration until follow-up was 6.5 months (SD 5.7). Median BSAS scores in ISG+ patients at baseline did not differ significantly from ISG- patients, except for skin lesions (5.0 in ISG+ vs. 0.5 in ISG- p=0.005). BSAS scores at follow-up did not differ significantly (ISG+ vs. ISG-).

Median BSAS scores were significantly lower at follow-up compared to baseline for oral ulcers (p=0.010), skin lesions (p=0.018) and overall activity (p=0.019). Regarding genital ulcers there was no significant result, due to only 37 patients reporting complaints of genital ulcers. Performing these analyses in ISG+ patients only did not change these results, except for BSAS overall activity, which lost significance (p=0.057).

RAPID3 scores were not statistically different between baseline and follow-up (9.67 vs. 8.75, p=0.145), nor were its separate components function (p=0.67 vs. 0.67, 0.713), pain (4.0 vs. 4.0, p=0.157) and patient global (5.0 vs. 4.5, p=0.095).

The majority of patients used prednisone at baseline (58.5%) and at follow-up (57.4%). In 15 patients, prednisone was stopped at follow up, in 13 patients it was started.

Conclusion: HCQ improves median BSAS scores for oral ulcers, skin lesions and overall activity at 3 months follow-up compared to baseline. These results were similar in ISG+ patients (except for overall activity). Additional research is needed to assess the effect of HCQ in more patients and over multiple time points.

Table 1. Median BSAS scores of patients treated with HCQ.

	Baseline (median, IQR)	Follow-up 3 months (median, IQR)	P-values
All patients (n=94)			
Oral ulcers	5.0 (2.00-7.88)	3.0 (1.00-6.00)	**0.010**
Genital ulcers	0.0 (0.00-3.88)	0.0 (0.00-3.00)	0.371
Skin lesions	5.0 (1.25-7.00)	2.5 (0.00-7.00)	**0.018**
Overall activity	5.5 (4.00-8.00)	5.0 (2.00-7.25)	**0.019**
ISG+ patients (n=72)			
Oral ulcers	5.25 (2.00-7.63)	3.25 (1.00-6.00)	**0.007**
Genital ulcers	0.5 (0.00-4.00)	0.0 (0.00-3.00)	0.684
Skin lesions	5.0 (2.00-7.13)	3.0 (0.00-7.00)	**0.015**
Overall activity	6.0 (4.00-8.00)	5.0 (2.00-7.50)	0.057

References:

[1] Hatemi G et al. 2018 update of the EULAR recommendations for the management of Behçet's syndrome. Ann Rheum Dis 2019;77:808-818

Disclosure of Interests: Floor Kerstens: None declared, Shreen Mohamed: None declared, Ingrid Visman: None declared, Franktien Turkstra: None declared, Christopher Swearingen: None declared, Yusuf Yazici Consultant of: BMS, Celgene Corporation, Genentech, Sanofi – consultant, Consultant of: BMS, Celgene Corporation, Genentech, Sanofi – consultant

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AB0537 DIAGNOSTIC ACCURACY OF SYMPTOMS AND SIGNS FOR GIANT CELL ARTERITIS: SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Making a correct diagnosis of giant cell arteritis (GCA) is critical given the potential complications of the disease and its therapy. Estimation of the clinical probability of GCA is challenging. Prediction models might be helpful, but have methodological and practical draw backs. One earlier meta-analysis described the diagnostic accuracy of symptoms and signs for a positive temporal artery biopsy [1]. In the latter study, the diagnostic accuracy of symptoms and signs might have been overestimated due to inclusion of case-control studies.

Objectives: To evaluate the diagnostic accuracy of symptoms and signs for GCA.

Methods: PubMed, EMBASE and the Cochrane Database were searched for relevant studies. Studies were eligible if: all patients were suspected of having GCA; either a temporal artery biopsy (TAB), imaging test, or clinical diagnosis was used as reference standard for GCA; a 2x2 table was available for at least one symptom, physical sign or routine laboratory test (i.e. the index tests). Case reports and case-control studies were excluded. The screening, full text review, quality assessment with QUADAS-2 tool and data extraction were performed by two investigators. Hierarchical logistic regression modelling provided the pooled estimates of likelihood ratios with their 95% confidence intervals. Likelihood ratios <0.5 (i.e. making GCA less likely) or >2.0 (i.e. making GCA more likely) were considered diagnostically relevant.

Results: Out of 1359 reports screened, 59 studies were included in the study. These reports contained 13406 patients, including 3940 GCA patients. Most studies were retrospective, performed at tertiary centres and published after the prior meta-analysis [1]. TAB was the reference standard in 36 studies and a clinical diagnosis in 23 studies. Quality assessment revealed substantial risk of selection bias in the majority of studies. Studies using a clinical diagnosis were at risk of bias, as the reference standard might be influenced by the index tests (e.g. symptoms). Jaw claudication, limb claudication, temporal tenderness, temporal artery abnormalities, especially arterial thickening or loss of pulse, and anterior ischemic optic neuropathy provided a positive likelihood ratio >2.0. None of the 19 symptoms and 7 physical signs evaluated, provided a negative likelihood ratio <0.5. An ESR >60mm/hr and platelet count >400*10^9/L provided a positive likelihood ratio of >2.0. Absence of an elevated CRP level or ESR >60mm/hr yielded a negative likelihood ratio of <0.5. Studies using a clinical diagnosis as reference standard reported higher positive likelihood ratios for jaw claudication, weight loss and PMR when compared to TAB studies. Absence of an elevated CRP provided a lower negative likelihood ratio in studies using the clinical diagnosis.

Conclusion: Few clinical findings may help to estimate the clinical probability of GCA. The presence or absence of any particular symptom or sign does not sufficiently rule out or rule in GCA. These findings highlight the need of additional tests (i.e. imaging, biopsy) in patients suspected of having GCA.

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Disclosure of Interests: Kornelis van der Geest Speakers bureau: Roche (2019), Maria Sandovici: None declared, Elisabeth Brouwer Consultant of: Roche (consultancy fee 2017 and 2018 paid to the UMCG), Speakers bureau: Roche (2017 and 2018 paid to the UMCG), Sarah Mackie Grant/research support from: Roche (attendance of EULAR 2019; co-applicant on research grant), Consultant of: Sanofi, Roche/Chugai (monies paid to my institution not to me)
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AB0538 PREGNANCY OUTCOMES IN PATIENTS WITH TAKAYASU'S ARTERITIS: CASE SERIES

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Background: Takayasu's arteritis (TA) is most prevalent in women of childbearing age. Although its activity and risk of relapse are low during pregnancy, up to 40% of patients may have unfavorable obstetric outcomes and therefore it is important to know their clinical behavior.
Objectives: To describe the clinical features and obstetric outcomes of pregnant women with TA treated in a tertiary center.
Methods: Retrospective evaluation of medical records of 6 pregnancies in 6 women with TAs treated in a tertiary center in Medellin, Colombia between 2011-2018.
Results: Six women who were 17.5 (RI 9.25) years old at diagnosis and 24 (RI 8.25) years old at delivery, their disease duration were 5.5 (RI 10.5) years. Three patients had extensive aortic involvement classified as Numano type V, two as type IIB and one as type I. At delivery, three patients were active and required immunosuppressants, five had high blood pressure, one developed preeclampsia in the second trimester, one had severe mitral and tricuspid insufficiency with decreased ejection fraction of the left ventricle; two had aneurysms (left subclavian artery and ascending aorta). There were two fetal deaths, one due to intrauterine growth restriction and placental insufficiency and another of unknown etiology; both patients with disease activity, extensive aortic condition and arterial hypertension; no pregnancy resulted in abortion or preterm birth. Five deliveries were by caesarean section by maternal indication; there was no aortic dissection, aneurismal rupture or cerebral hemorrhage (table).

Table. Patient's characteristics

Patient	Age at diagnosis	Age at delivery	Clinical features	Hata-Numano classification	Maternal outcome	Fetal outcome
1	6	17	HT, absence of left brachial and radial pulses, L carotid and subclavian murmurs, LVEF 47%	V	HT, C-section	Term delivery, SGA
2	22	26	HT, abscence of L brachial and radial pulses, L carotid and subclavian murmurs, dyspnea, angina	V (plus pulmonary)	HT, vaginal birth	Placental insufficiency, IUGR, fetal death
3	14	38	HT, abscence of L brachial and radial pulses, L carotid and subclavian murmurs, intermittent claudication, dyspnea, aortic regurgitation	IIB	HT, C-section	Term delivery, SGA
4	18	24	HT, malaise,, abscence of L brachial and radial pulses, intermittent claudication, arthralgia	IIB	Preeclampsia, C-section	Term delivery, SGA
5	17	22	Fever, malaise, intermittent claudication, arthralgia	I	C-section	Term delivery, SGA
6	21	24	HT, abscense of bilateral femoral, popliteal, tibial and pedial pulses, headache, dizziness, amaurosis	V	HT, C-section	Fetal death

HT: hypertension; L: left; LVEF: left ventricular ejection fraction; C-section: cesarean section; SGA: small for gestational age; IUGR: intrauterine growth restriction

Conclusion: Pregnant women with active disease and extensive aortic condition presented unfavorable obstetric results, suggesting that an inadequate control of vasculitis may lead to greater maternal-fetal complications.
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Disclosure of Interests: None declared
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AB0539 URINARY INFLAMMATORY CELL ANALYSIS REFLECTS THE RENAL HISTOPATHOLOGY IN ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY-ASSOCIATED VASCULITIS

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Background: The anti-neutrophil cytoplasmic autoantibody (ANCA)- associated vasculitides (AAVs) include microscopic polyangiitis (MPA), granulomatosis with polyangitis (GPA), and eosinophilic granulomatosis with polyangitis (EGPA). These small-vessel vasculitides are characterized by necrotizing inflammation of the vessel wall, particularly affecting small arteries, arterioles, and capillaries in systemic organs, and the kidney is one of the most frequently involved organs. Although kidney biopsy is necessary for deciding the therapeutic protocol, it is invasive and is sometimes hard to perform biopsy because of patient's severe general condition. We have already reported that T cells and macrophages appear in the urine of patients with glomerulonephritis, accompanied by active cellular infiltration such as cellular crescent formation and diffuse interstitial cell infiltration, but not in the urine of patients with glomerulonephritis without the active inflammatory lesions.
Objectives: In this study, we examined the utility of urinary inflammatory cell analysis for accessing kidney histopathological findings in AAVs.
Methods: This was a cross-sectional, retrospective chart study. Thirty-six AAV patients who had been referred to Niigata University Hospital between 2002 and 2018, and performed percutaneous kidney biopsy and urinary inflammatory cell analysis, were participated in this study. Thirty-two patients had MPA, and 4 had GPA. The kidney biopsy findings were classified into Berden's classification (a method to categorize glomerular lesions into four classes) and Neumann's classification (a method to evaluate glomerular, tubulo-interstitial, and vascular lesions by using activity indexes and chronicity indexes). Flow-cytometric analysis of urinary inflammatory cells was performed for each subject. Numbers of urinary T cells or macrophages were determined by multiplying the number of viable cells in the gated mononuclear cell region in each sample by the percentage of urinary CD3-positive or CD14-positive cells in the population, respectively. The correlations between the results of both methods and the numbers of urinary inflammatory cells were examined using Kruskal-Wallis test and Spearmann's rank correlation coefficient. A p-value of <0.05 was taken to denote statistical significance.
Results: The numbers of urinary inflammatory cells showed a trend of increase in crescentic category without statistical significance in Berden's classification. Meanwhile, activity indexes had significant positive correlations with the number of urinary CD3-positive cells ($r = 0.541$, $p = <0.001$), CD14-positive cells ($r = 0.354$, $p = 0.034$), and total inflammatory cells ($r = 0.449$, $p = 0.006$) in Neumann's classification.
Conclusion: The numbers of urinary inflammatory cells reflect the active lesions of kidney histopathological findings, and these results indicate the usefulness of urinary inflammatory cell analysis for assessment of kidney biopsy findings in patients with AAVs.
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Disclosure of Interests: None declared
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AB0540 CLINICAL ANALYSIS OF AORTA INVOLVEMENT IN PATIENTS OF ANCA-ASSOCIATED VASCULITIS

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Background: ANCA-associated vasculitis (AAV) is an autoimmune disease that involves abnormal death of neutrophils and leads to necrotic inflammatory reactions in blood vessels, including microscopic polyangiitis (MPA), Granulomatous polyangiitis (GPA) and Eosinophilic granulomatous polyangiitis (EGPA). AAV is mainly involved in small blood vessels, and intermediate arterial lesions can also occur, but the large arteries and their primary branches are rarely involved.
Objectives: To summarize the clinical characteristics of aortic involvement in patients with ANCA-associated vasculitis (AAV).
Methods: The clinical manifestations, systemic involvement, laboratory examination, imaging characteristics and treatment of aortic involvement in AAV patients admitted to Peking Union Medical College Hospital from January 2013 to December 2018 were retrospectively analyzed.
Results: Nine patients were enrolled in our study. The ratio of male to female was 2:1 and the median age was 47 years old. Of the 9 patients, 4 were GPA (44%), 4 were MPA (44%) and 1 was EGPA (11%). The aorta is involved in an average of 3 locations per case, mainly in 7 locations: 3 ascending aorta and aortic arch, 4 in the head and arm trunk (including carotid and subclavian artery), 2 in the abdominal aorta, and 1 in the abdominal cavity. There were 2 cases of renal artery, 1 case involving brachial radial artery, 2 cases of iliac artery and lower limb artery, and 1 case involving left main coronary artery, anterior descending branch, circumflex branch, and right coronary artery. Aortic lesions: 3 cases had aneurysms, arterial dilatation and / or dissection, 6 cases had arterial stenosis or occlusion and 3 cases had periarteritis.When major arterial involvement was found, the AAV of the patients were mostly active, with an average of 19 points for BVAS vasculitis activity and 1 for FFS score. 6 cases had lung involvement (67%), 6 cases had kidney involvement (67%), 4 cases had ENT involvement (44%), 3 cases had nervous system involvement (33%), and 1 case had gastrointestinal involvement (11%). All patients were treated by steroid and immunosuppressant, while 1 case received the operation of ascending aorta and aortic arch replacement.
Conclusion: Mainly involved in small blood vessel inflammation, AAV may also have aorta involvement, which was more common in patients who had active disease and need more positive treatment. The affected aorta areas of these patients were mainly ascending aorta, aortic arch, and head and arm trunk, which can be manifested as aneurysms, dissections, and arterial stenosis Periarteritis, etc. If necessary, surgically treatment of the affected aorta could be considered when the situation of AAV was stable enough.
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Disclosure of Interests: None declared
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AB0541 IMPROVED SURVIVAL IN PATIENTS WITH GIANT CELL ARTERITIS: A POPULATION-BASED COHORT STUDY

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Background: In previous studies patients with giant cell arteritis (GCA) have had survival rates that are similar to the general population.
Objectives: To investigate survival trends and cause-specific mortality in patients diagnosed with GCA over a 60-year period.
Methods: We assembled a population-based incidence cohort of patients with GCA diagnosed between 1950 and 2009. All patients were included if they met the American College of Rheumatology (ACR) 1990 Criteria for the Classification of GCA. Patients diagnosed between 2000 and 2009 could also be included if they met the following criteria: age greater than or equal to 50 years, elevated inflammatory markers, and radiographic evidence of large-vessel vasculitis attributed to GCA. A non-GCA comparison cohort was assembled from the same underlying population for each patient with GCA. Patients were followed until death, last contact, or December 31st, 2018. Survival trends were analyzed by grouping patients into the following categories according to year of GCA diagnosis: Group A 1950-1979; Group B 1980-1989; Group C 1990-1999; and Group D 2000-2009. Mortality rates were estimated using the Kaplan-Meier method and were compared with expected mortality rates for persons of the same age, sex, and calendar year, as estimated by regional population life tables. Cause-specific mortality was obtained from death certificates for patients in both cohorts. The causes were grouped according to ICD-9 chapters and hazard ratios were estimated against the non-GCA comparators.
Results: The study population included 245 incident cases of GCA: 194 (79%) women and 51 (21%) men with mean age (±SD) of 76.2 (±8.3) years and median follow-up of 10.6 years. There was no overall difference in survival between the GCA cohort and the general population. The 2-, 5-, and 10-year survival rates (95% CI) were 89% (86, 93), 76% (70, 81), and 56% (50, 63) respectively with a standardized mortality ratio of 0.99 (0.86, 1.14). The standardized mortality ratios for Groups A, B, C, and D were 0.83 (0.57, 1.17), 0.92 (0.63, 1.3), 1.21 (0.85, 1.69), 0.70 (0.50, 0.95), respectively. The overall all-cause mortality adjusted for age, sex, and calendar-year was similar between the GCA patients and their comparators with a hazard ratio of 1.03 (0.84, 1.24). Mortality due to neoplasms was significantly lower in the GCA cohort with a hazard ratio of 0.53 (0.3, 0.92). Other cause-specific mortalities were not significantly different between the groups.
Conclusion: In this population-based cohort of patients with GCA diagnosed over a 60-year period, the survival of patients diagnosed in recent years was significantly better than that of the general population. The explanation for this novel finding is unclear, but likely to be multifactorial. In this study the number of deaths due to neoplasm in the GCA group was significantly lower.
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AB0542 REACTIONS TO PNEUMOCOCCAL 13-VALENT VACCINE IN PATIENTS WITH BEHCET SYNDROME

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Background: The European League Against Rheumatism (EULAR) recommends pneumococcal 13-valent (PCV13) and 23-valent vaccines in patients with rheumatic diseases (1). Adverse reactions to 23-valent pneumococcal vaccine were previously reported in patients with Behçet Syndrome (BS) (2). These were proposed to be associated with the pathergy phenomenon which may be observed in patients with BS.

Objectives: To determine the frequency of adverse reactions to PCV13 in patients with BS who were candidates for TNF inhibitor treatment, together with ankylosing spondylitis (AS) and rheumatoid arthritis (RA) patients as controls.
Methods: All of our patients who are candidates for TNF inhibitor therapy have been offered vaccination with PCV13 since 2016. We surveyed all patients with BS, AS and RA who were vaccinated with PCV13 in our infectious diseases outpatient clinic since 2016. Patients' charts were reviewed and additionally patients were telephoned to identify any adverse local or systemic reactions. Local reactions were defined as redness, swelling, pain, and limitation of arm movement. Systemic reactions were defined as fever, headache, chills, rash, vomiting, joint pain, and muscle pain.
Results: A total of 88 patients with BS, 143 patients with AS and 133 patients with RA had been vaccinated in our infectious diseases outpatient clinic. Among these, 55/88 (62%) patients with BS, 86/143 (60%) patients with AS and all 98/143 (68%) patients with RA could be contacted. Twenty-one of 55 (38%) patients with BS, 18/86 (20%) patients with AS and 27/98 (27%) patients with RA reported at least one local and/or systemic reaction after vaccination. Patients with BS reported more systemic reactions than the other two groups (48%, 12%, 23% respectively). On the other hand local reactions were less common among patients with BS (52%, 88%, 77% respectively). The local reactions were confined to erythema at injection site, pain and difficulty in moving among patients with AS and RA while 2 patients with BS had severe papulopustular skin lesions at injection site, in addition to erythema, pain and difficulty in moving. Both of these patients were pathergy positive at the time of the diagnosis.
Conclusion: Severe papulopustular skin lesions at PCV13 injection site were observed only, but rarely, in patients with BS. Possibility of recall bias due to the retrospective nature of our study and the lack of other vaccines as controls are limitations of our study. Whether the skin lesions are caused by the skin pathergy reaction needs to be studied prospectively, as the pathergy status at diagnosis may be changed by the time these patients become candidates for TNF inhibitor treatment.
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Disclosure of Interests: Berna Yurttas: None declared, Sıtkı Safa Taflan: None declared, Nese Saltoglu: None declared, Gulen Hatemi Grant/research support from: BMS, Celgene Corporation, Silk Road Therapeutics – grant/research support, Consultant of: Bayer, Eli Lilly – consultant, Speakers bureau: AbbVie, Mustafa Nevzat, Novartis, UCB – speaker
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Scleroderma, myositis and related syndromes

AB0543 CLINICAL CHARACTERISTICS OF A GROUP OF CHRONIC GRAFT-VERSUS-HOST DISEASE PATIENTS WITH POSITIVE AUTOIMMUNITY.

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Background: Graft-versus-host disease (GVHD) is a commonly severe multiorgan complication in patients undergoing allogeneic transplantation of hematopoietic progenitors. Its chronic form reflects a complex immune response with different degrees of inflammation, immune dysregulation and fibrosis. In some chronic graft-versus-host disease (cGVHD) patients, positive antibodies have been detected, which represent the presence of immune activity and suggest the possible involvement of B lymphocytes in the disease etiopathogenesis, but their clinical utility is controversial.
Objectives: To describe the clinical characteristics of a group of cGVHD patients with positive autoimmunity treated in a multidisciplinary consultation of Rheumatology-Dermatology- Hematology of GVHD.
Methods: Observational and retrospective study to describe the clinical characteristics of the patients with positive autoimmunity collected in the database of the multidisciplinary consultation of GVHD. The variables reviewed for this study, in addition to the demographic ones, were type of antibody, disease causing the transplant, presentation, severity and type of involvement. The statistical analysis was done with Epi-info 7.2.2.6.
Results: Only 16 (16%) of the 100 patients included in the database had positive autoimmunity. Twelve (75%) tested positive to ANA, although 5 (31.25%) in a lower titer (1/80). The most common immunofluorescence pattern was the nucleolar in 88.89% (66.67% nucleolar and 22.22% nucleolar + cytoplasmic). Other antibodies detected were: 6 anti-Ro52, 2 anti-dsDNA, 1 anti-RP155, 1 anti-Fibrillarin, 1 anti-SAE1, 1 p-ANCA and 1 anti-NOR-90. The mean of age was 51.31±14.03 years. As for sex 4 (25%) were female and 12 (75%) were men. The most frequent disease that caused the transplant was acute myeloid leukemia (58.3%). Ten (62.5%) patients presented de novo cGVHD, 1 (6.25%) progressive and 5 (31.25%) quiescent. The time since receiving the transplant until the first visit was 14 to 79 months. Ten (62.5%) patients had nonspecific symptoms (arthralgia and myalgia), 2 (12.5%) edema, 8 (50%) contractures, 8 (50%) fasciitis and 6 (37.5%) eosinophilia. Eight (50%) patients had ocular involvement and 6 (37.5%) of the oral mucosa in the form of dry syndrome (Sjögren-like syndrome). Ten (62.5%) patients had limitation of joint mobility detected by the range of motion scale (ROM), of which 6 were mild and 4 moderate. Only 5 (31.25%) patients had general condition impairment. As for the skin involvement 10 (62.5%) patients had sclerodermiform involvement (8 of them being eosinophilic fasciitis- like), 2 (12.5%) lichenoid, and 3 (18.5%) mixed (sclerodermiform + lichenoid). Only 1 patient didn´t meet diagnostic criteria for GVHD. The sclerodermiform was the most common type of involvement in the positive ANA patients. Regarding the severity according to the of the American National Institute of Health (NIH) classification: 8 (50%) had serious affectation, 5 (31.25%) moderate and 2 (12.5%) mild, with 4 (25%) exitus.
Conclusion: In our cohort of patients with cGVHD, serum detection of autoantibodies is uncommon, being the ANA with nucleolar pattern the most frequent. Although the small sample size does not allow correlations with the clinical variables it´s worth highlighting a greater positivity of autoantibodies in the sclerodermiform skin forms.
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Disclosure of Interests: Maria Elisa Acosta: None declared, Luis Gómez-Lechón: None declared, Olga Compán: None declared, Sonia Pastor: None declared, Carlos A. Montilla-Morales: None declared, Olga Martínez González: None declared, Ana Isabel Turrión: None declared, Javier del Pino Grant/research support from: Roche, Bristol, Consultant of: Gedeon, Cristina Hidalgo: None declared
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AB0544 EVALUATION OF MACULAR AND OPTIC DISC MICROVASCULAR NETWORK IN PATIENTS WITH SYSTEMIC SCLEROSIS: AN OPTICAL COHORENCE TOMOGRAPHY ANGIOGRAPHY STUDY

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Background: Systemic sclerosis (SSc) is characterized by fibrosis of the skin, internal organs and vasculopathy. Invivo, the retina provides a unique opportunity to assess the microcirculation in the eye. Previous studies have been evaluated the changes in the retinal and choroid layer and showed thinning of the choroid layer and reduced retinal microvascular density.
Objectives: To analysis the retinal and optic disc capillary network in patients with SSc without clinical signs of retinal involvement by using optical coherence tomography angiography (OCTA).
Methods: In total 40 SSc patients who classified according to the ACR/EULAR criteria and 40 healthy control subjects were included in the analysis. All patients underwent a detailed ophthalmologic examination by the same ophthalmologist. After pupil dilatation, macular angiography was performed with 6x6 mm area scanning using standardized system and images of the retinal capillary plexus were analyzed by Cirrus OCTA software. Mean macular thickness, retinal nerve fiber layer (RNFL) and the Ganglion cell inner plexiform

layer (GC-IPL), vessel density (VD), perfusion density (PD), optic disc PD, reflux index and foveal avascular zone (FAZ) parameters were measured by the same experienced operator.

Results: There was no significant difference between SSc and controls in terms of age, sex, spherical equivalent (SE), intra ocular pressure (IOP), and axial length (AL). Central and mean macular thickness, nasal and inferior RNFL thicknesses were significantly thinner in SSc patients (Table). Additionally GC complex thicknesses were significantly thinner in all quadrants compared to controls.

Central vessel density (CVD) and central perfusion density (CPD) values were found significantly decreased in all regions in patients with SSc. Optic disc perfusion density values were also decreased in SSc group. An inverse correlation was found between central macular thickness, FAZ area and perimeter values (rho:-0.300, p:0.007; rho:-0.276, p:0.013, respectively).There was no relationship between the disease duration and the OCTA measures.

Conclusion: Vascular and perfusion density were found decreased in patient with SSC at the results of OCTA measures. These findings may help to understand vasculopathy in the pathogenesis of the disease and OCTA may be a new method providing objective and non-invasive information about capillary network in SSc.

Table. Demographic and ocular parameters of study population

Parameters	SSc (n = 40)	Control (n = 40)	*p*
Age, years; mean (SD)	47.2 (8.6)	47.5 (8.1)	0.631
Male sex, n (%)	24(60)	16 (40)	0.087
Disease duration, months; mean (SD)	81.3 (38.0)	N/A	-
Foveal MT(µ)	246.3 ± 19.4	252.6 ± 15,3	**0.033**
Average MT(µ)	280.8 ± 12,4	286.5± 8.7	**0.008**
Vessel density (mm^{-1}), 6 mm total area; mean (SD)	17.60 ± 1.31	18.66 ± 0.64	**0.006**
Perfusion density, 6 mm total area; mean (SD)	43.25 ± 3.32	45.94 ± 1.52	**0.002**
Circularity index; mean (SD)	0.72 ±0.09	0.73 ± 0.06	**0.049**
RNFL nasal (µ); mean (SD)	74.37±12.36	74.05±8.48	**0.011**
RNFL inferior (µ); mean (SD)	122.62±17.87	127.40±12.63	**0.023**
Inferior nasal GCC(µ); mean (SD)	85.72 ± 8.53	85.82 ± 4.84	**0.001**
Inferior temporal GCC(µ); mean (SD)	82.70 ± 8.62	84.95 ± 4.15	**0.001**
Superior nasal GCC(µ); mean (SD)	86.35 ± 7.73	86.8 ± 5.70	**0.012**
Superior temporal GCC(µ); mean (SD)	47.2 (8.6)	47.5 (8.1)	0.631

MT: Maculer thickness; RNFL: Retinal nerve fiber layer; GCC: Ganglion cell complex

Disclosure of Interests: None declared

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AB0545 GASTROINTESTINAL INVOLVEMENT IN SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a chronic, connective tissue disease with an autoimmune pattern characterized by inflammation, fibrosis and microcirculation changes leading to internal organs malfunctions. The gastrointestinal tract (GIT) is affected in up to 90% of patients with SSc. Any part of the GIT from the mouth to the anus can be affected. There are few descriptive studies about SSc-related GIT involvement.

Objectives: We aimed to characterize the GIT involvement in patients with SSc.

Methods: This retrospective study included all patients from SSc cohort of our autoimmune diseases unit in a tertiary referral centre. All patients fulfilled SSc criteria proposed by the American College of Rheumatology. All subjects' histories were evaluated. Laboratory and imaging results were obtained from the hospital files. Patients with digestive manifestations were compared with patients without GIT involvement. Chi2 and t-student were used, using the statistical package SPSS25.0.

Results: 83 subjects with SSc were included, 68 (81,9%) of them were women. The mean age at the onset of SSc was 62,1 ± 15,3 years (range 26-89) with a mean follow-up of 9,6 ± 7,4 years. 80,7% of patients had limited SSc, 12% diffuse SSc, 4.8% SSc sine scleroderma and 2,4% early SSc. Considering the immunological profile 12 (14,5%) had Scl70 antibodies, 49 (59%) anticentromere and 21 (25,3%) had ANA antibodies without specificity for anti-Scl70 or anticentromere. 37,3% patients had lung involvement, 20,5% scleroderma and 30,1% digital ulcers. 79,5% of SSc patients were treated with proton pump inhibitors or H2 blockers. 53 (63,9%) patients with SSc had GIT involvement. In 11 patients (20,7%) digestive involvement was diagnosed before SSc (mean 26,2 months). Esophageal involvement occurred in 83%, gastric involvement in 28,3%, intestine involvement in 24,5% and liver and biliary tree involvement in 26,4%. See table 1. No significant differences in age, sex, SSc subtype, autoantibody profile, lung involvement, skin disease, mortality and therapy were observed between patients with or without GIT manifestations. There were no deaths associated with GIT involvement. The most common pharmacologic therapy used was proton pump inhibitors (86,8%), domperidone (20,8%) and antibiotic rotation (17%).

Esophageal	Gastric	Intestinal	Liver and biliary tree
44/53 (83%)	15/53 (28,3%)	12/53 (24,5%)	14/53 (26,4%)
Esophageal motility disorder 8 (15,1%)	Gastroparesis 6 (11,3%)	Small bacterial overgrowth 7 (13,2%)	Primary biliary cholangitis 9 (17%)
Gastroesophageal reflux 40 (75,5%)	Abdominal pain / nausea 10 (18,9%)	Colonic inertia 1 (1,9%)	Autoimmune hepatitis 3 (5,7%)
Dysphagia 11 (20,8%)	Subacute gastritis 7 (13,2%)	Diarrhea 6 (11,3%)	Cholestatic liver enzymes 11 (20,8%)
		Flatulence / abdominal discomfort 6 (11,3%)	Cirrhosis 2 (3,8%)

Conclusion: Almost two thirds of our cohort of SSc have symptomatic gastrointestinal disease. GIT manifestations are heterogeneous. Symptoms are non-specific and overlapping for a particular anatomical site. Esophagus is the most commonly affected. More than seventy-five per cent of patients experience symptoms of gastroesophageal reflux. We did not find differences among patients with and without SSc GIT disease. 17% of patients had a Reynold's syndrome.

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AB0546 IMMEDIATE TO INTERMEDIATE EFFICACY AND SAFETY OF PROSTAGLANDINS E1 (PGE1) INHIBITORS- ALPROSTADIL IN TREATMENT OF SYMPTOMATIC RAYNAUD'S IN SYSTEMIC SCLEROSIS; SINGLE TERTIARY RHEUMATOLOGY CENTRE EXPERIENCE FROM SRI LANKA

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Background: Systemic sclerosis (SSc) is a multi-system connective tissue disease[1]. Raynaud phenomenon (RP) is a frequent (>90%) manifestation in SSc[2] & if untreated could lead to complications such as digital ulcers, gangrene and amputation.

Calcium antagonists are considered as first-line therapy for symptomatic SSc-RP. In refractory cases phosphodiesterase type 5 (PDE-5) inhibitors- Sildenafil and PGI2 analogue- Iloprost are used. A meta-analysis of trials indicate that PDE-5 inhibitors reduce the frequency and severity of SSc-RP attacks.

In addition a study done with PGE1 inhibitors- Alprostadil 60 micrograms infusion given for six consecutive days, had shown immediate efficacy in SSc- RP; as demonstrated by increased blood flow, digitally measured by telethermography. Furthermore there was a reduction of the number, frequency and severity of attacks[3].

Due to unavailability of Iloprost in Sri Lanka, based on the above evidence some rheumatology centres use Alprostadil 60 microgram infusion for 3 consecutive days in refractory symptomatic SSc-RP.

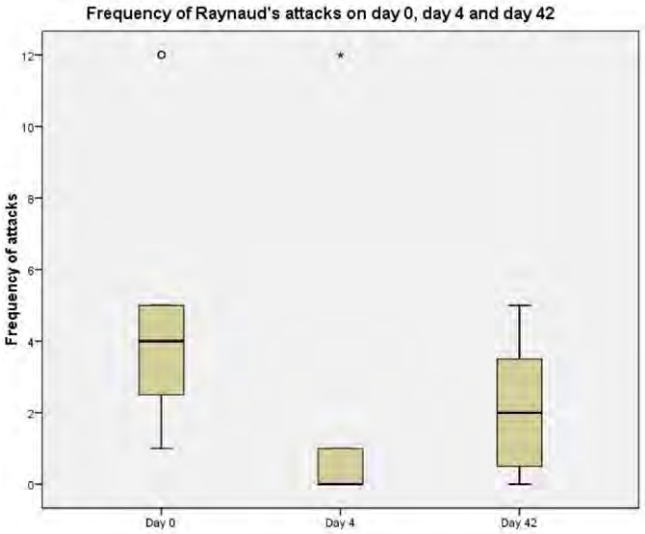
Objectives: To assess immediate (Day 4) and intermediate (Day 42) efficacy of Alprostadil 60 microgram infusions given for 3 consecutive days in treating SSc-RP.

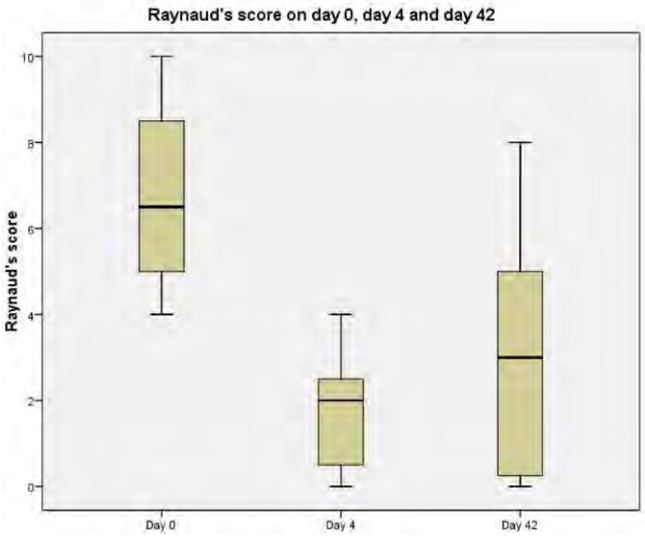
Methods: An observational longitudinal study was conducted at the Rheumatology unit, Teaching Hospital Anuradhapura- Sri Lanka during 01.09.2019- 30.12.2019. Twelve diagnosed Systemic Sclerosis patients with symptomatic Raynaud's (Raynaud's score of >5) despite receiving maximum tolerable doses of calcium antagonists consisted of the study sample.
Pre and post (on day 4 and 42) treatment frequency of Raynaud's attacks and Raynaud's score was recorded using a pre-tested interviewer administered questionnaire. Statistical analysis was done using SPSS version 22 with Wilcoxon Signed Rank test at 5% significance level.
Results: All recruits were females (n=12). Median (IQR) age of the study population and disease-duration were 45 (40 to 53.5) years and 6 (2.8 to 9.5) years respectively. Among participants, 58.3% and 25% had previous or current digital ulcers and gangrene respectively.

Table 1. Pre and post treatment mean frequency of attacks and mean Raynaud's score

	Pre treatment median (IQR)	Post treatment Day 4 median (IQR) and significance of the difference between the pre-treatment values	Post treatment Day 42 median (IQR) and significance of the difference between the pre-treatment values
Mean frequency of Raynaud's attacks/ past 24hrs	4.0 (2.3 to 5.0)	0.0 (0.0 to 1.0) P<0.05*	2.0 (0.3 to 3.8) P<0.05*
Mean duration of attack/24hrs	21.3 (1.1 to 32.5)	0.5 (0.5 to 3.0) P<0.05*	7.5 (3.0 to 25.0) P>0.05
Mean Raynaud's score	6.5 (5.0 to 8.8)	2.0 (0.3 to 2.8) P<0.05*	3.0 (0.1 to 5.0) P<0.05*

*statistically significant





Conclusion: Alprostadil 60 microgram infusions demonstrated a statistically significant immediate and intermediate efficacy in treating symptomatic SSc- RP with reduction of frequency of Raynaud's attacks and Raynaud's score at both. Only immediate efficacy was seen for mean duration of attacks. Based on these and the observed satisfactory safety level, we recommend the use of Alprostadil for symptomatic Raynaud's in SSc-RP as an alternative to Iloprost. Further studies of larger samples are recommended.

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AB0547

INVESTIGATION OF THE PRESENCE OF FIBROMYALGIA SYNDROME IN PATIENTS WITH SCLERODERMA

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Background: As with other connective tissue diseases, fibromyalgia (FMS) syndrome is not uncommon in scleroderma. However, there is no clear information about it in the literature. According to 1990 ACR criteria, sensitive point evaluation was made in scleroderma and FMS frequency was reported as 18.6% in scleroderma patients. However, it is known that fibrosis creates difficulties in sensitive point determination. moreover, ACR 1990 criteria cannot be met in approximately 25% of fibromyalgia patients. Therefore, the frequency of fibromyalgia in scleroderma patients is unclear. In 1990, ACR announced new criteria in 2010 due to the low sensitivity of ACR criteria to FMS detection and not being used in the follow-up of the disease. In the new set of criteria, not the 18 sensitive point evaluations, but the Widespread Pain Index and Symptom Severity Scale are evaluated.
Objectives: In this study, we planned to investigate the frequency of fibromyalgia in systemic sclerosis patients according to the new ACR criteria defined in 2010.
Methods: 43 patients with diffuse systemic sclerosis with no known additional diseases were included in the study. Patients were evaluated with the new fibromyalgia diagnostic criteria set. Patients were evaluated with Fibromyalgia Impact Questionnaire (FIQ), Pain Location Score (PLS), Symptom Impact Questionnaire (SEA), Widespread Pain Index (WPI) and Symptom Severity Scale (SSS).
Results: The mean age of the patients was 53.45 ± 12.87 years (39 women, 4 men). Mean values were FIQ: 46.05 ± 17.44, PLS:18.32 ± 9.87, SEA: 20.76 ± 11.31, WPI: 7.93 ± 5.87, SSS: 6.51 ± 3.41 respectively. According to these results, 62.8% (n: 27) FMS presence of SS patients was detected.
Conclusion: In the literature, there are only a few studies evaluating the frequency of FMS in scleroderma patients. Malcarne et al. reported that 18.6% of 102 SSc patients met the 1990 classification criteria for FMS. However, there are predominantly early-stage systemic sclerosis patients in this study and the patient group is heterogeneous. We included patients with diffuse systemic sclerosis and widespread skin involvement in this study. we found a much higher frequency of fibromyalgia syndrome than indicated in the literature. Considering that systemic sclerosis is a serious disease that significantly impairs quality of life, this finding is very important. In order to relieve the symptoms associated with FMS, it is important to provide them with additional medical support, to provide as much exercise as possible, and to provide group therapies to improve patients' quality of life.

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AB0548

ASSESMENT OF THE PHYSICAL ACTIVITY IN SYSTEMIC SCLEROSIS PATIENTS BY USING COMMERCIAL SMART BANDS AND ITS ASSOCIATION WITH DISEASE CHARACTERISTICS: A PILOT STUDY

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Background: Systemic sclerosis (SSc) is a complex disease, characterized by multi-system organ involvement including interstitial lung disease (ILD) and pulmonary arterial hypertension (PAH). The decrease in physical activity in SSc patients with lung involvement has been demonstrated by self-reported physical capacity and 6 min-walking test (6MWT) (1, 2). Commercial smart bands can provide data on daily physical activity, sleep characteristics, blood oxygen concentration and heart rate measurement, therefore may aid in monitoring disease activity.

Objectives: The aim of this study is to evaluate physical activity in SSc patients by using a commercial smart band and investigate its association with clinical characteristics and patient-reported outcome measures of disease activity

Methods: This prospective observational study included SSc patients with having a smartphone. Patients characteristics including age, sex, and organ involvements were recorded. Each participant was subjected to pulmonary function tests and 6MWT. All of patients answered Scleroderma Health Assessment Questionnaire (SHAQ, consisting of HAQ-Disability Index (DI) and visual analog scales (VAS) domains). All patients received Fitbit inspire HR smart band® which records the number of steps, heart rate, distance and was instructed to wear it continuously for one week. Tracked data was collected from smartphones via Fitbit application.

Results: Fifteen SSc patients (14 females and 1 male) participated in the study, 8 (53.3%) had limited SSc and 7 (46.7) had diffuse SSc. The mean age was 48.5±15.5 and the median disease duration was 4 (min-max:1-9) years. Eleven (73.3%) patients had ILD and one patient had PAH. Musculoskeletal complaints were evident in two patients. Forced vital capacity (FVC, % predicted), diffusion capacity of lung for carbon monoxide (DLCO, %) in patients with ILD were significantly lower than patients without ILD median (IQR) 102 (30) vs 80 (27) p= 0.026, 57 (20) vs 95 (13), p= 0.002, respectively. The median distance of 6MWTs were 450 (225) vs 568 (102) in ILD and non-ILD groups. The median total weekly step counts of ILD patients were remarkably lower in ILD patients compared to non-ILD 36.137 (17.879) vs 58.114 (80.681) steps/week, (p= 0.01). Patients with ILD had a bit higher median heart rate compared to non-ILD, 73 (9) vs 67.5 (12). The total weekly step counts were correlated with pulmonary function tests, including forced expiratory volume in one second (FEV1%) (r= 0.57, p= 0.025), FVC (%) (r= 0.65, p= 0.009), and DLCO (%) (r= 0.70, p= 0.005), patient-reported disease severity (r=-0.66, p= 0.007), and breathing problem (r= -0.55, p= 0.03) domains of SHAQ. There was no correlation between weekly step counts and 6MWT

Conclusion: The assessment of physical activity with smart activity bands may help to identify SSc patients with ILD. Tracked physical activity using smart bands correlates with pulmonary function tests and performs better than 6MWT, suggesting it as a useful tool for the assessment of disease activity.

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AB0549

THE RELEVANCE OF AORTIC STENOSIS AND OUTCOME OF TAVI PROCEDURE FOR VALVE REPAIR IN SCLERODERMA PATIENTS

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Background: Patients with systemic sclerosis (SSc) are at risk for developing aortic valve changes. The prevalence of aortic valve stenosis (AS) in SSc patients is unknown. Previously, patients with AS were treated with valve replacement; in recent years, Trans Catheter Aortic Valve Implantation (TAVI) is widely used in general population. The safety of Trans Catheter Aortic Valve Implantation (TAVI) in SSc has not been assessed.

Objectives: A retrospective study on aortic valve pathology and treatments including TAVI performance.

Methods: We reviewed 374 records of SSc patients at our site EUSTAR cohort and extracted cases with reported AS confirmed by ECHO cardiography and heart catheterization.

Results: We found data on 13 (3.4%) patients with AS: 12 females (92.3%); mean age 70.3 (SD 7.7) years, disease duration 15.4 (SD 6.3) years. Ten patients had limited SSc (76.9%, all cared anti-centromere antibodies) and 3 diffuse SSc (1 patient had RNAP3 and 2 had anti-topoisomerase antibodies); 5 (38.5%) patients had significant coronary disease (3 underwent CABG, 2 had several PTCA). Eight (61.5%) patients dead during years 2004 - 2019. Aortic valve replacement was performed in 5 patients (4 – metal and 1 – biological); 2 patients did not undergo AS repair due to impaired general condition; 6 patients underwent TAVI between January 2013 and December 2019 (5 at Rambam Cardiology Institute). All SSc patients underwent trans femoral TAVI under conscious sedation. The procedure was successful in all patients. The length of hospitalization was 5-14 days (mean 8.2 days); 3 (50%) patients needed pacemaker implantation (they did not have previous conduction abnormalities). The follow-up duration after TAVI was between 5 and 67 months (mean 20.7). During follow-up one patient developed bacterial endocarditis related to pacemaker device two months after the procedure; the event resolved after removing the device and according antibiotics treatment; the same patient had transient ischemic attack two years later and another pacemaker implantation 3 years later due to complete AV block. One patients dead from urosepsis 11 months after TAVI, the death was not related to procedure. One patient developed anemia due to large hematoma after the procedure.

Conclusion: Screening for aortic valve pathology is essential as AS is not rare in SSc patients especially in those with long standing limited disease and positivity to centromere antibodies. AS in SSc patients may be associated with clinically significant coronary artery disease. TAVI was safe in our SSc patients without in-hospital mortality and benign long-term outcome.

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AB0550

DIFFUSING CAPACITY OF THE LUNG FOR CARBON MONOXIDE (DLCO) VS FORCED VITAL CAPACITY (FVC): SYSTEMATIC LITERATURE REVIEW AND META-ANALYSIS TO EXAMINE THEIR ABILITY TO MEASURE CHANGE IN CLINICAL TRIALS IN SYSTEMIC SCLEROSIS (SSC)

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Background: Lung involvement remains the main cause of morbidity and mortality in SSc. In 1 year clinical trials to assess lung involvement, FVC is usually evaluated and changes while the DLCO usually remains unchanged. In longer term observational studies, the DLCO often changes more than the FVC.

Objectives: To examine, through a systematic literature review(SLR) and meta-analysis, whether DLCO%pred or FVC%pred (both to be designated solely as DLCO and FVC henceforth), responds more in assessing SSC interstitial lung disease in first year and longer term follow-up(FU).

Table 1. Results from Random Effect Meta-Analysis

	21 studies				5 studies			
	FVC % pred mean value	SE	**DLCO % pred mean value**	SE	**FVC % pred mean value**	SE	**DLCO % pred mean value**	SE
BASELINE	78.8	3.43	59.7	5.52	81.1	5.68	55.6	11.59
1 YEAR FOLLOW UP	81.5	3.85	63.4	6.07	-	-	-	-
>1 YEAR FOLLOW UP	-	-	-	-	83.4	4.68	54.7	12.37

Methods: PubMed, EMBASE and COCHRANE databases were searched for english language articles on SSc published between 1960 and 31st October 2018. Any study that made reference to FVC and DLCO evaluation in SSc and reported their changes over the years was included. Reviewers double extracted articles to obtain agreement on>95% of pre-defined critical outcomes:DLCO and FVC at baseline,1 yr of FU and at the last assessment interstitial lung disease by HRCT of the lungs study design, duration of FU. Other variables included demographics. In all cases I^2 test for heterogeneity was used and a result from 75 to 100% was considered as high heterogeneity.A random effects meta-analysis was used. Differences in the degree of change in FVC and DLCO were tested with t-test without compensation for repeated analysis.

Results: 1870 articles were screened for eligibility and 21 were selected for the SLR and meta-analysis The analysis used 21 studies to evaluate changes of FVC and DCLO at 1 yr of FU. Only 5 studies were eligible to evaluate changes during longer FU (24.7 months(SD=20.4)). Heterogeneity was high at baseline and FU, (at 1 yr and >1 yr),both for the 21 studies at 1 yr (FVC:I^2 99.74%, 99.78%; DLCO: I^2=99.91%99.92%) and the 5 studies at > 1 year (FVC:I^2 92.86%;DLCO:I^2=99.54%), diminishing the confidence in the results. Table 1 gives the results of the random effects meta-analysis both for 21 and for the 5 studies evaluated. Regarding changes over 1 yr in the 21 studies, change of mean FVC was 2.7 (78.8vs81.5) while change in mean DLCO was 3.07(SE 8.20) (59.7vs 63.4). Considering the 5 studies during long term follow up, change in mean FVC was 2.0(7.36)(81.1vs83.1), and change in mean DLCO was -0.96 (16.95)(55.6vs54.7). Comparing the 1 yr changes in the 21 studies, change in mean FVC was 2.7(5.2)and change in mean DLCO was 3.07(8.2); difference in changes was not statistically significant (p=0.5791). During long term FU (24.7 months), change in mean FVC was 2.0(7.36)and change in mean DLCO was -0.96 (16.95); difference in changes was not statistically different (p=0.4698).

Conclusion: Our data are limited by great heterogeneity. Given this limitation, this SLR and meta-analysis indicates that there is no difference in the changes comparing FVC to DLCO at either 1 yr or during longer term follow-up. Corroboration of these results in prospective studies and in registries to make clear, comparable comparisons will be needed.

Disclosure of Interests: Silvia Bellando Randone: None declared, Eleonora Cappellini: None declared, Letizia Nidiaci: None declared, Gemma Lepri: None declared, Maria Grazia Lazzaroni: None declared, Corrado Campochiaro Speakers bureau: Novartis, Pfizer, Roche, GSK, SOBI, Gianluca Bagnato: None declared, Domenico Sambataro: None declared, Gianluca Sambataro: None declared, Marco Matucci-Cerinic Grant/research support from: Actelion, MSD, Bristol-Myers Squibb, Speakers bureau: Acetelion, Lilly, Boehringer Ingelheim, Daniel Furst Grant/research support from: AbbVie, Actelion, Amgen, BMS, Corbus Pharmaceuticals, the National Institutes of Health, Novartis, Pfizer, and Roche/Genentech, Consultant of: AbbVie, Actelion, Amgen, BMS, Cytori Therapeutics, Corbus Pharmaceuticals, the National Institutes of Health, Novartis, Pfizer, and Roche/Genentech, Speakers bureau: CMC Connect (McCann Health Company)

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AB0551 CLINICAL SIGNIFICANCE OF COGNITIVE IMPAIRMENT AND MALNUTRITION IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Previous studies reported a high prevalence of cognitive dysfunction in systemic sclerosis (SSc). Cognitive impairment was estimated to involve 60% to 80% of SSC patients and to be correlated with older age, disease severity, diffuse cutaneous subset and poor quality of life.

Objectives: The aim of our study was to evaluate the association between cognitive impairment, nutritional status and the quality of life of SSc patients.

Methods: Sixty-eight consecutive SSc patients followed at our Institution were evaluated for cognitive impairment using the validated Italian version of the Montreal Cognitive Assessment (MoCA). Scores <26 were considered abnormal. We also assessed other domains and quality of life measures such as UCLA SCTC GIT 2.0 for gastrointestinal involvement, BDI-II and PHQ-9 for anxiety and depression, EAT-10 for dysphagia symptoms, SHAQ and SF-36 for function and quality of life (QoL). The risk and the presence of overt malnutrition were assessed using the MUST questionnaire and the GLIM criteria, respectively. Clinical and demographic parameters such as age, sex, BMI, disease subset, organ involvement, autoantibody profile and modified Rodnan Skin Score were also recorded for each patient. Data were analysed by Student t-test or chi-square test and regression analyses were used to assess the association between variables.

Results: A total of 68 SSc patients [47 (69.1%) limited SSc (lSSc) and 21 (30.9%) with diffuse SSc (dSSc), 59 female; mean age 60.2 (±13.4) years; mean disease duration 9 (±8.2) years; mean mRSS 8.1 (±7.6)] were included in the study.

Cognitive impairment was identified in 30 (44.1%) SSc patients; the mean MoCA score was 24.7 (±4.3). According to GLIM criteria, 16 (23.5%) patients were malnourished. Compared to patients with a MoCA≥26, patients with cognitive impairment were older (p<0.001), had more comorbidities (p<0.0001) and a worse QoL as assessed by the physical and general health domains of the Sf-36 (p<0.05). Malnourished patients were significantly more dysphagic (p<0.01) and had a worse HAQ (p<0.01) compared to well-fed patients. On regression analyses, cognitive impairment was related to increasing age (OR 1.08, 95%CI 1.03 to 1.14, p=0.001), but not to malnutrition, disease subset or symptoms. Malnutrition was associated with dysphagia (OR 1.10, 95%CI 1.01 to 1.20, p=0.01) and HAQ score (OR 2.69, 95%CI 1.24 to 5.82, p=0.01), but was not predicted by cognitive impairment.

Conclusion: Cognitive dysfunction is frequently observed in SSc patients and mostly associated with increasing age and number of comorbidities. Malnutrition and cognitive impairment are both associated to QoL but seem to be unrelated.

Disclosure of Interests: None declared

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AB0552 CHARACTERISTICS OF MYOSITIS SPECTRUM DISEASE - RHEUMATOID ARTHRITIS OVERLAP CASES IN A HUNGARIAN COHORT

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Background: Overlap syndromes are autoimmune disorders in which classification criteria of at least two connective tissue diseases (CTDs) are fulfilled. The Division of Clinical Immunology in Debrecen, Hungary oversees patients with idiopathic inflammatory myopathies (IIMs) since the 1980's.

Objectives: In a work called The Myositis Antibody Research Project, which is coordinated together with the Bath Institute for Rheumatic Diseases (UK), authors investigated 330 patients with myositis, all treated in this Hungarian center.

Methods: The aim of this retrospective study was to investigate the frequency, clinical and serological parameters and therapeutic options in myositis – rheumatoid arthritis overlap cases in this group of 330 patients.

Results: The frequency of overlap cases, as seen in literature, was 13.64%. The importance of myositis-associated antibodies (MAAs) can be seen on this results: 44.44% of overlap patients, while only 7.02% of not overlap patients were MAA positive. Out of our 45 overlap patients twenty-seven myositis - RA overlap patients could be identified. Among these 27 patients the women:men ratio was 12.5:1, PM:DM ratio was 2.375:1. Muscle weakness and sceletal involvement was present in every patient, myalgia in 77.78% and Raynaud's phenomenon in 48.15% of the patients; general symptoms during disease relapse (fatigue, weight loss, fever) were present in 59.26%, 18.52% and 14.82%, respectively. Ten cases had seropositive rheumatoid arthritis, with high titer of rheumatoid factor. Authors underline the importance of lung involvement as internal organ manifestation: 8 patients had anti-synthetase antibodies (six anti-Jo-1, one anti-PL-7 and one anti-PL-12). In anti-PL-7 and anti-PL-12 positive patients interstitial lung disease (ILD) appeared some years before myositis and early agressive management of ILD resulted in fast remission of muscle weakness. Anti-Mi-2 and anti-SRP could be detected in two patients. Most frequent used disease modifying antirheumatic drugs were cyclophosphamide, methotrexate and cyclosporine, 19 patients received DMARD combination therapy. Biological therapy was used in 3 patients, intravenous or subcutaneous immuneglobulin in 4 patients and one patient with RA – myositis – antiphospholipid syndrome died because of asipartion pneumonia.

Conclusion: Authors conclude that it is really challenging to treat these overlap cases: they form a very heterogenous group of patients and management has to be personalized.

Disclosure of Interests: None declared

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AB0553

THE NOCEBO PHENOMENON PARTLY ACCOUNTS FOR DIARRHOEA AMONG PARTICIPANTS IN THE RANDOMIZED PLACEBO-CONTROLLED TRIAL OF NINTEDANIB FOR INTERSTITIAL LUNG DISEASE ASSOCIATED WITH SYSTEMIC SCLEROSIS (SENSCIS)

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Background: The nocebo phenomenon, the opposite of placebo, defined as unfavourable changes in a patient's symptoms or condition resulting from negative anticipations to treatment and possibly leading to suboptimal outcomes and non- adherence, is more frequent than previously thought in rheumatology practice[1]. The tyrosine kinase inhibitor nintedanib has shown efficacy for the treatment of systemic sclerosis (SSc)-associated interstitial lung disease in SENSCIS, a recent randomized controlled trial (RCT)[2]. Diarrhoea was the most frequently reported adverse event in SENSCIS.

Objectives: To test whether the nocebo phenomenon is involved in the prevalence of diarrhoea as an adverse event in trials with nintedanib.

Methods: We compared the incidence of diarrhoea in the placebo arm between SENSCIS and all other placebo controlled RCTs involving >40 SSc patients in each arm, as well as between SENSCIS and all other nintedanib RCTs published so far. We also compared the strength of the warnings for diarrhea (ie times word is mentioned and number of lines devoted to nintedanib related "diarrhoea") in the informed consent forms (ICFs) of different nintedanib RCTs

Results: The mean percentage of patients reporting diarrhoea was 32% in the placebo arm and 76% in the active treatment arm in SENSCIS. These numbers are comparing to a prevalence of only 7% (range 2.3-9.1%) and 9% (range 5.8-14%), respectively of other RCTs in SSc (bosentan, n=2; macitentan, n=2; tocilizumab, n=1). Since the estimated point prevalence of diarrhoea in an SSc cohort similar to SENSCIS would not exceed 15% based on the literature, there was an at least 2-fold increase in the occurrence of diarrhoea in the placebo group during SENSCIS. More importantly, when looking into other nintedanib RCTs (Table 1), we found that patients reporting diarrhoea in the placebo arm were 20% and 18% in cancer and idiopathic pulmonary fibrosis (IPF) trials, respectively, which is almost half than in SENSCIS. Consistent with our hypothesis, the percentage of diarrhoea in the placebo arms of the different nintedanib RCTs increased along with the number of mentions and the number of lines devoted to "diarrhoea" in the respective ICFs.

Table 1. Percentage of patients developing diarrhoea in phase III nintedanib RCTs and diarrhoea-related warnings in ICFs

Published RCT (year of publication)	Treatment indication	placebo arm, N	nintedanib arm, N (mg/bid)	Adjunctive treatment	% Diarrhoea		Mentions of 'diarrhoea'/ lines devoted in ICF
					Placebo	Active treatment	
SENSCIS (2019)	SSc-ILD	288	288(150)	48% MMF 5% MTX	31.6	75.7	9/11
INBUILD (2019)	Progressive Fibrosing ILD including SSc-ILD and other CTD-ILDs	331	332 (150)	18% ≥1 from biologics, DMARDs, corticoids	23.9	66.9	8/10
INPULSIS1 (2014)	IPF	204	309 (150)	21% corticosteroids	18.6	61.5	3/3
INPULSIS2 (2014)	IPF	219	329 (150)	21% corticosteroids	18.3	63.2	3/3
LUME-Lung 1 (2014)	Lung cancer	659	655(200)	docetaxel	21.8	42.3	2/4
LUME-Lung 2 (2016)	Lung cancer	360	353(200)	pemetrexed	15.4	34.9	4/5
LUME-meso phase III (2019)	Malignant pleural mesothelioma	229	229(200)	pemetrexed & cisplatin	23.0	53.0	4/5

Conclusion: These results indicate that the nocebo phenomenon is partially involved in the high prevalence of diarrhoea among SSc patients participating in the SENSCIS trial. Whether patients with SSc have increased susceptibility to the nocebo phenomenon when compared to patients with IPF or cancer deserves further study.

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AB0554

CONCORDANCE IN THE CLASSIFICATION CRITERIA IN A PATIENT COHORT WITH IDIOPATHIC INFLAMMATORY MYOPATHIES (IIM).

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Background: Differents classifications criteria for IIM exist. New classification criteria are superior to previous in capturing different subgroups of IIM.

Objectives: To compare the concordance and disparity of Bohan and Peter and EULAR/ACR 2017 classification criteria at the level of diagnostic certainty, in a group of chilean patients with IIM.

Methods: 40 adults patients with IIM (27 Dermatomyositis (DM) and 13 Polimyositis (PM)), according Bohan and Peter criteria were analized. The patients were reclassified with EULAR/ACR criteria. The level of diagnostic certainty (definitive, probable and possible) was registered for both Classification Criteria. The concordance and disparity between criteria was evaluated. Concordance and disparity analysis were made considering the strict agreement between level of certainty of both criteria, using Cohen´s Kappa coefficient. The analysis was done for the complete cohort and for separated groups.

Patients with discordance belonging to the same subgroup were evaluated using contingency tables. The direction of the change (gain or lost of certainty) and the relation with diagnostic subgroup was also analized. Descriptive statistics is expressed as diagnostic categories, number of patients and rates.

Results: For the complete cohort and for DM and PM groups the concordance was low. For 27 patients with DM, the observed concordance rate was 63% (16 definitives, 1 probable). The observed disparity rate was 37%. The direction of the change was gain of one level of certainty in 14.5% and two levels in 22.2% of patients applying EULAR/ACR criteria compared to Bohan y Peter criteria. For 13 pacients with PM, the observed concordance rate was 46% (3 definitives and 3 probables). The observed disparity rate was 54%. The direction of the change was loss of certainty. The loss of certainty was one level in 85,7% (one patient change from probable to posible). Only one patiente had gain of certainty of one level (14.3%).

Conclusion: The strict concordance between both classification criteria was low. The observed concordances were better in patients with DM that PM. The disparities involved gain of level of diagnostic certainty in DM patients, while in PM patients there was mostly lost of level of certainty.

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AB0555

ANTI-RO POSITIVITY EFFECT ON CLINICAL CHARACTERISTICS AND MORTALITY IN A SINGLE-CENTER COHORT OF ANTISYNTHETASE SYNDROME PATIENTS

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Background: Antisynthetase syndrome (ASSD) is an heterogeneous disease characterized by the occurrence of anti-synthetase antibodies (ARS) and the classic triad of arthritis, myositis and Interstitial Lung Disease (ILD). Pulmonary involvment bears an increased risk of life threatening events, being the main cause of mortality in these patients. No significant differences in mortality have been noticed among the different ARS specificities. However the role of extractable nuclear antigen antibodies on mortality in these patients is still matter of debate.
Objectives: To asses the effect of anti-RO antibodies on clinical characteristics and mortality in a large italian single-center cohort of ASSD patients.
Methods: Cohort study of outcome, clinical and laboratory characteristics, at baseline and at last follow-up, of 55 ASSD patients progressively enrolled and followed-up at our out-patient clinic. Survival was estimated with Kaplan-Meier function and comparison between frequencies of clinical characteristics was studied with Chi-square test.
Results: We identified 30 anti-Ro+ (M:F=1:4) and 25 anti-Ro- (M:F=1.5:1) ASSD patients. No difference in the age of onset was observed (p value=0.83). Classic triad prevalence and evolution was similar between the two groups with only significant difference of ILD prevalence at last follow up, higher in anti-Ro+ patients group (p value=0.01). Overall mortality was of 13 subjects (23%) during the follow-up period (median 53 months, IQR 16-114). Despite the significantly higher pulmonary involvment in the anti-Ro+ group no difference between mortality in anti-Ro positive and negative groups was observed. Adjusting mortality to include disease-related events only did not provide any additional difference (p value=0.5) (Table 1). Survival curves of the two groups were not different at any time point (Log-rank test, p value 0.98) (Figure 1).

Table 1. Clinical and Demographic Characteristics of the cohort

ASSD	Ro+	Ro-	P value
PZ (M:F)	30 (6:24)	25 (14:10)	/
Age (years) at disease onset (median, IQR)	56 (43-69)	54 (46-68)	0.83
Disease duration (months) (median, IQR)	55 (23-112)	52 (13-130)	0.681
Arhtritis at onset (%)	22 (73)	17 (68)	0.664
Arhtritis at last follow-up (%)	26 (86)	18 (72)	0.175
Myositis at onset (%)	12(40)	15 (60)	1
Myositis at last follow-up (%)	19 (63)	21 (84)	0.086
ILD at onset (%)	20 (66)	12 (48)	0.162
ILD at last follow-up (%)	30(100)	20 (80)	0.01
Complete form at onset (%)	8 (26)	4 (16)	0.34
Complete form at last follow-up (%)	17 (56)	13 (52)	0.729
Raynaud phenomenon (%)	7 (23)	8 (32)	0.472
Mechanic's hands (%)	12 (40)	12 (48)	0.551
Death (%)	7 (25)	6 (24)	0.953
Disease related death (%)	3 (42)	4 (66)	0.506

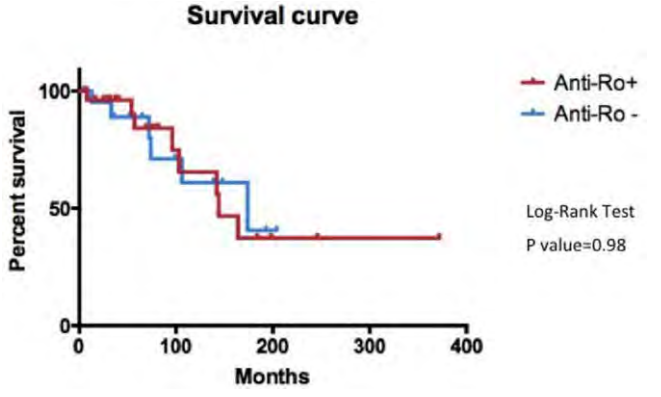


Figure 1. Kaplan-meier curve of anti-Ro+ and anti-Ro – ASSD patients.

Conclusion: The clinical spectrum and the time course of ASSD is not significantly affected by the presence of anti-Ro antibodies, althuough ILD seems to be more associated to anti-Ro antibodies. Despite higher prevalence of ILD in Ro positive group no difference in mortality was observed in respect to anti-Ro negative patients.

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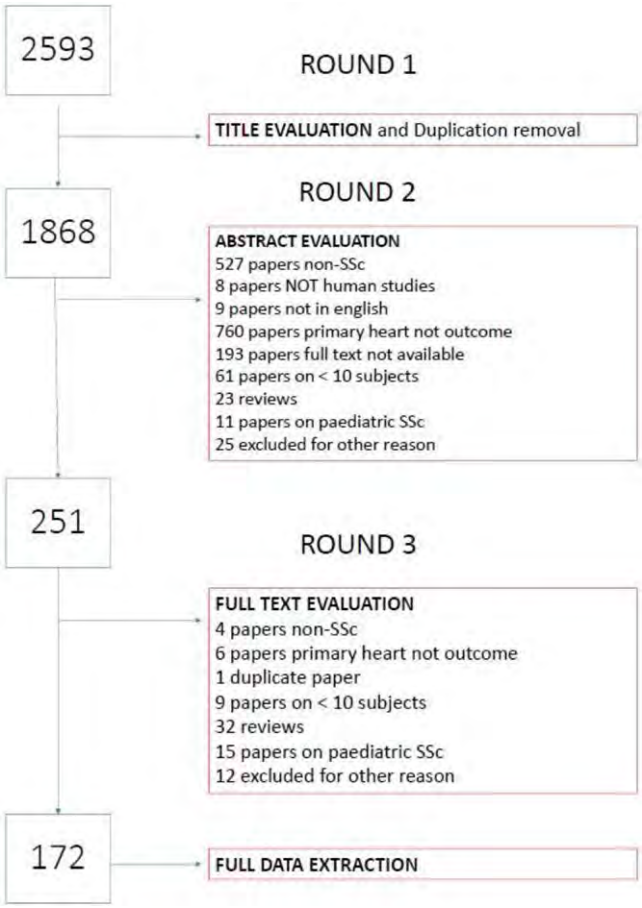
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AB0556

PRIMARY SYSTEMIC SCLEROSIS HEART INVOLVEMENT (PSSCHI): A SYSTEMATIC LITERATURE REVIEW (SLR), CONSENSUS-BASED DEFINITION AND PRELIMINARY VALIDATION.

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Background: pSScHI may cause tissue, functional and conduction abnormalities with varied clinical manifestations. The absence of a clear definition of pSScHI impairs the significance and ability of focussed research, frequently not allowing the distinction between primary and secondary involvement.
Objectives: We aimed to establish an expert consensus definition for pSScHI, to be used in clinical trials and everyday clinical practice, and to start its validation process.
Methods: A SLR for cardiac manifestations and alterations in SSc was conducted using PubMed, Web of Science and Embase. Articles published from inception to December 31st, 2018 were identified. Inclusion criteria included papers in English on adult SSc patients, with heart involvement as outcome. We excluded non-human studies, secondary heart involvement (eg PAH, drugs, infections), reviews and case reports. PRISMA recommendations were followed where applicable. Extracted data were categorized into relevant domains (signs, symptoms, anatomical site involved, physiological abnormalities, pathological changes, prognostic outcomes), which informed the consensus definition. Sixteen senior experts (7 rheumatologists, 8 cardiologists, 1 pathologist) discussed the data and, using a nominal group technique, added expert opinion, provided statements to consider and ranked them. Consensus was attained for agreement >70%. Sixteen clinical cases were evaluated in two rounds to test for face validity, feasibility, inter- and intra-rater reliability and criterion validity (gold standard set by agreed evaluation between expert rheumatologist, cardiologist and methodologist).
Results: 2593 publications were identified and screened, 251 full texts were evaluated,172 met eligibility criteria. Data from the 7 domains were extracted and used to develop the World Scleroderma Foundation – Heart Failure Association (WSF-HFA) consensus-derived definition of pSSc-HI, as follows:
"pSScHI comprises cardiac abnormalities that are predominantly attributable to SSc rather than other causes and/or complications*. pSScHI may be sub-clinical and must be confirmed through diagnostic investigation. The pathogenesis of pSScHI comprises one or more of inflammation, fibrosis and vasculopathy. *Non SSc-specific cardiac conditions (e.g. Ischaemic heart disease, arterial hypertension, drug toxicity, other cardiomyopathy, primary valvular disease) and/or SSc non cardiac conditions (e.g. PAH, Renal involvement, ILD)."
Face validity was determined by a 100% agreement on credibility; application was feasible, with a median 60 (5-600) seconds taken per case; inter rater agreement was moderate [mKappa (95%CI) 0.56 (0.46-1.00) and 0.55 (0.44-1.00) for the two rounds] and intra rater agreement was good [mKappa (95%CI) 0.77 (0.47-1,00)]. Content validity was reached based on the wide variety of patients in the SLR, criterion validity was reached with 78 (73-84) % correctness.



Conclusion: Using a SLR and modified nominal technique, we have developed a preliminary pSScHI consensus-based definition and started a validation process for it to be used in clinical research and clinical practice.

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AB0557 CO-EXISTENCE OF SYSTEMIC SCLEROSIS HALLMARK AUTOANTIBODIES ASSOCIATES WITH DISTINCT CLINICAL PHENOTYPE

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Background: Systemic sclerosis (SSc) is typically manifests with distinct SSc-specific antibodies (SSc-Abs): anti-topoisomerase I (ATA), anti-centromere (ACA), anti-RNA polymerase III (ARA), anti-U3RNP (u3RNP), anti-U1RNP (U1RNP), anti-PmScl (PmScl), anti-Ku (Ku) and anti-Th/T0 (Th/T0), each being characterised by different clinical features and prognosis. The presence of >1 SSc-Abs is rare with minimum data about these patients' clinical phenotype.

Objectives: To describe and compare the clinical features of SSc patients with >1 SSc-Ab

Methods: The autoantibody profiles of 2799 SSc patients from February 2001 to June 2017 were retrospectively reviewed. Patients with >1 SSc-Abs were identified. Clinical features were collected and compared to historical cohorts of SSc patients with single SSc-Ab positivity. Patients were excluded if treated prior to their immunology test with rituximab, iv immunoglobulins or stem cell transplantation. Statistical analysis was performed using Fisher exact test.

Results: 72 patients (2.6%) with >1 SSc-Ab were identified. Full clinical data were available for 63 patients. 60 patients (2.1%) had double Ab positivity and 3 patients had triple Ab positivity (0.1%). 13 Ab combinations were present. U1RNP and ATA was the most frequent combination (35%), patients were significantly younger (51.38 years) than both U1RNP (58.64 years, p=0.050) and ATA (62.03 years, p=0.002) patients and more commonly of diffuse subset (dcSSc) (p=0.001 and p=0.041 respectively). Compared to ATA patients overlap features were more frequent (43% vs 15%, p=0.004) including inflammatory arthritis (p=0.025) and myositis (p=0.013) (Table 1). U1RNP and ACA had a significantly higher prevalence of pulmonary arterial hypertension compared to U1RNP (p=0.039) and ACA (p=0.022) patients, and compared to ACA patients they were younger (57.88 vs 68.75, p=0.015) with a higher incidence of myositis (p=0.001). U1RNP and ARA patients were more frequently dcSSc subtype compared to U1RNP patients (75% vs 21%, p=0.040). U1RNP and PmScl patients had a higher prevalence of myositis compared to U1RNP patients (p=0.006). ATA and ACA patients behaved similarly to ATA patients with a significantly higher prevalence of lung fibrosis (p=0.006) and myositis (p=0.041) compared to ACA. ACA and PmScl (7%) had higher prevalence of myositis compared to ACA patients (p=0.04).

Table 1. Frequency of clinical features in some of the double antibody group combinations, compared to our cohort of patients with only one of the SSc specific antibody. Significant p values (<0.05) highlighted in bold. ILD (interstitial lung disease), PAH (pulmonary arterial hypertension), SRC (scleroderma renal crisis).

		Clinical features									
		Arthritis		ILD		PAH		SRC		Cardiac		Myositis	
Double antibody group	Comparator group	n	p	n	p	n	p	n	p	n	p	n	p
U1 RNP and ATA		6 (29%)		15 (68%)		1 (9%)		0		0		4 (19%)	
	U1RNP	14 (18%)	1	38 (50%)	0.195	12 (16%)	0.287	1 (1%)	1	2 (3%)	1	12 (16%)	0.744
	ATA	28 (10%)	**0.025**	213 (79%)	0.382	12 (4%)	1	17 (6%)	0.622	20 (7%)	0.378	30 (11%)	**0.013**
U1RNP and ACA		2 (25%)		2 (25%)		4 (50%)		0		0		3 (27%)	
	U1RNP	14 (18%)	1	38 (50%)	0.267	12 (16%)	**0.039**	1 (1%)	1	2 (3%)	1	12 (16%)	0.148
	ACA	23 (16%)	0.047	43 (31%)	0.233	56 (15%)	**0.022**	6 (2%)	1	10 (3%)	1	3 (1%)	**0.001**
U1RNP and ARA		0		2 (50%)		0		1 (25%)		1 (25%)		0	
	U1RNP	14 (18%)	0.311	38 (50%)	1	12 (16%)	1	1 (1%)	0.098	2 (3%)	0.144	12 (16%)	1
	ARA	4 (3%)	1	64 (45%)	1	15 (10%)	1	34 (24%)	1	4 (3%)	0.133	5 (3%)	1
U1 RNP and PmScl		1 (33%)		2 (66%)		0		0		0		3 (100%)	
	U1RNP	14 (18%)	1	38 (50%)	1	12 (16%)	1	1 (1%)	1	2 (3%)	1	12 (16%)	0.006
	PmScl	7 (13%)	1	27 (50%)	1	3 (6%)	1	3 (6%)	1	1 (2%)	1	21 (39%)	0.069
ATA and ACA		0		3 (75%)		0		0		0		1 (25%)	
	ATA	28 (10%)	1	213 (79%)	1	12 (4%)	1	12 (4%)	1	20 (7%)	1	30 (11%)	0.153
	ACA	23 (16%)	1	43 (31%)	**0.006**	56 (15%)	1	6 (2%)	1	10 (3%)	1	3 (1%)	**0.041**
ACA and PmScl		1 (25%)		3 (25%)		0		0		0		1 (25%)	
	ACA	23 (16%)	0.227	43 (31%)	0.385	56 (15%)	1	6 (2%)	1	10 (3%)	1	3 (1%)	**0.04**
	PmScl	7 (13%)	0.457	27 (50%)	0.612	3 (6%)	1	3 (6%)	1	1 (2%)	1	21 (39%)	1
ACA and U3RNP		0		3 (50%)		0		0		0		0	
	ACA	23 (16%)	1	43 (31%)	0.215	56 (15%)	1	6 (2%)	1	10 (3%)	1	3 (1%)	1
	U3RNP	3 (6%)	1	12 (24%)	0.456	13 (26%)	1	5 (10%)	1	6 (12%)	1	9 (18%)	1

Conclusion: Coexistence of hallmark autoantibodies is exceedingly rare in SSc patients. When combined, both SSc-Abs have the potential to synergistically interact and modify the clinical phenotype.

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AB0558 RISK FACTORS FOR THE DEVELOPMENT OF BREAST CANCER IN SYSTEMIC SCLEROSIS

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Background: Prior literature shows a global increase of cancer risk among patients with systemic sclerosis (SSc). Although breast cancer (BC) is one of the most frequent malignancies in SSc patients, the characteristics of this neoplasm among SSc patients is not well established and it is uncertain whether SSc significantly increases the risk of this cancer.
Objectives: Describe the characteristics and risk factors for BC among Spanish patients with SSc.
Methods: Ambispective and multicenter study of patients with a diagnosis of SSc according to ACR/EULAR criteria and/or LeRoy classification included in the Spanish Scleroderma Registry (RESCLE) from 2006 to 2018. Characteristics of patients with BC were described and incidence was compared with that of the general population.
Results: Among 1930 patients with SSc, 206 (10.7%) had cancer. BC was the most frequent tumor location (47 patients of 206 with cancer [22.8%]), followed by lung cancer (29, 14.1%). The risk of BC was increased in patients with SSc compared to the general population (standardized incidence ratio [SIR] 1.31; 95% CI 1.10-1.54; *P* = 0.003).
The comparison of patients with BC and those without cancer showed that patients with BC had older age at diagnosis of SSc (50.9 vs 45.9 years, respectively; *P* =0.004), were more frequently diagnosed of interstitial lung disease (ILD) (30/47 [63.8%] vs 694/1714 [40.5]; *P* = 0.002) and pulmonary hypertension (12/24 [50.0%] vs 262/917 [28.6%]; *P* = 0.037), had higher frequency of puffy hands as the first manifestation of SSc (4/45 [8.9%] vs 38/1664 [2.3 %]; *P* = 0.023) and had more frequently primary biliary colangitis (PBC) (7 /46 [15.2%] vs 72 /1708 [4.2%]; *P* = 0.004). Regarding autoimmunity profile, patients with SSc and BC had a significantly higher presence of anti-Ro (11/44 [25.0%] vs 214/1528 [14.0%]; *P* = 0.049) and anti-mitochondrial antibodies (7/28 [25.0%] vs 96/837 [11.5%]; *P* = 0.039). Multivariable regression analysis showed an independent association between the puffy hands (OR = 6.40; 95% CI 1.73-23.60; *P* = 0.005), diagnosis of PBC (OR = 5.70; 95% CI 2.16-15.07; *P* = 0.001), presence of ILD (OR = 3.29, 95% CI 1.69-6.39; *P* <0.001) and the presence of the anti-Ro antibody (OR 2.14; 95% CI 1.01-4.56; *P* = 0.048) with the presence of BC.
Conclusion: BC risk was increased in patients with SSc. The development of ILD, PBC, the presence of anti Ro and puffy hands as the first clinical manifestation of SSc were identified as independent factors associated with the development of BC in our cohort.
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Zhang JQ et al. The risk of cancer development in systemic sclerosis: a meta-analysis. Cancer Epidemiol. 2013;37(5):523-7.
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AB0559 ARRHYTHMIAS AND LEFT VENTRICULAR DYSFUNCTION IN PATIENTS WITH SYSTEMIC SCLEROSIS.

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Background: Cardiac involvement in systemic sclerosis (SS) is common and one of the leading causes of mortality (up to 31%). Usually, it appears early and in a silent way. It can affect any cardiac structure and present with various manifestations. Cardiac disease worsens the prognosis and increases mortality, so it should be kept in mind in these patients.
Objectives: Study the prevalence of arrhythmias in patients with SS, not affected with pulmonary arterial hypertension (PAH) or other cardiac diseases, and establish its association with left ventricular (LV) dysfunction and heart dysautonomia (HD), as well as with other variables that could predict the development of this complication.
Methods: Prospective study of a cohort of patients with SS, excluding those with heart disease, PAH or cardiovascular risk factors. All underwent a clinical assessment, blood test with cardiac biomarkers, electrocardiogram (ECG), Holter 24h (HLT) and echocardiogram (TTE), interpreted by an expert cardiologist blind about the patients. Arrhythmias were classified as clinically significant arrhythmias (CSA) or clinically nonsignificant arrhythmias (CNSA) by ECG and HLT. LV diastolic dysfunction (LVDD) was defined as E/e'> 8, LV systolic dysfunction (LVSD) as a global longitudinal strain <20% and HD as a SDNN <100ms. Demographic, clinical and biological data were collected. A follow-up was performed at 6.2 ± 0.9 years. Statistical analysis was performed using SPSS 23 IBM®.
Results: 36 patients were included: age 56.7 ± 12.3 years (y), male / female 35/1, disease duration 7 ± 4.1 y. 66% belonged to the limited SS subtype, 66.6% were anti-centromere+, 25% anti-topoisomerase, 2.7% anti-PM/Scl and 2.7% anti-RNA polymerase III+. Raynaud was present in a 100%, telangiectasia in 55.6% and interstitial lung disease in 36.1%. The modified Rodnan skin score (mRSS) was ≤ moderate (0-29 points) in 55.6%; 27.8% had presented digital ulcers that required prostaglandins.
27.8% had LVDD, 22% LVSD, 11.1% LVDD + SD and 16.7% HD. 50% (18/36) of patients had ECG alterations, of which 44% corresponded to CSA (Table 1) and, 55.6% (20/36) HLT alterations, of which 75% were CSA (Table 2). 3/36 patients had both HLT and ECG CSA. In 1 patient, impaired LV ejection fraction was detected; in none, valvular disease. 38.8% had elevated NT-proBNP and 13.9% troponin T (TnT). No correlation was found between any parameters and CSA.
A correlation was found between mRSS and DLCO (p=0.002), DLCO and digital ulcers (p=0.001), and mRSS and digital ulcers (p=0.005). A correlation was also found between elevated NT-proBNP and TnT (p=0.006) and between elevated NT-proBNP and LVDD (p=0.049).
At follow-up after 6.2 ± 0.9 y, 2 patients had died: 1 of neoplasia and 1 of severe biventricular dysfunction 5.2 y after the study.
Conclusion: Our data confirm a high prevalence of ventricular arrhythmias and left dysfunction in patients with SS, without heart disease, cardiorespiratory symptoms or HAP, being up to 75% of the arrhythmias CSA. The lack of correlation between CSA and LVSD or DD indicates that arrhythmias could be due, not only to a supposed structural alteration of the myocardium, but to a primary and early cardiac involvement in SS. In addition, the lack of correlation between CSA in ECG and HLT reinforces the importance of a complete cardiac evaluation in these patients to rule out silent cardiac involvement.

Table 1. ECG abnormalities. *CSA.

Alterations		# Patients
Major	Complete Left Bundle Branch Block (BBB)*	1
Minor	Abnormal QRS prolongation in precordial leads	1
	Nonspecific ST-T wave changes	3
	Incomplete Left BBB*	3
	Incomplete Right BBB*	4
Other	QT prolongation	11

Table 2. HLT alterations. *CSA.

Alterations	Subtype	# Patients
Supraventricular Extrasystoles	**Uncommon**	**7**
	Frequent*	**3**
	Mono/Polymorphic	**0**
Nonsustained Supraventricular Tachycardia*		**7**
Ventricular Extrasystoles	**Benign**	**4**
	No Benign*	**4**
	Doublets	**1**
	Two Morphologies	**2**
	Accelerated Idioventricular Rhythm	**1**
1st-degree Atrioventricular Block		**1**
Sinus Tachycardia		**2**

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AB0560

DESCRIPTIVE ANALYSIS AND STUDY OF CORRELATIONS IN A COHORT OF PATIENTS WITH INFLAMMATORY MYOPATHIES

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Background: Inflammatory myopathies (IM) are a group of rare diseases that involve muscle inflammation. Several types are defined with a wide range of different manifestations and prognosis.

Objectives: Describe the characteristics of the cohort of patients with IM in a tertiary hospital, in order to identify their demographic and clinical characteristics and try to find a correlation between them.

Methods: Retrospective observational study of patients with IM: dermatomyositis (DM), polymyositis, antisynthetase syndrome (ASS), necrotizing autoimmune myopathy and overlap syndrome (OS). Clinical, biological, neurophysio and histopathological data were collected. Statistical analysis was performed using SPSS 23 IBM®.

Results: 28 patients were included with a follow-up of 10.9 ± 9.8 years (y). According to the 2017 EULAR / ACR criteria for IM, 89.2% were classified as definitive MI, with an average score of 12.1 ± 3.2. Age at diagnosis 47.3 ± 17.7y; ratio 1.3; 78.6% Caucasian, 10.7% Asian and 10.7% Latino. 39.3% had DM, 3.6% hypomyopathic and 3.6% amyopathic DM, 28.6% OS and 17.9% ASS. Lung involvement was the most prevalent extramuscular manifestation (67.9%). Systemic sclerosis was the most frequent overlapping autoimmune disease (AD) (21.4%) and 2 patients (7.1%) overlapped more than 1 AD. In Table 1 are detailed the clinical characteristics of the patients, and in Figures 1 and 2, the autoantibody (aa) profile and treatments used. The incidence of neoplasm was 10.7% 10.3 ± 9.6y after the diagnosis of myopathy (3 breast neoplasms, 1 colon and 1 cutaneous lymphoma), and of them, 66.7% had two synchronous neoplasms. No neoplasms were observed in the 2 anti-TIF1-γ+ patients. The subtype of IM in these patients was 1 OS anti-RNP+, 1 DM anti-PL-12+ and 1 ASS anti-OJ+. 17.9% smoked and 21.4% had taken statins at some point, without it being related to the start of the myopathic clinic. A capillaroscopy was performed in 67.9%, being pathological in 63.1%

The positivity of anti-RNP (p=0.01) and steroid bolus (p=0.039) were correlated with a more severe disease, defined as a summation index composed of a series of manifestations (pulmonary hypertension (PH), ischemic heart disease, venous/arterial thrombosis, myo/pericarditis, interstitial lung disease (ILD), severe infections, neoplasms or hospitalizations). Other statistically significant correlations between aa and clinical manifestations are detailed in Table 3, among which the anti-RNP+ with myopericarditis stands out. No correlation was found between the findings on capillaroscopy and the type of IM.

Conclusion: The most frequent subtype of IM was DM. 10.3% of the patients presented a neoplasm, all with different subtypes of myopathy and aa. The presence of anti-RNP+ correlated with greater severity of the disease and myopericarditis. Likewise, significant differences were found between the subtypes of aa and certain clinical manifestations. There is no correlation between findings on capillaroscopy and the type of IM.

Table 1. Clinical characteristics.

Clinical manifestations		Frequency %
Presentation	Acute	40.7
	Subacute	22.2
	Insidious	37
Muscular Weakness		82.1
Muscle Enzymes Elevation		85.7
Muscle Pain		67.9
Joint Manifestations (Mf)		67.9
Systemic Mf		67.9
Digestive Mf		46.4
Raynaud's Syndrome (RS)		53.6
Sclerodactyly		32
Digital ulcers (DU)		25
Calcinosis		10.7
ILD		67.9
	Nonspecific Interstitial Pneumonia	63.2
	Usual Interstitial Pneumonia	15.8
	Organizing Pneumonia	10.5
	Lymphocytic Interstitial Pneumonia	5.3
	Undefined Pattern	5.3
PH		10.7
Serious Infections		17.9

Table 2. Correlations between clinical manifestations and aa.

Manifestations	Autoantibodies	p value
DU	Anti-MDA5	0.005
Sclerodactyly	Anti-RNP	0.011
Pericarditis	Anti-RNP	0.000
Myocarditis	Anti-RNP	0.005
Diabetes	Anti-RNP	0.027
RS	Anti-PM/Scl	0.033
Calcinosis	Anti-PM/Scl	0.027
Flexion Contractures	Anti-PM/Scl	0.027
Arrhythmias	Anti-PL-12	0.001

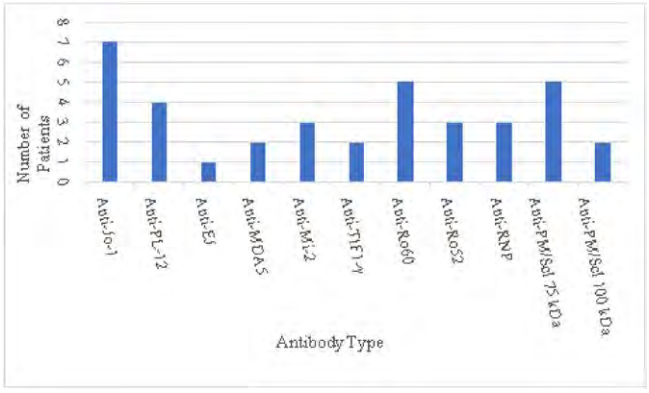


Figure 1. Aa.

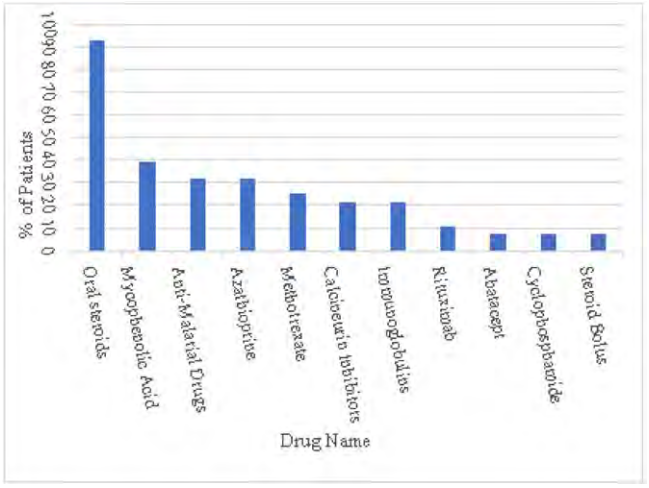


Figure 2. Treatment.

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AB0561

AUTOMATIC QUANTIFICATION OF INTERSTITIAL LUNG DISEASE FROM CHEST COMPUTED TOMOGRAPHY IN SYSTEMIC SCLERODERMA

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Background: Scleroderma-associated interstitial lung disease (SSc-ILD) is often observed in patients with systemic scleroderma (SSc) and its diagnosis contributes to early treatment decisions[1,2].
Objectives: The present study aims to automatically quantify SSc-ILD from high-resolution chest-computed tomography (HRCT) and to evaluate the association between interstitial lung disease (ILD) extension and lung function impairment.
Methods: Ninety-four patients with SSc and 27 lung-healthy subjects matched for gender, weight, height, and age underwent HRCT, spirometry and carbon monoxide diffusion capacity (DL_{CO}). SSc-ILD was determined as the tissue mass present between -500 and +100 Hounsfield Units normalized by the total lung tissue mass (TLM). Cut off was the highest value obtained in the control group (25% of TLM). All data are presented as mean and standard deviations (Table I). An ANOVA test followed by Bonferroni post-hoc correction was used for comparisons among groups.
Results: From 94 patients with SSc, 64 were classified as having pulmonary involvement (SSc-ILD) and 30 as not having pulmonary involvement (SSc No-ILD). In SSc-ILD subjects, there was a significant reduction in forced vital capacity (FVC), carbon monoxide diffusion capacity (DL_{CO}) and carbon monoxide diffusion capacity normalized by alveolar ventilation (DL_{CO}/A) when compared with SSc No-ILD and control group.
Conclusion: The proposed method allows the automatic quantification of SSc-ILD from HRCT and ILD extent is associated with pulmonary function impairment.
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Table 1. Demographic variables, pulmonary function tests and densitovolumetry considering scleroderma patients with less or greater pulmonary involvement.

	Control Group N = 27	SSc No-ILD N = 30	SSc-ILD N = 64	p-value
Demographic Data				
Females	16 (59.2)	28 (93.3)	58 (90.1)	-
Age (years)	37.9 ± 14.8	51.2 ± 12.2	56 ± 14	**<0.011**[a,b]
BMI (kg/m^2)	26.7 ± 5.1	24.1 ± 5.0	25.9 ± 5.7	-
Lung Function				
FVC (% predicted)	100.2 ± 9.2	99.9 ± 19.8	69.8 ± 16.7	**<0.001**[b,c]
DLco (% predicted)	103 ± 13.3	83.8 ± 14.2	63.4 ± 20.3	**<0.002**[a,b,c]
DLco/A (% predicted)	112.7 ± 17.4	85.7 ± 12.9	79.2 ± 20.6	**<0.001**[a,b]
Densitovolumetry				
TLV mL	4675 ± 986	4471 ± 916	3492 ± 1120	**<0.001**[b,c]
Lung Tissue Mass (g)	793 ± 125	756 ± 159	731 ± 155	-
ILD Extent (% LTM)	17 ± 2	22.9 ± 1.2	32.6 ± 8	**<0.003**[a,b,c]

a: Statistically significant difference between No-ILD SSc and control group; b and c: Statistically significant difference between SSc-ILD vs control group and SSc No-ILD, respectively.

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AB0562 SLEEP HYGIENE: COULD IT BE A CONFOUNDING FACTOR FOR SLEEP QUALITY IN SYSTEMIC SCLEROSIS?

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Background: Sleep disturbances have been described in Systemic Sclerosis (SSc). Confounding factors related to sleep quality are also investigated. Although sleep hygiene plays an important role in sleep quality, as far as we know, there are not enough data to show the effect of sleep hygiene on sleep quality of SSc.
Objectives: To investigate sleep hygiene, its impact on sleep quality, and its association with demographic-clinical factors in patients with SSc, rheumatoid arthritis (RA), and healthy controls.
Methods: The study was designed as cross-sectional. Forty-nine patients with SSc who fulfilled the 2013 ACR/EULAR classification criteria for SSc, 66 patients with RA who fulfilled 1987 revised classification criteria, and 30 healthy controls were included in the study. All participants were female. Demographic and clinical variables were documented. Disease activity index of both SSc and RA was calculated. SSc patients were assessed by questionnaires including Short Form 36 (SF-36), The Health Assessment Questionnaire Disability Index (HAQ-DI), Beck Anxiety and Beck Depression Inventory, Pittsburg Sleep Quality Index (PSQI), Sleep Hygiene Index (SHI). Additionally, RA patients and healthy controls were estimated by HAQ-DI, Beck Anxiety and Beck Depression Inventory, PSQI, and SHI. Logistic regression analysis was used to determine the predictors of sleep quality.
Results: Preliminary results of the study were given. The baseline demographics were similar among groups. When comparing groups according to HAQ-DI, Beck Anxiety and Beck Depression Inventory, PSQI, and SHI, we found higher scores in SSc and RA rather than healthy controls (p<0.001, p=0.001, p=0.001, p<0.001, p=0.003; respectively). While depression and sleep hygiene were determined as the risk factors of sleep quality in SSc in univariate analysis, depression (OR=1.380, 95%CI: 1.065–1.784, p=0.015) and sleep hygiene (OR=1.201, 95%CI: 1.003–1.439, p=0.046) were also found in multivariate logistic model. In RA patients, while health status, depression, and anxiety were found as risk factors according to the univariate analysis, depression (OR=1.120, 95%CI: 1.006–1.245, p=0.038) was the only factor according to multivariate logistic model (Table).
Conclusion: Although depression is a well-known clinical variable impacting on sleep quality, sleep hygiene should also be kept in mind as a confounding factor.
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Table. Univariate logistic regression analysis of clinical variables to assess predictors of sleep quality

	Systemic sclerosis		Rheumatoid arthritis	
	OR (95% CI)	p	OR (95% CI)	p
HAQ-DI	1.019 (0.882–1.177)	0.801	1.089 (1.011–1.173)	**0.025**
BDI score	1.293 (1.082–1.547)	**0.005**	1.129 (1.036–1.230)	**0.006**
BAI score	1.080 (0.997–1.169)	0.059	1.122 (1.038–1.214)	**0.004**
SHI	1.200 (1.060–1.357)	**0.004**	1.048 (0.965–1.137)	0.264
Disease activity[a]	0.707 (0.439–1.138)	0.153	1.446 (0.839–2.492)	0.185

[a]Disease activity was calculated by Valentini disease activity index for SSc and DAS28-CRP for RA.

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AB0563 AORTIC ROOT DILATION IN ASSOCIATED WITH THE REDUCTION OF CAPILLARY DENSITY OBSERVED AT NAILFOLD CAPILLAROSCOPY IN SSC PATIENTS

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Background: Systemic sclerosis (SSc) in a chronic autoimmune disease characterized by endothelial dysfunction and diffuse microangiopathy, leading to tissue ischemia and inducing fibrosis of skin and visceral organs. Furthermore, it was demonstrated the impairment of wall elasticity of large-medium vessels, such as aorta and its branches (1). SSc-related microangiopathy of vasa vasorum of the aortic wall could also be supposed. However no data on this hypothesis are available in literature.
SSc microangiopathy may be easily studied at the nailfold by means of videocapillaroscopy. Indeed, capillaroscopic findings are representative of the microvascular damage caused by SSc troughout the body.
Objectives: we aimed to investigate the presence of aortic root dilation, classical sign of aortic wall damage, in a cohort of SSc patients, and to correlate these

findings with the capillaroscopic patterns (early, active, and late, according to Cutolo's classification (2)).
Methods: we recruited 125 SSc patients (M/F: 14/111, mean age 55+/-12.7 years, median disease duration 11 years) in 3 Rheumatology Centres in Sicily, Italy, from January to December 2019.
Transthoracic echocardiogram with aortic root diameter measurement was carried out in all patients. Moreover, videocapillaroscopy with identification of early, active, or late SSc patterns was performed in the whole case series. Patients with early SSc pattern formed the subgroup 1, while those with the active or late patterns (both characterized by the reduction of capillary density) the subgroup 2.
Results: we identified 8 (6.4%) SSc patients with aortic root dilation (diameter > 35 mm). Their age and their frequencies of cardiovascular risk factors were similar to the whole series. Moreover, videocapillaroscopy showed 62 (49.6%) early, 47 (37.6%) active, and 16 (12.8%) late SSc patterns.
Aortic root dilation was observed in only one patient in the subgroup 1 (1/62, 1.6%), and in 7 cases of the subgroup 2 (7/63, 11.1%); p=0.03.
Conclusion: in this multicentre study, we found that aortic root dilation is significantly associated with the reduction of capillary density at nailfold capillaroscopy (active or late SSc patterns). On the basis of these findings, we might argue that SSc-related microangiopathy of vasa vasorum could contribute to aortic wall damage, at least in a subset of SSc patients.
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AB0564 HEART VALVULAR ALTERATIONS IN A MULTICENTRE ITALIAN COHORT OF SSC PATIENTS

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Background: systemic sclerosis (SSc) in a chronic autoimmune disease characterized by endothelial dysfunction, diffuse microangiopathy, and fibrosis of skin and visceral organs. Typical cardiac involvement may includes microvascular ischemia, contraction band necrosis, and patchy fibrosis, leading mainly to arrythmias and conduction defects, diastolic dysfunction, or right ventricular failure (secondary to pulmonary arterial hypertension) [1]. Valvular diseases are poorly described and generally not considered a typical sign of SSc [2-4].
Objectives: we aimed to describe valvular alterations in a multicentre cohort of SSc patients.
Methods: we consecutively recruited 118 SSc patients (M/F: 14/104, mean age 56.7±12.4 years, median disease duration 10 years, limited/diffuse skin subsets: 95/23, anti-centromere/anti-Scl70/others autoantibodies: 35/37/46) in 3 Rheumatology Centres in Sicily, Italy, from January to December 2019.
Considering the cardiovascular risk factors, 40 (34%) patients were smokers, 7 (6%) diabetics, 12 (10%) showed hypercholesterolemia, 38 (32%) arterial hypertension, while none was obese. Transthoracic echocardiogram was carried out in all patients during their follow-up.
Results: valvular abnormalities were as follow: mitral valve: insufficiency 85 (72%) cases - mild in 77/85, stenosis 2 (2%) - mild in 25/28, sclerosis/tickening 36 (30%), and calcification 9 (8%) patients; aortic valve: insufficiency 28 (24%), stenosis 4 (3%), sclerosis 29 (25%), and calcification 7 (6%) patients; tricuspid valve: insufficiency 91 (77%) cases, no cases of stenosis, sclerosis 5 (4%), and calcification 1 (1%) patients; pulmonary valve: insufficiency in 13 (11%) patients.
As expected, tricuspid insufficiency (TI) was associated with pulmonary arterial hypertension (PAH) (moderate TI in 20% of patients with every TI and PAH vs. 4% of patients with TI without PAH, p=0.019).
Aortic sclerosis (AS) was associated with the presence of arthritis (AS in 35% of patients with arthritis vs. 16% of patients without, p=0.029).
No association was found with age, gender, disease duration, skin subset, autoantibodies, capillaroscopic patterns, presence of digital ulcers, lung, renal, or digestive involvements.
Conclusion: in this multicentre SSc cohort study, we found that cardiac valve alterations are very common, even though generally not clinically relevant. The presence of PAH was associated with more severe TI. Finally, AS was associated with arthritis that could be considered sign of chronic inflammatory state, which is often linked with accelerated atherosclerosis and remodeling process of aortic valve [5].
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AB0565 HOSPITALIZATION IN A COHORT OF PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHY: WHAT IS HAPPENING IN ARGENTINA?

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Background: Inflammatory myopathies are rare diseases that affect multiple organs and systems, with poor prognosis and high in-hospital mortality. [1,2] In Argentina there are few reported data regarding hospitalization and its outcomes in these patients.
Objectives: To analyze the characteristics of hospitalizations and the factors associated with poor outcome in adult patients with Idiopathic Inflammatory Myopathy (IIM).
Methods: Retrospective, analytical study. We included patients ≥ 18 years with IIM, according to Bohan and Peter and/or ACR / EULAR 2017 criteria, who were admitted in our hospital between 2003 and 2019 at least once. Sociodemographic and clinical data were recorded. We defined "unfavorable outcome" as the presence of one of the following events: death, mechanical respiratory assistance and/or critical care unit requirement. Continuous variables were compared by Student's or Mann Whitney's T test, and categorical variables by Chi^2 test or Fisher's exact test. Binary logistic regression was performed to identify independent factors associated with an unfavorable outcome.
Results: 61 hospitalizations of 40 patients with IIM were evaluated; 67.5% of the patients were female (27/40), with a mean age of 52.5 years (SD± 13). The most frequent reason of admission was for diagnosis (44.3%) followed by disease activity (31.1%). In 78.7% of hospitalizations (48/61) the diagnosis was dermatomyositis. The median of hospitalization days was 14 (IQR 8-30). In 21 out of 61 hospitalizations (34.4%), an unfavorable outcome was observed, of which 17 (80.9%) ended in death. Respiratory muscle involvement ($p = 0.01$), thrombocytopenia ($p < 0.001$), treatment with intravenous methylprednisolone pulses ($p = 0.032$), Intravenous Immunoglobulin ($p = 0.001$), longer hospitalization ($p = 0.001$) and severe infections ($p = 0.001$) were associated with adverse outcomes. In the multivariate analysis, serious infections (OR: 21.7; IC95 1.77 - 266; $p = 0.016$) and the requirement of Intravenous Immunoglobulin (IVIg) (OR: 54.5; IC95 1.4 - 214; $p = 0.033$) were found to be independently associated with an unfavorable outcome.
Conclusion: IIMs are diseases with high morbidity and mortality rate. In this cohort of hospitalized patients, we found a high percentage of unfavorable outcomes. Seriously ill patients received IVIg more frequently, and severe infections were associated with worse prognosis.

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AB0566 NAILFOLD EXTENT OF REDUCED CAPILLARY DENSITY IS ASSOCIATED WITH DIGITAL ULCERS AND WITH AN INCREASED RISK OF DIGITAL ULCERS IN SYSTEMIC SCLEROSIS

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Background: A growing evidence supports the role of microvasculopathy as a primary pathogenic event in systemic sclerosis (SSc). The most commonly used imaging technique to identify microangiopathy in SSc is high magnification videocapillaroscopy (NVC), and reduced capillary density and/or capillary loss, which is a typical feature of "scleroderma microangiopathy", easily identified by NVC, has been associated with digital ulcers (DUs). Different approaches have been proposed to measure capillary density or capillary loss. Some of these were qualitative methods, others semi-quantitative, others only concerned a limited nailfold area, without ever evaluating the overall density, which is more suitable for quantitative estimate.
Objectives: To assess the association between the extent of different values of nailfold capillary density and the presence of DUs and to identify the risk of developing DUs, based on quantitative parameters.
Methods: The study involved 54 SSc selected patients (47 women and 7 men, mean age 59.5 years, 50 with limited and 4 with diffuse). The study population came from an ongoing database, that includes clinical and laboratory data of patients with definite SSc. A videocapillaroscope (VideoCap® 3.0, DS Medica, Milan, Italy) with a 200x optical probe was used. During examination, eight fingers (fingers 2–5 of each hand), 4 fields per finger, according to the standard literature were assessed. For each patient, a total of 32 images were collected, then classified as having either "normal", "non-specific" or the "scleroderma pattern" (SP). Capillary density was defined as the number of capillaries/mm in the distal row, regardless of its shape and morphology. Avascular areas were defined by the absence of loops within a width/area extending over more than 500 microns. For each patient, the SP images were further graded with no/slight reduction of the capillary density (7-9 loops/mm) (NOR), with a well-defined reduction of capillary density (6-4 loops/mm) (RED) and with loss of capillaries (<4) plus avascular areas (AA). Then, the overall percentages were calculated (the number with SP, the number with NOR, with RED and with AA, respect to 32), thus obtaining the quantitative measures. All data were analysed using the MedCalc® version 18.6; 64-bit (MedCalc Software, Mariakerke, Belgium).
Results: A total of 1728 images were analyzed. Patients with DUs were 16/54 (29.6%). All patients had a SP, but only five patients showed a SP along the entire nailfold. A comparison between patients with or without DUs showed a significant difference both for the overall extent of AA (p=0.032), and particularly for the overall extent of RED (p<0.001). No significant difference was found regarding the overall extent of the SP (p=0.085). Factor significantly associated with DUs in multivariate analysis was the overall extent of RED (p=0.0286). The ROC curve was very effective at discriminating the capillary feature able to distinguish patients with DUs from patients without DUs. The discriminatory power of the overall extent of RED was very good, with an AUC of 0.948 (95 % CI 0.852 ± 0.990). Then, we calculated the cut-off values of the overall extent of RED for presence/absence of DUs with the highest combination of sensitivity and specificity. The resulting cut-off value (Yourden index of 0.825) was >68.7 (sensitivity 92.31 %; specificity 90.24 %) with a LR+ of 9.46.
Conclusion: Our data strongly support that the capillary density between 4 and 6 loops/mm is the best capillaroscopic quantitative measure associated with DUs and able to discriminate the probability of having DUs. If all SSc-specific antibodies and/or other laboratory/clinical parameters are not yet available, the overall capillary density can allow physicians to assess SSc patients easily, regarding DUs and risk for developing DUs.
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AB0567 CHARACTERIZATION OF PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHY AND MYOCARDIAL INVOLVEMENT: A MONO-CENTRIC EXPERIENCE.

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Background: Idiopathic inflammatory myopathies (IIM) are immune-mediated disorders of the skeletal muscle, with dermatomyositis (DM), polymyositis (PM), inclusion body myositis (IBM) and immune-mediated necrotizing myopathy (IMNM) representing major subtypes. Beyond skeletal muscle, other organs may be affected and myocardial involvement may lead to severe life-threatening complications. The exact prevalence of myocardial involvement among IIM patients and its impact on other disease characteristics remain unclear.
Objectives: To investigate the prevalence of myocarditis in patients affected by IIM in and to determine whether the presence and extent of myocardial involvement identify a distinct disease phenotype.
Methods: 42 longitudinally followed IIM patients were routinely screened for myocardial involvement during a median [IQR] follow-up time of 4.2 [2-8.5] years. Patients with secondary causes of myocardial dysfunction were not included. Patients were considered to have myocarditis in case of: *i)* abnormal elevation of both circulating troponin T and troponin I, *ii)* signs of myocardial inflammation or necrosis/fibrosis at cardiac MRI, or *iii)* positive myocardial tissue histology. Demographic, clinical and serologic features of patients with myocarditis were compared to those with no sign of myocardial involvement. Moreover, we determined whether the extent of myocardial involvement based on troponin levels predicts skeletal muscle disease severity.
Results: 57.1% (24 of 42) of patients had myocarditis. The frequency of myocardial dysfunction was similar among patients with DM, PM, IBM or IMNM and was not related to autoantibody positivity. Myocarditis was not associated with sex or ethnicity. Patients with or without myocarditis were similar in terms of age at disease onset and extra-muscular manifestations including dysphonia, dysphagia, arthralgias or arthritis, Raynaud phenomenon or interstitial lung disease. Independent of the IIM subtype, the presence of perimysial macrophages at skeletal muscle biopsy seems to protect from myocarditis development (p=0.04). Patients with myocarditis had higher median [IQR] levels of aldolase (10.9 [7.8-15.8] vs. 5.6 [4.9-8.6], p=0.014) and creatine kinase (1785 [966-5852] vs. 685 [168-2255], p=0.04) compared to patients with no myocardial dysfunction. Among patients with myocarditis, levels of troponin I negatively correlated with manual muscle testing 8 (MMT8) score (r=-1, p=0.01), strength in biceps (r=-0.95, p=0.014) and wrist extensors (r=-0.95, p=0.014) at last visit. Troponin T and troponin I titers were similar among patients with different IIM subtypes. C-reactive protein (p<0.04) but not erythrocyte sedimentation rate was found to predict myocardial involvement.
Conclusion: Our findings suggest that myocarditis is a frequent occurrence among patients with IIM and should be routinely ruled out. A more severe skeletal muscle disease is associated with an increased likelihood of myocarditis development, presumably due to higher systemic disease activity or inefficient disease control. The extent of myocardial damage faithfully reflects the severity of skeletal muscle dysfunction.
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AB0568 BASELINE EUROPEAN PATIENT DEMOGRAPHICS AND DISEASE CHARACTERISTICS IN A PHASE 3 STUDY OF SAFETY AND EFFICACY OF LENABASUM, A CB2 AGONIST, IN DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS

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Background: We previously presented on the baseline characteristics of a large cohort of diffuse cutaneous systemic sclerosis (dcSSc) patients enrolled in a Phase 3 trial of lenabasum, a selective cannabinoid receptor type 2 (CB2) agonist. Lenabasum, was safe and well-tolerated in a prior Phase 2

study in dcSSc patients and associated with improvements in ACR Combined Response Index Systemic Sclerosis (CRISS) score and multiple secondary efficacy outcomes.

Objectives: We now report on the background standard of care and baseline disease characteristics of European (EU) patients in order to assess variability by geographic regions.

Methods: The RESOLVE-1 Phase 3 study was designed with input from study investigators and regulatory authorities. An important intent of the design was to have eligibility criteria that allow testing of efficacy and safety of lenabasum in an inclusive group of dcSSc subjects to maximize relevance to patients in current practice. The study is ongoing and remains blinded.

Results: Primary efficacy outcome is the ACR CRISS score at 12 months, comparing lenabasum 20 mg BID to placebo. Key inclusion criteria are males and females ≥ 18 years of age with dcSSc and disease duration ≤ 6 years who are on stable standard of care medicines, with background stable immunosuppressive mediations allowed. Baseline mRSS needed to be ≥ 15 if disease duration was > 3 to ≤ 6 years at enrollment. The study enrolled 110 EU subjects over 15 months who received ≥ 1 dose of study drug at 20 sites in 7 countries. Baseline characteristics as shown in Table 1. The majority were middle-aged, female, and white, and 80% were on immunosuppressive drugs in EU region; methotrexate (MTX) used in 30% of subjects, mycophenolate/mycophenolic acid (MMF) used in 46% of subjects, and 43% of subjects took ≥ 2 concurrent immunosuppressive drugs. There were regional differences in background immunosuppressive with use of MTX, MMF and corticosteroids highest in EU, NA and Asia, respectively.

Table 1. Patient Baseline Demographics and Disease Characteristics by Regions (Blinded)

Characteristic at First Dose	Mean (SD) or %		
	Region		
	Europe	US, CA, AU, IL	Asia
	N =110 (30.1%)	N = 189 (51.8%)	N = 66 (18.1%)
Years of age	51 ± 11.7	51 ± 13.5	49 ± 13.2
Female	75%	78%	71%
ILD	55%	40%	58%
Caucasian	101 (91.8%)	148 (78.3%)	0 (0.0%)
Asian	2 (1.8%)	10 (5.3%)	66 (100.0%)
Black	2 (1.8%)	16 (8.5%)	0 (0.0%)
Other	5 (4.6%)	15 (7.9%)	0 (0.0%)
Any immunosuppressive drug	80%	89%	79%
≥ 2 immunosuppressive drugs	43%	48%	38%
Mycophenolate	46%	70%	26%
Corticosteroids	31%	31%	53%
Methotrexate	30%	22%	23%
Other	31%	41%	26%
Modified Rodnan Skin Score	21.9 ± 7.75	23.8 ± 8.41	20.0 ± 7.72
Physician Global Assessment	5.9 ± 1.57	5.3 ± 1.56	5.0 ± 1.50
Patient Global Assessment	4.9 ± 2.02	5.0 ± 2.25	4.8 ± 1.89
HAQ-DI with aids/devices	1.0 ± 0.69	1.3 ± 0.76	0.7 ± 0.77
Forced vital capacity % predicted	83.2 ± 18.92	77.5 ± 16.41	82.5 ± 14.73

Conclusion: This is the first Phase 3 study to use ACR CRISS as the primary efficacy outcome, a composite outcome of multiple clinically relevant measures of SSc, and the largest interventional study to date in diffuse cutaneous SSc. While the use of background immunosuppressive therapies is significant irrespective of geographic regions, MTX use is highest in the EU. Benefits of having inclusive eligibility criteria are that they facilitated timely full enrollment and will make the study more relevant to real-world practice. This study provides a model for future Phase 3 trials in dcSSc and will afford valuable information regarding scleroderma care in practice as well as evaluating the efficacy and safety of lenabasum.

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AB0569 SPECIFIC FEATURES OF VASCULAR DISORDERS IN SYSTEMIC SCLEROSIS-OVERLAP SYNDROMES.

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Background: The Systemic Sclerosis-overlap syndromes are a typical representative of the well-known group of overlap syndromes in rheumatology, causing great difficulties in diagnostic and therapeutic aspects.

Objectives: To identify specific features of vascular disorders in patients with Systemic Sclerosis-overlap syndromes.

Methods: 100 patients (pts) were followed, including 68 pts with Systemic Sclerosis-polymyositis/dermatomyositis (SSc-PM/DM) (f:m 52: 16), aged 17 to 74 years (mean 43±13.9) and mean disease duration 5 [2-7] years, and 32 pts with Systemic sclerosis-Rheumatoid arthritis (SSc-RA) (f:m 31:1), aged 17 to 74 years (mean age 48±14.8) and average disease duration 11.5 [5-18,5] years. The comparison group consisted of 100 pts with Systemic sclerosis (SSc) (f:m 90:10), aged 51 to 75 years (mean 51±12.9) and mean disease duration 10.6 [5-13,5] years.

Results: In 1/3 of pts with SSc-PM/DM, the Raynaud's phenomenon (RP) preceded the emergence of skin lesions and was the first symptom of the disease (33%), developing in the first year in the majority (68%) of cases, being a unique sign of the disease in only 6 (9 %) pts, while in all other cases it was associated with articular involvement, skin lesions and muscle disease. In the first year of the disease 7 pts (10%) already had signs of digital ischemia (scars, ulcers), and by the end of 3 years such signs were present in 1/3 of SSc-PM/DM pts (32%). 29 pts (43%) developed recurrent digital trophic disorders, such as digital scars in 12 (18%), digital ulcers in 16 (23.5%) and digital necrosis of the distal phalanx in 1 pts (1.5%).

In 25 (78%) SSc-RA pts there was a gradual, monosymptomatic – with isolated RP - onset of the disease, similar to chronic cutaneous cSSc. In 29 SSc-RA (91%) pts, RP developed in the first year, and in 23 (72%) it was the first sign of the disease, and in 12 (37.5%) it preceded the development of skin and joint symptoms. Vascular disorders progressed with increasing duration and activity of the process. 7 patients (22%) developed recurrent digital trophic disorders - predominantly finger scars, while 3 (9%) pts had digital ulcers, developing in 11.66±7.62 years on average from the onset of the disease. Correlation analysis revealed a link between patients' age of and presence of telangiectasias (p<0.02). Digital trophic disorders were significantly more frequent in patients with longer disease duration (p<0.05).

Comparing of SSc-overlap syndromes and SSc pts showed, that although RP was present in all of them, nevertheless digital vascular-trophic disorders such as scars, ulcers (p<0.02) and necrosis (p<0.001) were less likely to develop in pts with SSc-overlap syndromes, similarly, telangiectasia and osteolysis were also significantly less frequent (p=0.04) distinguishing SSc-overlap syndromes from limited SSc (Table). Although, SSc-overlap syndromes pts had more severely affected muscles and joints as compared to SSc.

Table. Comparative characteristics of vascular disorders in SSc and SSc patients

Analyzed features	SSc n=100 (%)	SSc- overlap syndromes n=100 (%)	SSc-PM/DM n= 68 (%)	SSc-RA n=32 (%)
Raynaud phenomenon	100 (100)	100 (100)	68 (100)	32 (100)
Digital trophic disorders:				
scars	19 (19)	19 (19)	12 (18)	7 (22)
ulcers	34 (34)**	19 (19)**	16 (23,5)	3 (9)*
necrosis	16 (16)***	1 (1)***	1 (1,5)***	0 (0)***
Telangiectasia	60 (60)*	46 (46)*	34 (50)	12 (37,5)*
Osteolysis	37 (37)*	24 (24)*	16 (23,5)	8 (25)

* p<0,05, ** p<0,03, *** p<0,001

Conclusion: Digital trophic disorders (ulcers, necrosis), as well as telangiectasia and osteolysis are significantly less likely to develop in SSc-overlap syndromes than in SSc, which should be taken into account when panning therapeutic strategies in this category of patients.

Disclosure of Interests: None declared

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AB0570

MIXED CONNECTIVE TISSUE DISEASE: NOT THAT UNCOMMON, A SINGLE-CENTER EXPERIENCE FROM INDIA

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Background: Mixed connective tissue disease (MCTD) is considered to be uncommon; specifically there is sparse data on MCTD from developing countries like India.
Objectives: This study examines the clinical and serological features of these patients in a single center in North-India.
Methods: This was a retrospective single-center study of patients diagnosed as MCTD in last 20 years. The patients included fulfilled at least one of the diagnostic criteria namely Alarcón-Segovia, Kasukawa, and Kahns. Demographic details, clinical signs and symptoms, laboratory parameters, treatment and outcome were extracted from medical records and clinic files in a pre-designed proforma.
Results: This study included 41 MCTD patients. There was a marked female preponderance (F: M=40:1), and mean age of disease onset and diagnosis was 33.8 ± 10.7 and 39.3 ± 10.2 years. 39 (92%) of the patients fulfilled both Kahn and Kasukawa criteria, while 31 (76%) fulfilled Alarcon-Segovia criteria. Initially patients had been (mis)diagnosed as rheumatoid arthritis, systemic lupus erythematosus (or UCTD) (in five patients each), overlap syndromes or myositis (in 4 patients). ANA was commonly high-titer and specked, U1RNP was positive in all. (Table 1) Other autoantibodies on immunoblot included SSA and Ro52 in half the patients. Raynaud's was seen in three-fourth at presentation and all the patients over time. Digital gangrene and puffy fingers were seen in 8 (20%) and 18 (46%) patients. Other clinical features included arthritis in 33 (81%), sclerodactyly in 23 (56%) and proximal weakness in 20 patients (49%). Interstitial lung disease and pulmonary arterial hypertension were seen in 20 (57%) and 15 (44%) patients. All patients (except one) received prednisolone, and it was currently used in almost 90%. Intravenous cyclophosphamide was used in one-third, commonly for ILD.

Table 1. Laboratory features of patients with MCTD

Labs n (%)	
Leucopenia	9 (22)
Thrombocytopenia	10 (24)
Raised globulins [b]	22 (69)
Mean globulins, mean (SD)[a]	5±3.4
Elevated CPK[b]	10 (31)
CPK Levels U/L, median (IQR)	256 (57.5-1036)
ANA Speckled Pattern N (%)	31[d] (82)
U1RNP N (%)[b]	32 (100%)
U1RNP Blot Intensity	
1+	8 (25%)
2+	1 (3.2%)
3+	7 (21.8%)
4+	16 (50%)
U1RNP EIA, mean(SD), n=19	141.3 ± 82.4
Raised RF Titers[h]	10 (35.7%)
Low C3 mg/dl[f]	8 (40%)
Low C4 mg/dl[f]	3 (15%)
FVC, mean (SD) n=20	82.4 ± 18.9
ILD on HRCT[g]	20 (57)
Dilated PA on CT[f]	10 (50)
PAH[e] on ECHO	15 (44.1%)
RA/RV Dilated	5 (18)

SD-standard deviation, IQR- Interquartile range, CPK- Creatinine phosphokinase,, ILD-Interstitial lung disease, PAH- Pulmonary arterial hypertension, ANA- Anti nuclear antibody, IIF- Indirect Immunofluorescence, PA- pulmonary artery, RA/RV- Right atrium/Right Ventricle, [a]34 [b]32 [d]38 [e]34 [f]20 [g]34 [h]28

Conclusion: MCTD was not uncommon in the single-center in North India. Kahn and Kasukawa criteria were found to be the most sensitive for its diagnosis. Digital gangrene was relatively common and sometimes the presenting feature; whereas puffy fingers was present in only half the patients.
Disclosure of Interests: None declared
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AB0571

IS RITUXIMAB AN ADEQUATE GLUCOCORTICOID SPARING AGENT IN IDIOPATHIC INFLAMMATORY MYOPATHIES?

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Background: Idiopathic inflammatory myopathies (IIM) are essentially treated aiming improvement of muscle function and extra muscular disease manifestations. The backbone of the treatment is corticosteroids enhancing the survival and patient quality of life. The lack of consensus on target-specific immunosuppressive treatment highlights the need for further studies evaluating alternative treatment methods. Rituximab is potentially a glucocorticoid-sparing agent which was reviewed in multiple studies with small sample sizes due to the rarity of the disease.
Objectives: Higher statistical power can enhance the trustworthiness of alternative treatment methods yielding the main objective of this study.
Methods: This retrospective study was conducted at a tertiary rheumatology center. Patients were diagnosed with an idiopathic inflammatory myopathy (dermatomyositis [DM], polymyositis [PM]) and were treated with rituximab in order to be included in this study. Clinical signs and symptoms of the presentation were noted during the first patient encounter as well as the follow-up. Parameters of disease activity including acute phase reactants, muscle enzyme levels, and disease-specific autoantibodies were analyzed.
Results: The study includes 28 patients (20 DM, 8 PM). The age of diagnosis was 43.44 ± 15.77 years, follow-up duration was 60.7 ± 70.7 months. The presenting signs and symptoms of the patients are shown in Figure 1. The parameters of disease activity before and after treatment are summarized in Table 1. The mean corticosteroid dose decreased from 31.429 ±23.934 mg to 10.278 ±12.001 (p=0.001). Other treatment methods were methotrexate (n=18), Intravenous Immunoglobulin (IVIG) (n=7), and cyclophosphamide (n=2). There were not any deaths during the follow-up. Two patients were lost to follow-up.

Table 1. The Parameters of Disease Activity Before and After Treatment

	Before Treatment	After Treatment	P Value
CPK, mean ± std (U/L)	1426 ± 2049.92	263.44 ± 265.63	0.004
LDH, mean ± std (U/L)	557.5 ± 365	379.78 ± 192.1	0.03
AST, mean ± std (U/L)	62.52 ± 59	30.16 ± 27.59	0.01
ALT, mean ± std (U/L)	56.48 ± 49.21	27.64 ± 24.52	0.008
ESR, mean ± std (mm/hour)	26.38 ± 28.98	20.39 ± 18.76	0.36
CRP, mean ± std (mg/L)	19.23 ± 46.15	12.53 ± 26.67	0.5
RF, mean ± std (U/mL)	0 (0)	N/A	N/A
ANA, n (%)	3 (10.71)	N/A	N/A

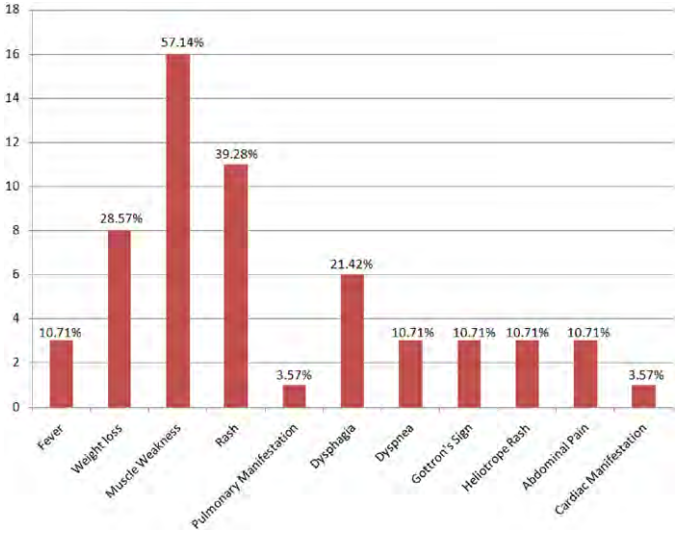


Figure 1. The Presenting Signs and Symptoms of the Patients

Conclusion: Rituximab is shown to be effective in treating myositis along with corticosteroids as well as a corticosteroid-sparing agent in retrospective studies and open-label clinical trials; however, lack of statistical power should be underlined. Long term decrease in steroid use and decrease in disease activity markers hints the effective use of rituximab as a glucocorticoid sparing agent as well as its safety with minimal side effects.
Disclosure of Interests: None declared
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AB0572 **REDUCED ENZYMATIC ACTIVITY OF ANTIOXIDANT SYSTEM IN SCLEROSIS.**

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Background: The antioxidant system is a natural barrier to the pathologic effect of reactive oxygen intermediate (ROI) on the tissues of patients with systemic scleroderma (SSD). It is comprised of enzymatic links, of which the cascade of enzymes like superoxide dismutase (SOD), glutathione peroxidase (GP), glutathione reductase (GR) and others are most important. Autoantibodies to enzymes of the antioxidant system can bring about a reduction in their biochemical activity.

Objectives: Studying the effect of production of antibodies to antioxidant system enzymes SOD, GP and GR in patients with SSD using immobilized magneto-controlable adsorbents.

Methods: We observed 40 patients with SSD and 30 apparently healthy individuals. Degree I of activity was established in 15 patients (37,5%), degree II – in 24 patients (60%), degree III – in 1 patient (2,5%). Patients with subacute and acute course of the disease, degree of activity II and III were united in one group due to their small number. Antibodies to SOD, GR and GP were determined in blood serum of patients upon admission and discharge using immobilized antigen forms of enzymes (Gontar I.P., 2001). Commercial preparations served as antigens when determining antibodies to SOD, GR and GP.

Results: A study of blood sera from healthy individuals showed SOD antibodies level of 0,06±0,004, GP antibodies – 0,045±0,003, GR antibodies – 0,05±0,01. The total activity of SOD in the group of healthy people was 38,2±1,2 IU; GP – 0,153±0,007, GR – 114,3±3,7. Upon admission to hospital patients showed a reliably reduced activity of SOD and GR ($p<0,002$), and unreliably reduced activity of GP ($p<0,02$). Among patients with SSD antibodies to SOD were detected in 15 people (37,5%), antibodies to GP – in 14 (35%), antibodies to GR – in 16 (40%). With degree I of activity, high levels of SOD antibodies were detected in 4 patients (26,7%), antibodies to GP – in 4 patients (20%), to GR – in 6 (40%). When SSD was degree of activity II and III, the patients showed a reduced activity of SOD, GR and GP ($p<0,05$) compared with healthy people, and higher antibody levels ($p<0,002$). We noted an increase in the number of patients whose serum showed high antibody levels: antibodies to SOD in 11 people (44%), to GP – in 11 (44%), antibodies to GR – in 12 (48%). In the group of SSD patients who showed high levels of SOD, GR and GP antibodies, we observed a reliable reduction in enzymatic activity ($p<0,05$). SOD activity was reliably reduced both in chronic and subacute course of the disease ($p<0,02$). In the group of patients with high levels of enzyme antibodies we noted a reliable reduction in enzymatic activity. A test for antibodies to SOD, GR and GP in SSD patients with involvement of various organs and systems showed their reliably elevated level in all clinical groups ($p=0,032$, $p=0,034$ and $p=0,025$).

Conclusion: Production of antibodies to antioxidant system enzymes plays an important role in pathogenesis of SSD involving internal organs and tissues and aggravating the course of the disease on the whole.

Disclosure of Interests: None declared

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AB0573 **IDIOPATHIC INFLAMMATORY MYOPATHIES: A SINGLE-CENTER EXPERIENCE**

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Background: Idiopathic inflammatory myopathies (IIM), mainly dermatomyositis (DM) and polymyositis (PM) are the diseases of the musculoskeletal system most commonly affecting the proximal muscles of the limbs. In addition to muscle inflammation, these conditions are multisystemic, presenting with a variety of complaints.

Objectives: As IIMs are infrequent, a single-center experience presenting quantitative data describing in-depth information on the nature of disease and treatment seems useful.

Methods: This retrospective study was conducted at a tertiary rheumatology center. Patients were diagnosed with an idiopathic inflammatory myopathy (DM, PM) in order to be included in this study. Clinical signs and symptoms of the presentation were noted during the first patient encounter as well as the follow-up. Parameters of disease activity including acute phase reactants, muscle enzyme levels, and disease-specific autoantibodies were analyzed. Treatment and prognosis information was also noted with additional information from phone call interviews.

Results: The study includes 108 patients (78 DM, 30 PM). The mean age of diagnosis was 43.17 ±18.73 years, follow-up duration was 44.37 ±60.58 months. The presenting signs and symptoms of the patients are shown in Figure 1. The parameters of disease activity before and after treatment are summarized in Table 1. The clinical tests ordered during the disease management are summarized in Table 2. The mean corticosteroid dose decreased from 45.65 ±114.53 mg to 15.22 ±16.77 ($p=0.007$). Other treatment methods were methotrexate (n=72), rituximab (n=28), Intravenous Immunoglobulin (IVIG) (n=9), and cyclophosphamide (n=5). Ten patients died during the follow-up. Thirty-six patients were lost to follow-up.

Table 1. The Parameters of Disease Activity Before and After Treatment

	Before Treatment	After Treatment	P Value
CPK, mean ± std (U/L)	2429.55 ± 5503.85	210.23 ± 352.97	<0.0001
LDH, mean ± std (U/L)	659.48 ± 458.74	262.83 ± 139.81	<0.0001
AST, mean ± std (U/L)	82.22 ± 92.63	25.94 ± 18.76	<0.0001
ALT, mean ± std (U/L)	75.28 ± 83.3	26.48 ± 21.68	<0.0001
ESR, mean ± std (mm/hour)	28.7 ± 25.36	25.62 ± 22.53	0.35
CRP, mean ± std (mg/L)	14.76 ± 26.86	9.12 ± 18.23	0.07
RF, mean ± std (U/mL)	15.72 ± 19.96	N/A	N/A
ANA, n (%)	26 (24.07)	N/A	N/A
Anti- JO 1, n(%)	5 (4.63)	N/A	N/A

Table 2. The Clinical Tests Ordered during the Disease Management

	Tested	Positive
Muscle Biopsy, n(%)	28 (25.93)	23 (82.14)
Skin Biopsy, n(%)	9 (8.33)	9 (100)
Thorax CT, n(%)	24 (22.22	18 (75)
Abdominal CT, n(%)	11 (10.19)	8 (72.73)
EMG, n(%)	43 (39.81)	36 (83.72)

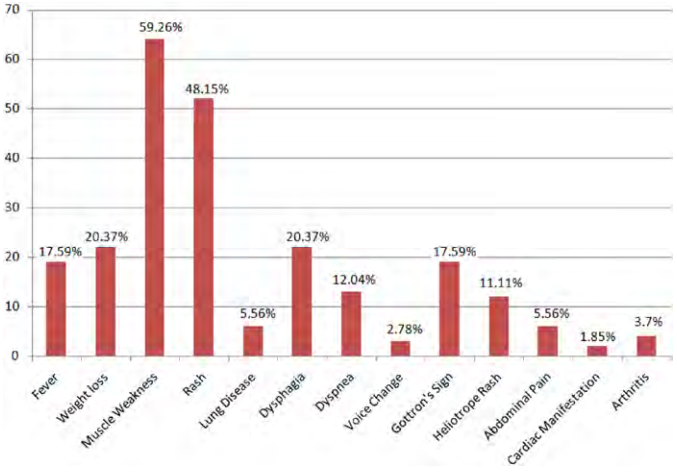


Figure 1. The Presenting Signs and Symptoms of the Patients

Conclusion: IIMs are very rare and can present with very different signs and symptoms. Referral to rheumatology can be challenging along with treatment. With inadequate clinical insight diagnosis and management of these patients can be delayed and quite expensive. Long term follow-up in our center enabled adequate control of disease activity as proven by the highly significant decrease in parameters of disease activity, especially muscle enzyme levels. Furthermore, we reported the variety of clinical symptoms, investigation methods and treatment essays in our center trying to reflect the potential challenges that can hinder a health clinical practice as well as highlight the requirement of a standardized approach.

Disclosure of Interests: None declared

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AB0574

BENEFITS OF ILOPROST IN LONG – TERM STABILIZATION OR IMPROVEMENT IN NEOANGIOGENESIS IN SYSTEMIC SCLEROSIS: A 15 YEARS OBSERVATION COHORT

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Background: In Systemic Sclerosis (SSc) fibrosis is due to microcirculation damage with capillary necrosis, arteriolar intimal proliferation and local ischemia. loprost (ILO) is used IV for the treatment of severe Raynaud phenomenon (RP) and digital ulcers (DU) in (SSc). We have already described (1) an improvement of peripheral vascularization with ILO, observed after 3 years treatment by capillaroscopy with an increase in the capillary number and mild regression of avascular areas and pericapillar oedema

Objectives: Our aim was to observe capillaroscopic changes in a cohort of 26 patients treated with ILO, once a month (25 – 50 ng each infusion) for an average time of 15 years

Methods: We evaluated the initial and 2019 capillaroscopic picture of 26 SSc patients (24 W,2 M; median age 63.8Y) in continuous treatment with monthly infusion of ILO from 2004 to today. 6/26 were SCL70 positive;the remainder was positive for anticentromere Ab

Results: We documented stability of capillaroscopic picture in 62% of patients,an improvement in 19% and a worsening (mainly from early to active pattern) in 19%. Low adherence to therapy was observed among the worsened patients. Out of 8 patients with onset ulcers, only 3 patients still have skin ulcers, all with late stable capillaroscopic picture from onset.We have not documented serious adverse events

Conclusion: Our observations confirm the efficacy and safety of ILO in the treatment of SSc even after many years of treatment, resulting in a stabilization of microvascular damage, independent of disease severity.

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Disclosure of Interests: None declared

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AB0575

THE ROLE OF LONG-TERM AND INTENSIVE IV ILOPROST TREATMENT IN REDUCTION OF PULMONARY ARTERY PRESSURE AND PRO-BRAIN NATRIURETIC PEPTIDE (PBNP) IN SCLERODERMA PATIENTS

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Background: Systemic sclerosis (SSc) is a chronic immune-mediated connective tissue disease with heterogeneous organ involvement that reduces the life expectancy of this patients. In particular cardiopulmonary manifestations, such as pulmonary arterial hypertension (PAH), are currently the primary cause of death and stabilizing this condiction may represent an important therapeutic goal (1,2). An increased NT-proBNP is predictors of PAH in SSc and use this markers should result in improved PAH risk stratification (3)Some studies have suggested the role of intravenous iloprost in preventing the incidence of most severe vascular complications in long term treated patients (4).

Objectives: The aim of our study is to evaluate the evolution of the disease, with particular focus on cardiopulmonary function, in a group of consecutive patients chronically treated with iloprost at the Rheumatology Unit of Catania Hospital, Italy, from 2006 to 2019.

Methods: 68 SSc patients (58F, 52.88 ± 12.6 years). At baseline, 67.6%, 25% and 5.9% had a limited, diffuse and early scleroderma type respectively and 20,6% had interstitial lung disease. The follow-up period of the study was of 9.9 ± 2.9 years. Iloprost was administered with a regimen of 6 infusions per month (6 hours/day, 0.5-2.0 ng/kg/min) to treat secondary Raynaud's phenomenon (RP), diagnosed at an average age of 46.6 ± 13.7 years. We evaluated: skin score (SS), systolic pulmonary arterial pressure (PAPs), plane tricuspid annular systolic excursion (TAPSE), lung diffusing capacity of carbon monoxide (DLCO), forced vital capacity (FVC), alveolar volume (VA), DLCO/VA, pro-brain natriuretic peptide (pBNP), and NYHA class.We analyzed the patients as a whole group (68 subjects), as a group who continued the treatment (57 subjects) and as a group who stopped the treatment during the follow-up (11 patients).

Results: After the long follow up period in the study (almost 10 years) in the whole group of patients, PAPs and pBNP showed statistically significant improvement from baseline (30.91 ± 6.4 vs 27.36 ± 7.1 and 97.20 ± 69.3 vs 66.65 ± 44.3 respectively, $p < 0.0001$ for both) while the other parameters showed no significant changes: SS (4.70 ± 5.3 vs 3.86 ± 4.2 mm), TAPSE (22.07 ± 2.4 vs 22.06 ± 3.8 mm), DLCO (83.68 ± 13.5 vs 77.70 ± 14.6 mmol/kPa.min), FVC (107.09 ± 14.5 vs 107.72 ± 18.7 liters), VA (91.12 ± 13 vs 90.30 ± 14.4 liters), DLCO/VA (88.48 ± 13.5 vs 89.5 ± 16.3) and NYHA class (1.0 ± 0.0 vs 1.0 ± 0.0). A subgroup analysis indicated a significant improvement in addition to PAPs and pBNP also for skin score for 57 patients who continued the treatment (5.09 ± 5.7 vs 3.30± 4.2, $p < 0.0001$) and a significant worsening of this parameter as early as the first year of suspension ($p < 0.05$ year 1, $p<0.01$ year 2 and 3) in 11 patients who stopped the treatment.

Conclusion: Cardiac involvement is recognised as a poor prognostic factor among systemic sclerosis (SSc) patients, significantly to mortality and N-TproBNP peptide may represent a surrogate marker for cardiac involvement in SSc, selectively identifying patients with severe impairment of cardiac function. Our intensive (6 infusions/month) and chronic regimen of iv iloprost administration seems improve the long-term evolution of disease in SSc patients, as suggested by the improvement of cardiopulmonary parameters and the significant improvement of SS.

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Disclosure of Interests: Rosario Foti Consultant of: lilly, sanofi, MSD, Janssen, Abbvie, BMS, celgene, roche, Speakers bureau: lilly, sanofi, MSD, Janssen, Abbvie, BMS, celgene, roche, elisa visalli Consultant of: lilly, sanofi, MSD, Janssen, Abbvie, BMS, celgene, roche, Speakers bureau: lilly, sanofi, MSD, Janssen, Abbvie, BMS, celgene, roche, Giorgio Amato: None declared, Alessia Benenati: None declared, Salvatore Bellofiore: None declared, Massimiliano Mule': None declared, Marcella Di Gangi: None declared

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AB0576

INCIDENCE AND CLINICAL MANIFESTATIONS OF RAYNAUD'S PHENOMENON IN RHEUMATIC DISEASES

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Background: Systemic sclerosis (SSc) is a connective tissue disease (CTD) most frequently associated with Raynaud's phenomenon – RP (96%), followed by mixed CTD (MCTD) (86%), systemic lupus erythematosus – SLE (31%), undifferentiated CTD (30%), rheumatoid arthritis – RA (22%) and Sjogren's disease – SD (13%)[1]. RP can manifest as a classical triple-colour change with pallor (ischaemic phase) followed by cyanosis (deoxygenation) and erythema (reperfusion)[2,1]. However, this triple-colour change only occurs in 19% of cases[2,3]. Majority of patients report an episodic double-colour change, consisting of pallor and cyanosis, pallor and erythema or cyanosis and erythema[2]. In a 4.8-year follow-up, 37.2% of RP patients developed rheumatic diseases (RD), 8.1% had other causes, in 54,7% RP remained primary[4].

Objectives: To study the incidence and manifestations of secondary RP in RD.

Methods: A questionnaire survey conducted in 230 patients with RD.

Results: RP was detected in 45.6% of RD patients (n=105), 54.4% of patients with RD had no RP (n=125). RP was 4 times more frequent in females than in males (F:M 4:1). In RP group, 87 patients (82%) had autoimmune RD: SSc (55.2%), SLE (17.1%), RA (6%),dermatomyositis (3.8%), cross syndrome (3.8%), MCTD (1.9%), SD (0.9%).

Only 84% of RP patients had positive answers to all three questions that characterize RP (1. Is there an unusual sensitivity of fingers to cold? 2. Do fingers change color when exposed to cold? 3. Do they turn white and/or bluish?). Biphasic color changes (whitening-blueness; whitening-redness; blue-redness) were observed in 33 (31.4%) patients with RP, three-phase changes – in 32 patients (30.5%). Blueness of fingers to cold was more frequent in SLE than in SSc ($p=0.027$).Redness of fingers to cold occurred more often in cross syndrome, MCTD, SD, RA, vasculitis than in SSc ($p<0.001$) and in vasculitis than in SLE ($p=0.035$). In SSc patients, whitening of fingers to cold was more common than redness ($p=0.037$) and two-/three-phase changes of fingers color in the cold were more frequent than single-phase changes ($p<0.001$).

The frequency of RP attacks was detected more than once a day in 44 (42%) patients. In 73% of cases, RP did not show signs of deep digital ischemia. Digital ulcers (active) were observed in 13 (12.3%) patients, fractures in a finger area – 23 (21.9%), digital scars – 15 (14.2%), phalange amputations – 7 (6.6%).

Conclusion: Patients with RD and secondary RP most often have SSC (55%), less often – SLE (17%), RA (6%), DM (3%). In SSc and SLE patients, Raynaud's reddening of fingers to cold is less common than in other RD. In SSc, two-/three-phase changes of fingers color in the cold are more frequent than single-phase changes. In SLE, fingers turn blue in the cold more often than in SSc.

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AB0577 ENDOTHELIAL DYSFUNCTION AND ATHEROSCLEROSIS IN SYSTEMIC SCLEROSIS: A MULTIPARAMETRIC ANALYSIS USING IMAGING TECHNIQUE AND LABORATORY MARKERS OF INFLAMMATION AND VASCULAR FUNCTION: SCLERODERMA CV RISK STUDY

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Background: Systemic sclerosis (SSc) patients have an increased risk for atherosclerotic cardiovascular disease (CVD), possibly mediated by inflammatory and fibrotic mechanisms[1]. However, pathogenesis of accelerated atherosclerosis in SSc remains to be elucidated. Endothelial dysfunction is the key initial event in atherosclerosis. Predictors for rapid evolution of cardiovascular complications would be highly desirable for CV risk stratification. This study aims to assess endothelial function and atherosclerosis in SSc, in context of markers of inflammation and vascular function in SSc patients.

Objectives: To assess endothelial function and atherosclerosis in SSc in context of markers of inflammation and vascular function in SSc patients.

Methods: A cross-sectional study was performed in 20 SSc patients meeting the 2013 European League Against Rheumatism (EULAR) and American College of Rheumatology (ACR) classification criteria and 18 healthy controls matched for age and sex. Flow-mediated dilatation (FMD) assessed by AngioDefender and CIMT measured ultrasonographically. Disease-specific measures included: Disease duration, Modified Rodnan Skin Score (mRSS), EUSTAR activity score in SSc. We also assayed markers of inflammation, including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), proinflammatory cytokines (interleukin IL-1, IL-6, and IL-17), and endothelial dysfunction including lipids, serum nitrite and TBARS (marker of oxidative stress). Quality of life measured by Scleroderma Health Assessment Questionnaire (SHAQ).

Results: FMD is significantly lower in SSc patients compared with controls (6.13±0.35% vs. 9.12±0.25%, p≤0.05). CIMT is significantly higher in SSc patients compared with controls (0.071±0.04cm vs. 0.035±0.02cm p≤0.05). Compared with controls, SSc patients had significantly (p≤0.05) elevated mRSS, EUSTAR score, ESR, CRP, IL-1, IL-6, IL-17, nitrite, TBARS and SHAQ whereas HDL levels are significantly reduced in SSc compared with controls (p≤0.05). In SSc, FMD inversely correlated with EUSTAR score, mRSS, IL-6 (Fig. 1A), serum nitrite (Fig. 1B), TBARS (Fig. 1C) and CIMT (Fig. 1D). CIMT positively correlated with age (Fig. 2A), disease duration, CRP (Fig. 2B) and IL-17 (Fig. 2C) and inversely correlated with HDL (Fig. 2D) (p< 0.05).

Conclusion: In the present study, FMD and CIMT are impaired in SSc, indicating endothelial dysfunction and accelerated atherosclerosis, respectively. EUSTAR score, mRSS, IL-6, serum nitrite, CIMT and TBARS predicted endothelial dysfunction. Age, disease duration, CRP, IL-17, HDL and impaired FMD predicted accelerated atherosclerosis. SSc-related inflammatory mechanisms (IL-6, IL-17) and markers of vascular function (CRP, serum nitrite and TBARS) may all be involved in the development of vascular disease in SSc. Cytokine-triggered inflammation mediated by nitrite and TBARS is associated with endothelial dysfunction and accelerated atherosclerosis in SSc. These markers would possibly serve as predictors of endothelial dysfunction and atherosclerosis and more importantly therapeutic targets to prevent premature atherosclerosis and cardiovascular disease in SSc.

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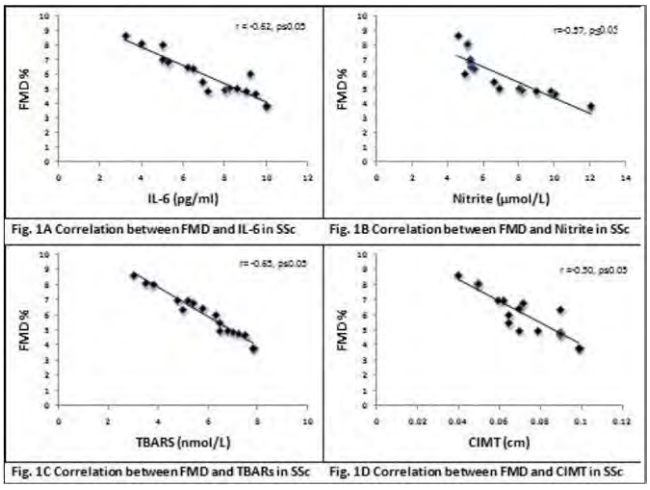


Fig. 1A Correlation between FMD and IL-6 in SSc
Fig. 1B Correlation between FMD and Nitrite in SSc
Fig. 1C Correlation between FMD and TBARs in SSc
Fig. 1D Correlation between FMD and CIMT in SSc

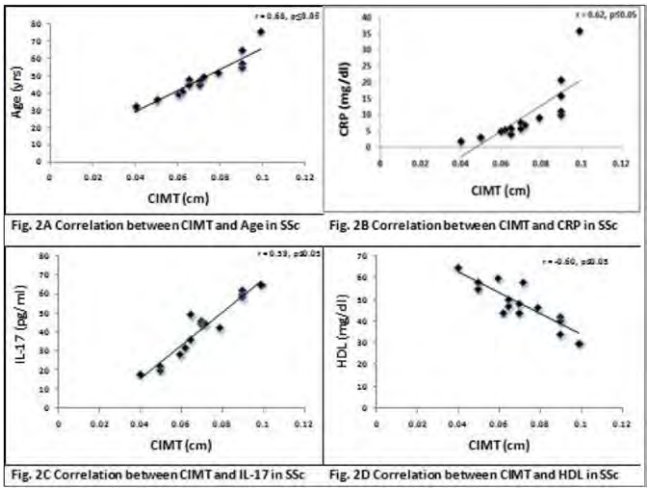


Fig. 2A Correlation between CIMT and Age in SSc
Fig. 2B Correlation between CIMT and CRP in SSc
Fig. 2C Correlation between CIMT and IL-17 in SSc
Fig. 2D Correlation between CIMT and HDL in SSc

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AB0578 LONG-TERM TOLERABILITY OF AMINAPHTONE IN A COHORT OF SYSTEMIC SCLEROSIS PATIENTS IN CONCOMITANT STANDARD THERAPY

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Background: Aminaphtone (AMI) is a bioflavonoid compound, classically used for "capillary disorders". *In vitro* AMI interferes with adhesion molecules (sELAM-1 and sVCAM-1) and with vascular endothelial cadherin degradation thus defending vessels permeability. Moreover, it counteracts vasoconstriction, downregulating endothelin-1 production at a gene level (1-3). *In vivo* AMI ameliorates clinical symptoms of several clinical conditions, above all Raynaud's phenomenon (RP), either primary or secondary to systemic sclerosis (SSc), as demonstrated by a recent six-month study (4).
Objectives: To evaluate long-term tolerability of standard dosage of AMI in a real-life cohort of SSc patients with secondary RP.
Methods: Seventy-eight SSc patients (mean age 65±13 years; mean disease duration 9±7 years) treated with AMI due to active RP were enrolled (ACR/EULAR 2013 criteria). They were taking various concomitant treatments, including aspirin, calcium-channel blockers, cyclic intravenous iloprost, immunomodulators, endothelin receptor antagonists. SSc patients performed periodic clinical assessments and blood tests on average every four months per clinical practice. Duration of AMI administration, side effects, and self-assessment of Raynaud Condition Score (RCS) in a scale from 0 (absence of pain) to 10 (intolerable pain) were retrospectively taken into account.
Results: Duration of AMI administration was between six and sixty-seven months (mean 31±20 months). AMI was administered at 75 mg *bis in die* dosage, as standard initial posology. At baseline, mean RCS was 7.3±0.8. After 3 months of treatment sixty-four patients (82%) yet referred a subjective improvement of RCS (3.5±0.8, p=0.03), whereas 14 patients (18%) were clinically unsatisfied (RCS 6.1±0.4, p=1.12). In this last group, posology was increased to 75 mg *tris in die*, with a satisfactory amelioration in further nine patients (93,6%) (RCS 4.0±0.6 p=0.04), while five patients (6,4%) definitively discontinued therapy for subjective ineffectiveness within six months. Patients referred a sustained improvement of RCS along the observational period (31±20 months) (last RCS 3.7±0.7, p=0.03 vs baseline). During the follow-up, five patients (6,4%) referred headache as side effect: three of them had to reduce AMI posology to 75 mg per day, while maintaining clinical benefits. Periodic blood tests did not reveal any significant alteration attributable to AMI. No other side effects related to the drug appeared during the treatment period.
Conclusion: AMI shows an acceptable medium-long-term tolerability along with sustained efficacy in the management of SSc-related RP, without disabling side effects. However, the retrospective design, the absence of a placebo-control group and the concomitant standard therapy limit the results, and a randomized controlled trial for AMI use in the management of SSc-related RP is desirable.
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Disclosure of Interests: Emanuele Gotelli: None declared, Sabrina Paolino: None declared, Federica Goegan: None declared, Francesco Cattelan: None declared, Massimo Patanè: None declared, Carmen Pizzorni: None declared, Maurizio Cutolo Grant/research support from: Bristol-Myers Squibb, Actelion, Celgene, Consultant of: Bristol-Myers Squibb, Speakers bureau: Sigma-Alpha, Alberto Sulli Grant/research support from: Laboratori Baldacci
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AB0579 ANTI-JO1 ANTIBODIES IN A REAL-WORLD POPULATION.

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Background: The presence of anti-aminoacyl transfer RNA synthetase (ARS) autoantibodies is essential for the antisynthetase syndromes (ASSD) diagnosis; as well, Anti-Jo1 ARS positivity is the highest weighted criterion in the 2017 EULAR/ACR criteria for idiopathic inflammatory myopathies (IIM).
Previous studies have shown differences in ARS specificity between different blot assays. Nevertheless, an adequate clinical correlation and its detection by another monospecific-assays or indirect immunofluorescence assay (IIFA), can safeguard it.
Objectives: To evaluate the prevalence of Anti-Jo1 ARS and their performance in the ASSD and IIM diagnosis criteria fulfillment in a real-world population.
Methods: We performed an observational retrospective study in one center in which IIFA and a blot assay (EUROLINE ANA Profile 3-IgG that include Anti-Jo1 but not other ARS) were performed in all cases with autoimmune disease suspicion (03/2007-07/2019).
We assessed: 1) Anti-Jo1 ARS prevalence, 2) The rate of Anti-Jo1 positivity in the performed blot assays, 3) The rate of patients with Anti-Jo1 ARS meeting ASSD or IIM criteria, and 4) The rate of true and false positive Anti-Jo1 ARS considering the IIFA and clinical correlation.
Results: A total of 419.361 inhabitants are under the center coverage area at the date, a total of 12.711 blot assays were performed during the observation period, and 61 cases presented Anti-Jo1 ARS positivity. The Anti-Jo1 ARS prevalence in the whole studied population was 0.00014, representing 0.04% positivity of the performed blot assays.
Of those with Anti-Jo1 positivity:
– Only 4 patients (6.6%) met Solomon´s ASSD criteria and 26 (42.6%) met Connors ASSD criteria (less strict), representing the 0.0009% and 0.006% of the whole population respectively.
– Five cases (8.2%) presented a possible or probable IIM by Bohan and Peter criteria and 55 cases (90.16%) presented a probable or definitive IIM by EULAR/ACR criteria, representing 0.001% and the 0.013% of the whole population respectively.
– The Anti-Jo1 positivity was not confirmed by a monospecific-assay. Nevertheless, 52 cases (85.25%) presented positive IIFA (>1/80): 27 (51.92%) nuclear, 12 (23.08%) cytoplasmic and 12 (25%) with both patterns. A total of 23 cases presented a fine speckled AC-19/AC-20 pattern; representing the 40.98% of all Anti-Jo1 ARS cases.
– Only 4 cases (6.56%) did not meet any of the ASSD or IIM classification criteria. And only 4 cases (6.56%) fulfilled Solomon ASSD criteria or presented a probable IIM by Bohan and Peter criteria, or a definite IIM by EULAR/ACR criteria. Thus, we can estimate that 6.56% of the cases were clinically false positives and other 6.56% were clinically true positive; leading a gap of 86.88% of cases with Anti-Jo1 ARS that only fulfill Connors ASSD criteria (less strict) or a not complete score to confirm the IIM diagnosis by Bohan and Peter or EULAR/ACR criteria.

Conclusion: The low prevalence of Anti-Jo1 ARS positivity observed and the low number of cases with confirmed ASSD or IIM in the Anti-Jo1 positive detected cases, suggest that:
– It is not efficient to test it by screening.
– It should be tested only under adequate clinical suspicion.
– Probably it is not convenient to include it in not myositis specific blot assays. Despite it is desirable to incorporate the evaluation of myositis specific antibodies in the IIM classification criteria; the differences observed between Bohan and Peter and 2017 EULAR/ACR criteria fulfillment in our series, suggest that the latter could be overweighting the Anti-Jo1 ARS positivity.

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AB0580 GENDER DIFFERENCES IN SYSTEMIC SCLEROSIS-IMPACT ON DISEASE PHENOTYPE AND PROGNOSIS

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Background: The low overall prevalence of systemic sclerosis (SSc) and the low proportion of male patients have resulted in a scarcity of studies assessing sex differences in SSc patients, and contradictory results.
Objectives: To evaluated sex influence on disease characteristics at baseline and then to estimate the effects of sex on disease progression and survival.
Methods: We performed a retrospective observational study using data extract from the EULAR scleroderma trials and research (EUSTAR) cohort 096. 173 patients were analysed (26 males).
The severity of organ system involvement was defined as described previously (1).

Results: Males were significantly older at symptom onset (p=0.007) and at first center visit (p=0.009). There were no differences regarding disease duration at first visit or the interval between the onset of Raynaud syndrome and other non-Raynaud manifestations (p=0.06). Male patients were significantly more likely to have ever smoked (p<0.001), males more often had severe or end-stage peripheral vascular involvement (p=0.01). Modified Rodnan skin score (mRSS) was significantly higher in males (p=0.004). We found no difference regarding musculoarticular involvement, except for digital contractures (p=0.001) and tendon friction rubs (p=0,044). Males more often had interstitial lung disease (ILD) (p=0.013) which was also more frequently severe or end-stage (p = 0.003). Cardiac involvement was more common in males: pulmonary hypertension (PAH) (p = 0.018), arrhytmias (p=0.012), left ventricle ejection fraction<45% (p=0.014). The frequency of scleroderma renal crisis (SRC) was higher in males (p=0.025). Gastrointestinal involvement did not differ between groups EScSG (European Scleroderma Study Group) disease activity scores were higher in males (p=0.001). The isolated presence of antitopoisomerase-1 or anticentromere antibodies did not differ between groups. Mortality rate was similar between sexes, although male sex is a independent predictor for the death associated with ILD, SRC, arrythmias

In multivariate analysis, male sex was independently associated with a higher risk of diffuse cutaneous subtype (OR: 1.56, (1.35 to 1.84); p<0.001), a higher frequency of severe vascular disease (OR: 1.38 (1.11 to 1.67); p<0.001), severe digital contractures (OR:1.92(1.68 to 2,42); p<0.001), interstitial lung disease OR: 1.22 (0.9 to 1.47); p<0.001), severe heart involvement (OR: 1.56 (1.22 to 2,1); p<0.001) and SRC (OR: 3.31 (1.87 to 5620); p<0.003). In the longitudinal analysis, after a mean follow-up of 7.2 (±2.6) years, male sex was predictive of new onset of scleroderma renal crisis (HR: 3.66 (1.82 to 4.86); p=0.006) and heart failure (HR: 1.9 (1.36 to 3.18); p=0.01).

Conclusion: In essence, the disease prophyle in females is that of younger age of onset, longer disease duration at first center visit, less severe peripheral vascular involvement, the most frequent cause of death being PAH. In contrast, males are older at onset, present earlier in their disease, have dcSSc, more severe peripheral vascular disease, higher mRSS, more frequent and severe ILD, more frequent heart involvement, higher risk of PAH and SRC, the most common cause of death being ILD. These results raise the point of including sex in the management and the decision-making process.

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Disclosure of Interests: Laura Groseanu Speakers bureau: novartis, eli-lilly, ucb, pfizer,sandoz, Andra Balanescu Consultant of: pfizer, Speakers bureau: Abbvie, Eli-Lilly, Novartis, Pfizer, Roche, Sandoz, UCB, Violeta Bojinca Speakers bureau: Eli-Lilly, Novartis, Pfizer, Daniela Opris-Belinski Speakers bureau: Abbvie, Eli-Lilly, Novartis, Pfizer, Roche, Ioana Saulescu Speakers bureau: Eli-Lilly, Pfizer, Diana Mazilu: None declared, Sanziana Daia-Iliescu Speakers bureau: sandoz, Andreea Borangiu: None declared, Florian Berghea Paid instructor for: abbvie, Speakers bureau: gideon richter, egis, novartis,ucb, cosmin-laurentiu constantinescu: None declared, CLAUDIA COBILINSCHI Speakers bureau: novartis, Maria Magdalena Negru: None declared, mihai abobului Speakers bureau: gideon richter, Ruxandra Ionescu Consultant of: Consulting fees from Abbvie, Eli-Lilly, Novartis, Pfizer, Roche, Sandoz, Speakers bureau: Consulting and speaker fees from Abbvie, Eli-Lilly, Novartis, Pfizer, Roche, Sandoz

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AB0581

HIGH PREVALENCE OF TUBERCULOSIS IN ADULTS AND CHILDREN WITH IIM AS COMPARED WITH SLE: RETROSPECTIVE DATA REVIEW FROM A LARGE COHORT AT A TERTIARY CARE CENTER IN INDIA.

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Background: Infections are the most common cause of morbidity and mortality in idiopathic inflammatory myositis (IIM). India is endemic for Tuberculosis (TB) with a prevalence of 2.3 cases per thousand population.

Objectives: Thus, we studied the prevalence of TB in our cohort of IIM patients and compared with that in systemic lupus erythematosus (SLE).

Methods: Medical records from paper charts and electronic medical records were reviewed for adults and juvenile patients with SLE (ACR criteria 1997) and IIM (Bohan and Peter criteria 1975) first presented at a tertiary care hospital in India from 1989 to 2016. Clinical variables including disease characteristics variables, the frequency, site, duration and complication of active TB as well as dose of corticosteroids and other immunosuppressive drugs were extracted retrospectively from the medical records. Descriptive statistics were used to describe the cohort and TB characteristics. Chi-square and t-test were used to evaluate association of TB with clinical diagnosis as well as medication data.

Results: There were 167 (132 adults and 35 juvenile) IIM and 280 (131 adults and 149 juvenile) SLE in our cohort. Active TB occurred in 24 (14.4%) of all IIM cases (18, 13.6% adults; 6, 17.1% juvenile) as compared to 18 (6.4%) of all SLE cases (8, 6.1% adults; 10, 6.7% juvenile, p value < 0.01). Of all the TB in myositis, most often it was seen in Dermatomyositis (n=11, 45.8%) followed by Polymyositis (5, 20.8%), and occasionally in Overlap myositis (3, 12.5) and juvenile dermatomyositis (1,4.1%).

Considering an annual TB rate of 211 per 100,000 of the general population, the risk of developing active TB was 62-fold higher in patients with IIM and 27-fold higher in those with lupus. Patients with IIM had higher odds of developing TB as compared with Lupus [odds ratio 2.86 (CI 1.5-5.47), p=0.007).

Amongst 24 IIM patients with TB, 10 had pulmonary TB and 14 had extra-pulmonary TB. The median glucocorticoid dose at the diagnosis of TB was 0.25 (0-1.5) mg/kg/day. Half the cases of active TB occurred during inactive myositis. Seventeen patients with active TB were followed up over 27 months (8-184), with remission of TB in all cases but required prolonged courses of Anti-Tuberculous Therapy (ATT) in 25% cases with 10 ATT related adverse events in 8 patients and 5 patients with relapse of myositis due to lowering of immunosuppression.

Conclusion: Patients with IIM have higher prevalence of active TB as compared with SLE patients. The risk is highest in patients with Dermatomyositis possibly related to high doses of steroids. Extra-pulmonary forms of TB are more common, and patients commonly require prolonged course of ATT and may suffer relapses of myositis during ATT. Screening for latent TB may be useful in IIM patients before prescribing steroids and other immunosuppressive drugs.

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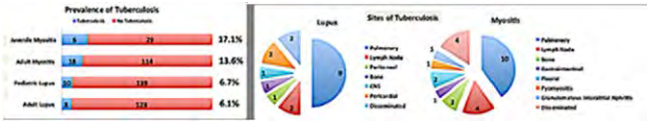


Figure 1. (A) Prevalence and (B) sites of tuberculosis

Table 1.

Population demographics

Variable	Adult Lupus	Pediatric Lupus	Adult Myositis	Juvenile Myositis
Patient number	131	149	132*	35#
Median follow up (years)	3.0	6.0	5.5	8.0
Female : Male	8:1	9:1	6.3:1	1.5:1
Median age (years)	32.4	13.7	32	8
Lupus nephritis (%)	51.9	100	NA	NA
Chronic kidney disease (%)	4.6	7.3	0	0
Incidence rate/ 100 patient years follow up	2.0	1.1	2.3	1.9

*56 DM, 28 PM, 13 Anti-synthetase syndrome and 35 Overlap myositis #26 jDM, 1 PM and 8 Overlap Myositis

Table 2. Clinical profile of patients with Tuberculosis

Clinical profile of Tuberculosis cases				
Clinical parameter	**Adult lupus (n=8,%)**	**Pediatric lupus (n=10,%)**	**Myositis (n=24,%)**	**P (SLE vs. IIM)**
Cases on high dose steroid#	3 (37.5)	4 (40.0)	5 (20.8)	0.15
Disease duration <=1 year	4 (50)	4 (40)	8 (33.3)	0.50
Pulmonary: Extra-pulmonary	4:4	5:5	5:7	0.76
Tissue/Fluid diagnosis	1 (12.5)	7 (70)	10 (41.7)	1.00
Active underlying disease	4 (50)	7 (70)	12 (50)	0.54
Relapse of TB	2* (25)	0	2 (11.8)	0.76
Resistant Tuberculosis				
MDR suspect	0	0	2	0.09
Pre-XDR	0	0	1	1.00
Death	1 (12.5)	1 (12.5)	0	0.09

#(>0.5mg/kg) * One patient each had CKD and family history of TB

Disclosure of Interests:
Latika Gupta: None declared, Abhishek Zanwar: None declared, Rohit Aggarwal Grant/research support from: Pfizer, Genentech, BMS, Mallinckrodt, Consultant of: Pfizer, Genentech, BMS, Mallinckrodt, Bristol Myers-Squibb, octapharma, CSL Behring, AstraZeneca, Corbus, Kezar, Abbvie, Able Lawrence: None declared, Durga Misra: None declared, Vikas Agarwal: None declared, Ramnath Misra: None declared, Amita Aggarwal: None declared
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AB0582 DIAGNOSING SYSTEMIC SCLEROSIS WITH PHOTOACOUSTIC AND HIGH-FREQUENCY ULTRASOUND IMAGING

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Background: Vasculopathy is already evident in early systemic sclerosis (SSc); Raynaud's phenomenon and typical nailfoldcapillaroscopic findings are part of the criteria of very early diagnosis of SSc (VEDOSs) (1). As not all early SSc patients have alterations in their nailfoldcapillaries, there is need for other diagnostic tools. Photoacoustics(PA) and high-frequency ultrasound (HFUS) might be able to fulfill this need (2). The former can measure the oxygen saturation of hemoglobin by using short pulsed laser light while the latter can provide high-resolution images that allow measuring skin thickening distal from DIP joint, which could be used to determine skin involvement early.
Objectives: We hypothesize that photoacoustics and high-frequency ultrasound can distinguish (early) SSc patients from individuals with primary Raynaud's phenomenon (PR) by measuring the oxygenation (by PA) of the fingertip and skin thickening (by HFUS).
Methods: In our cross-sectional study, we compared measurements of the third finger in (early)SSc patients with individuals with PR and healthy volunteers. Smoking and beta-blockage were exclusion criteria. The level of oxygenation (by PA) and skin thickness (by HFUS) were compared between groups. Nailfoldcapillaroscopy was performed on all subjects and analyzed for the pattern.
Results: Thirty-one adult subjects participated in this study: twelve patients with SSc, 5 patients with early SSc, 5 volunteers with PR and 9 healthy controls.
We found a significant difference in median (IQR) oxygen saturation between earlySSc patients 75.9% (IQR 75.1%-86.6%) and subjects with PR 94.1% (IQR 93.1%-94.5%) (p=0.0002) using the Wilcoxon rank-sum test (figure 1).



Figure 1. Boxplot of saturation (%) per group.

Measurements of skin thickening also showed a significant difference in early SSc patients compared to subjects with PR, respectively 0.5mm (IQR 0.4mm-0.5mm) vs. 0.3mm (IQR 0.3mm-0.3mm), P=0.0002 (figure 2).

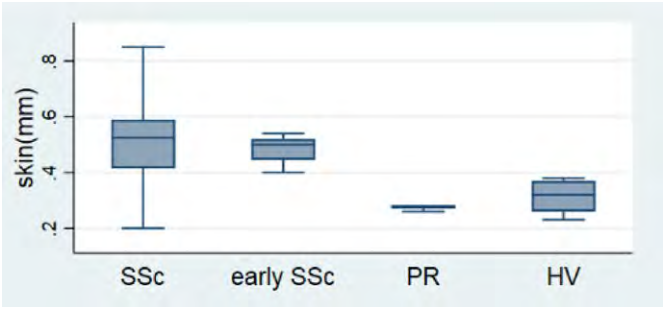


Figure 2. Boxplot of skin thickness (mm) per group.

Conclusion: Our results demonstrate that photoacoustic and high-frequency ultrasound can distinguish between (early)SSc and PR in both oxygenation saturation and skin thickening. In a larger prognostic study we want to determine the value of photoacoustic and high frequency ultrasound in diagnosing earlySSc.
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AB0583 COMPARISON OF THE RITUXIMAB (RTM) IN MONOTHERAPY REGIMEN AND CYCLOPHOSPHOMIDE (CYP) EFFICACY AND SAFETY IN SYSTEMIC SCLEROSIS (SSC) WITH INTERSTITIAL LUNG DISEASE (ILD)

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Background: CyP is considered as a drug of choice for the treatment of ILD in the patients with SSc. However, the use of CyP leads to rather limited and transient improvement of the pulmonary fibrosis. RTM is considered as a promising therapeutic agent for treatment of ILD in the patients with SSc. However, the limited number of RTM-treated patients, considerably different dose regimens, cumulative doses, and observation periods does not allow univocal conclusions on RTM efficacy or definitive recommendations on RTM use in the patients with SSc.
Objectives: To compare the impact of CyP and RTM a single-agent therapy on SSc clinical manifestation and activity, and the safety of these agents in the open-label prospective non-randomized study.
Methods: 71 patients with the confirmed SSc diagnosis and ILD evidence based on multispiral computed tomography findings were enrolled into the study. All patients received low-dose and moderate-dose glucocorticoids regimens. Group A (n=35) received RTM as a single therapy agent over the follow-up period 13.3±2.3 months in a total dose 1.35±0,5g (the patient's average age was 45.0±15 years, with female proportion 80%; SSc duration 6.3±2.3 years; diffused/localized forms 1.3/1). Group B (n=36) received parenteral CyP for 12±6 months at total dose 10.6±5 g (the average age 47±12 years, females 92%, SSc duration 5.0±4.8 years, diffused/localized forms 1.6/1). The age, gender proportion, SSc form and SSc duration, FVC, were similar in the both groups. The time courses of FVC, modified skin count (mRss, points), activity index (EScSG, points) were assessed in the study.
Results: The glucocorticoids starting dose that patients received at the time of inclusion in the study was significantly higher in group B compared to group A (p=0.03). Only after a year of CyP therapy, the dose of glucocorticoids was reduced to the starting dose in group A.

In Groups A and B the therapy was associated with significant decrease in mRss (p=0.02 and 0.009, respectively) and EScSG (p=0.00017 and 0.000165, respectively).
Evaluation of FVC time course in Groups A and B revealed significant FVC increase (p= 0.002 and 0.034, respectively), with median increment about 5%.
The 10% FVC increase and decrease was similar in both groups.
The therapy was better tolerated in RTM-treated group: during RTM therapy adverse reactions emerged in significantly lower proportion of the patients (4/11%) compared with CyP-treated group (19/53%), p=0,0000.

Parameters	Group A	Group B
Activity Index 1 *M ± SD*	2.8±1.4*	3.2±1.9*
Activity Index 2 *M ± SD*	1.4±1.2*	1.6±1.3*
Skin count 1 *M ± SD*	11.5±9.5 *	11.0±9.3 *
Skin count 2 *M ± SD*	8.2±6.2 *	7.2±5.6 *
FVC 1 *M ± SD*	78.7±20.0 *	76±20.3*
FVC 2 *M ± SD*	84.2±20.0*	82.7±22.5*
Δ FVC %	5.3 [0.8; 11.1]	5.7 [0; 11.2]
FVC increment by ≥10%, n/%	9/26	14/31
FVC decrement by ≥10% n/%	2/5.7	2/4.4
Dose of glucocorticoids 1, mg	11.6±4.7	10.4±4.6
Dose of glucocorticoids 2, mg	15.3±8.5*	10.9±5.4*

Notes: in Parameters column 1 = before treatment, 2 = after treatment; M ± SD = mean value and standard deviation; * = significant difference between the vales measured before and after the treatment

Conclusion: Both agents effectively alleviated skin induration and EScSG, and significantly improved FVC. However, the glucocorticoids doses that needed to be used during anti-B cell therapy were significantly lower compared to CyP treated patients. The RTM single therapy was better tolerated compared to CyP. The study findings substantiate potential use a RTM single therapy both as a first-line agent for ILD treatment in the patients with SSc, and in the event of CyP inefficacy of poor tolerability.
Disclosure of Interests: None declared
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AB0584

DOES ANTI-ACID TREATMENT INFLUENCE DISEASE PROGRESSION IN SYSTEMIC SCLEROSIS INTERSTITIAL LUNG DISEASE (SSC-ILD)? DATA FROM THE GERMAN SSC-NETWORK

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Background: Gastroesophageal reflux (GER) is common in SSc and thus treatment with anti-acid therapy (AAT) is frequent. An association between GER and the development / progression of SSc-ILD has been hypothesized. However, outcomes of AAT on disease progression in SSc-ILD has only sparsely been studied.
Objectives:
Methods: The German Network for Systemic Scleroderma (DNSS), which includes SSc pts. prospectively, was analyzed for SSc-ILD. Those without progression at ILD 1st diagnosis were categorized in AAT vs. no-AAT users and disease outcome was assessed.
Results: SSc-ILD was reported in 1165 (28.2%) out of 4131 pts. 712 of SSc-ILD pts had no disease progression at ILD 1st diagnosis. 567 used AAT while 145 did not. Baseline characteristics were similar between groups with regards to age (mean 54.7 years), BMI, time since SSc diagnosis and immunosuppressant use. Significant differences in no-AAT vs. AAT were found for gender (male 18% vs. 25%, p=0.05), SSc subtype (p=0.002, diffuse more common in AAT), lung function (DLCO 66% vs. 58%, p=0.001; FVC 86% vs. 77%, p=0.001), mRSS (8 vs. 11.5, p<0.01), esophageal involvement (32% vs. 56%, p<0.01) and steroid use (30% vs. 43%, p=0.005). While mortality did not differ between groups (3.9%, p= 0.59), disease progression was more common in the AAT group than in no-AAT users (24.5% vs. 13%, p=0.03). Furthermore, there was a significant difference in decline of FVC≥10% with 30% in the AAT compared to 14% in no-AAT (p=0.018); a decline in DLCO≥15% was more common in the AAT group by trend (23% vs. 14%, p=0.087).
Conclusion: While results may have partially been biased by differences in baseline characteristics, this current analysis disfavors the approach of AAT use for SSc-ILD.
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AB0585 SINGLE CENTER EXPERIENCE OF CLINICAL PROFILE OF INFLAMMATORY MYOSITIS FROM INDIA

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Background: Clinical profile of myositis differs in respect of the setting. We present a single center experience from a community based referral center
Objectives: STUDY CLINICAL PROFILE OF INFLAMMATORY MYOSITIS (IM)
Methods: We present data from 114 patients of connective tissue disorders (CTD) with dominant Inflammatory Myopathy(IM) evaluated in CRD where we have patient database since 1996. Standard investigations & ELISA, immunoblot and nephlometry to assay autoantibodies (AAb) were done. Data extraction done from 2005-2017
Results: 36 and 28 patients respectively diagnosed as dominant idiopathic dematomyositis (DM) and polymyositis (PM); remaining 41 patients showed overlap (OCTD). Mean onset age range 33-40 years in each subset with women dominance. Exclusive proximal muscle involvement seen 64% DM, 67% PM and 43% OCTD. 12 of OCTD showed classical DM rash. Raynauds's phenomenon was seen in 38% (25% DM, 10% PM, 65% OCTD). 83% OCTD showed inflammatory polyarthritis; DM 29% and PM 42%. Two patients DM also diagnosed malignancy (ovarian CA). 25% DM, nil PM and 31.7% OCTD showed CT based lung findings. Mean creatinine phosphokinase at diagnosis were DM 1580, PM 2239 & OCTD 830. EMG required in 48 patients confirmed diagnosis (DM 17, PM 16 and OCTD 15). Seven patients with diagnostic dilemma/ poor therapy response required muscle histopathology confirmation. 59% DM,69% PM and 84% OCTD were seropositive ANA positive in 71%(ENA profile available for most). All Patients received steroids. Methotrexate prescribed in (92%), Azthioprine in (28%), hydroxychloroquine in (88%) with majority showing good response. Mycophenolate prescribed in (6%) for aggressive disease, IVIG in 2 patients for acute IIM with interstitial pneumonitis. Rituximab was prescribed in 4 resistant cases; all responding favourably. Mortality data of 4 patients(severe myositis(1), interstitial pneumonitis(1), ovarian cancer(1), septic shock(1)) was available. Antesynthatase syndrome noted in 9 patients.
Conclusion: Overlap CTD with myositis seems more common profile than DM or PM. Response to therapy was satisfactory with steroids and methotrexate being the mainstay. Rituximab is a promising biological agent in chronic resistant cases.
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Disclosure of Interests: : NACHIKET KULKARNI Speakers bureau: PFIZER, NOVARTIS, YANSEN, Anuradha Venugopalan: None declared, MANJIT SALUJA: None declared, Arvind Chopra Grant/research support from: Zydus Pharamceutical Ltd India
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AB0587 IMMUNOMODULATORY COMBINATION THERAPIES IN PATIENTS WITH DERMATOMYOSITIS / POLYMYOSITIS: A RETROSPECTIVE CROSS-SECTIONAL STUDY

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Background: Dermatomyositis (DM)/Polymyositis(PM) is an autoimmune disease that typically involve the striated muscle with a variable involvement of the skin and other organs [1]. Lymphocyte subsets disorders may contribute to the pathogenesis of DM/PM. It has been discovered that immunomodulatory drugs such as low-dose interleukin (IL)–2, rapamycin can help to regulate the lymphocyte subsets and control the disease and improve the prognosis [2-4].
Objectives: To investigate the levels of peripheral lymphocyte and CD4+T subsets of DM/PM patients and further to observe the regulatory effect of modulatory therapy on these cells in PM/DM at a relative large-sample size.
Methods: Total 450 patients with PM/DM and 206 healthy controls (HCs) were enrolled in this study. Among these participations, 320 patients received immunomodulatory combination therapies (immunomodulatory drugs include low-dose interleukin-2, rapamycin, metformin, retinoic acid etc). The absolute numbers of T, B, NK, CD4+T, CD8+T, Th1, Th2, Th17 and Tregs in peripheral blood of these individuals were detected by flow cytometry combined with standard absolute counting beads before and after the treatment.
Results: Patients with DM/PM had lower levels of total T, CD4+T, CD8+T, Th2, Th17, NK, Th1 and Tregs compared with those of HCs ($P < 0.05$). After immunomodulatory combination treatments, there was a dramatically increases various peripheral lymphocyte subsets such as T, B, CD4+T, CD8+T, NK, Th1, Th17 and Tregs ($P < 0.05$). Moreover, the increase in Tregs was much more than that in effector T cells (Teffs), resulting a rebalance of immune systems.
Conclusion: The unbalance of lymphocyte cells should contribute to the pathogenesis of DM/PM patients. Immunomodulatory combination therapies could promote the proliferation and functional recovery of Tregs in patients and might help to alleviate disease activity.
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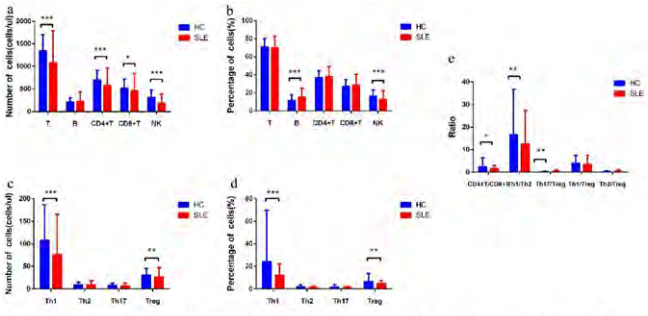


Figure 1: Comparison of lymphocyte subsets in peripheral blood between healthy controls(HC) (n=206) and untreated DM/PM patients (n=450). All the lymphocytes subsets were analyzed by detected by flow cytometry combined with standard absolute counting beads. Data were presented as: mean±SD and statistical analysis was determined by two-tailed unpaired t-test. Patients had lower levels of T, NK, CD4+T , CD8+T ,Th1 and Tregs, decreased percentages of NK, Th1 and Tregs, and higher ratios of Th17/Tregs and lowerer ratios of CD4+T / CD8+T, Th1/Th2 in DM/PM compared with those of healthy controls. *P < 0.05, **P < 0.01, ***P < 0.001.

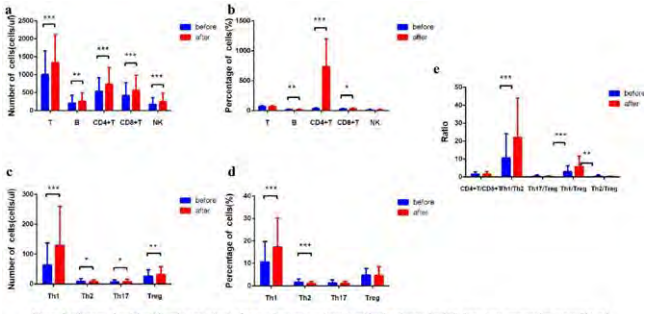


Figure 2: Changes of peripheral lymphocyte subsets after new immune regulatory combination therapy (n=320). Data were presented as mean±SD and statistical analysis was determined by two-tailed paired t-test. Absolute number of T, B,NK, CD4+T, CD8+T, Th1,Th17 and Tregs were significantly increased. The proportion of B, CD4+T, CD8+T and Th1 were also increased, the ratio of Th1/Th2 and Th1/Tregs were increased while the ratio of Th2/Tregs had a tendency to increase after new immunoregulatory combination therapies. *P < 0.05, **P < 0.01, ***P < 0.001.

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Disclosure of Interests: None declared
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AB0588

INFECTION AGGRAVATED DECREASE OF THE LEVEL OF TH17 AND TREG CELLS AND LOW-DOSE IL-2 REBALANCED TH17/TREG IN THE PERIPHERAL BLOOD OF PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHY

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Background: Idiopathic inflammatory myopathies (IIM) are featured by a series of clinical presentation such as proximal muscle weakness, increased serum levels of creatine kinase and other muscle enzymes and involvement of other organs and systems[1, 2], which results in high morbidity and early mortality[3]. We have known the changes of the level of Th17 and Treg cells in IIM in previous studies[4-6]. However, whether infection affects lymphocyte subsets or not and whether the effect of low-dose interleukin-2 (IL-2) can be influenced by the use of immunosuppressants or not are still unclear.

Objectives: The study aimed to explore the changes of lymphocyte subsets in patients of IIM with or without important organ infection, and the restoration of Th17/Treg after receiving low-dose IL-2.

Methods: A total of 118 IIM patients were enrolled and classified into infection group and non-infection group based on the important organ infection. Of them, 48 cases were treated with low dose IL-2 ($5.0*10^5$ IU for 5 days). The absolute number of peripheral total T, B, $CD4^+$ T, $CD8^+$ T, NK, Th1, Th2, Th17 and Treg cell subsets were analyzed by flow cytometry combined with absolute counting beads. Clinical data, laboratory examinations and the levels of peripheral lymphocyte subsets were analyzed retrospectively.

Results: In these patients, especially in the infection group, the absolute number of T, $CD4^+$ T, $CD8^+$ T, NK, Th1, Th2, Th17 and Treg cells were significantly decreased as compared with that in the healthy controls, which were significantly increased by low dose IL-2 (especially Treg cells) treatment. The levels of ESR, LDH and HBDH and the ratio of Th17/Treg were significantly lower than those before IL-2 treatment (Z=-2.237, -2.083, -2.140, -3.663, P=0.025, 0.037, 0.032, 0.000). The 48 cases who received IL-2 treatment were divided into 2 groups according to whether they used immunosuppressants. There was no significant difference in the absolute number of T, B, $CD4^+$ T, $CD8^+$ T, Th1, Th2, Th17 and Treg cells, the proportion of Th17 and Treg cells and the ratio of Th17/Treg between the 2 groups (P>0.05).

Conclusion: Global decrease in lymphocyte subsets was found in IIM patients, especially those who had important organ infection. A significant re-balance of Th17/Treg was observed after receiving treatment with low-dose IL-2. Furthermore, the restoration of lymphocyte subsets showed similar degree after treatment with or without immunosuppressants. Low-dose IL-2 may become a potential therapy for IIM patients. The mechanism of lymphocyte decrease in IIM is required further to study.

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AB0589

THE IMPORTANCE OF A SYSTEMIC SCLEROSIS CLINIC IN A TERTIARY REFERRAL CENTER – A PORTUGUESE EXPERIENCE

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Background: Systemic sclerosis (SSc) is a rare systemic rheumatic disease (SRD) characterized by small vessel inflammation and fibrosis of skin and internal organs. Pulmonary and cardiac involvement contribute to both morbidity and mortality associated with the disease. A multidisciplinary approach with strict monitoring is therefore key to attain clinical success.

Objectives: To describe the organization and patient pathways of our SSc outpatient clinic.

Methods: Observational study using data extracted from Reuma.pt/SSc (a subset of the Rheumatic Diseases Portuguese Register). Data extracted included demographic variables and clinical and immunological manifestations. The disease was classified according to the 2013 ACR/EULAR criteria. Our SSc clinic is managed by two dedicated Rheumatologists and up to two Rheumatology residents on a weekly basis, but it is a dynamic multidisciplinary clinic where various medical specialties collaborate closely. There are two associated subspecialty clinics (pulmonary hypertension and pulmonary fibrosis) where the Rheumatologists engage with pneumologists and cardiologists, allowing greater collaboration in the management of these patients. Patients' data is systematically registered in Reuma.pt/SSc as a part of the routine activity of this clinic, contributing to real-world data on SSc.

Results: A total of 220 patients were registered between July 2011 and June 2019. 196 (89.1%) were female, with a mean age of 58.9±14 years and a mean disease duration of 14.6±9 years. Ninety-seven patients (44.1%) had limited cutaneous SSc, 52 (23.6%) had diffuse cutaneous SSc, 35 (15.9%) had overlap SSc, 24 (10.9%) had preclinical SSc and 12 (5.4%) had SSc sine scleroderma. Raynaud phenomenon was present in 92% of the SSc patients and 40% had a history of digital ulcers. Gastrointestinal manifestations included esophageal dismotility in 39.5% of patients, gastric disease in 24.4% and intestinal involvement in 15.5%. Pulmonary involvement was found in 47.6% of SSc patients, heart disease in 43.6% and kidney involvement in only two patients. Antinuclear antibodies were positive in 92.2% of the patients, anti-centromere in 44.1%, anti-topoisomerase I antibodies in 39.1%, anti-U1RNP in 4.5% and only three patients had anti-PM-Scl and one had anti-RNA polymerase III. 31 patients were lost to follow-up and 32 died. 18 patients are currently being followed up in the pulmonary hypertension clinic and seven in the pulmonary fibrosis clinic.

Conclusion: The implementation of a standardized approach with regular multidisciplinary work has proven very helpful in evaluating patients with SSc. The continuous registry of patients in Reuma.pt/SSc has been essential for patient care, research and healthcare planning.

Disclosure of Interests: None declared

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AB0590

CLINICAL AND DEMOGRAPHIC CHARACTERISTICS OF PATIENTS WITH ANTISYNTHETASE AUTOANTIBODIES: DATA FROM A PORTUGUESE TERTIARY OUTPATIENT CLINIC

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Background: Antisynthetase syndrome (AS) may have different clinical phenotypes and outcomes associated with different anti-aminoacyl RNA-synthetase (anti-ARS). Patients may also present with incomplete/early phenotypes that do not fulfil the classification criteria.

Objectives: To evaluate the clinical and demographic characteristics of patients positive for anti-ARS in our Myositis clinic.

Methods: Observational study using data from the Portuguese Rheumatic Diseases Register (Reuma.pt/Myositis protocol). Data extracted included demographic variables, clinical features and immunological expression of the disease.

Results: 17 patients were identified. All met the criteria for AS according to Connors criteria, while 3 did not met according to the Solomon criteria. Mean age at diagnosis was 60.1 years (26 - 80) and 76.5% were female. Mean follow-up time was 2.8 (0.5-9) years. Only 3 patients had history of smoking in the past. The autoantibodies expressed were anti-Jo1 (n=12), anti-PL12 (n=2), anti-OJ (n=2) and anti-PL7 (n=1). 4 patients positive for anti-Jo-1 also expressed anti-Ro52. The clinical information and treatment are described in table 1. One patient presented as a paraneoplastic syndrome associated with anti-Jo-1.

Table 1. Demographic and clinic characteristics of our cohort. AZA – azathioprine; CYC – Cyclophosphamide; DM – dermatomyositis; GS – Gottron's sign; ILD – Interstitial lung disease; PM – Polymyositis; NSIP - Nonspecific interstitial pneumonia; MH – mechanic hands; MMF - Mycophenolate mofetil; MTX – Methotrexate; PDN – prednisolone; RP – Raynaud phenomenon; RTX – Rituximab; UIP - Usual interstitial pneumonia; Y – yes; N – no. Connors criteria – anti-ARS plus one or more of RP, MH, arthritis, ILD, fever. Solomon criteria – anti-ARS plus 2 major criteria or 1 major and 2 minor criteria. *induction therapy.

Case	Serology	Major criteria (ILD [NSIP/UIP/ non-specific] or PM/ DM)	Minor criteria (Arthritis, MH, RP)	Other manifestations	Connors (2010)/ Solomon (2011) criteria	PDN	DMARDcs (MTX/MMF/ AZA)	CYC/ RTX
1	Jo1	PM	MH, arthritis	GS	Y/Y	Y	MMF	-
2	Jo1	NSIP	RP, MH	Asthenia	Y/Y	Y	AZA	-
3	Jo1	NSIP	MH, arthritis	Calcinosis, asthenia	Y/Y	Y	AZA	-
4	Jo1	NSIP; DM	-	GS	Y/Y	Y	-	-
5	Jo1/Ro52	PM	MH, arthritis	GS, asthenia	Y/Y	Y	MTX	-
6	Jo1	UIP	RP, arthritis	Asthenia	Y/Y	Y	-	RTX
7	Jo1/Ro52	NSIP; PM	arthritis	-	Y/Y	Y	MMF	CYC*
8	Jo1	NSIP; PM	-	-	Y/Y	Y	MMF	-
9	Jo1/Ro52	NSIP; PM	-	-	Y/Y	Y	AZA	-
10	PL7	-	RP, arthritis, MH	Dysphagia	Y/N	Y	-	-
11	Jo1	-	RP	Asthenia	Y/N	-	-	-
12	Jo1/Ro52	PM	MH, arthritis	GS, asthenia	Y/Y	Y	MMF	-
13	PL12	PM	RP, arthritis	GS, asthenia	Y/Y	Y	MMF	-
14	Jo1	UIP	RP, arthritis	Weight loss, asthenia	Y/Y	Y	-	RTX
15	OJ	Non-specific pattern	-	-	Y/N	Y	MMF	-
16	OJ	NSIP	-	-	Y/Y	Y	-	-
17	PL12	PM	RP, MH	-	Y/Y	-	-	-

Conclusion: The most frequent autoantibody was anti-Jo-1, which is consistent with the literature. Interestingly, patients with anti-PL, usually described as having severe lung disease, in our series do not have it. Additionally, we found a trend for a younger age at diagnosis in Jo1 positive patients and remarkably more than half of these patients have been diagnosed with ILD, being the NSIP pattern the most frequently reported.

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AB0591 ANALYSIS OF A COHORT OF PATIENTS WITH SYSTEMIC SCLEROSIS AND INTERSTITIAL LUNG DISEASE

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Background: Interstitial lung disease (ILD) is a common manifestation of systemic sclerosis that is associated with early mortality. The development or progression of ILD can occur at any time, so patients should be monitored regularly, particularly in the first years after diagnosis.

Treatment should be considered when the disease is clinically significant, particularly when there is evidence of progression based on a decrease in lung function, progression of fibrosis on the HRCT or worsening of respiratory symptoms.

Objectives: -To relate the type of systemic sclerosis (SS) with pulmonary involvement with the radiological pattern.

-To study if there is a relationship between the antibodies and the aforementioned affectation.

Methods: Retrospective descriptive study of patients treated in our Hospital (2009-2019) by the Rheumatology and Internal Medicine department diagnosed with systemic sclerosis and interstitial lung disease.

The data were obtained through the review of medical records.

We have included data from patients who have a diagnosis of limited or diffuse systemic sclerosis or overlap with interstitial lung involvement.

Results: Of the 213 patients with systemic sclerosis in our database 43 had interstitial lung involvement (20.2%). 79% of the patients with ILD (34) had a non-specific interstitial pneumonia type (NSIP) radiological pattern and 21% of the patients (9) had a pattern of usual interstitial pneumonia (UIP)

Among the patients with ILD with a NSIP -type radiological pattern, 19 patients were diagnosed with diffuse SS, 9 patients with overlap syndrome and 6 with limited SS. Of the patients with ILD with radiological pattern type UIP, 5 patients were diagnosed with diffuse SS, 3 patients with overlap syndrome and 1 patient was diagnosed with limited SS.

TABLE 1. RELATIONSHIP BETWEEN SS TYPE AND RADIOLOGICAL PATTERN

	NSIP	UIP
LIMITED SS	6 (17.6%)	1 (11.1%)
DIFFUSE SS	19 (55.8%)	5 (55.5%)
OVERLAP	9 (26.4%)	3 (33.3%)

Among the patients with the NSIP pattern, 17 had positive SCL70 antibody, 3 positive ANA patients and 1 patient had positive anti-centromere antibody.

Of the patients with UIP type interstitial pneumopathy, 8 patients had anti-SCL70 antibody, 3 patients ANA positive antibody and 2 patients anti-centromere positive antibody.

TABLE 2. RELATIONSHIP BETWEEN TYPE OF AB AND RADIOLOGICAL PATTERN

	NSIP	UIP
Anti SCL70	17	8
Anti centromere	1	2
ANA	3	3

Regarding treatment, 21 patients were taking Mycophenolate, 16 patients required cyclophosphamide and 6 patients rituximab.

No patient in our cohort died due to interstitial lung disease.

Conclusion: The data obtained are consistent with what is collected in the medical literature.

The subtype of scleroderma most related to ILD was diffuse SS. The most frequent antibody was anti-SCL 70.

Regarding the treatment,the most used in ILD in our center was the mycophenolate.

From our sample analyzed when applying the likelihood ratio (RV) a value of 47,186 is obtained, which has an associated probability of 0, which is less than 0.05, leads to reject the null hypothesis (there is no dependence between antibodies and type of radiological pattern of ILD in SS), concluding that there is dependence between the analyzed variables.

After this analysis, we can conclude that in our sample there is a relationship between the type of interstitial pneumopathy pattern and the antibody present in patients with SS.

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AB0592 NAILFOLD CAPILLARY ABNORMALITIES PREDICT INTERSTITIAL LUNG DISEASE (ILD) COMPLICATION IN SYSTEMIC SCLEROSIS PATIENTS

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Background: Systemic sclerosis (SSc) have various organ involvements including pulmonary hypertension (PH), digital ulcers (DU), and interstitial lung disease (ILD). On the other hand, Nailfold capillary (NFC) abnormalities (enlarged/giant capillaries, fresh or old hemorrhages, avascular areas, ramified/bushy capillaries) detected by capillaroscopy are included in ACR/EULAR classification criteria for SSc as one of important findings. In addition, many studies have reported the relationship between NFC abnormalities and organ involvements (DU, PH) [1][2]. However, there are a few reports about the relationship between NFC abnormalities and ILD.

Objectives: We clarify the association with NFC abnormalities and ILD in SSc patients.

Methods: We enrolled SSc patients without PH from January 2016 to December 2019 in our institution. SSc patients were diagnosed according to EULAR classification criteria in 2013. ILD was detected by chest CT scans. We assessed severity of ILD with pulmonary function tests (PFT). Abnormal PFT was defined as vital capacity (%VC) or diffusion capacity (DLCO) < 70%. NFC abnormalities were detected with "OptiPiX capillaroscopy Clinic 1.7.x" and the number of capillaries was measured per 1mm in 2nd to 5th fingers of both hand. We defined enlarged and giant capillaries as >30 µm and >50 µm, respectively.
Results: We enrolled 59 SSc patients (54 females, 5 males). Mean age is 65.0 ± 8.0 years. Thirty-one patients (52.5%) were complicated with ILD. Mean capillary counts are 6.6/mm. The number of patients with each NFC abnormalities (enlarged capillaries, giant capillaries, microhemorrhages, ramified, avascular areas) are 42, 32, 48, 38, and 33 cases, respectively. Two cases did not have NFC abnormalities. SSc patients with giant capillaries had fewer ILD complications (p <0.05, odds ratio 0.183 [0.059 – 0.57]). Other NFC abnormalities were not associated with ILD in SSc patients. We inspected %VC of 23 patients and DLCO of 20 patients with ILD. Eleven patients had abnormal PFT (5 patients had abnormal %VC and 9 patients had abnormal DLCO). Most of them had not enlarged capillaries than patient with normal PFT (odds ratio 0.11 [0.016 – 0.81]). Other NFC abnormalities including giant capillaries were not associated with abnormal PFT.
Conclusion: We investigated the relationship between NFC abnormalities and ILD conplications in SSc patients. NFC abnormalities are associated with ILD complicacion and severity of ILD. It was suggested that no giant capillary in SSc patients may predict ILD complication. Moreover, no enlarged capillary may predict the severe ILD.
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	With ILD(n=31)	Without ILD(n=28)	P
enlarged capillaries	19	23	0.08
giant capillaries	11	21	**0.002**
microhemorrhage	25	23	0.88
ramified	21	17	0.57
avascular areas	19	14	0.38

Table1. each NFC abnormalities in SSc patients

	Patients had normal PFT(n=12)	Patients had abnormal PFT(n=11)	P
enlarged capillaries	10	4	0.02
giant capillaries	5	3	0.47
microhemorrhage	9	9	0.69
ramified	9	8	0.90
avascular areas	10	6	0.13

Table2. each NFC abnormalities in SSc patients with ILD

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AB0593 DOES REALLY EXIST MIXED CONNECTIVE TISSUE DISEASE?

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Background: Currently, most authors accept that mixed connective tissue disease (MCTD) is an independent entity, although there are those who argue that it is actually an overlap syndrome or an undifferentiated early phase of another systemic autoimmune disease (SAD).
Objectives: To analyze the long term evolution of a serie of patients with MCTD.
Methods: Observational, retrospective and multicenter study in patients with MCTD (*diagnostic criteria of Alarcón-Segovia et al),* followed for a minimun of 2 years.
Results: Fifty-five patients (49 women) with a median age at diagnosis of 38±14 years and with a follow up time (median) of 101 months (range, 24-237 months with a total of 501.2 pacients-*year*) were identified.
At the end of the follow-up period, only 27% (15/55) of the patients kept on fulfilling MCTD criteria. In the remaining 73% (40), 40% (22) had been differentiated to systemic lupus erythematosus (SLE), 13% (7) to systemic sclerosis (SSc) and 20% (11) developed an overlap syndrome [SSc+SLE in 8 cases and SSc+rheumatoid arthritis (AR) in 3]. In 8% of these patients, a secondary Sjögren's syndrome was diagnosed during the follow-up period. The average score in patients who met the EULAR/ACR 2013 criteria for SSc was 11 (minimum 9 - maximum 16) and the average time elapsed from the diagnosis of MCTD to meet SSc criteria was 64.4 months (interquartile range [IQR] 25-75%: 10-127 months).
Applying the 2012 SLICC criteria, only 24 patients of those initially diagnosed as MCTD ended up meeting SLE criteria. The average score in these patients was 5.6 (4-9) and the average time elapsed from the diagnosis of MCTD unltil fulfilling the SLICC criteria was 39 months (IQR 25-75%: 6-28). When we apply the new ACR/EULAR 2019 criteria, the percentage of patients who meet SLE criteria increased to 30%, with an average score of 17.3 (10-38). The average time elapsed since the diagnosis of MCTD until meeting the new SLE criteria was reduced to 17 months (IQR 25-75: 0-10).
In the multivariate study, the presence of sclerodactyly (OR: 2.91; IC 95% 1.90 - 4.1, p= 0.001) and esophageal involvement (OR: 2.05; IC 95% 1.14–3.66, p=0.016) were associated with the evolution to SSc. Any predictor of evolution to SLE was identified.
Conclusion: Only slightly more than a quarter of patients initially diagnosed as MCTD maintain this diagnosis during the follow-up. The majority, ended up evolving towards to another SAD, fundamentally SLE and SSc. The new ACR/EULAR 2019 criteria seems to be more sensitive than the SLICC 2012 criteria for diagnose SLE in these patients.
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AB0594 EFFECTIVENESS OF RITUXIMAB IN CSDMARDS-RESISTANT ACTIVE MIXED CONNECTIVE TISSUE DISEASE

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Background:
Objectives: To evaluate rituximab (RTX) effectiveness and safety in treating patients with refractory mixed connective tissue disease (MCTD).
Methods: Open observational study including patients with refractory MCTD (active disease despite treatment with glucocorticoids and csDMARDs) from two third-level hospitals who had been treated with RTX (off-label use) from January 2001 to December 2019.
Results: Thirteen patients (all women) were included, with a mean age of 32 years (SD: 10, range 17-50) and a median time of evolution of the disease of 55 months (SD: 34.3; range 5-98 months). The main indication for initiating treatment with RTX was refractory arthritis (100%), most of the times accompanied by other features of the disease including shrinking lung syndrome (2), fibrosing progressive non-specific interstitial pneumonia (FP-NSIP) (1), recurrent serositis (2), glomerulonephritis (GMN) (2), lymphadenitis (1) and immune thrombocytopenic purpura (ITP) (1). All patients were treated with RTX at rheumatoid arthritis dosage while the baseline immunosuppressive treatment (methotrexate, azathioprine, mycophenolate, leflunomide or tacrolimus) remained unchanged. Hydroxychloroquine was also associated in 8 of the patients. The follow-up time (median) after starting RTX was 118 months (range, 65-177 months, with a total of 132.6 patient-years of follow-up) and the mean number of cycles of treatment was 4.2 (range, 1-15), with a variable interval (from 6 to 12 months). After the first RTX cycle, a partial or complete response was achieved in 92% of the patients. A significant improvement in the mean DAS28-ESR was observed (initial: 4.56 ± 1.6 / final: 2.21 ± 0.85; p=0.008). In all but one patient, who had previously failed to 2 anti-TNFα

DAS28-ESR clinical remission or low activity was achieved, generally from week 16 to 20, although relapses were frequent and all cases need retreatment after 6-9 months. In 4 patients, RTX retreatment dosage was optimized to 1 g/cycle. The 3 patients with pulmonary involvement showed stabilization (2 cases) or improvement (1) of the lung function *(as defined by the American Thoracic Society)*. In patients with GMN, renal response to RTX treatment was complete in a patient and partial in the other. The patient with ITP entered remission after the first RTX cycle and no more cycles were needed. Response in patients with serositis and lymphadenitis was also complete and maintained. Moreover, the glucocorticoid doses were reduced to less than half of the initial dose in all cases. At the end of the follow-up, 7 out of the 13 patients (54%) were still being treated with RTX. For the remaining 6 patients, RTX was withdrawn because of primary failure (1), recurrent bacterial infections (2), gestational desire (2) sustained remission (1).

Conclusion: According to our preliminary results, RTX seems to be effective and relatively safe in patients with csDMARDs-resistant active MCTD.

Disclosure of Interests: L Montolio-Chiva: None declared, J. Narváez: None declared, Juanjo J Alegre-Sancho Consultant of: UCB, Roche, Sanofi, Boehringer, Celltrion, Paid instructor for: GSK, Speakers bureau: MSD, GSK, Lilly, Sanofi, Roche, UCB, Actelion, Pfizer, Abbvie, Novartis, J Lluch Pons: None declared, Ana V Orenes Vera: None declared, I Vázquez-Gómez: None declared, Maribel Mora: None declared, Xavier González: None declared, Carla Marco: None declared, Jesús Rodriguez: None declared, Montserrat Romera: None declared, Joan Miquel Nolla: None declared

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AB0595 EFFECTIVENESS OF TOPICAL SODIUM TIOSULFATE FOR THE TREATMENT OF CALCINOSIS-ASSOCIATED CUTANEOUS ULCERS IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Treatment of calcinosis associated with systemic sclerosis (SSc) mainly involves the use of systemic therapies, which often have limited efficacy. However, little attention has been paid to local treatment, which is especially useful when associated with skin ulcers.

Objectives: To show our experience with topical sodium thiosulfate (TST) for the treatment of calcinosis-associated cutaneous ulcers in patients with SSc.

Methods: Descriptive analysis of a case series of patients with SSc and calcinosis-associated skin ulcers treated with TST. Wound management procedure: wounds and perilesional skin cleaning and disinfection is performed and, if needed, additional debridement. TST is compounded at 25% as w/o emulsion, for extensive calcinosis, or as beeler-base or cold-cream ointment, for limited calcinosis. Wounds are then covered with a polymeric foam dressing. This cure in moist healing environment shows some advantages over the dry cure (exudate control without damaging the periulceral skin, protection against contamination, and reduction of the needed cures, healing time and pain).

Results: Nine patients (7 women) with calcinosis-associated skin ulcers and SSc were included: 2 patients with diffuse SSc (DcSSc), 6 with limited SSc (LcSSc) and 1 with overlap syndrome. Median age was 60 years (IQR 20). 6 patients had localized wounds and 3 had extensive involvement and/or tumoral calcinosis which had been refractory to systemic treatment with diltiazem, colchicine, zoledronate, rituximab, and/or acenocoumarol and had suffered recurrent superinfections. Follow-up results of more than 3 months are available for 8 patients, who have been on TST a median time of 9 months (IQR 8.25). They have shown clinical improvement (disappearing of many calcinosis foci and partial or complete healing of the ulcers together with an improvement in pain, function, quality of life and satisfaction of the patients). Radiological improvement was also observed in 1 case. No TST related adverse effect has been detected, except for slight maceration of the wound edges due to the ointment preparation, which was resolved by protecting these with zinc oxide cream

Conclusion: In our experience, treatment with TST for calcinosis-associated skin ulcers in patients with SSc is an effective, safe and easily implementable therapeutic alternative in clinical practice.

Disclosure of Interests: Inmaculada Torner Hernández: None declared, A Sendra-García: None declared, V Núñez-Monje: None declared, L Montolio-Chiva: None declared, Ana V Orenes Vera: None declared, I Vázquez-Gómez: None declared, Eduardo Flores Fernandez: None declared, À Martínez-Ferrer: None declared, Elia Valls-Pascual Grant/research support from: Roche, Novartis, and AbbVie, Speakers bureau: AbbVie, Lilly, Pfizer, MSD, Novartis, Janssen, Bristol Myers Squibb, UCB Pharma, D Ybáñez-García Speakers bureau: Lilly, Roche, Sanofi, Juanjo J Alegre-Sancho Consultant of: UCB, Roche, Sanofi, Boehringer, Celltrion, Paid instructor for: GSK, Speakers bureau: MSD, GSK, Lilly, Sanofi, Roche, UCB, Actelion, Pfizer, Abbvie, Novartis

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AB0596 PREDICTORS, LONG TERM CLINICAL AND TREATMENT OUTCOMES IN SOUTH ASIAN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOSITIS: A SINGLE CENTER STUDY

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Background: Idiopathic inflammatory myositis (IIM) are a heterogeneous group of immune-mediated disorders with varied presentations and multiple organ involvement. Data on long term outcome among South Asian patients with IIM is sparse.

Objectives: To study the long term clinical outcome, treatment responses and factors predicting outcome among adult patients with IIM

Methods: Patients diagnosed as 'Idiopathic Inflammatory Myositis' under the department of Clinical Immunology and Rheumatology at CMC, Vellore, India were screened retrospectively. Patients aged 18 years and above, satisfying Bohan and Peter criteria, having follow up of one year or more with atleast two outpatient or inpatient visits between January 2010 and April 2019 were included in this study. Those patients with connective tissue disease associated myositis were not included. Details on muscle weakness, extramuscular involvement, muscle enzymes and treatment administered were recorded at baseline, 3, 6, 12, 18, 24 months and yearly thereafter. After assessing their cumulative response, categorization of patients into complete and partial responders was done. Complete responders were defined as patients with persistent muscle power of more than 4/5 and/or MMT 8 more than 76/80, complete resolution of skin, articular and lung involvement (if any) as well as muscle enzymes less than twice the upper limit of normal without any documented flares during the entire follow up period. Patients not satisfying the said criterias were grouped as Partial responders. Disease free survival duration was also analyzed.

Results: Out of 310 patients of IIM identified, 187 (60.3%) patients satisfied the inclusion criteria. Women were 2.2 times more than men and mean age at symptom onset was 35.7±12.6 years. Dermatomyositis was the predominant myositis subtype seen. All patients were put on steroids with the mean dose being 45.9 ± 18.6 mg/day. At baseline, the key immunosuppressants used were methotrexate in 44.9% and mycophenolate in 37.6% patients. The median follow up duration was 48 (25-80) months. An associated malignancy was diagnosed in 3.2% after a median duration of 24.5 months. Five patients expired after a median duration of 80 months from diagnosis. Normal muscle power was attained in 76.1% patients and 88.6% were vocational by the last follow up visit. Steroids were discontinued in 56.7% patients after a median duration of 24 months (p=0.0002). Discontinuation of the immunosuppressant was feasible in 10.2% patients after a median duration of 44 months. Assessment of

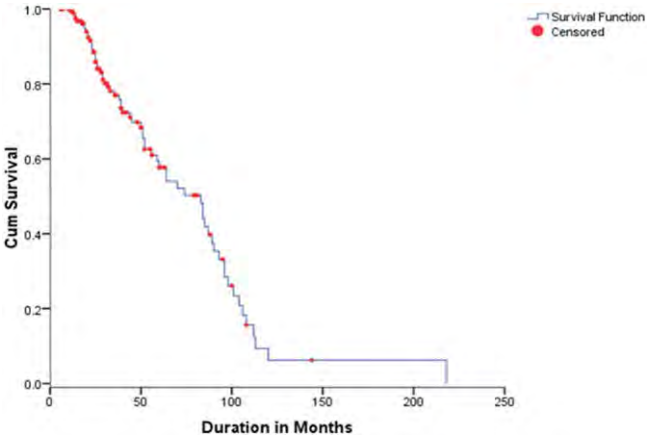


Figure 1. Disease free survival plot of patients with IIM

the cumulative responses revealed a relapsing and remitting course in 45.9%. Outcome predictors in univariate analysis were Jo-1 status, presence of arthritis, interstitial lung disease and pericardial effusion at baseline. On multivariate analysis, absence of pericardial effusion (p=0.011) and interstitial lung disease (p=0.067) at baseline were found to be predictors of complete response. Disease free survival probability estimated at 5 years and 10 years was 91.6% and 72.4% respectively. Estimating the probability gender wise, males achieved disease free status earlier than females.

Conclusion: A favorable clinical and functional outcome was seen in a significant proportion of these patients with IIM on long term follow up. Pericardial effusion and ILD were identified as predictors of poor clinical outcome.

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AB0597 PULMONARY FUNCTION IN PATIENTS DIAGNOSED OF EARLY SYSTEMIC SCLEROSIS: A NEW TOOL FOR SYSTEMIC SCLEROSIS CLASIFFICATION?

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Background: Interstitial lung disease (ILD) is a frequent complication of systemic sclerosis (SSc) and is often progressive and has a poor prognosis. A restrictive ventilatory defect could suggest ILD either alone or in combination with pulmonary arterial hypertension.

Nowadays, Early-SSc is well defined as preliminary stage of SSc. Patients who meet criteria for Early-SSc could benefit from an early diagnosis of pulmonary involvement.

Objectives: Our aim was to assess the pulmonary function in patients diagnosed of Early SSc.

Methods: Retrospective observational study of a wide and unselected series of patients diagnosed as Early-SSc from a single university hospital from 2012 to 2019. Patients were classified as Early-SSc following Le Roy criteria. Despite this, patients already did not meet 2013 ACR/EULAR classification criteria for SSc. We reviewed pulmonary function through conventional spirometry and diffusing capacity of lung for carbon monoxide (DLCO).

Results: We included 56 patients with a mean age of 52.3±12.1 years (96.4% women; 3.6% men).

At the diagnosis of Early-SSc, no one of our patients evidenced a restrictive ventilatory pattern. DLCO was below normal limits in 18 patients (32.1%). Small airway obstruction expressed according decreased maximal (mid-) expiratory flow (MMEF) 25-75 was present in 24 patients (42.8%).

After a mean follow-up period of 38.3±2.4 months, 29 (51.8%) patients fulfilled 2013 ACR/EULAR criteria. The average time between diagnosis of Early-SSc and achieve SSc classification was 24.4±1.8 months. The remaining 27 patients continued classified as Early-SSc.

An analysis of the subgroup of patients which progressed to SSc showed that DLCO was decreased in 15 of those 29 patients (51.7%) and 18 of 29 patients (62.1%) presented decreased MMEF 25-75. Comparing with the subgroup of patients which not progressed to SSc were significant differences (Decreased DLCO: 51.7% vs 11.1%; p=0.02 and decreased MMEF 25-75: 42.8% vs 22.2%; p=0.05).

The analysis of pulmonary function of the subgroup of patients continued classified as Early-SSc after follow-up period did not show significative changes after follow-up.

Conclusion: In our study, a third of the patients classified as Early-SSc presented at diagnosis abnormal values of DLCO and/or signs of small airway obstruction without the presence of a restrictive ventilatory pattern. Moreover, this pulmonary disfunction was significantly more frequent in patients who progressed to definitive SSc. Patients which remains classified as Early-SSc did not experience significative changes.

Our results support the concept that pulmonary function was impaired in Early-SSc and that I should probably be considered for future Early-SSc classification criteria.

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AB0598 THE INCREASING USE OF IMMUNOSUPPRESSANTS IN EARLY SYSTEMIC SCLEROSIS

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Background: Immunosuppression (IS) remains the main treatment for progressing skin involvement, active interstitial lung disease (ILD) and underlying inflammatory joint (IJ) or muscle disease in systemic sclerosis (SSc).

Objectives: This study investigated the pattern and trends in immunosuppressive agent use in patients with early SSc diagnosed before and after 2007 to determine whether the changes in the preferred type and combination of IS, timing and predictors of administration took place over the past decade.

Methods: 397 SSc patients from Canadian Scleroderma Research Group (CSRG) database (183dcSSc, 214 lcSSc) who had baseline and follow-up visits within 3 years (1.8±0.8) after disease onset were included: 82% females, age at diagnosis 53±13 years, disease duration 1.6±0.8 years. Organ involvement was assessed by modified Rodnan skin score, Medsger Disease Severity Score (DSS) and CSRG definitions using bivariate, chi-squared, ANOVA, and adjusted regression analyses.

Results: 115 dcSSc patients (63%) and 62 lcSSc (29%) received IS, most commonly methotrexate (MTX) (72% dcSSc and 52% lcSSc), followed by mycophenylate mofetil (MMF) and cyclophosphamide (CYC). Within the patients receiving IS, monotherapy prevailed (77% dcSSc and 68% lcSSc); CYC and azathioprine were the preferred choice of IS more frequently in lcSSc compared to dcSSc (p<0.006 and p<0.02, respectively). In dcSSc, IS were predominantly prescribed at years 2 and 3 after the onset of first non-Raynaud's phenomenon (RP) manifestation, when about half of the patients received IS. The proportion of lcSSc patients receiving IS was significantly lower and distributed more equally through the first three years. After 2007, dcSSc patients received IS more often (74% vs 50%, p=0.001), especially MTX (p=0.02) and MMF (p<0.05), and earlier (peaked at 2 years after disease onset)(Table 1).

Table 1. Proportion of patients receiving immunosuppressive treatment at each year after disease onset in SSc diagnosed before and after 2007.

Years after the first non-RP symptom	lcSSc				
	Before 2007		After 2007		
	Total N of pts seen at each year	% receiving immune suppressives	Total N of pts seen at each year	% receiving immune suppressives	P-value
1	13	15	47	17	>0.9
2	24	21	82	18	0.772
3	49	14	107	14	>0.9
	dcSSc				
1	24	29	40	43	0.286
2	51	26	65	65	0.0001
3	62	45	63	54	0.325

IS administration was associated with male gender, ILD, a-Scl-70 positivity, ACA-negativity and IJ disease in lcSSc, and with ACA-negativity and a higher mRSS in dcSSc. Multivariate logistic regression analysis showed that IS treatment could be predicted by ACA-negativity in lcSSc patients (Exp(B) 0.317, p=0.012) and younger age in dcSSc patients (Exp(B) 0.974, p=0.002).

Conclusion: Over the past decade, there has been a trend to prescribe IS more often, especially MTX, and earlier in dcSSc patients. MMF has gained favour over CYC. Autoantibody status was the most consistent predictor whether a patient is likely to take IS over the course of the disease.

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AB0599 TREATMENT OF REFRACTORY DERMATOMYOSITIS WITH TOFACITINIB

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Background: Dermatomyositis (DM) is a systemic, autoimmune disease affecting the skin and proximal skeletal muscles. A subset of DM patients present with subclinical or resolved muscle involvement but continue to have skin disease. In these cases, first and second line treatments including glucocorticoids are sometimes insufficient for controlling the disease, necessitating escalation of treatment. Several recent studies have investigated the response of Tofacitinib, an oral Janus Kinase inhibitor approved for the treatment of rheumatoid arthritis, in DM patients and patients with inflammatory skin diseases.

Objectives: Due to the reported ability of JAK inhibitors to suppress type 1 interferon (IFN) signaling, which is suspected to be upregulated in DM, we evaluated the efficacy of treatment with Tofacitinib in four refractory DM patients.

Methods: Four patients with dermatomyositis without evidence of current muscle involvement began treatment with Tofacitinib 11 mg daily after they had failed or had adverse effects to first and second line immunosuppressive agents. Their medical records were reviewed at 0, 3, and 6 months, with improvement measured using the Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) activity score. Throughout their treatment they were additionally monitored for improvement in markers of inflammation and the necessity for concomitant treatments. Patients were monitored for adverse effects to Tofacitinib treatment.

Results: All four patients within the case series showed significant improvement of their cutaneous disease activity (CDASI scores improved by 8-15 points) over the first 6 months, with three of the four having achieved minimal clinically improved difference of >= 5 point by three months. Based on the CDASI, three of the cases' disease classification changed from moderate-to-severe disease to mild disease. The last patient initially presented with mild disease. Other outcomes noted included improved pruritus in 3 patients and improvement of calcinosis in 1 patient. One patient was additionally able to stop concomitant treatment with prednisone and IVIG at 3 and 6 months, respectively. This patient had been on daily prednisone for 4 years. Only other patient on prednisone was on low dose of 3mg daily. The patients all had normal muscle exams prior to treatment with Tofacitinib. No worsening muscle involvement or adverse effects were noted with Tofacitinib use.

Conclusion: Tofacitinib is believed to play a role in the inhibition of IFN signaling pathways that are overactive in dermatomyositis. All four patients within this retrospective study showed significant improvement of cutaneous disease with Tofacitinib use.

Gender/ Age/ Ethnicity	DM Subtype / disease duration	Previous Treatment	Concomitant Treatment with TOF	CDASI Activity	CDASI Activity 3 month	CDASI Activity 6 month	Other Outcome
M/ 55/ Caucasian	Amyopathic DM; 5 years	AZA, HCQ, IVIG, MTX, MMF, Prednisone, RCI, RTX, TAC	HCQ	12	5	4	None
F/ 37/ Caucasian	Amyopathic DM; 7 years	AZA, HCQ, IVIG, MTX, MMF, Prednisone, RCI, TAC	Prednisone, IVIG, MTX	15	8	5	Pruritus and CRP improved
F/ 60/ Caucasian	Amyopathic DM; 4 years	AZA, MTX, Prednisone	Prednisone, MTX	17	15	5	Pruritus improved
F/ 47 African American	Classic DM; 5 years	AZA, colchicine, HCQ, IVIG, MTX, MMF, pamidronate Prednisone, RCI, RTX, TAC	IVIG, Colchicine	22	8	7	Pruritus and calcinosis improved

Abbreviations: CDASI, Cutaneous Dermatomyositis Disease Area and Severity Index; AZA, azathioprine; CRP, C-reactive protein; DM, Dermatomyositis, HCQ, hydroxychloroquine; IVIG, intravenous immunoglobulin; MTX, methotrexate; MMF, mycophenolate mofetil; RCI, repository-corticotropin injection; RTX, rituximab; TAC, tacrolimus; TOF, tofacitinib;

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AB0600 THE EFFECTS OF HYPERBARIC OXYGEN THERAPY TO QUALITY OF LIFE AND STATE OF MICROCIRCULATION IN PATIENTS WITH SYSTEMIC SCLEROSIS - A PILOT STUDY

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Background: Many treatments have been tried in therapy systemic sclerosis (SSc) patients but use of hyperbaric oxygen therapy (HBOT) is very limited.

Objectives: To assess the effects of HBOT to quality of life and state of microcirculation in SSc patients.

Methods: 18 female patients aged 29-68 years (mean 57 years) with limited SSc and digital or leg ulcers were included in this work. The HBOT protocol comprised 20 sessions 5 day/weekly, 60 min, 100% oxygen at 2.2 ATA. The treated patients were evaluated at baseline and after 20 HBOT sessions. Evaluation consisted of physical examination, capillaroscopy, pulmonary function tests, biochemical analyses, socio-demographic and clinimetric questionnaires: Systemic Sclerosis Questionnaire (SySQ) and Health Assessment Disaability index Questionnaire (HAQ-DI).

Results: Mean value [before: after, mean (range)] for SySQ [15.5 (4-48) vs 9.0 (3-31)], HAQ-DI [0.60 (0-2.88) vs 0.35 (0 -1.75)], erythrocyte sedimentation rate [21 (4-42) vs 12 (3-27)], forced vital capacity (96.61±14.44% vs 115.94±16.69%), diffusing lung capacity of carbon monoxide (73.61±6.63% vs 87.33±9.30%) significantly improved after HBOT sessions ($p<0.001$). There was no significant changes in the total number of capillaries (325 vs 338, $p=0.235$), mean number of enlarged capillaries (21 vs 27, $p=0.182$), giant capillaries (14 vs 14, $p=0.235$) and ramified/bushy capillaries (14 vs 13, $p=0.178$) before and after HOBT. All patients had digital ulcers, and 5 patients had bilateral lesions (digital and leg ulcers). Mean size of ulceration before HBOT was 12x11mm, and after therapy was 4x4mm ($p<0.001$). Three patients had digital gangrene. Amputation was not require for any.

Conclusion: Our data confirm the efficacy of HBOT in treating SSc patients. Further studies are required to evaluate the protocol and to understand the durattion of the clinical effect.

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AB0601

RAPID AND SUSTAINED EFFICACY OF AN INDUCTION TREATMENT WITH A TRIPLE THERAPY INCLUDING HIGH-DOSE INTRAVENOUS IMMUNOGLOBULINS, METHOTREXATE AND GLUCOCORTICOIDS IN ANTI-3-HYDROXY-3-METHYLGLUTARYL-COENZYME A REDUCTASE MYOPATHY

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Background: Anti-3-hydroxy-3-methylglutaryl-coenzime A reductase (HMGCR) myopathy is a new entity, which has been clearly associated to statin use, even if it can be diagnosed in patients without a history of exposure to statin or even in the childhood (1).

Objectives: The aim of the study is to describe the efficacy of a triple therapy regimen consisting in high-doses of intravenous immunoglobulins (IVIG), methotrexate (MTX), and glucocorticoids (GC) in 16 patients with Anti-HMGCR myopathy enrolled in 6 specialized centres.

Methods: A total of 16 patients with anti-HMGCR myopathy (7 females; 9 males) were collected. Mean (±standard deviation) age at the onset of disease was 72.4±10.3 years old. All patients were diagnosed having anti-HMGCR myopathy [anti-HMGCR antibodies were measured by chemiluminescence assay (Bio-Flash, Inova, CA)] (2). Median follow-up was 29.5 months (interquartile range: 15.75-60 months). Anti-HMGCR antibodies were available in the follow-up in 8/16 patients.

Results: Thirteen out of 16 patients (81.3%) had been exposed to statin (1/13 to red rice), 3/16 (18.7%) were not exposed. As induction therapy, 11/16 patients have been treated with triple therapy (high-dose IVIG, MTX and GC), 2/16 with double therapy (high-dose IVIG and GC), 2/16 have been treated with GC alone, the patient exposed to red rice resolved only with red rice suspension. Clinical remission and normalization of CPK values within month +24 were obtained in all the patients. All the patients were in remission at the last follow-up. Gradual improvement started soon from the first month, and among the 13 patients treated with an aggressive immunosuppresssive therapy including IVIG (13/13), GC (13/13) and methotrexate (11/13), 9/13 normalized the CPK value within 6 months. Clinical and laboratory response was accompanied by significant decrease or normalization of the anti-HMGCR antibody titer. All the patients were either not taking GC (56.3%), or were taking low doses of GC (43.7%) at the last follow-up. Four patients had stopped GC within 6 months. No serious side effects were recorded. After persistent remission, a maintenance immunosuppressive therapy was then administered. Only 3 relapses in 3 different cases were recorded, all of them during drug-free remission in long-term follow-up. Reinduction was again effective in all.

Conclusion: Anti-HMGCR myopathy is a rare and serious myopathy which usually affects older people during statin treatment. After statin suspension, a rapid and sustained remission can be achieved by induction with a triple aggressive therapy consisting in medium-to high doses of GC, high-dose IVIG, and MTX (3). GC should be tapered as soon as possible. Relapse appears infrequent during maintenance treatment. Monitoring anti-HMGCR antibody titer may be clinically relevant.

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AB0602

SYSTEMIC SCLEROSIS: SUBCLINICAL ATHEROSCLEROSIS AND MORBIMORTALITY.

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Background: Rheumatic diseases are associated with accelerated atherosclerosis, and an increase in cardiovascular morbidity and mortality. This process is mediated by classic cardiovascular risk factors (CVRF), chronic inflammation and atherogenic treatments such as corticosteroids. In Systemic Sclerosis (SSc) cardiovascular complications have increased in recent decades, although the studies on subclinical atherosclerosis (sATS) in SSc show discordant results.

Objectives: To evaluate prospectively the relationship between subclinical atherosclerosis, cardiovascular morbidity and mortality in patients with SSc.

Methods: 120 consecutive patients with SSc who attended their medical regular review during November and December 2011 were included. We evaluated the presence of plaques and measured the right CCA IMT by B doppler US for the detection of sATS (IMT> 0.9mm and/or presence of plaque), review of classic CVRF and estimation of Medsger severity and EUSTAR activity index. Patients have been followed for 8 years, with at least annual consultation. In retrospect, the SCTC damage index, published in 2019, was obtained at the time of inclusion in the study. The clinical characteristics of the patients are collected since 1990 in a Prospective Longitudinal Observational Study (PLOS). Descriptive analysis was performed, using contigence tables for qualitative variables, and comparison of means for quantitative variables. The relationship between clinical characteristics, mortality, cardiovascular events (CVE), activity, severity and damage index, and sATS, was analyzed using binary logistic regression, adjusting for age and sex.

Results: 120 patients with SSc were included (93% female, age 60 ± 12 years). 42 of these patients (35%) had subclinical atherosclerosis. Age was statistically significant higher in patients with sATS compared to those without it (67.9±11.5 vs. 56.1±10.4 years, p <0.001). We found no differences between groups in activity, damage and severity index (Table 1). Patients with sATS had higher levels of ESR and CRP, but the difference was not confirmed after adjusting for age (*). During the 8 years of follow-up, 9 CVE in 7 patients (5.8%): three myocardial infarction, one transient ischemic accident, one angor, one intermittent claudication and three refractory heart failure. The incidence of severe CVE was more than double in patients with SAtS (10.25% vs. 3.7%), but the difference was not significant. We found no relationship between the mortality of any cause, or the secondary to CVE, with sATS, in the 32 patients who died during the follow-up, 3 due to CVE (9.4%). The results are similar when we analyze only the presence of plaques.

Table 1. Relationship between clinical characteristics and activity, severity and damage index with the presence of accelerated atheromatosis.

	Absent n=78	Present n=42	
Diffuse cutaneous SSc	37.18%	26.12%	NS
mRSS	7.71 ± 6.32	6.38 ± 4.92	NS
High mRSS	9.69 ± 8.33	7.57 ± 4.74	NS
Arthritis	32.05%	28.57%	NS
Lung involvement	33.33%	30.95%	NS
PAH	10.26%	7.14%	NS
Cardiac involvement	15.38%	9.52%	NS
Digital ulcers	35.90%	35.83%	NS
AntiScl70	25.64%	21.43%	NS
ESR	20.12 ± 13.77	26.88 ±17.25	p =0.037*
CPR	0.65 ± 0.61	0.89 ± 0.7	p =0.041*
High activity index	11.54%	19.05%	NS
Damage index	6.67 ± 5.56	5.62 ± 4.9	NS
Σ Medsger index	5.37 ± 3.5	5.05 ± 3.45	NS

Conclusion: In our study subclinical atherosclerosis is not related to higher mortality in patients with SSc, but it does seem to influence the occurrence of cardiovascular events. In addition, our results suggest that SSc does not influence the onset of accelerated atheromatosis.

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AB0603 PDGFA AS A POTENTIAL BLOOD MARKER IN DSSC

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Background: PDGF is a potential important factor in the pathogenesis of scleroderma. PDGF is almost undetectable in healthy skin or lung. Immunohistochemical studies have revealed increased presence of PDGF*α* and PDGF*β* receptors in scleroderma skin biopsies.
Objectives: The aim of this study was to determine the mRNA level of *IFNα1*, *IL-4, TGFβ1*, *TGFβ2*, *PDGFα*, *PDGFβ*, *TNFα* in whole blood in SSc patients in the aspect of clinical
Methods: A group of 14 patients (50% were women) with systemic sclerosis based on EULAR / ACR 2013 criteria was included in the study. The modified Rodnan Skin Score (mRSS) was evaluated by same assistant at the beginning of the study and six months later. DLCO, HRCT, echocardiography and NFC were measured. Gene expression was determined using validated TaqMan probes in qPCR. Constitutive mRNA level of selected genes was analyzed using ΔCt method. Comparison between different groups of patients was determined using non-parametric Mann-Whitney U test. Correlation was analyzed using non-parametric Spearman test.
Results: The mean age of the patients was 60 ± 15.66. 100% of patients had organ involvement as pulmonary fibrosis. 78% - had active changes -features of ground glass.
64% of patients had mild mRSS-1-10 skin involvement, 36% had moderate to severe skin involvement. In SSc patients *TGFβ1* and *IFNα1* revealed the highest level of expression in comparison to other analyzed genes. Additionally, very high and significant correlation between *TNFα* and *TGFβ1* (r=0.7 p=0.004) has been noted. High and significant correlation between mRNA *PDGFβ* and *TNFα* levels have been observed. We did not reveal significant differences in analyzed genes expression when compare limited and diffuse SSc. Nevertheless, patients with dSSc were characterized by higher level of *IFNα1* (almost 2 times) and *TGFβ1*. On the border of significance higher *PDGFα* mRNA level was observed in dSSc patients when compared to lSSc. Average *PDGFα* expression is higher in SSc patients with Scl70 positive than than in patients without Scl70 (p=0.04).
In the aspect of clinical parameters, patients with ESR ≤12 mm/h revealed almost 6 times higher level of *IFNα1* (p=0.01) in comparison to the patient with ESR>12mm/h. Patients with mRSS above10 points revealed significantly higher of *PDGFα* expression in comparison to patients with mRSS ≤10 (p=0.04). In these group of patients CRP and ESR were not different significantly.
In the case of patients with active fibrosis (ground glass) in HRCT *IFNα1* expression was almost 2.5-times higher than in patients with HRCT non-active. Significantly higher *PDGFα* has been revealed in patients with active HRCT when compared with patient with non-active HRCT. Nevertheless these two groups did not differ in ESR or OB parameter.
SSc patients in active phase of NFC revealed almost 3 times higher level of *IFNα1* expression in comparison with the patient in late phase.
Conclusion: The mRNA level of *PDGFα* may be a potential blood marker to predict worse prognosis in scleroderma
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Role of PDGF in fibrotic diseases and systemic sclerosis.
Trojanowska M1.

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AB0604 EVALUATION OF PATIENTS WITH ANTISYNTHETASE SYNDROME AND INTERSTITIAL LUNG DISEASE BASED ON THE RADIOLOGICAL PATTERN

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Background: Antisynthetase syndrome is an autoimmune rheumatologic disease characterized by the presence of specific antibodies that are known as antisynthetase antibodies and with a varied clinic, including arthritis, myositis or interstitial lung disease (ILD), among others. ILD is the manifestation that associates the highest morbi / mortality and can occur with different characteristic radiological patterns: usual interstitial pneumonia (UIP), non-specific interstitial pneumonia (NSIP), organized pneumonia (OP)
Objectives: Describe the clinical, serological and prognostic characteristics of patients with antisynthetase syndrome with interstitial pulmonary involvement (ILD) based on their radiological pattern.
Methods: Retrospective descriptive study of patients with a clinical diagnosis of antisynthetase syndrome in which they show positive for some antisynthetase antibody and with clinical follow-up of at least 6 months in a reference center consultation between the period from January 2008 to September 2019. In those patients who presented interstitial lung involvement clinical, analytical and prognostic variables were evaluated (including spirometry) based on the radiological pattern presented by high-resolution computed tomography (HRCT) of the chest
Results: 32 patients (24 women and 8 men) were included in the study. 7 cases (21.9%) did not present pulmonary involvement, while the remaining 25 cases (78.1%) presented with interstitial lung involvement. Of the patients diagnosed with ILD, 4 cases (12.5%) had an interstitial pattern UIP, 17 cases (53.1%) had an interstitial pattern of NSIP and another 4 (12.5%) interstitial pattern of OP. From an analytical point of view, the most frequent antisynthetase antibody in our sample was antiJo1 with 29 cases (96.9%) and less frequently the antiPL12 antibody with 2 cases and antiPL7 with 1 case. The specific characteristics depending on the type of EPID pattern are summarized in Table 1.

Table 1.

CHARACTERISTICS	ILD PATTERN		
	Pattern UIP N=4	Pattern NSIP N=17	Pattern OP N=4
Gender (Female) n (%)	4 (100)	11 (64.7)	3 (75.0)
Age at diagnosis	47.5 ± 12.9	52.9 ± 10.5	42.0 ± 12.9
Myositis, n(%)	2 (50.0)	13 (76.5)	4 (100)
Arthritis, n (%)	3 (75.0)	15 (88.2)	3 (75.0)
Fever, n (%)	1 (25.0)	9 (52.9)	2 (50.0)
Mechanic´s hands, n(%)	2 (50.0)	7 (41.2)	2 (50.0)
Raynaud´s phenomen, n (%)	1 (25.0)	8 (47.1)	1 (25.0)
Skin involvement, n(%)	2 (50.0)	10 (58.8)	4 (100)
Treatment, n(%)			
Glucocorticoids	4 (100)	16 (94.1)	4 (100)
Immunosuppresants	4 (100)	16 (94.1)	4 (100)
Biological therapy	1 (25.0)	8 (47.1)	2 (50.0)
Drug´s number (mean, SD)	3 ± 0.8	5 ± 2.9	4.7 ± 1.8
Antisynthetase antibodies, n(%)			
Anti Jo1	3 (75.0)	15 (88.2)	4(100)
PL7	0 (0)	1 (5.9)	0 (0)
PL12	1 (25.0)	1 (5.9)	0 (0)
Ro52	3 (75.0)	14 (82.4)	2 (50.0)
RF positive	1 (25.0)	4 (23.5)	1 (25.0)
CK increase	2 (50.0)	11 (64.7)	4 (100)
Aldolase increase	2 (50.0)	12 (70.6)	4 (100)
Functional respiratory tests: mean(CI95%)			
Variation DLCOc(%)	-4.4 (-12.5, 3.7)	-2.5(-6.1, 1.0)	7.4 (-10.6, 25.3)
Variation FVC(%)	-1.1 (-12.8, 9.1)	6.0 (3.2, 8.8)	7.5 (-9.5, 24.6)
Variation FEV1(%)	0 (0-2.25)	5.0 (1.9, 8.3)	7.35 (-18.0, 32.7)
Variation FEV1/FVC(%)	0.5 (-7.1, 8.2)	-1.3 (-2.22, -0.37)	-0.4(-12.88, 11.98)

Conclusion: ILD is a frequent and serious manifestation that can occur in patients with antisynthetase syndrome, which may have different radiological patterns. In our series, the most observed radiological pattern has been the NSIP pattern with 68%. The pattern most associated with the Ro 52 antibody was the UIP pattern and the NSIP pattern. As for the group that required the largest numbers of drugs (including biological therapy) it was the NSIP pattern. When evaluating changes in respiratory function tests, the pattern that shows a tendency to improve over time is organized pneumonia with improvement of the DLCO, FVC, FEV1, FEV1 / FVC, while the UIP pattern showed a worsening of the DLCO and the FVC.
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AB0605 CLINICAL PROFILE AND CHEST HIGH-RESOLUTION COMPUTED TOMOGRAPHY (HRCT) FINDINGS IN PATIENTS WITH CONNECTIVE TISSUE DISEASES AND INTERSTITIAL LUNG DISEASE: EXPERIENCE OF A SINGLE REFERENCE RHEUMATOLOGY CENTER

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Background: Interstitial lung disease (ILD) is a common manifestation of connective tissue diseases (CTDs), and is associated with significant morbidity and mortality. Chest high-resolution computed tomography (HRCT) play an important role in the diagnosis of ILD and may provide prognostic information.

Objectives: We aimed to characterize the clinical profile and chest HRCT abnormalities and patterns of patients diagnosed with CTDs and ILD.

Methods: In this retrospective, observational study we included 80 consecutive patients with CTDs and ILD referred to a tertiary rheumatology center between 2015 and 2019. From hospital charts we collected clinical data, immunologic profile, chest HRCT findings. HRCT patterns were defined according to new international recommendations.

Results: Out of 80 patients, 64 (80%) were women, with a mean age of 55 years old. The most common CTD associated with ILD was systemic sclerosis (38.8%), followed by polymyositis (22.5%) and rheumatoid arthritis (18.8%). The majority of patients had dyspnea on exertion (71.3%), bibasilar inspiratory crackles were present in 56.3% patients and 10% had clubbing fingers. Antinuclear antibodies (ANA) were present in 78.8% patients, and the most frequently detected autoantibodies against extractable nuclear antigen were anti-Scl 70 (28.8%), followed by anti-SSA (anti-Ro, 17.5%), anti-Ro52 (11.3%) and anti-Jo (7.5%). Intravenous cyclophosphamide therapy for 6-12 months was used in 35% of patients, while 5% of patients were treated with mycophenolate mofetil.

The most frequent HRCT abnormalities were reticular abnormalities and ground glass opacity. Non-specific interstitial pneumonia (NSIP) was identified in 46.3% CTDs patients. A pattern suggestive of usual interstitial pneumonia (UIP) was present in 32.5% patients, mainly in patients with systemic sclerosis. In 21.3% patients the HRCT showed reticulo-nodular pattern, micronodules and other abnormalities, not diagnostic for UIP or NSIP pattern.

Conclusion: Nonspecific interstitial pneumonia (NSIP) is the most common HRCT pattern associated with CTDs. Further prospective longitudinal studies are needed in order to determine the clinical and prognostic significance of various HRCT patterns encountered in CTD-associated ILD and for better patient management.

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AB0606 SYSTEMIC SCLEROSIS – ARE PATIENTS WITH CALCINOSIS DIFFERENT FROM THOSE WHO DO NOT HAVE IT?

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Background: Systemic Sclerosis (SS) is a heterogenous disease with a broad range of organ involvement. Calcinosis is a common problem and although it may affect almost any body tissue, it is typically seen in the limbs.[1] Its presence relates with higher risk of digital ulcers and infection.[2] It is still unknown whether patients with calcinosis also have other clinical features that differentiate them from the remaining.

Objectives: To determine the prevalence of calcinosis in a SS cohort and to evaluate if its presence relates with specific clinical features.

Methods: A cross-sectional study was conducted evaluating a cohort of SS patients. Plain radiographs were taken to assess calcinosis at elbows, hands, knees and feet. Clinical data was obtained and analyzed using IBM SPSS Statistics 26®.

Results: We included 25 patients, 21 females [n= 21 (84%)], median (min, max) age was 58 (27, 75) years-old. Regarding disease classification, 16 (64%) had limited SS, 4 (16%) had diffuse SS, 3 (12%) had overlap syndrome and 2 (8%) had early SS. Ten (40%) patients had radiological calcinosis in at least one site, seven of which (70%) were subclinical. The most affected areas were knees and hands [n=6 (24%)]. Table 1 summarizes the clinical characteristics of patients with and without calcinosis. Limited SS was significantly more prevalent in the calcinosis group [n=9 (90%) vs. n=7 (46.7%), p=0.04]. All patients had Raynaud phenomenon [n=10 (100%) vs. 15 (100%)]. Current or past digital ulcers [n=5 (50%) vs. n=6 (40%), p=0.697], telangiectasias [n=9 (90%) vs. n=11 (73.3%), p=0.615], pulmonary hypertension [n=2 (20%) vs. n=1 (6.7%), p=0.550] and esophageal involvement [n=6 (60%) vs. n=6 (40%), p=0.428] were more frequent in the calcinosis group but with no statistical significance. Although late capillaroscopic pattern was more frequent in the calcinosis group, there was no statistical significance difference [n=4 (40%) vs. n=1 (6.7%), p=0.121]. Seropositivity for centromere-B antibodies was more frequent in the calcinosis group but with no statistical significance [n=7 (70%) vs. n=8 (53.3%), p=0.678].

Table 1. Demographic and clinical data of patients with and without calcinosis.

Demographic and clinical data	Calcinosis (n=10)	No calcinosis (n=15)	p-value
Female gender, n (%)	9 (90)	12 (80)	0.626
Age (years), median [min,max]	68.5 [27, 75]	52 [36, 73]	0.129
Cutaneous classification			
Limited, n (%)	9 (90)	7 (46.7)	0.04
Diffuse, n (%)	1 (10)	3 (20)	0.626
Early, n (%)	0 (0)	2 (13.3)	0.500
Overlap, n (%)	0 (0)	3 (20)	0.250
Clinical manifestations			
Current or previous digital ulcers, n (%)	5 (50)	6 (40)	0.697
Interstitial lung disease, n (%)	2 (20)	4 (26.7)	1.000
Pulmonary hypertension, n (%)	2 (20)	1 (6.7)	0.550
Arthritis, n (%)	2 (20)	3 (20)	1.000
Calcinosis, n (%)	3 (30)	0 (0)	0.052
Esophageal involvement, n (%)	6 (60)	6 (40)	0.428
NFC patterns			
Non specific abnormalities, n (%)	1 (10)	3 (20)	0.626
Early scleroderma, n (%)	1 (10)	1 (6.7)	1.000
Active scleroderma, n (%)	3 (30)	10 (58.8)	0.111
Late scleroderma, n (%)	4 (40)	1 (6.7)	0.121
Autoantibodies			
Centromere B, n (%)	7 (70)	8 (53.3)	0.678
Scl-70, n (%)	1 (10)	4 (26.7)	0.615

Conclusion: The prevalence of calcinosis was similar to that reported in literature (18-49%). This study confirmed the association, already found in previous studies, between calcinosis and the limited form of SS and raises attention for the importance of calcinosis radiographic screening since there was a high prevalence of subclinical calcinosis. [1] Although there were some clinical differences between patients with and without calcinosis, given the small cohort, statistical significance was not obtained. Larger studies are needed to increase statistical power.

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AB0607 MYOSITIS-RELATED INTERSTITIAL LUNG DISEASES: CLINICAL FEATURES, BIOMARKERS AND AUTOANTIBODIES IN LATINOAMERICAN PATIENTS

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Background: The lung is one of the most common extra-muscular targets in idiopathic inflammatory myopathies (IIM) and interstitial lung disease (ILD) is a prevalent and often devastating manifestation of IIM [1].

Objectives: To know the frequency of autoantibodies associated with IMM-ILD, biomarkers, and their relation with clinical features in patients with IIM.

Methods: Adults with IIM were enrolled in a retrospective way. Demographics, clinical and laboratory features were registered. The determination of antibodies was perfomed by the Inmunoblot technique with Euroinmmun kit. Patients without a myositis antibody panel were excluded. The diagnosis of ILD was based on HRCT. Patients with anti-MDA5 antibodies and with anti Ro-52 antibodies associated with anti-ARS were considered as high risk group, those with anti-ARS, anti-U1-RNP, anti-PM/ Scl and anti-Ku antibodies as moderate risk and those with anti-Mi2, anti SRP and anti TIF1 antibodies as low risk[2].

Results: Demographics characteristics are shown in table 1. We included 36 patients. Dermatomyositis (DM) was described in 69.4%, polymyositis (PM) in 16.7% and antysnthetase syndrome (AAS) in 13.9%. Out of the total of our patients, 30.6% had interstitial lung disease. The most frequent autoantibody was Anti Ro52 in 13 (36.1%) patients and 44.4% were in the high risk group. We analized our patients by the presence or absence of ILD and we found that

anti-MDA5 antibodies were more frequent in IMM-ILD group (p=0.006). In our IMM-ILD group we compared the autoantibodies with the clinical and serological features and we found that patients with IMM- ILD and anti Ro-52 antibody had more frequency of heliotrope rash (p=0.045) and those with IMM- ILD and anti-Jo1 antibody had a higher level of CK (p<0.001).

Table 1. Demographic characteristics

Age, mean SD	40.611 +/- 16.37
Women, n(%)	24 (66.7%)
Diagnosis	
Dermatomiositis	25 (69.4%)
Polimiositis	6 (16.7%)
Síndrome antisintetasa	5 (13.9%)
Time of evolution *	6.00 (2.25 – 19.00)
Interstitial lung disease	11 (30.6%)
Serological	
CK	305.00 (50.75 – 1969.250)
LDH	460.727 +/- 384.76
Risk ILD complicated with IIM	
High	16 (44.4%)
Moderate	8 (22.2%)
Low	12 (33.3%)

*months

Table 2. Clinical and serological comparation between IMM groups with and without ILD

	IMM with ILD, n=11	IMM without ILD, n=25	*p*
Proximal muscle weakness	10 (90.9%)	22 (88.0%)	NS
Heliotrope Rash	7 (63.6%)	10 (40.0%)	NS
Mechanic hands	4 (36.4%)	4 (16.0%)	NS
Anti-Mi-2	2 (18.2%)	8 (32.0%)	NS
Anti-Tif1 γ	0 (0.0%)	6 (24.0%)	NS
Anti-MDA5	4 (36.4%)	0 (0.0%)	**.006**
Anti-NXP2	1 (9.1%)	0 (0.0%)	NS
Anti-SAE1	0 (0.0%)	1 (4.0%)	NS
Anti-Ku	0 (0.0%)	2 (8.0%)	NS
Anti-PM/Scl100	0 (0.0%)	1 (4.0%)	NS
Anti-PM/Scl75	2 (18.2%)	0 (0.0%)	NS
Anti-Jo1	1 (9.1%)	0 (0.0%)	NS
Anti-SRP	0 (0.0%)	3 (12.0%)	NS
Anti- PL12	0 (0%)	1 (4.0%)	NS
Anti-EJ	1 (0.1%)	1 (4.0%)	NS
Anti- PL7	1 (9.1%)	4 (16.0%)	NS
Anti-OJ	0 (0.0%)	2 (8.0%)	NS
Anti-Ro52	5 (45.5%)	8 (32.0%)	NS

Conclusion: Anti-MDA5 antibodies were more frequent in our IMM-ILD group than in IMM without ILD group. Almost half of our patients were in a high risk group, which means they need an early immunosuppressive treatment. In our IMM-ILD patients we found an association between the presence of anti Ro-52 antibody with heliotrope rash and of anti-Jo1 antibody to a higher level of CK.

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AB0608 CARDIAC VESSELS CALCIFICATION IN A COHORT OF SYSTEMIC SCLEROSIS PATIENTS: POSSIBLE ROLE IN VASCULOPATHY AND HEART ABNORMALITIES.

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Background: Cardiovascular disease is the leading cause of morbidity and mortality worldwide. Myocardial calcifications have been related with cardiovascular diseases (CVD) such as focal wall motion abnormalities and arrhythmias. The impact of vascular calcifications is under investigation in order to define the risk of cardiovascular events. The relationship between cardiac calcification and systemic sclerosis (SSc) has not been investigated.

Objectives: The aim of the study is to evaluate the frequency of different patterns of cardiac calcification in SSc patients, and to correlate them to other CVD risk factors.

Methods: We analyzed thoracic-CT scanners of 35 SSc patients (88% female, aged 47,8 ys ±12,9, disease duration 12,8 ys ±9) to determine the location and extension of vascular and cardiac calcification. All recruited patients fulfilled the 2013 ACR-EULAR classification criteria for SSc. No one patients had renal failure, cardiomyopathy, myocarditis, history of cardiac surgery or radiotherapy.

Results: We found myocardial vessels calcifications (MCv) in 37% SSc patients, aortic wall calcifications (ACw)in 60% SSc patients, cardiac valve calcifications (VC) in 28% SSc patient and heart wall calcifications (HCw) in 20%.

The SSc patients with almost one calcification had older age (65±9,8 ys vs 50±8,8 ys; p=0,0001) and higher values of circulating NTproBNP (336,9±351,9 vs 144,2±107,8; p=0,04) compared to those without.

In particular, the SSc patients with MCv had and uric acid (5,3 ±1,5 vs 4,1 ±1,3; p=0,05), higher rate of PAH (25% vs 0%; p=0,037), arrhythmia (38,5% vs 9%; p=0,036) and higher prevalence of CENP-B antibodies(46% vs 4%; p=0,01) compared to patients without MCv.

Patients with HCw had lower C reactive protein (0,16 ±0,10 vs 0,7±0,7; p=0,008) compared to those without HCw. No differences in the rate of heart and vascular complications of SSc were observed.

The SSc patients with ACw had higher frequency of arrhythmia (33% vs 0%; p=0,016) and longer disease duration (15,5 y ±9,9 vs 8,8 ±5,8; p=0,03).

The SSc patients with VC had higher rate of PAH (33%vs0%; p=0,003) and uric acid (6±0,5vs3,8±1,2 p=0,0001).

Regression analysis excluded any association with gender, BMI, systemic arterial hypertension, steroid therapy, hypovitaminosis D or smoke habit. No cardiovascular event was recorded in one year of observation.

Conclusion: All patterns of calcifications may be related mostly with the older age. Myocardial vessels calcifications have been found in a high percentage of SSc patients and in particular in those with PAH and positive for anti CENP-B. Furthermore, myocardial vessels calcifications could be associated to the higher occurrence of arrhythmia. More studied are needed to assess the importance of vascular calcification as a part of the vascular involvement in SSc.

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AB0609 THE SPECTRUM OF ANTINUCLEAR ANTIBODIES IN PATIENTS WITH SYSTEMIC SCLEROSIS POSITIVE FOR ANTI-U1RNP

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Background: Patients with systemic sclerosis positive for anti-U1RNP have special clinical picture and disease progression. The autoimmune profile in this group is poorly understood.

Objectives: The purpose of our work was to study the level of major autoantibodies in patients with systemic sclerosis positive for anti-U1RNP.

Methods: The study included 80 patients (71 women and 9 men, mean age 44,5±14 years) positive for antibodies to RNP and meeting the criteria of the systemic sclerosis (ACR/EULAR 2013). Patients were examined for autoantibodies: RF, ACCP, ACA, anti-Scl70, anti-RNAP-III, anti-Ro, anti-La, anti-dsDNA, anti-Sm, ACL, anti-Jo1. 44 patients were examined in dynamics in 24 months.

Results: In the study group the clinical picture was dominated by inflammatory musculoskeletal lesions (synovitis and myopathy), skin manifestations were poorly expressed. Interstitial lung disease was detected in 68% of cases. Overlaps (34%) with other rheumatic diseases (rheumatoid arthritis, systemic lupus erythematosus) and combination with Sjogren's syndrome (32.5%) were frequently noted. Other antibodies were often detected: commonly - RF (31%), anti-Ro (38%), anti-dsDNA (42%), rarely - anti-Sm (11%), ACCP (8%), anti-La (8%), ACA (6%), anti-Scl70 (6%), AKL (2%). Anti-Jo1 and anti-RNAP-III were not detected at all. In patients with systemic sclerosis highly-positive for anti-U1RNP (more than 2 upper normal limits) RF, anti-Ro, anti-dsDNA were significantly more common in comparison with low-positive(p=0.00). In dynamics 80% of patients maintained anti-U1RNP, while other autoantibodies were detected with the same frequency. In patients with initially low titer of anti-U1RNP, their disappearance was noted.

Conclusion: Patients with systemic sclerosis positive for anti-U1RNP differ in the predominance of inflammatory musculoskeletal manifestations and frequent combination with Sjogren's syndrome and overlaps. Highly positivity for anti-U1RNP is accompanied by a persistent increase in RF, anti-Ro, anti-dsDNA

Disclosure of Interests: None declared

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AB0610 **SEASONAL VARIATION IN IDIOPATHIC INFLAMMATORY MYOPATHIES INCIDENCE AND PRESENTATION: A RETROSPECTIVE STUDY IN BEIJING AND HONG KONG**

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Background: Seasonal patterns of disease onset and severity in idiopathic inflammatory myopathies (IIMs) as a whole are conflicting [1-3]. In recent years, over 10 myositis-specific antibodies (MSAs) have been identified. They are able to divide patients into homogenous subgroups and inform on prognosis [4].

Objectives: The objective of the study was to investigate the seasonal variation of onset of IIMs characterised serologically.

Methods: This was a multi-centred retrospective observational study. Consecutive Chinese patients with IIMs admitted to the rheumatology wards of the participating major regional hospitals in Beijing and Hong Kong from July 2013 to June 2018 were recruited. The diagnosis of IIMs was based on the Bohan and Peter's criteria with definite or probable cases being included [5]. Patients with clinically amyopathic disease must have the typical Gottron's papules or heliotrope rash as determined by rheumatologists or dermatologists, and with no symptoms or signs of muscle involvement according to Sontheimer [6]. Patients with juvenile myositis, inclusion body myositis, cancer-associated myositis and myositis associated with other connective tissue disease were excluded. A commercial line blot immunoassay kit (EUROLINE) was used to detect the MSAs.

Results: All together 495 patients were studied. The mean age of the patients at disease onset was 48.1 years (S.D. 13.3). There was a female predominance (68.3%). The subgroups of IIMs were: dermatomyositis (61.0%), polymyositis (21.8%), clinically amyopathic dermatomyositis (12.9%), immune mediated necrotising myopathy (3.8%) and nonspecific myositis (0.4%). No particular seasonal pattern in disease onset was observed in IIM patients as a whole (Figure 1) or in any classical subgroups. However, significantly more patients with any one MSA had their disease started in the first half of the year (p=0.007) as shown in Figure 2. Patients with either anti-synthetase or anti-MDA5 antibodies, which are associated with interstitial lung disease, had more frequent disease onset from November to February, which might coincide with the local flu season. It was also found that MSA positivity was associated with infection of the patient (p=0.005). Further analyses showed that patients with MSAs which are typically associated with severe skin disease (MDA5, TIF1g, NXP2, SAE) had more hospitalisation from April to September where excessive sun exposure is expected. There were no major differences between the Beijing and Hong Kong subgroups.

Conclusion: Apparent seasonal patterns were noticed in our ethno-serologically defined IIM patients. Certain environmental factors, particularly infection or UV exposure, could be potential triggers. Our findings could shed light on the identification of etiologic factors and enhance our understanding of disease pathogenesis.

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Figure 1.Disease onset of myositis patients.

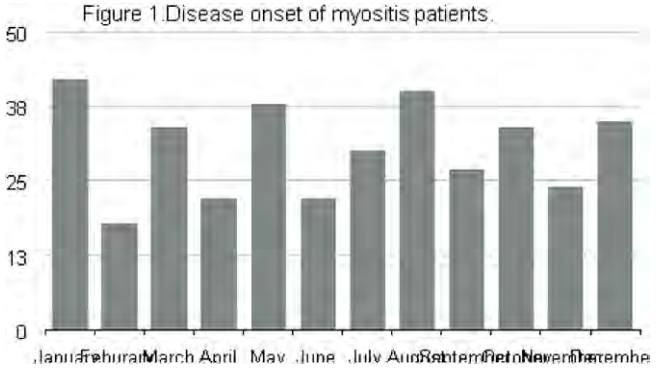
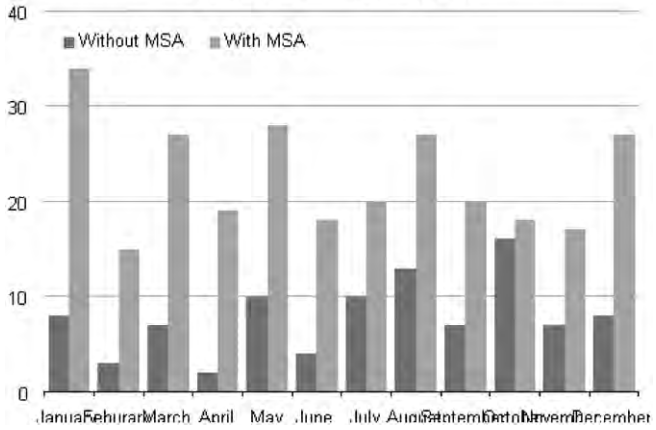


Figure 2. Disease onset of myositis patients with or without myositis specfic antibodies (MSA)



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AB0611 **STRAIN ANALYSIS OF THE RIGHT VENTRICLE USING 2D-SPECKLE TRACKING ECHOCARDIOGRAPHY IN A COHORT OF PATIENTS WITH SYSTEMIC SCLEROSIS**

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Background: Systemic Sclerosis (SSc) is a rare and life-threatening connective tissue disease with multiple organ impairment. Cardio-pulmonary involvement is common: pulmonary fibrosis, pulmonary hypertension (PH), and electrical disorders are the most serious complications and causes of increased mortality.

Objectives: We evaluated features related with the onset and development of PH in a cohort of SSc patients. We further studied ecocardiographic abnormalities, by means of 2D-speckle tracking echocardiography (STE) with specific reference to the right ventricular strain measure (RV-strain).

Methods: We analyzed data from 50 SSc patients (pts) referred to our University-based Rheumatology Centre and SSc Unit from January 2007 to June 2019 (F/M 45/5; lc/dcSSc 45/5; mean age 59.20±14.357 years; mean disease duration 12.08±8.75 years). All pts underwent general and cardio-pulmonary assessment in our Cardio-Rheumatology Clinic. The following parameters were considered: blood exams, in particular inflammation indexes, uric acid test and serum autoantibodies; pulmonary function tests; high resolution scan of the lungs (HRCT); standard electrocardiogram (ECG) and RV-strain measured by 2D-STE. These examinations were performed according to clinical picture and current methodologies. We compared SSc subjects with (10/50) and without (40/50) PH diagnosis during follow-up regardless of treatments.

Results: SSc pts with PH didn't show significant alterations concerning RV-strain if compared with pts without PH (p=0.707). Nevertheless, RV-strain value was modified in relation to TAPSE alterations in all pts but this data correlated with right ventricular dilatation only in PH subjects. Furthermore, interesting significant values about dilatation of right and left atria (p=0.007, p=0.048), dilatation of inferior vena cava (p=0.037) and right ventricle (p=0.023) were observed. Left ventricular hypertrophy (p=0.012) as well as valvular insufficiencies (mitral and aortic) were more frequent in PH group too (p=0.016). These pts showed higher incidence of

skin ulcers (p=0.0001), higher values of blood pressure (p=0.004), elevated uric acid levels (p=0,027) and anti-centromere antibodies positivity (p=0.0001).
Conclusion: Our research provides further evidence of the prognostic value of echocardiographic findings in SSc subjects, with focus on PH. Population enlargement is ongoing in order to identify more accurate results about RV-strain, considering the efficacy of PH treatments on cardiac contractility. Speckle tracking echocardiography proves to be a sensitive, low-cost, non-invasive and reliable tool to detect early cardiac impairment in Ssc, full of potential future prospects.
Disclosure of Interests: None declared
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AB0612 SHORT-TERM REVERSIBLE IMPROVEMENT IN EARLY-PHASE ELEMENTS OF NAILFOLD CAPILLARY ABNORMALITIES IN PATIENTS WITH SYSTEMIC SCLEROSIS BY INTRAVENOUS CYCLOPHOSPHAMIDE (IVCY)

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Background: Nailfold capillary abnormalities are one of representative signs in systemic sclerosis (SSc). However, previous reports about changes in nailfold capillary by immunosuppressive therapy have been limited. Especially, there have been no reports about short-term changes in nailfold capillary abnormalities.
Objectives: To clarify whether intravenous cyclophosphamide (IVCY) treatment for SSc patients can improve nailfold capillary abnormalities in half a year.
Methods: Among patients diagnosed as having SSc according to the 2013 ACR/EULAR classification criteria at our hospital from May 2018 to December 2019, those who treated with IVCY for interstitial lung disease (ILD) were consecutively registered. All patients received IVCY six times. Nailfold capillary abnormalities on eight fingers including both second to the fifth fingers were observed with a nailfold videocapillaroscopy (NVC). Each finger was evaluated for enlarged capillary, giant capillaries, hemorrhage, loss of capillary, disorganization of the vascular array, and capillary ramification. Quantitative scoring was performed on a scale of 0 to 3 in accordance with the ratio of each of them. NVC tests were evaluated before IVCY treatment intervention and after IVCY. In all cases, the evaluation of NVC after IVCY treatment was performed 6 months after the administration day. Skin changes were evaluated by modified Rodnan's total skin thickness score (mRSS) at performing NVC. Anti-centromere antibodies, anti-Scl-70 antibodies, anti-RNA polymerase III, and anti-RNP antibodies were measured. Pulmonary function tests (PFTs) including forced vital capacity (FVC) and diffusing capacity of the lung carbon monoxide (DL_{CO}) were performed before and after IVCY. The statistical significance of the differences between means of two groups was evaluated by paired t-test. A p level of 0.05 or less was considered statistically significant.
Results: Five patients were included. The mean age was 59 years and 4 patients were female (80%). High dose corticosteroids were used in 2 patients (40%). Anti-RNA polymerase III was positive in 2 patients (40%), anti-Scl-70 antibody was positive in 1 (20%), and negative test for any specific antibodies was in 2 (40%). Changes in NVC scores, which were total scores of 8 fingers, were as follows: Enlarged; 13.2±4.8 to 6.4±5.9 (p=0.018), Giant; 7.0±5.7 to 1.6±1.1 (p=0.0314), Hemorrhage; 8.4±6.2 to 3.2±2.3 (p=0.0274), Loss; 4.0±2.5 to 0.6±1.3 (p=0.0288), Disorganization; 0.6±0.9 to 1.0±1.0 (p=0.7065), Ramification; 0.6±0.9 to 0.8±1.8 (p=0.5730). (Table) After IVCY treatment, mRSS reduced in 4 cases (80%). Changes in mRSS scores were as follows: 18.8±8.3 to 12.4±13.3 (p=0.0677). The cases with improved mRSS and those with improved NVC findings were consistent. The mean FVC before and after IVCY was 2077 ml and 2062 ml, respectively. The mean DL_{CO} before and after IVCY was 9.88 mL/min/mmHg and 9.58 mL/min/mmHg, respectively.
Conclusion: Nailfold capillary abnormalities in patients with SSc could be improved in half a year with IVCY. Especially, early phase elements including enlargement, giant, and hemorrhage were specifically reversible.

Table.

No.	*(E)*	*(G)*	*(H)*	*(L)*	*(D)*	*(R)*	*mRSS*
1	21→14	16→3	19→7	0→0	0→2	0→0	14→9
2	12→3	4→2	6→1	4→0	2→1	1→0	15→1
3	14→11	8→2	6→2	7→0	0→0	0→4	10→5
4	10→4	6→1	8→3	4→3	0→2	2→0	25→12
5	9→0	1→0	3→3	5→0	1→0	0→0	30→35
mean ± SD	13.2±4.8	7.0±5.7	8.4±6.2	4.0±2.5	0.6±0.9	0.6±0.9	18.8±8.3
	6.4±5.9	1.6±1.1	3.2±2.3	0.6±1.3	1.0±1.0	0.8±1.8	12.4±13.3
p-value	0.018	0.0314	0.0274	0.0288	0.7065	0.5730	0.0677

E: enlarged, G: giant, H: hemorrhage, L: loss, D: disorganization, R: ramification.
The table shows the total of eight points for each finding in the NVC test. The previously described values are before treatment and the later values are after treatment.

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AB0613 AUTONOMIC NEUROPATHY AND ITS PREDICTORS IN SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc), a chronic autoimmune disease, is associated with autonomic neuropathy[1]. Autonomic neuropathy, especially cardiovascular autonomic neuropathy (CAN) is significant risk predictor of sudden cardiac death. However, its relationship with disease specific measures remains unexplored in SSc.
Objectives: To assess cardiovascular autonomic neuropathy and sudomotor function and its predictors in systemic sclerosis.
Methods: In this cross-sectional study, 16 SSc patients meeting the 2013 European League Against Rheumatism (EULAR) and American College of Rheumatology (ACR) classification criteria and 15 age and sex-matched healthy controls were recruited. Cardiovascular autonomic function assessed by five cardiovascular reflex tests according to Ewing. Peripheral sympathetic autonomic function assessed by FDA approved Sudoscan (Impeto Medical, Paris) through measurement of electrochemical skin conductance. Disease-specific measures (Disease duration, Modified Rodnan Skin Score (mRSS), EUSTAR activity score), and inflammatory measures (ESR, CRP) were determined. Quality of life measured by Scleroderma Health Assessment Questionnaire (SHAQ).
Results: Systemic sclerosis patients had significantly impaired parasympathetic [Heart rate response to deep breath (HRD) (Fig. 1A), Heart rate response to standing (HRS) (Fig. 1B) and Heart rate response to valsalva manoeuvre (Fig. 1C)] and symapathetic [BP response to hand grip (BPH) (Fig. 1D)] function as compared to healthy controls. Scleroderma patients had significantly impaired sudomotor function ($p<0.05$) as compared to healthy controls. Levels of mRSS, EUSTAR score, ESR, CRP and SHAQ were significantly higher in SSc patients as compared to healthy controls ($p\leq0.05$). Parasympathetic (HRD & HRS) dysfunction inversely correlated with ESR, CRP and mRSS. Sudomotor function positively correlated with mRSS, disease duration and CRP.
Conclusion: CAN and Sudomotor function are significantly impaired in SSc. Parasympathetic dysfunction is more pronounced than sympathetic dysfunction in SSc. CAN and Sudomotor dysfunction are associated with disease-duration, skin-score, ESR and CRP. These could serve as potential predictors of Cardiovascular Autonomic neuropathy and sudomotor dysfunction in SSc.

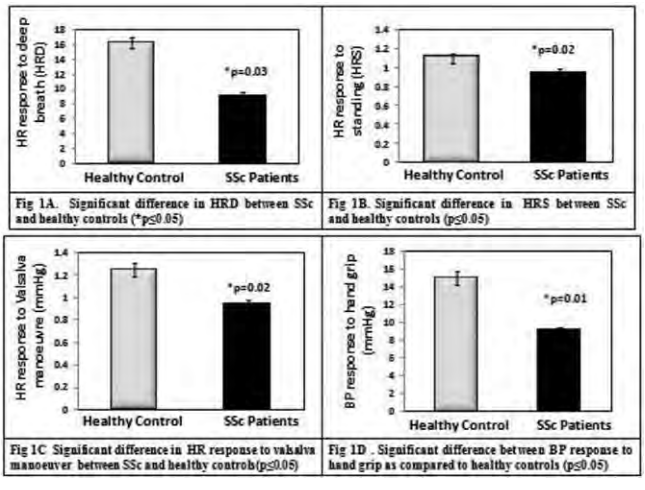


Fig 1A. Significant difference in HRD between SSc and healthy controls (*p≤0.05)
Fig 1B. Significant difference in HRS between SSc and healthy controls (p≤0.05)
Fig 1C Significant difference in HR response to valsalva manoeuver between SSc and healthy controls(p≤0.05)
Fig 1D . Significant difference between BP response to hand grip as compared to healthy controls (p≤0.05)

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Acknowledgments: None
Disclosure of Interests: None declared
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AB0614 METHOTREXATE DOESN'T LOWER THE RISK OF DEVELOPING INTERSTITIAL LUNG DISEASE IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES WITH JO-1 ANTIBODIES.

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Background: In patients with idiopathic inflammatory myopathies (IIM) most commonly found autoantibody against histidyl-tRNA synthetase (anti-Jo-1) is associated with development of interstitial lung disease (ILD), which has been recognized as a serious mortality factor.
Objectives: To assess if methotrexate as an initial steroid sparing agent lowers the risk of developing ILD in anti-Jo-1 positive patients diagnosed with IIM.
Methods: Medical records of IIM patients treated in a referral clinic in capital city of Poland between 2008 and 2018 were reviewed. Inclusion criteria were: fulfillment of ACR/EULAR 2017 classification criteria for IIM, positivity of anti-Jo-1 antibodies in the EUROLINE test, introduction of corticosteroids equivalent to ≥0,5mg of prednisone. Exclusion criteria: insufficient data on disease course, history of IIM <18 months.
Results: 29 patients were included for this analysis. ILD was present at the onset in 52% (n:15) patients. Other 14 patients were treated initially with corticosteroids ≥0,5mg/kg along with methotrexate up to 25mg/week. In all 14 patients methotrexate was well tolerated and led to successful reduction of steroid dose. However, ILD attributed to the primary disease appeared in follow up in 50%(n:7) of these patients (medium 36 months), which resulted in alteration of treatment. In 7 patients ILD didn't develop.
Conclusion: Our study shows that methotrexate in dose up to 25mg/week doesn't lower the risk of developing ILD in Jo-1 positive IIM patients in the long term suggesting that other medication should be used as a first line treatment for this group.
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Disclosure of Interests: None declared
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AB0615 MORTALITY AND CAUSES OF DEATH AMONG ROMANIAN SYSTEMIC SCLEROSIS PATIENTS

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Background: Systemic sclerosis (SSc) is associated with an increased risk of death compared to the general population. Survival in SSc patients has improved significantly over the last 20 years with a decrease in renal involvement as a cause of early death and an increase in death caused by cardiopulmonary involvement (1,2). Causes of death in SSc patients have not been described in a Romanian cohort so far.
Objectives: To study the causes of death in patients with SSc prospectively followed-up from 2002 to 2018 in a single tertiary centre from Romania.
Methods: The cohort consists of 197 patients who fulfill the American College of Rheumatology /EULAR 2013 criteria for SSc. We examined the data of patients who had died during follow up. Patients were reviewed at least twice a year and the cause of death was classified as SSc-related or nonSSc-related. SSc-related deaths were then attributed to the major organ involved. A univariate Cox proportional hazard (PH) regression was used to examine the association between each variable and mortality. Variables reported in the literature to associate with mortality were considered in the multiple Cox PH regression model.
Results: Of 197 SSc patients (87.8% females), 47.7% had diffuse SSc and 52.2% had limited SSc. The mean age at diagnosis was 47 (SD 12) years and mean follow up duration was 6.75 years. There were 41 deaths (20.8%). Survival rate was substantially lower in men (P <0.003). The mean age at the time of death in those with diffuse SSc was lower compared to limited SSc (55.8 years vs 68.7 years). Sixty percent of deaths were SSc-related (pulmonary cause[n=11], cardiac cause[n=6], gastrointestinal involvement [GI, n=3], renal crisis [n=2] and others [n=4]). Deaths no related to SSc were associated with cancer and infections. Age at onset of Raynaud phenomenon [HR 1.05], male gender [HR 3.41], diffuse SSc [HR 0.48], presence of tendon friction rub [HR 4.54], digital ulceration [HR 3], esophagitis [HR 2.07] and cardiovascular involvement [HR 3.68], use of corticosteroids[HR 2.13] and cyclophosphamide [HR 2.02] were associated with poor prognosis in multivariate analysis.
Conclusion: In our cohort the main causes of death were lung and cardiovascular involvement. Deaths occurred early after the onset of the disease and the survival rate was significantly reduced among men. Multivariate analysis showed that age at onset of Raynaud phenomenon, male gender, diffuse disease form, presence of tendon friction rub, digital ulceration, esophagitis and cardiovascular history, use of corticosteroids and cyclophosphamide were independently associated with mortality.
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Disclosure of Interests: None declared
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AB0616 REDUCED BONE MINERAL DENSITY IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES: A LONGITUDINAL STUDY

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Background: Reduced bone mineral density (BMD) leads to fragility fracture which is associated with a significant morbidity and excess mortality [1,2]. Patients with idiopathic inflammatory myopathies (IIM) should be at a heightened risk of reduced BMD as a result of the systemic inflammation, reduced mobility and corticosteroid use [3]. A previous cross-sectional study demonstrated a high prevalence of osteoporosis (23.7%) and osteopenia (47.4%) in a cohort of IIM patients [4]. However, longitudinal data are lacking.
Objectives: To assess the BMD of IIM patients longitudinally and to investigate the factors associated with accelerated bone loss.
Methods: This is a single centered observational study. Existing adult Chinese patients with IIMs who had serial BMD measurements done were recruited. The diagnosis of IIMs was based on the Bohan and Peter's criteria with definite or probable cases being included [5]. Patients with clinically amyopathic disease must have the typical Gottron's papules or heliotrope rash as determined by rheumatologists or dermatologists, and with no symptoms or signs of muscle involvement according to Sontheimer [6]. BMD was measured by dual energy X-ray absorptiometry (DEXA). Clinical variables thought to be associated with bone health were documented.
Results: All together 28 patients were studied. The mean age of the patients at disease onset was 46.1 years (S.D. 12.2). There was a female predominance (92.9%). The subgroups of IIMs were: dermatomyositis (39.3%), polymyositis (25.3%), clinically amyopathic dermatomyositis (21.4%) and immune mediated necrotising myopathy (14.3%). Only a minority of the patients smoked (7.1%) and none of them drinks regularly. About one fifth of the patients were underweight. All patients have been exposed to systemic corticosteroid, while 82.1% of them were still on it between the two scans with 32.1% even on high dose (>0.5mg prednisolone/kg/day). Three out of the 28 patients (10.7%) was found to be osteoporotic at baseline and 17 patients (60.7%) were osteopenic. Follow-up DEXAs were performed mostly 5 to 10 years after the initial scan. Despite 8 patients (28.6%) were given active anti-osteoporotic medications, the bone health deteriorated significantly. The mean baseline neck of femor BMD dropped from 0.711 to 0.657 g/cm2 (p=0.042) on follow-up, while the total

lumbar BMD from 0.951 to 0.905 g/cm2 (p=0.036). The T-score in 11 patients (39.3) reached osteoporotic range at the second DEXA. Together with the patients with osteopenia, 78.6% of the IMM patients had reduced BMD at the follow-up scan. Actually, 5 patients (17.9%) already had one episode of fragility fracture. The use of high dose corticosteroid in between the 2 scans was found to be associated with a greater degree of mean BMD loss in the hip (-0.171 vs -0.007 g/cm2, p=0.007).

Conclusion: Reduced BMD is prevalent in patients with IIM. Follow-up study revealed significant worsening of bone health. High dose corticosteroid use might be especially detrimental. Liberal assessment of BMD and use of anti-osteoporotic drugs in IIM patients are advisable. Prompt use of steroid-sparing agents to minimize steroid exposure may also be helpful.

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AB0617 OPTICAL COHERENCE TOMOGRAPHY IN THE ASSESSMENT OF SKIN FIBROSIS IN SYSTEMIC SCLEROSIS: A CROSS-SECTIONAL STUDY

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Background: Previous studies have shown that Optical Coherence Tomography (OCT) is a reliable biomarker of skin fibrosis and significantly correlates with the severity of the skin involvement in Systemic Sclerosis (SSc) [1,2].

Objectives: Aim of this cross-sectional study was to evaluate the performance of skin OCT to discriminate between SSc and healthy controls (HC) and to compare results with the current gold standard, the modified Rodnan skin score (mRss), in a different SSc study cohort.

Methods: Dorsal forearm skin of consecutive diffuse cutaneous SSc (dcSSc) patients and matched-HC was scanned by an investigator blinded to the clinical data using Vivosight scanner (Michelson Diagnostics, Kent, UK). Minimum Optical Density (MinOD), Maximum OD (MaxOD) and OD at 300 micron-depth (OD300) were measured. Clinical involvement was assessed by a blinded operator using the mRss and results were compared with imaging data. Statistical analysis was performed using GraphPad Prism software V.7.0.

Results: A total of 88 OCT images were obtained from 22 dcSSc patients [20 Female, mean age 49 (±11) years, 12 with < 5 years disease duration) and 22 HC (20 Female, mean age 50.7 (±6.7) years]. All OCT measures (MinOD, MaxOD and OD300) were significantly lower in SSc patients than in HC (p=0.011, p<0.0001, p<0.0001 respectively). MaxOD and OD300 were significantly different between the four groups (0-3) of patients based on the mRss at the site of analysis (p=0.035, p=0.001 respectively). Skin OCT showed a good performance in discriminating SSc skin vs HC (overall AUC 0.72, 0.8 and 0.89 for MinOD, MaxOD and OD300 respectively).

Conclusion: These results confirm in a cohort different from those of the previous studies that skin OCT is able to reflect the severity of skin involvement in SSc. Longitudinal studies are needed to validate its potential as surrogate outcome measure of skin fibrosis in SSc patients.

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AB0618 COMPREHENSIVE ANALYSIS OF AUTOANTIBODY PROFILE IN A TURKISH SYSTEMIC SCLEROSIS COHORT

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Background: Serum autoantibodies closely reflect patterns of organ involvement and disease progression in systemic sclerosis (SSc). The entire autoantibody profile is less well defined in many cohorts and the data regarding their clinical associations and frequencies is limited.

Objectives: To determine the autoantibody profile of patients with SSc, as well as their clinical associations, in well-characterized inception- cohort with disease duration less than 3 years.

Methods: Serum samples of 100 patients out of 105 enrolled in the study were analyzed for ANA patterns with indirect immunofluorescence (IIF) assay using HEp-20-10/primate liver mosaic IIFT kit. Sera of 96 patients were subjected to commercial line immunoassay to quantify autoantibodies against 13 different autoantigens.

Results: 92 (92%) out of 100 patients were positive for ANA by IIF (Table 1). The speckled staining was the most pattern followed by nucleolar in 10 patients, centromere in 4, reticular in 1, nuclear in 2 and homogenous in 1. All patients (n= 96) patients were positive for at least 1 autoantibody by immunoblotting (Table 2). Twenty-two (49%) of patients with antiTopo I, 12 (44%) of the patients with antiCENP and 4 (22%) of the patients with antiRNAPIII were single positive. There was no difference in terms of the clinical findings when the patients with single and coexpression of these antibodies were compared. The distributions of the most frequent autoantibodies are shown in Figure 1. Interstitial lung disease was more frequent in the patients positive for anti-Topo I (78.8%) and anti-RNAPIII (27.3%). One of the two patients with breast cancer was anti-RNAPIII positive and none of the patients have diagnosed scleroderma renal crisis. Anti-Topo I was more common in patients with dcSSc (75%) and anti-CENP in lcSSc (46.4%).

Table 1. Demographic, clinical and laboratory characteristics of the SSc patients.

Sex	
Female N, %	91 (86.7%)
Male N, %	14 (13.3)
Female-to-male ratio	
Age, mean±SD years	48.6±12.7
Disease duration, mean±SD years	2±1.4
Disease classification N, %	
Diffuse	39 (36.5%)
Limited	65 (62.5%)
Sine scleroderma	1 (1%)
Interstitial lung disease	37 (34.3%)
Pulmonary arterial hypertension	3 (2.8%)
Scleroderma renal crisis	0
Digital ulcer	14 (13.3%)
Raynaud phenomenon	105(100%)
Telengiectasia	31 (28.8%)
Calcinosis	1 (1%)
Malignancy	3 (2.9%)
Antinuclear antibody profile N*, %	
Positive	92 (92%)
Staining pattern	
Speckled	65 (65%)
Nucleolar	13 (13%)
Centromere	29 (29%)
Homogeneous	3 (3%)
Reticular	3 (3%)

Table 2. Numbers and combinations of autoantibodies identified in the 96 SSc patients.

	Topo-I	CENP	RNAP III	Fibrillarin	NOR90	Th/To	Pm/Scl	Ku	PDGFR	Ro52
Topo-I	22	1	7	0	1	5	9	5	0	7
CENP		12	2	0	2	2	2	2	0	11
RNAPIII			4	0	1	2	1	3	0	7
Fibrillarin				0	0	0	0	0	0	0
NOR90					0	1	1	0	0	2
Th/To						0	4	2	0	2
Pm/Scl							4	3	0	6
Ku								1	0	2
PDGFR									0	0
Ro52										2
Single positive	22	12	4	0	0	0	4	1	0	2
Total	45	27	18	0	5	8	17	9	0	24

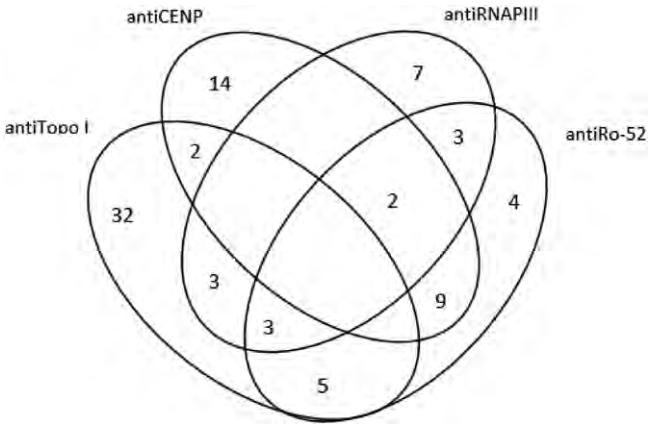


Figure 1. Diagram of disease-related antibodies against the four main autoantibodies [anti-centromere (antiCENP) anti-Topoisomerase I (antiTopo I), anti-RNA polymerase III (antiRNAP III) and anti-Ro52).

Conclusion: We presented the clinical and serologic features of the Turkish SSc patients from a new inception cohort. Clinical features of the SSc patients with single or multiple antibody positivity were not different.

References: None

Disclosure of Interests: None declared

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AB0619 PROGNOSTIC FACTORS OF PATIENTS WITH ANTI-MDA5 ANTIBODY-POSITIVE DERMATOMYOSITIS COMPLICATED WITH INTERSTITIAL PNEUMONIA -A JAPANESE SINGLE CENTER STUDY-

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Background: Anti-melanoma differentiation-associated gene 5 antibody (anti-MDA5 Ab)-positive dermatomyositis (DM) is frequently associated with rapidly progressive interstitial pneumonia (RPIP), whose prognosis is assumed to be poor[1]. Although outcome of DM-RPIP has been reported to be improved by early immunosuppressive therapy, we still experience the cases with severe outcome. Only several reports mentioned the prognostic factors and they have not been fully elucidated.

Objectives: To identify the predictors of prognosis in patients with anti-MDA5 Ab-positive DM associated with interstitial pneumonia (DM-IP).

Methods: Anti-MDA5 Ab-positive DM-IP patients admitted to Fujita Health University Hospital between January 2010 and October 2019 were consecutively included and stratified into 2 groups, the survived and the deceased groups. DM was diagnosed according to the criteria proposed by Bohan and Peter[2]. Clinically amyopathic DM was diagnosed according to the criteria proposed by Sontheimer [3]. Diagnosis of IP was based on findings of high resolution CT scan (HRCT). The definition of RPIP was rapid exacerbation of hypoxemia or HRCT findings in a period of days to one month after the onset. Clinical features and prognosis of the patients were collected retrospectively and compared between groups. Candidates of predictors are extracted by the univariable analysis using Fisher's exact test for dichotic parameters and Wilcoxon signed-rank test for continuous parameters and multivariable analysis using logistic regression analysis. Receiver operating characteristic (ROC) curve analysis was examined to obtain the cut-off level. Survival was examined using Kaplan-Meier method and Log-rank test.

Results: Twenty-one patients were involved. Eight were deceased and 13 were survived. The deceased group had a higher ratio of male (75% versus 25%, p= 0.018). All deceased cases were with RPIP and 67 % in the survived cases. Levels of serum ferritin (4490 versus 646 ng/mL, p = 0.0026), CRP (2.1 versus 0.9 mg/dL, p = 0.0490), CK (1150 versus 290 U/L, p = 0.017), AST (194 versus 108 U/L, p = 0.025) and LDH (674 versus 368 U/L, p = 0.011) were higher in the deceased group. Interestingly, skin ulcers were tended to be more frequent (12.5% versus 87.5%, p= 0.0587), and anti-SS-A antibody was also more frequently detected (14.3% versus 85.7%, p=0.0072) in the survived group. Using ROC analysis cut-off values were 963 ng/mL for serum ferritin level (sensitivity 100%, specificity 83%), 0.7 mg/dL for CRP (sensitivity 75%, specificity 69%), 308 U/L for CK (sensitivity 88%, specificity 77%), 62 U/L for ALT (sensitivity 100%, specificity 62%), and 454 U/L for LDH (sensitivity 88%, specificity 77%). Patients were divided into two groups based on these cut-offs or based on dichotic parameters and survival was examined between 2 groups. Except CRP and anti-SS-A antibody, survival was significantly worse in parameter-positive or higher groups. Interestingly, anti-SS-A antibody-positive group had better outcome compared with those without.

Conclusion: In our analysis, novel candidates such as serum CK, AST, and LDH levels were newly extracted and parameters previously reported was also included and those were also associated with the clinical outcome. In addition, anti-SS-A antibody was identified as a novel protective factor associated with a good outcome.

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AB0620 EFFECTIVENESS OF RITUXIMAB IN PATIENTS WITH EARLY DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS. A MULTICENTER ANALYSIS.

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Background: Rituximab (RTX) is effective in improving skin affection in patients with diffuse cutaneous systemic sclerosis (DcSSc). However, there are few data on early use of this drug.

Objectives: To evaluate RTX effectiveness for skin disease in patients with DcSSc of less than 3 years of evolution.

Methods: Multicenter, observational and retrospective study. Patients with DcSSc starting RTX within 3 years since first non-Raynaud symptom were recruited. Demographic variables, time of disease duration at the beginning of RTX, immune pattern and time on RTX treatment were collected. Effectiveness was defined as modified Rodnan skin score (mRSS) improvement. Evaluations were done by the same experienced rheumatologist. Patients subjective perception of skin hardening and/or tightness was evaluated. mRSS changes from baseline to 6 and 12 months after RTX beginning and, later on, to the last available observation were analysed using Wilcoxon test. Statistical analysis was performed with SPSS 20.0.

Results: 11 patients (8 women) were recruited from 2 university hospitals. Median age was 48 years (IQR 22). Median time since diagnosis to RTX beginning was 12 months (IQR 8). 5, 3 and 2 patients presented ATA +, RNPIII + and Ro-52 +, respectively. Median duration of RTX treatment was 12 months (IQR 68). Median baseline mRSS was 15.5 (IQR 18). Median mRSS after 6 and 12 months of RTX treatment and at last available mRSS evaluation was 15 (IQR 13), 14.5 (IQR 13) and 11 (IQR 16), respectively. mRSS showed statistically significant improvement at 6 (29%, IQR 37) and 12 months of RTX treatment (35%, IQR 34) and, thereafter, at last available observation (39%, IQR 51), compared to basal mRSS. Most patients reported subjective improvement at 6 (9 of 10

patients) and 12 months (6 of 7), and at last available evaluation (6 of 8); all other patients reported stability.

Conclusion: In our experience, patients with DcSSc seem to benefit of early RTX treatment. Improvement may be seen as early as 6 months and seems to reach a plateau at 12 months.

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AB0621 TOLERABILITY AND SAFETY OF ACETYLSALICYLIC ACID IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Systemic Sclerosis (SSc) is characterized by an increased incidence of macro- and microvascular complications. Current evidences on efficacy, safety and tolerability of acetylsalicylic acid (ASA) in SSc patients are limited, and the indication to this treatment is based on the experience of each single centre or physician. Esophagus and stomach are the portions of the digestive tract that are more frequently affected by adverse events due to ASA exposure.

Objectives: We evaluated the incidence of adverse events associated with low-dose ASA treatment in a cohort of patients affected by SSc.

Methods: Demographic data and disease features of 302 patients affected by SSc treated with low-dose ASA were collected and patients were followed-up for a median period of 6.9 years (range: 0-20 years). The proportion of patients taking ASA for secondary prevention for cardiovascular disease was also noted. The incidence of discontinuation of the drug, gastrointestinal intolerance, bleeding and death in the observation period was recorded.

Results: Patients had a median age of 54.0 years (19.6-89.4); 91.9% were female, 13.2% were smokers and 44.0% had a BMI≥30Kg/m^2. The prevalence of ischemic heart disease, peripheral vascular disease and stroke was of 8.6%, 5.3% and 3.3%, respectively; 48.7% of the patient took ASA in primary cardiovascular prevention. Therapy started after a median disease duration of 4.8 years (range: 0.0- 30.1 years) since the first non-Raynaud symptom and 56.6% of patients had an early disease (less than three years of disease duration). During the observation period, 30 patients (14.3 per 1000 person-years) discontinued ASA after an average period of assumption of 4.6 years (range: 0.3-18.0 years). The main adverse events were heartburn, dyspepsia and hematochezia, recorded in 18 patients (8.6 per 1000 person-years). Eight of them (3.8 per 1000 person-years) had evidence of digestive tract bleeding. Five patients (2.4 per 1000 person-years) discontinued ASA due to recurrent epistaxis. Twenty-eight patients (13.4 per 1000 person-years) died in the follow-up period, 16 of these (7.6 per 1000 person-years) because of SSc-related causes. None of them had evidence of major bleeding. We used Kaplan-Meier analysis to evaluate the incidence of ASA discontinuation. The history of digital ulcers (Log rank test X^2 4.7, p=0.037) and male sex (Log rank test X^2 4.3, p=0.03) were associated with a higher cumulative ASA discontinuation rate due to gastrointestinal intolerance.

Conclusion: In our cohort of SSc patients, ASA resulted safe and well tolerated in most cases, despite the risk of gastroesophageal abnormalities due to disease. Although this comforting results, taking in account the lack of controlled-randomized trials about efficacy and safety, the choice to start antiplatelet therapy with ASA should be mandatorily preceded by a careful evaluation of risks and benefits. Furthermore, an attentive monitoring for possible adverse effects is needed during ASA treatment. Patients with digital ulcers and male sex could present less drug tolerability.

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Disclosure of Interests: Lucrezia Verardi: None declared, Enrico De Lorenzis: None declared, Gerlando Natalello: None declared, Laura Gigante: None declared, Umberto La Porta: None declared, Elisa Gremese Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Merck Sharp & Dohme, Novartis, Sanofi, UCB, Roche, Pfizer, Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Merck Sharp & Dohme, Novartis, Sanofi, UCB, Roche, Pfizer, Silvia Laura Bosello Speakers bureau: Abbvie, Pfizer, Boehringer

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AB0622 ASSOCIATIONS WITH DIGITAL PITTING IN SYSTEMIC SCLEROSIS: A RETROSPECTIVE ANALYSIS.

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Background: Digital pitting, the loss of tissue at the fingertip, is a cardinal feature of systemic sclerosis (SSc), contributing 3 of the 9 required points to fulfil the 2013 ACR/EULAR classification criteria. However, research into digital pitting has been scarce, despite it being painful and impacting on hand function.

Objectives: To identify factors associated with digital pitting in patients with SSc.

Methods: This was a retrospective analysis of data from patients with SSc attending a tertiary referral centre. Patients were subdivided into those with and without digital pitting, as recorded at their last documented attendance. The following variables were analysed: age, gender, age at Raynaud's onset, age at SSc onset, limited/ diffuse cutaneous subtype, history of intravenous (IV) vasodilators, amputations, debridements and autoantibody status (anti-RNA polymerase, anti-Scl70, anti-centromere and anti-RNP).

Results: Data were available from 713 patients with SSc. Digital pitting was present in approximately half of these patients (n=362, 51%). Table 1 summarises their characteristics.

Table 1. Descriptive statistics of patients with and without digital pitting

	Digital Pitting (n=362)	No Digital Pitting (n=351)
Age, mean (SD)	67.1 (14.5)	66.5 (13.6)
Females, n (%)	287 (79.3)	301 (85.8)
Age at Raynaud's onset/ Age at SSc onset, median (IQR)	39.3 (25.2, 49.3)/ 41.4 (26.2, 52.5)	47.5 (35.3, 57.3)/ 52.5 (41.9, 60.4)
Limited/ Diffuse subtype, n (%)	276/85 (76.5/ 23.6)	257/93 (73.6/ 26.6)
History of IV vasodilators, n (%)	167 (46.4)	52 (14.9)
History of amputations, n (%)	52 (14.4)	5 (1.4)
Debridements, n (%)	72 (20.2)	18 (5.1)
Autoantibody status, n (%): Anti-RNA polymerase/ Anti-Scl70/ Anti-centromere/ Anti-RNP	13 (6.2)[1]/ 61 (17.1)[3]/ 152 (42.6)[5]/ 15 (4.3)[7]	34 (14.0)[2]/ 41 (12.0)[4]/ 120 (35.4)[6]/ 22 (6.5)[8]

Denominator populations [1]210, [2]246, [3]357, [4]345, [5]357, [6]341, [7]352, [8]341

From the univariable analysis (Table 2), gender (female, p=0.02), age at Raynaud's onset (p<0.001), age at SSc onset (p<0.001), IV vasodilators (p<0.001), amputations (p<0.001), debridements (p<0.001), anti-RNA polymerase (p=0.01), anti-Scl70 (p=0.05) and anti-centromere (p=0.05) were found to be significantly associated (anti-RNA polymerase negatively (p=0.20)) with digital pitting (p≤0.05). Further analysis adjusting the p value for multiple testing (Bonferroni adjustment, p≤0.0036) found age at Raynaud's onset, age at SSc onset, history of IV vasodilators, amputations and debridements to be significantly associated with digital pitting.

Table 2. Univariable logistic regression

	Odds Ratio	95% Confidence Interval	P value[1]	Number of patients in each analysis
Age	1.000	0.998 to 1.003	0.62	713
Female	1.116	1.015 to 1.231	0.02	713
Age at Raynaud's onset	1.008	1.007 to 1.010	<0.001	713
Age at SSc onset	1.004	1.003 to 1.005	<0.001	713
Limited/ Diffuse subtype	1.039/ 1.041	1.049 to 1.127/ 1.046 to 1.139	0.39/ 0.35	710/ 711
History of IV vasodilators	1.448	1.336 to 1.553	<0.001	710
History of amputations	1.553	1.363 to 1.768	<0.001	713
Debridements	1.405	1.259 to 1.568	<0.001	707
Autoantibody status: Anti-RNA polymerase/ Anti-Scl70/ Anti-centromere/ Anti-RNP	1.223/ 1.111/ 1.081/ 1.114	1.052 to 1.419/ 1.000 to 1.234/ 1.002 to 1.162/ 1.310 to 1.786	0.01/ 0.05/ 0.05/ 0.20	456/ 702/ 698/ 693

[1]p≤0.05

Conclusion: The results from this exploratory study in a large cohort of SSc patients provide valuable insights into factors associated with digital pitting. Patients with digital pitting often have an earlier onset of Raynauds and of SSc and significantly more debridements/amputations, suggesting that digital pitting is associated with vascular disease severity. Our findings indicate the need for further research investigating pathophysiology of digital pitting, to inform development of preventative treatment strategies.
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AB0623 RATE AND PREDICTIVE FACTORS ASSOCIATED WITH SUSTAINED REMISSION IN IDIOPATHIC INFLAMMATORY MYOSITIS

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Background: Idiopathic inflammatory myositis (IIM) is a group of heterogeneous connective tissue diseases, characterised by chronic muscle inflammation, myositis-specific or myositis-associated autoantibodies and different extra-muscular features. Achieveing low disease activity or remission in patients with IIM has proven to be difficult due to the wide clinical spectrum of the different IIM types.
Objectives: To retrospectively assess any predictive factors for sustained remission in IIM patients
Methods: We retrospectively analyzed data taken from medical charts, which included age at disease onset, gender, laboratory data as well as clinical features present at onset, organ involvement and treatment history. A total of 151 adult patients with IIM followed-up for > 1 year were retrospectively enrolled. Remission was defined as no clinical and laboratory evidence of disease activity persistent for more than 6 months during follow-up, while undergoing myositis therapy or under no medication. The remission of cutaneous involvement was defined as no current activity of skin rash, absence of Gottron's papules as well as heliotrope rash and erythema, whereas the remission of pulmonary involvement was considered as no requirement for intensification of immunosuppressive therapy during follow-up. Likewise, absence of muscle weakness or hyposthenia was taken into account for evaluating muscle involvement. Moreover, the clinical features were accompanied by normalization of myogenic enzymes such as creatine kinase (CK) and lactate dehydrogenase levels.
Results: Among all 151 patients, 89 (58.9%) patients achieved sustained remission. By univariate analysis, overlap myositis (7.9% vs 27.4%; p=0.003; OR:0.22), cancer-associated myositis (CAM) (7.8% vs 19.35%; p=0.046; OR:0.3), as well as the presence of anti Ku (3.37% vs 12.9%; p=0.05; OR:0.23) and anti TIF-1 gamma (1.1% vs 8%; p=0.043; OR:0.13) antibodies and polyarthritis (11.2% vs 24.19%; p=0.045; OR: 0.397) at onset were significantly associated with active IIM, not achieving remission.
Out of 89 patients in remission, 79 (88.8%) achieved long-term sustained remission, lasting at least 2 years, whereas 10 patients (11.2%) showed relapse. Most of relapsed patients showed a relapse/remitting disease, with no evident trigger for the relapse. We divided our cohort of 89 patients in remission in 2 subsets: 83 patients in remission undergoing therapy (93.3%) and 6 patients in drug-free remission (6.7%). No significant differences were found between two groups, except for younger age at onset (p=0.0002) found in patients achieving drug-free remission.
Conclusion: Sustained remission occurs in about one half of patients with IIM. The presence of anti Ku and anti TIF-1 gamma antibodies as well as polyarthritis at onset lowers the chance of achieving sustained remission. Younger age at diagnosis has proved to predict drug-free long-lasting remission.
Disclosure of Interests: None declared
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AB0624 PREDICTIVE PARAMETERS FOR DEVELOPMENT OF INTERSTITIAL LUNG DISEASE IN IDIOPATHIC INFLAMMATORY MYOSITIS

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Background: Idiopathic Inflammatory Myositis (IIM) is a group of heterogeneous connective tissue diseases, primarily characterized by chronic muscle inflammation as well as myositis-specific or myositis-associated autoantibodies and a spectrum of different extra-muscular features.
The most frequent organ involment in IIM is Interstitial Lung Disease (ILD), occurring in 5-80% of different IIMs cases and considered the hallmark of morbidity and mortality in patients with IIMs.
Objectives: To retrospectively assess the predictive factors for development of ILD in IIM patients
Methods: We retrospectively analyzed the prevalence of ILD in a single-center cohort of 165 IIM patients. Patient data was collected from clinical charts. ILD was diagnosed by chest X-ray scan and chest CT scan. All chest CT and chest X-ray scans available and performed at our hospital were consequently re-evaluated by our expert pneumologist for uniform evaluation.
Results: Myositis-related ILD (M-ILD) was found in 52 IIM patients (31.5%): 46.15% was affected by anti-synthetase syndrome (ARS), 21.15% by polymyositis (PM), 19.23% by dermatomyositis (DM) and 13.46% by overlap myositis. The pulmonary involvement was characterized by Non-specific interstitial pneumonia (NSIP) (30.6%), Unusual Interstitial Pneumonia (UIP) (38.77%), Bronchiolitis Obliterans with Organizing Pneumonia (BOOP) (20.4%), overlap NSIP/BOOP (4.1%) and Undetermined/Unspecific pattern (6.12%). Eighty four percent of M-ILD consisted of non-smokers and 69.23% presented with dyspnea at onset.
ILD was diagnosed in 90.38% of patients within the first year of IIM diagnosis (early onset ILD) and was associated with dyspnea and/or cough in 70.2% and 17% respectively. On the other hand, late onset ILD presented mostly with dyspnea and/or cough in 60% of cases and was significantly associated with anti-Ku antobodies.
At onset ILD was significantly associated with: ARS (p<0.0001; OR:12.98), anti-Jo-1 (p<0.0001; OR:6.1), anti-Ro (p=0.038; OR:2.2), mechanic's hands (p<0.0001; OR:10.41), arthritis (p=0.01; OR:2.58), polyarthritis (p=0.001; OR:4.578), dyspnea (p<0.0001; OR:9.66), and high levels of CPK (p=0.0001) and GOT (p=0.0146). By contrast, the following features: DM (p=0.012; OR:0.36), facial rash (p=0.003; OR:0.31), anti-NXP-2 (p=0.019; OR<0.0001), anti-PL-12 (p=0,03; OR<0.0001) and myositis (p<0.0001; OR:0.173) present at onset were less frequently associated with M-ILD.
At multivariate analysis M-ILD was predicted by anti-Ro (p=0.0448), polyarthritis (p=0.0093) and dyspnea (p=0.0001) at onset. On the other hand, patients presenting myositis (p=0.0383) and facial rash (p=0.0398) at onset were less likely to developed M-ILD.
Conclusion: ILD occurs in about one third of patients with IIM, mostly affected by ARS. The presence of anti-Ro antibodies as well as polyarthritis and dyspnea at onset predict the development of ILD.
Disclosure of Interests: None declared
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AB0625 IS PULMONARY ARTERIAL HYPERTENSION, ASSOCIATED WITH SYSTEMIC SCLEROSIS REVERSIBLE?

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Background: Systemic sclerosis (SSc) is one of the frequent causes of the pulmonary arterial hypertension (PAH) which found in 6-15% patient with SSc. Patients with PAH, associated with SSc have a poorer prognosis than other forms of PAH. 6 World Symposium of PH lowered diagnostic cut-off to 21 mm Hg in hope of improved survival. PAH reversibility is described in congenital heart defects, HIV and some tumors
Objectives: The aim of the study to detect reversibility of PAH associated with SSc.
Methods: Hemodynamics (mean pulmonary artery pressure (MPAP), pulmonary artery wedge pressure (PAWP), cardiac output (CO) and pulmonary vascular resistance (PVR)), functional class (NYHA), 6-minute walk distance (6MWD), biomarkers and DLCO were assessed. Patients with pulmonary fibrosis and left heart diseases were excluded.
Results: The study includes 56 patients receiving start-up monotherapy with 1st generation PAH-specific drugs: bosentan (25 patients) and sildenafil (31 patients). The median age of the patients was 51.5 (37; 58) years. At the time of diagnosis, the MPAP in the sildenafil group was 49 (30; 50) mm Hg, bosentan - 50 (42; 56) mm Hg, differences not significant (p = 0.11). During observation against the background of sildenafil intake,

the MPAP decreased by -3 (-7; 0) mm Hg, bosentan -6 (-13; -2) mm Hg. Decreasing of MPAP ≤ 21 mm Hg was at seven patients receiving sildenafil. Initial hemodynamic values in this group of patients was MPAP 25 (21; 27) mm Hg., RAP 2 (1; 5) mm Hg, PAWP 7 (6; 10) mm Hg., CV 5.9 (4.7; 6.7) l/min, PVR 3.0 (1.5; 4.2) Wood Unit. Among patients taking sildenafil, there were seven who had MPAP less than 35 mmHg, and among patients taking bosentan, there were 4 patients with less than 35 mmHg. However, the decreasing was observed only group who received sildenafil. ROC – analysis shown that cut-off for reversible is 29 mm Hg (AUC 0,977, sensitivity 97%, and specificity 100%)

Conclusion: In patients with PAH, associated with SSc, on sildenafil treatment, at MPAP < 29 mm Hg reversibility is possible. Further study is required.

Disclosure of Interests: None declared

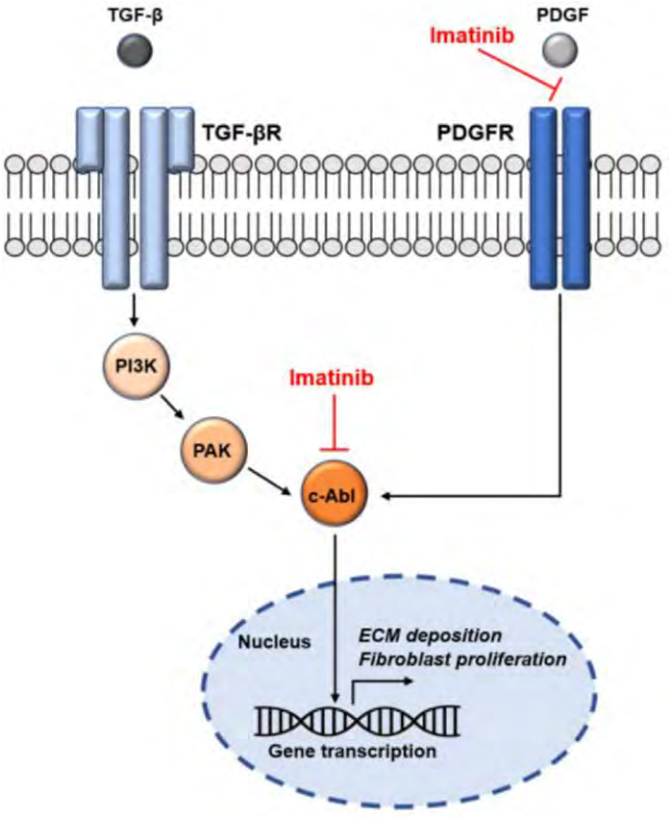
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AB0626

IMATINIB FOR THE TREATMENT OF SYSTEMIC SCLEROSIS: RATIONALE, CLINICAL EVIDENCE AND FUTURE DEVELOPMENT

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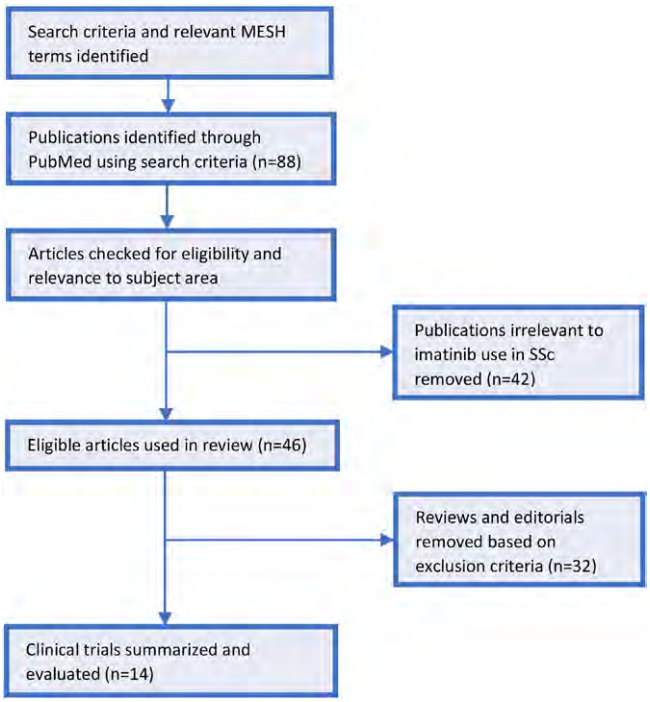
Background: Systemic sclerosis (SSc) is a chronic disorder of connective tissue affecting the skin and internal organs. The molecular mechanisms behind SSc are not entirely understood, but recent advances highlight key signalling pathways[1] (see Figure 1). Fibrosis disrupts tissue architecture resulting in organ dysfunction. This causes significant morbidity and mortality[1], therefore there is a clear need for identifying efficacious antifibrotic treatment.



Imatinib is a tyrosine kinase inhibitor with established use in some malignancies, and existing evidence that it can treat SSc[2].

Objectives: The aim of this literature review is to summarise the current evidence and future developments of imatinib as antifibrotic treatment in SSc.

Methods: PubMed headings "systemic sclerosis", "scleroderma", "imatinib" and synonyms were used. See Figure 2.



Results:

Lead author and year	Study design	Population	Intervention (imatinib dose given daily)	Results
Hinchcliff ME. 2016	Case study	1 female (F) with an 8-month history of diffuse cutaneous systemic sclerosis (dcSSc)	400mg	Severe adverse events (AEs)
Pope J. 2014	Early phase proof of concept trial	10 with dcSSc.	9 given 400mg, 1 placebo	Poor drug tolerability
Prey S. 2012	Double blind RCT	28 with SSc	15 given 400mg, 13 placebo	No improvement
Khanna D. 2011	Phase I/IIa pilot trial	20 with SSc	Up to 600mg	AEs present
Pope J. 2011	Double blind RCT	10 with SSc.	9 given 400mg, 1 placebo	No improvement, AEs present
Gordon J. 2014	Open label, single arm, extension phase clinical trial	17 with average disease duration of 3.5 years	100-400mg	↓ modified Rodnan skin score (mRSS)
Fraticelli P. 2014	Phase II pilot trial	30 with SSc	200mg	↑ lung function
Guo L. 2012	Case series	6 F, Chinese pts with SSc	200mg	↓ mRSS and ↑ lung function
Divekar AA. 2011	Single centre, open-label study	15 with SSc	100mg up to 600mg/day	↑ lung function
Spiera RF. 2011	1-year, phase IIa, single-arm, open-label clinical trial	30 with dcSSc	400mg	↓ mRSS and ↑ lung function
Freyhaus H. 2009	Case report	58yo F	400mg	↑ lung function
Chung L. 2009	Case report	2 with early dcSSc	200mg	↓ mRSS and ↑ lung function
Van Daele PL. 2008	Case report	69yo F	400mg	↓ mRSS and ↑ lung function
P. P. Sfikakis. 2008	Case report	24yo F	400mg	↓ mRSS and ↑ lung function

9 studies showed imatinib had positive efficacy in the treatment of SSc. 5 showed no improvement or adverse effects.

Conclusion: Overall, current evidence suggests that imatinib can be a useful drug to improve manifestations of SSc, for some. Despite inconclusive evidence, a dose-dependent relationship seems to exist for imatinib toxicities, with more research needed to ascertain a safe dose.

Gene expression profiles may distinguish patients that can benefit from imatinib[3]. Also, Notch signalling could be exploited to increase imatinib uptake into fibroblasts, thereby increasing efficacy[4].

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Acknowledgments: Skin Research Institute of Singapore

Disclosure of Interests: None declared

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AB0627 PROGNOSIS AND MORTALITY OF DERMATOMYOSITIS AND POLYMYOSITIS PATIENTS WITH MALIGNANCY

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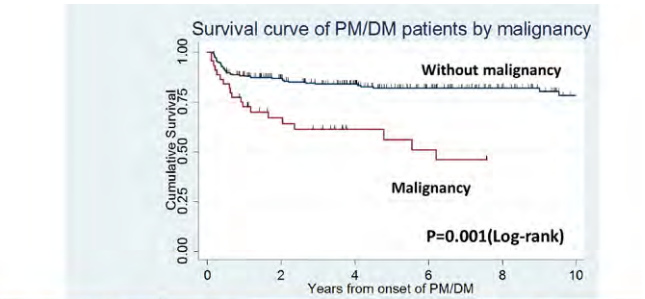
Background: Previous studies indicate that cancers in DM/PM patients are associated with increased mortality. Hence, identifying predictors of malignancy in PM and DM is crucial. However, few large series studies have reported prognostic and predictive factors of malignancy in patients with PM and DM. Moreover, in recent years, several published studies also allow us to better understand the clinical characteristics of malignancy in PM and in DM.

Objectives: To analyze the mortality and identify the major independent risk factors for death in patients with dermatomyositis/polymyositis (DM/PM) complicated with malignant tumor.

Methods: The clinical data of all patients with DM/PM in Peking University First Hospital from January 2007 to Jan 2019 were retrospectively reviewed. All patients were followed up to confirm whether they had malignant tumors. According to the statistics of the National Bureau of Statistics of China, the standard mortality (SMR) and life lost years (YLL) of patients with DM/PM were combined with malignant tumors. The Kaplan-Meier method was used to analyze the 10-year survival of DM/PM patients with malignant tumors. Cox multivariate regression was used to predict independent risk factors for DM/PM patients with malignant tumors.

Results: A total of 334 patients with dermatomyositis and 69 patients with polymyositis were enrolled in the study. The mean age of onset was 50.5 ± 14.8 years and 48.9 ± 16.1 years, with a median follow-up of 40.6 (11.6-77.6) months. Among them, 320 patients were successfully followed up, including 69 patients with death, 46 DM/PM with malignant tumors (38 with dermatomyositis and 8 with polymyositis). The average age of onset of DM/PM patients with malignant tumors was 55.4 ± 15.1 years and 59.5 ± 4.7 years, respectively, of which 17 died. The age-sex adjusted SMR of DM/PM patients without malignant tumors was 9.0 (95% CI 6.8-11.2). The age-sex adjusted SMR of DM/PM with malignant tumors was 12.3 (95% CI 9.0-14.7). The life loss of male patients with dermatomyositis complicated with malignant tumors was 30.1 years, and that of females was 38.6 years; the life loss of male patients with polymyositis was 27.6 years, and that of females was 22.1 years. A 10-year survival analysis showed that DM/PM patients with malignant tumor had significantly worse prognosis than patients without malignancy (p=0.001 Log-rank). The 1-, 5-, and 10-year survival rates of DM/PM patients who did not have malignant tumors were 87.9%, 81.9%, and 78.4%, respectively. DM/PM Patients with malignant tumors 1, 5, and 10 years The survival rates were 73.3%, 56.0%, and 45.7%, respectively. The independent risk factors for death in DM/PM patients with malignant tumors were advanced age (HR=1.11 95% CI 1.02-1.20, p=0.014) and infection (HR=17.07 95% CI 1.66-175.75, p= 0.017).

Conclusion: Malignant tumor is a common in patients with DM/PM, and the mortality of DM/PM patients with malignant tumors is high. The independent predictors of mortality for PM/DM patients with malignant tumors were age at disease onset and infection.



survival rates	1 year	5 years	10 years
Without malignancy	87.9%	81.9%	78.4%
Malignancy	73.3%	56.0%	45.7%

Acknowledgments: We thank our patients with PM/DM participating in this study.

Disclosure of Interests: None declared

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AB0628 EMERGING AUTOANTIBODIES PANEL (MYOSITIS ASSOCIATED AND MYOSITIS SPECIFIC ANTIBODIES) IN INFLAMMATORY MYOPATHIES: THE FREQUENCIES OF AND RELATIONSHIP WITH CLINICAL FEATURES

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Background: The idiopathic inflammatory myopathies (IIM) are characterized by muscle weakness, skin disease and various internal organ involvement and they can overlap with other autoimmune diseases. Recent autoantibody panels improve understanding and management of inflammatory myopathies. Myositis specific autoantibodies including Anti-TIF-1, Anti-NXP2, Anti-MDA5, Anti-SAE1, anti-HMGCR and anti-cN1A are regarded as key biomarkers aiding the diagnosis of patients. On the other hand, myositis-associated autoantibodies (MAAs) are also found in other autoimmune rheumatic diseases.

Objectives: To investigate the clinical meaning and impact of new myositis autoantibodies panel in real life data.

Methods: A total of 110 subjects (77 female, 33 male) admitted to Hacettepe University Hospitals with the signs and symptoms of IIM were screened by a line immunoblot assay (EUROLINE: Autoimmune Inflammatory Myopathies16 Ag) between 2017 and 2020. Only moderate or strong reactivity results were reported as positive. Demographic, clinical, laboratory, therapeutic data and imaging features were obtained by the retrospective review of medical records. IIM patients were diagnosed by Bohan and Peter's criteria and classified according to the EULAR/ACR classification criteria for adult and juvenile IIM and their major subgroups.

Results: IIM was diagnosed in 61 patients (42.6% DM/JDM and 57.4% PM) and patients with overlap were in decreasing order, Scleroderma (n=8), RA (n=5), Sjogren (n=4), SLE (n=3), autoimmune hepatitis (n=2).

Myositis-specific autoantibodies (MSAs) were found in 60%, myositis-associated autoantibodies (MAAs) in 41% of inflammatory myositis patients. The most common MSAs were anti-Jo-1 (16.4%) and anti-MDA-5 (13.1%) and the most common MAA was Ro-52 (32.7%) (Table 1). MAAs were more common in patients with polymyositis (54% vs 23% p=0.013). Twenty-one (34.4%) patients (61.0% females) had interstitial lung disease (ILD). Anti-Jo-1 (38.1%) and anti-Ro-52 (52.4%) was the most common MSA and MAA in patients with IIM and ILD.

MSAs were also determined in 10 of the 49 patients who were not diagnosed with IIM. Five patients with Anti-SRP, Anti-Mi-2 alpha, Anti-Jo-1 Anti-PL7, Anti-MDA-5 autoantibodies diagnosed as connective tissue disorder, one of them also had bladder cancer. Three patients with Anti-NXP2, Anti-PM-Scl 75, Anti-Ro-52, Anti-Mi-2 beta, Anti-PL7, Anti-PL12 autoantibodies had ILD. One patient (Anti-Mi-2 alpha, Anti-NXP2 and Anti-Ku autoantibodies positive) had viral myositis and one patient (Anti-Mi-2 alpha, Anti-Ro-52 autoantibodies positive) had inflammatory polyneuropathy.

Conclusion: Our study revealed relationship of anti-Jo-1 and anti-Ro-52 but not anti-MDA-5 in ILD-inflammatory myopathies. Even though new autoantibodies panel give opportunity to a closer look for inflammatory myopathies, larger series of patients should be evaluated to determine the association of specific antibodies in the differential diagnosis and prediction of outcome of IIM. MSA positivity in non-IIM diagnosed patients should be monitored to determine whether this positivity is related to a future disease development.

Table 1: Frequency of MSAs and MAAs in idiopathic inflammatory myositis

	JDM/DM (n=26 patients)	PM/ASS (n=35 patients)	All (n=61 patients)
Myositis-specific autoantibodies, n(%)			
Anti-Jo-1	1 (3.8%)	9 (25.7%)	10 (16.4%)
Anti-MDA-5	5 (19.2%)	3 (8.6%)	8 (13.1%)
Anti-SRP	2 (7.7%)	4 (11.4%)	6 (9.8%)
Anti-TIF1g	4 (15.4%)	2 (5.7%)	6 (9.8%)
Anti-NXP2	4 (15.4%)	2 (5.7%)	6 (9.8%)
Anti-SAE1	2 (7.7%)	1 (2.9%)	3 (4.9%)
Anti-Mi-2 alpha	2 (7.7%)	1 (2.9%)	3 (4.9%)
Anti-Mi-2 beta	2 (7.7%)	0	2 (3.3%)
Anti-PL7	0	3 (8.6%)	3 (4.9%)
Anti-PL12	0	2 (5.7%)	2 (3.3%)
Anti-EJ	1 (3.8%)	3 (8.6%)	4 (6.6%)
Anti-OJ	1 (3.8%)	0	1 (1.6%)
Myositis-associated autoantibodies, n(%)			
Anti-Ro-52	4 (15.4%)	16 (45.7%)	20 (32.8%)
Anti-PM-Scl 100	1 (3.8%)	4 (11.4%)	5 (8.2%)
Anti-PM-Scl 75	1 (3.8%)	4 (11.4%)	5 (8.2%)
Anti-Ku	0	4 (11.4%)	4 (6.6%)

Disclosure of Interests: Gözde Kübra Yardımcı: None declared, Enes Erul: None declared, Emre Bilgin: None declared, Bayram Farisoğulları: None declared, Levent Kılıç: None declared, Zeynep Saribas: None declared, Umut Kalyoncu Consultant of: Abbvie, Amgen, Janssen, Lilly, Novartis, UCB, Ali Akdoğan: None declared, Burcin Sener: None declared, Şule Apraş Bilgen: None declared, Omer Karadag: None declared

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AB0629 VASCULAR MANIFESTATIONS OF SYSTEMIC SCLEROSIS: SIMILAR IN PATHOGENESIS, DIFFERENT IN FREQUENCY

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Background: Pulmonary arterial hypertension (PAH) is one of the main manifestations of vascular involvement in systemic sclerosis (SSc). The association of PAH with Raynaud's phenomenon (RP) and digital ischemic disorders is assumed.

Objectives: The aim of the study to detect of the possible relationship of pathogenetically similar processes and the predictor role in the early diagnosis of PAH and digital ischemic disorders by the nailfold videocapillaroscopy (NVC).

Methods: 111 patients with SSc (51 patients with PAH (SSc-PAH) and 60 patients without PAH) include in this study. In all patients, the diagnosis of SSc was validated according to the 2013 ACR-EULAR criteria. PAH was diagnosed by right heart catheterization. NVC was performed in all recruited subjects. Capillary quantitative parameters (loops length and width, capillary density, neoangiogenesis) were evaluated and a semi-quantitative scoring was used (specific patterns - early, active and late) to define microvascular alterations. The test evaluated the presence of capillaroscopic changes in the nailfold bed on 2-5 fingers of both hands. The normal capillaroscopic pattern was characterized by the presence of 7-11 capillaries in the form of hairpins per 1 mm. Pathological patterns were characterized by morphological and structural changes, such as expanded and giant capillaries, hemorrhages, avascular fields, neoangiogenesis. The capillaroscopy pattern (normal, non-specific, early/active/late) was determined qualitatively. Decreased capillary density, dilated, giant or branched capillaries, microhemorrhages were evaluated semi-quantitatively.

Results: RP was detected in 100% of cases in both groups. In the analysis of capillaroscopic patterns in both groups, the early and late scleroderma types of changes prevailed, but no significant differences were noted. Typical scleroderma patterns were found in 51 patients (100%) with SSc-PAH. In 3 patient with SSc without PAH, the abnormalities were regarded as non-specific. The NVC pattern was detected to be early in 8 patients with SSc-PAH and in 11 with SSc without PAH. The NVC pattern was found to be active in 16 patients with SSc-PAH and in 18 with SSc without PAH. The NVC pattern was detected to be late in 27 patients with SSc-PAH and in 28 with SSc without PAH. In addition to RP, the development of digital ulcers was noted with equal frequency in history (25 patients with SSc-PAH and 32 with SSc without PAH). Also, the time to their appearance from the first symptom of SSc was the same (56 (16; 84) months and 44 (23; 72) months, respectively). Severe forms of digital ischemic disorders were observed rarely and with the same frequency in the studied groups. Ischemia in 2 patients with SSc-PAH and in 5 patients with SSc without PAH, gangrene in 2 patients only in the SSc group without PAH, amputation in 1 of each group.

Conclusion: In the course of the study, it was not possible to identify differences between the NVC patterns, the frequency and severity of digital ischemic disorders in the compared groups. That fact does not allow using the NVC as an early diagnosis of PAH in SSc. However, the NVC can help predict the development of digital ischemic disorders.

References: No

Disclosure of Interests: None declared

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AB0630 IMBALANCE BETWEEN TH17 AND REGULATORY T CELLS IN PATIENTS WITH PM/DM COMBINED WITH EBV/CMV VIRAEMIA

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Background: Dermatomyositis and polymyositis (DM/PM) are associated with muscle weakness and inflammatory infiltration within the skeletal muscle. The numerical and functional defects of immune cells, due to long-term uses of glucocorticoids and disease-modifying anti-rheumatic drugs (DMARDs) together with immune disturbances associated with disease itself, lead to high risks in opportunistic infections, such as Epstein-Barr virus (EBV) and cytomegalovirus (CMV).[1-2] We want to observe changes of peripheral lymphcytessubsets in PM/DM patients with EBV and/or CMV infection,especially whether there is imblance between Th17 and Treg cells.

Objectives: To investigate the characteristics of peripheral lymphocyte subsets in PM/DM with EBV and/or CMV infection, especially the Th17 and Treg cells.

Methods: From February 2016 to November 2019, PM/DM patients with EBV and/or CMV viremia (infection group, n=34) and without infection (non-infection group, n=31) as well as healthy adult controls (n=20) were enrolled in our study. Absolute numbers of total T, total B, NK, CD4 + T, CD8 + T cells, and CD4 + T subsets (Th1, Th2, Th17 and Treg cells) in peripheral blood by flow cytometry combined with standard absolute counting beads.

Results: (1) Compared with PM/DM patients without infection, 34 PM/DM patients with EBV and/or CMV infection, including 12 patients with EBV, 20 patients with CMV, 2 patients combined EBV and CMV, the absolute number of total T lymph cells (P=0.019), total B lymph cells (P=0.037), NK cells (P=0.033), CD4 + T cells (P=0.000), Th1 cells (P=0.014), Th2 cells (P=0.003), Th17 cells (P=0.003), Treg cells (P=0.004) lower than its of (P=0.003) patients without infection, the absolute number of CD8 + T cells (P=0.427) has no obvious difference between them.

(2) And its the absolute number of total T lymph cells (P=0.000), total B lymph cells (P=0.003), NK cells (P=0.000), CD4 + T cells (P=0.000), CD8 + T cells (P=0.006), Th1 cells (P=0.000), Th2 cells (P=0.001), Th17 cells (P=0.000) and Treg cells (P=0.000) significantly lower than healthy control.

(3) Compared with the healthy control,the absolute number of total T lymph cells (P=0.000), NK cells (P=0.000), CD4 + T cells (P=0.031), CD8 + T cells (P=0.000), Th1 cells (P=0.002), Th2 cells (P=0.031), and Treg cells (P=0.000) in PM/DM without infection evidently lower, but there is no siginificant difference in absolute number of total B lymph cells (P=0.19) and Th17 cells (P=0.171).

Conclusion: We show that the absolute number of peripheral blood lymphocytes and CD4+T subsets in patients with PM/DM with EBV and/or CMV viremia is further reduced. In addition to Treg cells, a decrease in Th17 cells may also be an important feature of EBV and/or CMV infection in DM/PM. These cell reductions may be the cause and risk indicator of viral infections.

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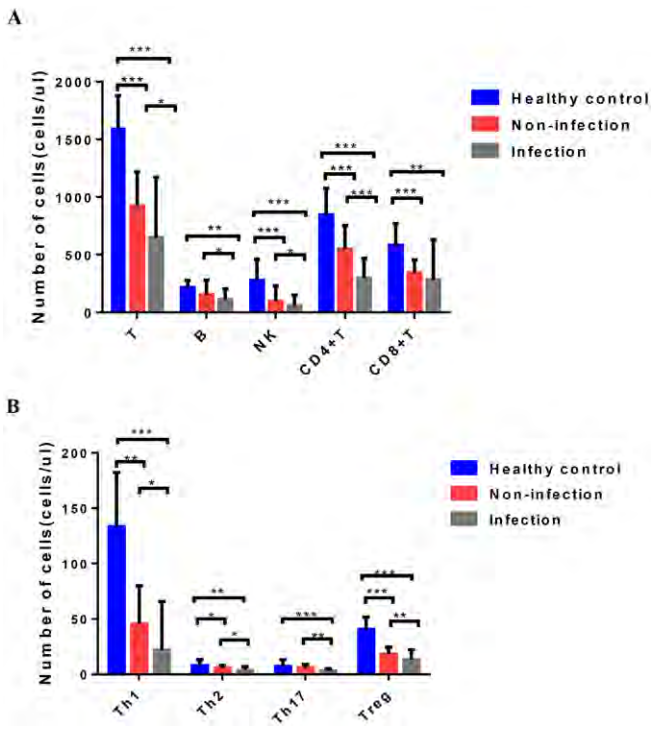


Figure. Absolute numbers of peripheral lymphocyte subsets between healthy controls and patients were assessed by fow cytometry using oneplatform method. PM/DM infection group (n=34), PM/DM non- infection group(n=31)and healthy control group (n = 20).(*p<0.05, **p<0.01, ***p<0.001)

Disclosure of Interests: None declared
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AB0631 **THE CLINICAL CHARACTERISTICS OF SYSTEMIC SCLEROSIS WITH LUNG CANCER: DATA FROM SINGLE CENTER IN CHINA**

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Background: Malignant neoplasms is the second most common non-SSc associated cause of death in SSc patients, only second to infection. And among all the neoplasms, lung cancers are the most common, which is in the urgent need of attention from clinicians.
Objectives: To analyze the clinical features of patients of SSc with lung cancer.
Methods: Medical records of inpatients admitted in Peking Union Medical College Hospital from March 1992 to December 2018, were collected and analyzed, including the clinical manifestation, laboratory data, radiological images, pathology. SSc patients without lung cancer during the same period, matched by age and gender, were selected as the controls.
Results: Nineteen SSc patients with complete medical records were identified, with 17 (89.5%) females and 2 (10.5%) males. The mean age of SSc onset was 37.8±12.0) years old and of lung cancer diagnosis was (54.4±10.2) years old. One (5.3%) had a smoking history. Eight (42.1%) patients had family history of cancer, which was significantly higher than those without lung cancer (4 patients, 5.3%, P<0.001). The proportion of limited cutaneous SSc (lcSSc) were 63.2% among these patients, and 18 (94.7%) had interstitial lung disease (ILD), the difference between the two groups was not statistically significant (P = 0.259 and 0.051, respectively). All ILD was diagnosed before the onset of lung cancer, with a median interval of 9.2 (range 1.6-28.1) years. SSc patients with lung cancer had less myositis than control group (0% vs. 27.6%, P = 0.032), yet no significant differences were identified in Raynaud's syndrome, esophageal involvement, digital ulcers, pulmonary hypertension, telangiectasia and arthritis. All patients developed lung cancer after the diagnosis of SSc, with a median interval 10.5 (range 2.0-36.2) years. In most of them(18, 94.7%), lung cancer happened after at least 6 years of SSc onset. Newly happened cough (9 patients), worsening decrease in activity endurance (3), chest pain (2), hemoptysis (2), nodes in lung through regular CT scans (3) were the first presentations of lung cancer. Ten(62.5%) neoplasms developed in the lower lobes of the lung, while 3 was in the upper lobes, one in the lingual lobe, and one in the left pulmonary hilum, and 3 were unknown. The median survival of the case group were 31.4 years, while the median survival of the control group was not reached. Eight patients tested EGFR gene mutation or ALK gene rearrangement, and only 2 were positive.
Conclusion: It is not uncommon that SSc could be concomitant with lung cancer, especially for those with long disease duration and family history of malignancy. Due to the subtle onset of lung cancer, clinicians should pay attention to it during clinical practice.
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20. Spondyloarthritis - treatment

AB0632 **EFFECTIVENESS OF ETANERCEPT BIOSIMILARS IN REACTIVE ARTHRITIS: RETROSPECTIVE CASE CONTROL**

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Background: There is a paucity of evidence based therapies for reactive arthritis(ReA). Data is limited for anti-TNF drugs usage [Table 1] with even less data on biosimilars.

Table 1. Anti-TNF use in reactive arthritis

Place (year)	Anti-TNF	N	Outcomes	Remarks
Pennsylvania, USA (2005)	Etanercept	16	10 completed trial: 9 responders	Synovial histology improvement but not normalized
Strasbourg, France (2011)	Infliximab(5) Etanercept(4) Adalimumab(1)	10	Rapidly effective in 9 patients (90%) 5 had DFR	Relapses responded to re- initiation
Besançon, France (2016)	Etanercept (9) infliximab (3) Adalimumab(3)	15	5 had DFR	9 developed chronic SpA
Delhi, India (2019)	Infliximab(10), Adalimumab(3) Etanercept(1)	9	At median of 3.5 months: 4 had remission, 3 relapse, 1 adverse reaction	Biologicals were not given regularly
Current study	Etanercept biosimilars	10	At median 7 months: 6 had DFR	All patients responded

DFR: drug free remission

Objectives: To find out the outcomes of etanercept biosimilars (ETN-b) use in ReA
Methods: A retrospective review of patients meeting the Braun criteria[5] for probable ReA helped identify patients on ETN-b. Patients with less than 1 year follow-up and those who had received less than 5 doses of ETN were excluded. Biological naïve patients who had completed at least 1 year follow-up were included as controls. Baseline and current status was compared between these two groups.
Results: Of 94 identified ReA patients, 11(11.7%) had received ETN-b and 10 met the case definition. Five each had received one of two ETN-b. 30 were available as controls. All cases had been documented as refractory ReA. Amongst cases, 7 patients had resolution of ReA; 2 had relapsing courses and 1 persistent arthritis. Four were in remission off all drugs. Controls has similar proportions [Table 2]. There were no infections or adverse effects recorded during follow-up.

Table 2. Comparison between etanercept group and biological naïve groups

	Etanercept group (n=10)	Non-etanercept group (n=30)	Non parametric tests of significance
Age at presentation (years)	27(17.2-34.2)	25(19-34.2)	NS
Males	10 (100%)	22 (55%)	NS
Follow-up (months)	27(15-71.7)	27(15-79.5)	NS
Preceding infection	Diarrhoea= 6 UTI= 4	Diarrhoea= 23 UTI= 7	NS
Inflammatory backache	3	11	NS
Small joint involvement	4	11	NS
Monoarticular/ oligoarticular/ polyarticular	3/3/4	10/8/12	NS
Average intra-articular injections	1.9	0.3	NS
Sulfasalazine	9	22	NS
Methotrexate	1	1	NS
Disease outcome	Resolved = 7 Relapsing = 2 Persistent = 1	Resolved = 19 Relapsing = 9 Persistent = 2	NS
Drug free remission	4 (40%)	12(40%)	NS
BASDAI at last follow-up	0.3(0-0.8)	0(0-1.4)	NS
HAQ-DI at last follow-up	0(0-0.15)	0.05(0-0.3)	NS

BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; HAQ-DI: Health Assessment Questionnaire Disability Index; NS: not significant

Conclusion: All 10 patients responded. 40% achieved drug free remission. Thus, ETN-b appear safe and effective for ReA refractory to conventional therapy.

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AB0633 REAL WORLD EXPERIENCE OF THE IMPACT OF SECUKINUMAB ON DISEASE ACTIVITY AND FATIGUE IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Fatigue is one of the most commonly reported symptom of ankylosing spondylitis (AS). It impacts functional ability, quality of life, and ability to maintain employment[1]. Secukinumab, a fully human monoclonal IgG1 antibody that neutralizes IL-17A, has shown significant and sustained improvement in the signs and symptoms of active AS in the MEASURE 2 study[2]. It has also shown to improve fatigue scores. Despite this, the published literature on real life experience is scarce. We report our experience of Secukinumab use at Gartnavel General Hospital, Glasgow, UK.

Objectives: We performed a retrospective review to assess the response of our AS patients to Secukinumab. We also reviewed the impact of treatment on fatigue.

Methods: AS patients commenced on Secukinumab 150mg subcutaneously from mid-2016 to September 2019 were identified using the clinical records on our database. Response using Bath AS disease activity index (BASDAI) and Bath AS function index (BASFI) were recorded. Impact on fatigue and pain was measured using single-item fatigue and pain visual analogue scale (VAS) within the BASDAI questionnaire.

Results: 30 AS patients, 11 anti-TNF naïve and 19 anti-TNF inadequate responders (IR), on Secukinumab were identified. Retention rate was 76.66% (23/30). Sustained improvement was observed across all outcome measures over 3.5 years. Fatigue and pain improvement were somewhat lower than expected but did show slow improvement. Responses were greater in anti-TNF naïve patients. There was no significant difference in response between smokers (33.34%, 10/30) and non-smokers (36.67%, 11/30). There were 4 patients with inflammatory bowel disease, none of whom flared. No new safety signals were identified.

Table. Clinical response to Secukinumab in patients with active AS

Time	BASADI		BASFI		Fatigue		AS pain	
	Mean	%change	Mean	%change	Mean	%change	Mean	%change
Baseline	7.09		7.3		7.6		7.99	
3M	6.71	-5%	7.24	-8%	6.9	-9%	6.89	-14%
6M	5.4	-24%	5.8	-20%	6.29	-17%	6.06	-24%
9M	6.01	-15%	6.56	-10%	6.41	-16%	6.1	-24%
12M	5.04	-29%	5.42	-26%	6.35	-16%	5.55	-30%
18M	4.98	-30%	3.73	-49%	6.38	-16%	4.91	-38%
24M	5.52	-22%	5.72	-22%	6.79	-11%	5.6	-30%
%Change from baseline	Anti-TNF naïve	Anti-TNF IR	Anti-TNF naïve	Anti-TNF IR	Anti-TNF naïve	Anti-TNF IR	Anti-TNF naïve	Anti-TNF IR
3M	-37%	-9%	-44%	6%	-10%	-14%	-53%	-14%
6M	-34%	-27%	-38%	-29%	-28%	-6%	-43%	-6%
9M	-27%	-4%	-30%	1%	-23%	-6%	-41%	-6%
12M	-41%	-22%	-31%	-29%	-31%	0%	-44%	0%
18M	-32%	-11%	-57%	-22%	-35%	5%	-34%	5%
24M	-26%	-12%	-32%	-1%	-16%	3%	-32%	3%

There were <3 patients in >2 years follow up group therefore results were omitted from analysis

Conclusion: In our real-life cohort of AS patients, significant improvement was seen over 3.5 years in both BASDAI and BASFI. Fatigue was significantly improved in anti-TNF naïve group, but results were disappointing in anti-TNF IR group. This may be explained by the fact that there are older patients with established disease and background degenerative changes in anti-TNF IR group. Although fatigue data had slightly discordant results compared with the MEASURE 2 study[2], considering the use of single item VAS rather than multi-dimensional measures such as FACEIT fatigue scale, clear improvement has been observed.

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Acknowledgments: S. Kerr, K. Anderson and Rheumatology department, Gartnavel General Hospital, Glasgow, UK

Disclosure of Interests: None declared

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AB0634 BUDGET IMPACT ANALYSIS OF BIOLOGICAL THERAPY COMPARED TO CONVENTIONAL SPONDYLOARTHRITIS TREATMENT, IN A FOURTH LEVEL HOSPITAL IN BOGOTA COLOMBIA

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Background: Spondyloarthritis refers to a family of diseases, of which ankylosing spondylitis and non-radiographic axial spondyloarthritis are responsible for axial impairment. Previously, the only treatment available were NSAIDs, which control activity and stop radiological progression, but at the expense of increased adverse effects, such as cardiovascular risk, dyspepsia and chronic renal failure. For the past 2 decades, biological therapy has been available, which means an increase in care costs.

Objectives: The objective of this study is to perform a budget impact analysis of biologic therapy.

Methods: To do a budget impact analysis from the perspective of the payer, comparing biological therapy with coventional therapy for the treatment of spondyloarthritis. Demographic characterization of the population attended at the Central Military Hospital. Time horizon from 2012 to 2018, taking the activity count according to the hospital's billing and the prices of the activities of the state body SISMED. Exchange rates at the end of 2018.

Results: The patients attended were 117, mostly men (63, 25%), average age 46, 4 years (SD 13), with disease diagnosis time of 9, 8 years (SD 9, 6). In the budget impact analysis, it is observed that 25% of patients were on DMARDs

therapy, 22% with NSAIDs and 96% with biologic therapy. The average year/patient cost with NSAIDs alone would be EUR 381, with DMARDs only EUR 9,318 and, if only biological therapy was used, EUR 423. Within the total number of patients, the average annual cost, including the possibility of combining these drugs, amounted to EUR 5,403

Conclusion: Including biological therapy in the care of patients with spondyloarthritis can increase up to 24 times the annual cost per patient. This increase is not only due to higher market value, it also relates to the need for more medical procedures and diagnostic follow-up tests.

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Table 1

Distribution by therapy		Cost monotherapy treatments (EUR)	
NSAIDs	66%	Patient with NSAIDs	$381
Biological Therapy	57%	Patient with biological therapy	$9.318
DMARDs	33%	Patient with DMARDS	$423

Average patient cost year $5,403 EUR

Table 2

Distribution of average annual cost per patient	
Analgesic	0,72%
Biological	94,2%
Procedures	1,32%
Diagnosis	3,12%
For osteoporosis	0,64%

Disclosure of Interests: None declared

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AB0635 HOW ARE NON STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAID) PRESCRIBED IN AXIAL SPONDYLOARTHRITIS?

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Background: For decades, NSAID have been used as the first-line drugs to treat axial spondyloarthritis (ax-SpA). However, the NSAID prescription strategy is not clearly detailed and it varies from one clinician to another.

Objectives: The aim of this study was to assess the NSAID prescription modalities adopted in ax-SpA and the differences between these modalities.

Methods: This is a descriptive study including 200 cases of ax-SpA fulfilling the ASAS 2009 criteria and diagnosed between January 2000 and October 2019. The demographic and clinical features of the ax-SpA were collected and the modalities of prescription of NSAID were retrospectively assessed.

Results: Our population consists of 138 men and 62 women with a mean age of 43,3 ± 11,2 years. The HLA B-27 antigen was present in 50,8% of cases. The ax-SpA was a pure axial form in 67% of patients, associated with peripheral arthritis, enthesitis and dactylitis in 19%, 21,5% and 1,5% respectively.

One hundred eighty patients (90%) had been treated with NSAIDs. The NSAIDs used were: the Diclofenac (57.5%), Indomethacin (37.5%), Piroxicam (36%), clecoxib (34%), Naproxen (29.5%) and ketoprofen (13%). Seventy-three patients (36.5%) had used at least 3 NSAIDs.

Among the 180 patients treated with NSAID, 88 patients (48,8%) were treated with conventional synthetic DMARDs (csDMARDs) in association with NSAID: Salazopyrine (43,3%) and Methotrexate (13,3%). Seventy-one patients (39,4%) had necessitated the use of anti-TNF alpha.

NSAIDs were used continuously in 115 patients (63.8%) and the maximum dose of NSAIDs was used in 78 patients (43.3%). By comparing patients who used maximum doses of NSAIDs and those who used NSAID continuously with other patients, we noticed that the use of biological treatments was more frequent in those groups (p = 0,01 and p=0,004 respectively).

In addition, while comparing the group of patients co-treated with csDMARDs with other patients treated with NSAID on monotherapy, we noted that this group of patients had more arthritis (p<0,0001), enthesitis (p=0,02), psoriasis (p=0,04) and necessitated more biological treatments (p=0,01).

Conclusion: Our results suggest that maximal doses and/or continuous prescription of NSAID were mainly used if there was no response to that treatment. The csDMARDs were more prescribed if there were peripheral manifestations or psoriatic arthritis and those forms were also more candidates to biological treatments.

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Disclosure of Interests: None declared

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AB0636 MODALITIES OF PRESCRIPTION OF ANTI-TNF ALPHA IN AXIAL SPONDYLOARTHRITIS: ON MONOTHERAPY OR COMBINED WITH CONVENTIONAL SYNTHETIC DMARDS

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Background: The advent of biologics targeting tumor necrosis factor-alpha (anti-TNF alpha) has revolutionized the treatment of spondyloarthritis (SpA). Their association with conventional synthetic disease-modifying antirheumatic drugs (cs-DMARD), although effective and used in clinical practice for the treatment of peripheral rheumatic diseases, is not clearly assessed in axial spondyloarthritis (ax-SpA).

Objectives: The aim of this study was to assess the strategy of prescription of anti-TNF alpha in a population of ax-SpA and to compare patients treated with anti-TNF alpha on monotherapy with those who had combined therapy with cs-DMARDs.

Methods: This is a retrospective descriptive study including 85 cases of ax-SpA diagnosed between January 2000 and October 2019 and treated with anti-TNF alpha.

The clinical features, the erythrocyte sedimentation rate (ESR), the C-reactive protein (CRP), Bath ankylosing spondylitis disease activity index (BASDAI) and Bath ankylosing spondylitis functional index (BASFI) were compared between groups of anti-TNF alpha on monotherapy or combined therapy with csDMARDs.

Results: Of 85 ax-SpA, 67 were males (78,8%) and the mean age was 44,4 ± 10,9 years. The mean period of evolution was 12,3 ± 9,1 years and 52,2% of patients were HLA-B27 positive. The ax-SpA was a pure axial form in 74,1% of patients, associated with peripheral arthritis, enthesitis and dactylitis in 17,6%, 17,6% and 1,2% respectively.

The ant-TNFs were administrated with a men delay of 78 ± 70,8 months. The anti-TNFs used were: Infliximab (41,1%), Etanercept (32,9%), Adalimumab (23,5%) and Golimumab (2,3%). Fifty-nine patients (69,4%) were treated with anti-TNF alpha on monotherapy and 26 patients (30,6%) had combined therapy. The csDMARDs prescribed were the Salazopyrine (22,4%) and the Methotrexate (7,1%).

While comparing the groups of anti-TNFs combined therapy and monotherapy, we noticed that the arthritis were present in 30,7% of patients from the group of combined therapy versus 11,8% of patients from the group of monotherapy (p=0,03). The psoriasis also was more present in the group of combined therapy (11,5% vs 1,6%; p=0,04).

There was no statically significant difference between the two groups in the following parameters: age, gender, HLA B27, enthesitis, dactylitis, uveitis, inflammatory bowel diseases, ESR, CRP, BASDAI and BASFI.

Conclusion: Our results suggest that the concomitant use of csDMARDs with anti-TNFs is frequent in clinical practice in ax-SpA, but mainly justified by the presence of arthritis or psoriasis.

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AB0637 EFFICACY OF COMEDICATION OF CONVENTIONAL SYNTHETIC DMARDS WITH TNF BLOCKERS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: Tumour necrosis factor blockers (anti-TNFs) are typically used in axial spondyloarthritis (ax-SpA) when the disease has not responded adequately to conventional therapy. However, the effects of the comedication conventional synthetic disease modifying antirheumatic drugs (csDMARDs) with anti-TNFs are inconclusive.

Objectives: The aim of this study was to evaluate the efficacy of comedication csDMARD and anti-TNF compared with anti-TNFs on monotherapy.
Methods: A descriptive retrospective study including 85 patients with ax-SpA according to the criteria of the group ASAS on 2009 and having received anti-TNFs between January 2000 and October 2019.
The patients were divided on two groups, those who had received combined therapy with cs-DMARDs and those who had received anti-TNFs on monotherapy.
The response to treatment was assessed with the ASAS 40 response and partial remission at 3 and 6 months of treatment and was compared between the two groups.
Results: Our populations consists of 67 men and 18 women with a mean age of 44,4 ± 10,9 years. The mean period of evolution was 12,3 ± 9,1 years and 52,2% of patients were HLA-B27 positive. The ax-SpA was associated with peripheral arthritis, enthesitis and dactylitis in 17,6%, 17,6% and 1,2% respectively.
Fifty-nine patients (69,4%) were treated with anti-TNF alpha on monotherapy and 26 patients (30,6%) had combined therapy. The ASAS 40 response was achieved in 45,6% of patients at 3 months and 64,1 % of them at 6 months of anti-TNFs treatment. Among them, 7,4% had obtained partial remission at 3 months and 20,3% at 6 months of treatment.
There was statically significant difference between the two groups on the ASAS 40 response or the partial remission at 3 and 6 months of treatments.
Conclusion: The comedication therapy with csDMARDs does not influence the efficacy of anti-TNFs in ax-SpA patients suggesting no benefit in the concomitant use of these drugs in clinical practice.
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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.6320

AB0638 THE EFFECT OF VITAMIN D ON QUALITY OF LIFE AND SEVERITY OF PAIN IN PATIENTS WITH ANKYLOSING SPONDYLITE

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Background: The high incidence of ankylosing spondylite (AS) in people of working age, as well as the negative impact of the disease on the quality of life of patients, determine the need for adjuvants to reduce the severity of pain and thereby achieve the physical, psychological and emotional well-being of patients.
Objectives: To study the effect of vitamin D (colecalciferol) on the quality of life and the severity of pain in patients with ankylosing spondylite.
Methods: The study included 69 patients with AS, who studied the quality of life indicators according to the Medical Outcomes Study Short Form (SF-36); pain syndrome and stiffness in the spine were assessed by a visual analogue scale by patients, and by a physician - by counting the number of painful joints (NPJ), the disease activity index (BASDAI) and the Functional Index (BASFI). All patients were receiving a basic therapy in a stable dose for at least 10 months. They were divided into 2 groups, comparable in age, disease activity; Group 1 (n = 33) additionally received colecalciferol 1500 ME during 6 months of observation.
Results: At the end of the observation period when evaluating data on SF-36: in the 1st group, the physical health component has improved - the increase in physical functioning (PF) and bodily pain (BP) by 51.4% and 37.8% from the baseline; vital activity, psychological health, and social functioning due to emotional state have also increased by 37.6%, 33.4% and 42.5%, respectively. In the 2nd group above mentioned parameters have not changed. In the 1st group the indexes of BASDAI and BASFI have decreased by 16% and 22% ($p = 0.0079$, $p = 0.0022$, respectively), and their dynamics in the 2nd group were less significant ($p = 0.013$, $p = 0.017$, respectively) Also, in patients of the 1st group have decreased the severity of morning stiffness and the pain in the spine a highly reliable ($p < 0.001$), and in the 2nd group they were less significant ($p = 0.043$, $p = 0.016$, respectively). Positive dynamics of NPJ in the 1st group was more significant ($p = 0.003$) than it was in the 2nd group ($p = 0.033$).
Conclusion: In the group of patients treated with colecalciferol was noted improvement in indicators of quality of life (the parameters of the physical component of health, vitality and social functioning) and also more significant decrease of the intensity of pain and of morning stiffness duration, of NPJ, than in not received to colecalciferol patients. Inclusion of vitamin D in the comprehensive AS therapy promotes not only reduction the severity of the chronic pain manifestations, but also improves the quality of life of patients with this pathology.
Disclosure of Interests: None declared
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AB0639 TREATMENT EFFICACY WITH SECUKINUMAB IN A COHORT OF SPONDYLOARTHRITIS PATIENTS

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Background: Spondyloarthropathies are a heterogeneous group of similar diseases, with interrelated clinical manifestations, such as Psoriasis Arthritis (APs) and Ankylosing Spondylitis (EA). There are different treatments for this group of pathologies.
Objectives: It is very important to differentiate between those that present predominantly axial (spine and/or sacroiliac) or peripheral involvement, since the response to treatment is very different.
In some clinical trials, secukinumab significantly improved versus placebo, the symptoms and signs, physical function and quality of life, however, at present, we do not have enough data from secukinumab in real clinical practice.
This is the real reason of this study: the use of secukinumab in clinical practice.
Methods: Multicentric longitudinal observational study of 5 Hospitals in Madrid. Patients are over 18 years old and meet the following inclusion criteria: New York criteria for AS, ASAS for EA, CASPAR for APs, and all of them are with secukinumab or have received it.
We will evaluate the effectiveness rate as well as its confidence interval at 95%. In addition, the effectiveness of secukinumab will be compared in the different pathologies by using χ^2.
Results: 72 patients were collected, 41 of them were women (57,75%).
12 patients (16,90%) had not received FAME before secukinumab and 22 patients (33,99%) were naive to biological treatment.
In 4 patients, the reason for starting secukinumab was the patient's comorbidities, in 2 the adverse effects of previous treatment and in the rest, was the lack of efficacy of the previous treatment.
The patients were divided into 4 categories according to the level of DAS-28 or BASDAI, at the beginning of the treatment and the last recorded value, in: Absence of activity, mild, moderate and severe activity. Of the patients with data, they managed to improve the DAS-28 score (change category) by 30,95%, while only 4,76% worsened their score. With respect to BASDAI, of the total number of patients, only 3,03% worsened, while his score improved 27,27%.
According to baseline diagnosis, a greater improvement of the disease activity in peripheral APs(66,67%) and mixed APs(61,54%) is achieved.
Conclusion: In real clinical practice, treatment with secukinumab was effective in patients with spondyloarthritis, achieving improvement in previous activity rates. In this study, the most significant improvement was obtained in peripheral and mixed APs.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.5400

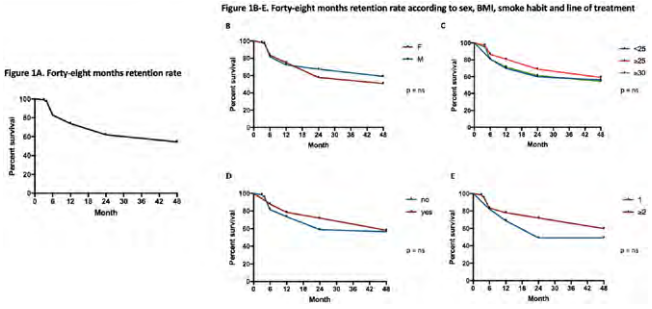
AB0640 LONG-TERM EFFECTIVENESS AND DRUG SURVIVAL OF GOLIMUMAB IN PATIENTS AFFECTED BY PSORIATIC ARTHRITIS WITH CUTANEOUS INVOLVEMENT

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Background: Psoriatic arthritis (PsA) is a chronic immune-mediated disease associated with psoriasis (PsO). Overexpression of inflammatory cytokines such as tumor necrosis factor (TNF)-α plays a key role in the pathogenic mechanisms. Golimumab (GLM) is a fully human monoclonal antibody IgG1k neutralizing TNF-α approved for PsA and PsO, but effectiveness evaluation in real life remains a crucial issue.

Objectives: In a real-life setting, to determine the survival rate of GLM (drug survival) at 48 months in the global population, in different clinical settings, and the effectiveness of GLM in improving joint symptoms and cutaneous manifestations in patients affected by moderate to severe PsA with cutaneous involvement.
Methods: We collected retrospectively from 1 January 2014 to 31 December 2019 data from 105 patients affected by PsA, according to the Classification for Psoriatic Arthritis (CASPAR) criteria, who started treatment with GLM. Inclusion criteria were age > 18 years and had a diagnosis of PsA > 6 months, the presence of peripheral arthritis (at least one active joint) and active PsO. Relevant anamnestic, clinical, biochemical data and biological treatment line were collected at baseline (T0) and after 6 (T6), 12 (T12), 24 (T24) and 48 (T48) months of GLM treatment. Comparisons between baseline and 48 months continuous variables were performed using a paired t-test or a Wilcoxon signed-rank test for paired samples. The drug survival rates were analyzed using Kaplan-Meier estimates. Drug survival rates were read from the Kaplan-Meier survival curves. Differences in drug survival between groups were analyzed using a log-rank (Mantel-Cox) test, by stratifying for sex, BMI, smoking habit and line of treatment. A p-value <0.05 was considered as statistically significant.
Results: Peripheral arthritis was present in 67 (63.8%) cases, axial disease in 37 (35.3%), enthesitis and PsO as prominent manifestations in 82 (78%) and 84 (80%) patients respectively. Erosive disease was present in 38 (36.2%) of patients at baseline. The most frequent comorbidities were MetS described in 20 (19%) patients and cardiovascular disease described in 33 (31.4%) patients, probably due to the high incidence of smokers (33 (31.4%) of patients) and to the elevate BMI score (27.1±6.0). At 48 months, the 42% (44 of 105) (figure 1A) of the patients have discontinued therapy; the most frequent reason was insufficient response/loss of efficacy (30 patients (28.6%) out of 105). Unexpectedly, no statistical significant difference emerged according to gender (p=0.652), BMI (p=0.655), smoking habit (p=0.466) and line of treatment (p=0.208) (figure 1B-E). Finally, the effectiveness of GLM in improving joint symptoms and cutaneous manifestations was confirmed once again, with a statistical significant improvement at 48 months in clinical (BASDAI p<0.0001; PASI p<0.01; DAPSA p<0.0001) and biochemical (CRP<0.05) data.
Conclusion: This multicentric study revealed a high drug persistence of GLM in real-life patients, although the presence of comorbidities. Unlike what is known in literature, our study population presented no differences in terms of clinical response and efficacy between male and female, smokers and no-smokers, obese and health-weight patients, different line of treatment. On the other hand, efficacy and safety of GLM has been demonstrated once again also in real-life treatments.

References: No references.

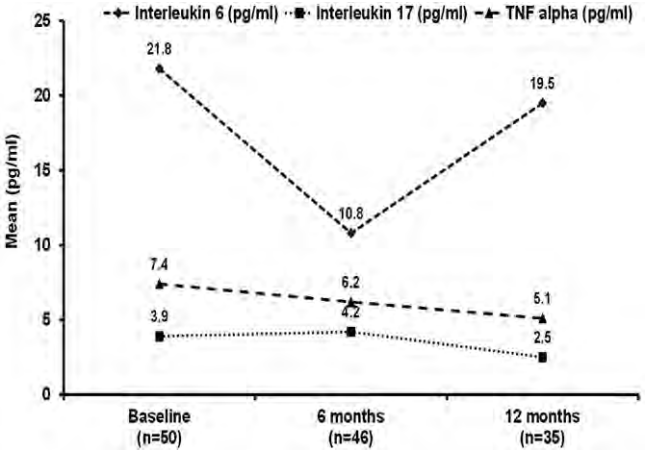


Disclosure of Interests: giulia lavinia fonti: None declared, Maria Sole Chimenti: None declared, Arianna D'Antonio: None declared, miriam teoli: None declared, Francesco Caso: None declared, Luisa Costa: None declared, marco tasso: None declared, Augusta Ortolan: None declared, Mariagrazia Lorenzin: None declared, Paola Conigliaro: None declared, paola triggianese: None declared, Raffaele Scarpa: None declared, Roberto Perricone: None declared, Roberta Ramonda Speakers bureau: Novartis, Celgene, Janssen, Pfizer, Abbvie, Lilly
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AB0641 MANAGING ANKYLOSING SPONDYLITIS (AS) WITH SHORT TERM BIOSIMILAR ADALIMUMAB REGIMEN IN A RESOURCE STRAPPED SETTING: A PROTOCOL DRIVEN COMMUNITY CLINIC ORIENTED STUDY

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Background: We were handicapped by the exorbitant cost of innovator anti-Tumour Necrosis Factor (TNF) drugs. Despite limited use, we sometimes observed long-term benefits following short term induction like use. Emboldened by advent of biosimilars, we carried out an investigational study.
Objectives: To evaluate the effectiveness of a short regimen of biosimilar (Bs) Adalimumab in AS
Methods: 50 consenting patients (86% B27+) naïve for biologics and negative for latent TB screen were enrolled into an observational design study of one year; Baseline mean values for age, duration, ASDAS and CRP was 31 years, 98.8 months, 4.6 and 64 mg per dl respectively. During the first year, patients were begun with 40 mg Bs Adalimumab (Bs-ADL) (Exemptia™), injected fortnight, for 12-16 weeks. No patient received DMARD or steroid in the first year of study. Patients continued standard of care follow up program in the clinic. The ASAS (Assessment Spondyloarthritis International Society) improvement indices were used. Standard intention-to-treat analysis was performed; significant p <0.05.
Results: Optimum ASAS 40 improvement was observed at week 12 (68%); substantial improvement lasted till week 36. At one year, the ASAS 40 was 38%; ASAS partial remission 22% patients. Pro-inflammatory cytokines (IL-6, TNF α and IL-17) showed conspicuous reduction; maximum drop in IL-6 at week 24 (See Figure). 11 patients withdrew in the first year. 30 patients completed two years and 22 patients completed 3 year follow up. Over time, there was substantial loss in the ASAS 20 and 40 responses but patients seemed satisfied with the on-going symptomatic relief and improved function. Admittedly, patients showed more adherences to advice on physical exercise and stress reduction. Flares were more frequent after 1 year requiring short term round the clock NSAID; only 5 patients could afford to repeat a short term Bs-ADL regimen and one patient underwent hip arthroplasty. None received steroids and 5 patients were begun on Sulfasalazine in the second year and monitored. We could not evaluate structural modification (AS). Selected outcomes over 2 and 3 years from the current study will be compared to matched control (derived from the clinic database). None developed TB or any serious drug related toxicity. 2 patients developed recurrent uveitis.
Conclusion: This real life documented experience unravelled impressive long term benefits following a kick start short term induction regimen of Biosimilar Adalimumab in AS. Though contrary to standard practice, this seemed a practical solution in our setting. We speculate a psychological and motivational boost rather than a prolonged real time biological effect (Bs-ADL) for this phenomenon. Our study has important socioeconomic bearing and merits validation.
Acknowledgement: This was essentially a non-commercial investigator-initiated study. Zydus Cedilla India provided a generous research grant with free of cost Bs_ADL to several patients and a large concession in the cost to the rest.



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AB0642 SACROILIAC JOINT INJECTIONS PERFORMED WITH ULTRASOUND GUIDANCE IN PATIENTS WITH SACROILIITIS

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Background: Sacroiliitis is the hallmark of axial Spondyloarthritis (axSpA). ASAS-EULAR management recommendations for axSpA, consider glucocorticoid injections directed to the local site of musculoskeletal inflammation as a

treatment option for pain relief, besides treatment with oral non-steroidal anti-inflammatory (NSAIDs) before starter biotechnological treatment. However, there are few studies to evaluate efficacy of this technique with a small number of patients and a short follow-up. Ultrasonography has been used as a valuable option to guide this technique.

Objectives: To evaluate the efficacy and safety of ultrasound-guided injections of sacroiliac joints (SIJs) in patients with sacroiliitis using clinical and laboratory outcomes at baseline and at 4-6th weeks.

Methods: This study involved patients with axSpA with acute sacroiliitis, ≥18 and ≤ 65 years old, with body mass index (BMI) < 30kg/m^2 attending the Rheumatology Outpatient Clinic, which had been poorly controlled (ASDAS>2.1) by conventional therapy (physiotherapy, NSAIDs at maximum tolerated dosing during ≥ 4 weeks). Sociodemographic, clinical (disease duration, BMI, BASDAI, BASFI, ASDAS) and laboratory (CRP) data was collected from the medical records at baseline and at 4-6th weeks.

Statistical analyses were conducted using SPSS version 25. Continuous variables were described with mean/median ± standard deviation (SD).

SIJs injection was performed, under ultrasound guidance, using standard procedures with 2mL of lidocaine 1% and 40mg of methylprednisolone, with a 22-gauge needle. The procedure was performed by the same operator. Written informed consents were obtained from all patients.

Results: We performed eleven sacroiliac injection in eleven consecutive patients (one procedure per patient). Nine patients (81.8%) were female, mean age (±SD) of 40.6(±9.4) years, median disease duration(±SD) of 0.9(±6.2) years and median BMI(±SD) of 24.2(±3.3). Eight patients (72.7%) had Nr-axSpA. All patients were non-responders to NSAIDs.

At 4-6th weeks there was a decreased in median (±SD) BASDAI (5.4±1.9 vs 4.1±1.9), BASFI (4.2±1.4 vs 3.5±2.3) and ASDAS (3.2±0.8 vs 2.2±0.6) indexes.

Conclusion: As previous studies demonstrated, this technique seems to be safe and quite effective.

Our goal is to increase the number of patients undergoing this technique and have a longer follow up to evaluate its efficacy. The study has several limitations: the mid- and long-term effects should be evaluated in the future based on the results of the short-term effects and the study was not conducted as a double-blinded, controlled study.

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Disclosure of Interests: Ana Rita Cunha: None declared, Carolina Mazeda: None declared, Renata Aguiar: None declared, Anabela Barcelos Speakers bureau: Bene, Eli-Lilly, Pfizer, MSD, Novartis

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AB0643 DRUG SURVIVAL OF SECUKINUMAB IN A SPONDYLOARTHRITIS COHORT. A 24 MONTHS MULTICENTRIC STUDY

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Background: Secukinumab inhibits the interaction between Interleukin 17A (IL-17A) and its receptor. Clinical trials have demonstrated good data in efficacy and safety in patients with spondyloarthritis (SpA) as first biological choice or inadecuate response to other biological in SpA. However there is few evidence in real clinical practice.

Objectives: Evaluate the drug survival in a real clínical practice, as an indirect way to show the efficacy and security of Secukinumab at 24 months

Methods: A multicentric observational, longitudinal, retrospective study of 24 months conducted in five Madrid hospitals (Spain). Patients older than 18 years treated with Secukinumab which fullfilled ASAS criteria for SpA and/or modified New York criteria for ankylosing spondylitis (AS) and/or CASPAR criteria for psoriatic arthritis (PsA) were included. For evaluation of the drug survival, dates from starting until closing date or definite withdrawal of the treatment were determined. Kaplan-Meier function was used to estimate the drug survival and Wilcoxon test for the comparison of the survival rate between the different diagnoses, because of the survival curves did not reach the median

Results: A total of 71 patients were included. The mean age was 50.26 ys (SD 11.01), 57.75% women. 35 patients fullfilled classification criteria for PsA ant 36 fullfilled classification criteria for axSpA. 22 patients were naïve for biologic therapies and 49 patients had an inadecuate response to TNFi. 13 patients discontinued Secukinumab before the closing date, the main reason for the interruption was secondary failure (n= 6), and primary failure (n=2). Secukinumab survival rate was 81.95% up to 24 months in this cohort. The median of survival was 2.36 years (IC: 1.79-2.84). There were no significant differences about the drug survival related to diagnosis (p=0.976). The safety data were similar to those described in clinical trials.

Conclusion: Secukinumab is an effective and safe treatment for the management of espondiloarthritis regardless of the subtypes, with a high survival rate. In this study naive patients show similar data obtained in clinical trials. In this cohort of patients, those who initiated secukinumab after failure to TNFi, showed a greater secukinumab survival than the data provided in clinical trials

Disclosure of Interests: None declared

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AB0644 ULTRASOUND GUIDED EPIDURAL INJECTION IN RADIOGRAPHIC AXIAL SPA PATIENTS WITH LIMITED SPINE MOBILITY: A PROSPECTIVE PILOT RANDOMIZED CONTROLLED TRIAL

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Background: Ankylosing Spondylitis (AS) is a systemic inflammatory disease of unknown origin. It affects mainly males. Chronic inflammatory back pain is the commonest presenting symptom and regularly develops between 20 and 40 years age. AS can likewise, have extra-articular manifestations. These manifestations commonly develop after the onset of axial symptoms but hardly can precede them. Even though AS is a systemic disease, the presenting symptoms, treatment, and morbidity are largely dependent on spine affection. Epidural injections for managing chronic low back pain are one of the most frequently performed interventions in the United States. Friedly et al reported administration of epidural injections in 36% of patients with axial low back pain. However, there is no clinical evidence for the use of epidural injections in axial SPA and most recommendations are limited to radicular pain with disc herniation. The evidence for caudal epidural injections is Level I in managing pain secondary to disc herniation and radiculitis. To our best of knowledge, this is the first study evaluating the role of caudal epidural steroid and lidocaine injections in managing pain and function of the spine in radiographic axial SPA.

Objectives: To evaluate the significance of caudal epidural injections in controlling pain and spinal stiffness in radiographic axial SPA.

Methods: In our study 32 Patients were included. They were randomly doled out into 2 equivalent groups; Group I received caudal epidural injections ultrasound guided with 1% lidocaine hydrochloride (xylocaine, AstraZeneca) 9 mL mixed with 1 mL of triamcinolone 40 milligrams (Kenacort, Bristol Myers Squip), whereas Group II did not receive. Both groups were matched regarding age, sex and disease duration (table) and both were under treatment with anti TNF and NSAIDs with or without sDMARDs. All participants fulfilled the ASAS criteria for radiographic axial SPA. Outcomes measures included: visual Analogue Scale (VAS), and ASDAS score with assessment at baseline, 2 weeks and 8 weeks post-treatment. Significant pain relief was defined as 50% or more or no pain. ASDAS improvement is considered when the score reduction ≥ 1.1.

Results: There was a significant difference between both groups regarding pain (Figure 1) and ASDAS scores (Figure 2) in favor of group I. This effect was maximum after 2 weeks interval. More than two thirds of the cases (68.8%) had significant pain relief among group 1, compared to only 18.8% among group 2. Despite the decline of this effect after 8 weeks, still the difference significant between both groups. Shorter disease duration and older age of onset were associated with better outcomes among group 1 but not group 2. However, these correlations were non-significant.

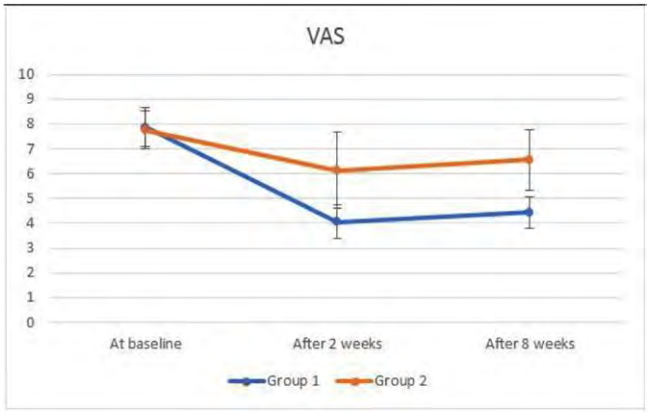


Figure 1. Change of VAS between the two groups.

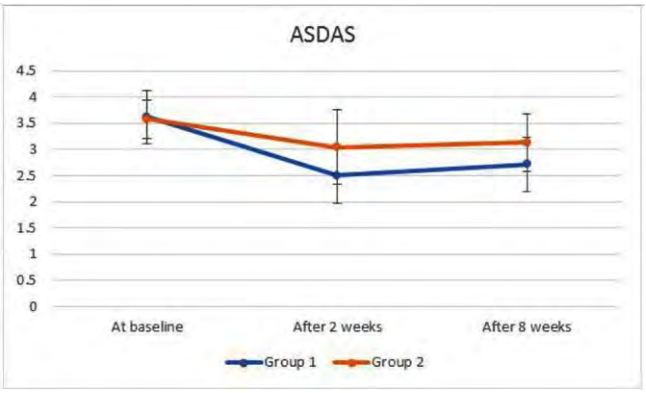


Figure 2. Change of VAS between the two groups.

Conclusion: Caudal epidural injection is cheap, effective and practical technique in controlling pain and stiffness of the spine in radiographic axial SPA with acceptable complications and relatively sustained effect. Studies including bigger number of participants and longer span of follow up still required.

Table. Comparison between the two groups as regards demographic and outcome data

Item		Group 1	Group 2	P value
Age		40.31±4.54	38.88±5.44	0.423
Sex	Male	10(62.5%)	9(56.2%)	0.719
	Female	6(37.5%)	7(43.8%)	
Disease duration	(in years)	3.13±1.48	3.22±1.24	0.847
VAS	At baseline	7.88±0.81	7.75±0.77	0.658
	After 2 weeks	4.06±0.68	6.13±1.54	**<0.001**
	After 8 weeks	4.44±0.63	6.56±1.21	**<0.001**
	% improved at 2 weeks	11(68.8%)	3(18.8%)	**0.004**
	% improved at 8 weeks	6(37.5%)	2(12.5%)	0.102
ASDAS	At baseline	3.62±0.51	3.58±0.37	0.814
	After 2 weeks	2.50±0.53	3.04±0.71	**0.020**
	After 8 weeks	2.72±0.52	3.13±0.55	**0.036**
	% improved at 2 weeks	10(62.5%)	3(18.8%)	**0.012**
	% improved at 8 weeks	7(43.8%)	2(12.5%)	0.057

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Disclosure of Interests: None declared
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AB0645 PREDICTORS OF THE EFFECTIVENESS OF INTRA-ARTICULAR GLUCOCORTICOID INJECTIONS IN RHEUMATIC HIP INVOLVEMENT

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Background: Hip involvement in chronic inflammatory rheumatic diseases is a turning point in the course of the disease because of disability and functional impairment. Total joint replacement surgery rate in spondyloarthritis increased 40% despite the use of Disease-modifying anti-rheumatic drugs (DMARD) and biologic treatment. Intra-articular glucocorticoid injection may help prevent hip joint replacement surgery and radiographic progression.
Objectives: This study aimed to determine predictive factors of the steroid injections' efficiency in chronic inflammatory rheumatic diseases with hip involvement.
Methods: This is a retrospective study over a 13-years (2006-2019) that included patients followed for chronic inflammatory rheumatic diseases complicated by hip involvement and underwent intra-articular glucocorticoid injection.
Results: Forty-two patients were enrolled: 32 male (76,2%) and 10 women (23,8%). The average age was 27 years [6-73] at the time of the steroid injection. Ankylosing spondylitis (AS) was present in 73,8% of cases (radiographic axial spondylarthritis 90,3%, Psoriatic spondylitis 6,5% and peripheral enthesitis 3.2%) and juvenile idiopathic arthritis (JIA) in 26.2% of cases (enthesitis-related arthritis 63,6%, oligoarticular JIA 18,2%, seronegative polyarticular JIA 9,1% and juvenile psoriatic arthritis 9,1%). Active smoking was found in 47.6% of cases. All patients were on DMARD: NSAIDs (19%), methotrexate (42.9%), salazopyrin (23.8%), combination of methotrexate and salazopyrin (2.4%) and anti-TNF alpha (7.1%).
Hip involvement was bilateral in 81% of patients. Examination revealed pain and limited hip mobility in all cases. Radiographic forms in AS were: early coxitis (17,2%), condensing form (17,2%), destructive form (58,6%), synostosante (3,4%) et combined (3,4%). During JIA, hip involvement was destructive in 45.4% of cases and minimal to moderate in the remaining cases.
Lequesne algofunctional index averaged 11 (3-18). An improvement was reported in 63.4% of cases. Statistically significant decrease was found in the BASDAI score, visual analogue scale (VAS) for general health status as estimated by the patient and C-reactive Protein (CRP) (p=0.001; p=0.01 and p=0.03; respectively).
There was no statistically significant difference between the efficacy of intra-articular glucocorticoid injection and sex, age, smoking, diagnosis and whether the hip involvement was bilateral or not (p=0.5; p=0.2; p=0.8 and p=0.1; p=0.6; respectively). Steroid injections were less effective in patients treated with biologics (p=0.04). However, it was more effective in AS with early hip involvement (p=0.03).
Conclusion: Hip involvement is a negative prognostic factor in chronic inflammatory rheumatic diseases. Therefore, early diagnosis and management is essential in order to slow down the structural progression and the need for prosthetic surgery.
Disclosure of Interests: None declared
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AB0646 IS IT FEASIBLE TO ACHIEVE RECOMMENDED THERAPEUTICAL TARGET IN PATIENTS WITH AXIAL SPONDYLARTHRITIS IN CLINICAL PRACTICE? DATA FROM THE SPA-PAZ COHORT

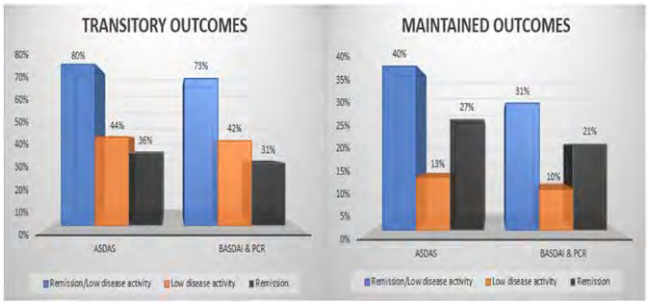
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Background: Current ASAS/EULAR recommendations for the management of patients with axial spondylarthritis (axSpA) establish that the therapeutic goal to achieve in clinical practice is remission, defined as the absence of both clinical and laboratory disease activity evaluated by BASDAI&CRP or preferably ASDAS and if this is not possible, low disease activity may be an alternative. Recently, ASDAS nomenclature has been modified, calling now low disease activity to what was previously called moderate activity. To this day we do not know if this target is feasible in clinical practice.
Objectives: To analyze the frequency of patients with axSpA achieving maintained remission (R) or low disease activity (LDA) after receiving biological therapy. Secondary objectives included: i) to assess if the activity index used influences the frequency of maintained R/LDA, ii) analyze the prognostic factors for achieving maintained R/LDA.
Methods: An observational, longitudinal study of a prospective cohort (SpA-Paz) including all patients with axSpA who initiated their first biological treatment between the years 2003-2017. Demographic, clinical and analytical data were collected at the beginning of treatment and clinical disease activity measured by BASDAI&CRP and ASDAS every 6 months for 2 years. Maintained R was defined as (BASDAI<2 & normal CRP and/or ASDAS <1.3) and maintained LDA (BASDAI <4 & normal CRP and/or ASDAS <2.1) on at least 3 consecutive visits. Statistical analysis: i) measures of central tendency and dispersion for quantitative variables and frequencies for qualitative variables; ii) univariate and multivariate analysis of binomial logistic regression model and calculation of OR and 95% CI.

Results: Out of 186 patients with axSpA who started treatment during the study period, 63% were men with a mean age of 54 ± 14.1 years. 75.3% of the patients had radiographic axSpA and 74.7% were HLA-B27 positive. Other baseline characteristics (not shown due to space restrictions). Overall, 80% of the patients achieved ASDAS R/LDA (R36%/LDA44%) in at least one of the visits after 2 years of follow-up, but only 40% (R27%/LDA13%) fulfilled the maintained ASDAS R/LDA state. On the other hand, 73% of patients were classified as BASDAI&CRP R/LDA (R31%/LDA42%) in at least one of the visits, but only 31% (R21%/LDA10%) obtained the maintained BASDAI&CRP R/LDA state. In the multivariate analysis, we observed an independent statistically significant association with male sex (OR=3.19; 95% CI=1.46-6.99), younger age at the beginning of the biological treatment (OR=0.97; 95% CI=0.95-0.99) and the use of methotrexate (OR=3.07; 95% CI=1.39-6.78) in patients who achieved maintained BASDAI&CRP R/LDA and with male sex (OR=4.01; 95% CI=1.83-8.77), younger age at the beginning of the biological therapy (OR=0.96; 95% CI=0.94-0.99) and HLA B27 presence (OR=4.30; 95% CI=1.68-11.01) in patients who achieved maintained ASDAS R/LDA.

Conclusion: Although the majority of patients with axSpA who initiate biological therapy achieve the recommended therapeutic goal in the first two years of treatment, the percentage of patients who manage to maintain the R/LDA status is limited. In our study, maintained R was more frequent than maintained LDA, being somewhat higher when measured by ASDAS. This fact may suggest that patients who achieve maintained R have a greater inhibition of their inflammatory activity and, therefore, it remains in time. Male sex and younger age at the beginning of the biological therapy were the main baseline predictors for achieving maintained R/LDA.

Graphics:



Disclosure of Interests: Karen Nathalie Franco Gomez: None declared, Chamaida Plasencia: None declared, Marta Novella-Navarro: None declared, Diego Benavent: None declared, Patricia Bogas: None declared, Romina Nieto: None declared, Irene Monjo: None declared, Laura Nuño: None declared, Alejandro Villalva: None declared, Diana Peiteado Grant/research support from: AbbVie, Lilly, MSD, and Roche, Speakers bureau: AbbVie, Roche, and MSD, Alejandro Balsa Grant/research support from: BMS, Roche, Consultant of: AbbVie, Gilead, Lilly, Pfizer, UCB, Sanofi, Sandoz, Speakers bureau: AbbVie, Lilly, Sanofi, Novartis, Pfizer, UCB, Roche, Nordic, Sandoz, Victoria Navarro-Compán Consultant of: Abbvie, Lilly, Novartis, Pfizer, UCB, Speakers bureau: AbbVie, MSD, Lilly, Novartis, Pfizer, UCB

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AB0647 THE EFFECT OF EXTRACORPOREAL SHOCK WAVE THERAPY (ESWT) ON PLANTAR FASCIITIS IN PATIENTS WITH AXIAL SPONDYLOARTHROPATHIES: DOUBLE-BLIND, RANDOMIZED CONTROLLED TRIAL

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Background: The effectiveness and safety of radial extracorporeal shock wave therapy (r-ESWT) on chronic plantar fasciitis (PF) in patients with axial spondyloarthropathies (SpA) remains unclear.

Objectives: To investigate the efficacy and tolerability of r-ESWT in patients with PF in axial-SpA on the clinical and radiological parameters.

Methods: In this double-blind, randomized controlled trial, 22 axial-SpA patients with PF whom have heel pain above 5 according to Visual Analog Scale (VAS) over 3 months were randomly divided into two groups: r-ESWT (1.8 bar pressure, 10 Hertz frequency, 500 pulse intensity) and sham ESWT. Both groups received a total of 3 treatments at one week intervals. All patients were assessed by using the VAS, heel pressure algometry, Foot Function Index and plantar fascia ultrasonography (thickness, convexity, echogenicity of PF, presence of perifascial fluid and subcutaneous tissue edema) at baseline, one week after each session and 4th and 8th week after the last therapy. A decrease of more than two units on the VAS and improvements on plantar fascia ultrasonographic assessments was considered as primary and secondary endpoints respectively.

Results: Descriptive data of the patients are presented in table 1. Both groups showed significant improvements in all assessment parameters ($p<0.05$) after the therapy sessions and at the 4th and 8th week follow-up. No serious adverse event was observed in any patient. When two groups were compared regarding the differences in improvements, no statistically significant difference was found between the r-ESWT and sham ESWT groups in any of the parameters ($p>0.05$).

Table 1. Baseline demographic characteristics of patients

	r-ESWT group (n:10)	Sham group (n:12)
Sex (n, %)		
Female	7 (%70)	9 (%75)
Age* (year)	43.8±8.23	48.5 ± 7.62
Height* (cm)	163.1±7.17	160.75±11.71
Weight *(kg)	80.1±9.38	81.67±22.31
BMI* (kg/cm^2)	30.2±3.92	31.11±5.42
Duration of heel pain n, (%)		
>6 month	8 (%80)	10 (%83.3)
3-6 month	2 (%20)	2 (%16.7)
VAS (0-10)	8.22 ± 1.394	7.82 ± 0.603
FFI scores*	Right Left	Right Left
Pain	60.66±22.20 51.11±33.37	61.18±21.55 63.18±9.83
Disability	66.66±16.34 51.55±34.20 60.33±31.35	68.09±27.23 72.27±18.74
Activity restriction	44.77±41.08	58.72±35.51 62.36±29.28
Total	62.66±15.06 49.14±31.60	62.54±25.05 65.90±15.89
Pressure algometry (kg/cm^2)	Right Left 2.07 ± 1.58 3.86 ± 4.09	Right Left 3.70 ± 3.17 3.60 ± 3.23
US measurements*	Right Left	Right Left
PF thickness (mm)	3.60± 0.73 3.40± 0.71	4.15± 1.07 4.04± 1.12
Increased PF convexity n (%)	4 (40) 2 (20)	4 (33.3) 5 (41.7)
Decreased echogenicity n (%)	2 (20) 3 (30)	6 (50) 8 (66.7)
Perifascial fluid (+) n (%)	2 (20) 0 (0)	3 (25) 4 (33.3)
Subcutaneus tissue edema (+) n (%)	8 (80) 6 (60)	8 (66.7) 9 (75)

Conclusion: To the best of our knowledge, this is the first study evaluating the clinical and radiological efficacy and tolerability of r-ESWT in patients with PF in axial-SpA. Radial extracorporeal shock wave therapy is safe and tolerable treatment on chronic PF in patients with axial-SpA.

References:

[1] Dizon JN, Gonzalez-Suarez C, Zamora MT, Gambito ED. Effectiveness of extracorporeal shock wave therapy in chronic plantar fasciitis: a meta-analysis. Am J Phys Med Rehabil. 2013 Jul;92(7):606-20

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AB0648 COMPARING SYMPTOMS, TREATMENT PATTERNS, AND QUALITY OF LIFE OF ANKYLOSING SPONDYLITIS PATIENTS AND NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS IN JAPAN

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Background: Axial spondyloarthritis (axSpA) is a chronic inflammatory disease of the axial skeleton associated with impaired health-related quality of life (QoL) and disability.

Objectives: To better understand the symptoms, clinical characteristics, treatment patterns, and quality of life (QoL), of non-radiographic axial spondyloarthritis (nr-axSpA) patients and how they compare to ankylosing spondylitis (AS) patients in Japan.

Methods: Data from a cross-sectional survey conducted with physician (rheumatologists, orthopedic surgeon, and internal medicine) and their consulting

patients in Japan were analyzed. Data were collected from Jun-Aug 2018 via physician-completed patient record forms and patient self-completed forms. Patients who had physician confirmed diagnoses of AS and nr-axSpA were eligible to participate. Demographics, disease status (improving, stable, unstable, deteriorating), symptoms, and medication use were reported by the physician, while work disability and QoL measures were reported by the patient using validated questionnaires. QoL and treatment patterns of nr-axSpA and AS patients were compared using parametric tests and non-parametric tests where appropriate.

Results: Data from 41 physician, 72 AS patients, and 91 nr-axSpA patients were included in this analysis. A higher proportion of AS patients were male (70.8% vs. 58.2%; p=0.1040), yet this was not statistically significant. AS patients had a similar mean age (55.0 vs. 55.1; p=0.9762) compared to nr-axSpA patients. The majority of AS and nr-axSpA patients (61.1% vs. 62.9%; p=0.872) were not receiving a biologic. On average, AS and nr-axSpA patients reported similar rates of symptoms (Table 1). Patient reported outcomes such as the Assessment of SpondyloArthritis international Society Health Index (ASAS HI;6.0 vs. 6.4; p=0.6103), Patient Global Assessment (18.7 vs 22.7; p=0.4239), and the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI; 3.1 vs. 3.4; p=0.3453) were similar between AS and nr-axSpA patients. AS patients reported a lower EQ-5D VAS (62.6 vs. 71.3; p=0.0237) when compared to nr-axSpA patients.

Table 1. Characteristics of AS and nr-axSpA Patients in Japan

	AS N=72	Nr-axSpA N=91	p-value
Mean age, (SD)	55.0 (17.5)	55.1 (16.5)	0.9762
Gender, males; n (%)	51 (70.8%)	53 (58.2%)	0.1040
BMI, mean (SD)	23.4 (3.5)	22.7 (3.1)	0.1890
Joint Inflammation or Stiffness; n (%)	25 (34.7%)	32 (35.2%)	1.0000
Inflammatory Back Pain; n(%)	25 (34.7%)	34 (37.4%)	0.7456
HLA-B27 positive; n (%)	7 (9.7%)	4 (4.4%)	0.2169
Alternating Buttock Pain; n (%)	6 (8.3%)	5 (5.5%)	0.5390
Dactylitis; n (%)	5 (6.9%)	6 (6.6%)	1.0000
Enthesitis; n (%)	5 (6.9%)	9 (9.9%)	0.5825
Tendonitis; n (%)	0 (0.0%)	2 (2.2%)	0.5037
Synovitis; n (%)	3 (4.2%)	4 (4.4%)	1.0000
Arthritis; n (%)	15 (20.8%)	26 (28.6%)	0.2806
Osteoporosis; n (%)	8 (11.1%)	13 (14.3%)	0.6412
Physician's Global VAS, mean (SD)	12.1 (11.2)	22.6 (11.0)	0.0100
Patient Global VAS, mean (SD)	18.7 (18.5)	22.7 (11.7)	0.4239
EQ-5D VAS, mean (SD)	62.6 (25.0)	71.3 (20.2)	0.0237
BASDAI, mean (SD)	3.1 (1.8)	3.4 (2.6)	0.3453
ASAS HI, mean (SD)	6.0 (4.3)	6.4 (5.1)	0.6103

Conclusion: Nr-axSpA and AS being part of the same disease spectrum (i.e. axial spondyloarthritis) share the same clinical features. The burden of the disease, as assessed by QoL measurements, is also similar in AS and nr-axSpA patients.

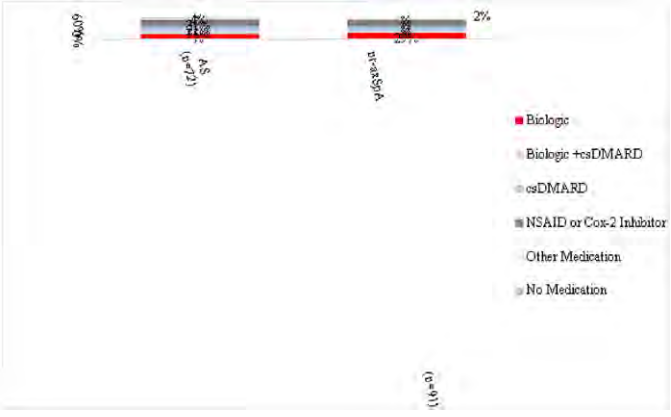


Figure 1. Medication Use among AS and nr-axSpA Patients in Japan

Disclosure of Interests: Tetsuya Tomita Consultant of: Eli Lilly and Company, Toshihiko Aranishi Employee of: Eli Lilly Japan, Kohei Hagimori Employee of: Eli Lilly Japan, Ko Nakajo Employee of: Eli Lilly Japan, Nicola Booth Consultant of: Janssen, Elizabeth Holdsworth Employee of: Adelphi Real World, Theresa Hunter Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company

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AB0649

REAL WORLD EFFICACY OF SECUKINUMAB: A SINGLE CENTRE EXPERIENCE

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Background: Secukinumab was approved by NICE for patients with active Ankylosing Spondylitis and Psoriatic Arthritis in 2017. Clinical trial data suggests secukinumab is a useful treatment option in both conditions, but often real world experience differs greatly from clinical trial results. In addition, patients with more refractory disease are often excluded from clinical trials.

Objectives: To assess the response to secukinumab in patients with seronegative spondyloarthropathy receiving treatment at University Hospital Coventry and Warwickshire

Methods: Patients starting secukinumab at UHCW were identified from the Blueteq funding database. Medical notes were reviewed retrospectively to assess response rates using BASDAI responses in Ankylosing spondylitis and PsARC responses in PsA. Patients who had previously had inadequate response to TNF inhibitors (PsA only) and severe psoriasis received 300mg secukinumab monthly; the remainder were prescribed 150mg monthly.

Results: 146 patients commenced secukinumab between June 2017 and January 2020 and had outcome data recorded. 73 patients (50%) had received previous biologic agents prior to secukinumab exposure. Patients with Ankylosing spondylitis had high BASDAI (6.8±1.4) and spinal pain (7.5±1.4). 48 patients had an initial response to treatment as per outcome measures done before and after Secukinumab inception. Secukinumab was effective in 89 patients (94%), and 87 (91%) continued treatment.

In psoriatic arthritis, despite high levels of activity at baseline (mean tender joint count 10±8; swollen joint count 6±3) and 65% prior biologic exposure; high rates of response were seen. The majority of patients have continued treatment. Secukinumab was well tolerated in both patient groups with low rates of discontinuation due to adverse events (8 patients, 5%). Adverse events included recurrent infection (3), rash (1), mouth ulcers (1), vertigo (1), new onset cancer (1) and new onset Crohn's (1) although rates were low overall. Patients with pre-existing uveitis did not develop exacerbations but low numbers of patients with prior uveitis were treated.

	PsA (n=51)	AS (n=95)
Age in years, mean (SD)	53 (13)	49(12)
Male sex, n (%)	21 (41)	62 (65)
Disease duration in years, mean (SD)	8 (8)	10.9 (9.2)
Previous biologic exposure, n (%)	30 (65)	43 (48)
Number of prior biologics, median (range)	1 (1-4)	1 (1-4)
Responder, n (%)	37 (72)*	89 (93)
Discontinuation, n(%)	12 (24)	8 (8.5)
Adverse events	6	2
Lack of efficacy	6	4
Other	0	2

*Response could not be assessed in 3/51 PsA patients due to insufficient clinical data; these patients have been recorded as non responders

Conclusion: Secukinumab demonstrates high levels of efficacy even in a cohort of patients with longstanding PSA and AS with high rates of inadequate responses to other biologics.

Secukinumab is well tolerated with low rates of discontinuation due to adverse events.

References: Certolizumab pegol and secukinumab for treating active psoriatic arthritis after inadequate response to DMARDs Technology appraisal guidance [TA445]

Secukinumab for active ankylosing spondylitis after treatment with non-steroidal anti-inflammatory drugs or TNF-alpha inhibitors Technology appraisal guidance [TA407]

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AB0650 BIOSIMILAR INFLIXIMAB EXPERIENCE IN SPONDYLOARTRITIS PATIENTS: TREASURE REAL LIFE RESULTS

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Background: Biosimilar infliximab (bio-INF) was approved for all indications of the reference product in several countries. It has been marketed since 2014 in Turkey and used in the same indications with its bio-originator.
Objectives: Herein, we aimed to analyse clinical features and the drug survival rates of spondyloarthritis patients who have recieved bio-INF.
Methods: This multicenter, prospective observational cohort study used the TReasure database in which web-based registration of rheumatoid arthritis and SpA patients are being performed in 13 centers across different regions of Turkey. Age, gender, and acute phase responses (erythrocyte sedimentation rate and C-reactive protein), HAQ scores, VAS patient global, VAS fatigue, VAS pain, VAS physician global, BASDAI, BASFI, ASDAS ESH and ASDAS CRP values, clinical findings of SpA patients, number of patients who has received bio-INF as first line therapy or after switch, treatments which are used before bio-INF, the reasons for switching bio-INF to another biologic DMARD and drug survival rates were retrospectively evaluated.
Results: A total number of 231 SpA (94 (40.7 %) female, 137 (59.3%) male, mean age 43±11 yrs) patients have received biosimilar infliximab in the database. Of the 231 patients 127 (55%) had received bio-INF as first line therapy, whereas 104 (46 (19.9%) 2nd choice, 58 (25.1%) 3rd choice) patients used switching after another biologic DMARD. Previously used biologic and synthetic DMARDs were adalimumab (28.6%), etanercept (22.5%), golimumab (9.1%), original infliximab (8.2%), secukinumab (13.4%), methotrexate (23.8%), leflunamid (10.4%), sulphasalazine (60.6%). The baseline and first visit (3. Months) diseases activity scores were shown in Table 1. Drug survival rates were 79.1 in 12. months, 65.5 in 24. months and 54.6 in 60. months. (Figure 1). The most common reasons for switching from biosimilar infliximab to another biologic DMARD is secondary (25(10.8%)), and primary ineffectiveness (22(9.5%)). Other reasons to discontinuation of treatment are psoriasis (5 (2.1%)), infusion reaction (3(1.2%)), allergic reaction (22(8.8 %)), chest pain (3(1.2%)), dyspnea (1 (0.4%)), vasculitis (1 (0.4%)) and patient or doctor wish (7 (3.4%)).
Conclusion: The results of this real life data provides evidence that biosimilar infliximab is an effective and safe treatment option with long term use in SpA patients. Drug survival rates of bio-INF is similar to its bio-originator.

Table 1. Disease activity scores

	Baseline visit	3.month	
	median (Q1-Q3)	median (Q1-Q3)	p
HAQ score	0,63 (0,4-1)	0,25 (0-1)	**<0,001**
BASDAI	6,2 (4,8-7)	2,8 (1-5)	**<0,001**
BASFI	5,05 (3,3-6)	2,1 (0,45-4)	**<0,001**
VAS Patient Global	70 (50-80)	30 (10-50)	**<0,001**
VAS Doctor Global	60 (40-70)	30 (20-40)	**<0,001**
VAS Pain	50 (3-80)	30 (10-50)	0,572
VAS fatigue	70 (50-80)	40 (10-65)	**<0,001**
ESR	24 (11-45)	11 (6-23)	**<0,001**
CRP	12,1 (4,4-30)	3,91 (2,19-9)	**<0,001**
ASDAS ESR	3,12 (2,51-4)	2,05 (1,39-3)	**<0,001**
ASDAS CRP	3,53 (2,86-4)	2,21 (1,5-3)	**<0,001**

*Wilcoxon Signed Rank Test

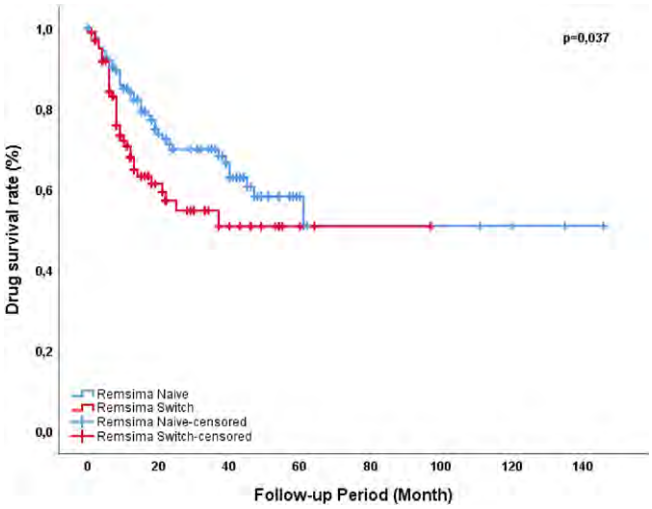


Figure 1. Drug survival rates

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AB0652 MACHINE LEARNING TO PREDICT EARLY TNF INHIBITOR USERS IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Tumor necrosis factor (TNF) inhibitors are important drugs in treating patients with ankylosing spondylitis (AS). However, they are not used as a first-line treatment for AS. There is an insufficient treatment response to the first-line treatment, non-steroidal anti-inflammatory drugs (NSAIDs), in over 40% of patients. If we can predict who will need TNF inhibitors at an earlier phase, adequate treatment can be provided at an appropriate time and potential damages can be avoided. There is no precise predictive model at present. Recently, various machine learning methods show great performances in predictions using clinical data.
Objectives: We aim to generate an artificial neural network (ANN) model to predict early TNF inhibitor users in patients with ankylosing spondylitis.
Methods: The baseline demographic and laboratory data of patients who visited Samsung Medical Center rheumatology clinic from Dec. 2003 to Sep. 2018 were analyzed. Patients were divided into two groups: early TNF inhibitor users treated by TNF inhibitors within six months of their follow-up (early-TNF users), and the others (non-early-TNF users). Machine learning models were formulated to predict the early-TNF users using the baseline data. Additionally, feature importance analysis was performed to delineate significant baseline characteristics.
Results: The numbers of early-TNF and non-early-TNF users were 90 and 509, respectively. The best performing ANN model utilized 3 hidden layers with 50 hidden nodes each; its performance (area under curve (AUC) = 0.75) was superior to logistic regression model, support vector machine, and random forest model (AUC = 0.72, 0.65, and 0.71, respectively) in predicting early-TNF users. Feature importance analysis revealed erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and height as the top significant baseline characteristics for predicting early-TNF users. Among these characteristics, height was revealed by machine learning models but not by conventional statistical techniques.
Conclusion: Our model displayed superior performance in predicting early TNF users compared with logistic regression and other machine learning models. Machine learning can be a vital tool in predicting treatment response in various rheumatologic diseases.

Disclosure of Interests: None declared
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AB0653 SURVIVAL OF BIOLOGIC THERAPHY AS SECOND LINE IN PATIENTS WITH ANKYLOSING SPONDYLITIS. EXPERIENCE IN A TERTIARY CARE CENTRE

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Background: In ankylosing spondylitis (AS) patients with lack of response to a first line of biologic disease modifying antirheumatic drugs (bDMARD), switching to another bDMARD is recommended, aiming either to the same or different therapeutic target. In several previous studies a decrease in drug survival has been noted when tumor necrosis factor alfa inhibitors (TNFai) are used as second or third treatment line (1,2).
Objectives: Primary endpoint: To evaluate survival of bDMARD as second line treatment in patients with AS non responding to TNFai either because of lack or loss of efficacy. Secondary: To evaluate the impact on drug survival of several variables such as sex, HLA, peripheral arthritis, radiologic sacroiliitis, CRP, BASFI, BASDAI or bDMARD class.
Methods: Observational, longitudinal and retrospective observational study. We included 67 patients diagnosed with AS who received treatment on second line with bDMARD (TNFai or anti IL7) after discontinuation of TNFai as first line of treatment. We analyze patients older than 18 yo, with at least 3 months of continuous treatment before and after switch, seen in our Hospital from 2006 to 2019. Data were collected regarding to demographics, HLA B27 positivity and functionality and activity index, CRP and treatment with cDMARDs.
Results: All 67 patients included were still on follow up after switching to second bDMARD. Median age was 37 yo, 56.7% were male and 31%, smokers. 35.8% patients had axial AS; 1.5% peripheral arthritis; 62.7%, mixed and 9%, dactilitis. 76.1% had radiographic sacroiliitis and 74.6%, HLA B 27+. As first bDMARD, the most common was Infliximab (IFX) (47.8%), followed by Adalimumab (ADA) (19.4%) and Etanercept (ETN 14.9%). Mean survival was 32.4 months (IFX, 37 months; ETN, 45; Golimumab, 32.3 and ADA, 24.1). The commonest cause of treatment suspension was loss of efficacy (LoE) (56.7%), followed by lack of efficacy (LaE) (17.6%) and adverse effects (AE) (16.4%).
As second bDMARD the most frequent was ADA (35.8%), followed by ETN (34.3%), Golimumab (9%), IFX (7.5%) and Secukinumab (6%) with a mean survival of 45 months (ETN 63.8, ADA 45.7, Golimumab 32). Treatment was discontinued in 47.8% of patients because of LoE (17.9%), LaE (17.9%) and EA (11.9%). A total of 16 AE were recorded, of which 6% were infections and 9%, allergic reactions. Regarding the analysis of the impact of other variables on drug survival, there was statistically significant differences on HLA B 27 carrier status (p=0.012), in which we observed an increase on survival when the patient is HLA B27 + and in whom BASDAI is higher before switching (p=0.02).
Conclusion: In our study, we did not observe differences in survival of second line bDMARD in patients with AS regarding type of TNFai, case of discontinuation or type of radiographic involvement in the first line of treatment. Patients with HLA B27+ and high value of BASDAI at the beginning of second bDMARD showed an increased on drug survival. Contrary to literature, we did not see significant differences regarding CRP.
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AB0654 IMPACT OF GENDER ON PATIENT PROFILE AND TREATMENT RESPONSE IN ANKYLOSING SPONDYLITIS PATIENTS TREATED WITH TNF-A INHIBITORS

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Background: Ankylosing spondylitis (AS) was historically seen as a predominantly male disease and although recent data showed a more homogenous sex prevalence there is still a long delay and more often a misdiagnosis in women. Also, studies showed that there might be gender-attributable differences regarding clinical characteristics, radiographic damage and response to treatment.
Objectives: The aim of this study was to assess gender differences in AS patients regarding the clinical presentation, disease activity, functional status and response to tumor necrosis factor-alpha inhibitor (TNF-α inhibitor) therapy.
Methods: This retrospective analysis included 59 AS patients treated with first TNF-α inhibitor for at least 12 weeks. TNF-α inhibitor therapy introduction and response was determined according to ASAS-EULAR management recommendations for AS. Clinical and demographic parameters were compared between the female and male patients.
Results: Twenty-four patients (40,68%) were females and 35(59,32%) were males. Women were older than male at moment of study (p=0,049), at the time of diagnosis (p=0,05) and when starting biologic therapy (p=0,009). Moreover, they had a longer diagnosis delay (p=0,017) compared to men. Prevalence of HLA-B27 status and the rate of peripheral arthritis, dactylitis, enthesitis, uveitis or inflammatory bowel disease (IBD) were not different between two groups. Disease activity and functional status were also similar in both groups. Males had a significantly longer drug survival time for first biologic (p=0,031). One female patient (4.2%) and 4 male patients (11,4%) showed primary or secondary inefficacy to TNF-α inhibitor (p=0,61). All 5 non-responders switched to second TNF-α inhibitor and showed a good clinical response. The comparison of the demographic features, clinical characteristics, disease activity, functional status and response to TNF-α inhibitor therapy according to the gender are presented in Table 1.
Conclusion: In our cohort, the presence of the female gender was related to longer diagnosis delay compared to males. Non-response rate for the first TNF-α inhibitor was similar between groups, but men had longer drug survival time for the first biologic.
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Table 1. Comparison of the baseline demographic, clinical characteristics and treatment response between female and male patients treated with TNF-α inhibitor

	female (n=24)	male (n=35)	P Value
Age (years), mean±SD	49,08±12,94	42,56±11,96	0,049
Age at onset (years), mean±SD	31,6±9,5	27,7±9,18	0,117
Age at diagnosis (years), mean±SD	39,02±11,22	33,06±11,36	0,05
Diagnosis delay (years), mean±SD	7,39±3,45	5,36±2,86	0,017
Age at TNF-α inhibitor initiation (years), mean±SD	46,4±12,25	38,08±11,14	0,009
HLA-B27 positivity n (%)	17 (70,8%)	32 (91,4%)	0,086
Family history n (%)	10 (41,7%)	15 (42,9%)	1
Peripheral arthritis n (%)	16 (66,7%)	17 (48,6%)	0,26
Enthesitis n (%)	3 (12,5%)	6 (17,1%)	0,9
Dactylitis n (%)	0 (0%)	3 (8,6%)	0,385
Uveitis n (%)	8 (33,3%)	9 (25,7%)	0,732
Inflamatory bowel disease n (%)	3 (12,5%)	5 (14,3%)	1
BASDAI score at TNF-α inhibitor initiation, mean±SD	6,33±1,69	6,11±1,77	0,637
BASFI score at TNF-α inhibitor initiation, mean±SD	5,68±1,39	6,09±1,39	0,272
ASDAS-CRP score at TNF-α inhibitor initiation, mean±SD	3,87±0,93	3,78±1,02	0,743
Duration of first TNF-α inhibitor use (months), mean±SD	35,33±26,66	51,54±28,25	0,031
Non-responders to first TNF-α inhibitor n (%)	1 (4,2%)	4 (11,4%)	0,611

Disclosure of Interests: None declared
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AB0655 IMPACT OF BIOLOGIC THERAPY ON WORK IMPAIRMENT IN REAL LIFE IN AXIAL SPONDYLOARTHRITIS PATIENTS: DATA FROM REGISPONSERBIO

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Background: Biologic therapy (BT) has demonstrated its effect in improving work impairment in axial Spondyloarthritis (axSpA) patients in clinical trials, however there is few data of these effects in clinical practice.
Objectives: -To assess the influence of BT in work status using the WPAI questionnaire in patients with axSpA in real life.
-To compare work status between incident and prevalent cases with BT.
-To evaluate factors related to changes in work status in these patients.
Methods: REGISPONSERBIO is an observational, prospective and multicentric Spanish registry of SpA patients under biologic treatment recruited between September 2013 and December 2014. The study includes demographic, radiologic and disease data from both incident (starting biological therapy at the inclusion) and prevalent (already under biologic therapy at the inclusion) patients. WPAI (Work Productivity and Activity Impairment) questionnaire was used to assess work status (employment, lost hours, absenteeism and presenteeism) in both groups of patients at six months after study inclusion. Patients more than 65 years old who were not working were excluded from the analysis, as no changes in work impairment are expected in these individuals.
A descriptive study of work status and related factors was performed using mean and standard deviation as appropriate. Work status was compared between both time-points in incidents and between incidents and prevalents. Uni and multivariate analysis for factors related to baseline work status were assessed, and correlation for change at six months.
Results: The study included 75 incident and 134 prevalent axSpA patients. After start of BT, incident patients presented an increase in the number of patients who affirmed to be actively working and an improvement in absenteeism, lost hours and presenteeism, however statistical significance was only reached in the number of hours lost. Comparing incident and prevalent cases, incident patients showed worse data on work status compared to prevalent ones, but only presenteeism reached statistical significance. Factors related to absenteeism and presenteeism at study inclusion were disease activity variables (PGA, BASDAI, ASDAS-CRP), ASQoL and BASFI. Best correlation with improvement in absenteeism at six months was with change in BASDAI (0.84 p 0.07) and age (-0.56 p 0.11), and with improvement in presenteeism were BASFI (0.59 p 0.002), ASQoL (0.57 p 0.002), BASDAI (0.54 p 0.04), PGA (0.51 p 0.01) and ASDAS-CRP(0.51 p 0.01).
Conclusion: Biologic therapy is associated to an improvement in work status in axSpA patients. The results suggest that the fast and high improvement in disease activity and disability observed after start of BT is not directly translated to an improvement in work status at short time. Disease activity, disability and quality of life were the main factors influencing both, work status at inclusion and improvement in absenteeism and presenteeism after BT was started.
Disclosure of Interests: Marta Arévalo: None declared, Mireia Moreno: None declared, Victoria Navarro-Compán Consultant of: Abbvie, Lilly, Novartis, Pfizer, UCB, Speakers bureau: AbbVie, MSD, Lilly, Novartis, Pfizer, UCB, Font Ugalde Pilar: None declared, Eugenio de Miguel Grant/research support from: Yes (Abbvie, Novartis, Pfizer), Consultant of: Yes (Abbvie, Novartis, Pfizer), Paid instructor for: yes (AbbVie, Novartis, Pfizer, MSD, BMS, UCB, Roche, Grunental, Janssen, Sanofi), Speakers bureau: yes (AbbVie, Novartis, Pfizer, MSD, BMS, UCB, Roche, Grunental, Janssen, Sanofi), Teresa Clavaguera Speakers bureau: novartis, BMS, Faes, Luis F. Linares Ferrando: None declared, Beatriz Joven-Ibáñez Speakers bureau: Abbvie, Celgene, Janssen, Merck Sharp & Dohme, Novartis, Pfizer, Jordi Gratacos-Masmitja Grant/research support from: a grant from Pfizzer to study implementation of multidisciplinary units to manage PSA in SPAIN, Consultant of: Pfizzer, MSD, ABBVIE, Janssen, Amgen, BMS, Novartis, Lilly, Speakers bureau: Pfizzer, MSD, ABBVIE, Janssen, Amgen, BMS, Novartis, Lilly, Xavier Juanola-Roura: None declared
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AB0656

IMPACT OF A FAMILY HISTORY OF SPONDYLOARTHRITIS ON TNFI DRUG SURVIVAL AND TREATMENT RESPONSE IN PATIENTS WITH ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS

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Background: Spondyloarthritis (SpA) is known to have high familial aggregation, with a positive family history of SpA being a strong risk factor for disease development, in particular for ankylosing spondylitis (AS). Despite this well-known characteristic of the disease, whether family history is associated with disease prognosis and treatment outcome has been much less studied. Patient characteristics predicting response to tumour necrosis factor alpha inhibitors (TNFi) in SpA include age, sex and high disease activity, but whether family history is predictive of TNFi treatment outcomes remains unclear.
Objectives: To assess if a family history of psoriatic arthritis (PsA), AS, or SpA in general is associated with a different drug survival and treatment response to TNFi in patients with AS and PsA.
Methods: Patients diagnosed with AS (N=1688) or PsA (N=3216) starting their first TNFi treatment between January 2006 and December 2017 were identified in the Swedish Rheumatology Quality Register (SRQ). Disease activity measures were extracted from SRQ at treatment start and at 3 and 12 months of treatment. Data on demographics and comorbidities were available through linkage to other national registries. Multiple imputation was applied to address missing data. Family history was defined as having at least one first-degree relative diagnosed with AS, PsA or any form of SpA in the National Patient Register at start of first TNFi. Analyses were made for AS and PsA index patients separately. Kaplan-Meier plots were used to compare drug survival, and hazard ratios for drug discontinuation were estimated with Cox regression adjusting for age, sex, disease duration and baseline disease activity. The change in disease activity from baseline to 3 months of treatment, and the proportion of patients remaining on treatment at 12 months and reaching low disease activity (LDA) with BASDAI (for AS) and DAS28-CRP (for PsA), were analysed in linear regression adjusting for age, sex, disease duration and baseline disease activity.
Results: A positive family history of AS was found in 14% of AS patients, and 12% of PsA patients had a family history of PsA. Characteristics such as age, sex and baseline disease activity were similar in AS patients with and without a family history of AS. Among PsA patients, those with a family history of PsA were to a larger extent female, with lower CRP but longer disease duration. No significant differences were seen in drug survival among patients with and without a family history of their respective disease (Figure 1), with hazard ratios for drug discontinuation of 1.03 (95% CI 0.84 to 1.27) in AS patients and 1.08 (95% CI 0.94 to 1.25) in PsA patients. Using family history of any form of SpA as exposure did not change this conclusion. The changes in disease activity at 3 months of treatment compared to baseline were similar between groups. At 12 months, 55.2% of AS patients with a family history were still on treatment and had a BASDAI corresponding to LDA, compared to 56.4% of AS patients without a family history. Among PsA patients, 38.7% of patients with a family history had reached DAS28-CRP LDA, compared to 42.6% for those without a family history. For both AS and PsA, these differences were non-significant.
Conclusion: While family history of SpA is a strong predictor of disease development, family history was not found to affect neither TNFi drug survival nor treatment response in patients with AS and PsA in this register-based study.

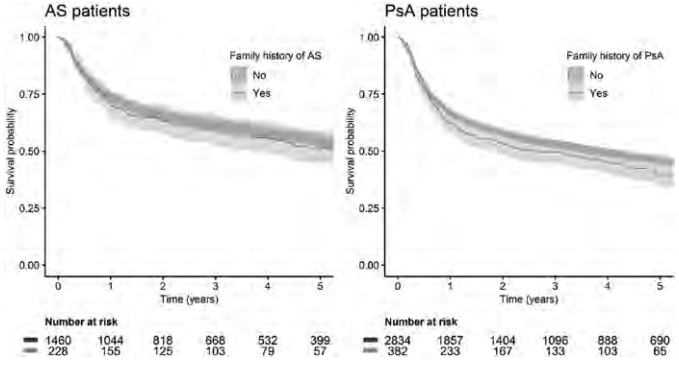


Figure 1. Survival plots for time to TNFi discontinuation in patients diagnosed with AS and PsA respectively, by family history status

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AB0657

IMPROVEMENT IN DISEASE ACTIVITY IS ASSOCIATED WITH ENHANCEMENT IN THE QUALITY OF LIFE DURING TUMOUR NECROSIS ALPHA INHIBITOR TREATMENT; A PROSPECTIVE COHORT EXPERIENCE IN AXIAL SPA

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Background: Axial spondyloarthritis (axSpA) is a chronic inflammatory condition affecting mainly axial skeleton. The disease usually starts in early adulthood and cause considerable impact on physical function, work ability and quality of life (QoL). With the introduction of tumour necrosis factor inhibitors (TNFi) significant improvement in articular and extra-articular manifestations of disease was shown in randomized controlled trials and several registries. However, there is limited data about the effects of TNFi therapy on QoL and the relationship between inflammation and QoL in cohort studies before.

Objectives: To evaluate the influence of TNFi agents on different aspects of QoL which might be a significant determinant of patient burden in axSpA patients in parallel with disease activity.

Methods: In total 83 TNFi naïve axSpA patients (62.7% male; mean age 40.6 ± 12 years) according to the ASAS criteria were included in this prospective observational cohort study between 2014-2018. Demographic and disease related characteristics were collected at baseline. Disease activity (BASDAI, ASDAS-CRP), function (BASFI) and QoL (SF-36 and ASQoL) were evaluated at baseline and 24th and 52nd weeks of follow-up. The changes in disease activity, function and QoL were assessed with Wilcoxon test and relationship between changes in QoL and activity on week 24 was evaluated by Spearman's correlation analysis.

Results: Baseline disease related characteristics, disease activity and QoL scores were presented in table 1. Both disease activity and QoL were significantly improved at 24th and 52th weeks (Figure 1). The change of SF-36 subscales and summary scores at weeks 24 were correlated with the change in disease activity and function (Table 2). The SF-36 scale and summary scores were found to be similar at 24 and 52 weeks of TNFi treatment (Figure 2).

Conclusion: The results of the present study suggest that TNFi treatment have a substantial influence on QoL in parallel to the control of disease activity at 24th weeks of treatment and this effect was sustained at 52 weeks not only randomized controlled trials but also real life experience.

Table 1. Demographic and clinical features in patients with axial spondyloarthritis at baseline

Parameters	
Duration of disease, years*	9 (10)
Ever smoking, n(%)	36 (43.4)
Body mass index, kg/m2 *	26 (4.9)
HLA-B27 positivity, n(%)	39/57 (68)
Peripheral arthritis, n(%)	39 (47)
BASFI*	5.1 (2.3)
BASDAI*	5.8 (1.7)
ASQOL*	12 (8)
ASDAS-CRP*	3.6 (1.1)
PCS*	32.5 (7.9)
MCS*	37.3 (10.9)

*All parameters presented as mean (SD)

Table 2. Correlation with changing of disease activity scores and quality of life parameters at 24 weeks

	ΔBASDAI		ΔBASFI		ΔASDAS-CRP		ΔASQOL	
	p	r	p	r	P	r	p	r
ΔPCS	<0.001	-.60	<0.001	-.43	<0.001	-.45	.002	-.39
ΔMCS	.001	-.42	.012	-.31	.019	-.29	<0.001	-.50
ΔPF	<0.001	-.48	<0.001	-.52	.008	-.31	.021	-.28
ΔRP	<0.001	-.48	.028	-.25	.001	-.38	.002	-.35
ΔBP	<0.001	-.60	.004	-.33	<0.001	-.45	<0.001	-.46
ΔGH	<0.001	-.58	.026	-.27	<0.001	-.45	<0.001	-.54
ΔVT	<0.001	-.48	.001	-.39	.004	-.33	.003	-.34
ΔSF	.001	-.38	.064	-.21	.098	-.19	.008	-.31
ΔRE	.003	-.34	.013	-.28	.012	-.29	.004	-.34

Table 2. Correlation with changing of disease activity scores and quality of life parameters at 24 weeks

	ΔBASDAI		ΔBASFI		ΔASDAS-CRP		ΔASQOL	
	p	r	p	r	P	r	p	r
ΔMH	.003	-.34	.016	-.28	.044	-.23	<0.001	-.43

BASDAI Bath Ankylosing Spondylitis Activity Index; BASFI Bath Ankylosing Spondylitis Functional Index; ASDAS-CRP Ankylosing Spondylitis Disease Activity Score with CRP; ASQOL Ankylosing Spondylitis Quality of Life Questionnaire; PCS Physical Component Summary Sscore; MCS Mental Component Summary Score.; PF Physical Functioning; RP Role Physical; BP Bodily Pain; GH General Health; VT vitality; SF Social Functioning; RE Role Emotional; MH Mental Health
Δ Changing according to basal values at week 24

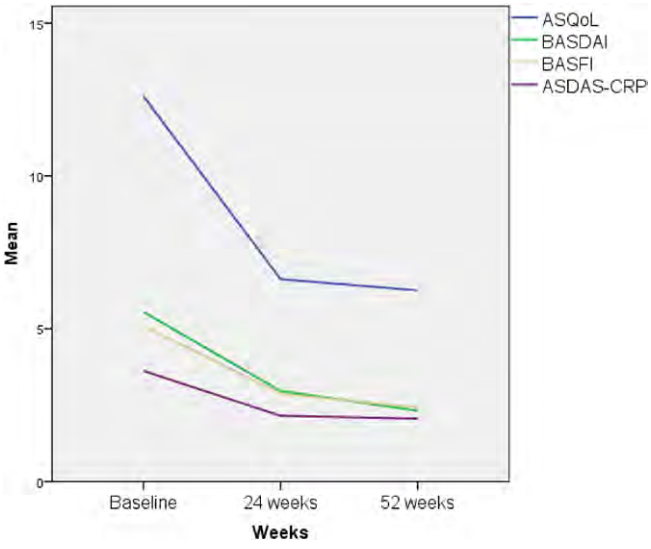


Figure 1. Improvement in disease activity and quality of life during the follow-up time

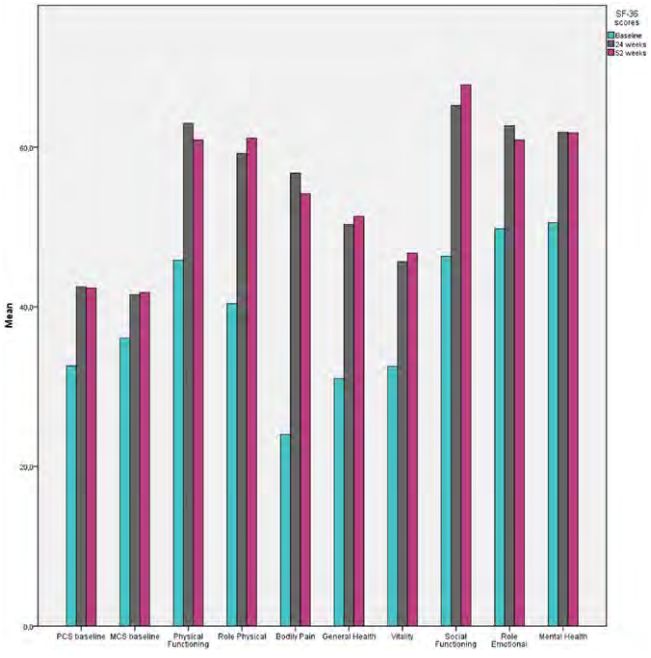


Figure 2. Mean change in Short Form 36 scores for patients with axial spondyloarthritis following anti-TNF therapy

Disclosure of Interests: None declared
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AB0658

PREDICTION OF THE EFFECTIVENESS OF TREATMENT WITH INFLIXIMAB BASED ON THE DETERMINATION OF ANTINUCLEAR ANTIBODIES IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: The search for new methods for predicting the effectiveness of treatment for biologics is important issue.
Objectives: To study antinuclear antibodies (ANA) levels during of AS treatment by infliximab and evaluate the influence of ANA on treatment outcome
Methods: The presence of antinuclear antibodies (ANA) in 53 ankylosing spondylitis (AS) patients (44 men (83.02%), and 9 women (16.98%), 37.19 ± 9.38 years (95% CI: 34.60-39.78) treated with infliximab was determined by indirect immunofluorescence on an automated AKLIDES system in a serum titer of 1/80 initially (before treatment with infliximab) and at week 30 (before 7 administration). Specific autoantibodies were analyzed on the AKLIDES Cytobead platform using the following antigens SS-A 52, SS-A 60, SS-B, ds-DNA, CENP-B, Sm, RNP / Sm. ANA research was carried out at the Brandenburg Technical University (Senftenberg, Germany). Evaluation of the effectiveness of infliximab therapy was carried out by determining ASDAS-CRP at baseline, at the 14th, 30th and 54th weeks.
Results: A positive nuclear type of ANA was determined initially in 2 out of 53 patients (3.77%) (in one case, the type of luminescence was nucleolar, in the other - speckled), at the 30th week of observation, 16 out of 53 patients became seropositive for ANA (30.18%). The frequency of occurrence of ANA at the 30th week of treatment was significantly higher than the baseline (p <0.0001). Positive results for the determination of specific autoantibodies to at least one nuclear antigen were found in 7 of 16 (43.75%) ANA-positive patients. In all cases, Anti-SS-A 60 (100%) was detected.
In the group of patients in whom treatment with infliximab was ineffective at the 54th week of observation, ANA positivity was observed in 10 (55.5%). In the case of treatment effectiveness at the 54th week of ANA, positivity was not observed at the 30th week. Differences in the incidence of ANA in patients with effective and ineffective treatment at week 54 were statistically significant (p <0.0001). Anti-infliximab antibodies were significantly more common in ANA-positive patients at week 30 of treatment with infliximab (p = 0.002, Fisher's exact test).
The appearance of ANA at the 30th week of infliximab therapy was inversely related to the absence of secondary resistance at the 54th week of treatment according to the ASDAS-CRP criteria (OR 0.026; 95% CI: 0.002-0.039; p = 0.0007), which allows us to use the results of the determination of ANA at the 30th week of treatment with infliximab as a predictor of secondary resistance to treatment at the 54th week. When testing the method for predicting secondary resistance to treatment with infliximab at week 54 based on the results of determining ANA at week 30 of treatment in a control sample of 12 patients with AS, it was found that the method is statistically significant (p = 0.0015, Fisher's exact test).
Conclusion: Assessment of ANA positivity at week 30 of treatment with infliximab can be seen a predictor of the development of secondary resistance to infliximab at the 54th week of treatment.
Disclosure of Interests: None declared
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AB0659

SECUKINUMAB PROVIDES SIGNIFICANT IMPROVEMENT OF SPINAL PAIN IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: RESULTS FROM THE 24-WEEK PHASE 3 SKIPPAIN STUDY

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Background: Spinal inflammation causing back pain is a hallmark of axial spondyloarthritis (axSpA) mainly affecting the sacroiliac joints and spine.[1] Spinal pain is the most burdensome symptom resulting in substantial functional limitations and impairment of health-related quality of life.
Objectives: SKIPPAIN (NCT03136861) evaluated efficacy and safety of secukinumab (SEC) in reducing spinal pain in patients (pts) with axSpA who had an inadequate response to NSAIDs.
Methods: SKIPPAIN, a 24 week (wk), randomised, double-blind, multicentre trial, enrolled axSpA pts (aged ≥18 years) with active disease defined by Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score ≥4 and average spinal pain numerical rating scale (NRS) score >4 at baseline (BL) and inadequate response to ≥2 NSAIDs ≥4 wks. The trial had a PBO-controlled period from BL to Wk 8 and a SEC 150/300 mg period from Wk 8 to Wk 24. Primary and key secondary endpoints were superiority of SEC 150 mg compared to PBO in achieving average spinal pain score <4 on a 0–10 NRS and BASDAI score <4 at Wk 8, respectively.
Results: 380 axSpA pts (269 (70.8%) AS and 111 (29.2%) nr-axSpA) were randomised to SEC 150 mg (N=285) or PBO (N=95). Demographic and BL characteristics are presented in **Table 1**. Proportion of responders, in terms of average spinal pain, was 31.9% vs. 20.0% for SEC vs PBO (p<0.05) and proportion of pts with BASDAI score of <4 was 33.3% vs. 23.2% for SEC vs PBO (p<0.05), respectively at Wk 8 (**Table 2**). After Wk 8, responder rates increased with SEC treatment. No unexpected safety events were reported.
Conclusion: Secukinumab provided significant improvement of spinal pain in pts with axSpA. SEC was well tolerated with a safety profile consistent with previous reports.[2]
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[1] Danve A & Deodhar A. *Clin Rheumatol*. 2019;38:625-34.
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Table 1. Patient Demographics and BL Characteristics

Characteristic	SEC 150 mg N = 285	PBO N = 95
Age (years)[1]	42.3 (11.9)	40.9 (12.2)
Female[2]	106 (37.2)	39 (41.1)
Time since onset of back pain (years)[1]	13.2 (10.1)	12.3 (9.6)
HLA-B27 positive[2]	233 (81.8)	76 (80.0)
hsCRP (mg/L)[1]	13.0 (21.5)	13.2 (23.5)
Elevated hsCRP (>5 mg/L)[2]	140 (49.1)	49 (51.6)
Previous exposure to TNF-α inhibitors[2]	34 (11.9)	11 (11.6)
Spinal pain NRS Score, 0-10 (average)[1]	7.27 (1.37)	7.31 (1.31)
Spinal pain NRS Score, 0-10 (nocturnal)[1]	7.31 (1.42)	7.40 (1.35)
Spinal pain NRS Score, 0-10 (total)[1]	7.23 (1.51)	7.22 (1.48)
BASDAI[1]	7.09 (1.22)	6.91 (1.38)
ASDAS[1]	3.75 (0.89)	3.67 (0.84)
Peripheral arthritis[2]	104 (36.5)	30 (31.6)

[1]mean (Standard Deviation), [2]n (%).
hsCRP, high-sensitivity CRP; N, number of randomized pts; n, number of evaluable pts; NRS, numerical rating scale

Table 2. Inferential Analysis of Achieving Spinal Pain and BASDAI Score <4.0 Using Logistic Regression Model at Wk 8

Variable	Treatment Group	n/N (%)	Odds ratio versus PBO	95% CI	P-value
Spinal Pain NRS Score (Average)	SEC 150 mg	91/285 **(31.9)**	1.89	(1.08, 3.33)	0.0264
	PBO	19/95 **(20.0)**			
Spinal Pain NRS Score (Nocturnal)	SEC 150 mg	77/285 **(27.0)**	1.72	(0.95, 3.10)	0.0720
	PBO	17/95 **(17.9)**			
Spinal Pain NRS Score (Total)	SEC 150 mg	92/285 **(32.3)**	2.38	(1.31, 4.31)	0.0043
	PBO	16/95 **(16.8)**			
BASDAI score	SEC150 mg	95/285 **(33.3)**	1.75	(1.01, 3.04)	0.0466
	PBO	22/95 **(23.2)**			

P-values are from a Logistic regression model with treatment as the principle factor and prior exposure to TNF inhibitors and naïve/inadequate responders to TNF inhibitors as stratification factors.
Missing values were imputed as non-responders. N, Number of randomised pts; n, Number of pts who are responders/evaluable pts.

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AB0660

LONG-TERM CLINICAL OUTCOME OF ANTI-TNF TREATMENT IN PATIENTS WITH EARLY AXIAL SPONDYLOARTHRITIS: 10-YEAR DATA OF THE ETANERCEPT VS. SULFASALAZIN IN EARLY AXIAL SPONDYLOARTHRITIS TRIAL

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Background: Long-term data on anti-TNF treatment in patients with early axial spondyloarthritis (SpA) is scarce.
Objectives: The objective of this analysis was to assess the long-term clinical efficacy (up to 10 years of treatment) of a tumor necrosis factor (TNF) inhibitor etanercept (ETN) in patients with early axial spondyloarthritis, who participated in the long-term (until year 10) extension of the ESTHER (Etanercept vs. Sulfasalazine in Early Axial Spondyloarthritis Trial) trial.
Methods: In the previously reported ESTHER trial, patients with early active axial SpA [including both non-radiographic axial SpA (nr-axSpA) and radiographic axial SpA (r-axSpA)/ankylosing spondylitis (AS)] with a symptom duration of <5 years and a positive MRI of the sacroiliac joints (SIJs) and/or the spine at baseline) were treated with ETN (n= 40) or sulfasalazine (SSZ) (n= 36) during the first year (1). At year 1, all patients who were not in remission continued with - or switched (in case of SSZ therapy) to – ETN for up to 10 years in total (1). Patients in remission discontinued their therapy and were followed-up until end of year 2; in case of remission loss, ETN was (re)-introduced and continued till the end of year 10.

Figure 1: Observed response rates to etanercept (A) and the course of disease related parameters in study completers (n=19) (B).



Table 1. Baseline characteristics of patients with axial spondyloarthritis who completed the study as compared to patients who dropped out.

	Completer (n=19)	Non-Completer (n=57)	p value
Age, years	32.5 (7.4)	32.8 (8.9)	0.91
Male patients, n (%)	15 (78.9)	29 (50.9)	***0.034***
Symptomduration, years	1.1 (1.2)	1 (1.7)	0.81
HLA-B27 positivity, n (%)	18 (94.7)	44 (77.2)	0.091
Elevated CRP (CRP>5mg/l), n (%)	7 (38.9)	33 (62.3)	0.088
Fulfilled New York criteria, n (%)	12 (63.2)	27 (47.4)	0.24
Patient global (0-10)	6.1 (1.9)	7.2 (1.7)	***0.025***
Physician global (0-10)	5.5 (1.5)	6.5 (1.2)	***0.007***
ASDAS	3 (0.7)	3.5 (0.8)	***0.042***
BASDAI (0-10)	5.4 (1.1)	5.8 (1.3)	0.27
BASFI (0-10)	4 (2.1)	4.4 (2)	0.41
BASMI (0-10)	1.2 (1.3)	2 (1.6)	***0.039***
AS-QoL (0-18)	7.6 (3.9)	10.1 (3.9)	***0.019***

Results: Out of 76 initial patients, 25% (n=19, 12 with r-axSpA and 7 with nr-axSpA) completed year 10 of the study. At baseline, completers were significantly more often male and showed lower values of patient (PGA) and physician global assessments of disease activity (PhGA), ASDAS (Ankylosing Spondylitis Disease Activity Score), BASMI (Bath Ankylosing Spondylitis Metrology Index), and AS-QoL (Ankylosing Spondylitis Quality of Life Questionnaire) as compared to non-completers (Table 1). When analyzing clinical data of the completers, mean BASDAI, BASFI and ASDAS values were constantly <2 during the follow up with no statistically significant differences between the r-axSpA and nr-axSpA sub-groups (Table 2, Figure 1B). In the entire group, a sustained clinical response was observed over 10 years of follow up (Figure 1A). A total of 39 serious adverse events were documented over the 10 years of the study, while six of them were seen as possibly associated with ETN treatment, which lead in five patients (one lymphoma, one sarcoidosis, one demyelinating neurological disease, one elevated liver enzymes and one recurrent minor infections) to an ETN discontinuation.
Conclusion: A sustained clinical response was shown over the 10 years of the study for the completers with comparable rates between r-axSpA and nr-axSpA. ETN was well tolerated across the entire treatment period and showed a good safety profile with no new safety signals.
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AB0661

CO-MEDICATIONS MAY ALTER THE RESPONSE TO TNF-INHIBITORS IN SPONDYLOARTHRITIS PATIENTS: A PHARMACOMICROBIOMIC EFFECT?

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Background: The reason why some spondyloarthritis (SA) patients fail to respond to TNF inhibitors (TNF-i) remains unclear. Recently, it has been shown in

cancer immunotherapy that the therapeutic response may be strongly altered by co-medication with drugs interfering with the gut microbiota, such as antibiotics, proton pump inhibitors (PPI), non-steroidal anti-inflammatory drugs (NSAIDs), psychotropic or antidiabetic drugs.

Objectives: Considering the potential role of the gut microbiota in the pathophysiology of SA as in the therapeutic response, the aim was to study the influence of co-medications known to interfere with the microbiota with the therapeutic response to TNF-i in SA patients.

Methods: We retrospectively reviewed the charts of all patients treated in our department with a first TNF-i from 2009 to 2018. Data collected were demographic information, HLA-B27 status, disease characteristics… Patients were classified as responder (R) or non-responder (NR) according to the BASDAI (< 40/100) value at M6 or to the clinician judgment (when BASDAI was not available). Regarding co-medications, we collected all drugs known to interfere with the gut microbiota that were administered 1 month before and during the first 3 months of the TNF-i treatment. We only considered drugs given to more than 5% of patients. Quantitative data were expressed as mean ± standard deviation, and qualitative variables as percentages. Univariate and multivariate analyses were performed to evaluate the relationship between co-medications and TNF-i. All analyses were computed on STATA 13.1 software with a statistically significant threshold of 0.05.

Results: We included 188 patients suffering from ankylosing spondylitis (n=89) or peripheral SA (n=99). They were 68 women and 120 men, mean aged 46.6 ± 13; 53% were B27 positive. TNF-i were infliximab (19%), etanercept (44%), adalimumab (34%) golimumab (2%), certolizumab (1%), combined with MTX in 51 patients. 135 patients (72%) were R and 53 (28%) NR. In univariate analysis, 59.1% of patients who received NSAIDs were R, compared to 88.2% of patients not treated with NSAIDs (p< 0.0001); 42.2% of patients receiving PPIs were R compared to 86.3% of patients PPI free (p< 0.0001); 55.8% of patients who were given antibiotics were R, compared to 75.7% of patients who did not (p=0,02); 27.8% of patients treated with psychotropic drugs were R, compared to 75.9% of patients not receiving such treatment (p< 0.0001) (Figure 1). Differences were not statistically significant for corticosteroids, MTX, angiotensin-converting enzyme inhibitors and statins. Although 91% of patients taken PPIs were also given NSAIDs, NSAIDs, PPIs and antibiotics intake were considered as independent factors associated with TNF-i failure in multivariate analysis.

Conclusion: Co-medication with NSAIDs, PPIs, antibiotics and psychotropic drugs were significantly associated with a decreased chance to respond to TNF-i. The hypothesis that this effect is due to their interference with the gut microbiota is only speculative but, regardless the reason of this interaction, clinician should be aware of the potential negative effect of these co-medication on TNF-i.

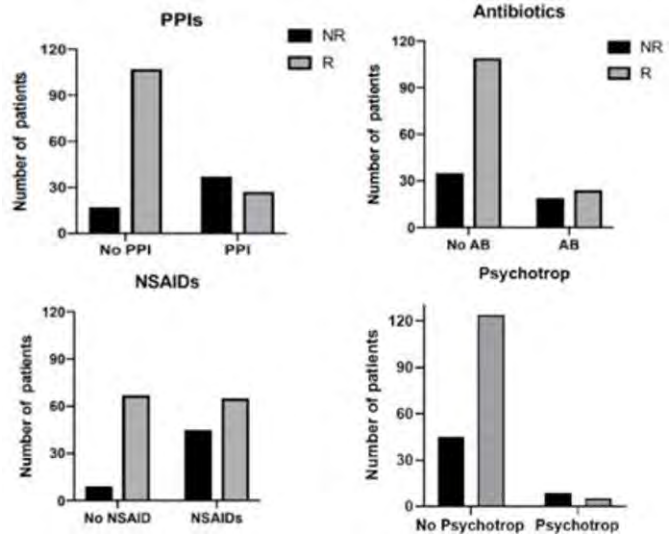


Figure 1.

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AB0662

TREATMENT AND FOLLOW-UP OF AXIAL SPONDYLOARTHRITIS IN DAILY CLINICAL PRACTICE - A SURVEY AMONG DUTCH RHEUMATOLOGISTS

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Background: ASAS-EULAR have developed management recommendations for axial spondyloarthritis (axSpA) to provide guidance to the management of patients with axSpA[1]. However, there is limited insight into how rheumatologists treat axSpA patients in daily clinical practice and if these recommendations are used.

Objectives: To get insight into the management of axSpA patients in daily practice in the Netherlands.

Methods: We performed a survey among rheumatologists in the Netherlands with 21 multiple choice questions; 5 general questions on characteristics of their practice and 16 questions addressing treatment and follow-up of axSpA patients in daily practice. The questionnaire was taken during structured face-to-face interviews by employees of the medical department of Novartis NL Rheumatologists in the Netherlands were invited to participate, aiming to get a sample of rheumatologists varying in geographical location and hospital type, as well as a mix of SpA-experts and non-SpA-experts. Rheumatologists gave approval for anonymous use of the data, which were entered in a database and analyzed using descriptive statistics.

Results: Between October 15 2019 and January 16 2020, 36 rheumatologists participated; 6 from university hospitals, 27 from general hospitals and 3 from private care centers.

81% of the rheumatologists referred most of their axSpA patients (76-100%) after diagnosis for information and education concerning axSpA, exercise and lifestyle to a specialized nurse practitioner. Furthermore, 53% of rheumatologists referred most of their axSpA patients (76-100%) to a physiotherapist for exercise therapy. At diagnosis, approximately 55% of axSpA patients used the daily maximum dose of NSAIDs, compared to 25% for patients on biological treatment.

The reported level of importance of different axSpA related aspects for starting a biological was largely similar for AS and nr-axSpA, although some differences could be observed (Figure 1): Most rheumatologists graded insufficient response to 2 NSAIDs during 4 weeks (94% for AS and 92% for nr-AxSpA) and bone marrow edema on MRI (75% and 89%) as important for starting a biological. About 60% of rheumatologists considered active disease using ASDAS/BASDAI important for the decision to start a biological, which was similar to the importance of the level of pain. For nr-axSpA, more rheumatologists graded elevated CRP and bone marrow edema on MRI as important for starting a biological, than for AS.

Most rheumatologists (67%) do not base a decision that a biological is ineffective on ASDAS or BASDAI. To assess disease activity in axSpA, 86% of the rheumatologists always measured C-reactive protein (CRP), compared to 42% and 31% for BASDAI and ASDAS, respectively. 77% of rheumatologists reported to follow the 2016 ASAS-EULAR treatment recommendations for axSpA for treatment and follow-up of axSpA patients.

Conclusion: This survey among Dutch rheumatologists suggests that ASDAS and BASDAI are as important for starting a biological in axSpA as is the level of pain. Moreover, in contrast to ASAS-EULAR treatment recommendations, most rheumatologists do not use validated disease activity instruments to assess biological ineffectiveness, which may be a topic for increasing awareness and education.

References:

[1] Van der Heijde D et al, Ann Rheum Dis 2017;76:978-91.

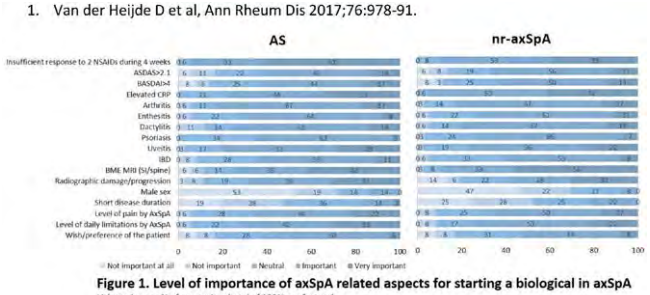


Figure 1. Level of importance of axSpA related aspects for starting a biological in axSpA

Values given as % of responders (total of 100% per feature)

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AB0663 **EFFICACY OF BIOLOGICAL THERAPY IN TREATMENT OF ANKYLOSING SPONDYLITIS IN SERBIA**

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Background: Patients with ankylosing spondylitis (AS) are treated in accordance with the 2016 ASAS / EULAR recommendations.
Objectives: Determine our experience and results in the treatment of AS by analysing data from the URES database collected from reference centers for the treatment of rheumatic diseases in Serbia.
Methods: Retrospective insight into the database of patients treated with biological therapy in reference centers (Institute of Rheumatology in Belgrade, Institute "Niska Banja", Special Hospital Novi Sad, KC Vojvodina and KC Kragujevac) from 2009-2018. Disease activity was monitored by the BASDAI, BASFI and ASDAScrp indexes.
Results: Of the 250 patients, 185 were male. The mean age at diagnosis was 33.02 ± 11.17 years. The mean length of treatment prior to initiation of biological therapy was 6.55 ± 7.82 years. There was a statistically significantly shorter duration of illness before the introduction of biological therapy in those who subsequently remained on the first drug (5.91 ± 7.53 vs 8.48 ± 8.48 years p = 0.046, p <0.05). The mean age at TNF alpha inhibitor administration was 39.61 ± 11.33 years. Patients who remained on the first drug were significantly younger when starting treatment with TNF inhibitors compared with patients who changed the first drug (38.75 ± 11.29 vs 42.46 ± 11.11 years p = 0.029, p <0.05). Those who changed the first drug were statistically longer treated with biological drugs (36.9 ± 30.03 vs 56.33 ± 32.4 months p = 0.0001). There were more patients with dactylitis and HLAB27 + in the group remaining on the first drug (p <0.05) and more with inflammatory bowel disease in the group who had the change in drug (p <0.05). The duration of etanercept therapy as the first drug was 49.11 ± 36.37 months, with the second drug 24.26 ± 27.08, and with the third drug 43 ± 45.2. Treatment with adalimumab as the first drug lasted for 28.34 ± 21.28, for the second drug 21.65 ± 14.57, for the third 3.5 months. Golimumab therapy as the first drug lasted 25.85 ± 14.58, with the second drug 20.33 ± 19.13, and as the third drug for 24 months. Therapy with infliximab as the first drug lasted 28.36 ± 23.52, with the second drug 20.3 ± 20.09, and with the third 16.5 months. According to the ASDAScrp index, 185 patients had very high disease activity (VHDA) before the first drug, high activity (HDA) 63, moderate activity (MDA) 2. At the time of the intersection, 8 had VHDA, HDA 48, MDA 106, and there were 88 patients in remission. There are 8 patients in the VHDA group who started treatment with the current drug less than 6 months ago. There are 48 patients in the HDA, of whom 17 who started treatment with the current drug less than 6 months ago, one at the time of the intersection had a urinary tract infection and high CRP, and the remaining 30 were patients with no significant decrease in ASDAS index (16 on first drug, 12 on the second drug and 2 patients on the third drug).
Conclusion: In patients with AS who do not have a good response to the first anti TNFα drug, a good option to continue their treatment is to switch to the second and third drugs of the same mechanism of action (anti TNFα drug).
KEY WORDS: ankylosing spondylitis, TNFα inhibitors, efficacy
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21. Spondyloarthritis - clinical aspects (other than treatment)

AB0664 **DIAGNOSIS DELAY IN ANKYLOSING SPONDYLITIS PATIENTS IN EGYPT: FACTORS, SOCIOECONOMIC AND CLINICAL OUTCOME**

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Background: Ankylosing spondylitis (AS) is a destructive inflammatory disease which was reported to have the longest diagnostic delay among the inflammatory rheumatic disease. This lag period have a great impact on the clinical outcome and socioeconomic state of the patients. With the advent of tumor necrosis factor-α (TNF-α) inhibitors, early diagnosis in AS has become important(1).
Objectives: to evaluate the period from symptom onset to diagnosis of AS in Egyptian patients and to examine possible reasons for delayed diagnosis and its impact on the economic and social life of the patients.
Methods: The study included 87 AS patients diagnosed according to the Assessment of Spondyloarthritis international Society (ASAS) criteria (2). A face-to-face interview was applied to take medical history, and a questionnaire that contains some clinical aspects of disease was used. Diagnosis delay was described as the gap between first AS symptom and correct diagnosis of AS. Clinical and functional assessment of axial SpA measured by Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Metrology Index (BASMI). The direct medical cost during years of delay (including costs of medical consultations, medications, investigations, physiotherapy and surgical treatment) had been estimated by Egyptian pound.
Results: The study included 87 AS patients with mean age (30.03±8.3), 70 male (80.5%) and 17 female (19.5%).
Mean delay in diagnosis was(5.7 ±4.9) years. Mean of diagnostic delay for patient diagnosed before 2010 is (14±4.4) and that of patients diagnosed after 2010 is (3.5±1.8) with significant difference between both (p value<0.0001). The main cause of delay was incorrect diagnosis as follow degenerative disc disease (43/87, 49.4%), non-specific back pain (31/87, 35.6%), rheumatoid arthritis (10/87,11.5%), rheumatic fever (2/87, 2.3%) and tuberculosis of spine (1/87, 1.1%). The mean of the medical visits was (6±5.4). Most incorrect initial diagnoses were made by orthopedicians (57.9%), followed by neurologists (22.2%) followed by rheumatologist (10%) and general phyisicians (9.9%). Absence of extra-articular manifestations, negative family history and juvenile age are significantly associated with diagnostic delay. Delay in diagnosis is significantly associated with higher disease activity index(BASDAI), functional index (BASFI), and damage index(BASMI). The mean of the costs during years of delay is (15671.3±546.1) with the mean of cost per each year delay (660.9±6.6) with high significant association between the cost and longer delay in diagnosis (<0.0001). Regarding work ability, we found that(32.2%) are fit for work, unfit (29.9%), partially fit (37.9%) with high significant difference between ability of work and shorter delay. Regarding social effect, 40.2 % of patients developed negative effect on social life with significant association to diagnostic delay (0.004).
Conclusion: Our study confirmed the importance of early diagnosis of AS due to its impact on patient's health outcome and socioeconomic state.We recommend to increase the awareness about the disease among healthcare professionals in our region.
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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.5003

AB0665 **VALVULOPATHY, SYSTOLIC AND DIASTOLIC DYSFUNCTION IN AXIAL SPONDYLOARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS**

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Background: Axial Spondyloarthritis (ax-SpA) displays an increased cardiovascular disease (CVD) risk compared with the general population. Although ischemic cardiac manifestations are well known, prevalence of non-ischemic manifestations such as myocardial dysfunction and valvulopathy is less clear.
Objectives: To compare prevalence of myocardial dysfunction and valvulopathy by ultrasound in ax-SpA patients and versus healthy controls.
Methods: Two investigators independently searched for studies indexed in PUBMED, Cochrane Library and EMBASE databases and published before January 17th 2020. The search was focused on ultrasound evaluation of myocardial

function and valvulopathy, with two-dimensional, Doppler, tissue Doppler, and speckle tracking echocardiography. We included for meta-analysis all controlled studies including ax-SpA without previous cardiovascular disease. Data were pooled using appropriate random or fixed effects model.

Results: Literature search retrieved of 186 abstracts. A total of 31 papers were included in the systematic review and 27 papers were analyzed in the meta-analysis (1,494 ax-SpA patients and 1,091 healthy controls). Studies displayed cross-sectional design and included ax-SpA without prevalent cardiovascular disease.

Ax-SpA was defined according to the modified New York criteria (24 studies) followed or the ASAS criteria (2 studies). HLA B27+ positivity ranged from 51 to 100%, mean age ranged from 26.7 to 55.7 years, disease duration ranged from 3.2 to 23.3 years and mean BASDAI ranged from 1.24 to 5.6.

Patients with ax-SpA displayed a lower diastolic function with a lower E/A ratio, a higher deceleration time, a higher isovolumetric relaxation time and a lower systolic function with a lower ejection fraction (figure 1). Left-ventricular end diastolic and systolic diameters were higher in ax-SpA patients with respectively mean difference 0.55 mm [CI95%; 0.19, 0.91] and 0.79 mm [CI95%; 0.40, 1.17]. We did not find any difference for left and posterior ventricular thickness, left atrial dimension, and left ventricular mass index.

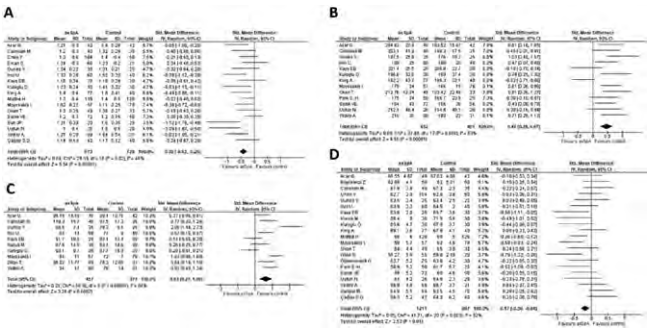


Figure 1. Systolic and diastolic dysfunction is slightly altered in ax-SpA patients compared to healthy individualsDiastolic dysfunction was assessed by (**A**) E/A ratio (m/s), (**B**) deceleration time (ms), (**C**) Isovolumetric relaxation time (ms) and (**D**) systolic function was assessed by ejection fraction (%).

A total of 15 articles reported prevalence of valvulopathy in ax-SpA. Prevalence of mitral regurgitation and aortic regurgitation were similar in ax-SpA patients and healthy individuals: OR=1.13 [CI95% 0.76, 1.68] and OR=1.18 [CI95% 0.68, 2.04].

Conclusion: Prevalence of valvulopathy was similar in ax-SpA and healthy individuals. Diastolic and systolic function seems to be slightly altered in ax-SpA compared to healthy controls. However, this difference is unlikely clinically relevant. Usefulness of systematic echography remains to be determined in future longitudinal studies.

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AB0666 A COMPARISON OF CLINICAL FEATURES AND PREDICTORS OF TREATMENT RESPONSE IN SPONDYLOARTHRITIS PATIENTS IN THE MIDDLE EAST: A CROSS-SECTIONAL MULTINATIONAL STUDY

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Background: Spondylarthritis it is a chronic inflammatory disease with heterogenous clinical features. Its prevalence ranges between 0.2%-2%. Over the years biological therapy has improved work productivity and activity impairment in people with SpA. Unlike in rheumatoid arthritis, the concept of treat-to-target is still debatable among rheumatologist. However, there is a consensus that treatment in patient with SpA should be personalized. There are several challenges in the Middle East that might affect providing personalized medicine to patients with SpA in this region.

Objectives: The of objective of the study is to explore factors that interfere with achieving clinical targets in patients with SpA clinical practice in the Middle East.

Methods: We conducted a cross-sectional, multicentre study to explore the factors that interfere with achieving clinical targets in SpA patients from four countries in the Middle East (Lebanon, Oman, Qatar, and the United Arab Emirates). A total of 404 patients who attended participating centers from January 2019 to June 2019 and who met the ASAS 2010 classification criteria for axial and peripheral SpA; and were at least 18 years of age were enrolled in the study. We excluded patients with peripheral arthritis only. We extracted demographics, clinical data, and conducted patients survey. We used Compliance Questionnaire for Rheumatology (CQR) is a self-reported adherence measure created specifically for and validated in rheumatic diseases.

Demographic data and disease and treatment characteristics were described as median and the 25th–75th interquartile range (IQR). Multiple regression analysis was used to investigate the impact of different factors on ASDAS-CRP in patients with SpA. Statistical analysis was performed using Minitab version 18.1 software.

Results: A total of 404 patients initially enrolled in the study, we excluded 95 patients as they had peripheral involvement only. We analysed the data of 309 patients with axial only or axial and peripheral SpA. There median age was 43 years and 53.7% were females. The median disease duration was six years. At the time of the study, 72.1% patients were within the arbitrary clinical target of ASDAS < 2.1. Detail description of the studied population and subgroups outlined in table 1. Enthesitis (OR: 2.9; P value: 0.004), Psoriasis (OR: 2.74; P value: 0.007), low compliance score (OR: -4.36; P value: < 0.0001) and HLA B27 (OR: 2.12; P value: < 0.04) were independent predictors of a higher ASDAS –CRP.

Conclusion: Enthesitis, psoriasis, noncompliance, and HLA B27 were independent predictors for ASDAS in our cohort.

Table 1. Demographic and clinical characteristics of all patients and for achiever and non-achievers

Variables	All patients (309)	Achiever (223)	Non-achieves (86)
Age, Median, (IQR) yrs	43, (36-51)	43, (35-51.5)	42, (37-51)
Female %	53.7%	54.2%	51.9%
Disease Duration, Median, (IQR)yrs	6, (3-9)	6, (2-8)	7.5, (3-10)
Patient has medical insurance/ Medical coverage	94.5%	95.0%	93.1%
Smoking	13.9%	12.1%	18.6%
ASDAS-CRP, Median (IQR)	1.56, (1.24-2.1)	1.56, (1.07-1.6)	2.75, (2.36-3.3)
Arthritis	40.1%	36.3%	48.1%
Dactylitis	13.6%	11.3%	18.50%
Enthesitis	29.1%	22.4%	43.2%
Family history of SPA	18.4%	14.3%	25.9%
Good response to NSAIDs	21.7%	18.8%	22.2%
HLA B27	30.0%	25.6%	40.0%
Inflammatory bowel disease	7.1%	7.3%	6.20%
Inflammatory low back pain	68.6%	68.1%	69.8%
Onycholysis	10.9%	10.7%	11.1%
Psoriasis	39.4%	25.1%	40.7%
Sacroiliitis (Radiographic)	50.4%	49.8%	51.9%
Uveitis	6.1%	4.0%	11.1%
SpA- classification			
Axial	49.8%	55.7%	35.6%
Axial & peripheral	50.2%	44.3%	64.4%

Acknowledgments: ArLAR 2018 Scientific committee for initiating SpA special interest group meeting

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AB0667 ACHILLES PAIN PERSISTENCE IN PATIENTS AFFECTED BY SPONDYLOARTHRITIS: ULTRASONOGRAPHIC AND BIOMECHANICAL STUDY.

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Background: Enthesis anatomy and biomechanics have a key role in Spondyloarthritis (SpA) pathogenesis (1) but few data are available about the influence of structural and biomechanical changes of Achilles tendon (AT) on persisting pain in longstanding SpA patients.
Objectives: To correlate AT pain in longstanding SpA patients with ultrasonographic detectable disorders and biomechanical abnormalities.
Methods: We performed a monocentric cross-sectional analysis including 35 consecutive patients affected by SpA (13 with Psoriatic Arthritis, 9 with Enteropathic SpA, 6 with Ankylosing Spondylitis and 7 with Undifferentiated SpA) under treatment with anti- TNF agents. A rheumatologic clinical and clinimetric evaluation (AT VAS pain, BASDAI, BASFI, HAQ), an ultrasound study of AT according to the Madrid Sonographic Enthesis Index (MASEI) score and a podiatrist biomechanical evaluation [Foot posture index (FPI), degree of ankle dorsiflexion with the knee extended and flexed] were performed.
Results: Study population (13 F; 22 M; mean age 54.9 ±13.9 years; mean disease duration 9.5 ± 5.0 years; mean BMI 25.8 ±4.4) showed a mean AT VAS pain of 3.4 ± 2.2, a mean HAQ of 0.6 ± 0.6, a mean BASDAI of 3.3 ±2.1 and a mean BASFI of 2.2 ±1.9. At the ultrasonographic evaluation 47% (33/70) of the AT entheses analysed presented a dishomogeneous echostructure, 31% (22/70) structural thickness, 53% (37/70) calcifications, 10% (7/70) erosions, 44% (31/70) a retrocalcanear bursitis. A power Doppler positivity was found only in 0.07% (5/70) of the AT.
At the biomechanical evaluation 50% (35/70) of the feet showed a FPI score between 0 and + 5 (neutral foot), 46% (32/70) a FPI score between +6 and +9 (slight foot pronation) and 6% (4/70) a FPI score between -1 and -4 (slight foot supination).
The mean degree of ankle dorsiflexion with extended knee was 8.4 ± 3.9 with the 61% (43/70) of the patients with a maximum dorsiflexion < 10° of whom 46% (20/43) do not recover after the knee flexion.
We found a between the mean degree of left ankle dorsiflexion with extended/flexed knee both with ultrasound-revealed left AT enthesis calcifications (p=0.014/0.037) and with left AT enthesis thickness (p=0.049/0.035), and a significant association between the mean degree of right ankle dorsiflexion and extended/flexed knee and ultrasound-revealed right AT calcifications (p=0.008/0.012). Moreover, we noticed an inverse correlation between the mean overall degree of ankle dorsiflexion with extended/flexed knee and the BASFI values (p=0.007/0.004). AT VAS pain was statistically related with Achilles PDUS signal persistence (p=0.048) but not with US signs of chronic entesopathy or biomechanical alterations [calcification (p=0.39), erosions (p=0.74)]. The limits of the study were the low number of patients recruited and the lack of a control group.
Conclusion: In this monocentric study on a cohort of SpA patients, we demonstrated a statistically significant correlation between ankle–subtalar joint complex biomechanics alterations, ultrasonographic signs of chronic enthesopathy and clinimetric index of functional disability. Residual Achilles pain seems to be related to US signs of active enthesitis.
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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.5891

AB0668 CLINICAL CHARACTERISTICS OF RADIOGRAPHIC AND NON RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS IN A GROUP OF TUNISIAN SPONDYLOARTHRITIS

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Background: In the literature, non radiographic axial Spondyloarthritis (nr-SpA) is predominantly female with a shorter period of evolution and similar peripheral manifestations to radiographic axial spondyloarthritis (r-SpA). However, we do not have Tunisian studies comparing the two groups of axial spondyloarthritis (ax-SpA).
Objectives: The aim of this study was to assess the epidemiological and clinical differences between nr-SpA and r-SpA in a group of Tunisian ax-SpA.
Methods: Two hundred patients with ax-SpA (ASAS 2009 criteria) were retrospectively included and classified as r-Spa characterized by the presence of radiographic sacroiliitis and nr-SpA defined by the presence sacroiliitis only on MRI or HLA B27 antigen with other clinical features. The different demographic and clinical parameters were compared between the nr-SpA and r-SpA groups.
Results: One hundred thirty-eight men and 62 women were included with a sex ratio of 2,2. The mean age was 43,3 ± 11,2 years and the mean period of evolution was 10,7 ± 8,4 years. The patients were divided to r-SpA in 80% of cases (n = 160) and nr-SpA in 20% of cases (n = 40).
Women were more present in the nr-SpA group with 47,5% of women versus 26.8% of women in the r-SpA group (p = 0,01). The patients with nr-SpA were younger with a mean age of 39,4 ± 13,4 years versus 44,3 ± 10,4 years in patients with r-SpA (p = 0,03). The mean period of evolution was shorter in nr-SpA group (5,8 ± 4,9 years vs 11.9 ± 8.5; p <0.001). The family history of SpA was more frequent in nr-SpA group (17.5% vs 4.3%, p = 0.004). Arthritis were more frequent in nr-SpA (42.5% vs 13.7%; p <0.0001). Similarly, enthesitis were more frequent in nr-SpA group (45% vs 15.6%; p <0.0001).
No statistically significant differences were found in the following parameters: age at onset of symptoms, diagnostic delay, HLA B-27 antigen and dactylitis.
Conclusion: The clinical features were different in the 2 groups of ax-SpA: Patients with nr-SpA were more female and had more peripheral manifestations while patients with r-SpA were older and with longer period of evolution.
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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.6041

AB0669 PARTICULARITIES OF TUNISIAN FEMALE AXIAL SPONDYLOARTHRITIS

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Background: Axial spondyloarthritis (ax-SpA) is a chronic rheumatic disease that mainly affects men. However, the female form of ax-SpA remains insufficiently studied.
Objectives: The aim of this study was to determine the clinical characteristics, the disease activity and the functional impact of female ax-SpA in comparison with male ax-SpA.
Methods: This is a retrospective study including patients diagnosed with ax-SpA fulfilling the criteria of the Assessment of SpondyloArthritis international Society (ASAS) 2009.
Clinical parameters, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), Bath ankylosing spondylitis disease activity index (BASDAI) and Bath ankylosing spondylitis functional index (BASFI) were compared between groups of female and male ax-SpA.
Results: Two hundred ax-SpA patients were included with 31% of female (n=62) and a mean age of 43,3 ± 11,2 years.
The mean age at onset of symptoms was 31,8 ± 8,9 years for women and 25,3 ± 9,1 years for men (p <0,0001). The mean age at diagnosis was 36,4 ± 9,6 years for women and 31,7 ± 10,4 years for men (p = 0,003). Ax-SpA with juvenile onset was noted in 1,7% of women and 12,1% of men (p = 0,02). Male ax-SpA were significantly more smokers (46.8% vs 5.4%; p <0.001). The mean duration of morning stiffness was 11,3 ± 9,2 minutes for women versus 21,6 ± 19,3 minutes for men (p = 0,005).
The mean ESR was 42,4 ± 29,8 mm for women and 28,3 ± 23,4 mm for men (p = 0,001). Radiographic sacroiliitis was present in 69,3% of women versus 84,7% of men (p = 0,01). The use of anti-TNF alpha was less frequent in women (29% vs 48,5%; p = 0,01).
Our study didn't found a statistically significant difference in peripheral manifestations, extraarticular manifestations, CRP, BASDAI and BASFI between the two groups.
Conclusion: Female ax-SpA seems to have a better prognosis than male with older age in disease onset, less inflammation, less radiographic sacroiliitis and less use of biological treatments.
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Disclosure of Interests: None declared
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AB0670

AXIAL MANIFESTATIONS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS: ARE THEY SIMILAR?

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Background: Spondyloarthritis (SpA) is a group of heterogeneous diseases that includes axial SpA (axSpA), such as ankylosing spondylitis and axial non-radiographic SpA, and Psoriatic Arthritis (PsA) with peripheral and/or axial involvement (axPsA). Currently, it is not well known if the characteristics and burden of the disease in patients with axPsA are similar to that of patients with axSpA.
Objectives: To compare the demographic, clinical and structural features between patients with axSpA and axPsA.
Methods: Data from an observational prospective cohort including all patients with SpA initiating biological therapy because of predominant axial manifestations from 2002-2019 in a university hospital were analyzed. AxSpA and axPsA were defined in clinical practice according to the prescribing rheumatologist, based on clinical features and complementary examinations. Demographic information, laboratory tests, disease presentation, sacroiliitis according to modified New York criteria in the pelvis X-ray, disease activity indexes (ASDAS and BASDAI) and concomitant treatment before starting biological drug were collected from the electronic medical record and biologic database. In the statistical analysis, chi square or the exact Fisher's test was used for categorical and t-student or U-Mann Whitney for continuous variables, according to the distribution of the data. Then, the association between demographic and clinical features and each disease was analysed using univariable and multivariable logistic regression models.
Results: Out of 352 included patients, 287 (81.5%) had axSpA, and 65 had axPsA (18.5%). Baseline characteristics are shown in Table 1. Mean baseline ASDAS was 3.3±0.9 and 3.1±1.0 for axSpA and axPsA, respectively. Biological therapies initiated can be seen in Figure 1. No significant differences at baseline were observed between axSpA and axPsA for most of the characteristics including: gender, age at diagnosis, age at starting biologic, disease duration before biologic, smoking habit, CRP, disease activity, enthesitis, dactylitis, inflammatory bowel disease (IBD), patient global assessment and sulfasalazine use. However, there were differences between diseases in some relevant characteristics. AxSpA patients had less peripheral involvement (41.5 vs. 78.5 %, p=0.004), more uveitis (15.3 vs. 3.1 %, p=0.03) and were more frequently HLA-B*27 positive (72.3 vs 34.1 %, p<0.001), in comparison to axPsA patients. They also had better physician global assessments (PhGA) (37.4 vs 44.4, p=0.02), and a higher grade of radiographic sacroiilitis. AxSpA patients used less global baseline concomitant therapy (p=0.001), methotrexate (p<0.001) and prednisone (p<0.01), whereas they used more sulfasalazine (p=0.003) than axPsA patients in our cohort. After running multivariate analyses, the absence of peripheral manifestations (OR=4.7; p<0.001) and the positivity of HLA-B27 (OR=5.4; p<0.001) were independently associated with axSpA.

Table 1. Baseline stratified characteristics. Results are shown as absolute numbers (percentages) or mean ± standard deviation.

	AxSpA & AxPsA n= 352	AxSpA n= 287	axPsA n= 65	p-value
Sex (male)	223 (60.6)	180 (62.7)	43 (66.2)	0.7
Age (years):				
At diagnosis	35.9 ± 13.4	35.7 ± 13.7	36.9 ± 12.1	0.9
At biologic starting	44.4 ± 13.2	44.1 ± 13.4	45.8 ± 11.6	0.3
Disease duration before biologic (years)	17.9 ± 10.3	7.9 ± 11.3	8.9 ± 9.0	0.7
Current smoking habit	158 (44.9)	129 (44.9)	29 (44.6)	0.9
HLA B27 positive	219/322(67.8)	204/281 (72.3)	16/47 (34.1)	<0.001
CRP(mg/dL)	12.4 ± 17.9	12.6 ± 18.9	11.1 ± 12.7	0.5
Clinical involvement:				
Only axial	170 (48.2)	168 (58.5)	14 (21.5)	<0.001
Axial and peripheral	182 (51.7)	119 (41.5)	51 (78.5)	
Psoriasis	74 (21.3)	11 (4.2)	63 (97)	<0.001
ASDAS	3.3 ± 0.9	3.3 ± 1.0	3.1 ± 1.0	0.1
BASDAI (0-10)	5.9 ± 4.2	6.1 ± 4.5	5.23 ± 2.1	0.1
Enthesitis	85 (41.5)	73 (25.4)	12 (28.6)	0.07
Dactylitis	10 (2.7)	7 (2.4)	3 (4.6)	0.4
IBD	9 (2.6)	8 (2.8)	1 (1.5)	0.7
Uveitis	46 (13.6)	44 (15.3)	2 (3.1)	0.03
PGA (0-100)	63.2 ± 21.8	64.1 ± 21.5	58.8 ± 23.2	0.1
PhGA (0-100)	39.1 ± 21.5	37.4 ± 13.7	44.4 ± 22.6	0.02
Radiographic sacroiliitis, mNY criteria	227 (64.5)	203 (70.7)	24 (36.9)	< 0.001
Concomitant therapy:	193 (52.4)	145 (50.5)	48 (73.8)	0.001
Monotherapy				
Only MTX	66(20.7)	36 (13.9)	30 (46.2)	< 0.001
Only SZS	82 (25.6)	73 (28.2)	9(13.8)	0.03
Prednisone use	32 (9.5)	20 (7.7)	12 (20)	0.004

Conclusion: Despite being spondyloartrithis with many common traits, axSpA and axPsA present some differences in clinical practice. Whereas axSpA patients are more frequently HLA-B27 positive, axPsA have more peripheral involvement. These differences in clinical presentation between both diseases may contribute to variances in therapeutic management, such as increased use of baseline concomitant therapy in axPsA patients who initiate biological therapy.

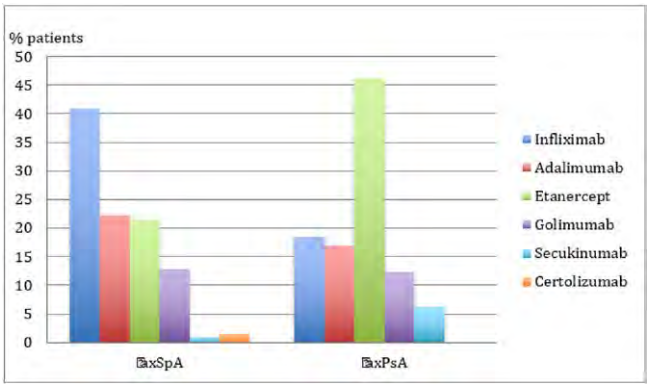


Figure 1. Biological therapies initiated in axSpA and axPsA

Disclosure of Interests: Diego Benavent: None declared, Victoria Navarro-Compán Consultant of: Abbvie, Lilly, Novartis, Pfizer, UCB, Speakers bureau: AbbVie, MSD, Lilly, Novartis, Pfizer, UCB, Chamaida Plasencia: None declared, Diana Peiteado: None declared, Alejandro Villalva: None declared, Alejandro Balsa Grant/research support from: BMS, Roche, Consultant of: AbbVie, Gilead, Lilly, Pfizer, UCB, Sanofi, Sandoz, Speakers bureau: AbbVie, Lilly, Sanofi, Novartis, Pfizer, UCB, Roche, Nordic, Sandoz
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AB0671

PREVALENCE OF EXTRA-ARTICULAR MANIFESTATIONS AND IMPACT ON TARGETED DRUG PRESCRIPTION IN PATIENTS WITH SPONDYLOARTHRITIS: A RETROSPECTIVE ANALYSIS OF A REAL-LIFE COHORT

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Background: Extra-articular manifestations (EAMs), such as uveitis, inflammatory bowel diseases (IBD), and psoriasis (PSO) can frequently complicate the disease course of patients with spondyloarthritis (SpA), although prevalence data on this regard are still controversial. The occurrence of EAMs may influence the decision to introduce a targeted therapy and also drive the choice of the most appropriate drug.
Objectives: The aim of this study is to retrospectively evaluate the prevalence of EAMs in a real-life cohort of SpA patients who were eligible to receive a targeted therapy and to investigate their impact in the choice of targeted treatment.
Methods: Clinical data of SpA (axial SpA [axSpA], peripheral SpA, and psoriatic arthritis [PsA]) patients treated with a biologic or targeted synthetic Disease-Modifying Anti-Rheumatic Drug (DMARD) between December 1999 and December 2019 were extracted from a local registry. Prevalence of main SpA-related EAMs (uveitis, IBD and PSO) was calculated at the time of drug prescription, evaluating their distribution according to treatment subgroups. Comparisons between disease and treatment subgroups were made using the Fisher's test.
Results: The study included 629 patients with SpA (axSpA 26%, peripheral SpA 24%, PsA 50%), 266 [42%] women, mean age [±SD] 52 [±13.2] years, mean disease duration 7.8 [±7.9] years), receiving a total of 1106 lines of targeted treatment (I-line n=629, II-line n=258, ≥ III-line n=219) with etanercept (n=177), anti-TNF monoclonal antibodies (397 infliximab, 273 adalimumab, 38 certolizumab pegol, and 130 golimumab), secukinumab (n=46), ustekinumab (n=28), or apremilast (n=18). At the time of drug introduction, 13% of SpA patients showed at least one EAM. The prevalence of uveitis was higher in axSpA (11.8%) compared with both peripheral SpA (5.5%, p=0.01) and PsA (2.8%, p<0.0001), while IBD was more frequent in peripheral SpA (15.6%) than in axSpA (8.1%, p=0.008) and PsA (4.7%; p<0.0001). The prevalence of PSO was similar in axial and peripheral SpA (8.4 versus 6.3%, respectively;

p=0.41). In the overall population, the baseline presence of at least one EAM was associated with a more frequent prescription of anti-TNF monoclonal antibodies rather than etanercept (14.4% versus 6.7%, respectively; p=0.004). Moreover, we observed a numerically, although not statistically significant, higher proportion of EAMs in patients treated with anti-TNF monoclonal antibodies rather than secukinumab (6.5%), ustekinumab (7.1%), and apremilast (5.9%).

Conclusion: In our real-life cohort of SpA patients treated with targeted therapies, EAMs were highly represented at baseline, especially uveitis in axSpA and IBD in peripheral SpA. The presence of extra-articular involvement was associated with a preferential prescription of anti-TNF monoclonal antibodies rather than etanercept or drugs with different mechanisms of action.

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AB0672 PATIENT CHARACTERISTICS AND DISEASE ACTIVITY, BUT NOT THE CRANIOCERVICAL POSTURE ABNORMALITIES PREDICT TEMPOROMANDIBULAR DISORDERS IN ANKYLOSING SPONDYLITIS PATIENTS: A CROSS-SECTIONAL, OBSERVATIONAL STUDY

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Background: There are contradictory results in the relevant literature about the relationship between objective determinants of craniocervical posture and temporomandibular disorder (TMD), whereas no study has worked on AS and TMD relationship.

Objectives: To evaluate the predictors of TMD in AS patients and its relationship with craniocervical posture, we conducted this study

Methods: AS patients aged between 18-50 years and consecutively admitted to our outpatient clinics were recruited. TMD was diagnosed by 'Diagnostic Criteria for Temporomandibular Disorders (DC/TMD)' criteria. Spinal mobility was assessed by BASMI; disease activity by ASDAS-CRP and neck disability by Neck Disability Index. We measured the craniocervical angle, cervical curvature angle, suboccipital distance, atlas-axis distance, anterior translation distance by using the lateral cervical X-rays (Figure).

Results: A total of 98 (58.2% female) patients with a mean age of 37.4 ±48.2 years was recruited (Table 1). TMD was diagnosed in 58 (59,2%) patients. Spinal mobility and craniocervical posture measurements were similar among the two groups (Table2). Smoking, bruxism (in females), neck disability and AS activity (in males) were higher in TMD patients (Table 1). Multivariate analysis revealed active smoking (aOR 6.86; CI: 1.83-25.60; p=0.004), bruxism in females (aOR 17.87; CI: 2.0-159.20; p=0.01), high ASDAS in males (aOR 11.82; CI: 1.14-122.5; p=0.038) and neck disability (aOR 12.67; CI: 3.75-42.85; p<0.001) as independent risk factors for TMD in AS patients.

Conclusion: No relationship between the craniocervical posture measurements and TMD was found in AS patients. Active smoking, high disease activity in males, bruxism in females and neck disability were found as predictors of TMD in AS patients.

Table 1. The clinical and demographical data of the study population

Parameter	All patients	TMD (+) (n=58)	TMD (-) (n=40)	P value
Gender (Female)	57 (58.2)	38 (65.5)	19 (47.5)	0.076
Age	37.4±8.2	37.8±7.7	36.9±8.9	0.57
Smoking				
Smoker	33 (33.7)	25 (43.1)	8 (20.0)	**0.017**
Non-smoker	65 (66.3)	33 (56.9)	32 (80.0)	
AS disease duration (year)	8.1±5.7	7.8±6.2	8.6±5.0	0.47
AS treatment				
NSAID				0.52
Regular	13 (13.2)	8 (13.8)	5 (12.5)	
On-demand	49 (50.0)	31 (53.4)	18 (45.0)	
Sulphasalazine	38 (38.7)	24 (41.4)	14 (35.0)	0.67
Anti-TNF agents	59 (60.0)	33 (56.9)	26 (65.0)	0.42
Bruxism				
Present	61 (62.2)	43 (74.1)	18 (45.0)	**0.003**
Nighttime	18 (29.5)	11 (25.6)	7 (38.9)	
Daytime	15 (24.6)	10 (23.3)	5 (27.8)	
Whole day	28 (45.9)	22 (51.2)	6 (33.3)	
Absent	37 (37.8)	15 (25.9)	22 (55.0)	

Table 2. Comparison of AS-related and craniocervical posture measurements

Parameter	All patients	TMD (+) (n=58)	TMD (-) (n=40)	P value
AS-related measurements				
ASDAS	2.4±0.95	2.7±0.93	2.0±0.85	**0.001**
Male	2.3±1.3	2.7±1.14	1.7±0.85	**0.007**
Female	2.5±0.9	2.7±0.82	2.4±0.78	0.11
Tragus-wall distance (cm)	11.7±2.55	11.6±1.97	12.0±3.24	0.41
Cervical rotation (angle)	71.6±12.78	71.6±12.32	71.5±13.59	0.94
Chin-thorax distance (cm)	2.1±1.64	2.1±1.44	2.1±1.91	0.90
BASMI	2.0±1.19	2.0±1.11	2.1±1.31	0.76
mSASSS	3.5±4.84	3.4±3.88	3.8±6.03	0.70
Measurements of craniocervical posture				
Craniovercival angle	79.6±10.31	78.9±10.47	80.6±10.11	0.41
Cervical curvature angle	165.4±12.42	165.6±12.89	165.0±11.84	0.82
Suboccipital distance (mm)	6.3±3.97	6.2±4.04	6.5±3.91	0.71
Atlas-axis distance (mm)	5.2±2.43	5.3±2.47	5.0±2.40	0.62
Anterior translation distance (mm)	10.9±13.74	11.4±11.79	10.1±16.35	0.66

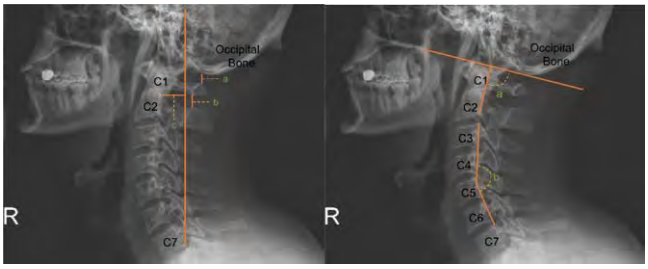


Figure. For the assessment of cranicervical posture; suboccipital distance (A.a.), atlanto-axial distance (A.b.) anterior translation distance (A.c), craniocervical angle (B.a), cervical curvature angle (B.b) were measured on standardized lateral X-rays.

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AB0673 SHINING LIGHT ON AXIAL SPONDYLOARTHRITIS: DISEASE ACTIVITY AND VITAMIN D. WHAT'S THE LINK?

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Background: Axial spondyloarthritis (axSpA) is a chronic inflammatory disease predominantly involving the axial skeleton and sacroiliac joints. Although the exact aetiology remains largely unknown, there is thought to be an immune-driven element. Vitamin D deficiency has been associated with a number of autoimmune diseases and is thought to play an important role in modulating the immune system. Low vitamin D levels may contribute to the development and progression of axSpA[1].

Objectives: To study the possible associations between low vitamin D and disease activity in axSpA.

Methods: A systematic literature search using Medline, Embase and Cochrane was performed using MESH search terms "ankylosing spondylitis", "axial spondyloarthropathy" and "vitamin D". Articles examining disease activity measured by BASDAI, ASDAS-CRP, ESR and CRP identified through title/abstract screening, were included in the study, with relevant information extracted.

Results: Out of 495 articles identified from the initial search, 19 observational studies which were mostly (89%) cross-sectional studies were identified. There was considerable heterogeneity between studies, including in the definition of vitamin D deficiency, latitude where study took place and seasonal variation. Vitamin D levels were often lower in patients with axSpA compared to controls. Seventeen studies found no association with vitamin D deficiency and disease activity. The exceptions included one study which measured serum vitamin D receptor levels as opposed to serum 25 (OH) D or 1,25 (OH)2 D concentrations, and another study whose recruitment occurred over four years and therefore seasonal variation may conflict results. Patients taking NSAIDs or anti-TNF had no difference in vitamin D levels.

Conclusion: Vitamin D deficiency is more prevalent in axSpA but does not seem to associate with increased disease activity. Longitudinal studies are required to better define these links.

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Disclosure of Interests: None declared

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AB0674 CLINICAL AND IMAGING FEATURES IN SPONDYLOARTHRITIS PATIENTS WITH AND WITHOUT HLA-B27 AND HLA-B51

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Background: Despite being commonly expressed in the general population, the human leucocyte antigen (HLA)-B27 allele strongly increases the susceptibility to develop spondyloarthritis (SpA). Likewise, the association between the HLA-B51 allele and the development of Behçet's disease is well documented. However, the exact mechanisms responsible for their pathologic role are still a matter of debate. Moreover, anecdotal reports show an association between HLA-B51 and the clinical spectrum of SpA.

Objectives: To investigate the clinical and imaging findings of SpA patients according to the absence or presence of HLA-B27 or HLA-B51.

Methods: We retrospectively analyzed 236 patients with axial or peripheral SpA, according to the ASAS criteria, referring to two tertiary Rheumatology Clinics between 2017 and 2019. All patients had been tested for HLA-B alleles. Patients with HLA-B51 haplotype and fulfilling the criteria for Behçet's disease were excluded.

Results: Table 1 shows demographic and clinical features of patients, according with the HLA-B haplotype (neither HLA-B27 nor -B51, double negative; positive for HLA-B27 only, positive for HLA-B51 only). Inflammatory low back pain and sacroiliitis, assessed by X-ray or magnetic resonance imaging (MRI), were more prevalent in double negative and HLA-B27 patients, compared to HLA-B51 patients. In this regard, the presence of HLA-B51 was negatively associated with axial manifestations at onset (OR 0.347, 95% CI 0.200-0.604, p<0.0001) and in the course of the disease (low back pain: OR 0.395, 95% CI 0.225-0.689 p<0.0001; sacroiliitis on imaging: OR 0.342 CI 0.189-0.619 p<0.0005). When considering extra-articular manifestation, aphtous lesions were more prevalent in patients with HLA-B51 (p< 0.0001), inflammatory bowel diseases in the double negative group (p=0.0006), and increased C-reactive protein in double negative and HLA-B27 patients (p=0.02).

Table 1.

	All (236 patients)	Double-negative (101 patients)	HLA-B27 (53 patients)	HLA-B51 (82 patients)	*p value*
Female (%)	167 (71)	73 (72)	28 (53)	66 (60)	0.0024 (cumulative)
Age, years (mean±SD)	53.7±13.3	56.4±12.7[#]	48.2±14.4[$]	54±12.7	#<0.01 vs HLA-B27 $< 0.05 vs HLA-B51
Age at diagnosis, years (mean±SD)	48±14.5	50.3±13*	40.8±15.5[§]	50.2±14.3	*<0.001 vs HLA-B27 §<0.001 vs HLA-B51
Time from symptoms to diagnosis, years (mean±SD)	3.8±5.7	3.6±4.8	3.2±3.7	4.4±7.5	ns
Type of onset:					0.0031 (cumulative)
-Axial (%)	129 (55)	67 (66)	31 (59)	31 (38)	
-Peripheral (%)	63 (27)	19 (19)	12 (23)	32 (39)	
-Axial and peripheral (%)	44 (19)	15 (15)	10 (19)	19 (23)	

Conclusion: The presence of HLA-B51 identifies a subgroup of SpA patients with peculiar features compared to double-negative or HLA-B27 SpA patients. HLA-B51-related SpA may be an additional condition to be included in the SpA spectrum.

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Disclosure of Interests: Francesco Carubbi Speakers bureau: Francesco Carubbi received speaker honoraria from Abbvie and Celgene outside this work., Alessia Alunno: None declared, Alessandro Conforti: None declared, Angelo Francesco Bonifacio: None declared, Paola Cipriani Grant/research support from: Actelion, Pfizer, Speakers bureau: Actelion, Pfizer, Roberto Gerli: None declared, Roberto Giacomelli Grant/research support from: Actelion, Pfizer, Speakers bureau: Abbvie, Roche, Actelion, BMS, MSD, Ely Lilly, SOBI, Pfizer

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AB0675 RED CELL DISTRIBUTION WIDTH AND FATIGUE IN AXIAL SPONDYLOARTHRITIS: A SLEEPER SIGNAL

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Background: Fatigue is a ubiquitous feature of autoimmune conditions, and axial Spondyloarthritis (axSpA) is no exception, with over 50% of patients reporting some degree of fatigue[1]. Erythrocyte size variability (as measured by red cell distribution width (RDW)) has been found to correlate with fatigue in a cohort of systemic lupus erythematous (SLE) patients and may reflect early iron deficiency[2]. We investigate whether this finding holds true in axSpA.

Objectives: To investigate the relationships between fatigue, disease activity, and RDW (as a proxy for functional iron deficiency) in patients with axSpA.

Methods: Cross-sectional analysis performed on patients with axSpA, as defined by the Assessment of SpondyloArthritis international Society (ASAS) criteria, enrolled in a longitudinal data collection study from October 2017 until January 2020 in a single outpatient setting. Patients required a minimum of 1 set of patient-reported outcome measures (PROMs), including the completion of a Functional Assessment of Chronic Fatigue Illness Therapy (FACIT) Fatigue Scale v4 (numerical score between 0–52 with a lower score indicating greater fatigue), and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). C-reactive protein (CRP) as a biochemical marker of disease activity, as well as Haemoglobin (Hb) and RDW performed within 3 months either side of a PROMs set were extracted and matched. Only one pair of matched data was selected per patient according to the least timeframe between a set of PROMs and bloods of interest (if multiple were available). Anaemia was defined according to World Health Organisation criteria, i.e., Hb <120 g/L in

females and Hb <130 g/L in males. Non-parametric analysis of variables was performed using Spearman's rank correlation with significance defined at a p-value <0.05.

Results: 63 patients were included in the analysis (63.5% (40) male, mean time to diagnosis 11.46 (±9.04) years, 79.4% (50) HLA-B27 positive, 46% (29) current or ex-smokers). Blood parameters showed mean Hb of 139.6 (±16.03) g/L, mean RDW of 13.55 (±1.46) %, mean CRP of 5.23 (±10.82) mg/L. Mean BASDAI score of cohort was 3.69 (±2.02) and FACIT score 34.18 (±11.30). Mean absolute interval time difference between a PROMs set and bloods of interest was 16.14 (±41.11) days.

Univariate analysis showed a statistically significant, negative correlation between fatigue (FACIT) and disease activity (BASDAI), ($p<0.001$; $r= -0.63$), but failed to demonstrate an association between fatigue and Hb, RDW, or CRP. Subgroup analysis of 51 patients, following exclusion of patients with anaemia (12), engendered a significant and moderately negative correlation between fatigue and RDW ($p=0.02$, $r=-0.32$) (Figure 1), maintained a significant correlation between fatigue and BASDAI ($p<0.0001$, $r=-0.56$) and showed a non-significant association between RDW and BASDAI ($p=0.07$, $r=0.25$).

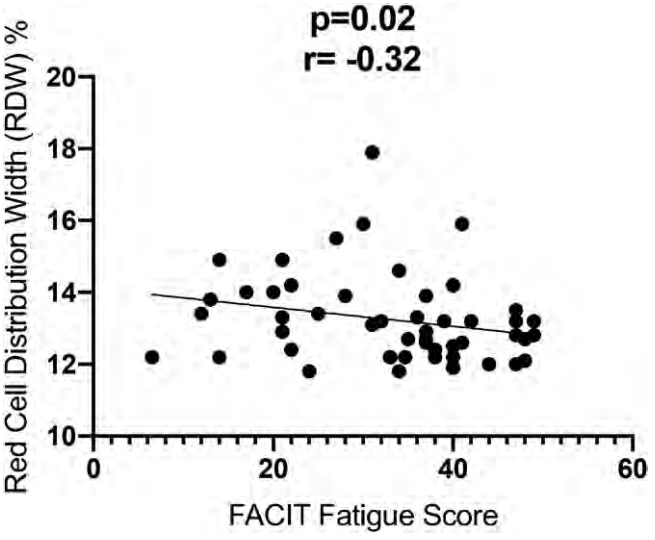


Figure 1. Negative correlation between FACIT score and RDW

Conclusion: These findings suggest that RDW may potentially represent a surrogate marker of disease activity in patients with axSpA. RDW may also be implicated in the multi-faceted aetiology of fatigue in axSpA patients, and may reflect functional iron deficiency. A recent cohort study of axSpA patients found anti-TNF therapy ineffective at alleviating fatigue in nearly 80% of patients[1]. Management of potential functional iron deficiency as reflected by RDW may offer an alternative treatment target for fatigue in these patients.

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AB0676

THE ROLE OF ACPA AND ANA IN SPONDYLOARTHRITIS: HOW THE AUTOIMMUNE DYSREGULATION CAN AFFECT THE COURSE OF DISEASE AND THERAPEUTIC SUCCESS OF MONOTHERAPY DMARDS AND BDMARDS

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Background: Occasional findings of anti-citrullinated-protein-antibodies (ACPA) and anti-nuclear-antibodies (ANA) were rarely described in literature on Psoriatic Arthritis (PsA) and on Spondyloarthritis (SpA) in general. How these autoimmune dysregulations can affect the course of them is not yet understood.

Objectives: The aim of our study is to evaluate if the presence of ACPA and ANA can determine different disease subsets and influence the DMARDs monotherapy (methotrexate) drug survival (DSM) and b-DMARDs multi-failure patients (MF).

Methods: We conducted a retrospective study on patients with Psoriatic Arthritis (PsA) and Spondyloarthritis that fulfilled the ASAS and CASPAR criteria. Patients with diagnosis of connective tissue disease and rheumatoid arthritis and patients ≤ 18 years old were excluded from the study. For each patient, the following variables were considered: age, ACPA, ANA, time between arthritis onset and start of DMARDs (start-time), DSM, switch to b-DMARDs (sw-bDMARDs), arthritis subset (oligoarticular (OA), polyarticular (PA), enthesitis (EA), axial involvement (AI)), number of comorbidities (NC), Charlson Comorbidity Index (CCI).

Results: 150 patients (55% with PsA and 45% with another SpA) were included in the study. No differences were found in age, ANA rate, ACPA rate, start-time, OA, PA, EA, AI, NC and CCI between the PsA and SpA groups.

In the whole group of patients, the ACPA+ subjects(11%) had a significant increase of NC (2.47 ± 1.5 vs 1.6 ± 1.4, p=0.035), a trend to higher CCI, to switch to b-DMARDs, and to be MF compared to those without ACPA. In the same group, the ANA+ patients (12%) showed shorter DSM (233.5 wk ± 45.9 vs 548.0 wk ± 56.8, p=0.362) with similar trend in each subgroup (PsA and SpA).

In SpA group, the ACPA+ patients(6,3%) had a trend to shorter DSM (269.0 weeks ± 125vs 603.96 wk± 92.8, p=0.492),to higher sw-bDMARDs, and to be MF, higher NC and CCI compared to those without ACPA. No differences in clinical subset (OA, PA, EA, AI) were observed. In the same group the ANA+ patients had significant higher rate of PA (100% vs 65%, p=0.026) rather than OA (0% vs 35%, p=0.025). No significant differences were found in NC, CCI, MF.

In the PsA group, ACPA+ patients showed a trend to develop PA and EA subsets, shorter DSM (187.5 wk ± 48.7 vs 299.6 wk ± 31.4, p=0.415), higher rate to sw-bDMARDs and to be MF. The ANA+ PsA patients had higher trend to develop PA and AI subsets rather than OA and EA. All ANA+ patients were MF (100% vs 42%, p=0.046).

Conclusion: The ACPA and ANA positivity in PsA and SpA patients could be suggestive of more severe clinical disease manifestation, higher frequency of comorbidities and lower predicted 10-year survival (CCI). Moreover, this autoimmune dysregulation could be associated with worse drug survival in monotherapy with methotrexate and higher chance to be MF. Therefore, they can be taken into account for clinical management of these patients.

Disclosure of Interests: None declared

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AB0677

REVISING THE DEFINITION OF REACTIVE ARTHRITIS AND DIFFERENTIATION FROM UNDIFFERENTIATED SPONDYLOARTHRITIS

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Background: Reactive arthritis (ReA) is defined by 1999 ACR criteria as arthritis preceding a bacterial genitourinary (GUS) or gastrointestinal (GIS) infection in 3 days-6 weeks and evidence of triggering infection. Recently, ReA is classified as SpA and patients who do not fulfill SpA criteria are classified as undifferentiated spondyloarthritis (USpA) according to ASAS/EULAR SpA classification criteria.

Objectives: In several case reports which are associated with other infective agents are reported and the definition is extended for some clinicians so that SpA which is occurred after any infection is called as ReA. On the other hand, some researchers still accept the classical definition of ReA. The problem with the heterogeneity of opinions and unstandardized definition of ReA hinders studies about pathogenesis and standardization of treatments. In this study, we aimed to determine the spectrum of the use of the definition of reactive arthritis in publications in PubMed between 2009-2019.

Methods: The ReA keyword is searched in PubMed for the years between 2009-2019. 248 different publications have been identified and included in this research. 89 articles, 47 reviews, 108 case reports, 2 guidelines, and 2 editorials reviewed for the definition of ReA.

Results: Only 42.7% (106 patients) of these publications meet the classical definition which suggests ReA after only GIS and GUS infections. In 4 (1.6%) of the publications ReA was defined after GIS, GUS and oropharyngeal infections; in 3 (1,2%) of the publications after any bacterial infection; in 9 (3.6%) of the publications after any infection. In 8 (3.2%) of the publications, ReA and USPA was used correspondingly. In 39 (15,7%) of the publications the term agent related, ReA was used without making a general definition for ReA. 79 publications (31,9%) have not defined ReA.

According to causative agent and ReA relationship, in 64 (24,6%) general infective agents, in 75 (30,2%) classical agents, in 22 (8,9%) other bacterial agents, in 23 (9,3%) streptococcus, in 10(4%) intravesical BCG, in 6 (2.4%) HIV, in 6 (2.4%) tuberculosis, in 12 (4,8%) clostrudium difficle, in 2 (0.8%) parasites were

reported. In 31 (12,5%) of the publications the causative agent for the ReA was unknown, the diagnosis was made clinically.

Conclusion: In this study, it is aimed to draw attention terminology intricacy and the need for the standardization of the definition of ReA and USpA. It is clear that to standardize the definition of Rea and USpA is necessary. Between 2009-2019 there are reported cases diagnosed as ReA associated with bacterial infections (especially with Clostridium difficile, streptococcus and tuberculosis infections), and viral infections (by a majority with HIV), and parasitic infections. It is not clear if we need to define them classically or define them as USPA. Another important consideration is the necessity of extended laboratory investigations to find out the real causative agent even if the patient is clinically diagnosed with ReA. The requirement of the differentiation between ReA and USpA must be revealed for therapeutic researches.

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AB0678 RISK FACTORS FOR ADVERSE PREGNANCY OUTCOMES IN SPONDYLOARTHRITIS: DISEASE PHENOTYPE AND DISEASE ACTIVITY MAY PLAY A ROLE

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Background: Pregnant patients (pts) with spondyloarthritis (SpA) seem at increased risk for adverse pregnancy outcomes (APO), however limited and conflicting data have been published so far and risk factors for APO in these pts remain poorly understood.

Objectives: To assess APO and identify possible risk factors for those in a cohort of SpA pregnant pts.

Methods: Data on SpA pts prospectively-followed in a pregnancy clinic from 2010 to 2019 were retrospectively analysed before conception and during each trimester. Pregnancies complicated by APO were compared with those that were uneventful for demographic and clinical variables. Active disease was defined as a DAS-28-CRP>3.2 or an ASDAS-CRP ≥ 2.1 according to peripheral or axial dominant disease respectively.

Results: 56 pregnancies (mean age 34±5 years; median disease duration 60 months, IQR 24-123) in 47 pts were analysed: 37 psoriatic arthritis, 7 axial SpA, 6 undifferentiated SpA, 3 enteropathic SpA, 2 reactive arthritis and 1 enthesitis-related juvenile idiopathic arthritis. APO were recorded in 23/56 (41%) pregnancies: 5 (9%) early miscarriages, 1 (2%) medical abortion (central nervous system malformation), 3 (5%) preterm births (≥34 gestational week, all for preterm premature rupture of membranes - PROM); 2 (4%) PROM; 7 (13%) small for gestational age newborns (SGA); 3 gestational diabetes and 2 cholestasis of pregnancy. Table 1 displays the comparison between pregnancies with and without APO. A higher number of pts with active disease were detected during the 2nd trimester in both groups, however differences between those were only significant at the 3rd trimester (p=0.03). History of inflammatory bowel symptoms (IBS) was also associated with an increased risk for APO (p=0.02). Although not reaching statistical significance, APO occurred more frequently in pts with a previous use of > 1 conventional synthetic (cs) or biological (b) disease-modifying antirheumatic drug (DMARD) (p=0.05), suggesting a more difficult to treat phenotype. Likewise, pts with APO were less often treated with low dose aspirin (LDA) during pregnancy.

Conclusion: SGA was the main APO recorded. History of IBS, a more difficult to treat phenotype and the presence of active disease during pregnancy influenced APO in this cohort, reinforcing the need for tight disease control before and during pregnancy. Larger and prospective data are warranted to confirm these results and to assess the potential protective role of LDA.

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Table 1. Differences between patients with and without APO

	Pregnancies with APO	Pregnancies without APO	*p*
N, %	23, 41.1	33, 58.9	
Maternal age at conception, mean±SD (years)	33.8±5	33.8±4.9	NS
Hx previous APO – N, %	4,17.4	3, 9.1	NS
Disease duration, median (IQR), (months)	96 (36-132)	48 (24-96)	NS
Axial dominant disease – N, %	6, 26.1	6, 18.2	NS
Peripheral dominant disease – N, %	11, 47.8	20, 60.6	NS
Hx enthesitis – N, %	9, 39.1	13, 39.4	NS
Hx dactylitis– N, %	5, 21.7	11, 33.3	NS
Hx psoriasis– N, %	10, 43.5	18, 54.5	NS
Hx uveitis– N, %	1, 4.3	4, 12.1	NS
Hx inflammatory bowel symptoms – N, %	4, 17.4	0, 0	**0.02**
HLA-B27– N, %	8, 34.8	7, 21.2	NS
>1 cs or bDMARDs before conception – N, %	13, 56.5	10, 30.3	0.05
LDA during pregnancy – N, %	7, 30.4	17, 51.5	NS
Active disease before conception - N, %	5, 21.7	2, 6.1	NS
Active disease 1st trimester - N, %	1, 4.3	4, 12.1	NS
Active disease 2nd trimester - N, %	6, 26.1	5, 15.2	NS
Active disease 3rd trimester - N, %	3, 13	0, 0	**0.03**

Legend: Hx – history of; NS – non significant.

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AB0679 HEALTH ASSESSMENT IN FEMALE PATIENTS WITH SPONDYLOARTHRITIS: FOCUS ON REPRODUCTIVE SPHERE

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Background: SpA patients experience a decreased quality of life due to social, emotional and relational life impairment in addition to pain, fatigue and joint damage. Sexual dysfunction (SD) is often neglected by both patients and clinicians, although articular and extra-articular manifestations of the disease can decrease the quality of sexual life. Previous findings showed that SD can affect from 27% to 67% of patients with rheumatic diseases. Data available on SD in rheumatic patients are poor and primarily focus on male ankylosing spondylitis patients

Objectives: The aim of this study is to evaluate, in a group of female SpA patients, the presence of SD, its relationship with extra-articular manifestations and to estimate the correlation between disease activity and sexual activity.

Methods: 52 SpA patients (including PsA, IBD-SpA and undifferentiated SpA-un-SpA) and 50 healthy controls (HC) were administered the Female Sexual Function Index (FSFI) questionnaire for the analysis of sexual function (score from 0 to 100). SD is defined by a score lower than 26. Disease activity was evaluated through DAPSA and BASDAI. SpA-HAQ and BASFI was also performed to assess functional status

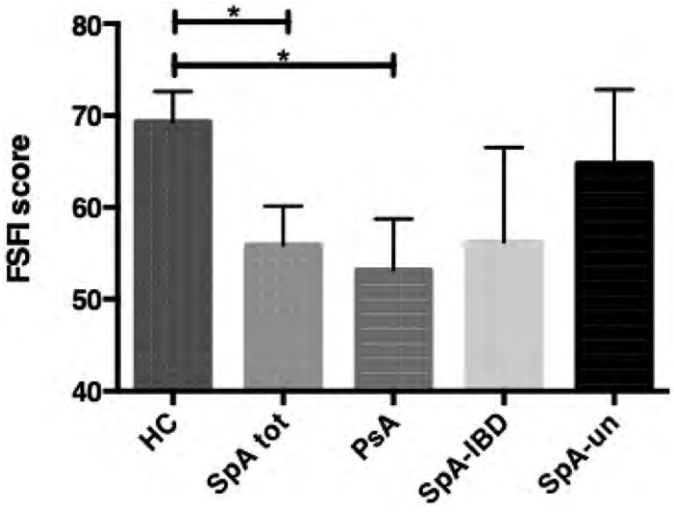
Results: There was a trend for a significantly greater proportion of SD in the patients (21%) than the controls (8%), $\chi^2(1, N = 102) = 3.52$, $p = .06$). Within the different groups, the percentage of those with SD according to the FSFI cut off were 23% of PsA patients, 25% of IBD-SpA patients, 11% of un-SpA patients, and 8% of healthy controls, however, when the patient groups were analysed separately these differences were not significant, $\chi^2(3, N = 102) = 4.43$, $p = .22$. Mean scores on the FSFI were lower for the total SpA patients group t(100) = 2.47, p = .02 compared to HC. When scores on the FSFI were analysed separately for each patient group, there was a trend for a significant difference between the groups, $F(3,98) = 2.43$, $p = .07$, and follow up t-tests showed that only the PsA group scored significantly lower than the HC, $t(100) = 2.56$, $p = .01$ (see Fig. 1). Among the items of the questionnaire, questions regarding sexual desire, lubrication and discomfort were statistically significantly lower scores in patients compared to HC ($p = 0.001$, $p = 0.009$, $p = 0.02$, respectively). For the overall patient group, the FSFI was significantly negatively correlated with the DAPSA ($r = -.37$, $p = .008$), the SpA-HAQ ($r = -.30$, $p = .03$) and the BASFI ($r = -.30$, $p = .03$). Additionally, the PsA group showed a negative correlation between DAPSA scores and FSFI score ($r = -.38$, $p = .03$) and the IBD-SpA group had a negative correlation between FSFI score and BASFI ($r = -.80$, $p = .002$).

Conclusion: Overall, the data generally show that SD is more common in SpA patients compared to HC and that SpA patients score lower on the FSFI. The negative correlations between the FSFI and scores on DAPSA, SpA-HAQ and BASFI suggest that sexual function may be poorer for patients with greater disease activity and poorer functional status. These findings could be due to the number of tender and/or swollen joints as well as chronic pain or fatigue patients

often experience. A key limitation of this study is the small sample size. Future research will include a larger sample size. SD in patients with rheumatic disease is still a neglected field in clinical practice, however, its assessment could contribute to improved quality of life for patients

Table 1. Clinical characteristics of patients and healthy controls

	PsA	un-SpA	IBD-SpA	HC
Age (mean ± SD)	50.6 ± 4.0	43.9 ± 3.6	46.3 ± 2-0	52.5 ± 0.5
Distribution (N%)	31 (59%)	9 (17%)	12 (24%)	50
Age at diagnosis (mean ± SD)	40.0 ± 2.5	35.6 ± 4.1	40.8 ± 1.2	/
DAPSA	15.1 ± 9.9	12.2 ± 9.9	/	
HAQ	0.6 ± 0.5	0.8 ± 0.5	1.0 ± 0.7	/
BASDAI	0.6 ± 0.9	0.6 ± 0.8	5.1 ± 2.8	/
BASFI	16 ± 16.0	37.8 ± 26.8	46.7 ± 21.7	/



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AB0680

BASELINE CHARACTERISTICS OF PATIENTS ENROLLED IN THE ONGOING SIRENA STUDY, A NATIONAL PROSPECTIVE OBSERVATIONAL REGISTRY IN SPONDYLOARTHRITIS SUBJECTS

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Background: There is a paucity of epidemiological data in Early Arthritis. SIRENA is an Italian prospective observational study in SpA patients, naïve to conventional, targeted and biological DMARDs.

Objectives: To present the baseline data, including demographic characteristics and patterns of clinical presentation, for the population enrolled between June 2017-February 2019.

Methods: At the study entry, patients are diagnosed, newly or confirmed, according to ASAS criteria and classified in subjects with predominant axial (AX) or with mainly peripheral (PER) manifestations. Diagnostic delay, subtypes of SpA are evaluated as well as clinical features (i.e. presence of dactylitis, enthesitis, involvement of skin/nails/other organs).

Results: In 23 italian sites, 282 patients were enrolled. Baseline data are shown in Table 1. 18% of the patients were obese (maximum BMI=39.7), 22% overweight. Diagnostic delay was registered for 58.1% patients with a mean delay of 57.1 months. Main reasons of the delay were incorrect referrals (44%) and previous misdiagnosis (27%). The most frequent type of SpA was psoriatic arthritis (54.3%), followed by ankylosing spondylitis (18.5%), undifferentiated SpA (11.5%), non-radiographic axial SpA (8.2%), and enteropathic SpA (7.5%). The majority of patients reported as first symptom peripheral arthritis and inflammatory back pain, followed by enthesitis. The most frequently reported comorbidities were psoriasis (50.4%) and cardiometabolic and gastrointestinal diseases (30.1% and 15.7%,respectively) - Table 2. To the 154 psoriatic arthritis (PsA) patients, CASPAR classification criteria were also applied, with a performance of 95% and a mean score of 3.64.

Conclusion: SIRENA is the first Italian Disease Registry for SpA patients. The above results are in line with the few evidences found in literature (1), confirming the representativeness of our sample. In case of PsA, our results confirm that the accordance between ASAS and CASPAR criteria is very high.

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Table 1.

Patient Characteristics (baseline)	Mean N=282
Age	50.8 years
Sex (%)	49 F/51 M
Weight	73.7 Kg
BMI	25.3
Smoking Status (never/ongoing/past - %)	56.8/22/21.2
Alcohol consumption (not/occasional/usual drinker - %)	50.0/44.9/5.1
SpA type (%)	35.8 AX/64.2 PER
Diagnostic Delay (yes - %)	58.1
Months of diagnostic delay (mean)	57.1 months
Newly diagnosis (%)	68.4

Table 2.

A) First Symptom	Number of Patients *N=282, more than 1 symptom referred*
Arthritis	145
Enthesitis	70
Dactylitis	35
Inflammatory Back Pain	114
Psoriasis skin	67
Psoriasis nails	21
Uveitis	5
IBD	16
B) Comorbidities	**Percentage of Patients** *N=282, more than 1 comorbidity referred*
Cardiometabolic	30.1%
- Hypertension	27.0%
- Dyslipidemia	13.8%
- Diabetes	7.1%
- MetS	6.0%
- CHD	3.2%
Psoriasis	50.4%
Gastrointestinal	15.7% (5.3% Crohn's disease)
Endocrine	9.6%
Depression/Anxiety	5.7%
Osteoporosis	4.6%
Hepatic	4.3% (2.5% NAFLD)
Infections	3.9%
Malignancies	2.8%
Kidney	1.8%

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AB0681 COMPARISON BETWEEN DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF PREDOMINANT AXIAL VS MAINLY PERIPHERAL SPONDYLOARTHRITIS (SPA) PATIENTS, ENROLLED IN THE ONGOING SIRENA STUDY

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Background: SIRENA is an Italian, prospective Registry in Spondyloarthritis (SpA) patients, naïve to conventional, targeted and biological DMARDs. Patients are diagnosed, newly or confirmed, according to ASAS criteria and classified in subjects with predominant axial **(AX)** or with mainly peripheral manifestations **(PER)**.

Objectives: To compare descriptively AX vs PER subgroups of patients.

Methods: Demographic data, diagnostic delay and subtypes of SpA as well as clinical features and comorbidities are collected.

Results: 282 patients were enrolled: 101 (35.8%) AX and 181 (64.2%) PER. Baseline data are shown in Table 1. There were more obese patients in AX (21.4% AX vs 16.1% PER) and more overweight ones in PER (19.4% AX vs 23.8% PER). The % of subjects with diagnostic delay was higher in AX (65.7% vs 53.9% PER) and the delay longer (mean of 73.1 months vs 47.8). In both groups, main reason of the delay was incorrect referrals (41.5% for AX and 45.3% for PER). Noteworthy the fact that in PER, the 75.7% of patients had a newly diagnosed SpA. In PER, the most frequent SpA type was PsA (82.3%), followed by undifferentiated SpA (8.8%) and enteropathic SpA (7.5%), while in AX, 49.5% were ankylosing spondylitis, 21.8% nr-ax-SpA and only 4% PsA. The majority of PER patients reported as first symptom peripheral arthritis (80/181), psoriasis (57/181) and enthesitis while in AX referred inflammatory back pain (80/101). High percentages of comorbidities were reported: psoriasis (65.8%) and cardiometabolic diseases (34.8%) were higher in PER while depression/anxiety and GI diseases were higher in AX (Table 2). At the baseline, the mean PhGA score (0-100) was 51.5 for AX and 43.8 for PER.

Conclusion: SIRENA study highlights relevant differences in AX vs PER patients, expecially in terms of diagnostic delay, clinical presentation and comorbidities.

Table 1.

	Mean AX n=101	Mean PER n=181
Age (years)	47.3	52.8
Sex (female/male - %)	50.5/49.5	47.5/52.5
Weight (Kg)	73.0	73.9
BMI	25.3	25.4
Diagnostic Delay (yes - %)	65.7%	53.9%
Time of delay (mean - months)	71.3	47.8
Newly SpA diagnosis (%)	55.5%	75.7%

Table 2.

A) First Symptom *(more than 1 symptom referred)*	**AX n=101 N. Patients**	**PER n=181 N. Patients**
Arthritis	23	122
Enthesitis	16	54
Dactylitis	7	28
Inflammatory Back Pain	80	34
Psoriasis skin	10	57
Psoriasis nails	2	19
Uveitis	4	1
IBD	7	9
B) Comorbidities	**% Patients**	**% Patients**
(more than 1 comorbidity referred)		
Cardiometabolic	20.8%	34.8%
-Hypertension	19.8%	30.9%
-Dyslipidemia	17.8%	11.6%
-Diabetes	6.0%	7.7%
-MetS	5.0%	6.6%
Psoriasis	22.8%	65.8%
Gastrointestinal	20.8 (16.9% CD)	12.8 (4.4% CD)
Depression/Anxiety	11.9%	2.2%
Endocrine	6.9%	11.1%
Osteoporosis	3%	5.5%
Hepatic	4% (3% NAFLD)	4.4% (2.2% NAFLD)
Infections	3%	3.9%
Malignancies	0%	4.4%

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AB0682 FUNCTIONAL IMPAIRMENT IN PATIENTS WITH AXIAL SPONDYLOARTHROPATHY IN A GERMAN COHORT: WORSE OUTCOMES AND WORSE QUALITY OF LIFE FOR FEMALE PATIENTS

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Background: Axial spondyloarthritis (AxSpA) may lead to significant structural damage resulting in marked impairment and disability. Historically, AxSpA has been thought to have a distinct male predominance regarding both, occurrence but also disease severity. However, it has recently been shown in international cohorts that women with AxSpA may have in fact an increased disease burden and worse outcome than their male counterparts.

Objectives: The aim of this project was to analyse functional capacity in a German cohort of AxSpA patients and identify associated factors by comparing demographic data, clinical characteristics, disease activity and treatments.

Methods: Analysis of a German University Hospital outpatient clinic cohort of 150 AxSpA patients. Questionnaire-based screening tools were used to assess disease activity, functional impairment and quality of life (BASDAI, FFbH, WHO-QOL-BREF). Female and male patients were compared by independent samples two-tailed T tests for continuous variables as well as chi-squared test for categorical variables.

Results: A German cohort of 150 AxSpA patients with 89 male and 61 female patients (mean age 49.3 years for males, 48.5 for females, p=0.77) was analyzed for functional capacity. Female patients had a significantly higher functional impairment in everyday life compared to males (p=0.013). After adjusting for age, linear regression showed female sex still to be significantly associated with functional impairment. Female patients rated their satisfaction with health as well as their physical and mental health-related quality of life significantly lower than male patients (p=0.015, respectively p=0.003 and p=0.002).

There were no significant differences in disease duration, diagnostic delay or family history between male and female patients (p=0.731, p=0.971 and p=0.776). Women had a slightly higher disease activity (BASDAI 4.08 vs. 3.36), although just not statistically significant in our cohort (p=0.056). Female patients had more peripheral joint involvement (52.5% vs. 34.8%, p=0.032), as well as more enthesitis (31.1% vs. 16.9%, p=0.04), whereas there were no differences concerning eye involvement (p=0.51). Female patients were less likely to be HLA B27 positive (65.6 vs. 80.7%, p=0.04). and were less likely to be on anti-TNF treatment (p=0.032, respectively p=0.042).

Conclusion: Also in our cohort female patients had a higher burden of disease as well as a worse patient reported outcome with worse quality of life and more self-reported functional impairment in everyday life. These data underline the importance of raising awareness for sex differences in disease presentation and suggest that female patients might require different treatment to achieve improved outcomes.

Disclosure of Interests: None declared

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AB0683 IS THE NEW ASDAS NOMENCLATURE IN LINE WITH THERAPEUTIC DECISION MAKING IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS?

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Background: The Assessment of SpondyloArthritis international Society (ASAS) proposed in 2018 a change in the nomenclature of the Ankylosing Spondylitis Disease Activity Score (ASDAS) for monitoring disease activity in axial spondyloarthritis (axSpA), renaming the previously status of moderate disease activity as low disease activity status, with the presumption that this better reflects the perception that the doctor and the patient have about the disease situation. However, this decision was not data-driven.

Objectives: To evaluate the association between the state of low disease activity according to the new ASDAS nomenclature and the therapeutic decision in patients with axSpA.

Methods: Longitudinal retrospective study in which patients with axSpA recruited in a secondary hospital were included. All patients with clinical diagnosis of axSpA who started treatment with a first inhibitor of tumor necrosis factor between January 2014 and June 2019 were included. At each follow-up visit, disease activity assessments (including BASDAI and CRP) and the therapeutic decision of the doctor were collected. Later, the ASDAS was calculated and disease status at each visit was classified according to the new nomenclature (inactive, low, high and very high activity). Using descriptive statistics, the association between the disease activity status and the therapeutic decision was evaluated.

Results: A total of 304 visits were analyzed in 104 patients with axSpA. Out of these, 57% were women, 47% had a subtype of non-radiographic axSpA and 42% were HLA-B27 positive. The mean (standard deviation) age at diagnosis was 46.9 (12.5) years. In the visits with an ASDAS showing a status of low activity, the therapeutic attitude was not to intensify the treatment in 98.2% of the cases. However, in visits with an ASDAS status of high or very high disease activity, treatment was intensified in 33.7% and 82.8% of cases, respectively.

Conclusion: In clinical practice, the status of disease activity initially classified by the ASDAS as moderate disease activity is currently considered to represent low disease activity status based on the therapeutic attitude of following a non-intensification strategy in this situation. These data support the recent change in the nomenclature of disease activity states according to the ASDAS.

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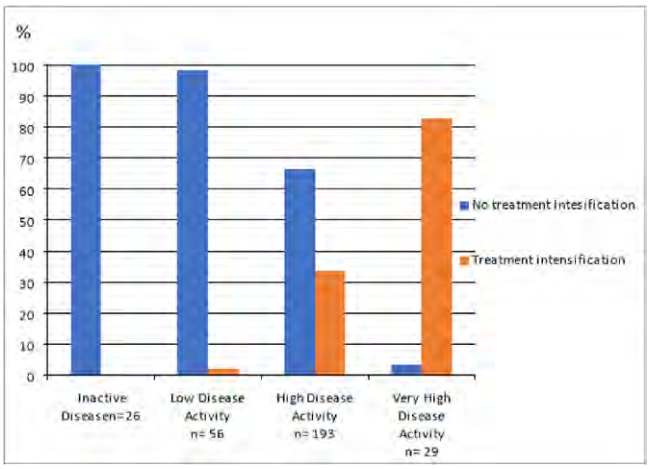


Figure 1. Association between the state of disease activity according to the new ASDAS nomenclature and the therapeutic decision.

Disclosure of Interests: Blanca Garcia-Magallon Consultant of: MSD, Speakers bureau: Pfizer, Amgen, Celgene, MSD, María del Carmen Castro Villegas: None declared, Rosa Rosselló: None declared, Victoria Navarro-Compán Consultant of: Abbvie, Lilly, Novartis, Pfizer, UCB, Speakers bureau: AbbVie, MSD, Lilly, Novartis, Pfizer, UCB

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AB0684 COMPARATIVE ANALYSIS OF PATIENT-REPORTED OUTCOMES AMONG EMPLOYED AND UNEMPLOYED PATIENTS WITH AXIAL SPONDYLOARTHRITIS. RESULTS OF THE SPANISH ATLAS 2017

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Background: Unemployment is associated with poorer disease outcomes in chronic conditions. Current high rates of unemployment in Spain may lead to a higher burden of disease in axial spondyloarthritis (axSpA) patients.

Objectives: To evaluate the differences in sociodemographic factors and patient-reported outcomes (PROs) between employed and unemployed axSpA patients in the same sample.

Methods: Data from 680 unselected patients of the Spanish Atlas of Axial Spondyloarthritis from an online survey were collected in 2016 were analysed. Active workforce participants were divided into employed and unemployed according to International Labour Organization (ILO) standards. Socio-demographic characteristics, and Patient-reported Outcomes (PROs) [BASDAI (0-10), spinal stiffness (3-12), functional limitation (0-54) and psychological distress (0-12, General Health Questionnaire GHQ-12)] were compared between employed and unemployed participants. The X^2 test was used for qualitative variables and the Mann-Whitney test for quantitative variables.

Results: In total, 415 (63.6%) patients were categorised in the active population, of which 325 (78.3%) were employed and 90 (21.6%) unemployed (Table 1). 62.8% (N = 86) of unemployed patients declared that axSpA was the cause of their joblessness. Compared to the unemployed, the employed patients had a higher percentage of university studies (47.1% vs 23.3%; p=0.001) and higher income level per family member (€890.4 vs €358.5; p<0.001). In relation to PROs, the unemployed presented greater disease activity (6.3±1.9 vs 5.2±1.9; p<0.001) and spinal stiffness (7.8±2.3 vs 6.5±2.6), worst functional limitation (45.0±8.4 vs 40.6±10.1; p<0.001) and more psychological distress (7.6±4.2 vs 4.9±4.3; p<0.001). In addition, a higher proportion of unemployed participants self-reported anxiety (27.8% vs 16.0%; p=0.011) and depression (23.3% vs 10.2%; p=0.001) (Table 2).

Table 1. Employment status of Spanish Atlas survey respondents

Population	N	%	Employment status	N	%
Active population*	415	63.6	Employed	325	78.3
			Unemployed	90	21.6
			Total	415	100.0
Inactive population	238	36.4	Temporary sick leave	63	26.5
			Permanent sick leave	64	26.9
			Retired	63	26.5
			Homemakers	29	12.2
			Students	9	3.8
			Early retirement	10	4.2
			Total	238	100.0
Total	653	100.0			

*According to the ILO

Table 2. Association between sociodemographic characteristics and PROs comparing employed and unemployed axSpA patients

	Employed (N = 325) Mean ± SD or n (%)	Unemployed (N = 90) Mean ± SD or n (%)	p-value
Sociodemographic			
Age (years)	42.9 ± 8.6	42.0 ± 9.1	0.513
Gender (Male)	159 (48.9)	36 (40.0)	0.133
Education level (University)	153 (47.1)	21 (23.3)	**0.001***
Marital status (Married)	231 (71.1)	54 (60.0)	0.051
Monthly Income (€)	890.4 ± 592.3	358.5 ± 377.7	**<0.001***
PROs			
Diagnostic Delay (years)	7.7 ± 7.6	8.0 ± 6.5	0.319
BASDAI (0-10)	5.2 ± 1.9	6.3 ±1.9	**<0.001***
Spinal Stiffness (3-12)	6.5 ± 2.6	7.8 ± 2.3	**<0.001***
Global Limitation Index (0-54)	40.6 ± 10.1	45.0 ± 8.4	**<0.001***
GHQ-12 (0-12)	4.9 ± 4.3	7.6 ± 4.2	**<0.001***
Anxiety	52 (16.0)	25 (27.8)	**0.011***
Depression	33 (10.2)	21 (23.3)	**0.001***
Sleep disorder	50 (15.4)	18 (20.0)	0.295

Conclusion: The Spanish Atlas results show significant differences between employed and unemployed patients with axSpA, with greater disease activity, spinal stiffness, functional limitation, and poorer mental health in those who are unemployed.

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AB0685 IMPACT OF AXSPA ON WORKING LIFE: RESULTS FROM 233 PATIENTS OF THE RUSSIAN FEDERATION PARTICIPATING IN THE EUROPEAN MAP OF AXIAL SPONDYLOARTHIRTIS (EMAS)

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Background: Axial spondyloarthritis (axSpA) has been shown to impact patients' (pts) professional opportunities, employment status and work productivity [1].

Objectives: To evaluate employment status, work-related issues and their interrelation with the disease-related characteristics among Russian axSpA pts.

Methods: The European Map of Axial Spondyloarthritis (EMAS) was a cross-sectional on-line survey of pts with self-reported axSpA conducted in 13 European countries. Russian participants were recruited between Dec 2017 and Feb 2018 through the Russian Ankylosing Spondylitis Association and an online panel. Socio-demographic, BASDAI, psychological distress (GHQ-12), working status and work-related issues (e.g. taking sick leave, difficulties fulfilling or reducing working hours, etc.) were assessed.

Results: 233 Russian pts participated in EMAS. The mean age was 36.7±9.1 years, 51.9% were female, and the mean disease duration was 12.4±9.5 years. Of the 233, 226 reported their employment status and productivity, of which 73.45% were employed, 12.39% were unemployed, 4.42% were on sick leave, 3.54% were homemakers, 2.21% were retired, 2.21% were on early retirements, 1.77% were students. Of the 160 pts, who reported their occupation, 73 (45.63%) were employed and had jobs requiring higher education qualifications, 39 (24.38%) had management positions, 23 (14.38%) were skilled manual workers and 12 (7.50%) were skilled non-manual workers, 3 (1.88%) were occupied in armed forces, 3 (1.88%) pts worked as unskilled workers. 124 (76.54%) of 162 pts survey respondents declared to have suffered work issues related to their disease in the 12 months prior to the survey. The most common work-related issue was difficulty fulfilling working hours in 69 (56.56%), followed by taking sick leave 49 (40.16%) and asking for days off 44 (36.07%) out of 122 pts. Pts who reported any type of issues at work had higher BASDAI and psychological distress (GHQ-12 score) (**table 1).** 145 (76.32%) out of 190 responded pts reported that their choice of workplace had been influenced by the disease (68.25%).

Table 1. BASDAI and GHQ-12 by work-related issues and difficulty fulfilling working hours due to axSpA.

Any type of issue at work	BASDAI			GHQ-12		
	Mean	SD	N	Mean	SD	N
No	3.14*	1.93	38	2.95*	3.39	38
Yes	4.97*	2.08	124	6.53*	3.76	124
Difficulty fulfilling working hours	**Mean**	**SD**	**N**	**Mean**	**SD**	**N**
No	4.53**	2.15	55	5.49**	3.80	55
Yes	5.32**	1.96	69	7.36**	3.54	69

* Mann-Whitney test p-values < 0.001
** Mann-Whitney test p-values < 0.05

Conclusion: Results from the Russian sample of the EMAS survey highlight the impact of axSpA in working life. Patients with any type of work-related issue mark above the cut-off point of BASDAI and GHQ-12, so work-related issues are associated to a status of high disease activity and a risk of poor mental health. Among all work-related issues surveyed, the presence of presenteeism (measured by difficulty fulfilling working hours) is associated to both a clinical and significant increase in disease activity through BASDAI.

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AB0686 ONLINE QUESTIONNAIRE CAN IMPROVE DELAY IN AXIAL SPONDYLOARTHRITIS DIAGNOSTICS. RESULTS OF SAINT PETERSBURG AXSPA EARLY DIAGNOSTICS PROJECT

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Background: Due to current data mean diagnostics delay in axial spondyloarthritis (axSpA) is 7.4 ± 8.4 years (mean ± SD) [1]. However, development

of specific and high sensitive criteria of axSpA do not improve the situation because one of the main reasons of late axSpA diagnostics is the increased period when the patient with typical axSpA symptoms do not referred by general practitioner (GP) to the rheumatologists (so called «human factor»). The increasing role of internet online technologies can make way from GP to rheumatologist shorter and decrease the diagnostics delay in axSpA.

Objectives: To develop the online questionnaire that calculates probability of having axSpA and evaluate the advantages of the method of online based detection of axSpA under the traditional ways of axSpA search.

Methods: Based on positive and negative predictive values of symptoms from ASAS axSpA criteria (2009) the axSpA Early Diagnostics Questionnaire (aEDQ) was developed. The aEDQ was available on website of Russian Ankylosing Spondylitis Association from October 2018. Link to the aEDQ could be obtained directly on the site and additionally by using one of 1,500 related to axSpA keywords approved by 5 rheumatologists from Russian SpA Expert Group. Those of participants who had high risk of axSpA according aEDQ were recommended to visit the rheumatologist, related to axSpA diagnostics. Participants with low risk of axSpA were sent to their GP. Collected data of diagnostics delay and capacity of the aEDQ were compared with data from demographically matched populations from EMAS online survey from 13 European countries (n=2,846), and SPACE cohort results (n=461) [1, 2], and from Russian North-Western axSpA LADOGA register (n=1,544). This study used only anonymized data. Statistical analysis was performed with Statistica SPSS2017, GraphPadPrizme 2016.

Results: Since October 2018 until January 2019 in Saint-Petersburg 22,925 people visited the aEDQ, 21,939 (95.6%) people filled out the questionnaire. Out of 21,939 people filled out questionnaire 7,888 (35.95%) people has high risk of axSpA. Within one month after passed the questionnaire 424 people with high risk of axSpA (5% out of all who had the recommendation) consulted by rheumatologist (mean age 42±6.6 years, male 275 (65%), symptoms duration 4.4 ± 3.0 years, HLA-B27 positive 292 (68.3%)). In 254 patients out of 424 (59.9%) presence of axSpA was confirmed as compared with 44.6% in SPACE cohort results ($\chi 2 = 19.24$, $p<0.000$ for differences with SPACE cohort results [2]).

Mean diagnostics delay in aEDQ cohort was 4.4 ± 3.0 years (mean ± SD), n = 254, in axSpA patients with traditional way of axSpA search in LADOGA register was 8.8 ± 4.8 years, n=1,544 (LADOGA study results), and 7.4±8.4 years in EMAS survey [1], $p < 0.0001$ for all the differences.

Conclusion: Online axSpA Early Diagnostics Questionnaire with function of calculation of axSpA probability can decrease diagnostics delay and increase percentage of confirmed by rheumatologist axSpA diagnosis as compared with another forms of axSpA search.

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AB0687 THE PROBABILITY OF SPONDYLOARTHRITIS IN PATIENTS WITH UVEITIS

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Background: Uveitis is a heterogeneous group of inflammatory eye diseases, some of which may be associated with spondyloarthritis (SpA). The probability of SpA depends on the clinical features of uveitis.

Objectives: To evaluate the probability of SpA depending on the clinical features of uveitis.

Methods: 208 patients with uveitis referred from ophthalmologists were assessed at the Institute of Rheumathology. 139 of 208 pts had an acute recurrent course of uveitis, 69-chronic course; 149 of 208 had isolated anterior uveitis, 59 – panuveitis involving the posterior and/or intermediate part of the eye; 160 had unilateral uveitis, 48 – bilateral; 106 had HLA- B27, 102 - without HLA-B27. In addition to HLA- B27, a survey was performed to identify clinical and imaging signs of SpA, including radiography and MRI of sacroiliac joints.

In 60 cases (28.8%), various SpA were identified (20 –ankylosing spondylitis, 2- reactive arthritis, 38 – non-radiographic SpA). In 148 pts SpA was not confirmed (4 of them had Behcet's disease, 2-sarcoidosis, 4-toxoplasmosis, 29 - viral uveitis, 1 - Fux syndrome, 2 – Vogt-Koyanagi- Harada syndrome, 2 - multiple sclerosis, 104 – unspecified uveitis).

Sensitivity (Se) and specificity (Sp), relative risk (RR), 95% confidence interval (CI), and likelihood ratio (LR) were calculated for each clinical parameter of uveitis with the following assessment of the probability of SpA.

Results: Pretest probability of SpA in the group was 28.8%, that corresponds to pretest odds of 0.4. Among 139 pts with acute recurrent uveitis SpA was identified in 45 (32.3%), among 69 with chronic uveitis – in 15 (21.7%), RR-1.49, 95% CI [0.896, 2.475], LR-1.17. Among 149 pts with isolated anterior uveitis SpA was in 55(36.9%), among 59 with panuveitis – in 5(8.5%), RR=4.36, 95% CI [1.8, 10.3], LR-1.43. In a subgroup of 160 pts with unilateral uveitis SpA diagnosed in 51 (31.9%), in a subgroup of 48 with bilateral uveitis – in 9 (18.7%), RR = 1.7, 95% CI [0.9, 3.1], LR-1.14. Among 160 HLA-B27-positive pts SpA detected in 56 (52%), among 102 HLA-B27- negative – in 4 (3.9%), RR=13.4, 95% CI [5.1, 35.8], LR-2.7. Taking into account the pretest odds and likelihood ratio of all parameters, posttest odds was 2.7, that corresponds to posttest probability of 67%.

Conclusion: A combination of such signs of uveitis as isolated localization in the anterior part of the eye, acute recurrent course, unilateral inflammation, HLA-B27, increases the probability of SpA more than 2 times

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Disclosure of Interests: None declared

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AB0688 GAIT PATTERN DIFFERENCES BETWEEN PATIENTS WITH RADIOGRAPHIC AND NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS, THE MYOSPA STUDY

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Background: Axial spondyloarthritis (axSpA) is a chronic inflammatory disease classified as radiographic (r-axSpA) or non-radiographic (nr-axSpA). Defining the gait patterns associated with these two groups can improve its detection and promote early intervention. In normal walking, body segments move around the joints as struts of an inverted pendulum. The resultant cyclic rotations contribute to the forward translation of the body, while minimizing muscle work and maintaining stability. Recent literature describes a decline in this pendulum-like mechanism associated with aging and some neurological diseases (Parkinson and multiple sclerosis).

Objectives: The aim was to compare the 3D gait kinematics of patients with r-axSpA and nr-axSpA.

Methods: A cross-sectional study was conducted on 54 participants (18-50 years old), 27 patients with axSpA (according to ASAS criteria, with less than 10 years since symptoms onset) and 27 healthy controls, matched by gender, age and level of physical activity. A sub-analysis was performed involving the whole group of patients classified as r-axSpA (n=14) and nr-axSpA (n=6). Subjects movement was reconstructed using a 3D full-body kinematic model (Kinetikos, Coimbra, Portugal) fed by 15 inertial sensors placed in the head, arms, trunk, pelvis, thighs, shanks and feet. 3D gait kinematics was characterised based on variables that analyse the body movement as a whole (e.g. center of mass displacement, speed), conventional spatiotemporal parameters (e.g. stance/swing time, step length) and joints kinematics time-normalized to 101 points, comprising the gait cycle from 0 to 100%. Nonparametric statistical tests were used.

Results: In the r-axSpA group, 71,4% were male, with a mean age of 34.43±7.84 years and a BASDAI of 2.84±2.39, whereas in the nr-axSpA, 50%

were male, with a mean age of 41.83±6.27 years and a BASDAI of 2.99±0.58. A statistically significant difference was observed in the displacement of the center of mass (with respect to the pelvis local coordinate system) along the anteroposterior axis between the two studied groups (H = 4.96, p = 0.03), with a mean rank displacement of 8.6 for r-axSpA and 15.00 for nr-axSpa, corresponding to a reduction in displacement of 38% (mean 0.00986 vs 0.01579m), in the r-axSpa group.

Conclusion: Our preliminary results in r-axSpA subjects show a reduction of the pendulum mechanism. Although no significant segmental (kinematics) changes were observed, the sum of all studied variables result in a clear different gait pattern between the two groups. The observed decline can be an early sign of the inefficiency of the r-axSpA group to minimise the cost of transport of the center of mass during walking (i.e. increased instability). This study shows the potential of gait analysis to identify subjects who may benefit from early physiotherapy intervention.

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AB0689 THE IMPORTANCE OF THE SUN. VITAMIN D AND SPONDYLOARTHRITIS: OUR EXPERIENCE IN A THIRD LEVEL HOSPITAL.

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Background: Vitamin D plays an important role in the pathogenesis of autoimmune diseases, so that it has been shown that an adequate level is associated with a lower risk of developing this group of entities as well as a lower severity of them. Specifically, in spondyloarthritis (SpA) the deficiency has been associated with greater aggressiveness and greater radiological progression.

Objectives: Assess levels of vitamin D in patients diagnosed with SpA in the León University Assistance Complex and study its possible relationship with different clinical-epidemiological variables.

Methods: Prospective observational study between January 1, 2019 and December 31, 2019 with consecutive sampling of patients diagnosed with SpA (New York criteria, ASAS) in our hospital between 1973 and 2018. It was taken as a cut-off point for vitamin normality D those values ≥ 30 ng / ml. The disease activity was assessed based on BASDAI and CRP level (taking as a cut-off point 5 mg/l, reference value of our hospital and ruling out elevation due to intercurrent processes) in the last consultation. Positive values above 130 mlg/dL were considered for the orosomucoid and for calprotectin as undetermined values between 50-100 mg/kg feces and suspected IBD greater than 100 mg/kg feces. An attempt was made to link the value of vitamin D with disease activity, tobacco, the development of uveitis and the presence of subclinical intestinal inflammation.

Results: 132 patients were included, of which 60.6% were men with a mean age of 49.35 ± 12.95 years. 84.8% were B27 positive. 88.6% met New York criteria. 35.6% suffered uveitis at some time during their evolution. As for tobacco, 68.2% were non-smokers, 12.9% were former smokers and 18.9% were active smokers. 6.8% of the sample presented positivity for the orosomucoid and 37.8% alterations in calprotectin (of which 24.2% were undetermined and 13.6% suspected of inflammatory bowel disease). Only 25% of patients had elevated CRP levels and 11.4% of patients had BASDAI> 4. 50.8% of our sample had optimal levels of Vitamin D while 49.2% were at low values.

A statistically significant association was observed between hypovitaminosis D and elevated CRP levels (p 0.038). In our sample we found no statistical association with uveitis or with markers of subclinical inflammatory activity.

Conclusion: -Almost half of the patients in our sample have hypovitaminosis D which is probably attributable to the meteorological characteristics of León region.

-Low levels of vitamin D are statistically significantly related to higher levels of CRP and, therefore, with greater disease activity.

-No significant relationship was found with uveitis or with a higher risk of subclinical intestinal inflammation in our simple.

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Disclosure of Interests: None declared

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AB0690 ANTIPHOSPHOLIPID ANTIBODIES AND SPONDYLOARTHRITIS. TRUTH OR MYTH? OUR RESULTS IN A THIRD LEVEL HOSPITAL.

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Background: The importance of antiphospholipid antibodies and their clinical involvement in thrombotic phenomena, isolated or associated with certain autoimmune diseases such as systemic lupus erythematosus, is known. However, in spondyloarthritis (SpA) there is little published data about it.

Objectives: Identify the presence of antiphospholipid antibodies in patients diagnosed with SpA in the León University Assistance Complex and analyze its possible relationship with different clinical-epidemiological variables.

Methods: Prospective observational study between January 1, 2019 and December 31, 2019 with consecutive sampling of patients diagnosed with SpA (New York criteria, ASAS) in our hospital between 1973 and 2018. Anticardiolipin antibodies, anti-B2 glycoprotein and Lupus anticoagulant (AL) were the requested antiphospholipid antibodies excluding cases of positivity for other causes (coagulopathy, liver disease) and repeating the determination at 12 weeks. The disease activity was assessed based on BASDAI and CRP level (taking as a cut-off point 5 mg/l, reference value of our hospital and ruling out elevation due to other intercurrent processes) in the last consultation. An attempt was made to link antiphospholipid antibodies with sex, disease activity, cardiovascular risk factors (CVRF), thrombotic events and taking anti-TNF.

Results: 132 patients were included, of which 60.6% were men with a mean age of 49.35 ± 12.95 years. 84.8% were B27 positive. 88.6% met New York criteria. 43.2% had CVRF, highlighting arterial hypertension (HT) in 25%; dyslipidemia (DL) in 24.2%; Obesity in 3.8%, hyperuricemia in 3% and diabetes mellitus (DM) in 2.3%. 43.9% of the patients were being treated with an anti-TNF. Only 25% of patients had elevated CRP levels and 11.4% had BASDAI> 4.

38.7% of the sample had positive antiphospholipid antibodies; of which 58.8% (22.7% of total patients) were confirmed. Of these, AL was the predominant in 90.2% of cases (34.9% of the total number of patients). Likewise, 10% of patients with repeated antiphospholipid antibodies met criteria for antiphospholipid syndrome (thrombi).

It was observed in our sample that female sex can behave as a protective factor against the positivity of AL (p 0.002) and that elevated CRP levels show a statistically significant tendency to the presence of AL (since the first positive determination was related with a p 0.013).

Conclusion: -According to our results, it seems important to determine antiphospholipid antibodies (especially AL) in patients with SpA, especially in order to avoid future thrombotic events.

-There seems to be a trend between disease activity and the probability of presenting positive AL, however, more studies are needed to confirm this hypothesis.

-The female sex, in our sample, can be considered a protection factor against this antibody.

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AB0691 CHARACTERIZATION OF DIFFERENT GROUPS WITH IMAGING AND NON-IMAGING FINDINGS OF ANKYLOSING SPONDYLITIS COMBINE WITH HIP LESION IN WESTERN CHINESE

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Background: Hip joint lesion are the main cause of disability in patients with Ankylosing Spondylitis(AS) in western China. Seriously affect the quality of life of patients.The early clinical characteristics of hip joint disease are not typical, the disease is insidious, and the radiological diagnosis is delayed.The main prevention is early screening and early diagnosis.
Objectives: This study attempted to find out the main characteristics and related factors in different groups of AS combine with hip joint lesion in western China.
Methods: A-First evaluation: How many patients have 1) active SIJ changes on MRI. 2) chronic SIJ changes (each for erosion, clerosis, ankylosis, or any of those) on MRI. 3) a combination of active changes and chronic changes (each for erosion, sclerosis, ankylosis, or any of those) on MRI. 4) active hip changes on MRI. 5) chonic hip changes (erosion, effusion any of those) on MRI. 6) a combination of active changes and chronic hanges (erosion, effusion any of those) on MRI. B-Then, combination SIJ / hip. 7) active SIJ changes on MRI and in parallel active hip changes on MRI. 8) chronic (see above) SIJ changes on MRI and in parallel active hip changes on MRI. 9) chronic (see above) SIJ changes on MRI and in parallel chronic (see above) hip changes on MRI. 10) chronic (see above) SIJ changes on MRI and in parallel any (active or chronic) hip changes on MRI. C-Then, characterization of these groups with non-imaging findings. Characteristics of groups 7-10 above, for age, sex, Disease duration, Hip pain, Joint pain, enthesitis, Diarrhea, uveitis, ASDAS-CRP, BASDAI, BASFI, BASMI, Pat. Global, CRP, ESR, Harris Score, HLA-B27.
Results: Retrospective analysis total 558 SpA patients (mean age 29, mean duration 5 years). 1) HIP-Active+Chronic group (N=288, AS=151) vs SIJ+HIP-Active group (N=241, AS=138): hip pain (p<0.0001), diarrhea (p<0.0001), joint pain (p<0.0001) and BASFI (p<0.05); 2) HIP-Active+Chronic(N=117, AS=58) vs SIJ-Chronic+HIP-Active group (N=214, AS=134): hip pain(p<0.0001), joint pain (p<0.0001), enthesitis (p<0.0001), ASDAS-CRP (p<0.05) and ESR (p<0.05); 3) SIJ-Active+Chronic group (N=204, AS=125) vs SIJ-Chronic+HIP-Active group (N=214, AS=134): hip pain (p<0.0001), joint pain (p<0.0001); 4) SIJ-Active+Chronic group (N=204, AS=125) vs SIJ+HIP-Chronic group (N=72, AS=40):hip pain (p<0.0001), Pat. Global (p<0.05); 5) SIJ+HIP-Active group (N=241, AS=138) vs SIJ-Chronic+HIP-Active group (N=214, AS=134): HLA-B27 positive (Chi-square, df, 24.98, 4) (p<0.0001); 6) SIJ+HIP-Chronic group (N=72, AS=40) vs SIJ-Chronic+HIP-Active/Chronic group (N=228, AS=144): Pat. Global (p<0.05), ESR (p<0.05).
Conclusion: Hip joint lesion are closely related to sacroiliac joint lesion and HLA-B27 positive in AS. Hip pain is the main clinical manifestation of hip joint lesion in AS. Hip joint lesion may lead to function declines, disease activity in AS.
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AB0692 CLINICAL SIGNIFICANCE OF LIPID PROFILES IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: Axial spondyloarthritis (axSpA) is a chronic inflammatory disease of the sacroiliac joints and spine. Lipid profiles, including total cholesterol(TC), high-density lipoprotein cholesterol(HDL-c), low-density lipoprotein cholesterol (LDL-c), TC/HDL-c, triglycerides(TG), have been reported to be changed regularly in axSpA patients. However, the clinical significance of lipid profiles in axSpA patients is controversial.
Objectives: The study aims to determine the clinical significance of TC, HDL-c, LDL-c, TC/HDL-c, TG for axSpA patients.
Methods: A total of 208 axSpA patients and 113 healthy subjects were enrolled in the study retrospectively. TC, HDL-c, LDL-c, TC/HDL-c, TG, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), Bath Ankylosing Spondylitis Disease Activity Index(BASDAI) were collected. AxSpA patients were divided into remission axSpA group(BASDAI<4, n=123) and active axSpA group(BASDAI≥4, n=85). Relationships between the parameters were assessed by the Sperman' s correlations analysis. Receiver operation characteristic (ROC) curves were used to discriminate axSpA patients from healthy subjects and active axSpA group from remission axSpA group.
Results: TC, HDL-c, and TG in axSpA group were lower than those of control group, while TC/HDL-c was higher (P<0.05). ROC curve results showed that the AUC value of HDL-c for axSpA was 0.790 (CI95%: 0.740-0.839), yielding a highest AUC value. The optimal cutoff value of HDL-c for axSpA was 1.095, with the Youden index of 0.496, sensitivity of 65.5% and specificity of 84.1%. HDL-c was negatively correlated with BASDAI (r=-0.159, P=0.022). TC/HDL-c was positively correlated with BASDAI (r=0.183, P=0.008). Besides, TC/HDL-c, CRP, ESR in active axSpA group were higher than those of remission axSpA group, while HDL-c was lower (P<0.05). ROC curve results showed that the AUC value of TC/HDL-c and CRP for active axSpA group were 0.621 (CI95%: 0.543-0.700) and 0.634 (CI95%: 0.556-0.712), yielding a higher AUC value than other parameters. The optimal cutoff value of TC/HDL-c for active axSpA group was 4.429, with the Youden index of 0.201, sensitivity of 40.2% and specificity of 79.9%.
Conclusion: HDL-c was decreased in axSpA patients with a highest diagnostic value, compared with healthy control. TC/HDL-c was elevated in active axSpA patients, showing a significant correlation to the disease activity of axSpA.

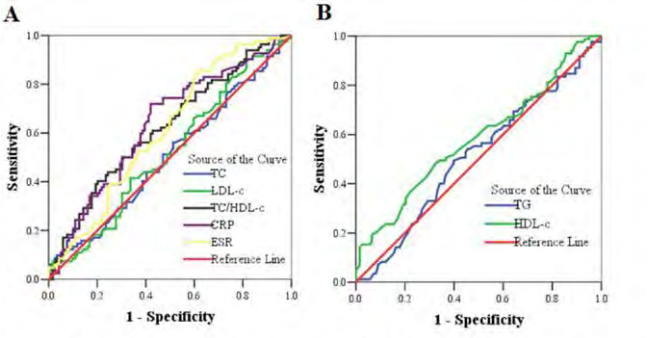


Figure.1 ROC curves was used to discriminate active axSpA group from remission axSpA group.

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AB0693 TIM-3-EXPRESSING NEUTROPHILS AS A NOVEL INDICATOR TO ASSESS DISEASE ACTIVITY AND SEVERITY IN ANKYLOSING SPONDYLITIS

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Background: Ankylosing spondylitis (AS) is a type of chronic inflammatory disease that compromises the axial skeleton and sacroiliac joints. Many studies have shown that neutrophils play an important roles in the inflammatory process of AS. However, the immunomodulatory roles and mechanisms of neutrophils in AS are poorly understood. T-cell immunoglobulin and mucin domain-containing protein

3 (Tim-3) has been reported as an important regulatory molecule, expressed and regulated on different innate immune cells, plays a pivotal role in several autoimmunity diseases. Recent study indicates that Tim3 is also expressed on neutrophils. However, the frequency and roles of Tim3-expressing neutrophils in AS was not clear.

Objectives: In this study, we investigated the expression of Tim3 on neutrophils in AS patients and analyzed the correlation between the level of Tim3-expressing neutrophils and the disease activity of AS.

Methods: AS Patients were recruited from Guangdong Second Provincial General Hospital (n=49). Age/sex-matched volunteers as Healthy controls (HC) (n=39). The medical history, clinical manifestations, physical examination, laboratory measurements were recorded. The expression of costimulatory molecules including programmed death 1 (PD-1), Tim-3 on neutrophils were determined by flow cytometry. The frequencies of Tim3-expressing neutrophils in AS patients were further analyzed for their correlation with markers of inflammation ESR and CRP, disease activity and severity of AS.

Results: The expression of Tim3 on neutrophils in patients with AS was increased compared to the HC (Figure 1A). The frequency of Tim3-expressing neutrophils in patients with AS showed an positive correlation with ESR, CRP and ASAS-endorsed disease activity score (ASDAS) (Figure 1B). Moreover, the frequency of Tim3-expressing neutrophils in active patients(ASDAS≥1.3) was increased as compare with the inactive patients (ASDAS<1.3) (Figure 1C).

Conclusion: Increased Tim-3 expression on neutrophils may be a novel indicator to assess disease activity and severity in AS, which may serves as a negative feedback mechanism preventing potential tissue damage caused by excessive inflammatory responses in AS patients.

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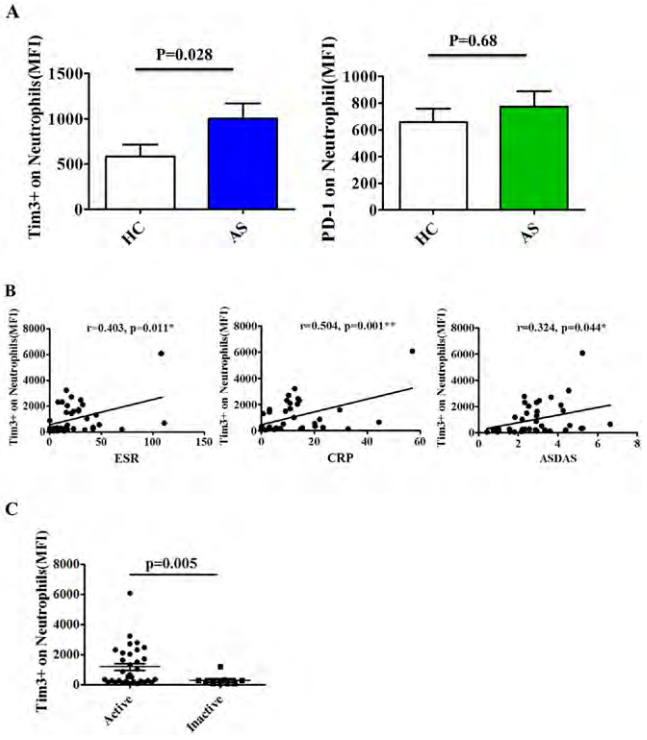


Figure 1. (A) The expression of Tim3 on neutrophils in AS and HC.**(B)**The correction between Tim3-expressing neutrophils and ESR,CRP,ASDAS.**(C)** The expression of Tim3 on neutrophils in active and inactive patients.

Disclosure of Interests: None declared

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AB0694

IS THERE ANY HETEROGENEITY OF SPONDYLOARTHRITIS DISEASE MANIFESTATIONS BETWEEN TWO ETHNIC SUBGROUPS?:A MULTICENTRE INTERNATIONAL COMPARATIVE STUDY BETWEEN INDIA AND UK

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Background: Pathogenesis of Spondyloarthritis (SpA) multifactorial and remains unclear. Various hypothesis have been postulated genetics, HLAB27, IL17, Gut microbiome and Biomechanical stress. Many of these factors can be attributed to ethnic background and environment. HLAB27 accounts for 20–25 % of total heritability and 40% of genetic risk while <10% of HLA-B27 carriers in general population develop SpA[1]. Higher faecal calprotectin levels in SpA compared to control point towards microscopic gut inflammation[2]. Thus dietary habits and geographical factors can influence pathogenesis of disease. We looked in clinical manifestations of SpA patients of two very different ethnic background Caucasians and Indians from UK and India to shed more light in understanding the disease

Objectives: To study any differences in the clinical manifestations of SpA patients of two ethnic groups

To compare outcome measure (BASDAI and ASDAS) between Caucasians and Indians

To study the difference in disease activity between Indian patients and British Asians

Methods: Multicentre observation study where data of SpA patients attending rheumatology clinics from two major teaching hospitals collected. In India data collected from Sheth VS Hospital and NHL Medical College, Gujarat and in United Kingdom from University Hospitals Leicester, NHS trust. Leicester has a multi-ethnic demography wherein almost 30%[3] of population is of south Asian ethnicity, making this study unique.

Baseline demographic and clinical data was collected. Clinical and outcome measures compared to see any heterogeneity in disease manifestations. SPSS software used

Results: Total 200 patients analysed with 148 Indians and 52 Caucasians. The Indian cohort was subdivided into British Asians (second generation Indians) and those form Gujarat, India

We found Indian subgroups were younger with shorter disease duration. Comparison in Table 1

Table 1.

	Caucasian	Indian	P
Age	45.9±12	31±12	<0.001
M:F	34:19	3:1	0.74
TDI years	9.6 ±5.9	3.5± 5.2	<0.001
BASDAI	4.05±2.17	3.1±1.7	0.002
ASDAS	2±0.8	2.4±1.2	0.02
CRP	12.8±23.6	24±12	<0.001
HLAB27	67%	26%	<0.001
Uveitis	25%	12%	0.02
IBP	78%	90%	0.03
Enthesitis	21%	60%	<0.001
Peripheral Arthritis	19%	36%	0.02
Dactylitis	2%	10%	0.07
Psoriasis	10%	20%	0.1
IBD	2%	5%	0.35

Comparing British Asians to Indians, Gujarat no significant difference in clinical parameters. (Table 2)

Table 2.

	British Asian	Indian	P
BASDAI	5.16±2.76	3.1±1.7	0.006
ASDAS	2.53±1.3	2.4±1.2	0.74
CRP	15.2 ±15.4	24±12	<0.001

Conclusion: We found Caucasians had more HLAB27 positivity and extra-articular manifestation of uveitis however the Indian population has

more enthesitis and peripheral arthritis. Enthesitis is initiated during a mechano-sensation and the cultural difference including style of footwear could probably be one of the factors explaining our findings inflammatory back pain has been reported to be higher in Indians compared to Caucasians which could be due to life style

The fact that ASDAS CRP behaves similarly in Indian patients across the two countries and is more when compared to Caucasians might point towards overall higher burden of disease in Indian population

To our knowledge this is a first study comparing clinical manifestations of SpA between Indians and Caucasians

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Disclosure of Interests: Nibha Jain: None declared, Sapan Pandya: None declared, Puja Srivastava: None declared, Prashant Chotalia: None declared, Arumugam Moorthy Speakers bureau: Abbvie, Novartis,UCB,MSD

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AB0695 SUSTAINED ASDAS-CRP REMISSION IS ASSOCIATED WITH BETTER LONG-TERM FUNCTIONAL OUTCOMES: A REAL-LIFE ANKYLOSING SPONDYLITIS COHORT STUDY

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Background: Ankylosing spondylitis (AS) leads to back pain and structural damage that may result in functional impairment[1]. Function is usually assessed in clinical trials conducted in developed countries, with patients receiving biological therapy[2,3].

Objectives: To evaluate variation in the Bath Ankylosing Functional index (BASFI) over time in a AS cohort followed in a developing country. Compare the improvement in BASFI between patients achieving or not sustained (≥12 months) ASDAS-CRP remission/low disease activity (LDA). Analyze predictors for achieving a minimum clinically important improvement (MCII) in BASFI (ΔBASFI ≤ -0.6)[4].

Methods: This cross-sectional analysis was conducted in a retrospective cohort. Adult patients fulfilling the New York criteria for AS and followed during at least 5 years in the Spondyloarthritis clinic were included. BASFI variation (ΔBASFI) was described as median (25^{th}/75^{th}). Comparison of ΔBASFI between patients fulfilling or not sustained ASDAS-CRP remisson/LDA was done using the Mann-Whitney test. Hierarchical Poisson model was used to identify predictors for achieving a MCII in BASFI.

Results: 69 patients were analyzed, 53.6% were men, the mean age was 48.9±11.4 years, and the mean follow-up time was 6.1±0.5 years, median (25^{th}/75^{th}) disease duration of 10 (5-18) years; 14.5% of the patients were on biological therapy at baseline. The median (25^{th}/75^{th}) ΔBASFI was low: -0.1 (-1.9 /+1.1) but 46.4% (N= 32) presented a MCII in BASFI during follow-up. Patients who achieved sustained ASDAS-CRP remission/LDA had a significant improvement in BASFI over time compared with those who did not achieve this target (p=0.026) (Figure 1). Patients with higher BASFI scores at baseline had a greater probability of achieving a MCII in BASFI (RR1.13 95%CI 1.00-1.27 p=0.047). Achieving and maintaining ASDAS-CRP remission/LDA during at least 12 months increased in 82% the probability to obtain a MCII in BASFI (RR 1.82 95% CI 1.14-2.91, p=0.012).

Conclusion: Patients achieving sustained ASDAS-CRP remission/LDA had better functional outcomes over time compared to those not achieving this target. Higher BASFI scores at baseline and sustained ASDAS remission/LDA were predictors of a MCII in BASFI.

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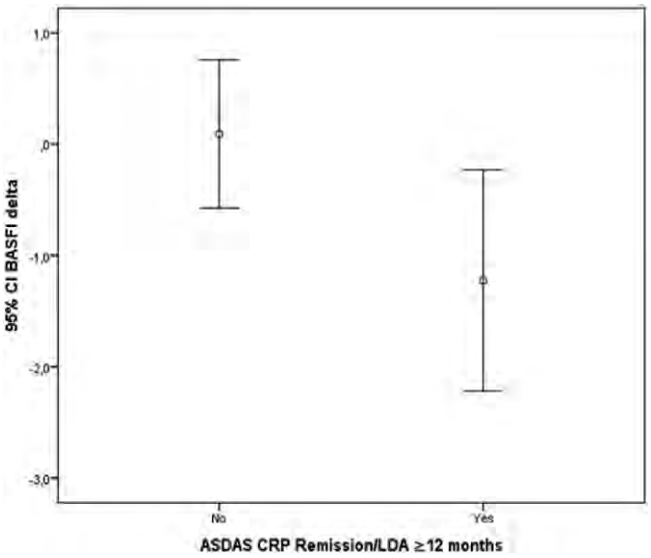


Figure 1. Comparison of ΔBASFI between patients who achieved or not sustained ASDAS-CRP remission/LDA.

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AB0696 THE PATH OF A PATIENT WITH AXIAL SPONDYLOARTHRITIS TO DIAGNOSIS IN RUSSIA, DATA FROM THE EMAS SURVEY

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Background: Scientific research in axial spondyloarthritis (axSpA) over the recent years has grown significantly. Early detection, diagnosis and treatment are critical to improve the functioning situation, reduce comorbidities and loss of quality of life of patients with axSpA. However, the diagnostic delay remains high.

Objectives: To describe the path to diagnosis among Russian axSpA patients.

Methods: The European Map of Axial Spondyloarthritis (EMAS) was a cross-sectional on-line survey of unselected patients with self-reported axSpA conducted in 13 European countries. Russian participants were recruited between December 2017 and February 2018 through the Russian Ankylosing Spondylitis Association and an online panel. Socio-demographics, age at symptom onset, age at diagnosis, diagnostic tests performed, HCPs visited prior diagnosis, and diagnosing HCP were collected. Diagnostic delay was calculated by subtracting the age at symptom onset from age at diagnosis.

Results: 233 Russian participants were enrolled. The mean age was 36.7±9.1 years, 51.9% were female. The average duration of the disease was 12.4±9.5 years. 54.9% patients visited more than one specialist before diagnosis. Russian respondents reported a low demand for GPs, physiotherapist and an orthopaedic specialist in contrast to the total of EMAS participants (table 1). AxSpA was most frequently diagnosed by a rheumatologist (87.5%).

Table 1. Health professional visited before being diagnosed with axSpA.

	Russian population N=233	Pan-European population N=2706
	%	%
GP	67.81	83.4
Rheumatologist	44.21	66.1
Other	37.34	13.6
Orthopaedic specialist	23.61	34.5
Physiotherapist	17.6	46.0
Osteopath	13.73	16.3

Most used medical test for diagnosis are similar to those used in the aggregated Pan-European sample (table 2).

Table 2. Medical tests made to diagnose axSpA.

	Russian population N=230	Pan-European population N=2661
	%	%
X-rays	80.87	72.3
MRI scan	70.00	64.3
HLA B27	62.61	65.4
CT scan	25.22	20.8
Ultrasound scan	17.83	21.0
Radionuclide scintigraphy	3.5	16.4
Other	9.13	4.2

Among those who underwent HLA-B27 test (n=144), 87.23% declared to be HLA-B27 positive. This percentage is higher than that found in the Pan-European aggregated sample (73.95% of HLA-B27 positive).

The mean age at symptom onset was 24.22±9.75 years. Consequently, the mean diagnostic delay calculated was 6.88±6.94 years without differences between males and females and the median was 5 years. More than half of the sample had a calculated diagnostic delay of higher than 5 years (55.39%).

Conclusion: The results of the survey confirm the existence of a diagnostic delay. Although this aspect has been greatly improved in recent years, reducing diagnostic delay is one of the major challenges associated with the clinical management of axSpA and must be addressed with GPs and rheumatologists. We suggest that features in patient routing in other countries can be explained these differences: the survey did not include a neurologist, to whom patients with back pain have a visit in Russia. The most frequently performed medical tests are included in the ASAS criteria for axSpA, which indicates a good knowledge of doctors.

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AB0697 PERFORMANCE OF DIFFERENT CRITERIA SETS FOR INFLAMMATORY BACK PAIN IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS IN DEMOCRATIC REPUBLIC OF CONGO

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Background: Inflammatory back pain (IBP) is the most prominent clinical feature for an early diagnosis of axial spondyloarthritis. The performance of the criteria sets for IBP has not yet been assessed in clinical practice in the Democratic Republic of Congo (DRC).

Objectives: To assess and to compare the performance of different IBP criteria sets in axial spondyloarthritis (SpA) outpatients attending the rheumatology unit of the University Hospital of Kinshasa, DRC.

Methods: One hundred and eight Congolese outpatients with axial SpA defined by rheumatologist's clinical judgment were included in the spondyloarthritis cohort of the University Hospital of Kinshasa from March 1st 2015 to February 28, 2017. Calin criteria, Berlin criteria and ASAS criteria sets for IBP were performed to assess their performance against clinical judgment. Detailed history, clinical examination and imaging of sacroiliac joints by plain radiography were obtained. Sacroiliac joint radiographic lesions were scored with the modified New York criteria. Magnetic resonance imaging and HLA B27 were not performed. Fifty additional patients with a diagnosis of chronic (>3 months) mechanical low back pain (MLBP) were included as control group. The performance of each item and different criterias was evaluated using sensitivity, specificity, and likelihood ratio (LR). Baseline characteristics of the mechanical and inflammatory back pain cohorts were compared with chi-square or Student t tests as appropriate.

Results: The mean age was 43.8±15.1 years in SpA patients versus 62.4±9.1 years in controls (MLBP patients) with respective sex ratio (M/F) of 1/0.8 and 1/2.1. There were significantly more male patients in the ankylosing spondylitis (AS) group than in the non-radiographic axial spondyloarthritis group ($p<0.01$). Among the criteria sets, Calin criteria showed the best sensitivity (92.6%) while the Berlin criteria showed the best specificity (97.6%) in the detection of IBP patients. The new ASAS criteria for IBP compared to the two previous criteria sets did not show good sensitivity nor specificity (sensivity 80%, specificity 62%, LR+ 1.05 (0.90 – 1.22), LR- 0.52 (0.39 – 0.69), 95%CI).

Conclusion: The Calin criteria set would be useful for epidemiological and clinical studies in DRC. The ASAS criteria set for IBP is not better than other criteria sets in the screening of IBP for Congolese patients with axSpA.

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AB0698

REAL CLINICAL PRACTICE IN THE CONTROL OF REPORTED OUTCOMES BY THE PATIENT (PROS) DIAGNOSED WITH PSORIATIC ARTHRITIS AND/OR ANKYLOSING SPONDYLITIS WHO BEGIN TREATMENT WITH SECUKINUMAB. A PROSPECTIVE MULTICENTRIC STUDY.

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Background:

Objectives: Analyse the effect of secukinumab in terms of the patient´s own variables, specifically: fatigue, sleep, pain and quality of life in patients with psoriatic arthritis or spondyloarthritis.

Methods: A multicentric longtitudinal observational prospective study was carried out at 6 months in patients who begin treatment with secukinumab. At the start and after 6 months the following data was collected on the outcome: pain through an visual analogue scale (VAS), fatigue using the FACIT-fatigue scale, sleeping problems using the insomnia severity index (ISI) and quality of life with the EuroQol-3L-5D and the PsAQoL.

The sample can be described in terms of the distribution of the variables through measures of central tendency.It was analysed if the change after 6 months was statistically relevant using Student´s t-test for paired data in the case of FACIT, VAS, PsAQoL and ISI and chi-squared for the dimensions of the EQ-5D. The size of the effect of each of the measurements taken was calculated using Cohen's D. the results are given grouped by disease and globally. The analysis was carried out using Stata v12 (College Station Tx, USA)

Results: In table 1, the changes in the scales of normal distribution can be seen. Apart from general VAS, all the scales experience significant relevant changes. The PROs preferred by the patient with the best therapeutic response is the quality of sleep. The adjustment of the regression models does not produce changes in the results, apart from small adjustments to the condidence intervals (final column table 1). The subdomain in which the most significant change in the EQ-5D is produced is in that of pain and discomfort.

Scale	Basal*	6 months*	change (adjusted)*+
VAS general (0-100, from worst to best)	56.9 [4.6 a 64.2]	50.9 [42.4 a 59.4]	-6.0 [-12.7 a 0.7]
FACIT-fatigue (better when	25.3 [21.6 a 29.0]	32.5 [28.0 a 37.0]	7.2 [5.1 a 9.3]
ISI (0to28, best to	16.0 [14.0 a 1.0]	10.6 [8.4 a 12.8]	-5.4 [-6.8 a -
PsAQoL (0 to 20, best to worst)	12.5 [1.8 a 14.1]	9.0 [7.0 a 11.0]	-5.4 [-6.8 a -4.1]
EQ-5D (0-100 from worst to best)	42.3 [35.7 a 48.8]	60.6 [52.0 a 69.3]	18.4 [13.9 a 22.8]

Conclusion: After 6 months patients who begin treatment with secukinumab, present with improvements in all sizes of the effects of the treatment in the various studied scales. The improvement achieves global and generalised statistical significance after 6 months of study. The greatest effect is on sleep, quality of life and fatigue.

The measurements of the outcomes reported by the patients are a clinical value added to our objective evaluations of the health and activity of the disease, and allow us, in a more integrated and comprehensive manner, to undertake a more exact and close evaluation of their state of health and wellbeing.

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AB0699

RESIDUAL DISEASE BURDEN PRESENT IN AXIAL SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS PATIENTS ACHIEVING LOW DISEASE ACTIVITY STATES

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Background: Despite achieving Low Disease Activity (LDA) states, patients with SpondyloArthritis (SpA) may have considerable residual disease. Sparse data is currently available from Asia.

Objectives: We aimed to evaluate the burden of residual disease in patients with axial SpondyloArthritis (axSpA) or Psoriatic Arthritis (PsA) who achieved LDA.

Methods: We used data from a registry of SpA from an outpatient setting in a tertiary hospital in Singapore. For axSpA, LDA was defined as Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) <4/10. For PsA, LDA was defined by achieving 5/7 cutoffs in the Minimal Disease Activity (MDA) or clinical Disease Activity index for Psoriatic Arthritis (cDAPSA) ≤13.

Results: From 262 cases of axSpA (21% women; mean ± standard deviation (SD) age 42 ± 14 years), 58% of patients achieved LDA states. While from 142 cases of PsA (49% women; mean ± SD age 51 ± 14 years), 38% and 63% achieved MDA and cDAPSA LDA, respectively. Both axSpA and PsA patients with LDA had pain scores range from 17.2 to 25.7/100 and fatigue scores from 3.3 to 3.5/10. (Table 1). Substantial burden in physical disability and mental well-being were seen as a low physical and mental component summary of SF-36. cDAPSA classified nearly twice as many PsA patients into LDA than MDA. Compared to PsA patients in MDA, PsA patients in cDAPSA LDA had higher pain scores, Patient Global Assessment (PtGA), dactylitis, and enthesitis. axSpA patients in LDA classified by BASDAI had the highest pain and fatigue scores, and PtGA.

Table 1. Residual disease burden in patients with axSpA and PsA who have achieved LDA

	axSpA	PsA	
	LDA (n=153)	LDA by MDA (n=54)	LDA by cDAPSA (n=90)
Age, years¥	42.2 (14.0)	52.5 (13.2)	52.5 (13.2)
Female, n (%)	26 (17.0)	30 (55.6)	45 (50.0)
TJC¥	0.1 (0.3)	0.8 (1.0)	1.0 (1.4)
SJC¥	0.1 (0.3)	0.7 (1.3)	0.9 (1.3)
VAS-pain (0-100)¥	25.7 (19.0)	17.2 (17.8)	20.8 (16.7)
BASDAI (0-10)¥	2.3 (1.0)	2.4 (1.6)	2.7 (1.7)
BASDAI fatigue (0-10)¥	3.5 (2.2)	3.3 (2.3)	3.4 (2.3)
PtGA (0-100)¥	27.8 (19.5)	20.9 (17.9)	23.5 (17.6)
Dactylitis (0-20)¥	–	0.3 (0.5)	0.5 (0.9)
LEI (0-6)¥	–	0.1 (0.4)	0.2 (0.5)
HAQ (0-3)¥	0.1 (0.1)	0.1 (0.2)	0.2 (0.4)
HAQ < 0.5, n (%)	149 (97.4)	52 (96.3)	77 (85.6)
SF-36 PCS¥	46.8 (9.9)	45.8 (11.5)	45.1 (11.7)
SF-36 MCS¥	46.4 (11.2)	46.1 (11.3)	45.6 (10.6)

axSpA, axial Spondyloarthritis; PsA, Psoriatic Arthritis; LDA, Low Disease Activity; MDA, Minimal Disease Activity; cDAPSA, clinical Disease Activity index for Psoriatic Arthritis; TJC, tender joint count; SJC, swollen joint count; VAS, Visual Analog Scale; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; PtGA, patient's global assessment; LEI, Leeds Enthesitis Index; HAQ, Health Assessment Questionnaire; SF-36, Short-Form 36; SF-36 PCS, norm-based Physical Component Summary (mean=50, SD=10); SF-36 MCS, norm-based Mental Component Summary (mean=50, SD=10)

¥mean (SD)

Conclusion: Despite being in LDA, axSpA and PsA patients experienced substantial pain, fatigue and poorer functional health and mental well-being.

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AB0700

RADIOGRAPHIC PROGRESSION IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS UNDER TREATMENT WITH TNF INHIBITORS. DATA FROM REGISPONSERBIO (SPANISH REGISTER OF BIOLOGICAL THERAPY IN SPONDYLOARTHRITIDES)

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Background: Clinical efficacy of TNF inhibitors (TNFi) in axial spondyloarthritis (axSpA) has been widely probed in randomized control trials. In clinical practice, some studies suggested that long-term (more than 4 years) treatment with TNFi could slow down radiographic progression in axSpA; however, whether this treatment inhibits structural damage remains unclear.

Objectives: To evaluate radiographic progression in axSpA patients receiving long-term TNFi (over 4 years) in comparison with patients starting TNFi.

Methods: A total of 204 patients with axSpA were included in the Spanish Register of Biological Therapy in Spondyloarthritides (REGISPONSERBIO). Out of these, 80 patients (31 starting TNFi and 49 under long-term TNFi) were included in this study based on the availability of spinal radiographs (cervical and lumbar lateral views), at two time points. Radiographs in patients starting TNFi were available: i) at baseline (before TNFi) and ii) after 3 to 5 years of TNFi therapy (mean follow-up 3.7±0.8), while in long-term TNFi patients, these were available: i) at one follow-up visit at least 4 years later since TNFi was started and ii) after 3 to 5 years of this visit (mean follow-up 3.5±1.1). Two trained readers, not blinded for chronological order, independently scored lateral cervical and lumbar spine images according to the mSASSS system (0-72). Following definitions for progression were used: change of the absolute scores, change of ≥2 units, development of new syndesmophytes, and development of new syndesmophytes or growth of the existing syndesmophytes.

Results: Reliability of both readers was excellent with intraclass correlation coefficients (ICCs) of 0.98 (0.98-0.99) at inclusion and 0.98 (0.97-0.99) at follow-up. Most patients (82.5%) were classified as radiographic axSpA. Mean BASDAI at first visit (i) was of 5.0±2.4 for starting TNFi patients and of 3.2±1.9 for long-term TNFi patients. The table depicted the results for radiographic scores and progression. Mean mSASSS score at first visit (i) was 15.8±21.5 and 15.1±18.4 units for starting TNFi and long-term TNFi patients, respectively. The change score between both visits was 2.3±4.2 and 2.3±4.1, respectively. Similarly, no differences were found for change of ≥2 points (32.3% in starting TNFi and 35% in long-term TNFi patients). However, development of new syndesmophytes or growth of the existing syndesmophytes were found to be more frequently (but not significant) in starting TNFi patients compare to long-term TNFi patients.

Conclusion: In patients with axSpA treated with TNFi in clinical practice radiographic progression is observed, independently of the time under this therapy. Nevertheless, the development and growth of syndesmophytes seem to be lower in long-term treated patients.

Table.

	Starting TNFi patients	Long-term TNFi patients*	p-value
Presence of syndesmophytes at first visit, % (n)	45.2% (14)	53.1% (26)	NS
Presence of syndesmophytes at follow up, %	51.6% (16)	55.1% (27)	NS
Mean change score, mean ± SD	2.32 ± 4.19	2.26 ± 4.09	NS
Change of ≥ 2 units in the score % (n)	32.3% (10)	34.7% (17)	NS
Development of new syndesmophytes, % (n)	29% (9)	18.4% (9)	0.3
Progression or development of new syndesmopyhtes % (n)	29% (9)	22.4% (11)	0.5

* Patients with more than 4 years under TNFi treatment

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AB0701

ANTERIOR UVEITIS AND HLA B27, ARE THERE ANY CLINICAL OR THERAPEUTIC DIFFERENCES IN PATIENTS WITH POSITIVE HLA B27 VERSUS THOSE WITH HLA B27 NEGATIVE?

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Background: Anterior uveitis is the most frequent form of presentation of uveitis. An important part of patients do not associate extraocular manifestations, so more information about the clinical profile is needed to optimize therapeutic decisions.

Objectives: To describe the clinical profile of patients with anterior uveitis related and not related to the antigen HLA-B27. Compare both groups to establish differences.

Methods: Retrospective cohort study. Consecutive patients diagnosed with non-infectious anterior uveitis, assessed in the multidisciplinary uveitis unit of the Infanta Leonor University Hospital (Madrid) from its establishment in October 2017 to December 2019, were included. To compare categorical variables Chi square was used and the test of Fisher; and Student's T or Mann-Whitney U test for continuous variables. Finally, a multivariate analysis was performed to established differences between the two groups. A value of p <0.05 was considered statistically significant.

Results: 62 patients with anterior uveitis, 26 (42%) with HLA B27 positive and 36 (58%) with HLA B27 negative were included. There were no differences between the two groups regarding sex. Differences were found in the mean age at diagnosis, 35 + -9.6 in the HLA B27 positive group vs 47 + -14.9 in the HLA B27 negative group (p 0.01). The time since uveítis diagnosis was longer in the HLA B27 positive group: 7.08 years (3.45-11.79) versus 2.41 years (1.66-3) in the HLA B27 negative group (p 0.000). Regarding the etiology, the majority of patients in the HLA B27 negative group had a diagnosis of idiopathic anterior uveitis (72.2%), and 53.8% of the patients in the HLA B27 positive group were diagnosed with spondyloarthritis (p 0.000). There were no significant differences in the number of patients that require systemic treatment. There were no differences regarding oral corticosteroids intake, with very few patients needing it (2 patients in the HLA B27 positive group and 5 patients in the HLA B27 negative group (p 0.699). The percentage of patients who needed to start an immunosuppressive treatment were similar between the two groups, 6 patients (23.1%) in the HLA B27 positive group and 11 patients (30.6%) in the HLA B27 negative group (p 0.717) No significant differences could be detected between groups in the multivariate analysis in terms of laterality, clinical course, treatment with immunosuppressants or development of complications.

Conclusion: In our cohort patients with HLA B27 positive debut at an earlier age. There were no differences between both groups in laterality, course of uveitis, systemic treatment or ocular complications.

Disclosure of Interests: None declared

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AB0702

THE FREQUENCY OF INFLAMMATORY BOWEL DISEASES IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Ankylosing Spondylitis (AS) is closely associated with inflammatory bowel disease (IBD). About 6-46% of patients with IBD have various lesions of the musculoskeletal system [1]. 5-10% of patients with spondylarthritis (SpA) eventually develop IBD, with Crohn's disease (CD) being more common than Ulcerative colitis (UC) [2]. Determining the level of fecal calprotectin (FC) is a study that allows to diagnose IBD. The concentration of FC directly depends on the neutrophil infiltration of the intestinal mucosa and has a direct connection with the activity of the inflammatory process [3]. It is known that level of FC increases in 2/3 of patients with AS and is closely related to parameters reflecting higher disease activity [4].

Objectives: The aim of this study was to evaluate the frequency of IBD in patients with AS using an assessment of FC level.

Methods: In the analysis were included 40 patients with AS, fulfilling the modified New York criteria, among them man -26 (65%), woman -14 (35%), mean age of patients was 41.2 ±10.5, mean disease duration - 13±8.8 years. All patients were examined with ESR, CRP, esophagogastroduodenoscopy, colonoscopy and quantitative analysis of the fecal calprotectin levels using the method of lateral immunochromatography with the BUHLMANN Quantum Blue rapid test. Standart range: 100-1800 µg /g.

Results: All patients had a high disease activity, mean BASDAI was 5.2 ± 1.7, mean ASDAS CRP 3.8 ± 1.1. 35 patients (87.5 %) had FC level more than 100 µg / g, the remaining 5 patients (12.5%) less than 100 µg /g. 12 patients (30 %) had FC level more than 1,800 µg / g, 23 (57.5 %) from 101 µg / g to 1800 µg / g. All patients with FC levels more than 100 µg / g showed an increase CRP (mean 28.4 mg / l) and ESR (mean 36.3 mm\h) levels. IBD were diagnosed in 9 cases (22.5%): 5 patients (12.5 %) with CD and 4 patients (10 %) - UC, in the remaining cases (77.5%) was no intestinal pathology.

Conclusion: The results showed high frequency of IBD in patients with AS. Patients with high FC levels (more than 100 µg/g) had high disease activity (AS). In most cases, inflammatory bowel disease were diagnosed in patients with FC levels more than 100 µg/g.

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AB0703

WHICH OF THE ASDAS OR BASDAI CORRELATES BETTER WITH PHYSICIAN GLOBAL ASSESSMENT?

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Background: Ankylosing Spondylitis Disease Activity score (ASDAS) was developed because of the limitations of Bath Ankylosing Spondylitis Disease Index (BASDAI) of being totally patient-derived with limited face and construct validity. ASDAS includes inflammatory markers that were aimed to increase its face validity by representing a different 'objective' domain of disease activity that was not included in BASDAI.

Objectives: The aim of our study was to compare correlation of ASDAS and BASDAI with physician global assessment (PhGA) in order to know which is more reliable.

Methods: Cross-sectional study including patients with SpA according to the ASAS criteria of 2009 and/or New York modified criteria. The erythrocyte sedimentation rate (ESR) and the C-reactive protein (crp) were measured. The disease activity was assessed by BASDAI and ASDAS. Physician global assessment (PhGA) was rated by 0–100 numeric score. We correlated disease activity indices with physician global assessment by Pearson coefficient.

Results: A total of 110 patients (68 men and 42 women) with a mean age of 43.18 ±12.34 [19-79] years was collected. The mean disease duration was 5.99±2.31 [1-10] years. The mean ESR and CRP were respectively 28.41±21.51 [2-110] and 15.56 ±23.84 [0-153] mg/l. ESR was correlated with PhGA (p=0.06, r=0.300), however CRP was not correlated with PhGA (p=0.134, r=0.165). The mean ASDAS-ESR and ASDAS-CRP were respectively 2.93±1.05 [0.83-5.65] and 2.81±0.97 [0.29-4.77]. The mean BASDAI was 4.42±2.23 [0-9.2]. The mean PhGA was 5.43 ±2.31 [1-10]. The BASDAI correlated with PhGA (p=0.007, r=0.307). In addition, ASDAS-ESR and ASDAS-CRP correlated with PhGA (p=0.001, r=0.372, p=0.001, r=0.391) respectively.

Conclusion: In conclusion both BASDAI and ASDAS are equal, with a superiority nonetheless for the ASDAS since it correlated stronger with PhGA.

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AB0704

PRESCRIBING PRACTICES IN AXIAL SPONDYLOARTHROPATHY

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Background: Axial spondyloarthropathy(axSpA) treatment has undergone a number of significant developments over the past number of decades. Previously

limited to non-steroidal anti-inflammatories (NSAIDs) and corticosteroids, treatment options now include synthetic disease modifying anti-rheumatic drugs(sDMARDs) and biologic agents. The development of national registries for inflammatory arthritis provides an opportunity to study medication usage in a large cohort of patients with axSpA. The Ankylosing Spondylitis Registry of Ireland (ASRI) is a source of epidemiological data on patients with axSpA in Ireland. The aim of this study was to examine medication exposure and outcomes.
Objectives: To characterize a large cohort of patients with axSpA in terms of medications usage, burden of disease and patient reported outcomes.
Methods: The patient population registered in the ASRI was analysed using IBM SPSS version 26. Patients were analyzed on the basis of medication exposure. The four treatment groups were classified as no treatment, NSAIDs only, biologics only, or biologics and NSAIDs. Mean age, duration of disease and delay to diagnosis was compared between groups. Burden of disease was assessed via mean BASDAI, BASFI, BASMI, HAQ and ASQoL between the four groups. Differences between groups was tested for statistical significance a one-way analysis of variance (ANOVA). A chi-squared test for independence was used to compare differences in rates of HLA-B27 positivity rates and gender. Results were deemed significant where $p < 0.05$.
Results: At present 860 patients are currently enrolled in the ASRI with 76.6% (659) males and 23.4% (201) females. Average age of patients is 45.8 years, mean disease duration of 19.4 years with 95.5% (821) of patients listed as Caucasian. Mean scores were BASDAI 4.02, BASFI 3.7, BASMI 4.02, HAQ 0.55, and ASQoL of 6.51. Treatment groups were made up of 9.9%(85) on no treatment, 22.2%(191) NSAIDs treatment only, 34.8%(299) biologics treatment only and 32.1%(276) treated with both NSAIDs and biologics. Patients only on NSAIDs were noted to be older than patients on biologics, and those on both biologics and NSAIDs (p=0.02). Patients on NSAIDs were older at symptom onset than those on both biologic and NSAID treatment (p=0.02), however the effect size is small(0.012). No significant difference was noted between groups regarding disease duration, delay to diagnosis or distribution between genders (table 1). Difference in BASDAI scores between groups was significant between all groups, with patients on both biologics and NSAIDs having the highest scores and those on no treatment with the lowest scores(4.74 vs 3.37) possibly a reflection of disease severity(table 2).

Table 1.

	ASRI	No tx	NSAIDs tx	Biologic tx	Biologic & NSAIDs	p value
Number	860	9.9% (85)	22.2% (191)	37.8% (299)	32.1% (276)	
Age	45.8	49.7	46.2	45.3	45.1	***0.02***
Symptom onset	26.4	27.5	28.2	26.1	25.2	***0.02***
Disease duration	19.4	22.2	18	19.1	19.8	*0.06*
Delay to dx	8	9.8	8.1	7.4	8	*0.13*

Table 2.

	ASRI	No tx	NSAIDs tx	Biologic tx	Biologic & NSAIDs	p value	Effect Size
BASDAI	4.02	3.37	4.21	3.4	4.74		0.06
		3.37	4.21			*0.04*	
		3.37			4.74	*<0.01*	
			4.21	3.4		*<0.01*	
				3.4	4.74	*<0.01*	

Conclusion: A large proportion of patients in the ASRI were treated with either biologics only or both biologics and NSAIDs. No treatment was the least common treatment within this cohort. Patients not on treatment tended to be older than those on any type of treatment. Overall patients on biologics alone tended to have better patient reported outcomes as compared to all other treatment groups. The development of longitudinal data for the ASRI will help to further understand the reason behind these differences.
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AB0705 INCIDENCE, TREND AND FACTORS ASSOCIATED WITH AMYLOIDOSIS IN PATIENTS WITH SPONDYLOARTHRITIS IN SPAIN. OBSERVATIONAL STUDY BASED ON THE REGISTRATION OF DISCHARGES OF THE GENERAL HOSPITALS OF THE NATIONAL HEALTH SYSTEM (CMBD). (TREND-ESPA STUDY)

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Background: Amyloidosis (AA) is a complication of inflammatory diseases, such as Spondyloarthritis (Spa). It is related to active and long-lasting disease. The treatment of Spa has had a major change in recent years, which has allowed a better control of disease activity.
Objectives: Analyze the incidence, trend and factors associated with secondary AA hospitalizations in patients with Spa, in Spain.
Methods: Population study based on the analysis of a national administrative database (CMBD) of hospital admissions. **Period:** 01/01/1999 to 31/12/2015. **Study population:** patients with diagnosis of Spa who were admitted to any national hospital. **Control population:** 2 groups have been used as controls: **GP:** group of the general population (without Spa diagnosis) matched of equal sex, age, year and autonomous community as the study population. **RA:** all income, in the same period, of patients diagnosed with Rheumatoid Arthritis (RA). Secondary AA admissions were identified by the presence of code 277.3. The trend was analyzed using Generalized Linear Models (MLG). The Odds Ratio (OR) of secondary amyloidosis was calculated in Spa vs GP and Spa vs AR.
Results: The database (BD) for analysis consists: **1. Study population:** 102,609 admissions with Spa diagnosis. **2: GP:** 102,609 admissions matched with the study population. **3.-** RA: 320.332 admissions. There was a total of 3,790 admissions with AA diagnosis: 782 (0.79%) at Spa, 74 (0.06%) GP and 2,924 (0.91%) RA. The main clinical-demographic characteristics patients with Spa and AA versus the rest of Spa are shown in the following table:

	Spa_ Amylodosis	Spa_without_ amyloidosis	OR	IC95%	*p*-value
N (%)	782 (0,72)	101827 (99,28)			
Mean Age (SD)	55,9 (13,15)	58,9715,5)	0,98	0,98-0,99	p<0,001
Mean Charlson Index (SD)	1,80 (1,34)	1,14(1,81)	1,15	1,12-1,18	p<0,001
ALOS (SD)	12,78 (15,12)	10,57 (15,37)	1,01	1,00-1,008	p<0,001
Male n (%)	596 (75,2)	70792 (66,56)	1,52	1,29-1,79	p<0,001
Dead during admission, n (%)	82 (10,35)	3537 (3,32)	3,35	2,66 -4,22	p<0,001
Areact (%)	20 (2,52)	2178 (2,04)	1,23	0,79-1,93	p=0,318
Spa_EII (%)	81 (10,22)	5238 (4,92)	2,19	1,74-2,77	p<0,001
AS (%)	538 (67,92)	67207 (63,19)	1,23	1,06-1,43	p<0,001
PAs (%)	243 (30,68)	37673 (35,42)	0,8	0,69-0,93	p=0,005
Psoriasis (%)	24 (3,03)	2917 (2,74)	1,1	0,73-1,66	p=0,595
Uveitis (%)	12 (1,51)	542 (0,50)	3,01	1,68-5,34	p<0,001
Diabetes mellitus (%)	34 (4,29)	14822 (13,93)	0,27	0,19 - 0,39	p<0,001
Dementia (%)	3 (0,37)	626 (0,58)	0,64	0,2-2	p=0,638
HTA (%)	185 (23,35)	31395 (29,52)	0,72	0,61 - 0,85	p<0,001
Tabaquismo (%)	56 (7,07)	13283 (12,49)	0,53	0,40 - 0,69	p<0,001
Hiperlipemia (%)	99 (12,5)	17748 (16,68)	0,71	0,57-0,88	p<0,001
TVP (%)	7 (0,88)	648 (0,60)	1,45	0,68-3,07	p=0,351
Depresión (%)	23 (2,90)	5939 (5,58)	0,5	0,33-0,76	p<0,001
Tbc (%)	3 (0,37)	544 (0,51)	0,73	0,23-2,30	p=0,803

The age-adjusted rates (/100,000hab*year) of AA in Spa/GP/RA were 16.72 / 1.40 / 97.87 respectively (19.54 / 1.26 / 139.70 in men and 12.23 / 1.74 / 04.54 in women). Age-adjusted AA rates decreased in both Spa from 19.86/100,000hab*year in 1999, to 9.91 in 2015 and for RA from 131.9 in 1999 to 68.7 in 2015). While in GP increased (from 0.75 in 1999 to 2.87 in 2015). It is estimated a decrease (adjusted by age) in Spa of -4.6% per year and -5.5% in Ra, while in PG there was an increase of 10.2%. The AA OR in Spa vs GP is 10.77 (IC95%: 8,489-13,676). While the AA OR in Spa vs RA was 0.808 (95% CI: 0.747-0.875).

Conclusion: In Spain, during the period 1999 to 2015, there has been a decrease in the incidence of AA in patients with Spa and Ra. We estimate a decrease of -4.6% per year in Spa and -5.5% per year in Ra. Being male, AS or Spa_EII, and uveitis are associated with AA.
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AB0706 ASSOCIATION BETWEEN SARCOIDOSIS AND SPONDYLOARTHRITIS: A NEW COMORBIDITY, CHANCE OR SELECTION ERROR? (TREND-ESPA STUDY)

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Background: On literature there are a significant number of cases describing the coexistence between Spondyloarthritis (Spa) and sarcoidosis. There are 3 main ways in which different diseases can be found in the same individual: chance, selection bias, or by 1 or more types of causal association. In this work we analyze whether there is a causal association between sarcoidosis and Spa.
Objectives: To analyze the hypothesis that there is a causal association between sarcoidosis and Spa.
Methods: Case-control study nested in a population database of hospital admissions (CMBD). **Period:** 1999 to 2015. **Database Study (DB):** Study population + control population. **Study population:** patients with a diagnosis of Spa who were admitted to any national hospital. **Control population (GP):** group of the general population (without Spa diagnosis) matched of equal sex, age, year of admission as the study population. **Cases:** Cases of sarcoidosis were identified by the presence of ICD-9 code 135. **Controls:** admissions without sarcoidosis diagnosis. The clinical-demographic characteristics of patients with Spa and sarcoidosis vs Spa without sarcoidosis are described. To rule out the association being random, the Odds Ratio (OR) was calculated for the association between sarcoidosis and Spa. To minimize selection error, the association with logistic regression models was analyzed by adjusting by more than 50 variables.
Results: The DB of the study consists of 205,218 admissions: 102,609 admissions with Spa and 102,609 admissions without Spa. There was a total of 220 admissions with sarcoidosis: 133 (0.12%) in Spa and 87 (0.08%) in the GP group. The OR is 1.53 (IC95% 1.17 – 2.01). The following table shows the main clinical-demographic characteristics of patients with Spa and sarcoidosis versus the rest of Spa:

	Spa_sarcoidosis	Spa_without_sarcoidosis	OR	IC95%	*p*-value
N (%)	124 (0.12)	102485 (99,9)			
Mean Age (SD)	56,31 (13.5)	58,94 (15.47)	0,989	0,978-1	0.032
Mean Charlson Index (SD)	1,09 (1.67)	1,15 (1.81)	0,982	0,888-1.087	0.715
Estancia media (SD)	**8,52 (7.97)**	**9,94 (14.05)**	**0,989**	**0,972-1**	**0.049**
Male n (%)	75 (60.48)	68534 (66.87)	0,758	0,528- 1.087	0.150
Dead during admission, n (%)	4 (3.22)	3439 (3.35)	0,96	0,354-2.601	1
Areact (%)	0 (0)	2192 (2.13)			1
EspA_EII (%)	5 (4.03)	5034 (4.91)	0,813	0,332-1.991	0.835
EA (%)	69 (55.64)	63145 (61.61)	0,7815	0,548-1.114	0.195
Aps (%)	55 (44.35)	37758 (36.84)	1,366	0,958-1.947	0.092
Psoriasis (%)	6 (4.83)	2867 (2.79)	1,766	0,777-4.015	0.165
Uveitis (%)	1 (0.8)	542 (0.52)	1,529	0,213-10.962	0.482
Diabetes mellitus (%)	24 (19.35)	14277 (13.93)	1,482	0,949-2.315	0.086
Dementia (%)	1 (0.8)	606 (0.59)	1,366		0.521
HTA (%)	39 (31.45)	30462 (29.72)	1,084	0,742-1.585	0.699
Tabaquismo (%)	20 (16.12)	12833 (12.52)	1,343	0,832-2.168	0.222
Hiperlipemia (%)	17 (13.70)	17322 (16.9)	0,781	0,468-1.303	0.399
TVP (%)	1 (0.8)	627 (0.611)	1,32	0,184-9,465	0.533
Depresión (%)	11 ((8.87)	5693 (5.55)	1,655	0,890-3.075	0.114
Amiloidosis (%)	0 (0)	782 (0.76)			1
Eritema Nodoso	**5 (4.03)**	**88 (0.08)**	**48,89**	**19,50-122.53**	**p<0.001**
VIH	0 (0)	635 (0.61)			1
VHC	0 (0)	1307 (1.27)			1
VHB	**4 (3.2)**	**320 (0.31)**	**10,642**	**3,906-28.992**	**p<0.001**
Obesidad	6 (4.83)	5910 (5.76)	0,83089564	0,365-1.887	0.847

In the logistic regression model (model 1) adjusting by age, sex, and year of admission the OR was 1,459 (IC95% 1.10-1.92). Model 2: Adjusting by model 1 variables + those that were significant in the univariate analysis (EN and HBV) the OR was 1.40 (IC95% 1.06-1.84). Finally, in Model 3, which included model variables 2 + those variables with clinical meaning (out of a total of 50 variables) the OR was 1.38 (IC95% 1.04-1.82).
Conclusion: There is a causal association between sarcoidosis and Spa (OR 1.5). This association is ruled out by chance. Although selection bias cannot be completely ruled out, it is reasonably minimized in our study.
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AB0707 IS ANKYLOSING SPONDYLITIS ASSOCIATED WITH INCREASED MALIGNANCY RISK?

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Background: Increased cancer risk has been reported with rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). Few studies on malignancy risk in ankylosing spondylitis (AS) patients have provided conflicting data.
Objectives: To look at the risk of cancer in AS patients in the US and identify any risk factors associated with increased cancer frequency.
Methods: This is a retrospective observational study using the IBM Explorys data base, a pooled de-identified clinical data base of > 60 million unique patients in the US with patient level data. The Explorys collects aggregated, standardized and normalized clinical data from different electronic health records automatically updated in near real time. In Explorys, patient records are mapped into a single set of Unified Medical Language System ontologies to facilitate searching and indexing. Diagnoses, findings and procedures are mapped into the systematized nomenclature of medicine – clinical terms (SNOMED-CT) hierarchy. Criteria of AS included at least one visit with a rheumatologist and the diagnosis code of AS (N=14,310) between 2009-2019. We further stratified the cohorts by adding the following variables to the search tool: race, gender, smoking, laboratory data (elevated ESR and CRP, HLA-B27 status), extra articular manifestations (psoriasis, inflammatory bowel disease or uveitis) and medication use (TNF inhibitor, secukinumab or NSAIDs). The index date was defined as the date of the first ever malignant neoplastic disease diagnosis occurring after the qualifying AS diagnosis.
The controls group (24,542,770) included all adults ≥ 18 years of age with exclusion of positive ANA, diagnosis of RA, SLE, AS, or vasculitis, and at least one outpatient office visit during the study period. For both groups we excluded previous diagnosis of cancer prior to 2009. A chi-square test of association was performed between the 2 groups (AS patients and controls) and the odds ratio (OR), its standard error, and the 95% confidence interval (CI) were calculated.
Results: Of the 14,310 patients with AS, only 1300 (9.08%) patients had a cancer diagnosis compared to 2,719,240 controls (11.07%). The AS patients found to have decreased odds of cancer compared to control group (Odds ratio 0.9004, 95 % CI: 0.8502 to 0.9536, P = 0.0003). Demographics and clinical characteristic of AS patients and controls with cancer are shown in table 1. Risk factors for increased cancer risk in AS patients are shown in table 2.
Conclusion: The study demonstrated that cancer risk was lower in the AS patients in the USA compared to the controls with no rheumatic disease. Male sex, white race, HLA-B27 positivity, history of IBD, NSAIDs use, and elevated makers of inflammation were associated with higher odds of cancer in AS patients.

Table 1. Demographics and other features of patients with cancer.

	AS patients with Cancer (n=1300)	Controls with Cancer {n=2,719,240)
Caucasians	85.38%	82.09%
Males	53.08 %	45.53%
Smokers	30.00%	22.22%
Elevated ESR	44.61%	10.20%
Elevated CRP	44.61%	10.25%
NSAID use	76.92%	47.20%

Table 2. Risk factors for cancer in patients with AS using chi-square test.

	AS with cancer N = 1300	AS without cancer N=11,350	P value
Male	690 (53.08%)	5690 (50.13%)	0.04
Female	610 (46.92%)	5650 (49.78%)	0.05
White	1110 (85.38%)	8980 (79.12%)	<0.0001
African American	70 (5.38%)	930 (8.19%)	0.0004
Psoriasis	180 (13.85%)	1510 (13.30%)	0.56
IBD	120 (9.23%)	520 (4.58%)	<0.0001
Uveitis	180 (13.85%)	1480 (13.04%)	0.41
Smoking	390 (30%)	2910 (25.64%)	0.0007
Elevated ESR	580 (44.61%)	3490 (30.75%)	<0.0001
Elevated CRP	580 (44.61%)	4240 (37.36%)	<0.0001
HLA B27 positivity	110 (8.46%)	760 (6.7%)	0.018
TNFi	530 (40.77%)	4840 (42.64%)	0.2
Secukinamab	50 (3.85%)	360 (3.17%)	0.19
NSAIDs	1000 (76.92%)	7660 (67.49%)	<0.0001

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AB0709 SERUM IL-12/23 AND IL-17 LEVELS IN PATIENTS WITH SPONDYLOARTHRITIS WERE NOT INFLUENCED BY TNF-BLOCKADE

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Background: Spondyloarthritis (SpA) refers to a heterogeneous group of disorders with clinical features that can include axial and peripheral arthritis, inflammatory bowel disease, uveitis, and psoriasis. Several cytokines including interleukin (IL)-12/23, IL-17 and tumor necrosis factor (TNF) are involved in pathogenesis of SpA. It is assumed that TNF is the upstream cytokine in the cytokine cascade (Schett, et al., 2013).
Objectives: To investigate whether TNF inhibitors decrease serum IL-12/23 and IL-17 levels in patients with SpA.
Methods: Serum were obtained from 23 SpA patients (AS, 10 patients; PsA, 13 patients) enrolled in this study, at baseline, 24 and 48 weeks of TNF inhibitor treatment. Serum IL-12/23 and IL17 levels were measured using LEGEND MAX Human IL-12/IL-23 (p40) ELISA Kit (BioLegend) and Human IL-17A ELISA kit (Invitrogen), respectively. IL-6 levels, the other downstream cytokine, was measured using Lumipulse G600II (FUJIREBIO) as a control.
Results: Any significant reduction in IL-12/23 levels (143.9±143.6 pg/mL at baseline, 156.3±117.1 pg/mL at 24 weeks and 139.3±118.1 pg/mL at 48 weeks), as well as that in IL-17 levels (13.6±51.9 pg/mL at baseline, 12.3±41.4 pg/mL at 24 weeks and 11.6±39.2 pg/mL at 48 weeks) were not observed in 23 SpA patients. On the other hand, serum IL-6 levels were significantly decreased after treatment (4.0±4.2 pg/mL at baseline; 1.8±1.4 pg/mL, *p=0.002*, at 24 weeks; 1.6±1.9 pg/mL, *p=0.0002* at 48 weeks. Pain-VAS was significantly reduced at 24 and 48 weeks compared with that at baseline. No significant differences in serum levels of analyzed cytokines were observed in the AS group compared with the PsA group at baseline (IL-12/23 levels: 110.8±70.0 vs.169.3±180.3 pg/mL, *p=0.28*; IL-17 levels: 26.8±78.6 vs. 3.4±7.6pg/mL, *p=0.08*).
Conclusion: TNF inhibitors did not alter serum IL-12/23 and IL-17 levels but reduced IL-6 levels in patients with SpA. These results imply that IL-12/23 and IL-17 expression might be regulated by alternative pathways.
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Disclosure of Interests: Miho Murakami Grant/research support from: Chugai, Eisai, Consultant of: Chugai, Norihiro Nishimoto Grant/research support from: Chugai, Eisai, Consultant of: Chugai, Speakers bureau: Chugai, Eisai, AYUMI, Mitsubishi Tanabe, AbbVie, Novartis, Nippon Kayaku, TOWA, Astellas, Kyowa Kirin
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AB0710 PATIENT PERCEPTIONS OF FIBROMYALGIA SYMPTOMS AND THE OVERLAP WITH AXIAL SPONDYLOARTHRITIS

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Background: In clinical practice, it is often challenging to distinguish fibromyalgia syndrome (FMS) from axial spondyloarthritis (axSpA), which includes ankylosing spondylitis and non-radiographic axSpA.[1,2] Early stages of axSpA may present with an onset similar to FMS,[3] and likewise patients with FMS may have symptoms that are similar to axSpA. Differentiating between axSpA and FMS can also be challenging for patients and cause confusion about their diagnosis.
Objectives: To examine the prevalence of axSpA symptoms among patients with FMS and differences in the pathway to diagnosis among patients with and without concomitant axSpA.
Methods: Adult US patients with FMS without concomitant rheumatoid arthritis or psoriatic arthritis in the ArthritisPower registry received email invitations to participate. Participants (pts) were asked whether they had a diagnosis of axSpA or ankylosing spondylitis and completed patient-reported outcome measures including Patient Reported Outcomes Measurement Information System (PROMIS) measures for Pain Interference, Sleep Disturbance and Fatigue, and the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). Pts then responded to a 57-item customized survey developed by the researchers in collaboration with patient partners. Results are descriptively reported.
Results: As of January 2020, 231 pts completed the survey; 97% female, 89% White, mean (SD) age of 52 (11). Mean (SD) Pain Interference score was 68 (5); Sleep Disturbance 63 (8); Fatigue 68 (7); and BASDAI 46 (9). Of the pts, 40 (17%) reported concomitant axSpA, 64% osteoarthritis, 6% gout, 5% Crohn's or ulcerative colitis, and 4% lupus. Half of all pts perceived their FMS to be 'rarely' or 'never' well managed and 80% felt that they have had an undiagnosed condition in addition to their FMS and their other current diagnoses. Three-fourths (75%) of pts reported being able to tell the difference between their FMS pain and pain they experience as a part of the concomitant disorder. Back pain lasting >3 months was reported by 95% of axSpA pts and 94% of non-axSpA pts and 12% reported all of the symptoms consistent with patient reported versions of the Assessment of SpondyloArthritis International Society (ASAS) criteria (back/buttock pain >3 months; age of symptom onset <45; sacroiliitis diagnosis; at least on spondyloarthritis feature) (Figure 1), and of these, 39% reported an axSpA diagnosis. More pts with axSpA received their FMS diagnosis by a rheumatologist (45%) than without (41%) (Figure 2), and of the pts without an axSpA diagnosis (n=191), only 6% had recalled their provider ever discussing with them the possibility of axSpA, including non-radiographic axSpA diagnosis. Half (53%) of pts with axSpA believe that their axSpA should have been diagnosed earlier, with 33% reporting that one reason for the delay was their doctors' belief that FMS was the cause of any axSpA symptoms they experienced.
Conclusion: Patients with FMS often experience symptoms of axSpA and the two conditions can occur concomitantly. Additional research is needed to improve the triage, diagnosis, and education of patients with FMS and symptoms of axSpA.
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Figure 1. Symptoms of axial spondyloarthritis (axSpA) reported by participants with fibromyalgia syndrome (FMS) with and without axSpA diagnosis (N=231)

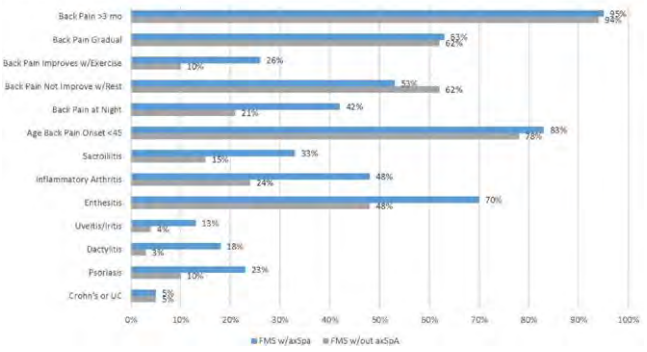
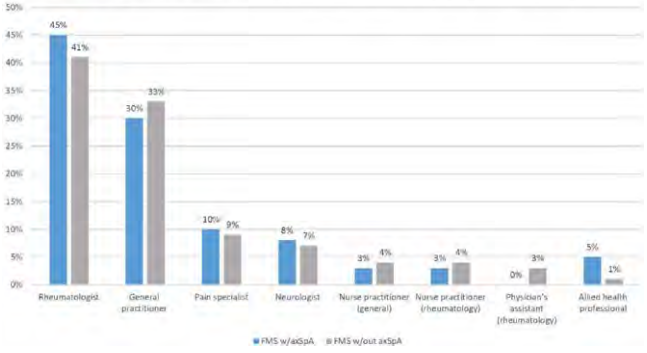


Figure 2. Provider giving fibromyalgia (FMS) diagnosis, by axial spondyloarthritis (axSpA) diagnosis status (N=231)



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AB0711 USEFULNESS OF THE TRABECULAR BONE SCORE AS A PREDICTOR OF VERTEBRAL FRACTURE IN PATIENTS WITH AXIAL SPONDYLOARTHROPATHY

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Background: In axial spondyloarthritis (axSpA) the risk of vertebral fracture is increased, not always corresponding with the values of bone mineral density (BMD). One possible explanation is that syndesmophytes interfere with these values. We consider whether the evaluation of trabecular microarchitecture by an accessible methodlike the Trabecular Bone Score (TBS), that does not involve additional irradiation neither seem to be influenced by the presence of syndesmophytes, may be an advantage to estimate the risk of fracture.
Objectives: To estimate the prevalence of vertebral fractures in patients with axSpA. To assess the diagnostic accuracy of TBS and BMD for vertebral fracture, and if it is influenced by the presence of syndesmophytes. To analyze the correlation between the absolute values of BMD and TBS in the lumbar spine.
Methods: Cross-sectional study. Patients were consecutive recruited. We collected demographic (sex, age), clinical (syndesmophytes, vertebral fracture, BASDAI, BASFI, time of evolution of axSpA, treatment) and analytical variables [vitamin D (1,25-OHD), CRP and ESR]. The BMD was determined using the Lunar Prodigy ProTM densitometer from GE Healthcare, to which the TBS iNsight® software version 2.2 was added to perform the TBS analysis. The presence of fracture was evaluated by radiology. The statistical analysis was performed with the SPSS 22.0 and OpenEpi softwares.
Results: 84 patients were included, 60 men and 24 women, with a mean age of 59 years (± SD 13). 51.2% had lumbar syndesmophytes. The prevalence of fractures was 13.7%, 95 CI (7.8-22.9). 51.2% were treated with NSAIDs, and 48.8% with biological drugs. The evolution of axSpA was > 10 years in 65.5%. The mean scores of BASDAI and BASFI were 3.7 and 4.3 respectively (± SD 2.2 and 2.3). The mean CRP value was 8.5 mg / L (± SD 8.4), ESR 12.2 mm / h (± SD 11.4) and 1.25-OHD 27.9 ng / dL (± SD 13.6).
According to the lumbar and femoral T Score, 9.5% and 15.5% of the patients were in the range of osteoporosis respectively.19% patients had a low TBS value (≤1.23).
Regarding the influence of syndesmophytes on TBS and BMD values, we found significant differences in lumbar spine BMD (p = 0.01) but not in total hip and femoral neck BMD (p = 0.2 and 0.3 respectively) nor in the TBS (p = 0.1).
Regarding the correlation of TBS and BMD values of the spine, no correlation was observed in patients with syndesmophytes, while a moderate correlation (r = 0.4, p = 0.02) was observed in patients without syndesmophytes.
In the univariate analysis, the factors related to the presence of vertebral fracture were age, female sex, absolute BMD values in the lumbar spine and total hip, and TBS values. No relationship was found with the rest of the variables. In the multivariate analysis, only the TBS showed a significant association with the presence of fractures (p =0.02).
Regarding the predictive capacity of fractures, TBS showed a higher sensitivity than that of BMD (55.6% versus 18.2% and 30% of BMD in the spine and hip respectively), being the specificity comparable (85.3% versus 91.3% and 85.1% of BMD in column and hip respectively).
Conclusion: the prevalence of fractures was 13.7% among the patients studied, 95 CI (7.8-22.9). The presence of syndesmophytes influenced the values of lumbar BMD but not the hip BMD or those of the TBS. We found a correlation between the values of BMD of the spine and TBS only in patients who did not have syndesmophytes. Only TBS values were significantly related to the presence of fractures in the multivariate analysis. TBS showed greater sensitivity with similar specificity than BMD for the detection of vertebral fractures.
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AB0712

DISEASE CONTROL AND QUALITY OF LIFE IN PATIENTS WITH ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS IN REAL CLINICAL PRACTICE IN SPAIN: MIDAS STUDY

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Background: There are few data on disease activity status and Quality of Life (QoL) in clinical practice in Spain for patients with ankylosing spondylitis (AS) and psoriatic arthritis (PsA).
Objectives: To assess the disease activity status in standard clinical practice through BASDAI<4 in AS and DAPSA≤14 in PsA and the relationship with QoL.
Methods: An observational, non-interventional, cross-sectional, multicenter study. Patients ≥18 years with ≥6 months diagnosis and classified by ASAS and modified New York criteria or CASPAR criteria undergoing treatment ≥3 months. At the cross-sectional visit, the principal variable taken was the percentage of patients under remission and low disease activity according to the national and European recommendations1-3, assessed through BASDAI and ASDAS-CRP in AS or DAPSA and MDA in PsA. The relationship between patients' QoL and disease activity were assessed using ASAS-HI in AS and PSAID in PsA.
Results: 313 AS patients were included, 75.7% male, 78.5% HLA-B*27+, with a mean (SD) age of 50.4 (12.0) years, a mean (SD) disease duration of 15.5 (11.6) years and a mean (SD) CRP of 5.1 (8.2) mg/l. 313 PsA patients were included, 54.3% male, 17.95% HLA-B*27+, with a mean (SD) age of 54.1 (12.2) years, a mean (SD) disease duration of 10.5 (9.0) years and a mean (SD) CRP of 4.91 (7.3) mg/l. 29.7% AS patients were on biological and 26.8% were on non-biological therapy vs 17.9% and 40.9% PsA patients, respectively. According to BASDAI, 64.5% AS patients were on LDA and 29.4% PsA patients had inactive disease by ASDAS-CRP, 59.4% of patients had a DAPSA<14 while 19,8% were on remission also by DAPSA. In both groups, the QoL impact was low, mean 5.8 in ASAS-HI by AS and 3.0 by PSAID in PsA. QoL impact was significantly higher in patients with active disease (9.3 in AS and 4.4 in PsA).
Conclusion: Our observations show that most AS and PsA patients have an inactive disease, whereas 36% and 41% of AS and PsA patients, respectively, are inadequately controlled despite therapy in standard clinical practice in Spain, which is associated to a significantly worse QoL.
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Table 1. AS and PsA scores according to the current treatment.

	Valid N	Mean (SD)	95% (CI)
AS			
Disease control (BASDAI)			
Not under remission (BASDAI<4)	111	9.3 (3.7)	(8.6; 10.0)
Under remission (BASDAI≥4)	202	3.9 (3.4)	(3.4; 4.4)
Total	313	5.8 (4.4)	(5.3; 6.3)
Disease activity (ASDAS-CRP)			
ASDAS-CRP≥1.3	221	7.1 (4.1)	(6.6; 7.7)
ASDAS-CRP<1.3	92	2.7 (3.4)	(2.0; 3.4)
Total	313	5.8 (4.4)	(5.3; 6.3)
PsA			
Disease control (DAPSA)			
Not under remission (DAPSA>14)	127	4.5 (2.4)	(4.1; 4.9)
Under remission (DAPSA≤14)	186	1.9 (1.7)	(1.7; 2.2)
Total	313	3.0 (2.4)	(2.7; 3.2)
Active disease (MDA)			
Inactive (MDA criteria ≥5)	161	1.5 (1.4)	(1.3; 1.7)
Active (does not meet MDA criteria)	152	4.5 (2.2)	(4.2; 4.8)
Total	313	3.0 (2.4)	(2.7; 3.2)

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Disclosure of Interests: José L. Pablos Consultant of: Pfizer, Lilly, Novartis, Roche, Celgene, Sanofi, Gilead, Biogen, Paid instructor for: Bristol, Speakers bureau: Abbvie, Janssen, Pfizer, Lilly, Novartis, Roche, Celgene, Bristol, Sanofi, Cristina Fernández-Carballido Consultant of: Yes, I have received fees for scientific advice (Abbvie, Celgene, Janssen, Lilly and Novartis), Speakers bureau: Yes, I have received fees as a speaker (Abbvie, Celgene, Janssen, Lilly, MSD, Novartis), Xavier Juanola Consultant of: Pfizer, Lilly, Novartis, Roche, Celgene, Sanofi, Gilead, Biogen, Paid instructor for: Bristol, Speakers bureau: Abbvie, Janssen, Pfizer, Lilly, Novartis, Roche, Celgene, Bristol, Sanofi, Jordi Gratacos-Masmitja Grant/research support from: a grant from Pfizzer to study implementation of multidisciplinary units

to manage PSA in SPAIN, Consultant of: Pfizzer, MSD, ABBVIE, Janssen, Amgen, BMS, Novartis, Lilly, Speakers bureau: Pfizzer, MSD, ABBVIE, Janssen, Amgen, BMS, Novartis, Lilly, Eugenio de Miguel Grant/research support from: Yes (Abbvie, Novartis, Pfizer), Consultant of: Yes (Abbvie, Novartis, Pfizer), Paid instructor for: yes (AbbVie, Novartis, Pfizer, MSD, BMS, UCB, Roche, Grunental, Janssen, Sanofi), Speakers bureau: yes (AbbVie, Novartis, Pfizer, MSD, BMS, UCB, Roche, Grunental, Janssen, Sanofi), Rafael Ariza-Ariza: None declared, Cristina Sanabra Employee of: Yes: employed as a Medical Advisor (Novartis), Pau Terradas Employee of: Yes: employed as a Medical Advisor (Novartis), Carlos Sastré Employee of: YES; I´m Medical Advisor in Novartis Spain

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AB0713 PERIODONTAL DISEASES AND ITS ASSOCIATION WITH ANKYLOSING SPONDYLITIS/SPA: A SYSTEMATIC REVIEW

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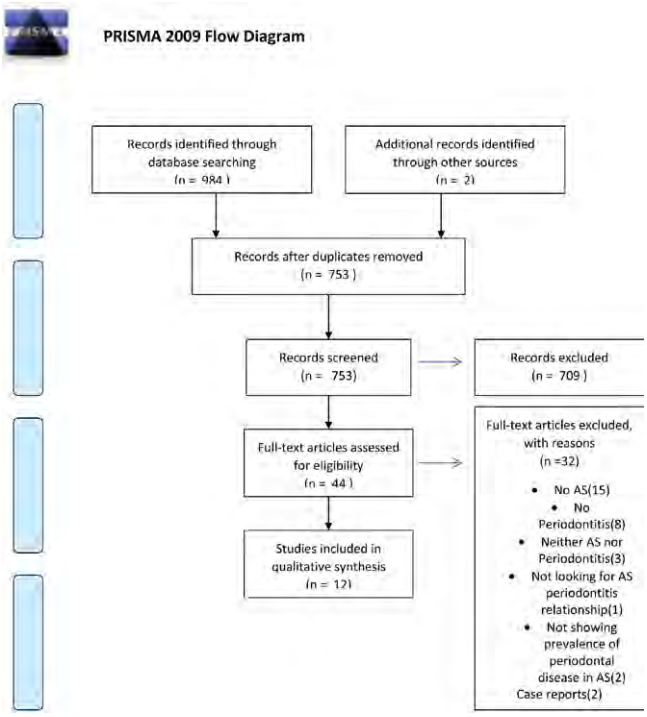
Background: A close association between periodontal disease and Ankylosing spondylitis (AS) has long been specualted. Both diseases are characterized by dysregulation of the host inflammatory response, leading to further destruction of soft and hard connective tissue with there being evidence of increased levels of TNF-α and various interleukins in both patients of AS and periodontitis.

Objectives: The aim of this systematic review was to appraise the available literature exploring the relationship between AS and periodontal disease.

Methods: We searched Medline & Embase databases (from their inception till October 2019) using appropriate combinations of following search items with limits '(English, Human)'; Ankylosing spondylitis, spondyloarthritis, spondyloarthropathies, spondyloarthritides, spinal disease, musculoskeletal disease, Rheumatic disease AND periodontitis, periodontal disease, periodontoses, parodontoses, chronic periodontitis, gum disease, gingivitis, oral health, dental health, plaque index, bleeding on probing, probing pocket depth, clinical attachment loss. This search was supplemented by the manual search of bibliographies of articles selected and conferences proceedings of EULAR. Only be reviews, observational study of cross-sectional, cohort or case control type on adult patients with AS were selected. Data was extracted from a predesigned proforma. A close association between periodontal disease and Ankylosing spondylitis (AS) has long been specualted. Both diseases are characterized by dysregulation of the host inflammatory response, leading to further destruction of soft and hard connective tissue with there being evidence of increased levels of TNF-α and various interleukins in both patients of AS and periodontitis.

Results: A total number of 984 articles were identified and 12 were selcted for detailed appraisal (Figure 1, PRISMA flow chart). They were all case control studies. The prevalence of periodontitis ranged from 38% to 88% in patients with AS whereas in the control group from 26% to 71 % in controls. Out of 12 studies, two showed significant changes in Plaque Index (PI), two studies showed altered Pocket Probing Depth (PPD), three showed significant increased in Clinical Attachment Loss (CAL) and increased Bleeding On Probing (BOP) was seen in 2 studies. In 7 studies, periodontitis was seen in a significant number of patients with AS ($P<0.05$). All studies reported that the prevalence of periodontal disease in AS patients was higher as compared to non-AS patients.

Conclusion: Our systematic review found an association between AS and periodontal disease. Patients with AS show higher prevalence of periodontitis and a poor oral hygiene as compared to healthy controls. At practice level, this systematic review underscores the need for a collaboration between dentists and rheumatologist.



Disclosure of Interests: None declared
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AB0714 THE ROLE OF AGE, DURATION OF THE DISEASE AND CUMULATIVE GLUCOCORTICOID DOSE IN THE FORMATION OF DISORDERS OF THE STRUCTURAL AND FUNCTIONAL STATE OF BONE TISSUE IN MEN WITH ANKYLOSING SPONDYLITIS

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Background: In recent years, it is becoming increasingly clear that osteoprosis (OP) holds the important place among complications of ankylosing spondylitis (AS). The frequency of emergence of OP, according to the data of last investigations, ranges from 18.7 to 62%, osteopenic syndrome – from 50 to 92%. It is known that decrease of bone mineral density (BMD) in patients with AS is caused not only by the action of traditional risk factors (age, sex, genetic predisposition, low body mass, and others) but also by the action of factors associated with the disease itself such as: duration of AS, activity of the inflammatory process, administration of glucocorticoids (GC), deficiency of Vitamin D, low physical activity of patients and so on. However, until now there are no clear data about the role of each of them in the formation of disorders of bone metabolism in men with AS. In the Ukrainian population of patients with AS such investigations have not been conducted.

Objectives: To investigate the role of age, duration of disease and *cumulative glucocorticoid dose* in the formation of disorders of bone mineral density (BMD) in men with AS.

Methods: The investigation of 108 men with AS at the age of 40.74 ± 0.87 years and 25 normal control subjects of the same age and sex has been carried out. The diagnosis of AS was established on the basis of modified New York criteria. BMD of the lumbar spine and femoral neck was determined by dual-energy X-ray absorptiometry on the apparatus 'Hologic Discovery Wi' (S / N 87227). The diagnosis of osteoporosis in men over 50 years was considered in case of decrease of BMD by T-score ≤ – 2.5 SD, osteopenia corresponded to T-score from –1 to –2.5 SD, for men under the age of 50, the Z-score was used, and its decrease ≤ – 2.0 SD and more indicated the significant loss of bone mass.

Results: A decrease of BMD at the level of the lumbar spine and femur neck was found in 61 (56.5%) patients, of these 29 (27.7%) had osteoporosis, 31 (29.5%) had osteopenia. In the control group, decrease of BMD was detected in 6 (24%) patients, of these osteoporosis was diagnosed in 1 (4%), and osteopenia was diagnosed in 5 (20%) patients. In the age group of below 35 years, 18 (64.3%) patients had a decrease in BMD, 35 (56.5%) patients – in the 36-55 age group, and 8 (53.3%) patients – over the age of 45. The index of BMD also did not differ significantly between the groups. As for the duration of the disease, the

largest proportion of 33 (75%) patients with decreased BMD was found in the group of patients with duration of the disease from 5 to 10 years. In the group of patients with duration of the disease up to 5 years, patients with decrease in the Z-score were 11 (55%), and in the group with duration of the disease more than 10 years - 17 (41.6%) patients. Decrease of BMD was associated with *cumulative glucocorticoid dose*. In particular, in the group of patients with a *cumulative* dose of glucocorticoids less than 12.6 g Z-score at the level of the lumbar spine was -0.98 ± 0.17 SD, in the group with a *cumulative* dose of GC 12.6-21.6 g Z-score was equal to –0.43 ± 0.40 SD, and in the group with *cumulative* glucocorticoid dose – above 21.6 g the Z-score was –1.69 ± 0.30 SD. As the glucocorticoid dose increased, the proportion of patients with decreased BMD increased. In the group of patients with the highest dose of GC there were 67.7% such patients, while in the group with the lowest dose – only 30 (57.6%). Significant correlation (r = -0.24) was established between Z-score of the lumbar spine and the total dose of GC.

Conclusion: In 61 (56.5%) patients with AS decreased BMD at the level of the lumbar spine and neck of the femur is revealed. Decrease of BMD in patients with AS does not depend on the age and duration of the disease, but is associated with the *cumulative* dose of GC.

Disclosure of Interests: Sergii Shevchuk Grant/research support from: Celltrion, Inc, Oksana Pavliuk: None declared

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AB0715 POSSIBLE METHODS OF EARLY DIAGNOSIS OF RENAL ALTERATION IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: kidney damage is one of the extraarticular manifestations and complications of ankylosing spondylitis (AS). Due to some disadvantages of traditional renal function parameters, the search for new markers is actively conducted [1].

Objectives: to evaluate urinary excretion of liver type of fatty acid binding protein (L-FABP), which is expressed in cells of proximal tubules, heart type of fatty acid binding protein (H-FABP), which is expressed in cells of distal tubules [2], and trefoil factor-3 (TFF-3), which is expressed in cells of the proximal and distal tubules and collecting duct [3], in patients with AS.

Methods: urine samples of 50 patients (37 males, 13 females) were evaluated. Patient inclusion criteria were a diagnosis of AS according to the New York modified criteria (1984) and ASAS 2009 (The Assessment of SpondyloArthritis international Society, 2009) for axial spondyloarthritis and age 18 and over. Median age of patients was 39 [34;56] years, duration of joint syndrome – 10 [7;18] years, glomerular filtration rate (GFR) - 105 [83;119] ml/min/1.73 m^2. Patients received nonsteroidal anti-inflammatory drugs (NSAIDs), and tumor necrosis factor alpha inhibitors (TNFα inhibitors). L-FABP, H-FABP, TFF-3 levels were measured by enzyme-linked immunosorbent assay. Urinary excretion was expressed as nanograms per millimol of urinary creatinine. The results were compared with the results of the control group.

Results: the values of L-FABP in patients with AS without chronic kidney disease (CKD) exceeded the values in the control group: 0.05 [0.01;0.09] ng/mmol creatinine compared to 0.03 [0.00;0.06] ng/mmol, (p=0.04). H-FABP was detected in only 6 patients, all of them were with CKD. Its level was up to 601.50 ng/mmol. H-FABP level was undetectable in the control group. The level of TFF-3 in patients without CKD was higher than in the control group: 53.42 [20.84;105.71] and 23.31[1.97;62.90] ng/mmol respectively, (p=0.02). A correlation with disease activity (BASDAI and ASDAS) was found for TFF-3 (rs=0.33, p<0.05). This marker in patients receiving NSAIDs is higher compared with TNFα inhibitors: 89.51 [39.82;118.91] and 32.61 [13.51;88.23] ng/mmol respectively, (p=0.04). L-FABP and TFF-3 correlated with each other (rs=0.6, p<0.05). The level of FABPs and TFF-3 did not depend on sex, age, GFR and AS duration.

Conclusion: L-FABP and TFF-3 may be of interest for diagnosis pre-clinical renal alteration, including those associated with the NSAIDs toxicity, in patients with AS. L-FABP and H-FABP may be useful in determining stages and levels of tubular injury

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AB0716 SEX DIFFERENCES IN CLINICAL PHENOTYPE AND RADIOGRAPHIC DISEASE PROGRESSION IN AXIAL SPONDYLOARTHRITIS: RESULTS FROM THE GERMAN SPONDYLOARTHRITIS INCEPTION COHORT

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Background: It is presumed that the phenotype of the axial spondyloarthritis (axSpA) may differ in females and males; the published data are controversial.

Objectives: To explore the sex differences in disease features and radiographic progression in axSpA.

Methods: A total of 210 patients with axSpA (115 with radiographic and 95 with non-radiographic axSpA) were selected for analysis. Spinal radiographs were scored by two readers in a random order according to the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS). Pelvic radiographs were scored according to the grading system of the modified New York criteria; a sacroiliitis sum score was calculated as a sum of the grades for both sacroiliac joints. Mann-Whitney and Fisher exact tests were performed for group comparisons. A multivariable regression analysis was performed to analyze the influence of gender on radiographic progression.

Results: Males (n=107; 51%) were significantly younger at disease onset (34.8 ± 10.3 vs. 31.5 ± 11.2 years, p=0.008) and at diagnosis (37.5 ± 10.2 vs. 34.1 ± 11.2 years, p=0.006); symptom duration at baseline was similar (4.1 ± 2.6 vs. 4.3 ± 2.8 years, p=0.66). Females were less often HLA-B27 positive (74 (72.5%) vs. 92 (86.0%), p=0.02), had higher baseline disease activity (BASDAI 4.3±2.2 vs 3.7±2.0; p=0.05), but lower baseline C-reactive protein level (7.1 ± 10.9 vs. 12.3 ±18.2 mg/l, p=0.08), and similar time-averaged ASDAS (2.5±0.8 vs 2.4±1.0; p=0.385). Males more frequently had definite radiographic sacroiliitis (70.1% vs. 38.8%; p<0.001), higher sacroiliitis sum score (4.9 ±1.9 vs 3.2±1.8, p<0.001), and higher mean mSASSS (6.1 ± 10.7 vs 2.4 ± 4.0; p=0.100) at baseline. Other variables were comparable between the groups. There was a trend for a higher radiographic progression in males in all explored outcomes, statistically significant only for the formation/progression of syndesmophytes (23 (21.5%) vs. 10 (9.7%), p=0.023), with no differences in the radiographic progression of sacroiliitis. In a multivariate logistic regression analysis, similar odds for spinal radiographic progression, new syndesmophyte formation and radiographic progression of sacroiliitis by ≥1 grade were seen – **Table 1**.

Conclusion: There was a trend for male patients to have more radiographic damage at the baseline and more progression after two years, as reflected by the percentage of patients with new syndesmophytes.

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Table 1. Association of sex with radiographic progression in spine and sacroiliac joints after 2 years of follow-up.

Parameter, n (%) or mean±SD	Female (n=103)	Male (n=107)	P
Spinal radiographic progression			
mSASSS change	0.46 ± 1.63	1.00 ± 2.85	0.25
Progression of mSASSS by ≥2 points	10 (9.7)	20 (18.7)	0.08
New syndesmophytes or progression of syndesmophytes	10 (9.7)	23 (21.5)	*0.02*
Progression of radiografic sacroiliitis			
Change of the sacroiliitis sum score	0.14 ± 0.94	0.13 ± 0.73	0.58
Progression of sacroiliitis by at least 1 grade in opinion of both readers	17 (16.5)	9 (8.4)	0.09

mSASSS – modified Stoke Ankylosing Spondylitis Spine Score;

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AB0717 THE ASAS-HEALTH INDEX MAY BE USEFUL TO IDENTIFY DISEASE ACTIVITY STATES IN PATIENTS WITH SPONDYLOARTHRITIS.

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Background: Patients with spondyloarthritis (SpA) suffer not only from pain or physical disability, but they are also affected in multiple facets of life due to this condition (disease impact). Recently, the ASAS group has proposed a new way of capturing the impact that SpA have on patients' lives, based on the principles proposed by the International classification of functioning, disability and health (ICF). The tool obtained (ASAS-health index or ASAS-HI) includes 17 items that cover most ICF domains.
Objectives: To analyze the performance of ASAS-HI in real clinical practice, by comparing it with other standard measures of evaluation of SpA. To assess whether ASAS-HI is able to identify disease activity states in these patients.
Methods: This cross-sectional study included 111 consecutive patients with SpA (ASAS criteria). The correlation (Spearman's rho) between ASAS-HI, BASDAI, ASDAS, and BASFI was analyzed. ROC curves were constructed to analyze ASAS-HI values that determined BASDAI remission, ASDAS inactive disease, and ASDAS low activity. A logistic regression was made to determine the ASAS-HI items with greater capability to discriminate the state of remission / inactive disease.
Results: Seventy-four men and 37 women were included, mean age of 43.3 ± 10.6 years. The average duration of illness was 7.6 ± 6.8 years. Sixty percent of the series was under biological therapy. HLA-B27 was positive in 79.3%. The average value of ASAS-HI was 5.4 ± 3.8. There were significant correlations between ASDAS and BASDAI (rho: 0.89, p <0.0005), BASDAI and BASFI (rho: 0.86, p <0.0005), BASFI and ASDAS (rho: 0.78, p <0.0005), BASDAI and ASAS-HI (rho: 0.77, p <0.0005), ASDAS and ASAS-HI (rho: 0.70, p <0.0005). The optimal cut-off point of ASAS-HI for BASDAI remission (Table 1) corresponded to a value ≤ 2. As for the value of ASAS-HI to define ASDAS inactive disease (Table 2), this was ≤ 0. For ASDAS low activity, the value was ≤ 6 [area under the ROC curve 0.82 (95% CI: 0.73-0.89), Sen: 89.5%, Spe: 66.1). In the multivariate regression, the two ASAS-HI items associated with BASDAI non-remission were, "I often get frustrated" [OR 9.2 (95% CI: 1.2-69.4), p = 0.032], and "I sleep badly at night" [OR 7.7 (95% CI: 1.4-41.6), p = 0.018). As for ASDAS, the only question of ASAS-HI significantly associated with active disease was "pain sometimes disrupts my normal activities" [OR 8.7 (95% CI: 1.7-45.2), p = 0.010].
Conclusion: ASAS-HI correlates well with most outcome measures in SpA. A cut-off point of ASAS-HI ≤ 6 identifies a low disease activity and could be considered a good treatment objective. The evaluation of SpA should include not only conventional measures (BASDAI / ASDAS) but also disease impact measures (ASAS-HI).

Table 1.

Area under the ROC curve (AUC)	0.883	95% CI	0.809-0.936	p-value	<0.0001
Optimal cut-off point	**≤2**	Sensitivity	65.71	Specificity	96.05

Table 2.

Area under the ROC curve (AUC)	0.873	95% CI	0.797-0.929	p-value	<0.0001
Optimal cut-off point	**≤0**	Sensitivity	58.82	Specificity	94.68

Disclosure of Interests: None declared
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AB0718 DIAGNOSTIC PERFORMANCE OF VARIOUS CLASSIFICATION CRITERIA IN LOW BACK PAIN PATIENTS WITH SUSPECTED AXIAL SPONDYLOARTHRITIS: A PRAGMATIC STUDY.

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Background: In routine practice, axial spondyloarthritis (SpA) can be a diagnostic challenge because there is potential overlap with osteoarthritic low back pain or diffuse polyalgic syndrome with axial pain as fibromyalgia. Internationally recognized classification criteria (AMOR, ASAS (1), ESSG (2)) are often used as diagnostic tools in clinical practice (3), but few studies have sought to establish their "real life" diagnostic performances.
Objectives: This monocentric study aimed to evaluate the diagnostic performance of different sets of classification criteria for SpA in patients with chronic back pain hospitalized for suspected axial SpA. The second objective was to evaluate the impact of the sacroiliac MRI reading according to the ASAS MRI reading or expert musculoskeletal reading.
Methods: Patients presenting with inflammatory low back pain who underwent standardized sacroiliac MRI protocol were consecutively included. The diagnoses obtained with the classification criteria (AMOR, ESSG, Modified AMOR and Modified ESSG (with sacroiliac MRI)) were compared to the gold standard diagnoses (made by a college of three experienced rheumatologists). Two readings of the sacroiliac MRI were performed (ASAS MRI reading and Expert MRI reading (including all inflammatory or structural T1 or T2 STIR abnormalities)). Diagnostic performance was measured for each set of classification criteria: sensitivity, specificity, predictive positive and negative values (PPV, NPV) and positive and negative likelihood ratios (PLR, PLN). The clinical, biological and MRI factors associated with axial SpA diagnosis were identified in a multivariate logistic regression model.
Results: 83 patients were included of which 27 had axial SpA according to the opinion of the college of rheumatologists. The AMOR modified criteria (with ASAS MRI reading) had the highest diagnostic performance values, with sensitivity = 96%, specificity = 71%, NPV = 97%, PPV = 54%, PLR = 3.3, and NLR = 0.06. Sacroiliac MRI reading demonstrated poor sensitivity (< 60%) for SpA (ASAS or expert reading), while expert reading of MRI had high specificity (98%), NPV = 90%, PPV = 78%, and PLR = 18. In multivariate logistic regression, the presence of enthesitis (OR = 3.51, IC95% [1.10;11.21]; p = 0.024), positive HLA B27 (OR = 4.22, IC95% [1.25;14.18]; p = 0.02)) or sacroiliitis on MRI (ASAS reading) (OR = 3.34, IC95% [1.04; 10.76]; p = 0.043) were independently associated with the final diagnosis of SpA.
Conclusion: The results of this pragmatic study suggest that the Modified AMOR criteria with ASAS MRI reading can be used to rule out axial spondyloarthritis (NPV = 97%). However, the use of an MRI ASAS reading alone creates a risk of false positives because of the greater impact on ASAS criteria compared to AMOR or ESSG criteria. Further international studies are needed to decrease the rate of false positives in suspected cases of axial spondyloarthritis in routine practice.
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AB0719 CLINICAL FEATURES OF PATIENTS WITH ANKYLOSING SPONDYLITIS AND SECONDARY AA-AMYLOIDOSIS

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Background: Secondary AA-amyloidosis is one of the most serious complications of ankylosing spondylitis (AS). Better knowledge of specific to secondary AA-amyloidosis clinical features is important for improving further management of these patients.
Objectives: To conduct a comparative analysis of AS patients with and without secondary AA-amyloidosis.
Methods: The study included 220 AS patients (according to modified New York criteria) without amyloidosis - Group 1, and 9 AS patients with histologically confirmed secondary AA-amyloidosis – Group 2.
Results: Table 1 presents the comparative characteristics of Group 1 and Group 2 patients. Both groups were comparable in terms of patients' age, rates of HLA B27 positivity, presence of enthesitis, uveitis, inflammatory bowel diseases (IBD), and psoriasis on assessment. Group 2 patients tended to be younger at AS onset, while shorter disease duration and fewer male patients were established for Group 1. Group 2 had higher rates of extra-spinal AS manifestations, such as arthritis and coxitis. It should be noted that all AS patients with secondary AA-amyloidosis were males, with clinically manifest arthritis, involving hip joints, and AS onset in the childhood in 8 out of 9 cases.

Table 1. Comparative characteristics of Group 1 and Group 2 AS patients.

	Group 1 (n=220)	Group 2 (n=9)	p
Mean age, M±σ, y.	35,1±9,5	40,1±8,6	>0.05
Mean age at the onset, M±σ, y.	29,9±9,6	13,4±7,5	**<0.05**
Mean disease duration, M±σ, y.	6,9±5,6	26,3±6,5	**<0.05**
Men, n (%)	162 (73,6%)	9 (100%)	**<0.05**
HLA B27, n (%)	202 (91,8%)	9 (100%)	>0.05
Arthritis, n (%)	182 (82,7%)	9 (100%)	**<0.05**
Coxitis, n (%)	119 (54,0%)	9 (100%)	**<0.05**
Enthesitis, n (%)	105 (47,7%)	7 (78%)	>0.05
Uveitis, n (%)	52 (23,6%)	4 (44,4%)	>0.05
IBD, n (%)	5 (2,2%)	0	>0.05
Psoriasis, n (%)	24 (10,9%)	0	>0.05

Conclusion: Patients with AS and secondary AA amyloidosis are predominantly of male gender, who usually get sick in childhood, have 100% HLA-B27 positivity, peripheral arthritis, and coxitis.

Disclosure of Interests: None declared

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AB0720 SOLUBLE TRANSFERRIN RECEPTOR IN DIAGNOSIS OF IRON DEFICIENCY ANEMIA IN PATIENTS WITH SPONDYLOARTHRITIS

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Background: Anemia is a frequent hematological disorder in patients with rheumatic diseases. The main pathogenetic variants of anemia are anemia of chronic disease (ACD), iron deficiency anemia (IDA), and anemia of chronic disease with iron deficiency (ACD/IDA). The presence of systemic inflammation hinders to diagnose absolute iron deficiency, because standard tests of iron status are affected by it. Soluble transferrin receptors (sTfR) measurement and the calculation of the sTfR/ log ferritin index (sTfR index) are recommended, but data about diagnostically significant levels of these indicators in patients with spondyloarthritis (SpA) is currently limited.

Objectives: To assess the diagnostic significance of sTfR and the sTfR index for detecting absolute iron deficiency in patients with SpA and anemia.

Methods: Complete blood count, standart iron metabolism parameters, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were evaluated in 68 patients with SpA. Serum concentration of sTfR was measured with enzyme-linked immunosorbent assay (ELISA) using sTfR ELISA kit («Monobind Inc.», USA). The sTfR index was calculated by the formula $sTfR/\log_{10}$ ferritin. Anemia was defined using the World Health Organization criteria. Depending on the serum ferritin concentration, transferrin saturation, and CRP level, ACD, IDA, or combined anemia (ACD/IDA) were diagnosed. Disease activity was determined by the BASDAI (Bath Ankylosing Spondylitis Disease Activity Index) and ASDAS-CRP (Ankylosing Spondylitis Disease Activity Score based on CRP) scales. Receiver operating characteristic (ROC) analysis was performed with MedCalc.

Results: Anemia was found in 48 of 68 (70,6%) SpA patients. 16 (33,3%) patients had ACD and 32 (66,7%) had ACD/IDA. Hemoglobin level in ACD was 118 [112; 123] g/L, in ACD/IDA – 110 [106; 120] g/L, in non-anemic patients – 133 [129; 145] g/L (p<0.001 for all groups). CRP and ESR values were higher in ACD compared to ACD/IDA patients (31.5 [20.3; 46.4] mg/L and 27.0 [16.0; 35.5] mm/h versus 9.8 [5.6; 16.9] mg/L and 15.5 [12.0; 22.5] mm/h, respectively [p=0.00 and p=0.038]). No statistically significant difference was found between all groups in BASDAI and ASDAS-CRP scores.

ACD/IDA patients had significant increases in serum sTfR levels (1.7 [1.4; 2.2] mg/L) compared to ACD (1.5 [1.1; 1.7] mg/L, p=0,04) and to non-anemic patients (1,3 [1,1; 1,6] mg/L, p=0,003). The sTfR index was significantly higher in ACD/IDA (0.93 [0.82; 1.24]) compared to patients with ACD (0.64 [0.48; 0.75], p<0.001) and without anemia (0.67 [0.56; 0.81], p<0.001).

The areas under the curves (AUCs) for distinguishing between ACD/IDA and ACD were 0.85 for sTfR index (p<0,001), 0.72 for sTfR (p<0,001). The sTfR index (cutoff >0.83) and sTfR (cutoff >1.39 mg/L) had sensitivities of 75% and 53%, and specificities of 83% and 81%, respectively.

Conclusion: According to obtained data, serum concentration of sTfR >1.39 mg/L and the sTfR index >0.83 point to the presence of iron deficiency component in the structure of anemic syndrome in patients with SpA.

References: Management of patients with SpA requires constant monitoring of side effects of therapy, in particular induced by the non-steroidal anti-inflammatory drugs. Use of sTfR and the sTfR index can improve the detection of IDA. A significant advantage of these indicators is their independence from systemic inflammation.

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AB0721 OCULAR INVOLVEMENT IN INFLAMMATORY BOWEL DISEASE. STUDY OF 1442 PATIENTS FROM A SINGLE UNIVERSITARY CENTER.

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Background: Inflammatory bowel disease (IBD), which includes Crohn's disease (CD), and Ulcerative colitis (UC) are related to Spondyloarthritis (SpA). Ocular manifestations (OM) are well-stablished in SpA but not in IBD. It has been classically reported that whereas uveitis with SpA is predominantly anterior, unilateral, sudden, and limited; in IBD it is bilateral, posterior, insidious, and chronic *(Lyons & Rosenbaum JT.Arch Ophthalmol 1997; 115:61-4).*

Objectives: In a large unselected series of IBD, we study the OM and assess; **a)** epidemiological, clinical features, **b)** the relationship with extraintestinal manifestations.

Methods: Study of all consecutive patients from a single University Hospital during the last 40 years with**: a)** IBD (CD and UC), and **b)** OM: uveitis and scleral pathology diagnosed by clinical features and slit-lamp.

Results: OM were present in 42 (2.9%) (25 women/17 men) (84 eyes) of 1442 IBD patients; OM included the uveitis group (UG) (n=23; 1.6%) and the scleral pathology group (SG) (n=19, 1.32%) (**TABLE)**.

TABLE.

	Uveitis (n= 23)	Epi/scleritis (n=19)	p
DEMOGRAPHIC PARAMETERS			
Sex, n (%)	6 ♂ / 17 ♀	11 ♂ / 8 ♀	p= 0.04*
Age at diagnosis (years) mean ± SD	49.13±14.64	47.63±12.48	p= 0.415
INTESTINAL AFFECTION			
CD, n (%)	12 (52.17)	16 (84.21)	p= 0.02*
UC, n (%)	11 (47,83)	3 (15,74)	p= 0.16
EXTRAINTESTINAL AFFECTION			
Cutaneous manifestations			
•Erythema nodosum, n (%)	6 (26.09)	2 (10.53)	p= 0.30
•Pyoderma gangrenosum, n (%)	1 (4.35)	0 (0)	p= 0.92
•Psoriasis, n (%)	1 (4.35)	4 (21.01)	p= 0.23
Joint involvement	10 (43.50)	6 (31.60)	p= 0.36
•Psoriathic arthritis, n (%)	1 (4.35)	3 (15.80)	p= 0.47
•Enteropathic Spondyloarthritis, n (%)	6 (26.09)	3 (15.80)	p= 0.66
•Ankylosing Spondylitis, n (%)	3 (13.04)	0 (0)	p= 0.28
Digestive manifestations			
•NASH, n(%)	4 (17.39)	6 (31.58)	p= 0.28

***p value < 0.05. SD:** standard deviation; **CD:** Crohn's disease**; UC:** ulcerative colitis**; NASH:** non-alcoholic steatohepatitis.

The most common pattern in SG was episcleritis (n=16; 84.21%) and scleritis (n=3). In UG, uveitis was typically anterior (n=18; 78.3%), unilateral (n=19; 82.6%), sudden (n=19; 82.6%), and limited (n=12; 52.2%).

The comparative study between SG vs UG showed in UG a significant predominance of women and UC. Also, a non-significative higher frequency in Pyoderma gangrenosum, erythema nodosum and joint involvement was observed in UG.

After a mean follow-up of 15.2±9.97 years, extraintestinal manifestations were observed in 100% of patients, being articular forms (n=16; 38.10%) the most common type. In addition, joint/axial flare is more related to the presence of uveitis (p=0.038).

Conclusion: Both uveitis and episcleritis are equally frequent OM in IBD. Although uveitis is more infrequent in IBD than in SpA, it is also anterior, unilateral, sudden and limited in contrast with published data from selected series.

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AB0722 LOSS OF GLYCOSAMINOGLYCANS OF LUMBAR INTERVERTEBRAL DISCS IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: To evaluate the glycosaminoglycan (GAG) content of lumbar intervertebral discs (IVD) in patients with ankylosing spondylitis (AS) using GAG chemical exchange saturation transfer (gagCEST).
Objectives: Does local GAG content in non-degenerative IVDs measured by gagCEST MRI differs between AS patients and HC?
Methods: 195 lumbar IVD of 15 patients with AS (mean age 50 ±10 years) and 25 healthy control patients (HC) were prospectively examined with 3 T magnetic resonance imaging (MRI). MRI protocol contained morphological T2 weighted (T2w) images to grade IVD according to the Pfirrmann classification and biochemical imaging with gagCEST to calculate a region of interest (ROI) of the nucleus pulposus (NP) and annulus fibrosus (AF). Prior to statistical testing of gagCEST effects in patients and HC, IVD were classified according to Pfirrmann.
Results: Significantly lower gagCEST values of NP and AF were found in non-degenerative IVD (Pfirrmann 1 and 2) of AS patients compared to HC (NP: 1.88 % ±1.21% vs. 3.38 % ±1.71%; p<0.01; confidence interval (CI): 0.89%/2.11%. AF: 1.11 % ± 1.07 % vs. 1.96 %± 1.23 %; p<0.01; CI 0.39%/1.3%).
Conclusion: GagCEST analysis of morphologically non-degenerative IVDs in T2w images showed significantly lower GAG values in patients with AS in the NP and AF compared to HC. Our results potentially allow for the detection of GAG loss prior to morphological degeneration.

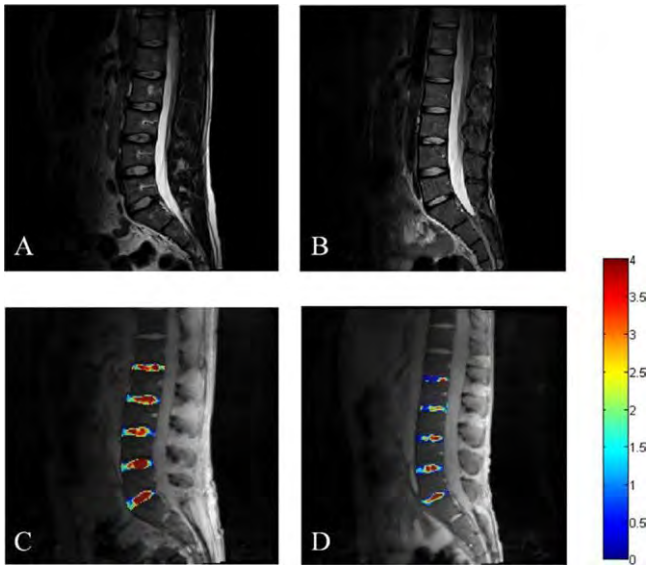


Figure 1. Comparison of morphological T2 weighted (T2w) images to grade IVD according to the Pfirrmann classification and biochemical imaging with gagCEST between HC (A and C) and AS patients (B and D) showing significant lower GAG levels in AS patients.

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AB0723 SERUM LEVELS OF TRANSFORMING GROWTH FACTOR BETA1 AND SCLEROSTIN AND THEIR CORRELATIONS WITH MRI AND LABORATORY FINDINGS IN PATIENTS WITH SPONDYLOARTHRITIS

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Background: There is an actual demand for searching the biomarkers which could reflect disease activity and MRI changes in sacroiliac joints (SIJ) and spine in patients with spondyloarthritis (SpA). Transforming growth factor-beta 1 (TGF-β1) is a cytokine that suppresses inflammatory cytokines but could augment inflammation [1]. A very recent study suggests a possible role of sclerostin (Scl) in the identification of SpA patients, but further studies are needed to prove its role as a disease activity and progression biomarker [2]. In general, the role of these biomarkers in SpA patients remains unknown due to controversial data about their levels in patients with SpA in comparison with healthy subjects and correlations with SpA activity.
Objectives: This study was designed to determine TGF-β1 and Scl serum levels and its correlations with changes in spine and SIJ on MRI imaging, laboratory parameters and indices of disease activity and functional status in SpA patients.
Methods: 102 patients with SpA (mean age (M±σ) - 38.1±11.2, 67 males and 35 females) and 15 healthy age- and gender-matched controls were included in the study. C-reactive protein (CRP, mg/l) and erythrocyte sedimentation rate (ESR, mm/hr) were evaluated as inflammatory markers. Disease activity and functional impairment were moderate to high, mean Ankylosing Spondylitis Disease Activity Score (ASDAS-CRP) was 3.07±1.07, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI, mm) - 45.3±18.6, Bath Ankylosing Spondylitis Functional Index (BASFI, mm) - 31.7±22.9.
Serum levels of TGF-β1 (pmol/l) and Scl (pmol/l) were measured by ELISA. Spine MRI imagines were assessed for active inflammatory lesions using Berlin method (0-69, n=19). Active and chronic MRI changes in SIJ were scored by Spondyloarthritis Research Consortium of Canada (SPARCC) score (0-72) and Danish scoring method (0-48), respectively (n=67). Spearman correlation coefficient and Student t-test were used for statistical analysis.
Results: Mean value of laboratory and MRI parameters were: CRP – 20.9±31.5, ESR – 27.1±22.1, Berlin score was 3.93±3.87, SPARCC – 22.5±11.9, Danish score – 20.5±9.83.
Patients with SpA had significantly lower serum levels of biomarkers compared with the healthy controls: 285.3±186.9 vs 443.2±84.3, p=0.0017 - for TGF-β1, and 21.7±13.5 vs 31.2±10.5, p<0.0001 – for Scl.
There were significant positive correlations for TGF-β1: strong - with active spine lesions by Berlin method (r=0.810, p<0.01), and weak - with CRP level (r=0.224, p=0.024). There were no correlations with MRI inflammatory changes in SIJ.
Scl had weak negative correlation with SPARCC (r=-0.265, p=0.030), but not with Danish or Berlin scores.
There were no other correlations, including ASDAS-CRP, BASDAI and BASFI for both TGF- β1 and Scl.
Conclusion: Serum TGF- β1 and Scl levels are significantly lower in SpA patients comparing with non-SpA subjects. TGF- β1 positively correlates with disease activity (CRP and active MRI lesions in spine), but has no correlations with SIJ inflammation assessed by MRI. Scl negatively correlates with inflammatory MRI changes in SIJ, but not in the spine.
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AB0724 IS THERE A LINK BETWEEN RADIOGRAPHIC SACROILIITIS AND HIP INVOLVEMENT IN SPONDYLOARTHRITIS?

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Background: Hip involvement is a common feature in spondyloarthritis (SpA). Whether the hip is part of the axial or appendicular skeletal is still a matter of discussion.
Objectives: We aimed to assess the relationship between sacroiliitis, spinal and hip involvement in SpA.

Methods: Patients with SpA diagnosed according to the assessment of Spondyloarthritis International Society criteria were included in this retrospective cross-sectional study.
The modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) and the Bath Ankylosing Spondylitis Radiology Index-spine (BASRI-s) were used to assess the radiographic involvement of the spine.
The sacroiliac joints were scored according to the modified New York criteria.
Radiological hip involvement was scored using the Bath Ankylosing Spondylitis Radiology Index hip (BASRI-h).
Patients were divided into two groups: G0 including patients without hip involvement and G1 patients with hip involvement.
Results: We included 112 patients with a sex ratio of 2.4. The average SpA symptom duration was 9.33 ± 8.93 years. The diagnostic delay was 42.92 ± 52 months.
Radiographic hip involvement was noted in 39.28% of cases. It was bilateral in 31 patients (70.4%). The total number of coxitis was 75. Severe and moderate hip involvement (BASRI-h ≥ 3) affected 21 hips. The most common radiographic pattern was early coxitis (n=31, 41.3%) followed by the destructive form (n=22, 29.3%, mimicking-osteoarthritis form (n=15, 20%), condensing form (n=5, 6.6%) and ankylosing form (n=2, 2%).
Radiographic sacroiliitis was noted in 75.8% of patients. It was bilateral in 91.7% of cases. Among the 161 sacroiliac joints fulfilling the m-New-york criteria, 32.9% had grade 4 and 37.2% had grade 3.
The mean mSASSS was 10.26 ± 15. The mean BASRI-t, BASRI-C, and BASRI-L were 3.99 ± 2.9, 0.89 ± 1.3, and 1.1 ± 1.3 respectively.
Radiographic sacroiliitis was more common in patients with hip involvement (G1) (90.9% vs 68.2%, p=0.00). Patients in G1 had higher mSASSS (15.78 ± 18.24 vs 6.29 ± 11.85, p=0.01), BASRI-L (1.73±1.46 vs 0.75 ± 1.131, p=0.009), and BASRI-s (5.46 ± 3.02 vs 3.19 ± 2.46, $p< 10^{-3}$) than patients in G2. There was no significant difference between the two groups regarding the BASRI-C.
Multivariable analysis revealed that radiographic sacroiliitis was associated with hip involvement (OR=14.81, 95%, [1.1-198], p=0.042).
When comparing patients with severe and moderate hip involvement (BASRI-h ≥ 3) and those with mild involvement, we didn't find significant differences regarding BASRIs, BASR-L, BASRI-c, mSASSS, and sacroiliac involvement.
Conclusion: As reported in previous studies [1], we concluded that structural axial lesions were higher in patients with coxitis. Structural damage to the sacroiliac joint in SpA was predictive of hip involvement.
We suggest that sacroiliitis, spinal and hip involvement are part of the same spectrum.
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AB0725 FACTORS ASSOCIATED WITH RADIOGRAPHIC SPINAL INVOLVEMENT IN SPONDYLOARTHRITIS

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Background: Spondyloarthritis (SpA) is characterized by significant radiographic changes in the spine. The structural spine damage can be assessed using several scorings such as the Bath AS Radiology Index (BASRI) and the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS).
Objectives: We aimed to identify factors associated with structural damage in the spine using these scores.
Methods: We conducted a cross-sectional study including patients with SpA diagnosed according to the assessment of Spondyloarthritis International Society criteria.
To assess the radiographic involvement of the spine, we used the mSASSS, the BASRI-spine (BASRI-S), the BASRI-lumber (BASRI-L) and the BASRI-cervical (BASRI-C).
Disease activity was assessed using the BASDAI and ASDAS-CRP.
Results: Among the 112 patients, 72.32% were men. The mean age was 43.78 ± 12,91 years. The mean age at diagnosis was 37.8 ± 13.45 years. The diagnostic delay of 37,8 ± 46 months.
Forty-nine patients were smockers (43.8%).
The mean BASDAI score and ASDAS–CRP score were 4.04 ± 1.99 and 3.30 ± 0.87.
The mean ESR and CRP were 36.21 ± 27 (mm/H) and 31.28 ± 47.25 mg/L
The mean BASRI-S was 3,99 ± 21,96 and the mean mSASSS was 10,26 ± 15,41.
Twenty-five patients (22.3%) had non-radiographic axial SpA.
Men had higher BARSI-L (1.36 vs 0.7, p= 0.045) and BASRI-S (4.3 vs 3.09; p=0.047) than women.
Moreover, smokers' patients had higher mSASSS (14.07 vs 7.02; p=0.031), BASRI-C (1.23 vs 0.62; p=0.031), and BASRI-S (4.82 vs 3.35; p= 0.009) than non-smokers' patients.
A positive correlation was noted between age and BASRI-C (r= 0.260, p=0.012). There was no correlation between age at the onset of SpA and structural spine damage.
We found a positive correlation between disease duration and the following scores: BASRI-C (r=0.245, p=0.018) and BASRI-S (r=0.274, p=0.003).
Patients with non-radiographic axial SpA had lower mSASSS (4.05 vs 12.14; p=0.034), BASRI-s (1.2 vs 4.9; p< 10-3), and BASRI-L (0.42 vs 1.4; p=0.003) than patients with radiographic axial SpA.
There was no correlation between the radiographic index and BASDAI and ASDAS-CRP.
Conclusion: We confirmed previous observations that male gender, smoking and disease duration are associated with structural damage in the spine [1].
However, CRP and other inflammatory biomarkers were not associated with radiographic evidence of spine involvement.
As observed in previous studies, the radiographic spine damage did not correlate with disease activity (BASDAI) [1].
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AB0726 CHOROIDAL THICKNESS IS A BIOMARKER AND CAN PREDICT THE RESPONSE TO TREATMENT IN ANKYLOSING SPONDYLITIS

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Background: Choroidal thickness (CT) has been proposed and evaluated as a potential marker of systemic inflammation associated with inflammatory diseases as Ankylosing spondylitis (AS). Patients with active AS have a thicker choroid than healthy subjects, regardless of eye inflammation. The evolution of choroid after treatment is poorly known.
Objectives: This study evaluates the CT of patients with severe AS disease activity before and after six months of biological therapy.
Methods: This prospective multicenter study evaluates the CT in 44 patients with high AS disease activity, naïve for biological treatment, and no history of eye inflammation before and after six months of biological therapy, aged from 18 to 65 years. The correlations between the CT and C-reactive protein (CRP) with the disease activity indices and scales as Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), night pain and Patient Global Assessment (PGA) were calculated at baseline and after six months of biological therapy. The concordance between the CT and CRP was determined. Finally, we assessed potential predictors of response to treatment. Clinically important improvement was defined as a decrease in ASDAS score ≥ 1.1 points.
Results: Globally, 44 eyes of 44 patients aged between 18-65 years were included in the study, 12 (27%) women. The biological treatments prescribed were: Adalimumab 13 (29.5%), Certolizumab 9 (20.5%), Secukinumab 10 (20%), Etanercept 8 (18%), Infliximab 3 (6.8%), and Golimumab 1 (2.2%).
Mean CT values were significantly higher at baseline than after six months of treatment (baseline 355.28±80.46 µm; 6 months, 341.26±81.06 µm) (p<0.001).
CT decreased both in patients on biological treatment without effect in eye (Secukinumab and Etanecept; p=0.024) and in patients on treatment with effect in eye (other; p=0.005). Also, CRP, BASDAI, night pain and PGA decreased after six months of treatment ((p<0.001, p<0.001, p<0.001, p<0.001). We found a 95% concordance between CT and CRP at baseline and 6 months.
Multivariable analysis showed that clinically important improvement was associated with higher CT and age as independent factors (OR 0.97, CI95% 0.91-0.93; p=0.009, and OR 0.81, CI95% 0.7-0.95; p=0.005). Clinically important improvement was associated with basal CT >374 µm (sensitivity 78 %, [CI 95% 60-90], specificity 78% [CI 95% 52-92], area under the curve of ROC, 0.70, likelihood ratio 3.6).
Conclusion: CT decreased significantly after six months of biological treatment. CT and CPR had a 95% concordance. A high CT is associated with risk of failure

to biological treatment. CT can be considered as a useful biomarker of inflammation and predictor of response to treatment in AS.

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AB0727 WORK OUTCOMES AND ASSOCIATED FACTORS IN ANKYLOSING SPONDYLITIS PATIENTS IN CHINA

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Background: Poorer work productivity due to pain and functional impairment is commonly seen in ankylosing spondylitis (AS) patients, which may contribute to huge social economic burden. However, data about work outcomes and associated factors in Chinese AS patients were barely reported.

Objectives: To assess work outcomes and identify factors associated with poor work productivity in patients with AS in China.

Methods: A cross-sectional study was conducted in China. Adult patients (aged ≥ 18 years) fulfilled the 1984 New York modified criteria of AS were enrolled from rheumatology center from Jan 2017 to Aug 2017. All participants completed questionnaires about socio-demographic characteristics, disease characteristics, quality of life and the Work productivity and activity impairment questionnaire in AS (WPAI:SpA) to accesses the impact of chronic health conditions on job performance and productivity. Factors associated with work outcomes were evaluated.

Results: A total of 91 patients with AS were included: 87.8% males, 78.02% employed, mean age and disease duration of 30 and 10 years respectively. The mean (SD) activity impairment of all patients was 48.57% (22.02%). For patients with employed work, mean (SD) absenteeism, presenteeism and work productivity loss were 10.22% (19.44%), 43.86% (22.48%) and 47.92% (25.81%) respectively. In multivariable analysis, activity impairment was associated with Bath Ankylosing Spondylitis Functional Index (BASFI) (P<0.01) and Ankylosing Spondylitis Quality of Life (ASQoL) (P<0.01). Absenteeism was associated with disease duration (P=0.03). Presenteeism was associated with disease duration (P=0.04), BASFI (P<0.01) and ASQoL (P<0.01). Work productivity loss was associated with BASFI (P<0.01) and ASQoL (P<0.01).

Conclusion: Longer disease duration, reduced physical function and poorer quality of life are associated with reduced work productivity in Chinese AS patients.

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AB0728 MICROVASCULAR CHANGES OF THE RETINA IN ANKYLOSING SPONDYLITIS, AND THE ASSOCIATION WITH CARDIOVASCULAR DISEASE – THE EYE FOR A HEART STUDY.

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Background: Patients with ankylosing spondylitis (AS) have an increased risk at cardiovascular disease (CVD). Microvasculature changes might precede overt CVD, but have been poorly studied in AS. The small vessels of the retina are accessible for non-invasive visualization, and microvascular changes (retinal arteriolar narrowing, venular widening, loss of tortuosity) are described in association with CVD in other diseases.

Objectives: The aim of this study was to compare the retinal microvasculature of AS patients with healthy controls, and to assess gender differences.

Methods: A cross-sectional, case-control study comparing AS patients (fulfilling the modified New York criteria, Rheumatology outpatient clinic of Reade and Amsterdam UMC) with healthy controls (EMIF-AD PreClinAD cohort of the Dutch Twins Register(1)), men:women=1:1. Most important inclusion criteria were: age 50-75 years, diabetes mellitus was excluded. All subjects underwent Optical Coherence Tomography Angiography and fundus photography (≥1 eye), analyzed with Singapore I Vessel Assessment software (Table 2). Differences between AS and controls were evaluated with generalised estimating equations (GEE), adjusted for demographics and cardiovascular risk, and stratified for gender.

Results: In total, 59 AS patients (mean disease duration 36 years) and 105 controls were included. Controls were significantly older than patients, but did not differ in cardiovascular profile (Table 1). Patients had a significantly lower retinal arteriolar tortuosity (β-0.1; p=0.02), and higher vessel density (β 0.5, p=0.02), than controls (Table 2). Also, male AS patients showed a lower arteriovenular ratio compared to male controls (β -0.03, p=0.04). There were no differences between women with and without AS. In AS, a high disease activity was associated with a wider (unfavorable) venular diameter (p=0.05), whereas biologic use showed a wider (more favorable) arteriolar diameter (p<0.01).

Conclusion: This study detected several retinal microvascular changes, in AS patients compared to controls, of which some are associated with CVD based on previous studies. Some changes were only observed in male-, but not in female, patients. A new finding was an increased capillary density in AS, of which the association with CVD-risk has not yet been studied before.

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Table 1. Patient characteristics AS (n=57) and controls (n=105)

	AS	Controls	*p*
Gender, women (%)	30 (51)	52 (50)	ns
Age, mean yrs (SD)	60 (6)	68 (4)	<0.01
Smoking currently, yes (%)	11 (19)	8 (8)	0.06
Body mass index, mean (SD)	26 (4)	26 (3)	ns
Hypertension, yes (%)	23 (39)	39 (37)	ns
Dyslipidemia, yes (%)	9 (15)	18 (17)	ns
Cardiovascular disease history, yes (%)	9 (15)	15 (14)	ns
NSAIDS (%)	24 (41)	6 (6)	<0.01
Biological (mostly TNF inhibitor)* (%)	29 (49)	0 (0)	<0.01
AS Disease Activity Score, mean (SD)	2.1 ±0.9		

Table 2. Retinal vascular parameters, differences AS and Control subjects

		Crude			Adjusted for: Age, gender, BMI smoking, hypertension, dyslipidemia		
Retinal vascular parameters		β	(95%CI)	p	β	(95%CI)	p
Diameter Arteriolar		1.6	(-2.0, 5.2)	0.37	-0.2	(-4.8, 4.4)	0.92
Venular		5.4	(-0.66, 11.5)	0.08	2.5	(-5.4, 10.4)	0.53
Arteriovenular ratio		-0.01	(-0.03, 0.01)	0.43	-0.01	(-0.03, 0.02)	0.65
Tortuosity	Arteriolar	-0.05	(-0.12, 0.03)	0.19	-0.1	(-0.2, -0.01)	0.02
Complexity	Fractal dimension	0.01	(0.00, 0.03)	0.04	0.0	(-0.02, 0.02)	0.88
Vessel Density	Inner ring	0.8	(0.5, 1.1)	<0.001	0.5	(0.1, 0.9)	0.02
	Outer ring	0.7	(0.4, 1.0)	<0.001	0.2	(-0.2, 0.6)	0.42

Disclosure of Interests: Rianne van Bentum: None declared, Milad Baniaamam: None declared, Buket Kinaci-Tas: None declared, Jacoba van de Kreeke: None declared, Pieter Jelle Visser: None declared, Erik Serné: None declared, Michael Nurmohamed Grant/research support from: Not related to this research, Consultant of: Not related to this research, Speakers bureau: Not related to this research, Irene van der Horst-Bruinsma Grant/research support from: AbbVie, Novartis, Eli Lilly, Bristol-Myers Squibb, MSD, Pfizer, UCB Pharma, Consultant of: AbbVie, Novartis, Eli Lilly, Bristol-Myers Squibb, MSD, Pfizer, UCB Pharma

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AB0729

ASSOCIATIONS BETWEEN CARDIAC CONDUCTION AND DISEASE CHARACTERISTICS IN AXIAL SPONDYLOARTHRITIS

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Background: Cardiac conduction defects are well-documented in axial spondyloarthritis. However, historical literature (many from an era when axSpA was less well managed compared to modern day) include patients with advanced disease that may explain their high prevalence. Many recent studies reply on administrative codes that may under-report conduction defects. Thorough examination of ECG measurements and axSpA characteristics are scarce.
Objectives: To describe a range of cardiac conduction measurements in axSpA and their association with disease characteristics.
Methods: We conducted a single-centre cross-sectional study of consecutive patients meeting the ASAS axial SpA criteria in Liverpool, UK. Patients were excluded if they had a known/symptomatic conduction defect. Disease assessment included BASDAI, spinal pain, BASFI, CRP, ESR, HLA-B27, BMI, the presence of extra-articular manifestations (uveitis, psoriasis, IBD) and use of NSAIDs and TNFi. Each patient underwent a 12-lead ECG (GE healthcare; MAC2000) to obtain: PR (atrio-ventricular conduction), QRS (ventricular depolarization) and QTc (ventricular de- and repolarization) intervals in milliseconds (ms). QTc was corrected for heart rate using Bazett's formula. Prolonged PR interval was defined as >200ms, prolonged QRS as >100ms and prolonged QTc as >440ms in men and >460ms in women. QT dispersion has been shown to predict a range of cardiac outcomes; we measured this as the difference between the longest and shortest QT in two consecutive cardiac cycles. Associations between patient characteristics and ECG measurements were assessed using univariable linear or logistic regression. Bonferroni correction was applied for multiple comparisons.
Results: 163 patients underwent ECG testing: mean age 52 (SD14) years, mean symptom duration 10 years (SD 9.6), 79% male and 74% HLA-B27 positive (among 78 tested). 1 patient had Wolf-Parkinson-White (accessory pathway). Summary of the 4 measurements are shown in Table 1. None of these 4 ECG measures were associated with age, symptom duration, gender, BMI, disease severity (BASDAI, spinal pain, BASFI and log transformed CRP/ESR), HLA-B27, EAMs or NSAIDs/TNFi.
Conclusion: Conduction defects were rare in this group of axSpA patients. Only 3% had prolonged AV conduction, which is no higher than general population estimates [1]. The prognostic value of these conduction defects and QT dispersion requires further study.
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[1] van der Ende et al. Population-based values and abnormalities of the electrocardiogram in the general Dutch population: The LifeLines Cohort Study. Clin Cardiol. 2017; 40(10): 865–872

Table 1. ECG measurements in 163 axSpA patients.

	Mean (SD)		n (%)
PR, ms	149 (24)	PR>200ms	5 (3%)
QRS, ms	91 (15)	QRS>100ms	25 (16%)
QTc, ms	385 (32)	QTc prolonged	6 (4%)
QT dispersion, ms	43 (21)	QT dispersion >50ms	41 (26%)

Disclosure of Interests: None declared
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AB0730

ASSOCIATION OF SPONDYLOARTHRITIS AND FAMILIAL MEDITERRANEAN FEVER AND IMPACT ON DISEASE PHENOTYPE: A SYSTEMATIC REVIEW OF THE LITERATURE

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Background: Spondyloarthritis (SpA) and Familial Meditaerranean fever (FMF) may co-exist in certain populations, and have some overlapping manifestations (oligo-arthritis, hip involvement). Their association may impact disease phenotype and may affect disease management.
Objectives: To evaluate the association of SpA and FMF and its impact on disease phenotype and management.
Methods: A systematic literature search was conducted with the keywords spondyloarthritis and familial mediterranean fever from Janurary 1990 to January 2020 in PubMed and using manual cross-reference methods.
Results: The search retrieved 74 articles, out of which 37 articles were relevant to the study question; most of the articles were case reports, with some large cohort studies of FMF and SpA (Flowchart in Figure 1).
In large FMF cohorts, the prevalence of SpA was higher compared to the general population (7.5-13%, OR around 10). M694V was a risk factor for SpA. These FMF-SpA patients were older at diagnosis, had lower fever attacks, and higher disease duration, inflammatory back pain, chronic arthritis, enthesopathy, persistent inflammation and higher resistance to Colchicine. In case series, they were responsive to anti-TNF therapy.
In large SpA cohorts, MEFV mutation, particularly M694V, was found in 15-35% (even without associated FMF). In most cohorts, MEFV mutation carriers didn't have any distinct disease phenotype, except for some reports of higher ESR, more hip involvement, higher BASFI and higher BASDAI. Genome-wide association studies and case reports suggest an implication for IL-1 and thus a role for Anakinra therapy in these patients.
Conclusion: In FMF or SpA patients with resistance to conventional therapy, the evaluation of disease association should be performed as it may have significant impact on disease management.
References:
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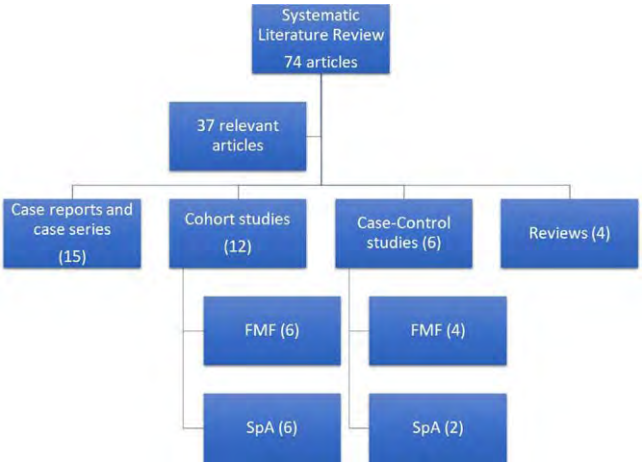


Figure 1. Flowchart of the systematic literature search (Spondyloarthritis, Familial Mediterranean Fever; January 1990-2020).

Disclosure of Interests: Nelly Ziade Speakers bureau: Abbvie, Janssen, Lilly, Novartis, Pfizer, Roche, Sanofi, Aref Nassar: None declared
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Psoriatic arthritis

AB0731

IMPACT OF FIBROMYALGIA ON DISEASE ACTIVITY INDICES, HEALTH RELATED QUALITY OF LIFE AND FATIGUE IN PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Psoriatic arthritis (PsA), causes inflammation in joints and enthesis, emotional instability and poor quality of life (QOL).[1] Fibromyalgia (FM) may coexist with PsA, complicating its diagnosis and management.[2] The effect of FM on the QOL and fatigue in PsA patients has not been vastly studied.[3]
Objectives: Assess the effect of FM on PsA patients' disease activity indices, QOL and fatigue.
Methods: This study included Group I: 37 PsA only patients (61.7%), 48.38 ± 11.69 years and group II: 23 FM-PsA patients (38.3%), 50.78 ± 11.8 years, according to classification criteria for PsA and 2016 Revisions to 2010/2011 FM diagnostic criteria. Psoriasis area severity index (PASI), disease activity in PsA (DAPSA), composite PsA activity index (CPDAI), PsA QOL and multidimensional assessment of fatigue (MAF) were assess in both groups. The severity and impact of FM was assessed in group II.
Results: Patients with FM-PsA had a statistically higher PsA disease activity in subjective measures only but not in objective measures. Table 1

Table 1. Comparison between the studied groups according to disease activity

	Group I (37)	Group II (23)	Test of Significance	P
	Mean ± SD		t	
CPDAI	8.68 ± 3.33 Median (Minimum – Maximum)	11.26 ± 2.03	3.735* U	<0.001*
PASI	8.3 (0 – 45.7)	14.4(0.9 – 49.6)	292.5*	0.043*
DAPSA	29 (14 – 89)	45.5 (20.5 – 99)	226.0*	0.002*
C-reactive protein (mg/dl)	6.3 (0.3 – 72)	6 (0.8 – 61.6)	409.5	0.802
68 Tender joint count	7 (2 – 64)	23 (8 – 68)	112*	<0.001*
66 Swollen joint count	2 (0 – 23)	4 (0 – 10)	300.5	0.055
Leeds enthesitis index	2 (0 – 6)	6 (3 – 6)	76.5*	<0.001*
Dactylitic count	0 (0 – 8)	0 (0 – 7)	421	0.924

U: Mann Whitney test
t: Student t-test
p: p value for comparing between the studied categories
*: Statistically significant at p ≤ 0.05

Patients in both groups had similar functional level by health assessment questionnaire (HAQ) (U=339, p=0.188) and QOL by PsAQOL (U=306, p=0.068). While, MAF was statistically higher in group II patients 34 ranging from 28 to 48.7 in group II vs 26.5 ranging from 0 to 49.5 in group I (U=172.5, p<0.001).
In group II patients: the mean tender point count was 16.50 ± 1.84, fibromyalgia severity scale (FSS) was 20.7 ± 3.99 and fibromyalgia impact questionnaire (FIQ) was 57.22 ± 7.30. There was a statistically significant correlation between FSS and DAPSA (r_s=0.59, p=0.003), PsAQOL (r_s=0.64, p=0.001) and HAQ ($r_{s=}$0.613, p=0.002), and between FIQ and PASI (r=0.488, p=0.018), PsAQOL (r=0.576, p=0.004), HAQ (r=0.557, p=0.006) and MAF (r=0.619, p=0.002).
Conclusion: These results might highlight the importance of considering FM as a contextual factor in disease activity assessment in patients with PsA, especially in those with discrepancies in TJC/patients reported outcomes versus SJC/inflammatory markers or persistently high disease activity indices.
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Disclosure of Interests: None declared
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AB0732

FATIGUE ASSESSMENT IN EGYPTIAN PSORIATIC ARTHRITIS PATIENTS: RELATION TO SERUM INTERLEUKIN 23, DISEASE ACTIVITY AND QUALITY OF LIFE.

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Background: Fatigue is a prevalent and fundamental phenomenon in psoriatic arthritis (PsA) patients. It often interferes with physical and social functions and may lead to social withdrawal, long-standing sick leave, disability and loss of work productivity. Fatigue is a prevalent symptom in patients with chronic rheumatic diseases. Cytokines as interleukin IL-23/17 play a pivotal role in the pathogenesis of PsA.
Objectives: To assess fatigue in PsA patients and determine its relation to serum IL 23 levels, disease activity, Skin severity, physical function and quality of life (QoL).
Methods: Fifty PsA patients and 46 matched healthy controls were included in this study. Skin severity based on the Psoriasis Area and Severity Index (PASI), the Disease Activity index for Psoriatic Arthritis (DAPSA) and the Functional Assessment of Chronic Illness Therapy (FACIT-F) were assessed. Physical function was assessed by the Health Assessment Questionnaire Disability Index (HAQ-DI) and health-related QoL was assessed using the Short Form Health Survey (SF-36), Psoriatic Arthritis QoL (PsAQoL) and the Dermatology Life Quality Index (DLQI). Serum IL-23 levels were measured in the studied groups.
Results: The study included 23 (46%) females and 27 (54%) males with a mean age of 42.78±12.33 years. The mean serum IL-23 level was significantly higher in PsA patients (50.89 ±13.86 pg/ml) than in controls (43.88 ± 6.34 pg/ml) (p=0.006). The FACIT score ranged from 2-41. Severe fatigue (score <30) was reported in 27 (54%) PsA patients. There were significant correlations between FACIT-F and (DAPSA, PASI, HAQ-DI, PsAQoL, DLQI and SF-36). No significant correlations could be detected between FACIT-F and serum levels of IL-23 and CRP.
Conclusion: Fatigue was a frequent complaint in PsA patients. There was a mutual negative impact between fatigue and each of PsA joint disease activity and physical function and it worsened the QoL. Fatigue was worsened with increased severity of skin PsO. Although serum level of IL-23 was significantly elevated in PsA patients than the controls, it wasn't correlated with fatigue score. Hence IL-23 can't be considered a biomarker for fatigue severity.
References:
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Table. Correlation between FACIT-F score and different parameters in patients group

	FACIT-F	
	r_s	p
DAPSA	-0.365*	0.009*
PASI	-0.424*	0.002*
HAQ-DI	-0.464*	0.001*
PsAQoL	-0.633*	<0.001*
DLQI	-0.492*	<0.001*
SF-36	0.600*	<0.001*
CRP	-0.167	0.247
Serum IL-23 levels	-0.183	0.204

r_s: Spearman coefficient, *: Statistically significant at p ≤ 0.05

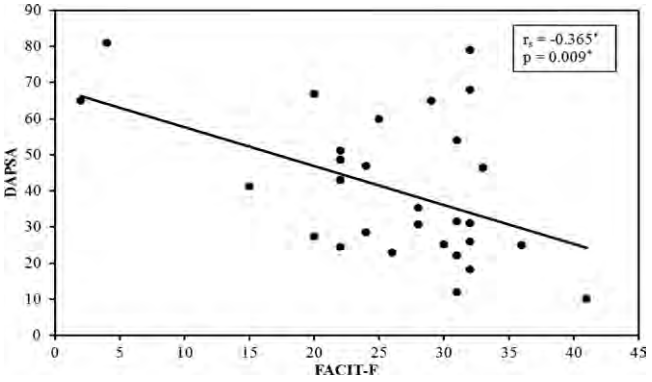


Figure. Correlation between FACIT-F and DAPSA in the studied PsA patients.

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AB0733

PSORIATIC ARTHRITIS IN NIGERIAN PSORIASIS PATIENTS - MYTH OR A MISSING LINK?

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Background: Beyond true arthritis, Psoriatic arthritis (PsA) is known with dactylitis and enthesitis. Enthesitis is postulated as the central pathogenic process in seronegative spondyloarthritis[1], and the primary finding in psoriatic arthritis[2]. Psoriasis (and more so PsA) were initially thought to be rare in West Africa. Psoriasis (Ps) is now reported increasingly in Nigeria. But the notion of the rarity of PsA still remains in the absence of systematic documentation of PsA among psoriasis patients, with few cases reported from Rheumatology clinics[3].

Objectives: This study set out to determine the prevalence of PsA among Nigerian Ps patients using the Classification for Psoriatic Arthritis (CASPAR) criteria, and to evaluate enthesitis amongst them.

Methods: This hospital-based, cross-sectional study was carried out at the dermatology clinic over an 18-month period. All patients seen within the study period with biopsy-established Ps were recruited. Fifty-three (53) Ps patients, 16 years or older, were enrolled. The CASPAR criteria was used to diagnose PsA. A modified Spondyloarthritis Research Consortium of Canada (SPARCC) enthesitis chart was used to document entheseal inflammation sites. Diagnosis of enthesitis was made by clinical examination.

Results: Fourteen participants fulfilled the CASPAR criteria (8 females, 6 males, F:M = 1.3:1) giving a PsA prevalence of **26.4%**. Using the Moll & Wright clinical classification, Oligo/Mono-articular pattern was the most documented (Fig 1). No patient had arthritis mutilans. Enthesitis was found in **ALL(100%)** PsA patients (Table 1). Highest frequencies were found in the right iliac, right patella and both plantar fascia (Fig 2). Multiple sites were involved in 87.5% of patients.

Conclusion: Psoriatic arthritis can not be considered rare among Nigerian Ps patients. Enthesitis has been suggested as the primary finding, and the initial site of inflammation in PsA[2,4]. Our findings reinforce these theories in an African population. Whilst other studies reported occurence of enthesitis in 30-50% of PsA patients[5], our study found 100%. Admittedly though a small study population, it suggests that enthesitis may well be the missing link to finding more PsA patients in Nigeria and Psoriasis patients of West African descent.

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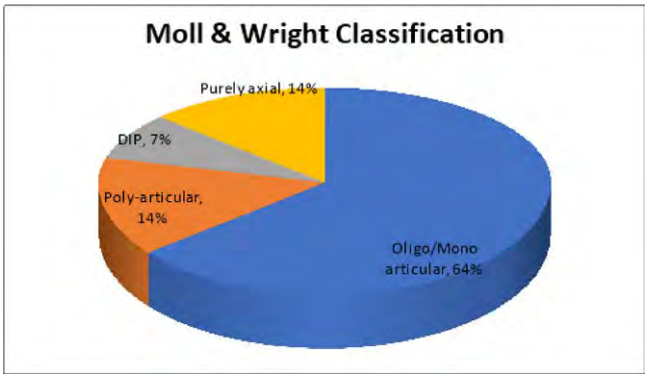


Fig 1. Moll & Wright articular patterns.

Table 1.

VARIABLE	PsA, n=14	No PsA, n=39	Sig
	n (%)	n (%)	
Inflammatory Eye Disease			
Yes	4 (28.6)	1 (2.6)	0.014f
No	10 (71.4)	38 (97.4)	

Table 1.

VARIABLE	PsA, n=14	No PsA, n=39	Sig
	n (%)	n (%)	
Nail Involvement			
Yes	8 (57.1)	13 (33.3)	0.066*
No	6 (42.9)	26 (66.7)	
Dactylitis			
Yes	3 (21.4)	0 (0)	0.016f
No	11 (78.6)	39 (100.0)	
Enthesitis			
Yes	14 (100)	1 (2.6)	0.000f
No	0 (0)	38 (97.4)	

PsA=psoriatic arthritis, f=Fischer's exact, *=Pearson's chi-square, sig=significance level.

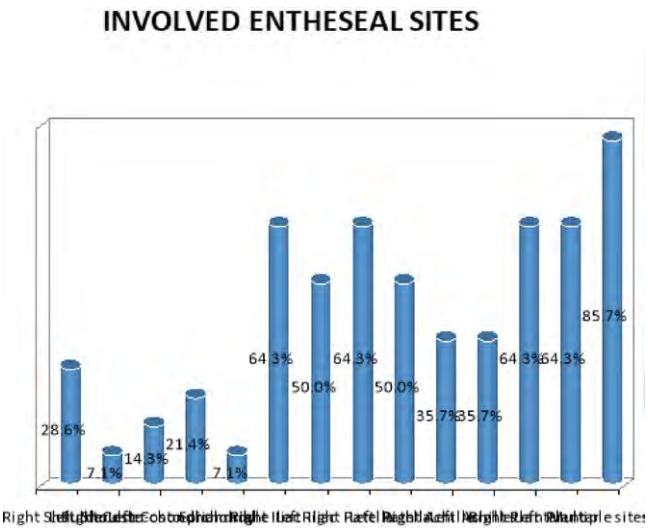


Fig 2. Enthesitis Distribution

Disclosure of Interests: None declared

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AB0734

EFFICACY AND SURVIVAL OF APREMILAST IN PATIENTS WITH PSORIATIC ARTHRITIS AND PSORIASIS IN REAL CLINICAL PRACTICE

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Background: Apremilast (APR) is a phosphodiesterase 4 Inhibitor. APR has been demonstrated to be an effective and safe therapy in the treatment of active psoriatic arthritis (PsA) and psoriasis in patients who were intolerant of or unresponsive to synthetic Disease-modifying Antirheumatic Drugs (DMARDs).

Objectives: To assess the effectiveness and survival rates of APR in a cohort of patients diagnosed with PsA and psoriasis with arthritis in real clinical practice.

Methods: An open, longitudinal, prospective, descriptive study. A total of 80 patients diagnosed with PsA or psoriasis with arthritis were included. All patients received the starting dose of oral APR as per the Summary of Product Characteristics and a maintenance dose of 30mg every 12 hours. The following variables were collected: age, gender, years of evolution, prior treatment with DMARDs, swollen and tender joint counts (SJC, TJC), C-Reactive Protein (CRP), and presence of dactylitis, enthesitis and cutaneous psoriasis. Treatment response was evaluated in all patients at 6, 12 and 18 months follow-ups. Efficacy in patients with PsA was evaluated using the Disease Activity in Psoriatic Arthritis (DAPSA)-based criteria: low activity (DAPSA 5-14) and clinical remission (DAPSA 0-4). To assess the level of enthesitis, Maastricht Ankylosing Spondylitis Enthesitis Score (MASES) index was used. Efficacy in patients with psoriasis was evaluated using the Psoriasis Area and Severity Index (PASI)-based criteria: PASI-75 (improvement ≥ 75% of the baseline PASI). Kaplan-Meier method was used for survival analysis.

Results: Of the 80 patients included in our cohort: 42 patients were diagnosed with PsA and 38 with psoriasis. 57,1% of patients with PsA and 63,2% of patients with psoriasis were men with a mean age of 48.2 ± 11.1 and 48.2 ± 14.8 and mean duration of disease 3.5 ± 1.4 and 3.2 ± 2.6 years respectively. Most of

the patients with PsA (93%) had cutaneous disease and enthesitis and dactylitis were present in 45% and 31% respectively. 95% of patients with PsA had received prior treatment with Metotrexate. At 6, 12 and 18 months, there was a statistically significant decrease from baseline in TJC, SJC and DAPSA scores. The decrease in the MASES index and the levels of PCR were not statistically significant (Table 2). According to DAPSA, at 18 months follow-ups, clinical remission rate was 77.8%, and low activity rate was 22.2%. 55% of patients with psoriasis reached PASI-75 at 18 months. APR survival rates at 6, 12 and 18 months was 67,85 %, 56,45% and 50,2 % in patients with ApS and 74,8%, 70,4% and 65,1 % in patients wiyh psoriasis.

Conclusion: APR is an effective drug for the treatment of psoriatic arthritis and psoriasis, reaching statistical significance according to DAPSA, and with a high survival rate after 18 months of treatment.

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Table 1. Disease characteristics in patients with PsA receiving APR

PATIENTS WITH PsA	Basal, mean±SD	6 Months, mean±SD	12 Months, mean±SD	18 Months, mean±SD	"p" value
TJC	3.3 ± 2.0	1.2 ± 2.3	1.1 ± 1.6	0.7 ± 1.1	*p=0.002
SJC	2.4 ± 1.6	0.4 ± 0.9	1.0 ± 2.0	0.3 ± 1.0	***p=0.001**
CRP	6.8 ± 6.3	3.5 ± 3.8	3.4 ± 3.9	2.7 ± 4.1	p=0.062
DAPSA	21.1 ± 5.6	5.6 ± 7.2	6.5 ± 8.5	2.9 ± 4.1	*p=0.000
MASES	1 ± 1.4	0.1 ± 0.5	0 ± 0	0 ± 0	p=0.16

Table 2. Disease characteristics in patients with Psoriasis receiving APR

PATIENTS WITH PSORIASIS	Basal, mean±SD	6 Months, mean±SD	12 Months, mean±SD	18 Months, mean±SD	"p" value
PASI	9.5 ± 6.6	4.1 ± 4.7	2.2 ± 2.6	3.4 ± 3.8	p=0.072

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.1237

AB0735

SEVERITY OF NAIL PSORIASIS SCORE (SNAPS) DEMONSTRATES LONGITUDINAL CONSTRUCT VALIDITY AGAINST THE MODIFIED NAIL PSORIASIS SEVERITY INDEX (MNAPSI) IN AN OBSERVATIONAL COHORT OF PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Longitudinal observational data on psoriatic nail dystrophy is scarce, in part due to the lack of a validated outcome measure that is feasible in routine care. The Severity of Nail Psoriasis Score (SNAPS; range 0-40: scored one point each for the presence of pitting, onycholysis, hyperkeratosis and/or severe nail disease[#] in each fingernail) has face validity and has recently demonstrated feasibility, reliability and cross-sectional construct validity against the modified Nail Psoriasis Severity Index (mNAPSI; range 0-130)[1].

Objectives: We aimed to assess the longitudinal construct validity of SNAPS against the mNAPSI and physician nail VAS (PhNVAS), and to determine the effect size and measurement error of these tools.

Methods: Consenting consecutive patients enrolled in the Bath Psoriatic Arthritis (PsA) longitudinal cohort underwent photography of their fingernails at baseline[1] and 6 months alongside routine clinical assessments. Dorsal images of individual fingernails were acquired using a tripod mounted DSLR camera. An angled mirror positioned distally aided identification of hyperkeratosis. Photograps were scored using SNAPS, mNAPSI and PhNVAS[1]. Paired statistical analyses were conducted to assess for change in scores from baseline to follow-up. Pairwise correlations between change in SNAPS and change in mNAPSI and PhyNVAS were assessed using Spearman's rho. Effect sizes and measurement error were calculated.

Results: Fifteen patients with a mean (±SD) age of 54.5 (±10.59) were assessed at 6 months. There was a significant reduction in both the mNAPSI and SNAPS scores (p<0.005), with improvements in the most frequently-observed manifestations[1] i.e. pitting, onycholysis, hyperkeratosis and crumbling (Table 1). No other feature specific to mNAPSI improved over time. There was no significant change using the PhyNVAS. There was a strong correlation between changes in SNAPS and the mNAPSI (Figure 1; rho = 0.838, p<0.001). The correlation between change in SNAPS and PhyNVAS was not statistically significant (rho =0.45, p=0.095) (Figure 1). The change in mNAPSI correlated moderately with the PhNVAS (rho = 0.540, p=0.038). mNAPSI was superior to SNAPS in most parameters of measurement error (Table 2). The mNAPSI and SNAPS had similar effect sizes as measured by the SRM (Table 2).

Conclusion: SNAPS demonstrates longitudinal construct validity against the mNAPSI in a small observational cohort of PsA patients as evidenced by a strong correlation between the measures, comparable effect sizes and sensitivity to change over time. Whilst measurement error parameters favored the mNAPSI, SNAPS may be a more feasible measure for studying nail disease in cohort studies.

References:

[1] Antony A, Hart D, Cavill C, Korendowych E, McHugh N, Lovell C, Tillett W. The 'Severity of Nail Psoriasis Score' (SNAPS) Is Feasible, Reliable and Demonstrates Construct Validity Against the mNAPSI in an Observational Cohort of Patients with Psoriatic Arthritis [abstract]. *Arthritis Rheumatol.* 2019; 71 (suppl 10).

Table 1. Outcomes at Baseline and at Follow-Up:

Outcome	Mean (SD) or Median (IQR) N=15		t-test or Wilcoxon Sign Rank test (p-value)
	Baseline	Follow-up	
SNAPS	13.0 [8.00-21.00]	5.0 [2.00-11.00]	0.002*
mNAPSI	22.0 [12.00-35.00]	6.0 [4.00-15.00]	0.001*
Physician Nail VAS	23.3 (22.90)	15.8 (15.22)	0.147
Physician Global VAS	18.0 [10.75-32.75]	15.0 [10.00-30.00]	0.455

Table 2. Measurement error of SNAPS, mNAPSI, PtNVAS and PhyNVAS

	SRM	SEM	SDC	SDC % (% of total score)	SDD	SDD% (% of total score)
SNAPS	1.15	1.71	6.72	16.79	3.36	8.40
mNAPSI	1.15	3.51	13.74	10.57	6.87	5.29
Physician Nail VAS	0.40	4.71	18.47	14.21	9.23	7.10

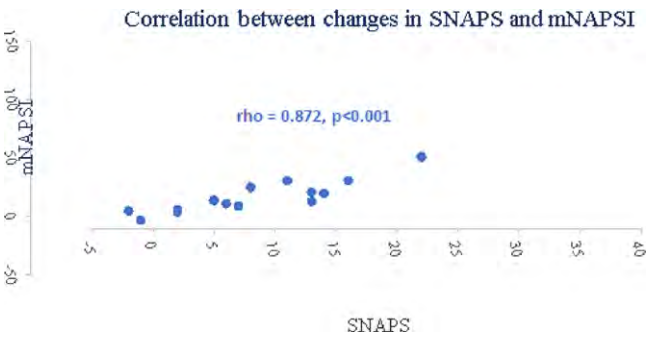


Figure 1. Correlation between changes in SNAPS and changes in mNAPSI

Disclosure of Interests: Anna Antony: None declared, Sadaf Saeed: None declared, Darren Hart: None declared, Preeti Nair: None declared, Charlotte Cavill: None declared, Eleanor Korendowych: None declared, Neil McHugh: None declared, Christopher Lovell: None declared, William Tillett Grant/research support from: AbbVie, Celgene, Eli Lilly, Janssen, Novartis, Pfizer Inc, UCB, Consultant of: AbbVie, Amgen, Celgene, Lilly, Janssen, Novartis, MSD, Pfizer Inc, UCB, Speakers bureau: AbbVie, Amgen, Celgene, Lilly, Janssen, Novartis, Pfizer Inc, UCB
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AB0736

SEVERITY OF NAIL PSORIASIS SCORE (SNAPS) IS SENSITIVE TO CHANGE IN A COHORT OF PATIENTS WITH PSORIATIC ARTHRITIS TREATED WITH ETANERCEPT

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Background: The Severity of Nail Psoriasis Score (SNAPS; range 0-40: scored one point each for the presence of pitting, onycholysis, hyperkeratosis and/or severe nail disease[#] in each fingernail) has been utilised to collect data regarding psoriatic nail dystrophy in the Bath Psoriatic Arthritis (PsA) Longitudinal cohort for many years. SNAPS has construct validity in PsA with the modified Nail Psoriasis Severity Index (mNAPSI) as a comparator instrument and appears to be more feasible than mNAPSI with excellent reliability[1].
Objectives: We aimed to determine if SNAPS could demonstrate longitudinal sensitivity to change in a cohort of patients treated with biological disease modifying anti-rheumatic drugs (bDMARDs) and therefore be utilized prospectively in observational and clinical trial settings.
Methods: Patients enrolled in the Bath PsA longitudinal cohort routinely undergo clinical assessments including a 66/68 Swollen and Tender Joint Count (SJC/TJC), Psoriasis Area Severity Index (PASI), Patient Global Assessment (PtGA) and Physician Global Assessment (PhGA), as well as complete patient-reported outcome measures such as the Health Assessment Questionnaire (HAQ) and Dermatology Quality of Life (Derm-QoL). All patients who commenced treatment with Etanercept and had available outcome data at baseline, 3 months and 6 months were included in this retrospective analysis. Baseline demographics were recorded and paired t-tests were utilized to assess the change in SNAPS at 3 and 6 months. The effect size and measurement error of SNAPS in this cohort were measured. Correlations between SNAPS and other outcome measures were assessed using Pearson's r.
Results: Fifty-seven patients (32 male and 25 female) with available data were retrospectively analysed. The mean (±SD) age of the cohort and duration of disease was 61.3 (±11.55) and 13.3 (±10.82) years respectively. The mean SNAPS at baseline was 3.7 (±6.13) and improved to 2.0 (3.74, p=0.018) at 3 months and 1.2 (2.40) at 6 months (p=0.001 for change from baseline and p=0.039 for change from month 3). The smallest detectable difference at 3 months for SNAPS in this cohort was 1.35, representing 3.37% of the range of the score (Table 2). The standardised response mean (SRM) was 0.32 at 3 months and 0.44 at 6 months. There was a modest correlation between the improvement in the SNAPS score and the improvement in PASI and Derm QOL at 3 months (r = 0.511 and 0.558 respectively, p=0.001) and 6 months (r= 0.672, p<0.001 and r=0.510, p=0.003 respectively).
Conclusion: SNAPS demonstrates sensitivity to change in response to treatment with a bDMARD and could be a potential outcome measure for the assessment of treatment efficacy in prospective studies.
References:

[1] Antony A, Hart D, Cavill C, Korendowych E, McHugh N, Lovell C, Tillett W. The 'Severity of Nail Psoriasis Score' (SNAPS) Is Feasible, Reliable and Demonstrates Construct Validity Against the mNAPSI in an Observational Cohort of Patients with Psoriatic Arthritis [abstract]. *Arthritis Rheumatol.* 2019; 71 (suppl 10).

Table 1. Outcomes at Baseline, 3 months and 6 months

	Mean (SD) or Median [IQR]		
	Baseline	3 Months (p for change from baseline)	6 Months (p for change from baseline)
PASI (0-72)	3.0 (4.80)	1.6 (2.12) p=0.01	1.3 (1.6) p=0.002
SNAPS (0-40)	3.7 (6.13)	2.0 (3.73) p=0.018	1.2 (2.39) p=0.001
Derm-QoL (0-30)	5.7 (7.07)	1.95 (3.23) p=0.001 (n=33)	1.9(4.72) p=0.037 (n=31)

Table 2. Measurement Error for SNAPS in an Etanercept Cohort

Timeframe	Standardised Response Mean	Standard Error of Mean	Smallest Detectable Change	Smallest Detectable Change (% of total score)	Smallest Detectable Difference	Smallest Detectable Difference (% of total score)
0-3 months	0.32	0.69	1.91	4.77	1.35	3.37
0-6 months	0.44	0.74	2.06	5.15	1.46	3.64

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AB0737

MEASUREMENT PROPERTIES OF RADIOGRAPHIC OUTCOME MEASURES IN PSORIATIC ARTHRITIS: A SYSTEMATIC REVIEW FROM THE GRAPPA-OMERACT INITIATIVE

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Background: Structural damage was identified as an important outcome domain in the Psoriatic Arthritis (PsA) Core Domain Set and should be assessed at least once in the development of a new therapeutic.
Objectives: To conduct a systematic literature review (SLR) to identify studies addressing the measurement properties (MPs) for ROIs and appraise the evidence through the OMERACT Filter 2.1 Framework Instrument Selection Algorithm (OFISA). [1]
Methods: An SLR was conducted in EMBASE and MEDLINE to identify full-text English studies developing or assessing MPs of ROIs in PsA. Determination of eligibility, data extraction and methodology asssessment were performed by 2 reviewers. MPs were rated according to the 'Provisional Standards' and assigned a Red/Amber/White/Green (RAWG) rating (Figure 1). [1, 2]
Results: 3621 references were screened, 531 full-text articles reviewed, and 12 were included (Figure 2). Nine instruments assessing peripheral radiographs and six assessing axial radiographs were identified (Table 1). Three of the nine peripheral radiographic instruments had adequate evidence for reliability and some evidence for construct validity: the modified Steinbrocker, Ratingen, and modified Sharp van der Heijde scores. There was scant evidence for reliability, construct validity and responsiveness for the axial ROIs, compounded by the lack of a standardized definition of axial PsA.
Conclusion: This SLR summarizes the MPs of ROIs and identifies relevant knowledge gaps that need to be addressed prior to endorsement of an instrument for the PsA Core Domain Set.
References:

[1] Richards P and De Wit M, editors. The OMERACT Handbook (March 2019)
[2] Mokkink LB and D'Agostino MA. Protocol for performing a systematic review on imaging techniques (unpublished)

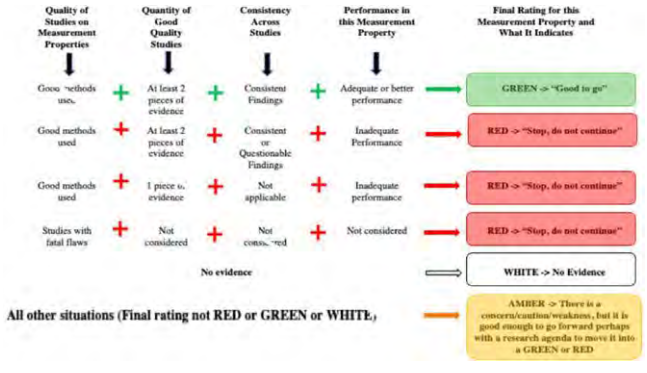


Figure 1. Criteria for the RAWG Rating

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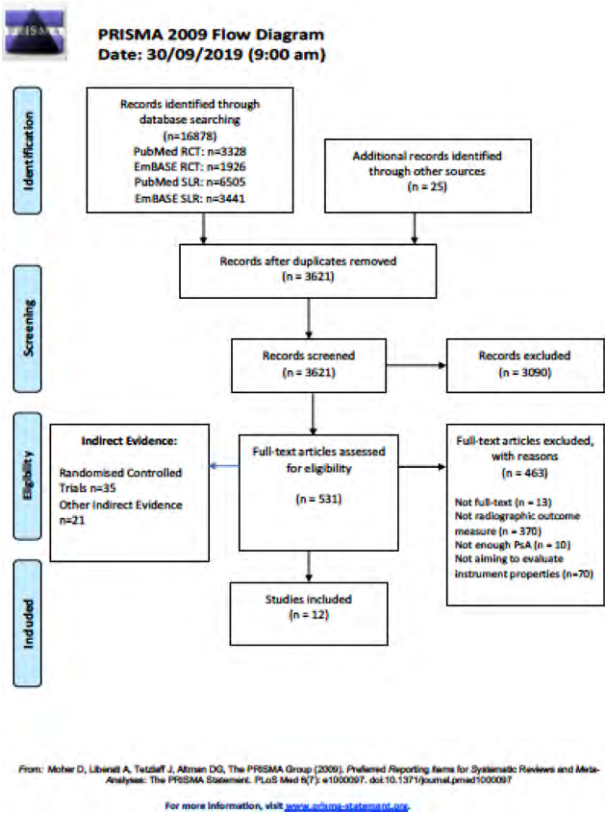


Figure 2. PRISMA Diagram

Gilead, Janssen, Novartis, Pfizer, UCB, Speakers bureau: Received speaker fees from Abbvie, Janssen, Novartis, Pfizer, UCB., Heidi Bertheussen: None declared, Lori Schick: None declared, Niti Goel Shareholder of: UCB and Galapagos, Consultant of: VielaBio, Mallinckrodt, and IMMVention, Alexis Ogdie Grant/research support from: Pfizer, Novartis, Consultant of: Abbvie, Amgen, BMS, Celgene, Corrona, Janssen, Lilly, Pfizer, Novartis, Ana-Maria Orbai Grant/research support from: Abbvie, Eli Lilly and Company, Celgene, Novartis, Janssen, Horizon, Consultant of: Eli Lilly; Janssen; Novartis; Pfizer; UCB. Ana-Maria Orbai was a private consultant or advisor for Sun Pharmaceutical Industries, Inc, not in her capacity as a Johns Hopkins faculty member and was not compensated for this service., Pil Hoejgaard: None declared, Laura C Coates: None declared, Vibeke Strand Consultant of: AbbVie, Amgen, Biogen, Celltrion, Consortium of Rheumatology Researchers of North America, Crescendo Bioscience, Eli Lilly, Genentech/Roche, GlaxoSmithKline, Hospira, Janssen, Merck, Novartis, Pfizer, Regeneron Pharmaceuticals, Inc., Sanofi, UCB, Dafna D Gladman Grant/research support from: AbbVie, Amgen Inc., BMS, Celgene Corporation, Janssen, Novartis, Pfizer, UCB – grant/research support, Consultant of: AbbVie, Amgen Inc., BMS, Celgene Corporation, Janssen, Novartis, Pfizer, UCB – consultant, Robin Christensen: None declared, Ying Ying Leung Speakers bureau: Novartis, Janssen, Eli Lilly, Philip J Mease Grant/research support from: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Eli Lilly, Novartis, Pfizer, Sun Pharmaceutical, UCB – grant/research support, Consultant of: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Eli Lilly, Novartis, Pfizer, Sun Pharmaceutical, UCB – consultant, Speakers bureau: Abbott, Amgen, Biogen Idec, BMS, Eli Lilly, Genentech, Janssen, Pfizer, UCB – speakers bureau, William Tillett Grant/research support from: AbbVie, Celgene, Eli Lilly, Janssen, Novartis, Pfizer Inc, UCB, Consultant of: AbbVie, Amgen, Celgene, Lilly, Janssen, Novartis, MSD, Pfizer Inc, UCB, Speakers bureau: AbbVie, Amgen, Celgene, Lilly, Janssen, Novartis, Pfizer Inc, UCB

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AB0738 **SAPHO OR PSORIATIC ARTHRITIS?: EVALUATION OF CASPAR CRITERIA IN A COHORT WITH SAPHO.**

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Table 1. Summary of Measurement Properties

				Discrimination					
				Reliability		Responsiveness			
ROI	Domain Match	Feasibility	Construct Validity	Inter-rater	Intra-rater	Measurement Error	Longitudinal Construct Validity	Clinical Trial Discrimination	Thresholds of Meaning
Original Steinbrocker Score				A	A		R		
				[1]	[1]		[1]		
Modified Steinbrocker Score		#		G	G	A	A		
				[2]	[2]	[1]	[2]		
Modified Larsen Score				A	A		A	*	
				[1]	[1]		[1]		
Ratingen Score		#	A	G	G	A	A		
			[1]	[3]	[3]	[3]	[1]		
mTSS-A				A	A	A			
				[1]	[1]	[1]			
mTSS-B		#		A	A	A	A	*	
				[1]	[1]	[1]	[1]		
mSvdHs		#	A	G	G	A	A	*	
			[2]	[2]	[2]	[1]	[1]		
ReXPsA			R						
			[0]						
SPARS		#	A	A	A				
			[1]	[1]	[1]				
Axial PsA Definition 1									
MSASSS		#	A		R				
			[2]		[0]				
BASRI - Total		#	A		R				
			[2]		[0]				
PASRI		#	A		R				
			[2]		[0]				
Axial PsA Definition 2									
MSASSS		#	A	R	A		A		
			[1]	[1]	[1]		[1]		
BASRI - Spine		#		R	A		A		
				[1]	[1]		[1]		
PASRI		#		A	A		A		
				[1]	[1]		[1]		
Modified NYC		#		R	A				
				[1]	[1]				
RASSS		#		R	A		A		
				[1]	[1]		[1]		

A = Amber, R = Red, G = Green
[Total available studies for synthesis following excluding studies with poor methodology]
* RCT data available but no published effect sizes
# Feasibility data available

Background: SAPHO syndrome (synovitis, acne, pustulosis, hyperostosis and osteitis) is an acronym created with the aim of encompassing within the same entity the findings present in a heterogeneous group of patients with various osteoarticular and cutaneous disorders. For years it has been debated whether it is an entity itself or if, on the contrary, it is a specific phenotype of psoriatic arthritis.
Objectives: Determine the relationship between SAPHO syndrome and psoriatic arthritis by comparing the classic criteria of SAPHO with CASPAR in patients previously diagnosed with SAPHO.
Methods: A retrospective study where patients with a diagnosis of SAPHO in the same center (1984-2018) were reviewed. Of a total of 95 patients that met the criteria of Benhamou et al., 46 were excluded due to lack of information to complete the minimum necessary data, so 39 patients were finally included in the study. Demographic data were registered, age at diagnosis, CASPAR criteria (active psoriasis, history of own or familial psoriasis, nail psoriasis, negative RF, dactylitis and new formation/juxta-articular bone proliferation), classical criteria of SAPHO and HLAB27. For the statistical analysis, a Chi-square is applied to determine the differences between the groups with / without CASPAR criteria.
Results: Of the sample of 39 subjects diagnosed with SAPHO, 15 patients (38%) met CASPAR criteria (4M/11W), with a median age at diagnosis of 42 years (range 21-50). Of them, 8 (60%) had active cutaneous psoriasis, 10 (73%) had a family or personal history of psoriasis, 6 (40%) had psoriatic nail dystrophy, 14 (93%) had negative FR, 3 (20%) had presented some episode of dactylitis and 10 (73%) had juxta-articular new bone formation. Of the 15 patients who met CASPAR criteria, 9 (67%) had synovitis, 2 (13%) acne, 4 (26%) pustulosis, 13 (87%) hyperostosis and 12 (80%) osteitis. HLAB27 was positive in 1 patient (2.5%) of the group that met CASPAR criteria. Of the patients who did not fulfill CASPAR criteria (9M/15W), the median age at diagnosis was 44.5 years (range 10-70). None of them had active cutaneous psoriasis, psoriatic nail distrophy or dactylitis, 1 (4%) had a family or personal history of psoriasis, all had RF- and 3 (12.5%) had juxta-articular bone new formation (Table 1). Synovitis was observed more frequently in patients who met CASPAR criteria than in those who did not (67% vs 25%, p 0.01). In contrast, osteitis was present more frequently in patients who did not meet CASPAR criteria (80% vs 96% p 0.05) and pustulosis, although it was not statistically significant (50% vs 26%, p 0.07). Among patients who did not meet CASPAR criteria only 1 met the 5 classic SAPHO criteria and another 3 met 4.

Table 1.

	CASPAR + (15)	CASPAR – (24)	
CASPAR CRITERIA			
Current psoriasis	60% (8)	0% (0)	
History of psoriasis	73% (10)	4% (1)	
Psoriatic nail dystrophy	40% (6)	0% (0)	
FR -	93% (14)	100% (24)	
Dactylitis	20% (3)	0% (0)	
Juxta-articular new bone formation	73% (10)	12.5% (3)	
SAPHO CRITERIA			
Synovitis	67% (9)	25% (6)	p 0.01
Acne	13% (2)	30% (7)	p 0.1
Pustulosis	26% (4)	50% (12)	p 0.01
Hyperostosis	87% (13)	92% (22)	p 0.3
Osteitis	80% (12)	96% (23)	p 0.05
HLAB27+	1 (2.5%)	0 (0%)	

Conclusion: Approximately one third (38%) of patients diagnosed with SAPHO meet criteria for psoriatic arthritis, the most notable variables being active psoriasis or a history of psoriasis. Synovitis manifests more frequently in patients with CASPAR criteria and osteitis more present in patients who did not meet them.

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AB0739 PSORIATIC ARTHRITIS RELATED-UVEITIS, OUR EXPERIENCE IN A THIRD-LEVEL SPANISH CENTRE.

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Background: The occurrence of uveitis in patients with psoriatic arthritis (PsA) has been documented as the most frequent and important extra-articular manifestation, with an estimated frequency of 7 and 18%. Clinical onset may be acute or insidious, and it may be accompanied by other ocular manifestations. In contrast with spondyloarthropathy related-uveitis, PsA associated tends to be insidious, bilateral, chronic or posterior.
Objectives: To describe clinic and immunological features of psoriatic arthritis patients in our centre, especially those with associated-uveitis and to define its frequency.
Methods: A retrospective, descriptive and single-centre study (1985-2017) of 494 patients diagnosed with PsA according to the criteria of an expert rheumatologist was conducted. All patients were studied according to a standard protocol. The group was divided into 3 articular categories: pure axial, pure peripheric and mixed. Data regarding enthesitis and dactylitis, as well as HLA-Cw6 and HLA-B27 were extracted, from those available. Ophthalmologic and cutaneous involvement was registered. 216 patients were excluded because of data absence or alternative plausible diagnosis. Descriptive analyses were applied.
Results: Eight patients had uveitis (2,9% in this series), only one case developed chronic pattern. Acute anterior uveitis was the form of presentation in 6 patients (75%). Unilateral involvement was registered in 3 (37,5%), in every case with right eye implication. One patient developed up to 13 episodes of acute anterior uveitis, every episode in the same eye. Median of age at first episode was 54 years, 3 (37,5%) patients were female. Regarding articular categories: 1(12,5%) pure axial, 3 (37,5%) pure peripheric and 4 (50%) mixed. Enthesitis was registered in 2 patients, none of our series developed dactylitis. 3 patients (37,5%) were HLA-B27 positive and 2 patients (25%), HLA-Cw6 positive. 6 cases had cutaneous psoriasis (75%). Adalimumab was prescribed to 5 PsA related-uveitis patients with optimal control of disease.
Larger PsA cohort without ocular involvement (270 patients), 118 (42,4%) cases were female and median of age was 44 years. Pure axial involvement was present in 20 (7,2%), pure peripheric, 134 (48,2%) and mixed, 122 (43,8%). 31 (11,15%) cases developed enthesis involvement and 18 (6,5%), dactylitis. HLA-B27 was tested positive in 45 patients (19,7%) and HLA-Cw6, in 56 (27,4%). Cutaneous psoriasis was present in 231 cases (83,1%).
Conclusion: Frequency of psoriatic arthritis-uveitis is lower in our sample than referred in bibliography. Further investigations are needed to understand the underlying reasons, although it could be related to the use of biologic treatment and narrower inflammatory activity control in comparison to previous studies. No posterior pole involvement, bilaterality, chronicity nor insidious onset are common in our data; neither axial involvement seems to be predictor for the appearance of uveitis.
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AB0740 SECOND-LINE BIOLOGIC DMARDS SURVIVAL IN PSORIATIC ARTHRITIS. DATA FROM A SPANISH THIRD-LEVEL HOSPITAL.

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Background: Psoriatic arthritis (PsA) covers a wide spectrum of disease manifestations, including arthritis, enthesitis, dactylitis and axial spondylitis. This range of symptoms presents a challenge to the treating physician. Biologic disease-modifying antirheumatic drugs (bDMARDs) have proven effective through randomized clinical trials; and most international PsA guides include them as main option upon first-line treatment failure. However, studies regarding drug efficacy after bDMARD switching are scarce, lower response rates and drug survival on consecutive lines has been explored in previous research.
Objectives: To assess bDMARDs survival after first-line failure in PsA patients treated in a third-level hospital and to determine baseline clinical and laboratory parameters associated with drug survival.
Methods: We conducted a retrospective, single-centre study. 47 patients who received a second-line bDMARD were included, with diagnosis of PsA according to the criteria of an expert rheumatologist. All patients were studied according to a standard protocol. Data regarding bDMARD prescribed, baseline characteristics, axial or peripheral involvement and immunological profile (included both HLA-B27 and HLA-Cw6) were extracted. C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) at bDMARD start were included, as well. Kaplan-Meier, log-rank analyses and Cox regression models were applied.
Results: Of 47 patients receiving a second bDMARD, 55,3% (26) were female and mean (S.D.) age was 40,6 (12,52) years. Median (interquartile range) disease duration was 10,1 (3,7-14,8) years. Prescribed drugs were Adalimumab (ADL) (36,2%, 17), Etanercept (ETN) (27,6%, 13), Infliximab (IFX) (6,4%, 3), Golimumab (GOL)

(10,6%, 5), Certolizumab (CTZ) (4,3%, 2), Secukinumab (SCK) (8,5%, 4) and Apremilast (APR) (6,4%, 3). 42,3% cases suffered from axial involvement, rest of the sample (57,6%) presented a pure peripherical form of PsA. HLA-B27 and -Cw6 were assessed in 80,9% (38) and 68,1% (32), respectively; of whom, HLA-B27 carriers were 10,5% and HLA-Cw6 positive, 46,9%. Mean CRP level was 10,25 mg/L and mean ESR was 23,17 mm. Patients showed mean and median global drug retention of 44,57 (29,8-59,3) and 23 months. At 12-month visit, drug survival was 70%, 47% at 24 months, and 33% at 4 years from onset. Mean drug persistence by bDMARD prescribed was: ADL, 62,1 months; ETN, 51,9 months; IFX, 39 months; GOL, 22,8 months; CTZ, 9,5 months; SCK, 13,5 months; and APR, 16,3 months. Through log-rank analyses, differences in drug retention were investigated by several variables. Female sex (30,35m, 16,5-44,2 m.) was identified as statistically significant different than male patients (62,5m, 35,6-89,4m, p=0,021). Although not significant, other differences were remarkable: non-axial involvement, HLA-Cw6 negativity, HLA-B27 positivity and CRP level over 5 mg/L. No differences were found between altered and normal ESR patients.

Conclusion: Second-line bDMARD survival is lower in female PsA patients, according to our data and previous bibliography. Despite our reduced sample and possible bias, non-axial involvement, absence of HLA-Cw6, presence of HLA-B27 and higher levels of CRP at biologic onset might be predictors of better drug persistence. Further investigations are required on this field.

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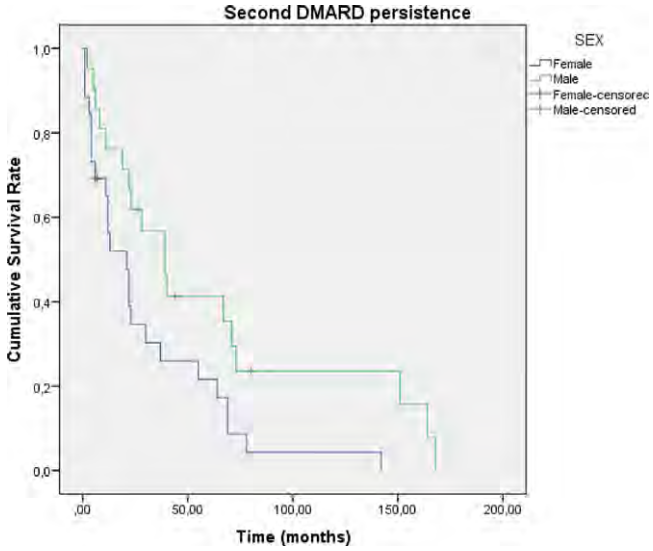


Table 1. Kaplan–Meier survival analysis of persistence according to sex.

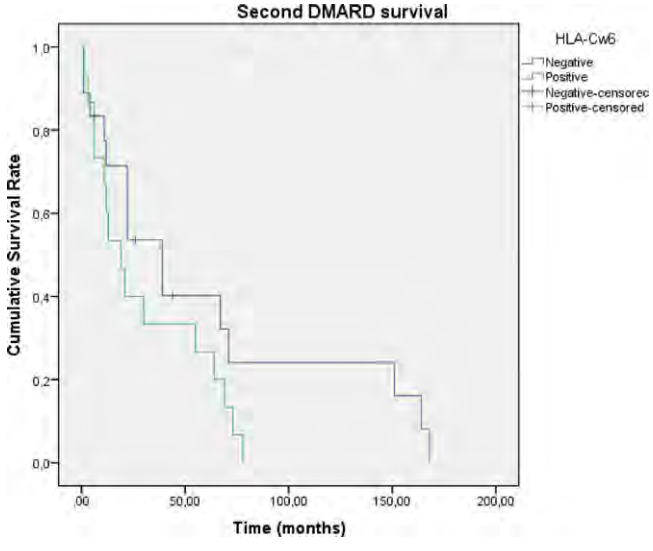


Table 2. Kaplan Meier survival analysis of persistence according to HLA-Cw6.

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AB0741

IS THE THERAPEUTIC TARGET ACHIEVEMENT INCREASING OVER TIME IN PATIENTS WITH PSORIATIC ARTHRITIS STARTING BIOLOGICAL THERAPY? DATA FROM 15 YEARS.

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Background: Treatment in Psoriatic Arthritis (PsA) has undergone a major revolution in recent years, with the development of new targets and molecules. Despite these advances, data from clinical practice demonstrating a change in management success are scarce.

Objectives: To evaluate if the proportion of patients (pts) with PsA maintaining an acceptable medium-term control of the disease activity after starting a first biologic agent is increasing over time.

Methods: Prospective cohort including 101 patients (pts) with PsA starting a 1st biologic (TNF inhibitor, anti-IL 17 inhibitor) in a tertiary hospital between 2002-2018. Demographic, clinical and laboratory data were collected at the beginning of treatment. Disease activity indexes (ASDAS for axPsA and DAPSA for pPsA) were collected before starting biologic, six and twelve months later (baseline, 6m and 12m visit, respectively). Low disease activity (LDA) was defined as ASDAS < 2.1 (axPsA) and DAPSA ≤14 (pPsA). Three groups were established according to biologic initiation date: period 1 (p1) (between 2002-2007), (p2) 2008-2013 and (p3) 2014-2018. Each period had a minimum follow-up of 1 year for every patient. For each interval, the percentage of pts achieving persistent (at both follow-up visits) LDA was determined, as a marker of acceptable medium-term control of the disease. All collected variables were compared between groups by ANOVA and Chi-Squared test.

Results: Out of the 101 pts initiating biological therapy, 46 % were males and 57 % had peripheral PsA. At the biologic treatment start, mean ± SD age was 48.5 ± 12 years and disease duration was 9.9 ± 10 years. Biological therapies initiated included etanercept in 38 % of pts, infliximab in 24 %, adalimumab in 25 %, golimumab in 7 %, secukinumab in 3 % and certolizumab in 3 %.

Stratified by time intervals, 36 (35.6%) pts started in p1, 36 (35.6%) in p2 and 29 (28.8%) in p3. Baseline characteristics of pts by periods are shown in Table 1. For patients in p3, compared to the previous intervals, a significant lower CRP (p=0.03) and ESR (p=0.004) were found at baseline, whereas there were no significant differences on baseline disease activity indices. Fifty-one (50%) pts achieved persistent-LDA after one year of starting biologic. Figure 1 reports the total number of patients that were in LDA in all the visits in the 1st year, stratified per period of time and predominant manifestation. A lower percentage of patients in LDA (33% in p1 vs, 67% in p2 vs 52% in p3, p = 0.02) was found in the first interval, in comparison to the most recent periods. The difference in response between p2 and p3 is mainly due to the group of patients with pPsA, whereas the improvement in the group of patients with axPsA remains constant in both periods.

Conclusion: The percentage of pts with PsA achieving LDA status after one year of initiating a biological therapy has substantially increased over time. A lower threshold of inflammation at biological therapy start and a broader spectrum of therapies might explain this better management on PsA.

Table 1. Baseline patient's characteristics by periods of time

	2002-2007 (n=36)	2008-2013 (n=36)	2014-2018 (n=29)	p-value
Characteristics at the beginning of biological therapy				
Age at starting biologic, years (m± SD)	47±11.5	49±11.7	49±14.3	0.7
Male sex, n (%)	13 (36)	23 (64)	11 (38)	< 0.05
Peripheral PsA, n (%)	22 (61)	16 (44)	20(69)	0.1
Erosions, n (%)	14 (40)	7 (20)	7(20)	0.1
Non-smokers, n (%)	23 (64)	25 (71)	14 (50)	0.2
BMI (m± SD)	27±5.5	27±4.2	25.5±3,6	0.2
Disease duration, years (m± SD)	9.9±10	8.8±7.4	8.2±10.0	0.8
RF +, n (%)	3 (8)	0	7 (10)	0.2
HLA B27, n/N (%)	3/8 (37)	3/18 (16)	4/18 (22)	0.5
DMARDs (MTX/SSZ), n (%)	26 (72)	30 (83)	24 (83)	0.4
Methotrexate, n (%)	22 (61)	24 (67)	20 (69)	0.8
Sulfasalazine, n (%)	12 (11)	7 (19)	7 (24)	0.4
Baseline CRP (m± SD)	12.5±15.8	12.8±17.0	6.5±5.9	< 0.05
Baseline ESR (m± SD)	31.5±20.7	26.2±22.0	15.6±10.8	< 0.01
Baseline DAPSA (m± SD)	27.3±11.2	24.7±14.3	20±14.3	0.2
Baseline ASDAS m± SD)	3.4±1.0	3.1±1.2	2.9±1.1	0.4

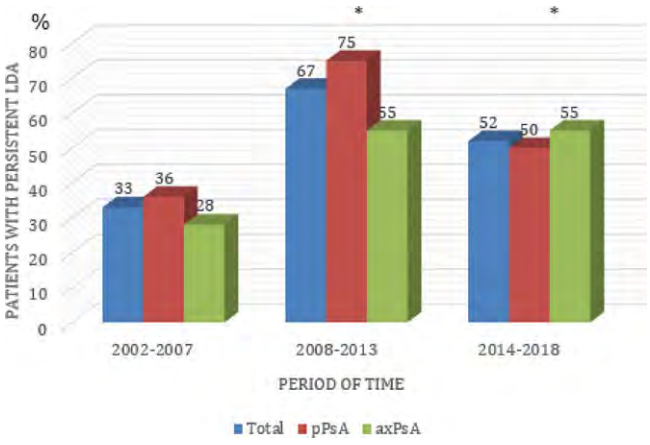


Figure 1. Patients achieving persistent-LDA during the 1st year of biological therapy, stratified by period of time and by disease. ** Statistically significant difference with respect to p1.*

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AB0742

CONVENTIONAL SYNTHETIC DMARDS IN PSORIATIC ARTHRITIS - CHANGING PRACTICE IN BIOLOGIC ERA: REAL-LIFE RESULTS FROM HURBIO-PSA REGISTRY

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Background: Conventional synthetic disease modifiying anti-rheumatic drugs (csDMARDs) are recommended as the first-line treatment options for most of the psoriatic arthritis (PsA) patients. In the last two decades, biologic drugs become more accessible and their percentage in the daily practice is increasing continuously. However, how they influenced the utilization of csDMARDs still remains unknown, yet.

Objectives: To determine the utilization rates of PsA patients before, after and at the starting of biologic DMARDs

Methods: We analyzed all patients who received at least 1 dose of biologic DMARDs, registered to HURBIO-PsA database, and who have complete data regarding csDMARD use before (ever), after (at last control visit) and at the starting of biologic DMARD. Methotrexate, leflunomide and sulphasalasine were the csDMARDs recorded. Demographic data of these patients were also recorded.

Results: A total of 426 (70% female) PsA patients was included. Mean age and mean PsA disease duration were 48±12.4 and 9.3±8.3 years, respectively. Mean duration of csDMARD utilization before bDMARDs was 5.8±5.1 years, and mean follow-up duration under bDMARDs was 3.7±2.5 years. Distribution of the bDMARDs that ever-prescribed as follows: adalimumab 273 (64.2%), etanercept 125 (29.3%), certolizumab pegol 103 (24.2%), infliximab 102 (24.0%), secukinumab 63 (14.8%), golimumab 55 (12.9%), ustekinumab 24 (5.6%) and tofacitinib 11 (3.4%). Percentage of each csDMARDs used before (ever used), after (at last control visit) and at the starting of biologic DMARDs were given in **Figure**. Also the percentage of patients using csDMARD as monotherapy and combination therapy were given in **Figure**.

Conclusion: csDMARDs particularly sulphasalazine and methotrexate were important treatment options before bDMARD period, however they (particularly SSZ) were usually discontinued after bDMARD initiation. Rate of concomitant csDMARDs use remains relatively stable after starting the bDMARDs. Besides, rate of concomitant mono/csDMARD use is significantly higher after bDMARD initiation, in contrast to pre-bDMARD period.

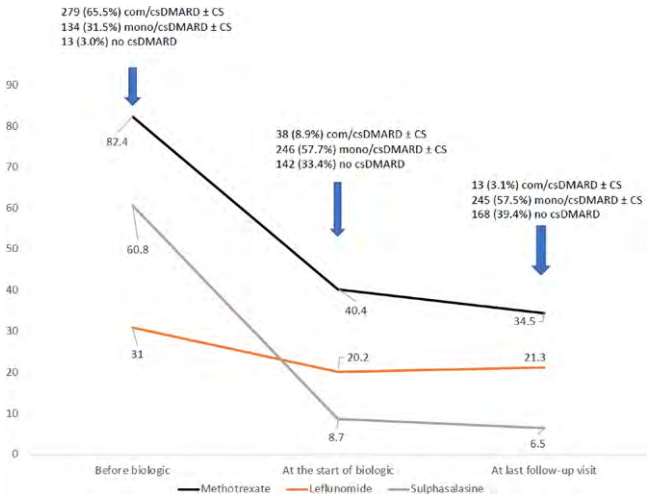


Figure. Percentage of each csDMARDs, and mono or combination of csDMARDs used before (ever used), after (at last control visit) and at the starting of biologic DMARDs (*com/csDMARD: combination csDMARD; mono/csDMARD: monotherapy of csDMARD; csDMARD: conventional synthetic disease modifying antirheumatic drug*).

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AB0743

DISEASE CHARACTERISTICS OF PSORIATIC ARTHRITIS PATIENTS MAY DIFFER ACCORDING TO AGE AT PSORIASIS ONSET: CROSS-SECTIONAL ANALYSIS OF PSORIATIC ARTHRITIS-INTERNATIONAL DATABASE

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Background: Psoriasis and psoriatic arthritis (PsA) are heterogenous diseases with various disease manifestations and phenotypes. Psoriasis has a bimodal age of onset being early (before the age of 40, type 1) and late. The impact of this classification on the PsA features is not well understood.

Objectives: To compare the PsA characteristics of patients with early- and late-onset psoriasis in a large, multicenter database

Methods: PSART-ID (Psoriatic Arthritis-International Database) is a prospective, multicenter web-based registry (www.trials-network.org) of patients with PsA. A detailed data collection was performed including demographics (sex, age, duration of education, smoking status, BMI), skin features (psoriasis onset date, type, initially involved site of skin, nail involvement (ever) and family history) and PsA characteristics (type of articular involvement and presence of axial, dactylitis (ever), enthesitis (ever), family history) and indices for disease activity and function (DAPSA, Leeds enthesitis index, BASDAI, BASFI, patient and physician global assessment, pain, HAQ-DI). We grouped according to the age at psoriasis onset (early onset, psoriasis before the age of 40 (EOPsO); late-onset, psoriasis after the age of 40 (LOPsO)), patient and disease characteristics of the groups were compared (1). Due to the differences among groups, following adjustments weer made: BMI for age, nail involvement for PsO disease duration, axial PsA for PsA disease duration.

Results: A total of 1634 (62.8% females; EOPsO, 1108 (67.8%); LOPsO, 526 (32.2%)) patients with PsA was recruited. Rate of over-weight patients was higher in LOPsO group (66.8% vs. 86.8%, p<0.001; adjusted for age - aOR 1.55 (1.11-2.20; % 95 CI)). The EOPsO group had the scalp involvement as the initial site of skin disease more often than the LOPsO group (56.7%

vs. 43.0%, p<0.001), whereas extremity involvement was more frequent as the initial finding in the LOPsO group (EOPsO vs. LOPsO 63.8% vs. 74.2%, p<0.001). Nail involvement (ever) was more prominent in EOPsO group, however, the significance was disappeared when adjusted for psoriasis duration. Interaction between gender and both axial disease and psoriatic disease family history were found (axial disease in man; EOPsO vs LOPsO; 38.0% vs. 25.4%; p=0.005; adjusted for PsA duration - aOR 0.56 (0.38-0.84; %95 CI) // psoriatic disease family history in females; EOPsO vs LOPsO; 39.5% vs. 30.1%; p=0.003; OR 0.65 (0.50-0.86; %95 CI)). Duration between PsO and PsA was significantly longer in EOPsO group (148 vs. 24 months, p<0.001). In EOPsO group, more patients had PsO preceeding PsA than LOPsO group (81.8% vs. 60.6%, p<0.001), however, synchronous disease -defined as the diagnosis of PsO and PsA within the same year- was more common in LOPsO group (16.6% vs. 30.3%, p<0.001) (Table 1). Psoriatic disease activity parameters, patient and physician reported outcomes and HAQ-DI scores were similar in both groups.

Conclusion: Clinical features of PsA may be affected by the age at the onset of psoriasis. As the genetic background is different in early and late-onset psoriasis, this may suggest a different pathogenetic mechanism based on the psoriasis phenotype, also affecting the PsA features. Further prospective studies are needed to define whether the classification of PsA requires including psoriasis phenotypes as well.

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Table 1. Comparison of psoriatic arthritis patients' characteristics according to age at psoriasis onset

Variable	EOPsO (n=1108, 67.8%)	LOPsO (n=526, 32.2%)	Overall (n=1634)	Odds ratio (%95 CI)	P value
Age, mean (SD)	41.5 (11.8)	58.3 (8.3)	46.9 (13.3)	--	<0.001
Female, n (%)	674 (60.8)	352 (66.9)	1026(62.8)	0.76 (0.61-0.95)	0.017
BMI, mean (SD)	27.6 (5.2)	29.5 (5.0)	28.2 (5.2)	------	<0.001
≥ 25, n (%)	736 (66.8)†	454 (86.8)	1190 (73.3)	3.26 (2.46-4.32)	<0.001
				1.55 (1.11-2.20)†	0.011
Psoriasis (PsO)					
Age at diagnosis, mean (SD)	23.5 (9.4)	50.4 (7.2)	32.1 (15.3)	--	<0.001
Disease duration, mean (SD) (year)	18.1 (12.2)	7.8 (6.5)	14.7 (11.7)	--	<0.001
Initial scalp inv., n(%)*	560 (56.7)	193 (43.0)	753 (52.5)	1.74 (1.32-2.18)	<0.001
Initial torso inv. n(%)*	208 (21.1)	84 (18.7)	292 (20.3)	1.16 (0.87-1.54)	0.32
Initial extremity inv. n(%)*	629 (63.8)	333 (74.2)	962 (67)	0.61 (0.47-0.78)	<0.001
Initial genital inv. n(%)*	73 (7.4)	29 (6.5)	102 (7.1)	1.15 (0.74-1.80)	0.52
Plaque psoriasis (+), n(%) **	649 (80.8)	295 (80.2)	944 (80.6)	0.95 (0.70-1.30)	0.81
Pustuler psoriasis (+), n(%)**	144 (17.9)	69 (18.8)	213 (18.2)	1.05 (0.76-1.45)	0.73
Nail involvement (ever), n(%)	552 (50.0)	222 (42.2)	774 (47.5)	1.36 (1.10-1.68)	0.003
				0.99 (0.78-1.25)††	0.96
Psoriatic Arthritis (PsA)					
Age at diagnosis, mean (SD)	35.8 (11.2)	54.2 (8.4)	41.7 (13.4)	--	<0.001
Disease duration, mean (SD)	5.7 (7.6)	4.2 (5.2)	5.2 (7.0)	--	<0.001
Monoarthritis, n(%)	30 (2.7)	20 (3.8)	50 (3.1)	1.42 (0.80-2.53)	0.22
Oligoarthritis, n(%)	344 (31.1)	163 (31.2)	507 (31.1)	1.01 (0.82-1.26)	0.98
Polyarthritis, n(%)	542 (49.1)	246 (47.0)	789 (48.5)	0.90 (0.72-1.11)	0.42
Arthritis mutilans, n(%)	3 (0.3)	1 (0.2)	4 (0.2)	0.70 (0.07-6.78)	0.76
Axial disease, n(%)					
- Female	187 (27.8)	78 (22.3)	265 (25.9)	0.76(0.56-1.03)‡	0.08
- Male	164 (38.0)	44 (25.4)	208 (34.4)	0.56(0.38-0.84)‡	0.005
DIP involvement, n(%)	164 (14.8)	76 (14.5)	240 (14.7)	0.97 (0.72-1.30)	0.86
Dactylitis (ever), n(%)	245 (23.4)	123 (24.7)	368 (22.9)	1.07 (0.83-1.38)	0.56
Enthesitis (ever), n(%)	255 (25.0)	129 (26.3)	384 (23.5)	1.07 (0.84-1.37)	0.56
CASPAR, mean (SD)	3.64 (1.1)	3.58 (1.1)	3.62 (1.1)	--	0.25
CASPAR (+), n(%)	959 (86.7)	444 (84.7)	1403(85.9)	0.85 (0.63-1.14)	0.28
Psoriatic disease					
PsO before PsA, n(%)					<0.001
- Yes	925 (83.6)	328(62.1)	1253(76.6)	3.14 (2.48-3.98)	<0.001
- No	20 (1.8)	51 (9.6)	71 (4.3)	0.17 (0.10-0.29)	<0.001
- Synchronous	161 (14.6)	149 (28.3)	310 (19.1)	0.43 (0.34-0.55)	<0.001
Family history, n(%)					
- Female	266 (39.5)	106 (30.1)	372 (36.3)	0.65 (0.50-0.86)	0.003
- Male	127 (29.3)	52 (29.9)	179 (29.4)	1.03 (0.70-1.51)	0.87
Duration between PsO and PsA, (month), med (min-max)	148 (-218, 797)	24(-240, 313)	80 (-240,797)	--	<0.001

*n=1435, **n=1171, †:adjusted for age ,††: adjusted for psoriasis duration, ‡: adjusted for psoriatic arthritis duration
BMI: Body mass index, CASPAR: ClASsification criteria for Psoriatic Arthritis, DIP: Distal Interphalangeal

AB0744 **PSORIATIC DISEASE AND BODY COMPOSITION: A SYSTEMATIC REVIEW OF THE LITERATURE**

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Background: There is emerging evidence of a relationship between psoriasis and metabolic syndrome, increased prevalence of cardiovascular risk factors and adverse cardiovascular outcomes. Obesity is a risk factor for psoriatic disease itself but there has been less emphasis on body mass alterations and the distribution between separate compartments: fat-free tissue (lean body mass), extracellular water and adipose tissue. Body composition is a term used to describe the percentages of fat, bone, water and muscle in human bodies and is an emerging tool in assessment of physical fitness and metabolic health, although its role in disease is less well appreciated.

Objectives: To identify whether psoriatic patients, including those with psoriatic arthritis, confer specific and recognizable body composition changes compared

Figure 1. Flow diagram of articles included in this review

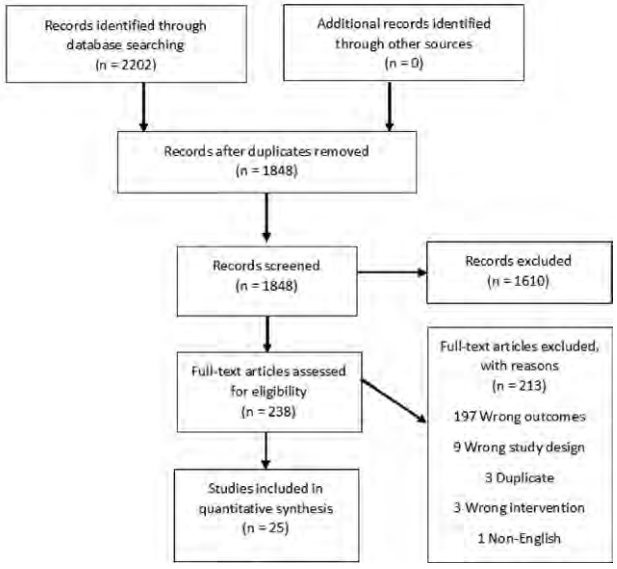


Table 1. Body composition outcomes by modality

	Study	Design	Pso vs HC
Bioimpedance analysis (BIA)	Barone et al., 2018	Cross-sectional	+
	Barrea et al., 2015	Cross-sectional	+
	Barrea et al., 2016	Cross-sectional	+
	Demirel et al., 2013	Cross-sectional	ND
	Engin et al., 2014	Case-control	+
	Galluzzo et al., 2017	Cross-sectional	+
	Galluzzo et al., 2018	Prospective cohort	+
	Krajewska-Wlodarczyk et al., 2017	Cross-sectional	+
	Romani, Caixas et al., 2012	Cross-sectional	+
	Romani, Caixas, Ceperuelo et al., 2012	Cross-sectional	+
Dual energy X-ray absorptiometry (DXA)	Diniz Mdos et al., 2016	Cross-sectional	+
	Kofoed et al., 2012	Cross-sectional	+
	Leite et al., 2015	Cross-sectional	+
	Leite et al., 2018	Randomised control trial	+
	Renzo et al., 2011	Prospective cohort	+
	Tournadre et al., 2017	Cross-sectional	+
Ultrasonography	Gonul et al., 2017	Cross-sectional	+
Transthoracic echocardiography	Akyildiz et al., 2014	Cross-sectional	+
Computed tomography (CT)	Balci et al., 2010	Cross-sectional	+
	Balci et al, 2014	Cross-sectional	+
Other Mean muscle index	Aguiar et al., 2014	Cross-sectional	+
Body fat (%)	Andreevskaia et al., 2013	Cross-sectional	+
Body fat (%)	De La Brassinne et al., 2016	Cross-sectional	+
Lipid accumulation product index	Ganguly et al., 2016	Cross-sectional	+
MRI of abdominal fat distribution	Ferguson et al., 2019	Prospective cohort	+

ND: no difference

with the general population, and to review existing modalities for the assessment of body composition.

Methods: Electronic searches of the literature were conducted in PubMed, Medline (Ovid®), Embase (Ovid®), Cochrane Central Register and Google Scholar. Titles and abstracts were reviewed by two authors independently against a set of prespecified inclusion/exclusion criteria, reference lists were examined and synthesis of the included studies was conducted.

Results: Twenty-five whole-text papers met the inclusion criteria and were included in the final narrative analysis. The studies were of heterogeneous design and used a range of objective measures to assess body composition, including bioimpedance analysis (BIA), dual energy X-ray absorptiometry (DXA) and computed tomography (CT). Few studies met all the quality assessment criteria. 24 studies confirmed discrete biological and body composition changes in patients with psoriatic disease, which correlated positively with other indicators of metabolic syndrome, including waist circumference, waist-to-hip ratio, weight, BMI, plasma concentrations of LDL-cholesterol, leptin and apolipoprotein-B.

Conclusion: There is an increased prevalence of metabolic, anthropometric and internal body composition derangements in psoriatic patients compared with controls, and these changes seem to be independent of obesity and the customary metabolic syndrome, including higher overall body fat, visceral fat and sarcopenia. Our study highlights the applicability of several imaging techniques in the evaluation of body composition in psoriatic patients, including some novel automated systems, and future studies should focus on validation and standardization of assessment tools both in research and clinical practice.

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Disclosure of Interests: None declared
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AB0745

REAL-LIFE EXPERIENCE FOR SECUKINUMAB IN PSORIATIC ARTHRITIS FROM HURBIO-PSA DATABASE

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Background: Biologic disease modifying anti-rheumatic drugs (bDMARD) are revolutionary treatment options for management of inflammatory arthritis. Secukinumab (SEC), anti-interleukin-17A monoclonal antibody, is a new alternative choice to anti-TNFs and IL-12/23 blocking agents in the therapy of psoriatic arthritis (PsA). In Turkey, government health insurance system covers secukinumab for at bDMARD-refractory PsA patients.

Objectives: In this study, analyzing of parameters that related with effectiveness and drug survival rates for patients using SEC from Hacettepe University Rheumatology Biologic Registry (HURBio-PsA) were aimed.

Methods: HURBio-PsA is a monocentric biologic database including 470 PsA by December 2020. Sixty-two PsA patients that recorded with prescribed SEC in the database were evaluated. Sixteen patients have no control clinical-visit were excluded. Descriptives and demographics were recorded and Kaplan-Meier analysis was used to estimate SEC drug-retention rates.

Results: Fourty-two (26.1% male) PsA patients treated with SEC) were included. Characteristics of the patients at the baseline and the last visit were shown in Table. Last visit scores of DKYI, Patient VAS Global, VAS Fatigue, VAS Pain and BASDAI showed statistically significant improvements in comparison with first visit values. Median duration of SEC usage was 5.4 (Min-Max: 0.18-18.6) months. SEC drug-retention rate at 12 months were 69% and 54.4% for two PsA groups that were used previously 1 and ≥2 bDMARDs, respectively (p=0.743, Figure).

Conclusion: In this real-world study derived from single center experience; there is no statistically significant difference for drug survival rates of SEC therapy in the patient groups used 1 and ≥2 bDMARDs. Effectiveness and drug-survival shoul be obviously verified by data derived from multicenter large cohorts.

Table 1. Baseline characteristics of PsA patients with treated with Secukiumab

	All Patients (n=62)	1 bDMARD exposed (n=18)	≥ 2 bDMARD exposed (n=44)	p
Gender, Female, n(%)	47 (75.8)	12 (66.7)	35 (79.5)	0.334
Age at the disease diagn osis, years, mean±SD	42 ± 11.65	35 ± 5.65	38.6 ± 10.7	0.721
Age at SEC starting, years, mean±SD	48.2 ± 10.8	43 ± 2.8	49.5 ± 11.3	0.182
Median duration of SEC treatment, median (min-max)	6.3 (0.9-18.6)	3.3 (3.2-3.3)	9 (4-20)	0.519
HLA-B27 positivity, n(%)	3/24 (12.5)	1 (14.3)	2 (11.8)	1
BMI, kg/m^2, mean±SD	28.9 ± 5.9	32.6 ± 3.7	28.4 ± 6.0	0.546
Ever smokinig history, n(%)	40/61 (65.6)	13 (72.2)	27 (62.8)	0.6
Uveitis, n(%)	3 (4.8)	0 (0)	3 (6.8)	0.55
PsA/Psp family history, n(%)	22 (35.5)	2 (11.1)	20 (45.5)	0.01

Table 2. Activity parameters of PsA patients have a least clinical visit

	1 bDMARD exposed (n=)			≥ 2 bDMARD exposed (n=)		
	First Visit	Last Visit	p	First Visit	Last Visit	p
DAS28, Median (IQR)	2.8(1.5)	2.8 (1.8)	0.155	3.9 (1.7)	3.5 (1.4)	0.414
HAQ, Median (IQR)	0.3 (0.7)	0.05 (0.61)	0.065	0.7 (0.9)	0.5 (0.85)	0.500
DKYI, Median (IQR)	4 (4.5)	0 (3)	0.049	11 (15)	5 (9)	0.003
ESR, Median (IQR)	19 (23.2)	17.5 (18.7)	0.398	28 (38)	35 (27.9)	0.082
C-RP, Median (IQR)	0.49 (0.64)	0.41 (0.75)	0.724	0.73 (1.8)	1 (2)	0.564
BASDAI, Median (IQR)	61 (61)	27.5 (48)	0.005	58 (31)	46 (39)	0.038
BASFI, Median (IQR)	38 (50)	9.4 (54.5)	0.035	43 (53)	36 (47)	0.480
Tender Joint Count, Median (IQR)	0 (0.5)	0 (0.5)	0.180	1 (4)	0 (9)	0.720
Swollen Joint Count, Median (IQR)	0 (1.2)	0 (0)	0.357	0 (2)	0 (0)	0.635
VAS Global Patient, Median (IQR)	80 (55)	25 (45)	0.006	60 (20)	50 (50)	0.032
VAS Fatigue, Median (IQR)	65 (62.5)	40 (62.5)	0.027	60 (40)	50 (40)	0.110
VAS Pain, Median (IQR)	80 (57.5)	40 (72.5)	0.022	70 (30)	60 (50)	0.170

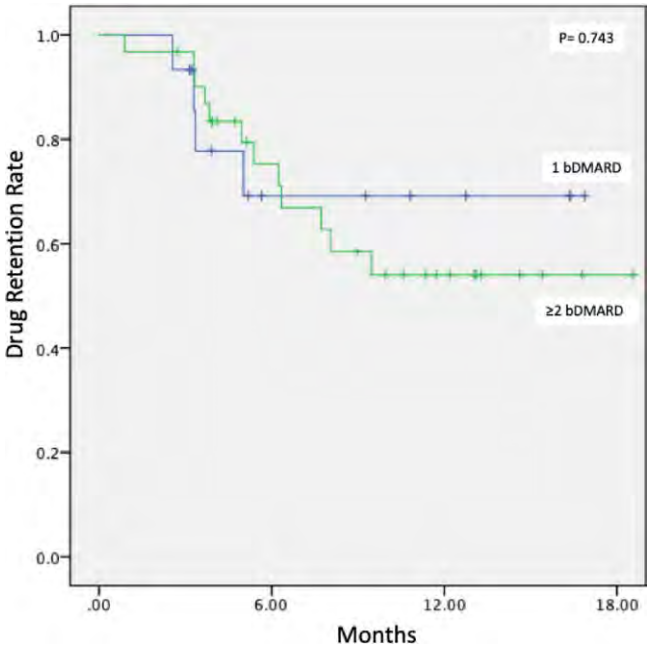


Figure. Drug Retention Rate for Secukinumab

Disclosure of Interests: Ertugrul Cagri Bolek: None declared, Emre Bilgin: None declared, Gözde Kübra Yardımcı: None declared, Bayram Farisoğulları: None declared, Emine Duran: None declared, Berkan Armagan: None declared, Levent Kılıç: None declared, Şule Apraş Bilgen: None declared, Ali İhsan Ertenli: None declared, Umut Kalyoncu Consultant of: Abbvie, Amgen, Janssen, Lilly, Novartis, UCB

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AB0746 EVALUATING TENDER AND SWOLLEN JOINTS FOR THE ASSESSMENT OF INFLAMMATORY PAIN IN PSORIATIC ARTHRITIS USING ULTRASOUND

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Background: Tender and Swollen Joint Counts (TJC, SJC) are items of disease activity scores in rheumatoid arthritis (RA) and psoriatic arthritis (PsA). Recent studies suggest that TJC do not adequately reflect ongoing inflammation in RA when using Ultrasound (US) as a reference standard, and that pain might be due to other, non-inflammatory causes.[1, 2] In PsA, the role of tenderness and swelling of joints for reflecting active inflammation has not been well studied so far.

Objectives: To evaluate tender (TJ) and swollen joints (SJ) for the assessment of inflammation in PsA.

Methods: We performed a prospective study on 83 PsA patients undergoing clinical and ultrasound examinations at two study visits scheduled 12 months apart. Tenderness and swelling were assessed for 68 and 66 joints respectively and US examinations, including grey scale (GS) and power doppler (PD) were conducted at all 68 joints. GS- (range 0-204) und PD sum scores (0-204) were calculated. At patient level, correlations were performed between TJC, SJC and clinical or US values. At joint level a GS value≥1 and/or PD value≥1 was defined as active synovitis, which was compared to whether a joint was tender, swollen or both. A generalized linear mixed model was created to assess the predictive value of TJ and SJ for active synovitis after 12 months, taking into consideration the joint site.

Results: At baseline the median TJC and SJC for 83 patients was 4 (range 0-59) and 1 (0-20), respectively and the median GSS- and PD sum score was 16 (3-56) and 3 (0-31) respectively. SJC correlated with the GSS sum score (r= 0.37, p=0.004) and PD sum score (r =0.47, p<0.001), while TJC only correlated with PD sum score (r=0.33, p=0.01). TJC correlated better than SJC with patient reported outcomes like patient global assessment (TJC: r=0.57, p<0.001; SJC r=0.39, p=0.002) and health assessment questionnaire (TJC: r=0.50, p<0.001, SJC no significant correlation). Swollen joints (with or without tenderness) showed active synovitis (GSS≥1 and/or PD≥1) in 67.6% of cases, while tender joints (with or without swelling) showed signs of US activation in only 34.5%. A joint that was considered swollen at baseline was more likely to express active synovitis after 12 months (OR: 4.3, 97.5 CI: 2.9-6.2), compared to a joint that was either tender or swollen at baseline (OR: 2.8, 97.5 CI: 2.1-3.5).

Conclusion: SJC are more closely linked with US signs of inflammation as compared to TJC in PsA. While swelling of a joint predicts US inflammation after a year, the information whether the joint is additionally tender or not, gives no additional predictive information.

References:

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Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.4345

AB0747 SPECIFIC ULTRASOUND LESIONS IN PSORIATIC ARTHRITIS: PREVALENCE AND CORRELATION WITH DISEASE ACTIVITY

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Background: Psoriatic arthritis (PsA) is a systemic inflammatory disease with articular and extra-articular features. In recent years, Ultrasonography (US) is playing an important role in the diagnosis and monitoring of this disease. Specific US features of PsA have been reported such as enthesitis, peritenon extensor tendon inflammation (PTI) and soft tissue edema.

Objectives: The aims of this study were to evaluate the prevalence of these US signs in PsA patients and to determine their association with disease duration and activity.

Methods: Patients with peripheral PsA responding to the Classification Criteria for Psoriatic Arthritis (CASPAR) were enrolled. Clinical and biological data were extracted, and then US examination was performed by an experimented rheumatologist blinded to clinical data using a machine type Esaote MyLAb 60 with a linear probe of 6-18 MHz. The following US features were evaluated: PTI at the dorsal aspect of metacarpo-phalangeal (MCP) joints, soft edema at the volar aspect of MCP joints and enthesitis of the digitorum extensor at the dorsal aspect of distal inter-phalangeal (DIP) joints.

A p<0.05 was considered statistically significant.

Results: We included twenty PsA patients, 8 men and 12 women, with a mean age of 55 ± 11 [33-77] years old. The mean disease duration was of 10±8 [1-34] years. A family history of PsA or psoriasis was reported in 53% of cases.

Oral corticosteroids were used in 21% of patients, at a mean daily posology of 7 mg [5-10] of Prednisone equivalent, Methotrexate in 84% of cases at a mean posology of 15 mg [10-20] per week, Sulfasalazine in 10% of cases and a biological DMARD in 32% of cases (Etanercept=4, Infliximab=1, Adalimumab=1).

The mean number of tender and swollen joints were respectively of 8 [0-16] and 2 [0-8]. The mean rate of patient global evaluation and visual analogue scale was of 5 [0-9].

The mean DAPSA (Disease Activity in PSoriatic Arthritis) score was of 32±27 [4-112].

US examination demonstrated that all patients had at least one of the three specific signs that we were looking for. At MCP level, PTI was noted in 11% of joints with Power Doppler (PD) signal in one case and soft tissue edema was noted in 3% of joints.

At DIP level, enthesitis of digitorum extensor tendon was noted in 39% of joints. The elementary lesions reported were: enthesophyte in 25%, erosion in 8%, calcification in 5% and thickened or hypoecoic tendon in 4% of joints. However, no PD signal was detected at the enthesis.

A positive association was found between DAPSA score and soft tissue edema (p=0.000), but not with PTI (0.668) and enthesitis (0.137). No relation was found between these three lesions and the disease duration.

Conclusion: The presence of soft tissue edema, enthesitis and/or PTI on US can be an argument for the diagnosis of PsA. Soft tissue edema is shown to be associated with disease activity.

Disclosure of Interests: None declared

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AB0748 IMPORTANCE OF COMORBIDITIES IN PATIENTS WITH ARTHRITIS PSORIATIC

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Background: Cardiovascular diseases are more prevalent in inflammatory arthritis, such as psoriatic arthropathy (PsA), than in general population. An increase in the presence of anxiety-depressive disorders has been also described in patients with psoriatic disease.

Objectives: To assess the prevalence of comorbilities in a cohort of patient with PsA, especially cardiovascular events and anxiety-depression disorders.

Methods: Observational, cross- sectional study of a cohort of patients with PsA from a monographic clinical unit in a rheumatology department to describe the presence of comorbidities: hypertension, diabetes, hyperlipemia, hyperuricemia, smoking, obesity, depression and isquemic heart disease (IHD). The

Table 1. Comorbilities in patterns of disease.

	PsA (n=145)	Peripheral disease (n=94)	Mixed disease (n=31)	Axial disease (n=20)
Age at diagnosis, year (DE)	45,4 (±13)	45,7 (±12,9)	45 (±13)	43,9 (±13,8)
Time of evolution, years (DE)	9,3 (±6,2)	9,6 (±6,5)	8,6 (±5,4)	7,3 (±2,9)
Men, n (%)	84 (57,9%)	48 (51,1%)	26 (83,9%)	10 (50%)
Women n (%)	61 (42,1%)	46 (48,9%)	5 (16,1%)	10 (50%)
Hyperlipemia, n (%)	87 (60%)	60 (63,8%)	17 (54,8%)	10 (50%)
BMI >25, n (%)	83 (57,2%)	61 (64,9%)	15 (48,4%)	7 (35%)
Hypertension, n (%)	46 (31,7%)	28 (29,8%)	13 (41,9%)	5 (25%)
Hyperuricemia, n (%)	41 (28,3%)	25 (26,6%)	11 (35,5%)	5 (25%)
Diabetes, n (%)	27 (18,6%)	20 (21,3%)	6 (19,4%)	1 (5%)
Smokers, n (%)	26 (17,9%)	13 (13,8%)	10 (32,3%)	3 (15%)
Depression, n (%)	23 (15,9%)	16 (17%)	6 (19,4%)	1 (5%)
Metabolic syndrome n (%)	23 (15,9%)	15 (16%)	5 (16%)	3 (15%)
IHD, n (%)	15 (10,3%)	7 (7,4%)	6 (19,4%)	2 (10%)

comorbidities were analyzed according to the type of disease: peripheral, mixed and axial involvement. For statistical analysis SPSS v.25 was used.
Results: We included 145 patients: 84 men and 61 women. The mean age at diagnosis was 45,4 (± 12,9) years, and the mean time of evolution was 9.3 (± 6,2) years. No significant difference between genders was observed.
Peripheral involvement was observed in 94 (64,8%), mixed 31 (21,4%) and axial involvement in 20 (13,8%). We did not find any differences between gender for peripheral and axial pattern, however 31% of men versus 8,2% of women presented a mixed pattern. [OR=5 (1,8-14), p= 0,001].
The most common comorbidities founded were hyperlipemia, overweight and arterial hypertension. Table 1 shows all the comorbidities studied and their distribution by pattern.
Patients with mixed involvement had a higher proportion of smokers [OR=2,9 (1,2-7,3), p=0,02] and a tendency to higher IHD [OR=2,8 (0,9-8,6), p=0,06].
Overweight was significantly lower in axial pattern patients [OR=0,4 (0,2-0,8), p=0,01] and higher in the peripheral ones [OR=1,5 (1,1-2,1), p=0,01].
IHD was prevalent in patients of our cohort (10,3%), it was significantly higher in men than in women [OR=12 (1,5-93,9), p=0,003], and more likely in mixed involvement (19,4%).
Males with PsA also developed hyperuricemia more frequently [OR=6,5 (2,5-16,9), p<0,0001]. Metabolic syndrome was found in 15.9%, but there was no significant difference among the patterns. Although, it was associated with hyperuricemia [OR=21,6 (6,7-69,8), p< 0,0001] and ischemic heart disease [OR=12,4 (3,8-40,1), p< 0,0001]. Finally, the rest of the comorbidities analyzed did not show significant difference in gender and pattern of disease.
Conclusion: In our cohort, a high prevalence of comorbidities was found, especially hyperlipemia, metabolic syndrome and IHD. In general, overweight (BMI > 25) was very common and was associated to a peripheral disease while the axial disease showed as a protective factor.
Disclosure of Interests: None declared
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AB0749 COMPARING PATIENT-PHYSICIAN DISCORDANCE IN RA AND PSA PATIENTS

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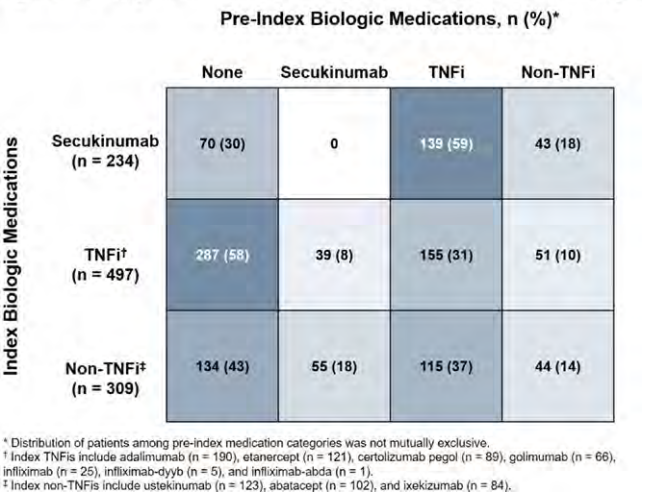
Background: Patient global Assessment (PGA) of disease activity is considered a key patient reported outcome in Rheumatoid Arthritis (RA) and Psoriatic Arthritis (PsA), both being included in combined indices of disease activity. However, patients and physicians frequently disagree in their assessment.
Objectives: This study aimed at comparing the degree of this discrepancy and its determinants in RA and PsA.
Methods: Cross sectional study including 100 patients with RA (ACR/EULAR 2010 criteria) and 100 patients with PsA with predominant peripheral joint involvement (CASPAR criteria), aged ≥18 years, randomly selected from the electronic registry Reuma.pt. Data were collected from the most recent rheumatology visit during the last year: sociodemographic data, disease duration (years), tender and swollen joint counts 0-28 (TJC and SJC), disease activity (DAS28 3V-PCR), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), patient's pain assessment, PGA and physician global assessment (PhGA). The discrepancy between patients and physicians (ΔPPhGA) was defined as PGA minus PhGA, and a difference > |20mm| was taken as "discordance". Categorical variables are presented as proportions and continuous variables as mean (±SD). Patient and clinical characteristics were compared between patients with RA and PsA using t- test and $\chi 2$ test, as adequate. Variables with p<0.05 or clinically relevant were included in multivariable logistic regression analysis to identify correlates for ΔPPhGA in the whole sample. A p≤0.05 was considered statistically significant.
Results: Compared to PsA, patients with RA were more often female (90% Vs 49%, $p < 0.05$), older (66.7 ± 10.7 Vs 58.3 ± 12.2 years, $p < 0.05$) and had a shorter disease duration (18.2 ± 9.8 Vs 19.9 ± 9.7 years, $p = 0.202$). Regarding disease activity, the RA and PsA groups were comparable: DAS28 3V-PCR (2.3 ± 0.9 Vs 2.4 ± 1.0, $p = 0.34$). Patients with RA had a higher mean ΔPPhGA (30.4 ± 30.6 Vs 25.4 ± 27.5, $p < 0.05$), and were more frequently discordant to the physician (69% Vs 51%, $p < 0.05$). In univariable analysis, having RA, higher patient's pain assessment and higher ESR were associated to patient-physician discordance. In multivariable analysis, only patient's pain assessment (OR 1.04 [95% CI 1.03-1.06], p = 0.00) and TJC (OR 0.82 [95% CI 0.68-0.97], p = 0.02) remained as predictors of discordance.
Conclusion: Despite comparable disease activity scores in RA and PsA patients, RA patients tend to have a worst self-perception of their disease activity compared to their physician´s. Patient's pain assessment and TJC were the only predictors of patient-physician discordance, irrespective of the disease.
Disclosure of Interests: Luisa Brites: None declared, LILIANA SARAIVA: None declared, Flavio Costa: None declared, João Dinis de Freitas: None declared, Mariana Luis: None declared, Ana Rita Prata: None declared, Helena Assunção: None declared, José Antonio P. da Silva Grant/research support from: Pfizer, Abbvie, Consultant of: Pfizer, AbbVie, Roche, Lilly, Novartis, João Rovisco: None declared, Catia Duarte: None declared
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AB0750 CLINICAL CHARACTERISTICS AND TREATMENT PATTERNS OF PATIENTS WITH PSORIATIC ARTHRITIS WHO WERE PRESCRIBED BIOLOGICS: DATA FROM THE COLUMBUS REPOSITORY

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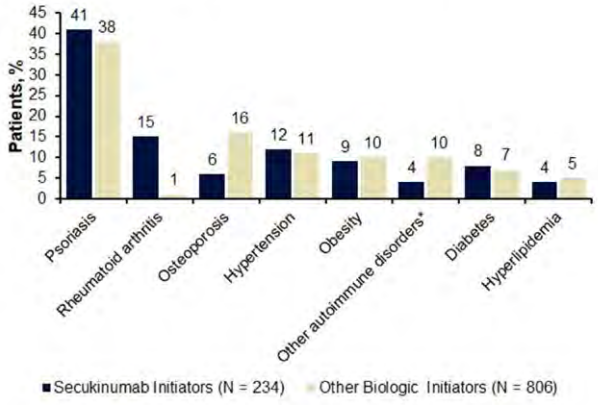
Background: Real-world data from electronic health records (EHR) allow examination of treatment patterns and clinical practice behaviors for psoriatic arthritis (PsA).
Objectives: To describe physician and patient characteristics, and treatment patterns of patients with PsA who initiated secukinumab and other biologics using data from the Columbus Repository.
Methods: EHR data from adult patients with PsA who were prescribed a new biologic therapy between January 2018 and March 2019 (index date) were included from the Columbus Repository, which collects clinical records from a network of US rheumatology providers. Demographics, disease characteristics, and treatment patterns, as well as physicians' characteristics, were reported for patients who were prescribed secukinumab vs other biologics (abatacept, adalimumab, etanercept, certolizumab pegol, golimumab, infliximab, infliximab-dyyb, infliximab-abda, ustekinumab, and ixekizumab). Treatment groups were mutually exclusive and only the most recently prescribed biologic was represented. Categorical variables were summarized using frequency counts and percentages and continuous variables were presented using means and standard deviations.
Results: As of March 2019, 234 patients initiated secukinumab and 806 initiated other biologics for PsA treatment; 62 physicians prescribed biologics for PsA. Overall, 73% of physicians' offices had a single provider contributing patients to the analysis, and 76% of physicians were located in the South US region. Secukinumab initiators were younger (55.2 vs 57.3 years), more likely to be male (44% vs 31%), and had higher BMI (34.0 vs 31.9 kg/m^2) vs other biologic initiators. Almost all disease activity measures evaluated had a large proportion (> 80%) of missing data; among those with nonmissing data, secukinumab initiators had numerically higher mean (SD) RAPID3 score vs other biologic initiators (12.6 [6.5] vs 11.6 [7.1]). Overall, 70% of secukinumab initiators and 48% of other biologic initiators were biologic experienced (**Figure 1**). Comorbidities were similar between groups (**Figure 2**). The most common reasons for discontinuation of prior biologic were the biologic was no longer required and lack of efficacy (**Table 1**).

Figure 1. Prior Biologic Use Among Patients Initiating Secukinumab, TNFis, or Non-TNFi Biologics



* Distribution of patients among pre-index medication categories was not mutually exclusive.
† Index TNFis include adalimumab (n = 190), etanercept (n = 121), certolizumab pegol (n = 89), golimumab (n = 66), infliximab (n = 25), infliximab-dyyb (n = 5), and infliximab-abda (n = 1).
‡ Index non-TNFis include ustekinumab (n = 123), abatacept (n = 102), and ixekizumab (n = 84).

Figure 2. Comorbidity Profile (≥ 5% of Patients) Among Secukinumab vs Other Biologic Initiators With PsA



* Including celiac disease, systemic sclerosis, Sjögren syndrome, vitiligo, chronic urticaria, systemic lupus erythematosus, and giant cell arteritis.

Table 1. Treatment Patterns Among Patients With PsA at the Index Date

	Secukinumab (N = 234)	Other Biologic (N = 806)	SMD*	P Value
Reason for discontinuing prior biologic treatment, n (%)	N = 164	N = 385	0.20	0.67
No longer required	64 (39)	136 (35)		
Lack of efficacy	28 (17)	75 (19)		
Cost or administrative	5 (3)	10 (3)		
Side effects	5 (3)	9 (2)		
Lack of tolerability	0	3 (1)		
Patient fear of side effects	1 (1)	0		
Other	25 (15)	63 (16)		
Missing	36 (22)	89 (23)		
Prior medication use, n (%)				
NSAIDs	109 (47)	365 (45)	0.03	0.78
Opioids	89 (38)	252 (31)	0.14	0.06
Steroids	68 (29)	265 (33)	0.08	0.31
DMARDs				
Methotrexate	83 (35)	340 (42)	0.14	0.08
Sulfasalazine	25 (11)	93 (12)	0.03	0.81
Apremilast	53 (23)	104 (13)	0.26	< 0.01
Tofacitinib	10 (4)	36 (4)	0.01	1.00
No. of prior biologics, mean (SD)	0.95 (0.82)	0.62 (0.77)	0.41	< 0.01

SMD, standardized mean difference.

* Comparisons with SMD > 0.1 were suggestive of clinically relevant differences.

Conclusion: Secukinumab initiators with PsA were more likely to be male and biologic experienced, have a higher BMI and higher RAPID3 scores indicative of more active disease vs those initiating other biologics. Additional structured and unstructured elements may need to be captured on EHR platforms to gain clarity on disease activity and treatment decisions.

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AB0751 SAFETY AND PERSISTENCE OF USTEKINUMAB IN PATIENTS WITH PSORIATIC ARTHRITIS IN BIOBADASER

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Background: Ustekinumab has been efficacy and safety for psoriatic artritis in clinical trials.

Objectives: To assess effectiveness, by means of drug persistence analisys, and safety of ustekinumab in patients with psoriastic arthritis in Biobadaser.

Methods: BIOBADASER is the Spanish registry of biological drugs of the Spanish Society of Rheumatology and the Spanish Medicines Agency. We identified patients aged 18 years or more with psoriatic arthritis on Ustekinumab. A descriptive analysis was performed.The persistence of ustekinumab therapy was calculated with a Kaplan-Meier curve and was compared with the persistence of anti-TNF, according to line treatment. Log Rank test was used to establish a comparison. Adverse events occurring with ustekinumab are described according to year treatment.

Results: One hundred and twelve patients were on ustekinumab. Most of them were on their second or third line treatment: 53.57% more than one biological therapy (BT), 19.64% second BT, 26.79% were naïve for BT. Most of them were on 45 mg dose: 88.24%. Median duration of disease at Ustekinumab initiation was 10.1 SD 7.2 years; 69.23% had peripheral arthritis; 45.24% had obesity and 39.29% were overweight; 40,6% were on prednisone and 59.82% on DMARD. The cause of discontinuation of treatment was mainly inefficacy (82.61%) and less common an adverse event (6.52%). The probability of persistence of treatment with ustekinumab was 0.83 (95% CI 0.63-0.92) at year 1, 0.79 (0.58-0.90) at year 2 and 0.79 (0.58-0.9) at year 3 when ustekinumab was prescribed as the first line treatment. The persistence decrease when ustekinumab was prescribe as a second and third treatment: being 0.53 (0.27-0.73) the first year, 0.46 (0.22-0.67) the second year and 0.46 (0.22-0.67) as a second line treatment and 0.58 (0.44-0.70) the first year, 0.33 (0.17-0.50) the second year and 0.33 (0.17-0.50) the third year as a third line treatment.The persistence was similar to anti-TNF treatment, according to line treatment. Adverse events were mainly mild (97.83%) and occurred the first year of treatment. Most of the adverse events were classified as “infections and infestations” (36.96%).

Conclusion: The persistence of ustekinumab was high, being 83% at the end of the first year on treatment and 79% the second and the third year of treatment. The persistence of ustekinumab was higher when if it was the first line treatment compared as if it was used as the second o third BT option. The persistence of Ustekinumab is similar to the persistence of anti-TNF treatments in all the analyzed treatment lines (no statistically differences were found). Adverse events occurred mainly during the first year treatment. They were mainly mild adverse events and the frequency decreased within the second and third year of treatment.

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AB0752 PSORIATIC ARTHRITIS: OLIGOARTHRITIS AND POLYARTHRITIS PATTERN CHANGES OVER THE INITIAL YEAR OF THE PRESENTATION. A REAL-WORLD EVIDENCE REPORT FROM THE QUEBEC REGISTRY RHUMADATA®

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Background: Psoriatic Arthritis (PsA) most frequently presents as a polyarthritis or (less often) as an oligoarthritis [1]. Upon reassessment, patients may change category during follow-up [2-3]. Historically, the patients in the original description of Moll and Wight had an oligoarticular presentation [4]. However, other studies have not found the same distribution in all patient populations [5]. Currently,

none of the accepted diagnostic or classification criteria set for PsA consider the variation in the number of involved joints in the early phase of PsA.

Objectives: To evaluate the change in pattern between oligoarticular and polyarticular psoriatic arthritis, within the first year of follow-up.

Methods: Data from RHUMADATA® patients diagnosed with PsA were extracted on December 8th, 2019. In the current analysis, we consider the first year of care patients following their first encounter with clinic staff. Patients with at least two 66/68 joint counts completed during this initial year are the subjects of this analysis. Joint count classification (Oligo vs Poly) was assessed from the first and last available joint counts. Patients were classified as having a polyarticular form of PsA if 5 or more of their joints were assessed as being swollen and/or tender. Subjects with 4 or less swollen and/or tender joints were classified as oligoarticular PsA patients.

Results: A total of 287 patients with at least two 66/68 joint counts are used in the present analysis. At baseline, the mean age of patients was 47.8 ± 13.5 with average disease duration of 1.6 ± 5.2 years. 49 % of patients were women. Average joint count at baseline was 7.1 ± 7.2 (swollen) and 7.1 ± 7.5 (tender) joints. Considering only 28 joints, the average was 4.2 ± 5 and 3.9 ± 4.8 for swollen and tender joints respectively. At the first joint count, 115 (40%) patients were assessed as "Oligo" and 172 (60%) as "Poly", while 159 (55%) and 128 (45%) were similarly assessed at the last assessment. The two assessments agreed for 179 (62%) and disagreed for 108 (38%). Of the 115 patients initially classified as "Oligo", 32 (28%) were reassessed as "Poly" within the initial year, while 76 (44%) of the 172 patients initially classified as "Poly" were reassessed as "Oligo". All 172 patients initially classified as "Poly" initiated a DMARD during this period (167 (97%) initiated a csDMARD and 5 (3%) initiated a bDMARS). All patients initially classified as "Oligo" also initiated treatment during this period (98 (85%) and 17 (15%) of the 115 patients initially classified as "Oligo" initiated csDMARDs and bDMARD respectively).

Conclusion: These observations suggest that a single assessment of joint count may be misleading in establishing the oligo or polyarticular pattern of PsA. This classification should take treatment into account.

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AB0753

THE CONTRIBUTION OF JOINT SYMPTOMS, ENTHESITIS, SKIN AND NAIL PSORIASIS (PSO) TO MINIMAL DISEASE ACTIVITY (MDA) ACHIEVEMENT IN PSORIATIC ARTHRITIS (PSA) PATIENTS (PTS). EFFECT OF TOFACITINIB TREATMENT. DATA FROM REAL CLINICAL PRACTICE.

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Background: PsA is an inflammatory arthritis associated with skin and nail PsO. The treatment target of PsA is MDA. In order to achieve MDA it is necessary to significantly improve musculoskeletal (MSK) symptoms, skin symptoms and patient-reported outcomes (PROs). In RCT it has been recently demonstrated that targeting both joint and skin symptoms is very important in achieving optimal improvement in health-related quality of life [1]. However, there is not enough data from clinical practice. Tofacitinib (TF) is an oral Janus kinase inhibitor approved for the treatment of PsA pts.

Objectives: to study the influence of joint, enthesitis, skin and nail symptoms on MDA achievement in active PsA (pts) treated with TF for 6 months (mo).

Methods: 41pts (M/F=24(58.5%)/17(41.5%) with active PsA fulfilling the CASPAR criteria, were included after signing consent participation forms. Mean age 42.4±10.3 years (yrs), median (Me) PsA duration 72 [35;120] mo, PsO duration 192 [98;312] mo, PASI 14.5 [7;23.8], DAPSA 44.2 [37.8;55.3]. Pts were treated with TF 5mg twice daily. At baseline (BL) and over a period of 6 mo of therapy PsA activity was evaluated by Tender Joint Count (TJC68), Swollen Joint Count (SJC66); PGA, physician global assessment by Visual Analog Scale (VAS), DAPSA. Enthesitis was evaluated by LEI (Leeds Enthesial Index) plus Plantar Facia (PF); PROs were measured by PtGA VAS, PtPain VAS, HAQ. PsO were measured by PASI/BSA (%). The presence/absent of Nail PsO was evaluated. The number of pts (NPts) who reached MDA (5/7: TJC≤1, SJC≤1, PASI≤1/BSA≤3, PtPainGA≤15, PtGA≤20, HAQ≤0,5, enthesitis count≤1) was calculated. M±SD, Me[Q25;Q75], %, Pearson-χ^2, OR 95% (CI) were performed. All p<0.05 were considered to indicate statistical significance.

Results: At BL mean TJC/SJC/PtPainGA/PtGA/PASI/HAQ were 19[12;24]/11[8;16]/65[50;75]/70[50;80]/14.5[7;23.8]/1[0.625;1.5] accordingly. Enthesitis/Nail PsO were found in 27 pts (65.9%)/in 33 out of 41 pts (80.5%) respectively. BSA>3% was found in 20 out of 41 pts (51.3%). After 6 mo of therapy all MDA parameters as well as DAPSA score decreased significantly (table 1). The NPts with Enthesitis decreased significantly and became 12 out of 41 pts (30.8%). After 6 mo of therapy the NPts with nail PsO didn't decrease significantly compared with the BL; the dynamics was: from 33 out of 41 pts (80.5%) to 31 (79.5%) accordingly (p=0.991). MDA was found in 15 out of 41 pts (36.58%). After 6 mo of therapy no significant differences were seen between the groups of pts with/without MDA in the NPts with nail PSO: 11 out of 15 pts (73.33%) and 20 out of 24 (83.3%) accordingly (p=0.456). Enthesitis, PASI, nail PsO had a negative impact on achieving MDA, while joint symptoms and PROs were significantly associated with MDA attainment after 6 mo of TF therapy (Fig. 1).

Conclusion: In real clinical practice TF treatment improves all MSK symptoms in active PsA pts. The presence of Enthesitis and Skin/Nail PsO severity at BL has a negative impact on MDA attainment in short-term outcomes. These findings should be taken into consideration when choosing treatment.

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Research granted by Pfizer.

Table 1. Change in all evaluated parameters from BL to 6 mo.

Parameters,	BL M±SD	6 mo M±SD
TJC68	18.1 ±9.8	4.9±5.0*
SJC66	12.8±7.7	2.5±4.0*
DAPSA	44.2±17.1	11.8±9.4*
PtPain, VAS, mm	65 [50; 75]	18 [5;30]*
PtGA, VAS, mm	70 [50; 80]	20 [10; 30]*
PASI	14.5 [7;23.8]	5.6 [0;10.4]*
LEI+PF	1 [0;2]	0[0;0]*
HAQ	1 [0.625; 1.5]	0.5 [0; 0.875]*

* p<0.0001 – differences from BL/6 mo;

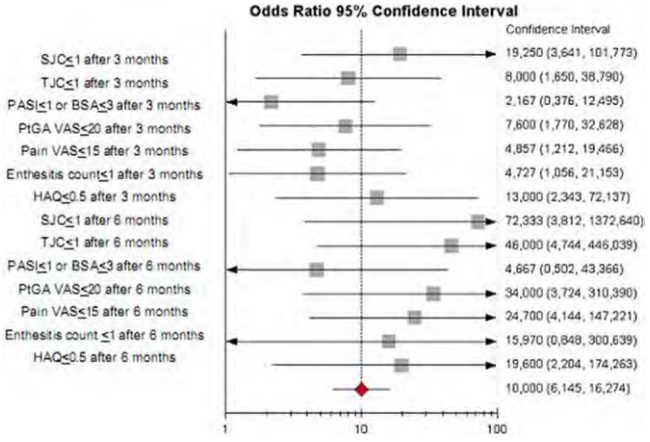


Fig. 1. Forest plot Joint, Enthesitis, PROs, Skin/Nail PsO contribution in MDA attainment at 6 mo of TF therapy.

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AB0754

HOW DO WE TREAT PSORIATIC ARTHRITIS? EVIDENCE FROM A 15-YEAR MONOCENTRIC BDMARDS EXPERIENCE

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Background: Psoriatic arthritis (PsA) treatment paradigm has dramatically change during the last 15 years, improving patients clinical outcomes and quality of life. We have now the possibility of a wide option among bDMARDs with different targets: TNF-inhibitors (TNFi), anti-IL17A inhibitors and anti-p40IL12/23. However, the choice of the "best" treatment in PsA patients is still a challenge in our daily clinical practice, making treatment decision a tricking issue.
Objectives: Aim of the study was to retrospectively evaluate the distribution of clinical PsA subtypes and comorbidities among bDMARDs treated patients in the last 15 years in a monocentric cohort of the Rheumatology Unit, University of Rome Tor Vergata.
Methods: Patients affected by PsA diagnosed by the CASPAR criteria and treated with a bDMARDs, in the last 15 years were enrolled. Clinical assessment included the presence of: oligo and/or polyarthritis and axial involvement (yes/no), enthesitis (yes/no), dactylitis (yes/no), PsO and onychopathy (yes/no). Comorbidities, as cardiovascular, metabolic syndrome and kidney diseases, were registered. The overall timeframe was halved in: 1st period (2004-2011) and 2nd period (2012-2019). Chi-square test was used to analyze the distribution of clinical PsA subtypes and comorbidities.
Results: Data from 314 consecutive PsA patients treated with bDMARDs were obtained (Table 1). A total of 259 (82,48%) patients were treated with TNFi, while 55 (17,52%) with non-TNFi (i.e. Secukinumab, Ustekinumab or Apremilast). In the 1st period, 143 (86,14%) patients were treated with TNFi and 23 (13,85%) with non-TNFi; in the 2nd period, 116 (78,4%) patients were treated with TNFi and 32 (21,2%) with non-TNFi. PsA patients with polyarticular involvement were on TNFi in a higher prevalence in the first period than in the second ($p<0.001$). On the contrary, oligo-articular PsA and axial PsA were on TNFi in a higher prevalence in the 2nd period than in the 1st ($p<0.001$), as well as non-TNFi drugs were more frequently used in the 2nd period than in the 1st ($p=0.03$). PsA patients with PsO and/or onychopathy were in a higher prevalence on non-TNFi than on TNFi in the 1st period ($p<0.001$). PsA with enthesitis and/or dactylitis were in a higher prevalence on TNFi than on non-TNFi in the 1st period ($p<0.001$); this difference disappeared in the 2nd period, when both TNFi and non-TNFi were equally used (p=ns). PsA patients with metabolic syndrome and/or cardio-vascular and/or renal diseases were more prevalent on TNFi in the 1st period than in the 2nd while in the 2nd these patients were more frequently on non-TNFi ($p<0.05$).
Conclusion: Here, we demonstrated that clinicians treatment choice in patients with moderate-severe PsA may be influenced by the clinical subtype and/or the occurrence of comorbidities. In particular, during the last years, the use of non-TNFi can be chosen more adequately as a therapeutical challenge in patients with different clinical manifestations and with comorbidities, improving PsA treatment paradigm.

Table 1. Clinical characteristics of patients enrolled.

	TNFi		Non-TNFi	
	2004-2011	2012-2019	2004-2011	2012-2019
F (N)	104	68	16	22
M (N)	53	34	9	8
Total, divided for period	157	102	25	30
Total, divided for drugs	259		55	
F/M (%)	66/34	67/33	64/36	73/27
Age, years	55,4±13,09	56,28±11,34	54,80±12,56	57,44±11,15
Disease duration, months	156±106,03	162,69±101,65	172,87±108,53	167,2±108,89
Age of onset, years	42,57±13,00	41,73±12,13	42,065±15,33	45,8±13,6
Age of diagnosis, years	44,74±12,98	43,35±11,25	43,4±14,33	46,8±15,98
Diagnostic delay, months	72±34,68	12±8,52	6,73±10,64	27±15,12

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AB0755

REAL WORLD EFFECTIVENESS OF SECUKINUMAB IN PSORIATIC ARTHRITIS: FINDINGS FROM A RECENT CROSS SECTIONAL SURVEY OF RHEUMATOLOGISTS AND PATIENTS IN EUROPE

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Background: Secukinumab has demonstrated significant and sustained reduction of disease activity and improvement in physical functioning and quality of life in PsA pts in RCTs.[1]
Objectives: This study assessed effectiveness of secukinumab in PsA in a real-world setting.
Methods: This was a cross-sectional survey of rheumatologists, dermatologists and pts in France, Germany, Italy, Spain, and UK. Data were collected online from June-Dec 2018 via physician-completed patient record forms. Pts receiving any treatment for PsA were included in survey (n=1675). Pts receiving secukinumab >4 months were included in this analysis. Pts reported quality of life, work, and disability measures at their current consultation. Physicians reported patient demographic and disease characteristics, concomitant and previous treatments, and time since diagnosis. Physicians also reported overall, skin and joint disease severity, pain (1-10 scale), BSA psoriasis involvement, global VAS score, PASI score, SJC, and TJC for 2 time points: initiation of treatment and at the time of data collection (current consultation). Data were analysed descriptively. The data analysed here is representative of pts that are currently receiving secukinumab and does not assess pts that have discontinued treatment.
Results: 572 PsA pts were receiving secukinumab >4 months at their current consultation. Patient mean age was 47.9 yrs, with 43% female, 59% working full time, and a mean BMI of 26.6. On average, pts were diagnosed with PsA 5.6 years before the current consultation, had received secukinumab for 11.0 months, and for 59% of pts secukinumab was their 1st advanced therapy (bDMARDs or tsDMARDs), 24% their 2nd and 16% their 3rd or more. 25% of pts were also receiving a csDMARD concurrently. Pts reported a mean EQ5D utility score of 0.83, mean WPAI overall work impairment of 24.3%, mean HAQ-DI score as 0.6, and mean PsAID12 score as 2.6 at current consultation. Proportion of pts with moderate and severe overall disease severity, and skin and joint severity decreased at current consultation vs at the initiation treatment (Table 1). Between initiation of treatment and current consultation, pts achieved a significant reduction in disease activity scores, pain score, global VAS scores, BSA, PASI score as well as a greater proportion of pts achieving a BSA < 3%, a PASI score < 3 (Table 2).
Conclusion: This multinational study demonstrated secukinumab effectiveness in routine care in PsA pts, with significant improvements across all outcomes.
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Table 1. Disease severity at initiation of secukinumab and at current consultation

	At initiation of secukinumab (n=572)	At current consultation (n=572)
Overall disease severity, n (%)		
Mild	32 (5.6)	432 (75.5)
Moderate	316 (55.2)	131 (22.9)
Severe	218 (38.1)	9 (1.6)
Don't know	6 (1.0)	-
Skin severity, n (%)		
Mild	93 (16.3)	478 (83.6)
Moderate	287 (51.2)	82 (14.3)
Severe	154 (26.9)	12 (2.1)
Don't know	38 (6.6	-
Joint severity, n (%)		
Mild	50 (8.7)	444 (77.6)
Moderate	329 (57.5)	118 (20.6)
Severe	181 (31.6)	10 (1.7)
Don't know	12 (2.1)	-

Table 2. Physician reported outcomes at initiation of secukinumab and at current consultation, mean (SD)

	At initiation of secukinumab (n=572)	At current consultation (n=572)
BSA[a]	19.2 (15.3)	4.6 (8.7)
BSA < 3%, n (%)	28 (8.2)	213 (62.5)
PASI score (0-72)[a]	17.2 (11.5)	4.2 (8)
PASI score < 3, n (%)	11 (7.1)	99 (64.3)
DAS28 score[a]	5.2 (1.5)*	2.8 (1.3)
TJC (0-68)[a]	12.1 (9.9)	2.5 (3.6)
SJC (0-66)[a]	10.0 (9.5)	2.9 (7.5)
Pain score (1-10)	6.3 (2.0)	2.6 (1.6)
Physician global VAS score (1-100)[a]	59.4 (24.2)	23.3 (22.2)

Table 2. Physician reported outcomes at initiation of secukinumab and at current consultation, mean (SD)

	At initiation of secukinumab (n=572)	At current consultation (n=572)
Patient global VAS score (1-100)[a]	56.7 (30.4)	23.4 (18.3)

1. [a]Calculated on available data.

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AB0756 GUSELKUMAB IMPROVED WORK PRODUCTIVITY AND DAILY ACTIVITY IN PATIENTS WITH PSORIATIC ARTHRITIS: RESULTS FROM A PHASE 3 TRIAL

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Background: DISCOVER 2 (DISC 2) is a Phase 3 trial of anti-IL-23-specific mAb guselkumab (GUS) in psoriatic arthritis (PsA) pts, who experience impaired physical function, resulting in disability, work productivity loss, and economic consequences.[1]

Table. Model-based estimates of mean change from baseline in WPAI-PsA domains

% change from baseline	PBO		GUS 100 mg q8W		GUS 100 mg q4W	
	W16	W24	W16	W24	W16	W24
Work time missed (absenteeism), n	155	152	141	145	145	143
LSMean	-4.6 (-7.2, -1.9)	-3.5 (-6.4, -0.6)	-3.5 (-6.2, -0.7)	-3.1 (-6.1,-0.1)	-4.7 (-7.4, -2.0)	-3.8 (-6.8, -0.8)
LSMean diff			1.1 (-2.6, -4.8)*	0.4 (-3.7, 4.5)*	-0.2 (-3.9, 3.5)*	-0.3 (-4.4, 3.8)*
Impairment while working (presenteeism), n	131	130	125	129	133	130
LSMean	-10.3 (-13.9, -6.7)	-10.2 (-13.7, -6.7)	-16.1 (-19.7, -12.4)	-19.4 (-22.9, -15.9)	-15.1 (-18.7, -11.5)	-19.5 (-23.0, -16.0)
LSMean diff			-5.8 (-10.8, -0.8)†	-9.2 (-14.0, -4.4)‡	-4.8 (-9.7, 0.1)*	-9.3 (-14.1, -4.5)‡
Overall work productivity impairment (absenteeism + presenteeism), n	131	130	125	129	133	130
LSMean	-11.2 (-15.0, -7.5)	-10.9 (-14.6, -7.1)	-15.9 (-19.7, -12.2)	-19.7 (-23.4, -16.0)	-15.8 (-19.5, -12.1)	-20.0 (-23.7, -16.3)
LSMean diff			-4.7 (-9.9, 0.5)*	-8.8 (-14.0, -3.7)‡	-4.6 (-9.7, 0.5)*	-9.2 (-14.3, -4.0)‡
Daily activity impairment, n	244	244	247	246	243	245
LSMean	-10.6 (-13.3, -7.9)	-10.3 (-13.1, -7.6)	-17.1 (-19.8, -14.4)	-21.5 (-24.2, -18.7)	-17.0 (-19.7, -14.3)	-20.5 (-23.2, -17.7)
LSMean diff			-6.5 (-10.2, -2.8)‡	-11.1 (-15.0, -7.4)‡	-6.5 (-10.2, -2.7)‡	-10.2 (-14.0, -6.4)‡

Data are % (95% CI)
*p>0.05, †p<0.05, ‡p<0.001
LSmeans, p values based on MMRM
LSmean diffs, p values vs PBO

Objectives: To evaluate the effect of GUS on impaired work productivity and daily activity in DISC 2 using the Work Productivity and Activity Impairment Questionnaire: Psoriatic Arthritis (WPAI-PsA).

Methods: Bio-naïve adults with active PsA despite nonbiologic DMARDs &/or NSAIDs received subcutaneous GUS 100 mg every (q) 4 weeks (W); GUS 100 mg W0, W4, q8W; or placebo (PBO). WPAI-PsA assesses, due to PsA over the previous week, work time missed (absenteeism), impairment while working (presenteeism), and impaired overall work productivity (absenteeism + presenteeism) and daily activity. Percentage change from baseline was analyzed for WPAI-PsA domains using mixed-effect model repeated measure (MMRM). Indirect savings from improved overall work productivity were estimated with 2018 US mean yearly wage estimate (all occupations).[2]

Results: At Week 24, impaired overall work productivity and daily activity were improved 20-22% in GUS-treated and 10-11% in PBO-treated pts (Table). Potential yearly indirect savings from improved overall work productivity was $10,242 with GUS q8W and $10,404 with GUS q4W vs $5,648 with PBO; $4,594 and $4,756 difference, respectively.

Conclusion: Improvement in overall work productivity and daily activity was greater with GUS versus PBO among pts with moderate-to-severe PsA, resulting in potential annual incremental economic gains.

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AB0757 ASSOCIATION BETWEEN DEPRESSIVE SYMPTOMS AND ENDOTHELIAL DYSFUNCTION IN PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Cardiovascular complications are the leading cause of death in patients with psoriatic arthritis (PsA), but current strategies for reducing cardiovascular risk are still inadequate. Depression is a common comorbidity in PsA patients and it is recognized as an independent cardiovascular risk factor in the general population. Endothelial dysfunction, assessed as a reduction in brachial

artery Flow Mediated Dilation (FMD), is a predictor of major cardiovascular events in high and low risk populations.

Objectives: To investigate the relationship between endothelial function and depressive symptoms in a cohort of patients with PsA.

Methods: Sixty consecutive patients with PsA, aged between 30 and 79 years, with no history of major cardiovascular events, were characterized for traditional cardiovascular risk factors and features of psoriatic disease. The risk of cardiovascular events according to traditional risk factors was calculated using the Framingham Risk Score (FRS) and the presence of depressive symptoms was defined through the Hospital Anxiety and Depression Scale (HDS) using the validated cut-off of 8. Endothelial function was assessed by FMD. Serum IL-6 was quantified by ELISA, IL-17 and TNF-α levels by Luminex method.

Results: Patients had an average age of 52.1±11.0 years, 43.3% of them were male, 23.3% obese and 25.0% active smokers; 38.3%, 25.0% and 11.7% were treated for high blood pressure, dyslipidemia and diabetes mellitus, respectively. The 10-year risk of major cardiovascular events estimated by FRS was 10.4%. The mean duration of PsA was 9.4 years, 30.0% of patients were in minimal disease activity (MDA) and 61.7% and 46.7% were treated with conventional and biotechnological DMARDs, respectively. The mean HDS value was 6.9±3.2 and 43.4% of patients had significant depressive symptoms. The severity of depressive symptoms according to HDS correlated with disease activity according to DAPSA (r=0.449, p=0.001). The mean FMD was 7.8±3.8%, this value correlated inversely with age (r=-0.408,p<0.001), risk of major cardiovascular events according to FRS (r=-0.327, p=0.011) and severity of depressive symptoms according to HDS (r=-0.285, p=0.027). The correlation between FMD and serum IL-6, IL-17 and TNF-alpha levels was not statistically significant. In multivariate linear regression models, the relationship between FMD and HDS was significant also when corrected for age (β=-0.26, p=0.03, R^2=0.23) and FRS normalized through logarithmic transformation (β=-0.32, p=0.009, R^2=0.22).

Conclusion: The degree of endothelial dysfunction quantified by FRS correlates with the severity of the depressive symptoms in patients with PsA, independently of the cardiovascular risk attributable to classical risk factors. The weak relationship between FRS and serum levels of IL-6, IL-17 and TNF-alpha suggests a role of factors independent of inflammation in the regulation of endothelial function in patients with PsA. Systematic research and treatment of depressive symptoms could contribute to a more complete stratification and a better management of cardiovascular risk in patients with PsA.

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AB0758

REAL-WORLD EFFICACY AND SAFETY OF APREMILAST IN BELGIAN PATIENTS WITH PSORIATIC ARTHRITIS: FINAL ANALYSIS OF THE MULTICENTRE, PROSPECTIVE APOLO STUDY

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Background: Real-world evidence on the efficacy and safety for patients (pts) with psoriatic arthritis (PsA) treated with apremilast (APR) is lacking but required to understand the uptake and potential of the drug.

Objectives: To assess the efficacy and safety of APR in pts with active PsA from routine clinical practice in Belgium.

Methods: In this multicentre, prospective study, the primary endpoint was the PsA Response Criteria (PsARC) response 6 months after APR initiation, defined as improvement in ≥2 (at least 1 must be joint swelling or tenderness) and no worsening in any of 4 criteria: swollen joint count (SJC [0-66]), tender joint count (TJC [0-68]), Physician's Global Assessment of Disease Activity and Pt's Global Assessment of Disease Activity. Other endpoints included the 12-item PsA Impact of the Disease (PsAID12) questionnaire, Health Assessment Questionnaire-Disability Index (HAQ-DI), Physician's and Pt's Numerical Rating Scale assessing disease activity for the most affected joint, psoriasis-involved body surface area, enthesitis, dactylitis and pain.

Results: In total, 107 pts were enrolled and included in the baseline (BL) demographics/disease characteristics and safety analyses. The efficacy population comprised 69 pts (pts who started APR ≤30 days before inclusion in the study and completed ≥150 days of treatment). Mean age was 53 years, mean body mass index was 29 kg/m^2 and 56% were female. Mean duration of PsA was ≈8 years (87.1 months). One-third of pts presented with short disease duration (time since diagnosis of PsA: ≤2 years); 84% were biologic naive. The most frequently reported comorbidities were cardiovascular disease (30%) and hypercholesterolemia (24%). At BL, mean (SD) SJC was 8.0 (6.5); mean (SD) TJC was 14.2 (12.5). Pts from the efficacy population were representative of the overall population. Fifty-four pts (60%) continued APR treatment for 6 months; 38 (36%) had discontinued APR (insufficient efficacy: n=15; adverse events [AEs]: n=16; intolerance: n=6; other reason: n=1). AEs were mostly mild or moderate in nature and consistent with APR's known safety and tolerability profile.[1] At Month 6, data were available for 49 pts, 65% of whom were PsARC responders. Mean change from BL in SJC was −5.23, with improvements (defined as ≥30% decrease per PsARC) observed in 80% of pts; 42% had no swollen joints at 6 months. Comparable results were seen for TJC, with mean changes from BL of −5.34 and improvements observed in 71% of pts; 27% had no tender joints at 6 months. Among pts with enthesitis at BL (n=21), 43% achieved a score of 0 by Month 6. Among pts with dactylitis at BL (n=18), 83% achieved a count of 0 by Month 6. Impact of PsA on quality of life (QoL) from the pt's perspective was assessed using the PsAID12 questionnaire and characterized by physical and psychological domains. After 3 and 6 months of treatment, 33% and 50% of pts with PsAID >4 at BL (n=60) achieved PsAID12 ≤4, respectively (cutoff value for Pt Acceptable Symptom State[2]). Improvements were observed in all 12 domains at Months 3 and 6 compared with BL (Figure). In all, 66% of pts showed a decrease ≥0.35 in HAQ-DI; the proportion of pts reaching a global HAQ-DI <0.5 increased over time (14% at 3 months; 20% at 6 months).

Conclusion: Results from APOLO, a study assessing the impact of APR in routine settings, indicated that APR is associated with rapid and sustained improvements in PsA signs and symptoms and QoL in an important proportion of pts. Safety and tolerability were consistent with the known profile of APR.

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Figure. Improvement From Baseline in Mean PSAID12 Domain Scores



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AB0759

FOUR-YEAR EFFICACY AND SAFETY OF GUSELKUMAB IN PSORIASIS PATIENTS WITH AND WITHOUT PSORIATIC ARTHRITIS: A POOLED ANALYSIS FROM VOYAGE 1 AND VOYAGE 2

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Background: Guselkumab (GUS), a fully human monoclonal antibody, selectively binds and blocks interleukin-23. VOYAGE 1 and VOYAGE 2 are two ongoing Phase 3, randomized, double-blind, placebo (PBO)/active comparator-controlled clinical trials of GUS in patients (pts) with moderate-to-severe psoriasis (PsO).
Objectives: This post-hoc analysis reports pooled results through 4 years among a subgroup of moderate-to-severe PsO pts with self-reported psoriatic arthritis (PsA) at baseline.
Methods: 1829 pts were randomized to GUS 100 mg at Weeks (Wks) 0, 4, and 12, then every 8 wks (q8wk); PBO at Wks 0, 4, and 12, GUS at Wks 16 and 20 then q8wk; or adalimumab (ADA) 80 mg at Wk 0, 40 mg at Wk 1, then 40 mg q2wk until Wk 47 (VOYAGE 1) or Wk 23 (VOYAGE 2). In VOYAGE 1, all pts received open-label GUS 100 mg q8wk during Wks 52-204. VOYAGE 2 incorporated a randomized withdrawal study design, followed by open-label GUS during Wks 76-204. Pooled subgroup analyses using the combined GUS group were conducted based on self-reported PsA status at baseline. Efficacy based on Investigator Global Assessment (IGA) score and Psoriasis Area and Severity Index (PASI) response was assessed using prespecified treatment failure rules (nonresponder status for all time points after discontinuing due to lack of efficacy, worsening of PsO, or use of a prohibited treatment).
Results: For pooled VOYAGE 1 and VOYAGE 2 pts (N=1721), combined GUS and ADA to GUS response rates at Wks 100, 156, and 204 were: PASI 90 80.6%, 80.0%, and 80.4%; PASI 100 50.1%, 49.9%, and 52.2%; IGA 0/1 83.6%, 83.3%, and 81.7%; and IGA 0 54.3%, 52.9%, and 53.9, respectively. In the pooled subgroup analysis of pts with and without PsA, response rates were similar across the Wk 100, Wk 156, and Wk 204 evaluations (Table). Rates of adverse events through Wk 204 were comparable for pts with PsA vs those without PsA at baseline.
Conclusion: Among GUS-treated pts with moderate-to-severe PsO with and without self-reported PsA at baseline, stable, durable, and high levels of skin responses, as well as comparable safety outcomes, through 4 years were observed.

Table. Pooled GUS Response Rates

	Without PsA at Baseline			With PsA at Baseline		
	Wk 100	Wk 156	Wk 204	Wk 100	Wk 156	Wk 204
	N=1301	N=1239	N=1191	N=289	N=276	N=264
PASI 90	1049 (80.6%)	1001 (80.8%)	964 (80.9%)	233 (80.6%)	211 (76.4%)	206 (78.0%)
PASI 100	648 (49.8%)	631 (50.9%)	635 (53.3%)	149 (51.6%)	125 (45.3%)	125 (47.3%)
	N=1300	N=1235	N=1189	N=288	N=276	N=264
IGA 0/1	1086 (83.5%)	1042 (84.4%)	979 (82.3%)	241 (83.7%)	217 (78.6%)	208 (78.8%)
IGA 0	702 (54.0%)	664 (53.8%)	649 (54.6%)	160 (55.6%)	135 (48.9%)	134 (50.8%)

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AB0760

SERIOUS INFECTIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS TREATED WITH TNFI: DATA FROM THE NOR-DMARD STUDY.

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Background: Infection is an important complication in patients with rheumatoid arthritis (RA), especially when exposed to therapy with tumor-necrosis-factor-inhibitors (TNFi) compared to conventional syntethic DMARDs. The majority of studies have been in RA populations and less is known about the risk of serious infections (SIs) in patients with psoriatic arthritis (PsA).
Objectives: To compare the incidence and risk of SI between RA and PsA patients treated with TNFi.
Methods: The NOR-DMARD is a prospective observational multi-centre study. Patients diagnosed with clinical RA or PsA, starting treatment with a TNFi between Jan 2009 to Dec 2018 were included. SI was identified through linkage to the Norwegian Cause of Death Registry and the Norwegian Patient Register and defined as an infection requiring hospital admission with at least one-night hospital stay and/or as an infection causing death. A predefined list of ICD10 diagnosis for infections was used. Time at risk was defined as time from baseline to the first SI, 30 days after discontinuation of TNFi therapy, emigration or end of study period. Crude incidence rates (IRs) of SIs for RA and PsA were presented as events per 100 patient years at risk (PYR) and hazard ratios (HRs) were adjusted for age and gender. The risk of SI in PsA vs RA patients was estimated in cox-regression models adjusted for age and gender, and corrected for multiple observations. The models were stratified by age < 50 vs ≥ 50 years, gender, DAS28-CRP remission (<2.6) vs non-remission at 3 months, and use of methotrexate as co-medication.
Results: A total of 3180 treatment courses on TNFi were identified (1780 RA and 1400 PsA) in 2368 patients (1356 RA and 1012 PsA) with 5697 person years at risk. The mean age in RA patients was 53.2 (SD 13.9), in PsA 48.2 (SD 11.9), p <0.001. 1542 (65 %) were women. Mean disease duration in years in RA patients was 10.0 (SD 9,7) and 8.5 (SD 9.0) in PsA patients, with no significant difference in disease duration, p = < 0.001. There were 124 cases of SI in RA patients and 55 cases in PsA patients during treatment with a TNFi. The crude SI IRs were 4.00 (3.35, 4.76) in RA patients and 2.12 (1.63, 2.76) in PsA patients. Compared with RA patients, patients with PsA had a lower risk of SI (HR 0.64, 95 % CI 0.46-0.91) when adjusted for age and gender. The HR for females was (HR, p-value) (1.00, 0.97), age ≥ 50 was (1.80, 0.001), MTX co-medication (1.00, 0.99), DAS28-CRP >2.6 at 3 months was (1.20, <0.001) and for seropositives (0.95, 0.77).
Conclusion: In patients starting treatment with a TNFi, the risk of SI was significantly lower in patients with PsA, compared to patients with RA, when adjusted for age and gender. The incidence rate of SI was lower in patients aged < 50, and in patients in DAS28-CRP remission for both PsA and RA patients.

Table 1. IRs of SI in RA and PsA patients starting a TNFi Jan 2009 – Dec 2018. HRs for PsA compared to RA.

	RA (1780 treatment courses)			PsA (1400 treatment courses)			
	SI, n	PYR	IR (95 % CI)	SI, n	PYR	IR (95 % CI)	HR (95% CI)
Overall SI	124	3105	4.00 (3.35, 4.76)	55	2592	2.12 (1.63, 2.76)	0.64 (0.46, 0.91)
Female	91	2253	4.04	27	1302	2.07	0.56
Male	33	852	(3.29, 4.96)	28	1290	(1.42, 3.02)	(0.36, 0.88)
			3.87			2.17	0.83
			(2.75, 5.45)			(1.50, 3.14)	(0.48, 1.44)
Age,	30	1122	2.67	23	1497	1.54	0.60
baseline	94	1983	(1.87, 3.82)	32	1095	(1.02, 2.31)	(0.33, 1.09)
< 50			4.74			2.92	0.68
> = 50			(3.87, 5.80)			(2.07, 4.13)	(0.44, 1.03)
MTX comedication	94	2424	3.88	38	1690	2.25	0.70
Yes	30	681	(3.17, 4.75)	17	902	(1.64, 3.09)	(0.47, 1.04)
No			4.40			1.89	0.53
			(3.08, 6.30)			(1.17, 3.03)	(0.28, 1.03)
DAS28-CRP at 3	35	1234	2.84	12	1174	1.02	0.48
months	59	1193	(2.04, 3.95)	25	814	(0.58, 1.80)	(0.24,
< 2.6			4.94			3.07	0.96)
> = 2.6			(3.83, 6.38)			(2.07, 4.54)	0.70 (0.43, 1.14)

Table 1. IRs of SI in RA and PsA patients starting a TNFi Jan 2009 – Dec 2018. HRs for PsA compared to RA.

	RA (1780 treatment courses)			PsA (1400 treatment courses)			
	SI, n	PYR	IR (95 % CI)	SI, n	PYR	IR (95 % CI)	HR (95% CI)
Serological status	64	1743	3.67	-	-	-	-
RA	60	1362	(2.87, 4.69)	-	-	-	-
Seropositive			4.40				
Seronegative			(3.42, 5.67)				

*DAS28-CRP < 2.6 = remission, PYR; Patient years at risk, MTX; Methotrexate, IR; Incidence rate

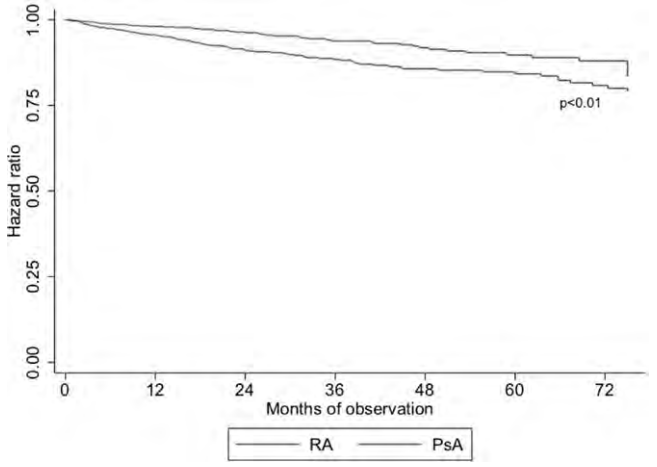


Figure 1. Age- and gender-adjusted risk of SI across RA and PsA

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AB0761

DEMOGRAPHIC AND CLINICAL FEATURES OF JUVENILE-ONSET PSORIATIC ARTHRITIS: RESULTS FROM PSART-ID REGISTRY

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Background: Although psoriatic arthritis (PsA) may be seen at any decades, juvenil onset PsA is relatively rare. Moreover, there were no more data about clinical features, treatments, and course in juvenile PsA when they reached to adult age.

Objectives: The objective of this study was to assess and compare demographic and clinical features for juvenile onset PsA and adult onset PsA.

Methods: PsART-ID is a multicenter, international database, investigating the disease characteristic in real life (1). Briefly, demographic data, PsA subtypes, uveitis, enthesitis, dactylitis, Co-morbidities, disease activity scores (TJC, SJC, VAS-pain, VAS patients and physician global assessments, VAS-fatigue, BASDAI), and functional status (HAQ-DI, BASFI) were recorded. Psoriasis and PsA starting age were noted, as well. Patients were classified as juvenile PsA or juvenile PsO (under 18 years old). Results were compared regarding to juvenile versus adult onset age.

Results: Overall, 1644 PsA patients were included to study, 301/1644 (18.3%) patients had juvenile onset psoriasis. Of 39/1644 (2.4%) patients had juvenile onset PsA, as well. As expected, juvenile onset PsA patients were younger, however PsA disease duration were longer than adult onset PsA patients. There were no any difference between demographic and clinical data, except BMI and enthesitis were less frequently at the juvenile onset PsA groups. Although, ever csDMARD using were similar between two groups, however, juvenile onset PsA patients were used more frequently bDMARDs.

Table. Comparison of demographic and clinical characteristics of juvenile and adult-onset psoriatic arthritis

	Juvenile onset	Adult onset	p
N (%)	39 (2.4)	1605 (97.6)	
Female Sex n (%)	24 (61.5)	1006 (62.7)	0.884
PsA beginning age mean (SD)	13.3 ± 3.85	42.3 ± 12.9	<0.001
Current age mean (SD)	26.6 ±10.7	47.3 ±13.07	<0.001
Duration of psoriasis (years)	17.10 ± 11.26	14.75 ± 11.78	0.124
Duration of psoriatic arthritis (years)	13.5 ±11	5.06 ± 6.7	<0.001
Cigarette smoking (ever) n (%)	15/38	641/1494	0.72
Education duration/year (mean,SD)	10.09 ± 3.67	9.52 ± 4.81	0.464
BMI (kg/m2) (mean, SD)	24.5 ±5.1	28.3 ± 5.21	<0.001
Family history of PsO/PsA n (%)	15 (38.5)	559 (34.9)	0.642
Nail involvement n (%)	18 (46.2)	762 (47.5)	0.864
Dactilitis n (%)	9 (23.7)	367 (24)	0.958
Entesitis n (%)	3 (7.9)	384 (25.7)	0.013
Uveitis n (%)	-	13 (4.3)	0.713
Axial involvement (%)	15 (38.5)	464 (29)	0.199
Methotrexate	36 (92.3)	1348 (84)	0.162
Sulfasalazine	17 (43.6)	612 (38.1)	0.488
Leflunomide	14 (35.9)	379 (23.6)	0.076
Biologic DMARDs	102 (33.9)	358 (26.8)	0.013

Conclusion: Although psoriasis may be seen frequently in the juvenile age, juvenile onset PsA was not so frequent in our PsA cohort. Although, ever csDMARD using were similar between two groups, however, juvenile onset PsA patients were used bDMARDs more frequently.

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[1] Kalyoncu U et al. The Psoriatic Arthritis Registry of Turkey: results of a multicenter registry on 1081 patients. Rheumatology. 2017;56:279-286.

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AB0762

METABOLIC SYNDROME IN EGYPTIAN PSORIATIC ARTHRITIS PATIENTS.

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory arthritis affecting 20:30% of patients with skin Psoriasis (PsO). It is strongly associated with obesity, particularly excess visceral adiposity, which leads to insulin resistance, hyperglycemia, dyslipidemia, and hypertension (HTN).

All the previous findings are grouped in Metabolic Syndrome (MetS) which increase the risk of development of Type 2 diabetes mellitus (T2DM) by five folds and cardiovascular disease (CVD) by two folds.

Objectives: The aim of this work was to define those who fulfill MetS criteria in PsA patients thus of greater risk to develop CVD and T2DM.

Methods: Fifty PsA patients diagnosed according to the CASPAR criteria and 50 matched healthy controls were included in this study.

All patients were subjected to thorough clinical evaluation of the musculoskeletal system. The disease activity was assessed by DAPSA and BASDAI. Skin severity was assessed by the PASI. Disability assessment was done by the HAQ-DI. Laboratory investigations included: CRP, uric acid and diabetic profile (including **HOMA-IR**) and lipid profile in patients and control subjects.

Subjects were defined as having MetS according to International Diabetes Federation (IDF) criteria:

Abdominal obesity was measured by Waist circumference (WC) for Egyptian cut-offs values (WC>100.5 cm in men and >96.25 cm in women).The subjects must have central obesity to identify MetS plus any two of the following four factors:

1) Raised triglycerides level (TG) ≥ 150 mg/dL or on specific treatment.
2) Reduced levels of high-density lipoprotein cholesterol (HDL <40 mg/dL in males and <50mg/dL in females or on specific treatment.
3) HTN: (systolic: ≥130mm H g or diastolic: ≥ 85 mm Hg) or on treatment for HTN.
4) Raised fasting glucose levels (≥ 100 mg/dL), or previously diagnosed T2DM.

Results: Metabolic syndrome was significantly higher among PsA patients than control group (42% Vs 16% respectively).

Regarding frequency of MetS components, obesity was the highest component among PsA patients (62%) as illustrated in Figure 1.

CRP mean level was significantly higher in PsA patients compared to control group with p <0.001*. CRP serum level showed a positive significant correlation with DAPSA score and HOMA-IR (P= 0.031, 0.002 respectively)

Correlations between MetS components and (disease activity, skin severity and physical function) are shown in Table 1.

Conclusion:

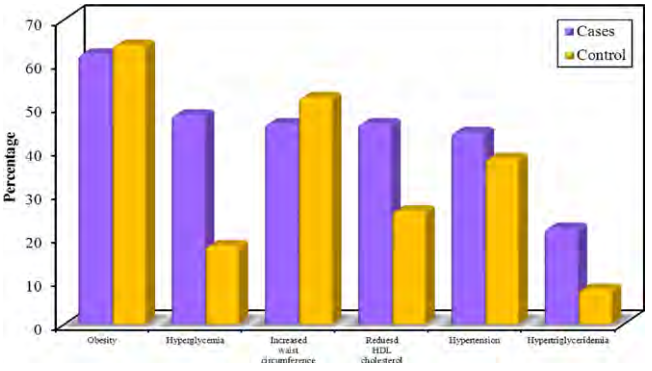
1-There is high frequency of MetS in PsA patients compared to control group.

2- Obesity and DMT2 were the most common components of MetS.

References:

[1] Eder L, Harvey P, Chandran V, Rosen CF, Dutz J, Elder JT, et al. Gaps in diagnosis and treatment of cardiovascular risk factors in patients with psoriatic disease: an international multicenter study. The Journal of rheumatology. 2018:jrheum. 170379.

[2] Alberti KGMM, Zimmet P, Shaw J. Metabolic syndrome—a new world-wide definition. A consensus statement from the international diabetes federation. Diabetic medicine. 2006;23(5):469-80.



Psoriatic Arthritis		Metabolic syndrome							
		WC	BMI	TG	HDL	FBS	HOMA-IR	Systolic BP	Diastolic BP
DAPSA	r_s	-0.233	0.081	0.086	-0.116	0.263	0.387	0.136	-0.170
	P	0.308	0.728	0.710	0.616	0.250	0.083	0.557	0.462
BASDAI	r_s	0.798*	0.152	0.060	-0.110	-0.424	-0.294	0.168	-0.027
	P	<0.001*	0.509	0.798	0.636	0.055	0.196	0.467	0.906
PASI	r_s	0.435*	0.226	0.363	-0.521*	-0.276	-0.253	-0.054	-0.060
	P	0.049*	0.324	0.106	0.015*	0.227	0.268	0.818	0.795
HAQ-DI	r_s	0.189	0.176	0.168	-0.286	-0.240	-0.184	-0.343	-0.276
	P	0.413	0.445	0.466	0.209	0.295	0.424	0.128	0.225

Disclosure of Interests: None declared

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AB0763

THE INFLUENCE OF OBESITY ON BIOLOGICAL DMARD TREATMENT RESPONSE IN PSORIATIC ARTHRITIS: HUR-BIO REAL LIFE RESULTS

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Background: Obesity could be a risk factor for response to treatment and disease severity in psoriatic arthritis (PsA) because of potential pro-inflammatory effects of cytokines produced by adipose tissue (1).

Objectives: This study aimed to assess association of demographic, clinical and disease activity indices with obesity in patients using biological disease-modifying antirheumatic drugs (bDMARD) treatment in HUR-BIO cohort.

Methods: HUR-BIO (Hacettepe University Rheumatology Biologic Registry) is a prospective, single center database of biological treatments since 2005. Until January 2020, HUR-BIO PsA registry enrolled 469 patients. Demographic, clinical, laboratory, therapeutic data were collected from this database which including tender/swollen joint counts, Erythrocyte Sedimentation Rate (ESR), C-Reactive Protein (CRP), Health Assessment Questionnaire (HAQ), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Disease Activity Score - 28 joint (DAS28), Disease Activity index for Psoriatic Arthritis - 28 joint score (DAPSA-28), Psoriatic Arthritis Impact of Disease 12-item questionnaire (PSAID-12). BMI≥30 was defined as obesity.

Results: HUR-BIO PsA had 469 PsA patients and 441 patients with available BMI data were enrolled. Overall, 187/441 patients (42%) had obesity. The median follow-up period of obese and non-obese PsA patients was 7 (3-12) and 8 (4-12) years, respectively (p: 0.31). Obese patients were older at the age of PsA diagnosis (43 (33 - 53) vs 36 (28 – 45) years, p<0.001), higher female gender (76% vs 64%, p: 0.008), higher comorbidities (53% vs 27%, p<0.001). While there was no difference between the two groups in uveitis, IBD, family history and smoking; HLA-B27 was higher in non-obese patients (table). DAS28, BASDAI, DAPSA-28 joints, PSAID-12 were higher in the obese group than in the non-obese group, both before the biological DMARD and at the last visit (p <0.05) (figure 1). BASDAI50% response were similar and patients with HAQ score <0.5 were less frequently in obese patients. For obese and non-obese PsA patients, first bDMARDs percentages were adalimumab 46 vs 48, etanercept 18.2 vs 17, infliximab 14 vs 18, golimumab 7 vs 7.5, certolizumab 12 vs 7, secukinumab 1 vs 0.5, ustekinumab 1 vs 1, others 1 vs 1%, respectively and were similar (p: 0.72). Retention rate for first bDMARD was higher in non-obese than obese patients. Median of the retention rate of bDMARD in obese and non-obese groups was 54.2 and 79, respectively (log rank p: 0.03) (figure 2).

Conclusion: Obesity was associated with higher disease activity and poorer effect of bDMARD treatment in patients with PsA. In obese PsA patients with high disease activity despite bDMARD therapy, intentional weight loss may be recommended as an adjunctive therapy.

References:

[1] Klingberg E, Bilberg A, Björkman S et al. Weight loss improves disease activity in patients with psoriatic arthritis and obesity: an interventional study. *Arthritis research & therapy*, 2019, 21.1: 17.

Table. Baseline and last visit demographic, clinical and disease activity by BMI categories

	BMI > 30	BMI < 30	p-value
Age at PsA, years, median (Q1-Q3)	43 (33-53.5)	36 (28-45)	**0.000***
Disease duration, years, median (Q1-Q3)	7 (3-12)	8 (4-12)	0.31
Gender (male/female, %)	24/76	36/64	**0.008***
Smoking Ever n, %	102 (54.8)	159 (62.8)	0.091
HLA B-27 (+) n, (%)	7 (14)	32 (35)	**0.006***
Uveitis n, %	4 (2.2)	6 (2.4)	0.571
IBD n, %	4 (2.1)	6 (2.4)	0.567
PsA/Pso Family history n, %	74 (39.6)	84 (33.2)	0.169
Taking steroids before biological drugs n, %	115 (61.5)	156 (61.7)	0.972
BASDAI50% response n, %	35 (31.8)	61 (41)	0.13
Last HAQ score < 0.5 n, %	91 (52.3)	160 (68.1)	**0.001***

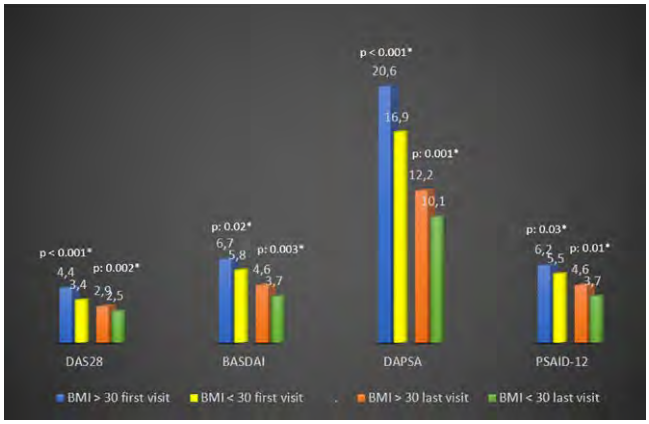


Figure 1. Baseline and last visit disease activity by BMI categoriesp: 0.03*p: 0.01*p: 0.001*p: 0.002**p < 0.05BMI: Body mass ındex, DAS: Disease Activity Score, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, DAPSA: Disease Activity index for Psoriatic Arthritis, PSAID: Psoriatic Arthritis Impact of Disease

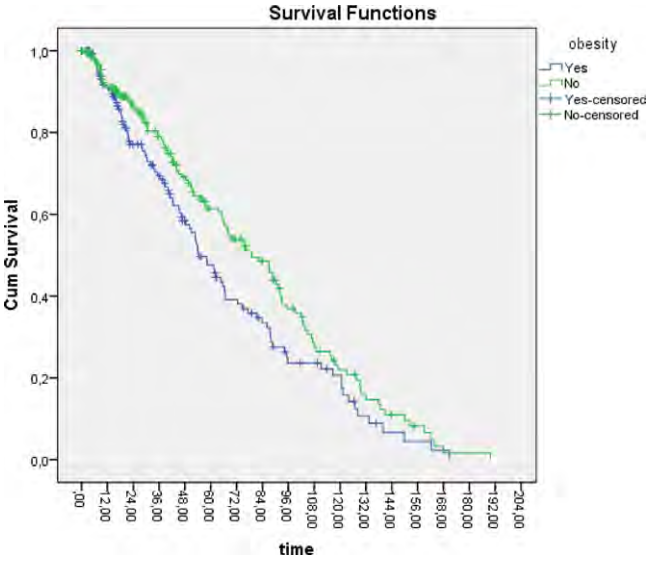


Figure 2. Retention rate for biological DMARD by BMI categoriesMedian of retention rate of first bDMARD: BMI > 30 kg/m^2 and < 30 kg/m^2 54.2 and 79, respectively.Log rank p-value between BMI > 30 kg/m^2 and <30 kg/m^2: **0.03***

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AB0764

SAFETY OF SYSTEMIC CORTICOSTEROIDS IN A SHORT REGIMEN IN PATIENTS WITH PSORIATIC ARTHRITIS. RETROSPECTIVE ANALYSIS OF A LARGE OBSERVATIONAL COHORT.

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Background: There is controversy surrounding the use of systemic corticosteroids in psoriatic arthritis (PsA). It's an accepted fact that the use of systemic corticosteroids can trigger severe flare-up of erythroderma or pustular psoriasis. Nevertheless, corticosteroids have been used to achieve faster improvement of joint symptoms of PsA.
Objectives: To analyze the use of systemic corticosteroids at intermediate doses in a short regimen in patients with PsA, as well as the serious complications of psoriasis upon withdrawal.
Methods: Retrospective analysis of an observational cohort of 453 patients from a university hospital, following a specific protocol from 1992 to 2019. The following variables have been collected: corticosteroid treatment (methylprednisolone ≤16mg /day in a slow tapering regimen in 2 months), demographic and disease factors, comorbidities that could be associated (diabetes mellitus, high blood pressure, severe infections) and serious complications of psoriasis (erythroderma or pustular psoriasis). To assess the activity of psoriasis, physician global assessment is mostly used and occasionally to a lesser extent body surface area and psoriasis area severity index.
Statistical analysis (SPSS v.25): descriptive analysis, Chi-squared test for qualitative variables and t-student test for quantitative variables.
Results: In our series, 35.98% (163/453) of patients have received short corticosteroid regimen at some point in follow-up care, of which 93.8% received concomitant treatment with disease modifying antirheumatic drugs (DMARD).
Only 6.2% of the patients who received short corticosteroid regimen presented a flare-up of psoriasis, most of them mildly. No patient developed an erythroderma or severe pustular psoriasis.
After analyzing the data, a greater use of this regimen of treatment has been observed in patients with dactylitis (44.6% with dactylitis vs 27.8% without dactylitis, p<0.001) and a lower use of corticosteroids in axial PsA (14% of axial PsA vs 41% of non-axial PsA, p<0.001).
There were no significant differences in the use of corticosteroids in respect to sex, age, age of onset of PsA, duration of PsA or high blood pressure. Nor in factors of poor radiographic prognosis: number of damaged joints, mutilating PsA and carpitis.
Conclusion: In our series, no patient developed an erythroderma or severe pustular psoriasis and most of the flare-ups of psoriasis were mild. The use of systemic corticosteroids at intermediate doses in a slow tapering regimen concomitantly with DMARD can be safely used in patients with PsA.
References: None
Disclosure of Interests: None declared
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AB0765

CAN A 6-JOINT ULTRASOUND SCORE DIFFERENTIATE RHEUMATOID ARTHRITIS FROM PSORIATIC ARTHRITIS? A CROSS SECTIONAL STUDY

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Background: Ultrasonography (US) is a well established technique both for diagnosis and follow up in Rheumatoid Arthritis (RA) and Psoriatic Arthritis (PSA)[1]. To date, there is no consensus regarding a standardized US evaluation of joint involvement by a validated score to be used for differential diagnosis.
Objectives: 1) To differentiate the ultrasound features of patients affected by active RA or active PSA by using a 6-joints score[2]. 2) To analyze correlations between those findings and clinical patterns of PSA disease.
Methods: 68 RA and 38 PSA patients (divided in two equal subgroups according to the clinical involvement i.e. polyarticular or oligoarticular) were enrolled in a multi-center cross-sectional study. All patients underwent clinical evaluation including demographic data, disease characteristics, laboratory test and tender/swollen joints count. SDAI and DAPSA were calculated in accordance to the disease and standard of care. The sonographic evaluation of wrists, II MCFs and knees, was performed using a multifrequency linear probe (13-18 MHz) with power Doppler (7.5 MHz, PRF500 Hz). High-end equipment was used and the scanning technique as well as the lesion assessment was previously agreed among the participants, who performed a consensus session 100 images. A validated ultrasound score[2], which included effusion, synovial hypertrophy and synovial hypervascularization at 6 joints sites was used. Those lesions were assessed according to OMERACT definitions and semi-quantitatively graded (0-3). By summing the scores obtained at each joint site and globally, a joint score for articular involvement, a score for the severity of each lesion and a global 6-joint score for all abnormalities were calculated.
Results: Clinical evaluation showed no statistically significant differences between RA and PSA (table I). Ultrasound detected significant differences in the score of joint effusion (SE) (p<0.021), synovial hypertrophy (SH) (p<0.001) and Doppler signal (p<0.011) between oligoarticular PSA and RA. Significant differences in the joint score of II MCF (p<0.000) and wrist (p<0.032) were also found between oligoarticular PSA and RA. The global 6-joint score was 10,88 in RA, 6,05 in PSA oligoarticular, 16,32 in PSA polyarticular. No differences were found between RA and polyarticular PSA.
Conclusion: Ultrasound evaluation of 6 target joints might help to discriminate RA and PSA oligoarticular subset. The study of a limited number of joints is

Table 1.

Dependent variables	Study Population	p values	
US_SEScore	RA	PSA OLIGO	**.021**
		PSA POLY	.356
	PSA	RA	**.021**
	OLIGO	PSA POLY	**.014**
	PSA	RA	.356
	POLY	PSA OLIGO	**.014**
US_SHScore	RA	PSA OLIGO	**.001**
		PSA POLY	.336
	PSA	RA	**.001**
	OLIGO	PSA POLY	**.004**
	PSA	RA	.336
	POLY	PSA OLIGO	**.004**
US_PDScore	RA	PSA OLIGO	**.011**
		PSA POLY	.102
	PSA	RA	**.011**
	OLIGO	PSA POLY	**.006**
	PSA POLY	RA	.102
		PSA OLIGO	**.006**
US_MCP2Score	RA	PSA OLIGO	**.000**
		PSA POLY	.276
	PSA	RA	**.000**
	OLIGO	PSA POLY	**.002**
	PSA POLY	RA	.276
		PSA OLIGO	**.002**
US_WRISTScore	RA	PSA OLIGO	**.032**
		PSA POLY	.610
	PSA	RA	**.032**
	OLIGO	PSA POLY	**.047**
	PSA POLY	RA	.610
		PSA OLIGO	**.047**
US_KNEEScore	RA	PSA OLIGO	1.000
		PSA POLY	.133
	PSA OLIGO	RA	1.000
		PSA POLY	.180
	PSA POLY	RA	.133
		PSA OLIGO	.180
US_KNEEScore	RA	PSA OLIGO	1.000
		PSA POLY	.133
	PSA	RA	1.000
	OLIGO	PSA POLY	.180
	PSA POLY	RA	.133
		PSA OLIGO	.180

US: ultrasound; SE synovial effusion; SH synovial hypertrophy;
PD power Doppler; MCP metacarpophalangeal; PSA psoriatic arthritis;
OLIGO oligoarticular; POLYpolyarticular

therefore a complementary tool to the clinic, fast and well integrated into the overall assessment of the arthritic patient.

References:

[1] Zabotti A. et al. Clin Exp Rheumatol. 2018; 36:519-525.
[2] Perricone C et al. Rheumatology (Oxford) 2012; 51:866-73.

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AB0766 ACCURACY OF PATIENT REPORTED OUTCOME REPORTING IN RANDOMIZED CONTROLLED TRIALS IN PSORIATIC ARTHRITIS

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Background: Patient-reported outcomes (PROs) allow incorporating the patient's perspective and health related quality of life (HRQoL) into shared decision making when choosing the optimal treatment strategy in patients suffering from psoriatic arthritis (PsA). PsA is a chronic inflammatory disease with heterogeneous manifestations with a range of symptoms, co-morbidities and reduced quality of life. International working groups (1) emphasized to integrate these outcomes as endpoints in clinical trials and as part of the core set of measures.

Objectives: To evaluate the quality of PRO reporting in randomized clinical trials in PsA.

Methods: We conducted a systematic literature review (PROSPERO ID 160930) searching PUBMED, MEDLINE and the Cochrane Library for publications (in English language) on randomized controlled trials investigating biological or targeted synthetic disease modifying drugs in adult PsA patients that included some PROs to evaluate the response to treatment. Two of the authors (BFS, AK) screened, selected and extracted the data of the trials that fulfilled inclusion criteria. Statistics were descriptive.

Results: Of 1392 articles in total 880 were screened (512 duplicates); 92 were selected for detailed analysis with 48 finally analysed. 87% were primary publications were some patient-outcome measure were reported. The Health Assessment Questionnaire Disability Index (HAQ-DI) was reported in all RCTs (100%), while 70% of trials reported on the Short Form (36) Health Survey (SF36). Fatigue (FACIT-F) was reported in 29% of trials with different rates of articles published before and after the OMERACT working group recommendations (27% vs 50%) (1). Data on burden of psoriasis through the Dermatology Life Quality Index in 45%. Other PRO measurements to assess potentially affected health domains such as sleep disturbance, psychological disorders or well-being at work were reported only rarely.

Conclusion: Our SLR shows that all trials report data on HAQ-DI. However, important domains as also emphasized by the OMERACT working group (1) are not routinely reported. Especially fatigue, included in 2016 as part of the OMERACT "Inner core" of the PsA Core Domain Set is only reported in about one quarter of studies, although 50% of studies published after 2016 report on fatigue. Data on emotional well-being, psychological status, productivity losses, and sleep disturbance remain rarely reported in PsA randomized controlled trials.

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[1] Orbai A, de Wit M, Mease P, et al International patient and physician consensus on a psoriatic arthritis core outcome set for clinical trials. Annals of the Rheumatic Diseases 2017;76:673-680.

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AB0767 PATIENTS WITH RHEUMATOID ARTHRITIS HAVE A LOWER BONE DENSITY THAN PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Osteoporosis is a skeletal disease characterized by the loss of bone density resulting in an increased fracture risk. Female sex, advanced age, Caucasian ancestry, previous history of fractures, menopause and certain genetic factors predispose for osteoporosis. In addition, recent studies could prove that chronic inflammatory diseases such as Rheumatoid Arthritis (RA) and long-term treatment with higher doses of glucocorticoids (GCs) represent independent risk factors for the development of osteoporosis. On the other hand, the intake of vitamin D, a calcium-rich diet and physical exercise can be protective. Data describing the prevalence of osteoporosis in patients with other rheumatic diseases like psoriatic arthritis (PsA) are lacking.

Objectives: We compared the prevalence of osteopenia and osteoporosis in patients with RA and PsA, respectively, based on data obtained from our ongoing prospective monocentric study Rh-GIOP investigating glucocorticoid (GC)-induced osteoporosis in patients with different rheumatic diseases (NCT02719314).

Methods: Bone mineral density data measured by dual x-ray absorptiometry (DXA) in patients with PsA (n=92) were compared with data measured in 92 age- and

gender-matched patients with RA. The results were analysed with respect to clinical and laboratory parameters such as data on GC treatment (frequency, duration defined as start of treatment until timepoint of measurement, actual and cumulative dose), csDMARD and bDMARD (including as well tsDMARDs) therapy, serological parameters (Vitamin D, alkaline phosphatase, calcium, inflammatory markers and rheumatoid factor) and functional status (e.g. Health Assessment Questionnaire (HAQ), sporting activities). Statistical analyses were performed descriptively using mean and standard deviation, t-tests for metric variables, and chi-square tests for nominal variables. For subgroup analyses with less than 30 patients per group, tests for non-normally distributed data were used due to the lower test power.

Results: RA patients showed significantly lower means of bone density values (minimal T-score, p=0.03) than PsA patients leading to a higher frequency of osteopenic bone densities (p<0.005). However, no differences in the frequency of osteoporotic bone densities could be detected. PsA patients reported a significantly longer disease duration and a higher current GC dosage. In contrast, the frequency of current GC intake was higher in RA patients. Although the calcium intake was higher in the RA group, neither blood levels of calcium and vitamin D, nor the cumulative GC dose (GCCD) or duration of GC therapy could indicate a causal relationship for the differences observed in bone density values between the two groups. The frequency of csDMARD therapy did not differ significantly between PsA and RA patients while the frequency of bDMARD therapy was higher in the PsA group (p=0.04).

Conclusion: The lower bone density in RA patients seems not to be fully explained by higher GCCD, disease duration or higher levels of inflammation. However, RA patients had a higher frequency of current GC intake. Additionally, differences in bone density between the two groups could be related to the higher number of bDMARD therapies in PsA patients, but further investigations like multivariate analyses with higher numbers of patients are necessary. Furthermore there is more need for research on possible molecular and genetic factors in PsA, which are protecting from low bone density.

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AB0768 TREATMENT WITH TOFACITINIB IN REFRACTORY PSORIATIC ARTHRITIS. MULTICENTER STUDY OF 87 PATIENTS IN CLINICAL PRACTICE

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Background: Tofacitinib (TOFA) is the first JAKi approved for psoriatic arthritis (PsA) in Europe (July 2018). TOFA has shown efficacy in refractory patients to anti-TNF in Randomized Clinical Trials (RCT) (*Gladman D. NEJM 2017; 377: 1525-36*).

Objectives: To assess efficacy and safety of TOFA in clinical practice (CP). To compare the profile of CP with RCT

Methods: Study of 87 patients of CP with PsA treated with TOFA; Results are expressed as percentage, mean±SD or median [IRQ].

Results: 87 patients (28♀/59♂), mean age of 52.8±11.4 years (Table 1). Pattern of joint involvement was: peripheral (n=60), axial (1) and mixed (26). Presented also enthesitis (49.4%), nail involvement (30.2%) and dactylitis (31%).

Prior TOFA, most patients (80%) received oral prednisone, synthetic immunosuppressants (mean 2.3±0.9) and biological therapy (BT) (3.6±1.9): etanercept (n=58), adalimumab (54), infliximab (31), golimumab (37), certolizumab (30), secukinumab (54), ustekinumab (39) and ixekizumab (2). Apremilast was used in 17.

After a mean follow-up of 12.3±9.3 years from PsA diagnosis, TOFA was started (5 mg/12 h). In 48 (55.2%) TOFA was used in combined therapy: methotrexate (30) and leflunomide (15). In the remaining 39, monotherapy was prescribed.

Patients of CP compared with RCT have a longer duration of PsA, worst functional disability (HAQ) and received a higher proportion of corticosteroids and BT (anti-TNF and non-anti-TNF) (Table 1).

Patients improved in activity indexes (PASI, DAS28, DAPSA) and laboratory test (table 2). Minor side effects were reported in 21 patients (gastrointestinal symptoms), and TOFA was discontinued in 29 due to inefficiency mainly.

Conclusion: Patients of CP had a longer evolution and received a greater number of biologics than those of RCT. TOFA as in RCT seems effective, rapid and relatively safe for refractory PsA.

Table 1. Baseline features

	CLINICAL TRIAL *Gladman* N=131	CLINICAL PRACTICE N=87
Age, years (mean±SD)	49.5±12.3	52.8±11.4
Sex, n (%)	67M/64F (51/49)	59M/28F (68/32.2)
Duration PsA, years (mean±SD)	9.6±7.6	12,3±9.3
HAQ-DI	1.3±0.7	1.4±0.7 (n=26)
Swollen joint count, mean±SD	12.1±10.6	5.7±5.8
Painful joint count, mean±SD	20.5±13.0	8.0±6.6
Elevated CRP, n (%)	85 (65)	55 (63.2)
PASI score, median [IQR]	7.6 [0.6-32.2]	9.0 [4.2-15]
Oral glucocorticoid, n (%)	37(28)	44(50.5)
Concomitant synthetic DMARDs, n (%)		
- Methotrexate	98 (75)	30 (34.4)
- Leflunomide	12 (9)	15 (17.2)
- Sulfasalazine	21 (16)	6 (6.9)
- Others	2 (2)	
N. of previous TNF inhibitors, mean±SD	1.7±1.0	2.4±1.4
Previous use of other biological no anti-TNF, n (%)	11 (8)	68 (78.2)

Table 2. Improvement at 1st, 6th and 12th month

	Baseline n=87	1st month n=77	6th month n=52	12th month n=20
Nail involvement, n (%)	17 (19.5)			
Improvement, n (%)		5 (35.7)	6 (60)	5 (83.3)
Enthesitis, n (%)	28 (32.2)			
Improvement, n (%)		8 (47.1)	10 (58.8)	3 (50)
Dactylitis, n (%)	16 (18.4)			
Improvement, n (%)		9 (69.2)	6 (85.7)	0 (0)
CRP mg/dl, median [IQR]	1.9 [0.3-5]	0.5 [0.1-2.2]	0.5 [0.3-1.2]	0.4 [0.4-3.7]
p (vs baseline)		0.004	0.005	0.66
DAS28, median [IQR]	4.8 [4.1-5.40	3.7 [2.8-4.6]	2.8 [2.2-3.8]	2.9 [2.2-3.7]
p (vs baseline)		<0.001	<0.001	<0.001
DAPSA, median [IQR]	28 [18.41-34.05]	15.5 [10.1-25.7]	9 [6.07-15]	4.3 [2.4-8]
p (vs baseline)		<0.001	<0.001	<0.001
PASI, median [IQR]	5 [1-14]	1.4 [0-7]	0 [0-4]	0.05 [0-2.7]
p (vs baseline)		0.192	0.105	0.300

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AB0769 THE IMPACT OF BODY MASS INDEX ON DISEASE ACTIVITY AND ENTHESITIS IN PSORIATIC ARTHRITIS

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Background: Overweight/obesity has increased exponentially in the last decades, becoming a huge Public Health problem. Moreover, an increase in adipose tissue is associated with an increased production of several proinflammatory cytokines and acute phase reactants. Higher BMI has been related with new bone formation including syndesmophytes and enthesophytes. In fact, besides

rheumatologic conditions including Psoriatic Arthritis (PsA), enthesopathy can be a consequence of several clinical conditions including metabolic syndrome, mechanical injuries and degeneration.

Objectives: To evaluate the effect of body mass index (BMI) on disease activity scores and enthesitis scores in Psoriatic Arthritis.

Methods: Retrospective study including all the patients with PsA meeting the CASPAR criteria, beginning first-line biologic therapy at our centre. Demographic and clinical data were collected from the Portuguese database Reumapt. Statistical analysis was performed with SPSS. Continuous variables were compared through Spearman/Pearson correlations.

Results: The mean BMI was 26.8 (SD 0.5). In our sample of 119 PsA patients, 21.5% were overweight and 8.3% were obese. The mean age of patients was 46.3 ± 1.03 years; 60 female and 59 male. The median disease duration was 6.8 (0.3-33.8) years. At baseline mean (SD) disease activity variables were: DAS 28 4vESR 4.9 (0.2), ESR 33.2 (2.3) mm/h; CRP 2.35 (0.3) mg/dL, BASDAI 6.6 (0.2), ASDAS 3.9 (0.1), BASMI 3.7 (0.2), BASFI 5.8 (0.3), MASES 1.9 (0.3), SPARCC 2.3 (0.3). There were statistically significant positive correlations between BMI and MASES at baseline (p=0.024, r=0.411) but there weren't with SPARCC, DAS 28 4vESR, ESR, CRP, BASDAI, ASDAS, BASMI and BASFI.

Conclusion: The data showed that patients with higher BMI values had higher enthesitis scores suggesting that overweight/obesity may have a negative impact on enthesopathy. Further studies are still needed to further understand that possible relationship.

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AB0770 DESCRIBING A COHORT OF PATIENTS WITH PSORIATIC ARTHRITIS ACCORDING TO THE BODY MASS INDEX: EXPERIENCE IN A JOINT RHEUMATOLOGY-DERMATOLOGY CLINIC

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Background: Obesity is a predictor for the development of psoriatic arthritis (PsA) with a negative prognostic impact.

Objectives: We aimed to describe and characterize patients with PsA according to the Body Mass Index (BMI) in a joint Rheumatology-Dermatology unit (PAIDER).

Methods: We retrospectively reviewed patients diagnosed with PsA according to CASPAR criteria visited between May 2012 and May 2019 at the PAIDER clinic of our center. Data on demographic and anthropometric features, serologic findings, source of referral, cardiovascular risk factors and biological treatment were collected from clinical records. Patients were classified according to the WHO International Classification of nutritional status in normal weight (BMI 18.5-24.9 Kg/m2), overweight (BMI 25-29.9 Kg/m2) and obesity (BMI≥30 Kg/m2). A descriptive analysis was performed, and the differences between groups were evaluated using Chi2, T-Student and ANOVA tests. P-values <0.05 were accepted as significant.

Table 1.

Baseline characteristics	Total n=393
Female, n (%)	199 (50,6)
Age, yrs, mean ±SD	52,47 (13,21)
Source of referral, n (%)	
Dermatology	117 (29,8)
Rheumatology	219 (55,7)
Primary Care and Others	22 (5,6)
Smoker, n (%)	97 (25,8)
High Blood Pressure (HBP), n (%)	106 (27,7)
Diabetes, n (%)	48 (12,5)
Hypercholesterolemia, n (%)	98 (25,8)
Hyperuricemia, n (%)	32 (8,6)
HLA-B27 positive, n (%)	68 (21,6)
BMI, Kg/m^2, mean ±SD	28,15 (5,87)
Biological treatment, n (%)	166 (43,2)

Table 2.

Characteristics according to BMI	Normal weight n= 118	Overweight n= 112	Obesity n=118	P value
Female, n (%)	66 (55,9)	52 (46,4)	62 (52,5)	ns
Age, yrs, mean ±SD	47,92 (14,08)	54,71 (11,75)	54,48 (11,54)	**<0,001**
Source of referral, n (%)				Ns
Dermatology	35 (33,7)	37 (35,2)	34 (30,9)	
Rheumatology	63 (60,6)	61 (58,1)	70 (63,6)	
Primary Care and Others	6 (5,8)	7 (6,7)	6 (5,5)	
Smoker, n (%)	37 (33)	23 (21,1)	31 (26,7)	ns
High Blood Pressure (HBP), n (%)	12 (10,5)	37 (34,3)	41 (35)	**<0,001**
Diabetes, n (%)	7 (6)	9 (8,3)	30 (25,6)	**<0,001**
Hypercholesterolemia, n (%)	19 (17)	24 (22,2)	45 (38,5)	**0,001**
Hyperuricemia, n (%)	5 (4,4)	7 (6,8)	19 (16,7)	**0,004**
HLA-B27, n (%)	27 (28,7)	17 (17,9)	13 (12,6)	**0,016**
BMI, Kg/m^2, media ±DE	22,58 (1,78)	27,46 (1,55)	34,42 (5,08)	-
Biological treatment, n (%)	47 (41,2)	45 (40,9)	66 (55,9)	**0,032**

Results: During the study period 393 patients (50.6% women) with a mean age of 52.47 ± 13.21 years were evaluated. Baseline characteristics are shown in table 1.

The mean BMI was 28.15 ± 5.87 kg/m^2. 112 patients (32%) were overweight with a mean BMI of 27.46 ± 1.55 kg/m^2 and 118 patients (34%) were obese with a mean BMI of 34.42 ± 5.08 kg/m^2. Of the obese patients, 80 (67.8%) had obesity grade 1, 28 (23.7%) grade 2 and 10 (8.5%) grade 3.

Characteristics of the patients according to BMI categories are shown in Table 2. We observed that mean age was significantly higher in obese patients (p <0.001), as well as the prevalence of cardiovascular risk factors such as HBP (p <0.001), Diabetes (p <0.001), dyslipidemia (p = 0.001) and hyperuricemia (p = 0.004). Obese patients also received more biological therapy (p=0.032). A higher prevalence of HLA-B27 was observed in patients with normal weight (p=0.016). No differences were found according to BMI regarding gender and source of referral.

Conclusion:

- Almost 70% of patients with PsA visited in the PAIDER clinic of our center have a BMI above normal and more than a third of them are obese, mostly grade 1.
- In our joint clinic there are no differences in BMI regarding the source of referral of the patients.
- Patients with obesity are older, have more cardiovascular comorbidities and receive more biological treatment significantly, which increases the complexity of their management and worsens the prognosis.

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AB0771 DAPSA REMISSION/LOW DISEASE ACTIVITY IS ASSOCIATED WITH LOW PSAID12 IN PSORIATIC ARTHRITIS

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Background: Psoriatic arthritis (PsA) has a prevalence of 0.17% in North-Western of Spain and patients suffer this disease have significant impact on daily life due to articular, dermatological and psychological symptoms. DAPSA VLDA/LDA (≤14) is a therapeutic goal recommended by EULAR for clinical practice.

Objectives: Our aim was to assess the relationship between DAPSA index and PsAID questionnaire in routine clinical practice.

Methods: We performed a cross-sectional study of patient and physician reported outcomes. We obtained clinical information of patients with PsA attending clinic from October 2018 to October 2019. Data were collected from clinical records concerning age, gender, disease duration, joint counts, dactylitis, enthesitis, body surface area (BSA) of psoriasis, laboratory results (ESR and CRP), HAQ, PsAID12, pain and global assessment from patient with numerical rating scale (NRS) and DAPSA index. Data were analysed using SPSS21. Logistic regression was used to assess patient reported outcomes which were associated with DAPSA VLDA/LDA.

Results: Data were available for 210 patient visits, 43% females. DAPSA≤14 was in 143 patients (68.1%) and was associated with higher disease duration, OR 1.079 (1.020-1.142, 95% CI), p 0.008. DAPSA index was not associated with BSA (r 0.126, p 0.176).

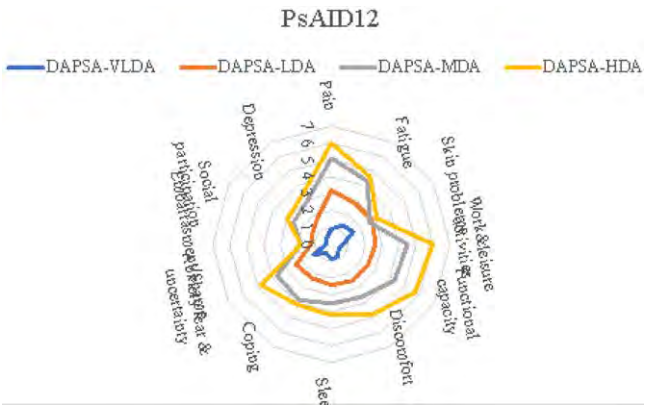


Figure 1.

PsAID12 was evaluated in 156 patients and we saw that patients with DAPSA≤14 had significantly lower PsAID12 (mean 1.7 ± SD 1.7 vs. 3.9 ± 2.1), p< 0.0001. PsAID12 of less than 4 is considered a good outcome and all items of PsAID12 (Figure 1, mean values for NRS) were less than 4 in patients with DAPSA≤14. All components of PsAID12 except item 3 (skin problems) were associated with DAPSA≤14 on univariate analysis but only pain remained independent predictor on multiple regression analysis (p< 0.0001).

Conclusion: In these PsA patients, DAPSA VLDA/LDA was associated with higher disease duration and with lower PsAID12. Pain is dominant symptom in patients with psoriatic arthritis, even in those with DAPSA≤14, and skin problems are not good represented in DAPSA index.

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Acknowledgments: SOGARE

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AB0772 OSTEOPOROSIS AND ITS RELATIONSHIP WITH THE SERUM URIC ACID LEVEL IN PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Although osteoporosis is an inherent comorbidity in inflammatory rheumatic disease and the risk of bone loss is high in patients with several rheumatic diseases, evidence is limited in psoriatic arthritis (PsA). One of the most prominent features in PsA is increased serum urate (SU) levels. Due to its antioxidant effects and protective role against osteoporosis, high SU levels are associated with increased bone mineral density (BMD) and reduced bone loss in the healthy population, and in patients with rheumatoid arthritis. However, whether this association is also present in patients with PsA has not been investigated.

Objectives: The aim of this study was to evaluate PsA patients with respect to the presence of osteoporosis and its association with SU levels.

Methods: This ongoing study included 86 patients (68 female, 18 male) who were diagnosed with PsA according to the CASPAR criteria and had indications for BMD testing according to the National Osteoporosis Foundation. Clinical characteristics including body mass index (BMI), pain VAS, patient global VAS, enthesitis, and tender and swollen joint counts were recorded. Evaluations included the PASI, PsAQoL, and HAQ. Disease activity was assessed using the DAPSA, BASDAI, and MDA. Osteoporosis was defined as a BMD T-score of -2.5 or less and osteopenia as a BMD T-score between -1 and -2.5 (WHO osteoporosis).

Results: The mean age of the study group was 55.4 (SD:9.2) years and the mean disease duration was 84.5 (SD:91.6) months. Indicators of secondary osteoporosis were type-1 diabetes mellitus (1%), hyperthyroidism (2.3%), early menopause (<age 40) (8.1%), and chronic liver disease (9.3%). As for the steroid use, the rates of never, previous and current users were 33.7%, 20.9% and 22.1%, respectively. Osteoporosis was found in 9.3% and osteopenia in 33.7% of the patients. A history of vertebral compression fractures or any fracture was present in 20.9% of the patients, half of whom were in postmenopausal. BMD L_1-L_4 T- and Z-scores were lower in female patients (p<0.05). DAPSA remission and MDA rates were 6% and 15%, respectively. Bone mineral density was similar across DAPSA disease activity categories (remission-low-moderate-high) (p>0.05). The frequency of osteoporosis did not differ significantly between patients with DAPSA remission and non-remission (p>0.05). The mean L_1-L_4 T- and Z-scores, and BMD g/cm^2 were significantly higher in patients with MDA than those without MDA (p<0.05). The mean SU level was 5 (SD:1.3) mg/dl, and 18.6% of the patients had a SU level of 6 mg/dl or higher. There was no significant correlation between SU and BMD (p>0.05). BMI showed a weak correlation with femur total T-score (r=0.244). PASI showed weak inverse correlations with femur neck T-score (r=-0.286) and total femur T-score (r=-0.245). BMD variables showed no correlations with disease duration, acute phase reactants, BASDAI, PsAQoL, and cumulative steroid dose.

Conclusion: Patients with PsA did not have an increased prevalence of low BMD despite fractures. Osteoporosis was associated with MDA and the severity of psoriasis, but not with DAPSA, SU level, functional impairment, and quality of life.

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Disclosure of Interests: None declared

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AB0773 THE INCIDENCE OF RESIDUAL DISEASE ACTIVITY FOLLOWING DIVERSE DISEASE ACTIVITY MEASUREMENTS FOR PSORIATIC ARTHRITIS

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Background: Due to the complex nature of psoriatic arthritis (PsA), diverse disease activity measures have been developed, the most common of which include Disease Activity Score for Psoriatic Arthritis (DAPSA), Minimal Disease Activity (MDA) and Very Low Disease Activity (VLDA). Recently, new composite measures have been developed such as Psoriatic Arthritis Disease Activity Score (PASDAS) and GRACE index. Due to different domains and assessments, even though these measures may indicate remission or low disease activity, residual disease activity (RDA) may persist.

Objectives: The aim of this study was to evaluate RDA in patients with PsA.

Methods: A total of 148 patients (105 female, 43 male; mean age 47.5 (SD:12.6) years) who met the CASPAR criteria for PsA were recruited. Demographic and clinical characteristics of patients were recorded, including pain visual analog scale (VAS), joint VAS, patient global VAS, and tender and swollen joint counts. Evaluations included the Leeds Enthesitis Index (LEI), Psoriasis Area and Severity Index (PASI), Psoriatic Arthritis Quality of Life (PsAQoL), Short-Form 36 Health Survey (SF-36) and Health Assesment Questionnaire (HAQ). Disease activity and remission were assessed using the DAPSA, MDA, VLDA, PASDAS and GRACE Index. MDA was calculated with 5 and 6 positivity criteria separately. Low disease activity (LDA) was defined as follows: DAPSA ≤14, PASDAS ≤3.2 and GRACE Index ≤ 2.3. RDA was defined as the presence of at least one of the following criteria despite remission or LDA: tender and/or swollen joints >1, dactilitis >1, LEI>1, HAQ>0.5, PASI>1, PtGA>20, physician VAS>20, or pain VAS>15.

Results: The mean duration of disease was 68.2 (SD:80.2) months. DAPSA-LDA, PASDAS-LDA, GRACE-LDA, MDA and VLDA were observed in 48.6%, 14.6%, 14.9%, 23.6% and 2% of PsA patients, respectively. RDA as determined by at least one domain was identified in 91%, 95%, 86% and 86% of patients who were classified as having MDA, DAPSA-LDA, PASDAS-LDA and GRACE-LDA, respectively. Undetected RDA was most common with DAPSA, whereas VLDA completely ruled out RDA. PASDAS and GRACE resulted in similar rates of RDA (Table-1). With DAPSA-LDA, the incidence of RDA in the pain domain was significantly lower with older age. Female patients had higher rates of RDA with the LEI and HAQ (p<0.05).

Conclusion: VLDA was the most and DAPSA was the least sensitive method to detect remission/LDA. RDA should be kept in mind in patients with PsA when using current measures to assess remission or LDA.

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Table 1. RDA in patients with LDA according to diverse activity scores

	Remission and LDA according to disease activity scores, n (%)					
RDA, n (%)	MDA-5 n:35	MDA-6 n:13	VLDA n:3	DAPSA LDA n:72	PASDAS LDA n:22	GRACE LDA n:22
RDA_TJC	4 (11.4)	1 (7.7)	0	25 (34.7)	3 (13.6)	1 (4.5)
RDA_SJC	1 (2.9)	0	0	3 (4.2)	0	0
RDA_dactilitis	2 (5.7)	0	0	2 (2.8)	1 (4.5)	1 (4.5)
RDA_PASI	4 (11.4)	1 (7.7)	0	23 (31.9)	5 (22.7)	5 (22.7)
RDA_VAS pain	23 (65.7)	3 (23.1)	0	56 (77.8)	13 (59.1)	13 (59.1)
RDA_VAS Global	21 (60)	4 (30.8)	0	56 (77.8)	10 (45.5)	11 (50)
RDA_physician VAS	26 (83.9)	8 (61.5)	1 (33.3)	64 (88.9)	15 (71.4)	16 (72.7)
RDA_HAQ	1 (2.9)	1 (7.7)	0	16 (22.2)	1 (4.5)	0
RDA_LEI	1 (2.9)	1 (7.7)	0	24 (33.3)	3 (13.6)	2 (9.1)

RDA: residual disease activity, MDA: Minimal disease activity, VLDA:Very Low disease activity, LDA: Low disease activity, TJC:Tender joint count, SJC: Swollen joint count

Disclosure of Interests: None declared

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AB0774

TIME TO RESPONSE FOR CLINICAL AND PATIENT-REPORTED OUTCOMES IN PATIENTS WITH PSORIATIC ARTHRITIS TREATED WITH TOFACITINIB, ADALIMUMAB OR PLACEBO

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Background: With multiple disease domains affected in PsA, clinical and patient-reported outcome (PRO) measures are important to assess disease improvement following treatment. Rapid, meaningful improvements in disease activity are a priority for physicians and patients (pts). Tofacitinib is an oral Janus kinase inhibitor for the treatment of PsA. Higher proportions of pts achieved responses in PROs and clinical measures when treated with tofacitinib for 3 months vs placebo (PBO).[1-5] Proportions of responders were also similar between tofacitinib and adalimumab (ADA) after 3, 6 and 12 months.[2,3,5]

Objectives: To determine the time to initial response using responder definitions for selected PROs and clinical endpoints in pts with active PsA treated with tofacitinib, ADA or PBO switching to tofacitinib.

Methods: In this post hoc analysis, data were collected from two Phase 3 studies (OPAL Broaden [12 months; NCT01877668]; OPAL Beyond [6 months; NCT01882439]).[3,4] Pts receiving tofacitinib 5 or 10 mg twice daily (BID), subcutaneous ADA 40 mg once every two weeks (Q2W; OPAL Broaden only), or PBO switching to tofacitinib 5 or 10 mg BID at Month (M)3, were included. Responder definitions included: HAQ-DI ≥0.35-point improvement from baseline (BL), Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) total score ≥4-point improvement from BL, minimal disease activity (MDA) yes/no composite response (meeting at least 5 of 7 criteria) and PsA Disease Activity Score (PASDAS) post-BL score of ≤3.2 and >1.6-point improvement from BL. First post-BL data were collected at Week 2 (eg for HAQ-DI) or M1. Time-to-event analyses were performed using the Kaplan-Meier (KM) method, with pts censored at the last observed visit. Log-rank tests compared time to initial response across treatment groups.

Results: KM analyses show days to initial response (Figure 1, Figure 2). Time to initial HAQ-DI response was significantly different between treatment groups in OPAL Broaden ($p<0.01$): faster response in pts receiving tofacitinib 5 mg BID, tofacitinib 10 mg BID and ADA 40 mg Q2W vs pts who switched from PBO to tofacitinib at M3 (Figure 1a). A similar, but not significant (ns), trend was observed for HAQ-DI responses in OPAL Beyond (Figure 1b). Generally, initial FACIT-F responses were achieved faster (ns) in pts receiving tofacitinib 5 mg BID vs other treatment in both studies (Figure 1c, Figure 1d). Times to initial MDA and PASDAS responses were similar between tofacitinib and ADA treatment groups (Figure 2).

Conclusion: Times to initial response in functional ability and disease activity were similar in pts treated with either tofacitinib or ADA. Time to initial response prior to first post-BL observation (Week 2 or M1) was not estimable in this analysis. These results may help physicians better understand the time frame for a meaningful response in pts receiving tofacitinib.

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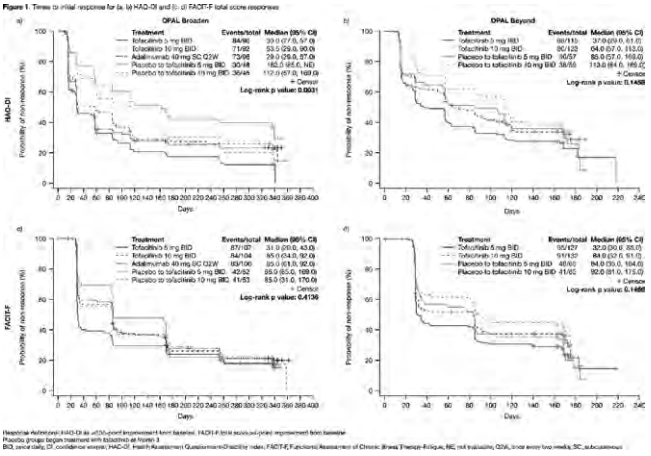
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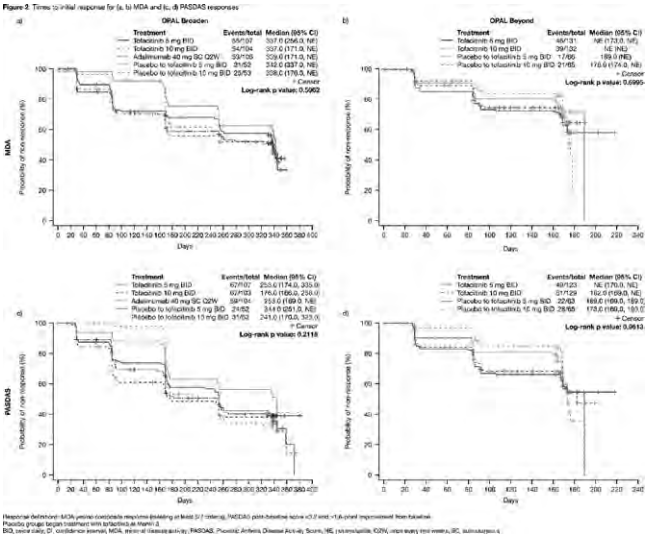
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AB0775

PERIPHERAL JOINT INFLAMMATION IS ASSOCIATED WITH MORE PROATHEROGENIC CARDIOVASCULAR RISK PROFILE IN PATIENTS WITH PSORIATIC ARTHRITIS

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Background: We have previously found that: (i) patients with spondyloarthritis (SpAs) have higher circulating levels of IL-18 and osteoprotegerin (OPG) than healthy controls (1), (ii) psoriatic arthritis (PsA) patients present with more proatherogenic lipid profile and higher IL-18 levels than ankylosing spondylitis (AS) patients (2)

Objectives: To investigate the relationship between disease phenotype, i.e. peripheral arthritis (perPsA n=45), axial PsA (axPsA n=16) and ankylosing spondylitis (AS n=94), cardiovascular risk factors and serum concentrations of IL-18, IL-17.

Methods: A group of 155 SpA patients (94 AS/61 PsA), of similar age (44.5 versus 44.9 years), disease duration (4.8 versus 6.8 years), and matched with high disease activity (AS ASDAS-CRP 3.62±0.94; PsA DAPSA 26.75±26.61) were included in the study. The lipid profile comprised triglycerides (TG), total cholesterol (tChol), low- and high-density lipoprotein (LDL and HDL, respectively) measurement. Ischemic Heart Disease (IHD) diagnosis was established from patient's medical history. Serum concentrations of IL-17AF, IL-18 were measured by specific commercially available enzyme-linked immunosorbent assays (ELISA) and were expressed as medians (pg/ml). The Mann-Whitney test was applied for intergroup comparison, correlation was assessed using Spearman's Rank tests (r value is shown) with linear regression model.

Results: Patients with perPsA had higher rate of IHD than axPsA and AS patients (27% vs 0% vs 7.8%, respectively). perPsA patients had significantly higher diastolic blood pressure than AS patients (perPsA 131±13mmHg vs AS 121±14 mmHg), more severe cardiovascular burden than patients with axial disease, were characterised by higher occurrence of obesity (perPsA 42% vs axPsA o 18% vs 18% AS) and hypertriglyceridemia (perPsA 48% vs axPsA 14% vs 16%AS) as well as higher TG concentration (perPsA 165± 87 mg/dl vs axPsA 111± 63mg/dl vs 110± 57 AS mg/dl). Moreover, patients with perPsA had significantly higher serum concentrations of IL-18 than axPsA and AS groups (132.5pg/ml vs 79.2pg/ml vs 84.9pg/ml), but there were no differences between them in IL-17 concentrations. Interestingly, in patients with perPsA, but no other patients' groups, statistically significant associations between IL-18 concentrations and proatherogenic risk factors were found, as IL-18 correlated positively with TC (r=0.31), TG (r=0.53) atherogenic index (r=0.6), and uric acid (r=0.3) concentrations, while negatively with HDL levels (r=-0.47). Although patients groups differ in cardiovascular risk profiles, there were no significant differences in CV risk estimation using SCORE scale (perPsA 2.3% vs 1.6% axPsA vs 2.1%AS)

Conclusion: We conclude that in PsA peripheral joints inflammation is associated with more proatherogenic cardiovascular risk profile and higher IL-18 serum levels, that seem to be interrelated, while patient's disease activity is associated with metabolic syndrome. Generally recommended SCORE scale is practically unable to indicate SpA patients with higher CV risk

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Disclosure of Interests: None declared

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AB0776 ACCESSORY STAGE IN THERAPY OF PSORIATIC ARTHRITIS WITH ENGINEERED BIOLOGICAL PREPARATIONS

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Objectives: increasing the sorption capacity of medications based on interleukin-12 and interleukin-23 in patients with psoriatic arthritis

Methods: To reduce the concentration of anti-inflammatory cytokines (IL-12, IL-23) we ran the blood from psoriatic arthritis patients through granules which had been obtained preliminarily by emulsion polymerization. Antibodies to IL-12 and IL-23 were obtained from the commercial formulation Ustekinumab with a concentration of monoclonal antibodies -0,2 mg in 1 ml of saline solution. They were of spherical shape, with gel particle size 10 – 100 mcm. Specific sorption capacity of magnetocontrollable polyacrylamide granules (MPG) was determined using a mini-column with working chamber capacity of 0,2 ml, filled with MPG through which Il-12 and Il-23 solutions (1 ml) were run in increasing concentrations.

Results: Perfusion of the blood through a magnetocontrollable adsorbent was done using a column of 10 ml capacity equipped with an electric magnet; magnetocontrollable polyacrylamide granules with immobilized antibodies to IL-12 and IL-23 were added to the column. This device was used for in vitro processing of heparinized blood from 10 patients with psoriatic arthritis of varying degree of activity who had not received parenteral administration of cytokine IL-12 and IL-23 inhibitors (Ustekinumab) for 12 months. Blood from 10 apparently healthy donors was used as control; the perfusion procedure was the same. The concentration of cytokines (IL-12 and IL-23) in the blood plasma was determined with immunoenzyme assay commercial kits: Bender Med. Systems, USA for IL-12, and Bender Med. Systems, Vienna Austria for IL-23. The parameters under study were determined twice for each sample: prior to and after perfusion. It was established that perfusion through a magnetocontrollable adsorbent leads to a considerable decrease in IL-12: by 99,8% from baseline (in apparently healthy individuals), and by 99,9% in psoriatic arthritis patients; the concentration of IL-23 decreased by 99,9% in psoriatic arthritis patients. That is why decreasing the cytokine level as much as possible is of great practical importance as the cytokines play the leading role in psoriatic arthritis pathogenesis. When comparing data on carbon–based adsorbents found in literature we saw that the cytokine concentration decreased by 92,64% from baseline. Elimination of the cytokines did not bring about any statistically important change in the content of blood corpuscles, which is an additional advantage of the method.

Conclusion: The obtained findings demonstrate high effectiveness of the method of simultaneous sorption of interleukin-12 and interleukin-23 using an original magnetocontrollable adsorbent based on Ustekinumab. The proposed adsorbent shows little traumatism in relation to blood corpuscles, as well as low nonspecific sorption. Extracorporeal elimination of cytokines from the blood flow can be a promising preparatory step in genetically designed treatment of patients with psoriatic arthritis.

Disclosure of Interests: None declared

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AB0777 EPIDEMIOLOGY, CLINICAL FEATURES AND BIOLOGICAL TREATMENT OF UVEITIS IN 320 PATIENTS WITH PSORIATIC ARTHRITIS. STUDY FROM A SINGLE UNIVERSITY CENTER.

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Background: Uveitis is an extra articular manifestation of psoriatic arthritis (PsA). Biological therapy, especially monoclonal TNF inhibitors, are useful to prevent and to treat refractory non-infectious uveitis. However, other biologics had been related to paradoxical uveitis

Objectives: Our aim was to assess **a)** the epidemiological and clinical features of uveitis associated to PsA and **b)** its relationship with biological treatment used in PsA.

Methods: Observational study of unselected consecutive patients studied in a single reference University Hospital with**: a)** diagnosis of PsA by CASPAR criteria and **b)** diagnosis of uveitis by ophthalmologist exploration. Demographics features, clinical findings, complementary tests and treatment were recorded.

Results: We studied 320 (182 women/138 men) patients with PsA; mean age at PsA diagnosis of 41.7±15.79 years and with a delay of diagnosis from the onset of symptoms of 2.6±2.01 years.

Ten patients (4 men/6 women) out of 320 patients (prevalence 3.13%) with a mean age of 42.2 ± 16.8 years were diagnosed of uveitis after a mean follow-up of 10±7.9 years. In all cases, the uveitis had an anterior pattern. Only 1 (10%) of them had a bilateral affection, acute onset in 10 patients (100%), and 4 of them (40%) had a recurrent pattern. The diagnosis of uveitis preceded the one of PsA in 5 (50%) patients in 1.6±0.87 years. In those with a previous diagnosis of PsA, it was done 13.3±10.4 years before the uveitis onset. Only 1 patient (10%) with recurrent unilateral uveitis presented vitritis. In 10 patients the mean number of anterior chamber cells was 2±0.4. Comparison of baseline characteristics and clinical features between patients who developed uveitis and those who did not is shown in **table.**

Only 2 patients (20%) with uveitis received biological therapy. The first one developed its first episode of uveitis after 29 months with etanercept. After the episode, a switch to adalimumab was done, without any other episode of uveitis after 22 months of treatment. The second one was a patient with multiple episodes of recurrent uveitis, who developed new flares with adalimumab, certolizumab and golimumab.

Conclusion: Most of the uveitis had an anterior and unilateral pattern. The onset of uveitis in patients with PsA can either precede or go after the diagnosis of the PsA. HLA B27+ was more frequent in patients with uveitis. Biological therapy did not achieve good answer in patients with recurrent uveitis.

Table.

	Uveitis (n=10)	Non uveitis (n= 310)	p
Baseline general features			
Age, years (mean±SD)	42.2 ± 16.8	46.4 ± 11.9	0.38
Sex, n (m/w) (%)	4/6 (40/60)	134/176 (43.2/56.8)	0.90
HLAB27, positive %	60	11.8	<0.01
Disease Characteristics			
Axial arthritis, %	40.0	37.0	0.88
Peripheral arthritis, %	80.0	72.9	0.89
Hip affection, %	30.0	20.0	0.71
Enthesitis, %	60.0	40.5	0.55
Dactylitis, %	20.0	29.5	0.77
Scores			
BASDAI (mean ± SD)	3.3 ± 2.08	2.4 ± 1.9	0.26
BASFI (mean ± SD)	2.7 ± 1.9	1.6 ± 1	0.31

Disclosure of Interests: Iñigo González-Mazón: None declared, Lara Sanchez-Bilbao Grant/research support from: Pfizer, Natalia Palmou-Fontana: None declared, David Martinez-Lopez: None declared, Susana Armesto: None declared, Miguel A González-Gay Grant/research support from: Pfizer, Abbvie, MSD, Speakers bureau: Pfizer, Abbvie, MSD, Ricardo Blanco Grant/research support from: AbbVie, MSD, and Roche, Speakers bureau: AbbVie, Pfizer, Roche, Bristol-Myers, Janssen, and MSD
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AB0778 ASSOCIATION BETWEEN PATIENT-REPORTED OUTCOMES AND DISEASE ACTIVITY IN BIMEKIZUMAB-TREATED PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Bimekizumab (BKZ) is a humanised IgG1 monoclonal antibody, which selectively neutralises interleukin (IL)-17A and IL-17F. There is support for the BKZ mechanism of action as a novel therapeutic approach for psoriatic arthritis (PsA).[1-3] The phase 2b dose-ranging BE ACTIVE study assessed the efficacy and safety of BKZ in patients (pts) with PsA; data are reported elsewhere.[4] Patient-reported outcomes (PROs) are increasingly recognised as important endpoints in clinical trials.[5] The Psoriatic Arthritis Impact of Disease-9 (PsAID-9) questionnaire was specifically developed to assess health-related quality of life (QoL) in pts with PsA[5] and its validity in clinical practice has been demonstrated.[5-6]
Objectives: To report the association between PsAID-9 score (a PRO) and disease activity response (very low disease activity [VLDA], minimal disease activity [MDA] or Disease Activity Index for Psoriatic Arthritis [DAPSA] remission) during 48 weeks' (wks') BKZ treatment.
Methods: Details of the study design (NCT02969525) are reported elsewhere.[4] Here, we report the proportion of pts who achieved a PsAID-9 score ≤3, and the association between PsAID-9 score at Wk 48 (range 0–10, where 10 corresponds to worst QoL) and VLDA/MDA (binary states of disease control) or DAPSA (range 0–>28 where 0–4 is remission, 5–14 is low, 15–28 is moderate, and >28 is high disease activity) at Wk 12.
Results: Across 206 randomised pts at baseline, 66.5% had psoriasis body surface area (BSA) ≥3%, 18.9% had prior tumour necrosis factor inhibitor (TNFi) exposure, and 63.6% received concomitant methotrexate. A substantial proportion of pts achieved MDA and/or DAPSA remission by Wk 12, which generally increased through to Wk 24 and 48 (**Table 1**). The 160 mg BKZ group saw the highest Wk 48 rates of MDA response (60.0%) and DAPSA remission (45.0%) (**Table 1**). The proportion of pts achieving a PsAID-9 score ≤3 was consistently high across all active treatment arms (**Figure 1**). PsAID-9 score was consistently lower (indicating better QoL) for pts with VLDA or MDA, and those in DAPSA remission (**Figure 2**), indicating that low disease activity was associated with improved PROs.
Conclusion: In BKZ-treated pts, improvements in PsAID-9 were associated with achievement of VLDA/MDA response and DAPSA remission. These results suggest that pts achieving higher disease control have improved QoL.
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Table 1. MDA and DAPSA responder rates

	MDA (%) [a]			DAPSA remission (%) [b]		
Treatment arm	**Wk 12**	**Wk 24**	**Wk 48**	**Wk 12**	**Wk 24**	**Wk 48**
BKZ 160 mg (n=40)	47.5	50.0	60.0	20.0	35.0	45.0
BKZ 160 mg LD (n=37) [c]	43.2	59.5	54.1	29.7	48.6	37.8
BKZ 320 mg (n=41)	29.3	36.6	46.3	12.2	19.5	34.1

[a] DBS, pts with missing data were counted as non-responders; [b] DBS, missing data are imputed using last observation carried forward; [c] 160 mg with 320 mg LD at baseline. BKZ: bimekizumab; DAPSA: Disease Activity Index for Psoriatic Arthritis; DBS: dose-blind set; LD: loading dose; MDA: minimal disease activity.

Figure 1. Proportion of patients achieving PsAID-9 score ≤3

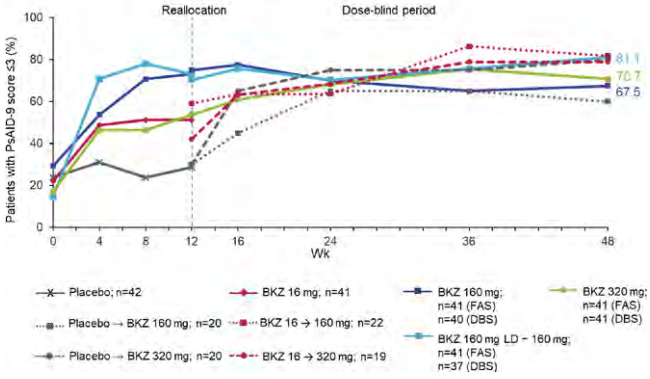
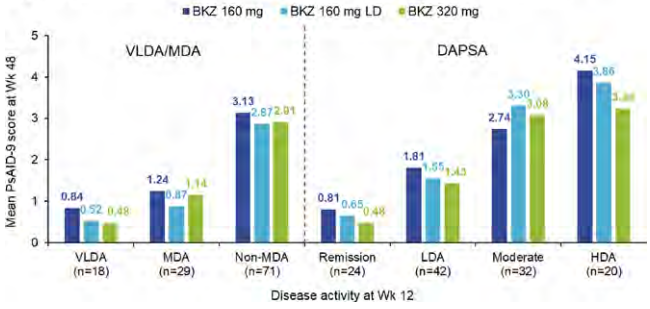


Figure 2. Association between PsAID-9 and VLDA, MDA, and DAPSA disease states at Wk 48



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AB0779 DOES DACTYLITIS/ENTESITIS PREDICT THE RESPONSE TO A SPECIFIC BIOLOGICAL TREATMENT IN PSORIATIC ARTHRITIS?

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Background: Spondylarthritis are diseases with a pathophysiological focus in enthesis with a different extent of synovial component. In the event of therapeutic failure with DMARDs, the clinician may consider biological therapy with anti-TNF drugs or other targets such as IL23 Despite this, most patients receive first-line anti-TNFs. Given that IL19 and IL23 activity is recognized at the level of the enthesis.
Objectives: To evaluate whether the presence of dactylitis/entesitis could be useful in the choice of a particular biological therapy.
Methods: A secondary analysis of a previous study was performed based on an electronic survey completed by patients with PsoA and distributed among members of the patient association "Acción Psoriasis". Records from 191 respondents who had received at least one biological therapy were included. Patients were grouped according to the presence or absence of dactylitis or enthesitis. The rate of need to progress to the next therapeutic biologic line was compared.
Results: 61 patients reported dactylitis and 155 enthesitis. Distribution of treatments in patients with dactylitis: 33 patients received an anti-TNF-alpha, 11 Secukinumab and 12 Ustekinumab. 15 patients in the group receiving an anti-TNF-alpha had to substitute another treatment within 2 years (45.4%). 3 patients in each of the remaining groups had to substitute treatment within 2 years (27.2% and 25%, respectively). Compared to those receiving anti-TNF-alpha therapy, patients treated with Secukinumab or Ustekinumab had greater therapeutic persistence at 2 years (P<0.001, in both cases). Distribution of treatments in patients with enthesitis (not including dactylitis): 115 received an antiTNF-alpha, 25 received Secukinumab and 18 received Ustekinumab. 38 patients who received an anti-TNF-alpha had to substitute it within 2 years (24.5%). 4 patients who received Secukinumab and 3 who received Ustekinumab had to substitute their treatments in less than 2 years (16% and 16.6%, respectively). Compared to patients receiving anti-TNF-alpha therapy, patients treated with Secukinumab and Ustekinumab had a higher proportion of therapeutic persistence at 2 years (P<0.05 for both cases).
Conclusion: The presence of dactylitis more than enthesitis, is associated with a higher proportion of therapeutic persistence in those patients treated with anti-IL17 or anti-IL23 therapies. Although there are multiple factors that condition the choice of biological therapies in patients with PsoA, the presence of enthesitis and dactilitis (understood as polyenthesitis) should be considered among the most important ones.
Disclosure of Interests: None declared
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AB0780 TREATMENT PERSISTENCE OF BIOLOGICS AMONG PATIENTS WITH PSORIATIC ARTHRITIS (PSA)

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Background: Persistence in biologic therapy in psoriatic arthritis is critical to optimize symptom remission, functional capacity and health care costs.
Objectives: To estimate the persistence to biologic treatment prescribed to PsA patients in a real-life setting as well as factors associated with improved biologic drug survival in these patients.
Methods: Patients with PsA from a large health care provider database with at least two consecutive dispensed prescriptions of a biologic agent indicated for PsA from January 1st, 2002 until December 31st, 2018 were identified and followed until medication stop date or the end of observation period. Patients were considered non-persistent whenever a new prescription was dispensed and a permissible gap of 6 months was exceeded prior to starting on this biologic agent from the prescription date. Treatment changes were based on physician decisions and patient preferences. Demographic data including age, sex, BMI, ethnicity, smoking history and socioeconomic status as well as Charlson comorbidity index were retrieved. Data regarding use of steroids and non-biologic disease-modifying anti-rheumatic drugs were also extracted. Descriptive statistics, including means (standard deviations) for continuous variables and frequencies (%) for categorical variables, were used. Persistence estimates were derived using non-parametric survival analysis using Kaplan-Meier functions, with treatment discontinuations as failure events. Cox regression hazard ratio models were conducted to investigate factors associated with drug persistence.
Results: 2301 PsA patients with 2958 treatment periods were identified and included in the analyses. The mean age was 50.9±14 years of whom 54% were females, 70.4% of the study population had a BMI>25, and 36% were obese(BMI>30), 40% were current smokers, and 76% had a Charlson comorbidity index higher than 1. The most commonly prescribed drug was etanercept, followed by adalimumab, golimumab, secukinumab, ustekinumab and infliximab at 33%, 29%, 12%, 10%,8% and 8%, respectively. Only about 20% of patients remained on a particular biologic agent after 5 years, whereas about 40% persisted on therapy following 20 months of treatment. A Kaplan-Mayer survival analysis with pairwise comparisons of all treatment choices with respect to lines of therapy was conducted. When analyzing the data for all treatment periods and taking into account all lines of therapy, secukinumab had a higher persistency than adalimumab, infliximab and ustekinumab, with a Log Rank of 0.022, 0.047 and 0.001, respectively, as is shown in figure 1. Female sex and smoking were associated with lower drug persistence (HR=1.25, 95%CI 1.13-1.38 and HR=1.109, 95%CI 1.01-1.21, respectively). When analyzing the data regarding second-line biologic agents, secukinumab was found to be superior to adalimumab, etanercept, infliximab and ustekinumab but not to golimumab with a Log-Rank P value of 0.001, 0.004, 0.025 and 0.002, respectively (figure 2). On analyzing the data using only the first indicated biologic line, no superiority of any single anti-Tumor Necrosis Factor-alpha (anti-TNFα) agent was observed.
Conclusion: In this large observational cohort, in the era of biologic therapy, a relatively low persistence was observed, with female sex and smoking having a negative impact on persistency. None of the anti-TNFα agents as first line therapy was found to be more persistent than others, while secukinumab was found to be superior to other biologics when indicated as second line of therapy.
References: None

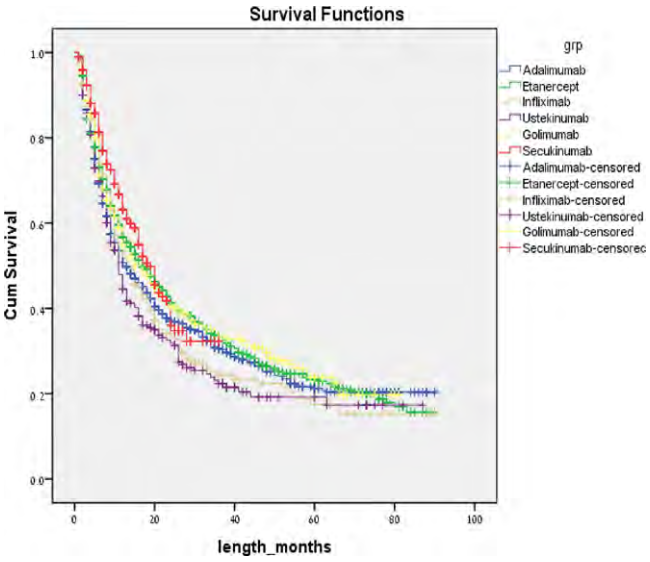


Figure 1.

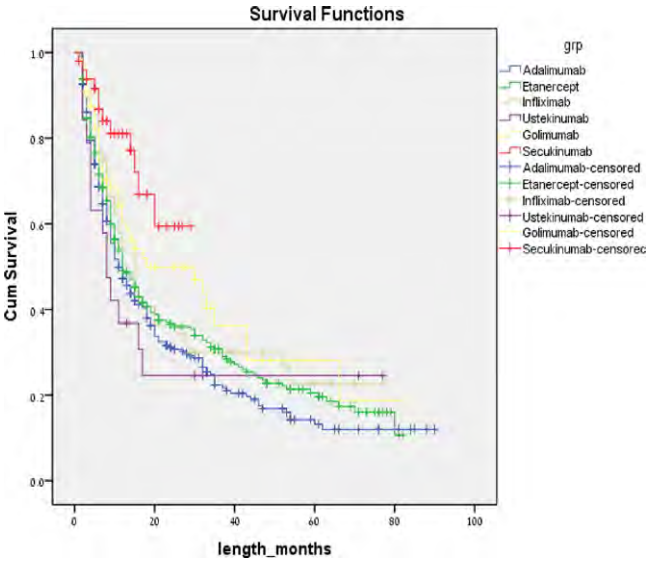


Figure 2.

Acknowledgments: none
Disclosure of Interests: None declared
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AB0781 OPTIMIZATION OF APREMILAST USE IN DAILY PRACTICE BY EXPECTATION MANAGEMENT

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Background: Apremilast is an oral phosphodiesterase 4 inhibitor and approved drug for treatment of Psoriatic Arthritis(PsA). Previous studies show apremilast to be efficacious and safe. (1) However, physician are sometimes reluctant to prescribe apremilast in clinical practice due to its perceived side effects, and relatively small effect size (1).
Objectives: In this study we investigated the occurrence and frequencies of adverse events, and the effects of patient expectation management on drug survival for PsA patient starting apremilast.
Methods: From March 2017 to December 2019, 21 consecutive patients have been included in the apremilast PsA cohort at Reade in Amsterdam, the Netherlands. The initial high dropout rate that was observed with usual care led to a revision in the baseline visit with more emphasis placed on patient expectation management.
Results: From the usual care group (UCG; n=12), 10 patients (83%) stopped apremilast within the first year: 6 (50%) due to adverse events, 4 (33%) due to inefficacy. Only 2 patients (17%) completed one year of follow-up. In contrast, in the expectation management group (EMG; n=9), only 1 patient (11%) dropped out due to adverse events, and none stopped due to inefficacy. 2 patients (22%) completed one year of follow-up, the other 6 patients (67%) are within the first year of treatment (median 5 months, range 1-10; figure 1). In total 55 adverse event were reported during the study, of which 40% were gastro-intestinal (table 1). There was one serious adverse event (within in the EMG group, stroke leading to hospitalization) which was considered not related to apremilast, and the patient remained on drug.
Conclusion: The most common adverse event for apremilast are gastrointestinal side effects that subsided during prolonged use. Managing patient expectations before start of apremilast increases drug survival and is helpful for optimizing apremilast use in daily practice.
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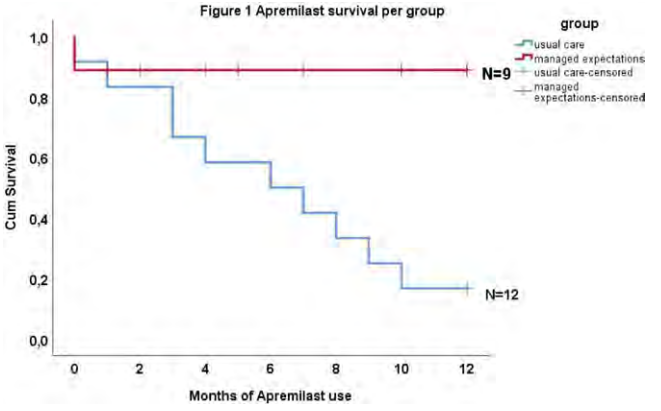


Table 1. Patient reported adverse events apremilast

Adverse events	Mild	Moderate	Severe	SAE	Total
Gastro-intestinal AE	15	7	0	0	22(40%)
Mood complaints	2	1	0	0	3 (5%)
Infections	8	1	0	0	9 (17%)
Headache	4	1	0	0	5(9%)
Others	15	1	1	1	16(29%)
Total	44	11	1	1	55(100%)

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AB0782 EXPLORING OCCURRENCE AND CORRELATES OF SLEEP DISTURBANCES AND FATIGUE IN PSORIATIC ARTHRITIS PATIENTS

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Background: Psoriatic arthritis (PsA) patients have been reported to suffer from increased sleep disturbances (1) and fatigue (2). Sleep disturbances and fatigue in PsA may not only be influenced by skin and musculoskeletal manifestations, but also by psychosocial consequences of the disease and the patients' mental status (3).
Objectives: To explore the occurrence and correlates of sleep disturbances and fatigue in PsA clinic patients.
Methods: A broad data collection was completed from 137 PsA patients including demographics, disease activity measures for both skin and musculoskeletal involvement and patient reported outcome measures. Pain was reported on a VAS scale 0-100 mm and sleep and fatigue on a numeric rating scale (NRS) 0-10. Depression was scored as: 1 not, 2 moderately and 3 extremely depressed. Sleep disturbances and fatigue were defined as present if the NRS score was ≥5. Descriptive statistics (mean (SD) for continuous variables and percentage for categorical variables) were applied. Associations were explored using univariate and adjusted linear regression analyses, with inclusion of variables in multivariate analysis that had a p value <0.2 in univariate analyses.
Results: Demographic patient characteristics: mean age 52.3 (SD 10.3) years, BMI 28.4 (4.3) kg/m2, women 50.4%, current smoker 17.5%, living together 76.6%, working 54.8%. Musculoskeletal disease status: PsA disease duration mean 8.8 (SD 6.8) years, CRP 5.0 (8.3) mg/L, 68 tender joint count (68TJC) 10.1 (11.1), 66 swollen joint count 0.6 (1.0), MASES enthesitis score 3.0 (3.2). Psoriasis skin status: PASI 2.6 (3.7) and itching skin 23.1%. Patient reported outcome measures: pain 34.8 (23.3) mm, sleep disturbances 3.5 (2.9), fatigue 4.2 (2.6), MHAQ 0.44 (0.40) and depression 1.4 (0.4). Mean numbers of comorbidities was 0.72 (0.93) and 45.3% exercised ≥1 time per week and 32.4% currently used bDMARDs and 58.4% csDMARDs.
The prevalence of sleep disturbances was 38.0% and that of fatigue 44.5%.
Identified associations with impaired sleep disturbances in univariate analyses were female gender, higher BMI, smoking, not working, higher scores for 68TJC, MASES score, pain, fatigue, depression, lower MHAQ, not exercising and itching skin. For fatigue the identified associations were female gender, smoking, not working, higher scores for 68TJC, MASES score, pain, sleep disturbances, depression, lower MHAQ and itching skin.
In adjusted analysis only pain, fatigue and higher MHAQ were independently associated with sleep disturbances and pain, sleep disturbances and depression were independently associated with fatigue.
Conclusion: The prevalence of sleep disturbances and fatigue was frequently reported in our PsA patients. No measures reflecting skin involvement or objective measures of inflammatory musculoskeletal involvement were independently associated with sleep disturbances and fatigue. Our data suggest that patient's perceptions of musculoskeletal involvement (pain or MHAQ) play an important role causing sleep disturbances and fatigue in PsA patients. However, mental status also seems to play an important role in the perception of fatigue.
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Disclosure of Interests: Glenn Haugeberg: None declared, Mari Hoff: None declared, Brigitte Michelsen Grant/research support from: Research support from Novartis, Consultant of: Consulting fees Novartis, Arthur Kavanaugh Grant/research support from: Abbott, Amgen, AstraZeneca, BMS, Celgene Corporation, Centocor-Janssen, Pfizer, Roche, UCB – grant/research support
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AB0783 THE IMPACT OF SKIN ITCHING ON HEALTH RELATED QUALITY OF LIFE IN PSORIATIC ARTHRITIS OUTPATIENT CLINIC PATIENTS

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Background: In psoriatic arthritis (PsA) both skin and musculoskeletal involvement can contribute to reduce health related quality of life (HRQoL) (1). Although itch is considered an important symptom in psoriasis, less is known about its extent and potential impact on HRQoL in PsA.
Objectives: The aim of the study was to assess the prevalence of itchy, sore, painful or stinging skin in PsA patients and also to explore the impact of these symptoms on overall HRQoL and skin related HRQoL.
Methods: PsA patients were consecutively recruited from a rheumatology outpatient clinic. Data collection included variables listed in the table. Patients also answered the question: "Over the last week, how itchy, sore, painful or stinging has your skin been? With answer alternatives: Not at all (score 0), a little (score 1), a lot (score 2) and very much (score 3)." For analysis the variable

was dichotomized; 'Not at all' and 'a little' were scored as 'not itching', and 'a lot' and 'very much' were scored as 'itching'. HRQoL was assessed using the 15D questionnaire and skin HRQoL using the Dermatology Life Quality Index (DLQI). Categorical variables are presented as numbers and (%) and continuous variables as mean with (SD). An association with 15D and DLQI was explored using univariate and multivariate linear regression analysis.

Results: Among 125 PsA patients (63 men and 63 women), means age was 52.2 years, BMI 28.3 kg/m2, disease duration 8.9 years; 15.2% were smokers. The number and percentage (%) of PsA patients reporting their skin to be itchy, sore, painful or stinging was as follows: Not at all 25 (20.0%), a little 71 (56.8%), a lot 23 (18.4%) and very much 6 patients (4.8%). The table shows data for all PsA patients and for patients defined to have no itching or having itching skin.

	Total (n=125)	No itching (n=96)	Itching (n=29)	P
Age (SD), years	52.2 (10.1)	52.3 (10.1)	51.6 (10.2)	0.73
Women, n (%)	62 (49.6%)	49 (51.0%)	13 (44.8%)	0.56
BMI (SD), kg/m2	28.3 (4.3)	28.0 (4.0)	29.4 (4.9)	0.12
Smoking, n (%)	19 (15.2%)	14 (14.6%)	5 (17.2%)	0.73
Dis.dur. (SD), years	8.9 (6.7)	9.1 (6.7)	8.0 (6.9)	0.42
CRP (SD), mg /L	4.8 (8.5)	4.4 (8.5)	6.1 (8.5)	0.37
TJC68 (SD)	9.70 (11.07)	9.21 (10.32)	11.39 (13.41)	0.36
SJC66 (SD)	0.57 (0.99)	0.56 (1.00)	0.61 (0.96)	0.84
MASES (SD)	2.9 (3.1)	2.5 (2.9)	4.0 (3.7)	0.02
IGA (SD), (VAS 0-100)	14.0 (11.7)	12.9 (10.2)	17.8 (15.4)	0.12
PGA (SD), (VAS 0-100)	35.3 (24.2)	30.5 (22.6)	50.9 (22.8)	<0.01
Pain (SD), (VAS 0-100)	33.4 (23.4)	28.6 (21.3)	49.1 (23.6)	<0.01
Fatigue (SD), (VAS 0-100)	45.1 (32.0)	40.3 (31.7)	61.0 (28.1)	<0.01
MHAQ (SD), (0-3)	0.40 (0.35)	0.35 (0.32)	0.58 (0.39)	<0.01
PASI (SD), (0-72)	2.4 (3.5)	1.9 (3.2)	4.1 (4.1)	0.01
DLQI (SD), (0-30)	3.5 (3.6)	2.2 (2.3)	7.9 (3.9)	<0.01
15D (SD), (0-1)	0.84 (0.09)	0.86 (0.09)	0.80 (0.08)	<0.01
bDMARDs, n (%)	43 (34.7%)	33 (34.7%)	10 (34.5%)	0.98
csDMARDs, n (%)	73 (58.4%)	61 (63.5%)	12 (41.4)	0.03

Dis.dur.: disease duration

In univariate analysis itching was found to be associated with impaired HRQoL assessed by 15D but not in adjusted analysis. In a regression model adjusting for age, gender, BMI and including variables with p<0.2 in univariate analysis (MASES enthesitis score, investigator [IGA] and patients global assessment [PGA], fatigue, pain, MHAQ, Psoriasis Area Severity Index [PASI] score and itching and treatment), only female gender, PASI score and itching were independently associated with reduced skin HRQoL.

Conclusion: Skin itching was frequently reported in our PsA patients (20-25%) and was also found to be associated with impaired HRQoL, in particular for skin HRQoL (DLQI). The association was independent of the extent of skin involvement (PASI). More needs to be understood about subjective skin symptoms such as itch in order to improve HRQoL in PsA.

References:

[1] Kavanaugh A, et al. Ann Rheum Dis 2019;9:1215-9

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AB0784

COMPARABLE IMPACT AND BURDEN OF DISEASE OF PSORIATIC ARTHRITIS PATIENTS WITH LIMITED JOINT INVOLVEMENT VS. THOSE WITH MORE EXTENSIVE JOINT INVOLVEMENT: INTERIM RESULTS FROM THE REWARD STUDY, A PROSPECTIVE, MULTICENTER, REAL-WORLD STUDY IN PATIENTS TREATED WITH APREMILAST

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Background: Psoriatic arthritis (PsA) is associated with a high burden of disease and an increased risk of comorbidities. Recent data suggest that patients with moderate PsA benefit most from apremilast (APR) treatment.[1] Results from an earlier analysis of the REWARD study suggest that patients with limited joint involvement may benefit from APR treatment, with improvements in the perceived impact of disease.[2] Patients with limited joint involvement or comorbidities are underrepresented in randomised controlled trials; therefore, evidence from real-world patient cohorts is needed to assess and compare the impact and burden of disease on patients with limited vs. extensive joints who may also have comorbidities.

Objectives: To compare the burden of disease and comorbidities in patients with PsA who have limited joint involvement with patients with PsA who have extensive joint involvement.

Methods: The prospective, multicenter, observational REWARD study assessed the impact of using the Psoriatic Arthritis Impact of Disease (PsAID) questionnaire (score range: 0-10), presence of domains of PsA (enthesitis, dactylitis, skin psoriasis, nail psoriasis, axial involvement), and ongoing or history of comorbidities of interest on PsA patients considered for apremilast treatment in The Netherlands. This interim analysis compared results in patients with limited joint involvement (swollen joint count [SJC] ≤4) vs. more extensive joint involvement (SJC >4).

Table 1. Patient Characteristics

Demographics	SJC ≤4 n=53	SJC >4 n=24
Age, mean	53.1	54.4
Female, %	46.2	66.7
Body mass index, mean, kg/m^2	28.6	28.7
PsA Characteristics		
SJC, mean	1.2	10.2
TJC, mean	4.3	13.7
PsAID, mean	4.4	4.8
Pain VAS, mean	45.9	53.4
Moderate to severe psoriasis (BSA >3), %	31.4	21.7
Dactylitis, %	18.9	33.3
Enthesitis, %	43.4	45.8
Nail psoriasis, %	45.3	41.7
Axial spondyloarthritis, %	3.8	8.3
Comorbidities		
Hypertension, %	30.2	37.5
Hypercholesteremia, %	13.2	16.7
Uveitis, %	1.9	8.3
Malignancy, %	0.0	8.3
Heart failure, %	5.7	8.3
Depression, %	5.7	4.2

Figure 1. Baseline SJC vs. PsAID vs. Pain VAS

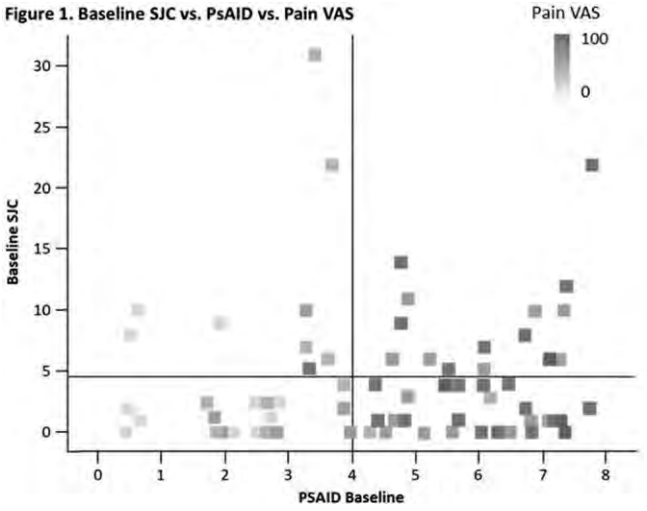
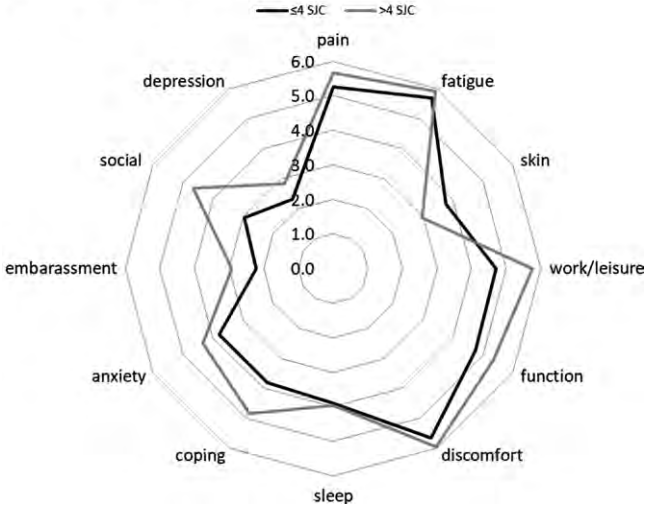


Figure 2. Baseline PsAID by Domain



Results: Currently, 77 patients have been included in the analysis (SJC ≤4: n=53; SJC >4: n=24) (Table 1). Mean baseline PsAID scores were 4.4 vs. 4.8 for the SJC ≤4 vs. SJC >4 groups (Figure 1). The proportions of patients who were not in the PsAID-defined Patient Acceptable Symptom State (PASS) were 58.7% for the SJC ≤4 group and 62.5% for the SJC >4 group. Mean pain visual analog scale (VAS) scores (0-100 mm) were 45.9 vs. 53.4 for the SJC ≤4 group vs. for the SJC >4 group. Mean scores for the individual PsAID domains for the SJC ≤4 vs. SJC >4 groups were generally comparable (Figure 2). Presence of specific manifestations of PsA for patients in the SJC ≤4 group vs. the SJC >4 group, respectively, were: moderate to severe psoriasis (psoriasis-involved body surface area [BSA] >3: 31.4% vs. 21.7%), nail psoriasis (45.3% vs. 41.7%), enthesitis (Leeds Enthesitis Index >0: 43.4% vs. 45.8%), dactylitis (18.9% vs. 33.3%), and axial involvement (3.8% vs 8.3%). Comorbidities in ≥5% of either group (SJC ≤4 vs. SJC >4) included hypertension (30.2% vs. 37.5%), hypercholesterolemia (13.2% vs. 16.7%), uveitis (1.9% vs. 8.3%), malignancy (0.0% vs. 8.3%), heart failure (5.7% vs. 8.3%), and depression (5.7 vs. 4.2%).

Conclusion: In this real-world study, no strong associations between SJC and patient-reported impact of disease or pain were observed. Similar to patients with more extensive joints involvement, patients with limited joint involvement had an associated substantial burden of disease, with more than half not achieving PsAID PASS.

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[1] Mease PJ, et al. Arthritis Care Res (Hoboken). 2020 Jan 7. Epub. 2. Jansen TL, et al. Ann Rheum Dis. 2019;78:913. Abstract FRI0442.

Disclosure of Interests: Tim Jansen Grant/research support from: Olatec, Grunenthal – grant/research support, Consultant of: AbbVie, Celgene Corporation – consultant, Speakers bureau: Grunenthal, Sobi – speakers bureau, Arie Van Vliet Employee of: Amgen Inc. – employment; Celgene – employment at the time of study conduct, Marijn Vis Grant/research support from: Novartis, Pfizer – grant/research support, Consultant of: AbbVie, Celgene Corporation, Eli Lilly, Novartis, Pfizer – consultant

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AB0785 REAL LIFE EXPERIENCE OF METHOTREXATE BASED DUAL COMBINATION DMARDS IN PSORIATIC ARTHRITIS- RESULTS FROM KARNATAKA PSORIATIC ARTHRITIS COHORT (KPSAC)

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Background: Biologics have been the focus of recent treatment guidelines and 'Treat to Target' strategies for both psoriasis (PsO) & psoriatic Arthritis (PsA). However, in day-today practice, combination DMARDs anchored around methotrexate are mainstay in majority of patients.

Objectives: To describe experience and effectiveness of Methotrexate in combination with conventional DMARDs in Karnataka Psoriatic Arthritis Cohort.

Methods: Treatment information was extracted from KPsAC (n=549) which is a cross sectional, non-interventional study conducted across 17 rheumatology practicing centres in Karnataka, India using a structured proforma. This study was approved by respective Ethical committee. Information on efficacy was extracted for various csDMARDs in combination with methotrexate. Standard disease activity outcome measures were used for assessing the response to therapy (DAPSA, PASI, HAQ, MDA5). All participating rheumatologists underwent training to calculate PASI and other outcome scores.

Results: Nearly half of the patients in our cohort were on methotrexate (44%) monotherapy. Proportion of patients who received combination csDMARD anchored on methotrexate were 29%. The choice of add on csDMARD was as per clinician discretion or subject preference. Patients were divided in to three groups based on treatments they were receiving at the time of study: Methotrexate (Mtx)+Leflunomide (Lef), Mtx+Sulfasalazine (SSz) and Mtx+Apremilast(Apr). Their characteristics along with outcome measures are depicted in table 1. In Mtx+Apr group: remission or low disease activity was present in 42%, HAQ score of <0.5 was seen in 82%, and only one patient had a PASI of > 10. PASI was significantly lower in the Mtx+Apr group compared to Mtx+Lef group (p<0.009) and Mtx +Ssz group (p < 0.020)

Conclusion: Apremilast is an orally administered, small molecule inhibitor of phosphodiesterase 4 (PDE4)**. In this observational study, 3 groups of methotrexate plus csDMARD- leflunomide, sulphasalazine and apremilast fared similarly for articular domain of PsA. However, in cutaneous domain, PASI was significantly lower in apremilast + methotrexate group. To our knowledge, this is the first real life report of the use of combination DMARDs in unselected PsA patients demonstrating effectiveness of apremilast in cutaneous domain. Methotrexate remains anchor DMARD for treatment of PsA in 2/3rd of PsA patients. Addition of apremilast to methotrexate inadequate responders appears to be beneficial in PsA with persistent cutaneous disease. However, being an observational study, this needs to be confirmed in controlled clinical trials.

References: ** Apremilast: A Review in Psoriasis and Psoriatic Arthritis, Drugs March 2017, Volume 77, Issue 4.

Table. Characteristics and comparison of combination csDMARDs

	MTX+SSZ (N=39)	MTX+LEF (n=77)	MTX+APR (N=45)
Median Age (years)	37	39	35
Median disease duration (months)	96	101	112
Enthesitis (Ever)	6(15%)	21(27%)	4(8%)
Dactylitis (Ever)	9((23%)	28(36%)	12 (26%)
DAPSA			
< 4	6(15%)	9(11%)	10(22%)
4-14	14(36%)	25(32%)	13(29%)
14-28	7(18%)	24(31%)	11(24%)
PASI >10	7(18%) #	14(18%) *	1(2%) *#
HAQ < 0.5	30(77%)	60(78%)	37(82%)
MDA 5 achieved	16(41%)	25(32%)	19(42%)

*P value < 0.009 #P value <0.02

Disclosure of Interests: None declared

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AB0786 IMPACT OF PSORIASIS SEVERITY ON HEALTH-RELATED QUALITY OF LIFE IN EARLY PSORIATIC ARTHRITIS: RESULTS FROM REAL WORLD DATA, THE DEPAR STUDY

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Background: Psoriasis is an important feature of psoriatic arthritis (PsA). Psoriasis itself is known to have a significant impact on Health-related Quality of life (HRQoL)[1], however its role within PsA is less well understood. In daily practice, assessment of psoriasis may not always be a priority for rheumatologists, having been trained to focus on articular involvement. In order to assess whether psoriasis deserves more attention from rheumatologists, the aim of this study is to evaluate the influence of psoriasis on HRQoL in early PsA patients.

Objectives: To describe the evolution of psoriasis severity during the first year of follow up in patients with early PsA and to evaluate the impact of psoriasis severity on HRQoL.

Methods: Real world data were used from the Dutch south west Psoriatic Arthritis cohort (DEPAR) study, consisting of newly diagnosed PsA patients included between July 2013 and February 2019. Psoriasis severity was assessed using the Psoriasis Area and Severity Index (PASI) and categorized in: no psoriasis (PASI 0), mild psoriasis (PASI<7), moderate psoriasis (PASI 7-12) and severe psoriasis (PASI>12). Musculoskeletal disease severity was measured with the Disease Activity in PSoriatic Arthritis (DAPSA) score as contrast for psoriasis severity. DAPSA was categorized in: remission (REM[DAPSA≤4]), low disease activity (LDA[DAPSA≤14]), moderate disease activity (MDA[DAPSA≤28]) and high disease activity (HDA[DAPSA>28]).[2]

General HRQoL was assesed with the Short-Form 36 (SF-36[Physical component scale and Mental component scale]). Skin-specific HRQoL was measured with the Skindex-17 (psychosocial scale and symptoms scale).

Results: In total, 435 patients were included. Mean (sd) age was 49.7 (13.4) years and 53% (n=229) was male. Psoriasis severity does not fluctuate much over the course of the first year and the majority of patients had mild psoriasis (Figure 1). HRQoL worsened with increasing psoriasis severity, when measured by the Skindex17. This reduction in HRQoL was not seen when measured with the SF-36 (Figure 2).

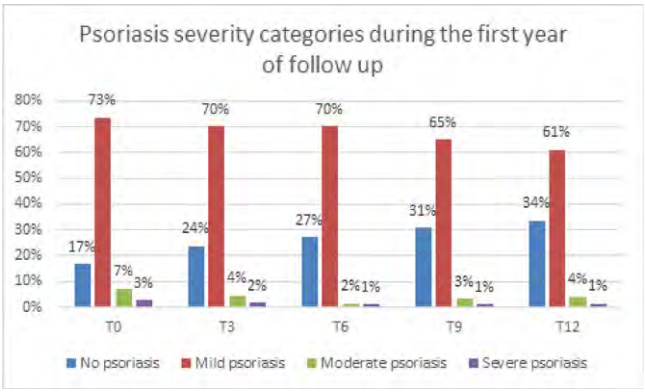


Figure 1. Psoriasis severity categories during the first year of follow up. No psoriasis (PASI 0), mild psoriasis (PASI<7), moderate psoriasis (PASI 7-12) and severe psoriasis (PASI>12).

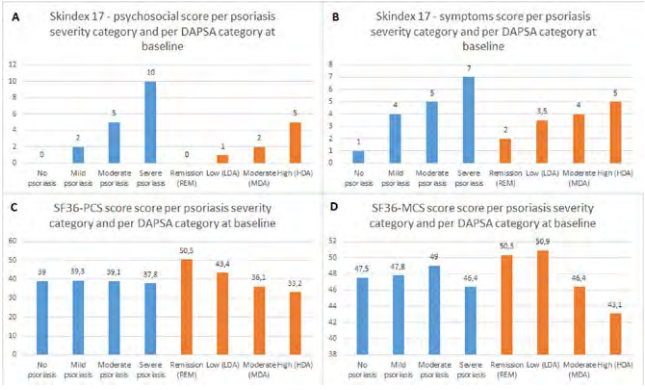


Figure 2. A, B: Median Skindex17 psychosocial score and symptoms score per psoriasis severity category and DAPSA category at baseline. C,D: Mean SF36 Physical component scale (PCS) score and Mental component scale (MCS) score per psoriasis severity category and DAPSA category at baseline. No psoriasis (PASI 0), mild psoriasis (PASI<7), moderate psoriasis (PASI 7-12) and severe psoriasis (PASI>12). REM (DAPSA<4), LDA (DAPSA<14), MDA (DAPSA<28) and HDA (DAPSA>28)

Conclusion: In early PsA patients, psoriasis severity is mostly mild, but considerably impacts HRQoL when measured using a skin specific questionnaire. For optimal management of PsA patients, we therefore recommend rheumatologists to additionally acquire information on the degree of psoriatic involvement. In our opinion, this information is valuable for the adequate assessment of HRQoL.

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Disclosure of Interests: Fazira R. Kasiem: None declared, Marc R Kok Grant/research support from: BMS and Novartis, Consultant of: Novartis and Galapagos, Ilja Tchetverikov: None declared, Kim Wervers: None declared, Johanna Hazes: None declared, Jolanda Luime: None declared, Marijn Vis Grant/research support from: Novartis, Pfizer – grant/research support, Consultant of: AbbVie, Celgene Corporation, Eli Lilly, Novartis, Pfizer – consultant

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AB0787 EFFECTIVENESS OF IL-17 INHIBITORS REVEALED BY MINIMAL DISEASE ACTIVITY (MDA) ACHIEVEMENT OF PSORIATIC ARTHRITIS PATIENTS

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Background: Recently, several type of biologics such as TNF inhibitors, IL-17 inhibitors, IL-12/23 (p40) inhibitors and IL-23 (p19) inhibitors are approved for PsA. Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) 2015 Treatment Recommendation suggests the treat-to-target strategy for PsA[1)], however, this recommendation does not indicate how to determine which biologics to use. Recent reports revealed that IL-17 inhibitors were as effective as TNF inhibitors[2)]. On the other hand, based on the Tight Control of Psoriatic Arthritis (TICOPA) study, present treatment strategies for PsA aim to reach on minimal disease activity (MDA)[3)].

Objectives: We investigate the effectiveness of IL-17 inhibitors focusing on MDA achievement which were administered for the Psoriatic Arthritis (PsA) patients in our institution.

Methods: We examined 46 patients whom were diagnosed and treated in our institution. We analyzed DAS28-CRP as the evaluation of arthritis and Minimal Disease Activity (MDA) achievement as that of overall disease activity.

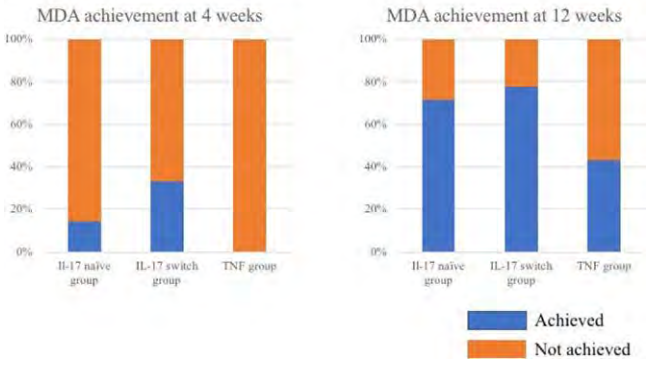
Results: Biologics were administered in 30 cases (65.2%) of all 46 cases. In 30 cases, 19 cases (63.3%) initiated TNF inhibitors (TNFi) and 7 cases (23.3%) were IL-17 inhibitors (naïve group). In 9 cases, TNFi were switched into Il-17 inhibitors (switch group), 7 cases continued TNFi (TNFi group). Patients characteristics in the cases which could collect the data were shown in Table 1. As for arthritis, DAS28-CRP has significantly improved at fourth weeks in naïve and TNFi group. In switch group, DAS28-CRP has not demonstrated significant improvement, however, IL-17 inhibitors were effective for the cases to which they were initiated for arthritis. As for MDA, 71% and 78% have also achieved MDA at twentieth weeks in both naïve and switch groups. In the TNFi group, 67% have not achieved MDA at twentieth weeks because of no improvement of rash (Figure 1). In switch group, all cases to which IL-17 inhibitors were initiated for either arthritis or rash have achieved MDA, however, 40% of cases which were introduced for both arthritis and rash have not achieved MDA.

Table 1. Comparison of clinical characteristics at baseline in 3 groups.

	Il-17 naïve group (n=7)	IL-17 switch group (n=9)	TNF group (n=7)	p value
Age, year	60.7 ± 18.9	53.8 ± 15.4	50.7 ± 13.6	N.S
Disease duration, year	20.3 ± 25.8	17.4 ± 9.5	9.9 ± 12.4	N.S
Male, n (%)	3 (43)	6 (67)	5 (71)	N.S
MTX, n (%)	2 (29)	4 (44)	5 (71)	N.S
CRP(mg/dl)	0.41 ± 0.50	1.87 ± 3.13	1.07 ± 1.77	N.S
Swollen joint count	6.7 ± 7.3	3.6 ± 4.2	6.2 ± 6.9	N.S
Tender joint count	6.6 ± 7.0	2.2 ± 2.6	6.9 ± 9.0	N.S
Patient pain VAS	55.7 ± 22.3	47.1 ± 34.9	35.4 ± 13.6	N.S
BSA (%)	12.5± 17.3	7.7 ± 14.8	7.4 ± 7.2	N.S
Biologics, n	Secukinumab: 2 Ixekizumab: 5	secukinumab: 3 Ixekizumab: 5 Brodalumab: 1	Infliximab: 3 Adalimumab:3 Etanercept:1	

TNF: Tumor Necrosis Factor, MTX: Methotrexate, VAS: visual analog scale, BSA: body surface area, N.S: not significant

Figure 1. MDA achievement in 3 groups



Conclusion: In our study, IL-17 inhibitors could bring high rate of MDA achievement for both naïve and switch from TNFi. We suggest that TNFi should be switched into IL-17 inhibitors rapidly in the case of ineffective for TNFi.

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[1] Coates LC, Kavanaugh A, Mease PJ, et al. Arthritis Rheumatol. 2016;68:1060-71.

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Disclosure of Interests: None declared

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AB0788 GENDER DIFFERENCES IN PSORIATIC ARTHRITIS DISEASE CHARACTERISTICS: EVIDENCE FOR WORSE DISEASE IN WOMEN.

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Background: Psoriatic arthritis (PsA) affects both sexes equally, however there seem to be significant differences in disease expression between the genders.
Objectives: To investigate gender differences in disease manifestations, patient-reported outcomes and comorbidities among patients with PsA.
Methods: This cross-sectional study of patients with PsA followed at an academic rheumatology outpatient clinic between 1/6/2017 and 1/12/2019. We compared clinical characteristics, patient-reported outcomes, disease activity and comorbidities in male and female patients with PsA. All patients were over 18 years of age and fulfilled the CASPAR criteria for PsA. Differences between gender in values of continuous variables were assessed by T-tests or Mann-Whitney tests. The association between categorical variables and gender was assessed by Pearson chi-square test or Fisher's exact test.
Results: 135 patients, 83 (62%) women and 52 (38%) men were included. Factors studied for gender differences are shown in Table 1. Women had significantly more tender (11 vs 3 p 0.001) and swollen (10 vs 3, p 0.013) joints, worse VAS (Visual Analogue Scale 0-10) pain (6 vs 5, p <0.001), higher ESR (20 vs 11, p 0.001) and worse DAPSA(Disease Activity in Psoriatic Arthritis) (33 vs 18 p 0.006) and presented with more enthesitis (32.5% vs 13.5%, p 0.013). In contrast, men achieved Minimal Disease Activity (MDA) more frequently (26.9% vs 3.6% p<0.001)and had significantly more comorbidities than women. Polyarthritic disease was more frequent in women (62% vs 31%), although at non-significant levels.
Conclusion: Male patients with PsA have more comorbidities, while female patients have greater disease activity, worse patient reported outcomes and achieve MDA less frequently.

Factor	Women (n=83)	Men (n=52)	P value
	Median (25th-75th percentile)		
Age	55.1 (46.8-63)	56.6 (50-65.7)	0.419*
BMI	27.9 (24.9-35)	30.1 (26.8-33.3)	0.181#
Pso duration/ PsA duration (years)	8.3 (3.9-24.5)/ 2.4 (0-5.7)	14.3 (4.7-22.7)/ 2.8 (0-6.4)	0.451# /0.605#
Smoking (Packyears)	15 (5-30)	27.5 (0-46)	**0.002#**
TJC/SJC	11 (4-16)/ 10 (5-17)	3 (0-13)/ 3 (0-14)	**0.001#/0.013#**
VASPain/ VASGA	6 (5-8)/ 5 (3-6)	5 (1-6)/ 4 (2-5)	**<0.001*/**0.121*
CRP/ ESR	1.4 (0.4-3.2)/20(11-33)	1.1 (0.2-2.7)/ 11 (7-18)	0.398#/**0.001#**
BSA/PASI	0 (0-2)/0(0-2)	2 (0-6)/1(0-4.8)	0.139#/0.258#
DAPSA	33 (24.1-45)	18 (9.3-45)	**0.006#**
	n (%)		
Enthesitis/ Dactylitis	27 (32.5)/ 20 (24.1)	7 (13.5)/ 10 (19.2)	**0.013*****/ 0.508***
Dyslipidemia	33 (40.2)	31 (59.6)	**0.029*** **
Liver	3 (3.6)	7 (13.5)	**0.046****
Eyes	0 (0)	3 (5.8)	0.055**
Uricemia	3 (3.6)	8 (15.4)	**0.023****
Depression or anxiety	16 (19.3)	11 (21.1)	0.817***
CAD	2 (2.4)	12 (23.1)	**<0.001****
DM	14 (16.9)	12 (23.1)	0.392
MDA	3 (3.6)	14 (26.9)	**<0.001**

*: T-test with unequal variances; #: Mann-Whitney test; **: Fisher's exact test; ***: Pearson chi2 test;
Pso: Psoriasis; PsA: Psoriatic arthritis; BMI: Body mass index; TJC: Tender joint count; SJC: Swollen joint count; VASPain: Visual analogue scale 0-10 for pain; VASGA: Visual analogue scale 0-10 for general assessement; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; BSA: Body surface area; PASI: Psoriasis area severity index; DAPSA: Disease activity in psoriatic arthritis; CAD: Coronary artery disease; DM: Diabetes mellitus; MDA: Minimal disease activity;

References:

[1] Determinants of Patient-Reported Psoriatic Arthritis Impact of Disease: An Analysis of the Association with Gender in 458 Patients from 14 Countries.
[2] Orbai AM, Perin J, et al Arthritis Care Res (Hoboken). 2019 Oct 14. doi: 10.1002/acr.24090.

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AB0789

PERSISTENCE IN USE OF BIOLOGIC DISEASE MODIFYING ANTIRHEUMATIC DRUGS TREATMENT IN PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Treatment for patients with moderate to severe psoriatic arthritis (PsA) relied on TNF inhibitors (TNFi) for many years. Recent approvals of newer biologics include interleukin (IL) -12 inhibitor ustekinumab and IL-17A inhibitors ixekizumab and secukinumab. Limited up-to-date evidence exists for the comparison of utilization patterns between TNFi and IL inhibitors.
Objectives: To compare the persistence on treatment with biologic disease-modifying anti-rheumatic diseases (DMARDs) in PsA patients who initiated TNFi versus IL inhibitors.
Methods: We conducted a cohort study using a US commercial insurance database (IBM MarketScan: 2014-2017). We identified patients with PsA by using a validated claims-based algorithm (positive predictive value of 82.4%) which required two PsA diagnosis codes and a prescription dispensing for TNFi (etanercept, infliximab, adalimumab, certolizumab, golimumab) or IL inhibitor (secukinumab, ustekinumab, or ixekizumab). The index date was the 1st drug dispensing date after the 2nd PsA diagnosis. We excluded patients with biologic DMARD use at any time prior to the index date. Patients were ≥18 years old on the index date and continuously enrolled in the plan for ≥365 days prior and after the index date. Our study outcome was the change in the initial biologic regimen during the year after the index date. Patients were considered as 'persistent users' if they were still on the index regimen, or 'switchers' if they were on a different biologic at the 365th date of follow-up. We applied 30 days of gap between dispensing after accounting for the days of supply of each dispensing. For sensitivity analysis, we allowed any gap and determined persistent use at 365th date less strictly.
Results: We identified a total of 3,180 TNFi initiators and 214 IL inhibitor initiators (Table). Mean age was 52.9 (±11.6) years for TNFi initiators and 50.4 (±11.7) years for IL inhibitor initiators. Using the 30-day gap, there were 37.1% persistent TNFi users and 24.8% persistent IL inhibitor users after 1 year form the index date. 11.1% of TNFi initiators switched to a different TNFi while 4.7% switched to an IL inhibitor. Among IL inhibitor initiators, 6.1% switched to a TNFi and 5.6% to another IL inhibitors. However, in the sensitivity analysis where we allowed a longer interval between the fills/ injections, there were 53.0% persistent TNFi users and 53.7% persistent IL inhibitor users. In other words, IL inhibitor patients had a longer interval between the doses than the recommended treatment intervals on the label.
Conclusion: In PsA patients, TNFi initiators were more adherent to the initial regimen than IL inhibitor initiators during 1-year follow-up period. However, the sensitivity analysis indicates that some patients may resume their initial treatment beyond the indicated refill intervals. Further investigations are needed to clarify whether this is due to a better treatment effectiveness or adverse effects associated with IL inhibitors.

Table. Selected baseline characteristics of initiators TNFi versus IL inhibitors in PsA patients

	TNFi	IL inhibitor
N	3,180	214
Age (years), mean (SD)	52.9 (11.6)	50.4 (11.7)
Female, %	57.0	55.6
Combined comorbidity score, mean (SD)	0.9 (1.8)	0.3 (1.2)
Hypertension, %	41.0	48.1
Diabetes, %	16.4	24.8
Psoriasis, %	63.2	72.9
Non-biologic DMARDs, %	66.5	60.8
Oral steroids, %	49.4	41.1
NSAID, %	55.4	43.0
Emergency room visit, %	21.2	20.6
Hospitalization	8.2	11.2
No. of visits to dermatologist, mean (SD)	2.6 (8.2)	1.3 (4.7)

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AB0790

CLINICAL PROFILING OF PSORIATIC ARTHRITIS (PSA): AN OBSERVATIONAL STUDY FROM A SOUTH INDIAN PSORIATIC ARTHRITIS COHORT

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Background: Clinical patterns and disease burden of PsA varies in different parts of the world. Demographic studies from Indian subcontinent are sparse
Objectives: To study the cutaneous, articular profile of PsA and describe their disease activity, disability and co-morbidities (CMs)
Methods: This is a multicenter, cross-sectional, non-interventional study from Karnataka, India. All consecutive PsA patients defined by CASPAR or expert diagnosis were evaluated over 8 months from 17 Rheumatology centers across Karnataka using standard parameters such as PASI, DAPSA, Indian version of HAQ-DI[1], psoriatic co-morbidity index[2] (Cidx) and MDA 5. Patient consent and EC obtained
Results: 549 PsA patients were evaluated and their disease characteristics are shown in Table 1 & 2. PsA preceded psoriasis in in 81 (14.7%).

Table 1. Patient characteristics (n=549)

DEMOGRAPHICS		PsA	
Commonest age group of PsA (yrs)	31-40	**PsA Subclassification**	
M:F	6:5	**Symmetric polyarthritis**	216(40.7%)
Type 1 Psoriasis	279(55.8%)		
Type 2 Psoriasis	221(44.2%)		
Mean duration (yrs)		Asymmetric oligoarthritis	202(38.1%)
Psoriasis	8.8(±7.8)	DIP predominant	88(16.6%)
PsA	5.2(±6.3)	Arthritis mutilans	16(4.2%)
PsA preceded psoriasis	**81(14.7%)**	**Dactylitis**	182(33.9%)
Family h/o			
Psoriasis	107(19.7%)	**Enthesitis**	109(20.3%)
PsA	33(6%)	**Mean TJC68**	6.3(±8.9)
AS	11(2%)	**Mean SJC68**	3.5(±5.2)
Uveitis	5(0.9%)	**Type of Psoriasis**	Plaque 253(59.9%)
IBD	3(0.5%)		Erythrodermic 31(7.3%)

Table 2. Disease characteristics

DISEASE ACTIVITY		DISABILITY		CO-MORBIDITIES	
Mean PASI: 3.8(7.4)		**Mean HAQ-DI: 0.3(0.45)**		**Mean Cidx: 0.98(1.6)**	
Mild (PASI 0-5)	480(80%)	**Mild-mod disability**	260(48.2%)	**N with 1 or more CMs**	232(42.3%)
Severe (>10)	57(10.6%)	**ADL with most frequent disability**	Climbing a flight of stairs 189(35%)	**HTN**	19.8%
				T2DM	16.6%
				Smoking	5.4%
				PsA severity	3.2%
Mean DAPSA: 18.8(16.6)		**ADL with highest disability score**	Sitting cross-legged/ squatting	**Anxiety**	3.1%
Remission	100(19.9%)			**IHD**	2.3%
Low DA	145(28.8%)			**Dyslipidemia**	2%
Moderate DA	137(27.2%)			**Others**	<2% each
High DA	123(24.5%)			**Family h/o CV dis/stroke**	72(15.2%)

Type I & II psoriasis did not differ in PASI, DAPSA, HAQ-DI or having a family h/o psoriasis. Type II psoriasis had higher Cidx than type I (p=0.0001). Pt pain VAS, DAPSA, PhyGA, PtGA & SJC significantly correlated with higher HAQ-DI (p<0.0001). TJC, ESR, CRP & PASI had minor correlation with HAQ-DI. Females had higher HAQ-DI compared to males (p=0.02). Knee joint involvement caused disability most frequently. Cidx was higher in males (p=0.008). Minor correlation was found between Cidx with age, HAQ-DI & DAPSA. Mean BMI of our cohort was 26.8(±14.8) kg/m^2. 56.5% were overweight. Higher BMI was not associated with age, duration of arthritis, DAPSA, PASI, HAQ-DI & Cidx.
Infections (any time) were recorded in 10.8%, of which skin was the commonest site in 38.9%; 30.5% of these needed hospitalizations.
Conclusion: Despite mild skin disease in majority, more than half of the patients have moderate to severe joint activity. Mild to moderate functional disability in nearly half of our cohort indicate high burden of damage. High incidence of co-morbidities in PsA compared with general population is in line with published literature. In addition to aggressive control of articular activity, detection and control of co-morbidities must be an integral part of PsA management.

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[1] **https://doi.org/10.1093/rheumatology/41.12.1457**
[2] **http://dx.doi.org/10.1136/annrheumdis-2016-eular.4598**
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AB0791

NETAKIMAB REDUCES SKIN MANIFESTATIONS OF PSORIATIC ARTHRITIS: RESULTS OF SUBANALYSIS FROM A DOUBLE-BLIND RANDOMIZED PHASE 3 STUDY (PATERA)

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Background: Patients with psoriatic arthritis (PsA) have skin manifestations that negatively affect their quality of life. Netakimab (NTK) is a humanized anti-interleukin 17A antibody approved for the treatment of moderate-to-severe plaque psoriasis.
Objectives: To evaluate the efficacy of NTK on PsA skin manifestations. This abstract presents 24-week data from the ongoing phase 3 PATERA study (NCT03598751).
Methods: PATERA is an international, multicenter, double-blind, placebo (PBO)-controlled study. 194 eligible adult patients with psoriatic arthritis (CASPAR, 2006), with inadequate response to csDMARD or one TNFi, were randomly assigned (1:1) to receive NTK 120 mg or placebo (PBO) subcutaneously at Week (Wk) 0, 1, 2, 4, 6, 8, 10, 14, 18, 22. 84 patients from PBO arm, failed to achieve ACR20 (20% improvement in American College of Rheumatology criteria) at Wk 16, were switched to NTK. Endpoints for assessment of skin involvement included PASI the proportion of patients achieving 75%, 90%, and 100% improvement in Psoriasis Area and Severity Index score (PASI75, PASI90 and PASI100, respectively).
Results: 184 patients (NTK arm, N=94; PBO arm, N=90) had PASI>0 at baseline (BL). Demographics and BL characteristics were balanced between treatment arms (Table 1). Treatment response was assessed in patients with ≥3% body surface area involvement (BSA) at BL. PASI75/90/100 response rates for NTK arm were significantly greater than for PBO and increased throughout the whole analyzed period. At Wk 24 PASI75 was achieved by 82.89% vs 11.11% for NTK and PBO, respectively (p<0.0001). A significantly higher percentage of patients achieved complete skin clearance (PASI100) in NTK arm compared to PBO (48.68% vs 6.94%, p<0.0001). PASI90 response rate was also higher for NTK (Figure 1). Relative change (%) from baseline in PASI score correlated with PASI75/90/100 response rates throughout the entire analyzed period. PASI decreased by 87.5 % in NTK arm vs only 4.4% in PBO arm after 24 wks of treatment (Table 2).

Table 1. BL characteristics (for patients with PASI>0 at BL)

Arm	NTK (N=94)	PBO (N=90)
Age (years) *	44.0 (11.82)	42.9 (12.14)
Male, n (%)	51 (54.26)	48 (53.33)
PsA duration, mo*	63.3 (73.81)	68.1 (79.79)
PASI*	12.27 (11.31)	10.35 (9.80)

* mean (standard deviation); mo=months, PASI=Psoriasis Area and Severity Index

Table 2. Percentage (%) change from baseline in PASI total score (mean (SD))

	NTK (N=76)	PBO (N=72)
Week 4*	-61.1 (36.04)	-8.6 (31.99)
Week 8*	-74.2 (35.36)	-8.4 (37.57)
Week 16*	-80.8 (49.38)	-2.3 (61.06)
Week 24*	-87.5 (32.83)	-4.4 (63.48)

Data are presented for patients with BL BSA ≥ 3%; *p<0.0001 vs placebo

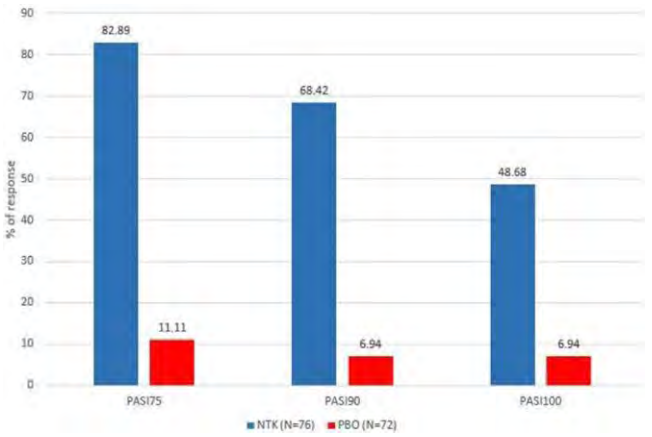


Figure 1. Percentage of patients with PASI75/90/100 at Wk 24 (in patients with BL BSA≥3)

Conclusion: 24-week treatment with NTK at the dose of 120 mg resulted in significant improvement in skin manifestations in PsA patients: more than half of the patients with BSA≥3 at BL achieved complete skin clearance.

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AB0792

NETAKIMAB IMPROVES PATIENT-REPORTED OUTCOMES IN PATIENTS WITH PSORIATIC ARTHRITIS: RESULTS FROM A RANDOMIZED DOUBLE-BLIND PHASE 3 TRIAL (PATERA)

T. Korotaeva[1], I. Gaydukova[2], V. Mazurov[2], A. Samtsov[3], V. Khayrutdinov[3], A. Bakulev[4], M. Kokhan[5], A. Kundzer[6], N. Soroka[7], E. Dokukina[8], A. Eremeeva[8]. *[1]Nasonova Research Institute of Rheumatology, Moscow, Russian Federation; [2]Mechnikov North-Western State Medical University, St-Petersburg, Russian Federation; [3]Kirov Military Medical Academy, St-Petersburg, Russian Federation; [4]Razumovsky Saratov State Medical University, Saratov, Russian Federation; [5]Ural Research Institute of Dermatovenerology and Immunopathology, Ekaterinburg, Russian Federation; [6]Healthcare Institution Municipal Clinical Hospital No. 1, Minsk, Belarus; [7]Scientific and Practical Center of Surgery, Transplantology and Hematology, Minsk, Belarus; [8]JSC BIOCAD, St-Petersburg, Russian Federation*

Background: Psoriatic arthritis (PsA) is associated with multiple manifestations, resulting in reduced health-related quality of life (HR-QoL) of patients (pts). Netakimab (NTK) is a humanized anti-IL17A antibody approved for the treatment of moderate-to-severe plaque psoriasis.

Objectives: To assess the impact of NTK on patient-reported outcomes (PROs) in active PsA pts, based on data of 24-week (wk) data from the ongoing PATERA study (NCT03598751).

Methods: PATERA is an international double-blind, placebo-controlled clinical study. 194 eligible adult pts with PsA (CASPAR, 2006), with inadequate response to csDMARD or one TNFi, were randomized (1:1) to receive NTK 120 mg or placebo (PBO) at Wk 0, 1, 2, 4, 6, 8, 10, 14, 18, 22. Pts from PBO arm failed to achieve ACR20 (20% improvement of the American College of Rheumatology criteria) by Wk 16 were switched to NTK. PROs included changes from baseline (BL) in Work Productivity and Activity Impairment General Health (WPAI GH), 36-item Short Form Health Survey (SF-36), European Quality of Life Questionnaire (EQ-5D-5L), Dermatology Quality of Life Index (DLQI), Health assessment questionnaire disability index (HAQ-DI).

Results: BL demographics and PsA characteristics were similar between treatment arms (Table 1). The proportion of pts with an improvement of ≥1 level in EQ-5D domains at Wk 24 (among pts who reported problems at BL) was higher in NTK arm compared to PBO (Figure 1). The assessment of physical disability showed positive dynamics in NTK arm: at Wk 24 mean change in HAQ-DI from BL was -0.6 for NTK vs -0.1 for PBO (p<0.0001). DLQI was assessed in pts with ≥3% body surface area involvement at BL (N=76 in NTK arm, N=72 in PBO arm). A greater reduction in DLQI was observed in NTK-treated pts (-11.4) compared to PBO-treated pts (-1.8) (p<0.0001). After 24 wks WPAI response for NTK was better than for PBO in all aspects, except work time missed due to PsA (Table 2). Positive dynamics were reported for both SF-36 components, however, the difference between NTK and PBO was not statistically significant. At Wk 24 mean change from baseline in SF-36 PCS in NTK arm was 10.4 vs 7.7 in PBO (p=0.29), mean change in SF-36 MCS was 6.4 vs 9.0 in the same arms, respectively (p=0.56).

Table 1. BL demographics and PsA characteristics

Arm	NTK (N=97)	PBO (N=97)
Age (years) *	44.0 (11.7)	43.1 (11.9)
Male, n (%)	52 (53.6)	50 (51.6)
PsA duration, mo*	63.1 (73.1)	68.2 (77.5)
HAQ-DI*	1.15 (0.6)	1.21 (0.6)
DLQI*	14.8 (6.5)	13.9 (7.3)
SF36 PCS*	32.39 (9.5)	31.10 (8.9)
SF36 MCS*	45.29 (10.7)	46.04 (11.5)

* mean (standard deviation), N=number of pts, mo=months, PsA=psoriatic arthritis, HAQ-DI=Health assessment questionnaire disability index, DLQI=Dermatology Quality of Life Index, SF36=36-item Short Form Health Survey, MCS=Mental Component Summary, PCS=Physical Component Summary

Table 2. WPAI change from BL at wk 24 (mean±standard deviation)

Parameter	NTK	PBO
Absenteeism (%)	-8.7±29.1 N=60	-9.1±31.8 N=47
Presenteeism (%)	-22.1 ±22.1 N=57	-1.0±26.5 N=42
Overall work impairment (%)	-18.6±21.8 N=57	0.6±26.7 N=42
Activity impairment (%)	-25.5±25.2 N=96	-5.4±29.1 N=97

N=number of pts in the analysis category

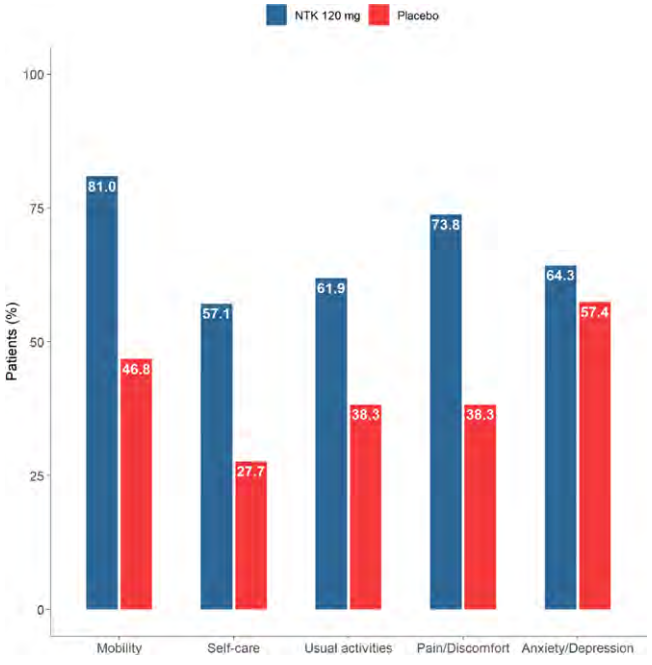


Figure 1. Improvement in EQ-5D categories

Conclusion: NTK demonstrated rapid improvement in QoL, work productivity and physical function in pts with PsA.

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Disclosure of Interests: Tatiana Korotaeva Consultant of: Pfizer, MSD, Novartis, AbbVie, Celgene, JSC BIOCAD, Janssen, UCB, Lilly and Novartis-Sandoz, Speakers bureau: Pfizer, MSD, Novartis, AbbVie, Celgene, JSC BIOCAD, Janssen, UCB, Lilly and Novartis-Sandoz, Inna Gaydukova Grant/research support from: JSC BIOCAD, Speakers bureau: Pfizer, Novartis, AbbVie, JSC BIOCAD, Celgene, MSD, Sanofi, V Mazurov: None declared, Aleksey Samtsov Grant/research support from: JSC BIOCAD, Novartis, Eli Lilly, Johnson&Johnson, Celgene, Glenmark, Galderma, Sanofi, Vladislav Khayrutdinov Grant/research support from: Akrikhin, Alkoy, Belupo, JSC BIOCAD, Bosnaliejk, Verteks, Glenmark, Elfa, Leo Pharma, MSD, Novartis, Pfizer, Sun Pharma, Sanofi, Celgene, Pharmtec, AbbVie, Eli Lilly, Jadran, Janssen, Andrey Bakulev Grant/research support from: AbbVie, Eli Lilly, Pfizer, UCB, MSD, Novartis, Galderma, Celgene, Leo Pharma and Johnson&Johnson, JSC BIOCAD, Consultant of: Novartis, Celgene and Johnson&Johnson, Speakers bureau: AbbVie, Eli Lilly, Galderma, UCB, Novartis, Celgene and Johnson&Johnson, Muza Kokhan Grant/research support from: AbbVie, Eli Lilly, Pfizer, UCB, MSD, Novartis, Galderma, Celgene, Leo Pharma and Johnson&Johnson, JSC BIOCAD, Consultant of: Novartis, Celgene and Johnson&Johnson, Speakers bureau: AbbVie, Eli Lilly, Galderma, UCB, Novartis, Celgene and Johnson&Johnson, Alena Kundzer: None declared, Nikolaj Soroka Grant/research support from: JSC BIOCAD, Ekaterina Dokukina Employee of: JSC BIOCAD, Anna Eremeeva Employee of: JSC BIOCAD

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AB0793 CHANGES IN PSAID-12 SCORES BEFORE AND AFTER BIOLOGICAL TREATMENT IN PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Psoriatic Arthritis Impact of Disease 12-item questionnaire (PsAID-12) is a patient-reported outcome measure (PROM) which allows a more precise assessment of the impact of PsA and helps treatment decisions geared to either disease activity or, for example, physpsychological distress (1,2).

Objectives: Our objective is to evaluate change of PsAID-12 values after three-months biologic drug treatment and to find out its relationship with other quality of life indices and disease activity parameters in PsA patients

Methods: Patients with a diagnosis of PsA according to CASPAR criteria were recruited to the study. The data of the patients before and after three-month treatment were evaluated retrospectively. The number of swollen (0-66) and tender joints (TJ) (0-68), ESR, CRP, Patient Global Assessment(PGA), physician's global assessment (PhGA),DAPSA and BASDAI were used for the assessment of disease activity. Functional status was assessed with BASFI, quality of life with EuroQol, DLQI and HAQ. Enthesitis evaluation was performed with MASES. Dermatological assesment was done with BSA and PASI. In addition, PSARC and MDA criteria was used to assess patient's response to treatment. A p-value less than 0.05 was statistically significant.

Results: Fifteen patients who met the study criteria were evaluated. 3 patients were excluded because of irregular drug usage. 9 of the 12 patients were women, the average age was 46,41, and BMI was 32,68. Both acute phase reactants were decreased after treatment, and there was significant decrease at CRP levels but not at ESR. It was also observed that there were significant differences at PGA, PhGA, BASDAI, BASFI, MASES, DAPSA and PsAID-12 scores after treatment. There were no statistically significant differences at number of swollen and tender joints, HAQ,EuroQol, PASI, BSA and DLQI scores. 3 patients achieved MDA and 7 patients achieved PSARC criteria. There were statistically significant correlations between pre-treatment mean scores of PsAID-12 and BASDAI, BASFI, DAPSA, HAQ, EuroQol, PhGA. There were statistically significant correlations between after-treatment mean scores of PsAID-12 and BASDAI, DAPSA, PASI and BSA. The correlations between PSAID-12 change (ΔPsAID-12) with other outcome measure changes were as follows: ΔHAQ (r=0,27, p=0,39), ΔBASDAI (r=0.37, p=0,22), ΔPGA (r =0.28, p=0,36), ΔDLQI (r=0.71, p=0,17), ΔBASFI (r=0.41, p=0,18), ΔESR (r=0,20, p=0,55),and ΔCRP (r=-0.39, p=0,20), ΔDAPSA (r=0,77, p=0,009), Δnumber of TJ (r=0,81, p=0,004), ΔMASES (r=0,57, p=0,08), ΔEuroQol (r=-0,29, p=0,34), ΔPASI (r=0,30, p=0,62). It is also observed that PsAID-12 scores decreased more in PSARC responders rather than non-responders, but this difference was not statistically significant. No cases of major adverse event were reported.

Conclusion: PsAID-12 evaluates effect of both physical and psychosocial aspects of PsA and shows close relationship with other PROMS but it may be inadequate in assessing biological treatment response in PsA.

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Disclosure of Interests: None declared

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AB0794 CLINICAL TRIAL DISCRIMINATION OF PHYSICAL FUNCTION INSTRUMENTS FOR PSORIATIC ARTHRITIS: A SYSTEMATIC REVIEW

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Background: Physical function is a core domain to be measured in randomized controlled trials (RCTs) of psoriatic arthritis (PsA). The discriminative

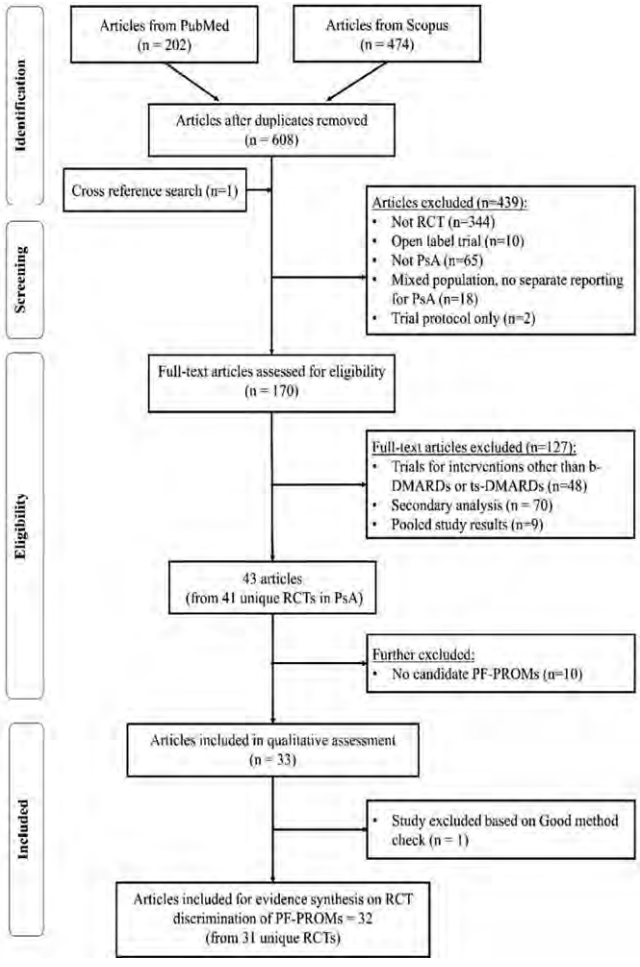


Figure 1. Article selection

performance of patient reported outcome measures (PROMs) for physical function (PF) in RCTs has not been evaluated systematically.
Objectives: In this systematic review, the GRAPPA-OMERACT working group aimed to evaluate the clinical trial discrimination of PF-PROMs in PsA RCTs.
Methods: We searched PubMed and Scopus databases in English to identify all original RCTs conducted in PsA. We limited the review to RCTs of biologic and targeted synthetic DMARDs. Groups of two researchers extracted data independently for PF-PROMs. We assessed quality in each article using the OMERACT good method checklist. Effect sizes (ES) for the PF-PROMs were calculated and appraised using *a priori* hypotheses. Evidence supporting clinical trial discrimination for each PF-PROM was summarized to derive recommendations.
Results: 32 articles were included (Figure 1). Four PF-PROMs had data for evaluation: HAQ-Disability Index (DI), HAQ-Spondyloarthritis (S), Short Form 36-item Health Survey Physical Component Summary (SF-36 PCS), and the Physical Functioning domain (SF-36 PF) (Table 1). The ES for intervention versus (vs.) control arms for HAQ-DI ranged from -0.55 to -1.81 vs. 0.24 to -0.52; and for SF-36 PCS ranged from 0.30 to 1.86 vs. -0.02 to 0.63.

Table 1. Summary of Measurement Properties Table for clinical trial discrimination

Articles	HAQ-DI	HAQ-S	SF-36 PCS	SF-36 PF
Antoni 2005 (IMPACT); Gottlieb 2009 (UST)	+			
Antoni 2005 (IMPACT2)	+		+	
Kavanaugh 2006 (IMPACT2)				+
Mease 2005 (ADEPT); Genovese 2007 (ADA); Mease 2010 (ETN); Kavanaugh 2009 (GO-REVEAL); Kavanaugh 2017 (GO-VIBRANT); Gladman 2014 (RAPID-PsA); Mease 2015 (FUTURE1); McInnes 2015 (FUTURE2); Kavanaugh, 2016 (FUTURE2)-subgroup; Nash 2018 (FUTURE3); Mease 2017 (SPIRIT-P1); Nash 2017 (SPIRIT-P2); Deodhar 2018 (GUS); Mease 2016 (CLZ)	+		+	
Mease 2000 (ETN); McInne, 2013 (PSUMMIT 1); Ritchlin 2014 (PSUMMIT 2); Araugo 2019 (ECLIPSA)	+		+	
Gniadecki 2012 (PRESTA)	+			
Mease 2019 (SEAM-PsA)	+/-		+	
McInnes 2014 (SEC)	+		+	
Mease 2014 (BRO)	+		+	
Mease 2011 (ABT)	+/-		+	
Mease 2017 (ASTRAEA)	+		+	
Mease 2006 (ALC)	+/-			
Mease 2017 (OPAL Broaden); Gladman 2017 (OPAL Beyond)	+			+
Mease 2018 (EQUATOR)	+			+
Mease 2018 (ABT-122)		+		
Total available articles	31	1	24	4
Total articles for evidence synthesis	29	1	23	2
Overall rating	+		+	+

Color code in each box indicate study quality by OMERACT good methods. GREEN: "likely low risk of bias"; AMBER: "some cautions but can be used as evidence"; RED: "don't use as evidence" WHITE (empty boxes): absence of information from that study. (+): findings had adequate performance of the instrument; (+/-): equivocal performance; (-): poor performance (less than adequate).

Conclusion: Clinical trial discrimination was supported for HAQ-DI and SF-36 PCS in PsA with low risk of bias; and for SF-36 PF with some caution. More studies are required for HAQ-S.

Disclosure of Interests: Ying Ying Leung Speakers bureau: Novartis, Janssen, Eli Lilly, Richard Holland: None declared, Ashish Mathew: None declared, Christine Lindsay Employee of: Previously employed (worked) for pharmaceutical company., Niti Goel Shareholder of: UCB and Galapagos, Consultant of: VielaBio, Mallinckrodt, and IMMVention, Alexis Ogdie Grant/research support from: Novartis, Pfizer – grant/research support, Consultant of: AbbVie, BMS, Eli Lilly, Novartis, Pfizer, Takeda – consultant, Ana-Maria Orbai Grant/research support from: Abbvie, Eli Lilly and Company, Celgene, Novartis, Janssen, Horizon, Consultant of: Eli Lilly; Janssen; Novartis; Pfizer; UCB. Ana-Maria Orbai was a private consultant or advisor for Sun Pharmaceutical Industries, Inc, not in her capacity as a Johns Hopkins faculty member and was not compensated for this service., Pil Hoejgaard: None declared, Jeffrey Chau: None declared, Laura C Coates: None declared, Vibeke Strand: None declared, Dafna D Gladman Grant/research support from: AbbVie, Amgen Inc., BMS, Celgene Corporation, Janssen, Novartis, Pfizer, UCB – grant/research support, Consultant of: AbbVie, Amgen Inc., BMS, Celgene Corporation, Janssen, Novartis, Pfizer, UCB – consultant, Robin Christensen: None declared, William Tillett: None declared, Philip J Mease Grant/research support from: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Eli Lilly, Novartis, Pfizer, Sun Pharmaceutical, UCB – grant/research support, Consultant of: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Eli Lilly, Novartis, Pfizer, Sun Pharmaceutical, UCB – consultant, Speakers bureau: Abbott, Amgen, Biogen Idec, BMS, Eli Lilly, Genentech, Janssen, Pfizer, UCB – speakers bureau
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AB0795

ABNORMAL LEVELS OF PERIPHERAL LYMPHOCYTES SUBSETS IN PATIENTS WITH PSORIATIC ARTHRITIS AND RESTORATION AFTER RECEIVING OUR NEW IMMUNOREGULATORY COMBINATION THERAPIES: A CROSS-SECTIONAL STUDY

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Background: Psoriatic arthritis (PsA) is a chronic autoimmune disease characterized by skin and joint inflammation with lymphocytes disturbance [1,2]. However, the statuses of immune cell subsets are unclear. In addition, although, during the past 20 years, the treatment of the PsA has progressed rapidly, it still remains an unmet need[3].
Objectives: To compare the lymphocyte subsets in peripheral blood of PsA patients and healthy controls and, evaluate effects of immunoregulatory combination therapies, such as low-dose interleukin-2, rapamycin, metformin, and retinoic acid, on the proliferation and functional recovery of lymphocyte subsets in PsA patients.
Methods: From September 2014 to December 2019, 218 PsA patients (107 male and 111 female) and 206 healthy controls (78 male and 128 female) were enrolled, including 112 patients (50 male and 62 female) who received immunoregulatory combination treatments (low-dose interleukin-2, rapamycin, metformin, retinoic acid and coenzyme Q10, ect). The absolute numbers and ratio of T, B, NK, $CD4^+$T, $CD8^+$T, Th1, Th2, Th17 and Tregs in peripheral blood were measured by flow cytometry with absolute counting beads. The data were subject to normal distribution, which was expressed as the mean ± standard deviation. Independent-samples T test and paired-samples T test were applied. P value <0.05 were considered statistically significant.
Results: The absolute numbers of B, $CD4^+$T and Th17 in PsA patients were significantly higher than those of healthy controls (P<0.01), while the absolute numbers of NK and the percentage of Th1 and Tregs were decreased significantly (P<0.01). The ratio of Th17/Tregs was significantly increase (P<0.001) (Figure 1). After receiving our new immunoregulatory combination therapies, the percentage of B, Th2 and Th17 were lower than before (P<0.05) and the absolute numbers of T, $CD8^+$T, NK, Th1 and Tregs in PsA patients were increased (P<0.05). Further, the ratios of Teffs/Tregs had a tendency to decrease (rebalance of them): Th2/Tregs (P<0.01) and Th17/Tregs (P=0.095) (Figure 2).
Conclusion: The abnormal levels of peripheral lymphocyte subpopulations resulted in an imbalance of Teffs/Tregs, which might play an important role in PsA pathogenesis. Our new immunoregulatory combination therapies could promote the proliferation of Tregs and may help for PsA patients' symptom remission.
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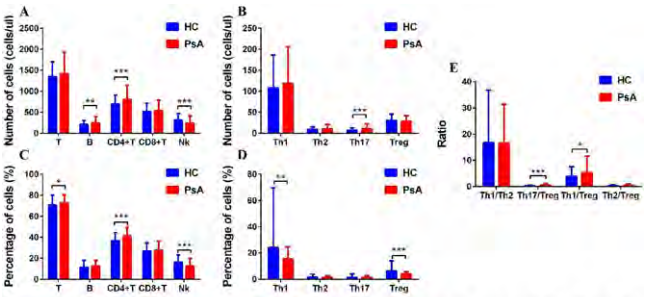


Figure 1: Comparison of lymphocyte subsets in peripheral blood between healthy individuals (n=206) and PsA patients (n=218). Data were expressed as mean ± standard deviation to the distribution. Independent-samples T test was applied. PsA patients had higher absolute numbers of B, $CD4^+$T, Th17 (A and B), decreased percentage of Th1 and Tregs (D), decreased absolute numbers of NK (A), and higher ratios of Th1/Tregs and Th17/Tregs compared with those of healthy controls (E). HC: healthy control. $^*P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$.

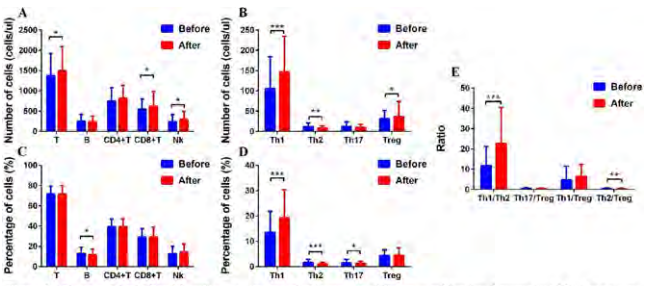


Figure 2: Changes of peripheral lymphocyte subsets after immunomodulatory combination therapy (n=112). Data were presented as mean ± SD and statistical analysis were performed using paired t-test (two-tailed). The absolute numbers of T, NK, $CD8^+$T, Th1 and Tregs were significantly increased (A and B). The percentage of B, Th2 and Th17 were significantly decreased (C and D). The ratio of Th17/Tregs and Th2/Tregs had a tendency to decrease after treatment (E). $^*P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$.

Acknowledgments: None.
Disclosure of Interests: None declared
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AB0796 PSORIATIC ONYCHOPATHY: MORE THAN MEETS THE EYE

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Background: Psoriatic onychopathy is an independent predictor of the onset of psoriatic arthritis (PsA). Assessment of nail disease is difficult given the limited utility of clinical assessment tools for the nail.
Recently, ultrasound (US) proved to be informative in the assessment of nail involvement.
Objectives: We aimed to describe morphologic ultrasonographic nail disease changes and to look for correlations between these features and the characteristics of the PsA.
Methods: The study included patients who met the CASPAR criteria for PsA.
An US scan of patient's nails was performed in order to study the nail, matrix and skin thickness.
Results: We included 33 patients with PsA with a mean age of 51.2±12.5 years. The mean DAPSA was 22.8± 19.7 (remission:9 patients, low activity: 5 patients, moderate activity: 11 patients and high activity: 8 patients).
Twenty-nine patients had a personal history of skin psoriasis, present in 64 % of the patients the day of the examination with a mean PASI of 2.76 ±3.9.
Eleven patients (33.4%) presented with psoriatic onychopathy (45 fingernails) with a mean mNAPSI of 14.1± 16.
The most common patterns of nail involvement were:
Oil-drop patches (5 fingernails), pitting (4 fingernails), onycholysis (3 fingernails), crumbling (3 fingernails), subungual hyperkeratosis (2 fingernails), leukonychia (2 fingernails), *paronychia* (2 fingernails), splinter hemorrhages (1 fingernail).
We scanned 330 fingernails. The US study revealed dystrophy in 75 nails (22.7%) of the nails, in 17 patients (51.5%): Undulations or pitting (n=47), followed by disappearance of the anechoic space (n=38) and anechoic ventral nail plate (n=18).
The mean thickness of skin, nail plate and nail matrix region were 2.25±0.32 mm, 0.38±0.07 mm and 1.89±0.33, respectively.
We found a positive correlation between nail plate thickness and both skin and nail matrix region thickness (r=0.561, p=0.001 and r=0.523, p=0.002).
Skin, nail and nail matrix thickness were significantly higher in men and in smokers. Manual workers did not have greater skin, nail plate nor nail matrix thickness.
There were no correlations between disease activity evaluated by the ASDAS-CRP, DAS28, PASI, ESR or by CRP and any of the US parameters.
In contrast, there was a significant negative correlation between psoriatic disease duration and nail plate thickness (r=-0.372, p=0,036).
Conclusion: Ultrasound offers an appropriate alternative for the evaluation of the nail unit. In our study it was able to detect subclinical involvement of the nail in 30 fingernails and in two patients.
Disclosure of Interests: None declared
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AB0797 ULTRASONOGRAPHIC ASSESSMENT OF ENTHESEAL INVOLVEMENT IN PSORIATIC ARTHRITIS

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Background: Entheseal involvement is a frequent and distinctive feature of psoriatic arthritis (PsA), often under diagnosed. It is especially associated with nail involvement. Because clinical examination is not sensitive enough for the detection of early signs of this involvement, US may be considered as an alternative imaging technique in the diagnosis of enthesopathy.
Objectives: The aim of the present study is to evaluate US entheses abnormalities in PsA and their correlation with clinical characteristics
Methods: The study included patients diagnosed with PsA according to the CASPAR criteria. They underwent a thorough clinical examination with special regard to the presence of enthesitis using the Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Index.
The US study bilaterally explored entheses at six sites: proximal plantar fascia, distal Achilles tendon, distal and proximal patellar tendon insertion, distal quadriceps tendon and distal brachial triceps tendon. We evaluated the following elemental lesions of enthesis at each site: thickness and structure of the tendon, calcifications, bursae, erosions, power Doppler signal in bursa or enthesis full tendon.
Results: Of the 33 patients, 39.4 % were male. The mean age was 51.2±12.5 years. The mean disease duration was 13.5±10.2 years.
The mean DAPSA was 22.8± 19.7 [0.1-84.5]: remission(n=9), low activity (n=5),-moderate activity (n=11),high activity(n=8).
At inclusion, 11 patients (33.4%) patients presented with psoriatic onychopathy (45 fingernails) with a mean mNAPSI of 14.1±16. Out of the 528 entheseal sites, 92 were tender at the palpation (17,4%) with a mean SPARCC at 2.87.
A total of 396 entheseal sites were examined by US. In 140 of them (35.35%), US found at least 1 sign indicative of enthesopathy. The most affected tendon was the distal Achilles tendon (42/396), followed by proximal plantar fascia (32/396), distal patellar tendon (20/396), quadriceps tendon (20/396), distal brachial triceps tendon(14/396) and finally proximal patellar tendon (12/396).
The most common elemental lesions were enthsophytes (176), erosions (114) and calcifications (50).
We found a positive correlation between age and both calcification (r=0,4, p=0.021) and enthesophytes (r=0.479, p=0.005).
We found a positive correlation between enthesophyte and the tender and swollen joints count (r= 0.352, p=0.045, r=0.378, p=0.03) and the SPARCC score (r=0.397, p=0.022).
Patients with higher BASDAI had thicker tendons (r=0.355, p=0.05).
Patients with nail dystrophy had more bursitis and erosions.
US scores did not correlate with sexe, disease duration and disease activity measures (ASDAS, DAPSA, DAS28 and PASI). Patients with subclinical entheseal involvement didn't have higher inflammatory biomarkers (ESR, CRP).
Conclusion: US subclinical enthesopthy are not rare in psoriatic arthritis, in particular in patients with active disease.

Clinical nail involvement was associated with bursitis and erosions. New studies including larger study groups are required to verify the findings of the present study

Disclosure of Interests: None declared

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AB0798 EFFECT OF ANTIRHEUMATIC THERAPY ADMINISTERED IN ACCORDANCE WITH "TREAT TO TARGET" PRINCIPLES ON DIASTOLIC DYSFUNCTION OF THE LEFT VENTRICLES IN PATIENTS WITH ACTIVE EARLY PSORIATIC ARTHRITIS

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Background: Psoriatic arthritis (PsA) are chronic inflammatory diseases, with massive increase of cardiovascular events (CVE) and cardiovascular death. Diastolic dysfunction of the left ventricles (LVDD) is a risk factor for the development of the heart failure.

Objectives: to study the effect of antirheumatic therapy administered in accordance with "Treat to target" principles on LVDD in early PsA (EPsA) patients (pts).

Methods: 48 (F.-23) DMARD-naive PsA pts, according to the CASPAR criteria, age 36[27; 45] years (yrs.), PsA duration – 6[4; 8] months. All pts were assessed for transthoracic echocardiography. Diastolic function was determined by early and atrial peak filling rates derived from differential volume-time-curve analysis. Methotrexate therapy was started in all pts with an escalation of the dose up to 25 mg/week subcutaneously. In case of no remission 3 months later, MT was added with biologic therapy: Adalimumab, Certolizumab pegol, Ustekinumab. Antihypertensive therapy received all pts with arterial hypertension (AH). All p less then 0.05 considered to statistical significance.

Results: At baseline LVDD was identified in 5(10.4%). The LVDD pts were older, in more cases they had AH, abdominal obesity (p<0.05). Significant negative correlations were found between LVDD and body mass index (BMI) (r=-0.41), age (r=-0.71), total cholesterol (r=-0.44), triglycerides (r=-0.48), low density lipoproteins (r=-0.44), systolic (r=-0.59) and diastolic blood pressure (r=-0.4), for all p<0,01. By 18 months of therapy significantly decreased DAS from 4.06[3.48; 4.91] to 0,97[0,65;1,48]; C-RP from 19.4 [8.8;37.5] to 2.2 [0.9; 4.6]mg/l, for all p<0,001. DAS remission was achieved in 69% of pts. We didn't find significant differences between baseline and after treatment the frequency of LVDD – 5(10,4%) to 4(8.3%).

Conclusion: in pts with EPsA frequently (10.4%) were detected LVDD, which are associated with a AH, age, higher BMI. Low prevalence LVDD in patients with EPsA is possibly caused by short duration of disease and early start of antirheumatic therapy. This has implications for development of preventive strategies for heart failure in EPsA patients.

Disclosure of Interests: None declared

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AB0799 REAL-WORLD EXPERIENCE OF SECUKINUMAB FOR PSORIATIC ARTHRITIS WITH AXIAL INVOLVEMENT.

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Background: Evidence on the efficacy of biologics in the treatment of psoriatic arthritis (PsA) patients with axial manifestations affecting 30-70% of PsA patients is limited. Secukinumab (SEC) has provided significant and sustained improvement in the signs and symptoms of active PsA and ankylosing spondylitis.

Objectives: This study aims to analyze the experience of using SEC for PsA patients with axial involvement in real-world setting.

Methods: Multicentric observational, longitudinal, retrospective study conducted in a tertiary hospital between January 2016 and December 2019. Patients with PsA (CASPAR criteria) and clinical and/or image diagnosis of axial involvement receiving at least one dose of SEC were included. Patients with non-pathological sacroiliacs x-ray and MRI had to have spinal pain VAS ≥4/10 after failure to NSAIDs, prior to the onset of SEC, to be included. Medical records were reviewed to collect demographic and clinical data, features of PsA (manifestations, treatments and activity assessment). Descriptive statistics and then a comparative analysis with the Student *t*-test to analyze the effectiveness of SEC were performed.

Table 1. Disease activity assessment at 6 months of secukinumab therapy.

	Baseline	6 months after SEC	Mean difference	P value
SJC	4,8±5,4	1,9±3,1	-2,8 (IC95% -3,9 a -1,7)	p<0,0001
TJC	7,7±5,8	3,9±4,1	-3,8 (IC95% -5,1 a -2,4)	p<0,0001
Spinal pVAS	6,1±3,2	4,2±2,9	-1,9 (IC95% -2,4 a -1,4)	p<0,0001
CRP (mg/L)	7,7±9,9	4,9±5,9	-2,9 (IC95% -4,5 a -1,2)	p=0,0009
ASDAS-CRP	2,5±1,9	1,8±1,3	-0,7 (IC95% -0,9 a -0,4)	p<0,0001
DAPSA	27,7±12,1	16,7±10,4	-11 (IC95% -15,3 a -6,8)	p<0,0001

SJC: swollen joint count, TJC: tender joint count, Spinal pVAS: spinal pain visual analog scale, CRP: C-reactive protein, SEC: secukinumab.

Results: Of 98 PsA patients treated with SEC, 58 (59.2%) had axial involvement, of which 41 (71%) female. Mean age was 54 y.o (SD 10) and average duration of the disease was 10 years (SD 8). All 58 patients had peripheral disease (33% joint erosions), 55 (95%) had psoriasis, 20 (34%) showed dactilitis and 39 (67%) had enthesitis. Sacroiliacs x-ray was damaged in 38 (66%) patients (grade I-IV) and 23 (40%) pathological MRI, with HLAB27+ at 8 (14%) patients. Average BMI was 29 (SD 8), with an obesity rate of 33% (19 pt). Observed comorbidities were hypertension (27 pt, 47%), diabetes mellitus (6 pt, 10%), dyslipidemia (23 pt, 40%), active smoking (18 pt, 31%) and malignancy (6 pt, 10%). Regarding previous treatments, 90% had received cDMARDs, particularly methotrexate (86%) and 40 (69%) had been exposed to at least one bDMARD (15 pt to one, 9 to two, 6 to three and 10 to four or more). 7 patients were on 300 mg dose and 51 patients on 150 mg dose (dose escalation to 300 mg was performed in 16 patients and 44% respond and maintain SEC). Average drug survival time was 1.4 (SD 1) years. At 6 months of SEC therapy, tender and swollen joint count, spinal pain VAS, CRP, ASDAS-CRP and DAPSA had significantly decreased (Table 1). 29 (50%) patients suspended SEC during follow-up due to primary ineffectiveness (8), secondary ineffectiveness (16), adverse events (3), latex allergy (1) and remission (1). Adverse events do not differ from those reported in clinical trials.

Conclusion: Secukinumab in real-world setting provided improvements in the axial and peripheral manifestations of PsA, using both the 150 mg and 300 mg doses.

Disclosure of Interests: MARIA MARTIN LOPEZ: None declared, Beatriz Joven-Ibáñez Speakers bureau: Abbvie, Celgene, Janssen, Merck Sharp & Dohme, Novartis, Pfizer, José Luis Pablos: None declared

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AB0800 CLINICAL ASSOCIATION BETWEEN URIC ACID/25-HYDROXYVITAMIN D SERUM LEVELS RATIO IN PATIENTS WITH PSORIATIC ARTHRITIS

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Background: The association between hyperuricemia and psoriatic arthritis (PsA) is actually generally accepted. Previous studies have demonstrated that uric acid suppress 25(OH)D metabolism [1]. More evidence is required to demonstrate the immune modulatory effects in psoriasis, psoriatic arthritis and other autoimmune diseases. In particular, the potential association between 25-hydroxyvitamin D serum levels and PsA still remains unknown.

Objectives: To assess a clinical association between uric acid/25(OH)D serum levels ratio related to PASI, BASDAI and DAPSA, if any, in patients with psoriatic arthritis.

Methods: We retrospectively observed 61 patients with psoriatic arthritis referred to our outpatients clinic, independently from already being on therapy or naïve. All selected patients underwent only conventional non-biological therapy at baseline and none received vitamin D supplementation and either allopurinol or febuxostat previously. Blood samples were drawn from all participants for assessment of 25-hydroxyvitamin D and uric acid serum levels. Disease activity of psoriasis and psoriatic arthritis were assessed by the Psoriasis Area and Severity Index (PASI), the Disease Activity Index for Psoriatic Arthritis (DAPSA) and the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). We assessed the covariates of interest by the Wilcoxon non parametric test, through the SPSS 24 Software.

Results: We observed 61 patients, mainly females (83.6%). At the univariate analysis, the uric acid/25(OH)D serum levels ratio revealed significantly associated with DAPSA and BASDAI indexes ($p<0.001$ and $p<0.001$, respectively), whilst no significant association emerged with the PASI index ($p=0.462$).

Conclusion: Data in the literature about these associations in the context of psoriatic arthritis are really poor. As a consequence, our findings, though preliminary, suggest us to hypothesize a potential role of uric acid/25(OH)D serum levels ratio as potential inflammation marker in order to better assess the disease activity. However, future larger studies are needed to investigate more in depth this association.

References:

[1] Charoenngam N, Ponvilawan B, Ungprasert P. Vitamin D insufficiency and deficiency are associated with a higher level of serum uric acid: A systematic review and meta-analysis. Mod Rheumatol. 2019 Mar 4:1-6.

Disclosure of Interests: None declared

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AB0801

EFFECTS OF GUSELKUMAB, A MONOCLONAL ANTIBODY THAT SPECIFICALLY BINDS TO THE P19-SUBUNIT OF INTERLEUKIN-23, ON DACTYLITIS AND ENTHESITIS IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: POOLED RESULTS THROUGH WEEK 24 FROM TWO PHASE 3 STUDIES

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Background: Guselkumab (GUS), a novel monoclonal antibody that specifically binds to the p19-subunit of IL-23, demonstrated efficacy in the Ph 3 DISCOVER-1 (D1) & DISCOVER-2 (D2) trials of pts with active psoriatic arthritis (PsA).[1,2] Dactylitis & enthesitis, key PsA clinical manifestations, can be difficult to treat and may portend more significant disease burden.[3,4]

Objectives: In pts with dactylitis or enthesitis at baseline, assess: 1) changes in symptoms over time and 2) relationships between improvements in dactylitis or enthesitis and other PsA domains.

Methods: Adults with active PsA despite standard therapies were eligible for D1 & D2. Approx. 30% of D1 pts previously received 1-2 TNF inhibitors; D2 pts were biologic-naïve. Pts were randomized 1:1:1 to GUS 100mg Q4W; GUS 100mg at W0, W4, Q8W; or PBO. Independent assessors evaluated dactylitis (total score: 0-60) & enthesitis (Leeds Enthesitis Index [LEI]; total score 0-6). Dactylitis and enthesitis findings through W24 were prespecified to be pooled across D1 & D2. P-values are unadjusted. We assessed changes in dactylitis and LEI scores over time (ANCOVA); associations between dactylitis or enthesitis resolution and ACR/PASI responses at W24 (Chi-square); and correlations between dactylitis or LEI and HAQ-DI/SF-36 change scores at W24 (Spearman's correlation). AEs through W24 were reported.[1,2]

Results: At W0, 42% of pooled D1+D2 pts had dactylitis; 65% had enthesitis. GUS improved dactylitis and LEI scores vs PBO at W8, W16, W24. GUS vs PBO differences were significant for dactylitis changes at W16 & W24 and LEI changes at W8 (Q4W only), W16 & W24; no dose response was observed (**Fig**). Rates of dactylitis or enthesitis resolution by W24 were consistently significantly (p<0.001) associated with ACR20/50/70 and PASI75/90 response (**Table**). In GUS-treated pts at W24, significant correlations were observed between dactylitis change scores and PASI (p<0.001 Q4W; p=0.006 Q8W) and SF-36 MCS (p=0.038 Q4W; p=0.003 Q8W) changes, and between LEI and HAQ-DI change scores (p<0.001 Q4W; p=0.005 Q8W). No consistent correlations/associations were observed between dactylitis or LEI scores and other clinical outcomes.

Conclusion: In PsA pts with dactylitis or enthesitis at W0, GUS improved dactylitis or LEI scores vs PBO by W8; treatment differences were significant at W16 & W24. Resolution of dactylitis or enthesitis was significantly associated with clinically meaningful improvements in PsA joint & skin symptoms. Improved dactylitis scores correlated with improved skin symptoms and mental health; improved LEI scores correlated with improved physical function.

References:

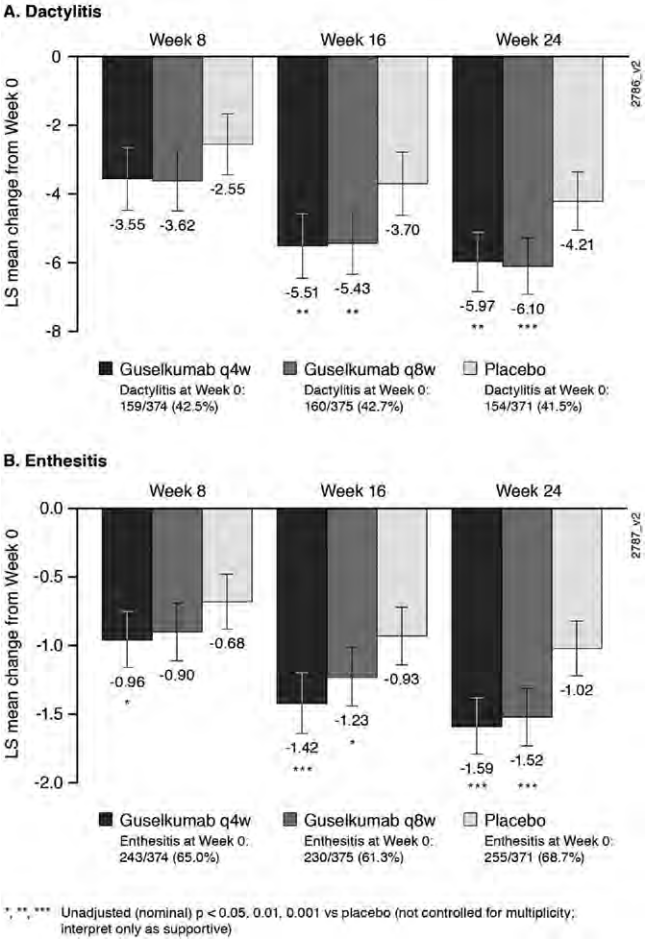
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[2] Mease P (A#L13), Arthritis Rheumatol 2019;71(suppl 10);
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Table. Pooled DISCOVER-1&2: associations between dactylitis/enthesitis resolution and joint/skin response

		ACR20	ACR50	ACR70		PASI75[a]	PASI90[a]
Dactylitis resolution[b]	**N**	**%pts**	**%pts**	**%pts**	**N**	**%pts**	**%pts**
Q4W	**373**	55*	34*	16*	**121**	78*	55*
Q8W	**375**	53*	31*	16*	**116**	80*	65*
PBO	**372**	26*	12*	5*	**115**	19*	10*
Enthesitis resolution[c]							
Q4W	**243**	34*	31*	11*	**187**	82*	63*
Q8W	**230**	40*	7*	12*	**162**	77*	62*
PBO	**255**	14*	13*	5*	**182**	19*	9*

* p < 0.001 (Chi-square)
[a] In pts with ≥3% BSA psoriasis & IGA ≥2 at W0
[b] In pts with D at W0
[c] In pts with E at W0

Fig. Pooled DISCOVER-1&2 LS mean changes from baseline over time in A) dactylitis and B) LEI scores



*, **, *** Unadjusted (nominal) p < 0.05, 0.01, 0.001 vs placebo (not controlled for multiplicity; interpret only as supportive)

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AB0802

SAFETY PROFILES OF IXEKIZUMAB VERSUS ADALIMUMAB: 52-WEEK RESULTS FROM A HEAD-TO-HEAD COMPARISON IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS

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Background: Ixekizumab (IXE) was shown to be superior to adalimumab (ADA) in achievement of simultaneous improvement of joint and skin disease (ACR50 and PASI100) in patients with active psoriatic arthritis (PsA) and inadequate response to conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs).[1]

Objectives: To compare the safety and tolerability profile of IXE vs ADA in patients with PsA up to 52 weeks of treatment.

Methods: SPIRIT-H2H (NCT03151551) was an open-label, head-to-head, blinded assessor clinical trial which included patients with active PsA (≥3 tender joint count + ≥3 swollen joint count) and plaque psoriasis (BSA ≥3%) who were inadequate responders to csDMARD therapy but naïve to biologic DMARDs. Patients were randomized (1:1) to approved dosing of IXE or ADA. Safety events were assessed at each patient visit up to Week 52. Frequencies of adverse events (AEs) were based on the number of patients in the safety population (patients who received ≥1 dose of study drug). Cases of inflammatory bowel disease (IBD) and cerebro-cardiovascular events were adjudicated by external committees. Kaplan-Meier analysis of time to onset of serious adverse events (SAEs) was performed.

Results: Of the 283 patients randomized to each treatment, 87% (246/283) of patients who received IXE and 84% (237/283) of patients who received ADA completed 52 weeks of treatment. The frequency of treatment-emergent AEs (TEAEs) was similar between the groups (74% IXE vs 69% ADA), however fewer severe TEAEs were reported in the IXE group (3.2% IXE vs 7.1% ADA) (Table). SAEs were significantly more frequent in the ADA group compared to the IXE group (12% vs 4.2%; p<0.001), and the time to develop a patient's first SAE was significantly shorter for ADA versus IXE (p<0.001; Figure). Discontinuations due to AEs were numerically more frequent in the ADA group versus the IXE group (7.4% vs 4.2%; p=0.15). IXE-treated patients reported more injection-site reactions (ISR) than ADA-treated patients (11% vs. 3.5%; p=0.002). Study withdrawals due to ISR were comparable, and only one injection-site reaction was severe on ADA (Table). There were two IBD cases reported for IXE; one case was confirmed as IBD.

Conclusion: Safety results were consistent with previous trials with IXE and ADA. Compared with IXE, patients with PsA treated with ADA had significantly more serious AEs.

References:

[1] Mease PJ, et al. *Ann Rheum Dis.* 2020;79(1):123-31.

Table. Safety results at 52 weeks

	IXE N=283 n (%)	ADA N=283 n (%)
TEAEs	209 (74)	194 (69)
Severe[a]	9 (3.2)	20 (7.1)
Related to study treatment[b]	98 (35)	87 (31)
Serious adverse events	12 (4.2)	35 (12)***
Deaths	0	0
Discontinuation due to AE	12 (4.2)	21 (7.4)
Serious infections	3 (1.1)	4 (1.4)
Injection-site reactions[c]	30 (11)	10 (3.5)**
Severe	0	1 (0.4)
Resulted in discontinuation	2 (0.7)	3 (1.1)
Anaphylaxis	0	0
Inflammatory bowel disease	2 (0.7)	0
Ulcerative colitis	1 (0.4)[d]	0
Crohn's disease	1 (0.4)	0
Cerebro-cardiovascular events	5 (1.8)	7 (2.5)
MACE	0	2 (0.7)
Malignancies	0	4 (1.4)
Depression	5 (1.8)	9 (3.2)
Interstitial lung disease	0	1 (0.4)
Cytopenias	9 (3.2)	12 (4.2)
Hepatic events	18 (6.4)	20 (7.1)

[a]Patients with multiple occurrences of the same event are counted under the highest severity. [b]The TEAE's relationship to study treatment was judged by the investigator. [c]MedDRA high-level term. [d]This event was adjudicated but it was not a confirmed IBD. ***p<0.001; **p<0.01 by Fisher's exact test. ADA=adalimumab, AE=adverse event; IBD=inflammatory bowel disease; IXE=ixekizumab; MACE=major adverse cardiovascular event; TEAE=treatment-emergent adverse event.

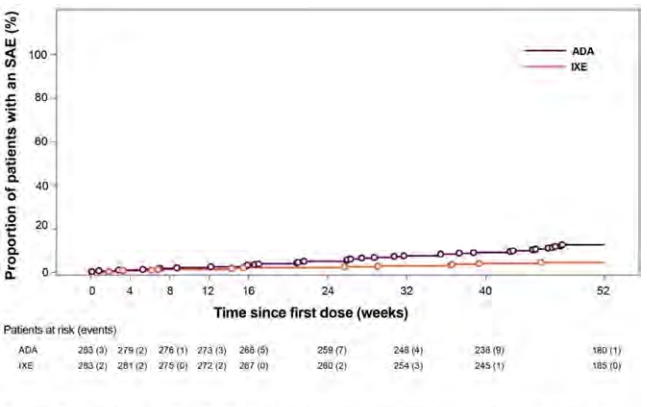


Figure: Time to onset of first SAE. Numbers below x-axis represent patients at risk at each time point. Open circles represent events. p<0.001 by log rank test. ADA=adalimumab; IXE=ixekizumab; SAE=serious adverse event.

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AB0803

EFFICACY OF TILDRAKIZUMAB IN PSA: DAS28-CRP SCORES THROUGH WEEK 52

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Background: Tildrakizumab (TIL), an anti–interleukin (IL)-23p19 monoclonal antibody, is approved in the US, EU, and Australia for treatment of moderate-to-severe plaque psoriasis.[1] A randomised, double-blind, placebo-controlled, multiple-dose, phase 2b study (NCT02980692) evaluating efficacy and safety of TIL for treatment of psoriatic arthritis (PsA) was recently completed.

Objectives: To evaluate the effect of TIL in PsA, using the DAS28-CRP responses up to week (W)52.

Methods: Patients (pts) ≥18 years old with PsA[2] and ≥3 tender and ≥3 swollen joints were randomised 1:1:1:1:1 to receive TIL (200 mg once every 4 weeks [Q4W], 200 mg every 12 weeks [Q12W], 100 mg Q12W, or 20 mg Q12W) or placebo (PBO Q4W) to W24. Thereafter, PBO Q4W and TIL 20 mg Q12W arms crossed over to TIL 200 mg Q12W to W52. DAS28-CRP was shown to be reliable in PsA studies,[3] and pts achieving scores <3.2 satisfied responder criteria.

Adverse events (AEs), including treatment-emergent AEs (TEAEs) and serious AEs (SAEs), were monitored throughout the study.

Results: Overall, 391/500 pts screened met the inclusion criteria; 55% were female with a mean age of 48.8 years. At baseline, disease characteristics were generally consistent across treatment arms (**Table**).

At W24, DAS28-CRP response rates increased across all TIL treatment arms relative to PBO (**Figure**). After W24, response rates continued to increase and were sustained through W52, including in pts who switched from PBO to TIL.

From W0–W24/W25–W52, 50.4%/39.9% and 2.3%/1.0% of pts experienced a TEAE and SAE, respectively. There were no reports of candidiasis, inflammatory bowel disease, major adverse cardiac events or elevated liver enzymes. From W0–W24, 1 pt (0.3%) had urinary tract infection (TIL 100 mg Q12W). From W25–W52, 1 pt (0.3%) had an intraductal proliferative breast lesion (TIL 20→200 mg Q12W). One pt (0.3%) discontinued before 24 weeks due to hypertension. No deaths were reported.

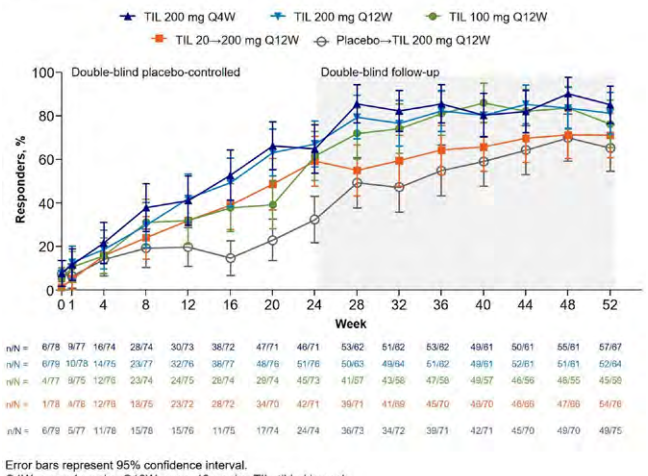
Table. Baseline disease characteristics related to DAS28-CRP

	TIL 200 mg Q4W n = 78	TIL 200 mg Q12W n = 79	TIL 100 mg Q12W n = 77	TIL 20→200 mg Q12W n = 78	PBO→TIL 200 mg Q12W n = 79
hsCRP, mg/L	7.8 ± 18.6	10.5 ± 14.4	10.6 ± 20.0	10.7 ± 14.0	13.0 ± 20.8
ESR, mm/h*	22.8 ± 18.9	22.5 ± 19.8	24.7 ± 19.8	27.2 ± 20.7	26.9 ± 20.5
Swollen joint count (66)	10.4 ± 7.4	10.0 ± 8.0	11.0 ± 8.2	9.4 ± 6.4	11.8 ± 9.8
Tender joint count (68)	16.6 ± 11.9	19.5 ± 13.9	21.3 ± 14.8	19.0 ± 13.0	19.7 ± 14.7
PtGA	57.8 ± 18.3	61.1 ± 20.7	60.3 ± 20.2	61.9 ± 17.4	65.2 ± 18.1

Data are reported as mean ± standard deviation unless otherwise stated.
*Total pts analysed (n) = 71, 69, 70, 68, 62, respectively.
ESR, erythrocyte sedimentation rate; hsCRP, high-sensitivity C-Reactive Protein; PBO, placebo; PtGA, Patient Global Assessment; pts, patients; Q4W, every 4 weeks; Q12W, every 12 weeks; TIL tildrakizumab.

Conclusion: Treatment with all doses of TIL increased the rate of DAS28-CRP responders in pts with active PsA and was well tolerated, suggesting a reduction in PsA-related disease activity for up to 52 weeks of treatment. Ongoing analyses will assess whether DAS28-CRP responses correlate with baseline clinical characteristics.

Figure. DAS28-CRP response rates across treatments and time points



Error bars represent 95% confidence interval.
Q4W, every 4 weeks; Q12W, every 12 weeks; TIL, tildrakizumab.

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AB0804

PREGNANCY AND PSORIATIC ARTHRITIS: A SYSTEMATIC LITERATURE REVIEW OF DISEASE ACTIVITY AND ADVERSE PREGNANCY OUTCOMES

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Background: There is little robust evidence on the course of pregnancy and its outcomes in women with psoriatic arthritis (PsA) on which recommendations for the management of these patients could be based.

Objectives: To review available data on disease activity during pregnancy and adverse pregnancy outcomes in women with PsA.

Methods: Systematic literature search within the databases Pubmed and Embase using the keywords 'psoriatic arthritis' and 'pregnan*/ obstetr*/ matern*/ gestation*/ deliver*/ abortion*/ reproduct*/ birth/ parity'. All full text articles published until 31 Dec 2019 were systematically evaluated by 2 reviewers. All studies including at least 5 pregnant PsA patients and reporting on disease activity and/ or obstetric outcomes were considered.

Results: The review of 592 search results revealed 13 eligible publications reporting on a total of 2332 pregnancies in PsA. Nine studies reported disease activity during and after pregnancy using differing instruments (table 1). Three of them reported an increase in the proportion of women with moderate to severe activity postpartum compared to pregnancy. Another 3 studies described a worsening of the arthritis in 15-32% and in the psoriatic activity in 4-9% of patients during pregnancy and postpartum in 33-50% and 27-43% of patients, respectively.

Table 1. Study characteristics

Study	Data source	No. of pregnancies	Disease activity instruments
Berman, 2018	Hospital records	35	Synovitis
Bröms, 2018	National registries	964	-
Eudy, 2019	Hospital records + questionnaires	37	Patient reported arthritis + psoriatic activity
Mork, 2019	National registries	130	-
Mouyis, 2017	Hospital records	16	Physician global activity
Murray, 2019	Hospital cohort*	18	DAS28-CRP3
Ostensen, 1988	Hospital cohort*	12	Composite score
Polachek, 2017	Hospital cohort*	42	SJC/ TJC, PASI
Polachek, 2019	Hospital cohort + questionnaires	151	Patient reported PsA activity
Remaeus, 2019	National registries	541	-
Smith, 2019	Cohort*	117	HAQ, RAPID3
Strouse, 2019	Claims data	161	-
Ursin, 2019	Cohort*	108	DAS28, BASDAI

*Prospective study

Table 2. Obstetric outcomes

Study	Comparator: Pregnant women without ...	Reported as	(Pre-) Eclampsia	Gestational diabetes	Elective Caesarean section	Preterm birth	SGA	LBW
Bröms	... psoriasis	HR	**1.49 (1.08-2.05)**	1.21 (0.79-1.87)	**1.47 (1.18-1.81)**	1.25 (0.94-1.65)	0.72 (0.42-1.22)	1.07 (0.75-1.52)
Mork	... Spondyloarthritis	OR	1.03 (0.23-4.57)	-	1.01 (0.47-2.19)	1.24 (0.54-2.83)	1.72 (0.98-3.02)	-
Remaeus	... PsA	HR	1.21 (0.78-1.88)	1.26 (0.54-2.94)	**1.47 (1.10-1.97)**	**1.63 (1.17-2.28)**	1.06 (0.61-1.84)	-
Smith	... auto-immune/ other chronic diseases	RR	2.22 (0.98-5.04)	1.41 (0.70-2.87)	-	1.69 (0.94-3.03)	-	1.52 (0.76-3.04)
Strouse	... rheumatic diseases	HR	-	-	-	**1.77 (1.15-2.73)**	1.24 (0.75-2.06)	-

Abbreviation: HR, Hazard ratio; OR, Odds ratio; RR, risk ratio.

Adjusted analyses did not show an increased risk for gestational diabetes, small for gestational age (SGA) and low birth weight (LBW) in PsA patients (table 2). However, estimates for other obstetric outcomes diverged.

Conclusion: Individual studies showed a trend towards increased disease activity after pregnancy in PsA patients but due to the heterogeneity of the instruments used, it is difficult to summarise the single results. No signal for specific adverse pregnancy outcomes was identified. However, a higher risk for (pre)eclampsia, elective caesarean section and preterm birth cannot be ruled out. Differences in studies (e.g. primary vs secondary data) limit statements on obstetric outcomes. Harmonization of approaches and instruments is crucial in order to enable future joint data analyses and meta-analyses. In particular, a standardised instrument for assessing disease activity of PsA that takes into account the particularities of pregnancy is needed.

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AB0805 PREMATURE ATHEROSCLEROSIS IN PSORIATIC ARTHRITIS (PSA) PATIENTS AND ITS POSSIBLE ASSOCIATION WITH INSULIN RESISTANCE & SERUM LEPTIN LEVEL

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Background: PsA is a heterogeneous inflammatory arthritis. Patients (pts) with PsA suffer from associated cardiovascular disease, obesity, metabolic syndrome, diabetes (DM), osteoporosis. In psoriasis, leptin has been shown to stimulate keratinocyte proliferation, expression of adhesion molecules and angiogenesis.

Objectives: To detect the presence of premature atherosclerosis in PsA pts, measure HOMA-IR as a reflection of insulin resistance (IR) and serum leptin (LEP) level & to detect their association with the presence of premature atherosclerosis in PsA pts.

Methods: 45 PsA pts (classified according to CASPAR Criteria) & 45 healthy subjects as controls were included. Pts were subjected to history taking, clinical examination to determine body mass index (BMI), the clinical type of PsA, distribution, involved body surface area (BSA), measuring the Psoriasis Area and Severity Index (PASI) and Disease Activity in PSoriatic Arthritis: DAPSA score. Routine laboratory, fasting insulin (FI), fasting blood glucose (FBG) to calculate HOMA-IR,total cholesterol (TC), HDL, LDL, Triglycerides (TG), serum LEP, carotid Doppler to determine Carotid intima–media thickness (CIMT) & presence or absence of plaques were done. Exclusion: DM, RA, SLE, smoking, postmenopausal females, HCV infection, morbid obesity

CIMT	Person correlation coefficient	p-value
BMI	0.095	0.371
Duration of disease (years)	0.179	0.239
BSA score	0.12	0.434
PASI	0.186	0.221
FBG	0.059	0.582
WBC	-0.104	0.329
Platelet	0.022	0.835
Hb	-0.106	0.319
HDL	0.505	0.000**
LDL	0.382	0.000**
TC	0.275	0.009**
Triglyceride	0.06	0.577
SGOT	0.03	0.776
SGPT	0.033	0.754
Serum leptin	0.537	0.0001**
HOMA IR	0.446	0.000**
ESR	0.351	0.001**
CRP	0.320	0.002**
Urea	0.445	0.784
Creatinine	0.392	0.954
Uric acid	0.034	0.748
FI	0.431	0.000**

Results: Mean **BMI** 22.51±1.69 and 23.46±1.82 kg/m^2, no statistical significance (P =0.205).

Mean **BSA** 5.9±3.1%, **DAPSA score** (13.98±4.7), **PASI score:** 88.9% (40 pts) had mild to moderate PASI, 5 had severe disease (8.6±4.8).

TC, LDL and TG were higher in pts, while HDL was higher in controls (P =0.0003, 0.0001, 0.00001 & 0.05).

A significance between 2 groups regarding LEP (P =0.00001), ranging from 2-16.99 (9.7±4.5) in group I and 1.35-1.78 (1.6±0.1) µg/ml in controls. **Normal: 2.6-8.35**

FI & HOMA IR were significantly higher in PsA group (P = 0.001, 0.00001)

The mean CIMT 1.1±0.3 mm and in group II 0.8±0.1 mm. 14 pts (31.1%) had plaque, while 68.9 % & all controls had no plaques, with a significance regarding CIMT & presence of plaques (P=0.011 & 0.0041).

A positive statistical significance between LEP and dd (P=0.001), BSA, PASI and DAPSA (P =0.007, 0.003, 0.001) but not with age, BMI (P=0.98 & 0.88).

There was no statistical significance between LEP and FBG, HbA1C, HOMA IR, FI, CBC (P > 0.05), or between LEP and TC, TG, HDL, LDL (P=0.438,0.390, 0.699, 0.050), liver enzymes, renal functions, ESR and CRP.

There was statistical positive correlation between LEP and CIMT (P =0.0001), but not with the presence of plaques (P=0.846).

CIMT and other variables: Table 1

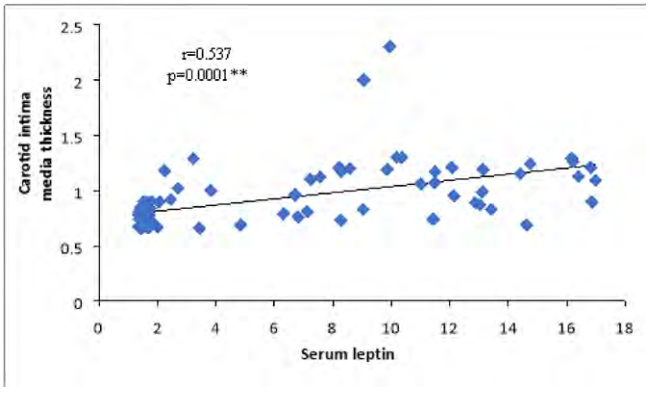
DAPSA: there was no statistical significance with TC, HDL, LDL and TG (P=0.51, 0.876, 0.717 & 0.255), but a statistically significance with LEP and CIMT(p=0.001& 0.009). Pts with higher score had higher LEP and increased CIMT.

PASI: there was no significance between TC, HDL, LDL, TG (P=0.724, 0.157, 0.651& 0.374) or CIMT (p=0.290) in mild-moderate and severe PASI. LEP was significantly higher in severe PASI score (P= 0.001).

Conclusion: The presence of abnormal lipid profile, IR, increased CIMT, high disease activity and increased LEP may be considered as useful criteria for early recognition and thus prevention of atherosclerosis in PsA pts.

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AB0806 DOES VITAMIN D INFLUENCE THE ACTIVITY OF THE DISEASE IN PATIENTS WITH PSORIATIC ARTHRITIS?

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Background: Several studies have shown an inverse relationship between vitamin D levels (25OHD) and disease activity in patients with rheumatoid arthritis (RA). However, the existing data in patients with psoriatic arthritis (PsA) are poor, and they use the DAS28 index as a peripheral joint activity marker by extrapolation with RA.

Objectives: To analyze the relationship between 25OHD levels, disease activity and functional capacity in patients with PsA.

Methods: Transversal, observational, descriptive study. We included PsA patients with peripheral joint involvement. We collected demographic variables (gender, age), clinical variables [follow-up, received treatments, TJC

(68), SJC (68), VAS] and analytical variables (25OHD, CRP, ESR). We used *Disease activity in psoriatic arthritis* (DAPSA) score to measure disease activity, and the *Health assessment questionnaire* (HAQ) to determine functional capacity. Levels of 25 OHD <20 ng/ml and between 20-30 ng/ml were considered deficient and insufficient, respectively. Statistical analysis was made with SPSS 22.0. The descriptive analysis results were expressed as percentage and mean ± SD. We used Pearson's correlation to assess the association between quantitative variables and T test to compare means between dichotomous variables.

Results: 125 patients were included, the majority women (60.8%), with an average age of 55.4 (SD 12.2) years. The average follow-up was 75.5 (SD 68.3) months. 97.6% of patients had received DMARDs and 40.8% biologics, and almost half of the patients (42.7%) took calcium and 25OHD supplements. The average value of 25OHD was 27.1 (SD 12.1) ng/ml, with 30% of patients having 25OHD deficit and 63.3% insufficiency. The majority of patients had an acceptable disease control, with a mean DAPSA of 10.5 (SD 7,9); and mean of CRP, ESR, TJC and SJC was 6.1 (SD 3.7) mg/l, 10.2 (SD 9.9) mm/h, 1.3 (SD 2.5) and 0.7 (SD 2.1), respectively. The average value of HAQ was 0.6 (SD 0.7). We observed an inverse correlation between 25OHD levels and joint counts, TJC (p=0.02) and SJC (p=0.03). On the other hand, patients with hypovitaminosis D presented a tendency to get higher scores in DAPSA index (P=0.07). We do not observe any relationship between 25OHD and HAQ.

Conclusion: As can be seen in our sample, low values of 25OHD are related to increased disease activity in patients with PsA.

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AB0807 VITAMIN D ROLE IN VASCULAR DAMAGE PROGRESSION IN PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Psoriatic arthritis (PsA) is associated with insufficent levels of vitamin D (25OHD) and an increased cardiovascular risk. Several studies, have shown an inverse relationship between 25OHD levels and cardiovascular damage.

Objectives: To study the relationship between 25OHD and vascular damage, as well as its possible influence on its progression, in patients with PsA.

Methods: Pre-post longitudinal study with analytical components. PsA patients with peripheral joint involvement were included. Demographic (sex, age), clinical [follow-up time, DAPSA, current treatment, body mass index (BMI), classic vascular risk factors, vascular events] and analytical variables [atherogenic index, glomerular filtration (GF-MDRD), glycosylated hemoglobin (HbA1c), CRP, ESR, 25OHD] were collected. We considered deficient level of 25OHD <20 ng/ml and insufficient <30 ng/ml. Basal vascular risk was estimated through SCORE tool. Extracranial carotid artery was explored with an Esaote MyLab70XVG ultrasound with linear probe (7-12mHz) and an automated program that measures intima media thickness (IMT) by radiofrequency, and the presence of atheroma plaques was evaluated following Mannheim consensus. Pulse wave velocity (PWV) was measured through Mobil o graph® dispositive. IMT≥900 µ and PWV≥ 10m/s were considered as pathological values. We repeat vascular study 3 years later. Vascular damage progression was defined as the appearance of atheroma plaques during the follow-up and/or an increase in their number. Statistical analysis was performed using SPSS 22.0 program.

Results: 78 patients were included. Eighteen patients were excluded due to high vascular risk [previous event, diabetes type II or type I with target organ injury and/or GF-MDRD< 60 ml/min]. 57.5% were women with a mean age of 54.2 (SD 10.9) years. The mean follow-up time was 96.8 (SD 163.6) months and mean DAPSA was 10.2 (SD 8.3). 96.2% of patients had received DMARDs and 42.3% biologicals, and 42.3% took calcium and 25OHD supplements. Mean BMI was 27.5 (SD 4.7) kg/m^2. 42.3% had tobacco exposure, 29.5% were hypertensive and 32% dyslipidemic. Mean SCORE was 1.6 (SD 1.8) and mean 25OHD was 27.6 (DSD 11.6) ng/ml. 28.2% patients had 25OHD deficit and 60.3 % insufficiency. At the beginning, 32.1 % of patients had atheromatous plaques with a number of plaques around 1.7 (SD 1.2), and 6.7% and 19.7% had a pathological IMT or PWV, respectively. Baseline, we had not observed any association between 25OHD and the presence of atheroma plaques, IMT or PWV. Three years later, we detected progression of vascular damage in 31.2% patients. In these patients, the existence of hypovitaminosis D was associate with the appearance of atheroma plaques (p=0.043). This association desappeared in the multivariate analysis, in which only the CRP influenced the appearance of atherome plaques (OR: 1.4, IC 95% 1.04-1.98, p=0.025).

Conclusion: Low 25OHD levels are not related to vascular damage or influence a posible progression of it in our serie. As might be expected, the progression of vascular damage depends on the inflammatory load in these patients.

Disclosure of Interests: L Montolio-Chiva: None declared, M Robustillo-Villarino: None declared, Ana V Orenes Vera: None declared, Marta Aguilar-Zamora: None declared, C Vergara-Dangond: None declared, I Vázquez-Gómez: None declared, Eduardo Flores: None declared, A Sendra-García: None declared, À Martínez-Ferrer: None declared, Elia Valls-Pascual Grant/research support from: Roche, Novartis, and AbbVie, Speakers bureau: AbbVie, Lilly, Pfizer, MSD, Novartis, Janssen, Bristol Myers Squibb, UCB Pharma, D Ybáñez-García Speakers bureau: Lilly, Roche, Sanofi, V Núñez-Monje: None declared, I Torner-Hernández: None declared, Juanjo J Alegre-Sancho Consultant of: UCB, Roche, Sanofi, Boehringer, Celltrion, Paid instructor for: GSK, Speakers bureau: MSD, GSK, Lilly, Sanofi, Roche, UCB, Actelion, Pfizer, Abbvie, Novartis

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AB0808 IMPLEMENTING IPAD-BASED ASSESSMENTS TO IMPROVE PERFORMANCE IN A PSORIATIC ARTHRITIS CLINIC AT A DISTRICT GENERAL HOSPITAL

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Background: Psoriatic Arthritis (PsA) is a complex disease with profound physical and psychosocial effects. The core domain set for this condition was updated by the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA)-Outcome Measures in Rheumatology (OMERACT) PsA working group in 2016[1] and the TICOPA (TIght COntrol of Psoriatic Arthritis) study suggested that adopting a 'treat-to-target' approach aiming for Minimal Disease Activity (MDA) could result in better clinical outcomes[2].

Objectives: To improve assessment of all the core domains of PsA during clinic appointments and aim to treat these patients using a 'treat-to-target' approach to improve clinical outcomes.

Methods: We were able to confirm through a retrospective baseline audit that all core domains of PsA were not being fully addressed in our general rheumatology clinics. A dedicated weekly PsA clinic was then set up at our district general hospital. Subsequently, iPads incorporated with GRAPPA App were implemented in these clinics to facilitate multi-domain assessments aiming for MDA. This was supported by a Health Education England (Wessex) Quality Improvement Fellowship that involved rheumatology and dermatology team members working in close collaboration. We then carried out a re-audit to assess our performance. Additionally we set up quarterly combined Rheumatology and Dermatology clinics for patients with severe joint and skin involvement. We also conducted a baseline survey by asking patients for their opinion about the 'setting up of the dedicated PsA service', the 'quarterly combined clinics' and the 'use of iPad-based assessments'. We asked them to score each of these on a scale of 0 to 10, with 0 being 'very negative' and 10 'very positive'.

Results: We had pragmatically set a standard of 75% for our baseline audit but we found an overall compliance of only 27.4%. There was also a wide variation between different domains with a compliance of even 0% for some. Domains that are not assessed are unlikely to be fully taken into account when deciding about treatment. The re-audit following the implementation of iPad-based assessments in dedicated PsA clinics showed a significant improvement in each of the domains and the overall compliance went up to 97.9% (Table 1). The patient survey findings were also excellent with mean scores of 9.5, 9.0 and 9.5 respectively for the three items (Figure 1).

Table 1.

	Audit (n = 25)	Re-audit (n = 29)
	Compliance	
Q1. Documented evidence of joint count being performed?	84.0%	100.0%
Q2. If yes, then was it a 66/68 count for swollen and tender joints?	4.7%	100.0%
Q3. Documented evidence of dactylitis being assessed?	8.0%	100.0%
Q4. Documented evidence of enthesitis being assessed?	4.0%	100%
Q5. Documented evidence of assessment of spinal involvement?	8.0%	100.0%
Q6. Documented evidence of assessment of skin involvement?	36.0%	100.0%
Q7. Documented evidence of assessment of nail involvement?	4.0%	93.1%
Q8. Documented evidence of assessment of fatigue?	8.0%	96.6%
Q9. Documented evidence of assessment of degree of pain?	60.0%	100.0%
Q10. Documented evidence of patient's global assessment?	68.0%	96.6%
Q11. Documented evidence of assessment of physical function?	0.0%	96.6%
Q12. Documented evidence of assessment of health-related quality of life?	0.0%	93.1%
Q13. Documented evidence of assessment of systemic inflammation?	72.0%	96.6%
Overall Compliance	**27.4%**	**97.9%**

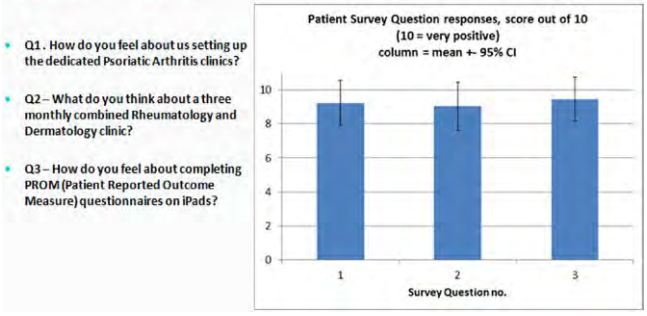
Conclusion: Dedicated PsA clinics using the GRAPPA App on iPads could facilitate comprehensive multi-domain assessments of patients with PsA and potentially lead to better outcomes as well as greater patient satisfaction.

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Figure 1. Patient survey (n=26)



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AB0809 HOW WELL ARE BIOLOGICS RETAINED IN PSORIATIC ARTHRITIS - A REAL WORLD STUDY

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Background: Biologics have led to a sea change in the management of psoriatic arthritis (PsA) with unprecedented improvement in the signs, symptoms and radiographic damage, resulting in improvement in functionality and quality of life. However longitudinal data for their retention and tolerability is sparse.

Objectives: Our objective was to evaluate real-world biologic therapy duration and reasons for discontinuing treatment.

Methods: We conducted a retrospective analysis of our PsA electronic register from 1994 up to and including April 2019 at our university teaching hospital. We had access to full patient records including details on co-morbidities, drugs and disease management.

Results: 335 patients were identified with PsA. 58% of them were female with mean age of 46 yr (13-81). 113 (33.7%) patients had been treated with a biologic with 105 (93%) continuing at the time of analysis. 60 individuals were prescribed combination therapy with DMARDs. Mean age was 43.3 years (13-81) with 56% women. The biologics sample was ethnically diverse including 80% White Caucasian patients, 17% Asian and others (3%). Significant co-morbidities included cardiovascular disease (18.6%) and diabetes (4.4%). Eight different biologics were in use with adalimumab being the most prescribed (67%).

35 (30.9%) patients had stopped biologics at some point with 76 episodes of cessation. 6% of our sample had discontinued two or more biologic treatments. The mean duration before biologic therapy was discontinued was 18.2 months (8 days to 9.5 years), which was almost twice as long as the average period before discontinuing a DMARD (9.9 months). Main reasons for stopping treatment included 23% each due to GI symptoms, neurological causes, cutaneous symptoms and other side effects. The remaining 8% reported fatigue as the reason for stopping therapy.

Conclusion: To our knowledge this is the first dedicated retrospective review of a large real world PsA cohort comparing drug survival and tolerability of biologics against DMARDs. Biologic therapies are well tolerated in psoriatic arthritis. There is no significant difference amongst various modes of action. Over a quarter of the patients discontinue the drug owing to intolerance with mean drug survival of 18 months. In contrast nearly two-thirds were intolerant of DMARDs and stopped within ten months. Thus both the rate and duration of biologic retention is significantly better than conventional DMARDs. This has significant economic impact as NICE guidelines require an adequate trial of two DMARDs for six months prior to advanced therapy. However, this approach is unlikely to be cost effective as the disease progresses whilst patients struggle with DMARDs prescription and thus delay biologics which are more likely to be tolerated and retained longer. Hence there is an urgent need to review NICE guidelines to allow earlier employment of biologics in the treatment paradigm with significant benefits to both patients and the health economy.

Disclosure of Interests: Issrah Jawad: None declared, Muhammad Khurram Nisar Grant/research support from: Muhammad Nisar undertakes clinical trials and received support (including attendance at conferences, speaker fees and honoraria) from Roche, Chugai, MSD, Abbvie, Pfizer, BMS, Celgene, Novartis and UCB, Consultant of: Muhammad Nisar undertakes clinical trials and received support (including attendance at conferences, speaker fees and honoraria) from Roche, Chugai, MSD, Abbvie, Pfizer, BMS, Celgene, Novartis and UCB, Speakers bureau: Muhammad Nisar undertakes clinical trials and received support (including attendance at conferences, speaker fees and honoraria) from Roche, Chugai, MSD, Abbvie, Pfizer, BMS, Celgene, Novartis and UCB

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AB0810 IMPACT OF TOLERABILITY ON RETENTION OF CDMARDS IN PSORIATIC ARTHRITIS - IS IT A CONCERN?

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Background: Most guidelines recommend the first line use of DMARDs in Psoriatic Arthritis (PsA). However, studies show that many conventional treatments like methotrexate are poorly tolerated. There is hitherto no published real-world data addressing the tolerability of DMARDs in PsA.

Objectives: Our objective was therefore to assess the drug management in PsA with focus on tolerability and the reasons for therapy cessation.

Methods: We conducted a retrospective analysis of all PsA patients enrolled in electronic database up to April 2019 at our university teaching hospital. We had access to full patient records including details on co-morbidities, drugs and disease management

Results: 335 patients were identified with a formal diagnosis of PsA. Mean age of the cohort was 46 years (13-81) and 58% were female. 48% of the group had clinically active disease. Same percentage were taking a single DMARD. 10% had trialled 3 or more drugs. 62% of patients had discontinued one or more DMARDs prior. The mean duration before discontinuing a DMARD was 9.9 months. Methotrexate was the best tolerated and on average discontinued after 13.4 months (range: 4 days to 10.9 years). Sulfasalazine and Hydroxychloroquine were discontinued after an average of 8.4 (11 days to 4.27 years) and 12.5 months (1.3 months to 2.88 years) respectively. Leflunomide was the least tolerated DMARD and stopped after an average of 5.5 months (7 days to 2.53 years). The main reason for stopping a medication was gastro-intestinal symptoms which accounted for 42% of all the reported side effects. This applied to both methotrexate (43%) and sulfasalazine (46%) discontinuation. The leading reasons for discontinuing Hydroxychloroquine were jointly GI symptoms and other side effects at 43% each. Leflunomide was stopped in 50% of cases due to neurological symptoms.

Conclusion: To our knowledge, this is the first report confirming poor retention rate of oral DMARDs in a real world PsA cohort managed over 20 years.

In the context of chronic disease, the median duration of treatment is short. Our analysis did not include patients who suffer from side effects but continue therapy thereby impacting treatment adherence and hence the true scale of the issue is likely higher. Though NICE guidelines stipulate the need of an adequate trial of minimum two DMARDs prior to therapy escalation, in reality these drugs are not well tolerated and thus pose a challenge to clinicians. One potential solution is earlier adoption of biological therapies, which are increasingly cost effective and have been shown to be better tolerated.

Disclosure of Interests: Issrah Jawad: None declared, Muhammad Khurram Nisar Grant/research support from: Muhammad Nisar undertakes clinical trials and received support (including attendance at conferences, speaker fees and honoraria) from Roche, Chugai, MSD, Abbvie, Pfizer, BMS, Celgene, Novartis and UCB, Consultant of: Muhammad Nisar undertakes clinical trials and received support (including attendance at conferences, speaker fees and honoraria) from Roche, Chugai, MSD, Abbvie, Pfizer, BMS, Celgene, Novartis and UCB, Speakers bureau: Muhammad Nisar undertakes clinical trials and received support (including attendance at conferences, speaker fees and honoraria) from Roche, Chugai, MSD, Abbvie, Pfizer, BMS, Celgene, Novartis and UCB

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AB0811

DEMOGRAPHIC, TREATMENT AND DISEASE CHARACTERISTICS OF PATIENTS WITH PSORIATIC ARTHRITIS RECEIVING TOFACITINIB IN THE UNITED STATES, FRANCE, GERMANY, ITALY, SPAIN AND THE UNITED KINGDOM

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Background: Tofacitinib is an oral JAK inhibitor for the treatment of psoriatic arthritis (PsA). The efficacy and safety of tofacitinib for PsA have been demonstrated in Phase 3 trials of up to 12 months' (mos) duration.[1,2]

Objectives: To describe demographic, treatment and disease characteristics of a sample of patients (pts) at initiation of tofacitinib for PsA in the United States (US), France, Germany, Italy, Spain and the United Kingdom (European Union Five; EU5).

Methods: An online, retrospective medical chart review of de-identified pts treated with tofacitinib for PsA from the US and the EU5 was conducted by Ipsos Rheumatology Monitor between Sept and Dec 2019, after product approval for PsA (US, 5 mg twice daily [BID] and 11 mg once daily [QD]: Dec 2017; EU, 5 mg BID: June 2018). Rheumatology healthcare professionals (HCPs), recruited from a large panel, selected a sample of charts of pts ≥18 years of age who had a HCP-reported diagnosis of PsA and were prescribed tofacitinib. Extracted data included pt demographics, treatment characteristics (including treatments prior to tofacitinib) and disease characteristics at tofacitinib initiation (including HCP-reported disease severity).

Results: Of 1564 pts (US n=436; EU5 n=1128, respectively) sampled by 391 HCPs, the majority were White (75%; 91%), female (both 52%) and 45–64 years of age (53%; 57%). At time of chart review, US pts had received tofacitinib for median (interquartile range [IQR]) 9 (7–11) mos, and EU5 pts for 7 (6–9) mos; 52% of US pts received 11 mg QD, and 84% of EU5 pts received 5 mg BID. Median (IQR) time from PsA diagnosis to tofacitinib initiation was 34 (12–68) mos for all pts with data available (n=1237), and was shorter for US (11 [3–33] mos) vs EU5 (40 [19–79] mos) pts. Most pts had received ≥1 prior targeted therapy (59%; biologic or targeted synthetic disease-modifying antirheumatic drugs) for median (IQR) 12 (7–22) mos. The most common HCP-reported reason for switching from prior targeted therapy was efficacy failure (US and EU5 both 59%); either initial failure (US 28%; EU5 13%) or long-term failure (US 34%; EU5 48%) (Figure 1A). Mechanism of action and mode of administration were the most common HCP-reported reasons for switching to tofacitinib in both the US and EU5 (Figure 1B). HCP-reported disease severity at tofacitinib initiation was higher in the EU5 than US (Figure 2).

Conclusion: Characteristics of pts treated with tofacitinib for PsA were generally similar in the US and EU5. However, time from PsA diagnosis to tofacitinib initiation was shorter in the US vs EU5. It was of clinical interest to note that switching to tofacitinib appeared to be more commonly influenced by mechanism of action and mode of administration vs pt preference and access, as reported by HCPs. A key limitation of this study was the retrospective chart review design, which may introduce recall bias.

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[1] Mease et al. NEJM 2017;377:1537-50.

[2] Gladman et al. NEJM 2017;377:1525-36.

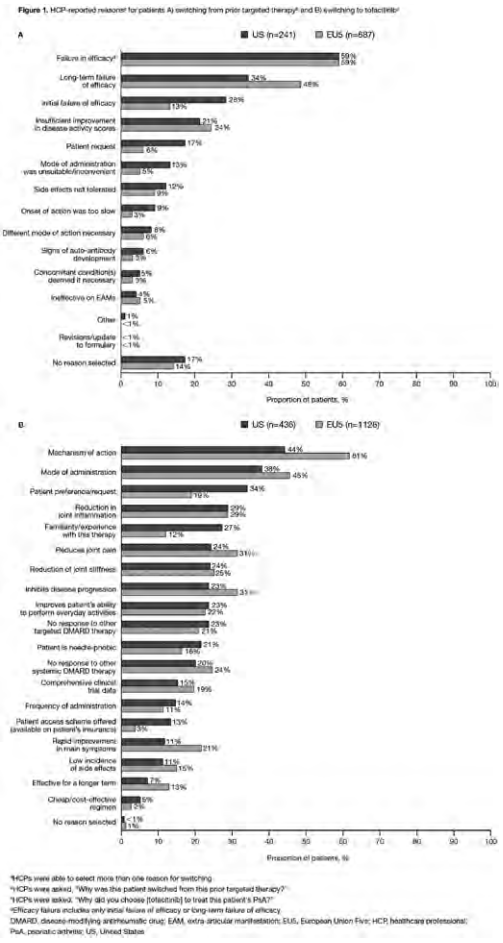
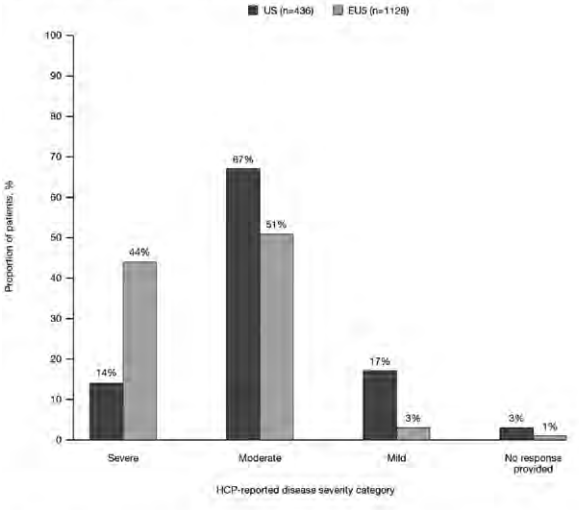


Figure 1. HCP-reported reasons[a] for patients A) switching from prior targeted therapy[b] and B) switching to tofacitinib[c]

[a]HCPs were able to select more than one reason for switching.
[b]HCPs were asked, "Why was this patient switched from this prior targeted therapy?"
[c]HCPs were asked, "Why did you choose [tofacitinib] to treat this patient's PsA?"
[d]Efficacy failure includes only initial failure of efficacy or long-term failure of efficacy.
DMARD, disease-modifying antirheumatic drug; EAM, extra-articular manifestation; EU5, European Union Five; HCP, healthcare professional; PsA, psoriatic arthritis; US, United States

Figure 2. Proportion of patients with PsA categorised within each HCP-reported disease severity category[a]



[a]HCPs were asked to assess the patient's disease severity at tofacitinib initiation and were given the options of "Severe", "Moderate", and "Mild"
EU5, European Union Five; HCP, healthcare professional; PsA, psoriatic arthritis; US, United States

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AB0812 IS THE VISCERAL ADIPOSITY INDEX ASSOCIATED WITH THE PRESENCE OF CARDIOVASCULAR RISK SCORES AND COMORBIDITY IN PSORIATIC DISEASE?

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Background: Psoriatic disease (PsD) is a chronic immune-mediated inflammatory disorder and predominantly involves the skin and joints. There is a better known relationship between the severity of PsD with some comorbidities such as metabolic syndrome, cardiovascular disease and obesity. Visceral Adiposity Index (VAI) has been shown to be an important marker, gender- dependent for insulin resistance, adipose tissue function and distribution.
Objectives: The aim of this study was to evaluate the relationship between the VAI and cardiovascular risk scores of patients with psoriatic arthritis.
Methods: This study was conducted with 101 PsD patients who fulfilled the classification criteria for Psoriatic Arthritis (CASPAR) criteria and 98 healthy subjects. Demographic and clinical data were recorded. Disease activity was evaluated with the Health Assessment Questionnaire (HAQ), Disease Activity Index for Psoriatic Arthritis (DAPSA), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Disease Activity Index (BASFI) and Psoriasis Area Severity Index (PASI). The SCORE, Framingham index, metabolic syndrome (MetS), Body mass index (BMI) and VAI values of the patients and the VAI values of the healthy subjects were calculated.
Results: Mean BMI (kg/m^2) was calculated as 29.63 5.66. According to the SCORE measurements, 53 (52.5%) patients were at low risk, 45 (44.6 %) at moderate risk, and 3 (3 %) at high risk. No patients were at very high risk. According to the Framingham score, 72 patients (71.3%) were at low risk, 22 patients (21.8%) at intermediate risk and 7 patients (6.9%) at high risk. The risk was found to be statistically significantly higher in the PsD group compared to the healthy control group in respect of metabolic syndrome, obesity (BMI >30) and VAI levels (p<0.05). Significantly higher VAI levels were determined in PsD patients with metabolic syndrome, BMI> 30 (obesity), diabetes mellitus and hypertension compared to without these comorbidities (p<0.05). A statistically significant correlation was determined between low and moderate risk Framingham score, and the VAI levels of PsD patients. Correlations were determined between disease activity and metabolic and cardiovascular risks of patients. A weak correlation was observed between VAI levels and the Framingham score (Table).

Table. Correlations (r) between disease activity and metabolic and cardiovascular risks of patients

Parameters	BASDAI	PASI	DAPSA	BASFI	HAQ	VAI	SCORE	Framingham risk score
Framingham risk score	0.02	0.095	**0.285****	**0.202****	0.067	**0.299****	0.523	1
SCORE	-0.079	-0.026	0.095	0.065	-0.01	0.058	1	**0.523****
VAI	0.128	0.192	0.101	0.105	0.019	1	0.058	**0.299****
HAQ	0.129	0.135	**0.421****	**0.284****	1	0.019	-0.01	0.067
BASFI	**0.764****	0.14	**0.484****	1	**0.284****	0.105	0.065	**0.202***
DAPSA	**0.462****	**0.341****	1	**0.484****	**0.421****	0.101	0.095	**0.285****
PASI	0.092	1	**0.341****	0.140	0.135	0.192	-0.026	0.095
BASDAI	1	0.092	**0.462****	**0.764****	0.129	0.128	-0.079	0.024

Abbreviation; VAI: Visceral Adiposity Index, SCORE: Systematic Coronary Risk Evaluation Index, Health Assessment Questionnaire (HAQ), Disease Activity Index for Psoriatic Arthritis (DAPSA), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Disease Activity Index (BASFI) and Psoriasis Area Severity Index (PASI). ***p<0.05, **p<0.001**

Conclusion: Patients with psoriasis are more susceptible to obesity and other diseases such as metabolic syndrome, dyslipidemia, cardiovascular diseases, insulin resistance and diabetes. Therefore, control of bodyweight in PsD patients is important for management of the disease. Since VAI can be calculated simply from routinely taken measurements, the VAI level can be used to determine cardiovascular risk and VAI may also provide clues about comorbidities in patients with newly diagnosed PsD.
Disclosure of Interests: None declared
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AB0813 GUSELKUMAB-TREATED PATIENTS ACHIEVED CLINICALLY MEANINGFUL IMPROVEMENT IN SYSTEMIC SYMPTOMS AS MEASURED WITH PROMIS INSTRUMENT: RESULTS FROM PHASE-3 PSORIATIC ARTHRITIS TRIAL DISCOVER 1

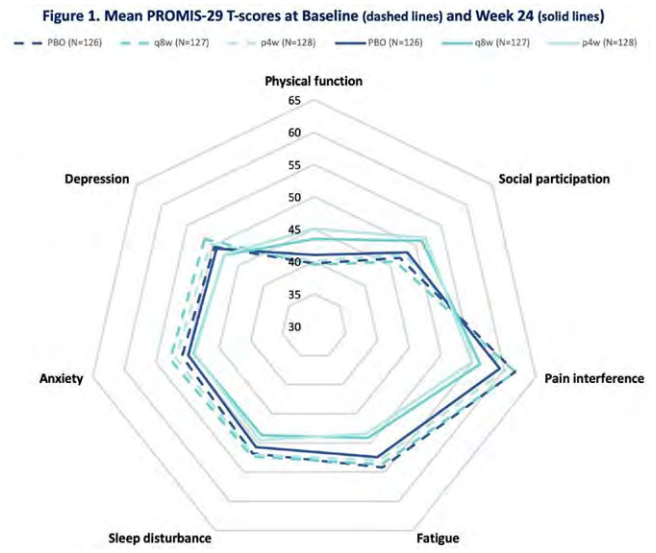
A. M. Orbai[1], L. C. Coates[2], A. Deodhar[3], P. Helliwell[4], C. T. Ritchlin[5], A. Kollmeier[6], E. C. Hsia[6,7], X. L. Xu[6], S. Sheng[6], B. Zhou[6], C. Han[6]. *[1]Johns Hopkins Univ School of Med, Baltimore, United States of America; [2]Oxford Univ, Oxford, United Kingdom; [3]Oregon Health & Science U, Portland, United States of America; [4]U of Leeds, Leeds, United Kingdom; [5]U Rochester Med Ctr, Rochester, United States of America; [6]Janssen Research & Development, LLC, Spring House, United States of America; [7]U Penn Med Ctr, Philadelphia, United States of America*

Background: Patients (pts) with psoriatic arthritis (PsA) experience broad systemic symptoms including pain, fatigue, depression, sleep disturbance, poor physical function, and diminished social participation.
Objectives: DISCOVER 1 is a Phase 3 trial (NCT03162796) evaluating the efficacy and safety of guselkumab (GUS), an anti-interleukin 23 inhibitor that binds to the p19-subunit of IL-23, in pts with active PsA. PROMIS-29 (Patient-Reported Outcomes Measurement Information System-29), a validated generic health instrument,[1] assessed the treatment effect of GUS on symptoms in pts with PsA.
Methods: Pts with active PsA despite nonbiologic DMARDs were enrolled, and ~30% of pts could have previously received ≤2 TNFi. Pts were randomized (1:1:1) to subcutaneous GUS 100 mg at Week 0 (W0), W4 then q8W (n=127), GUS 100 mg q4W (n=128), or PBO (n=126). Concomitant stable use of select csDMARDs, oral steroids, and NSAIDs was allowed. PROMIS-29 consists of 7 domains (Depression, Anxiety, Physical Function, Pain Interference, Fatigue, Sleep Disturbance, and Social Participation) and a pain intensity 0-10 numeric rating scale (NRS). The raw score of each domain is converted into a standardized T-score with a mean of 50 (general population mean) and a standard deviation (SD) of 10. Higher PROMIS scores represent more of the concept being measured. A >= 5-point improvement (1/2 SD of T-score) is defined as clinically meaningful.[1]
Results: At baseline, mean PROMIS-29 T-scores for physical function, social participation, sleep disturbance, pain, and fatigue were worse than the general US population. At W24, GUS q8W-treated pts achieved greater improvements from baseline in all PROMIS-29 domains vs PBO (p<0.05) (Table and Fig 1). Results were consistent in the GUS q4W group except for anxiety and sleep disturbance. More pts receiving GUS achieved clinically meaningful improvement vs PBO except for depression and anxiety in the GUS q4W group, which were numerically improved (Fig 2).
Conclusion: Active PsA pts treated with GUS achieved clinically meaningful reduction in symptoms and improvement in physical function and social participation vs PBO at W24.
References:
[1] http://www.healthmeasures.net/score-and-interpret/interpret-scores/meaningful-change/165-meaningful-change

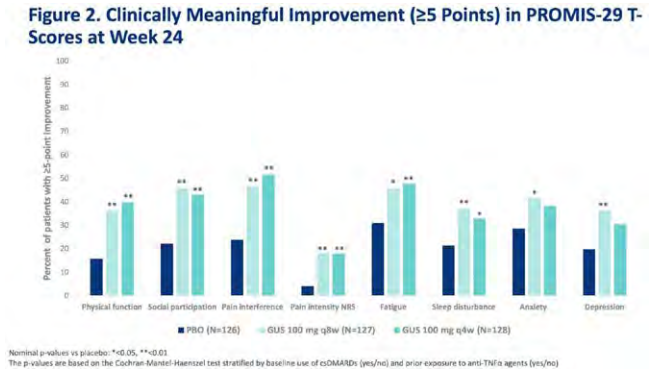
Table. PROMIS-29 Domain T-Scores Least Square (LS) Mean Change from Baseline

	LS Mean Change from Baseline		
	PBO	GUS q8W	GUS q4W
Anxiety	-1.37	-3.23*	-2.92
Depression	-0.85	-3.4**	-2.67*
Fatigue	-1.86	-4.79**	-5.08**
Pain interference	-2.30	-5.49**	-5.69**
Physical function	1.34	3.89**	5.05**
Sleep disturbance	-1.17	-3.48**	-2.46
Social participation	1.45	4.90**	4.52**
Pain intensity	-0.56	-1.98**	-2.32**

Nominal p-values vs placebo: *<0.05, **<0.01



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DOI: 10.1136/annrheumdis-2020-eular.2929

AB0814

SUSTAINED IMPROVEMENTS IN PHYSICAL FUNCTION, QUALITY OF LIFE, AND WORK PRODUCTIVITY WITH IXEKIZUMAB IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS AND PREVIOUS INADEQUATE RESPONSE TO TUMOUR NECROSIS FACTOR-INHIBITORS: 3-YEAR RESULTS FROM SPIRIT-P2 TRIAL

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Background: Ixekizumab (IXE), a high-affinity monoclonal antibody that selectively targets IL-17A, has shown improvements compared to placebo (PBO) not only in disease activity but also in various patient-reported outcomes (PROs) assessing physical function, quality of life (QoL), and work productivity in PsA patients treated for 24 weeks and sustained up to 52 weeks.[1, 2]

Objectives: To report the effects of treatment with IXE on these PROs after up to 3 years of treatment.

Methods: In SPIRIT-P2 (NCT02349295), a Phase 3 trial, 363 adult patients with active PsA and prior inadequate response or intolerance to 1 or 2 TNF inhibitors (TNFis) were randomized 1:1:1 to IXE 80 mg every 4 weeks (IXEQ4W; N=122) or every 2 weeks (IXEQ2W; N=123), or PBO (N=118) in the double-blind treatment period (Weeks 0-24). Both IXE regimens had a starting dose of 160 mg. Results are reported from a subset of the intent-to-treat population who were randomized to IXE at baseline (Week 0). The following PROs were assessed during Weeks 0-156: HAQ-DI (minimally clinically important difference [MCID] an improvement ≥0.35), medical outcomes survey Short Form-36 (SF-36) Physical and Mental Component Summary (PCS and MCS), European Quality of Life 5 Dimensions Visual Analog Scale (EQ-5D VAS), and Work Productivity and Activity Impairment Questionnaire-Specific Health Problem (WPAI-SHP; absenteeism, presenteeism, work productivity, and activity impairment). Missing values were imputed by observed analysis and modified baseline observation carried forward (mBOCF) for continuous data or by modified non-responder imputation (mNRI) for categorical data.

Results: Mean baseline scores for SF-36 (PCS and MCS), EQ-5D VAS, and WPAI-SHP (Figure 1) and HAQ-DI (mean [SD]: IXEQ4W=1.2 [0.6]; IXEQ2W=1.2 [0.6]), indicated impaired physical function and QoL. The percentage of patients of who completed 156 weeks of the study in IXEQ4W and IXEQ2W arms were 57.4% (n=70) and 44.7% (n=55), respectively. Patients receiving IXE treatment up to 3 years reported sustained improvements in SF-36 (PCS and MCS), EQ-5D VAS, and WPAI-SHP (presenteeism, work productivity, and activity impairment) (Figure 1). Observed HAQ-DI mean change from baseline in IXEQ4W: -0.46 (0.62) and IXEQ2W: -0.48 (0.55). The percentage of IXE treated patients achieving MCID for HAQ-DI (improvement ≥0.35) was sustained at 3 years (Figure 2).

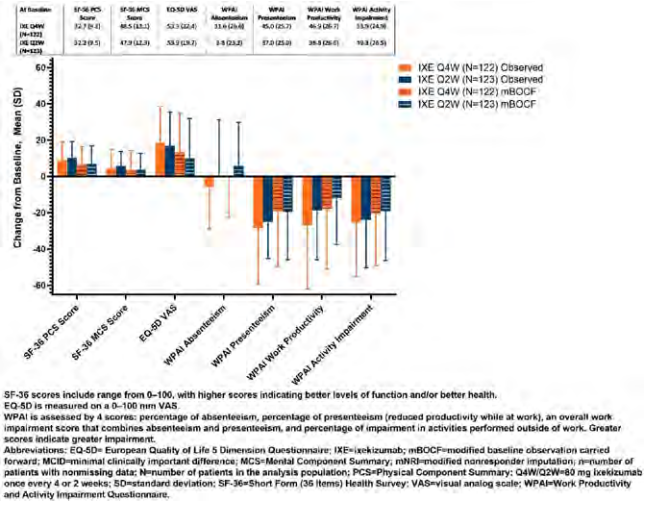


Figure 1. Summary of Patient-Reported Outcomes presented as change from baseline at Week 156 (Observed and mBOCF): Intent-to-Treat Population (Patients Randomized to IXE at Baseline)

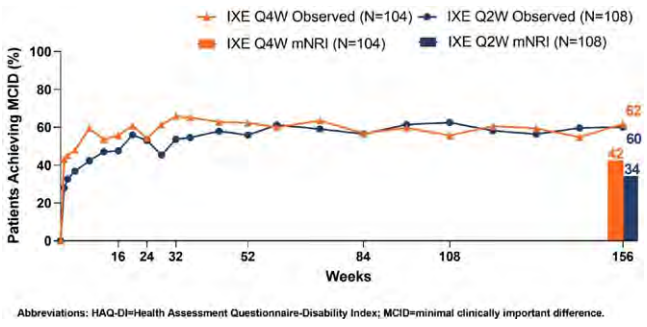


Figure 2. Patients achieving HAQ-DI MCID Response up to Week 156 (Observed) and at Week 156 (mNRI) among patients with HAQ-DI≥0.35 at baseline: Intent-to-Treat Population (Patients Randomized to IXE at Baseline)

Conclusion: Improvements in PROs, measuring physical and mental function, quality of life, and work productivity are maintained up to 3 years with IXE treatment in patients with active PsA who have had an inadequate response or intolerance to 1 or 2 TNFis.

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AB0815 CHANGES IN BODY COMPOSITION, BONE MINERAL DENSITY AND BONE REMODELING MARKERS DURING INTERLEUKIN 12/23 INHIBITION IN PSORIATIC ARTHRITIS

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory disease characterized by multiple comorbid conditions including cardiovascular comorbidities, diabetes, obesity and osteoporosis. Little is known about body composition in patients with PsA and no data are available regarding body composition changes under DMARDs.

Objectives: We investigated the effects of ustekinumab (UST), a humanized anti-interleukin 12/23 antibody, on body composition, bone mineral density (BMD) and bone remodeling markers in patients treated for PsA.

Methods: Thirty patients with active PsA treated with UST were included in a 6 months open follow-up study. Body mass index, DAS28-CRP, bone remodeling markers, serum levels of leptin, BMD and body composition (dual-energy X-ray absorptiometry) were measured at baseline and 6 months of treatment. At baseline, PsA patients were compared with 60 non-PsA controls matched for age, sex and body mass index.

Results: Compared with controls, we observed lower total and appendicular lean mass (53.1 ±13.1 vs. 56.7 ±11.9 kg, p=0.013 and 21.6 ±6.3 vs. 23.4 ±5.0 kg, p=0.010 respectively) and greater fat mass in PsA (32.5 ±10.8 vs. 25.2 ±8.9 kg, p<0.001). Among PsA patients, 30% had a skeletal muscle mass index below the cut-off point for sarcopenia (Baumgartner's criteria: men 7.26 kg/m2, women 5.5 kg/m2) whereas no case was observed in the control group. After 6 months of treatment with UST, there was not a significant change of BMI, while there was a tendency for reaching the significant level for fat mass (+1.75 ±3.60 kg, p=0.054), and fat mass index (+0.59 ±1.25 kg/m^2, p=0.061). In contrast, a decrease in total lean mass was observed (-1.57 ±3.10 kg, p=0.046) without a significant change in appendicular lean mass and skeletal muscle mass index. No changes for bone remodeling markers, leptin and BMD were observed at 6 months.

Conclusion: Patients with active PsA required biologic therapy had increased fat mass and decreased lean mass. Moreover, ustekinumab might worsen the decrease in lean mass with no significant change in fat mass.

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AB0816 CARDIOVASCULAR COMORBIDITIES IN PSORIATIC ARTHRITIS: A CASE CONTROL STUDY.

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Background: Psoriatic Arthritis (PsA) is an inflammatory arthritis associated with psoriasis. It occurs in approximately 8% –30% of patients diagnosed with psoriasis. In addition to joint and skin manifestations, patients with PsA have an increased prevalence of traditional cardiovascular (CV) risk factors that has been associated with a higher severity of PsA and increased cardiovascular disease (CVD). However, this increased risk has been attributed not only to increased traditional risk factors but also to chronic systemic inflammation.

Objectives: To compare the most relevant CV comorbidities in patients with PsA and controls.

Methods: A cross-sectional observational study was designed, 94 patients between 45-75 years who fulfilled the CASPAR classification criteria for PsA and 94 age-matched controls were included. The clinical characteristics compared between groups were: age, BMI, waist/hip index, gender, diabetes mellitus, hypertension, dyslipidemia, overweight, obesity, smoking history and prior cardiovascular event. Student-t test, Mann-Whitney U, Chi^2 test and Fisher's exact test were used to compare data and odds ratio were calculated. $p \leq 0.05$ was considered statistically significant. Logistic regression analysis was used to test association between significant clinical risk factors for PsA. The data were analyzed using the SPSS version 25 software.

Results: 94 PsA patients and 94 controls were included. The majority of the patients were women (57.4% in the PsA group and 80.9% in the control group) (p 0.001). Body mass index and waist/hip index were higher in PsA group (p 0.002) (p <0.001) respectively.

PsA patients had more hypertension than controls (p 0.022), more overweight (p 0.005), and a higher smoking history (p <0.001) than the control group. There was a trend in higher hyperlipidemia prevalence in PsA patients (Table 1).

Table 1. Clinical comorbidities and risk factors for PsA.

Variable	PsA	Control	*p*	OR (95% CI)
Age*	53.23 ± 11.31	53 ± 10	0.790	
BMI*	29.37 ± 5.32	27.21 ± 4.17	0.002	
Waist/Hip Index**	0.94 (0.88-1.03)	0.90 (0.85-0.92)	<0.001	
Gender			0.001	
Female	54 (57.4%)	76 (80.9%)		
Male	40 (42.6%)	18 (19.1%)		
Diabetes	18 (19.1%)	14 (14.9%)	0.438	1.35 (0.62-2.91)
Hypertension	33 (35.1%)	19 (20.2%)	0.022	2.13 (1.10-4.12)
Dyslipidemia	36 (38.3%)	24 (25.5%)	0.06	1.81 (0.97-3.37)
Overweight	77 (81.9%)	60 (63.8%)	0.005	2.56 (1.31-5.03)
Obesity	36 (37.6%)	26 (27.7%)	0.146	1.57 (0.85-2.92)
Smoking history	36 (38.3%)	78 (83%)	<0.001	0.127 (0.06-0.25)
History of CVD	68 (72.3%)	8 (53.3%)	0.137	2.28 (0.75-6.94)

*Data are reported in mean ± SD

**Data is reported in median (IQR)

We performed a multivariate analysis that showed that being overweight and presenting a waist / hip index above 0.90 cm confers an increased risk of developing PsA (Table 2).

Table 2. Multivariate analysis of significant clinical risk factors for PsA.

Variable	*p*	OR (95% CI)
Hypertension	0.239	1.69 (0.70-4.05)
Overweight	0.027	2.57 (1.11-5.92)
Waist/hip index >0.90	0.007	2.80 (1.32-5.95)

Conclusion: Several traditional cardiovascular risk factors were found with a higher prevalence in the group with psoriasis. It is critical that physicians known the common comorbidities associated with PsA so that they can provide optimal management and treatment and improve mortality and quality of life.

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AB0817 DOES SMOKING AFFECT SECUKINUMAB TREATMENT OUTCOMES AND SAFETY IN PATIENTS WITH PSORIATIC ARTHRITIS? - REAL WORLD DATA FROM THE GERMAN AQUILA STUDY

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Background: Several studies have shown a negative association between smoking status and psoriatic arthritis (PsA) clinical outcomes.[1,2] The German non-interventional study AQUILA provides real-world data on the influence of smoking on therapeutic effectiveness and safety issues under secukinumab (SEC), a fully human monoclonal antibody that selectively inhibits interleukin-17A.

Objectives: The aim of this interim analysis is to describe selected baseline (BL) demographics, to evaluate SEC effectiveness on disease activity and depressive mood and to report the safety profile depending on smoking status of PsA patients.

Methods: AQUILA is an ongoing, multi-center study including up to 2700 patients with active PsA or ankylosing spondylitis. Patients were observed from BL up to week (w) 52. Real-world data was assessed prospectively and analyzed as observed. In addition to the assessment of C-reactive protein (CRP), data was collected on patient´s disease activity (tender/swollen joint counts, TJC/SJC), skin disease activity (Psoriasis Area and Severity Index, PASI) and depressive mood (Beck´s Depression Inventory version II, BDI-II). For calculation of the proportion of patients who experienced (serious) adverse events ((S)AEs), all PsA patients were included who received at least one dose of SEC irrespective of further documentation of any study visit. This interim analysis focuses on subgroups non-smoker (NS) and smoker (S).

Results: At BL, 641 PsA patients were included: 49.8% (n=319) non-smokers (NS) and 24.3% (n=156) smokers (S). 17.5% (n=112) were ex-smoker and 8.4% (n=54) of unknown smoking status. In both, NS and S, the proportion of women was higher (58.0% in NS and 67.3% in S). NS were slightly older than S (mean age: 53.8/49.7 years). There were no significant differences between NS and S in mean CRP within the 52 weeks (Fig. 1A). Both TJC and SJC improved over time and were similar between NS and S (Fig. 1B). Although mean absolute PASI value was worse in S at BL, a similar temporal improvement was seen in both groups (NS: 7.0 at BL to 1.0 at w52; S: 9.2 at BL to 1.0 at w52). BDI-II scores decreased in both groups with overall higher values in S (NS: 10.9 at BL to 9.1 at w52; S: 12.8 at BL and 10.8 at w52). Regarding the occurrence of AEs and SAEs with or without suspected relationship to SEC, NS had percentagewise less events than S (Table 1). In addition, percentage of PsA patients who discontinued SEC treatment due to an AE was lower for NS compared to S.

Table 1. Overview of AEs (and SAEs) under SEC treatment depending on smoking status in PsA patients

Number of patients with	NS (N=333), n (%)	S (N=161), n (%)	P value
AE	233 (70.0)	118 (73.3)	0.11
AE with suspected relationship to SEC	129 (38.7)	72 (44.7)	0.10
SAE	74 (22.2)	45 (28.0)	0.06
SAE with suspected relationship to SEC	29 (8.7)	18 (11.2)	0.37

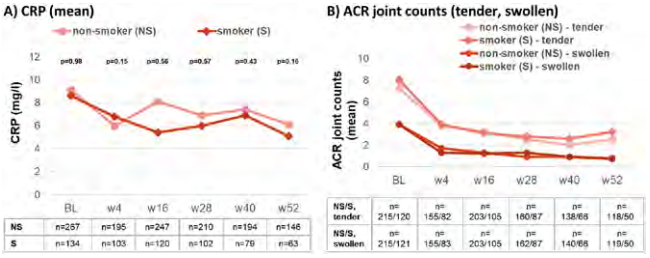


Figure 1. Disease activity in PsA patients treated with SEC depending on the smoking status* CRP data/ACR joint counts were documented not for all PsA patients at BL and subsequent visits.

Conclusion: In a real-world setting, SEC improved disease activity and depressive mood of PsA patients with no obvious differences between NS and S. Overall, this interim analysis shows that SEC is an effective and reliable treatment, irrespective of the PsA patients' smoking status. Further progress of the AQUILA study as well as long-term data from other real-world observational studies with SEC, such as SERENA, will reveal whether this trend will continue.

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AB0818 SKIN INVOLVEMENT IN PSORIATIC ARTHRITIS (PSA) - THE INCREMENTAL IMPACT OF PSORIASIS ON QUALITY OF LIFE, DISABILITY AND WORK PRODUCTIVITY: REAL-WORLD SURVEY IN US AND EUROPE

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Background: PsA involves joint and skin symptom presentation that varies across patients. Differences in patients outcomes with joint only, and joint and skin involvement have not been extensively studied in a real-world setting.

Objectives: To assess prevalence of joint only, and joint and skin disease in a real-world clinical setting, and to assess incremental impact of skin symptoms on quality of life (QoL), disability and work productivity.

Methods: A cross-sectional survey in patients with PsA recruited by rheumatologists and dermatologists was conducted in France, Germany, Italy, Spain, UK and US. Data were collected Jun-Aug 2018 via physician-completed patient record forms and patient self-completed forms. Patients were compared by joint and skin involvement using parametric and non-parametric tests. Multiple linear regression analyses examined impact of incremental body surface area (BSA) on patient reported outcomes (PROs). Models controlled for gender, age, time

since diagnosis, employment status, biologic DMARD use, BMI, number of joints affected.

Results: Of 1,909 patients (539 US, 1,370 EU), 35% of patients had joint only disease, while 26%, 23%, and 16% experienced joint disease plus 1-3%, >3-10%, and >10% BSA respectively (Figure 1). Patients were comparable demographically (Table 1). After controlling for demographics and number of joints involved, results showed BSA independently and significantly impacted QoL, work productivity, disability (Table 2).

Table 1. Comparison of patient demographic and disease characteristics by joint and skin disease involvement

	Joints only (n=673)	1-3% (n=493)	>3-10% (n=447)	>10% (n=296)	p-value
Age, mean (SD)	49.2 (13.7)	49.2 (13.2)	47.6 (12.4)	47.6 (13.8)	0.09
Male, n (%)	379 (56.3)	260 (52.7)	248 (55.5)	155 (52.4)	0.53
BMI, mean (SD)	26.9 (4.9)	26.8 (4.6)	26.7 (4.2)	26.5 (4.7)	0.52
Caucasian, n (%)	621 (92.3)	442 (89.7)	399 (89.3)	270 (91.2)	0.41
Full-time employment, n (%)	391 (60.9)	275 (57.7)	259 (59.1)	153 (53.1)	0.01
Biologic tx, n (%)	420 (62.4)	283 (57.4)	218 (48.8)	141 (47.6)	<0.01
Months since diagnosis, mean (SD)	68.4 (76.2)	56.7 (68.2)	54.2 (67.3)	52.1 (75.1)	<0.01
Current BSA %, mean (SD)	0.0	1.7 (0.8)	6.3 (2.0)	21.3 (10.1)	<0.01
*66 swollen joint count, mean (SD)	1.5 (3.6)	2.1 (4.2)	7.1 (11.1)	6.9 (10.5)	<0.01
*68 tender joint count, mean (SD)	2.1 (4.1)	3.7 (6.4)	6.0 (7.7)	9.8 (10.0)	<0.01

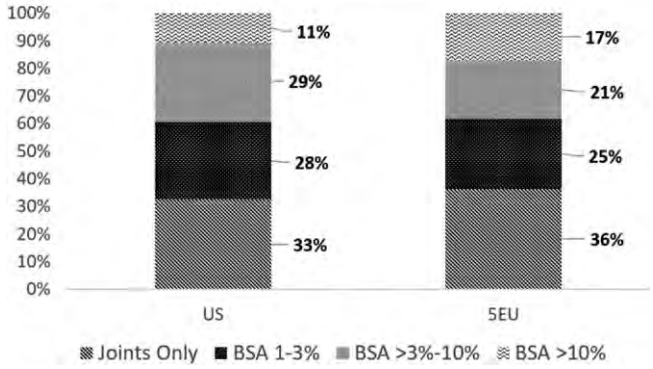
*Calculated on available data, n=394

Table 2. Incremental impact of BSA on PROs

	BSA in addition to joint involvement	Change in predicted PRO values	P value
EQ5D utility (n=656)	Joint only (ref)	0.85	
	1-3%	-0.02	0.31
	>3-10%	-0.06	<0.01
	>10%	-0.06	<0.01
EQ5D VAS (n=668)	Joint only	78.14	0.74
	1-3%	-0.58	0.03
	>3-10%	-3.78	0.14
	>10%	-3.04	
WPAI % overall work impairment (n=369)	Joint only	15.88	0.91
	1-3%	+0.32	<0.05
	>3-10%	+5.11	0.01
	>10%	+7.51	
HAQ-DI (n=635)	Joint only	0.32	0.41
	1-3%	+0.04	<0.01
	>3-10%	+0.22	<0.01
	>10%	+0.27	
PsAID12 (n=642)	Joint only	1.66	0.03
	1-3%	+0.42	<0.01
	>3-10%	+1.22	<0.01
	>10%	+1.37	

α PRO key for worse outcome (range): EQ5D utility (0-1.0) = lower; EQ5D VAS (1-100) = lower; WPAI (0-100) = higher; HAQ-DI (0-3) = higher; PsAID12 (0-10) = higher

Figure 1: Prevalence of joint and skin involvement across regions



Conclusion: Two thirds of this sample of actively treated PsA patients have skin involvement. Over half would be considered moderate-severe (BSA >3%). After controlling for joint symptoms, results show that increasing skin involvement in PsA patients adversely impacts QoL, disability and work productivity.

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AB0819 FLARES AMONG PATIENTS WITH PSORIATIC ARTHRITIS (PSA) - FREQUENCY AND IMPACT ON PATIENT OUTCOMES: REAL-WORLD SURVEY IN THE US AND EUROPE

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Background: Flares in PsA, presenting as periods of acute disease activity, are thought to negatively impact patients' lives. This has not been extensively studied in a real-world setting.

Objectives: Describe flares, assess impact on quality of life and work productivity, and explore predictors.

Methods: A cross-sectional survey among patients with PsA recruited by rheumatologists and dermatologists was conducted in France, Germany, Italy, Spain, UK and US. Data were collected Jun-Aug 2018 via patient record forms and patient self-complete forms. Physicians recorded flare status (in flare currently/flared in last 12 mo/longer than 12 mo or never), demographics, physician perceived severity and clinical outcomes. Patients reported quality of life [QoL] (EQ5D-5L), work productivity (WPAI), disability (HAQ-DI), pain (PsAID12 pain scale). Patients were compared by flare status using parametric or non-parametric tests. Logistic regression explored predictors of flare. Multivariate regression explored the impact of flare status on patient reported outcomes (PRO). The model was adjusted for gender, age, BMI, physician speciality.

Results: Data were collected for 2,238 patients (586 US, 1,652 EU). Mean age was 48.7 years (13.2 SD), 53.8% were male. Physicians reported 7.5% were currently in flare and 22.0% had flared in the last 12 mo. Patients had experienced 2.2 mean flares in the last 12 mo (4.9 SD), lasting a mean 16.4 days (16.2 SD). Patients in flare were comparable demographically with those not; however, those in flare were less likely to work full time (43.6 vs. 59.3%, p<0.01). Patients not in flare had clinically active disease (Table 1).

Table 1. Clinical characteristics of patients by flare status

	Currently in flare (n=168)	Flared in last 12 mo (n=492)	Not flared in last 12 mo/never flared (n=1578)	p-value
In remission, n (%)	4 (2.4)	157 (33.2)	799 (53.5)	<0.01
*Current BSA affected, mean (SD)	10.3 (12.0)	6.5 (7.6)	5.0 (7.7)	<0.01
*66 SJC, mean (SD)	5.4 (4.6)	4.5 (7.3)	2.4 (6.9)	<0.01
*68 TJC, mean (SD)	7.8 (5.8)	5.5 (8.3)	3.1 (5.6)	<0.01
Physician-perceived severity, n (%)				
Mild	35 (20.8)	346 (70.3)	1297 (82.2)	<0.01
Moderate	101 (60.1)	139 (28.3)	261 (16.5)	
Severe	32 (19.0)	7 (1.4)	20 (1.3)	

*Calculated on available data: Total base sizes: BSA=1665; SJC=514; TJC=493; Satisfaction=931

Results showed that flare status significantly impacted QoL, work productivity, disability, and pain (Table 2). Exploring predictors of flare in the last 12 mo in un-adjusted analyses showed that demographic characteristics were not predictive of flare status, however patients presenting as moderate or severe at diagnosis were at greater risk of flare. Patients who were prescribed a bDMARD at diagnosis were at lower risk (Figure 1).

Table 2. Impact of flare status on PROs

	Current flare status	Change in predicted PRO values	P value
EQ5D utility (n=933)	Not in flare (ref) In flare	0.83 -0.23	<0.01
EQ5D VAS (n=946)	Not in flare In flare	76.1 -21.3	<0.01
WPAI % overall work impairment (n=496)	Not in flare In flare	20.1 +28.5	<0.01
HAQ-DI (n=901)	Not in flare In flare	0.4 +0.6	<0.01
PsAID12 pain score (n=922)	Not in flare In flare	2.5 +3.0	<0.01

PRO key for worse outcome (range): EQ5D utility (0-1.0) = lower; EQ5D VAS (1-100) = lower; WPAI (0-100) = higher; HAQ-DI (0-3) = higher; PsAID12 pain (0-10) = higher

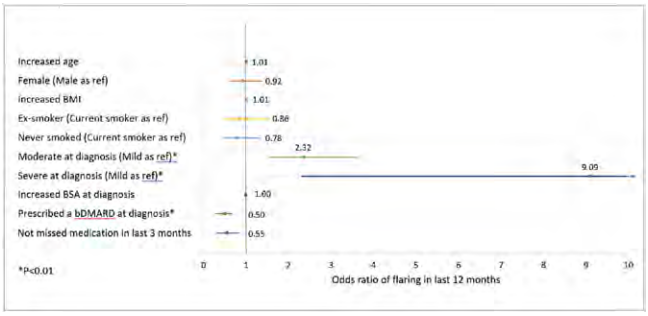


Figure 1. Predictors of flaring in last 12 months

Conclusion: One third of patients surveyed were either currently in flare or had flared in the last 12 mo. Being in flare adversely impacted QoL, disability and work productivity. Flare may be predicted by overall physician-reported PsA disease severity at diagnosis.

Disclosure of Interests: Ana-Maria Orbai Grant/research support from: Abbvie, Eli Lilly and Company, Celgene, Novartis, Janssen, Horizon, Consultant of: Eli Lilly; Janssen; Novartis; Pfizer; UCB. Ana-Maria Orbai was a private consultant or advisor for Sun Pharmaceutical Industries, Inc, not in her capacity as a Johns Hopkins faculty member and was not compensated for this service., William Tillett Grant/research support from: AbbVie, Celgene, Eli Lilly, Janssen, Novartis, Pfizer Inc, UCB, Consultant of: AbbVie, Amgen, Celgene, Lilly, Janssen, Novartis, MSD, Pfizer Inc, UCB, Speakers bureau: AbbVie, Amgen, Celgene, Lilly, Janssen, Novartis, Pfizer Inc, UCB, Suzanne Grieb Grant/research support from: Janssen, Steve Peterson Employee of: Janssen Research & Development, LLC, Elizabeth Holdsworth Employee of: Adelphi Real World, Sophie Meakin Employee of: Adelphi Real World, Sara Bruce Wirta Employee of: Janssen-Cilag Sweden AB, Soumya D Chakravarty Shareholder of: Johnson & Johnson, Employee of: Janssen Scientific Affairs, LLC, Laure Gossec Grant/research support from: Lilly, Mylan, Pfizer, Sandoz, Consultant of: AbbVie, Amgen, Biogen, Celgene, Janssen, Lilly, Novartis, Pfizer, Sandoz, Sanofi-Aventis, UCB

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AB0820

COMPARATIVE EFFICACY OF GUSELKUMAB IN PATIENTS WITH PSORIATIC ARTHRITIS: RESULTS FROM SYSTEMATIC LITERATURE REVIEW AND NETWORK META-ANALYSIS

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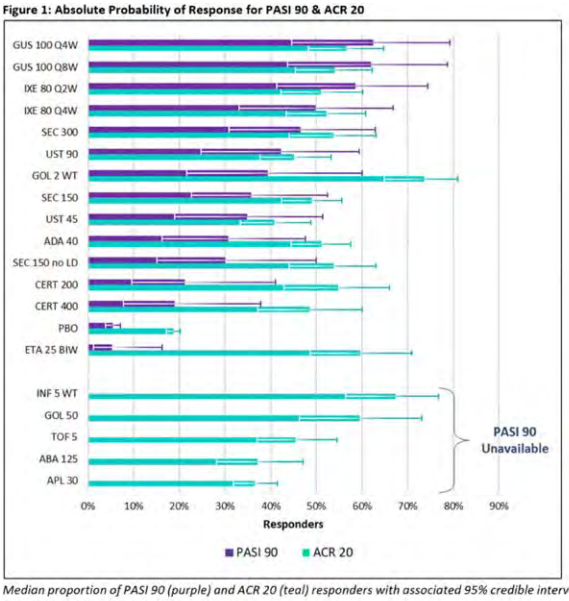
Background: The efficacy of the interleukin (IL)-23 subunit p19 inhibitor guselkumab (GUS) for psoriatic arthritis (PsA) has recently been demonstrated in two Phase 3 trials (DISCOVER-1 & -2) but has not been evaluated versus existing targeted therapies for PsA.

Objectives: To compare GUS to targeted therapies for PsA through network meta-analysis (NMA).

Methods: A systematic literature review was performed to identify PsA randomized controlled trials from 2000 to 2018. Bayesian NMAs were performed to compare treatments on American College of Rheumatology (ACR) 20/50/70 response, Psoriasis Area Severity Index (PASI) 75/90/100 response, Health Assessment Questionnaire Disability Index (HAQ-DI) score, resolution of enthesitis (RoE), resolution of dactylitis (RoD), adverse events (AEs) and serious adverse events (SAEs). Analyses used random effects models that adjusted for placebo response via meta-regression on baseline risk when feasible. Results are summarized by ranking treatments according to median absolute probabilities of response derived from NMAs.

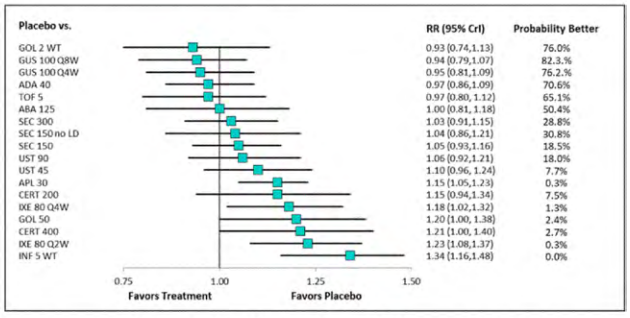
Results: Twenty-six Phase 3 studies were included in the quantitative synthesis. Studies were placebo-controlled up to 24 weeks and evaluated 13 targeted therapies for PsA. Absolute probabilities are reported for PASI 90 & ACR 20 responses according to *Figure 1,* and a forest plot of relative risks versus placebo for AEs is reported according to *Figure 2*. For ACR 20 response, GUS 100 mg every 4 weeks (Q4W) and every 8 weeks (Q8W) ranked 5th and 8th out of 20 interventions and were comparable to IL-17A inhibitor (IL-17Ai) and most tumor necrosis factor inhibitor (TNFi) agents. Similar findings were observed for ACR 50 and 70 responses. For PASI 90 response, GUS Q4W and Q8W ranked 1st and 2nd out of 15 interventions and were highly likely to provide a greater benefit than most other agents. Similar findings were observed for PASI 75 and 100 responses. For HAQ-DI score, GUS Q4W and Q8W ranked 6th and 10th out of 20 interventions and were comparable to IL-17Ai and most TNFi agents. For RoE, GUS Q4W and Q8W ranked 8th and 6th out of 13 interventions and were comparable to IL-17Ai and TNFi agents. For RoD, GUS Q4W and Q8W ranked 8th and 9th out of 13 interventions and were comparable to most IL-17Ai and TNFi agents. For AEs, GUS Q4W and Q8W ranked 3rd and 2nd out of 19 interventions and were comparable to IL-17Ai and TNFi agents. Likewise, for SAEs, GUS Q4W and Q8W ranked 4th and 5th out of 20 interventions and were comparable to IL-17Ai and TNFi agents. Analyses that controlled for previous exposure to biologics or assessed outcomes at alternative timepoints were broadly consistent with primary analysis results.

Figure 1: Absolute Probability of Response for PASI 90 & ACR 20



Median proportion of PASI 90 (purple) and ACR 20 (teal) responders with associated 95% credible intervals according to best-fitting NMAs.

Figure 2: Forest Plot of Adverse Events vs. Placebo



Forest plot comparing relative risks (RR) and 95% credible interval (CrI) versus placebo for adverse events. Probability better than placebo shown on the right.

Conclusion: NMA results indicate that GUS is comparable to most targeted PsA treatments for improvement in arthritis, soft tissue damage, physical function, and safety outcomes. For PASI outcomes, GUS is highly likely to provide a greater benefit than other targeted PsA treatments.

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AB0821 ANXIETY AND DEPRESSION IN PSORIATIC ARTHRITIS (PSA) - PREVALENCE AND IMPACT ON PATIENT REPORTED OUTCOMES: REAL-WORLD SURVEY IN THE US AND EUROPE

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Background: Anxiety and depression are comorbidities among PsA patients. The impact of anxiety and depression on outcomes in PsA patients has not been characterized in a real-world clinical setting.
Objectives: To describe the prevalence of anxiety and/or depression in PsA patients, assess concordance in reported anxiety and/or depression between patients and physicians, and compare clinical and patient reported outcomes (PROs) in patients who do and do not report anxiety and/or depression.
Methods: A cross-sectional study of patients with PsA recruited by rheumatologists and dermatologists was conducted in France, Germany, Italy, Spain, UK and US. Data were collected Jun-Aug 2018 via physician-completed and patient self-completed forms. Physicians reported patient demographic, disease characteristics and diagnosed anxiety and/or depression. Patients reported experience of PsA-related anxiety/depression, quality of life [QoL] (EQ5D-5L), work productivity (WPAI), disability (HAQ-DI), and disease impact (PsAID12). Patients were compared according to patient reported anxiety/depression using parametric and non-parametric tests. Multivariate regressions explored impact of anxiety/depression on PROs. Models adjusted for age, gender, employment status, BMI, # of joints affected, body surface area (BSA).

Table 1. Demographic and clinical characteristics by patient-reported anxiety and/or depression

	No anxiety and/or depression (n=436)	Anxiety and/or depression (n=252)	P value
Demographics			
Age, mean (SD)	47.7 (12.1)	49.1 (12.6)	0.13
Female, n (%)	196 (45.0)	146 (57.9)	<0.01
BMI, mean (SD)	26.7 (5.1)	26.9 (4.4)	0.57
Caucasian, n (%)	408 (93.3)	238 (94.4)	0.46
Working full time, n (%)	293 (68.6)	107 (44.8)	<0.01
Biologic tx, n (%)	257 (58.9)	160 (63.5)	0.26
Disease characteristics			
Days since diagnosis, mean (SD)	2090 (2204)	2532 (2813)	0.04
Current overall severity, n (%)			
Mild	277 (63.5)	137 (54.4)	0.02
Moderate	145 (33.3)	106 (42.1)	
Severe	14 (3.2)	9 (3.6)	
Current BSA %, mean (SD)	8.7 (12.3)	6.4 (8.2)	0.02
66 swollen joint count, mean (SD)	2.7 (3.6)	5.6 (10.4)	<0.01
68 tender joint count, mean (SD)	3.8 (4.3)	6.0 (6.2)	<0.01

Results: Data were collected from 688 physician-patient pairs (524 EU; 164 US). Physicians reported anxiety and/or depression in 14.2% of patients (EU 13.3%; US 16.2%), while 36.6% (EU 36.3%; US 37.8%) of patients self-reported anxiety and/or depression. 71.4% of physician-patient pairs agreed on anxiety and/or depression presence or absence (Kappa = 0.31, fair agreement). Patients with anxiety and/or depression had worse QoL more work impairment, greater disability (Table 2).

Table 2. Impact of anxiety or depression on PROs*

	Anxiety and/or depression	Change in predicted PRO value with anxiety and/or depression α	P value
EQ5D utility score, mean N=488	Without (ref) With	0.83 -0.10	<0.01
WPAI percentage overall work impairment, mean N=262	Without With	22.3 +7.4	<0.01
HAQ-DI score, mean N=480	Without With	0.53 +0.26	<0.01
PsAID12 score, mean N=482	Without With	2.32 +1.78	<0.01

* Adjusted for age, gender, employment status, BMI, # of joints affected and BSA
α PRO key for worse outcome (range): EQ5D utility (0-1.0) = lower; EQ5D VAS (1-100) = lower; WPAI (0-100) = higher; HAQ-DI (0-3) = higher; PsAID12 (0-10) = higher.

Conclusion: One third of patients self-report anxiety and/or depression. Treating physicians may not be aware of patient experience of anxiety and/or depression. Patients with anxiety and/or depression appear to have worse QoL, work productivity and disability outcomes than those without.
Disclosure of Interests: Laure Gossec Grant/research support from: Lilly, Mylan, Pfizer, Sandoz, Consultant of: AbbVie, Amgen, Biogen, Celgene, Janssen, Lilly, Novartis, Pfizer, Sandoz, Sanofi-Aventis, UCB, Jessica A. Walsh Grant/research support from: AbbVie, Pfizer, Janssen, Consultant of: AbbVie, Novartis, Eli Lilly and Company, UCB, Kaleb Michaud Grant/research support from: Janssen, Elizabeth Holdsworth Employee of: Adelphi Real World, Steve Peterson Employee of: Janssen Research & Development, LLC, Sophie Meakin Employee of: Adelphi Real World, Sara Bruce Wirta Employee of: Janssen-Cilag Sweden AB, Soumya D Chakravarty Shareholder of: Johnson & Johnson, Employee of: Janssen Scientific Affairs, LLC, Alexis Ogdie Grant/research support from: Pfizer to Penn, Novartis to Penn, Amgen to Forward/NDB, Consultant of: Abbvie, Amgen, Bristol-Myers Squibb, Celgene, Corrona, Janssen, Eli Lilly, Novartis, Pfizer
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AB0822 WHICH CLINICAL FACTORS INFLUENCE MINERALIZATION OF THE METACARPAL BONES AND FINGER JOINT SPACE WIDTH IN PSORIATIC ARTHRITIS?

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Background: Metacarpal bone mineral density as measured by digital x-ray radiogrammetry (DXR-BMD) and finger joint space width quantified by computer-aided joint space analysis presented computer based and observer independent parameters for the evaluation of radiographic damage of the hand skeleton.
Objectives: The aim of this study was to quantify clinical parameter which potential influence periarticular mineralisation of the metacarpal bones and finger joint space width in Psoriatic Arthritis (PsA)-patients.
Methods: The study includes 201 PsA-patients. All patients received a radiograph of the hand. Bone mineral density was measured by DXR (Pronosco X-Posure System™, Version 2.0; Sectra; Sweden) and finger joint space width of all finger joints were evaluated by computer-aided joint space analysis (CAJSA, Radiogrammetry Kit, Version 1.3.6; Sectra; Sweden). The Z-Score was used as an age- and gender-independent parameter for the quantification finger joint space narrowing.
Results: Regarding gender, the DXR-BMD was significant reduced with -0.028 g/cm^2 in women. An equivalent significant result was evaluated for finger joint space width (Z-ScoreMCP -1.07, Z-ScorePIP -0.81 and Z-ScoreDIP -0.76). The DXR-BMD was significantly lowert (-0.011 g/cm^2) between the disease duration < 2 years (0.545±0.076 g/cm^2) and >10 years (0.509±0.070 g/cm^2). The Z-Score showed no significant change regarding the disease duration. Inflammatory activity as measured by c-reactive protein presented no impact on DXR-BMD and the Z-Score of all finger joints. Additionally, the use of corticosteroids was associated with a reduced DXR-BMD (-0.037 g/cm^2) and an absence of finger joint space narrowing.
Conclusion: The study highlights that the demineralisation of the metacarpal bones was associated with female gender, disease duration and the use of corticosteroids. Whereas, the prior mentioned parameters had no influence on finger

joint space width. Consequently, periarticular demineralisation and finger joint space narrowing presented two different and independent radiological signs in PsA.

References: N/A

Disclosure of Interests: Alexander Pfeil Grant/research support from: This study Investigator Initiated Study "Automatic assessment of joint space narrowing in rheumatoid arthritis based on the Post-hoc analysis" (number: IIS-2016-110818) is a part of the of the Investigator Initiated Study "The quantification of inflammatory related periarticular bone loss in certolizumab pegol treated patients with rheumatoid arthritis" (number: IIS-2014-101458) which is supported by UCB Pharma GmbH, Monheim, Germany., Marcus Heinz: None declared, Diane Renz: None declared, Joachim Böttcher: None declared, Gunter Wolf: None declared, Peter Oelzner: None declared

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AB0823 MINIMAL DISEASE ACTIVITY IN PSORIATIC ARTHRITIS IS ASSOCIATED WITH LOW IMPACT OF DISEASE ON PSAID12 QUESTIONAIRE

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Background: Psoriatic arthritis (PsA) has a prevalence of 0.58% in Spain and patients suffer this disease have significant impact on daily life due to articular, dermatological and psychological symptoms. To reach minimal disease activity (MDA) is a therapeutic goal recommended by EULAR for clinical practice.

Objectives: Our aim was to assess the relationship between MDA and PsAID questionnaire in routine clinical practice.

Methods: We performed a cross-sectional study of patient and physician reported outcomes. We obtained clinical information of patients with PsA attending clinic from October 2018 to October 2019. Data were collected from clinical records concerning age, gender, disease duration, joint counts, dactylitis, enthesitis, body surface area (BSA) of psoriasis, laboratory results (ESR and CRP), HAQ, PsAID12, pain and global assessment from patient with numerical rating scale (NRS) and MDA status. Data were analysed using SPSS21. Logistic regression was used to assess patient reported outcomes which were associated with achieving MDA.

Results: Data were available for 210 patient visits, 57% males. MDA 5/7 was reached in 118 patients (56.2%) and MDA7/7 in 58 (27.6%). Age and gender were not associated with reach MDA. Higher disease duration was associated with MDA, OR 1.062 (1.012-1.114, 95% CI), p 0.015.

PsAID12 was evaluated in 156 patients and all components were associated with reach MDA. Patients in MDA had significantly lower PsAID12 than those were not in MDA (mean 1.5 ± SD 1.5 vs. 3.8 ± 2.1), p< 0.0001. PsAID12 of less than 4 is considered a good outcome and individual components of PsAID12 (Figure 1, mean values for NRS) were less than 4 in patients with MDA.

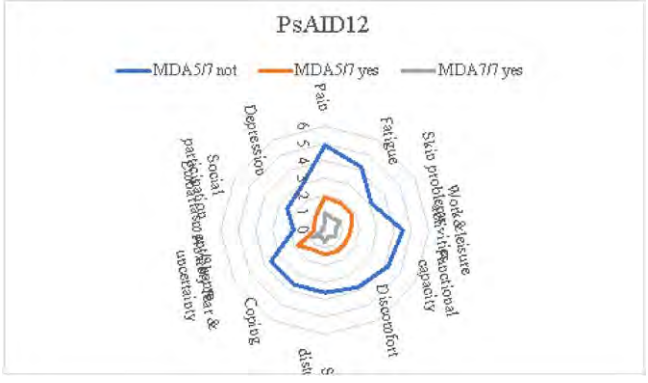


Figure 1.

All components of PsAID12 were associated with MDA on univariate analysis but only pain and functional capacity remained independent predictors on multiple regression analysis (p< 0.0001 and p0.008 respectively).

Percentage of BSA was associated with skin component of PsAID12 (p<0.0001) and with shame component (p0.001).

Conclusion: In these PsA patients, MDA was reached mainly in patients with higher disease duration. MDA is a relevant treatment target in PsA, with markedly lower PsAID12 in patients in MDA. Pain and functional discapacity are dominant symptoms in patients with psoriatic arthritis, even in those in MDA. Skin affection is associated with skin and shame components on the PsAID12.

References:

[1] Queiro R et al. Arthritis Res Ther. 2017 Mar 29;19(1):72.

Acknowledgments: SOGARE

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AB0824 WHICH PARAMETERS ARE RELEVANT IN THE IDENTIFYING AXIAL INVOLVEMENT IN PSORIATIC ARTHRITIS? – RESULTS OF A SURVEY AMONG ASAS AND GRAPPA MEMBERS

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Background: Inflammatory involvement of the axial skeleton (sacroiliac joints and / or spine) is one of the relatively frequent musculoskeletal manifestations associated with psoriasis / psoriatic arthritis (PsA). There is an urgent need for an evidence-based definition for axial involvement in PsA that would identify a subgroup of patients within the heterogeneous PsA population to conduct observational, interventional and translational studies. ASAS and GRAPPA embarked on a collaborative initiative to develop a definition of axial involvement in PsA.

Objectives: To perform a survey to identify variables relevant in the identification of the presence of axial involvement in PsA among members of ASAS and GRAPPA.

Methods: The online survey utilized the **PAPRIKA** methodology (***P**otentially **A**ll **P**airwise **R**an**K**ings of all possible **A**lternatives)* that determines decision-makers' part-worth utilities representing the relative importance of the attributes. Participants were exposed to number of clinical scenarios and were prompted to decide which of the scenarios is more compatible with axial involvement in PsA unless they are equal (**Figure**). The constant stem of each scenario was "a patient diagnosed with psoriatic arthritis fulfilling the CASPAR criteria"; the variable part included 13 common spondyloarthritis variables (**Table**). Variables were ranked according to their relative importance.

Results: The survey was completed by 186 ASAS/GRAPPA members (63 ASAS only, 80 GRAPPA only, and 43 both societies). The ranking of the variables is presented in **Table**. The highest ranked parameters indicative of axial involvement in a patient with PsA were presence of typical radiographic or MRI changes in the sacroiliac joints and/or spine followed by the presence of chronic back pain and then inflammatory back pain. A separate analysis of ASAS and GRAPPA members provided the similar results concerning the relevance of the variables.

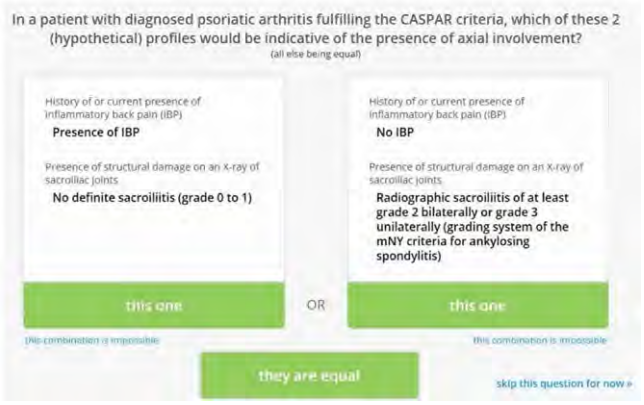
Conclusion: Objective signs of inflammatory involvement of the axial skeleton are the most important indicators of axial disease in PsA in the opinion of the experts. A prospective cohort study is currently being planned to address the value of these and other variables in defining axial involvement in PsA.

Table. Ranking of the parameters relevant to deciding on the presence of axial involvement in a PsA patient in the opinion of ASAS and GRAPPA members (n=186).

N	Parameters	Median rank	Mean rank
1	Presence of structural damage on an X-ray of SIJ	2	2.8
2	Presence of structural damage on an X-ray of spine	3.5	4.1
3	Presence of subchondral BME / osteitis on MRI of SIJ compatible with SpA	4	4.5
4	Presence of BME / osteitis on MRI of spine compatible with SpA	4	5
5	History or current presence of back pain	5.5	5.8
6	History of or current presence of inflammatory back pain	5.5	6
7	Good response of back pain to non-steroidal anti-inflammatory drugs	8	7.8
8	HLA-B27	8	8.1
9	Family history for SpA	9.5	9
10	Elevated C-reactive protein	10	9.3
11	Presence of peripheral arthritis and/or enthesitis and/or dactylitis	10	9.4
12	Presence of anterior uveitis	10	9.5
13	Presence of inflammatory bowel disease	10	9.6

BME=bone marrow edema, MRI=magnetic resonance imaging, SIJ=sacroiliac joints, SpA=spondyloarthritis

Figure. An example of a survey question with two clinical scenarios comparing two pairs of parameters to determine part-worth utilities of the parameters.



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AB0825 TIME-COURSE CHANGE IN AXIAL MOBILITY IN PSORIATIC ARTHRITIS PATIENTS UNDER BDMARD

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Background: Spinal mobility is assessed frequently in patients with psoriatic arthritis (PsA) using *Bath Ankylosing Spondylitis Metrology Index* (BASMI) to provide baseline measurement, monitor changes over time and to assess the impact of clinical interventions. BASMI comprises 4 measures of spinal mobility (cervical rotation, tragus-to-wall distance, modified Schober's test and lumbar lateral flexion) and one hip mobility measurement (intermalleolar distance).

Objectives: The aim of this study is to investigate the time-course change of BASMI in PsA patients after 6 months of *Biologic Disease-modifying Antirheumatic Drug* (bDMARD) therapy. The authors also pretend to evaluated, at baseline and after 6 months of treatment, the association between BASMI, disease activity scores and physical function.

Methods: An observational retrospective study was performed in patients with PsA under bDMARD followed in the Rheumatology department of a tertiary university hospital. Were included patients treated with only one bDMARD. Demographic and clinical data were collected from the Rheumatic Diseases Portuguese Register. For spinal mobility calculation BASMI was used. Disease activity was evaluated with *Ankylosing Spondylitis Disease Activity Score* (ASDAS) and *Bath Ankylosing Spondylitis Activity Index* (BASDAI). Physical function was assessed with *Bath Functional Index* (BASFI). The variation of BASMI, ASDAS, BASDAI and BASFI was calculated as the difference between values registered at 6 months and at baseline and presented as Δ. Correlations between ΔBASMI, ΔASDAS and ΔBASFI was calculated using Pearson test.

Results: A total of 55 patients were included. Thirty patients were males (54.5%). The mean age at diagnosis was 44.6 ± 12.6 years and the median disease duration at start of bDMARD was 5.4 years (min: 0.30; max: 25.5). In total, 19 (34.5%) patients had predominant axial involvement, 36 (65.5%) peripheric and 36 (65.5%) enthesopathic. Almost all patients fulfilled the CASPAR criteria for PsA (n=50, 90.9%). According to ASDAS criteria, at the baseline 20 patients (36.4%) had high disease activity and 34 (61,8%) very high. The most used bDMARD was etanercept (n=21, 38,3%) followed by golimumab (n=19, 34.5%) and adalimumab (n=8, 14.5%). Three patients were treated with infliximab, two with certolizumab and other two with secukinumab. Forty-one patients (75.9%) were concomitantly treated with conventional synthetic DMARDs. Axial PsA patients had more limitations in spinal mobility (BASMI mean 4.5 ± 1.5) and more functional limitation (BASFI mean 6.8±1.9) than patients with predominant peripheric involvement (BASMI mean 3.3± 1.2, p=0.004; BASFI mean 5.4±3, p=0,0048). Statistically significant differences in ASDAS and BASDAI in these two groups were not observed (p=0.332 and p=0.605, respectively). For all patients, BASMI did not vary significantly (p=0.691) at baseline (mean 3.7± 1.4) and after 6 months (mean 3.8±1.3) of treatment. Although the ΔBASMI for etanercept was negative (mean -0.12±0.9) and for golimumab positive (0.14±0.8), it was not statistically significant. At baseline there is a significant positive association between BASMI and ASDAS (r=0.435, p=0.001), BASMI and BASDAI (r=0.567, p<0.001) and BASMI and BASFI (r=0.510, p<0.001). However, there was not a statistically significant association between ΔBASMI and: ΔASDAS, ΔBASDAI and ΔBASFI (r=0.158; p=0.269, r=0.019; p=0.096 and r=0.121; p=0.397, respectively).

Conclusion: In PsA patients treated with bDMARDs, at least in short-term follow-up, BASMI does not improve with time. Changes in BASMI did not correlate with changes in activity disease and in functional outcome. Studies with longer follow-up and with more patients are needed to better evaluate these associations.

Disclosure of Interests: Maria Rato: None declared, Filipe Pinheiro: None declared, Salomé Garcia: None declared, Bruno Miguel Fernandes: None declared, Sara Ganhão: None declared, Rita Gaio: None declared, Miguel Bernardes Speakers bureau: Abbvie, Amgen, Biogen, Eli-Lilly, Glaxo-Smith-Kline, Pfizer, Janssen, Novartis, Alexandra Bernardo: None declared, Lúcia Costa: None declared

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AB0826 PROBABILITY OF SURVIVAL OF USTEKINUMAB IN PSORIATIC ARTHRITIS: A REAL CLINICAL PRACTICE COHORT COMPOSED OF 64 PATIENTS

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Background: Psoriatic arthritis (PsA) is an inflammatory disorder of unknown etiology. Several domains are affected as peripheral or axial joints, enthesitis, dactylitis, nails as well as skin. Diverse cytokines have been described in the pathology of PsA as TNFα, IL-17 and IL-23. Ustekinumab (UST) is a fully human IgG1κ monoclonal antibody to interleukin 12/23. Its efficacy and safety have been tested in several clinical trials and registries. Nevertheless data from real word evidence studies is needed to understand the effectiveness, safety and behavior of UST in a different population of patients from randomized controlled trials

Objectives: Analyze the persistence of UST 45 and 90 mg along 52 weeks of treatment

Methods: Drug survival, effectiveness and security of UST were studied in a population of 64 PsA patients treated in the period between August 2014 to October 2019. Drug survival was defined as the time from initiation to discontinuation (stop/switch) of bDMARDs. For the determination of drug survival, Kaplan-Meier survival curves and Cox-regression analyses were used. Effectiveness was described as a reduction in the use of corticosteroids and in the levels of CRP along the study. All adverse events were recorded during the study

Results: 64 patients were included with a mean follow-up of 57,2 weeks. At baseline the mean age was 47,8 years (8,9). 54,7% of patients were women and 45,3% were male. 31,3% were obese. Mean disease duration was 7,9 (5,0) years. 45,3% presented peripheric arthritis; 32,8% axial involvement; 31,3% enthesitis; 80% psoriasis. Patients were 45% bDMARDs-naïve; had a previous bDMARDs in 20,3% and ≥ than two bDMARDs in 34,4%. 30% of the patients had co-therapy with methotrexate and 29,7% of patients received corticosteroid therapy. Mean CRP was 7,9 (12,7) mg/L. The global probability of survival for UST was 96%, 83,9% and 60% at week 12, 24 and 52 respectively. High UST dosage was associated with favorable drug survival (at 52W: UST 45 mg=40,1%; UST 90 mg=75,8%; UST 45 to 90 mg*=88,9%) (p=0,008). The bDMARDS-naïve population also correlated with favorable UST survival (at 52W: bDMARDS-naïve=66,1% vs bDMARDS-experienced=56,7%), however no statistical significance was found (p=0,196). No difference in survival was observed among patients with or without axial involvement (W52: axial=58,2% vs non-axial=61,6; p=0,869). UST produced a reduction in the use of corticosteroids (30% vs 16%) and CRP levels (8,7 vs 7,7). Differences were greater in patients treated more than 28 weeks (maximum efficiency described for UST) (corticosteroids: 26% vs 16%; CRP levels: 8,5 vs 4,4). 4,9% of the patients suffered an AE. Most of them were non-serious AE: infections (3,3%) or headache (1,6%). The main cause of treatment discontinuation was lack of efficacy (30%), followed by primary failure (9,4%) and just a 3% due to AE

Conclusion: The persistence of UST was dose-dependent and greater for the UST 90 mg dosage and for the population of bDMARD-naïve patients

Drug survival of UST in the population of patients with axial involvement seems similar to the population of patients without axial affection which provide evidence of the efficacy of the IL23 inhibition in the axial domain of PsA

UST decreased the use of corticosteroids and CRP levels along treatment

The security profile of UST was to the drug. Only few non-serious AE reported during this study

*UST 45 to 90 mg, patients who change from UST 45 to UST 90 mg dosage

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Disclosure of Interests: None declared

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AB0827 IMPACT OF BASELINE BODY MASS INDEX ON THE EFFICACY AND SAFETY OF TOFACITINIB IN PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Obesity is highly prevalent in PsA (~45%)[1] and is associated with a reduced response to TNF inhibitors.[2] Tofacitinib is an oral Janus kinase inhibitor for the treatment of PsA.

Objectives: This post hoc analysis assessed tofacitinib efficacy and safety in patients (pts) with PsA by baseline (BL) body mass index (BMI) category.

Methods: Data were pooled from two placebo (PBO)-controlled, double-blind, Phase 3 studies in pts with active PsA and an inadequate response to ≥1 conventional synthetic DMARD (OPAL Broaden [12 months; NCT01877668]) or to ≥1 TNF inhibitor (OPAL Beyond [6 months; NCT01882439]).[3,4] This analysis included pts randomised to tofacitinib 5 mg twice daily (BID), tofacitinib 10 mg BID or PBO, stratified by BL BMI: <25 kg/m^2, ≥25–<30 kg/m^2, ≥30–<35 kg/m^2, or ≥35 kg/m^2. Efficacy and safety were reported to Month (M)3. M3 efficacy outcomes included ACR20/50/70 and HAQ-DI responses, dactylitis and enthesitis resolution rates and changes from BL in HAQ-DI, Short Form-36 Version 2 (SF-36v2) Physical (PCS) and Mental Component Summary (MCS) scores, and Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) scores. Safety outcomes included adverse events (AEs), such as cardiovascular (CV) events and changes in lipid levels and liver function tests (LFTs).

Results: This analysis included 710 pts; 43.8% were obese (BMI ≥30). At BL, 161 (22.7%) pts had a BMI <25, 238 (33.5%) had a BMI ≥25–<30, 186 (26.2%) had a BMI ≥30–<35 and 125 (17.6%) had a BMI ≥35. Most pts were white (92.5–96.8%), middle-aged (mean: 44.5–51.2 yrs) and female (49.5–65.6%). Greater proportions of obese pts were from Russia/Eastern Europe (35.0%) and USA/Canada (31.8%), vs the rest of world. At BL, higher BMI correlated with an increased prevalence of metabolic syndrome (4.3% in BMI <25 to 76.0% in BMI ≥35) and CRP levels >2.87 mg/L (49.1% in BMI <25 to 84.0% in BMI ≥35). Higher proportions of pts (42.5–47.9%) in BL BMI categories <35 reported no prior biologic DMARD use, vs pts with a BL BMI ≥35 (33.6%). At M3, efficacy improvements were greater in tofacitinib-treated pts vs PBO-treated pts (Figure 1). In pts with a BL BMI ≥35, a trend towards fewer pts responding was observed (Figure 1) and mean changes from baseline in SF-36v2 PCS and MCS and FACIT-F generally appeared lower (Figure 2) vs pts in lower BL BMI categories. Up to M3, the proportions of pts with AEs, and percentage change from BL in lipid levels and LFTs, were generally similar across all BL BMI categories. Three CV events were reported: non-fatal cerebrovascular accident, transient ischemic attack (both tofacitinib 5 mg BID, BMI ≥30–<35) and coronary artery revascularisation (PBO; BMI ≥35). Limitations include the 3-month observation time, particularly for safety findings, thus longer observation times are warranted.

Conclusion: Regardless of BL BMI, tofacitinib demonstrated greater efficacy than PBO at M3 in pts with PsA. Similar to other advanced therapies,[2] reduced efficacy was generally observed in tofacitinib and PBO pts with a BL BMI ≥35. Tofacitinib safety appeared consistent across all BL BMI categories.

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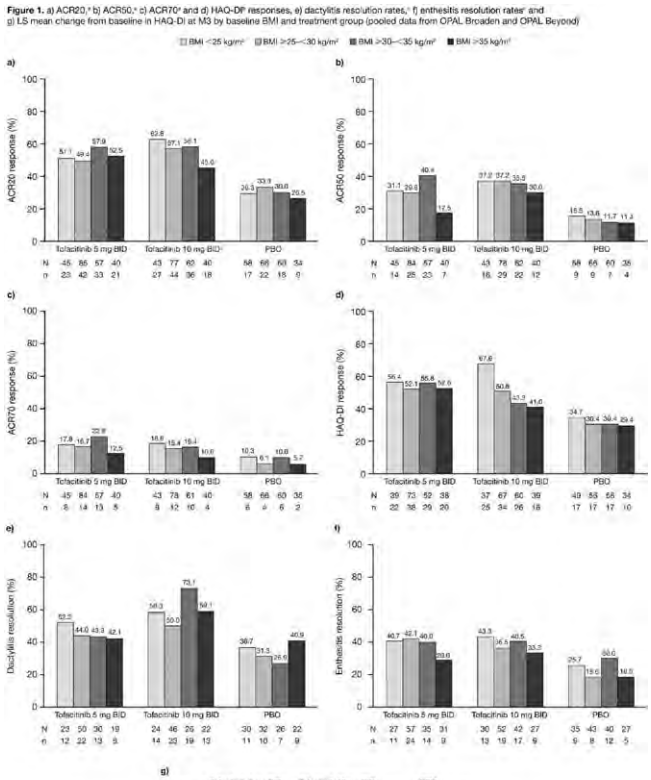


Figure 1. a) ACR20,* b) ACR50,* c) ACR70* and d) HAQ-DI* responses, e) dactylitis resolution rates,† f) enthesitis resolution rates† and g) LS mean change from baseline in HAQ-DI at M3 by baseline BMI and treatment group (pooled data from OPAL Broaden and OPAL Beyond)

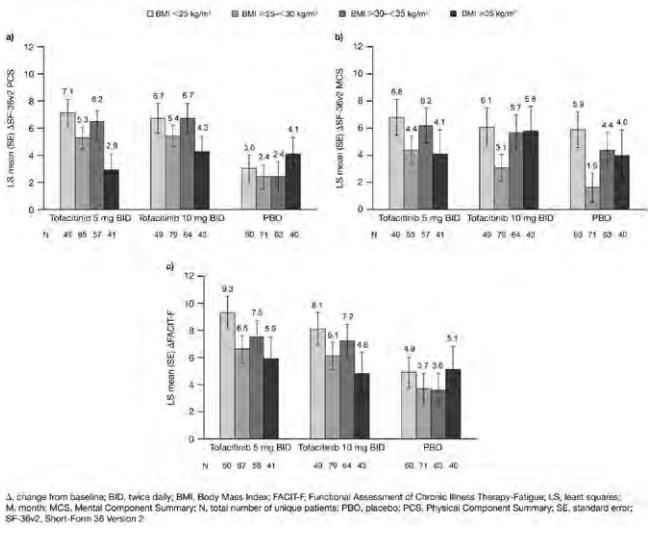


Figure 2. LS mean (SE) changes from baseline in a) SF-36v2 PCS, b) SF-36v2 MCS and c) FACIT-F at M3 by baseline BMI and treatment groups (pooled data from OPAL Broaden and OPAL Beyond)

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AB0828 IS PSORIATIC ARTHROPATHY DIFFERENT WHEN IS ACCOMPANIED BY AXIAL INVOLVEMENT?

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Background: Axial involvement in patients diagnosed of Psoriatic arthritis (PsA) in variable in previous studies. Axial involvement (according GRAPPA criteria) is based upon inflammatory spinal symptoms pain with loss of lumbar mobility and the presence of radiological sacroiliitis and other radiographic signs of spondylitis in patients with PsA.

Objectives: Evaluate the prevalence of axial involvement in PsA an their clinical features.

Methods: All patients included in the monographic PsA consultation database of our second level hospital were analyzed. Demographic, clinical and analytical variables were collected. Statistical analysis was performed using SPPSS v.25

Results: We included 145 patients with PsA (fulfilling CASPAR criteria) with a mean age at diagnosis of 45,4 (±13) years and time of evolution of the disease 9,3 (±6,2) years. The proportion of the affectation types were: peripheral 94 (64,8%), mixta 31 (21,4%) and axial 20 (13,8%). Therefore, 51 (35,2%) patients meet criteria for axial involvement, of with 31 (21,4%) also had associated peripheral involvement. Table 1 shows the differences between patients with and without axial disease. Axial involvement was higher in males than women [OR=2,3 (1,1-4,7), p=0,023]. HLAB27, determined in 106 patients, was more prevalent in axial PsA than in exclusive peripheral patients, 35% and 4,5% respectively [OR=11,3 (3,0-42,7), p<0,0001] We didn't find any differences in other domains of psoriatic disease or gender. Age at diagnosis was lower in patients with HLA B27 positive [35,6 (±12,3) vs 46,2 (± 12,1) years, p=0,0001] and in the patients with dactylitis [40,2 (11,8) vs 46,7 (13) años, p=0,018] or uveitis [28,7 (8,5) vs 45,8 (12,8) years, p=0,02], respect patients who did not present them, regardless of HLAB27. No differences were found in age between patients with axial o peripheral disease [44,6 (±13,3) vs 45,9 (±12,8) years, p=0,56], neither other domains like skin psoriasis, onicopathy or enthesitis. Patients with axial involvement had overweight (BMI >25) less frequently than peripheral disease [OR=0,4 (0,2-0,8), p=0,01)]. We didn't find any differences in other comorbidities (arterial hypertension, diabetes, hyperlipemia, hyperuricemia, ischemic heart disease, depression) between patines with axial or peripheral disease.

Table 1. Differences between axial and peripheral patterns

	With axial involvement, n=51	Without axial involvement, n=94	OR (IC 95%)	p value
Age at diagnosis, years (SD)	44,6 (±13,3)	45,9 (±12,8)		0,6
Time of evolution, years (SD)	10 (±6,8)	8,9 (±5,8)		0,3
Men, n (%)	36 (42,9%)	48 (57,1%)	2,3 (1,1-4,7)	0,02
HLAB27, n (%)	14 (82,4%)	3 (17,6%)	11,3 (3,0-42,7)	<0,0001
Skin Psoriasis, n (%)	47 (36,4%)	82 (63,6%)	1,7 (0,5-5,6)	0,4
Onicopathy, n (%)	11 (26,2%)	31 (73,8%)	0,6 (0,2-1,2)	0,1
Dactilytis, n (%)	9 (32,1%)	19 (67,9%)	0,8 (0,3-2,0)	0,7
Enthesitis, n (%)	13 (44,8%)	16 (55,2%)	1,7 (0,7-3,8)	0,2
Uveitis, n (%)	2 (66,7%)	1 (33,3%)	3,8 (0,3-42,9)	0,2
Inflammatory bowel disease, n (%)	2 (66,7%)	1 (33,3%)	3,8 (0,3-42,9)	0,2
Hyperlipemia, n (%)	27 (31%)	60 (69%)	0,6 (0,3-1,3)	0,2
BMI >25, n (%)	22 (26,5%)	61 (73,5%)	0,4 (0,2-0,8)	0,01
Hypertension, n (%)	18 (39,1%)	28 (60,9%)	1,3 (0,6-2,6)	0,5
Hyperuricemia, n (%)	16 (39%)	25 (61%)	1,3 (0,6-2,7)	0,5
Smokers, n (%)	13 (50%)	13 (50%)	2,1 (0,9-5,0)	0,08
Ischemic heart disease, n (%)	8 (53,3%)	7 (46,7%)	2,3 (0,8-6,8)	0,1
Depression, n (%)	7 (30,4%)	16 (69,6%)	0,8 (0,3-2,0)	0,6
Diabetes, n (%)	7 (30,4%)	20 (74,1%)	0,6 (0,2-1,5)	0,3

Conclusion: Prevalence of axial involvement in our cohort (35,2%) is found within the data reported in other studies (25-70%). Nevertheless, we found less prevalence of HLAB27 positive than other reports. Patients with HLAB27 positive, dactylitis or uveitis are diagnosed at earlier ages.
Disclosure of Interests: None declared
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AB0829 INFLAMMATORY BOWEL DISEASE IN PSORIATIC ARTHRITIS. STUDY OF 306 PATIENTS FROM A SINGLE UNIVERSITARY CENTER. PREVALENCE, CLINICAL FEATURES AND RELATIONSHIP TO BIOLOGIC THERAPY.

L. Sanchez-Bilbao[1], D. Martinez-Lopez[1], N. Palmou-Fontana[1], S. Armesto[2], M. A. González-Gay[1], R. Blanco[1]. [1]*H.U. Marqués de Valdecilla, Rheumatology, Santander, Spain;* [2]*H.U. Marqués de Valdecilla, Dermatology, Santander, Spain*

Background: Inflammatory bowel disease (IBD), which includes Crohn's disease (CD), Ulcerative colitis (UC), and undetermined colitis may be related to psoriasis and psoriatic arthritis (PsA). Biologic therapy (BT) is useful in PsA and IBD but paradoxically has been related to IBD.
Objectives: In a wide series of PsA, our aim was to assess **a)** the epidemiological and clinical features of associated IBD and **b)** its relationship with BT.
Methods: All unselected consecutive patients studied in a single reference University Hospital with**: a)** PsA (CASPAR criteria) and **b)** IBD: CD, UC and undetermined colitis diagnosed by endoscopic patterns, clinical criteria and laboratory tests. A comparative study between patients with and without IBD was performed
Results: We studied 306 (165 women/141 men) patients with PsA; mean age at PsA diagnosis of 41.7±15.79 years; delay of diagnosis from the onset of symptoms of 2.6±2.01 years. IBD (CD=6; UC=1 and undetermined colitis=3) was observed in 10 of 306 (3.3%, 8 women/2 men). A significant more frequency of enthesitis, positive HLA-B27 and non-significant more severe PsA (axial, and hip involvement, and a higher BASDAI, BASFI, DAPSA, PASI) was observed in patients with associated-IBD (**TABLE).**
IBD was present before PsA in 5 patients and in the other 5, after 9.6±15.3 years of evolution of PsA. BT for PsA has been used in 1 (20%) (etanercept) of these 5 patients which developed IBD and in 67 of 296 (22.6%) without IBD (Adalimumab 45; Certolizumab 8; Infliximab 6; Golimumab 4; Etanercept 4).
Conclusion: IBD in PsA was uncommon (3.3%), may be associated to a more severe PsA, and no relationship to BT was found.

TABLE 1.

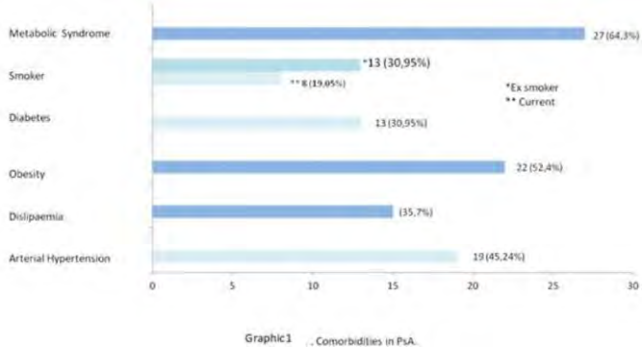
	Patients with IBD (n=10)	Patients without IBD (n=296)	p
DEMOGRAPHIC PARAMETERS			
Sex, n (%)	2 ♂/8 ♀ (20.0/80.0)	139 ♂/157 ♀ (46.9/53.1)	p = 0.11
Age at PsA symptoms onset (years), mean± SD	39.0±15.1	44.2±11.4	p = 0.17
Age at PsA diagnosis, mean±SD	41.7±15.7	46.4±15.8	p = 0.22
PsA RELATED DATA			
PsA type			
Asymmetric Oligoarticular, n (%)	4.0 (40.0)	159 (53.7)	p = 0.59
Symmetrical Polyarthritis, n (%)	0.0 (0.0)	46 (15.5)	p = 0.37
Axial, n (%)	3.0 (30.0)	40 (13.5)	p = 0.31
Mixed, n (%)	3.0 (30.0)	51 (17.2)	p = 0.54
Enthesitis, n (%)	7.0 (70.0)	111 (37.5)	**p = 0.03***
Dactylitis, n (%)	0.0 (0.0)	79 (26.7)	p = 0.70
Hip involvement n (%)	4.0 (40.0)	55 (18.5)	p = 0.57
Scores			
BASDAI, median [ICR]	3.1 [0.0-4.4]	2.2 [0.0-4.5)	p = 0.64
BASFI, median [ICR]	6.0[0.0–6.9]	0.0 [0.0-3.3]	p = 0.69
DAPSA, median [ICR]	10.7 [0.0–14.62]	4.3 [0.0-13.0]	p = 0.31
PASI, median [ICR]	2.3 [0.0–6.7]	0.6 [0.0-2.38]	p = 0.70
Laboratory tests: HLA-B27, n (%)	6.0 (60.0)	23 (7.8)	**p = 0.001***

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AB0830 LIPID PROFILE IN PSORIATIC ARTHRITIS. FREQUENCY AND ASSOCIATION WITH DISEASE ACTIVITY.

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory disease associated with higher risk of cardiovascular events and metabolic syndrome. The inflammation not only accelerates atherosclerosis, but also may influence cardiovascular (CV) risk factors such as lipid profile, blood pressure and insulin resistance. Lipid profile has previously been studied in PsA, however this association is still controversial.
Objectives: To study the frequency of altered lipid profile in patients with PsA and its association with disease activity.
Methods: We studied all the patients with diagnosis of PsA who consecutively attended to Rheumatology Unit at Cordoba Hospital from July 2018 to December 2019. PsA was diagnosed according CASPAR criteria. Clinical and laboratory data were collected. The activity of the disease was evaluated by PASI, MDA and DAPSA. Quantitative variables will be expressed in median and 1st and 3rd interquartile; qualitative variables expressed in frequency and percentage. Correlation analysis was calculated using Spearman's rank correlation coefficient. P<0.05 was considered statistically significant.
Results: 42 PsA patients were included. Mean age was 56 years old (47.25-62.75) and 54.76% were female (n=23). 92.86% (n=39) of the patients had plaque Psoriasis and 87.8% (n=36) had peripheral joint involvement.
Frequency of comorbidities in PsA are shown in Graphic 1. 31 (73.8%) of the patients were treated with topical therapy, 3 (7.14%) with phototherapy, 31 (73.8%) with Methotrexate and 17 (41.46%) with biologics and JAK inhibitor. Activity Disease Index and Lipid profile are shown in Table 1 and 2.
There was not association between Apo B/Apo A coefficient with DAPSA (rho=0.013; p=0.940) and MDA (rho=-0.029; p=0.867).
Conclusion: In spite of the presence of cardiovascular factors in the majority of PsA patients, lipid profile is not correlated with disease activity in this population.
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Graphic 1. Comorbidities in PsA

Table. 1. Activity Disease Index in PsA

ACTIVITY INDEX	n=42
DAPSA	14.45 (9.72-23.92)
DAPSA	
≤4 REMISSION	3
>4 y ≤14 low disease activity	16
>14 y ≤28 moderate disease activity	17
>28 high disease activity	3
cDAPSA	14.00 (8.00-23.00)/41*
MDA	9 (25)/36
PASI	2.20 (0.20-6.80)/41*

*Expressed in median and interquartiles.Qualitative variables expressed in frequency and percentage.

Table. 2. Lipid Profile in PsA patients.

Cholesterol (mg/dl)	194.5 (164.8-218.2)
HDL (mg/dl)	48.00 (37.00-57.00)
LDL (mg/dl)	114.5 (78.5-140.8)
TG (mg/dl)	139.50 (89.25-191.20)

Expressed in median and interquartiles.

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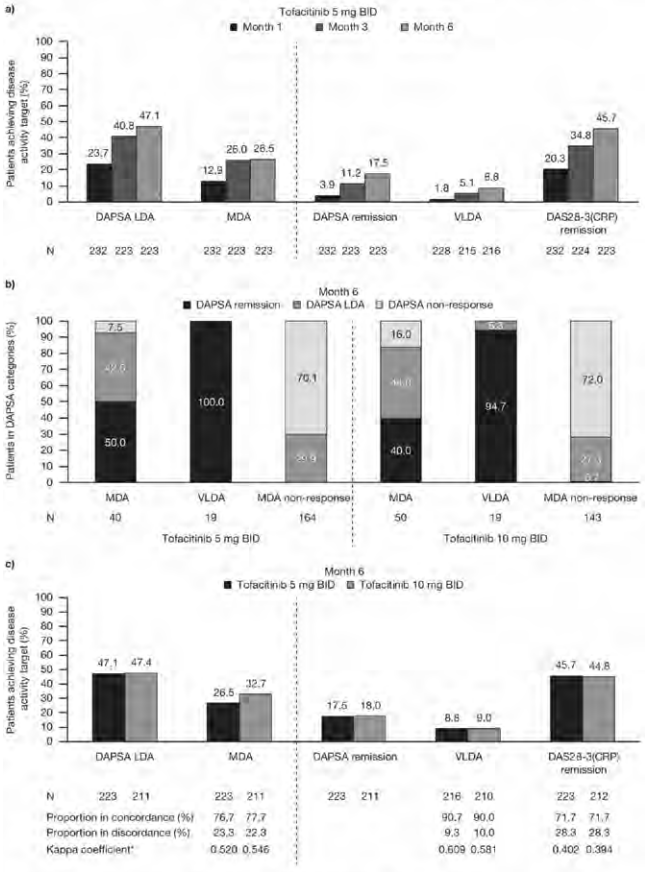
AB0831

COMPARISON OF DIFFERENT REMISSION INDICES IN PATIENTS WITH PSORIATIC ARTHRITIS: A POST HOC ANALYSIS OF DATA FROM PHASE 3 TOFACITINIB STUDIES

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Background: An international task force has agreed that remission and low disease activity (LDA) are treatment targets for patients (pts) with PsA, and recommends the Disease Activity Index in Psoriatic Arthritis (DAPSA) and minimal disease activity (MDA) to assess disease activity states.[1] Tofacitinib is an oral Janus kinase inhibitor for the treatment of PsA.
Objectives: In this post hoc analysis, we compared DAPSA LDA with MDA, and DAPSA remission with very low disease activity (VLDA) and DAS28-3(CRP) remission, in pts with PsA receiving tofacitinib.
Methods: Data were pooled from 2 Phase 3 studies (OPAL Broaden [12 months; NCT01877668]; OPAL Beyond [6 months; NCT01882439]) for pts receiving tofacitinib 5 or 10 mg twice daily (BID) or placebo (PBO). DAPSA was determined by summing: swollen joint count (SJC66); tender/painful joint count (TJC68); Patient's Global Assessment of Arthritis (PtGA; visual analogue scale [VAS]); pain (VAS); and CRP. Pts were classified as achieving MDA or VLDA when meeting ≥5 (MDA) or 7 (VLDA) of the following criteria: TJC68 ≤1; SJC66 ≤1; Psoriasis Activity and Severity Index ≤1 or body surface area ≤3%; pain (VAS) ≤15; PtGA (VAS) ≤20; HAQ-DI ≤0.5; tender entheseal points (using Leeds Enthesitis Index [LEI]) ≤1. A logistic regression model was used to assess demographic and baseline characteristics as predictors of a trend in DAPSA scores at Month (M)3. DAPSA LDA (≤14), MDA, DAPSA remission (DAPSA ≤4), VLDA and DAS28-3(CRP) remission (DAS28-3[CRP]<2.6) rates were compared at M1, M3 and M6 for pts receiving tofacitinib 5 mg BID and at M6 for pts receiving tofacitinib 5 or 10 mg BID. Agreement between disease activity indices at M6 was evaluated using a kappa test. The percentage of tofacitinib-treated pts who achieved MDA, VLDA and non-response was reported at M6, stratified by achievement of DAPSA LDA, remission or non-response.
Results: This analysis included 709 pts: tofacitinib 5 mg BID, n=237; tofacitinib 10 mg BID, n=236; PBO, n=236. At M3, older patients treated with tofacitinib, and tofacitinib- or PBO-treated pts with higher baseline SJC66, TJC68, PtGA VAS, HAQ-DI, LEI and Pain VAS, were significantly ($p<0.05$) more likely to have higher DAPSA. DAPSA LDA, MDA, remission (DAPSA and DAS28-3[CRP]) and VLDA rates generally increased from M1 to M6 for patients receiving tofacitinib 5 mg BID (Figure a). At M6, most tofacitinib-treated pts who achieved MDA, and all who achieved VLDA, were also in DAPSA remission or LDA (Figure b). At least moderate agreement (defined by kappa values 0.41–0.60) was observed between DAPSA LDA and MDA, and between DAPSA remission and VLDA, with both doses of tofacitinib at M6 (Figure c).
Conclusion: Remission and LDA rates generally increased over time in pts with PsA receiving tofacitinib. DAPSA LDA showed moderate agreement with MDA, and DAPSA remission showed at least moderate agreement with VLDA, confirming that DAPSA and MDA are useful measurement tools to assess disease activity in pts with PsA treated with tofacitinib.
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Figure. Percentage of patients receiving a) tofacitinib 5 mg BID achieving DAPSA LDA, MDA, DAPSA remission, VLDA or DAS28-3(CRP) remission at Month 1, 3 or 6; b) tofacitinib 5 or 10 mg BID achieving MDA or VLDA, by DAPSA categories at Month 6; c) tofacitinib 5 or 10 mg BID achieving DAPSA LDA, MDA, DAPSA remission, VLDA or DAS28-3(CRP) remission at Month 6



*Kappa test of agreement between: DAPSA LDA and MDA; DAPSA remission and VLDA or DAS28-3(CRP) remission
BID, twice daily; DAPSA, Disease Activity Index for Psoriatic Arthritis; DAS28-3(CRP), Disease Activity Score in 28 joints, CRP; LDA, low disease activity; MDA, minimal disease activity; N, number of available patients; VLDA, very low disease activity

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GlaxoSmithKline, Novartis, Pfizer Inc, Sandoz, Speakers bureau: AbbVie, Amber, Bristol-Myers Squibb, Eli Lilly, Novartis, Pfizer Inc, Roche, Claudia Helling Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Annette E Szumski Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Rajiv Mundayat Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Daniela Graham Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Dario Ponce de Leon Shareholder of: Pfizer Inc, Employee of: Pfizer Inc
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AB0832 IDENTIFICATION OF NATIVE AND CITRULLINATED AUTOANTIBODIES TO PSORIASIS RELATED-ANTIGEN PSOP27 IN SYNOVIAL FLUIDS OF PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Psoriatic arthritis (PsA) is an inflammatory joint disease. Unlike rheumatoid arthritis (RA), PsA is a "seronegative disease", with no diagnostic biomarkers, hence diagnosis is based on clinical evaluation alone. PsA is closely associated with psoriasis (PsO), with up to 1/3 of psoriatic patients developing PsA via unknown mechanism.
PsoP27 is an antigen present in mast cells in psoriatic lesions and absent in skin uninvolved by psoriasis or in healthy controls (1), thus playing a significant role in inflammatory reaction in the psoriatic skin lesion (2). Its levels in skin lesions correlate with psoriasis activity (3). Though speculated to be involved in other inflammatory processes, this antigen has not been investigated in relation to PsA.
Objectives: Our aim was to identify and determine the level of native and citrullinated PsoP27 antibodies (Ab) in serum and synovial fluid of patients with PsA compared to RA and osteoarthritis (OA), exploring a potential common inflammatory pathway in PsA and PsO.
Methods: Synovial fluid (SF) and serum of PsA (n=35, m:f 24:11, median age 48, PsA median duration 8Y, PsO median duration 15Y) and RA (n=11, m:f 2:9, median age 60, median RA duration 13.5Y) patients were analyzed for the level of native and citrullinated PsoP27 Ab. SF derived from OA (n=13, m:f 1:12,median age 77) patients and sera of healthy donors (n=31) were used as controls. Samples were analyzed by ELISA.
Results: SF levels of native and citrullinated PsoP27 Ab were significantly higher in PsA and RA compared to OA patients (Table 1).

Table 1. PsoP27 level (Optical density, OD) in SF of patients with psoriatic arthritis (PsA), rheumatoid arthritis (RA), and osteoarthritis (OA).

PsoP27 -SF			
	PsA	**RA**	**OA**
median	0.640	0.855	0.283
SD	0.298	0.286	0.28
P value (comp. to OA)	0.0082	0.0023	-
P value (comp. to RA)	0.0637	-	0.0023
Cit-PsoP27- SF			
median	0.766	0.982	0.378
SD	0.373	0.348	0.279
P value (comp. to OA)	0.003	0.001	-
P value (comp. to RA)	0.14	-	0.001

Significant correlation was observed between the SF levels of both forms of PsoP27 Ab and the swollen joints count (Native: *p=0.029, r=0.39*, Cit: *p=0.041, r=0.369*), psoriasis area and severity index (PASI) score (Native: *p=0.011, r=0.56*, Cit: *p=0.008, r=0.369*), and CRP levels (Native: *p=0.017, r=0.446*, Cit: *p=0.03, r=0.408*). In contrast, in RA patients there was no correlation between SF levels of PsoP27 Ab and the swollen joint count or CRP levels.
Both forms of PsoP27 Ab were detected in sera of all study groups, at a similar level (Table 2).

Table 2. PsoP27 level (OD) in sera of patients with psoriatic arthritis (PsA), rheumatoid arthritis (RA), and healthy controls (HC).

PsoP27- Serum			
	PsA	**RA**	**HC**
median	0.184	0.235	0.219
SD	0.137	0.097	0.141
P value (comp. to HC)	0.044	0.746	-
P value (comp. to RA)	0.055	-	0.746
Cit-PsoP27- Serum			
median	0.317	0.232	0.321
SD	0.298	0.143	0.160
P value (comp. to HC)	0.767	0.076	-
P value (comp. to RA)	0.044	-	0.076

Conclusion: We determined for the first time the presence of antibodies to psoriatic-related autoantigen PsoP27, in SF of PsA, RA and OA patients. Low SF level of PsoP27 Ab in OA compared to a high Ab level in RA and PsA may suggest a potential new biomarker discriminating between inflammatory arthritis versus OA. Furthermore, we showed a positive correlation between the SF levels of antibodies to PsoP27 in SF and disease activity in PsA, but not in RA. Also, we demonstrated the presence of citrullination and antibodies against citrullinated peptides in PsA, a process thought to be specific to RA. Our results suggest that antibodies to PsoP27 in SF may be a potential biomarker in PsA, both for diagnosis and disease assessment.
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AB0833 COMORBIDITY IN PSORIATIC ARTHRITIS WITH AND WITHOUT ENTHESITIS

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Background: Psoriatic arthritis (PsA) is a chronic systemic inflammatory disease associated with psoriasis and high levels of comorbidity. There is no data on comorbidity in PsA with and without enthesitis.
Objectives: Evaluation of the frequency and the structure of comorbidity in PsA patients with and without enthesitis.
Methods: A retrospective analysis of 239 case histories of PsA patients observed at the Moscow City Rheumatology Center was performed. There were 68 (28.5%) PsA patients with enthesitis and 171 (71.5%) patients without enthesitis. The study included 132 female and 107 male patients, mean age was 52.0 ± 14.8 years. 217 patients (90.8%) had psoriasis. The average psoriasis duration was 19 ± 14.3 years. The diagnosis of PsA was established based on CASPAR criteria (2006).
Results: Comorbid diseases were observed in 141 (59%) patients with PsA. Moreover, in the group of PsA patients with enthesitis, comorbidity was noted much more often compared to the group without enthesitis (70.6% and 54.4%, respectively, p = 0.01). The most common comorbid diseases were: arterial hypertension (25%), gastropathy (16.2%), osteoporosis (13.2%), osteoarthritis (11.8%), diabetes mellitus (11.8%), hyperuricemia (10, 3%), obesity (8.8%). A distinctive feature of PsA patients with enthesitis was a more frequent detection of osteoporosis (13.2% and 5.8%, respectively, p = 0.01), which may be due to concomitant osteitis.
Conclusion: High rates of comorbidity were found in PsA patients with enthesitis (70,6%). The most prevalent comorbid diseases were arterial hypertension (25%), gastropathy (16.2%) and osteoporosis (13.2%). Patients with PsA with enthesitis were significantly more likely to have osteoporosis compared with patients without enthesitis, which is important to consider when managing patients.
Disclosure of Interests: None declared
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AB0834 CLINICAL CHARACTERISTICS OF PSORIATIC ARTHRITIS IN CHINESE PATIENTS: A CROSS-SECTIONAL OBSERVATIONAL STUDY

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Background: The clnical features of psoriatic arthritis(PsA)greatly varied in reports fomr different countries.There was no exact data in China.
Objectives: To disclose the characteristics of PsA in China, we initiated an investigation it in our cohort of PsA patients.
Methods: A cross-sectional observational study was conducted in our PsA cohort of Peking University First Hospital. All the clinical and imaging data at the patient's first visit were collected, including the age, gender, disease course,

skin lesion, arthritis, dactylitis, enthesis, laboratory tests, concomitant diseases and so on.

Results: Two hundred and seventy-nine patients with PsA were enrolled in this study. Their mean age was 41 year-old with 132 (47.3%) female. Median disease duration was 3 years. Among these patients, 196(73.4%)patients had the skin lesion first, 47 (17.6%)patients had the arthritis first, and the other 24(9.0%) patients had the psoriasis and the arthritis at the same time. Arthritis was the most common manifestation. Polyarthritis was the most common arthritic manifestation with proximal interphalangeal (PIP) joint as the most frequently involved joint. Dactylitis was observed in 89 (31.9%) patients, mostly at the second, third and fourth toe. Enthesis was found in 18 (6.5%) patients by physical examination, however, in 158 (56.5%) patients with the aid of ultrasound and MRI.

Conclusion: Polyarthritis was the most common arthritis type in Chinese PsA patients, and PIP joint was the most involved joint, and the second, the middle and the fourth toe were the most frequently digits. The imaging techniques, especially ultrasound dramatically increased the identification of enthesis.

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AB0835

THE IMPACT OF ADALIMUMAB VS PLACEBO ON PATIENT-REPORTED OUTCOMES AND UTILITY MEASURES AMONG PATIENTS WITH MODERATELY TO SEVERELY ACTIVE PSORIATIC ARTHRITIS

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Background: Physical function and health-related quality of life(HRQoL) are negatively impacted in patients(pts) with PsA. Treatment with conventional and biological (b) DMARDs improved patient-reported outcomes(PROs).

Objectives: To assess impact of adalimumab(ADA) vs placebo(PBO) on PROs following 12-week (wk) treatment.

Methods: Pts(n=315) with moderately to severely active PsA and bDMARD naive were randomized to ADA 40mg or PBO every other wk. We assessed PROs at baseline(BL) and wk 12 using the 36-item Short-Form(SF-36) Health Survey physical(PCS) and mental component summary(MCS) scores, 8 domain scores ranging from 0(worst) to 100(best), and SF-6D utility measure derived from all 8 SF-36 domains with scores ranging from 0.296(worst) to 1.00(full health) and minimally important difference(MID) of 0.041. Patient Global Assessment of disease activity(PtGA) and pain(both utilizing 100 mm visual analog scale[VAS]) and HAQ disability index(DI) were assessed. Mean changes from BL, percentages of pts with improvements ≥minimum clinically important differences(MCID), and scores ≥US age-and gender-matched normative values(A/G norms) were analyzed, based on as observed data. *P* values were assessed by analysis of variance model for continuous variables and *Cochran–Mantel–Haenszel* test for binary outcomes, adjusting by baseline MTX use and extent of psoriasis. Numbers needed to treat(NNTs) are reported using proportions of pts reporting improvements ≥MCID in SF-36, PtGA, pain, and HAQ-DI.

Results: BL PRO scores were similar between ADA(n=151) and PBO(n=162; **Table 1**). Improvements from BL at wk 12 with ADA vs PBO were significant in PtGA, pain, HAQ-DI, and SF-36 PCS(change: 9.3 vs 1.4; $P<0.001$) but not in SF-36 MCS(1.6 vs 1.2; **Table 1**). Six of 8 SF-36 domains significantly improved from BL to wk 12 with ADA vs PBO(all $P\leq0.05$; **Table 1** and **Figure 1**). SF-6D improvements exceeded MID with ADA(change: 0.071) vs PBO(0.018). Proportions of pts reporting improvements ≥MCID at wk 12 were significantly greater with ADA vs PBO in all PROs, except SF-36 role emotional and mental health domains, with corresponding NNTs ≤6.4(**Figure 2**). Proportions of pts who reported scores ≥A/G norms in HAQ-DI, SF-36 PCS, and 6 of 8 SF-36 domains were significantly greater with ADA vs PBO(**Figure 2**).

Table 1. Mean Disease Characteristics and SF-36 Domain Scores by Treatment Group at Baseline and Wk 12 Compared With Age-and Gender-Matched Normative Values

	ADA 40 mg eow		PBO		A/G norms
	Baseline	Week 12 [change from baseline to week 12]	Baseline	Week 12 [change from baseline to week 12]	
SF-36 PCS	33.2	42.5[9.3**]	33.3	34.7[1.4]	≥50
SF-36 MCS	48.1	49.8[1.6]	46.6	48.4[1.2]	≥50
SF-6D	0.653	0.724[0.071]	0.641	0.659[0.018]	—
PtGA	47.1	25.9[–21.7**]	48.1	47.5[0.2]	—
Pt pain	51.1	26.8[–24.1**]	48.8	49.1[1.3]	—
HAQ-DI	1.0	0.6[–0.4**]	1.0	0.9[–0.1]	≤0.25
	Baseline (vs A/G norms)	Week 12 (vs A/G norms)	Baseline (vs A/G norms)	Week 12 (vs A/G norms)	
Physical Functioning	50.8(–31.5)	65.9***(–16.4)	48.2(–34.1)	52.0(–30.3)	82.3
Role Physical	37.1(–45.9)	65.9***(–17.1)	32.6(–50.4)	40.6(–42.4)	83.0
Bodily Pain	41.3(–31.6)	61.0***(–11.9)	40.2(–32.7)	43.7(–29.2)	72.9
General Health	49.5(–20.8)	62.1***(–8.2)	52.1(–18.2)	53.0(–17.3)	70.3
Vitality	41.4(–17.8)	55.1***(–4.1)	41.6(–17.6)	45.0(–14.2)	59.2
Social Functioning	66.3(–19.0)	77.8†(–7.5)	61.7(–23.6)	66.7(–18.6)	85.3
Role Emotional	65.1(–23.4)	70.4(–18.1)	59.1(–29.4)	66.0(–22.5)	88.5
Mental Health	67.6(–8.5)	72.9(–3.2)	64.9(–11.2)	67.3(–8.8)	76.1

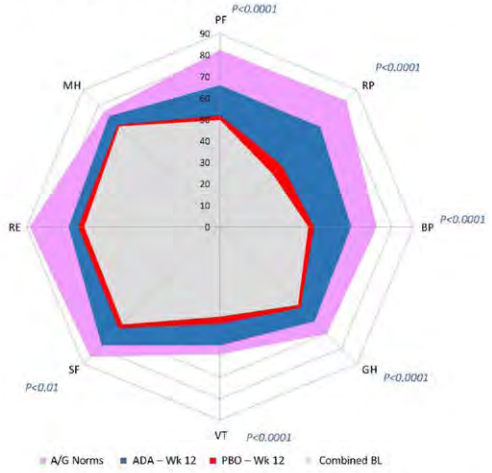
ADA, adalimumab; A/G norm, age-and gender-matched normative value; eow, every other week; DI, disability index; MCS, mental component summary; MID, minimally important difference; PBO, placebo; PCS, physical component summary; PtGA, Patient Global Assessment of disease activity; SF-36, 36-item Short-Form Health Survey; SF-6D, Short-Form 6D.

SF-6D MID=0.041.

Statistical analysis ADA vs PBO: †$P<0.05$; *$P<0.01$; **$P<0.001$; ***$P<0.0001$.

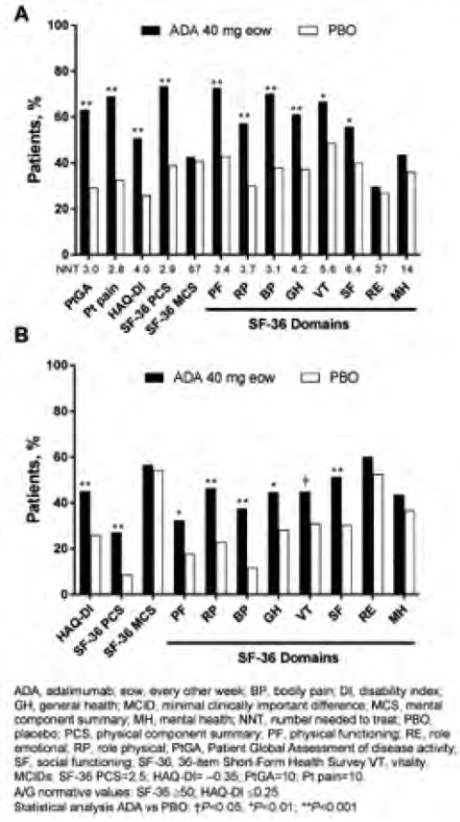
Conclusion: Statistically significant and clinically meaningful improvements and scores ≥A/G norms(higher definition of response) at week 12 were reported with ADA vs PBO in pts with moderately to severely active PsA.

Figure 1. Spydergram of Mean Changes in SF-36 Domain Scores at Week 12: ADA vs PBO vs Age- and Gender-Matched Normative Scores



ADA, adalimumab; A/G norm, age- and gender-matched normative value; BL, baseline; BP, bodily pain; GH, general health; MH, mental health; PBO, placebo; PF, physical functioning; RE, role emotional; RP, role physical; SF, social functioning; SF-36, 36-item Short-Form Health Survey VT, vitality.

Figure 2. (A) Proportion of Patients Reporting Improvements ≥MCID and (B) Scores ≥Age- And Gender-Matched Normative Values at Week 12



ADA, adalimumab; eow, every other week; BP, bodily pain; DI, disability index; GH, general health; MCID, minimal clinically important difference; MCS, mental component summary; MH, mental health; NNT, number needed to treat; PBO, placebo; PCS, physical component summary; PF, physical functioning; RE, role emotional; RP, role physical; PtGA, Patient Global Assessment of disease activity; SF, social functioning; SF-36, 36-Item Short-Form Health Survey VT, vitality. MCIDs: SF-36 PCS=2.5; HAQ-DI= −0.35; PtGA=10; Pt pain=10. A/G normative values: SF-36 ≥50; HAQ-DI ≤0.25. Statistical analysis ADA vs PBO: †P<0.05, *P<0.01; **P<0.001

Disclosure of Interests: Vibeke Strand Consultant of: AbbVie, Amgen, Biogen, Celltrion, Consortium of Rheumatology Researchers of North America, Crescendo Bioscience, Eli Lilly, Genentech/Roche, GlaxoSmithKline, Hospira, Janssen, Merck, Novartis, Pfizer, Regeneron Pharmaceuticals, Inc., Sanofi, UCB, Pankaj Patel Shareholder of: AbbVie, Employee of: AbbVie, Naijun Chen Shareholder of: AbbVie Inc, Employee of: AbbVie Inc, Elizabeth Lesser Shareholder of: AbbVie Inc, Employee of: AbbVie Inc

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AB0836

PREVALENCE AND DETERMINANTS OF FATIGUE IN PSORIATIC ARTHRITIS IN AN ASIAN POPULATION

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Background: Fatigue is one of the core domains to be measured in all clinical trials for psoriatic arthritis (PsA). Studies of fatigue in PsA in Asia are scarce.
Objectives: To describe the prevalence and evaluate the factors associated with fatigue in PsA patients within a multi-ethnic Asian population.
Methods: We used data from the PRESPOND registry for PsA patients attending an outpatient clinic of a tertiary institution in Singapore. Demographics data and disease characteristics were evaluated. Fatigue was assessed by question 1 of BASDAI (BASDAI-F) and the vitality domain of SF-36 (SF-36 VT).
Results: 131 patients (50.4% men, 63.4% Chinese, median PsA duration 1.78 years) with completed data for fatigue were included. The median (IQR) tender and swollen joint count was 2 (5) and 1 (3) respectively. 45 patients (34%) experienced high fatigue (defined by BASDAI-F ≥ 6/10[1,2]). 5 clusters of factors were identified using principal component analysis that explained 66.2% of the variance of all factors, which mapped to disease activity, disease chronicity, demographics (ethnicity and gender), and BMI (Figure 1). Of these, disease activity and chronicity were significantly associated with BASDAI-F and SF-36 VT. In a multivariate analysis, back pain, peripheral joint pain and patient global assessment were associated with BASDAI-F, whereas peripheral joint pain, HAQ-DI, age and BMI were associated with SF-36 VT (Table 1).

Table 1. Multivariable analysis for variables associated with fatigue

	BASDAI-F				SF-36 VT			
	b	95% CI	*β*	*p*	*b*	95% CI	*β*	*p*
Back pain (0-10)	0.335	(0.180, 0.490)	0.356	<0.001	-	-	-	-
Peripheral joint pain (0-10)	0.027	(0.012, 0.042)	0.268	0.001	-2.296	(-3.410, -1.182)	-0.320	<0.001
PGA (0-100)	0.211	(0.061, 0.361)	0.236	0.006	-	-	-	-
HAQ-DI (0-3)	-	-	-	-	-12.74	(-17.97, -7.51)	-0.386	<0.001
Age, y	-	-	-	-	0.260	(0.065, 0.456)	0.179	0.009
BMI, kg/m²	-	-	-	-	-0.644	(-1.183, -0.105)	-0.165	0.020

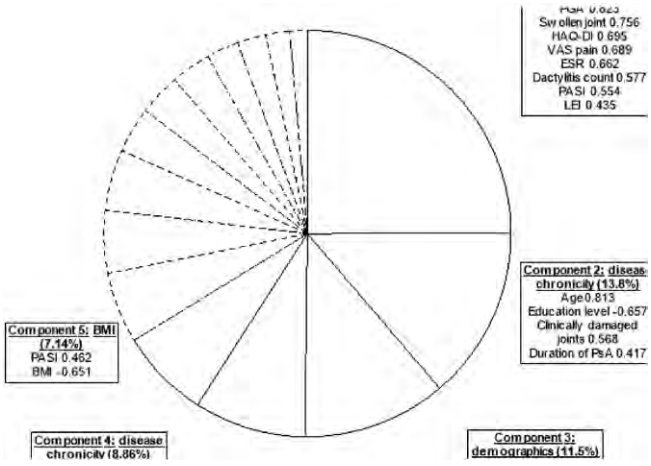


Figure 1. Principal component analysis with 5 components and residuals (in dotted lines). Only factor loadings with magnitudes greater than 0.40 are shown.

Conclusion: PsA-associated fatigue is prevalent in this Asian PsA cohort and is associated with disease activity and chronicity.
References:

[1] Gudu T, Etcheto A, de Wit M, Heiberg T, Maccarone M, Balanescu A, et al. Fatigue in psoriatic arthritis - a cross-sectional study of 246 patients from 13 countries. Joint Bone Spine. 2016;83(4):439-43.
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AB0837

ITCH AS THE MAJOR MEDIATOR OF THE EFFECT OF TOFACITINIB ON HEALTH-RELATED QUALITY OF LIFE IN PSA: A MEDIATION ANALYSIS

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Background: PsA is a chronic, systemic inflammatory disease with signs and symptoms across multiple domains, including cutaneous manifestations, which can impact health-related quality of life (HQoL). Tofacitinib is an oral Janus kinase inhibitor for the treatment of PsA. In two Phase 3 randomised studies, patients (pts) with active PsA treated with tofacitinib experienced greater improvements in various dermatologic endpoints, compared with placebo. As pruritus is a bothersome symptom of skin disease in pts with PsA, we sought to determine how tofacitinib affects HQoL via clinical improvements in skin symptoms including itch.
Objectives: To determine the relationships between tofacitinib treatment, dermatologic symptoms and pt-reported HQoL related to skin disease in PsA.
Methods: Analyses used data (mean scores from Months 1 and 3) from two Phase 3 studies (OPAL Broaden [NCT01877668]; OPAL Beyond [NCT01882439]) of pts with active PsA treated with tofacitinib 5 mg twice daily or placebo; pts

were tumour necrosis factor inhibitor (TNFi)-naïve or had previous inadequate response (IR) to ≥1 TNFi. All pts were treated continuously with a single conventional synthetic DMARD. Mediation modelling, a statistical method used to assess mechanisms underlying observed relationships between different variables via other explanatory variables (mediators), was applied. The mediation model included: treatment, as the independent (explanatory) binary variable (tofacitinib 5 mg BID vs placebo); HQoL, measured by Dermatology Life Quality Index (DLQI), as the dependent (outcome) variable; and two mediators, pt-reported Itch Severity Index (ISI) and Physician's Global Assessment of Psoriasis (PGA-PsO) (a latent variable represented by erythema, induration and scaling). The initial model designated the treatment effect on DLQI mediated via ISI and PGA-PsO as an indirect effect, and treatment effects not attributable to ISI or PGA-PsO as a direct effect (Figure 1).

Results: Data were collected from 468 pts, pooled from both studies. In the initial model (pooled data), the effect of tofacitinib treatment on DLQI was largely mediated by itch (measured by ISI) and PGA-PsO (indirect effect) (p<0.0001); the effect of treatment attributable to factors other than ISI and PGA-PsO (direct effect) was not statistically significant (p=0.66). Results were consistent for pooled and individual study data. Because the direct effect was small and not statistically significant, the model was re-specified to exclude the direct effect of tofacitinib treatment on DLQI. In the revised model (pooled data), 17.7% of the indirect effect was attributable to PGA-PsO (p=0.0006) and 82.3% was attributable to itch (assessed by ISI) (p<0.0001) (Figure 2). Analyses of individual studies using the revised model gave results generally consistent with pooled data.

Conclusion: Dermatology-focused mediation modelling showed that a majority of the effect (~80%) of tofacitinib treatment on DLQI is mediated by improvements in itch, with ~20% mediated via improvements in PGA-PsO.

Figure 1. Initial mediation model

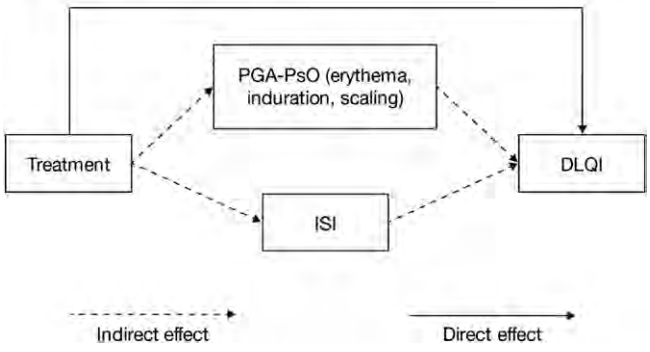
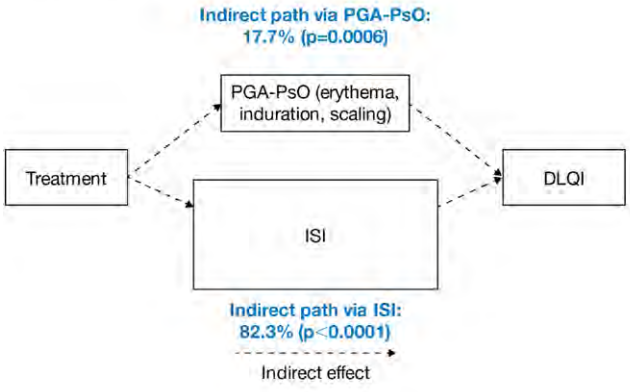


Figure 2. Revised mediation model



Treatment is represented by a binary variable (tofacitinib 5 mg BID vs. placebo).
DLQI, Dermatology Quality of Life Index; ISI, Itch Severity Index;
PGA-PsO, Physician's Global Assessment of Psoriasis.

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AB0838 IDENTIFYING MEDIATORS OF PAIN REDUCTION IN PATIENTS WITH PSORIATIC ARTHRITIS TREATED WITH TOFACITINIB: ROLE OF INFLAMMATION ASSOCIATED WITH PERIPHERAL ARTHRITIS, ENTHESITIS AND SKIN DISEASE

P. C. Taylor[1], K. De Vlam[2], A. G. Bushmakin[3], L. Fallon[4], J. F. Merola[5], J. C. Cappelleri[3], M. A. Hsu[3], P. J. Mease[6]. *[1]University of Oxford, Oxford, United Kingdom; [2]UZ Leuven, Leuven, Belgium; [3]Pfizer Inc, Groton, United States of America; [4]Pfizer Inc, Montreal, Canada; [5]Brigham and Women's Hospital, Harvard Medical School, Boston, United States of America; [6]University of Washington, Seattle, United States of America*

Background: Treatment effect on pain is a priority for patients (pts) with psoriatic arthritis (PsA) and physicians. As pain is multidimensional, there is growing interest to understand the mechanisms of pain relief during treatment. Tofacitinib is an oral Janus kinase inhibitor for the treatment of PsA. Previous analyses showed that the effect of tofacitinib on pain in pts with PsA was partially mediated through improvement of inflammation as assessed by C-reactive protein (CRP) and Swollen Joint Count (SJC). Additional potential inflammation-associated mediators that might contribute to tofacitinib's effect on pain include enthesitis and skin disease.

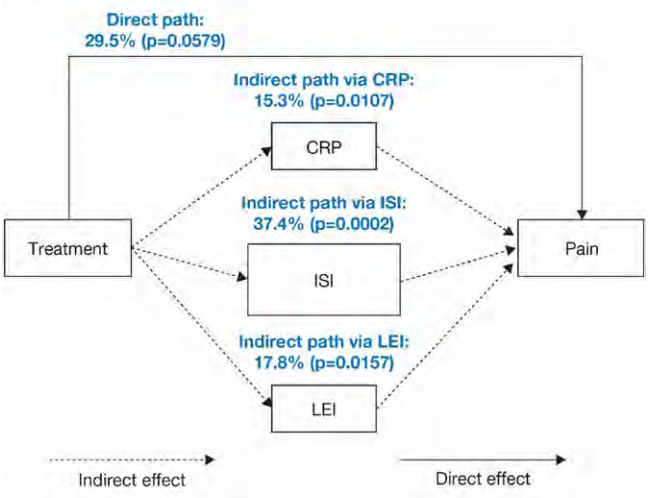
Objectives: To describe the interrelationship between pain, tofacitinib treatment and potential inflammatory-associated outcomes, using mediation modelling.

Methods: Data from two Phase 3 studies (OPAL Broaden [NCT01877668]; OPAL Beyond [NCT01882439]) of pts with active PsA treated with tofacitinib 5 mg twice daily (BID) or placebo were used; pts were tumour necrosis factor inhibitor (TNFi)-naïve or had previous inadequate response to ≥1 TNFi. All pts were treated continuously with a single conventional synthetic DMARD. Analyses were completed using pooled and individual study data at Months 1 and 3 (using mean scores across visits). Mediation modelling seeks to explain mechanisms underlying observed relationships between independent and dependent variables via other variables (mediators). This initial model included: treatment as the independent (explanatory) binary variable (tofacitinib 5 mg BID vs placebo); pain, measured by Patient's Assessment of Arthritis Pain (VAS, 0–100 mm), as the dependent (outcome) variable; mediators were: pt-reported Itch Severity Index (ISI); CRP; SJC; Psoriasis Area and Severity Index (PASI); and enthesitis, measured by Leeds Enthesitis Index (LEI) or Spondyloarthritis Research Consortium of Canada Enthesitis Index (SPARCC). The final model was revised based on results of the initial model.

Results: The initial model (N=329; pooled data) showed that tofacitinib treatment affects pain mainly indirectly via ISI, CRP, SJC, PASI and enthesitis (LEI), with 16.0% (p=0.53) attributable to the direct effect. The indirect effect via SJC (<1%) was not significant (p=0.99); the indirect effect via PASI was contradictory (-14.4%, p=0.10). The final model (Figure 1) excluded SJC and PASI. Analysis of the final model (N=468; pooled data) revealed that 29.5% (p=0.0579) of tofacitinib treatment effect on pain was attributable to the direct effect, and 70.5% (p<0.0001) was attributable to the indirect effect. ISI, LEI and CRP mediated 37.4% (p=0.0002), 17.8% (p=0.0157) and 15.3% (p=0.0107) of the tofacitinib treatment effect on pain, respectively. Results for individual studies were consistent with pooled data, as were those when enthesitis was represented by SPARCC in the model.

Conclusion: The majority of tofacitinib treatment effect on pain in pts with PsA is collectively mediated by itch, enthesitis and CRP, with itch being the main mediator of treatment effect (~37%), using mediation modelling analyses.

Figure 1. Final mediation model



Treatment is represented by a binary variable (tofacitinib 5 mg BID vs placebo); pain was measured by Patient's Assessment of Arthritis Pain (VAS, 0–100 mm); inflammation was measured by CRP.

BID, twice daily; CRP, C-reactive protein; ISI, Itch Severity Index; LEI, Leed Enthesitis Index; VAS, Visual Analogue Scale

Acknowledgments: Study sponsored by Pfizer Inc. Medical writing support was provided by Eric Comeau of CMC Connect and funded by Pfizer Inc.

Disclosure of Interests: Peter C. Taylor Grant/research support from: Celgene, Eli Lilly and Company, Galapagos, and Gilead, Consultant of: AbbVie, Biogen, Eli Lilly and Company, Fresenius, Galapagos, Gilead, GlaxoSmithKline, Janssen, Nordic Pharma, Pfizer Roche, and UCB, Kurt de Vlam Grant/research support from: Celgene, Eli Lilly, Pfizer Inc, Consultant of: AbbVie, Eli Lilly, Galapagos, Johnson & Johnson, Novartis, Pfizer Inc, UCB, Andrew G Bushmakin Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Lara Fallon Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Joseph F. Merola Consultant of: Merck, AbbVie, Dermavant, Eli Lilly, Novartis, Janssen, UCB Pharma, Celgene, Sanofi, Regeneron, Arena, Sun Pharma, Biogen, Pfizer, EMD Sorono, Avotres and LEO Pharma, Joseph C Cappelleri Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Ming-Ann Hsu Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Philip J Mease Grant/research support from: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Eli Lilly, Novartis, Pfizer, Sun Pharmaceutical, UCB – grant/research support, Consultant of: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Eli Lilly, Novartis, Pfizer, Sun Pharmaceutical, UCB – consultant, Speakers bureau: Abbott, Amgen, Biogen Idec, BMS, Eli Lilly, Genentech, Janssen, Pfizer, UCB – speakers bureau

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AB0839

RELIABILITY OF COMPOSITE MEASURES FOR THE ASSESSMENT OF PSORIATIC ARTHRITIS

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Background: Composite measures of disease activity have been developed for use in Psoriatic Arthritis (PsA) to capture the wide spectrum of disease but there is a lack of consensus regarding which to adopt for routine practice. It is recognised that more data is required to understand the measurement properties of existing instruments and consider the impact of modifications that may improve face validity, responsiveness or feasibility. It is important to have an estimate of a measurement instrument's reliability in the setting of stable disease in order to understand measurement error and responsiveness. To our knowledge no data exists on the stability of composite measures in PsA.

Objectives: To measure test re-test reliability of composite measures of disease activity in PsA.

Methods: Clinical and patient reported outcomes to enable the calculation of composite measures were administered to 141 patients with PsA at five time points in a UK multicentre observational study. All patients fulfilled the CASPAR criteria. Twenty-nine patients with clinically stable disease and receiving no treatment intervention underwent repeat assessment by the same examiner within 2 weeks. Patients in high and low disease were included. Reliability was evaluated by intra-class correlation coefficient (ICC) and Bland Altman plots.

Results: Of the 29 patients included 15 were male, the mean age was 52.4 years (SD 13.39), mean disease duration at T_0 was 9.2yrs (SD 8.11). The mean swollen joint count was 3.4 (SD 5.1), tender joint count 11.3 (SD 15.03) and PASI 1.0 (SD1.04). The ICC (95% CI) for tender and swollen joint counts were 0.94 (0.87-0.97) and 0.91 (0.80-0.96) respectively. The ICC for PASI was 0.95 (0.90-0.98). All composite measures demonstrated high levels of test-retest reliability with ICC >0.85, table. The most reliable measure was the PADAS ICC 0.98 (95% CI 0.954-0.991). The individual ICC for each composite measures are reported in the table and Bland Altman plots, figure.

Conclusion: All composite measures show high levels of test-retest reliability in this cohort. The PASDAS was the most stable measure. Modifications to these instruments can now be tested and the impact compared to the original versions.

Table. Test Re-Test reliability of each composite measure

	Intraclass Correlation Coefficient (95% Confidence Interval)
GRACE	0.929 (0.842-0.968)*
CPDAI	0.852 (0.635-0.940)*
PASDAS	0.978 (0.954-0.991)*
DAPSA	0.922 (0.831-0.964)*
3VAS	0.915 (0.815-0.960)*
RAPID3	0.899 (0.782-0.953)*

Disease Activity Index for PsA (DAPSA), PsA Disease Activity Score (PASDAS), Composite Psoriatic Disease Activity Index (CPDAI), GRAppa Composite Exercise (GRACE), 3 Visual Analogue Scale (3VAS), Routine Assessment of Patient Index (RAPID3), *P<0.001

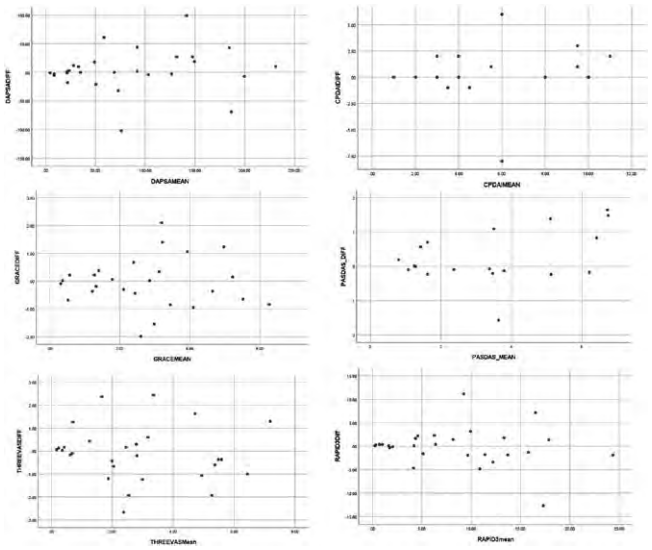


Figure. Bland Altman plots for each composite measure

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AB0840

INFLUENCE OF PSORIATIC ARTHRITIS (PSA) ON BONE LOSS AND ANALYSIS BETWEEN AXIAL AND PERIPHERAL PSA IN JAPANESE PATIENTS

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Background: Osteoporosis is one of the major comorbidities in patients with psoriasis and psoriatic arthritis (PsA). It has been reported that PsA induces fragility bone structure[1] and high risk of osteoporosis[2]. However, there is no report about relationship between psoriatic arthritis and osteoporosis in Japanese patients and its mechanism has not been elucidated.

Objectives: The objective of this study is to investigate influence of PsA on bone mineral density (BMD) and its mechanism including analysis between axial and peripheral PsA in Japanese patients.

Methods: This study was retrospective study. We examined 58 cases of PsA and 29 cases of RA that underwent DXA tests at our facility from January 2017 to July 2019 (Table 1). The axial PsA was classified as axial SpA using the ASAS classification criteria. First, we investigated influence of PsA containing both axial (n=30,19 males, 11 females, mean age: 50.6 years) and peripheral (n=28, 19 males, 9 females, mean age: 58.0 years) subtypes on BMD measured by dual-energy X-ray absorptiometry. Second, we measured serum bone metabolism markers (P1NP: type I procollagen-N-propeptide, TRACP-5b: tartrate-resistant acid phosphatase 5b) and bone remodeling effector molecules (Dkk1: Dickkopf1, sclerostin, 25(OH)D: 25-hydroxyvitamin D) to elucidate differences in BMD between axial and peripheral PsA. Furthermore, rheumatoid arthritis (RA) (n=29, 2 males, 27 females, mean age: 66.2 years), as a reference disease, was also evaluated for comparison with axial and peripheral PsA.

Osteoporosis and Osteopenia were defined as T-score ≤ -2.5 or %YAM ≤70%., -1.0< T-score >-2.5 or 80>%YAM >70% respectively.

Results: 58 patients with PsA indicated low T-score, Z-score and %YAM in both lumbar spine and proximal femur (Table 1). Axial PsA and peripheral PsA showed osteoporosis in 16.7% and 35.7%, and osteopenia in 20.0% and 32.1%, respectively, despite the fact that there were many middle-aged men. Comparison between axial and peripheral PsA, axial PsA showed higher BMDthan peripheral PsA. In bone remodeling makers, P1NP in both PsA were almost same, but TRACP-5b, bone resorption marker, in axial PsA was lower than that in peripheral PsA(Table 2). In bone remodeling influencer molecules, Dkk1, and sclerostin in axial PsA was slightly higher than those in peripheral PsA, whereas 25(OH)D is almost same as the both PsA. On the other hand, RA also indicated low T-score and %YAM in both lumbar spine. P1NP in RA showed slightly lower, but TRACP-5b and Homocysteine in RA higher than those in axial and peripheral PsA. Dkk1 and sclerostin in RA were slightly lower than those in both PsA.

Conclusion: Peripheral PsA indicated more severe bone loss than axial PsA in our study. There were some differences in bone remodeling markers and bone remodeling effector molecules between axial and peripheral PsA, but the relationships between BMD and these parameters were not confirmed. Further studies are needed to elucidate bone loss mechanism in these PsA.

(Table 1) Characteristic DATA

	Axial-PsA	Peripheral-PsA	RA
n	30	28	29
male (%)	63.3%	67.9%	6.9%
ave.age (y.o.)	50.6±11.1	58.0±10.1	66.2±12.4
Osteoporosis (%)	16.70%	35.70%	41.40%
Osteopenia (%)	20.00%	32.10%	13.80%
DXA			
Lumbar spine			
T-score	-0.77±1.39	-1.95±1.04	-1.84±1.31
Z-score	-0.24±1.63	-0.97±1.36	-0.31±1.24
%YAM	91.9±14.4	79.3±11.2	79.9±14.6
Proximal femur			
T-score	-0.81±1.13	-1.14±0.64	-1.20±1.32
Z-score	-0.07±1.01	-0.19±0.81	0.36±0.94
%YAM	89.3±15.1	84.9±8.57	84.5±16.9
Fracture			
vertebral (n)	2	3	3
Hip (n)	2	0	0

(Table 2) Laboratory DATA and Treatment Drugs

		Axial PsA (n=30)	Peripheral PsA (n=28)	RA (n=29)
Laboratory DATA (ave.)	Homocysteine, g/mol	13.364±4.095	14.525±4.986	368.098±1900.195
	Dkk-1	3782.11±575.975	3427.29±880.759	3093.52±1427.96
	SOST/Sclerostin	153.06±69.38	134.52±106	89.68±62.96
	TRACP-5b, mU/dL	283.5±113.7	355±136.7	410.6±179.1
	ucOC , ng/mL	2.01±1.23	4.91±4.85	3.33±3.08
	25(OH)D, ng/mL	16.08±6.94	17.04±6.06	13.90±5.34
	total P1NP, ng/mL	50.62±19.85	52.74±33.97	39.03±22.73
	CRP, mg/L	8.20±16.4	6.6±20.9	6.6±10.2
Treatment Drugs	TNFinhibitor (n)	6	2	3
	IL-17inhibitor (n)	2	1	0
	IL-12/23inhibitor (n)	2	1	0
	IL-6inhibitor (n)	0	0	2
	Bisphosphonate (n)	3	6	15
	Vitamin D (n)	4	4	15
	Teriparatide (n)	0	1	0
	Prednisolone use (n.mg/d)	0 , -	1, ave.3.0mg/d	10, ave.4.0mg/d

References:

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Disclosure of Interests: Shigeyoshi Tsuji Grant/research support from: Eli Lilly, Speakers bureau: AbbVie, Asahi Kasei, Chugai, Daiichi Sankyo, Eli Lilly, Eisai, Mitsubishi Tanabe, Celgene, and Novartis Pharma K.K., Tetsuya Tomita Consultant of: Eli Lilly and Company, Mari Higashiyama: None declared, Takaaki Noguchi: None declared, Toshikazu Mouri: None declared, Jun Hashimoto Speakers bureau: AbbVie, Asahi Kasei, Chugai, Daiichi Sankyo, Eli Lilly, Eisai, Mitsubishi Tanabe, Celgene, and Novartis Pharma K.K.

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AB0841

TARGET OUTCOMES IN PSA: SIMULTANEOUS ACHIEVEMENT OF ACR50-PASI100 AND BEYOND: INSIGHTS FROM SPIRIT-H2H AT WEEK 24

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Background: Psoriatic Arthritis (PsA) treatment should aim to achieve robust improvement of arthritis as well as control of extra-articular manifestations like the skin. SPIRIT-H2H evaluated the efficacy of ixekizumab (IXE) and adalimumab (ADA) in patients with active PsA and psoriasis, and naïve to biologic Disease-Modifying Anti-Rheumatic Drugs (bDMARDs). At week 24 (W24), IXE showed superiority to ADA in simultaneous achievement of ACR50 and PASI100 as well as significant improvement of treat-to-target and other extra-articular outcomes.

Objectives: To examine and to compare PsA efficacy outcomes in patients beyond achievement of the primary endpoint of the SPIRIT-H2H trial at W24, irrespective of treatment allocation.

Methods: All patients recruited had active PsA (defined as tender joint count ≥3/68, swollen joint count ≥3/66 and body surface area [BSA] ≥3%), and inadequate response to conventional synthetic (cs)-DMARDs. Patients were randomised 1:1 to open-label, assessor-blinded IXE or ADA. We conducted post-hoc analysis of SPIRIT-H2H (NCT03151551), categorizing patients into four independent groups based on the achievement of the primary outcome (ACR50 & PASI100), ACR50 only, PASI100 only or none of them after 24 weeks of treatment. Statistical analyses consisted of mixed model for repeated measurement and logistic regression models using non-response imputation.

Results: At week 24, patients reaching simultaneously ACR50 and PASI100 had a statistically significant higher response in most treat-to-target endpoints than those meeting ACR50 only (p<0.05). In this latter group, a high response rate was observed in ACR70, MDA, DAPSA remission and PASI90 response (48.9%, 60.6%, 35.1%, 36.2%, respectively). In patients that did not achieve either ACR50 or PASI100, up to 1/3 of the patients did achieve ACR20, DAPSA score ≤14, or no physical impairment.

Table. Efficacy Endpoints at W24

	ACR50 & PASI100	ACR50 only	PASI100 only	Neither ACR50 nor PASI100
	n=181	n=94	n=121	n=170
ACR20	100.0 [b,c]	100.0	53.7	34.7
ACR70	64.6 [a,b,c]	48.9	0.0	0.0
MDA	75.7 [a,b,c]	60.6	23.1	12.4
VLDA	32.6 [a,b,c]	13.8	3.3	1.8
DAPSA LDA or Remission (≤14)	92.3 [a,b,c]	81.9	43.0	28.8
DAPSA Remission (≤4)	44.8 [b,c]	35.1	6.6	2.4
HAQ-DI score ≤0.5	75.7 [b,c]	64.9	30.6	27.4
PASI75	100.0 [a,c]	60.6	100.0	37.1
PASI90	100.0 [a,c]	36.2	100.0	14.7
SF-36 PCS change from baseline[§]	12.3±0.53 [b,c]	12.3±0.74	5.4±0.66	4.0±0.55

Data are presented as %; [§]mean±standard error.

[a] p<0.05 vs. ACR50 only; [b] p<0.05 vs. PASI100only; [c] p<0.05 vs. Neither ACR50 nor PASI100.

ACR, American College of Rheumatology; DAPSA, Disease Activity in Psoriatic Arthritis; HAQ-DI, Health Assessment Questionnaire Disability Index; LDA, Low Disease Activity; MDA, Minimal Disease Activity; PASI, Psoriasis Area Severity Index; VLDA, Very Low Disease Activity.

Nine patients with active PsO and BSA≥3% were assessed as PASI=0 at baseline, a medical inconsistency that was resolved using medical judgement. These patients were considered PASI100 responders if PASI=0 and BSA=0 at post baseline visits.

Conclusion: Reflecting the complexity of PsA, different degrees of improvement were observed across all treat-to-target outcomes with greater improvements in patients that met ACR50 response regardless of skin resolution. These findings at week 24 need to be confirmed with a longer duration of treatment.

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AB0842 DISCOVERY OF ARTHRITIS IN PSORIASIS FOR EARLY RHEUMATOLOGIC REFERRAL (DAPPER): A CROSS-SECTIONAL STUDY

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Background: One in three patients with psoriasis (Pso) will develop psoriatic arthritis (PsA) (1). When untreated, this can lead to disability and irreversible joint damage (2). Current screening methods are mostly based on questionnaires. These lack specificity and sensitivity (3,4). Thus, a significant portion of PsA patients remains undetected.

Objectives: Our main objective is to ascertain the prevalence of PsA in a cohort of Pso patient, treated at a dermatology outpatient clinic. Secondary, we wish to make a referral tool for dermatologist to detect patients suspected of PsA.

Methods: A sample of 300 patients, stratified for current skin therapy (topical, systemic non-biologic, biologic), will be screened by a rheumatology resident for PsA signs and symptoms. When PsA is suspected, patients are referred to a rheumatologist for confirmation. We gather information about demography, treatment (past and current) and comorbidity. On top of that, we gather data on disease specifics (age of onset, disease duration, severity). We store biomaterials and DNA. Eventually, all these data will be used to form a more specific prediction model which can be used at the dermatology department for more efficient referral.

Results: We will present preliminary data of the first 100 patients. In this cohort, we found 14 patients with known PsA. 10 patients were suspected of (previously undiagnosed) PsA, and were referred to a rheumatology clinic. Three cases were confirmed, and 4 are still under analysis. This makes the prevalence of PsA in Pso 17-21%. Of these three new cases, one was treated with topical therapy only, one was treated with a biologic, and one received targeted therapy. In the patients with PsA, we found a higher amount of men. On top of that, we found a trend towards more intensive therapy. This may be due to indication bias, were the presence of arthritis may lead to a more aggressive treatment. Interestingly, 2 of the 3 previously undiagnosed PsA patients were treated with a biological for their skin symptoms.

Conclusion: Preliminary data of the DAPPER study reveal that the prevalence of confirmed PsA in Pso patients is 17%. If all suspected PsA are confirmed, this rises to 21%. Even under systemic biologic treatment, arthritis can still be active.

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AB0843 PSORIATIC ARTHRITIS PATIENTS ACHIEVING DAPSA REMISSION/LOW DISEASE ACTIVITY HAVE BETTER LONG-TERM FUNCTIONAL OUTCOMES

L. Vargas Cruz[1], J. Boechat Farani[2], J. Rabello Costa[3], F. Menegat[4], J. V. Andrade Águas[5], B. Ruschel[6], A. A. Gasparin[2], C. Brenol[2], C. Kohem[2], P. Palominos[2]on behalf of Rheumatology Department. Hospital de Clínicas de Porto Alegre, Brazil Universidade Federal do Rio Grande do Sul, Brazil. *[1]Hospital de Clínicas de Porto Alegre, Rheumatology, Porto Alegre, Brazil; [2]Hospital de Clínicas de Porto Alegre, Rheumatology, Porto Alegre, Brazil; [3]Universidade Federal do Rio Grande do Sul, Medicine, Porto Alegre, Brazil; [4]Hospital de Clínicas de Porto Alegre, Pesquisa Clínica, Porto Alegre, Brazil; [5]Universidade Federal do Rio Grande do Sul, Medicine, Porto Alegre, Brazil; [6]Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil*

Background: Patients with psoriatic arthritis (PsA) experience substantial functional impairment, which impacts on health-related quality of life.[1] Evidence from randomized clinical trials (RCTs) suggests better patient-reported functional outcomes when lower disease activity is achieved.[2,3,4]

Objectives: To evaluate the impact of achieving DAPSA remission (REM) or low disease activity (LDA) on long term function measured by HAQ-DI. To verify predictors of achieving a minimum clinically important difference (MCID) in HAQ-DI (≤ -0.35).

Methods: This is a longitudinal analysis of a real-life retrospective cohort. Inclusion criteria were adult patients fulfilling CASPAR criteria for PsA with at least 4 years of follow-up in the PsA Clinic. Demographic and clinical data were extracted from electronic medical records. Comparison of HAQ-DI variation between patients with DAPSA REM/LDA and those with moderate/high disease activity was performed using generalized estimating equation (GEE), adjusted by Bonferroni test. Correlation between HAQ-DI and DAPSA was analyzed by Spearman correlation method. A multivariate hierarchical regression model was applied in order to evaluate predictors of achieving a MCID in HAQ-DI scores.

Results: Seventy-three patients were included in the analysis, of which 58.9% were female, with a median (25/75th) of 8 (3-15) years since PsA diagnosis and a mean follow up time of 6.2±1.2 years. In total, 37% of patients (N=27) presented a MCID in HAQ-DI during the follow-up. Function measured by HAQ-DI was determined by PsA disease activity measured by DAPSA (interaction test: $p < 0.0001$) (Figure 1). A moderate and statistically significant correlation between ΔDAPSA and ΔHAQ-DI was observed ($r_s = 0.60$; $p<0.001$) (Figure 2), demonstrating that a decrease in PsA disease activity was associated to improvement in function. Only patients in DAPSA REM demonstrated a constant declining in HAQ-DI scores during the 6 years of follow-up (Figure 1). White ethnicity and older age at baseline were predictors for not achieving MCID in HAQ-DI (RR 0.33 95% CI 0.16-0.67, p=0.002 and RR 0.96 95% CI 0.93-0.98, p<0.0001, respectively), while higher scores of HAQ-DI at baseline were predictors of achieving a MCID (RR 1.71 95%CI 1.12-2.60, p=0.013).

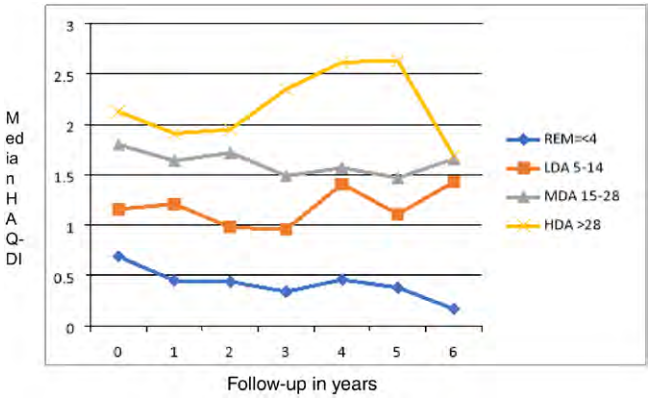


Figure 1. Variation in HAQ-DI according to PsA disease activity measured by DAPSA

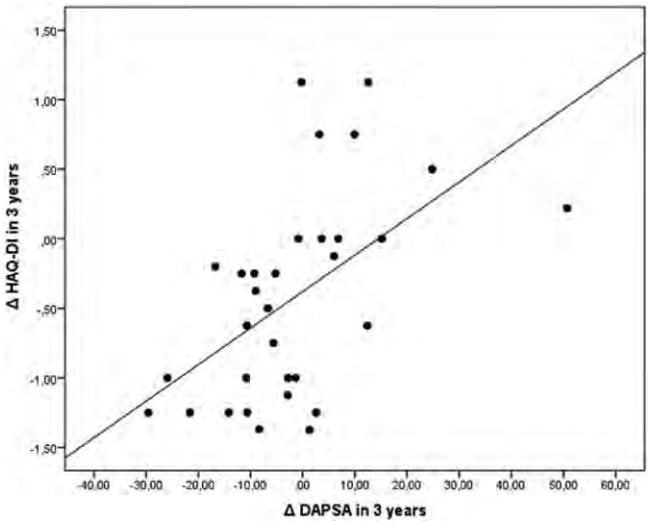


Figure 2. Correlation between changes in PsA disease activity (ΔDAPSA) and changes in functional indices (ΔHAQ-DI) over three years of follow-up

Conclusion: In PsA, patients who maintained DAPSA REM/LDA over time had better long term functional outcomes. Higher HAQ-DI scores at baseline, non-white ethnicity and younger age were predictors for achieving a clinical significant improvement in HAQ-DI.

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Median HAQ-DI

Follow-up in years

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AB0844

SERUM SCD40L LEVEL CAN PREDICT SHORT-TERM CLINICAL OUTCOMES IN PATIENTS WITH PSORIATIC ARTHRITIS ON TREATMENT WITH APREMILAST.

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Background: The pathogenesis of Psoriatic Arthritis (PsA) involves several pathways simultaneously, including the CD40/CD40L interaction. In vitro evidence suggests that the cleavage of soluble CD40L (sCD40L) may happen as a Phosphodiesterase 4- (PDE4) dependent reaction [1-3].

Objectives: Here we investigate whether apremilast, a PDE4 inhibitor, could modify circulating level of soluble CD40L (sCD40L) in PsA patients, and the possible associations of these changes with clinical response.

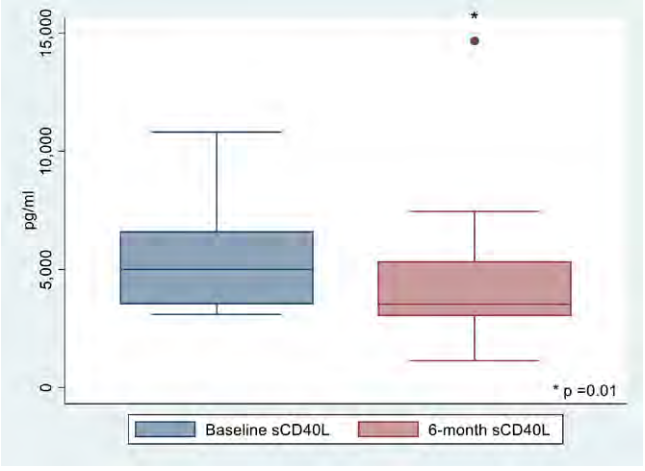
Methods: Consecutive patients with PsA starting apremilast in routine clinical practice between October 2018 and September 2019 in a single center were longitudinally observed. Sera were collected at baseline and at the 6-month follow up visit. Demographics and clinical characterstics at different observation times were recorded. Samples were ran in a Bio-Plex ProTM plate for sCD40L level. To investigate the association of sCD40L level with DAPSA minor response and DAPSA Low Disease Activity (LDA) and/or Remission (ie DAPSA ≤14) at 6 months of treatment, multivariate logistic regression models with backward selection (p <0.05) were built.

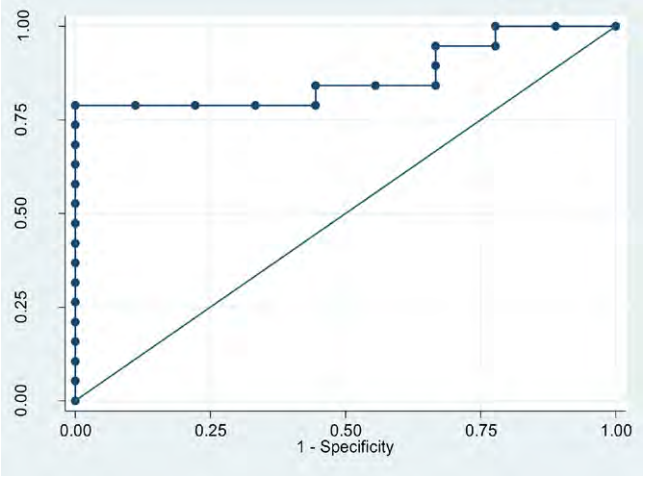
Results: We studied n.27 patients (16/27 women, 59.6%) with PsA with mean age (± SD) of 58.4 ± 10.4 years. A significant reduction of the mean values of DAPSA, LEI and PASI was evidenced at 6 months. Mean serum level of sCD40L decreased from 5364.02 ± 2025.70 to 4412.14 ± 2629.81 pg/ml after 6 months of apremilast treatment (p=0.01, Figure 1). Baseline sCD40L was an independent predictor of DAPSA minor response (OR 1.0006, 95% CI 1.0001-1.0012; AUC 0.76 (95% CI 0.55-0.97)). Moreover baseline DAPSA (OR 0.80, 95% CI 0.65-0.98) and baseline sCD40L (OR 1.001, 95%CI 1.0001-1.0028; AUC 0.85 95% CI 0.69-0.98, Figure 2) were independently associated with DAPSA LDA/Remission.

Conclusion: Apremilast may decrease sCD40L level in PsA patients. Higher baseline serum sCD40L level may predict short-term clinical response to apremilast.

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AB0845 TOFACITINIB IMPROVES DISEASE ACTIVITY AND PATIENT-REPORTED OUTCOMES (PROS) IN PATIENTS (PTS) WITH ACTIVE PSORIATIC ARTHRITIS (PSA) IN REAL CLINICAL PRACTICE.

T. Korotaeva[1], L. Vorobyova[1], E. Loginova[1], E. Gubar[1], Y. Korsakova[1], S. Glukhova[1], P. Karpova[1]. *[1]Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Background: PsA is a disease with multiple manifestations; it has significant impact on physical and emotional aspects of pts' life. PROs as well as disease activity are an important instrument for assessing treatment response. Tofacitinib (TF) is an oral Janus kinase inhibitor; in RCT TF demonstrated efficacy in active PsA pts concerning PROs [1] but there is currently no evidence from real clinical practice.

Objectives: to study the influence of TF on disease activity and PROs in 3/6 months (mo) of therapy in pts with active PsA in clinical practice.

Methods: 41(M/F=24(58.5%)/17(41.5%) PsA pts fulfilling the CASPAR criteria were included. Mean age 42.4±10.3 years (yrs), median (Me) PsA duration 72 [35;120] mo, pts had inadequate response to conventional synthetic disease-modifying antirheumatic drugs (csDMARDs, mostly Methotrexate)/biological (b) DMARDs (29% of pts). Pts were treated with TF 5 mg twice daily after signing consent participation forms. At baseline (BL) and in 3/6 mo of therapy PsA activity was evaluated by Tender Joint Count (TJC68), Swollen Joint Count (SJC66); PGA, physician global assessment by Visual Analog Scale (VAS), DAPSA. PROs were measured by PtGA VAS, PtPain VAS, BASDAI, HAQ, DLQI, RAPID, FACIT, PsAID12, **P**atient-**A**cceptable **S**ymptom **S**tate (PASS) of PsAID12≤4. PsAID12 was analyzed as a change above the minimal clinical important difference (MCID) -1.25 points [2]. Higher PsAID12 scores are considered to be worse and correspond to poorer PsA-specific health-related quality of life. M±SD, Me [Q25; Q75], %, t-test, Pierson-χ^2, Manna-Whitney tests were performed. All p<0.05 were considered to indicate statistical significance.

Results: At BL 87.8% of pts had high PsA activity by DAPSA. By 3/6 mo of therapy significant improvement in all PsA activity indexes and PROs were observed (table 1) (for all p<0.0001). By 6 mo of therapy DAPSA remission was seen in 11 out of 41 pts (26.8%). After 3/6 mo of therapy all PsAID12 domains demonstrated significant improvement (p<0.0001) (Figure 1). The PsAID12 improvement above MCID in -1.25 points reached 90.2% of pts by 6 mo. In 3/6 mo of therapy PsAID12 PASS was achieved in 66.7%/71.8% pts accordingly.

Table 1. Change in all evaluated parameters from BL to 3/6 mo.

Parameters, M±SD	BL	3 mo	6 mo
TJC68	18.1 ±9.8	6.3±6.9*	4.9±5.0**
SJC66	12.8±7.7	3.7±4.3*	2.5±4.0**
BASDAI	6.0±1.7	2.2±1.63*	1.77±1.42**
DAPSA	44.2±17.1	15.2±12.4*	11.8±9.4**
CRP (mg/l)	27.4±29.3	5.1±7.8*	6.2±11.6**
PtPain, VAS, mm	65 [50; 75]	20 [10;30]*	18 [5;30]*
PtGA, VAS, mm	70 [50; 80]	23 [14; 35]*	20 [10; 30]**
ESR (mm/h)	32±25.5	14.8±16,3*	13.6±16.3**
Total PsAID12 score (over past week, 0-10)	5.18±2.14	2.07±1.65*	1.68±1.48**
PsAID12 PASS, %	25.6	66.7	71.8
HAQ	1 [0.625; 1.5]	0.5 [0.125; 0.875]*	0.5 [0; 0.875]**
DLQI	5 [2; 12]	2 [0; 6]*	2 [0; 4]**
FACIT	29 [23;38]	39.5 [31.5; 48]*	38 [32;45]**
RAPID	16 [13.3; 18.6]	6.5 [3.7; 9.1]*	5 [2.3; 8.3]**

*p<0.0001 – differences from BL to 3 mo; ** p<0.0001 – differences from BL/6 mo;

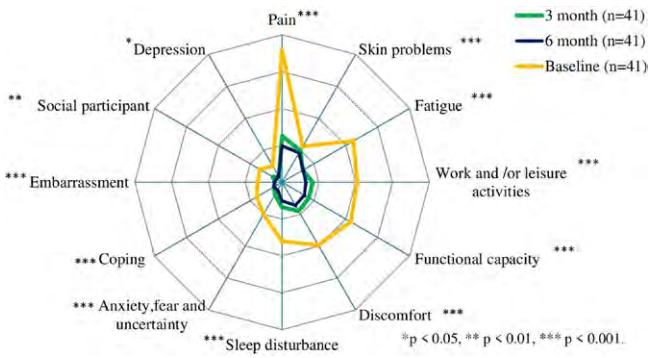


Figure 1. PsAID12 domains at BL and at 3/6 mo of TF treatment.

Conclusion: In real clinical practice TF provides significant and clinically considerable improvement of PsA activity and PROs, including pain, psychological and emotional status.

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Disclosure of Interests: Tatiana Korotaeva Consultant of: Pfizer, MSD, Novartis, AbbVie, Celgene, JSC BIOCAD, Janssen, UCB, Lilly and Novartis-Sandoz, Speakers bureau: Pfizer, MSD, Novartis, AbbVie, Celgene, JSC BIOCAD, Janssen, UCB, Lilly and Novartis-Sandoz, Lyubov Vorobyova: None declared, Elena Loginova Speakers bureau: Janssen, ELENA GUBAR: None declared, Yulia Korsakova: None declared, Svetlana Glukhova: None declared, Polina Karpova: None declared

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AB0846 HIGH DEGREE OF CLASSIFICATION CRITERIA FULFILLMENT AMONG PATIENTS WITH CLINICAL PSORIATIC ARTHRITIS DIAGNOSES IN SWEDEN

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Background: The clinical diagnosis of psoriatic arthritis (PsA) may be challenging. In Sweden, the vast majority of PsA cases are diagnosed within rheumatology or internal medicine (IM). Knowledge of the correspondence between clinical ICD diagnoses and classification criteria fulfillment is crucial to interpret studies identifying cases based on ICD codes.

Objectives: To assess the degree to which patients with clinical PsA diagnoses in Sweden fulfill established PsA classification criteria.

Methods: Four hundred patients with ≥1 outpatient physician visit to one of five rheumatology or IM departments (3 university/2 county departments, spread across Sweden) 2013-2015 with a main ICD-10 diagnosis of PsA (L40.5/M07.0-M07.3), were randomly selected from the Swedish National Patient Register (80 cases/site). Based on a structured medical record review, positive predictive values (PPV) of a clinical PsA diagnosis (i.e. ≥1 visit with a PsA ICD-10 code) for fulfillment of the following classification criteria were assessed: CASPAR,[1] Moll & Wright,[2] Vasey & Espinoza,[3] and Modified ESSG criteria for PsA,[4] respectively (as well as for any of these); ASAS criteria for peripheral or axial spondyloarthritis (SpA) [5]; and the 1987 ACR criteria for rheumatoid arthritis (RA).[6] Subanalyses regarding CASPAR fulfillment were also performed restricted to patients with available rheumatoid factor and peripheral X-ray status (central CASPAR items; n=227), and among patients with ≥2 ICD codes for PsA, of which ≥1 from a rheumatology/IM department (n=353).

Results: Out of 400 clinically diagnosed PsA patients, 343 (86%) fulfilled any of the 4 PsA classification criteria, with a PPV for CASPAR fulfillment of 69% (rising to 73-82% in the subanalyses; **Figure 1**). Substantial overlap was seen

regarding fulfillment of the 4 PsA criteria (**Figure 2A**). Moreover, 86% fulfilled the ASAS peripheral or axial SpA criteria, while the 1987 ACR definition of RA was met by 27% – in both cases with the great majority also classifiable as PsA (**Figure 2B**). Most patients not fulfilling any PsA criteria had either no verified arthritis or polyarticular disease (**Table**). Overall, only 6.5% of the clinical PsA diagnoses were judged as clearly wrong by the rheumatologists performing the medical record assessments.

Conclusion: The validity of clinical ICD-10 diagnoses for PsA in the Swedish National Patient Register is good, with a PPV of 86% for the fulfillment of established PsA classification criteria.

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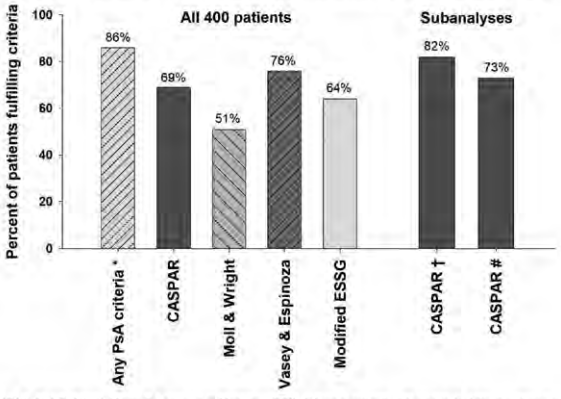
[6] *Arthritis Rheum* 1988;31:315-24

Patient characteristics (n=400), stratified by classification criteria fulfillment

	Fulfilling any PsA criteria n=343	Not fulfilling any PsA criteria n=57
Male sex, %	46	44
Age, yrs; mean (SD)	59 (14)	62 (15)
Symptom duration, yrs; mean (SD)	18 (12)	16 (13)
Psoriasis, %	89	47
Nail psoriasis, %	38	11
Arthritis, %	93	58
Monoarthritis, %*	7.9	0
Oligoarthritis, %*	45	22
Polyarthritis, %*	47	78
DIP-joint arthritis, %	28	7.0
Dactylitis, %	28	1.8
Enthesitis, %	42	19
Inflammatory back pain, %	27	5.3
RF positive, %	5.8	14
ACPA positive, %	4.4	3.5
Arthritic X-ray changes in hands/feet, %	33	21

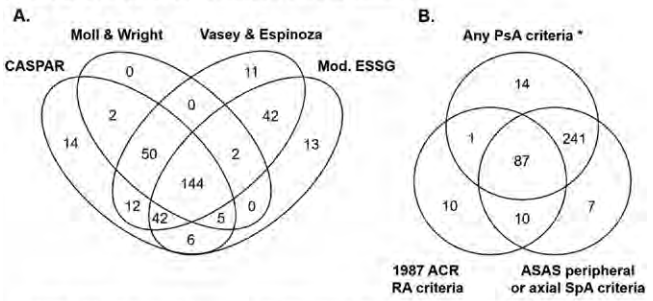
* % of patients with arthritis of known distribution. Missing data: 0-4%, except for RF (33%), ACPA (37%) and X-ray changes (20%).

Figure 1. Fulfillment of classification criteria for psoriatic arthritis



* CASPAR, Moll & Wright, Vasey & Espinoza or Modified ESSG. † Among patients with available data regarding rheumatoid factor and peripheral X-ray status, n=227. # Among patients with >=2 ICD codes for psoriatic arthritis in the Swedish National Patient Register, of which >=1 as main diagnosis from a rheumatology or internal medicine department, n=353. PsA, psoriatic arthritis; CASPAR, CIASsification criteria for Psoriatic ARthritis; ESSG, European Spondyloarthropathy Study Group.

Figure 2. Overlap of classification criteria fulfillment



* CASPAR, Moll & Wright, Vasey & Espinoza or Modified ESSG. CASPAR, CIASsification criteria for Psoriatic ARthritis; ESSG, European Spondyloarthropathy Study Group; PsA, psoriatic arthritis; ACR, American College of Rheumatology; RA, rheumatoid arthritis; ASAS, Assessment of SpondyloArthritis international Society; SpA, spondyloarthritis.

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AB0847

HIGH TOLERABILITY OF USTEKINUMAB IN THE TREATMENT OF PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS – RESULTS OF THE NON-INTERVENTIONAL STUDY SUSTAIN

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Background: Several biologics available for the treatment of psoriatic arthritis (PsA) have demonstrated effectiveness. A major aim of the treating physician is to find the safest treatment for his patients.

Objectives: In this work we analyzed the safety of ustekinumab in the treatment of PsA in a real-world setting.

Methods: The SUSTAIN study is a prospective, multi-center non-interventional study in Germany designed to evaluate long term effectiveness and safety, quality of life, and other patient reported outcomes in patients with active PsA under treatment with ustekinumab in routine clinical care over the course of 160 weeks. Treatment with ustekinumab is according to the label recommendations. In the third interim analysis we evaluated the data of 336 included patients till week 112.

Safety was evaluated based on the following parameters: numbers of adverse events (AEs), serious AEs (SAEs), and physicians' / patients' assessment of tolerability of treatment with ustekinumab. AEs are either reported by the subject voluntarily or are obtained by means of subject interviews at study visits. AE definitions, attribution rules, and severity criteria were pre-specified in the study plan. All AEs / SAEs were recorded and described including information on date of onset, seriousness, severity, outcome, action taken, and relationship to treatment as evaluated by the physician. All AEs were followed to satisfactory resolution or a clinically stable endpoint.

Results: For this analysis 336 patients (57% women) at 75 centers were included. Data for key study visits were obtained for the following numbers of patients: 310 patients at week 4, 237 patients at week 40, 160 patients at week 76, and 108 patients at week 112. A total of 88 SAEs (9.0% of all reported AEs) have been documented through the data cut-off date including SAEs of

the categories musculoskeletal and connective tissue disorders (n=21, 6.3% of all reported AEs), nervous system disorders (n=8, 2.4%), infections and infestations (n=9, 2.7%), neoplasms (n=4, 1.2%), cardiac disorders (n= 7, 2.1%). Overall, 14 (1.4% of all reported AEs) of the 88 SAEs were assessed as related to ustekinumab (Table 1). AEs and SAEs lead to permanent discontinuation of treatment with ustekinumab in 119 and 11 patients, respectively. The vast majority of AEs leading to treatment discontinuation amount to ineffective drug or drug effect decrease (n=84) and psoriatic arthropathy (n=16). The most frequent SAE leading to discontinuation was psoriatic arthropathy (n=4). Tolerability of therapy with ustekinumab was assessed as "very good" or "good" by 98.1% of the treating physicians after 76 weeks and by 100% after 112 weeks (Figure 1 A). Tolerability was assessed as "very good" or "good" by 98.7% of patients at week 76 and by 100% at week 112 (Figure 1 B). Overall, the safety profile of ustekinumab in this population of psoriatic arthritis patients through week 112 was generally consistent with that demonstrated in earlier studies.

Table 1. Summary of adverse events in all patients (N=336)

	n (%)
No. / % of patients	
at risk	336 (100.0)
with adverse event (AE)	269 (80.1)
with AE related to Ustekinumab[1]	188 (56.0)
with AE related to MTX[1]	95 (28.3)
with serious adverse event (SAE)	52 (15.5)
with SAE related to Ustekinumab[1]	11 (3.3)
with SAE related to MTX[1]	3 (0.9)
No. / % of events	
all AE	980 (100.0)
AE related to Ustekinumab[1]	383 (39.1)
AE related to MTX[1]	156 (15.9)
SAE	88 (9.0)
SAE related to Ustekinumab[1]	14 (1.4)
SAE related to MTX[1]	3 (0.3)

[1] 'related' events are events with missing, possible, likely or very likely causality

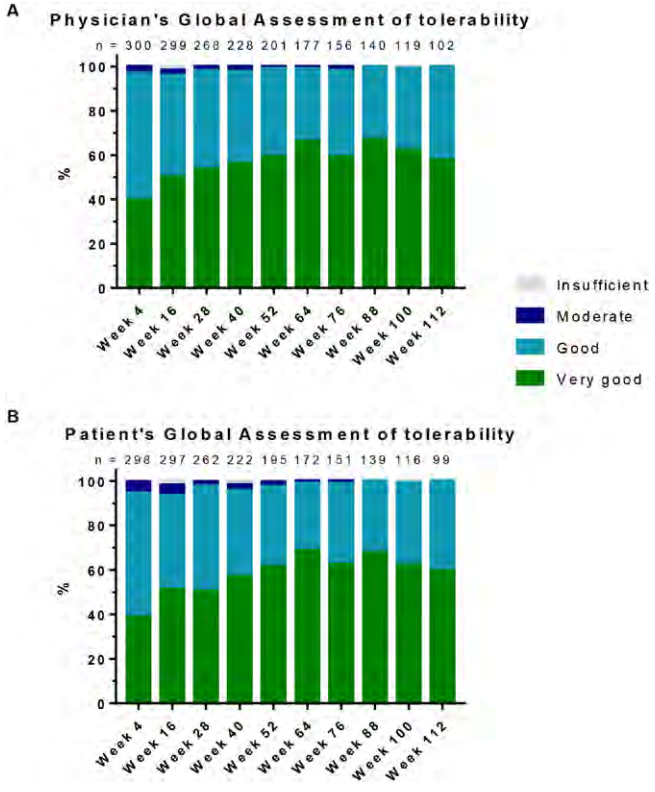


Figure 1. Global Assessments of tolerability

Conclusion: In this interim analysis of safety data from the non-interventional SUSTAIN study, ustekinumab was highly tolerated in the treatment of patients with active PsA in routine clinical practice through up to 112 weeks.

Disclosure of Interests: Joerg Wendler Consultant of: Janssen, AbbVie, Sanofi, Speakers bureau: Roche, Chugai, Janssen, AbbVie, Novartis, Maren Sieburg: None declared, Evgenia Movshovich: None declared, Nils Damann: None declared, Frank Behrens Grant/research support from: Pfizer, Janssen, Chugai, Celgene, Lilly and Roche, Consultant of: Pfizer, AbbVie, Sanofi, Lilly, Novartis, Genzyme, Boehringer, Janssen, MSD, Celgene, Roche and Chugai

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AB0848 IS THERE A WINDOW OF OPPORTUNITY IN EARLY PSORIATIC ARTHRITIS? RETROSPECTIVE DATA FROM A REAL LIFE SETTING

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Background: In early rheumatoid arthritis (ERA) a window of opportunity (WoO) is well established since its first proposal in 2002 (1). ERA patients achieved a better clinical outcome when DMARD therapy was initiated within the first 12-16 weeks after start of symptoms (disease duration (Xd) (2). To the best of our knowledge, comparable data are missing for early psoriatic arthritis (EPsA), even though the benefit of tight control is known in EPsA (3,4). In contrast to ERA early PsA is usually defined as Xd <24months (3,4).

Objectives: To study in a setting of routine rheumatologic care if a WoO like in ERA also can be observed in EPsA comparable to ERA.

Methods: n=90 consecutive outpatients with definite PsA were recruited in this retrospective longitudinal cohort study with the following inclusion criteria: DMARD- and steroid-naïve at the first time of visit in our outpatient clinic (t0), minimum follow-up of 3 years, classification as very early psoriatic arthritis (VEPsA, Xd≤3 months, n=30), late early psoriatic arthritis (LEPsA, > 3 Xd ≤ 12 months, n=30) and late psoriatic arthritis (LAPsA, Xd > 36 months, n=30). Standardized assessments had been performed at regular intervals of 3 months within the framework of routine rheumatologic care. Outcome at 3 years (t36) was analyzed within groups and between groups (DAS28, Physician Global Assessment (PhG), HAQ, fatigue, morning stiffness).

Results: Cohorts did not differ between gender and age (mean age 54 years). There was no significant difference in DAS28, HAQ, PhG and morning stiffness at t0. Fatigue at t0 differed between cohort 1 and 3 significantly ($p<0.03$). In all cohorts DAS28 and PhG have been decreased at t36 significantly (minimal $p< 0.006$). In comparison to VEPsA LEPsA showed a significant difference in DAS28 ($p<0.04$) and PhG ($p<0.05$), but not in morning stiffness and fatigue. Highly significant differences between VEPsA and LAPsA were observed for DAS28 ($p <0.007$), morning stiffness ($p < 0.001$), PhG ($p<0.05$) and fatigue ($p < 0.006$) at t36.

Conclusion: Significant and relevant differences between the outcomes at 3 years of patients with VEPsA, LEPsA and LAPsA could be identified in this retrospective pilot study. Particularly the highly significant difference between VEPsA and LAPsA (<3 months vs. >36months) is remarkable. The data suggest a window of opportunity also in patients with EPsA. With a time interval of Xd≤12 this window seems to be longer than in ERA. Further studies with higher number of patients were needed to confirm our findings from this real life setting.

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AB0849

FATIGUE IN PSORIATIC ARTHRITIS – PREVALENCE AND IMPACT IN DAILY RHEUMATOLOGIC OUTPATIENT CARE

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Background: Fatigue is a major problem in various rheumatic diseases. Only a few studies so far have focused on the occurrence of fatigue in psoriatic arthritis (PsA) (1).

Objectives: The aim of this study was to explore the prevalence and impact of fatigue in patients with PsA and its potentially association with disease activity in daily routine rheumatologic care.

Methods: 105 consecutive outpatients with definitive PsA (mean age 62 years, mean disease duration 8 years) were included in this prospective study. Patients received a clinical examination and laboratory tests. Furthermore, following assessments were used: assessment of disease activity (patient (PG) and physician global (PhG), NRS, 0-10), DAS28, CDAI, pain (NRS, 0-10), HAQ, SF-36, fatigue (NRS (0-10) and Chalder Fatigue Scale (CFS; bimodal: 0-3 no fatigue, 4-11 fatigue; Likert scale: 0-3 no fatigue, 4-33 fatigue, 19-33 severe fatigue/ chronic fatigue syndrome) (2).

Results: In the CFS questionnaire 56/105 patients (53%) were classified as fatigue cases (bimodal score >4). 22/105 (21%) suffered from severe fatigue/ chronic fatigue syndrome (score > 19, Likert scale). Mean fatigue was 14,9 (CFS, Likert Scale) and 4,5 (NRS). In n=47 (45%) patients fatigue was present <3 months, in 22 (21%) patients 3-6 months, whereas in n=34 (32%) >6 months. Intraday fatigue occurred in 75-100% of full daytime in 20 patients (19%).

An extensive impairment of the health related quality of life has been shown in all categories of SF36 (PF=46; RP=52, BP=42, GH=53, VI=45, SF=74, RE=51, MH=68). Fatigue strongly correlated with 6 dimensions of SF36: RP r= -0,61, BP r= -0,73, GH = -0,66, VI r= -0,79, SF r= -0,54, MH r= -0,59.

On average disease activity was low (mean DAS28 = 2,5) with a range from 0,5 to 7,8.

Fatigue strongly correlated with the PG (r=0,72) as well as with DAS28 (r=0,49), CDAI (r=0,57), pain (r=0,71), tender joint count (r=0,41) and HAQ (r=0.57). The PhG showed only a poor correlation with fatigue (r=0,29). There was no correlation with ESR (r= -0,01), CRP (r=0,14) and swollen joint count (r=0,17).

63/105 (60%) patients were in DAS28 remission (DAS28 < 2.6) but 24/63 (38%) of them suffered from fatigue. 39/105 (37%) patients were exhibiting DAS28 disease activity (DAS28 > 2.6). All these patients suffered from fatigue, 29/39 (74%) had severe fatigue.

Conclusion: Our results show that fatigue is a major problem in PsA with relevant impact on the health related quality of life. The relatively high percentage of patients suffering from fatigue despite clinical remission or low disease activity suggests that fatigue could be an independent outcome criterion in PsA that should be considered as an additional dimension of remission.

It seems that the clinical routine assessments of disease activity including laboratory tests and PhG do not identify fatigue in PsA sufficiently. Therefore a standardized acquisition of fatigue should be part of studies and daily routine care for PsA patients.

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AB0850

CUTANEOUS LUPUS ERYTHEMATOSUS DISEASE AREA & SEVERITY INDEX (CLASI) DEMONSTRATES THRESHOLDS FOR DETECTION OF TREATMENT RESPONSE IN A PHASE 2, PLACEBO-CONTROLLED TRIAL OF USTEKINUMAB IN SLE

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Background: In a Phase 2 study, Ustekinumab (UST) showed improvement at week (wk) 24 in the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) response (≥4-point improvement from baseline [BL]) vs placebo (PBO).[1] Post hoc analysis revealed that more patients (pts) on UST vs PBO achieved ≥50% improvement in total CLASI activity score.

Objectives: To examine the relationships of CLASI activity responses to SLEDAI-2K (S2K) mucocutaneous disease responses.

Methods: Adults with SLE (S2K ≥6, ≥1 BILAG A and/or ≥2 BILAG B scores) despite standard of care (SOC) therapy were enrolled. Pts (n=102) were randomized (3:2) to UST ~6 mg/kg IV or PBO at wk 0, followed by UST 90 mg SC or PBO every 8 wks beginning at wk 8 + SOC. S2K index measures complete improvement from BL; S2K Responder Index-50 (S2K RI-50) evaluates partial improvement (≥50%) in S2K rash. CLASI rash: sum of erythema and scale/hypertrophy score. In post hoc analysis, improvement in CLASI activity score at wk 24 was calculated using increasing thresholds of BL disease activity and various cut points of improvement to define treatment response.

Results: Complete improvement from BL in rash was concordant between CLASI and S2K (correlation coefficients [r] ≥0.997, Table 1). There was less agreement between CLASI and S2K RI-50 for assessing partial improvement in rash. Treatment difference (UST vs PBO) in % pts achieving partial improvement in rash was observed for CLASI (60% vs 38.5%), but not S2K RI-50 (51.1% vs 50%). Complete improvement from BL in mucosal ulceration was congruent between CLASI and S2K (r=1). Both instruments demonstrated greater proportions of responders to UST vs PBO. Treatment differences between UST and PBO in achieving ≥20%, ≥35%, and ≥50% improvement from BL in total CLASI activity score were noteworthy at various thresholds of disease activity (Table 2).

Table 1. CLASI Activity Scores vs SLEDAI-2K Activity

24-Week Improvement	Treatment	Activity Measure % (n/N*)		r**
		CLASI Rash	SLEDAI-2K Rash	
100%	PBO	30.8 (8/26)	30.8 (8/26)	1.0000
	UST	28.9 (13/45)	31.1 (14/45)	0.9997
≥50%	PBO	38.5 (10/26)	50.0 (13/26)	0.9996
	UST	60.0 (27/45)	51.1 (23/45)	0.8693
		CLASI Mucosal Ulcer	SLEDAI-2K Mucosal Ulcer	
100%	PBO	66.7 (8/12)	69.2 (9/13)	1.0000
	UST	89.5 (17/19)	89.5 (17/19)	1.0000

*N=Evaluated pts with BL SLEDAI rash present, total CLASI activity score >0, and CLASI rash or mucosal ulcer activity scores >0 in analyses of subcomponents; **Calculated using tetrachoric correlation.

Table 2. Differences in Partial Improvement in Total CLASI Activity Score at Various BL Disease Activity Thresholds

CLASI Total Activity Score	Improvement Threshold (%)	PBO % (n/N*)	UST % (n/N*)	Difference % (UST vs PBO)
BL >0	≥20	54.8 (17/31)	74.5 (38/51)	19.7
	≥35	41.9 (13/31)	60.8 (31/51)	18.9
	≥50	41.9 (13/31)	54.9 (28/51)	13.0
BL ≥4	≥20	58.8 (10/17)	71.9 (23/32)	13.1
	≥35	35.3 (6/17)	62.5 (20/32)	27.2
	≥50	35.3 (6/17)	53.1 (17/32)	17.8
BL ≥6	≥20	53.8 (7/13)	72.0 (18/25)	18.2
	≥35	30.8 (4/13)	60.0 (15/25)	29.2
	≥50	30.8 (4/13)	52.0 (13/25)	21.2
BL ≥8	≥20	58.3 (7/12)	70.6 (12/17)	12.3
	≥35	33.3 (4/12)	58.8 (10/17)	25.5
	≥50	33.3 (4/12)	47.1 (8/17)	13.8

*N=Evaluated pts with BL total CLASI activity score >0, ≥4, ≥6, ≥8 based on post hoc analyses

Conclusion: CLASI demonstrated partial improvement in active mucocutaneous disease that was not captured by S2K RI-50. Treatment effect favoring UST vs PBO was observed across range of thresholds of BL CLASI activity and cut points used to define improvement, which have previously been shown to be clinically meaningful.[2] Findings are based on a limited sample size and treatment duration; results will be confirmed in an ongoing Phase 3 UST trial (NCT03517722).

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Abbvie, GSK, Resolve, AstraZeneca, Amgen, Eli Lilly, EMD Serono, BMS, Viela, Kyowa Kirin, Bevra H. Hahn Grant/research support from: Janssen Research & Development, LLC, George Tsokos Grant/research support from: Janssen Research & Development, LLC, Shawn Rose Employee of: Janssen Research & Development, LLC, Kaiyin Fei Employee of: Janssen Research & Development, LLC, Y Irene Gregan Employee of: Janssen Research & Development, LLC, Robert Gordon Employee of: Janssen Research & Development, LLC, Kim Hung Lo Employee of: Janssen Research & Development, LLC, Ronald van Vollenhoven Grant/research support from: AbbVie, Amgen, Arthrogen, Bristol-Myers Squibb, GlaxoSmithKline (GSK), Janssen Research & Development, LLC, Lilly, Pfizer, Roche, and UCB, Consultant of: AbbVie, AstraZeneca, Biotest, Bristol-Myers Squibb, Celgene, Crescendo Bioscience, GSK, Janssen, Lilly, Medac, Merck, Novartis, Pfizer, Roche, UCB and Vertex, Speakers bureau: AbbVie, AstraZeneca, Biotest, Bristol-Myers Squibb, Celgene, Crescendo Bioscience, GlaxoSmithKline, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, UCB, Vertex

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AB0851 CAROTID ULTRASOUND IN PSORIATIC ARTHRITIS: A CASE-CONTROL STUDY

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Background: Patients with psoriatic arthritis (PsA) have an increased risk of cardiovascular disease (CVD). The carotid ultrasound, which measures both carotid intima-media thickness (cIMT) and carotid plaque (CP), is a non-invasive tool useful in the detection of subclinical atherosclerosis[1]. However, carotid ultrasound differences between PsA patients and general population have not yet been well described.

Objectives: This study aimed to compare the carotid ultrasound characteristics in PsA patients with controls.

Methods: This cross-sectional study included 70 PsA patients that fulfilled the CASPAR (Classification Criteria for Psoriatic Arthritis) criteria and 70 controls subjects matched by age and comorbidities. Patients with a history of previous atherosclerotic CVD (ischemic heart disease, cerebrovascular accident or peripheral arterial disease) and pregnancy were excluded. A clinical history and blood tests were performed. Carotid B-mode ultrasonography was used for measurements of cIMT and the presence of plaques. *Increased cIMT was defined as ≥0.9 mm to 1.1 mm. CP was defined* as a *focal narrowing ≥0.5 mm of the surrounding* lumen or a *cIMT ≥1.2 mm.* Descriptive analysis was done with frequencies (%), mean (±SD) and median (q25-q75), and comparisons with Chi square, Student´s t and Mann-Whitney U tests.

Results: A total of 138 subjects were included. Clinical and demographic characteristics are shown in Table 1. Increased cIMT and right carotid plaque were significantly more prevalent in PsA patients compared to controls *(p*=0.017 and p=0.049, respectively). No significant differences were found in the prevalence of carotid plaque and in the intima-media thickness between the PsA patients and the control group.

Table 1. Clinical and demographic characteristics.

Variable	PsA (n=69)	Controls (n=69)	*P*
Age(mean±SD)	53.58±10.946	53.86±7.313	NS
Women, n (%)	38(55.1)	59(85.5)	**<0.001**
Obese, n (%)	26(37.7)	28(40.6)	NS
Type 2 Diabetes, n (%)	14(20.3)	9(13)	NS
Hypertension, n (%)	27(39.1)	19(27.5)	NS
Dyslipidemia, n (%)	29(42)	24(34.8)	NS
Active smoker, n(%)	15(21.7)	12(17.4)	NS
Disease duration, median (q25-q75)	5(2.5-8)	-	-
Methotrexate, n (%)	46(66.7)	-	-
Biologics, n (%)	23(33.3)	-	-
DAS28-ESR, (mean±SD)	3.74±1.477	-	-
DAS28-CRP, (mean±SD)	2.43±1.088	-	-
DAPSA, median (q25-q75)	35(27.5-58.5)	-	-

Conclusion: Patients with psoriatic arthritis have a higher cardiovascular risk, as proven by the increased cIMT found on carotid ultrasound results. Therefore, it is advisable to perform a carotid ultrasound in patients with PsA to achieve an optimal management of the disease. The rheumatologist must be aware of the importance of performing a complete cardiovascular evaluation to provide a correct treatment in order to lower possible cardiac events.

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Table 2. Carotid ultrasound findings.

Variable	PsA (n=69)	Controls (n=69)	*P*
Any carotid plaque, n (%)	27(39.1)	17(24.6)	NS
Right carotid plaque, n (%)	18(26.1)	8(11.6)	**0.049**
Left carotid plaque, n (%)	19(27.5)	15(21.7)	NS
Increased cIMT, n (%)	9(13)	1(1.4)	**0.017**
Right cIMT, median (q25-q75)	0.58(0.46-0.76)	0.6(0.51-0.69)	NS
Left cIMT, median (q25-q75)	0.58(0.5-0.73)	0.61(0.54-0.78)	NS

Disclosure of Interests: None declared

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AB0852 LONG TERM FOLLOW UP OF VISCOSUPPLEMENTATION WITH DIFFERENT TYPES OF INTRA-ARTICULAR HYALURONIC ACID IN OSTEOARTHRITIS OF THE KNEES

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Background: Knee osteoarthritis (OA) is a progressive degenerative condition resulting in functional loss besides pain and discomfort.[1] The aim of treatment as of today should be joint preservation in order to prevent surgery, alleviation of symptoms and improvement of functions.

Viscosupplementation (VES) with Intra-articular hyaluronic acid (IAHA) injections has been shown to have protective physiochemical functions and may confer disease-modifying, long term effects on the articular cartilage. [2][3] However conflicting guidelines, availability of multiple varieties, and absence of good studies or any treatment protocol has resulted in lack of confidence of the results of IAHA.

Objectives: To determine the Long term effectiveness of VES with various types IAHA in OA in maintaining functional improvement of the knees and evaluate the duration of effect of first and repeat injections of VES.

Methods: From the 15 year retrospective longitudinal study of data of VES with different types of IAHA in our Centre, we evaluated the following outcomes:

1. The WOMAC scores were regularly done on each visit of the study group. Those with maintained improvement in the WOMAC total score were followed and reinjected when the scores started decreasing.
2. All patients who were given Non Animal Source Hyaluronic acid (NASHA) were included in the study. Patients with repeat IAHA were further evaluated for Type of NASHA used and were categorized into 2 groups accordingly:

a. Those with High Molecular weight Hyaluronic acid (HMW-HA) 6-8mg/ml – 6 ml single injections

b. Those with Very High Molecular weight, Cross linked Hyaluronic acid (VHMW-HA) 20- mg/ml – 3 ml injections.

Results: The total number of patients treated over the last 15 years was 1206 with 689 having Kellgren and Lawrence (KL) Grade III OA, and 517 KL Grade IV OA. The data showing distribution of type of IAHA used in the group, the average Gap between the injections with the Range in years for the least gap and the longest gap between the injections, along with the follow up to giving the 3rd injection was given is summarized in Chart 1: Time gap between repeat IAHL injections in OA knees.

Chart 1. Time gap between repeat IAHL injections in OA knees

OA GRADE &	I INJ		II INJ			III INJ	
VISCOUS TYPE	N = 1206	Gap 1	Range	N =782	Gap 2	Range	N = 578
KL GRADE III OA	N = 689		N = 442			N = 314	
Group A:HMW-HA	237	0.92	0.8 -1.6	144	0.87	0.6-1.1	105
Group B:VHMW-HA	452	2.54	1.8-3.4	298	2.43	1.7-2.8	209
KL GRADE IV OA	N = 517		N = 340			N = 340	
Group A:HMW-HA	154	1.02	0.6-1.2	96	0.95	0.5-1.1	75
Group B:VHMW-HA	363	2.01	1.4-2.3	244	1.89	1.4-2.2	189

Gap 1 - Average Time between I & II inj.in years, Gap 2 - Average Time between II & III inj. in years

Range - Being the time in years for the least & the longest Gap between the injections

HMW-HA - High Molecular weight Hyaluronic acid

VHMW-HA - Very High Molecular weight, Cross linked Hyaluronic acid

Conclusion: 1.Repeated VES by IAHA were found to have a long term effect of alleviation of symptoms, improvement of functions and joint preservation and thereby prevention of surgery for a long period.
2.VHMW-HA have a longer duration of action than HMW-HA.
3.Repeat Injections bring about a similar duration of effect as the previous injection.

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Disclosure of Interests: Anish Kumar Aggarwal Speakers bureau: Eli Lilly, Pfizer, Janssen of J&J, Dr. Reddy's, Intas, Torrent, Emcure & Alkem., NAKUL AGGARWAL: None declared, DIPIKA JAIN: None declared

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23. Osteoarthritis

AB0853 IMPACT OF ULTRASONOGRAPHY-DETECTED PES ANSERINE BURSITIS ON PAIN ANDFUNCTION IN PATIENTS WITH PRIMARY KNEE OSTEOARTHRITIS

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Background: Pes anserine bursitis (PAB) is one of the most common causes of knee pain. Hence, this study aimed to compare the pain and function among all primary knee osteoarthritis (KOA) patients with or without ultrasonic-detected PAB and the associated clinical and radiological findings.
Objectives: To compare pain, function, and clinical and radiological findings among primary KOA patients with or without ultrasonography-detected PAB.
Methods: A single-center cross-sectional study was conducted on 245 patients with primary KOA. Patients with more symptomatic knee examined by musculoskeletal ultrasound (MSUS), then according to the presence or abscence of PAB, the patients were categorized into two groups. To differentiate between grades of inflammation of PAB on ultrasonography, the authors developed a semi-quantitative scale (0–2) as follows: Grade 0, normal hyperechoic picture of pes anserine tendons without tendonitis or bursitis; Grade 1, mild hypoechogenicity and/ or mild swelling or mild loss of fibrillar pattern of the pes anserine tendon and/or mild anechoic effusion related to the tendons; and Grade 2, marked hypoechogenicity and/ or large swelling or marked loss of the pes anserine tendon and/or marked anechoic effusion related to the tendons.. Radiological grades of Kellgren–Lawrence were recorded. Pain and functional status was assessed by visual analog scale (VAS), Health Assessment Questionnaire-II (HAQ-II), and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC).
Results: A total of 110 (44.9%) patients were diagnosed with PAB where 91 (82.7%) of them had Grade 1 and only 19 (17.3%) had Grade 2. The presence of PAB was statistically significant related ($P < 0.05$*) with age, VAS, HAQ-II, WOMAC subscales, synovitis, and radiographic Grades 3 and 4. However, there was no statistically significant difference ($P \geq 0.05$) between KOA patients without PAB and KOA patients with PAB, regarding sex, body mass index, baker cyst, and effusion.
Conclusion: The presence of PAB on MUS is associated with increased pain and disability in KOA. MSUS should be more widely used to establish the association between PAB and symptom severity and disability among KOA patients.
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Disclosure of Interests: None declared
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AB0854 METABOLIC FACTORS ASSOCIATED TO CLINICAL HAND OSTEOARTHRITIS IN INDIVIDUALS WITH KNEE PAIN

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Background: There is some evidence supporting associations between metabolic factors, clinical hand osteoarthritis (OA) and radiographic knee OA. However, more studies are needed regarding early knee OA.
Objectives: The aim was to study associations between metabolic factors and clinical hand OA at baseline in a cohort of individuals with knee pain, with and without radiographic knee OA
Methods: In an ongoing five-year longitudinal study of knee pain, hand OA was assessed by clinical examinations in 296 of the included individuals at baseline [1]. BMI, waist circumference (WC) and blood pressure was measured. Body composition was assessed with Inbody 770. Fasting plasma glucose, triglycerides, cholesterol, HDL-and LDL-cholesterol and HbA1c was analysed. Metabolic syndrome (MetS)was present if central obesity (WC ≥94 cm in men and ≥80cm in women) plus any two of the following factors: raised blood pressure (systolic blood pressure ≥ 130 or diastolic blood pressure ≥ 85 mm Hg or treatment of hypertension), raised triglycerides (≥ 1.7 mmol/L or specific treatment), reduced HDL-cholesterol (men < 1.03 mmol/L and women < 1.29 mmol/L or specific treatment), raised glucose (glucose ≥ 5.6 mmol/L, or type 2 diabetes). Hand strength and self-reported disability of the arm, shoulder and hand (quickDASH) was assessed.
The individuals were divided according to having clinical hand OA or not, according to Altman [1]. The associations between background factors and clinical hand OA were calculated by crude logistic regression analyses, adjusting for age and sex.
Results: Fifty-five percent of the individuals in the study was overweight or obese, 40% had MetS and 23% had radiographic knee OA. In total 34% of the individuals had clinical hand OA. The group with hand OA were older, had higher proportion of body fat, fasting plasma glucose, HbA1C, worse quickDASH score and lower hand strength, table 1. Clinical hand OA was significantly associated to higher age (OR 1.04, 95%CI 1.01-1.07), higher fasting plasma glucose (1.56, 1.05-2.30), worse quickDASH (1.04, 1.02-1.06) and lower hand strength (0.99, 0.99 -0.998), but not to proportion of body fat and HbA1c.

Table 1. Descriptives at baseline

	No hand OA Mean (sd)	Hand OA* Mean(sd)	p-value
N	194	102	
Age	**51 (9)**	**53 (8)**	**0.015**
Sex, women, %	69	73	0.374
BMI	26.2 (4.8)	27.1 (4.7)	0.114
Visceral fat area (VFA)	110 (53)	122 (54)	0.070
Percentage of body fat*	**30 (9)**	**32 (8)**	**0.026**
Waist circumferance, cm	95 (13)	97 (13)	0.226
Central obesity, %	77	86	0.067
Raised Blood pressure, %	61	65	0.492
Cholesterol (mmol/l)	5.2 (1.0)	5.4 (1.2)	0.317
Triglycerides (mmol/L)	1.0 (0.6)	1.1 (0.7)	0.078
Raised triglycerides, %	9	16	0.075
LDL-cholesterol (mmol/L)	3.4 (1.0)	3.5 (1.1)	0.416
HDL- cholesterol mmol/L)	1.7 (0.4)	1.8 (0.5)	0.352
Glucose (mmol/L)	**5.4 (0.5)**	**5.6 (1.2)**	**0.010**
HbA1c (mmol/L)	**36 (3)**	**38 (6)**	**0.016**
quickDASH	**11.5 (12.8)**	**21.8 (18.6)**	**<0.001**
Hand strength (N)	**291 (110)**	**252 (103)**	**0.004**

Conclusion: In this cross-sectional study, the only metabolic factor associated with clinical hand OA was fasting plasma glucose. Contrary to other studies, there were no gender differences found. The association between development of clinical hand OA and metabolic factors in individuals with knee pain need to be further assessed in longitudinal studies.

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AB0855 **THE "HORSE SADDLE" SIGN: A NEW ULTRASOUND SIGN FOR OSTEOARTHRITIS**

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Background: Hand Osteoarthritis is one of the most prevalent rheumatic diseases that can give early visible findings by ultrasound where synovial hypertrophy, effusion, osteophytes and articular cartilage decrease stand out. However, these findings, although sensitive, may not be very specific since they are also observed in inflammatory arthritis. Throughout our clinical practice in osteoarthritis, we have seen, over repeated examinations, an specific morphological change of bone not previously described in the literature. It is a bone extension in the head of the phalanx of the finger joints that causes a deformity that we have called "horse saddle" and that is typically located in the proximal and distal interphalangeal joints of the fingers. This sign can be seen in the longitudinal exploration of the palm of the hand by grayscale ultrasound. This sign that we have not found specifically described in the literature reviewed to date is considered to be useful for the diagnosis of osteoarthritis.
Objectives: To Assess the sensitivity and specificity of the "horse saddle" sign in the diagnosis of osteoarthritis.
Methods: An exploratory clinical comparative cross-sectional study where an ultrasound of the hands and comparative radiographs in PA view were performed on patients with osteoarthritis, inflammatory arthritis and healthy patients seen in the Rheumatology clinic of the Vall de Hebron Hospital. Age, sex and time of evolution of the disease were collected as clinical variables. The MCP, PIP and DIP joints from the second to the fifth finger of both hands were viewed with grayscale in longitudinal and transverse plane of both the dorsal and palmar face, assessing for osteophytes, synovitis and the horse saddle sign. A General Electric Logiq S8 machine was used with an 8-13 MHz linear probe. All patients signed an informed consent and approval was obtained from the hospital ethics committee. The statistical analysis was carried out with Stata 15.1.
Results: A total of 38 patients with osteoarthritis, 20 patients with inflammatory arthritis (8 psoriatic, 9 RA, 1 LES, 1 PMR and 1 Sjögren) and 2 healthy patients were assessed. It was found that the horse saddle sign had a sensitivity of 66.7% and specificity of 86.4% in osteoarthritis showing a p-value of 0.052 by means of the chi-square test. 87% of patients with the horse saddle sign had osteoarthritis and only in 2 patients with RA and in the patient with LES. In contrast for osteophytes a sensitivity of 100% was observed with a specificity of 45.45% (p of 0.001) and for synovitis a sensitivity of 53.3% and specificity of 77.27% was observed with p of 0.039.
Conclusion: The horse saddle sign is an ultrasound sign with good sensitivity and specificity for the diagnosis of hand osteoarthritis comparable to other classic ultrasound signs such as osteophytes and synovitis.
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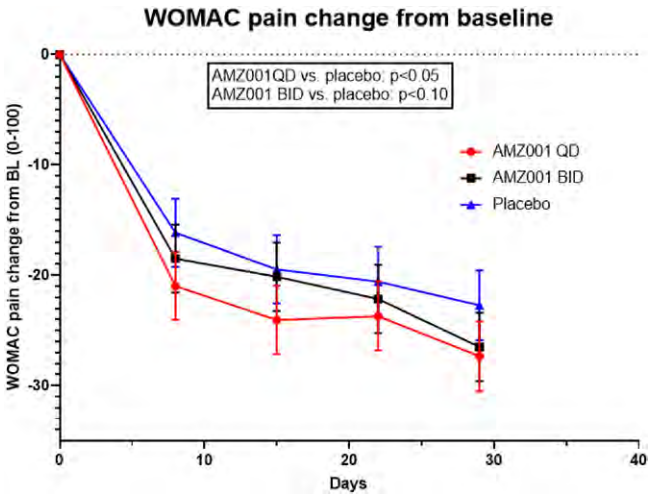
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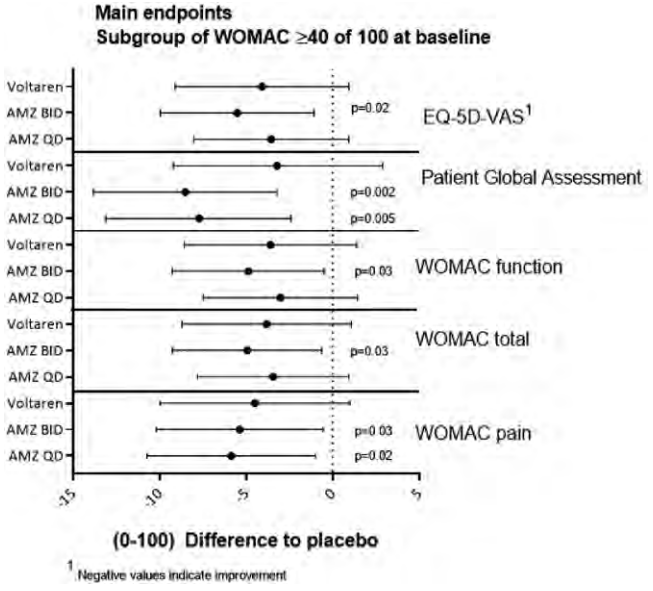
AB0856 **A PLACEBO-CONTROLLED, DOUBLE-BLIND, RANDOMIZED, TRIAL OF AMZ001 – A NOVEL DICLOFENAC SODIUM 3.06% GEL - FOR THE TREATMENT OF KNEE OSTEOARTHRITIS SYMPTOMS**

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Background: Development of improved topical treatments of painful joints is warranted. A novel diclofenac sodium gel formulation, AMZ001, has been developed with the purpose of improving 1) The onset and duration of pain relief, and 2) The ease of use by reducing the required daily frequency of gel application. Previous trials in human subjects have confirmed improved permeability of a reduced volume of AMZ001 gel as compared to approved diclofenac topical products with a comparable safety and tolerability profile, supporting trials to evaluate the efficacy and safety of AMZ001 in painful joint conditions.
Objectives: The current abstract reports the main results of a randomized trial of AMZ001 once or twice daily application versus placebo in symptomatic knee osteoarthritis.
Methods: The trial was a placebo-controlled, parallel group, double-blind, randomized trial to evaluate the efficacy and safety of AMZ001 or placebo in subjects with knee osteoarthritis. The main inclusion criteria were Kellgren-Lawrence radiographic severity of 1-3, and pain ≥40 and ≤90 out of 100 using the WOMAC pain subscale (5 questions) at the time of screening. The subjects were randomized to apply AMZ001 gel once (QD) or twice (BID) daily or placebo twice daily per OA knee for a period of 28 days, or to apply Voltaren® Gel 1 % four times daily (QID) in a single-blind fashion for exploratory comparison. The primary endpoint was change from baseline at week 4 in WOMAC pain (5 questions). The main secondary endpoints included WOMAC subscales, Patient Global Assessment (PGA) and quality of life using the EQ-5D. In addition to the main analysis, a post-hoc subgroup analysis of subjects meeting the pain criterion at both screening and baseline was performed.
Results: A total of 444 subjects were randomized. The main baseline characteristics were well balanced between treatment groups.
AMZ001 QD and BID led to statistically significant reductions in pain compared to baseline with an estimated difference (95% CI) normalized to 0-100 at week 4 of -27.33 (-30.50, -24.17), and -26.49 (-29.60, -23.38), respectively. Reduction in pain at week 4 was statistically significantly superior to placebo for AMZ001 QD (p=0.04), and borderline significant for AMZ001 BID (p<0.10) as shown in Figure 1.



Both AMZ001 QD and BID led to statistically significant improvements in PGA at week 4 compared to placebo (p<0.05 for both), and AMZ001 BID led to significantly improved quality of life (p<0.05) compared to placebo. There were no statistically significant differences between AMZ001 QD or BID in any of the endpoints. In the post-hoc analysis of subjects meeting the pain criterion at both screening and baseline the differentiation to placebo was strengthened for all efficacy endpoints, as shown in Figure 2.



While the study design and differences in sample sizes does not allow formal comparisons between the double- and single blinded groups, the exploratory comparator, Voltaren QID, did not reach statistically significant differences to placebo or AMZ001 in any of the endpoints, in neither the ITT nor the subgroup analyses. The safety and tolerability of AMZ001 was favorable, as the frequency of AEs leading to discontinuation of treatment was similarly low (ranging between 2.8 % to 6.6 %) between AMZ001 once or twice daily and placebo or Voltaren Gel 1%. The most common treatment-emergent AEs were application site dryness, and application site erythema. No serious adverse events were reported during the trial.

Conclusion: AMZ001, a novel topical diclofenac formulation, either once or twice daily was efficacious in the treatment of knee OA pain with a good tolerability and safety profile, suggesting AMZ001 may be a promising alternative to existing pain-relieving treatments in knee OA.

References: NA

Disclosure of Interests: Asger Bihlet Shareholder of: Nordic Bioscience, Consultant of: Amzell BV, Medivir AB, Xintela AB, Merck KGaA, Employee of: Nordic Bioscience, Inger Byrjalsen Employee of: Nordic Bioscience, Henning Bay Nielsen: None declared, Jeppe Andersen Shareholder of: Minor shareholder of Nordic Bioscience, Consultant of: Medivir AB, Xintela AB, Employee of: Nordic Bioscience, Laetitia Delpy Employee of: Amzell BV, Caroline Derne Employee of: Amzell BV, Dario Carrara Employee of: Amzell BV

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AB0857 A NEW BIOPSYCHOSOCIAL QUESTIONNAIRE FOR PATIENTS WITH KNEE OSTEOARTHRITIS

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Background: OA is a problem that cartilage damage occurs, which leads to stiffness in the joint, pain and functional limitations (1). This problem can also cause psychosocial impact like other chronic diseases (2). As with other rheumatic diseases, this complex picture of inflammation required biopsychosocial approaches and measurement methods for knee OA.

Objectives: This study was planned to investigate the validity and reliability of a new biopsychosocial questionnaire which is named Cognitive Exercise Therapy Approach Biopsychosocial Questionnaire (BETY-BQ) in individuals with knee osteoarthritis (OA).

Methods: The study included 150 individuals who diagnosed knee osteoarthritis at stage 1 or 2 according to the Kellgren-Lawrence scale. For determining daily living activities; Health Assessment Questionnaire (HAQ), for quality of life Short Form-36 (SF-36) Quality of Life Scale, for anxiety and depression levels; Hospital Anxiety and Depression Scale (HADS), for severity of disease Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and for biopsychosocial evaluation BETY-BQ were used.

Results: The correlation between BETY-BQ and other scales was examined by Spearman correlation analysis (r=-0.252, 0.633, p<0,05). Cronbach's alpha coefficient and item-total correlation were used as reliability methods. Cronbach's alpha coefficient was examined for the internal consistency of the scale and was found to be 0.887 for the first evaluation, 0.917 for measurements after 1 week and 0.843 for measurements after 3 months. Item total correlation, which was another indicator of reliability, ranged from 0.632 to 0.854 (p<0.05).

Table 1. Correlation coefficients between all questionnaires and Cognitive Exercise Therapy Approach Biopsychosocial Questionnaire (BETY-BQ).

Spearman Correlation Analysis	Cognitive Exercise Therapy Approach Biopsychosocial Questionnaire (BETY-BQ)	
	r	p
WOMAC-Pain	0,473	<0,001
WOMAC-Stiffness	0,458	<0,001
WOMAC-Physical Function	0,514	<0,001
WOMAC-Total Score	0,553	<0,001
hospital anxiety and depression scale- anxiety	0,615	<0,001
hospital anxiety and depression scale-depression	0,252	0,002*
Health Assessment Questionnaire	0,633	<0,001
Short Form-36 Role limitations due to physical health	-0,440	<0,001
Short Form-36 Role limitations due to emotional problems	-0,357	<0,001
Short Form-36 Physical functioning	-0,469	<0,001
Short Form-36 Social functioning	-0,355	<0,001
Short Form-36 Pain	-0,487	<0,001
Short Form-36 General Health	-0,513	<0,001
Short Form-36 Emotional well-being	-0,508	<0,001
Short Form-36 Energy/fatigue	-0,453	<0,001

Conclusion: As a result of our study, it was concluded that BETY-BQ is a valid and reliable biopsychosocial questionnaire in individuals with knee OA diagnosis. This result showed that BETY-BQ can be used in clinics to evaluate biopsychosocial involvement in patients with knee OA.

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AB0858 TREATMENT ALGORITHM FOR ANKLE OSTEOCHONDRAL LESIONS AND DEFECTS

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Background: traumatic ankle joint osteochondral lesions and defects (OHLD) is frequent cause of OA, chronic pain and loss of joint function; results of traditional treatment strategy are often unsatisfying

Objectives: to develop treatment algorithm for OHLD based on evaluation of previously determined main prognostic factors.

Methods: the analysis of long-term (36 ± 4.5 months) treatment results of 239 patients after traumatic ankle joint OHLD revealed the following factors with the greatest predictive value (defined by PC – prognostic coefficient) for good result of treatment (defined as AOFAS function score 75-100 points): age < 40 years (PC = 8.5); size of OHLD ≤ 1.0 cm^2; volume ≤ 1.5 cm^3 (PC = 8.0); osteoarthritis stage ≤ II (PC = 7.2). Based on these factors, a step-by-step, discrete and alternative algorithm for the choice of treatment tactics was created. The algorithm includes use of arthroscopic or open debridement, abrasive chondroplasty, bone marrow regeneration stimulation (microfracturing or tunneling), mosaic osteochondroplasty, arthroplasty or arthrodesis, the use of cellular regenerative technologies (bone marrow cells, platelet riched plasma), and others. Patients of older age with advanced OA need complex, step up approach, surgical treatment combined with regenerative cell technologies. The effectiveness of the differentiated approach to treatment was studied in 72 patients with OHLD (main group) in comparing to 72 patients in whom traditional treatment approaches were used, based on the stage of injury according to the Berndt & Hardy classification (comparison group).

Results: compared to the traditional approach, the developed algorithm and treatment system allowed to half terms of hospitalization, to reduce the intensity of pain syndrome (by NRS) and increase the functional activity (by AOFAS) by 25%. In 3 years after trauma good/excellent results of treatment demonstrated 86% patients of main group and 32,2% of patients from comparing group (p<0,05).

Conclusion: implementation of the developed treatment algorithm increases the number of good and excellent long-term results by 2.6 times and reduces the number of complications and unsatisfactory results by 4.9 times.

Disclosure of Interests: None declared

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AB0859 IMPROVEMENTS IN PHYSICAL FUNCTION IN PATIENTS WITH OSTEOARTHRITIS RECEIVING SUBCUTANEOUS TANEZUMAB IN 3 RANDOMIZED CONTROLLED TRIALS

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Background: Tanezumab, a monoclonal antibody against nerve growth factor, is in development for the treatment of the signs and symptoms of osteoarthritis (OA).

Objectives: To assess the improvement in physical function following treatment with subcutaneous (SC) tanezumab in three Phase 3 OA studies.

Methods: All three randomized, double-blind, controlled studies enrolled patients (pts) with radiographically-confirmed OA of the hip or knee, who had inadequate response or could not tolerate standard of care analgesics. Study 1 was a dose-titration study (NCT02697773), where pts received two SC doses of: placebo at baseline/week (wk) 8; tanezumab 2.5 mg at baseline/wk 8; or

tanezumab 2.5 mg at baseline/5 mg at wk 8 [1]. In Study 2 (NCT02709486), pts received three SC doses of placebo, tanezumab 2.5 mg, or 5 mg (at baseline/wk 8/wk 16). In Study 3 (NCT02528188), pts received a stable dose of nonsteroidal anti-inflammatory drugs (NSAIDs) before randomization to double-dummy tanezumab 2.5 mg or 5 mg (at baseline and every 8 wks during a 56 wk treatment period) or twice daily oral NSAIDs. Pts completed Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Physical Function subscale questionnaires in clinic. The least squares (LS) mean (standard error (SE)) change from baseline was calculated for each timepoint up to wk 16 and significance was calculated versus placebo (Studies 1 and 2) or NSAID (Study 3).

Results: A total of 4541 pts were evaluated (n=696 in Study 1, n=849 in Study 2 and n=2996 in Study 3). In Studies 1 and 2, there were statistically significant improvements from baseline for all tanezumab treated groups versus placebo at wks 2, 4, 8, 12 and 16 (**Table 1).** In Study 3, the tanezumab 2.5 mg group showed a significant improvement from baseline at wk 2, compared with the NSAID group (**Table 2).** At wk 4, both tanezumab treatment groups showed a significant improvement from baseline compared with the NSAID group (**Table 2**). The tanezumab 5 mg group showed a significant improvement from baseline compared with the NSAID group at wks 8 and 16 (**Table 2).**

Table 1. Change from baseline in WOMAC Physical Function: Study 1 and 2

		Study 1			Study 2		
		Tanezumab 2.5 mg n=231	Tanezumab 2.5/5 mg n=233	Placebo n=232	Tanezumab 2.5 mg n=283	Tanezumab 5 mg n=284	Placebo n=282
Wk 2	LS mean (SE)	-2.89 (0.21)	-3.05 (0.21)	-2.14 (0.21)	-1.95 (0.14)	-1.69 (0.14)	-1.26 (0.14)
	p vs placebo	0.0004	<0.001		<.0001	0.0014	
Wk 4	LS mean (SE)	-3.30 (0.21)	-3.38 (0.21)	-2.28 (0.21)	-2.52 (0.15)	-2.50 (0.15)	-1.71 (0.15)
	p vs placebo	<.0001	<.0001		<.0001	<.0001	
Wk 8	LS mean (SE)	-3.17 (0.21)	-3.12 (0.21)	-2.55 (0.21)	-2.38 (0.15)	-2.52 (0.15)	-1.76 (0.15)
	p vs placebo	0.0057	0.0114		<.0001	<.0001	
Wk 12	LS mean (SE)	-3.61 (0.22)	-3.80 (0.22)	-2.75 (0.22)	-2.83 (0.16)	-2.87 (0.16)	-2.04 (0.16)
	p vs placebo	0.0004	<.0001		<.0001	<.0001	
Wk 16	LS mean (SE)	-3.22 (0.22)	-3.45 (0.22)	-2.56 (0.22)	-2.68 (0.16)	-2.69 (0.16)	-2.02 (0.17)
	p vs placebo	0.0065	0.0002		<.0001	<.0001	

Table 2. Change from baseline in WOMAC Physical Function in Study 3

		Tanezumab 2.5 mg n=1002	Tanezumab 5 mg n=998	NSAID n=996
Wk 2	LS mean (SE)	-1.76 (0.08)	-1.64 (0.08)	-1.55 (0.08)
	p vs NSAID	0.0150	0.3286	
Wk 4	LS mean (SE)	-2.29 (0.09)	-2.31 (0.09)	-1.96 (0.09)
	p vs NSAID	0.0004	0.0001	
Wk 8	LS mean (SE)	-2.46 (0.10)	-2.69 (0.10)	-2.27 (0.10)
	p vs NSAID	0.0517	<.0001	
Wk 16	LS mean (SE)	-3.27 (0.11)	-3.39 (0.11)	-3.08 (0.11)
	p vs NSAID	0.0691	0.0030	

Conclusion: Consistent improvements in WOMAC Physical Function were seen across the first 16 wks for all dose groups of tanezumab-treated pts versus placebo in Study 1 and 2. The tanezumab 5 mg group in Study 3 showed a significant improvement at wks 4, 8 and 16 compared with the NSAID group. Improving physical function could help OA pts attain treatment goals beyond pain relief, improving their ability to perform important daily activities.

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Disclosure of Interests: Steven P Stanos Consultant of: Pfizer, Sanofi, Scilex, Salix, Speakers bureau: Scilex, Wilson J Chang: None declared, Cory Hultman Employee of: Eli Lilly and Co., Mojgan Sadrarhami Shareholder of: Pfizer Inc., Employee of: Pfizer Inc., Takaharu Yamabe Shareholder of: Pfizer, Employee of: Pfizer, Peter Park Shareholder of: Pfizer Inc., Employee of: Pfizer Inc.

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AB0860

STUDY DESIGN OF ROCCELLA: A PHASE 2 CLINICAL TRIAL WITH A DISEASE-MODIFYING OSTEOARTHRITIS DRUG CANDIDATE GLPG1972/S201086

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Background: Loss of articular cartilage is one of the major signs of osteoarthritis (OA). Aggrecan, the main proteoglycan component of the extracellular matrix of articular cartilage is cleaved by ADAMTS-5 (A Disintegrin And Metalloproteinase with ThromboSpondin-motif-5).[1] GLPG1972/S201086, a potent and highly selective inhibitor of ADAMTS-5, is an oral Disease-Modifying OsteoArthritis Drug (DMOAD) candidate. In a pooled Phase 1 safety analysis involving 171 participants GLPG1972/S201086 was shown to be well tolerated.

Objectives: To present the study design of ROCCELLA, a large Phase 2 clinical trial in knee OA (KOA) patients, evaluating the efficacy and safety of GLPG1972/S201086 in reducing cartilage loss in OA.

Methods: ROCCELLA is a multinational 52-week, multicentre randomized double-blind placebo-controlled dose-ranging phase 2 trial for the treatment of OA (NCT03595618). Eligible patients were aged 40–75 years with a diagnosis of primary femorotibial KOA, a pain score of 40–90mm on a 100 mm Visual Analogue Scale (VAS), predominant medial disease and a combined Kellgren/Lawrence (KL) 2 or 3 and Osteoarthritis Research Society International (OARSI) medial joint space narrowing (JSN) 1 or 2 severity grading range upon central reading of the X-ray. If both knees were eligible, the target knee was selected based first on the highest KL grade, then on the highest JSN grade and finally on the highest pain VAS score at baseline. Patients were randomized 1:1:1:1 to take placebo or three dose levels of GLPG1972/S201086 orally once daily for 52 weeks. The target knee was evaluated by quantitative Magnetic Resonance Imaging (qMRI) at baseline visit, week 28 and week 52, or at early withdrawal.

The primary endpoint of the study is change from baseline to week 52 in cartilage thickness of the central medial tibio-femoral compartment (cMTFC) of the target knee. Secondary objectives are safety and tolerability including treatment emergent serious adverse events. Additional secondary structural and clinical efficacy objectives are based on changes from baseline in the target knee: cartilage thickness and bone area on qMRI, KOA "progressor" rates, Joint Space Width on X-ray, pain VAS, the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) total and sub scores, Patient Global Assessment VAS and the proportion of Outcome Measures in Rheumatology (OMERACT)-OARSI responders. Blood will be collected to assess the pharmacokinetics of GLPG1972/S201086. Planned, exploratory analyses include biochemical biomarkers of cartilage and bone turn-over. The study is designed to maintain the experiment wise type I error at 5%. A Mixed-effects Model for Repeated Measures will be used for the primary analysis. The randomisation was stratified by geographic region.

Results: The study started in August 2018 and was fully recruited (N=938) by June 2019. Large numbers of patients with KOA had to be screened to meet the stringent pre-specified selection criteria. The study completion is expected by end of 2020.

Conclusion: This is the first large Phase 2 study where patients with primary KOA are treated for 52 weeks with GLPG1972/S201086, an orally administered DMOAD candidate. This clinical trial was designed with a combination of two radiological selection criteria to ensure sufficient structural progression (cartilage loss) in the study population.

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Disclosure of Interests: Henri Deckx Employee of: Galapagos, Ellen van der Aar Employee of: Galapagos, Marjolijne van der Stoep Employee of: Galapagos, Marianne Wooning Employee of: Galapagos NV, Katy Bernard Employee of: Institut de Recherches Internationales Servier, Sergey GRANKOV Employee of: Institut de Recherches Internationales Servier, Olivier Imbert Employee of: Institut de Recherches Internationales Servier, Maria Pueyo Employee of: Institut de Recherches Internationales Servier, Felix Eckstein Grant/research support from: Merck, Orthotrphix, Servier, Galapagos, Kolon Tissuegene, Samumed, Novartis, Consultant of: Merck, Bioclinica, Servier, Samumed, Roche, Kolon Tissuegene, Galapagos and Novartis, Employee of: co-owner and employment with Chondrometrics

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AB0861

CURRENT PHARMACOTHERAPY FOR KNEE OSTEOARTHRITIS: SPECIFIC FEATURES OF SYMPTOMATIC AND DISEASE MODIFYING EFFECTS

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Objectives: to study the specific features of the symptomatic effect and tolerability of paracetamol (P), glucosamine sulfate (GS), chondroitin sulfate (CS), and meloxicam (M) in patients with knee osteoarthritis (OA).
Methods: An 18-month open-label randomized prospective parallel-group trial enrolled 80 patients with knee OA who fulfilled the American College of Rheumatology criteria and signed the informed consent. They had Kellgren and Lawrence grades I-III OA with visual analogue scale pain intensity of > 40mm in the target knee, a body mass index of < 35 rg/m^2, and no clinical dysfunctions of vital organs and systems. The patients were randomized into 4 groups: 1) P 2g daily; 2) a standard GS regimen; 3) a standard CS regimen; 4) M 15mg daily. The patients were followed up for 18 months, The effectiveness was evaluated by the WOMAC questionnaire, Lequesne index, and OMERACT-OARSI (D scenario) during 8 visits. Laboratory and clinical examination as well as electrocardiography were performed. Adverse events were recorded during each visit.
Results: After 4 weeks of treatment, symptomatic improvement was noted in all groups; however, the best effect was achieved by the use of M and continued to the end of the study. The percentage of patients reacting to the therapy by the OMERACT-OARSI criteria was highest in M group (100%), reached 90% in GS, 85% in CS groups and 75% in P group. In the groups of P, GS and CS failed to respond to treatment 25, 10, and 15% correspondingly. However, medium narrowing of articular space (NAS) was measured at the end of the study and was significantly lower in GS group (-0.07; p=0,0002), CS (-0.1; p=0.004) and M (-0.06; p=0.006). Besides, the quota of patients without heavy NAS (> 0.5 mm in medial KJ) was the lowest in GS group as compared with three other groups.
Conclusion: The results of this trial suggest that it is expedient to use GS, CS and M long, support the recent guidelines of the European Society for Clinical and Economic aspects of Osteoporosis and OA (ESCEO), and can give proofs of the efficiency and safety of GS, CS, and M used in the treatment of knee OA.
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AB0862

CONSENSUS STATEMENT ON INTRA-ARTICULAR INJECTIONS OF PLATELET-RICH PLASMA FOR THE MANAGEMENT OF KNEE OSTEOARTHRITIS

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Background: There has been much debate regarding the use of intra-articular injections of platelet-rich plasma (PRP) as symptomatic treatment for knee osteoarthritis. The heterogeneity of the preparation and injection protocols limits the extrapolation of data from randomized controlled trials and meta-analyses.
Objectives: The objective of this expert consensus was to develop the first clinical practice recommendations for PRP injections in knee osteoarthritis.
Methods: Fifteen physicians (10 rheumatologists, 4 specialists in rehabilitation and sport medicine and 1 interventional radiologist) from different countries were selected given to their expertise in the fields of PRP and osteoarthritis. Twenty-five recommendations were finally retained after several meetings using the modified Delphi method to establish clinical consensus. All experts voted their agreement or not for each recommendation using a score between 1 (totally inappropriate) and 9 (totally appropriate). Depending on the median value and extreme scores, recommendations were judged as appropriated or unappropriated with a strong or relative agreement but could also be judged as uncertain due to indecision or absence of consensus.
Results: The main recommendations are listed below:

- Intra-articular injections of PRP constitute an efficient treatment of early or moderate symptomatic knee osteoarthritis. Median = 8 [6-9] – Appropriate. Relative agreement.
- Intra-articular injections of PRP may be useful in severe knee osteoarthritis (Kellgren-Lawrence grade IV). Median = 7 [6-7] – Appropriate. Relative agreement.
- Intra-articular injections of PRP in knee osteoarthritis should be proposed as second-line therapy, after failure of non-pharmacological and pharmacological (oral and topic) symptomatic treatment. Median = 9 [5-9] – Appropriate. Relative agreement.
- Intra-articular injections of PRP should not be performed in osteoarthritis flare-up with significant effusion. Median = 7 [5-9] – Appropriate. Relative agreement.
- Intra-articular PRP treatment may include 1 to 3 consecutive injections. Median = 9 [7-9] – Appropriate. Strong agreement.
- Leukocyte-poor PRP should be preferred for knee OA treatment. Median = 8 [5-9] – Appropriate. Relative agreement.
- PRP injections should be performed under ultrasound or fluoroscopic guidance. Median = 8 [3-9] – Uncertain. No consensus.
- PRP should not be mixed with injectable anesthetic or corticosteroid. Median = 9 [6-9] – Appropriate. Relative agreement.

Conclusion: Twenty-five recommendations were discussed by an international multidisciplinary task force group in order to provide a basis for standardization of clinical practices and future research protocols.
Disclosure of Interests: Florent Eymard Consultant of: Regenlab, Paul Ornetti: None declared, Jérémy Maillet Consultant of: Regenlab, Eric Noel Consultant of: Regenlab, Philippe Adam Consultant of: Regenlab, Virginie Legré Boyer Consultant of: Regenlab, Thierry Boyer Consultant of: Regenlab, Fadoua Allali: None declared, Vincent Grémeaux Bader: None declared, Jean-François Kaux: None declared, Karine Louati: None declared, Martin Lamontagne Consultant of: Pendopharm, Fabrice Michel: None declared, Pascal Richette: None declared, Hervé Bard Consultant of: Regenlab
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AB0863

RADIOGRAPHY VERSUS ULTRASONOGRAPHY – WHICH IMAGING MODALITY TELLS US MORE ABOUT PAIN SEVERITY IN KNEE OSTEOARTHRITIS?

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Background: Osteoarthritis (OA) is a leading cause of disability worldwide and pain is its cardinal symptom. Ranging from structural injuries to central sensitization, multifactorial mechanisms play an important role in pain perception in patients with knee OA (KOA) defining a discrepancy between pain and structural damage. Imaging modalities such as radiography and musculoskeletal ultrasonography may assess those structural findings and both are well embedded in routine clinical practice. However, their association with pain severity is poorly studied.
Objectives: To evaluate the place of X-ray- and ultrasound-derived parameters of structural damage for pain perception in knee osteoarthritis patients.
Methods: Sixty-four knees from 38 patients with KOA fulfilling the ACR criteria were assessed. The pain severity was evaluated in all knees by 100-millimeters (mm) visual analogue scale (VAS). Anteroposterior radiographs of the fully extended knees in an upright weight-bearing position were obtained and images were evaluated according to the Kellgren-Lawrence (KL) and OARSI atlas. All patients were investigated with a portable MyLab 25 Gold system equipped with an LA435 transducer (Esaote SpA, Genoa, Italy) by two experienced ultrasonographers. The presence or absence of synovial thickening, effusion in the suprapatellar bursa, and popliteal cyst were assessed. Medial meniscal extrusion and medial and lateral femoral cartilage thickness (medial and lateral) were measured in mm in full extension and flexion position, respectively. Femoral osteophytes were semi-quantitatively scored using a scale consisted of four grades (0-3).
Results: The levels of pain differed significantly in the KL groups (p = .001) and in the groups classified according to the medial tibiofemoral compartment narrowing defined in line with the OARSI atlas (p = .005). The other knee osteoarthritis radiographic characteristics derived from the OARSI atlas did not correlate with the pain. From the assessed ultrasound parameters, medial

meniscal extrusion and medial femoral cartilage showed a weak correlation with pain levels (r = .254, p = .043; r = -.265, p = 0.034, respectively). Nevertheless, in the multivariate analysis after adjusting for age and BMI, both variables did not reach significance for explaining the differences in VAS levels. No association between the presence of synovial effusion and popliteal cyst and pain severity was found.

Conclusion: Plain radiography and ultrasonography reflect different structural changes in osteoarthritis that may play an important role in pain perception. Both imaging modalities can complement each other in order to improve the evaluation of the patient with KOA.

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AB0864 DO CORTICOSTEROIDS AND HYALURONIC ACID INJECTIONS CAUSE INFECTIONS? A SYSTEMATIC REVIEW OF LITERATURE ON ADVERSE EFFECTS AND INFECTION RATES OF INTRA-ARTICULAR CORTICOSTEROID AND HYALURONIC ACID INJECTIONS IN PATIENTS WITH KNEE OSTEOARTHRITIS

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Background: Knee osteoarthritis has been a leading cause of chronic pain and disability in our increasingly aging population. Conservative management options of physiotherapy and oral analgesics offer some relief, but delivery of intra-articular injections such as corticosteroids or hyaluronic acid has increasingly become the mainstay of pain management of knee osteoarthritis. In a clinical setting, intra-articular injections offer a means to delay a total knee replacement. Despite the abundance of literature on corticosteroids and hyaluronic acid, there is no known percentage of infection rates or adverse effects that clinicians may use to inform patients prior to obtaining consent for the injection.

Objectives: To determine a rate of adverse events and infection rates in patients undergoing intra-articular injections of corticosteroids or hyaluronic acid.

Methods: A systematic review of current literature including studies involving patients ranging from 45 patients (Carmona L, 2018) to Cochrane reviews of 1767 patients (Campbell Kirk, 2015). From these studies, the number of patients, adverse reactions (i.e. pain, erythema) and serious adverse reactions (infections) were calculated.

Results: Within our study, there was a large variation of numbers of adverse effects of hyaluronic acid and corticosteroids amongst studies, with percentages as variable as 0-9.3%. Corticosteroids demonstrated 11-26% reduction of adverse events compared to hyaluronic acid. However, confidence intervals were found to not be statistically significant.

Conclusion: Intra-articular injections of corticosteroids and hyaluronic acid, although deemed clinically effective, continue to demonstrate variable rates of adverse effects and infection amongst patients with progressive knee osteoarthritis.

Disclosure of Interests: None declared

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AB0865 EPIDURITIS IN INFECTIOUS SPONDYLODISCITIS

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Background: The main problem with infectious spondylodiscitis (ISD) is the diagnosis difficulty. Tuberculosis, with deceptive clinical semiology, remains to date the most common cause in underdeveloped and developing countries.

Objectives: To report the frequency and characteristics of epiduritis in ISD and to specify its short and medium-term impact through a series of 70 cases.

Methods: A descriptive retrospective study was conducted including patients with ISD, hospitalized in the rheumatology department at Fattouma bourguiba Hospital,Monastir TUNISIA between January 2009 and August 2019. Sociodemographic, clinico_biological and radiological data were collected.

Results: 34 male and 36 female were included. The average age was 53.91 ±15.3 years. The mean time to visit was 80.3±89 days [4,520]. Co-morbidity was noted in 66.7% of patients: diabetes (22), hypertension (18), hemodialysis (8), heart disease (4), and long term corticosteroid therapy (4). Tuberculosis contagion was present in 7.2% of patients. The most frequent reason for consultation was low back pain (63.8%) with a root syndrome in most patients (>50%). Neurological abnormalities were noted in 8.7% of patients. Skin swelling was noted in 4.3% of patients. Biological inflammatory syndrome and hyperleukocytosis were the moost biological abnormalities reported respectively in 81.2% and 30.4% of patients,. Among 70 ISD: 29 were with common germ, 18 with tuberculosis, 8 with brucellosis, and 14 with an undetermined germ. 91.3% of patients underwent a spinal magnetic resonance imaging (MRI): epiduritis was documented in 72% of cases, frequently anterior (53%). The epidural abscesses association was noted in 33 patients. It was pronounced mostly at the lumbar (19) and dorsal (14) levels. Epiduritis was frequently associated with para-vertebral soft tissues infiltration: pre-vertebral thickening (32), pre-vertebral collection (17), psoas muscle abscesses, (13). Spinal cord compression was noted in 2 patients. On 3-month visit, the ISD associated with epiduritis evolution was characterized by persistence of pain, hence radiological control was justified in 6 patients. A persistent biological inflammatory syndrome was noted in 27% of cases. Furthermore, 2 deaths were observed in this group of patients.

Conclusion: Epiduritis rate in ISD requires a well-codified diagnostic and therapeutic strategy that will consider carfelly the neurological prognosis involved.

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Acknowledgments: Rheumatology Department

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AB0866 THE PREVALENCE AND CLINICAL FEATURES OF FRAILTY SYNDROME IN PATIENTS WITH SYMPTOMATIC RADIOGRAPHIC KNEE OSTEOARTHRITIS AND RHEUMATOID ARTHRITIS: A STUDY OF THE KOREAN NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY (KNHANES)

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Background: Frailty is defined as syndrome of physical decline in late life, characterized by marked vulnerability to adverse health outcomes. Knee osteoarthritis (OA) could be one of the major diseases related to frailty conditions. The prevalence and clinical features of frailty syndrome in knee OA and rheumatoid arthritis (RA) were not reported previously.

Objectives: We studied the clinical features and nutritional status of knee OA and RA patients with frailty syndrome in nationwide survey data.

Methods: Symptomatic knee osteoarthritis patients were defined who had knee joint pain accompanied with grade 2 or more Kellgren-Lawrence score in plain radiographic studies from the data of KNHANES (N=17,873, from 2010 to 2013). RA was defined who diagnosed by physician. We calculated the frailty index (score 0~1.0) using 46 items from the frailty related co-morbidities and laboratory abnormalities according to Rockwood clinical frailty scale. We analyzed the clinical features of three frailty groups [robust (≤0.10), pre-frail (0.1< * ≤0.21), and frail (>0.21)] in symptomatic radiographic knee OA patients and RA patients.

Results: The prevalence of Knee OA patients was 8.59% [95% CI: 8.19-9.01]. Relative risk ratio is significantly increased in pre-frail (OA; 2.66 [2.26-3.14], RA;4.02 [3.07-5.27]) and frail group (OA; 6.27 [5.20-7.57], RA;7.00[5.03-9.74]) in polytomous logistic regression.

Body mass index (BMI), white blood cell, platelet, and serum creatinine were significantly increased in knee OA and RA patients with frailty syndrome. But, hemoglobin, estimated GFR (CKD-EPI equation) and EQ-5D were significantly decreased in knee OA and RA patients with frailty syndrome (Table). The daily nutritional intakes of total calories, carbohydrate, protein, fat, sodium and potassium were significantly decreased in knee OA patients with the frailty syndrome. In RA patients, the significant decreased nutritional intakes of total calories, carbohydrate, protein and fat were observed.

Conclusion: We showed increased BMI, decreased renal function and lower nutritional status in symptomatic radiographic knee OA and RA patients with frailty syndrome.

Table.

		Robust	Pre-frail	Frail	p
Body mass index (kg/m^2)	Knee OA	24.13 [23.74-24.53]	25.07 [24.83-25.32]	25.46 [25.14-25.78]	< 0.0001
	RA	23.73[23.04-24.42]	23.58 [23.20-23.97]	24.97 [24.28-25.66]	0.001
Hemoglobin, g/dL	Knee OA	13.53 [13.36-13.70]	13.51 [13.42-13.61]	13.27 [13.14-13.40]	0.004
	RA	13.63 [13.34-13.92	13.30 [13.14-13.46]	13.15 [12.85-13.45]	0.060
White blood cell, 10^3/μL	Knee OA	5.50 [5.29-5.71]	5.94 [5.81-6.07]	6.41 [6.24-6.58]	< 0.0001
	RA	5.47 [5.13-5.82]	5.85 [5.64-6.06]	6.68 [6.32-7.03]	< 0.0001
Platelet, 10^3/μL	Knee OA	246.03 [238.52-253.53]	258.13 [253.44-262.82]	259.96 [253.40-266.53]	0.045
	RA	237.49 [222.91-252.06]	255.30 [247.50-263.10]	262.04 [248.32-275.77]	0.038
Serum creatinine, mg/dL	Knee OA	0.734 [0.712-0.756]	0.764 [0.751-0.777]	0.861 [0.826-0.895]	< 0.0001
	RA	0.732 [0.686-0.779]	0.783 [0.762-0.805]	0.917 [0.840-0.994]	< 0.0001
CKD-EPI eGFR, ml/min	Knee OA	88.54 [86.77-90.31]	83.89 [82.89-84.88]	76.22 [74.80-77.63]	< 0.0001
	RA	94.30 [90.77-97.82]	85.86 [84.00-87.73]	74.76 [70.91-78.61]	< 0.0001
EQ-5D	Knee OA	0.933 [0.921-0.944]	0.804 [0.793-0.815]	0.635 [0.616-0.653]	< 0.0001
	RA	0.966 [0.953-0.979]	0.857 [0.839-0.874]	0.666 [0.619 -0.713]	< 0.0001

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AB0867

INCREASED ADIPONECTIN LEVELS ARE ASSOCIATED WITH HIGHER RADIOGRAPHIC SCORES IN THE KNEE JOINT, BUT NOT IN THE HAND JOINT: THE DONG-GU STUDY

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Background: Several studies have evaluated the association between serum adiponectin levels and knee and hand osteoarthritis (OA), with mixed results.
Objectives: The aim of this study was to investigate the relationship between OA and serum adiponectin levels according to the radiographic features of knee and hand OA.
Methods: A total of 2,402 subjects were recruited from the Dong-gu Study. Baseline characteristics were collected via a questionnaire, and X-rays of knee and hand joints were scored by a semi-quantitative grading system. The relationship between serum adiponectin levels and radiographic severity was evaluated by linear regression analysis.
Results: Subjects with higher tertiles of serum adiponectin were older and had a lower body mass index than those with lower tertiles. In the knee joint scores, serum adiponectin levels were positively associated with the total score (P<0.001), osteophyte score (P=0.003), and joint space narrowing (JSN) score (P<0.001) among the three tertiles after adjustment for age, sex, body mass index, smoking, alcohol consumption, education, and physical activity. In the hand joint scores, no association was found between serum adiponectin levels and the total score, osteophyte score, JSN score, subchondral cyst score, sclerosis score, erosion score, and malalignment score among the three tertiles after adjustment.
Conclusion: In this study, we found that increased adiponectin levels were associated with higher radiographic scores in the knee joint, but not in the hand joint, suggesting different pathophysiologic mechanisms in the development of OA.
Disclosure of Interests: None declared
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AB0868

EFFICACY AND SAFETY OF PULSED ELECTROMAGNETIC FIELDS IN THE TREATMENT OF OSTEOARTHRITIS: RESULTS OF A MULTICENTER BLIND PLACEBO-CONTROLLED STUDY.

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Background: Pulsed electromagnetic fields (PEMF) is a well – known method of non-pharmacological treatment that is widely used in knee osteoarthritis (KOA).
Objectives: To evaluate the effectiveness and safety of PEMF in KOA.
Methods: The study group consisted of 231 KOA patients, 77.9% of women, age 61.9±12.2 years, BMI 30.6±5.8 kg / m2, average disease duration 5.0 [2.0;10.0] years. Patients were randomly assigned to two groups. Group 1 patients received PEMF for 14 days using a device that creates a low-frequency pulsed magnetic field, group 2-a false PEMF (a device that completely simulates a working device, but does not create a magnetic field). We evaluated the dynamics of the WOMAC index, the severity of pain at rest and when moving on a 100-mm visual analog scale (VAS), the need for non-steroidal anti-inflammatory drugs (NSAIDs), and the evaluation of the patient's treatment result (on a 5-point scale).
Results: Statistically significant reduction in pain, stiffness, and improved function was observed in both true PEMF and false PEMF. Thus, the WOMAC pain in Group 1 decreased from 231 [180; 290] to 110 [60; 166.3], p<0.001; in Group 2 from 212.4 [145; 260] to 143 [76.5; 200], p<0.001, the severity of pain in rest (VAS) decreased in Group 1 from 47 [27.8; 60] to 20 [10; 30], p<0.001; in Group 2 from 40 [20; 57.5] to 20 [7.5; 40], p<0.001. After therapy, the need for NSAIDs also decreased: in Group 1 NSAIDs were canceled or reduced in 33.1% of patients, in Group 2 - in 16.8% (p=0.006). For all indicators, the dynamics were statistically more significant in Group 1 than in Group 2. The result of treatment as "good" and "excellent" was evaluated by 58.5% of patients in Group 1 and 39.8% of patients in Group 2, p<0.001. No serious adverse reactions were observed when using true and false PEMF. Two patients who received false PEMF therapy was interrupted due to increased joint pain.
Conclusion: PEMF with short-term use provides a significant improvement in the condition of KOA patients. PEMF is well tolerated and does not cause serious complications.
Disclosure of Interests: None declared
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AB0869

CLINICAL FEATURES OF WOMEN WITH KNEE OSTEOARTHRITIS AT DIAGNOSIS IN CAMEROON, SUB-SAHARAN AFRICA

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Background: To the best of our knowledge, no study has been done in sub-Saharan Africa among those who suggest that knee osteoarthritis is more severe in women.
Objectives: To assess differences in features of knee osteoarthritis between female and male patients in a sub-Saharan Cameroonian population.
Methods: A cross-sectional study from December 2018 to April 2019 conducted in the Rheumatology Unit of the General Hospital, Douala, Cameroon. We included patients with a recent diagnosis of knee osteoarthritis according to 1986 ACR criteria and Kellgren–Lawrence radiographic grading ≥ 2. Sociodemographic, clinical, radiographic and therapeutic data at diagnosis were collected. Assessment of the functional disability was done using the Lequesne algofunctional index, more adapted to Africans than WOMAC index. We compared these data between women and men. A p <0.05 was considered to be statistically significant.
Results: We screened 168 patients with the diagnosis of knee osteoarthritis. Seventeen patients with Kellgren-Lawrence radiographic grading at 1 were excluded. Then, we included 151 patients (120 women and 31 men) in the final analysis. The main characteristics of patients at diagnosis are summarized in Table 1. Knee osteoarthritis in women was characterized by a low level of education, a low financial income, and a high frequency of obesity. There was no difference between women and men for age at diagnosis, place of residence, intensity of pain, functional disability, number of compartments of the affected knee, Kellgren-Lawrence radiographic grading, and treatment previously received.

Table 1. Main characteristics of patients with knee osteoarthritis at diagnosis

Parameters	Total population Mean (SD)	Male Mean (SD)	Female Mean (SD)	*p*
Age (years)				
Mean age	59.88(12.8)	61.48(14.38)	59.46(12.41)	0.43
<40	10(6.6)	4(12.9)	6(5)	0.24
40-65	87(57.6)	14(45.16)	73(60.83)	0.17
>65	54(35.8)	13(41.94)	41(34.17)	0.55
Residence				
Rural	37(24.5)	10(32.26)	27(22.5)	0.37
Urban	114(75.5)	21(67.74)	93(77.5)	0.37
Level of education				
Primary	40(26.5)	3(9.68)	37(30.83)	0.03
Secondary	66(43.7)	9(29.03)	57(47.5)	0.09
University	35(23.2)	19(61.29)	16(13.33)	0.0000
Illiterate	10(6.6)	0	10(8.33)	0.20
Duration of OA (months)	38(44.9)	39.7(58.92)	37.59(40.92)	0.81
Pain				
VAS pain (mean)	5.2(1.6)	5(1.34)	5.34(1.68)	0.29
Mild pain	25(16.56)	4(12.9)	21(17.5)	0.73
Moderate pain	94(62.25)	24(77.42)	70(58.33)	0.08
Severe pain	32(21.19)	3(9.68)	29(24.17)	0.13
Joint effusion	28(18.5)	4(12.90)	24(20)	0.51
BMI				
Mean BMI	32.42(6.25)	26.89(4.05)	31.33(6.41)	0.0003
Normal	30(19.87)	11(35.48)	19(15.83)	0.02
Overweight	46(30.46)	14(45.16)	32(26.07)	0.07
Obesity	**65(49.67)**	**6(19.35)**	**69(57.5)**	**0.003**
Lequesne index				
Mean Lequesne index	8.6(2.4)	8.32(2.53)	8.77(2.4)	0.35
Moderate handicap	40(26.49)	9(29.03)	31(25.83)	0.89
Severe handicap	64(42.38)	12(32.71)	52(43.33)	0.79
Very severe handicap	37(24.5)	8(25.81)	29(24.17)	1
Kellgren-Lawrence grading				
Grade 2	81(53.6)	19(61.29)	62(51.67)	0.44
Grade 3	55(36.4)	9(29.03)	46(38.33)	0.45
Grade 4	15(10)	3(9.68)	12(10)	1
Compartment involved				
1	18(11.92)	6(19.35)	12(10)	0.26
2	28(18.54)	4(12.9)	24(20)	0.51
3	105(69.6)	21(67.74)	84(70)	0.98
Medial femoro-tibial	128(84.77)	25(80.65)	103(85.83)	0.66
Lateral femoro-tibial	117(77.48)	23(74.19)	94(78.33)	0.80
Femoro-patellar	144(95.36)	29(93.55)	115(95.83)	0.95

Conclusion: Apart from obesity, characteristics of knee osteoarthritis seems to be similar in women and men at diagnosis in Cameroon.

Disclosure of Interests: None declared

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AB0870 PAIN AND FUNCTIONAL OUTCOME OF PERIPHERAL BLOOD DERIVED STEM CELLS IN PRIMARY OSTEOARTHRITIS OF KNEE AT LOW RESOURCES SETTING: A PHASE II PILOT RCT

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Background: Osteoarthritis (OA) of the knee is one of the main causes of musculoskeletal disability. Osteoarthritis is now often considered as organ failure. Because of limitations in the effectiveness of conventional management options, alternative possibilities such as cell based therapies are approaching into vogue

Objectives: To assess the effectiveness of peripheral bold derived stem cells (PBSCs) therapy for primary OA knee.

Methods: This phase-II pilot RCT was conducted after the IRB ethical clearance. Patients attending PM&R department of BSMMU having KL grade III osteoarthritis knee those fulfilled the selection criteria were considered as the sample. All respondents were divided to into two groups by using randomization technique. In control group, 15 respondents received standard care for Knee Osteoarthritis. In PBSCs group, 15 cases received with single dose autologous peripheral blood derived stem cells (PBSCs). Stem cells were harvested using G-CSF 30MU and CD34 stem cells were collected through apheresis. Quality was ensured measuring cell viability and surface antigen. All respondents were assessed before treatment and at week 4, week 12 and week 24 for pain reduction and for functional improvement using Visual Analogue Scale (VAS 0-10 cm) and validated Bengali WOMAC questionnaire. Joint sonography was done before treatment, at 12 week and 24 week after treatment commencement.

Results: Female were 60% and 67% in control and PBSCs group respectively. The mean age was 56.3±6.7 and 55.8±7.3 year in control and PBSCs. After 12 weeks of stem cell therapy, pain reduction and functional significant improvement was observed in both groups. However, after 24 weeks further significant pain reduction, functional improvement was observed in PBSCs group. Moreover, the cartilage thickness measured by high frequency ultrasound and the mean cartilage thickness was increased by 0.14 mm from the baseline among PBSCs group.

Conclusion: PBSCs is promising in patients with primary OA knee. Further large scale research is solicited.

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Acknowledgments: Department of Transfusion Medicine, BSMMU

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AB0871 OSTEOARTHRITIS IN OBESE PATIENTS

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Background: Obesity is a recognized risk factor for osteoarthritis (OA) of the knee joints, which is associated with increased biomechanical stress. However, the association of OA with metabolic syndrome is more multifaceted, since overweight and obese people have a similar increased risk of OA of the hand joints that do not carry weight, due to systemic factors.

Objectives: To identify the features of the course of OA in overweight patients.

Methods: 52 patients with an established diagnosis of osteoarthritis were examined: women - 84.6%, men - 15.4%, average age - 60.9 ± 8.9 years (32 to 78 years). Clinical examination, calculation of body mass index (BMI), determination of the X-ray stage of OA according to the Kellgren and Lawrence system; ultrasound examination of the knee joints; assessment of the severity of pain according to visual analog scale (VAS); the index WOMAC was used to evaluate pain, stiffness and physical function. We evaluated the quality of life by EQ-5D.

Results: The duration of OA was 8.75 [2.58; 26] years. The distribution of patients according to the X-ray stage of OA: I - 9.6%, II - 57.6%, III - 26.9%, IV - 5.9% of patients. The BMI range was from 21 to 43 kg/. A BMI up to 30 kg/ was found in 22 patients: 17.3% - normal weight, 25% - excess body weight. Thirty patients has BMI more than 30 kg/: I degree - 38.4%, II degree - 15.3%, III degree - 4%. Obese patients rated pain according to the VAS scale of 1.3 the score is more intensively than patients with a BMI <30 kg/m^2 ($p < 0.001$). A detailed examination of each subsequent degree of obesity revealed a tendency to reduce the pain syndrome from 7.52 points at 1 degree of obesity to 5 points at 3 degrees of obesity ($p < 0.001$). With increasing body weight, there was an increase in difficulties in daily activities according to the WOMAC ($p < 0.05$). Reactive knee synovitis was detected in 25 (48%) patients. The incidence of synovitis in patients with a BMI <30 kg / m^2 is 27%, with a BMI> 30 kg / m^2 is 68%. Patients with obesity of 1st degree had synovitis in 65%, 2nd degree - 75%, 3rd degree - 84% of cases ($p < 0.05$). A high correlation between the x-ray stage of OA and BMI ($r = 0.74$; $p < 0.001$) was revealed. According to the EQ-5D questionnaire, patients with the 1st degree of obesity (2.31 ± 1.3) were very anxious, but the level of anxiety decreases in patients with 3rd degree of obesity (1.44 ± 0.9) and it's equal to that in individuals with normal body weight (1.33 ± 0.8).

Conclusion: The existence of obesity in patients with OA is associated with an increase in pain, a significant decrease in functional ability, a presence of reactive synovitis of the knee joints, aggravation of the X-ray stage of OA, and the appearance of anxiety and depression. However, with the further progression of obesity, the levels of anxiety for one's condition decrease.

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AB0872 EFFICACY AND SAFETY OF THE COMBINATION OF APOCYNIN AND PAEONOL (APPA) IN PATIENTS WITH OSTEOARTHRITIS: AN UNCONTROLLED PATIENT CASE SERIES

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Background: Apocynin and paeonol are secondary metabolites of plants used in traditional Asian medicine for centuries. The combination of synthetic versions of these two molecules (APPA) was developed initially for the treatment of osteoarthritis (OA) in animals where it has been found at least as effective as meloxicam. Human clinical trials are currently ongoing.
Objectives: To report the outcomes from a case series of patients treated with APPA.
Methods: Subjects with a diagnosis of OA, who had tried unsuccessfully a number of standard therapies, requested treatment with APPA from the author (NL), often following successful treatment of their animals with the combination or via networking. The usual daily dose was 1240 mg paeonol and 352 mg of apocynin taken as two 400mg capsules twice daily.
Results: Twenty-three subjects with a diagnosis of OA of whom 7 were scheduled for surgery have been treated with APPA. There were 10 female and 13 males with an age range from 40 to 81 years. Nine patients had OA of the knees, 5 of whom had bilateral involvement, 7 had hip OA, 5 bilaterally and 2 with end stage bone on bone disease. Four patients had hand OA, one of whom also had disease of the hip, lower back and feet. In 3 patients the joints involved was not recorded. In 19 patients treatment was reported as effective. In 4 patients the treatment was ineffective, all of who were scheduled or had been recommended for surgery. In 2 of these cases cases this was bone on bone The duration of treatment for OA at the last recorded follow-up was reported for 16 patients in whom treatment was deemed effective and ranged from 9 to 120 months (median 24 months). In a further 3 patients the treatment the duration was not reported. In the 4 patients where no benefit was reported APPA was discontinued within a few weeks. In no case was there a report of APPA being discontinued due to adverse events. In 13 patients it was specifically stated that there had been no adverse events whereas for the remaining 10 patients it was not documented whether adverse events had occurred or not.
Conclusion: Treatment with APPA was reported as effective by 82.6% of patients. In all patients in which the combination was ineffective the disease was severe with joint replacement recommended or scheduled; in two patients this was bone on bone. This would suggest that APPA is not a simple analgesic, a conclusion supported by effects seen in the rat meniscal tear model where possible disease modifying effects have been reported (1).
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AB0873 ULTRASOUND GUIDED INTRA-ARTICULAR INJECTION WITH HYALURONIC ACID AGENTS IN MODERATE HIP OSTEOARTHRITIS

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Background: Current guidelines usually only include hyaluronic acid (HA) intra-articular injection as an alternative therapy option for knee osteoarthritis (OA). When compared to the blind approach, ultrasound guided intra-articular injections (USGIA) have shown a higher efficacy and reduced number of adverse events due to injection techniques [1]. This has allowed targeting deep joints like the hip. The objective of the study is to evaluate the short and long term efficacy and safety of HA-USGIA in moderate hip OA.
Methods: Patients with Kellgren-Lawrence II and III hip OA (refractory to NSAIDs, pain killers and chondroprotective agents) were prospectively recruited to receive 3 consecutive weekly doses of HA- USGIA using free hand technique [2]. Informed written consent was signed. VAS pain scale and WOMAC score was performed at baseline and at 3 and 6 months after the end of treatment. The first injection was performed after a 1-month wash out. X ray assessment was made at baseline and after 6 months. Ultrasound evaluation was made at baseline and at each visit.
Results: Fifteen patients (median age 67 years, IQR 63-69 years, 13/15 women) with hip OA were enrolled and 28 hip joints were injected (Fig 1a,b). None of the hips presented ultrasound detected capsular distension (suggesting inflammation) during the study. Table 1 presents the results on medication efficacy at 3 and 6 months. The pain evaluated by VAS score showed a significant and progressive decrease from baseline to 3 and 6 months respectively (Table 1). Indeed, a significant and sustained decrease of total WOMAC scores and its separate domains- pain, stiffness and function was recorded from baseline to 3 and 6 months (Fig 2a,b). No significant changes were observed regarding the WOMAC score stiffness and function domains when comparing results at 3 and 6ms. Moreover, WOMAC-pain score was significantly lower at 6ms as compared to 3ms (Table 1), highlighting the dramatic and sustained medication impact on the most relevant parameter for clinical practice, in patients with hip OA. Neither drug-related nor injection technique related adverse effects were recorded. No patient developed signs of hip osteonecrosis or inflammatory lesions during follow-up.

Table 1. The trends of the scores expressed as medians and comparisons between follow-ups

Score	Median (Q1 to Q3)			P-values			
	Baseline (b)	3 ms	6 ms	all*	b vs. 3ms^	b vs. 6ms^	3ms vs. 6ms^
VAS pain	8 (7 to 8)	3 (2 to 4)	2 (2 to 3)	<0.0001	<0.0001	<0.0001	0.2472
WOMAC total	57 (45.5 to 64.5)	9 (6.8 to 16.3)	7 (4.8 to 12.0)	<0.0001	<0.0001	<0.0001	0.1671
WOMAC pain	10.5 (8.0 to 13.5)	2 (1 to 2.3)	0.5 (0 to 2)	<0.0001	<0.0001	<0.0001	0.0123
WOMAC stiffness	3.5 (3 to 5)	0 (0 to 1)	0 (0 to 0)	<0.0001	<0.0001	<0.0001	0.1118
WOMAC function	42 (32 to 49)	7 (3.8 to 16)	6 (4 to 11.5)	<0.0001	<0.0001	<0.0001	0.4279

Q1 = first quartile; Q3 = third quartile;
* Friedman test; ^ Wilcoxon test; 3 ms-3 months, 6ms-6 months, b-baseline

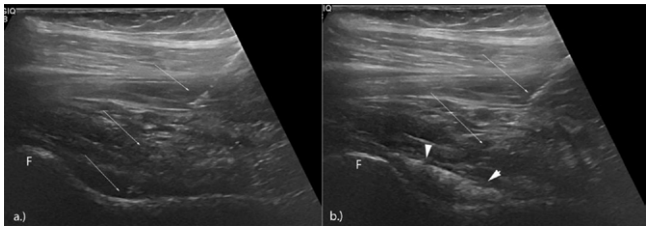


Fig.1. Legend: a.) Longitudinal scanning at hip joint level. F- femoral head, arrows showing the hyperechoic needle penetrating the muscles and arriving inside the anterior join recess. b.) Post-procedural longitudinal scanning at the hip joint level. Arrowheads- showing the hyperechoic intra-articular drug moving anti-gravitational and distending the capsule.

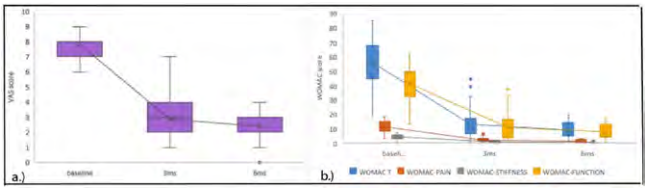


Fig 2. ab Legend. a.) Evolution of VAS for pain over time; b.) Evolution of WOMAC total score and its components over time. The line in the box is the value of median, the box is the first and the third quartile, the wishers are the minimum and maximum and the × is the value of mean. 3ms- 3 months, 6ms- 6 months, WOMAC T- WOMAC total.

Conclusion: The results suggest that HA – USGIA may be an effective and safe treatment for moderate hip OA, due to its short and long term benefits. This treatment should not be delayed until advanced OA is diagnosed. Longitudinal controlled studies on larger cohorts are warranted to confirm these preliminary results.
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AB0874 FUNCTIONALITY IN OSTEOARTHRITIC GAIT IS RELATED TO TREATMENT DECISION. A MULTIFACTORIAL ANALYSIS

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Background: Osteoarthritis (OA) is a degenerative disease with complex underling mechanisms [1–3]. The interactions among several factors make the study of the disease very complex and often lead to different treatment, i.e. surgical or conservative, decisions for subjects clinically and radiographically similar. Recent explorations performed at the body level pointed out that macro-factors, like overweight or gait, can influence the development of the disease [4]. The number of related factors is high, and they are very likely to interact with each other. However, the literature lacks randomized and balanced studies to verify such effects of multiple factors [5].
Objectives: The aim of this work was to develop a multifactorial analysis to explore whether and how gait functionality and dynamics can be related to treatment decision.
Methods: A multifactorial analysis of gait dynamics in OA subjects was developed. 81 OA subjects, graded 2-3 in KL, were selected based on 4 clinical factors: Gender (male – female), Age (60-67 – 68-75), BMI (25–29.9 – 30+) and Treatment (total knee replacement (TKR) – conservative treatment). Gait analysis was performed using 8 cameras BTS Smart-DX 700, 1.5 Mpixels 250 fps and 2 force plates BTS P-6000 500 Hz sampling (BTS S.p.A., Milan, Italy). Helen Hayes marker protocol with medial markers was used for the study. Each volunteer was asked to perform a minimum of 5 valid gait sequences. Functionality and dynamics parameters were measured.
Functionality: Velocity of gait and the time needed to perform a gait cycle were computed.
Dynamics: The reaction forces and torques at the ankles, knees and hips were computed through inverse dynamic analyses.
Analysis of variance was performed for the four factors described among the functionality and dynamics parameters.
Results: The multifactorial analysis showed that functionality values are more subjective to the studied factors than the dynamics ones.
Functionality seems to be directly related to the clinical treatment. Patients who selected TKR needed more time to make a step, spent more time in double stand position and walked slower (p<0.002). Older subject also walked slower but this dependency seemed to variate with age (interaction between clinical treatment and age – p<0.02 – Figure 1).

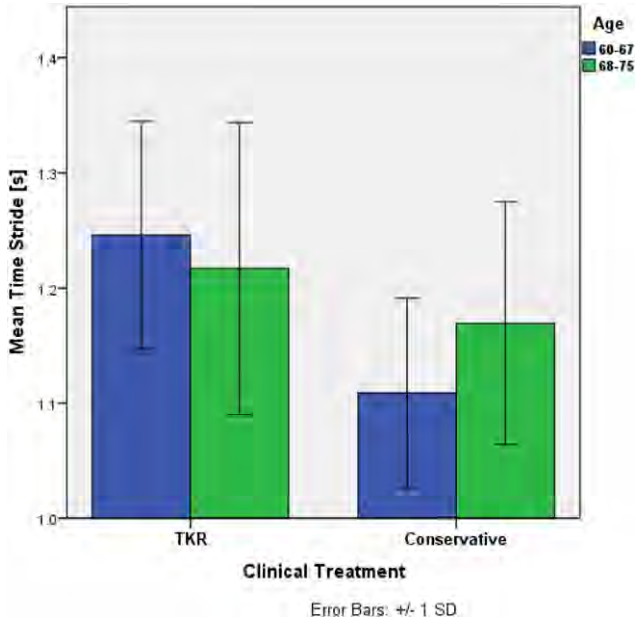


Figure 1 Interaction between Clinical treatment and age.

Dynamics: Forces at the joints seemed to be affected by the gender and an interaction between age and BMI (p< p<0.005, p<0.02) but not by the kind of therapy. Differently, torques were statistically related to the clinical treatment (p<0.007). Age was also significant as was the interaction between age and BMI (both p<0.007).
Conclusion: Reduced functionality seems to be related to the selection of therapy. In contrast to current paradigm, forces at the joints may have no role in the definition of the best therapy for OA subjects. Subjects requiring TKR do not present higher loads at the joints. However, torques seems to be related to the therapy selected. Instead of forces, kinematics and posture assessments might support rational definitions of the therapy and future multifactorial analysis should take them into consideration.

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Disclosure of Interests: None declared
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AB0875 HYBRID COOPERATIVE COMPLEXES OF SODIUM HYALURONATE + SODIUM CHONDROITIN NON-SULFATED (HA-SC) IN THE TREATMENT OF HIP OA: CLINICAL RESULTS

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Background: Hip Osteoarthritis (OA) is a widespread disease characterized by pain and functional impairment, which, particularly in the elderly, may compromise overall health and quality of life. In the last decades, Intra-articular (I.a.) injections of hyaluronic acid (HA) gained more space among the conservative treatment of OA because of their beneficial effects and positive outcomes without relevant complications. (1,2). An innovative and patented formulation containing hybrid cooperative complexes of sodium hyaluronate 2.4% + sodium chondroitin non-sulfated 1.6% of biotechnological origin (HA-SC) has been recently developed for the I.a. treatment of hip OA and evaluated in a pilot study (3).
Objectives: 1) Primary aim: Evaluation of the safety of HA-SC in the treatment of symptomatic hip OA; 2) Secondary aim: Evaluation of the efficacy of HA-SC in terms of pain reduction (VAS) and function improvement (Lequesne) of the affected hip joint.
Methods: This is a pilot, multicentric, open, prospective study. The following inclusion criteria were established: Patients (both genders) aged ≥ 40 years suffering for primary hip OA confirmed by X-Ray; Grade I-II-III according to K&L grading scale; Basal VAS pain at the target hip > 40 mm; Failure of at least two lines of conservative treatments. All patients underwent a single I.a. hip injection of a 3mL vial of HA-SC and followed-up for six months.
Results: 48 patients have been enrolled and completed the study. The treatment was generally well-tolerated, with only ten patients out of 48 (20.8%) reporting local effects mainly consisting of injection site pain and arthralgia localized in the treated area. All these patients completed the study. The treatment with HA-SC was associated with a statistically significant decrease of VAS scale from a basal value of 67.5 (mean) to 22.8 (mean, p<0.0001) at the end of the observation period at six months, with a statistically significant decrease at seven days of follow-up evaluation (29.3, mean, p<0.0001). The mean Lequesne's Index total score after the single injection of HA-SC decreased from a baseline value of 10.4 (mean) to 5.1 (mean, p<0.0001) at six months. The decrease was marked and significant also at any of the other evaluated time point (p<0.0001).
Conclusion: A single I.a. injection of the innovative formulation containing hybrid cooperative complexes of sodium hyaluronate + sodium chondroitin non-sulfated (HA-SC) showed to be well tolerated and safe in the treatment of symptomatic hip OA. A rapid and significant decrease in hip pain (VAS) and Lequesne's Index was also observed starting immediately after the I.a. injection and lasting until the end of the follow-up period. However, conservative treatment of hip OA is still challenging. This new formulation could represent a promising, long-lasting, and effective I.a. treatment.

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[3] IBSA Data on file.

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AB0876 THE BENEFIT AND SAFETY OF DIACEREIN IN AGED AND OBESE PATIENTS WITH SYMPTOMATIC KNEE OSTEOARTHRITIS: DATA FROM THE DISSCO CLINICAL STUDY

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Background: The DISSCO trial (6-month international, multicentre, double-blind, randomised study on the effect of diacerein vs celecoxib in symptomatic knee osteoarthritis [OA] patients) showed that diacerein had comparable efficacy to celecoxib at reducing the level of pain (WOMAC pain).
Objectives: To assess the effect of age, body mass index (BMI), and gender on the efficacy/safety profile of diacerein following 6 months of treatment.
Methods: Of the patients (n=380) that were randomised, 186 received treatment with 50 mg diacerein once daily for the first month and twice daily thereafter. This study was done on the intent-to-treat population (n=183). Efficacy outcome assessments which included absolute change in WOMAC pain (score 0-50) and function (score 0-170), and VAS (score 0-10) were analysed following stratification based on age (< 65 vs ≥ 65 years old) and BMI (< 30 vs ≥ 30 kg/m^2) at time of randomisation. Treatment effects on continuous efficacy outcomes were performed using covariance analysis (ANCOVA). For gastrointestinal (GI) safety outcomes, the adverse events (AEs), including diarrhoea, soft faeces, abdominal pain and dyspepsia, and the time-to-onset from baseline were stratified according to age of patients at randomisation. Treatment-related GI AEs were also assessed according to the gender. The independent variables were treatment, stratification variable, interaction between both, and the outcome measure at baseline. Comparisons between groups were carried out using Chi-square.
Results: No significant differences were found between the two age groups (<65 years old [n=105], ≥65 years old [n=78]) in the level of reduction in WOMAC pain (-10.3 ± 1.1, -8.6 ± 1.3, respectively; p=0.30), VAS (-2.3 ± 0.2, -2.2 ± 0.3, p=0.73) or improved physical function (-29.7 ± 3.7, -22.1 ± 4.2, p=0.18). The reported incidences of treatment-related GI AEs were also similar between the two age groups; more specifically for diarrhoea, incidence for patients <65 years old [n=12] 11.3% and for those ≥65 years old [n=7] 8.8% (p=0.63) with a mean time-to-onset (day 43 ± 49, 61 ±51, respectively; p=0.11). Moreover, gender had no influence on treatment-related GI AEs (p=0.42).
In regard to treatment response of obese (n=101) vs. non-obese (n=82) patients in terms of pain reduction (WOMAC: -10.1 ± 1.2, -9.1 ± 1.1, respectively; p=0.58; VAS: -2.6 ± 0.3, -2.0 ± 0.3; p=0.15), or improved WOMAC physical function (-29.8 ± 4.2, -23.5 ± 3.8; p=0.26), there were also no significant differences.
Conclusion: In symptomatic knee OA patients, the level of effectiveness and safety profile of treatment with diacerein were found not to be influenced by age, BMI or gender.
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AB0877 CLINICAL EFFICACY AND SAFETY PROFILE OF TOPICAL ETOFENAMATE IN THE TREATMENT OF PATIENTS WITH MUSCULOSKELETAL DISORDERS: RESULTS OF A SYSTEMATIC REVIEW

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Background: Musculoskeletal disorders affect millions of people of all ages around the world [1]. Nonsteroidal anti-inflammatory drugs (NSAIDs) are, in general, the cornerstone of musculoskeletal pain management; however, systemic adverse events with oral formulations of NSAIDs are common. To address this, topical formulations of some NSAIDs have been developed. [2] Although there are many nonsteroidal anti-inflammatories, only a few are used as local therapeutics. This is because the physicochemical properties of these substances, which were originally developed for oral administration, frequently do not guarantee a satisfactory pharmaceutical formulation with satisfactory topical absorption. [3]
Objectives: The aim of this systematic review was to assess the available evidence on the efficacy and safety of the topical formulations of the NSAID etofenamate in patients with musculoskeletal disorders.
Methods: A systematic search of PubMed and Web of Science was conducted, using the key words (topical etofenamate efficacy) OR (topical etofenamate safety) OR (topical etofenamate effectiveness) to identify studies of etofenamate published from inception to November 2018. Some published manuscripts of interest known by the authors but not identified in the PubMed search were also added to ensure the review article was as comprehensive as possible.
Results: Overall, 12 studies were identified. [3-14] These studies demonstrated the ability of topical etofenamate (administered either in gel [5% or 10%], cream [10%] or lotion [10%] formulations]) to improve pain and reduce inflammation in patients with musculoskeletal disorders, including blunt injuries and rheumatic diseases. Etofenamate was shown to have an overall efficacy that was superior to other topical NSAIDs, such as 1% indomethacin and 1% diclofenac, and to be as effective as topical formulations of 2.5% ketoprofen gel and 2% ketorolac gel (although ketorolac suggested a better elimination of pain at some time points). Overall, when compared to placebo, etofenamate gel 5% demonstrated significant better results in the reduction of pain symptoms (with or without combination with ultraphonophoresis). Furthermore, clinical evidence indicates that etofenamate is generally well tolerated in these indications.
Conclusion: The available clinical evidence suggests that etofenamate could be an effective therapeutic option for the management of musculoskeletal disorders, such as blunt traumas, lumbago or osteoarthritis. However, larger and well-controlled clinical trials comparing the efficacy and safety of etofenamate with other newer topical NSAIDs are warranted.
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Disclosure of Interests: Anabela Pereira Consultant of: Recently, I was a paid consultant of Bial., Speakers bureau: I have been a paid speaker for Bial., Daniela Marinho Employee of: I'm currently an employee of BIAL pharmaceutical company. I belong to the medical affairs department of Bial.
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AB0878 THE COMPARISON EFFECTS OF INTRA-ARTICULAR INJECTION OF PLATELET RICH PLASMA (PRP), PLASMA RICH IN GROWTH FACTOR (PRGF), HYALURONIC ACID (HA), AND OZONE IN KNEE OSTEOARTHRITIS; A ONE YEAR RANDOMIZED CLINICAL TRIAL

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Background: Knee osteoarthritis (OA) as a common progressive degenerative condition is one of the most important leading causes of disability and relative dependence. Worldwide prevalence of symptomatic knee OA has estimated 3.8%. It affects more than 20% of over 45-year-old population. Among the minimally invasive methods recommended for knee OA management is intra-articular injections for which a large array of products have been used. Despite all the

existing options, there is still no general consensus on the choice and priority of the best intra-articular injection in knee osteoarthritis.
Objectives: Our study compare the short and long-term efficacy of the intra articular injections (IAIs) of hyaluronic acid (HA), platelet-rich plasma (PRP), plasma rich in growth factors (PRGF), and ozone in patients with knee osteoarthritis (OA).
Methods: In this single-blinded randomized clinical trial, 238 patients with mild to moderate knee OA were randomized into4 groups of IAIs: HA (3 doses weekly), PRP (2 doses with 3 weeks interval), PRGF (2 doses with 3 weeks interval), and Ozone (3 doses weekly). Our outcome measures were the mean changes from baseline until 2,6, and 12 months post intervention in scores of visual analog scale, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and Lequesne index.
Results: A total of 200 patients enrolled final analysis. The mean age of patients was 56.9 ± 6.3 years, and69.5% were women. In 2 months follow up, significant improvement of pain, stiffness, and function were seen in all groups compared to the baseline, but the ozone group had the best results($P<0.05$). In 6 month follow up HA, PRP, and PRGF groups demonstrated better therapeutic effects in all scores in comparison with ozone ($P<0.05$).At the end of the 12th month, only PRGF and PRP groups had better results versus HA and ozone groups in all scores ($P<0.05$).Despite the fact that ozone showed better early results, its effects begin to wear off earlier than other products and ultimately disappear in 12 months.
Conclusion: Ozone injection had rapid effects and better short-term results after 2 months, but its therapeutic effects did not persist after 6 months and at the 6-month follow up, PRP,PRGF and HA were superior to ozone. Only patients in PRP and PRGF groups improved symptoms persisted for 12 months. Therefore, these products could be the preferable choices for long-term management.
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AB0879 DOES BODY WEIGHT INFLUENCE THE KNEE INJURY AND OSTEOARTHRITIS OUTCOME SCORE IN PERSONS WITH SYMPTOMATIC KNEE OSTEOARTHRITIS?

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Background: Overweight is a major risk factor for the development and progression of knee osteoarthritis (OA). Weight loss for patients with knee OA has been associated with improvement in self-reported pain and function and is recommended by EULAR as part of the therapeutic management.
Objectives: The aim of the study was to evaluate the relation between overweight and functional impairment in adults with knee OA.
Methods: It was a prospective study conducted in a rheumatologic department over a 4 months period. Patients with symptomatic knee OA based on the ACR criteria, were included. A screening of body mass index (BMI) was carried out for all patients. It was categorized following the WHO classification into: normal (<25 kg/m2), overweight (25 to <30), obese (up to 30).
Pain level was evaluated using the Visual Analogue Scale (VAS). Function was assessed by the short form of the Knee injury and Osteoarthritis Outcome Score (KOOS-PS) (KOOS-PS scores to 0 representing no difficulty and 100 representing extreme difficulty). The patients' knee radiographies were graded according to Kellgren Lawrence criteria (KL). The patients were allocated in two groups; as grade I-II KL (Group 1) and grade III-IV KL (Group 2).
Results: We included 143 patients with a mean age of 65.17± 10.7 years and 88.1% of women. Patients were from low socio-economic class in 30.8% of cases. Mean disease duration of the KOA was 5.4 years [3months-20 years] and mean BMI was 31.8±5.6kg/m^2. Patients were with normal weight in 16.1%, overweight in 19.6% and obese in 64.3%.
Knee OA was bilateral in 85.3% and other OA sites were associated in 37.8% of patients. Mean VAS pain of knee OA was 6.6±1.5 and KOOS-PS was 48.8±16.5/100. Concerning the radiographic damage; we found grade I-II (KL) in 22.6% and grade III-IV (KL) in 77.4%.
High BMI (BMI≥25 kg/m^2 was not significantly associated with worse KOOS score ($p=0.9$), more pain ($p=0.5$) or an increasing severity of radiological knee osteoarthritis ($p=0.14$). Moreover, the level BMI was not associated with the presence of other OA sites ($p=0.9$) or a bilateral KOA ($p=0.07$).
Conclusion: These data, from a subset of participants with symptomatic radiographic knee OA, demonstrate no correlation between obesity and pain, functional impairment and radiographic severity.
Acknowledgments: none
Disclosure of Interests: None declared
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AB0880 NEUROPATHIC PAIN IN PATIENTS WITH KNEE OSTEOARTHRITIS: PREVALENCE AND RELATED FACTORS

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Background: Discordance between radiographic and pain severity in osteoarthritis (OA) has led researchers to investigate other pain mechanisms, including neuropathic pain (NP). Recent meta-analysis concluded that NP prevalence in people with knee or hip OA was 23% [1].
Objectives: The primary objective of this study was to determine the prevalence of NP in patients with painful knee OA. Secondarily, we evaluated the relationship between NP and pain intensity, function and radiographic severity of knee OA.
Methods: This cross-sectional study enrolled patients with knee OA (ACR criteria) from a rheumatology outpatient Hospital over a four-month period. Exclusion criteria were: knee surgery, chronic conditions of the nervous system, cognitive or psychiatric disorders. The patient's characteristics and pain severity using the Visual Analogue Scale (VAS) were evaluated. The NP was assessed according to the Douleur Neuropathique 4 questionnaire (DN4) (arabic valid version). Functional impairment was estimated using the short form of the Knee injury and Osteoarthritis Outcome Score (KOOS-PS) (KOOS-PS scores to 0 representing no difficulty and 100 representing extreme difficulty). Radiographs were rated using the Kellgren Lawrence (KL) grade classification (I-IV). Statistical analysis was performed to find the factors closely related with NP.
Results: Ninety three patients with knee OA were included in the study. The mean age was 65.03±18.5 years with a sex ratio of 0.08. Mean duration of symptoms was 3.5 years [3months-20 years]. Concerning the marital status: 53.8% were married, 34.4% were widow and 10.8% were divorced. The majority of patients were illiterate (65.6%) and only 2.2% went to university. Patients were from low socio-economic class in 37.6% of cases. At least one comorbidity was revealed for 90.3% of patients and their mean BMI was 31.6±6.3 [19.9-52.3]. Concerning the clinical features of the KOA, mean VAS pain was 6.6±1.6 and KOOS-PS was 45.6±18.5. Of the subjects, 22.6% have radiographic at grade II, 57% at grade III and 20.4% at grade IV based on KL grading.
The mean (SD) score by the study participants on the DN4 was 4.9± 2.4. The prevalence of NP (DN4≥4) was 71%.
A DN4 score≥4 was significantly associated with the VAS pain ($p=0.00$) and the KOOS-PS ($p=0.00$) and the presence of comorbidity ($p=0.04$). However, there was no significant relation between DN4 score and, age, sex, marital status, socio economic class, level of education, BMI and KL grade ($p=0.7$, $p=0.08$, $p=0.7$,$p=0.3$, $p=0.7$, $p=0.7$, $p=0.6$).
Conclusion: Our results highlight the high frequency of NP in patients with knee OA according to the DN4. Knee OA patients with NP encounter clinically relevant functional limitation. Thus, it is important to be aware of this neuropathic component to ensure appropriate management in the treatment of knee OA pain.
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AB0881

COMPARISION OF FUNCTIONAL OUTCOMES BETWEEN PRIMARY AND REVISION TOTAL KNEE ARTHROPLASTY

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Background: Total knee arthroplasty (TKA) is the gold-standard treatment for end-stage knee osteoarthritis (OA). An increase in the prevalance of primary and revision TKA is projected due to aging of the population, increase in the obesity and OA prevalence, patients' quality of life perceptions and primary TKA procedures. Although TKA reliably improves pain and function; gait ability and function are still low compared to normal levels [1]. It is important to understand the prognosis to decide to undergo a rTKA (revision total knee arthroplasty) or enhance treatment protocols [2].

Objectives: The aim of the study is to compare the functional results of primary and revision TKA.

Methods: Hospital Of Special Surgery knee score (HSS), The Figure-Of-8 Walk Test (F8WT), The Modified Four Step Square Test (mFSST) and the 3-Meter Backwards Walk Test (3MBWT) were used for function assessment.

Table 1. Characteristics of the patients

	TKA	rTKA	p
HSS	83.00 (74.00-90.00)	78.50 (68.75-90.25)	0.179
Age-years	65.00 (57.00 – 70.25)	69.00 (59.50-75.75)	0.178
BMI-kg/cm^2	30.90 28.41 -34.65)	31.61 (25.54-36.41)	0.748
Time after surgery-years	2.00 (1.50-4.25)	3.00 (2.00-6.50)	**0.038**
Female	25 (80.6 %)	20 (69.0 %)	0.296
Male	6 (19.4 %)	9 (31.0 %)	
Pain	0.00 (0.00-0.00)	0.00 (0.00-0.75)	0.127

*p<0.05

Table 2. Functional Performances Of The Patients

	TKA	rTKA	P
3MBWT	6.2 (3.80-8.69)	7.68 (6.10- 11.25)	**0.042***
mFSST	10.20 (9.00-12.98)	13.10 (11.25-15.07)	**0.001***
F8WT	6.23 (4.74-8.6)	9.11 (7.15-12.05)	**0.001***

*p<0.05

Conclusion: Functional status, fall risk, balance and walking skills of the rTKA patients were lower than the TKA patients. rTKA patients experience longer operation time, hospital stay and make fewer functional gains. Improvement after rTKA is also reported to be lower than TKA and balance could be worsened or does not improve after TKA [2].

Walking skills of the rTKA patients were worse than the TKA patients which may cause rTKA patients to be more cautious and tentative due to fear of falling and failure of the implant leading a more impaired function [2]. rTKA patients' balance was lower and had more fall risk than the patients with TKA. These may be due to the recurrent incision of soft tissues causing a loss of more mechanoreceptors and a greater impairment of proprioception. These findings can help clinicians to make a more informed decision for both primary and revision procedures [3].

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AB0882

RELIABILITY OF THE 3-M BACKWARDS WALK TEST IN PATIENTS WITH REVISION TOTAL KNEE ARTHROPLASTY

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Background: Total knee arthroplasty (TKA) is an effective treatment for patients suffering from end-stage osteoarthritis with 10- to 15-year implant survivorship rates exceeding 90%. Infection, osteolysis due to polyethylene wear, loosening, stiffness and instability may cause to implant failure and revision of the TKA (rTKA). However, up to 20% of patients continue to have postoperative pain, functional limitations and low treatment satisfaction and 24% of patients were not able to walk unaided with no limp or a slight limp after TKA [1].

Falls and related traumas can produce "fracture, dislocation, crushing, and other injuries" [2]. Falls often occur due to impaired physical function which includes changes in lower knee joint angle, weakened lower limb muscles, peripheral nerve blockade, deformity of the foot limited balance and gait.

Several measures of fall risk have been previously developed however, recent research has demonstrated that backwards walking is more sensitive at identifying changes in mobility and balance compared to forward walking. Backwards walking is necessary to perform such tasks as backing up to a chair, opening up a door or getting out of the way of a sudden obstacle.

3-M Backwards Walk Test (3MBWT) is used to evaluate walking skills, fall risk and dynamic balance. The 3MBWT demonstrated similar or better diagnostic accuracy for falls in the past year than the most commonly used measures and found to be reliable in healthy subjects. [3] However, its reliability in rTKA has not been investigated.

Objectives: The purposes of this study were to determine the test-retest reliability and the minimal clinically important difference (MCID) of the 3MBWT in patients with rTKA

Methods: Twenty-two patients with rTKA, operated on by the same surgeon, were included. For the 3MBWT, a distance of 3 meters was marked with tape and participants were asked to align their heels with the black tape. They were instructed to walk backwards as quickly. Patients performed trials for 3MBWT twice on the same day. Between the trials, patients waited for an hour on sitting position to prevent fatigue.

Results: The 3MBWT showed an excellent test-retest reliability. Intraclass correlation coefficient ICC for 3MBWT was 0.97. The standard error of measurement and MCID at the 95% confidence level for 3MBWT were 1,08 and 2,99 respectively.

Conclusion: The 3MBWT has an excellent test-retest reliability in patients with rTKA. It is an effective and reliable tool for measuring fall risk, dynamic balance and walking skills. As a clinical test, the 3MBWT is easy to score, has no cost, needs no special equipment and can be applied in a short time as part of the routine medical examination.

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AB0883

RELIABILITY OF THE MODIFIED FOUR SQUARE STEP TEST IN PATIENTS WITH REVISION TOTAL KNEE ARTHROPLASTY

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Background: Patients with total knee arthroplasty (TKA) often experience pain and reduced balance control, which may predispose them to greater fall risk. The patients with revision total knee arthrooplasty (rTKA), have more pain, stiffness and physical dysfunction and less postoperative improvement compared to the patients with TKA [1]. Falls in people with gait or balance disorders have significant consequences. Fear of falling can also predispose people to inactivity, which can lead to problems of debilitation, increased handicap, and disability by itself. Most of the falls take place in the course of movement, and the trips and slips were determined as the most common cause of elderly falls. Trips are responsible of falls between 40% to 60% and slips between 10% to 15%, showing that the capability to take a quick step would prevent many falls [2]. Literature has found stepping speed to the different directions declines with aging and are lesser for fallers than for nonfallers [3].

Modified four square step test (mFSST) was developed to assessing fall risk and dynamic balance by scoring time while participants stepping in multiple directions but its reliability has not been investigated in patients undergoing rTKA.

Objectives: The aims of this study were to determine the test-retest reliability and the minimal clinically important change (MCID) of the mFSST in patients with rTKA

Methods: mFSST administered on 22 patients undergoing rTKA. mFSST is performed by using tapes to make one horizontal and one vertical line like a cross to create 4 quadrants. Patients' performances were timed as patients were successfully stepping clockwise and counter-clockwise while avoid touching on tapes, turning their body or losing balance. Two trials performed and patients rested between trials and were encouraged to rest as often as they required to prevent fatigue.
Results: $ICC_{(2,1)}$ for mFSST was 0.83. The standard error of measurement and MCID were 0.67 and 1.85 respectively (95 %. confidence level).
Conclusion: The mFSST has a good test-retest reliability in patients with rTKA. It is a reliable and responsive tool for measuring fall risk, dynamic balance and mobility. The mFSST is an excellent measure of gait variability, stepping in multipl directions and dynamic balance, also can easily identify real clinically important changes in patients with rTKA in simple environments and minimal equipment.
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AB0884 METABOLIC UNHEALTHY PHENOTYPE OF OBESITY IN PATIENTS WITH KNEE OSTEOARTHRITIS: THE EFFECTIVENESS OF ORLISTAT.

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Background: Obesity is an important socio-medical problem of mankind. Since the number of obese people in the world is increasing by about 1% per year, the immediate prospects do not look optimistic. One of the important risks of the development and progression of osteoarthritis (OA) is the metabolically unhealthy phenotype of obesity, which is accompanied by a violation of lipid and carbohydrate metabolism, a violation of cytokine regulation. An important step in the treatment of patients with obesity and OA of the knee joints is weight loss.
Objectives: To evaluate the effectiveness of complex therapy of metabolic unhealthy phenotypes of obesity using orlistat (an intestinal lipase inhibitor) in the clinical manifestations of knee OA, dynamic markers of lipid and carbohydrate metabolism, dynamic CRP and leptin.
Methods: The study included 50 female patients with knee OA Kellgren-Lawrence stage II-III and obesity (body mass index (BMI)>30kg/m^2), aged 45-65yo. Group 1 (25 patients) was administered orlistat at 120 mg (1 capsule) 3 times a day for 6 month combined with low-calorie diet and therapeutic physical exercise. Group 2 (25 patients) was administered only life-modifying therapy for 6 month. The clinical parameters of the course of knee OA (WOMAC), an assessment of the quality of life (EQ-5D) were assessed at initially and after 6 months. Also initially and after 6 months a laboratory study of peripheral blood was performed glucose, HDL, LDL, TG, CRP, leptin, and the index of visceral obesity (IVO) was calculated.
Results: Initially, all patients had signs of a metabolically unhealthy phenotype of obesity: waist circumference (WC) > 88cm, high IVO, dyslipidemia, arterial hypertension, hyperleptinemia. After 6 months of complex therapy of obesity using orlistat in patients of group 1, a significant decrease in body weight by 10.07% ($p < 0.05$), a decrease in WC by 8 cm ($p < 0.05$), a significantly significant decrease were achieved IVO ($p < 0.05$), glucose ($p < 0.05$). Analysis of cytokines showed a significant decrease in leptin ($p < 0.05$) and CRP ($p < 0.05$) in patients with a weight loss of more than 10%. The reduction in body weight in group 1 patients reduced pain by 52% ($p < 0.05$), stiffness by 51% ($p < 0.05$), improved joint functional failure by 51% ($p < 0.05$) and improved quality life by 52% ($p < 0.05$). In patients of group 2, against the background of non-drug therapy of obesity, body weight decreased by 0.84% ($p > 0.05$), slightly decreased WC ($p > 0.05$). Indicators of lipid metabolism, IVO, glucose, leptin remained unchanged ($p > 0.05$). The increase in CRP in patients of the 2nd group was determined by 24.54% ($p < 0.05$).
Conclusion: The results of our study demonstrate the effectiveness of the use of a comprehensive drug regimen for the treatment of metabolically unhealthy phenotype of obesity for the clinical manifestations of osteoarthritis of the knee joints; it contributes to the improvement of metabolic parameters: a decrease in WC, lipid and carbohydrate metabolism, CRP and leptin. Thus, the use of complex therapy using orlistat in patients with osteoarthritis and obesity leads to a decrease in the metabolic activity of adipose tissue, helps to reduce cardiometabolic risk and to improve the clinical course of osteoarthritis.

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AB0885 EFFECTIVENESS AND SAFETY OF GLUCOSAMINE AND CHONDROITIN COMBINATION IN PATIENTS WITH KNEE AND HIP OSTEOARTHRITIS: INTERIM ANALYSIS RESULTS OF AN OBSERVATIONAL STUDY

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Background: Combined treatment with oral glucosamine hydrochloride (GH) and chondroitin sulfate (CS) was shown to be efficient for pain relief and function improvement in osteoarthritis patients with moderate to severe knee pain [1,2].
Objectives: To investigate demographic and clinical characteristics, changes in pain, functions of daily living, quality of life and treatment satisfaction of patients with knee osteoarthritis (KOA) or hip osteoarthritis (HOA) receiving long-term treatment with oral GH and CS combination in routine clinical practice.
Methods: An open-label, multicenter, observational prospective study is being conducted in the Russian Federation. Patients of both sexes with KOA or HOA (Kellgren and Lawrence grades I-III) who receive GH 500 mg+CS 400 mg capsules three times a day for the first 3 weeks of treatment, then twice daily, are included in the study. The interim analysis has been conducted after the first 550 enrolled patients (50% of the total sample size) had completed the first follow-up visit (Week 16-24 after the start of treatment).
Results: The study group included 406 (73.8%) patients with KOA and 144 (26.2%) patients with HOA enrolled in 43 centers in Russia. The mean age of the patients was 61.1 years; most patients were women (88.7%). The predominant risk factors for OA were non-genetic causes (excess weight, hormonal disorders, malformations of bones and joints, joint operations) (52.8% of patients), exogenous risk factors (professional activity, trauma, sports) and hereditary diseases of bones and joints were reported in 15.5% and 4.1% of patients, respectively.
Interim analysis showed clinically significant improvement in each of the KOOS and HOOS subscales at 4-6 months after the start of treatment. In patients with KOA, the mean score increase was 15.7 for the Pain subscale, 14.6 for the Quality of Life subscale, 13.8 for the Physical function (KOOS-PS), and 11.7 for the Symptoms subscale. The percentage of patients who rated the pain frequency as 'always' or 'daily' decreased from 60% to 25%.
In patients with HOA, the mean score increase was 16.0 for the Pain subscale, 14.3 for the Quality of Life subscale, 16.1 for the Physical function (HOOS-PS), and 10.3 for the Symptoms subscale. The percentage of patients who rated the pain frequency as 'never' or 'monthly' increased from 34% to 60%.
Most patients (89.1%) were receiving the medicinal product for ≥3 months. Treatment-related AEs were reported in 16 (3.0%) patients and mainly included gastrointestinal tract disorders (in 12 (2.2%) patients).
Conclusion: The results obtained at 4-6 months after the start of treatment demonstrate clinically significant reduction of frequency and intensity of pain and other OA symptoms, as well as improvement of functions in daily living and quality of life in patients with KOA or HOA after the first course of treatment with GH + CS capsules. The majority of patients (72.5%) were satisfied with the treatment. The incidence of drug-related AEs was low, and the nature of AEs was consistent with known safety profile of GH and CS combination.
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24. Osteoporosis

AB0886 INCIDENCE OF FRACTURES IN A BARIATRIC SURGERY COHORT

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Background: Bariatric surgery is the set of surgical techniques whose objective is weight reduction, and it could have complications. One of them may be the increase in the incidence of fractures (1), secondary to nutritional defects (2), among others, that could modify bone metabolism with an increase in remodeling (3).
Objectives: To carry out a retrospective observational pilot analysis of a cohort of 140 morbidly obese patients after bariatric surgery, of a total of 304, descriptive of axial and peripheral fractures, among other variables.
Methods: Data were collected from the University Hospital of Fuenlabrada of a cohort of morbidly obese people who underwent bariatric surgery from 2009 to the present. Were included as variables age in years, sex, body mass index (BMI) before surgery, evolution time since surgery in years, incidence of sleep apnea syndrome (OSAS), incidence and type of fracture, osteoporotic or not, and axial or peripheral. A descriptive and frequency analysis, and a chi-square contingency table between incidence of fracture, and gender, OSAS, or childhood obesity, were performed.
Results: A 48.76 years old cohort was observed, 25.7% men/74.3% women, 30.8% childhood obesity, BMI of 45.65 kg / m2, and 45% with a diagnosis of OSAS. A 15% of fractures were noted: 66.66% considered as osteoporotics (40.76% axial, 50.31% peripheral, and 8.93% of both) in a time of evolution of 5.81 years, and without relationship with gender, OSAS or childhood obesity (p = 0.7, p = 0.15, p = 0.16).
Conclusion: It is a study that higlights that bariatric surgery in Fuenlabrada area is mainly performed on morbidly obese women in adulthood. There is a high rate of OSAS, and an increase in the incidence of fractures unrelated to gender, OSAS or childhood obesity, despite the fact that in the bariatric surgery protocol densitometric osteoporosis is an exclusion criterion.
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AB0887 PATIENTS DEMOGRAPHIC CHARACTERISTICS WITH ESTABLISHED OSTEOPOROSIS TREATED WITH DENOSUMAB IN A THIRD LEVEL HOSPITAL

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Background: Osteoporosis (OP) is the most common cause of fragility fractures. It is characterized by a loss of bone mass that modifies the bone microstructure, increases fragility and predisposes to fractures. There are numerous risk factors for fragility fracture that must be evaluated for diagnosis and treatment. The treatment consists of non-pharmacological measures (balanced diet and exercise), adequate intake of calcium and vitamin D and specific pharmacological treatment (bisphosphonates, teriparatide, denosumab or selective estrogen receptor modulator) 1-3.
Objectives: To perform a descriptive evaluation of the demographic and clinical characteristics of patients with osteoporosis treated with Denosumab, their degree of compliance with the therapy as well as the evaluation of the possible causes of treatment cessation.
Methods: All patients diagnosed with OP from January 2015 to January 2020 have been reviewed in the Rheumatology Service of the University Hospital of Santiago de Compostela and patients treated with denosumab have been selected. Demographic, clinical and treatment data have been collected from data collected in their electronic medical record
Results: Of the 507 patients diagnosed with Osteoporosis from January 2015 to January 2020, a total of 133 patients (26.2%) have received treatment with Denosumab. The majority are women (92.5% n = 122) with a mean age of 76 years (age range: 49-105 years). Previously, 38% (n = 51) had vertebral fractures, with 8% (n = 11) standing out who had presented 3 or more vertebral fractures prior to Denosumab treatment.
The mean time to start Denosumab therapy since the diagnosis of Osteoporosis (by Densitometry or established by fractures) has been 35 months (0 to 84 months from diagnosis)
Through the electronic Medical Record the dispensations were accessed in the Denosumab pharmacy office and its administration in Primary Care was verified. Complete adherence to treatment (without skipping any dose) was observed in 73% of patients (n = 97). In 5.2% (n = 7) an omission was avoided. In 21.8% (n = 29) 2 or more dose omissions were corroborated 9 patients (6.8%) completed treatment with Denosumab in the follow-up period (55% due to the need for dental interventions, 33% for loss of follow-up and 12% for fear of secondary effects).
In 66 patients (49.6%) risk factors were identified to present Osteoporosis; being corticosteroid therapy at doses greater than 5 mg / day of Prednisone or equivalent (26% n = 33) the most frequently identified risk factor.
No vertebral fractures were registered at the end of treatment with Denosumab, with an average time since the end of treatment of 2.77 years (6 months - 8 years).
Conclusion: The rate of patients diagnosed with Osteoporosis who receive Denosumab therapy at some time reaches 26%, being the most frequent drug used after bisphosphonates.
Complete adherence to treatment has been observed in 73% of patients.
We have not observed vertebral fractures after suspension of Denosumab in our series of patients, although the total exposure time (from the end of treatment to the end of follow-up) is short: 2.77 years
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AB0888 REASONS FOR LETHALITY IN ELDERLY AND SENIOR AGE PATIENTS WITH OSTEOPOROTIC FRACTURES OF FEMUR

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Objectives: to identify the causes of mortality in middle-aged and elderly patients during the first year after they had a low-energy hip fracture.
Methods: the causes of lethality were examined of the patients with a non-traumatic femur fracture. 432 patients with osteoporotic hip fractures were under observation: 328 women and 104 men. The mean age of women was 75, 4 (70; 82) years, the mean age of men was 71,5 (65; 80) years.
Results: after 12 months, mortality rate was 137 cases (total mortality - 31.8%). Most of the deaths were due to cardiovascular system diseases. The total number of fatal cases was 93 (67.8%): for men - 22 (66.0%) cases, for women - 71 (68.3%) (p = 0.65). Diseases of the respiratory system caused death in 23 (16.8%) patients: in men - 5 (15.1%) cases and in women - 18 (17.3%) (p = 0.31). Mortality from oncological diseases was 15 (10.9%) cases: in men - 3 (9.09%) cases and in women - 12 (11.5%) (p = 0.45). Diseases of the digestive system, as the cause of death, were detected in 5 (3.6%) men and women (2 (6.06%) and 3 (2.9%) cases, respectively (p = 0.1)).
Conclusion: the most of the deceased men and women had cardiovascular and respiratory diseases. The gender differences in mortality rates were not found.
Disclosure of Interests: None declared
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AB0889 **SARCOPENIA AND HIP FRACTURE IN GERIATRIC POPULATION**

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Background: Sarcopenia is a loss of skeletal muscle mass, muscle strength, and function, with an impact on the quality of life, increased risk of bone loss and fracture, which is associated with normal aging.
Objectives: To determine the effect of sarcopenia on the recovery of patients after hip fracture, their fitness, functionality, and quality of life
Methods: A prospective study had 60 patients with hip fractures of both sexes,> 65 years of age (70.8), in the experimental group of patients with sarcopenia and the control group without sarcopenia. All anthropometric measurements were performed: BMI (kg / m2), waist circumference, the volume of the upper arm and lower leg muscle mass, handgrip force (kg) - dynamometry. The following questionnaires were used to assess functionality, mobility, and quality of life: Health assessment questionnaire (HAQ), Harrison hip score (HHS), Sarcopenia and Quality of life (SarQol)
Results: Muscle mass (BMI) was significantly lower in the experimental group patients (p <0.005) compared to the control group. The clamp strength measured by the dynamometer was significantly lower in patients with hip fractures (p <0.005) compared to the control group. About 2/3 of the subjects with sarcopenia and hip fracture have a severe and complete physical disability. There was a significant difference in all domains of quality of life between subjects with hip fractures and the control group due to the presence of sarcopenia (p <0.005).
Conclusion: The presence of sarcopenia indicates consequently reduced functionality and a degree of disability in patients with hip fractures, slows recovery and increases the need for mobility aids, thus extending hospital stay and patient recovery.
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AB0890 **VITAMIN D PROMOTES BONE MINERAL DENSITY ACCRUAL AFTER DISCONTINUATION OF ALENDRONATE.**

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Background: Vitamin D repletion is known to maximize the response to bisphosphonates (BPs) in terms of both bone mineral density (BMD) changes and anti-fracture efficacy. The contribute of vitamin to BMD after discontinuation of BPs has been poorly investigated.
Objectives: To explore whether change of vitamin D status may contribute to the tail effect of alendronate (ALE) on BMD.
Methods: Participants in this retrospective study were postmenopausal osteoporotic women exposed to ALE. Either cholecalciferol or calcifediol have been administered, as vitamin D supplementation in accordance to good clinical practice, during ALE treatment and after ALE discontinuation. BMD was evaluated by Dual-energy X-ray absorptiometry (DXA) at lumbar spine and femoral site. Vitamin D status has been checked by measuring 25(OH)D serum levels through HPLC. Surrogate bone formation and resorption markers (i.e. C-terminal telopeptide of type I collagen (CTX) and alkaline phosphatase (ALP), respectively) were also evaluated. The Fracture Risk Assessment Tool (FRAX) served to estimate the participants' 10-year fracture risk for major osteoporotic and hip fracture.
Results: 88 postmenopausal osteoporotic women (age 61.14 ± 6.96 yr.) were included in the final analysis. The 10-year probability of major and hip fractures was 18.31±11.51 and 8.60 ± 10.55 %, respectively. Participants were exposed to ALE treatment for 31.27 ± 20.69 months; then they stopped treatment for 33.33 ± 18.97 months. Change of BMD was inversely related to drug holiday (r=-0.27, p=0.005). Modification of 25(OH)D was inversely associated with change of ALP (r=-0.22, p=0.018) and CTX levels (r=-0.3, p=0.06). By distributing participants in tertiles according to variation of 25(OH)D levels over time, women allocated in the tertile with the higher increase of 25(OH)D showed a 5.7% BMD gain that was two times larger in comparison with participants with lower increase of 25(OH)D. At a multiple regression analysis, after correcting for ALE treatment duration, bone turnover marker modifications, BMI and age at menopause, BMD change at lumbar spine was significantly associated with time since menopause (ß=2.28, SE 0.44, p<0.0001), FRAX score (ß=-0.65, SE 0.29, p=0.03), drug holiday duration (ß=-2.17, SE 0.27, p<0.0001) and change of 25(OH)D levels (ß=0.15 SE 0.03, p=0.0007).

Conclusion: After ALE discontinuation, modification of BMD are strictly associated with change of vitamin D status.
Disclosure of Interests: None declared
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AB0891 **BARE TO THE BONE - AN AUDIT OF RENAL BONE DISEASE AGAINST KDIGO GUIDELINES**

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Background: Chronic kidney disease-mineral and bone disorder (CKD-MBD) is complex and management can be difficult. We aimed to compare management of our CKD patients to 2018 KDIGO guidelines. The guidelines suggest checking calcium and phosphate (Ca/PO4) within 12 mths in CKD 3a and 3b, within 6 mths for CKD 4, and within 3 mths for CKD 5. Parathyroid hormone (PTH) should be checked at baseline in CKD 3a-b, within 12 mths in CKD 4 and within 6mths in CKD 5. Alkaline phosphatase (ALP) should be measured within 12 mths in CKD 4 and 5. 25-(OH)D levels 'might' be measured at baseline in CKD 3a to 5D. BMD scanning is suggested if the result will impact treatment decisions. Lateral abdominal X ray is recommended as an alternative to CT for detection of vascular calcification. Calcitriol and vitamin D analogues are no longer routinely advised in CKD 3a-5; 25-(OH)D insufficiency should be corrected as in the normal population.
Objectives: To compare management of our CKD patients to 2018 KDIGO guidelines
Methods: We randomly selected 70 patients in whom data was available from renal clinics between May and September 2019.
Results: Mean age was 67.3 yrs. 41 male, 29 female. 33 patients had CKD 3a-b; 31 had CKD 4; 6 had CKD 5. Mean duration of CKD was 10.6 yrs. 10 patients were taking activated vitamin D analogues; 13 were taking 25-(OH)D analogues. 25-(OH)D levels ranged from 24-158 nmol/L (mean 65nmol/L). PTH levels ranged from 2- 69pmol/L (mean 23pmol/L). 3 patients were taking bisphosphonates. 44 had previous lumbar spinal imaging; vertebral fractures were evident in 4 (9%). 12 patients had had DXA scans; lowest T score was -2.5. Table 1 - tests within suggested time frames:

	CKD 3a-3b	CKD 4	CKD 5
Ca/ PO4	33 (100%)	29 (93%)	6 (100%)
ALP	33 (100%)	31 (100%)	6 (100%)
PTH	14 (42%) (ever)	8 (26%)	3 (50%)
25-(OH)D	8 (24%) (ever)	8 (26%) (ever)	1 (14%)(ever)

Conclusion: Optimum PTH levels in CKD patients are not known, and therapeutic options in CKD-MBD often limited. Nevertheless, our results suggest that bone biochemistry could be checked more consistently in CKD patients. Although detection of vascular calcification may not alter renal management, abdominal imaging provides an opportunity to screen for vertebral fracture, present in a

significant number of our patients. The KDIGO guidelines offer a framework to work with our renal colleagues, as many patients will be jointly managed.

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AB0892 PREGNANCY AND LACTATION ASSOCIATED OSTEOPOROSIS: FIRST CASE SERIES IN IRAN

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Background: Osteoporosis is a common rheumatologic disorder in postmenopausal women which could lead to morbidities later in life. However, this condition has not been properly studied in premonapausal women.

During pregnancy, the fetus needs a total of 30 grams of calcium for its skeleton and during lactation, 200 mg of calcium is secreted in the breast milk per day which the mother acquires by doubling its intestinal absorption rate. If the calcium intake of the mother is not sufficient to satisfy the fetus' needs, it will be provided by bone resorption, which will decrease the maternal calcium reserves [1].

Pregnancy and Lactation Associated Osteoporosis (PLAO) is a rare condition associated with pregnancy that should be considered in premenopausal women. The most commonly affected sites are the vertebrae and, more rarely, the hips, pubic rami and ribs [2].

An important complication of osteoporosis is fracture and a preemptive diagnosis and treatment thereof, can have drastic effects on the quality of life.

Objectives: Our objective is to document the relevant risk factors, present signs and symptoms, course of illness, and response to treatment in three cases of PLAO. It is quite possible that osteoporosis in pregnancy

and lactation is more frequent than recognized, simply because it is only recognized when an-unexpected fracture occurs[3]. Thus, in this article we are presenting three cases that showcase the need for more rigorous research on PLAO risk factors, the need for screening in high risk patients, and the advantages of early detection in patients' outcome.

Methods: The clinical cases of the patients whose PLAO diagnoses had been confirmed by both a radiologist and a rheumatologist in the past year was extracted. Information related to demographic indices, clinical manifestations, and the treatment methods was evaluated and compared.

Results: In the past year, three patients with a chief complaint of low-back pain have visited our clinic. The first, a 22-year-old woman with a nursing history of 2 months, the next one, a 31-year-old woman with a nursing history of 3 months, and the last, a 22-year-old woman with a nursing history of 4 months. All three patients had low back pain and tenderness. Two out of three patients had deficient vitamin D levels and the other had a normal one. All three patients had low BMD in lumbar vertebra and MRI imagings indicative of osteoporotic fracture.

Table 1. General and pregnancy-relatedcharacteristics of the case studies

Variables	*Case 1*	*Case 2*	*Case 3*
Age	22	31	22
Nursing duration	2 months	3months	4months
BMD(lumbar spine)	-3.6	-3.5	-3.1
Vitamin D level	12.6(ng/ml)	31.6(ng/ml)	8(ng/ml)
Fracture	$T_{12,}L_1$	$T_{4,5,6,7,10,}L_2$	$L_{1,2,3,4,5}$

Conclusion: Since the symptoms of PLAO are often confused with pain in other low-back pain conditions associated with pregnancy, PLAO is a mostly overlooked diagnosis[4]. It is only recognized when an unexpected fracture occurs [3]Therefore, high risk patients with less severe symptoms are usually not diagnosed and thusly, should undergo a proper screening test, so that they are recognized early and the morbid sequelae are averted.

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AB0893 THE EFFECTS OF THREE DIFFERENT VITAMIN D3 SUPPLEMENTATION REGIMENS IN DEFICIENT SUBJECTS - A RANDOMIZED OPEN-LABEL PARALLEL GROUP STUDY.

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Background: Currently, most experts agree that levels of serum 25OH-Vitamin D (25OHD) lower than 20 ng/mL represent an acceptable threshold for deficiency (1). However, recommendations for vitamin D supplementation vary between scientific societies, and the best regimen to treat deficient patients is still not clear (1).

Objectives: The aim of our study was to compare the pharmacokinetic profile of three different regimes of cholecalciferol supplementation in terms of 25OHD exposure and their safety profiles.

Methods: We evaluated, in healthy subjects affected by vitamin D deficiency (defined as 25OHD<20 ng/mL), 18 to 60 years of age, the efficacy of three different oral supplementation regimens: daily 10,000Iu administered for 8 weeks, weekly 50,000Iu for 12 weeks and biweekly 100,000Iu for 12 weeks. Serum 25OHD was dosed at baseline, at week 2, 4, 8 in all three groups and also at week 12 in the 50,000 and 100,000Iu groups (the blood sample was taken before the drug administration if scheduled on the same day). Baseline characteristics and 25OHD changes from baseline to the various observation points were tested with ANOVA and t-test. 25OHD was measured by the IDS-ISYSMulti-Discipline automated analyser (Immunodiagnostic System, Boldon, UK) based on chemiluminescence technology. The CV intra-assay measured in our laboratory was 6% (inter-assay CV 9%). The study was authorized by the local ethical committee (protocol DIBA/11. Supported by Abiogen Pharma, Italy).

Results: A total of 75 subjects were randomized to receive one supplementation regimen. The descriptive of the sample at baseline and relative 25OHD levels at the various observation points are reported in table 1. 25OHD increased significantly already at week 2 in all three groups (p=0.000). At week 2, 100% of the subject of the daily regimen group presented 25OHD levels >20ng/mL, 96% in the weekly and 88% in the biweekly ones.

Table 1. mean values ± SD at the different observation points.

Parameter	Daily 10.000 Ui (N = 25)	Weekly 50.000 Ui (n = 25)	Biweekly 100.000 Ui (N = 25)	p-value
M:F	12:13	7:18	12:13	
Age (years)	30.2 ± 9.9	36.7 ± 8.7	35.4 ± 11.0	*0.059
Body Weight (kg)	65.8 ± 13.2	67.8 ± 10.8	66.6 ± 13.7	*NS
Height (m)	1.7 ± 0.1	1.68 ± 0.1	1.7 ± 0.1	*NS
BMI	22.55 ± 2.7	23.8 ± 2.2	22.8 ± 2.7	*NS
Baseline 25OHD (ng/mL)	14.6 ± 3.9	12.8 ± 3	13.5 ± 4.1	*NS
25OHD week 2	32.3 ± 5	26.5 ± 3.4	25.6 ± 5	[a]0.007 [b]0.000
25OHD week 4	55 ± 10.1	39.9 ± 4.2	36.9 ± 7.2	[a]0.000 [b]0.000
25OHD week 8	79.1 ± 16.2	53.5 ± 7.2	46.4 ± 8.2	[a]0.000 [b]0.000 [c]0.001
25OHD week 12	NA	58.5 ± 7.8	50.6 ± 9.6	[b]0.000 [c]0.001

*ANOVA test.

[a]Daily 10.000 Ui vs weekly 50.000 Ui.

[b]Daily 10.000 Ui vs Biweekly 100.000 Ui.

[c]Weekly 50.000 Ui vs biweekly 100.000 Ui.

In addition, the 25OH levels of the daily regimen group at week 8 were higher than both the ones of the weekly and the biweekly regimen groups both at week 8 and week 12 (p<0.000 vs both groups).

No serious adverse event occurred.

Conclusion: All the three different regimens proved to be effective in correcting vitamin D deficiency already after 1 months (2 weeks for the daily regimen). A more refracted approach seems to more effective than the bolus-based regimens. The safety profile was excellent in all groups.

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Disclosure of Interests: Angelo Fassio Speakers bureau: Angelo Fassio reports personal fees from: Abiogen and Novartis, outside the submitted work., Giovanni Adami: None declared, Ombretta Viapiana: None declared, Giovanni Orsolini: None declared, Alessandro Giollo: None declared, Maurizio Rossini Speakers bureau: AbbVie, Abiogen, Amgen, BMS, Eli-Lilly, Novartis, Pfizer, Sanofi, Sandoz and UCB, Davide Gatti Speakers bureau: Davide Gatti reports personal fees from Abiogen, Amgen, Janssen-Cilag, Mundipharma, outside the submitted work.
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AB0894 OBSERVANCE OF ZOLEDRONIC ACID INFUSION. A RETROSPECTIVE 3 YEARS STUDY

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Background: Osteoporosis is a public health issue. Lack of therapeutic compliance is often a problem in the treatment of osteoroposis, with potentially dramatic consequences. No studies have evaluated the observance of zoledronic acid infusion after 3 years, the time of the therapeutic reassessment.
Objectives: The main objective of assessing the level of compliance was to evaluate the level of zoledronic acid infusion adherence at 1, 2 and 3 year periods, in a cohort of osteoporotic patients on discharge from Begin hospital, following treatment for fracture caused by low-energy trauma. The first infusion was prescribed by rheumatologists, with the following infusions to be prescribed by general practitioners.
Methods: We performed a retrospective observational study initially conducted by written and telephone questionnaires on a population of patients hospitalized in the rheumatology department of HIA Bégin for an osteoporotic fracture. Data was collected between July 2015 and December 2018. A first letter, containing a stamped addressed envelope to the Bégin hospital for ease of reply, was sent to the patients selected for the study. The protocol had to be modified following a very low response rate, unaided by bad quality addresses. We then tried to contact the patients by phone 3 times and, if unable to reach them, we called their general practitioners on 3 occasions.
Results: 94 patients were initially selected. Every year, we retained within the study patients who had followed their annual zoledronic acid infusion protocol. Taking into account all 94 patients, adherence level for the first infusion was 41.4%, down to 29.7% for the second infusion and down to 12.8% for the third infusion.
For those who had the first infusion performed, adherence level for the second infusion was 71.8%, down to 30.8% for the third infusion.
Conclusion: The observance and follow-up of zoledronic acid infusion in France by general practitioners is not adequate. Follow-up measures on an annual basis by the rheumatologist could significantly improve adherence.
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Disclosure of Interests: None declared
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AB0895 RELATIONSHIP BETWEEN BONE MINERAL DENSITY, INFLAMMATORY ACTIVITY AND AUTOIMMUNITY IN A COHORT OF EARLY RHEUMATOID ARTHRITIS PATIENTS

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Background: The etiology of bone loss in Rheumatoid Arthritis (RA) is multifactorial and systemic inflammation plays a relevant role. Recently, a relationship between autoimmunity and bone mineral density (BMD) has been described in patients with RA.
Objectives: To study BMD and biochemical parameters of bone metabolism in a cohort of patients with early rheumatoid arthritis, and assess the relationship between them and autoimmunity and other markers of inflammation.
Methods: A prospective longitudinal study was performed. 128 patients from an early Rheumatoid Arthritis Unit (ERAU) were included. All of them fullfilled ACR 2010 classification criteria for RA. Demographic, clinical, biochemical, immunological, radiological and densitometric data, and also inflammatory activity index DAS 28, HAQ functional index, were collected. Any value >20 IU/mL for RF and >30 IU/mL for ACPA was defined as positive.
Results: Between January 2009 and June 2017, 801 patients were evaluated in our ERAU. After two years of follow-up, the most frequent definitive diagnoses were: Early RA 221 (27.6%), Undifferentiated Arthritis 97 (12.1%), Psoriatic Arthritis 62 (7.7%), Spondyloarthritis 54 (6.7%) and autoimmune Diseases 28 (3.4%).
From the 128 patients with early rheumatoid arthritis evaluated, 104 (81.9%) were ACPA positive and 98 (77.2%) FR positive. The mean BMD in the total column was 0.96 ±0.14 g/cm2 and in the femoral neck was 0.76 ±0.12 g/cm2. No correlation of BMD with autoimmunity markers was found in either of the two locations studied, while a negative relationship between BMD and the PCR inflammation marker (BMD femoral neck: rho-0.203, p = 0.027 and BMD lumbar spine rho =-0.27, p 0.003) was found. The BMD did not correlate with DAS28 nor the HAQ index.
The mean baseline serum calcidiol value was 20.7±8 ng/ml, and a negative correlation of basal serum calcidiol with the functional HAQ index was observed (rho=-0.23, p= 0.008). No correlation between other autoimmunity (FR and ACPA) and inflammation (VSG, PCR and DAS 28) markers and vitamin D was found.
Conclusion: The BMD in patients with early rheumatoid arthritis of our cohort correlates with the PCR inflammation marker. Unlike other studies shows, in our cohort, serological autoimmunity factors do not have shown to have an independent effect on BMD.
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AB0896 EFFECTIVENESS OF SACROPLASTY IN THE MANAGEMENT OF OSTEOPOROTIC SACRAL FRACTURE IN ELDERLY PATIENTS

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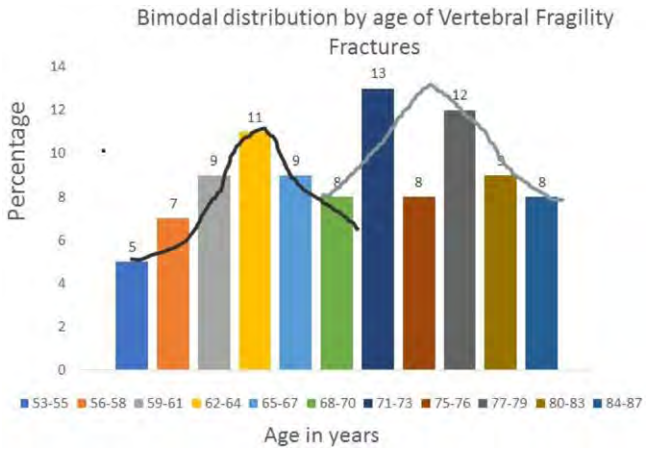
Background: Sacral fractures are a source of pain leading to loss of autonomy in elderly patients. Sacroplasty may be an effective alternative of conservative medical treatment.
Objectives: To evaluate the short-term analgesic effect of sacroplasty compared to conservative treatment in patients with osteoporotic sacral fractures
Methods: This is a retrospective study of cases of osteoporotic sacral fractures treated with sacroplasty, compared with cases treated with conservative medical procedure over the same period. Outcome was evaluated by pain (Visual analogic scale) short-term (one month) evolution and side effects occurrence.
Results: From January 2009 to June 2019, eleven patients were treated with sacroplasty for osteoporotic fractures at the Besançon University Hospital Centre. These were compared to 12 patients with osteoporotic sacral fracture with exclusive medical management, as a control group. The two groups were similar in age, gender and pain level at baseline. The median VAS was 7/10 in both groups at baseline, In the sacroplasty group, a significant decrease of pain was observed over the two first weeks, with a tendency remaining at day 30. There were no significant differences in the conservative treatment group at one week (p=0.2), fourteen days (p=0.6) and thirty days (p=0.7) compared to basal assessment.
When comparing the sacroplasty group and the conservative treatment group, no differences were noted at baseline between the two groups, there was a significant difference between the two groups the following day (p=0.001), one

week (p=0.003) and day 15 (p=0.01) after the intervention. However, there was no significant difference between the two groups at day 30, but only a trend (p=0.08).
Regarding analgesic treatments, 30% of patients in the sacroplasty group could reduce their analgesics between the time they entered and left hospital. None of the patients in the control group were able to reduce their analgesic treatment over this period. In addition, half of the patients in the sacroplasty group were successful in returning home compared to only one-third of the patients in the conservative treatment group.
Conclusion: In this study, sacroplasty was associated with an early and significant pain relief compared to conservative management in patients with osteoporotic sacral fracture. The procedure is well tolerated and may prevent loss of autonomy in these patients.
Disclosure of Interests: None declared
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AB0897 BIMODAL DISTRIBUTION OF VERTEBRAL FRAGILITY FRACTURES (VFF) IN A FRACTURE LIAISON SERVICE (FLS). RESULTS OF A COMPARATIVE ANALYSIS OF PATIENTS WITH VFF VERSUS THOSE WITH OTHER FRAGILITY FRACTURES (OFF).

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Background: Fragility fractures (FF) represent a health problem and among them, the VFF. They have worse vital prognosis, are at greater risk of new FF, had higher comorbidity, with clinical manifestations in only 30%-40% of cases. One in 6 women and one in 12 adult males will have a VFF.
Objectives: To analyze the clinical characteristics of FF patients attended in the FLS at Virgen Macarena University Hospital. Compare the sociodemographic and clinical characteristics of VFF patients with those with OFF.
Methods: Design: Prospective cohort. Patients attended in the FLS from May 2018 to November 2019 in a protocolized manner (Openclinica®). Inclusion criteria: a clinical FF in the previous two years. Descriptive statistics: percentages and means with 25th and 75th percentile. Inferential statistic by parametric and nonparametric tests. The project was approved by the Ethics Committee and patients signed consent to participate.
Results: Data from 414 patients with a first FF are analyzed, 101 (25%) with VFF and 313 (76%) with OFF [188 (45%) hip, 66 (16%) distal radius, 32 (8%) humerus and 27 (6%) miscellaneous (pelvis, ribs, tibia)]. All VFFs analyzed had clinical symptoms and the number of fractured vertebrae was 2 (1-3). In 28 (37%) were FF of dorsal vertebrae, at 25 (33%) lumbar and 23 (30%) dorsal and lumbar. Comparative analysis showed differences in age VFF 71 (62-77) vs OFF 76 (66 – 83) years, p=0.0003. It highlighted a bimodal distribution according to age, with a peak incidence of 55 to 68 years and another between 75-80 years (Graph). Referral unit to FLS: VFF Rheumatology (42%) and/or Traumatology Emergency Room (44%) vs OFF Internal Medicine (45%) and General Traumatology Unit (38%), p=0.0001. There were also differences in the treatment with teriparatide (VFF 20% vs OFF 4%); zoledronate (VFF 6% vs OFF 3%) and alendronate (VFF 44% vs OFF 63%, p=0001); days of immobilization (VFF 30 (0 - 60) vs OFF 10 (0 - 30), p-0.01); they have greater independence to carry out activities of daily life (Barthel Scale) VFF 95(81 – 100) vs OFF 80 (60 – 95), p=0.00001; increased clamping force of hands 18 (12 - 20) vs 12 (8 - 18) mmHg, p=0.001, and lower risk of falls (J D Downton Scale) (VFF 43% vs OFF 60%, p=0,01). While the number of relevant comorbidities was higher in VFF 3 (1 - 5) vs OFF 2 (1 - 4) it was no statistical, p=0.3. The use of GCC was risky for VFF (n=13, 13%) vs OFF (n=17, 5%), p=0.01 and RR (95%CI) 2.3 (1.01 – 5.3) and not for other drugs (GnRH inhibitors, aromatase inhibitors or chemotherapy). No differences in sex were found (VFF 80%- vs OFF 80% women, p=0.9), previous FF history (9% vs 12%, p=0.2), secondary OP (16% vs 21%, p=0.1); percentage of patients with OP by femoral neck DEXA (VFF 35% vs 42%, p=0.2) or by lumbar spine DEXA (VFF 36% vs OFF 34%, p=0.8).



Conclusion: VFF have a bimodal age-based distribution, usually occurring in younger patients, with a higher degree of independence and muscle strength and lower risk of falls, although they are associated with longer duration of immobilization, compared to OFF. In our cohort, VFFs affect 2 or more vertebrae and they are commonly treated with parenteral osteoporotic drugs. The use of glucocorticoids doubled the risk of developing a VFF, these findings are similar to those of others published cohorts.
This project received a grant of the Ministry Health of the Junta de Andalucía Ref.PIN-0092-2016.

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Disclosure of Interests: Blanca Hernández-Cruz Speakers bureau: Abbvie, Lilly, Sanofi, BMS, STADA, Francisco Jesús Olmo Montes: None declared, Maria José Miranda García: None declared, María Dolores Jimenez Moreno: None declared, María Angeles Vázquez Gómez: None declared, Mercedes Giner García: None declared, Miguel Angel Colmenero Camacho: None declared, José Javier Pérez Venegas: None declared, María José Montoya García: None declared
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AB0898 IMPACT OF BIOLOGICAL AGENTS, ORAL GLUCOCORTICOIDS, OR BOTH ON THE EFFICACY OF DAILY TERIPARATIDE TREATMENT FOR OSTEOPOROSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Daily teriparatide (dTP) strongly affects bone metabolism in patients with rheumatoid arthritis (RA), resulting in increased bone mineral density (BMD). We reported the 2-year results of dTP treatment for osteoporosis (OP) in patients with RA in EULAR2014 [1]. Drugs affecting bone metabolism, such as biological agents (BIOs) and glucocorticoids (GCs), are frequently administered to patients with RA in addition to dTP in daily clinical practice. Although dTP increases bone turnover, BIOs reduce osteoclast activity and GCs decrease bone turnover. We reported the effects of GCs or BIOs on the efficacy of dTP in EULAR2015 [2]. The present retrospective study investigated the effects of GCs or BIOs on the efficacy of dTP in patients with RA using a larger patient cohort.
Objectives: To evaluate the effects of BIOs, GCs, or both on the efficacy of dTP treatment for OP in patients with RA.
Methods: The study included 56 female patients who had completed 2 years of dTP treatment. We separated these patients into four groups according to their treatment regimen at dTP initiation: B(–)G(–),included patients who did not receive BIOs or GCs (n = 14); B(+)G(–), included patients treated only with BIOs (n = 8); B(–)G(+), included patients treated only with GCs (n = 24); and B(+)G(+),included

patients treated with both BIOs and GCs (n = 10). We determined baseline (BL) characteristics, % changes in BMD in the lumbar spine (LS) and total hip (TH) from BL to 24 months, and % changes in serum bone turnover markers (BTMs), such as BAP, P1NP, NTX, and TRACP-5b, from BL to 6 months after dTP initiation. Dunnett's test was used for comparisons between B(–)G(–) and other groups.

Results: The mean ages of the B(–)G(–), B(+)G(–), B(–)G(+), and B(+)G(+) groups at BL were 70.0, 65.5, 69.6, and 71.5 years, whereas the mean duration of RA in these groups were 15.4, 20.8, 69.9, and 71.5 years, respectively. Furthermore, the mean baseline DAS28-CRP levels in these groups were 2.8, 2.2, 2.8, and 2.3. The mean LS-BMD (g/cm^2) at BL were 0.795, 0.819, 0.826, and 0.853, whereas the mean TH-BMD at BL were 0.619, 0.570, 0.601, and 0.629, respectively. The mean % changes in LS-BMD at 24 months were 15.5%, 12.7%, 11.9%, and 8.1%, respectively (Fig 1A). There were no significant differences between B(–)G(–) and other groups. The mean % changes in TH-BMD at 24 months in the B(–)G(–), B(+)G(–), B(–)G(+), and B(+)G(+) groups were 6.4%, 5.3%, 4.4%, and 1.5%, respectively (Fig 1B) A significant difference was observed between the B(–)G(–) and B(+)G(+) groups (p = 0.03). The % changes in BTMs in the B(–)G(–), B(+)G(–), B(–)G(+), and B(+)G(+) groups were as follows: BAP, 90.5%, 44.0%, 29.5%, and 87.7%; P1NP, 374.1%, 338.2%, 225.9%, and 640.0%; NTX, 75.2%, 106.6%, 42.5%, and 80.5%; and TRACP-5b, 75.8%, 43.85, 20.4%, and 122.3%, respectively. No significant differences were observed in the changes in BTMs among the groups.

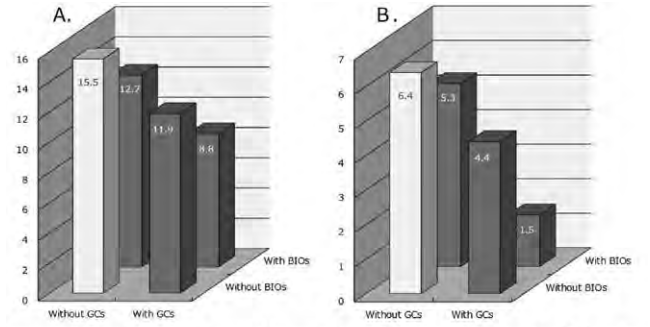


Figure 1. % Change of Bone Mineral Density from Baseline to 24 Months
A: Lumbar spine, B: Total hip
BIOs: biological agents, GCs: glucocorticoids

Conclusion: This study suggested that concomitant use of BIOs and GCs inhibited the increase in BMD induced by dTP treatment in patients with RA, particularly TH-BMD. Although BTM analysis revealed no statistical significance, GCs tended to decrease the % change in BTMs.

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Disclosure of Interests: Yuji Hirano Speakers bureau: Tanabe-Mitsubishi, Pfizer, Eisai, Abbie, Chugai, Bristol-Meyers, Jansen, Astellas, UCB, Eli-Lilly, Asahikasei, Daiichi-Sankyo, Amgen, Hironobu Kosugiyama: None declared, Kyosuke Hattori: None declared, Daisuke Kihira: None declared

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AB0899 TREATMENT STATUS OF PATIENTS WITH GLUCOCORTICOID-INDUCED OSTEOPOROSIS IN THE AKITA ORTHOPEDIC GROUP ON RHEUMATOID ARTHRITIS REGISTRY

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Background: Glucocorticoids (GC) have potent anti-inflammatory and immunosuppressive effects and are used to treat a variety of diseases. However, GC are associated with several adverse effects. Glucocorticoid-induced osteoporosis (GIO), a bone metabolism disorder, accounts for 25% of the side effects associated with GC, and long-term use of these agents leads to fragility fractures in 30 to 50% of patients [1]. GC are frequently used to treat rheumatoid arthritis (RA). No report on the current treatment status for glucocorticoid-induced osteoporosis (GIO) has been published following the publication of the new guidelines for the management and treatment of GIO issued by the Japanese Society for Bone Mineral Research provided in 2014 (Figure 1) [2].

Objectives: The present study aimed to investigate the current treatment status of GIO patients in the Akita Orthopedic Group on Rheumatoid Arthritis (AORA) registry.

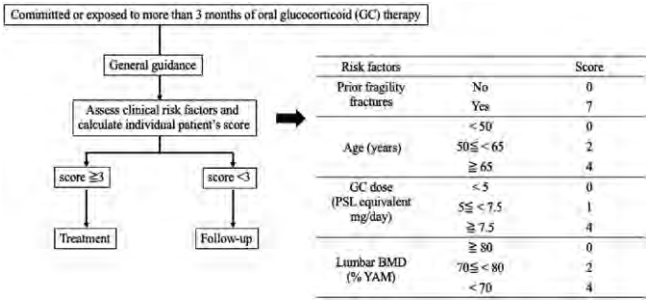
Methods: This retrospective, multicenter study included 683 patients (138 men, 545 women) with fracture risk factor scores ≥3 based on the new guidelines who were in the AORA registry. We examined patient characteristics, differences in patient backgrounds between treated and non-treated groups.

Results: There were no significant differences in mean GC dose between men and women (4.0 ± 2.3 mg/day vs 3.6 ± 1.8 mg/day, p = 0.08). The mean disease duration of RA in women was significantly longer than in men (180.2 ± 140.2 months vs 143.8 ± 129.6 months, Untreated GIO patients were significantly more likely to be men and younger. The univariate analysis showed that clinic visits, male sex, younger age, and longer disease duration were significant risk factors for lack of therapeutic intervention for GIO. Multivariate analysis showed that being treated in a clinic, male sex, and younger age were significant risk factors for lack of therapeutic intervention for GIO.

Conclusion: Our results emphasize the importance of considering the prevention and treatment of GIO in all patients with RA, including younger and male patients, who have lower intervention rates.

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AB0900 FREQUENCY OF LOCAL COMPLICATIONS AFTER TOTAL HIP ARTHROPLASTY IN PATIENTS WITH RHEUMATIC DISEASES.

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Background: Surgical treatment of patients with rheumatic diseases (RD) is associated with an increased risk of complications. It is caused by presence of an inflammatory process, osteoporosis, reduced physical activity, severity of functional impairment, long-term glucocorticoid therapy, biological and disease-modifying antirheumatic drugs. All this provides elongated wound healing period, the development of infectious complications and increased risk of periprosthetic fractures.

Objectives: To study a frequency of local complications of total hip arthroplasty (THA) in patients with inflammatory RD and osteoarthritis (OA).

Methods: We analyzed 1591 THA, which were performed to RD patients between 2000 and 2019 years.

Results: We performed 882 arthroplasties in patients with inflammatory RD, which consisted of patients with rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), juvenile rheumatoid arthritis (JRA), ankylosing spondylitis (AS), systemic scleroderma (SSD), and also 709 operations in OA patients.

Local complications after THA were 120 (7.54%), of these 83 (9.41%) in patients with inflammatory RD and 37 (5.22%) in OA patients.

We revealed a significantly greater number of complications in patients with inflammatory RD (p<0.005).

Conclusion: Inflammatory RD (RA, SLE, JRA, AS, SSD) patients have local complications after THA (9.41%) 1.8 times more often than OA patients (5.22%). It shows that the operative treatment of patients with RD requires a special approach, management and careful treatment of the bone and surrounding tissues during surgery.

Disclosure of Interests: None declared

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AB0901 PREVALENCE OF OSTEOPOROSIS IN ITALIAN POSTMENOPAUSAL WOMEN ACCORDING TO DEFRA ALGORITHM

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Background: Osteoporosis is a recognized health problem and the burden of the disease is mostly associated with the occurrence of hip and vertebral fracture.
Objectives: This study was aimed at evaluating the prevalence of osteoporosis in Italian postmenopausal women, defined by DeFRA calculation as a 10 years fracture risk equal or higher than 20%.
Methods: This is a monocenter cohort study evaluating 1850 post-menopausal women aged 50 years and older. All the participants were evaluated as far as anthropometrics. Defra questionnaire was administered and calculated with bone mineral density (DXA) measured at lumbar spine and femoral neck.
Results: The prevalence of osteoporosis as assessed by DeFRA was 29.8% in the whole population, according to literature. The frequency of a risk fracture equal or higher than 20% varied from 7.9% in the group aged 50-59 years to 35% in subjects aged >80. Among clinical risk factors for fracture, the presence of a previous fracture (spine primarily) was the most commonly observed.
Conclusion: Our data showed that about one third of post-menopausal women aged 50 and older in Italy has osteoporosis on the basis of DeFRA algorithm, with a high 10 years fracture risk. A previous fracture is the most common risk factor. The data should be considered in relation to the need to increase prevention strategies and therapeutic intervention.
Disclosure of Interests: None declared
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AB0902 BONE HEALTH IN PATIENTS WITH JUVENILE ONSET DERMATOMYOSITIS ASSESSED AFTER LONG-TERM FOLLOW-UP; A CASE CONTROL STUDY

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Background: Patients with juvenile dermatomyositis (JDM) are at risk of developing low bone mineral density (BMD) and not reach peak bone mass, mainly due to prednisolone (pred) treatment [1], making them prone to osteoporotic fractures later in life
Objectives: To compare BMD in longterm JDM patients (Pts) with that of controls (Ctr); and in Pts explore how disease variables affect BMD.
Methods: Pts (n=59) were clinically examined median 16.8y (range 6.6 - 27.0 y) after disease onset and compared 1:1 with age/sex matched Ctr. Dual-energy X-ray absorptiometry (DXA) was used to measure BMD and Z-scores in whole body (WB), lumbar spine at L2-L4 (spine). In those ≥ 20y; also proximal (PR) and distal 1/3 radius (DR), and total hip were examined. Pred at follow up was reported, and cumulative dose calculated. Bone remodeling factors: C-terminal telopeptide (CTX), amino-terminal propeptide (P1NP) and 25(OH)Vitamin D (VitD), were measured in serum.
Results: BMD WB was lower in Pts than Ctr, and both WB and spine BMD and Z scores were lower in Pts than Ctr <20 years (Tbl 1). DR BMD and Z-score were both lower in Pts ≥20y. Serum analysis showed lower VitD was lower in Pts than Ctr. In Pts ≥ 20y Vit D was lower and eSR was higher compared to Ctr.
In Pts ≥ 20y: moderate negative associations were found between both BMD WB and spine, and pred use at follow up (R`s = -0.43), and between BMD PR and VitD (R= -0.34). There was a positive moderate association between Z-score PR and CTX (-0.45) not found in Ctr, and between Z-score total hip and cumulative pred dose (R = 0.38). All p <0.05.
In Pts <20y moderate negative associations were found between Z-score for spine and months of pred use and cumulative pred doses (R`s = -0.40 and -0.48, p<0.05). Other associations found in Pts <20y were also found in respective Ctr.
Conclusion: We found that Pts bone health was affected differently in young and adult JDM-Pts. Association analysis between BMD, Z-scores and medication and/or bone remodeling factors were not conclusive. We will perform linear regression analysis to determine if and how BMDs and Z-scores are dependent on pred use, time and doses, and factors important for bone remodeling.

Table 1. Characteristics, disease variables, BMD and Z-scores in JDM Pts and Ctr

	Pts (n=59)	Pts < 20y (n=28)	Pts ≥ 20y (n=31)	Ctr (n=59)	Ctr < 20y (n=28)	Ctr ≥ 20y (n=31)
Age, y	21.5 (6.7-55.4)	15.3 (6.7-19.8)	34.3 (20.4-55.4)	21.6 (6.2-55.4)	14.4 (6.2-20.1)	34.2 (20.5-55.4)
Female	36 (61)	20 (71.4)	16 (51.6)	36 (61)	20(71.4)	16 (51.6)
BMI, kg/m^2	22.3 (4.8)	20.3 (4.6)	24.0 (4.4)	22.7 (4.5)	21.4 (5.2)	23.9 (3.5)
Height, cm	164.9 (14.7)	157.1 (15.9)	171.8 (9.1)	167.3 (15.8)*	159.8 (18.3)	174.0 (9.2)
Fracture any	19 (32.2)	NA	NA	21 (36.8)	NA	NA
BMD, g/cm^2						
Whole body	1.10 (0.15)	1.01 (0.13)	1.18 (0.10)	1.13 (0.14)*	1.06 (0.16) †	1.19 (0.08)
Spine, L2-L4	1.12 (0.23)	0.99 (0.21)	1.24 (0.18)	1.17 (0.22)	1.07 (0.27)†	1.26 (0.11)
Distal radius		NA	0.87 (0.09)		NA	0.93 (0.11) ††
Z-score						
Whole body	-0.07 (1.08)	-0.39 (0.99)	0.21 (1.10)	0.27 (0.90)	0.28 (1.01) † †	0.26 (0.71)
Spine, L2-L4	-0.16 (1.2.)	-0.39 (1.01)	0.06 (1.34)	0.4 (1.02)	0.25 (1.21) †	0.24 (0.84)
Distal radius		NA	-0.76 (1.03)		NA	-0.05 (0.87)**

y: years, BMI: Body mass index, NA: not applicable. Values are: median age (range), median (IQR), n (%) or mean (SD). p-values *p<0.05, **p<0.01 when comparing Pts and Ctr and † p<0.05, †† p<0.01 when comparing Pts and Ctr < and ≥ 20 years.

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Words: 3555
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.5357

AB0903 VITAMIN D LEVELS IN PRIMARY CARE AND RHEUMATOLOGY PATIENTS

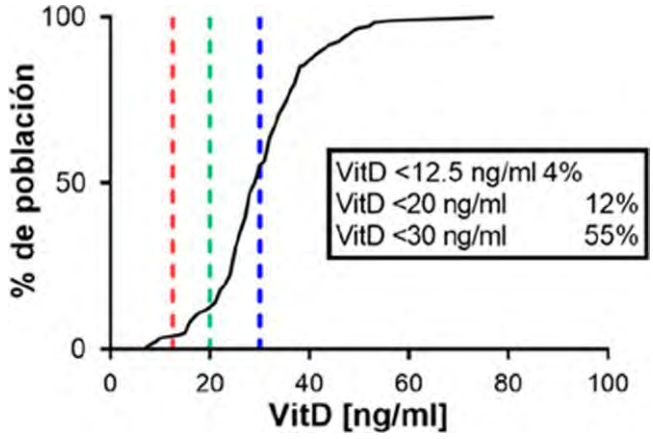
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Background: Although many studies are calling into question the benefits commonly attributed to the vitamin D out of the bone sphere, in the recent years its determination and supplementation has been generalized in the population. Causes of this trend are not clear, but generalist media pressure or even specialized over patients and doctors, along with overrated normality levels could be contributing to this fact. Actual literature[123] indicates that 25-OH vitamin D levels of 30ng/ml or higher are not necessary, and most of the authors agree that 20ng/ml levels are enough for the general population, and only levels below 12.5ng/ml must be considered deficient and subsidiaries of supplementation.
Objectives: Obtain the vitamin D levels distribution from a sample of individuals with no bone pathology, or supplementation prescription in Tenerife's North Area.
Methods: Retrospective descriptive study of the 25-OH vitamin D levels requests from the Tenerife's North Area, made for any reason by the Primary Care Doctor or the rheumatologist, both in the Primary Care Centers and the Hospital Universitario de Canarias (HUC). 25-OH vitamin D values were gathered from 2662 blood samples from a total of 2635 patients, from September to November of 2018 (2241 from Primary Care and 421 from rheumatology). In order to determine the use of calcium and vitamin D supplements, and the presence of bone pathology, either renal or from a malabortive process, 400 individuals were randomized (250 from primary care and 150 from rheumatology. Demographic data (age and gender), calcium serum, phosphor and 25-OH vitamin D levels were gathered for the individual records. With regards to the treatment, data about vitamin D supplements, calcium with vitamin D, or the sum of both, that the patient may have in electronic prescriptions at that time; as well as osteoporosis treatment (biphosphonates, denosumab or teriparatide) were gathered.
Results: Using the age, gender, male/female relation, the levels of vitamin D, calcium and phosphor, as comparison factors; the characteristics of the random population were statistically indistinguishable from the global population. Regarding the random sample characteristics, from the 150 rheumatology patients, 11 were men (7.3%) and 139 women (92.7%). While from the 250 primary care patients, 66 were men (26.4%) and 184 were women (73.6%). The average age of the primary care sample was 55.76±19.72 years and 65.16±13.84 years in the rheumatology sample.
In the total random healthy population: without bone pathology, renal or malabortive and without calcium, vitamin D or antiresorptive drug (n=181) treatment, the levels of vitamin D were 31±14ng/ml with a normal distribution and without clear differences between the primary care and rheumatology patients. When the healthy population distribution was studied by vitamin D levels, the 55% presented values below 30ng/ml, 12% below 20ng/ml and 4% showed levels under 12.5ng/ml: levels agreed as deficient (see graph).
Conclusion: The 55% of the patients studied in primary care and rheumatology, without renal, digestive or bone disease and without vitamin D supplement,

presented vitamin levels below the actual limits of 30ng/ml. These limits, used by most of the laboratories, tend to overestimate the vitamin D deficiency.

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Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.4796

AB0904 PERSISTENCE AND REASONS FOR DISCONTINUATION OF DENOSUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Denosumab, a fully human monoclonal antibody to receptor activator of nuclear factor kappa B ligand, which inhibits osteoclast differentiation, activation and survival, not only increases bone mineral density but also inhibits the progression of bone erosion in patients with rheumatoid arthritis (RA)[1-3]. Therefore, denosumab have been preferably prescribed for patients with RA recently. The persistence with denosumab, which is administered subcutaneously once every 6 months, was reported higher than with oral bisphosphonates[4], and in the prospective cohort studies, the persistence rate for one year was reported to be 82-95%[5-6]. However, there have been no report about the persistence in patients with RA treated with denosumab, moreover the reasons for discontinuation of denosumab.

Objectives: The aims of this single center retrospective cohort study were 1) to assess the persistence with denosumab in a routine clinical setting and 2) to identify the reasons of discontinuation in patients with RA. And we also reviewed the clinical outcomes of osteonecrosis of the jaw in patients with RA during denosumab treatment.

Methods: The present study is based on databases from our hospital, which include age, gender, date of injection of denosumab, as well as information on patients' characteristics. Patients were included in this study when denosumab were newly started at our department during the period from June 1, 2013 and September 30, 2017. In this study, persistence was defined as patients with an interval between injections of no longer than 6 months plus 8 weeks. Patients were followed until censoring (death, transferring to another hospital) or the end of the study (August 3, 2018).

We investigated reasons for the discontinuation of denosumab. Major reasons for the discontinuation of denosumab were classified as adverse event, anxiety over adverse events, patient's transfer or request, doctor's careless lack of refilling an injection, and other reason.

We identified patients who had been diagnosed as osteonecrosis of the jaw, and demographic, pharmacological, and clinical data were collected from medical records.

Results: One hundred and seventy-five patients were identified. Kaplan–Meier analysis showed a slow decline of persistence after initiating denosumab therapy, dropping to 80.4 and 61.9 % after 1 and 2 years of follow-up. When analyzing the reason of discontinuation as adverse events, the persistence rate of denosumab was at 89.4, and 79.4% at 1, and 2 years of follow-up, respectively.

During 2-year period, 72 patients discontinued denosumab. A total of 27 adverse events occurred, of which five events were osteonecrosis of the jaw. The other reasons for adverse event included death in four, fracture in three, and so on. Six patients discontinued due to anxiety over dental adverse event. Thirteen patients were in doctor's careless lack of refilling an injection

All five patients who were diagnosed as osteonecrosis of the jaw had received the treatment with prednisolone, and four were treated with biologic drugs. All patients stopped denosumab and switched to other drugs including teriparatide. All patients underwent surgical curettages of necrotic bone and cured.

Conclusion: Persistence of denosumab in patients with RA is comparable to that in postmenopausal women with osteoporosis. Dental screening and care should be important to continue denosumab treatment.

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AB0905 THE PREVALENCE AND RISK FACTORS OF OSTEOPOROSIS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES: A TUNISIAN STUDY

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Background: Osteoporosis is as known a chronic complication of inflammatory bowel diseases (IBD). Its etiopathogenesis is often multifactorial.

Objectives: The aim of our study was to describe the prevalence of reduced bone mineral density and to identify risk factors of osteoporosis in patients with inflammatory bowel diseases.

Methods: This is a retrospective study over three years, collecting patients suffering from IBD and having benefited from a bone densitometry. We have specified for each patient the clinical data and the IBD characteristics. Bone mineral density (BMD, g/ cm) was assessed by dual X-ray absorptiometry. Osteoporosis was diagnosed when BMD was 2.5 standard deviations below the mean peak value in young adults (T score,22.5 SD). Patients with other pathology that may change the bone metabolism were excluded.

Results: sixty-one patients were included with an average age of 38 ± 13 years [16-73]. The sex ratio M / F was 1.25. 69% of patients had ulcerative colitis. The bone density profile was normal in 49.2% of the cases. Osteoporosis and osteopenia were noted in 13.1% and 37.7% of patients, respectively. Osteoporosis was associated with advanced age (50.5 ± 16.5 years vs 36.26 ± 12.93 years; p = 0.007) and longer course disease (6.75 ± 7, 4 years vs 2.5 ± 4 years; p = 0.015). The cumulative dose of prednisone equivalent used in patients with osteoporosis was significantly higher than the other patients (2775 ± 3338 mg vs 706 ± 1449 mg; p = 0.003). Osteopenia was more frequently associated with crohn's disease (58% vs 28.6% p = 0.0029). There was no significant difference between the group with osteoporosis or osteopenia and the group with normal bone densitometry for sex and body mass index.

Conclusion: Osteoporosis during IBD is associated with advanced age, longer duration of illness and administration of high doses of corticosteroids. The high proportion of osteoporosis and osteopenia in our study underlines the importance of systematic BMD measurement in all IBD patients as a base for initiating the appropriate treatment.

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AB0906 PREVALENCE OF HYPOVITAMINOSIS D IN DIAGNOSTIC PATIENTS OF BREAST NEOPLASIA IS GREATER THAN EXPECTED FOR THE GENERAL POPULATION? SERIES OF 200 DIAGNOSTIC PATIENTS OF BREAST NEOPLASIA IN A TERTIARY HOSPITAL INITIATING TREATMENT WITH AROMATASE INHIBITORS

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Background: In our population the prevalence of hypovitaminosis D is high. A recent cross-sectional observational study conducted in Spain shows that 63% of postmenopausal women who receive osteoporosis (OP) therapy and 76% who do not receive treatment had 25 (OH) D levels below 30 ng / mL1.
The latest studies show a relationship between hypovitaminosis D and the development of systemic inflammatory and tumor diseases, determined by the presence of receptors in various tissues, including breast.
Objectives: To determine which levels of serum 25 (OH) D, and secondarily calcium, phosphorus, PTH and CTX, present 200 patients diagnosed with breast cancer and taking hormonal treatment, referred to a monographic OP consultation of a tertiary hospital for the assessment of their bone metabolism, and if these values differ from what is expected for the general population.
Methods: Retrospective cross-sectional study of 200 women diagnosed with breast cancer receiving treatment with aromatase inhibitors (AI), performed in a tertiary hospital. Blood levels of vitamin D, calcium, phosphorus, PTH and CTX have been collected, as well as other variables and risk factors.
Results: 200 patients with a mean age of 64.8 years and an ED of 9.5 were collected. The median is 64.5 (Q1 58 and Q3 72).
The vitamin D levels presented by the study patients were <10 ng/mL in 13 patients (6.67%), 11-20 ng/mL in 50 (25.64%), 21-30 ng/mL in 68 (34.87%), 31-70 ng/mL in 62 (31.79%), and> 70 ng/mL in 2 (1.03%). This implies that in 67.18% of the patients they had values below the optimal range.
92.31% of patients (180) presented PTH values within the normal range and only 7.69% presented values above normal.
The serum calcium and phosphorus levels of the patients selected for the study had ranges within normal (99.49%) except 1 case that presented high values (0.51%) for both.
The values of CTX (carboxyterminal telopeptide used as a marker of bone resorption) were in the normal range in 81.96% of patients (159), low values in 0.52% (1) and values above the normal range by 17.53% (34).
Conclusion: The prevalence of insufficient levels of vitamin D in our study (Breast cancer + AI) is not greater than that estimated for the general population according to various studies.
Our study found that 67.18% of patients (2/3 of the selected population) had values below those considered optimal (<30 ng / mL) and 32% had values <20.
Only 7.69% of the patients presented PTH values above the normal range.
In 82% of patients, CTX used as a marker of bone resorption had normal values.
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AB0907 BONE METABOLISM ASSESSMENT IN PATIENTS WITH RECENT DIAGNOSIS OF GIANT CELL ARTERITIS

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Background: There are several studies assessing bone mass and osteoporosis (OP) development of patients with giant cell arteritis (GCA) during glucocorticoid treatment, however data at time of diagnosis is scarce.
Objectives: To analyze bone metabolism, bone mineral density (BMD) and trabecular microarchitecture by measuring trabecular bone score (TBS) in patients with recent diagnosis of GCA.
Methods: Retrospective observational study in which we included all patients with GCA and bone metabolism assessment at diagnosis. We recorded: risk factors for OP (previous fractures and anti-OP treatments), bone metabolism (calcium, phosphate, PTH, 25-vitaminD [25-OHD]) and the DXA results (Lunar, DPX) at the time of diagnosis and during the follow-up. The statistic analysis was made with SPSS.
Results: 36 patients (27 W: 9M) with a mean age of 76±9 years were included. The clinical characteristics of the GCA at diagnoses were: headache (81%), constitutional syndrome (58%), allodynia (42%), visual loss (42%, binocular in 2 patients), jaw claudication (39%), polymyalgic syndrome (28%), amaurosis fugax (25%) and lingular necrosis (n=1, 3%). Additional diagnosis tests included: temporal biopsy (86%, being pathologic in 55%), temporal ultrasound (97%, pathologic 34%), extra-cranial arteries ultrasound (81%, pathologic 7%) and PET/CT (19%, pathologic 86%). Up to 61% received three metilprednisolone bolus (mean dose 1700mg). 7 patients (19%) had previous OP and 3 had already suffered a fragility fracture (Colles, vertebral and femur). Only 4 patients were receiving anti-OP treatment (2 oral bisphosphonate, 2 zoledronate).
At time of diagnosis of GCA, the mean of 25OHD was 17±13ng/mL (88%, <30). BMD showed low bone mass in 80% of patients (47% with OP, 33% osteopenia). The mean TBS was 1.026±0.098 and up to 38% showed poor bone microarchitecture [values <1.23]). No significant differences were observed between patients with or without TBS <1.23. Up to 94% of patients received anti-OP treatment (26 zoledronate, 6 oral bisphosphonate, 1 denosumab, 1 teriparatide). 3 patients had incidental fractures during the follow-up, however no relation was found with BMD or TBS.
Conclusion: Low bone mass and vitamin D insufficiency are frequent in patients with recent diagnoses of GCA and up to 38% have poor bone microarchitecture at baseline. Thus, it's important to perform a bone mass assessment in all patients with recent diagnose of ACG and initiate therapeutic or preventive anti-OP treatment if required.
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AB0908 ASSESSMENT OF THE IMPACT OF THE LEAN MASS WITH BODY COMPOSITION BY DUAL-ENERGY X-RAY ABSORPTIOMETRY ON THE BONE MINERAL DENSITY

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Background: Lean mass, mainly composed of muscle, has been correlated to bone mineral density (BMD) [4]. Studies reported that lean mass has an important impact on BMD not only in young women but also in postmenopausal women [1]. High lean mass is more favorable for the BMD than low lean mass. Some studies suggested that genetic factors responsible for both lean mass and BMD are shared [3]. Low muscle mass and low BMD could impair the quality of the patient's life [2, 5].
Objectives: The aim of this study is to assess the impact of the lean mass with body composition by dual-energy X-ray absorptiometry on the bone mineral density.
Methods: 107 women underwent body composition analysis by dual-energy X-ray absorptiometry (DXA). Lean mass in kg and BMD in kg/cm2 were analyzed. Normal BMD was defined as T-score > -1.0 standard deviation (SD). Osteopenia was defined as T-score between -1.0 SDs and -2.5 SDs and osteoporosis was defined as T-score ≤ - 2.5 SDs.
Results: The mean age of the women was 57 years (yrs.) ± 11 yrs. (range 41 yrs. – 80 yrs.). Subjects had mean weight of 75 kg ± 12 kg (range 50 kg – 110 kg) and mean height of 156 cm ± 9 cm (range 151 cm – 172 cm). 73/107 women (68.2%) were with normal BMD, 24/107 women (22.4%) were with osteopenia and 10/107 women (9.4%) were with osteoporosis. Lean mass differed significantly between the groups (p = 0.000). Women with normal BMD had the highest mean lean mass (58.47 kg) and the mean lean mass of the women with osteopenia and osteoporosis decreased as follow: 47.56 kg for women with osteopenia and 36.22 kg for women with osteoporosis.
Conclusion: Women with osteoporosis have the lowest lean mass compared to the women with osteopenia and osteoporosis.
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AB0909 TREATMENT WITH DENOSUMAB IN GLUCOCORTICOSTEROID-INDUCED OSTEOPOROSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Glucocorticosteroids (GCS) are widely used in the treatment of rheumatoid arthritis (RA) as bridge-therapy. Though, according to last recommendations for the treatment of RA *GCS should be considered in short-term and different dose regimens and routes of administration and should be tapered as rapidly as clinically feasible. But in some cases, patients received GCS for a long period in low doses (*<7.5 mg/day prednisone equivalent). *It is well known, that* long-term GCS use is associated with osteoporosis and increased risk of fracture, even at low daily doses. On the other hand, RA itself leads to the changes in the biomechanical properties of bones through the increased production of pro-inflammatory cytokines. Furthermore, immobilization due to pain from inflamed joints and impairment of physical activity are in response for osteoporosis formation. In addition, patients with RA are often co-prescribed a proton pump inhibitor, which have a reported effect on occurrence of osteoporosis. Taking into consideration all mentioned above patients with RA, receiving GCS therapy reveal high risk for osteoporosis and fracture formation and require corresponding treatment.
Objectives: The aim of this study is to evaluate the effect of 12 months treatment with denosumab (bone-modifying agent) in patients with RA, continuing to receive GCS.
Methods: 50 female patients with RA (mean age 54 ± 6.3 years) were enrolled in this study. Duration of RA was 10.5 ± 3.2 years. All patients received prednisone 15,3± 10,25 mg/day with gradually escalation of dose for ≥ 12 months. As DMARD therapy patients received methotrexate dose in average 15-20mg/week (75%), leflunomide 20 mg/day (25%). Bone mineral density (BMD) is measured in all patients by Dual-energy X-ray absorptiometry (DEXA) at baseline and 12 months after treatment with denosumab. All patients received denosumab 60 mg subcutaneously once every 6 months.
Results: The measurement of BMD at baseline revealed the following results: T-score in lumbar spine was -1,95 ± 1,36 and in total hip -1,64± 0,94 with high major osteoporotic fracture risk. All patients completed the study. The BMD after 12 months significantly increased both in lumbar spine +4,2 % (p<0,001) and in total hip +2,1% (p<0,001).
Conclusion: Denosumab should be considered as a drug of choice in RA patients, continuing to receive GCS. Further large investigations are needed to assess the BMD after discontinuation of denosumab and evaluate fracture risk in this population of patient.
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AB0910 SARCOPENIA AND BONE MINERAL DENSITY IN MEN WITH CORONARY HEART DISEASE

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Objectives: To examine bone mineral density (BMD) in men with coronary heart disease (CHD), depending on the state of the muscle mass, strength and function.
Methods: 79 men aged over 50 years with verified CHD were examined (mean age 63 (57; 66) years).
The BMD and T-criterion (standart deviation, SD) of the femoral neck and lumbar spine (L1-L4) were evaluated using dual-energy x-ray absorptiometry (DXA) on the Lunar Prodigy Primo bone densitometer (USA). The following reference intervals were used: normal BMD values (T-criterion ≥-1), osteopenia (OPe) (T-criterion from -1 to -2.5), and osteoporosis (OP) (T-criterion <-2.5).
To assess muscle mass, the total area (cm^2) of the lumbar muscles of the axial section at the level of the 3rd lumbar vertebra (L3) was determined using multispiral computed tomography on a 64-slice computer tomograph "Somatom Sensation 64" (Siemens AG Medical Solution, Germany). The ratio of the obtained index of the area of skeletal muscle to the square of the patient's growth index determined the " skeletalmuscular index L3" (SMI). The media considered the threshold value to be 52.4 cm^2/m^2.
Results: The femoral neck BMD in the examined patients was 0.96 (0.89; 1.03) g/cm^2, which corresponds to -0.50 (-1.00; 0) SD according to the T-criterion, in the lumbar spine -1.23 (1.11; 1.32) g/cm^2 and 0.4 (-0.50; 1.20) SD according to the T-criterion.
In accordance with the recommendations of the European working group on sarcopenia in Older people (EWGSOP, 2010, 2018), the patients were divided into 3 groups: 31 patients without sarcopenia (group 1), 21 patients with isolated muscle loss (presarcopenia) (group 2) and 27 patients with sarcopenia (group 3). BMD in the femoral neck in the group of patients without sarcopenia was 0.96 (0.72; 1.26) g/cm^2, which corresponds to -0.50 (-0.8; 0.2) SD according to the T-criterion, in the lumbar spine – 1.19 (1.10; 1.275) g/cm^2 and 0.1 (-0.6; 0.8) SD according to the T-criterion. BMD in the femoral neck in the group of patients with presarcopenia (group 2) – 0.995 (0.94; 1.04) g/cm^2 and -0.3 (-0.70; 0) SD according to the T-criterion, in the lumbar spine – 1.32 (1.24; 1.40) g/cm^2 and 1.20 (0.50; 1.90) SD according to the T-criterion. In patients with established sarcopenia (group 3), the following indicators of BMD and T-criterion were recorded: 0.95 (0.845; 0.98) g/cm^2 and -0.60 (-1.40; -0.40) SD and 1.23 (0.085; 1.31) g/cm^2 and 0.4 (-0.8; 1.1) SD in the femoral neck and lumbar spine, respectively.
A comparative analysis of the results of the DXA found that patients with sarcopenia had a significant decrease in the BMD and T-criterion in the femoral neck compared to patients with presarcopenia (p=0.039 and p=0.040, respectively). There were no differences between the groups of patients without sarcopenia and with sarcopenia and presarcopenia (p>0.05).
It was found that patients with sarcopenia had significantly lower BMD and T-criterion in the lumbar spine compared to patients with presarcopenia (p=0.017 and p=0.0165, respectively). The values of the BMD and T-criterion in the groups of patients without sarcopenia and with presarcopenia and sarcopenia in the lumbar spine were comparable (p>0.05).
Conclusion: The presence of sarcopenia is associated with loss of BMD in the femoral neck and in the lumbar spine. The results obtained confirm the high probability of common pathogenetic links between OP and sarcopenia.
Disclosure of Interests: None declared
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AB0911 PREVALENCE AND RISK FACTORS OF HIP FRACTURE ASSOCIATED WITH OSTEOPOROSIS IN A GERIATRIC POPULATION FROM COLOMBIAN NORTH EAST.

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Background: Hip fracture is a frequent cause of hospital admission in older adults.[1] The prevalence of hip fracture associated with osteoporosis in the elderly is 18% in women and 6% in men.[2] Likewise, the attention of this event requires an approximate value of 2,943 dollars, which represents an average of 18,95% of the per capita income of most countries.[3] It is also established that appropriate and timely treatment of osteoporosis can prevent the appearance of fractures.[4]
Objectives: The aim of this study was to determine the prevalence of hip fracture associated with osteoporosis, as well as the associated factors to its presentation in a geriatric population in Colombia.
Methods: Cross-sectional study that included 130 patients over 65 years old, who consulted the University Hospital of Santander with hip fracture. The main variable of exposition was the medical history of osteoporosis. Descriptive analysis was performed with absolute and relative frequency measurements for the qualitative variables and central tendency measures and dispersion according to the distribution of the variables. Subsequently, the bivariate logistic regression analysis was performed to identify the associated risk variables. The analysis was performed with the Stata 12.0 Software.
Results: From the 130 patients included in the study, 33.85% corresponded to the male gender. The average age was 82.49 years with a DS of 8.35 years. The median length of hospital stay was 17.5 days with an interquartile range of 11 to 26 days. The most common comorbidity was hypertension in 65.38%, followed by diabetes and COPD in 21.54%, heart failure in 19.23% and chronic kidney disease in 17.69%. The median Charlson score was 5 with an interquartile range between 4 and 6 points. 13.85% of the patients admitted had concomitant osteoporosis, 77.7% of them were women and 8,46% of them had severe osteoporosis, with history of prior fracture, without treatment. In the bivariate analysis, an association was found between having COPD (OR: 4.89, 95% CI 1.71-13.95, p = 0.003), dementia (OR: 3.20, 95% CI 1.05-19.56, p = 0.044), malnutrition (OR: 3.42, IC95 % 1.10 - 10.60, p = 0.032), and osteoporosis associated with hip fracture at hospital admission. Likewise, a greater probability was found for the development of in-hospital pneumonia (OR: 2.48, 95% CI 1.14 - 7.98, p = 0.04) in patients with osteoporosis compared to those who did not have bone disease.
Conclusion: 13.85% of patients who entered due to hip fracture had osteoporosis as comorbidity, data comparable to that previously reported. Variables associated with the presence of osteoporosis at admission in patients with hip fracture were found like history of COPD, dementia, and malnutrition, which makes it likely that those patients with pathologies that decrease physical activity or food intake can impact in an important way the appearance of osteoporosis. One of the most important contributions of this study

is the identification of in-hospital complication (pneumonia), which should be actively monitored in these patients.

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AB0912 CLINICAL UTILITY OF THE WARD TRIANGLE OF HIP BONE DENSITOMETRY: DATA FROM AN FLS UNIT

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Objectives: To evaluate the clinical utility of Ward's triangle (W) of bone densitometry (BMD) of the hip in a population of postmenopausal women referred to BMD from a FLS Unit coordinated by Rheumatology (FLS-REU).

Methods: Retrospective study, which includes, after informed consent, postmenopausal women referred by any department of specialized medicine or primary care medicine, of the health department, to the FLS-REU Unit of our center, during the period of February 2010 to October 2019.

General patient data were collected (age, gender), and risk factors for OP. BMD of the lumbar spine (CL) and hip (femoral neck, total hip and W) was performed, except if there was lumbar surgery, severe scoliosis, or a bilateral hip prosthesis. The BMD outcome was distributed in normal (T index [Ts] to -1 SD), osteopenia (Ts: -1.1 to -2.5 SD) and OP (Ts: <-2.5 SD), separated into two groups: mild OP-moderate (Ts: from <-2.5 DE to -3 DE) or severe OP (Ts: <-3 DE).

Results: 5,740 postmenopausal women referred for BMD are included, with the W result available (Table 1). The result of the mean Ts (SD) was: in CL: -1.49 (1.48) SD, femoral neck: -1.33 (1.11) SD and in W: -2.05 (1.12) SD. In 947 (16%) women, the W was normal, with a mean Ts: -0.28 (1.12) SD; osteopenia in 2,606 (45%): -1.83 (1,12) SD and OP in 2,197 (39%) SD, of which 1,010 (61%) had mild-moderate OP and 967 (49%), severe OP.

The table shows the BMD results of W and CL, the correlation coefficient between them being 0.52 (0.5-0. P <0.001), although with a Kappa coefficient of 0.26 (0.24-0.28. P = 0). The probability that a result in W of normal BMD is normal also in CL is 73% (70% -76%), in osteopenia in both: 47% (45% -49%) and OP: 46% (44 % -48%). In the analysis by ROC curve, the cut-off point of Ts in W for osteopenia in CL is -1.85 SD (sensitivity: 0.648, specificity: 0.649, with AUC: 00.702. [0.687-0.716]) and for OP in CL -2.35 DE (sensitivity: 0.69, specificity: 0.70, with AUC: 0.757 [0.744-0.770]).

	LUMBAR SPINE (LS)				
	Normal	**Osteopenia**	**Osteoporosis (OP)**	**OP <-2.5 a -3 SD**	**OP <-3.0 SD**
Ward normal	681	211	39	26	13
N (%): 947 (16)	0.41±1.78	-1.61±1.78	-2.95±1.78	-2.7±1.78	-3.46±1.78
Tscore: -0.28 ± 1.12 SD					
Ward osteopenia	899	1.192	463	310	153
N (%): 2.606 (45)	-0.07±1.48	-1.73±1.48	-2.96±1.48	-2.72±1.48	-3.43±1.48
Tscore: -1.83±1.12 SD					
Ward Osteoporosis	346	800	975	-	-
N (%): 2.187 (39)	-0.19±1.48	-1.83±1.48	-3.23±1.48		
Tscore: -3.07±1.13 SD					
Ward Osteoporosis <-2.5 a-3 SD	188	416	-	173	378
N: 1.010 (51)	-0.16±1.48	-1.83±1.48		-2.77±1.48	-3.08±1.48
Tscore: -2.78±1.12 SD					
Ward Osteoporosis <-3 SD	114	304	-	193	327
N: 967 (49)	-0.24±1.48	-1.84±1,48		-2.78±1.48	-3.73±1.48
Tscore: -3.51±1.13 SD					

Conclusion: 1.For clinical practice, the usefulness of the W result is low, although if the BMD result is normal, there is a 73% probability that in CL it will also be. 2. The correlation between the result of W and CL, although significant, is slight. 3. The cut-off points of Ts, with better sensitivity and specificity, that correlate a W osteopenia or osteoporosis with the result in CL is -1.85 and -2.35 SD, respectively.

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Disclosure of Interests: None declared

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AB0913 PREDICTING PATIENTS AT RISK OF FRAGILITY FRACTURE WITH NORMAL BONE MINERAL DENSITY: AN OBSERVATIONAL STUDY

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Background: There is an increased risk of low-trauma fracture as bone mineral density (BMD) decreases, however a large proportion of these fragility fractures occur in those without osteoporosis or osteopenia. The widely used FRAX tool uses femoral neck (FN) BMD, amongst other parameters, to predict fracture risk. In those with normal BMD, data is lacking on the weight these other parameters hold in predicting future risk. Indeed, FN BMD can be facultative in the estimation of risk when using FRAX.

Objectives: To establish predictors of fragility fracture in a patient cohort referred for BMD estimation, subsequently found to have bilateral FN BMD of greater than 1.

Methods: A cohort of patients in the North West of England referred between 2004 and 2014 for BMD estimation, with both left and right FN BMD of greater than 1 were identified. Patient parameters identified and analysed included age at scan, gender, BMD at left hip, body mass index (BMI), fat mass, family history of fracture, alcohol history of 3 or more units per day, smoking status, rheumatoid arthritis (RA), and steroid exposure. Patients with fragility fracture were compared with those without fracture. Chi-square test and T-test were applied to categorical and continuous data respectively. Further univariate and multivariate logistic regression models were fitted to determine parameters associated with future fracture risk.

Results: 619 patients with bilateral FN BMD of greater than 1 were identified and included in analysis. Mean age at scan was 54 years (SD 11.82) and 542 (87.56%) were female. 92 (14.86%) patients had a fragility fracture. Mean left FN BMD was 1.91 (SD 0.71), and mean right FN BMD was 1.92 (SD 0.68). Results of the univariate analysis are described in Table 1 below.

Table 1. Logistic regression analysis of patient parameters with unadjusted and adjusted odds ratios for fragility fracture

Predictor	Unadjusted odds ratio (95% CI)	Odds ratio adjusted for age (95% CI)	Odds ratio adjusted for age and gender (95% CI)
Age at scan (years)	0.99 (0.98-1.01)	-	-
Gender	1.37 (0.66, 2.84)	1.34 (0.64, 2.80)	-
BMD at left hip	0.34 (0.03, 4.05)	0.37 (0.03, 4.37)	0.50 (0.03, 7.67)
BMI	1.07 (1.03, 1.10)	1.07 (1.03, 1.10)	1.07 (1.03, 1.10)
Fat mass	1.00 (1.00, 1.00)	1.00 (1.00, 1.01)	1.00 (1.00, 1.01)
Parent fractured hip	0.99 (0.57, 1.70)	0.97 (0.56, 1.68)	0.94 (0.54, 1.64)
Alcohol (3 or more units/day)	1.16 (0.47, 2.86)	1.16 (0.47, 2.87)	1.16 (0.47, 2.89)
Current smoker	1.40 (0.89, 2.21)	1.40 (0.89, 2.21)	1.42 (0.90, 2.23)
Rheumatoid arthritis	0.83 (0.32, 2.19)	0.85 (0.32, 2.24)	0.86 (0.34, 2.27)
Steroid exposure	0.53 (0.30, 0.96)	0.53 (0.30, 0.96)	0.54 (0.30, 0.98)

Conclusion: Steroid exposure and body composition parameters influence fracture risk in this group pf patients with normal BMD, further work will be done looking at the types of fractures and other parameters in this group of patients.

Disclosure of Interests: Christopher Saleh: None declared, Marwan Bukhari Speakers bureau: Bristol-Myers Squib, UCB celltech, Roche/Chugai, Pfizer, Abbvie, Merck, Mennarini, Sanofi-aventis, Eli-Lilly, Janssen, Amgen and Novartis., Syed Mujtaba Bilgrami Speakers bureau: Pfizer

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AB0914 BONE LOSS AND NEW FRACTURES WITH DENOSUMAB TREATMENT

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Background: The incidence and factors related to an inadequate response to denosumab (Dmab) treatment remain unclear.
Objectives: To describe clinical, analytical and densitometric characteristics of patients with inadequate response (IR) to Dmab in clinical practice. IR was defined as the presence of a new fracture [fxs-IR] or a significant decrease in BMD (≥5% lumbar or ≥4% femoral) [BMD-IR].
Methods: retrospective study of patients with IR to Dmab treatment. Data of demographic variables, risk factors for osteoporosis, history of fractures, previous anti-osteoporotic treatment, densitometric and analytical parameters were collected before and after IR.
Results: 22 patients were included (19W:3M) with mean age of 75±10years. The causes of osteoporosis were: postmenopausal (50%), induced by glucocorticoids (22.7%), alcoholic (9.09%) and multifactorial (18.8%). Most patients were previously treated with bisphosphonates (59.09%, duration 5.2±2.6y) and had previous vertebral fractures (54.54% %, median 3).
During Dmab treatment, 10 patients presented a BMD-IR (with a mean bone loss up to -3.5% at femur and -5.8% at lumbar spine) and 12 had fxs-IR (vertebral [n=8], humerus [n=1], pelvis [n=1], tibia [n=1]). No significant differences were observed in duration of Dmab between both IR groups (Fxs-IR: 3,2±1,9 vs BMD-IR: 2,4 ± 1,2y). In the BMD-IR, the BMD loss was higher at lumbar spine than at total hip (-6.6%±3.7 vs -1.9%±4.8). Only 1 patient of the fxs-IR had a secondary cause of IR (mieloma multiple).
In the fxs-IR group, most patients started combined treatment with teriparatide (n=4), 1 changed to teriparatide and 7 remained with Dmab. In the BMD-IR group, most mantained Dmab treatment (n=8) and 2 switched to zoledronate.
Conclusion: Most patients who developed IR to Dmab had been previously treated with bisphosphonates and had previous fragility fractures and appears within the first 3 years of treatment. BMD loss seems to be more marked at spine than total hip. Only one patient had a secundary cause of IR.
Disclosure of Interests: None declared
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AB0915 BONE MINERAL DENSITY AND FRACTURE FREQUENCY IN PREMENOPAUSAL WOMEN WITH RHEUMATIC DISEASES

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Background: The onset of the disease in young and middle age is typical for rheumatic diseases (RDS), but most studies on osteoporosis were conducted in patients (pts) older than 50 years, which included postmenopausal women.
Objectives: To assess bone mineral density (BMD), fracture frequency and the factors associated with low BMD in premenopausal women with RDs.
Methods: 160 women (median age, 36 [29; 43] years): 120 pts with RDs (43 rheumatoid arthritis (RA), 53 systemic sclerosis (SSc) and 24 psoriatic arthritis (PsA)) and 40 age-matched healthy controls were enrolled in the study. We performed a dual-energy X-ray absorptiometry (DXA, Hologic Discovery A, USA) to measure BMD in lumbar spine, femoral neck and total hip. BMD decreasing grade was evaluated by the Z-score <-2SD. All pts were interviewed using a unified questionnaire including assessment of daily dietary calcium intake. Serum vitamin D, C-reactive protein and erythrocyte sedimentation rate (ESR) measurements were done.
Results: 25% pts with RDs and only 8% healthy controls have low BMD (p=0.02). RA, SSc and PsA pts had low BMD in 37%, 21% and 13%, respectively, that was more often than in healthy women (p=0.004, p=0.046 and p= 0.081, respectively). 9,3% RA pts and 7,5% SSc pts had low energy fractures. BMD of RDs pts in all areas of measurement demonstrated a direct correlation with height, weight, body mass index, and serum vitamin D concentration and an inverse correlation with the cumulative dose of glucocorticoids. Also, proximal femur BMD inversely correlated with RDs duration. BMD of femoral neck and total hip inversely correlated with C-reactive protein level in SSc pts. In RA women we found a direct correlation between lumbar spine and femur neck BMD and ESR.
Conclusion: 25% of premenopausal women with RDs had reduced BMD and needed monitoring and osteoporosis prevention, while 9.3% pts with RA and 7.5% women with SSc needed anti-osteoporotic treatment.
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AB0916 FACTORS THAT DEMONSTRATED SIGNIFICANT CORRELATION WITH BONE MINERAL DENSITY GAIN WITH DENOSUMAB ADMINISTRATION FOR PATIENT WITH RHEUMATOID ARTHRITIS

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Background: Denosumab, a monoclonal antibody of receptor activator of NF-κB ligand promotes a strong action for bone mineral density (BMD) gain. This agent is often used for patient with rheumatoid arthritis (RA) because of its strong anti-osteoclastogenesis action, with that joint structural damage is induced. However, factors what affects BMD gain for patient with RA is still unclear.
Objectives: Factors that may affect BMD gain for patient with RA is evaluated statistically.
Methods: Patients with RA to whom denosumab is administrated consecutively three shots or more were picked up. BMD in lumbar spine (LS) and femoral neck (FN) measured with dual-energy X-ray absorptiometry was routinely measured at the initial administration (BL). BMDs were measured every six months when another denosumab is administrated. Change of BMD for each bone was calculated. Patient's age at BL, at onset of RA, disease duration, sex, anti-cyclic citrullinated polypeptide antibodies (ACPA), whether denosumab is naïve, body mass index (BMI) at BL were harvested. BMD in each bone, serum tartrate resistant acid phosphatase 5b (TRACP5b), total type one procollagen-N-peptide (P1NP), calcium (Ca), creatinine (Cr), cystatin C (CysC), estimated glomerular filtration ratio based on CysC (eGFR), serum Cr-to-CysC ratio (Cr/CysC), and Barthel Index, were measured at BL and every six months thereafter. Relationship between BMD gain from BL to second administration and such like factors at BL were evaluated with linear regression analysis at first with univariate model and then multivariate model with factors that demonstrated statistical significance within 5%. Binary logistic regression analysis for these factors was also performed according to BMD gain. These procedures were performed as a same manner regarding with BMD gain from BL to third administration.
Results: A total of 397 patients with 43 males (10.4%) and 354 females (89.6%) were recruited. Average age was 81.3 and average disease duration of RA was 6.9years. 227 patients (57.4%) was denosumab naïve, and prior to BL, 170 patients were already administered with alendronate in 26, risedronate in 26, minodronate in 23, ibandronate in 12, raloxifene in 39, bazedoxifene in 7, teriparatide in 36.
BMD gain in LS from BL to the second administration demonstrated significant correlation with age and TRACP5b at BL with univariate model, and only aging correlated significant negative correlation with BMD gain with multivariate model. In binary logistic regression analysis, aging demonstrated no significant regression with BMD gain. From BL to third administration, BMD gain also demonstrated significant correlation with aging, but no correlation with TRACP5b, but Cr/CysC at BL. These two factors also demonstrated significant correlation with BMD gain in LS, in these aging demonstrated negative and Cr/CysC demonstrated positive correlation. Cr/CysC demonstrated significant regression with BMD gain in LS from BL to the third with binary logistic regression analysis.
BMD gain in FN from BL to the second demonstrated significant correlation with age, BMD in FN at BL, and ACPA with univariate model, and all of the three demonstrated significant correlation with BMD gain with multivariate model. However, no factors demonstrated significant regression with BMD gain with binary logistic regression analysis. From BL to third administration, BMD gain in FN demonstrated significant correlation with aging and BMD in FN at BL. However, BMD in FN at BL demonstrated the only factor to correlate with BMD gain in FN. BMD in FN at BL demonstrated significant regression with BMD gain in FN from BL to the third with binary logistic regression analysis.
Conclusion: These results suggested that BMD gain in LS and FN was affected by different factors. These results may be helpful reference in choosing denosumab against osteoporosis in RA patient.
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Crystal diseases, metabolic bone diseases other than osteoporosis

AB0917 AGE PLAYS A CRUCIAL ROLE IN CRYSTAL ARTHRITIS SEVERITY – A SYNOVIAL FLUID STUDY

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Background: Incidence and severity of gout and calcium pyrophosphate deposition disease (CPPD) increase with age (1). Aging is associated with immune senescence, leading to a deregulation of the innate immune system and hence inflammation (2). MRI studies hinted on a significantly higher synovial inflammation in older compared to younger arthritis patients(3). Whether inflammatory

responses to synovial crystals are more pronounced in elderly patients or not is unknown.

Objectives: To test the hypothesis whether aging associates with a more pronounced synovial inflammation in response to urate and CPP crystals.

Methods: Gout or CPPD patients with a synovial fluid (SF) aspiration were included. Clinical, blood and synovial parameters were recorded. In the Cytokine study, SF was analyzed for interleukin (IL)-1-beta,

IL-6, IL-8, IL-10, IL-12p70, interferon-gamma (IFN-gamma), tumor necrosis factor-alpha (TNF-alpha), IL-17, and transforming growth factor-beta (TGF-beta) by multiplexed cytokine analysis.

In the Cell study, SF samples were immunophenotyped by flow cytometry, including surface markers CD4+ (CD3+), CD8+ (CD3+), and following stimulation for intracellular IFN-gamma and IL-17. The patients were divided into two groups by age median-split.

Statistical analysis

Categorical variables were reported as frequencies. Continuous variables were compared using Student's t-test or in case of non-normal distribution Mann-Whitney U test.

Table 1. Patients Characteristics

Medians, (IQR), Frequencies in %	Cytokine study (n=15)	Cell study (n=19)
Age [years]	76.6 (69.5; 83.0)	59.0 (54.5; 76.0)
Age Median Split	75	65
Male	80.0%	68%
Gout; CPPD patients [n pat] crystals*	10; 5	10; 9
Oligo-/Polyarticular [n pat]	7	8

IQR=Interquartile ranges, CPPD=Calcium pyrophosphate deposition disease, n pat=number of patients

Cytokine study

Median C-reactive (CRP), SUA levels and synovial cell counts were higher in the older patient group. Serum creatinine levels were similar between the two groups. Synovial IL-1-beta, IL-8, and IL-17 levels were significantly higher in the older subjects. Age was correlated with SF IL-1-beta (r=0.62, p=0.02), IL-17 (r=0.63, p=0.04) and IL-8 (r=0.54, p=0.04) levels.

Cell study:

Median CRP was higher in older patients: 87 mg/l (IQR 65; 115) vs. 20 mg/l (IQR 7; 65, p=0.0129). Although not significant, a higher frequency of total Th17 (both CD4+IL17+ and CD8+IL17+) T-cells were seen in the SF of the older patient group. The remaining T-cell subsets were comparable between the two groups.

Conclusion: Gout and CPPD are paradigms for auto-inflammatory diseases. We here show an important autoinflammation enhancing cofactor: age. Inflammation measured as serum CRP, SF-IL-8, SF-IL-1-beta, and SF-IL-17 was pronounced in the older patients. Moreover, the adaptive immune system with a predominant Th-17 immune response was more prominent in the older patient group. High IL-17 concentrations may promote differentiation of T-cells in Th-17 cells and thus perpetuate inflammation in older patients with crystal arthritis (4).

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AB0918 FACTORS ASSOCIATED WITH ACHIEVEMENT OF TARGET SERUM URIC ACID IN PATIENTS WITH NON-TOPHACEOUS GOUT ATTENDING PRIMARY CARE CLINICS.

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Background: Gout is characterised by deposition of monosodium urate crystal in the synovial fluid of joint and other tissues, in the presence of elevated serum uric acid (SUA). Dose-escalation strategy with allopurinol as first-line urate lowering therapy (ULT) was shown to be cost effective and a target SUA of less than 360µmol/L was recommended in non-tophaceous gout.[1] Some of the barriers to treatment effectiveness were related to physician and patient-related factors.[2,3]

Objectives: To investigate the factors associated with achievement of target SUA in patients with non-tophaceous gout attending primary care clinics.

Methods: A cross-sectional study was conducted over four months on patients with gout attending 21 primary care clinics in Selangor, an urbanised state in Malaysia. The demographic and clinical data, including the most recent SUA within six months of study participation, were obtained from patients' interview and medical records. Obesity was defined as body mass index (BMI) of >27.5kg/m^2. Data was analysed for patients with non-tophaceous gout. Comparison between patients who achieved and did not achieve target SUA, defined as <360µmol/L, was performed using chi-square and student t-test for categorical and continuous data, respectively.

Results: Four hundred and twenty-six patients with gout participated in this study and 343 (80.5%) patients had non-tophaceous gout. Their mean age was 57.7 (±12.9) years. Majority were men (280 patients), Malay (260 patients) and had at least a secondary education (223 patients). There were high prevalence of cardiovascular co-morbidities; hypertension in 279 (81.3%), dyslipidaemia in 235 (68.5%), diabetes mellitus in 154 (44.9%) and obesity in 167 of 265 (63%). There were 280 patients diagnosed with gout for more than six months and 201 (71.8%) had recent SUA; 44 (21.9%) achieved target SUA and 157 (78.1%) did not achieve target SUA. The factors found to be significantly different between the two groups were age, ethnicity, education level, BMI and SUA level before ULT initiation. (Table 1) The mean allopurinol dose were similar between patients who achieved and did not achieve target SUA (191.3±80.8mg vs 197.1±72.5mg, p=0.56) despite significant difference in the mean SUA (301.5±70.3µmol/L vs 488.3±93.1µmol/L, p<0.01).

Table 1. Comparison between patients who achieved and did not achieve target sUA level.

Factors	Target sUA achieved, mean (±SD)	Target sUA not achieved, mean (±SD)	p-value
Age, years	63.9 (8.9)	58.1 (12.5)	<0.01
Gender*			0.92
• Male	35 (21.7)	126 (78.3)	
• Female	9 (22.5)	31 (77.5)	
Ethnic*			0.03
• Malay	30 (19.1)	127 (80.9)	
• Others	14 (35)	26 (65)	
Education*, n=181			0.14
• Primary	17 (35.4)	31 (64.6)	
• Secondary and beyond	24 (18.0)	109 (82.0)	
Disease duration, years	94.5 (99.9)	96.39 (94.8)	0.91
BMI, kg/m^2	28.3 (4.3)	31.1 (7.8)	<0.01
SUA before ULT, µmol/L	553.2 (109.2)	603.2 (98.5)	0.03
Recent SUA, µmol/L	301.5 (70.3)	488.3 (93.1)	<0.01
Allopurinol dose, mg	191.3 (80.8)	197.1 (72.5)	0.67

*no of patients

Conclusion: There was a low percentage of patients who achieved target SUA in primary care clinics. Older age, ethnicity other than Malay, lower BMI and lower SUA level before ULT initiation were significantly associated with achievement of target SUA. Higher education was significantly associated with failure to achieve target SUA and in these patients, allopurinol was not titrated according to SUA level.

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AB0919 WHAT IS LOWER EXTREMITY ENTHESEAL INVOLVEMENT IN ACUTE GOUT ATTACK? AN ULTRASOUND-STUDY

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Background: Articular involvement in acute gout attack is extremely common and mainly characterized by arthritis, which are usually transient, severe, reversible and well responsive to treatment. The involvement of tendons and entheses in lower extremity in monosodium urate-related disease through US (ultrasound) assessment have been described [1,2]. US findings in gout raising the hypothesis that entheseal involvement could be a missing target in the clinical evaluation of gout patients.
Objectives: To evaluate by ultrasound (US) the frequency and characteristics of lower extremity entheseal involvement in acute gout attack patients.
Methods: US assessment were performed by independent rheumatologist on 31 patients with acute gout attack. Presence of lower extremity entheseal involvement were evaluated by grey-scale (GS) and power Doppler (PD). US assessment contain quadriceps, patellar and Achilles tendons, and plantar fascia entheses according to the OMERACT definitions.
Results: US revealed one or more abnormalities in at least one enthesis in 22 out of 31 gout patients (71.0%) and 47 out of 310 entheses (15.2%). Among the affected entheses, the patellar insertion of quadriceps tendon was most commonly involved (57.4%) during acute gout attack, followed by the calcaneal insertion of the Achilles tendon (17.0%) and distal insertion of the patellar tendon (14.9%). The proximal insertion of the patellar tendon and calcaneal insertion of the plantar fascia were involved in 8.5% and 2.1%, respectively. Bone erosions and osteophytes were found in affected entheses (10.6% and 25.5%, respectively).
Conclusion: Our study identifies that lower extremity entheseal involvement is a missing target in the evaluation of patients with acute gout attack. US plays a key role in the assessment of both clinical and subclinical enthesitis in gout patients.
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AB0920 APPLICATION OF THE EULAR 2016 GUIDELINES FOR URATE-LOWERING THERAPY IN CLINICAL PRACTICE (DATA OF A SIX-MONTH PROSPECTIVE STUDY)

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Background: The EULAR 2016 guidelines on gout management provide for a consecutive regimen of urate-lowering medications; however, the possibility of reaching the target uric acid level when using the regimen has not been studied in clinical practice.
Objectives: To assess the possibility of reaching the target uric acid level when following the EULAR 2016 guidelines on gout management with use of different xanthine oxidase inhibitors available in Russia.
Methods: This monocentric prospective study included 83 gout patients (79 (95%) male and 4 (5%) female patients) with the mean age of 51.3±10.9 years old. The inclusion criterion was indications for urate-lowering therapy in accordance with the EULAR 2016 guidelines. The exclusion criteria were the following: absolute contraindications to all of the study drugs, GFR <30ml/min/1.73m2, and NYHA class III-IV heart failure.
At urate-lowering therapy initiation, the patients were prescribed allopurinol with the starting dose of 100mg/day; the dose was titrated until the target uric acid level was reached (maximum up to 900mg/day), and in the patients with GFR between 30 and 60ml/min/1.73m2 – up to 300mg/day. In case of insufficient efficacy of allopurinol (unachieved target uric acid level of <360μmol/L, for the patients with severe gout of <300μmol/L) or development of adverse reactions, allopurinol was replaced with febuxostat with the starting dose of 80mg/day and dose titration up to 120mg/day if necessary. The laboratory tests included serum creatinine level, uric acid level, AST, ALT, creatine phosphokinase, glucose; clinical blood test. The following parameters were assessed: possibility of reaching the target uric acid level when following the suggested regimen, and frequency of development of adverse reactions when using allopurinol and febuxostat.
Results: 37 (45%) patients had the target uric acid level of <360μmol/L and 46 (55%) pts – of <300μmol/L. The recommended therapy regimen allowed 77 (93%) patients under study to reach their target uric acid level.
The target uric acid level was achieved by 44 (53%) out of 79 patients on allopurinol, of whom 36 (82%) received 100-600mg/day, and 8 (18%) – 700-900mg/day. Of the patients with GFR of >60ml/min/1.73m2, 32 (73%) patients achieved their target uric acid level and of those with GFR <60ml/min/1.73m2 – so did 12 (27%). Then the patients on allopurinol with unachieved target uric acid level were prescribed febuxostat (in 30 (77%) cases because of inefficacy of the allopurinol therapy, in 9 (33%) patients because of their development of adverse reactions where 5 pts had a more than doubled level of transaminase (ALT, AST), 2 pts had skin itch and 2 pts had hives).
In total, 39 patients received febuxostat, of whom 4 pts were with initial intolerance for allopurinol in past history, and 35 pts after therapy with maximum dose of allopurinol. A febuxostat dose of 80mg/day was associated with achievement of the target uric acid level in 14 (42%) patients and that of 120mg/day – in 19 (58%) patients, therefore, total 33 (85%) patients reached their target uric acid level. Four patients on febuxostat developed adverse reactions: 3 patients had a more than doubled serum transaminase level (ALT, AST) and 1 patient had hives. Also, an insignificant increase in the mean GFR was registered from 73±21.4ml/min/1.73m2 to 78.4±22.5ml/min/1.73m2 which did not differ between the two drugs.
Conclusion: The recommended regimen of xanthine oxidase inhibitors in their maximal doses secures reaching the target uric acid level in 93% patients. In 47% patients, allopurinol in maximal doses (up to 900mg/day) does not significantly increase the possibility of reaching the target uric acid level, even though it demonstrates high tolerance.
Disclosure of Interests: Maria Chikina: None declared, Maxim Eliseev Speakers bureau: Novartis, Menarini Group, Alium, Olga Sheliabina: None declared
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AB0921 COMPARISON OF EFFICACY AND SAFETY OF DIFFERENT ANTI-INFLAMMATORY DRUGS AT INITIATION OF URATE-LOWERING THERAPY IN PATIENTS WITH GOUT (PRELIMINARY DATA)

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Background: NSAIDs, colchicine and glucocorticoids are used for prevention of acute arthritis in gout patients, yet there is little data on their comparative efficacy.
Objectives: Comparison of efficacy and safety of different anti-inflammatory drugs used for prevention of acute arthritis at initiation of urate-lowering therapy in gout patients.
Methods: This monocentric prospective study included 79 gout patients (75 (94.9%) male and 4 (5.1%) female patients) with the mean age of 51.3±10.9 years old. The inclusion criteria were the following: established gout (ACR/EULAR 2015 criteria), aged 18-80, serum uric acid level >360μmol/L, absence of urate-lowering therapy at baseline and at least one gout flare within past three months. The exclusion criteria were: absolute contraindications to all of the study drugs, GFR <30ml/min/1.73m2.
All of the patients were prescribed urate-lowering therapy (allopurinol or febuxostat), the dose was titrated until the target serum uric-acid level (<360μmol/L) was achieved. Simultaneously, preventive anti-inflammatory therapy was initiated and the drug for each patient was chosen individually: colchicine 0.5mg/day or any NSAID in minimal anti-inflammatory dose or prednisolone 7.5mg/day. The analysis of the data included 3-month comparative evaluation of the efficacy of the preventive therapy against the following parameters: frequency of gout flare and duration thereof, VAS pain intensity of flare. The laboratory tests included serum creatinine level, uric acid level, AST, ALT, creatine phosphokinase, glucose; clinical blood test before, two weeks and three months after the initiation of the therapy.
Results: NSAIDs were received by 14 (17.7%) patients, colchicine by 56 (70.9%) and glucocorticoids by 9 (11.4%) patients. There were no differences initially in age, GFR or lab test values.
Three months later, the gout flares frequency median lowered to 1 [0;2] flare ($p<0.01$). The frequency of gout flares did not depend on the chosen drug and was 1 [0;1] for NSAIDs, 1 [0;2] for colchicine and 1 [1;2] for glucocorticoids.
40 (50.6%) patients out of 79 did not have a single flare. The patients who received NSAIDs (57.1%) and colchicine (42.9%) experienced no gout flares more often than those who received glucocorticoids (37.5%), but the differences were not significant.
However, the VAS pain intensity of gout flares in the patients who received NSAIDs (30.7±12.9mm) was lower than in those who received colchicine (42.1±12.3mm) and glucocorticoids (42.2±8.4mm) ($p<0.05$ for both).
The duration of gout flares on different drugs was not significantly different and was on average 3 [1.5;4] days for the patients on NSAIDs, 5 [3;7] days for those on colchicine and 5 [4;6] days for the patients who received glucocorticoids.
The NSAID therapy was discontinued in two cases, in which the serum transaminase levels (AST, ALT) more than doubled; the colchicine therapy - because of development of diarrhea in two patients and of myopathy in one.
Conclusion: Efficacy of and tolerance to a three-month course of preventive therapy with NSAIDs and glucocorticoids in gout patients are comparable to that with colchicine. In case of development of gouty arthritis, preventive use

of NSAIDs is characterized by lower pain intensity than as against colchicine or glucocorticoids.
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AB0922 BUROSUMAB (ANTI-FGF23 MONOCLONAL ANTIBODY) IN THE TREATMENT OF A PATIENT WITH RECURRENT TUMOR INDUCED OSTEOMALACIA.

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Background: Tumor-induced Osteomalacia (TIO) is a rare paraneoplastic syndrome caused by tumoral overproduction of fibroblast growth factor 23 (FGF23), resulting in hyperphospaturia, hypophosphatemia and osteomalacia. Surgery is the only curative treatment, but tumor can locally recur, even after years from primary surgery. Furthermore, some tumors cannot be removed by surgery due to their location.
Objectives: To describe a case of a 53-year-old woman affected by recurrent TIO after three surgical attempts of removal treated with Burosumab.
Methods: We describe the case of a 53 years old woman with TIO treated with Burosumab, an anti-FGF-23 monoclonal antibody at present approved for X-linked hypophosphatemic rickets only.
Results: A 46-year-old Caucasian female was referred to our Bone Unit after experiencing several fractures in different sites. She reported being in good health until three years prior consultation. At the time of symptoms onset, she experienced a progressive muscle pain, enabling her to stand for a long period. During imaging evaluation for atraumatic fracture of right great trochanter, the MRI abdomen and ^{18}FDG- PET-CT showed a metabolic pre-sacral lesion. She unsuccessfully underwent to an exploratory laparotomy of that lesion. Then, she suffered from atraumatic intertrochanteric fracture of right femur, surgically treated, and after 3 months, she had an insufficiency dyaphiseal fracture of the left femur, surgically treated. Furthermore, she experienced several ribs fractures. At the time of first evaluation, lab works showed: serum-Phosophate (PS) 1.2 mg/dL (reference range (RR) 2.5-4.5 mg/dL), urinary-phosphate of 24h (PU) 842 mg/24h, alkaline phosphatase (ALP) 565 UI (RR<300), 1,25$(OH)_2$ vitamin D_3 27 ng/L (RR 25-86.5), PTH 24 (RR<75 pg/mL), intact-FGF-23 117 (RR 25-45 pg/mL), normal serum and 24h-urinary Calcium. Patient underwent to ^{68}Ga-DOTATATE-PET-CT that showed a pre-sacral lesion, who was studied with MRI and CT before surgery. In 2013 patient underwent surgical excision of the pre-sacral region. After 18 months of well-being, patient complained worsening of articular pain and muscle weakness, and further ribs fractures. Another ^{68}Ga-DOTATATE-PET-CT reported a relapse of the previous pre-sacral lesion (32x12x47 mm) with an increase of FGF-23levels (54.6 pg/mL). Even the subsequent surgery was not able to remove the tumor. Since 2015, patient was maintained in phosphorus supplements and 1,25$(OH)_2$vitamin D_3, but PS levels never normalized. We asked for compassionate use of Burosumab and, after ethical committee approval, in September 2019 she was started on Burosumab, at a dose of 30 mg per month (0.3 mg/kg). At baseline, she had PS 1.2 mg/dL, PU 1874 mg/24h, TRP 25.96%. After two months, she improved in pain symptom (VAS reduction from 65 to 12 mm), which allow her to walk and stand without crutches. She did not normalize her PS levels (1.3 mg/dL), while PU reduced to 1000 mg/24h. We titred Burosumab dose at 40 mg per month (0.6 mg/kg) and patient is still under therapy, waiting for next blood works.
Conclusion: This is the first European patient affected by TIO treated with Burosumab. Burosumab could be a promising therapy in the medical treatment of TIO refractory or not eligible for definitive surgery. Further data are needed to standardize the proper dose regimen.
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AB0923 DIETARY FACTORS AND TOPHI: A FOOD INTAKE FREQUENCY SURVEY IN CHINESE GOUT PATIENTS

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Background: Tophi is a cardinal sign of advanced gout. Risk factors of gout are also closely related to the formation of tophi, such as impaired kidney function and serum uric acid (sUA). Several dietary factors, such as alcohol, fructose-containing beverage, red meat, sea foods have been confirmed increasing the risk of gout. Diet patterns vary widely in different countries. Dietary factors' association with tophi formation remain elusive in Chinese gout patients.
Objectives: This study aimed to study whether dietary factors were risk factors for tophi.
Methods: We recruited consecutive gout patients who fulfilled the 2015 Gout Classification Criteria of ACR/EULAR and collected demographic data, gout disease characteristics and comorbidities. Tophi was evaluated by physical examination and/or musculoskeletal ultrasound. All gout patients completed 10-items food intake frequency questionnaire which included red meat, animal offal, seafood, alcohol, fructose-containing beverages, milk and dairy products, coffee, hotpot, slow-cooking soup and tea. Patients were advised to report the average frequency of food consumption in the preceding year of first gout attack. Multivariate logistic regression analysis was performed to evaluate risk factors of tophi. Dependent variables were those met p values less than 0.1 on univariate analysis.
Results: a)There were 682 gout patients recruited with 94% male, mean age 44±16 years, and median gout duration 4 (2,7) years. The mean sUA was 9.0±2.3mg/dl. Tophi presented in 166 (24.3%) patients with 31 (4.5%) patients diagnosed by ultrasound. In patients with gout duration <3 years, 3~4.9 years, 5~9.9 years and ≥10 years, the prevalence of tophi were 6.7%, 19.4%, 38.8%, and 49.6%, respectively. b)Tophus patients were characterized by older age (48±16 vs. 42±15 years), longer gout duration [7(4, 10) vs. 3(1, 5) years], more ever involved joints [11(4, 24) vs. 3(2, 5)] and more flare times in the last year [11(4, 24) vs. 3(2, 6)]. For comorbidities, tophus patients presented higher prevalence of urolithiasis (36% vs. 23%), hypertension (54% vs.40%,) and diabetes (20% vs. 11%) but less hypertriglyceridemia (19% vs. 32%, all P<0.05). c)Compared with patients without tophi, tophus gout patients consumed more red meat (>300g/d: 12% vs. 6%), seafood (>2 times/w: 18% vs.13%), hotpot (≥1 time/w: 17% vs. 10%) and alcohol (>84g/d: 23% vs. 9%). d)Dependent variables of multivariate logistic regression analysis included age, gender, gout duration, diuretics, BMI, sUA, serum creatinine, urine pH, hypertriglyceridemia, hypertension, diabetes, coronary heart disease, urolithiasis, alcohol consumption, hotpot, red meat, and seafoods. Gout duration, sUA, serum creatinine and urine pH were positively correlated with tophi, while hypertriglyceridemia was negatively associated with tophi. For dietary factors, heavy alcohol consumption (> 84g/ day vs. < 1g/ day OR=2.624, 95%CI: 1.437-4.793) and hotpot (≥ 1 time/w vs. <1 time/w, OR=2.164, 95%CI: 1.217-3.847) were positively correlated with tophi.
Conclusion: Our data suggest tophi should not be ignored in gout patients with short duration. Heavy alcohol consumption and hotpot are associated with the formation of tophi.
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AB0924 CALCIFIC TENDONITIS OF THE ROTATOR CUFF: PERIOSTIN ENRICHMENT IS ASSOCIATED WITH A BETTER RESPONSE TO ULTRASOUND-GUIDED PERCUTANEOUS LAVAGE.

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Background: Calcific tendonitis of the rotator cuff is a frequent cause of chronic shoulder pain. It is due to apatite deposits within the tendons. Little data are currently available about proteins associated to crystals within deposits.
Objectives: The aim of the study was to quantify 6 proteins in calcific powders obtained from patients who have undergone an ultrasound-guided percutaneous lavage (UGPL) of their calcification and to look for correlations between their concentration and patient characteristics.
Methods: Calcific powders were obtained from patients included in the CALCECHO trial whose main objective was to compare post-procedure pain between two groups: methylprednisolone or placebo injected at the end of the lavage [1]. Based on preliminary proteomic data and literature data, the following proteins have been selected and quantified by ELISA: Pigment-epithelium Derived Factor (PEDF), Osteopontin (OPN), Periostin (POSTN), Activin A (ACT A), Osteoprotegerin (OPG) and Bone Morphogenic Protein-2 (BMP-2). The level of each protein was expressed in µg per pg of the total proteins present in the sample. These proteins have been selected for their link to the mineralization. Correlations between the level of each protein and radiographic and ultrasound appearance of the calcific deposits were sought. We also looked for correlations between level of each protein and duration of pain or response to UGPL (Mann-Whitney test).

Results: Sixty-six samples were studied: mean age was 48.9 (+/- 9.7) and 68% were female. Mean duration of shoulder pain was 30 months with a mean VAS pain of 68/100 (+/-14). Mean calcification size was 1.8 cm. Results of ELISA were as follows: mean level of PEDF at 1097 pg/µg, mean level of OPG at 135 pg/µg, mean level of POSTN at 6.9 pg/µg, mean level of ACT A at 19.6 pg/µg and mean level of OPN at 49.6 pg/µg although BMP-2 was undetectable. There was no correlation between level of proteins and the size of the calcification or the duration of pain. There was no difference in protein levels between type A and type B calcifications on radiography (classification of the French Society for Arthroscopy). In contrast, levels of POSTN and OPN were significantly higher in nodular calcifications compared to the homogenous (p=0.003 and p=0.01 respectively) or fragmented types (p=0.03 and p=0.04 respectively). Furthermore, calcifications without acoustic shadowing were enriched in POSTN compared to those with (p=0.04). Finally, the periostin level was significantly higher in calcifications that have responded well to UGPL (p=0.02).

Conclusion: In this cohort of patients treated by UGPL, we observed higher levels of POSTN and OPN in the less dense calcifications and POSTN enrichment appeared to be associated with a better response to UGPL. Considering these data, further studies will be necessary to better understand the role of this protein in calcific tendonitis.

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AB0925 MULTIPLE FRACTURES DUE TO IRON-INDUCED AND FGF23-MEDIATED HYPOPHOSPHATAEMIC OSTEOMALACIA: AN UNKNOWN ADVERSE EFFECT

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Background: The use of a specific and widely used type of intravenous ferrotherapy, ferric carboxymaltose (FCM), has been linked to the development of an asymptomatic and transient hypophosphataemia. However, in recent years it has been published that it can generate a severe hypophosphataemic osteomalacia (HPO) mediated by fibroblast growth factor 23 (FGF23) that is associated with high morbidity[1]. It is a potentially serious adverse effect whose prevalence is unknown and that clinicians may know little about.

Objectives: To know the clinical and biochemical characteristics of this adverse effect and make it visible in the medical community.

Methods: Observational descriptive study of three cases of patients assessed in the Rheumatology department of our hospital who were referred for study of recurrent fractures and diagnosed of FGF23-mediated HPO due to FCM. Demographic, clinical and laboratory data of the patients are described.

Results: The clinical and laboratory characteristics of the patients are shown in table 1. All patients presented clinical and biochemical features compatible with FGF23-mediated HPO (mean of FGF levels 240 kRU/L, NR 0-145). All had multiple insufficiency fractures (Fx) and/or avascular necrosis (AN), with hip involvement in all 3 cases. Other causes of HPO were ruled out in all of them using PET ^{18}F-FDG, octreotide scintigraphy, abdominal magnetic resonance and PET ^{68}Ga-DOTATOC, and a genetic study of hypophosphataemic rickets was also performed in case 1. In all patients FCM was discontinued and phosphate levels were progressively normalized allowing the withdrawal of oral phosphate and calcitriol replacement therapy. After metabolic normalization, none presented new Fx or AN.

Conclusion: Treatment with FCM can cause severe FGF23-mediated HPO, multiple fractures and a great decrease in the quality of life. Since it can be potentially serious and easily reversible, it is important to favor the dissemination of these new cases and the knowledge of this disease. The need to monitor phosphate and/or FGF23 levels in patients receiving this intravenous iron therapy should be evaluated.

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Table 1. Clinical and biochemical characteristics of the patients

	Case 1	Case 2	Case 3
Age (years)[a]	36	75	43
Medical history	Crohn's disease (CD), right hemicolectomy. CD-associated spondyloarthritis	Small bowel angiodysplasias	Antisintetase syndrome. Uterine fibroids.
Cause of anemia	Gastrointestinal bleeding and malabsorption	Gastrointestinal bleeding	Gynecological bleeding
Fe-CBX start date	10/2010	08/2013	02/2018
Fe-CBX discontinuation date	10/2018	11/2018	06/2018
Total time Fe-CBX (months)	96	63	4
Fractures	AN: left calcaneus posterior tuberosity, astragaline dome, right femoral head Fx: left talus, tibial pylon, tibia-astragaline and ischiopubial branch; right 2nd metatarsal, distal tibia, posterior tuberosity of calcaneus	Fx both femoral necks and right sacral wing	AN both femoral heads
Bone densitometry	LS: Z-score-2.4 FN: Z-score -2.4		LS: Z-score -0.5 FN: Z-score -1.3
Phosphate, mg/dL (NR 2.5-4.5)[a]	**1.8**	**1.6**	**1.3**
Calcium, mg/dL (NR 8.6-10.2)[a]	9.1	**8.3**	9.0
1,25(OH)$_2$D$_3$, ng/ml (NR 30-100)[a]	54	**12**	**7**
PTH, pg/ml (NR 12-65)[a]	**71**	**223**	**104**
AP, UI/L (NR 46-116)[a]	113	**140**	86
Ph-exc, mg/24h (NR 400-1300)[a]	**1609**	**1630**	489
TPR, % (NR 73-87)[a]	**58.3**	**50.2**	**70.7**
FGF-23, kRU/L (NR 0-145)[a]	**183**	**335**	**201**
Time to normalization[b]	10	4	8

[a]During treatment with FCM. [b]Of serum phosphate levels since FCM discontinuation in months. LS: Lumbar spine. FN: Femoral neck. NR: Normality range. PTH: Parathyroid hormone. AP: Alkaline phosphatase. Ph-exc: 24-hour urine phosphate excretion. Ph-cl: phosphate clearance. TPR: Tubular phosphate reabsorption. Data highlighted in bold indicate altered values.

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AB0926 PERFORMANCE OF THE ACR-EULAR GOUT CLASSIFICATION CRITERIA FOR THE DIAGNOSIS GOUT IN CLINICAL PRACTICE: A ONE-YEAR FOLLOW-UP STUDY

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Background: Classification criteria are used for classifying groups of patients, especially for clinical trials, and diagnostic criteria for diagnosis in individual patients.

Objectives: to establish the performance of the 2015 ACR/EULAR gout classification criteria for the diagnosis gout in patients with undifferentiated arthritis. Secondary, to explore the use and efficacy of uric acid lowering therapy (ULT) in daily clinical practice in new gout patients.

Methods: 1-year follow-up study was performed in subjects with unclassified arthritis, who had been classified as gout patients or not, according the gout classification criteria, including imaging with dual-energy CT, but without ultrasonography and joint X-rays.(1) The reference was the clinical diagnosis (gout yes/no) after 1-year follow-up.

Results: 71 patients were included; their demographic and clinical characteristics are summarized in Table 1. All 63/71 patients classified as having gout at baseline also had a clinical gout diagnosis after one year, and of the patients not classified, none had the clinical diagnosis of gout at one year.

Table 1. Characteristics of the 71subjects included in analyses

	Diagnosis**	
	gout (n=63)	no gout (n=8)
Age in years, mean (SD)	62 (14)	59 (14)
Male gender, N (%)	53 (84)	5 (63)
Symptom duration* at baseline in months, median (IQR)	12 (1-48)	8 (0.5-33)
Joint involvement at baseline N patients (%):		
MTP,	33 (52)	1 (12)
ankle/midfoot	12 (19)	1 (12)
other joint	18 (29)	6 (76)
SUA intercritical in umol/l, mean (SD)	484 (63)	337 (71)
2015 ACR/EULAR criteria baseline score, mean (SD)***	10.3 (2.5)	2.6 (1.5)
2015 ACR/EULAR criteria ≥8 points, N patients (%)***	57 (90)	0 (0)
MSU crystal positive joint aspiration, N patients (%)	44 (70)	0 (0)
DECT positive, N patients (%)	49 (78)	0 (0)

* self-reported, intermittent symptoms; ** all patients classified with gout at baseline also had a clinical gout diagnosis after one yea; *** using a somewhat limited set, see methods
MTP, metatarsophalangeal joints; SUA, serum uric acid; DECT, dual-energy CT; MSU, monosodium urate;.

Sensitivity, specificity, positive and negative predictive value, and accuracy values (95% CI) of the classification criteria set we used were 0.91 (0.80-0.96); 1 (0.63-1); 1; 0.57 (0.38-0.74) and 0.92 (0.83-0.97), respectively. The area under the receiver operating characteristics curve (95% CI) was 0.95 (0.91-0.99).
ULT was started in 49/63 (78%) of gout patients; 45/49 (92%) of them had serum uric acid levels ≤ 360 µmol/l and no recurrent gout attack during one-year follow-up.
Conclusion: The 2015 ACR-EULAR gout classification criteria performed well for the diagnosis gout in clinical practice. Most gout patients had been treated successfully, according to current guidelines.
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AB0927 HIGHER ULTRASOUND BURDEN WITH MONOSODIUM URATE CRYSTALS IN THE JOINTS IS CONNECTED TO MORE PRONOUNCED ARTERIOSCLEROTIC VASCULAR ALTERATIONS

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Background: The severity of gout and the presence of subcutaneous tophi increase the risk of cardiovascular death. In patients (pts) in the spectrum of gout and in subjects who have inflammatory arthritis with accompanying asymptomatic hyperuricemia, data whether ultrasound (US) burden with monosodium urate (MSU) crystals in the joints is associated with higher cardiovascular risk are contradictory.
Objectives: To establish the relationship between US MSU crystal deposits in the joints with diastolic heart function and carotid arteries alterations in gout pts, individuals with asymptomatic hyperuricemia and no sign of inflammatory arthritis and psoriatic arthritis pts with asymptomatic hyperuricemia.
Methods: The study is cross-sectional. A total of 121 consecutive pts were included, divided into 85 pts with gout - 63 males and 22 females aged 57.7±14.1 years, 27 subjects with asymptomatic hyperuricemia and no sign of inflammatory arthritis - 13 males and 14 females aged 53.4±17.2 years, and 9 psoriatic arthritis individuals with asymptomatic hyperuricemia - 2 males and 7 females aged 61.2±14.4 years. Pts underwent two-dimensional echocardiography, US examination of the common carotid arteries and US of the joints of the hands, elbows, knees, ankles and feet. The echocardiography was conducted with 2.5 MHz transducer phased array working with pulse Doppler frequency of 2.5 MHz. Parameters of the transmitral blood flow were measured: the ratio between maximal early and late flow velocities (E/A ratio) and deceleration time (DT). With tissue Doppler imaging, early diastolic mitral annular velocity (e´) was obtained. We judged for left ventricular filling pressure by determining E/e´ ratio. Using US of the common carotid arteries done with 10 MHz linear transducer working with pulse Doppler frequency of 5 MHz were measured: intima-media thickness (IMT), common carotid artery resistive index (CCARI) and the presence of atherosclerotic plaques was recorded. US of the joints was performed with a high-frequency, linear transducer, 4-15 MHz. The existence of double contour sign, intra-tendinous MSU aggregates, snow storm, tophi, tophi with erosions, or a combination of these US features was assessed. Data were analyzed by Chi-Square, Mann-Whitney, Kruskal Wallis, t-test and ANOVA.
Results: In the three groups there was no difference in the mean values of E/A ratio (p=0.591), DT (p=0.498), e´ (p=0.662), E/e´ ratio (p=0.754), IMT (p=0.260), CCARI (p=0.089) and in the frequency of heterogeneous or homogeneous carotid arteries plaques (p=0.595). Among pts with and without evidence of MSU crystals in the joints the means of E/A ratio (p=0.452), DT (p=0.367), e´ (p=0.218), E/e´ ratio (p=0.230), IMT (p=0.165), CCARI (p=0.097) and the frequency of heterogeneous or homogeneous plaques (p=0.830) were comparable. The distribution of MSU crystal deposits in two or more joints was the highest in gout pts (56.5%) compared to pts with asymptomatic hyperuricemia (11.1%) and individuals with psoriatic arthritis (22.2%), (p<0.001). Pts with MSU crystal deposits in two or more joints compared to those with crystal deposits in one joint and pts without MSU crystals had the highest CCARI (mean±SD; 0.72±0.05 vs 0.69±0.07 vs 0.68±0.07, p=0.019), the longest DT (mean±SD; 236±50.99 msec vs 208.09±34.30 msec vs 216±55.43 msec, p=0.026) and had a tendency of lowest e´ (mean±SD; 10.33±3.96 cm/s vs 12.03±3.83 cm/s vs 11.99±3.98 cm/s, p=0.077), but the values of E/A ratio (p=0.119), E/e´ ratio (p=0.107), IMT (p=0.151) and the distribution of atherosclerotic plaques (p=0.920) were equal.
Conclusion: Pts with higher US MSU burden have more pronounced left ventricular diastolic dysfunction and greater vascular stiffness. The changes in their vessels are mainly of the arteriosclerotic type.
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AB0928 DISORDERS OF FATTY ACID METABOLISM IN THE FORMATION OF ARTERIAL HYPERTENSION IN PATIENTS WITH GOUT

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Background: One of the possible mechanisms of the formation of cardiovascular disorders in patients with gout may be a violation of the metabolism of fatty acids. Decrease of the total content of unsaturated fatty acids (UFAs) has a multifaceted adverse effect on a number of metabolic processes which lead to the development of arterial hypertension (AH) and atherosclerosis as a result. There are no studies on the level of UFAs in the blood of patients with gout depending on the presence of hypertension.
Objectives: To study the level of UFAs in the blood of patients with gout depending on the presence of AH.
Methods: We examined 87 patients with gout and AH. 83% were men (mean age 55.4 ± 12.3 years). All patients had chronic gouty arthritis, 30% of patients had tofus. The duration of gout was 8 [4; 11] years. AH was detected in 49 (56.2%) people. The duration of AH was 7 [2; 10] years. All patients went through standard general clinical, laboratory and instrumental examination. Ozonation method was developed and put into practice in N.N. Semenov Federal Research Center for Chemical Physics, Russian Academy of Science (FRCCP RAS), to assess disorders of the lipid metabolism for diagnostic purposes. The essence of the method is to determine the level of unsaturation of serum or blood plasma lipids which depends on the total amount of double bonds (DB) in UFAs both in a free state and within lipid combination. This parameter is called the Double Bond Index (DBI). DBI is measured by a domestic device ADS-5M («Double bond analyzer») developed at FRCCP RAS. The control group consisted of 20 healthy men, comparable in age. Statistical analysis of the data was carried out using the STATISTICA 10.0 program.
Results: Patients were divided into 2 groups: patients with gout with normal blood pressure (group 1; n = 38) and with AH (group 2; n = 49). Patients from group 2 differed by a longer course of gout and had a higher level of uric acid in comparison with patients from group 1. The number of joints involved in the inflammatory process in patients from group 2 exceeded the number of those in patients from group 1. Patients from group 2 had more often attacks of gouty arthritis and the severity of pain during the last year compared with group 1. The normative value of the blood serum lipids DBI was determined for the control group of healthy people (260+20 conventional units (c.u.)) by the ozonation method. A significant deviation of the DBI from the norm both increased and decreased is a sign of pathology. In all groups DBI is lower than the norm but to a different extent. DBI is slightly reduced relative to the norm (DB = 229 c.u.) in group 1 therefore lipid metabolism is impaired just slightly. DB = 167 c.u. in group 2 which indicates a significant disorder of lipid metabolism (p<0,05). Thus the ozonation method is informative and allows

to quantify the severity of patient general condition and DBI is an integral indicator of changes in the number of fatty acids and body general condition.
Conclusion: The presence of AH in patients with gout makes the clinical course of the disease more severe and exacerbates lipid disorders that can make significant changes in the formation of cardiovascular complications in this category of patients. DBI can be used as an additional criteria in laboratory diagnostics and monitoring to develop adequate treatment tactics.
Disclosure of Interests: Margarita Gromova Speakers bureau: Speaker for Biotehnos, Boehringer-ingelheim, Vladimir Tsurko Speakers bureau: Speaker for Boehringer-ingelheim, Berlin-chemie, Oksana Kisliak Speakers bureau: Speaker for Berlin-chemie, KRKA, Elena Kiseleva: None declared
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AB0929 CALCIUM PYROPHOSPHATE DIHYDRATE CRYSTAL-DEPOSITS: REMEMBER THE SPINE!

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Background: Calcium pyrophosphate dihydrate crystal-deposits (CPPD) is a common crystal disease affecting men and women equally. It is normally seen in peripheral joints. Spine involvement is rare and may mislead the diagnosis.
Objectives: To describe clinical, radiological and therapeutic findings of CPPD of the spine.
Methods: A retrospective descriptive study was conducted in the rheumatology department of Farhat Hached Hospital, including patients diagnosed with CPPD of the spine over a period of 20 years (1998-2018). Data concerning clinical, radiological and therapeutic aspects of CPPD of the spine were callected from their medical files.
Results: Twelve patients had a spinal localisation of CPPD. The mean age was 59.91±16.21 years. Patients were mainly women with a sex ratio men/women of 1:3. Mean duration of symptoms before the diagnosis was 27.08±25.69 months. Spinal presentation was the revealing symptom of CPPD in 45.5% of the cases. It affected the cervical spine in 66.7% and the lumbar spine in 33.3% of the cases. Spinal localisation of CPPD was associated with a peripheral arthropatyhy in 75% of the cases (the knees in 41.7%, wrists and hands in 66.6%, shoulders in 25% and the hips in 16.7%). Discovery of spinal CPPD was coincidental on plain radiographs in 16.7% of the cases. When symptomatic, the disease manifested itself as inflammatory pain in 72.7%, mechanical pain in 9.1% and both diurnal and nocturnal pain in 18.2% of the cases. Physical examination revealed stiffness of the spine in 58.3% of the patients. Fever was noted in 8.3% and deterioration of general condition with anorexia was reported in 25% of the patients. Neurological complications were represented by cervical myelopathy in 25%, sciatica in 8.3% and a case of unilateral ulnar nerve neuropathy was reported. Laboratory tests revealed inflammation in 50% of the cases. However, crystals were present in synovial fluid in only 25% of the patients. Spinal CPPD was visible on plain radiographs in 83.3% of the cases, showing calcified discs in 75% and signs of destruction in 16.7% of the cases. Peripheral calcifications were present in the wrists in 33.3% and the knees in 58.3% of the cases. Crow dens syndrome was reported in 16.7% of the patients. CT-scan helped the diagnosis of calcifications and crown dens syndrome when performed. MRI was prescribed in 58.3% of the patients and characterized the cervical myelopathy. Treatment relied on analgesics in all patients, NSAIDS were prescribed in 83.3%, colchicine in 66.7% and general corticosteroids in 25% of the cases. Spinal immobilization was recommended in 25% of the cases for a short period. Spinal CPPD was idiopathic in 75%, secondary to hyperparathyroidism in 8.3% of the cases and familial cases were detected in 16.7% of the patients.
Conclusion: Axial CPPD is rare and is an under-recognized entity that should be considered in elderly patients with neck or back pain. It can involve the discs or ligaments. The crown dens syndrome is quite suggestive of the diagnosis. If spinal CPDD is suspected, colchicine therapy could be a good therapeutic test and would avoid unnecessary further tests.
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AB0930 URATE INDUCED PRIMING OF HUMAN MONOCYTES IS MEDIATED VIA THE TGF-B PATHWAY

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Background: Hyperuricemia, elevated serum urate levels, is the main risk factor for gout, but is also associated with higher incidence of comorbidities such as cardiovascular disease, type 2 diabetes, metabolic syndrome and chronic kidney disease[1]. Crisan *et al.* showed that urate leads to increased production of interleukin (IL)-1β, a pro-inflammatory cytokine, and downregulation of IL-1 receptor antagonist (IL-1Ra), the natural inhibitor of IL-1, in human monocytes[2]. This imbalance between IL-1β and IL-1Ra is mediated by epigenetic reprogramming of innate immune cells[2]. RNA sequencing in urate-treated monocytes demonstrated that the TGF-β signalling pathway was differentially expressed[3].
Objectives: The objective of this study is to further explore the role of TGF-β in urate induced priming of human monocytes.
Methods: Human peripheral blood mononuclear cells (PBMCs) were isolated from healthy volunteers, adhered to a flat bottom plate, and treated for 24h with a dosing range of urate after which mRNA was isolated. For validation experiments, PBMCs from 9 gout patients and 7 healthy controls were isolated and adhered to a flat bottom plate for 4h after which cells were stored for RNA isolation. qPCR primers designed for TGF-β, TGF-β receptor I and II, MMP9, SMAD7 and ITGAV were used to assess expression levels of TGF-β pathway in these adherent monocytes. For priming experiments, adherent monocytes were primed for 24h with urate and/or recombinant TGF-β1 (R&D systems) with or without a TGF-β receptor II antibody (R&D systems), cells were washed and restimulated with LPS for 24h. Cytokine levels in supernatant were determined by ELISA for IL-1β, IL-6 and IL-1Ra.
Results: mRNA expression of TGF-β and its downstream targets were upregulated in urate treated monocytes and in gout patients compared to healthy controls. Moreover, urate levels significantly correlated to TGF-β in individuals with gout. Both urate and TGF-β priming increased the release of IL-1β and IL-6 after LPS stimulation in human monocytes. We did not observe a synergistic effect between the two and therefore hypothesized that urate induced inflammation is mediated via TGF-β. Blocking the TGF-β receptor II partly reversed the urate induced phenotype: lowered IL-1β and IL-6 production and restored levels of IL-1Ra. Further validation experiments are ongoing.
Conclusion: Urate induced priming of human monocytes is at least partly mediated via the TGF-β pathway. This study contributes to the understanding of the pathways involved in urate induced inflammatory status and might in the future provide a mechanistic explanation for the occurrence of some comorbidities in patients with gout. Additionally, as TGF-β is a major player in the pathogenesis of systemic sclerosis, this study might give a rationale for treatment of hyperuricemia in this population.
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AB0931 THE QUALITY OF LIFE IN GOUT PATIENTS WITH ULCERATION OVER TOPHI

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Background: The prevalence of gouty patients with ulcerations over tophi are increasing over time and it has been reported that gouty patients have significantly poor quality of life (QoL) compared to those healthy controls. [1, 2] there is no study on comparison of the QoL in patients with or without ulceration over tophi.
Objectives: To compare the QoL in gout patients with or without ulcerations over tophi.
Methods: A total of 79 inpatients with gout who were admitted to Guangdong Second Provincial General Hospital from January 2019 to January 2020 were included. Among them, ulcerations were identified in 28 patients. Short Form-36 Scales (SF-36) were chosen to assess patients. Differences between the groups were tested with Student's t test or Mann-Whitney U test for continuous variables, and Chi-square tests for categorical variables.
Results: Of 79 subjects, 74 were male, mean age was 54.23±14.3 years, disease duration was 10.94±7.06 years. Gouty patients had moderate- to high-quality levels in general health, vitality, social functioning, role emotional, and

mental health (median: 65, 75, 75, 88, and88, respectively), while had low levels of quality in role physical, and bodily pain (median: 0, and 22, respectively). Patients presenting with ulcerations over tophi had worse scores on five SF-36 domains, the mental component summary (MCS) and the physical component summary (PCS) than gout patients without ulcerations [mean (SD); P < 0.05 for all]: Bodily pain, 30.86(31.59) vs 35.17(33.40); General health, 49.46(27.01) vs 64.17(23.69); Vitality, 57.14(32.53) vs 72.84(26.38); Mental health, 75.4(22.43) vs 83.05(20.96); Reported health transition, 3.58(0.89) vs 3.78(1.42); MCS, 52.62(21.82) vs 66.65(21.44); PCS, 35.85(21.17) vs 46.67(23.86).

Conclusion: Patients with ulcerations over tophi present much worse QoL compared those without ulcerations. Our study suggests that the presence of ulceration over tophi further deteriorates the QoL in gout patients.

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Table 1. Clinical characteristics

Variable	Total (n=79)	Non-ulcerations (n=51)	Ulcerations (n=28)	*P* value
Male, n (%)	74(93.7)	47(92.1)	27(96.4)	0.462
Age[a], mean, y	54.23±14.30	53.96±12.24	54.71±17.69	0.842
Body mass index[a], kg/m^2	24.87±3.97	25.13±4.02	24.40±3.91	0.444
Gout duration[a],y	10.96±7.06	10.04±6.75	12.63±7.41	0.119
Maximum Serum uric acid, mg/dL	625.5±133.86	630.9±124.23	614.3±166.43	0.639
Smoking, n (%)	38(48.1)	23(45.1)	15(53.5)	0.477
Alcohol, n (%)	26(32.9)	13(25.5)	13(46.4)	0.072
Hypertension, n (%)	34(43.0)	18(35.3)	16(57.1)	0.062
Diabetes mellitus, n (%)	13(16.5)	10(19.6)	3(10.7)	0.281
Regular treatment, n(%)	3(3.8)	3(5.9)	0(0)	0.971
Glucocorticoid abuse, n (%)	18(22.8)	11(21.5)	7(25.0)	0.173

[a]Mean (SD).

Table 2. QoL scores

	Median (IQR)	Non-ulcerations (n=51), mean (SD)	Ulcerations (n=28), mean (SD)	*P* value
Physical function[b]	50(20-80)	58.62(32.17)	40.89(35.97)	0.095
Role physical[b]	0 (0-100)	33.03(46.91)	17.85(37.17)	0.119
Bodily pain[b]	22(0-62)	35.17(33.40)	30.86(31.59)	0.007
General health[b]	65 (40-80)	64.17(23.69)	49.46(27.01)	0.014
Vitality[b]	75 (50-95)	72.84(26.38)	57.14(32.53)	0.023
Social function[b]	75(38-100)	72.55(3.02)	60.27(33.85)	0.107
Role emotional[b]	88 (68-96)	33.98(47.37)	15.43(34.45)	0.135
Mental health[b]	88 (68-96)	83.05(20.96)	75.4(22.43)	0.007
Reported health transition		3.78(1.42)	3.58(0.89)	0.007
PCS		46.67(23.86)	35.85(21.17)	0.048
MCS		66.65(21.44)	52.62(21.82)	0.007

[b](range = 0-100)

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AB0932 FACTORS IN ACHIEVING TARGET SERUM URIC ACID LEVELS IN OUTPATIENT GOUT MANAGEMENT IN A MALAYSIAN TERTIARY RHEUMATOLOGY CENTRE

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Background: Gout is one of the most common inflammatory arthropathies. A target serum uric acid of less than 300μmol/l is recommended when tophi are present, and less than 360μmol/l for non-tophaceous gout. Urate-lowering therapy (ULT) should be titrated until the target is achieved and long-term maintenance of the target concentration is recommended. Although ULT has been proven to reduce the uric acid level, less than half of treated patients achieved the target serum uric acid (sUA) in real-world clinical practice.

Objectives: To assess the mean treat-to-target achievement in outpatient management of gout by the tertiary rheumatology centre and to identify factors influencing the success rate.

Methods: Retrospective cross-sectional study of all patients with gout attending out-patient clinics in a rheumatology referral centre from 1st January 2018 until 31st December 2018. Electronic medical records were reviewed. The successful target achievement is defined as mean of all available sUA in 2018 which is ≤360 and ≤300μmol/l for non-tophaceous and tophaceous gout respectively. Chronic kidney disease (CKD) is defined as glomerular filtration rate of less than 60ml/min.

Results: There were 251 patients analysed with mean age of 56.3±13.8 years and disease duration of 10.5±9.2 years. Majority were males (215, 85.7%) and 133 (53%) patients had tophaceous gout. The rate of success achieving the target SUA level of ≤360 and ≤300μmol/l were 33.9% (40) and 15.8% (21) in non-tophaceous and tophaceous gout respectively. However, in patients who are compliant, the target sUA achieved is 52.4% (33) and 31.7% (19) in non-tophaceous and tophaceous gout respectively. Characteristics of patients who achieved the targeted sUA were patients of more than 50 years old (48, 78.7%), without family history of gout (29, 65.9%), were prescribed colchicine prophylaxis upon initiating ULT (46, 76.7%), with absence of joint erosions (34, 73.9%) and those with normal creatinine clearance (40, 65.5%). There were 120 (48.4%) patients who were compliant to ULT. In 42 compliant patients who achieved target sUA, the mean allopurinol dose is 289.66mg±101.2 and 369.23mg±175 in non-tophaceous and tophaceous gout respectively. Sub-analysis in 31 compliant CKD patients, revealed no difference in allopurinol dose between those who achieved versus non-achieved target sUA (mean 243mg versus 263mg respectively). However, we noted that 11 (61%) CKD patients with tophi did not achieved target sUA at dose less than 300mg allopurinol. Lower achievement of target sUA was significantly associated with presence of tophi (p=0.001), poor compliance (p= 0.000) and presence of more than one comorbidity (p=0.041).

Conclusion: There are several challenges in achieving target uric acid level contributed by both patient and clinician factors such as compliance, presence of comorbidity and ULT dose. Our study suggests that higher dosage of allopurinol is required in patients with tophaceous gout, with or without renal impairment. However, the limitation of this study is, the small number of subjects which therefore needs *further* investigation.

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AB0933 PHYSICAL ACTIVITY DECREASES PAIN AND INFLAMMATION IN GOUT PATIENTS

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Background: Despite the high prevalence of gout, there has been little investigation into the relationship between physical activity and gout.

Objectives: To investigate whether physically active gout patients, as assessed by the International Physical Activity Questionnaire (IPAQ) long form, have lower pain scores, decreased inflammation, assessed by C-reactive protein (CRP) levels and less flares.

Methods: During scheduled appointments, gout patients not experiencing a flare at the time of visit were recruited from our clinics and consented to participate in the study. IPAQ were completed. Clinical data collected during the visit included age, years since diagnosis, flares per year, perceived pain at the time of visit and in the past 4 weeks, and C-reactive protein (CRP) levels.

Results: Thirty gout patients were recruited. Ages 31-86 (mean 61); duration of gout: one- 43 years (mean 9). IPAQ, separated gout patients into physically active (n=16) and physically inactive cohorts (n=14) (p<0.001. Physically active gout patients had over 12-fold fewer gout flares per year (p<0.01); 10-fold less CRP (p<0.01, a 4.6-fold decrease in perceived pain at the time of visit (p<0.01), and a 2.8-fold decrease in perceived pain over the past 4-week period (p<0.05).

Conclusion: This is the first study using a validated physical activity tool, IPAQ, to assess physical activity in gout patients. In this study, physically active gout patients were found to have lower CRP levels, less flares per year, and decreased pain perception compared to those that are not physically active, highlighting, the importance of incorporating physical activity as a possible adjunct treatment option during intervals between flares.

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AB0934 DUAL-ENERGY COMPUTED TOMOGRAPHY IN GOUT PATIENTS: IS IT USEFUL IN GENERAL PRACTICE?

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Background: Dual-Energy CT (DECT) has high sensitivity and specificity for detecting monosodium urate (MSU) crystal deposition. Although widely used in research, few studies have evaluated the usefulness of DECT in clinical practice.
Objectives: To evaluate the use of DECT in a clinical setting and determine its utility
Methods: We retrospectively evaluated the records of all patients referred for DECT scans over a 6.5-year period. Patient charts were reviewed for clinical features.
Results: 113 patients (17.5/yr) received DECT evaluation at a university hospital over the study period (234 scans). All were referred by rheumatologists. Medical records were available for 69 patients (134 scans), including 44 males and 25 females (mean age 62 (SD, 12.9, range: 34-85 yrs). Mean duration of gout was 6.7 (SD, 8.1) yrs. DECT was ordered to evaluate known gout (36/69, 52.1%), suspected gout (32/69, 46.4%), and suspected calcium pyrophosphate (CPP) disease (1/69, 1.4%). 32/69 (46.4%) of patients were on urate-lowering therapy.
61% (42/69) had MSU crystal and none had CPP deposition. Mean MSU volume was 1.6cc (SD, 5.2cc; range: 0.01-35 cc.) The joints imaged were feet/ankles (80/134, 60%) and hands/wrists (53/134, 40%). 23/33 (69.7%) patients with DECT positivity had elevated serum urate (SU) levels >6mg/dL; however, elevated SU was not significantly associated with DECT positivity (odds ratio (OR) 1.9, 95% CI:0.59-5.95, p=0.28).
For patients with positive scans, mean gout duration from first known flare was 9.5 (SD, 8.8) yrs.
Among patients who had scans completed within 1 yr of the first known gout flare, 1/10 were positive (10%); 4/16 within 2 yrs (25%); and 8/21 within 3 yrs (29.6%).
Of patients with positive DECT scans, 24/42 (57%) had symmetric distribution of MSU crystal deposition: 10/24 (42%) hands and 14/24 (58%) feet; with gout duration of 7.9 (SD, 8.0) yrs.
Conclusion: DECT was infrequently utilized and only by rheumatologists. Only 60 % of patients referred for DECT scanning because of known or suspected gout had MSU deposition. DECT was uncommonly positive in patients with a 1-3 yr history of gout. When positive, the MSU crystal deposition was symmetrical in most gout patients. DECT scans, while important in furthering our understanding of gout biology, are not routinely used in general practice and often do not provide important decision support information. Establishment of practice guidelines might be important in developing more appropriate utilization of DECT.
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AB0935 HYDROLYSIS OF INORGANIC PYROPHOSPHATE IN HUMAN SYNOVIAL FLUID BY IMMOBILIZED PYROPHOSPHATASES

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Background: Calcium pyrophosphate deposition (CPPD) disease, alternatively known as pseudogout, is a type of arthropathy caused by a deposition of microcrystals of calcium pyrophosphate (CaPPi) in joint tissues, particularly in fibrocartilage and hyaline cartilage. Up to date, specific treatment of CPPD disease has not been developed. Conventional therapy is focused on anti-inflammatory and immunosuppressive treatment aimed at the prevention of acute symptoms. Previously we suggested for this purpose inorganic pyrophosphatases (PPases) immobilized on nanodiamonds of detonation synthesis (NDs) [1]. We synthesized and characterized conjugates of NDs with PPases from *Escherichia coli* and *Mycobacterium tuberculosis* (Ec-PPase or Mt-PPase) using amino-substituted NDs with (ND-L) or without linker (ND-NH_2). The conjugates showed high enzymatic activity in the *in vitro* model system simulating the ionic composition of synovial fluid
Objectives: The present work is focused on testing enzyme-based agents for the partial dissolution of calcium pyrophosphate deposits in the synovial fluid of patients with CPPD disease.
Methods: PPase activity of soluble and immobilized PPases was evaluated as the rate of PPi decrease with time. 1 mM PP_i was added to the synovial fluid of patients with CPPD containing the samples of PPases, and the amount of PP_i in the samples was determined every 2-4 hours using ^{31}P NMR spectroscopy.
Results: We demonstrated the possibility of differential detection of pyrophosphate (PP_i) among the spectrum of phosphorus-containing compounds in the synovial fluid and used the rate of decrease of exogenous PP_i to estimate hydrolytic activity of PPases and PPase-based conjugates. The hydrolysis followed the first order reaction kinetics and the rate constants by different samples of PPases are presented in Table 1. Non-enzymatic hydrolysis of exogenous PP_i was quite moderate or not observed at all. Ec-PPase (both soluble and immobilized) showed very low hydrolytic activity with the residual PP_i levels above 80%. However, all samples of Mt-PPase showed significant hydrolytic activity. In two cases of three, PP_i was almost completely hydrolyzed within 20 hours. The maximum activity (2.24 U•mg^{-1}) was shown by Mt-PPase immobilized on ND-L. Hydrolytic activity for all studied enzymes is only 1-2% of such values under optimal *in vitro* conditions, most probably due to the inhibiting effect of calcium in synovial fluid. Nevertheless, the activity of Mt-PPase-based samples was comparable with the values typical for some classes of hydrolases. It allows us to consider the suggested PPase-based materials as promising agents for the hydrolysis of PP_i in the joint tissues *in vivo*.

Table 1. PP_i hydrolysis in the synovial fluid by soluble or immobilized PPases.

Samples		*k*, hr^{-1}	*A*, U·mg^{-1}
Control	-	0.010 ± 0.001	0
	ND-NH_2	0	0
	ND-L	0.013 ± 0.002	0
Ec-PPase	Soluble	0.025 ± 0.003	0.33 ± 0.04
	Immobilized on ND-NH_2	0	0
	Immobilized on ND-L	0.017 ± 0.003	0.22 ± 0.04
Mt-PPase	Soluble	0.10 ± 0.01	1.3 ± 0.1
	Immobilized on ND-NH_2	0.04 ± 0.01	0.53 ± 0.05
	Immobilized on ND-L	0.17 ± 0.02	2.2 ± 0.3

Conclusion: In this work, we applied the ^{31}P NMR spectroscopy to estimate the quantity of P_i and PP_i in synovial fluids of patients with CPPD disease. The conjugates of bacterial PPases with detonation nanodiamond were demonstrated to retain enzymatic activity in the hydrolysis of exogenous PP_i in human synovial fluid. These results provide the basis for the further tests of PPase-based conjugates on animal models *in vivo*.
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AB0936 CLINICAL STUDY ON PERIPHERAL BLOOD IMMUNE FUNCTION IN PATIENTS WITH GOUTY ARTHRITIS

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Background: Gout is an inflammatory disease characterized by hyperuricemia and recurrent arthritis. In severe cases, joint disability and renal insufficiency may occur [1]. In recent years, many studies have found that immune dysfunction plays an important role in the occurrence and development of gout [2]. Therefore,

in-depth study of its internal mechanism is of great significance for the prevention and treatment of gout.

Objectives: This paper mainly discussed the expression of peripheral blood immune function in patients with gouty arthritis and the changes and significance of peripheral blood immune function in gout with different uric acid levels.

Methods: A retrospective analysis was performed on 258 outpatients and inpatients with gout in shanxi medical university from 2016 to 2019, all of which met the diagnostic criteria of the American college of rheumatology (ACR) in 1997, and 41 healthy controls. Complete clinical data and general laboratory data were collected, and peripheral blood lymphocyte and CD4+T cell counts were completed for all subjects.

Results: (1) Total peripheral blood B cells of gout patients [238.00 (171.50,323.07) and 191.04 (149.66,253.14), Z=-2.759, P=0.006], Th cells [814.11 (617.50,1052.89) and 625.84 (562.52,750.15), Z=-3.905, P<0.001], Th/Ts [1.4 (1.04,2.00) and 1.11 (0.89,1.52), Z=-2.862,Th17/Treg [0.36 (0.20,0.60) and 0.24 (0.14,0.34), Z=-3.949, P=0.000] and the absolute counts of Th17 cells [9.06 (5.07,15.57) and 7.48 (4.31,10.18), Z=-2.520, P=0.012] were higher than those of the healthy control group, and the differences were statistically significant. The absolute count of Treg cells [28.82 (17.48,38.04) and 30.22 (22.74,39.46), Z=-2.249, P=0.025] was lower than that of the healthy control group, and the difference was statistically significant. (2) The Th17% [1.05 (0.71,1.42) and 1.27 (0.73,2.00), Z=-1.995, P=0.046] and the Th17/Treg [0.25 (0.14,0.44) and 0.39 (0.23,0.63), Z=-3.147, P=0.002] in peripheral blood of patients with high uric acid in the gout group were higher than those in the normal uric acid group, the difference was statistically significant. The Treg % [3.84 (2.65,5.02) and 3.12 (2.36,4.37), Z=-2.239, P=0.025], and the Treg cells [30.75 (21.97,43.27) and 24.07 (16.84,36.29), Z=-2.522, P=0.012] were lower than those in the uric acid control group, with statistically significant differences.

Conclusion: The level of Th17 cells in peripheral blood of patients with gout increased significantly while the level of regulatory T cells decreased significantly. Th17 cell level in peripheral blood of the high uric acid group was significantly increased compared with the normal uric acid group, while the regulatory T cell level was also significantly decreased, and the Th17/Treg ratio was also increased. This suggests that regulatory T cells may play an important role in the pathogenesis of gout and are closely related to uric acid metabolism, so the study of internal mechanism can provide a new target for the treatment of gout.

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Infection-related rheumatic diseases

AB0937 COMPARATIVE STUDY OF PYOGENIC SPONDYLODISCITIS VERSUS TUBERCULOUS SPONDYLODISCITIS

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Background: Infectious spondylodiscitis is a life-threatening infection of the intervertebral disc and adjacent vertebrae that can be caused by a variety of microorganisms. Our country is at intermediate endemicity for Tuberculosis.

Objectives: To compare the clinical, biological, radiological characteristics, management and prognosis of pyogenic versus tuberculous spondylodiscitis.

Methods: Retrospective study of 89 patients admitted to our department over a period of 20 years [1998-2018]. The diagnosis of spondylodiscitis was made based on clinical, biological, radiological and bacteriological data.

Results: The average age of the patients was 56.1 years. There were 46 men (51.6%) and 43 women (48.4%) with a female predominance during tuberculous spondylodiscitis (57.1%) versus 26.9% during pyogenic spondylodiscitis (p = 0.009).

Diabetes was more frequent during pyogenic spondylodiscitis but with no statistically significant difference (p = 0.4). The evolution time was statistically greater during tuberculous spondylodiscitis (p <0.001). Patients with tuberculous spondylodiscitis had more frequently an impaired general condition (p = 0.02).

Hyperleukocytosis was noted more frequently in the pyogenic group than in the tuberculosis group (p=0.03), while the increase in sedimentation rate was not significantly different between the two groups (90 mm/h and 76 mm/h, respectively, p=0.1). We found no statistically significant difference regarding the site of spondylodiscitis.

Radiologically, the frequency of para-vertebral and psoas abscesses, epiduritis and the presence of spinal cord compression were similar in the two groups (p=0.2; p=0.1 and p=0.1, respectively), whereas mirrored geodes were more frequent during tuberculosis (p = 0.04).

Surgical and interventional treatments (percutaneous sampling, abscess drainage) were more frequently noted during pyogenic spondylodiscitis, but without significant difference (p=0.2). The occurrence of immediate complications was more frequent during tuberculosis but without a statistically significant difference (p=0.2).

Conclusion: In our series, patients with tuberculous spondylodiscitis tend to have a chronic pattern of progression and more often an impaired general condition. However, there was no significant difference in the presence of abscess, epiduritis and the occurrence of complications between tuberculous spondylodiscitis and pyogenic spondylodiscitis.

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AB0938 PARTICULARITIES OF INFECTIOUS SPONDYLODISCITIS IN THE ELDERLY: COMPARATIVE STUDY WITH THE YOUNG SUBJECT

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Background: The incidence of infectious spondylodiscitis is steadily increasing. The prognosis depends on various parameters, including age.

Objectives: To explore the differences in presentation and the results of further investigations and the prognosis of spondylodiscitis between young and elderly subjects.

Methods: This is a retrospective study of 113 patients admitted to our department over a period of 20 years [1998-2018]. The epidemiological, clinical, biological, radiological and progressive aspects of spondylodiscitis in subjects over the age of 65 were compared to cases of spondylodiscitis in young subjects whose age is less than 65 years.

Results: Of the 113 identified patients, 33 (29.2%) were classified as older, with male predominance in both groups (56.2 and 51.5% respectively; p=0.6). The presence of risk factors, particularly diabetes, was more frequent in the older subjects but without a statistically significant difference (p=0.2). Hepathopathies were also more frequent in the elderly but without statistically significant difference (p=0.3). The mean duration of progression was 3 months with no statistically significant difference between the two groups (4 and 5 months respectively, p=0.1).

The presence of neurological symptoms, especially radiculalgia, was more frequently reported in younger subjects (p=0.01). Also, young subjects were more likely to have a fever (p=0.005). On the other hand, a biological inflammatory syndrome was more frequently encountered in older subjects (p=0.03).

We found no statistically significant difference in the location of spondylodiscitis (p=0.4). Also, multifocal involvement was more frequent in older subjects but without a statistically significant difference.

Radiologically, para-vertebral abscesses, epiduritis and spinal cord compression were more common in the elderly group (p=0.03; p=0.01 and p=0.01, respectively). While the frequency of intervertebral pinching and erosions was similar in both groups (p=0.1; p=0.8, respectively).

Tuberculosis was the most involved germ in more than 50% of cases with no statistically significant difference between the two groups (57.5 and 51.5% respectively; p=0.5).

All patients received targeted antibiotic therapy.

The occurrence of immediate complications was more frequent in the elderly but without a statistically significant difference (p=0.1). They included neurological complications (spinal cord compression and Cauda equina s*yndrome*) that occurred in 6.3% of cases in younger subjects versus 36.4% of cases in the elderly (p=0.07). Followed by treatment side effects dominated by disturbance of liver function due mainly to antituberculosis drugs occurring in 16.3% of cases in the younger group and 15.2% of cases in older subjects (p=0.8). Finally, there were 2 deaths in each group (p=0.5).

Conclusion: Our series has shown that the picture of spondylodiscitis in the elderly is less noisy. However, the neurological damage is more pronounced on imaging. The misleading symptomatology in the elderly explains the delay in diagnosis and treatment, which leads to more frequent complications and excess mortality.

Disclosure of Interests: None declared

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AB0939

POLYMYALGIA RHEUMATICA FOLLOWING INFECTIVE TRIGGERS OR VACCINATIONS: A DIFFERENT SUBSET OF DISEASE?

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Background: Polymyalgia rheumatica (PMR) is the most common inflammatory disorder of elderly; an association with environmental triggers and deregulated immune response has been described.
Objectives: The aim of this study was to investigate the presence of environmental triggers before the onset of PMR and its association to a particular subset of disease.
Methods: The database of 58 consecutive PMR patients recruited from a single rheumatology secondary care setting was retrospectively analyzed to investigate the frequency of environmental triggers and correlations with clinical characteristics. Patients underwent multidistrict ultrasound examination of both proximal and distal sites. Laboratory tests were repeated after one month from first visit, when steroids were started, and about every three months during follow-up (for at least 24 months)
Results: Fifteen PMR patients (26%) described a connection with environmental agents: six PMR patients reported a vaccination, 3 an upper respiratory tract infection and 1 pneumonia before the onset of disease. Five patients reported seasonal influenza as trigger of PMR. The model of multivariate linear regression which better predicted a shorter time to normalize inflammatory reactants (R squared 27,46%, p=0,0042) comprised the presence of an environmental trigger and a higher CRP. A linear regression analysis confirmed an inverse correlation between CRP at onset ant time to normalize inflammatory reactant (r= -0,3031, p=0,0208). A significant correlation was demonstrated between presence of environmental trigger and shorter time to normalize inflammation (r=-0,5215, p<0,0001), lesser frequency of gleno-humeral synovitis on US (r=-0,3774, p=0,0038).
Conclusion: Our work describes a correlation between environmental triggers in PMR and higher CRP at diagnosis and faster response to therapy. We may suppose that these patients belong to a more specific subtype of PMR, in whom external stimuli, such as vaccinations or infections, may lead to a deregulated response within the context of an impaired immune and endocrine system. We recommend a systematic research of previous infections or vaccination in recent onset PMR
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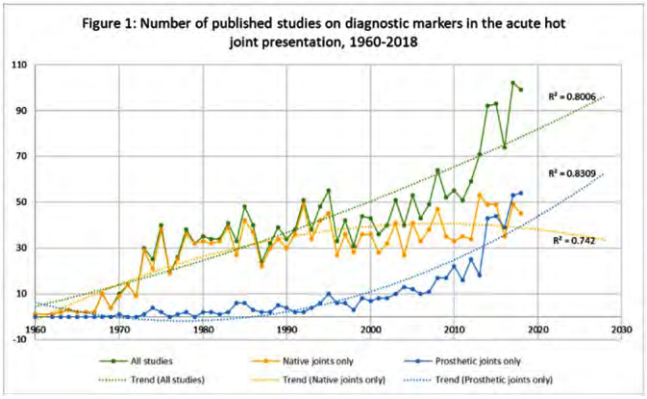
AB0940

BIOMARKERS IN THE DIAGNOSIS OF ACUTE HOT JOINTS: AN EVALUATION OF RESEARCH INTEREST 1960-2018

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Background: The acute hot joint presentation is a common clinical emergency, often the result of crystal arthritis or trauma. However, all diagnoses can mimic septic arthritis, which should be excluded promptly due to the potential for rapid joint destruction and significant morbidity. The gold-standard test for septic arthritis is synovial fluid culture, which can take several days to perform. Meanwhile, patients are often admitted and given antimicrobials. Other specialties have made use of rapid biomarkers to exclude infection, for example, exclusion of empyema using pleural fluid pH and glucose [1]. Such biomarkers could reduce the need for lengthy hospital admissions and inappropriate antibiotic use in the acute hot joint presentation.
Objectives:
1. Evaluate research interest over time, on the use of diagnostic biomarkers in the acute hot joint presentation.
2. Compare research interest in the use of diagnostic biomarkers in acute hot native versus acute hot prosthetic joints.

Methods: We performed a review of the number of publications reporting the use and diagnostic accuracy of biomarkers to exclude infection in the acute hot joint presentations. The database, *Scopus*, was searched for English-language studies (1946-2018) using search terms relating to septic arthritis, crystal arthritis, and diagnostic markers derived from synovial fluid/aspirate. The number of papers published per year on prosthetic joints only was also calculated. Therefore, the following were recorded for each year 1946-2018: total number of studies; prosthetic joints only; native joints only. Values were plotted, with polynomial trend-lines and R^2 calculated.
Results: Our search yielded 2279 relevant studies in total (561 on prosthetic joints), published 1946-2018. Only 1 study was identified for the year 1946; the next recorded publication was in 1960. Therefore, this single study was excluded as an outlier. Results are presented in Figure 1. The number of studies on diagnostic biomarkers for acute hot joints continued to increase after 1960. From 2016, the number of studies conducted in prosthetic joints outnumbered those done in native joints. Polynomial trend-lines applied to the results showed studies on native acute hot joints are predicted to decline, while those in prosthetic joints will continue to increase.
Conclusion: Reasons for an increasing number of studies on prosthetic compared to native acute hot joints include a narrower differential diagnosis in prosthetic joints, i.e. septic vs aseptic. In contrast, native acute hot joints may be the result of various causes including crystal arthritis, inflammatory arthritis, and trauma. Having a narrower differential diagnosis may facilitate diagnostic research in prosthetic joint presentations. Furthermore, incidence of prosthetic joint infection is also greater than that of native joint infection [2]. Nonetheless, the incidence of native joint infection is increasing [3]. This, and the lack of methods by which to rapidly distinguish native joint septic arthritis from non-infective causes, indicates that more research is required in this area.
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AB0941

NEURALGIC AMYOTROPHY AND HEPATITIS E INFECTION: REPORT OF 6 CASES AND REVIEW OF THE LITERATURE

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Background: Neuralgic amyotrophy (NA) or Parsonage and Turner syndrome is triggered at least in 25% by a viral infection: parvovirus B19, CMV, HSV, etc... Recently, few cases of Hepatitis E Virus (HEV) related NA were reported. This particular association remains little known and is overlooked by most physicians. Besides, clinical, electrodiagnostic (EDX) and MRI characteristics, as well as evolution of HEV-related NA have not been fully described yet.
Objectives: To describe 6 cases of HEV-related NA and to perform a review of the literature.
Methods: We describe longitudinally clinical examination, electrodiagnostic (EDX), biological and MRI results of 6 cases of HEV-associated NA, diagnosed in our center.
Results: The 6 cases were aged between 33 and 57 years old (mean 44.5), sex ratio was 5M/1F. All patients had positive IgM anti-HEV (serology) and a cervical MRI that could not explain clinical presentation. Overall, the 6 patients totalize 26 mononeuropathies (range 1 to 8 per patient), 5/6 patients had a severe presentation of NA, with bilateral and asymmetric symptoms (3 cases). HEV-related NA involved classical nerves such as supra-scapular (6 cases, twice bilaterally) and long thoracic nerves (5 cases), some less classical nerves like anterior

interosseous nerve (3 cases, twice bilaterally), and some very unusual ones such as the lateral antebrachial cutaneous nerve (1 case) and the sensory fibers of median nerve (1 case). NA also involved accessory spinal (2 cases, once bilaterally) and phrenic nerves (1 case bilaterally), both originating from cervical plexus. The EDX pattern of these nerve lesions consisted of unique or multiple extensive asymmetric inflammatory mononeuropathies with severe axonal loss and numerous denervation signs damage involving mostly the supra-scapular. On scapular MRI (available for 5/6 patients), amyotrophy in at least one muscle was observed in all patients. Out of 26 nerves involved, after 12 months all had well recovered (above 3/5 MRC scale).

Conclusion: HEV should be systematically screened when NA is suspected, whatever the severity, if the onset is less than 3 or 4 months (before IgMs anti-HEV disappear). HEV-related NA appears to be frequently associated with a severe pattern, without modifying the recovery usually observed.

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AB0942 INFECTIOUS SPONDYLODISCITIS: TUBERCULOSIS VERSUS BRUCELLOSIS

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Background: Infectious spondylodiscitis is a serious impairment that can compromise the functional and vital prognosis. The determination of the germ responsible is the key of the treatment.

Objectives: The objective of our work is to describe the epidemiological, clinical and evolutionary profile according to the germ responsible by comparing tuberculous and brucellar spondylodiscitis.

Methods: This is a retrospective study including 32 cases of spondylodiscitis with specific germs (Mycobacterium tuberculosis and Brucella) collected in an internal medicine department over a period of 18 years (2000-2018).

Results: These were 20 men and 12 women with an M / F ratio of 1.66. The average age of our patients was 50.63 [16-84]. The germ implicated was Koch's Bacillus in 11 patients (34.38%) and Brucella in 21 patients (65.63%). The mean age for tuberculosis (TB) was 45.18 years versus 53.48 years for brucellosis. Spinal pain was the major symptom in the 02 groups. The deterioration in general condition was present in 80.95% for the brucellosis group versus 81.82% for the tuberculosis group.

Biological inflammatory syndrome was observed in 94.24% of the brucellosis group and 63.63% of the TBC group. The lumbar location was the most frequent in the 02 groups (71.88%).It was a multifocal localization in 27.27% (TB) and 61.90% (Brucellosis) respectively. The imaging allowed the detection of para abscesses -vertebral in 54.55% for the TB group versus 23.81% for the brucellar group. An epiduritis was objectified in 36.36% of the TB group against 33.33% for that of brucellar. CT-guided biopsy was performed in 54.55% of tuberculosis patients compared to 47.62% in the other group. It was only positive in one case of brucellosis, whereas it allowed diagnosis in 36.36% of cases of TB.

The evolution after initiation of adequate antibiotic treatment was interspersed with neurological complications in the tuberculosis group in 18.18% of cases against 14.29% in the brucellosis group. Draining abscess was necessary in the tuberculosis group in 18.18% and in 9.52% of the brucellosis cases.

Conclusion: Our results show a higher frequency of neurological complications in tuberculosis forms. Vertebral biopsy is of no interest in Brucellar spondylodiscitis unlike tuberculosis forms where it allows the diagnosis.

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AB0943 INFECTIOUS SPONDYLODISCITIS OF THE ELDERLY: CHARACTERISTICS AND OUTCOMES

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Background: Spondylodiscitis still frequent. It affects both old and young patients. It makes diagnostic and therapeutic difficulties.

Objectives: to identify the characteristics and outcomes of infectious spondylodiscitis (ISD) in patients over 65 years old.

Methods: A monocentric retrospective study including patients hospitalized for ISD in the rheumatology department of university hospital of Monastir,TUNISIA between January 2009 and August 2019.

Results: Among 70 patients with ISD, 21 (11 male, 10 female) or 30% are over 65 years old. The average age was 70.6 years (65-82 years). History of diabetes (n = 9), hypertension (n = 9), hemodialysis (n = 5), heart disease (n = 5) were the most risk factors reported, while in younger patients, spinal surgery, epidural infiltrations and long-term general corticosteroid therapy were the main risk factors. The mean time for consultation was 142.3± 73 days longer than for younger patients. Fever was present in 0,14% of cases. Assessment time found that already 5 patients had paraplegia or spinal cord compression. 19/21 patients had epiduritis on spinal cord MRI. Soft tissue abscesses were present in close rate in both younger and old patients. Biological assessment showed an inflammatory syndrome and hyperleukocytosis in 92% and 38% of patients respectively (compared to 73% and 27% in younger patients). Germs ware identified in 14 patients (47.3%). Common germs were the most involved (12 patients), while in younger patients, specific- germs were the most reported. Follow up has shown that neurological sequelae are more prevalent in elderly.

Conclusion: ISD in patients over 65 years old require a careful attension in therapeutic management given that age according to this study seems to influence the prognosis. In fact, these patients are more susceptible to disability due to neurological complications.

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AB0944 TUBERCULOUS SEPTIC ARTHRITIS: CLINICAL FEATURES OF TWELVE CASES

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Background: Extrapulmonary forms of tuberculous septic arthritis account only for 1% of tuberculous infections. Although TB infection is rare in western countries, arthropathy is still a common problem in developing countries.

Objectives: Describe clinical features of tuberculous septic arthritis seen by the rheumatologist.

Methods: Retrospective descriptive study, lead in the rheumatology department of Farhat Hached Hospital, including medical files between 1999 and 2020. Data of patients diagnosed with tuberculous arthropathy were analysed.

Results: Twelve patients were diagnosed with tuberculous septic arthritis. Six men and women were enrolled with a sex ratio of 1. The mean age of diagnosis was 47.5±16.16 years. Mean delay of diagnosis was 12.83±15.12 months. A triggering factor like a trauma was described in 8.3% and comorbidities were associated in 16.7% of the cases, mainly diabetes and chronic renal dysfonction. Type of pain was inflammatory in 91.7% of the time. The disease presented as a monoarthritis in 91.7% and an oligoarthritis in 8.3% of the cases. Chronic forms were observed in 91.7% and acute forms in 8.3% of the cases. Transmission was hematological in 60%, directly inoculated in 20% and secondarily disseminated from another site in 20% of the cases. Arthritis affected the knees in 50%, followed by the hips in 33.3% and then the ankles and wrist in 8.3% of the cases each. Fever was noted in 41.7% and general condition was altered in 50% of the patients. Chest radiographs showed the presence of infiltrates or micronodules in 33.3% of the patients. Bone erosions were detected in 66.7% of plain radiographs, while narrowing of the joint was seen in 83.3% and and juxta articular osteoporosis in 50% of the cases. MRI showed the presence of abces in 33% of the cases. The Mantoux test was positive in 2 cases, of which, one didn't receive the recommended neonatal vaccine. Culture was positive in the synovial fluid in 25%, in sputum in 16.7%, and in urine in 8.3% of the cases. Synovial biopsy was performed for all patients. It showed a non specific synovial inflammation in 50%, granulomatous inflammation in 33.3% and caseous necrosis in 16.7% of the cases. Common quadri therapy was prescribed for all patients with a mean treatment duration of 11.41±1.37 months. Surgery was performed in only two

cases with an uncontrolled infection under antibiotics. Disseminated tuberculosis accured in 33.3%, recurrence of the infection in the same site in 16.7% and extension to another articular localisation in 25% of the cases. One patient had a tuberculous meningoencephalitis leading to his death.

Conclusion: Tuberculous septic arthritis is difficult to diagnose and should be recalled especially in endemic countries when dealing with chronic monoarthritis. Synovial biopsy is needed most of the time to confirm the diagnosis. Treatment is long and the disease may be complicated with fatal disseminated forms.

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AB0945 **CONTRIBUTION OF MICROBIOLOGICAL AND ANATOMOPATHOLOGICAL EXAMINATIONS IN THE DIAGNOSIS OF SPONTANEOUS PYOGENIC SPONDYLODISCITIS IN ADULTS**

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Background: Pyogenic spondylodiscitis (SPD) is a serious infection of an intervertebral disc and/or adjacent vertebrae, that remains a topical problem in rheumatological practice. Early diagnosis and treatment are the only guarantees of a favorable outcome. Clinicians must strive to isolate the responsible bacteria in order to adapt the treatment, and thus reduce the risk of resistance and complications due to SPD itself, but also to the multiplication of probabilistic treatments.

Objectives: Our aim was to study the contribution of the different microbiological and anatomopathological examinations in the diagnosis of pyogenic SPD.

Methods: It was a descriptive study in a single rheumatology department. Data were collected retrospectively from observations of patients hospitalized in the past 20 years who have been diagnosed with pyogenic SPD. We excluded cases of tuberculous and brucellar SPD from our study because of their completely different histological and microbiological profiles.

Results: Twenty-two cases of pyogenic SPD were collected (14M/ 8F). The mean age of the population was 55.9 years [29,80]. A bacteriological survey including at least one cytobacteriological examination of the urine (CBEU), chest X-rays and blood cultures allowed the identification of the bacteria in 16 cases (73%). The most common site were bacteria was identified was blood culture in 7 cases, skin sample and urine collection in 2 cases each. Disco-vertebral puncture and biopsy (DVPB) was performed in 19 patients when there was no bacteria identification and/or when diagnosis of infectious SPD persisted doubtful. On histopathological examination, were described: an infiltrate and/or inflammatory changes without specificity signs in 7 patients and an appearance of chronic pyogenic SPD very likely in 12 patients. Bacteriological study of DVPB fluid or paravertebral abscesses sample helped to isolate bacteria in 4 patients. DVPB or abscesses puncture were contributing by histological and/or bacteriological examination in 12 patients (63%).

Infecting bacteria was identified in 14 patients (64%). Gram-negative bacilli (GNB) and staphylococcus aureus were the most frequent germs (7 cases each) including 2 cases of co-infection. GNBs were represented by: Escherichia Coli and Enterobacter Cloacae in 2 cases each, Proteus Mirabilis, Serratia Marcescens and Klebsiella oxytoca in 1 case each. Clostridium clostridioforme and Lactococcus cremoris were isolated in 1 case each. For patients whose etiological investigation remained negative, SPD diagnosis was retained based on imaging (MRI) guided by anamnestic, clinico-biological and histopathological arguments.

Conclusion: SPD is a rare condition that needs to be treated rapidly. Once the diagnosis is suspected, bacteria must be isolated before starting any antibiotic therapy. Simple and non-invasive exams as blood cultures, CBUE and chest rays, should be undertaken first. In fact, these simple exams allowed a germ identification in 73% cases in our study. If doubt persist, DVPB could be contributive to the diagnosis.

References: None

Disclosure of Interests: None declared

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AB0946 **PARTICULARITY OF MULTIFOCAL INFECTIOUS SPONDYLODISCITIS**

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Background: Infectious spondylodiscitis is an infection of the intervertebral disc with damage to the vertebrae. Multiple stage involvement may lead to serious complications. Better understand of this infection is mandatory for optimal management.

Objectives: The objective of our study was to describe the clinical, biological aspects and the course of this disease.

Methods: This is a retrospective study including cases of infectious spondylodiscitis collected in a single rheumatology center between 2002 and 2018. Multi focal spondylodiscitis was defined as an attainment of 2 or more disc levels. Clinical, biological and evolution of this disease were reported.

Results: Among the 52 cases of infectious spondylodiscitis collected, thirteen patients had multi-stage involvement of the spine. The sex ratio M/F in this group = 0.44 with an average age of 52 ± 14.32 years [31 – 76 years]. Diabetes mellitus was observed in 3 patients, chronic renal failure in one case and immunosuppressive therapy in one case. At the moment of the diagnosis, inflammatory back pain was present in all patients, fever was noted in 8 patients (61.5%), neurological deficit in 2 patients (15.4%) and weight loss in 4 cases (30.8%). The diagnosis time delay was 22 ± 15.9 weeks [2 – 60 weeks]. The mean CRP was 70.16 mg / L ± 55.5 [3.4 - 178] and the ESR was on average 79 mm ± 31.28 [6 - 125]. Diagnosis was confirmed by MRI in all cases. A prevertebral abscess was observed in 7 cases (%), an epiduritis in 5 patients (38.5%) and a psoas abscess in two cases (15.2%). The cervical spine was affected in 3 cases, the dorsal spine as well as the lumbar spine were affected in 12 cases. The involvment of 2 vertebral sites was the most frequent with 7 cases. A maximum of 5 site was noted in 3 cases. The thoracolumbar spine was the most affected with 11 cases (84.6%), the cervico-thoraco-lumbar involvement was found in only one case (7.7%). The bacteriological diagnosis was done by the disco-vertebral biopsy in 6 cases (46.2%), the brucellar serology in 3 cases (26.1%) and a strong presumption of tuberculosis (with positive IDR or Quantiferon) in 4 cases (30.8%). Mycobaterium tuberculosis was isolated in 8 patients (61.5%), brucella melitensis in 3 patients (23.1%) and staphylococcus aureus was found in 2 cases (15.4%). The outcome was favorable in all patients with appropriate antibiotic therapy after an average follow-up of 10.9 months ± 2.19.

Conclusion: Multifocal infectious spondylodiscitis is a serious disorder which mainly affects immunocompromised patients and the specific germs are the most incriminated.

Disclosure of Interests: None declared

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Pain in rheumatic diseases, including fibromyalgia

AB0947 **RECIPROCAL IMPACT OF FIBROMYALGIA ON DISEASE CHARACTERISTICS AND PHYSICAL AND PSYCOLOGICAL DOMAINS IN SJOGREN SYNDROME: CROSS SECTIONAL OBSERVATIONAL STUDY.**

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Background: Sjogren Syndrome (SS) is an autoimmune exocrinopathy, resulting mainly in ocular and oral dryness, with approximately half of patients displaying symptoms from different organ systems, further adding to the heterogeneous clinical phenotype of the disease. Fatigue and pain are common systemic symptoms in patients with primary SS and fibromyalgia is a frequent condition associated with chronic diseases.

Objectives: The aim of the study was to evaluate the impact of concomitant fibromyalgia in patients with Sjogren Syndrome in terms of clinical features and disease activity.

Methods: 50 patients with Sjogren Syndrome were enrolled in the study (100% female, age: 53.7 ± 13.2 years and disease duration: 8.7 ± 5.3 years), 25(50.0%) with concomitant fibromyalgia (SS/Fibro-group) and 25(50.0%) without (SS-group). 36 patients with primary fibromyalgia (Fibro-group) were included as control group. At study entry, demographic, educational, life-style and clinical parameters were recorded for each patient. SS was diagnosed according to the American College of Rheumatology (ACR) classification criteria (1) and fibromyalgia was diagnosed according to criteria for fibromyalgia defined by ACR (2). Moreover, each patient with fibromyalgia, with and without concomitant SS, was asked to fill a self-reported questionnaire to assess the impact of Fibromyalgia on multiple physical and psycological domains (Italian-FIQR).

Results: Stratifying the study cohorts based on the demographic and life-style characteristics, no significant differences were found comparing SS-group, Fibro-group and SS/Fibro-group. However, considering the different organ involvement,

SS/Fibro-group were more likely reporting arthralgia symptoms (100.0%) than SS-group (76.0% p=0.02), despite similar clinical evidence of arthritis-synovitis among the two groups (12.0% in both groups respectively, p=1.00). Moreover, SS/Fibro-group showed significantly lower ESSDAI score (2.8 ± 1.7) and higher ESSPRI score (7.0 ± 0.9) compared to SS-group (ESSDAI: 7.5 ± 3.7 p<0.001 and ESSPRI: 5.2 ± 1.4, p<0.001 respectively). Finally, analyzing the differential distribution of individual scores of physical and psycological domains of the Italian-FIQR Questionnaire, SS/Fibro-group did not differ compared to Fibro-group (p>0.05 for all the 21 questions included).

Conclusion: SS is affected by concomitant fibromyalgia in terms of subjective-dependent parameters (i.e. joint complaints) however the concomitant SS does not affect the impact of fibromyalgia on physical and psycological domains, even if disease activity is higher in SS patients without fibromyalgia.

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AB0948 TIME TO CONSIDER HYPERMOBILITY AS A CAUSE OF SYMPTOMS IN PATIENTS PRESENTING TO EARLY ARTHRITIS CLINICS: A RETROSPECTIVE ANALYSIS OF 279 PATIENTS

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Background: Joint hypermobility is a common, although largely ignored physical sign. It is often asymptomatic but can be associated with significant musculoskeletal symptoms. Joint hypermobility may also be a feature of an underlying genetic disorder and patients may present with arthralgia, recurrent soft tissue injuries and intermittent joint swelling due to mechanical instability and poor proprioception. At University College London Hospital, we run a national service for the diagnosis and management of patients with hypermobility related disorders including hypermobility spectrum disorders, Ehlers-Danlos syndromes and Marfan syndrome. Over the years we observed that a significant number of our patients had been referred to the early arthritis clinics years prior to the recognition of their hypermobility. For example, one patient with a vascular type of Ehlers-Danlos syndrome EDS (confirmed COL3A mutation) presented to 3 different hospitals over a 5-year period, with possible inflammatory arthritis prior to the EDS diagnosis. Several studies have shown that a significant proportion of patients attending early arthritis clinics do not have inflammatory rheumatic diseases. In our experience, heritable disorders of connective tissue and hypermobility spectrum disorders are often overlooked and should be included in the differential diagnosis in patients seen in the early arthritis clinics.

Objectives: We aimed to audit the outcome of patients who were seen in the early arthritis clinics focusing on those who were not found to have inflammatory rheumatic diseases and to explore if joint hypermobility was considered as a possible cause of patient's symptoms.

Methods: A retrospective analysis of medical records was conducted of patients attending the early arthritis clinics at University College London Hospital between May 2018 and December 2019.

Results: 279 patients (90 males, 189 females) were seen in the early arthritis clinics with a mean age of 48 (range 19-91). 131 patients (47%) did not have inflammatory rheumatic diseases. Sixty-three of these patients (48%) were not given any diagnosis and joint hypermobility was not assessed during the appointment. Eleven patients (8%) had features of hypermobility, 11 patients (8%) were diagnosed with fibromyalgia, 20 patients (15%) received a diagnosis of osteoarthritis, and 27 patients (21%) were given other diagnoses including tendonitis and soft tissue pathology.

Conclusion: Almost 50 % of patients who were seen in the early arthritis clinics did not have inflammatory rheumatic diseases and 21 % of patients were discharged without a clear diagnosis. In these patients, hypermobility was not assessed and this is consistent with our observation. In our experience recognising joint hypermobility as a cause of arthralgia and intermittent joint swelling usually reassures patients and motivates them to follow appropriate treatment protocols including physiotherapy and occupational therapy thus allowing a more efficient utilization of early arthritis clinic resources towards those with true inflammatory rheumatic diseases. Going forward, we have planned to embed a cognisant attitude towards hypermobility within the relevant clinics to ensure that patients who do not have inflammatory arthritis are assessed for hypermobility and directed towards appropriate management.

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AB0949 AUTONOMIC AND INFLAMMATORY MECHANISMS OF PAIN AND FATIGUE IN FIBROMYALGIA AND ME/CFS: AN INTERVENTIONAL STUDY

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Background: Fibromyalgia and ME/CFS are complex disorders with overlapping symptoms; the pathoaetiology and clinical distinction are debated, however inflammatory and autonomic abnormalities are observed.

Objectives: To investigate the role of inflammatory and autonomic nervous system responses in mechanisms of pain and fatigue in fibromyalgia and ME/CFS

Methods: 63 patient participants with clinical diagnoses of fibromyalgia and/or ME/CFS were recruited into a multi-stage interventional study (ISRCTN78820481) alongside 24 healthy controls. All underwent research diagnostic criteria evaluation. The majority underwent autonomic challenge (60 degree head up tilt) and/or inflammatory challenge (placebo-controlled typhoid vaccination) with baseline characterisation of symptoms, inflammatory markers and pre-post measures of pain and fatigue.

Results: Of the 63 patients, 32% of patients had received a clinical diagnosis of Fibromyalgia; 38% ME/CFS and 30% dual diagnoses. Following research evaluation 89% met ACR diagnostic criteria for fibromyalgia; 94% Canadian Criteria for ME/CFS; 97% Fukada Criteria for ME/CFS

There was a significantly higher ESR in patients compared to controls (p= 0.036). There was a trend towards higher CRP in patients compared to controls (p= 0.076). ESR correlated with baseline pain score (r=0.309, p=0.011), fatigue severity (r=0.262, p=0.032), fatigue impact (r=0.382, p=0.014) change in fatigue score induced by tilt (r=0.319, p=0.011) and change in pain score induced by placebo-controlled inflammation (r=-0.279, p=0.043). Similarly CRP level correlated with baseline pain score (r=0.340, p=0.005), fatigue impact (r=0.439, p=0.004), change in fatigue (r=-0.277, p=0.045) and pain score (r=-0.394, p=0.014) induced by placebo-controlled inflammation and change in pressure pain theshold induced by tilt (r=0.286, p=0.027).

Baseline IL6 was higher in patients than controls (p = 0.002), correlating with baseline pain score (r = 0.345, p = 0.002) and change in pain score induced by tilt (r=0.281, p=0.21). Change in IL6 induced by inflammatory challenge correlated with inflammation induced fatigue score (r = 0.378, p = 0.01).

Conclusion: Inflammatory and autonomic mechanisms contribute to pain and fatigue in this frequently overlooked patient group, highlighting possibilities for targeted treatments. Such data will be enriched going forward by neuroimaging and transcriptomic insights.

References: n/a

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AB0950 EFFECT OF SELECTIVE SEROTONIN REUPTAKE INHIBITORS AND SEROTONIN NOREPINEPHRINE REUPTAKE INHIBITORS ON BONE MINERAL DENSITY IN EGYPTION PATIENTS WITH PRIMARY FIBROMYALGIA

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Background: Fibromyalgia is characterized by chronic widespread musculoskeletal pain that often co-exists with sleep disturbances, fatigue, cognitive dysfunction, stiffness and tenderness to palpation at specific tender points.Selective serotonin reuptake inhibitors represent a class of commonly used antidepressants. They act by preventing the reuptake of 5-hydroxytryptamine (5-HT) (Serotonin) through the inhibition of the 5-HT transporter (5-HTT) which is located on the presynaptic neuron, thereby increasing levels of 5-HT within the synaptic cleft and modulating neurochemical signaling.Usage of SSRIs was significantly associated with lumbar spine BMD reduction, particularly for old people.
DXA and TBS revealed that usage of SSRIs and SNRI was significantly associated with low BMD (Osteopenia and osteoporosis) specially spine BMD reduction with low TBS (partially degraded and degraded) particularly for old people. Conclusion: the present study provided evidence that usage of SSRIs or SNRI was significantly associated with low BMD (Osteopenia and osteoporosis) specially spine BMD reduction with low TBS (Partially degraded and degraded) particularly for old people and despite low BMD was found in the SRI users; it also found in 1ry fibromyalgia not on SRIs so 1ry fibromyalgia should also be considered as a contributing factor for low BM.
Objectives: This work aim to determine the correlation between selective serotonin reuptake inhibitors (SSRIs) and serotonin norepinephrine reuptake inhibitors (SNRIs) usage and bone mineral density (BMD) and trabecular bone score (TBS) changes in primary Fibromyalgia patient
Methods: The present cross sectional study was conducted on a Hundred (100) Egyptian patients diagnosed as primary fibromyalgia divided according to drug medication into two 2 groups, 50 patients on SSRIs and 50patients on SNRIs, recruited from Rheumatology, Physical Medicine and Rehabilitation departments at AlHussein and Sayed Galal, Al-Azhar University Hospitals. In addition to another 50 age matched the control group subdivided into 25 primary fibromyalgia patients not on those drugs and 25 healthy individuals selected by nurses and medical staff, after an informed consent from all subjects from June 2018 to December 2018..An approval was obtained from the medical ethics committee of Al-Azhar University before starting this study. All the patients were informed about the study procedures and a written consent was obtained from all of them. The subjects were categorized into three groups. Group A: 50 1ry fibromyalgia patients on SSRI. Group B: 50 1ry fibromyalgia patients on SNRI. Group C: 50 individuals as a the control group subdivided into: group C-1: 25, 1ry fibromyalgia patients non SRIs-users and group C-2: 25) healthy individuals.
Results: DXA and TBS revealed that usage of SSRIs and SNRI was significantly associated with low BMD (Osteopenia and osteoporosis) specially spine BMD reduction with low TBS (partially degraded and degraded) particularly for old people. Conclusion: the present study provided evidence that usage of SSRIs or SNRI was significantly associated with low BMD (Osteopenia and osteoporosis) specially spine BMD reduction with low TBS (Partially degraded and degraded) particularly for old people and despite low BMD was found in the SRI users; it also found in 1ry fibromyalgia not on SRIs so 1ry fibromyalgia should also be considered as a contributing factor for low BMD
Conclusion: The present study provided evidence that usage of SSRIs or SNRI was significantly associated with low BMD (Osteopenia and osteoporosis) specially spine BMD reduction with low TBS (Partially degraded and degraded) particularly for old people and despite low BMD was found in the SRI users; it also found in 1ry fibromyalgia not on SRIs so 1ry fibromyalgia should also be considered as a contributing factor for low BMD. Keywords: SSRI, SNRI, FMS, fibromyalgia, osteoporosis, TBS, BMD, bone mineral density, trabecular bone score.
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AB0951 THE ITALIAN FIBROMYALGIA REGISTRY: A NEW WAY OF USING ROUTINE REAL-WORLD DATA CONCERNING PATIENT-REPORTED DISEASE STATUS IN HEALTHCARE RESEARCH AND CLINICAL PRACTICE

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Background: Fibromyalgia (FM), the most frequently encountered cause of widespread musculoskeletal pain, affects an estimated 2% of the general Italian population. However, it is not a homogeneous clinical entity, and a number of interacting factors can influence patient prognosis and the outcomes of standardised treatment programmes. Registries are a source of high-quality data for clinical research, but relating this information to individual patients is technically challenging.
Objectives: The aim of this article is to describe the structure and objectives of the first Italian Fibromyalgia Registry (IFR), a new web-based registry of patients with FM.
Methods: The IFR was developed to collect, store, and share information electronically entered by physicians throughout Italy who are members of the Italian Society of Rheumatology and have a particular interest in FM. It has a web-based architecture that uses two separate servers and an encryption algorithm to ensure the confidentiality and integrity of the exchanged data. The questionnaires included on the platform are the Revised Fibromyalgia Impact Questionnaire (FIQR), the modified Fibromyalgia Assessment Status (ModFAS), and the Polysymptomatic Distress Scale (PDS).
Results: The registry includes data relating to 2,339 patients (93.2% female) who satisfied the 1990 or 2010/2011 American College of Rheumatology Classification Criteria for Fibromyalgia at the time of diagnosis. At the time of this analysis, the patients had a mean age of 51.9 years (SD 11.5) and a mean disease duration of 7.3 years (SD 6.9). The majority were married (71.3%), and generally well educated. The overall median FIQR, ModFAS and PDS scores and 25th-75th percentiles were respectively 61.16 (41.16-77.00), 8.91 (41.16-77.00), and 19.0 (13.00-24.00). The six highest scoring items indicating the greatest impact of the disease on the patients related to fatigue/energy (7.18), sleep quality (6.87), tenderness (6.69), pain (6.68), stiffness (6.66), and environmental sensitivity (6.35). A high proportion of the responding patients reported experiencing pain in the neck (80.46%), upper back (68.36%), and lower back (75.05%).
Conclusion: The IFR is the most comprehensive FM registry in Italy, and provides healthcare professionals with a secure, reliable, and easy-to-use means of monitoring the patients' clinical progression, treatment history and treatment responses. This can help clinicians to plan patient management, facilitates research study patient recruitment, and provides the participating pain clinics with statistics based on real-world data. It also helps address the Italian Ministry of Health long-term goal of using precision medicine for chronic pain prevention and treatment. It is hoped that the IFR will enhance both scientific research and clinical practice.
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AB0952 COENZYME Q10, TRYPTOPHAN AND MAGNESIUM: A NUTRITIONAL SUPPLEMENT IN THE TREATMENT OF FIBROMYALGIA SYMPTOMS

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Background: Fibromyalgia syndrome (FMS) is a multidimensional chronic disorder characterized by widespread musculoskeletal pain, fatigue, sleep disturbances, cognitive dysfunction, depressive episodes, and anxiety [1]. Management of FMS remains challenging and treatment strategies are required to be multidisciplinary. Among nonpharmacological therapies, nutrition is a promising tool, since oxidative stress and/or an imbalance of nutritional components have demonstrated to play a critical role in the pathophysiology of FMS [2,3].
Objectives: We conducted a pilot study (FATMIA Study) to investigate the efficacy and tolerability of a dietary supplementation (NSC) containing coenzyme Q10, magnesium and tryptophan in FMS patients.
Methods: This was a prospective, double-blind, placebo-controlled, two-period pilot study conducted between March 2017-October 2017. All patients underwent two 3-month treatments with NSC and placebo, with a 1-month washout period in between. To evaluate the most prevalent clinical manifestations of FMS, the Combined Index of Severity of Fibromyalgia questionnaire (ICAF) [4] was used. A sample of 23 patients aged from 18 to 80 years, with a formal diagnosis of fibromyalgia of at least two years, was included in the study.
Results: Twenty patients completed the study, while three (13.0%) dropped out because they failed to attend all clinical visits (n=2) or presented an adverse event (n=1). Participant demographics are presented in Table 1. All participants were female with a mean age of 51.9 (7.2) years. Depression and anxiety were reported in 65.0% (13/20) and 30.0% (6/20) of cases, respectively. All patients were under pharmacological treatment for FMS symptoms. The most commonly reported medications were paracetamol (60.0%, 12/20), selective serotonin reuptake inhibitors

(45.0%, 9/20), and tramadol (40.0%, 8/20). Physical symptoms such as fatigue, functional capacity, pain and sleep quality improved at the end of the study treatment, whereas they mainly declined after placebo treatment. However, no statistically significant differences were found among the studied variables. Total ICAF score improved after NSC treatment, and declined after placebo treatment. NSC treatment was well tolerated, with a low incidence of adverse events (5.0%, 1/20).

Table 1. Patient demographics

Parameter	Value
Age, years [mean (SD]	51.9 (7.2)
Sex (F/M)	20/0
Weight, kg [mean (SD]	69.3 (13.1)
Height, cm [mean (SD]	160.4 (6.5)
Years since first FMS diagnosis [mean (SD)]	7.7 (6.3)
Occupational status, n (%)	
Working full-time/part-time	10 (50.0)
At home	3 (15.0)
Not working/receiving pension	5 (25.0)
Retired or unemployed	2 (10.0)
Smoking patients, n (%)	8 (40.0)
Patients on alcohol consumption, n (%)	0 (0.0)
Patients on physical activity, n (%)	2 (10.0)

F/M: female/male

Conclusion: The results of this study constitute the first investigation of the effect of a nutritional supplement containing CoQ10, magnesium and tryptophan on FMS. Although the results should be confirmed in larger studies, they suggest that NSC treatment for 3 months, in addition to pharmacological therapy, may be of interest in the management of FMS. This treatment appeared to primarily improve physical symptoms, such as fatigue and pain, with low risk of adverse events.

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AB0953 CANNABINOIDS: FRIEND OR FOE OR A BYSTANDER?

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Background: Cannabinoids has recently gained popularity for use in chronic pain. There is a lot of inquisitiveness among our patients wherein health care professionals are asked about its efficacy, side effects and sometimes even ask for a prescription! As there is paucity of data and research about its use in rheumatology, patient reported outcome(PROM) can guide ahead in expanding our knowledge and experience.

Objectives: To study usage of cannabinoids by rheumatology patients

To study awareness among primary physicians regarding Cannabinoid usage in rheumatology.

Methods: Cross sectional survey with two arms. Arm 1 Information from patients attending tertiary rheumatology clinic,including perception regarding the use of Cannabinoids.

Arm 2 consisted of collecting data via web-based survey with20-question from 100 GPs of Leicestershire. Questions on demographics, perspectives on and knowledge of cannabinoid use. Statistical analysis SPSS software.

Results: Arm1 Total 102 rheumatology patients with 60%were females and 45% secondary education. 48% were unemployed. 75% Caucasians, 18% Asians. RA most common diagnosis followed by OA and FMS. 40 % depression and anxiety in addition to Rheumatic disease. 94% reported ongoing pain with 6-8 on a VAS scale. 79% were satisfied with their current therapy. 65% had heard about complementary medicine and 15% reported using cannabinoids.

Most common form Cannabinoids oil 60% followed by smoking 20%. 56% reported using >3 months and majority 72% use daily. Median age 55 years. 88% users Caucasians. Mean disease duration 6.25 years among users indicates chronicity of disease has a direct proportion in usage. All users had ongoing pain of 7 on VAS. 87% believed it helps them managing pain effectively with a pain free state. On an average spends between 50-100 pounds per week. More than half believe cannabinoids should be available as a prescription drug in NHS and 30% interested to know more about it.

In Arm 2 consisting of Primary care physicians, response rate 50%. Average clinical experience 5 years. Only 20% heard about usage of complementary medicine by rheumatology patient. Most replied that 10% of their patients use Cannabinoids for pain management. Most did not believe use of cannabinoids benefited the patients. Only 4% recommend its usage. 25% think it should be available as prescription. 40% experienced patients asking about cannabinoids during appointment. 88% of respondents did not know much about cannabinoid usage in rheumatology and have never prescribed it in their practice.

Conclusion: Cannabinoids widely used by the rheumatology patients with PROM favouring its efficacy for control of chronic pain. Preclinical data suggest that cannabinoids might have a therapeutic potential RA[1], OA, FMS[2]. Clinical data regarding cannabinoid treatment for rheumatic diseases are scarce, therefore, recommendations concerning cannabinoid treatment cannot be made. All patients who reported using it suffered from moderate to severe chronic pain. Thus main indication of usage was pain rather than recreational purpose. Although a small survey it clearly highlights lack of knowledge among primary physicians. These results emphasise the need for further research regarding the benefits and risks of cannabinoids in rheumatology.

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AB0954 IS CONNECTIVE TISSUE MASSAGE EFFECTIVE IN INDIVIDUALS WITH FIBROMYALGIA?

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Background: Fibromyalgia (FM) is a systemic rheumatic disease characterized by diffuse pain in the body, tenderness, fatigue and many more symptoms. Exercise is effective and safe method in individuals with FM. Connective tissue massage, another treatment method, is a reflex therapy where shear force is applied in a certain order at the connective tissue interfaces of the skin. In the literature, there is limited study releted compared with clinical pilates exercises and connective tissue massage in individuals with FM.

Objectives: The aim of the study was to examine the effectiveness of clinical pilates exercises and connective tissue massage in Individuals with Fibromyalgia on disease activity, number of painful regions, anxiety, biopsychosocial status and quality of life.

Methods: 32 women (age mean=52.43±8.32) diagnosed with FM according to American College of Rheumatology (ACR) criteria were included in this study. Participants were randomly divided into two groups as interventional group (n=15, mean age=48.80±7.48) and control group (n=17, mean age=55.64±7.87). While the connective tissue massage and clinical pilates exercises were applied to the treatment group, only clinical pilates exercises were applied to the control group. After the demographic characteristics and disease related data of the individuals were recorded; number of painful regions were assessed with Pain Location Inventory (PLI), disease impact with Fibromyalgia Impact Questionnare (FIQ), functional status with Health Assessment Questionnare (HAQ), anxiety with Beck Anxiety Inventory (BAI), quality of life with Short Form-36 (SF-36) and biopsychosocial status with Cognitive Exercise Therapy Approach (BETY) Scale were evaluated. All evaluations were made before and after treatment. All interventions were applied 3 days per week for 6 weeks by the same experienced physical therapist. One session for clinical pilates exercises consisted of 60 minutes (10 minutes warm up, 40 minutes clinical pilates exercises, 10 minutes cool-down). Connective tissue massage was started from lumbosacral region and continued lower thoracic, scapular, interscapular, and cervical regions, respectively. The Kolmogorov-Smirnov Test was used to determine whether the continuous variables were normal distributions.

Results: When the pre-treatment and post-treatment results are analyzed; the results were significant in the intervention group of PLI ($p = 0.007$), SF 36 physical component ($p = 0.025$) and mental component ($p = 0.017$) and FIQ ($p = 0.004$), while in the control group the difference in SF 36 physical component ($p = 0.008$) and mental component ($p = 0.024$), FIQ ($p = 0.001$) and BAI ($p = 0.043$) was significant. Delta values were calculated by subtracting post-treatment results from pre-treatment results. When the delta values of the groups are compared, it was determined that the difference only in the PLI ($p = 0.023$) were significant in favor of the treatment group.

Conclusion: According to our results, connective tissue massage has been shown to be effective in reducing the number of painful areas in addition to the

positive effects of clinical pilates exercises in individuals with FM. In order to increase the effectiveness of treatment in individuals with FM, we recommend the use of connective tissue massage as an additional treatment method.

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AB0955 FEATURES OF THE PAIN SYNDROME IN RHEUMATOID ARTHRITIS (RA)

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Background: The neuropathic component is present in the mechanism of pain in RA in 36% of cases. The presence of anxiety-depressive disorders and a decrease in the quality of life in patients with RA are shown.

Objectives: The study of the clinical features of pain in RA in men and women.

Methods: The group consisted of 134 patients with RA (94 women and 40 men), aged 36 to 60 years (average age 48.6 ± 7.1 years) and disease duration from 1 year to 10 years (4.03 ± 1.6 years) hospitalized in the rheumatology department of the Republican Clinical Hospital (Cheboksary). At the time of inclusion in the study, all patients were in the active stage of the disease.

An assessment of rheumatological and neurological status was carried out. Pain assessment was performed using: Visual Analog Scale (VAS); Ritchie articular index (RAI). The severity of neuropathic pain was determined using the diagnostic neuropathic pain questionnaire DN4 and PainDetect (sensitivity - 82.9%; specificity - 89.9%). To determine the psycho-emotional deviations used: general health questionnaire (anxiety and depression) - General Health Questionnaire (form GHQ – 28); HADS; Spilberger-Hanin situational and personal anxiety scale. Patient mobility limitations were assessed using the Rivermead mobility index score scale, and quality of life was quantified using the EQ-5D visual analogue scale.

To assess the activity of the disease, the level of C-reactive protein (CRP), the erythrocyte sedimentation rate (ESR), and the DAS index - 28-CRP were used. To assess mental and physical functioning, a standardized questionnaire The Short Form-36 was used.

To visualize the stage, survey radiographs were used in the direct projection of the metacarpophalangeal and metatarsophalangeal joints, wrist joints, proximal interphalangeal joints of the hands; distal parts of the feet.

Results: An analysis of chronic pain syndrome in 36% of patients revealed a neuropathic component of pain (DN4: 5.7 ± 1.1 points, PainDetect: 16.3 ± 4.2).

In the group of patients with neuropathic pain (n = 78) aged 55.1 ± 7.9 years, the duration of the disease was 3.4 ± 0.9 years, the more advanced and late clinical stages of the disease, III – IV radiological stages of RA were more common, were present neurological disorders and complaints characteristic of peripheral polyneuropathy. Rivermead mobility index in patients with neuropathic disorders, (n = 78) was 9.1 ± 0.8 points, in the absence of neuropathic disorders (n = 56), 11.2 ± 1.1 points. There were no significant differences in process activity (DAS index - 28 - CRP) and quality of life.

According to the questionnaire of situational and personal anxiety, Spilberger-Khanin revealed moderate anxiety and mild - depressive disorders. Quality of life was reduced in all patients with RA.

Pain syndrome in patients with neuropathic pain with symptomatic (NSAIDs, GC) and basic cytostatic therapy (methotrexate) showed that, despite the decrease in the severity of the inflammatory process, the positive dynamics was partial (VAS before therapy 6.4 ± 0, 7; VAS in the presence of therapy 4.3 ± 0.5 (p> 0.05); PainDetect = 14.9 ± 4.4; DN4 = 4.3 ± 1.5).

In men, statistically significant factors associated with pain were clinical parameters that accounted for 37% and 18% of pain variation (Ritchie articular index (CIR): Fsmc = 4.107, p <0.001; SF-36: Fsmc = 2.107, p <0.001) In women, the main significant factors associated with pain were the subjective feeling of pain and psychological characteristics that accounted for 12% of the pain variation (SF-36: Fsmc = 11.118, p <0.001).

Conclusion: A dynamic study of patients with RA in accordance with gender and age will further develop additional criteria for evaluating the effectiveness of complex therapy used to treat chronic pain, and will also increase the overall effectiveness of treatment.

Disclosure of Interests: None declared

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AB0956 VERTICAL NAIL RIDGING IN PATIENTS WITH FIBROMYALGIA: FREQUENCY, PROPOSED GRADING AND CORRELATION WITH OTHER DISEASE FEATURES

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Background: The vertical nail ridging (VNR) has long been reported to be related to stressful conditions[1]

Objectives: to evaluate the frequency of VNS in FM patients and its relation to other disease parameters depending on a proposed grading.

Methods: VNR has been searched for in 212 FM patients (2016 criteria). The number of fingers, the degree of VNR according to this proposed grading (0: no ridging, 1: ridging only detected by a magnifying lens, 2: ridging seen by naked eye and 3: ridging that can be seen and felt) and other FM features according to the new and old ACR criteria have been recorded. 80 subjects of those consulting for knee osteoarthritis have been examined for VNR and those found positive were asked about the FM features and examined for tender points. Patients aged >50 years and those with psoriasis and fungal infections were excluded.

Results: the mean age of patients was 32.4±9.9 (73.6% were female). The mean disease duration was 5.8±3.7, while the means of WPI, SSS and tender points were 9.4±2.9, 7.3±1.2 and 14.7±2.3 respectively. VNR was found in 209 patients (98.6%). Of 80 controls, VNR has been found in 61 subjects, of whom FM has been diagnosed in 32 patients (52.4%) by 2016 FM criteria and in 46 (75.4%) by 1990 criteria. The number of fingers with VNR has been found only correlated with the disease duration (r= 0.276, P = 0.000). The severity of VNR was significantly correlating with fatigue (P= 0.002), sleep disturbance (P= 0.001), awaking unrefreshed (P = 0.000), WPI (p = 0.01) and mean tender points (P =0.02). Considering the 2016 criteria as a gold standard, the sensitivity of VNR was 98.37%, the specificity was 9.68% and the diagnostic accuracy was 82.8%.

Conclusion: vertical nail ridging is a frequent finding and can be considered helpful for diagnosis of patients with FM. Further studies are needed to validate this sign for diagnosis and follow up of FM patients.

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AB0957 IS AQUATIC THERAPY MORE EFFECTIVE THAN LAND-BASED THERAPY IN REDUCING PAIN OF WOMEN WITH FIBROMYALGIA?

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Background: Fibromyalgia is a rheumatic disorder characterized by chronic widespread pain often associated with fatigue, unrefreshed sleep and cognitive problems with an increasing prevalence. Aquatic therapy has already been used for managing the symptoms of this syndrome. However, it is not clear whether there is a superiority of aquatic therapy over land-based therapy in improving the symptoms of fibromyalgia patients.

Objectives: Determine the effectiveness of two physiotherapy protocols: aquatic therapy versus land-based therapy, for decreasing pain in women with fibromyalgia.

Methods: The study protocol was a single-blind randomized controlled trial. Forty women diagnosed with fibromyalgia were randomly assigned into two groups: Aquatic Therapy (n=20) or Land-based Therapy (n=20). Both interventions include 60-min therapy sessions, structured into four sections: Warm-up, Proprioceptive Exercises, Stretching and Relaxation. These sessions were carried out three times a week for three months. The variables analyzed were: pain intensity (Visual Analogue Scale [VAS]), pain threshold (algometer), quality of life (Revised Fibromyalgia Impact Questionnaire [FIQR]), sleep quality (Pittsburgh Sleep Quality Index [PSQI]), fatigue (Multidimensional Fatigue Inventory [MFI]) and physical ability (6-minute Walk Test [6MWT]). Outcome measures were evaluated at baseline, at the end of the 3-month intervention period, and 6-weeks post-treatment. Statistical analysis will be carried out using the SPSS 21.0 program for Windows and a significance level of $p \leq 0.05$ was used for all tests.

Results: At the end of intervention period, both therapies were effective in improving pain intensity ($p<0.05$), pain threshold ($p<0.05$), quality of life ($p<0.05$), fatigue ($p<0.05$) and physical ability ($p<0.05$). For sleep quality, only the aquatic therapy group experienced a significant improvement ($p=0.033$). No differences were

observed between the groups in post-treatment, but they were found at the follow-up, in favor of aquatic therapy for pain intensity (p=0.023) and sleep quality (p=0.030).
Conclusion: Both physiotherapy interventions showed to be effective in reducing pain in patients with fibromyalgia. However, aquatic therapy was more effective in improving quality of sleep and decreasing pain intensity at six weeks of follow-up than land-based therapy. It seems that the therapeutic effects achieved in post-treatment were maintained for a longer time in the aquatic therapy group. Even so, in order to maintain the benefits obtained with the interventions, continuous physiotherapy treatment seems to be necessary.
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AB0958 LOW-ENERGY PULSED ELECTROMAGNETIC FIELD THERAPY REDUCES PAIN IN FIBROMYALGIA: A RANDOMIZED SINGLE-BLIND CONTROLLED PILOT STUDY.

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Background: Fibromyalgia is a clinical condition characterized by diffuse chronic muscle-skeletal pain, fatigue, sleep/mood disorders and muscular stiffness. The pathogenesis of fibromyalgia remains poorly understood but numerous lines of evidence suggest a role for alterations of both the central and peripheral nervous systems leading to heightened pain sensitivity along with a *corollarium* of other symptoms[1]. Low-energy pulsed electromagnetic field (PEMF) has promising data in the prevention of falls in senior individuals and is believed to promote osteogenesis and angiogenesis thus proving promising to treat bone diseases with chronic pain[2]. No data is available in fibromyalgia.
Objectives: To investigate the efficacy and safety of PEMF on fibromyalgia symptoms in a randomized single-blind pilot study.
Methods: We enrolled 21 women (median age 59 years, IQR 16,5) affected by fibromyalgia according to the 2010 ACR classification criteria[3] not receiving chronic medical treatment for pain; patients were randomly allocated to receive PEMF TEPT (triple energy pain treatment) / New Sunrise 280 (THS - Therapeutic Solutions, Milan, Italy) on the selected points (10 agopuncture points) or scrambled points for 20 minutes at baseline (T0) and after 4 (T4) and 8 (T8) weeks. Outcome measures were recorded at T0, T4 and T8 and included FIQ (fibromyalgia impact questionnaire), WIP (widespread pain index), VAS pain, SS (symptom severity scale), and SF-36 (short form 36 health survey questionnaire).
Results: Patients receiving the active treatment had a deep reduction of WIP from T0 to T8 (-76% vs -13% in placebo) with a statistically significant difference compared to the placebo group (p=0.0025) (**Figure 1**). In all endpoints, we observed a general reduction at T4 and T8 compared to T0 also for FIQ, VAS pain, SS, SF-36, regardless of the treatment arm and the decrease was higher in the active treatment arm compared to the placebo group, albeit not reaching statistical significance (**Figure 2).**
Conclusion: The results of our pilot study show that PEMF is more effective than placebo in reducing widespread pain in fibromyalgia while confirming that a placebo effect is clear in this complex disease.
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Figure 1. WIP

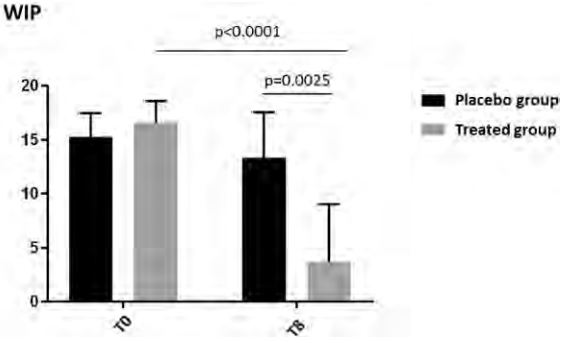
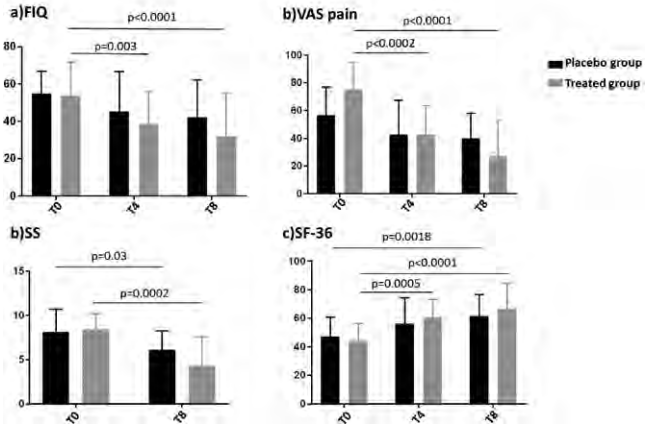


Figure 2.



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AB0959 FREQUENCY OF SEXUAL DYSFUNCTION IN WOMEN WITH FIBROMYALGIA

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Background: The impact of rheumatic diseases on patients'sexual life has been gathering the attention of the scientific community over the last decade. The existing studies, especially related to fibromyalgia, are scarce.
Objectives: To assess the prevalence of sexual dysfunction in women with fibromyalgia followed up at the Outpatient Clinic of the Medical Hospital in Russia.
Methods: The main group consisted of 54 women aged from 18 to 55 who sequentially applied for rheumatologist consultation. All subjects fulfilled ACR 2016 Fibromyalgia criteria. The comparison group included 100 healthy women adjusted by age who came for a scheduled health check up and signed the informed consent form. The Female Sexual Function Index (FSFI), obtained by applying a 19-item questionnaire that assesses six domains (sexual desire, arousal, vaginal lubrication, orgasm, sexual satisfaction and pain) and Hospital Anxiety and Depression questionnaire (HADS) were used. The data are presented as means and standard deviations.
Results: 26 (48,1%) of the patients interviewed reported no sexual activity over the past 4 weeks. fibromyalgia patients reported no sexual activity during the previous 4 weeks. Fibromyalgia group had significantly lower values of all FSFI

domains than those of the comparison group: desire 1.98±1.28 and 3.19±1.45; arousal 1.98±1.46 and 3.74±1.45; lubrification 2.35±2.25 and 4.37±1.32; orgasm 1.75±1.68 and 4.06±1.66; satisfaction 2.28±1.19 and 3.95±1.61; no pain 2.49±1.77 and 4.30±1.42. In General, total FSFI score was 12.86±10.97 on fibromyalgia group versus 23.55±8.24 in the healthy group (maximum possible being 36 points, p< 0.0001).

We tried to see if sexual function was affected by psychological status or stile of life. We found that only arousal, lubrification, orgasm and satisfaction had minimal values for clinically expressed anxiety while all parameters of sexual dysfunction were reduced in women on fibromyalgia group with borderline and clinically significant depression. There was the best index of sexual function married patients compared to divorced women. Unexpectedly, the minimal scores for all FSFI domains were in the fibromyalgia subgroup of 8 women with body mass deficiency and 20 women with Overweight, while normal body mass index and obesity were protective factors in sexual function.

Conclusion: Thus, a significant sexual function decrease was detected in female with fibromyalgia. The most severe dysfunction being associated with the abnormal anxiety, borderline and abnormal depression, divorced status, body mass deficiency and overweight.

Disclosure of Interests: None declared

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Back pain, mechanical musculoskeletal problems, local soft tissue disorders

AB0960 RELATIONSHIP BETWEEN THE CAREGIVER BURDEN AND UPPER LIMB-NECK DISABILITY AND PAIN IN BABY CAREGIVERS

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Background: Although caregiving is a normal part of being a parent of a young child, it is still unclear whether caregiving causes upper limb or neck disability in the caregiver.

Objectives: The aim of this study was to investigate the relationship between caregiver burden and upper limb-neck disabilities and pain in baby caregivers.

Methods: Sixty caregivers who are responsible for the caregiving of a 0-2 year old healthy baby, were included in this study. Physical characteristics and the gender of the caregivers were recorded. Caregiver burden was assessed by the Zarit Burden Interview; upper limb problems by DASH and neck problems by the Neck Disability Index and Neck Bournemouth Questionnaire. In addition, pain severity related to neck and upper limb was evaluated by using Visual Analog Scale over a 10 level scale.

Results: The mean age of the caregivers was 30.96 ± 6.43 year. The mean body mass index of the caregivers was 23.34 ± 3.29 indicating normal body composition. Height and weight were 163.75 ± 6.01 and 62.55 ± 8.98, respectively. Ninety-five percent of the caregivers were mother and the others were the babysitter. A weak relationship was determined between the Zarit Burden Interview and DASH (p=0.02, r=0.2), while no relationship was found between caregiver burden and other assessments. Caregivers were found to have very low pain severity in the upper limb and neck.

Conclusion: It has been previously reported that caregiving for a disabled child or adult causes care burden and various musculoskeletal disorders [1-4]. Current study demonstrated that giving care for a healthy child did not create care burden, and caused lower levels of pain in the upper limb and neck.

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AB0961 MYOFASCIAL TRIGGER POINTS ARE THE UNDEREVALUATED HYPOXIC NISCHES ALTERING POSTURE AND PHENOTYPE

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Objectives: Myofascial trigger point (MTrP) is a pillar pathophysiological unit in development of myofascial pain [1] and postural imbalance [2]. Dry needling (DN) of MTrP under ultrasound (US) guidance is prioritized method for treatment myofascial pain. Hypoxia-related signaling pathways play important role in development of rheumatic diseases and cancer [3,4].

Hypothesis: *MTrP are spastic hypovascularized hypoxic low energy areas that can produce organismic signaling, associated with niches in Flammer syndrome [3,4].*

Objectives: The aim was to evaluate structure of MTrP in regard to stiffness and "ischemic pattern" before and after DN.

Methods: We included 40 patients (26 females, aged 18–68 y.o.) with low back pain. Healthy 20 individuals (aged 18–52 y.o.) were controls. All patients underwent general exam, MRI, precise physical tests, extensive functional multiparameter neuromuscular US including M-mode, elastography (SWE), B-Flow (LOGIC E9 GE) of multifidus muscles. Then patients received DN of detected MTrP under US guidance.

Results: We successfully detected MTrP as hypoechoic, stiff and hypovascular small areas with different patterns of decreasing motility, contractility (muscle contracted/rested thickness) in all patient and did precise DN. After DN muscle structure improved, motility, contractility restored, VAS scores changed from 7.4 to 2.3 (p <0.05). SWE was 11±6 kPa in MTrP (27 kPa in active, 5-8 kPa in latent MTrP) vs 3.8±0.3 kPa in controls and decreased to 4±0.4 kPa after treatment. Hypovascularity ("ischemic pattern") size decreased from 3-4 mm to 0-1.5 mm, correlated with muscle function. Preliminary we found MTrP with more expressed hypovascular pattern, higher sensitivity and retaining levels of in individuals lower BMI and patient with Flammer phenotype [3,4] (13-15/15 positive responses to questionnaire).

Conclusion: MTrP are stiff and most likely hypoxic areas, parameters improved after precise DN. US hunting for "ischemic pattern" markers can be important for patient stratification and targeted treatment and prevention. Metabolic profiling including HIF signaling, proteomic data collecting needed for further investigation for effective patients stratification. For the follow-up studies a correlation of the Flammer syndrome phenotype with individualised profiles of patients and diagnosed ischaemic patterns is recommended.

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AB0962 LOW BACK PAIN AMONG MEDICAL STUDENTS: PREVALENCE AND RISK FACTORS

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Background: Low back pain (LBP) is a common health problem among all age groups. Medical students do not seem to be spared. In fact LBP is one of the most common musculoskeletal disorder and its prevalence is variable ranging from 41% to 72%.

Objectives: The aim of our study was to determine the prevalence of LBP among Tunisian medical students and to assess its associated factors.

Methods: We conducted a cross-sectional study over 2 months carried out on medical students in a Tunisian medical college. A digital questionnaire entered by Google forms was sent by e-mail and was completed by the students. Our study included students from the first year of the first cycle of medical studies up to the third year of

the second cycle. Socio-demographic, personal characteristics and life habits were collected. LBP was assessed using the Nordic musculoskeletal health questionnaire. The impact of low back pain was assessed using the Oswestry disability index (ODI).
Results: One hundred and seventy-nine students were included. The mean age was 22.9 ± 2.3 years [19.64-38.21]. The sex ratio was 0.29. The average body mass index was 23.55 ± 4.22 kg / m2 [17.67-43.07]. 82% of the students were in the second cycle of medical studies. 26.4% of the students had a regular sports activity. 91.2% spent more than 4 hours a day in a sitting position. The point, annual, and lifetime prevalence of LBP among medical students was 41.2%, 80.4% and 90.6%, respectively. Low back pain was acute in more than 58.8%, subacute in 14.9% and chronic in 26.3%. The mean ODI score was 10.32% ± 8.48% [0-32%]. Students with LBP were significantly younger than students without LBP (p = 0.015). LBP was more common in students who spent more than 4 hours in a sitting position with a difference at the limit of significance (p = 0.059). Being in the 2nd cycle was significantly associated with the occurrence of LBP (p = 0.006). Poor screen projection in the amphitheater was significantly associated with the occurrence of LBP (p = 0.029).We found a statistically very significant relationship between the occurrence of LBP and the poor layout of the amphitheaters (p = 0.000). The feeling of depression was significantly higher among LBP students (p = 0.018). Feelings of fatigue, being overwhelmed, irritability and worry were more frequently found in LBP students, but this difference was not statistically significant. In a multivariate analysis, the only factors that remained statistically significant were feeling of depression (p = 0.046, OR = 3.88; CI = [1,3-11,55]) and the poor layout of the amphitheaters (p = 0.006, OR = 8.99; CI = [2.55-31.69]).
Conclusion: The annual prevalence of LBP was 80.4%. These results testify to the magnitude of this health problem. The factors associated to LBP seemed to be essentially modifiable factors. This encourages special attention from medical schools to increase students' awareness of low back pain and to provide appropriate measures at reduce this musculoskeletal disorder.
Disclosure of Interests: None declared
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AB0963 HOW OFTEN DO DOCTORS TREAT PATIENTS WITH LOCAL DAMAGE TO THE PERIARTICULAR SOFT TISSUES IN REAL CLINICAL PRACTICE?

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Background: Damage of the periarticular soft tissues (DPST) - tendinitis, entesitis, bursitis, etc. are one of the most common reasons for patients to contact rheumatologists and orthopedic surgeons.
Objectives: To evaluate the frequency and localization of DPST in real clinical practice, as well as the effectiveness of therapy for this pathology in the acute period.
Methods: 68 outpatient orthopaedic surgeons evaluated the frequency of initial patient recourse due to DPST within one month. The study did not include patients with systemic rheumatic diseases such as spondyloarthritis. The localization of DPST and the dynamics of clinical manifestations were evaluated in 1227 patients (women 42.5%, cf. age 51.3±15.5 years). Non-steroidal anti-inflammatory drugs (NSAIDs), mainly meloxicam, were used as a first-line treatment for DPST. The results of treatment were evaluated after 10-14 days with repeated visits of patients.
Results: 7766 cases of primary outpatient treatment by orthopedic surgeons were evaluated. DPST was the cause of treatment in 1227 (15.8%) patients. This was the third highest incidence after acute injuries (37.2%) and knee osteoarthritis (20.6%).
In patients with DPST, the most common lesions were in the knee area (knee entesopathy, prepatellar bursitis, pes anserinus area tendinitis/bursitis) - 21.2%, the foot (plantar fasciitis) - 16.9%, the shoulder (tendinitis of the rotator cuff) – 16.4%, and the elbow (lateral and medial epicondylitis) - 15.3%. After treatment, there was a significant decrease in the severity of pain during movement – from 6.58±1.61 to 2.48±1.60 points on the numerical rating scale (p<0.001), a decrease in the intensity of pain at rest, at night and during palpation, as well as the severity of functional disorders. The need for local injection of glucocorticoids occurred in 22.1% of patients. Significant improvement was observed in all DPST localities, with 68.1% of patients rating the treatment result as "good" and "excellent". Adverse reactions were observed in 15.0% of patients, and no serious complications were reported.
Conclusion: DPST is the third most frequent reason of recourse to a doctor after acute injuries and osteoarthritis of large joints in the practice of outpatient orthopedic surgeons. The use of NSAIDs in the maximum therapeutic dose for 10-14 days allows for significant improvement in DPST of different localization.
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AB0964 THE ASSOCIATION BETWEEN RESIDUAL SYMPTOMS AND CERVICAL SPINE LESIONS IN RHEUMATOID ARTHRITIS

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Background: Treatment outcomes in rheumatoid arthritis (RA) have been improved with advances in drug therapy. In daily clinical practice, the outcomes are assessed based on the presence of swollen or tender joints, global assessment using a visual analog scale by a patient (GVAS) and a physician (DrVAS), etc., in addition to inflammatory findings. Although inflammation and joint symptoms are suppressed, many patients show no improvement in GVAS scores. The reported residual RA symptoms include morning stiffness (MS), pain (P), and dullness (D), but their causes are not completely known. Latent cervical spine lesions sometimes exist in RA, but their association with residual RA symptoms is unknown.
Objectives: We examined cervical spine lesions and residual symptoms in patients with RA who achieved the therapeutic goal.
Methods: Of 124 patients with RA, 82 (25 men and 57 women) who achieved a low disease activity (LDA) state on the Disease Activity Score for 28 joints with erythrocyte sedimentation rate (DAS28-ESR) were included. The mean age was 65.7 (28- 83) years, and the disease stage was Stage I in 28 patients, Stage II in 14, Stage III in 13, and Stage IV in 27. Dysfunction was graded as Class 1 in 63 patients, Class 2 in 18, and Class 3 in one (Steinbrocker classification). Biopharmaceuticals had been administered in 27 patients. As for disease activity, the DAS28-ESR scores indicated complete remission in 54 patients and LDA in 28. The survey form was used to investigate the presence or absence/duration of MS, the presence or absence/severity of P (Pain VAS), and the presence or absence/severity of D (Dullness VAS). On lateral functional radiographs of the cervical spine, patients with spinal lesions were selected and divided into the asymptotic stability (ASS; atlantoaxial dislocation ≥3 mm) + vertical setting (VS; Ranawat value <13 mm) group, the cervical spondylolisthesis group (≥3 mm of slippage on dynamic radiographs), and the spondylolisthesis group (≥3 mm of slippage on dynamic radiographs). They were examined for association with residual symptoms.
Results: According to cervical spine lesions, the patients who achieved the therapeutic goal were divided into the ASS+VS group comprising 15 patients (18.3%), the spondylolisthesis group comprising 11 (13.4%), and the stenosis group comprising 18 (22.0%). Among them, only the spondylolisthesis group showed significant differences in residual RA symptoms. In the spondylolisthesis group, the disease duration was longer, but there was no difference in age. MS, P, and D were significantly severer. The duration of MS was longer, and both Pain and Dullness VAS scores were higher. The score on each component of the DAS28 showed no difference in inflammatory findings. GVAS and DrVAS scores were higher. No common perceptions of spinal symptoms were shared between any patients with cervical spine lesions and physicians.
Conclusion: Improved patient-reported outcomes (PROs) are considered to be important to achieve more complete remission. There are various reports on the causes of residual RA symptoms, but many aspects remain unknown. Based on the results of this study, because asymptomatic subaxial subluxation is one of concerns in patients with spondylolisthesis with dynamic instability of the cervical spine, cervical spine diseases should also be considered in patients with severe residual symptoms. Not only radiography but also magnetic resonance imaging needs to be performed.
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AB0965 EVALUATION OF THE IMPACT OF THE JOB STRESS ON THE ONSET OF MUSCULOSKELETAL DISORDERS IN THE HEALTHCARE WORKERS OF THE GENERAL HOSPITAL OF DOUALA, CAMEROON

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Background: Job stress (workload) and its repercussions on health have already been described. However, very few publications has been performed in sub-Saharan Africa.
Objectives: To assess the link between job stress and musculoskeletal disorders (MSD) among healthcare workers of the Douala General Hospital.
Methods: In this cross-sectional study, the job stress, evaluated according to the Karasek model, made it possible to measure job-strain (high psychological

demand and low decision-making latitude), iso-strain (job-strain and lack of social support), and low-strain (relaxed or low-load work).
Results: Among the 261 participants in the study, 67.43% were women. The average age was 39.80 ± 9.4 years. The average length of professional service was 8.91 ± 7.30 years [1 - 35 years].
Regarding the job stress, 65.14% of the healthcare workers followed at least 11 patients per day. 78.54% had more than 40 hours of weekly work and 46.36% carried heavy loads during work. Job-strain was found in 58.62% of the participants, iso-strain in 7.66% and low-strain in 5.36%. MSDs were described by 225 participants (86.21%). They were mainly low back pain (68.44%), neck pain (52%) and shoulders' pain (37.78%).
In multivariate analysis, only weekly work> 40 hours (OR = 2.59; 95% CI 1.11–6.02, p = 0.026) and job-strain (OR = 3.14; 95% CI 1.33–7.39, p = 0.009) remained associated with the presence of MSD.
Conclusion: The healthcare workers in our study are exposed to a high psychological and physical job stress, causing MSDs. Ergonomic programs should be designed for these workers.
Disclosure of Interests: None declared
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AB0966 PREVALENCE OF SARCOPENIA IN PATIENTS WITH RHEUMATOLOGICAL DISEASES

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Background: The presence of sarcopenia in rheumatological patients is an independent predictor of morbidity and mortality in this cohort of patients. Patients with sarcopenia are characterized by lower physical activity, a tendency to depression and poor social adaptation.
Objectives: To assess the prevalence of sarcopenia in rheumatological patients.
Methods: 317 patients were examined, including 79 with systemic lupus erythematosus, 98 with rheumatoid arthritis, 72 with systemic scleroderma, 68 with spondyloarthritis. Among them, 201 women and 116 men, the age of patients ranged from 21 to 58 years, the average age at the time of inclusion of patients in the study was 41.1 ± 7.3 years. Sarcopenia was diagnosed using the method recommended by The European Working Group on Sarcopenia in Older People2.
Results: The frequency of occurrence of a decrease in the total mass of skeletal muscle according to the skeletal muscle mass index (ISMM) was 31.2% (99 patients), a decrease in muscle strength according to the wrist dynamometry was observed in 44.5% (141 patients), low skeletal muscle performance according to the results NIH Toolbox 4 Meter Walk Gait Speed Test in 42.8% (135 patients). The prevalence of suspected sarcopenia (probable sarcopenia) was 13.3% (42 patients) and sarcopenia 31.2% (99 patients), no cases of severe sarcopenia were detected. Statistically significant differences were obtained between groups of patients depending on the duration of rheumatological disease and the prevalence of sarcopenia ($\chi 2$=19.328 p=0.001).
Conclusion: The prevalence of sarcopenia in rheumatological patients in the general population was 31.2%.
Disclosure of Interests: None declared
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AB0967 OBESITY IMPACTS SURGICAL REPAIR OF ROTATOR CUFF TEAR IN A LOW-INCOME POPULATION

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Background: Rotator cuff tears (RCT) rank high among causes of shoulder pain in primary care. Surgical repair of RCT is indicated when judged refractory to clinical treatment. Comorbidities and environmental issues may impact the surgical result of RCT repair.
Objectives: to determine the impact of Obesity and Smoking in the outcome of low-income patients subjected to RCT repair.
Methods: Low-income (<5500,00 US$ annual *pib per capta**) patients living in Fortaleza-CE, Brazil were prospectively (2016-2018) evaluated in the Orthopedic and Rheumatology Services of the Hospital Geral de Fortaleza. Demographics and clinical data focusing Obesity (BMI >/≤ 30) and Smoking status (present/absent) were registered. Pain (0 – 10cm VAS) and functional shoulder score evaluation by the University of California at Los Angeles Shoulder Score (UCLA) and American Shoulder and Elbow Surgeons (ASES) scoring systems following at least 2 years post-operative follow-up were recorded.
Results: Thirty-nine individuals, 60.9±7.1 years-old, 30 female (68.3%) with 5.1 ± 1.9 years follow-up were evaluated; 21 (44.7%) were Smokers and 12 (25.5%) Obese (BMI >30). Other comorbidities included 16 arterial hypertension, 18 dyslipidemia, 17 osteoarthritis, 4 rheumatoid arthritis, 1 gout. Pain VAS values were 5.1 ± 2.6 vs 3.1 ± 2.8 in Obese vs Non-Obese (p=0.03) and 4 ± 2.8 vs 3.37 ± 2.99 in Smokers vs Non-Smokers (p=0.26), respectively. UCLA was 22.4 ± 8.2 vs. 28.79 ± 5.6 in Obese vs Non-Obese (p=0.004) and 26.2 ± 6.5 vs. 27.75 ± 7.18 (p=0.25) in Smokers vs. Non-smokers, respectively. ASES was 47.89 ± 28.3 vs. 68.1 ± 25.78 (p=0.021) in Obese vs. Non-obese and 58.98 ± 26.69 vs 65.3 ± 28.1 (p=0.243) in Smokers vs Non-Smokers, respectively.
Conclusion: Using Patient Reported Outcome instruments, these long-term data show that Obesity negatively impacts the outcome of surgical repair of RCT in low-income patients. Smoking status was apparently irrelevant but the number of cigarettes smoked daily was not considered. Emphasis on weight reduction is a practical, affordable though hard to implement measure that could improve surgical results when repairing RCT.
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Disclosure of Interests: Christine Silva: None declared, Natalia Mourão: None declared, Joaquim Landim: None declared, Leila da Rocha: None declared, Marco Lacerda: None declared, Airton Rocha Speakers bureau: Not related to the present work
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AB0968 DIAGNOSIS OF INFLAMMATORY BACK PAIN (IBP) IN A LOW-INCOME POPULATION USING ASAS IBP DEFINITION

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Background: Inflammatory back pain (IBP) is an important entry criterion for identifying patients with axial spondyloarthritis. Due to the very frequent prevalence of chronic non-inflammatory back pain (CBP), IBP is difficult to differentiate and recognize in many clinical practices. CBP is a frequent diagnosis in populations with low socioeconomic status.
Objectives: To investigate whether IBP ASAS definition help discriminate from CBP in a low-income population.
Methods: A total of 202 consecutive individuals were directly interviewed in Fortaleza/Brazil, for the prevalence of IBP (ASAS definition), monthly family income (US$), school education [>/≤ 8 school-years(SY)], and smoking habit (present/absent). People from all social levels were included.
Results: Mean age was 38.9±12.9 years, 100 (49.5%) were male and 36 (17.8%) were smokers; 135 (66.8%) declared less than 730US$ family earnings per month and 71 (35.1%) had less than 8 SY. Although 122 (60.3%) declared lumbar pain, in comparison, 29 (14.3%), 22 (10.9%) and 59 (29.2%) fulfilled ASAS, Berlin, and Calin's IBP criteria, respectively. There were 39 (58.02%) vs. 83 (61.5%) with vs. without CBP and 9 (13.4%) vs. 20 (14.8%) fulfilling vs. not fulfilling the ASAS IBP definition among those with more or less than 730US$ earnings (P>0.05), respectively.
Conclusion: This is the first report on the prevalence of IBP in a very low-income population. Over one-third had less than 8SY, revealing very low literacy. Smoking prevalence was also low if compared to 28% smoking prevalence WHO estimates across Europe*. These IBP prevalence data are similar to those reported in wealthier populations, living in higher latitude. Data suggest that ASAS IBP definition may be used to discriminate patients with IBP from those with CBP, regardless of income and literacy.
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AB0969 GAINED WEIGHT DURING PREGNANCY AND LOW BACK PAIN: IS IT REALLY ASSOCIATED?

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Background: Back pain is known to be a common complaint during pregnancy explained by gained weight in this period. Besides, the incidence of low back pain (LBP) in postpartum has also been quoted to be non-negligible even after delivery.
Objectives: The aim of our study was to assess if the development of LBP during the post-partum period was correlated to gained weight after delivery.

Methods: In this prospective study, we assessed a survey of 60 women under the age of 35 for back pain symptoms during the postpartum period from day 1 to 18 months. A structured questionnaire using Google form was used. Data from this survey were then correlated with gained weight and pregnancy outcome, as well as women's history of LBP.
Results: We interviewed 60 women during their post-partum period. The mean age was 27,9 years old [24, 35 years]. Women were on average at 9 months of post-partum [1, 18 months]. The median height was 1,6 meters [1,54-1,74m]. The median weight at the moment of the study was 63,2 kilograms [48-80kg]. Before pregnancy, body mass index was 23,5 Kg/m^2 [17-34 Kg/m^2]. The total gained weight at the end of pregnancy was 14 kg [12-29 kg]. Only 20% gained more than 15kg. LBP was experienced in 35% of cases with a mean delay of 3,2 months post-partum [1-8 months]. The prevalence of persistent LBP was noted in 26% of cases. However, no correlation was found between LBP and gained weight (p=0,07). Sixty five percent reported one or more significant episodes of back pain during their pregnancy. Significantly, more patients suffering from pain in pregnancy had history of previous back pain episodes when not pregnant (p<0,001), as well as during previous pregnancies (p<0,001).
Conclusion: No correlation was found between gained weight and occurrence of LBP. The main factors associated with the development of back pain were previous episodes of back pain while non-pregnant or pregnant.
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Paediatric rheumatology

AB0970 THE RELATION BETWEEN CONGENITAL STRUCTURAL MALFORMATIONS, DISC-VERTEBRA DEGENERATION AND DISC HERNIATION IN THE PEDIATRIC AGE GROUP

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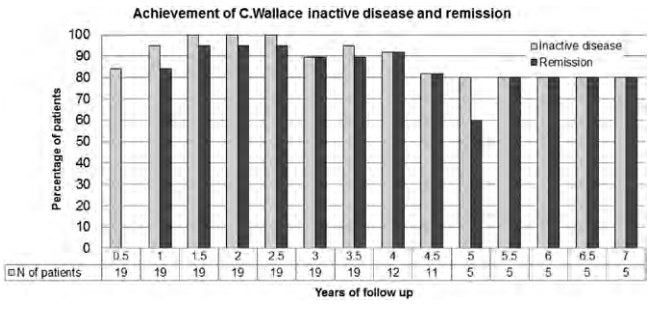
Background: Disc/vertebral degeneration and disc herniation are rare causes of low back pain in childhood. Their relationship with congenital anomalies were reviewed in few studies in literature (1-3).
Objectives: To examine the relation between congenital structural malformations in the lumbar spine, early degeneration and lumbar disc herniation in pediatric age group patients with low back pain, and to determine the incidence of congenital structural malformations, disc/vertebral degeneration, and disc herniation.
Methods: Four hundred patients with LBP persisting for at least six weeks were included in the study. Demographic characteristics, physical examination findings, and laboratory and imaging results were recorded for all patients. Severity of pain was determined using a visual analog scale (VAS). Lumbosacral X-rays were examined for the presence of lumbosacral transitional vertebrae (LSTV) and spina bifida occulta (SBO). The incidence of disc/vertebral degeneration and disc herniation was investigated at the L4-5 and L5-S1 level in lumbosacral magnetic resonans imaging of patients with and without congenital malformation (LSTV-SBO).
Results: The study population consisted of 219 girls and 181 boys aged 10-17 years (mean age 14.9±1.9). Presentation symptoms were low back pain in 90.5% (n= 362), and low back-leg pain in 9.5% (n=38). The mean VAS score was 5.3±1.0. LSTV was determined in 67 (16.8%) patients and SBO in 62 (15.5%). Disc herniation was determined in 68 patients, at the L4-5 level in 26.5% (n=18), at the L5-S1 level in 48.5% (n=33), and at both levels in 25% (n=17). Vertebral degeneration was present at the L4-5 level in 14 (8.6%) patients and at the L5-S1 level in 39 (23.9%), while disc degeneration was present at the L4-5 level in 21 (12.8%) patients and at the L5-S1 level in 31 (19.0%). No significant difference was observed in the incidence of disc/vertebral degeneration and disc herniation in patients with congenital malformation. Disc herniation was significantly more common in patients with disc degeneration (p=0.003, p<0.001). Congenital malformations were not observed in approximately 80% of patients without disc herniation and disc/vertebral degeneration.
Conclusion: The presence of congenital malformations does not appear to represent a risk factor for early degeneration and disc herniation in pediatric age group. Congenital malformations, early degeneration, and disc herniation may constitute an underlying pathology in pediatric patients with persistent low back pain.
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AB0971 LONG-TERM EFFICACY AND SAFETY OF CANAKINUMAB IN PATIENTS WITH SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS: RESULTS FROM A SINGLE-CENTER STUDY

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Background: Results from various phase 3 clinical studies have demonstrated the efficacy of canakinumab to treat patients with systemic juvenile idiopathic arthirtis (sJIA). However, limited information is available on the long-term efficacy and safety of this drug to treat children with sJIA.
Objectives: To evaluate the long-term efficacy and safety of canakinumab in patients with sJIA treated at the National Medical Research Center of Children`s health, Moscow, Russia.
Methods: This was a prospective, single-center study that included canakinumab (CAN)-naive patients diagnosed with sJIA following the International League of Associations for Rheumatology (ILAR) criteria and start receiving CAN treatment from 10/2012 to 03/2016. Patients included in this study also participated, for defined periods of time, in the clinical trial NCT02296424. Patients with active disease started treatment with canakinumab 4 mg/kg. A treat-to-target approach was used, canakinumab was discontinued in patients on clinical remission, either following the NCT02296424 protocol or by investigator's decision, and re-introduced in those patients who experienced a relapse afterwards. Disease characteristics and demographics were recorded at the time of diagnosis and initiation of treatment (study entry). Disease activity was evaluated periodically using the adapted **JIA** ACR core set measures, and percentages of patients with inactive disease and on clinical remission were calculated using the sJIA ACR criteria. Response to treatment was also evaluated by calculating modified ACR responses and JADAS-71 scores. Safety was assessed by collecting and classifying adverse events (AEs) at each visit.
Results: Nineteen patients presenting with sJIA were included in this study, with a median age at treatment initiation of 9.6 (interquartile range, IQR 6.4-11.1) years and a median disease duration of 4.4 (IQR 1.2-7.0) years. Most patients (17/19) had been treated previously with one or more biologic agents for sJIA. As of 23 December of 2019, the median time of follow up was 55.5 (47-71.7) months, with all patients being followed for at least 3.5 years and 5 patients followed for more than 7 years. As it is shown in figure 1, most patients (16/19) were on clinical remission one year after starting therapy, and this effect was sustained at year 3.5 (17/19). ACR 90 responses were observed in 84.2% (16/19) patients at one year and 94.7% (18/19) patients at 3.5 years, whereas JADAS-71 scores decreased from 15 (14: 28.5) at baseline to 0 (0: 0) at one year with 4/19 patients maintained with JADAS-71 >0); at 3.5 years, only one patient had JADAS-71>0 (0.47, due to slight ESR increasing). Concerning the 5 patients with >7 years of follow up, three of them were in clinical remission for more than 3 years, including one who had discontinued therapy more than 2 years. Another patient had a relapse after attempting drug discontinuation, but recovered clinical remission after reintroducing canakinumab, and remained in this state for the last two years. The remaining patient has persistent low levels of disease activity during the last four years of follow up. AEs required hospitalization were reported in 36.8% (7/19) patients.



Conclusion: Sustained clinical remission was observed in most patients with sJIA treated with canakinumab for up to 7 years, with no new or unexpected adverse events reported.

Disclosure of Interests: Ekaterina Alexeeva Grant/research support from: Roche, Pfizer, Centocor, Novartis, Speakers bureau: Roche, Novartis, Pfizer., Elizaveta Krekhova: None declared, Tatyana Dvoryakovskaya: None declared, Ksenia Isaeva: None declared, Aleksandra Chomakhidze: None declared, Evgeniya Chistyakova: None declared, Olga Lomakina: None declared, Rina Denisova: None declared, Anna Mamutova: None declared, Anna Fetisova: None declared, Marina Gautier: None declared, Dariya Vankova: None declared, Meyri Shingarova: None declared, Ivan Kriulin: None declared, Alina Alshevskaya: None declared, Andrey Moskalev: None declared

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AB0972 DEVELOPMENT OF THE PARENT VERSION OF THE JUVENILE ARTHRITIS DISEASE ACTIVITY SCORE CUT-OFFS FOR MODERATE AND HIGH DISEASE ACTIVITY STATES IN JUVENILE IDIOPATHIC ARTHRITIS IN A LARGE MULTINATIONAL PATIENT SAMPLE

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Background: Measurement of disease activity level is of pivotal importance in the care of patients with juvenile idiopathic arthritis (JIA). According to the most recent requirements, both, parent's and children's perception should be taken into account while evaluating the disease course and assessing effectiveness of therapy. Therefore, a new disease activity evaluation tool, based only on parent assessment of the outcome, is under development and named Parent Juvenile Arthritis Disease Activity Score (parJADAS) [1].

Objectives: The aim of this study is to develop the parJADAS cut-off values of moderate disease activity (MDA) and high disease activity (HDA) in JIA patients.

Methods: The parJADAS (score range 0-40) is the sum of 4 values: 1) parent's assessment of disease activity on a 21-numbered circle 0-10 VAS; 2) assessment of pain intensity on a 21-numbered circle 0-10 VAS; 3) proxy assessment of joint disease up to a maximum of 10 joints; 4) assessment of morning stiffness (MS) on a Likert scale, ranging from no MS (0 points) to > 2 hours of MS (10 points). The study dataset is composed of 2,412 patients with JIA, seen in 3389 visits with parJADAS available, enrolled in the the multinational registry PharmaChild, assessing the long-term safety of treatment of children with JIA. At each visit, subjects were subjectively rated as being in inactive disease, low disease activity, MDA, or HDA by the attending physician. For each patient, only one visit per disease state was retained.

To identify the cut-offs the following methods were implemented: 1) Mapping: the 25th percentile value of the parJADAS in patients having MDA or HDA, respectively, was calculated; 2) Youden Index: Youden Index (J) identifies the maximum potential effectiveness of the biomarker through the receiver operating characteristic (ROC) curve analysis; 3) Max agreement: The analysis of agreement was based on kappa statistics, which assesses the agreement beyond chance between 2 dichotomous ratings. The first rating was obtained using all possible parJADAS values as hypothetical test criteria; to obtain the second rating, the categorical ratings of each attending physician were dichotomized and were coded as 0 or 1.

Results: Preliminary cut-off values for parJADAS with sensitivity and specificity are presented in the table.

	25th centile	Youden Index	Kappa	Mean	Sensitivity	Specificity	AUC
MDA	6	5	9	7	73.4	82.0	0.853
HDA	14.8	11	18.5	15	71.2	87.6	0.892

Conclusion: Tentative cut-off values for classifying the states of MDA and HAD using parJADAS were calculated. The obtained values will be tested in the validation analysis. Once validated the cut-offs are ideally suited to identify subjects at risk of disease flare when remotely monitored with the parJADAS.

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AB0973 THE IMPACT OF YOGA, ANTI-INFLAMMATORY DIET & SELF MONITORING IN CHILDREN WITH RHEUMATIC DISEASES

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Background: There is growing evidence of positive effects of yoga, special diet and an internet-based model of self-monitoring in adults with rheumatic diseases in various small scale independent studies. These studies have shown improvement in disease activity, symptom relief, quality of life, mental health issues and social life and thereby optimizing the disease management in a holistic way.

Objectives: The present study was designed to investigate the combined effects of yoga, anti-inflammatory diet and self monitoring in children with chronic rheumatic diseases.

Methods: In the clinical study, a total of 22 children aged more than 8 years with newly diagnosed rheumatic disease were enrolled. Depending on their consent, they were divided into two groups; 1) experimental group and 2) control group.

Experimental and Control Group (n=22)

All 22 participants were advised every month follow up for the next 4 months. Baseline disease activity and damage scores were calculated for all.

Experimental Group (n=14) Three different printed materials were given.

1. Pictures of "Yoga Ashnas" with explanation in their understandable language
2. Pictures of foods under two headings: 1) beneficial and 2)harmful
3. Self monitoring kit: Disease and medicines information leaflets and simplified pictorial

version of disease specific monitoring and damage scores

- ✓All 14 participants were enrolled to a single time yoga training session under a guidance of an experienced yoga teacher.
- ✓All are advised 45 minutes yoga every day at home.
- ✓All are put on strict diet chart.
- ✓All should read the material and calculate their disease score/s every time before their next visit.

Table:

Table A: Characteristics	Experimental group (n=14)	Control group (n=8)
Median age	12.8 years	11.2 years
Males	5 (35.71%)	3 (37.5%)
Females	9 (64.28%)	5 (62.5)
Juvenile Systemic Lupus Erythematosus (JSLE)	2 (14.28%)	2 (25%)
Juvenile Dermatomyositis (JDM)	2 (14.28%)	1 (12.5%)
Juvenile systemic sclerosis (JSSc)	1 (7.14%)	2 (25%)
Mixed connective tissue disease (MCTD)	2 (14.28%)	0
Enthesitis related arthritis (ERA)	3 (21.42%)	1 (12.5%)
Polyarticular Juvenile Idiopathic Arthritis (PJIA)	4 (28.57%)	2 (25%)

Conclusion: Yoga, anti-inflammatory diet and self-monitoring have shown extremely beneficial effects in children with rheumatic diseases in multiple ways.

Table B: Monitoring Parameter	Experimental group (n=14)	Control Group (n=8)
Improvement in disease activity	13 (92.8%)	6 (75%)
Relief in pain and fatigue	12 (85.71%)	3 (37.5%)
Optimum weight maintenance	10 (71.42%)	1 (12.5%)
Improvement in routine activity and school performance	12 (85.71%)	4 (50%)
Improvement in mood and behavioural problems	12 (85.71%)	2 (25%)
Knowledge, awareness and involvement of patient and family members in disease management	12 (85.71%)	2 (25%)
Adherence to management	14 (100%)	6 (75%)
Use of alternative medicines	1 (7.14%)	3 (37.5)
Early identification of risk factor/s	5 (35.71%)	0 (0 %)

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AB0974 ANALYSIS OF DYSLIPIDEMIA IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease and is characterized by multiple autoantibodies associated with a multisystem illness. However, studies of dyslipidemia in pediatric SLE patients are limited.
Objectives: The aim of our study is to describe the lipid profiles associated with disease activity and organ damage and their correlation with laboratory parameters in pediatric SLE patients.
Methods: We retrospectively reviewed medical records from a single tertiary hospital in Taipei, Taiwan from 2002 to 2018. One hundred and twenty-four patients diagnosed with SLE were included. Dyslipidemia is defined as elevations in total cholesterol (TC), low-density lipoprotein (LDL), and triglyceride (TG) levels, and a reduction in high-density lipoprotein (HDL) levels. We gathered all of the lipid profiles, clinical characteristics, and laboratory parameters from each patient. Pediatric SLE patients participated in this study, based on their lipid profile, were classified as dyslipidemic or not. The mean values of each evaluated parameters were calculated and analyzed with generalized estimating equation (GEE) method.
Results: Total thirty-one SLE patients were enrolled; twenty-four (77%) patients had dyslipidemia. The levels of total cholesterol, TG, and LDL in the dyslipidemic group are significantly higher than those of non-dyslipidemia (214.0 mg/dL *vs* 145.0 mg/dL, 130.1 mg/dL *vs* 76.4 mg/dL, 138.7 mg/dL *vs* 82.0 mg/dL; respectively). The mean values of white blood cell count (6726/μL) in dyslipidemia group are significantly higher than non-dyslipidemia group (4521/μL; p=0.0157). In contrast, the level of high-sensitivity CRP in the non-dyslipidemia group (0.2 mg/dL) are significantly lower than those of patients with dyslipidemia (0.49 mg/dL; p=0.0486).
Conclusion: It has been well known that CRP could suppress HDL and increase TG and that elevation of CRP might indicate increased cardiovascular risk. Our results demonstrated that elevated high sensitivity CRP levels were noted in SLE patients with dyslipidemia. It is suggested that routine monitoring of cardiovascular risk factors, such as dyslipidemia, should be recommended for pediatric SLE patients.
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AB0975 LIPID PEROXIDATION AND ANTIOXIDANT PROTECTION IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS ON BIOLOGICAL THERAPY

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Background: Juvenile idiopathic arthritis (JIA) is a chronic immuno-inflammatory joint disease that leads to a child's disability. Currently, drugs aimed at the main pro-inflammatory cytokines, such as tumor necrosis factor (TNF), interleukin-1 (IL-1), interleukin-6 (IL-6), and others, are successfully used to treat JIA. The effect of these drugs on metabolic processes has been little studied.
Objectives: The purpose of the study was to determine the state of lipid peroxidation and antioxidant protection in children with JIA receiving biological therapy.
Methods: 28 children with polyarticular JIA, 15 children with systemic JIA and 20 healthy children were examined at the republican center of pediatric rheumatology on the basis of the rheumatology department of the 4th city children's clinical hospital in Minsk. All patients received methotrexate, non-steroidal anti-inflammatory drugs, and glucocorticoids as needed.
Determination of lipid peroxidation (LPO) and serum ACL and ACW were performed at the BelMAPO Central Research Laboratory. Statistical data processing was performed by traditional methods of variation statistics on a personal computer using the Statsoft Statistica 6.0 program.
Results: During the study, prior to the use of tocilizumab, results were obtained that indicate the activation of lipid peroxidation processes and the violation of antioxidant defense processes in children with JIA. A significant (P <0.05) increase in the level of lipid peroxidation products in the blood serum of children with JIA compared with healthy children was established: the content of dienconjugates in the blood of children with JIA was 3.12±0.51 opt.pl., in healthy children - 1.65±0.4 units of opt.pl., the content of dienketones in children with JIA - 2.32±4839 units of opt.pl., in healthy children - 0.19±0.08 units of opt.pl., the content of malondialdehyde in children with JIA is 9.14±1.84 μmol/L, in healthy children - 7.13±1.35 μmol/L. A significant (P <0.01) decrease in the serum ACW and ACL in the blood serum of children with JIA was established when compared with the control group: the ACW content in children with JIA was 10.61±5.8 μmol/L, in healthy children - 13, 72±5.24 μmol/L, ACL content in children with JIA - 7.21±2.65 μmol/L, in healthy children - 8.81±3.5 μmol/L.
During the treatment with tocilizumab, a remission of the disease was achieved. According to the results of a repeated study of lipid peroxidation and antioxidant protection 6 months after the start of biological therapy, a decrease in LPO activity and an increase in the antioxidant ability of substances in blood serum were found. Thus, the content of dienketones decreased to 1.05±0.17 units of optical density, dienconjugates to 2.4±0.6 units of optical density, and malondialdehyde to 6.3±1.7 μmol/l. The content of ACW increased to 12.91±3.3 μmol/L, and ACL to 8.9±3.5 μmol/L.
Conclusion: The results indicate a positive effect of tocilizumab therapy on lipid peroxidation and antioxidant protection in children with JIA.
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AB0976 CAPTURING THE ENTHESITIS RELATED ARTHRITIS CONTEMPORARY PROFILE OF NORTHERN GREEK PATIENTS IN THE ERA OF BIOLOGICS

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Background: Enthesitis-Related Arthritis (ERA) is a subtype of Juvenile Idiopathic Arthritis (JIA) subtype with an estimated prevalence ranging from 8% to 37.4%. The improvement of the disease course and outcome has been

related with the introduction of biologic Disease-Modifying Antirheumatic Drugs (bDMARDs) and the uninterrupted monitoring following the transition of young patients to adult rheumatology settings.

Objectives: To capture the contemporary ERA profile in Northern Greek patients by analyzing the characteristics and treatment outcome in the era of bDMARDs.

Methods: This retrospective cohort study included patients who had been monitored on a 3-month schedule for ≥12 months, from 2000 to 2017. The periodic metric assessment included the disease status and burden by applying contemporary tools in respect to activity, clinical remission (CR) and damage (cJADAS, JSpADA, Wallace criteria for CR and JADI, respectively).

Results: Forty-three patients, mainly male (60%) with a mean age at disease onset of 10.75 (SD:2.75) years were enrolled. The predominant joints were the hip, ankle and sacroiliac (56%, 49% and 46%, respectively). Median lag time from diagnosis to bDMARDs initiation was 8.5 months. Patients with sacroiliitis were more likely to receive bDMARDs (hazard ratio [HR]:3.26, 95% confidence interval [CI]: 1.35, 7.88). Thirty six patients (84%) achieved clinical remission (CR) on medication (CRONM), within a median time of 11 months and correlated with compliance (HR:3.62, 95%CI: 1.34, 9.76). Twenty patients (47%) experienced a flare following CR, mainly as a single episode (75%). The median flare-free survival following remission on and off medication (CROFFM) was 42 and 34 months, respectively. At the last evaluation, both median baseline cJADAS (8), and JSpADA (2) dropped to 0, while 13 patients (30%) were in CROFFM, 17 (40%) in CRONM, and 13 (30%) had persistent disease activity. The median percentage of CR per patient was 54% and no patient had JADI >0.

Conclusion: Early administration of bDMARDs and compliance to monitoring and treatment improved the long-term outcome in ERA. Axial involvement emerged as a negative prognostic factor with an increased need for bDMARDs and diminished rates of CR.

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AB0977 DISEASE COURSE AND TREATMENT RESPONSES IN JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS; A SINGLE CENTER EXPERIENCE

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Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune inflammatory disease that may cause morbidity and mortality by affecting multiple systems. The 10-20% of patients have juvenile onset and this cluster have may more severe kidney, neuropsychiatric or hematological involvement.

Objectives: The aim of this study was to assess the clinical and laboratory characteristics, disease activity, and treatment response of patients with juvenile SLE (jSLE).

Methods: This is a retrospective study involving patients between 1 July 2016 and 1 January 2020. The data of patients diagnosed with jSLE and followed up for a minimum of 6 months, were collected. The SLEDAI-2K scores at initiation and at the follow-up (1st, 3rd, 6th, and 12th months of treatment) were examined. The SLEDAI-2K score was considered to be ≤4, for disease remission status.

Results: A total of 49 children were included in to the study. The female/male ratio was 4.4/1 and the median age of the patients at the diagnosis was 13 (IQR: 11.1–15.2) years. The median follow-up of patients was 19 (IQR: 12–25) month. Four of the patients were diagnosed with monogenic SLE. Two siblings were diagnosed with c3 deficiency and two were diagnosed with familial chilblain lupus. The most common clinical findings were found musculoskeletal complaints (69.4%), malar rash (51%), oral ulcers (38.8%), and fever (30.6%), respectively in over all the group. The frequency of involvement of the system and organs was as follows; mucocutaneous 77.6%, musculoskeletal 69.4%, renal 44.9%, hematological 34.7%, serous membranes 16.3%, neuropsychiatric 12.2%, respectively. All patients had anti-nuclear antibody positivity, while 46.9% had anti-ds DNA, 14.3% had anti-Sm and 8.2% had antiphospholipid antibody positivity. While all patients received hydroxychloroquine treatment, 22.4% of the patients were received were mycophenolate mofetil, 22.4% were azathioprine, 14.3% cyclophosphamide, 12.2% methotrexate and 10.2% were rituximab. The median SLEDAI-2K score was 14 (IQR: 10–18.5) at admission, besides it was found to 6 (IQR: 4–12), 4 (IQR: 2–6), 2 (IQR: 0–6) in the 1st, 6th and 12th months of treatment, respectively. While 98% of the patients had active disease at admission, 67.3% at 1 months, 32.7% at 6 months and 22.4% at 12 months still had active disease (SLEDAI-2K >4). Patients with initially high SLEDAI-2K scores had significantly lower remission rates in the first month (p=0.003). It was observed that patients with high SLEDAI-2K scores in admission were more resistant to conventional immunosuppressive treatments and the use of rituximab was more frequent in these patients. At least one major organ (renal, hematological, neurological) were affected in 57% of patients. The remission rate of these patients at 6 months was found significantly decreased compared to the others (p <0.005). Renal biopsy was performed in 21 patients (42.9%). 12 of them had type 4 lupus nephritis (LN), 5 had type 2, 2 had type 3, and 1 had type 5. It was observed that patients with renal involvement were the group that reached remission latest.

Conclusion: The presence of high initial SLEDAI-2K scores and the major organ involvement have poor predictive value to achieve inactive disease.

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AB0978 EFFICACY OF ANAKINRA TREATMENT IN PEDIATRIC RHEUMATIC DISEASES; A SINGLE-CENTER EXPERIENCE

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Background: Anakinra, a recombinant IL-1 receptorantagonist, is a treatment option that acts byblocking the biological activity of IL-1 in autoinflammatory conditions. The diseases that the IL-1 was over expressed are the potential conditions for this treatment. Such as familial Mediterranean fever (FMF), cryopyrin-associated periodic syndrome (CAPS), and hyperimmunglobulin D syndrome (HIDS) with monogenic inheritance, and systemic juvenile idiopathic arthritis (SoJIA) or idiopathic recurrent pericarditis as non-Mendelian polygenic diseases, can be listed as examples of these diseases.

Objectives: The aim of this study was to review the efficacy of anakinra treatment in children with rheumatic disease followed in our center.

Methods: The study group consisted of children with pediatric rheumatic diseases followed up in the Pediatric Rheumatology Department of University of Health Sciences and treated with anakinra (anti-IL 1) for at least one month, between 1 July 2016 and 1 January 2020. The data of these patients were collected retrospectively. The disease activity of the patients at 3rd month and 12th month after the treatment were assessed. We aim to report our experiences of pediatric rheumatic diseases treated with anakinra.

Results: There were 28 patients treated with anakinra for the different pediatric rheumatic diseases. The diagnoses of these patients were as follows; eight were macrophage activation syndrome (MAS) complicating SoJIA, six were HIDS, four were CAPS, four were FMF, four were idiopathic recurrent pericarditis, one was deficiency of interleukin-36 receptor antagonist (DITRA), and one was undefined systemic autoinflammatory disease. 46.4% of the patients were male and 53.6% were female. The median age of diagnosis of the patients was 6.5 ((interquartile range (IQR): 4-12.7) years. The median follow-up duration of the patients was 14 (IQR: 3.7-28) months. The patients median anakinra treatment duration was 3 (IQR: 1-4) months. Fever reduced and C-reactive protein normalized within median 2 (IQR: 1-3) and 5 (IQR: 5-7) days, respectively. In the 3rd month after treatment; It was observed that 53.6% of patients achieved a complete remission (no attack was seen or MAS was improved). The frequency of attacks were decreased more than 50% in 35.7% of patients and less than 50% in 7.1%. 3.6% of patients were unresponsive to treatment. In the 12th month assessment after the initiation of treatment, it was observed that 28.6% of patients were still under anakinra treatment and in remission, 10.7% of them were in remission without anakinra treatment. In 60.7% of patients, anakinra was switch to other biological treatments for different reasons (35.7% partial response or unresponsiveness, 17.8% injection site reactions and 7.1% daily-injection difficulty). Biologic drug switch to canakinumab and tocilizumab was observed in 88.2% and 11.8% of patients, respectively. One patient developed recurrent MAS episodes when the anakinra dose was tapered, and one another patient was unresponsive to the anakinra and dead due to secondary to MAS.

Conclusion: Anakinra seems to be a successful treatment to achieve inactive disease in a significant portion of patients in the early period. The recurrence of disease attacks while drug tapering and injection site reactions were appears the main causes of treatment switch or discontinuation.

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AB0979 MEVALONATE KINASE DEFICIENCY AT TREATMENT WITH CANAKINUMAB: RARE BELATED CUTANEOUS FEATURE

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Background: Mevalonate Kinase Deficiency (MKD) is an autosomal recessive autoinflammatory syndrome. Diagnostic criteria are based in clinical and genetic features (mutations in MVK gene) and its main treatment consists of blocking IL-1[1-5].
Objectives: To describe a case-series of a rare bleated cutaneous feature.
Methods: From January 2004 to September 2019, all cases diagnosed of MKD have been reviewed.
Results: 15 patients had MKD diagnosis (11 pathogenic mutations, homozygosis or double heterozygosis). Most common symptoms were oral and genital aphthous, abdominal pain, adenopathies and recurrent fever. Mean age of diagnosis was 10,67 years old (8,67 years later from the beginning of symptoms). Mean time of follow-up was 10 years. 3 patients developed this rare bleated cutaneous feature: suppurative hydrosadenitis. When the first injury appeared, all were at treatment with Canakinumab (mean time of treatment 4 years) and had 7,67 years of MKD course. This comorbidity began as repeating abscesses in folds with apocrine glands and hair follicles (armpits, inguinal, anal and genital folds). 2 patients continued Canakinumab and 1 switched to Adalimumab because of severity of cutaneous involvement.
Conclusion: This is the first case-series showing suppurative hydrosadenitis associated to MKD that has not been described in literature. Both theories have been found: as immune-mediated disease partnering this autoinflammatory syndrome (MKD) or as adverse event of treatment (anti-IL-1, less presumable).
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AB0980 CASE-REVIEW ON FAMILIAL MEDITERRANEAN FEVER IN A SPECIALIZED CENTRE

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Background: Familial Mediterranean Fever (FMF) is a genetic autoinflammatory disorder caused mostly by mutations in MEFV gene. Its inheritance is autosomal recessive and is the most frequent periodic fever syndrome. First-line treatment is based in colchicine use, so biologics (anti-IL-1) are reserved for refractory cases[1, 2].
Objectives: To account for clinic and treatment features of patients with FMF in a specialized center as opposed to non-referent centers.
Methods: This study was developed in the Pediatric Rheumatology Service in Hospital Universitario y Politécnico La Fe de Valencia. Demographic, clinic and treatment data were collected from patients diagnosed of FMF since January 2004 to September 2019.
Results: 106 patients met last FMF criteria[3]. 55% had a pathogenic mutation in genetic analysis. 52% were female. Before 10 years old, 71% of patients had the diagnosis (51% before 4 years old). Arthralgia/myalgia (73%), periodic fever (62%) and abdominal pain (54%) were the most common symptoms. Systemic Juvenile Idiopathic Arthritis (JIA, 6), other forms of JIA (9) and vasculitis (10) were the most prevalent comorbidities. When talking about treatment, 76,4% received Colchicine (60,5% with good response), 22,6% needed a classical disease modifying antirheumatic drug (mostly Methotrexate) and 22 patients got biologic treatment (73% anti-IL-1).
Conclusion: When analyzing this case-review, JIA has a strong association with our patients, so it could explain severe disease activity and more articular involvement. This could be an illustration to the higher use of Methotrexate. Also, the most relevant symptom was arthralgia while fever is the most frequent in literature. Likewise, age of diagnosis has been earlier than other case-series (this would be more frequent in other autoinflammatory syndromes, as literature relates)[1, 2, 4].
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AB0981 VALIDATION OF THE CAREGIVERS QUESTIONNAIRE (IMPACT OF PEDIATRIC RHEUMATIC DISEASES ON CAREGIVERS MULTIASSESSMENT QUESTIONNAIRE) IN PEDIATRIC RHEUMATIC DISEASES

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Background: The CAREGIVERS questionnaire is used as a multidimension screening instrument for burden of caregivers, it allows to examine the impact of juvenile idiopathic arthritis (JIA) on several areas of the caregiver's life, looking for specific concerns and needs in which treatment could be required. This instrument has shown a good understanding among participants, reliability and consistency to measure the psychosocial and economic impact on primary caregivers of patients with JIA.
Objectives: The aim of this study is to validate CAREGIVERS questionnaire with the most common pediatric rheumatic diseases, such as JIA, systemic lupus erythematosus (SLE) and juvenile dermatomyositis (JDM).
Methods: The external validation phase of the constructed questionnaire will be carried out following Feinstein's clinimetric and psychometrics methodology, to measure the impact of the disease on the caregiver and create a risk profile for treatment detachment.
Results: A total of 200 questionnaires are applied to caregivers of pediatric patients with rheumatic diseases: 109 caregivers of patients with JIA, 28 caregivers of patients with DMJ and 63 caregivers of patients with SLE. When analyzing all the questions together, a general Cronbach's alpha of 0.6751 was obtained (Table 1).

Table 1. External validation of the Questionnaire

Dimension	Numero de Ítems	Alfa de Cronbach
I. Impacto Emocional	6	0.5669
II. Impacto Social	3	0.47
IIIA. Impacto Financiero	4	0.6736
IIIB. Impacto Laboral	3	0.3151
IV. Impacto Familiar	5	0.4948
V. Impacto en la Relación entre Cuidador-paciente	1	NA
VI. Impacto en la relación de pareja	1	NA
VII. Impacto en la Religión/Creencias/Espiritualidad	1	NA
VIII. Impacto de las Redes Sociales	4	0.6642
Total	28	0.6751

Conclusion: The CAREGIVERS questionnaire showed to be validated to assess the impact of pediatric rheumatic diseases.

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AB0982 SERUM ALBUMIN LEVELS AND DEPRESSION IN JSLE

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Background: Albumin is a negative acute phase response protein synthesized in the liver, being an important marker of inflammation. Under inflammatory conditions, the transcapillary escape rate of albumin may increase, leading to hypoalbuminaemia. Systemic lupus erythematosus (SLE) is a chronic condition involving multiple organ systems, inducing functional disability and psychological burden responsible for noteworthy depressive symptoms[1]. Depression may be related with psychosocial, environmental and biological factors, disease activity and its severity, age and sex[2]. Several studies show that immune activation and increased concentrations of positive and decreased concentrations of negative acute phase proteins are involved in the pathogenesis of depression[3]. As albumin has the capacity to bind homocysteine, lowered serum albumin levels leads to hyperhomocysteinemia, a well-known risk factor for depression. Moreover, hypoalbuminaemia decrease the availability of tryptophan, an essential amino acid from which the neurotransmitter serotonin is derived, and induce oxidative stress, which further decreases antioxidant levels in people with depression.

Objectives: To assess the association between serum albumin levels and depressive symptoms in juvenile-onset SLE (jSLE) patients.

Methods: A cross-sectional sample of jSLE patients, currently aged ≥ 16 years, completed a psychosocial assessment including quality of life (SF-36) anxiety and depressive symptoms (HADS) and cognitive assessment (MMSE), between October 2018- May 2019. Local Ethics Committee approved the study. All patients fulfilled both 2012 and 2019 EULAR/ACR classification criteria for SLE. Juvenile-onset was defined as age at diagnosis <18 years. Demographics and clinical characteristics were collected. Statistical analysis was performed with SPSS®. Variables were compared with spearman correlations tests.

Results: 30 jSLE patients were included (90%female) in the study, with median (min-max) age of 21 (16-35) years, with mean (SD) age of diagnosis of 15.8 ± 2.1. Median albumin serum level was 41.7 (16.7-46.3) g/dL. Psychosocial assessment revealed a mean (SD) score in HADS - Depression of 3.9 (3.3), HADS - Anxiety of 9 (4.3), MMSE of 27.7 (1.8), Physical health SF-36 of 66.8 (9.9) and Mental health SF-36 of 68.9 (17.5). 23.3 % jSLE showed mild cognitive impairment, 63.3% anxiety and 13.3% depression. We observed significant inverse linear relationships between serum albumin levels and depressive symptoms score (p=0.042, ρ=-0.380) and with anxiety symptoms score ((p=0.029, ρ=-0.406). No significant correlations were detected between albumin serum concentrations and cognitive assessment.

Conclusion: Our findings are consistent with studies previously reporting the potentially protective effect of high serum albumin levels on mental health in different populations. A possible inflammation related aetiology for depression in jSLE patients is highlighted, further explained through the protective roles played by albumin in inflammation, infection, and oxidative damage.

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AB0983 LIPID METABOLISM AND DISEASE ACTIVITY IN JSLE PATIENTS

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Background: Systemic lupus erythematosus (SLE) is an autoimmune systemic disease associated with premature atherosclerosis. Risk factors include dyslipoproteinemia, inflammation, oxidized low-density lipoprotein (LDL), hyperhomocysteinemia and antiphospholipid antibodies. Hyperlipidemic condition is being reported to promote the production of proinflammatory cytokines such as IL-1β, IL-6, and IL-27 and lowering blood lipid levels improves the disease. Oxidative stress is elevated, mainly due to mitochondrial dysfunction, further disrupting lipid metabolism. Some drugs also have an impact on lipid profile, such as chronic steroid use, which worsens LDL, HDL, and TG levels.

Objectives: To assess the relationship between lipid profile and disease activity in juvenile SLE (jSLE) patients.

Methods: Retrospective study of jSLE patients, fulfilling both 2012 and 2019 EULAR/ACR classification criteria for SLE. Juvenile-onset was defined as age at diagnosis <18 years. Demographics and clinical characteristics were collected. To evaluate the activity of jSLE, the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) was used. Statistical analysis was performed with SPSS®. Spearman's rank non-parametric test or Pearson's parametric test were used to assess the bivariate correlation for inflammatory and metabolic variables. P value <0.05 was considered significant for all the statistical tests.

Results: 35 patients were included, with current median (min-max) age of 22 (16-35) years, mean (SD) age of diagnosis of 15.8 (2.4) years; 91.4%female. Median ESR was 19 (2-75) mm/h, CRP 1.65 (0.1-9.6) mg/L, albumin 41.6 (16.7-46.3) g/L, proteinuria 0.2 (0-3) g/dL, leukocyturia 0 (0-1362.7)/uL, erythrocyturia 0 (0-501.9)/uL and anti-double stranded DNA 89.3 (10-800) U/mL. Mean C3 was 102.1 (21.6), C4 17.1 (7.4) mg/dL and creatinine 0.63 (0.1) mg/dL. Median SLEDAI was 2 (0-12). All were ANA positive, 40 % positive for antinucleossome antibodies, 25.7% anti-ribossomal P protein antibody, 11.4% anti-Sm, 8.6% autoantibodies against *β2-glycoprotein* I, 8.6% anti-cardiolipin, 14.3% lupus anticoagulant, 37.1% anti-SSA and 8.6% anti-SSB. Articular manifestations were present in 48.6%, mucocutaneous in 77.1%, haematological in 45.7%, lupus nephritis in 42.9%, serositis in 8.6% and pulmonary interstitial disease in 2.9%. Mean (SD) total cholesterol values (TC) was 165.5 (44.7) mg/dL and LDL 94.5 (29.9) mg/dL. Median high-density lipoprotein was 52 (28-92) and triglycerides (TG) 81.5 (41-253) mg/dL. Median daily prednisolone dose was 5 (0-40) mg. 88.6% were treated with hydroxychloroquine, 31.4% with mychophenolate mophetil and 14.3% with azathioprine. TC was negatively correlated with serum albumin (p=0.043, rho=-378) and positively with SLEDAI (p=0.032; rho= 0.392), proteinuria (p=0.009; rho= 0.469) and leukocyturia (p=0.031; rho= 0.394). A positive correlation was found between LDL and proteinuria (p=0.043; rho= 0.385) and between TG and CRP (p=0.001; rho= 0.575). TG were also positively correlated with prednisolone daily dose (p=0.035; rho= 0.394). Mean LDL was higher in anti-Sm positive patients (p=0.022). No differences were found regarding anti-phospholipids antibodies. Nephritic lupus patients had worse lipid metabolism, but this did not reach statistical significance.

Conclusion: In out cohort, increased expression of TC, LDL and TGs is associated with disease activity in SLE. As expected, higher doses of prednisolone also correlated with lipid metabolism.

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AB0984 BIOLOGICAL THERAPIES IN JUVENILE IDIOPHATIC ARTHRITIS: ARE THERE ANY DIFFERENCES BETWEEN CATEGORIES?

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Background: Juvenile Idiopathic Arthritis (JIA) is a heterogeneous group of pediatric diseases. Different response to biological treatment (BT) has been reported according to disease subtype.
Objectives: To analyze the prescription and withdrawal of BT in JIA patients with focus on JIA category.
Methods: A retrospective observational study was conducted on JIA patients followed in a referal hospital and who had received at least one BT between 1999 and 2019.
Results: 130 JIA patients were analyzed: 29 (22,4%) were Oligoarticular Persistent (OligP), 22 (16,9%) Enthesitis related Arthritis (ERA), 20 (15,4%) Systemic (sJIA), 19 (14,6%) Polyarticular RF- (PolyRF-), 14 (10,8%) Polyarticular RF+(PolyRF+), 13 (10%) Oligoarticular-Extended (OligE), 11 (8,4%) Psoriatic Arthritis (APso) and 2 (1,5%) Undifferentiated (Und).
The main characteristics are summarized in table 1.
The first line BT most frequently indicated was Etanercept up to 40% in all the categories except for ERA, where the most frequent BT was Adalimumab and sJIA, where the most frequent BT was Anakinra. The time between diagnosis and start of BT was different among the categories (p=0,007). In the Und category, the time until BT was the shortest (median: 1 month), since both patients had coxitis, followed by APso [median: 9 months IQR(1-57)] and sJIA [median: 17,5 months IQR(0,3-146,8)]. The survival of the first BT was different among the categories (p=0,006): 94,7% of the ERA continue receiving the first BT, followed by 76,2% of OligP and 50% of PolyRF+ and APso. Only 42% of sJIA continue on the first BT prescribed [up to 53,3% were TNF inhibitors (TNFi)]. The categories with less retention of the first BT were: OligE (25%); PolyRF- (27,3%) and Und (0%). The most frequent cause of discontinuation, among these categories, was secondary failure.
In the survival analysis between categories, there were differences on OligP (p=0,004), OligE (p=0,042) and PolyRF- (p=0,017). Tocilizumab and Adalimumab were the BT with highest survival with regards to Infliximab, Etanercept, Rituximab (OligE, PolyRF-), Abatacept (OligE, PolyRF-) and Certolizumab (OligP). The survival rate of IL1 inhibitiors and IL6 inhibitiors was higher regarding to TNFi in sJIA patients (p=0,013).
Conclusion: Taking into account JIA category is mandatory to choose BT and to understand the response and discontinuation of BT. OligE and PolyRF - showed a high rate of change of the first BT related to secondary failure of Etanercept and Infliximab when compared to Adalimumab and Tocilizumab, as described in the survival analysis. The category with the highest retention of the first BT was ERA. UND patients started sooner BT due to the presence of coxitis. In sJIA, IL1 inhibitors and IL6 inhibitors were superior to TNFi in the survival analysis, as reported in existing literature.

Table:

Table 1	OligP	ERA	sJIA	PolyRF-	PolyRF+	OligE	Apso	UND
Sex,n% M F	 4(13,8) 25(86,2)	 17(77,3) 5(22,7)	 11(55) 9(45)	 2 (10,5) 17(89,5)	 2(14,3) 12(85,7)	 1(7,7) 12(92,3)	 4(36,4) 7(63,6)	 1(50) 1(50)
Age at diagnosis me, IQR	4 (2,6-5)	12 (9,8-15)	7 (3-13)	8 (2-13)	12 (8,5-15)	3,5 (2-8,3)	12 (3-15)	12,5
Uveitis,n%	12(41,4)	7(31,8)	0(0)	3 (15,8)	0 (0)	3(25)	2 (18,2)	1(50)
ANA, n (%) ACPA, n (%) B27, n (%)	22(75,9)	 18(81,8)		8 (42,1)	12 (85,7) 9(64,3)	9(75)	5 45,5) 3(27,3)	
BT lines: n	1ª: 29 2ª: 11 3ª: 1	1ª: 22 2ª: 2	1ª: 20 2ª: 10 3ª: 5 4ª: 1 5ª: 1	1ª: 11 2ª: 9 3ª: 6 4ª: 3	1ª: 14 2ª: 7 3ª: 2 4ª: 2	1ª:13 2ª: 9 3ª: 2 4ª: 1 5ª: 1	1ª:11 2ª: 5 3ª: 4 4ª: 3 5ª: 1	1ª:2 2ª:2

APso, Psoriatic Arthritis; BT, biological treatment; ERA, Enthesisits related Arthritis; F, female; M, male; OligE, Oligoarticular-Extended; OligP, Oligoarticular-Persistent; PolyRF-, Polyarticular RF-; PolyRF+, Polyarticular RF+; sJIA, Systemic JIA; Und, Undifferentiated

Disclosure of Interests: None declared
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AB0985

THE EFFECT OF GENDER ON CHILDREN AND ADOLESCENTS WITH FAMILIAL MEDITERRANEAN FEVER

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Background: In the literature, it was reported that children with with Familial Mediterranean fever (FMF) have lower functional capacity and muscle strength than healthy children. With reduced functional capacity, daily activities are negatively affected. The individual starts to adopt an inactive lifestyle and decreases in muscle strength are observed. A vicious circle occurs and results in exacerbation of symptoms and worse quality of life.
Objectives: The aim of this study is to investigate the effect of gender on dynamic muscular endurance, physical activity and quality of life with FMF.
Methods: Forty-eight children and adolescents (26 girls, 22 boys, mean age=12.43±3.04 years, age range=7-18 years) were included. Exclusion criteria:The presence of another disease. Intraarticularsteroid injection or surgery in any joint in the last 3 months. Evaluations were made by the same pediatric rheumatologist and physiotherapist by face to face interview method. Dynamic muscle endurance was evaluated by use of curl up test (30 sec), push up test (30 sec) and one-legged stationary hop test (15 sec); physical activity level by Physical Activity Questionnaire and quality of life by Pediatric Quality of Life Inventory (PedsQL) 3.0 Arthritis Module. Physical Activity Questionnaire contains nine items and evaluates physical activities in last seven days and frequency of these activities. As score increases, level of physical activity increases. In this study, child and parent forms of PedsQL were used to evaluate the quality of life. High scores mean high quality of life. Independent Samples Test was used in the analysis because the data fit the normal distribution.
Results: Difference was significant in Physical Activity Questionnaire (p=0.028) in favor of girl gender whereas in child form (p=0.017) and parent form (p=0.040) of PedsQL (p=0.003) in favor of boy gender.
Conclusion: We see that the physical activity are lower in children and adolescents with FMF who have a gender of girls and, accordingly, lower quality of life. Therefore, we believe that these individuals should increase their physical activities.
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Table 1. Demographic characteristics

Variables	Girls (n=26)	Boys (n=22)
	M±SD	M±SD
Age (years)	12.96±2.91	11.86±3.24
Body weight (kg)	42.76±12.55	40.17±11.89
Height (m)	1.50±0.13	1.48±0.15
BMI (kg/m^2)	18.25±2.90	17.85±3.39
Age of onset (years)	7.57±4.07	7.22±3.99
Dose of colchicine (per day)	1.18±0.60	1.63±0.68
Duration of treatment (years)	5.30±2.90	4.61±3.34
C-reactive protein (mg/dl)	0.88±2.28	1.25±2.91
Pras et al severity score	6.35±2.68	5.31±2.60
	n (%)	n (%)
FMF in the family (Yes/No)	4(15.4)/16(61.5)	12(54.5)/10(45.5)
Arthritis (Yes/No)	9(34.6)/17(65.4)	6(27.3)/16 (72.7)
Arthralgia (Yes/No)	20(76.9)/6(23.1)	14(63.6)/ 8(36.4)
Knee (Yes/No)	6(23.1)/20(76.9)	7(31.8)/15 (68.2)
Elbow (Yes/No)	1(3.8)/25(96.2)	0(0)/22(100)
Ankle (Yes/No)	6(23.1)/20(76.9)	7(31.8)/15(68.2)
Hand (Yes/No)	1(3.8)/25(96.2)	1(4.5)/21(95.5)

Table 2. Comparison of data in terms of gender

Variables	Girls (n=26)	Boys (n=22)	p*
	M±SD	M±SD	
Curl Up Test (repeat)	10.70±3.58	12.80±3.66	0.075
Push Up Test (repeat)	10.55±5.06	11.75±6.29	0.511
One-legged Stationary Hop Test (repeat)	37.60±12.74	35.35±6.02	0.480
Physical Activity Questionnaire	16.93±5.70	20.70±5.77	**0.028**
PedsQL- child form	19.15±13.48	10.68±9.38	**0.017**
PedsQL- parent form	22.30±17.85	13.04±11.06	**0.040**

Disclosure of Interests: None declared
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AB0986

NT-PROBNP LEVEL IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: The defeat of the cardiovascular system is considered a proven comorbid state in rheumatic diseases, including rheumatoid arthritis in adults. One of the markers of the cardiovascular failure formation is BNP, namely, its N-terminal inactive fragment (NT-proBNP76), which accumulates in specific granules of cardiomyocytes. Its diagnostic value increases with the appearance of minimally expressed symptoms. The long-term course of JIA is also characterized by changes in the state of the cardiovascular system, and there may be no visible clinical manifestations. For their diagnosis a 6-minute walk test is widely used, including in children.

Objectives: To study the content of NT-proBNP in patients with juvenile idiopathic arthritis and compare with the level of exercise tolerance.

Methods: 10 patients with JIA (9 girls, 1 boy), average age 12.78 ± 0.95 years, were examined. All children had a polyarticular RF negative subtype of JIA with a disease duration of more than three years (average disease duration 69.56 ± 17.07 months), received basic methotrexate therapy and did not have dysfunction of the lower extremities joints. The control group included 7 healthy children, comparable by sex, average age 14.25±0.73 years. An ECG, an ultrasound scan of the heart, and a 6-minute walk test (6MTX) were carried out with determining the distance traveled (6MWD) and the increase in heart rate. The level of the N-terminal polypeptide of cerebral natriuretic hormone (B-type) (NT-proBNP) was determined in the morning, after waking up, and studied by competitive immunoassay on an IMMULITE 2000 analyzer ("Siemens").

Results: In children with JIA a decrease in myocardial contractility was not detected. Left ventricular ejection fraction (62.17±0.83% (60.02 – 64.02) versus 69.84 ± 0.85% (62.3 – 80.3), p <0.05) in children with JIA were within normal limits, but significantly lower than in the control group. According to the results 6MTX indicator 6MWD in JIA-patients was 490.51 ± 11.40 m and in the control group 516.85 ± 8.84 m (p <0.05) and heart rate growth was 27.75 ± 2.30% versus in the control group (37.38 ± 3.86%), p <0.05. A negative correlation between the increase in heart rate and the duration of the disease was found (r = -0.7, p = 0.05). The level of NT-proBNP in patients with JIA was within physiological values and amounted to 47.5 ± 14.09 pg / ml (20 – 128 pg/ml), but this was higher than in children of the control group (20.29 ± 0.29 pg / ml (20-22 pg/ml), p <0.05). A high correlation was found between 6 MWD and NT-proBNP level (r = 0.8, p <0.03).

Conclusion: In children with JIA there is a decrease of the exercise tolerance that increases with the duration of JIA on the background of preserved myocardial contractility. This is accompanied by a higher basal NT-proBNP level than in healthy children.

Disclosure of Interests: None declared

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AB0987 STUDY ON THE FACTORS AFFECTING THE FINAL ADULT HEIGHT IN JUVENILE IDIOPATHIC ARTHRITIS

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Background: Juvenile idiopathic arthritis (JIA), a chronic inflammatory disease involving limited joints and/or constitutional symptoms in childhood or adolescent, might affect body height and result in short stature in adulthood. Well-controlled disease activity is beneficial in improving growth impairment in JIA patient.

Objectives: To identify any factors that influence final adult height in the patient with juvenile idiopathic arthritis.

Methods: We retrospectively reviewed the medical records of JIA patients between 2009 to 2019 in National Taiwan University Hospital. The diagnosis of JIA was according to the International League of Associations for Rheumatology (ILAR) criteria. Personal history, laboratory reports, and medication were analyzed. The difference between final adult height and target height was calculated in each patient. We defined whose final adult height higher than target height as positive group and the others as negative group. A cox univariate proportional hazards model was applied to compare the variables between these two groups.

Results: Total 120 patients are collected. There are 74 (61.7%) and 46 (38.3%) cases in the positive and the negative group, respectively. The mean onset age of disease is 11.78 3.78 in positive group and 10.83 4.04 in negative group. Male is more than female in both groups, with a ratio of 1.7:1 and 2.7:1 respectively. Enthesis-related arthritis accounted for the most in positive group, however, in negative group, oligo-arthritis was the most common type. There are slightly more patients having received biologics in positive group than negative group without significance (64.8% vs. 54.3%, *p*=0.33). Among the patients treated with etanercept, those in the negative group had a significantly younger age when they started the treatment compare to the positive group (11.83.1 vs. 13.9 3.1, *P* =0.01). The patients in positive group had significantly higher final adult height (171.08.7 vs. 162.9 8.1, *P* < 0.001). The univariate analysis showed that the age when etanercept treatment started was associated with the occurrence of a negative difference between final height and target height (odds ratio=0.80, 95%CI=0.67-0.96, *P*=0.02).

Conclusion: In JIA patients, 38.3% of them had a negative difference between final adult height and target height. The subtype might play a critical role in affecting the growth of patients. A younger age when the child received etanercept was associated with a lower attained adult height than target height, however, it needs further analysis on the medication of these children.

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AB0988 CLINICAL FEATURES AND ANALYSIS OF MEFV GENE IN 31 PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER (FMF)

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Background: FMF is recessive systemic autoinflammatory disorder characterized by recurrent fever, peritonitis, pleuritis, pericarditis and arthritis accompanied with headache and abdominal pain. Mutation of MEFV gene encoding pyrin resulted in inflammasome activation and the uncontrolled production of IL-1β. Overview of pathogenesis, clinical features and management in Japanese patients with FMF had been reported. However, the differences of clinical features between mutated and non-mutated of MEFV still remain unclear.

Objectives: We have analyzed 31 Japanese patients with FMF in Gifu district to clarify the association between various clinical features and mutation of *MEFV.*

Methods: Genomic DNA were purified from white blood cells in 31 FMF patients, and mutated MEFV has been explored. We have analyzed *MEFV, TNFRSF1A, MVK and NLRP3 genes* in 31 patients with FMF except for 1 patient. Therefore, we excluded another autoinflammatory diseases such as TNF receptor-associated syndrome (TRAPS), mevalonate kinase deficiency and cryopyrin-associated periodic syndrome. Clinical symptoms and laboratory data were analyzed around onset time. Each patient had been treated with colchicine (0.5-2 mg).

Results: Characteristics of Patients with FMF (22 female/9 male) were as follows; Onset time were 0-56 years-old (21.4 ±11.8), and Frequencies of clinical symptoms such as periodic fever, headache, abdominal pain, arthralgia, chest pain, cervical lymph nodes swelling, and myalgia were 31/31, 9/31, 8/31, 6/31, 5/31, 3/31 and 1/31, respectively (double symptoms were observed). Patients with FMF were divided into 3 groups as follows; Patients with typical compound heterozygous mutations of MEFV (E148Q /M694I) which indicated exon 10 mutation, were 5 cases (G1). Patients with atypical mutations, except for exon 10, such as 133G>A in 3UTR, exon 1 (E84K), 2 (L110P, E148Q), 3(R202Q, P257L, G304R, P369S, R408Q), 5(S503C) and 9(I591M) were 13 cases (G2). Patients with no mutations in MEFV gene were 12 cases (G3). There were no significant differences of age at first visiting hospital (FV)and onset age of fever attack (O) (FV: 29.0 ± 15.6, 27.1 ± 12.5 years-old (yo) and 34.7 ± 12.7 yo, O: 21.0 ± 17.6 yo, 17.8 ± 12.1 yo and 25.2 ± 6.5). But significant differences in duration of fever attack (D) and frequency of fever attack (FF) between G1 and G2 or G3 were observed as follows; (D: 2.2 ± 0.4 days vs 5.5 ± 3.1 days, P<0.05, and 3.8 ± 1.7 days), FF: 0.72 ± 0.3/

month (M), 1.24 ± 1.1/M, and 1.5 ± 0.7/M vs group1, P<0.05), respectively. Laboratory examinations such as WBC, CRP and serum amyloid A (SAA) at fever attack were not significantly different between 3 groups. All of those patients were effective for colchicine treatment except for 2 patients in group 1 because of loss of hair, severe diarrhea and liver dysfunction due to side effects of colchicine. Finally, 4 patients in G1and G2 received canakinumab treatment. Patients with *MEFV* mutations have no family histories. Mutations of E148Q were found in 12 patients (40%).

Conclusion: We have examined association between clinical features and mutations of MEFV in 31 patients in Gifu district, suggesting that duration of fever attacks and frequency of fever attacks in G1 are significantly shorter than G2 and G3, respectively in Japanese patients with FMF. Mutations of E148Q in exon 2 were observed in 16-23 % of normal Japanese patients, indicating that E148Q is the polymorphism or accelerating factor.

Disclosure of Interests: None declared

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AB0989

TUBERCULOSIS RISK IN CHILDREN WITH RHEUMATIC DISEASES TREATED WITH BIOLOGIC DISEASE MODIFYING ANTI-RHEUMATIC DRUGS

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Background: Chronic rheumatic diseases entail the use of biologics in children. Immunosuppressive effects of drug therapy put children at risk of various infections. Tuberculosis (TB) is a leading chronic infection in certain parts of the world. Recent estimates suggest the prevalence of TB in India to be 3.2 cases per thousand population[1].

Objectives: Thus we reviewed the prevalence of Tuberculosis amongst children with various rheumatic disorders treated with different biologics.

Methods: The search strategy for writing review articles proposed by Gasparyan et al[2]. was followed. Articles available on MEDLINE and Scopus, published on or after January 1, 2010 to 1 October 2019, were reviewed. (Figure 1) Details on Tuberculoisis and disease variables were collected (Table 1).

Table 1. Data extraction form

Data extraction form
Drug
Study characteristics
Country of study
Type of study
Year
Author
DOI
Outcomes reported
Number of participants
Total number of Tuberculosis reported
Disease variable
Disease or type of JIA (PA-RF+, PA-RF-, OA, OA extended, ERA, jspA, SJIA, PsA, Undifferentiated, only uveitis)
Duration of JIA before biologics (Median, IQR)
Duration of follow-up (Median)
Exposure in patient years
Infectious events
Total no of infection events
Major/ serious Infections- Number of events
Opportunistic infections
Minor Infections- Number of events
Treatment received
Biologic Doses received
Duration of biologic treatment
Concomitant drugs
Steroids
Other

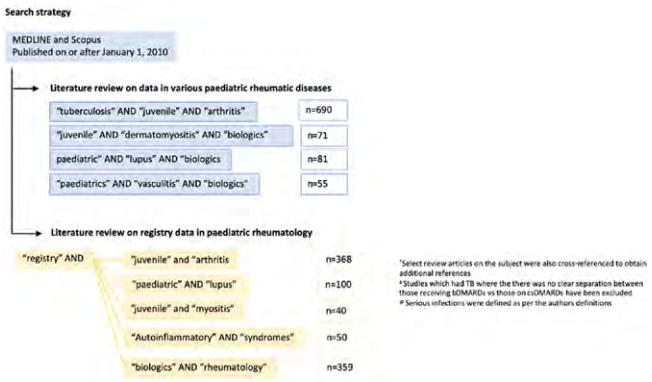


Figure 1. Number of articles obtained after searching through MEDLIEN and Scopus.

Results: Data on infections in children with rheumatic disorders on biologics is scant (Table 2, Figure 2A). Tuberculosis was reported on occasion (0-5 cases per country) in the developed world with the highest Tuberculosis reports being from Turkey (Figure 2B). There is particular paucity of data from regions with highest number of incident cases or prevalence of tuberculosis more than 100 per 10 000 population (figure 2C, D).

Table 2. Summary of data on tuberculosis in paediatric rheumatology with various biologics

	JIA	Lupus	Myositis	Autoinflammatory syndromes	Vasculitis
Infliximab	783(A) 547(B)	0	0	0	10(C)9(B)
Adalimumab	2925 (A) 489(B)	0	0	0	1(B)11(C)
Etanercept	6974 (A) 2019(B)	0	0	0	1(C)
Certolizumab	37 (A)0(B)	0	0	0	0
Golimumab	224 (A) 3(B)	0	0	0	0
Rituximab	107 (A) 51(B)	75(B)	48(E) 185(C)	0	3(C)
Belimumab	0(A) 0(B)	39(B)	0	0	0
Anakinra	471 (A) 63(B)	0	0	29(A) 27(B)1(D)	0
Canakinumab	196 (A)	0	0	4(A)109(E)	0
Tocilizumab	998 (A)	0	0	0	2 (B) 9(C)
Abatacept	521 (A)	0	0	0	0
Combination of anti TNFs	3(A)	0	0	0	0

A: Registry data, B: Cohort, C: Case series, D: Anecdotal reports E. Trials

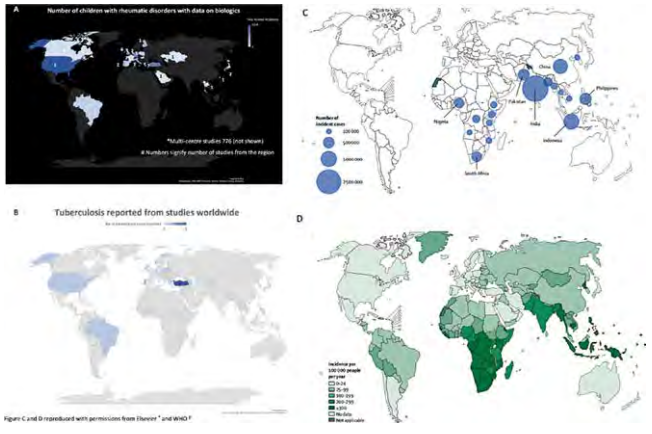


Figure 2 A. Data available on children with pediatric rheumatic disorders on biologics B. Number of Tuberculosis cases reported from studies summarized in figure 2A C. Number of cases worldwide* D. Global incidence of Tuberculosis per 10000 people#

Retrospective studies of duration 10 m- 10years suggest that TB risk is minimal in pediatric rheumatology patients on biologics in low TB incident areas. However, most prospective studies suffer from short observation period (Table 2). Most registries focus on response to therapy rather than complications.

Conclusion: TB risk is minimal with biologics use in peadiatric rheumatology in areas with low TB incidence (<99 cases per 10 000 population). However, most prospective studies are hampered by short observation period. There is

insufficient data to establish safety in countries with high background prevalence of TB. Long term prospective national registries are needed from in TB countries with focus on risk factors for infections.

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AB0990 SECONDARY SUBACUTE ARTHRITIS IN CHILDREN WITH DIASTROPHIC DYSPLASIA AND RMED

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Background: Progressive osteoarthritis is common in skeletal dysplasias. In the most of these disorders progress is relatively slow and acute pain with severe disability secondary to osteoarthritis is rare during childhood. Diastrophic dysplasia and rMED are quite unique among other skeletal dysplasias for secondary subacute arthritis (SSA). Protracted course of SSA can mimic JIA.

Objectives: To analyse incidence and features of SSA in group of patients with DD/rMED.

Methods: We retrospectively analysed for SSA our series of 39 patients with DD/rMED. Clinical, radiological and laboratory data were collected. Clinical assessment included pain (VAS), ROM (range of motion) and postural/walking disturbances. Radiological type by Yasunaga classification, neck-shaft angle (NSA) and articulo-trochanteric distance (AT distance) were estimated. MRI data regarding cartilage damage, joint effusion and bone marrow condition were noticed. Biomarkers of inflammation and immune response (ANA, RF, vimentin antibodies) were assessed in blood samples.

Results: We identified 17 patients with hip joint SSA among 39 patients with DD/rMED (43%). Bilateral involvement was identified in 13 children with asynchronous appearance in all cases (from 2 to 18 months before the symptoms on the other side). Trauma (including iatrogenic damage during physiotherapy) preceded SSA in 9 cases. Pain, limited range of motion, limping and antalgic posture throughout the day were noticed in all the cases. Duration of these symptoms was from 4 weeks to 9 months. Progressive phase (increasing symptoms) took from 2 weeks to 4 months. General laboratory data were normal or indicated moderate inflammatory response without any specific changes. Radiolodgical data shows predictive sighs like NSA<110°, AT distance <10mm, fair or poor congruency by Yasunaga classification. Also radiological data demonstrated progressive subluxation with narrowing of articular space, osteoporosis, subchondral cysts.

MRI revealed pseudo-erosive damaged cartilage in contact area with joint effusion and bone marrow oedema. Total cartilage matrix also visualized like intermittent and multi-layered = erosive-like chondrolysis (defective articular hyaline cartilage) in 11 patients (65%).

Management included bed rest or partial weight bearing. NSAID were prescribed for 2-4 weeks with following usage according to the symptoms. Physical therapy to maintain range of motion was provided. One patient was operated (containment surgery for subluxation). In follow-up (2-7 years) 12 patients were painless at the daily life. 4 patients had intermittent pain and one patient (operated) - daily moderate pain. Range of motion was restored in 11 patients. Those patients who underwent in-hospital rehabilitation immediately after appearing of the symptoms demonstrated better outcome.

Conclusion: SSA is typical for DD/rMED and leads to remarkable disability. Early recognition and non-surgical management are important for recovery. The quick reversibility of the clinical picture arthritis against the background of a short course of NSAIDs and rehabilitation is a characterized of non-autoimmune secondary inflammatory process (SSA). SSA not requires *anti-rheumatic treatment in children* with DD/rMED.

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AB0991 EPIDEMIOLOGY AND CLINICAL FEATURES OF CHRONIC JOINT PAIN IN CHILDREN AND ADOLESCENTS

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Background: Arthralgia in children for many years continues to maintain the status of the most common symptom of rheumatic diseases. However this symptom should not always be interpreted as a manifestation of arthritis. Well known that arthralgia in growing children is a frequent problem which can be caused by pathological or innocuous process.

Objectives: *The goal of this study was to* analyze the structure of childhood arthralgia.

Methods: We *carried out* a *retrospective review of 600* children who applied to the outpatient department of the institute with a complaint of pain lasting longer than two months in one or more joints. The clinical, instrumental and laboratory pictures were studied. Special attention was paid to certain aspect of joint pain by the child or his parents. The data obtained made it possible to systematize and detail the nature of the articular pathology in children of various age groups.

Results: All children were divided into several groups based on their anatomical and physiological characteristics of osteoarticular system: the first group consisted of 240 children under 6-7 years old, the second group – 220 children 7-12 years old, the third group – 140 children over 12 years old.

Research suggests that more preschool children were experience bilateral lower extremity pain by "post-walk genesis" due to natural hypermobility, immaturity of sensory innervation of the joints and imbalance of the leg muscles (e.g. growing pains). The second most common cause was joints pain associated with infectious factor (post-infectious genesis or chronic foci of infection). The frequency of juvenile arthritis and other rheumatic diseases in children of this age group did not exceed 10%. Special attention was paid to nightpain with fever and changes in blood tests to exclude malignancies manifestation and other tumors (less 5%).

The most common causes of joint pain of school-age children were hypermobility syndrome and enthesopathy (primary, secondary). Secondary enthesopathy were result of changes in nutrition, rapid growth and excessive exercise. Also enthesopathy were manifestation of endocrine, gastrointestinal or infectious diseases. The proportion of children with the onset of chronic inflammatory arthropathy also did not exceed 10%. Hypermobility child's syndrome was characterized by harmless pain, linked to physical activity (less morning stiffness).

Over the past decade, we've seen a gradual *increase in the number of children* with diagnosed patellofemoral pain (non-traumatic) and mediopatellar plica syndromes (95% were girls). In most cases children was complicated by syndrome of increased anxiety. Cases of apophysitis as cause of chronic arthralgia were over 15%. The share of true chronic inflammatory arthropathies, including spondylitis, in children of this age group did not exceed 10%. Fibromyalgia were diagnosed less 5%.

Conclusion: Despite continuous improvements in examination technique and image quality there is no universal test to diagnose cause of childhood arthralgia. Age features, individual nature of pain perception, the high frequency of incomplete and transient forms of arthropathy, cases atypical joint diseases have been intriguing problems for diagnostic pathology. Integrated assessment modelling framework of the clinical and instrumental pictures with understanding of the anatomical and physiological characteristics of childhood will help identify the true cause of chronic musculoskeletal pain. there is no single test to diagnose CA

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AB0992 CONNECTING SLEEP QUALITY, PAIN AND MOOD DISTURBANCES IN JUVENILE FIBROMYALGIA

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Background: Subjective sleep problems, including difficulties falling asleep, waking up, un-restorative sleep and daytime sleepiness are highly prevalent in patients with juvenile fibromyalgia (JFM). Sleep disturbances has been considered a consequence of severe pain and depression, but also in healthy individuals sleep deprivation is also a risk factor for the development of chronic widespread pain, tenderness and fatigue, suggesting the important role of sleep in pain control and in the pathophysiology of fibromyalgia.
Objectives: To estimate the incidence of polysomnographic alterations in JFM and to explore the relationship between sleep problems and the musculoskeletal pain, fatigue and mood and anxiety disorders.
Methods: 21 patients (M 3; F 18; mean age 16,1) with JFM were included. The objective sleep quality was measured by overnight polysomnography (PSG) (using the EMBLETTA MPR PG device). PSG data were compared to age and sex-matched controls. The subjective sleep disturbances were assessed by the Sleep Condition Indicator (SCI). Musculoskeletal symptoms were evaluated by using the widespread pain index (WPI). Pain intensity was evaluated on a 0-10 visual analogical scale (PVAS). Fatigue was assessed by using the Symptom Severity (SS) questionnaire. Mood and anxiety disorders were evaluated by using the Children Depression Index (CDI) and the Multidimensional Anxiety Scale for Children (MASC). Comparison of categorical data was performed by means of the Fisher's Exact test. The relationship between sleep quality and clinical symptoms were assessed using Spearman's rank order correlation coefficient (rs). All statistical test were 2-sided and p values less than 0.05 were considered statistically significant.
Results: Nineteen out of 21 (90.5%) patients complained subjective sleep disturbances and un-restorative sleep. Seven out of 21 (33.3%) patients had mood and anxiety disorders. Eight out of 21 patients (38.1%) showed an electroencephalographic pattern of alpha wave intrusion in slow wave sleep (SWS). SCI was significantly correlated to CDI score rs -0,775 (p≤0,0001), MASC 0,61 (p=0,005), WPI -0,731 (p=0,001), SSI 0,492 (p=0,038), PVAS -0,590 (p=0,006).
Conclusion: A substantial percentage of JFM patients experience sleep disturbances, which are, correlated with the severity of the muscolskeletal sympotms and mood and anxiety disorders. One third of JFM patients have alpha intrusion in the SWS. The important role of sleep in pain control suggests that the development of treatments to improve sleep quality may lead to more effective management of fibromyalgia in the future.
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AB0993 A CASE SERIES OF KAWASAKI DISEASE FROM KENYA

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Background: Kawasaki disease (KD) has been described across the globe, including the African continent, but none yet from Kenya.
Objectives: To describe the clinical features and management strategies of pediatric patients diagnosed with Kawasaki Disease at a tertiary referral hospital in Kenya.
Methods: A retrospective chart review was undertaken for the period January 2013 to December 2017 for all pediatric patients admitted at Aga Khan University Hospital Nairobi, Kenya. All medical records with a discharge diagnosis of Kawasaki disease were reviewed, de-identified and data extracted using a data collection tool.
Results: Among the 15 cases identified, 8 (53%) had complete KD. The mean age was 1 year 10 months with a slight increase in males (53.3%). The mean duration of symptoms at diagnosis was 7.2 days (range 1-11 days). Fourteen patients (93.3%) received both intravenous immunoglobulin and aspirin but dosing varied from high dose aspirin (80-90 mg/kg/day) to low dose aspirin (3 mg/kg/day). Baseline cardiac evaluations were done among these 14 (93.3%) and one patient was found to have bilateral dilated coronaries. Only 5 patients (33.3%) had repeat echo examinations within 6 weeks after diagnosis all of which were normal.
Conclusion: The challenges faced in the management of KD in Kenya include awareness of the disease, access and expertise to pediatric echocardiography, follow-up, access and cost of IVIG. Increasing awareness and improving health care resources is important in improving outcomes of KD in Kenya.
Keywords: Kawasaki Disease, Pediatric Rheumatology, Kenya, Global Health, Vasculitis
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AB0994 NEW ALTERNATIVE IN THE TREATMENT OF PATIENT WITH MUTATION OF GEN LACC1

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Background: Few patients have been described in the literature with mutations in the Lacasa Domain containing one (LACC1) gene. Its clinical presentation usually associates sustained systemic inflammation associated with chronic polyarticular erosive arthritis. Until now, there have been multiple treatments described to try to control the disease, however, they are generally unsuccessful in the long term.
Objectives: Describe the clinical course of a patient as well as the different treatments used
Methods: Clinical chart review
Results: Female 18-year-old born from a consanguineous Moroccan couple. Mother, brother and sister with similar conditions. She started at 3 years with fever, anemia, intense elevation of acute phase reactants and symmetric polyarthritis (knees, elbows, carps, shoulders, hands and ankles). Subsequent whole exome sequencing identified c.128_129delGT mutation in the LACC1/FAMIN gene. During the course of her illness, she has received treatment with oral, intravenous and infiltrated corticosteroid, methotrexate and etanercept, without getting adequate control of the disease. In 2016, she started treatment with tocilizumab (8 mg / kg every two weeks), obtaining an acceptable control of the disease (requiring periodic infiltrations every 2-3 months due to persistent arthritis). Nonetheless, in April 2019, she consulted for clinical worsening of the arthritis and laboratory test (C reactive protein 99.7 mg / L, erythrosedimentation rate 53 mm / h, leukocytes 13,500/µL and neutrophils 10,930/µL). At that time, she discontinued therapy with tocilizumab and started tofacitinib 5 mg every 12 hours with good evolution. Since its introduction, it has not required joint infiltration again and the inflammatory parameters (persistently elevated previously) have normalized.
Conclusion: The jak kinasa inhibitors may be a treatment option in those patients with bad response to conventional therapy.
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AB0995 JUVENILE ONSET SYSTEMIC LUPUS ERYTHEMATOSUS WITH SJÖGREN'S SYNDROME: CLINICAL AND LABORATORY FEATURES.

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Background: Systemic lupus erythematosus with juvenile onset (jSLE) with Sjogren's syndrome (SS) in children is a poorly studied and rare combination, the frequency of which, according to the literature, is 7.5-10.0%[1].
Objectives: To study demographic data, specific features of jSLE with SS in single center.
Methods: Retrospective study of all consequently patients (pts) of single-center in pediatric department with combination of jSLE and SS.
Results: SS was verified in 14 pts with jSLE (14.3% were boys), which amounted to 15.5% of all pts with jSLE. The median age of jSLE onset was 13.5 y.o. [9.3; 14.9]. The median of disease duration at the time of SS verification was 1.3 y [0.6; 2.9].

Expressed constitutional disorders (fever, weight loss) observed in 13 pts (91.7%). 11 pts (78.6%) had acute cutaneous lupus, 5 pts (35.7%) – chronic cutaneous lupus, 3 (21.4%) – oral and nasal ulcers, 6 (42.8%) – nonscarring alopecia, 9 pts (64.3%) – polyarthritis, 2 pts (14.3%) – renal involvement, 2 pts (14.3%) – serositis, 1 (7.1%) – interstitial lung disease, 5 pts (35.7%) – neuropsychiatric disorder, including psychosis in 2 (14.3%). 4 patients had skin lesions atypical for SLE (1 - annular erythema, 1 - erythema nodosum, 2 - Ro-associated skin vasculitis). 12 pts (85.7%) had generalized lymphadenopathy.12 pts (85.7%) had various hematological disorders: anemia – in 5 pts (35.7%), leukopenia – in 9 (64.3%), isolated lymphopenia in 1 (7.1%), thrombocytopenia – in 4 pts (28.6%). 13 pts had isolated involvement of salivary glands, 1 – combined with lacrimal glands. The decrease in salivary gland function was recorded in 50% of cases, hypolacrimia – in one case. Recurrent parotitis was present in only one case (7.1%). ANA were detected in 100% pts, anti-dsDNA – in 10 pts (71.4%), anti-Sm – in 7 pts (50.0%), anti-Ro - in 10 (71.4%), anti-La - in 7 (50%), RNP-70 – in 5 pts (35.7%), RF+ - in 6 pts (42.9%), hypocomplementemia – in 3 pts (21.4%). The most common was the combination of positive ANA, anti-dsDNA, antiRo with acute cutaneous lupus, polyarthritis, generalized lymphadenopathy and expressed constitutional disorders – 8 pts (57.1%). 4 pts (28.6%) had polyclonal hypergammaglobulinemia. 3 pts (21.4%) had concomitant autoimmune non-rheumatic disease; 1 - autoimmune hepatitis, 1 - type 1 diabetes mellitus, 1 - autoimmune thyroiditis. Median disease activity by SLEDAI at the time of jSLE verification was 11.5 scores [9.25;15.7].

Conclusion: According to our results, the frequency of detection of secondary SS in jSLE was higher than the literature data. The clinical features include a high frequency of constitutional disorders, lymphadenopathy, skin manifestations, high frequency of antiRo with a significantly lower incidence of kidney involvement, serositis than jSLE without SS. In pts with a diagnosis of SLE, the possibility of developing secondary SS should be considered (specially in girls with antiRo positive), the early detection of which affects the choice of therapy and prognosis.

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AB0996 FAMILY CASE OF BLAU SYNDROME IN 3 CHILDREN, INITIALLY DIAGNOSED AS JUVENILE IDIOPATHIC ARTHRITIS

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Background: Juvenile Idiopathic Arthritis (JIA) is heterogeneous group of diseases which may include genetically determined conditions. Extremely rare monogenic hereditary autoinflammatory disease, such as Blau syndrome (BS) is usually difficult to recognize and JIA is initially established. BS is caused by a mutation in the NOD2/CARD5 gene and phenotypically characterized by triad of granulomatosis polyarthritis, uveitis and skin rash.

Objectives: To present the family case of genetically confirmed BS in 2 siblings, initially diagnosed as patients with JIA.

Methods: Two brothers of 15 and 3 years old were examined in our clinic. Additional genetic assay was performed because of unusual clinical picture.

Results: *Case report.* Older brother, 15 y.o. developed arthritis of both wrist joints at the age of two. There was erythematous maculo-micropapular scaly rash on the trunk and extremities before the onset of arthritis. By 2009 (5 y.o.), the knees, ankles, and three PIP joints of the left hand were involved. Polyarthritis was characterized by severe effusion and periarticular tissues swallowing. He was treated in regional hospital by NSAID, methotrexate, cyclosporine A without significant positive effect. Since 2012 etanercept was added for treatment with variable result. Inactive status of the disease is never reached. Repeated intra-articular GC injections were needed from 4 to 10 times per year. The patient was admitted to our clinic in November 2019. He was suffering from severe polyarthritis and uveitis de novo (granulomatous chorioretinitis) was detected. At the same time his younger 3 y. o. brother with recently started disease was hospitalized in our clinic. He had polyarthritis with typical features of "boggy" synovitis and tenosynovitis of wrists, ankles and knees, anterior uveitis was determined. The onset of arthritis was preceded by a small-spotted rash with desquamation. This classical clinical features in younger brother let us suggest the BS. There was no increasing of ESR and CRP in both sibs throughout the course of the disease. A molecular genetic study of the NOD2/CARD15 gene in both brothers revealed the same mutation of c.1001G>A (p. Arg334Gln). Because of the absence of specific treatment for this disease and due to insufficient effect of etanercept with uveitis de novo therapy was changed to golimumab and good initial effect is reached. The youngest brother has started his therapy by methotrexate. It should be noted that the family has the eldest brother (20 y.o.), who has been suffering from arthritis since an early childhood with similar clinical picture. We are going to perform genetic analysis of the NOD2/CARD15 gene for the eldest brother.

Conclusion: Our clinical case shows that extremely rare BS may be misdiagnosed as JIA. Lack of efficacy of the etanercept therapy and uveitis de novo developing may be caused by genetic (*non-idiopathic*) nature of disease. Classic triad of boggy-arthritis, granulomatous uveitis and/or skin lesions without acute phase markers is required to perform genetic assay for the detection of a pathogenic mutation of the NOD2/CARD15 gene. This case is remarkable by the presence of BS in two (or 3) children of the family.

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AB0997 IS HEIGHT ADJUSTMENT NECESSARY IN PEDIATRIC DENSITOMETRY IN ALL CHILDREN?

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Background: The current guidelines of the International Society for Clinical Densitometry (1) recommend that in children with linear growth or maturational delay, Z score results should be adjusted. Height for age Z score (HAZ) adjustment is valid and can be calculated using the formula the formula proposed by Zemmel et al(2). It is possible that pediatric populations without linear growth or maturational delay, also benefit from HAZ, to prevent bone size from influencing the final Z score.

Objectives: To evaluate Z score variability adjusted and without adjusting for height for age.

Methods: We analysed data from densitometry performed on patients 2-20 years of age, from 2016 to 2018, assessed in the pediatric rheumatology office of our hospital for presenting risk factors for low bone mass/osteoporosis. The HAZ was calculated according to Zemel's formula.

Results: Data from 103 patients are presented. Its characteristics are summarized in Table 1

Table 1.

Mean age	9,8 years
Female	52,4%
Height Percentil ≤ 3	6,8%
Height Percentil ≥ 97	4,9%
LBM (Z score ≤ -2) spine	8,2%
LBM HAZ spine	6,4%
LBM whole body	10,5%
LBM HAZ whole body	7,2%

The table shows that the proportion of patients with BMD decreases in both the spine region and the whole body when adjusting for HAZ.

When evaluating the relationship between densitometric measurements we found that spine Z score (ZsS) and whole body Z score (ZsWB) had a correlation coefficient of 0,73 (p<0,001). There were no differences between their averages (p=0,170).

At the LBM cut-off point (Z score ≤ -2) there were discrepancies in 7%, where 5% presented LBM in ZsWB but not in ZsS. The concordance index at this point was 0,557.

When comparing these measures with their HAZ adjusted equivalents, we observe:

- HAZ adjusted ZsS vs ZsS without adjusting: There were no differences between their averages (p=0,913) with a correlation coefficient of 0,78 (p<0,001). Concordance index at cut-off point for LBM was 0,498, with a discrepancy of **7%**, where **2%** had LBM according to HAZ adjusted ZsS, but not to ZsS without adjusting.
- HAZ adjusted ZsWB vs ZsWB without adjusting: There were no differences between their averages (p=0, 367) with a correlation coefficient of 0,82 (p<0,001). Concordance index at cut-off point for LBM was 0,557, with a discrepancy of **7%**, where **2%** had LBM according to HAZ adjusted ZsWB, but not to ZsWB without adjusting.

Conclusion: There are discrepancies at the LBM cut-off point depending on the HAZ adjustment.

The pediatric population without linear growth or maturational delay, can also benefit from HAZ adjustment, especially those with high height percentiles in which their size can hide a diagnosis of LBM.

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AB0998 TRABECULAR BONE SCORE IN PEDIATRICS, IS IT USEFUL?

B. P. Magallares López[1], H. Park*[1], D. Cerda[2], J. Betancourt[3], G. Fraga[3], S. Boronat[3], S. Herrera[4], A. M. Marín[4], I. Gich[5], J. Malouf[4], J. Casademont[4], A. García-Guillén[1], H. Corominas[1]. *[1]Hospital de la Santa Creu i Sant Pau, Rheumatology, Barcelona, Spain; [2]Hospital de Sant Joan Despí Moisès Broggi, Rheumatology, Sant Joan Despí, Spain; [3]Hospital de la Santa Creu i Sant Pau, Pediatrics, Barcelona, Spain; [4]Hospital de la Santa Creu i Sant Pau, Internal Medicine, Barcelona, Spain; [5]Hospital de la Santa Creu i Sant Pau, Epydemiology, Barcelona, Spain*

Background: Bone fragility depends not only on bone mineral density (BMD), but also on bone microarchitecture. In adults, Trabecular Bone Score (TBS) is being used as an indirect marker of bone microarchitecture
It is a software that applicated to the vertebral image obtained by conventional densitometry, informs about the thickness of the trabeculae, the trabecular connectivity and the space between them. A high score indicates a better bone microstructure. In adults, a TBS equal to or greater than 1,350 is considered to represent a normal microarchitecture
Objectives: To evaluate the usefulness of TBS in pediatric population with risk factors for Low Bone Mass (LBM)
Methods: TBS was assessed by analyzing vertebral densitometries performed on patients from 4 to 20 years of age, assessed in the pediatric rheumatology office of our hospital for presenting risk factors for LBM, consecutively from 2016 until 2018 Data were compared with normal pediatric population
Results: Data from 83 patients are shown, with an average age of 11.2 years, 62% female, 80% Caucasian
The main risk factors for LBM were (%): Insufficient calcium intake (84,5), medications with osteopenizing potential (31), corticosteroids (39), sedentary lifestyle (13,6), fractures of long or vertebral bones (12,6) and hypovitaminosis D (8,1)

Table 1. TBS por age groups and in patients with and without LBM

Age groups	n	Mean	SD	Minimum-Maximum
Scholars (4-9a)	22	1,321	0,093	1,119-1,502
Adolescence (10-17a)	54	**1,309**	0,088	1,073-1,493
Youth (18-20a)	6	1,359	0,085	1,258-1,460
Spine Z score	**n**	**Mean (SD)**	p	**Minimum-Maximum**
≤-2	8	1,270 (0,075)	0,126	1,419-1,162
>-2	74	1,321 (0,090)		1,502-1,073
Whole Body Z score				
≤-2	9	1,246 (0,060)	**0,012**	1,323-1,145
>-2	73	1,324 (0,089)		1,502-1,073

Table 2. TBS in healthy population and study population for age

	Healthy girls (n=2535)		Healthy boys (n=1459)		Study girls (n=47)	Study boys (n=36)
Age (y)	**Spine BMD**	**TBS**	**Spine BMD**	**TBS**	**TBS**	**TBS**
1-2	0,40	1,325	0,37	1,272		
2-3	0,51	1,363	0,46	1,267		1,127
3-4	0,52	1,346	0,51	1,264	1,204	
4-5	0,60	1,346	0,60	1,267	1,237	1,243
5-6	0,60	1,288	0,56	1,269	1,330	1,368
6-7	0,65	**1,280**	0,60	**1,232**	**1,318**	1,422
7-8	0,67	**1,268**	0,64	**1,244**	**1,339**	**1,345**
8-9	0,71	**1,266**	0,68	**1,228**	**1,244**	
9-10	0,75	**1,278**	0,70	**1,208**	**1,253**	**1,341**
10-11	0,8	**1,285**	0,73	**1,231**	**1,229**	**1,292**
11-12	0,84	**1,337**	0,76	**1,250**	**1,303**	**1,315**
12-13	0,99	1,355	0,81	**1,248**	1,381	**1,368**
13-14	1,06	1,386	0,89	1,273	1,394	**1,338**
14-15	1,10	1,398	0,99	1,303	1,474	**1,285**

Table 2. TBS in healthy population and study population for age

	Healthy girls (n=2535)		Healthy boys (n=1459)		Study girls (n=47)	Study boys (n=36)
Age (y)	**Spine BMD**	**TBS**	**Spine BMD**	**TBS**	**TBS**	**TBS**
15-16	1,14	1,405	1,08	1,311	1,368	1,406
16-17	1,17	1,405	1,15	1,334	1,332	1,371
17-18	1,17	1,404	1,20	1,328	1,374	1,285
18-19	1,17	1,404	1,16	1,314		

Conclusion: TBS was lower in the patients with LBM by whole body Z score, but not in those with LBM by spine Z score. We observed a decrease in TBS in adolescence, not corresponding with a decrease in BMD, and that should not be interpreted as a pathological finding
Similar results have been described in other pediatric populations (1, 2), but larger studies are needed to evaluate this phenomenon. We hypothesize that it may be due to a higher rate of growth in adolescence, with a lower rate of calcium apposition into the osteoid material

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Disclosure of Interests: None declared
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AB0999 HALLMARK CLINICAL FEATURES OF JUVENILE PSORIATIC ARTHRITIS (JPSA)

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Background: JPsA is presented in 4 to 9% children with juvenile arthritis [1,2]. According to ILAR criteria, patients with uveitis, HLA-B27-positivity, and other exclusion criteria cannot be included in the JPsA category. Therefore, in pediatric rheumatological practice, the Vancouver criteria are more often used [3].
Objectives: to identify clinical features of psoriatic arthritis in children.
Methods: a single center, prospective and retrospective, continuous clinical trial for the period from 1989 to 2019 was conducted.
Results: We observed 83 patients with JPsA aged from 4 months to 17 years. Fifty-nine (71%) patients had definite JPsA and 24 (29%) had probable JPsA, according to the Vancouver criteria. The clinical and demographic characteristics are presented in Table 1.
In 17 (29%) children with definite JPsA, skin lesions presented as the first sign of the disease, joint damage in these patients developed after 3.5 ± 2 (2) years. In 28 (48%) patients articular syndrome was observed on the onset with subsequent skin manifestations after 5.3 ± 3 (5) years. Fourteen (23%) children with definite JPsA had simultaneous debut of skin and articular syndromes (Fig.1).

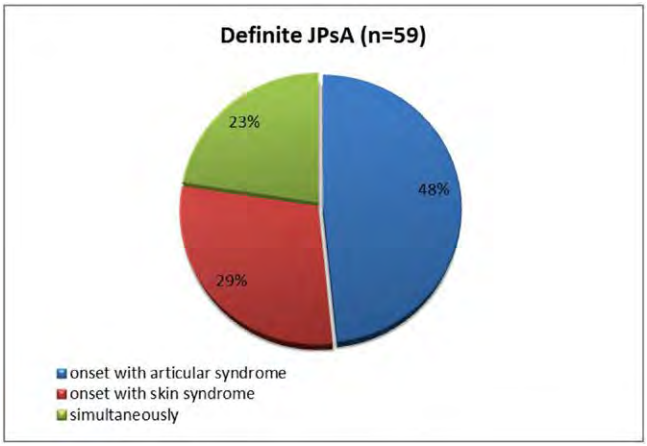


Fig.1. Skin and / or articular syndromes in the onset of the disease in children with definite JPsA

Table 1. The clinical and demographic characteristics of patients with JPsA (n=83)

Demographic indicators		JPsA M ± σ (Me)	
		Definite	Probable
Number of patients (n)		59	24
Girl/Boy Ratio		1,7:1	2:1
Average age, years		6,6±4 (5)	6,3±2,7 (5)
Duration of the disease, years		3 ±2 (3)	
Family history of psoriasis n, (%)	First-degree relative with psoriasis	22 (26%)	
	Second-degree relative with psoriasis	34 (41%)	
Potential trigger n, (%)	Infection	22 (27%)	
	Trauma	12 (14%)	
	Vaccination	7 (8%)	
	Insolation	5 (6%)	
	Stress	3 (4%)	
	Not identified	34 (41%)	

Among 59 patients with definite JPsA, vulgar psoriasis was observed in 45 (76%) patients, guttate psoriasis in 9 (15%), isolated nail psoriasis in 3 (5%), and palmoplantar psoriasis in 2 (4%). Fifteen (28%) patients had a combination of cutaneous psoriasis with damage to the nail plates.

Articular syndrome in the onset of the disease was represented by oligoarticular arthritis in 57 (69%) patients, in 15 (18%) children - symmetric rheumatoid-like arthritis, and in 11 (13%) - spondylitis. The most commonly involved joints at both presentation and during the course of the disease were the knee (41%), ankle (31%), and small joints of the hands (29%). During course of the disease, the articular syndrome transformed with symmetric rheumatoid-like arthritis prevalence (Fig. 2).

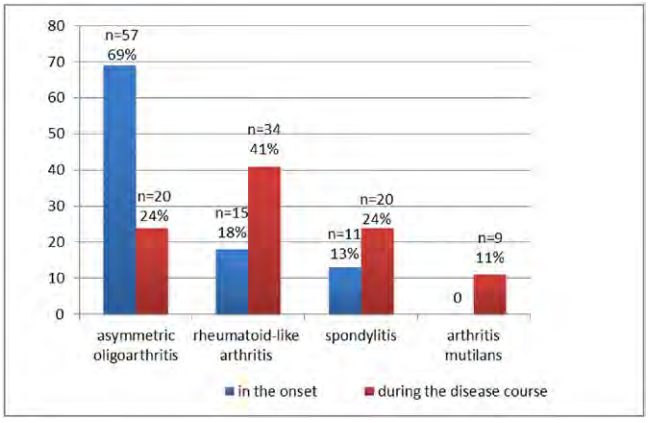


Fig. 2. Articular syndrome JPsA in the onset and during the disease course (n, %)

In 39 (47%) children, the disease at onset was characterized by high level of ESR – 34±12 (32) mm/h.

Conclusion: In most patients with JPsA, the onset of the disease occurred at the age of 6.6±4 years. Articular syndrome in the onset of the disease was presented as oligoarticular arthritis in 69% children. Overall, transformation to symmetric rheumatoid-like arthritis was the most common. Skin lesions were represented by vulgar psoriasis in 76%, guttate psoriasis in 15%, isolated nail psoriasis in 5%, palmoplantar psoriasis in 4%, and 28% of patients had a combination of cutaneous psoriasis with damage to the nail plates.

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AB1000 EFFECT OF THE LIPAT KALINGA ADOLESCENT TRANSITION CLINIC ON FILIPINO ADOLESCENTS WITH RHEUMATIC DISEASES

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Background: Establishing a transition program is important in bridging the gap between pediatric and adult healthcare especially in patients with chronic diseases. The Division of Pediatric Rheumatology of the Philippine General Hospital (PGH) established the Lipat Kalinga Adolescent Transition Clinic (LKATC) to help in the transfer from pediatric to adult healthcare by providing the support and guidance needed through education and reinforcement of self-management skills. This study is an assessment of the effect of the LKATC on the transition readiness of Filipino adolescents with rheumatic diseases at the PGH.

Objectives: To assess the effect of the LKATC program on Filipino adolescent patients with rheumatic diseases

Methods: This is a mixed-method study design done at the Philippine General Hospital. A retrospective descriptive before and after study was conducted along with a focus group discussion (FGD). The participants were pediatric rheumatology patients enrolled at the LKATC from May,2018 to April,2019. Comparison of the pre and post University of North Carolina (UNC) TRxANSITION scale (Filipino version) overall score and domains was done and facilitation of an FGD to elicit barriers and facilitating factors for the effective implementation of the LKATC. The FGD used a predefined discussion guide based on literature review and was done by a trained facilitator.

Results: We evaluated a total of 17 adolescent patients with rheumatologic diseases. Comparing the pre-intervention and post-intervention test scores, statistically significant increases were noted in several domains. Health transitional skills of these adolescents were noted to improve in terms of total score, medication, nutrition, self-management, informed reproduction, trade and school issues, insurance issues, and new health providers. There was no significant improvement in the type of illness, adherence and ongoing support.

Four patients who were enrolled at the LKATC and who attended at least 5 sessions participated in the FGD. The barrier themes elicited were 1. Expectation and beliefs regarding adult healthcare, 2. Different doctor-patient relationship, 3. Logistical problems. The facilitating themes elicited were 1. Familiarization, 2. Peer support, 3. Communication.

Conclusion: This study showed the effects of an adolescent transition clinic program in Filipino adolescent with rheumatic disease. Significant increase in the overall UNC TRxANSITION score as well as majority of the scores per domains were seen. Barriers and facilitating factors affecting the transition process elicited during a focus group discussion were also presented. This study provided baseline data on the importance of establishing an adolescent transition clinic for patients with chronic disease in the local setting.

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Disclosure of Interests: None declared

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AB1001 CHANGES IN THE PARATHYROID HORMONE LEVEL IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: It is proved that rheumatic diseases are accompanied by pronounced changes in calcium-phosphorus metabolism, which underlies the development of osteopenia syndrome. If in previous years glucocorticosteroid therapy (GCS) was considered to be the main reason for this, then the role of pro-inflammatory agents (activity of the pathological process), provision with vitamin D (VitD), and the effect of basic therapy are currently being discussed. It is also known that a decrease blood level of vitamin D leads to a violation of the absorption of calcium and phosphorus, a further increase in the level of parathyroid hormone, which underlies the risk of a decrease in bone mineral density.
Objectives: To study the level of parathyroid hormone in children with juvenile idiopathic arthritis, its relationship with the course of the disease and vitamin D status.
Methods: 91 patients with JIA (61 girls and 30 boys), with polyarticular (n = 41), oligoarticular (n = 29) and undifferentiated (n = 18) variants of JIA were examined. The age of the patients was 10.5 ± 1.7 years. The duration of the disease was 4.1 ± 1.1 years. All children receive basic methotrexate therapy. The control group included 25 peers of the corresponding gender. JADAS27 was counted, the levels of 25-hydroxycalciferol (25-OH D) and PTH were determined by chemiluminescent method. Corresponded to the content of vitamin D in blood serum, the normal level was noted in 14 patients, insufficiency - in 41 patients, deficiency - in 32 patients.
Results: The level of PTH in children with JIA remained within physiological values (30.6 ± 2.1 pg/ml; from 12.7 to 61.8 pg/ml) despite the high frequency of a VitD decrease in blood (80.2%). The level of PTH was not significant in groups of patients with a different level of vitamin D (32.8 ± 2.1 pg/ml at deficiency group; 29.2 ± 2.4 pg/ml at insufficiency group; 29.1 ± 1.8 pg/ml at a normal level of VitD group). PTH was comparable and did not differ in children of different sexes.
The highest level of PTH was in patients with a polyarticular variant of JIA (34.2 ± 4.5 pg / ml, p<0.05), which was accompanied by the lowest level of vitamin D (20.9 ± 2.1 ng / ml, p <0, 05) in the same group. There was obtained reliable correlations of activity indicators (JADAS27) taking into account Vit D and PTH, as well as with diseases duration and age of patients (p <0.05).
Conclusion: A study of the level of PTH in children with JIA did not show a significant increase depending on the vitamin D status in these patients. However, the age-related state of PTH is associated with the activity of the pathological process, the prevalence of articular syndrome and prolonged illness.
Disclosure of Interests: None declared
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AB1002 IS KAWASAKI DISEASE OR SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS IN CHILDREN WITH FEVER WITHOUT A SOURCE?

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Background: Fever without a source (FWS) is caused by various diseases, making differential diagnosis difficult. Clinical similarities between Kawasaki disease (KD) and systemic Juvenile Idiopathic Arthritis (sJIA) are well known. Kawasaki disease (KD), a self-limiting systemic vasculitis, remains of unknown etiology and can cause irreversible coronary artery aneurysms (CAAs). SoJIA is sometimes confused with incomplete KD because both diseases have overlapping clinical features and can be accompanied with CAAs and/or SJIA with macrophage activation syndrome (MAS).
Objectives: In this study, the frequency of both KD and SJIA among the patients evaluated with FWS and the clinical features of patients diagnosed with Kawasaki disease.
Methods: Medical records of patients who first visited our department between January 2016 and December 2019 were reviewed
Results: A total of 107 patients were enrolled in this study, including 43 patients (40.2%, 23 males) who fulfilled the criteria of Kawasaki disease and 64 patients (59.8%, 39 males) who did not fulfill them. In patients who fulfilled the criteria of classical FWS, 36(33.6%, 20 males) patients were diagnosed with systemic juvenile idiopathic arthritis. The mean age of the patients with Kawasaki disease was 30.0±20,4 months (median 25 months), the mean age of other patients was 52,6±40 months (median 39,5 months). The mean age of the patients with sJIA patients was 87,6±49,8 (median 80months). Kawasaki patients were younger than others (p=0.01). There was no difference in gender between groups.
In Kawasaki patients, the most common clinical feature at diagnosis was fever (100%) followed by conjunctival congestion and mucosal changes (69%). The last two findings are more significant in kawasaki patients than others (p<0,00). Twenty-six (59%) patients had completed KD while 25% had incomplete KD. 7 (16%) patients had atypical KD. The mean fever duration was longer in sJIA patients than KD and others (median 14,8 and 7 days, p<0.00). All patients with KD received IVIG (2 g/kg, infusion in 12 h) and aspirin (60 mg/kg/day). 13.6% of the patients also received oral corticosteroids because of IVIG resistance. Thirty-one patients (72.1%) responded to IVIG treatment, whereas 12 (6 female, 6 male) were IVIG resistant. CAI was detected in echocardiography at diagnosis in 10 (22.7%) (6 female; 4 male) patients. We also detected 4 patients pericarditis with /without CIA.
Conclusion: The clinical presentations of KD and sJIA are quite similar with fever, rash, hepatomegaly, and lymphadenopathy. All 2 entities may provide clues to potentially shared immunopathology.
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AB1003 ANTI-DFS70 AUTOANTIBODIES, JUVENILE IDIOPATHIC ARTHRITIS (JIA) AND UVEITIS: ARE ANTI-DFS70 A PREDICTIVE MARKER OF UVEITIS RISK IN JIA PATIENTS?

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Background: Juvenile idiopathic arthritis (JIA) is the most common paediatric rheumatic disease. Its most threatening complication is represented by uveitis, which could cause severe visual impairment if not diagnosed and treated promptly. It is an asymptomatic uveitis and the diagnosis is only instrumental. Therefore, regular ophthalmologic surveillance is crucial in the management of JIA. To date there are no specific predictive markers of uveitis development among JIA patients, including serologic subsets. Anti-Nuclear Antibodies (ANA) positive patients have the highest risk of iridocyclitis, but ANA are not specific. They could be found in patients with JIA without uveitis, in many other rheumatologic and inflammatory conditions and also in healthy subjects (6-12% of children). Anti-DFS70 antibodies (ANA forming a specific pattern in immunofluorescence) have been taken into consideration, but their role has not yet been established in a pediatric setting. Currently, there are few reports, involving small groups of patients and with non-univocal results. Some studies report anti-DFS70 antibodies more frequently in children with rheumatological diseases, in particular JIA-related uveitis; on the contrary, others describe them in healthy ANA positive patients.
Objectives:
1) To evaluate the correlation between anti-DFS70 autoantibodies and the risk of developing uveitis in a cohort of patients with JIA ANA + in pediatric age;
2) to compare the prevalence of anti-DFS70 in patients with JIA, with a group of healthy ANA + children, to better define the role of these autoantibodies (potential risk factor or a protective factor for the development of AARDs in children?)

Methods: We evaluated retrospectively 51 patients with JIA ANA +. We divided these patients in two groups, according to the presence (n=11) or the absence (n=40) of uveitis. For each patient we evaluated: gender, current age, age at diagnosis, type of JIA, therapy, presence of other diseases, dosage of ANA (with IF-Hep2), research of anti-ENA and anti-DFS70 antibodies (with chemiluminescence). Subsequently the whole group of patients with JIA was compared with a control group of healthy subjects aged ≤ 18 years (n=30), followed in the pediatric rheumatology clinic for occasional finding of ANA positivity, without pathologies at the moment of the study (in particular without rheumatological or autoimmune diseases).
Results: Among patients with JIA without uveitis, anti-DFS70 autoantibodies were positive only in one patient. Anti-DFS70 were negative in all patients with JIA and uveitis. The difference between the two groups is not significant (p=1). In the group of healthy patients 6/30 (20%) presented a positivity of anti-DFS70 autoantibodies, in the absence of anti-ENA.
Conclusion: Our data revealed no correlation between the positivity of anti-DFS70 autoantibodies and the risk of uveitis in patients with JIA ANA +, even

if the number of patients is small. Further studies are needed to identify a reliable predictive marker of uveitis risk in JIA patients. The finding of a significant greater prevalence of anti-DFS70 autoantibodies in healthy ANA + subjects allows to suppose that this autoantibody could represent a possible protective marker for development of AARDs in asymptomatic children with isolated ANA positivity, as for adults. To confirm this hypothesis, it would be useful to carry on the study prospectively, encompassing children with other rheumatological diseases, and prolonging the clinical and laboratory follow up.

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Disclosure of Interests: None declared
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AB1004 JUVENILE DERMATOMYOSITIS (JDM) IN SOUTHEAST ASIA: A 20-YEAR SINGAPORE EXPERIENCE

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Background: Juvenile dermatomyositis (JDM) is a multisystem inflammatory disease of childhood with variable demographics, clinical features and outcomes. No studies have described the characteristics of JDM patients from Southeast Asia population.
Objectives: To describe the clinical characteristics and outcomes of JDM patients in Singapore over a 20-year period.
Methods: Patients diagnosed with JDM from 1999 to 2019 at KK Women's and Children's Hospital, Singapore, were recruited. Nonparametric descriptive statistics were used to described data. Kaplan-Meier analyses were used to estimate the probability of remission. Multivariate logistic and Cox regression analyses were used to determine predictors as appropriate. The significant level was set at < 0.05.
Results: 32 JDM were identified. Clinical characteristics and treatment used are shown in Table 1.

	All (n=32)	Monophasic (n=17)	Polyphasic (n=14)
Male	14 (43.8)	7 (41.2)	7 (50.0)
Age at onset (yrs)*	6.4 (4.5 – 9.8)	5.4 (4.1 – 8.5)	7.4 (5.6 – 12.3)
Lag period (mo)*	3.5 (1.0 – 12.5)	2.0 (1.0 – 16.8)	6.8 (1.2 – 15.8)
Heliotrope	16 (50)	9 (52.9)	7 (50)
Gottron papule	23 (71.9)	12 (70.6)	11 (78.6)
Malar rash	19 (61.3)	9 (52.9)	10 (71.4)
Vasculitic rash	19 (61.3)	8 (47.1)	11 (78.6)
Arthritis	10 (31.3)	3 (17.6)	7 (50)
Nailfold changes	28 (87.5)	15 (88.2)	13 (92.9)
Calcinosis	9 (28.1)	4 (23.5)	5 (35.7)
Positive ANA	17 (53.1)	10 (58.8)	7 (50)
Positive Myositis antibodies	4 (12.5)	2 (11.8)	2 (14.3)
Laboratory at diagnosis, U/L*			
CK	324 (134 – 2229)	746 (139 – 2965)	351 (155 – 2622)
LDH	650 (450 – 943)	650 (398 – 1015)	714 (512 – 944)
ALT	28 (16 – 106)	35 (18 – 109)	38 (15 – 104)
AST	50 (30 -108)	50 (31 – 113)	85 (36 – 215)
Aldolase	13.7 (8.1 – 28.0)	14.2 (8.4 – 26.6)	16.3 (8.6 – 38.5)
CMAS score at diagnosis	29 (21 – 43)	28 (21 – 35)	35 (11 – 43)

*median (IQR), otherwise - n (%)

Pulse methylprednisolone (pMP) was used in 53.1% of patients after diagnosis. Median time to inactive disease (ID) was 5.3 months (IQR 2.8 – 12.8). Male, older age and patients on pMP (p = 0.003-0.044) achieved ID sooner. Older patients also developed disease flare sooner after achieving ID (p =0.024). No clinical features nor lab investigations predicted JDM disease course. Malay patients was associated with higher risk of calcinosis (p = 0.017).

Compared to adult dermatomyositis patients in Singapore[1], our cohort had more cutaneous manifestations including malar rash, vasculitic rash and nailfold changes. Table 2 shows the time for each muscle enzymes to normalise.

CK	1.49 (0.69 – 3.53)
LDH	4.53 (2.35 – 25.04)
ALT	1.71 (0.90 – 4.13)
AST	0.97 (0.53 – 3.12)
Aldolase	3.12 (2.35 – 8.30)

median in months (IQR)

Conclusion: Our cohort of JDM patients had more calcinosis compared to other Asian population[2]. Malay population is at higher risk of this complication. It is crucial to achieve ID state in the shortest time possible to avoid significant morbidity. Our study suggests that early treatment with pMP is associated with shorter time to ID. There is no predictor identified for disease course, similar to previous studies[3].

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Disclosure of Interests: None declared
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AB1005 BULLOUS LUPUS (BSLE) AS THE FIRST MANIFESTATION OF SYSTEMIC LUPUS ERYTHEMATOSUS IN THE PEDIATRIC POPULATION (PSLE): A DIAGNOSTIC CHALLENGE IN DAILY PRACTICE

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Background: Cutaneous manifestations are observed in 59–85% of patients with SLE but less than 5% developed BSLE. In the GLADEL cohort, the prevalence is 0.41%. BSLE literature in children is scarce

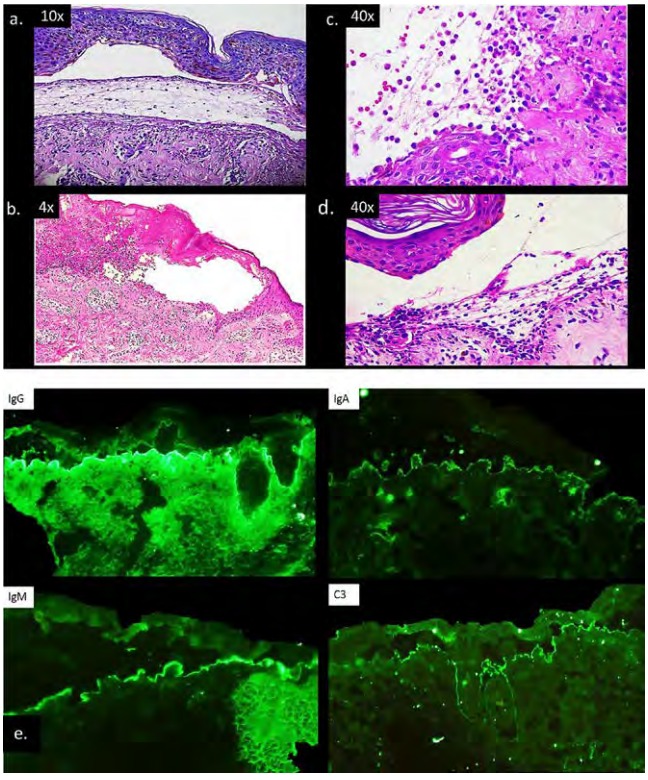


Fig 1. Histology and DIF of BSLE H-E **a** and **b**: subepidermal blisters **c** and **d**: abundant neutrophils are observed **e**: DIF full house linear pattern



Fig 2. skin lesions of BSLE **a**: tense serous blisters, scars and erosions **b**: purpuric macules in palms **c**: blisters in groin **d-g**: blisters and hypopigmented scars

Objectives: to describe the clinical characteristics of the patients with BSLE

Methods: series of cases between 2010-2019 of two reference centers. The cases met Camisa and Grimwood criteria for BSLE

Results: 5 cases had bullous lesions that resolved with residual hypopigmentation. One case had focal seizure and other patient had arthritis with leukopenia and thrombocytopenia. 2 patients had proteinuria <500 mg/24 hours. There were no cases of lupus nephritis. The median SLEDAI-2K score was 12 (IR: 8-17). All had ANAs in titers greater than 1:160 and four had anti-DNA (+). 5 patients had anti-RNP and 4 had anti-Sm. One case had anti-Ro/anti-La. All presented low C3 and 80% had low C4. 80% had ESR ≥20 mm/hour and CRP greater than 0.5 mg/dl in 60%. All presented clinical response with glucocorticoids and dapsone; one patient had methemoglobinemia that improved. At 3 months, the blisters did not recur in 4 patients except one case that presented relapse due to inadherence.

Histologically, the most common finding was subepidermal blisters with neutrophils in the papilar dermis. DIF showed linear deposits of Igs and complement in 4 cases and granular deposits in one case; IgG/IgM were in 5 of the samples. IgA was positive in 60% and C3 in 80%

Conclusion: In this series, BSLE was associated with neuropsychiatric, joint and haematological involvement in 40% of patients, without lupus nephritis. Such abnormalities had a parallel course to skin involvement, without recurrences. BSLE tends to have a single-phase behavior and in children unlike adults, severe renal involvement is uncommon

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Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.6359

Table 1. Overview of patients with BSLE. BMZ: basal membrane zone MTP: methylprednisolone DDS: dapsone

Age	SLEDAI-2K	Distribution	Mucosal lesions	Systemic findings	Laboratory	DIF	Treatment
14 M	8	Face Trunk Extremities Genitals	Ulcers on mouth and tongue Nasal erosions	No	ANA 1:2560 speckled pattern Anti-DNA 1:40 UI ENAS: anti-Sm + anti-RNP + C3: 86 mg/dl C4: 3.9 mg/dl	Igs deposition in the dermal side Linear pattern IgG, IgA, IgM and C3	MTP Pulses PDN 50mg/day CQ AZA DDS
12 F	12	Trunk Upper and lower extremities	Ulcers on mouth and tongue	Proteinuria non significant (<500 mg/24 hrs)	ANA 1:2560 homogeneous Anti-DNA >200 IU ENAS: anti-Sm + anti-RNP + C3: 36.3 mg/dl C4: 2.10 mg/dl	Igs deposition along the BMZ Linear pattern IgG, IgM, C3 and C1q	PDN 35 mg/day CQ AZA DDS
15 F	10	Face Trunk Extremities	Ulcers on mouth, hard palate and tongue	Proteinuria non significant	ANA 1:640 speckled and cytoplasmic Anti-DNA – ENAS: anti-RNP + anti-Sm + anti-Ro + Anti-La + C3: 56 mg/dl C4: 8.1 mg/dl	Igs deposition along the BMZ Linear pattern IgG, IgA, IgM and C3	PDN 50mg/day CQ DDS Mycophenolate IVIg

Table 1. Cont

10 F	17	Blister lesions: face, upper and lower extremities Purpure: both legs	No	Hematologic: leukopenia, lymphopenia and thrombocytopenia Arthritis	ANA: 1:640 speckled Anti-DNA 1:40 UI ENAS: anti-RNP + anti-Sm - C3: 51 mg/dl C4: 4.4 mg/dl LA: + IgG aCL: 92 GPL IgM aCL: -	Igs deposition along the BMZ Granular pattern IgM. IgG: + IgA, C3: -	PDN 30 mg/day DDS
9 F	16	Face Trunk Extremities	Ulcers on mouth and tongue	Focal convulsion	ANA 1:160 homogeneous Anti-DNA 1:10 UI ENAS: anti-RNP + anti-Sm + C3: 73 mg/dl C4: 12.8 mg/dl	Igs deposition in the dermal side Linear pattern IgG, IgA, IgM and C3	MTP Pulses PDN 25mg/day CQ DDS

AB1006 **DRUG SURVIVAL OF SYSTEMIC TREATMENTS IN JUVENILE IDIOPATHIC ARTHRITIS**

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Background: *Juvenile idiopathic* arthritis (JIA) comprises a group of inflammatory diseases that frequently requires systemic treatments. There are some studies that evaluate the systemic drug survival in adults with JIA; but there is scarce data about the drug survival in paediatric population.
Objectives: Our main objective was to study the drug survival of biologic therapies and synthetic DMARD in a monocentric cohort and the related factors influencing on it.
Methods: Patients with JIA visited in the last 12 years were included. We carried out a retrospective, longitudinal study and collected data on treatment (start date, tapering and stop the treatment date; causes of finish and combined treatment or not). We also collected demographic data with date of birth, sex, symptoms onset data and JIA subcategory. We studied time to relapse since the drug suspension. The drug survival for each kind of treatment was analyzed with Kapplan-Meier curves.
Results: We included 158 patients with JIA. Demographic data are shown in table 1. One hundred and thirty (82.3%) patients started methotrexate (MTX) with a half-life of 34.8 months; 79 (51.5%) patients started biologic therapy with half-life of 29 months and 14 (17.7%) patients started a second biologic with a half-life of 5 months. Time to first tapering of MTX was 12 months, for the first biologic was 10.5 months and for the second biologic was of 15 months. The main cause of suspension was remission for each group. Treatment according to different JIA subcategories is shown in table 2. In 45 patients (28.5%) systemic treatment was stopped and 11 (24.4%) had a disease flare in a mean time of 36 months. Taking into account only patients who flared, the mean time was 15.6 months.

Table 1. Demographics features

	Total (n:158)
Sex (female)	96 (60,76%)
Starting age (median y RI)	4,9 (2,6-9,8)
AAN positives	91 (57,6%)
JIA oligo persistent	66 (41,77%)
JIA oligo extended	16 (10,13%)
JIA enthesitis	14 (8,86%)
JIA psoriasic	9 (5,7%)
JIA systemic	18 (11,39%)
JIA poli FR-	29 (18,35%)
JIA poli FR+	4 (2,53%)
JIA undifferentiated	2 (1,27%)

Table 2. Treatment according to JIA subcategories

	Group 1 (Systemic JIA n=18 (%)	Group 2 (Oligoarticular JIA n=82 (%)	Group 3 (Poliarticular JIA n=33 (%)	Group 4 (Juvenil SpA n=23 (%)
Synthetic DMARD (n:130)	9 (50%)	71 (86,6%)	33 (100%)	17 (74%)
Biologic Therapy (n:79)	6 (33,3%)	34 (41,46%)	22 (75%)	17 (74%)
No systemic treatment (n:21)	7 (38,9%)	10 (12,2%)	0	4 (17.4%)

Conclusion: The drug survival for systemic therapies in children with JIA is more than 2 years, without significant differences between synthetic DMARDs and biologics. Remission is the main cause for ending treatment. Biologic drug survival was significantly shorter between systemic JIA and the other subcategories. Only one fourth of patients had a flared after stopping the systemic treatment.
Disclosure of Interests: Laura Trives Folguera Speakers bureau: ROCHE, Indalecio Monteagudo: None declared, Belén Serrano Benavente: None declared, Liz R. Caballero Motta: None declared, Ana Melissa Anzola: None declared, Katerine López Gloria: None declared, Juan Carlos Nieto Speakers bureau: Pfizer, Abbvie, MSD, Novartis, Janssen, Lilly, Nordic Pharma, BMS, Gebro, FAES Farma, Roche, Sanofi
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AB1007 **SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS: ARE DIFFERENT CLINICAL PATTERNS ASSOCIATED WITH S100A8/S100A9 SERUM LEVELS?**

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Background: Systemic juvenile idiopathic arthritis (SJIA) is a category of Juvenile Idiopathic Arthritis (JIA). Different clinical patterns (articular/systemic/both of them combined) have been recognized, possibly identifying distinct subpopulations. Serum biomarkers that reflect disease activity include S100A8/S100A9 (S100A8/9), however to date patterns of SJIA and their association with S100A8/9 has not been tested.
Objectives: To evaluate S100A8/9 levels in a cohort of patients with SJIA. To determinate S100A8/9 inactive vs inactive visits. To distinguish patterns on SJIA and their association with S100A8/9. To compare serum levels of S100A8/9 with other JIA categories and autoinflammatory diseases.
Methods: An unicenter, observational, cross sectional study was conduced. Patients with SJIA according ILAR whom S100A8/9 was measured as part of standard care were enrolled. Consecutive visits were included. Variables recorded were: clinical (systemic: fever, serositis, adenopathy, hepatomegaly, splenomegaly and arthritis); biochemical (S100A8/9, hemoglobin, platelet, erythrosedimentation, c-reactive protein, ferritin). Activity measures: Juvenile Arthritis Disease Activity Score (JADAS -10) and physician visual analogue scale (phy VAS). Visits were divided into active/inactive. Active visit was defined as at least one clinical feature.(systemjc and/or arthritis). Inactive visit no clinical symptoms neither JADAS-10> 1 and phy VAS: 0. SJIA patterns were defined as: “articular pattern”: those patients with arthritis without systemic features, “systemic pattern”: any systemic feature without arthritis, “mixed pattern”: both articular and systemic. Levels of S100A8/9 were tested using Calprotectin Elisa Kit. For comparisons others JIA: enthesitis related arthritis (ERA), polyarticular and autoinflammatory diseases who had at least one S100A8/9 determination were included. Descriptive statistics, Mann- Whitney U test and ANOVA were used as appropiate.
Results: Forty-two patients with SJIA were included (25 F). Age at evaluation 13 (1-16.5) years. Clinical features at study baseline: arthritis 57 %, rash 19%, fever 15 %, adenopathies 6%, splenomegaly 4%, hepatomegaly 1.5%. Laboratory features (median): hemoglobin 12.2 gr/dl, platelet 314000 cel/mm3, erythrosedimentation 12.5 mm/h, c-reactive protein 0.7 mg/dl, ferritin 235 ng/ml. JADAS -10 ≥ 1: 62%. Number of active patients were 29 (69%). Scheduled Medical visits were 129 (active 65%, inactive 35%). Active visits were divided according patterns into: articular 54%, mixed 35%, systemic 11%.
Serum Levels of S100A8/9 according to SJIA' patterns.

SJIA	Overall	Active	Articular	Systemic	Mixed	Inactive
Visits	129	84	46	9	29	45
S100A8/9 ng/ml Median (range)	7590 (300-2625)	16788 (300-26250)	10750 (300-26250)	5200 (850-12250)	25000 (3290-2625)	3103 (1140-1010)

S100A8/9 analysis revealed significant differences among active vs inactive medical visits (p: 0,00001). ANOVA test among SJIA`patterns showed, F:86.48, (p:0.00001). Mixed pattern was distinctive to others. S100A8/9 (medians ng/ml) in comparable diseases were: ERA: 4320, polyarticular: 4120, autoinflammatory: 6532. SJIA had the higher S100A8/9. SJIA was different than others comparable diseases (F: 11,62,p: 0.00001). Comparisons among SJIA`patternss and others disease found that systemic and articular pattern did not show differences (F.2.78, p:0.067)
Conclusion: S100A8/9 was higher in SJIA compared to others diseases. It reflected disease activity. Mixed pattern evidenced to be different to others (systemic/articular). Mixed pattern was the unique that showed significative difference compared to other diseases. SJIA is probably not a single disease, but not only clinical patterns and biomarkers as S100A8/9, if not, genetic variants and their expression would be able to identify homogeneous groups towards tailored treatments.
Disclosure of Interests: None declared
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AB1008 **METABOLIC DISORDERS IN CHILDREN WITH SYSTEMIC LUPUS ERYTHEMATOSUS**

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Background: Systemic lupus erythematosus (SLE) is the most common pathology from the group of systemic diseases of the connective tissue. Currently, the problem of deadly complications in patients with SLE is progressively shifting towards vascular catastrophes, such as strokes and heart attacks. If a few years ago, patients mainly died at a young age from renal failure as a complication of lupus nephritis, now thromboses of various localization are in first place.
Objectives: The purpose of the study was to determine the state of lipid peroxidation and antioxidant protection, the main indicators of the lipid spectrum and the state of hemostasis in children with SLE.
Methods: 25 children with SLE and 20 healthy children were examined in the rheumatology department of the 4th city children's clinical hospital in Minsk. The lipid spectrum, lipid peroxidation (LPO) and serum ACL, ACW were determined in the Central Research Laboratory of the Belarusian Medical Academy of Postgraduate Education.

Results: In children with SLE a significant increase in the content of total cholesterol (5.56±0.36 mmol/l) and a decrease in HDL-cholesterol levels (0.94±0.18 mmol/l) were found in comparison with the control group (3.71±0 69 mmol/L and 1.29±0.33 mmol/l, respectively).

A significant (p <0.05) decrease in the concentration of ApoA (85.1 [59.8; 94.9] mg/dl), ApoE (2.1 [1.2; 3, 7] mg/dl) and an increase in ApoB (59.8 [51.9; 67.8] mg/dl) in children with SLE were found compared with the control group (127.2 [122.1; 132.3] mg/dl, 3, 2 [2.3; 5.9] mg/dl and 32.1 [19.9; 50.8] mg/dl, respectively). ApoB / ApoA> 1 was established in 7 (28%) children with SLE.

The study found a significant (p <0.05) increase in the level of intermediate (DK233, DK278) and final (MDA) LPO products in the blood serum of children with SLE in comparison with the control group, which indicates the activation of LPO processes in these patients. During the correlation analysis, a positive correlation was established between the levels of DK233, DK278 in blood serum and CRP (r_s = 0.87, p <0.001). When studying the main indicators of the blood lipid spectrum in children with SLE, a significant increase in the serum concentration of total lipids (p <0.01) and triglycerides (p <0.001) was revealed when compared with the control group.

When determining indicators of coagulation hemostasis, in children with SLE, a predominance of hypercoagulation was detected, accompanied by a significant increase in serum fibrinogen level (5.08 ± 0.14 g/l) and an increase in platelet level (479.57 ± 8.01*10^9/l) in peripheral blood compared with the control group (3.24 ± 0.07 g / l and 294.23 ± 5.39*10^9/l, respectively). These indicators correlated with serum CRP concentration (rS = 0.62; p <0.01) and ESR level (r_s = 0.73; p <0.01). A relationship was established between elevated serum levels of fibrinogen and disease activity indicators (r_s =0.74; p <0.01).

Conclusion: The atherogenic orientation of the blood lipid spectrum, characterized by hyperlipidemia, hypertriglyceridemia, hypercholesterolemia and dyslipoproteinemia in the form of a decrease in HDL-cholesterol and an increase in LDL-cholesterol, as well as an increase in ApoB/ApoA ratio> 1 and a decrease in ApoE, the activation of LPO processes and a significant decrease in ACW and ACL in the serum of children with SLE are cardiovascular events risk factors (pulmonary thromboembolism, myocardial infarction and brain).

Acknowledgments: This study would not have been possible without the collaboration of numerous Belarusian pediatric rheumatologists, patients and their parents.

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AB1009 THE EFFICACY OF TOCILIZUMAB ON THE TREATMENT OF TAKAYASU ARTERITIS IN CHINESE CHILDREN

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Background: Takayasu arteritis (TA) is the most prevalent large-vessel vasculitis in children. Patients with TA have a high mobidity and mortality.It remains a therapeutic challenge because corticosteroids monotherapy can rarely cure TAK and the relapse rate is high during GC tapering.

Objectives: The aim of this study is to investigate the efficacy and safety of tocilizumab (TCZ)in Chinese children with Takayasu arteritis(TAK).

Methods: We retrospectively studied 6 TAK children treated with TCZ in our hospital from July 2017 to October 2018. The demographic and clinical data, laboratory examination results and vascular imaging data were collected.

Results: Six pediatric patients with critical or refractory TAK treated with TCZ were analyzed, including 3 males and 3 females.The diagnosis age was ranging in age from 2 to 13 years(median age:7 years).Three patients were initially treated with TCZ and Mycophenolate Mofetil(MMF) as the first-line regimen without corticosteroid or with a quite rapid GC taper duration,two of which had lifte-threatening coronary arteries involved and heart failure.The other three paitients were swcithed to TCZ from conventional disease modifying anti-rheumatic drugs (DMARDs) or other biologics due to being refractory to them and recurrent relapses.Four patients were given TCZ at 4 weeks regular intervals for 10 to 22 months,while two patients withdrew TCZ because of disease deterioration and unbearable abdominal or chest pain after the second dose.After 6 months follow-up,four patients experienced significant clinical and biological improvement with angiographically progression in one patient. A corticosteroid-sparing effect is obvious. Drug-related side effects occur in 1 patients manifesting as a mild elevated liver fuction. Neither neutropenia nor infection was observed.

Conclusion: Our study shows a clinical, biological, and radiological response in patients with refractory TAK treated with TCZ.

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AB1010 CLINICAL SPECTRUM AND IMMUNE ANALYSIS OF PATIENTS WITH CRYOPYRIN-ASSOCIATED AUTOINFLAMMATORY SYNDROME IN TAIWAN

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Background: Cryopyrin-associated periodic syndromes (*CAPS*) are emerging autoinflammatory diseases with available treatment. No reports have yet been reported from Taiwan.

Objectives: We reviewed cases suspected with CAPS to identify its existence in Taiwan.

Methods: Genomic DNA from one hundred and ten cases with symptom signs suggestive of CAPS(1) between 2016-2019 were sent for NLRP3 gene analysis. Clinical presentations, laboratory data, treatment regimens, as well as inflammasome activities were analyzed among those treated in a tertiary medical center in northern Taiwan.

Results: Among the 110 cases sequenced, 16 of them were found to carry missense mutations within the NLRP3 gene. Fourteen cases harbored known pathogenic genetic variants (c.1316C>T; c.1574A>T; and c.907G>C) and two carried novel NLRP3 missense mutations (c.210G>A, c.1371G>T)(2) with unknown pathophysiological roles. Through chart review, chronic urticarial, systemic juvenile idiopathic arthritis, Behcet's disease and refractory Kawasaki disease were most likely diagnosed before genetic analysis were arranged. As compared to chronic infantile neurological, cutaneous and articular syndrome (CINCA) and Muckle-Wells syndrome (MWS), familial cold autoinflammatory syndrome (FCAS) was the most frequently observed clinical presentation. Plasma serum *amyloid* A (*SAA*) and IL-1b were both significantly elevated among the cases diagnosed with CAPS as compared to the controls (p<0.05). IL-18, on the other hand, showed no significant differences between the groups. While the presence of LPS without ATP significantly increased the level of IL-1b in the PBMC stimulation test, IL-18 were significantly elevated in the confirmed CAPS with or without ATP upon LPS stimulation (all p<0.05). Caspase 1 activity were also tested positive among the cases with CAPS. Furthermore, we compared the immune profiles between those CAPS cases harboring pathogenic mutations with the 2 harboring unreported NLRP3 missense mutations and discovered that the PBMC stimulation test in cases with c.210G>A and c.1371G>T mutation did not differ from the healthy controls.

Conclusion: The number of NLRP3 gene alterations among patients suspected with CAPS in Taiwan is not low. In order to identify potential patients for proper medical intervention in the future, physician awareness, genetic testing as well as functional analysis are important.

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AB1011 LONG TERM FOLLOW-UP OF THE PATIENTS WITH ANTI NUCLEAR ANTIBODY POSITIVITY WHO HAD INITIALLY NO IDENTIFIABLE RHEUMATIC DISEASES

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Background: Anti-nuclear antibodies (ANA) are a group of the antibodies that develop against intracellular components of the cells. It is usually useful for diagnosing some of the connective tissue diseases like systemic lupus erythematosus, mixed connective tissue disease. But it is reported that its positivity rate is about %20 in healthy individuals. Therefore, it can be confusing to check ANA test, if there is not really high suspicion for connective tissue diseases or juvenile idiopathic arthritis.

Objectives: We aimed to evaluate results of long-term follow-up of the patients with ANA positivity who had initially no identifiable rheumatic diseases.

Methods: Six hundred and ninety-four patients with ANA positivity who did not diagnosed as any of the rheumatic diseases at the first examination were found in database. Two hundred and eighty- two patients of them were called so far and questioned about their demographic features and symptoms that are related with rheumatic diseases.

Results: Mean age of the patients at the time of study and at the time of testing were 13.4± 4.5 and 9.1±4.0 years. The female: male ratio was 1.05. Mean follow-up duration was 4.3±2.8 years. Most common reasons for the request for ANA test were arthralgia and skin eruptions. ANA testing was most commonly requested by a general pediatrists. Demographic features of the patients were summarized in Table 1.

Table 1. Demographic features of the patients.

	n (%)
Age (years)	13.4± 4.5
Female	145 (51.4)
Age at the time of testing (years)	9.1±4.0
Follow-up Duration (years)	4.3±2.8
Reason for testing	
Arthralgia	99 (44.1)
Skin Eruption	54 (24.1)
Check-Up	20 (8.9)
Arthritis	13 (5.8)
Gait abnormalities	7 (3.1)
Hair Loss	6 (2.6)
Fever	5 (2.2)
Uveitis	2 (0.8)
Recurrent abdominal pain	2 (0.8)
Who suggested testing?	
Pediatrician	196 (87.5)
Parents	13 (5.8)
Dermatologist	7 (3.1)
Ophthalmologist	3 (1.3)
Rheumatologist	2 (0.8)
Other	3 (1.3)
Positivity of acute phase reactants	15 (5.3)
History of infection before testing	56 (24.3)
History of drug-using before testing	39 (17)

Most of the diseases were diagnosed in patients with ANA positivity were not related with autoimmune mechanisms that associated with ANA positivity therefore, these diseases are thought to be coincidence. Only in 1 patients, systemic lupus erythematosus that has certain association with ANA positivity were diagnosed. All diseases that are diagnosed were shown in Table 2.

Table 2. All diseases that are diagnosed in patients during the follow-up period.

	n (%)
Hypermobility Syndrome	29 (10.2)
Urticaria	7 (2.4)
Hypothyroidism	6 (2.1)
Transient synovitis	4 (1.4)
Chronic ITP*	4 (1.4)
Scoliosis	4 (1.4)
Familial Mediterranean Fever	3 (1)
Cryopyrin associated periodic Syndrome	2 (0.7)
PFAPA syndrome**	2 (0.7)
Celiac Disease	2 (0.7)
Acute Rheumatic Fever	2 (0.7)
Fibromyalgia	1 (0.3)
Bone Tumor	1 (0.3)
Juvenile Idiopathic Arthritis	1 (0.3)
Henoch-Shöenlein Purpura	1 (0.3)
Myastenia Graves	1 (0.3)
Sever Disease	1 (0.3)
Vitiligo	1 (0.3)
Systemic Lupus Erythematosus	1 (0.3)

*Idiopathic Thrombocytopenic Purpura, **Periodic fever, aphthous stomatitis, pharyngitis and cervical adenitis syndrome.

Conclusion: We are reporting that in only 0.3% of patients with ANA positivity who don't have any diseases diagnosed initially, were diagnosed as rheumatologic diseases during to the follow-up period. Since positivity of ANA is also common in the healthy population, requesting this test in only patients with high suspicion for connective tissue disease will reduce confusion in terms of diagnosis.

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Other orphan diseases

AB1012 INVESTIGATION OF RELATIONSHIP BETWEEN SEXUAL FUNCTION AND OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY IN PATIENTS WITH BEHÇET'S: PRELIMINARY STUDY

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Background: Patients with Behçet's have sexual dysfunction in recently literature. However, depression and anxiety accompanying these studies were not excluded. In addition, increased sexual dysfunction in patients with Behçet's has been reported in these studies in relation to depression and anxiety. Also it has been stated that endothelial dysfunction decreases the vasodilator neurotransmitter level. It was emphasized that this may lead to erectile dysfunction in disease of Behçet's.

Objectives: The aim of this study is to evaluate the relationship between erectile dysfunction (ED) and radial peripapillary capillary (RPC) density determined by Optical Coherence Tomography Angiography (OCTA).

Methods: Patients under 45 years old who had no known additional disease and had no eye and neurological involvement were included in the study. The patients were evaluated with Beck Depression and Anxiety Scale. Accordingly, patients without anxiety and depression were included in the study. An International Index of ErectileFunction (IIEF) questionnaire was applied to a total of 18 patients who met the inclusion criteria. Detailed ophthalmological examination and OCTA imaging were performed by the ophthalmologist. Patients whose eye bottom could not be evaluated clearly (Corneal pathology, cataracts, etc.), image quality was 0.5 and below, and additional eye disease (glaucoma, optic neuropathy, maculopativb) were excluded from the study.

Results: The mean age of the patients was 37 ± 6.5 years, and the duration of the disease was 82.37 ± 47.78 months. There was a strong relationship between RPC Small Vessel Whole Density (RPC-SVWD) and overall satisfaction and sexual satisfaction (p: 0.036 and 0.045). There was a strong positive relationship between RPC Small Vessel Peripapillary Density (RPC-SVPD) and erectile function, sexual desire, sexual satisfaction and general satisfaction (p: 0.036, 0.032, 0.005, 0.004). There was a strong positive relationship between RPC All Vessel Peripapillary Density (RPC-AVPD) and erectile function and sexual satisfaction (p: 0.048, 0.015).

Conclusion: In our study, a significant relationship was found between sexual function and RPC density. In the literature, it has been found that nitric oxide synthesis decreases due to endothelial dysfunction in patients with Behçet's. Although there are preliminary study data, we found a significant relationship between the vascular layer of both the penis and the eye in our study. The data we obtained in this study, in which all factors that may cause erectile dysfunction are excluded, show that Behçet's, which is theoretically known to affect all vascular structures, can affect sexual functions by its nature. In our study, although there is a relationship between ED and OCTA data in Behçet's disease, the large number of cases of our ongoing study will provide clearer information.

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AB1013 CYCLOPHOSPHAMIDE VS AZATHIOPRINE FOR THE TREATMENT OF CONNECTIVE TISSUE RELATED INTERSTITIAL LUNG DISEASE

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Background: Interstitial lung disease (ILD) is a common morbidity and mortalitiy reason for connective tissue disorders (CTD). Data related to treatment options in the literature is limited
Objectives: To describe the role of azathiopurine (AZA) in the first line treatment of connective tissue disease related interstitial lung disease CTD-ILD, comparing with cyclophosphamide (CYC)
Methods: Between 2009 and 2019 all interstitial lung disease patients admitting rheumatology or pulmonology department were retrospectively evaluated. Among those patients,as an first line regimen treated with either azathiopurine or cyclophospamide were included. Primary end point was FVC percentage change at 6th month.
Results: Among 328 CTD-ILD, 57 patients had AZA treat and 79 patients had CYC for the first line treatment. Patients treated with AZA tend to have limited disease and older age. CYC treatment had a mean of 2,41% increase in FVC but in AZA -1,44% decrease in FVC predicted (p:0,041) 5 major CTD groups were defined (systemic sclerosis (SSc), rheumatoid arthritis (RA), primer sjögren syndrome (pSS), dermatomyositis/ polimyositis (PM/DM), autoimmune features of intestitial lung disease (IPAF)). AZA had similar efficacy in, PM/DM and IPAF groups but worse outcome in SSc, RA and pSS compared to CYC.
Conclusion: AZA treatment might be an option patients with limited disease extent and the diagnosis of PM/DM or IPAF. CYC was a better treatment in SSc, RA and pSS patients

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Table 1. CYC: treatment responses of cyclophosphamide and azathiopurine regimens AZA: azathiopurine CYC: cyclophosphamide, AZA: azathiopurine CTD: connective tissue disease, SSc:Systemic Sclerosis, RA: Rheumatoid Arthritis, pSS: primary sjogren syndrome, DM/PM/ ASS: Dermatomyositis / Polimyositis/Antisynthetase Syndrome, IPAF: Idiopahtic interstital fibrosis with autoimmune feautres, FVC: forced vital capacity

	AZA(n:43)	CYC (n:72)	p
Progression(overall)	39,3%	15,3%	0,013
SSc (n:47)	60%	11,9%	0,029
RA(n:16)	62,5%	25%	>0,05
pSS(n:16)	71,4%	11,1%	0,035
DM/PM/ASS(n:14)	11,1%	-	>0,05
IPAF(n:20)	28,6%	23,1%	>0,05
FVC change (overall) (lt)	-,129±0,741	0,024±0,249	0,189
SSc (n:47)	-0,086±181	0,025±0,351	0,286
RA(n:16)	-0,553±1,521	-022±0,262	0,341
pSS(n:16)	-0,328±0,242	0,014±0,313	0,167
DM/PM/ASS(n:14)	-0,0089±0,370	0,120±0,037	0,316
IPAF(n:20)	0,123±0,320	0,120±0,101	0,981
FVC change (overall) (%)	-1,44±10,65	2,41±7,55	0,041
SSc (n:47)	-3,00±3,67	2,23±8,27	0,031
RA(n:16)	-3,50±9,65	-1,75±4,65	0,654
pSS(n:16)	-6,71±15,97	3,33±8,35	0,027
DM/PM/ASS(n:14)	0,00±11,85	4,40±2,70	0,313
IPAF(n:20)	2,06±9,04	5,28±6,70	0,380

Disclosure of Interests: None declared
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AB1014 CLINICAL AND LABORATORY PHENOTYPES IN PATIENTS DIAGNOSED WITH SARCOIDOSIS IN A VETERAN'S HOSPITAL

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Background: Sarcoidosis is a disease which affect any organ or tissue in the body, but is predisposed to lung involvement in up to 90% of cases. Its cause is not yet established, although a multicausal model with genetic, environmental and infectious factors is proposed.
Objectives: Determine the clinical, paraclinical characteristics and survival of patients diagnosed with Sarcoidosis treated at the Central Military Hospital.
Methods: Historical cohort study of patients who were diagnosed with Sarcoidosis at the Central Military Hospital in the last 5 years. A review of medical records, laboratory results and radiological studies was performed and verification of survival status free of mortality was documented by independent outcomes group. A descriptive analysis was done using standard methods and non-parametric survival was calculated using the Kaplan Meyer method with confidence interval in STATA 15.
Results: Twenty patients with confirmatory biopsy of sarcoidosis. Average age 44 ± 15.3 years, 55% (11/20) of the patients were men. Dyspnea was the most frequent reason for consultation 50% (10/20), S. Löfgren 10% (2/20), the lung was the most frequent location 65% (13/20), mild hypercalcemia and normal enzyme converting angiotensin levels were found. 60% of patients had grade 1 commitment on the chest radiograph. 60% (12/20) of the patients received immunosuppressive treatment. The overall survival at 5 years was 92% (95% CI 57-99).
Conclusion: Sarcoidosis is a disease of young patients with a slight predominance in men. Pulmonary involvement is the most frequent, followed by mediastinal nodal involvement. Most patients received steroid treatment at some time in their life. The long-term survival of the disease is more than 90%, which indicates its benign course.

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AB1015 FEATURES OF CLINICAL AND LABORATORY ACTIVITY IN IDIOPATHIC LOBULAR PANNICULITIS.

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Background: The pathological process of idiopathic lobular panniculitis (ILP) comes from disorganization of the adipose tissue which leads to its fibrosis and atrophy. It is assumed that the disease is of immunopathological nature, as evidenced by disorders of lipid peroxidation, high CIC, excess production of leptin (LEP), IL-2 and TNF. The latter is considered a key cytokine involved in the development of the disease.
Objectives: to establish the relationship between the clinical picture and immuno-inflammatory parameters (CRP, LEP and TNF) in patients with ILP.
Methods: We examined 67 patients (9 men, 58 women) with the ILP diagnosis verified in the Institute in 2007-2017. The age of patients ranged from 20 to 76, the average duration of the disease was 78.91[48.50] months. In addition to general clinical examination we performed immunological, histological studies, computed tomography of the chest, tuberculin samples. To determine the body mass index of patients, the values of the Quetelet index (QI) were used.
Results: The disease was found in all age groups, but more than half of the patients (57%) were in the most active working age of 45-60. ILP started with painful induration of various localization, except for the face, and increased temperature reaction of the body. The mean value of QI 24.10±12.01 cm/kg corresponded to normal body weight (p=0.180). 41 patients (61.19%) demonstrated normal QI and preobesity at the age before 45 in 30.3% of cases (p=0.36). Obesity of degree II and III was recorded for 7 patients (10.44%). QI correlated with the age of patients (r=0.43, p<0.05). ESR correlated with VAS pain intensity (r=0.29, p<0.05), lesion area (r=0.50, p<0.05), temperature increase (r=0.68, p<0.05,) and CRP level (r=0.68, p<0.05). The concentration of CRP correlated with VAS pain intensity (r=0.46, p<0.05), lesion area (r=0.57, p<0.05), stage II node (r=0.41, p<0.05) and TNF–α concentration (r=0.32, p<0.05). The increase

of the last indicator had a direct correlation with stage II of the node (r=0.41, p<0.05,) and with the level of LEP (r=0.28, p<0.05), and an inverse correlation with the number of nodes (r=-0.24, p<0.05). The level of LEP increased in 35 patients (52.23%), had a direct correlation with QI (r = 0.46, p<0.05), the affected area (r = 0.31, p<0.05), the concentration of CRP (r=0.36, p<0.05) and an inverse correlation with the number of nodes (r = -0.33, p<0.05).

Conclusion: it is obvious that in case of ILP there is a need to increase knowledge about the markers of inflammatory activity (ESR, CRP, TNF–α and LEP) which correlated with the area of the lesion, VAS pain intensity and temperature increase.

Disclosure of Interests: None declared

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AB1016 RATE OF PREDEFINING DISEASE ACTIVITY, REMISSION AND RELAPSE OF ADULT-ONSET STILL'S DISEASE: SYSTEMATIC LITERATURE REVIEW

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Background: Adult-onset Still's disease (AOSD) is a rare, multisystem and auto-inflammatory disorder. Although several scoring systems are proposed to describe AOSD disease activity, there is no agreement on the definition of disease activity, remission or relapse of AOSD.

Objectives: Aim of this literature review was to determine the rates of defining ''disease activity'', ''remission'' and ''relapse'' of AOSD.

Methods: We performed a systematic review (May 2019) on Pubmed by using the MeSh word '' Adult-onset Still's disease''; results were restricted to human studies and English language. We excluded case reports, reviews and studies including less than 10 patients; 215 articles were recruited for final assessment. Of this 215 article, we reached the full-texts of the 181 articles. Final assessment was done with 181 articles. In these articles, we searched whether the definitions of disease activity, remission or relaps were made or not.

Results: Total of 181 articles were included to analysis. Mean age was 37.2±6.6 and 73.6% of patients was female. Articles were devided to 4 main groups according to main focus related to AOSD: Observational studies, laboratory studies, genetic studies and clinical trials. Diagnosis of AOSD was according to Yamaguchi criteria in 159 (87.8%) of articles and Yamaguchi criteria was the most commonly used criteria set. Disease activity was defined in 96 (54.1%) of articles. Remission and relapse were defined in 52 (28.7%) and 18 (10%) of articles, respectively. Most commonly used definition of disease activity was the ''systemic score'' which was defined by Pouchet et al. Rates of defining ''disease activity'', ''remission'' and ''relapse'' according to 4 main groups were given in Table 1.

Table 1. Rates of disease activity, remission and relapse reporting based on 4 main article groups

Article group	n (%)	Disease activity (n,%)	p	Remission (n,%)	p	Relapse (n,%)	p
Observational Studies	70 (38.7)	18 (25.7)	<0.001	17 (24.3)	<0.001	8 (11.4)	<0.001
Laboratory Studies	72 (39.8)	46 (63.9)		15 (20.8)		2 (2.8)	
Genetic Studies	17 (9.4)	5 (29.4)		2 (11.8)		0 (0)	
Clinical Trial	22 (12.2)	14 (63.6)		18 (81.8)		8 (36.4)	

Conclusion: In recent years, new treatment options become available for AOSD. However, data about how to measure the AOSD activity in largely missing. Definitions of disease activity, remission or relapse are missing in the most of the studies, including clinical trials, in current literature. Future studies are needed for this issue.

References: None

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AB1017 ANTI RANK LIGAND IN ACUTE CHARCOT NEURO-OSTEOATHROPATHY OF THE FOOT: A PROMISING TREATMENT

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Background: Acute Charcot neuroarthropathy (CN) of the foot is a rare and severe complication of peripheral neuropathy leading to joint destruction. Usual treatment rely on standard pressure offloading and no pharmacological treatment is available. Inflammation and increased osteoclastic activity via receptor activator of nuclear factor (RANK) ligand are major features of acute CN.

Objectives: To assess clinical, metabolic and radiographic effect of denosumab, a fully human monoclonal antibody against RANK ligand, in acute CN.

Methods: In this open study, we included all consecutive patients with acute CN treated with denosumab 60 mg in our mixed rheumatology/diabetes clinic dedicated to diabetic foot. Diagnosis of acute CN was based on clinical presentation and supported by biology, radiography, magnetic resonance imaging (MRI). Baseline and follow-up assessment included clinical examination and emission tomography–computed tomography (PET-CT).

Results: Seven patients with acute CN were treated with denosumab between 2017 and 2019 (age from 43 to 70 years). Five were diabetic. All patients received denosumab, because of failure of standard pressure offloading, with evolving joint destruction of midfoot. CN evolves since a median of 6 months (2 to 20) at denosumab initiation. All patients clinically improved after denosumab injection (table). After a mean follow-up of 16 months, only 1/7 patients had a new flare. In the 4 patients with available follow-up X-ray, structural damage remained stable. In all 3 patients with available PET-CT evolution, the maximum standardized uptake lean value (SUL max) decreased.

Three patients were retreated, with a mean interval of 6 months: One patients because of persistent clinical and biological inflammation (CRP 17 mg/L), one because of relapse due to intensive walking, and one due to an associated osteoporosis.

No adverse event and hypocalcemia was observed.

Conclusion: One to three injection of denosumab 60 mg was efficient in preventing flare and further bone destruction in a 16 months medium follow up. These results justify the conduction of a randomized control study to assess the efficacy of denosumab as the first-line pharmacological therapy in acute CN.

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Table 1. Baseline characteristics and follow up treatment

N° patient	1	2	3	4	5	6	7
Age (years)	70	43	64	69	54	57	54
Sex	M	F	M	F	M	M	M
BMI (kg/m2)	31.8	29.7	23.4	19	40.4	39	30
Cause of neuropathy	Undetermined	MODY	Type 1 Diabetes	Amyloidosis	Type 2 Diabetes	Type 2 Diabetes	Type 2 Diabetes
PET-CT (SUL max) before treatment	R =7.1. L = 4.9	3.5	3.9	R = 2.9. L = 3.1	R = L = 3.7	3.1	6.6
Number of injections	1	2	3	3	1	1	1
Number of new flare	0	0	2	0	0	0	0
Follow up after denosumab (months)	34	22	19	21	10	4*	3**
Radiography	stable	stable	stable	ND	stable	ND	ND
PET-CT (SUL max) after treatmen	R=4,3. L=3.	R=L=0	ND	ND	R=L=2.5	ND	ND

L, left; R, right. MODY, Maturity-Onset Diabetes of the Young;

* Assessment is scheduled on february 2020 (** march 2020)

AB1018

TREATMENT RESPONSE OF HYDRONEPHROSIS ASSOCIATED WITH IDIOPATHIC RETROPERITONEAL FIBROSIS, FOCUSING ON RATIO OF IGG4/IGG3 SERUM CONCENTRATION

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Background: Hydronephrosis, a common complication of idiopathic retroperitoneal fibrosis (iRPF), may lead to poor renal outcomes unless it is resolved. Pathological confirmation can help to identify the aetiology of the disease and determine the treatment strategy. But, in most cases, it is difficult to obtain sufficient tissue due to the location of fibrosis. In a recent study, parts of iRPF are correlated with IgG4-related disease characterised by elevated serum IgG4 levels (>135 mg/dL). Normal serum IgG3 level (21–176 mg/dL) has been known to be higher than normal serum IgG4 level (4–86 mg/dL). The reverse IgG4/IgG3 ratio has been suggested to be an IgG4-related disease component that distinguishes it from primary sclerosing cholangitis [1]. However, the ratio of IgG3 and IgG4 may be reversed in iRPF patients with hydronephrosis.
Objectives: We aimed to investigate the ratio of IgG subclasses as a predictive factor associated with treatment response of hydronephrosis in patients with iRPF.
Methods: We retrospectively recruited 19 iRPF patients with hydronephrosis who evaluated serum IgG subclasses in a tertiary hospital between 2004 and 2019. Hydronephrosis was evaluated on the basis of imaging findings. Medications and clinical and laboratory findings, including IgG subclasses, were reviewed following the diagnosis of hydronephrosis. Hydronephrosis improvement on subsequent images was evaluated to assess treatment response. Categorised data were compared using chi-square or Fisher's exact test. Continuous variables were compared using Mann–Whitney U test.
Results: At baseline, median serum IgG3 and IgG4 levels were 64 (IQR 37–82) mg/dL and 71 (IQR 40–171) mg/dL. Five patients had serum IgG4 levels > 135 mg/dL and 11 patients had the reverse serum level of IgG4/IgG3. On subsequent images (median follow-up at 3.2 [IQR 1.7–4.0] months), 11 patients showed hydronephrosis improvement. The proportions of positive ratio of serum IgG4/IgG3 (81.8% vs. 25%, p = 0.024), periaortic involvement (81.8% vs. 25%, p = 0.024) and high-dose glucocorticoid treatment (45.5% vs. 0%, p = 0.045) were significantly higher in patients with improvement than in those without improvement (Table 1). Interestingly, even in cases with normal serum IgG4 levels, patients with improvement showed a higher serum IgG4/IgG3 ratio than in those without improvement (median 1.5 vs. 0.7, p = 0.038).

Table 1. Clinical characteristics and treatment according to the short-term outcome of hydronephrosis

	Improvement (n = 11)	No improvement (n = 8)	p-value
Time to subsequent imaging (months)[a]	2.2 (1.3–4.2)	3.2 (2.0–3.8)	0.778
Males (n, %)	8 (72.7%)	7 (87.5%)	0.603
Periaortic involvement (n, %)	9 (81.8%)	2 (25%)	0.024
Impaired renal function (n, %)[b]	5 (45.5%)	2 (25%)	0.633
Serum IgG4 (mg/dL)[a]	114 (59–172)	43 (35–109)	0.152
Elevated serum IgG4 (n, %)	4 (36.4%)	1 (12.5%)	0.338
Serum IgG4/IgG3 ratio[a]	2.1 (1.2–4.9)	0.8 (0.4–1.0)	0.041
Positive ratio of serum IgG4/IgG3 (n, %)	9 (81.8%)	2 (25%)	0.024
Medical treatment (n, %)	7 (63.6%)	1 (12.5%)	0.059
High-dose glucocorticoid treatment (n, %)	5 (45.5%)	0 (0%)	0.045
Surgical intervention (n, %)	8 (72.7%)	4 (50%)	0.377

[a] Values are median and interquartile range (25^{th}–75^{th} percentile)
[b] Defined as serum creatinine level > 1.24 mg/dL

Conclusion: The reverse ratio of serum IgG4/IgG3 was associated with hydronephrosis treatment response, thus suggesting favourable responses to high-dose corticosteroid.
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AB1019

THERAPEUTIC PROFILE OF PATIENTS WITH VOGT KOYANAGI HARADA DISEASE FOLLOWED AT THE HOSPITAL DE CLÍNICAS. SAN LORENZO PARAGUAY.

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Background: Vogt-Koyanagi-Harada Disease (VKHD) is an autoimmune eye disease that causes chronic vision complications in young people. The treatment is based on corticosteroids and immunosuppressants, to which biological drugs are currently added. The visual prognosis depends on the stage in which it is diagnosed and the effective and timely treatment.[1,2]
Objectives: Describe the evolution and the therapeutic profile of patients with VKHD who go to the Rheumatology Department of the Hospital de Clínicas. San Lorenzo Paraguay until November 2019
Methods: Descriptive cross-sectional study conducted at the Hospital de Clínicas, San Lorenzo Paraguay, where clinical histories of patients with this disease and who have regular follow-up were reviewed.
Results: 21 patients were included, 17 (81%) women, average age of 35 years. The diagnosis and treatment were made 15 (71%) in acute phase, 4 (19%) convalescent phase and 2 (10%) in chronic phase.
Corticosteroids: All received corticosteroids at diagnosis. Methylprednisolone IV 1g /day for 3 consecutive days in 8 (44%) cases and for 5 days in 10 (55.5%) cases. The first month everyone received prednisone orally at 1mg / kg / d on average (60-75 mg/d), at 3 months the average dose of prednisone was 37 mg / d, at 6 months of 23 mg/d and at 12 months 10 mg / d months.
Immunosuppressive treatment: They received 20 (95%) patients. Induction with monthly intravenous cyclophosphamide was performed in 8 (40%) cases and with Azathioprine in 12 (60%) cases. Of the patients treated with Azathioprine initially, in 5 (23%) patients it was necessary to switch to Cyclophosphamide IV due to failure or intolerance. The maintenance treatment was azathioprine in 13 (62%) of the patients, MTX in 4 (19%) and the association of both drugs was indicated in 3 (14%) patients. One case was refractory and received infliximab and subsequently Rituximab, which resulted in remission.
The best final Visual Acuity (AV) was recorded with the Snellen chart in 40 eyes (20 patients), 27 (67.5%) patients with good vision (20/20 to 20/50), 8 (20%) patients with decreased VA (20 / 50-20 / 200), and 5 (12.5%) with legal blindness (<20/200) and of these only 3 patients had unilateral involvement and one patient with bilateral blindness. Sequelae / complications: 6 (28.5%) patients presented cataracts and finally 3 (14%) glaucoma, 5 (24%) anterior / posterior synechiae.
Conclusion: The majority of patients in this series presented a good vision when the inflammatory process was resolved (AV 20 / 20-20 / 50), this probably related to early diagnosis and initial aggressive treatment with intravenous corticosteroid pulses and its association with immunosuppressants of entry as mentioned in the literature. The worst vision, (visual acuity <20/200) occurred in 5 of 40 eyes, corresponding to 4 patients, two of them diagnosed and treated in the chronic stage. Timely treatment improves visual prognosis.
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Acknowledgments: Department of Rheumatology
Department of Ophthalmology
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AB1020

APPLICATION OF THE 2019 ACR/EULAR CLASSIFICATION CRITERIA CONTRIBUTES TO THE DIAGNOSIS OF IGG4-RELATED DISEASE

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Background: IgG4-related disease (IgG4-RD) is a rare and systemic disease characterized by swelling or masses in the involved organs, elevated serum IgG4, marked IgG4+ plasma cells infiltration and fibrosis. However, lacking of pathological data limited the definite diagnosis of IgG4-RD. As results of high-quality clinical and epidemiological investigations collected, new classification criteria for

IgG4-RD were approved by ACR and EULAR in 2019. Whether this new criteria improve the diagnosis efficiency needs to be validated in clinical practice.
Objectives: To applicate the 2019 ACR/EULAR classification criteria for the diagnosis of IgG4-RD in previously suspected patients and explore the clinical characteristics of patients with IgG4-RD according to the new classification criteria.
Methods: Patients suspected of having IgG4-RD due to elevated serum IgG4 and swelling or masses in single or multiple organs were recruited in Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University from May 2013 and November 2019. Demographic and clinical data were collected. The diagnosis was reevaluated with the 2011 comprehensive diagnostic criteria (CDC) for IgG4-RD and the 2019 ACR/EULAR classification criteria for IgG4-RD, respectively.
Results:
(1) There were 68 patients recruited and 59(86.8%) of them had elevated serum IgG4 (≥135mg/dl) and 53(77.9%) patients showed swelling or masses in single or multiple organs. Most patients first visit general surgery (17.6%), gastroenterology (16.2%), respiratory medicine (16.2%) and rheumatology (14.7%).
(2) According to the 2011 CDC for IgG4-RD, 4(5.9%) patients were definite IgG4-RD, 1(1.5%) was probable and 42(61.8%) were possible. According to the 2019 ACR/EULAR criteria, 20(29.4%) patients were diagnosed as IgG4-RD, including the 4 definite patients using the 2011 CDC.
(3) Among the 20 IgG4-RD patients according to the 2019 ACR/EULAR criteria, 19(95.0%) were male and median age of symptom onset was 62(46~69) years. There were 6(30.0%) patients diagnosed at rheumatology, 5(25.0%) at gastroenterology, 3(15.0%) at general surgery, 2(10.0%) at respiratory medicine and 1(5.0%) at stomatology, endocrinology, orthopedics and urinary surgery, respectively. There were 9(45.0%) patients with bilateral lacrimal or salivary glands involved, 9(45.0%) with pancreas and biliary tree involved, 5(25.0%) with retroperitoneum involved, 2(10.0%) with kidney involved and 1(5.0%) with chest involved.
(4) The median serum IgG4 of the 20 IgG4-RD patients was 15.40(4.14~55.10) g/L, median serum IgG was 27.9(17.2~50.2)g/L. There were 20.0%(4/20) patients had elevated serum eosinophil and 93.3%(14/15) had elevated serum IgE. There were 60.0%(9/15) patients had elevated C-reactive protein, 85.7%(12/14) had elevated erythrocyte sedimentation rate and 26.7%(4/15) had hypocomplementemia. There were 35.7%(5/14) patients had positive rheumatoid factor and 14.3%(2/14) had positive antinuclear antibodies. There were 6(30.0%) patients didn't received biopsies, 8(40.0%) patients received surgical removal of salivary glands, lacrimal glands or pancreatic masses and 6(30.0%) patients received needle biopsies of the salivary glands or biopsies by bronchoscopy, gastroscopy or enteroscopy.
(5) Among the patients didn't fulfill the 2011 CDC and the 2019 ACR/EULAR criteria, there were 40 patients had elevated serum IgG4, whose serum IgG4 level were significant lower than those of IgG4-RD patients [3.66(2.39~7.68) g/L vs. 15.40(4.14~55.10)g/L, P<0.001], and percentage of serum IgG4 ≥5× upper limit of normal were also lower than those of IgG4-RD patients (27.5% vs. 73.7%, P=0.002).
Conclusion: The 2019 ACR/EULAR criteria can help diagnosing patients with IgG4-RD even lacking the tissue confirmation. Patients with moderately elevated serum IgG4 need more clinical evidence to diagnose IgG4-RD and exclude mimics.
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AB1021 CHARACTERISTICS AND MANAGEMENT OF RHEUMATIC MANIFESTATION UNDER ESTROGEN RECEPTOR-TARGETING CANCER THERAPIES, DATA FROM A PROSPECTIVE REGISTRY

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Background: The knowledge about interdependencies between rheumatic manifestations and malignancies is limited. Further, reliable data on the occurrence of rheumatic symptoms as side effects of specific cancer therapies beyond checkpointinhibitor-induced immune-related adverse events are sparse. In this regard, although arthralgia under estrogen receptor-targeting therapies (aromatase inhibitors and the estrogen receptor modulator tamoxifen) has been frequently reported in oncological clinical trials and case reports, prospective data including an assessment of rheumatic manifestations by rheumatologists are lacking.
Objectives: To contribute to a better understanding of interdependencies between rheumatic manifestations and cancer/ estrogen blockade and potentially improve the management of both entities, pilot data were analysed.
Methods: Data on characteristics and treatment of rheumatic manifestations and cancer as well as their timely association were systematically, prospectively collected and analysed in the MalheuR (´malignancy and rheumatic disease´) registry, a long-term, observational study designed to study patients suffering from concomitant rheumatic disease and malignancy and/or premalignant lesions.
Results: We identified 11 patients with rheumatic manifestations under estrogen receptor-targeting therapies (3 anastrozol, 4 letrozol, 8 tamoxifen) as part of breast cancer treatment. In addition to breast cancer one patient had a lymphoma 3 years after and another patient had a non-small cell lung cancer 2 years before breast cancer diagnosis. The patients had different cancer stages (5 IA, 3 IIA, 1 IIB, and 1 IVA). Their mean age at cancer diagnosis was 60.4 ± 11.6 years and all patients are females. The time interval between diagnosis of cancer and onset of systemic/ rheumatic symptoms was 49.5 ± 34.0 months. Of interest, the time interval between onset of rheumatic symptoms and first assessment by a rheumatologist was 16.9 ± 22.3 months. The following systemic and rheumatic symptoms were reported: arthralgia in 10, arthritis in 8 (small joints in 5, large joints in 3 affected), morning stiffness (>30 min) in 7, IBP in 1, myalgia in 7, sicca symptoms in 2, fever in 1 (new-onset FMF with heterozygous M694U mutation), class IV glomerulonephritis and polyserositis in 1 (with new-onset SLE) patient(s). Disease burden at baseline was rather high with a mean VAS pain of 65 (±12.9)/100. Laboratory analyses revealed an increased CRP in 6/11 (55%) with a mean of 10.3 ± 8.2 mg/l (<5). Autoantibody positivity was observed for ANAs in 5/10 (50%, titers ranging from 1:80 to 1:160), anti-dsDNA in 1, rheumatoid factor in only 1/10 (10%) patients, none was anti-CCP positive. Before consulting a rheumatologist, patients were treated with NSAR 3/11 (27%), 10/11 systemic glucocorticoids (91%) with an initial dose of 17.5 ± 19.5 mg and intra-articular glucocorticoids 1/11 (9%). Rheumatological assessment lead to initiation of csDMARDs (3/11 MTX, 1/11 SSZ, 1/11 HCQ, 1/11 AZA (later MMF/ rituximab in the SLE patient) 1/11 colchicine) as corticosteroid-sparing agents with good response in the majority of patients.
Conclusion: Our data demonstrate heterogeneous rheumatic manifestations, partially with severe manifestations beyond arthralgia, so far not reported by oncological studies including follow-up, which might suggest an underreporting. Furthermore, despite close monitoring in tumor aftercare, our data show a considerable delay in referral to a rheumatologist and initiation of suitable treatment. The prospective design of the MalheuR registry enables future validation of our pilot data.
Disclosure of Interests: Alina Dr. Patroi Consultant of: Advisory board Novartis, Leonore Diekmann: None declared, Hanns-Martin Lorenz Grant/research support from: Consultancy and/or speaker fees and/or travel reimbursements: Abbvie, MSD, BMS, Pfizer, Celgene, Medac, GSK, Roche, Chugai, Novartis, UCB, Janssen-Cilag, Astra-Zeneca, Lilly. Scientific support and/or educational seminars and/or clinical studies: Abbvie, MSD, BMS, Pfizer, Celgene, Medac, GSK, Roche, Chugai, Novartis, UCB, Janssen-Cilag, Astra-Zeneca, Lilly, Baxter, SOBI, Biogen, Actelion, Bayer Vital, Shire, Octapharm, Sanofi, Hexal, Mundipharm, Thermo Fisher., Consultant of: see above, Bernhard. Kraemer: None declared, Karolina Benesova Grant/research support from: Study grants for SCREENED study by Abbvie, Novartis and Rheumaliga Baden-Württemberg, Consultant of: One-time participation in Novartis advisory board., Jan Leipe Grant/research support from: Consultancy and speaker fees: Abbvie, AstraZeneca, BMS, Celgene, Hospira, Janssen-Cilag, LEO Pharma, Lilly, MSD, Novartis, Pfizer, Roche, Sanofi, UCB. Scientific support: Novartis, Pfizer., Consultant of: Consultancy and speaker fees: Abbvie, AstraZeneca, BMS, Celgene, Hospira, Janssen-Cilag, LEO Pharma, Lilly, MSD, Novartis, Pfizer, Roche, Sanofi, UCB. Scientific support: Novartis, Pfizer., Speakers bureau: Abbvie, AstraZeneca, BMS, Celgene, Hospira, Janssen-Cilag, LEO Pharma, Lilly, MSD, Novartis, Pfizer, Roche, Sanofi, UCB
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AB1022 PANNICULITIS IN RHEUMATOLOGICAL PRACTICE: THE RESULTS OF LONG-TERM FOLLOW-UP

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Background: Panniculitis is a group of heterogeneous inflammatory diseases that occur with damage to the subcutaneous fat (SCF), musculoskeletal system, and often internal organs
Objectives: to evaluate the course and outcome in patients with panniculitis
Methods: the course of the disease was monitored in 193 patients treated at the V.A. Nasonova Research Institute of Rheumatology for 3-5 years (142 women, 51 men) aged 19 to 77 with the referral diagnosis of erythema nodosum (EN) and

undifferentiated panniculitis and with the disease duration of 1 week to 13 years. In addition to general clinical study, serum concentrations of α-1 antitrypsin, amylase, lipase, ferritin, creatinephosphokinase were determined, computed tomography of the chest organs, immunological, ultrasound scanning of the skin and SCF of the node area, tuberculosis tests and pathomorphological study of skin biopsy from the node area were performed.

Results: : as a result of laboratory and instrumental examination, the following diagnoses were made: EN associated with infection (72 people – group 1), lipodermatosclerosis (LDS) (40 –group 2), idiopathic lobular panniculitis (ILP) (32 – group 3), Löfgren's syndrome (SL) (49 –group 4). During the follow-up period, 6 deaths occurred (3.1%): in a patient with LDS due to acute heart failure and in 5 patients with ILP due to the activity of the disease which led to the development of cardiopulmonary pathology and disseminated intravascular coagulation (DIC) syndrome. In group 1, during the observation period, UE recurred in 18 people (25%), the probable causes were: hypothermia (6), exacerbation of chronic tonsillitis (6), acute respiratory viral infections (ARVI) (4), stress (1), a rapid decrease in the dose of glucocorticoids (GC) (1), the cause is unknown (2). In group 2, recurrence occurred in 19 patients (47.5%) due to the lack of anti-inflammatory therapy (plaquenil) (10), trauma (4), stress (3), and weight lifting (2). There was no recurrence in 7 patients in this group, however, nodes would not disappear completely, which is obviously due to the absence of plaquenil. In group 3, recurrence was registered in 24 cases (75%) and it was associated with insufficient effect of the ongoing anti-inflammatory therapy (9), a decrease in blood glucose to minimal doses (6), hypothermia (6) and the absence/cancellation of anti-inflammatory therapy (3). In group 4, recurrence of nodes was registered in 14 cases (28.5%), possible causes: cancellation of GC (9) and cooling/ARVI(5).

Conclusion: in the observed group of patients with panniculitis mortality was 3.1%. The main causes of recurrence in EN were viral-bacterial infections, and in case of ILP, LDS and SL it was insufficient effect/absence of anti-inflammatory therapy.

Disclosure of Interests: None declared

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AB1023 CARDIAC MRI IN HYPERFERRITINAEMIC DISEASE STATES REVEALS MYOCARDIAL INFLAMMATION NOT IDENTIFIED BY ECHOCARDIOGRAPHY

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Background: Acutely unwell adult patients with hyperinflammatory hyperferritinaemic states are typically challenging to diagnose. Case series suggest that cardiac involvement may be common (up to 20%) but the phenotype has not been well characterised[1].

The elevation of cardiac biomarkers suggests cardiac involvement, but are non-specific in acute illness. Cardiac MRI (CMR) offers the ability to characterise the myocardium and identify inflammation, and modern motion-corrected sequences now allow the assessment of patients who may struggle to breath-hold in the recovery from acute illness.

Objectives: We report 3 patients who underwent CMR in the acute phase of illness with raised cardiac biomarkers.

Methods: Case records of acutely ill patients with hyperferritinaemia from two major London centres were reviewed and cases who had undergone CMR in the acute phase of illness were identified.

Results: 3 cases were identified from a cohort of 22, we report CMR findings from differing aetiologies of hyperferritinaemic states:

Case 1: A female in her 60s presented acutely unwell with fever, swollen joints and salmon pink rash. Ferritin was raised at 50574ug/L (20-300ug/L), troponin I 384ng/L (<34ng/L) and Brain Natriuretic Peptide (BNP) 324ng/L (<159ng/L). Echocardiography was normal. However CMR with T2 mapping revealed several small areas of raised signal consistent with myocardial inflammation. A diagnosis of systemic Adult Onset Stills Disease (AOSD) was made. She received IV methylprednisolone and anakinra with normalisation of cardiac biomarkers.

Case 2: A male in his 20s with known SLE with associated end stage renal failure requiring transplant. He had a previous prolonged admission secondary to HLH. He presented with chest pain and concave shaped ST elevation on ECG. Troponin peak 2168ng/L, BNP 1334ng/L. Peak ferritin 1300ug/l.

He was initiated on colchicine for likely pericarditis. Echocardiography showed a dilated left ventricle and mildly increased wall thickness, but overall systolic function within normal limits.

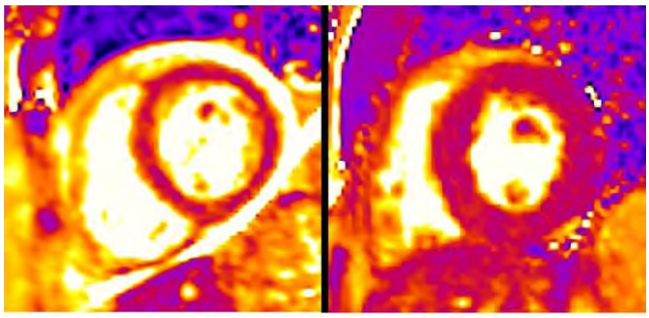
CMR reported nodular patchy late gadolinium enhancement in the mid inferoseptum and inferior wall associated with areas of raised T2 mapping values. NM cardiac rest gated PET reported abnormal FDG uptake to the myocardium with sites including the apical inferior wall, apical RV insertion point and basal septal/anterior right ventricular walls. Features were deemed in keeping with active myocarditis.

He responded to colchicine with improved troponin, and was discharged with close follow up.

Case 3: A male in his 20s presented with septic shock attributed to meningococcal septicaemia requiring ITU admission. Troponin was elevated at >9000ng/L. Bloods demonstrated raised ferritin and features consistent with HLH were identified.

CMR reported elevated native myocardial T1/T2 signal of the lateral and mid-anterior walls in keeping with myocardial oedema. Pericardium adjacent to the anterolateral wall had elevated T1/T2 signal with hyperenhancement on delayed enhancement imaging. Tissue characterisation was in keeping with an acute myopericarditis process.

In addition to broad spectrum antibiotics to treat his underlying infection, he received therapy for HLH including methylprednisolone, anakinra and IVIG. He subsequently made a good recovery to treatment.



Left panel shows a short-axis T2 map from Case 1. There is heterogeneity to T2 mapping values with multiple areas >55ms consistent with myocardial oedema. There is also a pericardial effusion. Right panel shows a short-axis T2 map from Case 2. There is again heterogeneity to T2 mapping with multiple areas >55ms consistent with myocardial oedema. There is also LVH consistent with hypertension.

Conclusion: CMR in acute illness with hyperferritinaemia reveals abnormal tissue characterisation with myocardial inflammation, even when echocardiography is normal. We suggest CMR may be a useful test to expand our understanding of hyperferritinaemic disease states.

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AB1024 EVALUATION OF CLINICAL FEATURES IN PATIENTS DIAGNOSED WITH JUVENILE AND ADULT-ONSET FAMILIAL MEDITERRANEAN FEVER

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Background: Familial Mediterranean Fever (FMF), which is more common in groups in the Mediterranean basin, is a monogenic auto inflammatory disease characterized by recurrent attacks of febrile peritonitis, pleuritis and arthritis.

Objectives: The aim of this study is to investigate the clinical features of patients diagnosed with juvenile and adult-onset Familial Mediterranean Fever (FMF).

Methods: Patients with FMF were included in the study consecutively without sample selection. Data about age, sex, disease duration (month), symptom duration, age at diagnosis, diagnosis delay time, comorbid diseases, and medications were noted. Patients with onset of symptoms ≤ 20 years old were classified as juvenile-onset, those > 20 years old were classified as adult-onset FMF. The frequency and characteristics of attacks and the presence of amyloidosis will be recorded.

Disease activity was assessed with the PRAS disease activity score. The Health Assessment Questionnaire (HAQ) and SF-36 were used to evaluate physical disability and quality of life, respectively.

The descriptive analysis was done for all parameters. Differences between categorical variables were assessed by Chi-square test and Fisher's exact test. The Mann Whitney-U test was used to compare two sample means. P<0.05 accepted as significant. SPSS 20.0 (Statistical package for social sciences for Windows 20.0) program was used for the statistical analysis.

Results: The mean age of 86 patients (63 female, 23 male) with FMF was 38.38 (SD: 12.13) years. The patients with the juvenile-onset FMF were 26.7% of the patients.

There were no differences between juvenile and adult-onset FMF groups in terms of gender, frequency of attacks, duration of attacks, acute phase values between attacks, colchicine dose, presence of colchicine resistance, and presence of amyloidosis (p>0.05). The latency to diagnosis was significantly higher in patients with adult-onset FMF (p<0.005).

The PRAS disease activity scores were significantly higher in the juvenile-onset FMF group (p=0.001). There were no significant differences between the two groups in terms of SF-36 and HAQ scores (p> 0.05).

Conclusion: While there were no differences between juvenile and adult-onset FMF patients in terms of quality of life and functional disability, the PRAS disease activity scores were higher in patients with juvenile-onset FMF.

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Disclosure of Interests: None declared

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AB1025 EVALUATION OF ANXIETY AND DEPRESSION LEVELS IN PATIENTS WITH FAMILIAL MEDITERREAN FEVER

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Background: Anxiety and depression are common problems in chronic rheumatological diseases (1). Familial Mediterranean Fever (FMF) is characterized by recurrent fever and serosal inflammation attacks.

Objectives: The aim of the study was to evaluate the levels of anxiety and depression in patients diagnosed with FMF, and to examine its relationship with drug compliance and attack frequency.

Methods: Sixty female patients aged 18 years or older who were consecutively admitted to the rheumatology outpatient clinic and diagnosed as FMF according to the Tel-Hashomer Classification criteria were included. Patients' age, gender, body mass index (BMI), educational status, disease duration, drugs used and frequency of attacks were recorded. Beck anxiety scale and Beck depression scale were used to determine the level of anxiety and depression.

Results: Sixty female patients with a mean age of 32.03 ± 10.03 and an mean disease duration of 9 ± 6.9 years were included in the study. The patients were divided into minimal, mild, moderate and severe according to their anxiety level. According to the level of anxiety, minimal anxiety was observed in 18 (30%), mild 9 (15%), moderate 12 (20%) and severe anxiety in 10 (16.7%) patients. Data related to anxiety are given in table 1. The patients were divided into minimal, mild, moderate and severe depending on the level of depression. Depending on the level of depression, minimal depression was seen in 34 (56.7%), mild 13 (21.7%), moderate 8 (13.3%) and severe depression in 4 (6.7%) patients. Data related to depression are given in table 2.

Table 1. Data about anxiety

	Minimal	Mild	Moderate	Severe	P
Age (years) (mean ± SD)	30.82 ±10.7	26.22±8.5	34.42±10.2	33.4±9.7	0.28
BMI (kg/m^2) (mean ± SD)	25.53±5.05	19.88±2.7	25.03±4.91	26.03± 3.4	0.02
Disease duration (years)	11.93±9.6	8.67±4.0	10.5±6.7	4,89±3,7	0.13
Marriatal status (Married)	13 (70)	2 (22.2)	10 (83.3)	9 (90)	0,06
Child status (%)(having child)	12 (70.6)	1 (11.1)	8 (72.2)		0,006
Time of the last attack (%)					0,72
2 weeks ago	2 (11.8)	2 (22.2)	4 (33.3)	4 (50)	
3 months ago	4 (23.5)	1 (11.1)	2 (16.7	-	
>6 months	7 (41.2)	4 (44.4)	4 (33.3)	3 (37.5)	

Tablo 2. Data about depression

	Minimal	Mild	Moderate	Severe	P
Age (years) (mean ± SD)	32.79±9.89	28.83±8.93	32.63±10.5	36.5±14.3	0.61
BMI (kg/m^2) (mean ± SD)	25.68±5.09	22.06±3.2	23.81±4.33	26.35±2.8	0.076
Disease duration (years)	10.52±8.06	8.5±4.6	8.67±4.6	1.5±1	<0.00
Marriatal status (Married)	25 (73.5)	8 (61.5)	7 (87.5)	3 (75)	0,63
Child status (%)(having child)	23 (71.9)	5 (38.5)	7 (87.5)	3 (75)	0,08
Time of the last attack (%)					0,94
2 weeks ago	6 (18.2)	2 (16.7)	2 (28.6)	2 (50)	
3 months ago	8 (24.2)	1 (8.3)	1 (14.3)	1 (25)	
>6 months	12(36.4)	5 (41.7)	2 (28.6)	1 (25)	

Conclusion: In the case of a chronic disease such as FMF, which has a younger patient population than other rheumatic diseases, anxiety and depression should be evaluated during routine outpatient clinic administration and psychiatric support should be provided if necessary.

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Disclosure of Interests: None declared

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AB1026 INFLAMMATORY MANIFESTATIONS IN PATIENTS WITH HUMAN LEUKOCYTE ANTIGEN-B*51 POSITIVE AND WITHOUT BEHÇET'S DISEASE

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Background: Human leukocyte antigen (HLA) B*51 allele is the most important genetic factor in susceptibility to Behçet's disease (BD), an immune-mediated systemic disorder of unknown etiology, characterized by recurrent episodes of inflammatory manifestations. In fact there is a considerable clinical overlap of BD with autoinflammatory syndromes. As it's known, the majority of HLA-B*51 positive individuals do not develop BD. But do these individuals also present inflammatory manifestations?

Objectives: Characterize the group of individuals in our hospital with positive HLA-B*51, without BD diagnosis and review whether inflammatory manifestations are present in these individuals.

Methods: A retrospective study of HLA-B*51 positive patients between 2000 and 2019. Genomic DNA was obtained from peripheral blood and HLA genotyping was performed using a PCR with Sequence Specific Primers (PCR–SSP) methodology. From the group of 289 B*51 positive patients, BD diagnosis were excluded. Demographic and clinical data were collected by review of clinical files in December 2019.

Results: 176 patients, mean age of 48.5 ± 16.5 years (5 to 84 years). Most were female (68%). The HLA study was motivated by multiple diagnostic suspicions: spondyloarthritis (SpA, 25.0%), BD (22.7%) and systemic sclerosis (SSc, 10.8%). The mean time elapsed since the immunogenetic study was 8.3 years, with 12 deaths recorded. 69 (39.2%) subjects had no diagnosis for immune-mediated disease (IMD). Of the other 107 patients, the majority had 1 IMD (64.5%), and the rest were diagnosed with 2 to 4 IMD. The most frequent IMD were SpA (20.8%), psoriasis (10.4%), psoriatic arthritis (9.7%), SSc (9.7%) and rheumatoid arthritis (7.1%). Autoantibodies were detected in 94 individuals (53.4%): antinuclear antibodies (64 patients), rheumatoid factor (26 patients) and CCP antibodies (11 patients). In 55 individuals no inflammatory manifestation was identified but the 68.8% of them presented between 1 to 7 manifestations:

System involved	Clinical manifestation	Frequency	
Ears, nose and throat	Chronic rhinitis	32 (13.2%)	∑ = 76 (31.4%)
	Recurrent tonsillitis	20 (8.3%)	
	Other	24 (9.9%)	
Cutaneous, mucous and serous	Recurrent oral aphtous ulcers	34 (14.0%)	∑ = 57 (23.6%)
	Serositis	10 (4.1%)	
	Other	13 (5.4%)	
Neurological	Chronic headache	34 (14.0%)	∑ = 36 (14.9%)
	Asseptic meningitis	2 (0.8%)	
Ocular	Ocular inflammation	31 (12.8%)	∑ = 31 (12.8%)
Urinary	Recurrent cystitis	15 (6.2%)	∑ = 15 (6.2%)
Vascular	Venous thromboembolism	7 (2.9%)	∑ = 14 (5.8%)
	Aneurysm	6 (2.5%)	
	Spontaneous coronary dissection	1 (0.4%)	
Rheumatic	Arthromyalgia	6 (2.5%)	∑ = 9 (3.7%)
	Gout	3 (1.2%)	
Constitutional	Recurrent fever syndrome	1 (0.4%)	∑ = 1 (0.4%)
Digestive	Recurrent abdominal pain	1 (0.4%)	∑ = 1 (0.4%)
Lymphatic	Axillary and inguinal adenopathies	1 (0.4%)	∑ = 1 (0.4%)
Pulmonary	Chronic pulmonary infiltrate	1 (0.4%)	∑ = 1 (0.4%)

Conclusion: Inflammatory manifestations are common in HLA-B*51 positive individuals, even in those without BD diagnosis. Further research is needed, considering other HLA alleles associated with increased risk of BD and including control groups.

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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.6572

AB1027 EFFECTIVENESS OF SUBCUTANEOUS ANTI-INTERLEUCINE 6 TREATMENT IN PATIENTS WITH ACTIVE MODERATE-SEVERE GRAVES' ORBITOPATHY REFRACTORY TO CONVENTIONAL THERAPY.

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Background: Graves' Orbitopathy (OG) is the main extrathyroid manifestation of Graves' disease (GD). Up to 25% of patients have moderate-severe inflammatory activity with a risk of major sequelae. Intravenous (i.v.) glucocorticoids (GC) pulses are the standard therapy. In refractory cases, several classic and some biological immunosuppressantsare used, obtaining variable responses. Interleukin 6 (IL6) is involved in the pathogenesis of OG, which has justified the off-label treatment with Tocilizumab (TCZ)[1], whose use by route i.v. has shown favorable results in published small case series and a single multicenter trial[2].

Objectives: To analyse the ocular effectiveness of anti-IL6 therapy used subcutaneously (s.c.) in patients with moderate-severe active refractory OG in usual clinical practice.

Methods: Retrospective descriptive observational study of a series of cases of moderate-severe OG patients treated with anti-IL6 s.c. The patient medical records of those who had received at least 1 cycle of anti-IL6 treatment were reviewed (December 2013-December 2019). The primary effectiveness outcome was the change of the Clinical Activity Score (CAS). Favorable response was considered: reduction of CAS≥2 points together with obtaining inactivity (CAS <3). Demographic data, personal medical history, clinical aspects of GD, previous therapies and data on the use and safety of anti-IL6 were collected. The SPSS11 package was used for statistical analysis, using non-parametric tests for quantitative variables. The study was approved by the local Ethical Committee.

Results: 12 of the 15 patients (80%) were women with a mean of 50.27 years (21-72). 60% (n=9) had smoking history, 40% (n=6) active. 26.7% (n=4) were diabetic, all without retinopathy. 100% of patients received imidazole antithyroid treatment. 46.7% (n=7) required β-blockers and 20% (n=3) diuretics. 66.7% thyroidectomy (n=10) and 20% (n=3) decompressive eye surgery and/or blepharoplasty were performed. Thyroid and ocular radiotherapy were used in 2 patients. 3 patients received botox. 80% (n=12) of them had previously received GC. 93.3% (n=14) were naïve to biological therapy, only 1 patient previously used Rituximab. All except one patient who was treated with SRL received TCZ as IL6 therapy. A significant favorable response was obtained in 100% of the patients (p=0.008), decreasing CAS average from 4.9 (2-7) to 1.7 (0-2) at the end of the therapy [Figure 1]. The severity of the OG changed from being moderate in 72.7% of the patients to mild in 66.7% of the total. The median time to inactivity was 8 months (2-15). 73.3% (n=11) of the patients finished the treatment reaching inactive OG, the rest (although inactive) maintained therapy. After 6 months, 100% of those who completed the treatment remained inactive with average CAS of 1.3 (0-2). Smoking did not influence the response, nor any other variable collected. Adverse events appeared in 26.7% (n=4) of the cases, all of them mild and without widrawal.

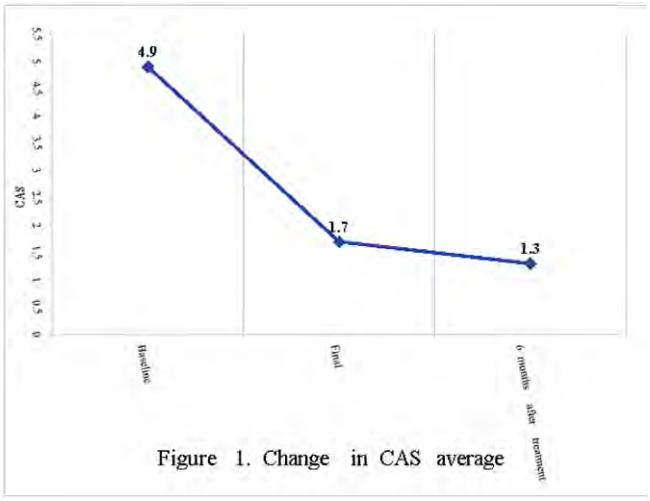


Figure 1. Change in CAS average

Conclusion: Treatment with anti-IL6 s.c. steadily decreases the clinical activity measured by CAS in patients with moderate-severe refractory OG, despite poor prognosis factors (such as smoking), with a good safety profile.

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Disclosure of Interests: None declared
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AB1028 A SINGLE-CENTER EXPERIENCE WITH TRANSIENT OSTEOPOROSIS – PATIENT CHARACTERISTIC AND APPROACH TO THERAPY.

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Background: Transient osteoporosis (TOP) or transient bone marrow edema syndrome is an enigmatic condition of unknown etiology first described in pregnant women. Though usually self limited, TOP causes pain and debilitation and predisposes the patient to avascular necrosis or fractures. The course can be protracted and patient may suffer relapses. Diagnostic method of choice is magnetic resonance imaging (MRI). Based on small case series and expert opinion, several therapeutic approaches have been proposed to hasten the recovery, including bisphosphonates, calcitonin, teriparatide. However, the literature is scarce and additional experience is needed to promote the understanding of this condition.

Objectives: To present our experience with TOP, including patient's characteristic, approach to diagnosis, prognosis and therapy

Methods: It is retrospective, single center study, conducted in Rambam healthcare campus, Haifa, Israel. All the medical files of patients referred to Rheumatology unit between years 2010-2020 were screened for diagnosis of TOP. Search words included: "osteoporosis", "bone marrow edema", "transient osteoporosis". The files were reviewed for patient's characteristics, modality of diagnosis, duration until full recovery, treatments and relapses.

Results: Eight patients with at least one episode of TOP were identified using the search words. Six patients (75%) were female. Three female patients developed TOP during or shortly after pregnancy. Two patients – one male and one non pregnant female suffered from TOP after bariatric surgery. One pregnant woman had a strong family history of TOP. The most frequent involved site in order of frequency were: hip (4/8), ankle (3/8) and knee (2/8). Six patients presented with more than one simultaneous site of TOP (hips, knees and ankles). Blood count, liver and Kidney function tests, markers of bone resorption, rheumatoid factor, Anti cyclic citrullinated peptide, Antinuclear antibodies were negative in all of the patients. C-reactive protein was elevated in 4/8 patients, Erythrocyte sedimentation rate was elevated in 2/8 patients. All patients had vitamin D deficiency. The diagnosis was confirmed by MRI. All the patients were treated with vitamin D and intra-venous Pamidronate, one patient with addition of calcitonin and one patient with addition of intra venous Iloprost. Time to recovery ranged from 1.2 to 6 months. The time to recovery was the same in pregnancy related TOP. Recovery was confirmed with follow-up MRI in all the patients. Relapses occurred in 4/8 patients and only one them had pregnancy related TOP. All the patients were treated by multidisciplinary team, including orthopedic surgeon, physiotherapist and psychologist when needed.

Conclusion: Our experience with TOP was enriched in patients presenting with more than one site of disease probably representing referral bias. Pregnancy related TOP was associated with lower risk of relapse. In terms of time to recovery there was no trend between pregnancy related and non related TOP or one site versus several sited TOP. None of the patients developed fracture, advocating in favor of adding bisphosphonates to therapy. Multidisciplinary approach is an essential part of TOP treatment strategy.

Disclosure of Interests: Sami Giryes: None declared, Katya Dolnikov: None declared, Alexandra Balbir-Gurman Consultant of: Novartis, Daniela Militianu: None declared, Natalia Puchkov: None declared, Yolanda Braun-Moscovici: None declared

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AB1029 MYOCARDIAL DYSFUNCTION DETECTED BY USING SPECKLE TRACKING ECHOCARDIOGRAPHY IN FAMILIAL MEDITERRANEAN FEVER PATIENTS; IS THERE ANY DIFFERENCE REGARDING RESISTANT DISEASE?

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Background: Familial Mediterranean fever (FMF) is an auto-inflammatory disease commonly affects people from Mediterranean basin. It is characterized by acute self-limiting inflammatory attacks of serous membrane. Some recent studies showed diastolic dysfunction in patients with FMF however systolic function was rarely evaluated before.

Objectives: To assess cardiac functions by using speckle tracking echocardiography (STE) in addition to routine measurements and to evaluate whether there is any difference between colchicine responsive patients and those with colchicine-resistant or severe disease.

Methods: Seventy-four FMF patients (57 responsive [60% female and median age 35 [18-63] years], 17 resistant [53% female and median age 31 [20-49] years]) and 74 healthy controls ([53% female and median age 37 [22-55] years]) were included in the study. Patients with cardiac disease or risk factors affecting STE were excluded. Patients who had ≥1 attacks in three months despite ≥2 mg/day od colchicine or who were treated with IL-1 blocking agents were defined as colchicine resistant disease and who had amyloidosis (whom had proteinuria ≥500 mg/day in at least 2 occasion or biopsy-proven amyloidosis) defined as severe disease. Demographic and disease related characteristics were obtained by using a structured form. A detailed echocardiographic examination including the M-mode, Doppler, and STE was applied to whole study population.

Results: There was no significant difference between groups in terms of age and sex. Disease duration was not different between colchine responsive and resistant patients (median duration in resistant diasease was 11 years (1-27), in responsive patients 6 years (0-33) and, p: 0.133). Although ejection fraction was similar among groups, global longitudinal peak systolic strain; a marker of systolic function, was significantly lower in FMF patients in comparison with healthy subjects and this difference was due to colchicine resistant FMF patients ($p<0.05$). There was no significant difference in echocardiographic parameters between non-resistive and resistive FMF patients ($p>0.05$) (Table).

Table. Comparison of standard and speckle tracking echocardiographic findings among groups

	Responsive FMF (n: 57)	Resistant FMF (n: 17)	Healthy Controls (n: 74)
LA	31 (23-41)	30 (26-35)	31 (22-44)
LVD	43 (35-86)	41 (38-48)	43 (20-50)
LVS	26 (20-32)	24 (18-31)	26 (19-34)
EF	62 (40-77)	64 (46-73)	60 (52-70)
E	95 (23-148)	98 (9-130)	93 (57-130)
A	83 (26-153)	79 (8-134)	81 (57-120)
DT	187 (100-303) *	183 (100-296)	161 (100-254)
ELateral	14 (8-29)	13 (10-23)	14 (8-23)
ALateral	11 (5-18)	10 (7-18)	10 (6-17)
ESeptal	11 (6-20)	9 (5-16)	11 (5-16)
ASeptal	10 (5-17)	10 (5-17)	9 (4-23)
GLS	20 (8-55) *	20 (15-32)	22 (16-33)
GCS	21 (10-29)	20 (11-42)	20 (13-30)

*Significant difference among groups, p<0,05. LA: Left atrium, LVD: left ventricular diastolic diameter, LVS: Left ventricular systolic diamater, EF: Ejection fraction, E: Early diastolic filling A: Atrial filling, DT: Deceleration time, GLS: Global Longitudinal strain GCS: Global circumflex strain

Conclusion: This study shows that there is subclinical myocardial dysfunction in FMF patients. Those patients with severe or colchicine resistant disease has a numerical but statistically different trend toward systolic dysfunction.

Disclosure of Interests: None declared

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AB1030 IGG4-RELATED DISEASE: A RETROSPECTIVE CLINICAL CASE SERIES FROM A TERTIARY CARE CENTRE IN INDIA

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Background: IgG4-related disease (IgG4-RD) is an often unrecognized, rare fibro-inflammatory condition that can involve various organ systems.

Objectives: The aim of this study was to identify the different clinical patterns of this disease in a single centre in North India.

Methods: 70 patients were diagnosed on the basis of published diagnostic criteria for IgG4-RD. Patients' presenting complaints, epidemiological profiles, laboratory, radiological and histological findings along with the treatment and outcomes were collated and analyzed from 2011 – 2019.

Results: In a total of 70 patients who were diagnosed with the disease, the ratio of female to male ratio was 1:1. The mean age of patients was 41.4 years. Involvement of orbits and peri-orbital tissues was highest (52.9%) due to large number of referrals from ophthalmology services. 13% of patients had multiple organ involvement. Patients with involvement of retroperitoneal tissues and lymph nodes were 8.5% and 5.7%, respectively. Increased serum IgG4 levels were found in 74.3% of the patients. Histopathological examinations of the affected organs were performed in 44 (62.85%) patients and a diagnosis of possible (38.57), probable (32.85%) and definite (28.57%) IgG4-RD was made. Majority of the patients (94.3%) required immunosuppressive medications along with corticosteroids. Azathioprine was the most commonly used (72.8%) immunosuppressive medication. Rituximab was used in17.1% of the patients, of whom one had multisystem involvement.

Conclusion: This study depicts the most common patterns of organ involvement along with the epidemiological, laboratory, histological, radiological data and response to treatment, in IgG4-RD, with a definite ophthalmology referral bias, in a tertiary care centre in North India.

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Table 1. Clinical and laboratory characteristics

Characteristics	Number of patients (N=70)
Age (years)	41.4
Age group in years, n (%)	
>50	24 (34.28)
<50	46 (65.71)
Sex, n (%)	
Male	36 (51.42)
Female	34 (47.22)
ESR (mm/hr)	24.37
CRP (mg/dL)	12.31
Serum IgG (mg/dL)	1214.2
Serum IgE (IU/L)	587.2
Type of IgG4 related disease, n (%)	
Definite	20 (28.57)
Probable	23 (32.85)
Possible	27 (38.57)

Data represented as mean, unless otherwise specified.
CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; Ig, immunoglobulin.

Table 2. Distribution of patients according to organ involvement.

Organ involvement	Number (%)
Orbital and periorbital	37(52.9)
Retroperitoneum	6 (8.5)
Laryngotracheal tissue	4 (5.7)
Aorta and branches	4 (5.7)
Lymph nodes	3(4.2)
Paranasal sinus	2 (2.8)
Paravertebral tissue	2 (2.8)
Pancreas	2 (2.8)
Lung and bronchus	2 (2.8)
Eye (Scleritis)	1 (1.4)
Prevesical Mass	1 (1.4)
Ear polyp	1 (1.4)
Small Bowel	1 (1.4)

Table 2. Distribution of patients according to organ involvement.

Organ involvement	Number (%)
Primary sclerosing cholangitis	1 (1.4)
Musculoskeletal	1(1.4)
Submandibular gland	1(1.4)
Central nervous system	1 (1.4)
Multisystem involvement	9 (12.86%)



Figure 1. Right eye proptosis

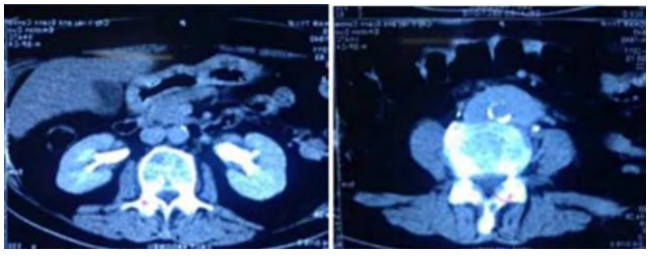


Figure 2. CT abdomen showing hydronephrosis due to retroperitoneal fibrosis

Disclosure of Interests: None declared
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AB1031 DYSKERATOTIC CELLS IN PERSISTENT PRURITIC SKIN LESIONS AS A PROGNOSTIC FACTOR IN ADULT-ONSET STILL'S DISEASE.

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Background: Adult-onset Still's disease (AOSD), a systemic inflammatory disorder, is characterized by high fever, evanescent rash, arthritis, and hyperferritinaemia. AOSD is also reported to be associated with other skin lesions, including persistent pruritic papules and plaques.
Objectives: This study aimed to assess the significance of dyskeratotic skin lesions in Japanese AOSD patients.
Methods: We retrospectively assessed the histology of persistent pruritic skin lesions and evanescent rashes and the relationship between dyskeratotic cells, serum markers, and outcomes in 20 Japanese AOSD patients, comparing AOSD histology with that of dermatomyositis (DM), drug eruptions, and graft-versus-host disease (GVHD).
Results: Persistent pruritic lesions were characterized by scattered single keratinocytes with an apoptotic appearance confined to the upper layer of the epidermis and horny layer without inflammatory infiltrate. In contrast to AOSD, the histology of DM, drug eruption, and GVHD demonstrated dyskeratotic cells in all layers of the epidermis with inflammatory infiltrate. AOSD with evanescent rash showed no dyskeratotic cells. The dyskeratotic cells in pruritic AOSD lesions stained positive for ssDNA and terminal deoxynucleotidyl transferase-mediated dUTP nick end-labeling, indicating apoptosis. Serum IL-18 was significantly higher in AOSD patients with dyskeratotic cells than those without, and generally required higher doses of glucocorticoids, immunosuppressants, and biologic agents. Two of ten AOSD patients with dyskeratotic cells died from haemophagocytic lymphohistiocytosis.
Conclusion: Persistent pruritic AOSD skin lesions are characterized by dyskeratotic cells with apoptotic features, involving the upper layers of the epidermis. There may be a link to elevated IL-18. This dyskeratosis may be a negative prognostic indicator.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.4072

AB1032 CONTRIBUTION OF BONE BIOPSY DURING REVELATORY BONE METASTASES

S. Jriri[1], M. Ben Majdouba[1], S. Ben Jemaa[1], A. Feki[1], R. Akrout[1], M. Ezzeddine[1], M. H. Kallel[1], H. Fourati[1], S. Baklouti[1]. *[1]Hedi Chaker Hospital, Sfax, Tunisia*

Background: Bone metastases (BM) are tumor cells that originate in a primary malignant tumor and are localized remotely in bone tissue. They more or less faithfully reproduce the morphological and biological characteristics of the primary tumor. Histological analysisis essential to confirm the diagnosis of BM and to identify the primary tumor if possible and sometimes to help in the selection of treatment.
Objectives: The aim of this work is to study the contribution of bone biopsy during revealing BM in diagnostic strategy and therapeutic decision.
Methods: We retrospectively studied the files of 105 patients hospitalized in a Rheumatology department of for BM revealing from January 2000 until December 2015. For each patient we collected epidemioclinical and anatomopathological data to arrive at the diagnosis of primary neoplasm and histological type.
Results: The patients were divided into 86 men (81.9%) and 19 women (18.1%) with a sex ratio (M / F) of 4.52. The average age of our patients was 64.91 ± 13.29 years. Pain was the most frequent reason for consultation found in 97.1%. This pain was either of bone site (61.9%) or of radicular topography (41.9%). Bone swelling or a pathological fracture revealed BM in 4.8% and 8.6% of the cases, respectively. The onset of neurological damage was noted in 13.3% of the cases.
Histologically, the bone biopsy performed in 64 patients made it possible to specify the histological type (carcinoma, adenocarcinoma) in 64% of the cases and to lead to primary cancer in 57.8%. A non-radio-guided percutaneous bone biopsy was performed in 44 patients (68.75%) including 41 osteo-medullary biopsy in iliac crest (BOM) and 3 in the sternum, a bone biopsy directed under scanner in 16 cases (25%) and a surgical bone biopsy in 4 cases.
The BOM was positive in 21 cases (51.2%) showing a poorly or moderately differentiated adenocarcinoma or carcinoma. It allowed referral to a primitive in 20 cases: a prostatic origin in 11 cases, a pulmonary origin in 5 cases, a digestive origin in 2 cases, a mammary origin in one case and a neuroblastoma in one case.
Conclusion: Thanks to improved sampling and immunohistochemistry techniques, the precise histological type and location of the primary tumor could be identified, there by improving the quality of care for patients with increased life expectancy.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.6285

AB1034 DEPRESSION AND ANXIETY IN FAMILIAL MEDITERRANEAN FEVER

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Background: Familial Mediterranean Fever (FMF) is a hereditary autoinflammatory disease characterized by recurrent attacks of fever, peritonitis, pleuritis, arthritis, and skin eruption (1). It is shown by studies that chronic diseases like diabetes mellitus, chronic heart disease, hypertension which other than inflammatory – rheumatologic disease increase depression and anxiety (2). There are a few studies evaluating depression and anxiety in FMF patients, and these results are conflicting (3,4).

Objectives: To assess the frequency of depression and anxiety in patients with Familial Mediterranean Fever (FMF)
Methods: In this study, 77 FMF patients aged 18 and over who were followed up in Sakarya University Education and Research Hospital, Department of Rheumatology, and 78 healthy volunteers aged 18 and over as thecontrol group. Beck depression scale and Beck anxiety scale were used to depression and anxiety, respectively. Beck'sdepression scale was evaluated as 9 and below normal, 10-16 mild depression, 17-29 moderate depression, 30-63 severe depression. Beck anxiety scale was evaluated as 0-8 normal, 8-15 mild anxiety, 16-25 moderate anxiety, 26 and above severe anxiety.FMF disease severity was determined by Pras scoring.
Results: The study group, comprised 77 diagnosed with FMF with a meanage of 37.18 and a control group comprised of 78 healthy controls (C) with a meanage of 35.32 (p=0,058). İn studygroup (P) %63.6, control group (C) %53.8 as female. %36.4 of thestudy group(C), %46.2 of the control group are male. (p=0,216). The prevalence of depression was significantly higher in FMF patients compared to the control group (in order P;C: normal %24,7; %47,4, mild depression: %40.3; %26.9, moderate depression %26; %19.2, severe depression %11.7; %6.4 p<0.015). Similarly in depression results; the prevalence of anxiety was significantly higher in FMF patients compared to the control group (in order P;C normal %23,4; %57.7, mild anxiety %26; %20.5, moderate anxiety %26; %15.4, severe anxiety %24.4; %6.4 p<0,001). Depression status was not correlated with FMF disease severity (p=0.645). A correlation was found between FMF severity and anxiety which it is which was found statistically significant (p=0.005).There was no relationship between erythrocyte sedimentation rate and C-reactive protein with depression and anxiety.
Conclusion: Both anxiety and depression frequency are increased in FMF patients compared to healthy controls.
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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.5852

AB1035 INTESTINAL MICROBIOTA COMPOSITION OF ADULT PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER AND HEALTHY CONTROLS (THE RHEUMA-BIOTA STUDY)

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Background: Although Familial Mediterranean Fever (FMF) is a monogenic disease, microbiota composition may play role in the pathogenesis or phenotypic expression.
Objectives: We aim to evaluate the intestinal microbiota composition in patients with FMF and to compare with healthy controls.
Methods: In this prospective cohort study, a group of 10 adult patients with FMF and 10 age-appropriate healthy controls, for which there was strict inclusion/exclusion, were enrolled. Fecal samples were stored at -80ºC until DNA extraction. A region of the 16S rRNA gene (V3-V4) was selected and sequencing was performed on the Illumina MiSeq platform at the Sequencing and Bioinformatics Service of FISABIO foundation.
Results: Alpha and beta diversity tests were similar between FMF and control groups except that Chao1 index. Chao1 index was modestly decreased in FMF group comparing the healthy controls (p<0.05). Our results showed differences in the intestinal microbiota composition of patients with FMF, with a higher abundance of *Eggerthella*, at genus level. At species level, *Eggerthella sinensis* and *Eggerthella lenta* were more abundant in patients with FMF.
Conclusion: *Eggerthella lenta* was previously shown to be higher in type II diabetes, multiple sclerosis, rheumatoid arthritis and some disseminated infections. In this study we firstly showed abundance of *Eggerthella* in patients with FMF, especially in *E. sinensis* and *E. lenta;* in addition to. Whether any of observed associations are causal, or the direction of causality is unclear yet and further studies with patients with FMF at the first diagnosis might clarify this issue.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.3906

AB1036 CLINICAL MANIFESTATIONS, CLINICAL COURSE, AND OUTCOMES OF IMMUNOGLOBULIN G4 RELATED DISEASE

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Background: Immunoglobulin G4 related disease (IgG4-RD) is an uncommon chronic systemic autoimmune disease, pathologically characterized by lymphoplasma cell, IgG4 plasma cell or storiform fibrosis infiltration with elevated serum IgG4 level. IgG4-RD is a new disease and not widely recognized.
Objectives: The aim of this study was to describe clinical manifestations and outcomes of IgG4-RD in Thai patients
Methods: This multicenter retrospective cohort study included patients who aged ≥ 18 years and were diagnosed with IgG4-RD according to 2011 comprehensive or consensus diagnostic criteria, between 2000 and 2019 in four academic centers in Thailand. Baseline characteristic, laboratory and pathologic findings, treatments, and outcomes were systematically reviewed.
Results: Of the 110 patients included, 71% were male with mean age (SD) of 59.6 (13.3) years and median disease duration (IQR) of 28.8 (14.6-53.5) months. Single organ involvement was observed in 60 patients (54.5%). The most common presenting organ involvement was the orbit (29%), followed by the salivary glands (19%), lacrimal glands (18%), bile duct (16%), and pancreas (11%). The most frequently affected organs were the orbits (34%), followed by the salivary glands (26%), lacrimal glands (20%), bile duct (19%), and lymph nodes (19%). Ninety-six percent (96%) had IgG4 level of more than 135 mg/dl at presentation. Most patients (92%) were treated with corticosteroid (CS) alone or in combination with immunosuppressive agents. Azathioprine (47%) and methotrexate (11%) were the most commonly used immunosuppressive agents. Additionally, 20% required surgery, and 6.4% underwent stent insertion. One-fourth (26%) were in remission with successfully CS tapering, while 37%, and 29% had complete, and partial response. Nevertheless, 22% relapse with median time to relapse (IQR) of 22.2 (12.8-41.1) months. Relapse was common in patients with orbital (p = 0.001) and lung (p= 0.007) involvement, and patients with longer disease duration (median 44.1 and 23.1 months, P=0.001), while serum IgG4 level was insignificantly higher in relapse group (median 1,085 vs. 850 mg/dL, p=0.28).
Conclusion: IgG4-RD is a chronic systemic autoimmune disease with diverse manifestations, response to treatment, and outcomes. Most patients responded well to CS and immunosuppressive agents with notable relapse rate, while minority required surgery or mechanical intervention.
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Acknowledgments: None
Disclosure of Interests: None declared
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AB1037 CANAKINUMAB FOR TREATMENT OF ADULT ONSET STILL'S DISEASE-RESULTS OF THE 24 WEEKS TREATMENT AND BEYOND: A MULTI-CENTRE, PLACEBO-CONTROLLED STUDY (CONSIDER)

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Background: Inhibition of interleukin-1 (IL-1) represents a promising treatment option in adult-onset Still's disease (AOSD). Canakinumab is approved for treatment of systemic juvenile idiopathic arthritis and has a marked impact on systemic as well as articular activity of the disease.
Objectives: To investigate the efficacy and safety of canakinumab in patients with AOSD and active joint involvement by means of a multi-centre, double-blinded, randomized, placebo controlled trial over a period of 24 weeks with the option of a long-term extension.
Methods: Patients with AOSD and active joint involvement (tender and swollen joint count ≥4 each) were stratified by pre-treatment status with biologic DMARDs to canakinumab (4 mg/kg, maximum 300 mg s.c. q4w) or placebo. After approval of canakinumab for AOSD by the European Medicines Agency, recruitment was stopped prematurely with enrollment of 35 out of 68 planned patients. The primary endpoint was the proportion of patients with a clinically-relevant reduction in disease activity at week 12 as determined by the change in disease activity score (ΔDAS28 >1.2).
Results: At enrollment, patients had high active disease with a mean DAS28(ESR) of 5.4 in the canakinumab group (n=18, [CI 43.1; 85.2]) and 5·3 in the placebo group (n=17, [CI 20.1; 65.0]). In the intention-to-treat analysis, 12 (67%) canakinumab and 7 (41%) placebo patients fulfilled the primary outcome criterion (p=0.18). Figure 2 shows the DAS28-ESR disease activity by treatment groups and visits with imputation. In the per-protocol analysis, significantly higher ACR30 (61% vs. 33% p=0.033), ACR50 (50% vs. 6.7% p= 0.009) and ACR70 (28% vs. 0% p=0.049) response rates were observed in the canakinumab group compared with placebo (Figure 1). Two patients in the canakinumab group experienced an SAE.

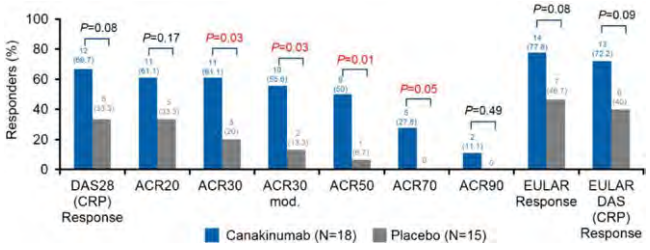


Figure 1. Response rates (PP)

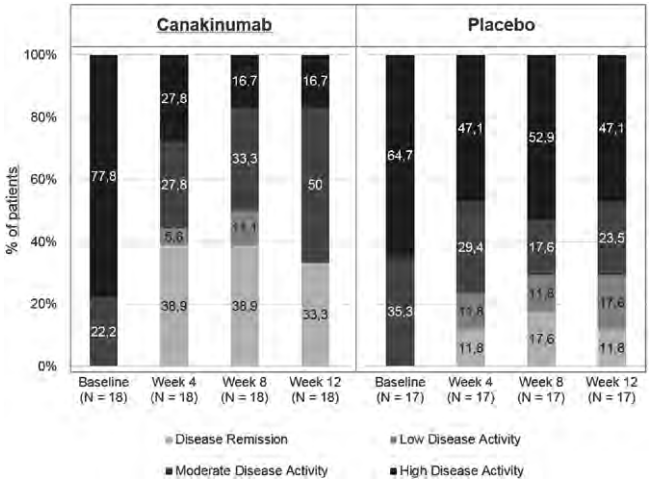


Figure 2. DAS28-ESR disease activity by treatment groups and visits with imputation

Conclusion: Although the study was terminated prematurely and the primary endpoint was not achieved, treatment with canakinumab led to an improvement of several outcome measures in AOSD. The overall safety findings were consistent with the known profile of canakinumab. Thus, our data support indication for IL-1 inhibition with canakinumab in AOSD.

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P-values are shown above each pair of bars; P-values in red are significant ACR, American College of Rheumatology; CRP, C-reactive protein; DAS, disease activity score; EULAR, European League Against Rheumatism; PP, per-protocol

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AB1038 INFLAMMATORY ORBITAL DISEASES: THE EXPERIENCE OF A TERTIARY RHEUMATOLOGY CENTRE

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Background: Inflammatory lesions of orbital disease encompass a wide spectrum of clinical entities including rheumatic disorders.
Objectives: To describe our experiences in adult patients who applied to a tertiary rheumatology center due to orbital disease.
Methods: This is a retrospective descriptive study and data were extracted from patient' charts. We described the clinical, laboratory, radiologic, histopathological presentations and final diagnoses of patients with inflammatory orbital disease who applied to our rheumatology clinic between January 2014 and December 2019.
Results: Thirty-eight patients (Female: 63.2%) were identified; median age at onset of orbital symptoms was 44.5 (min.-max 5-72) years. Swelling (57.9%) and orbital pain (47.4%) were the most common symptoms, followed by erythema (13.2%), vision loss (13.2%), proptosis (7.9%) and diplopia (%7.9). Table summarizes the demographic and clinical characteristics of the patients. Imaging (MRG) was performed in all patients and 63.2% had an orbital biopsy. Orbital imaging revealed extraocular muscles (71.1%), lacrimal glands (50.0%) and optic nerve (42.1%) involvement. Of patients 34.2% had bilateral and 18.4% had retroorbital involvement. The final diagnoses of patients were: IgG4-related disease (34.2%, n =13), idiopathic orbital inflammatory pseudotumor (36.8%, n = 14), granulomatosis with polyangiitis (18.4%, n =7), Sjogren's syndrome (n=1), relapsing polychondritis (n=1), thyroid-associated orbitopathy (n=1) and fungal granulomatous angiitis (n=1).
Conclusion: Inflammatory lesions of the orbit are rare and the diagnosis may be challenging. Differential diagnosis is based on clinical, laboratory, radiologic and histopathologic findings. Although IgG4-related disease is a relatively new diagnostic cause for orbital inflammation, it should be considered more in differential diagnosis.

Figure:

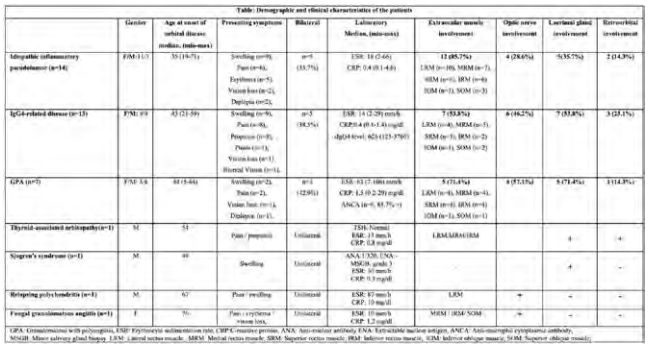


Table: Demographic and clinical characteristics of the patients

	Gender	Age at onset of orbital disease: median, (min-max)	Presenting symptoms	Bilateral	Laboratory Median, (min-max)	Extraocular muscle involvement	Optic nerve involvement	Lacrimal gland involvement	Extraorbital involvement
Idiopathic inflammatory pseudotumor (n=14)	F/M: 11/3	35 (19-75)	Swelling (n=9), Pain (n=6), Erythema (n=5), Vision loss (n=2), Diplopia (n=2),	n=5 (33.7%)	ESR: 16 (5-66) CRP: 0.4 (0.1-4.6)	12 (85.7%) LRM (n=10), MRM (n=7), SRM (n=6), IRM (n=6) IOM (n=1), SOM (n=3)	4 (28.6%)	5(35.7%)	2 (14.3%)
IgG4-related disease (n=13)	F/M: 8/5	43 (21-59)	Swelling (n=9), Pain (n=8), Proptosis (n=8), Ptosis (n=1), Vision loss (n=1) Blurred Vision (n=1),	n=5 (38.5%)	ESR: 14 (2-29) mm/h CRP:0.4 (0.1-1.4) mg/dl IgG4 level: 623 (123-3790)	7 (53.8%) LRM (n=4), MRM (n=5), SRM (n=3), IRM (n=2) SOM (n=1), SOM (n=2)	6 (46.2%)	7 (53.8%)	3 (23.1%)
GPA (n=7)	F/M: 3/4	44 (5-66)	Swelling (n=2), Pain (n=2), Vision loss (n=1), Diplopia (n=1),	n=1 (12.9%)	ESR: 83 (7-100) mm/h CRP: 1.5 (0.2-29) mg/dl ANCA (n=6, 85.7%+)	5 (71.4%) LRM (n=4), MRM (n=4), SRM (n=4) IRM (n=4) IOM (n=1), SOM (n=1)	4 (57.1%)	5 (71.4%)	1(14.3%)
Thyroid-associated orbitopathy(n=1)	M	51	Pain / proptosis	Unilateral	TSH: Normal ESR: 13 mm/h CRP: 0.8 mg/dl	LRM/MRM/IRM		+	+
Sjogren's syndrome (n=1)	M	49	Swelling	Unilateral	ANA/1320, ENA:- MSG(0, grade 3) ESR: 10 mm/h CRP: 0.3 mg/dl	-		+	-
Relapsing polychondritis (n=1)	M	67	Pain / swelling	Unilateral	ESR: 85 mm/h CRP: 10 mg/dl	LRM	+	-	-
Fungal granulomatous angiitis (n=1)	F	70	Pain / erythema / vision loss,	Unilateral	ESR: 10 mm/h CRP: 1.2 mg/dl	MRM / IRM/ SOM	+	-	-

GPA: Granulomatosis with polyangiitis, FMF: Erythrocyte sedimentation rate, CRP:C-reactive protein, ANA: Anti-nuclear antibody, ENA: Extractable nuclear antigen, ANCA: Anti-neutrophil cytoplasmic antibody, MSG(0: Minor salivary gland biopsy, LRM: Lateral rectus muscle, MRM: Medial rectus muscle, SRM: Superior rectus muscle, IRM: Inferior rectus muscle, SOM: Inferior oblique muscle, SOM: Superior oblique muscle)

Disclosure of Interests: Melek Seren Aksun: None declared, Taha Koray Sahin: None declared, Ertugrul Cagri Bolek: None declared, Levent Kılıç: None declared, Elif Günay Bulut: None declared, Kader Karlı Oğuz: None declared, Umut Kalyoncu Consultant of: Abbvie, Amgen, Janssen, Lilly, Novartis, UCB, Omer Karadag: None declared
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AB1039 LL-37, IL-36, GALECTIN-3 AND TLR-3 LEVELS IN IDIOPATHIC GRANULOMATOUS MASTITIS

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Background: Idiopathic granulomatous mastitis (IGM) is a non-infectious inflammatory disorder of the breast characterized by non-caseous granulomas. It is a chronic granulomatous inflammatory disease frequently seen in young fertile women, the cause of which has not been clearly understood. Immunosuppressive agents and surgical interventions are used in the treatment.
LL-37 is a cathelicidin-derived antimicrobial peptide with immunomodulatory properties that are effective in innate immunity. In addition, IL-36, galectin-3, TLR-3 are effective in autoimmunity with proinflammatory properties.
Objectives: With this study, we aimed to investigate the potential alterations of LL-37, IL 36, Galectin 3 and TLR-3 levels in IGM.
Methods: 35 female patients with biopsy-confirmed IGM and 35 healthy controls were included in the study. The serum samples of the subjects LL-37, IL 36, Galectin 3 and TLR-3 levels were studied using the Elisa method. While studying LL 37 and Galectin 3 levels in the tissue, samples of 10 patients who underwent mammoplasty for cosmetic reasons were used for the control group. Ten patients whose paraffin blocks were eligible for re-study were included in the study for tissue examinations. Based on the prevalence (0.1: <%25,- 0.4:%26-50, 0.6:%51-75, 0.9:%76-100) and severity (0: no, +0.5: very little, +1: little, +2: medium, +3: severe) of immunoreactivity in staining, histoscore was created (histoscores = prevalence x severity).
The data were evaluated using appropriate statistical analysis and p <0.05 was considered statistically significant.
Results: When the patient and control groups included in the study were compared, there was no significant difference in age. In serum samples, LL 37, IL 36, Galectin 3 and TLR 3 levels were statistically significantly lower in IGM group compared to the control group (p <0.001 for each) (Table-1). In biopsy samples, LL 37 level was found to be significantly lower in IGM group compared to the control group (p <0.001). However, no significant difference was detected in Galectin 3 levels in tissue studies (Table-2).
Conclusion: In our study, we found that the levels of LL 37, IL 36, Galectin 3 and TLR 3 decreased in serum samples in IGM disease whose etiology was not clearly understood. In addition, we showed that in patients with IGM, LL 37 levels decreased at the tissue level. Studies have shown that in cases of severe sarcoidosis, LL 37 deficiency is reduced both in level and gene expression. So they thought, deficiency of cathelicidin LL 37 may impede resolution of inflammation in the tissue of patients with severe form disease.

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Table 1. LL 37, IL 36, Galectin 3 and TLR 3 levels in serum samples

	IGM (N:35)	CONTROL (N:35)	P
Age	35,92 ± 5,19	34,03 ± 3,81	0,08
LL 37 (ng/ml)	5,20 ± 5,48	40,05 ± 31,97	<0,001
IL 36 (pg/ml)	294,74 ± 125,94	864,71 ± 442,39	<0,001
Galectin 3 (ng/ml)	3,61 ± 3,16	15,53 ± 10,14	<0,001
TLR 3 (pg/ml)	931,49 ± 443,86	4019,36 ± 2599,51	<0,001

IGM: Idiopathic granulomatous mastitis

Table 2. Evaluation of LL-37 and Galectin 3 levels with histoscores in biopsy samples

	IGM (N:10)	CONTROL (N:10)	P
LL 37	0,006 ± 0,025	0,140 ± 0,516	<0,001
Galectin 3	0,293 ± 0,201	0,400 ± 0,290	0,32

Disclosure of Interests: None declared
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AB1040 COEXISTENCE OF DEMYELINATION DISEASE AND FAMILIAL MEDITERRANEAN FEVER

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Table 1. Some clinical and laboratory features of patients with FMF or MEFV mutations accompanied by demyelination disease

Cases	Age/Sex	Diseases	MEFV mutations	The onset age/ diagnostic age for FMF	The onset age for DD/MS/ Presenting manifestations/MRI findings	Treatment for FMF / DD/MS
Case 1 (F1)	17/F	FMF+DD	M694V homozygous	3/5	15 OB (-) Fusiform plaques in the cingulate gyrus; plaques in T4-6	Colchicine IL-1 RA Glatiramer acetate
Case 2 (F1)	46/F	FMF+MS	M694V homozygous	8/9	28 Optic nerve involvement OB(+) Plaques (+)	Colchicine Glatiramer acetate
Case 3 (F1)	17/F	FMF+MS	M694V heterozygous	3/5	15 Loss of the right eye, vertigo OB(+) Plaques	Colchicine Pulse steroid Beta-interferon Teriflunomide
Case 4 (F2)	36/F	MS+MEFV mutation	M694V/R202Q	-	27 Headache, blurred vision, optic nerve atrophy OB(+) Plaques (+)	Glatiramer acetate
Case 5 (F2)	16/F	MS?+FMF+Cutaneous vasculitis	M694V/R202Q	16/16	11 Headache, blurred vision No LP (denied by pt) Plaques	-

F: Female, F1: Family 1, F2: Family 2; DD: Demyelination disease;MS: Multiple sclerosis;MRI: Magnetic resonance imaging; OB:Oligoclonal band; LP: Lumbar punction

Background: In the course of familial Mediterranean fever (FMF), the frequency of other inflammatory diseases increases compared to the general population. Multiple sclerosis (MS) or demyelinating diseases (DD) of central nervous system (CNS) are also more common in FMF patients than in the general population.
Objectives: In this study, we would like to report 5 cases with MS/DD accompanied by FMF or MEFV mutations in two families.
Methods: 4 patients with FMF and 1 patient with MEFV mutation were included in this study. The patients with FMF were diagnosed according to Tell-Hashomer clinical criteria for FMF. The diagnosis of MS was made according to McDonald criteria.
Results: The clinical features of the patients were shown in Table 1.
Conclusion: FMF and MS/DD are characterized by repetitive attacks. Familial association can be seen in 12% of patients with MS (1). This is related to both HLA and non-HLA-related genetic tendency. The probability of developing MS increased 4 times in FMF patients (2). This seems to be related to the presence of MEFV gene creating a pro-inflammatory background. In such family samples, combining HLA and non-HLA gene related studies with MEFV gene analysis will be useful in common genetic factors investigation.
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Acknowledgments: None
Disclosure of Interests: None declared
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AB1041 BIOLOGICS IN ADULT'S ONSET STILL'S DISEASE: TREATMENT STRATEGIES AND SAFETY IN SINGLE CENTER COHORT WITH LONG-TERM FOLLOW-UP

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Background: Adult-onset Still's disease (AOSD) is a rare systemic inflammatory disorder. In recent years biological disease modifying antirheumatic drugs (bDMARDs) are becoming increasingly important for its treatment.
Objectives: To evaluate disease outcomes, treatment strategies and their long-term safety in a cohort of AOSD patients treated with bDMARDs.
Methods: A single-center retrospective study of patients diagnosed with AOSD until 2019 was conducted. Patients were included if they: a) were 16 years old or older, b) met the Yamaguchi criteria and c) had received a bDMARD
Demographics, clinical and laboratory parameters were collected at the time of diagnosis.
Data regarding treatment lines included: the previous and concomitant conventional disease modifying antirheumatic drugs (cDMARDs), the type of initial bDMARD, switches, survival and corticosteroids discontinuation. Adverse events related to treatment and disease outcomes including death and amyloidosis were also recorded.
Results: Sixteen patients with AOSD (Table 1) refractory to cDMARDs were administered biologics. The median duration of follow-up was 14 years (range 1-24). Consistent with recent literature[1], two distinct disease patterns were recognized: the systemic form (SF) and the chronic articular form (CAF). In the SF the leading clinical symptoms were fever, pericarditis and pleuritis. In CAF the leading clinical symptom was persistent RA-like arthritis.

Table 1. Summary of patient characteristics at the time of diagnosis

Characteristics	Results
Age at the time of diagnosis median, (range) years	32.5 (18-64)
Sex (N)	11 female, 5 male
Fever	14 (87.5%)
Rash	8 (50%)
Lymphadenopathy	2 (12.5%)
Arthritis	15 (93.75%)
Pleuritis	7 (43.7%)
Pericarditis	9 (56.25%)
Hepatosplenomegaly	2 (12.5%)
Elevated liver enzymes	2 (12.5%)
Hyperferritinaemia	4 (25%)

Patients with the SF were treated with anakinra (n=4), tocilizumab (TCZ; n=3), canakinumab (n=1) and anti-TNFa (1 adalimumab, 1 etanercept) (n=2). Patients with the CAF received anti-TNFa (3 infliximab, 1 etanercept) (n=4) and TCZ (n=2). The median time from biologic initiation to corticosteroids discontinuation was 6.5 months, (range 2-32), (Table 2). 9 patients (56.25%) remained on treatment with the initial bDMARD, 4 patients (25%) received treatment with two and 3 patients (18.75%) with ≥ 3 bDMARDs. All patients with the CAF were on bDMARD at the end of follow-up, while 4/10 patients (40%) with the SF discontinued it. During follow-up only one serious adverse event was attributed to bDMARD (allergic reaction to infliximab infusion). There were no cases of amyloidosis or deaths

Table 2. Disease and treatment characteristics of 2 discrete phenotypes (Systemic and Chronic articular)

	Systemic form	Chronic articular form	Total
Patients (n)	10	6	16
Duration of follow-up (years), median (range)	13 (3-24)	14 (1-14)	14 (1-24)
Duration of disease prior to bDMARDs (months)	7.5 (2-120)	21 (3-36)	10.5 (2-120)
Number of cDMARDs prior to bDMARDs	2 (1-2)	1 (1-4)	2 (1-4)
Patients on concomittant cDMARDs, n (n/N%)	10 (100%)	6 (100%)	16 (100%)
Type of 1st bDMARD (n)	3 TCZ, 2 anti-TNFa, 4 Anakinra, 1 Canakinumab	4 anti-TNFa, 2 TCZ	
Patients on bDMARD at the end of follow-up (n/N%)	6 (60%)	6 (100%)	12 (75%)
Time to steroids discontinuation after bDMARD initiation (months)	7.5 (2-22)	4.5 (3-36)	6.5 (2-36)

Conclusion: Dichotomous phenotype in AOSD can determine treatment strategy for initial biologic treatment. Inhibition of IL-1 and IL-6 was the preferred therapeutic option for systemic form while inhibition of TNF and IL-6 was the preferred option for the chronic articular form. All of the above bDMARDs have favorable long-term safety profile in patients with AOSD.
References:
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Disclosure of Interests: Nikolaos Kougkas: None declared, Nestor Avgustidis: None declared, Sofia Pitsigavdaki: None declared, Katerina Pateromichelaki: None declared, ARGYRO REPA: None declared, Ainour Molla Ismail Sali: None declared, Anastasios Eskitzis: None declared, George Bertsias Grant/research support from: GSK, Consultant of: Novartis
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AB1042 ASSESSMENT OF BONE MINERAL DENSITY AND FREQUENCY FRACTURES PERIPHERAL SKELETON BONES IN PATIENTS WITH ALKAPTONURIA

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Background:
Objectives: To assess the bone mineral density (BMD) of the skeleton using the Hologic Discovery A DXA, determine the frequency of low-energy skeletal bone fractures among adult patients with alkaptonuria (AKU), and identibjectivefy factors that affect the occurrence of fractures.
Methods: AKU is a rare genetic disease (1 case per 250,000) which occur to severe damage to the spine and large joints. Serious problem in this category of patients is a decrease in BMD. The study included 40 patients with a reliable diagnosis of AKU (23 men and 17 women) aged from 33 to 78 years (mean 60.32±9.1). Densitometry of the lumbar spine was performed in 40 patients; of the forearm bones in 34 patients; of the proximal femur in 32 patients (8 patients were not examined due to bilateral hip joint replacement).
Results: Normal values of spinal BMD were found in 26 patients (65%), osteopenia – in 12 (30%) and osteoporosis – in 2 (5%) patients. In the proximal parts of the femur, osteoporosis was detected in 12 patients (30%), osteopenia in 13 (32.5%), and normal in 7 (17.5%) patients. In the bones of the forearm,

osteoporosis was found in 22 patients (55%), osteopenia – in 8 (20%), and norm – in 4 (10%) patients. The BMD values (g / cm^2) in the group were as follows:

	N	Mean	Percentiles 25th	Percentiles 75th
BMD L1-L4	40	1,06	0,88	1,25
BMD Prox.Femur	32	0,56	0,61	0,81
BMD Forearm	34	0,48	0,43	0,54

Peripheral bone fractures were diagnosed in 15 (32.6%) patients – 9 men and 6 women; 25 (62.5%) patients had no fractures. For the first time, fractures were reported in patients aged from 33 to 69 years (mean 55.9±9.5). The localization of fractures was as follows: femur – in 8 patients (20%), forearm – in 6 (15%), shin bones – in 1 (2.5%) patients. Despite lower BMD rates in women, there were no significant differences in the frequency of fractures depending on sex. Correlation analysis (for Spearman) showed the relationship of fractures with age (r= -0.31, p<0.05), femur BMD in general (r= -0.53, p<0.01) and forearm BMD (r= -0.44, p<0.01).

Conclusion: There is a high incidence of osteoporosis, mainly in the proximal femur and forearm in patients of the older age group with AKU. In the lumbar spine (due to the development of calcification of the intervertebral discs and ligamentous apparatus), osteoporosis is rarely detected, but the frequency of osteopenia is quite high. 32.6% patients had a history of skeletal bone fractures, and the sex of the patients did not affect the risk of fractures. The occurrence of fractures in patients with AKU is associated with low BMD values of the proximal femur.

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AB1043 AWARENESS OF THYROID EYE DISEASE, AN AUTOIMMUNE CONDITION, AMONG RHEUMATOLOGISTS

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Background: Autoimmune inflammatory conditions of the eye may be associated with rheumatic diseases such as rheumatoid arthritis, systemic lupus erythematosus, and granulomatosis with polyangiitis. This is also observed with thyroid eye disease (TED). Loss of immune tolerance to the thyroid stimulating hormone receptor has thyroidal consequences and nearly 40% of patients with Graves' disease also have clinically evident Graves' orbitopathy or TED.[1] TED results from tissue inflammation that causes retro orbital fat expansion[2] and extraocular muscle enlargement[2] and stiffening.[3] Because the orbital cavity is bony and of limited volume, proptosis and, in severe cases, optic nerve compression, can result. In many patients, muscle changes also cause ocular motility issues and double-vision. Because TED can have a similar presentation to other inflammatory orbital diseases (e.g., granulomatosis with polyangiitis) and Graves' disease patients frequently have other autoimmune conditions (10% of Graves's patients also have rheumatoid arthritis),[4] rheumatologists are likely to care for, or even diagnose, patients with TED.

Objectives: This analysis sought to understand rheumatologists' knowledge, and degree of participation in the treatment, of TED including referral patterns from ophthalmologists and endocrinologists for infusion therapies.

Methods: Rheumatologists practicing in the United States attended an educational session and agreed to complete a 12-item survey regarding TED awareness, referral patterns, and management.

Results: Of the 47 rheumatologists surveyed, 45 (96%) were familiar with TED. Ten (21%) physicians reported managing patients with TED, but the majority of physicians (62%) reported that they co-managed other autoimmune diseases in patients who also had TED. Additionally, 98% and 64% of polled rheumatologists had received referrals from ophthalmologists and endocrinologists, respectively, for autoimmune disease management or infusion therapy. Ophthalmology referrals for intravenous (IV) medication administration were most frequently for biologics (82%), but some referrals were also made for corticosteroids (2%) or other medication (13%) infusions. Only 23% of rheumatologists had administered a biologic specifically for TED (rituximab: 17%, tocilizumab: 2%, other: 4%), but 89% expressed an interest in administering a TED-specific monoclonal antibody therapy, awaiting FDA approval.

Conclusion: Nearly all surveyed rheumatologists were aware of the signs and symptoms of TED, although most did not actively manage or administer medication for TED. Given the high level of interest in infusing novel, TED-specific biologics, rheumatologists may become an integral part of TED patient management with the approval of a new biologic, teprotumumab, for thyroid eye disease.

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AB1044 CLINICAL AND IMMUNOLOGICAL FEATURES OF A SERIES OF PATIENTS WITH RHUPUS

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Background: Since its first description in 1971 by Schur, many authors have discussed whether rhupus is an overlap syndrome between RA and SLE, a particular form of SLE with prominent and frequently erosive joint involvement,or if it is a distinct clinical and immunological entity. There are several published case series in medical literature describing the features of that uncommon syndrome that constitutes about 0.01-2% of all systemic rheumatic diseases.

Objectives: To describe demographic, clinical and immunological features of a series of patients with rhupus syndrome and to compare them with previously reported series in the literature.

Methods: Review of clinical records of patients attended in a Tertiary Care Rheumatology Unit that fulfil classification criteria for RA (either ACR 1987 or ACR/EULAR 2010) and SLE (either ACR 1997 or SLICC 2012). In addition, a manual search of patients with positivity for both anti-CCP (defined as >3 UI/mL) and specific SLE antibodies (either anti-DNAds by IIF+- or anti-Sm by multiplex assay) was conducted. We excluded patients with known mixed connective tissue disease, drug-induced SLE as well as RA patients with anti-DNAds+ or anti-Sm+ without clinical features of SLE.

Results: We identified 8 patients, all of them women (4 of Latin American origin, 3 Caucasians and 1 Arab) with a mean age at diagnosis of 35 years (range:19-63 years) and a mean duration of disease of 9 years (±10.5 years). RA and SLE were diagnosed simultaneously in 50% of cases (37.5% onset as RA and 12.5% as SLE, being the mean time between both diagnoses of 16.5 months in those cases). Immunological features of patients are summarized in Table 1. An erosive form of arthritis is present in 37.5%. As extra-articular involvement, 75% have skin lesions (photosensitivity, malar rash, oral ulcers and alopecia as major features) and 100% haematological alterations with lymphopenia (37.5% thrombopenia). Serositis (37.5%), renal (25% biopsy-proven lupus nephritis, 12.5% non-nephrotic proteinuria) and neurological (present only in one patient) involvement were less common findings. Most common therapies in our series were glucocorticoids (100% of cases, with a mean dose of 21.25 ± 13.5 mg/day at onset), antimalarials (87.5%) and methotrexate (87.5%). 50% of patients required biologic therapy (2 etanercept, 1 adalimumab, 1 rituximab) for inadequate disease control with conventional synthetic DMARDs.

	ANA (IIF titers)	Anti-DNAds (IIF titers)	Anti-Sm	Anti-chromatin	RF (UI/mL)	Anti-CCP (UI/mL)	Anti-Ro	Anticardiolipin (UI/mL)	Anti-β2GPI (UI/mL)	Lupus anticoagulant
1	1/320	-	-	+	53	2	-	-	22 (IgM)	-
2	1/640	-	-	-	810	486	-	-	-	-
3	1/1260	-	-	-	1230	310	-	25.8 (IgM)	-	-
4	1/640	1/50	-	+	588	>300	-	-	28.5 (IgA)	-
5	1/160	-	-	-	232	11,1	+ (Ro60)	148 (IgG) 121 (IgM)	160 (IgG), 111 (IgM), 42 (IgA)	+
6	1/160	1/50	-	+	230	>300	-	32.4 (IgM)	-	-
7	1/320	-	-	-	198	>300	+ (Ro52)	19.5 (IgM)	-	-
8	1/160	-	+	+	170	>300	-	-	-	-

Conclusion: Prevalence of erosive arthritis in our patients is lower than previously reported, though as a limitation an imaging technique with a higher sensitivity for erosion detection than simple X-ray (such as US or MRI) was not available. Moreover, our series sample is small considering the low prevalence of this entity. The proportion of patients with simultaneous diagnosis of both RA and SLE is also higher (with a shorter interval between both diagnoses when this is not the case), so it is the proportion of patients receiving biologic therapy. The

rest of clinical and immunological features were similar to previously described in other series.

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AB1045 CLINICAL, ANALYTICAL AND RADIOLOGICAL CHARACTERISTICS OF A COHORT OF PATIENTS WITH SARCOIDOSIS.

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Background: Sarcoidosis is a systemic disease whose etiology is unknown. It is characterized by the formation of granulomas in any tissue of the organism. Ganglionic, pulmonary and cutaneus involvement is the most prevalent.
Objectives:
1. Describe clinical characteristics of a cohort of patients with sarcoidosis diagnosed.
2. Define the association between the ACE's number at diagnosis, radiological lung stage, treatment and course of disease.
3. Evaluate if the extrapulmonary involvement is related to the course of the disease.

Methods: Descriptive retrospective study of patients with S diagnosis treated in our Hospital in 2019. Data were obtained by reviewing medical records. Chi-square tests and parametric tests have been used to establish the differences described in the objectives.
Results: 102 patients diagnosed with sarcoidosis have been included, (51% females) with an average age of 56±11 years. Suspected diagnosis at the onset of disease was S in 70.6% of patients, followed by suspected lymphoma (20.6%). The average time for the definitive diagnosis of S was 9.5 months. 70.6% of the patients had elevated ACE titles at the beginning. Regarding the clinical manifestations, 18.6% of the patients presented fever at the beginning and 66.7% extrathoracic clinical manifestations. 72.5% have lymph node adenopathies, and in 91% there is thoracic involvement (the most frequent pulmonary stage is stage II). A biopsy was performed in 84.3% of the patients, the lung biopsy being the most performed (52.3%). 88.2% of patients received corticosteroid treatment at the onset of the disease (currently under treatment with corticosteroids 37.3%). 50% of patients are treated with immunosuppressants, Methotrexate was the most used. 5 patients are treated with biological therapy (AntiTNF).
Regarding the course of the disease, 51% of the patients have a chronic course, 45.1% are in remission and 3.9% have suffered a relapse of the disease. In this study, no significant relationship was found between the ACE values at the onset of the disease, the pulmonary stage and the course of the disease.
According to our data, patients presenting with extrathoracic clinical manifestations need more frequently corticosteroid treatment ($p = 0.017$) and immunosuppressive treatment ($p = 0.001$) with respect to patients who do not have an extrathoracic clinic. In addition, patients with an extrathoracic clinic present more frequently a chronic course of the disease than those who do not ($p = 0.019$).
Conclusion: The results described in this study are similar to those found in the literature. The differences found can be explained because patients presenting with extrathoracic clinical manifestations have a more complicated management and need more treatment than those with only pulmonary involvement, even patients with radiological stage I do not usually need treatment, only surveillance.
Disclosure of Interests: None declared
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AB1046 JOINT MANIFESTATIONS IN A COHORT OF PATIENTS WITH SARCOIDOSIS IN A THIRD LEVEL HOSPITAL.

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Background: Sarcoidosis (S) is a systemic granulomatous disease of unknown etiology, which most frequently affects the ganglion, lung and skin, although it can affect other organs, including the musculoskeletal system.
Objectives:
- Describe the clinical, analytical and radiological characteristics of patients diagnosed with S presenting joint manifestations.
- To assess the association between patients who have joint manifestations and the use of corticosteroids (C) and immunosuppressants (IS), with respect to those without joint involvement.

Methods: Retrospective descriptive study of patients with diagnosis of S with joint manifestations, treated in our Hospital from 2017 to 2019. Data were obtained by reviewing medical records. Chi square tests and Fisher's exact test have been performed to establish the differences described in the objectives.
Results: From a database of 102 patients with S, 18 presented joint manifestations (50% women), with a mean age of 57 ± 6 years. Of these patients, 4 (22.2%) have presented positive ANA. Regarding the clinic, 3 patients presented the association of polyarthritis and bilateral ankle swelling, 8 patients presented with polyarthritis, 3 monoatritis and 4 patients presented bilateral ankle swelling. 61.1% had fever at the onset of the disease.
14 patients (77.8%) had high ACE values at the onset of the disease, without presenting significant differences with respect to all patients diagnosed with S who do not have joint involvement.
All patients received treatment with C and 10 patients (55.5%) needed an IS treatment, finding no differences with respect to patients who do not have joint involvement ($p=0.92$).
On the course of the disease, the majority of patients with joint involvement have a chronic course (72.2%). Nor were significant differences found when compared with patients who have no joint involvement ($p = 0.73$).
Conclusion: Patients with joint involvement in our study have been 17.6% (18), an approximate result to that described in the literature (over 10%), although our result may be increased by the fact that the patients who are followed in Rheumatology present or have presented joint involvement. No significant differences were found between patients with S who presented joint involvement and those who did not, with respect to the initial ACE values, treatment and disease course. Prospective, multicenter and larger sample studies are necessary to better understand these associations.
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AB1047 IGG4-RELATED DISEASE PRESENTATION REQUIRES ADMISSION TO THE EMERGENCY DEPARTMENT IN THE MAJORITY OF CASES

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Background: IgG4-related disease (IgG4-RD) is generally considered a chronic fibro-inflammatory condition with insidious presentation and subclinical course. Our clinical experience, however, suggests that a sizable proportion of patients experience multiple accesses to the emergency department (ED), either at disease onset or during the disease course.
Objectives: In the present study we aimed (i) to assess the prevalence of acute manifestations of IgG4-RD at disease onset requiring referral to the ED, and (ii) to calculate the diagnostic delay from the initial acute presentation.
Methods: We revised our database and identified patients admitted to the ED because of symptoms lately attributed to IgG4-RD onset (Group 1) and those that were referred to our outpatient clinic without previous urgent manifestations (Group 2). Acute manifestations were clustered based on the anatomical district affected by IgG4-RD. Epidemiological, clinical, and serological features of Group 1 and Group 2 were compared.
Results: The study included 141 patients with IgG4-RD. 76 (54%) presented to the ED at disease onset. The most common clinical manifestations requiring admission to the ED were jaundice (53%), abdominal pain (41%), and fever (10%). Gastrointestinal involvement was the most frequent cause of referral to the ED (71% of cases), followed by involvement of the retroperitoneum (14.5%), and of the nervous system (6.6%). Pancreato-biliary involvement was significantly more frequent in Group 1. Head, neck, salivary and lacrimal gland involvement was more frequent in Group 2. The diagnostic delay was significantly shorter in Group 1 than in
Group 2.
Conclusion: Clinical manifestations associated with IgG4-RD onset require referral to the ED in the majority of cases. This finding contrasts with the general view of IgG4-RD as a condition with non-acute presentation.

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AB1048 RHUPUS SYNDROME IN A TERTIARY HOSPITAL

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Background: Rhupus syndrome (RhS) is a rare combination of rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). Different studies describe RhS cases that begin with erosive arthritis and the presence of rheumatoid factor (RF) and/or anti CCP and then the SLE symptoms.
Objectives: Despite the fact that RhS shows a low prevalence, it would be useful to know clinical characteristics of RhS patients since their therapy and outcome differ from those having RA or SLE alone.
Methods: Retrospective study with systematic revision of electronic clinical records of RhS patients was performed. Demographic, clinical and immunological data were collected.
Results: Eight RhS patients were included (all fulfilled SLICC 2012 criteria for SLE and ACR 2010 for RA). Mean age was 67.3 (45-84) years (7 were female).
In 3 cases RA was the first diagnosis with a mean evolution of 4.5 years until SLE diagnosis. In contrast, in 5 cases SLE was the first diagnosis with a mean evolution of 7.2 years until RA diagnosis. Photosensitivity and arthritis were the predominant clinical manifestations. One patient presents pericarditis and other case showed rheumatoid nodules in elbows. Renal, pulmonary or neurological affection was no reported.
4 patients were under biological/JAK inhibitors therapies (2 abatacept, 1 rituximab and 1 baricitinib) with favorable response of treatment.
Conclusion: In contrast to other series, only the 37.5% of our RhS cases begins with polyarticular seropositive arthritis. The 62.5% started with SLE symptoms as haematological alterations, cutaneous and serological manifestation, and showed longer progression to have polyarticular affection. Thus, RhS diagnosis is earlier in patients that begin with RA symptoms. 4 RhS patients were refractory to DMARd treatments, where biological/JAK inhibitors therapies are needed.
Disclosure of Interests: None declared
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AB1049 CLINICAL SPECTRUM AND THERAPEUTIC MANAGEMENT OF AUTO-IMMUNE MYELOFIBROSIS: A NATION-WIDE STUDY OF 30 CASES

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Background: Little is known about autoimmune myelofibrosis (AIMF), a rare entity that can occur alone or in association with another autoimmune disease (AID) and is responsible for bone marrow (BM) failure and life-threatening complications.
Objectives: We conducted a nationwide retrospective observational study of AIMF cases to better characterize the epidemiology, clinical presentation and evolution of this rare entity.
Methods: The aim of the study was to analyze the characteristics of AIMF and the nature and indication of treatments currently used. Response to treatment was evaluated by the revised Tefferi et al. response criteria.
Results: Among 30 cases of AIMF, the sex ratio (F/M) was 4:1 and the median age at diagnosis was 37 years (interquartile range 30–49). AIMF was diagnosed after the onset of an associated AID in 12 cases and concomitant to an AID in the remaining 18 cases. The most frequently associated AID was systemic lupus erythematous, followed by Sjögren syndrome. All cases consisted of reticulin fibers, and no collagen fibrosis was described. More than 50% of cases showed complete response after first-line therapy, with glucocorticoids (GC) in 28 cases. Half of the cases had treatment complications mainly related to GC therapy.
Conclusion: Diagnosis of AIMF remains challenging in the absence of a validated set of diagnosis criteria, and must always be searched in the presence of hematological abnormalities at onset or during follow-up of AID. Clinical context, search for mutations and pathology findings can help differentiating this rare disease from a clonal pathology. GC is currently an effective first-choice therapy for AIMF, but a high rate of GC dependency and long-term complications indicate the need to find new sparing drugs.
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AB1050 CLINICAL IMPLICATIONS OF ULTRASONOGRAPHY (US) IN DIAGNOSIS AND MONITORING DISEASE ACTIVITY OF RELAPSING POLYCHONDRITIS (RP) AND COMPARATIVE INVESTIGATION BY US BETWEEN AURICLE OF RP, REPEATED TRAUMA, CELLULITIS AND HEALTHY SUBJECT

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Objectives: To assess the clinical implications of ultrasonography (US) in monitoring disease activity and diagnosis of relapsing polychondritis (RP).
Methods: Firstly, auricular (n=5) and nasal (n=1) chondritis of six patients with RP were assessed by US before and after treatments. The relationship between US findings and serum markers were evaluated. Moreover, the comparisons of US findings between the auricle of patients with RP (n=5), repeated trauma (n=5), cellulitis (n=2) and healthy subjects (n=5) were also assessed.
Results: US finding before treatment showed low-echoic swollen auricular and nasal cartilage with increased power Doppler signals (PDS) in all cases of RP. US findings corresponded to biopsy findings. After treatment, the swollen ear and nose completely resolved. Then, US findings also showed dramatic reductions in swollen cartilage with the decrease in PDS. Although serum markers completely improved, US finding remained in 1 of 6 cases, and this case showed flare due to PSL tapering. Finally, RP could be differentiated from the damage of repeated trauma and cellulitis by the presence or absence of PDS and subperichondrial serous effusion.
Conclusion: US of auricular and nasal cartilage in RP possibly facilitates evaluation of auricular lesions and monitoring of disease activity, especially when we consider the treatment response and the timing of drug tapering.
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AB1051 KIKUCHI FUJIMOTO DISEASE, IS IT SLE?

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	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Gender	Woman	Woman	Woman	Woman	Woman	Woman	Woman
Age at onset	40	24	13	18	21	46	53
Previous autoinmune disease	Raynaud's phenomenon	No	Autoinmune tyroiditis	No	Supurative hidrosadenitis	No	No
Course	Self-limiting	Self-limiting	Self-limiting	Self-limiting	Self-limiting	Flair	Self-limiting
Autoimmunity	Negative	ANA 1/80	Negative	Negative	Negative	Negative	ANA 640, Ro/La+
Autoimmune disease during follow-up							
SLE diagnosis	Subsequent	Subsequent	No	Subsequent	No	Subsequent	Concomitant
Time (in months)	24	48	-	60	No	6	0
Clinical manifestations	Serositis Lymphopenia	Oral aftosis Lymphopenia Perniosis	-	Cutaneous subacute lupus	No	Acute cutaneous lupus (NET-like) Arthritis	Fever Serositis
Autoinmunity	ANA 1/640 Positive DNA	ANA 1/80 RNP+ Positive DNA	-	Negative ANA Ro+	-	ANA 1/320 RNP+	ANA 1/640 Ro/La+ Positive DNA
Treatment	Hidroxicloroquine	Hidroxicloroquine	No	Hidroxicloroquine	No	Hidroxicloroquine	Hidroxicloroquine

Background: Kikuchi-Fujimoto disease (KFD) is a rare entity characterized by adenopathies and fever. It raises a broad differential diagnosis that includes lymphoproliferative disorders, infections and systemic autoimmune diseases, and diagnostic confirmation is always by histology, which shows histiocytic necrotizing lymphadenitis. Although its course is generally benign and self-limited, it can be associated both at the time of diagnosis and during follow-up with systemic autoimmune diseases, the most frequent of which is systemic lupus erythematosus (SLE).

Objectives: To describre the clinical and analytical characteristics of patients diagnosed with KFD and the development of systemic autoimmune disease.

Methods: Patients diagnosed with KFD during the 1990s and 2020s are collected in a regional hospital (Granollers General Hospital). The clinic is documented at the diagnosis of EKF, the appearance of systemic autoimmune disease during follow-up and its clinical and analytical characteristics.

Results: A total of 7 patients with EKF were diagnosed. All of them women with a mean age at diagnosis of 30 years. Diagnosis was made in all cases with compatible clinical symptoms, fever and lymphadenopathy, and lymph node biopsy confirming histiocytic necrotizing lymphadenitis. At the time of diagnosis, a patient was also diagnosed with SLE. During the follow-up, 4 of the 6 remaining patients developed clinical manifestations compatible with SLE (3 of them with systemic manifestations and a case of subacute cutaneous lupus. The mean time of onset of SLE was 34 months (between 6 months and 5 years). All of them received treatment with hydroxychloroquine, with good response to treatment.

The clinical and analytical characteristics are presented in Table 1 below.

Conclusion: In our center, 5 of the 7 patients (71%) diagnosed with EKF developed manifestations compatible with SLE. The importance of the diagnosis of EKF lies precisely in the possible association with systemic autoimmune disease, the most common being SLE, so it is recommended that patients be monitored to identify those who develop associated autoimmune disease.

Disclosure of Interests: None declared

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AB1052 EVALUATION OF SYMPTOMS, DEPRESSION AND ANXIETY LEVELS IN YOUNG WOMEN WITH IDIOPATHIC GRANULOMATOUS MASTITIS

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Background: Idiopathic granulomatous mastitis (IGM) is a rare, chronic, inflammatory disease of the breast characterized by lobulocentric granulomas, and diagnostic and therapeutic procedures are challenging for patients [1]. Glucocorticoids, immunosuppressive drugs, surgical and conservative treatment are used for the treatment of the disease [2]. These patients have many risk factors for delayed wound healing after surgical intervention, fistula formation, secondary infection and frequent postoperative recurrence for anxiety and depression [3].

Objectives: The aim of this study was to investigate the anxiety and depression levels and influential effects of clinical and sociodemographic characteristics of patients with IGM.

Methods: 32 female patients enrolled to the study and who diagnosed as histopathologically proven IGM were included in this study. The sociodemographic and clinical characteristics of the patients were recorded and Beck depression inventory as well as health anxiety inventory were applied to the patients. In the same period, a control group consisting of age and sex matched people without any chronic disease was formed from health employees and their relatives. Correlation and logistic regression analyzes were performed between clinical and sociodemographic characteristics and scale scores.

Results: A total of 32 patients and 32 age and sex matched volunteers were included in the study. A significant difference was found between the Beck depression inventory and health anxiety inventory scores between the patient and control groups. There was a strong correlation between breast mass size and Beck depression inventory (r: 0.83, p: 0.01), in addition moderate correlation was found between breast mass size and health anxiety (r: 0.39, p: 0.05). In the logistic regression model (χ2: 12.274, R2: 0.469, p: 0.01) created by the retrospective elimination method, presentation with fistula (OR: 9.24), bilateral lesion (OR: 7.25) and disease duration (for each month OR:1.29) were found to be significant.

Conclusion: Studies show that patients with IGM experience severe anxiety and have a high risk of developing depression [4], similar in breast cancer even though the method and assessment tools are different than breast cancer. In this study, it was determined that IGM increases anxiety and depression levels in young female patients during both diagnosis and treatment. For this reason, it is thought that psychosocial evaluation of patients from the time of diagnosis, referring them to psychiatric treatment if necessary may improve the quality of life of the patients.

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AB1053 EFFECTIVENESS OF METHOTREXATE IN IDIOPATHIC GRANULOMATOUS MASTITIS TREATMENT

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Background: Idiopathic granulomatous mastitis (IGM) is a rare inflammatory disease of the breast [1], for which there is a lack of consensus on the treatment protocol [2, 3]; it requires long-term follow-up and is associated with a high rate of relapse after surgical treatment. In this study, we report on the largest single-center cohort of idiopathic granulomatous mastitis treated with steroids + methotrexate.

Objectives: We present this study believing that our experience with patients with IGM and use of steroid + methotrexate treatment in them will contribute to the literature.

Methods: We retrospectively examined the data of 33 patients histopathologically diagnosed with idiopathic granulomatous mastitis who were evaluated by our Rheumatology or General Surgery Clinics between 2013 and 2016.

Results: Of the 33 female patients (age: 38.64 ± 6.9 years), 24 were admitted with an initial diagnosis of Idiopathic granulomatous mastitis, whereas 9 were admitted after surgical treatment. The breast symptoms and laboratory values of the patients before and after the steroid and methotrexate treatment are shown in Table 1. Remission was achieved in 87.9% patients with steroid + methotrexate treatment, and there were no relapses during the 24-month follow-up.

Table 1. Pre- and post-treatment laboratuary and clinical findings.

	Pre-treatment	Post-treatment	P value
ESR (mm/h)	42.45±28.88	17.24±11.31	<0.001*
CRP (mg/L)	24.72±35.32	5.37±6.5	0.004*
Mass Size (mm)	36.94±16.40	10.79±15.01	<0.001*
Fistula (n)	15/33 (45%)	2/33(6%)	<0.001**
Nipple discharge(n)	17/33(52%)	1/33(3%)	<0.001**

ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; *Paired T Test;**Chi-Square test.

Conclusion: Methotrexate has so far been added to IGM treatment in order to decrease steroid dosage or to treat relapses, and it has been reported to be effective in case study and a limited number of studies with few patients [2, 4, 5]. Steroid + methotrexate treatment used by us in patients with IGM, which is a rare disease and for which no consensus exists regarding the treatment protocol, is effective and reliable in providing clinical improvement and long-term remission. Therefore, this treatment appears to be successful owing to long-term remission outcomes and very low relapse rates, without the patients having to undergo a surgical procedure and experience the associated anxiety and complications.

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AB1054 CLINICAL CHARACTERISTICS OF PATIENTS WITH UVEITIS FROM AN AUTOIMMUNE OCULAR DISEASE UNIT

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Background: The eye, particularly the uvea due to its substantial vascularization, can be a target for various inmune reactions. Etiology is unknown in most cases of inflamatory ocular disease. Ocassionally, ocular symptoms may be the first manifestation of some systemic diseases and its appearence, therefore, can lead us to the diagnosis and institution of treatment that, if performed early, can avoid irreversible sequelae.
Aim: Describe the experience at 12 months of an autoinmune ocular disease unit.
Objectives: to describe the clinical characteristics of patients diagnosed with uveitis and its association with systemic disease.
Methods: Retrospective, descriptive study. We included patients diagnosed with uveitis attending the Autoimmune Eye Disease Unit from January 2019 to December 2019. Qualitative variables were expressed as frequencies and percentages and quantitative variables as means and standard deviation.
Results: A total of 40 patients were included, 72.5% were women (26/40). Mean age of disease onset was 38 ± 17.2 years and the average diagnostic delay was 19.4 ± 46.8 months. The most frequent chief complaint was decrease in visual acuity, cited in 43.8% of the consults (25/57). Involvement was bilateral in 55% of cases (22/40). In order of decreasing frequency, diagnosis found were: Anterior uveitis in 47.5% (19/40), panuveitis in 35% (14/40), posterior uveitis in 10% (4/40) and intermediate uveitis in 7.5% (3/40). There was a recurrence (2 or more episodes of uveitis) in 65.7% (25/38) of patients and 58.8% (20/34) of them presented some sequelae. Prior to their first episode of uveitis, 12.5% (5/40) of patients had already been diagnosed with an autoimmune disease, the most common of which was spondyloarthropathy (3/5). Meanwhile, 33.3% (13/39) were diagnosed with a systemic disease from their first episode of uveitis. Regarding laboratory tests, 46.4% (13/28) of patients presented acute phase reactants, 13% (3/23) had positive serum antibodies and 41.6% (5/12) were HLA-B27 positive. Concerning treatment, 76.3% of patients required systemic corticosteroids (29/38) and 75% received at least one immunosuppressive drug (30/40). Out of this group, 30% needed a second immunosuppressive drug. Response to treatment was good in 63.6% of patients (21/33), partial in 18.1% (6/33), poor despite treatment in 6% (2/33) and poor due to lack of adherence in 12.1% (4/33).
Conclusion: In our cohort, there was a predominance of female, middle-aged patients with bilateral involvement. Anterior uveitis was the most frequent diagnosis. In one-third of patients, the first episode of uveitis led to diagnosis of a systemic disease. Most of our patients presented some type of sequel or local complication and required systemic treatment with corticosteroids and immunosuppressants.

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AB1055 CERTOLIZUMAB PEGOL: A SAFE AND EFFICIENT TREATMENT IN PATIENTS WITH UVEITIS DURING PREGNANCY.

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Background: Anti-TNFα agents are useful in uveitis **(1-5).** Certolizumab pegol (CZP) differs from other anti-TNFα agents due to its limited placental transfer.
Objectives: To assess efficacy and safety of CZP in women with uveitis during pregnancy.
Methods: Multicenter study of women with uveitis under CZP during pregnancy and their neonates.
Results: 14 women (23 eyes); mean age 34.3±5.5 yrs (TABLE 1). Pattern of uveitis: 10 anterior, 2 posterior, 1 intermediate, 1 panuveitis. Uveitis was bilateral in 9 and chronic in 7. CZP was started before conception in 10 patients and after in 4. All patients obtained or maintained ocular remission throughout pregnancy (**FIGURE**). Prednisone was reduced from a mean dose of 21.7±19.7 mg/day to 4.1±3.8 mg/day at 6 months (p=0.03), leading to complete discontinuation in 4. 15 healthy infants were born. Only 1 woman presented a mild infection. No infections or malformations were found in neonates after a follow-up of 6 months. 6 infants were breastfed and all received scheduled vaccinations without complications (TABLE 2**).**

TABLE 1.

	Age	Underlying disease	Immunosuppressants before CZP	Combined treatment
1	34	SpA	MTX, AZA, ADA	AZA
2	37	SpA	MTX, AZA, IFX, ADA, GOLI	
3	39	SpA	AZA, ADA	AZA
4	46	SpA	CyA, ETN, ADA, IFX, GOLI	
5	32	SpA	SSZ, ADA	SSZ
6	36	SpA	MTX, HCQ, ADA	
7	40	SpA	MTX, LFN, HCQ, IFX, ADA, GOLI	HCQ
8	31	Idiopathic	MTX, MMF, CyA, ADA	
9	33	Idiopathic	MTX, AZA, ADA, ETN	
10	32	RA	MTX	AZA
11	23	Vogt-Koyanagi-Harada	AZA, ADA	AZA
12	36	Juvenil Idiopathic Arthritis	ADA	
13	32	Punctate inner choroidopathy	ADA	
14	29	Behcet	CyA, IFX, ADA	

TABLE 2.

	Full term pregnancy	Multiple gestation	Preconception CZP exposure	Labor complications	Maternal infections	Neonatal infections (< 6 m after birth)	Congenital malformations	Breast-feeding
Neonates, n/N	15/15	2/15	5/15	0/15	1/15	0/15	0/15	6/15

Conclusion: CZP seems to be effective and safe in female patients with uveitis during pregnancy and neonates.

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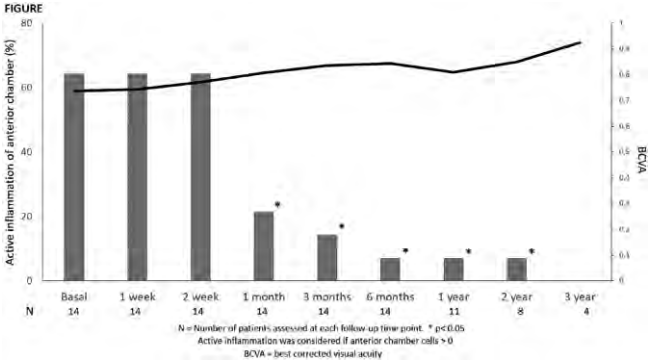
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FIGURE



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AB1056 SYMPTOMATIC SCLEROSING MESENTERITIS REVEALING ERDHEIM-CHESTER DISEASE: A RARE CONDITION MEDIATED BY BRAF

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Background: Sclerosing Mesenteritis (SM) refers to an entire spectrum of digestive inflammatory disorders. Diagnosis is based on imaging showing an increase of fat attenuation displacing bowel loops and is in most cases non-symptomatic. Several conditions (abdominal trauma/surgery, neoplasia, infectious and inflammatory diseases) are responsible for SM (1). Among neoplasia, Erdheim-Chester disease (ECD) is a rare clonal histiocytosis characterized by long bone involvement, peri-nephric fat infiltration and cardio-vascular involvement associated with compatible histology (2). Biopsy is mandatory to confirm tissue infiltration by histiocytes and detect somatic mutation. Almost 80% of ECDpatients harbor mutation in mitogen activated protein *(MAP)* kinase pathway especially *BRAF^{V600E}* gene mutation in about 60% of cases(3). No series of patients presenting both pathologies has been reported. Furthermore, no correlation with *BRAF* mutation status has been described in patient harboring SM and ECD.

Objectives: To describe the clinical, radiological and mutational status of patients harboring SM and ECD.

Methods: We reviewed the database of patients with histiocytic disorders in Besancon University Hospital. Patient required one abdominal computed tomography showing sclerosing mesenteritis and clinical/histological features of ECD to fulfill the inclusion criteria. All biopsy samples were investigated for mutation of *MAP* kinase pathway gene.

Results: Four patients suffered from SM and ECD. The median age at the diagnosis of ECD was 68 years old (61-72). All patients described abdominal pain and the mean duration between first symptoms and diagnosis of ECD was 12 months (4-19). The mean CRP level at diagnosis was 40.75 mg/L (5-117). Two patients were found to have myeloid neoplasms (chronic myelomonocytic leukemia (#2) and essential thrombocythemia (#4)) concurrent with ECD diagnosis.

Regarding abdominal computed tomography, all patients had a mesenteric mass associated with hyper-attenuated mesenteric fat and a "fat halo sign". One patient (#2) had ascites and one had splenomegaly (#4) but no patient had enlarged lymph nodes. CT also demonstrated peri-nephric fat infiltration ("hairy kidney") (4/4), vascular sheathing of aortic branches (3/4), adrenal hypertrophy (1/4) or ureter dilation (1/4). The mean SUV_{max} of the mesentery was 7.5 (4.1-10.9) at diagnosis on (^{18}F)- fluorodeoxyglucose-PET. Three patients underwent mesentery fat biopsy and all samples exhibited ECD histology. Regarding mutational status, 75% (3/4) patients had *BRAF^{V600E}* mutation.

After initiation of therapies for ECD (targeted therapies for ¾ patients), all patients had improvement of digestive symptoms and decreased of SUV_{max} on evaluation ^{18} FDG-PET during the follow up.

Conclusion: ECD should be investigated in patient with symptomatic SM especially if it is associated with peri-nephric fat infiltration. This condition is rare and might be driven by BRAF gene.

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AB1057 SCHNITZLER'S SYNDROME IN THE DIFFERENTIAL DIAGNOSIS OF ADULT STILL'S DISEASE

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Background: Schnitzler's syndrome (SchS) and adult onset Still disease (AOSD) are currently considered as multifactorial autoinflammatory diseases (MAIDs) and are classified as systemic inflammation with urticarial rash. Clinical similarities between SchS and AOSD (fever, urticarial rash, arthralgias), increased ESR and CRP and the efficacy of IL-1 inhibitors may lead to the diagnostic delay in SchS pts. Testing for monoclonal gammopathy helps establish the diagnosis in SchS pts but is not routinely used in AOSD pts.

Objectives: to examine demographic, clinical and laboratory characteristics, and the therapy of SchS pts in a single rheumatology center.

Methods: 5 SchS patients (2 females, 3 males), aged 32 to 68, underwent inpatient and outpatient examinations in the rheumatology center. All pts underwent a standard rheumatology examination, including ESR, CRP and M-gradient. 4 pts underwent genetic testing for mutations in *NLRP3,TNFRSF1A* genes to exclude MAIDs, such as CAPS and TRAPS.

Results: All pts were initially diagnosed with AOSD. The age at onset ranged between 28 and 66 years. Time to diagnosis varied from 2 to 22 years, being within 4 years in 4 of 5 pts. Patients presented with fever (4), urticarial rash (5) and musculoskeletal manifestations (5) (arthralgia in 3, bone pain in 4). Of 2 pts with serositis one presented with pericarditis and another – with pleuritis. Only 1 demonstrated a sore throat and polyneuropathy of the lower extremities. ESR and CRP were increased in all pts, leukocytosis was noted in 4 (Table 1). The

Table 1. Demographic, clinical and laboratory characteristics of patients with Schnitzler's syndrome

Pts	The age (y)	The age at onset (y)	Diagnosis delay (y)	ESR (<15 mm/h)	CRP (<6g/l)	M-gradient (g/l)	Anakinra	Canakinumab	The treatment duration (y)
1	51	40	4	31	107	7,1	0	1	5
2	53	28	22	40	29	5,7	0	0	0
3	36	29	3	140	44	7,8	0	1	3
4	58	53	3	100	192	7,6	1	1	0,5
5	69	66	2	49	96	5,1	1	1	0,5

Abbreviations: Pts – patients, y- years, ESR – erythrocyte sedimentation rate, CRP – C-reactive protein

monoclonal IgMk secretion was revealed in 5 pts, IgMκ and IgMλ – in 1 and IgGκ and IgGλ - 1. No *NLRP3, TNFRSF1A* gene mutations were identified. Prior to the diagnosis, all pts were treated with glucocorticoids with a transient partial clinical response and a disease relapse after reducing the dose or stopping the treatment. 2 pts failed to respond to methotrexate and 1 – to hydroxychloroquine. 4 pts were prescribed with 150 mg canakinumab, a monoclonal antibody targeting IL-1, subcutaneously once every 8 weeks. The treatment duration varied from 6 months to 5 years. 2 pts, who initially received daily 100 mg anakinra subcutaneously for 2 to 3 months with a positive response, were further treated with canakinumab. During the treatment with canakinumab, all pts rapidly responded with a complete resolution of fever, rash, arthralgias and bone pains, an overall health improvement and a normalization in ESR and CRP levels. The therapy was well tolerated. In 1 patient, the intervals between canakinumab injections were prolonged to 5 months without any evidence of relapse. During this period, the male patient became a parent to a healthy child.

Conclusion: In rheumatology practice SchS can be misdiagnosed with AOSD. AOSD patients should be tested for monoclonal gammopathy. IL-1 inhibitors are a highly effective and well-tolerated treatment option for SchS. In SchS patients with a complete response to canakinumab, injection intervals can be individualized.

Disclosure of Interests: None declared

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AB1058 JOINT HYPERMOBILITY SYNDROME AND PRIMARY OPEN-ANGLE GLAUCOMA

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Background: Eye symptoms: myopia, prolapse of the upper eyelid, epiblepharon in the upper eyelid are small diagnostic criteria for joint hypermobility syndrome (JHS).

There are few publications in the literature on the relationship between JHS and primary open-angle glaucoma (POAG).

It is known that in the development of JHS, the distribution of collagen of types I and III with the predominance of collagen of type III is important, the latter is encoded by the COL3A1 gene. When using POAG in the connective tissue of the middle and deep layers of the sclera by the immunohistochemical method, intense focal accumulation of type I and III collagen was previously revealed, and in the layers of the sclera's own substance, type III collagen, unusual for it.

Objectives: To study articular and extraarticular clinical manifestations, instrumental, laboratory signs, as well as to conduct molecular genetic studies on the carriage of the Col3Al gene in patients with a diagnosis of POAG and compare them.

Methods: Nine consecutive patients with an established diagnosis of POAG (burdened heredity by glaucoma) with arthralgia were sent for consultation to the V.A. Nasonova Research Institute of Rheumatology from the Moscow Helmholtz Research Institute of Eye Diseases. All patients are women, the average age is 56.7 ± 10.5 years, the average Beighton score - 4.86 ± 1.7, the mean value of the Westergren ESR - 11,8 ± 5.1 mm/h, CRP_{hs} - 4.9 ± 9.4 mg / 1, all of them were seronegative for rheumatoid factor (RE) and ACCP. All patients responded to the JHS diagnosis according to the 1998 Brighton diagnostic criteria. DNA was isolated from the leukocyte fraction of venous blood using the Wizard DNA Purification Kit (Promega) according to the manufacturer's instructions. The study of gene polymorphisms was performed by the method of minisequencing with subsequent time-of-flight mass spectrometry of a sample on a matrix (MALDI-TOF) in the clinical diagnostic laboratory of NPF L1TEX LLC using a standard protocol (Wise C.A., 2003).

Results: 9 patients had arthralgia, 8 - vertebralgia, 3 - myalgia. 2 had a history of wrist joint dislocation, 7 had flat feet (3 of them had Hallucis valgus), 5 had spondylosis and spondylolisthesis (protrusions and disc herniation according to MRI of the spine), and 4 had excessive skin and / or striate atrophy of skin. Extraarticular manifestations: mitral valve prolapse was detected in 3 patients (in 1 of them + atrial septal defect) with ultrasound of the heart, in 3 - descent of the internal organs (nephroptosis, uterine prolapse), in 4 - pronounced varicose veins of the lower extremities. All patients had a carrier state of the A allele identified by marker C.2092G> A and C allele c.2244T> C of the COL3A1 gene, and a family history of glaucoma. Identification of compliance with JHS diagnostic criteria and the presence of genetic factors (COL3A1 gene) in patients with POAG is of great scientific importance, since it confirms not only clinical associations, but also the genetic proximity of these two conditions. It is also difficult to overestimate the practical value, since patients with POAG need the help of a doctor in the treatment of their articular and other non-ophthalmological manifestations of JHS, and establishing a diagnosis of JHS will require a more thorough examination of the eyes in terms of detecting POAG, its treatment or prevention.

Conclusion: The association of JHS, POAG and COL3A1 gene necessitates further study of the association of JHS and POAG: POAG as a clinical manifestation of JHS, on the one hand, and the role of JHS as a possible risk factor for the development of POAG - on the other hand.

Disclosure of Interests: None declared

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AB1059 A RANDOMIZED, PLACEBO-CONTROLLED STUDY OF ANAKINRA IN PATIENTS WITH STILL´S DISEASE

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Background: Adult-onset Still's disease (AOSD) and systemic juvenile idiopathic arthritis (SJIA) are rare autoinflammatory disorders associated with an activated IL-1 pathway, characterized by spiking fever, rash, arthritis, lymphadenopathy, hepatosplenomegaly and serositis. There is a growing understanding that SJIA and AOSD are one disease with different ages of onset, i.e. Still's disease. The anaSTILLs study (anakinra in Still´s disease) was designed to further evaluate efficacy and safety of anakinra in patients with Still´s disease across all age groups.

Objectives: The primary objective was to demonstrate efficacy of anakinra versus placebo as assessed by ACR30 response with absence of fever at Week 2. Secondary objectives included: early onset of efficacy, sustained efficacy, time to study drug discontinuation, safety, pharmacokinetics, clinical signs and biomarkers.

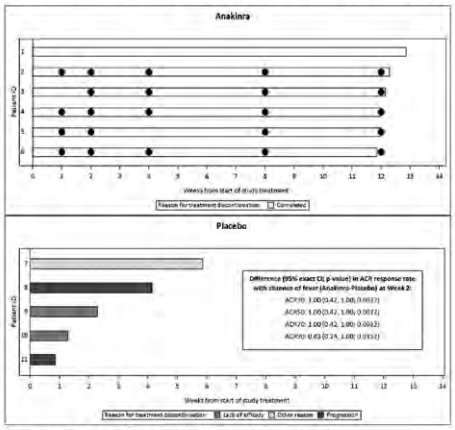
Methods: 'anaSTILLs' was a randomized, double-blind, placebo-controlled, 12-week study including patients with active and newly diagnosed (6 months) Still´s disease according to adapted ILAR criteria if <16, or Yamaguchi criteria, if ≥16 years of age at disease onset. Patients were randomized to anakinra 2 mg/kg (max 100 mg/day), 4 mg/kg (max 200 mg/day) or placebo.

Results: 12 patients were randomized and received study drug: 6 anakinra (2 mg/kg n=2, 4 mg/kg n=4) and 6 placebo, the study was terminated early due to slow recruitment. 1 patient on placebo had lymphoma, not Still's disease, and was excluded; thus in total 11 patients were analyzed for efficacy, 8 were children [median (range) age=4.0 (1-11) years] and 3 were adults [median (range) age=32.0 (25-51) years]. 55% were male and the mean symptom duration was 74.2 days. All patients on anakinra but none on placebo achieved ACR30 response with absence of fever at Week 2 (p-value=0.0022). The efficacy of anakinra was further demonstrated by superiority to placebo in ACR50/70/90 responses with absence of fever at Week 2. All placebo patients discontinued the study within 6 weeks, 2 due to progressive disease, 2 due to lack of efficacy and 1 due to withdrawal by patient. There was a numerically higher proportion with early onset of efficacy (Week 1) in the anakinra group compared to placebo. The

ACR30/50/70/90 responses in the anakinra group were sustained throughout the study period. Patients in the anakinra group had a prompt and persistent decrease in CRP and ferritin levels at Week 1, which was not observed in the placebo group. There were no unexpected safety findings. All anakinra patients developed anti-drug antibodies (ADAs) at some timepoint during the study. ADAs were persistent throughout the treatment period, except in one patient. Titers were low to moderate. One placebo patient had low ADA titers at one occasion. No neutralizing antibodies were observed and the ADAs did not appear to impact clinical efficacy or safety.

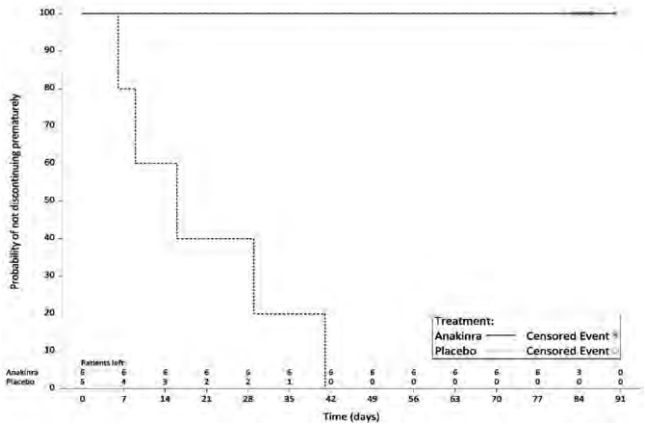
Conclusion: Anakinra is superior to placebo in the treatment of Still's disease. ADAs occur frequently but do not appear to adversely impact efficacy or safety. These results confirm the benefits of anakinra treatment in patients with active, newly diagnosed Still´s disease across ages.

Figure 1: Individual ACR90 response with absence of fever and treatment duration over time and ACR30/50/70 at week 2



Bars indicate time on study drug. Bullets indicate ACR90 response at the particular week.
Patient 1 had sustained ACR70 response but not ACR90.

Figure 2: Time to study drug discontinuation, Kaplan-Meier plot



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AB1060 A RARE IGG4-REALTED DISEASE PHENOTYPE WITH BONE DESTRUCTIVE LESIONS

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Background: IgG4-related disease (IgG4-RD) is an immunomediated fibroinflammatory condition with systemic course that can affect almost any organ in the body. In the majority of cases it is a benign condition with slow progression. The clinical symptoms are usually determined by compression of nearby anatomic structures by tumefective lesions, but not by invasive growth of the pseudotumor with the destruction of the organs. Bone destruction always raises suspicion of malignant tumor, but it should be considered in the course of IgG4-RD as well.

Objectives: To report a very rare bone destructive phenotype of IgG4-RD.

Methods: We report 5 cases of biopsy proven IgG4-RD with bone destructive lesions.

Results: In our cohort of patients there were 3 patients with multiple fascial bones destruction due to maxillary sinus pseudotumor expansion and 2 patient with vertebral destruction lesions.

Patients 1, 2 and 3 with facial bone destruction were young men aged 42, 36 and 28 years. In all cases the primary lesion was located in the maxillary sinus with expansion to the fascial soft tissues and orbit. Two patients had probable and 1 possible IgG4-RD diagnosis according to consensus diagnostic criteria, 2011. All patients were treated with rituximab and low doses of glucocorticoids with improvement of clinical symptoms (fascial edema, eye pain and/or headache), but lacking in radiologic improvement.

Patient 4 is a 51-year-old man who developed retrosternal pain, mimicking angina pectoris. Chest CT showed a tumor of posterior mediastinum, infiltrating the right lung and Th6-Th8 bodies destruction. Biopsy of the lesion revealed lymphoplasmatic infiltrate with lymph follicles formation, few eosinophils, significant diffuse fibrosis. Immunohistochemical study, showed IgG:IgG4 ratio >40%. The serum IgG4 concentration was 1.94 g/l (normal range below 2.0 g/l). Combined treatment was administered: rituximab 500 mg weekly #4 and cyclophosphamide 1000 mg + methylprednisolone 250 mg IV every 2 weeks #6. After that - cyclophosphamide 200 mg per week intramuscularly, methylprednisolone 4 mg daily per os. Due to spinal instability the patient undergone surgery. Six months later at check-up examination CT has shown a dramatic decrease of the mediastinal infiltrate. The treatment with cyclophosphamide and oral metylprednisolone was tapered gradually during 2 years due to no sites of pathological hypermetabolic activity were found on PET.

Patient 5 is a 60-year-old woman who had spinal surgery for C2 odontoid destruction. Biopsy revealed chronic inflammatory with massive fibrosis. 1,5 years later she developed salivary glands enlargement. During evaluation she had elevated serum IgG4 4.9 g/l and IgM 4.1 g/l (normal range below 0.6-3.7 g/l), serum protein electrophoresis with immunofixation showed monoclonal IgMκ 3.2 g/l. Left submandibular salivary gland biopsy revealed significant fibrosis, dense lymphoplasmatic infiltrate forming lymph follicle with IgG:IgG4 ratio 50-80% and no pathological signs of lymphoma. The patient was treated with rituximab 500 mg per week #2 and cyclophosphamide 1000 mg + methylprednisolone 250 mg IV every 2 weeks #3. The treatment was discontinued because of toxic hepatitis. Unfortunately, no follow-up was available. The tissue specimens after spinal surgery were also unavailable.

Conclusion: IgG4-RD can manifest by bone, including vertebral, destructive lesions and thus should be included when considering differential diagnosis in patients with bone destruction.

Disclosure of Interests: None declared

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AB1061 2019 ACR/EULAR CLASSIFICATION CRITERIA FOR IGG4-RELATED DISEASE IN RUSSIAN COHORT OF PATIENTS.

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Background: IgG4-related disease (IgG4-RD) is a systemic immunomediated fibroinflammatory condition that can affect almost any organ in the body. This is the reason for dramatic variety of clinical symptoms and complexity of diagnostics. 2011 Comprehensive diagnostic criteria (CDC) for IgG4-RD are used to establish the diagnosis for all lesions (except autoimmune pancreatitis type 1). In 2019 the new ACR/EULAR classification criteria for IgG4-RD were proposed to facilitate the formation of more homogenous groups of patients primarily for clinical trials inclusion purpose. They also provide a framework for clinicians considering diagnosis of IgG4-RD.

Objectives: To evaluate 2019 ACR/EULAR classification criteria for IgG4-RD in Russian cohort of patients with IgG4-RD.

Methods: 59 patient with IgG4-RD according to CDC with biopsy proven diagnosis were included.
Results: The mean number of affected organs was 2.1; 31 patients (52,5%) were women. Majority of patients had sialoadenitis (25 patients) and/or orbital disease (31 patients), 9 had retroperitoneal fibrosis (RPF). Other affected organs were lungs, pancreas, lymph nodes, paranasal sinuses, thyroid and low urinary tract. Twenty five (25) patients (42,4%) had definite, 14 (23,3%) probable and 20 (34,3%) possible diagnosis of IgG4-RD. Twenty three (23) patients (39%) didn't fulfill the 2019 ACR/EULAR classification criteria for IgG4-RD. Among them were the majority of patients with RPF (7 patients) who were lacking other organ involvement and IgG4 hypersecretion either in the tissue or serum. The majority of excluded cases were due to inadequate pathomorphological evaluation (lacking of the exact number and percentage (if >40%) of IgG4+ cells), lacking of multi-organ involvement or different patterns of involvement, e.g. in case of lungs involvement.
Conclusion: The new 2019ACR/EULAR classification criteria for IgG4-RD are very useful in evaluation of typical organ involvement and systemic course of IgG4-RD. It is essential to adjust Russian pathomorphologists's approach to cell counting and percentage determination for IgG4-RD cases to get suitable protocols.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.6327

AB1062 LIPODERMATOSCLEROSIS AS A TYPE OF LOBULAR PANNICULITIS: THE EFFECTIVENESS OF NON-PHARMACOLOGICAL TREATMENT METHODS

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Background: In medical practice lobular panniculitis-lipodermatosclerosis (LDS) is becoming more and more common. It is manifested by degenerative-dystrophic changes in subcutaneous fat (SCF) and occurs more often in middle-aged women affected by chronic venous insufficiency.
Objectives: to evaluate the effectiveness of mesotherapy (MT) and shockwave ultrasound therapy (UST) for LDS
Methods: among 539 patients referred to the V.A. Nasonova Research Institute of Rheumatology with the referral diagnoses of erythema nodosum or panniculitis 8.5% (46) of patients (44 women, 2 men) aged 18 to 82 with overweight (32) LDS with the disease duration of 11,8±6.4 months was verified. Patients were randomized into two groups of 23 patients each: group I received daily MT (10 sessions) therapy with drugs that have antioxidant, anti-inflammatory, lymphatic drainage and lipolytic effects, and 3 MHz UST of the node area twice a week (5 sessions). In group II MT was performed daily with 9% Natrii chloridum solution at a dose comparable to group I. The control methods included general clinical examination (characterization of induration on the lower legs with an assessment of the effect of pain pressing according to visual analogue scale (VAS pain), general blood and urine tests and ultrasound with elastography (USE) of the compaction. The main stages of control: initial (T0), after 14 days (T1), 1 month (T2) and 3 months (T3).
Results: before treatment 38 patients with LDS demonstrated asymmetric (83%) inflammation of SCF of the lower legs (100%) on its medial surface (91%). LDS regressed faster with normal body mass index (p = 0,04). In all patients of group I, after a course of physiotherapy a positive trend was registered, that is a decrease in VAS pain intensity (T0 50±18 mm; T1 35±11 mm), decrease in diameter (T0 6±2.2 cm; T1 4.5±1, 7 mm) and color intensity of the node (p<0.002), SCF thickening which results in "lumping" with macrovascularization according to USE, and decrease in ESR and CRP. In 44% of cases the treatment effect increased to T2 (p <0.05). After 3 months of observation, 15 patients required a second course of physiotherapy. In group II a positive clinical effect was registered for T2 in 14 patients (60.8%) and for T3 in 19 patients (83%) (p<0.05). Over the entire observation period LDS recurrence was registered in 19 patients (41%), the median of recurrence was 3 [1; 6] months, mainly in patients of group I. Recurrence was associated with node fusion into conglomerates (OR 4.33, 95% CI 1.05-17.8; p = 0.037). MT and UST were tolerated well, no side effects were detected.
Conclusion: the use of MT with 9% Natrii chloridum solution allowed us to achieve positive dynamics in patients with LDS, which significantly reduced the cost of treatment. Further studies are needed to evaluate the significance of these techniques.
Disclosure of Interests: None declared
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AB1063 CASE SERIES OF PATIENTS WITH CHRONIC NON-TUBERCULOSIS MYCOBACTERIA ACCOMPANYING WITH ANTI-INTERFERON GAMMA ANTIBODY

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Background: Anti-interferon (IFN) gamma antibody was a rare autoantibody which mainly been reported in Asia. It interferes the interferon pathway and eradication of intracellular pathogens, such as Salmonella or Mycobacteria. This rare disease should be raised for more awareness.
Objectives: To analyze clinical presentations of the patients with anti-interferon (IFN) gamma antibody.
Methods: We checked anti-IFN gamma antibody when patient fulfilled multiple NTM infection (especially bone marrow and lymph nodes). There are 6 cases of non-tuberculosis mycobacteria (NTM) infection accompanying with anti-IFN gamma antibody in our hospital from 2015 to 2019 of hospitalist ward, and the antibody titer is recorded.
Results: Among these cases, patients had initial presentations of fever (100%), elevated CRP and ESR (100%), lymphadenopathy (67%), body weight loss (50%), and elevated LDH (50%). All the 6 cases had negative results of TB-PCR test, but 1 had positive result of interferon gamma release assay (IGRA, 17%). NTM was identified from lymph node biopsy (50%), sputum (33%), skin (33%), and bone marrow (33%). Different NTM was identified, including Mycobacterium abscessus, Mycobacterium fortuitum group complex, Mycobacterium kanasii, and Mycobacterium avium complex. Prolonged antibiotics treatment was used, but all patients had recurrent or persisted NTM infection under medications. 4 cases had different NTM strain after 1 year of treatment from the initial involved organ. One case had an episode of Salmonella bacteremia with septic shock. Another case had positive result of ANA, and other cases had negative auto-antibodies.
Conclusion: Careful history taking and physical examinations are crucial in diagnosis this acquired immunodeficiency disease. This rare but unique disease should be taken into consideration.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.6610

AB1064 IMMUNOGLOBULIN G4-RELATED DISEASE (IGG4-RD): CLINICAL AND LABORATORY CHARACTERISTICS, TREATMENT RESPONSES AND PROGNOSIS IN ONE HUNDRED FIVE PATIENTS.

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Background: IgG4-RD is a systemic fibro-inflammatory condition with incompletely understood that is capable of affecting multiple organs.
Objectives: We aimed to investigate clinical and laboratory findings in Japanese patients with IgG4-RD.
Methods: Dates on clinical characteristics, laboratory features, and treatment response from patients with IgG4-RD in our hospital were reviewed retrospectively from January 2004 to September 2019.
Results: Among 105 patients were diagnosed and treated in our hospital, 48% were female and 88% were biopsy-proven. The median age of the patients was 66 years, and female were younger at their diagnosed age (p=0.04). Their medina duration of follow-up was 45 months. 48% of the patients had allergic history (including sinusitis, asthma, hay fever), younger patients tended to have allergy history. Mean serum IgE was 303 IU/dL (2-4965 IU/dL). Salivary and lacrimal grand involvement (63%) and dacryoadenitis and ocular and orbital inflammatory disease (56%), autoimmune pancratitis type 1 pancreatitis (18%), retroperitoneal fibrosis (16%), aortitis (15%) predominantly occurred. 84% of the patients had serum IgG4 higher than 135mg/dL, and high IgG and IgG4 concentration was associated with lower complements (CH50, C4) levels. Mean serum IgG was 1860 mg/dL (861-8432 mg/dL), and IgG4 was 449mg/dL (28-3210mg/dL). Male patients show higher serum IgG and IgG4 concentrations at baseline (p<0.01). Younger patients and low serum C4 level were associated with necessity of treatment, 60 of them used steroid, and the mean dose of prednisone they used was 30mg. Most of them responded well and tapering steroid. Steroid sparing agents were used in 23% of them. Although 23% of patients relapse as tapering steroid, 15% of them could stop treat with steroid. Retreatment with glucocorticoids is not associated with any factors. There were 14 malignancies in 13 patients during the follow-up period.
Conclusion: Our study revealed that IgG4-RD occurred in middle age with allergic disease in Japanese patients. The pattern of head and neck was predominance. For the most part of the patient serum IgG and IgG4 concentrations was high. Serum low complement level could be associated with its diagnosis and necessity of treatment with steroid. Younger patients tend to treat with steroid and they responded well.
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Disclosure of Interests: None declared
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AB1065 VISIT COMPLIANCE IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER: RESULTS FROM A GAZI UNIVERSITY FMF COHORT

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Background: Follow-up in all rheumatologic patients is critical, particularly Familial Mediterranean Fever (FMF). Current recommendations for all experts by the EULAR state that patients with FMF should be evaluated 6-monthly intervals to monitore the character and frequency of the attacks and the acute phase response. Disease-related complications such as amyloidosis can be *asymptomatic* and need only a careful follow-up.

Objectives: to quantify this phenomenon and to find predictive factors of visit compliance in patients with FMF.

Methods: The study included 474 adult patients with a diagnosis of FMF who followed at the outpatient rheumatology clinic of tertiary university hospital, from January 2018 to December 2018. . Demographic, socioeconomic data, familiy history, comorbid disease, medication history, characteristics, the International Severity Score for FMF (ISSF),autoinflammatory disease damage index (ADDI) were recorded. Visit compliance was defined as the presence of two visits in the outpatient rheumatology clinic for FMF last one year for the purposes set out in EULAR suggestion.Those who had fewer than two visits in the last one year were considered noncompliant.

Results: 230 (48.5%) were compliant while 244 (51.5 %) patients were noncompliant with their rheumatology visit. Both compliant and noncompliant patients had similar median age and disease duration. Female sex and being married was increased the visit compliance.The results of the logistic regression model exploring factors associated with compliance indicated that presence of family history in parents, absence of family history in sibling, treatment with biologic agents, other drug using,presence of more than 2 attacks except fever and adequate medical care were important predictors of visit compliance.

Table 1. Descriptive charecteristics of the patients with FMF, n=474

Variable	Compliant(n=230)	Noncompliant (n=244)	P value
Gender of patient (F)	142(61.7)	147(60.2)	0.73
Age, years*	35(28-42.5)	34(27-44.2)	0.88
Being Married	152(66.1)	146(59.8)	0.15
Disease duration, years*	22(14-31)	22(15-31)	0.71
Number of index flare* within last 12-month	6.7(1-10)	5(3-10)	<0.001
Family historyof parents	54(23.5)	39(16.0)	0.04
Family historyof sibling	73(32.9)	102(43.4)	0.02
Comorbid disease presence	73(31.7)	55(22.5)	0.02
Treatment			<0.001
Colchicine	230 (94.1)	180(78.6)	
Anakinra&Canakinumab	134(5.3)	49(21.4)	
Colchicine response presence	127(55.2)	126(52.3)	0.52
Drug using except FMF	74(32.2)	44(18.0)	<0.001
Presence of 2 attacks except fever	90 (39.1)	68(27.9)	0.009
Chronic peripheral arthritis	16(7.0)	7(2.9)	0.03
Amyloidosis	18(7.8)	9(3.7)	0.05
Proteinuria	23(10.8)	8(3.6)	0.004
Adequate medical care	161(70.0)	132(54.8)	<0.001
ISSF severity score*	3(2-4)	3(2-4)	0.02
ADDI index*	1(0-1)	1(0-1)	0.05

Conclusion: In conclusion, if FMF patients visit compliance increase, their functionality, medication adherence and quality of life will increase and flares and complication of disease can decrease. Thus, we highlight some recommendations for FMF specialist, patients and health care providers to improve outcomes.

Table 2. Multivariate logistic regression analysis for predictive factors of visit compliance of the patients with FMF, n=430

	Adj. OR	%95 CI**	p
Family history in parents (positive history vs negative)	1,8	1,0-3,1	0.03
Family history in sibling (negative history vs positive)	1,9	1,2-3,1	0.004
Comorbid disease status	1,3	0,7-2,5	0.32
Treatment (anakinra&canakinumab vs colchicine)	3,7	1,7-8,2	0.001
Drug using (other drugs vs FMF drugs)	2,2	1,1-4,4	0.01
More than 2 attacks except fever	2,3	1,2-4,0	0.004
Chronic peripheral arthritis	2,3	0,8-6,6	0.10
Proteinuria	2,2	0,7-6,7	0.14
Adequate medical care	1,9	1,2-3,1	0.003
Number of index flare within last 12-month	0,9	0,9-1,0	0.38
ISSF severity score	0,8	0,7-1,1	0,30

Disclosure of Interests: None declared
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AB1066 EFFICACY AND SAFETY OF APREMILAST IN BEHÇET DISEASE PATIENTS

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Background: Apremilast (APR), a small molecule inhibitor of phosphodiestersa-4, has been shown to be effective in the treatment of oral and genital ulcers in Behçet's disease (BD). BD is a systemic vasculitis with great heterogeneity of symptoms and manifestations. It can affect the blood vessels, mucosa, skin, joints, eyes, nervous system and digestive system. APR is indicated for treatment of oral ulcers in BD in some countries such as the USA and Japan.

Objectives: To evaluate the efficacy and safety of APR treatment in BD patients.

Methods: Single-center descriptive study of BD patients on APR treatment from February 2017 to December 2019. Demographic, clinical and analytical data were collected.

Results: 10 patients (9 women) were included, with a mean age at the beginning of APR treatment of 37±12 years and a mean disease evolution of 100±105 months. 8 of them showed HLAB51 positivity.

Before treatment with APR, 4 patients were refractory to DMARDs (2 MTX, 2 AZA) and one patient to 2 anti-TNF (ADA, IFX). All patients were under treatment with colchicine and 5 with steroids before APR therapy. The concomitant treatment with APR were: corticosteroids (5), NSAIDs (2), colchicine (8), MTX (2), AZA (2).

The main symptoms at the beginning of the APR treatment were: oral ulcers (100%), genital ulcers (60%) and arthritis/arthralgia (90%). We observed a clinical improvement after 3 months of treatment of 90% of oral ulcers, 100% of genitals and 55% of joint symptoms. The patients had a mean follow-up of 37±12 months and they maintain the therapy response during the APR treatment.

Patients presented adverse events, some of them transitory: headache (5), diarrhea (5), nausea (3), dysthymia (1), tremors (2), herpes zoster (1) and autolytic ideation (1). The treatment was withdrawn in 4 patients with a mean duration of 11 ± 13 months. 2 of the 4 adverse events were by autolytic ideation and nausea, 1 for genesic desire and 1 for persistence of joint injury. The APR doses were reduced to 30 mg per day in 4 patients, resolving the adverse events and persisting with a good response. In addition, dose reduction of colchicine and prednisone was achieved in 4 patients.

We observed other previous manifestations of BD such as uveitis (4), neurobehçet (3), cutaneous (folliculitis/pseudofoliculits) (4) and venous thrombosis (1). Cutaneous manifestations were resolved and the rest of previous manifestations remain without clinical changes during the follow-up.

Conclusion: We observed an improvement in the most common manifestations of BD and a safety profile similar to those described in other studies. We observed a resolution of mucocutaneous manifestations, a variable response in joint manifestations and stability in neurological manifestations. Adverse effects referred included gastrointestinal and headache, most of which were transient and were resolved with adjustment of treatment.

Disclosure of Interests: None declared
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AB1067 CASE OR FAMILY?FROM 2 CHINESE FCAS3 CHILDREN WITH PLCG2 MUTATION TO THEIR FAMILIES.

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Background: Familial cold autoinflammatory syndrome 3 (FCAS3) is an autoinflammatory disease (AID) caused by mutation of the PLCG2 gene, which has not been reported in China. We will report 2 cases of Chinese FCAS3 patients with no claimed family history, but we found the same mutations in a parent during their genetic analysis. After further inquiry of the parent's medical history, we confirmed that actually, they were two FCAS3 families. Through a literature review, we found that the clinical features of Chinese patients are milder than foreign countries, and their symptoms are concealed and may be ignored, resulting in mistakes in family history collecting.
Objectives: To summarize the genetic and clinical features of Chinese FCAS3 patients and to provide diagnostic recommendations for the disease.
Methods: Two suspected AID children with recurrent fever and urticaria were enrolled in this study. Clinical data and family history were collected, and genetic analysis was performed by next-generation sequencing (PID panel or WES) and Sanger-based validation. Literature was reviewed from PubMed, CNKI, and Wanfang Database.
Results: The two children were both diagnosed to be FCAS3 with PLCG2 mutation. The clinical manifestations of 2 children were recurrent fever, urticaria, and increased ESR and CRP. Case 1 has a paternal, and Case 2 has a maternal heterozygous mutation in the PLCG2 gene, while both had claimed without a family history. Further inquiry showed the two parents used to have a fever with urticaria. By comparing with foreign literature, we found our patients were milder than abroad patients. Large fragment deletions were relatively more common in foreign patients.
Conclusion: We reported the case of FCAS3 in China for the first time. Their genotype and phenotype were different from foreign patients. Their symptoms are mild, and heterozygous mutations are more common than foreign patients, which are the main differences. The difference in mutation type may be the reason for different clinical manifestations. Besides, both two families showed a trend of more severe clinical features in the next generation. As the symptoms of the elders were not obvious and may be ignored, it caused trouble for the genetic diagnosis. Therefore, family history should be collected carefully. For rashes and fevers, which are not too severe in overall symptoms, care should be taken about the possibility of AIDs. Genetic testing can help to make a definite diagnosis.
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AB1068 REGULATORY EFFECT OF SHORT-TERM LOW DOSE OF IL-2 RESTORES REGULATORY T CELLS IN IGG4-RELATED DISEASE

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Background: Little known about the roles of peripheral immune cell subsets in IgG4-related disease (IgG4-RD).
Objectives: The aim of our study was to analyze the role of low-dose interleukin-2 (ld-IL2) on these cells in IgG4-RD.
Methods: The percentage and absolute counts of lymphocyte subpopulations [CD3+ (T cells), CD4+, CD8+, CD19+ (B cells) and CD16+CD56+ (NK cells)] and CD4+T cell subsets (Th1, Th2, Th17, regulatory T (Treg)) using single platform flow cytometry in 25 IgG4-RD patients which were admitted and treated, as well as 24 healthy controls (HCs). Among IgG4-RD patients, 19 patients given only conventional treatments while 5 patients were were not only given conventional treatments but also received ld-IL2 (0.5 million IU/day) for 5 days.
Results: We found that the absolute counts of T, CD4+T and Th1 cells were increased in the peripheral immune cells of IgG4-RD patients when compared with HCs. Meanwhile, the percentage of B, Th2, Th17 and Treg cells demonstrated significantly decreased. The ratio of Th1/Th2 and Th1/Treg in IgG4-RD patients were higher than that in HCs. After IL-2 administration, the absolute numbers of Treg cells increased dramatically, furthermore, the proportion of Treg cells had a trend towards higher values compared with those before treatment. Conversely, the ratio of Th2/Treg was downward. There were no any significant differences in the above subsets between before and after conventional treatments.
Conclusion: Our findings support that the reduction of Treg cells in IgG4-RD patients, as well as ld-IL2 combined with conventional treatments were able to restore the Treg cells.
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AB1069 CONSIDERATION OF YAO SYNDROME AS A DIFFERENTIAL DIAGNOSIS FOR HEREDITARY PERIODIC FEVER SYNDROMES

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Background: Yao syndrome (YAOS, OMIM 617321), formerly termed nucleotide-binding oligomerization domain 2(*NOD2)*-associated autoinflammatory disease, is characterized by periodic fever, dermatitis, arthritis, and swelling of the distal extremities, as well as gastrointestinal and sicca-like symptoms. This disorder shares similar clinical phenotypes with hereditary periodic fever syndromes (HPFS) and thus can mimic one another.
Objectives: This study aimed to exemplify by a comparison of YAOS vs familial Mediterranean fever (FMF).
Methods: In this retrospective study, electronic medical records of a series of patients with YAOS were analyzed. All patients underwent genetic testing for periodic fever syndrome 6-gene panel (MEFV, TNFRSF1A, NLRP3, MVK, NLRP12 and NOD2).
Results: All patients were Caucasian and had recurrent fever, patchy erythema, arthralgia, and gastrointestinal symptoms (Table 1). With negative DNA sequencing for MEFV, these patients were treated with colchicine for presumed FMF, with a good response in patient 2 and minimal or transient response in other two patients. Further genetic testing identified the NOD2 variants. Unlike HPFS, YAOS is generally sporadic and is mostly reported in adults; spongiotic dermatitis is common; YAOS is associated with the NOD2 variants, IVS8+158 in nearly all patients, IVS8+158/R702W in up to 30%, and IVS8+158/1007fs, G908R or other rarer NOD2 variants in some patients.
Conclusion: YAOS can masquerade HPFS like FMF. Molecular analysis should cover NOD2 whole gene sequencing to help distinguish these diseases.
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Table 1. Demographic and Clinical Data of Patients

Patient	Demographics	Phenotype	Laboratory	Prior Diagnosis(Dx) and Treatment
1	Age Onset: 63 Age at YAOS Dx: 66 Gender: F Caucasian: Yes	**Fever:** High grade, lasting up to 36 hrs **Skin:** Patchy erythema on face, lasting up to 2 wks **Arthritis:** Knee and ankle **GI:** Abd pain, non-bloody diarrhea. GI workup: negative for IBD Sicca: Yes Asthma: Yes **Family history**: No	ESR)/CRP: Normal MEFV: Neg 6-gene panel: positive for NOD2 IVS8+158, R702W, heterozygous	**FMF**: Yes **Colchicine(col):** Transient response
2	Age Onset: 7 Age at YAOS Dx: 49 Gender: F Caucasian: Yes	**Fever:** High grade **Skin:** Patchy erythema on face, chest, abd, limbs, lasting up to 6 wks **Arthritis:** Knee, ankle and toe **GI:** Abd pain, nonbloody diarrhea, lasting up to 4 d. GI workup: neg for IBD Sicca: Yes Asthma: Yes **Family history**: Yes	ESR/CRP: Normal MEFV: Neg 6-gene panel: positive for NOD2 IVS8+158, heterozygous	**FMF**: Yes **Col:** Good response
3	Age Onset: 15 Age at YAOS Dx: 35 Gender: F Caucasian: Yes	**Fever:** Low grade **Skin:** Patchy erythema on arms and legs, lasting a few d **Arthritis:** Knee and shoulder **GI:** Abd pain with nausea and vomiting, lasting a few hrs. GI workup: neg for IBD Sicca: No Asthma: No **Family history**: No	ESR/CRP: Normal MEFV: Neg 6-gene panel: positive for NOD2 IVS8+158, 1007fs, heterozygous	**FMF:** Yes **Col:** Minimal response

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Disclosure of Interests: None declared
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AB1070

DIVERSITY ANALYSIS OF INTESTINAL FLORA IN PATIENTS WITH BEHCET'S DISEASE

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Background: Behçet's disease (BD) may be regarded as a polygenic autoinflammatory disease although adaptive immune system has also been implicated in pathogenesis. The specific components of the microbiota with BD that affect the host response leading to disease remain unknown. Regulation of intestinal microbiota would be able to provide new strategy and target for the treatment of BD.
Objectives: To study the diversity and the intestinal flora of intestinal microbes in patients with BD and further provide new ideas for clinical treatment.
Methods: The stool specimens of 13 BD patients were analyzed at the level of the Phylum, family and genus, and compared with that of 50 healthy controls(HC).
Results: Compared with controls, the abundance of intestinal microbiota in patients with BD was significantly different.At the level of phylum, the abundance of *Firmicutes* was significantly reduced in BD patients compared with that of HC(P<0.05)(fig. 1).At the genus level, in the BD group, the abundance of *Klebsiella is* significantly increased (P<0.05), but the abundance of *Clostridium IV, Lachnospiracea incertae sedis, Anaerostipes and Megasphaera* were significantly lower than that of healthy controls. (P<0.05)(fig. 2).

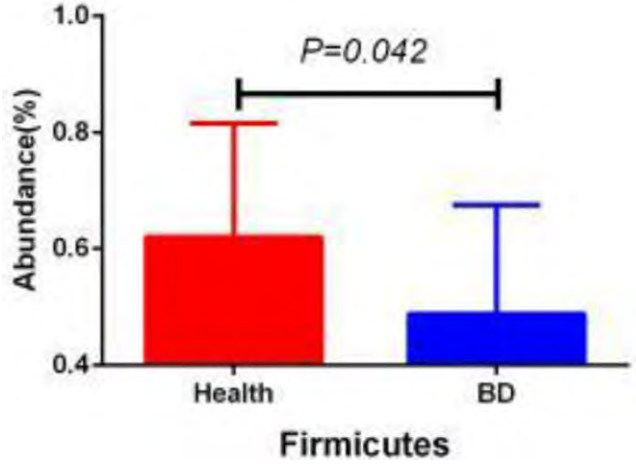


Figure 1. the differences between patients with BD and normal healthy adults were compared at the level of the phylum

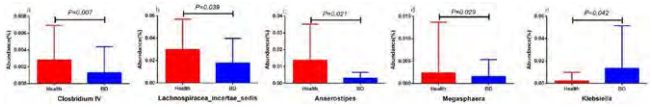


Figure 2. the differences between patients with BD and normal healthy adults were compared at the level of the genus

Conclusion: The diversity and balance of bacterial community in intestinal microecological environment of patients with BD are significantly different from the healthy control. Intestinal microbiota disorder may be related to the pathogenesis of BD, which might provide theoretical foundation for the regulation of intestinal flora for disease intervention.
Disclosure of Interests: None declared
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AB1071

COEXISTENCE OF FAMILIAL MEDITERRANEAN FEVER WITH SPONDYLOARTHRITIS: CLINICAL CHARACTERISTIC AND TREATMENT OUTCOMES

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Background: Studies indicate that there is an association with spondyloarthritis (SpA) and familial mediterranean fever (FMF) based on the following: 1) increased incidence of sacroiliitis in FMF, 2) MEFV gene mutations are significantly increased in ankylosing spondylitis (AS) and 3) both SpA and FMF show some common clinical manifestations such as the pattern of arthritis. However, characteristics of SpA associated with FMF such as clinical characteristics and treatment outcomes have been poorly documented and additional data is required on this topic.
Objectives: To study the clinical and treatment characteristics of patients associated with FMF and SpA.
Methods: Twenty-eight patients with FMF and SpA who were registered in our database were included in the study. Demographic, clinical, and laboratory data were collected. HLA-B27, MEFV gene mutations were recorded. Pelvic radiographs and sacroiliac joint magnetic resonance imaging (MRI) (if present) were scored based on the modified New York criteria (mNYc) and ASAS MRI definitions respectively. Treatment data were also recorded.
Results: There were 28 FMF-SpA patients in the study (mean age 45.1±16.4 years, 57.2% male). The mean age of onset of FMF and SpA were 31.9±17.9 and 35.5±16.2 years respectively. SpA patients were predominantly axial (n=21, 75%), and only 7 (25%) were mainly peripheral type. Fifteen (53.5%) patients were satisfying mNYc for AS. Four (14%) patients were fulfilling ASAS non radiographic axial SpA definition. Bone marrow edema was detected in (36%) of the patients who underwent MRI (n=14). Two (7.1%) patients had SpA symptoms but did not classify into any of the ASAS arms. Arthritis observed in 19 (67.8%) patients with mostly in oligoarthritis type (79%). Ankle and knees were the most affected joints. Total hip replacement was present in 7% of the patients. Amyloidosis confirmed by biopsy was detected in 4 (14%)

patients. Enthesitis (11%), uveitis (11%), Chron's disease (7%), dactylitis (3%), and psoriasis (3%) was also noted. Nearly %30 patients required non IL-1 biologic therapy (BTx) to control SpA symptoms (axial 70%, peripheral 30%). 40% of the patients needed to switch non IL-1 BTx to another biologic agent because of lack of efficacy on SpA symptoms (25%) or due to the adverse event (25%) and active FMF not responding to non IL-1 biological agent (50%).

Conclusion: We showed the following: 1) more female predominance in FMF-SpA patients compared to classic SpA, 2) FMF-SpA patients had lower frequency of HLA B27, 3) up to %30 of the patients required non-IL-1 BTx to control SpA symptoms and 4) in patients on non IL-1 BTx FMF symptoms responded in 80%.

Table 1. The clinical characteristics of FMF-SPA patients

Age*	45.1±16.4
Male, n (%)	16 (57.2)
SpA symptom duration,years*	9.5±7.0
FMF symptom duration,years*	12.6±9.6
HLA-B27 positivity, n (%)	5 (29.4)
Mainly axial involvement, n (%)	21 (75)
Mainly peripheral involvement, n (%)	7(25)
mNY positivity, n (%)	15 (53.5)
MEFV (M694V) mutation	18
MEFV (non M694V) mutation	19
Amyloidosis, n (%)	4 (14.2)
Non IL-1 biological treatment for SpA symptoms, n (%)	10 (35.7)

*(mean ±S.D)

Disclosure of Interests: None declared
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Diagnostics and imaging procedures

AB1072 ROLE OF ULTRASOUND IN DETECTION OF SHOULDER JOINT PATHOLOGIES IN ASYMPTOMATIC RHEUMATOID ARTHRITIS PATIENTS

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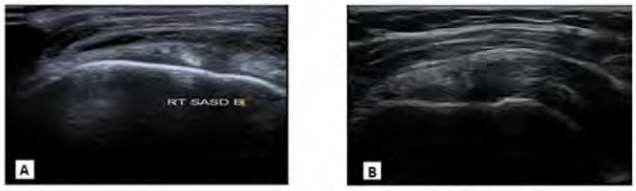
Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease that results in progressive destruction of structural components of the joints[1] It commonly affects the shoulder leading to pain, tenderness and decreased range of motion[2] Increased shoulder pain has been found to correlate strongly with disease severity[3], however there is little information available in the literature regarding shoulder pathologies in asymptomatic RA patients.

Objectives: To determine the prevalence of pathologies in asymptomatic shoulders in rheumatoid arthritis patients and role of ultrasound to detect it.

Methods: A cross-sectional study including two groups, first group included 36 RA patients, meeting the ACR/EULAR classification criteria for RA with no shoulder complaints. The second group included 36 healthy control subjects of similar age groups and sex, with no shoulder complaints. They were recruited from rheumatology outpatient clinic in Mansoura University Hospital. Only asymptomatic shoulders of both groups were examined clinically by inspection, palpation and special tests, then examined by ultrasound using Toshiba Xario 200 machine with 13 MHz superficial probe including biceps tendon, subscapularis tendon, supraspinatus tendon, subacromial subdeltoid (SASD) bursa, infraspinatus tendon, posterior glenohumeral joint for effusion or synovitis, acromioclavicular joint and humeral head for erosions. Findings of both groups were compared to each other.

Results: Asymptomatic shoulders in RA patients showed significant number of pathologies in 72% of the examined patients in comparison with healthy subjects (17%). According to frequency, humeral erosions were detected in 12 patients (33%), acromioclavicular osteoarthritis in 8 patients (22%), biceps tenosynovitis, supraspinatus tendinopathy, glenohumeral effusion in 6 patients (17%), subscapularis tendinopathy in 4 patients (11.%), SASD bursitis in 2 patients (6%), Infraspinatus tendinopathy in 1 patient (3%).

The healthy group showed less number of pathologies including supraspinatus tendinopathy 3 (8%), acromioclavicular osteoarthritis 2 (6%), humeral erosions 1 (3%).



A) Ultrasound scan of supraspinatus tendon longitudinal view and SASD bursa of asymptomatic shoulder shows SASD bursitis B) Ultrasound scan of supraspinatus tendon longitudinal view in healthy asymptomatic individual shows supraspinatus tendinopathy

Conclusion: A significant high rate of different pathologies can be present in shoulders of RA patients despite negative history and normal physical examination. Ultrasound can be used for early detection and better management before irreversible joint destruction.

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Disclosure of Interests: None declared
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AB1073 DYNAMICS OF X-RAY CHANGES IN THE HIP JOINTS WITH EARLY AXIAL SPONDYLOARTHRITIS PATIENTS.

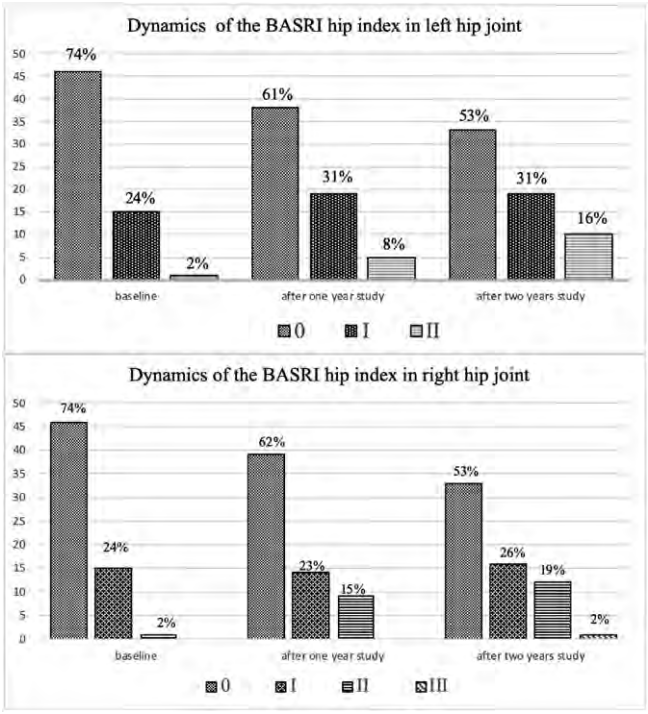
E. Agafonova[1], T. Dubinina[1], S. Erdes[1], D. Rumiantceva[1]. [1]*V.A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Background: in almost half of patients with ankylosing spondylitis (AS) in Russia, damage to the hip joints (HJ) is detected, but the rate of its progression has not been studied.

Objectives: to evaluate the radiological progression of coxitis in patients with early axial spondylarthritis (axSpA) for two years.

Methods: the study involved the patients of the Moscow cohort CORSAIR (Early Spondyloarthritis Cohort), which was formed in V.A. Nasonova Research Institute of Rheumatology. We analyzed 62 patients with a diagnosis of axSpa (ASAS criteria 2009), observed for at least 2 years and having survey images of the pelvic bones during inclusion in the cohort and 2 years after the start of observation. The average age at the time of inclusion in the cohort was 29.2 ± 6.4 years with an average disease duration of 23.8 ± 16.2 months, 32 men and 30 women, 92% of patients positive for HLA-B27. All patients received standard anti-inflammatory therapy.

Results: when including out of 62 patients in the study, only one (2%) patient showed X-ray changes in HJ, Fig. 1 (a; b)). After 2 years of follow-up, the number of patients with radiological changes in HJ increased to 13 (21%), Fig. 1 (a; b). Patients were divided into two groups depending on the presence of radiological progression in HJ.



A comparative analysis of the groups revealed that progression is more common in men and in younger people (p <0.05). In other parameters presented in Table 1, the groups did not differ from each other.

Parameter	ΔBASRI hip=0 n=39	ΔBASRI hip >0 n = 23	p
Sex (m/w), n	15/24	17/6	<0,05*
Duration of the disease months., Me [25; 75 percentile]	22 [7;36]	24 [18,8;24,8]	>0,05
Age, years, Me [25; 75 percentile]	29 [25,5;32,5]	26,5 [23,2;28,7]	<0,05*
BASDAI, Me [25; 75 percentile]	3,6 [2,1;5,2]	3,45 [1,1;5,2]	>0,05
BASFI, Me [25; 75 percentile]	1,5 [0,5;2,8]	0,7 [0,3;2,4]	>0,05
ASDAS (CRP), Me [25; 75 percentile]	2,5 [1,6;3,35]	2,4 [1,25;3,45]	>0,05
ESR, mm/h, Me [25; 75 percentile]	8 [6;22]	10 [5;28,75]	>0,05
CRP, mg/L, Me [25; 75 percentile]	5,3 [1,3;24,5]	5,2 [1,1; 23,4]	>0,05
Peripheral Arthritis, n%	12 (32%)	5 (22%)	>0,05

Conclusion: it has been shown that in some patients with axSpA already in the first years of the disease, radiological signs of HJ destruction are detected. The progression of coxitis was not dependent on the activity of the disease and was more often detected in men than in women.

Disclosure of Interests: Ekaterina Agafonova: None declared, Tatiana Dubinina Speakers bureau: Novartis, BIOCAD, MSD, Pfaizer, Abbvie, UCB, Shandor Erdes: None declared, Daria Rumiantceva: None declared

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AB1074 FEATURES OF COMBINED USE OF BIOMARKERS AND VISUALIZATION METHODS FOR DIAGNOSIS OF HEART DAMAGE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: In rheumatoid arthritis (RA), the endocardium is involved in the inflammatory process, which is caused by immunopathogenetic mechanisms involving CD4 +, T-cells and proinflammatory macrophages. Minor changes in the cardiovascular system can be successfully detected by ultrasound in patients with RA.

Objectives: to improve the quality of non-invasive diagnostics of heart disease in patients with RA.

Methods: 57 patients with RA were under observation: 7 men and 50 women aged from 26 to 70 years; mean age 50.45 ± 10.12 years; activity (according to DAS28) was low for 3.5%, medium for 86%, and high for 10.5%. Immunological examination included determination of serum IgM-RF, CRP, antibodies to cyclic citrulline peptide (anti-CCP), antibodies to modified vimentin (anti-MCV), antibodies to antigen RA33, levels of angiopoietin-like proteins 3 (ANGPTL3) and 4 (ANGPTL4) types (classical ELISA test), as well as the detection of IgG antibodies to 5'-nucleotidase (5'-NT) and xanthine oxidase (XO) (modified ELISA test). Data from ultrasound, magnetic resonance (MRT) and computer (CT) tomography were used in assessing the state of the heart structures.

Results: The pathology of cardiovascular system was diagnosed in 28 (49.1%) patients with RA. Signs of the heart damage were noted in 33.3% of cases (pericarditis and valvular heart disease were most often detected). In groups of patients with RA with elevated levels of antibodies to 5'-NT and XO (compared with RA patients with normal parameters), there was a significantly more frequent heart damage (for antibodies to 5'-NT: $\chi^2 = 3.8$, p = 0.047; for antibodies to XO: $\chi^2 = 3.92$, p = 0.041). It was discovered that in all patients with an increased level of antibodies to XO, one of the lesions of the heart valvular apparatus of varying severity was noted. According to ultrasound data (usually confirmed by CT and / or MRT), signs of valvular dysfunction were found in 21 (36.8%) patients with RA. The high frequency of mitral prolapse (28.6%) may be associated with the presence of a chronic inflammatory process that is able to accelerate the development of atherosclerosis and heart disease in RA patients. A tendency to an increase in the prevalence of mitral prolapse in patients with a longer duration of the disease (p = 0.062) and with high levels of serum ANGPTL4 (p = 0.058) was found.

One of the main factors leading to the development of vascular pathology in RA is the accumulation of reactive oxygen intermediate. Antibodies to XO can affect the biochemical activity of the enzyme in the serum of patients with RA, stimulating the increased formation of O-form XO, which has a pronounced prooxidant effect (especially to lipids). ANGPTL4, acting as a potent inhibitor of endothelial lipoprotein lipase, can suppress the release of non-esterified fatty acids and their transfer to the heart muscle.

Conclusion: To identify subclinical signs of involvement of cardiovascular system in the pathological process in the early asymptomatic stages of RA, it is advisable to use imaging techniques in combination with immunological markers of heart damage, which can be especially useful for screening, diagnostic evaluation and determining cardiovascular risk.

Disclosure of Interests: None declared

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AB1075 PRESENCE POWER DOPPLER ULTRASOUND AS A PREDICTOR OF RADIOGRAPHIC DAMAGE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease that leads to destructive changes and dysfunction of the joints. Ultrasound (US) is used in current practice as an early diagnostic method for detecting structural damage to articular surfaces. US changes in early RA are considered as one of the ways of predicting disease outcomes.

Objectives: to detect power doppler (PD) contribution in evaluation of radiographic RA progression in long term.

Methods: 85 RA pts, mean age 53,0 [44,0; 61,0] yrs, mean disease duration 8 [4; 24] months were treated by Treat-To-Target concept. After first year of therapy management was following real clinical practice rules until the termination of the study (4 years FUP). The wrist, MCP2 and MCP3, PIP2, PIP3, MTP2 and MTP5 joints of the clinically dominant side were examined by US (GS and PD). Clinical, laboratory parameters and US examination was performed at baseline, at Mo 3, 6, 9 and 12. The X-ray was conducted before treatment and in the end of the study. Structural damage progression was evaluated by change in the Sharp van der Heijde score (ΔSHS) between baseline and 4 year.

We categorized pts into 5 groups according to the occurrence of positive PD: 1) without PD throughout the observational period [the negative (N)], 2) positive PD limited to the period from the baseline to Mo 3 [the therapeutic response (R)], 3) positive PD limited to the period from the baseline to Mo 6-9 [the therapeutic late-response (LR)], 4) intermittent occurrence of PD in the observational period [the intermittently positive (IP)] and 5) with persistent positive PD throughout the observational period [the persistently positive (PP)].

Results: 80% of pts had PD synovitis at baseline. PD-synovitis dropped from 2 [1,0; 6,0] to 0 [0,0; 2,0] scores at Mo 12. RA progression by 4 years FUP was identified in 13% of pts. The X-ray erosion score at 4 years FUP in these groups – N, R, LR, IP and PP - were dependent by PD from baseline to Mo 12 (mean level 1 [0; 2]; 2 [0; 4], 3 [0; 5], 1 [0; 2] and 4,5 [1; 10] respectively), but statistically significant differences were found between N and PP groups.

Cox multivariate analysis identified that presence PD-synovitis at baseline was associated with risk of radiographic progression at 4 years (HR 3,68 95% CI 1,03 – 13,15, p = 0,045).
Conclusion: Thus, PD-synovitis has a prognostic value for increasing destructive radiographic changes.
References: no
Disclosure of Interests: None declared
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AB1076 COLOR DOPPLER HIGH- FREQUENCY ULTRASOUND OF DIGITAL ARTERIES IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) can lead to vascular complications such as digital ulcers or pitting scars (DU/PS). These changes develop in most patients with SSc and exacerbate their condition. However, there are no methods for dynamic assessment of the vascular involvement. The dynamics of capillaroscopic changes is very slow.
Objectives: The aim of the study was to compare blood flow parameters of digital arteries in SSc patients and healthy individuals and to compare with nailfold capillaroscopy and clinical signs of ischemia (DU/PS).
Methods: 32 SSc patients, mean age 49,5 [42,0; 59,0] yrs and 26 'healthy', mean age 43,5 [33,0; 57,0], were included. Groups of patients differed by gender and age. The exclusion criterion was the presence of obliterating vascular disease of the upper extremities. An Esaote MyLab Twice US system with 22 MHz linear probe was used. A total of SSc patients and controls underwent Color Doppler ultrasonography (CDUS) of 376 (256+208) digital arteries to compare blood flow velocity, resistive indices (RIs) and presence of occlusion. Nailfold capillaroscopy, clinical and laboratory data were also evaluated.
Results: In digital arteries, pulsatility index (PI), peak systolic velocity (PSV) and end-diastolic velocity (EDV) were significantly lower and RI higher in SSc patients compared with controls (PSV: 13,28 [9,88; 16,7] vs17,45 [12,65; 22,5] cm/s, p=0,008; EDV: 2,68 [1,78, 4,05] vs 6,37 [4,75; 8,5] cm/s, p=0,000; RI: 0,78 [0,69; 0,81] vs 0,68 [0,59; 0,74], p=0,005; PI: 1,73 [1,32; 2,19] vs 1,22 [0,99; 1,55], p=0,002).
We did not find any correlation between two methods. Also, we did not reveal any correlation between DU/PS, clinical, laboratory data and CDUS, but we found relationship between DU/PS and avascular areas or capillaroscopic findings (r= 0,37, p=0,045 and r= 0,40, p=0,03 correspondingly).
Conclusion: Blood flow is significantly decreased in digital arteries in SSc, but clinical features of vasculopathy depend on microcirculatory disorders. It is important to continue research to find methods for dynamic evaluation of microcirculatory changes.
References: no
Disclosure of Interests: None declared
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AB1077 VALIDATION OF A SIMPLIFIED SPANISH TOOL FOR SEMI-AUTOMATIC QUANTIFICATION OF SACROILIAC INFLAMMATION BY MAGNETIC RESONANCE IN SPONDYLOARTHRITIS (S- SCAISS).

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Background: With the objective to improve quantification of sacroiliitis maintaining a practical perspective, our group developed SCAISS, a semi-automated method to measure bone marrow edema (BME) in MR images from sacroiliac (SI) joints, combining semi-axial and semi-coronal slices [1]. The 2009 ASAS definition of active sacroiliitis was based on standard semi-coronal slices only, perpendicular semi-axial slices being considered but optional [2]. We hypothesized a simplified SCAISS (s- SCAISS) method using only semi-coronal slices.
Objectives: To analyze the validity and reliability and feasibility of a simplified Spanish tool for semi-automatic quantification of sacroiliac inflammation by magnetic resonance in spondyloarthritis (s- SCAISS) using a semi-coronal scan instead of combining semi-axial and semi-coronal slices.
Methods: The s- SCAISS was designed as an image-processing software. We performed the following analysis: (1) three readers evaluated SI images of 23 patients with axial SpA and various levels of BME severity with the s-SCAISS and SCAISS, and two non-automated methods, SPARCC and Berlin; (2) 20 readers evaluated 12 patients images, also with the three methods. Convergent validity, reliability and feasibility were estimated.
Results: The interobserver reliability (ICC and 95% CI) in the three observers' study was: s-SCAISS = 0.69 (0.490–0.845); SCAISS= 0.770 (0.580–0.889); Berlin = 0.725 (0.537–0.860); and SPARCC = 0.824 (0.671–0.916). In the 20 observers' study, ICC was: s- SCAISS = 0.66 (0.478–0.863); SCAISS = 0.801 (0.653–0.927); Berlin = 0.702 (0.518–0.882); and SPARCC = 0.790 (0.623–0.923). Spearman correlation coefficient between s- SCAISS _BERLIN was r= 0.712 and s- SCAISS_ SPARCC was r= 0.779 and s- SCAISS _SCAISS was r= 0.90. Similar results showed SCAISS BERLIN and SCAISS_ SPARCC (r= 0.729 and 0.840), respectively.
Conclusion: The simplified SCAISS (s-SCAISS) using only semi-coronal slice permits a valid, reliable, and fast calculation of overall BME lesion at the SI joint.
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, Pedro Zarco-Montejo Speakers bureau: Abbvie, MSD, Novartis, Pfizer., Angel Bueno: None declared, Luis Miguel Molinero: None declared
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AB1078 USE OF MYOSITIS SPECIFIC AUTOANTIBODIES TEST ACROSS A LARGE NHS HOSPITAL TRUST

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Background: The immunology laboratory at Barts Health supports a large clinical myopathy service, providing blood tests for myositis-specific autoantibodies (MSA) by a commercial line immunoblot panel for Jo1, PL7, PL12, SRP, Mi2, Ku, PM-Scl and Scl-70.
As Idiopathic Inflammatory Myositis (IIM) disease subtype definitions have evolved from the 1975 Bohan & Peter criteria, the discovery of new antibodies has proven useful in the hands of neuromuscular clinicians whose patients have a high pre-test probability of disease. Ready availability of the test has led to increased demand from:
1. Respiratory physicians with patients with severe Interstitial Lung Disease (ILD) which *can* be a symptom of some IIMs.
2. The connective tissue disease (CTD) screening section of the laboratory in which many patients are screened for antinuclear antibodies (ANA), which occasionally produces a pattern that *may* be associated with an MSA.

Objectives:
1. Determine the frequency of MSA requests from different departments.
2. To investigate the possibility of rejecting requests for MSAs at the laboratory in the absence of an elevated creatine kinase (CK), a hallmark of muscle damage associated with myositis (1).

Methods: MSA were measured by a commercial line blot (Bluediver) which included Jo-1, PL-7, PL-12, Mi-2, Ku, SRP-54 and PM-Scl-100. Demographics and results for all MSA requested between September 2017 and November 2019 were pulled from laboratory records, together with CK results (if performed). CK was interpreted as low, normal or elevated according to reference ranges of 25-200 U/L (female) or 40-320 U/L (male).

Results: 597 tests were performed between 2017 and 2019. In total 59/597 (10%) were positive for the audited antibodies (Table 1). General Practitioner (GP) requests accounted for 41/597 (6.9%) tests, internal 464/597 (78%) and external 82/597 (14%). External requests were the most frequently positive at 10/82 (12%), internal requests 46/464 (10%), and GP requests only 3/41 (7%) of the time. Of all internal requesting sources, Respiratory accounted for the largest number at 108/597 (18%), followed by neurology with 85/597 (14%) (Figure 1). GPs constituted the 4th largest source of requests.

Table 1.

	Positive on polymyositis screen	% positivity
All tests	597	
Total	59	9.9%
Jo-1	4	0.7%
PL-7	2	0.3%
PL-12	5	0.8%
SRP-54	10	1.7%
Mi-2	4	0.7%
Ku	3	0.5%
PM-Scl 100	25	4.2%
Scl-70	7	1.2%

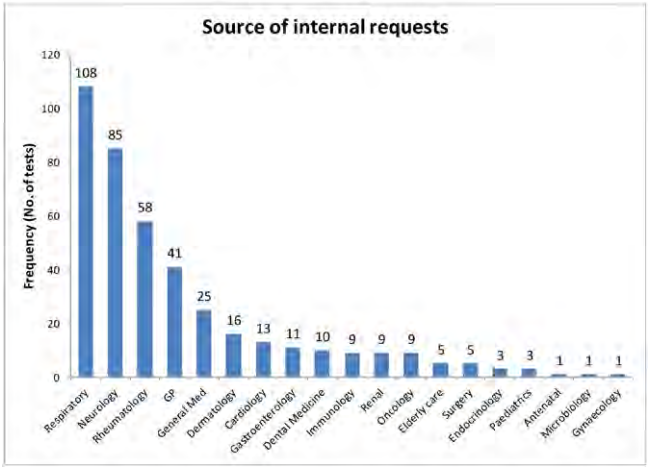


Figure 1.

MSAs had an associated CK result in 75% of internal and 12% of GP requests. A cohort of 17 patients had positive MSAs (3 x SRP, 1 x PL-7, 1 x Jo-1, 2 x Mi-2, 1 x Ku, 8 x PM-Scl100 and 1 x Scl-70) with normal CK.

Of the 41 GP requests, MSA had been requested by the lab on the basis of ANA pattern for 33 (80%) of them, 3 of which were positive (2 x Scl-70, 1 x SRP-54).

Conclusion: Demand for MSA from the Respiratory department (screening for ILD) currently exceeds demand from Neurology and from Rheumatology. In the GP cohort, 33 requests (80% of GPs, 5% of all requests) were generated by the laboratory.

A cohort of patients with normal CK results had a positive MSA, implying CK alone cannot be used to limit test access. Interestingly, 10 positive results had no CK requested implying they were not being investigated for myositis.

Further work is needed to determine the specificity and sensitivity of these antibodies for patients with clinically defined myositis, and the appropriateness of allowing the test to be applied in the absence of any clinical evidence of IIM.

The findings of this audit need to be further extended to look at other myositis including other anti-synthetases, HMGCoAR, MDA5, TIF-1γ, NPX-2.

References:

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AB1079 CORRELATION OF OPTICAL SPECTRAL TRANSMISSION IMAGING WITH ULTRASOUND AND DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Optical spectral transmission imaging (OST) is a new imaging method that measures inflammation in the hands of rheumatoid arthritis (RA) patients. OST might be used to assess disease activity instead of disease activity score 28 (DAS28) or ultrasonography (US), with the advantage of OST that it is fast and not operator dependent. Detection of joint inflammation with OST and with US as reference, has provided varying outcomes with ROC AUCs ranging from 0.69-0.88 [1-3]. Further evaluation of the currently available OST device (HandScan) is needed in other RA cohorts.

Objectives: To assess the correlation of OST measurement with US and disease activity, and to compare OST measurements of RA patients with healthy controls.

Methods: OST was done in 24 consecutive RA patients with active disease and 37 age and sex matched healthy controls using the HandScan device from Hemics, the Netherlands. The HandScan calculates OST values for each bilateral wrist, MCP and PIP joint, ranging from 0 to 3. OST total score is then composed of the sum of the 22 OST joint scores and therefore ranges from 0 to 66. US was performed in the same joints as OST and semi-quantitatively scored on a scale of 0 to 3 for grey-scale (GS) synovitis and power Doppler (PD) signal individually. A separate total score for GS synovitis and PD was calculated by summation of the individual joint US scores. Joint scores (at joint level) and total scores (at patient level) were used in separate analyses. Additionally, we measured swollen joint count 28 (SJC28), tender joint count 28 (TJC28), DAS28, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). For all statistical analyses, the non-parametric variant was used.

Results: Patient level

Median OST total score of RA patients was 16.88 (IQR 12.68-19.72). This was significantly higher than healthy controls (OST total score 12.06, IQR 10.32-14.93; p=0.0002).

OST total score of RA patients (patient level) did not significantly correlate with both US total scores (GS synovitis 0.37, p=0.08; PD 0.21, p=0.33), nor with disease activity parameters (DAS28 0.22, p=0.31; SJC28 0.32, p=0.12; TJC28 0.28, p=0.19; ESR -0.02, p=0.93; CRP 0.05, p=0.81).

Joint level

At joint level, there was a significant correlation for almost all joints with GS synovitis on US (table 2). For PD too few joints scored above 0 to allow for statistical comparisons, however for all joints median OST values were higher in PD positive joints than PD negative joints (differences in median OST values ranging from 0.2-0.5).

Table 1. Correlation of individual joint OST values and GS synovitis

	GS synovitis	
	Spearman r	p-value
Wrist	0.36	0.02
MCP1	0.27	0.06
MCP2	0.44	0.002
MCP3	0.40	0.005
MCP4	0.27	0.07
MCP5	0.39	0.006
IP1	0.35	0.01
PIP2	0.30	0.04
PIP3	0.13	0.37
PIP4	0.29	0.04
PIP5	0.37	0.01

Conclusion: OST total score was higher for RA than healthy controls. At patient level, OST total score did not correlate with other disease activity measures. At joint level, GS synovitis scores correlated with OST joint values for almost all joints. In addition, higher OST values were found in PD positive joints but frequency of PD positivity was too low to allow statistical comparisons. The results of this small cohort of new RA patients do not yet demonstrate additional value as compared to US and clinical examination to detection of joint inflammation at cross-sectional assessment, although fast and non-operator dependent OST assessment may also be weighed in further evaluation for clinical use.

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[3] Krabbe et al. 2016 ARD 75(3):632-3

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AB1080

OPTICAL SPECTRAL TRANSMISSION IMAGING SCORES DECREASE AFTER ONE MONTH OF BIOLOGICAL THERAPY, ESPECIALLY IN RHEUMATOID ARTHRITIS PATIENTS WHO RESPOND TO THERAPY

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Background: Optical spectral transmission imaging (OST) is a new imaging method that measures inflammation in the hands of rheumatoid arthritis (RA) patients. OST might be used to assess disease activity instead of disease activity score 28 (DAS28) or ultrasonography (US). The advantage of OST is that it is fast and not operator dependent. Up to now OST has only been investigated cross-sectionally and it is unknown if and to what extent OST can detect inflammatory changes due to anti-inflammatory treatment for RA.

Objectives: To compare OST measurements before and after 1 month of biological treatment for RA and to compare these OST changes with changes on US and disease activity.

Methods: The HandScan device from Hemics, the Netherlands, was used to measure OST scores for 13 RA patients before and after 1 month of anti-inflammatory therapy. Treatment included tumor necrosis factor inhibitor (n=10), tocilizumab (n=2) and tofacitinib (n=1). OST scores range from 0-66 (one score for both hands) and are based on bilateral wrist, MCP and PIP joints. US was performed in the same joints as OST and semi-quantitatively scored on a scale of 0-3 for grey-scale (GS) synovitis and power Doppler (PD) signal. Joint scores of GS synovitis or PD were summed, resulting is a total GS synovitis score and a total PD score, both also ranging from 0-66. Furthermore, tender joint count 28 (TJC28), swollen joint count 28 (SJC28), DAS28, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were determined. Response to therapy was defined as achieving the minimal clinically interesting improvement of DAS28 (DAS28 difference after 1 month > -1) as proposed by Ward et al. [1]

Results: Baseline OST was 17.73 ± 6.10 and this significantly decreased to 16.01 ± 6.68 (difference -1.71, 95%CI 0.05-3.38, p=0.045) after 1 month of therapy. This decrease was only present in patients who responded to therapy (n=8; OST decreased from 17.24 ± 5.98 to 14.26 ± 5.65, p=0.01) and not in non-responders (n=5; OST increased from 18.52 ± 6.90 to 18.83 ± 7.87, p=0.03).

In the total group, also DAS28 (difference -1.59, 95%CI 0.74-2.45, p=0.002), SJC28 (difference 4.62, 95%CI 1.50-7.73, p=0.007), ESR (Wilcoxon Rank p=0.008) and CRP (Wilcoxon Rank p=0.03) significantly decreased after 1 month of therapy, but TJC28 did not (difference 2.62, 95%CI -2.7-7.91, p=0.30).

OST change after 1 month of therapy significantly correlated with TCJ28 change (table 1). For GS synovitis the correlation coefficient nearly reached statistical significance. Changes in all other disease activity parameters were not correlated with OST change.

Table 1. Correlation of change in OST measurement with change in disease activity after 1 months of anti-inflammatory therapy

	Spearman r	p-value
Total GS synovitis	0.54	0.06
Total PD	0.22	0.47
DAS28	0.35	0.25
SJC28	0.29	0.33
TJC28	0.63	0.02
ESR	-0.42	0.15
CRP	-0.23	0.45

Conclusion: OST scores significantly decreased after 1 month of anti-inflammatory therapy and only in the RA group that responded well to this therapy. This indicates that OST is capable of detecting therapy induced inflammatory changes in the hands of RA patients. Larger studies are needed to further assess the monitoring value of OST for therapy efficacy in RA patients.

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AB1081

BLOOD PRESSURE, BMI AND SEX AFFECT OPTICAL SPECTRAL TRANSMISSION IMAGING MEASUREMENTS OF THE HANDS

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Background: Optical spectral transmission imaging (OST) is a new imaging method designed to measure inflammation in the hands of rheumatoid arthritis (RA) patients. The device uses a pressure cuff to occlude venous blood flow, resulting in an increased blood pool in the hands of the patient. In inflamed joints transmission of light through this blood pool is altered due to higher blood content, lower oxygenation and stronger hemodynamics at the location of inflammation [1]. However, altered hemodynamics not related to inflammatory arthritis might also influence OST measurements.

Objectives: In this study we investigated whether hemodynamic and other cardiovascular parameters affect OST measurements in healthy participants.

Methods: OST measurement was done in 37 healthy participants using the HandScan device from Hemics, the Netherlands. Carotid intima media thickness (IMT), pulse wave velocity (PWV) and augmentation index (AIx) were measured with ultrasound and SphygmoCor tonometry. Age, sex, diastolic and systolic blood pressure, pulse, hypertension (defined as systolic blood pressure >140 mmHg or diastolic blood pressure > 90 mmHg or antihypertensive treatment), total cholesterol, HDL, LDL, total/HDL cholesterol ratio, body mass index (BMI), European SCORE risk assessment, smoking status, cardiovascular history and medication use were collected during the same visit. Associations were investigated using univariate linear regression and multivariate regression adjusting for age and sex.

Results: Participants were 53 ± 8 years old and 65% was female. Systolic and diastolic blood pressure was 129 ± 19 mmHg and 80 ± 9 mmHg respectively and 22% used antihypertensive treatment, 8% an anticoagulant and 11% a statin. In total 38% had hypertension and 8% had a history of cardiovascular disease. Mean OST value was 12.69 ± 3.47 and all values were between 5.00 and 20.78. Cardiovascular and hemodynamic parameters that were associated with higher OST measurement were: hypertension (14.18 ± 1.12 versus 11.79 ± 0.69), systolic and diastole blood pressure, BMI and European SCORE (table 1). Also, male sex was associated with a higher OST with and without adjustment for age (15.05 ± 1.04 versus 11.41 ± 0.62 for females).

Table 1. Cardiovascular and hemodynamic parameters associated with higher OST measurement

	Univariate				Adjusted for age and sex			
	B	95%CI		p	B	95%CI		p
Hypertension (y/n)	2.39	0.12	4.67	0.04	2.41	0.37	4.45	0.02
Systolic blood pressure	0.08	0.03	0.14	0.005	0.07	0.02	0.12	0.01
Diastolic blood pressure	0.20	0.08	0.32	0.001	0.19	0.09	0.29	0.001
BMI	0.24	-0.01	0.48	0.06	0.26	0.05	0.47	0.02
Sex (male/female)*	3.67	1.56	5.78	0.001	3.54	1.29	5.79	0.003
European SCORE**	1.24	0.09	2.39	0.04	n/a			

*Adjusted for age only, **Not adjusted because age and sex are included in the European SCORE

Other parameters (age, cholesterol, pulse, IMT, having carotid plaque, PWV, AI, cardiovascular history, smoking status and statin, antihypertensive drug and/or anticoagulant use) were not associated with the OST measurement (p>0.13, data not shown)

Excluding the 5 (14%) participants with hand osteoarthritis showed comparable results, except for BMI and hypertension. BMI was also significantly associated with OST in the univariate analysis (B 0.24, 95%CI 0.01-0.47, p=0.039), while hypertension lost its statistical significance (uni B 1.74, 95%CI -0.69-4.17, p=0.15; multi B 1.44, 95%CI -0.61-3.48, p=0.16).

Conclusion: High blood pressure, BMI, male sex and European SCORE are associated with increased OST values in healthy participants. This indicates that differences in OST measurements of RA patients might not only reflect inflammatory burden but is also dependent on sex, blood pressure and body composition. This should be taken into account when using optical spectral transmission imaging for the assessment of inflammation in RA patients.

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AB1082

INFLUENCE OF THE VARIATION OF THE OPERATOR, PATIENT POSITION AND DEVICE ON THE MEASUREMENT PERFORMANCE OF RADIOFREQUENCY ECHOGRAPHIC MULTI SPECTROMETRY (REMS)

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Background: The monitoring of bone mineral density (BMD) is a key aspect for patients undergoing pharmacological treatments that might cause BMD changes at non-physiological rates. At present, the short-term follow-up of patients under treatment in terms of BMD change with time remains an unmet clinical need, since the current techniques, including the gold standard dual X-ray absorptiometry (DXA), require at least 1 year between two consecutive measurements [1]. Therefore, an effective strategy for the assessment of BMD should guarantee high accuracy, precision and repeatability of the measurements.

Objectives: The aim is to assess the influence of the variation 1) in patient position, 2) operator (both intra- and inter-) and 3) device on the REMS performance at lumbar spine and femoral neck.

Methods: 210 women were enrolled, divided in 7 groups of 30-patient each for the assessment of the parameters of interest, i.e. inter-device, intra- and inter-operator repeatability for lumbar spine scans and inter-patient position, inter-device, intra- and inter-operator repeatability for femoral neck scans.

All patients underwent 2 REMS scans at lumbar spine or femoral neck, performed by the same operator or by 2 different operators or by the same operator using 2 different devices or in different patient position (i.e. supine without constraints or with a constrained 25°-rotation of the leg). The percentage coefficient of variation (CV%) with 95% confidence interval and least significant change for a 95% confidence level (LSC) have been calculated.

Results: For lumbar spine, intra-operator repeatability resulted in CV%=0.37% (95%CI: 0.26%-0.48%), with LSC=1.02%, inter-operator repeatability resulted in CV%=0.55% (95% CI: 0.42%-0.68%), with LSC=1.52%, inter-device repeatability resulted in CV%=0.53% (95% CI: 0.40%-0.66%), with LSC=1.47%.

For femoral neck, intra-operator repeatability resulted in CV%=0.33% (95%CI: 0.23%-0.43%), with LSC=0.91%, inter-operator repeatability resulted in CV%=0.47% (95% CI: 0.35%-0.59%), with LSC=1.30%, inter-device repeatability resulted in CV%=0.42% (95% CI: 0.30%-0.51%), with LSC=1.16%, inter-patient position repeatability resulted in CV%=0.24% (95% CI: 0.18%-0.30%), with LSC=0.66%.

Conclusion: REMS densitometry is highly precise for both anatomical sites, showing high performance in repeatability. These results suggest that REMS might be a suitable technology for short-term monitoring. Moreover, thanks to its ionizing radiation-free approach, it might be applied for population mass investigations and prevention programs also in paediatric patients and pregnant women.

References: **Note:** Carla Caffarelli, Giovanni Adami[§], Giovanni Arioli[§], Gerolamo Bianchi[§], Maria Luisa Brandi[§], Sergio Casciaro[§], Luisella Cianferotti[§], Delia Ciardo[§], Francesco Conversano[§], Davide Gatti[§], Giuseppe Girasole[§], Monica Manfredini[§], Maurizio Muratore[§], Paola Pisani[§], Eugenio Quarta[§], Laura Quarta[§], Stefano Gonnelli

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AB1083

CURRENT PRACTICE AND OPINIONS ON IMAGING-GUIDED INTERVENTIONAL PROCEDURES IN RHEUMATIC AND MUSCULOSKELETAL DISEASES: INTERIM RESULTS OF A MULTINATIONAL MULTIDISCIPLINARY SURVEY TO INFORM EULAR POINTS TO CONSIDER

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Background: maging is widely used for diagnostic purposes in patients with rheumatic and musculoskeletal diseases (RMDs). In recent years, it is increasingly used also to guide interventional procedures. However, the extent of imaging application for this purpose as well as the different technical standards employed across Europe are not known.

Objectives: To learn how much imaging is used for interventional procedures in RMDs. To explore the technical standards employed in different settings and how important they are rated by users.

Methods: As part of the work of a multidisciplinary EULAR Task Force to develop recommendations for the use of imaging to guide interventional procedures in patients with RMDs, a survey was developed. The survey explored aspects of different interventional procedures (e.g. joint aspiration/injection) such as the use of imaging guide and the technical standards. Respondents provided also a 0-10 rating of how important they considered the same conditions/items with regard to each procedure. The survey was distributed to: rheumatologists across Europe, USA, Central America, South America, Asia and Pacific Area, HPs across Europe, European and American associations of other specialities (e.g. radiology, anaesthesiology). The survey was launched in December 2019. Interim results after 4 weeks are presented.

Results: 200 responses from 36 countries were collected. The respondents were mainly rheumatologists (90%) (Figure 1). 90% of respondents performed interventional procedures related to RMDs and of these, 76% use imaging guide. Ultrasonography (US) is the most commonly used technique (96%) followed by X-ray/fluoroscopy (13%). Among respondents using imaging guide, 60% received training on both imaging and imaging-guided procedures, 20% only on imaging and 16% no training. 49% of respondents perform the whole procedure using direct image guidance, 21% use imaging to find the appropriate anatomical landmark and then perform the procedure blindly. Air and contrast agent to control needle placement are rarely used (≤20%). Respondents provided also a rating (0-10) of how important they considered different technical conditions/items for each procedure and an estimate on a Likert scale of how often they used them for each of the procedures (Figure 1 shows an example). In most cases respondents use always/most of the times the conditions/items that they considered important. Discrepancies were mainly due to barriers at their own center.

Conclusion: Imaging, mainly US, is widely used to guide interventional procedures. However, training is not homogeneous and the use of imaging guide as well as technical conditions are based on the operator's opinion/experience. This survey will inform the EULAR points to consider for the use of imaging to guide interventional procedures in patients with RMDs.

Table 1. Characteristics of respondents (n=200)

	N	%
Age		
≤ 30	38	19
31 –35	56	28
36 – 39	50	25
40 - 49	33	16.5
≥ 50	23	11.5
Gender		
Female	89	44.5
Male	111	55.5
Specialty/Position		
Rheumatology	180	90
Radiology	11	5
Physical medicine and rehabilitation	3	1.5
Pediatrics	4	2
Non-clinical researcher	3	1.5
Health professionals	3	1.5
Other	3	1.5

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Carlo Alberto Scirè: None declared, Alessia Alunno: None declared, Xenofon Baraliakos Grant/research support from: Grant/research support from: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB and Werfen, Consultant of: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB and Werfen, Speakers bureau: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB and Werfen, Christian Dejaco: None declared

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AB1084 A SYSTEMATIC REVIEW OF THE ABILITY OF WHOLE BODY MRI TO ASSESS DISEASE ACTIVITY AND TREATMENT RESPONSE IN INFLAMMATORY ARTHRITIS

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Background: Whole body MRI (WBMRI) is an imaging technique that allows the assessment of the spine and peripheral joints in patients with inflammatory arthritis (IA) in a single examination. Depending on the protocol, it can potentially identify synovitis, enthesitis, spondyloarthritis and chronic structural changes.
Objectives: To evaluate the performance of WBMRI in patients with IA for detecting inflammation compared with clinical assessments and to show changes in response to treatment.
Methods: We conducted a systematic search of the electronic databases MEDLINE, EMBASE and Cochrane Library. Two authors selected independently the eligible studies, extracted the predefined data and assessed the quality using the QUADAS2 tool. Studies that reported a)disease activity scores, b)patient or physician reported outcomes or c)results from other imaging tests in IA patients who underwent WBMRI were included.
Results: Fourteen studies out of 471 met our inclusion criteria. The majority of the studies were performed in Spondyloarthritis [SpA] (n=9), followed by Rheumatoid Arthritis [RA] (n=4) and Psoriatic Arthritis [PsA] patients (n=3). Nine studies provided clinical and MRI outcome measures. There was great heterogeneity in the quality of studies, disease specific outcomes reported and methodology used to compare with MRI findings. One study documented low correlation between 28 swollen/tender joint count and MRI bone marrow oedema (BME)/synovitis in RA patients, whereas another reported that 31% of MRI negative joints (other than hand joints) exhibited tenderness. In PsA, one study demonstrated correlation between 28 swollen joint count and BME (r=0.54,p=0.03). Superiority of WBMRI in the detection of synovitis and enthesitis over clinical examination was documented in two studies with SpA patients. A third study in SpA showed a ranging agreement of 49 to 100% between clinical and WBMRI enthesitis.
Treatment response to biologics was assessed by WBMRI in 7 studies (5 in SpA, 2 in RA). In RA, one study showed numerical (but not statistically significant) reduction of WBMRI joint count at week 16 and 52 of Adalimumab treatment, whereas the reduction was statistically significant for the subset of patients achieving good EULAR response at week 16. The other study demonstrated a reduction in WBMRI synovitis and bone oedema scores after 1 year of anti-TNF or Tocilizumab treatment (median DAS28 score decreased from 5.1 to 2.1). A multicentre open label study reported a reduction in the number of MRI enthesitis lesions, spinal and sacroiliac joint scores at week 48, year 2 and 3 of Etanercept treatment in SpA patients. The mean BASDAI score decreased from 5.4 at baseline to 1.5 at year 2 and 2.2 at year 3. Improvement in WBMRI scores in SpA was also documented in one Adalimumab and one further Etanercept study.
Conclusion: There was a variable level of correlation between clinical and WBMRI outcome measures across the included studies. The clinical significance of inflammation detected by WBMRI in some studies remains unclear. Many of the devised WBMRI scores appear to decrease after biologic treatment. Further studies are needed to determine the accuracy of WBMRI in detecting inflammation and its potential utility for clinical practice.

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AB1085 ASSESSMENT OF DIAGNOSTIC DELAY IN PATIENTS AFFECTED BY ENTEROPATHIC SPONDYLOARTHRITIS: A CROSS-SECTIONAL STUDY

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Background: Diagnostic delay of spondyloarthritis (SpA) has been established even in combination with inflammatory bowel disease and may contribute to radiographic progression and disability.
Objectives: We aimed to evaluate diagnostic delay in enteropathic SpA (eSpA) and explore associated demographic, clinical, and radiographic characteristics.
Methods: We analysed consecutive eSpA patients referred to the combined gastro-rheumatologic clinic of the University of Rome Tor Vergata. Diagnostic delay was defined as the time interval from the date of first symptoms to the date of diagnosis. Conventional radiography (CR) and magnetic resonance images (MRI) of sacroiliac (SI) joints and spine were performed in axial (ax)SpA patient and examined by two independent radiologists. MRI were assessed for the presence of active/chronic inflammatory lesions, disease activity by ASDAS and inflammatory markers. Statistical analyses were performed using Mann-Whitney, chi square/Fisher tests and covariance analysis (SPSS software).
Results: 190 eSpA patients (124 female, mean age 47.5±12.8 years, disease duration 72±67.4 months, 73 UC/117 CD; 118 peripheral SpA, 72 axSpA including 44 non radiographic (nr)-axSpA) were evaluated. Axial eSpA patients had a higher prevalence of men sex (p<0.0001), HLA-B27 positivity (p=0.004), uveitis (p=0.01) and pancolitis (p<0.006) compared with peripheral eSpA. AxeSpA patients displayed higher ESR, ASDAS, and VAS pain compared with peripheral ESpA (p=0.0006, p=0.001, p=0.019, respectively). A higher prevalence of csDMARDs was detected in peripheral eSpA compared with axSpA (p=0.002) while treatment with cs and bDMARDs was similar in rad-axSpA and nr-axSpA patients.
Median diagnostic delay in eSpA was 48 months (IQR 6-77) with no difference between axial and peripheral patients. Rad-ax-SpA patients displayed a higher diagnostic delay compared with nr-axSpA (median/IQR 36/17-129 vs 31/10-57 months, p=0.03). Patients with rad-axSpA were older and with longer disease duration than patients with nr-axSpA (p=0.005 and p=0.019). Low education status and high rate of employment were found in rad-axSpA compared with nr-axSpA (p=0.003 and p=0.03, respectively).
Rad-axSpA patients with sclerosis, syndesmophytes and bridge at CR had a higher diagnostic delay than those without lesions (p=0.03, p=0.043, p<0.0001, Fig. 1A-C). Men showed a higher prevalence of spine damage lesions than women as sclerosis (p=0.02), squaring (p=0.0006), syndesmophytes (p=0.0028) and bridges (p=0.007). Longer disease duration was detected in patients with radiographic damage as bridge (p<0.0001) and sacroiliitis grade 3 (p=0.04). On MRI, SI bone oedema was associated with reduced diagnostic delay (p=0.04) while bone erosions was associated with higher diagnostic delay (p=0.002) compared with that in patients without these lesions (Fig. 1D-E). Rad-axSpA women had a higher prevalence of SI damage lesions at MRI than men (p=0.001). Patients with psoriasis displayed a higher diagnostic delay compared to those without skin involvement (p=0.004).

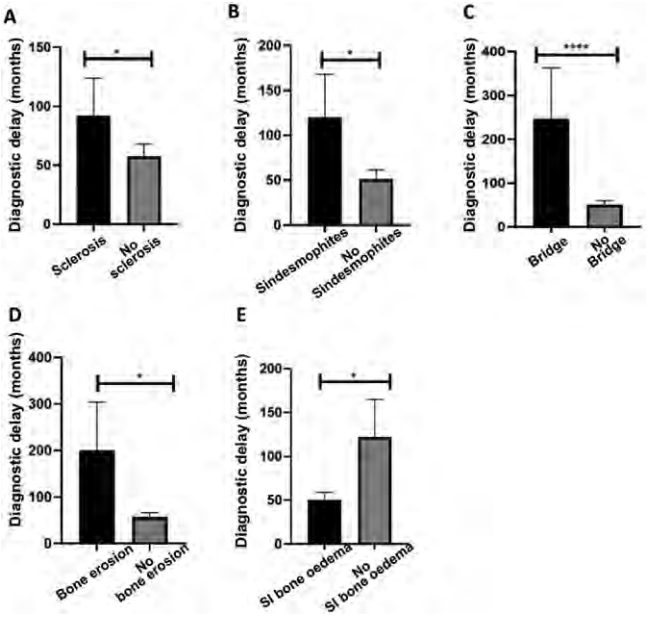


Figure 1.

Conclusion: Demographic and clinical factors differentiate axSpA from nr-axSpA patients. Diagnostic delay was higher in rad-axSpA compared with nr-axSpA despite the same treatment. Some lesions of spine/SI at CR and MRI, and psoriasis, were mostly associated with diagnostic delay and sex.

Disclosure of Interests: None declared

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AB1086 POWER DOPPLER AND SPECTRAL DOPPLER ULTRASOUND IN SUSPECTED ACTIVE SACROILIITIS: A COMPARISON WITH MAGNETIC RESONANCE IMAGING AS GOLD STANDARD

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Background: SIJ involvement is a characteristic feature of Spondylarthritis (SpA). Magnetic Resonance imaging (MRI) has been included in the new Assessment of SpA International Society (ASAS) criteria for the classification of Axial SpA. Gray scale US, Color Doppler ultrasound (CDUS), contrast-enhanced CDUS, and spectral Doppler (SD) US has been used in few works to evaluate the inflammatory activity of the SIJ with not conclusive results. Power Doppler ultrasound (PDUS) was not yet applied to the study of SIJ with active SI.

Objectives: The aim of this work was to study with PDUS and SD US the SIJ of patients with suspected active SI, to describe inflammatory flows with spectral wave analysis (SWA) in duplex Doppler US, and to correlate US data with clinical characteristics and the presence of bone marrow edema (BME) in MRI.

Methods: 22 patients (18 females and 4 males, mean age 35 years) with new onset of inflammatory back pain (IBP), were included. Every patient underwent an US examination in prone position. The sonographers were blinded to the clinical data of the patient. A Esaote Twice US machine, equipped with a convex multifrequency 1-8 MHz probe, was used, with standardized parameters: 1-5 MHz for gray scale, 1.9-2.3 MHz frequency for Doppler with Pulse Repetition Frequency (PRF) of 1.0 KHz and a color gain just under the artifact limit. SIJ was located as the hypoechoic triangle delimited between the sacrum and iliac bone, and the posterior SI ligament as the upper margin. The first sacral foramen was always localized to avoid measurement of the normal pre-sacral arteries. The PDUS was applied, and if any signals were detected in the SIJ, they were scored with a 3-points scale: 0= absence of signals, 1= isolate vessels, 2= more than one vessel. The signals were also classified as intra-articular or peri-articular. The same vessels were also evaluated using quantitative SD calculating the Resistive Index (RI=peak of systolic flow- end diastolic flow/peak systolic flow), ranging between 0 and 1. Every patient underwent MRI of SIJ within the same week, before treatment. A statistical analysis was performed, estimating the sensitivity and specificity against the gold standard (presence of BME in the same SIJ according to ASAS criteria). The Spearman rank not-parametric test was applied to correlate the presence and grading of BME with PDUS grading and RI. A regression analysis was applied between PDUS results and clinical characteristics.

Results: In 14/22 SIJ MRI revealed BME. In 13 of them, PDUS confirmed abnormal hypervascularisation in the intrarticular portion of SI, and in 3 in the periarticular site too. Two SIJ showed hypervascularisation at PD with no BME in MRI. A significant correlation was demonstrated between positivity and grading of PD and presence of BME in MRI (p=0.0005). SD analysis demonstrated low Resistance Index (RI) values in 14 SIJ (mean 0.57). An inverse correlation was demonstrated between RI and grading of BME in MRI (r= -0,6229, p= 0,044). The diagnostic accuracy of SD for detection of active SI varied on the basis of RI cut-off value. The best values of sensitivity (62,5%) and specificity (61,5%) were obtained with a RI cut-off values of 0.60. A multiple regression model demonstrated a significant relationship between PDUS signals and ASDAS (p=0.0382), but not with inflammatory reactants.

Conclusion: PDUS and SD US of SIJ can be useful as first imaging assessment in suspected active SI, demonstrating a good diagnostic accuracy compared with MRI. Intra-articular low RI values (<0.60) on SD indicate active SI with good accuracy. Moreover, PDUS signals into the SIJ correlate with clinical symptoms but not with inflammation reactants.

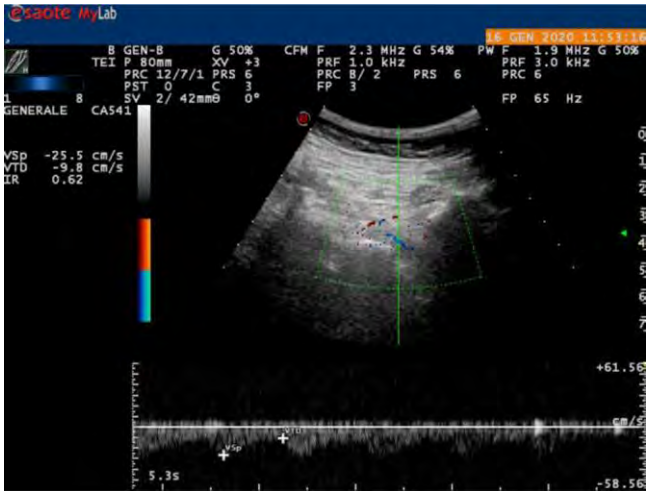


Figure 1. Doppler US in SI. Right SIJ with a Doppler signal along the posterior SIJ ligament, and another Doppler signal into the joint, where SD analysis gave a RI of 0,62.

Disclosure of Interests: None declared

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AB1087 DETECTING AXIAL AND PERIPHERAL NEW BONE FORMATION IN SPONDYLOARTHRITIS PATIENTS USING [18F]FLUORIDE PET-CT IMAGING

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Background: Bone formation in spondyloarthritis (SpA) is presumably related to local enthesitis/peri-articular inflammation and ultimately may lead to functional limitation (1,2). X-rays only allow long-term monitoring of bone formation (≥2 years) (3). Imaging techniques that can visualize bone formation at an early stage would therefore be valuable. Positron Emission Tomography (PET) using [^{18}F]Fluoride can visualize and quantify (early changes in) bone formation at molecular level (4).

Objectives: To investigate the feasibility of [^{18}F]Fluoride to assess new bone formation at axial and peripheral enthesial sites in SpA patients.

Methods: Thus far, 5 of the total of 15 patients with clinically active ankylosing spondylitis (AS) (according to modified New York criteria and BASDAI ≥4) and 8 of the 25 patients with active psoriatic arthritis (PsA) (according to CASPAR criteria and ≥1 clinically active enthesitis) were included. Of each patient, a whole body [^{18}F]Fluoride PET-CT scan was performed. All scans were visually judged and scored dichotomously by one reader (blinded for clinical data) for PET-positive lesions in the spine, peripheral enthesis sites and joints. Low dose CT was used for anatomical reference.

Results: The study is ongoing, with whole body [^{18}F]Fluoride PET-CT scans available in five AS patients and eight PsA patients. In 4/5 AS scans, at least (≥1) PET positive lesions were found in the cervical, thoracic and/or lumbar vertebrae. These were mainly found in anterior corners of vertebrae and bridging syndesmophytes (Fig. 1A). In all eight PsA patients, at least 1 PET positive lesion was visualized, projected either at the site of a tendon attachment (fascia plantaris, achilles- and patella tendon (Fig 1B)) or peri-articularly (in the ankle or wrist).

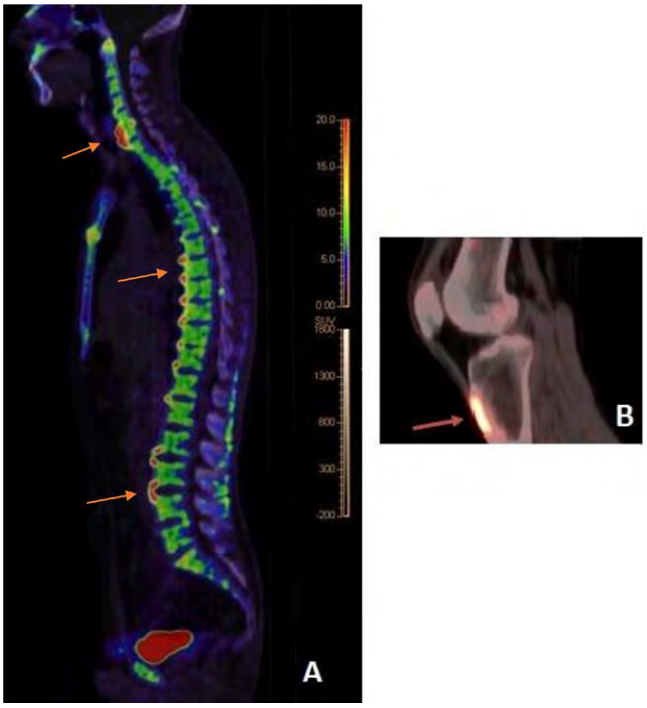


Fig 1. [18F]Fluoride uptake in the cervical, thoracic and lumbar spine in a clinically active AS patient (A) and in the patella tendon of the right knee in a clinically active PsA patient (B)

Conclusion: [18F]Fluoride PET uptake, reflecting new bone formation, can be visualized at heterogeneously distributed enthesis and (peri-)articular sites in AS- and PsA patients. The technique therefore is sensitive to visualize new bone formation and may reflect local disease activity. Additional scans will be collected and analyzed quantitatively, also after anti-TNF or Secukinumab treatment, to further investigate the applicability of [18F]Fluoride PET for monitoring of therapeutic effects on bone formation in SpA.

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AB1088 NAIL PSORIASIS: THE UNDERESTIMATED DISORDER IN PSORIASIS AND PSORIASIS ARTHRITIS. CAN ULTRASOUND AND CAPILLARY MICROSCOPY IN PATIENTS WITH NAIL PSORIASIS SPEED UP OUR DIAGNOSIS AND THERAPY?

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Background: Nail psoriasis is an extreme diagnostic and therapeutic challenge and represents an enormous physical and psychological burden for affected patients.50% of patients with psoriasis vulgaris develop nail involvement (NailPso)during the course of their disease. NailPso is the strongest predictor of psoriatic arthritis (PsA). Through the synovio-enthesial concept we have learned that there is an anatomical-pathophysiological relationship between DIP joint, extensor tendon and nail matrix. We have observed in daily practice that hypervascularization (HV) in ultrasound Power Doppler (US-PD)the nail matrix may be a pathognomonic element in its own right. There are no data on this in the literature.

Objectives: Is there a difference in the ultrasound PD examination of the DIP joint and nail area and in the capillary microscopy of the corresponding nail fold in patients with psoriasis vulgaris and nail psoriasis versus patients with psoriasis vulgaris without nail psoriasis.

Methods: Monocentric prospective study of all consecutive patients with psoriasis vulgaris who have come to a rheumatic practice to clarify a PsA. In addition to demographic data, assessments (PASI,DLQI,CASPAR,GEPARD, DAS28, SJ,TJ,FFBH), clinical examination, a standardized ultrasound PD examination and capillary microscopy of the affected fingertips in PsO patients suffering from nail psoriasis was performed as well as corresponding examinations of the 2nd and 3rd finger right in PsO patients without nail involvement.

Results: 79 patients could be included during the study period. Thereof 25 PsO patients without nail involvement and 44 PsO patients with nail involvement. Since the patients were examined consecutively, the difference results. There was no difference in age, BMI and sex in both groups (Pso and NailPso). The Caspar criteria as classification criteria for a PsA were positive in 65% of the NailPso patients and positive in 50% of all PsO patients without nail infestation. Hypervascularization in the US-PD examination in the area of the nail matrix could be seen significantly more frequently in NailPso compared to non-NagelPso patients. Such a difference did not exist in the HV of the extensor tendons.Capillary microscopy showed a significant difference in the number of torsions/twist capillaries in NailPso compared to Pso patients without NailPso. Hypervascularization of the nail matrix is seen significantly more frequently in patients with psoriasis of the nail than in patients without psoriasis of the nail. Such a difference does not exist in DIP joint -extensor tendon- enthesitis. At the same time, torsions are significantly more frequently seen in capillary microscopy in NailPso than in patients without NailPso.

Conclusion: The US-PD examination is a simple and non-invasive procedure which can be performed routinely in daily practice. The hypervascularization of the nail matrix should also make one think of nail psoriasis in the early stage of PsO, in order to be able to start early an appropriate therapy for this very stigmatizing and therapeutically extremely difficult manifestation of PsO. It seems to occur independently of extensor tendon synovitis as an independent manifestation phenomenon.

The occurrence of torsions in capillary microscopy >50 % also seems to be groundbreaking for a NagelPso, whereby capillary microscopy is a temporal challenge in daily routine.

References: § The present study (7734-BO-S2018 Ethics Commission of the MHH, Medical School Hannover, Germany) contains parts of the PhD thesis of M.Töllner

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AB1089 EVALUATION OF JOINT RHEUMATOLOGY/ RADIOLOGY MDT OUTCOMES & THEIR IMPACT ON RHEUMATOLOGY SERVICE

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Background: Multidisciplinary team (MDT) discussion between rheumatology and radiology is vital in diagnostic and prognostic management of patients' outcome. Nevertheless, discrepancies of the radiology report and clinical history cause unnecessary confusion and distresses to clinicians and patients. This could potentially affect subsequent clinical management.

Objectives: This survey was aimed to evaluate outcomes of rheumatology / radiology MDT discussion and to identify any discrepancies between original reports of the radiology images and amended reports following MDT. We also looked for potential reasons for the discrepancies and their impact on patient and health care resources due to erroneous original reporting.

Methods: We looked at all types of images which were discussed in rheumatology/ radiology MDT of University Hospital Plymouth from October 2016 to

April 2019. A total of 154 images were randomly selected and their reports were analyzed. The original reports were compared with the addendum made after the MDT and on the rheumatology electronic records. Clinical letters were also looked at to identify changes in follow up and treatment plans after the MDT.

Results: The majority of discussed images were X-rays (88). This is followed by 56 MRIs, 8 Ultrasounds and 2 others including CT.

After MDT review 38/88 X-rays (43%), 9/56 MRIs (16%) and 1/ 8 USS (13%) reports were amended. 31/38 amended X-ray (82%) and 5/9 amended MRIs (56%) were externally reported originally. In addition, 4 X-rays and 1 MRI reported by Radiology trainees were also amended.

Following the MDT outcome, the management plan was changed in 18/38 (47%) amended X-ray reports and 6/ 9 (67%) in amended MRI reports.

There were 17 rheumatology referrals by GP that were based on erroneous X-rays reporting and 3 of them were rejected after the MDT. The others were brought to the MDT after the first clinic visit and were discharged subsequently.

Conclusion: Joint rheumatology/ radiology MDT discussion makes significant outcome to patient care by minimizing unnecessary investigations and treatment based on erroneous or unclear reporting. Question is raised about efficacy of outsourcing of radiology reporting and need for intensive training for radiology trainees in reporting muscululoskeletal(MSK) images. Since significant numbers of GP referrals were based on erroneous reports, reporting done by MSK radiologists would have reduced unnecessary burden and waste of outpatient rheumatology resources.

The images submitted for MDT were selected largely by consultant rheumatologists based on their review of the images and reliance on the original report. Therefore, clinical impact is underestimated in this survey as there were potentially other images not reviewed in MDT that had ended in unnecessary clinical consultation. This survey emphasizes the need and importance of incorporating formal musculoskeletal radiology training into routine rheumatology training program.

Disclosure of Interests: None declared

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AB1090 BIOMARKERS TO DIFFERENTIATE EARLY INDISTINGUISHABLE CASES OF OSTEOARTHRITIS AND RHEUMATOID ARTHRITIS.

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Background: Osteoarthritis (OA) and rheumatoid arthritis (RA) are the most frequent inflammatory diseases of the musculoskeletal system, which could not be differentiated in their early stages, and characterized by degradation of articular cartilage and impairment of joint function. Sometimes, criteria and radiography are not insufficient to distinguish early-stages of RA and OA and predict disease course, and therefor biomarkers that help clinicians to early diagnose disease are essential.

Objectives: The aim of this study is to estimate serum level of Matrix metalloproteinase 3 (MMP3) and hrdroxyproline (HP) in early RA and OA patients to see if they can be used to differentiate both diseases at their early stages

Methods: The aim of this study is to estimate serum level of Matrix metalloproteinase 3 (MMP3) and hrdroxyproline (HP) in early RA and OA patients to see if they can be used to differentiate both diseases at their early stages

Results: We found a highly significant elevation of serum MMP3 in OA patients group compared to RA patients and control groups. We also found a highly significant elevation of MMP3 in RA patients than control group,($P < 0.001$). Meanwhile, we found a highly significant elevation of HP in OA patients than in RA patients and control groups, ($P < 0.001$), whereas there was no significant difference between HP in RA patients and control groups ($P > 0.05$).

Table 1. Demonstration of serum levels of MMP3 and HP in all groups.

"Enzyme"	OA *(n=40)*	RA *(n=40)*	Control *(n=40)*	p-value
MMP3 pg/mL	559.92±1112.84	153.25±162.05	59.79±63.54	<0.001
HP µg/mL	12.87±18.75	4.81±6.89	4.52±1.55	<0.001
HP µg/mL		4.81±6.89	4.52±1.55	> 0.05

Conclusion: Our results suggest that serum levels of Hydroxyproline (HP) rather than MMP3 could be used as a potential biomarker for early differentiation between osteoarthritis (OA) and rheumatoid arthritis (RA) when diagnostic criteria failed to be fulfilled.

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AB1091 FREQUENCY OF ULTRASOUND ENTHESITIS AND SYNOVITIS IN DIFFERENT ANATOMICAL SITES OF UPPER AND LOWER EXTREMITIES IN PATIENTS WITH PSORIATIC ARTHRITIS: CROSS-SECTIONAL STUDY

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Background: Psoriatic arthritis (PsA) is characterized by asymptomatic enthesitis and synovitis[1]. The location of pathological lesions is not clear. Furthermore, ultrasound (US) enthesitis indices assess limited number of entheses.

Objectives: To detect the most frequent sites of US enthesitis and synovitis in PsA.

Methods: 57 PsA patients were enrolled to the study. US examination included bilateral large 14 joints; entheses of tendons and ligaments in the projection of examined joints (total number - 54). Totally, 798 joints, 3078 entheses were examined. The study was conducted by US rheumatologist. Data collection: demographical, clinical, US (total synovitis count by grey scale, enthesitis counted as the sum of structural and acute components (US entheseal findings assessed by the definition and scoring for enthesitis in PsA (OMERACT US)[2]. Chi-square test used to calculate difference of articular and entheseal frequency between upper and lower extremities.

Results: In all 57 patients: male - 25 (43.9%), mean age 43.4±10.3(SD) years (y), PsA duration was 7 (3;10) y, Disease Activity in PsA score 18.1 (10.2;26.1).

Table. Frequency of articular and entheseal involvement of different anatomical sites in PsA

Upper extremities / Joints / Entheses	Frequency	Lower extremities / Joints / Entheses	Frequency
Acromioclavicular	29/456 (6.4%)	Hip	19/342 (5.6%)
Shoulder	3/456 (0.7%)	Knee	28/342 (8.2%)
Elbow	10/456 (2.2%)	Ankle	23/342 (6.7%)
Wrist	27/456 (5.9%)	Trochanter major:	31/2166 (1.4%)
		-gluteus minimum	36/2166 (1.7%)
		-gluteus medium	
Short head of the biceps brachii	11/912 (1.2%)	Spina iliaca anterior	13/2166 (0.6%)
		-superior	8/2166 (0.4%)
		-inferior	
Coracoacromial ligament	5/912 (0.5%)	Ischiadicus tuberositas	36/2166 (1.7%)
Infrascapularis	19/912 (2.1%)	Medial collateral ligament	44/2166 (2%)
		-Proximal	25/2280 (1.2%)
		-Distal	
Supraspinatus	18/912 (1.9%)	Lateral collateral ligament	23/2166 (1.1%)
		-Proximal	9/2166 (0.4%)
		-Distal	

Table. Frequency of articular and entheseal involvement of different anatomical sites in PsA

Upper extremities / Joints / Entheses	Frequency	Lower extremities / Joints / Entheses	Frequency
Infraspinatus	5/912 (0.5%)	Patellar ligament	19/2166 (0.9%)
		-Proximal	25/2166 (1.2%)
		-Distal	
Triceps brachii	21/912 (2.3%)	-Pes anserinus	37/2166 (1.7%)
Medial epicondyle	21/912 (2.3%)	Biceps femoris	7/2280 (0.3%)
Lateral epicondyle	34/912 (3.7%)	Semimembranosus	35/2166 (1.6%)
		Quadriceps femoris	52/2166 (2.4%)
		Tibialis anterior	9/2166 (0.4%)
		Tibialis posterior	13/2166 (0.6%)
		Achille	46/2166 (2.1%)
		Plantar fascia	30/2166 (1.4%)

There was difference between US synovitis detection of upper (57,1%) and lower (42,9%) extremities (p=0.04). Total count of US enthesitis of lower extremities (70,4%) was significantly higher than of the upper (29,6%;p<0.01).

Conclusion: US synovitis of upper extremities was slightly higher than in lower. US enthesitis of lower extremities is significantly higher. US imaging can be used to diagnose enthesitis and synovitis, especially in patients in whom symptoms may be difficult to discern, and data on location of pathological lesions will be useful.

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AB1092 ULTRASOUND EXAMINATION OF JOINTS AND PERIARTICULAR TISSUES IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES.

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Background: Joints and entheseal involvement is a common extraintestinal manifestation in inflammatory bowel diseases (IBD) [1]. Recent studies have shown the superiority of ultrasound over clinical findings in the evaluation of joints and periarticular tissues.

Objectives: To assess of joint and entheseal involvement in IBD patients using ultrasound with Power Doppler, their correlation with IBD clinical variables and the difference between Crohn's disease (CD) and ulcerative colitis (UC).

Methods: We prospectively included 38 IBD patients into the study. Disease activity was evaluated in CD by Harvey Bradshaw, in UC - Mayo Index. Peripheral joints and entheses were imaged by ultrasound, using Samsung Accuvix A30 5-13 MHz linear array transducer. Ultrasound examination of 14 peripheral joints (hip, knee, ankle, shoulder, acromioclavicular, elbow, wrist) and 35 entheses was performed. Vascularization on them was assessed with Power Doppler (PD). Entheseal abnormalities were scored with US according to indices GUESS, MASEI and BUSES [2]. Statistical analysis was done by Mann-Whitney test and Spearman criteria by "Statistica" software.

Results: In 38 patients UC was in 22 (58%), CD - in 16 (42%). The mean age of UC patients was 28 (23; 35) years, in CD - 33 (27; 36) years. The mean duration of UC was 24 (10; 48) months; CD - 66 (24; 114) months. The majority of patients had highly active disease: in UC - moderate and severe attacks in 16 pts (72%), in CD out of 16 patients, moderate and severe activity was observed in 9 (56%). Synovitis were found in 19 patients (50%), 8 patients with UC (36%), and 10 patients with CD (62%), synovitis with vascularization was detected in 7 patients (18%), five with CD (13%), two with UC (9%).

Enthesitis (echogenicity reduction and thickening) was detected in 30 patients (79%), 8 (50%) pts with CD and 17 (77%) pts with UC, enthesitis with vascularization (PD) in 13 pts (34 %), 5 (31%) pts with CD and 8 (36%) pts with UC. Tenosynovitis was observed in 11 pts (29%), three (19%) with CD and 8 (36%) pts - UC, tenosynovitis with vascularization in two patients (5%), one with UC and one with CD. Structure damage (erosion, enthesophytis) were found in 23 patients (61%), 12 patients (75%) with CD and 11 (50%) patients with UC.

There were no significant differences in ultrasound signs of joint and entheses damage between patients with UC and CD.

We found an association between the clinical characteristics of IBD and the ultrasound signs of entheses damage: duration of the disease has a direct moderate correlation with the number of enthesitis (SR = 0.36; p = 0.026) and GUESS (SR = 0.37; p = 0.022).

There was no statistically significant relationship between the severity of the attack and damage to the joints and entheses.

Conclusion: The severity of joint and periarticular tissues damage is significantly correlated with the duration of the index disease and are independent of IBD activity.

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AB1093 INTEROBSERVER AGREEMENT IN MAGNETIC RESONANCE OF SACROILIAC JOINTS ABOUT ACTIVE SACROILIITIS

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Background: Axial spondyloarthritis has characteristic clinical features such as enthesitis, sacroiliitis and spondylitis, and extra-articular manifestations(1). Magnetic resonance imaging (MRI) of sacroiliac (SI) joints is used to detect early sacroiliitis(2). Health institutions in our country carry out some of the radiology reporting services by outsourcing for reasons such as high cost and insufficient number of radiologists(3).

Objectives: We decided to evaluate the interobserver agreement in active MRI findings of SI between radiologist of outsourcing radiology services and local/expert radiologist in musculoskeletal diseases.

Methods: Between the years of 2015 and 2019, 8100 sacroiliac MRIs were taken at our center. The MRI of 1150 patients who were reported as active or chronic sacroiliitis from these sacroiliac MRIs or whose MRI was considered by the primary physician in favor of sacroiliitis was included in the study. Concordance between Evaluation and Service Procurement was examined using Kappa (k) coefficients. Mc Nemar test was used to compare the evaluation result between two observers. A p-value <0.05 was considered significant. Analyses were performed using commercial software (IBM SPSS Statistics, Version 23.0. Armonk, NY: IBM Corp.)

Results: Of the 1150 patients examined in the study, 526 (45.7%) were male and 624 (54.3%) were female. The general average age is 37.20 ± 11.65 and the average age of men and women is 34.98 ± 11.19 and 39.07 ± 11.71 respectively. A statistically significant difference was found between the expert radiologists and outsourcing radiologist reports. In other words, a high level of compatibility was not found among the evaluators (p <0.001). When the consistency between expert radiologist and outsourced radiologist reports was examined, it was observed that there was a medium level of concordance (k = 0.589).

Conclusion: The diagnosis of a spondyloarthropathy may be delayed for some reasons. In addition to the insidious course of the disease, being contented with an outsourced radiologist report may delay diagnosis. If the patient's clinic and MRI report are not consistent, the patient should not be removed from follow-up.

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		OUTSOURCING RADIOLOGIST REPORTS		TOTAL	p	
		NOT ACTIVE SACROILIITIS	ACTIVE SACROILIITIS			
EXPERT RADIOLOGIST REPORTS	NOT ACTIVE SACROILIITIS	508	178	686	<0.001	0.589
	ACTIVE SACROILIITIS	59	405	464		
TOTAL		567	583	1150		

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AB1094

SCAR IMAGING ECHOCARDIOGRAPHY WITH ULTRASOUND MULTI-PULSE SCHEME [ESCAR] FOR THE DETECTION OF MYOCARDIAL FIBROSIS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: PRELIMINARY RESULTS.

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Background: Myocardial fibrosis is a severe complication of immune-mediated diseases, occurring in up to 30% of systemic lupus erythematosus (SLE) patients. Cardiovascular magnetic resonance imaging allows myocardial scar detection in SLE patients, but it is costly, time consuming, and unfit for patients with renal disease. Scar imaging echocardiography with ultrasound multi-pulse scheme (eSCAR) is a novel and promising technique that proved to be effective in detecting ischemic myocardial scars in patients with coronary artery disease (CAD).
Objectives: To evaluate if the eSCAR technique is feasible and to better characterize SLE patients with cardiac involvement by eSCAR.
Methods: We recruited consecutive patients with SLE classified according to the 2019 EULAR/ACR recommendations. Patients with diabetes mellitus, obesity, prior cardiovascular (CV) disease or anti-phospholipid (aPL) syndrome were excluded. Eligible participants underwent a thorough clinical assessment and a full echocardiography examination, including the eSCAR technique. Data on clinical variables were collected; disease activity was estimated by the SLE Disease Activity Index (SLEDAI) score. Lupus flare was defined as new/worse clinical signs and symptoms and/or lab measurements and a change/increase in treatment. Patients were compared according to the presence or absence of eSCAR. In this preliminary report, only descriptive analyses are provided. Continuous data are reported as median [25^{th}; 75^{th} percentile].
Results: We enrolled fifteen patients diagnosed with SLE (age 45 years [36; 47], disease duration 14 years [12; 20]), 13 (87%) were females. Median SLEDAI was 5 [2; 8]. The most frequent disease involvement included arthritis (73%), skin and mucous membranes (60%), lupus nephritis (47%) and cytopenias (47%). Patients had received treatment for lupus with 5 drugs [5; 8]. Cumulative prednisone dosage was 25 g [20; 44], whilst the current daily dosage of prednisone was 4 mg [0.0; 5.0]. Hypertension was present in 4 (27%) and hypercholesterolemia in 2 (13%) subjects; 4 patients (27%) were current or past smokers. The eSCAR technique was feasible in all participants with no adverse effects. Myocardial scars were detected in 2 patients (eSCAR-positive 13%; figure and table); eSCAR positive patients were females and had no history of cardiovascular involvement (including pericarditis); they had at least one relapse within the prior 12 months before enrollment; at least one cardiovascular risk factor was found in both patients (one was a smoker and the other one had hypertension); none received prior treatment with cyclophosphamide or rituximab; they had no renal involvement; arthritis and cytopenia were the prominent features of disease; anti-dsDNA titer was higher than eSCAR-negative patients.
Conclusion: Echocardiography allowed detection of myocardial scars in patients with SLE. Our preliminary data show that eSCAR is feasible and well tolerated in a SLE population. Further data from this ongoing study will help investigate whether eSCAR might improve risk stratification, by identifying myocardial involvement in SLE patients with a more active disease.

Table

	eSCAR positive Patient 1	eSCAR positive Patient 2	eSCAR negative SLE patients (n=13)
Age, years	32	45	45
Sex	Female	Female	11 F / 2 M
ESR mm/h	29	7	15
CRP mg/L	3	0.6	2
Anti-dsDNA (IF)	Positive	Positive	Positive 7 (47)
Anti-dsDNA (CLIA)	105	149	34 [7; 66]
C3 (mg/L)	61	80	85 [70; 94]
C4 (mg/L)	4	13	10 [9; 16]
P-Cr (mg/dL)	0.6	0.8	0.7 [0.6; 0.7]
aPL	Positive	Negative	7 (47)
Disease duration, years	15	28	14 [12; 15]
SLEDAI	12	0	5 [2; 8]
Lupus flare in the past 12 months	yes	yes	5 (33)
Cumulative prednisone dosage (g)	60	61	24 [19, 32]
Previous use of cyclophosphamide	No	No	3 (20)
Previous use of rituximab	No	No	1 (1)

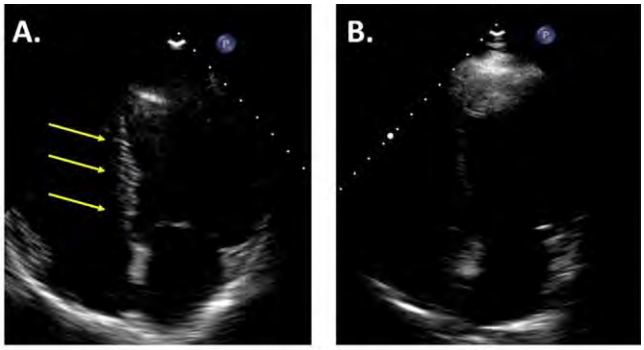


Figure. A. Myocardial fibrosis in the interventricular septum (eSCAR-positive patient). **B.** no myocardial fibrosis (eSCAR-negative patient)

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Disclosure of Interests: Alessandro Giollo: None declared, Giulia Vinco: None declared, Giovanni Orsolini: None declared, Giovanni Cioffi: None declared, Giovanni Adami: None declared, Angelo Fassio Speakers bureau: Angelo Fassio reports personal fees from: Abiogen and Novartis, outside the submitted work., Luca Idolazzi: None declared, Davide Gatti Speakers bureau: Davide Gatti reports personal fees from Abiogen, Amgen, Janssen-Cilag, Mundipharma, outside the submitted work., Flavio Luciano Ribichini: None declared, Maurizio Rossini Speakers bureau: AbbVie, Abiogen, Amgen, BMS, Eli-Lilly, Novartis, Pfizer, Sanofi, Sandoz and UCB, Ombretta Viapiana: None declared
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AB1095

DIAGNOSTIC PERFORMANCE OF THE AORTIC WALL THICKENING DETERMINED BY ROUTINE CT-SCAN FOR THE DIAGNOSIS OF AORTITIS OVER 50 YEARS OF AGE.

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Background: Making the diagnosis of aortitis may be challenging in the "real life". ^{18}F-FDG PET/CT (PET) has emerged has the gold standard to diagnose aortitis but it is expensive and not always quickly available. Injected CT-scan (CT) can also be used to diagnose aortitis, which is suspected when there is an extended circumferential, non-atherosclerotic increase of the aortic wall thickness (AWT). However, data are lacking on the diagnostic performances of AWT to diagnose aortitis.
Objectives: To describe the diagnostic performance of AWT measured by CT to diagnose aortitis in patients over 50 years of age.
Methods: We performed a monocentric retrospective study between 2013 and 2018 including 1) all patients over 50 years of age who had performed a PET for inflammation or fever of unknown origin or for suspicion of classical giant cell arteritis (GCA), aortitis or large vessel vasculitis (LVV); 2) with an injected CT-scan performed in the 30 days before or after PET; 3) not diagnosed to have cancer or infection 4) exposed to corticosteroids for less than 3 days at the time of CT and PET. The gold standard for aortitis was PET positivity according to the 2018 European consensus grading criteria (1). AWT was measured at different aortic segments (ascending aorta, descending thoracic aorta and suprarenal abdominal aorta) by a single radiologist unaware of the result of PET and of the previous interpretation of CT-scan.
Results: Eighty-nine patients were included (female: 47%; mean age 68.8 (50-93) years; GCA: n=28). Twenty patients had aortitis according to the PET result (GCA: n=16).
Mean maximal aortic wall thickening was: 3.25 mm (median: 3.3; range: 2-4.6) in the aortitis group and 2.2 mm (median: 2.1; range 1-3.8) in the negative PET group ($p < 0.001$).
The best ROC curve AUC (85%) was obtained considering the maximal AWT on the thoracic and suprarenal abdominal aorta only. The AUC of the ROC curve at the ascendant thoracic aorta was poor (75%) (Figure).
The Youden's index of the ROC curve was 2.6 mm with a sensitivity of 85 % and specificity of 71 % (Table) for aortitis diagnosis. An AWT ≤ 2.0 mm exclude the diagnosis of aortitis. The 3 mm threshold had a PPV of only 52% and an AWT ≥ 4 mm was fully specific.
Conclusion: Aortitis diagnosis using a routine injected CT-scan interpreted by a single radiologist may be certain when showing an AWT ≥ 4 and excluded for an AWT≤ 2.0. The threshold of 3 mm seems not sufficiently specific to diagnose aortitis without a confirmatory PET.

References:
[1] Riemer H.J.A. Slart et al. FDG-PET/CT(A) imaging in large vessel vasculitis and polymyalgia rheumatica: joint procedural recommendation of the EANM, SNMMI, and the PET Interest Group (PIG), and endorsed by the ASNC. Eur J Nucl Med Mol Imaging. 2018 Jul;45(7):1250–69.

Table. Performance of different threshold for maximal thickness of the aortic wall for diagnosis of aortitis using PET positivity as the gold standard*.

Thickness (mm)	Sensitivity	Specificity	NPV	PPV	accuracy
≥ 1.9	100 %	30.4%	100 %	29.41 %	46 %
≥ 2.0	100 %	31.88 %	100 %	29.85 %	47 %
≥ 2.2	95 %	53.62 %	97.36 %	37.25 %	63 %
≥ 2.6	85 %	71.01 %	94.23 %	45.94 %	74 %
≥ 3.0	60 %	84.05 %	87.88 %	52.17 %	78 %
≥ 3.3	60 %	92.75 %	88.89 %	70.59 %	85 %
≥ 3.5	35 %	95.65 %	83.54 %	70 %	82 %
≥ 3.8	25 %	98.55 %	81.92 %	83.33 %	82 %
≥ 4.0	20 %	100 %	81.17 %	100 %	82 %

*Made with ROC curve in descendant thoracic and suprarenal segment of the aorta; PET: ^{18}F-FDG PET/CT; NPV: negative predictive value; PPV: positive predictive value.

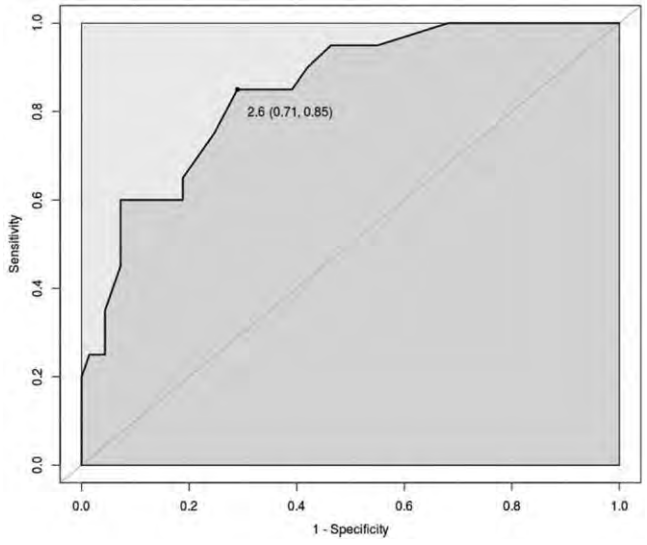


Figure. ROC curve of aortic wall thickness, in descendant thoracic and suprarenal abdominal segments for the diagnosis of aortitis.

Disclosure of Interests: None declared
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AB1096 THE ASSOCIATION OF ULTRASOUND ASSESSMENT AND PATIENT REPORTED OUTCOMES IN SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS: A SYSTEMATIC LITERATURE REVIEW

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Background: Patient reported outcomes (PROs) reflect patients' opinion on disease activity and impact of disease on various aspects of life. They are essential in the assessment of patients spondyloarthritis (SpA) and psoriatic arthritis (PsA), but may be influenced by several factors other than disease activity and severity. Ultrasound (US) is an objective tool to evaluate inflammation and structural damage in these conditions.
Objectives: The objective of this study was to determine if and to which extent the US assessment reflects patient perspective in patients with SpA and PsA.
Methods: Two separate systematic literature reviews were conducted for each disease. The research questions were formulated according to the PICO framework. The patient reported domains of health were selected from the ones included in the Core Set for SpA [1] and PsA [2] and from the ones frequently reported in clinical trials and observational studies for SpA and PsA, as well as patient self-assessment of pain at the joint level. We included articles that evaluated any kind of relationship between PROs and US assessment.

Table 1. Patient reported domains evaluated in the included studies.

	Domain	Studies reporting the domain N (%)
SpA	Disease activity	11 (91.7)
	Function/ disability	9 (75)
	Pain	7 (58.3)
	Patient global assessment	5 (41.7)
	Quality of life	5 (41.7)
	Morning stiffness	3 (25)
	Fatigue	1 (8.3)
	Sleep	1 (8.3)
	Global health	1 (8.3)
	Patient reported peripheral swelling	1 (8.3)
PsA	Function/ disability	10 (83.3)
	Pain	9 (75)
	Patient global assessment	8 (66.7)
	Disease activity	5 (41.7)
	Quality of life	4 (33.3)
	Disease impact	3 (25)
	Mood disorders	2 (16.7)
	Fatigue	2 (16.7)
	Morning stiffness	1 (8.3)

Results: SpA
In total, 2977 abstracts were identified, of which 12 articles were retained in the final analysis: 10 cross-sectional studies assessing disease activity state and 2 longitudinal, non-interventional trials assessing treatment response. The most frequently evaluated domains of health are depicted in table 1.
The cross-sectional studies evaluating only one joint area (foot and ankle, sacroiliac joint, shoulder and hip) showed that overall there is no important association between the PROs and the US parameters. In studies evaluating multiple entheses sites there were several correlations between PROs (pain, disease activity, function, quality of life (QoL)) and US variables, i.e., US inflammatory scores and total enthesitis scores, comprising both inflammatory and structural changes (r=0.24-0.53). In the longitudinal studies there was no consistent association between PROs and US variables.
PsA
Out of the 1267 abstracts identified, 12 were finally included in the qualitative analysis: 5 cross-sectional studies on disease activity state and 7 longitudinal studies, of which 2 on disease activity state and 5 on treatment response. The most frequently evaluated domains of health are depicted in table 1.
Overall, in the cross-sectional studies, there was no consistent association between PROs and US assessment. In the longitudinal studies on disease activity, pain and patient global assessment (PGA) were associated with US inflammatory variables (r=0.22-0.28), while disability correlated with US damage (r=0.22-0.39). Change in PGA and pain was associated with change in the global US inflammation score (r=0.28-0.35). In longitudinal studies on treatment response results were inconsistent: two studies showed that there was significant parallel trend of some PROs (function, pain and PGA) and some US entheses scores, but the other 3 studies showed no significant association.
Conclusion: The association between PROs and US in SpA and PsA was rather inconsistent. Patient perspective and US examination seem to provide different, but complementary perspectives on disease assessment and both should be taken into account in SpA and PsA management.
References:
[1] van der Heijde, J Rheumatol 1999
[2] Orbai, An Rheum Dis 2016
Acknowledgments: Supported by PARTNER Fellowship
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.4316

AB1097 THE ASSOCIATION OF ULTRASOUND ASSESSMENT AND PATIENT REPORTED OUTCOMES IN RHEUMATOID ARTHRITIS: A SYSTEMATIC LITERATURE REVIEW

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Background: Patient reported outcomes (PROs) are recognized to be essential outcome measures in the assessment of patients with rheumatoid arthritis (RA), but they can be prone to being influenced by multiple variables. Thus, objective

measures of disease activity, i.e. imaging techniques such as musculoskeletal ultrasound (US) are also of great interest.

Objectives: The objective of this study was to determine if and to which extent the US assessment reflects patient perspective in patients with RA.

Methods: A systematic literature review was conducted on PubMed and Embase, with the research question being formulated according to the PICO framework. The patient reported domains of health were selected from the ones included in the Core Set for RA [1] and from the ones frequently reported in RA clinical trials and observational studies [2], as well as patient self-assessment of pain or functionality at the joint level. We included articles that evaluated any kind of relationship between PROs and US assessment in RA patients.

Results: Out of the 3757 abstracts identified through the systematic literature review, 53 articles were finally included in the qualitative analysis, of which 38 were cross-sectional and 15 were longitudinal studies (figure 1). The most frequently evaluated domains are depicted in table 1.

Table 1. Patient reported domains evaluated in the included studies.

Domain	Studies reporting the domain N (%) out of 53 articles
Function/ disability	37 (69.8)
Pain	25 (47.2)
Patient global assessment	21 (39.6)
Morning stiffness	14 (26.4)
Quality of life	5 (9.4)
Global or general health/ well-being	5 (9.4)
Fatigue	4 (7.5)
Disease activity	1 (1.9)
Mood disorders (anxiety/ depression)	1 (1.9)
Treatment adherence	1 (1.9)
Disease impact	1 (1.9)
Foot impact (impairment and participation restriction)	1 (1.9)
Pain catastrophizing	1 (1.9)

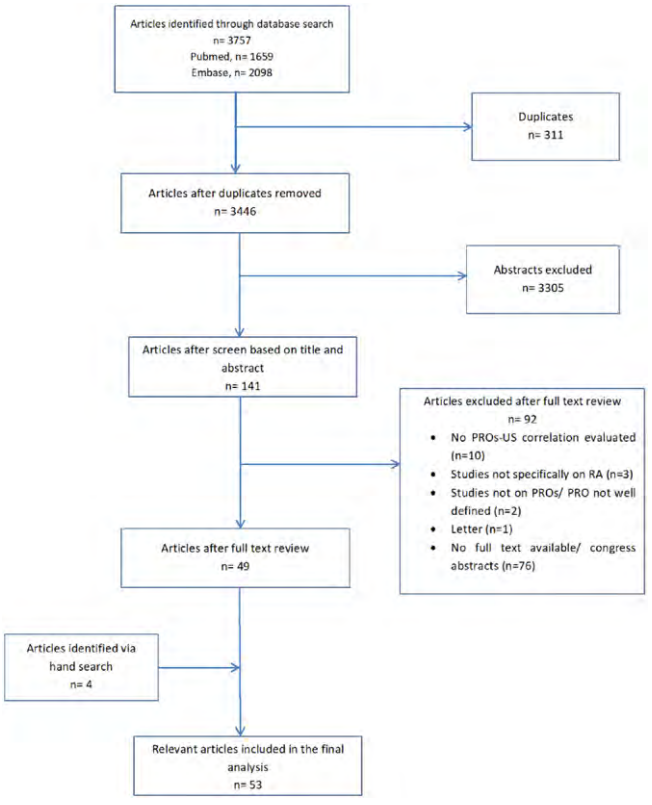


Figure 1. Flow chart of the systematic literature review

Cross-sectional studies: Overall, patient joint self-assessment of joint swelling or tenderness had a rather poor agreement with US evaluation but showed a stronger association with the clinical examination at the joint and/ or patient level. In studies evaluating RA patients in remission, disability and patient global assessment (PGA) were associated with Power Doppler (PD) synovitis (r= –0.395 to -0.460), while morning stiffness and patient assessment of flare with PD tenosynovitis (r= 0.29; odds ratio, OR 1.95 [95% CI, 1.17, 3.26]). In studies on RA disease activity, morning stiffness showed good associations with US inflammatory findings, especially PD tenosynovitis (r=0.280 – 0.561; OR 3.0 [95% CI, 1.2-7.5] or OR 10.9 [95% CI,1.2–39.13]) and disability with PD synovitis/ tenosynovitis (r=0.14 -0.55) and US damage/erosions (r=0.16-0.40). Pain, PGA and quality of life (QoL) mainly did not correlate with US assessment.

Longitudinal studies: In total, there was no clear, consistent longitudinal association between PROs and US variables in RA studies on remission or treatment response. However, in studies on RA disease activity, there was a strong longitudinal association between disability and US inflammatory scores (r= 0.32 – 0.40; beta: -0.009 to -0.025), but not US damage scores. Additionally, US ankle synovitis and/or tenosynovitis were shown to predict ankle pain (beta: 16.8 [95% CI: 4.81, 28.8]), and to a lesser extent disability.

Conclusion: Overall, we found contradictory results regarding the relationship between US evaluation and PROs in RA. While there were some consistent associations such as between disability and US inflammatory and structural findings or between MS and US inflammatory lesions, in particular tenosynovitis, there was no global strong correlation between US and PROs. Therefore, both assessments should be taken into consideration in RA evaluation and management.

References:

[1] Felson, AR 1993
[2] Orbai, Curr Rheumatol Rep 2015

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.4304

AB1098 STRUCTURAL ELEMENTS OF THE KNEE ENTHESES ASSESSED IN HEALTHY SUBJECTS WITH ULTRA HIGH FIELD MRI (150 MICRONS).

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Background: Fibrocartilaginous enthesis is composed of different histological zones which are commonly referred to the tendon distal extremity (a lamellar tissue with a low cell density, collagen and connective tissue), the fibrocartilaginous zone (with chondrocytes), a progressively mineralized zone and the bone. The MRI visualization of the water content of entheses is challenging given the very short relation time so that entheses has been very poorly assessed using MRI (1).

Objectives: The main objective of the study was to assess the structural elements of the knee enthesis based on the quantitative T2* measurements using Ultra High Field (UHF) MRI.

Methods: Twelve healthy subjects without any osteoarticular pathology were included in the study after they provided their informed consent. 3D gradient echo sequence with a 4.3 ms echo time and T2* mapping were performed. The lateral internal, external and crossed ligaments, patellar and quadricipital tendons were assessed. T2* measurements were performed specifically on the quadricipital tendon.

Results: The quadricipital tendon and the bone trabeculation could be visualized on the UHF MR image. The T2* mapping analysis illustrated a large value (16.4 ± 4 ms) for the subchondral bone and much lower values for the trabecular bone (11 ± 4.5 ms) and the different zones of the keen entheses (7.7 ± 1.9 ms).

Conclusion: Based on T2* measurements performed using UHF MRI, the different structural elements of the knee entheses were distinguished. This quantitative stratification could be used to assess changes in pathological conditions such as SpA and trauma.

References:

[1] Benjamin M, Bydder GM. Magnetic resonance imaging of entheses using ultrashort TE (UTE) pulse sequences. Journal of magnetic resonance imaging: JMRI. 2007;25(2):381-9.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.1191

AB1099

EVALUATION OF DIFFERENT FLUORESCENCE-OPTICAL IMAGING (FOI) ASSESSMENT METHODS TO DIFFERENTIATE CLINICAL PSORIATIC ARTHRITIS FROM PSORIASIS

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Background: Psoriasis (Pso) is one of the most common chronic inflammatory skin diseases in Europe. Psoriatic arthritis (PsA) is closely associated to Pso whereas the skin manifestation appears usually years before PsA-related symptoms emerge. Up to 30% of Pso patients develop PsA, but there is no clear correlation between disease duration of Pso and PsA development. In early PsA, changes in synovial vascularisation combined with increased expression of proangiogenic factors appear first. Therefore, imaging biomarkers for detection of changes in vascularisation might be useful for early detection of musculoskeletal disease. Fluorescence-optical imaging (FOI) is an indocyanine green (ICG) tailored method to detect microvascular changes in the hands using ICG kinetics over 360 sec. Different methods for assessment of FOI are available. It has not yet been demonstrated to what extent these methods can be used to differentiate psoriasis from psoriasis arthritis.

Objectives: To evaluate different reader dependent assessment methods to evaluate FOI in psoriasis and psoriatic arthritis.

Methods: FOI data (clinical PsA n=137, PsO without PsA n=202) from an observational prospective multicentre trial in Germany was used for manual assessment of the films using two different published assessment methods:(1) FOI activity score (FOIAS) and (2) individual characteristics of ICG kinetics. For (1) FOIAS, the levels of signal enhancement were scored using a scoring system from 0 to 3 (0=no enhancement, 3=strong enhancement) per joint as well as an assessment of the summation picture. (2) Kinetics were determined by joint-related signal enhancements as well as by ICG related flow-on and flow-off behaviour. Time to the first appearance of the signal, the time to the maximum enhancement and the time to the end of the signal were determined.

Results: By use of (1) FOIAS, the maximum score (overall signals of all joints assessed by FOIAS) showed a significant difference (p=0.0075) between PsA (mean 4.76) and PsO (mean 3.84). (2) Time to global maximum showed no significant difference (PsA mean 91.1 sec vs PsO 92.6 sec). Moreover, the mean time to maximum and clearance of ICG did not differ between the two diseases. The duration of the 3 phases of kinetic (phase 1: flow-in, phase 2: stable, phase 3: clearance) was 52.4 sec, 180.2 sec and 119.8 sec for PsA and 57.6 sec, 186.0 sec and 130.5 sec for PsO with an earlier phase 2 and 3 for PsA by trend. The most frequently affected joints in PsA (affected > 10%): PIP 3 right and PIP 5 right.

Conclusion: FOI is a sensitive method to detect changes in microvascularisation in the hands. The use of the manual FOIAS is able to differentiate significantly between PsA and PsO patients by comparison of the sum of scores over all joints (maximum score). The assessment of ICG kinetics is limited to discriminate between musculoskeletal and joint disease, differentiation of diseases is only seen by trend. Both methods characterize disease states differently. A combination of both methods might be useful to increase the potential of manual assessment of FOI signals.

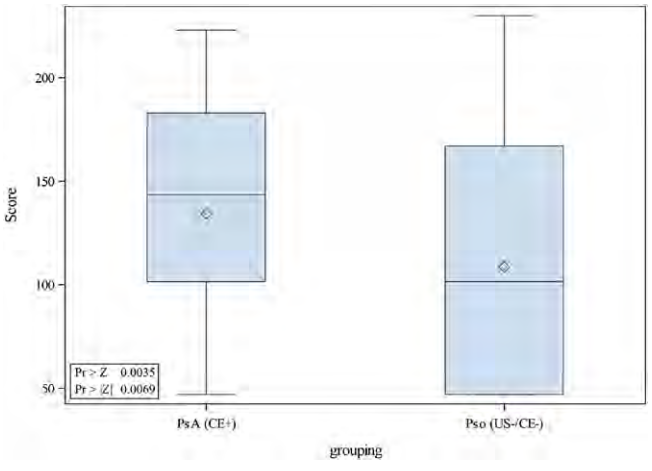


Figure 1. Maximum sum score of FOIAS in PsO and PsA patients (p=0.0075 in two-sided t-test).

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AB1100

PERFORMANCE OF MAGNETIC RESONANCE IMAGING FOR DETECTING SACROILIITIS IN EARLY STAGES OF SPONDYLOARTHRITIS

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Background: In view of the limited accuracy of clinical evaluation to recognize sacroiliitis, several imaging techniques such as conventional radiographs, scintigraphy, ultrasound (US), computed tomography (CT) and magnetic resonance imaging (MRI) have been used to examine the sacroiliac joints (SIJ).

Objectives: The aim of this study was to assess the performance of MRI for detecting sacroiliitis in early stages of spondyloarthritis (SpA).

Methods: This cross-sectional prospective monocentric double-blind study included 57 patients consulting for symptoms suggestive of SpA during more than 3 months between February 2014 and February 2017. Patients with conventional radiograph showing a confirmed sacroiliitis (grade 3 or 4) were not included. After clinical examination and blood sampling, eligible patients underwent MRI of SIJ. MR images were interpreted by 2 experimented musculoskeletal radiologists blinded to clinical and laboratory data. Two professors in rheumatology blinded to radiologists' conclusions, analyzed clinical data, laboratory tests, HLA typing, X-rays and MRI images and divided the patients into 2 groups: confirmed non radiographic SpA (nr-SpA) or no SpA. This classification was considered as the gold standard when analyzing the results.

Results: Fifteen men and 42 women were enrolled. The mean age at inclusion was 39.75 ± 11 years [17-59]. The mean duration from the first symptom was 47 ± 39 months [6.6-180]. Forty-three patients were assessed as nr-SpA (75.4%) and 14 patients as no SpA (24.6%). Thirty-three percent of patients were HLA B27 positive. Totally 22 patients had sacroiliitis at MRI, all of them classified as confirmed nr-SpA. Among the nr-SpA group, MRI showed bone marrow edema (BME) in 34.9% of patients and erosions in 44.2% of patients. Among the patients in whom the diagnosis of SpA was excluded, MRI showed bone marrow edema (BME) in 7% of patients and erosions in 7% of patients. A statistically significant association was observed between the presence of sacroiliitis at MRI and rheumatologists' diagnosis of SpA (p=0.001). The diagnostic value of MRI lesions is presented in the following table:

	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Positive Predictive Value (%)
BME	34.9	92.9	93.7	31.7
Erosions	44.2	92.9	95	35.1
MRI conclusion: sacroiliitis	51.2	100	100	40

Conclusion: SIJ MRI had an excellent specificity for the diagnosis of SpA but a moderate sensitivity. Consequently, some patients in early stages of SpA might be missed by MRI. In addition, we found that diagnostic based solely on BME lacked sensitivity. Detection of erosions in addition to BME enhanced sensitivity (from 34.9% to 44.9%) without changing specificity. Indeed, many recent studies have pointed out the importance of considering structural lesions of SIJ in addition to inflammatory lesions [1, 2].

References:

[1] Weber U, Lambert RGW, Pedersen SJ, et al (2010) Assessment of structural lesions in sacroiliac joints enhances diagnostic utility of magnetic resonance imaging in early spondylarthritis. Arthritis Care Res 62:1763–1771. https://doi.org/10.1002/acr.20312

[2] Weber U, Jurik AG, Lambert RGW, Maksymowych WP (2016) Imaging in Spondyloarthritis: Controversies in Recognition of Early Disease. Curr Rheumatol Rep 18:58. https://doi.org/10.1007/s11926-016-0607-7

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.5137

AB1101

THE PERFORMANCE OF COMPUTED TOMOGRAPHY FOR ASSESSING SACROILIITIS IN EARLY SPONDYLOARTHRITIS: WHICH STRUCTURAL LESIONS ARE MOST CONTRIBUTIVE TO THE DIAGNOSIS?

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Background: Computed tomography (CT) of sacroiliac joints (SIJ) is usually considered as a third-line modality in the diagnosis of spondyloarthritis (SpA), as it shows only structural lesions. According to 2015 EULAR recommendations, CT may be helpful if conventional radiograph is inconclusive and MRI cannot be performed [1]. However, its contribution for the early assessment of sacroiliitis is still little-studied.

Objectives: The purpose of this study was to assess the performance of CT scan for detecting sacroiliitis and the contribution of the different structural lesions to the early diagnosis of SpA.

Methods: This cross-sectional prospective monocentric study included consecutive patients, aged over 16, consulting for symptoms suggestive of SpA between February 2014 and 2017. Patients with a pelvic radiograph showing a confirmed sacroiliitis (making CT unnecessary to confirm the diagnostic) were not included. Eligible patients underwent CT of SIJ and the images were reviewed by 2 experimented musculoskeletal radiologists blinded to clinical findings. Then, 2 experienced rheumatologists analyzed clinical, biological and radiological data and classified patients into 2 groups: confirmed non-radiographic spondyloarthritis (nr-SpA) or no SpA. This classification was considered as the gold standard of this study.

Results: A total of 60 patients, 45 women and 15 men, were included in this study. Forty-six patients were assessed as confirmed nr-SpA (76.6%) and 14 patients as no SpA (23.4%). Mean age at the diagnosis was 39.5±10.8 years [17-59], and the disease duration from first symptoms was 48.6 ± 40 months [6.6-180]. Chronic back pain met the Calin criteria in 37 patients (61.7%), the Berlin criteria in 46 patients (76.7%) and the ASAS criteria in 32 patients (53.3%). Among the patients diagnosed as confirmed SpA, 71.7% were determined to have sacroiliitis at CT. As shown by the following table, the most sensitive lesion was subchondral bone sclerosis and the most specific one was new bone formation at entheses:

Table

	Confirmed SpA	No SpA	P	Se (%)	Sp (%)	PPV (%)	NPV (%)
Interruption of subchondral bone	67.4%	28.6%	0.01 (S)	67.4	71.4	88.6	40
subchondral bone erosions	65.2%	35.7%	0.05 (S)	65.2	64.3	85.7	36
Subchondral bone sclerosis	78.3%	28.6%	0.001 (S)	78.3	71.4	90	50
new bone formation at entheses	10.9%	7.14%	0.68 (NS)	10.9	92.9	83.3	24.1
CT conclusion: sacroiliitis	71.7%	28.6%	0.04 (S)	71.7	71.4	89.2	43.5

CT: computed tomography, SpA: Spondyloarthritis, Se: Sensitivity, Sp: Specificity, PPV: Positive Predictive Value, NPV: Negative Predictive Value

Conclusion: The relatively limited place of SIJ CT can be explained by the lack of investigations evaluating its real contribution in detecting sacroiliitis. In this study, we found that the main SI structural lesions were significantly associated to the final diagnosis of SpA with a sensitivity up to 78.3% and a specificity up to 92.9%. The main limitation of this technique remains the large radiation dose delivered to the gonads, especially with the commonly used axial position for CT. However, recent studies found that oblique coronal CT imaging seems to be a very promising technique, since it allows visualization of the subtle radiologic signs of sacroiliitis while delivering less radiation dose [2].

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AB1102

COLOR DOPPLER ULTRASOUND OF SACROILIAC JOINTS COMPARED WITH MAGNETIC RESONANCE IMAGING IN NON RADIOGRAPHIC SPONDYLOARTHRITIS

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Background: Magnetic resonance imaging (MRI) of sacroiliac joints (SIJ) can assess early inflammatory changes, thus allowing an early diagnosis of spondyloarthritis (SpA). However, its use in clinical practice may be limited by its cost, its duration and its limited availability. In this sense, ultrasound (US) has been suggested as a feasible and easy-to-apply alternative.

Objectives: The objective of this study was to evaluate the validity of Color Doppler Ultrasound (CDUS) in early assessment of sacroiliitis, compared to MRI findings as the gold standard.

Methods: A cross-sectional prospective monocentric study included patients attending the rheumatology department with suggestive signs of SpA between February 2014 and February 2017. Patients with pelvic radiography showing a confirmed sacroiliitis (grade 3 or 4) were not included. Eligible patients underwent US and MRI of SIJ. US examinations were performed by an experimented musculoskeletal radiologist blinded to MRI results. Vascularization within the SIJs was explored by the presence of a CDUS. When an artery was found, the resistive index (RI) was measured. The values of the RI ranged between 0 and 1. Doppler of each SIJ was considered as positive when RI was <0.75.

Results: Forty-three patients were included: 10 men and 33 women, with an average age at inclusion of 40.2 ± 11.1 years [17-59]. The mean duration of symptoms was 46±37.5 months [6.6-180]. A personal history of uveitis was noted in 3 patients and of chronic diarrhea in 3 patients. Morning stiffness was noted in 72% (n=31) of patients. Good response to nonsteroidal anti-inflammatory drugs (NSAIDs) and to physical activity were respectively reported by 41.8% (n=18) and 58% (n=25) of patients. Sacroiliac compression test, distraction provocative test, sacral thrust test, Gaenslen's test, Faber's test (Patrick) and Mennel's test were respectively positive in 39.5%, 32.5%, 48.8%, 23.2%, 32.5%, and 51.2% of the patients. Twenty-seven per cent of the patients were HLA-B27+. The MRI showed a confirmed sacroiliitis in 14 patients. Doppler signal was detected in 44 SIJ of 25 patients, of whom 14 SIJ of 8 patients showed bone marrow edema at MRI (p=0.054). At the joint level, considering MRI-proven sacroiliitis as the diagnostic standard, CDUS had a sensitivity of 70%, a specificity of 54.5%, a positive predictive value of 31.8%, and a negative predictive value of 85.7%. The spectral Doppler RI, averagely estimated at 0.74±0.12 [0.48-0.87], was not associated with the presence of sacroiliitis on MRI (p=0.747).

Conclusion: US, an imaging technique increasingly used in the assessment of musculoskeletal diseases, has been suggested to detect active sacroiliitis [1, 2]. Our study revealed that in early SpA, CDUS may be useful to assess active inflammatory changes of SIJ since it had a sensitivity of 70%, despite a relatively reduced specificity. However, RI values, which are expected to be low in patients with active inflammation [3], were unrelated to the presence of sacroiliitis. Future studies on larger numbers of patients might be conducted to complete previous data.

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AB1103

AUTOMATIC FINGER JOINT BONE EROSION SCORE PREDICTION CONSIDERING 2-TIME-POINT X-RAYS OF PATIENTS WITH RHEUMATOID ARTHRITIS BY DEEP LEARNING

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Background: Medical image analysis using deep learning (DL) has been attracting attention. In previous research, we proposed a DL method for detection of joint region and evaluation for bone destruction at a single point in time in hand X-rays of patients with rheumatoid arthritis (RA) [1-2]. However, in the score of van der Heijde-modified total Sharp scores (mTSS) in X-rays, it is difficult to apply the method as it is. In mTSS, score difference between 2-time points is important, and there is a problem that the score at each time varies depending on the doctor who evaluates.

Objectives: We aimed at developing an mTSS scoring method considering 2-time-point difference with a DL method.

Methods: A total of 104 X-ray image sets of both hands at two time points with an interval of ≥1 year were randomly obtained from patients with RA who had visited our clinic in 2015. Well-trained doctors determined the erosion scores of MP and PIP/IP joints of each hand in X-rays according to mTSS. These evaluations of hand joints were performed using our developed annotation software tool. In the learning phase, joint images were randomly divided into five sets for 5-fold cross-validation. We utilized a convolutional neural network model, such as SSD [3], for detecting joint regions and classifying the scores (Fig 1).

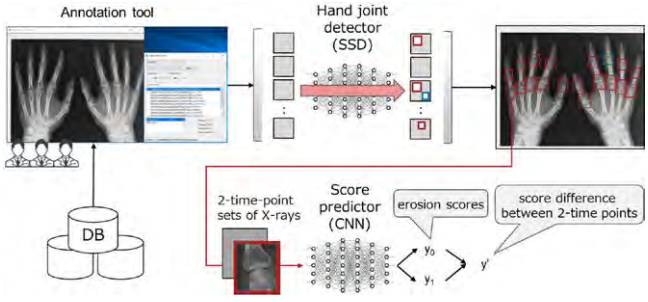


Figure1.

The models for classification were designed in consideration of the difference in erosion scores of each patient between the 2-time points of X-rays. The loss function of the DL model was defined bellow;

SCE: softmax cross entropy

MSE: mean squared error

t: training data

y: output of DL model

0: the former time point

1: the latter time point

T: transpose of matrix

Here, the coefficient γ is designed to reduce the error for another set of scores with equal differences. The first term of the loss function works to optimize the score at each time point, and the second term works to optimize the score difference at both time points. Thus, our method can be trained without being affected by characteristic training data.

Results: The number of joints with differences in erosion score between the former and latter time points was 1 (-2 points), 9 (-1), 2015 (0), 32 (+1), 17 (+2), and 6 (+3). There were no joints with score changes of -5, -4, -3, +4, and +5 points.

As a performance of predicting the difference in erosion score between the 2-time points of each patient's X-ray, our models presented a mean error of 0.412 per each joint in one set for 5-cross validation as compared with physicians' evaluation (Fig 2).

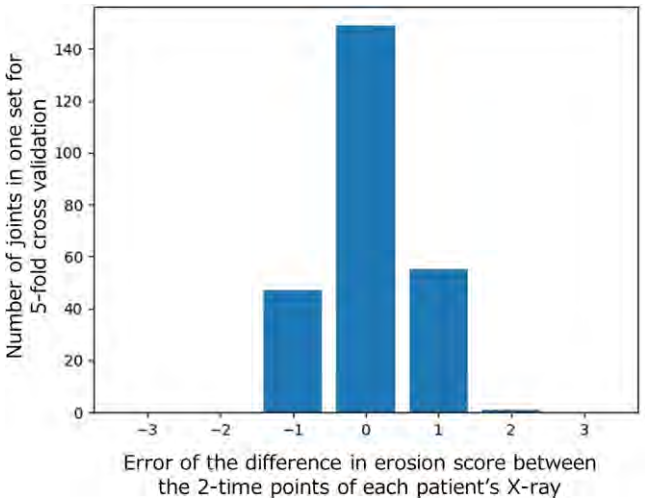


Figure 2.

Conclusion: Our DL-based models to predict hand joint erosion scores in X-rays were developed with relatively small samples. This suggests that the predictive performance may increase by collecting more training dataset. Next, we will apply our method to the prediction of joint space narrowing score.

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AB1104

ANALYSIS OF ANTINUCLEAR ANTIBODY TITERS AND PATTERNS USING HEP 2 INDIRECT IMMUNOFLUORESCENCE IN VARIOUS LIVER DISEASES

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Background: Abnormal liver function can be seen in not only hepatitis B virus infection (HBV), hepatitis C virus infection (HCV), hepatic carcinoma (HCC), but also in primary biliary cirrhosis (PBC), autoimmune hepatitis (AIH), and systemic autoimmune rheumatic diseases (SARD). Antinuclear antibody (ANA) testing using indirect immunofluorescence assay (IIFA) is a common and economical method which contributes to detect SARD and autoimmune liver diseases [1].
Objectives: Our objective was to investigate ANA positivity, titers and their patterns in multiple liver diseases, including PBC, AIH, HBV, HCV, and HCC, compared to healthy controls (HC).
Methods: 2537 patients with SARD, 137 PBC cases, 57 AIH cases, 3420 HBV cases, 769 HCV cases, 268 HCC cases, and 1073 HC were retrospectively assessed. The titers and patterns of ANA were detected with the IIFA method.
Results: ANA positivity rate was considerably discernible between these diseases, which is 90.1% in SARD, 93.4% in PBC, 49.1% in AIH, 19.1% in HBV, 13.9% in HCV and 23.5% in HCC. Moreover, only 4.9% of HCC cases, 2.5% of HBV patients and 1.6% of HCV patients had an ANA titer ≥ 1:320. The mixed pattern which composed of at least two patterns majorly lied in PBC. AC-15 and AC-21 was frequently related to liver diseases; the former pattern was more frequently found in AIH (84.2%) and PBC (8.8%), and the latter pattern was easily seen in PBC (62.2%) and HCC (22.6%). The positive rate of ANA in HC was 12.2% and its major pattern was AC-2.
Conclusion: There are differences in ANA positivity among patients with SARD and various liver diseases. Some mixed patterns may provide important evidence for the diagnosis of PBC. Clinicians should pay attention to ANA patterns and titer during the interpretation of this test.
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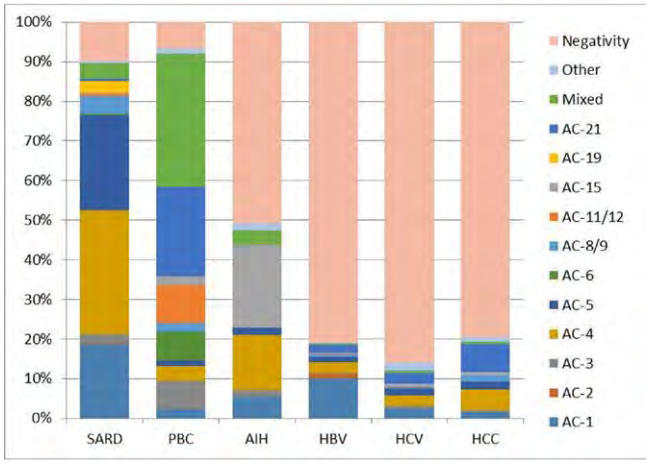


Figure 1. The Proportion of Each ANA Pattern Exhibited in Different Diseases and HCANA: antinuclear antibodies; HC: healthy controls; PBC: primary biliary cirrhosis; AIH: autoimmune hepatitis; SARD: systemic autoimmune rheumatic diseases; HBV: hepatitis B virus infection: HCV: hepatitis C virus infection: HCC: hepatic carcinoma.

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Disclosure of Interests: None declared
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AB1105

ASSOCIATION BETWEEN CAPILLAROSCOPIC ALTERATIONS AND ANGIOGENIC AND TISSUE REMODELING FACTORS IN PATIENTS WITH DERMATOMYOSITIS.

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Background: During last years we are seeking for new biomarkers of early or even preclinical diseases stages, precise definition of disease activity and accurate prediction of the disease course as well as biomarkers of treatment efficiency. Nailfold capillaroscopy (NFC) considering as a method for early or even preclinical diagnostic tool for systemic scleroderma, at the same time there is enough data that dermatomyositis (DM) characterized with similar NFC changes along with other idiopathic inflammatory myopathies (IIM) due to the peripheral vascular involvement.
Objectives: The goal of our research was aimed to analyze possible association between capillaroscopic alterations and angiogenic, tissue remodeling factors in patients with DM.
Methods: 44 patients with DM were examined and included in the study. NFC we performed using *Dino-Lite CapillaryScope with 200 magnification*. We assessed nailfold capillary density (NCD), presence of microhemorrhages, giant, dilated and ramified capillaries, scleroderma patterns (defined as an early, active or late pattern) and neovascular pattern (defined as an active and late scleroderma patterns). We use Manual Muscle Testing 8 (MMT8), Health Assessment Questionnaire (HAQ), Myositis Disease Activity Assessment Tool (MDAAT), Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI), physician's VAS, patient's VAS, serum muscle enzymes levels to asses disease activity. The level of transforming growth factor alpha (TGF-α) and vascular endothelial growth factor (VEGF) were assayed by the enzyme immunoassay system in the blood serum. We divided patients into 4 groups: 1st group – 17 DM patients with early NFC scleroderma pattern, 2nd group included 11 DM patients with active NFC scleroderma pattern, 3rd group – 6 DM patients with late NFC scleroderma pattern and 4th group included 10 DM patients with no any significant NFC alterations.
Results: We didn't find any significant difference of the VEGF level between examined groups, though the level of VEGF in the 1st group was – 473,65±48,24 pg/ml, 2nd – 412,89±106,24 pg/ml, 3rd – 283,0±71,93 pg/ml, 4th – 305,9±45,89 pg/ml (p=0,12, F=2,06), however at the same time we compare the level of VEGF between patients with long disease duration and newly onset disease and VEGF was higher among newly onset active DM patients – 465,32±54,54pg/ml VS 324,96±41,16 pg/ml (p=0,042, F=4,365). The level of TGF-α in the 1st group was 100,82±8,98 ng/ml, 2nd – 65,78±9,21 ng/ml, 3rd – 56,9±5,01 ng/ml, 4th – 65,5±10,2 ng/ml, though it was significantly higher in the 1st group patients (p=0,002, F=5,88).
Conclusion: According to our results we can assume that VEGF and TGF-α could be applied as biomarkers of disease activity and duration, however more data is required.
Disclosure of Interests: None declared
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AB1106

DO TENDER JOINTS IN PSORIATIC ARTHRITIS REFLECT INFLAMMATION ON ULTRASOUND?

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Background: Ultrasound (US) is a sensitive method for evaluating inflammation in arthritis, but several studies have shown discrepancies in inflammatory findings on US examination and clinically assessed disease activity, both in rheumatoid arthritis (RA) and psoriatic arthritis (PsA) (1, 2). In RA, a recent study found that swollen but not tender joints reflect synovitis detected by US (3). In PsA tenderness without joint swelling is a frequent finding.
Objectives: To investigate the agreement of clinical joint evaluation (swollen joints (SJ) and tender joints (TJ)) and US findings of inflammation in PsA assessing joints and periarticular tissue involvement (e.g. joint capsule, adjacent ligaments etc.).
Methods: We included 42 patients with active PsA (min. 3 swollen and tender joints) and hand involvement (min. 1 finger joint and/or 1 finger with dactylitis). All patients had US examination performed by one examiner (blinded to clinical data) using a high-end US scanner with a high-frequency 14 MHz linear transducer. 2-5th metacarpophalangeal- (MCP), proximal and distal interphalangeal (PIP and DIP) and 1-5th metatarsophalangeal (MTP) -joints were assessed by greyscale (GS) and power Doppler (PD) mode, bilaterally. Synovitis was scored for GS and PD change (0-3) according to OMERACT guidelines (4), PIP and DIP joints were additionally scored for volar synovitis (0-3) and presence of periarticular PD activity (PD activity in the joint capsule and/or adjacent structures). SJ (76) and TJ (78) counts were performed by an experienced rheumatologist blinded to US findings. As prevalence of lesions was low, agreement between TJ, SJ and US was calculated using the prevalence and bias adjusted Kappa

(PABAK) on dichotomized values (0-1 vs 2-3 for GS scores (based on the highest score for each joint), 0 vs. 1-3 for PD scores). US synovitis was defined as GS>1 and PD>0.

Results: Population characteristics and US findings are presented in table 1.

Table 1. Population characteristics

Sex (female)	18 (43)
Age (y)	49 (40-61)
Disease duration (y)	8.5 (5-15)
Swollen joints (76)	9 (5-16)
Tender joints (78)	22 (11-41)
Dactylitis (no. of patients with)	18 (43%)
Physicians global disease activity VAS	51 (38-64)
Patients global disease activity VAS	66 (66-78)
Patient Pain VAS	63 (49-74)
DAS28-CRP	4.8 (4.2-5.5)
CRP	4.6 (1.8-8.9)
US synovitis sum scores (0-102)	
GS	29 (21-38)
PD	2 (1-5)
US periarticular PD sum score (0-16) (PIP + DIP)	1 (0-3)

Median(IQR), no(%) VAS: Visual analogue scale (0-100). DAS28: Disease Activity Score 28 joint count CRP: C-reactive protein US: Ultrasound GS: Greyscale PD: PowerDoppler

Agreement between clinical and US joint evaluation is seen in table 2. There was poor agreement between TJ and US synovial hypertrophy and hyperaemia (PABAK 0.12 and 0.20, respectively) and fair agreement with periarticular PD (PABAK 0.25). Moderate agreement was found for SJ and intraarticular PD activity (PABAK 0.55). Our definition of US synovitis showed similar agreements with TJ and SJ as US hyperaemia.

Table 2. PABAK agreement of clinical examination and US findings.

	Swollen joint	US synovial hypertrophy (GS)	US synovial hyperaemia (PD)	US synovitis (GS>1, PD>0)	US periarticular PD	US synovial/ periarticular PD
No. of joints	3108	1428	1428	1428	672	672
Tender joint	0.53	0.12	0.20	0.20	0.25	0.20
Swollen joint		0.35	0.55	0.56	0.45	0.55

Prevalence and bias adjusted Kappa (PABAK) US: Ultrasound GS: Greyscale. PD: Power Doppler

Conclusion: In this study TJ did not reflect intra- or periarticular US inflammation in PsA patients. SJ had a better agreement with US findings of inflammation, especially PD, which is in line with previous RA studies.

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AB1107 DACTYLITIS IN PSORIATIC ARTHRITIS – PREVALENCE AND RELIABILITY OF ULTRASOUND PATHOLOGIES

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Background: Dactylitis is an important clinical feature in psoriatic arthritis (PsA). Early imaging studies indicated tenosynovitis and adjacent subcutaneous edema (SCE) as the main components in dactylitis, but more recent ultrasound (US) studies have found involvement of many other structures including synovitis and enthesitis (1). To date, there is no consensus on which US elementary lesions constitutes dactylitis.

Objectives: To investigate by US the prevalence of different elementary lesions found in dactylitis in PsA, and the reliability of scoring these lesions in a clinical setting.

Methods: In a cross-sectional study 31 patients with PsA and dactylitis were included from a rheumatology out-patient clinic. The most affected digit in each patient was examined both dorsal and volar, in longitudinal and transversal plane, using greyscale (GS) and color Doppler (CD) US with a 6-15 MHz linear transducer. One examiner scanned all patients and a 2nd examiner scanned 10 patients for inter-reader reliability. 1st examiner re-read images after appr. 3 weeks for intra-reader reliability. Following pathologies were scored: 1. SCE (hypo- or anechoic areas in the subcutaneous tissue, with/without hyperemia) 2. Soft tissue thickening 3. Synovitis of the metacarpophalangeal (MCP) or metatarsophalangeal (MTP), proximal interphalangeal (PIP), distal interphalangeal (DIP) or interphalangeal (IP) joints 4. Tenosynovitis of the flexor tendon and 5. Enthesitis at the deep flexor tendon (FT) and the extensor tendon (ET) entheses 6. Paratenonitis of the ET (hypoechoic area and CD around the ET). OMERACT US definitions and scoring were used for synovitis, tenosynovitis and enthesitis.

Results: Patients were 55% males, with short disease duration (median (interquartile range (IQR)) 1(0-6) year) and moderate disease activity (median (IQR) DAS28 3.2(2.4-4.5). 45% of the examined digits were fingers, 55% toes. 74% were tender, 26% non-tender. US findings and intra- and inter-reader agreements are presented in table 1. Intra- and inter-reader agreements were moderate to excellent, except for some entheses due to low prevalence of findings. Therefore, the prevalence and bias adjusted Kappa was used for these. All pathologies were found primarily in combinations, most commonly SCE and synovitis (71%), followed by SCE and flexor tenosynovitis (52%), and all three in combination (52%). No patient had flexor tenosynovitis as a sole component. No significant difference was found in tender vs. non-tender dactylitis.

Table 1. US findings and intra/inter-reader agreement using different Kappa statistics[$]

	GS +/-		GS 0-3		CD +/-		CD 0-3	
	n (%)	K*	grade	K**	n (%)	K*	grade	K**
Subcutaneous edema	23 (74)	1 / 1			17 (55)	0.8 / 0.7		
Soft tissue thickening	25 (81)	1 / 1						
Flexor tenosynovitis	16 (51)	0.9 / 1	2 (2-2)	0.9 / 0.9	14 (45)	0.9 / 1	2 (2-3)	1 / 0.9
Synovitis		K*		K**		K*		K**
MCP/MTP	21 (68)	0.9 / 0.6	2 (1-2)	1 / 0.5	5 (16)	1 / 1	2 (2-2)	1 / 1
PIP (n=27)	15 (56)	1 /0.7	2 (1-3)	1 / 0.7	9 (33)	0.9 / 0.5	2 (2-2)	1 / 0.7
DIP/IP	19 (61)	0.9 / 1	2 (2-3)	0.9 / 0.9	9 (29)	0.8 /1	2 (2-2)	0.9 / 1
Enthesitis	Any sign		Inflammatory^		Structural'			
		K#		K#		K#		
Deep flexor tendon	14 (47)	0.7 / 0.6	11 (36)	0.8 /0.7	12 (39)	0.8 / 0.7		
Extensor tendon PIP (n=27)	14 (52)	0.6 / 0.3	12 (39)	0.8 / 0.5	6 (22)	0.9 / 0.8		
Extensor tendon DIP/IP	9 (29)	0.9 / 0.4	8 (26)	1 / 0.7	7 (23)	0.9 / 0.8		
	GS + CD							
		K*						
Paratenonitis	10 (32)	0.7 / 0.4						

Values are prevalence (n (%)) and grade (median (IQR)). $: Cohen's Kappa (K*) or PABAK (K#) for binary outcomes, weighted Kappa (K**) (squared weights) for continuous outcomes. GS: Greyscale, CD: Color Doppler ^Inflammatory: Thickened, hypoechogenic or CD activity. 'Structural: Enthesophytes/calcifications or erosions.

Conclusion: In this US study dactylitis in PsA was found to represent several pathologies, most often subcutaneous changes in combination with synovitis and/or flexor tenosynovitis. Reliability of scoring pathologies of dactylitis in a clinical setting is overall good.

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Novartis, Novo Nordisk, Orion, Pfizer, Regeneron, Roche, Sandoz, Sanofi, and UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo Nordisk, Orion, Pfizer, Regeneron, Roche, Sandoz, Sanofi, and UCB, Inge Juul Sørensen: None declared, Lene Terslev Speakers bureau: LT declares speakers fees from Roche, MSD, BMS, Pfizer, AbbVie, Novartis, and Janssen.
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AB1108 ANALYSIS OF HOMOGENOUS PATTERN IN ANTI-NUCLEAR ANTIBODY-INDIRECT IMMUNOFLUORESCENCE ASSAY

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Background: Autoantibodies that produce the homogenous pattern on anti-nuclear antibody-indirect immunofluorescence (ANA-IIF) assay using human epithelial cell (HEp-2) substrate are histones, dsDNA and nucleosome. Homogenous pattern may be seen in patients with many different systemic autoimmune diseases as well as organ-specific autoimmune diseases. Homogenous pattern is difficult to distinguish from dense fine speckled (DFS) pattern and other staining pattern may be masked by homogenous pattern.
Objectives: The purpose of this study was to analyze the profile of autoantibodies in patients with homogenous pattern on IIF-ANA assay and to find out the clinical significance of homogenous pattern.
Methods: A total of 103 sera samples with homogenous pattern on IIF-ANA assay were obtained. The IIF-ANA assay was performed using the PhD system (Bio-Rad Laboratories, Hercules, CA, USA) with Kallestad HEp-2 slides (Bio-Rad Laboratories). EliA CTD Screen and EliA dsDNA (Thermo Fisher Scientific, Freiburg, Germany) were performed using the Phadia 100 system (Thermo Fisher Scientific). EliA CTD Screen has following specific antigens: U1RNP (RNP70, A, C), SS-A/Ro (60 kDa, 52 kDa), SS-B/La, Centromere B, Scl-70, Jo-1, fibrillarin, RNA Pol III, ribosomal P-protein, PM-Scl, PCNA, Mi-2, Sm, and native purified DNA. Specific autoantibody tests against histone and nucleosome assay were performed using Euroimmun microplate ELISA (Euroimmun AG, Luebeck, Germany). Western blot (WB) assay was performed to confirm the presence of anti-DFS70 using HeLa whole-cell lysates as previously described. Clinical information regarding the presence of autoimmune diseases and other clinical conditions of individual patients was obtained from a retrospective review of clinical records.
Results: Of the 103 patients with homogenous pattern on IIF-ANA assay, 21 were diagnosed as systemic autoimmune rheumatic disease (SARD) or organ-specific autoimmune diseases (autoimmune group), whereas 82 were not patients with autoimmune diseases (non-autoimmune group). Among 103 patients, 51 patients (49.5%) were negative on all autoantibody tests performed in this study: CTD screening assay and specific autoantibody tests against anti-DFS70, dsDNA, histone, and nucleosome. The detection rates of autoantibodies were 10.7% for dsDNA, 15.5% for histone, and 19.4% for nucleosome. Total of 32 patients (31%) were positive in at least one of dsDNA, histone, and nucleosome autoantibodies. The detection rate of CTD screening assay was 31.1% (32/103). Of 32 CTD screening positive patients, 18 (56%) were positive and the remaining 14 (44%) were negative on dsDNA, histone or nucleosome. Anti-DFS70 antibody was detected in 6 patients (5.8%) and they have no other autoantibodies. At least one of dsDNA, histone, and nucleosome autoantibodies were positive in 42.9% (9/21) of autoimmune group and 28% (23/82) of non-autoimmune group. Positive result on CTD screening was found in 38.1% (8/21) of autoimmune group and 23.2% (19/82) of non-autoimmune group.
Conclusion: It is generally accepted that homogenous pattern is caused by antibodies against dsDNA, histone and nucleosome and have a clinical relevance with SLE, chronic autoimmune hepatitis, and juvenile idiopathic arthritis. However, the results of this study found that the majority (79.6%) of patients with homogenous pattern had no autoimmune diseases and only 31% had autoantibodies to dsDNA, histone or nucleosome. Especially 49.5% of patients were all negative for autoantibodies included in CTD screening assay as well as autoantibodies responsible for homogenous pattern such as autoantibodies against dsDNA, histone, and nucleosome. This suggests that homogenous pattern may be originated by autoantibodies that cannot be identified by conventional test methods.
Disclosure of Interests: None declared
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AB1109 THE TIME-TO-EVENT ANALYSIS OF THE APPLICATION OF ULTRASOUND TO DISTINGUISHING PMR

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Background: Japan is the world's most aged country. The number of patients with polymyalgia rheumatic (PMR) is expected to increase more.
Classification criteria including ultrasound findings were published in 2012(1), but the ability to differentiate PMR from other mimicking diseases was unknown.
It is difficult to diagnose PMR accurately. We will clarify whether recently reported ultrasound findings (2, 3) which could be characteristic in PMR are helpful for distinguishing from other mimicking diseases and treatment outcome in suspected PMR patients. Neither diagnostic laboratory test nor specific antibody exist, and inflammatory markers such as C reactive protein and erythrocyte sedimentation rate are not specific.
Objectives: Patients who were clinically suspected of PMR and underwent ultrasound examination from 2008 to 2018. And Patients who visited the hospital with PMR and were diagnosed with PMR from 2008 to 2018.
Methods: Patients who visited the hospital and were diagnosed with PMR were extracted from the medical record database of the hospital. Patients who had been administrated GC at the first visit and whose records were not confirmed were excluded. Patients who were clinically diagnosed with PMR without ultrasound(Cli-PMR), patients who were diagnosed with PMR with ultrasound reports(US-Cli-PMR), patients who were diagnosed by the ultrasound expert only based on ultrasound images(US-PMR).
Patient were followed up for one year. Clinical diagnoses were confirmed at the 6 months and 12 months since the first GC administration.
Three groups were compared with each other in the rate of diagnosis change and the time intervals between the initiation of GC treatment and the occurrence of events: recurrence, methotrexate introduction and the normalization of C reactive protein.
the Kaplan–Meier method was used to evaluate the outcomes. Statistical analyses were conducted with R software, version 3.5.2 (R Foundation for Statistical Computing) and EZR(4).
Results: 545 PMR patients were extracted. 403 of 545 was excluded because of preexisting GC therapy and record availability.
At the 6 months follow-up, 92.8% of the non-US PMR group and 97% of US-PMR group remain PMR and at the 12 months follow-up 88.8% and 95% respectively. There was no significant difference in the three time-to-event outcomes.
Conclusion: Ultrasound did not contribute the improvement of the PMR outcomes. However, this finding was affected by confounding factors for example assignment to ultrasound and atypical cases and rheumatologists' uncertainness. Despite confounding factors, US-PMR group was not inferior. These findings showed that ultrasound may be useful for the complicated cases.
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Disclosure of Interests: None declared
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AB1110 QUANTUM BLUE® RAPID TDM ASSAY STANDARDIZATION HIGHLY CORRELATES WITH WHO INTERNATIONAL STANDARD FOR INFLIXIMAB

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Background: Therapeutic drug monitoring of RA patients under anti-TNF therapy is based on trough level determination of the drug. Rapid assays and multiple ELISAs are available that measure anti-TNF biologics. An international standard is required to improve comparability among different assays. Recently, WHO introduced a series of anti-TNF standards for etanercept, adalimumab and infliximab. This is the first step for achieving common standardisation of assays available on the market.
Objectives: The aim of the study was to evaluate the correlation of the WHO standard with BÜHLMANN Quantum Blue® Infliximab standardization and to compare spiking recovery in three commercially available infliximab ELISAs and one infliximab rapid test.
Methods: Calibration curves were generated with BÜHLMANN calibrators and with calibrators made from WHO international standard for infliximab (NIBSC 16/170). Twenty-six serum samples, covering a concentration range from 0.5 µg/mL to 19 µg/mL, were analyzed with both calibration curves and compared by Bland-Altman and Passing-Bablok analysis. Furthermore, recovery of six serum samples spiked with WHO international standard for infliximab was determined in Theradiag LISA TRACKER Infliximab (a), Grifols/Progenika Promonitor-IFX (b), Immundiagnostik IDKmonitor Infliximab drug level (c) and BÜHLMANN Quantum Blue® Infliximab (d). Spiking recovery experiments were performed according to Westgard 2008.

Results: The sample values gained with BÜHLMANN calibrators showed an excellent correlation with values gained with the WHO international standard for infliximab as calibrator. Passing-Bablok regression analysis revealed a slope of 0.96 and correlation coefficient (R) of 0.99. Bland-Altman analysis revealed a mean difference in the obtained values of less than five percent. Regarding spiking recovery analysis, all tests exhibit an excellent mean recovery of 101% (85-114%; a), 99% (91-105%; b); 101% (95-107%; c) and 94% (88-100%, d).
Conclusion: Current standardization of Quantum Blue® Infliximab rapid test correlates very well with the WHO international standard for infliximab (NIBSC 16/170). Spiking recovery was highly comparable for ELISAs and the Quantum Blue® Infliximab assay. This rapid test represents a unique and modern analytical method, for fast time-to-result and simplicity of usage in a more patient near medical environment.
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[1] Westgard, James. (2008). Basic Method Validation.
Disclosure of Interests: None declared
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AB1111 PREDICTIVE VALUE OF FLUORESCENCE-OPTICAL IMAGING TECHNIQUE IN DETECTION OF PSORIATIC ARTHRITIS IN PSORIASIS PATIENTS

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Background: Psoriasis (Pso) is one of the most common chronic inflammatory skin diseases in Europe. Psoriatic arthritis (PsA) is closely associated to Pso whereas the skin manifestation appears usually years before PsA-related symptoms emerge. Up to 30% of Pso patients develop PsA, but there is no clear correlation between disease duration of Pso and PsA development. Therefore, biomarkers for its early detection are of major importance. In early PsA, changes in synovial vascularisation combined with increased expression of proangiogenic factors appear first. Therefore, imaging biomarkers for detection of changes in vascularisation might be useful for early detection of musculoskeletal disease. Fluorescence-optical imaging (FOI) is a new method to detect changes in microvascularisation of the hands.
Objectives: To determine the number of positive PsA diagnosis within a 24 month follow-up period in PsO only patients with subclinical MSK-inflammation detected in FOI.
Methods: Sensitivity of FOI for detection of subclinical signs of musculoskeletal inflammation as biomarker for early PsA was observed in a prospective, multicentre study (XCITING) including patients with dermatological confirmed skin psoriasis. 411 patients were included from dermatology care units across Germany without diagnosis of PsA but potential risk factors for its development (nail psoriasis and/or joint pain or swelling within the last 6 months). Clinical examination (CE; swollen (66) and tender (68) joint count, enthesitis, dactylitis assessment) and standardised ultrasound (US) assessment was performed by a qualified rheumatologist to assess musculoskeletal inflammation. FOI was performed additionally. Data was analysed in focus on increased vascularisation of musculoskeletal structures as inflammatory markers. In case of discrepant results (positive FOI and negative CE and US), MRI was performed to prove the findings. In case of MRI negativity, a follow-up period of 24-months was performed including FOI, CE, US and MRI assessment.
Results: 83 of the 411 patients of the cohort were negative in all assessments (Pso only), 136 of the 411 patients were classified as PsA by rheumatologic assessments. 119 patients showed subclinical signs of musculoskeletal inflammation in the central reading of FOI, whereas CE and US were negative. In 37,5% of those patients, subclinical inflammation was confirmed by MRI assessment. 22 patients of the cohort without MRI positivity were willing to be followed up until month 24. 5 (7.5%) patients developed a clinical PsA until month 24 whereas 7 (10.5%) patients converted to be FOI negative. In 5 patients an additional MRI examination was performed in which one patient showed positive signs for inflammation.
Conclusion: FOI is an innovative method for measurement of changes in microvascularisation in the hands. 6/22 patients initial only positive in FOI (no clinical signs for PsA, negative US, negative MRI) developed either clinical evident PsA (n=5) or new inflammation in MRI (n=1) during follow-up of 24 months. Therefore, FOI positive signals in PsO patients increase the probability for PsA development.

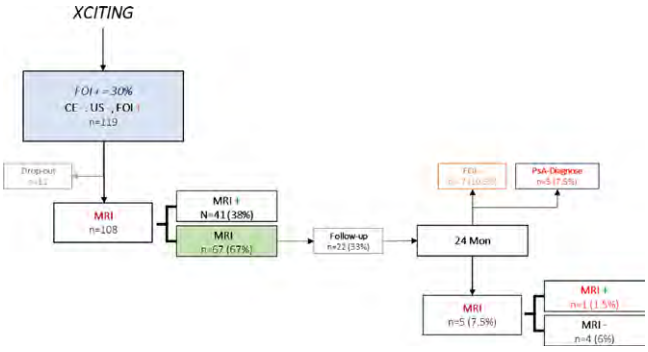


Figure 1. Flow Chart of the Follow-up period of the XCITING study.

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AB1112 THE DIAGNOSTIC OF THE OSTEOARTHRITIS OF THE HANDS BY CONVENTIONAL RADIOGRAPHY

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Background: The most severe phenotype of osteoarthritis (OA) is currently considered to be an inflammatory or erosive phenotype (EOA). There is currently no reliable x-ray picture of this disease in the literature, and the question of whether it is an independent form of OA, a natural more pronounced stage of progression, or a separate nosology is debated in the literature.
Objectives: To identify the localization, frequency, and severity of pain and radiological symptoms in patients with EOA and non-erosive (NOA) disease in the interphalangeal (DIP and PIP) and metacarpal (MCP) joints of the hands.
Methods: 64 women with diagnosis of OA of the hand (HOA) joints according to the ACR criteria were included into study after signing the informed consent form. Mean age was 65.28 ± 6.82 years (48-77), mean BMI 27,7 ± 4,4 kg/m^2, mean disease duration 12 ± 8,1 years. Individual patient's medical record included relevant anthropometric data, records from case history and clinical examination, AUSCAN scores, patient's articular status. Instrumental diagnostic methods included plain radiography of the hand joints in an anterior-posterior projection. The images were described in accordance with the Kellgren&Lawrence (K&L) system.
When evaluating radiographs of 64 patients with HOA, the most common was stage II (49%) according to K&L, and the most common symptoms in distal (DIP), proximal (PIP) interphalangeal and MCP were joint space narrowing (JSN) (100%, 100%, and 95%, respectively) and osteophytes (OP) (88%, 70%, and 45%, respectively). Subchondral osteosclerosis (SO) (5%), erosions (8%), and subluxations (3%) in MCP, as well as subluxation in PIP (6%) were less common. Statistica 10.0 was used for statistical analysis.
23 patients had EOA, 37 had NOA. Depending on the presence of erosions in interphalangeal joints patients were divided into 2 groups comparable in terms of age, age of OA onset and duration of disease (the average age of patients with EOA interphalangeal joints was 68 + 6.15 years, and mean disease duration 18,34 + 7.11 years; in the group without erosive changes in the average age amounted to 65,13±5.43 years, mean disease duration of 16.56±8.4 years).
Results: EOA DIP and PIP was detected in 15 (23%) with radiological changes corresponding to stages III-IV of HOA and in 8 people (12%) with stage II on

the K&L scale. Patients with stage I according to standard radiography had no erosive process.

In DMFs OP (100% and 78%, OR=1.28, 95%, CI [1.08-1.5], p=0.02), SO (74% and 11%, OR=6.8, 95%, CI [2.6-17.8], p<0,0001), subchondral cysts (SC) (61% and 24%, OR=2.5, 95%, CI [1.3-4.82], p=0.005) and subluxations (43% and 14%, OR=3.2, 95%, CI [1.3-8.23], p=0.01) were significantly more often found in patients with EOA. In PIPs SO (43% AND 5%, OR=8.04, 95%, CI [1.93-33.5], p=0.0005), SC (52% and 27%, OR=1.93, 95%, CI [0.1-3.73], p=0.045) and subluxations (17% and 0%, p=0.01) were significantly more frequently detected in patients with EOA compared to the non-erosive group. According to the results of the AUSCAN questionnaire, a significantly greater severity of pain was found in patients with EOA (65%) in comparison with the non-erosive (30%) form of HOA (OR=2.19, 95%, CI [1.23-3.9], p=0.008).

Conclusion: DIPs is most often affected in OA of interphalangeal joints, less often PIPs, the most common symptoms are JSN and OP. At EOA in addition to more frequent detection OP, cysts, SO, subluxations in DIPs, SO, cysts and subluxations in PIPs, there is also significantly more pronounced pain according to AUSCAN data, it can be concluded that EOA is more severe in comparison with the non-erosive form of HOA.

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AB1113 DIAGNOSTIC VALUE OF ANTI-SA AND ANTI-HN RNP K ANTIBODIES IN SERONEGATIVE RHEUMATOID ARTHRITIS

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Background: The diagnostics of seronegative rheumatoid arthritis (RA) remains the important issue in modern rheumatology. Other biomarkers are studied to close the diagnostic gap.

Objectives: The aim of work was to assess anti-Sa and anti-hnRNP K in patients with RA and to evaluate their diagnostic value in seronegative by anti-CCP and RF RA.

Methods: In the study were included 270 patients, which fulfill EULAR/ACR 2010 criteria for RA and 50 healthy controls. The mean of patients age was 52.80 (95% CI:51.70-54.80 years).

Levels of antibodies to anti-CCP and anti-Sa were evaluated by ELISA according to the instructions of the manufacturer (Euroimmune, Germany), anti-hnRNP K according to the instructions of the manufacturer ((Medipan, Germany). Levels of rheumatoid factor (RF) were assessed by kinetic nephelometry using an automatic analyzer Beckman Coulter (USA).

Results: Anti-CCP in patients were found 209 (77.41%) patients, RF - in 192 (71.11%) patients, anti-Sa – in 163 (60.37%) patients, anti-hnRNP K – in 63 (23.33%) patients. The incidence of Anti-CCP, RF, anti-Sa, anti-hnRNP K in RA was significantly higher (p<0.05) than in healthy individuals (0 (0%), 0 (0%), 1 (2.00%), 0 (0%) respectively).

The diagnostic sensitivity and specificity of anti-Sa to discriminate seronegative by anti-CCP and RF RA patients from healthy controls by ROC – analysis were determined and made up for anti-Sa - 50,00% (95%CI: 26.1 – 73.9) and 96.77% (95%CI: 83.2 – 99.5) respectively (area under ROC-curve 0.734; 95%CI: 0.588-0.850, p=0.0026), for anti-hnRNP K - 55,56% (95%CI:35,3 - 74,5), 100,00% (95%CI: 95,7 - 100,0) respectively (area under ROC-curve 0.778; 95%CI: 0.689-0.851, p=0.0001). There were no significant differences in clinical (DAS 28, CDAI, SDAI, treatment options) and laboratory characteristics (ESR, CRP, anti-CCP, RF levels) between anti-Sa-positive and anti-Sa-negative patients (p>0.05) as well as between anti-hnRNP K-positive and anti-hnRNP K-negative patients (p>0.05).

Conclusion: Anti-Sa and anti-hnRNP K may serve as potential additional laboratory biomarkers for seronegative RA to allow to close the seronegative RA gap and confirm the diagnosis of RA.

Disclosure of Interests: None declared

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AB1114 HANDWORK VS MACHINE; A COMPARISON OF RHEUMATOID ARTHRITIS PATIENT POPULATIONS AS IDENTIFIED BY MACHINE-LEARNING AND CRITERIA-BASED CHART REVIEW.

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Background: Electronic Medical Records (EMRs) offer a magnitude of observational data which is currently often manually reviewed to identify patient cases. Machine-Learning (ML) methods are highly efficient tools for data extraction, being able to process the information-rich free-text physician notes from EMRs. [1]

We postulate that incorporating this data into an ML pipeline, will enable the high-throughput identification of RA case cohorts qualitatively equal to conventional EULAR/ACR criteria based chart review.

Objectives: To investigate the comparability of Rheumatoid arthritis (RA) cases identified through EMR free-text enriched machine-learning algorithms to the field's gold-standard (GS) of criteria based chart-review.

Methods: We developed a classification algorithm using a Support Vector Machine (SVM) trained on 1000 manually reviewed patient EMRs and validated on a separate 1000 records. [2]

The SVM assigns a probability of being an RA case to each patient at a speed of >5000 records per second. The probability cutoff for case identification can be tailored to studies' needs, optimizing on sensitivity, specificity, etc. We optimized on PPV, resulting in a cutoff of 0.48 with a PPV of 0.96.

We used the 1987 and 2010 EULAR/ACR criteria based diagnoses of RA at one year after inclusion in a prospective arthritis cohort as GSs and compared the baseline characteristics of ML identified RA cases with both GSs separately and for those fulfilling at least one set of criteria using Pearson chi-squared and Mann-Whitney U tests ($\alpha = 0.05$).

Results: At the 0.48 cutoff the ML model performs very well on the annotated set and when compared to criteria based GSs. (Table 1)

Table 1. Performance of ML-model in the annotated data † (N = 1000) predicting cases and 1987, 2010 or either criteria based data * (N = 1235, 1218 & 1244 respectively) predicting cases (prob. ≥ 0.48). TP; True Positive, FP; False Positive, TN; True Negative, FN; False Negative, PPV; Positive Predictive Value, NPV; Negative Predictive Value, Spec; Specificity, Sens; Sensitivity

	Accuracy	PPV	NPV	Spec	Sens
Annotated Cases†	0.98	0.96	0.98	1.00	0.74
Criteria Definite Cases 1987*	0.82	0.79	0.83	0.92	0.61
Criteria Definite Cases 2010*	0.78	0.81	0.77	0.93	0.55
Either Criteria Cases*	0.76	0.90	0.72	0.95	0.51

Since patients diagnosed with RA do not necessarily meet classification criteria, it is not surprising that the ML cases and GSs do not completely overlap. The ML cases overlap to a larger degree with the 1987 GS than with the 2010 GS. Clinically, the ML identified cases do not differ from the 2010 and 1987 GS cohorts except for a slightly higher CCP2 positivity compared to the 1987 GS (65 vs 51%) and the combined criteria (65 vs 56%). (Table 1 & 2)

Conclusion: ML algorithms processing clinician notes enable fast and efficient selection of cases that are clinically similar to cases selected by criteria based chart review. This allows a significant reduction of time and effort required to construct high quality research cohorts.

Table 2. Comparison of baseline characteristics between 3 ML defined cohorts and a criteria based gold standard. † Not statistically tested; * significantly different to the ML selected cases at α = 0.05, Pearson Chi-Squared for proportions, Mann-Whitney U for medians

	Predicted Definite Case	1987 Criteria Based Case	2010 Criteria Based Case	Either Criteria Based Case
N†	335	399	609	666
Proportion Women	0.67	0.63	0.65	0.65
Proportion CCP2 Positive	0.65	0.51*	0.61	0.56*
Proportion RF positive	0.67	0.60	0.69	0.64
Median BMI	26.0	25.5	25.6	25.6
Median BSE	28	29	26	26
Median CRP	9.6	11	9	9
Median Age at Inclusion	57.7	58.7	57.2	58.3
Median Symptom Duration at Diagnosis (in Days)	95.5	90	91	89
Median Number of Swollen Joints	5	6	6	5

References:

[1] Maarseveen et al. ARD 2019;78

[2] https://github.com/levrex/DiagnosisExtraction_ML

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AB1115 REAL-WORLD NAILFOLD VIDEOCAPILLAROSCOPY IN A REFERRAL CENTER IN NORTHWESTERN COLOMBIA: A RETROSPECTIVE COHORT STUDY

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Background: Nailfold videocapillaroscopy is a non-invasive tool for the assessment of peripheral microcirculation, and it is useful for the diagnosis and prognosis of systemic autoimmune diseases. Despite its frequent use in clinical practice, the indications of this procedure are not standardized and there is no clear information in real-life about the reasons for remission, the presence of clinical findings of autoimmune diseases during the procedure, the frequency of patterns of autoantibodies and specific capillaroscopic findings.
Objectives: To describe the sociodemographic, clinical, paraclinical, and capillaroscopic findings of a cohort of subjects referred to a capillaroscopy service in northwestern Colombia.
Methods: We conducted a retrospective cohort study, including subjects from 2015 to 2018. Patients were evaluated by two expert rheumatologists. Variables: Reasons for referral, capillaroscopic patterns at baseline and at 6-month follow-up, presence of clinical findings of systemic autoimmune diseases during the procedure (Raynaud´s phenomenon, puffy fingers, sclerodactyly, pitting scars, digital ulcers, sclerosis cutis, platysma sign, Gottron, and microstomy), along with the pattern and dilution of antinuclear antibodies. Categorical variables were expressed in frequency and percentage and quantitative variables in mean and standard deviation or median with interquartile range, depending on the distribution of the data. Statistical package: SPSS 25. This survey was approved by the institutional Ethics Committee.
Results: A total of 392 capillaroscopies were performed, 318 for the first time. The referral reasons for capillaroscopy were: Raynaud`s phenomenon (n=134; 42.1%), connective tissue disease different than systemic sclerosis (SSc) (n=105; 33.1%), and systemic sclerosis (n=79; 24.8%). The baseline capillaroscopic patterns found were: Normal (n=123; 38.7%), non-specific (n=81; 25.5%), SSc (n=90; 28.3%), scleroderma-like (n=24; 7.5%). Among SSc pattern, early (21/90; 23.3%), active, (38/90; 42.2%), and late patterns (31/90; 34.4%) were found. Of the 12 capillaroscopies that presented a non-specific pattern at 6-month follow-up, only one (8.3%) progressed to a systemic sclerosis pattern. In the SSc patterns, the frequency of clinical findings were: sclerodactyly (n=34; 37.8%), Raynaud`s phenomenon (n=26; 28.9%), puffy fingers (n=10; 11.1%), platysma sign (n=10; 11.1%), pitting scars (n=8; 8.9%), digital ulcers (n=8; 8.9%), telangiectasia (n=7; 7.8%), microstomy (n=4; 4.4%), and Gottron (n=1; 1.1%). In the SSc patterns, 42/44 subjects (95,4%) had positive antinuclear antibodies in an mean dilution of 1:320; the most frequent patterns were: centromere (n=27; 64.3%) and nucleolar (n=6; 14-3%).
Conclusion: In a real-world setting, the main referral reason to a capillaroscopic center was Raynaud`s phenomenon; more than a third of the subjects had normal capillaroscopic findings; in the subgroup of baseline non-specific pattern, most of them were normal during follow-up; sclerodactyly and Raynaud`s phenomenon were the most frequent clinical findings in patients with systemic sclerosis capillaroscopic patterns.
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[2] Fichel F, et al. Dermatology. 2014;228(4): 360-7
Acknowledgments: School of Health Sciences. Universidad Pontificia Bolivariana. Clinica Universitaria Bolivariana. Medellin, Colombia
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AB1116 DOPPLER EVALUATION OF ENTHESITIS SEEMS TO BE A RELEVANT OUTCOME IN THE ASSESSMENT OF ACTIVITY IN SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS

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Background: The assessment of activity in spondyloarthritis (SpA) and psoriatic arthritis (PsA) involves several domains, including enthesitis. Clinical enthesitis evaluation has shown low sensitivity, specificity and reliability. Ultrasound (US) examination of enthesitis can be an accurate and objective way to evaluate this domain, supporting its inclusion in the assessment of the global state of the disease
Objectives: The main objective of this study is to analyze de prevalence of Doppler enthesitis in active SpA and PsA patients and to evaluate its association with the disease activity at patient level prior to start a biological therapy
Methods: A prospective multicenter cross-sectional study in patients with SpA and PsA with active disease (defined as patients who were going to start or switch biological therapy according to physician criteria and in agreement with clinical guidelines) was undertaken. Basal assessment included clinical features, physical examination and laboratory tests. Patients underwent bilateral US examination of peripheral entheses according to the MAdrid Sonographic Enthesitis Index (MASEI). MASEI and Outcome Measures in Rheumatology (OMERACT) enthesitis Power Doppler (PD) definitions were checked. Each enthesis was scanned in two planes: longitudinal and transverse, and 5 second videos were recorded for reliability. An inter-reader analysis by three readers was performed at each included center. For statistical analysis Mann-WhitneyU and Kruskal-Wallis tests were used. Intraclass correlation coefficient (ICC) and kappa test were used for reliability
Results: 64 consecutive patients were included, of whom 19(29.7%) were ankylosing spondylitis (AS), 7(10.9%), non-radiographic axial spondyloarthritis (nr-axSpA) and 38(59.4%) PsA patients. Mean age was 52.4±12.5 years and 36(56.3%) were males. Mean DAS28 (3.6±1.3) for peripheral involvement, mean BASDAI (5.6±2.2) for axial involvement, and CRP values (10±10.9) reflect moderate-high disease activity at baseline. Demographic, clinical and MASEI baseline characteristics are shown in Table 1. Mean global MASEI score was 29.4 (±11.4) and 55 patients (86%) scored ≥18 (proposed cut-off point to diagnose SpA). At the patient level, abnormal US findings consistent with at least one enthesis showing PD signal were observed in 52(81.3%) of patients using MASEI PD and 48(75%) using OMERACT PD definition without significant variation among the different SpA subtypes (p=0.8 and p=0.6, respectively). The inter-reader reliability among the two cohorts from each center performed by three readers was high (ICC cohort 1:0.92; cohort 2:0.85) and inter three readers kappa was good (0.92 and 0.86 for Doppler MASEI and Doppler OMERACT respectively).

Table 1. Baseline characteristics of SpA and PsA patients

	Total n= 64	AS n=19 (29.7%)	PsA n=38 (59.4%)	nr-axSpA n=7 (10.9%)	p
Age	52.4±12.5	50.3±14.5	54.6±11.6	46.3±9.9	0.2
Sex (Male)	36 (56.3%)	10 (52.6%)	23 (60.5%)	3 (42.9%)	0.6
CRP (mg/L)	10±10.9	13.7±11.4	9±10.9	6.8±9.1	0.3
VSG (mm/h)	17.3±15	12.6±7.5	20.6±18	11.9±4	0.4
DAS28 n= 40	3.6±1.3	3.1±1.1	3.9±1.3	3.2±1.4	0.2
BASDAI n=23	5.6±2.2	5.3±2.5	5.4±0.8	6.9±0.9	0.2
MASES n=26	1.1±1.5	1.1±1.6	-	1.1±1.3	0.9
MASEI	29.4±11.4	29.1±9	30±12.8	26.7±10.4	0.9
MASEI score ≥18	55 (85.9%)	18 (94.7%)	32(84.2%)	5(71.4%)	0.3
Mean number of enthesis with PD OMERACT	1.6±1.4	1.7±1.3	1.5±1.5	1.6±1.7	0.6
Mean number enthesis with PD MASEI	2.1±1.7	1.9±1.4	2.2±1.8	1.7±1.7	0.8
PD OMERACT ≥1	48 (75%)	15(78.9%)	28(73.7%)	5(71.4%)	0.9
PD MASEI ≥1	52 (81.3%)	15(78.9%)	32(84.2%)	5(71.4%)	0.7

Conclusion: PD enthesitis is found in the vast majority of patients with active SpA and PsA, independent of SpA subtype. MASEI PD might have some advantages versus OMERACT PD definition to detect active enthesitis. These findings support the usefulness of PD US in the assessment of activity in SpA and PsA at patient level.
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AB1117

CLINICAL IMPACT OF MUSCULOSKELETAL ULTRASOUND ON RHEUMATOID ARTHRITIS IN ROUTINE CLINICAL PRACTICE

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Background: Musculoskeletal ultrasound (MSUS) is a useful tool to assess disease activity in rheumatoid arthritis (RA) patients. However, it has not yet been established if its use would change treatment decisions within a treat to target strategy or whether it would lead to better outcomes in RA patients

Objectives: Our aim was to determine the impact of MSUS in the clinical management of RA patients and investigate factors associated with subsequent clinical actions by the referring rheumatologist

Methods: A prospective analysis of RA patients seen at an MSUS clinic over a 6-month period was undertaken. Pre- and post-US follow-up data (± 3 months) were analyzed. Baseline assessment included clinical features, physical examination and laboratory tests. All MSUS examinations were performed according to EULAR guidelines and using an Esaote MyLab 8 (Esaote, Genoa) with a high frequency (8-15 MHz) transducer. Patients were stratified in groups based on the clinical impact of the MSUS visit: 1) No clinical impact and 2) US findings leading to subsequent clinical action by the referring rheumatologist (including changes in dosages of current rheumatologic treatments, addition/substraction of medications or interventional procedures based on the MSUS results). First, differences between groups were tested using chi-squared and Student-t tests in the univariate analysis. Second, multivariate logistic regression models were employed to investigate factors associated to a change in clinical management

Results: A total of 61 RA patients were included for analysis. Mean age was 61.9± 11.4 years and 51 (83.6%) were female. Disease activity assessment was the most frequent referral reason (43; 70.5%). Overall, MSUS led to a subsequent therapeutic action by the referring rheumatologist in 39 (63.9%) patients, and to a change in the underlying diagnosis and/or in the clinical impression of the chief complaint that generated the referral in 7 (11.5%) patients. Baseline characteristics between both groups are compared in Table 1. In the univariate analysis, the detection of Power Doppler (PD) synovitis/tenosynovitis and 28 swollen joint count were significantly associated with a subsequent clinical action. In the multivariate analysis only PD synovitis/tenosynovitis (OR=3.28; 95%CI 1.06-10.27) remained significantly associated with a change in clinical management (Table 2)

Table 1. Baseline characteristics of RA patients

		Total n= 61	Change in clinical management n= 39 (63.9%)	No change in clinical management n= 22 (36.1%)	p
Age		61.9±11.4	61.5±12.5	62.6±9.2	0.7
Sex	Female	51(83.6%)	35(89.7%)	16(72.7%)	0.09
Smoking	Non smoker	33(54.1%)	17(43.6%)	16(72.7%)	0.08
	Smoker	13(21.3%)	11(28.2%)	2(9.1%)	
	Former smoker	15(24.6%)	11(28.2%)	13(21.3%)	
Radiographic erosions		29(48.3%)	22(57.9%)	7(31.8%)	0.05
28 Tender Joint Count		2.3±3.4	2.7±3.9	1.6±2.4	0.2
28 Swollen Joint Count		2±3	2.6±3.5	1.1±1.6	<0.05
ESR (mm/h)		28.1±20.6	26.1±15.5	31.7±27.4	0.4
CRP (g/L)		1±1.5	1±1.4	0.9±1.7	0.7
RF (IU/mL)		175.8±452.8	139.9±249.5	243.9±697.4	0.4
ACPA (IU/mL)		775.6±998.6	619.4±797.1	1079.9±1,275.9	0.2
US PD synovitis/ tenosynovitis		37(60.7%)	28(71.8%)	9(40.9%)	<0.05

Table 2. Independent factors associated with a change in clinical management based on logistic regression model

	p	Odds ratio	95% C.I.	
			Lower	Upper
28 Tender Joint Count	0.13	1.24	0.94	1.64
US PD synovitis/tenosynovitis	0.04	3.28	1.06	10.17

Conclusion: The most common indication of MSUS examination in RA patients was disease activity assessment. MSUS findings led frequent changes in therapeutic management and even to a change in the diagnosis in some of cases. The presence of PD synovitis/tenosynovitis was significantly associated to a change in the therapeutic management. These data highlight the impact of MSUS inflammatory findings in RA patients in daily clinical practice

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AB1118

OPEN MUSCLE BIOPSY AS A SAFE AND USEFUL MEANS OF DIAGNOSING VASCULITIS: A SINGLE-CENTER EXPERIENCE OF 210 BIOPSY CASES

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Background: We previously reported the utility of open muscle biopsies in diagnosing vasculitis [1]. The number of open muscle biopsies performed at our department has increased to over 200. The purpose of the present study was to evaluate the diagnostic utility of vasculitis and the safety of the open muscle biopsies.

Objectives: To clarify the diagnostic utility of vasculitis and the safety profile of the open muscle biopsy.

Methods: We retrospectively examined all cases of open muscle biopsy performed between May 2012 and June 2018 in our department. The biopsy results, the presence or absence of adverse events, and blood test data at the time of the biopsy were extracted from the patients' electronic medical records.

Results: Between May 2012 and June 2018, 210 open muscle biopsies were performed, 120 of which were done for vasculitis diagnosis. Diagnostic histopathological findings were obtained in 42 of the 120 cases (35%). The definitive diagnosis in these cases was microscopic polyangiitis (30 cases), eosinophilic granulomatosis with polyangiitis (seven cases), granulomatosis with polyangiitis (one case), polyarteritis nodosa (three cases), and other vasculitis (one case). In 57 cases with myeloperoxidase-anti-neutrophil cytoplasmic antibody (MPO-ANCA) ≥ 10 U/ml, 31 cases (54.3%) showed histopathology of vasculitis. In six cases with protainase-3-ANCA (PR3-ANCA) ≥ 10 U/ml, histopathology of vasculitis was found in one case (16.7%).

In all 210 open muscle biopsy cases, complications included minor wound dehiscence (11 cases) and small subcutaneous hematoma (six cases), which were able to be managed by local treatment. Albumin was significantly lower in the patients with wound dehiscence (mean 3.2 vs 2.7, p = 0.049)

Serious complications included anaphylaxis due to local anesthesia (one case), compartment syndrome due to hematoma (one case), hematoma requiring surgical removal (one case), and arterial hemorrhage requiring surgical intervention (one case). The patients in the latter three hemorrhagic cases were receiving antiplatelet drugs.

Conclusion: An open muscle biopsy is useful for diagnosing vasculitis, especially for MPO-ANCA-positive anca-associated vasculitis. Its safety profile is acceptable. Serious adverse events are rare, but the procedure should be performed carefully when patients are receiving antiplatelet drugs.

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AB1119

U9: A NOVEL CLINICALLY ORIENTED ULTRASONOGRAPHIC SCALE AS A USEFUL MARKER FOR MONITORING THERAPEUTIC RESPONSE IN RHEUMATOID ARTHRITIS (MULTI CENTERS STUDY)

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Background: Musculoskeletal Ultrasonography (MSUS) is now a widely used tool for monitoring of rheumatoid arthritis (RA). Although there are many proposed sets of composite scores, a fixed set of joints may not be an ideal tool to assess a disease like RA, which affects many joints and tendons in different presentations. In previous study (1) U9 score was proven to be correlated with disease activity parameters.
Objectives: To determine whether US assessment using U9 score is useful for monitoring response to treatment for RA or not?
Methods: A prospective, multicenter study were conducted in period from July 2019 to December 2019. All recruited RA patients were subjected to: Disease activity assessment by clinical disease activity indices (CDAI and DAS28 ESR). Functional status assessment by (HAQ) and ultrasonographic assessment using U9 score which include 8 joints (bilateral wrists,2nd MCP,3RD MCP and knees) plus most clinically affected joint or tendon (one joint or one tendon). Most clinically affected joints from 48 joints. Any affected tendons could be choosing. All targeted joints were evaluated according to EULAR guidlines and by EULAR/ OMERACT combined score (0-3). Targeted tendons were scored (0-3).All patients received their treatment (biologic and non biologic DMARDs) according to the decision of the treating physicians. No specific therapy is needed. CDAI and DAS28 ESR, HAQ and U9 score were repeated after 3 months to detect the response to change after receiving the therapy.
Results: One hundred and forty patients (23.6% were male) with mean age 39.26±11.30 were recruited from 4 tertiary referral university hospitals.
There was a significant difference (<0.001) between the first and second visits as regards clinical, laboratory and ultrasonographic parameters. DAS 28 decreased form (5.29±1.21) to (3.95±0.99), ESR decreased from (42.12±15.24) to (26.84±12.32), HAQ2 improved from (0.652±0.350) to (0.510±0.237) and U9 total US score decreased from (13.56±5.18) to (8.02±4.28).
There was significant correlation between U9 ultrasonographic score and clinical parameters at both visits (table 1).

Table 1. correlation between U9 ultrasonographic score and clinical parameters.

		U9 at 1st visit	U9 at 2nd visit
DAS-28	Pearson Correlation	0.806	0.790
	(P value)	<0.001	<0.001
CDAI	Pearson Correlation	0.787	0.773
	(P value)	<0.001	<0.001
HAQ	Pearson Correlation	0.431	0.317
	(P value)	<0.001	<0.001

We found that the most suitable cut-off value of U9 score to predict high disease activity was 11.5 (sensitivity 85.7% and specificity 80.6%), cut off value for moderate disease activity was 5.5(sensitivity 83.2% and specificity 88%) and cut off value for low disease activity was 3.5 (sensitivity of 83.3% and specificity 57.1%). These results are summarized in the following table:
Conclusion: U9 ultrasonographic score is very useful method for evaluating the monitoring the response of treatment.
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[1] Mortada, et al. Annals of the Rheumatic Diseases 2019;78:1009.
Disclosure of Interests: None declared
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AB1120 A TRIAD OF ULTRASOUND DETECTED HIGH-GRADE SYNOVITIS (MID TARSAL & ANKLE JOINTS), HIGH-GRADE TENOSYNOVITIS IN (TIBIALIS POSTERIOR & PERONEAL TENDONS) AND EROSIONS OF FIBULAR DISTAL END IS HIGHLY SUGGESTIVE OF CHARCOT ARTHROPATHY

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Background: Charcot arthropathy poses many clinical challenges in its diagnosis and management. Ultrasonography (US) may be able to identify pathological changes in cases of Charcot arthropathy (1).
Objectives: to characterize the ultrasonographicfeatures of patients in early pre-radiographic stages of neuropathic (Charcot) arthropathy.
Methods: This is an extension of our previous study of ultrasonographic features Charcot ankle and foot (1).
an observational studywhere 42 patients with neuropathic (Charcot) arthropathy of the footbetween January 2013 and october 2019 were enrolled. Inclusion criteria included: 1- Foot pain and swelling. 2- Typical MRI findings of Charcot arthropathy in the form of subcondral bone marrow edema with or without sub-chondralmicrofractures, joint effusion or soft-tissue inflammation. 3- Grade 0 Modified Eichenholtz classification system which means normal radiography of the affected foot. Patients with other forms of arthropathy that may mimic Charcot arthropathy e.g. gouty arthritis and rheumatoid arthritis, were excluded from the study.Ultrasonographic (grey scale and Doppler US) examination of mid-tarsal and ankle joints was performed according to the EULAR guidelines.
Results: Synovitis and effusionatmid tarsal joints were found in all patients and to a lesser extent in the ankle joints. High degree Doppler activity at both ankle and mid tarsal joints could be observed in most patients. Bony erosions were also common as well as tendonitis. A triad of active synovitis (in mid tarsal joints and ankle joints), active tendonitis (of tibialis posterior and peroneal tendons) and erosions in the distal end of fibula was present in 40 (95.2%) cases.
Conclusion: our study confirms the ability of ultrasonography to detect inflammatory lesions in early stages of Charcot arthropathy.
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AB1121 IMPLEMENTING HIGH VALUE CARE IN INPATIENT ANTINUCLEAR ANTIBODY TESTING

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Background: Antinuclear Antibody (ANA) testing forms the basis on which many rheumatological diseases are subsequently diagnosed. ANA testing quantifies the dilution of plasma to produce the titer and staining pattern and this can be a part of an ANA order set that reflexively cascades to sub-serology if positive. Studies have shown that a low titer ANA may potentially translate into an erroneous diagnosis: if one estimates a 1 percent prevalence of ANA associated disease in the general population then 30% of those individuals would have a false positive result of ANA detected at 1:40 titer [1]. We theorized that there is no need for several methods to coexist within a single inpatient hospital setting especially since diagnostic value of staining patterns alone is limited.
Objectives: To compare the utility and yield of "ANA screening reflex to profile" (ARP) and "ANA reflex to titer" (ART) order sets in the inpatient setting of a community tertiary care hospital. We aim to identify the appropriateness of the ANA testing ordered including cost-effectiveness of ordering ARP over ART in order to implement the identified quality measures towards improving utilization of ANA testing.
Methods: We identified all inpatient ANA reflex testing orders performed at Community Regional Medical Center, Fresno, California completed between 11/2018 till 07/2019. This included ART and ARP orders with 6 sub-serologies: SSA, SSB, dsDNA, Smith, Scl-70 and U1RNP. A Health Information Management report was generated which included patient's age, gender, length of hospital stay, dates of testing ordered, principal diagnosis and type of ANA testing ordered. Descriptive statistics were computed and analyzed.
Results: We reviewed a total of 1,012 ANA lab orders performed between 11/01/2018 until 07/30/2019 performed on 700 patients. According to the laboratory standard using Immunofluorescence Assay, an ANA titer starting from 1:40 is reported as positive. Out of the 1,012 tests, 334 tests were positive i.e. 33%. The ART order by itself contributed to 29.9% of the positive testing while ARP formed 70% of the positive testing. 56 of the 910 ARP (6%) performed had one or more sub-serology antibody positive while in 178 ARP orders (20%) only the ANA titer was positive with negative serology. The most common sub-serology antibody noted positive was dsDNA forming 54% of the positive serology results. Multiple testing was noted with 218 orders of ARP and ART being ordered on the same patient within the same week, which shows 21.5% of ANA lab orders were repetitive. Length of stay was noted to be more than 3 days for 89% of the patients who had repetitive testing, majority of those tests (99%) on the same day by the same medical provider. It cost $5.0 for an ART order that resulted negative and $5.0 for an ARP panel that resulted negative. It cost $10.0 for those patients who had both ART and ARP ordered with negative results. A positive ART result added $12.0 additional to the cost of each positive ANA profile ($67.36) when both tests were ordered together.
Conclusion: Our study findings reflect the need for using higher yield ANA testing that has been standardized. It demonstrated that physicians ordering the testing were not familiar with the ART vs. ARP, and the laboratory orders

needed to be re-structured. We removed the ART from the inpatient Electronic Medical Record i.e. Epic system so that only the ARP order remained. This would prevent repetitive testing and reduce healthcare costs through reduction by at least $12.0 per positive ANA result and may also translate into reduced length of hospital stay. We were able to add Centromere Antibody (Ab) to the ANA profile sub serologies to standardize it further as it is an important part of Scleroderma diagnosis.

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Disclosure of Interests: None declared

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AB1122 BENEFIT OF JOINT ULTRASONOGRAPHY IN RHEUMATOID CARE PATIENT SATISFACTION SURVEY WITH NPS® USING POCUS (POINT OF CARE ULTRASOUND)

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Background: The roles of rheumatologists include patient education and information provision, and there is a report that patient care led by nurses gives high satisfaction. In addition, it has been reported that rheumatologists will no longer provide sufficient care for rheumatism and nurses may make up for the shortage (1). In order for patients to deal with diseases for a long time, it is necessary to communicate with patients through team approach to healthcare including nurses specialized in rheumatology, and to make efforts to further improve patient satisfaction.

Objectives: The satisfaction of patients who had undergone joint ultrasound (MSKUS) by rheumatologist nurses who had been registered as sonographers by the Japan College of Rheumatology was evaluated using a net promoter score (NPS®) to investigate whether medical intervention by nurses improved patient satisfaction.

Methods: A questionnaire survey was performed in 103 RA patients who visited our department. The contents were 2 points, and (1) MSKUS's level of patient satisfaction and (2) MSKUS's level of recommendation to others were investigated. In (1), whether or not (1) the echo test was good, (2) whether the test was done with peace of mind, (3) whether the time of the test was appropriate, and (4) whether or not the disease status was better understood after the test, and (5) whether or not the patient wished to undergo the echo test periodically, were asked on a 5 point scale (high evaluation to low evaluation, 1 ~ 5). Regarding (2), the doctor said "Would you like to recommend the joint echo test to other patients? This question was evaluated using NPS®, which is said to have strong correlation with patient satisfaction, growth, and business performance in various industries.

Measurement method of NPS®

The customer with the 9 ~ 10 point score is classified as a "recommendation" the customer with the 7 ~ 8 point score is classified as a "neutral person" and the customer with the 0 ~ 6 point score is classified as a "critical person" The value of NPS® is the value that comes out after subtracting the percentage of a critical person (%) from the percentage of a recommended person (%).

Results: Questionnaires were administered to 103 RA patients and responses were obtained from all.

(1) For the 5 items of patient satisfaction, 85% or more of the patients had high scores (1 and 2) for all the questions.

(2) NPS® score was high at 67. The NPS® score was even higher in the group of patients without progression of joint destruction (Stage 1 and 2) at 79.

Conclusion: It was suggested that when the nurse who usually coaches explained the symptoms immediately using POCUS, the patient's satisfaction would be improved, and a sense of security would be provided for the test. In addition, NPS® is a unified questioning method and said to be highly correlated with customer satisfaction, and it was considered that POCUS leads to benefits in medical management.

References:

[1] Fusama M et al. Mod Rheumatol. 2017 Sep;27(5):886-893.; Survey on attitudes regarding EULAR recommendations for the role of nurses involved in medical care of patients with chronic inflammatory arthritis in Japan.

Disclosure of Interests: None declared

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AB1123 PROGRESSION OF FINGER JOINT CARTILAGE DAMAGE EVALUATED BY ULTRASOUND IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Cartilage damage in rheumatoid arthritis (RA) has been evaluated by joint space narrowing (JSN) in X-ray, despite the fact that it is not a direct evaluation of cartilage. We have recently reported that direct evaluation of finger joint cartilage thickness evaluated by ultrasound (US) is valid and useful for patients with RA[1)].

Objectives: In this study, we aimed to examine the progression of cartilage damage in RA patients.

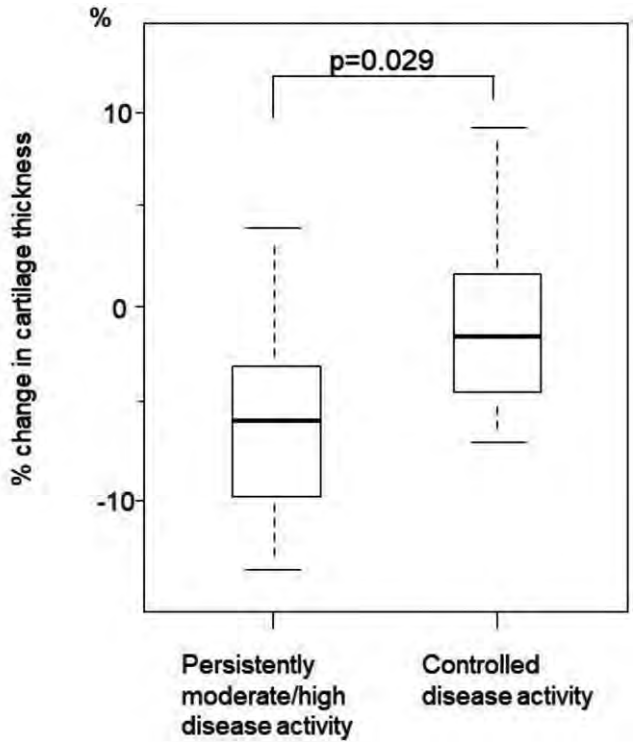
Methods: Forty-six patients with RA who had completed the US evaluation of finger joint cartilage thickness at baseline and after 1 year were included in this study. The cartilage thickness of metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints of 2nd to 5th fingers were bilaterally visualized and measured at the middle portion of MCP and PIP joints from a longitudinal dorsal view, with approximately 90 degrees flexion. Cartilage thickness was measured from the base of the cartilage to the interface artefact at the cartilage surface by calculating the pixel counts on DICOM images.

Results: In patients, 78% were female, the median age was 68 years and the median disease duration of the patients was 6 years. The median DAS28-CRP at baseline was 2.6. The sum of total cartilage thickness from 16 joints per patient ranged from 3.1 to 9.1 mm (median 6.4 mm) at baseline, and it was significantly correlated with disease duration (ρ=-0.423, p=0.003). A significant decrease from the baseline in the cartilage thickness (median -1.6%) was observed after 1 year (p=0.041). Furthermore, patients with persistently moderate/high disease activity for 1 year by DAS28-CRP (n=9) showed a greater decrease in the cartilage thickness than the remaining patients with controlled disease activity (n=37) (median -5.9% versus -1.5%, respectively, p=0.029).

Conclusion: This study further supported the validity and usefulness of joint cartilage thickness evaluation by US in patients with RA.

References:

[1] Ogura T, et al. Arthritis Care Res 2019 Oct 25.



Disclosure of Interests: Takehisa Ogura: None declared, Ayako Hirata: None declared, Sayaka Takenaka: None declared, Yuki Inoue: None declared, Takaharu Kagtagiri: None declared, Yuto Takakura: None declared, Hideki Ito: None declared, Hideto Kameda Grant/research support from: Abbvie, Asahi-Kasei,

Chugai, Eisai, Mitsubishi-Tanabe and Novartis, Consultant of: Abbvie, Boehringer, Celgene, Eli Lilly, Janssen, Novartis, Sanofi, UCB, Speakers bureau: Abbvie, Asahi-Kasei, BMS, Chugai, Eisai, Eli Lilly, Janssen, Mitsubishi-Tanabe, Novartis and Pfizer

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AB1124 USEFULNESS OF SUPERB MICRO-VASCULAR IMAGING(SMI) TO DETECT SILENT VASCULITIC DISEASE ACTIVITY IN 2 CASES OF TAKAYASU ARTERITIS

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Background: It is important to use vascular imaging modalities such as CT, MRI and PET-CT to evaluate disease activity of Takayasu arteritis (TAK). In particular, under treatment with tocilizumab (TCZ), redsidual vasculitic disease activity may remain even if serum CRP becomes negative. Contrast-enhanced CT,MRI and PET-CT can evaluate the morphology of blood vessel walls and the distribution of lesions and vasculitic activity, but it is invasive (radiation or contract media exposure), and costly. Ultrasound is superior in terms of morphological evaluation, cost, convenience, and low invasiveness. In particular, Superb Micro-vascular Imaging(SMI) is one of the micro blood flow display methods that can be installed in the ultrasound diagnostic device Aplio series.

There are some case reports in which micro blood flow signals of the carotid artery walls were detected using SMI in Takayasu arteritis [1] [2]. Both reports indicate that SMI blood flow is a comparable indicator of disease activity as serum CRP.

Objectives: To report the usefulness of SMI in 2 TAK patients who had negative serum CRP but had residual disease activity, leading to appropriate adjustment of treatment.

Methods: Two TAK patients who had been newly diagnosed in our department from May 2015 to October 2018 and had received SMI to detect carotid artery wall blood flow signal were retrospectively analyzed.

Results: Case 1

A 32-year-old woman developed neck pain, headaches, fever and she had high serum levels of CRP (8.1 mg/dl) and elevated ESR (98 mm/h). Contrast-enhanced CT showed thickening of the carotid artery, left subclavian artery and thoracic aorta and SMI detected blood flow signal in carotid artery wall. Diagnosis of TAK was made. After 2-week treatment with 1 mg/kg/day of PSL, CRP became negative but the micro blood flow in carotid arterity walls was detedted by SMI. Therefore,subcutaneous TCZ (162 mg/week)was added in combination with PSL.One year later, micro blood flow disappeared and we could judge there was no vasculitis activity (Figure A).

	Before treatment starts	2 weeks after starting treatment	One year after starting treatment
treatment	-	PSL 1mg/kg/day ongoing	PSL 7mg/day ongoing TCZ 162 mg/week ongoing
CRP(mg/dl)	+ (8.1)	–(0.0)	–(0.0)
SMI signal	+	+	–

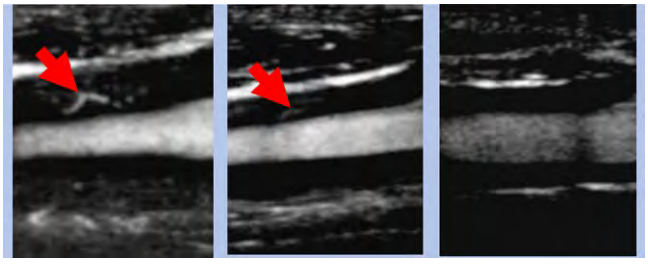


Figure 1. A. Clinical course of Case 1

Case 2

A 17-year-old woman developed proximal upper limb pain and fever with high serum CRP levels (7.1 mg/dl) and elevated ESR (>110 mm/h), and contrast-enhanced CT showed thickening of the carotid arteries and aortic arch. Two weeks after the start of PSL (1 mg/kg/day), CRP became negative at 0.3 mg/dl, but intramural blood flow detected by SMI remained. Then subcutaneous TCZ was added. Two weeks later, CRP became negative, and the SMI blood flow also disappeared (Figure B).

	Before treatment starts	2 weeks after starting treatment	4 weeks after starting treatment
treatment	-	PSL 1mg/kg/day ongoing	PSL 50 mg/day ongoing TCZ 162 mg/week added
CRP(mg/dl)	+ (7.1)	–(0.3)	–(0.0)
SMI signal	+	+	–

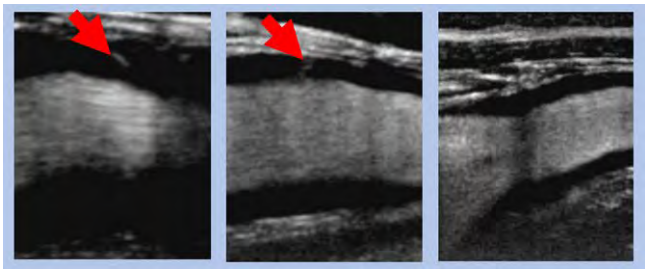


Figure 2. B. Clinical course of Case 2

Conclusion: Although SMI has the limitation that it cannot evaluate deep vascular lesions such as aorta, it is neither invasive nor costly and may be a good tool for evaluation of residual vasculitis activity of TAK.

References:

[1] Sato W, Sato T, Iino T, Seki K, Watanabe H. Visualization of arterial wall vascularization using superb microvascular imaging in active-stage Takayasu arteritis. *European Heart Journal - Cardiovascular Imaging*. 2019;20(6):719

[2] Ito S, Tahara N, Hirakata S, et al. Signal intensity of superb micro-vascular imaging associates with the activity of vascular inflammation in Takayasu arteritis. *Journal of Nuclear Cardiology*: *Official Publication of the American Society of Nuclear Cardiology*. 2019 Mar DOI: 10.1007/s12350-019-01665-4.

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Disclosure of Interests: None declared

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AB1125 PERFORMANCE OF ULTRASOUNDS TO ASSESS EROSION PROGRESSION IN RHEUMATOID ARTHRITIS

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Background: Ultrasonography (US) can detect more erosions than radiography (RX) at the joint level in rheumatoid arthritis (RA), especially at an early stage of the disease.

Objectives: The aim of the study is to determine the ability of ultrasonography to detect erosion progression by the US Score for erosions (USSe), in early (less than 2 years disease duration (DD)) and late stage (more than 2 years DD) RA over two years of follow-up.

Methods: Patients fulfilling ACR 1987 and/or ACR/EULAR 2010 criteria for RA were prospectively included. Clinical and demographic informations were recorded at baseline and hands and feet RX were scored according to the Sharp erosion score (SHSe). Erosive RA on RX was defined by the presence of at least three eroded joints (1). US examinations were performed at baseline and during the two years of follow-up. Erosions were scored by US on six bilateral joints (MCP 2, 3, 5 and MTP 2, 3, 5) with a four grade-scale to calculate total USSe. Erosive RA on US was defined by presence of one erosion ≥ 2mm (2). Inter-examiner reproducibility was performed on 14 patients in order to calculate the smallest detectable change (SDC), which was 2.3. Ultrasonographic progression was defined as a change in USSe > 2 (erosion change > SDC).

Results: A total of 71 patients were included, 22 patients (31.0%) had early RA and 49 (69.0%) patients had late RA diseases. On RX, 30 (42.3%) patients were erosive at baseline with a mean SHSe at 29.4 (SD at 24.7).

On US, 63 patients (88.7%) were classified as eroded. On US, erosions prevailed at baseline in MTP5 joints, then MCP2 and MCP5 joints on their lateral facets. During follow-up, 28 patients (39.4%) were classified as US progressors, 30 (42.3%) were stable and 13 (18.3%) considered as regressors (figure 1). In early RA disease, three of the four non eroded patients became eroded. USSe progressed in 11 patients (50%) while regression was observed in only one patient. In late RA disease, 17 patients (34.7%) progressed and 12 patients (24.5%) decreased significantly their USSe. Erosion progression prevailed on MTP 5 joints followed by MCP2 and finally MCP5 joints (figure 2).

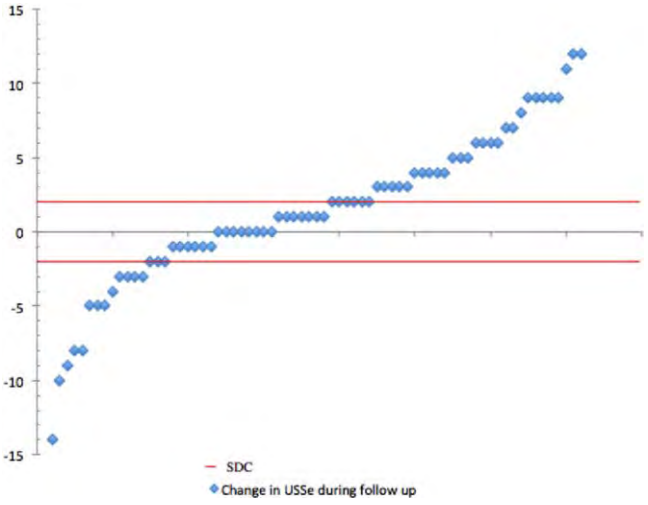


Figure 1. USSe progression plots (n=71)

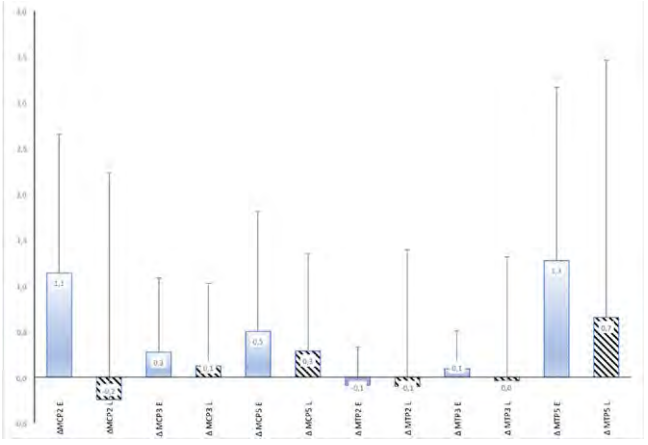


Figure 2. Differences of USSe by joints during follow-up in early and late RA

Conclusion: US structural examination is a highly reproducible method to assess erosion in RA disease. The USSe is able to detect structural changes (progression, stabilization and regression) in RA patients during a follow-up of two years especially in RA patients with short disease duration.

References:

[1] Van der Heijde D, van der Helm-van Mil AHM, Aletaha D, Bingham CO, Burmester GR, Dougados M, et al. EULAR definition of erosive disease in light of the 2010 ACR/EULAR rheumatoid arthritis classification criteria. Ann Rheum Dis. avr 2013;72(4):479-81.

[2] Roux C, Gandjbakhch F, Pierreisnard A, Couderc M, Lukas C, Masri R, et al. Optimization of ultrasonographic examination for the diagnosis of erosive Rheumatoid Arthritis in comparison to erosive hand Osteoarthritis. Eur J Radiol. sept 2019;118:10-8.

Disclosure of Interests: None declared

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AB1126

THE RELIABILITY AND DIAGNOSTIC ACCURACY OF DIGITAL TOMOSYNTHESIS COMPARED WITH CONVENTIONAL RADIOGRAPHY FOR THE INVESTIGATION OF SACROILIITIS

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Background: Conventional radiography remains part of the diagnosis of axial spondyloarthritis and determines qualification for biologic disease modifying anti-rheumatic drugs in many countries. The standard anteroposterior radiograph (XR) incompletely images the complex sacroiliac joint with recognised unacceptably low levels of agreement between readers. Digital tomosynthesis (DTS) uses conventional radiographic projections to create a three-dimensional image and is a potential alternative for the initial radiographic detection and grading of sacroiliitis.

Objectives: To compare the level of agreement between two radiologists when reporting sacroiliac joint imaging with digital tomosynthesis versus conventional radiography, as well as to compare the diagnostic accuracy of each imaging modality.

Methods: 229 consecutive patients that had radiography and digital tomosynthesis performed at Footscray Hospital, Melbourne, Australia were included. Two blinded radiologists independently re-reported all images according to the modified New York criteria, or listed an alternative diagnosis. An overall assessment of each image as inflammatory sacroiliitis, normal or non-inflammatory disease was also recorded. Demographic and clinical data were extracted from medical records. Agreement between and within readers was evaluated using kappa (κ) statistic. Diagnostic accuracy was calculated by comparing each reader's overall assessment against 2 reference standard comparators: most recent rheumatologist diagnosis and fulfillment of ASAS criteria at any time point.

Results: The intra-reader agreement of reader 1 was almost perfect for the left, right and overall sacroiliac joint assessments (κ 0.77 - 0.94), with DTS outperforming XR. Reader 2 agreement was mostly moderate (κ 0.39 - 0.69), with DTS and XR better on the left and right sacroiliac joint respectively, but XR having better overall assessment. The inter-reader agreement of DTS for all patients was moderate and better than XR as shown in the Table. When excluding non-spondyloarthritis patients, inter-reader agreement improved (κ 0.50 to 0.58) but there was no significant difference between DTS and XR. Using reader 1, the sensitivity of DTS (64.8 - 66.7%) was better than XR (54.9 - 60.7%) but low, in keeping with what is known about radiographic sacroiliitis and axial spondyloarthritis. The specificity of XR (78.5 – 80.3%) was better than DTS (72.3 – 73.1%). There were no significant differences when fulfillment of modified New York Criteria was used as a reader's positive test.

Table. Inter-rater reliability between the readers

	All patients (N=229)*	Inflammatory sacroiliitis & normal patients (N=164)**	Inflammatory sacroiliitis patients (N=92)**
XR Right	0.36	0.52	0.56
DTS Right	0.39	0.50	0.51
XR Left	0.34	0.55	0.56
DTS Left	0.42	0.55	0.58
XR Overall	0.40		
DTS Overall	0.45		

*Non-weighted kappa statistic
**Weighted kappa statistic

Conclusion: DTS demonstrated moderate reliability for assessment of sacroiliitis, marginally better than conventional radiography. Overall levels of agreement for both imaging modalities were however lower than radiography in previous studies, with several possible contributing factors. A prospective study in a selected spondyloarthritis cohort may better determine any benefit of DTS.

References:

[1] Christiansen AA, Hendricks O, Kuettel D, Horslev-Petersen K, Jurik AG, Nielsen S, et al. Limited Reliability of Radiographic Assessment of Sacroiliac Joints in Patients with Suspected Early Spondyloarthritis. The Journal of rheumatology. 2017;44(1):70-7.

[2] van Tubergen A, Heuft-Dorenbosch L, Schulpen G, Landewe R, Wijers R, van der Heijde D, et al. Radiographic assessment of sacroiliitis by radiologists and rheumatologists: does training improve quality? Annals of the rheumatic diseases. 2003;62(6):519-25.

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AB1127

IS SHOULDER INVOLVEMENT IN CLINICALLY SUSPECT ARTHRALGIA AN EARLY FEATURE OF RHEUMATOID ARTHRITIS? -A LONGITUDINAL ULTRASOUND STUDY

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Background: Multiple studies have demonstrated that shoulder complaints are frequent in Rheumatoid arthritis (RA). Recently, it has been shown that shoulder involvement is predictive for RA development in patients with undifferentiated arthritis(UA) and its value is comparable to that of small joint involvement. The phase of clinically suspect arthralgia (CSA) precedes the phase of clinically apparent arthritis; in this phase subclinical tenosynovitis of the hands, is associated with the development of RA. Given the similarities in predictive values between the shoulder and small joints in UA, and the predictive value of tenosynovitis in CSA, we hypothesized that subclinical tenosynovitis of the bicep tendon is also associated with RA development. We examined the biceps tendon, since this is the only tendon of the shoulder that is enclosed by a synovial sheath as it passes through the bicipital groove.
Objectives: Therefore, the aim of this study is to examine the predictive value of tenosynovitis of the bicep tendon by ultrasound (US) on developing inflammatory arthritis (IA) in CSA-patients.
Methods: The SONAR (Sonographic evaluation of hands, shoulders and feet in patients presenting with inflammatory arthralgia to identify subclinical arthritis) is a multi-center observational cohort study in which patients were followed for the development of clinically apparent inflammatory arthritis (IA). Visits were done at baseline and 6 monthly thereafter. At baseline a US of both shoulders was made. 1-year follow-up data were used. IA was defined as having an arthritis verified by the treating physician. US abnormalities of (1) the biceps tendon, (2) the glenohumeral joint and (3) the subdeltoid bursa, were assessed for tenosynovitis, arthritis and bursitis.. Reference values for tendon thickness and effusion of the bursa were determined according to Schmidt et al.(1)
Results: A total of 170 patients were included and underwent bilateral ultrasound (US) of the shoulder joint. Shoulder symptoms were infrequent (Table 1). After one year 37 patients developed IA (22%). ACPA positivity was associated with the development of IA (Table 1). As presented in Table 1, US abnormalities of the shoulder were found but none were associated with IA-development. In particular biceps tenosynovitis was not increased in the patients that developed IA.

Table 1. Baseline characteristics and ultrasound abnormalities at baseline in patients with CSA.

Baseline characteristics	All CSA-patients n=170	CSA-patients with IA (n=37)	CSA-patients without IA (n=133)	P value
Gender, female, n (%)	140 (82)	30 (81)	110 (83)	0.82
Age, years, mean (SD)	45 (12)	47 (12)	44 (12)	0.28
Symptom duration, weeks median (IQR)	30 (19-43)	37 (23-43)	28 (19-39)	0.14
TJC44, median (IQR)	5 (3-8)	5 (3-8)	5 (3-8)	0.81
Shoulder pain, n (%)	9 (5)	0 (0)	9 (6.8)	0.10
SJC44, median (IQR)	0 (0-0)	0 (0-0)	0 (0-0)	-
ESR, median (IQR)	10 (5-21)	9 (5-22)	11 (5-21)	0.66
RF-positive, n (%)	46 (28)	12 (34)	34 (26)	0.33
ACPA-positive, n (%)	26 (16)	10 (29)	16 (12)	0.019
US abnormalities of the shoulder				
Any US abnormalities, n (%) (n=170)	50 (29)	8 (22)	42 (32)	0.24
Biceps tendon Tenosynovitis, n (%) (n=164)	19 (12)	5 (15)	14 (11)	0.48
Biceps tendon thickness, n (%) (n=164)	6 (4)	0 (0)	6 (5)	0.19
Subdeltoid bursa effusion, n (%) (n=159)	29 (18)	3 (9)	26 (21)	0.094
Effusion joint, n (%) (n=157)	0 (0)	0 (0)	0 (0)	-

Abbreviations: IA: Inflammatory Arthritis, TJC44: Tender Joint Count in 44 joints, SCJ44: Swollen Joint Count in 44 joints,, ESR: Erythrocyte sedimentation rate, RF: Rheumatoid Factor, ACPA: Anti-citrullinated Protein Antibody

Conclusion: Subclinical tenosynovitis of the shoulder is not an early feature of RA in patients with CSA.
Reference:

[1] Schmidt WA, Schmidt H, et al. *Standard reference values for musculoskeletal ultrasonography.* Ann Rheum Dis. 2004 Aug;63(8):988-94.

Acknowledgments: *van der Helm- van Mil and de Jong contributed equal to this study
Disclosure of Interests: None declared
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AB1128

ULTRASOUND SYNOVITIS AND SQUEEZE TEST: IS THERE A RELATIONSHIP?

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Background: The squeeze test or the Gaenslen's test is an easy and rapid method to identify arthritis in metacarpophalangeal (MCP) and metatarsophalangeal (MTP) joints. It's characterized by tenderness upon lateral compression of MCP or MTP joints. This is a useful clinical exam for the early diagnosis of Rheumatoid Arthritis (RA).
Objectives: The aim of our study is to assess the real value of that test and its association with synovitis.
Methods: A prospective study including RA patients (2010 ACR/EULAR criteria) was conducted at the Rheumatology Department of Mongi Slim Hospital Tunis.
US examination was performed by an experimented rheumatologist blinded to clinical data using a machine type Esaote MyLAb 60 with a linear probe of 6-18 MHz. MCP joints were assessed in dorsal longitudinal view, in mode B and Power Doppler.
Synovitis was defined and Flexor digitorum Tenosynovitis was defined according to OMERACT.
A $p<0.05$ was considered statistically significant.
Results: Forty-three cases of RA were included. The mean age was 58.92 years [27 - 81]. The sex ratio was 0.16. Among our patients, 46.5% of cases were receiving methotrexate with a mean dose of 15,875 mg / week [7.5 - 22.5]. Corticosteroids were used in 55.8% of our patients with a mean dose of 8.65 mg / day [2.5 - 30]. Moreover, 23.25% of the patients were on biologics.
The mean value of morning stiffness was 37 min [0 - 150], the mean value of the global assessment of the disease by the patient was 5/10 [1 - 8]. The Gaenslen's test was positive bilaterally in 25,6% of cases, in the right hand and in the left one in respectively 39.5% and 27.9% of the patients. Tenosynovitis of the flexors were found clinically in 11.6% case.
The mean CRP was 29.7 mg / L [0.2 - 275] and the mean ESR was 65 mm [3 - 120]. The mean value of DAS28 and DAS28 $_{CRP}$ were respectively 5.20 ± 1.43 [2.69 – 9.00] and 4.33 ± 1.43 [1.35 – 8.32]. Overall, 430 joints and 430 flexor tendons were assessed by Ultrasound. Ninety-one synovitis were detected with a mean of 2.56 synovitis in MCP per patient [0 - 10]. Flexor tenosynovitis was found in 53.5% of patients.
A statistically significant correlation was found between the squeeze test and presence of ultrasound synovitis of the MCP whatever the site of the synovitis; on the right side ($r = 0.507$; $p < 10^{-3}$), or the left one ($r = 0.607$; $p < 10^{-3}$) but no correlation between the clinically detected tenosynovitis and the ultrasound tenosynovitis ($p = 0.364$). We found a significant correlation between the Gleason test and ultrasound tenosynovitis on both side with $r = 0.368$ and $p = 0.015$ on the right hand and $r = 0.441$ and $p = 0.003$ on the left one.
Conclusion: The squeeze test seems to be a very useful and practical clinical examination to easily detect synovitis and aid in the early diagnosis of RA
Disclosure of Interests: None declared
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AB1129

PREVALENCE OF FINDINGS IN ROUTINE ABDOMINAL ULTRASOUND IN PATIENTS WITH CONNECTIVE TISSUE DISEASES AND THEIR IMPACT ON DISEASE MANAGEMENT

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Background: Patients with connective tissue diseases (CTD) are often screened for abdominal organ involvement with ultrasound.
Objectives: To analyse the prevalence of routine abdominal ultrasound findings in different CTD entities and their impact on therapeutic decisions.
Methods: Retrospective chart review of all in-patients from a tertiary rheumatological referral center with CTD diagnosis and abdominal ultrasound examination between January 1st 2006 and December 31st 2015. Descriptive statistics were used to describe patient characteristics and frequencies of ultrasound findings. To determine whether findings impacted therapeutic decisions, we analysed if they were discussed in the hospital discharge letter.

Table 1. Frequency of abdominal ultrasound findings in different CTD.

	All patients	SLE	Sjögren´s syndrome		Systemic sclerosis			Myositis		UCTD	MCTD
			primary	secon-dary	diffuse	limited	with myositis	PM	DM		
Number of patients (females)	1092 (956)	194 (172)	252 (236)	167 (156)	78 (63)	125 (116)	17 (11)	24 (11)	33 (24)	99 (81)	87 (72)
	Frequency of findings (%)										
Gallbladder											
Concrements	8.2	6.7	10.7	7.2	10.3	-	5.9	16.7	12.1	6.1	5.7
Wall thickening	0.5	-	0.4	1.2	-	-	-	-	-	2.0	-
Status post cholecystectomy	14.4	8.8	17.9	20.4	14.1	17.6	5.9	25.0	3.0	14.1	5.7
Pancreas											
Pancreatic lipomatosis	14.3	10.8	11.1	25.1	15.4	12.0	23.5	25.0	15.2	14.1	3.4
Inhomogeneous parenchyma	1.9	2.6	1.6	-	-	0.8	-	4.2	6.1	3.0	4.6
Pancreatitis	0.2	0.5	-	0.6	-	-	-	-	-	-	-
Lesion/tumor	0.5	-	0.4	-	1.3	1.6	-	4.2	-	-	-
Kidneys											
Altered echogenity	4.7	5.7	6.0	4.2	7.7	4.8	-	8.3	6.1	-	2.3
Hydronephrosis	2.2	1.5	2.4	1.2	6.4	3.2	-	8.3	3.0	-	1.1
Cyst	10.3	9.3	10.7	12.6	15.4	9.6	5.9	4.2	15.2	8.1	4.6
Concrements	2.5	2.1	2.8	3.0	3.8	2.4	5.9	4.2	-	1.0	2.3
Lesion/tumor	0.6	0.5	0.8	-	3.8	-	-	-	3.0	-	-

Abbreviations: SLE: systemic lupus erythematosus, PM: polymyositis, DM: dermatomyositis, UCTD: undifferentiated connective tissue disease, MCTD: mixed connective tissue disease. " - " signifies 0.0% (n=0).

Table 2. Frequency of abdominal ultrasound findings in different CTD.

	All patients	SLE	Sjögren´s syndrome		Systemic sclerosis			Myositis		UCTD	MCTD
			primary	secon-dary	diffuse	limited	with myositis	PM	DM		
Number of patients (females)	1092 (956)	194 (172)	252 (236)	167 (156)	78 (63)	125 (116)	17 (11)	24 (11)	33 (24)	99 (81)	87 (72)
	Frequency of findings (%)										
Liver											
Hepatomegaly	8.1	9.8	9.1	5.4	12.8	5.6	11.8	12.5	-	4.0	11.5
Steatosis	26.8	23.7	23.8	36.5	32.1	24.8	29.4	41.7	24.2	26.3	18.4
Cirrhosis	0.5	-	0.4	0.6	-	3.2	-	-	-	-	-
Focal nodular hyperplasia	0.2	0.5	-	0.6	-	-	-	-	-	-	-
Dilated common hepatic duct	1.3	1.5	0.8	3.0	1.3	1.6	-	-	-	-	1.1
Suspected malignant tumor	0.5	-	0.4	-	1.3	-	-	-	3.0	2.0	-
Spleen											
Splenomegaly	15.2	24.7	12.7	9.6	16.7	13.6	17.6	25.0	9.1	10.1	18.4
Status post splenectomy	0.4	1.0	-	0.6	-	-	-	-	-	-	1.1
Other findings											
Pleural effusion	7.8	14.4	5.6	4.2	10.3	7.2	5.9	4.2	3.0	7.1	9.2
Ascites	2.2	4.1	0.4	0.6	6.4	3.2	-	4.2	-	1.0	2.3
Colitis	2.4	1.5	2.4	2.4	2.6	3.2	-	4.2	6.1	2.0	2.3
Lymphadenopathy	0.2	-	-	-	1.3	0.8	-	-	-	-	-

Abbreviations: SLE: systemic lupus erythematosus, PM: polymyositis, DM: dermatomyositis, UCTD: undifferentiated connective tissue disease, MCTD: mixed connective tissue disease. " - " signifies 0.0% (n=0).

Results: 1.092 patients with a total of 1.695 hospitalizations were analysed. Mean age was 55.1 years (range: 17-90 years, SD: 15.8), mean disease duration was 6.4 years (range: 0.0-52.8 years, SD: 9.1). 87.5 % were female.
Table 1 shows the frequency of findings per CTD entity. 48 out of all 1.695 examinations were discussed in the hospital discharge letter. In 30 cases, the physician described the ultrasound results as pivotal for therapeutic decision-making.
Conclusion: Routinely performed abdominal ultrasound rarely yields disease specific findings which subsequently impact the therapeutic decision-making process.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.3862

AB1130 **LOCALIZATION OF MRI INFLAMMATORY LESIONS OF THE HAND IN SCLERODERMA AND RHEUMATOID ARTHRITIS - COMPARATIVE STUDY**

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Background: Inflammatory lesions of hand are frquent clinical feature in rheumatoid artritis (RA), with lower frequency in pts with systemic sclerosis (SSc), also. MR is useful method for detecting and quantification of inflammatory lesion of the hand (bone oedema, erosions, synovitis) in RA and SSc.

Objectives: The aim of the study was to compare MR hand feature in SSc (experimental) and RA (control group) and to detect the localisation of the highest OMERACT RAMRISinflammatory score on the hand in pts with SSc and RA
Methods: 110 pts with SSc and 60 with RA were investigated (mean age 53y). All the pts underwenr clinical examination, X ray and MR on the dominant hand and wrist. Contrast enhanced low field MRI of the wrist and MCP2-5 joints was performend to all the pts. MRI inflammatory changes (bone oedema,erosions, synovitis)were assessed and scored by OMERACT RAMRIS scoring system.
Results: Clinical examination confirmed synovitis in 17.1%, and 78% of patients with SSc using MR I ($p < 0.001$). In the SSc group, erosions (by MR method) was confirmed in 52 (63.4%), by radiography in 22 pts (27.5%), which is a significantly lower percentage ($p < 0.001$). In the control RA group, erosion was confirmed in 34 (97.1%) by MR method, and by radiography in 6 (17.1%), which is a statistically significant difference ($p < 0.001$). Mean values of total MR score of synovitis (2.69 ± 2.29: 4.37 ± 1.31), oedema (6.58 ± 10.89: 20.57 ± 10.23) and erosion (6.84 ± 7, 43: 18.60 ± 5.01) on the wrist of the dominant hand were significantly higher in subjects with control RA than in those in the experimental SSc ($p < 0.001$). Mean values of total MR score of synovitis (3.15 ± 2.95: 5.26 ± 2.09), oedema (3.99 ± 9.82: 10, 51 ± 7.90) and erosion (4, 04 ± 4.76: 9.69 ± 4.27) on the MCP joints of the dominant hand were significantly higher in the control RA subjects ($p < 0.001$).The highest OMERACR RAMRIS synovitis score was on distal radioulnar (DRU joint) of hand in SSc and also In RA pts. The highest erosion score was found on capitate bone in SSc, but in lunate bone in RA pts. The highest bone oedema score was also found on capitate bone

in SSc, but in lunate bone in RA pts. According to the MCP joints, the highest synovitis score was found on the second finger in SSc and RA, highest erosion score also on the second finger in SSc, but on the third finger in RA; The highest bone oedema score was found on the third finger in SSc, and olso on the third and fifth finger in RA pts

Conclusion: MR inflammatory lesions in SSc are less frequent compared to that in RA but still in significant percentage, confirming the need for early detection and aggressive treatment of both, RA and SSc patients with joint involvement

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Disclosure of Interests: None declared

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AB1131 STATISTICAL PROCESS CONTROL AND PROCESS MAPPING QUANTIFY THE EFFECTS OF HISTORICAL CHANGES TO THE CONNECTIVE TISSUE DISEASE TESTING ALGORITHM AND IDENTIFY AREAS FOR FUTURE IMPROVEMENT IN A LARGE DIAGNOSTIC IMMUNOLOGY SERVICE

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Background: Pathology test turnaround times (TATs) are a limiting factor in patient flow through rheumatology services. Quality improvement (QI) methodologies such as Lean use tools including statistical process control (SPC) and process mapping to study the performance of the whole of a clinical pipeline, expose unnecessary complexity (non-value-adding activity), and streamline processes and staff roles.

Objectives: Understand effects of changes made to CTD testing algorithm over last 12 years by measuring some of the effects on TATs. Model current processes and suggest changes to workflow to improve TAT.

Methods: High-level flow diagrams of the current testing algorithm, and low-level process maps of analyser and staff processes were drawn.

Activity and TATs (working days between report and booking date) for ANA, ENA, DNA and CCP tests were plotted as XmR control charts.

Results: Finding 1: Largest referral laboratory does not currently operate a separate DNA monitoring workstream, resulting in unnecessary ANA and ENA testing (figure 1).

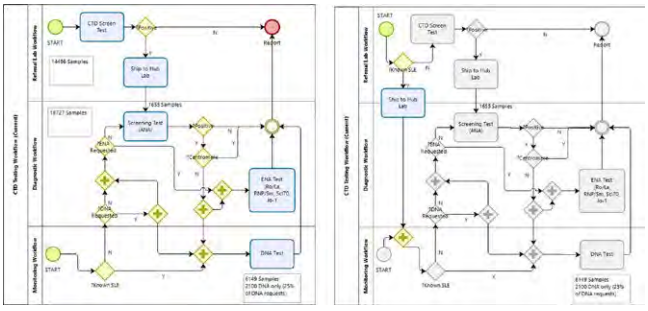


Figure 1. Current testing strategy (left) and suggested improvement (right)

Finding 2: Samples are handed off between 3 different lab benches, each of which may be staffed by a different staff member on a different day, and results processing involves handoff to a further 2 different staff members.

Finding 3: ANA demand is close to capacity, ENA demand exceeds current capacity (table 1).

Table 1. Demand for ANA, ENA and DNA tests, compared to capacity

Test	Median Demand (tests/ day)	Approx. Capacity (tests/ day)	Notes
ANA	74	100	Close to 80% recommended by the ILGs
ENA	38	36	*Less capacity than demand!!
DNA	34	100	Plenty

Finding 4: Stopping screening DNA requests on ANA result increased the number of DNA tests performed by about 10 samples per day (30%), but decreased turnaround time by a similar proportion (3.3 to 2.3 days, figure 2). It also reduced turnaround times of ANA and ENA tests.

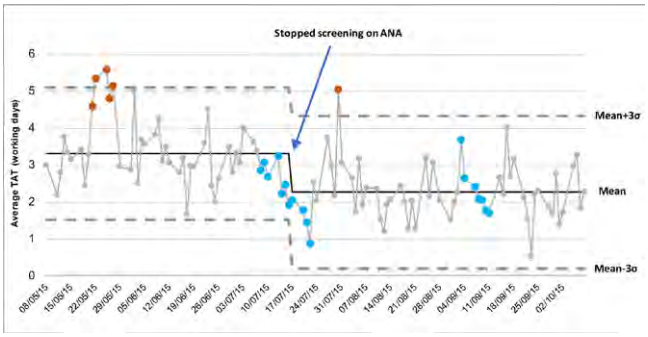


Figure 2. Control chart of average TAT of dsDNA antibodies by request date

Conclusion: Typically for a QI project, the initially simple CTD testing pipeline has accumulated many changes made without consideration of whole system performance, and is now a struggle to run.

Improvement ideas to be explored from this work include:

- Liaising with main referral lab to develop a DNA monitoring workstream to reduce unnecessary ANA and ENA testing
- Reduce handoffs, sample journey around lab analysers, and staff hands-on time by:
- changing ANA test methodology to same as DNA
- creating new staff roles (analyser operators to perform validation/ authorisation steps)
- Create more capacity for ENA testing by increasing the frequency of this test on the weekly rota
- Create more capacity for service expansion by running analysers at weekends (staff consultation required)
- Reduce demand on service by engaging and educating requestors
- Improve TAT for DNA by:
- processing samples the day they are booked in, instead of 1 day later
- auto-validating runs
- …using control charts to measure improvement

Disclosure of Interests: None declared

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AB1132 EFFECTIVENESS AND SAFETY OF ULTRASOUND-GUIDED FASCIA HYDRORELEASE ON METATARSALGIA WITHOUT SONOGRAPHIC EVIDENCE OF INFLAMMATION IN PATIENTS WITH RHEUMATOID ARTHRITIS.

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Background: Patients with rheumatoid arthritis (RA) who have metatarsophalangeal (MTP) joint involvement sometimes complain metatarsalgia without active sonographic inflammation[1]. Treatment of non-inflammatory metatarsalgia in RA is challenging and the pain sometimes lasts for years even though systemic inflammation completely resolves. On the other hand, intervention to fascia has increasingly attracted attention as a management of non-inflammatory pain[2]. Recently, we have invented a new technique called ultrasound-guided fascia hydrorelease (UGFHR), which injects fluid into "stacking fascia" (defined as high echoic and thickened fascia, often adhering to adjacent structures), making it unglued and instantaneously improving fascial pain.

Objectives: This study is aiming for prospective evaluation of effectiveness and safety of UGFHR on metatarsalgia in patients with RA.

Methods: We enrolled consecutive 11 patients with RA who came to rheumatology service in Suwa Central Hospital and satisfied the following inclusion and exclusion criteria:

Inclusion criteria were having at least one MTP joint pain on which the patient has tenderness on the extensor side.

Exclusion criteria were positive inflammation with ultrasound evaluation (defined as gray scale (GS) ≥2 and/or power doppler scale (PDS) ≥1) or having other cause of pain such as intermetacarpal bursitis, Morton's neuroma.

The patients received UGFHR on the fascia between the MTP joint capsule and the extensor tendon of the toe. We first searched for the stacking fascia between the two structures using ultrasound with longitudinal view of the extensor side of the MTP joint, and injected 2ml of normal saline into the stacking fascia, making it unglued (Fig. 1). If there was no stacking fascia, we injected on the fascia where the joint capsule and the extensor tendon became closest.

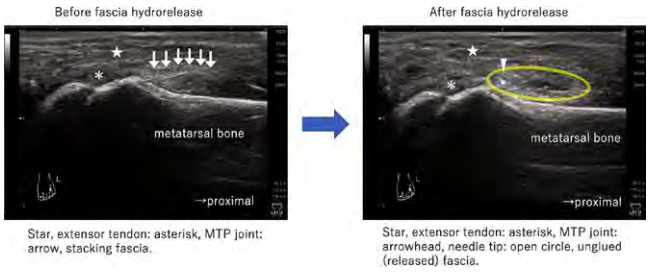


Figure 1. The procedure of ultrasound-guided fascia hydrorelease (UGFHR)

Numeric rating scale (NRS) of pain on walking and tenderness on the target MTP joint was measured on 3 occasions: before, immediately after, and one week after the UGFHR. Adverse events were also recorded.

The data were analyzed longitudinally, using Friedman test.

Results: The characteristics of the patients are shown in table 1. Female gender was dominant. Most of them were established RA. Simplified disease activity index (SDAI) were variable.

Table 1. The characteristics of the 11 patients.

Case	Age	Gender	RA duration (year)	deformity	SDAI	TJ	SJ	pVAS	dVAS	CRP (mg/dl)	ESR (mm/hr)	mHAQ	GS*	PDS**
1	81	female	6	no	0.12	0	0	0	0	0.12	16	0	0	0
2	69	female	14	no	7.02	2	1	2	2	0.02	11	0.125	0	0
3	72	female	10	yes	NA	0	0	NA	1	0.24	NA	NA	1	0
4	77	female	14	yes	22.45	4	4	6	5	0.45	18	0.25	1	0
5	53	male	4	no	4.03	0	0	3	1	0.03	NA	NA	0	0
6	49	female	1	no	4.12	2	0	1	1	0.12	5	0	0	0
7	61	male	0.5	no	6.03	1	1	2	3	0.03	2	0.125	0	0
8	57	female	4	yes	2.48	0	0	1	0.5	0.11	28	NA	0	0
9	49	female	1	yes	0.07	0	0	0	0	0.07	2	0	0	0
10	62	female	6	no	4.01	0	0	3	1	0.01	NA	0	0	0
11	76	female	7	no	7.02	0	0	3	1	0.02	6	NA	0	0

*GS: gray scale score on the target MTP joint, **PDS: power doppler scale score on the target MTP joint

The changes in NRS from before to immediately after and one week after the UGFHR are described in figure 2.

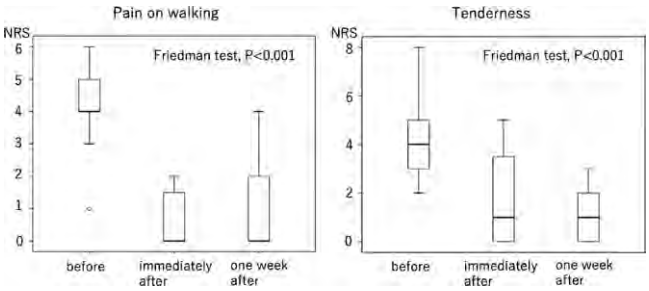


Figure 2. The changes in NRS.

Pain on walking and tenderness on the target joint both significantly decreased immediately after the procedure (ΔNRS from before to immediately after the UGFHR: -3.45 (95% confidence interval (CI) -2.32 to -4.59, p=<.01) and -2.45 (95% CI -1.32 to -3.59, p=<.01) respectively), and the change was maintained until one week after the UGFHR (ΔNRS from before to one week after the UGFHR: -3.09 (95% CI -1.77 to -4.42, p=<.01) and -3.27 (95% CI -1.80 to -4.75, p=<.01) respectively.

In terms of safety, 7 out of 11 patients complained injection pain, all of which did not last for a week. Otherwise, there was no adverse event such as infection, nerve injury, bleeding, or tendon rupture.

Conclusion: Ultrasound-guided fascia hydrorelease on MTP joint can be an effective and safe treatment option in patients with RA who have metatarsalgia but no sonographic evidence of MTP inflammation.

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Disclosure of Interests: None declared

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AB1133

BACK TO THE BASICS: UNDERSTANDING THE PROGNOSTIC VALUE OF RHEUMATOID FACTOR AND ANTI-CYCLIC CITRULLINATED PEPTIDE IN RHEUMATOID ARTHRITIS FROM A MUSCULOSKELETAL ULTRASOUND PERSPECTIVE

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Background: Anti-CCP and rheumatoid factor (RF), especially at high levels have been implicated as poor prognostic factors in rheumatoid arthritis (RA). With musculoskeletal ultrasound (US) being increasingly used for RA joint assessment, it is important to revisit the prognostic potential of these antibodies from an US perspective.

Objectives: To study the prognostic value of RF and anti-CCP for poor disease outcomes, by investigating possible associations with US detected joint inflammation and erosion.

Methods: In this cross sectional study, US power Doppler (PD) and grey scale (GS) joint inflammation were graded semi-quantitatively (0-3), while bone erosion was scored as either Yes=1 or No=0 at each joint recess. Patients disease activity was classified as either DAS28 <3.2 or DAS28 ≥3.2. Correlations of US variables with antibodies levels were quantified using the Pearson correlation coefficient. Simple linear regression was used to characterize relationships between variables and Receiver Operating Characteristic (ROC) analysis to determine statistically optimal cut-off values for identifying patients subgroups with US erosion scores >25th, >50th and >75th percentiles.

Results: 1080 joints and 1800 joint recesses from bilateral elbows, wrists, ankles and small joints of the hands and feet were scanned in 30 adult RA patients (76.7% Chinese and 93.3% female). Their baseline mean (SD) DAS28, disease duration, RF and anti-CCP levels were 3.58 (1.20), 70.3 (61.2) months, 142.1(179.0) IU/ml and 135.4(105.3) U/ml, respectively. Table 1 summarizes correlation coefficients of antibody levels with US variables. Among patients with DAS28 <3.2, there were no significant correlations between antibody levels with US variables. Among patients with DAS28 ≥3.2, anti-CCP levels correlated significantly (r=0.46, P=0.048) and were predictive (coefficient (95%CI), 0.028 (0.002, 0.053); R2=0.21; P=0.048) of US erosion scores. Area under the ROC curve (AUC) for anti-CCP levels (table 2) as predictive of patients with US erosion score >7 (75th percentile) was 0.72 (0.26, 0.97). For the anti-CCP level cutpoint of ≥95.2, specificity=53.8%, sensitivity=83.3%, accuracy=63.2%, Negative Predictive Value=87.5% and Positive Predictive Value=45.5%.

Table 1. Correlation of RF and anti-CCP levels with ultrasound variables

DAS28<3.2 Ultrasound variables	Correlation with RF Correlation coefficient (95% CI)	P-value	Correlation with anti-CCP Correlation coefficient (95% CI)	P-value
Erosion	-0.18 (-0.71, 0.47)	0.593	-0.295 (-0.76, 0.37)	0.379
PD	0.38 (-0.29, 0.80)	0.249	-0.287 (-0.76, 0.38)	0.392
GS	0.381(-0.28, 0.80)	0.247	-0.245 (-0.74, 0.42)	0.467
DAS28≥3.2 Ultrasound variables	Correlation with RF Correlation coefficient (95% CI)	P-value	Correlation with anti-CCP Correlation coefficient (95% CI)	P-value
Erosion	-0.03 (-0.48, 0.43)	0.908	0.46 (0.01, 0.76)	0.048*
PD	-0.26 (-0.64, 0.23)	0.291	-0.34 (-0.69, 0.14)	0.157
GS	-0.01 (-0.46, 0.45)	0.975	0.03 (-0.44, 0.47)	0.921

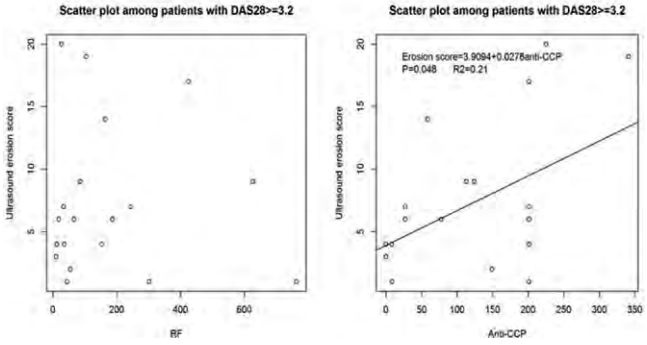
Statistically significant: * p<0.05

Table 2. ROC analysis of the performance of anti-CCP using various ultrasound erosion score criteria

Ultrasound erosion score criterion	Area under the ROC Curve (AUC) (95%CI)
> 2.25 (25th percentile)	0.57 (0.26, 0.87)
> 4.5 (median or 50th percentile)	0.68 (0.40, 0.95)
> 7 (75th percentile)	0.72 (0.26, 0.97)[1]

[1]Corresponding Threshold=95.2, Specificity=53.8%, Sensitivity=83.3%, Accuracy=63.2%, Negative
Predictive Value=87.5%, Positive Predictive Value=45.5%.

Figure 1. Scatter plots for RF and anti-CCP levels with ultrasound erosion scores



Conclusion: The prognostic significance of anti-CCP and RF appears to differ in RA. Specifically, among patients with at least moderate disease activity (DAS28 ≥3.2), anti-CCP - but not RF - is associated with joint damage, being moderately correlated with US detected erosions.

References: Nil:

Disclosure of Interests: None declared
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AB1134 ULTRASOUND FINDINGS IN HAND JOINTS INVOLVEMENT: A COMPARATIVE STUDY BETWEEN PSORIATIC AND RHEUMATOID ARTHRITIS

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Background: Psoriasis is a common skin disease that is associated with multiple conditions. The most prevalent coexisting condition is psoriatic arthritis (PsA) which develops in up to 30% of patients with psoriasis and characterized by diverse clinical features often resulting in delayed diagnosis and treatment. [1]
Objectives: The aim of this study was to investigate the potential of ultrasound (US) in the differential diagnosis between rheumatoid arthritis (RA) and PsA at the level of small joints of the hand and wrist.
Methods: Fifteen patients with PsA of the hands and wrists and 20 age and sex-matched RA patients were examined with musculoskeletal US. Radiocarpal, midcarpal, distal radioulnar, metacarpophalangeal (MCP), proximal interphalangeal (PIP) and distal interphalangeal (DIP) joints and flexor and extensor tendons (in wrist and hand) were examined bilaterally. Synovitis, erosions and tenosynovitis were scored according to semiquantitative method.[2]

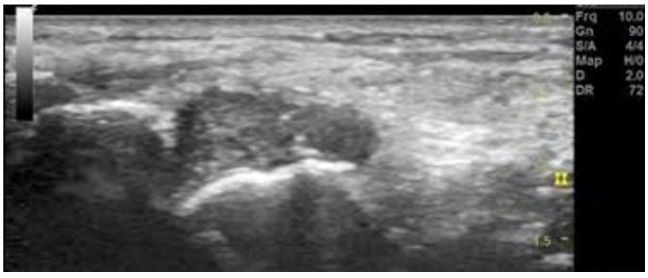


Figure 1 Sixty year old male patient with RA for 5 years,presented with pain and swelling at the wrist.Gray scale ultrasound sagittal view shows sever synovial proliferation at the radiocarpal joint

Results: Among 510 and 680 joints examined in PsA and RA respectively, certain US features such as synovitis and erosions at the DIP were exclusively detected in PsA (p<0.001). Synovitis was frequently present at the radioulnar joints in RA in comparison to PsA patients (52.5% vs 26.7% respectively, p=0.029). Joint effusion was frequently detected at radiocarpal and midcarpal joints in RA in comparison to PsA (p=0.047, 0.039 respectively). Effusion at the 3rd PIP joints was more significantly present in PSA than RA (p=0.037),while erosions were significantly detected at radiocarpal joints in RA in comparison to PsA patients (45%vs 20%respectively,p=0.029).Tenosynovitis was significantly detected at the extensor tendons in RA and at the flexor tendons in PsA patients (p=0.021, 0.022 respectively).
Conclusion: There are significant differences in the US findings of the hand and wrist that can help to distinguish between RA and PsA

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Acknowledgments: Not applicable
Disclosure of Interests: None declared
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AB1135 ECHO-ANATOMY OF THE PROXIMAL TIBIOFIBULAR JOINT

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Background: The proximal tibiofibular joint (PFTJ) should be considered in the differential diagnosis of a patient presenting with complaints in the lateral aspect of the knee However, this joint is often forgotten, yet involved in many degenerative and inflammatory pathological processes. MRI remains the imaging of choice to study the PFTJ. Ultrasound could also be useful in clinical practice to study the joint and its environment. To our knowledge, there is no systematic descriptive echo-anatomical study of PFTJ that would allow to standardize the ultrasound scanning of this joint.
Objectives: The objective of our study was to describe standardized ultrasonographic scans of the PTF joint and its environment starting from an anatomical study of the joint and then confirming the visibility of the different structures on a series of healthy volunteers.
Methods: We first conducted an anatomical study of the PTFJ on 3 cadavers. The different part of the joint (capsule, cartilage, ligaments) and the environment (nerves, muscles, vessels) were studied allowing an exact correlation between US images and the structures. This step led us to choose 3 scans useful for the study of the different part of the joint in clinical practice (figure 1): an anterior transverse oblique, a strict coronal, and a posterior transverse oblique. Subsequently, a TFPJ ultrasound was performed on 20 healthy volunteer patients to evaluate the feasibility and the visibility of the different structures seen on the dissection part.

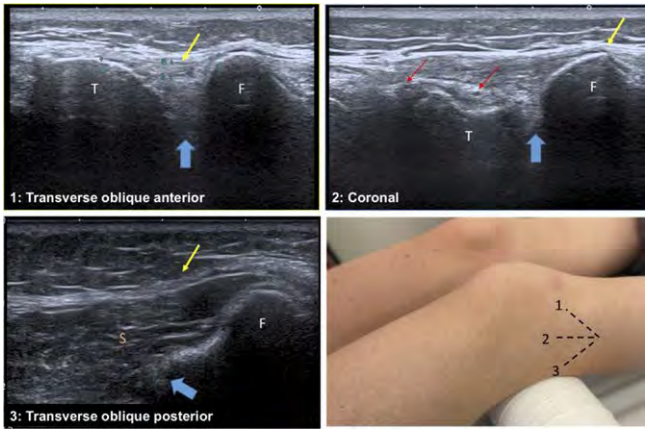


Figure 1.

Results: The different structures seen on the anterior transverse oblique scan were the anterior joint space, cartilage and anterior proximal tibiofibular ligament. The coronal approach led us to the visualization of the joint space, the collateral lateral ligament, the inferolateral genicular and posterior tibial recurrent artery, the meniscus and more posteriorly the ligaments of the posterolateral corner (popliteofibular, arcuate and fabellofibular). Finally, the posterior transverse oblique allowed us to study the posterior ligaments and joint recess under the

soleus muscle. Twenty healthy volunteers with an average age of 29 years underwent an ultrasound of the right PTF joint. The joint line spacing was visualized in 100% of the cases on the 3 sections. The anterior cross-section allowed anterior proximal tibiofibular ligament analysis in 100% of the cases (median length 15,7 mm (min-max: 12.3 – 23.4), median thickness 1.4 mm (min-max: 1-2.3). The coronal section allowed identification of the inferolateral geniculate and posterior tibial recurrent arteries in 90 and 85% of cases respectively, and the distal insertion of the fibular collateral ligament in 100% of cases. Posterior sectioning was more challenging and identification of the popliteal tendon, arcuate ligament and posterior proximal tibiofibular ligament was possible in 16, 7 and 2 patients respectively.

Conclusion: We performed a 2-step study: a cadaveric study followed by an ultrasound on healthy volunteer which allowed us to define 3 standardized scan of the PTF joint. These sections allow a thorough study of the PTF joint and the surrounding structures although study of the posterolateral corner ligaments remains challenging. We think that this scanning method can be integrated into daily clinical practice in rheumatology and in sports medicine.

Disclosure of Interests: None declared
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AB1136

THE DIAGNOSTIC VALUE OF SERUM KL-6 IN CONNECTIVE TISSUE DISEASE ASSOCIATED INTERSTITIAL LUNG DISEASE IN THE UYGUR POPULATION OF CHINA.

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Background: Connective tissue diseases are a group of inflammatory, immune mediated disorders.Interstitial lung disease (ILD) is associated with significant morbidity and mortality.Currently,, scientists are still looking for serum markers to diagnose interstitial lung disease.Althought serum KL-6 level has been studied in ILD of various aetiologies and revealed to be an important serum marker for ILD,but differences in KL-6 expression related to ethnic and/or genetic variants may exist.

Objectives: To evaluate the diagnosis of the serum Krebs von den Lungen-6 (KL-6) for CTD-ILD in the Uygur population of China.

Methods: 117 Patients with CTD-ILD (CTD-ILD group) and 182 patients with CTD (CTD group) who visited the department of rheumatology and immunology of People's Hospital of Xinjiang Uygur Autonomous Region between January, 2015 and December, 2019 were included. Serum KL-6 levels were measured by chemiluminescent enzyme immunoassay kit.

Results: The significantly higher levels of KL-6 were determined in the RA-ILD group than RA group [569(287.5,984)U/ml vs 194(152,266.5)U/ml](P<0.001) (figure 1).The optimal cutoff value of serum KL-6 for diagnosis of RA-ILD was 345.5 U/ml, and the sensitivity and specificity were71.8% and 90.1 %, respectively. Area Under the Curve (AUC) was 0.875.(figure 2)

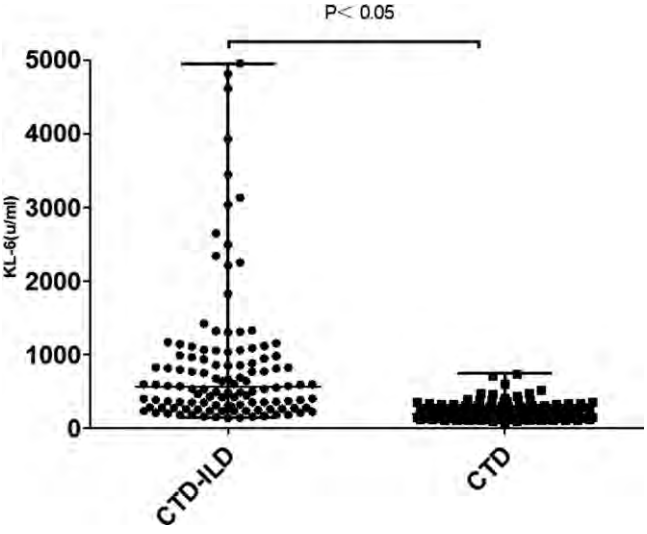


Figure 1. Comparison of serum KL-6 concentrations in CTD-ILD group and CTD group.

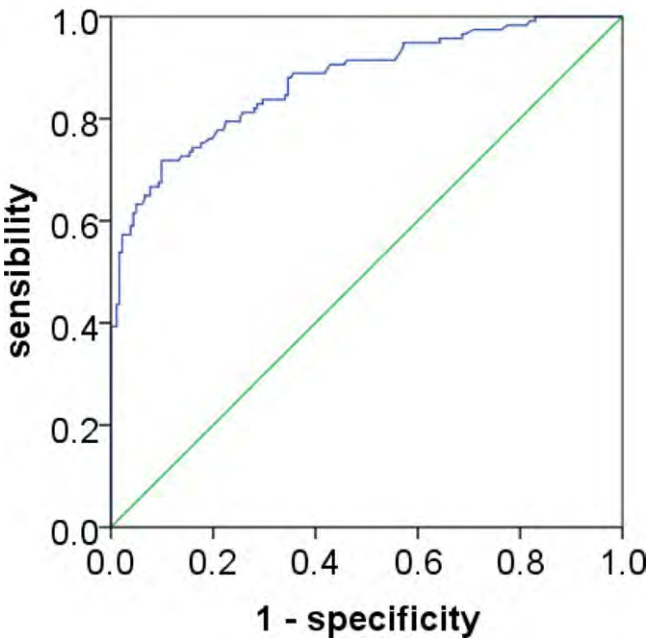


Fig 2. Receiver-operating characteristic curve(ROC) of KL-6 for the diagnosis of CTD-ILD

Conclusion: The serum KL-6 is a important biomarker for the diagnosis of CTD-ILD and Serum KL-6 could be a clinically useful biomarker in screening CTD-ILD in the Uygur population of China.

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AB1137

CLASSIFICATION OF THE EARLY STAGE OF RAPIDLY DESTRUCTIVE COXOPATHY ACCORDING TO THE FEMORAL HEAD DESTRUCTION

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Background: Rapidly destructive coxopathy (RDC) is an unusual subset of osteoarthritis of the hip characterized by rapid chondrolysis with progressive loss of the joint space as the first manifestation of the disease. Because rapid progression of RDC makes it difficult to obtain sequential radiographs in its early stage, the process of disease progression in the early stage remains unclear. Although the pathogenesis of RDC is still unclarified, the potential causes of RDC include subchondral insufficiency fracture of the femoral head resulting from osteoporosis, pelvic posterior inclination in RDC as a mechanical factor, and increased serum levels of matrix metalloproteinase (MMP)-3 as a biological factor.

Objectives: This study aimed to differentiate the process of disease progression in the early stage of RDC and provide its new classification system.

Methods: This monocentric retrospective study included 42 female patients who met the criteria of RPOH, chondrolysis >2 mm during 12 months from the onset of hip pain based on a series of radiographs and computed tomography (CT). This study also included 9 female patients with osteoarthritis secondary to developmental dysplasia of the hip (DDH), who demonstrated chondrolysis >2 mm during 12 months from the onset of hip pain. Cortical thickness index (CTI) correlated with bone mineral density of the hip, pelvic tilt, and serum concentrations of matrix metalloproteinase (MMP)-3 were analyzed.

Results: RDC were classified into two types based on the absence (type 1, n=17) and presence (type 2, n=25) of subsequent femoral head destruction shown by CT within 12 months after the onset of hip pain. MMP-3 significantly

increased in RDC type 2 compared with type 1 and DDH. Increased posterior pelvic tilt was found in RDC type 2 compared with DDH. Logistic regression and receiver operating characteristic curve analyses indicated that MMP-3 may be associated with differentiation between RDC types 1 and 2. No difference was found in CTI between RDC types and DDH.

RDC type 2 hips developed partial (type 2A) and massive (type 2B) femoral head destruction within the first 12 months. Whereas partial destruction showed <20% collapse ratio, massive destruction demonstrated >40% collapse ratio. Increased posterior pelvic tilt was found in massive destruction. Femoral head destruction started earlier within the first 6 months in massive destruction compared with that in partial destruction. From receiver operating characteristic curve analysis, pelvic tilt differentiated the femoral head destruction types using the initial radiograph at the onset before first demonstration of femoral head destruction. No difference was found in CTI or MMP-3 between the two subtypes.

Conclusion: Disease progression of RDC during 12 months after the onset of hip pain could be classified into two distinct types based on the absence (type 1) and presence (type 2) of femoral head destruction in association with MMP-3 and pelvic tilt as biological and mechanical factors, respectively. MMP-3 may be helpful to differentiate those two types in the early stage of RPOH. The extent of femoral head destruction could further differentiate RDC type 2 into two subtypes based on pelvic tilt.

Acknowledgments : This study was supported by the Japan Hip Joint Foundation.

Disclosure of Interests: None declared

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AB1138 ASSESSMENT OF FLUORESCENCE-OPTICAL IMAGING TECHNIQUE OF THE HANDS IN PSORIASIS AND PSORIATIC PATIENTS USING AN INNOVATIVE OBJECTIVE METHOD

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Background: Psoriasis (Pso) is one of the most common chronic inflammatory skin diseases in Europe. Psoriatic arthritis (PsA) is closely associated to Pso whereas the skin manifestation appears usually years before PsA-related symptoms emerge. Up to 30% of Pso patients develop PsA, biomarkers for its early detection are of major importance. In early PsA, changes in synovial vascularisation appear first. Imaging biomarkers for detection of changes in vascularisation might be useful for early detection of musculoskeletal disease. Fluorescence-optical imaging (FOI) is a new method to detect changes in microvascularisation of the hands. Each collected data set of the FOI system contains 360 images representing a time progression of the indocyanine green (ICG) distribution.

Objectives: To evaluate a reader-independent assessment method for evaluation of FOI in patients with PsO and PsA.

Methods: A prospective study including patients with dermatological confirmed skin PsO was performed. 411 patients were included from German dermatology units without PsA diagnosis but potential risk for its development. Clinical examination (CE) was performed by a qualified rheumatologist. For a reader independent evaluation of the FOI images an objective joint-based scoring method was developed. For this method, the joint areas are defined by image segmentation and scored based on generated heatmaps. To calculate a heatmap indicating conspicuous joints from a data set containing 360 images, each pixel is converted to a time series containing 360 values. From this time series, three independent values (features) are extracted: amplitude, average value and maximal slope. Thus, each pixel is reduced to three different feature values. After the three features are determined for each pixel, k-means clustering is performed on each feature. The numbers of centroids (k) are set to 3, 5, 7 and 9. 12 heatmaps (3 features à 4 ks) are calculated, which results in 12 scores for each joint as well. The clusters are then sorted dependent on their centroid value and coloured accordingly to a predefined heatmap colour palette. To finally score each joint, the pixels in the segmented joint area and their assigned cluster are summed and normalized by the area's amount of pixels and k.

Results: 271 of the patients were investigated by the newly developed method and compared with the CE scoring. 6426 joints were labeled as healthy whereas 1162 joints were either labeled as swollen, tender or both. The result over all investigated patients for k = 9 is summed in table 1. It is observable that every average and median healthy value is lower than the corresponding affected value.

Table 1. Resulting scores for k = 9 for all 271 patients.

Feature Statistic value	Amplitude		Mean		Slope	
	Healthy	Affected	Healthy	Affected	Healthy	Affected
Average	0.503	0.528	0.486	0.509	0.395	0.414
Median	0.496	0.532	0.482	0.505	0.389	0.415

Conclusion: FOI is an innovative method that detects early changes in vascularization of the hands. So, this method can be useful in early detection of arthritis especially in risk populations such as PsO patients. The results of the objective scoring method show that a clear distinction between healthy and affected joints is possible with the average scores as well as the median values. However, if the range of the scores is considered, the overlap between healthy and affected is not neglectable. Thus, the current scoring system can be used as an indicator but not as a single classification marker. Nevertheless, the research at hand has shown the expected outcome and motivates further development on the heatmap approach.

Disclosure of Interests: Lukas Zerweck: None declared, Ulf Henkemeier: None declared, Phuong-Ha Nguyen: None declared, Tanja Rossmanith Grant/research support from: Janssen, BMS, LEO, Pfizer, Andreas Pippow: None declared, Harald Burkhardt Grant/research support from: Pfizer, Roche, Abbvie, Consultant of: Sanofi, Pfizer, Roche, Abbvie, Boehringer Ingelheim, UCB, Eli Lilly, Chugai, Bristol Myer Scripps, Janssen, and Novartis, Speakers bureau: Sanofi, Pfizer, Roche, Abbvie, Boehringer Ingelheim, UCB, Eli Lilly, Chugai, Bristol Myer Scripps, Janssen, and Novartis, Frank Behrens Grant/research support from: Pfizer, Janssen, Chugai, Celgene, Lilly and Roche, Consultant of: Pfizer, AbbVie, Sanofi, Lilly, Novartis, Genzyme, Boehringer, Janssen, MSD, Celgene, Roche and Chugai, Michaela Köhm Grant/research support from: Pfizer, Janssen, BMS, LEO, Consultant of: BMS, Pfizer, Speakers bureau: Pfizer, BMS, Janssen, Novartis

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AB1139 DIAGNOSTICIS AND PROGNOSTICIS SIGNIFICANCE OF CHEST CT EVALUATION OF SMALL PULMONARY VESSELS IN CONNECTIVE TISSUE DISEASES WITH PULMONARY ARTERIAL HYPERTENSION.

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Background: Pulmonary arterial hypertension (PAH) is a fatal complication of connective tissue diseases (CTDs). Chest CT has been increasingly used in the evaluation of patients with suspected PH noninvasively but there is a paucity of studies.

Objectives: Our study was aimed to investigate the cross-sectional area (CSA) of small pulmonary vessels on chest CT for the diagnosis and prognosis of CTD-PAH.

Methods: This retrospective study analyzed the data of thirty-four patients with CTD-PAH who were diagnosed by right heart catheterization (RHC) and underwent chest CT between March 2011 and October 2019. We measured the percentage of total CSA of vessels<5 mm^2 and 5-10 mm^2 as a percentage of total lung area (%$CSA_{<5}$ and %$CSA_{5\text{-}10}$) on Chest CT. Furthermore, the association of %CSA with mean pulmonary artery pressure (mPAP) was also investigated. Besides, these patients were followed up until October 2019, and Kaplan-Meier survival curves were generated for the evaluation of prognosis.

Results: Patients with CTD-PAH had significantly higher %$CSA_{5\text{-}10}$ than CTD-nPAH (p=0.001), %$CSA_{5\text{-}10}$ in CTD-S-PAH and IPAH was significantly higher than CTD-LM-PAH and COPD-PH (p<0.01). There was a positive correlation between %$CSA_{5\text{-}10}$ and mPAP in CTD-PAH (r=0.447, p=0.008). Considering %$CSA_{5\text{-}10}$ above 0.38 as a threshold level, the sensitivity and specificity were found to be 0.824 and 0.706, respectively. Patients with %$CSA_{5\text{-}10}$≥0.38 had a lower survival rate than those with %$CSA_{5\text{-}10}$<0.38 (p=0.049).

Conclusion: Quantitative parameter, %$CSA_{5\text{-}10}$ on Chest CT might serve a crucial differential diagnostic tool for different types of PH. %$CSA_{5\text{-}10}$≥0.38 is a prognostic indicator for evaluation of CTD-PAH.

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AB1140

ABNORMAL RIGHT VENTRICLE RESERVE FOLLOWING EXERCISE IN PATIENTS WITH CONNECTIVE TISSUE DISEASES

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Background: Recent studies have indicated that cardiac autonomic dysfunction is an early sign of cardiovascular impairment in patients with connective tissue disease (CTD). Previous studies have mainly focused on autonomic regulation during rest in this population. The cardiac autonomic responses to an acute physiological stress might provide additional information on the autonomic dysfunction, serving as a powerful predictor of cardiovascular disease and mortality in patients with CTD.
Objectives: We aimed to use exercise stress echocardiography to detect early right heart dysfunction in patients with CTD and healthy controls.
Methods: Treadmill exercise stress echocardiography was performed in 19 CTD patients (8 systemic sclerosis, 6 mixed CTD and 5 SLE) and 20 healthy volunteers. Parameters of right ventricular (RV) systolic function (RV fractional area change, Doppler tissue s' velocity, and systolic strain and strain rate) and diastolic function (peak E and A velocity, Doppler tissue e', a' and early and late diastolic strain rate) were evaluated at baseline and after exercise, with the difference (Δ) being systolic and diastolic reserve. The immunoblotting assay was performed to detect the levels of rheumatoid factor (RF) and C-reactive protein (CRP) as well as autoantibodies such as, antinuclear antibody (ANA), anti-U1 ribonucleoproteins (U1RNP), anti-dsDNA, anti-Sm, anti-SSA, anti-SSB, anti-SCL-70 and RO-52. The correlation between these proteins and RV function was analyzed.
Results: Both the patients with CTD and healthy controls had a normal range of BMI, total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and triglyceride (TG). The average age of patients with CTD was 46.0 ± 10.4 years. At baseline, these patients presented no cardiovascular disease or pulmonary hypertension. No significant difference in the body weight, height, age, sex, blood pressure, RV and left ventricular (LV) function at rest between the two groups (all $P>0.05$). The parameters of RV systolic reserve decreased significantly in CTD group compared to those of the healthy controls (Δs': 5.8±2.1 vs 8.3±2.5cm^{-1}, P <0.01; ΔSr: 2.5±0.8 vs 2.8±0.7s^{-1}, P<0.01). Consistently, RV diastolic reserve was significantly decreased in CTD patients compared to controls (Δe': 2.8±1.5 vs 3.9±2.3cm^{-1}, P <0.05; Δa': 5.8±2.5 vs 10.9±6.3cm^{-1}, P <0.05; ΔE-Sr: 0.8±0.2 vs 1.2±0.5s^{-1}, P <0.05; ΔA-Sr: 0.9±0.3 vs 1.3±0.6s^{-1}, P <0.05). To identify independent predictors of RV function in CTD patients, linear regression was conducted. This suggested that ANA, anti-U1RNP, anti-dsDNA, anti-Sm, anti-SSA, anti-SSB, anti-SCL-70 and RO-52 were not correlated with RV reserve (all P >0.05). A logistic regression analysis revealed that RF (P <0.05) and CRP (P <0.01) were independently associated with RV reserve in CTD patients in response to an acute physiological stress.
Conclusion: Treadmill exercise echocardiography could detect right heart dysfunction early before diagnosed as cardiovascular diseases in patients with CTD. RV reserve after exercise might be a promising parameter to detect cardiovascular disease early in CTD patients.
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Public health, health services research, and health economics

AB1141

EVALUATION OF INFLUENZA AND PNEUMOCOCCAL VACCINATION RATES IN PATIENTS WITH RHEUMATOID ARTHRITIS AND SPONDYLOARTHRITIS, AND THE AWARENESS OF RHEUMATOLOGISTS ABOUT VACCINATION

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Background: Patients with inflammatory arthritis have increased risk of infections which may lead to morbidity and mortality. Some of those infections could be prevented by vaccination.
Objectives: The main objectives of the present study were to investigate (a) the uptake rate of influenza and pneumococcal vaccination among patients with rheumatoid arthritis (RA) and spondyloarthritis (SpA) attending a rheumatology outpatient clinic, (b) the factors associated with their vaccination rate and, (c) the attitudes of Turkish rheumatologists about vaccination.
Methods: Patients, followed-up in a tertiary rheumatology outpatient clinic with the diagnosis of RA and SpA, volunteered for participating to study, were included in this cross-sectional study. Data regarding the socio-demographic and disease-related characteristics (including disease duration, medications used, and comorbid conditions) of the patients, vaccination history, the knowledge about the vaccination, and the factors potentially associated with the uptake of vaccination were collected by face-to-face interview using a standardized questionnaire. 102 out of 345 rheumatologists have participated in a web-based survey.
Results: In total, we collected data from 387 patients (260 with SpA and 114 with RA; 204 [52.8%] female and mean age 46.6 ± 12.7 years). Only 123 (32.3%) of our patients were responded that their disease or treatment might be related to the increased risk for infectious diseases. Influenza and pneumococcal vaccines were administered to 71 (21.4%) and 21 (6.1%) patients, respectively. Vaccination for influenza was recommended by family physicians in 26 patients and by rheumatologists in 12 patients. Rate of influenza vaccination was significantly higher in patients >65 years (p=0.021) and with any co-morbid conditions (p=0.002). The main reasons reported by patients regarding not to be vaccination were (a) the belief that they did not need the vaccine (49.4% for influenza and 26.2% for pneumococcal vaccine), (b) the absence of recommendation from their physicians (24.1% for influenza and 26.2% for pneumococcal vaccine), (c) fear of adverse event of vaccination (28.8% for influenza and 3.2% for pneumococcal vaccine), and (d) lack of knowledge about vaccination (6.1% for influenza and 12.5% for pneumococcal vaccine). Even though 50% of rheumatologists who responded to the survey were aware of the presence of national vaccination recommendations, all of them stated that patients with inflammatory arthritis need to be vaccinated for both influenza and pneumococcal infections. Influenza and pneumococcal vaccines were administered to 23 (22.5%) and 4 (3.9%) rheumatologists, respectively.
Conclusion: Although the knowledge and awareness about influenza and pneumococcal vaccinations were seemed to be high among rheumatologists, vaccination rates for both were insufficient in RA and SpA patients. There remains significant effort to improve vaccination rates and to prevent morbidity and mortality due to vaccine-preventable infections in inflammatory rheumatic diseases.
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AB1142 TREATMENT COSTS OF SELECTED RHEUMATIC DISEASES IN SUB-SAHARAN AFRICA: A CASE FOR IMPROVED INSURANCE COVERAGE FOR AFRICAN PATIENTS

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Background: Rheumatic diseases lead to substantial economic costs [1] especially in resource-poor settings like sub-Saharan Africa (SSA).[2] Annual direct cost of lupus treatment ranges from $13,735-20,926 /patient in the US to £3231($4232)/patient in the UK.[1,3]
Data is rare for SSA and Nigeria in particular where the minimum wage is N30,000 ($83/mth) with only 5% of citizens covered by health insurance.[4,5] The scheme excludes some medications and certain procedures are grossly underfunded. Cost-of-illness studies are invaluable in planning and policy development. They typically include: direct, indirect and intangible costs.[6]
Objectives: To compare total costs of some rheumatic diseases, highlight underfunded therapies and push for wider insurance coverage of rheumatic diseases.
Methods: A cross-sectional study from the University of Uyo Teaching Hospital - Nigeria using data of 252 clinic patients (20 lupus, 27 rheumatoid arthritis, 25 gout and 180 osteoarthritis). Direct costs were estimated using the hospital pricelist while indirect costs were estimated using the human capital method. Statistical analysis was done with p<0.05.
Results: Females were the majority except for gout patients (44%). Most lupus patients were unemployed (75%) and had the highest annual total cost (N472,800–2,240,400) compared with the others. Key medications excluded from insurance are shown in table 2.

TABLE 1. COST-OF-ILLNESS COMPARISON OF SELECTED RHEUMATIC DISEASES

	Lupus (n=20)	RA(n=27)	Gout(n=25)	OA(n=180)
Age (years)	33.9 ± 11.4	43.4 ± 14.3	57.4 ± 9.6	59.7 ± 9.1
Female n (%)	24(95)	25(92)	11(44)	157(87)
Average Duration of illness (years)	4(1-11)	3.5(2-10)	3 (0.2-8)	4(0.1-20)
Unemployed n (%)	15(75.0)	19(70.3)	12(48.0)	62(34.4)
Workdays missed/mth	7	5	2	3
Direct costs (N'000)				
Total /mth (stable)	32.4	27	19.75	18
Total /yr (stable)	388.8	324	237	216
Total /mth (severe)	179.7	155.6	32.5	23
Total /yr (severe)	2,156.4	1,867.2	390	276
Indirect costs				
Productivity loss/mth	7	5	2	3
Productivity loss/yr	84	60	24	36
Total costs/mth	39.4 – 186.7	32 – 160.6	21.75 – 34.5	21 – 26
Total costs/yr	472.8 – 2,240.4	384 – 1,927.2	261 – 414	252 – 312

1$ = 360 Nigerian Naira (NGN), 1€ = NGN 402 as at 31/1/2020. Costs quoted in thousands of Naira.

Table 2. Uninsured treatments.

MMF
Methotrexate
Sulphasalazine
Azathioprine
HCQ
Febuxostat
Colchicine
Rituximab
Arthroplasty (N100,000*)
Dialysis (6 sessions)
Renal transplant

Conclusion: Total annual cost of lupus treatment in Nigeria is quite high ranging from (NGN 472,800–2,242,400) [$1313- 6228] for mild to severe disease. This contrasts with a mean annual national income of $1,000 given that 75% of lupus patients are unemployed. Expanded insurance coverage for rheumatic drugs will further reduce the enormous treatment burden and improve outcomes.

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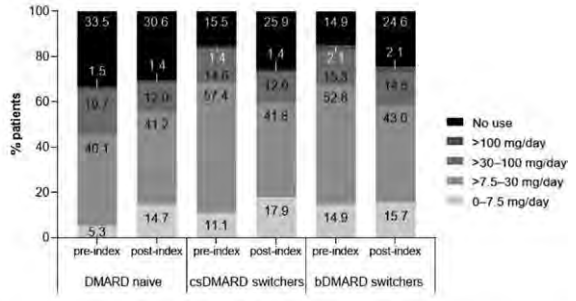
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AB1143 BURDEN OF GLUCOCORTICOIDS AMONG RHEUMATOID ARTHRITIS PATIENTS AT DIFFERENT STAGES OF DISEASE-MODIFYING ANTIRHEUMATIC DRUG MANAGEMENT

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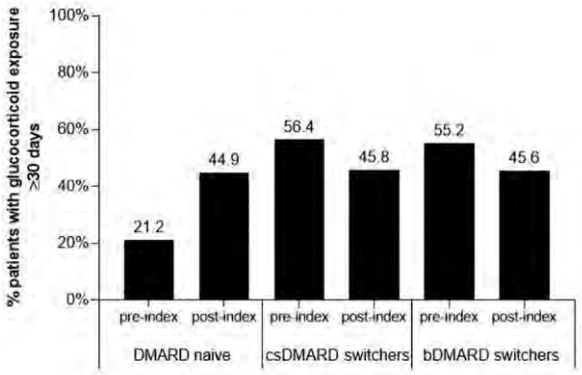
Background: EULAR and ACR guidelines recommend a treat-to-target approach for patients with RA including regular assessments of disease activity. Glucocorticoids are commonly used to control inflammation associated with uncontrolled disease. However, patients using glucocorticoids may develop short- and long-term side effects.
Objectives: To examine the real-world use of glucocorticoids among patients with RA who are disease-modifying antirheumatic drug (DMARD)-naïve or failing their first conventional synthetic DMARD (csDMARD) or biologic DMARD (bDMARD).
Methods: From a large US health claims database, this study included adults with ≥2 RA claims ≥30 days apart who started (index date [ID], 1/1/2012–3/31/2017) a first DMARD (DMARD-naïve) or patients who newly initiated a csDMARD and then switched to or added another DMARD (csDMARD switchers), and patients who initiated a first bDMARD and then switched to another bDMARD or Janus kinase inhibitor (JAKi; bDMARD switchers). All patients had continuous enrollment 1-year before and ≥1 year after ID and were evaluated for pre- and post-ID use of glucocorticoids (oral or injectable), prednisone equivalent dose (PED), and duration of exposure ≥30 days.
Results: The study included 28,201 patients in the DMARD-naïve cohort, 7,816 csDMARD switchers, and 4,656 bDMARD switchers (median age 54 years for all, 73%–78% female).
Among DMARD-naïve patients, 66.5% used glucocorticoids during the pre-ID period (Figure 1) and 61.2% had >7.5 mg/day PED, 21.2% had >30 mg/day PED, and 21.2% had ≥30 days of exposure to glucocorticoids (Figure 2). Post-ID, 69.4% of patients used glucocorticoids, while 54.7% had >7.5 mg/day PED, 13.5% had >30 mg/day PED, and 44.9% had ≥30 days of exposure to glucocorticoids.
Among csDMARD switchers, 84.5% of patients used glucocorticoids during the pre-ID period (Figure 1), and 73.4% had >7.5 mg/day PED, 16.0% had >30 mg/day PED, and 56.4% had ≥30 days of exposure to glucocorticoids (Figure 2). During the post-ID treatment, 74.1% of patients used glucocorticoids, 56.2% had >7.5 mg/day PED, 14.4% had >30 mg/day PED, and 45.8% had ≥30 days of exposure to glucocorticoids.
Among bDMARD switchers, 85.1% of patients used glucocorticoids in the pre-ID period (Figure 1), and 70.2% had >7.5 mg/day PED, 17.4% had >30 mg/day PED, and 55.2% had ≥30 days of exposure to glucocorticoids (Figure 2). During post-ID treatment, 75.4% of patients used glucocorticoids and 59.7% of patients had >7.5 mg/day PED, 16.7% had >30 mg/day PED, and 45.6% had ≥30 days of exposure to glucocorticoids.

Figure 1. Prednisone-equivalent dose use by cohort



bDMARD, biologic disease-modifying antirheumatic drug; csDMARD, conventional synthetic disease-modifying antirheumatic drug; DMARD, disease-modifying antirheumatic drug.

Figure 2. Pre-index and post-index glucocorticoid use by cohort



bDMARD, biologic disease-modifying antirheumatic drug; csDMARD, conventional synthetic disease-modifying antirheumatic drug; DMARD, disease-modifying antirheumatic drug.

Conclusion: Real world glucocorticoid use was high in all categories of DMARD-treated RA patients, at baseline and during their next treatment, suggesting ongoing medical needs. Glucocorticoid doses exceeded 7.5 mg/day for most patients. In addition, many patients had ≥30 days exposure to glucocorticoids, posing an additional safety risk.

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AB1144 DAILY CLINICAL CARE OF PATIENTS WITH MUSCULOSKELETAL COMPLAINTS – HOW HELPFUL IS A TRIAGE SYSTEM FOR EARLY RECOGNITION OF INFLAMMATORY RHEUMATIC DISEASES?

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Background: Early diagnosis and treatment are important for the management of inflammatory rheumatic diseases (RMD). However, the availability of rheumatologists is limited in most European countries and selection strategies lack sensitivity and/or specificity.

Objectives: To evaluate a triage strategy that offers the possibility to see patients within 4 weeks for short term appointments in order to check the probability of an inflammatory RMD and the necessity to further evaluate the patients in due time.

Methods: Physician's and patient's information who called our tertiary rheumatology department´s outpatient clinic for a date in the triage system were included in this analysis. The time to first appointment as assessed by a nurse (Step 1), the short evaluation by a rheumatologist in the triage (Step 2) and the patient´s complaints and the diagnoses after an extensive diagnostic evaluation (Step 3) were documented.

Results: In a period of 9 months in 2018, a total of 982 patients presented. A total of 62 patients (6.3%) were considered urgent (appointment within 3 days), while 240 (24.4%) were appointed within 4 weeks at Step 2. Of the former 46 (19.2%), and of the latter 151 patients (62.9%) were diagnosed with inflammatory RMD at Step 3. In total, 334 patients (34.0%) were diagnosed with inflammatory RMD at Step 3, including 126 with RA (37.7%), 71 with axSpA/PsA (21.3%), 95 with connective tissue disease/vasculitis (28.4%) and 20 with gout (6.0%). The diagnosis suspected in Step 2 was confirmed in Step 3 in 77.9% of cases. In 217 patients, the diagnosis suspected in Step 2 was not confirmed in Step 3. Of them, 34 (15.7%) had unclear findings at Step 2 but an inflammatory RMD was found at Step 3, while 148 (68.2%) had a suspected inflammatory RMD at Step 2 but this was not confirmed at Step 3. The most frequent musculoskeletal complaint at the time point of referral was pain in small peripheral joints (hands and/or feet) in 858 patients (87.4%), in large peripheral joints (knees, shoulders and/or hips) in 780 patients (79.4%) and back pain in 682 patients (69.5%). Fever, night sweats and unclear weight loss was reported by 50 patients (5.1%), while 210 patients (24.5%) presented with findings suspicious of inflammatory RMD such as elevated CRP of unclear origin, and 43 patients (4.8%) because of a threat of organ damage such as unclear elevation of creatinine, as reported by the referring physician. In addition, 167 patients (17.0%) had received glucocorticoids prior to referral, 87 (52.1%) of which finally did not receive the diagnosis of inflammatory RMD at Step 3, while 737 patients (75.1%) were receiving NSAIDs prior to referral.

Conclusion: In this prospective evaluation of a triage system where all patients were pre-screened by a nurse and were seen within 4 weeks by a rheumatologist, clinical differentiation could be performed timely due to a successfully structured triage system. The initially suspected diagnosis was finally confirmed in ≥75% of cases, while ≥1/3 of patients had a definite inflammatory RMD.

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AB1145 PRESCRIPTION PATTERNS AND DISEASE ACTIVITY IN PORTUGUESE WOMEN OF CHILDBEARING AGE WITH RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS, ANKYLOSING SPONDYLITIS AND JUVENILE IDIOPATHIC ARTHRITIS

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Background: Disease activity (DA) at conception is one of the main predictors of pregnancy outcomes in women of childbearing age (WoCBA) with rheumatic diseases. Teratogenicity and unawareness about pregnancy compatibility of some disease-modifying anti-rheumatic drugs might limit the choice of treatment in WoCBA.

Objectives: To assess differences in prescription patterns between WoCBA with rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis (AS) and juvenile idiopathic arthritis (JIA) and comparator groups, namely

postmenopausal women (PMW) and age-matched men. Evaluate DA in WoCBA comparing to the aforementioned groups.
Methods: Observational transversal study, using data from the portuguese registry of rheumatic diseases (Reuma.pt) from 3 portuguese centers. Adult patients (pts) with the diagnosis of RA, PsA, AS or JIA were allocated to the following groups: WoCBA (aged 18–44y), young men (YM) (18–44y), PMW (≥ 45y) and matched men (≥45y). Demographic and clinical variables are described as means or frequencies. Differences between groups regarding therapy and DA were assessed with Chi-square and ANOVA tests. Linear and logistic regression models were used to find predictors of DA and prescription patterns.
Results: 2133 pts were included, 69.9% female with a mean age of 55.96±15.85 y. 1437 pts were diagnosed with RA, 305 with PsA, 254 with AS and 137 with JIA. Patterns of prescription are detailed in table 1. WoCBA were less likely to be treated with glucocorticoids than PMW (OR 0.66 95%CI 0.44-0.99). WoCBA were 1.76 times more likely to be treated with MTX than YM (95%CI 1.04-2.97). Certolizumab was specially prescribed in WoCBA (OR 13.8, 95%CI 1.4-132.8). WoCBA had significantly higher DA scores than YM (DAS28 3.03±1.39 vs 2.32±1.18 and BASDAI 3.55±2.0 vs 2.43±1.66).

Table 1. Prescription patterns

Medications, n (%)	A -WoCBA (N=256)	B - Young Men (N=161)	C - Post menopausal Women (N=927)	D - Men N=340	Chi-square test
NSAIDs	143 (55.9)	111(68.9)	472 (50.9)	169 (49.7)	p<0.001
Glucocorticoids	106 (41.4)	31 (19.3)	625 (67.4)	154 (45.3)	p<0.001
csDMARDs					
- Methotrexate	149 (58.2)	60 (37.3)	663 (71.5)	197 (57.9)	p<0.001
- Leflunomide	12 (4.7)	4 (2.5)	45 (4.9)	2 (0.6)	p=0.003
- Sulfassalazine	9 (3.5)	5 (3.1)	39 (4.2)	9 (2.7)	NS
- Hydroxychloroquine	36 (14.1)	4 (2.5)	117 (12.6)	18 (5.3)	p<0.001
bDMARDs					
- Etanercept	48 (18.8)	29 (18.0)	140 (15.1)	66 (19.4)	NS
- Infliximab	9 (3.5)	11 (6.8)	36 (3.9)	30 (8.8)	p=0.002
- Adalimumab	17 (6.6)	15 (9.3)	47 (5.1)	27 (7.9)	NS
- Golimumab	15 (5.9)	18 (11.2)	37 (4.0)	30 (8.8)	p<0.001
- Certolizumab	10 (3.9)	0 (0)	2 (0.3)	2 (0.6)	p<0.001
- Tocilizumab	12 (4.7)	2 (1.2)	71 (7.7)	10 (2.9)	p<0.001
- Rituximab	5 (1.9)	0 (0)	50 (5.4)	4 (1.2)	p<0.001
- Abatacept	0 (0)	0 (0)	9 (1)	0 (0)	NS
- Secukinumab	1 (0.4)	4 (3.5)	8 (0.9)	2 (0.6)	NS
- Ustekinumab	1 (0.4)	3 (1.9)	5 (0.5)	0 (0)	NS
tsDMARDs	4 (1.6)	1 (0.6)	9 (0.9)	0 (0)	NS

bDMARDs – biologic disease modifying antirheumatic drugs, csDMARDs – conventional synthetic disease modifying antirheumatic drugs, NSAIDs – non-steroidal anti-inflammatory drugs, tsDMARD – targeted synthetic disease modifying antirheumatic drugs, WoCBA – women of childbearing age

Conclusion: Certolizumab was prescribed preferentially in WoCBA, who alsoreceived more MTX than YM. Nevertheless, DA in this group was not well controlled, which may influence future pregnancy outcomes. Ensuring tight DA control in WoCBA through proper and ideally no teratogenic medication remains an unmet clinical need.
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AB1146 REAL-LIFE PRACTICES IN MANAGEMENT OF REPRODUCTIVE HEALTH IN SLE AND APS BY OBSTETRICIANS AND RHEUMATOLOGISTS IN EGYPT. (AN ONLINE-BASED QUESTIONNAIRE)

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Background: Systemic lupus erythematosus (SLE) is an auto-immune disease that affect women in their reproductive age. Antiphospholipid syndrome (APS) is a hypercoagulable immune disease that occur as a primary condition or in assosiation with SLE.
The reproductive aspects as contraception, fertility, pregnancy are crucial to consider for proper management of SLE/APS.
Addressing these issues require collaboration between rheumatologists and obstetricians, improving their knowledge and ensuring that both are acquainted with the updated guidelines.
Objectives: To assess the knowledge and practice of Egyptian obstetricians and rheumatologists in management of reproductive health issues in SLE and APS, and to detect common misconceptions.
Methods: This research was conducted via google form online survey based on points discussed in EULAR recommendations for women's health and the management of family planning, assisted reproduction, pregnancy and menopause in patients with SLE and/or APS.[1] It was sent to target obstetricians and rheumatologists by internet clouds like (Facebook, twitter, LinkedIn) from August to November 2019. It included five domains; demographic data, general knowledge and attitudes about pregnancy in SLE and APS, contraception, drugs, and assisted reproductive techniques (ART)
After submitting answers, respondents were shown a link directing them to the 2016 EULAR recommendations.[1]
Results: This study was conducted on 254 physicians, 62% obstetricians and 38% rheumatologists. 64.6% were between the ages of 30-35 years.
For general knowledge, 52% of Obstetricians considered pregnancy in inactive SLE to be risky. (79.4% **vs** 54.1%) of (rheumatologists and obstetricians) respectively test for aPL in SLE patients. More than 70% in both groups were well informed on the increased rate of fetal and maternal complications in both SLE and APS.
For fetal surveillance, 87% and 90% of obstetricians preformed first and second trimester U/S, and 79% preformed second trimester Doppler.
For contraception, (57.7% **vs** 56.7%) discuss contraceptive choices with their patients. The majority considered it safe to use IUDs (73.9% **vs** 76%) and condoms (84.7 **vs** 85.4%) in both SLE and APS patients. On the other hand, for hormonal contraception- Levonorgestrol IUD, Depoprovera, COCP, and POP- only 14.6%, 22.9%, 26.1%, 24.8% of rheumatologists and 18.5%, 27.2%, 29.9%, 26.8% of obstetricians considered them unsafe to use in APS.
Concerning treatment, the majority considered low dose presnidone to be safe during pregnancy (94.8 % **vs** 80%) and breastfeeding (87.6% **vs** 64.3%). The majority also agreed on avoidance of Methotrexate (94.8% **vs** 84.1%) and Cyclophosphamide (89.7% **vs** 66.2%). However, regarding Hydroxychloroquine and Azathioprine use in pregnancy there was a significant discrepancy between rheumatologists and obstetricians, (89.7 % **vs** 42%) and (78.4% **vs** 36.9%) believed them safe to use in pregnancy. For Mycophenolate Mofetil, (80.4% **vs** 46.5%) said that it should be avoided in pregnancy. Regarding ART (45.4% **vs** 71%) considered it safe to use in stable SLE/APS.
Conclusion: The gaps in knowledge identified include the use of hormonal contraception in APS patients and the proper utilization of important medications to prevent and treat lupus flares. Initiation of shared Rheumatology/ obstetric clinics and focusing on the identified educational topics, would lessen the gap in knowledge and discrepancies in practice improve overall patient management.
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Disclosure of Interests: None declared
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AB1147 SCREENED – HIGH REMISSION RATES UNDERLINE THE BENEFIT OF SCREENING CONSULTATION MODELS FOR EARLY RECOGNITION AND TREATMENT OF RHEUMATIC AND MUSCULOSKELETAL DISEASES

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Background: Early recognition and treatment of rheumatic and musculoskeletal diseases (RMDs) is of critical importance for the individual outcome. However, nationwide health care structures in Germany do not facilitate early access to initial rheumatologic evaluation. Furthermore, waiting times of several months due to substantial capacity constrains in regional rheumatology care services compromise the prognostically relevant "window of opportunity" for subsequent sustained remission. To promote early detection of RMDs, the Division of Rheumatology at the University hospital Heidelberg, Germany has launched a unique screening consultation model that offers early access to rheumatologic evaluation on regional level.
Objectives: The registry-based study SCREENED ("Screen for early diagnosis") has been initiated to monitor the outcome of patients that were diagnosed with an RMD at the screening clinic and to assess the costs and benefits of this consultation model for the regional quality of care.

Methods: The screening consultation model has been launched in two phases: in the first phase (02/2016 - 01/2018), a screening clinic open to all patients without previous rheumatologic evaluation with appointments according to the registration order has been established through rearrangement of available capacities. In contrast to regular appointments, the screening clinic took place in shorter consultation time frames and without additional diagnostic procedures. In the second phase (02/2018 - 01/2020), in order to manage and prioritize access to rheumatologic care at our division more efficiently, prior to appointment allocation (not only) to the screening clinic all new patient registrations became subject to a preselection procedure based on the evaluation of an anamnesis questionnaire, medical reports and laboratory findings by an experienced rheumatologist. Furthermore, SCREENED project has been launched for scientific evaluation of both phases of the consultation model.

Results: The screening consultation model achieved a significant reduction in waiting times to few weeks compared to six months for a regular appointment. In the first phase, the screening clinic had a high sensitivity of 94.3% and an improvable specificity of 31.1%. In the retrospective cohort, high remission rates have been observed over all RMD entities (120/206 = 58.3% patients based on physicians' assessment in the follow-up after screening clinic) and in rheumatoid arthritis (RA) in particular (38/61 = 62.3% and 33/55 = 60% patients with DAS28 score < 2,6 after 12 and 24 months respectively). Remission was usually reached within a year after the first appointment (9.5 ± 6.7 months), however, a trend to higher remission rates in patients with shorter illness duration was obvious. In RA patients, csDMARDs have been initiated in a third of patients immediately at diagnosis in the screening clinic and in another third within six months after the first appointment. After 12 months, > 80% have received csDMARDs, while only 14.2% needed b/tsDMARDs in the follow-up over 24 months.

Conclusion: High sensitivity and significant reduction in waiting times for initial rheumatologic evaluation in the screening clinic pave the way for early recognition and treatment of RMDs. Subsequently, high remission rates in the follow-up were reached. In RA, a high proportion of patients only required csDMARDs to achieve sustained remission. A correspondingly small proportion of patients necessitating b/tsDMARD in the follow-up points towards a significant health economic benefit of the early rheumatologic intervention in the screening consultation model.

Disclosure of Interests: Karolina Benesova Grant/research support from: Study grants for SCREENED study by Abbvie, Novartis and Rheumaliga Baden-Württemberg, Consultant of: One-time participation in Novartis advisory board., Vivienne Lion Grant/research support from: Grant/research support from: Study grants for SCREENED study by Abbvie, Novartis and Rheumaliga Baden-Württemberg, Oliver Hansen Grant/research support from: Grant/research support from: Study grants for SCREENED study by Abbvie, Novartis and Rheumaliga Baden-Württemberg, Hanns-Martin Lorenz Grant/research support from: Consultancy and/or speaker fees and/or travel reimbursements: Abbvie, MSD, BMS, Pfizer, Celgene, Medac, GSK, Roche, Chugai, Novartis, UCB, Janssen-Cilag, Astra-Zeneca, Lilly. Scientific support and/or educational seminars and/or clinical studies: Abbvie, MSD, BMS, Pfizer, Celgene, Medac, GSK, Roche, Chugai, Novartis, UCB, Janssen-Cilag, Astra-Zeneca, Lilly, Baxter, SOBI, Biogen, Actelion, Bayer Vital, Shire, Octapharm, Sanofi, Hexal, Mundipharm, Thermo Fisher., Consultant of: see above

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AB1148

ECONOMIC BENEFIT FROM IMPROVEMENTS IN HEALTH-RELATED QUALITY OF LIFE WITH UPADACITINIB AND COMPARISONS WITH TOFACITINIB AND METHOTREXATE IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic, debilitating autoimmune disease and is associated with high direct medical costs. Treatment of RA with disease-modifying anti-rheumatic drugs (DMARDs) can improve patients' health-related quality of life (HRQOL) and has the potential to reduce direct medical costs associated with RA. Treatment with janus kinase inhibitors, such as upadacitinib (UPA), has shown improvements in HRQOL in patients with RA [1].

Objectives: To estimate the economic benefit from improvements in HRQOL and to compare estimated direct medical costs between: (1) UPA and tofacitinib (TOFA) and (2) UPA monotherapy and methotrexate (MTX) monotherapy in patients with RA.

Methods: This economic analysis used individual patient-level data from 2 randomized clinical trials (RCTs) of UPA (SELECT-NEXT and SELECT-MONO) and published aggregate data from 1 RCT of TOFA (ORAL-Standard) in patients with moderate to severe RA that collected repeated measurements of HRQOL based on the Short Form 36 Health Survey (SF-36). Estimated direct medical costs per patient per month (PPPM) for UPA 15mg once daily (QD) and MTX were estimated based on observed SF-36 Physical (PCS) and Mental Component Summary (MCS) scores in the SELECT RCTs using a published regression algorithm [2]. Direct medical costs PPPM for TOFA 5mg twice daily (BID) were estimated from Rendas-Baum, et al [3], which applied the same regression algorithm to SF-36 PCS and MCS scores observed in the ORAL-Standard RCT. Resulting estimates of direct medical costs PPPM in the short-term (12–14 weeks) and long-term (48 weeks) were compared between UPA and TOFA and between UPA and MTX. Costs were inflation-adjusted to 2018 US dollars. Bootstrapping was used to generate 95% confidence intervals (CI).

Results: Over 12 weeks, estimated direct medical costs PPPM were $186 lower (95% CI: $21, $364) in patients treated with UPA compared with those treated with TOFA. Estimated long-term medical costs PPPM at Weeks 24 and 48 (Figure 1) and cumulative costs over the entire 48-week period (difference: $1,452; 95% CI: $906, $2,086; Table) were significantly lower for UPA than for TOFA. Over 14 weeks, estimated direct medical costs PPPM were $370 lower (95% CI: $147, $575) in patients treated with UPA monotherapy compared with those treated with MTX alone. Estimated long-term direct medical costs at Week 48 (Figure 2) and cumulative costs over the entire 48-week period (difference: $2,120; 95% CI: $1,398, $2,861; Table) were significantly lower for UPA monotherapy compared with MTX alone.

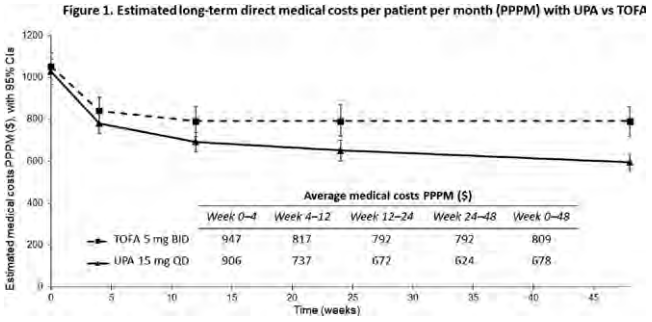
Conclusion: Based on improvements in HRQOL in the short-term and long-term, UPA 15mg QD was associated with significantly lower direct medical costs than TOFA 5mg BID in patients with active RA. UPA 15mg QD monotherapy was associated with significantly lower direct medical costs than MTX monotherapy in patients with active RA. These results provide evidence of the economic benefits of UPA as a novel treatment for moderate to severe RA.

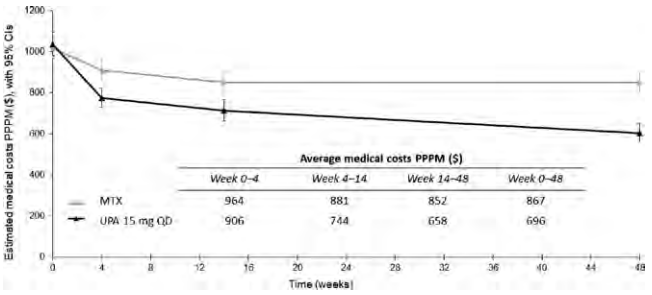
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Table. Cumulative cost savings over 48 weeks with UPA vs TOFA and UPA vs MTX

Treatment	Total 48-week medical costs ($)	Difference (95% CI)
UPA vs TOFA		
TOFA 5mg BID	8,964	1,452 (906, 2,086)
UPA 15mg QD	7,511	—
UPA vs MTX		
MTX	9,833	2,120 (1,398, 2,861)
UPA 15mg QD	7,713	—





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Disclosure of Interests: Arielle Bensimon Employee of: Analysis Group, Min Yang Employee of: Analysis Group, Eli Orvis Employee of: Analysis Group, Jerry Clewell Shareholder of: AbbVie, Employee of: AbbVie, Namita Tundia Shareholder of: AbbVie, Employee of: AbbVie

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AB1149 POOR RESPONSE TO HEPATITIS B VACCINATION IN RHEUMATIC PATIENTS TREATED WITH BIOLOGIC THERAPY – IMPLICATIONS FOR CLINICAL PRACTICE

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Background: Hepatitis B virus (HBV) vaccination is recommended for rheumatic patients starting biologic therapy. There is some evidence that HBV vaccination is effective in patients under conventional disease modifying anti-rheumatic drugs (DMARDs), but it is currently unclear whether this also applies to biologics.

Objectives: To assess the efficacy and safety of HBV vaccination in patients with rheumatic diseases treated with biologics.

Methods: We included patients with any inflammatory rheumatic diseases treated with any biologic, who were negative for anti-HBs and anti-HBc and had never been vaccinated for HBV. Engerix B® was administered at 0, 1 and 6 months and anti-HBs was re-assessed ≥1 month after last dose. Response was defined as anti-HBs>10IU/L and compared against healthy controls (HC) undergoing Occupational Health immunization. Disease flare was evaluated before and until at least 1 month post-vaccination. We recorded serious adverse events (SAE) and immune-related disorders not previously present.

Results: We included 67 patients, most treated with TNF inhibitors (TNFi), and 70 HC (Table 1). Most patients were taking concomitant DMARDs (69%) and were in remission/low disease activity (59%). Only 20 patients (30%) had a positive response to vaccination, in comparison to 68 HC (97%, p<0.001). Mean post-vaccination anti-HBs titre was significantly lower in responding patients than HC (569 ± 772 vs 1316 ± 811U/L, p<0.001). Responders diagnoses were RA (n=8 [25%]), PsA (n=7 [39%]), AS (n=4 [33%]) and IBD-associated SpA (n=1[100%]). Response was seen in 19/53 patients treated with TNFi (36%), but only 1/14 (7%) of patients treated with non-TNFi (p=0.037). Importantly, some responders had to temporarily interrupt biologic therapy due to other intercurrences for at least one administration. No clinical or demographic variables were associated with response, including age and disease activity. Fourteen patients (21%) experienced disease flares, of which 7 were mild and did not require therapy adjustment; 3 patients required minor treatment/dose adjustments; 4 patients had secondary failures that led to switches. There were 3 SAE (acute diverticulitis; abdominal infection; atrial fibrillation and urinary infection) 1-4 months after 1st/2nd dose, deemed not to be related to vaccination. One RA patient on infliximab had bilateral uveitis 2 months after the 1st vaccine dose, which resolved with topical therapy.

Table 1. Baseline characteristics of study participants.

	Patients (n=67)	Controls (n=70)	p
Age (years)	56 ± 9	46 ± 9	<0.001
Female (%)	40 (60)	62 (89)	<0.001
Diagnosis (%)			
RA	32 (48)		
PsA / AS	18 (27) / 13 (19)		
Other	4 (6)		
Disease duration (years)	17 ± 10		
Biologic (%)			
TNF-inhibitor	53 (79)		
Tocilizumab / Abatacept	6 (9) / 1 (1)		
Rituximab / Belimumab	2 (3) / 4 (6)		
Anakinra	1 (1)		
Conventional DMARDs (%)			
MTX / LEF	39 (58) / 1 (1)		
SSZ / Other	6 (9) / 3 (4)		
None	21 (31)		
Prednisolone (%) / Dose (mg)	29 (43) / 5.6 ± 2.1		
DAS28	3.1 ± 1.4		
ASDAS	2.2 ± 1.4		

Conclusion: In this study, HBV vaccination response was poor and lower in rheumatic patients treated with biologic therapy than in healthy adults. Vaccination was overall safe but there were 4 severe flares and 3 SAE that lead to treatment switch/interruption, although causal association is difficult to establish. Our data reinforce the recommendation for HBV vaccination prior to starting biologic therapy, possibly even as soon as the diagnosis is established. Alternative HBV vaccination strategies should be investigated in patients already treated with biologics.

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AB1150 ECONOMIC IMPACT ASSOCIATED TO BIOLOGICAL THERAPY / SYNTHETIC FAME OPTIMIZATION IN A COHORT OF PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATIC DISEASES TREATED BY OBJECTIVES.

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Background: Therapeutic decision-making for biologic-therapies/ synthetic FAME (BT/SD) dose optimization, should be based on optimal disease activity results according to a treatment strategy by objectives. The goal of BT optimization is to guarantee long-term effectiveness and safety, maximising economic savings

Objectives: To evaluate BT optimization patterns in patients with rheumatic diseases (RD) and associated economic savings.

Methods: An observational and prospective study, which included a cohort of patients with rheumatoid arthritis (RA), spondyloarthropathies (SA) and psoriatic arthritis (PsA) treated with BT from January 2014 to December 2019. BT optimization, achieved by reducing or prolonging the interval at least one dose, was indicated when patients have more than 6 months of treatment and are in clinical remission (DAS28 <2.6 for RA and PsA, and BASDAI<2 for SA) or minimal clinical activity (DAS28<3.2 for RA and PsA, and BASDAI<4 for SA).

Variables were described as frequencies and means. Diagnosis, BT (abatacept, adalimumab, apremilast, baricitinib, certolizumab, etanercept, golimumab, ixekizumab, secukinumab, tocilizumab, tofacitinib, and ustekinumab), dose regimens, total treatment duration, time on BT optimization (TO) and treatment costs were collected.

Cost savings were calculated per patient by comparing optimization treatment costs to conventional treatment and globally by comparing real cost to theoretical conventional doses cost.

Results: A total of 260 patients were included in the study. Switching were observed in 32.7%. From all patients, 53% were candidates for BT optimization (according to diagnosis: 60.9% with RA, followed by 52.2% with SA and 43.4% with PsA)

A 40% of patients with BT optimization were treated with adalimumab and etanercept being also the most common BT used in RD treatment

BT optimization allowed a pharmaceutical saving of **€ 177,539.40** per year against the use of conventional therapy, resulting in a reduction of the total cost of **€1,065,236.40** in the last 6 years. The saving per patient / year was € 707.63 for RA; € 850,40 for SA and of €493,21 for the PsA.

Conclusion: Therapeutic decision-making based on validated disease activity scales has allowed the BT optimization in approximately 53% of patients with RD. BT optimization allowed a pharmaceutical saving of € 177,539.40 per year being higher in the SA (€ 850.40) followed by the RA (€ 707.63) and finally the PsA (€ 493.21)
The BT optimization allows to reduce costs maintaining the effectiveness and safety.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.5354

AB1151 COMPLIANCE/CONCORDANCE WITH MYCOPHENOLATE MOFETIL IN PATIENTS WITH CONNECTIVE TISSUE DISORDERS IN COVENTRY.

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Background: Connective tissue disorders like Systemic lupus erythematosus (SLE) are multi-organ systemic conditions characterised by disordered immune function. Mycophenolate Mofetil (MMF) is commonly used for treatment of SLE[1] and other connective tissue disorders like Sjogren's syndrome, myositis and Scleroderma. Compliance with drugs remains a significant issue in management of these conditions and varying reports from across the world[2,3] continue to show significant lack of concordance resulting in increased disease activity and damage.
Objectives: The aim of this study was to investigate the compliance/concordance specifically with MMF treatment among patients attending clinics at University Hospitals Coventry and Warwickshire NHS Trust (UHCW)with SLE and other connective tissue disorders.
Methods: Ethical approval was obtained through research and development department within the Trust. This is a retrospective study collating non-identifiable hospital pharmacy data in patients who requested the prescription for MMF drug between January 2015 and December2018. Since MMF was required to be prescribed from the hospital (i.e. General practitioners within the region were unable to prescribe it), we have records for all prescriptions for these patients. We extracted information on sample size, frequency of prescription requested and length of follow up. Clinical data were obtained from paper and electronic notes of the patients. Data were analysed using the data analysis tool pack for linear regression, on Microsoft Excel package version 16.29.1.
Results: We recruited 144 patients into this study, (74%) of these are females. Age range for this group was 2-89 years, median age was 45 (±11.2) years with a mean (±SD) age of 35.6 (±11.2) years and a disease duration of 8.8 (±6.2) years. 73.1% were White British, the remaining included 8.3% Indian, 5.5% Pakistani, 2.7% Black British, 2% Caucasian, 2.1% Chinese, and 6.3% other. Overall, we had 54 patients with SLE and 90 Patients with other connective tissue disorders. Good compliance (81-100%) with MMF therapy was seen in 49 patients, (34%). Poor compliance (0-20%) was seen in 13 patients, (9%). We found a significant correlation between lack of compliance and risk of flares ($r = 0.25$, $p < 0.002$), displayed in Figure 1. We also found a significant difference in compliance patters depending on diagnosis and also on age. SLE patients were 34% less compliant with MMF in comparison to other connective tissue disorders. Demographics suggested the degree of compliance increased with age. Patients between 40-69 years of age were 65% more compliant in comparison to the age 20-39 years ($p < 0.002$).
Conclusion: SLE and connective tissue disorder patients within Coventry continue to have issues relating to compliance/concordance with MMF treatment and this appears to be worse in patients with SLE and in the 20-39 years of age. These patients also appear to be getting flares hence, this remains a major problem in the management of these conditions.
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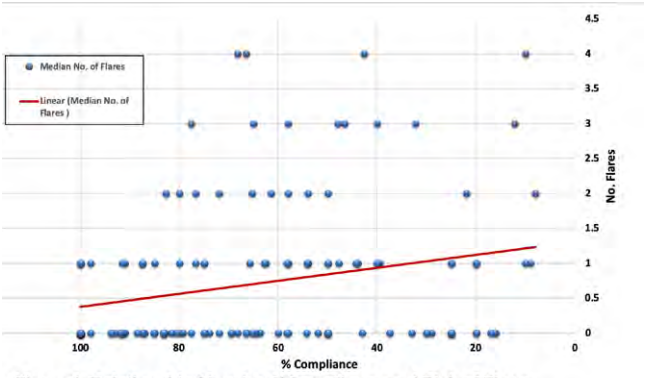


Figure 1. Relationship Showing %Compliance and Risk of Flares

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.6415

AB1152 INCREASED VACCINATION RATE AMONG PATIENTS UNDER BIOLOGICAL DMARDS AFTER INFECTIOUS RISK ASSESSMENT CLINIC

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Background: Infectious complications are a major concern among immunosuppressed patients. In an attempt to ameliorate these, EULAR released an updated version of their recommendations for vaccinations in patients with rheumatic diseases. These should resonate even further, since our patients are deliberately immunosuppressed in order to achieve remission. In 2018, an Infectious Risk Assessment Clinic (IRAC) was created in our centre to address these issues and prepare patients for biological therapy. This work summarizes our experience.
Objectives: Compare vaccination rate among patients with rheumatic diseases under biological therapy before and after the clinic creation.
Methods: A retrospective observational study was conducted in our Rheumatology Department and IRAC, at Local Health Unit of Guarda. All patients under biological therapy followed in our department from 2010 to 2020 were chart reviewed. Sociodemographic and clinical features were collected: sex, age, rheumatic disease diagnosis, current biological treatment and their vaccination history. Studied vaccines were Pneumococcal 13-valent conjugate, Pneumococcal vaccine polyvalent, Influenza virus, Hepatitis A and B, Herpes Zoster and Tetanus/Diphtheria. Patient was considered vaccinated when the correct schedule was followed by the attending physician. If prescription was outside the stipulated timing, it was considered not vaccinated. Chi-square and Fisher's exact test were used to assess associations and $p<0.05$ was considered statistically significant different.
Results: 65 patients were included, 41 (63.10%) were females, with a mean age of 52.38±11.11 years. Diagnosis distribution is the following: rheumatoid arthritis (52.30%), axial spondylarthritis (26.20%), psoriatic arthritis (12.30%), peripheral spondylarthritis (6.20%), 1 (1.50%) patient with Sjögren Syndrome and 1 (1.50%) with systemic sclerosis. Most common drugs were anti-TNFα (64.60%), anti-JAK (15.40%), anti-IL17A (10.80%), anti-CD20 (7.70%) and anti-IL12/IL23 (1.50%). Of all patients, 24 (36.90%) attended IRAC before starting biological therapy. Table 1 shows prescribed vaccines in both groups and their associations.

Table 1. Prescribed vaccines in both groups (p<0.05).

	IRAC attended	IRAC not attended	P
Pneumococcal 13-valent conjugate			0.24
Prescribed	23 (95.83%)	34 (82.93%)	
Not Prescribed	1	7	
Pneumococcal vaccine polyvalent			0.01
Prescribed	19 (79.17%)	19 (46.34%)	
Not Prescribed	5	22	
Influenza virus			<0.01
Prescribed	22 (91.67%)	12 (29.27%)	
Not Prescribed	2	29	
Hepatitis A			0.05
Prescribed	3 (12.50%)	0 (0.00%)	
Not Prescribed	21	41	
Hepatitis B			
Prescribed	12 (50.00%)	0 (0.00%)	
Not Prescribed	12	41	<0.01
Herpes Zoster			0.37
Prescribed	1 (4.17%)	0 (0.00%)	
Not Prescribed	23	41	
Tetanus/Diphtheria			0.14
Prescribed	3 (12.50%)	1 (2.44%)	
Not Prescribed	21	40	

Conclusion: A few conclusions can be drawn from this work. Firstly, prevalence of vaccination increased after clinic creation, especially for Pneumococcal vaccine polyvalent, Influenza virus, Hepatitis A and B. We would expect the same results in the remaining vaccines in a broader population. Our results were also affected by stock rupture in our country. Secondly, this study shows the importance of a protocol, which helps systemise assessment of infectious risk before biological therapy, by analysing thoroughly vaccination history and keeping it updated. Lastly, shared responsibility between rheumatologists and infectiologists enables them to leverage their skills and focus, leading to ultimate gains for the patient. We hope this work motivates colleagues to start similar practices in their centres.

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Disclosure of Interests: None declared

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AB1153 ANALGESIC AND ANTI-INFLAMMATORY DRUG USE IN PATIENTS WITH RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS AND SPONDYLOARTHRITIS VERSUS CONTROLS IN A BELGIAN GENERAL PRACTITIONER REGISTRY.

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Background: Rheumatoid arthritis (RA), psoriatic arthritis (PSA) and spondyloarthritis (SPA) are the most common inflammatory rheumatic diseases. Pain is the hallmark symptom in these conditions and pain relief is ranked first amongst preferred outcomes by patients. Level of analgesic and anti-inflammatory drug use is unknown in these populations in Belgium.

Objectives: To compare analgesic and anti-inflammatory drug use in patient populations of RA, PSA and SPA versus controls in a General Practitioners (GP) setting in an era of expanding treatment possibilities in rheumatology.

Methods: Data were obtained from Intego over a 13-year time interval from 1999 to 2012. Intego is a Flemish GP-based morbidity registration network hosted at the Academic Center for General Practice of the KU Leuven, covering 2% of the Flemish general population. Patients classified under the International Classification of Primary Care codes L88 (rheumatoid/seropositive arthritis) and L99 (musculoskeletal disease other) were selected for this study. Experienced rheumatologists verified if the keywords mapped to these codes corresponded to a diagnosis of RA/SPA/PSA. The date of these diagnoses in Intego was considered "baseline". Controls were matched on age, gender, baseline date and GP practice in a 4:1 case ratio. Intego registers all electronic drug prescriptions by the GP. Anytime use of glucocorticoids, NSAIDs, opioids except tramadol, tramadol and paracetamol in the first 3 years after diagnosis is presented. Proportions of patients and controls on analgesic and anti-inflammatory drugs were compared by Chi-Square analyses.

Results: Over a 13-year period, 738, 229 and 167 patients were included with a diagnosis of RA, SPA or PSA, respectively. Table 1 presents the medication use of these populations. The three conditions had statistically significantly more prescriptions for all types of analgesic and anti-inflammatory drugs compared to controls. Approximately 70% of patients with an inflammatory rheumatic condition received mild pain medication (NSAIDs, Tramadol and Paracetamol) in the first three years after diagnosis. To note is the high use of opioids, even excluding tramadol, in these populations ranging up to 15%.

Table 1. 3-year analgesic and anti-inflammatory drug use in RA, SPA and PSA patients versus controls

Medication	RA	RA Control	SPA	SPA Control	PSA	PSA Control
Number of patients	738	2952	229	916	167	668
Glucocorticoids	241(33%)	348(12%)	29(13%)	70(8%)	47(28%)	67(10%)
NSAIDs	455(62%)	1156(39%)	161(70%)	340(37%)	114(68%)	267(40%)
Opioids	109(15%)	263(9%)	31(14%)	53(6%)	24(14%)	45(7%)
Tramadol	87(12%)	150(5%)	22(10%)	28(3%)	16(10%)	26(4%)
Paracetamol	233(32%)	598(20%)	63(28%)	165(18%)	51(31%)	141(21%)
Total analgesic and anti-inflammatory drug use	506(69%)	1409(48%)	172(75%)	407(44%)	121(72%)	309(46%)

RA= Rheumatoid arthritis, PSA= psoriatic arthritis, SPA= spondyloarthritis. Total analgesic and anti-inflammatory drug is the sum of NSAIDs, Tramadol and Paracetamol. Anytime use of drugs are presented.

Conclusion: Frequent analgesic and anti-inflammatory drug use in patients with a chronic inflammatory joint condition is to be expected, and underlined by the results of our study. Remarkably is the high use of opioids, even excluding tramadol, in patients with RA, PSA and SPA in an era of effective disease modifiers, as well in the control population. Our data shows that around 9% of the Belgian population receives at least once over a 3-year period an opioid prescription. As our data only registers electronic GP prescriptions, this is likely to be an underestimation of the true prescription proportion. Detailed analyses on dose and duration of analgesic and anti-inflammatory drugs will follow.

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AB1154 EHR-INTEGRATED PATIENT-GENERATED HEALTH DATA FOR SYMPTOM MONITORING IN LONG-TERM CONDITIONS: A SYSTEMATIC REVIEW

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Background: Patients with long-term conditions (LTCs), including many RMDs, often require continuous management of care. Patient-generated health data (PGHD) collected between visits could inform ongoing care management and provide important insights into patient health and well-being. There is increasing interest in integrating PGHD in electronic health records (EHRs). However, integration is still largely aspirational with limited evidence of successful systems.

Objectives: To map the landscape of EHR-integrated remote symptom monitoring systems in the field of LTCs. The objectives were to 1) characterise state of the art systems, 2) describe their clinical use, and 3) outline anticipated and realized benefits for clinical practice.

Methods: A systematic search was conducted in three electronic databases up until November 2019. Titles and abstracts were independently screened by two reviewers. One reviewer screened full-text articles, identified those relevant for review and extracted data. Inclusion criteria included 1) symptom reporting systems in adult patients suffering a LTC, 2) integration of data into the EHR, 3) symptom data collected remotely, 4) evidence of use in clinical care. We did not exclude studies based on study design, quality, or sample size. Synthesis focused on describing system specifications and their use. For objective three we adopted a list of outcome indicators [1], which each of the studies were assessed against.

Results: The initial search yielded 2040 articles. Only 12 studies reporting on ten unique systems were identified. Two systems were used in rheumatology, but the majority were used in oncology. Systems were highly heterogeneous in terms of technical and functional specifications. Nine systems were fully integrated (data viewable in the EHR) while the remaining system represented a partial integration (data viewable via link in the EHR). Five systems allowed repeated data collection at

pre-defined intervals between visits with frequencies varying from daily to monthly. The remaining five made a single request before a scheduled clinic visit. The number of items requested from patients ranged from 9-48 per session. We identified three different clinical workflows: Simple (data only used during consultation, n=5), moderate (real-time alerts for providers when severe symptoms were reported, n=4) and on-demand (patient-initiated visits, n=1). Benefits of symptom reporting from each of the studies were categorised as anticipated, realized quantitative, and realized qualitative. We present summarised counts of these benefits in Figure 1. The most common anticipated benefits were better communication, changes to patient management and improved health outcomes. Most common realized benefits were detecting unrecognised problems and changes to patient management.

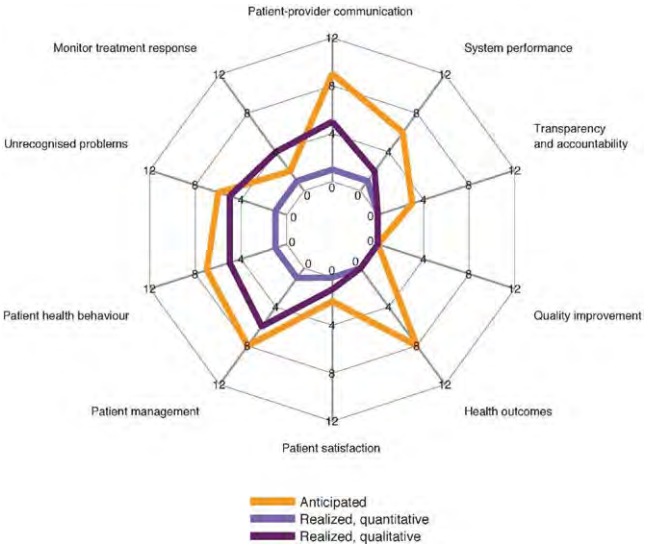


Figure 1. Summarized counts of benefits from each included study assessed against Chen et al.'s 10 outcome indicators. Categorized in anticipated (orange), realized quantitative (light purple), and realized qualitative benefits (dark purple).

Conclusion: There is growing interest and urge for integrating symptom data in the EHR and clinical care. Yet, this review has illustrated that there are limited published efforts to learn from. The heterogeneity in approaches underpins the need for a common framework. There is growing evidence from qualitative work in support of remote symptom-reporting in enabling better and patient-centred care in LTCs. The next step will be for robust, quantitative studies to provide evidence of benefits.

References:

[1] Chen J, Ou L, Hollis SJ. A systematic review of the impact of routine collection of patient reported outcome measures on patients, providers and health organisations in an oncologic setting. BMC Health Serv Res. 2013 Jun 11;13:211.

Disclosure of Interests: Julie de Fonss Gandrup: None declared, Syed Mustafa Ali: None declared, Sabine van der Veer: None declared, John McBeth: None declared, William Dixon Consultant of: Bayer and Google

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AB1155 WORK DISABILITY AND PREDICTORS OF POOR WORK OUTCOME IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: Axial spondyloarthritis (axSpA) is a chronic inflammatory disease which may lead substantial functional limitation. The disease more commonly affects men in their third decade of life. For patients with chronic disease participation in paid work may be the result of series factors like disease severity, effectiveness of the health care, availability and the type of work. Previously it was reported that ankylosing spondylitis may cause adverse work outcome.

Objectives: To understand the impact of axSpA on work disability and the factors associated with poor work outcome.

Methods: A cross-sectional survey was performed among323 patients withax-SpA according to ASAS classification criteriafrom one tertiary center. In total 219 (67.8%) patients were working age at the time study. The others were student, housewife or retired. Demographic, social and disease related characteristics were collected. Characteristic that might be associated with premature work loss were evaluated byunivariable and multivariable logistic regression analysis.

Results: Out of 219 axSpA patients (155 [71%] r-axSpA and 64 nr-axSpA, 69% HLA-B27 positive) who have a work at least once 47 (22%) was either withdrawn from work (n=35) or retired due to disability (n=12) during median (IQR) 12 (12) years symptom duration. Demographic and disease related characteristics of the patients with or without work diasbilitywere summarized in the table. In univariate analysis gender, smoking, education levels, the presence of peripheral arthritis, BASMI score and radiographically presence of syndesmophyte and hip involvement were found to be associated with poor work outcome. However poor work outcome were similar between r- and nr-axSpA patients. In regression analysis low education level (HR:3.4 [95%CI:1.4-8.6], P=0.007), peripheral arthritis (HR:2.7[95%CI:1.07-6.8], P=0.035), and ever smoking (HR:4.9 [95%CI:1.3-18.0], P=0.02) were independent predictors of work disability.

Conclusion: Our results suggest that there is still remarkable poor work outcome among axSpA patients and work disability might be similar in r- and nr-axSpA. Patients who are smoker, with low education levels, and peripheral arthritis seem to be at risk for premature work loss.

Table. Demographics and diseases related characteristics of study population

Variables	All population (n=219)	No work disability (n=172)	Work disability (n= 47)
Male, n (%)	161 (73.5)	122 (70.9)	39 (83)
Age, years*		41.5 (9.4)	43.1 (12.4)
Ever smoking, n (%)	155 (71.4)	115/171 (67.3)	40/46 (87)
Education duration ≤8 years, n (%)	82/212 (61.3)	53/165 (32.1)	29/47 (61.7)
Disease duration, years	6.7 (8.3)	5.5 (6.3)	10.7 (12.6)
BASDAI*	4.3 (2.4)	4 (2.3)	5.3 (2.6)
BASFI*	3.4 (2.8)	2.9 (2.5)	5.4 (3.0)
ASDAS-CRP*	2.8 (1.2)	2.7 (1.1)	3.3 (1.4)
BASMI*	2.3(2.0)	2 (1.8)	3.5 (2.4)
ASQOL*	9 (5.5)	8 (5.3)	12 (4.9)
Peripheral arthritis, n (%)	81/207 (39.1)	54/163 (33.1)	27/44 (61.4)
Hip arthritis, n (%)	39/205 (19)	26/163 (16)	13/42 (31)
Presence of syndesmophyte, n (%)	92/164 (56.1)	63/125 (50.4)	29/39 (74.4)

* Variables presented as mean (SD).

Disclosure of Interests: None declared

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AB1156 OVERVIEW OF INFLAMMATORY RHEUMATIC DISEASES AT THE EMERGENCY DEPARTMENT

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Background: Patients with rheumatological diseases can also apply to the emergency room due to acute attacks or complications. Especially in recent years, more patients, due to the increased use of immunosuppressant drugs in treatment, have applied to emergency services due to infection. On the other hand, data on applications to emergency services for rheumatological reasons are very few.

Objectives: In this study, applications to emergency departments for inflammatory rheumatic diseases were investigated.

Methods: 2715 patients from Atatürk Training and Research Hospital Rheumatology Clinic who were followed-up with the diagnosis of inflammatory rheumatic diseases between 2014 and 2018 were included in this study. The clinical and laboratory information of the patients were achieved from the hospital file records and the hospital data bank. The patients were classified according to the 5-stage triage system (T1: resuscitation, T2: critical, T3: urgent, T4: less urgent, T5: non-urgent).

Results: 21.3% (577) of 2715 patients applied to the emergency department. Among the emergency admissions, the first three diseases were; rheumatoid arthritis 19.7%, ankylosing spondylitis 19.2%, and familial Mediterranean fever 15.9% [Vasculitis 8.8%, Behcet's disease 7.6%, Gout 5.7%, Systemic lupus erythematosus 3.9%, Sjogren's Syndrome 3.6%, Scleroderma 3.2%, Still Disease 1.5%, Polymyalgia rheumatica 0.6%, others 9%]. 343 patients (59.5%) were discharged from the emergency department. 36.8% (212) of the patients were hospitalized in services and 3.6% (21) of them in intensive care. The first three reasons of the applications to the emergency department were: fever, malaise and fatigue in 1. 150 patients (25.9%), musculoskeletal system complaints in 2. 124 patients (21.4%) and abdominal pain in 3. 89 patients (15.4%), respectively. Vasculitis was the most common cause of hospitalization in the service in 38 patients (17.9%), whereas scleroderma was the most common cause of hospitalization in intensive care in 7 patients (33.3%) (table). 16 (76.1%) of the patients followed in intensive care unit were hospitalized with the diagnosis of respiratory system diseases. Death was observed in 10 (1.7%) of 577 patients. Five (50%) of the ex-patients had scleroderma (table). 8 (80%) of the deaths were related

to rheumatological disease and occurred after being hospitalized in intensive care unit.

Conclusion: The patients with inflammatory rheumatic diseases usually apply to the emergency department with urgent or less urgent clinical pictures. Rheumatoid arthritis, one of the most common inflammatory rheumatic diseases in almost all societies, was also the most common diagnosis in our study. In the vast majority of applications, infectious causes and disease activations related to immunosuppressive treatments were in the foreground. In addition, although vasculitis is the most common reason for the in-patients in clinical service, since the most frequent in-patients in intensive care unit and death is seen in the scleroderma group; caution should be exercised in the emergency applications of patients with these two groups.

References:

[1] Rheumatology consultation in the emergency department: Annual results. RAED 2014

Table. Examination of the diagnosis of 233 patients who were hospitalized and/or died from the emergency department

Parameters	In-patients in clinical service n, (%)	In-patients in intensive care units n, (%)	Died patients n, (%)
Vasculitis	38 (17.9)	5 (23.8)	1 (1)
Ankylosing spondylitis	33 (15.5)		
Rheumatoid arthritis	31 (14.6)	3 (14.2)	2 (20)
Behcet's disease	25 (11.7)	2 (9.5)	
Systemic lupus erythematosus	16 (7.5)	1 (4.7)	5 (50)
Scleroderma	10 (4.7)	7 (33.3)	
Antiphospholipid syndrome	10 (4.7)		
Psoriatic arthritis	9 (4.2)		
Family Mediterranean fever	8 (3.7)		
Sjogren's Syndrome	8 (3.7)		
Still Disease	7 (3.3)	1 (4.7)	1 (10)
Gout	7 (3.3)		
Undifferentiated connective tissue disease	7 (3.3)	2 (9.5)	1 (10)
Dermatomyositis	3 (1.4)		
Total	212 (100)	21 (100)	10 (100)

Disclosure of Interests: None declared
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AB1157 SEASONAL INFLUENZA VACCINATION: KNOWLEDGE AND ATTITUDES IN RHEUMATIC PATIENTS

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Background: Vaccines are one of the safest and effective public health interventions (1). Patients with rheumatic diseases (RD) have a higher risk of morbidity and mortality from vaccine-preventable infections (2). Seasonal Influenza vaccination (SIV) had shown to reduce the incidence, complications, admissions, and mortality from Influenza in patients with RD (3). Vaccine hesitancy is one of the threats to global health established by the WHO.

Objectives: To assess the knowledge and attitudes of rheumatic patients about SIV.

Methods: A self-questionnaire was applied during a community speech for rheumatic patients in October 2019 and also was applied in the rheumatology clinic of the university hospital "Dr. Jose Eleuterio Gonzalez" in Monterrey, Mexico, between November and December 2019. The questionnaire asks age, rheumatic diagnosis, and ten questions. Results are shown in descriptive statistics, the Chi-square and Mann-Whitney U tests were performed to compare groups. A P-value ≤0.05 was considered statistically significant. Analyses were performed using SPSS version 22.0.

Results: A total of 205 self-questionnaires were applied. 122 (59.5%) in the community speech and 83 (40.5%) in the clinic. The median age was 55 (45.75-62.25) years in the community population and 44 (28-59) years in the clinic, also the diagnosis distribution was different (Table 1). Most patients considered that rheumatic patients can be vaccinated. About 80% of patients have ever been vaccinated for seasonal influenza. 87.7% and 77.1% considered that SIV is safe and effective. About 85% of patients considered SIV the best way to avoid complications of Influenza. About 40% considered not safe to be vaccinated for influenza and other vaccine at the same time. 23.8% and 48.2% considered that SIV weakens the immune system and renders it susceptible to infections. Most of the patients know that SIV is free. 23.0% and 42.2% consider other measures better than SIV. 17.2% and 33.7% considered that SIV will get them worse instead of helping them, and 9.0% and 14.5% think that his RD will get worst with SIV.

Table 1. Population Characteristics

	Community N= 95	Clinic N= 83	P
Age, years, median (IQR)	55 (45.75-62.25)	44 (28-59)	0.001*
Diagnosis, n (%)			
-RA	67 (70.5)	46 (55.4)	0.037*
-OA	14 (14.7)	7 (8.4)	0.194
-SLE	3 (3.2)	11 (13.3)	0.013*
-Other AID	8 (8.4)	8 (9.6)	0.780
-Other NAID	3 (3.1)	11 (13.2)	0.012*

Conclusion: Misinformation about SIV is patent among rheumatic patients. It is a big challenge to clarify these myths to gain confidence about his safety and effectiveness and provide his benefits.

References:

[1] Hum Vaccin Immunother. 2013;9(8):1774-1778.
[2] Hum Vaccin Immunother. 2018;14(6):1311-1322.
[3] Ann Rheum Dis. 2020;79:39-52

Table 2. Questionnaire

		Community N= 122 (%)	Clinic N= 83 (%)	P
1. Can rheumatology patients be vaccinated?	Yes	114 (93.4)	75 (90.4)	0.420
	No	8 (6.6)	8 (9.6)	
2. Have you ever been vaccinated for Influenza?	Yes	97 (79.5)	68 (81.9)	0.668
	No	25 (20.5)	15 (18.1)	
3. Influenza vaccine is safe and effective:	Yes	107 (87.7)	64 (77.1)	0.045*
	No	15 (12.3)	19 (22.9)	
4. The best way to avoid compilations of influenza is by using SIV:	Yes	104 (85.2)	71 (85.5)	0.953
	No	18 (14.8)	12 (14.5)	
5. It is safe to be vaccinated for Influenza and other vaccines at the same time:	Yes	73 (59.8)	48 (57.8)	0.774
	No	49 (40.2)	35 (42.2)	
6. SIV weakens the immune system and renders it susceptible to infections	Yes	29 (23.8)	40 (48.2)	<0.001*
	No	93 (76.2)	43 (51.8)	
7. Do you know that SIV is freely provided?	Yes	115 (94.3)	76 (91.6)	0.453
	No	7 (5.7)	7 (8.4)	
8. Herbal medications, traditional medicine and some food (like orange) are better than SIV:	Yes	28 (23.0)	35 (42.2)	0.003*
	No	94 (77.0)	48 (57.8)	
9. SIV instead of helping me will get me worst:	Yes	21 (17.2)	28 (33.7)	0.006*
	No	101 (82.8)	55 (66.3)	
10. SIV will worst my rheumatic disease:	Yes	11 (9.0)	12 (14.5)	0.226
	No	111 (91.0)	71 (85.5)	

Disclosure of Interests: None declared
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AB1158 VACCINATION BARRIERS IN PATIENTS WITH RHEUMATIC DISEASES

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Background: Patients with rheumatic diseases (RD) are at increased risk of infections, attributed to the underlying RD, comorbidities and immunosuppressive therapy, including glucocorticoids, disease-modifying antirheumatic drugs, etc. (1). While many infectious diseases can generally be prevented by vaccines, immunization rates in this specific patient population remain suboptimal (2). Despite being recognized as one of the most successful public health measures, vaccination is perceived as unsafe and unnecessary by a growing number of individuals. Lack of confidence in vaccines is now considered a threat to the success of vaccination programs (3).

Objectives: To describe the main causes of non-vaccination in patients with RD.

Methods: A self-questionnaire was applied to a sample of patients with RD in the rheumatology clinic of the university hospital "Dr. Jose Eleuterio Gonzalez" in Monterrey, Mexico between September and December 2019. The questionnaire evaluated demographic characteristics (age, gender, diagnosis) and the vaccination status for Influenza (last year), pneumococcal (last 5 years), Herpes zoster (ever), Human papillomavirus (any dose) and Hepatitis B (any dose). It also includes a question asking: If you didn't receive any of the previous vaccines, what was the reason? (multiple-choice are shown in Table 2). Results are shown in frequencies and percentages.

Table 1. Demographic characteristics

	N= 102
Age, years, mean (SD)	51.27 (14.68)
Female, n (%)	84 (82.4)
Diagnosis, n (%)	
-RA	71 (69.6)
-SLE	13 (12.7)
-OA	12 (11.8)
-Other AID	6 (5.8)

Table 2. Vaccination barriers

	N=82
If you didn't receive any of the previous vaccines, what was the reason? n (%)	
1)Did not was recommended	22 (26.8)
2) Lack of availability	21 (25.6)
3) Vaccines don't work	13 (15.8)
4) Fear of adverse events	8 (9.7)
5) Previous adverse event	3 (3.6)
6) Other reason	
- Own decision	8 (9.7)
- Disinformation	7 (8.5)

Results: 102 patients were evaluated: Mean age was 51.27 (SD 14.68) years; 84 (82.4%) were females; 71 (69.6%) had rheumatoid arthritis, 13 (12.7%) had systemic lupus erythematosus, 6 (5.8%) had other autoimmune diseases and 12 (11.8%) had osteoarthritis. The rate of vaccination for Influenza was 49 (48%), for pneumococcal 25 (24.5%), for Herpes zoster 5 (4.9%), for Human papillomavirus 9 (8.8%), for Hepatitis B 14 (13.7%) (Table 1). 82 (80.3%) patients reported some barriers in vaccination, from these: 22 (26.8%) did not get the recommendation from the rheumatologist, 21 (25.6%) did not found available the vaccine, 13 (15.8%) believes that vaccines don't work, 8 (9.7%) had fear of adverse events, 3 (3.6%) reported previous adverse events, and 15 (18.2%) reported other reasons, that we classified as own decision 8 (9.7%) and disinformation 7 (8.5%) (Table 2).

Conclusion: The main barriers in vaccination of rheumatic patients reported were the lack of availability of the indicated vaccines and the medical and patient disinformation. This problem must be combated to ensure the complete vaccination of rheumatic patients.

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[1] Ann Rheum Dis. 2020;79:39-52.
[2] J Rheumatol. 2019;46(7):751-754
[3] Hum Vaccin Immunother. 2013;9(8):1763-73.

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AB1159 HIGH PREVALENCE MUSCULOSKELETAL PATHOLOGY: A CHALLENGE FOR PRIMARY ATTENDING PHYSICIANS. WHAT DO WE RHEUMATOLOGISTS CONTRIBUTE TO?

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Background: Musculoskeletal Diseases (MSKD) represent one of the main health problems burdens worldwide. They cause a significant functional, quality of life and socioeconomic impact. Knee and lumbar osteoarthritis are the most prevalent[1]. MSKD can be assessed by different kind of specialists: Orthopedic and Traumatology Surgery (OTS), Rheumatology and Rehabilitation, each of them focused at one of the distinct aspects of the same disease. It is the General Practitioner (GP) consultations that usually act as a gateway to specialized care. However, this derivation is carried out in non-standardized manners that leads to an evaluation from a sometimes wrong selected specialist or sometimes overlap management between several of them[2]. The result is an endless waiting list in an overburden health system that cannot solve people's health issues. In 2018, only in our area, 32.894 patients with MSKD were referred from GP to the different medical consultations: OTS (65%), Rehabilitation (25%) and Rheumatology (10%). Furthermore, there are specialized consultations called *"Primary Trauma"* to which GP can refer which are managed indistinctly by any of the 3 specialists mentioned before.

Objectives: The following study aims to assess by collecting data in one of these consultations, how these pathologies are referred to the different specialist and the role that the rheumatologist plays in its management.

Methods: From January to March 2019, 300 consecutive patients´ medical records from the HUVM area that were sent to "Primary Trauma" consultations and attended by a rheumatologist have been reviewed. The reason for consultation, tests and referrals requested, diagnoses reached and procedures and other therapeutic actions performed were collected. Descriptive statistics with percentages and mean are showed.

Results: The average age of the patients was 51 years [7-88], 57% (170) women and 43% (130) men. The most frequent reasons for referral were knee pain (26), foot pathology (23%), low back pain (12%) and carpal tunnel syndrome (6%). 68% (204 patients) attended the consultation with some test already performed request in primary care, mostly radiographs (61%) and MRI scan (34%). After the first assessment during consultation, only 31% required new studies. The diagnoses that were most frequently established are showed in table 1: degenerative knee pathology (29%) was the most prevalent. 60% of the patients assessed were given exercise tables and/or postural recommendations. 14% received an infiltration on the same day of the visit. Only 78 patients (26%) needed to be reviewed later in those consultations. Of the remaining 222 (74%), 81 (27%) were referred to other specialists. 56 of them (19%) went to OTS to a surgical evaluation, most frequently of the knee (32%), hand (27%) and foot (23%). 141 (47%) were discharged and referred to GP´s for follow ups.

Table 1. Diagnoses.

	N	%
Degenerative knee pathology	67	29
Plantar support alterations	34	15
Lumbar osteoarthritis	19	8
Deformities of the feet	17	7
Mechanical metatarsalgia	12	5
Plantar fasciitis	9	4
Carpal tunnel syndrome	9	4

Conclusion: The prevalence of MSKD found in medical consultation coincides with the national registers. Most patients did not need to be referred to surgical units. The role of the Rheumatologist is to take a comprehensive care for the patient, focusing on giving an effective evaluation and quick solution to his MSKD. In short, if the most prevalent MSKD are not subsidiary of surgical treatment (at least initially), the specialist whom patients with MSKD should be referred would be the rheumatologist.

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[2] Conill EM et al. Waiting lists in public systems: from expanding supply to timely access? Reflections on Spain's National Health System. Cien Saude Colet. 2011;16:2783–94.

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AB1160 A BENCHMARKING STUDY EVALUATING THE BURDEN OF AXIAL SPONDYLOARTHRITIS IN SPAIN COMPARED WITH THE REST OF EUROPEAN COUNTRIES. RESULTS OF THE SPANISH ATLAS AND EMAS STUDIES.

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Background: Benchmarking studies in axial spondyloarthritis (axSpA) may provide evidence of disparities, making it necessary to improve the healthcare and management of these patients.

Objectives: To evaluate differences between Spain and the rest of Europe (RoE) in relation to sociodemographic characteristics, life habits, and patient-reported outcomes (PROs) in axSpA patients.

Methods: Data from 2,846 unselected patients from the European Map of Axial Spondyloarthritis (EMAS) were collected through an online survey, with

a comparative analysis of 680 Spanish patients (2016) and 2,166 patients living in 12 other European countries (2017-2018). Socio-demographic characteristics, life habits, and PROs [BASDAI (0-10), spinal stiffness (3-12), and psychological distress (0-12, General Health Questionnaire GHQ-12)] were compared. The X^2 test was used for qualitative variables and the Mann-Whitney test applied for quantitative variables.

Results: Data from 680 (23.9%) Spanish patients were compared to 2,166 (76.1%) patients from the RoE. Compared to Spain, the RoE patients reported a higher percentage of females (64.1% vs 52.5%; p<0.001), university studies (51.7% vs 36.9%; p<0.001) and higher income per family member (€1,173.5 vs €823.2; p<0.001). In Spain, the proportion of respondents who were members of patient associations was higher than in RoE (44.3% vs 37.2%; p<0.001) (Table 1). Also compared to RoE, Spanish patients showed a greater diagnostic delay (8.5±7.7 vs 7.2±8.6; p<0.001), HLA-B27 carriership (77.1% vs 70.1%; p=0.003), and disease activity (5.7±2.0 vs 5.4±2.0; p=0.024). Despite lower diagnosis of anxiety and depression rates, Spanish patients reported greater psychological distress (5.7±4.5 vs 4.8±4.0; p<0.001). However, RoE patients declared greater spinal stiffness compared to Spanish patients (7.8±2.4 vs 7.5±2.7; p=0.009) (Table 2).

Table 1. Comparison of socio-demographic characteristics and lifestyle habits of axSpA patients in Spain and in RoE

	Spain (n = 680) Mean ± SD; n (%)	RoE (n = 2,166) Mean ± SD; n (%)	p-value
Age (Years)	45.7 ± 10.8	43.4 ± 12.6	<0.001*
Gender (Female)	357 (52.5)	1389 (64.1)	<0.001*
Educational level			
- No schooling	9 (1.3)	23 (1.1)	<0.001*
- Primary school	119 (17.5)	144 (6.6)	
- High school	301 (44.3)	880 (40.6)	
- University	251 (36.9)	1,119 (51.7)	
Monthly income (€) per household member	823.2 ± 656.4	1,173.5 ± 928.8	<0.001*
Smoking			
- Non-smoker or socially	417 (71.3)	1,679 (77.5)	<0.001*
- Less than 10 cig/day	24 (4.1)	111 (5.1)	
- More than 10 cig/day	144 (24.6)	376 (17.4)	
Alcohol			
- Never or occasionally	503 (86.0)	1,723 (79.5)	<0.001*
- 1–2 times per week	37 (6.3)	292 (13.5)	
- More than 2 per week	45 (7.7)	151 (7.0)	
Member of a patient support group	301 (44.3)	806 (37.2)	0.001*

Table 2. Comparison of PROs of axSpA patients between Spain and RoE

	Spain (n = 680) Mean ± SD; n (%)	RoE (n = 2166) Mean ± SD; n (%)	p value
Diagnostic delay, years	8.5 ± 7.7	7.2 ± 8.6	<0.001*
HLA-B27 (positive)	391 (77.1)	892 (70.1)	0.003*
BASDAI (0–10)	5.7 ± 2.0	5.4 ± 2.0	0.024*
Spinal Stiffness (3–12)	7.5 ± 2.7	7.8 ± 2.4	0.009*
GHQ-12 (0–12)	5.7 ± 4.5	4.8 ± 4.0	<0.001*
Anxiety	135 (19.9)	674 (33.1)	<0.001*
Depression	100 (14.7)	610 (30.0)	<0.001*

Conclusion: In this study, significant differences between Spanish and RoE patients were observed for the burden of the disease in patients with axSpA. Patients in Spain experience a greater diagnostic delay and greater psychological distress.

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AB1161 **ARTIFICIAL INTELLIGENCE FOR RHEUMATOLOGY**

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Background: Magnetic resonance imaging (MRI) of sacroiliac (SI) joints is used to detect early sacroiliitis(1). There can be an interobserver disagreement in MRI findings of SI joints of spondyloarthropathy patients between a rheumatologist, a local radiologist, and an expert radiologist(2). Artificial Intelligence and deep learning methods to detect abnormalities have become popular in radiology and other medical fields in recent years(3). Search for "artificial intelligence" and "radiology" in Pubmed for the last five years returned around 1500 clinical studies yet no results were retrieved for "artificial intelligence" and "rheumatology".

Objectives: Artificial Intelligence (AI) can help to detect the pathological area like sacroiliitis or not and also allows us to characterize it as quantitatively rather than qualitatively in the SI-MRI.

Methods: Between the years of 2015 and 2019, 8100 sacroiliac MRIs were taken at our center. The MRIs of 1150 patients who were reported as active or chronic sacroiliitis from these sacroiliac MRIs or whose MRIs were considered by the primary physician in favor of sacroiliitis was included in the study. 1441 MRI coronal STIR sequence of 1150 patients were tagged as ''active sacroiliitis" and trained to detect and localize active sacroiliitis and provide prediction performance. This model is available for various operating systems. (Image1)

Results: Precision score, the percentage of sacroiliac images of the trained model, is 87.1%. Recall, the percentage of the total sacroiliac MRIs correctly classified by the model, is 82.1% and the mean average precision (mAP) of the model is 89%.

Conclusion: There are gray areas in medicine like sacroiliitis. Inter-observer variability can be reduced by AI and deep learning methods. The efficiency and reliability of health services can be increased in this way.

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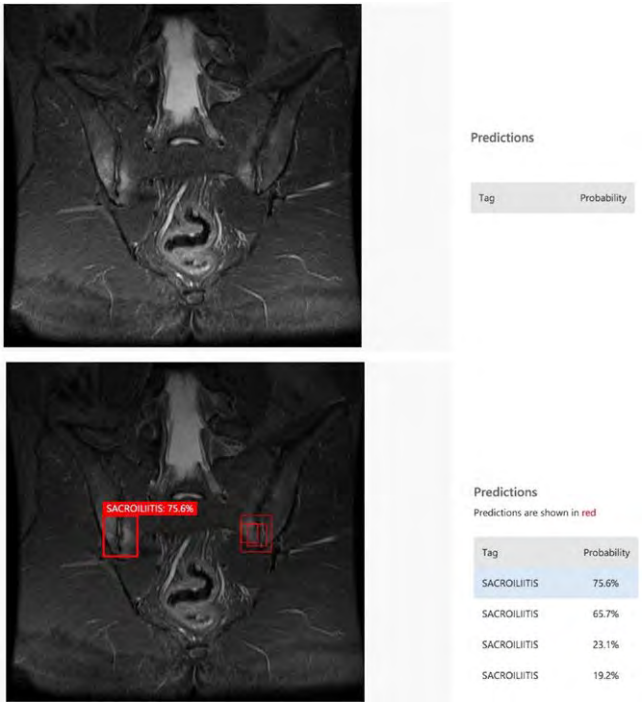


Image1. Bilateral active sacroiliitis detected automatically by AI model (in right sacroiliac joint 75.6%> (50%), in left sacroiliac joint 65% (>50%))

Disclosure of Interests: None declared
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AB1162 ANTI-TNF BIOSIMILARS: HOW KNOWLEDGE AND BELIEF INFLUENCE PRESCRIPTION

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Background: Biological agents change the management of rheumatic inflammatory disease with improving care but increasing costs. Biosimilars for subcutaneous TNF inhibitors (SC TNFi) are available in France since 2015 and provide the same treatments at lower cost. French health agencies do not legally oblige rheumatologist to first prescribe or switch to biosimilars.
Objectives: To assess the knowledge and beliefs of French rheumatologists about biosimilars.
Methods: The assessment was developed with a questionnaire consisting of five parts: demographics data, professional practice, theoretical knowledge, beliefs and confidence. The questionnaire was administrated via the website Limesurvey and sent by email to French rheumatologist. A descriptive analysis of the data and associated factors to initiation and switch of biosimilars have been done.
Results: One hundred one rheumatologists have participated to the study. 47.1% was less than forty years old. 92% of them have the authorization to prescribe TNFi. 53.2 always prescribed a biosimilars when they prescribed a SC TNFi for the first time and 78.5% in 90% of cases. 30.6% of French rheumatologist never switched to a biosimilars. Those who switch, do it in more than 75% of cases. 96.5%, 87.1% and 91.8% respectively answered that biosimilars are as efficient, as safe and have the same immunogenicity profile compared to originator. The initial biosimilars prescription is associated with a better knowledge about biosimilars. For example, 77.4% of rheumatologist who prescribe in more than 90% of the case, answer **NO** to the question "biosimilars and originator have to be compared in a phase III study for EACH indications for which originator obtained marketing approval". Only 31.2% of rheumatologist who prescribed in less than 90% of the case respond **NO** to this question. This difference was significant p<0.001. The switch to a biosimilars is associated with the beliefs and confidence. For example 25.4% of rheumatologists who switch for biosimilar in more than 75% of the case, answer **YES** to the question "There is not enough experiences with biosimilar". 57.7% of rheumatologist who switched in less than 75% of the case respond **YES** to this question. This difference was significant p<0.003.
Conclusion: Despite good knowledge on biosimilars, some French rheumatologists do not switch for these molecules. Our study suggests that this is due to lack of confidence.
Acknowledgments: The authors thank French rheumatologist who answer to the questionnaire
Disclosure of Interests: Arnaud De Chateaubriant: None declared, Pierre Ingrand: None declared, Elisabeth Gervais Speakers bureau: Novartis, Janssen, Roche, Pfizer, BMS, Abbvie
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AB1163 IMPACT ON COSTS AND WORKING LIFE OF RHEUMATIC PATIENTS WITH CHANGE IN BIOLOGICAL THERAPY FOR NO MEDICAL REASONS. REAL LIFE EXPERIENCE IN REGIONAL HOSPITAL OF SOCIAL SECURITY

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Background: Biologics as new therapeutic alternatives have revolutionized the management of rheumatic diseases. Biosimilars have been emerged as less expensive alternative. Most part of evaluations of biosimilars had proved effectiveness by clinical trials with outcomes as remission, but specific social aspects and economic variables not always has been considered. These aspects must be assessed in specific and real contexts (countries, health institutions) The effect on non-medical switch of biological therapy for rheumatic diseases in costs and working variables has not been documented in patients of the Mexican Social Security Institute (IMSS)
Objectives: Evaluate the impact of the change of biological therapy for non-medical reasons on the economic variables, costs and working aspects with rheumatic diseases on Mexican patients with social security
Methods: Cross-sectional observational study included patients from rheumatology clinical service of an IMSS Regional Hospital in Mexico City during last trimester of 2018. A structured questionnaire was applied who diagnosis of rheumatoid arthritis and spondyloarthropathies where received treatment biological for at least 24 months prior to the study. The individuals were divided into two comparison groups, G1: patients who changed to biosimilar biological treatment for non-medical reasons and G2: patients with original biological treatment without changes in the therapeutic scheme. In addition to socio-demographic characteristics, functional capacity (HAQ-di), disease activity (DAS28) and labor aspects were evaluated. A sex and age adjusted logistic regression analysis was performed where the outcome variable was the evolution
Results: The 71 cases evaluated included 90% female with schooling > 9 years in 90%. GI included 49%, age 51.1 years ± 15.1 vs G2 55.8+12.7; evolution in years: GI: 13.8+4.7 vs GII: 9.74+5.97. Both groups persisted in remission by DAS28 (G1:2.50+0.489 VS G2: 2.39+0.63). The G1 had a higher percentage of moderate affection in functional capacity: 58.8% vs G2: 35.9%, required more travel time to work, 2 hours less work per day and required more disability (48% vs 43% [RM0 1.6 95% CI: 0.45-3.4] After logistic regression models adjusted by age and sex, no significant results were found for economic and costs variables. However, a statistically significant association (p=0.017) were found for time progression disease as predictor variable between G1 Vs Group 2 (OR=1.15, 95% CI 1.02, 1.30). Mean time progression disease for G1 were 9.38±6.5 years (n=43) and for G2 were 14.17±5.5 years (n=28)
Conclusion: IMSS rheumatic patients who were on their original biological treatment, had more working time and improved statistically significative their time progression disease. Switch to biosimilar not have impact in clinical remission but can impact in economic and working aspects. IMSS serves 50% of Mexican population, covering medical care (physician fees, laboratory and medication purchase), and social security; so, should consider not only clinical aspects to acquisition of biologics drugs
Acknowledgments: FUNDACION IMSS
Disclosure of Interests: None declared
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AB1164 A COST PER RESPONDER ANALYSIS OF ABATACEPT VERSUS ADALIMUMAB FOR THE TREATMENT OF RHEUMATOID ARTHRITIS AMONG PATIENTS WITH SHARED EPITOPE (SE) POSITIVITY FROM A UNITED STATES PAYER PERSPECTIVE

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Background: The shared epitope (SE) is a significant genetic risk factor for rheumatoid arthritis (RA), and it has been proposed to be associated with T-cell activation and the production of anti-citrullinated protein antibody (ACPA).[1-3] The results from the Early AMPLE trial, a head-to-head trial comparing the efficacy of abatacept versus adalimumab among early moderate-to-severe RA patients with positive ACPA (ACPA+) and rheumatoid factor (RF), showed that at week 24, patients with SE positivity (SE+) responded better to abatacept compared to adalimumab across all efficacy measures evaluated (ACR20 [American College of Rheumatology], ACR50, ACR70, DAS[disease activity score]28-CRP[C-reactive protein]).[4]
Objectives: To compare the cost per responder (CPR) between abatacept and adalimumab among RA patients with SE+ at week 24 using the Early AMPLE trial data from a United States (US) payer perspective.
Methods: A CPR analysis was conducted for RA patients with SE+, ACPA+, and RF. Responders were defined as patients achieving ACR20, ACR50, ACR70, or DAS28-CRP ≤2.6 and efficacy data was sourced from the trial (Figure 1).[4] Approved product labels were referenced for treatment dosing regimen and wholesale acquisition cost was used to calculate pharmacy cost.[5] A real-world rebate scenario was considered for adalimumab (30%) to reflect the real-world pricing in the US market. The CPR was calculated as the total pharmacy cost divided by the proportion of responders.
Results: The total pharmacy cost at week 24 was $26,273 per patient for abatacept and $21,731 per patient for adalimumab. With achieving ACR70 as the definition of responder, the CPR at 24-week was $46,337 for abatacept and $74,935 for adalimumab, a difference of $28,598 (Table 1). The CPR was consistently lower for abatacept compared to adalimumab across all clinical measures, with difference ranging from $7,099 to $43,609.

Table 1. Overall cost per responder results

	Abatacept	Adalimumab	Difference
ACR20	$30,303.74	$37,403.06	-$7,099.32
ACR50	$34,254.68	$48,077.83	-$13,823.15
ACR70	$46,337.46	$74,935.10	-$28,597.64
DAS28-CRP ≤2.6	$52,546.68	$96,155.65	-$43,608.97

Conclusion: While the pharmacy cost was higher for abatacept compared to adalimumab driven by the rebate, due to its higher clinical efficacy, the CPR was consistently lower for SE+ RA patients treated with abatacept. The results may be useful for US healthcare decision makers in understanding how to optimize treatment for SE+ RA patient while minimizing costs in today's budget constrained environment.

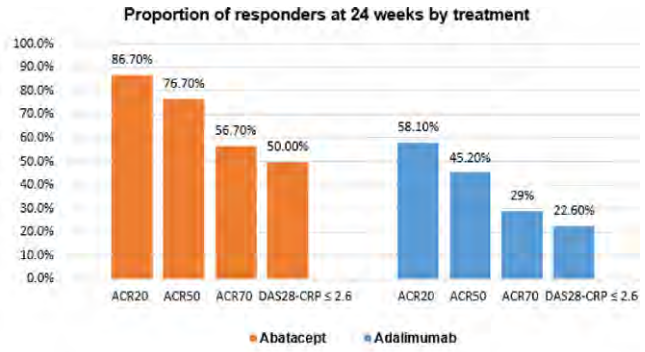


Figure 1. Proportion of responders by treatment data from the Early AMPLE trial

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Disclosure of Interests: Sang Hee Park Consultant of: Pharmerit International, which received consultancy fees from Bristol-Myers Squibb (US), Inc. for this study, Xue Han Employee of: BMS, Francis Lobo Shareholder of: Bristol-Myers Squibb (US), Employee of: Bristol-Myers Squibb (US), Sakina Nanji Consultant of: Pharmerit International, which received consultancy fees from Bristol-Myers Squibb (US), Inc. for this study, Dipen Patel Consultant of: Pharmerit International, which received consultancy fees from Bristol-Myers Squibb (US), Inc. for this study

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AB1165 MEDICATION ADHERENCE DATA IN A RANDOMIZED TRIAL: LARGE CHALLENGES TO COME FROM RAW DATA TO A WORKABLE AND RELIABLE DATASET

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Background: Medication adherence in the GLORIA trial, among elderly patients with rheumatoid arthritis, is measured with caps that register openings of the medication bottle. At each study visit, one or two medication bottles with cap (kits) are dispensed, each containing 90 capsules. Multiple steps are needed to come to a workable dataset to describe adherence.

Objectives: To describe the steps that are needed to come from raw data to a workable dataset to analyze adherence data that are recorded by electronic caps.

Methods: The medication bottle contains a cap with the ability to register cap openings. The raw dataset from the caps consist of an excel file with one opening event per row, recorded as date and time. One cap yields approximately 90 rows. First, the kit numbers were matched to the corresponding patient numbers, that are recorded in another excel file. Instances where two kits were dispensed were recorded with two kit numbers in one cell and need to be copied to two cells with one kit number. Second, the VLOOKUP function was used to combine dates and kit numbers. One row now contains all openings from one kit. Then, the number of days between first opening and each next opening date was calculated. A range of 90 days was made to calculate how many times the bottle was opened on each day of the 90-days period. The results were color-coded to visualize instances of zero, one or ≥two openings on a day.

Results: The colored calendar matrix (Figure 1) can now be used to categorize adherence patterns.



Figure 1. Example of calendar matrix of four caps of one patient.
Yellow=no opening, green=1 opening, blue=≥2 openings.

Conclusion: A monitoring cap seems a simple instrument to measure adherence. However, multiple steps and a lot of time are needed to come to a workable dataset for the study of adherence patterns.

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AB1166 DETERMINANTS OF REPOSITORY CORTICOTROPIN INJECTION TREATMENT INITIATION FOR PATIENTS WITH RHEUMATOID ARTHRITIS IN A LARGE CLAIMS DATABASE

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Background: The treatment goal in rheumatoid arthritis (RA) is sustained remission and prevention of RA flares [1]. While targeted biologics have improved disease outcomes, almost one-third of patients (pts) discontinue treatment by 1 year and 50% by 2 years, with lack of efficacy as the most common reason [2]. Repository corticotropin injection (RCI) is a naturally sourced complex mixture of adrenocorticotropic hormone analogues and other pituitary peptides and is an agonist for all 5 melanocortin receptors (MCRs). Activation of MCRs by RCI has been shown to have direct and indirect anti-inflammatory and immunomodulatory effects. RCI is indicated for adjunctive therapy for short-term administration in RA flares or uncontrolled disease [3].

Objectives: To characterize RA pts that initiate RCI therapy and identify predictors of RCI initiation, compared to biologic disease-modifying antirheumatic drugs (DMARDs).

Methods: This retrospective cohort study identified pts with ICD-9/10 diagnosis for RA over an 11-year period (2008-2018) in a large claims database (Truven MarketScan®). Adults with ≥1 claim for RCI (RCI cohort) or ≥1 RA-related biologic claim but no RCI (non-RCI cohort) were selected and characterized by demographics, disease severity (Claims-based Index for RA Severity, CIRAS), comorbidities (Charlson Comorbidity Index, CCI), treatment patterns, and healthcare resource utilization in the 12-month baseline (BL) period prior to their index date (i.e., the 1st RCI claim or last claim for biologic for non-RCI cohort). Predictors of RCI initiation were identified by multivariable logistic regression, controlling for demographics and BL characteristics.

Results: A total of 393 pts initiated RCI therapy while 188,062 initiated biologic treatment with no RCI claims. At BL, cohorts were similar with respect to mean age (~56 years), gender (76-79% female), and insurance type (79-80% commercial). Cohorts differed by region, plan type, and index year. Compared to non-RCI

patients, the RCI cohort had significantly higher CCI and CIRAS scores; higher use of traditional DMARDs (65.6% vs. 61.9%), corticosteroids (CS, 91.3% vs 68.8%), prescription nonsteroidal anti-inflammatory drugs (NSAIDs, 66.9% vs 58.5%), and opioids (67.7% vs 47.5%), but lower biologic use (45.8% vs. 87.7%) (all p<0.05). RCI pts had significantly higher mean number of inpatient, emergency room, office, and outpatient visits (all p<0.05).

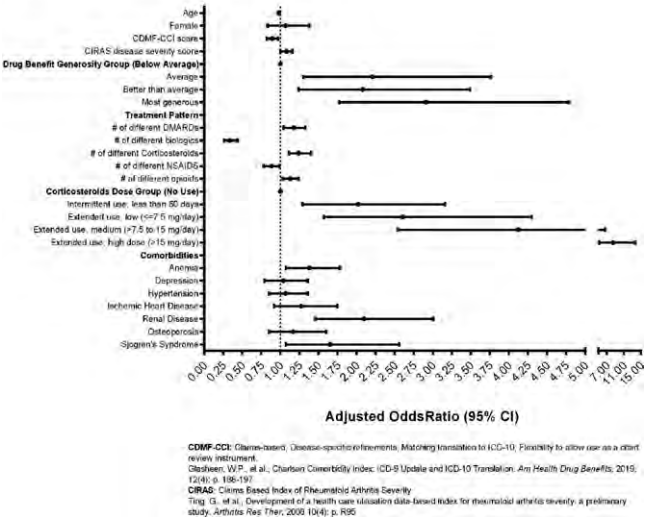
RCI therapy initiation was most significantly impacted by treatment patterns, including number of DMARDs, CS, and opioids tried in the previous year (Figure 1). Corticosteroid use was the strongest predictor of RCI initiation, especially extended use at any dose (OR≥2.6) and extended use of the highest doses (>15 mg/day, OR=8.5), present in 21% of the RCI cohort (Figure 1). Drug benefit generosity (proportion of out-of-pocket costs) was also associated with RCI initiation in any plan qualified as better than "below average" (OR=2.1-2.9). Anemia, renal disease, and Sjogren's syndrome were also associated with higher odds of RCI initiation (OR=1.4-2.1).

Conclusion: RA pts initiating RCI therapy were prescribed a greater number of traditional DMARDs, CS, and opioids in the previous 12 months compared to non-RCI pts, and have evidence of more severe disease and comorbidities. Extended and high dose CS use were the factors most associated with RCI initiation.

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Figure 1. Predictors of RCI Initiation



Disclosure of Interests: Kyle Hayes Employee of: Mallinckrodt ARD, LLC, Mary Panaccio Employee of: Mallinckrodt Pharmaceuticals, Huanxue Zhou Consultant of: I am full time employee in KMK Consulting Inc. and providing consulting service to Mallinckrodt, Mohammed Fahim Consultant of: I am full time employee in KMK Consulting Inc. and providing consulting service to Mallinckrodt

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AB1167 PREGNANCY AND INFLAMMATORY ARTHROPATIES: EXPERIENCE IN A MULTIDISCIPLINARY UNIT

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Background: Systemic inflammatory diseases are common in women at the reproductive age. These women may have fertility problems and complications during pregnancy.

Objectives: To describe the experience in a multidisciplinary unit (composed of Rheumatologists and Obstetricians) and asses the complications and treatments used in patients with inflammatory diseases in a tertiary hospital compared to those registered in healthy women from the same center (preterm births 6.59%, Caesarean section (C-section) 14.4%, maternal average age 33.33 years).

Methods: Retrospective and descriptive study of the evolution of pregnancy in patients with inflammatory diseases and follow-up in a multidisciplinary unit for more than 15 years (until December 2019). Demographics, maternal disease, time until conception, births, abortions, C-sections, treatments and complications were collected. Data was analyzed using IBM SPSS v23.

Results: We registered 29 pregnancies (25 patients): 20 Rheumatoid Arthritis (RA), 5 Psoriatic Arthritis (PsA), and 4 Spondylarthritis (SpA). Maternal average age at diagnosis was 27.6±6.36 years and average age at childbirth/abortion 35±5.6 years.

It took an average time of 8 months to conceive. 11.5% received fertility treatment using in vitro fertilization techniques.

5 abortions were registered prior to follow-up in this unit (0.2 abortions/mother). During follow-up 1 abortion (0.04 abortions/mother) was recorded in a RA patient. C-section was performed in 11 cases (39.2%): 6 RA (31.6%), 3 SpA (75%) and 2 PsA (40%).

17.2% of pregnancies were preterm (<37 weeks).

Intrauterine growth restriction (IUGR) was observed in a woman (3.4%) with RA and preeclampsia was observed in 2 cases (6.9%) (RA 1, SpA 1).

Disease activity (DAS28 and BASDAI) is shown in Table 1.

TABLE 1.

	DAS28 (median)				
	Previous	First Trimester	Second Trimester	Third Trimester	Posterior
Rheumatoid Arthritis	2.69	2.59	3.09	3.33	3.11
Psoriatic Arthritis	2.58	2.5	3.32	3.08	2.89
RA with biological agents (n: 6)	2.37	2.94	2.71	2.4	2.52
		BASDAI (median)			
Spondylarthritis	2.8	2.4	1.75	1	1.9

Treatments used prior to and during pregnancy are listed in Table 2.

TABLE 2.

TREATMENT BEFORE PREGNANCY	n (%)	TREATMENT DURING PREGNANCY	n (%)
Hydroxychloroquine	13 (44.8%)	Prednisone	17 (58.6%)
Prednisone	12 (41.4%)	Acetylsalicylic acid	16 (55.2%)
Methotrexate	9 (31%)	Hydroxychloroquine	15 (51.7%)
TNF inhibitors	7 (24.1%)	Sulfasalazine	2 (6.9%)
Sulfasalazine	2 (6.9%)	TNF inhibitors	2 (6.9%)

8 patients had received biological treatment prior to pregnancy (2 SpA, 6 RA)(3 Etanercept, 3 Adalimumab, 2 Certolizumab). 2 of them (RA) continued treatment during pregnancy. 1 of them discontinued it at week 17 on her own (Adalimumab) while the other continued with Certolizumab throughout pregnancy and presented IUGR. No other complications, such as infections or malformation, were observed in newborns. DAS28 data of these women can be found in Table 1.

Conclusion: In our series, as described in the literature, women with inflammatory arthropaties are older, need longer time to achieve pregnancy and have increased use of fertility techniques and increased likelihood of preterm and instrumental delivery compared to general population. Given the low number of patients receiving biological treatment no conclusions about complications and evolution of the disease can be drawn, so further investigation are needed in this group of patients.

Monitoring inflammatory arthropathies in a multidisciplinary unit increases the chances of successful pregnancies.

Disclosure of Interests: None declared

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AB1168 THE ANALYSIS OF "BIG DATA" AND PROCESSING OF UNSTRUCTURED INFORMATION (SEMANTIC HUB PLATFORM) TO IDENTIFY PATIENTS WITH SEVERE GOUT IN THE RUSSIAN FEDERATION.

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Background: the prevalence of gout and hyperuricemia (HU) in the world remains high, with a stable high incidence of severe gout [1]. There are no data on the prevalence and features of severe gout in the population of the Russian Federation (RF).

Objectives: To determine the percentage of patients (pts) with severe gout in the RF among pts with gout who are looking for information about their disease

on the Internet, to clarify their average age, gender distribution, comorbidity, difficulties in diagnosing and treating, to get an idea of the most relevant online requests in this cohort.

Methods: We used technology for analyzing "big data" and processing unstructured information (semantic intelligence) (the Semantic Hub platform, which scans Google and Yandex environments). For efficient processing of text corpora, several specialized converters were used. The resulting format for these converters is an XML representation of the source data. The study was based on real-life patient cases (specialized social networks, forums, and other sources of user-generated content). Messages from pts with gout and their relatives were used. Severe gout is characterized by frequent polyarticular flares or chronic arthritis, subcutaneous tophi, the presence of concomitant conditions.

Results: A total of 16253 messages were processed, with 'gout' entered as a search word. A total of 1691 gout pts were identified. The average age of online-active pts - 47.2 years. Men 60.5%. Severe gout was identified in 194 of 1691 (11.5%) pts, with 59% of pts aged 29 to 45 years. The proportion of men among pts with severe gout is 71%. Comorbidities most often include diabetes mellitus and metabolic syndrome - 24%, CKD - 51%, arterial hypertension-14%. Pts with severe gout have 1.9 comorbidities on average, while other pts with gout -1.1. The groups are comparable by age. Among 90 links related to medical specialties that pts visited before being referred to a rheumatologist, the first three leading positions were - orthopaedic surgeon (30%), general practitioner (25.8%), surgeon (21%). Sixty percent of pts reported that the time between the first attack and the diagnosis of gout was less than six months. The remaining 40% of pts report that this period lasted from 1 to 15 years. Less than 42% of pts were prescribed urate-lowering therapy (ULT) during internal consultation of a physician, and only 23% of physicians recommended ULT to pts with gout during online consultation. According to pts' reports, treatment includes 3 main groups of drugs: NSAIDs, intra-articular corticosteroids and ULT. Compliance with life-time ULT is very low. The most commonly requested topic on the Internet - attacks during holidays - 2426 messages, the second is held by the topic of lifestyle – 1899 messages, the third place - problems of comorbidities – 1813 references, and only in the fourth position - 1662 messages- the topic of ULT.

Conclusion: The percentage of pts with severe gout is 11.5% among gout pts who are looking for information about their condition on the Internet, which is consistent with the data from the largest original papers in the RF on the prevalence of severe gout [2]. More than a half of pts with severe gout (59%) are men aged 29 to 45 years. The decreased online activity of pts over 46 years old may be due to the low motivation for treatment of this cohort. Gout pts are rather more concerned about lifestyle than medical problems. This may also indicate the absence of the consistent compliance of this patient category to life-time therapy. Inadequate long-term therapy and late diagnosis may be the main factors for severe gout in young and active pts.

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AB1169 RHEUMATOLOGY PATIENT PERCEPTION OF CARDIOVASCULAR RISKS: A SURVEY AT A TEACHING HOSPITAL

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Background: It is well known that individuals with rheumatological conditions are at an increased risk for developing cardiovascular diseases (CVS) and they are the most common cause of mortality. However, there is still lack of awareness about the CVS risk among Rheumatology patients. We carried out a patient survey to assess their awareness and perception of CVS risk associated with their condition. We also assessed if the health professionals attending to these patients gave adequate education to the patients regarding the CVS risk.

Objectives: To study awareness about CVS risks among rheumatology patients

Methods: This was a prospective cross sectional survey where in multiple-choice questionnaires were distributed to consecutive patients attending rheumatology clinic. The questionnaire contained 18 questions including demographics, diagnosis, medications and their awareness of cardiovascular risks associated with their underlying rheumatic conditions. We also explored as patient attempted any Primary preventive measures for reducing the CVS risk.

Results: We collected data of 57 patients with 47% of patients were above 60 years of age with Female: Male ratio of 3:1. Rheumatoid arthritis was the most common diagnosis (60%) with others including AS (22%), SLE(5%). 32% of patients had been suffering from inflammatory disorder for >10 years and 44% believed their disease was still not fully controlled. 37% had family history of heart diseases. More than half of the patients (56%) were unaware of cardiovascular risks associated with their condition and 65% overall reported that they were not personally informed about these risks by the treating health professionals. When we analysed the newly diagnosed patients (<5years) 64% were unaware about the CVS risks which is higher compared to patients with diagnosis of >5 years. We tried to explore any ethnic differences, however the number is too small to compare. We noted that around 60% of white British with rheumatological diagnosis were not aware of CVS risk in our group. When further asked about the primary preventive measures, only 23% engage in exercise, 21% have made diet changes, 12% take aspirin, 16% have quit smoking and only 5% quit alcohol.

Conclusion: This was a small pilot study to look at the patient awareness of CVS risks associated with rheumatological conditions. Clearly there is lack of awareness among patients about CVS risks. Furthermore, most of the patients reported they were not educated about the risks from the health professionals. Majority do not engage in any kind of primary preventive measure for heart diseases. It is crucial that the health professionals actively educate patients regarding the CVS risks and the various methods through which these can be prevented. We believe patient-targeted educational programmes and behavioural interventions can be incorporated for holistic patient management.

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AB1170 THE IMPACT OF HIGH DISEASE ACTIVITY AS MEASURED BY SLEDAI AND DRUG BURDEN-ON HEALTHCARE UTILIZATION, QUALITY OF LIFE AND WORK PRODUCTIVITY IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: Although there is abundant literature on healthcare utilization in SLE patients, the impact of disease activity in SLE patients is not well understood.

Objectives: To quantify the impact of disease activity, as measured by SLEDAI score and drug burden, in SLE patients on health care resource utilization (HCRU), health related quality of life (HRQoL) and work productivity (WP).

Methods: Data were collected from a cross-sectional survey of 754 rheumatologists in US and EU5 from the Adelphi Real World 2010/2013/2015 Lupus Disease Specific Programmes (DSP). Physicians were asked to complete patient record forms (PRFs) for the next 5 prospectively consulting SLE patients; the same patients were asked to complete patient self-completion (PSC) forms describing how SLE affected them. PRFs collected data pertaining to the patient's diagnosis, disease history, current clinical outcomes, treatment and management history. PSCs focused on similar data collection and included patient reported outcome measures (PROs). Propensity score matching was used to assess differences in HCRU and PRO scores between SLE patients who had a low disease activity and those who had a high disease activity. Low disease activity was defined as a SLEDAI score of ≤4, a steroid dose of <7.5mg/day, and not on immunosuppressant or biologic. High disease activity was a SLEDAI score of >4, or on an immunosuppressant, biologic, or steroid dose of >7.5mg/day. Patients were matched on age, sex, and ethnicity.

Results: Data was extracted from 1278 PRFs, and 591 PSCs. Using the estimated propensity score each low disease activity patient (n=44) was matched with a high disease activity patient (n=1187). Using 1:1 matching, with replacement and allowing for ties, matching resulted in 414 high disease activity patients being used as matches for 44 low disease activity patients. Demographic data are reported in Table 1. Patients with a low disease activity were significantly less likely to be currently flaring, lower number of flares in last 12 months, less likely to have been hospitalized in the last 12 months, had fewer consultations in the last 12 months, reported better HrQoL (EQ5D), more favourable levels of fatigue (FACIT), and lower work impairment (WPAI). (Table 2).

Table 1. Demographic data

Variable	Low disease activity	High disease activity
Mean age (years)	38.1	40.0
% Female	90.7	88.2
% White/Caucasian	76.7	67.7
Mean years diagnosed	5.5	5.0

Table 2. Propensity score matching results

Outcome variable	Low activity mean	High activity mean	Coefficient	95% CI	p-value
Flared in the last 12 months	11.63	37.97	-0.26	[-0.38 – -0.14]	<0.001
Number of flares in last 12 months	0.21	0.70	-0.49	[-0.72 - -0.26]	<0.001
Hospitalised in last 12 months	4.65	14.98	-0.10	[-0.17 – -0.04]	0.001
Number of consults in last 12 months	2.84	3.52	-0.68	[-1.19 – -0.17]	0.009
EQ-5D-3L	0.78	0.88	0.10	[0.03 – 0.17]	0.004
FACIT Fatigue	34.68	39.86	5.19	[0.80 – 9.57]	0.02
WPAI overall percentage work impairment	14.42	45.35	-30.93	[-45.32 – -16.54]	<0.001

Conclusion: Systemic lupus erythematosus patients with lower levels of disease activity are less burdensome to the healthcare system and experience a significantly better HRQoL and lower levels of productivity impairment. There is a need to establish a universal definition of low disease activity as a treatment goal to benefit patient quality of life and reduce HCRU.

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AB1171 EFFECTS OF SUCCESSIVE SWITCHES OF TWO DIFFERENT BIOSIMILARS OF ETANERCEPT ON OUTCOMES IN INFLAMMATORY RHEUMATIC DISEASES IN DAILY PRACTICE

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Background: A single switch from an originator to a biosimilar product has been shown to be safe and effective in the treatment of rheumatic musculoskeletal diseases (RMDs). The availability of biosimilars has created a financial incentive to encourage switching to cheaper products ("non-medical switch"). This is naturally associated with multiple switches. However, the effect of multiple switching between biosimilars of the same reference product has not been thoroughly investigated to date.

Objectives: To assess the effectiveness and safety of systematic non-medical switching from innovator etanercept (ETN) to biosimilar ETN (SB4) and successive to another biosimilar ETN (GP2015) in adult patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) or axial spondyloarthritis (axSpA) in a real-life setting.

Methods: This retrospective study was performed in a tertiary center in adult patients with RA, PsA or axSpA who had been treated with the innovator ETN and who had been switched to two ETN biosimilars for economic reasons thereafter. The first switch from innovator ETN to the first biosimilar ETN occurred between February-May 2017 and the second switch from the first to the second biosimilar ETN occurred between September-December 2017. The end of the observation period was October 2019. Disease activity, function and adverse events (AE) were regularly assessed, and any changes in outcome were recorded during the follow-up period. The scores documented at week 12 week after the second switch were taken as primary outcome.

A total of 100 patients (54 RA, 27 axSpA, 19 PsA, mean age 54.3±15.1, 46% male) who switched twice to those ETN biosimilars over a follow-up period of 21.1±7.4 months were included. The retention rate after the second ETN biosimilar switch was 89% about 6 months after the second switch. While 2 patients were lost to follow-up and 1 patient died (cardiac arrest), 7 patients discontinued due to inefficacy or AE, including one pancreatic cancer. One patient was withdrawn due to pregnancy. Overall, 14 AEs were reported in 8 patients. Among them, 4 patients switched back to originator etanercept in month 6, 1 patient re-administered GP2015 successfully in month 3 after suffering from mucosal erosions and in 3 patients another mode of action was prescribed. The scores at week 12 of both, disease activity and function, remained unchanged (Table 1).

Table 1. Patient characteristics

	Assessment	Baseline (n=100)	SB4 Follow-up 12 weeks (n=100)	SB 4 Follow-up 24 weeks (n=100)	Second switch to GP2015 (n=100)	GP2015 Follow-up 12 weeks (n=97)	GP2015 Follow-up 24 weeks (n=89)
RA	DAS28	3,0 (1,2)	2,9 (1,4)	3,1 (1,2)	2,8 (1,4)	3,4 (2,5)	3,0 (1,4)
	HAQ	1,4 (0,8)	1,6 (0,9)	1,0 (0,9)	1,5 (0,8)	1,5 (0,8)	1,6 (0,9)
PsA	DAS28	3,8 (1,4)	1,9 (1,4)	2,8 (1,5)	3,1 (1,1)	4,5 (2,6)	3,6 (2,6)
	HAQ	1,2 (0,9)	1,0 (0,9)	0,9 (0,9)	1,0 (0,8)	1,0 (0,9)	1,2 (0,8)
axSpA	BASDAI	5,1 (2,7)	4,5 (2,6)	5,1 (3,8)	4,1 (2,2)	4,6 (2,5)	4,3 (2,4)
	ASDAS	3,4 (0,8)	2,5 (0,8)	2,7 (0,8)	3,2 (1,8)	2,7 (1,2)	2,5 (0,9)
	BASFI	4,4 (2,7)	4,3 (2,7)	4,3 (3,2)	4,6 (2,6)	4,5 (2,7)	4,8 (3,0)

*Values are mean ± standard deviation

Disclosure: Hexal funded this research

Conclusion: The retention rate after multiple switches from innovator ETN to two ETN biosimilars was close to 90%. No major changes in disease activity and function were observed in all three indications.

AB1172 IMPROVEMENT OF DEPRESSION BY JOINT SURGERY IN ESTABLISHED RHEUMATOID ARTHRITIS; RESULTS FROM MULTICENTER PROSPECTIVE COHORT STUDY FOR EVALUATION OF JOINT SURGERY ON PATIENT'S REPORTED OUTCOME

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Background: Total management including reconstructive joint surgery and rehabilitation should be needed for further improvements of physical function for long-standing RA patients. In these days, it is very important to evaluate the effectiveness of joint surgery as well as drug therapy based on patient-reported outcome (PRO)

Objectives: The purpose of this study is to explore the relationship among depression, clinical variables and other PROs including physical function and to explore whether joint surgery can improve the depression.

Methods: Multicenter prospective observational cohort study was conducted among patients who underwent elective joint surgery for RA from April 2012 to March 2016 (Study registration: UMIN000012649). In this study, we collected data at baseline and at 6 or 12 months after the surgery. These data were as follow; age, sex, disease duration, drug therapies, and disease activity (DAS), TUG, and patient-reported outcome [HAQ-DI, EQ-5D (QOL), pain and BDI-II (depression)]. Correlation between BDI-II and other variables were determined using multiple liner regression analysis.

Results: Totally, 346 patients before elective joint surgery were analyzed cross-sectionally. Mean age, disease duration, pain VAS, DAS28, HAQ-DI, EQ-5D and BDI-II were 64.2 years, 17.0 years, 36.2 mm, 3.02, 1.11, 0.641 and 13.0, respectively. 52.6% of elective joint surgeries were in upper limbs and 47.4% were in lower limbs. Multiple liner regression analysis showed that HAQ-DI [B:-0.099 (95%CI:-0.117- -0.08) β:-0.48] pain VAS [B:-0.002 (95%CI:-0.002- -0.001) β:-0.26] and BDI-II [B:-0.003 (95%CI:-0.005- -0.002) β:-0.19] had significant impact on EQ-5D. Furthermore, HAQ-DI [B:3.78 (95%CI:2.54- 5.06) β: 0.33] and pain VAS [B: 0.062 (95%CI: 0.023- 0.101) β 0.17] had significant impact on BDI-II. Especially, walking and eating were independent factors for BDI-II in HAQ-DI categories. These results were confirmed in longitudinal analyses using results from joint surgery in lower limbs (LL; n=138) and upper limbs (UL; n=165), respectively. BDI-II was remarkably improved from 12.1 (mean) to 10.5 in LL and from 14.2 (mean) to 11.9 in UL. Change in HAQ-DI had significant impact on that in BDI-II [LL; B:3.183 (95%CI:0.301- 6.065) β:0.229, and UL; B:2.55 (95%CI:0.19-4.92) β:0.19] while that in painVAS did not. Especially, the improving in walking category by LL [B:1.38 (95%CI:0.06- 2.70) β:0.18] and in hygiene category by UL [B:2.11 (95%CI:0.79- 3.42) β:0.24] were relevant factors for improving of BDI-II.

Conclusion: Depression is an important patient-reported outcome for QOL in established RA patients. Improving of physical function with joint surgery in both lower and upper limbs caused improving of depression status. Rheumatologists should take the joint surgery into consideration as effective intervention for treatment of established RA patients with treatment.

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AB1173 RHEUMATOLOGIST CARE IS ASSOCIATED WITH FEWER EMERGENCY ROOM VISITS BY PERSONS WITH GOUT

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Background: Gout is one of the most common inflammatory arthropathies. By searching a large administrative data base (Symphony Integrated Dataverse), we found that persons with acute gout see a rheumatologist infrequently, whereas less than 50% of advanced gout patients are seen by a rheumatologist. Notably, however, gout patients seen by rheumatologists have more frequent urate measurements and are prescribed urate lowering therapy more frequently. This study sought to determine whether involvement of a rheumatologist in gout care had a positive impact on health outcomes

Objectives: To determine whether involvement of a rheumatologist had a positive impact on health outcomes of patients with gout.

Methods: We carried out a retrospective analysis to identify persons with gout over an approximately 3-year period from October 2015 to December 2018. This study used data from the Truven Marketscan® database, an administrative database covering over 190 million patients across the United States and based on fully adjudicated and paid insurance claims. Patients were identified as having gout if they were >18 years of age and had at least two medical claims for the diagnosis of gout on different days, separated by at least 3 months. Patients with acute gout were identified by ICD-10 code M10.*, chronic nontophaceous gout (M1A.***0), tophaceous gout (M1A.***1) and uncontrolled gout (M10.*, M1A.*), the latter manifested by three gout codes (any) in the primary diagnosis position and three urate measurements within the same calendar year. Particular attention was placed on Emergency Room (ER) visits by individuals in each category and by individuals who had been evaluated by a rheumatologist.

Results: We identified 284,877 gout patients. The median age was 59.2 years and 79.0% were male. Of the 230,998 persons coded as acute gout, 10.7% were seen by a rheumatologist, whereas 26.9% of the 32,942 coded as chronic nontophaceous gout, 47.2% of the 7,723 coded as tophaceous gout and 43.6% of the13,514 coded as uncontrolled gout were seen by a rheumatologist. In each gout category, the frequency of ER visits was significantly reduced in persons who had been seen by a rheumatologist (Table 1). In acute gout, the frequencies of ER visits in those with and without rheumatologist care were 5.6% vs 6.6% (p<0.001), respectively. In chronic nontophaceous gout it was 5.5% vs 6.7% (p=0.001); in tophaceous gout it was 10.3% vs 14.7% (p<0.001); and in uncontrolled gout it was 12.8% vs 19.0%, respectively. If the frequencies of rheumatologist-associated gout patient ER visits were applied to all gout subjects, there would have been 3,088 less ER visits in this cohort of gout patients.

Table 1.

		Rheumatology Breakdown			Emergency Room Visits		
Population	Overall N	W/ Rheumatology	Patients	%	With Gout ER Visit (%)	p-value (comparing %)	ER Visits* Per Patient
Acute Gout	230,698	Yes	24,638	10.68%	1373 (5.57%)	<0.001	1.47
		No	206,060	89.32%	13632 (6.62%)		1.53
Non-Tophaceous Chronic	32,942	Yes	8,863	26.90%	486 (5.48%)	<0.001	1.95
		No	24,079	73.10%	1601 (6.65%)		2.39
Tophaceous Chronic	7,723	Yes	3,648	47.24%	376 (10.31%)	<0.001	2.78
		No	4,075	52.76%	597 (14.65%)		2.89
Uncontrolled	13,514	Yes	5,886	43.55%	753 (12.79%)	<0.001	2.06
		No	7,628	56.45%	1452 (19.04%)		2.56

* ER Visits are only included in this analysis if the primary diagnosis code on the claim is a gout code (M10.X, M1A.X)

Conclusion: There appears to be a positive impact of rheumatologist involvement in the care of gout patients, manifested by a significant decrease in the frequency of ER visits. Considering the inconvenience and cost of ER visits, rheumatologist care may have a significant impact on the well-being of gout patients and on the overall cost of their care.

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AB1174 TRACKING THE EFFECTS ON A CLINICAL SERVICE OF INTRODUCING ULTRASOUND FOR DIAGNOSIS OF GIANT CELL ARTERITIS: DESIGN OF A SERVICE EVALUATION USING LEAN METHODOLOGY

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Background: In our large, multi-site hospital, patients with suspected GCA are started promptly on high-dose prednisolone but until 2019, patients waited for temporal artery biopsy (TAB) until the GCA diagnosis could be confirmed ("GCA") or refuted ("not-GCA"). Reports of the impact of introducing temporal and axillary artery ultrasound (TAUS) have mainly come from smaller hospitals. Agreement between TAUS and TAB has been reported by others with a Cohen's kappa of 0.35 [1] and 0.40 [2]. We used Lean methodology to identify metrics across 5 key domains: delivery, quality, service, morale and cost.

Objectives: To design metrics for a service evaluation to measure impact of introducing TAUS, and to test their feasibility of measurement within routine care.

Methods: Our primary driver was time from presenting to our service to diagnostic confirmation (lead time). Pathway mapping, value stream mapping and a driver diagram identified key ideas for improvement.

We chose to measure: Delivery (mean lead time for each month), Quality (proportion of patients with GCA and positive TAB/TAUS; total (cumulative) prednisolone dose in patients with not-GCA, Service (patient feedback), Morale (staff feedback) and Cost (number of patients; cost of tests per patient; overall costs). We plotted these by month on run charts and defined a significant shift as 6 consecutive monthly values below baseline median. Cohen's kappa was calculated using GraphPad QuickCalcs.

Results: Routine TAUS for suspected GCA was introduced from January 2019, alongside a multidisciplinary team monthly meeting. TAUS was done a median

of 2.5 days from referral. Agreement between TAB and TAUS results was good (Table 1). The run chart showed a significant shift in our Delivery (median lead time fell from 28.7 days to 21 days after introduction of ultrasound) and both Quality metrics (proportion of GCA with positive TAB/TAUS increased from 29% to 69%; total prednisolone dose for not-GCA fell from 1.335g to 0.846g).

Table 1. Concordance between temporal and axillary artery ultrasound (TAUS) and temporal artery biopsy (TAB) in scans performed through 2019. Cohen's weighted kappa 0.59 (including equivocal results as separate category).

	TAUS positive	TAUS negative	TAUS equivocal
TAB positive	14	1	1
TAB negative	5	27	5
TAB equivocal	0	3	0

Within Costs, average per-patient costs of TAB/TAUS declined from £1004/patient to £792/patient, but total referrals for TAB/TAUS increased from 6/month to 10/month, increasing overall costs. Staff and patient feedback (Service, Morale) revealed that further improvements to the care pathway were needed to manage the additional complexity.

Conclusion: Lean methodology identified multiple metrics for evaluating the impact of TAUS on our service. Introducing TAUS improved Delivery and Quality, but measuring Costs, Morale and Service helped identify unintended consequences. Concordance between TAUS and TAB was good. We plan to continue to improve and monitor the care pathway based on our multi-stakeholder feedback.

References:

[1] Luqmani et al., HTA 2016

[2] Mukhtyar et al., Clin Rheum 2019

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AB1175 BIOLOGICAL THERAPY DOSE OPTIMIZATION AND COST MINIMIZATION STUDY IN SPONDYLOARTHRITIS: UTILITY OF REDOSER TOOL

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Background:

Objectives: . To describe the percentage of spondyloarthritis patients on biological therapy (BT) optimization in clinical practice whowould maintain remission or low disease activity (LDA) after 2 years of follow-up and to identify possible factors associated with relapse. To estimate the cost reduction between 2009-19

Methods: Design:A retrospective, observational longitudinal study under conditions of clinical practice. Patients: Spondyloarthritis in BT dose reduction. Inclusion criteria: Psoriatic arthritis (CASPAR criteria), and Axial Spondyloarthritis (ASAS criteria) which have been iniciated BT dose reduction between 2009-2019. Patients with BT are followed prospectively by two rheumatologists in a monographic clinic of subcutaneous biological therapy every 6 months, and with their usual rheumatologist every 6 months, as well. In such, the patients are controlled and attended in clinics with a pre-established questionnaire every 3 months. Variables: **Maintained Reduction:** patients who maintained BT dose reduction since de beginning of the optimization until the index date(data collection). **Relapse at 3,6,12,24 months**: patient who had to returnt to usual BT dose. Other variables: demographic, time to diagnosis and evolution disease, clinical-analytical: Tender Joint Count(TJC), Swollen Joint Count (SJC), C-reactive Protein (CRP), Erythrocyte Sedimentation Rate (ESR), activity index: DAPSA; BASDAI, ASDAS and physical function: HAQ and BASFI. Previous treatment with bDMARD. Dose reduction adjustment according to REDOSER**. Cost reduction in euros** (absolute and per patient-year) of BT in patients who are in dose reduction compared to the standard care. Analysis: Descriptive, Bivariate analysis, Multivariate logistic regression (DV:relapse). The absolute cost reduction and per patient-year was calculated.

Results: 65 patients with spondyloarthritis in dose reduction were included. Table 1 main characteristics in study population. The average time since the beginning of the BT was 47.61 months (±37.06). After 24 months of follow-up, 73.8% of patients (48) achieved a sustained reduction. All these patients accomplish remission or low disease according to differente index activities [DAPSA and BASDAI median(p25-p75)= 2.3 (2.1- 2.9) and 1.5 (0.7-2.6), respectively and ASDAS mean (SD) =1.4 (0.54)] and a shorter time of disease evolution. The dose reduction of BT carried out from 2009 to 2019 meant a total cost savings of 584080.37€, with a patient/year cost savings of 6192.28€. We evaluated the optimization according to REDOSER and it was observed that in 53 patients (81.5%) the reduction would have been adequate and the rest was doubtful. In bivariant analysis between patients who had relapsed and those who had not, only differences were observed in the BT line used [2nd line:(5(29.4%) Vs 2(4.2%),(p=0.025)] and and a higher percentage of patients with a doubt result of REDOSER [9(52.9%) Vs 3(6.3%), p<0.001)] respectively. In multivariant analysis the only independent variable associated with relapse was a doutbful result of REDOSER[OR(IC95%), 3.46(1.18-10.17); p=0.024], R2= 40.2%

Figure 1:

Variable	Patients n=65
Sex,male, (%)	45 (69.2)
Age in year, median(p25-p75)	50.6 (41.6-57.5)
Time to diagnosis,months,median(p25-p75)	24.01(12.0-48.1)
Disease evolution time,months, median(p25-p75)	171.4(114.7-255.5)
Percentaje of patients in dose reduction untill index date, n(%)	48(73.8%)
Clinical-analytical characteristics	
Diagnosis	
Psoriatic arthritis,n(%)	33 (50.8)
Ankylosing Spondylitis,n(%)	23 (35.4)
Non radiographic axial spondylitis n(%)	9 (13.85)
Type of afectattion	
Peripheral,n(%)	27(41.5)
Axial,n(%)	21(32.3)
Mixed n(%)	17(26.2)
HLA-B27 positive, n(%)	27(41.5)
Cutaneous Psoriasis,n(%)	32 (49.2)
Uveitis,n (%)	7 (10.8)
Inflammatory Bowel Disease n(%)	2 (3.1)
sDMARD at BT dose reduction beginning	
Metotrexate,n (%)	21 (32.3)
Sulfasalazine,n (%)	4 (6.2)
Leflunomide,n (%)	3 (4.6)
bDMARD	
Enbrel, n (%)	24 (39.6)
Benepali, n (%)	7 (10.8)
Humira, n (%)	18 (27.7)
Golimumab, n (%)	11 (16.9)
Certolizumab, n (%)	0 (0)
Infliximab, n (%)	2 (3.1)
Secukinumab, n (%)	3 (4.6)
Time until dose reduction, months, mean(DE)	47.61 (37.06)
Clinical-anaytical	
Basal DAPSA, median (p25-p75)	4.5 (2.2-8.2)
DAPSA 24 months, median(p25-p75)	2.3 (2.1- 2.9)
Basal ASDAS, mean (SD)	1.49 (0.73)
ASDAS 24m, mean (SD)	1.4 (0.54)
Basal BASFI, median (p25-p75)	1.1 (0.5- 2.8)
BASFI 24 months, median (p25-p75)	1.0 (0.0- 1.7)
Relapse	
Relapse at 3 months, n(%)	7 (12.1)
Relapse at 6 months n(%)	3 (6.7)
Relapse at 12 months n(%)	4 (9.5)
Relapse at 24 months n(%)	3 (8.6)
REDOSER(adecuate reduction), n (%)	53 (81.5)

Conclusion: Biological therapy dose reduction in spondyloarthritis is possible in the majority of patients, maintaining remission/LDA at 24 months. This leads to a greater cost reduction and efficiency. The relapse was associated with a doubtful result in REDOSER before optimization and this tool can be very useful in the assessment of BT reduction.

Disclosure of Interests: None declared

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AB1176

UTILITY OF REDOSER TOOL IN DOSE OPTIMIZATION OF BIOLOGICAL THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS IN CLINICAL PRACTICE

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Objectives: To describe the characteristics of patients with rheumatoid arthritis (RA) in dose reduction of biological therapy (BT) in clinical practice and identify possible factors associated with the time in dose reduction and verify the utility of REDOSER tool.
Methods: Design: A retrospective, observational longitudinal study under conditions of clinical practice. Patients: RA in BT dose reduction between 2007- 2019 were selected. Inclusion criteria: RA according to ACR 2010 criteria which have been initiated BT dose reduction. Patients with BT are followed prospectively every 3-4 months in a specialized outpatient unit of BT dose reduction with a pre-established protocol for data collection and registered in a database. Variables: Primary: **Time in reduction**: was defined as the time in which patients maintained the BT optimization and **Relapse at 12 and 24 months**: percentage of patients who, after starting BT optimization, return to the previous or standard dose. Secondary variables: **REDOSER:** Appropriate, Doubtful and Inappropriate (If dose reduction was adequate according to the REDOSER tool applied retrospectively were evaluated). Other variables: Demographic, clinical-analytical: time of disease evolution, RF, anti CCP antibodies, Number of Tender Joints, Number of swollen joints, erosions, activity index (DAS28, SDAI, CDAI) and physical function (HAQ). Previous treatments. Statistical Analysis: descriptive, bivariate using x2 and T-Student among patients with and without relapse at 24 months and multivariate linear regression to identify independent variables associated with the time in BT dose reduction (DV: time in reduction).
Results: 59 patients with RA were included. Table 1 shows the main characteristics of the subjects. The average (SD) of optimization in months was 17.9 (17.7). Ten patients (16.9%) relapsed at 12 months and 16 (27.1%) at 24 months. The mean (SD) of DAS28 and SDAI of patients who relapsed at 24 months was higher compared to baseline DAS28 (2.3 [0.9] vs. 1.5 [0.8]; p = 0.015) and SDAI (7.8 [6.3] versus 3.3 [1.6]; p 0.05). These patients who relapsed at 24 months compared to patients who did not have more erosions at the start of BT (p = 0.004), longer duration of disease (p = 0.072) and greater baseline activity of DAS28 (p = 0.017), of SDAI (p = 0.030) and CDAI (p = 0.036). After simulating the REDOSER tool to all patients at the beginning of the OBT, 28 patients (56%) were "Appropriate", 20 (40%) "Doubtful" and 2 (4%) "Inappropriate" of which they continue in OBT at the conclusion of study 22, 10 and 0, respectively (p = 0.020). In the multivariant analysis, the independent variables that are associated with time in dose reduction of BT were baseline DAS28 (β = -0.660, 95% CI[2.7-14.0]; p=0.014) and age (β=-0.800, 95% CI [0.8-0.0]; p=0.038).
Conclusion: The majority of the patients with RA who initiate BT dose reduction maintain the optimization after 24 months. REDOSER can be useful in clinical practice to assess the BT optimization in patients with RA. A longer time in BT dose reduction was associated with lower values of DAS28 at the beginning and younger age of the patients.

Figure 1:

Variable	Patients n = 59
Epidemiological characteristics	
Sex, female, n (%)	47 (79.7)
Age in years, mean (SD)	59,6 (12.6)
Evolution time, months, mean (SD)	172,0 (90.5)
Diagnostic delay, months, median (p25-p75)	12,0 (5.9-24.0)
Time to OBT, months, mean (SD)	17,9 (17.7)
Percentage of patients in OBT until index date, n (%)	32 (65.3)
Clinical and analytical characteristics	
RF positive, n (%)	46 (80.7)
Anti CCP antibodies positive, n (%)	45 (78.9)
Double seropositivity, n (%)	42 (73.7)
Erosions, n (%)	42 (73.7)
Treatment at dose reduction beginning	
sDMARD	
Methotrexate, n (%)	26 (44.1)
Sulfasalazine, n (%)	7 (11.9)
Leflunomide, n (%)	2 (3.4)
bDMARD	
Abatacept, n (%)	1 (1.7)
Etanercept, n (%)	28 (47.5)
Adalimumab, n (%)	4 (6,8)
Golimumab, n (%)	1 (1.7)
Certolizumab, n (%)	1 (1.7)
Tocilizumab, n (%)	22 (37.3)
REDOSER (adecuate reduction) n (%)	28 (56.0)

Disclosure of Interests: None declared
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AB1177

METHODOLOGICAL ASPECTS OF DESIGN, ANALYSES AND REPORTING OF STUDIES WITH WORK PARTICIPATION AS OUTCOME DOMAIN IN PATIENTS WITH INFLAMMATORY ARTHRITIS: RESULTS OF TWO SYSTEMATIC LITERATURE REVIEWS INFORMING EULAR POINTS TO CONSIDER

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Background: Inflammatory arthritis (IA) has substantial impact on work participation (WP). However, methodological issues hamper interpretation, comparison and meta-analyses of studies with WP as outcome domain. Sources of heterogeneity and methodological choices should be assessed in order to improve the quality of future studies.
Objectives: To summarize methodological choices in studies with WP as outcome domain in IA and other chronic diseases.
Methods: A EULAR task force on '*points to consider (PtC) when designing, analysing and reporting studies with WP as outcome domain among patients with IA*' outlined the scope of the systematic literature review (SLR) and identified 6 areas of potential concern (Table 1). Two searches were conducted (Figure 1): Search 1 (S1): original studies in IA (RCTs and longitudinal prospective observational studies); S2: systematic reviews in other chronic diseases. Two reviewers independently identified eligible studies and extracted data for the pre-defined methodological areas.

Table 1. Methodological issues across the 6 pre-defined areas (search 1, n=62)

Area	Methodological issues*
1. Study design	- 16/62 (26%) and 8/62 (13%) studies aligned the target population and sample size with the study's work outcome. - 9/39 (24%) of the interventional studies aimed to assess changes of work status (employment/disability) over a very short follow-up time (≤6 months).
2. Work outcome domains	- 7/33 (21%) of studies **defined work status**. - 30/30 (100%), 38/38 (100%) and 7/7 (100%) **defined absenteeism, presenteeism and unpaid work**, respectively.
3. Work outcome measurement instruments	- 22/62 (35%) studies used **non-validated instruments** (e.g. self-reported days of sick leave/impact of disease on productivity, n=16/62, 26%).
4. Contextual factors	- 54/62 (87%) studies neglected work-related contextual factors.
5. Data analyses	Of the studies measuring absenteeism and/or presenteeism: - 10/38 (26%) accounted for **skewness** of the work outcome. - 30/38 (79%) took **interdependence** between outcomes as part of work productivity and activity impairment questionnaire into account.
6. Reporting	- 62/62 (100%) studies reported the size and characteristics of the (sub)groups in which the analyses were performed. - 1/62 (2%) reported loss to follow-up and work-related reasons for drop-out. - 42/62 (68%) studies presented **aggregated** results; 11/62 (18%) presented results as **percentages according to meaningful thresholds**; 9/62 (14%): both forms. - 21/24 (88%) studies reporting **productivity costs**, **provided data on natural volumes (days/hours)** used to calculate costs.

*The number of studies in denominators vary by methodological issue.

Results: We included 62 original studies in IA (23 RCTs, 16 interventional and 23 non-interventional observational studies) and 28 SLRs in other chronic diseases. The methodological aspects most often neglected in original studies (Table 1) were: the choice of the study design in relation to the work-related study objective; definitions of the WP outcome domains considered; accounting for skewness of the work outcome; consideration of work-related contextual factors; reporting attrition and its reasons and reporting both aggregated results as well as proportions of individuals based on predefined meaningful thresholds. SLRs on other chronic diseases confirmed high heterogeneity and methodological flaws in all the 6 key methodological areas without identifying new problematic areas.
Conclusion: High methodological heterogeneity was observed in studies with WP. Consensus around the key methodological aspects is needed to homogenise and improve the quality of future studies. This review informs the EULAR PtC for the conduction and reporting of studies with WP as an outcome domain in IA.

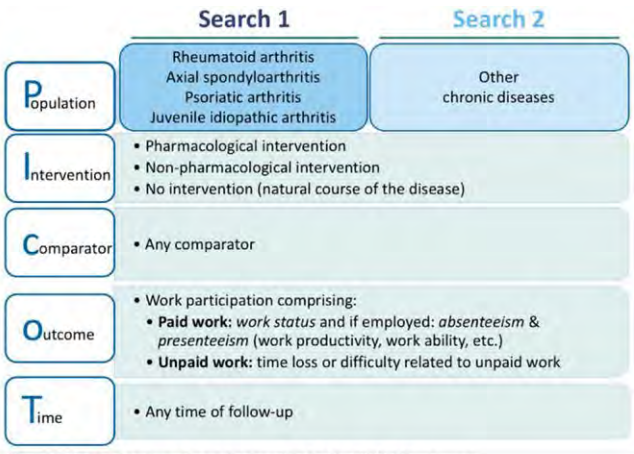


Figure 1. Search strategy 1 and 2 according to the PICOT framework.

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AB1178 AN AUDIT OF ORIGINATOR ADALIMUMAB TO BIOSIMILAR SWITCH IN TWO HOSPITALS

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Background: Biological drugs have revolutionized the treatment of immune-mediated inflammatory diseases (IMIDs). Current guidelines reserve these drugs for patients with severe refractory disease.
Biologic drugs are expensive, but as they reach patent expiry, the introduction of lower-cost biosimilars reduces their impact on health care budgets. It is estimated that NHS England could save £300 million by 2021 following the recent launch of adalimumab biosimilars [1]. As part of this process, there has been a mandatory switch of originator adalimumab to biosimilar adalimumab throughout the U.K.
Objectives: To evaluate the impact of the switch to biosimilar adalimumab in individuals with inflammatory arthritis at two NHS trusts in the East of England and calculate the proportion and reasons for switch back to originator adalimumab or a second biosimilar at 12 weeks.
Methods: Both hospitals ran dedicated 'switch' clinics. All patient records were reviewed retrospectively.
Results: 855 patients with different IMID switched from originator to biosimilar over 13 months. At 12 weeks, 730 patients (85%) maintained the switch, 71 patients (8.7%) switched back to the originator, and 54 patients (6.3%) switched to other biosimilars of the same drug.

Table 1. Primary outcome analysis of switching from originator to adalimumab biosimilar

Diagnosis	Total patient switched from originator	Average duration (year) of use of originator before bio switch (for patients continue using bio switch)	Total patients continuing (At 12 weeks)	Average duration (year) of use of originator before bio switch (for patients switched back to originator)	Total patients switched back to originator or other biosimilar
Rheumatoid Arthritis	356	7.9	314 (88%)	4.9	42 (12%)
Axial Spondyloarthritis	260	6.4	213 (82%)	4.5	47 (18%)
Psoriatic Arthritis	218	5.9	187 (86%)	2.9	31 (14%)
Juvenile Arthritis	16	3.7	14 (88%)	4.5	2 (12%)
Others	5	2.2	2 (40%)	0.8	3 (60%)
Total	855	7.0	730 (85%)	4.2	125 (15%)

Table 2. Reasons for back to originator or another biosimilar

Reasons for back to originator or another biosimilar			
Number back for Intolerance		Number back for Inefficacy	
Painful injection	69	BASDAI/Spinal Pain	13
Pain/Others	19	TJC, SJC, VAS	4
Rash/Allergic reaction	5	DAS	3
Headache	5	PsARC	2
Nausea	4	No Detail	1
Total	102	Total	23
%	82%		18%

Conclusion: Switching to a biosimilar was successful in the vast majority of patients and is associated with significant saving. The list prices for originator Adalimumab is £9,155/person/year and £8,238/person/year for biosimilar Adalimumab respectively [2]. By switching we will save approximately £719,402 per annum (9.2% cost reduction).
References:
[1] NHS England. NHS set to save record £300 million on the NHS's highest drug spend 2018 [cited 2018 November 30]. https://www.england.nhs.uk/2018/11/nhs-set-to-save-record-300-million-on-the-nhss-highest-drug-spend/
[2] https://bnf.nice.org.uk/medicinal-forms/adalimumab.html
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AB1179 EMERGENCY DEPARTMENT LENGTH OF STAY FOR PATIENTS WITH ACUTE GOUT

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Background: Emergency department (ED) visits for acute gout increased by approximately 20% between 2006 and 2014 in the United States. (1) Reducing ED length of stay (LOS) can help improve health outcomes, and reduce ED crowding and cost of care for patients with gout.
Objectives: The aim of our study was to assess ED LOS and to identify factors associated with prolonged ED LOS in patients with acute gout.
Methods: In this retrospective analysis, we included the first ED visit of adult patients (>18
years) with acute gout who presented to the 3 EDs affiliated with Lifespan Health Systems, the largest healthcare provider in Rhode Island. Our study period was 3/30/2015 to 9/30/2017.
We calculated ED LOS as the time spent by patients in the ED until they were discharged. Patients presenting to the ED and subsequently admitted to the hospital were excluded given the differential effect of systems factors in these patients. We assessed the following factors' association with being in the upper quartile of ED LOS: (a) Patient factors – demographics, comorbidities and clinical presentation of gout (number of joints involved, severity as gauged by an ED triage nurse on a scale of 1 to 5; 1 being the worst) and (b) systems factors – time of day, day of the week, and time of year at presentation to the ED, teaching versus non-teaching hospital setting, and performing an arthrocentesis. We performed univariate and multivariable analyses to identify factors associated with prolonged ED LOS in patients with acute gout.
Results: A total of 355 patients (mean age 56.6 ± 16.03 years, 81.3% males) were included. The median ED LOS was 2.65 hours (1.75, 4.3 hours). A quarter of the patients spent more than 4.3 hours in the ED; the national average across all medical illnesses being 3.7 hours (2). In the univariate analysis, older age (> 65 years), comorbidities (hypertension, congestive heart failure), worse ED severity score, procedural delays, and teaching hospital setting were associated with being in the upper quartile of ED LOS. In a multivariable analysis, age >65 years, procedural delays, and worse ED acuity score continued to be associated with longer ED LOS.
Conclusion: In our study settings, patients with acute gout spent a longer time in the ED than the national median of 120-150 minutes. (2) We noted that older age and higher acuity score in addition to procedural delays led to longer length of stay in the ED. The results of our study should guide future interventions to reduce ED LOS for patients with acute gout.

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Disclosure of Interests: None declared
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AB1180 THE EVOLUTION OF AN FLS IN SEARCH OF EXCELLENCE: THE EXPERIENCE OF GRAN CANARIA.

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Background: The implementation of an FLS in the Spanish public health system is not an easy task since there are no official plans for the incorporation of personnel dedicated to the unit
Objectives: To expose the consolidation and improvement of an FLS after its implementation as well as the problems that have arisen over time.
Methods: The health program for secondary fracture prevention was implemented in 2012. Initially worked with the same staff assigned to the Rheumatology service, since 2016 we have a part-time support nurse. Patients are identified from the emergency registry and, more recently, from patients admitted for hip fracture and treated in a monographic osteoporosis clinic. The baseline visit consists of consultation with the nurse, DXA and bone metabolism analytics. Falling patients are referred to a fall prevention school. Most patients are referred to their primary care physician to start a treatment.
Results: Of the 2,416 patients attended the baseline visit, 30% were forearm fractures, 27% hip, 20% humerus, 10% spine and 11% other fractures. In comparison to 2012, in 2019 the monthly average of patients has doubled, increased the number of hip and spine fractures, and increased the percentage of captured patients (Table). In spite of consolidating the unit, getting a support nurse for the admitted patients and establishing a solid alliance with primary care, it is pending the involvement of Primary Care Nurses and start first prescription at the hospital.

Table. Comparison of the first year with the last year of implementation of our FLS.

	2012	2019
Mean monthly number of fractures, N	22	42
Type of fracture: forearm/hip/spine, %	37/20/6	28/40/11
Captured patients of elegible, %	57	77
Delay in weeks until first visit to FLS, median	14	12
Patient origin: emergency list/inpatient/outpatient, %	100/0/0	59/31/9
DXA performed, %	100	61
Referral to fall prevention school, %	0	26
Criteria to start a treatment, %	67	90*
Referral to the osteoporosis clinic, %	37	7

*We apply the 2019 recommendations of the Spanish Society of Rheumatology

Conclusion: We present the achievements made by our FLS along 8 years and the difficulties within the Spanish public health system.
Disclosure of Interests: Antonio Naranjo Grant/research support from: amgen, Consultant of: UCB, Speakers bureau: AMGEN, Amparo Molina Speakers bureau: AMGEN, STADA, Cristina Sepúlveda: None declared, Candelaria Torres: None declared, Fabiola Santana: None declared, Francisco Rubiño: None declared, Rubén López: None declared, Soledad Ojeda Speakers bureau: AMGEN, LILLY, GEBRO
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AB1181 SHOULD A COMBINED RHEUMATOLOGY-PULMONOLOGY INTERSTITIAL LUNG DISEASE SERVICE BE CONFINED TO TERTIARY CENTRES - A SERVICE EVALUATION

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Background: Interstitial lung disease is a well described extra-articular manifestation in a range of rheumatic diseases. It carries significant morbidity and mortality. Management of rheumatic diseases associated ILD (r-ILD) requires expertise as the needs of such patients are complex and treatment options limited. Historically, such complex ILD has been managed in tertiary referral centres.
Objectives: We set up a combined service incorporating both rheumatology and respiratory domains in a district general hospital (DGH) to help patients avoid long journeys and improve their experience whilst focusing on an integrated care pathway. We evaluated the outcomes of the first set of patients managed in this proof-of-concept service model.
Methods: Referrals were accepted from any hospital specialist involved in the management r-ILD. They were triaged by lead ILD pulmonologist to monthly ILD MDT comprising a rheumatologist, respiratory physician, a radiologist and ILD specialist nurse. Appropriate patients were booked into combined clinic, run by the respective rheumatology and chest specialists with ILD interest, attracting a multi-speciality tariff. All the data was recorded electronically with full access to demographics, disease parameters, investigations and drug management.
Results: 89 patients were included in this proof-of-concept. Mean age was 66.1 yrs (19-90 yrs) and 44% (n=39) were male. 35 (40%) had RA, 34 (39%) had CTD, eight (10%) had sarcoidosis, five had IPAF and seven others. Most predominant HRCT pattern was NSIP (n=53,60%) followed by UIP (n=23, 21%), sarcoid (n=10, 12%) and miscellaneous (LIP and mixed). Mean FVC was 2.64 L/min (1.93-4.13) with DLCOc of 52.7% (28.9-90.1%) predicted. Only two patients had all antibodies negative whilst 87 had at least one antibody positive with ANA being the most common (n=28).
Most (83%) patients were treated with immunomodulators including nine with rituximab. 39 (44.3%) patients had significant improvement in clinical, imaging and pulmonary parameters with DLCOc improving to 56.57% and FVC to 2.70 L/min. There were similar improvements in six minute walk test. 17 patients died and 20 patients required long term oxygen therapy.
Conclusion: This proof-of-concept real world study confirms the utility of a combined specialist service in a district general hospital. Nearly half of this complex and resource intensive patient cohort had good clinical outcomes and derived benefit from the expertise in one room. Feedback from both patients and referrers was unanimously positive. No patient required tertiary centre referral and all could be managed adequately in the clinical setting.
Our report confirms that r-ILD can be managed in a DGH setting with a streamlined service offering clear benefits to patients. We would argue that r-ILD service, congruent to satellite pulmonary hypertension clinics in secondary care with hub-and-spoke model liaison with tertiary centre, can be established on similar principles and could help over-stretched tertiary care with repatriation of services whilst helping develop local expertise in the management of chronic ILD.
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, Consultant of: Muhammad Nisar undertakes clinical trials and received support (including attendance at conferences, speaker fees and honoraria) from Roche, Chugai, MSD, Abbvie, Pfizer, BMS, Celgene, Novartis and UCB
, Speakers bureau: Muhammad Nisar undertakes clinical trials and received support (including attendance at conferences, speaker fees and honoraria) from Roche, Chugai, MSD, Abbvie, Pfizer, BMS, Celgene, Novartis and UCB
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AB1182 OPTICAL COHERENCE TOMOGRAPHY FOR HYDROXYCHLOROQUINE EYE MONITORING - SHOULD WE WORRY?

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Background: Recent data have highlighted that hydroxychloroquine (HCQ) retinopathy is much more common than previously reported. The overall prevalence appears to be around 7.5% and depending on dose and duration of therapy can increase to 20-50 % after 20 years of therapy. Royal College of Ophthalmology UK recommend that all patients planning to take hydroxychloroquine long term have a baseline examination in a hospital eye department with a colour retinal photograph and spectral domain optical coherence tomorgraphy (SD-OCT) scans of the macula. After five years, annual screening is required with 10-2 Humphrey visual field testing, followed by pupillary dilation and imaging with both SD-OCT and widefield fundus autofluorescence imaging (FAF).
Objectives: Our aim was to review the early findings of the screening program for all rheumatology patients prescribed HCQ at our university hospital.
Methods: A business case was approved to set up eye monitoring in accordance with above guidelines. All patients with rheumatic diseases prescribed HCQ were identified through departmental database. They were invited for ophthalmological

examination and those with drug exposure >5 yrs were prioritised. An MDT pathway was established to manage anyone with signs of HCQ toxicity.
Results: 2,132 patients are prescribed HCQ in our county with population of 669,000. 997 patients fell under our unit's remit. 136 patients (82% women) have been screened with mean age of 58 yrs (24-84y). 65 (48%) have RA and remaining with connective tissue diseases. Median disease duration is 10 yr (0.75-30 yrs) and median drug exposure is 10 yr (0.4-27yr). Three doses of HCQ are prescribed: 200mg daily (53%), 300mg daily (13%) and 400mg daily (34%). Ten (7.3%) patients were found to have abnormal results. Three were consistent with HCQ toxicity pattern and one with likely toxicity. Two of them had already developed severe sight loss. HCQ was discontinued in all these cases. Six had other incidental anomalies requiring further input.
Conclusion: Hydroxychloroquine is used increasingly in the treatment of autoimmune diseases with emerging role in oncology. It has a favourable safety and tolerability profile with survival benefit demonstrated in SLE. In the UK, it's adoption has been particularly high owing to the requirement of trialling two DMARDs prior to being eligible for biologic therapy in RA and PsA. In the absence of modern retinal imaging techniques, HCQ toxicity was perhaps underestimated and hence older guidelines did not emphasise strict monitoring practice. Our preliminary data, in line with published evidence, represents a greater public health problem than previously estimated. It is clear that implementing the new guidelines not only recognises hitherto undiagnosed drug toxicity but also identifies incidental significant eye pathology which puts pressure on healthcare resources and needs robust service planning. Rheumatologists need to be aware of the potential impact requiring informed discussion with patients and perhaps a fundamental shift in prescribing behaviour to avoid this rapidly developing health concern.
Disclosure of Interests: Amr Moharram: None declared, Freddy Raj: None declared, Jose Maya: None declared, Ranjit Sandhu: None declared, Muhammad Khurram Nisar Grant/research support from: Muhammad Nisar undertakes clinical trials and received support (including attendance at conferences, speaker fees and honoraria) from Roche, Chugai, MSD, Abbvie, Pfizer, BMS, Celgene, Novartis and UCB
, Consultant of: Muhammad Nisar undertakes clinical trials and received support (including attendance at conferences, speaker fees and honoraria) from Roche, Chugai, MSD, Abbvie, Pfizer, BMS, Celgene, Novartis and UCB
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AB1183 TERIPARATIDE SWITCH TO BIOSIMILAR - IS IT COST EFFECTIVE?

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Background: Teriparatide is an effective treatment option for osteoporosis however NICE restricts its use to patients with high disease burden. This was based on cost effectiveness evaluation of the originator (Forsteo®) and would be different for recently introduced generic preparation.
Objectives: We wished to evaluate the current prescribing behaviour prior to a potential switch to generic version and associated cost savings.
Methods: All patients prescribed Teriparatide since the commencement of specialist osteoporosis service in Aug 2014 at our University teaching hospital covering 350,000 population were included. Data was extracted from electronic database with full access to demographics, population characteristics, disease parameters and medication history.
Results: 113 patients were prescribed Teriparatide over five years. Mean age of participants was 76 yrs (53-96). They had on average three comorbidities (0-8) with most common being hypertension (n=44, 38.9%) and inflammatory arthritis (n=21, 18.5%). Sixteen (14.1%) individuals had concurrent corticosteroids. Median number of fractures prior to therapy were four (0-12). Prior treatments included oral therapy (n= 90,79.6%), IV zoledronate (n=22, 19.4%) and denosumab (n=19, 16.8%). 66 (58.4%) of patients only had one prior bone active medication. Mean duration of prior therapy was 62.4 months (9-192 months). 17 (15.0%) patients had chronic kidney disease with lowest eGFR of 38. 41 (36.2%) had Vit D level between 40-75 nmol/L. Median T score was -3.8 (-2.1 - -6.0) which improved to -3.4 (-2.9 - -3.9) after two years.
Conclusion: Our real-world study shows that teriparatide is used predominantly in complex, multi-morbid older individuals with several prior fractures. Despite that teriparatide remains effective for a wide range of individuals including those with inflammatory arthritis and/or concurrent steroid use. Neither moderate CKD nor mild Vit D insufficiency seems to impact its efficacy. This is in line with recent meta-analysis of real life teriparatide use in complex osteoporosis with multimorbidity. Our study should enhance clinicians' confidence in its prescribing. It's notable that the use is higher than current estimates based on NICE cost effectiveness analysis for eligibility of teriparatide. Instead of annual predicted use of 4.8/100,000 population, it was prescribed to 6.4/100,000. This could potentially have a cost impact however the introduction of a generic version would mitigate against it. We calculated our savings to be over £125,000 if all patients were switched. These savings at national level would hopefully improve access to a wider patient cohort and perhaps allow earlier use in the treatment paradigm.
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, Consultant of: Muhammad Nisar undertakes clinical trials and received support (including attendance at conferences, speaker fees and honoraria) from Roche, Chugai, MSD, Abbvie, Pfizer, BMS, Celgene, Novartis and UCB
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AB1184 BURDEN OF DISEASE AND DIRECT HEALTH CARE COSTS FOR PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN WESTERN AUSTRALIA

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Background: Systemic Lupus Erythematosus (SLE) is a chronic multiorgan disease with an unpredictable disease course, which requires monitoring for disease activity, treatment efficacy and comorbidity. Data on the healthcare utilization and cost of SLE, especially from Australia are scarce.
Objectives: To determine the healthcare utilisation and estimated costs of inpatient admissions (IP), emergency (ED) and outpatient (OPD) hospital visits and investigations for SLE patients in Western Australia (WA).
Methods: This is a longitudinal cohort study of SLE patients seen at a metropolitan public hospital, with ≥6 months of follow-up (n=179, 95% female; baseline age 36.2 ± 15.2 years). Electronic medical records provided data on OPD, ED and IP visits, and investigations conducted at public hospitals from January 2000 - December 2019. Direct healthcare costs were estimated from public hospital expenditure aggregates in FY2018/19.
Results: During a median observation period of 11.0 years (IQR 7.4, 13.5), SLE patients required 13,320 OPD visits for a median of 5.3 (IQR 3.0, 9.3) appointments per annum. The majority of OPD visits were with Rheumatology (n=1,986, 14.9%), Immunology (n=1,527, 11.5%), and allied health services (n=1,952, 14.7%), followed by Ophthalmology (n=1,385,10.4%), maternal & fetal health (n=873,6.6%) and Renal medicine (n=844,6.3%). In total 143 patients (79.9%) attended ED on average of 3 times (IQR 2, 7; ED visit rate 44.0 (95%CI 41.0, 47.0) per 100 person years. Overall, 125 patients (69.8%) were hospitalised at average 3 times (IQR 2, 6), with a mean LOS of 5 days (IQR 3, 12) for an IP rate of 37.6 per 100 patient years (95%CI 34.8, 40.5). Only 12.8% of patients did not attend ED or IP in the public health care system. A total of 367,067 laboratory investigations were performed (median nr. of tests per patient 205 (±290) per year) across fields of haematology/biochemistry (89%), immunology (5%), microbiology (4.5%) and histopathology (<1%). Minimum estimates for direct health care cost during the study period were 25.4 million AUD (IP 11m, OPD 6.3m, ED 0.9m and investigations 9.1m) for a crude annual cost of 14,088 AUD per patient.
Conclusion: SLE patients have extensive healthcare utilization across a range of outpatient and inpatient services. The main direct costs for this multidisciplinary health care provision are for disease monitoring and in-hospital treatment. Based on these conservative cost estimates to which medication cost need to be added, total costs for SLE care in WA are projected to be significantly higher than reported from Europe.

Table 1. Healthcare resource utilisation of patients with systemic lupus erythematosus between in Western Australia between 2000-2019.

	Outpatient	ED Visits	Admissions
Patients, n (%)	179 (100)	143 (79.9)	125 (69.8)
Total events, n	13,320	794	678
Visit rate per 100 patient years (95%CI)	738.9 (726.3, 751.4)	44.0 (41.0, 47.2)	37.6 (34.8, 40.5)
Patients with ≥ 2 visit per annum, n (%)	153 (85.5)	110 ()	94 (%)
Patients with ≥ 4 visits per annum, n (%)	112 (62.6)		
Patients with >10 visits per annum, n (%)	37 (20.7)	17 (%)	13 (%)
Discharged from ED, n (%)	-	684	-
Admitted from the ED, n (%)	-	110	110
Average length of stay, median (IQR)	-	3.0(2.1, 4.0) hrs	3.2 (1.5, 5.85) days
Patients with an overnight admission, n (%)		-	122 (98)
Overnight admissions, median (IQR)		-	3 (1, 5)
Patients with admissions >7 days		-	53 (42.4)
Costs AUD (FY2018/19)	$6,273,720	$869,430	$10,997,485

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AB1185 BUDGET IMPACT ANALYSIS OF INTRODUCING SUBCUTANEOUS INFLIXIMAB CT-P13 SC FROM THE UK PAYER PERSPECTIVE

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Background: CT-P13 subcutaneous (SC) is the first and only SC version of infliximab developed by Celltrion Healthcare and currently approved by the European Medicines Agency (EMA) for the treatment of rheumatoid arthritis (RA). Infliximab has been only available in intravenous (IV) formulation and thus this new mode of administration will allow patients to self-inject at homes. Self-injection will reduce number of outpatient visits and expected to decrease IV administration cost significantly. This research describes the economic impact of introducing infliximab SC from the UK payer perspective.

Objectives: The budget impact analysis (BIA) was conducted to assess the financial impact of the adoption of infliximab SC. The BIA calculates the costs of treatment (drug acquisition cost and administration) for patients with RA as first-line treatments, and compares the cost in a scenario without infliximab SC vs a scenario with infliximab SC to estimate the budget impact over the 5 year period.

Methods: A prevalence-based BIM was developed incorporating epidemiological data, administration cost data from the literature and market share data from IQVIA. The analysis compared a market scenario where a proportion of patients were treated with infliximab SC ('World With' infliximab SC) to an alternative market scenario where infliximab SC were not available and all patients were treated with IV ('World Without' infliximab SC). The model assumed that the clinical outcomes are same between infliximab SC and infliximab IV, and patients entering the model were all naïve and remained in the treatment for 5 years. In the 'World With' scenario, patients receiving infliximab IV switched to SC administration at 30% in Year 1, 45% in Year 2, and remained 60% from Year 3 to 5. The drug cost of infliximab SC is assumed to be the same as that of comparator treatments. Administration cost per infliximab IV infusion was estimated to be £382 and £3.32 per SC administration.

Results: Compared to the "World Without" infliximab SC, the introduction of subcutaneous infliximab resulted in cost savings of £39.6 million in UK over a 5-year period, equating to 4,466 additional patients to be treated with infliximab SC in base case scenario.

Sensitivity analysis includes dose-escalation up to 5mg/kg to reflect the real-world setting. In that scenario, the saving increases to £279.6 million over a 5-year period, equating to 30,839 additional patients to be treated with infliximab SC.

Conclusion: Utilization of subcutaneous infliximab may lead to substantial cost savings for UK payers. Self-injection will significantly reduce the burden on healthcare delivery allowing resource to be spent elsewhere. Sensitivity analysis concluded that treatment with increased IV dose will result in higher savings from switching patients to subcutaneous infliximab.

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AB1186 THE NHS SCOTLAND THERAPEUTIC DRUG MONITORING SERVICE FOR BIOLOGIC MEDICINES: PRELIMINARY ANALYSIS OF UTILISATION AND CLINICAL RESULTS AT YEAR 1

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Background: Anti-tumour necrosis factor α (anti-TNFα) drugs infliximab (IFX) and adalimumab (ADL) are effective treatments for several rheumatic diseases. Therapeutic drug level and anti-drug antibody monitoring (TDM) has emerged as a useful tool for optimising drug effectiveness, by identifying individuals who may benefit from dose or treatment frequency adjustment, or have secondary drug failure due to immunogenicity.

Objectives: Ensuring safe and effective use of biologic medicines has been identified as a key priority for NHS Scotland. Inequity and inconsistency of access to TDM across the nation was recognised as a barrier to delivering best practice and so a nationally commissioned TDM service was proposed in January 2018 to support clinical practice, providing universal access to TDM for services treating inflammatory diseases across Scotland. Data collection and analysis of results regarding usage and clinical impact of the service were identified as key outcome measures to assess service success and sustainability.

Methods: A service webpage was developed to provide guidance on testing strategies and interpretation of TDM results (1). An automated search of clinical data and test results recorded within the clinical biochemistry electronic results management system was conducted to identify all TDM tests performed between 01/01/2018 and 31/12/2018. Descriptive analysis outcomes included the number of samples received, processed, overall testing population, service utilisation by Health Board, number and results of TDM tests performed per patient. TDM results were interpreted according to published guidance on the service webpage and comparison was made with previously published data (2).

Results: 3609 specimens were received for testing, from 13 of the 14 Scottish Health Boards. 3561 drug level (DL) tests were performed; 1786IFX, 1775 ADL. 2717 total antidrug anti-body (TABT) tests and 681 free antidrug anti-body tests (FABT) were performed according to service protocol. 2791 individuals had one or more TDM tests during the 12-month period, of whom 541 were tested twice or more (range 2-5).

Table 1. IFX & ADL DL, TABT and FABT results by category as defined in service guidance (AU/ml = Arbitrary Units/ml)]

		INFLIXIMAB	ADALIMUMAB	
Drug level by category	Supratherapeutic DL > 8mcg/ml	546 (30.6%)	708 (39.9%)	Supratherapeutic DL > 10 mcg/ml
	Therapeutic DL ≥3<8.1mcg/ml	738 (41.3%)	636 (35.8%)	Therapeutic DL ≥5<10.1 mcg/ml
	Sub-therapeutic DL < 3mcg/ml	502 (28.1%)	431 (24.3%)	Sub-therapeutic DL < 5 mcg/ml
TABT by category	Negative (<10 AU/ml)	791 (54.2%)	905 (71.9%)	Negative (<10 AU/ml)

Table 1. IFX & ADL DL, TABT and FABT results by category as defined in service guidance (AU/ml = Arbitrary Units/ml)]

		INFLIXIMAB	ADALIMUMAB	
FABT by category	Positive (>10 AU/ml)	668 (45.8%)	353 (28.1%)	Positive (>10 AU/ml)
	Negative (< 5AU/ml)	376 (82.8%)	176 (77.6%)	Negative (<10 AU/ml)
	Positive (> 5 AU/ml)	78 (17.2%)	51 (22.4%)	Positive (>10 AU/ml)

Conclusion: TDM has been enthusiastically embraced. It is estimated that > 50% of individuals treated with IFX or ADL have been tested at least once in the first year. DL results were found to be similar to previously published data, as were rates of antibody positivity. The large volume of data generated by the service may provide additional evidence regarding the utility of TDM in predicting clinical response. Next steps are to conduct a comparative effectiveness analysis where proactive vs reactive TDM testing strategies will be compared, with the primary outcome measure being the proportions of patients with secondary loss of response.

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AB1187 TREATMENT ADHERENCE: WHAT ABOUT THE RHEUMATOLOGIST?

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Background: Adherence to medications among patients with rheumatic diseases is often suboptimal.[1] Adherence to treatment has been described to be affected by several factors.[2] The rheumatologist plays a crucial role in influencing adherence behavior by addressing perceptions about medication, providing information, and establishing trust in the treatment plan.[3] There is no record of attitudes and thoughts of Mexico's rheumatologists about adherence to medication.

Objectives: To know the rheumatologist's attitudes regarding treatment adherence in follow up consultation.

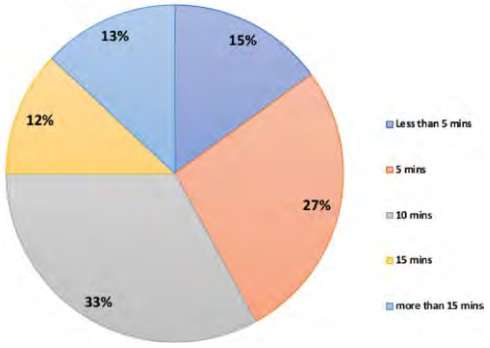
Methods: Descriptive, cross sectional study. Rheumatologists from across the country were invited to respond an electronic survey created with Google Forms, link was sent by Whatsapp ® message, responses were anonymous. The survey was constructed taking into account the main barriers of adherence related to the doctor. Seven questions were created, from one to six were multiple selections and the seven were open question *1.Where do you practice medicine? 2.Do you ask all your patients about adherence medication? 3.If your answer was positive, do you ask individually for each drug? 4.How long do you spend on explaining: side effects, benefits, and mechanisms of action of drugs? 5 Do you discuss available treatment options with your patients to decide one? 6.What's the definition of adherence? 7.Which activities can the doctor do to improve adherence to their patients?*

Results: Data were collected from 158 rheumatologists who completed the survey. Regarding the question where they practice medicine, 19.5% answered they work in public medical institutions, 31.8% do private practice and 48.7% work in both of them, 88.3% answered correctly adherence definition, 93% of rheumatologists ask for adherence to medication in the follow up consultation and only 86.1% do it individually for each medication, 97.4% discuss therapeutic options with their patients. The time used to explain treatment is presented in Figure 1. The interventions considered by rheumatologists to increase adherence are reported in Table 1.

Table 1 Interventions considered by rheumatologists to increase adherence

Patient education (in follow up consultation, conferences, pamphlets)
Develop rapport with patient. ("be accessible", "answer questions" "make the patient part of" don't be paternalistic or authoritarian")
Adherence measure (Use the available method, questionnaires, self-report, drug levels, electronic pillbox, pill count, etc. "*Don't matter which one, measure it!* ")
Interventions for no adherence reasons (phone calls, text messages, telephone alarms) fixed schedules for each medication, cognitive-behavioral therapy, access to medications)
Family support network
Presented in order to frequencies and grouped by topic

Figure 1
Time used by rheumatologists to explain treatment in follow up consultation



Conclusion: Rheumatologists ask for adherence medication but more than half use a limited amount of time to explain about medication, nevertheless, they think that patient education is the best intervention to increase adherence.

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AB1188 INFLUENZA VACCINATION TREND IN THE LAST DECADE AND FACTORS INFLUENCING THE RATE OF INFLUENZA VACCINATION IN CHRONIC INFLAMMATORY ARTHRITIS IN THE ITALIAN REGION OF FRIULI VENEZIA GIULIA (2006-2018)

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Background: vaccination is one of the most important medical intervention to prevent infectious complications in population at risk. EULAR recommendations for vaccination of patients suffering from autoimmune inflammatory rheumatic diseases (AIIRD) have been recently updated (1).

Objectives: to verify the level of coverage of the influenza vaccination in a local population of patients suffering from rheumatoid arthritis (RA), psoriatic arthritis (PsA) or ankylosing spondylitis (AS).

Methods: integration of the information coming from many administrative databases were used to this end. The Regional Health Information System of Friuli Venezia Giulia was used as the source of information for this retrospective cohort study. Patients were residents in Friuli Venezia Giulia and they had to carry the exemption code for RA, or PsA, or AS and at least one prescription of a

tsDMARD or a bDMARD in the 9 months before the start of the vaccination season (from October 1 to December 31). The observation period comprises all the years from 2006 to 2018. Multivariate logistic regression was used to assess the association between the probability of vaccination and demographic and clinical patient's characteristics in the influenza season 2018-2019.

Results: table 1 summarizes the results. During the whole period of observation, the coverage is always under the minimum desirable threshold of 75% and far from the optimum target of 95%, according to the National Italian Plan for Vaccination in the population at risk, even in the subgroup of older patients (age ≥ 65 years). In the logistic model including sex, age category, number and type of chronic conditions, socioeconomic status, rheumatic disease affecting the patient, area of residency, and treatment with tsDMARD or bDMARD, in 2018, older subjects were more likely to be vaccinated (people 65-74 vs 44-64, OR 4.63, 95%CI 3.76-5.70; people 75-84, OR 6.61, 95%CI 5.14-8.50) as were those with diabetes comorbidity (OR 1.64, 95%CI 1.03- 2.59); a lower borderline-significant probability of being vaccinated was observed among patients with low socioeconomic status (OR 0.83, 95%CI 0.68-1.00), and those treated by a biologic agent (OR 0.85, 95% CI 0.73-1.00)

Table 1. 2006-2018 vaccination coverage in RA, PsA and AS population.

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
	Global												
Number censored	1853	2031	2449	2684	2910	3092	3295	3471	3663	3883	4175	4334	4426
Total vaccinated (%)	662 (35.7)	664 (32.7)	848 (34.6)	946 (35.2)	892 (30.6)	942 (30.5)	886 (26.9)	994 (28.6)	926 (25.3)	1027 (26.4)	1232 (29.5)	1344 (31.1)	1550 (35)
Vaccinated ≥ 65 yrs (%)	61.4	57.9	61.6	60.5	55.7	54.5	47.7	49.9	43.9	46.1	51.9	52.6	57.0
	RA												
vaccinated (%)	38.5	35.0	37.1	37.7	33.7	33.8	29.7	31.3	28.3	29.6	32.3	33.5	37.3
Vaccinated ≥ 65 yrs (%)	61.9	56.9	61.1	59.6	55.2	54.6	47.4	49.2	44.3	46.2	51.5	51.3	56.0
	PsA												
vaccinated (%)	28.0	26.6	29.6	30.8	24.6	24.6	23.2	26.0	21.0	22.3	26.1	28.8	32.6
Vaccinated ≥ 65 yrs (%)	59.5	65.5	66.4	67.5	58.0	54.6	50.9	55.2	44.9	46.4	54.7	57.8	60.3
	AS												
vaccinated (%)	19.5	19.6	19.2	19.9	16.7	14.4	10.1	10.7	11.1	12.9	18.1	19.1	25.1
Vaccinated ≥ 65 yrs (%)	42.9	57.1	50.0	57.1	66.7	50.0	34.6	32.4	23.5	43.5	47.3	49.2	58.8

Legend: RA, rheumatoid arthritis; PsA, psoriatic arthritis; AS, ankylosing spondylitis.

Conclusion: influenza vaccination coverage is low in a population at high risk of infectious complications, even in the subgroup of elderly patients. Local guidelines are needed to improve the vaccination policies in AIIRD in order to increase the protection among patients who really need it.

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Disclosure of Interests: Luca Quartuccio Consultant of: Abbvie, Bristol, Speakers bureau: Abbvie, Pfizer, Alen Zabotti Speakers bureau: Celgene, Novartis, Janssen, Ginevra De Marchi: None declared, Tolinda Gallo: None declared, Salvatore De Vita Consultant of: Roche, GSK, Speakers bureau: Roche, GSK, Novartis, Francesca Valent: None declared

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AB1189 PICASO - THE PLATFORM FOR IMPROVED PERSONAL AND COORDINATED CARE OF CHRONICALLY ILL – SIX MONTHS RESULTS FROM A PROOF-OF-CONCEPT STUDY

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Background: Cross-sectoral coordination of treatment plans and efficient management of patients with chronic diseases and co-morbidities are of great importance. In rheumatoid arthritis (RA) it is essential to orchestrate information available for a patient at various locations, to allow (cost) efficient data use, to optimize management processes and to avoid redundant diagnostics. The information and communication platform developed in the Horizon2020 funded PICASO project (www.picaso-project.eu) supports the management of patients and their data along the continuum of care, consisting of hospitals, outpatient departments, practices, other health service providers via remote health monitoring. The platform might empower patients to improve their self-management of their illnesses.

Objectives: What technological expertise and resources do RA patients and physicians have, who are willing to participate in a proof-of-concept study using a modern ICT platform? What is the user satisfaction? What are platform`s clinical implications?

Methods: PICASO pursued a user-centered design approach. Platform`s user requirements were determined through workshops and interviews with physicians from various disciplines, patients and other stakeholders in the health care system (e.g. data protection officers). The development was accompanied by so-called "expert walkthroughs" to ensure a user-friendly design. An evaluation concept assessing the usability of the applications, user satisfaction and clinical relevance of the platform was part of the 6-month proof-of-concept study with RA patients and their physicians (rheumatologists and family doctors). A positive ethics vote was obtained.

Results: 111 user requirements were identified and used to develop the platform. Conformity with the GDPR as well as national regulations were precisely adhered to. All developments are based on the new 'Fast Healthcare Interoperability Resources' standard enabling data exchange with other software systems in the healthcare sector. This offers many advantages, e.g. a semantic model for describing the smallest units in the health care system (e.g. medication intake times, diagnostic procedures). Thus information can be linked and made available across sectors. Data can remain with the data owner and role-specific data access is ensured.

30 RA patients (80% female) participated, mean age was 58.6±10.8 years, disease duration 12.6±8.5 years, DAS28 2.6±0.9, average number of comorbidities 3.0±1.6. Patients' IT-experience was heterogeneous. After 6 months evaluations showed a good platform acceptance with an overall rating of 2.3±1.1 (n=27, Likert scale (LS) 1-6) and evaluation of 'ease of use' at 2.3±1.2 (n=27, LS 1-6). Usability tests showed that for patients the presentation of (1) tasks to be performed for the management of their disease, (2) results from their remote health monitoring, and (3) patient-reported outcome instruments in a dashboard was clear and easy to understand. Time required for documentation and daily tasks was rated as appropriate by 75.9% of the patients. No major technical problems or impairments due to RA where experienced when using the dashboard. 8 physicians (37.5 % female) participated in the evaluation; overall the platform was rated at 2.2±0.5 (LS 1-6).

Conclusion: The platform offers cross-sectoral orchestration of patient data and thus innovative capabilities for modern management processes (e.g. treat-to-target, tele-monitoring). The PICASO platform is available for RA patients as well as for other chronic diseases.

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Disclosure of Interests: None declared

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AB1190 DIRECT MEDICAL COSTS OF HOSPITALIZATION DURING THE MAINTENANCE THERAPY IN PATIENTS WITH ANTINEUTROPHIL CYTOPLASMIC ANTIBODY-ASSOCIATED VASCULITIS USING JAPANESE HEALTH INSURANCE DATABASE

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Background: Antineutrophil cytoplasmic antibody-associated vasculitis (AAV) requires a long-term maintenance therapy (MT), often accompanied by hospitalization due to relapse and/or comorbidities such as infection[1]. However, data about direct medical costs of hospitalization during MT in patients with AAV is limited to date despite of an increasing concern about the economic burden of patients with AAV[2-3].

Objectives: To describe frequency of hospitalization and its direct medical costs during MT after the remission-induction therapy (RT) in patients with AAV using Japanese health insurance database.

Methods: This retrospective longitudinal population-based study was conducted using claims data in Japan provided by Medical Data Vision Co., Ltd. We defined individuals as AAV cases receiving RT if they met all of the following: 1) having

at least one ICD10 code (M300, M301, M313, or M318); 2) having at least one prescription of oral corticosteroids with prednisolone-equivalent dosage ≥30 mg/day, methylprednisolone pulse therapy, immunosuppressive drugs (cyclophosphamide [IVCY], methotrexate, or mycophenolate mofetil), or rituximab (RTX) during hospitalization between April 2008 and April 2017; and 3) having at least 7 days of hospitalization. The observation started from the next day of discharge from the first hospitalization for RT and ended at 24 months later, the month of loss of follow-up, or April 2017. We described the frequency of hospitalization and calculated direct medical costs (per month) during the observation. We analyzed medical costs from a societal perspective. We classified reasons of hospitalization into 3 categories; intensification of treatments for AAV, AAV MT including IVCY or RTX treatments, and comorbidities (infection, cardiovascular disease [CVD], malignancy, and others) using ICD10 codes plus treatments or interventions during the hospitalization.

Results: In this study, 1,703 patients with AAV were included. The median [IQR] age was 72 [63, 79] years and 55.7% were female. The total number of hospitalization was 1,897 in 863 patients (50.7%). Among the hospitalizations, 296 hospitalization in 235 patients were categorized as intensification of treatments for AAV, 627 hospitalization in 297 patients were AAV MT, and 974 hospitalization in 572 patients were categorized as comorbidities. In the last category, infections were most frequent (220), followed by malignancy (54) and CVD (15). The mean direct medical costs per month was 20,945 EUR (1 EUR=125 JPY) in patients with hospitalization and 599 EUR in those without. Patients with hospitalization due to intensification of treatments for AAV had the highest direct medical costs (3,000 EUR), followed by those with hospitalization due to comorbidities (2,001 EUR), and those with hospitalization due to AAV MT (1,649 EUR).

Conclusion: More than half of the patients had hospitalization during MT, and hospitalization due to comorbidities were most frequent. The mean direct medical costs in patients with at least one hospitalization was approximately 3.5 times as high as that in those without hospitalization.

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AB1191 AWARENESS OF PRESCRIPTION DRUGS FOR RHEUMATOID ARTHRITIS AMONGST PATIENTS -A COMPARISON OF THE RESULTS FROM 2014 AND 2018 SURVEYS-

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Background: Treatment of rheumatoid arthritis (RA) is based on drug therapy. With the increasing number of effective drugs being authorized for use and generic drugs becoming available in the market, patients with RA now have an abundance of drugs as treatment options.

Objectives: To conduct a survey of RA patients to evaluate their knowledge about the prescribed drugs, their names, and the respective categories.

Methods: In 2014 and 2018, two different surveys were done in which RA patients were interviewed regarding the name of biologics (trade name) and other oral medications (category and trade name of anti-rheumatic drugs, steroid drugs and anti-inflammatory analgesics). The results of the two investigations are compared in this study.

Results: A total of 135 (34 men and 101 women) and 184 patients (31 men and 153 women) were interviewed in the surveys done in 2014 and 2018, respectively. In the 2014 survey, the mean age of the patients was 58.5 years (range: 25-88 years), while in the 2018 survey, the mean age of the patients was 61.0 years (range: 14-84 years). The various biologics prescribed to the patients who participated in the 2014 vs. 2018 surveys were as follows: infliximab (27 vs. 22), etanercept (11 vs. 9), adalimumab (14 vs. 16), tocilizumab (43 vs. 71), abatacept (29 vs. 46), golimumab (7 vs. 11), certolizumab-pegol (4 vs. 3), sarilumab (0 vs. 2), and tofacitinib (0 vs. 5), respectively. The number of patients who were prescribed various categories of oral medications, as stated in the 2014 vs 2018 surveys, was as follows: anti-rheumatic drugs, 104 (77.0%) vs. 131 (71.2%); steroid drugs, 36 (26.7%) vs. 44 (23.9%); and anti-inflammatory analgesics, 49 (36.3%) vs. 61 (33.2%), respectively. The number of patients that took medications without any knowledge about the drug name or its category, as reported in the 2014 vs. 2018 surveys was as follows: anti-rheumatic drugs, 24 (23.1%) vs. 42 (32.1%); steroid drugs, 11 (30.1%) vs. 24 (54.5%); and anti-inflammatory analgesics, 15 (30.6%) vs. 17 (27.9%), respectively. In the corresponding years, the number of patients who responded negatively to the question whether they knew about the trade name of the biologics prescribed to them was 15 (11.1%) and 26 (14.1%), in the 2014 and 2018 surveys, respectively. The mean age of the patients who expressed lack of knowledge with respect to the trade name of the biologics prescribed to them was 67.3 and 69.5 years old, in the 2014 and 2018 surveys, respectively; thus suggesting the impact of old age on awareness about prescribed drugs. Many of the biologics prescribed to these patients were intravenous drip formulations, and only one patient was prescribed self-administered subcutaneous injection formulation. This implied that the majority of patients who expressed lack of knowledge regarding the trade name of the biologics were administered the drug by health-care providers at the hospital.

Conclusion: Our investigation about RA patients' understanding of the trade names and category of the drugs they were administered revealed that 20 to 50% of the patients were unaware about the oral medications they were receiving. In particular, there were many patients who had misinterpreted steroidal drugs as analgesics. In addition, approximately 10% of the patients lacked an understanding of drugs that require cautious use due to their potential for causing adverse events. For those biologics administered at the hospital by healthcare providers, the patients had a lack of inclination to learn the drug name. In today's era, with the emergence of generic drugs and an increase in the drug categories, it is not easy for the aging patients to understand and remember information about the prescription drugs. Hence, it is necessary to come up with measures to tackle this situation.

Disclosure of Interests: None declared

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AB1192 THE UNDERWORLD OF DEPRESSIVE SYMPTOMS IN RHEUMATIC DISEASES: OVERLOOKED, UNRECOGNIZED OR UNPERCEIVED?

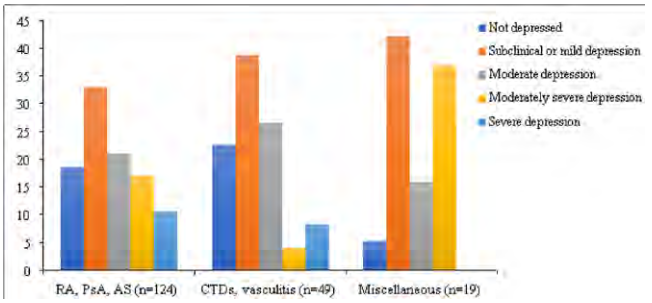
F. Ingegnoli[1,2], T. Schioppo[1,2], T. Ubiali[1], V. Bollati[2,3], S. Ostuzzi[4], M. Buoli[2,5], R. Caporali[1,2]. *[1]G Pini Hospital, Clinical Rheumatology Unit, Milan, Italy*; *[2]Università degli Studi di Milano, Milan, Italy*; *[3]EPIGET Lab, Milan, Italy*; *[4]ALOMAR Lombard Association for Rheumatic Diseases, Milan, Italy*; *[5]IRCCS Ca'Granda Policlinico, Milan, Italy*

Background: The concomitant presence of depressive symptoms and rheumatic diseases (RDs) impose a considerable economic and social burden on the communities as they are associated with numerous deleterious outcomes such as increased mortality, work disability, higher disease activity and worsening physical function, higher pain levels and fatigue. Despite growing interest on depressive symptoms burden in RDs, current patient perception on this topic is unknown.

Objectives: Italian patients with RDs were invited to participate in an online study gauging the presence and the perception of depressive symptoms using the Patient Health Questionnaire (PHQ-9).

Methods: This was a cross-sectional no-profit online study to screen the presence and the perception of depressive symptoms in RDs patients. All participants gave their consent to complete the PHQ-9 and they were not remunerated. Completion was voluntary and anonymous. The PHQ-9 rates the frequency of symptoms over the past 2 weeks on a 0-3 Likert-type scale. It contains the following items: anhedonia, depressed mood, trouble sleeping, feeling tired, change inappetite, guilt or worthlessness, trouble concentrating, feeling slowed down or restless, and suicidal thoughts. Patients were stratified as: <4 not depressed, 5-9 sub-clinical or mild depression, 10-14 moderate depression, 15-19 moderately severe depression and 20-27 severe depression. The survey was disseminated by ALOMAR (Lombard Association for Rheumatic Diseases) between June and October 2019.

Results: 192 patients took part in the study: 170 female with median age 50 years. Among respondents only 35 (18.2%) were not depressed. Depression was sub-clinical or mild in 68 (35.4%), moderate in 42 (21.9%), moderately severe in 30 (15.6%), and severe in 17 (8.9%). 16 (8.3%) of respondents declared to have depressive symptoms and 7 of 16 were under psychiatric therapy.
Moreover, patients were grouped according to diagnosis.
124 respondents had inflammatory arthritis (rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis). 23 (18.5%) were not depressed. Depression was sub-clinical or mild in 41 (33%), moderate in 26 (21%), moderately severe in 21 (17%), and severe in 13 (10.5%). Among them, 8 (6.5%) declared to have depressive symptoms depressed and 3 of 8 were under psychiatric therapy.
49 respondents had a connective tissue disease or vasculitis. 11 (22.5%) were not depressed. Depression was sub-clinical or mild in 19 (38.8%), moderate in 13 (26.5%), moderately severe in 2 (4%), and severe in 4 (8.2%). Among them, 3 (6%) declared to have depressive symptoms and 1 of 6 were under psychiatric therapy.
19 respondents had other rheumatic diseases. 1 (5.3%) was not depressed. Depression was sub-clinical or mild in 8 (42.1%), moderate in 3 (15.8%), moderately severe in 7 (36.8%). Among them, 5 (26.3%) declared to be depressed and 3 of 5 were under psychiatric therapy.



Conclusion: Our study confirmed that the overall real-life burden of depressive symptoms is relevant in all RDs. At the same time, these results highlighted that depressive symptoms are overlook by physicians and unperceived by patients since fewer that half of respondents (46.4%) had a clinical depression (PHQ-9>10). These results suggested that screening for depression should form part of the routine clinical assessment of RD patients.
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AB1193 WORK INSTABILITY AMONG POLISH RHEUMATOID ARTHRITIS PATIENTS

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Background: Rheumatoid arthritis (RA) affects patients' capacity to work. Rheumatoid Arthritis Work Instability Scale (RA-WIS) is a reliable method to measure work instability (WI) (1–3). We lack data on relationship between RA and work instability among Polish patients.
Objectives: The aim of our study was to assess WI and associated factors among patients with RA.
Methods: 315 patients from three rheumatology centres were enrolled and filled questionnaires including demographic and self-reported clinical data, RA-WIS, and The Health Assessment Questionnaire (HAQ). Swollen and tender joints count (SJC, TJC) were assessed by attending physician and current erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were collected. We excluded 41 patients due to incorrectly filled form and analysed questionnaires of 274 patients. DAS28 (Disease Activity Score in 28 joints) and DAS28-CRP were calculated. We performed statistical analysis with Statistica v. 13.3 using Mann-Whitney U test, chi-square test and Spearman's correlation
Results: 140 (51 %) patients were employed and their characteristics are presented on Table 1. In univariable analysis we identified following risk factors for high risk WI: moderate-to-high disease activity (DAS28≥3.2 – OR 2.29, 95%CI 1.06-4.96, p=0.033; DAS28-CRP≥3.2 – OR 2.34, 95%CI 1.04-5.27, p=0.038), ESR ≥30 mm/h in women and ≥20 mm/h in men (OR 2.65, 95%CI 1.20-5.89, p=0.010), CRP≥1mg/dL (OR 4.02, 95%CI 1.78-9.10 p<0.001), HAQ-DI>1.0 (OR 2.23, 95%CI 1.04-4.81, p=0.037) and at least moderate pain on visual analogue scale (VASp ≥4.5 cm - OR 5.31, 95%CI 2.36-11.96, p<0.001). Correlations were moderate between RA-WIS and VASp (R_S=0.59, p<0.001) and HAQ-DI (R_S=0.52, p<0.001) whereas weak with disease activity indices (DAS28 - R_S=0.31, p<0.001; DAS28-CRP - R_S=0.28, p<0.001).

Table 1. Demographic and clinical characteristics of employed patients according to work instability risk, N(%) or mean(±SD).

Characteristic	RA-WIS score	
	low-to-moderate (0-17)	high (>17)
Patients	94 (67.1%)	46 (32.9%)
Sex, female	73 (77.7%)	38 (82.6%)
Age (years)	47.9 (±11.8)	50.4 (±9.3)
Disease duration (years)	13.0 (±8.4)	14.0 (±8.7)
RF, positive	68 (72.3%)	34 (73.9%)
ACPA, positive	59 (62.8%)	29 (63.0%)
ESR (mm/h)	18.3 (±16.0)	28.2 (± 21.9)*
CRP (mg/dL)	0.6 (± 1.0)	1.1 (± 1.0)*
TJC	4.5 (±4.0)	7.6(±6.3)*
SJC	2.7 (±3.0)	5.2(±5.5)*
HAQ-DI	0.7 (±0.5)	1.1 (±0.5)*
pain - VAS 10 cm	3.9 (±1.9)	6.5 (± 2.2)*
DAS28	3.5 (±1.2)	4.2 (±1.4)*
DAS28-CRP	3.9 (±1.0)	4.3 (±1.2)*

WI – work instability, RA-WIS – Rheumatoid Arthritis Work Instability Scale, RF – rheumatoid factor in IgM class, ACPA – anti-citrullinated protein antibodies, ESR – erythrocyte sedimentation rate, CRP – C-reactive protein, TJC – tender joints count, SJC – swollen joints count, HAQ-DI – Heath Assessment Questionnaire Disability Index, VAS – visual analogue scale, DAS28 – Disease Activity Score in 28 joints
*p<0.05, Mann-Whitney U test

Conclusion: Pain and disability are main factors associated with work instability among patients with RA.
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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.2485

AB1194 STRIKING DIFFERENCES IN THE COURSE OF OSTEOARTHRITIS (OA) COMPARED TO RHEUMATOID ARTHRITIS (RA) OVER THE FIRST 24 MONTHS OF RHEUMATOLOGY CARE AT ONE PRIVATE PRACTICE SETTING

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Background: Recent reports indicate that disease burden in osteoarthritis (OA) is similar to or greater than in rheumatoid arthritis (RA) when an identical measure is used to assess patients with either disease, generally an MDHAQ/RAPID3 (multidimensional health assessment questionnaire/routine assessment of patient index data). The data suggest that a traditional view that RA is more severe than OA no longer is valid at this time. One concern is that similar disease burdens in OA vs RA may result entirely from superior treatments for RA, and RA may be considerably more severe than OA at initial presentation.
Objectives: To analyze MDHAQ disease burden in patients with OA vs RA at initial visit and at 24-month follow-up in routine care at a single solo-rheumatologist private practice setting.
Methods: All patients at this setting complete an MDHAQ at each visit in the waiting area, prior to seeing the rheumatologist. The MDHAQ includes three 0-10 scores for physical function, pain visual numeric scale (VNS), and patient global VNS, which may be compiled into a 0–30 RAPID3, as well as a 0-10 fatigue VNS, and 0-16 rheumatoid arthritis disease activity index (RADAI) self-report painful joint count. Mean MDHAQ scores were analyzed

for all 73 OA and 116 RA patients seen for an initial visit between 2011 and 2017. Mean scores at initial and 24-month visits were compared for all 25 OA and 63 RA patients seen at 24 month (21-27 month) follow-up visits, using paired t tests.

Results: Mean MDHAQ scores at first visit were similar for all 73 OA and 116 RA patients, and also for 25 OA and 63 RA patients who were also seen 24 months later, e.g., mean RAPID3 was 12.0-14.2. However, mean changes over 2 years were strikingly different in OA versus RA patients (Table). Almost all mean scores in OA were somewhat higher, while all mean scores in RA were clinically and statistically significantly improved at 24 months, e.g., mean RAPID3 worsened from 13.0 to 15.2 (+2.2 units, 17%) in OA patients, compared to improvement from 12.5 to 8.2 (-4.3 units, -34%) in RA patients. The smallest mean change in RA patients involved the joint count (7.7 to 6.1, -21%) (Table), suggesting possible control of inflammation, but continued damage to specific joints. An important limitation is that the data do not include follow-up on patients not seen over the 24 month "window," because of substantially better or poorer status, joint surgery, or other reasons, although the data present an accurate characterization of one rheumatology practice setting.

Mean values of patient MDHAQ scores in patients with OA or RA at first visit and 24-month follow-up

MDHAQ score:	OA first visit of those seen at 24 months (n=25)	OA 24-month visit (n=25)	% change, over 24 months	RA first visit of those seen at 24 months (n=63)	RA 24-month visit (n=63)	% change, over 24 months
RAPID3	13.0	15.2	+2.2, +17%	12.5	8.2	-4.3, -34%
Function	0.81	0.77	-0.04, -5%	0.71	0.50	-0.21, -29%
Pain	5.2	6.4	+1.2, +23%	5.1	3.2	-1.9, -37%
Patient global	5.1	5.9	+0.8, +16%	5.1	3.3	-1.8, -35%
Fatigue	4.1	4.4	+0.3, +7%	4.8	3.5	-1.3, -27%
Pt joint count	7.5	7.8	+0.3, +4%	7.7	6.1	-1.6, -21%

Abbreviations: MDHAQ=multidimensional health assessment questionnaire, OA=osteoarthritis, RA=rheumatoid arthritis, RAPID3=routine assessment of patient index data.
In change data, negative numbers indicate improvement, positive numbers indicate worsening.

Conclusion: Mean MDHAQ/RAPID3 scores were similar in RA or OA at the initial visit. Over 24 months, scores worsened slightly in OA and improved considerably in RA, resulting in considerably poorer status in OA versus RA, likely reflecting superior treatments for RA vs OA. At an individual level, patients with primary OA may have better or poorer status than patients with primary RA. Nonetheless, at a group level, the severity of disease burden in OA appears similar to RA, and becomes greater over the next 24 months, likely as a result of better treatments. The severity of OA is underrated, suggesting a need for increased resources for research toward better treatments for OA.

Disclosure of Interests: Kyle Schroeder: None declared, Theodore Pincus Shareholder of:
Dr. Pincus holds a copyright and trademark on MDHAQ and RAPID3 for which he receives royalties and license fees from profit-making organizations, all of which are used to support further development of quantitative clinical measures for patients and health professionals., Martin Bergman Shareholder of: Johnson & Johnson – stockholder, Consultant of: AbbVie, BMS, Celgene Corporation, Genentech, Janssen, Merck, Novartis, Pfizer, Sanofi – consultant, Speakers bureau: AbbVie, Celgene Corporation, Novartis, Pfizer, Sanofi – speakers bureau

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AB1195 CO-RELATION BETWEEN SELF EFFICACY, DEPRESSION AND PAIN AMONG CAREGIVERS WITH AND WITHOUT ARTHRITIS

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Background: People with arthritis, like others, are often informal caregivers. Caregiving adds burdens of stress and depression. Caregiver studies have shown these to be mitigated by self-efficacy or the confidence to achieve specific caregiving behaviors. Caregivers with arthritis have seldom been studied. We have been unable to find studies specific to caregiving and self-efficacy as they apply to those with and without arthritis. In this study, we evaluated the relationship between self-efficacy, pain, and depression among caregivers with and without arthritis.

Objectives: 1)To examine the correlation between caregiver self-efficacy and depression and pain. 2). To examine how these correlation differ for caregivers with and without arthritis.

Methods: A caregiver questionnaire was distributed via social media, mainly list serves and blogs to a convenience sample. Those receiving the links were urged to send them to other populations. Respondents self-reported arthritis and weekly hours spent caregiving. They reported pain using a pain (visual numeric scale (1-10)), depression with the Patient Health Questionnaire (PHQ-8), and Self-Efficacy was reported with the short caregiver self-efficacy scale). For caregivers and non-caregivers we compared caregiving hours, pain, depression and self-efficacy. We examined the distribution of caregiving hours by arthritis status and plotted mean pain scores by caregiving hours for caregivers with and without arthritis. The correlation between depression and self-efficacy was measured using Pearson correlation coefficient overall and by arthritis status.

Results: Over two weeks 155 individuals responded, with data on self-reported arthritis status. Of the respondents, 88% were female and 64% were 50-69 years of age. 46% self-reported arthritis (osteoarthritis was the most common type). Nearly 25% of caregivers reported spending less than 10 hours weekly on caregiving, while approximately 23% reported at the other end of the extreme (at least 40 hours weekly). The distribution by arthritis status of the caregiver is provided in Table 1.

Table 1.

	Caregiving hours						
Arthritis	0-9 hrs	10-19 hrs	20-29 hrs	30-35 hrs	40+ hrs	Missing	All
No	26 (31%)	26 (31%)	11 (13%)	5 (6%)	15 (18%)	1 (1%)	84 (54.2%)
Yes	12 (17%)	21 (30%)	11 (15.5%)	7 (9.9%)	20 (28%)	0	71 (45.8%)
Total	38 (24.5%)	47 (30.3%)	22 (14.2%)	12 (7.7%)	35 (22.6%)	1 (0.7%)	155

Caregivers with arthritis reported higher pain in the past week. Mean pain score among caregivers with arthritis was 4.4 (SD 2.2) compared to 2.7 (SD 1.7) among caregivers without arthritis (figure 1). This divergence widened for caregivers with 40 or more hours of caregiving. There was a strong negative correlation (Pearson correlation= – 0.473, p-value <0.0001) between depression and self-efficacy. The correlation was -0.59 for caregivers without arthritis (p=<0.0001, n=74 with data on all three variables) compared to the caregivers self-reporting arthritis (r=-0.35, p=0.006, n=60 with data on all three variables).

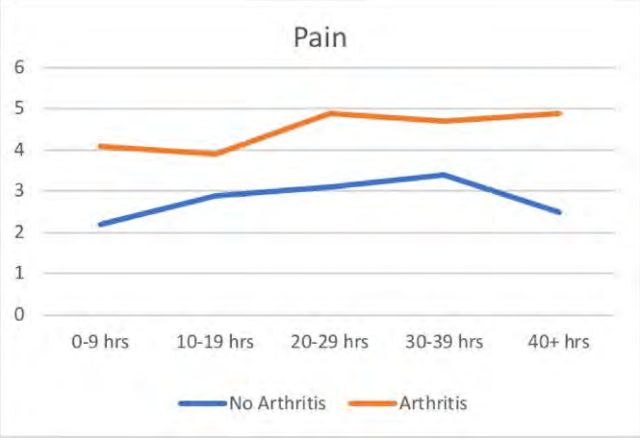


Figure 1.

Conclusion: This study suggests that lower caregiver self-efficacy has a direct and strong association with higher depressive symptoms and that this is more pronounced among caregivers with arthritis. This study also shows that caregivers with arthritis have more pain than caregivers without arthritis, and that this peaks and remains consistent for those doing twenty or more hours of caregiving weekly.. The stronger negative correlation of depression and self-efficacy among patients without arthritis may be explained by other independent contributors (such as pain) to depression in caregivers with arthritis.

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[1] Lorig K, Ritter PL, Laurent DD, Yank V. Building Better Caregivers: A Pragmatic 12-Month Trial of a Community-Based Workshop for Caregivers of Cognitively Impaired Adults. *J Appl Gerontol*. 2019;38(9):1228–1252. doi:10.1177/0733464817741682

Disclosure of Interests: None declared

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AB1196

A STUDY REVIEWING THE ASSOCIATED FACTORS AND COST-EVALUATION OF SWITCHING BACK TO ORIGINATOR-ETANERCEPT FROM ITS BIOSIMILAR AMONG PATIENTS WITH RHEUMATIC DISORDERS AT A TERTIARY CARE CENTRE IN UNITED KINGDOM

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Background: Biological therapy plays a major role in the management of patients with rheumatic disorders. Evidences generated at experimental settings have shown biosimilars as clinically effective, safe and cost effective. Nevertheless, real world data are lacking about cost effectiveness and causes of switching back to originator product among patients

Objectives: To describe the associated factors and cost evaluation of switching back to the originator etanercept from the biosimilar among patients with rheumatic disorders at The Robert Jones and Agnes Hunt Orthopaedic Hospital of United Kingdom

Methods: A descriptive cross-sectional study was undertaken with secondary data in a tertiary care hospital. All the patients who were switched from original etanercept (originator) to biosimilar Etanercept from October 2018 to June 2019 were included in the study. A pre-tested data extraction sheet was used in the data collection. Annual expenditure estimates for the treatment modalities were collected by consulting the experts. Descriptive analysis was done for the characteristics of the study sample and for the estimated annual costs. Associations of age and sex in the switching of treatment modalities were explored with chi-square test and Mann Whitney U test with 5% significance level.

Results: Records of 100 participants were extracted with a male to female ratio of 1: 1.4. The median [interquartile range (IQR)] of the participants was 54 (44 to 66) years. The leading three diagnoses were: rheumatoid arthritis (65%), Ankylosing Spondylitis (18%) and Psoriatic arthritis (14%). Out of the participants, 32 (32%) switched back to originator with a median (IQR) duration of 16.0 (10.5 to 19.5) weeks of commencing the biosimilar. The proportions of switching back were 28.1%, 34.4% and 37.5% among those who did, in the chronological 3-monthly intervals of the study. The main reasons for switching back included; side effects (21.9%), lack of efficacy (65.6%), both of these (9.4%) and other reasons (3.1%). Older age was observed among those who switched back ($p<0.05$) but gender did not show a statistically significant association ($p=0.532$). The annual estimated cost for biosimilar was 37.3% less than that for originator per patient.

Conclusion: In our cohort nearly one third switched back to the originator following the commencement of biosimilar incurring a financial and resource burden to the rheumatology department which in turn will have wider ramifications on the health care system. Exploring the reasons and factors associated with switching back to the originator in larger scale studies would help in planning cost-effective interventions and understanding the reasons why the patients revert back to the originator from the biosimilar therapy, especially among the older patients.

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AB1197

TREAT-TO-TARGET IS FEASIBLE IN RHEUMATOID ARTHRITIS PATIENTS DURING PREGNANCY, FIRST RESULTS OF THE PRECARA COHORT

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Background: A treat-to-target approach results in better outcomes for Rheumatoid Arthritis (RA) patients [1]. Well controlled disease is important for pregnant RA patients and patients with a wish to conceive too. Not only for the welfare of the mother, but also because active disease is associated with a prolonged time to pregnancy and adverse pregnancy outcomes [2]. This is this first study to examine a treat-to-target approach during pregnancy.

Objectives: To determine the feasibility of a treat-to-target approach in RA patients with a wish to conceive or pregnant.

Methods: Patients were derived from the PreCARA cohort (first inclusion 2011, data shown up to November 2019). The PreCARA cohort is an ongoing, single center, prospective study on RA and pregnancy. Patients in this cohort were treated according to a treat-to-target approach, in which the obvious restrictions of pregnancy were taken into account. Study visits were scheduled before, during and after pregnancy and disease activity (DAS28CRP) was measured. Results of the PreCARA study were compared with results of the PARA study [3], a historic reference cohort on RA during pregnancy, with a similar study design (inclusion 2002 – 2010). Patients in the PARA cohort were treated according to the standards of that time. The PARA cohort represents the natural course of RA during pregnancy with limited treatment options.

Results: 263 RA patients were included in the PreCARA cohort, up to now 154 children were born in this ongoing cohort. Mean age at inclusion was 32.3 (4.3 SD), 83.2 % was Rheumatoid Factor positive and/or ACPA positive. Mean disease activity in the PreCARA cohort is statistically significant lower than in the PARA cohort at every time-point: mean DAS28CRP in 3rd trimester in the PreCARA cohort 2.22 (0.73 SD), in the PARA cohort 3.35 (1.12 SD) $P < 0.001$ (figure 1). In the PreCARA cohort 73.3% of the patients were in low disease activity or remission before pregnancy increasing to 90.4 % in the third trimester, whereas in the PARA cohort these percentages were 32.2 % and 47.3% respectively ($P < 0.001$) (figure 2). Medication use in the PreCARA cohort is shown in table 1 and in the PARA cohort in table 2.

Table 1. Percentage of patients in the PreCARA cohort using certain medication (n=154).

Medication	Before pregnancy (%)*	1st trimester (%)	2nd trimester (%)	3rd trimester (%)	6 weeks post-partum (%)	12 weeks post-partum (%)	26 weeks post-partum (%)
MTX	5	0	0	0	15	19	15
Leflunomide	0	0	0	0	1	1	2
Abatacept	0	0	0	0	1	1	1
Hydroxychloroqine	63	51	51	50	49	43	31
Sulfasalazine	70	56	58	57	54	47	36
Prednisone	43	40	39	42	38	34	27
Azathioprine	1	2	1	1	0	1	1
Certolizumab	25	21	26	28	26	24	18
Adalimumab	10	5	0	0	3	3	4
Infliximab	5	8	3	0	1	1	1
Etanercept	13	10	9	3	10	11	9
Golimumab	0	0	0	0	0	0	1
Tocilizumab	3	1	0	0	3	2	3

* patients seen before pregnancy = 104

Table 2. Percentage of patients in the PARA cohort, a reference cohort, using certain medication (n=245). Medication that is not listed in this table was not prescribed in the study period.

Medication	Before pregnancy (%)**	1st trimester (%)	2nd trimester (%)	3rd trimester (%)	6 weeks post-partum (%)	12 weeks post-partum (%)	26 weeks post-partum (%)
MTX	0	0	0	0	18	30	36
Leflunomide	0	0	0	0	0	1	2
Hydroxychloroqine	6	2	2	2	4	8	7
Sulfasalazine	34	25	27	26	26	30	29
Prednisone	42	33	36	36	35	36	32
Azathioprine	1	0	0	0	1	1	1
Adalimumab	0	0	0	0	2	3	5
Infliximab	0	0	0	0	0	1	1
Etanercept	0	0	0	0	3	6	5

** patients seen before pregnancy = 124

Conclusion: This first study on a treat-to-target approach in pregnant RA patients shows that low disease activity and remission are an attainable goal during pregnancy, with over 90% of patients achieving this in the 3rd trimester. The effect of this approach on fertility and pregnancy outcomes should be the focus of further studies.

References:

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[2] Smeele et al. Current perspectives on fertility, pregnancy and childbirth in patients with Rheumatoid Arthritis. Semin Arthritis Rheum 2019

[3] de Man et al. Measuring disease activity and functionality during pregnancy in patients with rheumatoid arthritis. A&R 2007

Figure 1

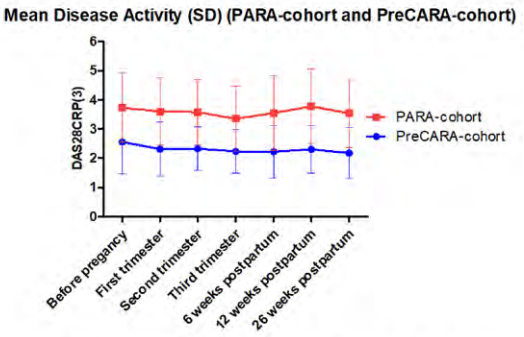


Figure 1: Graph showing DAS28CRP (mean, SD) scores over time. The x-axis displays specific time-points before, during and after pregnancy and the y-axis represents mean (SD) disease activity.

Figure 2

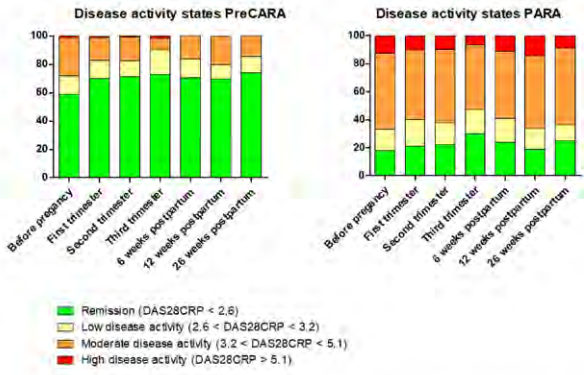


Figure 2: Bar charts showing disease activity states DAS28CRP scores. The x-axis displays the specific time-points before, during and after pregnancy, the y-axis shows the percentage of patients in the different disease activity states.

Disclosure of Interests: Hieronymus TW Smeele: None declared, Esther Röder: None declared, Hetty Wintjes: None declared, Laura JC Kranenburg - van Koppen: None declared, Johanna Hazes: None declared, Radboud Dolhain Grant/research support from: unrestricted grant from UCB Pharma

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AB1198 DECREASING OF TOTAL AND UNILATERAL KNEE ARTHROPLASTIES DUE TO RHEUMATOID ARTHRITIS BUT INCREASING IN OSTEOARTHRITIS IN OUR INSTITUTES IN LAST DECADE OF SUPER-AGING SOCIETY

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Background: The rate of elderly people over 65 year-old increased from 22.1 % in 2008 to 27.7% in 2017 in Japan, also from 27.1 % to 32.3 % in our super-aging area[1, 2]. The number of total and unilateral knee arthroplasty (TKA, UKA) have increased annually in all over the world according to the larger population of elderly people due to osteoarthritis (OA)[3]. In fact, the numbers of primary TKA predicted increasing from six hundred fifty-six thousand cases at 2010 to one million three hundred seventy-six thousand cases at 2020 in USA[4]. In the other hand, rheumatoid arthritis (RA) therapy have been remarkably improved from starting to use biologic agents since 2003 in Japan [5]. The rate of orthopaedic surgery may reflect trends in disease severity and drug management of RA [5].

Objectives: The aim of study is to reveal the rate of TKA, including UKA and revision TKA in elderly people in our super-aging area of Japan.

Methods: We surveyed the number and cause of primary and revision TKA and UKA in our institutes using the data of diagnosis procedure combination and the record of surgeries in the last decade.

Results: We had 23,193 cases of orthopaedic surgeries, including 4,242 primary and revision TKA/UKA from 2008 to 2017. The cause of TKA/UKA contained 3,817 (OA, 92 %), 212 rheumatoid arthritis (RA, 5.1%), 61 osteonecrosis, 42 loosening of prosthesis. The cause of 60 revision TKA/UKA contained 42 loosening, 9 broken of implant. They contained 3,584 cases of primary TKA, 614 UKA, 60 revision TKA/UKA. The numbers of TKA increased from 318 in 2008 to 529 in 2017 year by year, mainly due to OA (Fig.1). The numbers of primary TKA/UKA as cause of RA in 2013-17 more decreased compared to in 2008-12 (0.6), but in case of OA increased (1.3 times, Table 1, $p<0.05$).

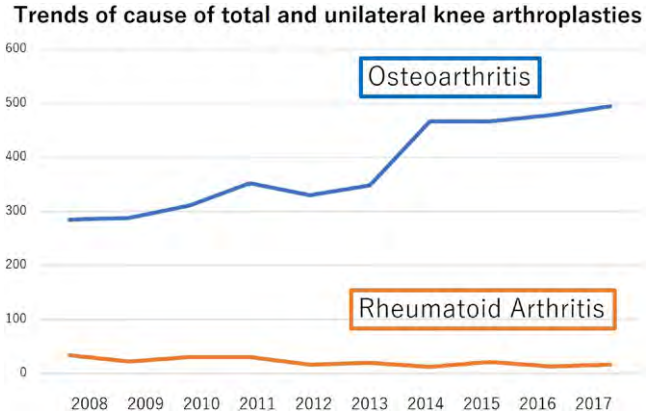


Figure 1.

Table 1.

	2008-12	2013-17	Times
Osteoarthritis	1565	2252*	1.3
Rheumatoid arthritis	131	81*	0.6
Trauma	1	5	5
Osteonecrosis of femoral condylar	20	41*	2.1
Revision	21	39	1.9
Total	1738	2418*	1.4
		* $p< 0.05$	

Conclusion: The number and rate of primary TKA/UKA due to RA decreased year by year because of progression of modern medication therapy. In the other hand, in case of OA increased because of increasing of elderly people affected by knee OA in the super-aging society.

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Disclosure of Interests: None declared

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AB1199 COST-EFFECTIVENESS OF EARLY INITIATION OF ABATACEPT ON JAPANESE RHEUMATOID ARTHRITIS PATIENTS BASED ON THE AMPLE STUDY, USING IORRA REAL WORLD DATA

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disorder leading to disability and reduced quality of life. Effective treatment with biologic disease-modifying antirheumatic drugs (bDMARD) poses a significant economic burden. The

abatacept (ABT) versus adalimumab comparison in biologic-naive RA subjects with background methotrexate (AMPLE) trial[1] was a head-to-head randomized study.
Objectives: To assess the cost-effectiveness (CE) of early initiation of ABT on Japanese RA patients with data from the IORRA database (ID).[2]
Methods: A model based on the AMPLE study was used to estimate the CE of ABT 1st versus ABT 2nd lines in a cohort of 1000 patients based on responses on ACR20/50/70, HAQ-DI, CDAI and SDAI estimated from the real-clinical data of the ID. Unit costs for direct medical costs of adverse events (AEs), proportions of patients with concomitant medications or outpatient/inpatient visits; doses and duration of concomitant medications were taken from the JMDC claims database.[3] Uncertainty was assessed in sensitivity analyses (SA) where cost parameters were tested on their ±30% levels. Results were compared between subgroups using cut-offs of 65-years of age and 1.5 of HAQ, or 5-years of treatment duration. The study used a Japanese healthcare payers' perspective over a 2-year time horizon.
Results: Incremental costs were all in favor of ABT 2nd line with 137 MJPY (1.1 M€, 120 JPY=1 €), 6 MJPY (0.05 M€), 41 MJPY (0.3 M€), 8 MJPY (0.07 M€) and 2.2 MJPY (0.02 M€) for bDMARDs, concomitant medication, AEs, serious AE, and hospitalizations due to infections, respectively. In total, the incremental costs were expected to be 195 MJPY (1.6 M€) higher for ABT as 1st line treatment, but the cost per responding patient and per patient in remission favored ABT 1st line across most response outcomes (Table 1).

Table 1. Total costs per responder and patient in remission per 2-year

	Difference in cost per health gain (ABT first line - ABT second line)
Cost per responding patient (kJPY)	
ACR20	-2,927 (-24 k€)
ACR50	-6,406 (-53 k€)
ACR70	-10,822 (-90 k€)
HAQ-DI	-5,120 (-43 k€)
Cost per patient in remission (kJPY)	
DAS28	828 (7 k€)
CDAI	-7,019 (-58 k€)
SDAI	-5,584 (-47 k€)

ABT=abatacept; ACR20/50/70= 20/50/70% improvement of the American college of rheumatology criteria; HAQ-DI=health assessment questionnaire disability index; DAS28=disease activity score; CDAI=clinical disease activity index; SDAI=simplified disease activity index

SA showed that the cost for bDMARDs drives the difference in healthcare costs between the cohorts (-685 MJPY to 1,074 MJPY). For sub-groups of patients ≥65 years, <65 years, HAQ≥1.5, HAQ <1.5, treatment duration ≥5 years, <5 years the total 2-yearly costs per responder (SDAI remission) were 106 kJPY (0.9 k€), 321 kJPY (2.7 k€), 1,353 kJPY (11.3 k€), 106 kJPY (0.9 k€), 231 kJPY (1.9 k€) and 178 kJPY (1.5 k€) lower for ABT 1st line, respectively.
Conclusion: Savings per responding patient are expected if ABT are prescribed as 1st line versus 2nd or 3rd line treatment, irrespective of age, disease duration and functional impairment level.
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Disclosure of Interests: Eiichi Tanaka Consultant of: ET has received lecture fees or consulting fees from Abbvie, Asahi Kasei pharma co., Bristol Myers Squibb, Chugai Pharmaceutical, Daiichi Sankyo Co., Eisai Pharmaceutical, Janssen Pharmaceutical K.K., Nippon Kayaku, Pfizer, Takeda Pharmaceutical, Taisho Toyama Pharmaceutical Co., and UCB Pharma., Speakers bureau: ET has received lecture fees or consulting fees from Abbvie, Asahi Kasei pharma co., Bristol Myers Squibb, Chugai Pharmaceutical, Daiichi Sankyo Co., Eisai Pharmaceutical, Janssen Pharmaceutical K.K., Nippon Kayaku, Pfizer, Takeda Pharmaceutical, Taisho Toyama Pharmaceutical Co., and UCB Pharma., Eisuke Inoue Speakers bureau: EI has received speaker fee from Bristol-Meyers, Pfizer, Merck serono., Ayako Shoji Consultant of: To conduct this work, Jonas Nilsson Consultant of: To conduct this study, Christos Papagiannopoulos Consultant of: To conduct this study, Dhanda Devender Shareholder of: BMS, Employee of: BMS, Yoshio Anazawa Shareholder of: BMS, Employee of: BMS, Yuri Yoshizawa Shareholder of: BMS, Employee of: BMS, masayoshi harigai Grant/research support from: AbbVie Japan GK, Ayumi Pharmaceutical Co., Bristol Myers Squibb Co., Ltd., Eisai Co., Ltd., Mitsubishi Tanabe Pharma Co., Nippon Kayaku Co., Ltd., and Teijin Pharma Ltd. MH has received speaker's fee from AbbVie Japan GK, Ayumi Pharmaceutical Co., Boehringer Ingelheim Japan, Inc., Bristol Myers Squibb Co., Ltd., Chugai Pharmaceutical Co., Ltd., Eisai Co., Ltd., Eli Lilly Japan K.K., GlaxoSmithKline K.K., Kissei Pharmaceutical Co., Ltd., Oxford Immuotec, Pfizer Japan Inc., and Teijin Pharma Ltd. MH is a consultant for AbbVie, Boehringer-ingelheim, Kissei Pharmaceutical Co., Ltd. and Teijin Pharma.
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AB1200 EARLY ARTHRITIS CLINICS IMPROVES THE EVOLUTION OF THE DISEASE AND DECREASES WORK ABSENTEEISM

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Background: Rheumatoid arthritis is the most common inflammatory arthritis, and a significant cause of morbidity and mortality. Several clinical studies have shown that treatment introduced at an early stage, referred to as a "window of opportunity", is associated with long-term benefits in the form of long-term remission and even complete remission of the disease.
Objectives: Assess the advantages of a Early Arthritis clinic (EAC) in the management of RA until remission is reached and its impact on work absenteeism.
Methods: We included a cohort of patients with early RA (≤12 months symptoms) who fullfield the ACR 2010 criteria, in an early arthritis clinic (EAC) from a tertiary hospital, between 2016-2019, followed for at least 2 years. Demographic, clinical, analytical and radiographic variables were included, and the dates of the visits during the follow-up were noted. Work absenteeism days was recorded before and after the first visit. Estadistic description and regressión analysis was performed.
Results: Eighty-four patients with early RA were included, with loss of follow-up of tweelve patients. Fifty-one (70,8%) were women with a mean age 50 years ±15,84. Fifty-one patients were FR positive (70,8%) and sixty-eigth were ACPA positive (94,4%). Nine subjects (13%) had erosions. Acute phase reactans elevation was observed in fifty-five patients (76,3%). Thirty-seven subjects (51,3%) were smokers. Mean swollen joint count was 4 ± 4,79 and mean DAS28 was 4.01 ± 1.28. Inflammatory arthralgia was reported since mean time 6.7 months before the first visit. Seventy patients (97%) were treated with methotrexate and forty-nine (70%) did not require other treatment during follow-up. Ten patients (14.3%) required DMARDb, and half received 2 or more drugs of this clase. The mean cumulative time of exposure to corticosteroids was 8.37 ±9,26 months. Mean time between the date of derivation to Rheumatologist and the first visit was 44 days. Forty-nine patients (81%) achieved remission during follow-up and mean time required for this goal was 299 days with a mean 4.7 visits. We found a significant correlation between the time to reach remission with DAS28, NAT and Nº treatments prescribed (0.38, 0.39 and 0.70 respectively, p <0.05). Twenty work absenteeism periods (mean 40.55 days) were reported in fourteen patients before the first visit associated with activity of RA, and tweelve periods (mean 19,75 days) in ten patients after the first visit (p <0.05).
Conclusion: In our EAC, patients with RA usually reach remission in less than a year, requiring approximately 4 visits to achieve this goal. A significant correlation was found between the time to reach remission, DAS28 and the number of treatments required. Most patients respond to Methotrexate and suspend corticosteroids in less than a year. We found a significant reduction of work absenteeism associated with RA activity, after the first visit during the follow-up.
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AB1201

INCREASING RATES OF INFLUENZA VACCINATION COVERAGE IN RHEUMATOID ARTHRITIS PATIENTS: DATA FROM A MULTICENTER, LONGITUDINAL COHORT STUDY OF 1,406 PATIENTS

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Background: Despite the increased incidence of influenza infection in rheumatoid arthritis (RA) patients, vaccination coverage has been shown to be suboptimal. Prospective data regarding the current rate and predictors of influenza vaccination adherence in RA patients are limited.

Objectives: To calculate the current rate and predictors of influenza vaccination in a real-life, prospective, longitudinal RA cohort.

Methods: Data regarding demographics, disease characteristics, treatments and co-morbidities from a multi-center, longitudinal cohort of Greek RA patients were collected at baseline and ~ 3 years later. Disease and patient characteristics were compared between patients with at least one influenza vaccine administration and non-vaccinated ones, during the 3 year follow-up period.

Results: From a cohort of 1,569 RA patients, 1,406 with available vaccination data at baseline and 3 years later (mean interval: 2.9 years) were included; (women: 80.4%, mean age: 61.8 years, mean disease duration: 9.7 years, RF and/or anti-CCP positive: 50.4%, mean DAS-28 = 3.33, mean HAQ: 0.44, bDMARD use: 44.8%). At baseline, 54.2% of patients reported influenza vaccination in the past (31.8% during the previous season), while during the 3 year follow-up period, 81% had ≥1 influenza vaccinations (p=<0.001). Patients who received ≥1 influenza vaccine were older (63.5 vs. 54.7 years, p<0.001), were more likely to be seropositive (59.2% vs. 45.2%, p<0.001), had higher HAQ (0.46 vs. 0.36, p=0.02) and BMI (27.7 vs. 26.9, p=0.02) at baseline, more likely to be treated with bDMARDs (46.8% vs. 36.4%, p<0.001) and more likely to have chronic lung disease (9.7% vs. 5.3%, p=0.02), dyslipidemia (36.4% vs. 24.2%, p<0.001), hypertension (46.1% vs. 29.2%, p<0.001) and to report vaccination against influenza the previous season before baseline evaluation (34.9% vs. 18.2%, p<0.001). By multivariate analysis, history of influenza vaccination during the last season before baseline (OR=1.87, CI: 1.27-2.74, p=0.001), bDMARD treatment (OR=1.51, CI: 1.07-2.13, p=0.018) and age (OR=1.05, CI: 1.04-1.06, p<0.001) were independent predictors of influenza vaccination.

Conclusion: In this ongoing, longitudinal, prospective, real-life RA cohort study, a significant increase in the influenza vaccination coverage was noted (from 53% to 81%). Influenza vaccination was independently associated with recent history of influenza vaccination, older age, and bDMARD treatment.

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AB1202

IMPACT OF BIOLOGICAL THERAPY ON WORK ABILITY AND PRODUCTIVITY IN RHEUMATOID ARTHRITIS

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Background:

Objectives: The objective of the study was to determinate the perceived impact of biological therapy on work ability and productivity of RA patients in Republic of Serbia.

Methods: The analysis was based on questionnaires filled by 626 patients treated with biological therapy and 175 patients treated with conventional therapy, as well as on information gathered on four focus groups. Two monetized indicators were used in the study: Work Productivity and Activity Impairment Questionnaire General Health V2.0 (WPAI-GH) and Human Capital Approach (HCA), as well as two non-monetized indicators: Stanford Presenteeism Scale (SPS) and The Health and Work Performance Questionnaire (HPQ). The use of WPAI-GH indicator on gathered data helps calculate the total cost of decreased productivity caused by RA, based on two complementary aspects: absenteeism and presenteeism. The HCA indicator builds on costs measured by WPAI-GH, by providing information on the cost of work disability caused by RA, as the cost that resulted from early retirement of patients. SPS provides the foundation for comparison of subjective feeling regarding the impact of RA on performing work tasks between patients treated with biological therapy and patients treated with conventional therapy, using Mann-Whitney test. HPQ indicator provides the basis for comparison of non-monetized absenteeism and presenteeism, in both absolute and relative terms, between the two groups of patients.

Results: Our results showed that the total cost of lost productivity of working population with RA in Serbia amounts 2.6 billion RSD (22.2 million EUR), while the total cost of work disability is 15.3 billion RSD (130.8 million EUR) per annum. Results of the HPQ analysis showed that the group treatededtd with conventional therapy had been absent from their work three times more frequently, on average, than the patients treated with biological therapy. Also, the group of patients treated with conventional therapy rated their work performance as lower than average – they rated their productivity as 94.21% of average productivity of other employees at the same/similar job, while the group treated with biological therapy rated themselves as equally productive, compared to other employees. SPS analysis details are presented in Table (Mann-Whitney test).

	Biological therapy (Yes/No)	N	Mean Rank	Sum of Ranks	p value (significance level: 0.05)
Despite having my health problem, I was able to finish all tasks in my work.	0	56	113.61	6362.00	0.027
	1	208	137.59	28618.00	
	Total	264			
At work, I was able to focus on achieving my goals despite my health problem.	0	55	110.43	6073.50	0.016
	1	206	136.49	28117.50	
	Total	261			
Despite having my health problem, I felt energetic enough to complete all my work.	0	56	112.64	6308.00	0.03
	1	206	136.63	28145.00	
	Total	262			
Because of my health problem, the stresses of my job were much harder to handle.	0	56	152.51	8540.50	0.01
	1	204	124.46	25389.50	
	Total	260			
My health problem distracted me from taking pleasure in my work.	0	56	161.55	9047.00	0.00
	1	205	122.65	25144.00	
	Total	261			
I felt hopeless about finishing certain work tasks, due to my health problem.	0	56	155.34	8699.00	0.01
	1	208	126.35	26281.00	
	Total	264			

Conclusion: Analysis undoubtedly suggests that RA influences lost productivity costs and work disability. Both work ability and productivity are better when biological therapy is in use, why significant savings would be possible if access to biological therapy could be used at an earlier stage of disease.

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AB1203

INVESTIGATING THE VIEWS OF COMMUNITY PHARMACISTS ON THEIR ROLE IN THE MANAGEMENT OF RHEUMATOID ARTHRITIS

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Background: Medicines optimisation is essential in the long-term management of rheumatoid arthritis (RA), particularly when considering combinations of conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs). Community pharmacists are ideally placed to optimise medicines use including monitoring side effects, counselling on dose and frequency and improving medicines adherence; however, in some countries, such as the UK, there are currently no community pharmacy services that address csDMARD use and little is known about the role community pharmacists play in managing RA as a long-term condition.
Objectives: The objectives of this qualitative study were to understand community pharmacists' views of their training, knowledge and current role in the management of RA.
Methods: We conducted 9 semi-structured, face-to-face or telephone interviews with community pharmacists based in the UK; all were transcribed verbatim. A topic guide, used to inform the interviews, covered four key areas: 1) knowledge and training, 2) pharmacological management 3) patients and services, 4) potential role. The transcriptions were then imported into NVivo for thematic analysis. A coding framework was developed from continual emerging themes and applied to the transcripts.
Results: Five male/4 female participants, the median age was 39 years (range 27 to 42) with a median number of years qualified as a pharmacist of 12 years (range 5 to 20) were included. The participants covered a range of roles including: pharmacist non-manager, pharmacist manager, locum pharmacist, superintendent pharmacist and relief pharmacist.
In assessing the current role of community pharmacists, 4 main themes were identified: (1) access to information about the patient's condition as a barrier, (2) their lack of knowledge in the management of RA, (3) providing practical advice about taking csDMARDs, and (4) exploring the reasons for non-adherence before taking further action. In assessing the potential role of community pharmacists, a further 2 themes were identified: improving access to information about the patient's condition before the current role can be increased and other barriers to an additional role, including time and funding.
In the theme 'access to information as a barrier' the most common point made was about the lack of information available to pharmacists on the individual indication for medicines. Pharmacists said this posed a barrier both to current practice and their potential role. No participants suggested the potential for an additional service specifically for RA, but some suggested that current services could be expanded to include RA as a target group. Participants discussed side effect counselling and ensuring access to medicines in detail with patients, but only 2 briefly mentioned discussing the benefits of csDMARDs.
Conclusion: This is the first in-depth exploration of the perspectives of community pharmacists on the management of RA in community pharmacy. This study has highlighted several important barriers both environmental and personal including time, education and resources that, if addressed, could allow community pharmacists to play a greater role in the management of RA.
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AB1204

COST-EFFECTIVENESS OF ABATACEPT IN SPAIN IN SEROPOSITIVE BIOLOGIC-NAÏVE EARLY RHEUMATOID ARTHRITIS PATIENTS WITH SHARED EPITOPE

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Background: The HLA class II Shared Epitope (SE) is a known Rheumatoid Arthritis (RA) risk allele linked to autoantibody production and disease progression. The recent Early AMPLE study suggests an enhanced treatment benefit of abatacept (ABA) over adalimumab (ADA) in SE positive patients with early seropositive RA.[1] Economic implications beyond the trial follow-up duration are unknown.
Objectives: To estimate the cost-effectiveness of ABA vs ADA in biologic-naive RA patients seropositive for anti-citrullinated protein antibody and rheumatoid factor based on the Early AMPLE study.
Methods: We developed a microsimulation model to estimate clinical response, medical cost, quality of life and survival from a Spanish payer perspective. The model captures the patient's disease and treatment journey using response outcomes and the Health Assessment Questionnaire (HAQ) score. Patients who fail to respond switch to the next treatment line. Six treatment lines are included to capture a lifetime horizon. Responding patients (ACR50 and EULAR response) achieve an improvement in their HAQ score. Patient mortality was modelled as a function of HAQ. For both the overall Early AMPLE population and SE+ patients, incremental monthly cost per response over 2 years and incremental cost per QALY over a lifetime were estimated. Costs were based on local tariffs in Spain.
Results: Baseline characteristics for the Early AMPLE (n=80) and the SE+ (n=61) patients were well balanced between the treatment groups.[2] Compared to ADA, the ABA cohort had a lower cost per response and the difference was more pronounced in the SE+ population, compared to the entire Early AMPLE population for both the response criteria (Table 1). Compared with ADA, the ABA cohort showed greater quality adjusted life years (QALYs) gains, and a modest increase in cost due to a prolonged time on treatment (Table 2). The incremental cost per QALY over a lifetime fell below commonly used thresholds in Spain (25-60 thousand Euros per QALY).[3]

Table 1. Cost per response results

Full Early AMPLE	ACR50		EULAR	
	ABA	ADA	ABA	ADA
Cost per response (€) – 2 years	25,860	40,654	26,993	40,643
Incremental monthly cost per response (€)	-616		-569	
SE positive	ACR 50		EULAR	
	ABA	ADA	ABA	ADA
Cost per response (€) – 2 years	24,272	40,249	25,337	41,425
Incremental monthly cost per response (€)	-666		-670	

All incremental results are for ABA – ADA

Table 2. Cost-effectiveness results (discounted)

Full Early AMPLE	ACR50		EULAR	
	ABA	ADA	ABA	ADA
LYs*	30.14	30.06	30.11	30.03
QALYs	8.32	7.81	7.57	7.12
Time on treatment (years)	4.17	2.03	5.14	3.06
Costs (€)	75,547	68,157	85,122	80,933
Incremental LYs*	0.08		0.08	
Incremental QALYs	0.52		0.45	
Incremental Costs (€)	7,390		4,189	
Incremental cost per QALY (€)	14,308		9,275	
SE positive	ACR50		EULAR	
	ABA	ADA	ABA	ADA
LYs*	30.38	30.22	30.16	30.09
QALYs	8.20	7.59	7.40	6.90
Time on treatment (years)	4.48	2.02	5.38	3.02
Costs (€)	78,113	68,651	87,586	81,321
Incremental LYs*	0.15		0.06	
Incremental QALYs	0.61		0.50	
Incremental Costs (€)	9,462		6,265	
Incremental cost per QALY (€)	15,410		12,503	

*LY results are presented undiscounted. All incremental results are for ABA – ADA

Conclusion: Compared with ADA, ABA is a cost-effective alternative and is associated with a lower 2 years cost per response for both populations. The economic benefit and quality of life gain is greater in a SE+ patient population.
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Epidemiology, risk factors for disease or disease progression

AB1205 PARADOXICAL BIOLOGICS-INDUCED AUTOIMMUNE DISEASES

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Background: Biological therapies have revolutionized the management of rheumatic diseases. This study analyzes the paradoxical autoimmune inflammatory manifestations that these therapies can induce. They are described as paradoxical because these are diseases in which the same biological drugs have proven effective.
Objectives: The aim of this study is to carry out a descriptive analysis of paradoxical biologics-induced autoimmune manifestations.
Methods: A retrospective research was carried out during January 2017 and March 2018 at Hospital Universitario Donostia.
Computerized medical records were reviewed. The following variables were recorded: underlying disease; type of developed manifestation; the triggering biologic drug and its duration; concomitant treatment with disease-modifying antirheumatic drugs (DMARDs), previous biological treatments; the adopted measure and the resolution of the complication or not.
Qualitative variables are recorded in absolute value and in percentage. The quantitative variables are recorded with the mean and standard deviation. The data has been analyzed with the SPSS Statistics 20 program.
Results: Twenty-six cases were analyzed. The most common triggering drugs were infliximab (30.8%), adalimumab (30.8%) and etanercept (15.4%). The most common underlying diseases were spondyloarthritis (42.3%), rheumathoid arthritis (34.6%) and Crohn's disease (11.5%). The most developed complications were cutaneous affectations (76.9%), psoriasis specifically.
Statistical significative difference regarding the molecules causing the complication, has only been found in the previous use of biologic drugs (p 0.003), number of treatment dropouts (p 0.048) and number of resolved complications (regardless of the adopted measure) (p 0.041).
Conclusion: Infliximab and adalimumab are the drugs that presented the most paradoxical manifestations, probably because they are the oldest and most used ones. The difference found in previously used biologics, could be due to the fact that new drugs are less frequently presented as the first option. Psoriasis is the most frequently developed complication. The difference found in the number of abandonments of the biologic treatment and the solution of the complication might be more associated with the complication itself, rather than with the responsible molecule. There is no consensus on the measures to be taken when facing the complication. The severity of the manifestation should be assessed, as well as the control of the underlying disease. Most complications resolve overtime.
Disclosure of Interests: None declared
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AB1206 OCULAR SARCOIDOSIS AND CLUSTERS OF CLINICAL ASSOCIATIONS. STUDY OF A SERIES OF 383 PATIENTS WITH SYSTEMIC SARCOIDOSIS FROM A SINGLE UNIVERSITY HOSPITAL

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Background: Sarcoidosis is an inflammatory disease which can affect multiple organs. The most frequent affected organs are lungs, skin and eyes (1-5). Ocular involvement is a severe complication.
Objectives: To assess the association of ocular sarcoidosis with other clinical domains.
Methods: Study of a large cohort of systemic sarcoidosis from a single tertiary university hospital. All consecutive patients were diagnosed with systemic sarcoidosis from January 1, 1999 to January 1, 2019 according the ATS/ERS/WASOG criteria (6).
Results: 41 (22 women/19 men) of 383 (10.7%) patients had ocular involvement, mean age 44.8±16 years. Lung was the most common affected organ associated with ocular sarcoidosis (n=36; 87.8%) followed by skin (n=14; 34.1%), joints (n=12; 29.3%) and neurological affection (n=8; 19.5%).
Ocular sarcoidosis presents a higher percentage of renal and neurological affection compared to organs affected in general sarcoidosis of our larger cohort (12% vs 6% and 19.5 vs 7%; respectively) (FIGURE).
Conclusion: The proportion of clinical domains affected in ocular sarcoidosis is mostly similar to global sarcoidosis, except the neurological (which almost is threefold) and renal (which doubles) affection. Hence, the importance of being aware of neurological and renal complications when ocular affection is present.
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Table 1

	Infliximab n 8 (31.8%)	Adalimumab n 8 (30.8%)	Etanercept n 4 (15.4%)	Certolizumab n 2 (7.7%)	Golimumab n 2 (7.7%)	Abatacept n 1 (3.8%)	Tocilizumab n 1 (3.8%)	Total n 26 (100.0%)	p value
Underlying disease									0.789
Rheumatic (%)	6 (75.0)	5 (62.5)	4 (100.0)	2 (100.0)	2 (100.0)	1 (100.0)	1 (100.0)	21 (80.0)	
Digestive (%)	2 (25.0)	3 (37.5)	0	0	0	0	0	5 (19.2)	
Type of developed manifestation									0.235
Hematologic (%)	0	1 (12.5)	0	0	0	0	0	1 (3.8)	
Neurologic (%)	2 (25.0)	0	0	0	0	0	0	2 (7.7)	
Digestive (%)	0	0	0	0	1 (50.0)	0	0	1 (3.8)	
Cutaneous (%)	6 (75.0)	6 (75.0)	4 (100.0)	2 (100.0)	1 (50.0)	0	1 (100.0)	20 (76.9)	
Other (%)	0	1 (12.5)	0	0	0	1 (100.0)	0	2 (7.7)	

Table 2

	Infliximab n 8	Adalimumab n 8	Etanercept n 4	Certolizumab n 2	Golimumab n 2	Abatacept n 1	Tocilizumab n 1	Total n 2	p value
The triggering biologic drug and its duration (months)	43.25 (SD 44.81)	10.93	75.50 (SD 66.08)	4.50	11.00	6.00	5.00	30.66	0.635
Concomitant treatment with DMARDs (%)	2 (25.0)	2 (25.0)	1 (25.0)	1 (50.0)	0	0	1 (100.0)	7 (26.9)	0.811
Previous biological treatment (%)	0	2 (25.0)	1 (25.0)	2 (100.0)	2 (100.0)	1 (100.0)	1 (100.0)	9 (34.6)	0.003
Suspension as the adopted measure (%)	5 (62.5)	7 (87.5)	0	2 (100.0)	1 (50.0)	1 (100.0)	1 (100.0)	17 (65.4)	0.048
Resolution of the complication (%)	3 (37.5)	8 (100.0)	1 (25.0)	1 (50.0)	1 (50.0)	1 (100.0)	1 (100.0)	16 (64.0)	0.041

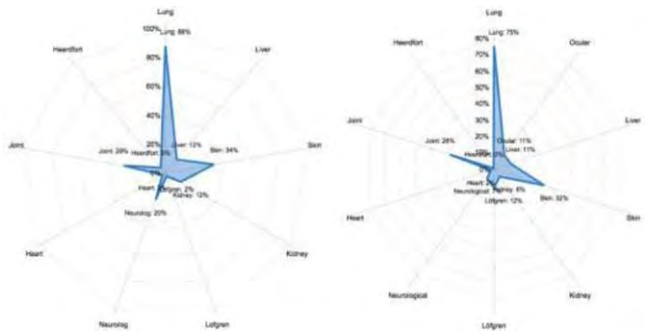


FIGURE. Comparison between distribution of organs affected in ocular sarcoidosis (left) and distribution of organs affected in general sarcoidosis (right)

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AB1207 EFFECT ON DIET MODIFICATION ON GOUT AND METABOLIC SYNDROME RISK FACTORS

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Background: Gout is the most prevalent inflammatory arthritis globally. Despite treatment advances, the prevalence of gout has continued to increase over the last several decades. There has also been increasing evidence that gout has a strong association with the metabolic syndrome. This indicates that gout is likely both an inflammatory and a metabolic disease that has a significant effect on quality of life and healthcare costs. Although current recommendations support aggressive medical therapy for gout treatment, dietary counseling is less emphasized. We hypothesize that emphasis on this nonpharmacological therapy will likely improve management and the metabolic syndrome in gout patients.

Objectives: To analyze the effectiveness of dietary counseling on gout management and risk factors for metabolic syndrome in gout patients at the Veteran's Affairs Medical Center in Long Beach, CA (VALB).

Methods: A retrospective cohort study was created from 2009-2016 involving Long Beach Veterans Affairs Hospital gout patients (n= 119) based on International Classification of Disease version 9 or 10. Patients were then stratified into two cohorts: received diet counseling (n=90) and no diet counseling (n=29). Data was reviewed for 24 months following initial gout diagnosis or intervention. Management was evaluated based on frequency of flares and related ED visits, change in creatinine clearance, serum uric acid levels (sUA), and changes to risk factors for metabolic syndrome including blood pressure, body mass index (BMI), cholesterol panel and hemoglobin A1c levels at six-month intervals.

Results: Although patients in both cohorts were noted to have decreased number of gout attacks, patients who received diet counseling had a significant decrease in number of gout attacks by month 12 (0=0.004). In addition, after 6 months, patients who received diet counseling were more likely to have sUA at goal (sUA<6 for nontophaeous gout and sUA<5 for tophaceous gout) (p=0.003). These patients were also noted to have improved creatinine clearance (p=0.08) and increased HDL (p =0.08). In addition, patients with improved HDL and LDL values more likely to have improved sUA levels and decreased ED visits (R^2=0.4, slope 0.14 and R^2=0.4, slope 0.05, respectively) by month 6. Patients with improved hemoglobin A1c levels were also noted to have a significant outcome in lowering serum uric acid level at month 18 (R^2=0.9, slope 2.6).

Conclusion: Gout patients who receive diet counseling had lower rate of future attacks and better control of sUA. In addition, these gout patients were also noted to have improvement in some risk factors associated with the metabolic syndrome. Notably, patients who had better control of their hemoglobin A1c levels were able to have lower serum uric acid levels. This may imply that controlling diabetes in patients may also help improve gout management. Given the serious complications and increased cardiovascular risks that can be associated with metabolic syndrome, optimization of gout through a nonpharmacologic intervention such as diet counseling can enhance clinical outcomes and optimize healthcare resources.

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AB1208 ADHERENCE TO TREATMENT AND DISEASE ACTIVITY ON RHEUMATOID ARTHRITIS

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Background: For treating Rheumatoid Arthritis (RA) it's clear that Treat to Target has presented the best strategy. The best outcome for patients has been attained by accepting clinical remission as the final objective in treatment. The development of new drugs for the treatment of RA has dramatically modified the approach clinicians have on the disease, however, the treatment of inflammatory conditions represents a challenge due to the multiple factors can affect its response.

It is known that non-adherence represents an increase in mortality, morbidity and healthcare costs.[1,2] Emphasis should be made on one of the most simple and effective variables that impact the effectiveness of treatment: adherence to treatment itself.

Objectives: This work aimed to evaluate the impact of methotrexate adherence on treatment outcome in patients with RA.

Methods: An observational, cross sectional study was performed using medical records from the Rheumatology Clinic at University Hospital from UANL Jose Eleuterio Gonzalez, Monterrey, México; the data was collected from 03/16/2018 to 01/29/2020. RA patients visits included fulfilled the 2010 ACR/EULAR classification, had their disease activity measured by Disease Activity Score 28 ESR (DAS28 ESR) and were treated with methotrexate as their primary disease modifying antirheumatic-drug (DMRAD). Patient disease activity was classified in 4 groups according to the DAS28 ESR score as <2.6 remission, 2.6-3.2 low activity, >3.2-5.1 moderate activity, >5.1 high activity.

Adherence to medication was evaluated utilizing a self-reported assessment that was applied per patient's visit. Patients were classified into 4 groups according to the percentage of the prescribed doses of Methotrexate that they abided to. Statistical analysis was performed using IBM SPSS 21 statistical package. Descriptive analyses were performed with frequencies (%) and the correlation between the calculated disease activity versus patient adherence to treatment was calculated using Pearson correlation coefficient. *P*-values <0.05 were considered statistically significant.

Results: A total of 795 patients visits were included. They were 92.33% female, mean (SD) age was 52.44 (±12.99) (Table 1). The most frequent routes for methotrexate were Oral 603 (75.84%), Subcutaneous 113 (14.21%) and Intramuscular 79 (9.93%). A significant correlation *r* (795) =0.-183, (*p*<0.001) was found between Disease Activity according to DAS28 ESR and Adherence classification according to prescribed doses taken

Table 1. Baseline Characteristics

	N= 795
Age, mean SD	52.44 (±12.99)
Sex, n (%)	
Female	734
Male	61
Methotrexate (mg/week)	
Average Dose	19.94
Median Dose	20
Intramuscular	79 (9.93%)
Subcutaneous	113 (14.21%)
Oral	603 (75.84%)
Disease Activity according to DAS28 ESR, n (%)	
Remission	343 (42.3)
Low activity	101 (12.5)
Moderate activity	292 (36.0)
High activity	59 (7.3)
Adherence classification according to prescribed doses taken, n (%)	
Absent (<25%)	20 (2.5%)
Poor (25-49%)	19 (2.3%)
Regular (50-74%)	55 (6.8%)
Adequate (>75%)	701 (86.5%)

Conclusion: Adherence to treatment with methotrexate therapy has a direct impact on RA treatment outcome. The evaluation of adherence to the prescribed treatment should be addressed before modifications in DMRAD therapy in patients with Rheumatoid Arthritis. Before considering treatment failure in a patient treated with methotrexate, adherence to treatment must be evaluated.

According to our results, self-reported adherence appears to be a cost and time effective method to care for patients.

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AB1209 A SYSTEMATIC REVIEW ON THE EFFECT OF DMARDS ON FERTILITY IN RHEUMATOID ARTHRITIS

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Background: Patients with rheumatoid arthritis (RA) seem to experience a diminished fertility. Reasons for this lowered fertility are insufficiently defined and probably multifactorial. Although the effect of DMARDs on pregnancy outcomes have been studied, there is a lack of data on the effect of DMARDs on the fertility of patients with RA.

Objectives: To evaluate all studies that concern an effect of DMARDs on the fertility of men and women with RA in a systematic review.

Methods: A search was conducted at 18/10/2019 in three databases including Embase, Pubmed (Medline) and Web Of Science with specific search strings for each database, constructed with the help from a health sciences librarian. We included studies involving women or men diagnosed with RA, of fertile age (18-45years) and on a DMARD therapy, with as outcome a fertility parameter. Systematic reviews, meta-analyses, case reports, case series and animal studies were excluded. Studies not in English or Dutch or written more than 15 years ago were excluded. Article selection was firstly based on title/abstract (double blind, two researchers, LB and IS) and then full text (two researchers, LB and IS). In case consensus could not be reached, a third researcher (DDC) was consulted. The references of included articles were reviewed ("snowballing") to include and minimize the missing articles. A quality check of the included full text papers was performed using the CASP Appraisal Checklists. A chart was made based on outcomes of interest.

Results: After duplicate removal, 9030 articles were found. After title/abstract screening, 82 articles remained. After full text screening, 4 articles could be retained. No additional studies were found through snowballing. Only studies about women could be included, as the evidence found for men was all in papers with exclusion criteria for our systematic review (e.g. case reports). Table 1 summarizes these papers. The included studies investigated the following DMARDs: methotrexate (MTX), certolizumab pegol (CZP), etanercept (ETN) and sulfasalazine (SSZ). No detrimental effects of these DMARDs on fertility, defined as time-to-pregnancy (TTP), anti-Müllerian hormone serum level or presence of a history of infertility, were reported.

Conclusion: This systematic review underlines the knowledge gap on the effect of DMARDs on fertility in human studies. Only 4 studies on women, and no studies on men were found. In the 4 included studies, DMARD treatment, even with MTX in contrast to general belief, had no harmful effect on fertility, probably because disease activity was better controlled with DMARD therapy. However, effects of other RA medication such as NSAIDs were excluded. More research is needed to improve guidance for patients with RA with a child wish.

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AB1210 THE IMPACT OF EXAMINATION STRESS ON AUTOIMMUNE DISEASES AMONG UNIVERSITY STUDENTS

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Background: Stress is a risk factor of various diseases including autoimmune diseases. Autoimmune diseases are one of the leading causes of morbidity in young adults. (1) Examination stress is a main concern nowadays due to the study style, lack of preparation, doctor- student relationship and family pressure. (2) The previous studies declared that stress may causes neuroendocrinal changes leading to immune dysregulations and cytokines production. (3)

Objectives: The aim of study is to scope the light on the importance of stress as a predisposing factor in autoimmune disease flares particularly Examination stress.

Methods: A three-year (2017-2019) cross-sectional prospective study conducted on 1365 students who presented to the Alexandria University rheumatology clinic during examinations. Clinical assessments, routine investigations, activity markers, activity indices, stress and anxiety questionnaires and perceived stress scale (PSS) were applied to all patients during consecutive visits.

Results: Through 5800 visits in three years during examination sessions, patients age ranged from (17 -25) years with 76% females and 24% males. They grouped into SLE (31.35%), Rheumatoid arthritis (RA) (37.28%), Fibromyalgia (13.91%), FMF (2.63%), Ankylosing Spondylitis (1.75%), Psoriatic arthritis (0.73%), systemic sclerosis (0.58%), and undifferentiated connective tissue (11.73%). According to SLE patients, 43.92% were newly diagnosed whilst 54.16% of previously diagnosed SLE presented with Flare in particular lupus nephritis (56.33%), arthritis (43.22%), hematological (49.76%) and serositis (21.36%). Interestingly, RA patients who newly diagnosed were 35.16% of total RA patients while 42.42% of previously diagnosed RA patients presented with moderate and high DAS-28 due to incompliance with treatment in (64.37%) of patients, (11.53% on biological, 88.47% on conventional treatment). In addition, (49.36%) of FMF presented in recent attacks. It was also found that Arthralgia, bone aches and sleep deprivation are the main complaints. Concerning, A High perceived stress scale (PSS) was associated with High DAS28 and SLEDI-2K scores. (r_s= 0.723, 0.865) (P<0.001)

Conclusion: Examination stress is one of triggering factor for autoimmune disease flares. It is associated with high disease activities and ruthless outcomes.

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AB1211 IMMUNE-RELATED ADVERSE EVENTS IN PATIENTS RECEIVING PD-1/PD-L1 INHIBITORS: PRELIMINARY RESULTS FROM A PROSPECTIVE COHORT STUDY

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Table 1. Characteristics of studies included in the systematic review

Authors	Location	Sample	DMARD	Outcome	Method	Design	Result
Akintayo et al. 2018	Nigeria	50 women with RA and 50 women without RA	MTX	Infertility or history of infertility	Interviewer-administered questionnaire	Retrospective study	MTX was associated with a negative history of infertility
Shimada et al. 2019	Japan	25 pregnancies in 19 patients with RA	CZP and ETN	TTP (time to pregnancy)	medical records	Retrospective study	bDMARD treatment shortened the TTP
Brouwer et al. 2013	The Netherlands	72 women with recent-onset RA compared to 509 healthy women	MTX	Level of serum AMH	medical records, serum samples (2 time points)	Retrospective study	AMH levels were not lower with MTX.
Brouwer et al. 2014	The Netherlands	245 women with RA	MTX and SSZ	TTP	Questionnaires and interviews	Prospective cohort study	MTX and SSZ did not prolong TTP

RA = Rheumatoid Arthritis; MTX = Methotrexate; TNFi = Tumor Necrosis Factor inhibitor; CZP = Certolizumab pegol; ETN = Etanercept; SSZ = Sulfasalazine; TTP = Time to Pregnancy; DMARD = Disease Modifying Antirheumatic Drug; AMH = Anti-Müllerian hormone

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Background: Recent introduction of immune checkpoint inhibitors (ICIs) revolutionized oncological guidelines. Immune-related adverse events (IrAEs) may occur in as many as 85% of patients (10% with toxicity grade 3/4), but detailed epidemiology of irAEs is still lacking, mostly because of data collection and analysis vary widely.
Objectives: The purpose of our study is to establish a prospective cohort of patients treated with PD-1/PD-L1 inhibitors in order to determine incidence, risk factors and characteristics of irAEs in a real-world setting.
Methods: We conducted a prospective cohort study enrolling patients receiving anti-PD-1/PD-L1 agents for the treatment of metastatic or locally advanced non-small cell lung cancer, renal cell carcinoma, squamous cell carcinoma of the head and neck, Hodgkin lymphoma. Detailed recommendations have been implemented for cases fulfilling criteria for suspected irAEs, including procedures for evaluation and diagnosis, specific treatments and rules for drug discontinuation. IrAEs have been defined and graded according to Common Terminology Criteria for Adverse Events vs 5.0. Management strategies have been adapted by a multidisciplinary panel, basing on the oncological guidelines, which represent the current best clinical practice. AEs screening, physical examination, ECG and clinical laboratory evaluation have been performed at baseline visit and follow up (4, 8, 12 weeks).
Results: Fifty-two patients have been enrolled from Jan 2019 to Dec 2020. Characteristics are reported in the Table below. Twelve patients developed irAEs (23%), 6 treated with nivolumab, 4 with pembrolizumab, 1 with atezolizumab and 1 with durvalumab. Mild-to-moderate (G1-G2) irAEs were hepatitis, hypothyroidism, III-V-VII cranial nerve palsy, polymyalgia-like syndrome, skin psoriasis and type-1 diabetes mellitus. Severe cases (G3) of bullous dermatitis, Lichen Planus, interstitial pneumonia and myositis occurred. One patient developed three different irAEs. Median time of onset was 4.5 weeks. IrAEs were successfully treated according to established guideline, but 4 patients stopped anti-neoplastic therapy due to irAEs and 11 for disease progression. Five patients died.
Conclusion: Cancer patients receiving PD-1/PD-L1 agents are being prospectively followed. Preliminary results confirm that 1/4 patients may develop irAEs. Innovative tools are required in order to manage irAEs, prevent potential relapse and avoid useless interruption of therapy. Further research needs to get insights into pathophysiological mechanisms and risk factors.
References:

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Characteristics	N = 52
Age [years, median (range)]	67 (31-92)
Gender (F/M)	17/35
Cancer type	
Melanoma	12
Renal cell carcinoma	9
Non-small-cell lung carcinoma Hodgkin	29
lymphoma	1
Head-neck cancer	1
Agents	
Nivolumab	24
Pembrolizumab	16
Atezolizumab	8
Durvalumab	4
irAEs	**12 pts (23%)***
G1	4
G2	6
G3	4
G4	0
Drug discontinuation	**20 (39%)**
due to irAEs	4
due to disease progression	11
death	5

*one patient had more than one event

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AB1212

PREVALENCE OF CAROTID SUBCLINICAL ATHEROSCLEROSIS IN PATIENTS WITH PSORIATIC ARTHRITIS VS RHEUMATOID ARTHRITIS: A CASE CONTROL STUDY

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Background: Rheumatic diseases such as Psoriatic Arthritis (PsA) and Rheumatoid Arthritis (RA) are associated with increased morbidity and mortality, mainly due to cardiovascular causes. Cardiovascular outcomes in patients with PsA and RA cannot be completely explained by traditional cardiovascular risk factors, suggesting that the systemic inflammation that characterizes these diseases may have an important role on accelerated atherosclerosis.[1]
Objectives: To compare carotid intima-media thickness (cIMT) and asymptomatic carotid plaque (CP) prevalence, between patients with PsA, RA and controls.
Methods: Cross-sectional observational study. Seventy patients, aged 35-75 years, with PsA and RA who fulfilled the CASPAR and ACR/EULAR 2010 classification criteria, respectively, who were active on a cardio-rheuma preventive clinic were recruited, matched with 70 healthy controls. All groups underwent a noninvasive examination using B-mode ultrasonography of the right and left common carotid artery. CP was defined as a focal narrowing ≥0.5 mm of the surrounding lumen or cIMT ≥1.2 mm; hyperplasia of the carotid intima was defined as cIMT ≥ 0.9 mm to 1.1 mm. Descriptive data were analyzed by continuous and categorical variables. Continuous variables with normal distribution are shown as mean ± standard deviation (SD), and non-normal distribution as median and quartiles (25q-75q). ANOVA, Kruskal Wallis, X^2 and Mann-Whitney U were used to compared data. A p value ≤0.05 was considered statistically significant. Statistical analysis was done using SPSS version 24 (IBM Corp., Armonk, NY, USA).
Results: Clinical and demographic characteristics are shown in Table 1. The global prevalence of carotid atherosclerosis was 25.7% and 38.6% in RA and PsA respectively, and 27.1% in controls (p=0.170). Intimal hyperplasia was found in 20%, 12.9% and 0% in RA, PsA and controls (p=0.001), respectively (Table 2).

Table 1. Clinical and demographic characteristics

	RA n=70	PsA n=70	Controls n=70	*P* value
Gender				
Male	9 (12.9%)	31 (44.4%)	11 (15.7%)	**<0.001**
Female	61 (87.1%)	39 (55.7%)	59 (84.3%)	
Age, years	54.51±9.657	53.1±10.87	53.54±7.48	NS
Body Mass Index, BMI, kg/m^2	28.99 (25.95-32.34)	29.04 (26.23-31.92)	27.44 (24.98-30.95)	NS
Comorbidities				
Diabetes Mellitus	11 (15.7%)	14 (20%)	8 (11.4%)	NS
Hypertension	24 (34.3%)	27 (38.6%)	15 (21.4%)	NS
Dyslipidemia	19 (27.1%)	30 (42.9%)	18 (25.7%)	NS
Active smoker	7 (10%)	16 (22.9%)	15 (21.4%)	NS
Disease duration				
Duration, years	8.45 (3.34-15.88)	5 (2.75-8)	-	**0.005**
Statins	9 (12.9%)	12 (17.1%)	10 (14.3%)	NS

Table 2. Ultrasonographic characteristics

	RA n=70	PsA n=70	Controls n=70	*P* value
Right CIMT, mm	0.8 (0.6-1.1)	0.6 (0.5-0.9)	0.6 (0.5-0.8)	**<0.001**
Left CIMT, mm	0.8 (0.6-0.9)	0.6 (0.5-0.7)	0.6 (0.5-1.2)	**0.002**
Any Hyperplasia	14 (20%)	9 (12.9%)	0	**0.001**
Right intimal hyperplasia	7 (10%)	5 (7.1%)	0	**0.021**
Left intimal hyperplasia	13 (18.6%)	2 (2.9%)	0	**<0.001**
Any plaque	18 (25.7%)	27 (38.6%)	19 (27.1%)	NS

Conclusion: This study shows the high prevalence of asymptomatic atherosclerosis in RA and PsA compared to general population. Even though it was shown a higher prevalence of CP in PsA, subclinical atherosclerosis in RA patients may have an increased clinical significance. The presence of carotid plaque between groups was not statistically significant. We observed increased prevalence of carotid intimal hyperplasia in RA and PsA compared with age-matched controls. We emphasize the value of ultrasonography in the detection of early atherosclerosis lesions.
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AB1213 DIFFERENT IMMUNOSUPPRESSIVE REGIMENS WITH NO EFFECT ON INFLUENZA-LIKE ILLNESS

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Background: Autoimmune disease (AID) has been associated with increased risk of influenza and influenza-like illness (ILI) and its worse clinical outcomes complications.
Objectives: We aimed to assess the influence and difference of several immunosuppressive (IS) treatments in the incidence of ILI, including glucocorticoids (GC), classic DMARDs and biologic DMARDs.
Methods: We conducted a cross-sectional study in two autoimmune clinics. Patients were invited to answer a survey reporting ILI symptoms between October 2017 and March 2018. ILI definition was considered according to the European Center for Disease Control. Data regarding current IS, diagnostic, disease activity, comorbidities, and vaccination coverage were collected from electronic registry. Patients with history of cancer, HIV, IGIV treatment, or lack of information were excluded. Univariate and multivariate logistic regression analysis were used to access predictors of ILI.
Results: We included 109 patients, with mean age 51 years and 81% female gender. The majority of patients had autoimmune arthropathy (n=54) or a connective tissue disease (n=44). Active disease was present in in 39% of patients. IS treatment was: GC 31%, classic DMARD 44%, biologic DMARD 28%. Vaccine coverage was 51%. Overall 41% reported ILI. We did not find any association between studied variables and ILI, including univariate and multivariate analysis. Univariate odds ratio calculation for IS treatment were: GC [OR 1,68 IC 0,7-3,8], classic DMARD [OR 1,03 IC 0,5-2,2], and biologic DMARD [OR 0,86 IC 0,4-2,0]. Comorbidity of pulmonary disease (n=8) may contribute to higher risk to ILI [OR 2,76 IC 0,8-10,0].
Conclusion: There was no difference in risk of ILI within different IS treatment regimens, although GC may increase the risk. The study is limited by the subjectivity of the ILI survey and the small size of the sample. The stratification of influenza risk will help in designing better vaccine coverage strategies in this population.

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AB1214 EPIDEMIOLOGY OF UVEITIS IN A SPANISH REGION: PREVALENCE AND ETIOLOGY, UVECAM PROJECT

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Background: Epidemiologic studies about the distribution of the various types of uveitis and their etiology are important in helping the clinician to investigate, diagnose, and manage these pathologies. Approximating prevalence of uveitis is an important public health challenge, though studies on this purpose are scarce and of low quality. Therefore it is difficult to estimate accurately the impact of this disease in our days.
Objectives: To estimate the prevalence of uveitis and to describe its etiologic and anatomical pattern by means of a population study carried out in a Spanish region
Methods: A cross-sectional descriptive, population-based, and multicentre study was conducted. The selection criteria consisted of having a diagnosis of uveitis. All data were collected from existing information in medical records. The clinical information was collected prospectively in all cases with a diagnosis of uveitis regardless its aetiology in the participating centres from the date of the study and during the following year. All patients underwent a complete ophthalmological examination with assessment of visual acuity, biomicroscopy, applanation tonometry and indirect funduscopy.
Results: The target population was the 687,892 inhabitants of the province of Toledo (Spain). During the study 389 cases of uveitis were registered. The prevalence was 58.7 (95% CI 53.0-64.9). The mean age was 47.0±20.6 years, and 57.8% were women. The most prevalent anatomical pattern was the anterior uveitis (54.2; 95%CI 48.1-60.8). For adults, idiopathic constitute the group with the highest prevalence (31.7; 95%CI 27.1-36.9), and in children autoimmune etiology was the most frequent (10.6; 95%CI 5.8-17.7).
The proportion of cases with autoimmune etiology was 23.3% in adults and 46.7% in children, with overall prevalences of 15.8 x10^5 and 10.6 x10^5, respectively. Estimates were higher in women than in men, both in adults (17.8 vs. 4.4) and in children (17.1 vs. 13.3). In paediatric population the autoimmune processes most frequently responsible for uveitis are juvenile idiopathic arthritis (JIA; 64.3%) and ankylosing spondylitis (AS; 14.3%), with prevalence's estimates of 6.8 and 4.5 x10^5, respectively. In adults, the most common cause was AS (43.2%; 6.6 x10^5), followed by sarcoidosis (10.7%; 1.7 x10^5), other spondyloarthritis (SpA) (8.3%; 1.3 x10^5), psoriasis arthritis and Behçet's disease (7.1%; 1.1 x10^5 in both cases).
Conclusion: It is a precise population study that analyzes uveitis in a Spanish region, analyzing in detail different etiologies and anatomical patterns. The most common causes were idiopathic. Among the autoimmune causes, AS was the most common.

Table. Overall number and global prevalence by age and sex

	Sample size N (%)	Cases of uveitis N (%)	Prevalence (95% CI) (X 100.000)
TOTAL	662319	389	58.7 (53.0-64.9)
Population (N=389)			
•Paediatrics	132464	31 (8.0)	23.4 (15.9-33.2)
•Adults	529855	358 (92.0)	67.6 (60.7-74.9)
Sex (N=377)			
•Men	337783	159 (42.2)	47.1 (40.0-55.0)
•Women	324536	218 (57.8)	67.2 (58.5-76.7)
Age groups in adults (N=358)			
•18-30	90075	55 (15.4)	61.1 (46.0-77.5)
•31-44	148359	94 (26.3)	63.4 (51.2-77.5)
•45-54	100672	78 (21.8)	77.5 (61.2-96.7)
•55-64	74180	50 (14.0)	67.4 (50.0-88.9)
•≥65	116568	81 (22.6)	69.5 (55.2-86.4)

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AB1215 EPIDEMIOLOGY AND CLINICAL PHENOTYPE OF BEHÇET'S DISEASE IN A WELL-DEFINED POPULATION OF NORTHERN SPAIN

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Background: Considerable epidemiological variations in prevalence of Behçet's disease (BD) have been reported. These disparities may either reflect geographical differences, methodological artifacts, changes over time or random fluctuations. In Spain, published BD's epidemiological studies are scarce.
Objectives: To study epidemiological and clinical domains of BD in a well-defined population of Northern Spain, as well as, to compare results with other regions.
Methods: We included all consecutive 111 patients, diagnosed of definitive or possible BD by expert rheumatologists between 1980 and 2019. Two Classification criteria were applied: a) International Study Group (ISG) for BD *(Lancet. 1990; 335:1078-80)*, and b) International Criteria for BD (ICBD) *(J Eur Acad Dermatol Venereol. 2014; 28:338-47)*. In addition, a literature review of Medline publications was carried out.
Results: In our study, prevalence was higher than in most European populations regardless of the diagnostic criteria applied. Incidence was low (expert opinion: 0.021, ICBD: 0.016, ISG: 0.012). Mean age at onset (36.8±13.2) and gender distribution (55.9% females) were similar to other countries. Pathergy test was performed in 9% of patients giving low results (25.2%). Clinical domains' frequency was in line with other regions except vascular and gastrointestinal involvement, which were lower. (**TABLE**)
Conclusion: BD's prevalence in Northern Spain is higher than in most European populations. These differences likely reflect a combination of true geographic variation, methodological artifacts as well as the easy access to Public Health System and its efficiency. In contrast, clinical phenotypes are similar to other regions.
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AB1216

INTERSTITIAL PNEUMONIA WITH AUTOIMMUNE FEATURES (IPAF): A SINGLE CENTER, PROSPECTIVE STUDY

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Background: Interstitial pneumonia with autoimmune features (IPAF)[1] describes a group of patients with interstitial lung disease and autoimmune features who do not meet the classification criteria for a specific connective tissue disease. Limited data regarding IPAF are available so far.
Objectives: To identify the epidemiological and clinical characteristics of patients with IPAF and to observe disease progression, response to treatment and frequency of infections in 1-year follow-up period.
Methods: Thirty-nine patients from 'Attikon' University Hospital of Athens fulfilling the IPAF criteria were enrolled. Clinical and laboratory findings, comorbidities,

TABLE

	Diagnostic criteria and study period	n cases / population size	Mean age at onset and sex (%females)	Prevalence (over 100000) / incidence	Oral / genital ulcers (%)	Skin lessions/ pathergy test (%)	Ocular involvement (%)	Joint involvement (%)	Neurobehcet/ Vascular/ Gastrointestinal involvement (%)
Herrero, A et al. Southern Europe (Cantabria, Spain)	Expert opinion, ISG, ICBD / 1980-2019	111 (expert opinion) / 86 (ICBD) / 65 (ISG) / 581078	36.8±13.2/ 55.9	19.1 (expert opinion), 14.8 (ICBD), 11.2 (ISG) / 0.021 (expert opinion), 0.016 (ICBD), 0.012 (ISG)	99 / 53.1	68.4 / 25. 2	35.1	68.5	18 / 10 / 4.5
Calamia, K. T. et al. North America (Minnesota, USA)	ISG / 1960-2005	13 / NR	31 / 30	5.2 / 0.38	100 / 62	85 / NR	62	46	23 / 23 / NR
Altenburg, A. et al. Northern Europe (Berlin, Germany)	ISG and ABD classification tree / 1961-2005	590 / 3391344	26 / 58	4.9 / 1 (estimated)	98.5 / 63.7	62.5 / 33.7	58.1	53	10.9 / 22.7 / 11.6
Mohammad, A. et al. Northern Europe (Skane County, Sweden)	ISG / 1997-2010	40 / 809317	30.5 / 33	4.9 / 0.2	100 / 80	88 / NR	53	40	0 / 20 / NR
Mahr, A. et al. Southern Europe (Seine-Saint-Denis County, France)	ISG / 2003	79 / 1094412	27.6 / 43	7.1 / NR	100 / 80	90 / 20	51	59	10 / NR / 10
Salvarani, C. et al. Southern Europe (Reggio Emilia, Italy)	ISG, 1988-2005	18 / 486961	33 / 50	3.7 / 0.24	100 / 78	100 / NR	56	50	11 / 6 / NR
Azizlerli, G. et al. Middle East (Istambul, Turkey)	ISG / prevalence study	101 / 23986	NR / 48.5	42 / NR	100 / 70.2	Not globally reported / 69.3	27.7	Not globally reported	NR / Not globally reported / NR
Davatchi, F. et al. Middle East (Iran nationwide)	Expert opinion / 1975-2018	7641 / NR	25.6 / 44.2	80 / NR	97.5 / 64.4	62.2 / 50.4	55.6	38.1	3.9 / 8.9 / 6.8
Krause, I. et al. Middle East (Galilee, Israel)	ISG / 15 years (not specific years have been reported)	112 / 737000	30.6 / 47	15.2 / NR	NR / 68	41 / 44.4	58	70	11.6 / Not globally reported / NR
Nishiyama, M. et al. Asia (Japan nationwide)	1987 JCBD / 1991	3316 / NR	35.7 / 50.6	NR / NR	98.2 / 73.2	87.1 / 43.8	69.1	56.9	11 / 8.9 / 15.5

medications, pulmonary outcomes assessed with repeated pulmonary function tests (PFTs) and chest HRCT and complications in a 1-year follow-up period were documented for each patient. Univariate models were performed in order to identify determinants of infection and clinically significant difference in PFTs (defined as change of ≥ 10% in FVC and/or ≥ 15% in DLCO).

Results: The mean age at the time of IPAF diagnosis was 63.2 (±11) years and 62% of the patients were female. The most common clinical features included in the IPAF criteria were arthritis (82%) and Raynaud's phenomenon (26%). A morbilliform and/or polymorphic rash of the face, neck and extremities (not included in the IPAF criteria) was noted in 54% of patients. ANA (59%) and anti–Ro (21%) were the most common auto-antibodies. Non-specific Interstitial Pneumonia (NSIP) was the most prevalent radiological pattern (61.5%) as shown in table 1. Treatment comprised corticosteroids and immunosuppressants including hydroxychloroquine, methotrexate, azathioprine, mycophenolate and cyclophosphamide. PFTs following treatment at 6 and 12 months from baseline showed a trend of improvement (Table 2, p> 0.05). At 1 year from baseline, 20.5% of patients showed a clinically significant deterioration while 25% had a clinically significant improvement. Infections were observed in 23.1% of patients during the first semester and in 12.8% during the second semester of the follow-up period. All were respiratory tract infections and two patients (5.1%) required hospitalization. All infections occurred in patients with non-UIP pattern (p=0.02) which might be attributed to higher doses of corticosteroids used in these patients (mean initial prednisolone dose = 27 (±18) mg/d in patients with non-UIP pattern versus 17 (±16) mg/d in patients with UIP pattern, p=0.4).

Table 1. Prevalence of HRCT patterns in 39 patients.

Radiological pattern	No (%)
NSIP	24 (61,5%)
OP	2 (5,1%)
NSIP with OP overlap	2 (5,1%)
LIP	1 (2,6%)
UIP	7 (18%)
NSIP and UIP	3 (7,7%)

NSIP: Non-specific Interstitial Pneumonia, OP: Organizing Pneumonia, LIP: Lymphocytic Interstitial Pneumonia, UIP: Usual Interstitial Pneumonia.

Table 2. PFTs at baseline, 6 and 12 months.

PFTs (% of predicted value ± SD)	Baseline	6 months	12 months	P value
FVC	79% (±19%)	82% (±18%)	84% (±17%)	ns
DLCO	49% (±16%)	52% (±17%)	53% (±17%)	ns

Conclusion: Rash is a common feature in IPAF and may be considered for inclusion into IPAF criteria. A trend of improvement in PFTs and a significant risk of respiratory tract infections mainly in the first semester of treatment and in patients with non-UIP radiological pattern were observed. Larger prospective studies are warranted in order to elucidate IPAF's prognosis and to identify effective management approaches.

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AB1217 THE EFFECT OF PROPHYLACTIC DOSE OF TRIMETHOPRIM-SULFAMETHOXAZOLE ON SERUM CREATININE IN JAPANESE PATIENTS WITH CONNECTIVE TISSUE DISEASES

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Background: Trimethoprim-sulfamethoxazole (TMP/SMX) is an effective antibiotic for prevention of pneumocystis pneumonia (PCP) in immunocompromised patients with various connective tissue diseases (CTD). [1)] At the normal dose of TMP/SMX, trimethoprim (TMP) component inhibits tubular creatinine secretion, leading to a rapid, but ultimately reversible, increase in serum creatinine. [2)] However, at prophylactic dose, the effect of TMP/SMX on creatinine in patients with CTD is not clear.

Objectives: We conducted this study to evaluate the effect of prophylactic dose of TMP/SMX on serum creatinine in patients with CTD.

Methods: This was a retrospective cohort study in which all patients with CTD, treated with prophylactic dose of TMP/SMX during the period between 2004 and 2018, were included, while patients with acute kidney injury due to other causes, were excluded. Retrospective medical chart review was performed to collect the following data, from the baseline through 12 weeks: baseline patient characteristics, serum creatinine (SCr), creatinine clearance (CCr), urine test, serum electrolytes, and level of SCr elevation after initiation of prophylactic dose of TMP/SMX from baseline, within 12 weeks. Using single and multiple regression analyses, we explored the risk factors that affected the SCr elevation value.

Results: A total of 272 patients, comprising 186 females, at an average age of 56±18 years, were included in the present study. Based on the medical chart review, this cohort was scored under the following categories: rheumatoid arthritis (RA) n=78, systemic lupus erythematosus (SLE) n=76, Vasculitis n=39, polymyalgia rheumatica/ giant cell arteritis (PMR/GCA) n=29, systemic sclerosis (SSc) n=32, polymyositis/dermatomyositis (PM/DM) n=10, mixed CTD (MCTD) n=5, and others n=56. Their average baseline creatinine level before treatment was 0.67 ± 0.25 mg/dL. They were administered with a mean dose of TMP comprising 99.2 ± 34.4 mg/day, which elevated the mean SCr level by 0.07 ± 0.12 mg/dL. Approximately 85% of the patients continued with the TMP/SMX treatment for 12 weeks, and only 5 (2%) showed creatinine elevation by more than 0.3 mg/dL. They were also administered with prednisolone at an average dose of 36.9 ± 92.3 mg/day.

For multiple regression analyses, the following variables were included: age, baseline CCr, use of loop diuretics, use of spironolactone, dose of TMP/SMX, use of non-steroidal anti-inflammatory drugs, and past history of diabetes mellitus. Baseline CCr and advanced age were independent risk factors. Regression coefficients and p values for age and CCr were 0.0018 (95% CI; 0.00083 – 0.0027) and p=0.00028; and 0.0007 (95% CI; 0.0003 – 0.0010) and p=0.00038, respectively.

Conclusion: In this study, we demonstrated that prophylactic dose of TMP/SMX elevates SCr by 0.07 ± 0.12 mg/dL on an average. Prophylactic dose of TMP/SMX rarely elevated the creatinine level significantly. Thus, based on our findings, other causes of renal impairment may be considered, if the patients administered with low-dose TMP/SMX show creatinine elevation by more than 0.3 mg/dL.

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AB1218 MATERNAL-FETAL MORBIDITY AND MORTALITY AMONG PREGNANT PATIENTS WITH RHEUMATIC DISEASES IN THE CLINIC OF PREGNANCY AND ARTHRITIS OF THE SALVADORAN SOCIAL SECURITY INSTITUTE

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Background: Connective tissue diseases are more frequent among women in childbearing age. In the past, it was not recommended for these women to get pregnant because of the risk of adverse pregnancy outcomes.

Objectives: The aim of this study is to compare the morbidity and mortality between pregnant patients with rheumatic diseases and pregnant patients without rheumatic diseases in El Salvador.

Methods: A case control study was conducted at *the Clinic of Pregnancy and Arthritis* and the *1° de Mayo Hospital*, both centers belong to the *Salvadoran Social Security Institute*. Clinical files were reviewed retrospectively and some of the data were collected during the clinical visit to each center. We included pregnant patients with rheumatic diseases of the Clinic of Pregnancy and Arthritis; the control group was randomly selected with a ratio 1:1 within pregnant patients without rheumatic diseases of the 1° de Mayo Hospital, between January 2016 and June 2019. A complication was defined as any event that required hospital admission. We used logistic regression to analyze univariable and multivariable associations to compare pregnancy outcomes between groups.

Results: During the study period, 230 patients were randomly included in both, the study group and the control group, with a ratio 1:1. The mean age for the study group was 32 (27-35) years, which was relatively older than the control

group, 28 (24-32) years. The mean pregnancy among both groups was 2 per patient. The most common rheumatic diseases in the study group were Rheumatoid arthritis (39.1%), Antiphospholipid Syndrome (31.3%) and Generalized Lupus Erythematosus (20%). The average visit to the Rheumatologist during pregnancy in the study group was 3.2. The visits started at a mean of 15.2 + 7.6 weeks of gestational age.

Thirty three point nine percent (33.9%) of the study group presented complications during pregnancy (vs 20.9%). Among the patients who presented complications, 9 of them (7.8%) had more than one complication during pregnancy. There were 44.3% cesarean deliveries in the study group compared with 22.6% in the control group, OR 2.1 (1.5-4.8) p=0.001. There were 16% of preterm deliveries between 34-37 weeks of gestational age in the study group compared to 10% in the control group, OR 2.2 (0.9-4.8) p=0.063. Preterm deliveries before 34 weeks of gestational age in the study group were 18% compared to 3% in the control group, OR 6.9 (2.3-20-9) p=0.001. There were 6 cases of spontaneous abortion in the study group and none in the control group. Thirty four percent (34%) of cases with low birth weight (<2.5kg) were found in the study group compared to 14% in the control group, OR 3.4 (1.6-6.1) p=0.001.

Conclusion: The most common rheumatic diseases among pregnant patients were Rheumatoid Arthritis, Antiphospholipid syndrome and Generalized Lupus Erythematosus.

Having a rheumatic disease was more associated with cesarean delivery, preterm delivery between 34 and 37 weeks of gestational age, and low birth weight.

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AB1219 ADHERENCE TO THE MEDITERRANEAN DIET IN PATIENTS WITH RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS, MULTICENTER STUDY

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Background: The Mediterranean diet (MD) has proven beneficial in a large number of chronic diseases. The relationship between the MD and rheumatic diseases is complex and there are few studies that have studied this relationship. These show that there could be a positive association between adherence to the Mediterranean diet (MD-A) and a lower prevalence of OA. In the case of RA, it has been proposed that the MD could reduce pain and improve functionality.

Objectives: To determine the MD-A diet of patients with RA and OA, and compare it with that of healthy subjects.

Methods: Multicenter, cross-sectional, observational study. Patients who attend the rheumatology outpatient and meet the ACR / EULAR 2010 criteria for RA and ACR for OA of hands, knees or hips are included in the study. The healthy are recruited among health personnel and companions of patients who do not live in the same address as the patient. The study is being carried out in the rheumatology consultations of two Hospitals and an outpatient center with specialized care. All participants have answered a survey of 14 questions (MEDAS-14), based on the Predimed study, which assesses MD-A. Fisher's exact test and the Mann-Whitney U test have been used to assess statistical significance. The study was approved by the Clinical Ethics and Research Committee of the centers.

Results: There have been 279 surveys (132 RA, 82 OA and 65 healthy). The MD-A in patients with RA is lower than in healthy (6.26 vs. 7.15, p <0.05). Patients with OA also have less adherence to the MD than healthy ones but this difference is not statistically significant (6.85 vs. 7.15, p> 0.05). The proportion of patients with RA and OA who consume 2 or more servings of vegetables daily is lower than that of healthy subjects (RA 20%; OA 13% and healthy 34%, p <0.05). The proportion of RA and OA that eats more than 3 weekly servings of nuts compared to healthy is also lower (RA 21%, OA 17%, healthy 35% p <0.05). The proportion of RA and OA that consume less than 1 serving of butter is lower than that of healthy (RA 86%; OA 82% and 98%, p <0.05). The proportion of RA that consumes 3 or more servings of legumes per week is lower than healthy (23% vs 40%, p <0.05). These differences between the OA group and healthy are not appreciated. The consumption of more than three pieces of fruit daily is more frequent in OA than in healthy ones (45% vs 26%, p <0.05).

Conclusion: The MD-A diet quantified by MEDAS-14 in subjects with RA and OA is lower than in healthy subjects, being significant in RA. Patients with RA and OA eat less vegetables and nuts but the intake of butter is higher. The RA group consumes less legumes than healthy ones. Patients with OA eat more fruit than healthy ones, this is the only food in the MD valued by MEDAS-14 that is consumed in a lower proportion in healthy ones. Longitudinal intervention studies are necessary to assess whether the differences observed in this study have any causal relationship.

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AB1220 DO ANTIBODIES HAVE DIFFERENTIAL EFFECT ON RADIOGRAPHIC PROGRESSION IN RA?

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Background: The presence of bony erosions in patients with RA is a marker of disease severity and once present they are largely irreversible. Previous studies have shown that those who are RF positive have more erosions than those who are RF negative. Likewise, ACPA is associated with increased bone loss and rapid erosive changes.

Objectives: The aim of our study was to determine which of these two antibodies is more strongly associated with erosive disease and whether being double +ve confers higher risk than single positive antibody status.

Methods: A retrospective study of 774 patients diagnosed with RA at a large university teaching hospital during the period of January 1981 and December 2018. Clinical records were reviewed to determine antibody status, date of diagnosis, duration of symptoms, DAS-28, age, ethnicity and whether the 1987 Rheumatoid Arthritis criteria was met. The presence of radiographic erosions at diagnosis were determined from reports of plain film radiographs of hands and feet of all patients. Chi square model was utilised to ascertain if there was a significant relationship among the four groups. Mann Whitney two-tailed U test was employed to determine the significance of relationship between the double negative group and other arms for all variables including disease duration and delta change in DAS28. Significance level was predefined at 0.05.

Results: All patients fulfilled the 2010 ACR/EULAR criteria. 240 (31%) patients were male and 534 (69%) were female with an age range of 17 to 90 years for the cohort. The duration of symptoms ranged for the patient cohort from 0.5 to 250 months with a median of 6 months while the duration of disease ranged from 4 to 455 months with a median of 49 months. DAS 28 ranged from 1.19 to 8.4 with a median of 4.4. 367 (47%) were positive for both RF and ACPAs, 87 (11%) were positive for RF alone, 66 (9%) were positive for ACPA alone and 254 (33%) were antibody negative.

There were a total of 127 patients with erosions at the time of diagnosis. Patients in the double positive group had a significantly higher (p=0.003) erosion burden compared to the double negative group i.e. 21.5% in RF+/ACPA+ versus 11.0% in RF-/ACPA- group. The erosion burdens in RF+/ACPA- and RF-/ACPA+ groups were 13.7% and 12.1% respectively.

Conclusion: This is the first real world study to demonstrate the radiographic erosive burden in the RA cohort with respect to RF/ACPA status. Our results show that patients RF+/ACPA+ have nearly two-fold higher incidence of radiographic erosions than patients who are RF-/ACPA-. Patients with single antibody positivity have a trend towards higher erosive burden compared to the double antibody negative group however it's the combination of two antibodies which is strongly associated with erosive disease.

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, Consultant of: Muhammad Nisar undertakes clinical trials and received support (including attendance at conferences, speaker fees and honoraria) from Roche, Chugai, MSD, Abbvie, Pfizer, BMS, Celgene, Novartis and UCB
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AB1221 POPULATION WIDE STUDY OF MORTALITY IN ANCA-ASSOCIATED VASCULITIS IN WESTERN AUSTRALIA FROM 2000 TO 2014

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Background: Survival in ANCA-associated vasculitis (AAV) has improved substantially in the last fifty years, but Australian data and studies with a control population are scarce.

Objectives: The aim of this study was to compare the all-cause mortality rate between patients with AAV and matched controls in Western Australia.

Methods: A retrospective population-based cohort study conducted using the Western Australia Health Data Linkage System (WADLS) for patients with a diagnostic code for AAV (International Classification of Diseases (ICD)-10-AM M30.1, M31.3 and M31.7). We included 240 patients with AAV (mean age 57.37 ± 16.69, 48.8% males) who had a hospital admission or emergency department visit between 1 January 2000 and 31 December 2014 and 4406 controls matched for age and sex. Death details were obtained from the WA Death registry. Mortality rates per 1000 person-years (MR) for AAV patients and controls were compared by mortality rate ratios (MRRs) with 95% CI. Kaplan Meijer survival estimates were analyzed by log-rank test.

Results: During a mean follow-up of 6.58 years (3.37, 11.25) 83 incident AAV patients (34.6%) died, giving a mortality rate of 48.13 per 1000 person-years (95% CI 38.33, 59.66). This was 82% higher overall than in controls (MRR 1.82, 95% CI 1.46, 2.26, P < 0.0001), while the MRR for males with AAV was 2.28 (95% CI 1.46, 2.26; P < 0.0001) and for females 1.43 (95% CI 1.01, 2.02; P = 0.0267). Survival estimates at one (90.5%) and five years (75%) were significantly lower in AAV patients than controls.

Conclusion: Over the last fifteen years, the mortality risk for AAV patients remains significantly increased compared with matched controls and more so for male than female AAV patients. Together with the reduced one- and five-year survival rate, this indicates the need for further improvements in initial disease management in order to reduce the risk of death in AAV.

Table Mortality rates (MR) per 100 patient years and Mortality rate ratio (MRR) with 95% CI in patients with AAV and controls

	AAV			Control			
	Deaths	Person years	MR (95% CI)	Deaths	Person years	MR (95% CI)	MRR (95% CI)
All	83	1724	48.1 (38.3, 59.6)	1219	46069	26.4 (25.0, 27.9)	1.82 (1.46, 2.26)
Male	49	789	62.1 (45.9 82.0)	690	25295	28.2 (25.2, 29.3)	2.28 (1.72, 3.02)
Female	34	935	36.3 (25.1, 50.7)	529	20773	25.4 (23.3, 27.7)	1.43 (1.01, 2.02)

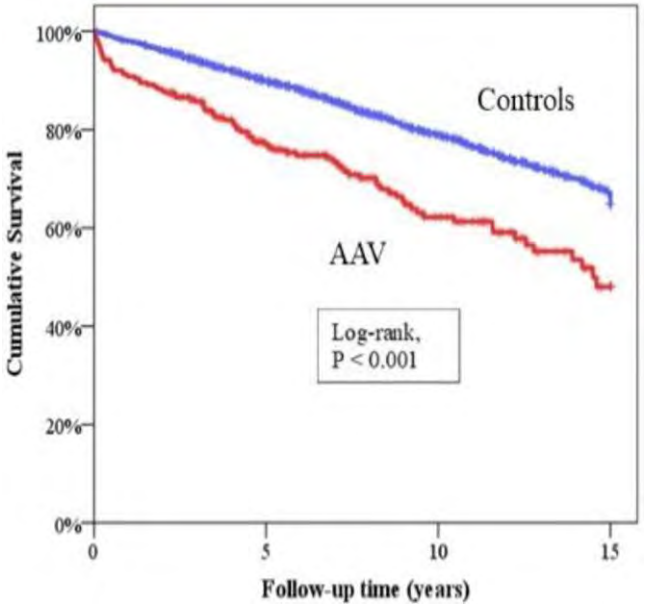


Figure. Kaplan Meyer Survival curves for AAV patients and controls

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AB1222 HOW DOES CHANGING THE TRADITIONAL P VALUE SIGNIFICANCE THRESHOLD TO .005 EFFECT OBSERVATIONAL STUDIES?

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Background: Changing the traditional p value significance level from 0.05 to 0.005 has been proposed as one remedy to the common ill understanding and use of the p values (1-2) especially leading to poor reproducibility. It was then reported that this change would decrease the number of statistically significant primary end points in randomized controlled trials (RCT) reported during 2017 in 3 main general medical journals by 1/3 (3).

Objectives: We reasoned that the same change would affect in the right direction the significance conclusions more in observational studies (OS) in that OS generally have retrospective or cross-sectional designs, looser study inclusion criteria, many potential confounders and post – hoc analyses.

Methods: We surveyed how the 0.05 to 0.005 change would affect the OS in the same 3 journals in reference 3 for the same year (2017) and in another year (2002), included to better assess the validity of our findings. RCT were also surveyed for both time periods. Two authors (MO, ZTD) surveyed all studies. Disagreements were settled by HY. Differing from the previous study (3) we analyzed the p values as related to the primary end points only in the abstracts. The RCT and OS between January 1, 2002 – December 31, 2002 and January 1, 2017 -December 31, 2017 in N Engl J Med, Lancet and JAMA were included.

Results: Among the RCT in 2017 the decrease in the number of significant p values was quite similar between what was reported (3) and the current study (Table) (29.3 vs 30.0%) supporting the validity of the slightly different methodology we used. We were however surprised to see that changing the significance level to 0.005 did not decrease the number of significant p values in OS as compared to the RCT. In fact the percentage decrease in RCT was statistically significantly less in 2002 and numerically in 2017 (Table).

Table. OS and RCT in 2002 and 2017

	OS (2002)		RCT (2002)
Number of articles	305		211
Total number of p values related to primary outcome(s)	323		322
p<0.05 n(%)	260(80.4)		240(74.5)
p<0.005 n(%)	190(58.8)		121(37.5)
Reduction in significant number of p values* (%)	70(26.9)	**P=0.011**	119(49.5)
	OS (2017)		**RTC (2017)**
Number of articles	167		200
Total number of p values related to primary outcome(s)	187		257
p<0.05 n (%)	162 (86.6)		173(67.3)
p<0.005 n (%)	125(66.8%)		121(47.0%)
Reduction in significant number of p values* (%)	37(22.8)	**P=0.55**	52(30.0)

RCT:Randomized Controlled Trials
OS: Observational Studies
*Number of p values <0.05 -Number of p values<0.005/(Number of p values<0.05

Conclusion: Contrary to our initial reasoning we now realize that changing the traditional p threshold will not decrease the number of significant p values more in OS than in RCT. A limitation of our work was that we surveyed only 3, high impact factor, general medicine journals. We envisage that in studies with smaller sample sizes more commonly published in journals with lower impact factors, the proposed change in the significance threshold would be more useful. Smaller sample sizes lead to more unstable, fickle p (4) values and changing the threshold would conceivably more or less stabilize this fickleness both in OS and RCT.

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AB1223 RHEUMATOID ARTHRITIS PATIENTS INCLUDED IN GLUCOCORTICOID TRIALS MOSTLY RESEMBLE THOSE SEEN IN OBSERVATIONAL COHORTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Randomised controlled trials (RCTs) are considered the gold standard in clinical research. Their results, however, may not be generalizable to patients in routine care.[1] Together with methotrexate, glucocorticoids (GCs) constitute the mainstay of therapy for many patients with rheumatoid arthritis (RA), but it is unclear whether trial evidence is actually generalizable to real-world patients.
Objectives: This review assesses to what extent RA patients participating in GC-RCTs differ from RA patients taking GCs in routine care.
Methods: This study was registered with PROSPERO (CRD42019134675). MEDLINE was searched for RCTs and, as comparators, cohort studies in RA evaluating systemic GC therapy. Cohorts were not allowed to exhibit apparent selection mechanisms concerning gender or age. Random-effects meta-analyses combined descriptive baseline characteristics that may modify the benefit-risk-ratio of various RA therapeutics. Meta-analyses were stratified by study type (RCT and CS). Stratified estimates were subsequently compared.
Results: 55 RCTs and ten cohort studies (21,657 participants overall) were included. Twelve characteristics (related to general demographics and disease activity) were reported frequently enough to allow for comparative analysis. Compared to cohorts, RCT participants were younger (-4.7 [-7.2 to -2.1] years) and had somewhat higher erythrocyte sedimentation rates (12 [6 to 18] mm/h) (Table 1). In the other ten characteristics, estimates did not differ significantly. Numerically, cohort patients had more longstanding disease and slightly more favourable disease levels in core set variables. Comorbidities could not be assessed.

Table 1. Pooled estimates

Outcome	RCT	*k*	Cohort	*k*	Contrast	(95% CI)	*p*
General demographics							
Age (years)	54.2	50	58.9	10	–4.7	(–7.2 to –2.1)	<0.001
Female (proportion)	0.70	52	0.73	10	0.89	(0.68 to 1.16)	0.38
Current or previous smokers (proportion)	0.59	3	0.51	2	1.38	(0.61 to 3.14)	0.44
BMI (kg/m^2)	25.9	5	25.9	3	0.0	(–1.9 to 1.9)	0.98
Disease duration (months)	56.5	43	85.1	7	–28.6	(–85.6 to 28.4)	0.33
Disease activity							
ESR (mm/h)	40.1	31	28.2	3	11.8	(5.7 to 18.0)	<0.001
DAS	5.3	24	4.9	5	0.4	(–0.1 to 0.9)	0.12
RF+, (proportion)	0.67	32	0.63	6	1.19	(0.80 to 1.78)	0.39
ACPA+, (proportion)	0.64	7	0.56	3	1.38	(0.64 to 3.00)	0.41
HAQ	1.3	31	1.1	4	0.2	(–0.1 to 0.5)	0.15
Pain (0-10)	5.2	26	4.8	2	0.4	(–0.8 to 1.6)	0.52
Patient global assessment (0-10)	5.2	17	4.9	3	0.3	(–0.9 to 1.5)	0.58

Conclusion: The results of our study suggest that evidence from RA GC-RCTs can be generalized to most patients in routine practice. We note that comorbidities – a frequent exclusion criterion for trial participation – could not be evaluated due to insufficient reporting. Our findings contrast with a similar study on RCTs investigating biologics in RA: There, trial participants were found to differ significantly in 4 out of 8 investigated baseline characteristics.[2]
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AB1224 MAJOR DEPRESSIVE DISORDER AMONG CYPRIOT PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND CORRELATION WITH CLINICAL CHARACTERISTICS AND DISEASE-SPECIFIC HEALTH-RELATED QUALITY OF LIFE

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Background: Major depressive disorder (MDD) is a common comorbidity in patients with chronic rheumatic conditions, and patients with systemic lupus erythematous (SLE) have an increased risk of developing depression. The coexistence of SLE and MDD might lead to impaired health-related quality of life (HRQOL). Gaining a deeper understanding of the factors associated with MDD in SLE will allow us to develop strategies in order to prevent depression and achieve an early diagnosis and management.
Objectives: The aim of this study is to determine the contributing factors associated with MDD in Cypriot SLE patients and examine the correlation between disease-specific HRQOL domains and depression.
Methods: We conducted a cross-sectional study of SLE patients who fulfilled the SLICC-2012 criteria. The patients were recruited from August 2019 to January 2020. Baseline demographic data, clinical features, and therapeutic regimens were captured. Depression was assessed by the patient health questionnaire (PHQ)-9, a validated tool to screen and diagnosed the condition. Scores above ≥10 are indicating MDD. HRQOL was evaluated by a disease-specific validated questionnaire, LupusQoL-Greek. LupusQol scores ranged between 0-100, with higher scores reflecting better QoL. The self-rated health status was examined, and the response was separate to poor/fair vs excellent/good. Demographic data, LupusQoL domains, clinical and other features of the SLE patients were described and compared between MDD (PHQ-9 ≥ 10) and non-MDD (PHQ-9<10) groups using Wilcoxon ranksum tests for continuous variables and chi-square tests for categorical variables.
Results: A total of 88 SLE patients were included in the study, with a mean age of 48.6 (19-80), 71(80%) were women, and mean disease duration of 13.2 years (0-44). Compared to the non-MDD group, patients with MDD (n=32, 36%) were significantly older (mean age 53.5 vs 46.9; p=0.03) and more likely to have the following SLE manifestations: mucocutaneous, vascular, pulmonary and musculoskeletal involvement. Furthermore, patients with MDD were less likely to be clinical quiescent (34.3%) compared with the non-MDD group (57.1%) (P<0.05). Self-rated health described as poor/fair was markedly associated with MDD (p<0.001). The LupusQoL domains' scores were notably lower in patients with MDD (PHQ ≥ 10), with a statistically significant reduction in all LupusQoL domains, indicating that depression was associated with worse HRQOL (Table 1).

Table 1. Differences in 8 LupusQoL domain scores among SLE patients with and without major MDD (PHQ-9 ≥10)

LupusQoL Domains (0-100)	PHQ-9 <10 (non-MDD)	PHQ-9 ≥10 (MDD)	P-value
Physical Health	72.87 (81.2, 9.3-100)	40.01 (32.75, 0-90.6)	<0.0001
Pain	75.27 (75, 16.6-100)	43.2 (41.6, 0-100)	<0.0001
Planning	81.08 (91.6, 0-100)	44.51 (50, 0-100)	<0.0001
Intimate relationship	68.38 (75, 0-100)	46.25 (50, 0-100)	0.0382
Burden to others	79.73 (83.3, 16-100)	51.97 (50, 0-100)	0.0003
Emotional health	81.76 (85.4, 25-100)	50.14 (50, 0-91.6)	<0.0001
Body image	84.09 (90.8, 5-100)	58.45 (66.6, 0-100)	0.0004
Fatigue	72.08 (75, 18.7-100)	41.2 (40.6, 6.2-81.2)	<0.0001

Conclusion: To our knowledge, this is the first study demonstrating significantly lower scores among MDD relative non-MDD (based on PHQ-9) patients across all the 8 domains of LupusQoL; therefore, it adds to the current evidence that depression significantly impacts the quality of life of SLE. Predictors of MDD include older age, and involvement of the vascular, mucocutaneous, pulmonary, and musculoskeletal system. Additionally,a poor or fair description of self-rated health was a predictor of depression.

Disclosure of Interests: None declared
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AB1225 LIPID PROFILE COMPARISON IN RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS: A CASE-CONTROL STUDY

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Background: Rheumatoid arthritis (RA) and psoriasic arthritis (PsA) are autoimmune diseases, in both diseases it has been described that the main cause of morbidity and mortality is cardiovascular (CV) disease. Dyslipidemia is the most recognized CV risk factor. An association is recognized between the concentrations of total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), total triglycerides (TG), atherogenic index (AI) and the risk of myocardial infarction (MI), stroke and fatal cardiovascular disease (CVD). The relationship between serum lipid levels and CVD risk is potentially paradoxical in RA but this relationship has not been clarified in PsA.
Objectives: To compare lipid profile between groups with RA, PsA and controls.
Methods: A cross-sectional observational study was designed, which included 95 patients between 45-75 years who fulfilled the CASPAR classification criteria for PsA. 95 patients between 45-75 years who fulfilled the ACR / EULAR 2010 classification criteria for RA and 95 age-matched controls. Concentrations of CT, HDL-C, LDL-C, TG and atherogenic index were compared between the groups. Clinical measures were compared using one-way ANOVA or Kruskall-Wallis tests. Post-hoc analysis was performed with Bonferroni's correction. A $p \leq 0.05$ was considered statistically significant. The data was analyzed using the SPSS version 25 software package.
Results: In our study, no significant difference in LDL-C was found between RA and PsA, however post-hoc analysis was performed where we found higher LDL-C levels among RA patients compared with controls (p 0.025). RA patients had higher HDL-C than PsA patients (p 0.006) but PsA had a higher HDL-C than controls (p 0.007). TC/HDL-C was higher in PsA than RA and controls (p 0.050). PsA patients were the group with the lowest HDL-C levels (p 0.007). In contrast RA were the groups with the highest HDL-C levels (p 0.007). (Table 1).

Table 1. Clinical parameters.

PARAMETER	*RA*	*PsA*	*Controls*	*p*
TC*	176.6 ± 37.2	176.3 ± 35.9	186.34 ± 33.172	0.089
TG**	132.7 (102.0-187.3)	131.0 (97.2-189.2)	118.35(88.2-162.25)	0.245
HDL-C**	50.7 (42.1-62.6)	46.7 (37.4-53.9)	51.7 (41.3-60)	**0.007**
LDL-C*	94.36 ± 21.70	97.71 ± 30.12	105.32 ±31.35	**0.025**
TC/HDL-C**	3.41 (2.81-4.08)	3.74 (3.17-4.47)	3.49 (2.99-4.52)	**0.050**

*Data are reported in mean ± SD
**Data is reported in median (IQR)

Conclusion: Patients with inflammatory joint diseases have more adverse lipid profiles than controls.

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AB1226 PREDICTING CARDIOVASCULAR EVENTS IN PATIENTS WITH SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS: THREE RISK ALGORITHMS

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Background: Inflammatory joint disorders have an increased cardiovascular (CV) risk when compared with general population. In 2009, the EULAR task force advocated the use of a 1.5 multiplication factor for these risk prediction models in Rheumatoid Arthritis patients with specific characteristics. The SCORE was not modified in patients with Psoriatic Arthritis (PsA) and Spondyloarthritis (SpA) in accordance with the present EULAR recommendations.
Objectives: To assess the accuracy of several CV risk algorithms to predict an event and determine its sensibility and specificity.
Methods: A retrospective analysis of PsA and SpA patients, followed in our department in Local Health Unit of Guarda during one year (2019) was done. We determined CV risk profile of our patients using the following data: gender, age, smoking status, blood pressure, lipid values and diabetes mellitus status. These variables were used to calculate risk prediction algorithms such as Framingham, the American College of Cardiology/American Heart Association (ACC/AHA) risk score and the Systematic Coronary Risk Evaluation (SCORE). Discriminatory ability for CV risk prediction was evaluated by the area under the ROC curves. Sensibility and specificity were calculated for low-to-intermediate and intermediate-to-high risk cut-offs. Cut-off values that mark the high risk were defined in 5% for SCORE, 20% for Framingham and ACC/AHA.
Results: 112 caucasic patients were included, 61% female with a mean age of 52.15±14.18 years and mean BMI of 27.11±4.81kg/m^2. 7 patients weren´t eligible to apply these cardiovascular scores. 8 patients were identified with non-fatal cardiovascular events (2 cases of stroke, 5 cases of myocardial infarction and 1 case of thrombophlebitis). 69 patients diagnosed with SpA and 43 with PsA, five CV events identified in SpA patients and three in PsA patients. Area under the ROC in SpA were 0.729 (95% CI 0.461 to 0.996) for SCORE, 0.839 (95% CI 0.735 to 0.943) for Framingham and 0.804 (95% CI 0.683 to 0.925) for ACC/AHA. Area under the ROC in PsA patients were 0.603 (95% CI 0.327 to 0.879) for SCORE, 0.660 (95% CI 0.326 to 0.995) for Framingham and 0.804 (95% CI 0683 to 0.925) for ACC/AHA. Sensibility and specificity were discriminated in table 1.

Table 1. Sensibility, specificity, positive predictive value (PPV) and negative predictive value (NPV) of CV risk algorithms

	Sensibility (%)	Specificity (%)	PPV (%)	NPV (%)
SCORE > 1%				
SpA	75	63	18	96
PsA	100	41	5	100
SCORE > 5%				
SpA	NA	NA	NA	NA
PsA	0	93	0	97
Framingham >10%				
SpA	83	78	28	98
PsA	50	51	5	95
Framingham >20%				
SpA	33	86	20	93
PsA	50	69	8	96
ACC/AHA >5%				
SpA	67	77	29	94
PsA	100	44	9	100
ACC/AHA >20%				
SpA	17	86	14	88
PsA	50	83	14	97

Conclusion: A good discrimination between patients with or without CV events has been demonstrated by area under the ROC curve, particularly to SpA patients. In PsA, the sample was smaller, which represents a limitation in this study. SCORE >5% did not identify CV events, therefore sensibility couldn't be calculated. Overall, the algorithms studied presented a low sensibility, underestimating CV risk. This could be explained since disease-related factors are not reflected in these scores. In our opinion, better algorithms are needed to correctly assess cardiovascular risk algorithms for SpA and PsA, since the majority of the events occur in patients with low-intermediate risk.

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AB1227 PREVALENCE OF RHEUMATIC MUSCULOSKELETAL DISORDERS IN A RURAL AREA OF UPPER EGYPT: WHO-ILAR COPCORD BASED COMMUNITY STUDY

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Background: Rheumatic musculoskeletal disorders (RMSDs) are a common cause of long term pain and physical disability. In developed countries, RMSDS are a major cause of absence from work and thus have a big financial burden on the country economic status. Several studies have been published the incidence and prevalence of RMSDs in different world countries and found to be widely variable. Estimation of the extend of the problem of RMSDs in developing world, especially in rural economies will help better understanding of the risk factors that contribute to the initiation and progression of these diseases and help the health care authorities to provide proper health program services in these areas to reduce the physical and financial burden of RMSDs (Bagher et al., 2011; Majumdar et al., 2015 and Usenbo, et al., 2015).
Objectives: To estimate the prevalence rate of RMSDs in a rural population in Upper Egypt.
Methods: A cross-sectional based study was carried out and included 3988 subjects of population (2013 females and 1975 males). Mean age of patients was (46.89±15.25ys). They proceeded 4 phases of World Health Organization/International League of Associations for Rheumatology community-oriented program for control of rheumatic diseases survey questionnaire WHO-ILAR Community Oriented Program for screening of rheumatic diseases. Modified Health Assessment Questionnaire (HAQ) was used to assess the disability severity. Individuals suspected to have any rheumatic diseases were subjected to full clinical examination, laboratory and radiological investigations to reach a final diagnosis. They were classified according to appropriate criteria of diagnosis of diseases.
Results: A prevalence rate of RMSDs was 16.22%, more prevalence in females (10.38% vs. 5.84% for males, P=0.000). The mean age of patients with RRMSDSs were older (46.89±15.25 yrs) than healthy individuals (29.56±18.95 yrs) (P=0.0001) and with increasing age (≥45-≤ 55 yrs).The identified RMSDs were OA (8.5%), Soft tissue rheumatism (STR) (6.57%), spinal disorders (SD) (6.47%), fibromyalgia (FM) (0.60%), RA (0.30%), arthralgia (0.18%), SPAs (0.15%), Gout(0.6%), Pseudogout (0.08%), SLE (0.5%), JIA(0.03) and MCTD (0.03%). The prevalence rates for the majority of RRMSDSs were higher in females and with increasing age. About two thirds of the patients had grade II disability.
Conclusion: The prevalence rate of RMSDs in a rural population ≥15years in Upper Egypt has been estimated to be 16.22%.The most prevalent RMSDs are OA, STR and SD causing the greatest burden of the disease. The predictive risk of RMSDs has to be assessed in future studies.
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AB1228 COMPARATIVE ANALYSIS OF COMORBID PATHOLOGY IN PATIENTS WITH RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDYLITIS

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Background: Interest in comorbid conditions in rheumatoid arthritis (RA) and ankylosing spondylitis (AS) is due to their influence on the course and prognosis of the disease itself, the quality of life of patients and the choice of treatment tactics.
Objectives: To compare the frequency and structure of comorbid pathology in patients with RA and AS.
Methods: 130 cases of patients with RA (95 women, 35 men, average age 47±6.6 years) and 86 with AS (27 women and 59 men, average age 44 ±7.4 years) were analyzed. The effect of concomitant pathology on the long-term prognosis was evaluated using the Charlson comorbidity index.
Results: Patients with RA had a combined pathology in 93.0% (122) cases, of which 24.5% (30) – one, 28.6% (35) – two, 46.7% (57) – three or more concomitant diseases. Concomitant diseases in AS patients were registered in 83.7% (72) of cases, including one in 36% (31), two in 14% (12), and three or more in 33.7% (29). The Charlson index from 1 to 2 points was determined in 78.5% (102) of RA patients and in 77.9% (69) of patients with AS (p=0.067). Values from 3 to 4 points had 19.2% (25) and 20.9% (18) of patients, respectively (p=0.064). The Charlson index of more than 5 points was registered in 2.3% (3) patients with RA and 1.2% (1) patients with AS.
The leading place in the structure of comorbidity in the group of patients with RA was occupied by diseases of the digestive system, which was observed in 79.2% (103) of patients. In the second place in the same group were registered cardiovascular diseases (CVD) – in 48.5% (63) patients, the most common arterial hypertension – in 36.9% (48). 27.6% (36) of patients had chronic pyelonephritis in combination with urolitiasis. Osteoporosis was detected in 20.0% (26) of RA patients.
In the group of patients with AS, diseases of the digestive system were also most frequently registered – in 76.7% (66) of patients. CVD was observed in 41.9 % (36) patients, of which 39.5% (34) had hypertension. Kidney diseases were registered in 9.3% (8) of patients. Osteoporosis was detected in 32.5% (28) of patients with AS.
Comparative analysis of the structure and frequency of diseases of the digestive system in RA and AS revealed no significant differences. CVD was registered more often in RA than in AS (48.5% vs 41.8%, p=0.037). There were significant differences in the frequency of hypertension in the study groups of patients: hypertension was observed more often in patients with as in 39.5% of cases, while in RA only in 36.9% (p=0.041), which is probably due to long-term use of medium and high doses of NSAIDs as "basic therapy" for AS. Kidney diseases were more common in RA than in AS (27% vs 9.3%, p=0.022). Osteoporosis, in contrast, was most frequently detected in patients with AS than in RA patients (32.2% vs 20%, p=0.047).
Conclusion: Despite differences in the pathogenesis of RA and AS, the long-term prognosis, determined by both rheumatic disease and comorbidities, did not differ significantly. Concomitant pathology is an important component that determines the management of patients.
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AB1229 SAFETY OF BIOSIMILAR ETANERCEPT IN THE TREATMENT OF RHEUMATIC DISEASES: DATA FROM THE MEXICAN ADVERSE EVENTS REGISTRY (BIOBADAMEX)

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Background: Access to biosimilar drugs in Mexico started on 2014. Although biosimilar drugs safety has proved comparability to originator drugs on trials, information about its safety on real-life data is limited.
Objectives: To compare safety in terms of adverse events of biosimilar etanercept (BEt) to originator etanercept (OEt) using information from the Mexican Adverse Events Registry (BIOBADAMEX).
Methods: BIOBADAMEX is a Mexican cohort that collects the information of biologic and biosimilar drugs used in patients with rheumatic diseases in public and private practice since 2016. Patients enrolled are followed- up yearly. For this study we included patients from 18 to 65 years old who were or are currently in treatment with OEt or BEt and analyzed the frequency of adverse events (AE), the severity and the outcome of these. Baseline time was considered at enrolment to the cohort. We used logistic regression to analyze univariable and multivariable associations.
Results: At the time of analysis a total of 119 have received treatment with OEt, 38 with BEt. Mean follow up time was 1.35 years. Rheumatoid arthritis (RA) was the most common disease for all the groups followed by ankylosing spondylitis (AS) and psoriatic arthritis (PsA). Both groups had similar baseline characteristics (Table 1). AE occurred in 4 (3.4%) patients with OEt and in 6 (15.8%) with BEt (OR 0.2, 95% CI 0.04-0.7). The most frequent AE in OEt group was allergic reaction, (2(2.5%) of patients), and infections were the most frequent AE in BEt group (2 (5.3%)). Of patients with BEt, 2(5.3%) had severe AE compared to none in the OEt (p=0.012). In the multivariable adjusted analysis comparing development of AE vs no AE including BEt, comorbidities and glucocorticoids, we found that use of BEt (OR 4.6, 95%CI 1.1-19.5) and presence of comorbidities (OR 4.6, 95%CI 1.01-20.5), were associated with AE. Use of glucocorticoids was not significantly associated.

Table 1. Baseline characteristics

	Originator etanercept (n=119)	Biosimilar Etanercept (n=38)	Univariable Analysis [a] OR(95%CI)
Sex (female), n(%)	98 (82.4)	27 (71.0)	1.9 (0.8-4.4)
Age, median (IQR)	53.6 (45-61)	51.3 (43-58)	1.0 (0.9-1.0)
Body Mass Index, median (IQR)	27.5 (23.4-32.5)	26.7 (24-29)	1.0 (0.9-1.1)
Diagnosis, n(%):			
Rheumatoid arthritis	98 (82.4)	26 (68)	1
Ankylosing spondylitis	13 (10.9)	9 (24.0)	0.3 (0.1-0.9)
Psoriatic arthritis	8 (6.9)	3 (8.0)	0.7 (0.1-2.8)
Comorbidities, n(%):	41 (34.5)	14 (40.0)	0.3 (0.3-1.5)

Table 1. Baseline characteristics

	Originator etanercept (n=119)	Biosimilar Etanercept (n=38)	Univariable Analysis [a] OR(95%CI)
Use of previous biologic, n(%):	95 (79.8)	16 (42.1)	**5.4 (2.5-11.9)**
Use of steroids, n(%):	45 (37.8)	22 (57.8)	0.4 (0.2-0.9)
Use of DMARD, n(%):	94 (78.9)	35 (92.1)	0.3 (0.1-1.1)
Adverse events[b], n(%):	4 (3.4)	6 (15.8)	**0.2 (0.04-0.7)**
Infections[b], n(%):	1 (0.8)	2 (5.3)	0.15 (0.1-1.7)
Allergic reactions[b], n(%):	3 (2.5)	1 (2.6)	0.9 (0.1-9.5)
Severe[b], n(%):	0 (0)	2 (5.3)	**p=0.012** [c]

[a]Univariable logistic regression analysis. [b]Cumulative at time of analyses, [c]Chi-square test.

Conclusion: This preliminary study showed that AE with BEt were more frequent as well as more severe compared to AE presented with OEt in patients with rheumatic diseases using BIOBADAMEX data. Our study suggests that use of BEt and comorbidities are associated with the development of AE. Follow up and inclusion of more participants is going on and will allow us to perform further analyses.

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AB1230 PERIPHERAL ARTERY DISEASE AND JOINT PAIN IN TYPE 2 DIABETES PATIENTS, FROM ASSOCIATION TO CAUSATION

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Background: Type 2 diabetes mellitus (T2DM) and arthritis are considered two separate conditions. However, inflammation and metabolic changes play a major role in diabetes co-morbidity (1). The pathogenesis of the joint pain and stiffness in diabetes patients is not fully understood. Diabetic osteoarthropathy (neuropathic arthropathy) considers a quite rare condition (0.1–0.4% of diabetic patients), involving destructive, lytic joint changes (2). Interestingly, over 52% of diabetic patients have joint diseases, compare to only 27% without diabetes; and people with arthritis have over 60%higher risk of diabetes development (3).

Objectives: The purpose of the study was to determine the association between the lesions of low extremity arteries (LEA) and the prevalence of arthritis (joint pain and stiffness) among patients with type 2 diabetes.

Methods: This is the pilot analysis of the musculoskeletal data obtained from the prospective cohort study of patients with diabetes complications 2013-2016 (179 consecutive T2DM pts undergoing transfemoral amputation (TFA) due to gangrene of lower limb (4,5), and 199 patients experienced balloon angioplasty (BA) of the LEA (without gangrenes). The computer tomography angiography was performed, along with clinical, laboratory and instrumental examination. Functional class of joint lesions (hip, knee or foot) was obtained based on self-service and (un)professional activity.

Results: All observed patients had diabetic neuropathy. The affected extremity in all the patients undergoing TFA had critical arterial ischemia along with foot gangrene, knee/hip pain, stiffness and rigidity. The second extremity also had stenoses of popliteal, anterior or posterior tibial arteries and the severity of stenoses was positively correlated with the severity of muscle and joints pain (r=0.771, p<0.001).

Among 199 patients without gangrene of lower limb, BA was done on superficial femoral artery 46 (23.1%) patients, popliteal in 44 (22.1%), posterior tibial 54 (27.1%), arterial tibial 41 (20.6), and peroneal artery 14 (7%). At least 1 large and 1 small joint was affected per person. The correlation between the prevalence of joint pain/stiffness and peripheral artery stenosis of the same lower extremity in patients without gangrene was significant r=0.632, indicating a large positive relationship (approximately 39.9% of the total variance). A linear regression analysis was conducted to evaluate the association between the severity of artery lesions and the severity of joint functional class, F (1, 198) = 57.82, p<0.001, t = 7.91, p < 0.001. The 95% confidence interval for the slope was 0.71 to 1.29, which did not include the value of zero.

Conclusion: The results show that the more severe the peripheral artery stenosis was the more prevalent join lesions are and worsen the function class. However, more studies are needed.

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AB1231 2019 LUPUS CLASSIFICATION CRITERIA SCORE PREDICTS FUTURE LUPUS HOSPITAL ADMISSION

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Background: There are several validated tools to quantitate lupus disease activity, end-organ damage and overall fragility. An algorithm to predict the hospitalization risk in lupus patients was proposed by Li et al[1]. That algorithm was able to effectively screen patients at increased risk of hospitalization using EHR information only. Recently, the new 2019 Lupus classification criteria score has been noted to accurately predict 10 year mortality[2].

Objectives: To test the above 2 algorithms with potential to predict lupus related hospital admissions.

First, we attempted to validate the existing algorithm from the index study of Li et al to predict lupus hospitalization.

Second, we tested the 2019 lupus clinical classification score for its ability to predict hospitalizations.

Methods: A retrospective chart review was performed using EHR data collected from 2013 to 2018 at University of Kentucky (UK) Medical Center. Inclusion criteria were 18 years or older at first outpatient rheumatology appointment at UK, at least 3 outpatient rheumatology visits at UK, and ICD 9/10 code for Lupus. A total of 217 patients met inclusion criteria. Variables similar to the index study were extracted from patients' first outpatient rheumatology visit at UK. Additionally, 2019 Lupus Classification Criteria score was calculated. Patients who were subsequently hospitalized, manual chart review was done to determine if the hospitalization was attributable to lupus or not.

Results: Table 1 shows differences between the variables predicting hospitalization in patients in this study (UK) and the Ohio State University (OSU) cohort from whom the admission predicting algorithm was derived[1]. All the risk factors that were found to predict lupus hospitalization in the index study, failed to achieve a statistical significance in our validation study.

Table 1. Differences in the variables predicting hospitalization between Index and Validation Cohort

Variables predicting Lupus Hospitalization	Index Study (Ohio State), % of patients (n=226)	Validation Study (University of Kentucky) % of patients; (n=217)
African American	33%	18%
Creatinine > 1.2	17%	7%
Hemoglobin < 11g/dl	79%	18%
Platelets < 180 / uL	75%	22%
High Risk immunosuppression	35%	9. 2%
Missed appointment	27%	25%

There was more success predicting lupus hospitalization using the 2019 lupus classification criteria score (CCS) (Figure 1). A CCS >=19 predicted higher risk of lupus related hospitalization vs CCS < 19 over the ensuing 2 years (p-0.05).

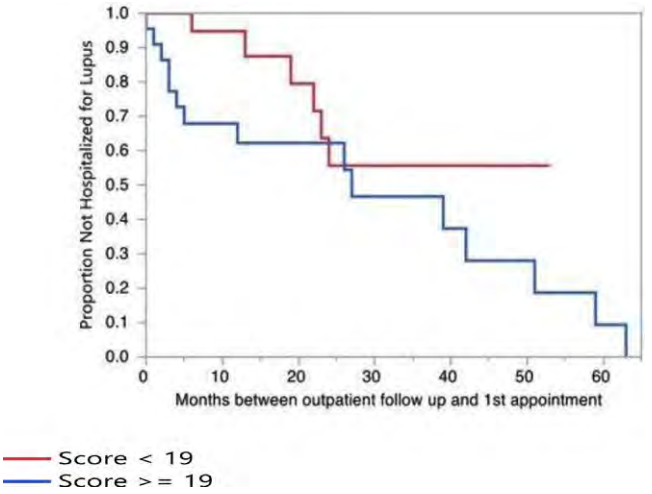


Figure 1. Kaplan- Meier Survival Analysis comparing the risk of hospitalization between the groups with 2019 Lupus classification criteria score (CCS) of less than 19 (red) and more/equal to 19 (blue). A time-dependent effect, with the admission free survival curves crossing at two years (Figure 1), indicated a 1 out of 3 chance of lupus related admission during the first 6 months for a high CCS score > =19.

Conclusion: We failed to validate the EHR algorithm identifying patients at high risk for lupus hospitalization in our less severely affected cohort with fewer admission events to analyze. Nonetheless, "criteria counting" using the weightings of the 2019 lupus classification criteria was granular enough to make these case finding criteria themselves prognostic for future hospitalization risk. It is likely that existing EHRs, using protocols based upon classification criteria scores, are now capable of predicting survival, costs, and admissions automatically.

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AB1232 ORAL DYSBIOSIS REFLECTS THE IMMUNOLOGICAL ALTERATION OF RA REGARDING TO ACPA AND HLA DRB1*SE: NAGASAKI ISLAND STUDY

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Background: Anti-citrullinated protein antibody (ACPA) production is observed in several organs even prior to the onset of rheumatoid arthritis (RA), and oral mucosa is considered to be one of the important tissues. The presence of HLA-DRB1*SE closely associates with ACPA production. Saliva is considered to reflect the oral microbiota including periodontal disease. Alteration of oral microbiota of RA becomes to be normalized by DMARDs treatment, however, the interaction of HLA-DRB1*SE, ACPA and oral microbiota of RA patients remains to be elucidated.

Objectives: The Nagasaki Island Study, which had started in 2014 collaborating with Goto City, is intended for research of the preclinical stage of RA, including ACPA/HLA genotype screening and ultrasound and magnetic resonance imaging examinations in high-risk subjects. Using the samples accumulated in this cohort, we have tried to investigate the difference of oral microbiota among RA patients and healthy subjects regarding to ACPA and HLA-DRB1*SE.

Methods: Blood and salivary samples were obtained from 1422 subjects out of 4276 who have participated in the Nagasaki Island Study from 2016 to 2018. ACPA positivity was 1.7 % in total. Some of RA patients resided in Goto City participated in the Nagasaki Island Study. At this point, we selected 291 subjects, who were ACPA positive non-RA healthy subjects (n=22) and patients with RA (n=33, 11 subjects were ACPA positive and 22 ACPA negative respectively) as the case, age and gender matched ACPA negative non-RA healthy subjects (n=236) as the control. ACPA was measured by an enzyme-linked immunosorbent assay, and HLA genotyping was quantified by next-generation sequencing (Ref.1). The operational taxonomic unit (OUT) analysis using 16S rRNA gene sequencing were performed. The richness of microbial diversity within-subject (alpha diversity) was scaled via Shannon entropy. The dissimilarity between microbial community composition was calculated using Bray-Curtis distance as a scale, and differences between groups (beta diversity) were tested by permutational multivariate analysis of variance (PERMANOVA). In addition, UniFrac distance calculated in consideration of the distance on the phylogenetic tree were performed.

Results: Median age 70 y.o., % Female 58.8 %. Among RA and non-RA subjects, not alpha diversity but beta diversity was statistically significance (p=0.022, small in RA). In RA subjects, both alpha and beta diversity is small (p<0.0001), especially significant in ACPA positive RA (Figure 1). Amongt RA subjects, presence of HLA-DRB1*SE did not show the difference but the tendency of being small of alpha diversity (p=0.29).

Conclusion: Our study has suggested for the first time the association of oral microbiota alteration with the presence of ACPA and HLA-DRB1*SE. Oral dysbiosis may reflect the immunological status of patients with RA.

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Disclosure of Interests: None declared

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AB1233 GENDER DIFFERENCE IN DISEASE SEVERITY AND TREATMENT OUTCOMES AMONG PATIENTS WITH RHEUMATOID ARTHRITIS (RA), AXIAL SPONDYLOARTHRITIS (AXSPA) AND PSORIATIC ARTHRITIS (PSA) STARTING TREATMENT WITH TARGETED THERAPY IN THE CZECH REPUBLIC

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Background: The ATTRA registry captures more than 95% of patients with RA, AxSpA, or PSA treated with biologics in the Czech Republic (CZ). In CZ, anti-TNF therapy is reimbursed for RA if DAS28>5.1 despite therapy with csDMARDs, for PSA if disease is not "adequately controlled" with csDMARDs and for AS if BASDAI>4 and CRP/ESR elevated above normal.

Objectives: We aimed to investigate gender-related differences in baseline characteristics and treatment effectiveness among patients with RA, AxSpa, and PsA starting first targeted therapy (TT) in CZ.

Methods: In this observational cohort study, the ATTRA register provided prospectively collected data on RA, AxSpA and PsA patients who initiated their first TT (mostly by TNFi) in 2012–6/2018. Treatment effectiveness and adherence was assessed at 12 months by a change in patient-reported outcomes (PROs), CRP and % drug survival. Differences in categorical and continuous data btw males and females were assessed using the Pearson X^2 test (of Fisher exact test, as appropriate), or Mann-Whitney test resp. This study was largely descriptive, and no statistical adjustments have been made.

Results: A total of 1602 RA, 1306 AxSpa, and 493 PsA patients were included. The difference in baseline characteristics btw women and men starting TT are shown in table 1. Their response and adherence to TT after one year is shown in table 2.

Conclusion: When starting their first TT, males tended to have higher levels of CRP, while females were more often (ex)smokers and reported worse parameters of quality of life across the diagnostic groups. The improvement of PROs was similar in males and females, while males with axSpA and PsA showed larger improvements in CRP. Survival on drug at one year was similar, save for AxSpA, where males showed better survival.

References:

Table 1. Baseline characteristics of pts starting first TT – comparison btw males (M) and females (F)

	RA (n=1602)			AxSpA (n=1306)			PSA (n=493)		
	M	F	p	M	F	p	M	F	p
N (%)	359 (22.4%)	1243 (77.6%)		931 (71.3%)	375 (28.7%)		262 (53.1%)	231 (46.9%)	
Age (yrs) at start of first symptoms	47.4 (37.1; 54.5)	42.8 (33.3; 51.4)	**< 0.001**	25.5 (19.6; 33.0)	28.6 (21.6; 36.6)	**< 0.001**	36.7 (27.7; 46.5)	38.8 (30.8; 47.5)	0.085
Age (yrs) at diagnosis	48.0 (37.0; 55.0)	44.0 (34.0; 53.0)	**< 0.001**	31.0 (24.0; 39.0)	35.0 (27.0; 42.0)	**< 0.001**	37.0 (30.0; 47.0)	38.0 (32.0; 49.0)	0.171
Age (yrs) at start of first TT	55.0 (46.0; 63.0)	53.0 (43.0; 62.0)	0.076	38.0 (32.0; 47.0)	42.0 (34.0; 50.0)	**< 0.001**	48.0 (37.0; 55.0)	49.0 (40.0; 58.0)	0.070
Smoker or ex-smoker	189 (58.8%)	729 (65.9%)	**< 0.001**	447 (53.6%)	197 (57.4%)	**< 0.001**	100 (43.3%)	132 (63.2%)	0.168
CRP (mg/l)	16.5 (9.0; 32.0)	14.0 (6.0; 28.0)	**< 0.001**	20.0 (11.9; 52.0)	16.0 (10.4; 26.0)	**< 0.001**	16.3 (8.0; 31.8)	15.0 (6.1; 28.7)	0.023
VAS pain (0–100)	70.0 (50.0; 80.0)	70.0 (55.0; 80.0)	**0.007**	70.0 (50.0; 80.0)	70.0 (55.0; 80.0)	0.292	65.0 (45.0; 80.0)	70.0 (60.0; 80.0)	**0.001**
VAS fatigue (0–100)	65.0 (50.0; 80.0)	70.0 (55.0; 85.0)	**< 0.001**	65.0 (50.0; 80.0)	70.0 (55.0; 85.0)	**< 0.001**	80.0 (45.0; 80.0)	75.0 (55.0; 85.0)	**< 0.001**
HAQ	1.4 (1.0; 1.8)	1.6 (1.3; 2.0)	**< 0.001**	1.1 (0.8; 1.5)	1.3 (0.8; 1.6)	**< 0.001**	1.3 (0.9; 1.5)	1.5 (1.0; 1.9)	**< 0.001**
EQ-5D (0–1)	0.2 (0.1; 0.7)	0.1 (0.0; 0.6)	**< 0.001**	0.2 (0.1; 0.7)	0.2 (0.1; 0.6)	**0.035**	0.2 (0.1; 0.7)	0.1 (0.1; 0.6)	**0.005**

Values are median (IQR) if not stated otherwise.

Table 2. Response to first TT and drug survival at 12 months (Δ= M12-M0)

	RA (n=1602)			AxSpA (n=1306)			PsA (n=493)		
	M	F	p	M	F	p	M	F	p
Δ VAS pain (0–100)	-30.0 (-55.0; -15.0)	-35.0 (-55.0; -15.0)	0.566	-40.0 (-60.0; -25.0)	-40.0 (-60.0; -15.0)	0.109	-40.0 (-55.0; -15.0)	-40.0 (-65.0; -15.0)	0.364
Δ VAS fatigue (0–100)	-30.0 (-50.0; -10.0)	-30.0 (-55.0; -10.0)	0.734	-35.0 (-50.0; -15.0)	-35.0 (-55.0; -10.0)	0.738	-30.0 (-55.0; -15.0)	-40.0 (-60.0; -35.0)	0.174
Δ HAQ	-0.5 (-0.9; -0.1)	-0.5 (-1.0; -0.1)	0.463	-0.5 (-0.9; -0.1)	-0.5 (-0.9; -0.1)	0.929	-0.5 (-0.9; -0.3)	-0.5 (-0.9; 0.0)	0.232
Δ EQ-5D (0–1)	0.4 (0.0; 0.6)	0.5 (0.0; 0.7)	0.156	0.5 (0.1; 0.6)	0.5 (0.1; 0.6)	0.602	0.5 (0.1; 0.7)	0.5 (0.1; 0.7)	0.648
Δ CRP	-11.0 (-25.9; -1.0)	-7.9 (-20.7; -1.0)	0.091	-14.9 (-26.6; -7.2)	-10.0 (-19.5; -2.7)	**< 0.001**	11.0 (-27.0; -3.1)	-8.2 (-20.0; -1.7)	**0.005**
Survival (%)	80 (76; 84)	76 (73; 78)	0.182	89 (87; 91)	79 (75; 83)	**< 0.001**	88 (84; 92)	83 (78; 88)	0.146

Values are median (IQR)

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Validation of outcome measures and biomarkers

AB1234 MICRO-RNA 155 AND MIR-34A: POSSIBLE BIOMARKERS OF INFLAMMATORY BURDEN AND DISEASE ACTIVITY IN ANCA-ASSOCIATED VASCULITIS WITH RENAL INVOLVEMENT

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Background: Predicting clinical outcomes in ANCA-related glomerulonephritis remains a major challenge. To date, there is no reliable biomarker able to predict renal prognosis in patients with ANCA-associated vasculitis (AAV). Micro-RNA (miRNA) are non-coding RNAs involved in the fine tuning of immune cells biology and this epigenetic modulation associates with different phenotypes and prognosis in several diseases.
Objectives: To investigate the expression of miR-155 and miR-34a in kidney biopsies of AAV patients according with renal outcome.
Methods: Fifteen patients with AAV and renal involvement (mean age 63.0 ±13.3 years, disease duration 4.9±2.2 months), who underwent renal biopsy. Demographic, clinical and autoimmune parameters were recorded for each patient. Each kidney biopsy was classified according to the Berden Classification, Risk group (according to the ANCA Renal Risk Score) and the chronicity Classification of the Mayo Clinic's proposed score.
MiR-155 and miR-34a expression was investigated on kidney biopsy tissue using the miRNeasy FFPE kit (Qiagen). The quantitative expression of miR-155, miR-34a and housekeeping gene U1, used as control, was assessed by Real Time-PCR. MiR-155 and miR-34a expression was correlated with histopathological and clinical-laboratory parameters.
Each patient was followed for 12 months and renal outcome was considered according to *KDIGO CKD* Classification. Markers of inflammation (ESR, CRP) and urine analysis data were recorded at baseline and after 12 months.
Results: Six (40%) patients were p-ANCA positive and 9 (60%) c-ANCA positive. Eight patients (53%) also had pulmonary involvement. The mean baseline GFR was 30.7±28.8 ml/min/1.73 m^2 and 10 patients (66%) showed an active urinary sediment.
At disease onset, the mean expression of miR-155 was 9.5±21.1, while the expression of mir-34a was 13.1±46.2. Considering the autoimmune profile, kidney tissue of p-ANCA positive patients was enriched of mir-155 (19.6±30.6 fold) compared to c-ANCA positive patients (1.9±2.9 fold; p=0.001). Particularly, considering the renal function, kidney tissue of patients with greater impairment of renal function (*KDIGO stage 5)* was enriched of miR-155 (21.5±38.3 fold) compared to patients with less renal impairment (*KDIGO stage 1-4*) (4.72±8.16 fold, p=0.004).
Tissue expression of miR-155 and miR-34a did not correlated with the above-mentioned histopathological classifications.
After 12 months from kidney biopsy, 3(20%) patients had a worsening of renal function, 5 (33%) still presented elevated markers of inflammation and 3 (20%) still had proteinuria at urine analysis. At baseline, kidney tissue of patients with higher CRP plasma levels and proteinuria at follow-up presented higher expression of miR-155 (p=0.002 and p=0.001), whereas no significant differences were found about miR-34a kidney tissue expression.
Conclusion: MiRNAs may play a potential role in the pathogenesis of ANCA-related glomerulonephritis. MiR-155 kidney enrichment seems to mirror the disease inflammatory burden and activity at the onset and after 12 months representing a possible biomarker in ANCA vasculitis with renal involvement. This finding may represent the basis for further studies on miRNA expression in blood samples, aiming to identify a non-invasive biomarker of kidney damage, predicting disease's relapses and patients' prognosis.
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AB1235 SALIVARY LEVEL OF CALPROTECTIN (MRP 8/14) AS A BIOMARKER FOR SJÖGREN SYNDROME – A PROSPECTIVE OBSERVATIONAL STUDY

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Background:
Objectives: Calprotectin (MRP 8/14) is secreted by neutrophils and monocytes in an inflammatory milieu(1). Increased levels of calprotectin in blood and faeces has been previously shown in patients with primary Sjogren's syndrome(pSS)(2). We hypothesised Calprotectin in saliva may therefore potentially reflect inflammation in salivary glands. In the present study, we aimed to assess the utility of salivary calprotectin as a biomarker in pSS and to evaluate the potential association of calprotectin with clinical features, laboratory markers and disease activity indexes in pSS.
Methods: Consecutive patients attending rheumatology clinic between September 2016 and July 2017 of age more than 18 years fulfilling either American European Consensus Group (AECG) 2002 or 2016 American College of Rheumatology/European League Against Rheumatism Classification Criteria for Primary Sjogren's Syndrome, constituted the case group. Patients with sicca non-pSS and rheumatoid arthritis patients satisfying ACR/EULAR criteria 2010 were recruited as disease controls. Age and sex-matched healthy subjects were recruited as a controls. Patient history, signs and symptoms, laboratory investigations, ESSDAI and ESSPRI scoring were noted for cases and disease controls. Unstimulated saliva was collected by the spitting method. Salivary calprotectin levels were quantified by commercially available ELISA kit(R&D Systems, MN, USA).
Results: A total of 42 pSS cases (41.5911.21 years, 40 women), 40 disease controls (47.629.81 years, 39 women) and 30 healthy controls (3610.65 years, 29 women) were recruited. In pSS and disease controls, the median levels of salivary calprotectin [38.5(81) and 52(69.5 ng/ml)] were significantly higher compared to healthy controls [26.5(29) {p=0.001}]. Salivary calprotectin levels in pSS was positively associated with oral symptoms and negatively associated with immunosuppression of 1 year and more(P=0.04 and 0.03 respectively),but not ESSDAI,ESSPRI scores or lab parameters.
Conclusion: Salivary calprotectin was elevated in pSS compared to healthy subjects and was found to be positively associated with oral symptoms and with immunosuppressive treatment.
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AB1236 KL-6 AS A BIOMARKER FOR SJÖGREN SYNDROME-ASSOCIATED INTERSTITIAL LUNG DISEASE: METHODOLOGY MATTERS

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Background: Krebs von den Lungen-6 (KL-6) was recently found to be a serum biomarker for various disease associated interstitial lung disease (ILD) including primary Sjögren syndrome (pSS).[1] KL-6 is a high-molecular-weight glycoprotein in the Mucin 1 protein group and is majorly expressed by regenerating type II pneumocytes; hence, serum KL-6 levels may reflect the severity of pulmonary damage with regeneration.[2] Human KL-6 also promotes the proliferation and survival of pulmonary fibroblasts and the differentiation of myofibroblasts, which enhance fibrosis.[3, 4]

Objectives: To evaluate the agreement between the latex particle-enhanced turbidimetric immunoassay with enzyme-linked immunosorbent assay (ELISA) and association with clinical phenotypes.

Methods: This retrospective case-control study included 39 patients with pSS, of whom 21 (53.85%) patients developed ILD at the end of follow-up. The serum KL-6 level was compared between latex particle-enhanced turbidimetric immunoassay (Nanopia) and ELISA (MBS2601395; MyBioSource, CA, USA). Electronic medical records were reviewed, including clinical information, images, pulmonary function test, and laboratory results on inclusion, and a chest physician reviewed the results of pulmonary radiography.

Results: The two serum KL-6 immunoassays revealed a moderate correlation with a Pearson product-moment correlation coefficient of 0.427. Serum KL-6 levels, measured using ELISA, were 1920.10 ± 1974.26 U/mL and 894.11 ± 788.53 U/mL in the ILD and non-ILD groups, respectively (p = 0.001). The latex particle-enhanced turbidimetric immunoassay for serum KL-6 was 459.62 ± 331.41 U/mL and 265.33 ± 105.37 U/mL in the ILD and non-ILD group, respectively (p = 0.074). The predictive values of serum KL-6 in the area under the receiver-operating characteristic curve were 0.810 and 0.669 in ELISA and latex particle-enhanced turbidimetric immunoassay, respectively.

Conclusion: Serum KL-6 is a predicting biomarker in pSS patients who may develop ILD. However, the methodology of immunoassay may influence the efficacy of the prediction and clinical association.

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AB1237 DIAGNOSTIC VALUE OF PROTEASOMAL AND AUTOPHAGIC MARKERS IN MUSCULAR DISEASES

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Background: Deficient cellular degradation pathways such as autophagy and the ubiquitin proteasome system (UPS) show a correlation with the onset of neurodegenerative diseases. Especially immune-mediated inflammatory myopathies often show therapy-resistant phenotypes with medical need for further understanding of pathogenesis und possible treatment.

Objectives: The aim of this work was to study an association of these two degradation pathways in a large group of different muscle entities and to examine a possible influence in the pathogenesis of the investigated muscle diseases. Furthermore, a potential benefit in diagnostics was studied using factors such as ubiquitin, p62, NBR1 and LC3 and their role as adapter molecules.

Methods: We examined ubiquitin, p62, NBR1 and LC3 on muscle biopsies from patients with the diagnosis of s-IBM, dermato- and polymyositis, muscular dystrophy, neurogenic atrophy, myotonic dystrophy type II (PROMM) and metabolic myopathies such as Pompe and McArdle disease. Immunohistochemical single and double stainings as well as immunofluorescence stainings were performed on cryosections. Furthermore, Western blot analysis was performed. The use of a histological score, defined as the product of the frequency of positive fibres and staining intensity, was used to investigate possible differences between the diseases in the expression of the investigated factors.

Results: Especially in s-IBM, myofibrillar myopathies and Pompe disease, proteasomal and autophagic markers were detected. On the other hand, neurogenic atrophy, McArdle disease and the majority of the myotonic dystrophies type II showed no positive signals, except for p62, which was detected especially in internalized nuclei and regenerative fibres. Overall, in all entities in regenerative and necrotic as well as in atrophic fibres, a positive staining for ubiquitin, p62, NBR1 and LC3 could be shown. Dermatomyositis showed a moderate immunoreactivity for p62 and NBR1 in the area of the perifascicular atrophy. Polymyositis showed a strong endomysial reaction in the area of the attacked muscle fibres, especially in the area of the lymphocytic infiltrates. The histological score showed that ubiquitin was significantly higher in s-IBM than in polymyositis. NBR1 was significantly higher in s-IBM than in dermatomyositis and muscular dystrophies. LC3 and p62 showed a significantly higher level in s-IBM as compared to dermatomyositis and polymyositis. Except for NBR1, a positive correlation of autophagic and proteasomal markers was shown in dermatomyositis. There was also a positive correlation between LC3 and ubiquitin in polymyositis. Using multivariate analysis and recursive partitioning, we could show a predictability of the diagnosis of s-IBM with a LC3 score above 3. On the other hand, a value below 3 excluded the diagnosis of s-IBM.

Conclusion: In particular, s-IBM, myofibrillar myopathies and Pompe disease showed a possible involvement disturbed proteasomal and autophagic degradation pathways in their pathogenesis. In addition, p62 and NBR1 seemed to have an important role in the immune response. Furthermore, the altered autophagic and proteasomal degradation pathways may be involved in ageing processes, sarcopenia and disease. In particular, LC3 seems to be suitable as a screening marker to recognize an idiopathic inflammatory myopathy. The other markers, such as p62, LC3, and NBR1, would be able to distinguish between the subgroups of idiopathic inflammatory myopathies. Therefore, LC3 could be included as a marker in the routine of neuropathological diagnostics. Further studies are needed to fully understand the role of proteasomal and autophagic factors in possible immune suppressive and immune modulatory therapies and to assess possible side effects.

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AB1238 THE ARABIC LUPUSPRO: CROSS-CULTURAL VALIDATION OF A DISEASE-SPECIFIC PATIENT-REPORTED OUTCOME TOOL FOR QUALITY OF LIFE IN LUPUS PATIENTS

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Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with high morbidity and disability that affects all aspects of quality of life (QoL). (1) LupusPRO is a disease-targeted patient-reported outcome tool for the measurement of health and non-health related quality of life (HRQoL and Non-HRQoL) in SLE patients. (2)

Objectives: To translate, cross-culturally adapt, and validate the LupusPRO v.1.8 into the Arabic Language.

Methods: LupusPRO v.1.8 was translated into Arabic following the forward-backward translation guideline. (3) The Arabic version of LupusPRO was subsequently applied to 107 Egyptian SLE patients. To assess test-retest reliability, the Arabic LupusPRO was completed on two occasions, two weeks apart. Validation was performed against the Arabic version of Medical Outcomes Study Short Form (SF-36), the Systemic Lupus Erythematosus Disease Activity Index (SELENA-SLEDAI) and the Systemic Lupus International Collaborating Clinics/American College of Rheumatology damage index (SDI). Discriminant validity of Arabic LupusPRO was evaluated against the SF-36 (item 1), while the conceptual framework was evaluated by the confirmatory factor analysis (CFA).

Results: The study included 107 patients, 95% of whom were women. Their median age was 32 (range:18-55) years. Arabic LupusPRO's Cronbach's alpha ranged from 0.71 to 0.98 except for the social support domain (0.65). Test-retest reliability ranged from 0.83 to 0.98. Convergent validity with corresponding domains of the SF-36 was satisfactory. Criterion validity showed a weak and non-significant correlation of lupusPRO domains with SDI except for physical domain and significant weak correlation with SELENA-SLEDAI (Table1).

Discriminant validity showed acceptable results against the SF-36 (item 1). The CFA showed good model fit indices for the hypothesized item-to-scale relationships (CFI =0.988, TLI = 0.987, and RMSEA=0.062), with most of item-to-scale loadings greater than 0.9.

Conclusion: The Arabic version of LupusPRO v1.8 is a reliable and valid tool for measuring QoL(HRQoL and Non-HRQoL) in Arabic-speaking SLE patients.

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Table 1. Validity of the Arabic LupusPRO against disease activity, damage index and SF-36

LupusPRO Domain	Validity			
	SF-36		Total SLEDAI	Total SDI
	Domain	Rho (*P*)	Rho (*P*)	Rho (*P*)
Lupus Symptoms			-0.25 (0.010)	-0.17 (0.08)
Cognition			-0.15 (0.117)	-0.21 (0.03)
Lupus Medications			-0.22 (0.021)	-0.37 (0.001)
Procreation			0.003 (0.977)	-0.20 (0.04)
Physical Health	RF	0.84 (<0.001)	-0.34 (<0.001)	-0.31 (0.001)
	RP	0.75 (<0.001)		
Sleep			-0.32 (0.001)	-0.09 (0.33)
Fatigue	VT	0.80 (<0.001)	-0.33 (0.001)	-0.12 (0.33)
Pain	BP	0.86 (<0.001)	-0.22 (0.026)	-0.18 (0.07)
Emotional Health	MH	0.74 (<0.001)	-0.33 (0.001)	-0.19 (0.05)
	RE	0.80 (<0.001)		
Body Image			-0.30 (0.002)	-0.25 (0.008)
Desire/Goals			-0.28 (0.004)	-0.10 (0.30)
Social Support			0.22 (0.02)	-0.20 (0.04)
Coping			0.07 (0.461)	-0.20 (0.03)
Satisfaction of Medical Care			0.18 (0.066)	-0.11 (0.24)
HRQoL	GH	0.81 (<0.001)	-0.37 (<0.001)	-0.28 (0.004)
None-HRQoL			-0.08 (0.42)	-0.26 (0.007)

PF: Physical functioning; RP: role physical; RE: role emotional; VT: vitality; MH: Mental health; BP: Bodily Pain; GH: General health.

Disclosure of Interests: None declared

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AB1239

THE EFFECT OF INFLUENZA VACCINATION ON THE MULTI-BIOMARKER DISEASE ACTIVITY SCORE AND ITS COMPONENT BIOMARKERS IN HEALTHY SUBJECTS

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Background: The multi-biomarker disease activity (MBDA) blood test measures 12 protein biomarkers (IL-6, CRP, SAA, EGF, VEGF, VCAM, MMP-1, MMP-3, leptin, resistin, TNF-RI and YKL40). It uses a validated algorithm to provide a score on a scale of 1-100 for assessing disease activity in patients with rheumatoid arthritis (RA). The MBDA score reflects several molecular aspects of inflammation, including cytokines, acute phase reactants, growth factors, molecular adhesion, metalloproteinases and hormones. Insights gained by understanding how vaccination affects these biomarkers in healthy subjects - in whom the level of inflammation prior to vaccination should be low and stable - may aid the understanding of how vaccination affects patients with RA.

Objectives: The goal of this study was to understand how immunization of healthy subjects with the influenza vaccine affects the assessment of inflammation with the MBDA score and its 12 biomarkers.

Methods: A 4-strain influenza virus vaccine (Fluarix Quadrivalent, GlaxoSmith-Kline) was administered intramuscularly to 22 healthy volunteer subjects on October 24, 2018. Serum samples were obtained immediately prior to vaccination (baseline) and 1, 2 and 3 weeks after vaccination. No restrictions were placed on subject activity. Samples were stored at -80 °C until measurement of the 12 MBDA biomarkers for determination of the adjusted MBDA score, hereafter called the MBDA score. (Adjustment accounts for the effects of age, sex and adiposity[1]). MBDA scores (natural scale) and biomarker concentrations (log scale) were modeled using generalized estimating equations (GEE) that account for correlations between measurements from the same subject at multiple timepoints. Significance of MBDA score change or biomarker concentration change over time was determined by a likelihood ratio test of timepoints.

Results: Of the 22 healthy subjects receiving the influenza virus vaccine, 14 (63.6%) were female, with mean (SD) age of 40.0 years (8.9). MBDA scores were low (<30), moderate (30-44) or high (>44) for 15 (68%), 6 (27%) and 1 (5%) subjects at baseline, and this distribution was stable over time (Figure 1). Overall, MBDA scores did not change significantly over time (p=0.48, Figure 2). Mean changes in MBDA score (95% CI) from baseline to weeks 1, 2 and 3 were 0.32 (-3.07, 3.71), 0.82 (-3.03, 4.67) and 2.86 (-1.10, 6.82), respectively (Figure 2); the week 3 value becomes 0.95 (-1.78, 3.68) if the week 3 outlier is removed. Among the 66 post-baseline measurements of change in MBDA score (Figure 2), 3 (5%) exceeded the 95% CI for change in MBDA score in this study (i.e., 14). When assessing the entire cohort across all timepoints, EGF was the only biomarker that demonstrated statistically significant change over time ($p=5.6 \times 10^{-7}$). At weeks 1, 2 and 3, the mean relative concentrations of EGF, compared with baseline, were 0.62 (0.52, 0.74), 0.86 (0.70, 1.06) and 0.62 (0.50, 0.76), respectively.

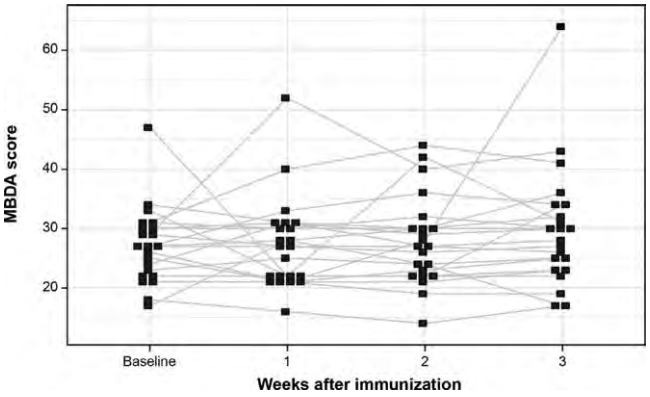


Figure 1

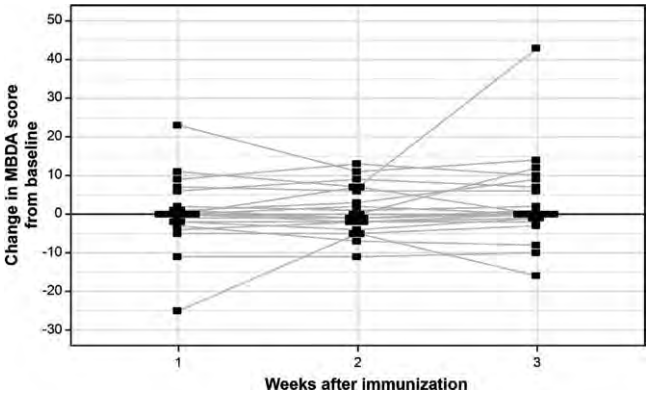


Figure 2

Conclusion: Immunization of 22 healthy subjects with a quadrivalent influenza vaccine did not have a statistically significant effect on MBDA scores during a 3-week observation, and it had minimal effect on the component biomarkers.

References:

[1] Curtis et al. *Rheumatology [Oxford]* 2018;58:874

Disclosure of Interests: Daniel Furst Grant/research support from: AbbVie, Actelion, Amgen, BMS, Corbus Pharmaceuticals, the National Institutes of Health, Novartis, Pfizer, and Roche/Genentech, Consultant of: AbbVie, Actelion, Amgen, BMS, Cytori Therapeutics, Corbus Pharmaceuticals, the National Institutes of Health, Novartis, Pfizer, and Roche/Genentech, Speakers bureau: CMC Connect (McCann Health Company), Lauren Lenz Shareholder of: Myriad Genetics,

Inc., Employee of: Myriad Genetics, Inc., Megan Horton Shareholder of: Myriad Genetics, Inc., Employee of: Myriad Genetics, Inc., Darl Flake Shareholder of: Myriad Genetics, Inc., Employee of: Myriad Genetics, Inc., Eric Sasso Shareholder of: Myriad Genetics, Inc., Employee of: Myriad Genetics, Inc., Michael E. Weinblatt Grant/research support from: BMS, Amgen, Lilly, Crescendo and Sonofi-Regeneron, Consultant of: Horizon Therapeutics, Bristol-Myers Squibb, Amgen, Abbvie, Crescendo, Lilly, Pfizer, Roche, Gilead

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AB1240 C4B BINDING PROTEIN AND WARFARIN IN THE ANTIPHOSPHOLIPID SYNDROME

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Background: Complement plays a role in the Antiphospholipid Syndrome (APS). C4b Binding Protein (C4BP) is a complement inhibitor with anticoagulant function (1). It belongs to the same protein family as β2GPI, the main antigen in APS. Its main isoform is bound to protein S in the circulation. Levels of both protein S and C4BP are known to be reduced by warfarin treatment (2) as well as by aPL, directly and indirectly.

Objectives: To investigate the levels of C4BP in primary (p) and secondary (s) APS, also considering warfarin treatment.

Methods: The total amount of C4BP (C4BPt) was measured by using magnetic carboxylated microspheres which were coupled with a monoclonal antibody against the α-chain of human-C4BP to capture the antigen. To detect C4BPt the same antibody was used, biotinylated. The binding of biotinylated antibodies was detected by streptavidin-phycoerythrin and data were collected using a MAGPIX Multiplex Reader. Using independent t-test, we compared C4BP in 118 SLE patients with repeated positivity for Antiphospholipid antibodies (aPL) (39/118 on warfarin), 291 aPL negative SLE patients (16/291 on warfarin), 67 pAPS (33/67 on warfarin), and 322 controls (none on warfarin). We then performed an interaction and a mediation analysis (3) in the SLE group to study the impact of warfarin on C4BP levels: since warfarin is mostly prescribed to aPL+ patients, it is considered a mediator in the reducing effect of aPL on C4BP. Therefore we compared individuals exposed and non-exposed to the presence of aPL with or without the mediator warfarin and calculated the percentage of reduction in C4BP that could be attributed to aPL or warfarin.

Results: Overall C4BP is 20% reduced in aPL+ patients (fig 1), independently of SLE, past thrombotic events and nephritis. Warfarin treated patients have lower levels of C4BP (fig 2). According to mediation analysis 11% of C4BP reduction is due to aPL and 9% to warfarin.

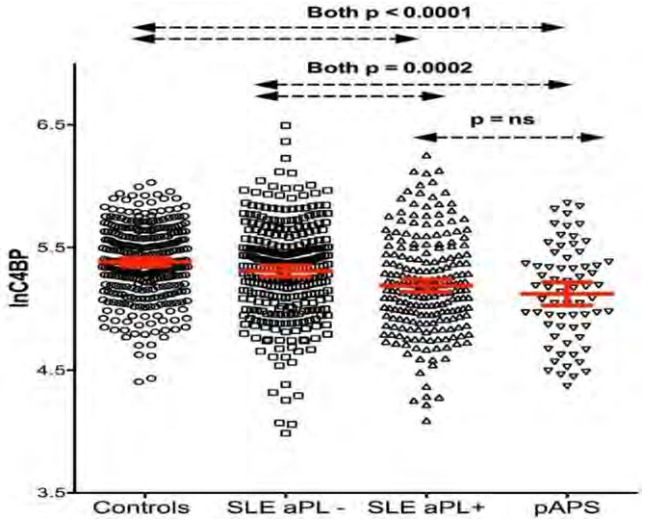


Figure 1. C4BP in different subgroups (67 pAPS, 118 SLEaPL+, 291 SLEaPL-, 322 controls)

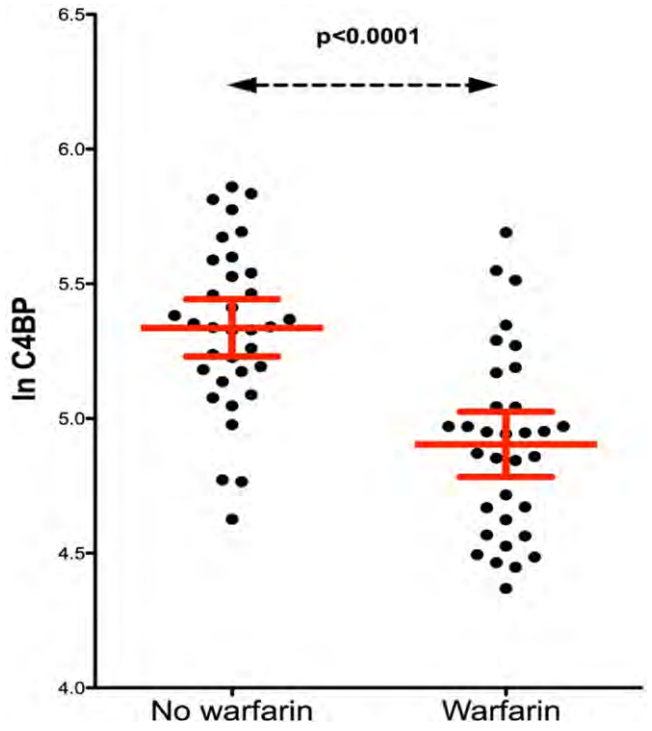


Figure 2. C4BP in 67 pAPS patients, 33/67 on warfarin

Conclusion: Both aPL and warfarin decrease levels of C4BP, a complement and coagulation regulator. Reduction of this complement inhibitor could contribute to complement activation and thrombosis in APS. Our results raise new questions regarding the effects of warfarin treatment on complement and coagulation in APS.

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Disclaimer: AV is employed at the Swedish Medical Products Agency, the views expressed in this paper are the personal views of the authors and not necessarily the views of the Governement Agency

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Disclosure of Interests: None declared

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AB1241 EVALUATION OF A PATIENT COMPLETED DISEASE FLARE QUESTIONNAIRE IN PSORIATIC DISEASE

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Background: Psoriatic Disease (PsD) is a chronic inflammatory disease of the skin, nails, joints, and entheses. A number of composite disease activity measures have been developed though there is yet consensus as to which to use in the clinic and in clinical trials. A patient completed disease flare questionnaire, covering multiple domains of disease impact, has been developed but has yet to be fully validated.

Objectives: To validate the FLARE questionnaire in PsD.

Methods: The 10 question FLARE instrument[1] was administered to 141 patients in an observational study of treatment change in PsD over 6 months follow up. Disease activity was measured by the PASDAS and the gold standard of flare

was based on patient opinion. ROC curve was constructed to examine the optimum cut-off for disease flare. Agreement between the FLARE instrument and patient opinion was assessed by Cohen's kappa. Test-retest was assessed in 28 patients with stable disease who underwent repeat assessment within 2 weeks and evaluated by intra-class correlation coefficient (ICC).

Results: The FLARE questionnaire was administered at 367 patient encounters. ROC analysis indicated that the optimum cut-off for a flare of disease was 4 (sensitivity 82%, specificity 76%; area under curve 0.85: figure). Mean PASDAS scores were 2.7 and 6.3 for no-flare (4) and flare (≥4) respectively (p = < 0.0001). For those patients who were having a flare the frequency of response to each question is given in the table. Agreement between patient opinion and questionnaire was 0.57, and between patient opinion and physician (based on treatment escalation) 0.43. ICC for the questionnaire was 0.87 (95% CI 0.72 – 0.94).

Conclusion: In PsD a flare represents escalation of symptoms and signs across multiple domains, as measured by the FLARE instrument; a score of 4 or more has external validity both in terms of composite disease activity and overall patient opinion of the state of their condition.

References:

[1] Moverley A, Waxman R, de Wit M, Parkinson A, Campbell W, Brooke M, et al J Rheum May 2016, 43 (5) 974-978

Table FLARE item response for those in flare vs not in flare

Item	FLARE instrument score <4	FLARE instrument score ≥4
	N (%)	N (%)
Worsening Itch	35 (19)	108 (58)
Worsening skin area	27 (15)	91 (49)
Increasing joint pain	34 (19)	161 (86)
Increasing number of tender joints	20 (11)	142 (76)
Decrease in ability to perform activities	3 (2)	81 (43)
Worsening in ability to move easily	8 (4)	126 (67)
Increase in frustration	14 (8)	142 (76)
Worsening in depression	8 (4)	90 (48)
Worsening in feeling of tiredness all the time	37 (21)	148 (79)
Worsening in the number or combination of symptoms from your disease	7 (4)	134 (72)

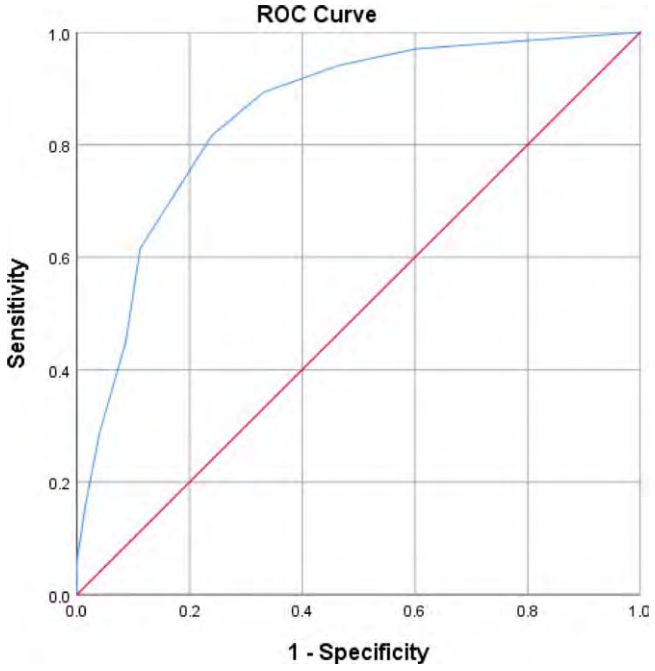


Figure. ROC analysis of FLARE questionnaire

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Disclosure of Interests: Philip Helliwell: None declared, William Tillett Grant/research support from: AbbVie, Celgene, Eli Lilly, Janssen, Novartis, Pfizer Inc, UCB, Consultant of: AbbVie, Amgen, Celgene, Lilly, Janssen, Novartis, MSD, Pfizer Inc, UCB, Speakers bureau: AbbVie, Amgen, Celgene, Lilly, Janssen, Novartis, Pfizer Inc, UCB, Robin Waxman: None declared, Laura C Coates: None declared, Oliver FitzGerald: None declared, Jon Packham: None declared, Neil McHugh: None declared

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AB1242 A NOVEL BIOMARKER OF MMP-CLEAVED PROLARGIN IS ELEVATED IN PATIENTS WITH PSORIATIC ARTHRITIS COMPARED TO OTHER FIBRO-INFLAMMATORY DISEASES

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Background: Psoriatic Arthritis (PsA) is a chronic inflammatory disease, characterized by involvement of skin, axial and peripheral skeleton. Prolargin is a class II small leucine-rich proteoglycan found to be expressed in connective tissues of patients with PsA, and previously suggested to be remodelled upon treatment. Fragments of prolargin could quantify tissue turnover in individuals with PsA and reflect pathological tissue changes in these patients.

Objectives: This study aimed at developing an immunoassay targeting a neo-epitope of prolargin cleaved by matrix metalloproteinases (MMPs), named PROM; and measure PROM levels in serum from two cohorts of patients affected by PsA and healthy controls.

Methods: Development of a novel immunoassay targeting a specific MMP-generated neo-epitope fragment of prolargin (PROM) together with technical validation was performed, and then evaluated in serum from two independent cohorts. The technical validation included inter- and intra-variation, linearity, spiking recovery, stability and specificity. Specificity was tested using an elongated peptide, a truncated peptide and a non-sense peptide. The Discovery Cohort consists of 13 healthy individuals and 11 PsA patients, mean age 58, 60.3% female and 100% caucasian. The Validation Cohort included 35 healthy individuals and 112 PsA patients with low disease activity included in a 24-week randomized, double-blind, placebo-controlled trial of 3g n-3 polyunsaturated fatty acids (PUFA), a cohort of patients diagnosed with PsA by the CASPAR criteria. These patients had a mean age of 50.8, 57.8 % female and 100 % caucasian. Clinical variables and serum samples were collected at baseline and after 24 weeks of follow-up. An unpaired t-test was used for evaluation of healthy individuals and patients affected by PsA, while a paired t-test was used for evaluation of treatment at baseline and after 24 weeks.

Results: A technically robust and specific assay was developed. The inter- and intra-assay variation of PROM was determined as 14% and 4 % respectively. PROM showed a good dilution recovery, spiking recovery, and storage /freeze-thaw stability (All, 100%±20%). PROM showed to be specific towards the targeted sequence, and did not show any reactivity towards the truncated peptide, elongated peptide or non-sense peptide. In the Discovery Cohort, serum levels of PROM were increased in patients with PsA compared to healthy individuals (p=0.032, Figure 1A). This increase was confirmed by the Validation Cohort, where PsA patients were significantly increased compared to healthy individuals at baseline (p=0.002, Figure 1B). After 24 weeks, the levels of PROM were unchanged in the n-3 PUFA treated group.

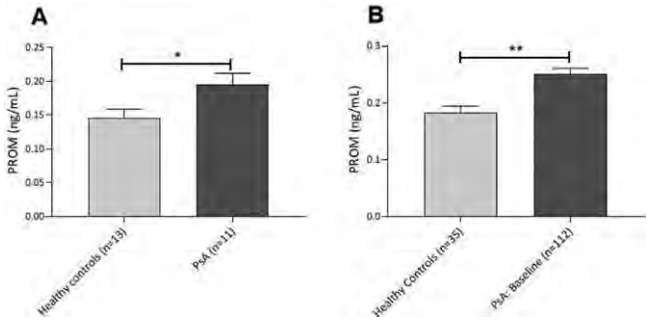


Figure 1.

Conclusion: The novel biomarker PROM, reflecting connective tissue remodeling, is elevated in PsA patients compared to healthy controls in two independent cohorts. No significant association was found for PROM in a low disease activity group of PsA patients treated with n-3 PUFA.

References: None

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Disclosure of Interests: Dovile Sinkeviciute Grant/research support from: Industrial PhD Student, Employee of: Industrial PhD Student, Annette Schlemmer: None declared, Erik Berg Schmidt: None declared, Anne-Christine Bay-Jensen

Shareholder of: Nordic Bioscience A/S, Employee of: Full time employee at Nordic Bioscience A/S., Morten Karsdal Shareholder of: Nordic Bioscience A/S., Employee of: Full time employee at Nordic Bioscience A/S., Jeppe Hagstrup Christensen: None declared, Salome Kristensen: None declared, Signe Holm Nielsen Employee of: Full time employee at Nordic Bioscience

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AB1243 TRAINING AND VALIDATION OF A MULTIVARIATE PREDICTOR OF RISK OF RADIOGRAPHIC PROGRESSION FOR PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The multi-biomarker disease activity (MBDA) score, adjusted for age, sex and adiposity ($MBDA_{adj}$), has been shown to be better than several conventional disease activity measures for predicting risk for radiographic progression (RP) in patients with rheumatoid arthritis (RA).[1] Serologic status and other non-disease activity measures are also predictive of RP risk. Combining them with the $MBDA_{adj}$ should result in a stronger prognostic test for RP than any one measure alone.
Objectives: Develop a multivariate model for predicting risk for RP that includes the adjusted MBDA score and other known predictors of RP.
Methods: Four RA cohorts were used, two for training (OPERA and BRASS, n=555) and two for validation (SWEFOT and Leiden, n=397). Each pair of cohorts was heterogeneous in disease duration and treatment history. BMI data were not available for one validation cohort, so a BMI surrogate was modeled using forward selection with the two training cohorts and 3 others (CERTAIN, InFoRM, RACER) (N=1411). An RP risk score was then trained using forward selection in a linear mixed-effects regression, considering disease-related and demographic variables as predictors of change in modified total Sharp score over one year (ΔmTSS), with a random effect on cohort. The RP risk score was validated as a predictor of RP with two cutoffs (ΔmTSS >3 and >5) using logistic mixed-effects regression. Odds ratios (OR) and 95% profile likelihood-based confidence intervals (CI) were calculated from the models and significance was assessed by likelihood ratio tests. Risk curves were generated to show probability of RP as a function of the RP risk score.
Results: The BMI surrogate included leptin, sex, age and age^2 and correlated well with BMI ($\rho = 0.76$). In training, the most significant independent predictors of RP were $MBDA_{adj}$ ($p = 0.00020$), seropositivity ($p = 9.3 \times 10^{-5}$), BMI surrogate score ($p = 0.013$) and use of targeted therapy ($p = 0.0026$). The final model was: RP risk score = 0.024 x $MBDA_{adj}$ + 0.093 if seropositive – 0.063 x BMI surrogate score – 0.61 if using a targeted therapy. In validation, the OR (95% CI) of the RP risk score for predicting ΔTSS >3 or >5 were 2.2 (1.6, 3.2) ($p = 2.6 \times 10^{-6}$) and 3.1 (2.0, 5.0) ($p = 5.7 \times 10^{-8}$), respectively (Figure 1). The odds of a patient having RP increases by 50% for each 21-unit or 15-unit increase in $MBDA_{adj}$, for RP defined as ΔTSS >3 or >5, respectively.

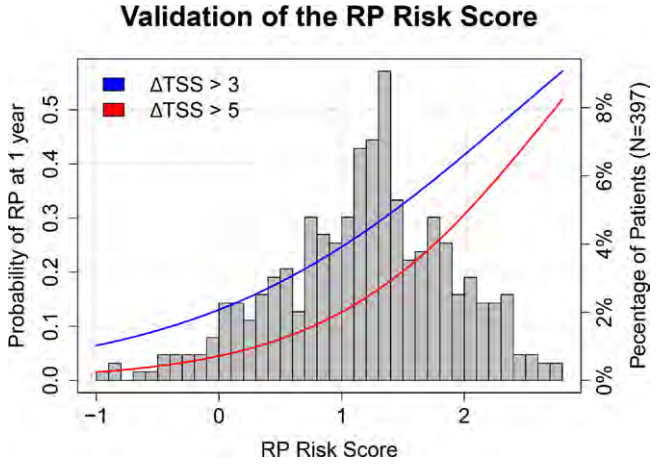


Figure 1.

Conclusion: A multivariate model containing adjusted MBDA score, seropositivity, a BMI surrogate and use of targeted therapy has been trained and validated as a prognostic test for radiographic progression in RA.
References:

[1] Curtis, et al. *Rheumatology [Oxford].* 2018;58:874

Disclosure of Interests: Thomas Huizinga Grant/research support from: Ablynx, Bristol-Myers Squibb, Roche, Sanofi, Consultant of: Ablynx, Bristol-Myers Squibb, Roche, Sanofi, Michael E. Weinblatt Grant/research support from: BMS, Amgen, Lilly, Crescendo and Sonofi-Regeneron, Consultant of: Horizon Therapeutics, Bristol-Myers Squibb, Amgen, Abbvie, Crescendo, Lilly, Pfizer, Roche, Gilead, Nancy Shadick Grant/research support from: Mallinckrodt, BMS, Lilly, Amgen, Crescendo Biosciences, and Sanofi-Regeneron, Consultant of: BMS, Cecilie Heegaard Brahe: None declared, Mikkel Østergaard Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Merck, and Novartis, Consultant of: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo Nordisk, Orion, Pfizer, Regeneron, Roche, Sandoz, Sanofi, and UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo Nordisk, Orion, Pfizer, Regeneron, Roche, Sandoz, Sanofi, and UCB, Merete L. Hetland Grant/research support from: BMS, MSD, AbbVie, Roche, Novartis, Biogen and Pfizer, Consultant of: Eli Lilly, Speakers bureau: Orion Pharma, Biogen, Pfizer, CellTrion, Merck and Samsung Bioepis, Saedis Saevarsdottir Employee of: Part-time at deCODE Genetics/Amgen Inc, working on genetic research unrelated to this project, Megan Horton Shareholder of: Myriad Genetics, Inc., Employee of: Myriad Genetics, Inc., Brent Mabey Shareholder of: Myriad Genetics, Inc., Employee of: Myriad Genetics, Inc., Darl Flake Shareholder of: Myriad Genetics, Inc., Employee of: Myriad Genetics, Inc., Rotem Ben-Shachar Shareholder of: Myriad Genetics, Inc., Employee of: Myriad Genetics, Inc., Eric Sasso Shareholder of: Myriad Genetics, Inc., Employee of: Myriad Genetics, Inc., Alexander Gutin Shareholder of: Myriad Genetics, Inc., Employee of: Myriad Genetics, Inc., Elena Hitraya Shareholder of: Myriad Genetics, Inc., Employee of: Myriad Genetics, Inc., Jerry Lanchbury Shareholder of: Myriad Genetics, Inc., Employee of: Myriad Genetics, Inc., Jeffrey Curtis Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Janssen, Lilly, Myriad, Pfizer, Regeneron, Roche, UCB, Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Janssen, Lilly, Myriad, Pfizer, Regeneron, Roche, UCB

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AB1244 PROGNOSTIC FACTORS IN IGG4-RELATED DISEASE: A LONG-TERM MONOCENTRIC CHINESE COHORT STUDY

Z. Ji[1], L. Ma[1], L. Zhang[1], L. Ma[1], D. Liu[1], Y. Sun[1], X. Kong[1], X. Dai[1], R. Chen[1], H. Chen[1], L. Jiang[1]. [1]*Zhongshan Hospital, Fudan University, Shanghai, China*

Background: Through initial response to treatment with GC, the patients with IgG4-related disease (IgG4-RD) exhibited high relapse rate after reduction or withdrawal of GC treatment, indicated the unsatisfactory prognosis for IgG4-RD. It is of clinical significance to develop new informative risk factors for refractory and relapsed disease.
Objectives: To evaluate the prognosis of IgG4-RD and identify predictive factors for treatment resistance and disease relapse in a Chinese cohort.
Methods: 102 patients newly diagnosed with IgG4-RD were followed for 6-111 months. Clinical data were compared between patients whose disease went into remission and those who suffered refractory or relapsed disease. Predictive factors for refractory and relapsed disease were calculated by univariate analysis.
Results: Among the 78 patients who received medical treatment with regular follow-up, 55 (59.8%) patients sustained clinical remission, and 23 (25%) patients suffered refractory or relapsed disease. The mortality and incidence of malignancy were both 4.35% during follow-up. Serum TNF-α ≥ 13 pg/ml, sIL-2R ≥ 1010 pg/ml, TC < 3.55 mmol/L, LDL < 2.0 mmol/L, IgG > 20.2 g/L, GC withdrawal, and treatment without immunosuppressor (IM) during the maintenance period (OR 3.23) were predictive factors for refractory and relapsed IgG4-RD. The combination of GC and IM treatment was protective (OR 0.338) against refractory and relapsed IgG4-RD.
Conclusion: Serum TNF-α, sIL-2R, LDL, TC, IgG, GC withdrawal, and treatment without IM during the maintenance period were predictive factors for refractory and relapsed IgG4-RD. Treatment with GC and IM may protect against refractory and relapsed IgG4-RD.
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AB1245 DAILY MANAGEMENT OF PATIENTS WITH AXIAL SPONDYLOARTHRITIS: SELF-MONITORING OF DISEASE ACTIVITY WITH A SMARTPHONE APP IS FEASIBLE – A PROOF OF CONCEPT STUDY

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Background: Assessment and monitoring of disease activity and functioning is of major importance for the course of axial spondyloarthritis (axSpA). This is equally important for patient monitoring in daily routine as also for tight control strategies. Even though there is evidence that a closer monitoring of patients is better than routine care, more intensive treatment schedules are often not realized in daily practice for several reasons including shortage of time and personal resources. Using application software devices (apps) in clinical routine for the recording of disease-specific patient reported outcomes (PRO) may facilitate monitoring and improve clinical decision processes but there is a lack of data on the use of apps.
Objectives: To investigate the use of such App technology in respect to usability, feasibility and equivalence of data in daily care of patients with axSpA. In more detail, it will be first determined how many patients are capable and ready to use the technology in a routine setting. Furthermore, the usage and behavior of patients using the app will be studied, the usability of the app and the equivalence of the collected parameters as well as the adherence to the documentation of disease activity over time.
Methods: Patients diagnosed with axSpA were consecutively included in this ongoing monocentric prospective cohort study. In addition to patient and disease characteristics, information on previous experience with digital health apps was collected. Patients were asked to submit BASDAI and BASFI scores regularly every 2 weeks. The free to use AxSpA Live App is available for Android and iOS as a Class I certified medical device.
Results: Out of 103 axSpA patients asked, 69 patients with axSpA (mean age 41.5 ± 11.3, 58% male, 76.8% use of bDMARDs, BASDAI 4.3 ± 2.0, BASFI 3.8 ± 2.5) out of 103 patients (67%) agreed to use participate, while 5 did not have a smartphone, 1 was unable to download the app for technical reasons, 28 reported other personal reasons). Of the 69, 62 patients (89.9%) reported using electronic media frequently and had used digital health apps (mean apps used 1.0 ± 1.3) in everyday life before. There were no systematic differences between pain levels documented on paper or by app at baseline (ICC 0.9 (95%CI 0.82 – 0.93). Out of 55 patients who completed week 2, only 33 patients (60%) used the App regularly to transmit their BASDAI/BASFI responses within the first two weeks (60%). Patients who started a new drug treatment because of high disease activity, reported BASDAI values more often than patients without a treatment change within a follow-up period of 5.5± 2.4 weeks (Table).

	Patients without change in their medication (n=53)	Patients with change in their medication (n=16)
Age, years	42.0 (11.9)	39.8 (9.3)
Sex, male (%)	62.3	43.8
BASDAI, baseline	4.1 (2.1)	4.9 (1.7)
BASFI, baseline	3.8 (2.6)	3.8 (2.3)
Time of follow-up, in weeks	5.4 (2.4)	5.6 (2.5)
Number of transmitted BASDAI values at week 2	22 (41%)	11 (69%)
Median number of transmitted BASDAI values during follow up	1.0(3.6)	1.5 (1.4)

Conclusion: The majority of patients with axSpA were able to use the AxSpA Live App. Most patients report scores regularly. The current disease activity seems to influence the adherence to reporting.

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AB1246 IDENTIFICATION OF GIANT CELL ARTERITIS IN REAL-WORLD DATA USING AN ADMINISTRATIVE CLAIMS-BASED ALGORITHM

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Background: Giant cell arteritis (GCA), the most common systemic vasculitis in adults, is often associated with significant morbidity and mortality. A claims-based algorithm that accurately identifies GCA patients in large real-world data can offer new opportunities for future epidemiological studies.
Objectives: We aimed to develop and validate a claims-based algorithm for GCA.
Methods: We developed and tested 5 claims-based GCA algorithms using U.S. Medicare claims (Parts A/B/D) linked to electronic medical record data from a large academic medical center, 2006-2014: **Algorithm 1)** ≥1 International Classification of Diseases, Ninth Revision (ICD-9) code for GCA (446.5x) by any physician, high dose steroid dispensing (i.e., prednisone equivalent ≥40 mg/day for ≥14 days), and ≥1 Current Procedural Terminology (CPT) code for ESR/CRP; **2)** ≥1 ICD-9 for GCA by a rheumatologist, high dose steroid dispensing, and ESR/CRP; **3)** ≥2 ICD-9 for GCA by a rheumatologist separated by 7-30 days and high dose steroid dispensing; **4)** ≥1 ICD-9 for GCA by a rheumatologist, high dose steroid dispensing, ESR/CRP, and CPT code for temporal artery biopsy; and **5)** ≥1 ICD-9 for GCA or its subtypes (447.6, 437.4, 417.8) by a rheumatologist, high dose steroid dispensing, ESR/CRP, and CPT code for chest imaging. For all algorithms, the index date was defined as the date of first steroid dispensing. Two physicians reviewed medical records for the gold standard definition of GCA: documentation of GCA by the treating physician or a temporal biopsy result consistent with GCA. Probable GCA cases based on treating physician's records were included as well. Positive predictive value (PPV) and 95% confidence intervals (CI) of the algorithms were calculated.
Results: We identified 1,930 patients with Medicare claims data linked to electronic medical records. Among these, 799 unique records with physician notes

documenting GCA or biopsy results were included in the PPV calculations. Algorithm 1, which identified the greatest number of patients (n=896), yielded the lowest PPV of 60.7%. Algorithms 4 and 5, which required disease-specific workups (temporal artery biopsy or chest imaging), mildly improved the PPV to 76.2% and 68.2%, respectively. The PPV was highest in algorithm 3 (84.8%), which required 2 or more diagnoses of GCA by a rheumatologist in addition to high dose steroid dispensing.

Table. PPV of Claims-based Algorithms

	No. of patients			
Algorithm #	**Records Identified**	**Records Reviewed**	**Adequate Records**	**PPV* (95% CI)**
1	896	446†	206 (46.2%)	60.7% (53.7-67.4)
2	471	471	270 (57.3%)	78.6% (73.2-83.3)
3	220	220	125 (57.4%)	84.8% (77.3-90.6)
4	296	296	172 (58.1%)	76.2% (69.1-82.3)
5	47	47	26 (55.3%)	68.2% (48.2-85.7)

* True positive cases included both definitive and probable GCA patients
†446 records were randomly selected for chart review.

Conclusion: A claims-based algorithm including two or more diagnosis codes for GCA by a rheumatologist separated by 7-30 days and high dose steroid dispensing (prednisone equivalent ≥40 mg/day for ≥14 days) can be a useful tool for identifying patients with GCA, allowing for future large real-world data studies.

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AB1247 ELEVATED SERUM COMPLEMENT (C3/C4) LEVEL AS AN INFLAMMATORY MARKER FOR INFECTION IN PATIENTS WITH FEVER: A RETROSPECTIVE STUDY

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Background: The functions of the complement system are to protect the host against infection, clearance of immune complexes, and regulate adaptive immunity after activation by C-reactive protein (CRP) or foreign cells.[1] C3 and C4 may increase up to 50 percent of baseline values as part of the acute-phase response, which is an expected host response for infection and injury.[2]

Objectives: We aimed to examine the correlation between elevated C3/C4 levels and the underlying causes (infectious vs. non-infectious) of fever (subjective and/or objective) in adults admitted to Community Regional Medical Center (CRMC).

Methods: This is a retrospective study of C3/C4 level that was ordered in adult patients who were admitted to CRMC in April 1st, 2018 to September 30th, 2018 with fever. This was also analyzed in comparison to elevated lactic acid, erythrocyte sedimentation rate (ESR), and CRP level.

Results: Complement levels were ordered in 210 patients admitted to CRMC medicine or intensive care units. Among these patients, 28.09% (59/210) were diagnosed with various infectious diseases confirmed by gold standard methods (cultures, serology tests, computerized tomography, or magnetic resonance imaging), regardless of fever status during admission.

About 26.6% (56/210) had subjective or objective (temperature greater than100.4 F or above), and **52** of them had complement levels (C3/C4) ordered with resulted in either normal or elevated. Within these **52** patients, lactic acid, ESR, and CRP were ordered in **33**, **28**, **25** of them respectively.

Table 1. Elevated C3/C4 level vs. normal C3/C4 level in detecting infection in fever patients when tested against gold standards.

	Patients with infectious disease diagnosis	**Patients without infectious disease diagnosis**	
Elevated C3 or C4 or both (screen test +)	13	7	Positive predictive value (PPV) =13/20=65%
Both normal C3 and C4 (screen test -)	8	24	Negative predictive value (NPV) =15/32=48.9%
	Sensitivity=13/21=61.9%	Specificity=24/31=77.4%	

Table 2. Sensitivity, specificity, PPV, NPV, likelihood ratio positive (LR+), and likelihood ratio negative (LR-) among C3/C4, lactic acid, ESR, CRPI/CRPH in detecting infection in patient with fever

	C3/C4 (N=52)	**Lactic Acid (N=33)**	**ESR (N=28)**	**CRPI/CRPH (N=25)**
Sensitivity	61.9%	50%	90%	100%
Specificity	77.4%	91.3%	11.1%	11.8%
PPV	65%	71.4%	36%	34.8%
NPV	48.9%	80.8%	66.6%	100%
LR+	2.7	5.7	1.0	1.1
LR -	0.49	0.55	0.9	0

Conclusion: Complement levels can be used as a rapid screening test to guide infection consideration as it correctly identified 61.9 % of febrile patients with infection, and 77.4% who didn't have an infection. A positive screening test in itself still requires further investigation in the causes of fever to confirm the diagnosis since the PPV is 65%. With the NPV of 48.9%, a negative screening test is still not reassuring that the febrile patient doesn't have an infection. Our study demonstrated the potential utilization of the elevated complement level as an inflammatory marker for infectious etiology of fever, as it has better LR+ when compares to ESR and CRP with similar turnaround time.

This study helps educate providers to acknowledge the fact that complement level does not have to be limited to be used on autoimmune related disorders only. Further large pool studies will be necessary to further investigate the role of complement levels as part of the screening test in a patient with fever.

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AB1248 MOLECULAR MARKERS OF PAIN AND OTHER SYMPTOMS IN KNEE OSTEOARTHRITIS

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Background: Osteoarthritis (OA) is one of the leading causes for disability in adults. The diagnosis of OA is generally based on patient reported pain, other symptoms and radiographic changes which occur in late stages. There have been extensive research over the last 30 years to identify and validate molecular markers for early diagnosis of OA and a large range of potential biomarkers has been identified[1, 2]. However, most of these biomarkers are markers of structural and metabolic changes, and have poor correlation with pain and stiffness in knee OA. The publicly available data from the National Institute of Health Osteoarthritis Initiative (OAI) provides an opportunity to search for clinically useful biomarkers associated with the main symptoms in OA.

Objectives: To identify molecular biomarkers which are associated with the main symptoms of knee OA.

Methods: 600 participants from 4791 men and women aged 45 to 79 who were Kellgren & Lawrence grade 1 or more were identified with biochemical markers data, radiographic and clinical features of OA. Nineteen biochemical markers measured in serum and/or urine were analysed for their association with primary clinical features of OA: Knee injury and Osteoarthritis Outcome Score (KOOS) pain and symptoms, and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain and stiffness score. Patient level analysis

was carried out based on the worst affected knee. The association of molecular biomarkers with KOOS and WOMAC scores were assessed using univariate and multivariate linear and logistic regression, and receiving operator characteristic curves (ROC). Area under the curve (AUC) was calculated in order to determine if a combination of the biomarkers improve the associations with the outcome variables.

Results: Only 3 of the 19 biomarkers investigated were associated with clinical symptoms. Serum cartilage oligomeric matrix protein (COMP) and chondroitin sulphate 846 (CS846) were associated with WOMAC pain and stiffness respectively, while, urinary C-terminal crosslinked telopeptide of type II collagen (CTXII) appeared to be highly associated with WOMAC stiffness, KOOS pain and symptoms (Table 1 / 2). The AUC from the univariate model for the association of biomarkers with WOMAC pain and stiffness were 0.5 (Table 1), while the AUC for unadjusted and adjusted multivariate model for the 3 biomarkers combined were 0.56 and 0.67 respectively (Figure 1).

Table 1. Univariate logistic regression model.

	WOMAC Pain		WOMAC Stiffness	
Biomarkers	**OR (95%)**	**AUC (p-value)**	**OR (95%)**	**AUC (p-value)**
sCS846	1.0026 (0.9996, 1.0056)	0.5200 (0.088)	1.0047 (1.0013, 1.0081)	0.5399 (0.007)
sCOMP	0.9419 (0.8912, 0.9954)	0.5462 (0.034)	1.0424 (0.9843, 1.1039)	0.5317 (0.156)
uCTXII	1.0077 (0.9990, 1.0165)	0.5300 (0.083)	1.0099 (1.0005, 1.0194)	0.5489 (0.039)

Conclusion: Serum COMP and urinary CTXII are associated with pain in knee OA, while serum CS846 and urinary CTXII are associated with joint stiffness. The multivariate logistic regression model shows good discrimination for the association of biomarkers with clinical symptoms of OA. The data from the multivariate model suggests that a clinically useful biomarker may be created using AUC values for better specificity and sensitivity.

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Table 2. Univariate and multivariate linear regression model. Confounders such as age, body mass index, gender and race were adjusted in the multivariate model.

Biomarkers	KOOS Pain				KOOS Symptoms			
	Univariate		Multivariate		Univariate		Multivariate	
	Coefficient (95%)	p-value	Coefficient (95%)	p-value	Coefficient (95%)	p-value	Coefficient (95%)	p-value
sMMP3	0.057 (-0.024, 0.138)	0.165	0.019 (-0.074, 0.111)	0.696	0.092 (0.022, 0.162)	0.010	0.059 (-0.021, 0.140)	0.147
uCTXII	-0.678 (-0.124, -0.012)	0.017	-0.086 (-0.152, -0.021)	0.010	-0.730 (-0.121, -0.025)	0.003	-0.091 (-0.148, -0.034)	0.002

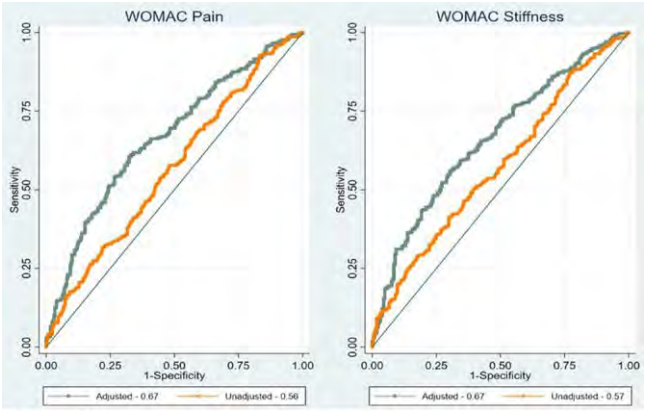


Figure 1. ROC curves representing the AUC values on the unadjusted and adjusted multivariate logistic regression model. In the latter data was adjusted for confounding variables age, body mass index, gender and race.

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AB1249

ASSESSMENT OF FATIGUE IN ADULTS WITH MODERATE-TO-SEVERE SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): A QUALITATIVE STUDY TO EXPLORE WHAT PATIENTS FEEL SHOULD BE MEASURED IN CLINICAL TRIALS

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Background: Fatigue is one of the most common symptoms reported by patients with systemic lupus erythematosus (SLE)—it is responsible for considerable loss of work time and greatly impaired quality of life. The Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) has been used to assess fatigue in SLE clinical trials[1]; however, assessment of the content validity of the FACIT-F in adults with SLE suggested that closer evaluation may be warranted.[2]

Objectives: This qualitative study aimed to understand SLE patients' experience of fatigue and assess the content validity of the FACIT-F.

Methods: The evaluation was informed by literature and guided by a project steering committee (PSC; patient advocate, clinical expert, outcomes measure expert). The institutional review board-approved study involved focus groups (Round 1) and cognitive interviews (Round 2) with adults with moderate-to-severely active SLE. All participants provided written informed consent. Round 1 included three focus groups to understand the disease and fatigue-related concepts that were most important to patients; participants also provided high-level feedback on the FACIT-F. Round 2 included 13 one-on-one cognitive interviews on the relevance of content, clarity, and comprehensiveness of the FACIT-F. Interviews were audio-recorded and transcribed and a content analysis was completed. The PSC reviewed results and contributed to decision-making. Specific focus was on determining patient understanding of the FACIT-F, comprehensiveness, and any gaps in concept coverage to evaluate fatigue in the context of a clinical trial.

Results: Twenty-eight patients with moderate-to-severely active SLE participated; they were mostly female (n=27), had a mean age of 45.5 ± 12.1 years (range: 18–75), and 23 (82%) had moderate and five (18%) severely active SLE. All participants were receiving SLE treatment, and most (n=23, 82%) reported fatigue among their top three most important SLE-related symptoms. Fatigue was described as having a profound impact on daily life, including ability to perform chores and work-related activities, maintain personal hygiene, exercise, and participate in hobbies. Study participants reported the FACIT-F covered concepts most relevant to their fatigue experience. Participants were able to understand the FACIT-F instructions, items, and response options and felt the recall period of seven days was appropriate.

Conclusion: Fatigue was one of the most important symptoms, having a significant impact on adults with moderate-to-severely active SLE, limiting their ability to perform necessary or desired activities. The FACIT-F was found to be an appropriate measure for the assessment of fatigue in this sample.[3] Evidence of the content validity of the FACIT-F in adults with SLE was confirmed for use to support endpoints in the Cenerimod Assessing $S1P_1$ Receptor Modulation in SLE (CARE) clinical trial.

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AB1250 DIAGNOSTIC SIGNIFICANCE OF THE PROCALCITONIN TEST IN RHEUMATOLOGY

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Background: Immuno-inflammatory rheumatic diseases (IIRDs) are often complicated by the infectious process, which may be due to both the disease itself and immunosuppressive therapy. At the same time, clinical symptoms and traditional laboratory tests are often uninformative in patients with active IIRDs, and negative results of bacteriological research do not exclude the presence of infection. One of the markers of bacterial inflammation – the procalcitonin test (PCT) - can play an important role in the early detection of infection in IIRDs.
Objectives: The aim of the study is to assess the diagnostic significant of PCT in rheumatology.
Methods: The study included 340 patients (227 women, 113 men, age 39.1±20.8 years) with different IIRDs: systemic lupus erythematosus (SLE) – 74, rheumatoid arthritis (RA) - 71, juvenile arthritis (JA) - 53, systemic vasculitis (SV) - 33, systemic scleroderma (SSD) - 27, ankylosing spondylitis (AS) - 18, adult-onset Still's disease (AOSD) - 13, other IIRDs - 51. The serum concentration of PCT was determined by the quantitative electrochemiluminescent method using the Cobas E 411 analyzer (Roshe, Switzerland).
Results: In patients without infection (n=181), the median (Me) PCT level was 0.11 ng/ml [0.05; 0.17]; higher values of PCT were found in patients with AOSD (0.39 ng/ml [0.14; 0.51]), systemic form of JA (0.17 ng/ml [0.11; 0.5]) and SLE (0.16 ng/ml [0.10-0.45]). In RA, SV, SSD, AS without infection, Me PCT was 0.07 ng/ml [0.03; 0.12]. The infectious process was detected in 159 patients: generalized - in 11, local - in 148. Depending on the severity of the intoxication syndrome, local infections are divided into severe (n=70) and light (n=78). Infections of the lower respiratory tract, urinary system, skin and soft tissues prevailed. In patients with generalized infection, Me PCT level was 3.6 ng/ml [0.49; 11.3]. In 10 patients of this group, the level of PCT exceeded 2 ng/ml, in 5 patients - 10 ng/ml. In severe local infection, Me PCT was 0.45 ng/ml [0.23; 1.19], in light - 0.12 ng/ml [0.05; 0.16]. In generalized infection, the level of PCT was significantly higher than in patients without infection ($p<0.0001$), as well as with mild ($p<0.0001$) and severe local infection ($p<0.0001$). In patients with severe local infection, the level of PCT was higher compared to patients without infection ($p<0.0001$) and with mild local infection ($p<0.001$). There were no significant differences in PCT in the groups of patients with light local infection and without infection. In SLE patients with infection, the level of PCT and CRP (but not ESR) was higher than in patients without infection; a correlation was found between the level of PCT and CRP ($r=0.53$, $p<0.001$) in the presence of infection. In AOSD, systemic form of JA, RA, SV, SSD, AS, significant differences in the levels of PCT, ESR, CRP in patients with infection and without infection were not obtained, correlations were not revealed. According to the ROC-analysis, the diagnostic significance of determining PCT in generalized infection is excellent, in severe local infection - very good, and in differentiation of generalized infection from local infection - very good.
Conclusion: PCT is a significant diagnostic test that allows to recognize generalized and severe local infections in patients with IIRDs. In order to more accurately diagnose the infectious process, a multi-marker approach is needed.
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Disclosure of Interests: None declared
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AB1251 VALIDITY OF RHEUMATOID ARTHRITIS DIAGNOSES IN FINNISH BIOBANK PATIENTS

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Background: Finnish healthcare registers are used in medical research, but there is little data about the validity of these registers in rheumatology.
Objectives: The aim of our study was to determine the validity of rheumatoid arthritis (RA) diagnoses in patients participating in the Finnish Biobanks.
Methods: We reviewed the electronic patient charts of 125 patients with at least one visit with a diagnosis of seropositive RA, 125 patients with at least one visit with a diagnosis of seronegative RA and 250 age-and-sex matched controls. Patients were randomly selected from Finnish biobank participants. We evaluated whether the patients' diagnosis of RA recorded in the hospital discharge registry at the participating hospital was correct according to chart review and expert opinion. In the control group it was investigated whether the diagnosis of RA was written in the patients' chart, but the diagnosis code was not recorded.
Results: The positive predictive value (PPV) of a single hospital registry diagnosis of seropositive RA was 0.74 but rose to 0.98 in patients with a special reimbursement for seropositive RA and 0.98 in anti-citrullinated protein antibody positive patients. For seronegative RA, the PPV of a diagnosis was 0.72 and in patients with a special reimbursement for seronegative RA 0.89. The PPV was higher in patients with more than one visit with the diagnosis: 0.92 if the patients had at least 5 visits with seropositive RA and 0.88 with at least 5 visits with seronegative RA. Negative predictive value for RA diagnosis was 0.99.
Conclusion: These results demonstrate that the validity of RA diagnoses in healthcare registers can be markedly improved with data about special reimbursement for medication, number of visits and serological data.
Disclosure of Interests: Antti Palomäki Consultant of: Pfizer, Speakers bureau: Pfizer, Sanofi, MSD, Johanna Paltta Consultant of: Lilly, Abbvie, Laura Pirilä Consultant of: Novartis, MSD Finland, Roche, Bristol-Myers-Squibb, Pfizer, Sanofi, Abbvie, Oy Eli LIlly Finland Ab, UCB Pharma Oy Finland, Jansen-Cilag, Mylan, Sandoz, Boehringer-Ingelheim, Paid instructor for: Boehringer -Ingelheim, MSD Finland, Speakers bureau: Boehringer-Ingelheim, Pfizer Finland, Hanna-Kaisa Heikkilä: None declared, Pia Isomäki Consultant of: Abbvie, BMS, Eli Lilly, MSD, Novartis, Pfizer, Roche, Sanofi, Johanna Huhtakangas Consultant of: Boehringer Ingelheim, Tuulikki Sokka-Isler: None declared, Oili Kaipiainen-Seppänen Speakers bureau: Boehringer Ingelheim, Kari Eklund Consultant of: Celgene, Lilly, Speakers bureau: Pfizer, Roche
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AB1252 CAN THE HUPI BE MORE USEFUL THAN OTHER INDICES IN THE SEARCH OF BIOMARKERS FOR RA?

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Background: The Hospital Universitario La Princesa Index (HUPI) was developed to tackle metric shortcomings of DAS28 and SDAI, and has shown better accuracy and responsiveness than these widespread indices.[1]
Objectives: To compare the performance of HUPI, DAS28, and SDAI in explaining the variability of radiographic progression, HAQ and the distribution of a biomarker of damage such as IL6.
Methods: Two cohorts were assembled with data from a clinical trial (ACT-RAY) and an early arthritis register (PEARL). Radiographic progression, measured as the change (Δ) of Genant or Sharp/Van der Heijde indices at week 52 in ACT-RAY and PEARL respectively, Δ HAQ and serum IL6 (ELISA; R&D Systems) levels, the latter only available in PEARL, were the outcome variables. HUPI, DAS28, SDAI, sex and age were the independent variables.
For each index, linear regression models adjusted for sex and age were developed using standardized variables. The overall performance of the model, as well as that of the specific index it included, were evaluated using the adjusted R2. Differences between models were assessed with the likelihood ratio test. Also, The *fpfitci* command (Stata v14) was used to estimate the predicted distribution of the described variables using fractional polynomials and plotting the resulting curves.
Results: The performance of the models and indices are shown in table 1. The variability of radiographic progression was better explained by the SDAI model in ACT-RAY whereas HUPI did it so in PEARL. The latter also performed better for explaining HAQ in ACT-RAY (figure 1) and IL6. Sex modified the performance of DAS28 and SDAI in their respective models. The relation between all the described outcomes predicted using fractional polynomials and each index was also more linear for HUPI than its comparators. (see an example in figure 2).

Table 1. Adjusted R^2 of the models and indices. R^2m: adjusted $R^2$of the models; R^2I: adjusted R^2 of the index included in the model; LR: Likelihood-Ratio test comparing HUPI models vs other indices'.

OUTCOME	INDEX	ACT-RAY		LR	PEARL		LR
		R^2m	R^2I		R^2m	R^2I	
RADIOGRAPHIC PROGRESSION	HUPI	0.025	0.024	ref	0.110	0.020	ref
	DAS28	0.031	0.030	<0.000	0.102	0.011	<0.000
	SDAI	0.051	0.050	<0.000	0.109	0.019	<0.000
HAQ	HUPI	0.353	0.323	ref	0.477	0.448	ref
	DAS28	0.329	0.298	<0.000	0.472	0.442	<0.000
	SDAI	0.334	0.303	<0.000	0.486	0.457	<0.000
IL6	HUPI	-	-	-	0.212	0.184	ref
	DAS28	-	-	-	0.204	0.176	<0.000
	SDAI	-	-	-	0.201	0.172	<0.000

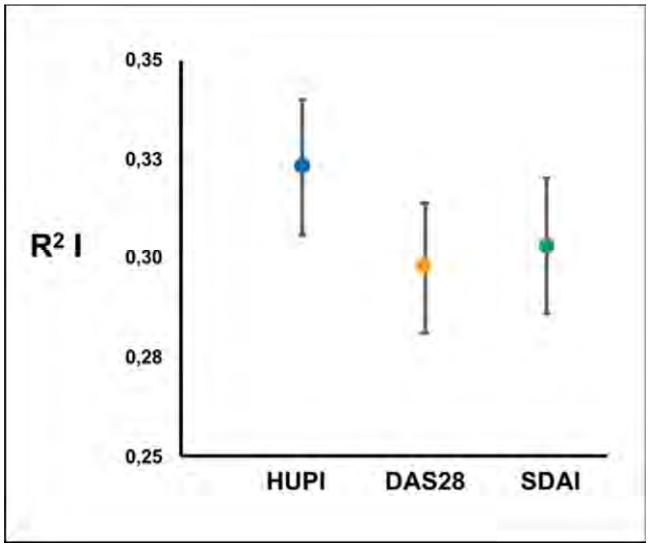


Figure 1. Box plots comparing the adjusted R^2 of each index estimated in models for HAQ in ACT-RAY.

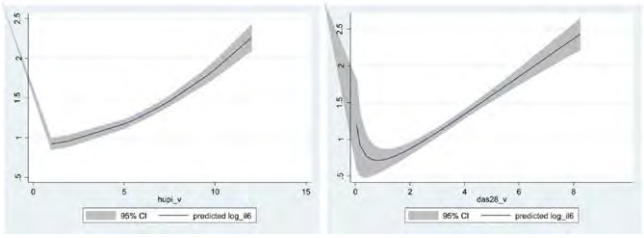


Figure 2. Curves for comparison of predicted serum IL6 using fractional polynomials for HUPI and DAS28.

Conclusion: Although all indices explained the outcomes' variability similarly, HUPI did it better than DAS28 and SDAI for almost all outcomes except for Δ Genant and HAQ in PEARL.

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[1] Gonzalez-Alvaro I, *et al.* PLoS ONE 14(4): e0214717

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AB1253

EVALUATION OF CYSTEINE-RICH 61 IN RHEUMATOID ARTHRITIS AS A DIAGNOSTIC MARKER AND PREDICTOR OF ATHEROSCLEROSIS

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Background: Matricellular protein Cysteine-rich protein 61 (Cyr61) is involved in chronic inflammatory disorders like rheumatoid arthritis (RA) and atherosclerosis.
Objectives: This study aimed to assess the value of serum Cyr61 in diagnosis of rheumatoid arthritis, evaluating its correlation with disease activity and its relation to atherosclerosis.
Methods: Cross-sectional study included 105 RA patients classified into active and inactive groups according to disease activity score (DAS28) with 50 healthy age and gender-matched controls. Full clinical and laboratory assessment was done including enzyme-linked immunosorbent assay (ELISA) measurement of Cyr61. Bilateral assessment of carotid intima-media thickness (CIMT) was done using high resolution-ultrasonography. Comparison of Cyr61 between RA patients and controls, correlation between Cyr61 and disease activity and CIMT were analyzed with appropriate statistical analyses.
Results: Significant elevation of Cyr61 in RA patients compared to controls (235.62±62.5 vs. 73.11±18.2) respectively. The cut off value of Cyr61 was 99.25 pg/ml, with area under the curve (AUC) =0.995, P <0.001, 98 % sensitivity and 95% specificity. Cyr61 was inversely correlated with DAS28 and its components in RA patients (r=- 0.92, r=- 0.94) (p<0.001). There was a significant positive correlation between Cyr61 levels and CIMT in inactive and active RA patients (r=0.88, r=0.47) respectively.
Conclusion: Serum Cyr61 as a potential diagnostic biomarker in RA is inversely correlated with disease activity. High Cyr61 in RA is a risk factor for atherosclerosis. Disruption of serum Cyr61 is engaged in the pathogenesis of both rheumatoid arthritis and atherosclerosis which is a clue for a future treatment strategy of RA.

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Disclosure of Interests: None declared

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AB1254

PHENOTYPING OF MULTIPLE BIOFLUIDS FOR LIQUID BIOMARKERS FOR DIAGNOSTICS AND PERSONALIZED MEDICINE OF RHEUMATOID ARTHRITIS, SPONDYLOARTHRITIS AND OSTEOARTHRITIS

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Background: Inflammatory and autoimmune diseases include multifactual pathomechanisms and systemic responses. The etiology of the joint diseases rheumatoid arthritis (RA), spondyloarthritis (SpA) in relation to osteoarthritis (OA) remain incomplete and establishing the correct diagnose remains nontrivial. Advances in high-throughput molecular technologies have increased investigations into the

utility of transcriptomic, proteomic and high-density protein arrays approaches as diagnostic tools and companion diagnostics for precision medicine. To increase our understanding of the molecular pathogenesis, we extracted synovial fluid from the joints from multiple patient groups and characterized the protein composition in relation to plasma. Basic blood tests include inflammatory markers and autoantibodies, however, now analysis speed and robustness allow more readily clinical insight biofluids.

Objectives: We present recent Omics concepts and studies investigating inflammatory state and treatment outcome in different biofluids from plasma to synovial fluid accessing causalities leading to inflammation and pain. Additionally, the aim was to investigate in any proteomic findings in synovial fluid can be correlated to proteomic changes in patient plasma and can be used as biomarkers for treatment effect.

Methods: Plasma and synovial fluid were investigated in multiple pathologies before and after treatment in patients (biologics; MTX; intraarticular gold). Deep proteome, PTM and EV profiling were accomplished using quantitative proteomics approaches using quantitative mass spectrometry-based analysis by DIA/PASEF followed by deep datamining. All biological samples were digested according to a Filter Aided Sample Preparation (FASP) protocol before analysis with tandem mass spectrometry (MS/MS). PTM profiling were evaluated by 4D CCS based feature finding.

Results: Mass spectrometry based profiling allowed quantitative profiling of up to 480 proteins in matched synovial fluid and plasma. Complementary analysis by Olink proteomics, cytokine profiling and cell-free DNA. Multiple acute inflammatory proteins were more abundant in the RA synovial fluid, including proteins originating from neutrophil granulocytes, whereas SpA patients had a higher concentration of haptoglobin. Complementary analysis by Olink immunoassay identified significantly downregulated inflammation markers out of 96 tested in relation to antiinflammatory treatment.

Conclusion: Discovery of biomarkers and/or inflammatory signatures through integration of multi-omic data allowed stratify patients for improved treatment and prognosis. Firstly, our data using next generation proteomics approaches alleviates many pitfalls of missing values and poor proteome coverage including unbiased PTM profiling without enrichment strategies.

Disclosure of Interests: None declared

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AB1255

AGREEMENT BETWEEN PATIENT-REPORTED OUTCOME MEASURES COLLECTED VIA A SMARTPHONE APPLICATION VS A TOUCHSCREEN SOLUTION IN AN OUTPATIENT CLINIC AMONG PATIENTS WITH INFLAMMATORY ARTHRITIS: A RANDOMISED, WITHIN-PARTICIPANT TRIAL

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Background: Patient-reported outcome measures (PROMs) are essential to understand the patient's perception of arthritis activity. In Demark, PROMs are registered on a touchscreen in the outpatient clinic. However, some patients find it inconvenient due to e.g. waiting in queue, lack of privacy, uncomfortable seating position, reduced upper limb strength and dexterity with seeing the touchscreen due to deformity of the cervical spine. The widespread use of smartphones makes it possible for patients to register PROMs via an application (app) on their own device.

Objectives: The primary aim is to evaluate the agreement (i.e. similarity) between the two devices assessed by the Health Assessment Questionnaire Disability Index (HAQ-DI) status among patients with inflammatory arthritis.

Methods: The study was a randomised, crossover, agreement trial (NCT03486613) conducted at Aalborg University Hospital, Denmark. Participants were recruited through an invitation on the touchscreen in the outpatient clinic. Patients with an established diagnosis (≥ 12 months) of rheumatoid arthritis (RA), psoriatic arthritis (PsA) or axial spondyloarthritis (axSpA) and experience with the PROM questionnaires (≥ 3 previous registrations) were enrolled and randomised in ratio 1:1 (stratified by diagnosis) to PROM registration through the DANBIO app and the touchscreen in random order. Figure 1A and 1B shows the two devices.

The sample size calculation was based on a prespecified equivalence margin of ±0.11 HAQ-DI points (i.e. ≤ half of the minimal important difference of 0.22 points) yielding a power of 99.2% for 60 enrolled patients. There was a wash-out period of 1-2 days between the two device registrations to minimise the potential carryover effect.

A paired t-test was used to calculate the mean HAQ-DI score for the two devices and the difference in HAQ-DI score with a 95% confidence interval (CI). A Bland-Altman plot was used to assess limits of agreement (LoA).

Results: 60 patients (20 with RA, 20 with PsA and 20 with axSpA) were randomised of whom 51.7% were male. Mean age was 53.7 years (range 22-77) and mean disease duration was 12.5 years (range 1.0-34.8).

Mean HAQ-DI was 0.608 (95%CI 0.437;0.779) for the DANBIO app and 0.614 (95%CI 0.446;0.783) for the touchscreen (Table 1). Agreement between scores obtained with the two devices is illustrated with Bland-Altman plots in figure 2A and 2B. The paired mean difference of HAQ-DI between the two devices was -0.006 (95%CI -0.0424; 0.030); thus the 95% confidence interval for the mean difference was within the prespecified equivalence margin of ±0.11 HAQ-DI points.

Table 1. HAQ-DI scores, difference and LoA for the two devices.

	App, mean (SD)	Touchscreen, mean (SD)	Difference, mean (95%CI)	LoA	Missing values
HAQ-DI (0-3)	0.608 (0.656)	0.614 (0.646)	-0.006 (-0.042;0.030)	-0.277;0.264	1

Conclusion: The current study showed no statistical or clinically important difference in HAQ-DI measurement captured by a smartphone app or outpatient touchscreen. Therefore, we feel confident that the two devices perform similarly enough to be used interchangeably in patients with inflammatory arthritis.

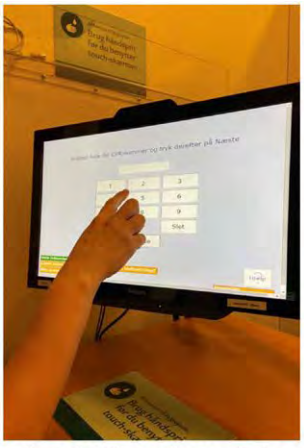


Figure 1A: The touchscreen in the outpatient clinic

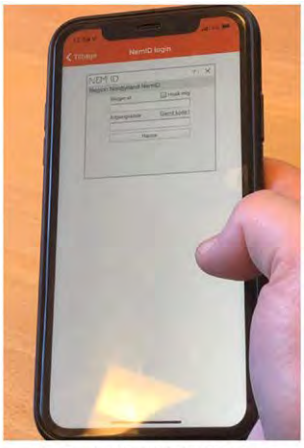


Figure 1B: The DANBIO app on a smartphone

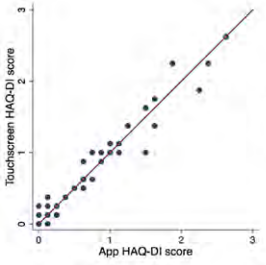


Figure 2A: HAQ-DI scores measured with the two devices with a line of equality.

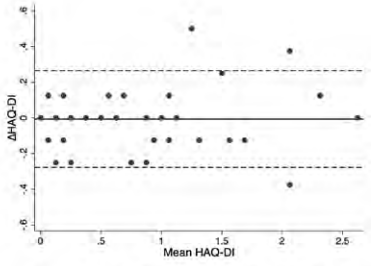


Figure 2B: HAQ-DI difference against mean. The dashed horizontal lines represents 95% limits of agreement and the solid horizontal line the mean difference.

Disclosure of Interests: Line Uhrenholt Speakers bureau: Abbvie, Eli Lilly and Novartis (not related to the submitted work), Robin Christensen: None declared, Lene Dreyer: None declared, Annette Mortensen Speakers bureau: MSD and Eli Lilly (not related to the submitted work)., Ellen-Margrethe Hauge Speakers bureau: Fees for speaking/consulting: MSD, AbbVie, UCB and Sobi; research funding to Aarhus University Hospital: Roche and Novartis (not related to the submitted work)., Niels Steen Krogh: None declared, Mikkel Kramme Abildtoft: None declared, Peter C. Taylor Grant/research support from: Celgene, Eli Lilly and Company, Galapagos, and Gilead, Consultant of: AbbVie, Biogen, Eli Lilly

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AB1256 CORRELATION BETWEEN SERUM CALPROTECTIN LEVELS, RAPID3 AND DISEASE ACTIVITY MEASURES IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Tight control of rheumatoid arthritis (RA) is essential and we need a validated, objective and reproducible disease measure to achieve it. There is not gold standard in RA. There is a rising interest in evaluating disease activity on the patient's point of view using patient-reported outcomes like RAPID3. Furthermore, some new biomarkers have appeared, like serum calprotectin, with promising results on its analyzing.
Objectives: To evaluate correlation between disease activity measures usually used in patients with RA (DAS28 ESR/CRP, SDAI and CDAI) and other alternative tools (RAPID3 and calprotectin). To analyze correlation between RAPID3 and serum calprotectin levels.
Methods: A cross-sectional study was performed. RA-patients (n=114) according to the ACR/EULAR 2010 classification criteria were consecutively enrolled from Rheumatology department at Hospital de Figueres during the period from February to June 2019. Disease activity, biomarkers and the assessment of the patient's health status with RAPID3 data were collected. Modified RAPID3 (mRAPID3) was calculated by subtracting the questions about the mood included in the questionnaire (k,l,m questions) to the results of the RAPID3 as if it were a response of the HAQ test. Coefficient Spearman's correlation (r) was used to assess the relationship between the variables, and coefficient of determination (r-squared=r^2 and adjusted r^2) was used to show the strength of correlation.
Results: 114 patients were included: 71% women, mean (SD) age 60(11) years, median disease duration 13(8) years. 80% had positive RF and 70% positive ACCP antibodies. 52% had erosions. 89% patients had been receiving treatment with csDMARDs, 38% with bDMARDs o dsDMARS and 66% with glucocorticoids. Disease activity measures' median values were DAS28ESR 3.07, DAS28CRP 2.76, SDAI 9.62 and CDAI 8.99 and showed low activity. The mean values of RAPID3 y mRAPID3 showed moderate activity (8.95 and 8.68 respectively). Median serum calprotectin level was 1.48µg/ml.
All correlations between variables were statistically significant and directly proportional although with different values (table).

Spearman's correlation coefficient between mRAPID3, serum calprotectin, disease activity scores and laboratory parameters

	mRAPID3	Calprotectin	CRP	ESR	DAS28ESR	DAS28PCR	SDAI	CDAI
mRAPID3	1							
Calprotectin	0.23	1						
CRP	0.33	0.59	1					
ESR	0.23	0.39	0.54	1				
DAS28-ESR	0.62	0.32	0.41	0.62	1			
DAS28-CRP	0.69	0.32	0.42	0.28	0.83	1		
SDAI	0.74	0.31	0.35	0.27	0.82	0.91	1	
CDAI	0.73	0.25	0.24	0.21	0.80	0.89	0.99	1

DAS28: Disease Activity Score, SDAI: Simplified Disease Activity Index, CDAI: Clinical Disease Activity Index, RAPID3m: Routine Assessment of Patient Index Data 3 modificative with k,l,m questions. CRP: C-reactive protein. ESR: erythrocyte sedimentation rate

Coefficient of determination found a weak association between RAPID3 and mRAPID3 with DAS28ESR (r^2=0,38) and moderate with DAS28CRP, SDAI and CDAI (r^2=0,47, 0,55 y 0,53). Determination serum calprotectin levels together with RAPID3 or mRAPID3 increased strength of correlation between DAS28ESR, DAS28CRP, SDAI and CDAI with RAPID3 (adjusted r^2=0,40, 0,49, 0,56, 0,52) and with mRAPID3 (adjusted r^2=0,41, 0,50, 0,56, 0,53). Correlation between RAPID3 and serum calprotectin levels was very weak (r^2=0,05).
Conclusion: Correlation between disease activity measures and mRAPID3 was strong, but it was weak with serum calprotectin levels. Correlation strength between RAPID3 and DAS28ESR was low and it was moderate with other composite indices, it maintained with RAPID3m and improved by adding serum calprotectin levels although modestly. There was a very weak correlation between RAPID3 and serum calprotectin levels suggesting that these two variables give us different information about the disease activity.

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AB1257 SCREENING FOR IMMUNOGLOBULIN A ANTIBODY REACTIVITY IN EARLY AXIAL SPONDYLOARTHRITIS IDENTIFIES NOVEL ANTIGENIC TARGETS

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Background: Although autoantibodies are not generally considered to be a hallmark of axial spondyloarthritis (axSpA), increasing evidence suggests the presence of autoantibodies in a subset of axSpA patients. Most of these described antibodies are of the immunoglobulin G (IgG) isotype while other antibody isotypes are less well studied. Antibodies of the IgA isotype can be of interest due to the strong link between gut inflammation and spondyloarthropathies.
Objectives: The aim of this study was to identify and characterize novel IgA isotype (auto)antibodies specific for early axSpA patients.
Methods: An axSpA cDNA phage display library, representing the antigenic repertoire from axSpA hip synovium, was constructed and screened for reactivity with IgA antibodies in plasma of early axSpA patients (*n=10*). Using enzyme-linked immunosorbent assays (ELISA), antibody reactivity against 173 identified targets was initially determined in pooled plasma of early axSpA patients (n=60) and healthy controls (HC, *n=30*), collected at Hasselt University. Antigenic targets that showed increased IgA reactivity in axSpA plasma pools were further validated in individual plasma samples of early axSpA patients (*n=79*) and HC (*n=101*).
Results: We identified 10 novel Hasselt University (UH) axSpA peptide targets with increased IgA antibody reactivity in pooled axSpA plasma. At present, validation of 8 UH-axSpA-IgA peptide targets in individual plasma samples revealed antibody reactivity against at least one of these targets in 32% of early axSpA patients (25/79) compared to 26% in HC (31/101, *p=0.4082*). By combining the 3 UH-axSpA-IgA peptides with the highest positive likelihood ratio (LR+) into a panel, an increased overall specificity of 90% (10/101) could be achieved, with an associated sensitivity of 24% (19/79, *p=0.0138*) resulting in a LR+ of 2.4. Antibody reactivity testing of the remaining 2 UH-axSpA-IgA peptide targets is currently ongoing.
Conclusion: The increased reactivity of IgA (auto)antibodies against several novel antigenic peptide targets underscores the role of the humoral immune response in axSpA, and might indicate a potential link with mucosal inflammation. IgA antibody reactivity against these novel peptide targets will be further validated in independent cohorts of early axSpA patients as well as in patients with chronic low back pain.
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AB1258 THE VALUE OF THE SQUEEZE TEST FOR DETECTION OF SUBCLINICAL SYNOVITIS IN PATIENTS WITH ARTHRALGIA SUSPICIOUS FOR PROGRESSION TO RA

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Background: The squeeze test (or compression test) is often used to quickly screen for arthritis in metacarpophalangeal (MCP)- and metatarsophalangeal (MTP)-joints. A positive test is traditionally assumed to indicate presence of synovitis. Previous studies in early arthritis indeed showed that a positive squeeze test was associated with presence of swollen MCP- and MTP-joints, as well as with local MRI-detected inflammation. The sensitivity of the test, with MRI-detected synovitis as reference, was 31-33%. The field is moving towards identifying patients at risk for rheumatoid arthritis (RA) in the phase of arthralgia. However, it is unclear if the squeeze test in the phase of clinically suspect arthralgia (CSA) is associated with subclinical inflammation, which can be detected with MRI.
Objectives: We aimed to assess if a positive squeeze test in patients with CSA is associated with MRI-detected subclinical inflammation, especially with

subclinical synovitis and tenosynovitis (the latter is recently identified as a strong predictor for RA-development).
Methods: 315 patients with recent-onset (<1 year) arthralgia of small joints and a clinical suspicion for progression to RA were consecutively included in our CSA-cohort. At baseline the squeeze test (compression across the knuckles of MCP- and MTP-joints with the force of a firm handshake) and unilateral contrast-enhanced 1.5T MRI of MCP(2-5)- and MTP(1-5)-joints was performed and scored according to RAMRIS. MRI-scores were dichotomized with data from age-matched symptom-free controls as reference. Follow-up ended when patients developed clinically apparent inflammatory arthritis (IA), or else after 2 years. Associations of the squeeze test and MRI-data were studied with generalized estimating equations, associations with IA-development with cox regression.
Results: 51% of CSA-patients had a positive squeeze test in MCP- or MTP-joints. In univariable analyses a positive test was associated with MRI-detected subclinical synovitis (OR 2.10 (95%CI 1.30-3.40)) and tenosynovitis (OR 1.68 (1.05-2.68)). In multivariable analyses including both inflammatory features only synovitis remained significant (OR 1.90 (1.16-3.13)). Thus, a positive squeeze test is a measure of subclinical synovitis, with a sensitivity of 44% (95%CI 33-55) and specificity of 72% (68-76).
A positive squeeze test in CSA was not associated with IA-development in cox regression adjusted for age, gender, CRP and ACPA-status (HR 1.57 (0.77-3.19). This was consistent with the finding that subclinical synovitis was not associated with IA-development in multivariable analysis adjusted for age, gender, CRP, ACPA-status and tenosynovitis (HR 1.40 (0.59-3.31), whilst tenosynovitis was associated (HR 4.94 (2.03-12.06).
Conclusion: The squeeze test is a simple test that, when positive in CSA, doubles the probability of presence of subclinical synovitis.
Disclosure of Interests: None declared
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Rehabilitation

AB1259 THE IMPACT OF DIFFERENT EXERCISE MODES AND INTENSITIES ON PAIN AND ENJOYMENT IN PEOPLE WITH EARLY RHEUMATOID ARTHRITIS

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Background: The benefits of exercise for people with rheumatoid arthritis (RA) are now widely recognised [1]. However, exercise participation among people with RA remains low. A key reason for that could be the commonly held belief that exercise, may exacerbate disease activity while acutely increasing levels of joint pain. The association of acute exercise with pain has not been established in RA and especially in people with a recent diagnosis.
Objectives: This study investigated the impact of acute aerobic-and resistance-type exercise on perceptions of pain in people with early RA.
Methods: Following local NHS ethical approval, ten people with RA volunteered for the study (Age=46±13years; BMI=29.4±8.6kg/m^2, RA diagnosis= 13±9months, mean±SD). Inclusion criteria were RA diagnosis (2010 EULAR criteria) within the last two years and not engaging in regular physical activity (i.e. no participation in structured exercise >2 times per week). They were assessed for maximal aerobic capacity and maximal strength at chest press, leg press and wide-grip lateral pulldown to determine intensities for exercise conditions. Thereafter they completed one no-exercise control trial (CON) and four exercise trials: 30 minutes of sub-maximal cycling at a workload equivalent to 65% VO_2max (CYCLE); high intensity interval exercise consisting of 10x1 minutes cycling intervals at a workload equivalent to 95% VO_2max (HIIE); resistance exercise consisting of three sets of 12-15 repetitions at 70%1RM (RES-70); resistance exercise consisting of three sets of repetitions to failure at 30%1RM (RES-30). All trials were randomised and separated by a washout period of 3-7 days. Participants completed a a visual analogue scale (VAS) for pain at baseline then 2-and 24-hours post exercise; they also completed a questionnaire related to exercise enjoyment 2-and 24-hours post exercise.
Results: Currently four RA participants have completed the study and all participants completed the prescribed exercises in full. Perceived pain was low at 2 hours (0.7±0.4) and 24 hours post-exercise (1.2±0.8) for all exercise conditions (see table 1). Importantly, a difference in heart rate between the aerobic conditions (heart rate during HIIE was 16% higher than during CYCLE), and a difference in workload between the resistance conditions (RES-30 was 117% higher than RES-70) did not result in a difference in pain perception. One participant reported increased pain at 24 hours (7cm vs 1cm at 2 hours) post RES-30, but claimed that this was purely muscular and not joint pain. Interestingly, all participants enjoyed the exercises with comparable high results across the exercise conditions (see table 1).

Table 1 Pain and Enjoyment Descriptives

Trial	Baseline VAS pain (cm)	2-hour VAS pain (cm)	24-hour VAS pain (cm)	2-hour exercise enjoyment (1-119)	24-hour exercise enjoyment (1-119)
CON	0.1±0.3	0.1±0.3	0.3±0.3	63.8±13.0	63.8±13.0
CYCLE	0.1±0.3	0.5±0.4	0.9±1.2	86.8±11.0	88.0±8.8
HIIE	0.1±0.3	1.3±1.9	1.1±1.7	85.0±27.8	88.3±19.1
RES-70	0.1±0.3	0.4±0.4	0.5±0.4	91.3±13.0	88.3±6.6
RES-30	0.1±0.3	0.4±0.5	2.4±3.1	88.5±17.1	85.0±13.1

(mean±SD)

Conclusion: This study identified minimal exercise effect on perceived pain at 2 hours-and 24 hours-post exercise among participants with early RA. This suggests that exercise did not exacerbate pain and importantly, high intensities and high loads did not cause additional pain. Nevertheless, further larger studies are required to examine the role of acute exercise on disease activity, e.g. inflammation, and the association with perceived pain in people with early RA.
References:
[1] Combe B, et al. 2016 update of the EULAR recommendations for the management of early arthritis. Annals of the Rheumatic Diseases 2016; 76: 948-959.
Disclosure of Interests: None declared
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AB1260 ARE THERMAL CURE AND REHABILITATION EFFECTIVE FOR RELIEVING LOW BACK PAIN? RESULTS OF A RANDOMIZED CONTROLLED TRIAL

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Background: Low back pain (LBP) is a major health problem around the world. It affects almost 80% of the population. Patient with LBP suffer from a heavy pain which is associated to long time incapacity. Different methods of treatment are applied in the objective of reducing pain and thus improving functional capacities of patients.
Objectives: Our study aimed to compare the benefits, with regard to LBP symptoms, of a thermal cure and a rehabilitation treatment.
Methods: It is a randomized therapeutic trial including patients with LBP, randomly divided into two groups: thermal cure and physical rehabilitation. Both of them were conducted in the same spa center of Djbal El Ouest. Outcome measures were visual analogic scale of pain (VAS), Oswestry Disability Index (ODI), Short Form-36 (SF36) questionnaire and schober test. Evaluation was carried out at day 18, 3 months, 6 months and 12 months following treatment.
Results: Seventy-four patients were included, divided into 2 groups: thermal group (n=37) and dry rehabilitation group (n=37). Seventy patients performed the full treatment.
In the group of patients treated with thermal cure treatment (n=37), a significant improvement of VAS of pain, ODI and SF 36 was noted in day 18, 3 months,6 months and 12 months (Table 1).

Table 1. Tendencies of the clinical indexes after treatment by thermal cure

	D0 (n=37)	D18 (n=37)	3months (n=35)	6months (n=32)	12months (n=36)
VAS ± SD	68,2 ± 16,2	**35,8 ± 26,5**	**55 ± 19**	**60,2 ± 18,1**	**56,1 ± 19**
P		**0,000**	**0,000**	**0,008**	**0,002**
ODI ± SD	38,3 ± 14,1	**29 ± 17,5**	**32 ± 14,1**	30,2 ± 14,1	**28,5 ± 13,6**
P		**0,03**	**0,03**	0,07	**0,000**
SF 36 physical mean score ± SD	34,4 ± 14,3	**64,2 ± 18**	**45,9 ± 19**	**50 ± 21,8**	**47,9 ± 18,5**
P		**0,000**	**0,000**	**0,000**	**0,001**
SF36 mental mean score ± SD	38,9 ± 16,3	**71 ± 21,6**	**55,1 ± 20,4**	**56,4 ± 19,9**	**52,2 ± 20,8**
P		**0,000**	**0,000**	**0,000**	**0,000**
Scober test ± SD	3,1 ± 1,3	**3,5 ± 1,3**	2,8 ± 1	3 ± 1,1	3,2 ± 1,5
P		**0,037**	0,322	0,812	0,657

VAS: visual analog scale; ODI: Oswestry Disability Index; SF36: short form 36

In the group of patients treated with physical rehabilitation (n=33), a significant improvement of the VAS of pain and of the physical mean score of SF36 was noted only on day 18 (Table 2). A significant improvement of the mental mean score of SF 36 was noted on day 18 and 6 months (Table 2).

Table 2. Tendencies of the clinical indexes after treatment by physical rehabilitation

	D0 (n=37)	D18 (n=33)	3 months (n=28)	6 months (n=29)	12 months (n=25)
VAS ± SD	64 ± 19,5	**47,4 ± 24,6**	55,7 ± 18,1	50,5 ± 27,5	62,2 ± 22,2
P		**0,002**	0,091	0,057	0,567
ODI ± SD	34,3 ± 12,3	31,1 ± 17,3	31,9 ± 15,6	30,3 ± 18,8	31,1 ± 12
P		0,268	0,258	0,296	0,150
SF 36 physical mean score ± SD	38,1 ± 16,1	**53,8 ± 22**	42,6 ± 16,4	45,1 ± 18,7	42,6 ± 16,2
P		**0,002**	0,284	0,202	0,185
SF36 mental mean score ± SD	39,3 ± 17,5	**61,6 ± 23,5**	45,1 ± 18,9	**49,6 ± 24,6**	46,9 ± 22,1
P		**0,000**	0,130	**0,033**	0,09
Schober test ± SD	3,2 ± 1,4	**3,5 ± 1,3**	3,4 ± 1,4	2,7 ± 1,2	2,9 ± 1,3
P		0,845	0,983	0,091	0,346

VAS: visual analog scale; ODI: Oswestry Disability Index; SF36: short form 36

Comparison of the two types of tested treatments showed a certain number of statistically significant differences. The VAS and physical mean score of SF 36 at day 18 and mental mean score of SF-36 at 3 months were significantly lower on the thermal cure group, while schober test at 3 months was significantly lower in the physical rehabilitation group.

Conclusion: Our study suggests a superiority of thermal cure in relieving pain and improving quality of life at short term among patient with LBP and a comparable efficacy in improving lumbar spine function. However, the effectiveness of physical rehabilitation was greater on spine mobility.

Disclosure of Interests: None declared

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AB1261 DOUBLE-BLIND PLACEBO-CONTROLLED TRIAL OF PULSED ELECTROMAGNETIC FIELD THERAPY IN KNEE OSTEOARTHRITIS (PRELIMINARY RESULTS)

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Background: Pulsed electromagnetic field (PEMF) therapy is widely used in different areas of medicine. There are a lot of portable PEMF therapeutic devices on the market around the world. Nevertheless, the role of PEMF in treatment of rheumatic conditions is not clear. Current evidence is of low and very low quality.

Objectives: To study efficacy and safety of PEMF therapy in primary and secondary osteoarthritis (OA) of the knee in controlled clinical trial.

Methods: This abstract presents the preliminary results of an ongoing double-blind placebo-controlled trial of PEMF portable therapeutic device "ALMAG+" (Certificate EN ISO 13485:2012+AC:2012 reg.-No 44221 117836, Yelatma Instrument-Making Enterprise, Russian Federation, Reg. Num.: 3007075140). The device is intended for physiotherapeutic treatment and rehabilitation with a low-frequency low-intensity PEMF in medical institutions, as well as at home after the recommendation of a doctor. Patients with primary and secondary (as a part of inflammatory rheumatic disease) OA of knee with Kellgren-Lawrence Grade I-III included in the study (in patients with inflammatory conditions disease activity should be minimal on stable drug therapy). Three courses of PEMF of 20 procedures for 1 year planned in active treatment group and placebo (inactive device) group of 35 patients each. Efficacy is evaluated by pain VAS, WOMAC, Lequesne index, and quality of life studied using SF-36, EuroQoL 5D tools. Instrumental control with knee ultrasound and MRI investigations will be performed. The study protocol was approved by local Ethical Committee.

Results: To date 23 patients (7 males, 16 females, age 54,6±11,2 years, primary knee OA – 16 pts, RA- 6 pts, AS – 1 pt) completed 1st course of PEMF. Table presents differences (Δ) in the main clinical parameters in active treatment and placebo device groups. No significant difference in ESR or CRP levels was found. No treatment-related adverse events has been reported.

Table. Differences (Δ) in the main clinical parameters after a 1st course of PEMF.

Parameter	Active device (n=11)	Placebo device (n=12)	p
Δ VAS pain in movement	15 [0; 38,5]	5 [1,25; 10,5]	0,053
Δ VAS pain in rest	10 [0; 34]	1 [0; 2,75]	0,043
Δ WOMAC	3 [2; 10]	2 [0; 4,5]	0,174
Δ Lequesne index	3 [0; 4]	1 [0,25; 2,5]	0,258

Conclusion: In this preliminary analysis pulsed electromagnetic field (PEMF) therapy showed significant impact on pain in rest in knee OA after one course of procedures.

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AB1262 EFFECTS OF TAI CHI EXERCISE ON PAIN, FUNCTIONAL STATUS AND QUALITY OF LIFE IN PEOPLE WITH OSTEOARTHRITIS AND INFLAMMATORY ARTHRITIS

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Background: Tai Chi as a type of physical activity (PA) is included in recommendations for PA in people with inflammatory arthritis (IA) and osteoarthritis (OA).[1]

Objectives: The aim of this study was to evaluate the effect of Tai Chi exercise program on pain, functional status and quality of life in people with OA and IA.

Methods: A study co-funded by the Erasmus + European Union Program for Sporting Activities called #WushuElixir was conducted in Croatia, Slovenia, Belgium and Spain. We present the results of the research conducted in Croatia from October 2018 to April 2019. A total of 44 participants (Pts) entered the Tai Chi exercise program. Majority of Pts were female with OA (Table 1). Tai Chi exercise program was performed for 60 minutes, twice a week, with a total of 50 training sessions. In data analysis where included only those Pts who completed at least 36% of exercise program, a total of 28 (63.6%) Pts, out of which 24 (85.7%) completed at least 70% of exercise program. An average attendance was 39 (78%) sessions. Outcome measures were: pain (VAS scale), stability and balance (Functional reach test; FRT), chest mobility (breathing index), spinal mobility (cervical and thoracic sagittal indices and Schober's test), muscle strength (Wall sit test), physical function (Lequesne Index of severity for OA of the hip, and Stanford Health Assessment Questionnaire (HAQ) 20-Item for IA) and quality of life (15D© The health-related quality of life instrument; 15D QL). For statistical analysis t-test for paired samples was used with statistical significance set on P<0.05.

Table 1. Descriptive statistics of participants

		N	%
Gender	Male	4	14.3%
	Female	24	85.7%
Age groups	≤45 years	3	10.7%
	46-60 years	9	32.1%
	61-70 years	11	39.3%
	≥71 years	5	17.9%
Diagnosis	Osteoarthritis of the spine, hip and knee	19	67.9%
	Inflammatory arthritis	5	17.9%
	Other	4	14.3%

Results: There was significant improvement in breathing index (P<0.001), sagittal mobility of cervical (P<0,001) and thoracic spine (P=0.007), Schober's

test (P<0,001), Wall sit test (P=0.042), 15D QL (P=0.048) and Lequesne index (P=0.030). There were no significant changes in VAS pain level (P=0.651), FRT value (P=0.442) and Stanford HAQ-20 scale result (P=0.186).

Conclusion: Tai Chi can improve functional status and quality of life in people with OA and IA.

References:

[1] Rausch Osthoff AK, Niedermann K, Braun J, et al. 2018 EULAR recommendations for physical activity in people with inflammatory arthritis and osteoarthritis. Ann Rheum Dis. 2018;77(9):1251-1260.

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AB1263 THE EFFICACY OF PULMONARY REHABILITATION IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Ankylosing spondylitis (AS) is a rheumatic disease that can cause a restrictive lung condition. Pulmonary rehabilitation increases lung capacity in patients with lung disease. In this study, we aimed to show increase in exercise capacity, decrease in dyspnea and change in quality of life with pulmonary rehabilitation in patients with AS.

Objectives: In this study, we included 20 AS patients of whom admitted to our outpatient clinic. At the beginning and end of the study, patients some findings such as SFT, FEV1 values, saturations, arterial blood pressures and heart rates were recorded separately. Also, BODE index results, 6-minute walk test (MWT) values, BORG dyspnea scores, Modified Medical Research Council (MMRC) dyspnea scales, Anxiety Stress Scales (ASS) were examined. Short Form-36 (SF-36) questionnaires were filled out.

Methods: Patients underwent rehabilitation for 8 weeks, two days in a week at hospital and one day at home. According to their exercise tolerances in rehabilitation, patients were given upper and lower limb endurance training, strength training, flexibility and stretching exercises, balance exercises, inspiratory muscles training.

Results: In our study, patients with AS showed significant improvement in MMRC, borg dyspnea scales and 6 MWT at the end of rehabilitation compared to beginning of rehabilitation (p<0.05). It is shown that there was significant improvement in the values of PEF % and FVC%, when the difference averages before and after rehabilitation were compared (p < 0.05) but there was no difference in FEV1 %, FEV1/FVC values (p > 0.05). There was also significant improvement in BASDAI-BASFI values (P=0.006, P=0.016, respectively). The bode index showed no significant difference (p > 0.05). There was significant improvement in anxiety on ASS. Only the mental parameter showed significant improvement when parameters evaluated by the SF-36 survey (p < 0.05). There was no significant difference in the rest of all parameters (p>0.05).

		Before treatment n=20 (Mean ±SD)	After treatment n=20(Mean ±SD)	p*
FVC		84,35±13,92	86,40±13,42	,007
FEV1		84,50±13,03	85,30±11,13	,431
FEV1_FVC		105,30±9,57	85,30±11,13	,837
PEF		64,80±17,14	67,60±16,65	,003
6-Minute Walk Test		415,5500±124,88625	439,900±122,364	,000
MMRC Dyspnea Scale		1,350±1,136	1,150±,87509	,046
BORG Dyspnea Score		2,400±1,273	1,650± 0,988	,000
BODE Index		,7500±1,86025	,700±1,688	,317
BASDAI		3,622±1,837	3,140±1,392	,006
BASFI		4,350±1,692	6,065±8,638	,016
ASS		9,00±5,036	7,050±3,034	,006
SF36	General Health	47,000±15,165	49,125±14,171	,485
	Energy	47,000±20,026	52,000±18,020	,120
	SocialFunctioning	55,000±22,725	58,875±18,217	,129
	Role limitations due to emotional problems	47,765±46,185	64,515±36,463	,117
	Mental	52,450±19,527	62,800±17,572	,041

P* Wilcoxon signed rank test. n, number of participants; SD, standard deviation; FVC,forced vital capacity;FEV1,forced expiratory volume;PEF,pik expiratory volüme; MMRC, Modified Medical Research Council;O2,oxygen; BASDAI,Bath Ankylosing Spondylitis Disease Activity Index; BASFI,Bath Ankylosing Spondylitis Disease Activity Index;SF-36, Short Form-36.

Conclusion: After pulmonary rehabilitation in patients with AS dyspnea symptoms decreased. As a result of this study, it is thought that pulmonary rehabilitation applied to patients with AS can minimize the adverse effects of the disease over the respiratory system.

Key words; pulmonary rehabilitation, ankylosing spondylitis, respiratory function test

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AB1264 THE EFFECTIVENESS OF KINESIOTHERAPY FOR PAIN SHOULDER SYNDROME

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Background: Pain shoulder syndrome is one of the most common conditions that is inherent in patients with various diseases and conditions. This problem is faced by both patients of a rheumatological profile (rheumatoid arthritis), and patients of other profiles: neurological (stroke, hernia of the cervical spine), traumatological (periarthritis). The regular use of painkillers and NSAID is associated with a risk of serious adverse reactions in patients.

PNF therapy can have a fairly quick positive effect. Kinesiotaiping is a common and easily accessible treatment method that, due to the inclusion of local neuromuscular adaptation mechanisms, can have an analgesic effect.

Objectives: The purpose of the study is to compare the effectiveness of traditional treatment methods in combination.

Methods: Patients with pain shoulder syndrome who were admitted to the doctor of physical and rehabilitation medicine were randomly assigned to one of three groups: group G1 - 20 patients who received combined treatment, including massage, acupuncture, PNF, kinesiotherapy.

Patients of group G2 (20 people) who received massage and acupuncture sessions, kinesiotherapy, but did not deal with PNF.

Patients in group G3 (20 people) received massage, acupuncture, and PNF, excluding kinesiotaping.

All patients received treatment 5 times a week (Monday to Friday, excluding Saturday and Sunday), the total duration of the rehabilitation course is 20 days. The program included: 30 minutes an acupuncture session, 20 minutes massage, 45 minutes physical exercises with a physical therapist. Classes using the PNF technique were carried out separately every other day for 45 minutes using the standard method for shoulder pain.

VAS was used to monitor efficacy. Pain was assessed at the beginning of the study, with the third, sixth, ninth and last visit to the clinic.

Results: The age composition of the patient group is from 31 to 70 years. The gender composition is 35 (58.33%) women, and 25 (41.67%) men.

The average time between the onset of clinical symptoms and the first treatment session was 47.3 days. In 90% of patients, a history of pain lasted from 6 weeks or more. 52 patients (86.67%) completed the treatment completely. Of these, G1 is 19 people (90% of this group), 16 (80%) in G2, and 17 of 20 in the G3 group (85%).

The average VAS score in G1 was 5.15 at the start of the study, and after the tenth session, it dropped to 2.78. A significant decrease in pain is also observed in the G2 group (from 5.17 at the beginning of the study to 3.19 after the tenth session). The G3 group in terms of pain reduction almost equaled the G1 group, where the level of pain from 5.16 decreased to 2.71.

Patients within 6 months after treatment evaluated the level of pain on their own and reported the data to the doctor. In patients of group G1, after 6 months, the average VAS score is 3.71. G3 patients after 6 months, the VAS score is 4.25 points. Patients of the G2 group at 3 months noted a return of the pain syndrome, after 3 months, the VAS score was 5.11.

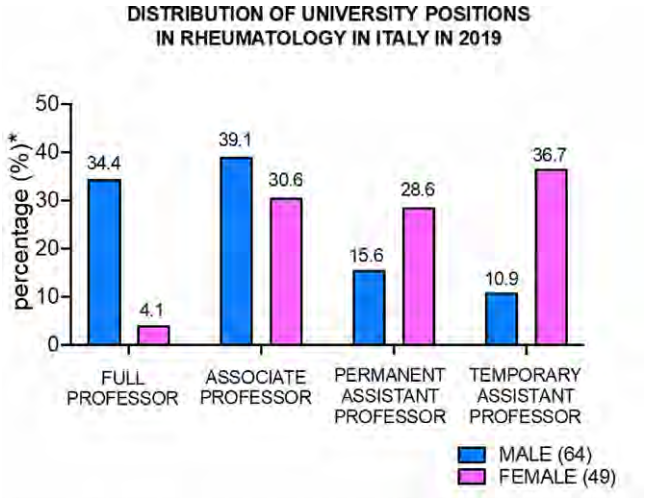
Conclusion: The obtained results testify to the high efficiency of PNF therapy, however, the combination with kinesiotyping allows better consolidation of the effect of therapy and prolongs remission of pain syndrome.
Disclosure of Interests: None declared
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Education

AB1265 GENDER DISTRIBUTION AND GENDER-RELATED ISSUES AMONG YOUNG RHEUMATOLOGISTS AND ACADEMIC POSITIONS IN RHEUMATOLOGY: A SNAPSHOT OF THE CURRENT SITUATION IN ITALY

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Background: The Italian Society for Rheumatology (SIR) comprises committees for Rheumatologists under the age of 40 (SIRyoung) and for Women in Rheumatology (Reumatologhe Donne – ReDO). As female representation is increasing in rheumatology worldwide [1], there has been interest in assessing gender-related issues.
Objectives: To describe the gender distribution among young members of SIR and academic positions in Rheumatology in Italy. To assess the expectations and needs of young rheumatologists with regard to their career.
Methods: SIRyoung members developed a web-based survey which was distributed among SIR members under the age of 40 during the spring of 2019. Responses were collected and analysed anonymously. ReDO retrieved and analysed the data regarding academic positions in Italy in September 2019 from official data by "Ministry of Education, University and Research" (www.miur.it).
Results: Out of 478 SIR members under 40 (66.5% F), 113 (23.7%) completed the SIRyoung survey (62.1% F). Regarding career plans, male and female members responded: hospital physician (36.9% vs 37.8%), outpatient clinic physician (18.5% vs 28.3%), academic career (23.9% vs 22.8%), private practice (16.3% vs 9.4%), and industry (4.3 vs 1.6%), respectively. When asked about their interest in doing a fellowship in another national center or abroad, 60.8% of male and 72.8% of female respondents were interested but thought they could not afford it. Reasons reported by males and females were: working reasons, namely barriers to temporarily leave the workplace (61.3% vs 50.7%), family reasons (16.1% vs 25.4%), financial reasons (22.6% vs 16.5%), respectively. As for academic rheumatology in Italy, 113 positions were retrieved. Men held 64 positions (57%) and women 49 (43%). Full professors were mostly men (92%), while assistant professors were women in 65% of the cases (58% of those with a permanent position; 72% of those with a temporary position) (Figure) [2].
Conclusion: Our study explored for the first time gender distribution and related issues in Rheumatology in Italy. Female representation accounts for two thirds of SIR members under 40. This could reflect the general trend of medical school being chosen more often by women than men. No differences were observed in the career expectations of male and female rheumatologists. Interestingly, nearly one fourth of female respondents were interested in academic career, confirming the trend toward female predominance observed for assistant professors. Therefore, it is likely that the next generation of full professors will have a balanced gender distribution, as it is already for associate professors. The choice of a fellowship is still hampered by several problems, but it seems that reasons for not pursuing such opportunities are similarly distributed in males and females. Although family reasons tend to be more frequent in female rheumatologists, this is not significant as compared to men. This could indicate that family affects career choices of both male and female rheumatologists. It is important that national societies promote surveys for the assessment of gender specific issues among their members, in order to identify unmet needs and design interventions for career support regardless of gender.



*percentages referred to the individual male (n=64) and female (n=49) cohorts, respectively

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AB1266 JOINTS STILL PLEADING FOR ATTENTION

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Background: Despite the prevalence of musculoskeletal diseases in an increasingly elderly patient population, musculoskeletal (MSK) examination remains frequently overlooked and poorly completed in medical clerking. Indeed, studies over the years have emphatically demonstrated the widespread omission of MSK examination. (1,2)
Objectives: The aim of this study was to evaluate the documentation of MSK examination in medical clerking on the acute medical take. Furthermore, we sought to assess doctors' perception of MSK examination and to evaluate the effect of GALS teaching.
Methods: Medical clerkings of 50 patients in the medical assessment unit (MAU) were reviewed on a single day irrespective of the pathology. Case notes were assessed for presenting complaints and documentation of clinical examination findings. Results of the baseline study along with GALS examination techniques were presented at the departmental meeting. Case notes review was subsequently repeated with the same sample size.
Results: Baseline study showed that MSK exam was recorded in only 10% of patients despite 20% of patients presenting with fall/collapse. In contrast, 100% of medical clerkings had respiratory examination, 94% had cardiovascular examination while 94% had abdominal examination documented. Although confidence in performing MSK examination was not felt to be a problem, perceived time constraints was a major barrier.
Repeat study with another 50 set of clerkings demonstrated a significant improvement, with 22% of clerkings having MSK examination recorded. However, the quality of documentation of MSK examination remained sketchy.
Conclusion: Our study reaffirms the fact that MSK examination remains broadly neglected despite the high proportion of patients admitted with fall or collapse. Although the completion of MSK examination improved following GALS screen teaching, the quality of clinical examination documentation remained inadequate. Evidently, the indifference towards MSK examination warrants prompt attention and action by medical educators and rheumatologists.

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AB1267 ONLINE CASE-BASED EDUCATION SIGNIFICANTLY IMPROVED RHEUMATOLOGISTS' KNOWLEDGE AND CONFIDENCE IN MANAGING PATIENTS WITH RA

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Background: With the rapid evolution in treatment strategies and the increasing range of available therapeutics for rheumatoid arthritis (RA), keeping pace with advances can be a challenge for busy physicians.
Objectives: We assessed whether online CME can improve rheumatologists' knowledge of RA management focusing on the assessment and monitoring of RA, the selection of appropriate treatments and the clinical efficacy and safety data for JAK inhibitors.
Methods: Rheumatologists participated in a text-based activity featuring two patient cases with questions that "tested" knowledge and discussion of the main "teaching" points. Educational effect was assessed using a repeated-pair design, pre-/post-assessment. A Chi-square test of independence determined if a statistically significant improvement (5% significance level, $P<.05$) existed in the number of correct responses between the pretest and posttest scores. Cramer's V estimated the effect size of the education. The activity launched on 15 December 2018 with data collection through 27 February 2019.
Results: •Significant improvement in average percentage of correct responses, rising from 47% at baseline to 92% post-activity ($P<.001$) and extensive educational impact (Cramer's V=0.496)
•Significant increase in percentage of rheumatologists (n=111) answering all 3 questions correctly (9% at baseline rising to 78% post assessment)
•Significant improvements in knowledge of EULAR/ACR assessment criteria (86% improvement, $P<.001$), EULAR treatment recommendations for a patient failing on MTX and a TNF inhibitor (100% improvement, $P<.001$), and the VTE risk associated with having RA or receiving RA treatments (108% improvement, $P<.001$)
•46% of rheumatologists reported greater confidence in their ability to appropriately incorporate JAK inhibitors into the treatment of patients with RA (average confidence shift 20%)
Conclusion: Overall, this learning activity was highly successful in improving rheumatologists'
knowledge and confidence in managing patients with RA, particularly with regard to the appropriate use of JAK inhibitors in patients for whom such treatment is suitable. The extensive impact of this interactive 'test then teach' activity is likely to directly translate into patient benefit. Further education on this topic would be useful to enhance and reinforce this knowledge and to support physician confidence in the use of JAK inhibitors in clinical practice.
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AB1268 ONLINE EDUCATION YIELDS SIGNIFICANT GAINS IN RHEUMATOLOGISTS' KNOWLEDGE OF THE ROLE OF JAK INHIBITORS IN THE MANAGEMENT OF RA

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Background: The treatment armamentarium for rheumatoid arthritis (RA) has expanded rapidly in recent years, making it challenging for rheumatologists to stay up to date with key advances. The most recently available treatment options for RA are the JAK inhibitors.
Objectives: Our goal with this activity was to assess whether online CME can improve rheumatologists' knowledge of the role of JAK inhibitors in the management of RA.
Methods: Rheumatologists participated in an online CME activity entitled 'Advancing patient care in rheumatoid arthritis: role of JAK inhibitors'. This was a 30-minute video roundtable discussion between 3 experts, with accompanying slides. This CME activity launched on April 30 2019 with data collection through September 13 2019. The educational effect was assessed using a repeated-pair design, pre-/post-assessment. A Chi-square test of independence determined if a statistically significant improvement (5% significance level, $P<.05$) existed in the number of correct responses between the pretest and posttest scores. Cramer's V estimated the effect size of the education.
Results: •Significant improvement in average percentage of correct responses, rising from a relatively high baseline of 67% to 81% post-activity ($P = .0006$)
•Increase in percentage of rheumatologists (n=68) answering all 3 questions correctly (37% at baseline rising to 66% post assessment)
•Significant improvement in knowledge of clinical trial safety data for JAK inhibitors (43% improvement, $P = .0079$)
•Numerical improvement from relatively high baseline for understanding of unmet needs in RA patients (74% at baseline, 87% post-activity) and the advantages of JAK inhibitors versus TNF inhibitors for a specific patient case (75% at baseline, 84% post-activity)
•Considerable educational impact (Cramer's V = 0.167) with 35% of rheumatologists reporting greater confidence in describing the mechanism of action of current and emerging JAK inhibitors (noteable average confidence shift of 15%)
Conclusion: A positive and significant effect on physician knowledge and confidence regarding JAK inhibitors for RA was achieved following this online CME activity. The extent of this educational impact is likely to lead to better patient outcomes since physicians are better equipped to consider JAK inhibitors for appropriate patients. The results also revealed that physicians would benefit from additional education to reinforce their knowledge of key clinical data for JAK inhibitors and on the use of JAK inhibitors in clinical practice.
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AB1269 REGIONAL DIFFERENCES IN THE PATIENTS' UNDERSTANDING OF TREATMENT STRATEGY IN RHEUMATOID ARTHRITIS

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Background: The treat-to target (T2T) concept is the standard for treating rheumatoid arthritis (RA) patients worldwide[1]. However, difficulties that patients encounter in achieving disease control may differ between regions, which may impact the type of support needed for successful T2T implementation.
Objectives: To compare differences in patient-reported challenges to controlling RA-related issues between Romanian and US patients.
Methods: A cross-sectional study that recruited 403 RA patients was conducted in six centers in Romania. Patients were invited to complete an RA-related questionnaire. We compared their responses to those from a previous published study that included patients with RA from the US[2]. The survey included items on subjective beliefs about RA treatment (e.g. adherence, cost, adverse events) and knowledge about T2T strategy. Approval for US data use was given by the study coordinator[2].
Results: All patients in the Romanian cohort were Caucasian, with a mean age of 58.7 years (SD 11.6). 78% were females and the mean disease duration was 11.2 years (SD 8.3). Data was concordant with results from the previously published study. More patients from US had college education (60% vs 43.9%).
Among the respondents, 93.3% Romanians were on a synthetic DMARD versus 97.7% Americans and 64.01% were currently on a biologic of choice compared to 74% patients in the US. More than half of the patients in both regions had a history of biologic DMARD use.
Asked to grade (0 *very good*, 10 *very bad*) their disease activity on the survey day, a large category of patients (37.4%, SD 14.1) marked an average state (4-6), while 19.08% (SD 11.2) were feeling poorly related to their disease.
Patients were asked to define their adherence to RA treatment in the last 30 days. While the US study reported that 93% of patients were adherent[2], in our study only 62.5% of the Romanian patients reported adherence ($p<0.01$). A significantly lower proportion of Romanian patients were aware of T2T strategy (35 %, p 0.04).
Regarding patient beliefs on their disease, statements were grouped into categories such as difficulty managing pain, medication safety, adherence, lifestyle.

Most European patients would agree to change treatment to lower pain. Almost 82% stated they would accept rare adverse events in order to avoid invalidity, to confirm a better future outcome. US patients were more prone to stick to current therapy than escalade to increase clinical response. However, asked about novel therapies, Romanians were reluctant to changing treatment despite insufficient benefit, if the risk of cancer was noted. There was a high agreement that a delay in treatment would be unsatisfactory for both familial and professional chores.

Conclusion: There are regional differences in knowledge and perceptions about RA treatment. Romanian patients know less on T2T algorithm. Improving awareness of the T2T strategy among RA patients may need different types of support depending on the patient's place of residence.

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Disclosure of Interests: CLAUDIA COBILINSCHI Speakers bureau: novartis, Maria Danila Speakers bureau: as personally stated, Daniela Opris-Belinski Speakers bureau: as declared, Ioana Saulescu Speakers bureau: Eli-Lilly, Pfizer, Laura Groseanu Speakers bureau: novartis, eli-lilly, ucb, pfizer,sandoz, Sanziana Daia-Iliescu Speakers bureau: sandoz, Catalin Codreanu Consultant of: Speaker and consulting fees from AbbVie, Accord Healthcare, Alfasigma, Egis, Eli Lilly, Ewopharma, Genesis, Mylan, Novartis, Pfizer, Roche, Sandoz, UCB, Speakers bureau: Speaker and consulting fees from AbbVie, Accord Healthcare, Alfasigma, Egis, Eli Lilly, Ewopharma, Genesis, Mylan, Novartis, Pfizer, Roche, Sandoz, UCB, Razvan Ionescu Speakers bureau: as personally stated, Magda Parvu Consultant of: Speaker fee and consultant: Pfizer, Novartis, Roche, Abbvie, UCB, Eli-Lilly, Speakers bureau: Speaker fee and consultant: Pfizer, Novartis, Roche, Abbvie, UCB, Eli-Lilly, Horatiu Popoviciu Speakers bureau: as personally stated, CODRINA ANCUTA Consultant of: AbbVie, Pfizer, Roche, Novartis, UCB, Ewopharma, Merck Sharpe and Dohme, and Eli Lilly, Speakers bureau: AbbVie, Pfizer, Roche, Novartis, UCB, Ewopharma, Merck Sharpe and Dohme, and Eli Lilly, Elena Rezus: None declared, Claudia Mihailov Speakers bureau: as personally stated, Ruxandra Ionescu Consultant of: Consulting fees from Abbvie, Eli-Lilly, Novartis, Pfizer, Roche, Sandoz, Speakers bureau: Consulting and speaker fees from Abbvie, Eli-Lilly, Novartis, Pfizer, Roche, Sandoz

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AB1270 RHEUMATOLOGY WORKFORCE IN LATIN AMERICA: TRAINING AND CURRENT STATUS

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Background: The demand for rheumatology care has been steadily increasing over the last few years. However, supply seems to be insufficient, according to previous research[1]. This situation may be at least partly explained by less physicians beginning a rheumatology residency program[2].

Objectives: We aim to identify baseline data, room for change, and to strengthen functional processes associated with the rheumatology workforce in order to improve care offered to patients living with rheumatic diseases.

Methods: Descriptive cross-sectional study. We obtained data on each country through local PANLAR rheumatologists. They completed an online survey using the RedCap® platform, used for capture and storage of data. The sample was described according to the type of variable.

Results: 19 Latin American countries were included in this study, globally 1 rheumatologist was available per 106,838 inhabitants. The highest rates were found in Uruguay (1 per 23.695 inhabitants) and Argentina (1 per 40.384 inhabitants). The lowest rates were found in Nicaragua (1 per 640.648 inhabitants) and Guatemala (1 per 559.902 inhabitants). The ratio between women and men rheumatologists was 0,99 women per each man. The lowest proportions were found in Peru (0,26:1), and the highest in the Dominican Republic (2.5:1). The average age for rheumatologists was 51,6 (SD12,75). Lowest average ages were found in Paraguay (43,1 SD10,77) and the highest age averages were found in Peru (56,23 SD12.93). The average monthly compensation was USD $2.382,6 (SD$1.462,5). Venezuela had the lowest salary ($197), the highest salary was found in Costa Rica ($4.500). The proportion of rheumatologists trained abroad was 26,7%, ranging between 0% in Uruguay and 90% in Bolivia.

The countries with more rheumatology training programs were Brazil n = 50 and Mexico n = 20, while Ecuador, Honduras and Nicaragua don't have any. The countries with the greatest amount of active residents were Brazil (n = 252) and Argentina (n = 100). The educational level required to enter the program was postgraduate studies in internal medicine in 42.11% of the programs. Currently, 108 residency programs in Latin America are active. Duration of residency programs is variable: 2 years (79.63% of cases), 3 years (16.67%), 4 years (1.85%), 5 years (0.96%) or 6 years (0.96%). The median monthly compensation for residents was $ 528 USD (IQR $ 774), the country with the highest payment was Costa Rica ($ 2637). Contrarily, in Cuba, Chile and Colombia there is no payment to residents. Finally, in 8 countries (42.11%) residents must not pay for their postgraduate studies, the average annual tuition expense in the rest of countries is $ 1248 (SD $ 2749).

Conclusion: The rate of rheumatologists per inhabitant is low. The demographic characteristics and the current status of the rheumatology workforce, as well as rheumatology training in Latin-America varies widely among countries. For instance, relevant differences can be found regarding payment to rheumatologists and residents, and tuition fees. The collected information will be useful when planning regional-based strategies, as well as for future research projects in each country and within PANLAR.

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AB1271 PATIENT EDUCATION IN PSORIATIC ARTHRITIS: A SERVICE EVALUATION AT ONE YEAR

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Background: Recent studies have demonstrated an increasing burden of musculoskeletal (MSK) diseases worldwide.[1] The importance of patient education (PE) is often overlooked in the management of long term inflammatory conditions. The European League Against Rheumatism recommends that PE should be integral to standard of care in inflammatory arthritis.[2] PE increases patients' knowledge, skills and confidence in managing their condition and improves patient activation (PA). Evidence shows that improved PA results in better outcomes and improved experiences of care. We previously reported on improved knowledge and confidence amongst a small patient group with psoriatic arthritis (PsA) who had attended a pilot education session.[3] This education session was delivered to a wider group of patients with PsA over a 12 month period; we report on the evaluation received from this service.

Objectives: To provide a PE programme to a wider group of patients with PsA, using a multi-disciplinary team (MDT) approach and to evaluate whether this improved patients' knowledge, skills and confidence in managing their PsA.

Methods: Adult patients with PsA attending their rheumatology clinic appointments were invited to a 2.5 hour MDT education session which covered: 1) a general overview of PsA; 2) medications used in PsA; 3) the role of physiotherapy and occupational therapy; 4) flares and self- management. These were interactive sessions, held in a small group setting to allow for informal discussion and questions to the MDT. Written materials including several booklets and online resources were also provided. Patients evaluated their knowledge or understanding before and after each topic covered, on the same day, using an evaluation tool with1-10 Likert scale items. Changes in ratings were analysed using student's t-tests. Patients were also asked: which aspects they found particularly helpful; if there was anything they would like to have added/ have more of in the session; whether they found the session helpful; whether they would recommend

it to other patients; whether they would be interested in developing a PsA patient support group.

Results: Four sessions were held over a 12 month period. A total of 32 patients attended; 10 males and 22 females, across a range of age categories. Disease duration varied from less than1 year to over 10 years. There were statistically significant improvements in all topics covered: mean improvement of 91% in how well informed patients felt about PsA overall (p<0.0001); mean improvement of 74% in confidence in accessing help from the MDT (p<0.0001); mean improvement of 122% in how well informed patients were about medications used in PsA (p<0.0001); mean improvement of 99% in patients' confidence in self-managing a flare (p<0.0001). Aspects that patients found particularly helpful included "The whole session", "Asking questions to all different professionals", "Meeting other sufferers", "Management of flares", "Fatigue information" and "Online resources". Overall, 97% of patients (31 out of 32) found the session helpful and would recommend it to others. Over 40% of patients expressed interest in developing a local PsA support group.

Conclusion: Following a 2.5 hour education session, improved knowledge, skills and confidence in managing their PsA was reported by 97% of patients, including patients with disease duration of > 10 years. This supports our previous finding that an interactive, group PsA education programme is a feasible and important adjunct to patient care.

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AB1272 ONLINE EDUCATION BOOSTS CLINICIAN KNOWLEDGE ABOUT EMERGING THERAPIES FOR PATIENTS WITH SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE

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Background: Systemic sclerosis-associated interstitial lung disease (SSc-ILD) has traditionally been treated with therapies such as cyclophosphamide, mycophenolate mofetil, and hematopoietic stem cell transplantation. However, these therapies are limited by potential toxicity, as well as duration and magnitude of effect. Clinicians need awareness of emerging therapies in late-stage clinical trials that may address these limitations.

Objectives: This study was conducted to determine whether online independent medical education could improve rheumatologists' and pulmonologists' knowledge of emerging therapies for the management of SSc-ILD.

Methods: Physicians (N = 2,076) participated in a 30-minute, 2-faculty, video-based, online CME with synchronized slides.[1] The majority of participants were rheumatologists (n = 522) or pulmonologists (n = 557), but the cohort also included clinical immunologists (n = 132) and other physicians with an interest in the topic (n = 865). This study focuses on the 120 rheumatologists and 111 pulmonologists who completed all pre- and post-questions. The effects of the education on knowledge was assessed using a 3-question, repeated pairs, pre-assessment/post-assessment study design. For all questions combined, the chi-square test assessed differences from pre- to post-assessment. P values <.05 are statistically significant. The activity launched on September 17, 2019, and data were collected through November 5, 2019.

Results: Overall significant improvements were seen after participation for both rheumatologists (average correct response rate of 55% at pre-assessment vs 75% at post-assessment; P<.001, N=120), and pulmonologists (average correct response rate of 60% at pre-assessment vs 77% at post-assessment; P<.001, N=111). Specifically, significant improvements were observed in clinicians' knowledge of clinical trial data for emerging SSc-ILD therapies (figure).

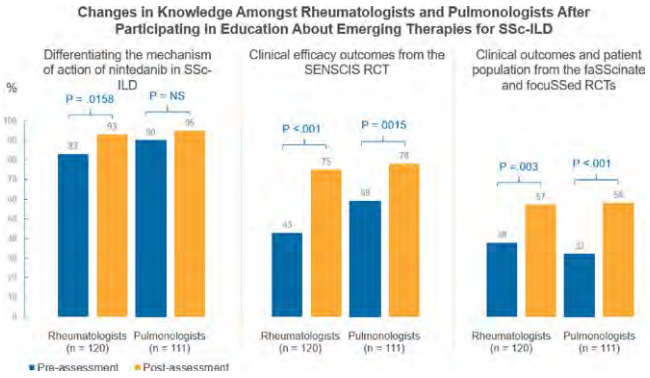


Figure.

Clinicians from APAC (n = 67) and Europe (n = 79) made up the majority of the cohort, and had similar rates of correct responses without significant differences, indicating consistent effects, independent of the region of origin. After participating in the activity, 48% of pulmonologists and rheumatologists had measurable improved confidence related to their knowledge of emerging therapies for patients with SSc-ILD.

Despite the increases in knowledge and confidence observed, the rates of correct responses suggest there is still room for improvement; therefore, ongoing education will be needed to reinforce knowledge of the latest data evaluating new therapies for SSc-ILD and what they will mean for future practice.

Conclusion: This study demonstrates the success of online, video-based education in improving rheumatologists' and pulmonologists' knowledge of the latest clinical data on emerging therapies for SSc-ILD. This could lead to earlier adoption of new, efficacious therapies that may slow disease progression and improve overall outcomes for these patients.

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AB1273 TEACHING RARE DISEASES THROUGH ROLE PLAY: RESULTS OF AN EXPERIMENTAL WORKSHOP ON RAYNAUD PHENOMENON

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Background: Systemic autoimmune diseases are mostly taught through theoretical lectures, which do not allow for the acquisition of physical examination skills and semiologic confrontation.

Objectives: We report herein the results of a pilot experiment using role-play to teach how to manage patients with Raynaud phenomenon (RP).

Methods: We developed a workshop that consisted of two 30-minute OSCE (Objective and Structured Clinical Examination) stations. Students were divided into groups of 4 to 5 persons. On each station, 2 students were actors and 2 were observers. After a short briefing, students played a 15-minute scenario and then had a 15-minute debriefing.

The first station simulated the case of a 26-year old woman referred for suspected RP. Students were instructed to perform clinical history taking and

physical examination of the patient, formulated relevant diagnosis hypotheses and prescribe any additional necessary exams. Students had to suspect the diagnosis of idiopathic RP. The simulated patient was played by a trained facilitator with expertise on RP.
The second station simulated the case of a 56-year-old woman referred for RP complicated by digital ulcers. Students received the same instructions as before. They had to suspect the diagnosis of systemic sclerosis. The patient role was held by a real patient with systemic sclerosis, followed by the physician who was supervising the station, who had received prior training and who agreed to participate in this training.
At the end of the workshop, the students had to complete a satisfaction questionnaire.
Results: A total of 21 students participated in the workshop and 17 completed the survey. The students were "very satisfied" (Likert 4/4) of this training in 94%. They considered this workshop "not very stressful" (Likert 2/4) and "very formative" (Likert 4/4) in 71%, but "a little short" (Likert 2/4) in 88%. After taking this training, all students felt "a little" (Likert 3/4, 24%) or "much more comfortable" (Likert 4/4, 76%) to manage patients with idiopathic RP; and "a little" (Likert 3/4, 65%) or "much more comfortable" (Likert 4/4, 35%) to manage patients with systemic sclerosis. All would recommend this workshop to other students.
When asked about the strengths of this training, the students mentioned the benefits of being put in an immersive situation, which allowed for a better acquisition of practical skills (especially physical examination) and a more interactive exchange with teachers; as well as the confrontation with a real patient, which allowed for a better retention of semiologic findings and associated a relational component to this experience. The main weak points reported were its short duration and the stress induced by being observed during the simulation.
Conclusion: This workshop suggests the interest and feasibility on a small group of students of a rare diseases awareness workshop using role-play. The evaluation of its pedagogical efficiency and its generalization on large student promotions are being considered.
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Educational cases

AB1274

STIFF SPINE AND A WEAK HEART: A CASE OF LONG STANDING ANKYLOSING SPONDYLITIS DEVELOPING PULMONARY ARTERIAL HYPERTENSION SECONDARY TO MIXED CONNECTIVE TISSUE DISEASE, CONFERRING POOR PROGNOSIS

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Background: Spondyloarthritides (SpA) and Connective Tissue Diseases (CTD) are considered distinct entities with diverse clinical features and genetic characteristics. There are very few case reports[1] of SpA coexisting with CTDs like Lupus, Scleroderma and Morphoea. Drugs used in treating SpA like Sulphasalazine and anti TNF drugs can also induce CTD.
Objectives: We report a case of a patient with eleven years history of Ankylosing Spondylitis (AS), presenting with Mixed Connective Tissue Disease (MCTD) and Pulmonary Arterial Hypertension (PAH) constituting a therapeutic challenge.
Methods: A 36 year old gentleman was diagnosed with AS at the age of 25 years, fulfilling the ASAS criteria (chronic inflammatory back pain, sacroiliitis on radiograph, HLAB27 positive). He was treated with NSAIDs, Sulphasalazine (SSZ) and physical therapy since 2008. There was gradual progression of his arthritis with high BASDAI along with recurrent anterior uveitis. He was treated with 5 doses of IV Infliximab 3mg/kg, between 2017 and early 2018. In May 2018, following further Infliximab he developed a serum sickness like reaction which was thought to be HACA response to Infliximab. He responded to IV hydrocortisone and antihistamines and Infliximab was discontinued.
In February 2019 he developed severe flare up of peripheral arthritis. He was treated with Injection Adalimumab 40mg every 2 weeks along with Latent TB prophylaxis with Isoniazid and Rifampicin. He received 4 doses to no effect and was discontinued.
In April 2019 Methotrexate (MTX) was added for peripheral arthritis. He discontinued both MTX and SSZ in July 2019 due to inefficacy. Peripheral arthritis responded well to Leflunomide that was started in September 2019.
There was an unexpected turn of events in October 2019, when he was admitted with severe dyspnoea and cough with new onset raynauds, skin tightening over forearms and nape of neck with salt and pepper appearance of skin at these sites (Images). He was hypoxic requiring oxygen support. Echocardiogram showed moderate pericardial effusion and pulmonary hypertension (PASP 60mmHg), dilated right heart and pulmonary artery. Pulmonary embolism was excluded on a CT pulmonary angiogram



Figure 1. Image 1, 2 – "salt and pepper" appearance of skin over the wrist and nape of neck, small joint arthritis



Figure 2. Image 1, 2 – "salt and pepper" appearance of skin over the wrist and nape of neck, small joint arthritis

Results: Investigations revealed 3+ ANA speckled pattern, anti RNP/ Sm 3+, Rheumatoid Factor negative. CRP 45.7u/l, Hemogram, renal and liver function tests were normal.
Cardiac MRI showed minimal pericardial effusion with mildly dilated right ventricle, non-dilated left ventricle with LVEF (~44%).

Right heart catheterization confirmed PAH with Mean PAP 58mmHg, LVEDP 8mmHg, PCWP 15mmHg
A diagnosis of Mixed Connective Tissue Disease (MCTD) was made, associated with PAH and pericardial effusion.
He was started on Ambrisentan and Tadalafil for PAH. Hydroxychloroquine and Mycophenolate Mofetil were also added in view of the PAH being associated with CTD. The additional pericardial effusion confers a poor prognosis.
Conclusion: Association of Spondyloarthritides and Connective Tissue Disease is rare. There are very few case reports of their chance association, especially MCTD[2]. Our patient had been exposed to Sulphasalazine, Infliximab, Adalimumab and Isoniazid, all with a potential to induce an auto immune CTD. MCTD features have persisted despite drug withdrawal. This case may suggest routinely checking for ANA in SpA patients prior to initiating anti TNF drugs.
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Disclosure of Interests: None declared
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AB1275 HYDROCEPHALUS IN AUTOIMMUNE DISEASES: A SERIES OF CHALLENGING CASES

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Background: Hydrocephalus can be a rare neurological manifestation but lethal complication of various SAIDs, including systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), sarcoidosis, and primary vasculitis. The commonly used medical management programs based on the etiology of hydrocephalus are anti-inflammatory or anti infectious therapies, while surgical management such as ventriculoperitoneal shunts is effective most of the time (Wei Jetal.,2019).
Objectives: To analyze the diagnosis and managment of hydrocephalus associated with autoimmune diseases
Methods: A retrospective case series study was conducted at Rheumatology department.Cairo university.Files were retrieved from the hospital archives by screening records from Jan 2014to Jan2019. Medical records were screened for data regarding the clinical manifestation and outcomeof hydrocephalus associated with autoimmune disease.
Results: Case (1)Male patient 28 yrs old diagnosed a systemic lupus erythematosus The patient was controlled on low dose steroid and azathioprine. In 2019: the patient presented with headache and blurring of vision. Fundus examination showed grade 2 to 3 papilledema. MRI brain showed: Non obustrcutive hydrocephalus. MRA & MRV: normal laboratory investigation was done and showed consumed c3 & c4. ESR: 35mm/hour. Hb: 12.3g/dl. WBC:6.38 cells/cm3. normal liver and kidney function. Neurosurgery consultation was done and recommended urgent ventriculo –peritoneal shunt. follow up fundus showed improvement of papilledema. The patient was discharged on steroids 30mg and mycophenolate mofetyl: 2gram with improvement of his condition.Case (2)Female patient 22 yrs old diagnosed as systemic lupus erythematosus onset 2010. In 2018 she started to develop quadriparesis started in left side followed by Right side associated with attacks of Tonic colonic convulsions. MRI brain showed: Marked communicating hydrocephalus with markedly reduced cerebral hemisphere white matter. MRV & MRA: normal. Her laboratory investigation showed ESR: 49mm/h. HB: 10.3mg/dl, WBC: 5.9 cells/ mm3. Normal platelet count. normal liver & kidney function. Normal c3 & c4. neurosurgery consultation was done. Urgent ventriculoperitoneal shunt was done with improvement of her condition. The patient was discharged on solupred 20mg along with azathioprine.
Conclusion: VPS along with medical treatment with steroids and immunosuppresion represent an effective treatment protocol.
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AB1276 NON-INTERFERON THERAPY OF CHRONIC HEPATITIS C IN A PATIENT WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND SECONDARY SJÖGREN SYNDROME - CASE REPORT

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Background: Hepatitis C virus infection is one of the most significant public health problems in the world. To date, the problem of selection of therapy is very relevant for patients with autoimmune diseases and chronic hepatitis C [1]. Patients with systemic lupus erythematosus (SLE) are forced to take different doses of steroids, often in combination with immunosuppressants (mycophenolate mofetil, azathioprine, etc.) even in the case of long-term remission. Such therapy for many years can contribute to the reactivation of hepatitis C.
Objectives: To describe a clinical case of the effectiveness of the combined use of interferon-free therapy and therapy of steroids in a patient with SLE, secondary Sjogren syndrome and chronic hepatitis C.
Methods: 56 years-old woman was admitted to the rheumatology department of Clinical Hospital No. 1 in December 2018 with the debut of SLE: photosensitivity, aphthous stomatitis, arthritis, pleurisy, sicca syndrome, leukopenia, ANA 1: 2560, antibodies to dsDNA 55.95 IU / ml, positive antiSS-A (Ro). At the same time, it became known that she was infected with hepatitis C virus in 1985 presumably. At the time of hospitalization, anti-HCV was positive, the virus genotype was 1b, the activity of the process was low (HCV RNA $6.6x10^4$, AST 33 U/L and ALT 25 U/L). The patient was prescribed corticosteroids (methylprednisolone 16mg/day) and hydroxychloroquine 400mg/day. In January 2019, after gastroenterologist, hematologist and infectious disease specialist advise, it was decided to conduct the patient a specific interferon-free antiviral therapy for chronic hepatitis C (a 24-week course with asunaprevir and daclatasvir), given the potential long-term glucocorticoid therapy, with the prospect of treating the patient with cytotoxic drugs, and the possibility of reactivation of chronic hepatitis C amid of immunosuppressive therapy for SLE and Sjogren syndrome.
Results: Low-disease activity of SLE was achieved in a month, and after 24-week course of antiviral therapy, there was no increase in SLE activity, and positive laboratory and clinical dynamics were noted.
Conclusion: Thus, the use of interferon-free therapy of chronic hepatitis C in patients with systemic lupus erythematosus and secondary Sjogren syndrome shows possible ways to safe treatment of this disease in patients with diffuse connective tissue diseases.
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Disclosure of Interests: None declared
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AB1277 AUTOANTIBODIES IN NLRP3-ASSOCIATED AUTOINFLAMMATORY DISEASE: A CASE REPORT AND LITERATURE REVIEW

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Background: We present the first report of high-titer autoantibodies in *NLRP3*-associated autoinflammatory disease(*NLRP3*-AID).Because systemic autoinflammatory disease(SAID) is characterised by the lack of autoreactive T-cells or autoantibodies,we made a systemic review on the theme of autoantibody in SAID to clarify this phenomenon.
Objectives: We present the first report of high-titer autoantibodies *NLRP*3-AID, and discuss autoantibody in classical SAID.
Methods: We collected the clinical data of the patient with *NLRP3*-AID who had high-titer autoantibodies,and made a systemic review about autoantibody in SAID.
Results: A 38-year-old Chinese Han patient was definitely diagnosed as *NLRP3*-AID because of cold-triggered urticaria-like rash and fever,arthralgia,-binaural sensorineural deafness,chronic meningitis,high inflammatory marker and de novo *NLRP3* T348M variant. Figure 1 shows pedigree of the patient. Meanwhile,she had positive antinuclear antibody(ANA) with a nucleolar pattern of 1:160, positive anti-β2GPI antibody 54-68 AU/ml (normal range < 20 AU/ml) and positive lupus anticoagulant 1.24-1.29 (normal range ≤ 1.2). Literature review found that 13 articles reported autoantibodies in Familial Mediterranean fever (FMF), and there was no autoantibody reported in hyperimmunoglobulinemia D syndrome (HIDS),TNF receptor–associated periodic syndrome(TRAPS) and *NLRP3*-AID. The prevalence of ANA,anti-dsDNA,RF and anti-CCP in patients with FMF was similar to healthy controls.

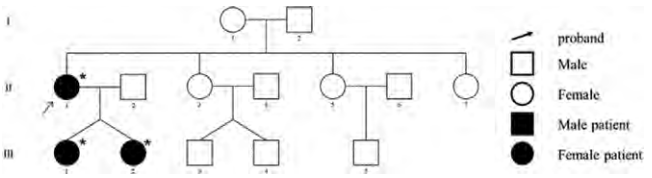


Fig. 1. Pedigree of the patient. The black arrow indicates the proband. The asterisks indicate the individuals who had clinical manifestations and carry the NLRP3 T348M variant.

Conclusion: Patients with *NLRP3*-AID can have high-titer ANA and APLs by accident. If patients with high-titer autoantibodies have characteristic manifestations of SAIDs instead of typical features of autoimmune diseases, we should make the final diagnosis through detailed investigation and genetic testing.
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AB1278 A CASE REPORT OF TOCILIZUMAB INDUCE RAPID REMISSION OF ADULT-ONSET STILL'S DISEASE WITH LIFE-THREATENING INTERSTITIAL LUNG DISEASE AND MACROPHAGE ACTIVATION SYNDROME

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Background: Adult-onset still's disease (AOSD) is a systemic inflammatory condition characterized by fevers, polyarthritis, skin rashes and increased leukocyte and neutrophil counts [1]. Sometimes life-threatening complications such as macrophage activation syndrome (MAS), disseminated intravascular coagulopathy (DIC) can be occurred without response to glucocorticoid and disease-modifying antirheumatic drugs (DMARDs).
Objectives: To describe an AOSD patient with life-threatening interstitial lung disease (ILD) and MAS response to tocilizumab.
Methods: This is a case report at our medical practice.
Results: A 43-year-old man was hospitalized for a 2-week history of fever accompanying skin rashes, polyarthritis, sore throat, leukocytosis (the maximum leukocyte count 37.25×10^9/L with 89.9% neutrophils), elevated levels of C-reactive protein (190.9mg/L) and ferritin level was very high (>15000ng/ml), Several antibiotics were consequently used, but fever was on going. Chest CT displayed diffuse interstitial lung disease. Infectious diseases and lymphoma were excluded and AOSD with ILD was diagnosed. However, MAS occurred the 20 days later after the pulse of intravenous MP (MP 500mg×3days) following MP 40 mg/day, which cannot stop the situation deteriorating. The minimum total white blood cells, hemoglobin and platelets went down to 0.25×10^9/l, 53g/l and 18×10^9/l. Finally, tocilizumab rescued this patient from desperation.
Conclusion: Tocilizumab was effective in AOSD with life-threatening ILD and MAS.
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HPR Measuring health (development and measurement properties of PROs, tests, devices)

AB1279-HPR A DESCRIPTIVE STUDY RELATED TO THE ADHERENCE BEFORE AND AFTER ENROLLING IN A MULTIDISCIPLINARY EDUCATIONAL PROGRAM

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Background: Rheumatoid arthritis (RA) is an inflammatory, chronic disease. It leads to deformity and destruction of joints through the erosion of cartilage and bone. Patients with RA report to suffer symptoms in hands, joints, swelling, loss of motion, muscle weakness among others.(1).Centers of excellence in RA have proposed a multidisciplinary model of care with an initial diagnosis, treatment prescription and follow-up with a rheumatologist, periodic consultations with a physiatrist, psychologist, physiotherapist, occupational therapy, nutrition and a patient focused program(2). With this model of care, the patient is seen as a whole, and the expectation is to achieve the best results in the management of RA. However, if the patient does adhere the model becomes ineffective.
Objectives: The aim of this to report the attendance to a multidisciplinary model of care for patients with RA that attend to a specialized center in Colombia, before and after enrolling in a educational program.
Methods: We performed a descriptive study. Patients enrolled our educational program in July 2019. In our institution patients are followed-up under T2T standards and a multidisciplinary approach, as part of our model of care they have periodic consultations with a rheumatology, physiatrist, psychologist, physiotherapist, occupational therapy and nutrition. We collected sociodemographic data, DAS28, and compare the attendance to each specialty at the beginning and at 6-month follow-up. Descriptive epidemiology was done, we calculated means, and standard deviations for continuous variables and categorical variables were presented as rates. We compared disease activity and adherence at the beginning of the program and after six months of attendance.
Results: We included 229 patients; mean age was 59 years ±10; 93% were female. At the beginning of our program, mean DAS28 was 2.57 ± 1.19, from all patients 65% were at remission, 11% at low disease activity 19% at moderate disease activity and, 5% at severe disease activity. Regarding adherence to our model, the medical specialty with the highest attendance was rheumatology (30%) followed by, physical therapy (16%) physiatrist consultation (15%) psychology (13%) and, occupational therapy (11%); the specialty with the lowest attendance was nutrition (8%). After six months of attendance to the educational program, we found an increasing number of patients in remission 67%, low disease activity 15%, moderate disease activity 18%, we did not have patients with severe DA28. Regarding the medical specialties, we found a 3% rise in the attendance to the nutrition consultation and psychology consultation. We did not find statistical association between disease activity and adherence to the model.
Conclusion: These results are a clear example of how an educational program is capable of increasing awareness and improving the clinical outcomes and adherence to a multidisciplinary model for approaching RA. As other studies have shown(3), patient education interventions improve adherence to medication and to attendance to health care specialists.
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Disclosure of Interests: Diana Buitrago-Garcia: None declared, Fernando Rodriguez: None declared, GUILLERMO SÁNCHEZ: None declared, Pedro Santos-Moreno Grant/research support from: I have received research grants from Abbvie, Biopas-UCB, Janssen, Novartis, Pfizer., Speakers bureau: I have been a speaker for Abbvie, Biopas-UCB, Janssen, Lilly, Novartis, Pfizer, Roche, Sanofi.

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AB1280-HPR REQUIRED FORCE TO OBTAIN A POSITIVE SQUEEZE TEST AUTOMATIZED IN PATIENTS WITH HAND ARTHRALGIA

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Background: Primary care physicians (PCP) are usually the first contact of people with inflammatory rheumatic diseases, and find the early symptoms of Rheumatoid Arthritis (RA) difficult to distinguish from those of other rheumatic diseases. A time-delay in the reference to Rheumatology is a health issue in several countries. The clinical aspects that general practitioner took into account in hand arthralgia patients are important to make the reference. In particular the Squeeze Test (ST) - which is simple to perform and rapidly done, ST is useful for identifying progression to RA in patients with undifferentiated arthritis. The ST has been described as not reliable because is clinician-dependent.

Objectives: To identify the required force that needs to be applied in order to obtain a positive Automatized Squeeze Test (AST) in a cohort of patients with hand arthralgia.

Methods: Ninety-seven patients were recruited in Family Medicine Consultation and in Rheumatology Consultation of the Hospital Universitario "Dr. José Eleuterio González" in Monterrey, Nuevo León, México. Eligible patients were adults (aged≥18 years) with hand arthralgia (that wasn't caused by trauma) as their chief complaint. After obtaining informed consent and after a questionnaire application, patients were submitted to AST maneuver, using an automated compressor with different forces already predetermined in the interface of the software used for compression.

Results: In this cohort of 98 patients, 79 (80.6%) were women. The mean age was 51.14 years (SD 14.66). Ninety-six (97.9%) patients were right handed. The diagnoses were Osteoarthritis (OA) (16.3%), RA (5.1%), Undifferentiated arthritis (1.2%), Psoriatic arthritis (1.2%) and Fibromyalgia (2%). Force measures according to diagnoses are reported in Table 1.

Table 1. Diagnoses and mean forces

Diagnosis	n (%)	Right hand force mean (kg/s^2) (SD)	Left hand force mean (kg/s^2) (SD)
OA	16 (16.3)	3.53 (2.74)	3.18(2.73)
RA	5 (5.1)	3.60 (2.53)	3.16(1.36)
UA	1 (1.2)	7.60(0)	8.70(0)
PsA	1 (1.2)	7.60(0)	7.80(0)
FM	2 (2.0)	4.11(4.40)	1.75(1.06)

OA, Osteoarthritis; **RA**, Rheumatoid Arthritis; **UA**, Undifferentiated Arthritis; **PsA**, Psoriatic Arthritis; **FM**, Fibromyalgia; **SD**, Standard Deviation

Conclusion: In the cases of RA and OA, the means of force to obtain a positive AST was lower than in the rest of the diagnoses.

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AB1281-HPR THE LEVELS OF VITAMIN D IN THE SPONDYLOARTHRITIS. DOES THE DEFICIT CORRESPOND TO THE INFLAMMATORY ACTIVITY?

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Background: Spondyloarthritis is a group of chronic inflammatory diseases with involvement of the axial skeleton (mainly), and also of peripheral joints. Patients with spondyloarthritis have a significant prevalence of vitamin D levels below normal and that would correlate with the degree of activity of the disease.

Objectives: To determine the association between vitamin D deficiency and the degree of activity of the disease (inflammatory activity) in a cohort of patients with spondyloarthritis.

Methods: Case-control type analytical observational study. We propose a retrospective review of the database of patients with spondyloarthritis (according ASAS2010 criteria) who were treated in the outpatient clinics of the Rheumatology Service of the General University Hospital of Ciudad Real during June 2018 to June 2019. Patients with the data will be selected. necessary for the analysis of the variables under study. The numerical variables of normal distribution evaluated will be described using measures of frequency and measures of central tendency / dispersion as appropriate. To assess the association between vitamin D levels and activity index, the odds ratio (OR) is calculated, with a 95% confidence level and the T-student for related samples.

Results: The final results of the study are presented. 115 patients were analyzed, of which 64 were men and 51 women, with an average age of 45.97 years (+/- 13.41 DE). 47% were ankylosing spondylitis, 21% psoriatic arthropathy, 16% undifferentiated spondyloarthritis, 7% spondyloarthropathy associated with inflammatory bowel disease and 9% were spondyloarthropathy associated with inflammatory bowel disease. The average of the activity was a BASDAI of 4.57 (+/- 2.35 SD) and measured by DAPSA was 12.61 (+/- 6.76 SD). 63 and 14 patients had activity measured by BASDAI and DAPSA, respectively. 49.56% patients presented an elevation of acute phase reactants. Vitamin D levels were 23.81 (+/- 10.5 SD). 77.4% presented figures of vitamin D deficiency or insufficiency. When performing the association analysis, the vitamin D deficit / insufficiency presented an OR 10 (95% CI: 3.66-27.29, p=<0.0001) with the degree of activity measured with BASDAI and DAPSA and against the elevation of RCP it was 3.63 (95% CI 1.43-9.25, p = 0.0092) and against the elevation of ESR it was 2.76 (95% CI 1.09-7, 0, p = 0.0438). Regarding the comparative analysis of means between vitamin D deficiency/insufficiency and BASDAI/DAPSA it was +3.29 (95% CI: 1.34-8.09, p=0.0084).

Conclusion: Patients with spondyloarthritis, as in other autoimmune diseases, vitamin D deficiency is associated with increased inflammatory activity (BASDAI, DAPSA, RCP and ESR), measured in different time periods. Therefore, an optimization of vitamin D levels can imply an improvement in the patient's clinical situation, measured by both BASDAI and DAPSA, as well as by RCP and ESR. In addition, it is necessary to monitor bone mineral density due to the risk of fracture in these patients for their multietiology (corticosteroid treatments, biological FAMEs, inflammatory activity).

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AB1282-HPR CONCORDANCE BETWEEN TUBERCULIN TEST AND INTERFERON-GAMMA RELEASE ASSAY IN THE SCREENING OF LATENT TUBERCULOSIS INFECTION IN PATIENTS WHO ARE GOING TO INITIATE A TNF INHIBITOR

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Background: The drugs that inhibit tumor necrosis factor (anti-TNF) alpha can reactivate a latent tuberculosis infection (ILTB) so requiring a rigorous screening before its onset. The tuberculin test (PT) has a high false negative rate in patients with immunomediated rheumatic diseases (IMID) and false positive in patients vaccinated with Bacillus Calmette Guérin (BCG). The neu methods of interferon gamma release (IGRA) seem to solve this problem, but its use is not standardized.

Objectives: Establish the degree of concordance in the diagnosis of ILTB between PT and IGRA in patients who are going to star an anti-TNF drug, in general, and in different situation like taking corticosteroids, being treated with disease modifying drugs, have been vaccinated with BCG or have risk factor for ILTB.

Methods: From May 2016 to November 2019, 195 patients with IMID who underwent ITLB screening prior to the initiation of an anti-TNF drug were included in this study. The concordance between PT and IGRA was calculated using the cohen's kappa index, for the general sample first and then for subgroups. An analysis of the factor that influence the result of PT and IGRA has also been carried out.

Results: The prevalence of ILTB was 26.7%. Of the total positive PT and Booster (n=50), QTF-G-IT was positive only in 15 patients (30%). The agreement between PT and QTF-G-IT was 0.33 (p<0.05). In the subpgroups, a moderate agreement was found in patients who did not take corticosteroids (k=0.45, p<0,05) and greater than the global one in those who had risk factor for ITLB (k=0.37, p<0.05).
Conclusion: In our study the agreement between PT and QT-G-IT is low in general, being somewhat higher in unvaccinated patients and with a high probability for ILTB. Taking this result into account due to the low concordance, the ideal ILTB screening strategy in patients who are going to start a anti-TNF would consist of performing both tests.
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AB1283-HPR GASTROINTESTINAL INVOLVEMENT AND QUALITY OF LIFE IN A COHORT OF SYSTEMIC SCLEROSIS (SSC) PATIENTS

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Background: SSc is an autoimmune disease characterized by fibrosis of the skin and several internal organs involvement. The gastro intestinal tract is often affected causing a wide symptomatology that can involve the oesophagus, stomach and/or intestine.
Objectives: To assess the gastro-intestinal tract with the UCLA SCTC GIT 2.0 questionnaire and the adherence to the Mediterranean diet with the Mediterranean Diet Score in a cohort of SSc patients.
Methods: 18 SSc patients classified with ACR/EULAR criteria (limited and diffuse subsets) were enrolled from January to April 2019, from the outpatient clinic of the University of Florence, Division of Rheumatology, Careggi Hospital. UCLA SCTC GIT 2.0 questionnaire for gastro-intestinal involvement (range 0-3), Mediterranean Diet Score (MDS range 0-14) for adherence to the Mediterranean diet, Health Assessment Questioning (range 0-3) for disability and SF-36 (range 0-100) for the quality of life were administered to patients. Data on weight and height were collected for the calculation of the Body Mass Index (BMI).
Results: *the* 18 SSc patients included had an average BMI of 23.9 ± 4.7 (M ± SD): only one patient was underweight (BMI=16.6) and 4 patients were overweight (BMI> 25). *O*ur results show good adherence to the Mediterranean diet with a score of 9.78 ± 2.24 (M±SD) to the MDS. The quality of life assessed by SF-36 show scores were below the cut-off (<50), showing an impaired quality of general life (mental summary index = 36.32 ± 11.35 and physical summary index = 39.53 ± 8.61). Patients disability, assessed by HAQ, reports some difficulty in carrying out daily life activities due to the disease (0.52 ± 0.53- M ± SD).
Gastro-intestinal involvement, measured with the UCLA GIT 2.0 questionnaire, shows moderate symptoms (0.50-1.00) in most items (reflux, abdominal distension, social function and emotional well-being), while a lower score (0.00-0.49) it was found in other items (diarrhea, constipation and faecal incontinence). Therefore, the total score of gastrointestinal involvement is moderate (0.42 ± 0.38 M ± SD)**.**
Conclusion: *In SSc,* Gastrointestinal involvement has a significant impact on quality of life, influencing the eating habits and sometimes leading to nutritional deficiencies. Further studies to analyse the eating habits of SSc patients are needed.
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AB1284-HPR RELIABILITY OF STEP TEST IN SUBJECTS WITH TOTAL KNEE ARTHROPLASTY

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Background: Patients with TKA show impairments in standing balance up to 1 year after surgery. The impaired standing balance in TKA patients was found to be associated with falls risk and decreased functional level. Assessing of standing balance with objective and reliable assessments tools would therefore be extremely useful for determining accurate exercise program, and risks of falling, especially during the rehabilitative period when ambulation is at its most unsteady (1, 2). The stepping maneuver requires adequate strength and motor control to stabilize the body over the stance limb while the other leg is stepping, therefore the Step Test (ST) provides significant information for dynamic standing balance and lower limb motor control (3). The reliability of ST is reported in patient groups such as stroke, however, there is not any study that investigates the reliability of ST in patients with TKA in the current literature.
Objectives: The purposes of this study were to determine the test-retest reliability and the minimal detectable change (MDC) of the ST in patients with TKA.
Methods: 40 patients with TKA due to knee osteoarthritis, operated by the same surgeon, were included in this study. Patients performed trials for ST twice on the same day. Between the first and second trials, patients waited for an hour on sitting position to prevent fatigue. The ST assesses an individual's ability to place one foot onto a 7.5-cm-high step and then back down to the floor repeatedly as fast as possible for 15 seconds. The score is the number of steps completed in the 15-second period for each lower extremity. Scores for each lower extremity were recorded separately. Prior to the testing, the ST was demonstrated by the tester and all participants were allowed to a practice trial.
Results: The ST showed an excellent test-retest reliability (ICC2,1=0.95) in this study. Standard error of measurement (SEM) and MDC_{95} for ST were 0.37 and 1.02, respectively.
Conclusion: This study found that the ST has an excellent test–retest reliability in patients with TKA. It is an effective and reliable tool for measuring dynamic standing balance and participant falls. As a performance-based clinical test, the ST is easy to score, can be applied in a short time as part of the routine medical examination. Therefore, inclusion of ST into a more comprehensive battery of

performance-based measures of standing balance and lower limb motor control function in subjects with TKA should be considered.

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AB1285-HPR ACCELEROMETRIC ASSESSMENT OF PHYSICAL PERFORMANCE DURING THE SIT-TO-STAND TEST IN PATIENTS WITH KNEE OSTEOARTHRITIS

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Background: Knee osteoarthritis is a major public health issue that causes chronic pain and functional limitation.

Objectives: This study aims to evaluate physical performance in knee osteoarthritis by clinical tests and accelerometer measurements, and investigate the relationship between physical perfomance alteration and clinical parameters.

Methods: This is a cross-sectional study, included 40 patients with knee osteoarthritis (100% female, average age 57.6 ± 5.2 years, median evolution time was 36 [24, 69] months, overweight in 82.5% of patients). Clinical evaluation performed with the visual analog scale (VAS), Western Ontario and McMaster Osteoarthritis Index (WOMAC), Lequesne score, Get up and Go (GUG) and Timed up and Go (TUG) tests. The percentage of fat mass was measured using impedencemetry.

All subjects were instructed to perform sit-to-stand transfers during 30 secondes. We measured the speed, strength and muscular power of the lower limbs during this test using the Myotest PRO® accelerometer.

A correlation analysis was performed in search of factors associated with physical performance alteration.

Results: The median speed during the sit-to-stand test was 4.3 [3.1-6.2] cm / sec. The median muscular strength and power during this test were 15.2 [13.6-17.7] Nm / kg and 14.5 [9.9-21.7] W / kg respectively.

Body mass index (BMI) correlated negatively with the 3 parameters of physivcal performance mesured by the Myotest PRO® accelerometer (speed, strength and muscle power) during the sit-to-stand test (p<0,05). There was no correlation between those measured parameters of physical performance, pain and functional indices of knee osteoarthritis.

Conclusion: Our pilot study assessed the physical performance of the lower limbs in knee osteoarthritis patients, by measuring the speed, strength and muscle power during the the sit-to-stand test. It suggests an association between obesity and physical performance alteration in knee osteoarthritis patients.

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AB1286-HPR EXAMINATION OF DYNAMIC GRIP ENDURANCE RELATED FACTORS IN PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Psoriatic arthritis (PsA) is a disease manifested by destruction of articular cartilage, subchondral bone, and fibrosis of the joint capsule without excessive synovitis (1). Most of studies that examining hand in PsA are radiographic, ultrasonographic, magnetic resonance imaging research and there is little knowledge about functional assessment of hand. According to our knowledge, there is no study assessing grip endurance in patients with PsA.

Objectives: To assess dynamic grip endurance related factors in patients with PsA.

Methods: A total of 19 patients [Mean age; 53.5±12.6 years, 14 women(73.7%), 5 men(26.3%)] diagnosed according to CASPAR criteria were included this study. Clinical and demographic characteristics were recorded. Dynamic grip endurance test was assessed with 10- repetition dynamic endurance test using a hand dynamometer (Lafayette Proffessional Hand Dynamometer, USA). Grip strength was examined by hand dynamometer and pinch strength was examined by pinchmeter (Lafayette, USA). Goniometer was used to assessment wrist position sense. Disability of Arm, Shoulder and Hand Survey (DASH) was used to determine disabilities and symptoms of upper extremity. We used Spearman's Rank Correlation Coefficient for data analysis.

Results: Dynamic grip endurance was negatively correlated with DASH score, perceived disability of hand, number of tender hand joints and positively correlated with grip strength, 3 point pinch strength on both dominant and non-dominant sides (p<0.05, Table 1). Dynamic grip endurance was not correlated with CRP level and joint position error on both dominant and non-dominant sides (p>0.05).

Table 1. Examination Of Dynamic Grip Endurance Related Factors In Patients

Variables (n=19)	Dynamic Grip Endurance Dominant	Dynamic Grip Endurance Dominant (%)	Dynamic Grip Endurance Non- Dominant	Dynamic Grip Endurance Non-Dominant (%)
DASH	**r=-0.525**	**r=0.524**	**r=-0.608**	r=0.153
	p=0.021	**p=0.021**	**p=0.006**	p=0.532
Perceived Disability	**r=-0.466**	r=0.326	**r=-0.509**	r=0.414
of Hand	**p=0.044**	p=0.174	**p=0.026**	p=0.078
Pain in Hand Joints	r=-0.363	**r=0.472**	r=-0.316	**r=0.542**
	p=0.127	**p=0.041**	p=0.188	**p=0.017**
Number Of Tender	**r=-0.641**	**r=0.569**	**r=-0.580**	r=0.268
Hand Joint	**p=0.003**	**p=0.011**	**p=0.009**	p=0.267
Number Of Swollen	r=-0.349	r=0.359	**r=-0.526**	r=-0.094
Hand Joint	p=0.143	p=0.131	**p=0.021**	p=0.702
Joint Position Error	r=0.147	r=-0.127	r=0.412	r=-0.026
Dominant	p=0.548	p=0.606	p=0.080	p=0.915
Joint Position Error	r=0.213	r=-0.339	r=0.047	r=0.350
Non-dominant	p=0.381	p=0.156	p=0.848	p=0.141
Grip Strength	**r=0.960**	r=0.033	**r=0.722**	r=-0.035
Dominant	**p<0.001**	p=0.892	**p<001**	p=0.887
Grip Strength	**r=0.742**	r=-0.151	**r=0.967**	r=0.035
Non- Dominant	**p<0.001**	p=0.538	**p<0.001**	p=0.887
2 Point Dominant	r=0.134	**r=-0.561**	r=0.344	r=-0.240
	p=0.585	**p=0.012**	p=0.149	p=0.322
3 Point Dominant	**r=0.539**	r=-0.444	**r=0.752**	r=-0.318
	p=0.017	p=0.057	**p<0.001**	p=0.185
Lateral Dominant	r=0.354	**r=-0.516**	r=0.355	r=-0.116
	p=0.137	**p=0.024**	p=0.136	p=0.637
2 Point	**r=0.622**	**r=-0.200**	**r=0.742**	r=0.031
Non-Dominant	**p=0.004**	**p=0.411**	**p<0.001**	p=0.901
3 Point	**r=0.633**	r=-0.216	**r=0.845**	r=0.013
Non Dominant	**p=0.004**	p=0.375	**p<0.001**	p=0.957
Lateral	**r=0.459**	r=-0.366	**r=0.579**	r=-0.063
Non Dominant	**p=0.048**	p=0.123	**p=0.009**	p=0.783
CRP	r=-0.280	r=-0.008	r=-0.386	r=0.023
	p=0.246	p=0.974	p=0.102	p=0.926

DASH: Disability of Arm, Shoulder and Hand Survey, *Spearman Correlation Test

Conclusion: Our findings suggest that dynamic grip endurance is associated with different functional parameters of the hand and worsening clinical parameters. Examining dynamic grip endurance might be a guide in creating an exercise program for clinicans in rehabilitation of patients with PsA.

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AB1287-HPR INVESTIGATION OF THE RELATIONSHIP BETWEEN GRIP ENDURANCE, DISABILITY OF UPPER EXTREMITY AND QUALITY OF LIFE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Upper extremity functions affect the quality of life at different levels in patients with rheumatoid arthritis (RA). In the current literature; it has been shown that grip endurance is associated with upper limb functions (1). However, there is no study investigating the relationship between grip endurance and quality of life in patients with RA.

Objectives: To investigate relationship between grip endurance, disability of upper extremity and quality of life in patients with RA.

Methods: In our cross sectional study, 23 RA patients [Mean age; 52.7±12.6, BMI;26.9±5.7 kg/m^2, Women;20(87.0%)] who were classified according to the ACR 2010 criteria. Demographics and clinical characteristics of patients were recorded (Table 1). Das28 for disease activity score, Static and dynamic grip endurance measurements using Hand Dynamometer (Lafayette Proffessional Hand Dynamometer, USA) for grip endurance, Disability of Arm, Shoulder and Hand Survey (DASH) for disabilities and symptoms of upper extremity and Short Form-36 Health Survey for quality of life were performed. Spearman's Rank Correlation Coefficient was used for data analysis.

Table 1. Demografic and Clinical Characteristics of Patients

Variables (n=23)	Median(IQR 25/75)
Age (year)	56(41/62)
BMI (kg/m2)	27,5(21.4/32.0)
Disease Duration(year)	8(5/15)
Morning Stiffness (VAS/mm)	38(23/48)
Perceived Disability of Hand (VAS,mm)	47(25/67)
Clinician Disability of Hand (VAS,mm)	30(20/39)
Number Of Tender Hand Joint	2(0/6)
Number Of Swollen Hand Joint	0(0/1)
CRP(mg l)	3,3(1.8/7.1)
ESR(nm/h)	13(6/21)
n(%)	
Morning Stiffness Duratton	
0-15 minutes	8 (34.8)
15-30 minutes	5 (21.7)
30-60 minutes	3 (13.0)
Longer than 1 hours	7 (30.4)
Das28	
Remission	11(47.8)
Low Activity	2(8.7)
Moderate Activity	7(30.4)
High Activity	3(13.0)

Data is presented median (interquantile range) or percentile (%).

Results: Grip endurance was negatively correlated with DASH and positively correlated with many different quality of life parameters, especially physical function, on both the dominant and non-dominant sides ($p < 0.05$). DASH was correlated negatively with SF-36 physical function, rol limitataion due to physical health, pain subparameters and positively correlated with Das28 score ($p<0.05$).
Conclusion: In our study, it was concluded that grip endurance was related to upper extremity functions and quality of life in patients with RA. This result shows that; assessment of grip endurance can be a guide for clinicians who have designed an upper limb rehabilitation program for patients with RA.
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AB1288-HPR BURTON PATIENT REPORTED OUTCOME MEASURES (B-PROM): STEPS TOWARDS VALIDATION

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Background: Patient reported outcome measure (PROMS) and experience measures (PREMS) are becoming of vital importance in the assemment of treating the rheumatic diseases. There have been a variety measuring different elements of a patients disease journey. To date few have been developed specifically in rheumatology outpatients, to that end the Burton rheumatology unit in the Midlands UK developed a 12 question PROM looking at the three domains of emotional, physical and functional health, this has been mindful of previois PROMS and PREMS developed [1,2,3].
Objectives: To validate a new PROM questionnaire in an unselected group of rheumatology outpatients with osteoarthritiss (OA)
Methods: Consecutive patients with OA attending outpatients in Burton were asked to fill in the questionnaire at the beginning and after completing education and exercise programme designed by the physiotherapists to treat OA. The results collated were analysed using STATA ™. Cronbach's alpha was calculated to look internal validity within domain and overall to assess validity of the questionnanire. This was done within domain and with the overall questionnaire.
Results: 130 patients were included, mean age was 65 and diagnosis was osteoarthritis. 71.5% patients were female. Cronbachs alpha results for the communication, relationship and reliability within the first domain were 0.80, 0.82 and 0.82 respectively. Domain 1: alpha for all three questions was 0.93. Domain 2: alpha for questions on knowledge was 0.60, reliability 0.81, fatigue 0.79 and pain 0.85. Domain two overall agreed with the other two domains was 0.95 . Domain 3: the alpha for movement was 0.81, strength was 0.73, independence was 0.81, mobility was 0.91 and social was 0.92. Domain three had an alpha overall of 0.93
Conclusion: The B-PROM shows good validity and could be used in patients with OA, further work using it on other patient groups will be performed.
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Disclosure of Interests: Ramasharan Laxminarayan Speakers bureau: Novartis, Pfizer and Lilly, Allison Dean: None declared, Helen Nutland: None declared, Lisa Bembridge: None declared, Marwan Bukhari Speakers bureau: Bristol-Myers Squib, UCB celltech, Roche/Chugai, Pfizer, Abbvie, Merck, Mennarini, Sanofi-aventis, Eli-Lilly, Janssen, Amgen and Novartis.
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AB1289-HPR PERCEPTION OF THE VALUE OF DRUGS ON DIFFERENT MANIFESTATIONS OF PSORIATIC ARTHRITIS BASED ON A MULTI-STAGE EXPERT OPINION SURVEY

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Background: Patients with psoriatic arthritis (PsA) present with heterogeneous clinical phenotypes, which includes different clinical manifestations such as peripheral arthritis, axial disease, dactylitis, enthesitis, and skin and nail psoriasis. Many drugs for treatment of PsA are available for individualised treatment strategies but robust evidence is available for peripheral arthritis only as primary endpoint of RCTs.
Objectives: To evaluate perception of German physicians on the value of current PsA treatments on different clinical PsA manifestations.
Methods: In a face-to-face meeting, 8 German physicians (dermatology, rheumatology), specialised in PsA research/patient care, proposed initial scores for the effect size of current PsA drugs on different PsA manifestations based on knowledge of study data and personal experience in use of the drugs. The ability to achieve a consensus of the proposed efficacy scores was explored by applying an online survey among a cohort of PsA experienced physicians. Finally, a second online survey evaluated how a larger group of physicians personally estimate the drug effect sizes on different PsA manifestations.
Results: Table 1 summarises the efficacy scores proposed by the initial expert group. In the first online survey 25 treating physicians were invited to participate, 14 (56%) of whom completed the survey. An agreement rate of over 65% of the participants was archived for 49 (68%) of the 72 proposed efficacy scores (Table 1). The consensus was especially high for the group of biological disease-modifying antirheumatic drugs (bDMARDs), except for etanercept and abatacept. However, the second survey (16 (39%) participants out of 41 invited physicians) revealed that the experience with the treatment using abatacept was low (4 / 16 (25%)) or non-existing (3 /16 (18.8%)) and several manifestations could not be estimated (Figure 1). Distribution of answers were broad for etanercept in general and for particular drug-manifestation combinations (e.g. effect of ustekinumab on axial disease).

Table 1. Efficacy scores proposed by a PsA expert group and consensus achieved by an online survey among PsA treating physicians Efficacy scores for different drugs and manifestations range from 0 (no effect) to 5 (maximal effect). Green fields indicate, that at least 65% of the survey participants agreed on the proposed efficacy score.

	Peripheral arthritis	Axial disease	Enthesitis	Dactylitis	Skin disease	Nail disease
Methotrexat	2.5	0	0	1	2.5	1.5
Sulfasalazin	1	0	0	0	0	0
Leflunomid	2.5	0	0	1	1	1
Apremilast	3	1	3	2.5	3	3
Etanercept	4	4	4	3.5	3	3.5
Infliximab	4	4	4	4	4	4
Adalimumab	4	4	4	4	4	4.5
Golimumab	4	4	4	4	3	3
Certolizumab pegol	4	4	4	4	4	4
Ustekinumab	3.5	2.5	4.5	3	4.5	4
Secukinumab	4	4	4	4	5	4.5
Abatacept	3.5	0	0	0	1.5	0

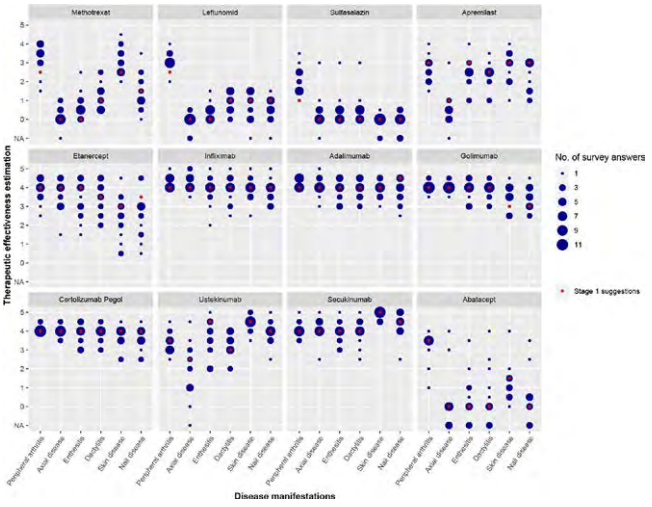


Figure 1. Results from an online survey among physicians querying their perception of efficacies of PsA drugs on different manifestations. Therapeutic effectiveness is estimated by the participants on a scale from 0 (no effect) to 5 (maximal effectiveness); NA = no answer. The size of the dots relates to the number of answers given. Red stars indicate the scores proposed by the initial expert group.

Conclusion: Many treatments are available to be used in PsA. The usage of treatment classes seems to depend on experience level and mode of action. Higher agreement on efficacy in specific diseases manifestation was achieved in the class of biologics whereas the opinion on efficacy of csDMARDs in general is divergent. Strategies are needed to guide physicians with lower level of experience in the use of specific drugs to achieve an optimised patient care level using personalized treatment strategies.

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AB1290-HPR UTILITY OF FRAX IN THE RISK DETECTION OF FRACTURE IN SPONDYLOARTHRITIS

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Background: Axial spondyloarthritis (SpAax) presents an increased risk of vertebral fracture not fully detected by Dual energy X-ray absorptiometry (DXA). The FRAX algorithms give the 10-year probability of hip fracture and of mayor osteoporotic fracture (clinical spine, forearm, hip or shoulder fracture), taking into account 11 clinical risk factors.

Objectives: To analyze the suitability of FRAX to detect the risk of fracture in patients with SpAax. To assess whether the incorporation of SpAax as a clinical risk factor to conventional FRAX provides additional information.

Methods: Cross-sectional study in which SpAax patients (ASAS criteria) were included. Clinical-demographic and related to the disease variables were collected. FRIDEX model for Spanish population was used to determine low, intermediate or high risk of mayor fracture by FRAX. These results were compared with those obtained by DXA and trabecular bone score (TBS). In the statistical analysis we used mean and standard deviation (SD) in quantitative variables and frequency in qualitative ones. To compare means among 3 groups, ANOVA test was used.

Results: The characteristics of the patients are shown in Table 1. According to FRIDEX, no patient had high risk of fracture and 2.4% had intermediate risk. When SpAax was added as a risk factor, no patient had high risk of fracture and 6.1% presented intermediate risk. According to DXA, 7.3% had high risk of fracture and 41.3% intermediate risk. TBS detected high risk of fracture in 18.3% and intermediate risk also in 18.3% of patients.

Table 1. Sociodemographic, clinical and related characteristics with the disease (BMD: bone mineral density, BMI: index of body mass)

Gender (Male), n (%)	61 (74.4)
Age, mean ± SD	49.48 ± 12.47
BMI, mean ± SD	27.13 ± 4.42
Smoking, n (%)	26 (31.7)
Diabetes mellitus, n (%)	9 (11)
Osteoporotic fracture, n (%)	1 (1.2)
Disease duration (years), mean ± SD	11.77 ± 10
syndesmophytes, n (%)	38 (46.3)
ASDAS-PCR, mean ± SD	2.55 ± 1.07
Lumbar BMD (g / cm^2), mean ± SD	1.032 ± 0.180
BMD femoral neck (g / cm^2), mean ± SD	0.816 ± 0.140
Lumbar TBS, mean ± SD	1.383 ± 0.133

Conclusion: FRAX does not seem an adequate tool to detect the risk of fracture in patients with SpAax since it did not improve the results obtained by DXA meanwhile TBS did. The incorporation of SpAax as a clinical risk factor to conventional FRAX did not provide additional information in most cases

Disclosure of Interests: None declared

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AB1291-HPR IMPLEMENTATION OF AN ELECTRONIC SYSTEM FOR ISSUING PRESCRIPTIONS IN PATIENTS WITH RHEUMATIC DISEASES

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Background: Pharmacovigilance is the science and activities related to detection, evaluation, understanding and prevention of adverse effects of medications or any other health problem related to them. (1)

Within the scope of the pharmacovigilance study, following domains are included: adverse drug reaction, interaction between medications, counterfeit or inferior quality medications, lack of efficacy of medications, misuse or abuse of medications and medication errors (ME). (2)

ME is any preventable incident that can cause harm to the patient or lead to improper use of medications when they are under the control of healthcare professionals or the patient. (3)

Objectives: To determine the frequency of ME in the prescriptions among rheumatology outpatient's clinic.

Methods: Prospective observational study.

Frequency of ME was sought by a randomized review of the prescriptions from rheumatology outpatient's clinic of the University Hospital "Dr. José Eleuterio González" before and after the implementation of an electronic medical prescription system (REPAIR®) (January 2018-December 2019)

REPAIR® displays an automated menu with the stages of the medical prescription: Name, presentation and dosage of the medicine and duration of the treatment. Figure 1. Once the review began, semiannual reports were made to the doctors involved in which frequency of errors and the stage of medical prescription with highest incidence of ME were reported.

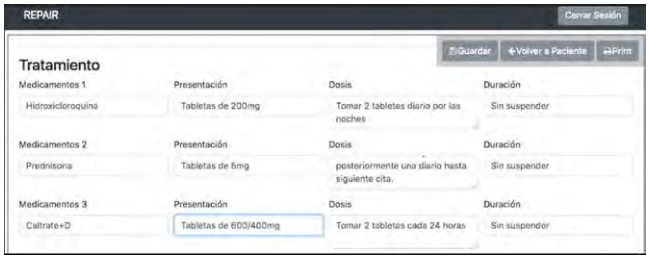


Figure 1 Example image displayed by REPAIR®

Descriptive statistics were performed, reporting frequencies and percentages.

Results: A total of 1599 medical prescriptions were evaluated. The number of prescriptions with ME was 196 (12.2%). Table 1

Table 1 General description about errors in medical prescriptions

Prescriptions evaluated	1599
Prescription with ME n (%)	196 (12.2%)
Medications evaluated n	10 413
Medications with ME n (%)	907(8.7%)
Average medications per prescription	6.4
Average medications with ME per prescription	0.78
Prescription Stage	
Name of the drug n (%)	2/10 413 (0.01%)
Medication presentation n (%)	77/ 10 413 (0.7%)
Dose of the drug n (%)	0/10 413 (0%)
Duration of prescription n (%)	725/10 413 (6.9%)

The incidence of ME decreased, at beginning of the study incidence was reported 31.6%, and at the end were 1.5%. Graph 1

The percentage of medications with ME also decreased from 17.2% to 0.8% at the end of the study. Table 2

Table 2 Errors in prescriptions per semester

	January-June 2018	July-December 2018	January-June 2019	July-December 2019
Prescriptions evaluated n	321	411	407	460
Prescriptions with ME n (%)	73 (31.6%)	93 (22.6%)	23 (5.6%)	7 (1.5%)
Medications evaluated n	2126	2784	2680	2823
Medications with ME n (%)	367 (17.2%)	469 (16.8%)	36 (1.7%)	35 (0.8%)
Average medications per prescription evaluated	6.6	6.7	6.2	6.4
Average medications per prescription evaluated	1.146	1.143	0.082	0.081
Prescription Stage n (%)				
Name	1/367(0.2%)	1/469 (0.2%)	0	0
Presentation	37/367 (10%)	37/469 (7.8%)	1/36 (2.7%)	2/35 (5.7%)
Dose	0	0	0	0
Duration	290/367 (89%)	367/469 (88.2%)	35/36 (97.2%)	33/35 (94.2%)

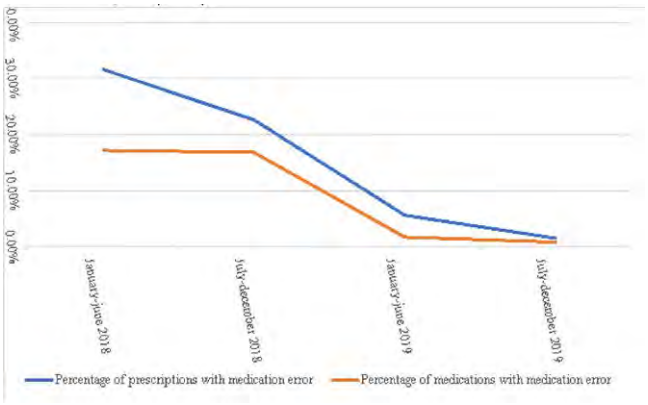
Conclusion: Decrease in the incidence of ME in rheumatology consultation is important because outcome of the patients depends significantly on treatment adherence. This study results shows that through the application of an electronic prescription system, it is possible to reduce the incidence of ME in rheumatology consultation.

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Graph 1

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AB1292-HPR NUMBER OF DRUGS IN THE PRESCRIPTION, A PREDISPOSING FACTOR FOR MEDICATION ERRORS IN RHEUMATOLOGY

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Background: Medication error can be defined as a failure in the treatment process that leads to or has the potential to lead to harm to the patient, this fault can happen in two different phases: prescribing and prescription.

Prescribing is the process of deciding what to prescribe and naming it. Various types of faults can occur in the decision-making process: underprescribing, overprescribing, irrational, inappropriate and ineffective prescribing. All these covers one type of errors, but these are different kind of errors that those that occur in the act of writing a prescription. This leads to the distinct concepts of 'prescribing faults' and 'prescription errors'

A prescription is 'a written order, which includes detailed instructions of what medicine should be given, to whom, in what formulation and dose, by what route, when, how frequently, and for how long'. Thus, a prescription error can be defined as 'a failure in the prescription writing process that results in a wrong instruction about one or more of the normal features of a prescription'. The 'normal features' include the identity of the patient, the identity of the drug, the formulation and dose, and the route, timing, frequency, and duration of administration. (1)

It is not record about the rate of medication errors in rheumatology consultation.

Objectives: To evaluate whether there is a relationship between prescribing errors and the number of drugs in the prescription.

Methods: A descriptive, observational, and retrospective study was made.

It was carried out a random search of medical prescriptions, generated by the electronic records (REPAIR®) of the rheumatology consultation of the Hospital Universitario "Dr. José Eleuterio González" during 2019, in which the prescriptions that contained any error were identified

T student test was performed to see the difference in the prescription error based on the number of medications. P <0.05 was taken as statistically significant.

Results: A review of 867 medical prescriptions was performed, among which 5503 medications were indicated with an average of 6.34 medications per prescription, a total of 30 (6.9%) prescriptions were found with error, where a total of 71 (3.9%) medications had errors. In the prescriptions with medication error, all the errors were prescription type; 68 (95.7%) had a mistake in the duration of administration and 3 (4.22%) in the identity of the drug.

In the prescriptions with medical errors the average number of prescription drugs was 7.50, only 2/30 (0.6%) had less than 7 indicated medications (4 and 6), meanwhile the prescriptions in which no error was found had a mean of 6.30 indicated medications. P < 0.001.

Conclusion: According to the study findings, it could be established that when the number of prescribed medications is greater than 7, there is an increased risk of making a prescription error. Further studies should carry out to look for other factors that influence medical errors in rheumatology clinics.

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Acknowledgments

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AB1293-HPR **DETERMINING FUNCTIONAL MOBILITY AND BALANCE FOR PATIENTS AFTER TOTAL KNEE ARTHROPLASTY: RELIABILITY OF L-TEST**

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Background: Total knee arthroplasty (TKA) is a very common procedure, particularly implemented for the treatment of knee osteoarthritis (OA). Patient expectations after TKA surgery now include being able to enjoy appropriate recreational activities representing ambulatory activities beyond that of just pain relief and adequate knee motion (1). Since recreational activity comprises of more complex functions and requires longer standing durations, walking for 6-meter in a straight line in the timed up and go test (TUG) does not fully reflect the functional capacity of patients with TKA, and TUG test may be limited to detect the balance and mobility capacity in TKA patients (2, 3). As such, there is a need to determine more effective and functional evaluation tools that better reflect realistic situations in order to assess ambulatory performance level for patients with TKA. However, no studies have been conducted in patients with TKA to examine the applicability of the L-test, which assesses ambulation of individuals and consists of complex mobilization activity.
Objectives: The purposes of this study were to determine the test-retest reliability and the minimal detectable change (MDC) of the L-test for TKA patients.
Methods: Twenty-four patients with TKA due to knee OA, operated by the same surgeon, were included in this study. Patients performed trials for L-test twice on the same day. Between the first and second trials, patients waited for an hour on sitting position to prevent fatigue. The tester recorded the performance time while the participant was asked to get up from a chair, walk 3 m in a straight line, turn right, continue walking for 7 m in a straight line, turn left, walk back along the same path and sit down in the chair at their usual walking speed. Prior to the real testing session, the L-test was demonstrated by the tester and all participants were allowed to a practice trial.
Results: The L-test showed an excellent test-retest reliability (ICC2,1= 0,98) in this study. Standard error of measurement (SEM) and MDC_{95} for L-test were 1,01 second and 2,8 second, respectively.
Conclusion: This study found that the L-test is a reliable test for patients following TKA. Overall, the excellent test-retest reliability of the L-test indicates that it may be an applicable standardized method to assess TKA patients who are able to walk greater distances and have better gait in more functional situations. Clinicians and researchers can be confident that changes in L-test time above 2,8 seconds, represent a "real" clinical change in an individual patient with TKA. We, therefore, recommend the use of L-test as complementary outcome measures for balance and functional evaluation in TKA patients.
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AB1294-HPR **LOW CONCENTRATIONS OF BIOLOGIC DMARDS IN BREASTMILK OF PATIENTS TREATED DURING LACTATION**

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Background: There is very limited information about the passage of biologics into breast milk and into the peripheral blood of breastfed infants. However, based on pharmacological properties of biologic DMARDs (bDMARDs) lactation may not be discouraged in patients with chronic inflammatory rheumatic disease to treat or prevent postpartum relapses. We here report two cases treated with bDMARDs during lactation: one woman with Muckle-Wells syndrome (MWS) treated with canakinumab and one woman with microscopic polyangiitis (MPA) treated with rituximab.
Objectives: To determine the level of rituximab and canakinumab in breast milk, in sera of breastfed infants as well as in sera of the mother and to calculate the average daily infant dose and the relative infant dose.
Methods: Serum and milk levels of Rituximab were measured by ELISA using commercially available coating and detection antibodies. For Canakinumab an ELISA was established by coating of plates with recombinant human IL-1beta and detection of Canakinumab in samples by a polyclonal anti-human IgG coupled to HRP. In both cases separate standard curves for serum and milk were established. Serum samples and milk samples of unexposed healthy controls were used to determine the lower limit of quantification.
Results: One patient with MWS received canakinumab 150 mg s.c. to treat a worsening of her disease ten days postpartum. She continued to breastfeed her child. The average concentration of canakinumab in milk samples collected on 10 consecutive days was 15.8 ng/ml. The average daily infant dose was 0.002 mg/kg/day. The relative infant dose, which refers infant to maternal exposure on a dose/weight basis, was 0.11%. There was no detectable canakinumab in the serum of the infant.
One patient with MPA received rituximab 500 mg i.v. as a remission maintenance therapy four months postpartum. She continued to breastfeed her child. The average concentration of rituximab in milk samples collected on 4 consecutive days was 3.71 ng/ml. The average daily infant dose was 0.001 mg/kg/day. The relative infant dose was 0.01%. There was no detectable rituximab in the serum of the infant.
Conclusion: Only minimal concentrations of canakinumab and rituximab can be detected in breastmilk. For both bDMARDs, the relative infant dose was below 1% of the maternal dose, which is considered unlikely to be of clinical concern. The lack of detectable levels of canakinumab and rituximab in the infants' sera supports the notion of low oral bioavailability of large monoclonal antibodies. Together, the results are similar to those seen in TNF inhibitors which are regarded to be compatible with breastfeeding, yet more data are needed (1, 2, 3).
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HPR Epidemiology and public health (including prevention)

AB1295-HPR **PREGNANCY RISK IN CHILDBEARING AGE WOMEN WITH RHEUMATIC DISEASES**

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Background: Rheumatic diseases (RD) are more frequent in women, affecting them during childbearing age. Medications used to treat can interfere with fertility or increase the risk of miscarriages and congenital abnormalities; Disease control and therapy should be discussed with patients before and during pregnancy, in order to minimize adverse outcome (1). Barriers to adequate communication

and counseling of women regarding reproductive health and family planning still exist among rheumatologists and increases the risk of complications(2).

Objectives: To identify childbearing age women with RD and a high risk of pregnancy.

Methods: A cross-sectional study was performed in the rheumatology clinic of the university hospital "Dr. Jose Eleuterio Gonzalez" in Monterrey, Mexico between October 2019 and January 2020. All non-pregnant childbearing age (18 to 45 years old) women any were included. A self-questionnaire of 10-items was applied. Demographic, data were collected from the electronic medical record. Results are shown in descriptive statistics. Analyses were performed with SPSS 22. A p< 0.05 was considered statistically significant.

Results: 135 women were evaluated, median age was 33 (25-39) years. Patients characteristics are shown in table 1. 115 (85.1%) had initiated sexual activity earlier in life (median age 18 years). Regarding the question, did you have sex last month? 115 answered it, 69 (60%) said they had, 49 (42.6%) used a contraceptive and 20 (28.9%) did not. 135 patients, 68 (50.3%) had a desire for pregnancy, 12 (17.6%) in the next 12 months and 56 (82.3%) in more than one year, of which 37 (66%) were using a family planning method and 19 (34%) were not (Table 2). For the question about receiving contraceptional counselling 112 answered it, 80 (70.4%) say they had. When they were asked if they received family planning and reproductive health counseling by their rheumatologist, just 64 (57.1%) affirmed they did; There was no differences in the use of contraceptive methods among those who received contraceptive counselling and those who did not (p>0.05). Among the 67 (49.6%) patients who did not want to be pregnancy 16 (23.8%) did not use a contraceptive method.

Table 1. Chracteristics

	n=135
Age, *years, median (IQR)*	33 (25-39)
Marital status *n (%)*	
Single	58(42.9)
Unmarried	19 (14.1)
Married	49 (36.3)
Divorced	9 (6.7)
Education *n (%)*	12 (8.9)
None	
Elementary school	17 (12.6)
High school	77 (57.0)
University	28 (20.7)
Diagnosis *n (%)*	
Rheumatoid arthritis	63 (46.7)
Systemic lupus erythematosus	39 (28.9)
Other autoimmune diseases	32 (24.3)
Onset of Sexual activity age, median (IQR)	18 (16-20)
Onset of Sexual activity?, n (%)	
Yes	115 (85.1)

Table 2. Tool questions

	n=135 (%
Did you have sex last month? *(n= 115, %)*	69 (60)
Yes	
Did you use any contraceptive method? *(n=115, %)*	
Yes	49(42.6)
Did you receive family planning and reproductive health counseling by the rheumatologist? *(n= 112, %)*	
Yes	64 (57.1)
Do you want to get pregnant after the next 12 months?	
Yes	56 (41.1)
Do you want to get pregnant in the next 12 months?	
Yes	12 (8.9)
Contraceptional counselling *(n=112, %)*	
Yes	80 (71.4)
Current treatment *(n= 107, %)*	
Pregnancy Risk	65 (60.7)

Conclusion: Using this short questionnaire, we identified that 35 (25.9%) of the patients had a risk of unintended pregnancy and that only 80 (70.4%) received reproductive health counseling from their rheumatologist. It is necessary to design and systematically apply questionnaires capable of detecting and evaluating risks in this population.

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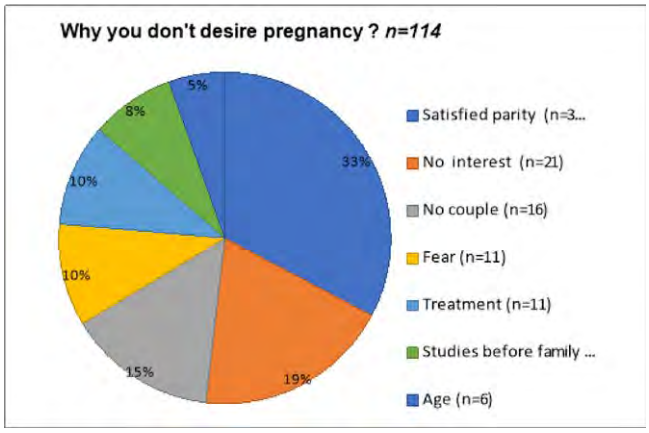
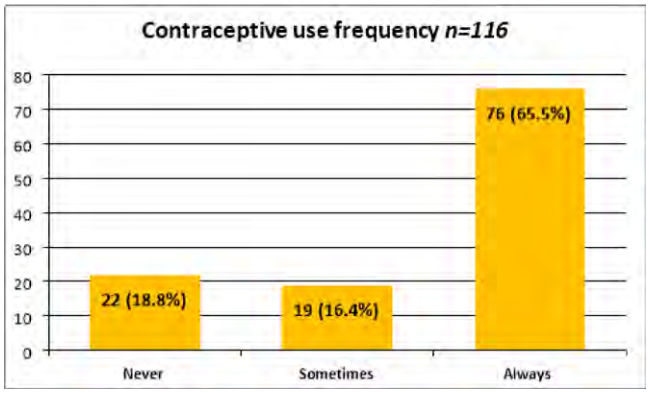
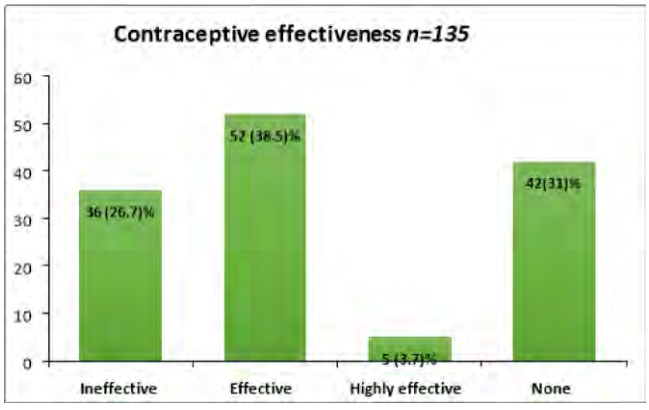


Figure 1.



Graphs 1.



Graphs 2.

Disclosure of Interests: None declared

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AB1296-HPR **PREVALENCE OF COMORBIDITIES IN A COHORT OF PATIENTS IN AN EDUCATIONAL MULTIDISCIPLINARY PROGRAM**

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory and complex disease. Patients with RA face other diseases that might lead to increase

morbidity. In patients with RA it has been stablished a high prevalence of comorbidities and their risk factors (1).

Objectives: The aim of this study was to evaluate the prevalence of comorbidities in Colombian patients with RA enrolled in an educational multidisciplinary program and possible correlation with disease activity

Methods: We performed a cross-sectional study; we included patients with confirmed diagnosis of rheumatoid arthritis in a specialized RA center. We collected sociodemographic data, and markers of disease activity DAS28. We collected data regarding the history of comorbidities such as hypertension, dyslipidemia, osteoporosis, type 2 diabetes mellitus, hypothyroidism, malignancies, among others. We performed a descriptive analysis, variables with a normal distribution were described using mean and standard deviation (SD), and non- normal distributed variables were described using median and interquartile range. Categorical variables were presented as rates. We evaluated the relationship between disease activity and comorbidities.

Results: We included 251 patients; mean age was 59 ± 9.8 years old, with a high proportion of women 93%; median disease duration was 15 years RIQ (8-20); in this study, 145 (65%) of patients were in remission; 35 (11%) had low, 44 (20%) moderate and 10 (4%) high disease activity. Regarding pharmacological therapy, 55% were receiving conventional DMARDs. The prevalence of comorbidities was 85%, the most common were high blood pressure 25% followed by hypothyroidism 12% and diabetes 10%, 0.7% of patients had malignancies such as thyroid cancer or breast cancer, 1.29% of patients had renal comorbidities. Among comorbidities related to RA 30% had osteoporosis and 20% arthrosis. We did not find a statistical association between DAS28 and comorbidities.

Conclusion: As other studies have shown, there is a high prevalence of comorbidities among RA patients, mainly high blood pressure. Due to the above, it is relevant to evaluate the risks factors of patients with RA, especially cardiovascular risks. We consider that a multidisciplinary program represents an opportunity not only to educate patients about healthy life styles and the management of RA, but also other diseases in order to increase the empowering of the health status in these poly pathological patients(2).

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AB1297-HPR BONE AND MINERAL METABOLISM IN SPONDYLOARTHRITIS

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Background: Spondyloarthritis is the term for a group of inflammatory chronic diseases primarily affecting the axial skeleton, as well as the peripheral joints. Regarding bone metabolism in these patients, several studies have reported higher levels of inflammatory activity (BASDAI, BASMI, ESR and CRP) in patients with osteoporosis compared to those without this disease, although no correlations were found.

Objectives: To describe clinical, serological and biological characteristics, as well as bone and mineral metabolism, according to analytical and densitometric criteria in a patient cohort with spondyloarthritis.

Methods: Observational, descriptive and cross-sectional study. A retrospective review was conducted of a database of patients with spondyloarthritis treated during outpatient visits at the Rheumatology Department of Hospital General Universitario de Ciudad Real between June 2018 and June 2019. Variables are described using measures of frequency and of central tendency and dispersion.

Results: Cohort of 115 patients (64 men and 51 women). Average age 45.97 years (+/- 13.41 SD). Ankylosing spondylitis in 54 patients, psoriatic arthropathy in 24, spondyloarthropathy associated with inflammatory bowel disease in 8, undifferentiated spondyloarthritis in 18 and other types of spondyloarthritis in 11. Regarding treatment, 40.88% of patients received disease-modifying drugs (methotrexate, sulfasalazine, etc.) and 43.4% received biologic drugs (86% anti-TNF alpha, 12% anti-IL-17 and 2% anti-IL-12/23). Moreover, 53.04% had received corticosteroids during some phase of their disease. Vitamin D levels were 23.81 (+/- 10.5 SD) and 77.4% of patients had a vitamin D deficiency/insufficiency. Of the total cohort, 34.78% presented osteopenia and 3.58% osteoporosis (T-Score and Z-Score).

Conclusion: In this study, patients with spondyloarthritis show high percentages of osteopenia and osteoporosis, undiagnosed until this time, along with vitamin D deficiency. This data suggests higher prevalences of these metabolic bone diseases. Osteoporosis prevention is essential due to the risk of developing early fractures resulting from increased bone fragility.

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AB1298-HPR RHEUMA-VOR: A PROOF-OF-CONCEPT NETWORK STUDY FOR THE IMPROVEMENT OF RHEUMATOLOGICAL HEALTH CARE THROUGH COORDINATED COOPERATION

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Background: Rheumatoid arthritis (RA), psoriasis arthritis (PsA) and spondyloarthritis (SpA) are the most common chronic inflammatory rheumatic diseases. For all three diseases, the so-called “window of opportunity” [1,2,4] has been identified as the decisive factor affecting the outcome.

Objectives: The aim of the prospective study is to improve the early diagnosis of RA, PsA and SpA and thus positively impact the quality of care for patients with the support of coordinating centers.

Methods: Primary care providers are given access to screening questionnaires to document potential early cases of RA, PsA, and SpA, based on characteristic symptoms. These are evaluated by multidisciplinary teams at the regional coordinating centers. If they fulfill the criteria for referral, patients get an appointment at a cooperating rheumatology specialist within weeks. If a rheumatic disease is diagnosed, physicians and patients receive questionnaires about sociodemographic, physilogical and psychological parameters.

In order to increase the quality of referrals, a 15-minute rheumatological consultation at the ACURA Rheumatology Center was implemented for all patients from Rhineland-Palatinate whose suspected diagnosis was confirmed by the coordination centre. In course of this, the Rheuma-VOR Screening-App will also be developed and optimized. The cooperating partners and additional information are already published [5].

Results: Preliminary data (31 Dec 2019) are presented. In Rhineland-Palatinate, Saarland and Lower Saxony, 4942 suspected diagnoses of 1526 different referring physicians have now been reported. A total of 2578 patients were referred by the three coordination centres to one of the 49 participating rheumatological specialists. 1004 patients were diagnosed with one of the three diseases. About 306 patients have already taken the follow-up appointment after one year.

In course of a screening consultation 736 patients have been screened to date. The patients have to wait in average about 42 days from the suspected diagnosis to the rejected or confirmed rheumatological diagnosis.

Conclusion: Although the average waiting time for all three diseases is currently almost twice as long as the 23.9 days in the Rhineland-Palatinate predecessor project ADAPTHERA which just focuses on RA, the current results are very positive compared to the national average [3]. The aim is to further increase the screening quality and screening numbers, especially in the 1-year follow-up.

Current data will be presented at the conference.

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Disclosure of Interests: Matthias Dreher: None declared, Reinhold E. Schmidt: None declared, Torsten Witte: None declared, Gunter Assmann: None declared, Kirsten Hoeper Consultant of: AbbVie, Celgene,, Speakers bureau: Abbvie, Chugai, Novartis, Lilly, Celgene, Sandoz Hexal, Konstantinos Triantafyllias: None declared, Jan Zeidler: None declared, Harald Binder: None declared, Andreas Schwarting: None declared

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AB1299-HPR THE RHEUMA-VOR APP: OPTIMIZING THE EARLY DIAGNOSIS OF RHEUMATIC DISEASES

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Background: The proof-of-concept network study "Rheuma-VOR" aims to improve the quality of rheumatological care through coordinated cooperation. In particular, rheumatic diseases should be diagnosed as early as possible and treated quickly in a targeted manner [3]. Smartphone apps have a potential to improve the management of chronic diseases. For example, they can be used to provide health information, or to offer self-monitoring and self-screening options [1, 2].

Objectives: The Rheuma-VOR Screening-App study examines whether a smartphone-based app can increase the detection rate of the three most common chronic inflammatory rheumatic diseases: rheumatoid arthritis, psoriatic arthritis and spondylarthritis.

Methods: Based on the multi-stage Delphi Procedure, a minimal list of questions for detection and differentiation between the three diseases was defined. The app for iOS and Android is in use since October 2018 during the screening consultation at the Division of Rheumatology and Clinical Immunology and at the ACURA Center of Rheumatology Rhineland-Palatinate. An additional validation will be performend with a non-preselected cohort based on the data of the Rheuma Bus Tour 2019.

Results: The Delphi Procedure identified 17 questions, including four laboratory parameters. They have been deployed in German as a smartphone app. The questions are read to the patient and can be answered with "YES", "NO", or "I DO NOT KNOW". Answering the questions takes approximately four minutes. The suspected diagnoses are based on a cumulative score. Some diagnoses are excluded or confirmed already after a few questions.

To date (31 Dec 2019), the app has been used on 466 patients. The sensitivity is 0.91, while the specificity is 0.25. The positive predictive value and the negative predictive values are 0.60 and 0.32, respectively. The false positive value is 0.33 and the false negative value 0.05.

Conclusion: The Rheuma-VOR App helps doctors and patients to invalidate or to confirm the suspicion of a possible rheumatic disease. Data from the cohort is currently analyzed to increase the screen's specificity. The additional validation, based on a non-preselected cohort collected during the Rheuma Bus Tour 2019, is in progress. A final validation concept is currently being developed.

In 2020, a section with the most important information about the aforementioned three diseases will be added. The section will include definition, etiology, prognosis, symptoms, therapeutic principles, medication and case studies.

Current data will be presented at the conference

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AB1300-HPR MALNUTRITION SCREENING AND ASSESSMENT TOOLS IN RHEUMATIC DISEASES

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Background: Inflammatory disorders have been associated with an increased risk of malnutrition, defined as an abnormal physiologic condition caused by an insufficient, unbalanced or excessive intake of nutrients due to exacerbated metabolic states.[1]

Mini Nutritional Assessment (MNA) and Nutritional Risk Screening Tool 2002 (NRS-2002) have been used to evaluate nutritional status in patients with rheumatic diseases.

Objectives: Compare MNA and NRS-2002 as tools for nutritional screening in rheumatic patients.

Methods: 152 patients with rheumatic diseases were evaluated in a Rheumatology center of México. Anthropometrical measurements were performed using Bioelectrical Impedance Analysis (BIA) TANITA. MNA and NRS-2002 were applied at the same date.

MNA is comprised of a dietary questionnaire, subjective and objective global assessment and anthropometrical measurements, classified as adequate (MNA 24-30), risk for malnutrition (MNA 17–23.5) and malnutrition (MNA<17).

NRS-2002 consists of nutritional and severity disease score and an age adjustment for patients >70 years (+1); classified as normal (0-3) and risk of malnutrition/established malnutrition (3 or more).

For statistical analysis the SPSS v24 was used. A $p < 0.05$ was considered statistically significant.

Results: A total of 152 patients with different rheumatic diseases were included, Table 1. The results according to each tool are represented in **Graphic 1.** A significant difference was found by the Chi-Square-test when comparing both tools, ($p<0.004$).

Table 1. Socio-demographic characteristics of rheumatic patients

DISEASES, n (%)	
Rheumatoid Arthritis	70 (46.1)
Systemic Lupus Erythematosus	19 (12.5)
Ostearthrosis	18 (11.8)
Sjögren´s Syndrome	5 (3.3)
Fibromyalgia	4 (2.6)
Ankylosing Spondylitis	2 (1.3)
Systemic Sclerosis	6 (3.9)
Others	27 (17.8)
SOCIO-DEMOGRAPHICS	
Age, mean years (SD)	51.98 (13.56)
BMI, mean (SD)	28.14 (5.8)
Brachial Circumference, cm, (SD)	32.57 (4.19)
Calf Circumference, cm, (SD)	37.08 (4.17)

A subanalysis in 70 Rheumatoid Arthritis patients was done with a mean age of 50.94 years (SD±12.11) and a mean BMI 28.53 kg/m2 (SD 5.48). The results according to each tool are represented in Table 2. When NRS-2002 was reclassified in 3 parameters (normal <2, risk of malnutrition 2 and malnutrition 3 or more), a significant difference persisted (p. 05) with a low correlation (.43).

Table 2. Descriptive data of MNA and NRS-2002 in rheumatic diseases.

	NUTRITIONAL SCREENING TOOLS				
	MNA	**NRS-2002**	**NRS-2002***	**Rho**	**p**
All Rheumatic Diseases					
Total Score, *n(SD)*	24.31 (3.48)	___	___	.23	.004
Malnutrition, *n(%)*	4 (2.6)	5 (3.3)	5 (3.3)		
Risk, *n(%)*	55 (36.2)	147 (96.7)	41(27)		
Normal, *n(%)*	93 (61.2)		106 (69.7)		
Rheumatoid Arthritis					
Total Score, *n(SD)*	24.43 (3.23)	___	___	.43	.05
Malnutrition, *n(%)*	1 (1.4)	2 (2.9)	2 (2.9)		
Risk, *n(%)*	22 (31.4)	68 (97.1)	15 (21.4)		
Normal, *n(%)*	47 (67.1)		53 (75.7)		

Conclusion: MNA was a more sensible tool for detecting risk of malnutrition when compared to NRS-2002. Screening tools play an important role at nutritional evaluation and should be complemented with objective methods such as BIA.[1] Rheumatologists must be aware that nutritional disorders affect the state of rheumatic diseases; and selecting an appropriate tool to detect malnutrition is of vital importance.

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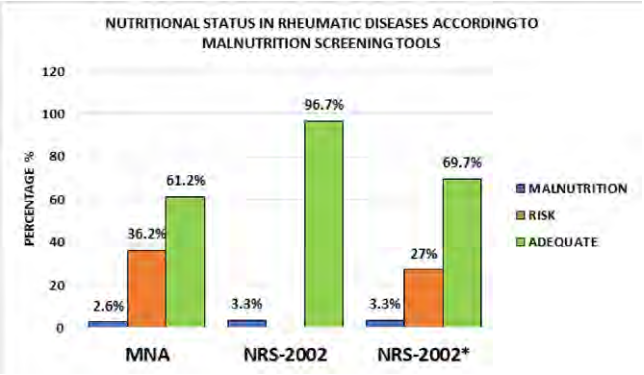


Figure 1. Graphic 1. Nutritional screening tools in rhematic disorders.**Total N=** 152 patients. **MNA=** Mini Nutritional Assessment **NRS-2002=** Nutritional Risk Screening Tool-2002. **NRS-2002*=** Nutritional Risk Screening Modified with 3 parameters.

Disclosure of Interests: None declared
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AB1301-HPR COMORBIDITIES AND FACTORS INFLUENCING RECURRENT GOUT ATTACK IN PATIENTS WITH GOUT: A CROSS-SECTIONAL STUDY

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Background: Gout attack is characterized by painful arthritis, loss of function and reduced quality of life. Frequent gout attacks can exert negative an influence on gout management [1].

Objectives: The objective was to identify the comorbidities of gout, to compare gender difference and to identify independent factors of multiple gout attacks.

Methods: A cross-sectional study was performed to collect demographic, clinical variables, self-reported comorbidities, and relevant testing. Group comparison and correlation of serum uric acid (sUA) levels with other variables was performed. Univariate and multivariate logistic regression was used to detect independent risk factors of sUA.

Results: 653 gout patients were enrolled, including 553 (84.7%) males. The mean age was 48.3±15.8 years old, with a disease duration of 8.0±6.4 years. 170 (26.0%) patients had hypertension, and 57 (8.7%) had hyperlipidemia. Elevated total cholesterol (TC) was observed in 173 (26.5%) cases. 42 (37.1%) cases presented with increased triglycerides (TG) and 270 (41.3%) had increased low-density lipoprotein (LDL-C). Abnormalities including nephrolithiasis (29.4%), hydronephrosis (3.2%), and gallstones (11.9%) were detected in the patients who underwent ultrasound examination. Although female patients had a longer disease duration, they had lower levels of sUA, creatine and C-reactive protein (CRP). A positive correlation with sUA was found in TG and CRP (P<0.05) in female patients, which was not observed in males. Only gout duration (OR=1.406, P <0.001), sUA (OR=1.006, P <0.001) and LDL-C (OR=0.530, P =0.006) were independent factors of gout attack (>20 times).

Conclusion: Comorbidity screening involving dyslipidemia is often neglected in gout patients. Gout duration and sUA level are risk factors of multiple gout attacks.

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Table 1 Comparisons of clinical and laboratory variables between male and female patients with gout

Variable	Male (n=553)	Female (n=100)	p
Age (years)	47.7±15.9	51.3±14.5	0.040*
BMI (kg/ m2)	24.5 (22.0-27.0)	23.3 (20.3-25.3)	0.001*
Gout duration (years)	6.0 (3.0-11.0)	9.5 (4.0-15.0)	0.001*
Gout attack times			
•≤5	209 (37.5)	33 (33.0)	
•6-10	97 (17.5)	22 (22.0)	
•11-20	70 (12.7)	22 (23.0)	
•>20	177 (32.0)	23 (23.0)	
Comorbidies			
Hypertension, n (%)	138 (25.0)	32 (32.0)	0.140
Coronary heart disease, n (%)	57 (10.3)	10 (10.0)	0.926
Fatty liver disease	53 (9.6)	4 (4.0)	0.069
Laboratory testing			
•ALT(U/L)	25.0 (17.0-40.0)	19.2 (14.6-29.0)	0.003*
•ALB(g/L)	43.5±6.3	42.4±3.9	0.025*
•TB (μmol/L)	12.7 (9.0-17.3)	14.5 (12.1-17.4)	0.002*
•BUN (mmol/L)	4.85 (3.98-6.27)	4.85 (3.91-4.82)	0.588
•Creatine (mmol/L)	94.0 (81.4-108.1)	73.8 (67.4-87.2)	<0.001*
•UA (μmol/L)	528.4±141.1	363.8±122.9	<0.001*
•Glucose (mmol/L)	5.62±1.67	5.43±1.17	0.317
•TC (mmol/L)	5.05±1.15	5.09±1.10	0.726
•TG (mmol/L)	2.11±1.66	1.94±1.86	0.335
•HDL-C (mmol/L)	1.14±0.30	1.52±0.41	<0.001*
•LDL-C (mmol/L)	3.25±0.97	3.39±0.92	0.182
•ESR (mm/h)	40.1±32.4	37.4±20.8	0.402
•CRP (mg/L)	28.0±40.3	10.5±18.6	<0.001*

* p < 0.05; BMI: body mass index; sUA: serum uric acid; ALT: alanine aminotransferase; ALB: albumin; TB: Total bilirubin; BUN: blood urea nitrogen; UA: uric acid; TC: total cholesterol; TG: triglycerides; HDL-C: high-density lipoprotein; LDL-C: Low-density lipoprotein; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein

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AB1302-HPR ASSOCIATIONS OF SLEEP ON GOUT PREVALENCE AND SERUM URIC ACID CONCENTRATIONS

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Background: Sleep deprivation and sleep inconsistency have been associated with modulation of the immune and inflammatory response systems with effects that include higher risk for psychosis, cardiovascular disease, and increased susceptibility to infection. One hypothesized mechanism to explain these findings is an association with pro-inflammatory states.

Objectives: In a first-of-its kind study, we examined associations between sleep quantity and gout using the largest public US dataset available; the National Health and Nutrition Examination Survey (NHANES).

Methods: NHANES data from 2009 to 2014 was selected based on questionnaire responses and laboratory studies. The resulting data set was analyzed for serum uric acid (SUA) levels (cut-off >6.0 mg/dL in females and >7.0 mg/dL in males), and gout risk factors. Analysis of variance, means, proportions, as well as univariate and multiple logistic regression models were used to evaluate the associations between sleep quantity, SUA and gout.

Results: 10,410 survey participants from 2003 to 2014 were included in the study. A total of 280 (2.7%) had gout. Gout prevalence ranged between 4.0% and 4.7% between high, normal, and low sleep groups. Multivariate analyses showed a significant association between extremely low sleep levels (OR = 0.53 and CI = 0.34 to 0.83), and gout, which was also seen with SUA level association (OR = 0.41 and CI = 0.32 to 0.52). However, in the broader sense, lower than normal (<7 hours) and higher than normal (>9 hours) levels of sleep had no significant associations with either gout prevalence or SUA, likely due to a non-linear relationship of SUA to sleep levels.

Conclusion: Despite numerous adverse effects found with low sleep levels, our study does not show a strong association between sleep quantity and gout prevalence or SUA levels.

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Disclosure of Interests: None declared
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AB1303-HPR TIME UNTIL DIAGNOSIS IN RHEUMATOLOGICAL PRACTICE: RESULTS FROM A CROSS-SECTIONAL MIDDLE-EUROPEAN COHORT COMPARED TO DATA FROM A SYSTEMATIC LITERATURE REVIEW

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Background: The time from first symptom to diagnosis (= diagnostic delay) is considered as key factor for better outcome in many chronic inflammatory rheumatic diseases, especially for rheumatoid arthritis (RA) and vasculitides like giant cell arteritis (GCA). A longer diagnostic delay may cause pain, reduced functionality, reduced life-quality and increased morbidity, as well as structural damages of the organs linked with higher mortality. This retrospective study assessed the diagnostic delay in consecutive Middle-European outpatients and compared results with those of a systematic literature review (SLR).
Objectives: To compare disease-specific diagnostic delays of consecutive rheumatic patients with international data from a systematic literature review.
Methods: Charts of a single-centre cohort with consecutively recruited patients were retrospectively reviewed for patients' and diseases' characteristics at a Middle-European university outpatient clinic for rheumatology. A SLR was performed according to PRISMA guidelines.
Results: The average mean ± SD time from first symptom to established diagnosis was 7.9 ± 11.7 (0.02-56.7) years. Spondyloarthritis patients showed the longest diagnostic delay with 13.1 ± 14.2 (0.1-56.7) years, whereas polymyalgia rheumatica-patients had the shortest diagnostic delay with 1.5 ± 0.4 (0.3-18.0) months. In the SLR, most data for diagnostic delays are comparable to the Innsbruck cohort, but the diagnostic delay for psoriatic arthritis in Innsbruck is longer than in the Danish DANBIO registry (p<0.001). Independent risk factors for prolonged diagnostic delays could not be identified.
Conclusion: For this Middle-European area, initiatives are justified especially to shorten diagnostic delays of SpA and PsA.
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Acknowledgments: We acknowledge and thank all patients who could be recruited to the SolutionX project. Ethical vote was obtained by the local ethics committee of the Medical University of Innsbruck (AN2017-0041 370/4.18).
Disclosure of Interests: Rick Mc-Cutchan: None declared, Sarah Maier: None declared, Valentin Winkler: None declared, Bernhard Gruber: None declared, Michael Schirmer Grant/research support from: total <3000.- €, Speakers bureau: total <3000.- €
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AB1304-HPR KNOWLEDGE OF HIGH SCHOOL STUDENTS ABOUT RHEUMATIC DISEASES: EFFECT OF AN EDUCATIONAL SESSION JOINTLY PROVIDED BY PORTUGUESE EULAR ASSOCIATIONS

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Background: International studies have shown that the awareness and knowledge of the general population about rheumatic and musculoskeletal diseases (RMDs) is poor. This is even lower in the young population, which are also affected by these disease but do not have as much awareness campaigns as adult community. Their professors and primary health care professionals may also play here also a key role, promoting early detection of signs and interpretations of symptoms, thus avoiding late health care referrals and diagnosis. (Vlieland, 2016).
Objectives: To assess the knowledge of high school Portuguese students about the RMDs and raise awareness for RMDs in young people, their professors, vigilants, and primary care nurses, within the school environment.
Methods: A 1-hour educational session about RMDs was planned (with the inputs from members of the Portuguese EULAR Associations) and performed during school activities. The educational session started with a knowledge questionnaire about RMDs in a paper sheet (9 questions; Graph 1), repeated in the end. An interactive session, using slides, interactive questions (Sli.do®), and practical demonstrations to simulate RMD symptoms (e.g. stiffness and functional limitations) was then lead by a rheumatology nurse, with the testimony from a young patient representative. A primary care nurse assisted in order to be engaged and promote future sessions ("autonomously"). Change in knowledge was assessed with Wilcoxon-test and awareness was documented with "word clouds" (using Sli.do®).
Results: A total of 75 students participated in four sessions (mode=16 years). Half of students (52%) had never heard about RMDs. Knowledge increased significantly in all questions (p<0.001; Graph 1). Figures 1 and 2 document the most common words representing what defines a RMD and what are the main symptoms, respectively.

Graph 1. Change in the percentage of correct answers before and after na educational session (n=75) (all p<0.001)

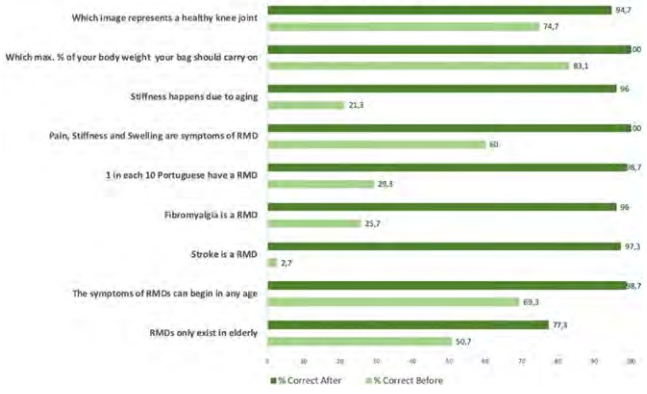
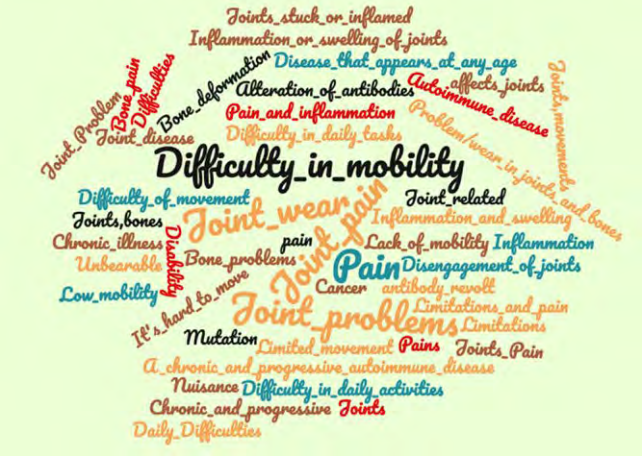


Figure 1. "One to two words" to define "Rheumatic diseases" by college students (n=75) after an educational session



Figure 2. Symptoms that can indiciate a rheumatic disease, according to college students (n=75) after an educational session



Conclusion: Our results confirm that awareness and knowledge about RMDs are very low high school students. The single and educational session was very well received by all students, and the the knowledge increased. Post-educational feedback was that students especially liked the testimony of a peer. Other sessions are taking place in primary schools.

References:

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AB1305-HPR

IS BETTER AND SAFER TOFACITINIB AS A FIRST LINE OF TREATMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS? – A COHORT STUDY

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Background: Tofacitinib is the first oral Janus Kinasa inhibitor approved for the treatment of rheumatoid arthritis (RA); and although it is approved both after conventional treatment and after biological therapy, it is not well known its real-life effectiveness in both cases and if it is preferable to use it after cDMARDs or biologics.

Objectives: We compare the effectiveness and safety of Tofacitinib in patients with RA analyzing if better and safer Tofacitinib after cDMARDs or biologics.

Methods: A retrospective analysis of a real-world cohort of patients with RA, who were treated with Tofacitinib in last 3 years, as first line of treatment (T1) after failure with cDMARDS and second line of treatment after biologic drug failure (T2). The therapy was considered effective with the change from moderate-high disease activity to low disease activity or remission measured by DAS28, in those who met criteria of high adherence, without change or addition of other conventional DMARDs, without new dose or increase of dose of oral glucocorticoids. A logistic model of regression was performed to evaluate de differences between T1 and T2, using as covariates sex, age, comorbidities, time of disease evolution, adverse events and other causes of discontinuation. Medication survival time and the main causes of suspension were measured. Mixed model regression and least-squared means were used to estimate the baseline changes and a Kaplan-Meyer survival analysis to estimate time to remission and drug survival.

Results: 105 patients with RA were included (median age: 56.1 ± 11.7 years; 80.9% female, median disease duration 11.48 ± 10.1 years); 43% (45/105) of patients with positive rheumatoid factor and 73% (77/105) positive anti-citrulline antibodies. Regarding treatment 51% (54/105) used Tofacitinib as 1T, after failure to cDMARDs; on the other hand, Tofacitinib was used as 2T, after failure to biologics in 49% (51/105) of patients. DAS28 levels were reduced at 8, 16 and 24 weeks with statistical difference (p value 0.004, <0.0001, and <0.001, respectively). HAQ-DI also reported reduction but without statistical difference. The use of Tofacitinib was more effective after failure to cDMARDs (p value 0.014) and patients with more than 3 years of disease (p value 0.04), a statistically better response. Also, corticoids use, positive RF, extended release tablet of tofacitinib reported better changes of DAS28 but without statistical significance. Patients with high disease activity treated with Tofacitinib 1T decreased from 30% at baseline to 19% at the last follow-up; patients in 2T way were in moderate activity of the disease in 57% at baseline and went to 37% in the last follow-up. There was an increase in patients who achieved remission in both groups, but higher in 1T where they went from 9% to 41%, while in 2T they went from 22% to 33% ($p < 0.05$). The survival rate of the medication was 1.7 years in 1T and 2.1 in 2T; in terms of time to remission, the use of Tofacitinib monotherapy presented statistical difference (p value <0.001). The main cause of suspension of treatment was therapeutic failure 12% (13/105), 9% in 1T (5/54) and 16% (8/51) in 2T (p <0.005). 6% of patients (6/105) presented suspension due to the occurrence of adverse events, 4% (2/54) in 1T and 8% (4/51) in 2T (p <0.005).

Conclusion: In patients with RA, the use of Tofacitinib as the first line of treatment (after failure to cDMARDs) is better in effectiveness and safer in comparison with its use as a second line of treatment (after biologics), with significant differences in the rates of therapeutic failure and occurrence of adverse events/reactions. On the other hand, concomitant corticoids use, positive RF, extended release tablet of Tofacitinib seem to increase the effectiveness of Tofacitinib in terms of DAS28 and HAQ-DI.

Disclosure of Interests: Omaira Valencia: None declared, Michael Cabrera: None declared, Fernando Rodriguez: None declared, Pedro Santos-Moreno Grant/research support from: I have received research grants from Abbvie, Biopas-UCB, Janssen, Novartis, Pfizer., Speakers bureau: I have been a speaker for Abbvie, Biopas-UCB, Janssen, Lilly, Novartis, Pfizer, Roche, Sanofi.

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HPR Interventions (educational, physical, social and psychological)

AB1306-HPR

THE EFFECTS OF CLINICAL PILATES EXERCISES IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid Arthritis (RA) is a rheumatic disease that may coexist many symptoms clinically. These clinical symptoms progress in a vicious cycle in many patients. Physical activity and exercise are known to improve many symptoms in RA patients.

Objectives: This study was designed to investigate the effects of clinical pilates exercises on fatigue, depression, aerobic capacity, pain, sleep quality and quality of life.

Methods: Thirty voluntary RA patients were included in this study. Patients were separated into three groups equally and each group was applied treatment for eight weeks. Clinical pilates exercises were practiced to the first group, aerobic exercises were practiced to the second group and combined training which was a combination of pilates exercises and aerobic exercises was performed to the third group. Fatigue, depression, aerobic capacity, pain, sleep quality and quality of life were evaluated by Fatigue Severity Scale (FSS), Beck Depression Inventory (BDI), Six minute walk test (6MWT), Short- Form McGill Pain Questionnaire (MPQ), Pittsburg Sleep Quality Index (PSQI) and Rheumatoid Arthritis Quality of Life (RAQoL), respectively.

Results: According to our results, statistically significant improvements were found for clinical pilates exercises on fatigue, depression, aerobic capacity and quality of life ($p<0.05$). Improvements in all parameters except from pain were concluded for aerobic exercises and combined training ($p<0.05$). Also, there was no statistically significant difference among the treatment groups in assessments ($p>0.05$).

Conclusion: Pilates exercises were found effective and safe for RA patients. Clinical pilates training may be as effective as aerobic exercises in patients with RA according to our study. Therefore, addition of clinical pilates exercises to the routine treatment of RA may enhance the success of rehabilitation.

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Disclosure of Interests: None declared

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AB1307-HPR INVESTIGATION OF THE EFFECTIVENESS OF TAI CHI EXERCISE PROGRAM ON CARDIOPULMONARY FUNCTIONS AND QUALITY OF LIFE IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is an autoimmune disease that not only affects the skin but also causes symptoms that involve important internal organs such as joints, muscles, and heart and lungs. Due to all these multiple system involvements, the quality of life of individuals with scleroderma decreases. Tai Chi Chuan is a combination of physical exercise and relaxation techniques, and it is a traditional Chinese exercise method used to improve mental and physical health of people. There are many studies showing that Tai Chi improves the body's aerobic capacity and psychological well-being. In the literature, Tai Chi has been shown to reduce pain, improve physical function, improve healing effects on depression and quality of life, especially, in the elderly, individuals with musculoskeletal diseases such as rheumatoid arthritis and osteoarthritis, and improve cardiac vascular risk factors such as hypertension and diabetes.

Objectives: The aim of the study is to examine the effectiveness of Tai Chi on cardiopulmonary functions and quality of life in patients with SSc.

Methods: 28 SSc patients (25 females, 3 males) with an average age of 53.00 ± 10.00 were included in the study. For training, patients were divided into two groups by block randomization method. Group 1 received 60 minutes of Tai Chi exercise program and Group 2 received 60 minutes of home exercise for 2 days a week for 8 weeks. 6-min walk test (6MWT) and St. George Respiratory Questionnaire was used to evaluate the cardiopulmonary functions, Short form 36 (SF-36) was used to evaluate the quality of life. All evaluations were performed at baseline and at the end of the 8th week

Results: When the groups were compared before training, there was no significant difference (p> 0.05). In post-training comparisons, there was a significant difference in all parameters in Tai Chi group (p: 0.001-0.045); there was a significant difference in the physical function sub-parameter of SF-36 and 6MWT in the home exercise group (p: 0.045, p: 0.038, respectively). Comparing the post-training groups, Tai Chi group was found to be superior in terms of all parameters compared to the home exercise group (p: 0.00-0.04). No side effects were observed during the exercises.

Conclusion: As a result of our study; Tai Chi has a possitive effect on cardiopulmonery function and quality of life in patients with SS. Tai Chi should be included in rehabilitation programs as a safe alternative type of exercise to improve cardiopulmonery function and quality of life in patients with SSc.

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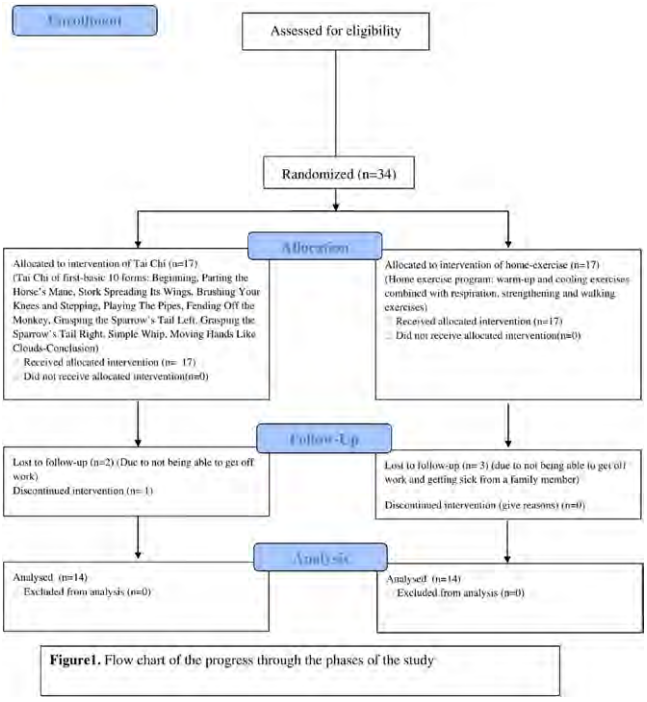


Figure1. Flow chart of the progress through the phases of the study

Disclosure of Interests: None declared

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AB1308-HPR DEVELOPMENT OF AN E-LEARNING PATIENT EDUCATION PROGRAM TARGETING PATIENTS WITH RHEUMATOID ARTHRITIS: FROM CONTENT TO DESIGN

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Background: Patient education (PE), with the aim of supporting patients to self-manage their disease is important in the treatment and care of patients with rheumatoid arthritis (RA) (1). Today, there is a shift in the organization of healthcare systems due to a demographic change towards ageing populations and an increasing use of technology. Advancements in web-technology can offer alternative ways to provide PE – e.g. through an e-learning platform. However, *E-Learning development must be based on the needs of the learners and on existing evidence on both education and content.*

Objectives: To develop an e-learning platform targeting newly diagnosed patients with RA.

Methods: Focus group interviews with patients, rheumatologists and nurses, with the aim of exploring informational and educational needs related to RA and how this may be communicated in an e-learning program, were conducted. We used a short interview guide to ensure the focus of the interviews, however, strived for a less structured start of the interview to promote a free discussion and later a more structured discussion of specific questions. Pictures, illustrating possible topics in PE within RA and ways to communicate, were also applied. The transcribed interviews were analyzed using thematic analysis (2).

The theoretical framework in the development and design drew on the cognitive theory of multimedia learning (3) and entertainment education (4).

Results: Four themes, covering experiences and needs emerged in the analysis of the focus-group interviews; '*Knowledge of RA, the disease course and prognosis*','*Medical treatment*','*A new life situation*' and '*Daily living with RA*'.

Subsequently, the program was developed through an iterative process between the project group, patient representatives, a communication consultant, graphic designers and an e-learning company.

The program was divided into three learning modules covering knowledge of RA, complications, medical treatment, examinations and daily living with RA, e.g. coping with emotions, pain, fatigue, work, education, physical activity etc. It offers

a combination of e.g. animations, videos with personal patient stories, podcasts, written text, spoken words and interactive quizzes.

Conclusion: The e-learning program is developed and ready for feasibility testing. Subsequently, the effectiveness of the program will be tested in a RCT study among approximately 250 patients.

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Disclosure of Interests: Line Raunsbæk Knudsen Consultant of: Phizer (Not relevant for the present study)., Speakers bureau: Phizer (Not relevant for the present study).
Lily (Not relevant for the present study).
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AB1309-HPR EFFICACY OF ADDING CAFFEINE TO THE TREATMENT REGIMEN IN REDUCING METHOTREXATE INTOLERANCE IN PATIENTS WITH RHEUMATOID ARTHRITIS: A RANDOMIZED CONTROLLED STUDY

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Background: Rheumatoid arthritis is one of common form of chronic inflammatory arthritis. Methotrexate has remained anchor treatment because of its potent efficacy[1]. Intolerance to Methotrexate is a common cause of non-compliance[2&3].

Objectives: To investigate the effect of adding caffeine orally as Methylxanthines (Caffeine), act as adenosine receptor antagonists[4] to reduce symptoms of moderate to severe methotrexate intolerance in patients with Rheumatoid Arthritis[5].

Methods: A prospective, randomized controlled study conducted at Aswan University Hospital, Egypt from Jan 2018 till may 2019. Sixty patients with Rheumatoid arthritis who have had experienced moderate to severe methotrexate intolerance was enrolled in the study. The methotrexate intolerance severity score (MISS)[6]was evaluated at base line before initiation of study then at the next three months consecutively. Patients were randomly assigned by closed envelope method into 2 groups each containing 30 patients: **Group (A)**; 30 patients was prescribed caffeine (coffee or dark chocolate) as an antidote to methotrexate intolerance[7]. **Group (B)**; 30 matched patients acted as control group that included who will continue methotrexate regimen without addition of any extra caffeine.

Results: Twenty four patients (80%) at time three follow up visit showed full improvement of symptoms of methotrexate-intolerance compared to ten patients (33.3%) at 2nd month follow up visit and seven patients (23%) at 1st month follow up visit with statistically significant difference all over the study period (P=0.005). half of study group patients discontinued anti-emetic and other drugs while none in control group did.

Conclusion: Adding caffeine to management regimen can reduce the symptoms of severe methotrexate-intolerance in Rheumatoid Arthritis patients.

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AB1310-HPR EFFECTS OF INSTRUMENT-ASSISTED SOFT TISSUE MOBILIZATION ON FROZEN SHOULDER: A RANDOMIZED CONTROLLED TRIAL

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Background: Frozen shoulder has a greater incidence, more severe course, and resistance to treatment in patients. Management is based on the underlying cause of pain and stiffness. Joint mobilization has been reported to improve joint range of motion in frozen shoulder. However, there is no information regarding the effect of instrument-assisted soft tissue mobilization (IASTM) in frozen shoulder. We proposed that there would be no significant difference between the two manual physical therapy techniques with relatively similar treatment effects in the frozen shoulder.

Objectives: The aim of this randomized controlled study was to compare the effectiveness of IASTM and joint mobilization in the treatment of patients with frozen shoulder.

Methods: Thirty patients with phase II frozen shoulder (mean age 50,9 years, age range 39–65 years) were randomly assigned to one of the two treatment groups: Group I received joint mobilization combined with manual stretching exercise and Group II received IASTM with manual stretching exercise (two days per week for six weeks) (Figure 1). The pain level was evaluated with a visual analogue scale (VAS) and the active range of motion (ROM) was measured with a universal goniometer. The Disabilities of the Arm, Shoulder and Hand score and the Constant-Murley score were used for functional assessment. The assessments were performed at baseline and after the 6-week intervention.



Figure 1. Instrument-Assisted Soft Tissue Mobilization

Results: Both groups had a significant decrease in pain according to VAS and a significant increase in ROM and function level (p<0.05). After the 6-week intervention, improvement of shoulder abduction ROM in Group I was found significantly higher than Group II (p=0.01), on the other hand, Constant-Murley score in Group II was found significantly higher compared to Group I (p=0,001).

Conclusion: Our results supported the hypothesis that either joint mobilization or IASTM, performed in addition to stretching exercise, provided similar improvements in pain levels in patients with the frozen shoulder.

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AB1311-HPR

RHEUMATIC AND MUSCULOSKELETAL DISEASES MANAGEMENT TOOL HELPS TO IMPROVE TREAT-TO-TARGET THERAPY AND PATIENTS' ADHERENCE TO TREATMENT

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Background: Many of the rheumatic and musculoskeletal diseases (RMD) are long term, painful, and function affecting, which takes both the doctors and patients a lot of time and effort. The number of Rheumatologists are not sufficient for the huge population of RMD patients in China. The doctor patient ratio is as low as 1:1000. Relatively inadequate medical resources, traffic inconvenience in rural area, and patients' insufficient understandings of the RMD may cause delayed medical intervention and poor prognosis. Effective RMD patient management tools which provide disease monitoring and enough doctor-patient communication is essential to improve the patients' adherence to treatment. We designed an RMD management app according to the social, cultural and economic situation of Chinese patients, which helps to facilitate shared decision making and relieve the pressure of insufficient medical resources.

Objectives: We aim to investigate the effect of RMD patient management app on treat-to-target therapy and patients' adherence and satisfaction to treatment.

Methods: An observational survey was administrated using a RMD patient management app. The app was designed and improved by Rheumatologist, orthopedics, nurses, patients, and app technical experts. Patients were offered with a questionnaire in regard to satisfaction with the app and their attitudes about the disease. General therapeutic principles, rehabilitation exercise videos and follow-up information were distributed through the app. Warning signals were sent whenever there was a flag sign of exacerbation. The demographic and clinical data, social and economic status, and drug retention rates of the patients were documented. The survey was designed by clinical experts from relevant departments and developed by both doctors and patients.

Results: All patients were supervised by the rheumatologist and orthopedist when using the app. In all the patients included, there were cases of rheumatoid arthritis (35.3%), osteoarthritis (32.4%), ankylosing spondylitis (26.5%), and other chronic arthritis (5.8%). The mean age 38.5±15.8 years old, with 52.9% male and 47.1% female. Most of the patients (85.3%) believed that the app was helpful. Young patients were more likely to respond to the survey than older patients. Some patients (79.4%) had increased compliance because the app offered more chances to communicate with the doctors, which increase their understanding and confidence about the disease. Three patients received flag signs of exacerbation much earlier than they could get to the hospital. From the feedback of the patients, we realized that the patient would like to have more information to keep them from stepping on the trap of false advertisement for therapy (which is very commonly seen in China).

Conclusion: RMD patient need to manage disease activity, daily function and mental state. Insufficient medical resources and patients' knowledge about the disease may lead to poor adherence and prognosis. RMD patient management tool on app was a feasible and cost-effective approach for data collection and patient education. The app increased treat-to-target therapy and patients' adherence to treatment.

References: None.

Disclosure of Interests: None declared

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AB1312-HPR

A COMPARISON OF THE EFFECTIVENESS OF TWO DIFFERENT KINESIO TAPE APPLICATIONS ON PAIN, FATIGUE AND HEALTH STATUS IN WOMEN WITH FIBROMYALGIA

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Background: Fibromyalgia (FM) is a syndrome characterized mainly by chronic widespread pain, fatigue and a decrease in health status. Kinesio tape (KT), one of complementary approaches, has favorable effects on clinic findings in FM, but studies investigating which types of the KT applications are more effective in FM are scarce.

Objectives: This study aimed to compare the effectiveness of fascial correction and FanCut KT applications on pain, fatigue and health status in women with FM.

Methods: A total of 27 women with FM were included, allocated into fascial correction (Group 1) (n:14, age: 41.50 (30.25) years, body mass index (BMI): 24.85 (5.28) kg/m^2) and FanCut techniques (Group 2) (n:13, age: 45.00 (21.00) years, BMI: 25.60 (4.55) kg/m^2) groups. The fascial correction technique performed with approximately 25% to 50% of tension and oscillated in longitudinal direction on overall back was used in the Group 1; while, the FanCut technique performed with 0% tension on the overall back was used in the Group 2. Exercise program was carried out 2 days a week for 6 weeks under the supervision of a physiotherapist in both groups. Pain intensity and severity of fatigue with the Visual Analog Scale and health status with the Fibromyalgia Impact Questionnaire were evaluated at the baseline and after the 6-weeks treatment.

Results: Physical characteristics of the groups were similar (p_{age}=0.190, p_{bmi}=0.808). After the treatment, it was found that pain intensity (p=0.001; p=0.001) and the severity of fatigue (p=0,001; p=0.003) decreased and health status (p=0.001; p=0.002) improved in both the group 1 and 2, respectively. Moreover, fatigue decreased (p=0.008) and health status improved (p=0.021) in the group 1 in comparison to the group 2; but pain intensity (p=0.085) did not differ between the groups.

Conclusion: In this study, it was observed that both the fascial correction and the FanCut KT applications were effective in decreasing pain and fatigue, and improving the health status of women with FM. In addition, the study suggested that the fascial correction KT application was superior in decreasing fatigue and improving health status in comparison to the FanCut KT application in women with FM. In clinics, the KT application may be considered as a non-pharmacologic and complementary therapy to improve the symptoms of FM. Moreover, the fascial correction KT application may be more effective in improving some parameters due to fascia dysfunction in FM.

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AB1313-HPR

EFFECTS OF N-ACETYLCYSTEINE ON PULMONARY FUNCTIONS IN PATIENTS WITH SYSTEMIC SCLEROSIS: A DOUBLE BLIND, PLACEBO CONTROLLED STUDY

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Background: Systemic sclerosis (SSc) is a systematic and rare autoimmune disease that affects many organs. N-acetylcysteine (NAC), thiol containing compound, can act both as the precursor of reduced glutathione and direct scavenger of reactive oxygen species.

Objectives: We assessed the clinical effect of NAC on pulmonary function test of patients with diffuse scleroderma.

Methods: This study is a randomized double blind clinical trial that was done on 25 patients with diffuse SSc without lung involvement on primary chest high-resolution computed tomography. Placebo was administered for 13 patients and 1200 milligram NAC for 12 patients. Body plethysmography parameters were assessed at the beginning of the study and after 24 weeks.

Results: Patients in the two groups were matched in the basic demographic data like age, duration of disease, and modified Rodnan skin score. The analysis showed no significant differences in parameters of plethysmography between the two groups. After importing the data of 2 patients in the placebo-treated group, who developed interstitial lung disease, DLCO in the placebo-treated group was 90.69 ± 21.29 milliliter at the end of the study, which significantly decreased compared with the beginning of the study (102.30 ± 13.83 ml). Also, changes of DLCO between the two groups were significantly different.

Conclusion: In this trial, sensitivity of DLCO as the first marker in evaluation of pulmonary function in patients with SSc was confirmed. On the other hand, NAC had no effect versus placebo in a period of 24 weeks. We recommend that more studies with larger sample size and longer duration should conduct for further evaluation.
References: No reference.

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AB1314-HPR

ECONOMIC EVALUATION OF THE DR. BART APP IN PEOPLE WITH KNEE AND/OR HIP OSTEOARTHRITIS

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Background: Self-management is of paramount importance in non-surgical treatment of knee and/or hip osteoarthritis (OA). Modern technologies offer the possibility to support self-management 24/7. We developed an e-self-management application (dr. Bart app) for people with knee and/or hip OA[1].
Objectives: To evaluate the (incremental) cost-utility and cost-effectiveness of the dr. Bart app compared to usual care in people with knee/hip OA, applying a health care perspective.
Methods: This economic evaluation was conducted alongside a 6-month randomized controlled trial, in which 214 participants were offered to use the dr. Bart app for 6 months and 213 participants received care as usual. Health care costs were measured using self-reported questionnaires. Clinical outcome measures were quality-adjusted life years (QALYs) according to the EuroQol (EQ-5D-3L), the EuroQol rating scale (QALY-TRS), and the five subscales of KOOS/HOOS. Cost and effect differences were estimated using longitudinal linear mixed models and cost-effectiveness acceptability curves. Bootstrapping was used to estimate statistical uncertainty.
Results: Mean age of participants was 62.1 (SD 7.3) years, with the majority being female (72%) (Table 1). The difference in health care costs was non-significantly in favour of the intervention group (€-31.12 (95% CI: -66; 3)). Table 2 shows estimated treatment effects over 6 months. We found small but positive effects on symptoms, pain and activities of daily living (ADL) in favour of the dr. Bart app group. For QALY and QALY-TRS, the probability of the dr. Bart app being cost-effective compared to usual care was 0.80 and 0.60 at a willingness to pay (WTP) of €10.000 and 0.72 and 0.44 at WTP €80.000, respectively. For symptoms, pain and ADL, the probability that dr. Bart app was cost-effective was > 82% and for activities and quality of life < 40%, regardless of WTPs.

Table 1. Baseline characteristics.

	Dr. Bart app group (n=214)	Control group (n=213)
Age, years; mean (SD)	62.1 (7.7)	62.1 (7.0)
Female, n(%)	147 (68.7)	159 (74.7)
BMI, kg/m^2; mean (SD)	27.8 (5.1)	27.3 (4.8)
Main OA-location, knee; n(%)	157 (73.4)	156 (73.2)

Conclusion: This economic evaluation, from a health care perspective, showed that costs were not significantly lower for the dr. Bart app group compared to usual care. Given the non-invasive character of the intervention and the moderate probability to be cost-effective for the majority of outcomes, the dr. Bart app has only the potential to serve as a trustworthy tool to provide education and goal setting regarding OA and its treatment options.

Table 2. Estimated treatment effects over 6 months.

	Estimated difference over 6 months between groups (95% CI)*	WTP €10,000	WTP €80,000
Health care costs, €	-31 (-66; 3)	N/A	N/A
QALY	0.0045 (-0.0119;0.0210)	0.80	0.72
QALY-TRS	-0.0015 (-0.0149; 0.0111)	0.60	0.44
KOOS/HOOS			
- Symptoms	2.6 (-0.8; 5.8)	0.93	0.93
- Pain	3.0 (-0.2; 6.1)	0.97	0.97
- ADL	1.9 (2.3; 6.1)	0.82	0.82
- Activities	-0.7 (-5.1; 3.8)	0.37	0.37
- Quality of life	-0.7 (-4.8; 3.2)	0.36	0.36

*Control group serving as reference category. Abbreviations: KOOS; Knee Injury and Osteoarthritis Outcome Score; HOOS; Hip Disability and Osteoarthritis Outcome Score.

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AB1315-HPR

HYPERBARIC OXYGEN THERAPY IN FIBROMYALGIA PATIENTS – DOUBLE-BLIND PROSPECTIVE CLINICAL TRIAL

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Background: Hyperbaric Oxygen Therapy (HOT) proved effective in improving of symptoms of patients affected by fibromyalgia syndrome (FMS) [1].
Objectives: The objective of the present study was to evaluate the effectiveness of HOT compared to hyperbaric treatment with no oxygen therapy (PBO) in the symptoms and working ability in FMS.
Methods: We conducted a prospective trial in employed patients with FMS, randomly assigned to HOT or PBO. Patients and evaluating clinicians were blinded to the treatment. HOT arm comprised 40 sessions, 5 days/week, 120 minutes, 100% oxygen at 2ATA; PBO comprised the same sessions without oxygen. Evaluations were at baseline, after 4 (T1) and 8 weeks (T2). Parameters considered were: socio-demographics, biochemistry, clinical evaluation and patient-reported outcomes (PROs). Baseline assessment included questions BELIEF (how much do you hope to improve with this treatment) and HOPE (how much do you expect to improve with this treatment), with VAS response. Spearman's, Mann-Whitney's, Kruskal-Wallis and Fisher's Exact test were used.
Results: 12 patients were included and completed the study, 6 in each arm (Tab. 1). No significant difference was observed in clinical measures or PROs at T1 and T2 between HOT and PBO arms, except for Working Productivity and Activity Impairment Questionnaire (WPAI) (result III) (Tab. 2). In both arms, disease duration was associated with worse PROs (Widespread pain index r=0.59,p=0.037, Severity Score r=0.81,p=0.025); higher BMI with improvement in function at T2 (r=0.63,p=0.027); higher baseline scores in BELIEF with reduction symptoms number (r=-0.67, p=0.021), higher scores in HOPE with reduction in Health Assessment Questionnaire (r=-0.057, p=0.039)

Table 1. Patients characteristics

	All	HOT	PBO
Number	12	6	6
Age*	55,5 (44;59,75)	55,5 (47,75;60)	51 (41;58,75)
Females**	6 (100)	6 (100)	6 (100)
Disease duration *	10 (8,25;26,75)	9,5 (7,5;20,75)	15 (10;26,75)
BMI*	25,5 (22,25;31)	25 (22,75;28)	28,5 (23;31,75)
Smoke**	0,5 (0;1)	0 (0;1)	1 (0,25;1)
HOPE score*	0 (0;1)	0,5 (0;1)	0 (0;0)
>=80**	9 (64,3)	5 (62,5)	4 (66,7)
BELIEF score*	70 (60;80)	75 (67,5;83,75)	62,5 (60;68,75)
>=70**	8 (57,1)	6 (75)	2 (33,3)

*median (IQR); **number (%)

Table 2. Change from baseline in clinical measures and PROs at T2.

	Medians (IQR)			P value	≧ 20 Percentage amelioration No. (%)			P value
	All	HOT	PBO		All	HOT	PBO	
Short Form-36 - Physical	1 (-1;4)	3 (-1;5,5)	0,5 (-0,75;3,25)	ns	0 (0)	0 (0)	0 (0)	ns
SF-36 - Mental	4 (-1;8)	6 (2,5;9,5)	1 (-1,75;5,25)	ns	0 (0)	0 (0)	0 (0)	ns
Severity score - total	-13 (-15;-2)	-15 (-17;-13,5)	-3 (-5,5;-0,5)	ns	2 (18,2)	2 (40)	0 (0)	ns
Number symptoms	-3 (-4;0)	-4 (-4,5;-1,5)	-2 (-3;-0,25)	ns	2 (18,2)	2 (40)	0 (0)	ns
SASP score	-1 (-3;0)	-2 (-3,5;-0,5)	-1 (-1,75;-0,25)	ns	1 (9,1)	0 (0)	1 (16,7)	ns
Widespread pain index	0 (-2;0)	0 (-2;0)	-0,5 (-1,75;0)	ns	2 (18,2)	2 (40)	0 (0)	ns
Tender Points Count (0-18	-2 (-3;-0,5)	-2 (-3,5;-1)	-1,25 (-2;-0,13)	ns	3 (27,3)	2 (40)	1 (16,7)	Ns
Health Assessment Questionnaire	0 (0;0)	0 (-0,5;0,5)	0 (0;0)	ns	3 (27,3)	1 (20)	2 (33,3)	ns
Fibromyalgia Impact Questionnaire	10 (0;15)	10 (7,5;15)	2,5 (-3,75;12,5)	ns	1 (9,1)	0 (0)	1 (16,7)	ns
WPAI result-2	-0,5 (-1,25;-0,13)	-1,5 (-2;-0,5)	-0,25 (-0,5;0,19)	ns	3 (21,4)	0 (0)	3 (37,5)	ns
WPAI result-3	0 (-2,38;0)	-2,75 (-3,88;-2)	0 (0;0)	ns	5 (35,7)	0 (0)	5 (62,5)	P=0.008
WPAI result-1	-1 (-3,25;-0,38)	-3,5 (-4,75;-1,5)	-0,5 (-1;0,38)	ns	6 (42,9)	2 (33,3)	4 (50)	ns

Conclusion: 8-week HOT treatment does not substantially improve symptoms in FMS compared to PBO. All patients on hyperbaric treatment may experience amelioration of symptoms: other factors should be considered, including beliefs and expectations on the treatment.

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AB1316-HPR COMORBIDITIES IMPACT ON PHYSICAL REHABILITATION PROGRAM OUTCOMES IN PATIENTS WITH KNEE OSTEOARTHRITIS

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Background: Physical rehabilitation is proposed as a method of non-pharmacological treatment of knee osteoarthritis (OA) by the EULAR and OARSI recommendations. At the same time, presence of concomitant diseases could influence the condition of patients and the outcomes of the rehabilitation program.
Objectives: To evaluate the frequency of comorbidities in OA patients and to appreciate their impact on outcomes of the physical rehabilitation program.
Methods: A prospective control case study was conducted in the University Rehabilitation Center. The patients underwent clinical examination, VAS scale was used to assess level of pain, and Knee Injury and Osteoarthritis Outcome Score (KOOS) with 5 domains (Pain, Symptoms, ADL, Sport, QoL) for joint function assessment. These parameters were evaluated at the onset of the program (T0) and at the end of the 10th day (T1). Medical data records, general clinical exam and Charlson Comorbidities Index (CCI) assessed the comorbidities.
Results: 48 patients with OA were included in the study, 37 patients of them were found with comorbidities. The most frequent associated diseases were: cardiovascular- 76.6%, obesity-59.9%, and endocrine - 12.9% cases. At T0, significantly lower levels in the group with comorbidities were identified on the domains Pain, Sport and QoL. The CCI in patients with comorbidities was 3.29 ± 0.14 points (82.1% for 1-year survival rate). At the T1 moment, we found an improvement in joint functionality in both groups. The mean value of the VAS score group of patients without comorbidities decreased from 48,18 mm to 21,36 mm ($p < 0.05$) and for the group of patients with comorbidities – 64,2 at / 36,2 mm ($p<0.001$). Significant improvement in joint function in the comorbidities group was in Pain ($p < 0.01$), Sport ($p < 0.05$) and Qol ($p < 0.01$) domains, at the same in patients without comorbidities, the improvement was significant in all 5 domains.
Conclusion: Comorbidities are highly associated to knee osteoarthritis and prove to have a negative influence on the results of the physical rehabilitation program; therefore, we would recommend to apply individualized rehabilitation programs adapted to the associated conditions of each patient.
Disclosure of Interests: None declared
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AB1317-HPR YOGA-THERAPY: IMPROVEMENT IN PSORIATIC ARTHRITIS PROMS AT 4 MONTHS

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Background: Psoriatic Arthritis and Psoriasis have a major impact on QOL with associated mood disorders and Cardiovascular disease and Cancer as inter-related co-morbidities [1]. Yoga therapy (Y-T) has been used in several Long Term Conditions [2] and we have reported Rapid improvement in Proms in RA (RCP 2018) and so compared results of a PsA cohort offered the same Y-T intervention.
Objectives: This first in UK PsA study investigated: a) impact of a 16 week Y-T intervention on functional outcomes and QOL in 10 PsA patients, b) acceptability and experiences of the intervention. We present results in comparison to a previously reported RA cohort n=10.
Methods: Ten adult PsA patients (2 M 8 F Age 32-67 Avg: 53.7 Y; PsA diagnosis: 6.45 yrs:1 Juvenile onset) consented to 10 individual Y-T sessions (weekly x 4; biweekly x 6) with a yoga therapist in a standard consulting room. The intervention was tailored to the needs and abilities of each patient and included: breath-centered physical yoga postures, breathing and visualization techniques, mantras and meditation, with supportive Lifestyle/behavioural strategies. All participants completed measures pre- and post-intervention (EQ-5D HAQ HADS PGIC) to assess change in health status.
Results: A 10 session course of Y-T over 16 weeks was completed with 92/100 PsA YT sessions. Note 1 patient had unrelated Trauma and withdrew after 2 sessions. This confirms acceptability of delivery in a clinic setting and all participants reported strong adherence to practices (0-1) and strong belief (0-2) in impact of yoga. (Likert 5 point 0-4 scale).
Further data on only 9 PsA participants will be presented in comparison to the previous RA cohort of 10.
PsA patients n=9: Pain reduced 25 % HADs Depression reduced 39% Anxiety reduced 25%
HAQ health score improvement was significant at $P<0.04$ (ANOVA).
EQol 5d(3L) improved 24% but overall QOL remained below 50% max calculated TTO.
RA patients had recorded stable overall TTO at a higher level 0.63 pre and post Y-T.
PGIC record of positive change is recorded as a reduction on VAS from 5/5 to 2.4/5.
We will add 12 month FU data set in PsA to compare with 24 month data in the RA cohort.
Conclusion: Yoga-Therapy is deliverable and acceptable in a NHS clinic setting for PsA. Improved PROMS begs further larger studies of mechanisms of bio-psychosocial intervention in long term inflammatory conditions. The outcomes support the Poly Vagal Theory [3] as an effector model, via the bio-mechanistic neuro-inflammatory reflex [4]. We propose further Health Economic analysis of this 2500 yr old Yoga model for long term conditions to examine any long term cost benefit to the NHS.
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Table 1. PsA vs RA post Yoga Therapy PROMs at 4 mth.

	PsA n=9 pre	PsA 4 m	PsA 4 m %	RA n=10 Pre	RA4m FU	RA 4m %
HADS m Depression	6.33	3.88	**-39**	6.7	2.3	**- 65**
HADS m Anxiety	8.56	6.44	**-25**	9.4	4.8	**- 48**
Mean HAQ	0.79	0.**75**	**- 2**	0.78	0.48	**- 26**
M Pain Score (HAQ)	60	45.00	**-25**	57	24	**- 58**
M Health Score (HAQ)	60	42.7	**-29 p<0.04**	51	17.2	**- 66**
M H Utility TTO (EQol5d)	0.41	0.5	+24	0.63	0.63	**0**
PGIC	5	2.4				

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AB1318-HPR VAGUS NERVE STIMULATION IN PATIENTS WITH RHEUMATOID ARTHRITIS: 48 MONTH SAFETY AND EFFICACY

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Background: Rheumatoid arthritis (RA) is a disease with significant remaining unmet medical needs for better treatments. Vagus nerve stimulation (VNS) to activate the inflammatory reflex (cholinergic anti-inflammatory pathway) represents a novel experimental therapy for RA.[1] Previously, we reported that inflammatory reflex activation by VNS reduced pro-inflammatory cytokine production and improved disease activity in a 17-patient rheumatoid arthritis (RA) proof-of-concept study using a reprogrammed epilepsy stimulator2; clinical improvement was sustained for 24 months without untoward safety signals.[3] Here we report the 48 months results from this long-term observational study.
Objectives: Determine the long-term safety and efficacy of VNS for the treatment of RA
Methods: In the primary study, a VNS device was implanted into 17 RA patients, mostly with insufficient response to multiple conventional and biologic DMARDs, on stable background of methotrexate (≤25 mg weekly) therapy[2]. The device electrically stimulated the vagus nerve, 1-4 min/day, over a 12-week open label

period. On completion, subjects were offered to enroll into a follow-up study, where the study physicians were given flexibility to alter VNS dosing parameters and/or to add a biologic disease-modifying antirheumatic drug (DMARD) to the treatment regimen to induce disease remission. Clinical disease activity measures and safety were accessed over 4 years.

Results: All patients electively continued VNS treatment in the long-term follow-up study, 4 subjects withdrew prior to month 48. Reasons for discontinuation were withdrawal of consent (N=3) and adverse event due to device discomfort (N=1). At the start of the follow-up study, the mean DAS28-CRP, CDAI and HAQ-DI were significantly reduced compared to the pre-implant baseline (mean difference± SD: DAS28-CRP=-1.60± 1.13, p<0.001; CDAI=-21.19± 13.5, p<0.001; HAQ-DI=-0.44± 0.49, p<0.01), and this effect was retained through 48 months. Patients using VNS monotherapy and those using a combination of VNS with biologic DMARDs exhibited stable improvements in DAS28-CRP, CDAI and HAQ-DI at month 48 (Table 1). Improvements were observed for patients who both previously had an insufficient response to targeted biological therapies as well those who had an insufficient response to standard DMARDs. No association was seen between DAS28-CRP and stimulation frequency (Range= 1X-8X/day). There was no difference in the adverse events profile between the two groups.

Table 1. Efficacy of VNS treatment.

	Treatment Reinitiated N=9			VNS Monotherapy N=8			Total N=17		
	Mo. 24	Mo. 36	Mo.48	Mo. 24	Mo. 36	Mo. 48	Mo. 24	Mo. 36	Mo. 48
	Mean change from baseline (SD)								
DAS28-CRP	-2.58 (1.0)***	-2.40 (1.0)**	-2.28 (1.3)**	-2.61 (1.3)*	-1.77 (1.8)	-2.0 (1.7)	-2.59 (1.1)***	-2.19 (1.2)**	-2.17 (1.4)**
CDAI	-24.06 (8.3)***	-18.02 (13.3) *	-16.2 (19.6)	-33.5 (11.1)***	-27.8 (16.0)*	-27.9 (12.7)*	-28.20 (10.5)***	-21.93 (14.5)*	-20.83 (17.5)*
HAQ-DI	-.60 (0.64)*	-.63 (0.45)*	-.31 (0.60)	-.89 (0.69)*	-.88 (0.92)	-.88 (0.61)	-0.73 (0.66)***	-0.73 (0.64)**	-0.54 (0.64)*

*P<0.05, **P<0.01, ***P<0.001 versus primary study baseline (month -3.5)

Conclusion: VNS was safe, well-tolerated, and resulted in significant and clinically important improvements in disease activity measures that were maintained over 48 months. These results support development of VNS devices as a new therapeutic option for RA treatment.

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AB1319-HPR EFFECT OF SEGMENTAL STABILIZATION AND PILATES ON CHRONIC NON-SPECIFIC LOW BACK PAIN: PILOT STUDY

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Background: Low back pain is an important health condition with major socioeconomic consequences and is associated with high costs for the health system, absenteeism at work and reduced functional performance. It is one of the most relevant health problems in the elderly, with point prevalence estimates higher than other musculoskeletal conditions.

Objectives: To verify the effect of segmental stabilization versus the Pilates method in the elderly with chronic low back pain.

Methods: The study included 9 elderly women with chronic low back pain randomized into two groups: Segmental Stabilization Group (SG n = 5; age 65.2 ± 4.32; Body Mass Index - BMI 29.99 ± 4.65) and Pilates Group (PG n = 4; age 67.75 ± 7.13; BMI 26.49 ± 4.06). Both groups underwent 16 individual sessions of 60 minutes twice a week and avaliated before and after 8 weeks. Pain was assessed using the Visual Analogue Pain Scale; functional disability, by Oswestry's disability index; excessive fear of movement and physical activity, using the Tampa Kinesiophobia Scale; level of confidence in the balance for specific activities, on the Activity-Specific Balance Confidence (ABC) scale and; activation of the transverse muscle of the abdomen, by the pressure biofeedback unit Stabilizer of the Chatanooga brand. The allocation and evaluations of the participants were performed by a blind examiner. The data were analyzed using the Student's t-test with the level of significance (p≤0.05).

Results: The data show significant differences in the reduction of pain intensity (p= 0.022) and functional disability (p=0.023) only in SG and improvement in kinesiophobia (p=0.007) only in PG. The level of confidence in the balance for specific activities was better in the SG when compared to the PG (p=0.059). There was no difference in the activation of the transversus abdominis in both groups.

Conclusion: The results indicate that the segmental stabilization was effective to improve pain and functional disability, Pilates to improve the degree of kinesiophobia and the SG obtained a better result when compared to the PG regarding the level of confidence in the balance for specific activities. Both techniques had a great effect on improving functional capacity and on the level of confidence in the balance for specific activities. It is suggested to carry out studies with a larger number of participants and follow-up evaluation to assess the long-term effects.

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AB1320-HPR THE ASSOCIATION BETWEEN PHYSICAL ACTIVITY AND CARDIORESPIRATORY FITNESS IN PATIENTS WITH RHEUMATOID ARTHRITIS AND HIGH CARDIOVASCULAR RISK

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Background: Rheumatoid arthritis (RA) is associated with increased risk of cardiovascular disease (CVD) disease and CV mortality[1]. High values of cardiorespiratory fitness (CRF) are protective against CVD and CV mortality[2]. Physical activity levels in patients with RA are low. Knowledge on whether physical activity is associated with CRF in patients with RA and high CV risk is scarce. This knowledge is important because improving the level of physical activity could improve CRF and lower CV risk in this group of patients with RA and high CV risk. However, it is unclear whether physical activity is associated with CRF in this group of patients. This study presents the preliminary results at baseline of the association of physical activity with CRF from an ongoing pilot study aimed at improving CRF through exercise therapy in patients with RA and high CV risk.

Objectives: To determine (i) the level of physical activity in patients with RA and high CV risk and (ii) whether physical activity is associated with CRF in patients with RA and high CV risk.

Methods: Patients with RA and high CV risk participated in this pilot study. Increased 10-year risk of CV mortality was determined by using the Dutch SCORE-table. Anthropometrics and disease characteristics were collected. Physical activity was assessed with an Actigraph accelerometer to determine the number of steps and intensity of physical activity expressed in terms of sedentary, light, and moderate-to-vigorous time per day. Participants wore the accelerometer for seven days. A minimum of four measurement days with a wear time of

at least 10 hours was required. The VO_2 max measured with a graded maximal exercise test was used to determine the CRF. Pearson correlation coefficients were calculated for the associations between the different measures of physical activity and VO_2max. For the variables that were associated, linear regression analysis was carried out, with pain and disease activity as possible confounders.
Results: Thirteen females and five males were included in the study. The mean age was 66.5 (± 15.0) years. Only 22% of the patients met public health physical activity guidelines for the minimal amount of 150 minutes a week. The mean step count was 6237 (± 2297) steps per day and mean moderate-to-vigorous physical activity time was 16.50 (± 23.56) minutes per day. The median VO_2max was 16.23 [4.63] ml·kg^{-1}·min^{-1}, which is under the standard. Pearson correlations showed a significant positive association for step count with VO_2max. No associations were found for sedentary, light, and moderate-to-vigorous physical activity with VO_2max. The significant association between step count and VO_2max($p = 0.01$) was not confounded by disease severity and pain.
Discussion: Since better CRF protects against CVD, increasing daily step count may be a simple way to reduce the risk of CVD in patients with RA and high CV risk. However, these results need to be confirmed in a larger study group. Future research should investigate if improving daily step count will lead to better CRF levels and ultimately will lead to a reduction in CV risk in patients with RA and high CV risk.
Conclusion: Physical activity levels of patients with RA and high CV risk do not meet public health requirements for physical activity criteria and the VO_2max was under the standard. Step count is positively associated with CRF.
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HPR Patients' perspectives, functioning and health (descriptive: qualitative or quantitative)

AB1321-HPR **DEVELOPING A SELF-MANAGEMENT INTERVENTION TO MANAGE JOINT HYPERMOBILITY SYNDROME AND EHLERS-DANLOS SYNDROME HYPERMOBILITY TYPE: AN ANALYSIS INFORMED BY BEHAVIOUR CHANGE THEORY**

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Background: Joint Hypermobility Syndrome (JHS) and Ehlers-Danlos Syndrome Hypermobility Type (EDS-HT) are heritable disorders of connective tissue that can cause joint instability and pain and are associated with increased anxiety and depression. There is currently little UK guidance for supporting patients with JHS/EDS-HT [1]. The analysis presented here used the Behaviour Change Wheel (made up of the Theoretical Domains Framework (TDF) and Capability, Opportunity, Motivation and Behaviour (COM-B) model[2]) to identify possible intervention options to improve self-management in people with JHS/EDS-HT.
Objectives: To determine recommendations for the components of a behaviour change intervention for people with JHS or EDS-HT.
Methods: Data from: 1) A systematic review and thematic synthesis of the literature examining adults' lived experiences of JHS/EDS[3] and 2) A thematic analysis of interview data where UK adults with JHS/EDS-HT (n=17, 14 women, 3 men) discussed the psychosocial impact of the condition on their lives[4], were mapped onto the TDF and COM-B in a behavioural analysis. A modified Nominal Group Technique focus group (n=9, all women) explored which interventions identified by the TDF/COM-B mapping exercise were most important to them.
Results: Participants prioritised a range of potential self-management interventions, including:
Education: Participants wanted greater support to improve their knowledge of JHS/EDS-HT, including self-help strategies for coping with injury, fatigue and overexertion, and how to evaluate information about their condition.
Training: In activity pacing, assertiveness and communication skills, and what to expect during pregnancy, when symptoms of JHS/EDS-HT can worsen.
Environmental restructuring and enablement: Support from occupational therapists to maintain independence at home. Enablement of access to CBT, mindfulness and emotional support.
Modelled behaviour: Positive first-person narratives that address how other patients with JHS/EDS-HT have coped with anxiety, depression, distress, fear, frustration and feelings of loss.
Conclusion: This study is the first to apply theoretically-informed approaches to the management of JHS/EDS-HT. Through a modified nominal group technique, potential behaviour change interventions for addressing barriers to self-management have been prioritised. Discussion with participants indicated poor access to psychological support, occupational therapy and a lack of knowledge of JHS/EDS-HT. Future research with healthcare professional and patient stakeholder groups will further evaluate which intervention options would be most acceptable and feasible for the management of JHS/EDS-HT.
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AB1322-HPR **NON-INFECTIOUS ACUTE INFLAMMATORY ARTHRITIS IN JOINT ARTHROPLASTY**

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Background: Acute inflammatory arthritis (AIA) in a native knee joint is a common pathology with a well-defined differential diagnosis which includes crystal-induced arthritis. Presenting symptoms in a knee joint arthroplasty (KJA) can mimic a periprosthetic hematogenous infection (PHI). There are few studies in current literature that describe possible causes of non-infectious arthritis in KJA. PHI requires, in most cases, an urgent combined surgical and antibiotic (AB) treatment. Describing and studying other possible diagnoses that may resemble PHI in a KJA is mandatory in order to minimize diagnostic errors and avoid unnecessary treatments.
Objectives: To analyze the characteristics of AIA in KJA with negative cultures in patients with an initial diagnosis suspicion of PHI.
Methods: A retrospective case series was conducted at a tertiary-level hospital including all patients diagnosed with an AIA in KJA with negative cultures from January 2012 to December 2019. Demographic data, clinical presentation, management and outcomes were recorded and analyzed.
Results: A total of 11 cases in 9 patients were included (6 females and 3 males) with a median age of 69 years at the time of diagnosis. All patients had risk factors for AIA (6 had chondrocalcinosis (CC), 2 hyperuricemia and 1 psoriasis). However, crystal deposits in synovial fluid (SF) for none of the patients had been previously found.
The median time from the index surgery to clinical presentation was 6 months, and from initial clinical presentation signs to referral was 24 hours. All cases presented with pain and swelling and 5 presented with erythema. Median body temperature on admission was 37.2ºC. All patients presented with no acute distress. Initial blood tests showed a median white blood cell count and CRP of 11.160/mm3 and 90mg/L, respectively. Blood and SF cultures were taken for all cases. The median white blood cell count in SF was 75.883/mm3.
Three cases had received AB treatment during a median of 6 days prior to microbiological sampling. After initial sampling, 6 cases received AB prior to surgery, 1 received AB after surgery, 1 received only AB and 3 were treated only with NSAIDs. In all cases, surgical treatment consisted in radical surgical debridement and polyethylene insert exchange.
Further blood and SF tests were performed 4 days after admission. The mean decrease for systemic white blood cell count, CRP and synovial leukocyte count was 46%, 58% and 56%, respectively. All cultures were negative and crystal deposits were not identified for any of the samples.
The median duration of symptoms was 127 days with a good outcome. 6 patients received AB for a median of 69 days.
Conclusion: Non-infectious AIA in KJA is a rare entity that should be accounted for the differential diagnosis of periprosthetic joint infection. The initial diagnosis

of infection could not be confirmed, although three patients had taken AB before sampling. It is important for physicians to have a suspicion for non-infectious arthritis, especially in patients with clinical and blood test result dissociation, radiological CC, medical history of hyperuricemia or psoriasis, in order to avoid unnecessary AB and surgical treatment.

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AB1323-HPR A QUALITATIVE EXPLORATION OF THE PERSONAL FINANCIAL TOLL OF ARTHRITIS

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Background: The financial experience faced by working-age people with arthritis includes living below the poverty line for many (1). Financial distress amongst people with arthritis is known to contribute to poorer health outcomes, including high psychological distress and more severe pain (2). Despite the demonstrated societal cost of arthritis care and management, the personal costs borne by the individual are not well understood in different health systems (3).

Objectives: To explore the perceived financial impacts of living with arthritis amongst working-age individuals aged 18 – 50 years in Australia.

Methods: A qualitative descriptive study design was used. Participants with inflammatory arthritis or osteoarthritis were recruited from the community, including urban and rural settings. An interview schedule was developed, informed by existing literature (4), which was piloted prior to data collection. Deductive and inductive coding techniques were used to identify financial-related themes arising from the data.

Results: Semi-structured interviews were conducted with 21 younger people (90% female) with a mix of arthritis conditions including rheumatoid arthritis, psoriatic arthritis, osteoarthritis, and ankylosing spondylitis. Four themes were identified: direct arthritis-attributable medical costs, indirect arthritis-attributable costs, insurance and pension costs, and broader financial impacts on the family. Non-subsidised costs were frequently referenced by participants as burdensome, and existed even within the publically-funded healthcare system. Financial distress was characterised by participants as chronic, onerous for the entire family, and associated with exacerbation of physical symptoms.

Conclusion: People with arthritis and of working age experience significant arthritis-attributable financial burden and related distress. Financial concerns should be actively identified and considered within shared clinical decision making, in order to provide more patient-centred care for these individuals.

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AB1324-HPR INVESTIGATION OF THE RELATIONSHIP BETWEEN SOCIAL APPEARANCE ANXIETY AND DISEASE DURATION, SELF-ESTEEM, ANXIETY AND DEPRESSION IN RHEUMATOLOGICAL DISEASES-PRELIMINARY STUDY

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Background: Appearance anxiety means discomfort in social interactions due to changes in appearance. Also this anxiety; it is the fear of being evaluated negatively and worry about the changes in appearance, and it is not only apparent. Body image is the emotions, thoughts and perceptions of the individual about his or her own body and directly affects self-esteem. The Social Appearance Anxiety Scale (SAAS) was developed to assess social appearance anxiety, and this scale was found to be a valid and reliable scale in scleroderma (SSc) patients. It was also thought to be related to the severity of the disease. The literature shows that appearance concerns are strongly related to depression in patients with rheumatic disease and should be evaluated routinely.

Objectives: The first aim of the study is to determine the level of social appearance anxiety in rheumatology patients, and our last goal is to investigation of the relationship between social appearance anxiety and disease duration, self-esteem, depression and anxiety.

Methods: 129 rheumatology patients with a mean age of 42.96 ± 11.33 years (51 men, 78 women) were included in the study. 55% of patients were ankylosing spondylitis (AS), 15.5% of patients were sjögren syndrome (SS), 11.6% of patients were rheumatoid arthritis (RA), 7.8% of patients were fibromyalgia syndrome (FMS), 6.2% of patients were SSc, 2.3% of patients were Behçet's disease (BD) and 1.6% were diagnosed with psoriatic arthritis (PsA). The Social Appearance Anxiety Scale (SAAS) was used to evaluate patients' social appearance anxiety, the Rosenberg Self-Esteem Scale (RSES) was used to evaluate self-esteem, and the Hospital Anxiety and Depression Scale (HADS) was used to evaluate depression and anxiety.

Results: The disease duration was found to be 6.82 ± 5.22 years. The SAAS average was found to be 43.23 ± 20.53 points. It was found that the SAAS values of patients with PsA and SSc were higher than patients with AS, RA, FMS, SS, BD. A moderate positive correlation was found between SAAS and disease duration, depression and anxiety (p: 0.048, r: 0.545; p: 0.007, r: 0.638; p: 0.014, r: 0.749, respectively).

Conclusion: As a result of the study, it was observed that rheumatology patients had moderate and high level social appearance anxiety. We thought that they have a higher level of social appearance anxiety because of skin involvement in patients with with PsA and SSc. In addition, as a result of the study, we found that as the social appearance anxiety increased, disease duration, depression and anxiety increased. According to this study, in which the preliminary results are given, we thought that it is necessary to determine patients' appearance anxiety in routine evaluation and to reduce social appearance anxiety by collaboration with multidisciplinary areas in rheumatological diseases.

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AB1325-HPR THE TRANSITION FROM PEDIATRIC TO ADULT RHEUMATOLOGY OF 347 PATIENTS AT A SINGLE CENTER

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Background: Pediatric to adult rheumatology transition can be a challenge for both the patient and the clinician, especially in rheumatology as it includes chronic diseases with close follow-up.

Objectives: The objective of this study is to understand our tertiary rheumatology center patient demographic transitioning from pediatric to adult rheumatology in order to design prospective studies enhancing the evidence of transition recommendations.

Methods: Patients included in this study are regularly followed-up in our adult rheumatology clinic and were regularly followed up in our pediatric rheumatology clinic in the past. They were all diagnosed with a rheumatologic condition receiving treatment. The patient files were assessed to have a better understanding of their demographic, disease and treatment information.

Results: Our cohort includes 347 patients diagnosed with a variety of conditions that are Familial Mediterranean Fever (FMF) (n=216), Juvenile Idiopathic Arthritis (JIA) (n=56), Juvenile Spondyloarthritis (jSPA) (n=39), Systemic Lupus Erythematosus (SLE) (n=20), Behçet's Disease (n=7) and the rest of the rheumatologic conditions with less than 5 patients each. The mean age of the patients during transition, mean age of diagnosis, and follow-up duration are 21.34±1.7, 10.4±4.18, and 10.82±4.4 in respective order. The treatment regimens the patients received are summarized in Table 1.

Table 1. Current Treatment Information of the Patients

Current Treatment Information	
DMARD	26
Colchicine	23
Adalimumab	21
Etanercept	10
NSAID	4
Tocilizumab	3
Cyclophosphamide	3
Rituximab	2
Prednisolone	7
Mycophenolate Mofetil	1
Canakinumab	1

Seven patients had FMF related attacks. In addition to attacks, one FMF patient had bilateral ankle pain and one patient had leg pain. One patient out of three diagnosed with Takayasu's disease was still symptomatic. One patient had uveitis-related symptoms. One patient diagnosed with SLE had skin dryness. Furthermore, there were patients with sequelae formation. One patient diagnosed with oligoarticular JIA (oJIA) had bilateral hip sequela with the additional left hip prosthesis. One oJIA patient had micrognathia, and one had left knee sequela. One pJIA patient had small joint sequelae. One sJIA patient had bilateral hip sequelae. One jSPA patient had enthesopathy. One FMF patient had proteinuria due to amyloidosis formation. Another FMF patient had hip surgery due to sequela.

Conclusion: Our center had patients with a variety of conditions with different natures of diseases. EULAR recommends the transition process to start no later than 14 years of age; however, this process started at the mean age of 21 in our patients. In most of these patients, especially the ones diagnosed with FMF, the control of disease activity was maintained. The transition of these different clinical entities might require certain amendments to the standard of care. For future references, we will be able to understand more about the adulthood prognosis of these clinical entities.

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AB1326-HPR TOBACCO ADDICTION IN PEOPLE WITH RHEUMATOID ARTHRITIS – FROM THE PERSPECTIVE OF PATIENTS

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Background: Smoking is one of the most significant modifiable exosomes risk factors for rheumatoid arthritis (RA) (1). Studies suggest that 25-30% of people with RA in Denmark smoke (2). This is almost twice as many as in the background population in Denmark. People with RA have a significant increased risk of severe comorbidity including cardiovascular disease. In addition, there are indications that smokers with RA have a poorer effect of the medical inflammatory treatment compared to non-smokers, and consequently more difficult to achieve remission of the disease activity (3). Tobacco addiction is complex and can be a challenge in smoking cessation. In addition to physiological dependence, habits and social and environmental factors may influence addiction. Tobacco smoking is associated with an addiction to nicotine and it is unexplored how this addiction appears in people with RA.

Objectives: The aim of this study was to examine from the patient's perspective how tobacco addiction appears in people with rheumatoid arthritis.

Methods: We conducted a qualitative study based on a hermeneutics approach. People with RA who previously had participated in a randomized controlled study (4) about smoking cessation conducted at the Center for Rheumatology and Spine Diseases at Rigshospitalet, Denmark were recruited for semi-structured interviews.

Results: In total, 12 people with RA (50% female) were included in the study. The median age was 62 years and median RA disease duration was 12 years. The degree of physical dependence measured by Fagerströms Test for Nicotine dependence (FTND) was on average: 4.9 (score: 0-10, 0=nonphysical dependence).

Three categories of how tobacco addiction appeared emerged during the analysis: 1) *It develops into ingrown habits* referring to the fact that smoking already in adolescence contributes to the development of specific physical, mental and social smoking behavior. Not all individuals considered themselves addicted to nicotine as they did not necessarily connect the nicotine to the ingrown habits. 2) *The body craves for nicotine* referring to nicotine proved calming, while a lacking or insufficient dose caused withdrawal symptoms. Furthermore, smoking became a habit where a craving for smoking occurred in certain situations. 3) *Ambivalence – for and against* referring to the physical dependence and smoking habits making a smoking cessation difficult. Dependency to nicotine and challenges to quit smoking led to a feeling of ambivalence and a lack of control.

Conclusion: Tobacco addiction appeared as a physical dependence and a habit, which, during a smoking cessation, led to ambivalent feelings. Therefore, based on this study, there is still a need for health professionals to talk to patients about smoking. But also, a need to articulate the complexity of addiction in order to support for smoking cessations. Information should be strengthened in the clinical practice in relation to nicotine's implication in tobacco addiction as well as the consequences of tobacco smoking for individuals with RA.

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AB1327-HPR SELF-ASSESSMENT OF ORAL HEALTH STATUS IN RHEUMATOID ARTHRITIS, SYSTEMIC LUPUS ERYTHEMATOSUS AND CONTROLS

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Background: Different periodontal disorders have been associated with the development of multiple rheumatic diseases, encouraging the production of citrullinated proteins and creating a proinflammatory state with an increase in oral and systemic symptomatology.

The Geriatric/General Oral Health Assessment Index (GOHAI) survey has been used as a self-assessment tool where studies have found a diminished quality of oral health in Rheumatoid Arthritis (RA).[1]

Objectives: Compare the behavior of GOHAI survey in RA, Systemic lupus erythematosus (SLE), and controls in a Rheumatology center at Northeast Mexico.

Methods: We performed a descriptive study of patients with RA and LES who answered the Spanish version of GOHAI survey. A control group was also included.

GOHAI survey consists of 12 Questions with Likert answers evaluating problems related to periodontal disease in the last 3 months.

Questions 1-4 evaluate physical function, 6, 7, 9-11 psychosocial status and 5, 8 and 12 pain.

Results: Sixty RA patients, 32 SLE patients and 46 controls were included. Groups were adjusted by sex and age.

GOHAI survey presented a total mean of 23.4 in RA, 22.06 in SLE and 21.54 in controls with a maximum score of 60 points.

When analyzing the survey in physical function and psychosocial status a statistical significant difference was found when comparing RA group to controls.

Table 1. Comparison between GOHAI index scores in RA, SLE and control groups

	RA n= 60	SLE n= 32	Controls n=46			
	Median (SD)	Median (SD)	Median (SD)	RA vs SLE	RA and controls	Three groups
Age	51.27 (15.84)	37.03 (14.14)	41.07(11.25)	**0.17**		
Sex	58 (96.67%)	29 (90.62%)	42 (91.3 %)			
1. Limit the kinds of food consumed	1.87 (1.14)	1.78 (1.15)	1.78 (0.81)			
2. Trouble biting or chewing	1.96 (1.2)	1.91 (1.27)	1.78 (1)			
3. Able to swallow comfortably	2.2 (1)	1.81 (1.47)	1.41(1.15)			
4. Unable to speak clearly	1.63 (1)	1.13 (0.42)	1.24(0.57)			
5. Able to eat without discomfort	1.9 (1.17)	1.59 (0.98)	1.76 (0.79)			
6. Limit contact with people	1.45 (0.9)	1.34 (0.75)	1.3 (0.73)			
7. Pleased with appearance of teeth	2.85 (1.65)	3.2 (1.79)	2.22(1.25)			
8. Use medication to relieve pain	1.83 (1.08)	1.94 (1.13)	1.87 (0.88)			

Table 1. Comparison between GOHAI index scores in RA, SLE and control groups

	RA n= 60	SLE n= 32	Controls n=46			
	Median (SD)	Median (SD)	Median (SD)	RA vs SLE	RA and controls	Three groups
9. Worried about teeth, gum or dentures	2.56 (1.39)	2.06 (1.54)	2.54(1.15)			
10. Self-conscious about teeth, gum or dentures	1.66 (0.94)	1.59 (1.02)	2.02 (1.06)			
11. Uncomfortable eating in front of others	1.54 (0.82)	1.53 (0.8)	1.39(0.8)			
12. Sensitive to hot,cold or sweet food	2.07 (1.06)	2.19 (1.31)	2.22(0.94)			
Total score (12-60)	23.4 (6.94)	22.06 (7.05)	21.54 (5.6)	**0.27**	**0.12**	**0.19**
Physical function	7.6 (3.32)	6.63 (2.6)	6.22 (2.26)	**0.15**	**0.06**	**0.05**
Psychosocial function	10.07(3.23)	9.72 (3.74)	9.48 (3.5)	**0.35**	**0.003**	**0.02**
Pain discomfort	5.78 (2.19)	5.72 (2.48)	5.85 (1.48)	**0.69**	**0.15**	**0.1**

RA: Rheumatoid Arthritis, SLE: Systemic Lupus Erythematosus

Conclusion: RA patients presented an increased alteration in oral health perspective when compared to SLE and controls. This association demonstrates the relationship between RA and periodontitis pathogenesis.
Importance in diagnosing periodontal disorders in rheumatic diseases should be performed due to its influence in quality of life and perpetuation of an inflammatory state and oral symptoms.

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AB1328-HPR INCREASED BODY MASS INDEX AFFECTS SPINAL MOBILITY RATHER THAN DISEASE ACTIVITY IN ANKYLOSING SPONDYLITIS

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Background: Studies have reported the association between overweight or obesity and ankylosing spondylitis (AS), but their relation is still unclear in China.
Objectives: To explore the prevalence of overweight or obesity and its effect on other indicators and their relationships in Chinese AS patients.
Methods: Demographic and clinical variables were collected from 207 AS patients. Patients were categorized to normal BMI group (BMI < 23kg/m^2) and overweight group (BMI ≥ 23kg/m^2). We used Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Metrology Index (BASMI), Health Assessment Questionnaire (HAQ), Ankylosing Spondylitis Quality of Life (ASQoL) and Medical Outcomes Study Short Form 36 (SF-36) to evaluate disease activity, physical function, spinal mobility, functional limitation and health-related quality of life, respectively. Statistical analysis used independent t test, Mann-Whitney U test, Chi-square test and Spearman's rank correlation test.
Results: 56.5% (117) AS patients were overweight or obese, among which 80.3% (94) were male. In the overweight group, patients were older, more being married, and have higher BMI, higher waist circumference, higher waist-to-hip ratio, longer disease duration, higher BASMI score, higher white blood cell count (WBC), higher lymphocyte and higher platelet count compared to the non-overweight group ($P \leq 0.038$). However, there was no distinct difference in BASDAI score between the two groups ($P = 0.891$). In the correlation analyses, gender and marital status ($P \leq 0.036$) were correlated negatively with BMI; while age, waist circumference, waist-to-hip ratio, WBC, lymphocyte count and red blood cell ($P \leq 0.036$) were correlated positively with BMI.
Conclusion: Overweight or obesity is common in Chinese AS patients. Increased BMI affects not disease activity but spinal mobility, which indicates that patients with high BMI are more likely to have limitations in flexion, extension, lateral bending and torsion of spine.

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AB1329-HPR THE CURRENT STATUS AND ASSOCIATED FACTORS OF FATIGUE IN CHINESE PATIENTS WITH GOUT

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Background: Fatigue of chronic diseases has been paid more and more attention. but the status of fatigue in gout patients has not been reported all the world[1].
Objectives: In the absence of previous studies, our study aims to investigate the fatigue status, explore the potential predictors of fatigue and the effects of fatigue on health-related quality of life (HRQoL) among Chinese gout patients.
Methods: This cross-sectional study was conducted from the Affiliated Hospital of Nantong University. A series of questionnaires were applied: Fatigue Scale-14 (FS-14), the 10 cm visual analog scale (VAS), the Patient Health Questionnaire (PHQ-9), the Generalized Anxiety Disorder questionnaire (GAD-7), the Pittsburgh Sleep Quality Index (PSQI), Health Assessment Questionnaire(HAQ), the Short Form 36 health survey (SF-36). Laboratory examinations were taken to obtain some biochemical indicators. Independent samples t-test, Mann–Whitney U-test, Chi-square analysis, Pearson /Spearman correlation, Stepwise linear regression and binary logistic regression were used to analyze the data.
Results: 411 gout patients were included in this study. Among them, more than 50% patients reported physical fatigue in FS-14, severe disease, poor psychological status and reduced HRQoL were associated with fatigue. Multiple stepwise linear regression and binary logistic regression were applied and showed that pain, sleep quality, anxiety, depression and functional disorder were the potential predictors of fatigue. In addition, we found that the more severe the fatigue, the lower the patient's HRQoL.
Conclusion: Fatigue among gout patients is exceedingly common. The results of this study suggested that rheumatologists should pay closely attention to gout patients who suffer from serious fatigue, especially those with pain, poorer sleep quality, anxiety, depression and functional disorder.

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AB1330-HPR ASSOCIATION OF INTERSTITIAL LUNG DISEASE AND QUALITY OF LIFE IN CHINESE RHEUMATOID ARTHRITIS

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Background: The health-related quality of life (HRQL) of patients with rheumatoid arthritis associated interstitial lung disease (RA-ILD) is less concerned(1). This study hypothesized that HRQL of such patients decreased.
Objectives: The aim of this study was to assess the difference in HRQL between RA with and without ILD, and to predict risk factors of HRQL in Chinese RA-ILD.
Methods: A cross-sectional survey of RA-ILD patients included socio-demographic characteristics, clinical variables, psychological factors and HRQL. Data were analyzed by Student's t or chi-square test. Linear regression analysis was used to investigate the predictors of HRQL in RA-ILD.
Results: The data showed that 35.17% (51/145) of RA patients had ILD. There are significant differences in age, sex, smoking history, disease duration and activity between RA with and without ILD. HRQL of RA-ILD was impaired. Physical component score (PCS) of patients with RA-ILD was also worse than that of RA without ILD (48.91±2.48 vs. 50.80±2.55). Linear regression analysis showed that DAS28 and fatigue were risk factors for PCS in patients with RA-ILD, while depression and rural residence were risk factors for mental components summary in Table 1.

Table 1. Stepwise multiple linear regression analysis of PCS and MCS in RA-ILD

Predictors	B	SE	t	*P*	95%CI
PCS					
DAS28	-0.777	0.227	-3.425	0.001	-1.236,-0.319
Fatigue	-0.655	0.206	-3.177	0.003	-1.071, -0.238
MCS					
Depression	2.188	0.669	3.272	0.002	0.836, 3.539
Rural residents	-1.609	0.756	-2.128	0.040	-3.137,-0.081

Footnotes: CI=Confidence interval. PCS=Physical component score; MCS=Mental component score; DAS28=28-joint disease activity score.

Conclusion: Compared with RA without ILD, HRQL of patients with RA-ILD was significantly impaired. Disease activity, fatigue, depression and rural residence were independent predictors of HRQL in Chinese RA-ILD.

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AB1331-HPR ACTIVE DISEASE ACTIVITY IN ANKYLOSIS SPONDYLITIS: WORSE OUTCOMES AND POORER HR-QOL

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Background: Ankylosing spondylitis (AS) is a chronic inflammatory disease that mainly affects the sacroiliac joints and the spine, resulting in decline in quality of life[1,2]. Poor QoL is significantly related to high disease activity[3]. However, there is no systematic report on which prognosis indicators are affected by disease activity in AS patients.

Objectives: This study aimed to evaluate the patient-reported outcome measures and health-related quality of life (HR-QoL) in AS patients defined on the basis of the Bath Spondylitis Ankylosing Disease Activity Index (BASDAI).

Methods: 204 AS patients were involved in this study. A serious of questionnaires were used to overall assess AS patients, which include: Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Metrology Index (BASMI), Bath Ankylosing Spondylitis Functional Index (BASFI), the 10 cm Visual Analog Scale (VAS), the Self-Rating Anxiety Scale (SAS), the Self-Rating Depression Scale (SDS), the Pittsburgh Sleep Quality Index (PSQI), the Health Assessment Questionnaire-Disability Index (HAQ-DI), the Fatigue Severity Scale(FSS) and the Short Form 36 Health Survey (SF-36). Independent samples t-test, Mann–Whitney U-test, Chi-square analysis and Pearson /Spearman correlation were used to analyze the data.

Results: The results demonstrated 31.4% AS patients were in active disease activity stage. Active AS patients were older, unemployed, and had less exercise therapy than stable AS patients. Besides, AS patients with active disease activity presented more severe pain(P<0.001), poor physical function(P<0.001) and spinal mobility(P<0.001). They were more anxious(P<0.001), depressed(P<0.001) and had more sleep disturbance(P=0.001). Compared with active AS patients, stable AS patients had more leukocytes(P=0.040), lymphocytes(P=0.002), erythrocytes(P=0.001) and hemoglobin(P<0.001). Active disease activity had a significant impact on all dimensions of quality of life in AS patients(P<0.001).

Conclusion: These findings suggested that medical personnel should pay more attention to active AS patients and make effective interventions to improve quality of life.

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AB1332-HPR ASSESSING THE PATIENT EXPERIENCE OF LUPUS NEPHRITIS: DEVELOPMENT OF A CONCEPTUAL MODEL AND REVIEW OF EXISTING PATIENT-REPORTED OUTCOME (PRO) MEASURES

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Background: Lupus nephritis (LN) is an autoimmune disease characterized by inflammation of the kidneys as a result of systemic lupus erythematosus (SLE). Approximately 50% of SLE patients will develop LN, which is considered to be one of the most severe manifestations of SLE and the leading cause of morbidity and mortality in SLE. While there is ample existing evidence on disease experience and PROs used in extra-renal SLE, little research has been done in LN. Qualitative interviews with patients can help identify concepts that are both important and relevant to the patient. In order to effectively evaluate treatment benefit, it is critical that PRO measures used to assess such concepts and define clinical trial endpoints are fit for purpose and have strong evidence of content validity in the specific context of use.

Objectives: The objective of this study was to understand the patient experience of LN and to identify and characterize the signs and symptoms of LN and their impact on health-related quality of life (HRQoL) through the development of a disease-specific conceptual model. This model was then used to evaluate the content validity of existing PRO measures available for use in LN.

Methods: A structured literature search was conducted in Medline, Embase and PsycINFO to identify qualitative research articles documenting the patient experience of LN. PRO measures developed or commonly used to assess patient experiences of LN were also identified. Semi-structured concept elicitation interviews were conducted with 15 adult patients in the US with a clinician-confirmed diagnosis of LN (defined in accordance with established clinical guidelines). Supplementary qualitative data were also collected from a review of publicly available online blogs/forums. Findings were used to inform the development of a conceptual model detailing the impact of LN signs, symptoms and HRQoL and evaluate the validity of existing measures used within LN.

Results: Searches revealed a paucity of qualitative research conducted with LN patients, supporting the need for prospective research in LN. Consistent with existing literature in SLE, the core signs and symptoms identified from the qualitative literature review, interviews and blog/forum review included joint pain, fatigue, joint stiffness, swelling (particularly in the extremities) and skin rashes. LN patients also reported urinary frequency, urgency, foamy urine and blood in their urine. Disease impact on physical functioning, activities of daily living, emotions, social life, work/finances and sleep were reported. PRO measures commonly used to evaluate patient experiences in LN included the SF-36, LupusQOL, LupusPRO, SLE Symptom Checklist, KDQoL and KSQ. Conceptual mapping of instruments against the newly developed conceptual model (Figure 1) highlighted that no single measure provides a comprehensive assessment of all symptoms/impact important to LN patients. Furthermore, items are largely focused on impact of symptoms with few items on symptom severity.

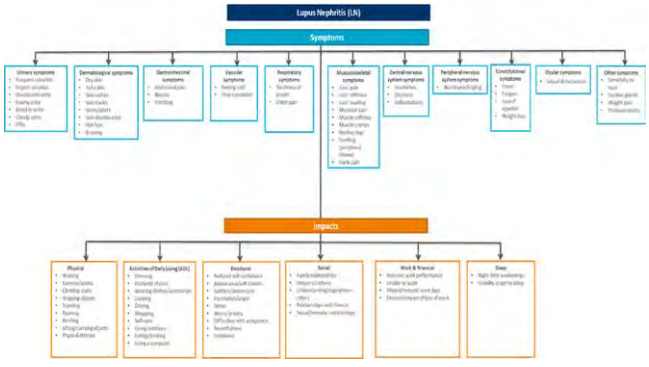


Figure 1. Conceptual model of lupus nephritis symptoms and associated impacts

Conclusion: The presentation of signs and symptoms in LN patients appears similar to those reported in extra-renal SLE populations, with the addition of swelling and urinary symptoms. Qualitative research with LN patients guided the development of a comprehensive LN conceptual model outlining the disease experience from the patients' perspective. These insights can be useful to inform PRO measurement strategies for clinical trials in LN.

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commissioned by Janssen to conduct the research reported in this abstract, Chloe Tolley Consultant of: Adelphi Values a health outcomes research company commissioned by Janssen to conduct the research reported in this abstract, Patricia Delong Employee of: Janssen, Elizabeth C Hsia Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC

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AB1333-HPR FIBROMYALGIA SYNDROME IN MEDICAL STUDENTS

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Background: At the university, students begin to be responsible for their own life decisions and lifestyles. First year students are required to adapt especially to a new learning environment and to cope with the academic and social demands of vocational education. High academic expectations are stressful and can pose a risk to students mental and physical health. Anxiety and depression are among the most common psychiatric problems among students.

Objectives: The aim of this study is to evaluate the prevalence of fibromyalgia syndrome (FMS) in medical students and to compare students from engineering faculty.

Methods: 392 (284 faculty of medicine, 108 faculty of engineering) students selected from Fırat University Faculty of Medicine and Engineering were included in the study. Hospital Anxiety and Depression Scale (HADS) forms were filled in for all participants. Anxiety and depression among students of medical and engineering were examined. Moreover, 2016 ACR FMS classification criteria was used to select the student who have FMS.

Results: In our sample, 185 (47.1%) and 207 (52.9%) of participants were male and female, respectively. HADS anxiety and HADS depression scores were significantly higher in engineering students than in medical students (mean HADS anxiety and depression scores were 9.07; 10.29, p= 0.007 and 7.61; 8.52, p= 0.039, respectively). While a significant difference was found among medical and engineering students in terms of HADS anxiety and depression scores in men ($p<0.001$ and p= 0.006), no significant difference was found in women (p= 0.676 and p= 0.278). On the other hand, 46 (16.1%) of medical students and 13 (11.7%) of students from engineering faculty have FMS (p=0.170).

Conclusion: FMS prevalences are similar in the medical students and students from engineering faculty. However, anxiety and depression are more common among male engineering students than medical students. This may be related to future employment anxiety among students from engineering faculty.

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AB1334-HPR BARRIERS AND FACILITATORS TO PHYSICAL ACTIVITY IN JUVENILE IDIOPATHIC ARTHRITIS (JIA): A SCOPING REVIEW

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Background: Physical activity is an important aspect in the management of JIA (1). However physical activity levels are low in this population (2). Limited research has been conducted to identify definitive barriers and facilitators to physical activity in children and adolescents who have JIA.

Objectives: The objective of this scoping review was to identify the common barriers and facilitators to physical activity in JIA.

Methods: Original studies, either quantitative or qualitative, including participants with a diagnosis of JIA, who were under 18 years of age were included. Two independent reviewers carried out a search of the literature and full text reviews of papers to determine eligibility for inclusion. The Critical Skills Appraisal Programme (CASP), Appraisal tool for Cross-Sectional Studies (AXIS) and Downs and Black critical appraisal tools were used to assess the quality of the included research articles.

Results: Eighteen studies were included in the review. The included studies were of a variety of low, moderate and high quality. The synthesis of the data identified pain to be the most common barrier and the modification of physical activities to the need of the individual to be the most common facilitator to physical activity in JIA.

Conclusion: Identifying the most common barriers and facilitators to physical activity allows clinicians to apply better management strategies when treating an individual with JIA. Our findings demonstrate the need for further research in this area to assist increasing physical activity participation for children and adolescents who have JIA.

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AB1335-HPR HEALTH PROFESSIONALS' PERSPECTIVE ON THE BENEFITS AND RISKS OF LOW-DOSE GLUCOCORTICOIDS IN RHEUMATOID ARTHRITIS – AN INTERNATIONAL SURVEY OF 444 HEALTH PROFESSIONALS

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Background: The Glucocorticoid Low-dose Outcome in Rheumatoid Arthritis Study (GLORIA) is an international investigator-initiated pragmatic randomized trial designed to study the effects of low-dose glucocorticoids (GCs) in elderly patients with Rheumatoid Arthritis (RA).

The research team is also committed to promote a better understanding of the risks and benefits of these drugs among health professionals and patients. In order to achieve these goals, it is important to assess the current ideas and concerns of patients regarding GCs.

Objectives: To evaluate the current patient perspective on the efficacy and risks of GCs in RA patients who are or have been treated with GCs.

Methods: Patients with RA completed an online survey (with 5 closed questions regarding efficacy and safety) presented in their native language. RA patients were recruited through a variety of patient organizations representing three continents. Patients were invited to participate through national patient organizations. In the USA, patients were also invited to participate through MediGuard.org. Participants were asked for their level of agreement on a 5-point Likert scale.

Results: 1344 RA patients with exposure to GCs, from Brazil, USA, UK, Portugal, Netherlands, Germany and 24 other countries** participated: 89% female, mean age (SD) 52 (14) years and mean disease duration 13 (11) years. The majority of participants (84%) had ≥10 years of education. The duration of GCs exposure was 1.6 (4.2) years. The majority of participants had read articles or pamphlets on the benefits or harms of GC therapy.

Regarding GCs efficacy (table 1), high levels of endorsement were found: about 2/3 of patients considered that GCs as very useful in their case, more than half considered that GCs were effective even at low doses, and agreed that GC improved RA symptoms within days.

Regarding safety (table 1), 1/3 of the participants reported having suffered some form of serious adverse events (AEs) due to GCs, and 9% perceived this as "life-threatening. Adverse events had a serious impact on quality of life, according to about 1/3 of the respondents.

Conclusion: Patients with RA exposed to GC report a strong conviction that GCs are very useful and effective for the treatment of their RA, even at low doses. This is accompanied by an important prevalence of serious AEs. Understanding the patient perspective can improve shared decision-making between patient and rheumatologist.

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Table 1 – Results of the surveys, across different countries, concerning patient perspective on the efficacy and risks of glucocorticoids in patients with RA.

	All	Brazil	USA	UK	Portugal	Germany	NL	Others***
GCs are or have been very useful to me								
Agree	56	64	56	62	42	51	68	54
Slightly agree	20	20	21	11	12	30	10	18
Neutral	6	4	8	7	5	6	6	10
Slightly disagree	3	4	5	1	4	0	3	3
Disagree	4	3	7	3	1	4	3	3
Missings	9	6	1	15	25	9	9	12
At a GC dose ≤7.5mg/day:								
- Are very effective in the control of signs and symptoms of RA								
Agree	41	48	42	40	31	28	48	38
Slightly agree	25	25	15	20	26	45	20	12
Neutral	12	11	24	8	12	12	16	12
Slightly disagree	5	7	6	6	4	0	4	4
Disagree	5	4	7	6	1	6	5	7
Missings	12	6	3	19	25	9	9	15
- Improve RA symptoms within days								
Agree	41	45	44	37	34	37	44	39
Slightly agree	23	23	19	19	20	33	23	24
Neutral	12	12	18	8	13	8	12	9
Slightly disagree	6	6	7	7	7	0	8	7
Disagree	8	8	89	10	1	3	5	7
Missings	11	6	3	19	25	9	9	15
I have suffered very SAEs due to GCs								
Agree	29	40	44	13	15	18	18	29
Slightly agree	3	0	0	0	0	0	32	18
Neutral	14	15	12	15	17	4	7	11
Slightly disagree	1	0	0	0	0	0	7	2
Disagree	44	40	43	56	43	58	27	41
Missings	9	6	1	15	25	9	9	12
N (% of total)*	**432 (100)**		**104 (24)**	**211 (49)**				**117 (27)**
How serious do you consider these SAEs								
Life threatening	9	NA	55	32	NA	NA	NA	13
Serious impact in my QoL	36	NA	39	38	NA	NA	NA	23
Minor impact in my QoL	27	NA	28	52	NA	NA	NA	17
Mild and well tolerated	29	NA	18	50	NA	NA	NA	32

Numbers indicate %.
***Others (% of total): Italia 1.9%; Spain 1.7%; Romania and Canada, each one 1.4%; Belgium 0.6%; France, Australia and Venezuela, each one with 0.2%; Algeria, Angola, Argentina, Belize, Cyprus, India, Ireland, Japan, Mauritius, Mexico, Mozambique, Moldova, Nicaragua, Norway, Sweden and Switzerland each one with 0.1%.
*The Portuguese, Germany and Deutschland version as well as the English survey through MediGuard.org, didn't have this question due to legal constraints (% of answers per frequency category).

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AB1336-HPR NON-PHARMACOLOGIC TOPICS RELEVANT FOR CLINICAL RESEARCH IN RHEUMATIC DISEASES: THE PATIENT PERSPECTIVE

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Background: The research approach on Rheumatic diseases (RDs) is challenging and patient involvement as partners in medical research is an emerging force to obtain relevant information and to add unique skills, values and experiences to research. Despite growing interest in non-pharmacologic aspects of clinical research in RDs, the patients' perspective is currently poorly explored.
Objectives: To identify and rank the priorities for clinical research according to patients' perspective.
Methods: A structured face-to-face meeting between physicians and a patient representative was convened to list the non-pharmacologic topics relevant to RD patients. A cross-sectional no-profit on-line anonymous survey was devised to evaluate opinions of RD patients. They were asked to rate the following topics: food/nutrition, air pollution, smoking, work activity, social participation, physical activity, emotional well-being/stress, alternative medicine, and patient-physician relationship. Moreover, patients were asked to explain for which reason a topic was considered important (disease prevention, halting disease progression, symptoms control and disease cure). The survey was disseminated by ALOMAR (Lombard Association for Rheumatic Diseases) between June and October 2019.
Results: 200 rheumatic patients completed the survey: 130 inflammatory arthritis, 50 connective tissue diseases/vasculitis, and 20 among osteoarthritis, gout, condrocalcinosis, polymyalgia and primary fibromyalgia. Respondents were 178 female with median age of 50 years and median disease duration of 7 years. Among the nine topics identified, the one most rated by patients was the doctor-patient relationship; 188 (94%) of respondents considered this topic very or extremely important (see table below). In descending order, patients rated very or extremely important: psychological well-being/stress 185 (92.5%), physical activity 155 (77.5%), nutrition, eating habits and alcohol 150 (75%), alternative therapies 144 (72%), work activity 144 (72%), environmental pollution 134 (67%), social life 121 (60.5%) and cigarette smoke 119 (59.5%). The topics considered relevant was perceived to be able to influence disease symptoms. Regarding RD prevention, environmental pollution and cigarette smoking were considered the most important topics, while fewer patients believed that research on other topics could help to stop disease progression or to achieve disease healing.

Ranking	Topic	Not or quite important	Very or extremely important
1	Doctor-patient relationship, n (%)	12 (6.0)	188 (94.0)
2	Psychological well-being/stress, n (%)	15 (7.5)	185 (92.5)
3	Physical activity, n (%)	45 (22.5)	155 (77.5)
4	Nutrition/eating habits/alcohol, n (%)	50 (25.0)	150 (75.0)
5	Alternative therapies, n (%)	56 (28.0)	144 (72.0)
6	Work activity, n (%)	56 (28.0)	144 (72.0)
7	Environmental pollution, n (%)	66 (33.0)	134 (67.0)
8	Social life, n (%)	79 (39.5)	121 (60.5)
9	Cigarette smoke, n (%)	81 (40.5)	119 (59.5)

Conclusion: This survey highlights the relevance of several unmet needs. The holistic approach, in terms of medical consultation and psychological well-being, is considered the most important component able to influence disease perception. By capturing patient opinions on non-pharmacological topics for clinical research, this survey indicates that the active patient involvement is essential to design successful translational studies and improve clinical outcomes.
Acknowledgments: We thank the Lombard Association of Rheumatic Diseases (ALOMAR) for its contribution to plan and disseminate the survey and the group that sustain systemic sclerosis (GILS).
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AB1337-HPR PATIENTS' EXPERIENCE OF INVOLVEMENT IN A RHEUMATOLOGY OUTPATIENT CLINIC

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Background: Involvement in own treatment and care is a wish from patients and a vision from politicians in Denmark. (1,2) In outpatient rheumatology patient involvement also leads to increased patient satisfaction, better quality of treatment and better utilization of resources in health care. (3,4,5) On the basis of this we ought to involve our patients at our Outpatient Clinic in Svendborg, but are we?
Objectives: To gain knowledge about how patients with rheumatoid arthritis experience involvement in treatment and care in the Rheumatology Outpatient Clinic, Svendborg.
Methods: An interview study of six patients with subsequent analysis based on Ricoeur. (6) Patient inclusion: patients with rheumatoid arthritis in remission by DAS28 for more than 2 years. The participants elected were 3 males and 3 female at the age of 30 – 78 visiting the clinic during Marts and April 2019. They were asked about their experience of involvement from time of diagnosis until present time.
Results: The study provided knowledge that patient involvement was new to the participants. This is also found in other literature about patient involvement. (7,8) All participants in this study felt involved in own care and treatment. The involvement was based on being seen and heard as persons with individual needs and not just as patients with arthritis. The way the participants experienced involvement showed that there are individual differences in how to provide the experience. In order to clarify what involvement meant for each patient, relationship with the health professional was necessary, as other studies also shows. (7,8) The relationship was conditioned by continuity, trust, care and mutual respect. For all the participants informed consent was equal to involvement. Disease activity or fear of this was the main reason for feeling involved this way. Literature describes the same: amongst other factors, the severity of the disease is significant for the patients desire to be involved. (7,8)
Conclusion: The participants experienced involvement in own care and treatment. The relation to the health professional was important providing this experience. All defined involvement as informed consent as it also is to many healthcare professionals. (9) All participants needed time to reflect on what

involvement meant as none of them had heard of it before. Patient involvement needs education of both patients and healthcare professionals to be taken further than informed consent.

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AB1338-HPR GLOBAL PATIENT PERSPECTIVE ON TOP CHALLENGES IN LUPUS CARE AND RESEARCH PARTICIPATION

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Background: The Addressing Lupus Pillars for Health Advancement (ALPHA) Project is a global consensus initiative to identify, prioritize and address top barriers in lupus drug development, clinical care and access to care. The Lupus Foundation of America convenes ALPHA with Tufts Center for the Study of Drug Development and a Global Advisory Committee of lupus experts representing clinician-scientists, industry and patients.

Objectives: Collect global patient input to determine alignment with the lupus clinician-scientist community on prior published consensus of top lupus barriers.

Methods: A 23-question online Qualtrics survey was developed to identify challenges across lupus diagnosis, clinical care and research participation. The survey, available in English, Spanish, Korean and simplified Chinese, was fielded in November 2019 to people with lupus and caregivers of children <18 with lupus. SPSS 26 and SAS 9.4 were used for descriptive statistics and sub-analysis.

Results: Analysis included only consented responses with ≥ 68% survey completion (n=3,447) received across 83 countries. 95% were female with a mean age of 45. Respondents reported being White (57%), Black or of African descent (14%), Hispanic or Latino (18%) and Asian (10%). 65% resided in the US while 35% resided in countries outside of the US. 97% were people with lupus while 3% were caregivers to children <18 with lupus.

Highest ranked challenges were similar globally and across children and adults: medication side effects, lack of treatment options and high out-of-pocket costs. Managing side effects ranked significantly higher ($p<.05$) outside of the US (48%) compared to US (40%). 50% of caregivers reported managing side effects as the top challenge for children compared to 43% of adults ($p<.05$). Research participation was low (24%) and lower among children (16%). The top reason for not participating in a clinical trial was not being asked by their doctor.

Conclusion: This global survey revealed that medication side effects and lack of effective treatments are top challenges for people with lupus, including children. Most respondents were never asked by their doctors to participate in a clinical trial, which may explain difficulties in trial recruitment. These barriers are consistent with prior published barriers identified by the clinician-scientist community.

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AB1339-HPR SAFETY AND ADHERENCE OF THE JAK INHIBITORS IN CLINICAL PRACTICE IN RHEUMATOID ARTHRITIS

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Background: The Janus Kinase (JAKi) inhibitors Baricitinib (BAR) and Tofacitinib (TOF) are indicated for moderate to severe active rheumatoid arthritis (RA). Data about safety, effectiveness in refractory patients and adherence in real clinical practice in our population are scarce.

Objectives: An evaluation of safety, adherence and reasons to consider suspension of JAKi in routine clinical practice.

Methods: Retrospective observational study of patients with RA treated with BAR and TOF according to usual clinical practice between September 2017 - December 2019. Data were collected from the electronic medical record and from the Dominion® Outpatient Drug Dispensing program.

Demographic, clinical, laboratory and treatment-related variables were collected, including reasons for discontinuing JAKi (inefficiency and toxicity). Adherence was calculated using the Compliance Questionnaire on Rheumatology (CQR-5), and the average possession ratio (RMP), which is defined as the number of days with treatment dispensed between the total days of the period analyzed, considering the adherent patient when RMP had a ≥ 0.8.

Laboratory abnormalities were defined according to normal limit values (NLV) and specifications of data sheet. A descriptive analysis was performed using proportions, medians and interquartile ranges (IQR) using the SPSS v.15 program.

Results: Thirty patients were included in treatment with BAR and nine with TOF. The median age was 62.9 (RIQ 49.9-74.4), 34 (87.2%) were women, 28 (71.2%) anti-CCP and 32 (82.1%) were rheumatoid factor positive, with erosive disease in 34 (87,2%) patients. In the previous treatment, 9 (23.1%) were naive to biological, 6 (15.4%) had received 1 biological, 18 (46.1%) 2 biologicals, and 6 (15.4%) ≥ 3 biologicals. The median treatment time was 8.4 months (RIQ 6.5-20.3) in BAR and 13.2 (RIQ 3.9-20.7) in TOF.

The reasons for consider suspension shown in Table 1.

Table 1. Treatment Discontinuation

	Initial DAS28 [median (IQR)]	Final DAS28 [median (IQR)]
BARICITINIB		
Continue treatment n (%): 17/30 (55.6)	4.20 (2.95-5.72)	2.60 (1.70-2.77)
Reasons for suspension		
-Refractory n (%): 7/13 (55.8%)	4.38 (4.16-5.43)	4,16 (3.56-5.23)
-Side effects n (%): 4/13 (30.7)	4.16 (3.45-4.84)	3.15 (2.69-4.41)
◦Thrombocytosis (1)		
◦Herpes Zoster (1)		
◦Anemia (1)		
◦Tubaritis (1)		
-Patient decisión n (%): 2/13 (15.4)		
TOFACITINIB		
Continue treatment n (%): 6/9 (66.6)	4.82 (3.28-6.20)	2.61 (2.45-3.70)
Reasons for suspension		
-Refractory n (%): 2/3 (66.6)	5.27 (5.23-5.31)	5.48 (5.04-5.92)
-Side effects n (%): 1/3 (33.33)		

Based on the CQR5 questionnaire, all patients treated with BAR and TOF were adherent "HIGH" class, and a median of RMP = 1.01 (IQR = 0.93-1.06) was obtained for BAR and RMP = 1, 00 (IQR = 0.91-1.01) for TOF, all adherents (≥ 0.8).

Table 2. Safety results of the treatment shows the safety results.

Side Effect	Baricitinib (n, %)	Tofacitinib (n, %)
Hb <11 g/dl	7 (23,3)	0
Hb < 8 g/dl	0 (0)	/
Hb Recovery >11 g/dl	2/7 (28,6)	/
Neutrophils < 1500/mm^3	0 (0)	/
Lymphocytes < 1000/mm^3	3 (10,0)	2 (22,2)
Platelets > 600 × 10^3/mm^3	1 (3,3)	0
AST o ALT > 1 NLV	4 (13.3)	0 (0)
Hypercholesterolemia (> 1 NLV)	13 (43.3)	5 (55.5)
Infections	13 (43.3)	0 (0)
Herpes zoster	6 (20,0)	0 (0)

Conclusion: In our population, mostly refractory to biological, more than half of the patients maintain treatment with JAKi, with optimal adherence. The main reason for the suspension of both drugs was inefficiency. The most frequent adverse effects were hypercholesterolemia in both groups and infections in BAR, with a high frequency of herpes zoster. No cardiovascular or thromboembolic events were observed.

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HPR Service developments, innovation and economics in healthcare

AB1340-HPR PATIENTS' OUT-OF-POCKET EXPENSES ANALYSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS ENROLLED IN A EDUCATIONAL PROGRAM

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Background: The increasing health and economic burdens of deaths and disabilities from non-communicable diseases (NCDs) are emerging as major concerns worldwide, particularly for low- and middle-income countries (LMICs) (1). Rheumatoid arthritis (RA) NCD is considered as one of the most common causes of disability. RA affects from 0.5% to 1% of the worldwide population. Little is known about the out-of-pocket (OOP) expenditures for prescription of pharmacological treatment for patients with RA, including drugs, diagnostic tests, mobility aids among others.

Objectives: To describe the out of pocket costs in patients with rheumatoid arthritis

Methods: We performed a cross-sectional study among patients who are participating in an educational program in a specialized center for RA. We collected sociodemographic variables; in addition, we collected data related to the expenditures in drugs, diagnostic tests and mobility aids that were not covered by the health system. Descriptive epidemiology was done, we calculated means, and standard deviations for continuous variables and categorical variables were presented as rates. The costs are presented in the US dollars with the average exchange rate for 2019

Results: We included 181 patients, 92% were female. Mean age was 59 years ±9.5. Regarding occupation, 24% were employees, 40% were economically inactive, and 36% were pensioners. Most of patients 45% had a low income, 43 % middle income and only 12% high income according to the Colombian socioeconomic classification. Most of out of pocket expenses (47%) were associated to the acquisition of medical devices such as reading glasses or orthopedic braces. Secondly, the OOP expenses were related to medications (38%) such as antibiotics prednisone or pain control medications. Finally, 25% of patients reported that they had pay for their diagnostic tests such as x rays or laboratory tests. When assessed the costs patients expended between 30-100 USD purchasing aid devices, medications or laboratory tests.

Conclusion: In the Colombian context OPP are relevant and represent an important expenditure for patients with RA especially for those who have low or middle income. Due to the above, it is important to find alternatives in order to help vulnerable segments of the population. Additionally, OPP needed to be taken into account due to its association with treatment adherence(2).

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AB1341-HPR FEASIBILITY OF THE BACK AND FORTH SCHOOL BOOKLET, A SHARED SELF MANAGEMENT INSTRUMENT FOR YOUNG CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA) AT SCHOOL

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Background: Young children with JIA have to cope with pain and fatigue during schooldays, facing problems with writing, climbing stairs, physical education and playing outside.[1] They need to develop age-appropriate self management skills, encouraged by their parents and teachers in a therapeutic alliance with the health professional team.[2] For this purpose a shared management tool, called the "Back and Forth Schoolbooklet"(B&FS), is developed, containing 1) Educational pages about JIA, pain and fatigue management 2) Diary pages with a colour-in puppet for expressing location and amount of pain, spaces for writing alternatives for limited activities, feedback spaces for parents and teachers and a self-evaluation scale of general well-being for the child. Children, parents and teachers are instructed how to use the booklet by therapists during outpatient rehabilitation. Structured evaluation of the use of the instrument is necessary to improve its applicability and effectiveness.

Objectives: To study the feasibility, defined as practical and experienced applicability and effectiveness, of the B&FS.

Methods: Pilot feasibility study with a mixed-method design. Parents, teachers, therapists and children with JIA were invited to fill in questionnaires after using the booklets in school. Adults had to sign informed consent. Practical applicability was assessed by multiple choice questions on duration and frequency of use. Used diary items and pages were counted in returned booklets. Experienced applicability and effectiveness were assessed by open-ended questions and 5 points Likert scales. Topics were experienced barriers, facilitators and benefits using the mentioned items of the booklets. Practical applicability was analysed descriptively. Atlas-ti8 was used for analysing and coding the answers on the open-ended questions using a thematic approach.

Results: Eight children(4-8 years) used the booklets. Six parents of six children, four therapists and four teachers signed informed consent and answered questionnaires. Six booklets were returned.

Practical applicability: Five children used booklets for a period of 2 to > 12 week, almost every day. One child stopped in the first week. Counting diary pages

confirmed every day or every second day appropriate use of the color-in puppet and spaces for parents and teachers. Experienced applicability: Identified themes were: child-friendly, easy and providing a clear guide for the daily school situation. Themes as: daily obligation, unwillingness of the child, lack of motivation or time of the parents or teachers and insufficient instruction illustrated experienced barriers for the use of the booklet. Effectiveness: Identified themes: 1) Children express themselves better about feelings of pain and fatigue, 2) Parents and teachers appreciate more insight into how the child feels and 3)Teachers feel provided with guidance in the interaction with the child 4) Children feel more secure to express itself at school and 4) Parents are more relaxed about the schoolsituation.

Likertscales showed that more than 75% of the users would advise the B&FS to other parents, teachers and therapists.

Conclusion: The Back & Forth School booklet is a feasible shared management instrument to support young children with JIA in the school situation. A less rigid daily routine and sufficient instruction can improve the experienced applicability.

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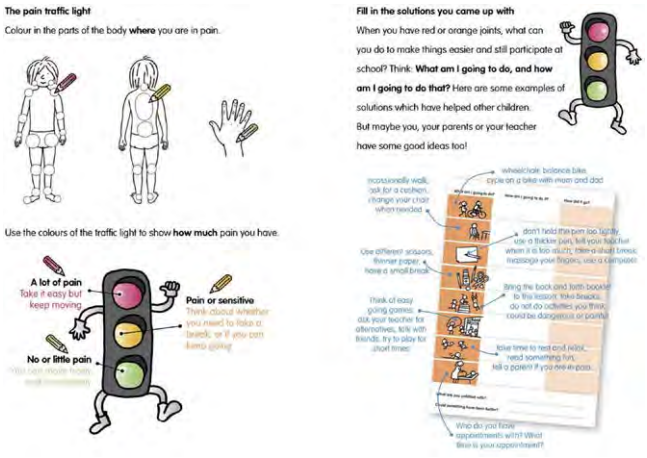


Figure 1 Educational page: Pain management

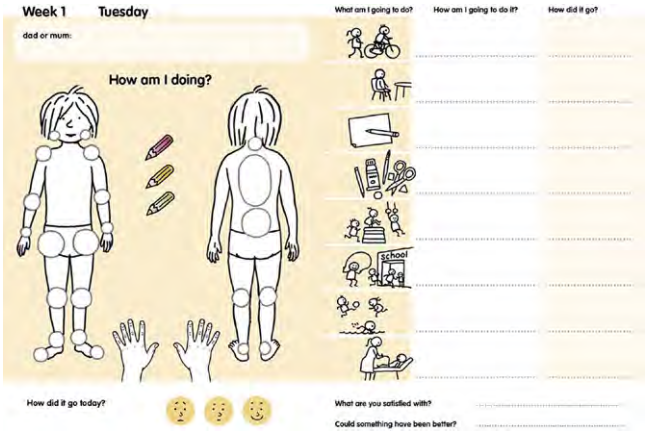


Figure 2 Diary page

Acknowledgments: Children, parents, teachers and therapists

Disclosure of Interests: None declared

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AB1342-HPR RHEUMATOLOGY 'HOT CLINIC' IN A TEACHING HOSPITAL - WHAT CAN BE EXPECTED?

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Background: Increased financial and bed pressures faced by the NHS have necessitated significant changes in the service provision of many inpatient medical specialties. At the Royal Derby Hospital, rheumatology has become predominantly outpatient-based and no longer has an allocated ward for inpatients. As a result, weekly rheumatology 'hot clinic' have been set up to help facilitate early hospital discharge and specialist outpatient review of patients with suspected rheumatological conditions. It was anticipated that the bulk of referrals would be for conditions requiring early intervention such as suspected giant cell arteritis (GCA) and hot swollen joints. However, there is a paucity of literature on the usefulness of such 'hot clinics' and the quality of referrals.

Objectives: This study sought to evaluate the range of conditions referred to the 'hot clinic' and early outcomes related to follow up or discharge.

Methods: The details of patients who attended the 'hot clinic' were retrospectively obtained using the hospital's electronic clinic appointments system. Electronic letters and discharge summaries were reviewed to determine the patient's presenting symptoms, suspected diagnosis and clinical outcome.

Results: A total of 40 patients who attended the 'hot clinic' from September 2018 to June 2019 were included. The average time from discharge to 'hot clinic' was 3.8 days (range 0-22 days). 27 patients (67.5%) were seen within 7 days of hospital discharge and 2 patients were seen after 18 and 22 days respectively, which spanned over the Christmas and New Year period.

87.5% (35) of patients were referred by acute medicine via the ambulatory care ward; 10% (4) by the Emergency Department and 1 by the medical ward. 5 patients were already known to rheumatology (3 with rheumatoid arthritis and 2 with psoriatic arthritis).

37.5% of referrals were made for suspected GCA, 35% for rash and possible connective tissue disease (CTD) or vasculitis except for GCA, 20% for swollen joints, and 7.5% for unexplained arthralgia or myalgia.

For the patients with suspected GCA, 3 out of 15 were treated as GCA after 'hot clinic' review - 2 of these went on to have a temporal artery biopsy and 1 had a positive biopsy for GCA. (All 3 received high dose steroids prior to their clinic appointment). 10 patients were felt to have an atypical headache and 3 of these were referred to neurology for further assessment. The remaining 2 patients were diagnosed with a sinus infection and migraine respectively.

Of the 14 patients referred with a rash and possible CTD or vasculitis except for GCA, 2 patients referred with a rash were diagnosed to have IgA vasculitis and referred to dermatology for further management. 2 patients were diagnosed with lupus and were followed up in the CTD clinic. 7 patients were felt to have a self-limiting post-viral or non-specific rash, 2 patients with possible drug-related rash and 1 patient thought to have erythema nodosum.

2 patients with swollen joints had a new diagnosis of seronegative inflammatory arthritis and 2 others were diagnosed with gout. 1 patient was diagnosed with osteoarthritis and another with post-viral arthritis and both were discharged.

The 3 patients with unexplained arthralgia or myalgia were felt to have self-limiting post-viral illnesses and were also discharged.

Conclusion: Suspected GCA is the most common referral to the rheumatology 'hot clinic'. However, the vast majority of these referrals turned out not to be GCA. The results of this study clearly suggest the need for development of better pathways e.g. for GCA and joint dermatology and rheumatology clinics.

Disclosure of Interests: None declared

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AB1343-HPR A QUALITATIVE REVIEW ASSESSING THEMATIC OUTCOMES FROM THE PHARMACY-LED ADALIMUMAB BIOSIMILAR SWITCH PLAN ACROSS 3 SPECIALITIES; RHEUMATOLOGY, GASTROENTEROLOGY AND DERMATOLOGY AT UNIVERSITY HOSPITALS OF COVENTRY AND WARWICKSHIRE (UHCW)

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Background: The advent of biosimilars has heralded a new era for cost effective biologic prescribing in the NHS. As patents expire for originator biologics, less expensive versions are now widely available as biosimilars. Non-medical switches (for reasons unrelated to a patient's health) ensure prescribing of best value medicines, and cost savings can be redirected to patient care.[1] This practice resonates with recommendations from Lord Carter's 2016 report regarding reducing unwarranted variation in the NHS and adopting cost saving opportunities.[2] In 2018/19, following loss of patent exclusivity for the expensive adalimumab originator biologic, UHCW worked in accordance with national directives to drive forward one of the largest non-medical biosimilar switches.

Objectives: This qualitative review aims to explore the success of the adalimumab biosimilar switch and key themes associated with switch backs/refusals across the Rheumatology (R), Gastroenterology (G) and Dermatology (D) specialities at UHCW.

Methods: The switch plan occurred between April-December 2019. 403 patients (R;189, G;176, D; 38) were eligible for switch. Patients were informed of the plan in advance via a patient information leaflet/hospital clinic visits. Switch refusals, withheld treatments and cancellations were documented and patients were advised to contact the hospital pharmacy/clinical teams if they encountered any concerns, adverse effects or lack of efficacy post switch. The clinician would then advise on subsequent management.

Results: During April-December 2019, 264/403 patients had been successfully switched (R;122, G;109, D;33). 33/403 patients switched back to the originator biologic (R;22, G;10; D;1). Of the 22 rheumatology switch back patients; 6 patients reported injection site pain and variably headache, fatigue, disease relapse, gastrointestinal (GI) upset, erythema; 10=reported lack of efficacy and variably influenza-type symptoms, relapse in associated psoriasis, difficulty in walking/sleeping, hair loss, excessive perspiration, facial cellulitis, foot drop and GI upset; 1=blepharitis;1=latex allergy before injection; 3=later declined switch; 1=damaged two devices and did not wish to continue biosimilar. Of the 10 gastroenterology switch back patients; 1=injection site pain; 2=lack of efficacy; 1=developed needle phobia; 1=latex allergy before injection; 1=switch detrimental to health; 2=unstable disease; 1=insomnia; 1=pregnancy. The 1 dermatology switch back patient reported injection site pain and bleeding.

38/403 patients refused the switch and remained on the originator biologic (R;11, G;27, D;0). 29/403 patients had treatment cancellations and were switched to an alternative biologic (R;17, G;9, D;3). 32/403 patients stopped treatment (R;13, G;19, D;0). Treatment was withheld for 7/403 patients (R;4, G;2, D;1).

Conclusion: The UHCW adalimumab biosimilar switch plan succeeded in switching a total of 66% of patients; thus an annual cost saving of £73,020. Injection site pain, most likely due to the biosimilar citrate content, and lack of efficacy according to patient perception and subsequent clinical review, were the most predominant causative themes for switch backs. Gastroenterology patients accounted for 71% (27/38) of the total switch refusals. Additional data regarding patient refusals, identifies future opportunities to improve patient counselling and drive further cost savings.

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AB1344-HPR POOLED ANALYSIS OF ASSOCIATION BETWEEN ABATACEPT OR OTHER TARGET DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS (TDMARD) AND TYPE 2 DIABETES MELLITUS (T2DM)-RELATED HEALTHCARE RESOURCE UTILIZATION (HCRU) AND COSTS IN TNFI-NAÏVE RHEUMATOID ARTHRITIS (RA) PATIENTS WITH T2DM

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Background: Limited information is available on the impact of target disease-modifying anti-rheumatic drugs (tDMARD) on patients with rheumatoid arthritis (RA) and type 2 diabetes mellitus (T2DM).

Objectives: The objective was to compare T2DM-related healthcare resource utilization (HCRU) and cost for TNF inhibitors (TNFi)-naive patients pooled from two commercial databases with RA and T2DM receiving abatacept, other non-TNFi, or TNFi.

Methods: A retrospective, observational study was conducted with MarketScan and PharMetrics (January 2008-September 2018). The study population included TNFi-naïve adult patients with RA and T2DM newly initiating abatacept, TNFi (adalimumab, certolizumab pegol, etanercept, golimumab, infliximab) or other non-TNFi (tocilizumab, anakinra, sarilumab, rituximab, tofacitinib). Date of tDMARD initiation was the index date. Patients had ≥2 RA diagnoses separated by ≥7 days, ≥1 T2DM diagnosis, and had ≥12 months of pre-index continuous enrollment. Follow-up ended at the end of patient insurance enrollment, study period or index treatment. T2DM-related HCRU and costs including inpatient stay, outpatient visits, ER visits, and pharmacy use were measured on a per-patient-per-month (PPPM) basis (2018 USD). Patients treated with abatacept were matched to TNFi and non-TNFi cohorts separately by propensity score adjusted with patients baseline comorbidities, HCRU, and costs.

Results: A total of 16,236 patients meeting criteria were identified. Most patients were female (74.3%), and the overall average age of 55.4 years (Table 1). After matching, 850 pairs of abatacept vs non-TNFi patients, and 1,096 pairs of abatacept vs TNFi patients were included in the adjusted results. Patients initiating abatacept had $144 lower adjusted T2DM-related costs as compared to non-TNFi and $79 lower costs than TNFi cohorts (Table 2).

Table 1. Patient Characteristics

	Abatacept n=1,134	Non-TNFi n=1,353	TNFi n=13,749	Total N=16,236
Age, mean years (SD)	58.5 (11.3)	57.7 (11.2)	54.9 (10.6)	55.41 (10.7)
Gender, female, n (%)	936 (82.5)	993 (73.4)	10,142 (73.8)	12,071 (74.3)
CCI, mean (SD)	2.2 (1.4)	2.3 (1.4)	1.8 (1.1)	1.89 (1.14)
DCSI, n (%)				
Cardiovascular	361 (31.8)	406 (30.0)	2,500 (18.2)	3,267 (20.1)
Neuropathy	294 (25.9)	374 (27.6)	3,161 (23.0)	3,829 (23.6)
Nephropathy	146 (12.9)	193 (14.3)	1,151 (8.4)	1,490 (9.2)
PVD	131 (11.6)	155 (11.5)	874 (6.4)	1,160 (7.1)
Retinopathy	103 (9.1)	119 (8.8)	922 (6.7)	1,144 (7.0)
Cerebrovascular	74 (6.5)	102 (7.5)	620 (4.5)	796 (4.9)
Metabolic	9 (0.8)	20 (1.5)	141 (1.0)	170 (1.0)

CCI: Charlson comorbidity index; DCSI: diabetes complications severity index; PVD: peripheral vascular disease.

Table 2. Adjusted T2DM-related HCRU and Costs after Propensity Score Matching

	Abatacept n=850	Non-TNFi n=850	Diff (ABA-Non-TNF)	Abatacept n=1,096	TNFi n=1,096	Diff (ABA-TNF)
T2DM-related HCRU (per 1000 Patients per Month)						
Number of Hospitalizations	13.9	20.4	-6.5*	12.6	14.9	-2.3*
Number of ER Visits	22.0	16.1	5.9*	18.4	16.3	2.0*
Number of Outpatient Visits	311	334.8	-23.7*	299.3	286.9	12.4
T2DM-related Costs (PPPM $)						
Inpatient Costs	507	535	-28	413	475	-62
ER Costs	27	17	10*	22	25	-3
Outpatient Costs	190	323	-133	186	170	16*
Pharmacy Costs	107	100	7*	97	128	-31
Total Costs	831	975	-144	719	798	-79*

*P<0.05

Conclusion: TNFi-naive RA patients with T2DM newly initiating abatacept had lower adjusted rates of T2DM-related hospitalizations compared to patients who initiated a non-TNFi or a TNFi. Total costs were lower among patients initiating abatacept vs. patients who initiated a non-TNFi or a TNFi. Findings suggest that initial abatacept among TNFi-naïve patients may be able to reduce healthcare utilization arising from T2DM complications and reduce T2DM-related costs in RA patients.

Disclosure of Interests: Xue Han Employee of: BMS, Qian Xia Shareholder of: I own shares of Bristol-Myers Squibb Company, Employee of: I am a paid employee of Bristol-Myers Squibb Company, Ying Bao Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Vardhaman PATEL Employee of: Bristol Myers Squibb, Amrina Roy Employee of: Mu-Sigma, Varshini Rajagopalan Employee of: Mu-Sigma, Francis Lobo Shareholder of: Bristol-Myers Squibb (US), Employee of: Bristol-Myers Squibb (US)

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AB1345-HPR THE MULTIDISCIPLINARY FOOT CLINIC: A SERVICE EVALUATION PROJECT

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Background: Patients with rheumatological foot disease are an overlooked population, and it was noted locally that these patients received a fragmented service; attending multiple appointments for the management of one clinical issue. This led to delays in treatment; significant inter-departmental correspondence and variations in the peri-operative management of disease modifying anti-rheumatic drug (DMARD) and biologic therapies. To remedy this a foot multidisciplinary (MDT) clinic was established, including input from rheumatology, orthopaedic surgery, specialist rheumatology podiatry and physiotherapy. The outcomes from the foot MDT clinic have been analysed in this service evaluation project.

Objectives: To evaluate the outcomes of the multidisciplinary foot MDT clinic, with particular reference to concordance to the British Rheumatology Society (BSR) guidelines on peri-operative medicine guidelines.

Methods: Data was collected retrospectively across all clinics from January 2017 to February 2019. Clinic letters were obtained, and data was collected using a standardised data collection sheet. Data was collected on patient demographics, rheumatological diagnoses, treatment outcomes from the foot MDT,

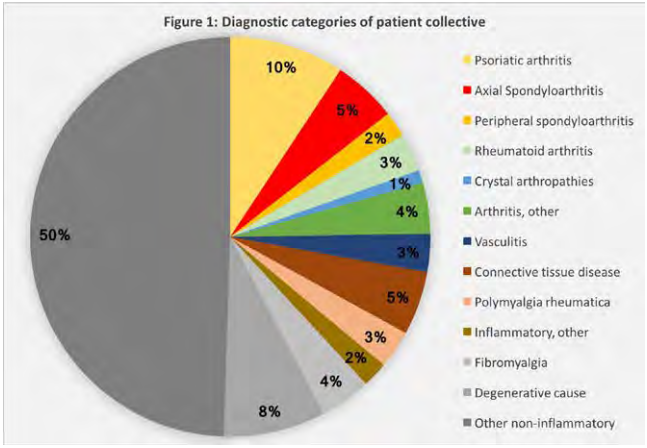
appropriateness of peri-operative plan and post-operative complications. No data was available on these outcomes prior to the advent of the foot MDT clinic.
Results: Data from 12 clinics was analysed (n=40). Patients had a median age of 66 years (IQR 27.5 years); 65% of patients were female and 35% of patients were male. The commonest rheumatological foot disease seen was rheumatoid arthritis (67%), followed by psoriatic arthritis (15%). All patients were treated with biologic or non-biologic DMARDs. Treatment outcomes were as follows: 27.5% were offered surgical treatment; 10% were offered intra-articular (IA) injections under ultrasound guidance; 10% were offered IA injections under general anaesthetic; 25% underwent specialist rheumatology podiatry, and the remaining 30% elected for a conservative approach after careful consideration of treatment options. Of those who were offered surgical treatment, 72% of patients were provided with a peri-operative plan which accorded with British Rheumatology Society (BSR) guidelines. Of those whom underwent surgery, one patient's surgical treatment was complicated by a post-operative infection; however, the peri-operative DMARD/biologic plan was not felt to be contributing factor.
Conclusion: The foot MDT clinic provides a comprehensive review of rheumatological foot conditions, with readily available access to a full range of treatment options. Co-location of all relevant professionals allows for real-time interdepartmental communication; shared decision making between clinicians and patients; avoids multiple appointments; reduces uncertainty with peri-operative planning as well as providing a cost-effective and efficacious service. Discrepancies in the peri-operative plan for medicines arose when the treating orthopaedic surgeon was not present in clinic. In these cases, the plan for surgical treatment was made outside of this clinic, without input from the treating rheumatologist. To improve concordance with BSR peri-operative medicine guidelines, it is recommended that all treatment decisions are made during the clinic, allowing input from all relevant partners. Informal feedback from patients commended the foot MDT, this shall be formalised through further qualitative data.
Disclosure of Interests: None declared
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AB1346-HPR

REAL-WORLD EFFECTIVENESS AND PERCEIVED USEFULNESS OF SYMPTOM CHECKERS IN RHEUMATOLOGY: INTERIM REPORT FROM THE PROSPECTIVE MULTICENTER BETTER STUDY

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Background: Symptom checkers (SC) promise to reduce diagnostic delay, misdiagnosis and effectively guide patients through healthcare systems. They are increasingly used, however little evidence exists about their real-life effectiveness.
Objectives: The aim of this study was to evaluate the diagnostic accuracy, usage time, usability and perceived usefulness of two promising SC, ADA (www.ada.com) and Rheport (www.rheport.de). Furthermore, symptom duration and previous symptom checking was recorded.
Methods: Cross-sectional interim clinical data from the first of three recruiting centers from the prospective, real-world, multicenter bETTeR-study (DKRS DRKS00017642) was used. Patients newly presenting to a secondary rheumatology outpatient clinic between September and December 2019 completed the ADA and Rheport SC. The time and answers were recorded and compared to the patient's actual diagnosis. ADA provides up to 5 disease suggestions, Rheport calculates a risk score for rheumatic musculoskeletal diseases (RMDs) (≥1=RMD). For both SC the sensitivity, specificity was calculated regarding RMDs. Furthermore, patients completed a survey evaluating the SC usability using the system usability scale (SUS), perceived usefulness, previous symptom checking and symptom duration.
Results: Of the 129 consecutive patients approached, 97 agreed to participate. 38% (37/97) of the presenting patients presented with an RMD (Figure 1). Mean symptom duration was 146 weeks and a mean number of 10 physician contacts occurred previously, to evaluate current symptoms. 56% (54/96) had previously checked their symptoms on the internet using search engines, spending a mean of 6 hours. Rheport showed a sensitivity of 49% (18/37) and specificity of 58% (35/60) concerning RMDs. ADA's top 1 and top 5 disease suggestions concerning RMD showed a sensitivity of 43% (16/37) and 54% (20/37) and a specificity of 58% (35/60) and 52% (31/60), respectively. ADA listed the correct diagnosis of the patients with RMDs first or within the first 5 disease suggestions in 19% (7/37) and 30% (11/37), respectively. The average perceived usefulness for checking symptoms using ADA, internet search engines and Rheport was 3.0, 3.5 and 3.1 on a visual analog scale from 1-5 (5=very useful). 61% (59/96) and 64% (61/96) would recommend using ADA and Rheport, respectively. The mean SUS score of ADA and Rheport was 72/100 and 73/100. The mean usage time for ADA and Rheport was 8 and 9 minutes, respectively.
Conclusion: This is the first prospective, real-world, multicenter study evaluating the diagnostic accuracy and other features of two currently used SC in rheumatology. These interim results suggest that diagnostic accuracy is limited, however SC are well accepted among patients and in some cases, correct diagnosis can be provided out of the pocket within few minutes, saving valuable time.
Figure:



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AB1347-HPR

DIGITAL SOLUTIONS TO AID SELF-MANAGEMENT: DEVELOPING A RHEUMATOLOGY APP FOR USE BY ANY PATIENT ATTENDING OUR DEPARTMENT

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Background: Managing complex rheumatological conditions requires information about the disease itself, treatments regimes and side effects. This is particularly important for those with a new diagnosis.

A local patient focus group identified the need for trustworthy information, written and reviewed by their rheumatology team to aid self-management. They felt information should be readily accessible, in one place, to re-read / re-listen to, as required.
Objectives: To develop a Rheumatology App, for any patient attending our department, to support self-management.
Methods: We worked with a number of rheumatology patients, of differing ages, the Rheumatology multi-disciplinary team (MDT) and an industry partner, hci.digital, to develop our App, called 'Rheumatology Connect'.
We developed over 30 short videos, provided links to other valuable patient websites e.g. Versus Arthritis, NRAS, NASS, and wrote short articles, to provide basic headline information about various different diseases, common treatments e.g. Methotrexate. We provided easily accessible contact details and information about our clinic locations (including postcodes, bus links, car parking). Video content was written by the clinical authors and filmed by hci.digital.
Patient involvement in designing the layout was particularly important for the App to be easily navigable by all.
We launched the App, in June 2018, at a local patient educational conference. We encourage all patients on regular follow up to download it /use it and remind everyone about it in our clinic letters.
Results: Downloads have been ongoing since launch, with over 1953 downloads and 21930 page views, with peaks around the time of our monthly education sessions when we advertise the App to new patients.
Over 54% spent between 2 to 5+ minutes in the App at a time. Most of the videos in the App are about 2 minutes long. Common hits include: videos on medications, various conditions, contact details, clinic locations, and services available.
We have had a number of spontaneous contacts from patients saying how valuable they find the information we have given them.
The App aids efficiency by allowing direct phone calls to the correct member of the MDT e.g. rheumatology physio, rather than going through the secretaries. We are also encouraging direct email contact via the App. These aspects are helping us make our services more efficient.
Conclusion: The App continues to be downloaded and used by our patients. It has become an important part of our patient education efforts, especially for those with a new diagnosis.
We have had a significant increase in email contact from patients, allowing us to be more efficient by responding more quickly to patient queries, avoid additional telephone calls and avoid ansa-phone messages.
To date, the App continues to be downloaded by patients and we have received very positive feedback. Having surveyed the users, our next step is to develop interactive PROMS, a calendar reminder function and medicines management function as these have been identified as additions users would find helpful to manage their disease. We have raised funds to develop the App. The updated app should be available by May 2020
Download free from App store (search '***Rheumatology Connect***') or go to ***www.rheumatologyconnect.info***.
Disclosure of Interests: None declared
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AB1348-HPR TELEMEDICINE IN RHEUMATOLOGY: ACCEPTANCE BY PATIENTS AND MEDICAL PRACTITIONERS IN GERMANY (TELERHEUMABB) - INTERIM ANALYSIS

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Background: The number of rheumatologists in Germany does not cover the minimum medical need [1]. This implies long journeys and waiting periods for patients in the context of rheumatologists' consultations. International studies suggest that telemedicine could resolve these issues and support health care professionals in rheumatologic care [2, 3]. So far, comprehensive sustainable approaches are still pending in Germany. By addressing the potential users, TeleRheumaBB investigates whether and how telemedicine can support rheumatologic care in Germany. The study is realized from Oct. 2017 until Jun. 2020.
Objectives: The objectives of the study are to evaluate the acceptance and willingness of patients and medical practitioners (MP) to implement telemedicine into rheumatological care as well as to understand how telemedical approaches should be designed to be applied in daily practice.
Methods: The study design contains a mixed-methods approach, which combines qualitative and quantitative data. In the qualitative part of the study 28 in-depth interviews and 3 focus groups involving patients, rheumatologists, general practitioners and stakeholders were conducted. The quantitative part of the study comprised a questionnaire survey with rheumatologists (n=48) and referrers (n=444) and a second questionnaire survey with patients (n=734).
Results:
Qualitative Data: The term "telemedicine" is filled with different meanings. Motives to implement telemedicine into daily practice are patient guidance, information, substantial time savings, desire of a modern practice etc. Reported risks of telemedicine are adverse impacts on the doctor-patient-relationship as well as low benefit with high effort.
Quantitative Data: 62% of the MPs' surveyed answered that they would like to use telemedical approaches. 81% of the participants supported doctor-doctor communication via telemedicine. Only 47% of the MPs' surveyed supported doctor-patients communication via telemedicine. MPs' state that there are barriers which prevent them from implementing telemedicine (89%). These are among others acquisition of technology, administrative expenses and poor remuneration. 53% of the patients surveyed stated that they had heard the term telemedicine before. 30% of the participants answered that they would like to try out telemedicine. 38% answered with "no" and 29% with "do not know". Further results from the patient survey will be available in June 2020.
Conclusion: The study results show high acceptance rates of telemedicine regarding doctor-doctor communication. Doctor-patient communication via telemedicine is less accepted. However, MPs' are reporting obstacles preventing the implementation of telemedicine in rheumatology. In order to implement telemedicine in rheumatological care comprehensively, adequate conditions must be established in the German health care system.
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AB1349-HPR IMPLEMENTATION OF A GROUP EDUCATION SERVICE FOR RHEUMATOLOGY OUTPATIENTS COMMENCING BIOLOGIC THERAPY AT UNIVERSITY COLLEGE LONDON HOSPITAL (UCLH)

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Background: Biologic therapies are commonly prescribed in a range of rheumatic conditions. From 2016 - 2018, a mean of 226 rheumatology outpatients at UCLH commenced biologic therapy per year for inflammatory arthritis alone[1]. Patient education is required prior to initiation. At UCLH this is delivered via individual appointments with specialist nurses, contributing to waiting times for nurse appointments and thus delays in starting treatment.
Objectives:
1.To evaluate patient satisfaction following group education.
2.To reduce the burden on specialist nurses delivering multiple individual sessions.
Methods: A once-weekly group education service was set up at UCLH. This comprised: an oral PowerPoint presentation; injection demonstration; question and answer session; and written leaflets. Patients were provided with pre- and post-session questionnaires to evaluate the service.
Results: Over the first five weeks of the service, 18 patients attended group education (a median of 4 patients per session). Nine patients (50%) had previously researched the medication via internet search engines. Patients' questions prior to the session were most commonly centred on side effects and long-term risks. All of the patients (100%) felt that "most or all" of their questions were answered during the session. Patients gave their awareness of the reason for therapy a median score of 7/10 pre-education; this rose to a median of 10/10 post-education. The median score given for confidence to self-administer the drug was

5.5/10 pre-education; this rose to a median of 10/10 post-education. The median anxiety score was 3/5 pre-education; this dropped to 2/5 post-education. The presentation was adapted based on questions that arose during the sessions. Multiple patients gave informal, verbal feedback stating that they found the group environment to be beneficial, providing a chance to meet others with similar conditions, share experiences and feel reassured that they are not alone in starting biologic therapy.

Conclusion: Patient feedback demonstrated that the group education sessions at UCLH were effective in improving their understanding of the rationale for biologic treatment, increasing their confidence in self-administration, and reducing anxiety. Verbal feedback illustrated that many patients enjoyed the group environment, and the opportunity to interact and share experiences with others. At an average rate of 4 patients currently being seen a week, it is estimated that this will save 192 specialist nurse appointments per year (out of an estimated 226 commencing biologic therapy). There is scope for further research into the effects that this has had on waiting times to receive education / start treatment, and on drug compliance.

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Disclosure of Interests: None declared

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AB1350-HPR SOCIOECONOMIC BURDEN OF NON-ATTENDANCE IN RHEUMATOLOGY CONSULTATION

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Background: Outpatient non-attendance refers to the phenomenon of patients who have a medical appointment but do not show up at the specified date, time, and location without giving previous notice.[1] In addition to affecting the efficiency and thereby increasing the healthcare total costs, nonattendance might also delay access to care for users on waiting lists.[1] Nonattendance at health appointments is costly to services, and can risk patient health.[2] There is very little data on the nonattendance prevalence and impact in Portugal. This knowledge might be fundamental to improve effectiveness of outpatient care in Portugal.

Objectives: 1) describe patient's non-attendance rate; 2) assess and characterize the sociodemographic and clinical characteristics among non-attending patients; 3) estimate the economic burden of non-attendance.

Methods: Retrospective, cross-sectional and analytical study. We reviewed a one-month Rheumatology consultation period regarding performed medical consultations and non-attended consultations without previous notification from patients. Direct economic costs of non-attended appointments were calculated based on the "Amending Agreement to the ULSAM, EPE Program Agreement."

Results: 982 consultations within January 2018 were included. Appointments episodes for therapeutic prescription, medical reports or programmed admissions were excluded. Fifty-seven (5.8%) of scheduled outpatient appointments were non-attended. Subsequent consultations represented 85.2% of attended appointments and 80.7% of non-attended appointments. Female gender was the most prevalent in both groups – 620 (67.0%) among attended consultations and 37 (65.0%) among non-attended consultations. Mean age was 57±15 years in the first group and 54±16 years in the second one. Among attended appointments, mean education level was 8±5 years versus 9±6 years among non-attended appointments. There were no differences between both groups in gender, age, education level, diagnosis, disease duration and activity or appointment type (first or subsequent consultation). A cost of 2,438 euros was estimated regarding non-attended appointments for this period, what could represent a burden of more than 29,000 euros yearly, in direct costs, only.

Conclusion: Non-attendance at scheduled appointments in public hospitals seems to be influenced by other factors besides gender, age and education level. The burden of non-attended appointments is undeniable. In addition to the costs estimated in this study, further indirect costs such as poorer patients outcomes, impaired access to medical care and hospital penalties should be taken into account. Implementation of awareness strategies aiming the optimization and effectiveness of healthcare system are required.

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Disclosure of Interests: None declared

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AB1351-HPR A HAND EXERCISES MHEALTH APP FOR PATIENTS WITH RHEUMATOID ARTHRITIS: DEVELOPMENT, DESIGN AND USABILITY STUDY IN TURKEY

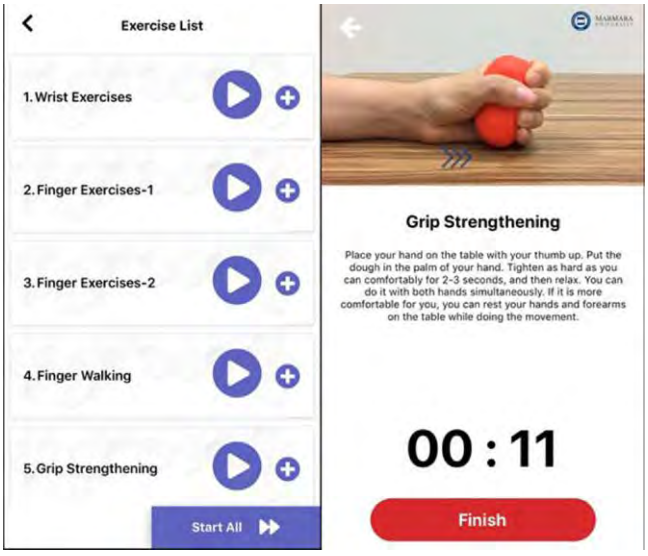
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Background: The Strengthening and Stretching for Rheumatoid Arthritis of the Hand (SARAH) programme has been shown to provide long term improvement in hand function for patients with rheumatoid arthritis (RA) affecting their hands. In Turkey, limited number of physiotherapists work in rheumatology departments so there is an opportunity to use the digital technologies for exercise prescription and follow up to improve access to treatment.Growing research evidence supports the effectiveness of mHealth interventions for improving exercise adherence and motivation.To our knowledge,there is no hand exercises mHealth program for patients with rheumatoid arthritis designed by experts with the user-centered method.

Objectives: The aim of our study is to develop and design a smartphone application for structured hand exercise program for patients with RA in Turkey and to test its usability.

Methods: We used a qualitative user-centered design approach with 2 phases. PHASE 1:we conducted focus group meetings to discuss the content, feature and design of app to produce a prototype version of smartphone software for RA hand training program.The Focus Group consisted of two physiotherapists and three hand therapists working in the field in different rheumatology or hand rehabilitation clinics,two software-computer engineers, and three patients with RA who had previously participated in hand therapy. The focus group met 4 times during phase 1. PHASE 2:we investigated the usability of prototype version of the rheumatoid hand exercise smartphone app software. All focus group members (n=10) and 6 patients used the app for one week.All users filled the usability questionnaire and provided written feedback on the app. Revisions were made and the revised version was tested. We put the revised app in digital markets in Turkish and English.

Results: The major themes identified from the Focus Group discussions during phase 1 were (a)Login techniques (b)self-monitoring (c)exercises types/frequency/diary, (d) patient education, (e)behavioral change and encouragement (f)exercise adherence. Patients and therapist all agreed the login needed to be easy. Patients wanted to be able to monitor their pain levels and hand function in the app. Patients thought the SARAH exercise were suitable for the app. A patient said:*'SARAH exercises is beneficial for my hand and tendon gliding exercise,I will be happy to see these exercises in app'*. Patients wanted exercise reminders using push up notifications to encourage exercise were proposed and included.A patient commented 'in the *morning and after work, motivational push up messages could be beneficial for exercise habit*."During the phase 2,we identified a need for education on how to use digital app, ways to provide patient follow up to monitor adherence, the need to allow patients to select the amount of notifications. This feedback was incorporated into the final version.



Conclusion: mHealth applications represent an easily accessible bridge between patients and health professionals for home-based programs. Using a user-centered approach ensured that we developed an application that met the needs of therapists and patients. Physiotherapists are using the app in rheumatology clinics in Turkey and long-term usability and feasibility studies are ongoing.

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AB1352-HPR **SHARED CARE – AN ALTERNATIVE WAY TO COPE WITH INCREASING SERVICE DEMAND**

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Background: Rheumatic diseases are immune-mediated disorders that affect the musculoskeletal system, soft tissues, blood vessels and connective tissue. Patients with rheumatic diseases need regular follow up for disease and drug toxicity monitoring. To cope with the increasing service demand, the Division of Rheumatology in the United Christian Hospital developed and expanded the shared care service. In the conventional practice, patients have to been seen by rheumatologist for every visit while the shared care service involved follow up by rheumatologist and rheumatology nurse in alternate sessions.
Objectives:
1.To evaluate the effectiveness and safety of the shared cared service
2To evaluate the effectiveness of reduction in workload of rheumatology clinic
Methods: This is a retrospective study involving the period from 1/1/2019 to 31/12/2019. Patients who attended the rheumatology nurse clinic for shared care were recruited and reviewed. All patients were selected and referred by rheumatologists. Criteria for shared care included regular follow up in rheumatology clinic and stable clinical condition. The length of follow up is adjusted according to patient condition. Services provided by rheumatology nurse (RhN) included disease education, drug and disease monitoring, drug advice and referral to other professionals and community service as indicated. During each visit, patient's vital signs, disease activity and laboratory results were assessed according to standard protocol. RhN will make discharge record to ensure continuity of care.
Results: Totally 489 episodes of attendance to nurse led clinic were recruited. Majority (97.3%) were arthritis patients. Others included lupus, vasculitis, Sjogren's syndrome and miscellaneous conditions. The length of follow up ranged from 3 weeks to 24 weeks and most of the patients were follow up between 8 to 16 weeks. Shared care patients included those with stable disease for interval monitoring, and patients for drug initiation and titration. The ratio for disease monitoring and drug monitoring are 41.3% and 58.7% respectively.
For the 489 episodes of attendance, 10 (2%) episodes needed rheumatologist intervention and 8 (1.6%) cases need advancement of follow up. Problems that required doctor interventions and advance follow up mainly are suboptimal disease control requiring medication adjustment or musculoskeletal ultrasound investigation.
178 (36.4%) episodes of nursing intervention were delivered, majority were medication advice (133, 27.2%). Reasons for nursing intervention included adverse drug reaction, abnormal investigation results, poor drug adherence and disease flare up. There were no emergency department attendance or admission related to rheumatic problems within one month of RhN follow up.
Conclusion: The shared care service is smooth and can safely lengthen the follow-up intervals to reduce clinic visit burden in rheumatology clinic. RhN input also allowed prompt advice for steroid tapering and dose titration for disease specific medication for better disease control. Proper case selection and close collaboration between rheumatologist and rheumatology nurse is the key.
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HPR Professional education, training and competencies

AB1353-HPR **EMPOWERING LEARNERS TO "OWN" THEIR PERFORMANCE: PRESENTING EDUCATIONAL PERFORMANCE DATA BACK TO LEARNERS AS A COMPONENT OF AND RATIONALE FOR SUBSEQUENT EDUCATION**

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Background: Beginning in 2016, RMEI created multiple accredited online education focused on RA and designed for rheumatologists. In 2018, the educational scope expanded to include live meetings, starting with a symposium at EULAR. For all programming from 2016-18 (6 courses, in both live and online settings), educational content was developed based on performance data from the previous RA courses. During the 2019 EULAR symposium, we presented the outcomes findings - from both the 2018 symposium and online courses – to the assembled rheumatologists, identifying ongoing educational gaps observed in their specialty population. The rationale: to create continuity between symposia over time by demonstrating incremental improvements and continuing areas of need, while also endowing learners with a greater sense of ownership and investment in forthcoming educational content.
Objectives: To evaluate the impact of presenting learner's educational performance data to them before education addressing persistent gaps identified in their performance the year prior.
Methods: Data collected during the 2018 EULAR symposium was analyzed to understand the underlying drivers impacting poor performance in an identified area of ongoing educational need (cycling versus switching TNF inhibitors). A linear regression model was run including all non-related curriculum, demographic, and evaluation questions as possible drivers against those related low-scoring (at Post-Test) curriculum questions. The content of RMEI's 2019 symposium at EULAR was developed to address the identified significant drivers to improve population proficiency in cycling versus switching. In addition to developing content based on the above findings, that data was also presented to learners in poster format prior to their participation in the 2019 symposium. During the period between on-site registration and the start of the symposium, attendees had the opportunity to explore data-driven insights, via audio-guided posters located around the meeting room. These insights included discussion of 2018 data analysis, identified drivers of poor performance, introduced the iterative data-driven methodology employed, and rationale behind content development for the 2019 symposium. At the conclusion of the 2019 symposium learners were asked to describe the impact/relevance of being presented with their performance data, their intention of incorporating course content into practice, and what specifically they intended to change.
Results: Data was collected on 135 clinicians (primarily physicians who actively treat patients with rheumatoid arthritis) who attended, and participated in, the symposium. With specific regard to the impact of seeing their own data presented back to them, 80% reported that seeing the learner data from the 2018 symposium enhanced their current learning experience. Further, 86% reported that they intended to incorporate course content into their clinical practice. Specifically, this population reported an intent to change their treatment approach and patient education practices.
Conclusion: Education is only as effective as the degree to which the audience is engaged. While year over year data from 2016 through 2018 demonstrated that an iterative approach facilitated the meaningful and necessary reinforcement of challenging concepts, learners in prior years were not aware of the methodological underpinnings of the educational offerings. Presenting this population with findings derived from their performance - as a rationale for the education they were about to participate in proved a compelling motivator for active learner engagement, and may have had a positive influence on the degree to which learners implemented course content into their clinical practice.
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AB1354-HPR **CURRENT SITUATION OF TRAINING IN RHEUMATOLOGY IN THE POSTGRADUATE CURRICULUMS OF INTERNAL MEDICINE, FAMILY MEDICINE, GERIATRICS, PAIN MEDICINE AND, PHYSICAL AND REHABILITATION MEDICINE ACROSS COLOMBIA**

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Background: Rheumatic diseases are an important complaint in patients, although the incidence is low, they cause disability and impact on the health system. Currently, in Colombia, there are 198 rheumatologist, so it's important to know how is rheumatology training in specialties related to rheumatology, which are the specialties that the patient with a suspected rheumatic disease will visit at first.
Objectives: To describe the training status in rheumatology in the postgraduate curriculums of internal medicine, family medicine, geriatrics, pain medicine and, physical and rehabilitation medicine across Colombia.
Methods: This is a descriptive cross-sectional study. A survey was applied in each participating medical school using the RedCap® platform. The questionnaire included multiple-choice responses and a textbox to complete. The survey was done to the 29 registered medical schools which offer the specializations

already mentioned. The program director or an assistant professor was asked to fill the survey out between April 2019 and January 2020. The sample was described through means and standard deviations or frequency and percentages according to the type of variable.

Results: Data was obtained from all the programs of specialization in internal medicine (n = 29), family medicine (n= 9), pain medicine (n= 8), physical and rehabilitation medicine (n= 6), geriatrics (n= 4). All the programs of internal medicine, geriatrics, and physical/rehabilitation medicine have rheumatology as a mandatory subject within the curriculum, while in family medicine and pain medicine programs: 33% (n= 3), and 57% (n= 4) respectively, does not have a rheumatology training. In internal medicine the average duration of rheumatology training is 56 days (28 to 90 days), in geriatrics, it is 56 days (45-60 days), in family medicine 26.1 days (3 to 30), in medicine physical and rehabilitation medicine 35 days (30 to 60) and in pain medicine 40 days (30 to 60). 93.8% (n= 45) of the programs surveyed have a rheumatologist as a teacher in charge of both, the academic activities and the external rheumatology consultation and in the rest of the programs these activities are done by an specialist in internal medicine, family medicine or pain medicine. The theoretical components most frequently offered in seminars or master classes are: rheumatoid arthritis, lupus, vasculitis, spondyloarthritis, gout, osteoarthritis, sjogren's syndrome and osteoporosis. The specialization programs have an average of 3 rheumatologists as professors (range 1 to 8). 43.8% of the programs use some virtual resources to complement the teaching in rheumatology such as video conferencing in virtual platform or YouTube (8.3%), online course (6.3%), mobile application (16.7%), others such as moodle and webcast platform (12.5%). 92.9% (n = 52) offer their students an elective rotation in the rheumatology service, in addition to the mandatory one. Finally, 89.6% (n = 43) of the interviewees agree with the way in which the curriculum is structured in their programs, to approach initial diagnostic and therapeutic in patients with suspected or established rheumatic disease. However, 23.2% (n = 13) of the professors of the surveyed programs (6 of internal medicine, 4 of family medicine, 2 of pain medicine and 1 of physical/rehabilitation medicine), consider that the rheumatology subject should not be mandatory within their programs.

Conclusion: All physicians need to be familiar with rheumatological conditions since the rate of rheumatologists in Colombia is low. Knowing rheumatology is an increasingly important role in a clinical scenario in many postgraduate curriculums as we explain in this study.

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AB1355-HPR THE IMPACT OF A STRUCTURED TRAINING PROGRAMME FOR THE DETECTION OF SYNOVITIS WITH MUSCULOSKELETAL ULTRASOUND (MSUS) IN RHEUMATOLOGY NURSING

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Background:

Objectives: To analyse the effect of a teaching intervention for the technical performance of a reduced index of ultrasound synovitis by nurses without previous experience in musculoskeletal ultrasound (MSUS).

Methods: Design: Quasi-experimental study of the before-after type. Protocol: The nurses received a theoretical-practical, face-to-face and intensive training of 8 hours, by an expert rheumatologist in musculoskeletal ultrasound (MSUS), to perform the Perricone index, which assesses the presence of grey-scale synovitis (GS) and quantifies the presence of a power-doppler (PD) signal semiquantitatively (0-3), in 6 joints (Wrists, 2nd Metacarpophalangeal (MCP) joints and knees). The theoretical knowledge acquired was assessed by an exam test type at the end of the training, and the technical skills were assessed by an ultrasound examination in patients with rheumatoid arthritis, immediately after the teaching session and at 18 months later. Variables: Illumination of the consultation, protection of privacy and unequivocal identification of the patient, technique (explorer ergonomics, bilateral comparison, use of both hands, measurement, marking and saving data), GS (probe position, centred image, cortical-cartilage-tendon display, depth, focus, frequency, gain), PD (probe pressure, PRF, position-width-depth of the box, focus, frequency, gain), synovial recesses (dorsal and palmar examination of the wrist, 2nd Metacarpophalangeal (MCP) joints and supra and parapatellar medial and lateral examination of the knees) and semi-quantitative gradation of synovitis in GS and PD. Statistical analysis: descriptive analysis, and in relation to the statistical significance tests for paired variables (pre and post teaching intervention) the McNemar test was used for dichotomous qualitative variables and McNemar-Bowker test for those of more than two categories.

Results: 5 nurses, 80% women, aged between 36 and 54 years participated. They adequately answered 100% of the 4-student test questions, and the remaining one matched 80% of them. The average time of baseline exploration was 45,2 ±3,8 minutes and the final time was 32,6 ± 3,5, improving the 5 students in an average of 12,6± 4,4 minutes. The technical aspects not performed correctly in the baseline ultrasound examination were the bilateral comparative, centred image, grey scale gain, measuring, correct anatomical image of the synovial recess of the wrist and position-width-depth of the Doppler box. An improvement was observed at 18 months in the unequivocal identification of the patient, adequate illumination of the consultation, bilateral comparison, correct anatomical acquisition of synovial recesses and the quantification of GS synovitis, but no statistically significant differences were observed, before and after the teaching intervention, in possible relation with the difficulty to use the ultrasound in their respective Rheumatology Units in clinical practice, but mainly because the aspects correctly performed in the baseline exploration were numerous.

Conclusion: A formal training of rheumatology nurses in musculoskeletal ultrasound (MSUS) could be very useful, and cost-efficient, in the health care of patients with rheumatoid arthritis.

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AB1356-HPR GOUT IN SPANISH PRIMARY HEALHCARE CENTERS: STILL A LONG WAY TO GO

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Background: Gout has a prevalence >2.5% in the Spanish adult population. It is a chronic disease that without proper treatment causes pain, joint deformity and increased cardiovascular risk and mortality. Recent advances have demonstrated that if correctly treated the disease can be controlled and even 'cured'. Most gouty patients are diagnosed and treated by general practitioners (GPs). There is evidence that the management if these patients is not good neither at Rheumatology Units nor at Primary Healthcare (PHC) centers.Several causes of this mismanagement can be found in the literature.

Objectives: Design and evaluation of the results of a questionnaire created from a bibliographic search focused on areas of improvement of gout management in PHC.

Methods: A search was made in Pubmed to identify the main barriers described in the management of patients with gout in primary care. The terms used were: "Gout", "primary healthcare" and "education". A Google Form of gout knowledge and management questionnaire was designed, taking into account what is described in the literature. The Google Form was sent to all GP from an urban area via mail and to other contacts via WhatsApp and twitter.

Results: Responses were obtained from 224 GPs; 69.5% were women; 73.1% had between 11 and 30 years of professional experience; 96.4% answered that gouty are mostly controlled in primary care; 99.6% performs the diagnosis of gout without analysis of synovial fluid and 17% diagnosed only by clinics without urate levels; 55.9% of GPs do not use any reference guide. Of those who use, the 73% use GUIPCLINGOT and 40% use SEMGs one; 80.5% have not done any gout course in the last 5 years; 26% did not have access to a rheumatologist to confirm the gout diagnosis; only 30.8% knew the therapeutic objective of the urate lowering therapy (ULT); 28.6% considered the beginning of ULT after the first attack; 62% believed that the most important part of the treatment was changing diet and lifestyles; 88.8% did not perform any specific education for these patients by the nurse; just 37.2% carried out a treat-to-target strategy to lower urate levels.

Conclusion: The questionnaire identifies multiple points of improvement for the management of this pathology in accordance with the described in the literature. Most GPs are unaware of the therapeutic objective of the ULT.

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AB1357-HPR DESIGNING THE ROYAL COLLEGE OF NURSING COMPETENCY FRAMEWORK FOR RHEUMATOLOGY NURSES

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Background: The 1st Edition of the RCN Competency Framework for Rheumatology Nurse Specialists (RNS) will be published in March 2020. The role of the RNS is complex, and can include caring for children and young people. The importance of RNS's was highlighted by the National Rheumatoid Arthritis Society (NRAS 2017). The British Society for Rheumatology (BSR) outlined the need for education, training supervision and work force development. Education for RNS isn't currently centralized but is key to improving skills and developing workforce for the future. RNS are in short supply resulting in problems of access to services and delays in care (BSR 2019). In all 4 UK nations the titles of RNS and proficiency vary greatly (Titrate trial 2019) This is likely to have an impact on patient experience and outcomes. The European League Against Rheumatism (EULAR) developed

recommendations for the role of the RNS which were recently updated (Beech et al, 2019). This framework maps all of these requirements.

Objectives: This work supports the development of roles, improve access for patients and reduce. This document will act as a foundation for building sustainability and a more robust education and role development strategy. This work will strengthen rheumatology nursing and support all 4 UK nation's issues regarding recruitment, retention, sustainability, succession planning and benchmarking. Dissemination is key and we will work hard with stakeholders to ensure centralization of a nationally adopted framework. This abstract submission will increase dissemination opportunities.

Methods: Online data sources were searched for the most relevant and current evidence. Where research evidence wasn't available, existing and new knowledge was utilised from a consensus of clinical expert and patient opinions, several rounds of discussions took place virtually and face to face. RCN Rheumatology Nurse Forum Workshop attendees in June 2019 also answered a questionnaire to elicit views and demographic information regarding roles.

Results: The questionnaire results demonstrated 100% (n37) agreement with the development of the framework and that only 2 respondents had completed a competency process. 60% were RNS. Of these 52% (n13) were band 6, 47% (n9) were band 7, and 1% were band 8 consultant nurses. The questionnaire highlighted the need to develop the framework. Results were fed back to the working party to inform the domains to be included.

Conclusion: Document will be at BSR 2020 having successfully submitted a session proposal and abstract. Evaluation will begin later in the year 6 to 12 months from launch. We will measure impact using a variety of methods including membership Facebook pages and the questionnaire at point of download request. We will measure where and how the competency is being used and adoption of the framework throughout the UK.

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Abbvie, Julie Begum: None declared, Ruth Wyllie: None declared, Trish Cornell Employee of: Consultant Nurse for Abbvie, Helen Smith: None declared, Lisa Howie: None declared, Louise Parker: None declared

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AB1358-HPR DIAGNOSIS OF AXIAL SPONDYLOARTHRITIS: A PRIMARY UNMET EDUCATIONAL NEED FOR RHEUMATOLOGISTS

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Background: Diagnosis of axial spondyloarthritis (axSpA) is challenging because of absent physical findings in early disease and the limited diagnostic performance of laboratory markers. Considerable reliance is placed on imaging of the sacroiliac joints (SIJ) but specialty training is primarily focused on interpretation of plain radiographic abnormalities.

Objectives: We aimed to identify what might be the primary unmet educational needs of rheumatologists completing fellowship training by using clinical and imaging data from an inception cohort of patients presenting with undiagnosed back pain. We hypothesized that concordance would increase after imaging is reviewed after the clinical data.

Methods: The diagnosis of axSpA was compared between local rheumatologists, axSpA experts and pF using clinical and imaging data from the multicenter Screening for Axial Spondyloarthritis in Psoriasis, Iritis, and Colitis (SASPIC) Study. In this inception cohort, patients ≤45 years of age with ≥3 months back pain undergo diagnostic evaluation by a local SASPIC rheumatologist, including imaging of the SIJ, who then records a global evaluation of presence/absence of axial SpA. This is done at 3 consecutive stages: 1.After the clinical evaluation. 2.After the results of labs (HLA B27, CRP) and radiography. 3.After review of the local MRI. In this exercise, 20 cases were selected from the SASPIC cohort and the rheumatologist global evaluations were removed from the eCRFs. Four experts in axSpA reviewed the clinical and imaging data in each eCRF and provided their global evaluations for stages 1, 2, and 3 of these 20 cases. Subsequently, 4 pF rheumatologists conducted the same exercise blinded to the assessments of the local rheumatologist and experts in axSpA. Concordance (% agreement) between the assessors was analyzed.

Results: Diagnosis of axSpA by the local SASPIC rheumatologist was made in 90%, 65%, and 75% of cases after stages 1, 2, and 3, respectively. Majority diagnosis of axSpA by experts was made in 84.2% (16/19), 57.9% (11/19), and 63.2% (12/19), after stages 1,2, and 3, respectively. Majority diagnosis of axSpA by pF rheumatologists was made in 94.4% (17/18), 100% (16/16), and 93.8% (15/16). Concordance among experts and between experts and local SASPIC rheumatologists increased after review of imaging data. For pf-rheumatologists concordance with experts increased after review of imaging for 2 assessors and decreased for the other 2 assessors. For the latter, the primary reason for decrease in concordance with experts was false positive diagnosis of axSpA in 35% and 30% of the cases after review of the imaging.

Conclusion: A structured case-based and sequential evaluation of clinical and imaging data suggests a gap in the training of recently graduated rheumatologists, with over-interpretation of imaging leading to false positive diagnosis of axSpA.

Assessors	Mean % Concordance (range) for diagnosis of axSpA		
	Stage 1	Stage 2	Stage 3
Experts in axSpA	64.2 (45-80)	75.8 (65-85)	84.2 (70-95)
Local rheumatologist vs Experts in axSpA	73.8 (70-80)	83.8 (80-85)	83.8 (80-90)
pF rheumatologist 1 vs Experts consensus	78.9	94.4	94.7
pF rheumatologist 2 vs Experts consensus	89.5	61.1	68.4
pF rheumatologist 3 vs Experts consensus	63.2	72.2	84.2
pF rheumatologist 4 vs Experts consensus	89.5	66.7	68.4

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AB1359-HPR PERCEPTION ABOUT FIBROMYALGIA AND ITS ACCOMPANYING SYMPTOMS AMONG MEXICAN PHYSICIANS

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Background: Previous studies showed that 93% of rheumatologists consider fibromyalgia (FM) as a clinical entity. However, accompanying symptoms such as fatigue, widespread pain, sleep disturbance and headache are underrecognized among physicians. According to a previous study, most recognized symptoms by general practitioners are fatigue and widespread pain (72.6%), while about thirty percent of physicians recognize sleep disturbance and depression as symptoms.

Objectives: To investigate physicians' point of view of FM accompanying symptoms in northeastern Mexico.

Methods: We designed an electronic survey about physicians' perceived importance of depression, fatigue, widespread pain, sleep disturbances, headache and irritable bowel disease symptoms (pain and cramping) in patients with FM. Questions were answered using a 5-point Likert scale: 1, strongly disagree; 2, disagree; 3, neutral; 4, agree; 5, strongly agree. General practitioners, rheumatologists, neurologists, psychiatrists were included.

Results: A total of 236 physicians were included: general practitioners, 149 (59.3%); rheumatologists, 21 (8.9%); neurologists 18 (7.6%); psychiatrists 8

(3.4%), and family physicians, 49 (20.8%). FM was considered a clinical diagnosis by 208 (88.1%) and most physicians think FM is both a physical and psychological condition, 190 (80.5%). Full results on physicians' perceptions is shown in Table 1. Fatigue was the symptom which most physicians agreed or strongly agreed was important in FM, 219 (92.7%). Disagreement (any degree) was greater regarding abdominal pain/cramping being an important symptom in FM, 52 (22%). Complete results can be seen in Image 1.

Table 1. Perceptions' of physicians about FM.

Variable	
FM is a clinic diagnostic, n (%)	208 (88.1)
Unsure FM is a clinical diagnostic, n (%)	12 (5)
FM is a physical illness, n (%)	33 (14)
FM is a psychological illness, n (%)	11 (4.7)
FM is both physical and psychological, n (%)	190 (80.5)
FM has a negative impact on quality of life, n (%)	227 (96.2)
FM has a negative impact on life expectancy, n (%)	135 (57.2)

Conclusion: FM was considered a clinical diagnostic and an illness both physical and psychological by most physicians. Headache and abdominal pain/cramping are symptoms less likely to be perceived as important in patients with FM.

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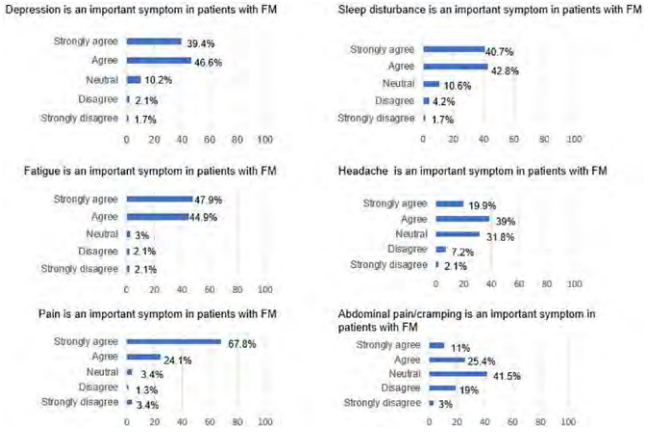


Figure 1. Image 1. Perception of accompanying symptoms of fibromyalgia (FM)

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AB1360-HPR

A MODEL TO IMPROVE MINORITY PATIENT RECRUITMENT IN LUPUS CLINICAL TRIALS - THE AMERICAN COLLEGE OF RHEUMATOLOGY MIMICT PROJECT EXPERIENCE

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Background: In the US, African Americans and Latinos are underrepresented in lupus clinical trials (LCTs),[1] despite experiencing the greatest lupus disease burden.[2,3] Low participation in LCTs results in inadequate data on treatment effectiveness for minority patients, and fewer opportunities for better care and treatment options.[1] Only one percent of minority patients are referred to clinical trials each year.[4] Provider barriers to making referrals include limited time and unfamiliarity with lupus and LCT opportunities.[4] Using US fedral grant funds, the American College of Rheumatology (ACR) developed MIMICT, a two-part model with associated materials to address provider-side LCT referral barriers. The materials include a toolkit for clinical trial sites and an educational toolkit for providers.

Objectives: Our objectives are to:

•Describe the US LCTs disparities.

•Discuss the research methodology to evaluate the two-part MIMICT model.

•Assess the feasibility of the model to increase minority involvement in clinical trials.

Methods: We designed two studies to evaluate the MIMICT model.The first study used an online, pretest/posttest, two-group evaluation approach to assess the extent to which the educational toolkit increased providers' knowledge, attitudes, self-efficacy, and behavioral intentions to refer minority patients to clinical trial. We conducted the study in 2018 with primary care providers (PCPs) and again in 2019/2020 with speciality providers. The second study used a longitudinal, mised methods, case-study approach to explore the real-world use of the toolkits with clinical trial site teams at two university medical centers.

Results: In the first study,among MIMCT-exposed PCPs, mean scores indicated statistical significance at p≤0.001 with more knowledge about referring [55.84 (sd=23.51) vs 41.76 (sd=19.98)], more self-efficacy to refer [55.00 (sd=37.22) vs. 37.99 (sd=34.42)], and more intentions to refer [61.36 (43.85) vs. 33.41 (41.16)] African American patients to LCTs among the treatment group than the control group, respectively. This presentation will discuss additional data comparing the study in 2018 and the study in 2019/2020 and look comparatively at outcomes across provider type.

In the second study, we found that the driver for successful engagemetn of providers and their subsequent use of the educational toolkit was the development of a trusting relationship between the clinical trial site teams and providers in the community. The development of trust took repeated and varied modes of contact, which we will discuss in-depth.

Conclusion: The MIMICT educational toolkit increase knowledge, self-efficacy, and intentions to refer lupus patients to LCTs. However, building trust between LCT sites and local providers takes time and repeated outreach, but the potential benefits to medicine and minority health are substantial.

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HPR Interdisciplinary research

AB1361-HPR

PRIMARY CARE PHARMACOLOGICAL TREATMENT FOR PATIENTS WITH HAND ARTHRALGIA

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Background: Primary care physicians (PCP) are the first point of contact for patients with a new-onset inflammatory rheumatic disease, like rheumatoid arthritis (RA). Consequently, primary care is crucial to the early diagnosis and prompt treatment of such individuals. The first three months following the onset of RA symptoms represent an important therapeutic window. Historically, patients with inflammatory arthritis received first-line treatment with non-steroidal anti-inflammatory drugs (NSAIDs), moving to synthetic disease-modifying anti-rheumatic drugs (DMARDs) relatively late in the disease process. As synthetic DMARDs are usually initiated in secondary care by rheumatologists, PCP focus on alleviation of patient's discomfort. Documented problems in primary care practice include accuracy of diagnosis, test ordering, medication use and delays in referral.

There is no evidence of which is the pharmacological treatment more commonly used for hand arthralgia in Family Medicine patients of a university hospital on their first or second visit.

Objectives: To examine the primary care physicians' pharmacological treatment prescribed for hand arthralgia in a Family Medicine Consultation.

Methods: In a period of a year and two months, eligible patients were recruited on their first or second visit to the Family Medicine Consultation of the Hospital Universitario "Dr. José Eleuterio González" in Monterrey, Nuevo León, México. Eligible patients were adults (aged≥18 years) with hand arthralgia as their chief complaint, who had not rheumatologic diagnosis and wasn't caused by trauma. Ninety patients were recruited, data were collected by capturing the prescription made by PCP.

Results: In this cohort of 90 patients, 71 (78.9%) were women. Of the 90 patients, 19 (21.1%) had no pharmacological prescription at all. Forty-nine patients (54.4%) had one prescribed drug, 17 (18.9%) had two drugs and 5 (5.6%) had three drugs. Prescribed drugs and their frequencies are reported in Table 1.

Table 1. Prescribed drugs and frequencies.

Drug	n (%)
No treatment	19 (21.1)
Celecoxib	26 (28.9)
Oxicams	22 (24.4)
Propionic acid derivatives	6 (6.7)
Phenyl Acetic acids	5 (5.6)
Acetaminophen	15 (16.7)
Tramadol	12 (13.3)
Steroids	11 (12.2)
Methotrexate	1 (1.1)

Conclusion: The most common group of drugs used for hand arthralgia in this cohort of patients was NSAID, and the most used of this group was celecoxib. Only in one patient, PCP prescribed disease-modifying anti-rheumatic drugs (DMARD) therapy, in this case was methotrexate. Almost 80% of the patients were prescribed with at least one drug without knowing the final diagnosis.

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AB1362-HPR COMMON PRACTICE IN DELIVERY OF INTRA-ARTICULAR THERAPIES IN RMDS BY HEALTH PROFESSIONALS: RESULTS FROM A EUROPEAN SURVEY

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Background: Intra-articular therapies (IAT) are routinely used in rheumatic and musculoskeletal diseases (RMDs); however large variability exists regarding current practice of delivery amongst health professionals.

Objectives: To inquire about common practice aspects to inform the EULAR Taskforce for the IAT of arthropathies.

Methods: A steering committee prepared a 160-item questionnaire based on the information needs of the Taskforce. The survey was disseminated via EULAR professional associations and social media and it was open to any health professional treating persons with RMDs, regardless of using IAT personally.

Results: The survey was answered by 186 health professionals from 26 countries, the large majority of whom (77%) were rheumatologists, followed by nurses (12%), general practitioners (2%) and orthopaedic surgeons (2%). The two collectives that perform IAT routinely are rheumatologists (97%) and orthopaedic surgeons (89%), with other professionals <50%. Specific training was compulsory for 32%. The most frequent indication for IAT is inflammatory arthritis (76%), followed by osteoarthritis (74%), crystal arthritis (71%) and bursitis (70%); and all joints are injected, with knee (78%) and shoulder (70%) being the most frequent. When questioned about specific contexts, such as pre-surgical, diabetic or hypertensive patients, variability among respondents was evident, with around 30 to 69% of professionals considering it acceptable to inject glucocorticoids (GC), while in others there was less variability (prosthetic or septic joints, <1%). GCs are the most used compounds, followed by hyaluronic acid and saline/dry puncture. Only 66 (36%) use ultrasound to guide IAT. In their opinion, to be accurately in the joint is moderately to largely important for large joints (80%) and very important in small joints. The maximum number of injections to perform safely in the same joint within one year was "2 to 3" for 65% (2% thought there is "No limit"). The majority reported that they informed patients about side-effects (73%), benefits (72%), and the nature of the procedure (72%), and less frequently about other aspects; with 10% obtaining written consent and 56% oral consent (mandatory only for 32%). Other questions help to understand the setting and procedures followed, including use of local anaesthetics and care after injection.

Conclusion: Although often performed in clinical practice for RMDs, there is apparent variability in several elements related to delivery of this treatment. This information, together with patient input, will help design current recommendations where research evidence is not available.

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AB1363-HPR EVALUATION OF SELECTION CRITERIA OF CLINICIANS IN THE TREATMENT OF OSTEOPOROSIS, OSTREQ RESEARCH IN TURKEY

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Background: Osteoporosis is a disease with increasing prevalence in the aging and growing world population and its insidious progression and lack of findings without fracture cause certain difficulties in the diagnosis and treatment of this disease. There are many medical and paramedical treatment options for osteoporosis, and clinicians make these treatment decisions with many factors in mind.

Objectives: We wanted to evaluate the importance of these factors for clinicians through a questionnaire. This 17-question questionnaire aimed to investigate the factors that clinicians consider in the planning of osteoporosis treatment and the effect of these factors on treatment planning. We made the Turkish version of the OSTEQ questionnaire in this study which factors clinicians in planning treatment for osteoporosis in Turkey we aimed to investigate that take into consideration.

Methods: OSTREQ questionnaire developed by Makraz et al. are used in this research. In this survey, which consists of 8 sections (health care system, patients' preferences regarding regimen's administration, usage, cost, severity of disease, treatment efficacy, safety profile and pharmaceutical industry) and 17 questions, the participants were asked to evaluate their answers with 5 different scales: Absolutely Preventive, Partially Preventive, Neither Preventive or Encouraging, Partially Encouraging, Absolutely Encouraging.

Clinicians of Rheumatology, Physical Therapy and Rehabilitation, Endocrinology and Metabolic Diseases participated in our study. The questionnaires were filled in by e-mail or by inviting the participants to the our university or by going to the clinics where the clinicians were working.

Results: In our study 37 (21.8%) were endocrinology, 49 (28.8%) were rheumatology and 84 (49.4%) were physical therapy and rehabilitation specialists. The overall Cronbach alpha coefficient of the questionnaire was found to be 0.855. No material was found to significantly increase the internal reliability coefficient if deleted. As a result of t-test in 27% lower and upper groups to measure the discriminative power of the items, it was seen that all items made a significant difference in the lower and upper groups, which were formed according to the total score of 27 people. Confirmatory factor analysis and internal reliability results did not require removal of

the substance, so the substance was not removed. When the responses of the specialist physicians participating in our study to the osteoporosis preference criteria questionnaire were examined according to their specialty, no statistically significant difference was found between specialty branches but only significant difference was found in health system and cost subscale according to branches (p = 0.013). Post-hoc test (LSD) was used to find out the group that made a significant difference in health system and cost sub-factor. higher scores (p = 0.034).

Conclusion: We developed and validated a general osteoporosis treatment questionnaire that could provide assessment of the criteria that physicians take into consideration when they decide to implement a regimen for osteoporosis. This tool could assist health care systems and pharmaceutical companies understand which parameters drive physicians' choices regarding the treatment of osteoporosis.

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AB1364-HPR IS ADHERENCE TO TREATMENT RELATED TO THE EFFECTIVENESS OF ANTI-TNFS IN PATIENTS WITH RHEUMATOID ARTHRITIS? - ANALYSIS OF A REAL-WORLD COHORT

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Background: Several medicines are prescribed for chronic disease management of rheumatoid arthritis (RA) including biologics; however, adherence to long-term therapy remains poor because many causes; the latter results in worsening clinical results.

Objectives: To analyze the relationship between adherence to treatment and the achievement of remission or low disease activity in patients with RA treated with three anti-TNF molecules of subcutaneous use.

Methods: In patients treated with 3 subcutaneous anti-TNFs, with at least one year of follow-up previously, adherence was measured with Compliance Questionnaire for Rheumatology (CQR19) applied by psychologist; the CQR19 is a 19 item, self-administered questionnaire that was developed with the aim of correctly identify rheumatology patients that were classified as "low" adherers (taking <80% of their medication correctly) and defining as high adhesion a result greater than 80%; adherence also was measured with medication possession rate (MPR) and attendance to scheduled consultations with the interdisciplinary team in each period measured. The effectiveness by DAS28, HAQ and the other measurements were made in three periods: at baseline (BL), 6 months (M6) and 12 months (M12). A Pearson correlation was made between the number of patients in remission and low disease activity by type of molecule and period, with adherence criteria.

Results: 112 patients diagnosed with RA were included, 34.8% (39/112) treated with adalimumab, 38.4% (43/112) etanercept and 26.8% (30/112) golimumab; The results of CQR19 at BL, M6 and M12 were greater than 80%, with no statistically significant differences between the three molecules. The MPR was higher than 80% in the three periods, being very similar between the three molecules, but in M12 period the difference in MPR between adalimumab 86% and golimumab 92.1% was statistically significant (p <0.005), for etanercept it was of 90%. Regarding to DAS28 and HAQ, there were no differences between the biologics analyzed; However, the highest percentage of patients with low disease activity and remission had a higher correlation with attendance to the consultations scheduled in the interdisciplinary RA care model (r = 0.78) p <0.005 (see tables).

CQR19				MPR		
	BL	M6	M12	BL	M6	M12
ADALIMUMAB	89,7	89,3	90,1	98,5	90,5	86,1
ETANERCEPT	87,4	89,7	89,7	97,9	89,6	90,9
GOLIMUMAB	88,2	87,6	91,5	97,1	96,1	92,1

No statistical differences in adherence between biologics were found depending on sex, type of concomitant conventional treatment for RA or presence of comorbidities.

RELATION BETWEEN Rem/LDA AND COMPLIANCE WITH APPOINTMENTS

	Rem	LDA	MDA	HDA	
ADALIMUMAB	63%	60%	53%	29%	P<0,005
ETANERCEPT	66%	62%	73%	-	-
GOLIMUMAB	68%	73%	55%	-	P<0,005

Conclusion: There seems to be a higher MPR with the monthly golimumab compared to the biweekly adalimumab and weekly etanercept; however, it does not necessarily imply greater effectiveness. Longer term studies are needed to confirm if there is better adherence and clinical results with monthly anti-TNFs than to other dosing regimens. Patients with remission and low disease activity had greater assistance to scheduled consultations with the interdisciplinary group, regardless of the type of molecule used. This study confirms the relation between adherence to medications and care model with clinical results.

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AB1365-HPR FREQUENCY OF JOINT DAMAGE IN PATIENTS WITH ULCERATIVE COLITIS

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Background: Ulcerative colitis (UC) is considered as a systemic autoimmune disease with lesions of the colon mucosa. The current of UC is often accompanied by different extra-intestinal manifestations. Their frequency, according to various studies, varies widely – from 25 to 60 %. It is a serious problem that affects the quality of life and the effectiveness of therapy [1, 2]. Rheumatological manifestations, in particular, damage to the joints and spine, are one of the extra-intestinal manifestations and they are of particular importance. To date, the relationship between UC and joint damage has not been fully studied. These diseases can occur independently in the body or have a common autoimmune or inflammatory nature. It is believed that having common pathogenetic mechanisms of development, UC and joint damage can be different clinical forms of the same disease.

Objectives: To evaluate the frequency of clinical manifestations of joint damage in patients with ulcerative colitis.

Methods: The study was conducted at the gastroenterological Department of the Hospital №25 (Russia, Volgograd). Archived data from the case histories of 69 patients with a confirmed diagnosis of ulcerative colitis were analyzed, including 58 men (30.4%) with an average age of 33.4 years, and 38 women (69.5%) with an average age of 37.6 years.

Results: Among 48 patients with UC, extra-intestinal manifestations were detected in 40 (41.6%) patients. A total lesion of the large intestine was found in 20 patients (20.8%), left-sided colitis in 14 (14, 6%), proctosigmoiditis in 6 (6.25%). The diagnosis was made for the first time in 4 patients (4.16%), 36 patients (37.5%) were admitted to the hospital again due to an exacerbation of the disease. Among the extra-intestinal manifestations, joint lesions prevailed: 20 patients (20.8%) showed clinical signs of peripheral arthritis, spondyloarthritis was detected in 8 patients (8.3 %), and 6 patients (6.25 %) had symptoms of unilateral sacroiliitis. 4 (4.16%) patients were diagnosed with nodular erythema. Primary sclerosing cholangitis was detected in two patients (2.08%).

Conclusion: The development of extra-intestinal manifestations in UC is largely determined by the course of the disease and the length of the inflammatory process in the colon. More than a third of patients with UC revealed extra-intestinal manifestations, among which the most common signs of joint damage were present, which necessitates timely diagnosis of extra-intestinal manifestations and involvement of a rheumatologist in the management of this category of patients.

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Bosch P., 1670 (AB0746), 1830 (AB1083)
Bosello S. L., 7 (OP0009), 209 (CO0002), 381 (THU0306), 691 (FRI0216), 698 (FRI0230), 700 (FRI0233), 1016 (SAT0153), 1072 (SAT0259), 1606 (AB0621), 1634 (AB0679), 1908 (AB1234), 1924 (AB1265)
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Burlaeva N., 1584 (AB0576)
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Cañas Alcántara I., 1815 (AB1051)
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Esaily H. A., 1918 (AB1253)
Esatoglu S. N., 1071 (SAT0258)
Esbensen B. A., 167 (OP0267), 1263 (SAT0606), 1284 (SAT0651), 1289 (PARE0006), 1952 (AB1326)
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Garrido-Cumbrera M., 54 (OP0081), 173 (OP0278), 514 (THU0548), 748 (FRI0315), 1134 (SAT0374), 1274 (SAT0629), 1278 (SAT0638), 1637 (AB0684), 1638 (AB0685), 1643 (AB0696), 1870 (AB1160)
Garrido-González C., 1134 (SAT0373)
Garrood T., 110 (OP0178)
Garrote A. R., 818 (FRI0441)
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Garufi C., 127 (OP0204), 367 (THU0281), 641 (FRI0121), 649 (FRI0134), 1016 (SAT0153), 1054 (SAT0223), 1235 (SAT0555), 1342 (AB0085), 1468 (AB0340), 1477 (AB0355)
Garvey T., 1567 (AB0541)
Garyfallos A., 657 (FRI0147), 712 (FRI0256), 1101 (SAT0312), 1275 (SAT0630), 1782 (AB0976), 1892 (AB1201)
Garza Acosta A. C., 780 (FRI0366), 1733 (AB0851), 1897 (AB1212)
Garza Martínez M. J., 1046 (SAT0206), 1505 (AB0410), 1506 (AB0411), 1952 (AB1327)
Garzanova L., 400 (THU0338), 404 (THU0345), 708 (FRI0247), 1588 (AB0583), 1600 (AB0609)
Gasparin A. A., 268 (THU0108), 404 (THU0346), 705 (FRI0243), 1506 (AB0412), 1643 (AB0695), 1727 (AB0843)
Gasparotto M., 1065 (SAT0245)
Gastanaga M., 485 (THU0497)
Gater A., 1954 (AB1332)
Gatica H., 1573 (AB0554)
Gatley J., 1069 (SAT0252)
Gattamelata A., 336 (THU0220), 356 (THU0258), 360 (THU0266), 689 (FRI0212)
Gatti D., 477 (THU0479), 565 (THU0640), 1183 (SAT0452), 1185 (SAT0455), 1185 (SAT0456), 1750 (AB0893), 1830 (AB1082), 1836 (AB1094)
Gatti S., 337 (THU0221)
Gatto M., 351 (THU0249), 1022 (SAT0163)
Gattorno M., 170 (OP0273), 182 (OP0293), 236 (THU0047), 489 (THU0501), 825 (FRI0457), 838 (FRI0482)
Gaudin P., 22 (OP0031), 431 (THU0393), 509 (THU0539), 1627 (AB0665)
Gaudio A., 1749 (AB0890)
Gaudreault F., 120 (OP0193)
Gaudreault N., 909 (FRI0608), 916 (FRI0623)
Gaugler B., 1381 (AB0161)
Gaujoux-Viala C., 52 (OP0077), 133 (OP0214), 312 (THU0188), 630 (FRI0101), 1135 (SAT0375)
Gauler G., 97 (OP0154), 569 (THU0650)
Gaur P., 1107 (SAT0323)
Gautier M., 489 (THU0502), 491 (THU0506), 826 (FRI0458), 829 (FRI0464), 1202 (SAT0492), 1780 (AB0971)
Gavigan K., 523 (THU0564), 580 (FRI0018), 1014 (SAT0150), 1298 (PARE0026), 1477 (AB0354), 1650 (AB0710)
Gavilán Carrera B., 465 (THU0457), 466 (THU0460), 472 (THU0470), 927 (FRI0647)
Gawrych M., 1313 (AB0021)
Gayá García-Manso I., 1222 (SAT0530)
Gaydukova E., 1008 (SAT0141), 1469 (AB0341), 1470 (AB0342), 1638 (AB0686)
Gaydukova I., 141 (OP0226), 767 (FRI0346), 904 (FRI0597), 1008 (SAT0141), 1145 (SAT0393), 1314 (AB0022), 1469 (AB0341), 1470 (AB0342), 1638 (AB0685), 1638 (AB0686), 1643 (AB0696), 1694 (AB0791), 1695 (AB0792)
Gazal S., 25 (OP0036)
Gazar Y., 1772 (AB0950)
Gazi S., 1404 (AB0208), 1892 (AB1201)
Gazitt T., 1688 (AB0780)
Gazzola F., 1046 (SAT0207)
Gdoura H., 835 (FRI0476), 1755 (AB0905)
Geale K., 37 (OP0056)
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Geenen R., 1292 (PARE0013), 1296 (PARE0022)
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Gehin J. E., 868 (FRI0536), 893 (FRI0579)
Gehring I., 594 (FRI0040)
Geifman N., 1038 (SAT0192), 1209 (SAT0506)
Geirsson A. J., 71 (OP0109), 435 (THU0398), 724 (FRI0275)
Geisemeyer N., 496 (THU0515)
Geldhof A., 992 (SAT0117)
Gelfand J., 773 (FRI0355)
Gellett A., 143 (OP0228)
Gellett A. M., 1158 (SAT0411), 1709 (AB0814)
Geluk A., 74 (OP0113)
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Gendron F., 1294 (PARE0016)
Geneus V., 432 (THU0395), 775 (FRI0357), 1709 (AB0814)

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Geng Y., 1239 (SAT0562), 1422 (AB0243)
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Genre F., 752 (FRI0322), 937 (SAT0014), 976 (SAT0084), 1309 (AB0011), 1309 (AB0012)
Genrinho I., 1862 (AB1145)
Gensler L. S., 40 (OP0060), 66 (OP0103), 68 (OP0105), 69 (OP0106), 426 (THU0384), 432 (THU0395), 1966 (AB1358)
Gentileschi S., 499 (THU0520), 1439 (AB0281), 1769 (AB0939), 1832 (AB1086)
Geny B., 708 (FRI0249)
Georganas C., 1892 (AB1201)
George M., 95 (OP0150), 888 (FRI0572)
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Gerhart W., 1274 (SAT0629), 1278 (SAT0638)
Geri T., 474 (THU0474)
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Gervais E., 769 (FRI0348), 821 (FRI0449), 1872 (AB1162)
Gervais F., 1294 (PARE0016)
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Gessa Sorroche M., 1806 (AB1027)
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Geusens P., 1920 (AB1257)
Gezer H. H., 548 (THU0613), 839 (FRI0483), 1684 (AB0772), 1684 (AB0773), 1804 (AB1024)
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Ghanbari Y., 1387 (AB0175)
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Ghigo E., 848 (FRI0499)
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Gigante L., 209 (CO0002), 381 (THU0306), 691 (FRI0216), 1072 (SAT0259), 1606 (AB0621), 1908 (AB1234)
Gigante M. R., 316 (THU0193), 370 (THU0287), 889 (FRI0574), 943 (SAT0027), 1055 (SAT0224), 1350 (AB0102), 1771 (AB0947)
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Gil M., 1180 (SAT0446)
Gil S., 815 (FRI0434)
Gil Velez R. J., 600 (FRI0049), 982 (SAT0098), 1549 (AB0503), 1592 (AB0591)
Gil del Gallego M. D., 912 (FRI0614)
Gilbert A., 1290 (PARE0009)
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Giordano A., 381 (THU0306)
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Giorgi R., 397 (THU0333), 606 (FRI0060), 976 (SAT0086), 1394 (AB0190), 1395 (AB0191)
Giorgi V., 464 (THU0454), 1773 (AB0951)
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Gokcen N., 1578 (AB0562)
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González Fernández M., 1468 (AB0339)
González Figueroa E., 1872 (AB1163)
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González M. J., 342 (THU0229)
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Gonzalez Juanatey C., 2 (OP0002), 757 (FRI0330)
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LV P., 681 (FRI0196), 1562 (AB0530)
La Porta U., 1606 (AB0621)
La Rosa A., 1029 (SAT0176)
La Torre G., 943 (SAT0027)
La Touche R., 527 (THU0572)
Laapas K., 890 (FRI0575)
Laatar A., 756 (FRI0329), 1390 (AB0182), 1401 (AB0201), 1429 (AB0261), 1437 (AB0277), 1442 (AB0287), 1449 (AB0300), 1456 (AB0314), 1458 (AB0319), 1613 (AB0635), 1613 (AB0636), 1613 (AB0637), 1629 (AB0668), 1629 (AB0669), 1670 (AB0747), 1771 (AB0946), 1779 (AB0969), 1853 (AB1128), 1921 (AB1260)
Labadie C., 427 (THU0386), 769 (FRI0348)
Labasse A., 801 (FRI0405)
Labbe A., 807 (FRI0417)
Labbene E., 502 (THU0525), 1839 (AB1100), 1840 (AB1101), 1840 (AB1102)
Laborne F. X., 296 (THU0163)
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Lacaille D., 7 (OP0010), 608 (FRI0064), 974 (SAT0078)
Lacarpia N., 1728 (AB0844)
Lacerda M., 1779 (AB0967)
Lachmann H. J., 825 (FRI0457)
Lack J., 178 (OP0286)
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Lacouture-Fierro J., 1048 (SAT0210), 1188 (SAT0463), 1423 (AB0246)
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Ladeb F., 502 (THU0525), 1839 (AB1100), 1840 (AB1101), 1840 (AB1102)
Ladehesa Pineda M., 749 (FRI0316), 752 (FRI0321), 892 (FRI0578), 1128 (SAT0362), 1134 (SAT0373)
Ladel C., 117 (OP0189)
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Laezza A., 1420 (AB0241)
Lafeber F., 55 (OP0083), 114 (OP0185), 242 (THU0060), 613 (FRI0074), 801 (FRI0406), 879 (FRI0554)
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Laganà B., 720 (FRI0270)
Lage-Hansen P., 100 (OP0158), 1555 (AB0516)
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Laheurte C., 1177 (SAT0441), 1360 (AB0121)
Lahiri M., 357 (THU0260), 590 (FRI0033), 864 (FRI0530)
Lahmar A., 157 (OP0250)
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Lai C., 1547 (AB0498)
Lai C. C., 286 (THU0141), 875 (FRI0549)
Lai K. L., 46 (OP0069)
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Lai N. S., 1427 (AB0256)
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Laiz A., 819 (FRI0442), 1051 (SAT0217), 1542 (AB0489), 1683 (AB0770)
Lajam A., 756 (FRI0328)
Lajas C., 1257 (SAT0598)
Lakka on behalf of Timo, 832 (FRI0470)
Lakota K., 1090 (SAT0292)
Lakshminarayanan V., 144 (OP0229)
Laktašić Žerjavić N., 1471 (AB0343), 1922 (AB1262)
Lalande A., 794 (FRI0393), 804 (FRI0411)
Lam J., 626 (FRI0096)
Lama S., 24 (OP0035), 963 (SAT0061), 1000 (SAT0129)
Lamacchia C., 594 (FRI0040)
Lamagna C., 30 (OP0046), 86 (OP0133), 579 (FRI0016)
Lamas J. R., 1338 (AB0077)
Lamb H. J., 805 (FRI0413)
Lamb S., 1963 (AB1351)
Lamberg H., 832 (FRI0470)
Lambert M., 1065 (SAT0244), 1527 (AB0457), 1552 (AB0510), 1927 (AB1273)
Lambert R. G., 43 (OP0065), 53 (OP0079), 738 (FRI0298), 740 (FRI0302), 749 (FRI0317), 1137 (SAT0378), 1140 (SAT0383), 1140 (SAT0384)
Lambotte O., 82 (OP0125), 1225 (SAT0536)
Lambova S., 507 (THU0535)
Lamkhanat O., 610 (FRI0068), 975 (SAT0082), 1425 (AB0252)
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Lanchbury J., 878 (FRI0553), 1913 (AB1243)
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Lapin S., 378 (THU0300), 904 (FRI0597), 1224 (SAT0533), 1314 (AB0022), 1315 (AB0025)
Lapkina N., 327 (THU0206), 1462 (AB0328), 1470 (AB0342)
Lapshina , 986 (SAT0105)
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Lapuente-Suanzes P., 895 (FRI0582)
Lara/Gonzalez L., 501 (THU0524)
Larbi A., 1327 (AB0050)
Larbre J. P., 827 (FRI0460)
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Larco Rojas X. E., 1031 (SAT0180), 1271 (SAT0622), 1640 (AB0689), 1682 (AB0768)
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Laska M. J., 1371 (AB0143)
Laskari K., 845 (FRI0493)
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Latino O., 661 (FRI0154), 1527 (AB0457)
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Lau C. S., 1492 (AB0384)
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Laurberg T. B., 13 (OP0018), 1297 (PARE0024)
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Lavarello C., 1789 (AB0992)
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Le Blay P., 929 (FRI0651)
Le Cessie S., 109 (OP0176)
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Le Goff B., 252 (THU0081), 509 (THU0539), 1762 (AB0924), 1857 (AB1135)
Le Guern V., 364 (THU0275), 368 (THU0282), 1043 (SAT0201), 1055 (SAT0226), 1515 (AB0433)
Le Joncour A., 1066 (SAT0246)
Le Marshall K., 1852 (AB1126)
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León L., 956 (SAT0051), 1225 (SAT0535), 1257 (SAT0598), 1444 (AB0290)
León M. D. L. P., 907 (FRI0603)
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Lea.Savey@aphp.Fr L. S. F., 1552 (AB0509)
Leal Bramasco A. S., 556 (THU0626)
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Lee E. B., 306 (THU0178), 610 (FRI0067), 699 (FRI0231)
Lee E. J., 934 (SAT0009)
Lee E. S. C., 1327 (AB0050)
Lee E. Y., 1092 (SAT0295), 1367 (AB0133)
Lee H., 934 (SAT0007), 1693 (AB0789), 1914 (AB1246)
Lee H. N., 248 (THU0072), 951 (SAT0041)
Lee H. R., 1318 (AB0031), 1353 (AB0109)
Lee I. H., 652 (FRI0139)
Lee J., 49 (OP0073), 126 (OP0201), 285 (THU0140), 458 (THU0443), 554 (THU0622), 610 (FRI0067), 862 (FRI0526), 871 (FRI0540), 880 (FRI0556), 1055 (SAT0225), 1255 (SAT0592), 1347 (AB0095), 1620 (AB0652), 1739 (AB0866)
Lee J. H., 831 (FRI0469), 934 (SAT0009), 1280 (SAT0641), 1782 (AB0974)
Lee J. J. W., 1156 (SAT0408)
Lee J. S., 25 (OP0036), 329 (THU0210), 621 (FRI0088), 640 (FRI0118), 708 (FRI0248), 1406 (AB0212), 1802 (AB1018)
Lee J. W., 507 (THU0536), 954 (SAT0048)
Lee K. A., 396 (THU0332), 1050 (SAT0214)
Lee L. H., 1198 (SAT0483), 1924 (AB1266), 1959 (AB1342)
Lee M., 336 (THU0219)
Lee M. S., 782 (FRI0370), 782 (FRI0371)
Lee M. Y., 1844 (AB1108)
Lee P. Y., 1210 (SAT0507)
Lee S., 126 (OP0201), 645 (FRI0128), 728 (FRI0282), 871 (FRI0540), 1358 (AB0116), 1620 (AB0652)
Lee S. G., 458 (THU0443), 554 (THU0622), 699 (FRI0231), 951 (SAT0041)
Lee S. H., 505 (THU0532), 554 (THU0622), 554 (THU0622), 1050 (SAT0214)
Lee S. I., 934 (SAT0007)
Lee S. J., 265 (THU0103), 310 (THU0186), 311 (THU0187)
Lee S. M., 507 (THU0536)
Lee S. S., 644 (FRI0126), 699 (FRI0231), 1031 (SAT0179), 1055 (SAT0225), 1519 (AB0440), 1519 (AB0441), 1519 (AB0442), 1740 (AB0867)
Lee S. W., 55 (OP0082)
Lee S. Y., 1124 (SAT0355), 1327 (AB0050)
Lee T. H., 728 (FRI0282), 1246 (SAT0575), 1255 (SAT0592)
Lee T. S. H., 709 (FRI0251)
Lee T. Y., 1485 (AB0370)
Lee W. I., 1844 (AB1108)
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Lee Y., 47 (OP0071), 984 (SAT0102), 1347 (AB0095)
Lee Y. A., 458 (THU0443)
Lee Y. H., 678 (FRI0190), 1005 (SAT0136)
Lee Y. J., 306 (THU0178), 307 (THU0180), 610 (FRI0067), 699 (FRI0231), 1122 (SAT0353), 1253 (SAT0588), 1367 (AB0133)
Lee Y. K., 728 (FRI0282), 880 (FRI0556), 1255 (SAT0592)
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Lees D., 856 (FRI0514)
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Leher H., 296 (THU0162), 624 (FRI0092), 987 (SAT0106)
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Leinhard O. D., 119 (OP0192)
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Leipe J., 168 (OP0270), 1248 (SAT0578), 1803 (AB1021)
Leite C., 1290 (PARE0009)
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Leloup C., 1122 (SAT0352)
Lemaire J. M., 801 (FRI0405)
Lempp H., 1279 (SAT0640)
Lems W., 136 (OP0219), 562 (THU0634), 783 (FRI0373), 894 (FRI0581), 1233 (SAT0551), 1873 (AB1165), 1949 (AB1320)
Lend K., 13 (OP0018)
Lenert A., 1906 (AB1231)
Lenfant T., 845 (FRI0494)
Leng X., 812 (FRI0428)
Lenne N., 149 (OP0236)
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Lenz L., 1910 (AB1239)
Leo P., 1311 (AB0015)
Leon L., 1564 (AB0535), 1795 (AB1005)
Leon Luque M., 1309 (AB0011), 1309 (AB0012)
Leon M., 798 (FRI0400)
Leon-Constantin M. M., 989 (SAT0111)
Leonardo M., 1309 (AB0011), 1309 (AB0012)
Leone M. C., 365 (THU0278)
Leong J. Y., 236 (THU0047), 1204 (SAT0496), 1327 (AB0050)
Leong K. P., 1433 (AB0270)
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Lester S., 92 (OP0145), 797 (FRI0399)
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Letaeva M., 1196 (SAT0480), 1197 (SAT0481), 1748 (AB0888), 1905 (AB1228)
Letaief H., 929 (FRI0651)
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Lettieri C., 542 (THU0601)
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Leung J., 1084 (SAT0279)
Leung S. O., 131 (OP0210)
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Li B. C., 1433 (AB0269)
Li C., 274 (THU0118)
Li D., 352 (THU0251), 1032 (SAT0182), 1512 (AB0425), 1526 (AB0454)
Li E., 1156 (SAT0408)
Li F., 274 (THU0118)
Li H., 1282 (SAT0646), 1856 (AB1133)
Li H. G., 591 (FRI0034)
Li I., 1882 (AB1184)
Li J., 66 (OP0102), 100 (OP0160), 131 (OP0210), 441 (THU0408), 511 (THU0544), 579 (FRI0017), 665 (FRI0163), 670 (FRI0173), 853 (FRI0510), 861 (FRI0524), 1044 (SAT0203), 1326 (AB0048)
Li L., 7 (OP0010), 118 (OP0191), 188 (OP0304), 247 (THU0070), 266 (THU0105), 572 (FRI0003), 1063 (SAT0242)
Li M., 131 (OP0210), 236 (THU0048), 511 (THU0544), 1063 (SAT0241), 1108 (SAT0326), 1156 (SAT0408), 1373 (AB0147), 1525 (AB0453), 1611 (AB0631)
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Li Q., 189 (OP0305), 353 (THU0252), 1068 (SAT0250), 1126 (SAT0359), 1160 (SAT0414)
Li R., 247 (THU0070), 1097 (SAT0303)
Li S., 274 (THU0118), 1068 (SAT0250), 1677 (AB0759)
Li T., 451 (THU0426), 452 (THU0427), 461 (THU0450), 853 (FRI0509), 1137 (SAT0379), 1326 (AB0047), 1402 (AB0204), 1601 (AB0610), 1641 (AB0693), 1765 (AB0931)
Li T. H., 286 (THU0141), 875 (FRI0549)
Li T. K., 1156 (SAT0408)
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Zhou Q., 227 (THU0028), 228 (THU0029), 544 (THU0604), 819 (FRI0443), 1047 (SAT0209), 1124 (SAT0356), 1127 (SAT0361)
Zhou W., 655 (FRI0143), 902 (FRI0593), 1272 (SAT0625), 1490 (AB0380), 1953 (AB1328), 1953 (AB1329), 1954 (AB1331)
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